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Development of SMEs and heterogeneity of trajectories: the case of biotechnology in France

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Abstract

Biotechnology is an emergent sector based on the creation of research-intensive Small and Medium Enterprises (SMEs). While some SMEs are growing, most of them remain small, even those set-up several years ago. What is the pattern of development of

the biotech sector? What are the patterns of development of firms? Studies on the development of high-tech SMEs have focused on a business model, in which entrepreneurs rely on growth forecasts to persuade capital investors (business angels and venture capitalists) to invest in a radical innovation project. Firms aim for a world market to industrialise their innovation, and initial public offering (IPO) enables initial investors to make profits that offset risky initial investment. While this model is appealing, it is simply one of the possible models of biotechnology development. Some firms are not designed to experience exponential growth, and choose to target local markets. Moreover, not all firms have the ambition of being listed on the stock exchange. Based on an in-depth analysis of the business and development of 60 French biotech SMEs, this article identifies two business models. By defining the development trajectories of each of these models, it highlights the temporary nature of the emergent model. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

Biotechnology is one of the emergent sectors whose development is largely based on the creation of research-intensive SMEs. In France, the number of new biotech SMEs is skyrocketing, from fewer than 10 new firms per year a decade ago, to more than 30 in 1998. However, while some SMEs are growing, most of them remain small, even those set-up several

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years ago. What is the pattern of development of the biotech sector? What are the patterns of development of firms?

Studies on biotechnology development have focused on a business model that emerged along with the development of high-tech SMEs. Based on a radical innovation project, a group of entrepreneurs creates a firm designed to grow fast. These entrepreneurs rely on optimistic forecasts of a promising scientific breakthrough to convince capital investors (business angels and venture capitalists) to fund their technological developments. The firm targets an international market in which it can industrialise its innovations and

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generate a comfortable income. Initial public offering (IPO) enables initial investors to make profits that offset risks taken at the outset. While this model is appealing, both in its ability to link up scientific discovery and economic valorisation of science, it is only one of the possible biotechnology development models. Some firms are not designed for exponential growth and target only a local market. Moreover, not all firms have the ambition of being listed on the stock market. Even if going public depends partly on age and on timing (there are periods when the window is open, and periods during which going public is very difficult), fewer than 30% of biotechnology firms are listed in the US and fewer than 7% in Europe. Biotechnology firms, therefore, develop along the lines of several models that have to be described and understood if the evolution of the sector, relations between the actors involved and the effects of public policies are to be understood.

The main features of the biotech sector (sciencebased, importance of start-ups, and heterogeneity of actors involved) are helpful in understanding its dynamics. Even if they are based on the growth of firms, trajectories and development logics can differ from one company to another. A survey of 60 firms was conducted in the year 2000 to understand the development of SMEs in France. In-depth face-to-face interviews were held during the same year within each of the 60 firms. The results shed light on the diversity of SMEs, which can be described in terms of business models. A business model describes a category of firm in relation to the market it targets, its expected growth, its modes of governance, and the organisation of its activity. The diversity of business models of biotechnology SMEs is a point that is rarely considered in studies on factors promoting the development of these firms (see [Section 2](#)). This approach requires not only the differentiation of firms' activities, but also an explanation of their resulting position compared to other actors in the industry and, more generally, the institutional framework around the firm. While the factors facilitating the creation of start-ups are now known, few studies have been made of those

facilitating their sometimes-fragile survival and development. The present article highlights the logic of the development of firms and shows that modes of development differ for each business model.

Section 2 discusses the role of SMEs in industrial dynamics and analyses how the diversity of SMEs has been studied in different contributions. Data and methods are presented in Section 3. The size of the innovation project appears to be a key variable to split the sample of firms into two homogeneous clusters. Networks of the firms (founders, alliances, etc.) are then discussed in Section 4 to describe the Sectoral Innovation System (SIS) in biotechnology.

2. Heterogeneity of SMEs

2.1. Sectoral characteristics of biotech firms

Innovation in biotech firms has common characteristics. Three main features have attracted a great deal of attention in recent years. (1) Development of the biotech sector is based on the entry of a large number of SMEs; the biotech sector is often described as a large and highly turbulent population of innovators; SMEs are a leading force in a science push context, while the role of large firms is mainly to integrate new discoveries into their products after they have been developed by SMEs. (2) Biotech is a science-intensive sector. This characteristic has two consequences (Zucker et al., 1994; Feldman, 1999). First, SMEs are located close to the source of knowledge, i.e. close to the main universities, even if they are not spin-off of universities. Second, most of the founders have a scientific background and a Ph.D. and are members of scientific networks. (3) Strategic alliances progressively appear as central features of the biotech sector. The status of alliances is changing from strategic alliances, as a means to acquire and co-ordinate resources for technological and scientific development, to a new organisational form. Powell et al. (1996) explain the development of SMEs by the inter-organisational collaboration between SMEs and large firms. For established firms in traditional life sciences sectors, such as pharmaceuticals, chemicals, or seeds, the introduction of biotechnology has been a competence-destroying innovation. Because of the novelty of this scientific field and the risks attached to biotechnology, established firms channel their investments in biotech research to SMEs through long-term contracts or by forming joint ventures (Arora and Gambardella, 1990). SMEs, in turn, enter into long-term contracts to obtain complementary assets, such as product testing, commercialisation, or

