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LINKING ENTREPRENEURIAL AGENCY TO THE EARLY LIFE STAGES OF INNOVATIVE FIRMS:

The case of the biotechnology sector

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General Introduction

Introduction

Policy makers in Europe and the United States undertake numerous policies to support entrepreneurship in order to have a positive effect on employment, economic growth and competitiveness through innovation (Gilbert et al. 2004). The support for young innovative firms can be carried out in different ways, such as the introduction of tax relief policies, financing programs for new ventures, incubator or business accelerator programs and indirectly through cluster programs, among others. However, there has been a long standing debate among economists regarding the link between innovative entrepreneurship and economic growth, which has led to a discussion about the effectiveness of these policies.

The links between entrepreneurship, innovation, employment and economic growth are crucial to the motivation behind public policies. The basis for such policies must therefore be discussed in terms of economic theory by looking at the strength of these links. The question of the link between entrepreneurship and economic growth is a complex one, and has its supporters and detractors among economists. Different authors with varying points of view have developed different methodologies and emphasised different levels for measuring performance in order to explain the relationship between the small business sector and employment and growth. Some emphasise the indirect links and benefits of entrepreneurship at a regional level through spillovers (Wennekers & Thurik 1999), which according to them have a positive influence on growth. Others look at the individual performance of new ventures, which is low for the majority of firms both in terms of growth in employment and turnover (Storey 1982; Parker 2004). What stands out from the literature is firstly the lack of evidence for a direct link between growth, employment and entrepreneurship. Statistics shows that only a minority of firms achieve growth (Storey 1994, pp.119–120; Parker 2004). This debate emphasises the need to understand why firms differ so much in their performance outcome (survival, growth), and if there is a way for policy makers to influence this outcome. Thus, when studying innovative firms, it is still valid to look at the reasons why some firms grow while others do not, and why some firms do not survive at all, since these aspects are relevant for policy makers in terms of employment and growth. Further, it is useful to focus on innovative entrepreneurship because, on the one hand, public policies put high hopes into the scientific elite, technology transfer and ultimately employment and competitiveness, but on the other hand, the link between economic growth and innovative entrepreneurship is weak in the existing literature, as mentioned above. The question of how to contribute to this debate in a constructive way in order to further the understanding of an innovative process through venture creation and its consequences still remains. Should we, like the literature cited above, link the firm to performance factors and try to differentiate between the high performing and poor performing firms?

While economists and policy makers do not agree among themselves on the link between entrepreneurship and growth on the overall economy, they both associate entrepreneurial success with growth in turnover and employment for individual firms. Although, economists and policy makers agree among themselves about what makes a venture successful, individual entrepreneur objectives may not be aligned with this definition of success. Entrepreneurial success can be defined differently depending on the stakeholder's point of view. An entrepreneur who is the driver of the firm evolution may not aspire to a growth in turnover or employment. Entrepreneurs are influenced by a variety of objectives when taking on firm creation, of which some are the concretisation of an innovation project, the creation of a long lived company, the ability to be their own boss by being self-employed, the personal capture of profit, etc (Cassar 2007; Oakey 1995). Many of these objectives may lead to different strategies such as that of longevity and small growth, or high growth and a short term exit through the sale of the newly created company. The statistical thresholds of growth and job creation, which the government aims at through start-up companies, can therefore be compromised by the entrepreneur's aspirations and actions. Therefore, one cannot hypothesise that firms with no significant growth (in terms of employment or turnover) during their early years are underperforming without taking into consideration that standards are set by the entrepreneurs themselves. These standards may vary and be different from the goals of policy makers. Success factors are therefore best taken here to be subjective and **this thesis will not try to find performance indicators to explain the differences in performance or define thresholds of indicators to define 'success'. However, it will look at the entrepreneurs' preferences, decisions and actions in relation to the path of the evolution of the firm.** Therefore the thesis focuses on a micro level of analysis.

Since this work aims at understanding the firm from the point of view of the entrepreneur and the fact that he may not necessarily aim at the rapid growth of his firm, this thesis instead focuses on the notion of evolution. Firm evolution will be studied along the lines of the entrepreneur's preferences, decisions and actions. The thesis focuses on the understanding of **firm evolution**[1], not in terms of employment and growth stages but in terms of early decisions and changes that the firm goes through that can affect its early evolution. This focus is chosen in order to further the understanding of why different firms can have different paces of growth. The entrepreneur's vision and action are considered as a central variable for understanding a firm's

[1] The notion of evolution is preferred to the notion of growth throughout the thesis since the firm does not always aspire to grow.

evolution, and is taken to act in concert with other variables. These can be internal variables relating to entrepreneur's characteristics and external ones, such as market, technological variation or financing opportunities. Tracing these relationships could, for instance, inform policy makers about the sensitivity of the firm's survival to problems that firms encounter during their early life. It could also inform entrepreneurs, who are willing to engage in creating innovative venture, to prepare them for important stages in the firm creation process and to help them anticipate common difficulties that arise at firm creation.

In order to study this question, we need to define first what is meant by the 'innovative firm's creation process'. As the literature on entrepreneurship (Shane 2003) has recently shown, the entrepreneurial process starts with the recognition and the decision to exploit opportunities. Therefore, if a study was started only at the time of firm administrative incorporation, the decision phase and the initial steps in acquiring resources before the creation of the firm as an administrative entity would be missed. The processes analysed in the thesis therefore include the phase of innovative project development in the incumbent organisation and the firm creation and early development. The concept focuses on two levels, which are the *innovative project* behind the firm creation and the *organisational level*. The organisational level includes firstly the transition between a parent organisation and a newly created organisation and secondly the organising process behind the newly created firm. The organisation process on which the study focuses lies mainly in the organisation of a management team and their ability to exploit the identified opportunity. This organisation can lead to changes between the person identifying the opportunity and the person that has the responsibility to exploit it.

Many contributions in the literature on firm creation focus their study only on the period from its formal organisation (e.g. establishment date) to an arbitrary end point early in its life. In contrast, we consider that the features of the innovation project at the origin of its conceptualisation and the beginning of resource accumulation can occur before the founding date and may play a role in the process of creation. Our level of analysis does not only focus on processes occurring after the founding date. In this case, the concept of innovation in this work is restricted to innovation as a new product or a new technology (which excludes new processes of production, new market or a new source of supply). In short, we will be examining the discovery and exploitation process of an opportunity as well as subsequent processes after foundation. Both of these processes will be analysed by studying the creation of innovative companies. The transition of an innovative project from an incubating organisation to a newly created organisation and its early development will be studied, in addition to the organisational process behind firm creation, which here includes the formation of a functioning managerial structure at the head of the firm. **The thesis therefore aims at understanding the co-evolution of an innovation project together with the organisational process behind firm creation.** The objectives of the study having being defined, the variables that have an influence on this process must now be identified. As emphasised earlier, the entrepreneur sets the objectives and strategy of development of the newly created firm, which has a direct impact on its pace of growth.

One of the identified drivers of firm evolution is the entrepreneur[2] himself through his decision making. The entrepreneur is therefore at the centre of this analysis due to his power of decision and action that drives the firm evolution. The theory of entrepreneurship defines an entrepreneur as an agent who takes risks that other agents will not take. An entrepreneur collects information (which is incomplete) that is required to make decisions about how to develop his business[3]. In order to better understand how an entrepreneur makes his decision, this thesis introduces and develops the concept of ***entrepreneurial agency***. This concept is defined by the extent of which an agent (here, the entrepreneur) has power over his actions and thus has an impact on his own life circumstances (this includes his venture). However, we must consider that the decisions that the entrepreneur takes are affected both by the entrepreneur himself through his experiences and culture, but also by external determinants that may to some extent constrain him in his decision. Discussing entrepreneurial agency therefore involves discussing the freedom and constraints in the context in which the entrepreneur operates and the factors that influence his goal setting, actions and ultimately the fate of his venture (survival, ability to grow...). The concept of entrepreneurial agency gives us the opportunity to understand how the entrepreneur's decision is made towards a specific strategy.

When discussing entrepreneurial agency, one therefore cannot focus on the entrepreneur alone but also must understand him within his environment, which influences his freedom of action. Hence, in order to understand components that limit the freedom of the entrepreneur, literature will be looked at that focuses on the constraints that put pressure on the entrepreneur during project development and through the creation process. The entrepreneurship literature has not been the most prolific in discussing the external constraints of innovative project building or firm creation. Organizational theory and innovation literature have been much more centred on these issues and are therefore another central literature used in this thesis.

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[2] In this thesis, when referring to the entrepreneur, we use male pronoun for the purpose of simplicity, which does not exclude the possibility that the entrepreneurs may be female.
[3] This definition may vary among authors. A further discussion of this definition is given in the review of literature in section 3.

Innovation studies and evolutionary theory have both contributed in terms of pointing out external and internal constraints on firms. Looking at external constraints, the evolutionary theory has pointed towards the market and competition being a strong determinant for firm survival (Hannan & Freeman 1977). Innovation literature and its concept of system of innovation (Freeman 1995; Edquist 2005) also discusses the influence of external constraints on individual ventures, and points towards institutions and organisations having a role to play in the development of firms. In terms of the internal constraints, the evolutionary theory has emphasised the role of technological determinants, which are absent from the theory of entrepreneurship. The study of the determinants of survival and growth of innovative start-ups must acknowledge the technological context that constrains firm creation and development (Woodward 1965; Oakey 1995). This technological context emerges from the previous knowledge and experience acquired by the entrepreneur, which limits his recognition of opportunities and also the technology and knowledge he may use for developing the opportunity. The system of innovation literature shows that the "free will" of the entrepreneur is also bounded by institutions in a system that influences (positively or negatively) the options available to the entrepreneur. Therefore this study does not limit itself only to the study of the agent, the entrepreneur, and towards the action he takes, but aims to understand in a **systemic manner** the development of an innovative project through the early life of a company.

As a result, the evolution path of a firm could have determinants that may not be obvious. This thesis looks in a dynamic way at the opportunity recognition and firm creation. The main focus of the thesis therefore concerns the process that results from the interplay between innovative project development and the firm's early organisation. To understand this dynamic it will also examine the interplay of variables that influence both these processes with the entrepreneurial decision and action being at the centre of the study. Apart of the entrepreneur's agency and motives, there are also other determinants that can be taken into consideration, such as technology, market determinants and influencing institutions.

Research objectives

This section explains in more detail the goals of the research in addition to identifying the main research questions.

As we noted above, economists and policy makers are interested in the survival and growth of a firm, while entrepreneur may not be. This thesis therefore aims at understanding the reasons of the choice for an entrepreneur towards a specific strategy. The concept of entrepreneurial agency introduced above will help us to understand what influences the entrepreneur's choices towards a specific strategy for the firm development. In order to do so, this section presents different elements used to understand the firm early evolution, which will be also reflected in our research questions.

On a theoretical side, the thesis will argue that the literature has rightly given a great deal of attention to the internal determinants of firm growth, and especially at the capabilities and experience of the individuals that constitute the founding team. However, little attention has been given to the reasons of goal setting in a newly created company and how these goals can be influenced by other variables. The thesis will therefore focus on the variables of evolution and the decision making and actions of the entrepreneur.

The thesis will also look at the process of entrepreneurial decision making under different constraints. Regarding the recent literature and expectations on new firms towards growth and employment, this thesis tries to understand how the goals of **the firm are set and whether or not this choice is independent and entirely due to the entrepreneur's choice**.

In order to understand these dynamics, the thesis will also look at the internal and external dynamic that drive the firm early evolution. It will weigh the different factors that are involved in the decision process, and assess the constraints under which the entrepreneur or the founding team makes their decisions, while taking into account their experience and background. The thesis therefore tries to understand how much freedom the entrepreneur has in his choices. It will view the entrepreneur as part of a larger system, in which the sector of activity also has a role in the firm's early development, including its specific regulatory and technological regime in addition to other support organisations for start-ups. Thus an additional research objective lies in understanding the firm early life stages within a **systemic view**. These research objectives can be translated into the following research question.

How does an innovative firm evolve during its early life stages and how do entrepreneurial agency, environmental factors and human capital influence the new venture path of development?

This research question involves a wide range of aspects under study and therefore triggers sub-questions to emerge from it. As highlighted earlier, this study aims to introduce and use a framework called entrepreneurial agency, which looks specifically at the three different components to be understood together: the entrepreneur as the agent, the environment and the action. The study of the entrepreneurial action in this thesis is characterised by the early stages of evolution of the firm. It aims firstly at understanding the ***action of entrepreneur*** towards two distinct objects, the innovative project, and the firm. These two objects will be studied together, but the thesis aims to understand if they evolve independently or not. Thus the first sub-question emerging from the main focus of research is:

How is the evolution of a new venture influenced by the transition of a project of innovation between the incumbent organisation and the newly created organisation? Conversely, is the project also influenced by the newly created organisation?

This question emphasises that the study aims at understanding the two parts that constitutes innovative entrepreneurship, which are the innovation process and the firm creation. The process of development of an innovation is not bounded by the firm, and usually exists before the firm creation since it is usually the trigger for its start. Conversely, the firm creation is the construction of a new organisation, which presents a number of challenges as we will see in the next chapter. The firms we study are selected to be built upon an innovative project, but is this firm then defined by this innovative project? Since innovation processes are highly uncertain, and may take time to be able to produce value, the question of the survival of the firm may depend on other factors and activities. The two processes must therefore be considered separately, even if the initial conditions of the firm creation means that they are linked.

Secondly, since we view the entrepreneur as part of a larger system, we also try to understand ***environmental determinants*** that may influence or constrain the entrepreneur in his decision or action. A second sub-question can then be formulated as follows:

How is the evolution of a new venture influenced by the relationship with other actors and pressures from the environment?

The entrepreneur interacts with organisations, institutions and markets through his activities, which potentially influences his venture. For instance, when starting his venture, the entrepreneur has to decide towards developing activities that aim at trading on specific markets. These markets are part of a specific sector that has its own value chain, regulations and set of competitors trading in it. All these elements constrain the entrepreneur in the way that he creates value to the consumer but also in the way he is able to capture value from his activities. Therefore, sectoral characteristics are taken into account in this work, in order to understand the conditions the entrepreneur is facing when making decisions. The general structure of a sector or industry is not the only factor that affects the entrepreneurial action, since individual organisations interacting with new firms can also influence the entrepreneurial agency. When being created, a firm needs particular resources (tangible or intangible) in order to be able to start trading, and thus on some occasions needs partners to help it obtain these resources. Thus resources, such as financing, human capital and physical capital can be sourced by different organisations. Thus we believe that such organisations, institutions and market conditions have an influence on the innovation and firm creation processes, and ultimately on the entrepreneurial agency.

Finally, the firm creation and innovation processes are also influenced by the person taking the entrepreneurial role, ***the entrepreneur***. Through various contributions, entrepreneurship literature has shown that the characteristics, background in terms of culture, but also the knowledge background, all have an influence on his behaviour. In order to be able to identify an opportunity in high-technology sectors and exploit it, the entrepreneur must often have a technical understanding. This understanding helps him to exploit opportunities of innovation (Oakey 1995). However, as explained earlier, we are also interested firm creation. While the technical knowledge is useful for the entrepreneur, firm creation can require other competences in terms of management, firm creation, industry knowledge and markets. Thus in some cases, the entrepreneurial process of identification and exploitation of an opportunity is carried out by more than one individual, which can involve a change of leadership between the stage of opportunity recognition and opportunity exploitation through firm creation (Shane 2004). Thus the decision over leadership is important to the inventor:

How is the evolution of a new venture influenced by a change in project leadership?

This leads towards another discussion, which links the fate of a firm with the entrepreneur's background. High-tech firms have a wide range of people taking entrepreneurial positions, which can include academic researchers, researchers from the private sector or business managers. The above question therefore appeals to another question regarding the influence of entrepreneurs with different backgrounds on a company.

How is the evolution of a new venture influenced by the entrepreneur's background?

The characteristics, background and culture of the agent are therefore included in the frame of study and we hypothesise that they can affect the project and firm early evolution. The thesis therefore aims at understanding the early evolution of an innovative firm, which is shaped by the agent and his characteristics.

This thesis aims at understanding the early steps of innovative firms for the reasons outlined above. The study of the interactions between the co-evolution of an innovative project with a newly created firm, involving a systemic view, appeals to the study of a complex process, which is best done through case studies[4]. To do so, the study chooses to focus on a specific sector, the biotechnology sector, since its characteristics can shed light on points highlighted in the research questions. The biotechnology sector is selected firstly due to sampling advantages. This sector is still in development, which means there are a large number of young firms. The sector is high-tech and knowledge intensive, which makes these firms more likely to be innovative in terms of the products they are offering[5]. It will look at the main problems that these firms encounter and the stages they go through during the early years of their development. This sector has several advantages linked to the interests of the research, which are outlined in the above research questions. A first feature of this study is the systemic approach that it takes. The biotechnology sector involves a range of regulations that have the potential to strongly affect the firm strategy, due to its different industries of application, such as the pharmaceutical or other life science industry. Thus this sector may highlight to what extend the environment constrain the entrepreneur in his innovation project and enterprise. A second feature of the study aims at understanding the influence of different backgrounds (in terms of experience, knowledge and culture) on the process under study. The biotechnology sector seems particularly adapted to this feature since it accommodates firms emerging from both public research and the private sector. Indeed, it is the sector in which academic spin-offs are the most represented compared to other high-tech sectors (Oakey 1995). Here academic spin-offs (or university spin-offs) are defined as the newly created firms aiming at developing a research project that emerged from academic research. Thus the biotechnology sector involves entrepreneurs with a variety of backgrounds coming from both private firm and public research, which will help us to link the characteristics of the agent to the early evolution of the innovative project and firm creation. Thus the biotechnology sector involves a variety of properties that are crucial to be able to tackle the above the research questions.

On the policy side, understanding the processes of firm formation and early growth has many benefits in our modern economy, especially in high-technology sectors. During a financial crisis, politics and policies struggle to find a way back to higher employment and to increase the growth and competitiveness of developed countries. The creation of new firms and the development of new technologies is usually the target of policy makers in order to rekindle growth in developed countries. However, as mentioned earlier, the majority of new firms do not have a significant influence on growth, since only a minority of them will first survive and only a minority of these survivors will experience significant growth. The understanding of the early stages of high-tech start-up evolution therefore highlights the processes that the entrepreneur goes through in a firm's

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[4] This is explained in further details in Chapter 3 section 2.1.
[5] An overview of this sector is provided in chapter 2.

infancy (e.g. its most vulnerable period). This may help policy makers to identify and help firms with a high potential in their vulnerable years in order to increase the number of surviving firms and thus firms with a potential for growth. The study of the newly created ventures, through the study of firms' goals over time, also enables us to differentiate firms based on their motivation for growth and/or survival objectives and understand how the choice for a business model and ultimately a path towards growth is made.

Outline of the thesis

The understanding of the motivation of an entrepreneur towards his early steps of evolution and the definition of his research strategy is explored throughout this thesis. The first part aims mainly at setting the theoretical and empirical background. The first chapter presents the theoretical literature that is the basis for the analytical chapters. It aims at defining and setting a framework to study innovative entrepreneurship. It firstly develops the definition of innovative entrepreneurship along the lines outlined in this introduction, by developing the concept of the co-evolution of innovative project development and the firm creation processes. Secondly, it deepens the discussion and understanding around the concept of entrepreneurial agency, together with its main variables of study (the entrepreneur, the entrepreneur's actions and the environment). Finally, the chapter goes in depth towards understanding the properties of each variable in this framework. This chapter aims at developing the framework of entrepreneurial agency and operationalises its components, which enables us to contribute to entrepreneurship theory, but also to hypothesise about variables that may play an important role in the firm early life stages.

The second chapter aims at offering a background for getting a better understanding about our cases. It focuses on the sectoral characteristics of biotechnology. This chapter describes the biotechnology sector, both from the scientific side as well as the industrial side. The description of the science lying behind the sector exposes the scientific breakthroughs that are at the origin of the quick development of this technology over the last 30 years. This section begins by describing how these scientific breakthroughs have various domain of application in different industries. The second part of the chapter focuses on various industries in which these breakthroughs can be applied. This particular section highlights the characteristics of each industry in terms of market evolution, regulation and other specificities. These characteristics account for environmental factors that the firm faces when entering a particular industry, and thus the section also discusses such environmental impact on the business models of firms. This chapter is therefore important because it outlines the specific environmental characteristics that the firm faces when entering this sector. It will enable us to understand external constraints that the entrepreneur faces when building his firm, which is one of the main variables of study in the analytical chapters.

The third chapter firstly intends to explain the methods chosen for studying the dynamics of the firm early life stages. In the light of the research questions and the theoretical framework, the chapter will argue why a case study design has been chosen, and under which rationale the specific firms for our case study have been chosen. This chapter also gives an overview of the cluster under study (the Alsace BioValley cluster) and finishes with a presentation of the firms included in the case studies. The overview of the cluster is complementary to the previous chapter as it gives us specific insights about the environment in which the firm evolves looking at the regional system of innovation. It gives some details about support organisations (such as financial organisations and other technology transfer organisations) that can play a role at firm creation, and therefore indicates other environmental characteristics which the entrepreneur's strategy and his venture evolution can be affected by.

The second part is composed of the analytical chapters and aims at understanding the firm early evolution when transitioning from a parent organisation to a newly created organisation following an innovation process, by answering the above research question. The research questions are organised around factors that are relevant to the entrepreneur, through his background or a change of leadership that can occur, environmental factors or through co-evolution processes (between the innovative process and the firm early life stages). The analytical chapters all rely on the case studies, for which the methods and the characteristics of the cases has been described in Chapter 3. These chapters are based upon interviews carried out with members of start-up founding teams and in the form of three papers that explore issues developed in the objectives of the thesis and answer the various research questions outlined above. The chapters first try to understand how certain determinants influence entrepreneurial agency, and then turns toward looking at how these components have an influence on the firm early life stages. The specific contents of the chapters in Part 2 are outlined in the following paragraphs.

A first component of our research question, relates to the role that the environment can play in terms of the constraint of one's firm development, which is the aim of the first analytical chapter. It particularly looks at the effect of the financial environment on the entrepreneur early strategy. Chapter 4 focuses on the impact of the involvement of financiers in the venture for the choice towards business model. This issue is known to have an important role in the biotech sector because many firms, especially those focusing on human therapeutics, need a high level of funds and thus have to acquire funding from venture capitalists. This issue has previously been studied in terms of linking the financier to the performance, while our aim here is to understand the impact of financiers on the entrepreneur and the early evolution of the firm. Since financiers are exposed to risks with their equity investment, they often impose constraints on the firms in which they invest. The chapter therefore looks at how financiers can have an influence on entrepreneurial agency (especially their freedom of choice) through various mechanisms, which can ultimately affect the business model. The results show how the availability of financing, the type of innovative project and the personality of the entrepreneur can influence the business model. The chapter also points towards an effect of regional learning for the financing choices of firms in which new firms are influenced by the experience of former or older firms located in the region, which are known to many new entrepreneurs. The chapter therefore concludes by describing how financial organisations can influence the choice of the entrepreneur towards a specific business model, and thus implies how the choice for a business model has an influence on the pursuit of the innovative process and the construction of the firm.

A second component of our research question focuses on the entrepreneur himself, and on the impact of his characteristics on the firm early life evolution through two components. The first component focuses on the background of the entrepreneur, through his experience and culture, and discusses its consequences in terms of preferences towards a firm strategy. The second component is concerned with the impact of a change of leadership on the strategy of the firm. Chapter 5 aims at observing the effects of a change, or no change, of leadership throughout the entrepreneurial activity (from opportunity exploitation to firm creation), and links the background and culture of the founder with the strategy of the firm (which can evolve over time). The strategy of the firm will be studied based on the activities pursued by the entrepreneur, and looks at the influence of the leadership background on both the innovative process and construction of the firm. It shows that the project and the firm are two different entities and that goals can be changed at different points in time during the firm development. It also shows that the individual preferences of the entrepreneur influence the firm trajectory and the project development. This chapter therefore aims at understanding in more general terms the role of characteristics of the entrepreneur(s) towards his decision for a firm strategy and by extension to the early evolution of the life of the firm and the innovation process.

The final chapter focuses on two specific elements of the research questions. Chapter 6 aims mainly at characterising the early evolution of a project of innovation towards the creation of a firm. This chapter mainly concerns the process of firm creation emerging from a university research project, and therefore only focuses on academic spin-offs. This chapter tries to understand the steps that a research project goes through when transitioning from the incubating organisation (here the university) to a newly created organisation. The chapter also shows the influence of the background of the founding team on the evolution of the innovative project and the firm creation process. It will differentiate between spin-offs created by PhD students, spin-offs created by senior academics who have decided not to take part in the management of the firm, and academics that are responsible for the project in the firm. In addition, because the chapter specifically looks at university spin-off creation, this brings us to the second component of the chapter, which is the understanding towards the role of university (together with the parent laboratory) during the transition of the project and early evolution of the firm. The link between the background of the entrepreneur and universities explains some differences of opportunity between entrepreneurs. Therefore, this chapter aims at putting forward the characteristics of the early evolution of a project in addition to issues relating to the background of entrepreneurs (introduced in Chapter 5) and with an external organisation, the university.

The thesis ends with the conclusions by discussing the contribution of the chapters and the overall contribution of the thesis. It discusses how the thesis has answered the research questions and identifies opportunities for further developments of the work.

Part I:
Background of the Study

Chapter 1: Theoretical background: Entrepreneurial role in the firm's early life stages

1. Introduction

This chapter aims at building a theoretical framework that will be useful for analysing the creation and evolution of innovative start-ups. The entrepreneurial event is here considered as the transition of an innovative project from an incubating organisation, in which the premises of the innovative project are developed, to a newly created organisation. Thus the review focuses on defining the notion of innovative entrepreneurship in order to characterise the two main processes: 1) the development of an innovative project and 2) the organisational process behind firm creation, which together compose the entrepreneurial process under study. The chapter goes on to identify key variables in these processes which are determined by a human agency framework that helps to clarify the role of agency in entrepreneurship studies. The chapter defines entrepreneurial agency as the triadic relationship between the entrepreneur, his actions and the environment. The chapter finally develops these three components of the relationship in order to identify variables that affect the two above processes.

Various literatures are used in this review to present a framework for studying these processes, starting with entrepreneurship literature but then extending to other streams of literature such as behavioural theories, innovation studies and theories of the firm and organisation. We draw from these literatures to identify a set of generic variables that influence the two above processes. The entrepreneurship literature is central to this study, since this literature deals with opportunity exploitation and firm creation processes, which is the backbone of this thesis. This chapter firstly discusses the two definitions of entrepreneurship that emerges from the literature, the one concerning firm creation and the one discussing change in the economy. Subsequently, the chapter examines the different roles of the entrepreneur before proposing a definition and a framework to study innovative entrepreneurship. The framework is explored and limited to the entrepreneurship literature when available, but is also based on other literature in the cases where entrepreneurship has not sufficiently developed the issue.

2. Entrepreneurship, what definition?

Entrepreneurship theory examines the action of firm creation, but also includes contributions towards the exploitation for opportunities of profit that become available in the economy. Thus the review of the entrepreneurship literature in economic theory is not a straightforward task since the literature is fragmented for several reasons: by the variety of its contributors and by the lack of a common definition for the entrepreneurial action. This lack of unity is believed to hinder the development of entrepreneurship theory as its own research field as explained by Shane (2003, p.3):

> "The division of the field into different camps has stymied the development of the field of entrepreneurship. By focusing on only one aspect of the entrepreneurial process, most researchers fail at providing a comprehensive explanation of the phenomenon".

These divisions might arise for several reasons. First, the literature has received contributions from a range of schools of thought that range from the study of entrepreneur as individuals, study of entrepreneurs in relationship with the organising set-ups of the firm and finally the relationship between entrepreneurship and economic trends (such as growth and competitiveness). Second, many disciplinary groups, such as economists, social scientists, psychologists, political scientists and others have contributed to this literature (for a review on the disciplines and contributions in entrepreneurship see Zahra 2005). Finally, the study of entrepreneurship has received contributions varying from the general role of the entrepreneur in micro-theory to a more practical study of entrepreneurship as a study of firm creation. With a variety of fields and focus of research surrounding the entrepreneur, the field of entrepreneurship has known a variety of research interests, many paths of development and a mixture of empirical methods. This variety of focus has translated into several definitions of entrepreneurial function and action.

Over the years the entrepreneur has been given different functions by economic theory scholars, depending on the contributor's interest. In this section only the definition of entrepreneurship in the history of economic thought will be looked at, since later sections deal with contemporary contributions from the more multi-disciplinary entrepreneurship field (section 2.1.3) and convert the components identified in both strands of entrepreneurship literature into operational and researchable concepts (section 2.1.4).

In fact, in the history of economic thought, the function of the entrepreneur has not been obvious. There are two main trends on qualifying the entrepreneurial function. The first one was interested in the organising function of the entrepreneur, **as somebody who is responsible for creating companies**. As Baumol (2010, p.18) reminds us:

> “Taken literally, the term ‘entrepreneur’ refers to someone who undertakes. Accordingly, in the early literature, and even in much of current discussion, the word is taken to refer to anyone who organizes a new business firm of any variety, whether or not a number of similar firms already exists;”

The second trend however emerged with the discontent of some economists with the neoclassical theory and especially with the hypothesis of perfect information and the static view of the economy as a collection of purely competitive market. They identified the lack of the entrepreneurial function in the macroeconomic theory, which seemed central for them in economic theory.

> “There are two main reasons why there is no economic theory of the entrepreneur. The first lies in the very extreme assumptions about access to information which are implicit in orthodox economics- that is in the neoclassical school of economic thought. Simple neoclassical models assume that everyone has free access to all information they require for taking decisions. This assumption reduces decision – making to the mechanical application of mathematical rules for optimization. It trivializes decision-making, and makes it impossible to analyse the role of the entrepreneurs in taking decisions of a particular kind. “ (Casson 1982, p.9)

Thus the entrepreneurial function is introduced in these theories to bear the **function of the agent acting for change** in the economy. These economic theories, in which the asymmetry of information introduces change in the economy, were in need of an agent responsible for the changing forces. This role was given to the emblematic entrepreneur. His effect on the economy took two different types of actions, a dis-equilibrating action (Schumpeter 1934) and an equilibrating action towards perfect competition (Kirzner 1978) depending on the theory. This economic trend focused on change in the economy and has associated the entrepreneurial function with a ‘slightly’ different definition than its original meaning (i.e. organisational undertaking or creation). For example, Schumpeter explains the shift he takes in explaining the entrepreneurial decision:

> “As it is the carrying out of new combinations that constitutes the entrepreneur, it is not necessary that he should be permanently connected with an individual firm; many “financiers,” “promoters” and so forth are not, and still they may be entrepreneur in our sense. On the other hand our concept is narrower than the traditional one that it does not include all heads of firms or managers or industrialist who merely may operate as established business, but only those who actually perform that function[6]. Nevertheless I maintain that the above definition does no more than formulate with greater precision what the traditional doctrine really means to convey.” (Schumpeter 1934)

[6] The author is here referring to the entrepreneurial function.

In these theories, by defining the entrepreneurial function with the action that leads to change rather than to the action of firm creation and organisation, the theorists change the focus from the action of creation to a more generalised function, the function of change. This function of change may occur with or without firm creation. This function of change is associated with the actions of the entrepreneur to carry new combinations (Schumpeter 1934) or to enter an already existing market where competition is weak (Kirzner 1978). In this definition entrepreneurship can be limited to firm creation, but not only; and all firm creations are not linked to entrepreneurial actions. Thus this division between the conceptions of the entrepreneur must be examined more deeply in order to understand the different definitions that underlie entrepreneurial actions.

2.1. Division between two conceptions of entrepreneurship

This section examines the two views of entrepreneurial functions. Starting with the traditional function of firm creation, the first sub-section examines contributions towards this definition from early theories to contemporary theories of entrepreneurship. It shows that this definition, even if it was used in early days, is still present in many contemporary contributions in the entrepreneurship research field. The second sub-section deals with the literature criticising the neoclassical literature. It explains the variant definitions of entrepreneurship. The last sub-section discusses the contemporary literature on entrepreneurship, and shows how this literature has grown even further in terms of variety of the fields of study, but also in terms of variety of levels of analysis.

2.1.1. Organising agent through firm creation

A significant part of the entrepreneurship literature, as much theoretical as empirical, has defined the entrepreneur as an organising agent that is responsible for the creation of organisations. This vision is considered as the traditional vision of entrepreneurship.

Starting with Cantillon (1755) who first introduced the word entrepreneurship in economic theory. He viewed the entrepreneurial function as a function of firm creation. The entrepreneur was seen as a merchant, who bought commodities to sell them when consumers needed them. The entrepreneur bought goods at the prevailing prices, but speculated that he was going to sell these goods at a higher price to gain profit. Cantillon saw the entrepreneur as an uncertainty bearer since he could not accurately predict the consumer demand.

Later, Say (1803) developed this notion of entrepreneurship in the economy. More than a trader, he saw the entrepreneur as an agent who organised firms. In his “Traité d’économie politique” Say sees the industrial entrepreneur as an agent who organises any type of production and seeks the profit from it. Part of the profit can then be redistributed to the capitalist who lent him the money. The returns that the entrepreneur receives are due to his judgement and his talent. The entrepreneur is described as having superior qualities[7], which will define his success. Say also points out that this type of activity, when exposed to the risk of markets, may cause him to fail, independently of his entrepreneurial abilities.

In the English economic literature, it was Mill (1900) who introduced the concept of the entrepreneur. He sees the entrepreneur as a superintendent who owns his business. He sees the 'undertaker' (for us the entrepreneur) as somebody who takes more risk than a capitalist but for greater profit. In his own words:

> "The rate of profit greatly exceeds the rate of interest. The surplus is partly compensation for risk. By lending his capital, on unexceptionable security, he runs little or no risk. But if he embarks in business on his own account, he always exposes his capital to some, and in many cases to very great, danger of partial or total loss." (Mill 1900)

All of the above authors see the profit as a rent independent of prevailing interest rates. Interest is the compensation that a capitalist receives for lending his capital to relatively secure undertakings or with some assurance of the return of the principal amount lent over a period of time and therefore not involving the uncertainties of entrepreneurial profit.

The early literature points toward a definition of the entrepreneur that is an organising agent who takes more risks in the economy than the other ones, but is rewarded with profit. Knight (1921) has greatly contributed towards the relationship between profit, rent and risk taking in the entrepreneurship literature. His contribution aims at advancing the understanding about the nature of the risk and profit borne by the entrepreneur. He undertakes a deeper analysis of the notion of risk associated to the entrepreneur. Knight prefers the term 'uncertainty' to 'risk' as it is due to non

[7] « Ce genre de travail exige des qualités morales dont la réunion n'est pas commune. Il veut du jugement, de la constance, la connaissance des hommes et des choses. Il s'agit d'apprécier convenablement l'importance de tel produit, le besoin qu'on en aura, les moyens de production ; il s'agit de mettre en jeu quelquefois un grand nombre d'individus ; il faut acheter ou faire acheter des matières premières, réunir des ouvriers, chercher des consommateurs, avoir un esprit d'ordre et d'économie, en un mot, le talent d'administrer. Il faut avoir une tête habituée au calcul, qui puisse comparer les frais de production avec la valeur que le produit aura lorsqu'il sera mis en vente. Dans le cours de tant d'opérations, il y a des obstacles à surmonter, des inquiétudes à vaincre, des malheurs à réparer, des expédients à inventer. Les personnes chez qui les qualités nécessaires ne se trouvent pas réunies, font des entreprises avec peu de succès ; ces entreprises ne se soutiennent pas, et leur travail ne tarde pas à être retiré de la circulation. Il n'y reste par conséquent que celui qui peut être continué avec succès, c'est-à-dire avec capacité. » J.B. Say p52

predictable economic fluctuation. In comparison with the previous contributions, Knight differentiates the notion of control of the firm from the notion of making decisions:

> "a specialization within productive groups, the individuals with superior managerial ability (foresight and capacity of ruling others) being placed in control of the group and the others working under their direction; and those with confidence in their judgement and disposition to "back it up" in action specialize in risk-taking". (Knight 1921, p.121)

Knight therefore argues that the function of making judgemental decision and taking responsibility for them, which is the function of the entrepreneur, is tightly bound to bearing uncertainty. The entrepreneur can have different sources of income depending on the functions he occupies. However, the revenues of the entrepreneurial activities due to judgemental decision making "is 'what is left' after the others are 'determined'" (Knight 1921, p.126).

Knight, in his analysis focused on risk taking, suggests that the underlying reasons for uncertainty have emerged from the presence of a dynamic element in the economy (exogenous change) that leads to incomplete information and therefore the possibility for residual income for entrepreneurial action. In the above literature authors were reviewed who developed entrepreneurship from the notion of firm organisation, with the function of bearing uncertainty in trading activities. These entrepreneurs are seen as organising agents who are at the origin of firms. However, the definition of entrepreneurship is not singular and the entrepreneurial function has also been used to characterise a different role. In the next literature reviewed, the dynamic element is central. More precisely the entrepreneur is a central figure leading to change in the economy.

2.1.2. Agent bringing change

Part of the explanation behind this division regarding the definition of entrepreneurs' lies in the fact that the objectives of the contributions vary. These variations can emerge from differences depending on author's theoretical contribution. As we previously emphasised, part of the main criticism towards mainstream economic theory (e.g. Walrasian microtheory, or price theory...) is the hypothesis of perfect information, which leads to a static economic model in which competitive equilibrium is the outcome of perfect information and Marshall's law of one price which immediately removes from the system those agents unable or unwilling to offer their goods or services at the market price. These assumptions are some of the most contested in the field and new economic theories have emerged, which introduce asymmetries of information leading to a dynamically changing economy as well as greater scope for firm differences. The entrepreneur is then seen as a central figure who acts as an engine for the dynamic change. However, there is no unified view of the entrepreneurial function. Thus different functions associated with the entrepreneur can be identified.

Two main views can be differentiated, which are the innovative entrepreneur in Schumpeterian (1934) theories, and the competitive entrepreneur in Kirznerian (1978) theories. Both of these theories relate to the literature viewing entrepreneurship as the action of taking advantage of opportunities, which can be opportunities of profit through innovation or competition.

Schumpeter (1934) sees the entrepreneur as the economic agent executing new combinations that lead ultimately to economic change. The agent of change (the entrepreneur) is seen as a disruptive force in the economy. In this theory, at equilibrium in the overall economy, the entrepreneur seeks to exploit the opportunity offered by innovation. Thus Schumpeter defines in much broader terms the notion of entrepreneurship compared to that of only an organisational function:

> "The carrying out of new combinations we call 'enterprise'; the individuals whose function it is to carry them out we call 'entrepreneurs'" (Schumpeter 1934, p.74)

His view of entrepreneurship breaks with previous ones when considering an entrepreneur that bears the risk. In his theory he makes clear that the entrepreneurial, capitalist and managerial[8] functions are distinct:

> "Our definition agrees with the usual one on the fundamental point of distinguishing between 'entrepreneurs' and capitalists' [...]. It also settles the question whether the ordinary shareholder as such is an entrepreneur, and disposes of the conception of the entrepreneur as risk bearer." (Schumpeter 1934, p.74)

As he distinguishes these functions from the entrepreneur, he therefore qualifies entrepreneurship as a temporary function. The function is defined as temporary because it is associated with the innovative function that is limited in time. It excludes the managerial function in most cases, emphasising the role of change agents rather than routine or optimisation. There can be an exception when the managerial position is mingled with the entrepreneurial function, which is the case when the innovation is introduced through firm creation. The entrepreneur is an innovative agent that exerts a function at some point in time. In Schumpterian theory the entrepreneur is also often seen as an agent with extraordinary capacity due to their vision and power of persuasion (Steinmueller 2010). On a global level, the actions of the entrepreneur, through his innovative

[8] See discussion about the managerial function p76-78.

action, give an endogenous form of technical change in the economy; as before Schumpeter, technical change was mostly kept as an exogenous factor.

Later Baumol (1968; 2010; 1993) pushed forward for a micro-theory of innovative entrepreneurship based on Schumpeter's theory. His main objective, like Schumpeter, was to integrate dynamics in mainstream economic theory through the introduction of innovative entrepreneurship. In this specific literature the concept of entrepreneurship is tightly linked to the concept of technological change and therefore growth. The entrepreneur, through his vision and courage, is a routine breaking agent, which is perseverant in his action of invention and further innovation.

On the other hand, the agent of change can be seen as working towards equilibrium. This is the case for the Austrian approach through market processes (Kirzner 1997) and also in the X-efficiency theory (Leibenstein 1987). The Austrian approach[9] focuses on market processes and is interested in how the market reaches equilibrium. Thus entrepreneurial agents are an equilibrating force towards perfect competition through identification of opportunities for profit. Kirzner (1997) in the following quote explains the main components of the arguments of Austrian economists:

> "The dynamic competitive process of entrepreneurial discovery (which is the driving element in this Austrian approach) is one which is seen as tending systematically toward, rather than away from the path to equilibrium." (Kirzner 1997, p.62)

This approach does not argue change through disequilibrium, but sees the entrepreneur as an equilibrating force through market processes. Through their actions entrepreneurs are then an equilibrating force through imitating behaviour of others. This imitative activity increases competition to, over time, overtaking the innovator's advantage and shifting the monopoly position of the innovator to an equilibrium state of competition.

Leibenstein (1987) and his X-efficiency theory, in a similar way to Austrian theories of entrepreneurship, sees the entrepreneurial function as a way to correct imperfect markets. The opportunity in the market emerges from underperforming firms. The X-efficiency is the degree to which a firm performs optimally with its given resources, by efficiently minimising their costs and adjusting their prices accordingly. If firms under-perform, this leaves opportunities for other firms to gain profit and thus the entrepreneurial function can fill this inefficiency.

[9] The Austrian approach is formed a group of economist in which Kirzner famously deals with the question of the entrepreneur in economic theory. The Austrian school is based on theories of human action starting mainly with von Mises.

The notion of entrepreneurship developed in economic theory has a dual definition, one focused on firm organisation and management and the other focused on bringing change into the economy (through innovation or competition). The second of these highlights a process that involves the recognition of opportunities from the entrepreneur and their exploitation, which can be done through firm creation (but not exclusively). The next section explores the state of the literature on entrepreneurship today and the unity of its definition.

2.1.3. The contemporary literature on entrepreneurship

The entrepreneurship research field today benefits from prolific contributions as much on a theoretical level as on a practical level. It has contributions ranging from single entrepreneur characteristics, firm formation questions, to entrepreneurship impact extending beyond the entrepreneurial project or firm. However, this diversity of research motivation and research issues has given rise to a variety of definitions used in this research field. This section aims at a brief overview of the entrepreneurship research field to discuss the definition of entrepreneurship via these aspects, but does not seek to describe in depth all these fields. In order to provide an idea about the main trends in entrepreneurship research, handbooks and reviews (Acs & Audretsch 2010; Casson et al. 2008; Sexton & Landström 2000; Landström et al. 2012; Alvarez et al. 2005) have been used to give a picture of the entrepreneurship literature today. This variety can be explained through different types of variety: firstly the variety in disciplines and secondly the variety of levels of analyses. Both of these levels are explained in the following sections.

2.1.3.1. A variety of disciplines

While there is a growing interest and academic contributions in the entrepreneurship research field[10], this field is formed of 'a mosaic of issues to be explored' (Zahra 2005). These contributions are coming from a range of disciplines, which are sociology, psychology, strategy, management and economics (for a review of the contributions per disciplines see Zahra 2005).

The diversity of backgrounds in this theory can be seen from a priori knowledge as a weakness of the field. The argument suggested by scholars making this statement is the lack of clarity of the field boundaries, because the field is fragmented and without a common foundation (Zahra 2005). However, the interdisciplinary aspect can also be viewed as a chance to be able to borrow concepts or theories from other sub disciplines when one or another has a limitation.

[10] More details about the increase of interest and contributions see Alvarez et al. (2005, p.1)

Decision-making is a key component of the entrepreneurial field, and many of the fields included in entrepreneurship theories are able to contribute to this component. The entry decision (Evans & Jovanovic 1989; Parker 2004), the decision to extend a managerial team (Miller et al. 1998; Eisenhardt & Schoonhoven 1990), the decision to collaborate with other institutions (Asheim & Isaksen 2002), and rational behaviour or the positivist agency theory (Jensen & Meckling 1976) can all contribute to these debates. Psychological theories help to understand the personality and motivation of an entrepreneur and sociologists (Stuart & Sorenson 2005; Stuart & Sorenson 2007), but also the role of social capital of the entrepreneur in relation to his choice towards firm creation. These theories also identified key issues about relationships between top management and team members. The diversity of the research fields has proven to be useful in order to understand individual characteristics of the entrepreneur but also how the entrepreneur interacts with its environment. In addition to the variety of disciplines that constitutes the entrepreneurship literature, these literatures are not unified in term of level of analysis tackled, which will be the topic of the next section.

2.1.3.2. A variety of levels of analyses

In terms of level of analysis, the literature can be differentiated as follows: the entrepreneur as an individual, the entrepreneur and the firm, and finally the entrepreneur (and venture) in a larger system (e.g. at a regional or national level).

The **individual level** deals with the entrepreneur as an agent and gives us some insights into understand primarily the characteristics of the entrepreneur (the operationalisation of this variable will be discussed in section 4). This level of analysis includes two main types of contributions: the ones contributing towards the understanding of the entrepreneur's specific characteristics and the ones contributing towards the occupational choice change of an entrepreneur.

The ***characteristics of the entrepreneur*** include the cultural, educational, sociological and demographic characteristics in order to know if the profile influences the entrepreneurial act. Concerning the motivation of the entrepreneur, McClelland (McClelland 1961) put forward the relationship between motivation and entrepreneurship. The author finds that entrepreneurs are more likely to have a high need for achievement, risk taking, a high need for control and have a preference for novel activities. Also, some other studies have confirmed that entrepreneurs are more inclined to want to be in control of their activities (Parker 2004; Brockhaus 1980; Fagenson 1993). There have also been studies about whether marital status, age, gender, education and other factors are specific to entrepreneurship activities. It has been shown in descriptive studies that in general self-employed people are in their mid-career, more likely to be a male and most likely to be married (Parker 2004; Storey 1994). In terms of education, some studies have shown a correlation between education and entrepreneurship (Bates 1990; Evans & Leighton 1990), although other studies suggest otherwise or even a negative effect (Parker 2004, p.73). The correlation between the two variables may also be dependent on the sector of entry (e.g. knowledge intensive sectors), since knowledge and experience might be more critical in some sectors than in others. Bates (Bates 1995; 1998) found some sectors with positive dependency (i.e. skilled services) but negative dependency in others (i.e. construction). Finally, family background might also have an influence on entrepreneurship. Many empirical studies (Laband & Lentz 1983; Lentz & Laband 1990) have shown a positive relationship between entrepreneurship level and parents that are self-employed; the evidence of intergenerational influence being stronger if it is the father that is self-employed (Dunn & Holtz-Eakin 2000).

Entrepreneurship literature has also discussed the view of entrepreneurial action through the ***occupational choice*** of the entrepreneur. Theoretical and empirical contributions (Evans & Jovanovic 1989; Parker 2004; Folta et al. 2009) have aimed at understanding the decision of an individual to make the step from an employment situation to self-employment. On the theoretical side, the literature has also seen the emergence of modelling of the entrepreneurial phenomena. One of the most cited papers in entrepreneurship theory is a paper by Jovanovich (Evans & Jovanovic 1989) developing a model of entrepreneurship. The model associates the liquidity constraint of the entrepreneur with his decision of entry or switching from employed to a self-employed role. On the same line, Parker (2004) contributed to advance the understanding of occupational choice of entrepreneurs between employment and self-employment. This definition of entrepreneurship includes the agricultural sector and free lance sector[11], which can be excluded in other definitions of entrepreneurship due to their lack of organisational function. In the case of free-lance employment, certain sectors (Medicine, Architecture, Craftsmen...) are organised through self-employment. This definition of entrepreneurship includes a larger number of agents than earlier definitions. Even in the first theoretical contributions, such as those given by Say (1803) and Cantillon (1755b), agricultural workers were not included in the entrepreneurial function even though they might be self-employed.

The interaction between the **organisational level** and the individual level has fostered different research directions. Firstly, the scholars have looked into merging the theory of the firm

[11] This is the case in many professions such as Medicine, Architecture... These occupational choices might not be seen as any particular sense of vision or particular risk bearing, thus would be excluded from many definition of entrepreneurship.

with entrepreneurship theory and secondly they have worked on the link between the entrepreneurial function and firm performance.

Some contemporary authors have generally emphasised the missing link between ***entrepreneurship theory and the theory of the firm*** (Casson 2005; Foss & Klein 2005; Baumol 1968). As Baumol (1968) would say “the Prince of Denmark has been expunged from the discussion of Hamlet”. Therefore after that observation, theories of the firm, including the entrepreneurial component, have flourished and now have a more comprehensive framework for entrepreneurship and are more able to link into the theory of the firm. Some of these emerging theories are presented here. Casson (2005) highlights the role of the entrepreneur as taking decisions in response to environmental change. He takes a perspective toward the role of information in entrepreneurship. In his theory, volatility is responsible for information asymmetry between agents. He explains in even greater detail the sources of volatility that can have a short or long-term effect or be supply and demand related. This volatility creates information gaps, which lead to asymmetry of information between agents. In his theory of the firm, the entrepreneur is the agent who takes advantage of information asymmetries because they are more optimistic (less risk averse) than other agents. From an evolutionary perspective, Witt (Witt 1999; 1998) explains the importance of the entrepreneurial function in an evolutionary theory of the firm. In his papers, Witt focuses on the concepts of bounded rationality together with the cognitive aspect of entrepreneurial vision. This contribution brings insights about the entrepreneurial vision that are often cited in the evolutionary literature but not deepened. He sees entrepreneurs as leaders that convince other agents to join their entrepreneurial venture. The sense of leadership of the entrepreneur enables him to share his vision of the firm with his employees. From a resource-base perspective, Alvarez (2001) argues that entrepreneurship and resource based theories are a good fit since both sides focus on resources. The author believes that the Resource based theory could benefit from the literature of entrepreneurship by integrating the entrepreneurial recognition (opportunity search and recognition). The author views the entrepreneur’s vision and specific cognition (compared to other agents such as managers) as a specific resource that can be a source of competitive advantage in the right environment. The entrepreneur is the coordinator of the bundle of resources, which allows him to organise its resources differently and independently from other firms. In other words, the entrepreneur contributes to the heterogeneity of resources. In his later work, Alvarez acknowledges the importance of rent generation in entrepreneurship and centrality in the theory of the firm (Alvarez & Barney 2007). In line with the classical view of the entrepreneur as an organising agent, many authors wanted to include the entrepreneurial component in the theory of the firm.

The other links made in the literature between the individual level and the organisational one is an empirical point of view and concerns the relationship between ***entrepreneurship and firm performance***. Some authors have therefore looked for high-performing start-ups. Performance in those theories is often referred to as first survival and then growth in terms of sales or employment. A specific category has even been created to describe these companies that are performing well in terms of growth; they are called 'gazelles' or high-impact firms. They have been defined as firms that have a high sale performance over a few years and are also accompanied by growth (Birch et al. 1995; Acs et al. 2008)[12]. In their paper, focusing on 20 studies, Henrekson and Johansson (2010) suggested that these firms are not specifically operating in high-tech sectors contrary to common belief, but are concentrated more on services. This study also shows that the age of gazelles is relatively young. Following the above discussion on innovative firms, another class of firm has also been a focus of interest, that of the New Technology Based Companies (NTBF). These enterprises are usually defined as newly created enterprises specialised in the exploitation of a technological innovation, or more generally in high-tech sectors (Storey & Tether 1998). Studies performed in the United States focusing on NTBF showed some examples of strongly growing companies (Little 1977), especially in the semiconductor industry (Bollinger et al. 1983). The growth of these firms in Europe is showing above average performance (Storey & Tether 1998), however there is no significant case for growth compared to the US. Even if the European studies do not have an exceptional record regarding NTBFs, their growth is usually measured in the short-term and is therefore not informing us on the long-term impact of employment or sales. Thus this literature has particularly emphasised the link between types of firm and performance, which leads to classifying them towards different levels of performance (in terms of growth) or sectoral characteristics such as NTBF.

Finally, **on the meso and macro level**, the entrepreneurial function, as clearly stated in theories of change, should have an influence on growth and competitiveness of a region or country. These issues have also been a focus of interest in the entrepreneurship literature. There have been contradictory results on whether entrepreneurship affects economic growth. Regarding the link between entrepreneurship and growth, Steinmueller (2010) divides the contributions between optimists and pessimists. The optimists (Braunerhjelm et al. 2010; Wennekers & Thurik 1999; Thurik 2009) find a relationship between entrepreneurship and economic growth and development while the pessimists (Storey 1982; Parker 2004; Shane 2003) argues that the actual performance of the

[12] ''A business establishment that has achieved a minimum of 20% sales growth each year over the interval, starting from a base-year revenue of at least $100,000.'' Birch et al. 1995
Acs, Parsons and tracy (2008) defined a "high-impact firm as an enterprise in which sales have doubled over the most recent 4-year-period and which have an employment growth quantifier of 2 or greater over the same period".

majority of the entrepreneurial ventures do not have any impact at an aggregate level. The partisans of a positive relationship between entrepreneurship and economic development focus on the "entrepreneurial" behavioural side of agents and excludes the self employed which are associated with managerial businesses (Wennekers & Thurik 1999). They discuss the specific conditions that lead entrepreneurship to economic growth, which lie in the creation of knowledge spillovers, the increase of competition and the increasing diversity between firms (Thurik 2009). As one can observe, the proponents of this view only point to an indirect relationship between entrepreneurship and growth, with the spillover dimension making it a regional rather than an economy wide impact. The relationship between spillovers and economic growth has also given rise to a growing amount of literature that features the entrepreneur in a regional environment, and thus contributions have increased more recently regarding the link between clusters (geographically co-located activities n the same industry or sub-industry) and entrepreneurship (Feldman et al. 2005; Feldman 2001). Conversely, others have arguments based on the size of the contribution of the small business sector towards the overall economy and that only a small percentage really contributes to its growth (Parker 2004; Storey 1982). However, both sides agree that a direct and positive relationship between entrepreneurship (as a whole) and economic growth is not always valid. Finally, contributions have also emphasised that the emergence of innovations is linked to the interactions of small and large firms in specific innovation systems, and therefore the notion of entrepreneurship is qualified as distributed (McKelvey 1998; Bureth & Pénin 2006). This idea relates to the concept of entrepreneurship as innovative opportunity exploitation, and thus not linked to organisational processes of firm creation, in which the opportunity exploitation is done through interaction between actors.

In the light of the range of theories and views available in the literature referring to entrepreneurs, the next section aims to make a synthesis of the definitions encountered and build one that is appropriate to our focus of study.

2.2. What definition of entrepreneurship should be in use here?

This section (section 2) explores the definition of entrepreneurship and aims at bringing a useful and pertinent definition for the concept of innovative entrepreneurship. However, there seems to be a persistent disagreement between scholars that see the definition based on firm creation and decisions or undertakings that bring change to the economy. This section then aims at summarising the different views of entrepreneurship discussed above, and then gives a definition of entrepreneurship that is applicable to our work, which is the basis on which our analysis will be built.

The definition of entrepreneurship has previously been based on the entrepreneurial action (firm organisation or opportunity exploitation). The literature defining entrepreneurship as firm creation define the notion of entrepreneurship as a permanent function that is usually related to the head of a newly created organisation. This vision defines the entrepreneur as a permanent function in the firm. The definition of 'entrepreneur' in economic theory, in its simplest form could be defined as "the decision making resulting in human action"[13] which is common to most theorists in the field. Here the human action resides firstly in the act of creation and secondly in the action of opportunity exploitation. In most of the theoretical contributions (Say 1803; Mill 1900; Schumpeter 1951), the action required to be done by the entrepreneur somehow defines the entrepreneurial abilities. The entrepreneur is seen as an agent with extra-ordinary capacities as a superintendent for Mill (1900), having superior qualities for Say (1803) or being an "Ubermensch" for Schumpeter (Steinmueller 2010).

Regarding theories dealing with economical change, the definition of entrepreneurship can be seen as different functions in the economy responding to different types of opportunity: innovation opportunities or competitive opportunities. In this literature the notion of entrepreneurship is only related to the exploitation of opportunities (competitive or innovative) and thus not defined by the notion of firm creation (as the literature presented earlier was). This definition of entrepreneurship has given rise to new contributions in contemporary entrepreneurship literature that do not involve firm creation but rather focus on the development of innovative projects inside existing organisations.

The different definitions are not mutually exclusive since they overlap in some ways. Hence, it is useful to differentiate types of entrepreneurship using the definition discussed above. To summarise the different types of entrepreneurship one can encounter in the actual literature, based on the literature described above, we can introduce a taxonomy as follows:

[13] This definition is taken from earlier theories of entrepreneurship as much as contemporary ones. This definition is first in line with the argument of Von Mises (Von Mises & Greaves 1949, pp.251–254) and Kirzner (Kirzner 1978, p.35) of an active acting agent following decision making, which is the essence of the entrepreneurial action. These action are to put in contrast with passive actions such as mechanical actions which are considered as passive. Schumpeterian theory (1934, p.75), apart from the characterisation of new opportunity creation, includes in its definition the initiative authority and foresight which can be represented by decision making and action stemming from it. In later contributions this definition is still referred to by Gartner (1989; 1994). He refers to it in his definition of entrepreneurship first as an acting man but also later as an agent that involves doing and thinking.

Table 1.1: Entrepreneurship types[14]

Type of opportunity		Firm creation	Inside an existing organisation
Change function	Innovative	Innovative entrepreneurship	Intrapreneurship
	Competitive	Imitative entrepreneurship	Diversification
Organisation function	Managerial	Classical Entrepreneurship	

The literature on entrepreneurship therefore displays a variety of definitions that are regrouped by the different functions that are showed in the Table 1.1 by the light grey area, which includes the definition covering the entrepreneurial function of change and the organising function at firm creation (which was described in section 2 of this chapter). Today's definition of entrepreneurship does not only include contributions about firm creation, but also about opportunity exploitation, which can be done inside an existing organisation. The definition therefore includes both aspects developed in entrepreneurship theory. The theory on the change function of entrepreneurship does not only deal with exploitation of opportunities through firm creation but also opportunity exploitation through firm creation. To be complete, the concept of entrepreneurship in existing organisations should therefore also be included in our definition and overview of the entrepreneurship theory (last column in Table 1.1). Theoretically, the notion of diversification could then also be included under the umbrella of entrepreneurship, but in practice the literature dealing with diversification is rather restricted towards organisational theory or firm growth and thus is not included in our definition of entrepreneurship (the light grey area of the table).

Innovative entrepreneurship (Baumol 1993; Baumol 2010; Schumpeter 1934) and intrapreneurship (Antoncic & Hisrich 2003; Antoncic & Hisrich 2001) are both included under the umbrella of entrepreneurship as a function of change described in the Schumpeterian theory, which has been recently recast by Baumol (Baumol 2010; Baumol 1993). It can include innovative actions such as new combination of productive assets but is not limited to a newly created firm. However, for sampling reasons, authors often prefer to study one or the other phenomena separately. Firm creation is often easier to identify on a quantitative scale. There may also be a great deal of difference in the process of implementing the entrepreneurial idea (in terms of access to resources such as financing and human capital).

[14] Inspired and extended from the table in Wennekers and Thurik (1999).

The imitative entrepreneurship theory relate by the Austrian view (Kirzner 1997; Kirzner 1978; Mill 1900)of is here represented through the competitive opportunity in the table. This can also be associated with the X-efficiency theory (Leibenstein 1966; Leibenstein 1987). Here the entrepreneurship is seen as a competitive force, which is mainly due to discovered opportunities for profit. The two first views are then considered to have an impact over economic processes as the two last ones are focused more on a firm level view.

The definition of entrepreneurship in some literature remains as referring sometimes only to firm creation as following the classical view of entrepreneurship in economic theory (Cantillon 1755a; Say 1803). In today's literature, this can include views such as managerial views of firm creation, or studies that consider the choice of agents to go towards self-employed positions. The managerial view (Penrose 1959; Garnsey 1998; Chandler & Hanks 1994; Helfat & Lieberman 2002) of the firm creation relates more to an organisational view of the firm. A founding director usually has a role oriented towards the efficiency of the use of the firm's resources (Penrose 1959). The organisation of resources is then what differentiates the founding director to the self-employed entrepreneur. This category can also include self-employment, but is not often considered as part of the entrepreneurial function. However, it can be considered so when one focuses on the decision towards engaging in new venture creation, or the choice for an individual to change from an employment status to self-employed. Entrepreneurship in this case can also include classes of occupation (such as craftsmanship, independent occupation) that are often self-employed due to this being the normal occupational structure in the industry. In some empirical studies of firm creation, these occupations are considered as entrepreneurship.

This section has aimed at drawing a general picture of the state of the definition of entrepreneurship, and has shown the existing array of contributions in the entrepreneurship literature that can create confusion. The discussion of this definition aims primarily to obtain a deeper understanding of the entrepreneurship literature in order to place this thesis within it and to clearly define the notion of entrepreneurship that is used in this work. As explained in the introduction, the thesis focuses on innovative entrepreneurship and aims at understanding the early evolution of the entrepreneurial function and those performing it. The concept of innovative entrepreneurship has two components: firstly the component of the innovative project which spans the process from opportunity recognition to the development of the project and realisation of the innovation, and secondly it involves organisation creation, which also induces a transfer of the project between the incubating (or nascent association) status to a newly created organisation. Our definition *of* ***innovative entrepreneurship*** *is the action of exploiting an opportunity of innovation* *through the creation of a firm*. Our study of innovative entrepreneurship therefore implies the study of the co-evolution of these two processes (which we also refer to as the entrepreneurial process).

This definition of innovative entrepreneurship must be extended to discuss its associated timeframe. Returning to the elements of the definition of entrepreneurship, while the organisational process behind firm creation can be considered as entrepreneurship, in this work we follow the Schumpeterian (1934) view about the distinction of entrepreneurs and managers and the consideration that the entrepreneurial function is temporary. Thus, we define the end of the entrepreneurial process as being at a time when the 'managerial routine' dominates the management of the firm. The end point is defined as the time at which a stable management team is in place in the newly created company, and the strategy and early activities are defined and under development. At this point, our study examines the entrepreneurial process in terms of the transition of an innovative opportunity through its early development in a newly created organisation, while the transition from entrepreneurial to managerial focus of the firm is a subject for future research.

In order to explain the organisational and macro processes of economic change, the above theories introduced the entrepreneur as an agent responsible for these dynamic processes. All of the theories included the presence of this agent, because of the need for an agent to make decisions and actions towards that change. In these theories the notion of human action through the entrepreneur is a central feature in order to explain the dynamics of economic change. However, these early theoretical contributions with different frameworks have raised confusion and prevented the emergence of a unified definition of the entrepreneur. The next section looks deeper into the variables necessary to study the **entrepreneur's decision making** and his **action** that is central in entrepreneurship literature. This is achieved by looking at the central place of the entrepreneur and his **power of agency**.

3. Agency and entrepreneurship

The section has until now highlighted the diversity of the definition of entrepreneurship. Thus, after characterising the concept of innovative entrepreneurship by focusing on both concepts of entrepreneurship, firm creation and opportunity exploitation, this section aims at finding a framework to understand and study the action of the entrepreneur.

In order to define, understand and build a framework for entrepreneurial action, we will therefore go back to the literature relating to human action, which explains in detail the variables and their interaction in the field called 'human agency'. This field has its roots in sociological and psychological literature. We therefore relate the diverse concepts developed in entrepreneurship under the general framework of triadic reciprocal causation originally developed in human agency theory (explained below). In this work the interpretation of human agency towards entrepreneurship theory is regrouped under the umbrella term 'entrepreneurial agency'.

The term of entrepreneurial agency is not totally absent from the entrepreneurship literature and has been used sporadically by some authors. For instance, Shane in his book (2003) briefly includes the notion of human agency to differentiate it from deterministic factors. The concept of human agency is primarily used to explain the power of the entrepreneur in economic theory through his decision (to exploit opportunities in this case) and action (Human agency can be found, p.3, 61, 94, 224). In the same way, this concept has been sporadically cited in the work of Baumol (1993) to refer to the role that the entrepreneur can take in the process of innovation. Other authors use this concept more extensively, such as Garud and Karnoe (Garud & Karnøe 2003) and Steinmueller (2010). The first of these mainly uses this term to refer to the concept of entrepreneur and the power of individual in the entrepreneurial process without defining it precisely. The second author takes the concept of entrepreneurial agency as a central concept of entrepreneurship theory and refers to this concept as coming from "a theory of risk-taking and entrepreneurial initiative". More specifically Steinmueller (ibid.) refers to the concept emerging from Schumpeterian theories as follows:

> "While the 'intangible assets' approach makes capabilities a diffuse feature of organisational life, Schumpeter sought to make clear that agency was more specifically lodged in the personality and drive of the individuals. This distinction is important because it separates a view in which change might be the consequence of organisational strategy and, hence, entrepreneurship a strategic decision of organisations, from one in which a more specific focus is placed on the individuals initiating and driving change processes."

The concept of agency has therefore been used previously and in most cases refers to the power of decision and action of individual agents. However, this concept has not been a main centre of interest in most cases, and is in general used to differentiate the individual power of the entrepreneur from the more deterministic view that some literature takes. However, these contributions never ask the question regarding the relative power of the entrepreneur towards his own ability to take decision and action in contrast with deterministic theory. This section therefore aims at contributing to the literature on this point through the use of human agency theory that has been developed in the field of psychology.

The field of human agency aims at understanding the role of an agent's self-influence over his goal realisation and thus his life circumstances (Bandura 2006). Agency theory regroups a variety of arguments and asks the question regarding the power of action of agents towards their own future. The power of human action can range from none (in deterministic theories) to full power (autonomous agency) depending on the theory. For instance, determinist theories argue that the environment is determinant for the outcome of any state of nature. In this case the agent is seen as performing a mechanical action in response to environmental change. At the other extreme, autonomous agency is the concept under which agents are independent and in control of their action and consequently over their own future. However, this concept has really few advocates (Bandura 1989). Others argue for a more tempered view, in which agents have to some extent a power over their own destiny through purposeful actions, but environment and initial condition also play a role over one's future life. In this theory the environment still can play a role in the outcome of the action. Bandura (1999) explains: "persons are neither autonomous agents nor simply mechanical conveyers of animating environmental influences". This theory seems to reflect the entrepreneurship theory where firstly the entrepreneur's vision and secondly the entrepreneur's actions are influencing his own life circumstances (through the creation of a firm) but are also having an impact on the overall economy (through innovation or competition), but to some extent the entrepreneur is also constrained by them.

The human agency theory as presented in the socio-psychology literature by Bandura has some properties that must be reviewed before stating its usefulness for the entrepreneurship theory. The agent in these theories is seen as an actor and not only a product of his life circumstances. This affirmation goes with four core properties that are given to the agent: intentionality, forethought, self-reactiveness and self-reflectiveness. Firstly, an agent has his own intentions, which take the form of goals or self interest in which his efforts are directed. Derived from intention, forethought involves the planning of the action towards the set goal(s); as part of this is that he anticipates the consequences of his actions and envisions expected outcomes resulting from them. Once the plan of action has been decided the agent is not passive in the realisation of his plan, instead he has to build the course of action that leads to the plan realisation (self-reactiveness). Finally, the agent is self-reflective in the way in which he assesses his action and has the ability to correct it while taking into account other determinants that may influence the course of action.

This theory does not therefore only consider the behaviour of the agent, but also discusses the issue of freedom and determinism of the actions of an agent. The theory does therefore not look at the action of an agent completely free of influence (i.e. autonomous agency) or only determined by external factors with passive reactions from the agent (i.e. mechanical agency) but has a nuanced and inclusive theory that integrates both views. Accordingly, the theory of human agency sees a reciprocal relationship between three types of determinants: the agent and his personality (which includes culture characteristics, and capabilities acquired), the action/behaviour of the agent and the environment in which he evolves.[15]

As suggested previously these main elements can be also found in the entrepreneurship literature. How this triadic relationship (i.e. the relationship between agent, his action and the environment) can be translated into entrepreneurship theory will now be discussed, which will also highlight how part of this relationship has already been tackled by the existing literature. The contributions on these components are briefly stated here for the purpose of the understanding of the triadic relationship that combine to make entrepreneurial agency, but are separately (each component) discussed in much more depth later in this chapter (i.e. section 4 for the agent, section 5 for the environment and section 6 for the action).

In entrepreneurship theory, the **action** studied can be divided into two categories: the influences that lead the agent to exploit an opportunity (which can take the form of firm creation), or the action and influences that lead to a given performance of the firm. The first of these looks more into the chain of interrelating causation that leads an individual to exhibit an entrepreneurial behaviour. The second studies the chain of interrelating causation that leads to the firm performance. These two action behaviours are studied in relation to personal assets of the entrepreneur (agent) and the environment. The personal assets of the entrepreneur are seen as firstly the characteristics of the entrepreneur (which are his gender, age, cultural background...) but also the experience, knowledge and capabilities that he has acquired over time. When looking at the entrepreneurship theory, the entrepreneurial action can be considered to be the result of individual action or collective action (led by a management team). The previous action and decision of the entrepreneur can also influence the future of the opportunities and power of decision of the entrepreneur due to the path dependency effect (Arthur 1994). Choosing a specific strategy and path of action can create a historical precedent in which the firm is locked in and that defines the future opportunities open to the firm. Thus, each entrepreneur may be constrained by his previous choice and action through a path dependency effect.

[15] Much more details on variables and relationships in this triadic reciprocal relationship can be found in Bandura's work.

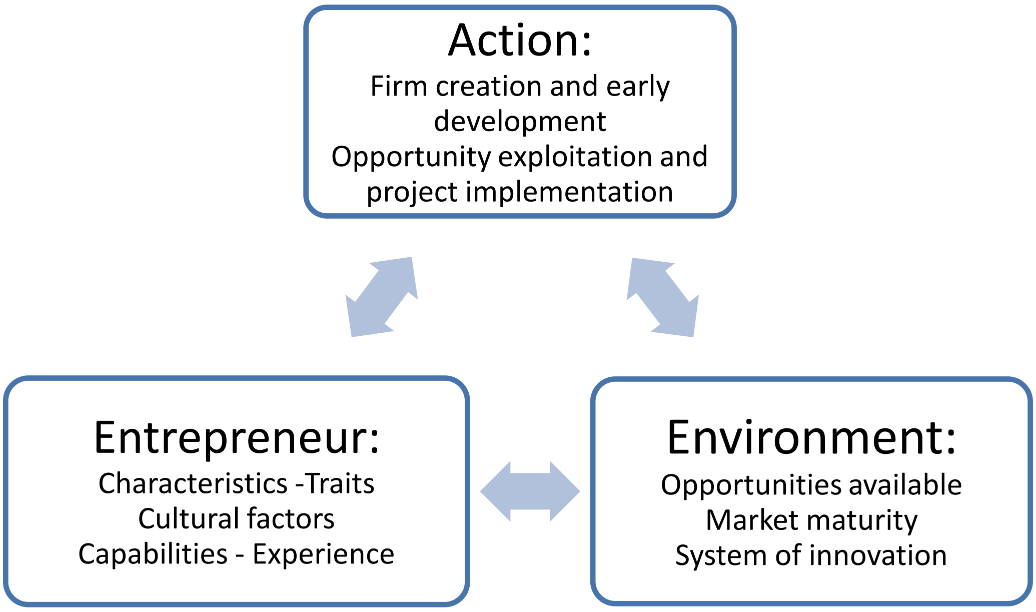
Subsequently, the **Agent**, as emphasised earlier, plays a determinant role in entrepreneurship theory as he incarnates the change in the economy. Entrepreneurship theory has made a theoretical contribution to the qualification of the entrepreneur, as explained above, through different traits such as seeking profit and being a risk taker. On the practical side, entrepreneurship literature has also tried to understand specific characteristics such as knowledge, culture and experience that the entrepreneur can have, which makes him more likely to become an entrepreneur or succeed in his entrepreneurial task.

In addition to the factors mentioned above, **environmental factors** also have an influence on entrepreneurial activity at various levels. The environment influences the entrepreneurial process in many ways, ranging from the existence of opportunity to the path of development of a project. Firstly, the environment is believed to have a crucial role in the emergence of opportunities. Several authors (Casson 2005; Shane 2003; Kirzner 1978) have highlighted the role of change in environment due to shocks in the emergence of new opportunities to be exploited. Secondly, regarding the course of development of the identified project, other external factors influence the path of the entrepreneur such as sectoral maturity, and the system of innovation. As Eisenhardt (1990) explained in detail, a firm's chance of growth is also determined by the state of the market in which the entrepreneur competes. Growing markets are more stable and offer more potential for growth compared to early or mature markets. Finally, the environment, as stated in the innovation system literature, with its specific regulation, support organisations and competing environment can influence the survival and ability to innovate of individual actors.[16]

The following reciprocal triadic relationship has therefore been adapted from the concept of human agency to develop the one of entrepreneurial agency:

[16] These aspects are developed in section 6 in this chapter.

Figure 1.1: The triadic reciprocal causation of entrepreneurial agency



This framework is used as a basis to define and understand the concept of ***entrepreneurial agency***, which can be defined as *the power of entrepreneurs to have influence over their decision and actions stemming from them*. The three components identified in the above framework can have an influence on the power of decision and action of the entrepreneur as described above. The analytical chapters analyse the evolution of the innovative project and the firm by considering the evolution of the entrepreneurial agency and by including at least two of the three components represented above.

The framework introduced above gives the opportunity to see the entrepreneurship literature in a **holistic view** rather than the mosaic of reductionist contributions seen up until now. Many contributions from different theories, as shown above, have focused on only part of the entrepreneurial question. This work aims at looking instead at the entrepreneurial function in a **systemic view**, where the components of the system interact and impact on each other. The systemic view here is central since the framework suggests that innovative entrepreneurship cannot be understood by studying only one component. The entrepreneurship literature has already highlighted that isolated components have an influence on the entrepreneurial action (through the observation of creation activity and survival or growth activity). However they do not give an account of the interaction between components that results in specific action and a specific path of opportunity exploitation. This work aims at filling this gap by studying innovative entrepreneurship as the interaction of two processes, the innovative one and the organisational one, together with influential factors that affect these processes.

In order to further our understanding and develop the three key components of our framework, we go back to the entrepreneurship literature and, when needed, other economics literature, in order to review how these concepts have already been developed. Having defined the main framework in this section, the next sections aim at going back to different streams of literature in order to make these triadic elements and their interactions operational and to make them useful in a practical setting. We therefore first ask the question of 'who is the entrepreneur' in order for to be able to identify the individual in charge of the entrepreneurial action. Secondly, we try to understand in what environment the entrepreneur evolves and how this environment impacts on the entrepreneur and his action. Finally we continue by describing what the entrepreneurial action is, both in relationship to innovative opportunity exploitation and organisational processes.

4. Who is the entrepreneur?

The previous section has highlighted the importance of the different variables (i.e. the entrepreneur, the entrepreneurial action and the environment) in the characterisation of the framework for studying entrepreneurship research. This section aims at discussing the features given by the literature on the entrepreneur in order for us to first be able to identify the entrepreneur and second to uncover characteristics that would affect his action over time.

Section 2 has already identified several attributes of the entrepreneurs that have been drawn from entrepreneurship theories. This section draws upon contemporary work in order to discuss the characteristics that have been attributed to the entrepreneur by theorists: is the entrepreneur a single individual with extraordinary capacities? Is the entrepreneur less risk averse than other agents? This section is organised into three parts. The first part discusses the abilities of the entrepreneur and how they affect his actions. The second part aims at discussing the identification of the person that fulfils the entrepreneurial function. The third part aims at discussing the entrepreneurial function together with the notion of risk.

4.1. The characteristics of an entrepreneur: is the entrepreneur an "Ubermensch"?

In many of the theories mentioned above, the entrepreneur is depicted with great qualities of leadership, vision and knowledge, amongst others. Many studies have therefore asked the question "who is the entrepreneur" in order to discover his characteristics and whether or not he has exceptional qualities that leads him to firstly become an entrepreneur and secondly produce a successful venture. As explained previously, the entrepreneur is often qualified as an agent with special qualities, as an "übermensch".

Many recent contributions have asked the question of "Who is the entrepreneur" in order to understand the specific characteristics needed to be an entrepreneur. This view is referred to as the 'traits approach'. This approach has been discussed in a previous section on contemporary literature of entrepreneurship (section 2.1.3). The trait approach has looked into different characteristics of an individual that could make them more likely to become an entrepreneur, such as personal motivations, family history or even personal traits. Since we are trying to link entrepreneurial actions to individuals, we should ask if the entrepreneur's traits affect his action.

The traits view must also be tempered by the fact that in most theories the entrepreneurial function is a temporary one; the creation of the firm or function of change in an economy is transitory and also in part to be linked to a personality; it is contextual. The entrepreneurial behaviour can be influenced by the entrepreneur's personality but also certainly some contextual events that lead to entrepreneurship at a specific point in time (this could be seen as the notion of opportunity in the entrepreneurship theory).

However, the managerial literature (Bourgeois III & Eisenhardt 1988; Glick et al. 1993; Eisenhardt & Schoonhoven 1990) has pointed towards the advantage of having functional diversity in a firm's management team, which refers to experience and knowledge of the team members. In fact, human capital is also seen as central in firm creation, by both academic researchers and practitioners. For instance, financiers such as venture capitalists often requires a change in the top management team in order to include experienced managers (Timmons 1978; Bidhé 2000). This is backed by academic studies that try to understand the link between the individual experience of entrepreneurs and firm survival and growth. Bird (1989) explains that the **industrial experience** of the entrepreneur may be crucial for firm survival and growth. This is due to the awareness of norms in the industry such as supplier relation, pricing or even employment. This hypothesis has been tested through a sample of 223 firms in Sweden by Delmar and Shane (2006) that concluded that industry experience has a positive influence on new venture survival and sales. In the same line, Klepper and Sleeper in their study of the US laser industry (2005) showed that spin-offs from previous firms had a much higher change to survive in the short to middle term than other firms due to their industry experience. **Business experience** has also been emphasised in the literature as a desirable feature of an entrepreneur. This can be referred to as the experience of firm management but also as a person that already has entrepreneurial experience. Business experience is desirable since it can help the entrepreneur in terms of finance, organisation, sales, logistics and marketing (Schoonhoven & Romanelli 2001; Shane 2003).

The human capital access is recognised as a determinant of firm survival and growth and thus should be discussed in this thesis. Since this study is focused on high-tech firms, and especially on the biotech sector[17], the entrepreneurial function includes the identification and development of an innovative opportunity, which needs specific technical competences entering a high-tech sector. This sub-section has highlighted the usefulness of some types of experience in order to increase the probability of success of a new venture. Thus the human capital of entrepreneurs (or founding team), regarding their technical, managerial and industrial experience, must be taken into account because these skills have an impact on the firm performance and must by the same means have an impact on the actions taken by the entrepreneur.

4.2. The entrepreneurial function: is it always embodied in one person?

In order to study the framework described above, with components that include the entrepreneur; his action and the environment, the first step is to be able to identify "the entrepreneur". In order to do so, we have to go back to our definition of entrepreneurship. Innovative entrepreneurship is defined as the actions of exploiting an opportunity of innovation from the time of conception through the time of firm creation and its early infancy. Thus the entrepreneur is the one fulfilling these actions, which we also refer to as the *entrepreneurial function*. The entrepreneur must therefore have two main activities, the activity consisting of identifying and taking the steps to develop and exploit the opportunity of innovation and also the organising function of firm creation. The entrepreneur is therefore identified through activities performed, such as opportunity recognition, exploitation, and the organisation process resulting and following firm creation. Thus the identification of the entrepreneur depends on the activities he performs.

During its early days, the entrepreneurship literature envisioned that the entrepreneurial function was embodied in a single person. The "entrepreneur" was seen as a super-agent ("Ubermensch") who could identify opportunities others could not see, find means of exploiting them no one else could do and, in addition had extraordinary persuasive powers and conviction thrusting him into a position of leadership as others became involved in his enterprise.

[17] The explanation of the choice for high-tech sector and biotech firms are explained in detail in Chapter 2 and thus are not discussed here.

However, in more recent literature, it has been acknowledged that the exceptional talent required to fulfil this entrepreneurial function is rarely found in a single individual. The entrepreneurial function could then be fulfilled by different people cooperatively (Garud & Karnře 2003; Gartner et al. 1994; Burger-Helmchen 2008). Starting from Schumpeter in his later work, he acknowledges that:

> "The entrepreneurial function may be and often is filled co-operatively. With the development of the large scale corporations this has evidently become of major importance: aptitudes that no single individuals combined must be built into a corporate personality;"
>
> Schumpeter (1951, p.256)

The difficulty for the entrepreneur is not so much in identifying the opportunity, but more in taking the decision to exploit them. Nowadays, especially in some sectors such as complex systems or science-based sectors, the exploitation of an opportunity requires many different skills or competences. The complexity of the technology, markets, environment, financial and organisational structure must all be treated, and the level of knowledge in each of these domains is crucial for the firm's productive choice. This productive choice will influence its survival and growth.