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distribution capabilities (Teece, 1986; Barley et al., 1992). Consequently, the biotech industry is characterised by a network structure of inter-organisational alliances that govern the exchange of complementary assets among the different actors involved: academic teams, large firms, SMEs. The SMEs are seen as a nexus of these networks because of their role between scientists who make the scientific discoveries, and the large established firms that have the capabilities to market the products.

The characteristics of biotech firms transcend the national context; they are similar in all developed countries. The concept of a SIS, defined by Breschi and Malerba (1997), clearly accounts for the dynamics of the biotech sector. A SIS is defined as a “system (group) of firms active in developing and making a sector’s products, and in generating and utilising a sector’s technologies; such a system of firms is related in two different ways: through processes of interaction and co-operation in artefact-technology development, and through processes of competition and selection in innovative and market activities”

(p. 131). The key actors of a SIS are the private firms. Breschi and Malerba (1997) emphasise the fact that competition and selection processes involve firms with different capabilities and capacities to mobilise other actors—large firms, universities, research institutes—and innovative performances.

The approach in terms of SISs highlights the key role of firms in the dynamics of innovation. As shown in our previous work (Mangematin, 2000a), most researchers (Stephan and Everahrt, 1995; Audretsch and Stephan, 1996; Klavans and Deeds, 1997) focus on fast growing SMEs as a key leading mechanism. For this kind of firm, critical resources are access to scientific competencies and techniques developed by academic research, and to capital markets. Their development relies on signals of these scientific competencies, i.e. patent applications, new products and researchers involved in the firm or in its scientific advisory board. Patents, collaborations with academic world, and partnerships with pharmaceutical firms appear to be positive signals of competencies for potential investors when the firm enters into the stock market. Researchers with a high level of scientific visibility often create these

firms. The connexion with the scientific network is a condition for growth. It is not sufficient, however, for firms must not only develop high-tech research, but also transfer and commercialise their results. This often involves research or development contracts with a large company, in which the SME undertakes to provide its partner with specific materials, technologies, know-how, or expertise. Relations are formed on the basis of a specific competency recognised by the large firm. The SME's technological lead depends on the quality of its research, and the launching of the activity relies on capital input for the development of the product or process. We argue, in this paper, that the development of the biotech sector is based on the coexistence of two types of firms, fast growing ones, which will form the elite of European industrial biotech leaders on which the sector could grow and compete with that of the US; and a large number of small firms mainly involved in services to biotech, and which are not expected to become worldwide leaders.

2.2. *Heterogeneity among firms within biotech sector and business models*

Most studies on the key factors promoting development of biotechnology SMEs focus on this emerging business model. Yet, empirical evidence shows that the strategies of biotechnology SMEs can vary widely, and it seems that all external factors do not influence the different modes of development in the same way. In other words, by treating biotech SMEs as a uniform population (from the point of view of strategies and modes of development), analyses tend to aggregate effects that may be very different from case to case. A first series of studies differentiates between biotech SMEs by using external indicators that could easily be collected by questionnaire or from published data. Based on the technologies used and the targeted domains of application, these studies try to group together firms with similar profiles in this respect (Arundel and Rose, 1998; Saviotti et al., 1998; Lemarie and Mangematin, 2000; Lemarie et al., 2001). From the statistic point of view, their results explain only a small part of the variance. In other words, it is difficult to partition all techniques and areas of application since many combinations of techniques and markets are tested by firms. The analysis also shows that relatively old SMEs have been able to incorporate very recent technologies, thus indicating that combinations of techniques used by each firm can evolve

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significantly. In a recent study, Mangematin (2000b) focuses on the composition of shareholding. The very nature of research-intensive firms generates substantial movements in their capital. Three main types can be distinguished: (1) firms owned by individual shareholders; (2) firms owned by institutional investors, i.e. venture capital or listed on the stock exchange; and (3) firms owned by major industrial groups. The analysis shows that firms in the latter two categories are bigger and develop faster, irrespective of the technologies used or the application domains targeted.

A second series groups together studies that analyse firms' development strategies on the basis of monographs. The main monographs published include: Genentech presented by McKelvey (1996), Celltech presented by Dodgson (1991), and Cetus presented by Rabinow (1996) through the history of PCR. Finally, Nilsson (2001) recently analysed biotech firms in Sweden, on the basis of seven monographs. Estades and Ramani (1998) also conducted a comparative study of 20 biotech SMEs based in France and the UK. Simplified versions of monographs are also published in the form of corporate profiles in specialised journals (e.g. Nature Biotech, Biofutur) or the reports of consultancy firms such as Ernst & Young. The analyses in these studies are often very interesting because they point out the different logics of development of the firms under review. However, it is difficult to generalise, given the limited number of firms studied and the heterogeneity of frames of analysis used in the different contributions. It is also difficult to generalise the result of the case studies because of the embeddedness of those firms in their environment. Lastly, the environment also differs from one case study to another, depending on the continent and the year in which the firm is studied.

These studies of biotech firms' profiles constitute a break in research focused on competition (Porter, 1980). Analysis in terms of resources and competencies has been developing since the mid-1980s. This change reflects the shift of interest from external towards internal analysis: organisations are studied from within rather than in relation to their environment. The increasing openness of organisations has gone hand-in-hand with a relative disappearance of boundaries. Thus, the theory of resources, for which the definition of boundaries is less fundamental than it is for approaches focused on competition, seems particularly rich. It proposes an analysis of the organisation and of its competitive advantages in terms of tangible and intangible resources and competencies (Barney, 1991; Grant, 1991; Hamel, 1991; Barney et al., 1994). Competitive advantage is based on logic of comparative advantages derived from resources and competencies. It is by knowing and controlling them that strategic options can be defined and a

competitive advantage created.

Resource-based theory (Penrose, 1959; Peteraf, 1993; Mahoney and Rajendran Pandrian, 1992; Shrivastava et al., 1994; Russo and Fouts, 1997), like the theory of dependent resources (Pfeffer and Salancik, 1978), distinguishes between resources which are inputs into the production process and can be of various kinds (capital, human resources, equipment, co-operative or commercialisation networks, reputation or scientific visibility), on the one hand, and competencies which are related to the use and implementation of those resources, on the other. The sustainable nature of competitive advantage depends on the difficulty another organisation would have imitating the source of the reference organisation's success.

This approach is fruitful for analysing an industry that relies primarily on a combination of resources because few of its products or services have as yet been marketed. The identification of critical resources for each type of organisation helps to understand development logics. Each business model has its own development logic which is coherent with the needed resources—customer and supplier relations, a set of competencies within the firm, a mode of financing its business, and a certain structure of shareholding (Teece et al., 1993). Two main business models have been identified.

1. SMEs that run small projects and target market niches (type A), i.e. small and segmented market in a small geographic area. Although innovation is crucial for these firms, the need to maintain profitability forces them to limit investments in research. In other words, they realise incremental innovations whose value can often be explained by the entrepreneur's early intuition and launching of a research programme to transform that intuition into an innovation. Firms in the A group sell both products and services. For those which sell products, agreements may be made with outside partners who

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will then perform part of the business (e.g. subcontracting all or part of the production; granting a license for distribution of the product in a foreign country). Mechanisms for appropriating profits from innovation differ, depending on tacitness and codification of knowledge. Typically, a firm that sells a product protects itself against risks of imitation. If certain activities are outsourced, it takes steps to remain in a position of leadership as regards the products concerned. Appropriation may be achieved by legal means, such as patents, by strategies of the first mover advantage type or, more generally, by the ownership of specific assets. LCA is one of the examples of such firm. It commercialises diagnostic kits to test the soil quality. When a firm sells services, by contrast, secrecy is most often enough to guarantee the fruits of innovation, for the service offered generally provides too little information on adequate techniques. Aquanal can be an example of this kind of firms. It develops methods to detect GMOs in food and more generally to analyse food compositions (mainly for certification).

It is rarely in the interests of SMEs in the A group and their customers to reserve all exclusive rights to the products or services provided. An SME (i.e. the supplier) that reserves exclusive rights will end up relying on certain customers and will be forced to increase its prices to cover fixed costs. If the customer is a firm, the question of exclusivity may arise. We note, however, that in that case the products or services bought generally correspond to factors that are not critical to maintenance of the customer firm's competitive advantage. It is preferable to outsource this activity to ensure better flexibility and possibly put several suppliers in competition.

2. Research-intensive SMEs that target broader markets (type B), i.e. niche markets which cover a large geographic area or large national or international markets. Famous SMEs that have made their mark in the history of biotechnology until now

(e.g. Genentech, Chiron, Millenium) are firms with very big research programmes. The profitability of such programmes is credible only if the markets targeted downstream are very broad. This positioning is, therefore, radically different from that of type A firms, which target niches so as not to enter into direct competition with big companies.