As a complement to the literature on entrepreneurship, the literature of organisational theories can help in this debate, especially the numerous contributions towards the understanding of management team decision taking in companies. This literature emphasises the crucial role of organisation in the company, especially in the management team, and describes the role of its members in the decision process and therefore the path of the firm. The entrepreneurial agency is here distributed to different agents, which interact in order to complete the process of making decisions. The management team in Cyert and March (1992) is seen as the "'dominant coalition' of individuals responsible for setting firm direction" (Wiersema and Bantel, 1992). The team therefore defines the technological path of the firm by considering the firm's environment and also its organisational capabilities. This literature emphasizes the roles of the top management team to lead their organisation to create change, which are "receptivity to change", "willingness to take risk, "diversity of information sources and perspectives" and finally "creative decision making". These characteristics are somehow representative of the characteristics described in the entrepreneurial literature, which are the risk bearing attitude, the information asymmetry in favour of the entrepreneurial agent, the recognition of change opportunity and finally the entrepreneurial creative vision (Margarethe F. Wiersema & Bantel 1992). In the same way, the top management **team background** has been recognised to be a determinant factor for the future success of all firms, including new ones. The determinants of success are mainly found in the individual experience and also in the group cohesion of the top-management team. In terms of cohesion, the firm diversity caused by backgrounds that create conflicts (to a certain extent) in a top management team might be a desirable feature (Bourgeois & Eisenhardt 1988) combined with rapidity of decision making. The constructive conflicts are more likely to be enhanced by a variety of background including industry experience. There is agreement that a diversity characteristic of the team has an influence on the firm evolution in terms of demography and experiences. There are positive and negative effects created by the diversity of firms. The good effects can mostly be seen as positive because of the fact that the diversity of backgrounds enhance the scanning of the environment (knowledge of markets and competitors) to act better in decision making processes (Glick et al. 1993). Diversity in the top-management team composition could enhance change and learning between members according to the concept of cognitive distance (Nooteboom 2000). The shared leadership has an effect on the cohesion of a firms and has a positive impact on the top management team performance and thus on the company (Ensley et al. 2003). Thus, having diversity in management teams of new companies may generate a diversity of firms, some of which have a better ability to survive in specific environments due to a better combination of competences.

The entrepreneurial function in some cases may not be fulfilled by only one agent independently. Depending on the sector of activity, on the market and organisation complexity, the entrepreneurial vision may be performed collectively or individually. The focus of this thesis is innovative entrepreneurship, especially in high-tech sectors, and the entrepreneur should therefore be able to possess the capabilities to recognise and exploit innovative opportunities but also to be able to successfully organise and manage a newly created company. Such individuals are rarely found and thus in this work we are not looking to identify a single entrepreneur in a firm but rather to identify the defined entrepreneurial functions and then look for individuals who perform such functions. Therefore, one should not expect to find a single “entrepreneur” in each organisation. In the following sections and chapter, the terminology “the entrepreneur” will still be used, however we see the entrepreneur as the individual fulfilling the entrepreneurial function at a given time, and thus we do not assume that the individual performing this action is unique. It has also been pointed out above that sector specific structure such as sectoral specificities (i.e. regulations, institutions or market specificities) is one environmental factor that affects the ability of a single agent to perform the entrepreneurial function.

4.3. The notion of risk and profit associated to the entrepreneur

The notion of risk and uncertainty has been linked to the entrepreneurial function since its early days. The risk function can be attributed to both definitions of entrepreneurship (the agent responsible for firm creation and the agent of change). In the discussion over the entrepreneurial function, risk has been seen for a long time as part of the entrepreneurial function (Cantillon 1755b; Say 1803). However, in early theory, the entrepreneur was considered as taking financial risk while investing in his venture, and therefore confounded with the capitalist function. In some contemporary theories, such as in the Schumpeterian theory of entrepreneurship, the risk was considered to be borne by the capitalist function[18], because they would experience the financial loss and thus be more affected than the entrepreneur if the innovative project were to fail.

A traditional characteristic that is attributed to the entrepreneur lies in his attitude towards risk. Some literature would therefore imply that the entrepreneur has a lower risk aversion than other agents in the economy. However, this proposition can be counterbalanced with many other variables and facts that can be found in entrepreneurship theories.

Firstly, some empirical studies have compared different categories of agents with entrepreneurs in terms of their risk aversion. Some empirical studies (Brockhaus 1980; Tucker III 1988; Palich & Ray Bagby 1995) show a positive relationship between entrepreneurs and gambling, while others found no significant evidence that entrepreneurs are more inclined towards risk taking. Thus evidence coming from empirical literature is somehow conflicting and therefore inconclusive on whether an entrepreneur is less risk averse than other agents. While developing this section we will therefore see that other explanations have emerged that can counterbalance the fact that the entrepreneur is different in terms of risk aversion, such as characteristics of his opportunity (i.e. risk inherent and expected profit related to the development of his opportunity) or asymmetry of information in favour of the entrepreneur.

The perception of risk can also differ among individuals. The first difference that can arise is the asymmetry of information. The entrepreneur, when discovering and assessing an opportunity, may have more information in terms of technology, market condition and the industry value chain to assess the opportunity. Therefore the decision of enterprise is less due to personality bias in risk bearing, than to the surplus of information held by the entrepreneur.

A second point must be mentioned regarding the notion of risk, which concerns the notion of probability. The notion of probability can be split into two types, the objective and the subjective probabilities. The objective probability occurs when all possible states of occurrence and their associated probabilities are known. The subjective probability stipulates that the future is unknown

[18] The capitalist function is the one that finances the project of the entrepreneur. Most often this function is associated with bankers or venture capitalists and Business angels, but is some cases this function can include personal money and love money (i.e. money from friends and family).

and that people take a subjective view in assessing the probability of different outcomes to an action (Miller 1977). In theories of entrepreneurship, in order justify the rationality of the agent and to explain why this agent rather than another exploits an opportunity, subjective probability is often introduced in relation to the concept of judgemental decision or optimism (Casson 2005; Shane & Venkataraman 2007). In Shane and Venkataraman's (2007) paper, the notion of optimism is intimately linked to the interpretation of the entrepreneur regarding the chances of success of his opportunity, and the chances are usually perceived as higher than in reality. For Casson (2005), the optimism differentiates the entrepreneur from other agents, since others are usually more pessimistic, which acts as a psychological barrier. The notion of optimism in this theory is based on the information available to the entrepreneur and his own interpretation of it. This notion is linked to the notion of decision making that is closely related to the notion of risk and uncertainty. The difference of available information between the entrepreneur and any other agent is that the entrepreneur has more information and so even though exploiting an opportunity is risky for him, it can appear more risky to other agents (for whom the action is uncertain). Literature on entrepreneurship and finance has differentiated between three notions of risk: risk, uncertainty, and unknown. Knight's (Knight 1921) contribution was focused on the discussion about the function of risk taking associated with the entrepreneur. In his book he differentiates the notion of uncertainty from the notion of risk. The notion of ***risk*** can be defined according to the literature (Knight 1921; Miller 1977) *as when the* possible *outcomes over an action are known and probabilities over outcomes are also known*. ***Uncertainty*** is defined as *outcomes which are known but probability over outcomes is not known* (true uncertainty and divergence of opinion). A third level can be added with the ***unknown,*** when the *possible outcomes of action are not known* (Gompers & Lerner 2001).

The notion of the perception of risk by the entrepreneur is one of the elements in the entrepreneurship theory that links the entrepreneur to his environment and influences his actions. This is the case for sectoral specificities. For innovative products there can be different factors linked to the uncertainty of the entrepreneur. Firstly, the industry in which the firm operates can be more inclined to change over a shorter period of time. For example, the pharmaceutical industry is turbulent due to the rate of innovation of the firms in the industry. Also, there may be a demand uncertainty if the innovative enterprise results in a new product. In comparison, when there is an existing and growing market where the industry does not require improvement of the product, competitive entrepreneurship is considered as less risky. There would be little uncertainty about entrepreneurial activity when the market size, the process of production and technique are known. On the technical side, there are also risks in terms of standards of specification (Oakey 1984, p.126).

4.4. Researchable specificities of the entrepreneur

The above sub-sections have aimed at providing a better understanding of how to identify the entrepreneur and which of his characteristics may have an influence on his actions.

Firstly, in theory, it is arguable that the entrepreneur is seen as a ‘super’ agent with exceptional characteristics to fulfil its function. In practice, depending on the technology used and industry target, there is not one entrepreneur who identifies and exploits opportunities and grows a firm successfully. This has been true for many high-tech firms such as Apple, intel or Google; each of these firms in their creation process, and later in their development process, have experienced a shared repartition of different tasks (marketing, managerial and technical), which has evolved over time. Thus, within this thesis, it will not be assumed that the entrepreneurial function is fulfilled by a single individual, but by a coalition that is not stable over time. Thus in none of the future chapters will the thesis try to identify a single person incarnating the entrepreneur; and when referring to the entrepreneurial notion it will consider the individual having leadership in the project (first in the scientific project, later in firm creation and then in the development process).

Secondly, the interdependence of risk and profit, from a theoretical point of view, is not straightforward in practice, especially in high-technologies. For risky investment, which is the case in the sector chosen for the study, risk bearing and profits are not always proportional. External early financing is required since those venture projects require high financing for completion. Thus in those cases, even if the risks borne by the entrepreneur seem greater, the availability of funds required guarantee the capitalist higher returns with mechanisms to limit risk, which are not accessible to the entrepreneur[19]. This discussion is particularly relevant for the decision of an entrepreneur in his choice of project, which determines his financing needs and therefore his choice of investment methods. These issues are especially discussed in Chapter 4, which deals partly with the relationship between capitalist and entrepreneur, as well as problems encountered during project development and control over the firm.

Thirdly, the experience of the entrepreneur can also be crucial for the survival and growth of his venture, and can therefore be a determinant for his actions. Since this work looks specifically at the biotechnology sector, the question of the experience needed to start a company on an innovative project is a central topic because many new ventures in the biotech sector are university spin-offs (Oakey 1995). Thus an academic wishing to identify and exploit an innovative opportunity is

[19] This is discussed further later in the section that links the talks about the environment in which the entrepreneur evolves

most likely to lack essential business and industrial experience. In our case, we therefore hypothesise that the founding team of a biotech venture influence their entrepreneurial action. This particular relationship is discussed in two of the analytical chapters. Chapter 6 focuses on the early process of firm independence from their parent organisation (here the university) by examining the founding team background, leadership structure and social capital of the firm's founders. Chapter 5 examines the process that leads to strategy definition in a newly created organisation in parallel with the process of founding team formation. It particularly links the background of the leader of the founding team with the strategy chosen.

5. What is the impact of the environment on the entrepreneur and his actions?

The entrepreneurship theory has looked extensively at defining the internal determinants of the entrepreneurial action, but has given less attention to the external influence over the entrepreneurial action. Hence the action of the entrepreneur, as explained in the human agency theory, cannot be an autonomous agency because the environment can have an extensive influence over the entrepreneur and his actions. Literature in entrepreneurship, under various headings, has included the environmental presence in its theory or through the concept of opportunities (Kirzner 1978; Shane 2003). The concept of opportunity used in entrepreneurship theory usually embeds the notion of the changing environment, such as technological, socio-political, demographic and, regulatory change, which can lead to new opportunities of profit that the entrepreneur can take advantage of (Shane 2003, p.23). Other theories, such as Penrosian (1959) theories, internalise the environmental notion by talking about "an image in the entrepreneur's mind", which includes different variables that enable him to make decisions and take actions. Among others[20] , these variables include the environment, defined as 'changes external to the firm and lie beyond its control', which is an important variable to consider in the possible action, or restriction of action that lies upon the entrepreneur (1959, p.4). External shocks (Casson 2005), investor behaviour (Gompers & Lerner 2001), and support organisations (such as incubators or other support organisations for ventures) are also a few other examples of the environmental factors that can impact firm behaviour and are discussed as separate matters in the entrepreneurship theories. The environment is an important influence over the entrepreneurial decisions and actions and thus also has an impact for the firm long term survival or evolution path. In order to build our understanding

[20] Other variables considered here in the notion of the image in the entrepreneur's mind are the internal and inherited resources.

of how the environment may shape the entrepreneurial action, the section refers to a range of literature that includes evolutionary economics, systems of innovation literature and regional economics to complement the scattered contributions that are offered in the entrepreneurship literature. Recently, the entrepreneurship theory has focused on the financing issue relating to innovative entrepreneurship and especially the consequences of the risk-financing on firm development, this issue is exposed in following section.

5.1. Financing

The financing side of the entrepreneurial action has been a central matter in entrepreneurship theory, both on the theoretical side than on the empirical one. The theoretical side has, as cited above, defined roles between the entrepreneur (i.e. the agent of action) and the capitalist (i.e. the agent providing funds for a given remuneration), and thus emphasises the centrality of funder's role in the entrepreneurial action. The entrepreneurial action (both the exploitation of the innovative opportunity and the creation of a new organisation) requires a certain amount of capital, which in many cases is achieved through external financing. In our specific case looking at innovative entrepreneurship (and furthermore at the biotechnology sector), the firms under study require a significant amount of external financing and thus we need to outline the different financing options available to them but also the cost of capital access, both financial and practical (or non-financial). In neoclassical theory looking at entrepreneurship (Cantillon 1755b; Marshall 1895; Mill 1900), the function of capital is often related to the banking loan, in which the entrepreneur borrows money from the banker against given interests until repayment. In these theories, the agent solely responsible for the risk in those theories is the entrepreneur. It must be recognised, however, that this is an idealisation given the existence in the real world of bankruptcy laws that allow borrowers to escape from loans. Even through this type of financing is the most commonly used when transitioning from employment to self-employment, general banking has been proven not to be adapted to some high-tech sectors. These firms, regarding their R&D expenses, do not qualify for general bank loans. However, other types of high risk financing have emerged to back-up those ventures. These are venture capitalists or business angels (Gompers & Lerner 2001). This particular type of finance goes hand in hand with a more interventionist role of the financier.

Venture capitalism is a type of financing which has specific rules and is suited to specific ventures. Primarily, venture capitalists are organisations which invest clients' funds with a high return. These kinds of funds usually have a life span of around ten years, in which time it usually sells its holding to pay back their clients (Bidhé 2000, p.144). Given its time constraint and return objectives, venture capitalists prefer to concentrate their investment on a few ventures with exceptionally high return potential (ibid.)[21]. Because the venture capitalists aim at financing ventures generally in the early stages, those organisations have different ways to reduce risks involved in these investments. Firstly, they have mechanisms to monitor their investments and align the manager interests with the venture capitalists' objectives. These include stage financing and remuneration of general management based on results. These mechanisms insure that reasonable milestones are met in order for the VC (Venture Capitalist) to meet his time constraints. They also put in place managers in the top management team, which are known and trusted by them (Gompers & Lerner 2001). Secondly, in order to reduce risk and to improve their firm selection process, the VCs specialise in a given industry and build a network of experts to help them in assessing technology understanding and market opportunities brought by the venture (ibid). Finally, in order to reduce further financial risk, VCs generally choose to syndicate with other VC companies to back a company by putting in place a compensating contract to ensure that their financial assets are mostly protected[22]. Thus venture capitalists, who are considered as higher risk investors, benefit from mechanisms that reduce risk taking, and thus the entrepreneur has to pay a cost in terms of control over the company.

Business angels are also a type of early financing used by innovative firms in order to get early financing for their risky projects. Business angels are not (in most of the cases) a replacement for venture capitalists, but rather they are more active in earlier stages (i.e. seed financing), since they cannot bear the financial burden of the larger financing that comes later (Cressy et al. 2006). They also tend to invest a much smaller amount of money since they are an individual financier. This type of financing is also less constraining than the former as it does not require any stage financing, due diligence[23], or attendance at board meetings. Hence, Business Angels are less interventionist in the day to day running of the company, which means that the entrepreneur is not as much affected in terms of control in comparison to venture capital financing. Business angels can also offer advice to entrepreneurs, since can often be former entrepreneurs or have an extensive knowledge of a specific sector, and also can have a network of contacts that can be of use in a newly created firm.

[21] This is consistent with the methods by which the venture capitalists operate, as they monitor the ventures they invested in to reduce the financial loss risk.

[22] "To protect their stake in the company, venture firms thus often take their investments in the form of *convertible preferred equity* or *convertible debt*, which have higher priority than common stock. In the event of a company's sale or liquidation, owners of this type of equity get paid before common stockholders do." (Gompers & Lerner 2001)

[23] Due diligence is an investigation carried out by financers in order to assess the quality of the investment (through the assets of the company), and can be used in later stages to protect the investor against deficiencies in the investment.

Comparing the VCs behaviour to the entrepreneur's, the entrepreneur still bears a significant part of the risk. Even if the entrepreneur does not compare in terms of the amount of capital brought by the venture capitalist, and is also at an advantage because he has a better knowledge[24] of the product he develops, the entrepreneur has little means to diversify its risk compared with the venture capitalist. The entrepreneur still has to raise funds starting with his personal wealth and additional investments that may be made by those who have a personal relationship with the entrepreneur ('love' money) to be able to benefit from any kind of financing. The financing needed by innovative entrepreneurs is usually high (with some exceptions depending on the sector or the initial project), especially in the biotech sector, and so the entrepreneurs need large amounts of personal funds in order to be able to raise financing from venture capitalists. The entrepreneur therefore takes a high risk on his personal assets and with his personal relationships as the investment assets are concentrated into the creation project. Secondly, in terms of control, the entrepreneur usually has to give up equity and thus control (this also includes accepting other managers on board), but also has to follow a tight path of development imposed by the venture capitalist in terms of milestones. Thus this leaves the entrepreneur with his personal wealth and relationships at high risk with limited control over the outcomes of the firm (as low profit outcomes with lower risk are not of interest of the VCs). In conclusion, even if the capitalist function can be seen as the function that bears risk in theory, in practical terms organisation that represents the capitalist function in the economy (such as banks and venture capitalists) has a variety of mechanisms to reduce uncertainty. Thus even if theoretically it is arguable that the capitalist function might be the risk bearer, in reality the entrepreneur has much fewer opportunities than the capitalist to reduce risks and uncertainty embedded in the innovation and creation process.

The entrepreneurship theory has discussed theoretically and empirically the role of the capitalist in the entrepreneurial action. His role is central as it is indispensable for most of the entrepreneurial action. Innovative firms, especially in the biotechnology sector, have specific needs in terms of financing, and thus the traditional banking system is not always adapted to their needs. Thus they turn to specific types of financing that are more adapted to higher risk projects, which can include venture capitalists or business angels. These types of financing come with advantages but also drawbacks, especially in terms of control over the company. The discussion of the relationship between entrepreneurs and their financing partners is therefore a central issue in innovative entrepreneurship and is the topic of discussion in Chapter 4. However, financing partners are not the

[24] This refers to the fact that the entrepreneur knows the advantages and the potential shortcoming of his product, which is usually a source of asymmetry of information between the entrepreneur and the venture capitalist.

only type of organisation that plays a role in the development of new ventures, other organisations and institutions also have an influence.

5.2. Other Institutions

In evolutionary economics the environment is emphasised in some literature more than others, depending on their influences and the variables they focus on. Hannan and Freeman (1977) develop their theory based on the environment selection criteria. These criteria are central for the evolution of the firm from an evolutionary perspective, in which initial conditions and external shocks are entirely responsible for the fate of an organisation, which is a particular case of deterministic theory in which the agency component is only considered as mechanical. The authors therefore leave little room for agency power and judge a firm by its capacity of production rather than putting emphasis on the decision making powers, such as the managerial agency and the entrepreneurial agency. As explained above, the entrepreneurship theory focuses on a more balanced view of agency power in which environmental influence has a place, but where agency power has its place too.

In the 1990s, an extensive literature was developed on systems of innovation, beginning with national systems of innovations and ranging to regional and sectoral systems of innovation, but also on the cluster and spillovers literature. This literature emphasise how the different components of the environment that a firm or entrepreneur is subjected to (other institutions competition markets...), have to be taken into account when analysing the diffusion of knowledge primarily, but are also relevant for analysing entrepreneurial activity and its success.

In this framework, the technical change literature has made a contribution with the concept of system of innovation. This concept gives us the possibility to understand the learning and innovation processes as a cooperative process. The firm does not stand alone in its environment and does not innovate alone. There are two other sets of environmental factors that can influence the firm's ability to innovate and therefore to change. These two factors are namely institutions, here defined as a set of laws or rules, and also organisations (Edquist 2005). The concept explains that the firm (including the entrepreneur) is part of a system with which it interacts and therefore is a determinant of its behaviour. The set of actors influencing the performance of the firm can also be found in related literature dealing with local learning. This literature points to external organisation and regulation that shapes this system, such as research organisations and universities, government agencies, financial institutions, other firms (competitors, customers and users) and finally regulations.

Another literature dealing with the knowledge system of the firm is the literature on regional studies. This literature argues that knowledge has a local component, and learning is easier within a limited geographical distance. Since the work of Marshall (1895), there has been an increasing interest on factors enabling local learning. This has developed from the assertion that "knowledge is in the air" to knowing the origins of regional dynamics, specialisation and excellence of a sector. Later on, the quantitative study of Audretsch and Feldman (1996) strengthened the arguments brought by this literature, by showing the existence of knowledge externalities between organisations specialised in the same sector. The regional studies thereafter joined the view of the system of innovation with their development on cluster literature that can include work ranging from the early literature on industrial districts, to the work of innovative milieu and also the work on regional systems of innovation. It is shown that large organisations such as universities or large firms can play an important role in the local dynamics (Markusen 1996).

The literature mentioned above therefore drives us towards the hypothesis that external organisations and institutions can be an important factor for the firm learning process, and also a driver of change in the firm. The firm cannot only be studied as an isolated component but must be seen in the environment with which it interacts in order to understand its' path of evolution. The entrepreneurship literature has sporadically included some of these organisations in order to understand firm development processes. As emphasised previously, the entrepreneurship literature has extensively discussed the impact on financing options for the firm and their consequences, but has also focused on other specific organisations, especially technology transfer organisations such as incubators (Siegel et al. 2003; Matt & Schaeffer 2012). Although the environmental factor has been tackled, from a theoretical perspective there has not been a discussion about the interaction between the entrepreneurial action and the environment.

The knowledge and learning aspect of the firm is not the only environmental constraint by which the firm is affected. Sectoral systems (Malerba 2005) and socio-technical systems (Geels 2004) emphasise other determinants by which the entrepreneur can be influenced. Thus systems of innovation miss large elements, which are the so called "knowledge base" and industrial framework in which the firm evolves (which includes markets structure through the utilisation and the diffusion of the technology), and differentiates the environments of firms and thus their behaviour. The firm is therefore influenced by first the creation of its technology but also later by its diffusion and utilisation. The knowledge base, which includes human resources, scientific and technological knowledge, but also tangible resources such as capital, tools and natural resources, is central for the creation of the technology. The technology and therefore the firm, are also affected by the user such as his facilities for maintenance, the cultural use and complementary artefacts. Finally, the technology is also constrained by regulation, which includes quality norms, laws in place and also property rights (Geels 2004). These components are integrated into the socio-technical system in which a firm and its technology evolves and thus has an influence on the firm decision making, technology, and firm evolution.

5.3.Conclusion on the firm's environment

This section has shown that the firm evolution cannot be studied as a standalone entity but is also influenced by a variety of factors external to the firm. The section on the environment has shown that little work on entrepreneurship has previously focused on the impact of environmental factors on the opportunity and action of the entrepreneur. The issue of taking a systemic approach has been proven useful in theories linked to innovation studies, and therefore we hypothesise that they may also be relevant to understand the entrepreneur's opportunities and constraints.

The section presented concepts that particularly influence new innovative firms, and has looked into entrepreneurship theory but also a variety of other literature related to innovation and regional studies. Several external determinants have been identified, such as financing organisations, other external organisations, technological constraint, regional resources (labour, natural resources) and also user practice. These determinants can all affect the product and the development of the firm. Due to the specificities of the sector chosen and the research design (which are explained extensively in the following chapters: Chapter 2 and Chapter 3), the relationships with users are overlooked in this thesis because the initial stages of development are so lengthy that most of the firms interviewed have not had time to fully developed their innovative project. The section has highlighted environmental aspects that can theoretically have an impact on entrepreneurial agency and also on the development of the entrepreneurial action. However, the thesis does not aim to look at each environmental feature, but rather looks at whether the environment is a factor that can affect entrepreneurial agency, and thus the power of decision and action of the entrepreneur.

The section has shown that the environment has both an impact on the possibilities that are offered to the entrepreneur, but also on the anticipation that the entrepreneur has on his future, as human agency theory suggests. The entrepreneur therefore has a specific relationship with his environment that influences his action. Since this hypothesis arises from theories linked to innovation studies, this work aims at looking partly at the environmental influence on the entrepreneur and to highlight how environmental specificities may play a role in the entrepreneur's strategy definition and exploitation. This can be seen in the anticipation of the relationship with the venture capitalist; knowing that there is a risk of losing control over the firm, the entrepreneur has to decide whether or not he is willing to be put in such a position (this relationship is extensively discussed in Chapter 4).

Consequently, the thesis accounts for these environmental influences in different chapters. Chapter 2 accounts for specificities of the biotechnology sector and the industries that use this technology for developing their products. The chapter points toward the high regulation in some industries such as in the pharmaceutical industry and the costs resulting from such regulation. Chapter 3 gives an overview of the regional actors that could influence the firms in their development (e.g. the university, incubator, financing organisations...). It also looks briefly at the structure of the science network in the cluster in order to give the reader on overview of the innovation system in which the firm evolves. However, the influences of these organisations are not included further as the respondents, despite an explicit question about regional environment, did not have much to say about regional organisations, apart from two exceptions of the university and financial institutions. The university impact is partly studied in Chapter 6, which studies the transition of a research project spinning out of university. In this chapter the role of the leader of the innovation project is studied to understand his relationship with the university and how this relationship impacts the early life of the firm. In Chapter 4 the main topic is the financing choice of entrepreneurs, and thus studies the relationship between the choice of the entrepreneur as a means of financing, the financing characteristics and the entrepreneurs' characteristics. This chapter also shows that the experience of other firms has an influence on the decision of the entrepreneur for the type of financing chosen and thus includes regional learning.

6. How can the entrepreneurial action be observed?

This section deals with the qualification and researchable aspects of the entrepreneurial action. As suggested earlier, innovative entrepreneurship can be qualified as the development of an innovative project through firm creation. Both of these notions are considered as processes that develop over time, in their respective literature. This section therefore firstly introduces the notion of time in the framework of entrepreneurial agency introduced earlier, before reviewing the literature on entrepreneurial processes. The section concludes with the researchable features of the entrepreneurial action.

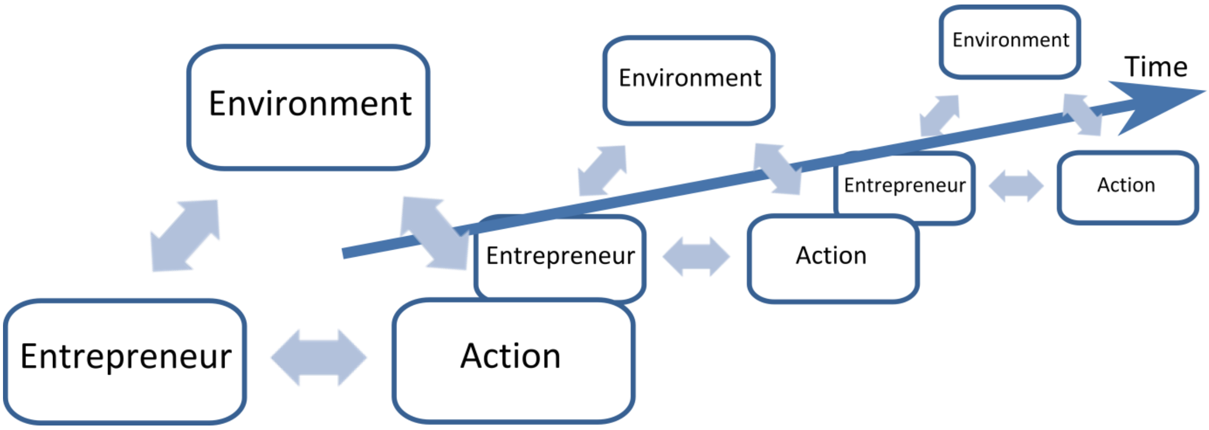
6.1. The notion of time in the entrepreneurial action

The entrepreneurial action, in opposition with the previous components described (i.e. the agent and the environment), unfolds over a period of time, which is often referred to as a process. Therefore, this section introduces the notion of time. The entrepreneurial action cannot be studied in a static manner, and so many contributions have focused on the entrepreneurial process with regards to both firm creation and opportunity exploitation.

The notion of time is attractive for studying evolution patterns, but its use has to be carefully considered. Some studies, such as the literature on firm life cycles (Whetten 1987; Phelps et al. 2007; Quinn & Cameron 1983) compares the life of a firm to the any living organism going through the various stages such as birth, youth, growth, decline and death. In this literature the question has risen about quantifying time for each stage. Some managerial literature (Phelps et al. 2007) on life cycles has analysed the life-cycle issue of the firm in order to make it fit to a creation time frame, by putting a quantitative timeframe on the evolutionary process. However, this view has been heavily criticised since the amount of time taken in each stage is specific to the firm, market opportunities and other components. This is especially true since different firms evolving in different sectors may have different technological or regulatory constraints when starting up a firm. An example is the contrast between two high-technology sectors, the software industry and the human health biotech sector (Oakey 1995). In the software sector, the product development process can be arguably less constraining than in the Biotech-human health related pharmaceutical sector. The software sector can be characterised with a low requirement for capital, equipment and so barriers to entry into the market is relatively low compared to other industries, and finally there is a potential for early revenues (ibid.). By contrast, biotechnology firms who target their products to the human health pharmaceutical industry are much more constrained in development costs and time since the regulation in that industry force the firm to a constraining testing of their products, which takes time and raises the costs of the product. Thus in our case we will not try to quantify the amount of time of each phase but rather try to find some relative sequence between the identified stages.

The notion of time is seen as a relative feature and has to be fully integrated in our framework of study. The evolution of the innovation and creation process must be described and the three components have to be understood in a dynamic manner. As we have already emphasised, the agent considered as entrepreneur can evolve over time, since this function can be fulfilled by more than one individual over time due to the capabilities needed at each stage of the entrepreneurial action (aim of Chapter 5). In addition, different organisations and institutions can have a different role when entrepreneurs are developing their action, such as the parent organisation having a strong role at the spin-off stage (aim of Chapter 6) or other organisations such as the local environment or financing institutions (aim of Chapter 4) having various influences at different stages of the company life. The entrepreneurial function and the environment is therefore seen in our study in a dynamic manner through the study of the actions, which are usually represented as processes and include firm creation or development of innovative projects (this is the developed in the next section). Therefore, the interaction of the different components identified by the human agency theory are here seen as a central pillar in our framework, and thus the interaction of the three components exposed in Figure 1.1 should be studied as an evolving process, as showed in Figure 1.2.

Figure 1.2: The entrepreneurial agency in an evolutionary perspective



The aim of this study being the holistic understanding of the entrepreneurial process, leads to a high number of variables being studied together. This complexity reduces the possibility to analyse the whole process of firm creation and development. Thus our framework aims at limiting the time span of the process. The study focuses only on the early stages of evolution that are here defined as the development of an innovative project, which is often started in an incumbent organisation in the case of the biotechnology sector. It also includes the organisational process of firm creation since this is part of our definition of innovative entrepreneurship. The organisational process of creation includes the formation of the management, which may differ from the team responsible for the development of the innovative project. This study includes the process of firm formation up until the point where there is a stable management and a clear strategy for the firm to develop.

The entrepreneurial action has often been represented as a process involving different steps, through life cycle models and other evolutionary models. Thus the following section depicts the literature focusing on entrepreneurial action as an entrepreneurial process. Following our definition, it includes processes concerning firm creation and development of innovative projects. The review tries to enclose different views of firm evolution processes in order to have an informative idea of the models given, which is the basis for qualifying what the entrepreneurial action is in innovative entrepreneurship. It will also specifically try to further the understanding of the specific steps that we aim to study (from the development of an innovative project before firm creation to the early organisation of the start-ups).

6.2. A stage view of the firm early life

The definition of innovative entrepreneurship has pointed towards two processes that need to be included in the concept, which includes the process of firm creation but also the process of opportunity exploitation and development. Thus in order to understand more deeply what lays in the entrepreneurial action, this section develops both processes and the difficulties behind each of them. It concludes by discussing the implications of the study of both of these processes together.

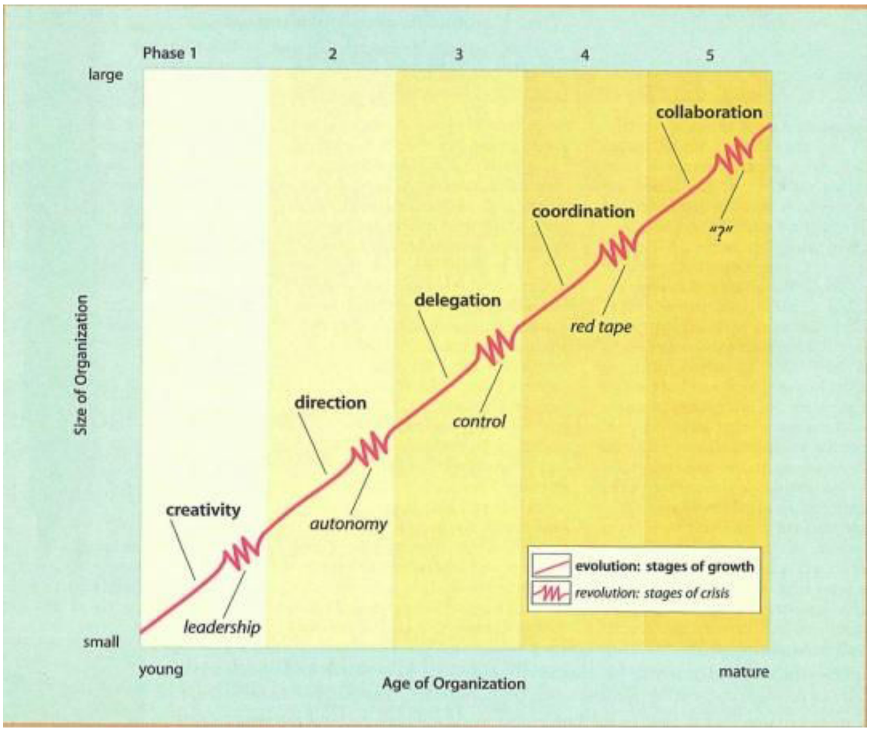
As this thesis focuses on the creation process, the review about organisational theories would not be complete without referencing the literature regarding the stage view of the evolution of an innovative firm, especially in its early life stages. In order to have a complete review of the contributions that bring an understanding of the process of creating an innovative organisation, this section gathers views on innovation theories, entrepreneurship theory and organisational literature (including theories of the firm). Thus this section is divided into three parts, a part on organisational models, another part on entrepreneurial models, which include stages before creation, and finally innovation models.

6.2.1. Organisational models

Understanding evolution of firms through growth patterns have given rise to many stage views of the firm evolution ranging from general models of long term growth for a firm to more specific models focusing on some specific stages such as early stages. This literature should not be taken as a general pattern of growth paths of firms but as a description of problems encountered linked to firm size or a specific stage of a firm. Before beginning to expose different stages and growth models, two notions that are usually invoked when talking about stages processes will be briefly discussed: the notion of time and the notion of change.

The stage view has been central to explain growth of the firm and explain the characteristics in terms of challenges at each stage of growth. This begins with a life cycle view of the growth of the firm that tries to explain the stages from birth to maturity. The stages are known as birth, youth, adolescence and maturity (Whetten 1987; Quinn & Cameron 1983). These views have been widely discussed in the literature of management and firm growth in terms of sets of problems, time and the characteristics of each stage. Also, following the evolutionary vs revolutionary view explaining change of the firm, Greiner (Greiner 1997) introduces the notion of crisis stages between evolution stages as follows:

Figure 1.3: The 5 stages of growth - Greiner 1998



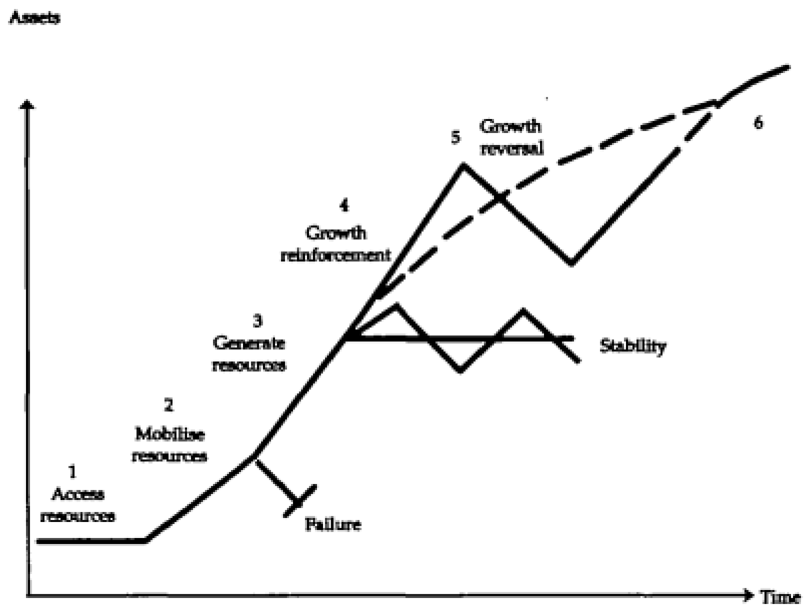
Source: (Greiner 1997)

This model emphasises that the firm evolves through definite periods of progressive evolution, until reaching crises points that lead to revolutionary changes in the firm, in order for it to be able to grow further. The crisis transitions often come as a result of managerial limitations at each stage of growth of the firm, and thus organisational disruption is seen as necessary for further growth. This literature argues for organisational processes, especially management change, which are crucial in order to understand processes and difficulties linked with growth processes. However, the focus of this thesis is specifically on early stages, and so only the early part of the model is relevant to our work. Besides, the variables explaining the evolution of the firm are limited to a single variable (i.e. managerial change) and thus this model may be missing other determinants. This model also does not tackle the reasons of early failure of firms. These are at the heart of the next model presented.

Churchill and Lewis (1983) go deeper into the issue of survival of firms with their stages of growth model. Their model emphasises the importance of the early stages of growth developing over five phases: existence, survival, success, take-off and resource maturity. In this model the firm also evolves from a small and young firm during the early stages to a mature firm during the later stages. The first step identified (i.e. the existence stage) is the stage at which the firm is recently created and experiences a high level of uncertainty for most of its activities (liability of newness, production plan, financial plan). The main objective of the firm at this stage is to remain active and be able to consolidate its activity. Once the business has proven its viability it enters into the survival stage, in which the firm must generate enough revenue to survive on a longer term basis and become an established player in the industry. Firms enter the stage of success when they generate enough income to expand their activity or diversify it (firms can also choose to not grow further, in which case they remain at the previous stage). The take off stage consists of rapid growth, which is also very financially demanding and in which the owner must delegate and reorganise managerial organisation in order to keep up with firm growth. Finally, during the maturity stage the firm tries to keep the advantages acquired from growth and consolidates the level of activity that was reached during the previous stage. Churchill and Lewis put emphasis on the centrality of the entrepreneur during the firm growth stage and argue that while the capabilities of the entrepreneur are determinants in the two to three first stages, in the latter growth stages of the firm this aspect becomes decreasingly important. Even though this contribution emphasises the choice that the entrepreneur has to make regarding the pace of growth of his company, it remains focused on the whole firm life. The following contribution presents a model mainly focused on the early life of the firm.

Garnsey (1998) also developed a stage model that emphasises critical problems for firm growth. Her work is distinct from the above literature on two main points: 1)the fact that it focuses only on early stages of the firm (i.e. the stages following firm creation) and 2) the fact that it is based on the resource-based view introduced by Penrose (1959). She describes the creation process regarding access to resources as follows: access to resources - mobilise resources - generate resources - growth (which is represented in Figure 1.4 below).

Figure 1.4: Growth paths of a firm



Source: (Garnsey 1998)

This stage view emphasises the fact that many ventures do not grow and thus go into either early failure (after stage 2 of growth), stability (after stage 3 of growth) or growth reversal (after stage 4). The author focuses on the role of resources, as much tangible as intangible, as she emphasises the deterministic nature of the entrepreneur's knowledge of his opportunity of firm development (e.g. first in terms of the choice of the sector but also in terms of lock-in that arises from the initial resources). The first stage is characterised by the identification of the opportunities and the decision over the activities. This phase mainly revolves around search activities in terms of resources and choices towards the activity (e.g. choice over sector, choice over strategy, commitment to a product ...). Once the organisation is committed to a strategy, the next stage consists of building channels for resource mobilisation through funders, customers and suppliers in order to sustain the resources needed for product development. The third phase, called generation of resources, features the beginning of the production cycle and requires the firm to build stable relationships with customers and distributors in order to ensure a continuous source of revenue. After the firm have demonstrated viability, it must choose between further growth and a low growth comfort zone. Once the new roles have been learned by employees and the resolution of early production and distribution problems have been routinised, the now eased and underused staff can be redeployed for other means in order to promote growth. The final stage of growth reversal can be experienced through the difficulties of management organisation (this aspect has also been pointed out in the above models). This can be due to environmental change such as demand fluctuation or resources shortage, which can hinder the firm's future growth and even survival. The paper overall grounds its view in the resource based theory and discusses the interplay between environment and resources brought by the entrepreneur. Even though the resource based view literature has rarely dealt with early firm growth, it is in this literature together with the evolutionary literature that we can find a study of the interplay between different components, especially the knowledge and environmental components that are central to our study.

The **knowledge component** in the dynamic view of the firm has become more and more central over the last 60 years. This began with Penrose (1959) who looked at resources, including intangible ones such as human resources. Following this was the work by Nelson and Winter (1982) who view the firm dynamics of change as being highly influenced by the firm learning abilities, both on the individual level and then on the organisational level. The organisational learning is central as it is the main driver of change in the firm. This knowledge can take two forms, the form of knowledge embodied in people, and also organisational knowledge that is described as a routine.

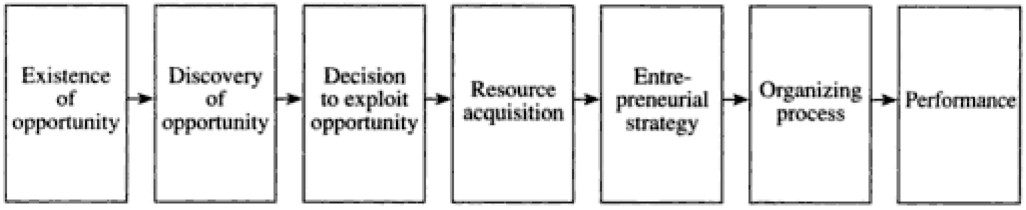
Several shortcomings can be pointed out in these studies that put forward stage views of the firm. Firstly, the views described above are general views of new firm development and thus do not specialise in high –tech or science based firms, which is the purpose of this thesis. Consequently, these observations do not tackle the specificities of high-tech sectors that, as Garnsey pointed out, may be one of the determinants of a firm's ability to grow (through the stage of maturity of the sector). Secondly, the two first models focus mainly on managerial problems that accompany firm growth, which is only one part of the opportunity for growth of the firm as they omit the environment impact as pointed out in the review above. The third model does take this into account, but lacks in precision regarding the interplay between environment, entrepreneur (or founding team) and the entrepreneurial action (illustrated by the stage view) due to the different stages of growth considered. Lastly and most importantly, as pointed out at the beginning of our study, we are looking at innovative entrepreneurship in order to examine the co-evolution of the organisational process together with the exploitation of an opportunity through the development of an innovative project. Since they are dealing only with the organisational part, these stage models omit stages that occur before firm creation and also the fact that the innovative project may have an impact on the opportunities for growth (which would be relevant for our study). In summation, our study only focuses on the early stages represented here[25] in order to understand the interplay between the environmental, the agent and the action variables. Thus the evolutionary and resource based views of the firm can be a good complement to other organisational literature because they include environmental factors and intangible resources in the study of firm evolution, whereas the other organisational literature frames their study in only managerial factors. This latter literature does not focus on any sustained growth path (or evolution as we call it) other than the one at the start of the firm (i.e. at the point of accessing new resources, also through new management) and how these organisational turbulences affect the early evolution. As pointed out previously, innovative entrepreneurship does not only start with the organisation of a new firm but before, with the innovative project that is developed at an earlier stage within an incubating organisation. In order to understand this project view, the next following section reviews the literature dealing with opportunity exploitation and then development of innovative projects.

6.2.2. How should the innovating organisation be understood

Outside the focus of organisational processes from the firm creation, some contributions in the entrepreneurship literature have also discussed the early firm development by starting their stages before firm creation. An early contribution (Carter et al. 1996) identified four stages of creation; first the intention to create the organisation, then the assemblage of resources, then developing an organisational boundary (creation) and then exchanges of resources across the boundaries (sales). These stages are similar to the ones identified by Garsney (1998). A later contribution by Shane (2003) in his search for a framework development for a theory of entrepreneurship introduced a central component, which is the concept of opportunity. Shane also put forward his stage event framework, which is much further developed than earlier stage model since the argument is made throughout his book on entrepreneurship. He constructed his theory around the main stages with the identification and decision to exploit an opportunity and then the response of firm creation with a resource acquisition, and next an organising process before performance. This model is shown below (Figure 1.5).

[25] By early stages we mean the creative stage to the leadership and early autonomy phase described by Greiner, or the existence stage to early survival for the Churchill and Lewis model or the stage of access and mobilisation of resources up to the beginning of the generation of resources in the model of Garnsey.

Figure 1.5: Model on the entrepreneurial process



Source: (Shane 2003)

In his theory, Shane insists on the concept of opportunity discovery and exploitation and makes them fully part of the entrepreneurial process. The stage view shown above includes the existence of a project and refers to the resource based view through the stage of resource acquisition. These stages entail the stages before firm creation, which were missing in the previously cited literature. The above process is divided into two parts, the part dealing with the opportunity exploitation and the organisational part that leads to firm performance during the two last stages. In this case, this process therefore implies that the firm organisation process and performance depend solely on the opportunity exploitation. This model does not consider the influence of the opportunity exploitation and project development on the process of firm organisation. Firm evolution has its own constraints such as tangible and intangible resource acquisition or management team change, as shown previously in Garnsey (1998) and Greiner (1997). This is one of the main questions raised in this work. We seek to study the opportunity exploitation and firm organisation as distinct but linked processes.

In the same line, the literature on entrepreneurial processes also includes specific stage views on high-tech and innovative firms. Firstly, there has been some development of stage views regarding the process of academic spin-off formation by Shane (2004). This contribution helps to understand the steps by which universities, with their aim of transitioning from doing research to having an interest in transferring knowledge or technology that they discovered/created. Shane (2004) explained the process by which universities go from research to a technology, including firm creation. Figure 1.6 shows the process adapted by Shane to understand the process of university technology creation to the point where the project becomes mature enough for transferring to the industry. This process is highly similar to the one developed earlier.

Figure 1.6: University research development (adapted from Shane 2004)

The first steps are here determined by research, which is necessary in order to be able to lead to useable technologies for the industry. This research can sometimes lead to knowledge or technology that can be used in the industry. The university will then seek IP (Intellectual Property), which is the next step in the development. Thus after marketing the technology, the university can push for the technology exploitation and try to licence to an existing company or create a firm (spin-off). The development cannot go further than invention since that would go beyond the university goal. The literature here informs of the transition process, including the operational steps a scientist goes through, in order to transfer his discovery to industry (through spin-off creation or licensing to an existing firm). Other contributions are concerned with the transfer of technology through spin-offs and have described similar stage processes as the one above.

For instance Clarysse et al. (2005) identifies a process with three main stages in order to characterise the transition from a research project to firm creation: the invention, transitions and innovation phases. In the details of the process (which is broken down further) one can observe many similarities with the spin-off model presented by Shane, with an opportunity and IP protection search, followed by a strategic choice and the decision over the business model. The model here integrates the strategic choice from the technology transfer side, but does not address the interrelation between the change of strategy and the project. In the same way Ndonzuau et al. (2002) also describe a spin-off process that is formalised through the following stages: results from research, business ideas, new venture projects, spin-off firms and creation of value. The authors focused on the practicality of each stage, such scientific culture, protection of the ideas, resources acquisition and the creation of value. Again this stage model is of a similar nature to the two previous ones. Every process put forward here focuses on the technology transfer through firm creation, where the creation process is the ultimate stage in the stage view.

Other views on firm early creation also pointed out the differences occurring between sectors in high technologies. Oakey (1995) explains that strategy of firm creation can differ between firms, which also depends on the sector of activity. The firm formation can take time for R&D before or after firm creation, depending on the strategy chosen. In some cases there needs to be a firm creation in order to raise funding for further R&D cost before the marketing phase. Thus the models described above can be close to other known models, such as models of innovation. Those models do not relate directly to a firm structure, but are still relevant for discussion around innovative firm formation.

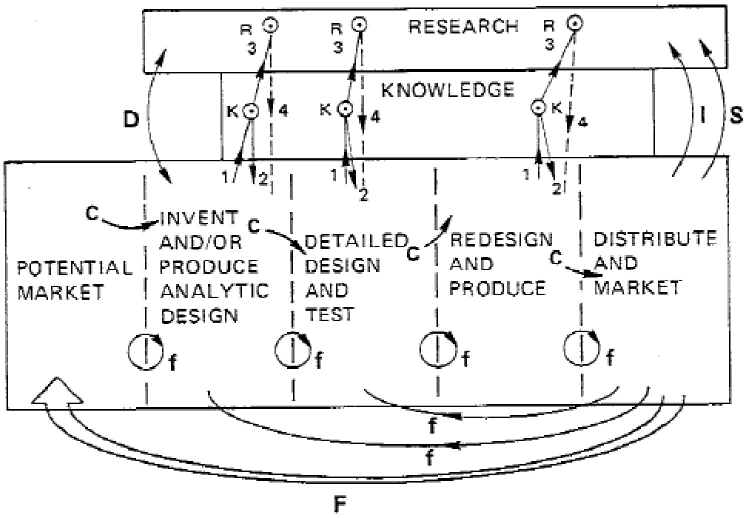
One can derive the impression from this literature that when a firm is created the process of technology transfer is successful. However, as innovation models shows, the process of innovation is not linear and there are many feedback loops that can intervene in the innovation development.

The idea that university has a role to play in the industry and local development emerged during the second world war (Rothwell & Dodgson 1992). The idea is usually attributed to Bush and his report (1945) which states that the scientific community, much of which was located in universities, had a prominent role in the technology developed during war time, and thus innovation literature attributes to him the concept of the science push linear model of innovation. Since then the industrialist and innovation literature used this work to introduce a variety of innovation models (Godin 2006). The science push linear model of innovation gives some sequential steps to answer this question, which is represented by Figure 1.7. It emphasises an innovation process divided into sequences that emerges from science (Basic followed by applied research). The innovation model helps to understand the process by which research leads to innovation regardless of institutions and the people at the origin of this process. Thus this model gives a generic overview of how innovation is conducted, but does not go deeper into processes of technology transfer as the previous models do.

Figure 1.7: Model of innovation based on Godin 2006

In earlier times, the innovation model was believed to be linear. It developed from research institutions to the industry, which is similar to basic research being transformed into applied research (Kline 1995). Even though the linear model was never explicitly formalised in early work by Bush, many later contributions attributed the above process to his report, mainly in order to point out flaws in the model. A later contribution that was widely accepted was the model of Kline and Rosenberg (1986) (Figure 1.8) that emphasised the role of research at every step in the model, but also feedback loops between steps. This model also acknowledges the role of market and knowledge interaction at every part of the process. This model is more advanced than others because it does not only contribute to show the main stages with their sets of problems, but links different resources and knowledge at each stage of the process. It also casts doubt on the ordering (sequential) of the models using feedback loops.

Figure 1.8: Chain linked Model



Source: (Kline & Rosenberg 1986)

The model of innovation remains generic but can help to understand the process by which technology transfer occurs between incubating organisations and industry through firm formation. Technology transfer processes that lead to innovation occur via two types of institution; research institutions, such as universities, and companies. The model focuses on the evolution of the innovation project from early research to its development, production and distribution. It features many feedback links especially in terms of research and knowledge, but also in terms of market. This type of models can help us to shed light of the innovative project side, but for the purpose of our study must be combined with earlier organisational processes that may have an impact on the opportunity for such a project to benefits from all these feedback loops.

6.3. Researchable characteristics of the entrepreneurial action

In conclusion, this review has shown that the literature concerned with evolution stages of innovative firm formation is fragmented into three distinct literatures, the literature on organisation, firm and growth theory, the literature of entrepreneurship and the literature on innovation models. Those literatures appear to be complementary but the literature covering the overlap is limited. While the literature of firm creation explains processes arising before firm creation, the explanation on the organisation phase remains general. Also it appears to be the opposite when concerned with the models developed to study firm growth (organisation processes after creation are focused on, but there is no focus on how the firm came to be created). Finally, models explaining innovation processes create a link between different stages which can be before or after firm formation, however it does not refer to firm creation.

As explained previously, firm creation in this work is seen as a process in which founding conditions must be a crucial determinant of the evolution of the firm. Thus the literature given above is complementary to explain the full process of firm creation. However, the criticism arises of a missing holistic view of innovative entrepreneurship. Any of these models would not be sufficient on its own, but each of them brings insights and variables that are crucial determinants in the firm development path.

Despite this, there appears to be a gap in the literature for qualifying the innovative entrepreneurial action through models that integrate both the innovative project side but also the organisational side of the company creation process. In this work, we are particularly interested in the co-evolution of both of these processes and the possible impact they have on one another. The aim is not to focus only on factual events (such as IP seeking, creation date etc), but on the interplay between the entrepreneur as the central agent, and his environment in order to characterise the entrepreneurial action. In this case there is a need to emphasise that entrepreneurial action is not only linear but consists of feedbacks between two processes. The entrepreneurship literature above describes a linear model where the organisational part is only a single step (usually the penultimate step to the exploitation of opportunity process). In our case, we want to question the linearity of the entrepreneurial process as described in the Figure 1.6 and 1.7 and through a study of the linearity and impact of the identified variables discuss the development of the entrepreneurial action.

In order to further the understanding of the process of innovative entrepreneurship, this section has highlighted two contributions that can further our understanding of the phenomenon. Firstly, there needs to be an understanding of the co-evolution of the innovation and the organisational process, and secondly one needs to study this evolution within a systemic framework that includes the specificities of the agent and the characteristics of the environment. A stage view framework of firm creation is developed in Chapter 5 and Chapter 6. These stage views are based on the above existing stage models. Chapter 6 particularly focuses on the step development with insights from case studies to understand specific issues and variation that can arise in the early evolution of newly created firms. The framework aims also at giving more specific steps than general and wide steps as the above theories do (e.g. such as resource acquisition or resource generation, firm development, etc).

7. Conclusion

The aim of this review began with the ambition to frame and clearly define the objective of the study, which is innovative entrepreneurship. The review firstly focused on the definition of entrepreneurship, which is different depending on the author, to later give the definition of the concept we adopt in this thesis. The review of entrepreneurship literature leads us to identify two main processes that characterise innovative entrepreneurship: the process of innovative project (i.e. opportunity) exploitation and the concept of firm creation through organisational processes. **Innovative entrepreneurship** was therefore defined as *the action of exploiting an opportunity of innovation through the creation of a firm*.

The chapter has worked around this definition in order to then find a suitable framework in order to study the entrepreneur and his actions. The aim was then to discuss a workable framework to study the process lying in innovative entrepreneurship. In order to study entrepreneurial action, the chapter called on literature on theories of action, especially human agency literature. This literature enabled us to build on the concept of human agency and adapt it to the concepts in the entrepreneurship literature, which we referred to as **entrepreneurial agency**. We define this as *the power of the entrepreneurs to have influence over their decision and actions stemming from them*. This definition hypothesises that the entrepreneur has neither full power, nor passivity over his action and the fate of his venture. Thus the human agency literature has also helped us to build a framework to study innovative entrepreneurship, especially the variables influencing entrepreneurial agency. The entrepreneurial agency framework features three components: the entrepreneur (i.e. the agent), the entrepreneurial action and the environment. These three components form the triadic reciprocal relationship that influences the entrepreneurial agency and thus the entrepreneurial process. The thesis objective is therefore to understand how these three components affect the entrepreneurial agency during the early stages of firm creation. In order to do so, the review focused on each component identified in the framework and their characteristics. The concept of entrepreneurial agency therefore aims at providing a framework in which the different literature tackled in entrepreneurship theories can be understood together. It aims at developing a holistic framework that explains the interaction between components that influence the entrepreneur's strategy, his business model and ultimately the firm path of evolution.

When discussing the researchable characteristics of the entrepreneur, we emphasised the difference that has to be made between the theoretical level and the practical level. In theory, the entrepreneur is represented as a unique entity who has many abilities to bring a firm to success (e.g.

like the übermensch described in Schumpeterian theories). However, in practice it is difficult to observe a unique individual fulfilling the entrepreneurial function from beginning to end (both the identification and exploitation of an opportunity, as well as building and running a newly created organisation). The thesis can therefore refer to the entrepreneur on a theoretical level, but will not try to identify a unique entrepreneur leading the entrepreneurial action. Rather, it defines identifies individuals that take a lead and responsibility for a specific part of the entrepreneurial action (as defined above). In practice, it therefore tries to identify an individual leader in charge at some point in time of the entrepreneurial action. This observation is reinforced by the choice of the sector. As the biotechnology sector has been chosen, the complexity of technologies developed for innovating and the complexity of specific markets are rarely known in depth by a unique individual. Consequently, we hypothesise that the entrepreneur may not be a single individual over time, but rather there may be different individuals that fulfil the entrepreneurial action over time. The thesis therefore also wants to understand the consequences that the change of individual fulfilling the entrepreneurial function has on the project and firm evolution overall. This is especially relevant, since the experience and personality of an entrepreneur has an effect on his preferences and choice over risk and profit, as was discussed in the section about the entrepreneur. This issue is especially discussed in Chapter 5.

The entrepreneur's history is not the only determinant that is taken into account when making choice and taking action for advancing the entrepreneurial project. As was pointed out, environmental factors also have an impact on the entrepreneurial decision and actions, and therefore on entrepreneurial agency. Specific determinants that may have an influence on the decision and action of the entrepreneur were identified in the literature review. However, the thesis does not aim at identifying or discussing an exhaustive list of environmental determinants, but to highlight how those external factors can affect the project over time. As the literature on new ventures highlights, the financial issue of getting enough capital to start and develop a venture is a key concern for new firms. Furthermore it is important to look at that particular view, as biotechnology product or service development needs subsequent financing, especially when developing drugs for the human pharmaceutical markets. Thus the choice towards a particular external financing organisation and their involvement in the new venture is key to our study and is the focus of Chapter 4. The above section on environmental factors has also highlighted different organisations in an innovation system which also influences on entrepreneurship at different points in time and at different levels. The section has pointed out that the biotechnology emerged from science and relies on the public sector to generate innovative products. Thus in our case we also consider university as having a prominent role in the development of technology and in the entrepreneurial process. Therefore, Chapter 6 focuses on the relationship between innovative projects, firm creation and the firm's link with their parent organisation, the university. Other environmental factors can also have an influence on firm development, such as incubators, property rights in a specific country, regional support organisations, etc...

Finally, and most importantly, the study of this framework includes the study of the entrepreneurial action. The question of characterising the entrepreneurial action is inferred from our definition of innovative entrepreneurship, by the inclusion of the innovative project development together with the firm creation and development. This is because both of these aspects involve a dynamic action or process individually (since firm creation and innovation are both described as processes in their respective literature). However, this definition also creates questions in terms of the way to study the relationship between the innovation and firm creation processes. Are those processes separate, sequential or is there overlap and co-evolution? The literature review has not been conclusive on this matter since the two processes have generally been studied separately. This is therefore an important question that we aim to tackle in our study in order to fill the gap left in the literature. In the analytical chapters we decided to focus, first on components affecting entrepreneurial agency, which could lead us to understand the early stages by dividing the study in separate steps (which are also overlapping) in order to closely follow this notion of co-evolution. The two first analytical chapters, Chapter 4 and 5, link different components of the developed framework between each other, respectively the environment (here financing) and the entrepreneur (the agent) to the strategy of the firms and its activities (i.e. entrepreneurial decision and action). These two chapters look at specific aspects that could influence the early path of the firm in terms of strategy and business model choice. Chapter 4 concentrates on the early interaction with the financial environment (especially financial organisation) while the firm is created. It particularly emphasises how the mode of financing can impact on the project versus the firm development. Chapter 5 looks at the organisational infancy and the managerial transition from scientific organisation to the newly created firm management team. In the final analytical chapter (Chapter 6), the notion of evolution is taken on a larger scale, to fully understand the process of transition between the parent organisation and the new venture. The focus lies more in the project development and the steps taken from project development to the firm creation. As the processes have been mainly studied separately, we need to understand the reasons and transitions from developing their innovative project in an incumbent organisation to creating their own organisation. The chapter therefore focuses on the step before firm creation and thus does not directly focus on the co-evolution of the two processes.

The analytical chapters are also in line with the framework we have set up. They seek to understand this triadic relationship of the different components in the early life of the firm. In order to avoid unnecessary complexity, these chapters do not look at the triadic relationship as a whole but rather at the relationship between each pair of components. For instance, Chapter 4 emphasises the influence of a central external actor, the financier, over the choice of the business model for the firm. Chapter 5 emphasises the relationship between cultural background and experience by looking at the decision over the business strategy. Chapter 6 looks at the relationship of entrepreneur specificities (through his different relationship with university) and entrepreneurial action over the transition phase between incubation and creation of the firm.

Further environmental factors are discussed in Chapter 2, which examines the sectoral characteristics of the biotech sector. The specificities of the sector are important as it defines the entrepreneurial needs in terms of competences but also external help needed. The following chapter therefore proceeds to give an overview of the chosen sector and relates it to the entrepreneurial action by discussing it in relation to specific business models developed in this sector. The following chapter (Chapter 3) follows on the methodology, which justifies the choice towards the multiple case study design. This chapter concludes with an overview of the case studies, including an overview of the cluster under study and details about each firm story.

Chapter 2: The Biotechnology sector: Disentangling inputs and outputs

1. Introduction

From the beginning we have indicated that our study focuses on a specific sector, the biotechnology sector. While the next chapter will deal more with the methodology and will explain in more detail the reasons for this choice, this chapter presents the characteristics of this sector. These specificities must be understood because, as stated in the literature review, the environment through supporting organisations, regulations and other institutions has an impact on new firm development. In order to do so, the chapter distinguishes between two parts of the sector, the origins of the technology and the industries in which the biotechnologies are widely used. The first part focuses on the scientific and technological advances made in biology that lead to innovations. This part describes where the innovations from the biotech sector emerged from and how this makes the sector distinctive. The second part is dedicated to industries using these technologies extensively. There is more than one industry basing their innovation systems on the biotechnology sector, which can have many differences concerning their value chain, respective regulation and also market size. The industry choice in many ways influences the early life of the firm due to their needs for financing, potential market and time to market. The division between the two sections aims primarily to make the point that even if the sector has a common scientific ground, the industry of application induces a very different environment for a firm to evolve in. Thus after discussing the common characteristics of the sector and looking at the scientific and technological inputs that firms base their activities on, the chapter discusses the industry in which the firms decide to market the results of their activities.

At the beginning of a firm's life, the entrepreneur need to make a choice about their activities and thus define an industry in which they trade in, based on the technology available to them. This choice requires them to build a long term strategy of profitability, which is based on the resources available, and the industry which defines the environment they choose to set themselves in. The industry's choice, with its specificities such as the regulations, value chain, market dynamism and competitors, should influence and to some extend and restrict the firm leader in his business model design. Thus in order to be able to understand implications in terms of business models induced by the activities and industry choice, this chapter also includes a discussion of the implications for specific business models that result from an industry choice. A **business model** is here defined as *the plan of the entrepreneur to develop an architecture of revenue that enables the* *firm first to survive and secondly to fulfil and capture value from its business strategy*. The business strateg**y** *lays in the objective of the entrepreneur, to pursue specific activities that will be the basis of the long term competitive advantage that the firm aims to build.* The discussion over business models tackles specific aspects of an industry in terms of regulations, financial systems, value chain or specific structures of firms in this sector. The characteristics of these industries may therefore have a deterministic influence on some features of the business model, such as the organisation of activities within the firm in order for it to make profit. The management team constrain themselves and their firm business models to characteristics of an industry by making a choice for the industry in which they aim to set their activities.

In summation, this chapter describes two sides of the sector: the advances in science and technology that gave rise to the sector, but also its industries of application. However, before going into these discussions one must give some general definition about the object of the study and that is the purpose of the next section.

2. General context and definition

The biotech sector covers a wide range of technologies, involved in different industries with different technological regimes. This sector must be explained in detail in order to gain an understanding about the process of innovation in this sector; but first a general definition must be given as well as background information about the sector.

The sector is defined mainly by the use of different technologies that come from different sciences and have potential applications in various industries; the most studied being the pharmaceutical one. The simplest definition (OECD 2013) describes the biotechnology industry as *"firms that apply technology relating to life sciences"*. This definition is broad, with the only restriction being the relationship between the biotechnology sector and the science from which the firms derive.

The biotechnology sectors have emerged following breakthroughs in genetics research (which is looked at in the following section) in the 1970s and with the development of the human genome project. These events improved the understanding of biological processes at a cellular and sub-cellular level, which had an important impact on the health industry, including pharmaceuticals. The high potential for application has given rise to a new generation of firms which entered the industry in the mid 1970s and have experienced a constant expansion since then. In the United

States biotechnology firms started to emerge in 1977 and quickly increased during the first few years (OTA 1984).

The range of applications of life sciences in the biotechnology sectors (coupled with new computational advances[26]) is rather wide. The literature on biotechnology differentiates three different fields of application. These include white biotechnology, which is related to industrial applications, red biotechnology, which is related to health issues, and finally green biotechnology, which is related to agricultural issues. These three category can be complemented by some emergent biotechnologies, which are the yellow biotech concerning pollution problems, blue biotech dealing with aquatic resources such as the seas and the oceans, and finally black biotech concerning bioterrorism (Cavazzana-Calvo & Debiais 2011).

The green and red biotechnologies are of great interest to the general public and also to policy makers due to their potential advances in their respective fields. The green biotechnologies, with their applications in agricultural sectors, could contribute to improvements in production and the conservation of natural resources, including food. The red biotechnology could lead us to advances in diagnostics and therapeutic solutions for many illnesses, and therefore reduce human health problems. For these specific reasons, biotechnologies have been of great interest to policy makers in regards to their potential contributions to different sectors. The biotech sector has a large panel of application, thus the study of all the different domains of application could add to the complexity and reduce the ability to make consistent conclusions about the firms chosen (see replication argument in Chapter 3). Thus from this point on we will only focus on a single domain of application of the biotech sector.

The decision towards a specific domain of application includes several elements, such as the variety of structure, a variety of founders regarding their previous experience and finally to choose a sector that has policy relevance today. As stated in the above paragraph, both green and red biotechnologies are extremely relevant to policy makers. The green biotechnology aims to contribute to bring solutions to problems such as agriculture to improve the production and quality of crops and to work towards sustainable development with the contribution of biological knowledge towards the design and use of renewable energy, reduction in the use of pesticides and helping to maintain biodiversity (OECD 2009a). In the case of the health sector, biotechnology is mainly of policy interest for public health reasons through the development of new vaccines and the future delivery of more affordable and personalised healthcare. Both of these domains of

[26] A later section refers to computational biology, which explains how advances in computing have impacted on the biotechnology revolution.

application still have markets in growth that make them attractive for a study of entrepreneurship. However, the healthcare sector seems to be slightly more adapted since its industries of application include the pharmaceutical industry, with extreme requirements in terms of product development, and other industries such as vaccines, cosmetics and nutraceutics that are less constraining. This variety, and in certain cases the extreme pressure that the environment puts on the firm, are conditions in which one can observe, among others things, the pressure exerted by the environment on entrepreneurial agency. The health industries also have the advantage of providing a wide range of sources of innovation, such as academia and large firms; academia being an early source of innovation in the domain. The literature has shown that public research was a determinant in the development of red biotechnology. Universities and public research organisations in the biology sectors have contributed to the industry with the transfer of technology through firm creation (Oakey 1995; Pisano 2006), firstly in terms of providing the main scientific findings behind the biotech sectors and ultimately in terms of new projects and labour, especially star scientists who are influential and take part in firm creation (Zucker et al. 2002). These applications also provide a variety of backgrounds within entrepreneurs in this sector, which is hypothesised to influence a firm's survival and success. This makes the health applications of biotechnology (red biotechnology) particularly interesting to study and thus we will focus on only these applications from now on.

The health sector, which is one of the main markets for biotechnology, is still growing due to its core demand for drugs, but other growing market include cosmetics and nutraceuticals (Figures are shown later in this review). The range of markets makes it possible to have long term and high risk technological projects (for example for the pharmaceutical sector that is highly regulated) and also shorter term projects for cosmetics or nutraceuticals products. Finally, the health sector has institutions that make it a particularly attractive sector for a good balance between R&D inputs (in terms of the technological context) and environment conditions (such as financing organisation, or regulatory framework), which provide an important role in their development and range of markets available (from nutraceuticals and cosmeceuticals to the pharmaceutical industry[27]). The founder's experience and strategy choices should therefore be determinants for the growth path of the firm in this sector.

Before going deeper in the characteristics of each industry, the next section first returns to the advances in science that gave rise to the biotech sector.

[27] This is detailed in section 4.2.4 of this chapter.

3. From sciences to technologies

The complexity and wide range of applications of the technology leads to a requirement for more boundaries to be drawn on relevant information relating to the case studies.

The first section will be dedicated to the advances in biological sciences that are inputs to the biotechnology sector, and a second section will look at the emergence of new technologies that give rise to innovation in many industries. Finally, the last section will explore the consequences of the introduction of these new technologies to different industries on an industry level, looking also at the value chain and the business models' change of entrants and incumbent firms.

Referring to the above statement of the emergence of the biotechnology sector due to the scientific advances in biology made in universities, one must first explain the scientific breakthroughs behind the rise of this new technology. Many of these breakthroughs, in concomitance with the rise of other technologies, gave rise to a biotechnology paradigm in the pharmaceutical industry and also other health sectors, which we will describe in a later section. This section aims firstly at summarising the new advances in science that gave rise to the biotechnologies.

3.1. The scientific revolution behind the emergence of the technology

The biotechnology sector is not new per se, since humanity has been using techniques relating to life science in many applications since the Stone Age. If we consider the definition of biotechnology as the use of living organisms or biological processes in a productive way then biotechnology activities can be traced as early as the Stone Age with the use of enzymes, bacteria and fungi in fermentation processes, or even with the first use of agriculture through the selection and breeding of plants and animals. The technology emerged long before the scientific understanding of these living organisms. However, scientific advances due to breakthrough occurring in the 20th century relating to how living organisms work, have given rise to a set of new techniques and opened new possibilities in the manipulation of living organisms. The scientific paradigm behind the development of biotechnology has been driven by the fundamental question of "What is life" (Morange 2003), and has been marked by the characterisation and understanding of genes (firstly through their roles and then through biochemical characterisation). This section exposes the scientific evolution behind the development of genetics.

During the 20th century, scientific advances have experienced a great leap in the explanation of 'human life' through the understanding of the functioning of genes. The interest in genes as an object of study arose in the late 19th century with attempts to understand heredity and the specific characteristics of living organisms (Morange 2000). The work of Mendel on the observed heredity of plant hybridisation through inheritance of traits, from which are derived the Mendel Laws of inheritance, would later become central in genetic science. Later research from Morgan in 1910 advanced the understanding on genetics, by showing that genes were carried on chromosomes and are the basis of heredity (Fagot-Largeault et al. 2007). The subsequent research in the genetics field was oriented towards the characterisation of the chemical form of what constitute a gene (whether they were proteins or nucleic acids). In 1952, Chase and Hershey proved that genes were made of nucleic acids (DNA) (ibid.). This result was already shown by Avery in 1944, but the experiment of chase and Ensley was a much clearer demonstration of it (Morange 2007). The final and most influential scientific breakthrough was to come with the discovery of the structure of DNA. This discovery is attributed to Watson and Crick and was published in April 1953, from which they were rewarded a Nobel Prize in 1962 (Cavazzana-Calvo & Debiais 2011). However, historians have also acknowledged the role of Franklin and Wilkins who worked on the X-Ray diffraction imaging that gave a clear picture of the double helix structure of DNA. While Franklin was the one able to produce the best picture the DNA structure, the discovery was attributed to Watson and Crick because their paper was the one that was able to link the specific structure of DNA with the auto-replication characteristic of the gene.

The understanding of the structure of genes and the way they replicate had an important impact on further advances in molecular biology and biochemistry in the 1960s, to which ultimately lead to the manipulation of genes and thus living organisms in the 1970s. These most recent advances were significant in the biotechnology revolution. This revolution first started in 1973 with DNA sequencing and Recombinant DNA technology developed by Cohen and Boyer (i.e. the ability to insert a specific DNA sequence into bacteria or mammalian cells allowing the expression of the corresponding protein), followed in 1975 by the technology developed by two British researchers Milstein and Kohler who developed 'cell fusion', also known as 'hybridoma' technology. Hybridoma technology intervenes in the production of monoclonal antibodies, which are used in diagnostics and cancer treatments by directing them against a specific part of a targeted protein. This technique is much more effective than the previous technology that was based on polyclonal antibodies. These advances are mainly used as vectors to distribute highly toxic drugs to clusters of cancer cells (Pisano 2006).

The other reason for such rapid advances in the study of genes is the technologies developed for sequencing them. In the 1970s Fred Sanger, Maxam and Gilbert developed a way to read sequenced genes through the codification of nucleotides, given the letters A, T, C, G (respectively Adenosine, Thymidine, Cytidine, Guanosine) (Fagot-Largeault et al. 2007; Hamdouch & Depret 2001; Pisano 2006), which they were rewarded by a Nobel prize in 1980. This made the production of proteins possible and also provided the possibility to read DNA and RNA. This method, when initially developed, was extremely labour-intensive requiring manual microscopic observation. Two techniques then arrived that improved the fastidious process and sped it up significantly. The first method, called the polymerase chain reaction, was invented by Kary Mullis in 1983 and could amplify a selected fragment of DNA. Secondly, Hunkapiller and Hood in the 1980s worked on a system that could automatically read DNA, and developed the first DNA Sequencer at Applied Biosystem (the name of their company) (Pisano 2006). Since then DNA Sequencers have improved in productivity. This technology helped to considerably reduce the time needed for completing the human genome project but also supported the rapid evolution of genomics.

Following this, these discoveries led to a large scale project, the Human Genome Project, which was put in place in the 1990 and targets the identification of genes for mapping the entire human genome (Cavazzana-Calvo & Debiais 2011). After the identification and mapping of all the genes in the human genome, which officially finished in 2000 and published in 2001, the research then focused on the functions of the genes. The human genome project has created an enormous quantity of information that has now to be understood, and which will probably help in understanding links between this information and the specific functions of genes and the proteins produced by them (ibid.). The function of genes involves the understanding of how proteins are produced and the specific functions of these proteins (Pisano 2006). The study of proteins is called proteomics and looks at their structure and functions. These two tasks are quite large; while the human genome has between 25 000 to 35 000 genes, they produce between 1 and 20 million different proteins. In addition, protein sequencing is not fully automated like gene sequencing (ibid.).

These advances in genetics open the way to the emergence of many new disciplines, which includes the understanding of the expression of genes and the understanding of the proteins that genes codes for, which can come together under the umbrella of the understanding of biological systems, but also in how they interaction with their environment. The next section gives an overview of the various sciences that emerged directly from the genetics revolution.

3.2. Scientific development from the early biological discovery

The aim of this section is to give a global overview of important disciplines that shape the health care advances and especially the pharmaceutical and related industries today. The list of disciplines and methods is not exhaustive.

The advances made on the tools to observe and interact with human genes have given rise to different disciplines and complementary technologies that have furthered the understanding of the functions of genes and proteins. The scale of information generated by the understanding of the human genome is phenomenal, and so calls for complex systems of data management. This section will therefore go through the common sciences developed following the human genome project, which are genomics, proteomics and bioinformatics for the management of the data generated.

3.2.1. Genomics

Genomics is the science behind the process of identifying genes and their functions with regards to their DNA sequence. In terms of health care, this discipline identifies genes involved in genetic diseases by comparing people's genes with or without specific diseases. This technology gives rise to more personalised medicine by implementing therapeutic customisation (Gassmann et al. 2008, p.43).

Different disciplines arise in genomics, from generic disciplines that further the understanding of gene expression, such as functional and structural genomics, to others that specialise in drug applications, such as pharmacogenomics and biomarkers.
Structural genomics aims at sequencing and identifying genes but also to represent the tri-dimensional structure of a genes output, such as the proteins that are coded by a given genome. Structural genomics is often referred to as the understanding of the structure of a large number of proteins. The knowledge of structure is important as it is closely linked to its function[28]. Thus this research, combined with functional genomics and with the today's computational power, can advance the understanding of a large variety of proteins (Brenner 2000). The international research community have contributed to a combined effort to build a library of all proteins folds through various research projects (such as Protein 300 in Japan, Protein structure initiative in the United States and SPINE and SGC programs in Europe)(Nature 2007).
The study of *functional genomics* (function of the genes) has become possible due to the variety of known sequences of different organisms. Thus the functions of a specific gene is studied by modifying the gene in a model organism (in an animal or plant) and observing the effect (Pisano 2006, p.33). The function of a gene can also be uncovered by comparing the structure of genes between patients that have been exposed to a particular disease and patients that have not.

[28] More information at http://www.bmrb.wisc.edu/structgen/ [Accessed March 22, 2014]

Pharmacogenomics[29] looks at the interaction between genetic profiles in relationship to their reaction to drugs (OECD 2009b, p.16; Gassmann et al. 2008, p.45). It especially focuses on the determination of drug efficiency and also on their adverse effect on patients (OECD 2009b). This science improves the grounding for the choice of specific medication, compared to the physician's trial and error practiced currently, in which any potentially harmful effects are only know about after the patient tries the drug. Pharmacogenomics will also improve the identification and development of more efficient drugs (Gassmann et al. 2008). Pharmacogenomics development is also dependant on the identification of *biomarkers*. "Biomarkers are indicators that mark the presence of a potential gene-drug interaction or that respond to therapeutic activity" (OECD 2009b). These are used to differentiate patients who respond differently to specific drug uses (ibid.). This discipline integrates the study of biochemistry, which is traditional in the pharmaceutical industry, and links it to the development of genomic knowledge, hence the origin of the word pharmacogenomics. Biomarkers have applications in the diagnostics field.

The advances in genetics have given rise to new ways of identifying candidates for drugs since the mid-1980s (Nightingale 2000), by "reverse genetics" (comparing statistically genetic markers with disease markers). Firstly, it provided pharmaceutical companies with a better understanding of the genes responsible for illnesses and their interaction with drugs (such as pharmacogenetics). It secondly opened a new door in terms of diagnostics, which used the knowledge of the correlation between gene expression and the risk factor of being prone to specific illnesses. The advances in pharmacogenomics aim at adapting therapies and treatments to both the patient's genetic specificities and the stage at which the illness is diagnosed. It also aims at making more cost efficient clinical trials and especially at reducing the amount of human testing required (Hamdouch & Depret 2001).

3.2.2. Proteomics

Proteomics derives from the word 'proteome', which is the set of proteins produced by a genome (Tyers & Mann 2003). Proteomics refers to the study of the structure of proteins and their functions, and is a natural continuation from genomics, "which provided a 'blueprint' of possible gene products that is the focal point of proteomic studies" (ibid.). The study of proteomics requires a considerable amount of research because genes can encode more than one protein, and proteins

[29] Here we use the general term 'pharmacogenomics', which is defined by the relationship between gene differences and drug behaviour. We include pharmacogenetics as looking specifically at peculiar drug responses and searching for a genetic cause. However, the terms have been used interchangeably, so here we only use the term pharmacogenomics. (source: http://www.genetics.edu.au/Information/Genetics-Fact-Sheets/PharmacogeneticsPharmacogenomicsFS25)

can be altered by posttranslational modifications before achieving their natural function (Pisano 2006). Proteins can therefore vary in a cell depending on gene expression resulting from environmental stimuli (Gassmann et al. 2008). The study of proteomics therefore includes “identification and quantification of proteins, but also the determination of their localization, modifications, interactions, activities, and, ultimately, their function” (ibid., p. 42).

The study of proteins is also difficult for other reasons. Contrary to genomics, and the tools developed to work with DNA and RNA, the study of proteins is limited by sample material, which is subject to degradation (Tyers & Mann 2003). The recent advances in proteomics are due to a combination of other technologies. These technologies include the improvement of spectrometry methods, which give the opportunity to identify proteins of an increasingly smaller and more complex structure, array-based proteomics and structural proteomics, which is similar to structural genomics and aims at understanding the structure of the protein to understand how it interacts with other organisms.

Concerning its application in health sectors, proteomics is expected to contribute to biomarkers and drug target identification. This will have a potential impact on the prevention and diagnosis of illnesses and the development of drugs for the treatment of illnesses.

3.2.3. Technologies emerging from the fusion of biology and computer advances

Since the informatics revolution, the new technologies (Information and Communication Tecghnologies here) have provided the possibility to organise and interact with information in an increasingly efficient way. This technology has helped to deal with the increasing amount of knowledge produced. The Biotechnology and pharmaceutical sector is increasingly efficient at producing new knowledge with the techniques and tools referred to earlier, and so there is a need to organise the large amount of information produced. The computational paradigm therefore also finds its place in the biotechnology sector, which is mainly referred to as bioinformatics.

The computational paradigm firstly provided the possibility to improve the management of information generated from the process of developing drugs, from design to trial, and thus organise them into useful databases. This enables bioinformatics scientists to collect data on model organisms and generate compound profiles, but also provides the possibility to share this information within an organisation (Gassmann et al. 2008).

Secondly, by using the data collected, computer simulations in the field of screening of new molecules for finding new drugs candidates have been developed. Data collected during the process of clinical trials for drug development is used for simulating and testing the effect of candidate molecules. The simulations (i.e. in silico experimentation) are based on a large number of previous experiments and even though probably less accurate, they still have the potential to reduce the amount of ‘wet’ experimentation, which has many limitations, such as time spent, costs and amount of waste generated (Nightingale 2000). This collected data enables new screening methods such as High-Throughput Screening (HTS), which makes it possible to conduct thousands of experiments daily when combined with the help of robotic installations (Dove 2007).

Thirdly, the advances in 3D modelling during the 1960s increase in the calculating power of computers during the 1970s and the high resolution visualisations all gave the rise to technology for 3D visualisation of the structure of molecules, proteins and electrons. These visualisations are particularly useful for simulations and for understanding of the bounding properties of molecules. As described in previous sub-sections, this technology aims at first to produce information about proteins properties and genes functions on a large scale (which can also be shared more easily within the scientific community (Hamdouch & Depret 2001)), but also helps in terms of their modelling. In combination with pharmacogenetics it makes it possible to increase the amount of experimentation in silico and thus improves the process of drug selection prior to clinical trial phases.

3.2.4. Towards an integrated view of these technologies: the study of systems biology

The combination of the technologies described above brought about a renewed interest in the field of system biology through the availability of information and the knowledge built and kept. The notion of studying biology as a system is not new and its origins can be retraced to Norbert Wiener during his developments of cybernetics, which discussed the development of feedbacks (Kitano 2002). This discipline aims at understanding the full complexity of living systems, through the study of dynamic organisation and interaction between the different components (such as proteins and genes)(Walhout et al. 2013). It does not only look at the organisms independently but also the response of organisms to environmental conditions (ibid.). The system view also introduces the notion of time and studies the system not anymore as separate components but as a dynamic entity with interactions (Kitano 2002).

Figure 2.1: The interaction of specialised biological sciences in characterising biological systems

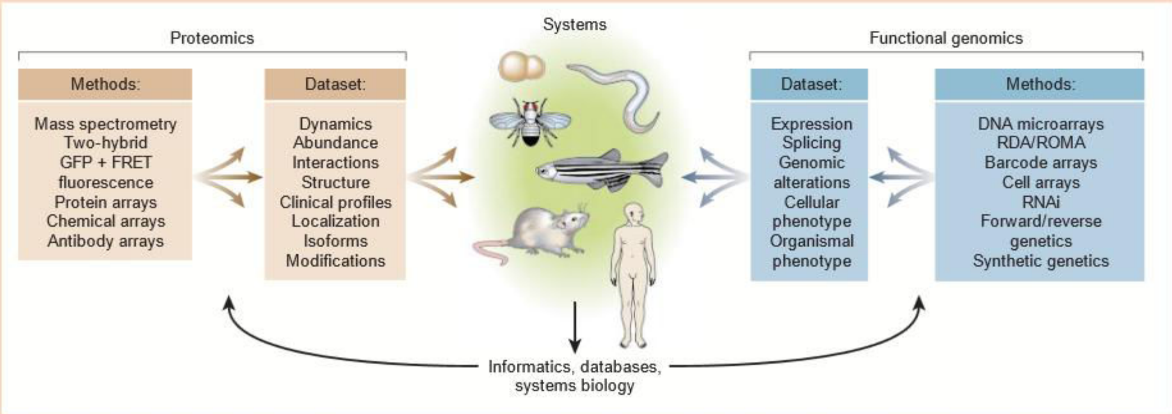


Figure 1 Platforms for proteomics and functional genomics. Methodology is shown in the outer columns, resultant datasets in the middle columns, and model systems in the centre.

Source: (Tyers & Mann 2003)

The above figure shows in more detail what is included in system biology research and the overlap of the different components discussed. In this discipline a point is made to bridge and develop interaction databases for storing findings in genomics and proteomics.

Kitano (2002, p.1662) has identified four key properties that would further the understanding of biological systems:

> "1) System structures. These include the network of gene interactions and biochemical pathways, as well as the mechanisms by which such interactions modulate the physical properties of intracellular structures.
> 2) System dynamics. How a system behaves over time under various conditions [...]
> 3) The control method. Mechanisms that systematically control the state of the cell can be modulated to minimize malfunctions and provide potential therapeutic targets for treatment of disease.
> 4) The design methods. Strategies to modify and construct biological systems having desired properties can be devised based on definite design principles and simulations, instead of blind trial-and-error."

These advances in the understanding of the interactions of the components and the environment gives rise to useful extensions in drug discovery processes. System biology may prove useful for decreasing attrition rates in drug discovery, through a better selection of compounds. An improved selection of compounds can be achieved through improved target identification (by a more informed selection of proteins), and through the recognition and avoidance of unwanted properties (see how the chosen proteins interact with other parts of the human system) (Hood & Perlmutter 2004).

3.2.5. Stem cells and cell biology

Much of the advances in biotechnology described above have been related to the understanding of increasingly small scale biological components, functions and dynamics. However, there have also been significant advances in cell biology, such as cloning and stem cell development. These advances evolved into developments with the potential to have an impact on human health (especially with cloning and stem cell technologies).

Stem cell technology has experienced much development since the 1960s. Concerning embryonic stem cells specifically, two advances were significant Firstly, in 1981 Evans, Kaufman and Martin grew embryonic stem cells in vitro and generated derivatives from mice. Secondly, in 1998 Thomson and colleagues successfully derived human embryonic stem cells.[30]

Stem cells have high potential in term of tissue regeneration, as they are undifferentiated cells that can divide, specialise and self renew to produce new stem cells. These cells can come from adults or embryos and can help repair failing organs (Holland et al. 2001). Embryo stem cells have the advantage of being able to differentiate and grow into any type of tissue. Contemporary advances in these techniques include the study of the cell differentiation process in order to be able to artificially provoke differentiation toward a chosen type of tissue. This is done through the injection of healthy stem cells to an organ. The use of stem cells can be applied in many degenerative diseases such as Alzheimer, Parkinson, and Diabetes but also to repair damaged tissue such as muscle, brain or heart tissue.

The study and development of stem cells provides several different therapeutic advantages. It firstly helps to understand the dynamics behind foetal anomalies (e.g. teratogens). Secondly, technology with the ability to grow differentiated tissue can be used to test the toxicity of drugs on different human organs, without testing on humans directly. Finally, it has therapeutic value in the creation of tissue to cure degenerative illnesses and failing organs.

In conclusion, the new fields of study following on from the research of genetics have improved the understanding of scientists and but also of private firms who put this understanding into practice. This section has loosely talked about the link between the advances in science and their applications in the health industry. The next section will focus more precisely on the industrial outputs of these scientific advances.

[30] http://stemcells.nih.gov/info/scireport/pages/chapter3.aspx

4. Outputs: the consequences on red biotechnology related industries

Biotechnology has grown with advances in the biological sciences. As the above section has shown, the applications were first aimed at the health sector, but this is not the only application since industrial (e.g. white biotechnology) and agricultural (e.g. green biotechnology) use can lead to application in other sectors. The focus here is on red biotechnology, which concerns the health sector application of sciences focusing on biotechnology. However, even within the broader groups there may still be differences between industries and types of product or services offered. This section therefore aims at understanding the biotechnology sector and distinguishes it based on the field of application within the health sector. This section describes the specificities of the industries in the health sector and how the structure of these industries affects the firms involved.

4.1. Biotechnology in the health sector: overview and definitions

Health related industries are where the first impacts of new bio-technologies are expected. Biological advances are expected to have the greatest impact in particular from new and better drug designs (thus in pharmaceuticals). However, not only has this industry been affected by the biotechnology revolution but the firms introducing these new technologies produced a number of new products in diagnostics and offered new services to the pharmaceutical industry. They are all part of what is known as health application for biotechnology, which can be defined as “the use of knowledge on cell functions and genetics at the molecular level, including an understanding of deoxyribonucleic acid (DNA), ribonucleic acid (RNA), proteins and enzymes, to develop new therapeutics and diagnostics” (OECD 2009).

The firms specialised in biotechnology are not only specialised in biopharmaceuticals (including vaccines and services), but also extend their domain of application to other industries such as cosmetics and nutraceuticals. The OECD (OECD 2009a) gives an overview of the different domains in the health industry in which biotechnology companies can specialise, and which directly relate to the pharmaceutical industry in terms of the creation of new drugs (therapeutics), diagnostics and services. The new applications to human health are called cosmeceuticals and nutraceuticals and have a growing use of biotechnologies to continue developing their markets.

The differentiation between industries in which the firm evolves is especially important in the health sector because the different industries come with different constraints for the firm. Different industries are subject to different regulations that can affect the plans of the firm, such as the financing available to them, the time to market and their business plan. These specific differences will be described for each domain of application of biotechnology in the health industry.

4.2. The pharmaceutical industry

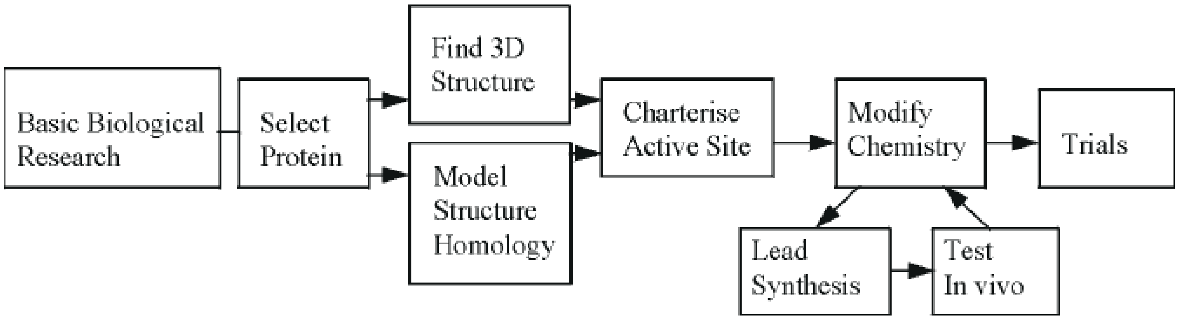
This section reviews the three main domains of activity of biotech firms in the pharmaceutical industry. These activities are drug development, diagnostics and services.

4.2.1. New drugs

Drug development is the most studied aspect for biotech firms entering the health sector. The process of drug development is known to be expensive, and therefore has a strong impact on new firms in Biotechnology. This section will therefore review the principal technologies involved in the drug discovery process. It will then discuss the specific details of the drug development process in terms of value chain costs and time. Finally, it will explain how a biotechnology firm can insert itself into this value chain by discussing the consequences on its business model.

The pharmaceutical industry has been changed by the biotechnology revolution. Before the integration of biological sciences in their search for new drugs and production processes, the pharmaceutical industry relied more on trial and error rather than logic and scientific knowledge to find new active compounds for making new drugs. Before the scientific revolution in 1970s, the pharmaceutical industry operated under the synthetic organic heuristic (Hopkins et al. 2007), which consisted of the random screening of molecules in order to find active compounds. With the study of genomics and proteomics, and an increasing level of knowledge generated from drug-targeting, the scientific revolution therefore informed screening strategies, which lead to a shift towards the biological heuristic. Since the 1970s, these sciences have therefore changed the approach towards rational design and guided screening (ibid.). The increasing understanding of biological processes at a cellular and sub-cellular level, in addition to advances in biochemistry, has improved the search methods. Firstly, it is now common practice to attempt to understand the interactions between diseases and the proteins that have an effect on the disease. Secondly, the biological and biochemistry knowledge developed is increasingly available in databases, together with tools for understanding the 3D structure of molecules. These advances make in silico search more efficient (search for interaction between chemicals and proteins). Simulation techniques have therefore been developed to help in identifying active compounds and also in improving the performance of the existing ones found using new biological knowledge (Nightingale 2000). The innovation process can therefore be characterised by the following drug discovery process in the pharmaceutical industry:

Figure 2.2: Drug discovery process under the biological heuristic



Source: (Nightingale 2000)

This process is characterised firstly by the search for proteins using scientific knowledge, understanding their molecular structure and then improving their performance based on an understanding of the chemical processes, which leads finally to trial experimentation. Thus in order to find suitable proteins for experimentation, both biological and biochemical knowledge is required.

Although the biological advances were initially thought to improve productivity in the pharmaceutical industry, regulation has also increased dramatically. These changes take the form of trials to test the safety of compounds, which are long, costly and significantly reduce the probability of marketable drugs being produced by biopharmaceutical companies today. The value chain of the development process of a drug must therefore be explained since it impacts firm productivity and profit.

This section will firstly describe the particular steps of drugs development in order to describe the value chain[31] and properties of this particular market. Drug development is decomposed into three different phases, each of which contain sub-phases. The drug development process firstly undergoes a drug discovery process, then a development process, which includes several different phases of clinical trials, and finally a marketing phase if the drug is accepted. This section will focus on the trial phase, since the drug discovery phase has been discussed in detail in the previous section on science, and therefore does not need to be developed further here.

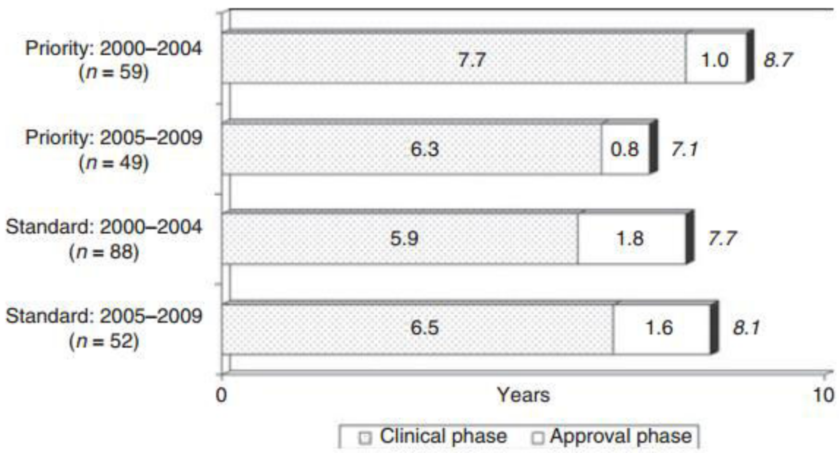
Drug development is one of the most risky parts in any drug discovery based biotechnology firm. The pharmaceutical industry is highly regulated because drugs have to be safe to use and also proven to be effective. These safety regulations have improved since the 1950s due to the problems

[31] The main reference used to explain this part is Gassman (Gassmann et al. 2008); some of the figures and graphs have been reproduce from this source for improving the clarity of the description in this section.

of drug toxicity ; a good example being the Thalidomide tragedy[32] (Landau et al. 1999). The length and cost of clinical trials have therefore increased over the years and so we discuss here the state of the current pharmaceutical sector clinical trials.

Concerning the time needed for the development phase, including clinical trials, the following two figures show the average time taken for drug approval, which is on average 8 years for standard drugs and 7 years for priority drugs (Figure 2.3). The attrition rates for the different phases are very high. Table 2.2 shows that during preclinical trials 48% of drugs make it to the next stage, 46% for phase one, 32% for phase 2, 87% for phase 3 and finally during the registration phase 97.5% make it through (Nightingale 2000).

Figure 2.3: Mean clinical and approval phase times for approved drugs 2000-2009



Source: (Gassmann et al. 2008)

Table 2.2: Typical survival rates of drugs entering trials

	Preclinical	Phase I[a]	Phase IIb	Phase III[c]	Registration	Market
Survival rate per 1000	1000	480	220	71	61	60
Percentage to market	6	12.5	27	85	97.5	100
Percentage to next phase	48	46	32	87	97.5	

Adapted from Parker (1998).
[a]50–100 healthy volunteers.
[b]200–400 patients.
[c]3000+ patients.

Source: (Nightingale 2000)

[32] This tragedy involved a small German company that sold a drug called Thalidomide, which was a sedative. The drug was clinically tested, but excluded pregnant women from this test. This resulted in the birth of thousands of babies with malformed limbs resulting from drug consumption by pregnant women before the effect was discovered, the drug was banned and much stricter regulations for drug testing enforced. More on this episode in the Landau Book chapter 1 page 95.

In more general terms, around 6% of the compounds starting preclinical trials make it to the market (ibid.) and only 3 in 10 of those drugs generate revenue that covers the R&D costs (Grabowski et al. 2002). The R&D costs of developing new drugs have dramatically increased over recent years to a peak in the 2000s of an average development cost of 1.2 billion dollars (PhRMA industry profile 2012). The main risk in the pharmaceutical industry following financial issues is linked to the efficacy of the product and its safety, which explains the high attrition rate during clinical trials (Gassmann et al. 2008). Overall, the chances of a product being approved following clinical trials is 1 in 40 to 50 projects (Jacob & Kwak 2003). It is therefore a highly risky strategy for biotechnology companies to have a single pharmaceutical project.

<u>*Business model implication:*</u> Regarding the high costs and time to development of biotech firms who want to engage in pharmaceutical products, these actors must adapt in terms of their business model since they will not be able to bear the costs and the development of a product on their own. The business model of human pharmaceutical firms is therefore very complicated has involved an open innovation type of value chain in recent years, compared to integrated pharmaceutical type companies during the pharma-chemical age (Gassmann et al. 2008). The small biotechnology companies developing drugs have a high interest in sharing R&D costs as early as possible with larger partners in order to reduce financial risk. Their business model also involves spending a large amount of money in R&D over a long period of time, without having any income from production. The biotech companies involved in drug development therefore need large amounts of early financing, which is generally obtained from venture capital investors. Due to their business model[33], venture capitalists usually require the venture to focus only on one molecule.

Another constraint in the development of the business model of pharmaceutical firms lies in the duration of property rights. As explained above, a successful compound needs on average 8 years of trials before being approved and marketed, while a patent is granted for 20 years. Thus a patent is approximately effective for 10 years. The delay in starting the development of the compound or problems during the trials could therefore significantly reduce the monopoly time and thus reduce the opportunity for profit (especially compared to the scale of the upfront investment).

In summation, biotech firms that choose to engage in biopharmaceutical developments are constrained in their business model (i.e. their ability to generate profit from an activity) by the investments needed, the inherent risk of failure during the trial period and finally by the patent life of the compound.

[33] For more information about the functioning of venture capitalists, Chapter 1 section 5.1 explains in further detail.

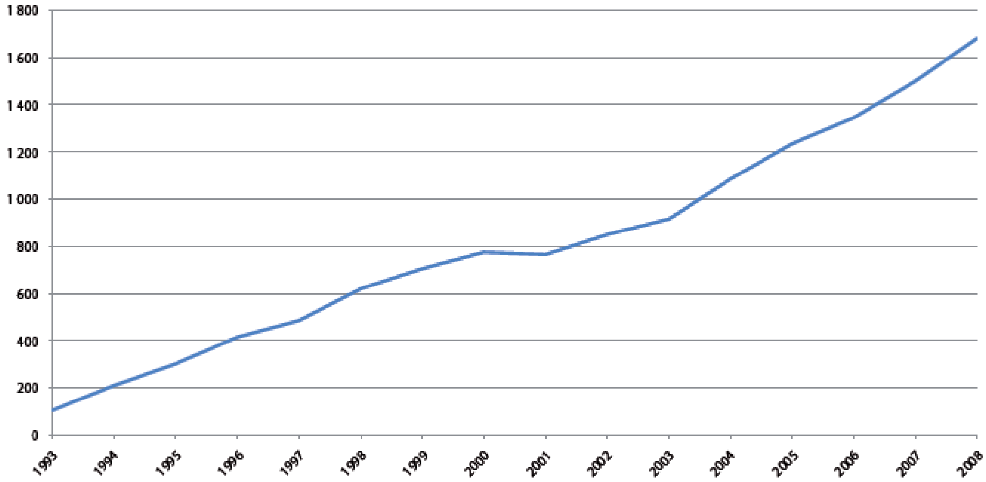
4.2.2. Diagnostics

A second important part of the pharmaceutical industry concerns diagnostics. A diagnostic can be defined as “a test or assay used to determine the presence of a specific substance, organism or nucleic acid sequence” (OECD 2009a, p.310). Diagnostics can be used in a variety of ways, from the early detection of diseases, predisposition testing and prevention to testing for better personalised treatment (Papatryfon et al. 2008). There are two types of diagnostic, which are differentiated because they are subject to different regulations. These are the in vivo diagnostic and the in vitro diagnostic. In vivo diagnostics are *invasive* processes that requite something to be inserted directly into the patient’s body. In vitro diagnostics are *non-invasive* processes that are done outside the human body.

In vivo diagnostics, due to their invasive nature, are regulated through clinical trials to avoid any patient safety issues, in a similar way to pharmaceutical drug trials. Furthermore, they represent a very small market, with only 13 diagnostics having market approval and 11 in development in 2003 (Arundel et al. 2009). These diagnostics emerge principally from American and Cuban companies; European companies have little activity in ‘in vivo’ diagnostics. Only 4 in vivo tests are currently in trial for European firms (English and Danish) (Arundel et al. 2009).

In vitro diagnostics, due to their non-invasive nature, are therefore regulated in a much less demanding way. There are two main types of in vitro test. The first is based on molecular genetics (DNA based) and detects changes in the genetic material of patients in order to identify their predisposition to certain types of diseases. There is also immunological testing (or protein based testing), which is aimed at detecting antibodies that can help to detect illnesses. The market for in vitro diagnostics is much larger because the general approval time for in vitro diagnostic tests is only 5 years on average (Jerel Davis et al. 2010). There has therefore been an increasing number of genetic tests made available, which have reached more than 1600 diseases (see figure below reproduce from (OECD 2009a).

Figure 2.4: Number of diseases for which genetic testing is available



Source: Authors, based on GENETests (2008).

Source: (OECD 2009a)

In 2004, the global market for in vitro diagnostics was evaluated to be more than € 22 billion (including 9.3 billion from the US and 5.8 billion in Europe), in which biotechnology diagnostics have a share of 30%, which represents €6.6 billion in revenues (Papatryfon et al. 2008). In vitro diagnostics are much more likely to experience growth in terms of the number of products compared to in Vivo diagnostics (Arundel et al. 2009).

Table 2.3: Estimate of modern biotechnology-based diagnostics and IVDs revenues in 2004

	Modern biotechnology-based diagnostics (EUR billion)	Share of total (in %)	IVDs (EUR billion)	Share of total (in %)	Regional share of biotechnology in IVDs (in %)
EU*	1.7	26	5.8	26	29
US	3.4	51	9.3	42	37
Others	1.5	23	7.04	32	24
Total	6.6	100	22.14	100	30

*Includes: the UK, France, Spain, Italy, and Germany

Source: (Arundel et al. 2009)

Diagnostics have therefore also benefited from the biotech revolution, which gave rise to genetic testing in the early 1990s in order to identify gene mutation and predispositions to certain diseases thanks to the leaps made in the understanding of the human genome. In terms of development costs, an important difference in the diagnostics industry must be made between the development of in vivo diagnostics, which are strongly regulated, and in vitro diagnostics, which is not.

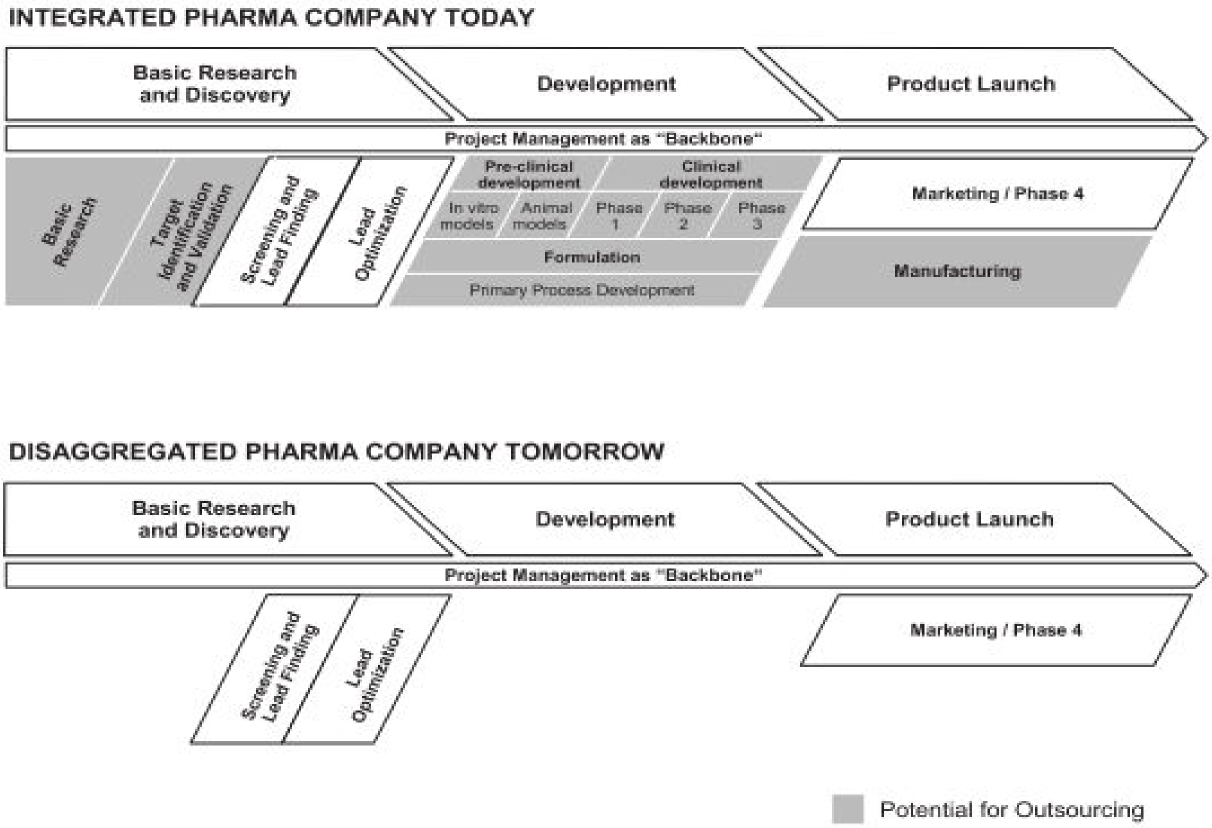
Business model implication: Firms who base their activities on diagnostics should be divided into two different types of firms according to their invasiveness (i.e. if they are in vitro or in vivo), which will influence their business models. In vivo diagnostics are under similar constraints as pharmaceutical firms (discussed above) and so these constraints may induce similar implications on their business models.

Conversely, in vitro diagnostics, due to their non invasive characteristics, benefit from a less constraining acceptation process and so are faster and less costly to develop. The need for risk financiers (such as venture capitalists) is therefore not essential for the development of firms that specialise in these activities. Firms specialised in *in vitro* diagnostics are therefore less constrained in their development, which may influence their profit opportunities and thus their business models.

4.2.3. Services

The increasing complexity and rapid evolution of science and technology make it much more difficult for large pharmaceutical companies to keep up to date competences internally (Hopkins et al. 2007). These companies therefore evolve towards an outsourcing model by only keeping core competences inside the firm's boundaries (Gassmann et al. 2008). The value chain of pharmaceutical companies becomes much more disintegrated with only a few major activities remaining in house. The potential activities that can be outsourced are represented in grey in the figure below (reproduced from Gassman et al. 2008):

Figure 2.5: Impact of outsourcing on the pharmaceutical value chain



Source: (Gassmann et al. 2008)

This has opened up opportunities for biotech firms to specialise in services derived from scientific and technical knowledge. The service activities can be in the discovery phase, by having innovative techniques to identify or improve new compounds, but also in the development phase with testing services (Gassmann et al. 2008). The service agreements can vary in their interactions and risk sharing; this ranges from limited tasks based on a determined fee to joint projects that include closer collaboration based on an agreement on the share of risk and profits (ibid.). The collaboration can eventually lead to integration (alliance, buy-out or fusion) if the service is relevant and strategic enough to the larger actor.

Business model implication. Firms that have a business model oriented towards services have the advantage of generating revenues quickly after starting their activities compared to firms that develop human therapeutics only. However, service activities involve a very different architecture of revenues compared to pharmaceutical drugs. Compared to drug discovery companies, services do not usually offer the same potential for high profit (Fisken & Rutherford 2002).

The firms that decide to get involved in services using either a service or a hybrid business model (a business model that includes both service and product development activities) are usually able to secure revenue at a much earlier stage and can also build relationships with larger pharmaceutical companies (Fisken & Rutherford 2002). These models can become particularly attractive as the source of financing become scarce following a financial crisis or the pessimism of investors.

4.2.4. Derived industries: Nutraceuticals and cosmeceuticals

When considering health sectors, one usually considers industries related to the detection and treatment of diseases. However, in recent years biotechnology firms have entered new industries relating to health in terms of prevention and the improvement of 'well being'. Some of these are considered here, such as nutraceuticals and cosmeceuticals. These industries have a high growth potential especially for biotechnology firms. These sectors illustrate the convergence between two different industries, such as the cosmetics industry and the pharmaceutical industry to form the cosmeceuticals, and the food industry and the pharmaceutical industry to form the nutraceuticals. These two industries are derived from existing industries, but where the added value is the health benefit that these products bring. They can be situated upstream from the pharmaceutical industry by acting as therapeutic or preventive. In the case of the cosmeceuticals, it must also face the beauty standards of contemporary society.

4.2.4.1. Cosmeceuticals

Historically, the cosmetics and drugs industries have always been close, but their relationship has become stronger over the course of the 21st century (Lin 2010). This is due to two factors. Firstly, society's demand for more drug-like products and secondly an increasing demand for safety and proven efficacy of the products (ibid). This gave the rise to clinical testing in the industry since the 1960-1970s.

Different countries have introduced various **regulations** concerning market introduction of cosmeceuticals[34]. In America in the 1960s the FDA started to take interest in some cosmetic products such as sun screen and started to get involved in the regulation of these products (Lin 2009). Certain cosmetic products are even classified as drugs by the FDA (such as suntan lotions or sunscreens that contain UV absorber).

In Japan, Kokuhisho disease, caused by inflammation of facial skin due to make-up, was sanctioned by a large action suit in Japan, which also greatly influenced the regulation there. The JCSS (Japanese Cosmetic Science Society) was therefore created in 1976. Clinical trials became a differentiator between cosmetic products. The clinical trials also have a marketing side in addition to

[34] To know more about evolution of regulation on cosmetics in different countries, please refer to Lin 2009.

a regulatory side, since potential users have confidence in “science” (via scientific validation such a clinical trials) (Lin 2009). The European countries have also improved their quality control and related regulations with the creation of a new European directive, but each country has to enforce it through competent local authorities. The regulation includes notification of the place of manufacture, exclusion of prohibited substances (1233 of them), a list of colorants, preservatives and UV filter use, and a ban on animal testing (Global Insight, Inc. 2007).

The cosmetics market is valued at around €136.2 billion worldwide as of 2006, and is still a market in growth (Global Insight 2007). It is therefore a lucrative market that started at the end of the 1990s for new biotechnology companies (Nasto 2007). In France, there is a high concentration of cosmetic firms, which is valued at 20 billion € with 2156 firms active in the sector (Direction générale des entreprises 2006). In France, the industry generated 17 Billion € of turnover in 2007 (Ministère de l’économie, des finances et de l’industrie 2011).

The cosmetics market has evolved to provide for consumers who want a higher level of safety (see the previous paragraph about regulations) but also efficient treatment promoted by science, because “Science sells” (Nasto quoting Maes 2007, (Lin 2010)). Biotechnology firms therefore have specific competences for managing clinical trials and using new science to target active substances that might have some desirable effects (anti-aging, skin solar protection, skin whitening –in Asian countries-, weight loss effects...) (Nasto 2007). The fact that regulation in this sector is much lower and has a growing market share makes it a good industry to enter for biotechnology firms.

<u>*Business model implication.*</u> The cosmetics industry has various advantages for biotechnologies companies to enter compared to human therapeutics. Its trial phase is less constraining, shorter and thus less costly. Additionally, the experience in terms of scientific abilities may become an advantage because incumbent firms may have limited capabilities in terms of trial management.
Opportunities are also diverse in terms of insertion through the product value chain for the company; it can choose to sell directly through different channels to license to some of the main players, or even have a mixed model while being active in another industry (such as the pharmaceutical industry) (Nasto 2007). The large market of cosmeceuticals is still growing and so is an additional advantage to those firms that choose to be active in it.

4.2.4.2. Functional foods & nutraceuticals

Regarding the development of health concerns in our modern society, besides the cosmetics industry that has been growing in recent years, the sectors of nutrition is also doing well. This tendency was expressed through new ways of consuming food with an emphasis on nutrition and the special health benefits of some foods.

Functional foods and nutraceuticals are new concepts and need defining. Functional foods are, as defined by health Canada (OECD 2009), "similar in appearance to a conventional food that is consumed as part of a usual diet and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, i.e. they contain bioactive compounds". On the other hand, a nutraceutical is (ibid) "a product isolated or purified from foods that is generally sold in medical form and demonstrated to have a physiological benefit or provide protection against chronic disease". These sectors were active before the entry of biotechnology, and so biotechnology is not central to those industries. However, biotechnology might be of use in the selection of plants or animals that have a high amount of desired compounds, or even in the engineering of those foods.

The functional food sector is experiencing growth. Over the last 5 years the sector growth was between 13% and 14% on a global level. In 2007 the global market of this industry was estimated at 46.7billion € (Ministère de l'économie, des finances et de l'industrie 2011). In France the volume of sales in this sector was 8 billion€ in 2007. Until now, biotechnology has not played a major role in this industry but, as mentioned earlier, it has the potential to do so (Arundel et al. 2009).

In terms of regulation, the main constraint for nutraceutical companies is to have a proven efficiency of their products. There is currently no official Food Law in the European Union (EU). The EU produced a white paper that proposed regulation for this industry in 2000, and most of these regulations have now been implemented (Coppens et al. 2006). In Europe, the food is under the Regulation (EC) nb 178/2002, which lays down the principles of European food law and also established the European Food and Safety Authority (ibid). This authority is responsible for scientific risk assessment linked to food in parallel with the precaution principle. There is no specific regulation for functional foods or nutraceuticals, although there is regulation (PARNUTS regulation) giving a legal framework for food with nutritional uses in which most of the functional foods are included. In terms of nutrition and health claims made by companies for certain products, the system requires pre-market approval and the publication of scientific proof of the claims used in marketing. [35]

[35] For more information about European Laws on Nutraceuticals and functional foods, please read (Coppens et al. 2006)

As a result, even if for the moment biotechnologies firms are not directly implicated much in this industry, the new technologies developed can find a domain of application; especially by engineering products with nutritious or health claims.

Business model implication. As this industry is still young, the level of regulation is low compared to the other industries we have looked at. The sector is in rapid growth and the opportunities for biotechnology firms seem large since this market has a growing interest in making scientific claims for the nutritional value of the foods. Thus as with cosmeceuticals, this sector seems a good alternative to the risky and expensive process taking place in the pharmaceutical sector, due to potentially high opportunities for profit and a shorter time to earn revenue due to lighter regulations.

5. Conclusion

This section has aimed on the one hand at showing firstly the science behind the firms developed in this sector and the reasons why the health industry should benefit from these advances. On the other hand, it has aimed at understanding the domain of application in health sectors. The bio-technologies have a much larger potential for application than only in the health sector; for instance it has fields of application in agriculture and bio-fuels, but also in industrial processes. This section has only focused on health sectors, since the case studies are focused solely on the health sector. The health sector in itself is quite complex because it involves the traditional pharmaceutical industry, with its different domains of application such as drugs, diagnostics and services, but also new health related industries such as cosmeceuticals and nutraceuticals.

Employing the description of the numerous scientific developments and the sectors of applications of this science, this chapter has aimed to show the opportunity potential in the biotechnology sector. Even though when scientists working in their laboratories have a human health application in mind, the spectrum of possibilities of application is rather large (even when just looking at industries linked to the health sector). Therefore, when starting a venture, an entrepreneur, even limited by his technical knowledge in biotechnology, has high potential to apply his knowledge in a variety of industries. In terms of entrepreneurial agency, the technology does imply some restrictions, but they are not as limited as one might think (i.e.not only the case in the pharmaceutical industry).

The overview of the different sectors is crucial since the involvement of firms in each specific industry involves different factors, and these factors have significant potential to influence a firm's survival and strategy. This is especially true for the regulatory requirement, which differs between these industries since drug and in-vivo diagnostics have the most constraining regulations that require large amounts of capital to develop a product. In terms of services, in vitro diagnostics and regenerative therapies are less constrained by regulation and so firms specialising or diversifying in those technologies/industries have a greater chance to develop a marketable product over a shorter amount of time. These sectors are also particularly interesting because they are a growing market and increasingly require proof of safety and efficacy, which is a capability lacking from incumbent firms (because regulation has changed recently).

The variety of domain of application in addition to the difference in regulation and market opportunities makes the choice for the industry even more crucial. As the second part of the chapter has shown, the regulation and market opportunities in the different industries influence the potential architecture of revenues a firm can expect in terms of volume and term to revenue. Thus even if an entrepreneur has a choice in terms of industry of application, the choice in itself affect his future agency. This makes the decision towards a particular industry a crucial one in terms of future agency of the entrepreneur. As shown in this review, advances in biology science unleash great expectations for possibility in the pharmaceutical sector. However, this sector is also the most constraining and with the most inherent risk when choosing to develop only human therapeutics products. Deciding to focus the firm's activity in this sector with potentially the help of a venture capitalist may have an important impact on his entrepreneurial agency.

This chapter has looked at the biotechnology sector in order to understand the science behind it and the industries affected by it. From an entrepreneurial agency perspective, we have shown that the science has the potential for application in many different industries, which has a positive effect on the possibilities given to the entrepreneur, but the choice of the industry unleashes specific constraints that the entrepreneur faces. Thus the future agency of the entrepreneur is reduced by his choice of activities in his chosen industry, and thus the choice of business model will be discussed more extensively in the analytical chapters.

The next chapter will focus on the details of the methodology used, but also on the cases chosen in our study. While doing so, it will also describe the firms and their choice of activities in addition to with their choice of industry.

Chapter 3: Empirical background

1. Introduction

While the first chapter of the theoretical background aimed at reviewing the literature in order to argue for a new framework in entrepreneurship theory, the other chapters (Chapter 2 and 3) focus on explaining the reasons for the choice of a particular methodology used to answer the research questions outlined in the introduction.

The previous chapter (Chapter 2) and this chapter are complementary in order to understand the choice and scope of our case study and its limits. It has given a detailed overview of the chosen sector (the biotech sector) in order for us to gain an understanding of the technological background and the market structure of this sector. Overall, the aims of Chapter 2 were to deepen the understanding of the potential technological context of innovative projects using biotechnology, and also give an overview of constraints present in different health industries in which biotechnologies have applications.

By looking at the aim of the study together with the framework used in the literature review, this chapter argues for the use of case studies since our aim is mainly exploratory and theory generating. Thus this Chapter (Chapter 3) aims at explaining data gathering and development of the case studies from their rationale to their operationalisation. The first section looks at the rationale for choosing the case studies, and explains the research design. It also follows on to the operationalisation of the methodology, by explaining the different steps taken to first identify local firms and second select the firm through specific filters (age, technology specialisation). The chapter finishes with an overview of the cases. The overview of the case studies involves an overview of the region under study in order to describe the regional system of innovation but also give an overview of the firms included in the case studies by providing a short summary of the history and creation path for each of them. This section gives a general overview of the cases tackled in our analytical chapters while also drawing some early conclusions about the representativeness of the sample and the specific characteristics of the firms.

2. Methodology

This section explains the research framework, sector and geographical choice for the case study design. The section then moves to the explanation of the case study design. The study focuses on case studies of 13 start-ups specialised in the Biotechnology / Medtech sector. Even though the purpose of this section is to outline the rationale and main features behind the case studies, each chapter also includes a methodology part that highlights the specific aspects of the case study used, since they are designed to be self-contained papers.

2.1. Research Design

2.1.1. Case study design[36]

Before starting to explain the rationale for the choice of research strategy and design, we will remind ourselves of the characteristics of a case study design and justify how this design is appropriate for our research objectives.

2.1.1.1. Research objectives

The aim of this research is to understand the evolution and steps that innovative entrepreneurs go through during the firm creation process. The work especially focuses on two crucial aspects, which are the decision component emphasised in the entrepreneurship literature (also referred to in this thesis as entrepreneurial agency), and the environmental and technological context in which the firm evolves. The study focuses on innovative firms, thus observations and conclusions from the study will only apply to this group. It is from these objectives that we designed our research, decided on the type of study and on which we ground the choice of the cases.

In order to discuss the best design for the study, we first remind ourselves of the main research questions that drive this work, as well as the research objectives. The research questions are the following (as exposed in the Introduction):

How does an innovative firm evolve during its early life stages and how do entrepreneurial agency, environmental factors and human capital influence the new venture path of development?

How is the evolution of a new venture influenced by…

> *… the transition of a project of innovation between the incumbent organisation and the newly created organisation? Conversely, is the project also influenced by the newly created organisation?*
>
> *... the relationship with other actors and pressures from the environment?*
>
> *... by a change in project leadership?*

[36] The case study design is mainly based on the theory explained by Yin in his book on case study research.

... by the entrepreneur's background?

Thus the research aims mainly at the understanding of the entrepreneurial process, characterised by innovative opportunity exploitation through firm creation, and problems that occur within it. The evolution is studied within the entrepreneurial agency framework that was introduced in the literature review (Chapter 1 section 3). Since the framework has been built from the literature, the study of these processes in the entrepreneurial agency framework is of an exploratory nature. Secondly, this work also involves the study of two co-evolving processes in a systemic manner, which calls for a complexity of interactions between the different components. Thus modelling methods are excluded at this stage. Since our theoretical background included a model of entrepreneurial agency, one could ask if agency models would be of use here. Neoclassical literature (Jensen & Meckling 1976) has already worked on concepts linked to agency problems using modelling methods to understand their power of decision and action. These models involve two types of individual, the principal and the agent, who are bound by a contract. The principal usually hires an agent in order to pursue an action, but this action can be biased by moral hazard problems. Such models involve studying the relationship between two types of individual who have respectively an ownership position and a managing position. This model does not seem fit for purpose here as the entrepreneur is both owner and manager in our cases, and thus this type of problem does not arise here. Other models could help us to understand development paths of entrepreneurs, such as real option models for example. However, the study is more exploratory than explanatory since this study aims at supporting a new framework built from the literature. This study aims to further the understanding of the complexity of the start-up phase by combining the views incorporating technological and environmental determinism and entrepreneurial agency in the creation process. The context and the complexity of the system in which the newly created firm evolves are therefore crucial in understanding the evolution path of the firm. The exploratory nature of the work together with the study of the complexity of the process, implies that we could not predict the parameters that should be used in a theoretical model in advance. Thus even if theoretical models would be a good way to formalise entrepreneurial agency, they will be left to later research, once the exploratory has been done. As the following section shows, the best framework to study complex processes is therefore through case study methods.

2.1.1.2. Strategy of research: why opt for a case study research

This section aims at explaining the details of the case study as a research design. This is done by firstly explaining the specificities of the case study research and its characteristics compared to other types of research. It is followed by a discussion on the design and methods used in case study research. In this way, the characteristics of the design are put into the perspective of the objectives of the study in order to justify the choice of case studies over other possible methods.

According to Yin (1994) there are three elements that should be determinants in the use of a research strategy:

> "the three conditions consist of (a) the type of research question posed, (b) the extend of the control an investigator has over behavioural events, and (c) the degree of focus on contemporary as opposed to historical events." (Yin 1994)

In addition, research design aims at choosing between different types of research strategy, which can be the following: experiment, archival analysis, surveys, history or case study analysis (ibid.).

It is believed that ***research questions*** are determinants in the choice of strategy. In his book Yin differentiates different types of question as follows: "who", "what", "how", "why", and "where" questions. It is argued that "how" and "why" questions are best suited for a case study, experiment or history research. This is due to the fact that these types of questions deal with the operational variables that are unfolded over time, in opposition to studies where one tries to identify frequencies or incidences of one variable in relation, which require quantitative methods (that emerge from question types such as who?, where? and sometimes what?). In our case, the research questions are centred on "how" questions because the work aims at understanding the dynamic process of innovative project development through firm creation and development and the effect of different variables on these processes (i.e. innovative project development and the firm organisational process). The research questions also look at different variables that may explain the differences between the paths of evolution, such as change in the top-management team and environmental factors.

The case design must also take into account to what extend the investigator has **control over the behavioural events** (Yin 1994). Behavioural events ask the question of whether or not the investigator has an influence over the events under study. In some cases the influence of the investigator is desirable, such as with experiments which the researcher investigates the impact of some variables on human action in a laboratory setting. However, in case study design or historical analysis this is not desirable. Finally, the degree of focus on ***contemporary vs historical events*** also has an influence on the selection of case study research. A case study may often be preferred when selecting a study over contemporary events rather than historical events. Concerning the focus of our study, the research objectives once again take a case study style of research. The research objectives aim at understanding a contemporary event, the development of an innovative project together with the firm creation process in the complexity of today's world, in which the investigator has little or no influence on. The case studies are carried out with interviews in retrospect to recent events in the creation of each company. The events studied are therefore contemporary in nature and since the study is done with only retrospective data, the investigator has no influence on the events or the behaviour of the firm during the period of study.

As Yin (2003) has suggested, case study is a research method that is independent in its form of data collection and must therefore be of a quantitative or qualitative nature. Thus the type of data collection used must also be justified. As explained above, the aim of the study is to understand the interaction between the entrepreneurial agency and the contextual nature of the project, by taking into account the complexity of the technology and environment in which the project takes place. This description seems fitting for a qualitative design, as defined by Collins and Nobli (1978):

> "Field studies reveal not static attributes but understanding of humans as they engage in action and interaction within the contexts of situations and settings. Thus inferences concerning human behaviour are less abstract than in many qualitative studies, and one can better understand how an intervention may affect behaviour in a situation"

Thus the qualitative study deals with concrete information, but also focuses on the interactions of the subject within its context and situation, which is the goal of this research. Stake (1995) defines it as an inquiry aimed at understanding rather than at explaining, the latter being a characteristic of quantitative research. Qualitative research (ibid.) also aims at looking at the phenomenon of searching for patterns in expected and unexpected relationships, while quantitative research focuses on the relationship between a small number of variables. Finally, quantitative studies are more focused on outcomes rather than processes (Creswell 2003). The research objectives therefore appeal principally to a case study design with primarily qualitative research methods.

Returning to the gaps identified in Chapter 1, the literature review showed firstly the lack of a process model focused specifically on the study of innovative firm creation. Secondly, the existing literature also lacks a common and contrasted view of the creation process, which includes entrepreneurial agency and technological and environmental contextualisation. This thesis thus studies the complex relationships for the decision making of the entrepreneur in light of his preferences and other factors (technology and environment, markets). The context involves understanding the entrepreneurial agency within a systemic framework, due to the importance of technological and environmental factors. This type of objective suits the study for an in depth investigation, in which a qualitative case study design strategy is the most able to provide an adequate framework for meeting those objectives (Yin 1981; Cassell & Symon 2004). The case study aims at understanding the effects of different variables towards the entrepreneurial agency and thus the firm development path. The study is thus exploratory in nature. The role of this case study is therefore to obtain a better understanding of a process that will lead to the development of new hypotheses and is therefore theory generating (Eisenhardt 1989; Eisenhardt & Graebner 2007).

The above explanation justifies the use of a qualitative case study research in this thesis. Firstly, as explained in Chapter 1, there is a lack of studies looking at the interplay of early path directions, institutions, and technological context. Since the study is exploratory in nature, it is best suited to case study research (Yin 2003). Secondly, the study aims at understanding the role of strategy, decisions made by the entrepreneur and the relative leadership change in the process of building an innovative company. The unit of analysis is therefore the **creation of innovative ventures**. This includes **two main embedded** units of analysis, which are the **firm's main project** that started before the creation, and the **firm** as an independent organisation, especially the organisation process of the founding and management team.

2.1.1.3. Research design: What type of case study research?

After defining and explaining the rationale for choosing the case study design in order to respond to the research objectives, the investigator must justify the type of case study best suited for his objectives. He has firstly to decide between a single or multiple case study design and secondly between an embedded or a holistic design (Yin 1994).

The single case design is preferred when insights in an exceptional case may have impact on theory building (ibid.). There can be several reasons for this choice; the case can be either a critical case, which includes unique details that have been proposed in the theory, or it can be an extreme case or very rare case that explores the reasons for the rarity of its occurrence. Finally, it can be a revelatory case that could not have been studied before. A single case study therefore has to be carefully selected and be proven to have a rare specificity for valuing its study.

On the other hand, a multiple study case design should not require unique specificities in its cases but should sample firms that are similar in some respect. This follows replication logic (Yin 1994). The replication logic entails a design in which cases are selected with regard to their expected results. The cases are selected to obtain similar results in order to conclude that a predicted outcome is not isolated to a case, but valid for many cases. The advantage for multiple case studies is that it is considered more robust for theory generation. In addition, since replication has taken place, the results are considered more robust than single case studies and are also going to generate more accurate theories(Eisenhardt & Graebner 2007). The replication of the case study can be literal when there may be similar results across the cases, or theoretical when there are contrasting results but which can be predicted. Since we are interested in a particular effect resulting from the leadership change in the top management, we opted to introduce diversity in one specific variable in order to see if the results are contrasted by this variable. Cases with literal replication were therefore introduces in which the founding team has the same structure (a business leader takes over from a scientific leader) and some cases following theoretical replication (where there are only scientific leaders or leaders who come from a business background). The justification for a multiple case design is well explained by Miles and Huberman (1994) in the following terms:

> “By looking at a range of similar and contrasting cases, we can understand a single-case finding, grounding it by specifying how and where and, if possible, why it carries on as it does. We can strengthen the precision, the validity and the stability of the findings”

In our case the choice favours a multiple case analysis since the phenomenon studied is not extremely rare (innovative firm creation). The studies are chosen in a specific sector and a specific country to follow replication logic. This can be justified because the technological context and the system of innovation differences may make a significant impact on the cases studied. Thus finding contrasting results, the determinants of the differences may be strongly influenced by their origins. Different origins may give rise to different processes and outcomes. In order to have a fixed point of departure for studying different origins, processes, and outcomes, this thesis focuses on an event, the presence or absence (and if present, the nature of) leadership change in the process of firm creation and early development towards the development of an innovative project.

2.1.2. The case selection

This section explains the reasons for the choice of sector and country for the case study.

The research aims at studying new ventures that have a positive impact potential on the economy through the introduction of an innovation. Two strategies could lead to the choice of firms; an ex-ante strategy or an ex-post strategy[37].

The ex-post strategy would consist of identifying innovative firms that have already introduced a successful innovation to the market, in order to understand their path of development. However, this strategy has two shortcomings. Firstly the firms would be quite old, since these firms

[37] The section on the firm performance in chapter 1 plays a role in the ex-ante vs ex-post strategy, as it discusses what type of ventures are considered to make a difference in terms of growth or competitiveness in the economy.

are identified based on their successful market introduction of an innovative product or service. Since the study is designed around a case study research, and considering the age of those ventures, it is highly unlikely that the firm founders would recall with precision the process and problems arising during company start-up. Secondly, the firms are not guaranteed to be in the same sector or industry when choosing this strategy, since the number of such firms is limited (for instance there are less than one percent of firms that qualify as gazelle firms in a majority of countries including France (OECD 2012)). This is a significant shortcoming because the research strategy aims at following a replication strategy for its case choices, which could be difficult due to the above reasons.

The second method of choosing firms would be an ex-ante strategy. The identification of possible firms that impact the performance of the overall economy could be focused on firms that have a high innovative potential due to their sector of activity. It has been explained in Chapter 1 that some studies have shown a relationship between innovative (R&D intensive) firms and economic growth. This strategy has the advantage of selecting young ventures and also ventures from a given sector.

The **sector choice** is also preferably a knowledge intensive one, which has not yet reached maturity. It must be in its emergence or development phase in order to have a high innovation potential. This can be translated in terms of technological regimes as a high opportunity regime. The life cycle of a given sector is crucial since it influences the chances of success of a firm. As Eisenhardt (1990) stated, growing markets are more suited to a healthy growth for start-up companies because these markets are more stable than emergent and mature markets. To sum up, this means that the firms have to be innovative and in a knowledge-intensive sector that has not yet reached maturity.

The choice of the biotechnology sector emerged for several reasons. Firstly, this sector was chosen since it is a knowledge intensive sector. The biotechnology sector is among the science based sectors such as chemistry, scientific instruments and new materials sectors. Science based firms, according to Pavitt (1984), are R&D intensive as the main source of their technology, and aim at a quick development of science and innovate as a principal activity. Since one of the criteria for the choice of our study is to understand the co-evolution of an innovative project together with the firm early development, the chosen sector should produce firms aiming at developing product innovations, which is usually the case for knowledge intensive sectors.

Secondly, the biotech sector is still in the growth phase of its life cycle (Ministère de l'économie, des finances et de l'industrie 2011). Many technologies developed within this paradigm are still in expansion. Chapter 2, section 4 has also shown how the different industries of application of health biotechnology have markets in expansions. Health applications in the biotechnology sector are still growing both in terms of their pharmaceutical demand and also in their related sectors, such as nutraceuticals and cosmetics. Chapter 2 emphasised the range of application and industries in which firms can find potential consumers. The fact that this sector is still in expansion in terms of life cycle, together with the fact that many of the industries of application have growing markets, provides an environment adapted for start-ups to survive in and also have the potential to grow. Therefore one can expect to find a significant number of firm creations in this sector.

Thirdly, the different industries of application of the biotechnology sector vary in terms of regulation and value chain (cf. Chapter 2). One of the main domains of application is the pharmaceutical industry, which has extremely constraining regulations and thus involves high-risks technological projects. This can be an advantage in our case, since the study is seeking to understand the impact of the environment on the firm early evolution. A second advantage of this variety of industries of application lies in the fact that other industries have a less constraining environment, including the diagnostic industry, the cosmetic industry, or firms providing services. The length of time to market in these industries is therefore shorter, and involves a lower risk in their development. This variety will give us the ability to nuance the effect of the environment between drug discovery firms and other firms and understand to what extend the environment can have a role in the firm early life stages.

Finally, public science plays a specific role in this sector. Public science was the first to provide the main breakthroughs that gave rise to the opportunities present in Biotechnology, but also a high number of biotechnology companies emerge directly from science developed within university. Compared to the semiconductors sector and other high-tech sectors, the contribution of academic entrepreneurship to biotechnology companies is quite prominent (Shane 2004; Oakey 1995; Pisano 2006), but a number of biotechnology companies also emerge from large pharmaceutical spin-offs. Therefore, this sector can provide us with both firms that emerge from the private sector, such as spin-offs of start-ups, and spin-offs of large pharmaceutical companies. Additionally, it is also one of the only sector that provides us with a high number of university spin-offs. This variety of background therefore reinforces the choice for the biotech sector, since the aim of the study focuses partly on how the entrepreneur's background influences the firm's strategy.

These reasons make the choice of the biotechnology sector particularly attractive for studying the early evolution of innovative firms under the entrepreneurial agency framework.

The issue of variety in the background of entrepreneurs in the sampling choice is a determinant in the choice of the firms. As stated in the above section, the choice of the cases should follow a replication strategy in order to reduce variation between cases to a minimum to give consistency in the results. The cases have to be chosen based on the same system of innovation, where institutions such as financial organisation, regulatory institutions and entrepreneurship support organisations are similar. The study therefore focuses on newly created firms originating from a single cluster. In this thesis, the term cluster is used simply to designate the co-location of firms. Other characteristics, that various authors have taken to be further indication or qualification of the existence of a cluster, will not be considered. The choice of a single cluster of this type minimises the geographical, institutional and environmental differences between ventures. This cluster would preferably be dynamic (with a high rate of firm creation) and would benefit from a strong academic as well as industrial background.

The Alsace BioValley cluster fits the above conditions. The cluster benefits from two developed networks; an academic one and an industrial one. The cluster hosts a strong university whose chemistry and biology departments are renowned worldwide. The cluster also has the advantage of being located close to the Basel region, which has a large population of headquarters of large pharmaceuticals firms. The final interesting characteristic concerns the local enterprises, which have been growing since the late 1970s. This makes this cluster particularly interesting to study because start-up founders have a wide range of backgrounds, and the cluster provides the opportunity for comparison between the firms that spread out from different institutions. The specific details of the cluster are further developed in section 3.1 of this chapter.

2.2. Fieldwork and collection of data

The fieldwork data collection has the followed two steps. The first subsection focuses on the first step, which is the identification of firms suitable for being included in the case studies. It focuses on data gathering to build a database that covers firms in the BioValley cluster. This gives us an overall idea about the population of firms and their characteristics in the cluster, which is useful in order to identify suitable firms for case study analysis. The second subsection explains the rationale behind the firm selection, which is our second step. This subsection also explains how the data has been collected (through interviews) and analysed.

2.2.1. Data collection

The first step of the research strategy lies in the identification of firms that are potentially suited for case study analysis. The data collection therefore focused initially on the identification of the existing firms located in the chosen cluster. This data collection has also been used in the past for analysing the BioValley cluster for a European Project called AEGIS, on which a paper was based regarding the evolution of co-publication of the ABV firms through time and space[38].

In order to start building this database, the work consisted in identifying firms located in the cluster. As there is no official list of firms, the database was built by combining the different information available. The main input came from a previous list of companies registered as member of the Alsace BioValley cluster association, used in previous research of the BETA (from the university of Strasbourg), and dated from 2008. This database included a variety of firm which were loosely connected to the life science field (including firms that are not relevant to us such as suppliers, consulting firms, marketing firms, subsidiaries of large companies). This data was enriched through time by research from different websites or databases such as Factiva (which holds articles informing about activities of the Alsace BioValley cluster), the local incubator website (which gives a description of all firms recently incubated), the website alsaeco (which is built by the local chamber of commerce and includes all the companies registered there), documents about grant funding for firms specialised in Biotechnology, and finally information found on the cluster website. The selection criteria for firms in the various databases found was based on the sectors in which they were active. The enterprise had to be active in biotech or medtech related activities. All the above information led to the constitution of a database containing 223 firms either registered with the Alsace BioValley organisation or active in the biotech/medtech sector.

For the entire set of firms, complementary information was searched for in the databases cited above. The information ranged from start and death year (if applicable), address, size of the firm and publications, patents or collaborative project records (national and European projects)[39]. Some of the evidence from this paper is described in the section 3.1 dealing with the cluster background and characteristics.

Concerning the data used for selecting the cases, a subset of the data was extracted for the selection, which included firms that were under 10 years of age in 2012 in order to include young firms only. The population identified was composed of 72 firms.

In order to help with the further selection of the firms, experts from the biotech sector in the region, and two firm founders were interviewed. These interviews are further developed in the next sub-section. One of the objectives of these interviews was to improve the firm selection

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[38] For more information you can find the paper titled "Evolution of the Alsace Biovalley cluster: An analysis based on co-publications by young innovative firms". Available at: http://www.aegis-fp7.eu/index.php?option=com_docman&task=doc_download&gid=113&Itemid=12
The data collection was done by the author of the thesis.

[39] e.g. Cordis database, Eureka Database, and IMI projects

process, among other objectives. These interviews resulted first in the recommendation of firms from the region that had a high potential impact, and therefore would be interesting cases to study. Secondly, the preliminary interviews with the two firm founders (of a 10 years old company) showed that firms that are 10 years old may still be too old to recall detailed information about firm creation. Therefore, we decided to limit our search to firms created in 2005 or after.

These interviews helped us to further reduce our sample of firms. A few new filters were introduced after gathering further information from each firm. The sample was reduced to firms that were still alive at the time of the interview. The original sample also included firms active in consulting activities, marketing activities or in green biotechnologies, but for replication purposes we also eliminated these firms. As explained in the research design, the case studies are based on replication design and so the selection of the case was mainly based on science dealing with health issues, and preferably operating in the biotech field rather than medtech one. The biotechnology field of the cluster is more developed and therefore produces more firms than the medtech sector, which explains the reason for its choice. This sampling also excluded implantation of an existing firm into the region or the local creation of plants from larger firms. Finally, we decided also to exclude firms that were created before 2005.

This selection considerably reduced our sample to 21 firms that followed all the criteria. All of the 21 firms identified were contacted for interviews, of which 14 agreed to be interviewed. These firms are represented in table 3.1.

Table 3.1: Firms contacted for interviews[40]

	Contacted	Interviewed
University Spin-off	14	9
Start-up Spin-off	5	4
Large company Spin-off	2	1
Total	21	14[41]

Table 3.1 shows the cases that were contacted and the ones that were interviewed. They are organised into three categories: university, start-ups and large company spin-offs. This classification is based solely on the secondary data gathered from the firms. For each of these 21 companies, information was gathered about founding teams together with the previous activities of these

[40] The characterisation of the parent organisation emerges from the information on leadership teams, since the project technicalities are as yet unknown. A later table shows the differences between the project and leadership team for characterising the parent organisation of a company.
[41] 14 firms were interviewed, while only 13 were taken into account in our case study, as one of them was at a too early stage to be considered as useful.

founders. The previous activities of the managing founders (i.e. founders who still have a predominant role in the management of the company) were therefore identified and helped to build the classification of these companies. Most of the firms identified emerged from local universities (14 of them), and in most cases from the University of Strasbourg (only one emerged from a research institute in Mulhouse). We also identified 5 firms in which the managing founders came from other start-ups located in the region (all of them are start-ups in Biotechnology), and finally two firms were identified that had founders with a long experience of working for a large pharmaceutical industry.

The selection of the firms aimed also at including a variety of founder experience in different fields and also a variety of parent firms from which these firms emerged. The idea was to include firms emerging from university, firms coming from other start-up companies, and finally firms originating from large pharmaceutical companies (that are limited to the Alsace region – only 2 identified). Following the interviews, one project was excluded from the study because this project was too early in the entrepreneurial development, since the scientific founder had just started to build his management team and therefore, the firm strategy and activities were still unclear. 13 projects were therefore selected in which the leadership team came from different organisations: 8 of them came from public research organisations (7 university of Strasbourg, 1 from a research institute in Mulhouse), 4 from previous start-ups and 1 from a large pharmaceutical company located in the Basel region. The connection to the parent organisation was defined by the team at creation, which was found in secondary data. Later in the presentation of the cases we will contrast this view by adding the provenance of the projects developed in the start-up.

While not every firm identified could be interviewed, one could argue the similarity between the cases interviewed and the cases identified that could not be interviewed in order to further justify the replication design. Firstly, the subset of cases interviewed includes more than half of the firms identified and also represents firms from each of the different categories identified. In the 7 cases not interviewed, the year of creation ranges from 2005 to 2012. Two of these cases were created in 2012 and therefore were in the administrative creation process at the time of the interview. Therefore, these two firms may have had a limited development and thus be in a too early stage to talk about their creation experience. In the unstudied subset, the firms created before 2012 included three diagnostics firms and two firms based on technological platforms or services. Both these technologies and models are represented in our set of cases. Therefore the firms interviewed have similar counterparts in terms of founding team composition and industry of application. This makes it a strong set of firms for generating results for young firms in the cluster, because the firms not interviewed are similar in characteristics to the ones interviewed.

The next subsection describes more specifically the general data collection and analysis based on the interviews.

2.2.2. Interviews

Data gathering for the cases was divided into two steps. The first step consisted of interviewing experts in the field of company creation, who had dealt with biotechnology companies. This step had two objectives, firstly it aimed at gaining an understanding of the system of innovation and secondly it helped to select interesting cases by asking for referrals to relevant cases, thereby creating a snowball effect. The second step consisted of interviewing the entrepreneurs, which consists of the main data used in the analytical chapters. The second interview design was influenced and refined with the help and comments gathered during the interviews with experts.

2.2.2.1. Experts' interviews

The main source of data comes from interviews carried out with the selected firms' founders. However, in order to prepare the questionnaire/interview for a particular round of interviews, the fieldwork firstly started with an initial round of interviews aimed at understanding the problems that entrepreneurs are experiencing. The first round therefore targeted a set of experts active in helping, or being involved in, the life science start-ups eco-system in the region.

In this framework, 17 experts were interviewed from different institutions, such as the Biovalley, the incubator SEMIA, Oséo (the French agency that is mandated to finance innovation), Business Angels, and other regional support organisations. Two of these experts were entrepreneurs. The interviews were designed as semi-structured interviews. The first part of the interview consisted of asking about the contribution of the activities of the interviewee's organisation in the innovation process of start-ups. These questions coupled with questions referring to other central organisations helped in understanding the regional system of innovation and central actors and institutions. These interviews were designed to identify the general steps of development of a high-tech organisation by asking questions relating to the knowledge needs of the founding teams and the new firms' financial needs. It also asked questions related to the problems that start-ups encountered while trying to generate growth in their early life. These questions shaped the design of the second round of interviews. The experts' interviews gave insights on the relevant topics for start-ups including additional questions that could be asked but also advice on the formulation and comprehensibility of the questions for improving the second round of interviews.

Finally, the interviews with experts ended on a discussion about promising start-ups or start-ups having problems in the region, in order to select cases to interview in the later round. This last discussion aimed at finding emerging cases of innovative firms that had the desired profile for the case study, and which had a high potential for success according to the interviewee. This method helped to preselect some cases of firms to interview. The interview with entrepreneurs included two founders of a firm started in the year 2002. From these interviews emerged the need to interview firms that were created more recently than 2002, which helped to define a threshold for the selection of firms.

As a result of this consultation, the main triggering points were identified, which could feed into the interview guidelines for the second round and could help to avoid technical jargon.

2.2.2.2. Entrepreneur's interviews

The entrepreneur's interviews were divided into two rounds. The first round of interviews targeted 4 firms and aimed at a pilot study for the semi-structured design of the interview, combining insights from theory and advice from the experts. The second round of interviews of 10 firms then followed with a semi-structured interview.

Concerning the interview design, it aimed at tackling 3 issues. The first part focused on the development of the scientific project before and after creation, the funding and financing issues, and the market interactions. The second part of the interview aimed at identifying the evolution of competences in the management team during firm creation. The questions aimed particularly at identifying desirable competences for a management team and the strengths and limitations of people with a scientific, managerial or industrial background. The final part of the interview focused on the relationship that firms maintained with other institutions or organisations and also their activity in terms of property rights. The interview design also took into account the different points of view that could emerge from people with different backgrounds. The division between founders coming from an academic background and founders coming from an industrial or managerial background were discussed in these interviews. Thus, where possible[42], founders from a scientific background and a business background were both interviewed. The interviews were limited to one hour in order to maximise the chance of getting interviews with firm creators, who often have limited time available for activities not directly benefiting the firm.

[42] When scheduling interviews, a question was asked about meeting a second founder, preferably from a different background, however this was not always possible due to the availability of the founders and their willingness to being interviewed; thus for some firms only one founder was available for interviews.

The number of interviewee per case is of two (or one when two could not be interviewed in 5 of the cases). The low number of interviews per case can be explained by the subject of study, which is the innovation that transforms into a firm creation. In order to understand this process, we needed to interview people that have knowledge about the innovation project as well as knowledge about organisation genesis. Thus the potential interviewees are limited to the number of founders of the firm. This could be a problem if the interviews were oriented towards collecting subjective information that could be subject to interpretation by the interviewer. However this is not the case, since the study cases are directed towards the understanding and chronology of events which is based on events and facts only, and thus not subject to interpretation by the interviewee or the interviewer. In addition to the triangulation with other secondary data collected, the low number of interviews still provides the opportunity to gain a detailed view of the process in terms of events in the development of the project and firm creation.

As noted earlier, a pilot round of interviews was conducted on 4 firms in order to test and validate the issues discussed in the interviews. The questions were mostly well understood, the timeline was realistic and the fact that two people were interviewed gave complementary views on events that happened in the firm. The design of the semi structured interview only evolved marginally, and thus the pilot interviews were kept in the final study. The changes concerned the rephrasing of some questions that were not well understood and the reordering of the questions. The only significant issue that arose was the age of the firms interviewed. The interviews with two founders of the oldest of the 4 firms, created in 2005, showed that the creators had started to have limited memories of the issues faced at creation time and problems that arose. The choice of interviewing firms created after 2005 was therefore supported by the pilot interviews.

In the 17 remaining enterprises, all of them were contacted for the case studies. From this sample of 17, 10 accepted to be interviewed. Overall the study therefore included 14 firms interviewed, including the 4 firms interviewed during the first round. From the 14 firms interviewed, for 9 of them, two people could be interviewed, but for 5 of them only one could be interviewed due to the limited availability of the other members in the founding team. One of the firms selected was in its creation process (therefore was not yet created in the administrative sense), which led to limited insights about the evolution of the project through firm creation, and therefore this case was discounted for the rest of the study.

Triangulation of the data was assured by two means. The first means was assured with the design of the interview, since the interview for each case included two of the founders where possible. Secondly, secondary data was gathered from press releases and from firm databases[43] in order to compare facts given by interviewees on topics such as size of the firm, financing contributions, partner organisation, and property right applications.

The cases are described in further detail in the next section. This description is divided into two parts; the first part relating to the chosen region and the second part relating to the firms involved in our case study.

3. Cases overview

This section aims at giving a descriptive background of the regional innovation system from which the firms in our case study were picked. The first sub-section aims at giving an overview regarding institutions that operate in this innovation system, the general structure and the organisation of the cluster, the institutions supporting entrepreneurship such as incubators, other supporting institutions and financing organisations. This sub-section ends with a knowledge base overview of the cluster through the description of the research community. The knowledge base section is divided into two parts. Firstly, it reviews contributions that explain the historical evidence of the knowledge evolution of the region. The historical evidence also includes a section about the Swiss region of Basel, because even though it is not in the regional boundaries of the study, the dynamic of the Basel region has an influence on the research community and the creation of start-ups in the Alsace BioValley region. Secondly, the section also reviews data on co-publication to help us understand the knowledge network of the firms in the BioValley today. The second sub-section moves onto the firms chosen involved in the case studies in order to give a short description, such as their history and creation process.

3.1. Alsace Biovalley: An overview[44]

3.1.1. Policy initiative

The Biovalley organisation has a dual history consisting of bottom-up actions and top-down policies. This section will firstly look at the bottom-up organisations that emerged from a local willingness to develop a competitive transnational region based on their strong knowledge base. This knowledge base is firstly based on the chemistry and pharmaceutical disciplines and later on the biological sciences. The top-down policy has also given the region the opportunity to create organisations for the promotion of specialised regional development. This section is supported by

[43] Through the processes mentioned in the database building section.
[44] The data and part of the analysis used for this chapter was done for a EU project AEGIS.

data found on websites for the different cited organisations, articles from the local press and also interviews with stakeholders.

3.1.1.1. The emergence of a trinational cluster

The history of the BioValley has multiple facets because the emergence of bottom-up initiatives is not fully unified and so different initiatives have emerged. The first and most well-known is the Swiss initiative that led to the creation of the trinational cluster.

The trinational cluster initiative started in Switzerland around the Basel area in the 1990s. The creation of the organisation coincided with the merger of two pharmaceutical companies Ciba and Sandoz. This merger resulted in major job losses worldwide (Grimond 1996) and locally[45]. The main actors at the time of the BioValley creation were the entrepreneur Georg H. Endres and the doctor Hans Brinner. The role of this newly created organisation was to promote firm creation and the development of the Biotech-Pharma sector, which was in continuity with the specialisation of the region at the time. In fact the Basel region hosts a large number of pharmaceutical company headquarters, such as Novartis, Clariant and Hoffman-Roche, which gave the region an industrial advantage.

The Swiss association[46] was the leading actor in the project of building an international organisation for supporting a cross border cluster organisation. The trinational cluster was then created in 1998 with a cluster association in Alsace (France) and another in the Fribourg region of Germany. Since then the trinational cluster has benefited from Interreg financing, which is a European Regional development fund targeting interregional cooperation initiatives across Europe, in order to develop the trinational biotech-pharma activities (1997-2001: Interreg II, 2002-2007: Interreg III, 2008-2012: Interreg IV)[47]. There are about 600 firms in the trinational cluster as well as 10 universities and other institutes dedicated to the life sciences.

3.1.1.2. The French historical industry and regional policy

The French BioValley association was then created in 1998 with the help of the “Conseil Général”[48]. The creation of this organisation was in line with its sister institution in Switzerland and

[45] An interview with an expert insisted on the fact that the job losses resulting from the merger was a determinant factor for the creation of the company.
[46] Association is here used to denote the administrative organisation responsible for the development of the local Swiss cluster.
[47] BioValley.com | About BioValley | Profile & History. Available at: http://www.biovalley.com/content.cfm?nav=3&content=13. Accessed January 12, 2012.
[48] Council of a territorial zone called ‘département’

came to form the trinational BioValley with the help of the Interreg Program II (1994-1999) for developing a TransBorder network.

The top-down cluster policy appeared later in France. The cluster policy in France is called "pôle de competitivité" and was launched in 2005. This policy was a continuation of another policy based on productive systems called "Systèmes Productifs Locaux" or SPL, which was put in place in the 1990s. In the 1990s much effort was put into these SPLs to reinforce their networking ability. The purpose of this new policy objective was to create organisations that can foster relationships between actors from the private and public sectors with the objective to foster innovation and ultimately competitiveness. This resulted in the French state implementing a policy on cluster support in 2002 that led to the creation of another association in 2005 responsible for managing the biotech cluster, called "Pôle Innovation Thérapeutiques". This was one of the 105 projects that were accepted for financing on a national level. It must be noted here that this initiative resulted in the creation of a second organisation responsible for fostering networking between firms (but with different tools).

3.1.1.3. The Birth of Alsace BioValley as a convergence of the two initiatives

In 2008 the two associations (the top-down and bottom associations that are created to deal with activities of the cluster) merged into one because both of them had similar objectives. Since then, the French cluster association has been known as Alsace BioValley.

Since its establishment, the ABV cluster has developed different strategies over various periods of time. At the beginning of its life, from 1998 to 2002, the main objective of the cluster association was to structure the local network so that local firms and laboratories could collaborate together. In the following period, from 2002 to 2004, the cluster association wanted to be recognised at an international level, and so this was the cluster's "international branding" period. Once the cluster became internationally visible, it focused its activities towards benefiting the local firms from that brand (after 2004). It also developed consortia with Israel and Canada to finance research collaboration between firms and research organisations located in those regions. However, these latest developments of the cluster strategy may not yet be visible since they were implemented after 2006. One can therefore expect that the ABV firms improved their local network from the year 2000, and their international network from 2005[49]. Finally, the Alsace BioValley as a '*Pôle de compétitivité*' has a role of intermediary for finding R&D subsidies by attributing a seal of approval for FUI project candidates (*'Fonds Unique Interministeriel'*).

[49] The information in this paragraph was based data gathered from the Alsace BioValley website together with the interview of the head of the cluster organisation.

3.1.2. Institutional support of technology transfer

The activities in the cluster have a long standing history with the university in terms of technology transfer, firstly with the technology transfer office (Connectus) and then its incubator (SEMIA). Other public and private organisations have also grown to facilitate entrepreneurship in the region. This section summarises the history and development of such organisations and gives an overview of their role in innovative venture creation.

There has been a long-standing activity in developing actions to support technology transfer and innovation, firstly by universities and then by regional public institutions. The first technology transfer institution in the local university was created in 1987, and there has been much development since. The most recent institutions could be summarised by the creation of a common and regional office for technology transfer of the university in 2006 and the creation of an incubator in 2000.

Created through a national policy in the 1980s, CRITTs (Regional centre of innovation and technology transfer) are semi-public organisations whose goal is to facilitate the transfer of technology from research organisations to the industrial world, especially SME's. This is achieved firstly by prospecting for firms that may have a technological need and secondly through technological delivery for firms that do not have the specific competences to develop the technology in-house. There are a total of 6 CRITTs in the region (optics and imaging, optics and laser, materials, agro-environment, agro-food and mechanic engineering). In the BioValley cluster the most active related CRITT is the one focusing on agro-food.

Conectus Alsace is the Technology transfer office of the University of Strasbourg, which was created in 2006. Its main objective is to help the public research developed within the university to be exploited and transformed into innovation, and as a result makes the connection between university and industry. From the beginning this organisation was shared by different public research organisations such as Inserm, CNRS, Insa and the university hospital, in addition to the university. The organisation obtained the support of a national French program that upgraded its status to SATT (société d'accélération de transfert de technologies). This recognition gives the organisation a juridical status, financial opportunities and a clearer model. Conectus already financed 45 projects for around 5.3M€, and has helped to create 12 enterprises.

The incubator[50] SEMIA was created in 2000 as an internal project at the University of Strasbourg[51]. It was created mainly in order to help the projects of start-ups in the health and

[50] Sources: Savoir(s)-October 2010; Interviews with incubators and entrepreneurs; see section methodology.

biotechnology sectors. Later, in 2004, the organisation became associated with the region and broadened remit to include any firm creation project emerging from research. Its role ranges from business office allocation to coaching in terms of business plan development or applying for grants. This organisation has a very good record of helping innovative start-ups to get national grants (*concours* in emergence and creation development, this is explained in the next sub-section). It also includes some financing possibilities for legal help and also business training. The incubator also has a willingness to strengthen the network of start-up companies by introducing a program of mentoring between new firms and more experienced entrepreneurs. The incubator seems to play an important role in the cluster, since every firm located in the Strasbourg area has benefitted from their services and found them useful in obtaining early financing, and in some cases also business training.

These organisations are not the only ones to support innovation and entrepreneurship in the region, since there are also other public, semi-public and private organisations involved in those activities. There are public organisations whose purpose is to support local innovative firms. For example, Alsace innovation is an organisation that aims to support innovative firms by consulting with them to help them maximise their chances of realising their innovative projects (in terms of business models, marketing, legal, managerial and organisational guidance). They also aim at building a strong network in order to help firms find the right partners, and finally support firms in their search for funding. This institution was created in 2012 as a result of the fusion of two institutions specialised in this kind of support (the regional agency of innovation (ARI), created in 2006, and the European Centre of enterprises and innovation (CEEI), created in 2001). The ARI was created in the Alsace region and was previously focused on developing regional strategy of innovation by firstly building projects within the cluster structure or CRITT structures, then by helping firms to find financing and eventually by having a consulting role. The CEEI focuses mainly on helping and performing consulting for firms that wish to innovate (including the established or new firms) and also organises an annual competition rewarding innovative projects.

On the business side, there also exists a private organisation (Wikane) with a mission to help young enterprises grow through consulting in strategy, finance, marketing and organisational structuring. Some of the consultants are also involved in business angel activity, and therefore high-risk companies who seek business angels financing can get the help of experts from this consulting network.

[51] It was created at University Louis Pasteur, which merged with two other universities in 2009 to form the University of Strasbourg. We only refer to it as University of Strasbourg for coherence and understanding purposes.

Besides these organisations having a role in technology transfer between the university and the industry, there is a growing pool of organisations focusing on investment towards start-ups in their early life stages, which will be presented in the following section.

3.1.3. Financial support available for start-ups

Besides needing institutional support for technology transfer, firms in their start-ups phase also need large investments, especially in Biotechnology. This section therefore focuses on the support available for new companies in terms of financing. Most firms start their activity with "love money" (money provided by founders' friends and family), which in most cases is not sufficient for the investments required to start the activity of the company. The biotechnology sector therefore needs financial help in order to get their company running, and there are various forms of help available. Public as well as private organisations are mentioned in order to show the financial offers available for local start-ups firms. The institutions either aim at supporting entrepreneurship activities, innovative activities or just investing in potentially high value projects. All organisations mentioned are organisations that have a local office in the cluster or relationships with local firms.