Firms in group B develop one of the two strategies: either they are involved in contract research with large firms, or they carry out large research programmes themselves and valorise the product or service in the market. When they undertake large research contracts for big industrial groups, the "client" will have exclusive rights to the results. In this type of contract, the SME is remunerated in instalments and in the form of royalties on innovations resulting from the programme. In other words, these firms do not develop the final product. This type of configuration leads SMEs to adopt a complementary position in relation to major industrial groups. They explore new technological domains that big groups prefer to outsource to remain more flexible. Research is based on the establishment of technological platforms (generally comprising large facilities, software and human capital) that can be amortised on

several major research operations.

Depending on the stage of the project, the firm's strategy to acquire and co-ordinate resources for development is not the same: during the years following start-up, the SME has no sales. As it approaches the marketing stage, the SME generates sales licence revenues for use of its product. In the case where heavy investments are needed to move into the industrial phase, the firm will tend to develop the product with outside partners. This is typically the case in the pharmaceutical industry, where the cost of developing a drug is very high, especially in the clinical testing phases prior to marketing. Most biotechnology-based drugs are developed by biotech SMEs and are commercialised by pharmaceutical groups.

As far as large companies are concerned, type B firms have a credible project because they are able to set-up extensive research programmes. Since these research programmes are radically new, the incumbent leaders' experience is not crucial and SMEs are not at a disadvantage. In certain cases, innovation requires additional assets. It is generally in such cases that type B SMEs enter into collaboration with industrial partners.

The French firms, Genome Express and Genset, during the late 1990's, illustrated types A and B. Genome Express has been created in 1994 by Y. Laurent and J.P. Mouret, who worked previously at Perkin-Elmer, a firm specialised in instrumentation for life sciences industries. Genome Express is basically a firm dedicated to high speed and high quality gene sequencing. In 2000, the firm sells mainly services,
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i.e. gene sequences, to a large number of clients, from academic labs to pharmaceutical industry. During this period, Genome Express is clearly a type A firm, which generates turn over from its activity, and which runs small research programs to perform incremental innovations. At the opposite, Genset has been founded in 1989 by two well-known researchers in biotechnology, P. Brandys and M. Vasseur. From the very beginning, this firm develops large research programmes to identify gene involved in important pathologies like obesity or cancer. It also runs a small sequencing activity linked to its research activity. Genset is financed through venture capital and stock market. It belongs to type B firms. Thus, these two firms belong to different business models even if they both generate turn over through the sequencing activity. For Genome Express, the sequencing activity covers the running costs of the firm. For Genset, it covers less than 10% of the running costs which are mainly research expenditures.

To conclude, it seems that a SIS exists in biotech. The central role played by SMEs is underlined by most of the actors. However, it seems that all SMEs do not play the same part. The different case studies show that the activity of the firm has an important impact on the type of firm and on its development logic. The consequences of this heterogeneity is discussed around two hypotheses.

H1. The size of the innovation project determines the two business models with internal coherence for each business model.

The first hypothesis discusses the existence of different business models and introduces a criterion of relative size of innovative project to structure the business models. What percentage of resources is devoted to the innovative project? Most of the resources? A small part of the resources of the firm? H1 divides firms in two categories: firms in which the innovative project represents a small part of the activity of the firm, and those built around the innovative project.

H2. Each firm in a business model requires different resources to run the operational activity. The firm has to convince different kinds of partners to ensure their development.

Hypothesis H2 underlines the fact that firms in each business model target different resources to ensure their development. To secure these resources, different kinds of alliances are concluded.

3. Survey and method

For analysing the factors stimulating firms' growth and determining business models based on their activities, a sample of 60 firms was selected amongst the 200 biotech firms in France ([Lemarie and Mangematin, 2000](#)). Data on

each of these firms were drawn from face-to-face interviews,¹ generally lasting 2 h. The interviewee was either the managing director, research director, or financial director. The entire survey was conducted between January and May 2000.

Surveyed firms were selected from a database of 200 French firms, constituted from the results of a short questionnaire survey² by the research ministry in 1999. Selection was made with a view to obtain a sample that was as representative as possible of the firms' business. Each of the six French firms listed on the New Market, EASDAQ, or NASDAQ was included in the sample. Finally, to ensure a sufficiently objective view of the firms' development, those created before 1995 were given preference in the survey (only nine firms out of 60 were created in 1996 or later).

On average, the 60 SMEs had 45 employees each and an average turnover of 4.1 M €. They were founded between 1977 and 1998: a quarter before 1989 and the other three quarters since then. These characteristics are similar to the average values observed on the broader sample of 200 French biotech firms.³ Table 1 presents the general characteristics of the sample.

The main characteristics of the French biotech SMEs, shown in Table 1, are given as follows.

- The size of the firms, measured in terms of turnover or number of employees, was not correlated with the date of creation. Turnover per employee is highly

¹ Time constraints forced us to conduct telephone interviews with 10 of the firms.

² See Lemarie and Mangematin (2000) for a presentation of the results of this study. Data on the 200 firms covered their legal status, date of creation, main financial indicators, technologies used, and markets targeted.

³ In this larger sample, 70% of the firms were created after 1990. The average turnover was 32 million francs and the average number of employees was 36 (Lemarie and Mangematin, 2000).

Date of creation

Table 1
General characteristics of the sample

	Average	Minimum	Maximum	Medium	First quartile	Third quartile
	1991	1977	1999	1992	1989	1995
Turnover (M)	4.1	0.0	30.5	1.0	0.3	5.5
Number of employees	45	0	525	16	7	40
Net income (M)	- 0.9	- 14.0	5.0	0.0	- 0.7	0.1
R&D expenditures (M)	1.7	0.0	33.1	0.2	0.1	1.3
Share capital (M)	2.2	0.0	25.2	0.3	0.1	1.7
Annual growth rate of employee numbers (%) 1997–1998				13	0	50
Total number of alliances	155					
Total number of founders	113					
Total number of shareholders	257					

(1) All the financial data concern the years 1999 (when available) or 1998. The increase in capital is calculated on the firm's entire life cycle. Growth of number of employees is calculated between 1997 and 1999. (2) Alliances: firms have been asked to record the number of alliances and the type of partner for the alliance. Alliances with academic teams and alliances with other firms have been split. The localisation of the partner is also important. Is it a local, national, or international partner? When several partners are involved in the same alliance, they are taken into account in each category.

variable (between 0 and 0.5 M

€ per person) and is • Investments in capital are one of the modes of fundnot necessarily a good indicator of the firm's health. ing the firm's research activity. The level of capital .

- Biotech SMEs are recent. Firms are less than 10 years old on average. Biotechnology is a new sector and firms were set-up recently.

is high and the presence of venture capitalists in the shareholding reveals the importance of capital for biotech SMEs. Compared to other SMEs in the

- Biotech SMEs are small in terms of employees and traditional sector, the number of SMEs listed on turn over. The biotech sector is composed of small the stock exchange is high. firms with 45 employees on average, and generate
- The most interesting characteristic revealed by

4.1 M

€ of turnover.

Table 1 is heterogeneity. The survey focuses on

- Biotech SMEs are not profitable in the period studied. They are at the beginning of their life cycle and need large investments before generating enough turnovers to cover running costs.

one type of firm (SMEs) in one given sector (biotechnology). The SMEs present a high degree of diversity, in their financial results (turnover, net income—some of them have negative results),

- Biotech SMEs are science-based. On average, R&D expenditures account for over 40% of the turnover. These SMEs obviously belong to a high-tech sector, where 76% of the founders have a scientific background and 14% are well-known scientists.

in their research activity (from 0 to 33.1

M  of R&D expenditures) to 525 employees). This diversity suggests that the activities of firms differ and that the logics of development may also be different. Because of

- The 46 firms, which answer to the question, are involved in 155 alliances. Thus, partnerships are one of the main characteristics of this sector. They are also means for small firms to acquire resources.

heterogeneity, all data are analysed through their medium and quartile rather than mean and standard deviation.

Biotech SMEs are involved in partnerships for

and financial) mobilised by firms to guarantee their gaining access to scientific knowledge and scien

The heterogeneity of resources (human, scientific,

tific platforms. Most partnerships with a scientific

team remain local and are mainly based on existing

relationships. Biotech SMEs contract mainly with 4

Even if it is rare for science-based firms, some firms have no large and multinational firms. See Table 6 for R&D expenditures, i.e. no formal R&D structure. They are mainly further details. service oriented.

survival and development relates to various strate

relationship between the firm's activity and the ambition of its innovation project appeared clearly. The distinction between firms in groups A and B is based on three variables taken from the interviews: (1) the firm's business strategy and the positioning prompted by its leaders. Will the firm develop a product or technology that caters for a local or an international market? Are patents national, European, or international?

(2) Does the firm invest essentially in R&D, or does it primarily develop an offering of products and services that generates turnover? (3) Is the firm's main activity research, or does it also develop sales and production? A qualitative analysis of the interviews enabled us to divide firms into these groups, according to their business strategy and activity. The following section analyses the coherence of firms in each group and the development logics in which they are grounded.