Starting with the organisations supporting entrepreneurial activities, two of them propose financial services in their offers. The "SODIV" is an organisation that aims at providing help activities that create employment. It was originally created by the French State in 1985 in order to sustain regional development after the closure of the potash mines. Today, the SODIV still invests in employment creation through entrepreneurs' projects under the condition that the newly created firms create a number of new jobs. The financial support takes the form of equity loans, used in general for leveraging more funds with other private investors. Currently the SODIV is financing eleven projects in the life sciences, four of which are among our case study sample. The second organisation aims at helping entrepreneurial projects is the "Réseau Entreprendre". As its name indicates, the organisation in based on a network (*Réseau* in French) of established entrepreneurs, who are willing to share their experience with new entrepreneurs. The Réseau Entreprendre was created 25 years ago in another region of France and has since grown inside France and has begun to grow internationally. The support provided by this association is firstly project oriented through the tutoring of newcomers by more experienced entrepreneurs and also by organising workshops on different subjects that might help new entrepreneurs to develop their enterprise. On the financial side, the association provides a loan service to its new members. The organisation can lend up to 45 000€ free of interest; the money comes from other members in the network. The Alsace Branch has already helped 65 new firms, including five in the Biotech cluster and one from our sample. These two organisations are not focused on innovative or high-tech companies, which explains the low number of participating innovative firms compared to the overall number of firms helped.

Continuing with organisations dealing with innovation, the French state created Oséo in 2005 in order to support innovative activities mainly through financing. This public organisation has several financial offers available for new firms. The first takes the form of a grant awarded through a national *concours*, which many new biotechnology projects try to benefit from and is targeted to innovative projects that could lead to firm creation. The *concours* has two categories, which are "émergence" and "création développement". The first concerns innovative projects in high technology that may lead to firm creation and awards the winners a grant that can be up to 45 000€ and should be spend on the move towards application, which is usually market search for the project developed. The latter can grant funds up to 450 000€ and helps newly created firms to develop their research projects. This money is usually used for leveraging more funds with other financial institutions. Eleven firms in our case study benefited from this funding.
Besides these awards, Oséo also offers other financial services. It firstly acts as a bank for giving loans to innovative firms when other lenders do not want to offer their services. They can also act as a form of security for helping the private banks to provide more secure loans. The financial help can range from bank loans with a 0% interest rate, equity loans, a cash advance, or a warranty for repayment when firms borrow from private banks. This second function is oriented towards complementing the private system in order to share risk between institutions when private banks do not want to take the risk of lending on their own.

Finally, the trend of private investor's providing equity funds has developed more intensively over the last 15 years. There are three main funds that have provided towards some of the firms studied. These are Alsace création, Alsace Amorçage and Alsace Business Angels. Alsace Création was created in 1998 and aims at supporting any newly created company (innovative, high-tech or otherwise) or at taking over other companies. It is jointly owned by public and private partners, such as private banks, insurance companies, local firms and even other companies. The investments in equity funds, which the organisations can make, range from 100 000€ to 750 000€.
Created in 2005, Alsace Amorçage aims at investing specifically in high-tech firms during the early stage of their creation. This organisation is jointly owned by two other organisations, the CDC enterprise (part of the Deposit and Consignments national Fund) and the Region Alsace.
The newest is Alsace Business Angels, which was created in 2006. This organisation is financed only by private investors and former entrepreneurs, who prior to its formation thought that the existing local offers of financing options for innovative projects was insufficient. Since its creation this fund

has already financed 8 projects with an overall budget of 890 000€, three of which are included in our case studies.

3.1.4. The Research Community

This section reviews the characteristics of the Alsace region in terms of research and industrial background. It also includes a sub-section relating to the Basel region, since this region has an influence on the industrial dynamic in the Alsace.

3.1.4.1. The Strasbourg region

The Strasbourg region has a longstanding history concerning the scientific needs for developing a Bio-pharma network. Science is known to be a relevant factor in developing a science-based network of firms and attracting certain types of industry. It is therefore useful to examine how the region has developed strong knowledge through the different industries of chemistry and biology in their research institutions. This is the purpose of this section.

Since the 17th century the region has been strong in both the academic and the industrial sides of the alchemy sciences (e.g. chemistry of metals and sciences linking chemistry to curing diseases). On the academic side, Strasbourg has been an outstanding pole of research in terms of chemistry and pharmacology throughout its history. On the pharmacology side, Strasbourg already had a school of pharmacy as early as 1803. However, the chemistry and pharmacology was expanded between 1872 and 1944, during the period of three wars, where succeeding German and French universities had tried to showcase their best research.

The chemical and pharmacy industry (Stadler & Harrowfield 2011), as well as local industries such as the petroleum and textiles, have contributed to develop the current chemistry excellence of the region (Olivier-Utard 2003). Even today the Alsace region has a specialisation in chemistry. This strength and history in chemistry is still visible today, as seen by the strong pharmaceutical industry in Basel and the chemistry scientific excellence in Strasbourg (Stadler & Harrowfield 2011). For instance, Schmiedeberg was recognised as the father of pharmacology by creating a field of study that tested the physiological effects of chemical compounds. The regional trajectory shows an important specialisation in chemistry and a growing interest in biology. The three universities located in Strasbourg recently unified in 2009. This merged university is composed of a large number of faculties and institutes as a result of its heritage.

On the industrial side, numerous natural resources and also industrial activities have given rise to collaboration between the industry and university. Chemistry knowledge gave rise to the exploitation of local petrol fields and potash mines. There was growth in the textile industry in the south of the region because this industry required specific competences, especially for working with dyes. The local university therefore provided a curriculum adapted to the needs of the local industry.

Alsace Biovalley has several strengths necessary for building a successful biotech-pharma cluster. The first lies in the leading and well recognised local research community, which has many specialised competencies and research fields needed in the pharma-biotech sector. It includes two universities, Université de Strasbourg and Université de Haute Alsace (which has been associated with the university of Strasbourg in 2013), which include many different faculties and laboratories relevant for the pharma-biotech sector such as medical faculty, pharmaceutical faculty, IGBMC (Genetic, Molecular and cellular Biology Institute), IBMC (Molecular and cellular Biology institute), Chemistry faculty, the Supra-molecular engineering Institute, the biotechnology school and the Mouse clinical Institute among others. The local biology and chemistry research has also been rewarded with several distinctions, including three Nobel prices in 1987, 2011 and 2013.

The cluster has two main sectors of activity, the first being medical technologies (including medical devices, imaging, robotics...) and the second focusing on the pharmaceutical market. The medical technology sector includes approximately 260 firms and has 6 dedicated research laboratories. The pharamceutical sector employs 18000 people over 130 enterprises and 20 dedicated laboratories[52]. In these firms there are a number of subsidiaries from big companies, such as Roche, Lilly and Bruker, a number of start-ups companies, approximately 46 created since 2005, and also established firms created locally, such as Transgene, Forenap and Codgene.

3.1.4.2. The Basel Region

The section explaining the choice of the cluster for the case study stated that the Basel region in Switzerland (adjacent to the Alsace region) has a strong pharmaceutical industry, which has an influence on the activity in neighbouring regions. Indeed, the Swiss region has a long standing history in the pharmaceutical industry that started at the end of the 19th century. Three of them were established in the 1880s starting in the dyestuff products, which were Ciba, Geigy and Sandoz (Landau et al. 1999). Hoffman-La Roche shortly followed. The dyestuff industries were first to specialise in chemistry in order to produce dyes for the textile industry. The dyestuff companies had opportunities for expanding their market during the First World War due to the weakening of the German dyestuff industry (ibid) (for a better understanding of the specialisation of these companies refer to Landau et al. 1999 p 44-45). Until the 1920s these companies were therefore specialised in

[52] Alsace BioValley. Entreprises des Sciences de la Vie-Santé en Alsace. Available at: http://www.alsace-biovalley.com/fr/Entreprises-des-Sciences-de-la-Vie-Sante-en-Alsace-51.html. Accessed January 12, 2012.

chemical products due to the weakening of the German industry. The transition to the pharmaceutical industry was not straight forward. Firstly the conversion of the industry towards pesticides and secondly the strong links with local universities gave these companies a way to diversify in the pharmaceutical sector, and later to focus on the process of drug development.

More than a century of the chemical and later pharmaceutical companies has therefore had a role in the formation of the cluster, which became especially competitive towards competition during the war periods. After many years of evolution within the industry, including fusion and acquisition, the performance of these companies is competing strongly with the world leading companies in the pharmaceutical industry. Novartis was the third largest pharmaceutical company in terms of revenue with $37 billion, and Roche was fifth with $34 billion in 2006 (Gassmann et al. 2008). The Basel region in Switzerland has therefore given the region an important pool of labour with competences specialised in scientific and industrial knowledge in the pharmaceutical industry.

3.1.5. The research network in the Strasbourg region

The previous section showed the strength of the local university in the region, with a long standing history in chemistry but also pharmacology. It also showed that there are strong interactions between the university and industry in the chemistry sector. This chapter has also emphasised the willingness of local actors to develop the industrial base of the region by creating numerous organisations supporting innovative industries through legal consulting and financing mechanisms.

From the science point of view, the biology and pharmacology knowledge developed by the university is substantial and seems to be growing strongly at a regional level. The industrial sector in biology has also been growing since the early days of the biotechnology sector during the 1970s, at the same period that it started to grow in the US. This section therefore aims at understanding the role of the university in terms of knowledge connections with existing firms in the cluster (measured through publications).

Methods. This sections aims at studying the relationship between the local biotechnology sector and the university laboratories in order to see if the historical connections linking the university and industry are also valid today. Publication data was examined at the organisational level for local firms specialised in biotechnology.

Local firms in the cluster were identified for the study by several means, such as a list of firms given by the local cluster organisation, the local incubator website and Alsaeco (a database of firms in the region from the Chamber of Commerce). The database included firms specialised in the biotechnology sector or related R&D sectors. This first search aimed at sampling the firms' characteristics such as their year of birth and death (if applicable), their full address and their domain of activity (pharmaceutical, agro-sciences, medical instrumentation...).

From this initial set of firms (223 of them), a second search was performed to reduce the number further, which involved identifying publication activity for each of these firms. A subset of 55 firms was retained, since these firms were known to have one or more publications according to the Web of Science. To do so the web of science for publication database was used. The firm's activities were identified through their name and address, with other addresses included in the document in order to trace partnership activity for publications and also the year of publication. These parameters enable us to obtain both a temporal and geographical view of the publishing activities of the local firms.

The analysis of the data includes two dimensions, firstly a temporal dimension and secondly a point is also made about the specific behaviour of young companies. Regarding the temporal dimension, the data covers the period from 1986 to 2010 and is split into five periods over five years. The rationale behind the periods of five years firstly lies in not being too sensitive to minor events that can influence the publication activity (discontinuity in publication activity and possible time lag between the acceptance and publication of the paper). Furthermore, the split coincides with different policy trends[53] pushed out by the Alsace Biovalley cluster (1998-2002 with the structuring of the local network, 2002-2004 where the cluster had an international branding activity, and from 2004 an objective to make the individual firms benefit from this international recognition). Secondly, since the thesis focuses in particular on new firms, this section will also comment on the specific position of new firms based on the data provided below. We therefore distinguish here the young innovative firms, which are defined relative to the notion of the time period. Young innovative firms are therefore defined as firms that are less than five years old at the beginning of each period (or less than 10 years old at the end of each period).

3.1.5.1. Cluster overview

Before exposing specific characteristics about publication activities of start-up firms, this section will firstly give a general overview of the data including some background statistics about the cluster and publication behaviour within it.

[53] These policy trends were identified through information given in an interview with the head of AlsaceBioValley.

The data identifies 120 firms involved in R&D activities (identified as having some R&D activity through publication, patent or collaborative project activities, or identified themselves through their NAF codes are R&D firms), from which 95 firms still exist. From the 95 surviving firms, 69 are located in the northern part of the region, of which 64 out of the 69 are situated in the Strasbourg area (CUS[54]). 26 of the firms are located in the southern part of the region (Haut-Rhin), but are spread across a variety of locations that include Mulhouse and its surroundings (14 firms), Colmar and its surroundings (5 firms), Rouffach (3 firms) and the French territory in the vicinity of Basel (4 firms). The two main domains of activity are Biotech pharma firms (more than 50% of the firms) and medical instrument firms (one third of the firms). The cluster also hosts firms from agro businesses, firms specialised in chemistry and even consulting firms.

Looking deeper into the population of firms, and especially at their size distribution (Table 3.2), the cluster shows a high number of small firms. In fact, two thirds of the firms have fewer than 20 employees and very few firms are medium sized to large. The large firms (over 100 employees) mostly belong to multinational subsidiaries in the region, such as Bruker Biospin, Clariant, DSM nutritional, Alcon, and Novartis among others. However, the larger firms also belong to local multinationals such as the Kronenbourg Brewery. Finally, three local firms are relatively young, having started between 10 and 25 years ago.

Table 3.2: Size distribution of the 95 biotech firms in the ABV Cluster

Size of the firm (Employees)	Number of firms
0-19	66
20-49	10
50-99	7
100-299	6
>300	6

Most of the firms in the cluster are small with fewer than 20 employees. The large number of small firms can be explained by the dynamism of firm creation, since most of them are locally created. The data shows that the local universities and public research institutions have contributed greatly to the local development since 31 of the 66 small firms emerged from scientific founders, of which 27 emerged from the University of Strasbourg. The presence of the university can therefore help explain the concentration of biotech firms situated around Strasbourg. The cluster also attracts a number of external firms, such as firms developed in other French universities or other small biotech firms that wish to have a subsidiary in the region.

[54] CUS –Communauté Urbaine de Strasbourg, which is a grouping of towns located very near to the main town of Stasbourg.

In terms of overall firm creation (including firms that have ceased their activities), the biotech cluster has been active in the biotech sector since the early development of the technology. In terms of start-up creations[55] (see Table 3.3), the first were created at the end of the 1970s and the beginning 1980s, which coincided with the development of the biotech sector. Two of those firms have grown into a medium size companies that today employ over 200 people each. Table 3.3 also shows that the number of creations of small companies is increasing over time and especially since 1995. This coincides with the start of the cluster policy and the development of the different support institutions behind small companies.

Table 3.3: Number of start-up creations in the ABV cluster

	Before 1986	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010	After 2010[56]
Number of firms created	7	6	6	15	23	26	7

The numerous companies created since the 2000s include spin-offs from the University of Strasbourg and other public research institutions, but also from the Basel pharmaceutical industry and firms created by employees of former start-ups.

3.1.5.2. Publication activities

The BioValley cluster has been growing partly through the implantation of subsidiaries of multinational companies but mainly as a result of the pool of local researchers who create spin-offs companies that are located close to their parent organisations. Due to the origin of many firms in the biotech cluster, and its strong history in terms of the university-industry relationship, the question remains regarding the relationship of the firms with the university after firm creation. In order to assess the relationship of firms with the university and public research sector, the activity of local firms in terms of their scientific publication activity will be examined, which will look particularly at co-authorship of local firms with local universities and also with other external partners on a national and international level.

In our sample 52 firms were identified as having published papers, and together published 1546 papers between 1986 and 2010. The profile of these firms is diverse and includes small biotech firms, subsidiaries of larger companies implanted in the region and finally a large agrofood firm. In

[55] Start-ups creations include the creation of local biotech firms but also the implantation of small biotech companies started elsewhere.
[56] The information gathered ended in early 2012.

table 3.4 we differentiate innovative firms, which are firms involved in R&D activities but excluding multinational or subsidiaries of multinational companies and which account for 71% of the publishing firms. Before going into the analysis of the publication, one must notice that in terms of publication activities a single firm has dominated the cluster. This firm is one of the oldest dedicated biotech firms in the cluster, having been created in 1979, and has had a strong history of publishing activities ever since. This firm had its maximum number of publications between 1986 and 2005. It is also one of the firms that grew significantly to more than 200 employees.

Table 3.4: General statistics of publication activities in the ABV cluster

	All periods	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010
# of innovative firms	106	25	35	54	81	102
# of publishing firms (% of publishing firms over innovative firms)	52 (49%)	7 (28%)	12 (34%)	17 (31%)	28 (35%)	42 (41%)
# of publications	1546	219	275	309	391	352
Average # of publications among publishing firms	29,73	31,29	22,92	18,18	13,96	8,38
Average # of publications among publishing firms, excluding leading firms	15,98	6,33	6,09	9,63	9,74	7,15
Median # of publications among publishing firms, excluding leading firms	5	6	2	4	7	3
Maximum # of publications	731	181	208	155	128	77

A second firm, who specialise in clinical trials and was also created in the early days of the cluster (in 1986), also has a significant share of the overall publication records with 253 publications. This firm started publishing in the 1990s and had the highest number of publications during the most recent period. The inclusion of the most active publishing firms has a high impact on the mean, especially during early periods.

Regarding the publication patterns of the overall cluster, when excluding the leading firms, shows a significant increase in papers published by firms between the 1986-1995 period and the 1996-2005 period. This reveals a jump in publishing activity of 6 publications per company to 9 publications for each firm that had published. However, by including the median values in our analysis we can deduce that the distribution of publishing firms is not constant over each period, and there are periods in which the distribution is more skewed than others. After giving general trends about the publishing activities in the cluster, we will focus on the collaborative behaviour in the publishing activity.

Table 3.5: General statistics on the publication activity of firms from the Alsace Biovalley Cluster

	All periods	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010
# of publications	1546	219	275	309	391	352
Alone	350	77 (35%)	71 (26%)	68 (22%)	65 (17%)	69 (20%)
With external partners	1196	142	204	241	326	283
Average # of mentioned addresses / publications	2,85	2,23	2,62	2,74	3,01	3,33

Table 3.5 shows the general trends of publication in 5 years intervals. The number of publications increased in each of the periods between 1986 and 2005 and then decreases during the final period. Before analysing the publication patterns of the firms shown in table 3.5 in more detail, we will first look at the general collaborative behaviour. As the number of papers increase, the trend towards overall collaboration increases in parallel.

Overall the number of publication authored alone (with only one address mentioned) decreased from 35% to 20% of the publications, with a peak during the penultimate period of 17%. However, over every period there is a constant increase in the number of collaborations, as shown in the average number of mentioned addresses, which increases from 2.23 in the first period to 3.33 in the final period. There is therefore an overall trend towards an increase in the publication behaviour accompanied by an increase in collaborative work. However, the collaborative behaviour still needs to be defined in terms of partner choice.

In terms of University-Industry partnerships, the publication records presented in table 3.6 show a strong relationship between local firms and universities. As explained earlier, the University of Strasbourg (which was formerly known as the University Louis Pasteur - ULP) is expected to have strong relationship with local firms. Table 3.6 shows that in addition to contributing towards the creation of Spin-offs Companies, the university also has strong publication linkages with the local firms. Even though firms in the cluster occasionally publish alone, which is less common over recent years, the firms in majority publish with partners, of which a part involve the University of Strasbourg. The number of firms having publications involving the university varies over the years but a strong core of them, usually between a third and a half, are involved in collaborative publishing with the university on a regular basis.

Table 3.6: Industry - University publications

	All periods	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010
# of publishing firms	52	7	12	17	28	42
# of firms having only published alone	5 (9,62%)	2 (28,57%)	2 (16,67%)	2 (11,76%)	2 (7,14%)	4 (9,52%)
# of firms having published with the ULP (possibly with other partners)	27 (51,92%)	3 (42,86%)	6 (50%)	8 (47,06%)	17 (60,71%)	15 (35,71%)
# of firms having only published with partners other than ULP	20 (38,46%)	2 (28,57%)	4 (33,33%)	7 (41,18%)	9 (32,14%)	23 (54,76%)

Looking in more detail at the fall in partnership with the ULP from the penultimate to the more recent period, the data reveals that the firms created after the year 2000 have a lower proportion that cooperate with the university than the previous generations of firms. In fact, regarding the firms that were less than ten years old, 60% of them collaborated with universities, but in the final period this number dropped to 40% while the number of publishing firms increased over time. While there are an increasing number of partner organisations, if these new firms are collaborating less with the local university, over time, then they must be collaborating more with other partners. The question that then arises is which other partners are they collaborating with?

In order to understand the publication activity in the cluster, Table 3.7 shows the number of Alsace BioValley firms that publish with partners in different locations, from local to international. Looking back at table 3.6, one can see that most of the local interactions involve the University of Strasbourg. In most cases the local firms have interactions with a local public research institute or the hospital if they are not directly collaborating with the university (with a couple of exceptions over all periods). Over all periods firms are more involved in collaboration with Local, French and European partners than with partners in other locations. This trend can be explained by the ease of access to those partners due to the cluster position at a European border and furthermore its association in a tri-national cluster.

Table 3.7: Number of firms from the ABV cooperating with partners from distinct geographic zones[57]

	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010
Local	2	5	10	7	16
France[58]	4	6	8	18	25
Africa	0	1	3	0	1
Asia	1	2	2	3	9
Europe[59]	4	5	13	21	29
Middle East	1	1	2	4	4
North America	2	4	4	14	20
Oceania	0	1	2	0	2
South America	0	1	0	3	1

Concerning the extra-European relationships, the firms in the BioValley cluster seem to be increasingly collaborating with North-American partners (almost half of them during the final two periods), but we can also see an increase in partnerships with Asian firms. The increase in the collaborative activity outside Europe could be explained by the partnering and branding policy developed by the cluster organisation. The cluster has indeed developed relationships and promoted local firms in worldwide events since 2002 (according to an interview done with the head of Alsace BioValley), which could have had a positive impact on the international publication partnering. This trend is also true for the younger firms in the cluster, which generally tend to work more locally but also on a European level. However, the most recent firms tend to be much more present at an international level (European and even American) than on a local stage. The younger firms' openness and collaboration with international partners may therefore partly explain the fall in firms collaborating with local institutions, especially the University of Strasbourg.

3.1.6. Conclusions

This description of the BioValley aimed at identifying the innovation system in which the firms are evolving, as much for identifying key players in the systems as how that system has evolved over time in recent years. The historical review has shown various trends, such as university-industry links but also the proliferation in number and activities of organisations supporting the creation and development of innovative firms. The second part has shown the evolution of firms in the cluster

[57] ABV firms that have cooperated with partners from different locations during a single period are counted multiple times
[58] Excluding the local level
[59] European partners excluding French partners

partnerships and also the centrality of the university in the development of the biotech cluster, based on statistical evidence from publication activities.

The historical evidence shows that the mix of French top down and bottom up policies have led to a strengthening of the support available for the local companies. With the inception of the cluster association in 1998 and then with the development of institutions such as the incubator and financing bodies in the 2000s, the region has built its institutions over several years to have comprehensive support for its start-ups.

One institution that had an outstanding role in the development of the firms in the region was the University of Strasbourg. As the history has shown, the university has had a long standing role in the development of the chemistry industry in the region, and now has a significant role in the Biotech industry. The university has had a proactive relationship with the industry, which continues to this day. The publication data still indicates that the University occupies a central role in the knowledge sharing activity of the cluster.

Finally, with the encouragement of the cluster association, the firms in the cluster have been increasingly involved in global collaboration especially with European, American and Asian partners in recent years, according to publication records.

The local system of innovation has therefore undergone considerable changes over the last 20 years. The bottom up and top-down policies have given the firms more support from the local system in terms of institutions, but firms are increasingly able to interact with other players on a global level.

3.2. Overview of firms interviewed

After identifying newly created firms in the biotechnology sector (excluding firms specialised in medical devices), 21 firms were identified and contacted for interviews, and 14 of them responded (see Table 3.1 in section 'Entrepreneur's interviews' in this chapter), in which 13 were included in the study (since one was too early in its organisational process of firm creation). In total 23 interviews were conducted of which 21 were included in the case study. The following table (Table 3.8) shows the number of interviewees per firm, in addition to some information about the founding team and founding project.

Some of the firms asked for anonymity and so their names were replaced with the English titles of Greek letters. Additionally, in the case of Domain therapeutics and Enovalys, their creators and projects were a direct continuation of the firms from which they spun-out from. The interviewees from these two firms were also directly involved in the creation of their parent start-ups and so information was also collected regarding the history of the two parents firms (Novalyst discovery and Faust pharmaceuticals respectively). Some of the following chapters also refer to these parent firms.

Table 3.8: Interviews repartition per firms

Firms' name[60]	Project origin	Original founding team	# of interviews	Year of creation[61]	# of employees[62]
Alpha	University	University	2	2011	1
Beta	University	University	2	2008	7
Kappa	University	University	2	2010	1
Anagenesis	University	University	2	2011	0
Biomica	University	University	1	2009	4
Cell Prothera	University	University	1	2008	10
Bionext	University	University	1	2009	6
Admet-X	University	University	2	-	-
Phytodia	University	Industry (start-up)	2	2006	10
Alsachim	University	Industry (start-up)	1	2005	10
Enovalys	Start-up	Industry (start-up) & University	2	2009	3
Domain Therapeutics	Start-up	Industry (start-up)	2	2008	20
Rhenovia	University	Industry (Large firm)	1	2007	25

3.3. Firm presentations

This subsection gives a brief history of each firm and some details about their domain of specialisation. For the firms desiring to remain anonymous, the description of their activity will not

[60] The firms wanting to remain anonymous are given a name referring to a Greek letter and are presented in italic in the table.
[61] If the year of creation is not specified, this means that there is an organised team around firm creation but the firm has not been created yet from an administrative point of view and therefore has also no employees.
[62] The data on the number of employees was drawn from the interview and thus are valid for April 2012.

go into as much detail in order to preserve anonymity, however a similar level of detail in information was collected for these firms as those which are named. The following narrative was developed based on the information gathered during the entrepreneurs' interviews, which includes a discussion on the development of the innovative project before and after creation in addition to the motivation and steps taken to create and organise the company. The section divides the firms into subsections according to their origin (e.g. parent organisation) as drawn from column 3 of the above figure.

3.3.1. University spin-offs

Firm Alpha. The project aims at providing an alternative treatment for a widespread disease, one which affects 20 million people in the world. It consists of the development of a bio-medical device transplanted into a failing organ that will produce a hormone essential for human survival. The current treatment involves daily medication or transplantation accompanied by anti-rejection medication. This technology aims at making the illness less debilitating.

This project was started in a university laboratory and was initially financed by two successive European projects in the framework program starting in 1996 and ending in 2007. These projects were collaborative and involved two other French partners, one being a university and the other being a firm. The European projects helped in testing the proof of concept for their device by testing firstly on small animals and then on larger animals. However, after the completion of those two projects the team had problems in securing research grants and decided to create a company to acquire more funding in order to continue product development (involving complementary testing of the product and improvement of the prototype). The firm was officially created in 2011 and is still being incubated in the university laboratory from which it emerged. The company has started to build its own team but still uses some services from the university laboratory, for which they compensate the university.

In regards to the team, the creation project was driven by the leading scientist from the previous European project. However, this scientist did not yet plan to leave his academic position and so looked for somebody to take charge of the general and operational management of the newly created company, while the important decisions remained his.

Firm Beta. The research project behind the firm creation started in 1994. It consisted of the injection of a biomarker (fluorescent molecule) into the blood for a disease diagnostic (in vitro diagnostics), which gave interesting results and led to a patent in 1997. The same year, they tried to transfer this technology for exploitation by a pharmaceutical company. However, in the end the partnership with the pharmaceutical company did not result in any technology transfer. The project was not pursued further until five years later when a small chemical company contacted the scientific team for collaboration. After these discussions failed to seal a partnership, the lead scientist in the project started to look for financing in 2006 and in 2007 secured partial funding for the creation of a spin-off company. The company was officially created in 2008.

Aware of his limitation in terms of managerial and industrial knowledge, the lead scientist began looking for somebody with those competences who could take leadership in the company, in parallel with his efforts to secure funding. Through his connection to the chemical firm, the scientist found a collaborator in Paris who later accepted to take the lead for the development of the company. This new leader did his training in agro science, and had a strong experience in firm creation.

The firm is now developing its first biomarker, since it is an in vitro diagnostic, and they hope to be able to market it shortly. The firm has also secured a place in a large European collaborative project that has given them the opportunity to approach and collaborate with big players in the pharmaceutical sector. This firm also remains incubated within its parent laboratory, but hopes to be able to move out shortly.

Firm Kappa. The project behind firm Kappa emerged from a collaboration between two laboratories in a university, because two competences were needed in order to identify and test the molecules (a chemistry component and a biological component). Around 2002, the laboratory specialised in chemistry worked on a family of molecules that had the potential to be effective against certain types of cancer, and thus started to synthesise some molecules. Soon, they needed competences to observe in vivo effects of these molecules, and therefore started a collaboration with another lab specialised in this domain. The project therefore started with the efforts of two biologist and two chemists. Around 2004 they applied for their first patent for an anti-cancer molecule. The thought of creating a company came some time later in 2007. In order to have a solid base for a company creation, they decided to synthesise and test new molecules from the same family, which was financed by a national scheme (ANR). In vivo and in vitro testing provided the possibility to apply for a second patent relating to the molecule's activity, which was granted in 2010.

For the creation of the firm, another person was needed in order to manage the 'business side' of the project, but also to be able to secure funding. A molecular biologist was hired to be the leading person in the firm creation. After talks with the local incubator, who helped them with their market search, the team decided to move towards the solution of company creation, which was completed by the end of 2010. The managing founder of the company enrolled in a part-time course for management and creation of new firms in Paris in order to gain knowledge about management and marketing. At the start of the company they secured national funding targeting innovative firm creation.

In terms of research, the firm is still located within a university laboratory to develop their molecules and test them in order to obtain a proof of concept. The firm has started looking for financing for the molecule development. The initial results of the studies for the proofs of concept were not as good as they expected and this may hinder their chance of receiving financing. The firm may therefore also consider getting involved in publicly funded collaborative projects or providing other services besides their drug discovery business model in order to secure cash for the survival of the firm. The firm also still works in close collaboration with the laboratories from which the molecules' identification emerged.

Anagenesis. This firm is based on a project looking at stem cell differentiation towards muscle and bone development. The lead scientist behind this project began working on stem cell differentiation towards muscle development in 1995 in order to help develop regenerative medicine using cell therapy. He worked on it at several different institutions starting in Marseilles, then the United States and then from 2005 in the IGBMC (institut de génétique et de biologie moléculaire et cellulaire) in Strasbourg. He developed the project with the help of AFM (Association Francaise contre les Myopathies) since his return to France. This project gave rise to two patents that were granted in 2011, which then led to the idea of firm creation in the same year.

The firm's team is built around the scientific team involved in the project. The project is led by the main scientist behind the research project, another researcher specialised in the search for funding and coordination of the newly created company and an engineer focused on the technical side of the project. A third partner is involved in the strategy building and business plan and is also responsible for the legal side, such as contracts for collaboration and licensing agreements. This latter member, who has significant experience in firm creation, was found through the network of the lead scientist. At the time of the interview, the firm was still located in its parent organisation, but had plans to look for another location.

Biomica. The project behind Biomica was based on a professor's discovery of two genes that have an influence on the rejection of organ transplants. These genes can be tested through diagnostics to predict if the patients would be under threat of a chronic rejection following transplantation. After meeting the head of a Parisian diagnostic company at a conference, they decided to start a company together. They started to talk about the project of firm creation around 2007-2008, and the firm was finally created in 2009. They also hired an operational manager to manage the day to day life of the firm. The firm is still incubated within the civil hospital in Strasbourg and also shares a facility with the lead scientist's laboratory.

In terms of team roles, the head of the company (business founder) brings knowledge about market, industry, user knowledge and insights about potential competition. The lead scientist has more knowledge about the scientific side and leads the scientific project. The operational manager focuses more on development processes, looks at financing for the company and also does feasibility studies and technological watching.

The firm's time to market is quite short since they develop in vitro diagnostics. They hope to market the product by 2013.

Cell Prothera. The project behind the firm is based on technology developed in relation to blood stem cells for regenerative medicine, principally in heart surgery. The research was developed at a research institute that specialises in haematology and transplantation. The principal scientist behind the innovation project performed his first blood stem cell transplantation in 1986. Since then he was firstly involved in the development of a lab before working on a process for developing and multiplying the number of stem cells gathered from the patient's blood. The technology developed includes a robot and a one off use kit in order to increase the number of stem cells extracted. The decision for creating the firm followed a need for the fabrication of a robot able to multiply stem cells, but the research institute was unable to develop this robot themselves due to its non-profit status. The company was then created in 2008.

The team includes two members from the parent organisation, including the lead scientist and the current (at the time) president of the organisation. The latter had experience in company creation and running private firms. He is therefore responsible for the general coordination of the project, financing search and recruiting. The team also includes a medical director, a development director and a project chief, who work with the scientific leader on the scientific part of the project.
The firm is located in a local incubator and is in the process of further developing their robot in collaboration with an industrial partner. They are also carrying out clinical trials. The initial results are encouraging and have demonstrated the proof of concept. They hope to reach the market by 2015-2016.

Bionext. The project behind Bionext is the personal project of the founder. Early in his studies, the founder was interested both in computer science and biology. During his training (undergrad and post grad) he took courses both in informatics and biology. He then continued towards a thesis in molecular biology relating to molecular structure at the IGBMC (institut de génétique et de biologie moléculaire et cellulaire). During his studies he started to develop software to visualise molecules in

3D but also a method to identify regions in cells that have similar functions to each other. Benefiting from the entrepreneurial experience of his brother in the IT sector, they both discussed the creation of a company in October 2008, before the end of his thesis. The firm was then created in April 2009, and hosted by the local incubator in December 2009.

The team is composed of four people, including the two project leaders described above. The management team also benefit from an experienced founder, the brother of the main founder who started his own software company, and another partner with industry knowledge, who helps in terms of strategy and international development.

In terms of the business model, the firm has initially financed itself with national grants for innovative firm creation and 'love money' (money coming from closer relatives and friends) and then two European projects. They are looking to leverage more funds through venture capitalists in order to grow quickly. They are targeting first to licence their product to academic institutions and universities (they made their first sale in the founder's former laboratory) and then move to the pharmaceutical and biotechnology sectors.

Admet-X. The idea behind Admet-X was to develop a technology platform, firstly targeting researchers from the university but also external partners. The development of this platform was done jointly by researchers from the biotechnology school and the pharmaceutical university. This platform aimed at combining chemical and biological technology to create an inclusive platform for several uses from finding targets to drug candidates. The building of the platform started in 1999 with a chemical library, then a screening platform in 2000, followed by a tech-med platform (analysis of biological chemistry) in 2006-2007. The tech-med platform was the basis on which the firm started. The platform for drug development helps for the target optimisation process, which also tests for toxicity and unwanted effects. The idea for the firm creation started with the identification of the need of services of local firms that could be provided by this platform.

The idea of the company creation become more concrete when the lead scientist met two tradesmen who were potential sellers of some equipment needed in order to improve the platform. Since the lead scientist could not get involved in the company creation himself, the tradesmen agreed to create a venture with him. The scientist entered into negotiation with the tradesmen regarding the practicality of the creation. However, in 2010 the salesmen pulled out just as the firm was about to be created. The company was therefore never created.

3.3.2. Start-ups' spin-offs

Phytodia. This firm started on the basis of the identification of an active natural molecule extracted from a plant. The natural extract was found and first tested at the university by several faculties. The groups involved were the pharmaceutical faculty, with the participation researchers who specialise in phytotherapy, and a researcher from the mouse and clinical institute, who specialises in metabolic illnesses. Together they tested natural molecules to cure diabetes. From the scientists' point of view, the project was therefore heading towards being a drug discovery company. The researchers themselves did not want to get involved in the creation of a company and therefore searched for somebody to take on the project. In 2005 the team tested 10 molecules in depth, which gave good results and improved the confidence in the project of firm creation. The firm was then created in 2006 and has been hosted within a firm incubator from 2008.

The current project leader was found by one of the scientific founders (he was one of his former students), who worked at another start-up in the BioValley that has now closed down. The project leader was supported at creation (financially and also in terms of management) by another start-up firm called Novalyst and their founding team. The project leader had a more scientific and technical background, while part of the Novalyst team was more specialised in management.

With the recent failure of some local companies specialised in drug discovery, Phytodia did not want to follow this type of business model and so tested the molecules for other effects. They decided to implement a three-stage model. Firstly, the firm would provide services based on their technical capabilities for analysing natural products. Secondly, they would develop cosmetic products with capabilities developed in-house. The cosmetic industry was chosen since one of the molecules had an effect on weight loss. The company therefore also developed a plant extract that would be sold to firms specialised in cosmetics products, which had positive results of efficacy during trials. This industry was chosen due to its much less constraining regulations and thus its shorter time to market. However, the firm management does not exclude the possibility of developing pharmaceutical products at a later stage, as was the initial purpose of the company.

Alsachim. This firm was created following the closure of another start-up specialised in drug discovery. Two people from this start-up decided jointly to create a firm in order to avoid unemployment. They decided to specialise in the synthesis of pharmaceutical active organic compounds and rare molecules. They are using specific techniques that originated from one of the founder's research developed for his thesis.

The team is therefore composed of two former employees of a firm that has closed, both of whom come from a scientific background. The firm was created in 2005. The firm was initially incubated by the university in a chemistry laboratory (in ISIS, Institut de science et d'ingénierie supramoléculaires) for one year, where they could rent the use of some necessary equipment. Once they had secured some clients and funding, they looked at the possibility of moving into their own premises around 2007.

The business model is firstly oriented towards services, since the aim of the firm creation lies in employment stability rather than a specific invention. This is mainly due to the need for stability of the founders but also due to their experience of having being involved in a start-up that failed and was forced to close. They therefore view the drug development business model as too risky. However, they do not exclude the possibility of moving into drug development in the future, if they have an opportunity and the company is strong enough.

Enovalys. The company started from a project emerging from academia, which initially span-out to form a first company in 2001. This first spin-off company implemented a hybrid model offering services and followed the project of the scientific founder. After 5 years of activity, the firm had begun to specialise in services and could not continue the research project in-house.

The project was originally based on chemical kits to help chemists improve their efficiency when performing experiments. The kit was accompanied by a database to optimise their choice for doing the right experiment. While the project was being developed in the first company, it evolved towards the design of 'distributed' software that helped chemists to record results from their experiences (successful and unsuccessful), and optionally to share their results with other users of the software. This project then span-out of the first company to create Enovalys in 2009.

The main team behind the project are the scientific founder who is inventor of the idea, and a young doctor who worked on this development project during his thesis[63]. The scientific founder has the role of scientific consultant, since he still has a position in academia and closely follows the evolution of the firm. The young doctor is in charge of the company's operational management (presentation, raising finance and monitoring of the scientific project). The main decisions are made between partners, which includes the two founders mentioned above and the current president and CEO of the former company, who also invested and followed the evolution of this spin-off. Additionally, they also receive advice from one of the external investors of the company.

The project is currently incubated in the biotechnology school. The main strategy behind the project is to reach a critical mass of users of the software through free use of the software but paying access to data generated by others. The team has considered to ultimately sell their project to a bigger player, such as a scientific search engine or database management firm.

Domain Therapeutics. Domain Therapeutics was also created on the basis of another company called Faust Pharmaceuticals. Faust Pharmaceuticals was created based on several different projects by researchers from a university laboratory in Gif-sur-Yvette (Region of Paris). None of these researchers wanted to move to the company and so it was managed by people hired by the venture

[63] The thesis was done in CIFRE where the student worked partly on a project in the industry while completing his academic degree.

capitalist funder. Faust Pharmaceuticals was developing a molecule targeting central nervous system diseases. This company therefore had a drug discovery business model that relied on heavy financing by capital risk organisations. In 2003, after two years of incubation within the university Laboratory, they decided to move to the Alsace region to develop their company. The project went through clinical trials. They had a false positive during toxicology testing that meant that they were forced to do additional testing in order to continue the project. This delayed the project for one year, which impacted on the future profitability of the firm (the patent life was not long enough) and on the willingness of the investors to continue funding the project. With competences that they developed over time and the acquisition of a small company, they built up specific competences that allowed them to work with a large Japanese pharmaceutical company called Takeda. This was the basis on which they continued their activity, by starting a new company (with 10 of their employees) providing services to larger groups and developing collaborative projects over time with larger players such as other pharmaceutical companies.

The team at Domain Therapeutics is based on the team built up by Faust Pharmaceuticals. The team leader was the previous Chief Scientific officer at Faust Pharmaceuticals. He built-up knowledge about the management of a small firm and also experimented the dynamic of a scientific project in the development of a small firm. He also has the competence to take strategic decisions for the firm. There is also a scientific officer who came from Faust Pharmaceuticals and supervises the scientific organisation of the firm. Finally, they are also helped by a previous CEO of Faust Pharmaceuticals for leveraging more funding to ensure the survival and development of Domain Therapeutics.

3.3.3. Large firm spin-off

Rhenovia. This firm is specialised in optimisation solutions and simulation technologies for treating neurological illnesses. The project and technology emerged from research carried out at California University, which developed a bio-simulation system in order to predict biological processes. The lead researcher had connections through his training with a researcher working at Novartis, who took the lead in company creation (he is now the President). They decided to create a company based on this technology with one of his colleague at Novartis and in collaboration with the scientist in California and another lead scientist in Germany. The President is the face of the company and represents its interests. He is the main manager of the company, which is logical due to his industrial and managerial experience gained at Novartis, and is helped by a Vice-President originating from the same company. On the scientific side, the lead scientist from the University of California has the role of chief scientific officer.

The aim of the firm is to identify molecules that are potential drug candidates through the use of the bio simulation platform. However, they have a hybrid business model in which they also try to develop partnerships through joint research projects involving bigger partners in the pharmaceutical and agro-food industries. They are also in the process of opening a new plant in Boston.

3.4. Synthesis of the chapter

The choice of the cases from the cluster aimed at reflecting different categories, which aimed at including ventures that emerged from large firms, from other small biotech companies, and firms that emerged directly from university. Table 3.1 earlier in this chapter showed that the cases were chosen with the aim of representing each of these different types of firms. These types of firms were defined through secondary data, according to the main founder's parent organisation, in the various databases searched (e.g. incubator information, and society.com). However, as the in-depth view of the cases shows, most of the firms were based on projects developed initially within university walls. Table 3.8 helps us to shed light on this issue by pointing towards the difference between the project origin and the origins of the founding team (which is related to our first selection of the cases). It shows that most of the projects originated in academia, even including the ones supported by a founding team who have an industrial background. Two projects (Enovalys and Domain Therapeutics) were identified as having come from a project developed by another start-up, but looking in detail at the history of the start-ups, the project followed by these two firms can be traced back to a university project. This confirms our understanding that universities are important actors in the biotechnology sector, because they provide scientific projects for the newly created firms to develop. This early observation supports our argument made in the theory that the fate of an innovative project, and the firm created base on it, may not be convergent, but can evolve in separate ways.

When considering the university, the section 3.1 has shown that the University of Strasbourg should have an important role in the regional dynamic. This is translated into the study cases by the fact that the University of Strasbourg have had an important role in a majority of the research projects taken on by the selected start-ups (11 cases on the 14). One of the cases has developed a project originated from a public research institute from the south of Alsace. Most of the cases show that there is a regional component to the localisation of the created firms. There are two exceptions to this, the first being Domain Therapeutics, whose parent organisation Faust Pharmaceuticals was created in Gif sur Yvette close to Paris and whose project origin was a local university, which later moved to Strasbourg. It is worth underlining here that the option to locate in the ABV cluster was due to the connection of one of the manager to the region and secondly due to the increasing opportunities made available for starting new firms by institutional actors such as the cluster association. In the second case, the research project of Rhenovia originated at the University of California. The firm happened to be created in the Alsace BioValley because the business manager who agreed to develop the project came from the region and previously worked in a large company. These results show that firm founders may also be an important factor for the choice of location of newly founded companies, since most of them have an attachment to region (from firms emerging from the University of Strasbourg and the other ones).

Regarding at the alignment of the original project and the activities of the created firm, one can see that there may during the creation process or in the early life of a firm. Many of the projects started at universities reflect the general aim at contributing towards health. The scientific founders of many of the cases aimed at human therapeutics and thus went into the pharmaceutical or diagnostics industries. However, in practice the surveyed companies had a wide range of activities in a variety of sectors. They include therapeutic applications, diagnostics, services to other pharmaceutical firms, and even the cosmetics industry. Thus, in terms of activities, our sample of firms include a variety of industries of applications compared to the sample surveyed in the biotechnology overview (cf. Chapter 2 section 4), and thus demonstrated the range of possibilities of application of research projects.

Finally, concerning the types of financing used, we have encountered only a small number of firms that were actually oriented towards venture capital investments (more information is given in the following chapter, Chapter 4). There are two explanations for such a small proportion of firms calling on risky financing. Firstly, some of the founders reported a shortage in the market for such financing, which has been even more weakened by the financial crisis. As a result, this type of financing is rare and very selective in terms of the risk they are willing to take, and thus less inclined to invest in many projects. A second reason lies in the perception of such type of financing, and therefore some firms willingly decide to not involve these types of organisations in their firms. This issue is further discussed in the Chapter 4.

This section has then emphasised that the cases benefit from a certain type of variety even when choosing firms from the same sector. Firstly, the firms have a variety of activities and are involved in a range of industries relating to human health. To a certain extent this gives a variety in the environment (regulatory and value chain environment) with which the firms are confronted. Secondly, there is a variety in the founding team backgrounds, since it is one of the main objectives of the study case. Some cases are mainly managed by people from an academic background, while others are directed by people with industrial experience with the help of scientific founders. This variety was chosen deliberately, and will help to understand how the early evolution is linked to experience and background differences.

4. Concluding comments

The cases described above have shown a variety in activities, domains of application and founding teams, despite the fact that the sector and cluster choice has been restrictive due to the replication design. As the description of the regional cluster has emphasised and the first overview of the cases has confirmed, the university is expected to have an important role in the dynamic of young firms, possibly through the sourcing of research projects and also through providing qualified labour to those newly created firms. In terms of the variety of background of founders, in the analytical chapters we aim to understand if the backgrounds has an influence on the entrepreneurial agency of the actor, firstly in the way that wider opportunities are open to some founders, or in the way that they take decision towards the future of the firm.

In terms of the use of the cases in the different chapters, not every chapter bases its evidence on all the cases. For Chapter 5, Admet-X was excluded because the project did not lead to a firm being created. In that case, there were little interactions between the managers and the scientific founders, and thus the steps studied in this chapter did not yet happen in the case of Admet-X. For instance, in Chapter 6, which is concerned with university spin-offs, not all firms emerging from universities are included. This is firstly because not including projects that have not yet experienced a firm creation relationship between the newly created organisation and the university is crucial for this paper, which was the case of Admet-X. Secondly, Alsachim and Phytodia were included because they relied on research built and developed within university walls (the first one through a PhD thesis and the latter one through a research project developed by 5 university scientists). For Chapter 4 all firms were included.

As the description of the case study has noted, there can be an apparent difference between the research project's (therapeutic) aim and the actual activities of the firm. The analytical chapters will therefore also aim at advancing the understanding of how a research project can be transformed in the firm and lead to a variety of activities. Thus, these early steps of the transformation between innovative project and firm creation have been shown in the literature review chapter (Chapter 1) to be empirically relevant and thus will be one of our focuses of study in the analytical chapter. In addition, some of the analytical chapters will try to further this concept of early evolution through the formalisation of the transformation of a research project into a new firm (Chapter 5 and Chapter 6).

The theoretical background has laid the premises and the boundary of the study. In the literature review it outlined the main concepts used and developed a framework in order to study the transition between an innovative project to the creation and early development of a company. Chapter 2 has given an overview of the biotechnology sector. This was needed because the framework has emphasised the prominent role of the environment in our study (besides the entrepreneur and its action), in addition to the replication design methodology that prefers to focus on a single sector; the Chapter 2 has given an overview on biotechnology sector. The review has attached importance in discussing how the industries linked to this sector can have an influence on business models and thus entrepreneurial agency. Finally, this chapter has described and argued for the use of the study case methodology and also described the cases chosen in further detail. The analytical chapters in the next part will focus on the transition from an innovative project to firm creation using the framework designed in the first chapter. They will use the above cases to show the influence of external factors such as financing institutions (Chapter 4) or university resources (Chapter 6), or factors linked to the entrepreneur's characteristics on entrepreneurial agency (Chapter 5). The following chapters also look at the early evolution of the firm and project in parallel with the evolution of the business strategy which is linked to the change of management in the firm (Chapter 5) or to the financial choice (Chapter 4). Finally, the final analytical chapter gives a broader view of the transition of an entrepreneurial project in firm creation by using a stage model (Chapter 6).

Part II:
Analytical chapters

Chapter 4: Financial partnering and business model: an interdependent choice

Abstract

Starting an innovative company involves many challenges for entrepreneurs in the biotech sector. One of the main challenges includes finding financial resources to develop the project behind the company creation. There are a variety of financing options that are available for young innovative firms, but each of them comes with advantages and disadvantages. This chapter draws on the differences between modes of financing in order to understand the entrepreneur's choice towards a given funding option and study the resulting impact on the firm business model. The chapter relies on study cases of 13 firms from a biotech cluster localised in the French region Alsace. The results show that one of the main influences for choosing types of financing is the experience of the previous generation of firms in the given sector together with the entrepreneur's preferences over control or independence of the firm. In this context a sample of the influential firms from the previous generation is presented and discussed.

1. Introduction

When creating a company based on an innovative project the entrepreneur has a vision of how his project will develop into a viable business. This project and firm development may need external help depending on the project type, among which financial help is one of most common needs of the entrepreneur. However, financial involvement of external actors, depending on the financial amount needed and riskiness of the project, may involve warranties and compromises from the entrepreneur because the investor needs to make sure that his investment is used in the best way. For instance, venture capitalist involvement in a firm often goes in parallel with close monitoring of the project development and intervention in the business strategy of the firm.

The involvement of an external financier in an innovative project is in many cases indispensable. This phenomenon is well documented in the literature dealing with entrepreneurship financing (Bhide 1992; Croce et al. 2013; Gompers & Lerner 2001; Schwienbacher 2013; Shane 2005). However, the involvement of an external financier is not without consequences for the entrepreneur. The entrepreneur may have to adapt his general goals or business strategy to the chosen financial partner and so must be prepared to share part of his entrepreneurial agency with the funding partner. Entrepreneurial agency is viewed here as the intentionality and freedom of decision and action held by an entrepreneur to realise and exploit an opportunity that he has identified. The involvement of external actors, such as financiers, can therefore affect entrepreneurial agency because the freedom of planning and action of the entrepreneur can be restricted to some extent. The notion of freedom embedded in the notion of entrepreneurial agency is central in this chapter because it discusses the relationship between an entrepreneur and a funding partner in addition to the limitations of an entrepreneur over his own actions.

The consequences of the intervention of a financier, together with the limitations of the entrepreneur's freedom, can be seen as more or less intrusive considering the difference in the alignment of goals between the entrepreneur and the financier. For instance, if the goals and the course of action are aligned between both actors then the loss of entrepreneurial agency can be considered as insignificant in order for the project to be realised. However, in the case of differences between agents (entrepreneurs and financiers) regarding the goals that the firm should pursue and the issue of the initial project, the share of the entrepreneurial agency between actors can lead to unwanted consequences on both sides. The goal and perception of success of the entrepreneurial project is therefore a central issue for discussion in the analysis of the interactions between the entrepreneur and the financier.

To sum up, this contribution aims at discussing the financier-entrepreneur relationship from the entrepreneur's point of view, in terms of trade-off between entrepreneurial agency, the nature of the entrepreneurial project and the entrepreneur's perception of success.

From the study of this relationship some questions emerge, such as: How does the financier influence the freedom of decision and action of the entrepreneur? How does the financing aspect influence the business model choice? Does the entrepreneur foresee the consequences of the limitation of his agency power when involving venture capitalists? The involvement of a financier certainly has an impact on the future path that a firm can pursue, and so most likely has a limiting influence over the entrepreneur's freedom of choice related to follow some pathways.

In order to explore the implications of the involvement of a financier for the entrepreneur, this chapter must therefore discuss three points. Firstly, it must define a business strategy and how it translates into a business model. Secondly, it must highlight the factors that influence an entrepreneur's choice towards a specific business strategy. Finally, it must discuss how to define the relationship between an entrepreneur and a financier.

2. Business goals: from the exploitation decision to entry business model

The entrepreneur, as part of his agency (i.e. entrepreneurial agency), plans and organises the firm's early development by outlining general objectives for the firm, which translates in more formal terms into a business model. This section aims at understanding the definition and components of the business strategy and the business model for newly created ventures. This section focuses first on the strategy literature, which elaborates on the characteristics of the business models. However, this literature deals mainly with established firms, and so this section discusses the applicability of this literature to new businesses. The section finally examines the specific characteristics of firms and business models in the biotech sector. Later sections discuss the influence of both the entrepreneur and also financier in the business strategy, which is then implemented as a business model.

Various authors from the literature of business strategy have contributed towards an understanding of the concept of business models, which has involved a variety of definitions (Morris et al. 2005). In order to start a discussion regarding the choice of a business model, it is first useful to remind ourselves about of the defining elements that constitute a business model. In his 2010 paper, Teece defines a firm's business model as follows:

> "The essence of a business model is in defining the manner by which the enterprise delivers value to customers, entices customers to pay for value, and converts those payments to profit. It thus reflects management's hypothesis about what customers want, how they want it, and how the enterprise can organize to best meet those needs, get paid for doing so, and make a profit."(Teece 2010)

Others have included in this definition the fact that the value extracted from consumers is a direct result of technological opportunities proposed by firms or developed through core competences (Chesbrough & Rosenbloom 2002; Morris et al. 2005; Sabatier et al. 2010). The business strategy therefore involves defining a path towards a competitive advantage for the leadership team, while the business model explains "the architecture of revenues" (Chesbrough & Rosenbloom 2002) behind the strategy. The concepts of the business model and business strategy are therefore related. The literature has discussed four determining factors for business models and business strategies (Teece 2010; Chesbrough & Rosenbloom 2002; Sabatier et al. 2010), which are the following: time to market, technological and financial risk, independence among actors and expected returns. These determinants are sector or even technology specific. The technology in use, regulation in the industry, in addition to the preferences of the entrepreneur, are among the factors affecting the business model. While this theory associates business models with bringing value to customers, in addition to generating revenues from these activities, this theoretical literature is mostly adapted to established firms in which the customer base is already known and in which the core competences of the firm are already developed. Thus the applicability of the notion of business model and business strategy must first be discussed in the light of new ventures before discussing its relationship to a specific sector.

Newly created firms have many challenges to be addressed, which include limited resources (in terms of physical and social capital), a need to become organised internally, but also a need to develop relationships with external partners. The firm has to deal with what Stinchcombe (1965) calls liability of newness. This means that the firm has first to build new roles within the organisation and secondly build new links with external partners. In many cases, a new firm does not yet have an internal organisation, nor links with customers and markets. External partners may also be reluctant to engage with the firm during the early stages due to their young age, since they do not know if the firm is trustworthy or not. Thus for a young firm a business model cannot yet be defined in terms of core competences or by identifying value creation to existing consumers.

The definition of business strategy has to be differentiated between newly created firms and established ones. Thus since the focus of the study is done on start-ups, we define the firm strategy according to entrepreneurial theories rather than from the strategy literature, which focuses on established firms. Mintzberg, Ashland and Lampel (2005) described the vision adopted by entrepreneurship theory on strategy, in which the entrepreneur is portrayed as the leader, as "a sense of long term decision, a vision of the organization's future." The authors elaborate on this vision aspect by defining it as malleable, "deliberate in overall vision and emergent in how the details of the vision unfold". Thus the view of the business model and business strategy have to be adapted to the entrepreneurial structure, which features a leader and his vision for the company's goals and activities. In entrepreneurship theory, the concept of business model can also be studied in a more practical sense as a tool for firms to make projections about their potential customers, market and also their potential revenue generation (Doganova & Eyquem-Renault 2009). Thus young firms are different from established firms because they have first to find their customer base and market in order to survive and adjust their business model to the above specifications. The decision behind the development of a project through firm creation implies planning from the entrepreneur by taking into consideration the project specificities (i.e. embedded technical knowledge, financial need for development, needs in terms of tangible assets...) but also risks inherent to the project, the financial availabilities and other environmental factors that the entrepreneur is subjected to (i.e. he has little influence over). Sectoral and market factors are an important part of this equation and therefore the later part of this section will focus on the biotechnology sector, which is the sector under study.

The biotechnology sector, which is the sector under study, is known to have specific industrial characteristics (cf. Chapter 2). These characteristics have made specific business models emerge for this particular sector, which are described below. The biotechnology sector has been distinct from other sectors in many aspects, including the existence of several value chains defining various markets to which firms can contribute. When talking about the biotechnology sector, one has to consider the specific sector in which firms are active, such as the pharmaceutical sector, agro sector, cosmetic industry or industrial application. Among these, the pharmaceutical industry is the best known and studied. The pharmaceutical value chain is known to be particularly complex and disintegrated (Gassmann et al. 2008) – with "a large group of islands of expertise" (Pisano 2006) and with a long time to market (up to 20 years). In the pharmaceutical industry, for firms choosing drug discovery models, the process of development, including clinical phases, can range from 5 to 20 years. Furthermore, the rent generation and rent appropriation for biotechnology firms are not high (Durand et al. 2008). Specialisation in pharmaceutical products, such as drugs by biotech companies, involves the most risky and constraining business strategies, since they have a long time to market and involve high technological risks (Sabatier et al. 2010). However, even though drug discovery is the best known activity, biotech firms can choose to exploit other activities when entering into the pharmaceutical industry (ibid.), such as specialised work on optimisation of the development process or the proposition of specific knowledge to pharmaceutical firms. This is because the amount of capital to raise for product making is often counted in millions (Gassmann et al. 2008). The need for financing is not only for project development but is also needed at each preclinical and clinical stage. For drug discovery models, the time from firm creation until first income (if the firm is focused on product only) is therefore lengthy and demands several schemes for raising venture capital. By comparison, inVitro[64] products, such as diagnostics, or products developed for other industries (such as agro-food, cosmetics, or for industrial applications) have a reduced length of trial phase and a shorter time to market, and therefore a reduced need for financing compared to firms specialising in drug discovery. There is a different level of financing needed for different technologies or products depending on the market chosen, but all these technologies still have a high need for financing and usually also require external investors.

These differences in technology and entry characteristics might restrict the business model possibilities. The entry condition and sector specific characteristics therefore result in a time to

[64] As noted earlier, InVitro refers to products used outside the human body, and therefore do not require clinical trials involving toxicity or side effects of the product.

market that is middle term to long term in most of the cases. Additionally, since the entry into high-tech firms are mostly innovative and the end product not fully developed (Oakey 1995), the level of risk (technological and financial) of a new venture is high.

For drug discovery companies, these characteristics influence the entry business model choice. The business model can thus vary from a high growth strategy, involving a high-risk business model that also has higher returns, to a shorter term rent seeking strategy, which involves a business model where income is made much earlier and financing needs are lower with less intrusive financiers. Different business models have therefore emerged for biotechnology firms, of which the main one are: the product model, the platform model and the hybrid model (Fisken & Rutherford 2002).

The product model aims at developing products for the pharmaceutical industry that can be either licensed to other companies through its development or sold directly. The time needed for earning the first income from the product usually takes 10 to 20 years for typical pharmaceutical products. This model is therefore considered as risky, but has the potential for high returns. These business models rely on high investments, which usually come from the pharmaceutical industry or a venture capitalist. The product model is considered less risky and needs a lower amount of financing for cosmetics, diagnostics or agro-food markets, which makes those markets more attractive, less risky and thus might not involve as much financial resources as a drug discovery model.

The second business model focuses on providing services stemming from technologies related to biology advances and is referred to here and elsewhere in the literature (e.g. Fisken & Rutherford 2002) as the platform model. It gives the companies the possibilities to have revenues in the short term, and also has a reduced risk compared to the first business model. The trade-off is to have a lower value generation in the middle to long term. These firms are not expected to make any significant profit and so are not very attractive to venture capitalists.

The last model is based on a mix of the two previous models, and is referred to as a hybrid model. While the firms in this business model still try to get into product development, which has a high value in the long term, they also generate short term revenue (usually through services) that reduce the risk of ceasing activities in the short term.

Beside the financial constraint that firms can encounter in this sector, there are also technological risks. Policy briefs (Direction générale des entreprises 2006; OECD 2009a; Arundel et al. 2009) have put forward the potential benefits of the new biotechnology revolution for human health benefits. However, some work has pointed out the rarity of such firms to succeed in this sector. The biotechnological revolution therefore struggles to be seen, which is due to the limitations of the innovation outcomes in terms of pharmaceutical products (Hopkins et al. 2007) and also the low performance of the average firm (Pisano, 2006). Therefore, even if some biotech firms have been success stories, such as Amgen, most of them earn no profit, despite needing high financial inputs. This is due to the technological uncertainty in transforming invention into marketable outcomes for pharmaceutical products (Sabatier et al. 2010). Concerning drug discovery firms, pursuing the product model may therefore involve great risk and little chance of success.

Recent literature has also pointed towards a dynamic nature of business models in this sector (Willemstein et al. 2007; Lehoux et al. n.d.). Willenstein and co-authors (2007), in their case study of Dutch firms specialised in health biotechnology, showed that business models of young firms are not static over time but showed changes during their early years in which they fluctuated between different business models. They exposed cases in which firms switched from service business models to platform models and also to product models. While not many details are given on the reasons for such change, one can hypothesise by looking at the above characteristics of the sector that firms may adapt their model to the available resources, while developing their real research objectives over time. Thus in the light of the above discussion, the firm **business model** is here defined *as the plan of the entrepreneur to develop an architecture of revenue that enables the firm first to survive and secondly to fulfil and capture value from its business strategy.* The business model could then change over time depending on the resources affecting the survival conditions and the business strategy. The **business strategy** *lays in the objective of the entrepreneur, to pursue specific activities that will be the basis of the long term competitive advantage that the firm aims to build.* Contrary to the established firms, newly created firms must develop an organisational structure and resources in order to implement this strategy, and thus the definition of their business model is crucial for the firm survival but also its ability to fulfil its business strategy.

The decision of action (entrepreneurial agency), when translated into the business model, is therefore constrained by many variables (e.g. technology determinants, time of development, regulatory framework, etc). The biotechnology sector, as we have shown, is particularly exposed to external determinants that make this sector particularly complex and requires a large amount of financing. The level of funds needed is variable depending on the business model chosen, but most often contributions from external financing are needed regardless of the activity due to the fixed costs involved with starting any activity (development of a product or service delivery). Two questions therefore arise from this statement. Firstly, how do entrepreneurs decide which types of business model they will pursue? Secondly, how does the involvement of external financiers affect the entrepreneurial agency?

3. The entrepreneurs' view on the business model

The business model is decided by the firm's leadership team, who evaluate the various risks and outcomes before taking the business decision regarding their own characteristics and preferences in parallel with their constraints (technological, market and financial constraints)[65]. These characteristics, that are taken into account during their decision making process, are related to the personality characteristics or preferences of the entrepreneur, such as risk aversion, need for control, independence and profit.

Entrepreneurs rely on their preferences (see Chapter 5 for an extensive discussion) to build a business model that suits their culture and their personality. The need for *control and aspiration of keeping the firm's independence* is a well-known issue that the entrepreneur faces, and must be weighed against the initial success of the project (Oakey 1995).

On the one hand, many authors (Penrose 1959; Oakey 1995) have emphasized the need for control over all the decisions of the firm. These needs can take two forms by either limiting the entry of other stakeholders in the decision process or limiting the growth of the firm. Firstly, this induces a limitation of entry involving venture capitalists for some companies, who then take part in decision making by appointing part of the managerial team, and by indirectly putting pressure on the management for further financing (Oakey 1995, p. 48). Secondly, the entrepreneur can willingly limit the growth of the company since it involves an increase in complexity of the organisation and also fragments part of the decision making into different levels in the organisation (Williamson 1967; Penrose 1959). The entrepreneur, since he may not wish to lose control over the firm, may decide to keep the firm to a small size and thus not fragment decision or supervision of power in the firm. As a result, some studies have shown that many founders prefer slow growth and independence from investors (Oakey 1995) by relying on early sales (Oakey et al. 1984), even in high-tech sectors.

On the other hand, in the specific biotechnology sector, many ventures are founded based on university research and therefore by scientists. Researchers from universities also have specific motivations, such as mainly following their *research breakthrough* or finding an application for the research done at university (Morales-Gualdrón et al. 2009). The research application motivation therefore often overcomes other motivation such as money (Chiesa & Piccaluga 2000) in relation to

[65] More details on how personal characteristics may influence entrepreneurial vision in Chapter 5.

the strategy underlying the creation of the new venture. In the case of biotech sectors, we therefore hypothesise that scientific entrepreneurs may want to settle for models with a higher impact on human health, which also coincides with a highly risky model, but if successful can also result in high financial return.

Once the entrepreneur has committed to a business strategy and decided to put his plan into action, he may seek help from different actors involved, including risk financiers such as venture capitalists. This section has emphasised the various preferences of the entrepreneur that may conflict with the financier, who in most of the cases aims at maximising his profits. The next section will therefore aim at understanding the direct and long term consequences of the involvement of a financier in the development of a business, especially in terms of freedom of decision and action remaining in the hand of the entrepreneur. The next section will show that in these conditions agency problems (i.e. principal-agent theory) can arise and it will try to understand the consequence of this problem for the development of the firm.

4. The financier-entrepreneur relationship

This section aims at understanding the advantages and the shortcomings of the financier-entrepreneur relationship in terms of entrepreneurial agency power. As explained in Chapter 1, entrepreneurial agency is defined as the power over decision and actions. It is a well known fact that the involvement of external financers, especially those specialised in early venture financing, can affect the decision making power of entrepreneurs. The section firstly presents the two types of financing commonly used during the early stages of venture development, which are business angels and venture capitalists. It highlights the different standards used by each type of financier and also the level of intervention they require when they decide to invest. This section reviews the literature dealing with the relationship between new ventures and capital risk financiers. This includes theories based on qualitative studies and theoretical models developed to characterise this relationship.

Venture capitalists and Business Angels are known to be the most common source of early financing, especially for ventures pursuing a risky project. They are both believed to be a crucial part of the development of innovative firms, but they differ in their financing methods. According to studies by Shane (2005) and Wong et al. (2009), Business Angels are quite different to venture capitalists in their investment behaviour.

Business Angels can firstly be a complementary to venture capitalist financing. They are an initial financing method used when the entrepreneur is not yet able to raise money from the venture capitalist (VC). Business Angels also differ in that they are individual investors and invest for their own profit, compared to VCs who are federated into professional funds. Due to their early and individual participation, they also tend to invest a much lower amount of money, and tend to invest in firms that are geographically close to them. In terms of control of the firm after investment, the business Angels are less constraining than the venture capitalists. They can offer advice or network relations but they usually intervene less in the development of the business. For example, they usually do not require stage financing, changes in management or regular attendance at board meetings. In other words, in many cases the involvement of business Angels has less effect on the entrepreneurial agency of the entrepreneur.

This is not the case for venture capitalist financing. According to case studies of start-ups and venture financing (Gompers & Lerner 2001; Bidhé 2000; Sahlman 1990), the relationship between financiers and entrepreneurs can affect the entrepreneurial agency at different levels. This literature has pointed towards the intervention of the financier at different levels, such as project development through milestones, stage financing, or even the appointment of a new management team. This difference may come from the fact that venture capitalists are professional organisations who invest the funds of clients' and seek high returns with repayment after a period of around 10 years (Gompers 1995; Bidhé 2000; Sahlman 1990). Venture capitalists therefore distinguish themselves from business angels also in terms of inputs for human capital and management. Through the appointment of new management, the venture capitalists usually bring management members with significant experience in managing high-growth firms but also in terms of industry specific knowledge, which the initial entrepreneur may be lacking. In order to maximise their returns, venture capitalists opt for detailed monitoring of the firms invested in. The extent to which these actions are taken depends upon the agreement between entrepreneurs and venture capitalists, and also the level of financing needed. In this case, many authors (Gompers 1995; Cable & Shane 1997; Arthurs & Busenitz 2003) have pointed towards an agency problem in this relationship. The agency problem emerges from the fact that there are different objectives that the entrepreneur and the venture capitalist can have. As explained earlier, entrepreneurs, depending on the case, may not always have a preference towards profit maximisation (but rather project completion or survival of the firm), but the VC does. The VC therefore uses the above tools to influence the action of the entrepreneur towards his own objectives, and thus has an impact on entrepreneurial agency. The start of a relationship between an entrepreneur and a VC can therefore imply a moral hazard problem[66] between the two parties. The VC may therefore bear the risk of the

[66] Moral Hazard problems occur when a party's action incurs a cost to another party that then bears part of the risk.

entrepreneur's action in case it deters the financier's investment. In this case the VC may wish to prevent this kind of behaviour by requesting contracts or by implementing ways to observe the entrepreneur's actions. This problem is well known and has been studied extensively in economic theory. This problem is dealt with in the principal-agent theories (which deal with agency problems) and it will be further developed here.

The notion of what will later be called 'the positive theory of agency', was introduced by Berle and Means (1932) and has been used extensively in the characterisation of the relationships of owners and managers in large companies. The formalised school of agency, also called 'principal-agent' theory, has also been used in other contexts, for instance to describe the relationship between the Venture Capitalist (VC) and the entrepreneur. Agency theory can be used to design a relationship when two entities (the principal and the agent) from a single organisation have different desires or goals for the given organisation, and when there is an asymmetry of information and observation problem for the party that has ownership (principal) over the acting party (i.e. agent). In this case, the principal-agent theory proposes ways to direct the effort of the acting party (i.e. agent) towards the desired goals of the principal party in order to minimise moral hazard problems. This model is mostly used to characterise the relationship between owners (principal) and managers (agents) in a firm.

As explained in the literature, in order to prevent moral hazards on the entrepreneur's side, the venture capitalist often enforces a variety of control actions, as outlined above. The monitoring, by stage financing, milestones and new management, are interventionist tools in order to make sure the venture is developed according to the financier's goals, and that the entrepreneur in the firm is orienting his efforts accordingly.

Many studies (Sahlman 1990; Sapienza & Gupta 1994; Gompers 1995; Gompers & Lerner 2001) have focused upon the reasons and the way in which venture capitalists (here considered as principal due to their involvement in the company through their investment) can constrain the entrepreneur into following the most profitable outcome for them (VC). These studies often focus on moral hazard and agency problems, and thus discuss how the venture capitalist can control and drive the entrepreneur towards a behaviour that is appropriate for them (i.e. towards positive effort). Venture capitalists aim at making a range of risky investments with an expected high return from a few of them after typically around 10 years of investment[67]. They are therefore expecting that the ventures they back have business models that guarantee a high growth and high-return at the term of investment, which in many of the cases involves focusing only on the development of a

[67] For a longer discussion on how venture capitalists operate, chapter 1 has a section dedicated to it.

single project (Gompers 1995). One of the strongest tools to control and gather information about the advances and viability of the firm is through stage financing and progress monitoring, which is possible due to the stage financing that is often adopted (Sahlman 1990; Gompers 1995). This tool gives the financier close control over the decisions of the entrepreneur, but most importantly gives an exit option before full investment. The VC constrains future investment in the venture through stage financing and the realisation of the previous results. The stage investment described above aims at reducing the amount spent by assessing the improvement of the project on a regular basis and re-evaluating the time and value of the expected return. As the principal agent theory shows, the attitude of the VC is therefore rational due to his situation.

Thus when the entrepreneur engages with the venture capitalist, he surrenders part of his entrepreneurial agency to the financier and thus may lose his future freedom of decision and action concerning the firm. Surrendering agency may be a strategic choice for the entrepreneur, who may prefer to develop a risky project with a high impact to increase his chances of success through this type of financing (Croce et al. 2013). However, at a later stage the entrepreneur may not be able to change strategy because he is bound by this relationship, and will therefore be constrained in his decision by the financiers (e.g. is involved into forced moves)[68]. The entrepreneur who chooses venture capitalist help is therefore locked into a single project (due to the requirement of VC expressed earlier) due to his initial choice, and the entrepreneur has limited opportunity (with his constrained choice of action) to have an influence over the firm strategy if the project were to fail or if the venture capitalist decides to no longer pursue the project anymore.

The literature has extensively shown or built models to explain the rationale behind the financier's behaviour, but there has been little literature talking about the influence of the loss of agency that the entrepreneur may face when involving specific types of financing. The aim of this case study is to understand how entrepreneurs' weigh the choices regarding this type of financing, and particularly pinpoints what factors influence their choice.

[68] The use of free moves and forced moves is derived from the concepts developed by Pickering (Pickering 1992). This theory borrows a notion linked to the theory of agency via the sociological view of human behaviour. It includes the notion of free moves and forced moves in scientific development, where free moves are used when the agent has choice and discretion and forced moves are used when the agent surrenders agency and has to comply with disciplinary rules.

5. Methodology

The aim of this research is to look at how entrepreneurs decide on their business model, especially when under financial constraint. As explained above, in some sectors the choices made on the financial side determine the path of evolution and growth of the firm, especially because the decision cannot be reverted and in some cases results in a limitation of the entrepreneur's entrepreneurial agency in the future. The methodology is built on a case study analysis since there are currently no previous hypotheses on these issues and it therefore needs theory building (Creswell 2003). The study focuses on 13 companies in Biotechnology originating from the Alsace BioValley (ABV) cluster in France. The study also features the story of 7 additional companies because their experience with financiers influenced the cases under study, according to the data gathered from the interviews.

5.1. Research design

The paper aims at studying the decisions of innovative firms towards their business models, especially the choice of involving venture capitalists in the development of the venture. As the literature review has explained, the relationship between the entrepreneur and VC is peculiar due to the moral hazard problem that may exist between the two parties. As explained above, when involving a VC, the entrepreneur gives up entrepreneurial agency to the financier. This agency limitation could cause problems at a later stage if the entrepreneur and the venture capitalist do not share common goals for the growth or the risk of the enterprise.

The study accounts for two selections of firms, the main selection of firms that constitutes the main case study used for drawing the results in this chapter, which includes 13 cases and a second selection of 7 firms since those firms had an influence over the choice of business model of many firms in the main study.

The study focuses especially on firms from a biotechnology cluster, called Alsace BioValley, from which only firms created after 2005 were selected. The aim of the interviews is to identify determinants that affect the decision upon which a newly created firm decides for a business model involving venture capitalists or not. The choice to interview firms in one cluster was based on the replication design proposed by Yin (1994) (cf. Chapter 3 section 2.1.1.3). In this way information was collected from one specific sector and from one specific cluster. Hence, companies were selected on the grounds of their age and technology. The technology choice was oriented towards firms that were specialised in biotechnology and which had a project relating to health related products. In our cluster 21 firms were therefore contacted and from them 14 firms accepted to be interviewed through one or two of their founders or their current manager. One of the firms interviewed was discounted as it was too early in its development and had not yet sought any financing, which leaves us with a sample of 13 firms. The age was crucial for the interviewee to be able recall precise facts that happened at creation time and to recall with precision the reasons for their decision towards a given business model. Selected firms were therefore less than six years of age.

A second set of firms is presented, since they had an influence on the choice over business model of firms in our sample of study. The 7 firms from this second selection are all firms named in the interviews from the first sample of firms.

5.2. Data Gathering

The main case study was designed in two successive rounds. They were done using face to face interviews with founders of the contacted companies. Where possible two founders were interviewed, but due to the firm size and time availability of some founders only one interview was conducted for some of the cases. The first round of interviews was a pilot round. However, since the design had not changed significantly between the two rounds, the cases included in the first round were kept in the analysis of the results.

Each interview followed a semi structured design and included questions targeting details about the history of the company from its research project to its creation. The interview design aimed at retracing the history of firm, while talking about different aspects such as the research project evolution, the management team, the market influence and the financing aspects. The financing aspect was of particular interest for this paper. The answers were drawn from the question about their search for financing over time, the different sources of financing used in order to start the firm, and their prospects of future financing. Adding to questions tackling aspects of financing in a descriptive way, the respondents were also asked about the influence of the financial aspect on the firm development. These issues were discussed in order to understand the evolution of the view of the business model and business strategy through market and financing variables.

After the first set of cases was completed, some preliminary grounded results emerged that shaped some of the insights for the subsequent cases, especially concerning the significance of the experiences that other local firms went through. The interviews were therefore modified to include a discussion about other firms' experiences and paths in the cluster, as described by the entrepreneur, and also the influence of the successes or failures of other firms.

These discussions resulted in the collection of secondary data concerning the *second set of firms* cited by the interviewees. Since these cases emerged because of referral from the interviews, they are not in any way representative of firms from the time. The description of these firms is only for illustrating the cases on which the main cases in the study drew their experience. The data gathering therefore includes the performance in terms of raising funds and survival of firms created around the year 2000, and is described in the first part of the results. The secondary data collection was based on historical details given through interviews, which were cross examined through secondary data originating from press releases and other scientific publication on the topic. The scientific publications are mainly drawn from work done at the Beta laboratory at the University of Strasbourg, which has already made case studies drawn from firms in the ABV cluster (Bureth et al., 2006).

5.3. Data Analysis and operationalisation of the concepts

The research design aims at inducing theory on the basis of a multiple case study. It grounds results by looking at patterns that emerge from the data extracted from the semi-structured interviews. The unit of analysis is the evolution of the business model choice, with its determinants.

As explained earlier, after the pilot interviews (with 4 firms) targeting start-up business models, a pattern of regional learning emerged. In order to validate this intuition, further interviews were carried out with 9 further firms, which were carried out with scientific founders and firm executives (when possible), included additional questions on the issue of the influences that affected their business model and their personal view about other firms in the cluster. The guidelines for interviews were therefore adapted from the pilot interviews to the final interviews in order to gather more information about business model decisions. These steps were included to see if the observations from the first set of cases were also true for the subsequent cases and interviews.

These interviews led us to distinguish between different entrepreneurs who had knowledge about the cluster dynamic in the past or were connected directly or indirectly to already existing firms in the same sector and drew on their experiences. Hence, as part of this observation, links from each entrepreneur with firms from the previous generation was retrieved from the interviews in order to compare which ones had been influenced by the previous generation of firms.

The data retrieved in the results comes from the latest generation of firms based on interviews coupled with secondary data. Tables were therefore drawn from case reports and verbal recordings made at the time of the interview in order to insure precision in the presentation of the data. The data regarding the previous generation of firms (shown in table 4.1) was drawn exclusively from secondary data, since we do not aim to analyse in detail their choice of business model but rather retrieve events and stories to give the reader a background on the history of the cluster and on which the newly created firms drew from to make their decision.

The firm reports also attempted to identify different variables, apart from other firm experiences, that helped them design their business model and also choose their mode of financing. Two of the main variables used in this chapter are the business strategy and the business model, which have been defined theoretically for start-ups in biotechnology in section 2. We will define here a proxy for the concepts in order to operationalise these different variables. For the first one, the business strategy, is defined by the long term goal of a firm that will be its main future activity, we use as a proxy the activities that are planned to be the main activity on a long term basis. The business model includes the short term activities in which the firm is now involved and whose objective is to bring revenue and therefore enable the firm to survive. Long term strategy and business model can be aligned in some cases.

Other data is operationalised in three summary tables. The first table covers the earlier generation firms, the second covers the financing choice and the business model decision, and the third focuses on the experience of the founders and their link to the previous generation of firms. More details about the different variables and their operationalisation will be given following in the description of the tables.

Data for the earlier generation of firms (7 firms)

Here we present the way that information was collected in order to create table 4.1. The firms are included on the basis that they have been cited by the respondents in our interviews. The information gathered about them was partly obtained through press releases but also through previous publications. It was also decided to not mention the names of these firms since the publications have left these firms as anonymous and because much of our information is drawn from these documents. Table 4.1 has used the following construct variables:

Funds raised: This variable refers to the amount of private financing raised by each firm through different private investors, such as venture capitalists and Business Angels. The four first cases were recognised to have raised a large amount of money compared to the national average on similar projects. For one of the firms (Firm G) no information could be found through press releases regarding the amount of investments.

Status: This variable aims at determining if the firm is still in activity. Three of the firms have died and their activities were not taken over by other firms. For firm B the investors decided to sell their assets in the firm because a problem emerged in product development emerged. Finally, for Firm E the original project was also having problems but the company changed names and activities following negotiations with the investors. The final two firms have survived and are considered as established since they have a healthy turnover and employment growth.

Business models: Two types of business model were chosen between the firms from the previous generation, which we refer to as product development and hybrid models. Product development models involve the firms to concentrate on human therapeutic products and all involved finance from venture capitalists (with a strong involvement in the management). The firms with this type of model were firm A, B, C, D, E, and firm F and G are identified as hybrid models. They are both involved in providing services to other biotech or pharmaceutical companies, but also have activities in terms of collaborative research projects.