4. Results

4.1. Firms that mobilise different resources

Basically, firms have been clustered in two groups: group A, consisting of those which have a small innovation project and target market niches; and group B, consisting of those which have a radical innovation project. In our sample, 37 firms are in type A and 23 firms in type B. Table 2 summarises the main characteristics of each type.

The analysis of firms' income and expenses clearly indicates the difference between traditional firms that target market niches (type A) and research-intensive firms (type B). The distribution of firms differs in respect of all characteristics except age and turnover. It, thus, appears that the creation of each type of firm is relatively homogeneous in time and that the appearance of a particular type of firm is not related to a particular period. In general, type A firms are smaller (average number of employees is 10, compared to 30 for type B), generate a turnover that covers running costs (including R&D spending), and grow more slowly than firms in group B. One of the reasons for which turnovers are not significantly different in the two groups is that our sample groups together firms at different stages of their life cycle, in both groups.

Each group has particular characteristics. For type A SMEs, the turnover is always clearly positive and correlated with the number of employees. Average turnover per employee is equal to 110 K

€ per person, the average current value in many sectors. When this indicator is studied for each firm, we note a clear link between this type of indicator and the age of the firm: the six SMEs with the highest average turnover per employee were all created before 1990, whereas the six SMEs with the lowest average turnover per employee were all created after 1994. This result is consistent with growth rates that are as high as 30% (on turnover) and 13% (on staff).

These firms, all invest in R&D, but their projects are of a reasonable size compared to the size of the firm. Note, however, that the levels of intensity of R&D of type A firms are high (10% on average) compared to other sectors. To sum up, type A SMEs have similar financial results. These firms have a net growth of their turnover and have to maintain a balanced accounting system. Maintaining this balance is especially difficult during the early years, before the firm has developed its first products. At that stage it is rarely possible to maintain a research team and most of the research is conducted by one or two people.

Type B firms have very different characteristics from those in the preceding category. Some of the firms are at the beginning of their life cycle and therefore focus on research without selling. That explains the high standard deviation on the turnover. For those which sell research through contract research, the average turnover is much higher. On the other hand, when considered in proportion to the number of employees, the turnover is lower than that of type A firms (90K

€ as opposed to 110K

€).

The importance of research programmes is clearly apparent in R&D investments. Some of the B type firms have

R&D investments that are far higher than their turnover. In general, the average intensity of R&D generally exceeds 50%. Type B firms fund their activity through capital.

Finally, the analysis of income and expenses en-ables us to draw a coherent picture of the development of the two types of firm. The development of type A firms is based on their activity. They sell products or services to clients. Their development depends on the size of the market; its expansion leads to a rapid development of the firms. By contrast, type B firms are based on their research and innovation projects. To be

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Table 2
Basic characteristics of the two business models

	Mann–Whitney	A			B			Full sample	
		Medium	First quartile	Third quartile	Medium	First quartile	Third quartile	Medium	First quartile
Number of firms	–		37			23		60	
Date of creation (year)	NS ($P = 0.2703$)	1992	1987	1994	1992	1989	1996	1992	1989
Number of employees	*** ($P = 0.0035$)	10	5	22	30	13	108	16	7
Turnover (K€)	NS ($P = 0.8912$)	1007	396	2679	1264	162	7287	1041	336
Net income (K€)	*** ($P = 0.000$)	16	–6	91	–1098	–4369	–141	–5	–714
R&D spending (K€)	*** ($P = 0.0001$)	82	37	305	1313	770	2672	229	65
Share capital (K€)	*** ($P = 0.0021$)	175	61	694	1650	257	3011	297	88
Annual growth rate of employee numbers (%) 1997–1998	** ($P = 0.0446$)	11	0	35	37	2	60	13	0

If $P < 1\%$ then ***; if $1\% < P < 5\%$ then **; if $5\% < P < 10\%$ then *; if $10\% < P$ then NS (non-significant); The Mann–Whitney test has been used to compare these data. The Mann–Whitney test is a non-parametrical test which can be performed on data to compare two independent samples. Gaussian distribution is not assumed to perform this test. All the financial data concern the years 1999 (when available) or 1998. The increase in capital is calculated on the firm’s entire life cycle. Growth rate of number of employees is calculated between 1998 and 1999.

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Table 3
Capital contributions

	Type of business								
	Mann-Whitney	A			B			Full sample	
		Medium	First quartile	Third quartile	Medium	First quartile	Third quartile	Medium	First quartile
Cumulated capital contributions on the firm's entire life cycle (M €)	*** ($P = 0.000$)	0.1	0.0	1.4	10.1	2.2	26.0	1.1	0.1
Cumulated contribution by venture capital on the firm's entire life cycle (M €)	*** ($P = 0.009$)	4.2	1.0	9.7	54.9	13.0	152.8	13.8	3.5

The contribution of venture capital is calculated as an average for firms who use it. Only those cases in which venture capitalists are the only parties involved at table are taken into account.

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able to achieve their goals, the CEOs⁵ of these firms have to convince investors to invest in their capital, since capital investors fund their operating activity.

To sum up, the size of the innovative project splits the sample into two business models. Thus, hypothesis H1 can be accepted. All the firms in the survey belong to the same sector. They have common characteristics: acquiring and developing scientific capabilities through internal research and alliances with both firms and academic teams. They also require funds to develop their activity. However, the degree to which these resources are needed and the nature of the partnership to acquire these resources are different in types A and B firms.

4.2. Musicians playing the same score in different orchestras

4.2.1. Types of business, structure of shareholding and movement of capital

Table 1 suggests that start-ups accompany their development by increasing capital. Table 3 presents the sum of capital invested in firms during the different round tables, by business model, while Table 4 identifies the different categories of shareholders. It exhibits the heterogeneity of firms in the capital needed and collected. In type A, small inputs suffice, and can be made by the founder of the firm alone or by family members or partners, or can be drawn from profits. Capital contributions (Table 2) are a key factor in the financing of type B firms, even if some of them have a high turnover. Since their creation, these firms have managed to raise an average of between 15 and 30 M

€ from shareholders (see following section for an analysis of shareholder structure). These capital contributions explain the high values of share capital, even if only part of the contribution is channelled into share capital. In other words, the older the firm, when the capital contribution is made, the higher the price will be for a given proportion of capital. These capital contributions are transformed into liquid assets that the firm progressively uses up. Ownership of these liquid assets results in interest received that partially compensates losses linked to the firm's business. This is probably the main reason why these firms have a higher net income than their operating income

⁵ CEO: chief executive officer.

Table 4 Current structure of shareholders

Number of shareholders	264	A	B	Chi-square test
Identity of shareholding				
Founders	42	30	12	** ($P = 0.018$)
Other SME	17	9	8	NS ($P = 0.382$)
Large firms	18	7	11	** ($P = 0.018$)
Venture capital	34	15	19	*** ($P = 0.001$)

Public	6	0	6
Others	8	1	7
Firms surveyed (60)	37	23	

If $P < 1\%$ then ***; if $1\% < P < 5\%$ then **; if $5\% < P < 10\%$ then *; if $10\% < P$ then NS (non-significant). Shareholders in the year 2000 are described in six categories. Some shareholders are present in several firms, making the number of shareholders higher than the sum of the shareholders by identity. Only “active” shareholders have been mentioned by the CEO, so that other shareholders, who represent a small minority, may have been omitted. The different categories are mutually exclusive: founders who created the firm and are still shareholders; individuals, family, friends or business angels; other SMEs, firms which have participation in the capital; large firms or multinationals which have participation in the capital; venture capitalists who have invested in SMEs; the public, when firms are quoted on the stock exchange. Table 4 is expressed in terms of presence or absence of each type of shareholder for a given firm. A shareholder that finances two firms is counted twice. On the other hand, for a firm with several shareholders of the same kind, e.g. several venture capitalists, the type of shareholder, and not the number of shareholders will be counted.

(Table 2). The opposite result is observed for type B, probably because of financial expenses.

When firms are listed in the stock exchange, the expected profit is high. As pointed out in Le Monde,⁶ the price earning ratio (PER) of the firms listed in the NASDAQ is about 144, compared to 20 for the blue chips which compose the Dow Jones. Type B firms are those in which the expectation of growth and of future profits is the highest. Thus, institutional investors (mostly business angels and venture capitalists) fund the starting steps of these firms. If the firm is successful,⁷ business angels and venture capitalists can stay in the shareholding of the firm to increase the value of their shares or they are able to sell out their shares when the firm makes an IPO.

⁶ De Tricornot, A., L'insaisissable valeur du Nasdaq et des entreprises de la nouvelle

economie, *Le Monde*, 27 February, p. 20.

⁷ The business angels and venture capitalists have lots of stocks, and it takes time for the market to generate the required liquidity to buy out all the stocks (at a good price for the shareholders).
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The current structure of capital clearly reflects the history of these firms (Table 4). Here, we simply identify the different types of actor present in the capital. Since setting up a business initially involves a few people, natural persons are often shareholders. In the case of type A firms, the founder almost always owns a substantial proportion of the shares. Genome Express, during the late 1990s, is a good example of this situation. By contrast, this is the case in only half of type B firms. When B type firms have been set-up only recently, their founders are more likely to be large shareholders, but their share of capital diminishes when the need for funds increases. The firm still has to convince other actors to invest in it.