Data for the main case study (13 firms)

<u>Business model and financing choice</u>

Business model: The business model reflects the discussion in the literature review and distinguishes between three types of business model: product oriented, service oriented and hybrid model. The product model involves firms focusing only on the original research project and aims at pushing it to development as quickly as possible, while limiting other activities to a minimum. For the hybrid model, the activities of the firm are oriented towards two goals, a product goal but complemented with services. This configuration provides the possibility of having early revenues in addition to the pursuit of a project. Finally, the service only model aims at focusing the firms' activities only on services and having short terms return on investments. For firm *Kappa* we mentioned 'product to hybrid' in the table, because within the first years of development the business model had changed due to a shortage of financing. For Anagenesis and Rhenovia, their model differs from other firms. Anagenesis' research project involves the development of processes that have more than one domain of application so we specified that the business model is not only based on one product. Rhenovia's hybrid model differs from the previous cases because it does not involve service activities but rather collaborative research projects to complement their original research project.

Choice reasons: This section gives some qualitative explanation about the reasons given by the entrepreneurs towards their choice of business model.

Main financing source achieved: This variable is drawn from the replies given in the interviews in which the respondents specified their source of financing. In order to not increase the complexity of this variable we did not invoke all the sources achieved, since most of them benefited from grants in their early life such as the concours oséo (more can be found out in Chapter 3 section 3.1.3). They used these funds for starting their activities but it is not their main source of financing.

VC wanted in early stages: This variable aims to be binary. Either the interviewee showed interest in involving venture capitalist companies or not. However, in one case (firm *beta*, which was one of our pilot interviews) we do not have this information, since the founder did not express any opinion on the issue. For one of our companies (Anagenesis), the management team acknowledged that the venture financing was not yet discussed and thus did not have yet a preference (this was coded in the table as 'Not yet').

Experience of the founder

Founder experience in firm creation: This variable is drawn from the description of the founders' (as a team) experience in firm creation. The answers are binary, where a positive answer corresponds to having founders involved in a firm creation project earlier in their career or being previously having a managing position in a start-up company.

Founder experience in the industry: This variable is also drawn from the description of the founders' (as a team) experience in firm creation. It is also binary and reflects whether or not the management team had members who worked in the bio-pharmaceutical or biotech industry prior to the founding of their venture.

Strong connection with previous generation: This variable establishes the link between the new created firm and a previous generation of firms. This variable can be positive in two cases. The first case is if the founder has been involved in the creation of another start-up in the region and thus is strongly connected to the founders of the company they have worked in. The second case lies in the fact that the firm founder knows personally some of the founders of firms of the previous generation.

Influence from previous generation: This variable is linked to the one above and names the firms that have been cited within the interviews. This is drawn from the question answers or from spontaneous talking about the firms from the previous generation in which the interviewee mentions the names of firms they knew and whether they seek to follow or not. In all of our cases Firms A to E were identified as examples to not follow due to their financing choice, while firms F and G were identified as being good examples to follow.

6. Business model choice: personal experience or regional learning

Over the course of case building and interviewing, the previous generation of firms were often mentioned in the discussion towards the firm's choice of a business model. These mentioned firms were described as having had good or bad practices by the interviewees. Before discussing the current firms' business model, this section will therefore return to the previous generation of firms in the biotechnology cluster, who were formed at the end of the 1990s and beginning of the 2000s. The first section will therefore look into the recent history of the cluster and point out particular firms created with different business models and their position today. This first section aims to give an overview of these firms from the previous generation, and will serve as a background of the analysis of the determinants for the firms' business model. The second section then focuses on the firms studied and the influences for their choice of business model.

6.1. Brief history of success and failure of previous generation of start-ups in the cluster

The industrial history of the local cluster in the Alsace region is rich concerning chemistry and pharmacy development, but also in biotechnology. Biotechnology started in the late 1970s with the creation of Transgene, who grew to become an early and important player in the biotechnology sector. The region's entry into biotechnology activity was early, since this technology was developed in the 1970s. The number of firms has been constantly growing since then. For instance, since the year 2000 we can record approximately 56 new creations of firms in domains related to the biotechnology sector (Lang et al. 2012).

In the late 1990s to beginning of the 2000s, a number of influential firms were created that were well known among the local scientific and industrial community. The descriptions of these firms are shown in table 4.1. Table 4.1 shows a number of start-ups that are, or have been, known in the region for their scientific potential or performance. This list is not an exhaustive but includes the most emblematic firms, including all the firms that are referred to in the interviews.

The first set of firms (Firms A, B, C, D and E) has been described as successes at the time of creation, since they raised a significant amount of money from venture capitalists and had high expectations concerning drugs development. All of these firms relied on a drug discovery only model, relying mainly on the venture capitalist type of financing for their early development. Those firms had a solid scientific background, including one who was funded on the basis of results from research of a Nobel Prize winner. On the financial side, the 4 firms (firms A, B, C and E) have a record of important investments from venture capitalists. These investments were considered as large compared to normal round financial investments in France for other biotechnology companies (Bureth et al. 2006). Due to these characteristics, these firms were seen as the future successful companies of the cluster, and were well known locally (in industry as much as in academia). At a time of large investments and growth in terms of employees (they employed between 20 and 46 people each), these firms were therefore seen as good role models to follow. During their first years, these firms experienced significant growth in terms of employees thanks to their funding. Even with the great start that they experienced, after a few years most of these companies closed due to failing to secure further financing needed for their development or due to problems encountered in their project development (of drug discovery). Firm A for instance failed to raise further financing after a second round, and Firm D also failed to raise money. Firm B, was declared bankrupt in 2006 after the failure of several of their products during clinical trials in phase I and phase II, while Firm C was also closed due to the unwillingness of financiers to pursue further financing in the firm. Ultimately, the assets of the two firms (Firm B and Firm C) were sold to foreign Biotechnology companies after liquidation[69]. All of these firms focused their business model on the long term development of potential new blockbuster drugs, which was highly risky but had a very high potential returns. The success of these business models was based on a consistent and long term financing relying on external funding partners, especially venture capitalists. The long term model was not sustainable for them because in most of the cases financiers did not reinvest after a few rounds or due to problems in the clinical trials of the products pursued, which ultimately led to the closure or sale of the companies to competitors.

Table 4.1: Overview of influential biotech firms created between 1999 and 2000

Firms name	Funds raised	Status	Business Model	Creation Year
Firm A	30 M€	Died (2005)	Product development	1999
Firm B	55 M€	Sold by investors (2006)	Product development	2000
Firm C	30 M€	Died (2005)	Product development	2001
Firm D	300 000€	Died (2005)	Product development	2001
Firm E	27 M€	Difficulties – changed into Domain Therapeutics	Product development	2001
Firm F	7.8 M€ (9 years)	Survived - established	Hybrid model	2001
Firm G	Business Angel investment (amount not known)	Survived - established	Hybrid model	1999

On the other hand, the two last companies listed in the table did not get as much attention or have as large a potential prospect as the former ones. They started with limited external investments and were dedicated towards services rather than products or drug development. These

[69] Data was gathered on the Factiva website.

companies were therefore not perceived as having a high growth potential and so attracted less attention at the time of their creation. However, after 10 years of existence, these two last companies (Firm F and firm G) are among the few companies left from the previous generation group created end 1990s and beginning 2000s. In addition to being the surviving firms, they have undergone substantial growth in terms of employees and turnover. The two enterprises currently have around 45 employees (45 and 46 respectively for firm G and Firm F). Both enterprises grew progressively over time. Firm G had particularly high growth in terms of employees at the beginning of 2000, by doubling their numbers between 2002 and 2004 to arrive at 40 employees at that point in time, at which point it had reached 5 million Euros in sales. In the case of firm F, it also evolved gradually from 4 employees at inception, to 22 by 2006 and then to 42 by 2011, at which point they aimed at furthering the growth in terms of employment to 10 more employees. Therefore, after more than 10 years of trading, these two companies are considered to be well established in the cluster. Their main activities were based upon services but also collaborative research projects, which gave them the opportunity to secure sales and income and experience sustainable growth in terms of employees and also in terms of turnover, without the dependency on an external source of financing. The revenues of the companies were around 2.6 million of Euros in 2009. These companies both relied on financing either to start their activities or finance substantial growth periods. They turned towards less invasive means of financing compared to venture capitalists (they turned to business Angels instead), since they were able to generate revenues from the beginning of their activities. Both of these companies based their activities on scientific technology, but compared to the other firms mentioned above, they specialised in drug development rather than drug discovery, the first being specialised in lead optimisation and the second focusing on chemical based vectors as their short-term base of revenues. After nearly ten years of activity, these two firms therefore stand out for their survival and growth during that period.

These firms represent extreme cases of success and failure in the region, and they are in no way representative of the overall population of firms at the time. However, one can note that in that generation there were numerous firms involved into drug discovery business models involving a venture capital type of financing.

The next section will look at more recent firm creation and their decisions towards a business model. It will explain the influence of the previous generation of firms (presented in this section) on their idea of good or bad practices to follow.

6.2. Business model influences of new firms

This section aims at understanding how founders of companies arrive at choosing a particular business model. In other words, what influences their choice towards a certain type of activities and a certain type of financing? As explained in Chapter 2, in the biotechnology sector, the choice towards the main activity of the firm and towards a domain of application is determinant for the architecture of revenue that the firm will be able to sustain, but is also determinant for the type of financing that the firm should use in order to develop their project. The choice of the firm's main objective and activities will be best suited to a specific mode of financing. As shown in the literature review, the funding partners also have different levels of impact on the agency of original founders and therefore on the strategy of the firm. The case study analysis gives us the opportunity to explore how the decision for the choice of the business model was taken regarding the funding constraint. In order to understand the underlying problems behind the decision for a business model choice, it is first necessary to give an overview of the model choice made by the firms studied and the reasons behind it. We will then go deeper in the leadership team's previous experience in the industry or being part of start-up companies in order to better understand the reasons for their choice towards a specific strategy.

6.2.1. Choice of their business model and financing choice and constraints

As explained in the literature review, the entrepreneur chooses his business strategy and business model, which then defines the venture's activity but also its initial need for financing. The level of financing needed, is suited to certain types of funding, which constrains the future agency of the entrepreneur. In the light of this loss of agency, the entrepreneur does not only have to act with his own objectives in mind when choosing a business model but also with the implications of certain types of financing. The vision of the founder and his preference towards having a high growth company, having control over the company and his wish for the company to survive for a long time or sell it after a few years is therefore influential in the reasons for choosing a particular mode of financing and thus restricts the business model that they can implement.

The main case studies, based on 13 firms created after 2005, show that financing institutions can influence the project and business strategy in many ways. Here we distinguish between two types of institutions that play a role in the early financing of high-tech start-ups, which are the equity (e.g. venture capitalist) and non-equity (e.g. business angels) financial organisations. Both of these types of financing have been used in our case study sample (see table 4.2).

Table 4.2: Business model and financing choice

Firm's Name	Bus. Model	Choice reasons	Main Financing source achieved	VC wanted in early stage
Alpha	Product	Research commercialisation	Public funding	Yes
Beta	Product	Research commercialisation	Public funding / Business angels	-
Phytodia	Hybrid	More control over enterprise; sustainable incomes	Business Angels / public funding	No
Alsachim	Services	Reduce risk – long term view	Business Angels/ Public funding	No
Kappa	Product to Hybrid	Problems of finding the investors... no other choice	Public funding	Yes
Enovalys	Product	Aim for a middle term sale to bigger players	Business Angels / Public funding	Yes
Domain Therapeutics	Hybrid	Services focus in order to develop trust with pharma to sell them afterwards their own molecules developments	Venture capitalist	Yes
Biomica	Product	No money problems	Own financing/ public funding	No
Cell Prothera	Product	The objective is to keep **control** over the company while being able to **finance** the project	Business Angels / Public funding	No
Anagenesis	Product (processes)	No dilution for the company shares *for **control** over the company*	NFPO[70] Grant	Not yet
Bionext	Product	They want a **fast growth** and not to involve business angels because they target venture capitalist that might not like business angels funding	Public Grant / love money / public funding	Yes
Admet-X	Services	They didn't want venture capitalists because of bad experiences / *control*	-	No
Rhenovia	Hybrid (co-development + product)	Their experience made them prefer to go towards the business angels route, because of bad experience with venture capital / control	Business Angels / Public funding	No

Table 4.2 shows the preference of the companies for different types of model. The three models identified in the literature review are present, which are the product model, the hybrid model and services model. Each type of model is represented, but most firms opted for the hybrid model.

[70] Not For Profit Organisation: Here the French Association for Myopathy.

6.2.1.1. Product model

Eight firms in our sample have chosen the product model. This decision is due to the willingness to focus on the technology or product development at the root of the firm and push it to market as soon as possible. However, not all of these firms are comparable between each other due to the product they are developing and the market in which they are operating. Some of them are concerned with drug discovery such as firm *Kappa*, or involved with technology with a long development time such as Anagenesis. In the case of firm *Alpha*, their product is not focused on human therapeutics but on a device that still depends upon a range of clinical trials for its commercialisation. There are firms' specialised in products or processes (Firm *Beta*, Biomica and Cell Prothera) that do not involve the heavy trial periods required for drug discovery. Finally, the final two firms (Bionext and Enovalys) that have a product model are oriented towards software development, which has a very short time to market. Thus in this generation of firms, it is very difficult to find an example of a drug discovery only business model, which contrasts with the early 2000s in which we identified at least 5 firms that chose to involve VC financing.

Looking more into the financing options, one can observe a variety of financing options involved in firm creation and development. Many of the projects are supported by Business Angels. This can be explained first by a high number of firms that do not have a product aiming at human therapeutics and thus simply do not need to involve venture capitalists. This is because the funds required for these firms are lower than that offered by Venture capitalists. Thus, naturally many of our cases do not look for Venture capitalist investments. As reported in Table 4.2, some of the firms explicitly aimed at obtaining funds from VC financiers, because either their development project requires extensive funding (firm *Alpha* or *Kappa*) or because they aim at a strategy for growth (Bionext and Enovalys). Finally, Anagenesis can be identified as having specific financing, which involves certain advantages concerning the continuity of their financing. Before the firm creation, the research project behind this firm was financed by NFPO, which are a specific type of financing. This specific organisation helps people with myopathic problem and thus directly benefits from the results of the research. Thus this organisation does not have a problem to continue to finance the research developed within the firm if the project contributes towards therapies that can be used to treat myopathic illnesses. This firm is therefore not under the same type of financing pressure as the other firms, because the others must find distinct types of financing when pursuing research within university and when the firm is created. Another exception can be identified in Biomica, which main investor is one of the founders of the company and has sufficient personal resources to back the company without resorting of high-risk financing. This company is oriented towards activities which are related to diagnostic and therefore also has a shorter time to market than the pharmaceutical products.

The cases have also pointed towards an adaptation of business strategy and thus business models, from their interaction with potential investors. The following examples explain how the relationship before and after being engaged with certain types of financiers incited entrepreneurs to adapt their vision of what was possible to achieve within their original strategy.

The product model may not always be the definitive model when the company builds their first business plan. The cases point towards changes occurring in the business model when searching for financing and after meeting investors. The interaction with investors can in certain cases influence the initial project, in terms of its scale, but can also change the business model, as the following example shows. For instance, Enovalys had to review their initial project plan after their initial search for financing:

> "The project varied a lot because of the financing solutions. Because the initial project was very expensive and so we modified the initial project for reducing its costs. And it was also good because the project became cleverer then. [....] The fact that we couldn't find funding obliged us to move to a less expensive project. We took two years to raise funds and we were also in contact with many people from different domains who helped us for going into this reflection [in how to change the project]"[71]

Confronting their business strategy while considering the financing available to them therefore made them realise that the project they were aiming for could not be achieved due to a lack of financial solution. The entrepreneurs therefore had to review their business strategy and business model with the feedback from financiers in order to be able to raise sufficient financing. This is not an isolated case, as other firms through their search for financing, have adapted their business model to 'financeable' options. Firm *Alpha* was in a situation where they did not hold all the competences needed in order to fully develop and bring their product to market. They were therefore advised to have a shorter time to market plan for getting investors on board, as the entrepreneur reported:

> "At the beginning, we wanted to do the clinical trial with all types of cell possible, but the [potential] investors clearly told us that this was going to be too long, we do not know how long it was going to

[71] Translated from French : "Le projet a beaucoup varié à cause du financement. Car le projet initial était extrêmement cher, et donc on a modifié le projet initial pour qu'il soit moins cher. Et c'est bien parce que du coup il est peut être plus intelligent, le projet. […] Le fait que l'on ai pas trouvé d'argent [pour le projet initial] nous a obligé à passer à un projet moins coûteux. On a mis deux ans à faire une levée de fond et on était en contact avec beaucoup de personnes de différents domaines qui nous ont amené à faire cette réflexion également. "

last, and that we did not master cell technology. Today we present a risk package saying that we are going to do human testing with human cells, without any regulatory problems in order to, in about three years' time, with the obtained results, we would have the possibility to partner with another Medtech company or a Big pharma."[72]

The financier can also influence the firms into implementing a one product only business model, as the two following firms experienced. The first firm was encouraged to do so before investment in order to improve their chance of raising funds as quickly as possible. In the case of the second firm, this was a requirement after investments from VCs.

The first of these firms was created in 2010 and since its creation has been seeking financial resources from venture capital types of organisation. Firm *Kappa* had then been advised the following when seeking financing:

"It is true that the compound that we tested had been selected by the laboratories, and it was the most advanced compound. Thus naturally the potential investors advised us to pursue with the most advanced compound, it could be the one to enter the quickest into pre-clinical, and do value creation."[73]

The firm followed the investor's advice to focus on only one compound. After the early stages of testing of the compound, they found out that the proof of concept was not conclusive and thus may jeopardise their chances of being financed. Thus they decided to reorient their strategy towards the possibility of offering services in order to survive in the short term.

This case can be compared to one of our firms, Domain therapeutics, that evolved from another company that does not exist anymore today. The earlier company was called Faust Pharmaceuticals, and had a business model oriented towards drug discovery and therefore had the involvement of a venture capitalist. Faust Pharmaceuticals experienced the same kind of pressure by a venture capitalist to follow a business model centred on a single product for pharmaceutical development:

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[72] Translated from French: "Au début on partait sur faire les études cliniques avec tous les types de cellules possibles, mais les investisseurs nous ont clairement dit que c'était trop long, on ne sait pas combien de temps ça va durer, vous ne maîtrisez pas l'aspect cellule etc. Aujourd'hui on présente un '*risk package*' en disant, on va faire une étude sur l'humain avec des cellules humaines, aucun problème réglementaire, avec dans trois ans, avec les résultats obtenus, on aura la possibilité de pouvoir intéresser une medtech ou une Big pharma. "

[73] Translated from French: "C'est vrai que le composé que l'on a voulu tester, c'était un composé qui avait été sélectionné par les laboratoires et qui était le composé le plus abouti, donc les investisseurs nous avait conseillé de poursuivre le composé le plus abouti et qui pourrait le plus rapidement rentrer en préclinique réglementaire et faire de la création de valeur. "

> "At Faust (previous name of the firm) we were not allowed [to enter services activities], we just had to consume the cash of the investors to dedicate 100% of the activities to research and clinical development. The investors wanted us to concentrate on the value creation and they said that services defocus the firm and takes resources to not bring much back [in terms of value creation]. If the society needs money please ask us (investors) and we will give it to you."[74]

As the interview recording shows, in their previous firm they did not have a choice towards the business model since the investors were against any other type of business model other than a product only model, since it was the only plan that was financially viable for the venture capitalists to pursue. Consequently, as explained in the literature review, risk financiers may urge entrepreneurs to aim at a single product business plan in order to secure potentially high revenue from investments and minimise resources used by not developing any other project. Venture capitalists are able to sustain this type of strategy by pooling different high-risk projects, expecting that only a few of them will succeed and financially make up for the other ones that failed. Concerning the fate of the firm Domain Therapeutics, the early investors (from Faust Pharmaceuticals) kept their shares in the company, which explains why this company with now a hybrid model have a venture capitalist financing. This was possible through the negotiation of the firm CSO to save the technological platform of the company.

In the cases of the above firms, this strategy did not work out and they had to move towards a hybrid model. In the case of firm *Kappa*, the initial research target did not meet expectations during the first trial and they still had not found any venture capital willing to help them develop their project on the financial side. Having used most of their resources raised through public grants when creating the company, they faced financial pressure, which could only be resolved by value creation (if the company wished to continue trading) and therefore provided services. In the second case, the Faust Pharmaceuticals company encountered some serious delays during their trials, which made the investment unviable for financiers due to the expected shortage in returns (as seen by the patent expiration time for the product). However, at the time the Chief Scientific Officer found a way to convince the investor that the firm had a good strategic advantage in some services it could offer, and convinced the venture capitalists to not close the company. They now hope to be able to develop a company based on a hybrid model by building on competences built in-house.

[74] Translated from French: "Chez Faust on n'avait pas le droit, chez Faust on devait juste consommer le cash des investisseurs et dédier 100% de notre activité à faire de la recherche et du développement clinique. Les investisseurs disaient qu'il fallait se concentrer sur de la création de la valeur, ils disaient faire du service ça défocalise la société et prend des ressources pour rapporter pas grand-chose ; si vous avez besoin d'argent vous nous demandez et on vous le donne."

A firm's business model and strategy imply specific financial needs if the firm is committed to pursue their original business strategy. If the strategy is oriented towards a product with only financial return over the long term and large initial investments, then the financial needs of these firms can only be fulfilled by venture capitalists. Venture capitalist funding is also helpful for firms aiming at having a high growth.

This section has shown that in some cases the original strategy can evolve when confronting their financial needs to the offers available. In some cases the decision of the entrepreneur towards an early strategy conformed to the willingness of financiers in order to improve their chances to access financing. This section has therefore shown that interaction with financiers can influence entrepreneurial agency through the decision and action of the entrepreneur towards his own strategy in order for him to obtain sufficient resources to pursue his enterprise. The last example has also confirmed that firms involving venture capitalists are also limited in their decisions. This is explained by the fact that financiers hold part of the ownership of the company together in return for the financial resources and thus, the general strategy of the firm and the business model is strongly influenced by the financiers.

6.2.1.2. Hybrid or service only models

Unlike the firms mentioned above, the ones that are studied in this section have integrated a business model in which revenues are incoming on a short term basis. The firms with a service model aim primarily at providing services over their lifetime, while the hybrid firms provide short term activities in order to support other activities in the longer term. In this section we present these two models in turn and discuss the reasons for the choices of these firms.

When choosing a **hybrid model**, firms decide to pursue two activities at the same time, which in most of the cases includes an activity of services or collaborative projects development that offers shorter term financing and a secondary project that is developed over the longer term.

As the above example of the product models has shown in some of the cases there is a shift from a product model to a hybrid model for financial reasons. Indeed, the hybrid model can help a firm to generate financial revenues earlier in their life by the offering of services, which can occur when no other financial options are available. However, some entrepreneurs choose willingly to engage for a hybrid model from the start for several reasons, of which three are given below.

The first two reasons are interlinked as they define each other: keeping the control over the company and the avoidance of certain types of financing (the venture capitalist financing), according to Table 4.2 As shown in section 4, the involvement of venture capitalists is synonymous with the loss of control by the entrepreneur over his firm future. The entrepreneur's engagements with this kind of financiers implicitly implies that the firm's strategy is set by them and that the managing team then has little control over the firm strategy and activities. The firm choosing a hybrid model normally wants to keep control over their company and not depend on any other institutions, especially risk financiers. This is consistent with the findings in section 3, which states that even in high-technology firms, firm creators tend to prefer control over the company rather than focusing on growth performance. The long term view and control over action on a long term perspective is also an issue for most of the founders since they want to have a sustainable and long term growth based on a limited risk project. Many of the entrepreneurs who were interviewed seemed to emphasise the importance of keeping their independence of choice in the future and their ability to decide their own path, as one of the founder of Phytodia commented:

> "All three of us [founders] agreed that the pharmaceutical project was not worth it for two reasons, that is to say that the horizon and the uncertainty was too complex and long and secondly we would need to raise venture capitalist financing, and all three of us agreed that we didn't want them because it meant the loss of independence and sharing the fate of the firm. The most important thing was to not lose our freedom in terms of independence [...] in order then to take any possible path"[75]

The choice towards pursuing a pharmaceutical product has here been influenced by a reflection over the company's future. This shows that entrepreneurs can reflect in terms of their future agency power in the firm and as a result adapt their business model in order to avoid such problems. The founders in this company integrated the uncertainty inherent to this type of innovation project and the use of this specific financing to lead to an uncertain fate of their firm (due to the relative probability of success of firms involved in pharmaceutical products), in which they would no longer have control. The prospect of agency loss made them discount this initial project choice, and they preferred to orient their firm towards a model in which they would keep agency but would have to compensate in terms of obtaining early revenues by other means. As Table 4.2 shows, the requirement for independence and control of the firm is shared by many other firms that have decided to implement a hybrid model.

[75] Translated from French: "On était d'accord tout les trois que le programme pharmaceutique, c'est pas la peine pour deux raisons, c'est-à-dire que l'horizon et l'incertitude c'est trop compliqué et long, deuxièmement le problème c'est qu'il faut lever des financements en capital risque et que tout les trois on était assez d'accord qu'on n'en voulait pas, parce que ça voulait dire une perte d'indépendance ou alors devoir partager le devenir de l'entreprise. … Le plus important c'était de ne pas perdre notre liberté (indépendance) […] afin d'emprunter tout les chemins possibles. "

Finally, two companies are focused solely on the service type model: Alsachim and Admet-X. In the case of Alsachim, the first objective for the two founders was to find another job after the loss of jobs that occurred after the closure/failure of their previous employing company. They concluded that the service market was the best option since they wanted to limit as much as possible the risk in their new company and ensure the company's sustainability. The founder of this company explained this as follows:

> "We wanted to create our job for tomorrow by proposing a more mixed model of services, rather than just drug discovery. [We] rather wanted first to build a firm that offers quality services and was professional and if in our domain of chemistry-biology we could at one point then integrate drug discovery. [...] I found the approach sounder and interesting because we already had a basis for clients, a basis of know-how, and a financial basis that was interesting, in order to avoid putting everything risk-wise on only drug discovery."[76]

The founder here avoided the option to create a drug discovery firm for the reasons outlined above on a short term basis. The firm had the opportunity to build their model on drug discovery, which was rejected by the founder due to his risk aversion. He also emphasised the build-up of market knowledge at the beginning of the firm's activity which would be beneficial in the longer run. For the moment they decided not to engage at all in drug discovery, but as they explained, the firm may evolve from a service only strategy to a hybrid strategy. In the case of Admet-X, the reasons for choosing a service model are similar to the reasons given above.

While financial independence can be a strong incentive for firms to choose a service or hybrid model, other reasons are put forward by founders for getting involved in services. The third reason proposed for this type of activity is to become closer to the market and to already have a basis of clients that the entrepreneur could build on for developing services. Getting involved in services can therefore benefit the firm by creating firstly a network of partners, and through the building of a relationship of trust could secondly engage with those partners on larger projects. Services give the firm the opportunity to be closer and more responsive to potential markets, while the main project is developed over a longer timeframe.

[76] Translated from French: " Nous on veut créer notre métier de demain, proposer un modèle plus mixte de services puis '*drug discovery*'. Plutôt construire d'abord une société de service de qualité, professionnelle et que si dans notre domaine de chimie –bio on pouvait intégrer un moment donné peut être de la '*drug discovery*' […]. Je trouvais l'approche beaucoup plus saine et intéressante, parce qu'il y avait un socle de clients, un socle de savoir faire et un socle disons financier qui était intéressant ; pour éviter de tout miser au niveau risque sur uniquement de la '*drug discovery*'. "

The emphasis that entrepreneurs make for the hybrid model and service model are common to most firms. Firstly, many entrepreneurs express the need for control and independence and seek this when creating the firm. They emphasise the willingness to keep entrepreneurial agency in their hands and to be the main actor in the evolution of the firm. This also gives them, among other advantages, the agency power over the future over their employment and the survival of the firm. Many firms choosing this type of model also emphasise the embedded risk they perceive from involving venture capitalists from the start and so instead move towards less constraining types of financing such as Business Angels. However, the choice towards keeping entrepreneurial agency has a cost, which in the case of drug discovery projects is the redirection of the strategy of the firm towards other activities such as services or collaborative research projects. This change of strategy also could imply a possible loss over the opportunity to ever return to the given drug discovery project (in which its viability often become limited over time due to an aging patent).

6.2.1.3. Remarks on financing solutions

The data (Table 4.2) shows that there is limited enthusiasm for the venture capitalist financing solution, and so a common source of financing comes from business angels. Regarding the availability of business-angel financing organisations, the region has developed a number of them over the last 10 years, which saw the creation of three starting from 1998[77]. This makes the availability of regional financing another solution for start-ups, since these kinds of institutions tend to invest in ventures geographically close to them, as shown in the literature review. This type of financing also generally invests a lesser amount compared to the venture capitalists and thus is more adapted to financing firms with a hybrid model or specific product models (excluding the ones aiming at human pharmaceuticals or firms aimed at growing quickly). These organisations do not ask for an active role in the strategic management, and are consequently coherent with many firm objectives for limiting the loss of agency of the founders.

Financial institutions therefore have an influence on the business strategy, before and after the financing decision. Before financing, when trying to raise financing, entrepreneurs receive information about financing options available to them and may therefore adapt their business strategy to accommodate the possible ways of financing it. After financing, the financier can help shape the business strategy and the business model of the firm in several ways, as expected from the literature review. For instance, for those involved with venture capitalists, the firm must focus its efforts on the most promising project and are dissuaded from getting involved in any other activities. On a more general level, this section has raised attention to the fact that the financing

[77] For more information please refer to chapter 3 in the section 3.1.3.

issues linked to business models have to be carefully thought out with regards to the choice of financier and their influence on the future decision and actions of the company (in terms of reduction of entrepreneurial agency for example).

In the biotechnology sector, external financing is often required regardless of the business model chosen, but the scale of financing needed could be different depending on the business model. However, the choice for a certain model may predetermine the type of financing (for instance a drug development business model requires venture capitalist funding), and thus in some ways restricts the future options and entrepreneurial agency of the founder. When making a decision over his firm strategy, the entrepreneur also chooses a business model that defines his financing needs. The financing needs will determine the type of financing that the entrepreneur must reach, and may imply a loss of agency. Consequently, if the entrepreneur is concerned with a loss of control, he has to adapt his firm business model accordingly. In our examples, we have seen that some entrepreneurs who have the opportunity to pursue drug discovery strategies, have changed strategies and business models in order to ensure that they keep control over the decisions in their venture. Other companies, that have identified the need to grow rapidly or kept their drug discovery ambitions, have involved venture capitalist financing

Following these conclusions regarding the importance that many entrepreneurs attach to control and independence issues, some questions remain, especially looking at the cases of firms developed in the late 1990s and the early 2000s. Why is there such a difference in the choice of business model observed over an interval of 10 years? Is there a reason why so few companies enter into drug discovery? As previously mentioned in the research methods section, the data revealed that there was an influence over local successes and failures that are not repeated in the next generation.

The next section will attempt to answer these questions by looking at how the industrial experience of the founders and the successes or failures of other firms influenced founders in the late 2000s in terms of the strategic choices for their business model. These issues of choice between control and product development are therefore seen in the light of founder's experience and the way that they associate risky business models and loss of control over the fate of the firm to certain type of financing.

6.2.2. Direct and indirect experience

As shown in studies of serial entrepreneurs, experience has an impact on the company founder, which is sometimes reflected in business strategy. While developing the interviews and talking about the influence of business models, entrepreneurs have often referred to their own experience about working for previous start-up companies, but also other companies in the region, and have reflected about these companies' performances. The next table (Table 4.3) therefore summarises whether or not the business model has been influenced by previous creations (i.e. their own creation, employee of a start-up or knowledge about other cases), and if these cases are seen as good or bad practices by the firms interviewed[78].

Table 4.3: Direct and indirect experience of founders

Firm's Name	Bus. Model	Founder experience of firm creation	Founder experience in the industry	Strong Connection to previous generation	Influence from previous generation[79]
Alpha	Product	No	No	No	-
Beta	Product	Yes	No	No	-
Phytodia	Hybrid	Yes	Yes	Yes	Firm C , Firm A, Firm E
Alsachim	Services	Yes	Yes	Yes	Firm D, Firm A, Firm C, Firm E
Kappa	Product to Hybrid	No	No	No	-
Enovalys	Products (two stage)	Yes	Yes	Yes	-
Domain Therapeutics	Hybrid	Yes	Yes	Yes	Firm A, Firm B, Firm C
Biomica	Product	Yes	Yes	No	-
Cell Prothera	Product	Yes	No	No	-
Anagenesis	Product (processes)	Yes	Yes	No	-
Bionext	Product	Yes	No	No	-
Admet-X	Services	Yes	Yes	Yes	Firm F, Firm G Firm B, Firm A
Rhenovia	Hybrid (co-development + product)	No	Yes	Yes	Firm B and others

The firms created in the late 1990s and beginning of the 2000s have had an impact on the business models of many newly created firms, through direct experience (i.e. as entrepreneurs were involved in firm creation or worked in a start-up) or knowledge of the history of those firms. These connections to the earlier generation also influenced their choice towards financing. Not every newly formed companies in our cases have been involved closely or even loosely (through personal

[78] The direction of influence is not consequential for our analysis.

[79] The lines with '-'are firms that didn't cite any good or bad practice of other firms. This column aims at showing which firms of the previous generation inspired them into the definition of their business model. Firm F and firm G are generally seen as good practices to follow, while the other firms had problems with their financiers and therefore are seen as bad examples to follow.

network) with previous firms in the cluster. Only 6 of our 13 firms have knowledge about firms from the previous generation, and only 4 have been directly involved in a company from a previous generation. In this section we therefore focus on the cases that have an experience of the previous generation and discuss the influence of these firms on their view of the good and bad practices in these firms' business models.

Concerning the firms that have had experience in previous start-ups in biotechnology or related industries (6 of them have previously worked in other start-ups cited in section 6.1), most of them are under the impression that involving venture capitalists implies a greater amount of risk for the future of the company in terms of survival and control of their own firm, but also in terms of the continuity of financing needed to achieve their initial innovative project. There is one exception, which can be explained by the fact that this particular company is less attached to agency issues because they consider that the firm could be ultimately acquired by another organisation (reported in Table 4.2). However, for firms that value the control over their own company, their choice of financing is affected by their connections to the previous generation of firms. In their experience, these financiers believe in making the company focus on only one of the more advanced or promising products (not diversifying the risk at the company level) in order to have high return potential. This practice makes sense for the financier and, involves different consequences for the entrepreneur.

One of our company founder which was involved in the development of another start-up before his present appointment shared his experience as:

> "I was previously employed by a company, firm C, which was financed with around 30 million Euros, and was one of the largest fundraisings in France in recent years, and I was on the executive committee. We therefore had a large working capital but we got shut down for being a few weeks late. That is to say, it was a time when the firm had around 40 employees and results were coming in, we had around two to three weeks delay [on the planning], and the investors didn't understand that in science on a program of 36 to 48 month, a margin of error of three weeks was insignificant. They panicked and stopped everything. [...] Finally, on a personal note it was a painful experience, because we went from a firm that was financed on a high level to a feeling of failure, yet nothing wrong had happened."[80]

[80] Translated from French: "Moi j'étais dans une boîte avant chez Firme C qui était financée à hauteur de 30 millions d'euros qui était l'une des plus grosses levées de fonds françaises de ces dernières années, et moi j'étais dans le comité de direction. Et donc on avait un très gros fond de roulement mais on s'est fait tuer pour quelques semaines de retard. C'est-à-dire qu'à un moment quand on avait commencé à avoir une entreprise avec une quarantaine de salariés et avec des résultats qui arrivaient, on a pris deux ou trois semaines de retard sur les délais, et les investisseurs n'ont pas compris que dans la science sur des programmes de 36 mois à 48 mois une marge d'erreur de trois semaines était vraiment minime, et ils ont paniqué et tout arrêté. Au final à

Here the founder described his opinion towards the inadequacy of the behaviour of the financier towards the inherent uncertainty linked to the innovative project. He underlined his lack of understanding towards the behaviour of the financier, since for him such delays were not significant compared to the overall project development. He also emphasised his feeling of failure about the closure of that 40 employee company, even though the agency power over the venture was not in the hand of the managers. This emotional experience therefore had an impact on his experience of firm creation, and made him realise the full consequences of this loss of agency. In the same way, the founder of Alsachim found the experience of working for a previous start-up beneficial:

> "On the business model side, I think that our experience at Firm D was very beneficial, because Firm D was a drug discovery society, which depended highly on fundraising and opened its capital quickly. We analysed the reasons for its failure. There were also many other drug discovery firms that were built and do not exist anymore, such as Firm A, Firm C, Firm D, who survived for 3, 4 or 5 years maximum."[81]

This trend of basing their decisions on personal experience is reinforced by the experience of other companies in the region, as the previous quote reveals. There were a number of firms created in the early 2000s and some of them raised an impressive amount of money and had outstanding scientific credentials (e.g. section 6.1.). Some others, who were not seen as promising at their formation, had a more service orientated business model, since they focused on a longer term growth, and are now seen as the successes from this generation because they succeeded in sustaining a steady growth over the years. Firm founders, who had been close to the local industry and in contact with the previous generation of firms, felt that the venture capital route was risky and thus were aware of the downsides of this model (e.g. loss of entrepreneurial agency). These observers then also considered that venture capital funding was not a good practice, but that having a long term growth based on sales from services first and later on products seemed to bear less risk and give better results. This argument has been given in some interviews, as shown in Table 4.3, and the following quote from a serial entrepreneur:

> "In this first story [enterprise the interviewee had created in the past] we had a search for venture capitalists, which did not work and at the same time there existed other firms Firm B, Firm A, and Firm C, who also worked with venture capital and also closed but with still millions available. Then we

titre personnel c'est une expérience douloureuse, parce qu'on passe d'une boîte financée à un haut niveau à un sentiment d'échec alors qu'il ne s'était rien passé de mal. "

[81] Translated from French: "A propos du business model je pense que notre expérience à Firme D était très bénéfique, car Firme D était une société de '*drug discovery'*, très dépendante de lever des fonds, ouvrir son capital rapidement et on a fait toute une analyse de l'échec. Car il y beaucoup de sociétés en '*drug discovery'* qui se sont montées et qui n'existent plus aujourd'hui comme Firme A, Firme C, Firme D et ces boîtes ont survécu 3, 4, 5 ans au maximum. "

realised there was a problem with this economic model. [...] In parallel I saw firms like Firm F or Firm G who were successful without using venture capitalists."[82]

For the companies who chose product only models from the start, the usual practice remained of raising the money and focusing on product development rather than company sustainability. When asking these companies about their influence, many of them were not previously connected to the industry and thus did not know about the history of the previous generation of local firms. Additionally, most of the firms interviewed did not have a drug discovery type business model and therefore few of them were in need of venture capitalist investment. However, there is an overall trend in the region that fundraising through venture capitalists has diminished and business models involving services with an objective of longer survival has become predominant, as a person in the management team of Domain Therapeutics specialised in working with venture capitalist's managed firms commented:

> "There is nowadays a willingness to try to be free of investors, to try to make models involving services with incomes that give the possibility to interact with the market, test immediately their technology to see if there is a demand. This gives the opportunity to be free from all the constraints that an investor brings, because [being in a relationship with them] it is a hassle."[83]

The interviews indicate that the previous experience (including personal experience and the experience of other local firms) can have an influence on the entrepreneur's decision over the firm's business model. In latter firms, many entrepreneurs have learnt, through personal or indirect experience, which the relationship with venture capitalists is a complex one, and they are also aware of the risk of losing their entrepreneurial agency to the venture capitalist. As the founder of Phytodia reported, this can lead to a feeling of failure as a result of not having any control over the decision to cease activity. The success and growth of two particular firms that are based on services has given the local entrepreneurs the feeling that a model involving services appears to be less risky and more sustainable regarding long term survival. For the other entrepreneurs who do not have this kind of experience, the exploitation of research results seems to remain a priority at creation. The product

[82] Translated from French: "Sur cette première histoire (entreprise) on avait une recherche de capital risque qui n'a pas fonctionné et en même temps existaient d'autres sociétés Firme B, Firme A et Firme C qui ont aussi fonctionné avec du capital risque et qui ont aussi fermé avec encore des millions d'euros en caisse et on s'est rendu compte qu'il y avait un souci avec ce modèle économique. […] J'ai aussi vu en parallèle des boîtes comme Firme G ou Firme F qui prospèrent. "

[83] Translated from French: "Il y a une volonté maintenant d'essayer de s'affranchir des investisseurs, d'essayer de faire des modèles de services avec des revenus car ça permet d'avoir une confrontation avec le marché, de tester immédiatement sa technologie pour voir s'il y a une demande et puis ça permet de s'affranchir de toutes contraintes qu'apporte un investisseur, parce que c'est une galère…"

development drives the company development in this case, and the logical means to do so is to raise capital.

7. Synthesis of the results and discussion

The literature dealing with the financial side of entrepreneurship, has contributed towards the centrality of risk financing (Bidhé 2000; Gompers & Lerner 2001; Croce et al. 2013). This discussion is focused on the entrepreneur's side and towards his choice over financing. The chapter has shown that both personal goals and available financing have an influence over the strategy of the firm and therefore its business model. This chapter aims at contributing towards the literature in two ways. It firstly focuses on the analysis of the way entrepreneurs take into account the financing constraints when making the choice over the firm's strategy and its business model. The second contribution consists of the possible influence of previous firm experience on the next generation of firms through regional learning. These two aspects are described and discussed here successively.

The first part of the results have emphasised different ways in which the financial environment influences biotech firms in terms of their business model. They show that the financiers have an influence over the companies' strategies before and after investment. The effect before investment consists of the adjustment that the entrepreneur has to make in his strategy and ultimately in his business model after considering financing. The entrepreneur has to make the choice over the strategy together with the financing he wants to involve while considering factors such as loss of control, success of a given project and the desired rate of growth for the company. The confrontation of one's project to the financing available (through the meeting of potential investors) can also influence the entrepreneur to adapt his strategy to the financing available to him.

Result 1: The assessment of entrepreneurs over financing options influences their decision towards the business model put in place for the firm.

The cases have emphasised that the firm strategy and business model is not static over time and that there can be radical changes even on a very short term basis. One of the changes observed concerns the case where firms seek financing from different financial organisations which give them feedback on their strategy. One of our cases described how their project had to be reviewed as its costs were too high for financiers. Another firm decided to focus their activities on the development of only one molecule following the advice given by financiers when the firm was seeking financing, which the firm followed through with. Thus even if the decision is left for the entrepreneur to decide on a firm strategy and business model, some can still be reliant on external funding and thus have to adapt to the offer available and follow their advice.

Result 1.1: An entrepreneur has to adapt his strategy regarding financing available to him. His agency is therefore affected by the financial market.

A group of firms in the cases were particularly interested in the control over their own firm and thus discounted the use of some types of financing accordingly. These firms therefore had to adapt their overall firm strategy and business model in order to fulfil this preference. They therefore adapted their business model in terms of revenues. These firms were more inclined to focus on a hybrid or service business model, which has the advantage of generating revenues on a short term basis and thus can rely on a mode of financing that is less invasive in terms of agency. The second part of the results showed that this awareness over the loss of control over the firm is amplified by difficulties encountered by some firms from a previous generation when using a venture capitalist type of financing, and even more so if the new entrepreneurs were directly involved in those companies. Consequently, to some entrepreneurs directly involved in the closure of decent size companies, the experience was quite memorable and made them draw away from this particular business model. The choice of many firms towards a business model that included services was comforted by the success of two local firms that followed this model, which over 10 years had grown to a medium size firm. Consequently, together with the increasing availability of Business Angel funds, many firms have decided to build a firm in which they could keep control, through activities that guaranty them revenues on a short term basis.

Result 1.2: An entrepreneur with the willingness to keep his entrepreneurial agency over the firm's life has to adapt his demand for financing and business model accordingly.

The ex-post effect of this choice restricts the future strategies of the entrepreneur as he is bounded by either a limited amount of external financial resources in some cases, or by giving up part of his agency power to the financier in other cases. Thus the choice towards a particular type of financing, together with its business model, may be determinant in the opportunities the firm can still pursue, and the options that the entrepreneurs gives up.

Result 2: The entrepreneur's choice towards a specific type of financing restricts his future options for firm development.

The results have primarily emphasised the consequences of involving a venture capitalist in their firm development, which restricts the entrepreneur in his future choice despite being an asset for a firm to develop quickly. For instance, when investing in a firm, venture capitalists consequently take control over the firm and put strict boundaries on the agency left to the managers. This has already been explained in the literature but is also confirmed by one of our cases. The founder who was interviewed described specifically that the firm manager did not have any choice over the firm's activity or business model. This risk strategy was also emphasised by the testimony of a founder who described his feeling of helplessness when they decided to close the firm. By comparison, the case of Domain Therapeutics showed that even if the business manager suffers a high loss of agency, some power is still left to the entrepreneur in the form of negotiation over the future of a company. However, this was an exception in the cases reviewed from the earlier generation, since all the other firms had their assets sold or liquidated by their shareholders.

Result 2.1: Involving a venture capitalist can result in a loss of entrepreneurial agency of the founders, which limits the influence of the entrepreneur over the firm strategy and business model.

The consequences of the choice of a business model involving venture capitalists were well exposed in the results. However, the consequences of avoiding them were not discussed. There may also be a path dependency implication when a firm decides to avoid this type of financing. The financing of venture capitalists' is well adapted for pursuing a highly uncertain research project, such as the drug discovery projects. In some of our cases, the decision to keep the control over the firm meant that the firm had limited financing to put towards a drug discovery project. Due to the regulation system in the human pharmaceutical industry (see Chapter 2), the time to market is around 10 to 15 years on average due to the amount of trials needed. Combining this aspect of the pharmaceutical industry with patenting expiration times, in order to obtain returns and expect the introduction of new drugs, firms are restricted in terms of time when exploiting such types of project. Returning to our cases, firms that are setting aside a drug discovery project in order to keep agency, are unlikely to return to this project because they quickly become financially unviable. Thus the choice of the entrepreneur towards entrepreneurial agency can in some cases result in the drop of drug discovery projects.

Result 2.2: Keeping entrepreneurial agency can restrict firms towards less innovative choices, which may results in human therapeutics projects left undeveloped.

The second main contribution of this work lies in the regional aspect in which the demography of business models might have changed over time. The results have clearly shown that some entrepreneurs have been affected at a range of levels by the successes and failures of older firms in the cluster. Our cases have shown that this awareness is somehow anchored to the regional history in our case, with people close to the local industry being influenced by the successes or failures of local firms when building their business model. Here we will refer to the literature related to regional learning (Marshall 1895) and the concept of "knowledge is in the air". This literature has agreed that learning occurs on a regional scale through face to face relationships. This paper has shown that the type of learning is not only of a technical nature but can also concern business practices. This learning can occur through direct experience from serial entrepreneurs or workers in start-ups who go on to start their own companies, but also as a result of indirect experiences through connections with the local industrial community. The experiences of the previous generation of firms have raised awareness over the irreversibility of the entrepreneur's financier choice and its impact on firm survival. Many of the firms interviewed would qualify firms from the earlier generation that involved a venture capitalist as a bad practice that should not to be followed. This has therefore produced an emergence of a number of firms focused on models that include services (e.g. hybrid models or services only models), since many of the entrepreneurs interviewed seek survival through control and freedom of choice over the future of their own venture. The learning seems to be conditional on a developed network of the current entrepreneurs having been in direct contact with older firms in order to draw from their experience. This is comforted by the fact that not all firms feel the same concern towards venture capitalists, or they did not discuss or were not aware of these stories.

Result 3: New entrepreneurs can draw from the experience of previous local firms in terms of financial preferences, which leads to an evolution of dominant business models over time in a specific location.

Looking at the future perspective, all start-ups have to confront their business plan with their financial resources and must define their needs in terms of external financing. Thus, when seeking financial help (from bank loans to opening the firm's capital), the entrepreneur must adapt his own ambition to the financial resources offered to him. Accordingly, this has consequences on the strategies available to him and thus his entrepreneurial agency.

The results drawn from the cases may be limited by several factors, such as the sector and region of study. This study emphasises the predominant role of financiers in the innovative project development, because biotechnology companies are known to have a high need for financing, especially those focused in drug discovery. Therefore, when applying this study to other sectors, the role of the financial variable may not play such an important part in the development of the innovative firm. The cases have shown that in the case of the pursuit of a drug discovery project, the entrepreneur usually has a binary choice, which is either to pursue the innovative project with the help of venture capitalists or to leave the project to keep his entrepreneurial agency and often leave aside the initial innovative project. This binary choice is a bi-product of the level of risk inherent to a drug discovery project, which is known to be a special case concerning its rate of success due to its costs and length of development. This result is therefore specific to this type of innovative opportunity, and has shown the importance of the financing choice in such extreme cases. However, the case study provided us with other applications, which gives us an opportunity to temper our results. In the cases of diagnostics for instance, such high investments over the long term were not needed and therefore the entrepreneur did not have to choose between his future entrepreneurial agency and the pursuit of the innovative project. The biotechnology sector is peculiar in this respect and therefore the venture capitalist financing may not be a requirement for the pursuit of certain innovative projects. The need for such type of financing may vary according to sector of application or even the specificities of the innovative project. However, the results can still be used in the reflection towards entrepreneurs aiming at rapid growth for their company, and their need for large amounts of financing for it, as opposed to the choice of control over the company. In these cases, the loss of agency of the firm involving such type of financing could be considered.

Finally, regarding the regional aspect of the use of venture capitalists, the region was first characterised by the fact that many firms had achieved high financing, with none of them achieving success. Therefore, the results showing that firms distrust venture capitalist financiers may be biased. The study of a region in which a firm had achieved success through venture capitalist financing may give the opposite results than the ones found here. Secondly, the region was characterised by a connected network of founders (where stories of older firms were known). Subsequently, an alternative region without a connected network of entrepreneurs may not lead to the sharing of experiences towards successes and failures. The effect of regional learning may require specificities that can only be tested through the study and comparison of other regions that are also specialised in high-tech sectors, and which also require the use of such types of financing.

8. Conclusions

This chapter has looked at the influence of financing on the choice of business model and development. Different aspects of the financing have been considered, including the financing required for a product or technology to be developed by the firm and the influence and availability of financing institutions (here especially VCs and Business Angels). The choice of financing is seen to be influenced by three components: the entrepreneurial agency and therefore the entrepreneur's preferences about firm growth or keeping control over the firm's future, the external environment through the financing institutions but also other firms in the region, and finally the initial project properties through the amount of financing needed to pursue its development.

Through theory and practice, the chapter has first pointed out that the choice towards the amount and type of financing has an impact on the firm's development on a short and a long term. Regarding the choice to go for a direct route of product development with high-risk and high-return potential, financed through venture capitalist institutions, in most of the cases these companies develop only one product, which leaves no space for alternative routes that could become useful if the initial project is no longer viable to develop. As explained previously, by developing a single project model financed by a venture capitalist, the entrepreneur locks himself into this model and looses **entrepreneurial agency** because he cannot revert his earlier decision. The choice for a business model, in addition to the choice for financing, implies also a choice over control and freedom of the entrepreneur in the firm.

The choice of business model also depends upon the entrepreneurs' preferences regarding freedom and control, while taking into account the pursuit of their initial project and its optimum route to fast development. The choice between the two involves different levels of risk (probability of success and therefore survival rates) and also different levels of reward and profit. The entrepreneur has to make a choice between control over the firm, growth potential and technology development priority. These variables are under the constraints of time, finances and technology. These variables are determinants in the choice of business model since the entrepreneurs who prioritise control limits their opportunity by not including venture capitalists and rely on a slower, less risky growth.

Through his choice of strategy and business model, the entrepreneur makes a conscious commitment towards both the evolution of the innovative project and the firm survival. For firms that had a drug discovery project, the involvement of a venture capitalist is often crucial for its successful development. However, the involvement of such a financial partner has heavy implication on future agency and on the ability of the entrepreneur to be able to change the company's activities in the event of project failure. Therefore, this choice may negatively affect the chance of survival of a firm. The opposite choice, to keep control over the firm's future and not involve venture capitalists, results in a low chance of success for the initial innovative project. In the case of other innovative projects, the choice between the project and maximising the chance for the survival of the firm are not antagonistic objectives and can be achieved together. The choice of the entrepreneur lies then in the agency power that he is willing to give away in order to access high-risk financing that would give him a chance to have a high-growth company. Thus in this study, the entrepreneurs in some of the cases have to make a conscious choice over the continuity of the project and the chance of survival of the firm. Therefore, one cannot consider that both of the processes, firm survival and project success, are aligned because in our case the entrepreneur has to consider both matters separately since the pursuit of one may jeopardise the chance of success of the other. Therefore, the choice of the entrepreneur towards a specific type of financing can have a differing impact on the project continuity and firm survival and evolution. This supports the idea of considering them as **co-evolving processes** rather than stages from the same process.

As the notion of control and freedom, and thus the concern over future **entrepreneurial agency**, seem to be important factors in the decision over certain types of financing, the **regional environment** can contribute towards awareness of the loss of control that is induced by this decision. Founders who were involved in a firm closure came to understand the full extent of the consequences from the loss of agency, through their network or even direct experience (for those previously involved with another firm in the cluster). These individuals were therefore less inclined to bear this kind of experience again and so valued more the control over the future of the firm. Thus, although some firms did not have any prejudice towards the venture capitalist type of financing, a significant proportion of the entrepreneurs interviewed indicated that they would prefer not to be involved with those financiers because they would lose too much freedom in running their firms. This trend was triggered by the path of evolution of other firms in the cluster that had difficulties to survive due to the requirements of the funders. This led the generation of firms created after 2006 to have a limited number supported by venture capitalists, which appears unusual for the biotech sector.

Chapter 5: Entrepreneur's background and start-ups strategy

Abstract

The experience and competences of the entrepreneur in a newly created company are known to influence the survival and growth of the firm. Considering that the entrepreneur has his own preferences regarding the path that his firm must follow, this chapter asks the question of the role of background and experience of founders in the goals setting of the newly created firm. The study focuses on high-tech firms specialised in domains related to biotechnology, and addresses the question of how the preferences of the entrepreneurs regarding the founding project of the firm influences the firm's evolution. It especially focuses on the difference in preferences between entrepreneurs with a scientific background and those with a business related background. The study analyses two types of event that may alter the goal setting of the new organisation, which are change of the firm's leader and pressure from the environment. The paper's findings are based on 12 study cases of firms in high velocity environments (here biotechnology sector). The findings include the fact that goal setting of companies is influenced by a) an early stage change in leadership and b) the risk and term to completion of the original project.

1. Introduction

In the entrepreneurship literature, the entrepreneurial decision occurs at the nexus of the perception of an opportunity and the steps made to transform this perception into reality. However, since this transformation involves company creation, it goes hand to hand with other sets of decisions that influence the early life of the firm, such as the decision of the goals by which the firm operates.

Entrepreneurship theory has described the entrepreneur as a unique agent with specific capabilities. The entrepreneur is described as being the 'perceiver' of an opportunity and the first to take a step towards realisation of discovered opportunities (definition according to Shane, 2003). In transforming opportunity into reality, the entrepreneur has to face different dimensions of volatility, such as fluctuation of demand, demographic changes and, industry and technology specific constraints (Casson 2005). The entrepreneur also has to deal with the complexity of firm creation

(Stinchcombe 1965)[84]. Although these issues are placed in the background of the 'heroic' theories of entrepreneurship, such as the one offered by Schumpeter (1934), not all entrepreneurs may have the 'reality distortion' capabilities attributed to individuals such as Steve Jobs.

In some specific sectors (especially knowledge intensive sectors including biotechnology) where the complexity and amount of information is too high to be retained by one person, the entrepreneurial function is then generally fulfilled cooperatively. This implies some type of division of labour between individuals who contribute to the entrepreneurial function with regards to their human capital stock. The entrepreneurial function should therefore be fulfilled cooperatively (Schumpeter 1951) or by a different person successively. This chapter focuses on the later phenomenon[85] and thus studies how the exploitation of opportunity and firm strategy is affected by a change of individual in the entrepreneurial function (as leader and main decision taker), which can also be referred to in the literature as surrogate entrepreneurship (Franklin et al. 2001).

As the firm project evolves over time, the entrepreneur's skills must also evolve with the changing needs of the organisation, which includes various tasks such as the management of a growing labour force, the project development and sensitivity to the environment and markets. These changes justify a change of leadership fulfilling the entrepreneurial function, since in innovative entrepreneurship the original inventor may lack managerial or business skills because they may only have a technical background. The question can then be asked about the impact of the entrepreneur background and previous experience to his set of preferences and therefore its impact on goals for an organisation attempting to innovate. This paper hypothesises that the background and culture of an entrepreneur affects his vision for the strategy of the firm and also the firm evolution.

This paper examines goal setting strategy in relationship to leadership change in the composition of the founding team of newly created firms in a high-technology sector (the biotechnology sector). The paper therefore tackles the following question: "*In the process of firm creation, how does the goal setting behaviour change over the early life of the firm? How do the goals change with a change of leadership at the time of firm creation?* ". These issues are specifically related to change in leadership of the firm, and the pressures exerted on the firm. The paradigmatic case of such management change is the replacement of a scientist/inventor by a managing director as the new leader of the project and also of the newly created organisation.

[84] The complexity on firm creation will be developed later in this chapter.
[85] We chose to study the latter phenomenon since it is the one we observe in the cases, which is associated with the choice of the scientist to develop the project himself or to find another person to do it.

In order to understand the evolution of firm strategy during their early days, the paper shines some light on the process of firm creation for high-tech new ventures. However, it does not focus on the performance effects of the change of leadership but rather on the process of organisational goal change. This analysis is broken down into 4 sections. The first section brings the literature of entrepreneurship and strategic choices together in order to propose a background in which to study the decision making process in firm formation and in the early life stages of a high-tech new venture. The next section explains the methods used for the study and the subsequent section presents the results. Finally, the paper discusses the results and concludes by presenting findings on early stage firm formation and decision strategy regarding leadership change.

2. Theoretical background

It is a known fact that firms in their infancy are particularly fragile, which leads to a rather low survival rate. This theoretical background is built on the basis of understanding of some of the complexities faced by firms during their early life stages. It firstly offers an overview of the challenges that a young innovative firm faces (with an emphasis on biotech sector). It attempts to build a framework in which one can study the early evolution of high-tech firms by discussing the organisational dynamics leading to the firm creation and the entrepreneurial function during this process. Secondly, the section discusses the organisational goal setting resulting from differences in the preferences of agents.

2.1. Specificities and constraints of the organising process

This section aims at understanding constraints and mechanisms behind firm creation by reviewing relevant literature regarding entrepreneurship and the creation and evolution of organisations.

The current literature looking at entrepreneurship sees the entrepreneurial action as being either in the company creation or in the opportunity exploitation (e.g. innovative entrepreneurship). In the second of these cases, the organisational part behind firm creation is seen as a simple step in the linear process of opportunity exploitation. For instance, Shane (Shane 2003)[86] proposes a stage view representation of the entrepreneurial process, in which the organisational part is restricted to a unique step in the process. However, other organisational literature has shown (Garnsey 1998; Greiner 1997) that firm creation (without considering the opportunity exploitation) follows its an

[86] The review and discussion about evolution processes have been discussed in Chapter 1 section 6.2, where they have been explained in details.

evolutionary path influenced by managerial challenges and resources availability. This chapter does therefore not follow the hypothesis that the organisational part in the firm creation is only one step in the process. Instead, it focuses on understanding the co-evolution between the organisational process of firm creation and project development. Hence, the literature review in this section first explains in more detail the constraints resulting from the firm creation processes, starting from its origin and looking at the organisational process and constraints that it faces. Firms face a variety of pressures that influence their path of development and can also change their initial development project. These pressures, which serve as constraint, feature determinant factors that emerge from initial conditions, environmental factors and organisational changes, which will be outlined here in more detail.

One constraint under which the entrepreneurs are subjected to is the technological one that is inherent to the entrepreneur's history. For instance, the entrepreneur's education and work experience creates his human capital and the opportunities that he is able to identify and exploit. Oakey (1995) argues that the newly created firm is determined by the technical experience of the firm founder. The firm founder has usually come from a public organisation or a large company in the same or related sector[87]. The company is therefore partly determined by the knowledge and opportunity recognition of the founder. In high-tech sectors, companies have been emerging from a large number of firms that started on an ongoing project or a technology developed in a parent organisation (Shane 2004; McQueen & Wallmark 1982). Thus, even if an entrepreneur is free to choose any opportunity for exploitation, they would tend to exploit one in which they have previously accumulated knowledge upon. This is called path dependency in some literature (Dosi et al. 2000; Nelson & Winter 1982), or determinism in others (Woodward 1965; Oakey 1995). The decision to exploit an opportunity, which we also refer to as the innovative project of the firm, is therefore chosen by the entrepreneur under the constraint of his knowledge.

In high-tech sectors, the founding team often require a certain amount of specific knowledge in order to identify or exploit an opportunity under the constraint of the environment in which they are involved. Thus the early entrepreneurial function is often fulfilled by individuals with a scientific or technical background. The downside of the founding conditions is often the common limitation of knowledge regarding the managerial, commercial and market aspects of firm creation that such individuals have, which is needed to develop a company in a high velocity environment.

[87] There is a tendency in some sectors that the company spins off from public or private organisations. For example, in the semiconductor sector many spin-offs emerge from existing large firms, as in the biotechnology sector, and the founders come more often from academia due to the embryonic nature of the technology (Oakey 1995).

This is especially true for biotech firms because many founders come from an academic background and therefore have an even more limited knowledge of the managerial and business components than entrepreneurs who come from the industry (Oakey 1995; Romanelli & Schoonhoven 2001). The entrepreneurial function, which consists of the identification, decision to exploit and exploitation of the opportunity, can be divided between different individuals. The teams' diversity characteristics in terms of cognitive diversity, such as education and job experience, is usually recognised to have a positive influence on the company survival and growth. This positive influence enhances an improved scanning of the environment (knowledge of markets and competitors) to act better in the decision making process (Glick et al. 1993). Diversity in the top-management team composition can also trigger learning between members according to the concept of cognitive distance (Nooteboom 2000). However, the diversity that can have a positive effect when viewed from the cognitive side, must also be accompanied by the cohesion side in order to be effective. The diversity of a top-management team can have a perverse effect on preferences and beliefs held by management members; e.g. diversity may enhance disagreements over different views (Miller et al. 1998). In the case of start-ups in high-tech sectors, case studies have also shown that possessing market, management and product development skills has an influence over a firm's survival and success (Shane 2004).

This leads to a search for new members during the start-up period, who have complementary knowledge that is indispensable for the survival and growth of the firm, since the technical founder is often not qualified for taking the position of business manager (Clarysse & Moray 2004). This behaviour can be reinforced by the fact that academic founders do not always aspire to leave their current occupation (Murray 2004). Hence, when the entrepreneur decides that he needs external competences for building a suitable founding team for the firm they wish to create, the enterprise undergoes organisational change, which also adds to the constraining elements that affect the firm during its early life stages. When new members are involved, the original entrepreneur must also decide on his place in the firm, and can decide whether or not he aims to be active or leading the newly created organisation. In many cases, especially in university spin-offs, one can observe the use of surrogate entrepreneurs, who takes the place of an academic at the head of the company and will carry out the function of developing the newly created firm (Franklin et al. 2001).

A **second problem** consists of creating "new roles, which have to be learned" by the people incorporating the new organisation (Stinchcombe 1965). Stinchcombe explains that in constructing an organisation, it requires time to reach maximum performance, until communication channels and trust between internal parties in the firm is reached. This assertion also applies to a newly formed founding team for company creation. Depending on the size, and assuming that even start-ups in high-technology sectors start small, the first major change concerns the team at the origin of the creation. As explained above, it is most likely that a technical founder of a high-tech company has an interest in finding collaborators with complementary knowledge, and thus the actors must negotiate their place and role in the company that is to be created. There may often be a designated leader in the project development that precedes the creation of the organisation. The new roles then have to be defined between the founders, and each founder has to find his role in the new organisation.

The literature presented above results in the identification of an organisational mechanism when an innovative project is exploited through firm creation. As explained above, if the entrepreneur-founder is reluctant to take a leading position in the newly created organisation for various reasons (his inability, lack of management competence, desire to stay in the previous organisation), the first founder has to engage in a search for building the new organisational core, the top-management team. This is represented by the Figure 5.1 below.

Figure 5.1: Founding team formation process

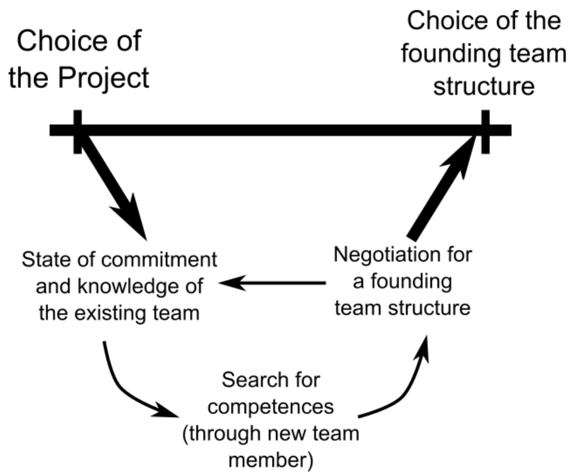


Figure 5.1 represents the organisational process by which the project converges to firm creation in terms of management structure. In order to continue the project following firm creation, the initial entrepreneur has to form a founding team with the necessary competences required to lead the project to success. This may involve a search for new members of the founding team, but also negotiations regarding the founding structure. As explained above, the negotiation of the founding structure can be influenced by the willingness of the initial entrepreneur to be the leader of the newly created organisation, but also by his own assessment of his capabilities or by contingencies introduced by other team members.

The fact that there may be a change of leadership and a new management group behind the firm may have an impact on the initial innovative project exploitation. One could therefore ask: How could the building of a founding team and a change of leadership structure influence the firm strategy and initial project development?

During the first phase of the organisation process, the number of people in the founding team can increase within the newly created company. Looking into behavioural theories of the firm, we are trying to understand how a coalition takes decisions about firm strategy and organisational goals setting. The literature on management teams has pointed towards the benefits of having a diverse team with regards to the firm performance (Eisenhardt and Schoonhoven, 1990; Glick et al., 1993). The introduction of new partners into a group can change the power balance compared to the previous team, as Bird (1989, p.226) explains:

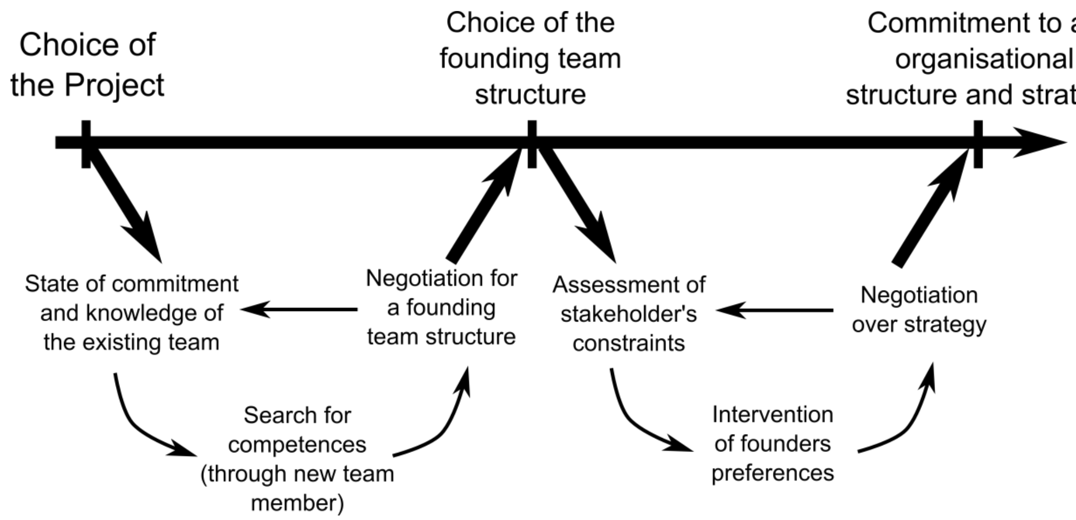
> "New partners "dilute" the influence of original partners, and new interpersonal relationships must be negotiated"

Once the team members have been found, the newly formed coalition has to build a shared vision of the goals of the company (Ensley et al. 2003). The definition of common goals in an organisation often manifests itself through the sharing of vision from the leader to the rest of the organisation (Baum et al. 1998). Having a shared vision benefits the firm as it has a positive impact in terms of performance (ibid.). Studies linked to group evolution can help us to understand the process of decision making. McGrath (1984) identifies four stages of group tasks: generate ideas or plans, choose goals and policies with alternatives, negotiate between members to resolve conflicts, and finally execute the tasks. He explains that the choice for a goal and the negotiation processes are complementary to each other. The decisions can be made with the group's prior agreement or after the resolution of a conflict. The resolution of conflict is solved by the negotiation between the different members of the group.

The participants of the coalition in the founding team must therefore agree upon a strategy, but also take into account external parameters, which is the **final constraint**. The environmental factors such as market conditions are known to be one of the main constraints on the firm during its early life stages (Hannan & Freeman 1977; Stinchcombe 1965). High-velocity environments and the technological regimes of each sector imply that the firm, in order to be able to survive, also has to adapt and take its environment into account when making decisions about firm strategy. Biotechnology is a sector that still has a highly uncertain market, which is influenced by much regulation, an increasing number of entrant firms and a changing demand from established players due to its rapid rate of technology evolution (cf. Chapter 2 for a full overview of the Biotech sector and its constraints). Management teams then have a crucial role on the survival and growth of the firm when deciding on the first set of goals that they impose on their organisation (Eisenhardt and Schoonhoven, 1990; Miller et al., 1998; Priem et al., 1995). This has been partly explained in the previous chapter based on the influence of the environment through the availability of financing and its consequences on business strategy. When deciding towards a business strategy, the leadership also takes into account environmental variables, which can include financing, institutional or regulatory variables.

The founding team structure, founder preferences and environmental constraints are therefore all part of the process of what defines the strategy of the firm during its early life stages. Figure 5.2 represents the process of strategy definition in a firm, given a certain founding team structure, including a number of variables such as founder preferences, which have been identified several times in the literature as constraining the firm development and having an influence on firm success.

Figure 5.2: Entrepreneurial process from team formation to strategy definition



The outcome of the process outlined above (i.e. the firm strategy) is dependent on the initial input (i.e. the innovation project and technology embedded into it), on the members of the coalition at the head of the company, and finally on external constraints (through the stakeholders' constraints). As Figure 5.2 suggests, the different founders' preferences influence the final choice of strategy process. The preferences are known to be personal to the entrepreneur, since they depend on his history, culture and values. Even though the exact preferences of each founder cannot be foreseen, the next section will aim at finding common cultural traits that may influence the preferences of agents that differentiate them based on their professional background.

2.2. The entrepreneur's preferences

The review above aimed at exposing the variables, mechanism and strategy that manifests following firm creation. The section has emphasised the crucial role of team formation, leadership change and alignment of goals in the founding coalition. It also emphasised the possible dominant role of the preferences of the entrepreneur(s) on the firm strategy. Classical and neoclassical economic theory hypothesise that every producer (or entrepreneur) pursues profit maximisation. However, this literature overlooks the fact that the entrepreneur may have personal preferences like it is considered for the normal economic agent, the consumer in utilitarian theory (Mill 1900). Neoclassical theory excludes this possibility by assumptions regarding market competition; those firms controlled by individuals with 'deviant' preferences will either fail by being able to meet the competitive market price or be unable to attract investors. In knowledge-based industries, however, these competitive conditions are unlikely to be present and space is opened for a variety of different managerial preferences. Hence, preferences of entrepreneurs become a possible object of analysis. This section attempts to understand the preferences of entrepreneurs, by firstly calling on general concepts from utilitarian economic theory and secondly understanding entrepreneurial preferences by linking it with the background of the entrepreneurs. This section therefore aims at understanding how personal preferences of an entrepreneur influence his decision taking in the organisation, which ultimately can affect the firm evolution.

In order to return to consideration of the variety of objectives that an entrepreneur can have, this chapter will introduce the concept of preferences for the entrepreneur. The entrepreneur is considered as an economic agent who has a specific set of preferences. Even though the entrepreneurial preferences are not highly studied in organisational theory or entrepreneurship, some authors have acknowledged their importance (Penrose 1959; Gimeno et al. 1997). For example, Penrose (1959, p.32) in her theory of growth stated:

> "Entrepreneurial preferences of this sort provide exactly the same kind of restriction on a firm's growth as does entrepreneurial inability to perceive or to act upon opportunities for profitable growth"[88]

There is a gap in the existing literature, since entrepreneurs' preferences have not been a central discussion in entrepreneurship theory, and they should not be limited to the issue of the

[88] Penrose here specifically refers to the ambition of each entrepreneur, in which one would prefer control over one's firm rather than profit and growth. She also emphasise that the ambition of the entrepreneur is not related to his skill, since very competent managers may not aim only towards greater prestige through firm growth.

differences of owner manager preferences, as considered in current economic theory. This section therefore integrates literature deriving from psychology, consumer behaviour and study of preferences in economics in order to obtain a better understanding of agents' preferences in order to partially fill this gap. This still agrees with the hypothesis that the entrepreneur acts with self interest (Edgeworth 1881). However, self-interest is not defined by the hypothesis as contributing only towards the maximisation of profit, but to a broader set of individual preferences referring to psychological constituents of human behaviour[89].

If we accept that the utility of each agent (including the entrepreneur's) is defined by the ordinality of preferences represented by a utility function, we must then also discuss the preferences of each entrepreneur and make some assumptions regarding the order of his preferences. This is translated into utility terms by literature contributions on psychological theories of human needs (Downey 1910). This is especially true when looking at the preferences regarding the hierarchy of needs. The hierarchy of preferences are usually constructed around basic needs or necessities, and then also less important needs such as comfort and leisure (Marshall 1895; Menger 1976). This view can also be related to a well-known literature in psychology that is explained by Maslow (1943) and his pyramid of needs. These theories state that human motivation is ordinal and hierarchical. This literature proceeds by differentiating life principles or basic wants (i.e. needs) from pleasure principles, which can also be referred to as aspirations (or wants) (Drakopoulos 1994). The author depicts the difference in these as the fact that a need is universally necessary and an aspiration relates to personal traits (ibid).

In order to transfer these basic concepts from the above literature to the preferences of the entrepreneurs, there must be two levels to differentiate between. The first of these is the basic needs, which are common to any agent and includes food, accommodation, etc. In developed countries, this could be translated into the fact that an individual has either enough personal wealth or has a secure employment perspective to meet his basic needs over time. The second of these are aspirations, which could be depicted as personal achievements that can be specific to the culture, personality and social environment of the entrepreneur. This is represented in the following figure (Figure 5.3).

[89] It is often said that money cannot buy happiness. However, economic theory is often drawn to the principle that money can buy happiness as it is the only variable considered on issues of individual choice.

Figure 5.3: Hierarchy of the entrepreneur's preferences

Aspirations - personal achievement- Depending on agents culture, social environment and personality
Basic needs - survival income often related to employment or personal wealth - Common to all agents

Proposition 1: The preferences of the entrepreneur like any other agent include an ordinal characteristic. Agents first satisfy basic needs over aspirations (personal achievement).

There is then a difference that is specific to the agents and is based on personal achievement (e.g. wants). However, since the wants are relative to social and cultural endowments we can consider different types of profile that share common backgrounds. Here we must differentiate the notion of personal achievement between founders with a business background and founders with a scientific background (i.e. could be an inventor of technology or a researcher who made a scientific discovery). This affects the personal notion of business success for each agent, which will be based on into different criteria according to the entrepreneur's background. On the business background side (Baumol 1967), the achievements predicted by behavioural theories are the profit rate and growth in sales from the enterprise. Using propositions built on the literature, we will here present the expected preferences of founders with a scientific background, followed by the preferences that belongs more to the business category.

In considering the economics of science, Dasgupta and David (1994) explain that the difference between science and technology lies mainly in the goals of the two different institutions. The authors identify the central incentive in science as seeking 'priority,' to be the first to discover new scientific knowledge from which follows the necessity to publish rapidly and completely. By contrast, it is possible to have a different motive – the reaping of direct financial gain from discovering (and applying) scientific knowledge which requires appropriation, the retention of the discovery in order to commercially exploit it before rivals imitate or duplicate the knowledge. As individuals, people who are called scientists may opt for either system. Therefore personal aspirations can be differentiated between two groups, which are the groups of researchers who operate in Science and the group that operates with the market rules of private organisation. It is therefore important to understand under which specific rules, incentives and cultures these two specific institutions operate in, since it may impact personal goals of individuals who come from these institutions.

In the case of founders originating from Science, they mostly have a set of objectives that are not oriented towards growth which is by definition replicative. The sociology of science, from the work of Merton (1979), explains that Science follows a strong cultural ideal, with its own rules and that scientists "recognize their dependence on particular social structures" (p.167). From this viewpoint, science is seen as an institution that is governed by its set of values and tacit rules. The two values of interest in our research are communism and disinterestedness. The value of communism is based upon the principles that the scientist exercises no property rights in his research, and that the main interest of the scientist therefore lies in recognition and esteem. On the other hand, disinterestedness should not be confused with altruism, defined by Merton as (1979, p. 276):

> "A passion for knowledge, idle curiosity, altruistic concern with the benefit to humanity and a host of other special motives attributed to scientists."

The culture of science can therefore be considered as the pursuit of knowledge with the reward of recognition and peer esteem, which differs from the general business and market culture. Thus the behaviour of scientists, regarding their cultural background, may differ from employees who come from the private sector.

Empirical contributions concerning the motivations of academic entrepreneurs are scarce, since they are not available through secondary data and have to be gathered through interviews. The classification of such preferences is not uniform among papers, since some are interested in invention push against market pull motivations (Autio & Kauranen 1994; Chiesa & Piccaluga 2000) while others do not differentiate the pecuniary motivation of the technology transfer motivation and find that commercialization is the main driver of academic entrepreneurship (D'Este & Perkmann 2011). This chapter wants to differentiate academic motivation from business ones, and so the previous distinction is crucial in this understanding and therefore restricts the number of empirical contributions relevant to our study. These empirical contributions seem to support the theoretical view. As for other agents, the consideration of wealth and recognition plays a central role in entrepreneurial creation, and the focus on knowledge and the advancement of science is the most predominant with academic entrepreneurs (Weatherston 1993; Morales-Gualdrón et al. 2009; Samsom & Gurdon 1993). This focus on solving research problems as well as developing applications is a core reason for their aspiration to work (Corman et al. 1988).

In addition to their willingness to pursue science, scientists that are involved in entrepreneurship explain their actions by their desire to see their technology or invention to be transferred and used in the industry (i.e. they are engaged with growth and its replicative nature). In their paper, Morales-Gualdron and colleagues (2009) explore this issue of the motivation driving academic entrepreneurship. They compared the motivations behind firm creation for 541 academic entrepreneurs in Spain. They show that for these entrepreneurs the most important dimension was scientific knowledge, which includes a desire to apply their knowledge and a desire for technology transfer. This type of behaviour has also been found in the case study exposed by Shane (2004). He was looking at spin-offs companies from MIT, from which he also found evidence that spin-offs creation aimed at transferring technology to the private sector in order to ensure that their idea would be realised in the market place. These papers show that in most of the cases academic entrepreneurs engage in this type of activity in order to pursue the goal of technology transfer and commercialisation of their research activities. In the literature on academic entrepreneurship, some studies have also shown that academic people have a set of objectives that is not oriented mainly towards growth, but more towards the application of research and the employment of future students (Doutriaux 1987).

Thus an academic entrepreneur has a specific view of the purpose of a new venture that is mostly motivated by the transfer and board utilisation of his knowledge, and can sometimes include secondary objectives as expressed above. However, academic entrepreneurs may require complementary competences and partner with others in order to build up their enterprise. Academic entrepreneurs engage in a new activity that is ruled by the market, and seek profit making for survival. Since partners coming from the private sector may be more sensitive to these latter issues, this can create a misalignment of objectives. In some cases the partnering can become problematic because other members of the founding team may have other objectives (which are developed below).

Proposition 2: Academic entrepreneurs, given their specific culture, have a tendency to have aspirations oriented towards technological development and technology transfer, especially technology developed by them during their academic career.

A manager involved in a start-up company can have motivations depending on his personality and cultural and social background. However, contrary to his scientific counterparts, for a manager from a business background prestige and personal achievement is usually assimilated based on his wealth or company size (Baumol 1967). However, the scale of wealth that they aspire to may depend on personal characteristics of the entrepreneur. As Penrose (1959, p.31) puts it:

> "Very good businessmen may well possess a personal scale of values in which an income greater that necessary to provide a comfortable position in the community has a relatively low claim on time and effort"

Some studies (Stutzer 2004; Higgins 2005) have put forward the impact of the social environment and socially formed aspiration levels on individual levels. Stutzer (2004) studies the general happiness levels of individuals together with their level of income. In his paper he surveyed 6000 individuals by assessing their level of income as well as their own assessment of level of income they need and their general level of happiness. The author observes first a correlation between the level of income and the assessment of income needed, which is consistent with the ratchet effect (Duesenberry 1949). However, he also observes a correlation between the level of aspiration of individuals with the income level of the community he lives in and thus concludes that aspiration levels are also determined through social comparisons. His empirical paper about income aspirations shows that an individual's aspiration level is influenced both by his previous achievements in terms of income and his social environment. To draw on more qualitative studies, in her book Higgins (Higgins 2005) showed that career and social environment have an impact on the personality behaviour and development of special capabilities of individuals and managers. She studies the career path of Baxter (a large healthcare company) managers through qualitative studies. In doing so, she identifies a specific practice at Baxter regarding the possibility for rapid evolution of young Baxter managers according to their results. This creates an expectation of evolution towards new challenges among the Baxter managers. Once the manager reaches the limit of his possible ascension through the hierarchy, his hunger for evolution is not satisfied and so he looks for other opportunities outside the company, some of whom turned towards biotechnology entrepreneurship. Career imprints of managers had a great influence over the confidence of its top-managers and their willingness to achieve, in addition to their outstanding experience. This appetite for self achievement drew many of them into entrepreneurship behaviour in the biotechnology sector.

However, this is not the case for all entrepreneurs since many of them prefer independence to growth and their ventures' growth is therefore affected by this decision (Cassar 2007). It has been shown in the literature that self-determination and freedom of activity is often a driver for self-employment (Benz & Frey 2008). The preferences of business founder's that push them to create and grow a company are therefore numerous and dependant on different characteristics of the entrepreneur. In the same way, the previous chapter has also shown that entrepreneurs may prefer control over their own firm when they have been exposed to firms involved in a risky strategy that led to failure. Such experience were found to have impacted new entrepreneurs in their strategy, and specifically in the way that they were less willing to take risks in order to ensure firm survival.

Proposition 3: ***Entrepreneurs with a business background are dependent on their experience and social environment to define their personal preferences.***

Proposition 3.1: Entrepreneurs who have had a successful managerial experience or who are in contact with many high achieving managers are more inclined to aspire to high growth firms in terms of profit and turnover.

Proposition 3.2: Entrepreneurs who have faced uncertainty towards their own employment may opt for more control over their own company and thus value survival over high-growth and high-turnover.

This review has shown that one can expect differences in goal settings depending on the person holding leadership in a firm. It has also shown that culture and backgrounds have an imprint on the entrepreneur's personal preferences. Entrepreneurs with an academic background are therefore likely to have a different set of aspirations than entrepreneurs with a business background, which is ultimately reflected in their organisational goal setting.

3. Methodology

This chapter focuses on the influence of individual preferences in a founding group on the goal setting of a newly created firm. It therefore tries to understand the goal setting of the firm in the light of the differences in background of their founders. As the literature review has shown, organisational change in the management team is common in high-tech firm creation. This study will therefore attempt to understand the impact of this structuring of the founding team on the general goals of the firm. It emphasises the differences of preferences linked to the background of the founder in particular (mainly academic vs private sector background), and their impact when there is a change of leadership if the initial project transitions to a newly created company. The study of processes is best analysed through case study methods, which gives the opportunity to gain an in-depth understanding of how entrepreneur's preferences can affect start-up evolution.

3.1. Research design

As the literature review has expressed, the main focus of this paper is centred on the organisational process behind the founding team at creation. The literature review explained that people with different backgrounds may have different preferences, which then leads to different goals and long term strategy of the firm. The literature (in section 2) emphasised the importance of cultural background, especially between founders that come from academia and founders coming from the private sector. The choice of the cases therefore reflects the need for both academic and business backgrounds. The choice of the sector is based upon this constraint, since the biotechnology sector is one in which the new technologies and products have been mainly developed in universities (Pisano, 2006a). Although a large number of spin-offs in the biotechnology sector come from academia, many of them involve people with industry or business experience in their management team (Shane 2004). This sector therefore provides an ideal pool of firms in which founding teams have a high background diversity, which justifies its selection for our study.

Firms with diverse founding teams were interviewed, some with academic leaders and some with business leaders, in order to have an objective view on how leadership is linked to background. The study also includes views about start-up companies from experts in the field of company creation[90] in order to have an external view of the shortcomings and advantages of different backgrounds on leadership positions. These experts have dealt with a large number of founding teams and therefore have a more balanced view, which gives them greater impartiality. The study focuses on 12 newly created firms (under 6 years) that are R&D oriented and have an activity related to biotechnology, and two older firms (10 years old) who were forced to re-evaluate their strategies over time due to external events.

The study takes a multiple case approach, as described in Yin's book (1994), in order to avoid extreme results and improve the validity of the study. For this multiple case study, the unit of analysis is the leadership team of the newly created firm, including the founders and current managers. The case study has been designed in a replication manner (Yin 1994). The research design includes several new ventures emerging from the same region in order to have similar environmental factors related to the same system of innovation, but with different founding team compositions for comparison.

The variation between cases in our study is mainly at the top management team level. As explained previously, we aimed at including teams with leaders coming from different backgrounds. This voluntary variation is the basis for comparing and contrasting results based upon the difference in founding team composition and leadership.

[90] Experts included in the study were required to be working in organisations that actively support entrepreneurship activities at many stages, from financing to support institutions.

In order to clarify the type of experience of founders, the paper distinguishes two types of background, which are the research and business backgrounds. It also shows the consequences of certain types of experience in the decision choice, such as previous employment difficulties. A founder with a research background was considered only if they had at least a doctoral qualification and come directly from a public research organisation or university prior the company creation (this excludes private research institution of commercial companies). A founder with a business background was considered if they had previously worked for a company in the Biotech-Pharma sector, and thus could be considered as having industry specific experience (we also refer to them to their experience as industry experience) that can be beneficial for the new venture, or as somebody who already has experience in the creation of a company or has had a managerial job in a company. This difference can be noted as both of these types of background (i.e. industry and business) imply work in the private sector and in our cases at a managerial level, and thus entrepreneurs with either of these backgrounds have experience in the day to day running of a company. However, founders with an industry background have potentially more experience concerning the structure and value chain in place in the industry in which the firm is operating due to their involvement in the biotech sector.

3.2. Data Gathering

The case study was conducted through face to face interviews with a variety of firm's founders and experts. For each firm, the interviewer tried when possible to conduct interviews with two founders with different responsibilities and/or background (business or managerial responsibilities vs. research responsibilities). However, due to the size of some founding teams and the availability of members, two interviews per firms was not always possible.

The aim was to have two views when possible. The choice of two people, especially for firms aged three years or more, gives a complementary view regarding the early research project on the researcher side, and a view of the setting up of the business on the business person side. This also provides the possibility to view the situation from people with different backgrounds and therefore different views of the project and firm creation.

The interviews were divided into two sections, where the first section recalled the historical development of the firm by emphasising steps such as contacts with markets, access to different types of financing and evolution of the people involved in the company. The second part of the interview focused more on specific questions about the managing team and the difference between scientific and business competences held by the firms.

In the process of gathering data, the transcripts of the interviews were created over the following 2-3 days based on the notes taken during the interviews and the recordings (all interviews were recorded on tape). Regarding the treatment of the data, the results were drawn from the transcripts, notes of the interviews and on the recording of the interviews when needed, especially for citation purposes.

3.3. Data Analysis and operationalisation of the concepts

The study aims mainly at understanding the mechanism behind the setting of the firm's goals during its early life stages. To achieve this, the main unit of analysis is the structure and decision making process of the founding team. As explained in the data gathering section (section 3.2), the cases are divided into two types of cases. The main cases are firms created recently, while two cases of older firms are described in the second section of the results.

The recent case study draws on 12 cases including 4 pilot cases. The pilot interviews did not differ much in content, but helped in the ordering and the formulation of the interview questions by identifying words or formulations with which the interviewee struggled. The semi-structured interview included a part on the founding team that asked question about the evolution of the top-management team, in addition to ask about the background of the people in it and the roles of each person at each point in time. It also tackled the working conditions and the opinion of the interviewee regarding the strengths or weaknesses of other people's experience and how this experience influenced the company development.

The data on older firms was gathered from various interviews. They were obtained through interviews with founders of the spin-off of two firms, which are included in to the above sample because the interviewees were also part of the founding team of those firms. The data was completed by including earlier interviews with the founder of the firm (in the case of Novalyst), since they were interviewed as experts in the field of local entrepreneurship in the biotech sector.

The analysis initially consisted of identifying the people who took part in the decision making process of the firm, thus the founding team. This gave the opportunity to determine leadership activity, which was identified as the person who took the strategic role and defined the main orientation of the firm, and the people involved in more operational decisions or who had an advisory position. The leader is therefore defined as the person who has the last word in taking the decisions over firm strategy, which is usually also the person in charge of the day to day management. Therefore, the leader is assimilated as the one having the most influence in defining the general strategy of the firm, which here relates to the decision towards the activities that makes up the core of each firm. The gathered information concerns the early dynamic of the founding team and leadership change. The information is related to the background, experiences, and preferences of founders and leaders. In the second set of cases, the section also looks at how change in the firms' environment can affect the strategy setting.

The results are based on both quotations and variables which are drawn from the interviews. The quotations given in the results are all drawn from the interviews, which have been translated from French to English. These quotes are based on the audio recordings in order to provide an accurate representation of the statements made by the interviewees. The result also includes overall variables that had to be transformed from the interviews into data that could be used and compared in the study. Therefore, before moving to the results we first describe briefly how these variables have been constructed from our qualitative data.

Leadership change: This variable tells us if there is an effective change between the project leader before firm creation and the firm leader after firm creation. This change is seen as the decision power over the fate of the firm being transferred from one person towards another. This transfer does not have to be in full because the original founder may still have shares in the company and/or a management place and thus can negotiate with the firm's actual leader. In our cases we observe that there are various levels of transition from the project leader staying in the firm, or a project leader still having an active role in the management while having a new leader at the head of the firm, to a minimal intervention of the initial project leader that restricts his involvement in the newly created company to a minimum.

Background of the leader: This variable categorises the most recent working experience of the actual firm leader within three categories: science, business and Industry. The science background concerns people with a background in a public research position. Business includes people with a background in firm creation and management. Finally, the industry background includes experience of working for a company that has operated in the biotech/pharmaceutical sector. All of the people with industry background still held some management experience from their previous employment. The order of the background given in the results is representative of the main background of the firm leader. The Enovalys firm was at the borderline between the two backgrounds. Its main leader previously did a thesis that was done in collaboration with another company. Due to his position, we decided that his scientific background was predominant, since he was working mainly on a research project and did not have any managerial position in the company when doing his thesis.

Aim of the scientific project: This variable gives a short description of the scientific project before the creation of the firm. It briefly explains the objective of each firm, but more information on this is available in Chapter 3 (section 3.3) regarding the cases description. This variable aims mainly to give an understanding to the reader about the primary aim of the project and the initial aim of the project leader in terms of the industry of application. Chapter 2 has shown that scientific discovery potentially has applications in more than one industry, and the choice towards one particular industry may influence returns that can be made from the initial project. Two firms had a complex situation regarding their research project, which were Domain Therapeutics and Alsachim. For Domain Therapeutics, the initial project could not be continued because problems during the project development triggered a change of name of the company and a refocusing of its activities. Its activities cannot therefore be focused on the original project, but are based on other specific competences available in the firm (more details are given in the second part of the results about this story in Chapter 3 section 3.3.2). For Alsachim, the founding team had the choice to follow either the research project of the firm they had worked in previously or to develop a technology based on one of the founder's thesis research topic (the full description of the story of the firm is also available in Chapter 3 section 3.3.2). They decided finally to go into services based on one founder's research, but this research does not aim at the development of an innovative product and can be considered as an innovative technique. Therefore, the basis of the activity of this firm is not based upon a project that may lead towards a product.

Term of the project: This is defined based on questions on the technology used and the founders' plans for first introduction of their product in the market while the firms are still following the initial project. If the project was not followed, then the term of the project was deduced based on the market targeted by the project's leaders before firm formation. The term to project is defined at three different levels: short term, middle term and long term. The short term projects are expected to have products on the market within 4 years. The middle term projects represent a time to the market between 5 and 10 years, while the long term projects concern a time to market of more than 10 years. The long term projects are most often represented by products that are aimed at pharmaceutical human therapeutics. Middle term project include diagnostic projects and projects based on medical devices. These projects need trial phases, but are less constraining than pharmaceutical clinical trials. Finally, short term projects include product equipment and software development, in which there is no regulation for having trials or proof of concept[91]. Alsachim and

[91] The proof of concept is based on studies that aim at giving 'preliminary evidence of efficacy and safety, with the aim to inform a decision about proceeding into full development of the drug". (Karlsson et al. 2013, p.1)

Domain therapeutics have no relevance for this variable for the reasons indicated above (they are primarily involved in services).

Main objective: This variable aims at operationalising the data on the strategy of the firm. It is based on the activities that the leader of the firm has decided to pursue and the preferences of the entrepreneur towards making a long term surviving company or a company that aims at pursuing the original project. If the company still prioritises the original project, then the variable is considered as project focused. For these cases, the interviewees have made clear that firstly the main aim of the company is to develop the project and the activities described by them goes in this direction. If the initial project is not followed, and the main activities performed by the firm are not directly related in the direct exploitation of the research project, then the main objective variable is seen as the firm survival. The mention 'firm' in this column can be followed by the activities chosen by the entrepreneur. Thus, as expressed in the results, many firms decide to offer services or go into other activities rather than the initial project. In the case of Rhenovia, this variable was not straight forward because they still actively pursue the first goal, but since they are involved in numerous collaborative research projects on a day to day basis to develop their activity, they are not considered as having a project only focus.

4. Detailed analysis of the case studies

This chapter explores the strategy development of a firm taking into account its original project and founding team formation. It looks especially at the impact of the building of the founding team through the emergence of a leader, and the impact of the leader's preferences regarding the strategy of the firm. This chapter therefore looks at the possible reasons for a shift between two primary goals of firms, which are the survival/success of the newly created organisation versus the success for the project that lead the organisation's creation. These two goals coexist in most organisations studied, but the factors cited previously (i.e. the change of leadership together with the preferences of the agent) affect the prioritisation of one goal compared to the other. The chapter looks especially at the change in goals of the firm relative to two events. These two events are the company creation, which is often coupled with a change of management and the exogenous shocks encountered by the newly created organisation. The results are therefore divided into two sections. The first section looks at the impact of the transition from an innovative project in the venture creation process on organisational goals. The second section focuses on shocks affecting the project or the firm which leads to a revision of goals.

4.1. Initial definition of the firm's strategy at creation

This part of the results focuses on the impact of leadership change on the management team at the origin of the firm towards the firm's main strategy. This organisational change is put into perspective through the aims and activities chosen to be pursued by the firm (represented by Figure 5.2). The change in the management team is then linked to the cultural background of the leader, in order to understand the strategy setting in a firm.

The cases chosen are differentiated through the background of the leader. The background of the new leader of the project is identified by differentiating if the founder is mainly scientific or business oriented. The results will also show that another variable affects the choice towards a particular strategy, which is the risk inherent to the project. The risk carried by the project is evaluated by its time to market and its expected profits. This risk is also linked to the domain of application that the scientist had in mind when bringing the project towards firm creation. As shown in Chapter 2 (section 4), the domain of application in health sectors varies a lot in terms of their constraints. These constraints can ultimately affect the time to market, chance of success of the product and thus the risk linked to the development of the project.

In our analysis, many of the firms were created in order to bring academic results to the industrial world. Some firms moved towards a general interest purpose objective, such as medical advances or other tools to improve research processes, while others undertook a business opportunity, such as services. In addition, since one of our main concerns in this study is to understand the impact of a change of management teams or leadership on strategy, most of the firms in our sample have had to build a management team and in some cases find a new leader, if the leader of the scientific project was not willing to take on this role.

Table 5.1 aims at describing the leadership status of the firm (i.e. if there was an actual change of leadership after firm creation) together with the competences of the new leader. It shows that in most of the firms the leader of the company is not the leader of the scientific project. There are five exceptions to this: Firm *Alpha* hired a project manager for assistance in addition to the main creator, in Anagenesis a team of post-doc and consultants helped the main leader, while in the case of Domain Therapeutics there was a transition from one company to one other. Finally, the creators of Bionext and Alsachim used competences and techniques built from their studies and their thesis' to create the company. Looking closer into the leaders' backgrounds, in most of the cases the newcomers (5 out of 7 of them) do not come from academia, but have experience in company creation (Firm *Beta*, Cell Prothera) or in the industry in which the firm wants to be active (Phytodia, Biomica, Rhenovia). The ones that decide to involve a surrogate entrepreneur coming from academia usually choose partners from the scientific community who have knowledge about the project and who are young researchers.

Table 5.1 also describes the initial project of each firm together with their expected term of the project and their chosen organisational goals. While the column about the scientific project describes the scientific project from which the new company started, the 'main objectives' column shows the actual activities carried out by the firm. These actual activities can be solely on the initial project or solely on other activities (derived from technologies of the project) or involve both. Therefore, we hypothesise from this data that if the current activities of the firm are solely focused on the project, then the firm leadership must have decided that the goal of the organisation should be focused on the success of the project. However, if subsequent efforts are allocated to other activities, such as services, then we consider that the goal of the leadership is more oriented towards firm survival and longevity than on the project. This influences the survival of the firm in a positive way but diverts resources from the original project activities. Finally, the table also includes the term of the project, which is the estimated time in which the project can be completed. The aim of the project (through its industry of application) and the term to completion, which coincides with the time at which the project may bring revenue, will help us assess the risk inherent to the project. Since this risk also has an impact on the survival of the firm, this may also be considered as an important factor in the decision over the firm's activities and thus their general objective (firm longevity vs. project success). This provides the possibility to look closer at the relationship between the background of the leader of the company and the risks related to the project (evaluated by the time to completion) and compare them to whether the choice of the main goal of the organisation is focused on the project or firm longevity.

Table 5.1 shows the choice of each firm towards a project, other activities or both. As explained previously, all firms emerged from a specific scientific project, or innovative techniques. A founding team is formed at start-up and a project leader is usually chosen from within or from outside the incubating organisation. Table 5.1 shows that different backgrounds can lead to different goal setting and organisation of the firm around the project and/or other activities. The study cases are therefore divided between firms that have chosen a leader with a scientific background or a leader with a business or industry background. As hypothesised in the literature review, we will differentiate the firms that are led by founders with a scientific background and a business background (which also includes the firms with an industry background). Table 5.1 is therefore analysed in this section to differentiate between firms that are lead by an entrepreneur with a scientific background or a business background. These two scenarios will be numbered as:

1) the newly created organisation has a leader with a scientific background

2) The newly created organisation has a leader with business or industry background

Table 5.1: Firm goal at creation after the new top-management team are in place

Firm Name	Leadership change	Background of the leader	Aim of the scientific project before firm creation	Term of project[92]	Main objectives
Alpha	No	Science	Create a bio-artificial organ	Middle term	Project
Beta	Yes	Business	Work on biomarkers	Middle term	Project
Phytodia	Yes	Industry	Develop a therapeutic compound	Long Term	Firm / services and cosmetic project
Alsachim	No	Industry	Using technology to bring innovative services to firms	-	Firm / specialised services
Kappa	Yes	Science	Develop a therapeutic compound	Long term	Project
Enovalys	Yes	Science - Industry[93]	Create a chemical reaction database	Short term	Project
Domain Therapeutics	No	Industry	Innovative techniques through acquisition	-	Firm /services
Biomica	Yes	Industry	Diagnostic test	Middle term	Project
Cell Prothera	Yes	Business	Develop transplantation from blood stem cells	Short term	Project
Anagenesis	No	Science	Understand the process of differentiation in the development of stem cells	Long term	Project
Bionext	No	Science	Big Data & Cloud Computing Platform to evaluate the effects of compounds on humans	Short term	Project
Rhenovia	Yes	Industry	Understand diseases of central nervous system through bio-simulation	Long term	Firm / parallel projects

[92] '-' means that there is not any set long term project and the creation of the firm is related to other activities.
[93] The leader of this project has a double background as he did his thesis within a company (CIFRE), but ultimately we consider him with a scientific background, since within his training he worked mainly on a research project. He also had limited knowledge in terms of general company management and so had to seek separate training after starting the company.

When looking at the choice of activities for leaders with a scientific background (including when there is a change of project leader), in all cases they keep the project as their main objective (5 out of 5 firms). This is not the case for people with an industry or business background, since many of them choose to have different activities such as services or related scientific projects (4 out of 7 firms), while the others are still focused mainly on the project. One explanation for this division evident from table 5.1 could be the risk inherent to the project which is linked to the term to completion of the project. Most of the projects that have a short term to completion are kept as the main activity, while the ones that have a long term to completion, such as therapeutic drugs, are abandoned or given a limited amount of effort compared to other activities such as services.

In terms of **evolution processes**, according to the results shown in Table 5.1, we can hypothesise that **scientific leaders would always prefer to pursue the initial scientific research projects.** Concerning the group **of leaders with a business background, their choice does not to seem predetermined** on whether they are pursuing the project or looking to develop a lasting firm. According to the table, leaders with a business background tend to consider the project in more detail (in terms of risk and term to completion of the project) before deciding to actively pursue this project. In order to further understand the distinction between the two categories, the reasons for such a differential of preferences between the categories must be studied further.

The following two sub-sections will look deeper into the reasons for the choice towards the main objectives that firms follow. It will look at the scientific motivations and preferences, and then the business leaders' preferences in order to understand what drives the choice towards the activities of the firm.

4.1.1. Scientists preferences

In this section we look at firms whose leaders are mainly from a scientific background. Some firms have the same leader who originally developed the project in the incumbent organisation, such as firm *Alpha* and Anagenesis, while others have delegated the development of their project to a fellow scientist, which is the case of all other firms in this category. However, Table 5.1 shows consistently that when the leader of the organisation comes from a science background, the main objective of the firm remains the project, e.g. the scientific project at the origin of the firm creation. The firms representing in which scientist keep a leadership position are therefore **mainly driven by keeping the firms' goals aligned with the project goals**. This is consistent for all the firms with a scientific leader, since they all recognise their priority as being focused on the research project. This is the case even for firms that have a mid to long term realisation of their project, which means profitability on a longer term (this includes two of the firms). The question of why scientists choose to focus on projects will be analysed through opinions gathered from various players who have worked with scientists or the scientists themselves.

Looking closer, many interviewees considered that some scientists are focused on their invention and discovery. For example, one of our firm leaders with an industrial background explained that scientists have a real desire for their technology to be transferred to a newly created company in order to have an impact on human health. He explained this regarding one of his fellow co-founders:

> "The chemist wanted to do something like Pierre Potier. ... like any good academic, they have the idea that with a bit of money and just their idea, that we could go [easily] from a plant[94] to a medication."[95]

His statement highlights two points. Firstly, the scientist is in this case driven by the success story of Pierre Potier[96], and wants to have a real impact on human health. In Pierre Potier's case, his discovery lead to the main drug used in cancer therapies nowadays, and so many scientists may aspire to follow his path and have a direct impact on human health from their own discovery. Secondly, this founder expressed the lack of understanding that some academics have regarding the often long and tedious development process. This is a good example that illustrates the dream of many scientists to follow the development of their academic project based on the potential achievement of being able to contribute to create a new drug and ultimately make a contribution to human health advances.

In addition it was also acknowledged by many interviewees and experts that scientists are often the ones most committed to the project. A business Angel commented:

> "In order for the firm to be successful, the entrepreneur must be somebody that has guts, and in many cases the one that has the guts is the inventor because it [the project] is his baby."[97]

This statement confirms that when the scientist is at the origin of the project and has put a considerable amount of time into it, they are usually the most motivated to carry the project to completion. The scientist's main motivation is aligned with his academic motivation to make a contribution towards health care problems. The creation of a successful or long lasting firm is not a

[94] Plant here refers to a molecule that has interesting active principles identified from a living plant.
[95] Translated from French : "Le chimiste avait dans l'idée de faire la même chose qu'a fait Pierre Potier […] Comme tout bon académique ils étaient persuadés qu'avec un peu d'argent et juste l'idée, que l'on pouvait passer d'une plante à un médicament pour le diabète. "
[96] Pierre Potier was a scientist who worked on natural products and was at the origin of a major drugs discovery that are still widely used for cancer curing, which is called the taxol. More information about his story can be found in CNRS Journal, 3 february 2006 "Pierre Potier, disparition d'un grand scientifique".
[97] Translated from French : "Pour qu'une entreprise réussisse il faut qu'il y ait quelqu'un qui s'arrache les trippes, et très souvent celui qui s'arrache les trippes c'est l'inventeur, parce que c'est son bébé. "

main priority for them. Their project moves on because it was not possible to pursue it within the academic organisation (this in further discussed in Chapter 6 section 4). These conclusions are also consistent with the statements of the entrepreneurs, one of which described his primary motivation as follows (the scientific founder of firm *Kappa*):

> "I saw most of all two aspects [considering the firm creation], the first one was a willingness of being involved in the industrial development of a research project; I really wanted to go to the end of the story. The other interest was that if those found molecules were potentially interesting, we wanted to push them as quickly as possible towards development, and therefore the patient."[98]

As this quote shows, the scientific founder expresses his desire to firstly push his scientific project and secondly that he wants to contribute to the improvement of human health. These objectives are common among all the scientists interviewed. Scientists sometimes explicitly express their willingness to push the project, as the above founder did, or explain the transition towards the company creation as a logical continuity of their scientific project. The scientific founders also have other additional reasons for the company creation, such as money (2 academic founders) or employment creation for local doctoral students (1 academic founder). However, these reasons are sporadic and vary among scientific founders.

These results confirm proposition 2, which proposes that academic entrepreneurs are focused on the exploitation of academic project, both for being able to see their project being developed and ultimately to contribute to human health. However, the above proposition argues that this may not be the case for new firms with a business leadership, which will be looked at in the next section.

4.1.2. Business or industrial managers preferences

Looking back at Table 5.1, most firms with leaders from business or industry have not had an a priori preference between project and firm development. The leaders also seem to be influenced by the time to project completion, or time until the first profit expected from the project. The differences of **choice for business leaders do not only depend on their background but also on the time to term for the project and the resources (financial and other) needed for completion**. The firms that have a longer term product and need higher financing are considered as riskier. In these cases it can be observed that the firm leader often diversifies by implementing complementary

[98] Translated from French "Je voyais avant tout deux aspects, la première était une volonté de faire développer ce projet de recherche vers un aboutissement industriel ; vraiment aller au bout de l'histoire. L'autre intérêt était de se dire que si potentiellement ces molécules étaient intéressantes autant de les pousser le plus rapidement possible vers un développement et vers le patient."

activities such as services. In order to better understand the reasons for this choice we will refer to interviews conducted with firm leaders who have business experience.

Concerning firms who choose to follow their initial project, their choice seems to be influenced by the risk inherent to the project (according to Table 5.1), which includes the expected time to completion and thus the time to first profit. Thus, in our cases the leaders with business backgrounds still put the priority on the initial project when the time to completion is of a shorter timeframe. This is the case for Cell Prothera, Biomica and Firm *Beta*. These firms are developing technologies for which they have a short term plan for market introduction, usually within 5 years of creation. They are specialised in technologies that are less constraining than pharmaceutical products, such as diagnostics or in vitro technologies that do not have the same kind of regulation compared to other invasive or in vivo ones[99]. The clinical trials for these products therefore need to cover the proof of concept, but since they do not include invasive technologies the clinical trials do not require safety tests. The founders of each of these firms insisted that the development time was to be completed within five years, and that they already had a clear plan for production and sales. All of the firms involved managed to raise funds without relinquishing control to the external investors.

Some of the firms also decided to diversify their activities and provide services, but these activities are more strategically oriented to potentially have a long term impact, as one of the founders commented:

> "The services with our partners goes beyond the aim of generating a bit of funding, it aims at doing co-development together for the future." [100]

Some of the firms focus on their first and primary projects, and ought to be involved in services for only strategic issues, while others with longer term product development choose to finance their project through providing services. For these firms, working on only their original project would require an external financier to take more control over the firm and therefore is not a preferred route for these business leaders (the choice towards financing was discussed in Chapter 4). They **are therefore more oriented towards securing the longevity of the firm** rather to work fully on the project.

[99] Please refer to the chapter 2 section 4 for the details of the different industries linked to life sciences.

[100] Translated from French: "La prestation de services avec nos partenaires c'est au-delà de générer un peu de sous, c'est de faire ensemble du co-développement pour l'avenir. "

The interviewed experts agree that the weakness of some project based firms is that their time to market is too long. This especially concerns those with drug discovery projects who have a time to market that is significantly higher than in any other sector. Start-ups, which are in a fragile state of their organisational life, improve their chances of survival by having a short time to market. An expert working in a financing organisation that helps companies to grow (SODIV) corroborated this:

> "The aspect of the market, for an enterprise is really important. ... In most of the cases, the leaders of [innovative] projects do not realise the delay of time to market, in general the time to develop products is underestimated."[101]

Some of the businesses view the benefits of financing themselves through services as a double advantage due to faster contact with the market in addition to the income advantage, as the manager of Domain therapeutics explained:

> "We [the company] will work even better for industrial partners, of whom we understand the needs when working for them,[...] and we will already have a foot in the door with contracts that will show them what we are able to do, that we work well, that we are efficient, and therefore we would be able to attract more important contracts."[102]

For long term projects, the leaders with business backgrounds may therefore prefer to provide services and have close relationships with their market, since the time to market and feedback from potential customer are both useful influences on the firm performance. There are also other explanations regarding the choice to include services in the firm. One business leader explains:

> "We [the founders] just wanted to be free and independent. The decisions are your decisions, the consequences are the one of your decisions, and if you made a mistake, you must take responsibility for it and adjust yourself. Not having any financiers around the table gives you the opportunity to take any possible path."[103]

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[101] Translated from French: "L'aspect marché, dans le domaine de l'entreprise est très important […] La plupart du temps les porteurs de projets ne mesurent pas non plus le délai de mise sur le marché ; en général ces délais sont sous-estimés. "

[102] Translated from French : "On travaillera d'autant mieux pour les industriels, qu'on comprendra leurs besoins en travaillant avec eux ; on aura déjà un pied dans la porte par le biais de contrats, qu'on arrivera à leur montrer ce qu'on sait faire, qu'on travaille bien, qu'on est efficace, et donc on arrivera à attirer des contrats plus important. "

[103] Translated from French : "Nous on voulait juste être libre et indépendant. Les décisions sont vos décisions, les conséquences sont celles de vos décisions, si vous vous êtes trompés vous devez l'assumer et vous recadrer, en gros c'est la liberté, c'était juste la liberté et l'indépendance. Ne pas avoir de financiers autour de la table vous permet d'emprunter tout les chemins possibles."

Issues of control and freedom over the firm goals and activities can also be reasons for the firm to provide services rather than seeking financing for advancing the project as fast as possible. The verbatim highlights that the freedom involves different facets, firstly the ability to readapt their path and being free to pursue and adjust to follow any opportunities they decide on, and also indicates that when taking a mixed model, the manager can be more willing to bear the consequences of decisions as it is his own and not the one of other stakeholders. The verbatim highlights this concern from entrepreneurs with a business background, which is shared among many the other firms in firm that has a leader with business or industry background. The results therefore emphasise the difference of mindset between scientists with no experience in entrepreneurial venture and those lead by business or industry leaders. Evidence from the cases supports the hypothesis that there are specific culture differences between academic, business and industry leaders. In two of the cases surveyed, the leaders came from unsuccessful start-ups in the region, which had a direct impact on the organisational goal. These cases will be presented here in order to emphasise the role of the experience of the firm leaders.

Going slightly deeper into the choice of business strategy, two of the firm creators (Phytodia and Alsachim) were particularly influenced by their experiences while working for other start-ups. These start-ups focused mainly on their pharmaceutical project but they eventually closed down due to a lack of funding to pursue. These two entrepreneurs therefore had to deal with the termination of an initial promising project in combination with the closure of the organisation and facing unemployment. They expressed in the interviews that this experience had an impact on their preferences for their current company goal setting. Their experiences lead them towards security and building a survivable firm rather than to aim for only the project. For Phytodia, the research project at the origin of the company is still pursued with secondary priority but the company relies primarily on services and cosmetic products (which is a market with less regulation than the pharmaceutical industry that was originally targeted) to survive and grow. For Alsachim, the entrepreneurs had the opportunity to follow the path of their previous company by taking over its project. Instead, the new owners preferred the development of technologies that they had worked on at university for providing services, rather than focusing on a risky project. Their motivations were the following:

> “We have created our (talking for two founders) job for the future, and so we wanted to go for a mixed business model of services and then drug discovery. [...] we also need stability for us, because

the job market even with experience is not always easy. Also, we had a constraint, we wanted to stay in Alsace."[104]

Therefore, the **personal vision and experience of the firm leader can influence the choice of the firm survival goal**. The term in which the firm must remain under the entrepreneur's control can range from a couple of years to a life employment plan. This intention of the entrepreneur is certainly influenced by his experience and personal preferences (e.g. the employment preference or personal achievement preference), which are more likely to vary between leaders with business or industry experience. This confirms the arguments given in proposition 3.2.

The interviews with entrepreneur's that were part of an unsuccessful start-up seemed affected by the period of closure of the organisation they were taking part in, especially by the fact that they were facing unemployment. Thus the preference towards firm longevity can also be influenced by the level of employment in the given location for suitable jobs for a specialised labour. This pressure may not be felt in such strong terms by academic entrepreneurs. Academic researchers in France have a status of being civil servants and therefore benefit from life employment. This status may help academic entrepreneurs to have different strategies compared to business entrepreneurs. In one of our cases we have a team that agreed that the best strategy for their company was to be acquired.

These results show that the background (social environment and experience) of the leader of the firm and the risk involved in the project may be determinants in the preferences of the agents, and therefore also determinants for the goal setting of the company. The difference in entrepreneur background has shown the difference in culture between academics and business or industry oriented people. The section explored the reasons for the project choices of scientific founders. It concluded that scientists are more oriented towards the development of research projects, since in the case where they were at the head of the development of the initial project they want to see their research project to be completed and to apply in the real world. Secondly, leaders with a scientific background feel strongly about improving human health, thus they may be seen more as social entrepreneurs than classical entrepreneurs. Academic researchers in France have a status of being civil servants and therefore benefit from life employment.

[104] Translated from French: "nous avons créé notre métier de demain, et donc voulions un business model mixte, de services et de '*drug discovery*'. […] On voulait aussi une certaine stabilité pour nous, car le marché du travail même avec de l'expérience n'est pas toujours facile, et nous avions aussi une contrainte nous voulions rester en Alsace."

This section has shown the influence of management changes when transitioning from incubating organisation to firm creation. The next section complements this study by examining the change in organisation objectives after creation, but most importantly the longer term problems regarding the co-evolution of the innovative project and the development of these organisations.

4.2. Consequences of exogenous shocks on the continuity of the firm's strategy

The organisational phase at creation is not the only phase characterised by organisational change in the early life of the company. As shown in Figure 5.2, external factors can trigger changes in organisational strategy at firm creation. This section will show that the mechanisms identified in the literature review are not only relevant for firm creation but also at a later stage, since external factors can also influence the firm strategy and organisation. It also focuses on the development of the strategy in the new firm, especially at specific times when the company has to make important strategic choices for the continuity and survival of the company vs. the project. Two cases of separation between the project and the company due to exogenous pressures or shocks will be studied. Exogenous shocks are here considered as all the events that affect the project or the firm but that are not dependant on the firm leader's control. Both of these cases are concerned with the decision to stop the project, the first because the project was no longer viable for venture capitalist financing and the second because the project was no longer adapted to the company. These two cases feature older start-ups in the same field. The study of these two cases gives insights about the reasons of changing long term goals. In Case 1, the project experiences some problems that lead to the investors choosing to cease investment, having previously invested heavily. Building on the capabilities developed during the years since creation, the firm changes its name for a new start based on in-house technologies. Case 2 features a firm started on the basis of a scientific project, but after some years of activity the firm has to choose its real domain of activity and therefore decides to drop the project.

Case 1

Faust pharmaceuticals started as a spin-off with several projects from researchers based in an academic laboratory in Gif sur Yvette. The start-up's objective was to exploit the discoveries made in the academic laboratory, which aimed at developing new drugs for the nervous system. The scientists quickly received backing from venture capitalists, who helped them to build the company and directly hired the CEO (Chief Executive Officer) and CSO (Chief Scientific Officer) from their previous contacts. The firm was then incubated for two years in the academic laboratory before moving to the Alsace BioValley cluster. At the end of the incubation phase they had raised around 16 million Euros from six investment funds. The business model at that stage was entirely focused on the development of the most promising drug. While doing clinical trials, they also acquired a service company in order to contribute to the drug discovery process. Due to problems that led to delays in the clinical trial phase, the investors decided to stop the financing because the time span for returns was too long in relation to the time of the patent expiration.

The scientific director then thought that there were valuable competences to take advantage of in the firm and that novel services could be provided to pharmaceutical companies. He therefore decided to take over Faust Pharmaceuticals and change its focus from a product oriented company (based on the initial project) to a company that could offer service activities and engage in collaborative projects with pharmaceutical companies.

There has been a shift in terms of project to a service based business model compared to the first company. The original strategy of the company was that the operations depended entirely on the success of the project (because the original goal was towards high profits from drug development), which was due to the investment model chosen by the firm. However, since this project failed and the company faced problems with a shortage of financing, the chief scientific officer (now CEO) decided to change the company towards a goal oriented model for improved self sustainability.

The new CEO described his reasons concerning his decision to continue the company activities with a greater emphasis on services:

> “In 2008, the society should have closed and fired the remaining employees, but the technology that we had developed by the acquisition of the small society Euroclide started to work really well. [...]In this period [end of financing period] I, in the position of scientific director, started to be contacted by companies that found our research technology interesting, including a big pharma.”[105]

The technology developed by the first company (before the change of name) was 100% product oriented due to the large involvement of venture capitalists. However, the acquisition of competences over the life of the company gave them an opportunity to refocus their activities and

[105] Translated from French : “Au courant de l’année 2008 la société devait fermer, licencier les personnes qui restaient, mais la technologie que l’on avait développé par le rachat de la petite société Euroclide commençait à très bien fonctionner […] Dans cette période là, moi en tant que directeur scientifique j’avais commencé à être approché par des sociétés qui trouvaient notre technologie de recherche intéressante dont une société de recherche Pharmaceutique.”

gave rise to another company called Domain Therapeutics. Hence, even with the death of the project that was the priority goal of the firm, the organisation was able to take advantage of their specific resources to survive without the project, as the CEO of Domain Therapeutics explained above.

In this case, after 7 years of focusing on a single project, the company changed its business model suddenly due to some problems emerging in the development of the product. This kind of transition can also be true on a much shorter timescale. This happened in one of the other start-ups in the case study, the firm *Kappa*. Firm *Kappa* was focused mainly on a molecule development project. After some months into the project and a search for financing, the firm now continues without much cash and with a prototype molecule that has failed the initial proof of concept tests. The firm must now focus on new molecules to continue the initial project. Since the firm is running out of cash without a molecule reliable enough to interest investors, the firm may have to refocus their activity on the firm survival and thus on services rather than prioritising products. A founder of firm *Kappa* stated:

> "Now, we are thinking about whether or not the investors are coming or not, and also thinking towards the diversification of our business model, in order to integrate eventually a small phase of services for doing 'customised chemistry'"[106]

In this particular configuration, the manager of the firm has decided to focus temporarily on other activities for the good of the main project, since there is a threat over the firm survival.

Therefore, even if a firm is mainly focused on its initial project, its interests are dealt with separately and can sometimes supersede the project development. **Personal preferences may change in the face of increasing uncertainty encountered during the life of the innovation project, especially when the firm experiences difficulties with their project. The difficulties are then reflected in the financial aspect that may ultimately affect survival**. This observation is consistent with proposition 1, since when there is an increased risk of firm closure, and thus unemployment for leaders, they tend to refocus their goals in order to ensure the survival of their venture.

This section started with a case in which the initial project was not viable after some years of activity, but the competences developed over time gave the firm an opportunity for survival. It has

[106] Translated from French : "Maintenant nous sommes en train de réfléchir si les investisseurs vont venir ou pas, on est en train de réfléchir pour diversifier notre business model en intégrant éventuellement une petite phase de service pour faire de la chimie à façon. "

also been shown that the project can be suspended for cash reasons in order to guarantee the survival of the firm and thus the employment of the people involved in the firm creation.

<u>Case 2</u>

The start of Novalyst evolved from an idea developed by an academic researcher. His idea was to produce a kit for improving and speeding up the chemist experimentation (as much in academia as in industry). These kits would be offered with a database and software that would be accessible to a wide range of users. The scientific founder found a partner with business experience through his personal network in order to develop the firm. They decided to pursue a mixed strategy for the company where they would receive revenue from services in order to fund development of their original project. They preferred that the firm should not depend on investors and should have a sustainable and independent development. During its development, Novalyst Discovery merged with another firm called Alix to form a new company called Novalix. The firm grew consistently to reach 120 employees in 2011. Ten years after the creation of Novalyst, the firm (now Novalix), under the direction of the business founder, decided to base its activity exclusively on the services that the firm developed over the years and in which they had their principal commercial focus.

This decision led them to drop the original project started by Novalix. The academic inventor at the origin of the project in collaboration with a PhD student working on the project engaged together to pursue their project with the creation of a new venture. In 2010 Enovalys was created, not because of a lack of success from Novalix but because after ten years the initial project was not a priority to the firm anymore.

These two examples show how projects and companies are linked at their conception. A co-evolution can often be observed as a growing independence over time between the two organisations (firm and project). Over time, when the company has grown in terms of employment and activities, the firm can become a standalone entity that is distinct from the project. The firm can survive without the project, by choice or by obligation. The project on the other hand may not only depend on the incubating organisation to survive, but on the entrepreneur's vision. The future of the firm and the project are dependent on the leader or management team in the firm and project founder. This is well illustrated by a comment made by the academic founder of Novalyst:

> "Each of us (founding team) must find our place. [...] and each of us must accept our role because there will necessarily be evolutions in the firm. For example, Novalyst at the start was a company that was very technologic, but in the end it was much more business development oriented. The

> roles have evolved a lot during this time. This is the reason why I came back to the CNRS, because after a while I didn't have anything to do in Novalyst anymore."[107]

The founders of a company, as this scientific founder expressed, can have a misalignment of objectives with other founders, which over the years can lead to a separation between the goals of the project and the organisation, but can also act to organise change in the founding team. In the above case this resulted in retirement of the scientific entrepreneur from active management. This is particularly due to the preference of the founder towards the completion of the project versus a sustainable development path for the company. The founder with a scientific background (inventor of the product) in this example wants to push for the completion of the product that emerged from his project. This is consistent with the observation made above that the evolution of the firm and the project may be independent. He therefore chose to continue his project with other collaborators who were working on the project at the time and created a new company that is focused on this particular product. The preference of the business founder was to focus on the company's existing strengths and a logical path of growth. He prefers to focus his strategic plan for the company on developed competences, the stable market and relationships with customers for the evolution of the company. The business founder who remained the president of the company talks about his strategy in these terms:

> "Today we are a company that is looking for reinforcement of its technological platforms for making a permanent effort to access new complementary technologies. Once you are anchored with [customers] companies, you are looking for developing the offer for them. That is what I call a catalogue strategy."[108]

In this case the CEO preferred adaptive evolution of the firm to market needs rather than a product push vision. The vision of the business founder and the scientific founder were at one point in time (here after 3 years) incompatible for a common evolution in the company, and so one of them was forced to retire from active management. The decision to not follow up the project does not imply the death of the project. Committed inventors could have taken the project further by

[107] Translated from French: "Chacun doit trouver sa place ; et il faut que chacun doit accepter son rôle, parce qu'il y a forcément des évolutions au cours du temps, au cours de l'évolution de la société. C'est que par exemple Novalyst au départ c'était une boîte qui était très technologique et qui à la fin est devenue très business développement. Le rôle des deux a beaucoup évolué au cours du temps. C'est pour ca que je suis revenu au CNRS car au bout d'un moment je n'avais plus rien à faire dans Novalyst."

[108] Translated from French: "Aujourd'hui on est dans une démarche d'entreprise qui cherche à muscler ses plateformes technologiques en faisant l'effort permanent d'accéder à des technologies complémentaires nouvelles. Une fois que vous êtes bien ancrés dans les boîtes vous cherchez à développer l'offre que vous pouvez leur faire. C'est ce que j'appelle la notion de catalogue."

changing organisation again, in the same way as when the project was moved away from academia. This was the case here with the creation of the new company.

In conclusion, the business leaders in these two cases ultimately decided to rely on existing markets and proven competences of the firm for their long term strategies. For these managers, the longevity of the company therefore relies primarily on known markets and developing market relationships. The company survival often supersedes the potential achievements of the project. The mechanism identified in the literature review, illustrated in Figure 5.2, shows that some of those mechanisms do not only take place at creation. In these two cases, exogenous factors forced the entrepreneurs to revise their vision, which also lead to organisational change.

These two sections have shown how the exogenous shocks and personal preferences in a coalition shape an organisation by influencing the behaviour of the leader of the founding team over time.

5. Synthesis of the results and discussion

The literature on top-management teams (Cohen and Bailey, 1997; Eisenhardt and Schoonhoven, 1990; Hambrick et al., 1996) has shown the influence of the composition of a management team over firm success. However, this literature mainly focuses on the interaction within a group at the head of a firm. This chapter instead focuses on the issue of transfer of leadership between individuals during the process of exploitation of an innovation process. The phenomenon of surrogate entrepreneurship has been introduced recently in the entrepreneurship literature (Franklin et al. 2001), which can be present in high-tech companies especially in academic spin-off companies. Thus we aim at understanding the consequences of surrogate entrepreneurship and its implications for the evolution of the firm. The chapter especially looked at the consequences of the entrepreneurs' backgrounds (initial inventor and surrogate entrepreneur) and choice of the firm leadership towards the strategy of a firm. While the literature has introduced the link between the background of the entrepreneur and his preferences, the results go further by looking more closely at the way they are related to the firm early evolution. It did so by firstly understanding the entrepreneur's choice towards a specific strategy and secondly by studying the impact of a change of leadership on the early evolution of a firm. Thus we first come back to the **preferences of the entrepreneurs**, before talking about their possible impact on the firm evolution through the revision of the propositions developed in the literature review. The literature review has made propositions that were specific to the preferences of different groups of people. The present chapter has partly built on these propositions but aims ultimately at transforming them into results in order to link people's preferences to their decisions over firm strategy. While the discussion initially compares the propositions to the results found, the section later focuses on revising the preference propositions in order to take into account the culture of the entrepreneur and link it to firm strategy. The revised propositions emerge from the results and aim at being tested in further research on a larger scale. We start by discussing the propositions concerning the background of the entrepreneurs and their culture, starting with academic entrepreneurs. The following proposition emerged from the literature:

Proposition 2: Academic entrepreneurs, given their specific culture, have a tendency to have aspirations oriented towards technological development and technology transfer, especially technology developed by them during their academic career.

In our cases, academic founders were usually depicted as wanting to develop their research project as the main reason for starting a company, together with the overall objective of contributing towards human health. Some interviewees also included secondary objectives such as employment creation for students, or even pecuniary returns, but such reasons were rare and thus could not be considered as goals stemming from cultural reasons, but probably are influenced by individual personalities. The goal of contributing towards human health must be specific to the science studies, since it could not be relevant to most other sectors. However, this objective of human health in the sciences related to biotechnology could be extended in other sectors to the desire of scientists to achieve a broad utilisation for their discovery or finding, when they have a relevant application in a given industry. Thus proposition 2 finds some grounds in our cases, since most of our academic researchers aim primarily at transferring their innovation for the benefit of human health rather than as a pecuniary objective. This is a general trend, as a minority of our academic entrepreneurs had pecuniary issues in mind. The proposition is revised later in order to adapt it to the strategy chosen by the entrepreneur.

Concerning the leaders with a business or industry background, the theoretical background advanced the following propositions:

Proposition 3: Entrepreneurs with a business background are dependent on their own background, experience and social environment to define his personal preferences.

Proposition 3.1: Entrepreneurs who have had a successful managerial experience or who are in contact with many high achieving managers are more inclined to aspire to high growth firms in terms of profit and turnover.

Proposition 3.2: Entrepreneurs who have faced uncertainty towards their own employment may opt for more control over their own company and thus value survival over high-growth and high-turnover.

Concerning the business leaders, we cannot make conclusions regarding any common preferences among them. This group representing leaders with business backgrounds was split into two, the ones aiming towards developing a project started in academia and the ones who opted for a hybrid model. In the first case, the main objective of the firm was to succeed in their project development and commercialisation, while the second focused on keeping the control over the company and mainly aimed at survival rather than having a growth objective. This objective was already discussed in Chapter 4 and we concluded then that this objective was influenced by the social environment of the firm and the connection of entrepreneurs with other successful or unsuccessful firms. In our case, the social aspect of the objective of the entrepreneur was therefore verified. Due to regional specificities, only proposition 3.2 could be verified. The sample has highlighted that entrepreneurs facing unemployment favoured keeping control over their own company and did not get involved into risky projects, but rather opted for less risky activities. However, the regional specificities did not provide an environment in which a high number of high-growth companies were thriving and therefore could not verify proposition 3.1.

Proposition 1: The preferences of the entrepreneur like any other agent include an ordinal characteristic. Agents first satisfy basic needs over aspirations (personal achievement).

Finally, regarding proposition 1, which was based on a theoretical assumption, we found that entrepreneurs prioritise their basic needs over aspirations. We have firstly observed that entrepreneurs who were previously confronted with an unemployment situation oriented their preferences for creating a stable employment for themselves through their effort to build a firm based on a business strategy with limited risk. Secondly, in the cases where some firms were approaching financial difficulties, entrepreneurs usually reacted with a change of strategy towards a business strategy that could preserve employment rather than accomplish the initial project. Thus in the face of unemployment our entrepreneurs (even those with scientific backgrounds) reviewed their preferences towards a model that maximised their chances of survival. However, the employment problem may not be applicable to academics with permanent positions. While they have the possibility to be partly involved in their start-up, they have the option to keep their status of civil servant that entitles them to return to their job if their enterprise faces problems. Therefore, this category of people may not be as sensitive to company closure as other entrepreneurs.

The preferences can then be linked to the strategy of the firm and thus the above propositions can be reformulated. **The preferences of the leaders induced different decisions over firms' strategy and thus influenced the evolution of the early life of the firm.**

The literature review has presented a two steps evolution in which the firm first commits to the founding team structure and then to the strategy. While the results have emphasised that several of the propositions (1, 2, 3.2) made in the literature about the preferences of the entrepreneurs are observed in practice, it has not yet been discussed how the **preferences affect the early evolution of a company**. Following our theoretical model, we interpret how the early evolution is affected by the choice of the leader as a result of his culture and preferences. The results have shown that there are differences in adopted strategies depending on the early decision over who takes leadership for the firm.

In the case studies we have differentiated between two types of entrepreneur, the entrepreneurs with a scientific background and the entrepreneurs with a business or industry background. The two main trends that are observed in our paper are the difference in choice over the initial project and the choice to pursue other activities and hold the initial project with secondary priority. We represented these paths of evolution observed in practice in Figure 5.4. The process starts with the initial scientific project, which is first followed by the leadership decision and thus the agreement on the team structure. The project leader has then to choose whether or not he wants to pursue the leadership in the newly created firm or prefers to delegate the project to somebody else. When this decision is made we can observe the background of the firm's leader that will influence the decision over the firm's strategy.

The results showed that the entrepreneurs from scientific backgrounds are more inclined to pursue projects that have a social impact, especially on general human health. The academic entrepreneurs did not express concerns about whether or not the project on which the company was based was risky. This is true whether or not the leader with a scientific background was leading the initial project, although the results also pointed towards the assumption that the initial project leader would have additional incentives to pursue the project due to his early research involvement.

Revised proposition 2: Leaders of a company with a scientific background are more inclined to pursue the initial project, since they are generally more motivated by social returns.

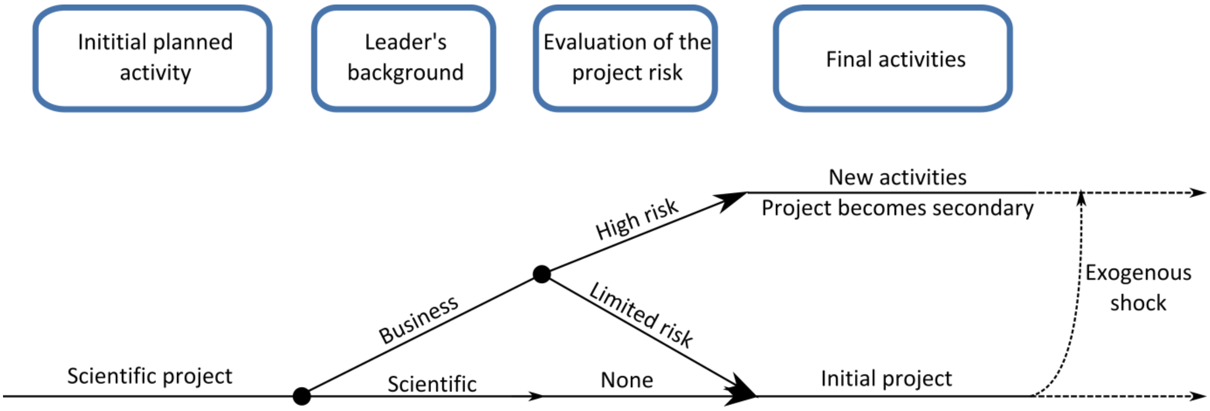
Concerning business leaders, it has been shown that their preferences are dependent on the risk behind the project because they are more attached to the survival of their firms. Thus we have seen that projects that have a short term to completion, have business leaders who usually choose the project as the main activity of the firm. However, projects that had an application in human therapeutics, and thus are considered as higher risks, are usually set to secondary priority, or put on hold in order to firstly build a financially stable company. Thus, as shown on Figure 4.5, we hypothesise that business founders observe the risks involved in building the venture on the initial project before deciding on their activities.

Revised proposition 3: Leaders of companies with a business background are more inclined to assess the risk involved in building the venture on the initial project before deciding on the firm strategy.

In our cases, the entrepreneurs with a business or industry background either choose to follow the initial research project, if it is not too risky or in the case of higher risk the entrepreneurs usually opts to primarily focus on other activities that aim at financial independency. Then depending on the involvement and negotiation of other members of the team, the project can be continued, but with limited time and resources, or be dormant (no activities from the company) until financing stability has been reached. For instance, in the case of firm Novalyst (case 2 in section 4.2) the scientific and business founders agreed that the business model should rely both on services to bring revenue to the firm on a short term basis and on keeping the development of the initial project. In the case of Phytodia, the researchers at the origin of the research project were aiming to find a molecule to have an impact on diabetes. Due to their unwillingness to get involved in the firm formation they did not influence the strategy decision much and as a result the molecule found was used in the cosmetic industry rather than the health industry. In this case, the project is considered dormant for the moment, but the business founder does not exclude the possibility of returning to the health sector later in the process. Finally, in the case of Alsachim, the founder could have taken up a pharmaceutical project from the company he worked in previously, but instead settled for a business model oriented towards services, and therefore currently does not have any ambition to get involved in the development of human therapeutic products. It can be noted that the choice of the two last founders were also influenced by the fact that they faced unemployment due to the failure of the venture that they were working in previously, and thus due to their experience they wanted to settle for a business strategy with limited risk of failure and with short term revenues.

Thus in Figure 5.4, when business founders settle for new activities with shorter term revenues, the level of pursuit of the initial project can vary between cases. It appears that this may vary according to the involvement of the scientist at the origin of the project in the new venture, but also according to the previous experience (in terms of employment) of the business founder.

Figure 5.4: Tree of decision towards a firm strategy



Looking at a more general trend, especially with the cases presented in the last section (section 4.2), over time one can see a growing independence and **co-evolution** of the project and the company. While the company aimed at the development of an initial research project, the path of the firm can diverge from the development of the initial project due to two events in its early evolution. Firstly, as we have seen, a change of management can cause a change in the firm activities away from the development of the research project, and secondly exogenous shocks can also have an influence on the activities of a company and ultimately on the pursuit of a project. Both of these phenomena can change the goal of a firm from being organised around a research project to the re-centring of activities based on similar knowledge but other activities. This observation could raise questions about the utility of start-ups used for technology transfer purposes. Here, especially when a surrogate entrepreneur intervenes, one cannot ensure that this entrepreneur will pursue the initial project and thus be the best vector for technology transfer of particular projects.

One of the characteristics of the cases studied is the lack of cases involving venture capitalists as a main financing source. Only one case was involving this type of financing, which was a direct consequence of its parent firm's business model (case of Domain therapeutics described above, in section 4.2, in Case 1). The previous chapter (Chapter 4) has explained this bias by the fact that this type of financing does not seem adapted to business founders, since it does not guarantee the survival and sustainability of the firm. However, as case 1 emphasised in the last section, the tree of decision is different if a venture capitalist is involved. The venture capitalist is often involved at an early stage and so takes the role of making the early leadership decisions. As explained in the case of Faust Pharmaceuticals, when venture capitalists are involved there is also no negotiation over the strategy because the financier requires that only the initial project is pursued (at the expense of any other activity). Thus in this case we typically have the introduction of leaders coming from the industry but who have very limited power to negotiate with the financer over the strategy of the firm. Thus, firms involved with this type of financier would not follow the path of evolution depicted in Figure 5.4.

Due to the fact that we focus on case studies to understand the complexity of the processes, this type of design has also limited explanatory power for certain types of variables. We cannot account for a large variety of cases and thus the conclusion of this study has to be carefully considered before being applied to other firms, other sectors or other countries.

In terms of variety of cases, the replication design (explained in Chapter 3 section 2.1.1) gives us the opportunity to study the complexity of the evolution of an innovation project together with the early evolution of start-ups, which limits the variety of cases we can study. Thus as explained above, firstly we observe in our sample a lack of firms financed through a venture capitalist financiers. Thus in this case the process of firm formation and the definition of firm strategy are different. However, some literature has already tackled the influence of venture capitalists on firms (Gompers & Lerner 2001). The conclusion also concerns mainly the biotechnology firms and cases from other industries should be considered in order to see if the results could be replicated elsewhere. While the biotechnology sector contains extreme cases of firm creation built on drug discovery projects, which are highly risky and are thus specific to this sector, the study of biotech firms that have a less risky initial project gave us the possibility to nuance our results. The results would then be potentially replicable in other knowledge intensive sectors, in which academic entrepreneurship would play a role. We associate the results with sectors in which the technologies developed require high technical competences, and thus the recognition of opportunity requires technical knowledge while the exploitation requires knowledge about specific industries and is done by private organisations such as companies. These sectors are therefore the most likely to convey surrogate entrepreneurship. Thus the conclusions should be tested in other knowledge-based industries in order to ensure the validity of the process.

In terms of generalisation, the fact that we have focused on one cluster has made our cases biased towards the cluster's history. We believe that the specific characteristics of the cluster can have an influence on the choice over the strategy of the firm. In our cases, and returning to the characteristics of the cluster explained in the previous chapter (Chapter 4), some firm leaders had faced unemployment and as a result this influenced their preferences towards firm activities that are less risky. In other case studies, such as the one done in the Silicon Valley in the 1990s, risky entrepreneurship seems less of an issue for many entrepreneurs because the employment market in semiconductors was very high in that environment. Some authors described the culture there as valuing job change. As one of the interviewees in the study of Saxenian (1996, pp.54–55) explained:

"If they are fired or leave here [in the Silicon Valley] it doesn't mean very much. They just go off and do something else..."

Thus the preferences of the entrepreneur may also be affected by the regional setting in which his firm evolves, since this may influence how he assesses the risk of taking up a new venture. Therefore, such type of study should also be replicated in other regions in order to test the results in other settings.

6. Conclusions

This chapter has highlighted several contributions to the literature. The chapter specifically aimed at understanding the role of involving a surrogate entrepreneur to exploit the opportunity, and the consequences of this change over the firm strategy. On a theoretical side, the chapter introduced the notion of preferences for the entrepreneur, and attempted to link the background of the entrepreneur, in terms of culture and experience, to his preferences. On an empirical side, the study tested these propositions but also explored three further issues. Firstly, it has explored the process by which a new venture defines its long term goal. Secondly, it focused on what defines individual entrepreneurs' preferences and how those preferences ultimately influence the goal setting of the new venture. The study has shown the link between founders' past experience, which influences their preferences, and the goal settings of the firm. The entrepreneurs have preferences depending on their wealth, personal goals and characteristics. Finally, the chapter also studies the impact of a change of leadership, on the firm's strategy and early life development. This influences their vision and also their choice of business strategy.

As the literature review emphasised, the genesis of a firm creation involves organisational processes that have a direct impact on the general strategy of the firm. It explained through different mechanisms how the initial aim of a company before creation (such as the development of a scientific project) can be transformed to a potentially different objective through the creation process. Two sub-processes have been identified, which are the team formation process and the definition of the firm strategy, where this second process is the central focus of this paper. Given the changes that occur during the team formation process, the result section focuses on the influence of the preferences of the leader and the impact of exogenous shocks on the strategy setting of the firm. The first part of our results has shown that the strategy setting of the firm is not always aligned with the initial trigger for starting the firm (here the development of a scientific project). The results have confirmed that a change in leadership can have a significant impact on the strategy setting of a company. The second part of the results has also shown that exogenous shocks can have a significant impact on the strategy setting of a company. In both of our cases, events related to the exogenous events of the firm have changed and has therefore forced the firms to readapt their objectives. These changes can then lead to other organisational disturbances.

The paper has also shown how the project and firm development can be simultaneously interlinked but distinct. As it is true for most of our cases, the firm creation was a direct step in the project development process. The organisational process behind firm creation, through a change in the founding team, makes the firm a distinct organisational entity from the project. In the two cases described in the last section (section 4.2) of the results, the two organisational entities (i.e. the firm and the project) became stand-alone entities (in the first case through the separation of the company and the project, where the project spun-out from another company creation, and in the second case where the project had to be abandoned). This chapter has therefore shown that organisational processes behind firm creation involve evolution of two distinct processes; the project development and the firm development.

Regarding the **choice** of the firm's **goals,** the results have shown that the **background and experience of the founders matters** in many ways. The first significant factor that influences the entrepreneur's goal preferences is his background. Founders with a scientific background tend to push their invention regardless of the risk, while founders with a business or industry background are much more sensitive to the risk and time to market involved in the invention when it comes to the main goal setting for the firm. This can also be due to the fact that the scientific founders are the inventors of the products that were meant for development in the newly created organisation. Concerning founders with business or industry backgrounds, their view of the goals of the firm seems to be dependent on the level of risk and term to completion of the project. When the product has a relative short time to market period and the business leader can raise sufficient funds for the project completion, they focus principally on the project. If the project is on a longer time span and the manager joins at the founding stage of the firm creation, the business founder tends to expand the firm's offer by adding services that have a shorter time to market and provides the opportunity to have cash flow earlier in the life of the firm. This behaviour can be highlighted with a specific experience of the founders. Founders who have faced unemployment are more inclined to have a secure business model and therefore favour the survival of the firm before any particular projects. Personal experience therefore has an influence on the entrepreneur's view of the function of the firm. In terms of **entrepreneurial agency**, this shows that the decision and the action of the entrepreneur are not entirely free of choice, since they are influenced by the entrepreneur's background and previous experience. These conclusions can differ when taking into account the type of financing used by the entrepreneur. Venture capitalist financing reduces the control over which the founding team defines their organisational goals, and thus may not provide the option of a service oriented business model. Founders with scientific experience see the firm as a means to complete long term projects that cannot be completed within a research institution. The business founder in our case focused firstly on the viability and market interaction of the firm before focusing on the project. A project with short term results would therefore be of greater interest for them because market feedback would be in sight.

These findings contrast with the neoclassical view of the entrepreneur. In these theories the entrepreneur seeks profit maximisation. He takes responsibility and risks that other agents are not willing to take. The paper has shown that this view may not be adequate for understanding the firm early development. This paper argues that entrepreneurs have preferences like any other economic agent and that these preferences influence the goals of the firm and may ultimately their ability to survive (high risk with high profits vs low risk with a higher chance of survival).

Chapter 6: From science to industry: the involvement of university in academic spin-off formation

Abstract

Universities have evolved in terms of their functions in the economy. Nowadays they increasingly have a direct function in the economy through their role of technology transfer. In this paper we look at a specific aspect of technology transfer, the process of firm formation from an innovation project started by scientists at university. This paper therefore aims at looking at the process of firm formation from universities. The paper identifies steps and characteristics by which the scientific project emerges from universities and transforms into a firm creation project. The paper also focuses on the organisational challenges that arise in this process, including a potential change of management or organisational problems arising when a firm is still being incubated in a parent organisation. Thus the chapter also looks at the contribution in terms of organisational arrangements of the transfer of a scientific project from a university to a newly created firm, and how these arrangements evolve over time. This research will be based on a multiple case analysis in the biotechnology sector. A set of nine biotechnology firms, which are spinouts of public research institutions in the Alsace Biovalley cluster, are used in order to identify those steps and their characteristics.

1. Introduction

In recent years studies have shown the potential economic benefits that research centres can bring (Bercovitz & Feldman 2006; Markusen 1996) through knowledge transfer. There might be several ways to transfer technologies and products developed at university, such as licensing patents, start-up creation or even collaborative research. This transfer can take the form of start-ups, with scientists getting involved in firms (Zucker et al. 2002), or just the movement of labour that helps transmission of relevant knowledge (Saxenian 1996). However, spin-off formation may be the most efficient option for transfer since it can involve transfer of tacit knowledge at the same time and outside firms may also be unwilling to take the risk of exploitation if the invention is too early in its development stage (Shane 2004; Thursby et al. 2001). Academic entrepreneurship is known to benefit the local economic environment and enhance technology transfer (Shane 2004). Even though transfer through academic spin-offs seems the best solution for transferring technology efficiently, little is known about the process of firm creation based on a university project or how the transition of the project between an academic organisation and an emerging company can be brought about successfully.

In the United States there have been specific measures with the aim of engaging universities in firm formation including the Bayh-Dole Act (1980) (which grants universities property rights over publicly funded research). This assignment of property rights provides a basis for capitalising start-ups (Slaughter & Rhoades 1996). Whilst US universities previously mostly aimed at producing knowledge as a public good, and particularly with Federal grants support, they are now expected to make contributions of an entrepreneurial nature (Etzkowitz 2003; Clark 1998).

Since start-up companies have few resources, at least during the start-up phase (before finding financing resources, assuming they do), research efforts may be limited. Universities can then intervene to contribute to the start-up effort in different ways; by providing innovative research results that requires transformation to get to the market place but also support the newly created company by providing physical resources. Thus, in addition to providing knowledge inputs, universities may also provide some help in the way the research is conducted. The university can help start-ups in different ways: on the research side and also on the facilities and equipment side due to the shortage of financial resources for the firm to buy the required equipment (Tornatzky et al. 1995; Shane 2004). Thus the equipment and facilities can be used by the newly created firms with reasonable price. Universities contribute to firm creation through their scientists and through any resources they provide. However, it is still unclear what varieties of patterns exist in the ways in which the two organisations manage the project transition between them in terms of resources, and whether those arrangements evolve during the early life of the company.

This issue can be examined by asking how the research projects started at a university transition into being taken over by a newly created organisation. The chapter also looks at the role that the university takes in the development of both the research project and the newly created organisation. The chapter therefore looks at the co-evolution of both the process of development of a research project and the firm creation process. The main concern motivating this study is: ***How does the firm relationship (through its founders) with university evolve over the stages of company creation? What resources are made available to them? Do relationships between the university and university spin-offs vary with the structure of the creation team?*** This paper will look at how the relationship between the university and its spin-off company evolves over time in terms of the benefit offered by the universities.

In order to answer this question, this paper grounds its focus in a first section on the evolution of a research project towards the decision of firm creation, while emphasising the opportunities offered by the university and the relationship between the two organisations during this process. The second part of the paper presents the methodology. The study builds on case studies in the biotechnology sector from the Alsace region in France. It will develop nine cases of firm creation that emerged from academic research projects. The third part draws on these cases to explain that a firm needs the university not only at the beginning of their project for the production of new knowledge, but also that the university has an evolving role in the firm during the various stages of development. The university has not only a role of knowledge transfer, but also gives crucial support through facilities and labour to start-up firms. The results emphasise that opportunities to the newly created firms differ with their relationship with the parent university. This leads to the final part of the paper featuring a summary and concluding comments.

2. Theoretical background

As the economic geography literature emphasises, the diffusion of knowledge is mainly regional (Audretsch & Feldman 1996) and flows from knowledge organisations. Universities are one of the knowledge organisations known to have an influence on local knowledge diffusion (Markusen 1996). The centrality of academia varies depending on the sector. In the specific case of biotechnology, academia is at the forefront of technological development (Cavazzana-Calvo and Debiais, 2011; Pisano, 2006b). Direct channels have been identified between universities and firms through co-publication networks (Owen-Smith & Powell 2004), and through the participation of renowned scientist in firms (Zucker et al. 2002). In recent years this has led to a more active role played by universities in industrial policies, which has resulted in them pushing for technology transfer and looking at its activity in terms of economic impact.

However, it is still unclear how the university contributes to the firm's innovation journey besides the scientific inputs (e.g. star scientists and sharing research results). Thus the aim of this chapter is to understand the transition by which a research project goes from being conducted by researchers in a university laboratory to being developed into a newly created company, which we refer as university spin-offs. The chapter focuses on two levels, which are the organisation (transition between a parent organisation and a newly created firm) and the development of a research project. These two levels will be tackled in the literature review. Firstly, in order to understand problems arising during the transition between research lead by universities and research pursued in the private sector, one must explain how the different organisations work.

Therefore the section starts with an overview of university policies and an overview of how research has evolved in the academic world. It continues with the differences one can expect between universities as a research organisation and companies involved in research. Secondly, after looking at the organisational differences, the paper focuses on building a process view of spin-offs led by the continuity of the research project from academia to the company. This part aims at finding a framework from which we can study interactions around the innovation project between the parent organisation and the newly created company later in the paper. This is done by integrating two literatures: the first on firm creation to highlight organisational processes and the second on innovation models to understand the evolution process of an innovative project.

2.1. The evolving role of universities

This section offers a view of the differences between basic research, applied research and industrial research and their link to technology. We discuss how the university knowledge production has evolved over time, and ask the question about the boundaries or possible overlap of these concepts in the contemporary world. The section looks into the types of research done at universities and how university research has become closer to the application of knowledge and to industrial research. This begins with a discussion about the change of policies regarding the role of universities in economic development.

Universities policy. University have evolved since the Second World War from a research and teaching institution to an entrepreneurial institution that can be an asset for the regional industrial policy (Etzkowitz & Leydesdorff 2000). In the 1990s regional studies shed light on phenomena linking knowledge diffusion and geographical proximity. Regional studies (Saxenian 1996) have emphasised competitiveness building in high technologies within specific regions. Competitiveness is believed to be regional (Porter 1998) since knowledge diffusion spreads unevenly over geographical dimensions. While knowledge diffusion may constitute a spillover (Audretsch & Feldman 1996), these spillovers may be confined to a geographically bounded area because of the tacit components of knowledge that are more effectively transmitted by face to face interactions or because codification of knowledge is incomplete and costly relative to interpersonal communication. The competitiveness of regions, especially in high-tech sectors, are believed to rely on knowledge providers such as public research centres or universities (Markusen 1996; Etzkowitz & Leydesdorff 2000) among other reasons. Following this observation, policy makers aimed at enhancing this competitiveness through the promotion of knowledge institutions and aimed at making universities a central part of the economic system. This promotion was done through policies at different levels, such as first regulatory policies (i.e. Bayh-Dole-Act), regional policies (i.e. cluster policies, science parks), and individual policies (support of university entrepreneurship- spin-off creation). All these different policies aimed at reinforcing the position of universities as a knowledge provider, and to make them part of the economical system through the facilitation and the incitation of universities to interact with the private sector[109]. This policy guidance has also altered the types of research done at universities towards closer links with the industry through technology transfer programming. This has been in-line with an increasing willingness, on the policy side, to see its public research organisation contribute to the competitiveness and growth of their country. University policies have changed throughout the years and now have a culture alternating between praising the support of public science (Bush 1945; Nelson 1959; Arrow 1962) for providing public knowledge, and praising the applied research within the universities with clear objectives and contributions to competitiveness (Slaughter & Rhoades 1996). Nowadays, with the emergence of universities used as a stakeholder in the innovation process, funding policies influence science towards problem oriented research (Calvert 2006), and thus applied research. The argument suggests that the universities have to move towards a competitiveness view. Thus we will remind ourselves of the concepts of basic and applied research and discuss their use in the industry.

From science to technology. The distinction between science and technology has been discussed in the early literature with the distinction between research done at universities and R&D conducted in the industry. This gave rise, in early days, to a distinction between basic research and applied research and development, which separates the research activities between universities (basic research and application) and industry (development). However, the distinction between research performed at university and research performed in the industry is not always clear. Before starting any discussion about knowledge transfer relying on research, it is required to remind ourselves about the literature differentiating types of research and also links and differences between types of research performed at universities and in the industry.

In the earliest literature, and especially before the Second World War, most university research programs were oriented towards basic research (Godin 2006). This type of research was characterised by having no objectives for application. Over the past 30 years, the universities have been gradually transformed from institutions performing basic research to entrepreneurial facilities that foster technology transfer (Geiger 2004; Etzkowitz 2003b; Godin & Gingras 2000). This has given rise to the changing function of universities and the activities performed there. This is reflected in recent contributions (Godin 2006; Kline 1995) by the distinction between basic and applied science. One of its distinctive elements is the motivation of the researcher, which is for a specific goal rather

[109] A later sub-section within this section explains more in depth the change in university activities which are partly induced by these policies.

than knowledge generation. If the motivation is the application of science in the industrial world, then the research would be considered applied. Thus fundamental science is increasingly encountering a push towards application, which is basic research but with concrete objectives in mind that are often related to as the Pasteur quadrant (Stokes 1997). The Pasteur Quadrant differentiates basic research from applied research within two dimensions: firstly the objective of fundamental understanding and secondly the consideration of use. This causes a third category to emerge, which is the use-inspired basic research that corresponds, for example, to Pasteur's research with his study of fermentation which had a practical and theoretical impact. This shows that the frontier between basic and applied research is fuzzy, and the consideration of use motivation and fundamental knowledge generation are not exclusive objectives.

Applied research has also been associated with the engineering sciences that is also increasingly performed at universities in several research fields (for example chemistry or thermodynamics) (Kline 1995). Thus the boundary between applied research and basic research is also blurred by the fact that it no longer reflects the division between research carried out at universities and in the industry. The blurring of this boundary also indicates that science is not isolated from technology, but that there are links between science and the industrial world. Different types of links can be identified. The Pasteur Quadrant indicates a motivational link between science and technology, such as fundamental research that is led by the application and use of the technology (like Pasteur and his study of fermentation). Other literature emphasises this link between science and technology with specific references in the history of science. For instance Kline and Rosenberg (1986) explain that when innovating some entrepreneurs call on science and its knowledge generation ability, which was the case for Edison. In order to develop his technology, Edison was drawn into hiring mathematicians in order to pursue research about the mathematical analysis of parallel circuits in electricity. This work led to the creation of a new mathematical mode of analysis. Thus the authors concluded that science is not isolated from the industrial world but also "the demands of innovation often force the creation of science". This observation led them to develop an interactive model of innovation, which is discussed later in this chapter (section 2.3). Likewise, Galison (2004) emphasised in his work the influence of Einstein's work at the patent office on the development of his theory. For instance, in his daily work at the patent office, Einstein reviewed many patents concerning innovation towards the improvement of clock accuracy. This part of his work became useful when formalising some papers about relativity theory in which he made references to train travel, which was a subject often discussed in patent applications at the time. Thus one cannot consider scientific projects, even during their early development, as completely independent from the industrial world.

While science can be seen as increasingly close to the technological world in terms of the inspiration on problems to work on, the link between science and technology has also become closer in terms of output. As a general trend, university has become increasingly active in the production of knowledge applicable to industries. This can be observed through the increase of the patenting activities of universities. Mowery and Sampat (2005) have pointed out the growing activity of US universities towards patenting activities, especially since the 1970s. This trend also fails to show a significant change since the introduction of the Bayh-Dole Act. This paper also shows that the contribution of universities directly affects the biotechnology sector more than any other sector. In this specific sector, the university research results are closer to industrial application than in any other sector (ibid.). We can also observe a technological bias in the university spin-off formation across sectors, with a large predominance of firms that have activities in biotech, software and medical devices (Shane 2004). It therefore appears that universities today are increasingly drawn to be active in the industrial world, depending on the sector. So can we consider the research in the world of science and the world of technology to also be increasingly similar?

Towards a convergence between science and technology? With the increasing push for scientists to be involved in value creation and knowledge transfer with policy and regulation change, practices have also changed in the academic community with an evolution towards a dual knowledge production. The academic production can be oriented towards two communities, both the scientific community through publications and the technological community through patenting. Through their literature review on academic patenting, Foray and Lissoni (2010) pointed to the increasing activity of academics in industrial outputs, which is seen as a by-product of their work. The authors advocate for these industrial outputs to hold a higher value in the scientific community in order to reduce the personal costs of the researchers to get involved in such activities. Carraz (2011) also showed that academics can adapt their research strategy in order to build a reputation both in the scientific and technological community, which he refers to as a hybridisation strategy. In practice, academic researchers have an increasing joint activity in terms of scientific as well as technological output, which increases the difficulty to differentiate between the basic vs. applied research classifications.

Another view to differentiate science from technology was developed in the new economics of science by Dasgupta and David (1994). This view does not differentiate the two institutions by their scientific activities but by the behaviours and norms developed by people from the two different communities. Science's main incentive is to achieve 'priority". A first scientific incentive system involves establishing this priority through the publication of new scientific findings. However, another incentive system exists in science in which researchers seek appropriation in order to be able to seek potential financial gain from discovery. This view of the academic community was introduced by Merton (1979), which describes the scientist to be within a community with institutional norms and who is creating public knowledge under a cooperative character. These norms described by Merton have stemmed into the concept of Open Science, where new knowledge can be considered as public and thus in opposition to private organisations that keep part of their knowledge closed in order for them to generate rent (David 1998). Hence, in this literature the difference is rather seen as cultural differences between communities that may have an impact when transferring a project from an academic environment to a privately owned firm.

The question therefore remains regarding the differentiation between research conducted by universities and research conducted in the industrial world. The line between both institutions has become hazy over time with the development of engineering sciences and industrial objectives; there have also been increasing interactions between universities and industry.

The links between industry and universities have become stronger over time especially in some specific sectors that have relevance in the industrial world (this is the case of many engineering sciences, or software, electronics or biotechnology). There has also been the evidence of indirect links between science and industry through the concept of spillovers and through labour movements (Saxenian 1996). The section has emphasised a difference in culture between the two institutions. One can ask if these differences may have an impact on the relationship between the two institutions? Finally, even though the interactions between both institutions are increasing, should we assume that research in these organisations is similar?

2.2. Public research constraint vs. private research constraint

Even if universities come closer to applied research and thus research done by the industry, we argue that some boundaries between universities and industry still need to be overcome. If the research remains somehow dissimilar, the question on the similarities of organisation and management must also be tackled to understand how a firm can reorganise from a university based project to an applied project that is able to be carried out by a private organisation.

Even though universities are increasingly pushed towards getting involved in technology transfer through commercialisation of their research, only a minority of researchers engage in this type of activity (D’Este & Perkmann 2011). One reason for such low involvement may be due to the incentive structure of many universities that does not favour such activities (Foray & Lissoni 2010), therefore commercialisation of research remains a secondary activity for researchers in universities.

If this is the case, the incentive structure together with limited interaction between both institutions may lead to cultural differences between universities and private research institutions.

Because universities and public research institutions are specialised in the scientific discovery or can be involved in the development of new technologies, the development part carried out by companies, here new ventures, have different characteristics in terms of R&D work. Companies carry out (not exclusively[110]) the development and commercialisation part emerging from opportunity discovery. Even as exploratory research, this part is also uncertain towards its outcomes; and the process is constraint by many variables in terms of planning. One of the main problems for firms in innovating and developing new technologies lies in the uncertainty coming from market and technologies (Kline & Rosenberg 1986). Technologies are uncertain regarding their development time and the practicalities needed to make the technology reliable in order to be able to meet production standards. Market also bears uncertainty through the evolving needs and standards users require, but also through competition.

Thus, even if it is necessary for a company to improve its technical performance this must be balanced against the economic usefulness of the project; since the health of such an organisation is at stake if economic performance is not met (Kline & Rosenberg 1986). As Mansfield (Mansfield et al. 1972) showed, managers in large R&D companies, and also R&D workers, are unable to accurately predict the technical and commercial outcomes of their projects, and usually overestimate economic return of their potential innovation and underestimate the development time. Thus this is one of the main differences between a public research organisation (including universities) and a private company involved in research activities, as public research organisations have fewer problems in maintaining themselves than private companies. The differences of culture can create tension and difficulties for university-industry relationships. In their paper, Cyert and Goodman (1997) identify points of culture that can differ between companies and university. The first factor can be identified as the notion of time, which for a company is usually translated into quarterly goals. As for research projects or research papers in science, deadlines may be less of an issue (Cyert & Goodman 1997). In private organisations that involve R&D activities, estimation costs, time to market, potential return and final product performance are all important factors to consider when planning of research projects (Smith & Reinertsen 1991). These variables are important for private firms and influence them in their decision of R&D investments but they must also engage in planning these activities, especially when it concerns small companies with a limited R&D budget. In the same way, performance evaluation differs between university scientists and managers. While

[110] Some companies can also have activities in more exploratory or 'basic' research.

the first are evaluated through the recognition of peers, managers are evaluated based on their hierarchy through the appraisal of their success in their tasks (Cyert & Goodman 1997). Thus these cultural differences can affect the possibility of them to successfully work together.

The constraints in firm development lie in the fact that at creation the founding team must have knowledge about development and commercialisation of products, which usually the academic entrepreneur lacks (Franklin et al. 2001) both in terms of personal experience and social capital (Mustar et al. 2006; Mosey & Wright 2007). Thus the search, composition and building of an adequate founding team are critical in the future ability of the entrepreneur to develop and commercialise their project.

Since the research and development path must transition between institutions with different goals and needs, how does this transition occur in the spin-out process?

2.3. Towards a model of university spin-off creation

In order to understand the process of creation for spin-off companies, this section uses different literature to build a model of firm creation. This model will be used as a conceptual framework to understand the firm creation process from a university innovative project developed around a discovery, invention or new technology. The literature used for creating this model comes from entrepreneurship literature with a stage view of firm creation, innovation studies with the model of innovation concepts and finally literature regarding technology transfer. These processes have already been presented and discussed in Chapter 1 (section 6.2), and consequently this section only discusses their possible contribution towards a model of project transition from a parent organisation to a newly created organisation. These processes are discussed in terms of issues raised concerning transition and differences between a university and a company.

Models of innovation. The idea that universities have a role to play in the industry and local development has emerged since the second world war and has been adopted by a number of countries since (Rothwell & Dodgson 1992). The idea of universities being prominent actors in the innovation process was put forward by Bush in his report (1945). Since then the industrialist and innovation literature used this work to introduce the innovation models (Godin 2006). The science push linear model of innovation gives some sequential steps to answer this question, and is still relevant in the discussion of technology transfer because in many technologies, and particularly in biotechnology, industries have emerged from a science push dynamic. The model evolves as follows: Basic research > Applied research > Development > Production > Diffusion. As discussed in the earlier section, the model hypothesises a chronological sequence between the steps, while research is consigned to the beginning of the model. While it succeeds in separating the research phase from the development and diffusion phase, this model has its limits for understanding the process of transfer since the organisational step is omitted. This model has been heavily criticised for not taking into account feedback loops from research institutions and the market knowledge during development phases. Later contributions (Kline & Rosenberg, 1986) therefore emphasised the role of research and market sensibility contributions at every step in the model but also feedback loops between steps. Innovation models inform us on the role of research in the innovation process, which is useful at each stage. Thus the innovation models that were developed are informative for our purpose in terms of project development. Models of innovation represent stages of activities that are carried out in the innovation process, but they do not focus on the organisation(s) carrying them out, which is the main interest of our research. Thus the information gathered in this model must be completed with models that focus more on the organisational settings in which innovation takes place. Thus we refer also to organisational and entrepreneurship literature to investigate this issue.

Entrepreneurship processes. In the literature there have also been contributions looking at each side of the technology transfer process separately (e.g. University side and company side). In order to build our framework of innovative project transition through spin-off creation, these two aspects must be combined. Shane (2004) for instance describes a stage model to understand technology transfer of projects originating from university and developing into a spin-off firm. This process includes 5 steps: research, invention, seeking Intellectual property, marketing the technology and finally transferring the project through licensing or firm creation (shown in Figure 1.6 in Chapter 1). This process is somehow similar to the linear model of innovation emerging from Bush's work, but includes more specific activities relating to technology transfer activities such as seeking intellectual property and licensing. In other words, the model of innovation is a good basis for understanding the development of an innovative project, and adds to it in terms of steps taken for technology transfer. In this work Shane also characterised the firm formation process but he characterised it through a product development process (such as proof of principle product development and market interactions), in a similar way to the above model. This representation of the transition project is solely focused on the technical side of the innovative project development and does not shed any light on how the organisational process behind the firm creation is triggered, how it evolves with the project or the problems that arise from firstly the organisation of the firm and secondly from transition of the innovation project. The entrepreneurship processes described above uses the characteristic of the entrepreneur as an explanatory variable for the evolution through the stage process. For instance, the exploitation decision is central in entrepreneurship theory and often characterised by the background of the entrepreneur and his psychological characteristics. Thus the entrepreneurship literature has shown that a certain type of economic agent can be more inclined to become an entrepreneur than others due to their career experience, marital status, income level or due to their personality (e.g. such as extraversion, aspirations or risk attitude) (Shane 2003).

From a firm creation perspective, there have been various contributions towards a stage development of new companies. The sequences that can be found in the literature are usually based around the same model, of which we will give some examples. The first is explained by (Katz & Gartner 1988) and follows the path: intention of creation -> creation -> assembling resources -> development -> exchange of resources. Shane (2003) in his general theory of entrepreneurship has a similar stage model, but introduces the discovery of opportunity at the beginning of his model. The entrepreneurial opportunity is often linked to a combination or recombination of resources where the entrepreneur believes there is a profit (Shane 2003). Shane's model here is divided between two main components, the first one dealing with the discovery and exploitation of an opportunity and a second part that includes an organisational dimension through resource acquisition, entrepreneurial strategy definition and an organising process stage. While these theories include an organisational side in their stage model, the stages themselves are too general to address specific issues that could explain difficulties that can arise in the creation process, and subsequently to understand the transition of an innovative project.

As these models show, the entrepreneurs impact on the course of the firm's evolution through their characteristics and their agency power. This element has therefore to be considered in our stage model (since it has already been considered in the earlier chapter). However, both of these models have little to say about the organisational challenges that the firm faces at its creation. The last model also fails to make the link between the opportunity exploitation and the organisational part of the model, which are treated successively, since our model is interested in the situation of overlap between these components.

Looking at the more organisational side, some authors have also focused on developing stage models. On the firm management side, Greiner (1997) has developed an evolutionary framework in which he identifies different growth stages of organisation balanced by crisis, in order pursue its evolution. This literature argues that the firm development follows a dialectic process and explains the different transition phases through the transition between different types of management. This model describes the firm from youth to maturity, but we are interested only in the early process of evolution. Thus, in our model only the first stage will be relevant. The first stage after creation is here described by the author as the creativity stage, which is characterised by a phase in which management in not yet well organised since the group working in the company is very small and is mainly working through informal communication when the work is mainly individual and focused on the technical aspects of the project. This phase ends with the growth in number of employees and of administrative tasks. At this point management skills are needed together with a leader for the organisation, and thus the firm needs formal structure through the new management put in place. This way of thinking about the development process highlights the evolving managerial needs, which we must also investigate in our model. However, the model described above was designed to be general and thus must be adapted to the particular investigation of knowledge based firms emerging from universities in particular, which may have specific founding characteristics as the previous chapter have emphasised.

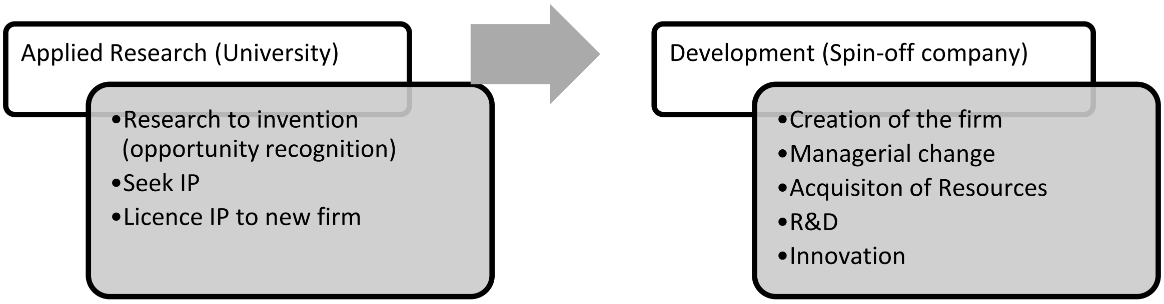
Another organisational model is put forward by Garnsey (1998), which describes the creation process in terms of access to resources as following: access to resources -> mobilise resources -> generate resources -> growth. This model is built on the resource base view of the firm developed by Penrose (1959) and considers tangible and intangible resources that influence the firm evolution and the firm growth. Looking at the first phases described in this model after start-ups, two types of resources are believed to have an impact on the firm's evolution, intangible and tangible resources. Intangible resources are manifested in the first stage of this model by the experience, knowledge, characteristics and resources that shape the early evolution of a firm. This model therefore links the factors described in the entrepreneurship theories. The entrepreneur in this model must also access physical resources (including financing) in order to develop his venture accordingly to his choice of activities. Therefore, in addition to the intangible resources, mainly provided by the entrepreneur, our model must also look at the physical resources needed in order to develop his activities. As Chapter 4 has explained, the strategy of the firm together with their choice of activities will define the firm's financial resource needs. However, the same chapter, in addition to Chapter 2, has also pointed towards the general need for initial financial resources for most of the firms in the biotech sector.

Finally, some stage models have been developed specifically around the concept of spin-off companies (Ndonzuau et al. 2002; Clarysse et al. 2005). Their representations are similar and integrate both of Shane's models (i.e. of university technology transfer and entrepreneurship). They describe a stage model as follows: Research -> Business Idea -> Business creation or invention -> transition -> innovation/ economic value. While emphasising the property right issues already talked about above, both of these models also emphasise the role of the university and its ability to help the firm with the use of university resources at creation and through providing human capital. While these models include different aspects of the resources needed at firm creation, they do not discuss how these phases are triggered and the evolving relationship with the parent organisation, which is one of the aims of this chapter.

The literature presented above focuses on long term processes in order to analyse one specific determinant on the firm evolution. Greiner's model explained the evolution of a firm through change in managerial organisation, Garnsey's model focused on the organisation of resources, innovation models on learning determinants and finally entrepreneurship models on the entrepreneur's ability to identify and exploit an opportunity. All of these processes have dealt separately with the innovative side (R&D project development) from the organisational side (firm creation), either because there were only focusing on one side of the project or because they considered that the organisational side followed the exploitation of opportunities and therefore the innovation project side. While the above models are useful in the understanding of innovation development or firm creation over a long period of time, they therefore lack a detailed and comprehensive view of smaller steps. This chapter instead aims at understanding a very specific step in spin-off formation while comprehending the various aspects tackled in each model. We therefore aim at understanding how a university spin-off is created, especially through the transition of a research project from university to a newly created firm. As the different literature above has tackled separately, this transition should include management evolution (which has already been investigated separately in Chapter 5), resources mobilisation and evolution of the innovation project.

Synthesis towards a stage view of spin-off creation. Combining the literature on innovation, university research for technology transfer and firm creation, we will construct a model of spin-off creation from university research. Two aspects of the creation are integrated into this model of project development, which is continuous and can be assimilated into the innovation model. It also integrates the aspect of organisational change and focuses on the transition of the innovative project between a university and a private (for profit) organisation. The study specifically focuses on this transition and therefore does not focus on the growth or performance of the firm after creation. The model includes different characteristics, some of which are performed by the university and some of which are performed by the firm, as explained in Figure 6.1.

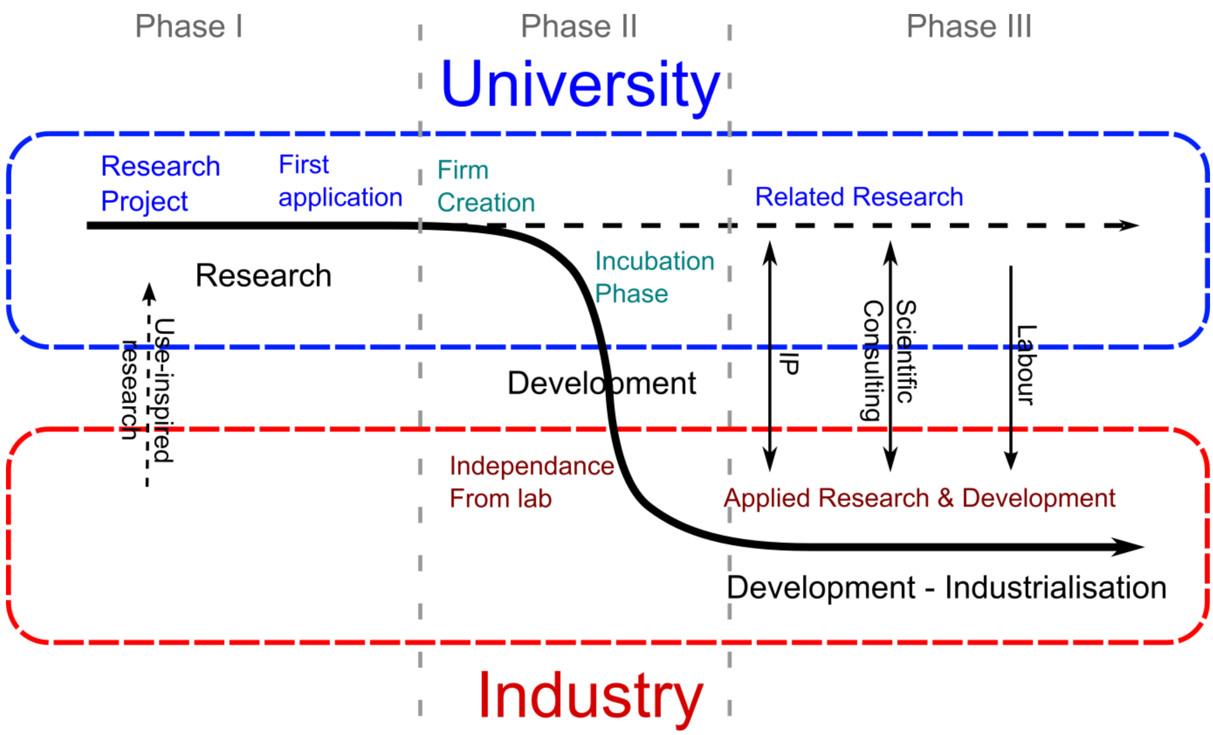
Figure 6.1: University spin-off creation process



The several models discussed above have analysed processes that have in some respects a relation to the transfer of innovative projects through firm creation. Through these contributions we have identified characteristics to be analysed in both the research done at university before transfer or the development of the innovative project after the transfer. These characteristics are presented in the Figure 6.1. In the model, the university contributes towards technology transfer to the firm by creating IP (Intellectual Property) before the firm creation and transferring it to its spin-offs when created. In order to be created the firm also needs to acquire resources in terms of human capital (human capital in terms of knowledge for commercialisation, and also technical knowledge related to firm development).

We aim at understanding the transition of a project started at university that is transferred to a newly created firm. To do so we divide the study into **three phases**: the phase before firm creation, the organisational phase of firm creation that also includes the transition of the research project between the two organisations, and finally the stage at which the firm becomes independent from the university in order to develop the research project. These phases are represented in Figure 6.2. One of the main objectives while characterising the phases is to understand the collaborative efforts between the two organisations (university and new firm) that make the transition of the project possible. Finally, we want to understand events that may trigger the transition between stages. In order to understand the interaction between the two organisations, the study looks at both tangible (e.g. need of physical resources to start the company) and intangible resources (through the knowledge and experience at a managerial level, but also in terms of human capital).

Figure 6.2: Innovative project evolution through university spin-off creation



While this representation of technology transfer may have a purpose of being used across sectors, we have to be careful about the extent of the generalisation of this process. It may be different according to scientific disciplines or industries of application. As the literature has noted, some scientific disciplines may be closer to application than others (e.g. software, biomedical research or other knowledge intensive sector), and the extent of the use of property rights and scientific consulting may also differ across sectors (Dalpé 2003). For example, the biotechnology sector has a much higher proportion of patenting activities in university than other sectors, and scientists also have a greater role in the creation of spin-offs through start scientists. Thus the model and the following results must be handled with care, since some of its features may differ across sectors.

Before going into the explanation of the phases inspired by the different models presented above, we want to first describe the points discussed in the theoretical background in terms of the relationship between universities and industries as organisations. During the early life of a research project the industry might on many occasions influence the scientific research, which can be the basis for the given research project under study. Through the different mission of the university, it can also contribute towards direct relationships with the industrial world in terms of transfer of property rights (such as patent licensing), through consulting activities with their scientific staff (e.g. through the participation of start scientists in firm committees) or through indirect means such as the skilled labour trained by university. Start-up companies may benefit from these different resources available from university over their early evolution. Figure 6.2 has already presented three phases of evolution and was constructed from the previous literature on stage models. These phases are constructed based on a theoretical hypothesis built from the literature, as described below.

To begin, the **phase before firm creation aims** at exploring the way public research projects transform into a firm creation project. Why would a researcher decide to go into a firm creation project? Chapter 5 has already emphasised the difference in academics' aspirations towards firm strategy, and we therefore hypothesise that the reasons for creation are linked with the willingness to develop and transfer research towards technological application. Even if the scientist's motivation for being involved in the development of a venture is known, the events triggering this step are often not known. Does the scientist spontaneously decide to get involve in firm creation? Why would he not opt for another technology transfer mechanisms?

After having clarified the reasons for the decision to create a company in the first stage, the study now focuses on the **practicality of the development of the new organisation, together with the transfer of the research project between organisations**. The project developed by a university researcher must then be transferred to the firm. It is therefore expected to include negotiations over the transfer of intangible assets (such as patents or industrial property) from the university to the newly created firm at that time. This negotiation may be accompanied by a transfer of tacit knowledge through collaborative work or the transfer of labour. As the literature suggests, the firms at the stage of resource acquisition may benefit from the parent organisation's help in terms of physical or human resources. However, even though one can argue towards the greater benefit of close relationships between science and industry, one might ask the question regarding the different incentive structures that exist in academia (open science culture) and the industry (proprietary technology), and how these different incentives may affect the transition of the project between the organisations.

The third stage represents the **firm after creation and project transfer**. Literature on the subject of university-industry relationships has highlighted that university may play an important role in a firm's life in terms of the different knowledge and technology transfer modes made available to firms. Literature on innovation models (Kline & Rosenberg 1986) has also highlighted the role of interactions with the need of knowledge inputs at different stages of development of a firm. Thus the university and the firm may keep a certain level of interaction between each other in order to ensure continuity when sourcing the relevant knowledge to further develop the innovation project in the newly created firm. The question remains regarding the specific contribution of the parent laboratory to the newly created firm, the remaining role of the scientist from the origin of the research project and whether there are other types of relationship that are developed with the university.

This description of the stages has shown that there are still some unclear points about this model that need enlightening. The first one concerns the point of decision for the firm creation. Why does a scientist decide to get involved in firm creation and why does he do so at a specific point in time?

The second unclear point concerns the practicality of the transfer of resources between two organisations, and the difficulties that emerge from this transfer. In theory, transfer of technology is paired with transfer of knowledge (Bozeman & others 2000). Thus in this stage view it is unclear how the transfer of knowledge is performed during the transfer of technology. It is unclear firstly how the needs of the firm evolves over time in terms of university resources; secondly it is unclear at what point in time and for what reason certain activities for technology transfer are pursued. Why and when should Intellectual property be discussed? Consulting pursued with scientific sources? Labour from university used?

The third unclear point lies in the research feedback loops at each stages, as mentioned in the interactive model of innovation (Kline & Rosenberg 1986). A question can also be asked about how the R&D is conducted in the firm, as R&D is still needed before profit for many high-tech firms especially in biotechnology (Oakey 1995). Is the need for research input homogeneous over time and over firm development?

This chapter aims to contribute towards these specific questions in order to primarily understand the evolution of an innovative project during the transition phase, with the transition being the change of incumbent organisation. This chapter also aims to understand the contribution of the university to the innovative project and the evolution of the interactions between the university and the newly created organisation.

3. Methodology

The research focuses on the role of a university in the process of firm creation. The study of a process model is more efficient through the use of qualitative data. This is because the qualitative research is more adapted to study a subject in a complex environment (Yin 1994). A detailed explanation for the reasons behind the choices and characteristics of our case study design is given in Chapter 3.

3.1. Research design

This study investigates nine[111] innovative university spin-offs in the biotech sector in the Alsace Biotech cluster known as BioValley, where projects have emerged from university research. The BioValley cluster has been chosen for its dynamism in terms of firm creation and technology transfer. The Biovalley is also a prime choice due to the strengths of its university. The University of Strasbourg has a long history of excellence in various fields of science, such as chemistry, pharmacy and biology (i.e. with several Nobel Prize winners in chemistry and biology)[112]. The strength of the university is reinforced by the variety of specialities within the biology and chemistry sciences developed. This strength could become a source of competitive advantage for firms that are evolving in the cluster, since the biotechnology sector exploits findings from a variety of scientific fields (See Chapter 2). The scientific resources are spread between many specialised institutes (e.g. molecular, sub-molecular, genetics, structural biology...) that bridge different disciplines such as physics, chemistry and biology (more information on the university has been given in Chapter 3 in the section 3.1). This gives the local university many advantages to produce high-quality research that could be a great source of innovation and technology transfer. This reinforces our choice of the BioValley due to the fact that the local university possesses strengths that could lead to important technology transfer projects.

For the choice of cases, local firms were firstly identified through databases of local firms, such as the incubator database, the chamber of commerce database and also with the help of the Alsace Biovalley organisation (which provided us with a list of active firms belonging to the cluster). It was then decided to interview young firms that were less than 6 years old at the time of the interview. This threshold was chosen so that the details, history of the company and problems encountered at creation could still be remembered in detail by the firms' founders. Thus among 21 firms contacted, 14 agreed to be interviewed. Among them, 9 firms were suitable following the criteria that the project had to be developed within university when it was last worked on prior to firm creation, and where a scientist working on that project was directly involved into the creation of the firm.

3.2. Data Gathering

For each firm, the founding team (including researchers involved in the development of the research project) and the current management team were identified. The data came from two main

[111] More information on the selection of the firms is given in chapter 3 section 4.
[112] This is developed much further in Chapter 2, with a more detailed history of sciences developed in university.

sources, the first being semi structured interviews with the members of the founding team, and the second being secondary sources of data acquired mainly from press releases.

When designing the interviews, the aim was to include two views whenever possible. These were the view of a person who had a business or industrial profile and the view of a scientific researcher who was involved in the research project that led to the firm creation. The choice of two people, especially for firms aged three years or more, made it possible to gather more data on the history of the firm in addition to applying the principle of triangulation.

The interviews of start-ups founders aimed at understanding the process of firm creation by emphasising different aspects relevant for this study, such as the conditions at the start of the scientific project and the development of this research project. It also focused on explaining how the research project transitioned to a firm creation project. It encouraged the respondents to take an event based approach. Five out of the nine cases included two interviews; the details of the number of interviews are given in the table below (Table 6.1). It was not possible to get two interviews for all of the firms because of the availability of founders at the time.

The semi-structured interview aimed at covering the story of the firm creation from the research project in the parent organisation to the firm creation and early development as shown in Figure 6.2, by explaining the different aspects of research including funding, collaboration, and property rights. The interview also aimed at discovering the way that the research is carried out in the university/ firm, and how the transition from being a university project to a firm project was achieved. The second part of the interview focused more on specific questions on patenting, publication, and collaboration activities of the firm.

Finally, the interview data was accompanied by secondary data, such as press releases, patents or publications. This provided the opportunity to triangulate data gathered from the interviews.

3.3. Data Analysis and operationalisation of the concepts

This research is designed on an inductive basis, in order to help understand patterns emerging from the transition of a project between a parent organisation (here a university) and a newly created firm. The main unit of analysis is the research project, which is embedded into an additional organisational unit (parent organisation and newly created company).

In order to find common patterns, the interview summaries were read repeatedly, while sometimes returning to the recordings in order to have an in-depth understanding of each case. The understanding of the project was a central point of focus, such as the starting date and the human capital on which the project emerged and developed. The interview also focused on the newly created organisation as a unit of analysis, which included a discussion about the creation phase, and the insertion of the project in this newly created organisation.

The interview process also aimed at identifying critical points or challenges that a newly created firm goes through, which can affect the decision process. The approach adopted here is inductive; however it also compares with existing theories of technology transfer and innovation for finding common grounds to the problems and attempts to deepen the understanding of the practicality of scientific and technological transfer through start-up creation.

The findings about the projects and newly created firms are related to the above presented three stage model (Figure 6.2). This model is discussed in the light of our cases to characterise the three stages based on their similarity and contrasting elements or steps. It tries to understand the rationale behind the transition between the different stages, and explain overall variations by categorising each project by the level of social proximity the researcher has with its parent organisation.

Table 6.1: Description of the firms

Firm	Creation Year	Number of respondents
Alpha	March 2011	2
Beta	Oct. 2008	2
Phytodia	2006	2
Kappa	Dec. 2010	2
Biomica	Jan. 2009	1
Cell Prothera	Apr. 2008	1
Anagenesis	Apr. 2011	2
Bionext	Apr. 2009	1
Alsachim	2005	1

The results are based on the interviews described above and will be exploited in two ways, which are the quotations and operational variables shown in tables. The quotations aim at illustrating points made in the section. They are extracted from recordings made during the interview and are translated into English. The variables used in the various tables in the results they are also drawn from the interviews. Some of the variables did not need any transformation in order to be compared to other cases, such as year of creation of the firm. For the other variables we will explain here their general meaning and also how they were constructed (if it is not straight forward). Four types of variable are used throughout the study. Firstly, we use some variables relating to time in the project in order to give an idea about the timing of particular events, which gives us the possibility to better study the evolution. A second type of variable includes descriptive variables about the project and firm creation. A third type of variable constitutes assets held by the management team, mainly in terms of competences that may have an effect on the early evolution of the project and the firm. Finally, the last type of variable concerns the labour used in the firm over time.

<u>Time variables</u>

Firstly, we use different indicators of time or period, which were not subject to interpretation but may benefit from further explanation.

The *year of start of the scientific project* is relative to the year given when the researcher actively decided to develop the research project, which would later lead to firm creation and the consequent dedication of resources and time towards that project.

The *firm creation project idea* relates to the time at which the scientist at the origin of the project knew that his research would not be developed any more in academia and decided that going towards firm creation was the way to pursue the research project. In the data some firms did not continuously pursue the project over the year and so the research project was put on hold for a certain period of time since there was no financial or human resources allocated to it. This is only the case for three firms: firm *Alpha*, firm *Beta* and Alsachim.

In terms of dates, the study also includes the year in which university or firms received patents for their projects, in the section *patents*, and can also include some comments such as for instance in the case of Biomica that the first discovery on which the innovation is based could not be patented as it was published in a scientific journal. In another case there is an absence of patents because the firm prefers to keep secrecy around their technology. On a more general note, the patents are mainly owned by the universities that developed the project in the first place, while others are jointly owned between the firms and the university. However, at firm creation firms negotiate the terms of use for these patents, which usually results in an exclusivity of use.

The last variable referring to a date concerns the *move year* and represents the year in which the firm moved from its parent organisation, or in some cases the year the founder made a concrete plan to move to a new location. In some of the cases there have been no mentions of any moves and thus the variable then states “not planned”.

Variables about the firm and the project

Aim of the scientific project: This header aims at explaining in a few words the objective of the scientific project in order to give a reminder to the reader about the research project but also the market in which this project is aimed. This has been drawn from the interviews given by the entrepreneur when asking them for the description of the initial scientific project at the origin of the company.

Project progress within University: This header aims at giving more information about the activity in the parent organisation towards the firm project (carried out before firm creation). It gathers information about grants or collaborative projects with some basic explanation of the activities linked to the project, when this information is available. This information is based on the interviews when asking about the financing and development of the project before firm creation.

Reasons for firm Creation: This header aims at comparing the reasons given by the interviewee regarding why firm creation was chosen. As many interviewees suggested, there were two reasons that were predominant, which were the limits of the financing in university and the potential application and social benefit of the discovery (which can also be affiliated with technology transfer). This information was collected during the interviews when discussing the history of the research project and the reasons for it to transform into firm creation.

Incubation: This variable aims at giving the first company location after firm creation. For most of the firms we mention that the new ventures were located in the same laboratory as the research project was, while two other companies were located elsewhere. In these cases there is a short mention of where the firms started their operations.

Variables about the management team and leadership

Scientist experience in start-up creation: This header aims at identifying the lead scientist experience in firm creation. This was achieved by asking about the career of each founding team member. If none of the scientific founders were involved in the set up of a previous company, the column will mention it. If this is not the case then, there will be a mention of this type of experience held by any co-founder involved in the management team in order to enlighten the reader about the set of competences available in the company.

Same scientific leader: This mentions whether there is a change of leadership between the research project development within university and the firm creation project. This information is binary and the affirmative means that both the initial project (before firm creation) and the start-up have the same person who makes the decisions about the general orientation.

Background of the leader: This variable concerns the background of the company leader and was collected through the response of the firm leaders about their previous employment and experience. This variable was divided into three categories: science, industry and business. This shows the main domain of professional experience of the firm leader. A mention of science concerns the leaders that did most of their career in public research up to the point of the firm creation. A mention of business includes the people that had experience in firm creation in their professional career but are specialised in areas unrelated to the technologies developed in their current creation project. Finally, a mention of industry relates to the firm leaders who have previously worked in the private sector and within firms involved in biotechnology or pharmaceutical development. In the cases of leaders with industry background, they are all considered to also have business knowledge, because they were involved in managerial positions in their previous position.

<u>Labour variables</u>

Working arrangements: This header gives some information about the arrangements with the parent laboratory or the incubation laboratory in terms of research work when the firm was newly created. It gives a brief description of how research facilities and labour might be shared between the two institutions. Unfortunately in the case of Cell Prothera the arrangements were not discussed, although we know that research was still developed within the parent organisation.

Scientific consultant: This variable is binary and aims at defining the relationship between the scientific leaders of the project and the newly created company. French law allows scientific founders of resulting projects to have shares and be scientific consultants for companies. If the variable features the value 'no', then this is because the scientific founder is part of the management team of the company.

New profiles hired / Firm's labour: This header defines the first hires of the company (excluding the management team), while giving their speciality if known. It is drawn from the answers to questions about employees of the firms.

4. Detailed analysis of the case studies

The literature review has pointed towards a lack of understanding of the process behind the transition of a research project from a parent organisation to a newly created firm. Since the aim of this study is to look into the role played by universities in innovation projects, the first requirement is to look into how and why a university research project leads to a firm creation project. In order to study this process, in the case where university is the parent organisation, we identified three phases that characterise this transition which are depicted in Figure 6.2. This separation between three phases of the research project influences the results section to be also divided into sections corresponding to these phases. The sections are organised as follows: (Phase I) the research to the decision of firm creation; (Phase II) from firm creation to independence[113] of the firm project in the lab, and (Phase III) the interactions between the research project and the lab it spun-out from. The following sections explain in much more detail the characteristics of those stages and the converging points between them. The results show that there is a **dialectic evolution of stages**, where the development of each phase reaches a contradiction and calls for a change to occur. In evolutionary thinking this could be related to the notion of discontinuous change (Weick & Quinn 1999), where there is a first part that contributes to a steady evolution that gradually leads to a phase of disruption. This disruption is the cause of the starting of a new phase. Thus the presentation of the results by phases involves the description of the main part of a phase but also the elements that lead to the end of this phase and the beginning of the next one.

The different phases can be described as follows. The first stage (Phase I) is characterised by a scientific project conducted in an academic laboratory. The move to the next stage is characterised by the research limitation of the university when close to the application of the product. The project can therefore not be developed any more in the university and can only be developed by a private organisation, where one of the options for moving forwards lies in firm creation. The second stage (Phase II) concerns the firm creation process, and its early life stages which that took place within the research laboratory. This period encompasses the enterprise's infancy, and explains the transition of the innovative project between being carried out by university to being developed by the created venture. The move to the third stage is normally triggered by the observation of the founding team that the incubation[114] is no longer adequate to the firm's needs and that there should be a clear boundary between the firm and the university. (Phase III) The firm then takes steps towards leaving the research lab (in most of the cases) to be located in their own premises and redefines the exchange between university staff and firm staff, such as the scientists taking on new roles as consulting experts for the firm.

As explained above, the projects were selected based on their origins (university). This enables us to develop a deep understanding of the transition phase between the types of organisation. It must also be noted that the different cases selected were created more or less

[113] Independence is here considered as the time at which the firm no longer needs university resources on a day to day basis, and which often results in the decision to leave the incubation phase in the parent organisation.

[114] Incubation represents the period in which an existing firm is growing into another organisation, the parent organisation.

recently, and are therefore in different stages of their life. As a result, this study has some cases which have not yet reached independency from their parent research organisation. However, these cases are still relevant due to the amount of detail given for their early stages.

4.1. Phase I : Research Project to Creation

The research project within academia. The first stage is characterised by the development of the research project by scientists in a university or a public research organisation. The project studied relate in general to projects that are carried out by researchers who have a career in academia, and usually a long term research agenda. In this phase, the research project moved forward to the point where it could no longer be carried out in the university as it began to require industrial development.

In order to give an overview of the projects behind the cases selected and their time frames, we refer to Table 6.2. Table 6.2 gives some details about each research project, such as the start of the academic research, periods where the research project was on hold (most of them were built without breaks in the research process and so the cell is left empty), the time they started to think about the company creation and the initial aim of the research project.

Table 6.2: Scientific Project

Firm's Name[115]	Year start scientific project	Scientific Project on hold[116]	Firm Creation Project Idea	Aim of the scientific project	Project progress within University[117]
Alpha	1996	2001-2003 2007-2010	2009	Create a bio-artificial organ	2 collaborative FP[118] for testing the device on small and medium animals
Beta	1994	1998-2003	2006	Work on biomarkers	Application for collaborative FP
Phytodia	2004	-	2005	Treat diabetes with natural extract	Collaboration with Centre on diabetes for first tests
Kappa	2002	-	2007	Develop a molecule for cancer treatment	Common work on chemistry (find active molecules) and biology (understand mechanism of action of the molecules)
Biomica	1994	-	2007	Find gene responsible for compatibility in transplantation	-
Cell Prothera	1980's	-	2006	Develop transplantation from blood stem cells	IRHT's[119] work specialises in transplantation
Anagenesis	1995	-	2010	Understand the process of differentiation in the development of stem cells	Project with AFM[120] working towards muscle application
Bionext	2002	-	2008	Big Data & Cloud Computing Platform to evaluate the effects of compounds on humans	PhD on Bioinformatics and structural biology
Alsachim	1998	2002-2005	2005	Using technology to bring innovative services to firms	PhD on the topic

Starting with the type of research leading to firm creation, it seems from the ***aim*** of the project that almost all of them could be considered more as applied research projects. As explained in the theoretical framework, the research is considered to be "applied" when the motivation for application is clearly stated in the research design (Calvert 2006). When carrying the project forward,

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[115] The number in brackets shows the category of the firm.
[116] The '-' in this column must be interpreted as being no period where the project was not followed.
[117] The '-' in this column refer to no further details was given by the interviewer.
[118] FP refers to Framework programs which are European Union funding grant system for research.
[119] IRHT is a research foundation (Institut de Recherche en Hématologie et Transplantation).
[120] AFM is a not for profit organisation (Association Française contre les Myopathies).

most researchers have an idea about application in mind, which usually relates to their original field. In this case, the context of the biotechnology sector leads all projects to have an objective to improve human health. This is the case for most of the research projects, except from Anagenesis whose research is directed towards an understanding of stem cell development. Their research however is directly related to the improvement of human health through the possible development of regenerative therapies. Alsachim also has a slightly different aim, because its project is linked to work developed within a PhD, which had potential to be developed towards offering innovative services to other firms. In this case the opportunity is not directly linked to human health.

Besides the aim of the scientific project, the **project progress within university** also proved to be increasingly involved in applied research. In many cases, the researchers who led the project, furthered their research by trying to work on the proof of concept[121]. In order to do so they either engaged in collaborative research programs, which could include private partners, or engage in collaboration with other laboratories specialised in other sciences. The realisation of applied research was usually financed through national or European collaborative research projects. In an interview with the leader of firm *Alpha*, he explains their search for successive financing for advancing their research project for a bio-artificial organ:

> "From 1996 to 2000, there was a first European project that aimed at a first proof of concept on small animals [...], then following from that there was another European project from 2004 to 2007 which was this time focused on a validation phase on bigger animals." [122]

Collaborative research projects therefore helped several research projects, such as the one followed by firm *Alpha*, firm *Beta* and Anagenesis. Many pharmaceutical projects are based and require the inputs of different sciences, and thus collaboration and bridges between research laboratories in a project can be made even before the firm creation. Multidisciplinary research can be considered as a step towards application, as Chapter 2 has shown biotechnology companies need complementary knowledge in order to be able to move towards the market. In most of the industries of application studied, clinical trials are required in order to prove that a product is effective, which requires different competences that often lie in different scientific disciplines. This was the case for Phytodia, which included scientists from the pharmacy research faculty, a specialist in phytotherapy (biology related to plants) and a specialist of metabolic illnesses. This was also the

[121] The proof of concept is based on studies that aim at giving 'preliminary evidence of efficacy and safety, with the aim to inform a decision about proceeding into full development of the drug". (Karlsson et al. 2013, p.1)
[122] Translated from French : "En 1996 jusqu'en 2000 il y avait un premier programme européen sur le projet qui avait pour but de faire un premier '*proof of concept'* sur le petit animal […] suite à ça il y a eu un deuxième programme européen entre 2004 et 2007 qui était cette fois ci une phase de validation sur le gros animal […]"

case for the company *Kappa* which involved a chemist for finding active compounds and a biologist for understanding in-vivo mechanisms of the molecules. In this case firm *Kappa* had the need of both biology knowledge and chemistry knowledge. The project emerged in a chemistry laboratory but, as the following quote suggests, the chemists were in need of biological competences for testing purposes:

> "The chemists not having this expertise in biology needed for testing their compounds in cellular models and animal models, got closer from biologists for realising this research work"[123]

The final case of a firm having a multidisciplinary research project is Bionext. Bionext integrated computer science knowledge of 3D visualisation with structural biology.

In all of these projects, there was a need for researchers from different areas to pool their knowledge in order to create a viable product that could be transferred to the industrial world. In the quote above this is shown by the need of cellular biology in order to understand the specific effects of compounds found by chemists. This close relationship between the different scientists reflects that research in these disciplines aims at producing results that impact the industrial world through multidisciplinary collaboration.

Regarding the timeline of the project, Table 6.2 also shows the **period of time from project conception until firm creation**. There can be a great difference between the time some research starts and the time of the creation of the company (from 5 years to 30 years). In some cases the project has been stopped and restarted for financing reasons (this is the case for firms *Alpha* and *Beta*). These financing reasons are often linked to the fact that the project is too applied. As many interviewees stated, it becomes more difficult to obtain public financing the more applied the project becomes. This is because public science (including research projects) can fund a project only as long as it includes the creation of new knowledge. However, as the project gets closer to application, especially in biotechnology, products have to be tested in order to prove their efficacy. The cases have shown that the university has limited tools to support this part of the research. Taking the example of firm *Beta*, who is developing a blood diagnostic, the project has been stopped and then restarted because the scientist could not further develop his product after obtaining a patent as they could not licence it to an existing firm. As the scientific founder stated:

> "There was no mean to transfer what we did [the project] easily. Then I tried to find funding in order to continue to work on the project but the project was too applied, and was also risky because the

[123]Translated from French " les chimistes n'ayant pas cette expertise de biologie pour tester des composés dans des modèles cellulaires, des modèles animaux, se sont rapprochés de biologistes pour faire réaliser ces travaux."

early results were surprising, and thus there were no means to find funds in the classical framework of fundamental research financing."[124]

Thus while the research project could be developed further in university, by multidisciplinary research in order to advance the project towards proof of concept, the financial means to pursue the project typically starts to dry up. Therefore scientists in academia have shown in the cases that they naturally drive the project and are interested in proving that the concept developed by them is viable. However, even if the resources in terms of human capital are available to them for the development of the project, the financial resources are increasingly difficult to find.

In the case of firm *Beta*, the project was first dropped for a while. The revival of the project took place when another firm contacted them regarding this patent and proposed exploitation opportunities.

The behaviours of scientists described above show their willingness to develop their concepts, which leads towards a tendency to try to push towards industrialisation as much as possible through different activities undertaken (through inter-discipline collaborations and involvement in funded R&D collaborative research programs). The cases show that there is a strong push for scientists towards applied research and even starting development or industrial processes while still in the university. This confirms the case made in the literature that universities are now pulled towards applied research, and the emergence of a new role of the university which is more entrepreneurial (Etzkowitz 2003). The scientists in these research organisations, driven by practical health needs of society, are therefore increasingly looking for solutions and trying to develop them as much as possible until they reach the limits of the system they are evolving in.

The literature review has shown that universities have also undergone a pull towards being closer to application through policy making. The cases have shown a trend that supports this view of a pull towards application. The general trend of some sectors to become close to university, and university general policy to get involved with the private sector, results in scientists within university pushing their research towards application. They get involved in working on the proof of concept in order for them to be able to transfer the project to the industry. However, this limits their productivity in generating new knowledge. Eventually, as we will discuss in the following part, the

[124] Translated from French : " Il n'y avait pas moyen de valoriser facilement ce qu'on avait fait. Donc j'ai essayé de trouver un financement pour continuer à travailler sur le projet mais c'était un projet qui était trop appliqué, qui présentait aussi un certain risque, parce que les résultats étaient iconoclastes et surprenants […], et donc il n'y avait pas de moyen de trouver de financements dans le cadre des moyens de financements classiques de la recherche fondamentale. "

involvement of scientists at the beginning of the industrial development of the scientific project will be restrained by the university capacity to support this type of activity within their research laboratories.

The creation causes. The first part of this section showed that the university is involved in applied research and even starts moving towards industrial development due to political willingness and its scientist's motivation. However, the push towards development is in contradiction with the fundamental aim of universities, which are bounded by their objectives of knowledge creation. When considering firm creation there is a distinction to make between two types of researchers, in terms of pace of evolution and decision towards firm creation. The development towards firm creation is different between projects that are carried out by established researchers and those carried out by former PhD students. For clarity reasons we refer to them as the **scientist category** and the **PhD category**. While in the earlier part of the section we described how researchers were looking for financing in public research in order to follow their projects, PhD students are not permanent members of a laboratory and so the end of their PhD usually relates to the end of their working relationship with their parent laboratory. Thus the decision towards a career path (firm creation or not) is made at the end of their studies. Thus this section assumes that there is a distinction between the **new** and the established scientists in terms of their reasons for creation. For the new doctors the choice lies in either following their research project or searching for a job. For the established scientists there are **two main causes of firm creation that are a consequence of the limit of the university action**. These two causes are the need for financing and the willingness to develop the project through technology transfer.

In the cases in which the scientists who founded the project had a senior position, the **scientist category** (7 cases out of 9), the question lies in whether it was the absence of opportunity or the limits of the academic institutions that triggered the development of a commercial product. The choice for the scientist is either to stop working on the given project (hoping the existing industry would pick up the idea), or start a firm that would pursue the project. The reasons of firm formation for the scientific founder of firm *Kappa* are explained in this way:

> "My vision [concerning the firm creation] included two aspects. Firstly I had the willingness to develop a research project towards an industrial application in order to go to end of the story. Secondly if the molecules were potentially interesting I wanted to try to push them as quickly as possible towards the patient. A third aspect would be that through the creation of a company one participates in the development of the local industry and to the possibility that young doctors in the sector can find a job

locally. For my scientific collaborator, his motivations were mainly the furthering and completion of his research project."[125]

Scientists who decide to get involved in firm formation have a strong desire to see their academic research project having an impact in the industrial world and therefore make an effort through firm creation. This is in line with the research motivation exposed in Table 6.2, which argues that scientists are motivated by the desire to push the application of their fundamental results (all the cases involving experienced researchers are concerned about this objective). However, these are general motivations; looking closer there are also practical reasons behind the decision of established scientists to create a company. There are two main reasons behind firm creation (cf table 6.3), which are the financing needs of the project and technology transfer (with the motivation that the project should be developed further). Table 6.3 summarises the firm creation in order to compare the reasons of founding, by dating the firm creation and the reasons behind it. It also states the involvement of the people at the time of creation and the patenting activity.

As shown on the Table 6.3 the two main reasons for firm creation are technology transfer (Phytodia, firm *Kappa*, Biomica, Cell Prothera, Anagenesis) and financing (Firm *Alpha*, Firm *Beta*). Table 6.3 confirms that a majority of research projects are converted into a university spin-offs because of the limitation of financial resources made available by universities. This limitation leads to two options: the researcher finds a company for licensing the technology, or the researcher gets involved in a company creation.

Finding a company to license the technology may be tedious and drawn out since pharmaceutical companies tend to target products that already have a proof of concept. The academic wishing to transfer his technology may also be limited to a lack of networks and knowledge of the industry. In our case, only one company (firm *Beta*) attempted to actively find an industrial partner to develop their scientific results, which in the end did not succeed. Table 6.3 shows that scientists have patenting activity sometimes long before company creation (*Alpha*, *Beta*, *Kappa* and Anagenesis), but none of them (apart of firm *Beta*) mentioned a willingness at that time to exploit the patent in order to transfer it to the industry.

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[125] Translated from French : " Ma vision [pour la création d'entreprise] je voyais avant tout deux aspects : premièrement j'avais une volonté de faire développer ce projet de recherche vers un aboutissement industriel, afin d'aller au bout de l'histoire, deuxièmement potentiellement si ces molécules sont intéressantes autant essayer de les pousser le plus rapidement possible vers le patient. Un troisième aspect, à travers la création d'entreprise on participe au maintient et développement d'un tissu industriel local et donc à la possibilité à des jeunes docteurs d'obtenir un travail sur Strasbourg. Pour mon collaborateur scientifique ses motivations étaient aussi essentiellement pour l'aboutissement de son projet de recherche. "

Table 6.3: Firm creation

Firm's Name	Creation Project	Creation year	Reasons for firm Creation	Scientist experience in start-up creation	Patents [126]
Alpha	2009	2011	Lack of financing in public research/ Technology transfer	No. One researcher with no prior experience involved in the creation.	2002 2010
Beta	2006	2008	Needed a way to finance his project / Technology transfer	No, but found a person with business knowledge to help in the creation	1997 2008
Phytodia	2005	2006	Technology transfer to industry / Discovery of natural extract for diabetes treatment	Yes, one of scientific founder did create another company in 2000. A person having 10 years of industry experience had been recruited before the start of the firm	2007
Kappa	2007	2010	Technology transfer to industry / Discovery of active molecule for cancer treatment	No. No prior experience in firm creation in the team, but recruited a person (scientific background) in charge of the creation	2006 2010
Biomica	2007	2009	Technology transfer to industry / Discovery of genes expression that has an importance in transplantation	No, but found a person with business knowledge to help in the creation	No patent for first discovery 2009
Cell Prothera	2006	2008	Technology transfer to industry / Developed heart transplantation from heart stem cells	No, but a person with great experience in firm creation helped during the creation	2012
Anagenesis	2010	2011	Technology transfer to industry / Differentiate stem cells into muscles cells	Yes. The scientific founder created a company with three other scientists in his early career.	2007 2011
Bionext	2008	2009	Get finance quicker / in order to get quicker to the market/ Ability to work on innovation	No, but involvement of an associate that had experience in firm creation.	2010
Alsachim	2004	2005	Firm creation after the closure of the start-up the founder worked in	Both founders had worked in the industry, in another biotech star-up	None Secrecy policy

Firm creation seems the most natural way to exploit the research project developed in academia. However, there are also some drawbacks in this solution. As Table 6.3 shows, most of the

[126] The patents are related to the project. They are either held by universities or shared with the newly created firm. The patents are usually licensed to the firm, with exclusive agreement for a low upfront cost in order for the firm to be able to get started.

scientific founders do not have any experience in terms of firm creation and this points to the potential in/ability of the scientist to pursue such an enterprise. Some of them (3 out of 6) therefore prefer to hire another qualified manager in order to help them with this task[127].

The creation process also takes time, typically from 1 to 2 years from the idea of creation to realisation. The process of creation can also be caused by legal and credibility issues. In order to raise further financing outside academia, one of the conditions lies in already having a legal entity who applies for such new types of financing. The creation of a firm through a legal private entity therefore enables founders in leveraging funds with financers or European projects and also discussing licensing with the university. A legal entity is needed to tackle these issues otherwise the matters are not taken seriously and the project cannot move forward. As we have seen in the earlier section, research projects developed within universities come up against more and more barriers when becoming applied projects, such as financial problems and the limitation of the commercial purpose of the university. The founder of firm *Alpha*, who financed his first proof of concept through collaborative research projects, explained the increasing difficulty he went through for finding further financing:

> "After this step, in 2007, the question arose about what should be done with the prototype developed. [...] I then tried to apply for an FUI or ANR research project, but every time the feedback given was that the project was too close to a clinical application. During a presentation at Alsace BioValley they convinced me that I should create a company"[128]

Researchers such as the president of the firm *Alpha* had in mind only to further the research project that he had carried out for the preceding 13 years (see Table 6.2). The creation of the company was therefore not a wish of the scientific founder but more a necessity in order to further the research and development as a research project in a laboratory. The researcher here is characterised by the willingness to pursue the project, but not necessarily to create a company. The company creation is here the solution that can solve the **financing problem** that hinders the further development of the research project.

The case of the firm *Beta* is also a striking example, whose scientific founder developed a biomarker technology and achieved some interesting results on a specific disease. In a first patent,

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[127] The process of finding and constituting a management team will not be developed in this chapter as it was the aim of the previous chapter, Chapter 5.

[128] Translated from the French quote : " Suite à cette étape, en 2007, s'est posée la question du fait que l'on a un prototype, qu'est-ce qu'on fait […]j'ai essayé ensuite de déposer un projet au fond unique interministériel, à l'ANR et à chaque fois le retour donné était que le projet était trop proche d'une application clinique, et au cours d'une présentation à Alsace BioValley on m'a convaincu qu'il fallait que je crée une société. "

which he applied for at university, he wanted to hand over the project to a pharmaceutical company, but this transfer never materialised. The project was then abandoned for several years until the researcher had another opportunity to further the project. Another company proposed to co-develop this research project from the existing patent, but they also failed to raise funds. Finally the project was able to proceed with the help and financing made available by the local technology transfer organisations such as Connectus and SEMIA, which provided the opportunity to first pursue the research project and then go towards the path of firm creation. These two examples also show **the lack of financing available** when the project is getting close to clinical development and therefore scientists turns towards firm creation in order to access funding to pursue their research projects. This problem was also mentioned in the case of Cell Prothera.

Another fact of interest is the increase in the **patenting activity** close to creation, as Table 6.3 shows. For each of the scientific projects, there has been patenting activities close to their creation date, which is true for each of the groups. This shows the willingness of scientists to be active in the industrial community (see literature review for further details), and also shows the push towards application and the willingness of scientists to contribute towards the industrial world. Including all the cases, two main reasons have been given for the patenting activity. Scientists seem to think about patenting activities for various reasons. Firstly because of the newness of the product developed and secondly because some of the scientists already look to have assets on which a possible firm could design their value creation. Scientific researchers therefore explained their patenting reasons differently:

> "At the beginning no [the patents' applications were not related to the firm creation]. Firstly we didn't know that we would potentially create a firm at that time, but the fact of having molecules that had biological properties were a good reason to apply for a patent at that moment."[129] (Scientist at Firm *Kappa*)

> "I am looking for creating a firm, but a firm has no value if it does not have a patent portfolio."[130] (Scientist at firm *Alpha*)

Even if patenting can be generated when making a discovery (the case of firm *Kappa* and *Beta*), most of the firms that were involved in patenting activity explained their behaviour by their willingness to transfer property rights to the newly created organisation in order to increase the

[129] Translated from French: " Au départ non [les brevets n'étaient pas déposés en vue de la création d'une firme]. Déjà on ne savait pas qu'on allait potentiellement créer une entreprise à l'époque, mais le fait d'avoir des molécules qui ont des propriétés biologiques de toute façon ça vaut la peine de déposer à ce moment là un brevet. "

[130] Translated from French: " Je cherche à créer une société, mais une société n'a pas de valeur si elle n'a pas de portefeuille de brevets. "

chances of firm success. Patenting activities help formalising the resources owned by the firm, and are therefore negotiated with the university around creation time.

For the **PhD category**, the researcher who leads the project does not have a strong link with his parent organisation compared to researchers with permanent positions. This instead leads them to make a choice at the end of their doctoral studies. The choice for them is the following: the project could either be developed further in academia, be developed in a private organisation or left undeveloped. In our first case of Alsachim, the decision to start a company came from the pending closure of the existing company in which the founders of Alsachim were working. The founders therefore decided to develop competences acquired through one of the founder's thesis to base their company on. In our second case (Bionext), the student wanted to pursue his innovation project further, which was partly developed within his thesis. A question was therefore asked during the interview regarding the choice of the kind of organisation that was best to pursue the research project. The head of Bionext replied as follows:

> "Finally, we decided for the enterprise because of the flexibility, for going forward faster on these research projects and hire people.[...] [the limitation of academia comes from] the way the French [research system] is organised nowadays, it is thematic projects, and if you don't fit in those you won't get any financing. There is a second phenomenon that is specific to France, with the example of the ANR projects [...] you need roughly six month to get an evaluation and approximately one year to get the first grants. One year in an innovative domain is enormous."[131]

For this company the choice to exploit was therefore linked to development opportunities and development time. The founder of this company was concerned that the development inside a university lab would be slower than in a private firm and that this could jeopardise the novelty of his product when coming to the market.

In summary, during the first stage the research project is developed within the universities with clearly applied motivations. For the scientist category, the first efforts towards development have already been completed in the university through collaborative research projects and involvement of complementary scientific competences. However, the more the research projects approach application the more the scientists find it difficult to find public funding and also to get support in their own laboratory to further develop their project, since its main mission is of

[131] Translated from French : " Et finalement, on s'est orienté sur le coté entreprise pour la flexibilité, permettre d'avancer plus vite sur ces projets de recherche et d'engager des gens. [la limitation du secteur academique] c'est la façon dont est orienté la France à l'heure actuelle, ce sont des projets thématiques, si vous ne rentrez pas dans ces cas-là vous n'aurez pas de financement. Après il y a un autre phénomène qui est propre à la France, c'est que par exemple les projets ANR […] il faut six mois à peu près pour l'évaluation et un an à peu près pour toucher les premières subventions. Un an dans le domaine de l'innovation c'est énorme."

knowledge creation through public research. More and more barriers therefore start to appear that hinder research projects within a public research institution, and so the researcher is confronted to a choice of continuing his project (which has to be done within a new institution) or stay in the present institution with no guaranty to see the project come to application one day. One of the solutions is to create a firm, which in some cases happens only as a result of funding limitation, but also in most of the cases by the willingness of scientists to transfer technology. For the PhD category, two questions arise; whether to continue a project after the thesis and whether to pursue it within the university or another organisation. However, outside academia they may have limited support.

The section has also shown that **university researchers** can increasingly have a motivation to **contribute to the industrial community**. This can be done through patenting as identified in the literature, but also in practices such as the development of inter-laboratory collaboration with the sole objective of advancing the development of research projects towards proof of concept. This view extends to the decision of scientists to get involved into firm creation. However, motivations behind these steps can be differentiated from most other entrepreneurs in our cases because they do not in general pursue protection of assets or personal enrichment, but rather for most of the scientific involved follows advancing human health.

The decision to create a company is often linked to the recognition of an opportunity, and is therefore linked to entrepreneurship. Entrepreneurship theory associates this notion of opportunity to the belief of the entrepreneur to make a profit (Shane 2003), which is not the case here as the primary motivation of many academics does not lie in the belief of financial return. However, in our case the recognition of an opportunity and the decision to exploit does not entirely coincide firstly with the creation of the firm and secondly with the identification of profit. The decision to further the project is made at the university and the decision of creation only emerges as one possible means of exploitation. Here one can observe the beginning of the differentiation between the importance of the firm creation project and the scientific project development. For **the scientist, the creation of a firm and the profit is not a central objective but is usually the only means of project realisation becoming the central focus**. The decision towards firm creation can then be seen as the decision to continue to develop the project in concomitance with the awareness of the limitations of the parent organisation to further the project.

4.2. Phase II : Firm creation to firm independence (incubation phase)

Incubation phase. The second stage starts with the creation of the firm. The creation phase firstly involves the organisation of the newly created firm as well as the transfer of the project from the university to the newly created organisation. This section therefore discusses the incubation time in the parent organisation after firm creation and the transition of the project from one organisation to another. Table 6.4 summarises the qualifications of the leader of the firm project and the state of incubation. This data will be used to analyse the link that the firms still have with their parent institutions.

Table 6.4 shows that for many projects with a senior scientist, have found an external leader to develop the company; some with a scientific background and some with a business or industry oriented background. This section shows that there is a distinction between the early evolution of firms that are led by people with different backgrounds (this has already been tackled in Chapter 5). We differentiate therefore two further categories, one of which is led by a scientist and the other led by a new comer with managerial experience. This last category includes firms that have a leader with an industry background or a business background according to Table 6.4. We refer to them respectively as the **scientist category** and the **managerial category**. This distinction of categories is important, especially in terms of the time taken to reach independence from the original laboratory as the section will show.

This section includes from now on the three categories as defined, which include the firms with a scientific leadership, the firms with a managerial leadership and the firms emerging from PhD student projects.

Table 6.4: The project in the firm

Firm's Name (Category)	Same scientific leader	Background of the leader[132]	Incubation	Working arrangements	Creation year	Move year
Apha	Yes	Science	Same lab	Rent of services	2011	Not planned
Beta	No	Business	Same lab	Researcher from lab. That switched to company	2008	2012 (plan)
Phytodia	No	Industry	Same lab	Phd students from lab dedicated to the project	2006	2008
Kappa	No	Science	Same lab	Scientist working on project paid by university	2010	Not planned
Biomica	No	Industry	Same lab	Sharing of the labour between firm and the lab	2009	Not planned
Cell Prothera	No	Business	Same Lab	Research done within the parent laboratory	2008	2010
Anagenesis	No	Science	Same lab	People that will work on the firm project are still part of the lab	2011	2013 (plan)
Bionext	Yes	Science	External incubator	An employee coming from the parent lab	2009	2013 (plan)
Alsachim	Yes	Industry	Other university Lab	10 employees, mainly technicians	2005	End 2006

The decision of where to start the organisation of the company is a difficult one. Here we have two cases where firms were incubated in different places compared to the parent organisation, both of which came from a PhD project (**PhD category**). For these firms the link with their parent organisation can be considered as weak compared to other projects that are incubated in their parent laboratory. Due to their lack of permanent positions, it is less natural for the firms started by the PhD students to be incubated in their parent laboratory. For both firms, the founder looked for a laboratory to incubate them which would have specific laboratory equipment that they could rent. Alsachim found an opportunity in another laboratory at the university and rented facilities for one and a half years. However, this opportunity was possible only after negotiations with the head of the

[132] The business background is differentiated from the industry background in order to emphasise the experience of the leader in the specific sector of application chosen by the company. Business experience is limited to managerial or firm creation experience.

laboratory in which he was incubated. This laboratory was not the one in which the entrepreneur did his PhD work. For Bionext, the opportunity did not work out and so the firm was incubated in university incubator. University organisations still maintain a role to help develop the research projects initiated by PhD graduates. However, the link with their parent laboratory seems weaker since for them to be able to be incubated in university laboratories, they need a much more proactive behaviour compared to a senior academic, for whom incubation in university is more natural.

For the **scientist category** and the **managerial category**, the firms have incubation periods arranged to start in the laboratory where the project was first lead. This is due to the strong involvement of a scientific founder who has a permanent and often senior position in the parent laboratory. Thus we can observe that for those ventures the links are stronger with their parent research laboratory. Most of the firms are still incubated in their parent institutions several years after creation, for which the interviewees give various reasons (see Table 6.4). The first reason is a practical one; since the activity of the firm starts slowly, their main activity is related to the research that was conducted in the parent research laboratory. In most cases this generates collaborative research between the firm and the research unit. This can be seen from Table 6.4 in terms of early labour that the newly created firm benefits from. Many of the firms pool their human resources with the parent lab through the renting of services (firm *Alpha*) or through the continuity of people employed by the university dedicated to the research project (where 6 of the cases are concerned). Some relevant labour in the laboratory is usually put in disposition to the enterprise by different processes. This can be in the form of PhD students (Phytodia), labour that are first financed by university and then by the firm (Firm *Beta*, Firm *Kappa*, Anagenesis), simply paid services to the lab to use labour (firm *Alpha*), or finally pooling the human resources from the laboratory to the one hired by the company (Biomica). Those human resources can be employed by the company at a later point when possible. The pooling of resources is also due to financial reasons, since newly founded firms need to begin their activity as soon as possible but are limited in terms of funding.

Another advantage to be located in the parent laboratory or having access to university resources is the availability of physical resources. Having access to the required material and instruments is therefore usually crucial in the firm's early development. At creation the firm does not have the strength to build its own research facilities when necessary and must as a result rely on the university physical resources in order to have a chance to survive in their first year. This was also the reason given by the founder of Alsachim for his choice to be incubated in a university laboratory:

"We wanted from the start to propose a consistent service and realise it in the best conditions and that our first clients feel straight from the start our professionalism. At ISIS the labs were fully equipped, there was a complete infrastructure and that was really interesting for us."[133]

The cost of the tools and machinery needed to deliver the service they aimed for at the start were too expensive for them, and thus being able to benefit from the university facilities for a monthly rent was a great opportunity to start their company. Like many new companies, the firm does not have the funds necessary for investment in physical resources that they need and thus the university can ensure a smooth transition for them. This gives the firm an opportunity to be fully functional while delaying the need for investment to a more suitable time for them in terms of financial abilities.

To sum up, when a new company starts to get organised there is rarely a clear-cut transition between the time the company is created and the time it moves out of the parent laboratory. For firms that do not have a close relationship to the parent laboratory (such as in the PhD category), the transition between the decision of exploitation, the creation of the company and the exit from the parent laboratory is clearer. The company immediately moves to an external laboratory, and does not share much labour but can sometimes need access to physical resources. However, this is different for companies where the scientist has a permanent position in university. In most of our cases the senior scientists have not only permanent positions but also have high hierarchical positions in their respective laboratories. In those cases the university is of great help in terms of labour and facilities during the initial stages of the company, and most of the firms in this case chose to stay in their parent laboratory. The move out of the laboratory is not imposed on them, since arrangements to pursue research have been found between the company and the laboratory. However, the question remains of why such companies decide to leave the laboratory at a later stage.

Independence from the scientific community. Here we aim to explore the reasons for the ending of incubation in universities, which will be differentiated by categories.

For the **managerial category**, where the leadership is held by people with business or industry experience, the point of change is reached partly due to the increasing importance of advancing the development of the project towards commercialisation compared to the cost advantages provided by the university. Collaborating with universities provides inexpensive but

[133] Translated from French : "Nous voulons dès le début proposer un service développé et le réaliser dans les meilleures conditions et pour que derrière les clients sentent tout de suite du professionnalisme. A l'ISIS les labos étaient complètement équipés, il y avait une infrastructure complète et c'était surtout ça qui était intéressant. "

qualified labour, such as Masters Students in need of an internship, PhD Students, or researchers working on related topics. The management of the company usually also wants the decision making process to be easier and not affected by academic priorities (generate more knowledge) but focused fully on the rapid development of the project. Many firms therefore want to take a step towards independence from academia and its specific culture, especially the ones led by a person with a business or industry background (firm *Beta*, Phytodia and Cell Prothera). The culture in the French academic system has been described by some managers as not compatible with the view of enterprise; as the president of firm *Beta* explained:

> "There must be a big warning about academic researchers [...] especially looking at their notion of time and money. We should not give the control of an enterprise to an academic researcher"[134]

The president of this firm does not deny the usefulness of being incubated in the parent laboratory during their first few years. He emphasised that at creation it was very useful to be able to access much of the university equipment, which they could not afford themselves. Even though they had a collaboration contract and rented the facilities, being incubated in the university made it cost efficient. However, the leadership also indicated the difference of culture between the French academia and the private research organisations. The notion of time and the notion of budget are totally different in academia compared to the private sector. The academic culture of being oriented towards knowledge generation made their way of working slower and is therefore un-adapted to the development of a firm. In private research organisations, researchers are more focused on the development of a specific project and take less time to explore results, especially those not directly linked to the development of the project. The academic culture is therefore not ideal for the development of an enterprise, which has to be much more careful about the timeline of the project and also the manner in which they spend money.

The leader of Phytodia had a similar experience and wanted to redefine the role of scientists in his company; as explained by the head of Phytodia:

> "[...] I make them intervene for what they are, technological experts that do consulting for the firm, for their scientific expertise and not for the everyday management of the company"[135]

[134] Translated from French : " Je mets un énorme '*warning*', un chercheur académique […] sur sa notion de temps et sa notion de l'argent. Il ne faut pas confier les rennes d'une entreprise à un chercheur académique. "

[135] Translated from French : " […] c'est de les faire intervenir pour ce qu'ils sont, c'est-à-dire des experts technologiques ils sont consultants pour la boite, mais pour leur expertise scientifique propre pas pour la gestion au jour le jour de la boite. "

As with the previous company, Phytodia also acknowledged the useful exchange with science. The company needed some researchers to further develop the molecules found by the research team. The two labs involved in the initial project therefore provided two PhD students. Later on in 2008 the company needed more workforce for the industrialisation of the research project and turned back again towards academia to hire two interns from the labs for a very reasonable price. The cost of labour was an issue, and the choice of PhD and Master Student interns was the most cost effective way to hire workforce without compromising on quality.

Despite initially hiring from academia, later on in 2008 when hiring other staff specialised in phytotherapy, the management made a point of hiring somebody external to the laboratory. It seemed then that the cost was not an issue anymore because the company had raised its first funds by the end of 2007 from local Business Angels. The main reason for this choice is typically to distance the company from academia, meaning having a clear line between research done in the university and research done in the company. The reasons given by the management of Phytodia were that they did not want scientists to interfere with management anymore; it will then be easier to divide the tasks between the employees. In this case, we can see an increasing confusion between the hierarchy and organisation of the newly created firm and the laboratory. Masters and PhD Students need to complete their degree and therefore have an academic responsibility, which is usually defined by their academic supervisor, but at the same time they are part of a private organisation in which they are liable to work for. The students are therefore caught in a double hierarchy that can be increasingly confusing.

Even for some academic entrepreneurs the leader typically thinks it is important to create a clear-cut line between academia and the firm; as is the case with Anagenesis:

> "I wanted to quickly create the society in order to control its perimeter and avoid discussions with people who wanted to jump on the moving train, because they were people that were ready to help and wanted to take part, but I preferred that things were discussed once everything was framed."[136]

This is an exception concerning firms that are lead by academic researchers. This firm is an exception because the academic researcher already had experience in firm creation, and as a result identified the importance of this step (cf. Table 6.3). In the case of other firm in the scientist

[136] Translated from French : "moi je voulais aller assez vite pour créer la société parce que je voulais en contrôler le périmètre et éviter les discussions des gens qui veulent un peu sauter dans le train en marche, car il y avait des gens qui étaient prêts à aider et voulaient participer, mais je préfère discuter des choses une fois que ce [le projet de création d'entreprise] soit cadré. »

category, the difference of culture is not as predominant because the leader of the firm comes from the same culture, and usually the academic hierarchy does not differ greatly from the firm hierarchy.

These experiences show clearly that there can be confusion between the company's activities and the research laboratory activities. These confusions can take many forms, such as continuing the research as if it was for the laboratory in university in which the methods and pace are not adapted to the industrial world (firm *Beta*), or having no clear boundary between the researchers working in the company and the researchers working in the laboratory (Anagenesis). The research activities conducted in a firm are different from the ones lead in academia. It has been pointed out that the research activities in academia are sometimes dispersed (travelling multiple paths to try many solutions in order to find the best), but this strategy cannot be used in a firm since the budget is a lot tighter, as is the timeframe for results. The founder of Phytodia also acknowledged that he felt that scientists sometimes did not understand how tight the company budget really is and often prefer to deepen research rather than developing the project. This observation is consistent with the difference between research institutions made in the theoretical background, in which the academic researcher is hired to produce knowledge while the private organisation has to be able to produce financial return from the project. The financial and competitive aspect of a private organisation can enter in conflict with the primary objective of the scientist, which is only to be able to transfer his knowledge in order to benefit human health problems but also have personal return in terms of reputation.

Therefore when financial resources are no longer a problem, many firms decide to put some distance between themselves and their laboratory of origin, especially those directed by leaders with managerial experience (managerial category).

For the scientist category (firm *Alpha*, *Kappa* and Anagenesis), two of the firms have decided to remain incubated in their parent organisation. The problems of independence are less striking for the first category and so their plan to move out of the laboratory is more oriented towards the long term. The only exception to this is Anagenesis. Even though there are reasons to move out of the academic lab for independence, the main reason for a move lies in strategic collaboration:

> "We are in discussion with a local pharmaceutical firm, who wishes to give us equipped locals close to them, and it is interesting for us because [...] they propose all the laboratory environment [...] and also

> they may be interested in the things we are doing, and if it can be an opportunity for us to develop a privileged relationship with them, it will suit us too".[137]

Thus they take advantage of the opportunity to leave the laboratory, in order to be able to clarify the boundary of the firm in terms of human resources. This also shows that the move to the next phase can also be triggered by an opportunity and not only by the increasing difficulties proven to work within university walls.

Phase II of the process is a crucial part for many firms. Firstly one must note the **difference of opportunity between the different categories**. Even though firms where senior researchers are involved in the creation have stronger links to the laboratory, the PhD graduates are not obviously linked to their parent laboratory and must find a suitable place typically outside the parent organisation. Secondly, this section showed that firms benefit in various way to start developing in universities; it is only after some time that the confusion between the two organisations (firm and research organisation) can become problematic and leads the firm to choose to move outside university as they may feel they could gain independence, especially towards the management of the company. One can therefore conclude that the decision to stay within the parent organisation in the first place may be constrained by the link the research at the origin of the project has with the university and ultimately the leader's seniority. The latter decision to move out of the university is generally differentiated between people with different backgrounds.

On a general note, one can observe a problem that emerges from **the fuzziness of the boundary of newly created organisations**. Since the project is a separate entity it is pursued within two organisations when the spin-off is incubated into the parent laboratory. Therefore, we observe a conflict between the firm organisation hierarchy and the university one. University staff may be shared or may be recently hired and thus transferred between organisations, which makes the scientific hierarchical structure and the organisational hierarchical structure confusing for the staff. When the structure of spin-off companies follow the hierarchical structure of the laboratory (in the scientist category), the confusion may be less evident than when there is business or industry leader (managerial category). In the managerial category, the former leader of the project (the scientist) is still part of the project organisation, which can interfere with the new hierarchical order in the newly

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[137] Translated from French : "On est en discussion avec une entreprise pharmaceutique locale, qui souhaite proposer des locaux équipés chez eux, et nous ça nous intéresse parce que […] il propose tout l'environnement du laboratoire […] et en plus il y a aussi dans le coin de leur esprit, que ce qu'on fait ça les intéresse et si ça peut permettre de créer des rapports privilégiés avec eux, nous aussi ça nous va bien. "

created firm. This may create tensions and enhance the willingness of the leader to separate their organisational structure from their parent organisation in order to create a clear hierarchy in the firm.

There has been until now two distinct forces that explain the development of the relationship between university and the newly created firm in two corresponding steps. In the first step the need for physical assets and human capital, together with the limited financial resources of the newly created company, makes it a logical step for the firm to try to take advantage of their close relationship with university. In the second step, a new force is introduced that can be identified as the difference of culture and practice of project development between the two types of organisation. As it has been pointed out in the literature review, the work practice and culture is very different between the two types of organisation. The private organisation needs to make revenue as soon as possible and to make profit from the project in order for it to survive in the long term. The fact that the firm chooses to develop their venture within university, with its specific working culture, makes it more difficult for shared labour of a dual hierarchy to respond to[138]. As for the firm, it is crucial to stay focused since development time is an important factor for survival and avoiding this confusion by stepping out of the university environment seems to be a vital step. Thus the time that each category stays incubated within the parent laboratory varies greatly between categories. For the PhD student category, there was no incubation time in the parent laboratory, but they can still benefit from university resources through the incubation in another laboratory or in an incubator. For the managerial category, there is usually an incubation time within the parent laboratory, due to the strong involvement of a founding scientist. However the time they stay within university is limited (in our cases ranged from 2 to 4 years according to Table 6.4 and one with no intention to move). For the scientist category, in most of the cases, the leaders did not aspire to a move yet.

4.3. Phase III : Firm taking its own R&D path

The previous section went deeper in the relationship between the infancy of a firm and its parent organisation (the university). This section looks into the way research is led when the firm takes some independency from the research laboratory and asks the question of the continuity of the relationship with the university. This section is less developed than the previous sections as it only looks at the remaining relationship between university and the newly created organisation. A

[138] For the scientist category this is less true than for other categories as the leader of the company also leads the scientific project and therefore responds to same hierarchy even if they are part of two different organisations.

second reason for its limited detail lies in the reduction of the number of study cases that are actually in this phase.

The development phase begins in the previous stage (phase II) but is a gradual process that evolves over the final two stages. It is a process of slow differentiation between research done at university and the research done within the firm. This differentiation takes place as the innovative project moves towards development and thus the contribution needed from the parent organisation becomes limited.

This is characterised by a need for the organisation to integrate new complementary competences which contribute in terms of proof of concept. These competences are new in the sense that they are different from the ones developed in the parent laboratory. This is achieved through the hiring of new engineers and technicians. As shown in Table 6.5, all companies hire new employees over a broad range of competences. The first reason for this behaviour is that the lab they are working with does not retain the needed competence, and the competence is essential for the development of the product. This was the case with firm *Alpha* where the founder of the company stated:

> "We hired an engineer in Biomaterials that has a more technical and regulatory side[...] at the beginning we wanted to hire a post-doc because we thought we needed to increase our research strength, but we noticed that we needed a more applied and regulatory strength and so an engineer in Bio-materials was necessary. We will also hire in July an engineer-assistant for doing most of the analysis".[139]

Being involved in a development project raises the need for a more applied workforce than a research one. In addition, this workforce must also possess the range of competences that are needed in the specific industry. The scientific founder of Anagenesis, who has previous experience of firm creation, said:

> "For starting an enterprise in biotechnology, ... [in our previous firm we needed] this ability of associating different competences that go above the limits of the labs. For example, we recruited chemists and engineers and if a machine was needed we had to build it... However, in research it is

[139] Translated from French: "on a embauché un ingénieur en biomatériaux qui est plutôt dans le côté technique et réglementaire […] au début on voulait recruter un post-doc parce qu'on pensait là de nouveau être sur un côté plus recherche, puis on se rend compte qu'on a un côté plus appliqué, plus réglementaire qui nécessite un ingénieur en Biomatériaux. On va recruter au mois de juillet un ingénieur assistant pour faire toutes les analyses. "

rarer, in a biology lab, to find engineering or chemistry competences. The disciplines are more partitioned... but in a firm it is vital [to have this range of competences]."[140]

The lab in university does therefore not offer the wide range of competences needed for the firm to develop its product and so there is a strong need for hiring engineers and technicians. In most of our cases this need does not emerge when the firm is about to move out, but can emerge any time during the process of development of the company (stage II or III), because in our cases firms led by scientific founders stay longer in their parent laboratory. The need for this new labour usually aims at complementary competences that need to be included in the development process. The engineers in Table 6.5 are hired mainly in order to pursue objectives such as proof of concept rather than for research purposes.

Table 6.5: Use of competences

Firm's Name	Scientific consultants	New profiles hired / Firm's labour
Alpha	No. Probable that she moves to the company	Engineer for facilitating the process of development and commercialisation
Beta	Yes	Engineer and bio-technician and post-doc Project manager
Phytodia	Yes	Hire master students for development and commercialisation
Kappa	Yes. Strong involvement for finding new molecules	None for the moment
Biomica	Yes	2 research engineers
Cell Prothera	Yes	Hire medical director and project manager
Anagenesis	Yes	-
Bionext	No	Software engineers, chemist and pharmacologists
Alsachim	No	1 Technician and 1 intern at the end of the first year

During the third phase the position of the scientist in the project and therefore in the firm may be different compared to phase I. This is summarised in Table 6.5. In fact most of the scientists

[140] Translated from French: " Pour construire une entreprise en biotechnologie … le côté association de compétences qui dépasse le cadre du labo, par exemple nous avons recruté des chimistes, des ingénieurs et si on veut une machine on la construit. Mais en recherche c'est rare dans un labo de biologie d'avoir des compétences en ingénierie ou en chimie les compétences sont beaucoup plus cloisonnées… alors que dans une boîte c'est vital. "

in our cases have expressed the wish of not leaving their research environment to go into the newly created company, except for firm *Alpha*, Alsachim and Bionext. In the case of Alsachim, the founder was already in the private sector when they decided to create the company and therefore did not pursue an academic career. In the case of Bionext, the issue was that the creator had just finished his thesis and therefore was not yet an appointed researcher. Most of the researchers expressed their preference to stay in the academic world because they recognise that they might not have the skills to engage in business creation, and it is not their profession. Though as Gittelman (2006) pointed out, and which was confirmed by many of the interviews (see the example of Firm *Alpha* in the previous section), the French academic culture does not value money making, and the academic structure is very different from a private organisation. Some researchers are fully aware of the limitation of their competence for company creation, as the scientist behind firm *Beta* explains:

> "As a researcher I do not have the capacity or the training to lead a project of this type in terms of management and financing. This was something I was aware of since the beginning. I would never have started this project without having with me somebody with those competences."[141]

Laws on innovation put in place in the 1990s[142] have therefore been very helpful for researchers who wanted to get involved in the creation of a company as a result of the application of research. This law allows the researcher to choose between different options for getting involved in the company. The first law permits the researcher to have the opportunity to leave academia for a set period of time (for a period of two years that can be extended twice). After this period the researcher has the option to return to his former position. The researcher also has the option to remain in academia while holding shares in the company (up to 15%), and can continue to act as a scientific consultant to the company. In the United States it is known and accepted that academics create and have active roles in companies (Gittelman 2006), however this is not the case in France. Looking at Table 6.5, most of the choices made by scientists at the beginning of their projects is to remain in academia. This is consistent with the comments of a French academic start-up creator (of 2 companies) who returned to academia:

[141] Translated from French: " Moi en tant que chercheur, je n'ai pas les capacités et pas la formation pour mener à bien en termes managérial et en termes de financements un projet de ce type. Ca a été depuis le début quelque chose dont j'étais parfaitement conscient. Je n'aurais jamais démarré sur cette base un projet sans avoir auprès de moi quelqu'un qui ait ces compétences. "

[142] This law gives more flexibility to a researcher in academia for concerning the creation or their involvement in a company. It gives them the possibility to the researcher to have a full time position in this company for a couple of years, or owning shares in a firm, or having being part of an executive committee of a firm in order to transfer research results to the industry. More details are given here: http://www.cnel.gov.pt/document/loi_innovation_recherche.pdf. A description of this law and their consequences in technology transfer is also given by Llerena and colleagues (2003)

"Usually the reintegration remains a big problem; the return to the CNRS[143] is very hard for a researcher [after a firm creation]. There is no return package, and he is welcomed as a beginner [...] There is a colleague of mine who tried to come back after the creation of a local firm; [his return] was a blatant failure, even if the firm worked, but put simply, him like me have thought at one point that our real value was not in business development. In [an academic] evaluation committee, the fact is that peers have a hard time to value the work required for firm creation [...] It is intended in law that researchers return after time spent in a company, but in fact the return is not that easy"[144]

In most of the cases, due to cultural factors in the French academic sector, researchers therefore have a preference to not leave their positions and instead prefer to take a consultant position, which is now allowed by the law. The company then distances itself from the research world by locating themselves outside their doors; but the link with academia remains due to constant consultation with the researcher on the science side. Most of the researchers therefore do not get involved with the business side of the company, but can still maintain some benefit by having shares in the company. The relationship is therefore transformed from constant interactions during the previous stage, to punctual help by the scientists with consulting position.

According to Table 6.5, there are three cases in which the scientific founder did not have a role of consultant. In all of these cases the project is still led by the scientific leader of the project in the newly created company. This is the case for both of the companies originating from PhD projects, since the company is also an employment means for the founders. In the last case of firm *Alpha*, it was the choice of the researcher. This has been proven to be quite rare as the other researchers prefer to remain in academia.

Concerning other types of links identified in the literature, such as research collaboration or property right transfer, these are rather sporadic in this phase and dependant on the project. As the earlier section has noted, the patents and property right transfer are discussed during the second phase. As it has been acknowledged by founders, the negotiations over property rights are done at firm creation and become rarer as the firm becomes independent. This said, there is one exception to the weakened collaboration and input of university research to newly created firms, since firm

[143] CNRS is a national public organisation in France which has many mixed research units with universities. For more information see Guthleben (2009)

[144] Translated from French: " Souvent la réintégration reste un gros souci, le retour au CNRS pour un chercheur c'est souvent dur, parce qu'il n'y a pas de '*package*' de retour, ils sont accueillis comme des débutants. […]Par exemple un de mes collègues qui a essayé de revenir après la création d'une firme locale, a été un échec flagrant, alors que sa boîte a marché, mais simplement lui comme moi à un moment on s'est dit notre vrai valeur ce n'est pas le développement d'une société […]. Les évaluations de carrières de chercheurs qui rentrent, les pairs ont du mal à apprécier le travail que représente monter une société, […] Il est prévu dans les textes la possibilité d'un retour mais dans les faits le retour n'est pas si facile. "

Kappa still works closely with the university laboratory in order to innovate new chemical compounds for testing and through a potential pipeline of development. In this case, the scientific project consisted in working on a set of molecules. While the firm started to focus on the exploitation of two molecules, the parent laboratory was providing more potential candidates for the drug discovery activities.

In summary, this stage is characterised for many firms as a transition towards industrialisation, where the firm is more independent and the relationship between the university and the firm is more rigid. The role of the scientist is then usually bounded by a consulting role. The firm also begins to organise itself by hiring labour that responds to the need for the industrial development of the project. However, one can observe that the university still has a role to play through the continuous link with the founding scientist, even if it is a restricted one.

5. Synthesis of the results and discussion

The above section has presented the general results representing the various phases of evolution identified. This section aims at drawing general results from the section, in addition to a discussion about the generalisation of the results. It also draws some general results that could be tested on a wider level (e.g. in other sectors, other countries or on a larger set of data).

The aim of this chapter was to understand the transition of a project from being led by researchers in a public research organisation to a newly created firm. The study has shown that the university-firm relationship is influenced by several aspects that each has an influence on the dialectic process (i.e. human resources, physical resources, financial resources, and the structure of management). During the course of the phases, the different resources evolved in terms of need and availability and, together with the structure of management, influenced the transition project towards firm creation. The theory has helped us to build a theoretical model of the transition of a research project that has been initially developed in university and is then transferred for development purposes to a newly created company. The results showed that the theoretical phases are observed in practice, but following a **dialectic process**. The phases showed processes that lead to contradictions, which are ultimately the cause of change.

Result 1: The transition of a research project to a newly created firm evolves in a dialectic way. There are different forces between the need of the project and the institutional rules of the organisations that influence this process.

The first phase begins with a general trend of researcher absorption into the research project, which pushes them to develop it as much as possible towards application. As seen in the literature review, researchers are increasingly pushed to take up projects that have an industrial application. In the biology-chemistry-pharmaceutical sciences, this push towards the industry is often translated into a willingness to further human health. In the case studies, this is translated into the entrepreneurs' motivation to see their technology used in the real world and to be actively involved in its development. In order to do so, researchers in our sample use different tools to be able to push this project towards the real world. They call on interdisciplinary research to show their proof of concepts and many of them also patent their findings. The behaviour of the researcher is consistent with the theoretical observation regarding the evolution of the role of science. The researchers see themselves as having an active role in the health industry. This motivation and new role pushes them to further their project not only on the research side but increasingly on the proof of concept, which is traditionally considered as distinct and included in the development of a technology done by the private sector. However, even though the university has evolved towards having a role in the economy, the rules of universities are unchanged and remain research oriented organisations. The university's primary role is knowledge creation and education, and its incentive structure is oriented towards these means and thus limits the action of researchers involved in technology transfer activities. One of the main limitations found in our case studies is the increasing inability of universities to financially support projects that do not add new knowledge. The researcher is therefore forced to make a decision about their research path by either stopping research on this particular project, or by possibly raising funds privately through firm creation. The creation of the firm is in most of the cases due to the desire to pursue a project through access to different types of financing that are no longer available when pursing the project in university.

Result 1.1: In the first phase, the researcher is driven by wanting to push his discovery/technology towards application, but at some point is limited by the rules of the institution (i.e. university) he evolves in.

The second phase begins with the creation of the company and mobilisation of resources needed to continue to develop the project within it. As the theoretical models have shown, at the beginning of their lives firms need to first mobilise physical and financial resources before starting their activities. They are also constrained by time and need to be able to simultaneously pursue the transferred research project. As the university has already hosted the research project, arrangements to pursue activities with them seems a natural idea. The financial constraint carried by the company, and the need for the company to start its development activity as quickly as possible, makes them increasingly reliant on university resources. University resources make it possible for the firm to develop quickly because the university can offer physical assets but also highly qualified labour for their growing activity. Thus firms are drawn to grow with an increasingly close link to their parent organisation through their close relationship for the project development. This closely-bound relationship induces problems over time as the company organises itself and grows. The cases show that company managers are concerned with the lack of clear boundaries between the company and the laboratory. This is particularly observable in the fact that it is increasingly difficult for staff to differentiate the activities and hierarchies that belongs to the firm from the ones of the university laboratory. This confusion affects the firm's functioning and the project development. Thus, while the project requires a close collaboration between university and firm during the beginning of the phase, the introduction of a new managing organisation in the firm makes the relationship complicated between the two institutions. This is particularly true for the firms with managers from a business background because their culture and organisational norms are considerably different from the ones present in universities. This confusion ultimately pushes the firm to move away from its parent organisation to seek independence. The move of a company can also vary according to the opportunities offered to them. In the cases of PhD students, the option to stay longer in a university laboratory is limited, since their position makes it more difficult for them to find opportunities to do so. Conversely, opportunities proposed to newly created firms to move outside academia (as in the case of Anagenesis) can shorten their incubation period.

> **Result 1.2: A second trend causes the firm to form a close link with university due to their need of resources, which ultimately leads to a blurred organisational boundary. This leads the firm to seek independence from its parent organisation.**

The third phase sees a redefinition of the firm's relationships with its parent organisation. Firstly, since the project has evolved further towards its development, the competences needed to pursue the project become different over time and less closely related to the parent laboratory. The university can still be of use by providing labour, but the firm increasingly uses competences from specialities other than those needed during the early research project. In terms of the relationship with the scientific founders (if they are not actively involved in the management of the firm), their position in the organisation is also redefined. This phase involves the firm defining a new relationship with its scientific founder (in terms of their involvement in the organisation of the firm), and redefining the firm's needs in terms of labour. Since our observation of this phase was limited, we cannot conclude on how this relationship evolves over time. However, we can observe that the independence of the firm from the parent laboratory involved firstly a limitation of the needs from them in terms of physical and human resources. The needs are now oriented towards other profiles, usually complementary to the ones originally needed within the laboratory. It also includes the definition of the role of the scientific founder if necessary, which marks distinct boundaries between the parent laboratory and the newly created firm.

> **Result 1.3: The third phase marks the independence of the firm with a redefinition of its relationship with its parent organisation.**

The results have also shown that there may be **differences** in the early transition of the project to the firm **according to the founders' background**. As expected from the literature, the norms of individuals from academic and business backgrounds differ and this has an influence over the transition process. This extends the differences of culture already observed in Chapter 5 by incorporating the difference of early path induced by the background of the leader of the founding team.

Result 2: The founders' background influences the transition, firstly through the strength of their relationship with university and secondly through their cultural differences (open science culture vs. business world culture).

The results have emphasised that firm managers with business or industry background have increasing problems to work efficiently when developing a venture within university due firstly to the fuzziness between the limits of the parent and the newly created organisation. This phenomenon is also aggravated by the difference in culture between the two types of organisation. The results show that the business manager has a different culture mostly oriented towards the rapid development of the project, which may conflict with the culture of exploration and knowledge production that exists within public research institutions. Thus business founders perceive the need to be independent from the parent organisation much quicker (i.e. the transition between phase 2 and phase 3 is triggered earlier than with only scientific leaders).

> **Result 2.1: University spin-offs with a business leader seek independence from their parent university much quicker than firms led only by scientists.**

Another difference, which has been observed in practice, is the difference between the links with the parent organisation regarding the seniority of scientists. The results have differentiated the relationships maintained between senior researchers and former PhD students who are the initial founders of the research project. The link developed due to their seniority, the time spent in the laboratory and their hierarchical achievements, may improve their ability to sustain a close relationship between the newly created firm and the parent laboratory. This relationship can define the level of opportunity that is offered for the project development. PhD students are in fact not that attached to their parent laboratory for development, contrary to the senior scientists who have invested a lot of time there. The PhD student's research project firstly stops in their parent organisation at the end of their thesis, meanwhile scientists have the opportunity to try to find financing for a research project in its first phase. Later on when the firm comes to be created, the opportunity to access the parent laboratory facilities is also different between these two categories, in the favour of senior scientists. Thus the transition model experiences variations in terms of opportunity and entrepreneurial agency (choice of the person in charge) according to the lead scientist's background.

Result 2.2: The stronger the firm's leader has a relationship with the university laboratory, the longer the firm tends to stay incubated within the parent organisation.

Lastly, in this case one can question the identification of the entrepreneur in terms of economic theory. The entrepreneur is often seen as the individual who uncovers an opportunity of profit and takes action to exploit it. This section shows further the process of opportunity identification and exploitation by scientists. In our study, the entrepreneurial action is held by the scientist (at least in terms of opportunity identification and firm creation). While the manager holds the opportunity exploitation (when the firm is created), this chapter has shown specific characteristics of the scientist as an early entrepreneur. In his decision to create a company, the scientist is influenced by the social impact of his research to a great extent, rather than the pecuniary objective. However, even though scientists can be identified as social entrepreneurs in terms of their goals, they exploit the identified opportunity through a private company subject to market constraints. This situation can lead to problems when the organisation of the company becomes more complex and when other actors are involved in the decision process.

The results have shown the robustness of our theoretical representation. However, the **generalisation of the results** must be discussed. The methodology was chosen because it gave the possibility to get an in depth understanding of the events and identify triggering points that may affect the transition between phases. It also provided the possibility to identify variations within this model by differentiating between different groups of people. However, this methodology also may bias the results due to one or more characteristics that are specific to the choice of the sector and the environment in which the firm evolves. For instance, the biotechnology sector has specific characteristics that may not be found in other sectors, firstly in terms of the high involvement of senior researchers during the process of firm formation. There may also be differences in the level of finance and resources needed of firms in this sector. The biotechnology sector is unique, primarily because it has important needs at the start of a company (excluding firms working on software development), such as access to specific tools and artefacts (e.g. machines and materials). This makes newly created firms highly dependent on either early investment or access to such artefacts. Secondly, the biotechnology sector is known to depend much more on property rights to add value to their technology (in terms of asset protection but also in terms of trading with other companies). This behaviour towards patenting is reinforced by the fact that it is a necessary condition in order to have access to private risk financing. Therefore, when looking for similar results in other sectors, findings concerning the dialectic evolution and close relationship between university and the newly created firms (especially in the second phase) may differ to some extent for other high-tech sectors.

In terms of environmental factors, the characteristics of the university also play a role in the triggering of the phases, as well as other institutions such as the incubator or the cluster association. This study focuses on an in depth case study with emphasis on the founding constraints and on the understanding of the early steps of the firm, and so the replication design was the most relevant solution. However, it has its limits in terms of conclusion and generalisation. Firstly, one cannot conclude on the importance of the environment on the phase transition, especially on the role played by the incubator or the cluster organisation regarding help during the transition. A comparative study could help to give a more accurate picture of the peculiarities of the university and the local actors. The choice of studying a French university might also be specific. In fact, the French academic sector is a specific case in terms of their status, laws and culture. It has some specific laws aimed at researchers (deriving from their civil servant status) that do not allow them to have another job. However, in order to facilitate knowledge and technology transfer, and also start-up creation, a law on innovation has been put in place that allows researchers to create their own company or to be a scientific consultant for a company. This therefore allows the scientist to be a part of firm creation in different ways. This aspect is particularly important in France since the academic culture seems to be very different than other countries, such as the American one for example (Gittelman 2006).

For this reason, this paper has aimed at generating propositions (which takes the form here of synthetic results) that are precise enough to be tested further in other contexts in order to generate comparable findings. Only then, one could make conclusions on the generalisation of these results.

6. Summary and Conclusions

This paper has looked at the process of spin-off creation from an existing university project in the biotechnology sector. It has done so by constructing a model by calling on different complementary theories, and then used case studies in order to understand what drives this process. It has done so by firstly identifying stages of transition between a scientific project being carried out inside a university or public research institution to the project being taken over by a newly created firm. The stages identified relate to the university involvement in the creation project, (1) when the research project moves away from total involvement by the university (the company is not existing yet), (3) to the marginal involvement of the university, where the university is a privileged collaborative partner of the firm. (2)The middle period shows a strong involvement of the university in the newly created firm. The paper has also looked at the interactions during each stage, between the people leading the project and how decisions are taken regarding the opportunities offered at university and the chosen backgrounds of the team during hiring.

The evolution seems to be caused by a dialectic process, which is partly driven by both the entrepreneurs' background and culture, but also by the resources that the firm needs for developing successfully. In the first stage, it is the growing culture of industrialisation but also the social benefit of their work that drives scientists to pursue their project, even if these activities becomes gradually unfit for the main purpose of their parent organisation. The trigger towards the next stage can be associated with a collective desire to pursue their research towards application but also with the entrepreneurial spirit of the researchers, or due to a limitation of financial resources within the university. The second period is defined by a close working relationship with the parent laboratory when possible (the study has shown that this is more complex for newly graduated PhD students). The newly created firm must put its activities in place as quickly as possible with limited resources. The parent laboratory is usually an ideal partner because it already has the required physical and human resources needed to pursue the research project. Over time the firm develops its own financial, physical and human resources and becomes increasingly independent from the parent organisation. The management then aim at distancing themselves from this academic organisation (especially for firm leaders that come from the private sector), since the incubation often causes problems in terms of defining clear boundaries between the firm and the parent organisation. Finally, the third phase is characterised by a redefinition of the relationship with the academic founder and also the parent laboratory. Thus both human (i.e. management and employees), physical and financial resources influence the early path of the firm through evolution and revolution periods that university spin-offs go through.

The relationship with the laboratory hosting the collaborative research depends firstly on the position of the researcher in terms of responsibility in the new firm but also depends on their position in the academic hierarchy. On the one hand, the results showed that PhD students may have a weaker relationship with their incubating laboratory and tend to leave their parent organisation earlier. On the other hand, in the firms where academics remain in the leadership of the company, their incubation time would remain longer and their ties would be stronger with the parent organisation. Finally, constant but more independent links are observed for firms in which the scientists step back from the firm creation project.

The university can take a prominent role during the start-up phase. They are firstly very helpful due to the fact that their institutions are flexible enough to initiate the first stage of development with financing available for the first proof of concept and they have connections with different institutions to test the project. During the second stage, the university remains of great use to help the firm in their setup activity, as financing may be a significant constraint for activity to begin. Thirdly, the university can exchange with the firm in terms of consulting positions for scientists. Through these different activities the universities are therefore involved by having a third role; one of technology transfer by helping through different means, including top-down (for the financing and laws of innovation) or bottom-up (spontaneous collaboration between laboratories from different disciplines), to push research as much as possible towards development.

Universities can have important influences during the firm's early life stages and the university indirectly influences the evolution path of a company. One can see that crucial decisions during the early life of a company is dependent on opportunity offered through their parent organisation, but also dependent on the background of the firm leader. The more the leadership is close to university institutions the more the founding team is inclined to stay as long as possible within the firm. This decreases with greater managerial and industrial competence as the need for independence is felt more strongly. In addition, there are opportunities for the university for firms to develop in their laboratories. For senior researchers the tendency is to choose to stay in the parent laboratory, whereas for start-ups emerging from PhD projects the decision can be more open and dependant on the opportunity.

General Conclusion

Conclusion

The aim of this thesis is to further the understanding of the entrepreneurial process, from opportunity recognition and decision to exploit, to the organisational process and the commitment to a path of evolution of a newly created firm. This is particularly central since firms in their infancy have a high failure rate due to numerous problems emerging along their creation process. Understanding the transition of an innovative process into the creation and early development of a company can therefore inform policy makers and institutions supporting start-ups in order to help bring the best support possible to these companies and reduce their failure rate.

In order to do so, the thesis has introduced the concept of entrepreneurial agency. The entrepreneurial agency is defined as the power of the entrepreneur to have an influence over his own decisions and the actions stemming from them. The entrepreneurial agency then aims to understand the freedom and constraining factors that the entrepreneur has in defining his own fate. In the results, the component representing this decision has been operationalised by examining the firm’s choice of general strategy and business model. The firm strategy has two advantages here: it firstly gives us some indication of the development path and the pace of growth that the entrepreneur wants to follow, and secondly it is observable in the early life of the firm. This indicator helps us understand what goals the entrepreneur pursues (e.g. independence, growth, innovation, public health improvement...) and if the entrepreneur prefers to be oriented towards a strategy that is very risky but with a high reward or a less risky strategy with lower gains. The strategy that the entrepreneur takes, also gives an indication of whether the firm is likely to grow quickly or not (through the ambitions of the entrepreneur, which is translated into the strategy of the firm). In addition, the strategy of the firm is observable early in the firm life, but actual growth and success factors can only be observed on a longer term. In summation, if the success and growth cannot be observed at the time of the study, then the strategy of the entrepreneur can alternatively be used as a proxy to understand his willingness to take risks for the survival and growth of the firm, or to ultimately push an innovation project to application.

The concept of entrepreneurial agency also introduces a framework in which to study innovative entrepreneurship. It emphasises different components, such as the agent (here the entrepreneur), the environment and the actions taken (which we assimilate into the early life stages of the firm). Chapter 1 (the literature review) has given us the opportunity to build on existing entrepreneurship and related theories to develop this framework.

On the one hand, entrepreneurship theories tend to highlight the incidence of the entrepreneur in his venture and assume that the entrepreneur is fully responsible for the success or failure of his company, through his experience and choice. On the other hand, other literature on evolutionary theory, organisational studies or innovation studies point to deterministic factors such as environment, competition or other organisations as part of the local innovation systems (such as incubators, financial organisations...), which also have an influence on the path of development of firms. These two views both support an extreme line of argument and do not consider a measured view of entrepreneurship in terms of both agency power and the freedom and constraining factors that can affect it. Thus the study does not aim at identifying variables that impact entrepreneurial outcome because lists of such variables have been described in the existing literature, but instead aims at understanding the interplay of influential variables and the entrepreneur's freedom of decision that affect the current development of the firm. The freedom of decision of the entrepreneur has been developed in this thesis with the introduction of the concept of entrepreneurial agency. This concept has been defined in this work by the application of human agency theory from the aspects of psychology found in entrepreneurship theory. Thus the thesis has developed this concept using a framework incorporating the active agent, which is embedded in the entrepreneur, the environment, which can impact both the entrepreneur and his actions, and finally the action in which entrepreneurship creates and organises a firm for opportunity exploitation. Consequently, the thesis looks to some extend at how these three components interact in the founding process.

Understanding processes is central in this thesis in order to understand triggering points at which the interplay of environment or technological context affects the agency of the entrepreneur and his freedom of decision. The complexity of this relationship meant that a quantitative study looking at the relationship between inputs and outcomes was not satisfactory. The methods used reflected the willingness to understand the complexity of the decision processes and the entrepreneurs' choices in the path of young firms.

The entrepreneurship theory has emphasised two views of the entrepreneurial action. Firstly the opportunity exploitation process (from recognition of an opportunity for profit to its exploitation) and secondly firm creation and its organisational process. This duality in definition has given rise in this thesis to the consideration of both processes, which both characterise the entrepreneurial action. As shown in the review of the literature (Chapter 1), both of these aspects are rarely considered together and thus the thesis has also aimed at characterising these coevolving processes.

The study therefore includes the study of different steps in the firm creation process in high-tech sector (here biotechnology), through two levels of observation: the innovative project at the origin of the firm creation, and the organisational level that triggers instability through organisational change between the parent organisation and the newly created firm. The study particularly focused on the influence of environmental factors on strategy decision (aim of Chapter 4 through the relationship between entrepreneur and capitalist), secondly the link between strategy building and leadership change (aim of Chapter 5), and thirdly the process behind the transition of an innovative project between a parent organisation and newly created company (aim of Chapter 6).

Returning to the research questions and contribution made in the analytical chapters.

As presented in the introduction, the aim of the research is to understand the interplay between environmental factors, technological context, human capital and entrepreneurial agency in the entrepreneurial process and the firm's early path of development. This section therefore emphasises the main contributions of the different chapters to the research questions, which firstly asks about the evolution from an innovative project into firm creation and early development and secondly looks at the entrepreneurial and environmental impact on this evolution.

Before discussing the co-evolution of the processes, we first return to the contributions that have identified factors that affect the entrepreneurial agency. Regarding the relationship between entrepreneur, environment and action, and thus on the determinants of entrepreneurial agency, Chapter 4 has shown that the **environment can have a significant impact on the entrepreneur's action and thus on the entrepreneurial process**. Chapter 4 firstly showed that external actors who have crucial resources for the firm (such as financial institutions) have a significant impact over the strategy of the firm and its business model, through their interactions with the entrepreneur. Hence, external actors affect the planning and action of the entrepreneurs in different ways. The results of the chapter emphasised the influence of the financiers both before and after investment. Thus the first result of the chapter showed that *the assessment of entrepreneurs over financing options influences their decision towards the business model put in place for the firm.* In this context, the entrepreneur plans his strategy and business model keeping in mind the financing options available to him. This is especially true for the entrepreneur willing to keep his agency over the duration of the firm life and therefore has to adapt his business model accordingly to exclude the use of risky venture capitalist financiers. There are also indirect effects, which includes the anticipation of the long term relationship with the financier. A second result of this chapter explained that *the entrepreneur's choice towards a specific type of financing restricts his future options for firm development.* The choice towards a type of financing are found to reduce the future options of the entrepreneur. On the one hand, the entrepreneur involving venture capitalist financing can lose his entrepreneurial agency, and is left with a limited influence over the business strategy and business model in the future. On the other hand, deciding to keep agency and not involving this type of financier may constrain the entrepreneur towards a less innovative option (especially when focused on high-risk, high-gain projects, such as human therapeutics projects). Additionally, the paper has shown that there can be a form of regional path dependency in which new firms prefer to adopt business models that are sustainable (from firms that are still alive) rather than adopting a model that appears very risky and which results in many firms disappearing on a regional level.

The environment is not the only component influencing the entrepreneur towards his strategy and evolution. Chapter 5 has shown how **the background of an entrepreneur can influence the firm during its early life stages**. Chapter 5 studied the process of decision over the firm strategy, taking into consideration the founder's characteristics and the effect of change of leadership over the firm strategy decision. Chapter 5 firstly put forward evidence of the process behind firm formation and the commitment towards a firm strategy, which firstly includes the formation of a founding team with a decision over leadership in the company, and secondly a negotiation between the founders over the firm strategy (the firm strategy being influenced by the environment but also the individual preferences of the founders). The chapter therefore discussed the impact of a change of leadership, together with the background of the leader, to understand the evolution of a firm's early strategy development. The entrepreneur's background has been proven to have an influence on the strategy of the firm. The chapter showed that entrepreneurs have ordinal preferences towards a strategy for their venture, since they are firstly concerned with employment before fulfilling their personal aspirations. These preferences and individual aspirations are also influenced by the background of each founder. Chapter 5 has differentiated between two types of entrepreneur background, the scientific background and the business background. The results have shown that the firm's *leaders with a scientific background are more inclined to pursue the initial project, since they are in general more motivated by social returns.* Our cases have shown that scientific leaders aim at pursuing scientific projects in order to pursue science and contribute towards human health, regardless of the risk. In contrast, *a firm's leaders with business backgrounds are more inclined to assess the risk involved in building the venture on the initial project before decidin on the firm strategy.* This assessment of the risk involves having a business strategy and business model that does not greatly jeopardise the chances of survival of the firm in the long term.

Chapter 4 and Chapter 5 have therefore both discussed the **decision of the entrepreneur over the firm's strategy**; the first involving external factors and the second involving factors belonging to the entrepreneur. Chapter 6 also partly contributed to this discussion regarding interplay between the environment, entrepreneur's background and the firm early evolution. Chapter 6 looked more specifically at the influence of the parent laboratory in the formation of academic spin-off companies. One of its results implied that *the founder's background influences the transition, firstly through the strength of their relationship with university and secondly through their cultural differences (open science culture vs. business world culture)*. Accordingly, the chapter has shown that the background of the entrepreneur influences his interaction with external organisations (such as the parent laboratory). It showed that *the stronger the firm's leader has a relationship with the university laboratory, the longer the firm tends to stay incubated within the parent organisation*, and thus benefit from crucial resources at the beginning of the firm's life. This result emerged from the differentiation of the scientific founder being a permanent or even senior member of the laboratory, compared to a former PhD student who had no statutory right in the university anymore. The results showed that the ease of access towards facilities within the laboratory was much higher for permanent members than for former PhD students. Thus the background of the firm founding team can also influence the opportunity available for the newly created organisation, and thus influence its early path of evolution. The chapter has also shown that if the newly created firm is led by an entrepreneur with a business background, the decision to move out of that parent laboratory quickly is more likely than with senior scientists.

Finally, we must emphasise some points that emerge from the study, which focuses on the **co-evolution of the innovative project behind the firm creation and organisation process emerging from it**. The entrepreneurial decision cannot be limited to only the decision of entry or opportunity exploitation, or the decision towards the strategy of the firm. Previous literature might hypothesise that both decision are aligned, however our case study has shown that in innovative entrepreneurship these two processes are not independent from each other and may even influence one another in some cases. The different chapters have contributed towards this understanding of co-evolution between the innovative project and the firm early development process. While Chapter 4 and Chapter 5 point towards this co-evolution through the proxy of decision over firm strategy, Chapter 6 goes further by representing this co-evolution in the form of a stage model.

In its study over financing decisions for the entrepreneur, Chapter 4 has linked this choice over firm financing to the early evolution of the firm through the business strategy chosen by the entrepreneur. The chapter has shown that in the case of a high-risk high-return project, the entrepreneur must usually make a choice between getting into the risky strategy of a product only model or a strategy that maximises the chance of survival of the firm. The first strategy can lead to the involvement of venture capitalists, which as the chapter has shown locks the firm into a project only strategy. On the other hand, if the entrepreneur values future agency or firm survival, he chooses to not involve such financing. Thus in this case, the entrepreneur has to choose between maximising the firm's chance of survival in the long term through a hybrid or service model. Thus consideration over agency or firm survival can in some cases supersede the innovative project development and thus lead to a separation between the interests of the project and the interests of the firm. This was also observed in Chapter 5. It has been observed that the background of the leader influences the choice over the firm strategy, with scientific founders pushing for innovative projects to be pursued, while business leaders consider the risk inherent to the project before deciding on the firm strategy. In some cases this leads to abandoning the original research project to re-focus the firm on other activities.

Finally, Chapter 6 developed the genesis of this co-evolution, by developing a stage model featuring the transition of the innovative research project from the parent organisation to a newly created organisation. In this case we only studied projects emerging from university, in order to focus on the transition of an innovative project from a university laboratory to a newly created firm. The study has shown that *the transition of a research project to a newly created firm evolves in a dialectic process and that there are different forces between the needs of the project and the institutional rules of the organisations that influence this process.* This transition has distinguished between three phases for this project transition. The first phase is characterised by the development of a research project that leads to the entry decision. This decision has been studied through the decision of scientists to pursue their projects outside academia. As a result, in our case the decision of exploitation can arguably be more science push oriented, due to our focus on academic entrepreneurship. The chapter showed that the entry decision can be broken down into two decisions, firstly whether or not to transfer a given technology and secondly whether this would be best done through firm creation. The first decision lies in the choice of transferring a given technology to the industry, through licensing to an existing company or through firm creation. Thus*, in the first phase, the researcher is driven by wanting to push his discovery/technology towards application, but at some point is limited by the rules of the institution (i.e. university) that he evolves in.* Venture creation may therefore be the only solution for the continuity of the project development.

The second phase in this process is characterised by an incubation period of the newly created company within the university. At creation time, the firm usually has little financing means and has to develop their organisation in terms of physical and human resources. In most of the cases, the firm takes advantage of the opportunity given to them to stay within the parent laboratory walls. While doing so they can access university facilities, materials and human resources at a reasonable cost, which are essential for the firm's early activities. Even though being incubated within the university has many advantages, it also comes with inconvenience when the firm is growing. Sharing resources and especially hiring labour from the parent organisation makes the boundary between the firm and the parent organisation blurred. The laboratory and the firm often have a distinct hierarchy, which can create confusion for labour hired within the firm who came from the university. Thus the phase is characterised by a trend *that causes the firm to form a close link with university due to their need of resources, which ultimately leads to a blurred organisational boundary. This leads the firm to seek independence from its parent organisation.* At this point in time, the newly created organisation often decides to relocate their activity outside university. Thus, *the third phase marks the independence of the firm with a redefinition of its relationship with its parent organisation.* In this phase, the relationships between the firm and the parent laboratory are redefined, which includes a redefinition of the role of the scientific founder (in the cases where he is not the leader of the firm). The firm activities also evolve over time towards the development of the project, and require different resources and labour from the parent laboratory compared to the earlier stages. As noted previously, these phases may vary depending on the background and leadership in the firm management team.

Altogether, the different chapters have shown that entrepreneurs have to weigh separately the decisions over the fate of the project and of the company when deciding on the firm strategy. At some stages the development of the research project goes hand in hand with the development of the firm, especially at firm creation. However, when leadership change or exogenous factors intervene, the survival and growth of the firm may be decided independently from the development of the research project and therefore their fate may no longer be linked. Chapter 5 presented two cases in which the firm leaders had to move away from the initial project. In the first case, this was because the firm activities and development would be hindered by advancing the research project, and the second because the project was not viable to develop anymore. Both cases have therefore shown that firm fate and project fate are not always linked over time, and in some case can develop independently from one another.

The different chapters therefore come together to help in understanding the triadic relationship identified in the literature review, together with the co-evolution of an innovative project with the process of firm early evolution. In order to understand the complexity of the processes, the triadic relationship is not studied as a whole but taken in pairs and used to understand the differences that lie behind the different evolution paths of new ventures.

What does this work imply and what is the continuity of this study?

The thesis also shows the limits of some expectations that policy makers have regarding their entrepreneurship policy. Consequently, we need to discuss the questions that arise from the results that have an impact on policy making. This work also has some limits, which will be discussed here. These reflections open a discussion for further research to be done in this field.

The introduction has pointed towards policy makers interests that could be discussed in the light of the results of this thesis. The aim of policy makers is to tackle issues such as employment, firm growth and national competitiveness. The general introduction pointed out that entrepreneurship theories can be used as a tool to both contribute to the employment objective through the creation of surviving firms and to the competitiveness objective by fostering highly innovative firms.

The question arises then of whether achieving innovation and employment growth is possible simultaneously. In order to foster innovation, policy makers look at university as a repository of knowledge that has a high potential for creating innovative companies. Entrepreneurship is often seen as a tool that bridges between science and industry and is believed to be a strong enabler of technology transfer. Technology transfer through the science push model has made entrepreneurship a tool for linking science to technology, with the idea that the firm is an ideal mode of transformation of a project, technology or product development in public science. The results of this study have pointed towards a complex co-evolution of the innovative project and the newly created organisation. They have pointed towards many organisational events (e.g. change in leadership, financial opportunities, organisational lock-in) that can have an impact on the continuity of the initial innovative project. This observation is also linked to the choice of the sector, in which product development (especially concerning human pharmaceutical) is a very lengthy and risky process to be carried by a newly created organisation. Policy makers, if concerned with a technology transfer policy, may also need to revise their idea about entrepreneurship as being a premium means of technology transfer, because as the results have shown, the initial project leader is not always ready and qualified to make a company, and involving external people to exploit the opportunity may change the focus of the company from a project oriented one towards a survival objective.

The idea of co-evolution has also shown that in life sciences the innovation objectives and the creation of sustainable jobs are not always compatible. In the case of biotechnology, firms aiming at developing human drugs are looking towards high-risk and high-benefit projects. The development of such types of projects rarely results in successful products. In our cases, Chapter 4 (section 6.1) described cases of firms that were involved in a drug discovery model, which generated high hopes because they attracted important capital investments, and in their early years grew to have between 20 to 46 employees each. However, due to their risky business models these firms encountered problems and had to close. Thus on a very short term basis, firms that are highly innovative and supported by venture capitalists seem to be a good solution for quick employment growth. Due to their innovativeness, these firms also have the potential to improve a territory's competitiveness. However, their ability to generate long term employment may be limited because these firms rarely survive in the long run. Thus, focusing on highly innovative firms may be attractive for policy makers, although they do not always deliver sustainable employments. Therefore, we argue that the objective of technology transfer and sustainable firm growth should be separated for policy makers. Technology transfer often requires costly development and may be a risky bet for building a sustainable employment strategy. For example, helping researchers to diffuse their knowledge, especially when they have contributed to find a potentially life-saving drug, will probably not create a durable company as the project may be highly risky and as a result may not survive the project. However, in order to build sustainable employment, policy makers may want to support less risky business models. While those firms may not grow as quickly as the earlier ones, they may bring more stability since the number of entrepreneurial failures for those types of firms may not be as high as with highly innovative firms. However, these firms may also have a limited impact on the overall competitiveness of a region.

The thesis may also be informative from a regional policy point of view, especially towards expectations in terms of innovativeness of a cluster. One of the main contributions of Chapter 4 is the relationship between the firm business model and the leader's needs and objectives. In this way, the chapter has pointed towards the employment security that must be acquired before a higher end aspiration. Thus, as Chapter 4 and 5 have emphasised, many entrepreneur's with a business background, after being employed in a venture that eventually had to close, faced unemployment problems and expressed their concerned about finding a qualified position locally. As a result, when the opportunity came to contribute to a venture creation, the priority of these entrepreneurs was to create a stable position for themselves and others, since the local employment market in the biotechnology sector was still limited. This constraint limited the entrepreneurs in their ambition and their willingness to risk a product oriented business model, which could potentially have been more innovative in outcomes and might have had a different impact on the firm in terms of growth pace but also at a regional level. This observation is not isolated only to the cases in this thesis, since other research has reported observations that have linked regional employment level with taking risk in a new venture in terms of innovation. An analysis of the Silicon Valley cluster has pointed towards a high mobility of labour (Saxenian 1996) and also the fact that the level of employment was low in the Information and Communication Technology (ICTs) industries, as described by Jackson (2000, p.24):

> "Of course there was a risk of failure. But everyone knew that a talented engineer could easily find work elsewhere if things didn't work out. There was no fear of long term unemployment to discourage risk taking"

Hence, one can hypothesise that the level of innovativeness and expectation by policies targeting firm to take risk in their venture must be measured against the availability of employment opportunities.

The study gave us the opportunity to firstly build a theoretical framework, the one of entrepreneurial agency, in order to study innovative entrepreneurship in a systemic way, and to then design an exploratory study to understand the features of this framework. The exploratory study through case studies is only a first step. In order to be able to use this framework broadly and to generalise the results, this framework must be tested in other contexts (e.g. other regions and other countries). However, these results can be considered as hypotheses generated in order to see if these observations can also be observed in other locations or even in other innovative sectors or on a larger scale. In addition to these direct observations, other hypotheses can be drawn from the cases and could be used in future research projects

The design of the methodology has an impact on both the number of variables and the complexity of the relationships studied, but also on the significance and scale of the conclusions drawn from the study. Indeed, a research methodology based on case studies was used to understand firstly the complexity of the co-evolution of the dual process involved in the entrepreneurial action, but also to gain a better understanding of its relationship with key components such as the entrepreneur and his environment. In order to carry out this in-depth analysis, one has to compromise on the scale and universality of the results. Consequently, the results and conclusions drawn in this thesis are only representative for the Alsace BioValley cluster.

The sector under study was chosen for its characteristics in terms of environmental factors and the diversity in terms of the background of firm's founder. In terms of regulation, the sector has a range of constraints that translate into a variety of risks for innovative projects developed by new firms. Thus this sector is unique, firstly in terms of the financing needed for the development of its products and in some cases the time to market for new products developed. Thus in the biotechnology sector, the reliance on external financing and the change of strategy at the beginning of its life were determinant factors. The specific cases of having projects based on drug discovery influenced firstly the need for financing of such a project to succeed and secondly the high number of strategy changes due to a change of leadership. Therefore, in this specific sector, one can observe the contradiction that may arise between the pursuit of a highly risky innovative project and the long term survival of a firm. The extension of the study to other high-tech sectors could help to conclude if such contradiction (between project development and firm survival) are specific to this sector. In the case of the biotechnology sector, a number of difficult choices are made by the entrepreneur concerning the trade-off between high-financing and control over the firm in the long term. He is also required to make a decision over the change of leadership to exploit the opportunity, but with a risk of strategy change by the new leader. This sector makes the early path highly sensitive to different factors, which may not be the case in other sectors. Thus the study of further sectors may confirm (or not) if such patterns are also observed elsewhere, and thus could be generalised.

The region under study also has specificities that have an influence on the results expressed in this study. As Chapter 3 section 3.1 and the analytical chapters have shown, the environment in which the firms evolved had characteristics that influenced the early life stages of the firms. Firstly, the region was specific in the sense that it hosted a university, which had a high degree of interaction with the newly created firms. Secondly, the firms also benefited from other organisations that are specific to the '*Pôle de compétitivité'*, which include among others the incubator, the availability of local risk financiers such as business angels, and a supportive cluster organisation. All of these organisations helped the firm during its early steps and supported the company in terms of financial and administrative aspects. One could therefore hypothesise that the early stages of a company would vary if these organisations were absent, and therefore the results in terms of the steps identified in the early evolution of the firm would be affected. Therefore, studies of a sample of firms outside of a cluster organisation, or a region without a connected university, would help redefine the steps of evolution of small firms in order to become closer to generalisation.

The sector under study together with the specific characteristics of the region has contributed towards a selection of innovation that was all linked to academic projects (directly or indirectly). Therefore, the study highlighted the difference of culture between an academic background and a business or an industry background. However, this gave us limited opportunities to study an innovative project emerging from the private sector and from a non-academic entrepreneur. Thus further studies should include innovative start-ups built upon innovation from an inventor originating from the private sector. Firstly, this will help us to understand if there are also changes in the leadership teams in these situations, and if those changes may also lead to differing preferences towards firm strategy. Such studies could also help us to understand the early firm creation process and development of such projects, which could be compared to the processes observed with university spin-offs.

Finally, the specific status and regulation in the French academia influenced the early evolution of both the innovative project evolution and the firm early development. This is because academic researchers have a specific status, which may also influence their behaviour in terms of academic entrepreneurship. Firstly, their status of civil servant in addition to the new law on innovation, enables them to create a company without leaving academia. They are able to take leave from university, which is limited to a few years, or can take a minority shareholder position in the firm that they create. Therefore, they can be encouraged to create innovative companies without having the risk of losing their academic position. Thus the study of other countries could be useful in order to understand the differences in the firm creation process, when the scientific founder status is different.

We believe that these topics may lead to further study in order to apply the concept of entrepreneurial agency in other contexts, such as other locations and sectors and therefore other systems of innovation. Further comparative studies could enlighten the specific characteristics of a sector or a location regarding the entrepreneurial path of development. In addition, further research could include the creation of theoretical models, such as real option models or models of decision making under risk. A real option model could help us understand the irreversibility or lock-in effects emerging from early decisions taken by the entrepreneur. Models featuring decision under risk could also be useful in order go further in understanding the question of why some entrepreneurs are more inclined to take on risky innovation projects while others prefer less risky options. Such a model would help us to understand how the background or situation of an entrepreneur influences his early strategy.

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Résumé en français

La situation économique en termes de croissance et d'emploi dans les pays européens est une source de préoccupation récurrente pour les dirigeants politiques. Une solution fréquemment implémentée consiste à inciter à la création d'entreprise. En effet, l'entreprenariat dans les domaines de l'innovation et des secteurs *high-tech* aurait pour avantage non seulement de créer des emplois durables, mais aussi d'avoir un impact sur la compétitivité. Afin d'atteindre ces objectifs, les décideurs politiques doivent compter sur les performances des firmes en termes de survie mais aussi de croissance et d'innovation. Des études empiriques ont montré que, pour la plupart des entrepreneurs, la décision de créer une entreprise résulte autant d'un besoin d'indépendance et de contrôle, que d'un objectif de profit (Cassar 2007; Oakey 1995), et seule une minorité d'entre eux aspire à une forte croissance pour leur société.

Ainsi, les aspirations des créateurs d'entreprises sont variées et l'évolution d'une organisation dans ses premières années de vie est donc difficile à anticiper. L'objectif de cette thèse n'est pas d'évaluer les firmes selon leurs résultats (i.e. emploi ou profit), mais de comprendre leur évolution en incorporant les objectifs individuels des fondateurs. Cette étude prend en compte les décisions de ces derniers par rapport à leur stratégie afin d'analyser les chemins d'évolution empruntés par chaque firme. Cette thèse peut donc servir autant aux gouvernants en vue d'améliorer leur soutien aux *start-ups* mais aussi aux entrepreneurs afin de les préparer aux problèmes qu'ils peuvent rencontrer dans leur projet.

Les premiers stades d'évolution des entreprises innovantes sont analysés ici tant sur le plan théorique, en faisant appel à la littérature sur l'entreprenariat, la théorie des organisations ou encore la théorie de l'innovation, que sur le plan empirique, *via* treize études de cas de *start-ups* dans le secteur des biotechnologies. Ce résumé présente l'objectif général de la thèse ainsi que le cadre conceptuel utilisé dans l'analyse. Il décrit ensuite les choix empiriques effectués, en précisant la méthode et les critères de sélection des études de cas. Il s'attache enfin à présenter les résultats organisés en trois chapitres analytiques, avant de conclure.

Objectif général

Le principal objet d'étude de la thèse se concentre sur le domaine de l'entreprenariat innovant. Ce concept incorpore deux composantes : premièrement le processus d'identification et d'exploitation d'une opportunité de profit (dans cette thèse via une innovation), et, deuxièmement, la création d'entreprise. Il s'agit plus précisément d'analyser le projet de construction d'une organisation depuis l'élaboration du projet d'innovation (i.e. avant la création) jusqu'au processus organisationnel mis en place lors du développement. Ainsi ce travail ne se limite pas seulement à la création de la nouvelle société en tant que telle. Elle s'attache à étudier deux processus potentiellement distincts : le développement organisationnel de la firme et l'exploitation d'une opportunité d'innovation. Néanmoins, la thèse considère que ces deux actions ne sont pas totalement indépendantes, et s'intéresse donc à leur co-évolution.

La problématique de recherche reflète le principal sujet de la thèse et peut être formulée de la façon suivante : *Comment le projet innovant évolue-t-il au court du processus de création de la firme?* L'étude considère que le développement du projet et l'organisation de l'entreprise dépendent des choix de l'entrepreneur à travers la stratégie développée. La question se pose alors de la marge de manœuvre qu'un dirigeant a réellement dans ses décisions, et donc des contraintes auxquelles il fait face. Cet arbitrage est développé théoriquement par la notion d'agence entreprenariale. Ce concept permet d'établir un cadre d'étude qui va expliquer l'influence de différents facteurs, tels que les facteurs environnementaux et ceux liés aux caractéristiques des entrepreneurs par rapport aux choix stratégiques de l'entreprise dans ses premières années de vie. La section suivante résume ce cadre conceptuel.

De l'entreprenariat à l'agence entreprenariale

Ce travail s'appuie sur la littérature entreprenariale afin de définir le concept d'entreprenariat innovant et d'introduire un cadre conceptuel adéquat pour analyser l'évolution de ces firmes dans leurs premiers stades de vie.

L'entreprenariat et son éventail de définition

La littérature sur l'entreprenariat est connue pour être hétéroclite tant du point de vue des définitions qui y sont associées, que des disciplines qui s'y intéressent. Une première différence peut être notée entre deux conceptions, l'approche microéconomique qui vise à comprendre la création d'entreprise et la perspective macroéconomique qui se concentre sur la fonction entreprenariale en tant que source de changement dans l'économie. Dans le premier cas, l'entreprenariat est considéré comme la décision d'un individu vers la création d'une entreprise et intègre ainsi une vision organisationnelle de cette notion (Cantillon 1755a ; Say 1803 ; Mill 1900). Dans le deuxième cas, l'entrepreneur a pour fonction l'exploitation d'opportunités qui entraine l'évolution macroéconomique d'un équilibre à un autre. Deux types d'opportunités sont identifiés par deux courants de littérature différents : les opportunités d'innovation (Schumpeter 1934) et les opportunités de compétition (Kirzner 1978). Ici, l'acte entreprenarial n'est pas par définition incarné par la création d'une organisation, mais associé à l'exploitation d'une opportunité. Dans la théorie économique, il n'y a donc pas de consensus sur la définition d'entrepreneuriat. Par conséquent, nous considérons que sa définition se base sur la combinaison de ces deux concepts, l'opportunité d'innovation et la création d'une entreprise. La thèse est construite à partir de cette définition, qui est développée plus en détail dans le cadre conceptuel. En somme notre travail étudie la firme innovante, que l'on peut scinder en deux objets distincts, l'exploitation d'une opportunité d'innovation et le processus organisationnel de construction d'une société.

Dans les théories traditionnelles de l'entrepreneuriat, l'accent est généralement mis sur l'entrepreneur en tant qu'individu, qui est responsable de la création et du développement organisationnel d'une firme (Cantillon 1755a ; Say 1803 ; Mill 1900), alors que d'autres théories le placent au centre de changements au niveau macroéconomique (Schumpeter 1934 ; Kirzner 1978). Dans ces dernières la notion d'entrepreneur via son action est le principal agent responsable de changements s'effectuant tant aux niveaux microéconomique que macroéconomique. Ainsi dans la lignée de la théorie entreprenariale, cette thèse se focalise sur la notion d'agence chez l'entrepreneur.

Le concept d'agence entreprenariale

Dans la littérature sur l'entreprenariat, plusieurs auteurs évoquent le concept d'agence (Shane 2003 ; Baumol 1993 ; Garud & Karnře 2003 ; Steinmueller 2010) mais ne le développent pas pour autant en détail. Ainsi, afin d'approfondir cette notion, nous nous sommes tournés vers le domaine de la psychologie, qui s'est attelée à ce sujet à travers la théorie de l'agence humaine. Cette dernière s'interroge principalement sur le pouvoir d'influence d'un agent sur son propre futur, considérant ses décisions et ses actions (Bandura 2006). Notre développement a pour objectif de combiner les approches déterministes, où l'agent est spectateur de son avenir, avec le concept d'agence autonome, où l'agent a un pouvoir total sur son futur. Une vue nuancée du pouvoir de l'agent entre liberté et déterminisme est ainsi avancée. Enfin l'agence humaine repose sur une relation entre trois types de déterminants qui ont un effet sur l'avenir de l'agent : sa personnalité, son action, et l'environnement dans lequel il évolue. Ces trois composantes sont la base du cadre conceptuel que nous appliquons à la théorie de l'entreprenariat, et que nous appelons agence entreprenariale. Ainsi la thèse cherche à expliquer l'influence de l'entrepreneur, celle de son action et celle de l'environnement sur l'avenir de la firme créée. La littérature sur l'entreprenariat, ainsi que la théorie des organisations et l'économie de l'innovation sont ensuite utilisées de manière complémentaire afin de comprendre et d'opérationnaliser les différentes composantes du cadre conceptuel.

Un premier axe de recherche se concentre sur ***l'entrepreneur***, et définit de manière pratique quelles caractéristiques lui sont associées. Premièrement, les contributions empiriques dans le domaine de l'entreprenariat, spécifiquement dans les secteurs *high-tech*, ont montré que les compétences requises pour identifier et exploiter une opportunité ne sont pas toujours incarnées dans une seule personne. En effet, le développement d'une technologie ou d'une invention jusqu'à la preuve de concept requiert souvent des capacités techniques, alors que le processus de création d'une entreprise ainsi que l'aspect d'industrialisation et de mise sur le marché nécessitent des compétences en gestion, en management et des connaissances industrielles (Schoonhoven & Romanelli 2001 ; Shane 2003 ; Delmar & Shane 2006 ; Bird 1989). Pour construire une entreprise qui va survivre et éventuellement grandir, un entrepreneur dans un secteur *high-tech* a besoin d'un panel de compétences. Même si, dans la théorie Schumpétérienne, ces dernières sont incarnées en un individu unique (Steinmueller 2010), en pratique il est rare que ces qualités soient regroupées en une seule personne. En effet, un nombre croissant de contributions se concentre sur l'introduction d'une notion d'entreprenariat partagé entre individus (Garud & Karnře 2003 ; Gartner et al. 1994 ; Burger-Helmchen 2008). Ainsi, l'action entreprenariale est, dans la plupart des cas, réalisée par un groupe de contributeurs. Dans ce travail, nous acceptons les conclusions de ces travaux empiriques et considérons comme entrepreneur toute personne contribuant à la reconnaissance ou à l'exploitation d'opportunités d'innovations, dont la création d'entreprise.

Un deuxième axe porte sur l'influence de ***l'environnement*** sur les décisions et l'action de l'entrepreneur. Cet aspect est en partie traité par la littérature sur l'entreprenariat mais connait des développements plus approfondis en économie de l'innovation avec les études sur les systèmes d'innovations (Edquist 2005) ainsi qu'en théorie des organisations, spécifiquement à partir de travaux sur la création d'organisations (Stinchcombe 1965). En effet, l'entrepreneur est confronté à des éléments extérieurs qui ont un impact sur ses décisions et contraignent son action. Cette influence ne concerne pas seulement les facteurs de marché ou les firmes concurrentes, mais aussi les dispositifs aidant les entreprises, comme les investisseurs ou les organisations publiques d'aide à l'innovation. L'un des domaines les plus développés dans les théories faisant le lien entre l'entreprenariat innovant et les facteurs environnementaux concerne le financement des *start-ups*. En effet, dans certains secteurs *high-tech*, et en particulier dans la biotechnologie, les firmes doivent rapidement lever des fonds suffisants pour survivre. Cette littérature s'est particulièrement intéressée aux avantages et inconvénients qu'implique un recours aux investisseurs à risque. Les

Venture Capitalist et *Business Angel* sont deux types de financeurs fréquemment utilisés. Les premiers sont souvent des organisations professionnelles qui regroupent de riches investisseurs privés finançant des projets très risqués. Les *Business Angels* sont plutôt des personnes individuelles, comme d'anciens entrepreneurs, cherchant autant à investir leur fortune qu'à participer à la réussite d'un nouveau projet d'entreprise. Ces deux types de financeurs diffèrent du point de vue du niveau de l'investissement et des retours demandés aux firmes. De plus, les financements à risque ne sont pas disponibles dans toutes les zones géographiques (ils sont très développés aux Etats Unis).
D'autres travaux comme ceux sur les systèmes d'innovation (Edquist 2005) ont aussi mis en évidence l'influence de certaines institutions et organisations sur les firmes. Les agences gouvernementales, les organisations de recherche, les concurrents ou encore les régulations ont un impact sur la *start-up* et influencent sa capacité non seulement à apprendre mais aussi à innover. Ces théories ainsi que celles liées aux systèmes technologiques (Malerba 2002 ; Geels 2004) mettent en avant les contraintes en termes de technologies, de marchés et de régulations que l'entreprise doit gérer. Enfin, la littérature sur les *clusters* et dynamiques régionales avance que des transferts de connaissances directs ou indirects sont possibles entre différentes organisations (e.g. organismes de recherches, entreprises…) (Marshall 1895 ; Audretsch & Feldman 1996 ; Porter 1998 ; Cooke 2007). Ainsi **l'entrepreneur doit être étudié par rapport au système dans lequel il évolue**, car ce système a un impact en termes de contraintes et d'opportunités, ce qui peut l'influencer dans ses décisions et dans son champ d'action.

Un dernier axe se concentre sur ***l'action de l'entrepreneur.*** Ce concept correspond ici à l'entreprenariat innovant, qui a été d'ores et déjà défini comme un processus double incluant l'exploitation d'une l'opportunité d'innovation et le processus de création d'une entreprise. Ces deux processus sont traités séparément dans les travaux sur l'entreprenariat, donc la thèse fait également appel à d'autres approches pour comprendre leur co-évolution. Ainsi trois littératures peuvent apporter des éléments pour caractériser cette action entreprenariale : la théorie de l'entreprenariat, la littérature sur l'innovation et enfin les théories de l'organisation. Elles sont complémentaires dans la compréhension de l'entreprenariat innovant.

La théorie des organisations contribue à identifier les besoins des entreprises, depuis leur création jusqu'à leur maturité. Elle se concentre principalement sur les changements organisationnels de l'entreprise, tels que ceux au niveau de l'équipe de management (Greiner 1997), ou les besoins évolutifs en termes de ressources (Garnsey 1998). Elle étudie l'évolution de la firme sur un niveau organisationnel, mais ne considère pas l'opportunité initiale qui est à l'origine de l'existence de l'entreprise. Elle est donc incomplète pour caractériser notre objet d'étude car **le**

projet d'innovation commence souvent avant la création de la firme. La littérature sur les processus d'innovation (Kline & Rosenberg 1986; Bush 1945), nous permet d'enrichir les modèles précédents et de les adapter à des *start-ups* exploitant des projets innovants. Ces contributions soutiennent qu'une partie seulement de ce processus est linéaire, allant d'une opportunité (émergeant de la science ou du marché) vers l'exploitation, le développement et l'industrialisation de l'innovation. La plupart de ces modèles mettent en exergue les liens constants avec la production de connaissances, ainsi que les liens rétroactifs entre les différentes phases. Enfin, certaines études sur l'entreprenariat combinent le projet d'innovation et la création de la firme. Contrairement à la théorie des organisations, leur analyse ne se borne pas à étudier l'entreprise à partir de sa création administrative, mais inclut aussi la reconnaissance d'une opportunité pour l'exploitation (Shane 2003). Par contre la création de l'organisation est considérée comme une unique étape dans ce processus et ne prend pas en compte la possibilité d'une co-évolution. Or la prise en compte simultanée de la fondation d'une firme et du développement du projet innovant est une des principales sources d'investigation et donc une des contributions de ce travail de thèse.

Le concept d'agence entreprenariale est au cœur de notre travail et l'interaction entre ses différentes composantes implique l'adoption d'une vision holistique. Ce cadre conceptuel est l'un des apports de la thèse car il intègre différentes notions étudiées dans l'entreprenariat, comme les qualités de l'entrepreneur et l'étude de son action. Le point de vue systémique que nous proposons, par le biais de l'inclusion de l'environnement, permet aussi d'amener de nouvelles dimensions à cette théorie. L'agence entreprenariale permet aussi de cerner les contributions des chapitres analytiques. En effet ceux-ci se focalisent non seulement sur les interactions des aspects liant l'action entrepreneuriale aux caractéristiques de l'équipe dirigeante (Chapitre 5) mais aussi sur l'environnement dans lequel l'entrepreneur évolue (Chapitre 4 et 6). En outre, tous les chapitres analytiques s'intéressent à l'évolution du projet innovant et au processus de création et développement de la firme, mais ces aspects sont davantage approfondis et formalisés dans le Chapitre 6.

Cadre Empirique

La méthodologie se concentre sur des études de cas, car c'est la méthode la plus appropriée pour répondre à la question de recherche posée. Elle est pertinente dans la mesure où elle est particulièrement adaptée à la compréhension et l'analyse de processus ou de mécanismes (Yin 1994). De plus notre travail met en perspective l'interdépendance d'un double objet d'étude, la co-évolution d'un projet innovant et d'une création d'entreprise en relation avec son environnement. L'analyse de l'interaction entre ces différents niveaux ajoute à la complexité de l'étude, ce qui est plus facilement pris en compte par des études de cas (Collins & Noblit 1978). La thèse se concentre sur une étude de cas multiple, afin de voir si les observations faites sur les firmes individuelles sont propres à leurs activités, ou sont partagées avec d'autres organisations. Ainsi pour minimiser les effets de variations dues à l'environnement, l'étude se base sur une logique de réplication (Yin 1994). Elle explore les spécificités d'un seul secteur et un seul système d'innovation local. La thèse repose ainsi sur l'étude de *start-ups* innovantes implantées dans un *cluster* spécialisé dans la biotechnologie, la BioValley alsacienne. Tant le secteur que la localisation géographique résultent d'une décision élaborée qui est expliquée dans les sections suivantes.

Le secteur de la biotechnologie

La biotechnologie offre plusieurs avantages pour étudier l'entreprenariat innovant. Un premier argument est que ce secteur est en croissance, et a donc un fort potentiel pour la création d'entreprises. Deuxièmement, les firmes dans ce domaine ont une activité importante de recherche et développement et, par conséquent, elles répondent au critère d'innovation posé par notre étude. En effet, les entreprises nouvellement créées émergent autant à partir d'organisations de recherche publique (Cavazzana-Calvo & Debiais 2011 ; Pisano 2006a) que d'entreprises privées. Bien que l'étude se concentre sur un seul secteur, celui-ci offre des possibilités d'applications dans des domaines variés comme la santé, l'environnement ou l'industrie. Pour éviter une trop grande variété de domaines d'application (c.f. principe de réplication), nous nous limitons à la santé. Ce choix se fonde sur deux raisons principales : premièrement ce domaine est d'utilité publique et par conséquent il fait l'objet de politiques publiques spécifiques pour favoriser son expansion, et, deuxièmement, il conserve toutefois une certaine diversité dans ses industries d'application. En effet, l'industrie pharmaceutique (qui est la plus connue à ce jour), celle du diagnostic, des cosmétiques et même les aliments fonctionnels intègrent les biotechnologies. Ces différentes applications permettent une étude de facteurs environnementaux, comme les structures et chaînes de valeurs, les tailles de chaque marché, la pression de la concurrence ou encore les variations d'ordre juridique. Par exemple, le marché pharmaceutique est hautement règlementé, exigeant un processus d'étude clinique complexe, ce qui rend le développement de produits pharmaceutiques long et coûteux, et est donc très risqué pour de nouvelles firmes. En ce qui concerne l'industrie du diagnostic, les réglementations sont différentes selon que le produit est invasif ou non. Dans le premier cas, les régulations sont quasiment aussi contraignantes que dans le domaine pharmaceutique, par contre, dans le second cas, les tests se limitent à la preuve de concept, et la mise sur le marché est potentiellement beaucoup plus courte. Enfin, pour la cosmétique et les aliments fonctionnels, la régulation est minimale, ce qui permet aux firmes entrantes d'avoir un temps de mise sur le marché beaucoup plus court que pour les produits pharmaceutiques. Ainsi, même en choisissant un seul secteur, celui de la biotechnologie s'appliquant à la santé, nous pouvons trouver des cas confrontés à des contraintes extérieures variées.

La BioValley Alsacienne

Le choix du système d'innovation se porte sur la BioValley, qui est localisée en France, plus particulièrement en Alsace. La BioValley alsacienne comporte plusieurs avantages pour l'étude de firmes en biotechnologie. Premièrement, elle se situe dans une région très dynamique, où tant les organisations publiques que privées contribuent au développement local dans le secteur de la chimie et de la pharmacie. En effet, l'Alsace a une longue histoire d'excellence scientifique dans ces domaines, et plus récemment aussi en biologie. Sa réussite se traduit par plusieurs prix Nobel dans ces disciplines, et un positionnement de l'Université de Strasbourg dans les 100 premières places du classement de Shangai. Par sa proximité avec le Canton de Bâle en Suisse, la BioValley profite également d'un rayonnement industriel important avec la présence de nombreux groupes pharmaceutiques comme Clariant, Novartis ou Roche. En outre elle abrite des entreprises spécialisées en biotechnologie depuis les années 1970, ce qui coïncide avec la période des premières créations de firmes dans ce domaine au niveau mondial. Elle comprend enfin une variété d'organisations soutenant les activités de jeunes entreprises, tant sur un plan financier qu'organisationnel. Ce tissu industriel dynamique, en particulier dans le secteur de la biotechnologie, a été décisif dans le choix de cette région pour nos études de cas.

Collection des données

Ayant justifié le choix du secteur et de la région géographique, cette section détaille le processus d'identification des entreprises étudiées dans le cadre des études de cas.

Une première étape a consisté à identifier les entreprises du *cluster* par le biais d'une collecte de données à partir de différents sites internet, comme celui de l'incubateur local et de la chambre de commerce régionale (alseco), et de coupures de presses trouvées sur les sites d'Alsace BioValley ou Factiva. Les résultats de cette recherche ont été recoupés avec une liste d'entreprises élaborée par l'organisation Alsace BioValley, ce qui a abouti à l'identification de 223 entreprises appartenant au cluster. D'autres données ont aussi été récoltées comme leur date de création, leur taille en termes d'employés, et si ces firmes sont toujours en activité.

La collection des données qualitatives s'est divisée en deux parties. La première s'est focalisée sur une série *d'interviews* avec des experts, afin de mieux comprendre l'environnement dans lequel les nouvelles entreprises évoluent et les problèmes qu'elles rencontrent. Elle a permis aussi d'avoir des avis sur l'identification de cas ayant un parcours intéressant tant au niveau des difficultés rencontrées que du potentiel de réussite. La deuxième partie des *interviews* était orientée directement vers les créateurs de jeunes entreprises innovantes. Elle s'est déroulée en deux étapes. La première a consisté en une phase pilote, afin d'améliorer la sélection des cas et les lignes directrices du questionnaire. Les entretiens étaient de forme semi-structurée, et avaient pour objectif de récolter des données sur trois thèmes, en commençant par l'historique de l'évolution du projet innovant avant la création d'entreprise, avec des questions sur l'influence du financement et du marché sur cette évolution. Il s'agissait dans un second temps de comprendre la dynamique et les spécificités de l'équipe managériale de la firme, tant en termes de compétences qu'en termes de prise de décision. Enfin, la dernière partie de l'entretien s'intéressait aux relations que l'entreprise entretenait avec d'autres organisations et cherchait à comprendre les stratégies en termes de droits de propriétés et de publication de la firme nouvellement créée.

Les *interviews* ont été généralement conduites avec deux personnes ayant pris part à la création de l'entreprise et ayant différentes expériences (surtout du point de vue scientifique et managérial). Cette stratégie a deux avantages. Le premier concerne la complémentarité des informations ; le scientifique ayant souvent un rôle plus important dans la période de recherche avant la création d'entreprise, alors que le manager détient plus d'informations sur la création et la gestion de la firme. Deuxièmement, au niveau de la compréhension des rôles managériaux, nous obtenons deux points de vue distincts sur la création d'entreprise. Malheureusement la disponibilité des fondateurs a été une contrainte et, dans certains cas, le nombre *d'interviews* par firme s'est réduit à une seule.

Les entretiens pilotes ont mis en avant le besoin d'interroger des responsables de firmes âgées de moins de 5 ans car certains participants trouvaient difficile de se souvenir des étapes précédant la création d'entreprise, et des difficultés rencontrées à ce moment là. La contrainte d'âge a réduit le nombre potentiel de cas à 21 entreprises. Toutes ces firmes on été contactées, et treize d'entre elles ont accepté de participer à notre étude. Parmi ces dernières neuf ont été identifiées comme *spin-offs* d'organisations publiques, dans la mesure où leur équipe de management incluait un scientifique issu du monde académique, et où des données secondaires ont permis d'identifier que ces projets résultaient de projets universitaires. Trois autres entreprises sont issues d'autres *start-ups* de la BioValley, et la dernière émane d'un grand groupe pharmaceutique de Bâle, cette classification s'appuyant toujours sur la base de l'équipe de management. Par contre, après l'analyse des études de cas, il est apparu clairement que toutes les entreprises avaient de près ou de loin bénéficié des apports d'universitaires dans leurs projets d'innovation (généralement localement).

Chapitres analytiques

Les résultats des études de cas sont présentés dans trois chapitres analytiques, qui prennent la forme d'articles indépendants. Chacun d'entre eux aborde un ou plusieurs thèmes relatifs au cadre théorique développé autour du concept d'agence entreprenariale. Certains des chapitres se focalisent sur l'influence de l'environnement et d'autres sur les caractéristiques de l'entrepreneur en relation avec son action. Ceci nous permet de mettre en exergue l'influence de ces deux composantes sur la co-évolution entre le processus d'exploitation de l'opportunité d'innovation et le processus de création de l'entreprise.

Chapitre 4

Créer une firme innovante, spécifiquement dans le domaine de la biotechnologie, nécessite des ressources financières très importantes. En effet dans ce secteur, bon nombre d'entreprises, en particulier celles visant le marché du médicament, ont des besoins de financement élevés et recourent souvent à des capital-risqueurs. Les financements se font dans une phase risquée de l'entreprise et, selon leurs contributions, les investisseurs demandent des contreparties contraignantes aux entrepreneurs. Ce chapitre analyse l'impact de la contrainte de financement, premièrement sur l'agence entreprenariale et deuxièmement sur l'évolution de la firme.

Afin d'identifier le lien entre le choix du financement et l'évolution de l'entreprise, ce chapitre utilise le *business model* comme variable intermédiaire. Le *business model* d'une *start-up* comprend les activités développées sur le court et moyen terme. Ces activités assurent la survie de la firme et vont lui permettre de réaliser des objectifs de plus long terme. Cette stratégie est caractérisée par les activités qui vont constituer son avantage compétitif.

Ce chapitre distingue deux types principaux de financeurs à risque : ceux de type *venture capitalist* et ceux de type *business angel.* Les *ventures capitalists* sont des organisations professionnelles qui financent des projets très risqués et à fort potentiel de profit. L'accès à ces fonds est souvent accompagné de nombreuses contraintes : suivi de la part des capital-risqueurs, décisions sur la formation de l'équipe managériale, financement par étape,... Ces exigences se traduisent par un pouvoir de l'investisseur sur le *business model* de l'entreprise et donc aussi sur sa stratégie. Dans ce cas, les firmes sont incitées à prendre des risques et à se développer rapidement, afin de générer des profits importants qui couvriraient les pertes engendrées par d'autres projets qui auraient échoué. Les *business angels* sont, eux, des investisseurs individuels qui ont une capacité de financement moindre que les *venture capitalists*, mais sont moins exigeants. En effet, les *business angels* n'ont aucun pouvoir de décision sur l'entreprise mais peuvent néanmoins avoir un rôle de conseil afin d'aider la *start-up* dans la construction de son *business model*. **La décision envers le niveau et le type de financement est cruciale, car elle va contraindre la firme en ce qui concerne sa capacité à développer son projet d'innovation mais aussi la liberté de l'entrepreneur à prendre ses propres décisions**.

Le chapitre montre que différents facteurs influencent le choix de financement, comme les préférences de l'entrepreneur par rapport à sa volonté de garder le contrôle de sa *start-up* sur le long terme. Les études de cas révèlent aussi que les expériences de firmes formées dix ans auparavant dans le même secteur ont influencé un bon nombre d'organisations créées par la suite. En effet, il y a eu une importante vague de *start-ups* dans le domaine de la biotechnologie vers la fin des années 1990 et le début des années 2000 dans la région. Une grande partie de ces firmes n'existe plus aujourd'hui, en particulier celles qui ont eu recours à un financement risqué, de type *venture capitalist*. Les firmes de la génération précédente qui ont réussi non seulement à survivre, mais également à croître, sont celles qui ont un *business model* incluant des prestations de services et par conséquent n'ont pas opté pour un financement à risque. Ainsi, les entrepreneurs actuels ont la perception que ce type d'investisseur est lié à une perte de contrôle sur les choix relatifs à la stratégie de l'entreprise. Les résultats montrent que certains des entrepreneurs qui ont créé leur entreprise après 2006 et qui avaient des contacts directs ou indirects avec leurs prédécesseurs ont tenu compte de ces expériences antérieures. Ils ont donc décidé d'adapter leurs *business models* afin d'éviter ce type d'investisseurs. Ils se sont orientés en général vers des *business models* intégrant en partie des activités de services, ce qui permet d'assurer leur survie à court terme et de développer leur projet d'innovation en toute indépendance sur le plus long terme.

Ce chapitre montre que certains acteurs extérieurs (i.e. les entreprises de la génération précédente et les investisseurs extérieurs) ont une influence sur le développement de l'entreprise, en particulier sur le choix du *business model* par l'entrepreneur. **Le chapitre met également en évidence une forme d'apprentissage régional et inter-générationnel concernant les pratiques de gestion de l'entreprise**.

Chapitre 5

Un deuxième chapitre analytique (Chapitre 5) étudie le lien entre les caractéristiques de l'entrepreneur et les premiers stades de vie de l'entreprise. Ce chapitre se focalise sur les balbutiements organisationnels d'une firme, c'est-à-dire sur la période de mise en place d'une équipe de direction. Il s'agit de comprendre comment l'évolution de l'équipe de management et le choix d'un *leader* influencent le développement du projet d'innovation à l'origine de la firme.

Les changements d'une équipe de management peuvent être dus à deux types de raisons. Premièrement l'inventeur reconnaissant l'opportunité d'innovation ne souhaite pas être à la tête d'une entreprise. Deuxièmement, la gestion d'une entreprise innovante requiert, dans la plupart des cas, un panel de compétences que l'inventeur ne possède pas.

En ce qui concerne le premier effet, la littérature a montré que les inventeurs ne sont pas toujours ceux qui exploitent l'opportunité d'innovation jusqu'au bout. Des contributions récentes se sont intéressées à l'entreprenariat en tant qu'action collective (Garud & Karnře 2003 ; Gartner et al. 1994 ; Burger-Helmchen 2008), alors que notre travail met plutôt l'accent sur le cas d'un passage de relais entre l'inventeur et le créateur d'entreprise qui va être chargé de continuer le projet d'innovation.

Un modèle conceptuel en deux étapes a ainsi été développé à partir de la littérature existante. Il a pour objectif de représenter le processus organisationnel enclenché lors la création d'une *start-up*. La première étape représente la construction de l'équipe managériale, alors que la seconde explique comment la stratégie de la firme est décidée. Lors de cette construction organisationnelle nous pouvons dans certains cas observer un changement de dirigeant.

Ainsi, un nouveau *leader* à la tête de l'entreprise peut, par hypothèse, avoir un impact sur la stratégie et le choix des activités. Le chapitre considère que l'expérience et la culture de l'entrepreneur peuvent avoir une influence sur ses préférences en termes de stratégie. Dans nos études de cas, beaucoup d'entreprises ont démarré sur la base de projets académiques qui sont dirigés par des universitaires avant la création d'entreprise. La littérature sur la sociologie de la science a montré que les individus ayant choisi une carrière académique développent une culture propre. Ainsi cette institution incite et récompense la création et diffusion de nouvelles connaissances (Merton 1979). Cette culture peut avoir un impact en termes de valeurs entreprenariales, qui vont être plutôt orientées vers le transfert de technologie et l'application industrielle de projets développés par la science. Le dirigeant qui vient du secteur privé, n'étant pas exposé à cette culture, a d'autres valeurs qu'un chercheur académique, ce qui peut déterminer ses préférences en termes de stratégies. L'entrepreneur industriel est focalisé sur une culture visant des objectifs liés au développement de l'entreprise, tels que la survie de cette dernière, le profit qu'elle génère et éventuellement sa croissance. Ces objectifs peuvent varier car des études empiriques montrent que certains fondateurs préfèrent limiter le développement de leur société (Benz & Frey 2008 ; Cassar 2007), alors que d'autres aspirent à une croissance poussée.

Ce chapitre s'intéresse ainsi à la nouvelle répartition des rôles entre les membres responsables de la gestion de l'entreprise et l'impact d'un changement de direction sur la continuité et la centralité du projet innovant. Ce changement peut mener à une stratégie générale différente lorsque le nouveau *leader* a une autre vision pour le devenir de l'organisation.

Les résultats montrent que **les différences de culture influencent le choix de l'entrepreneur en termes de priorités au sein de l'entreprise**. En effet un dirigeant venant d'un milieu académique va en général préférer l'aboutissement du projet d'innovation à la survie de l'entreprise. Par contre, celui issu du secteur privé va tout d'abord évaluer les risques liés aux projets avant de prendre une décision sur la priorité à donner à la poursuite du projet, gardant comme priorité la survie de la firme créée.

Cette partie fait donc le lien entre les caractéristiques de l'entrepreneur et leur impact sur la stratégie générale de l'entreprise. **Le changement de *leader* peut influencer la décision de poursuivre le projet d'innovation initial, mais aussi le chemin d'évolution de la *start-up***.

Chapitre 6

Après avoir discuté de l'influence de certains facteurs sur les décisions de l'entrepreneur dans les deux chapitres précédents, le dernier chapitre (Chapitre 6) s'intéresse aux étapes d'évolution du projet innovant vers la création d'une entreprise. Focalisé sur les *spin-offs* résultant de projets initiés dans le milieu académique, ce chapitre analyse la transition entre le développement d'un projet d'innovation incubé dans une université jusqu'au début de la création de l'entreprise censée développer ce projet. Il retrace l'ensemble du processus de création dont certaines étapes ont déjà été détaillées dans les chapitres précédents.

En effet, à partir des différentes littératures sur les *spin-offs,* comme celle sur l'entreprenariat et les théories de l'innovation, ce chapitre développe un modèle conceptuel qui prend la forme d'un processus de transition à trois phases. Dans une première phase, le projet d'innovation est encore incubé dans l'organisation parente, c'est-à-dire l'université, et se transforme en projet de création d'entreprise. Une deuxième phase se caractérise par l'incubation de l'entreprise nouvellement créée dans l'organisation parente. Enfin, la troisième constitue une phase d'indépendance de la *spin-off* par rapport à l'organisation parente, *via* entre autres la sortie de la période d'incubation et la redéfinition des relations entre les deux organisations. Le chapitre s'intéresse aussi aux spécificités des facteurs qui déclenchent cette transition. Celles-ci sont liées en particulier aux caractéristiques de l'entrepreneur et, notamment, sa relation avec l'université. Enfin le chapitre a pour objectif d'identifier si la transition entre les étapes identifiées est différente selon l'entrepreneur ou l'équipe managériale mise en place lors de la création de la firme.

Le premier résultat important de l'étude est **l'évolution dialectique que suit le projet d'innovation dans ses premières années de vie.** En effet, dans les deux premières étapes, les cas étudiés poursuivent un processus cumulatif qui mène à une contradiction, aboutissant à la transition vers la phase ultérieure. La première phase se qualifie par un processus dans lequel un chercheur va être poussé par sa culture à poursuivre un projet scientifique vers une application industrielle. En effet, récemment, l'économie de la science a montré que les chercheurs académiques sont de plus en plus incités à interagir avec le secteur privé, et à pousser leur projet scientifique vers une application industrielle, notamment par la voie du dépôt de brevet. Notre étude de terrain a confirmé que les universitaires étaient motivés par la poursuite de leur projet de recherche vers une application industrielle. Toutefois, il leur devient peu à peu difficile de continuer de telles activités au sein du laboratoire de recherche, car l'université a pour but premier la création de connaissances, et non l'exploitation de projets. Ceci se fait surtout ressentir du point de vue des financements accessibles au chercheur au sein de l'université. Cette première phase se termine par la création de l'entreprise, car c'est, dans la plupart des cas, le seul moyen pour l'universitaire de continuer son projet innovant et le pousser vers une application.

La deuxième phase commence par la création de l'entreprise qui, comme nous l'avons vu dans le Chapitre 5, peut engendrer des changements organisationnels, surtout concernant le *leadership* du projet. A ce stade l'entreprise est souvent incubée au sein du laboratoire parent. Cette situation est avantageuse pour la jeune firme, car elle n'a généralement ni les ressources en termes de capital humain, ni celles en termes de financement, pour être opérationnelle dans sa phase de création. Ainsi, le laboratoire parent peut être d'une grande aide dans les premiers stades de vie de l'entreprise car il permet un accès facilité à des ressources cruciales pour son développement. Par contre, le fait d'être incubé au sein d'une organisation de recherche publique peut poser des problèmes. En effet, la *spin-off* va souvent recruter son propre personnel au sein du laboratoire parent, ce qui peut créer une confusion organisationnelle. Les employés peuvent avoir l'impression d'être sous une double hiérarchie, celle du laboratoire et celle de la firme (spécifiquement lorsqu'il y a eu un changement de *leader* à la tête de l'entreprise). Ainsi, l'équipe de management ressent le besoin de créer des frontières claires entre les deux organisations, ce qui passe par l'indépendance de l'entreprise. Cette dernière va devoir trouver ses propres locaux et déménager du laboratoire.

Enfin, la troisième phase se caractérise par la redéfinition des liens entre le laboratoire parent (et les membres scientifiques fondateurs de l'entreprise) et la *start-up*.

Un deuxième résultat important est que **l'équipe managériale mise en place lors de la transition, spécifiquement le *leader* et son lien avec l'université, influencent la rapidité à laquelle l'entreprise quitte les locaux du laboratoire académique**. Cela dépend de la volonté d'indépendance envers le laboratoire, d'une part, et des opportunités proposées, d'autre part. Trois types de profils ont été identifiés : les dirigeants d'entreprises issus du milieu académique, ceux qui viennent du secteur privé, et enfin ceux qui sont d'anciens doctorants. Les phases sont légèrement différentes selon l'expérience des fondateurs. Pour ceux venant de fonctions académiques, il n'est souvent pas un problème de rester incubé dans l'organisation parente car l'équipe dirigeante dans le laboratoire et la firme ne diffèrent que légèrement. Les entrepreneurs venant du secteur privé ressentent davantage le besoin de créer des limites entre le laboratoire et l'entreprise. Ils ont donc tendance à écourter la deuxième phase. Enfin, les doctorants, qui ont des liens moins privilégiés avec le laboratoire parent (car ils n'ont souvent pas de position permanente au sein de ce dernier) n'ont pas toujours l'opportunité d'y être incubé. Dans notre étude de cas, ces entreprises ont été incubées dans d'autres laboratoires ou incubateurs pour une durée prédéfinie.

Conclusion

Cette thèse a pour but de comprendre les premières étapes de vie des entreprises innovantes. A travers une étude de cas sur des *start-ups* en biotechnologie, cette thèse contribue à la littérature existante en introduisant théoriquement le concept d'agence entreprenariale et en y apportant de premiers résultats empiriques. Elle met aussi l'accent sur une évolution interactive entre le processus d'innovation et le processus de création d'entreprise.

Le concept d'***agence entreprenariale*** a été introduit de façon théorique, afin de s'interroger sur la marge de manœuvre de l'entrepreneur par rapport à son pouvoir de décision et d'action. Les résultats ont montré non seulement l'influence de l'environnement, mais également celle du parcours et de la culture du créateur de la firme sur ses décisions et le développement de la *start-up*. Le Chapitre 4 et le Chapitre 6 ont conclu que la question du financement et les liens avec le laboratoire parent ont une influence sur les décisions prises par le fondateur. La décision envers un type de financement est importante car ceci influence la poursuite du projet innovant et le pouvoir de décision du dirigeant. L'université et le laboratoire parent peuvent aussi ouvrir des opportunités aux créateurs d'entreprises, grâce à un support de leurs activités dans les premières années de vie de la *start-up*. Ces chapitres ont montré que l'environnement peut avoir une influence déterminante sur l'agence entreprenariale. Le Chapitre 5 a mis en avant que la culture et l'expérience des dirigeants a un impact sur leurs décisions à travers la stratégie de la firme. En effet, il apparait que la culture académique pousse le fondateur vers une préférence pour le projet scientifique d'origine, alors que, du moins dans les cas que nous avons étudiés, ceux venant du secteur privé préfèrent assurer la survie de la firme avant de se lancer dans un projet risqué.

L'agence entrepreneuriale a ainsi des conséquences en termes de l'évolution sur les premiers stades de vie de la firme. En effet, la thèse a mis en avant ce double objet d'étude qui est le projet d'innovation concomitant avec la création d'entreprise. Ainsi l'étude a pu donner des informations sur la ***co-évolution*** de ces deux processus. Les chapitres analytiques ont montré que dans certains cas, non seulement les facteurs extérieurs à la firme, mais aussi les caractéristiques de l'entrepreneur ou le changement de *leader* peuvent influencer le choix d'une stratégie orientée plutôt vers la firme où vers le projet. Ainsi, après la création de l'entreprise, le développement de l'organisation ne se fait pas toujours par rapport à l'évolution du projet innovant de départ, mais nous pouvons observer dans certains cas la divergence des deux objets, projet et entreprise. En effet, œuvrer pour le bon développement la firme ne va pas toujours de pair avec la poursuite du projet initial.

Les résultats énoncés ci-dessus peuvent s'avérer utile lors de la conception de politiques publiques. En effet les cas ont mis en évidence le choix qui se posent aux firmes, entre créer une organisation qui a des chances de survivre à long terme et créer des emplois viables, *versus* développer un projet d'innovation risqué. Nous pouvons en conclure que les politiques relatives à l'entreprenariat ne doivent pas toujours pousser au double objectif d'innovation et d'emplois, car en pratique ils ne sont pas toujours compatibles.