The presence of major industrial groups is consistent with the given analysis of relations between SMEs and big companies. Type A firms focus on market niches and are therefore of little interest to large groups. By contrast, type B firms are large groups' potential partners or rivals in their core business. These groups, therefore, frequently acquire shares in firms in these categories when they reach a certain level of maturity. Since at the beginning of their life cycle type B firms' research results are still too hypothetical to interest industrialists, these investors prefer to wait and pay more to gain access to less risky projects.

Venture capital firms are virtually indispensable partners for type B firms, since over 19/23 use them. This proportion is over twice as high as that of type A firms. Moreover, the analysis of the average contribution of venture capital firms per biotech SME also shows substantial differences between types A and B. Very high contributions in the case of new type B firms reflect the significant development of this type of institution in France. More detailed analyses on the origin of venture capital firms reveal substantial differences between different types of SME: most capital contributions for type A firms were from regional venture capitalists, while foreign venture capitalists intervene primarily in type B firms.

Venture capital firms are not intended to remain shareholders in the long run. Their involvement in a high-risk project is based on expectations of large financial returns. Type A firms pose several problems from this point of view: (1) they generally run less risky, and also less profitable projects; (2) in many cases, the founder controls the firm and would like to maintain that control, thus leaving less latitude to any new shareholders to influence management; (3) finally, these firms rarely reach the stock market which is the most favourable capital outlet for

venture capitalists. This type of stumbling block is generally not found in type B firms, and shares can be resold either to big industrial groups or to the public at the time of flotation.⁸

The last issue, concerning shareholding, concerns the evaluation of the firm and the signal that investors look at. Type A indicators are traditional: turnover and profit margins are the main indicators. These firms have no specific characteristics in addition to others in the sector (high level of R&D expenditures, partnerships and capital investments). By contrast, investments in type B firms are mainly driven by expectations of profit rather than existing or even planned profits. Thus, investors have to believe unusual and non-financial signals. As profit expectations are based on science, signals are scientific: curriculum vitae of founders, scientific committees, and tangible commitments like patents or publications. Investors have to follow and believe such signals and indicators to invest large amounts of money in promising, but highly fragile, firms. The concentration of the shareholding is the main consequence of such a situation. It implies as follows.

- The number of actors is reduced. Even when they are public, the shareholding of these firms is concentrated amongst a limited number of shareholders, mainly institutional investors. Up-to-date scientific knowledge is necessary to be able to interpret signals like publications or scientific trends (Boissin and Trommetter, 2001). As a result, the shareholdings of these firms are mainly composed of persons involved in biotechnology. The liquidity of such firms, when they are listed, may be reduced compared to other sectors that are easier to understand for a large public of investors.

- Actors are specialised. Compared to other sectors in which traditional financial indicators can be interpreted with general knowledge of the sector, biotech firms require specific investments to understand the logic of the sector. It is necessary to be involved in both the scientific community and the financial

⁸ In most cases, flotation calls for additional capital by institutional investors (banks and insurance companies) during the prefloat stage. These investors, largely absent from the databases studied here, have been put into the 'public' category in Table 4. V. Mangematin et al. / *Research Policy* 32 (2003) 621–638

community. Even institutional investors need to be specialised and only few actors are involved in biotech firms which require large investments. That is one of the reason why venture capitalists and institutional investors like pension funds are specialised.

- The notion of “good results”, which is quite common in traditional sectors (high profit rate, high profit prospects, low level of debt, etc.), has to be redefined and adapted. Thus, both shareholders and CEOs need to agree about what “good results” are in a general framework of financial losses. Patents, contract research, or contract licences with large pharmaceutical companies are usually considered as favourable indicators, as are phase III products.

- Science and shareholding are international. To be able to generate high returns on investments, type B firms have to focus on international markets. Thus, the advance of science is no longer national, but international. This characteristic has two consequences. (1) The decision-making process in type B firms depends upon international criteria and decisions. Before IPO, B firms have international venture capitalists who invest in firms in Europe and the USA. European firms compete with American ones to acquire resources. After IPO, they compete on the same stock exchange (NASDAQ, Euronext, etc.) to attract shareholders. (2) Shareholders have to be more and more professional in their investment because of the internationalisation of the competition and the production of science.

All in all, when indicators are transient, and when the amount of money needed for development is high, investors become less numerous, more professional, and more international. Indicators and their significance require agreement in the community of investors. They are difficult for outsiders to understand and risks of manipulation of prices are high. Since this is a new and transitory situation (because everyone expects to have traditional firms which generate turnover and profit as soon as possible), the community of investors remains small.

4.3. Business models, founder's characteristics and acquisition of resources

As shown in Table 5, most of the founders have a scientific background. But the significance of the

Table 5 Characteristics of the founders

Number of founders	113	A	B	Chi-sqaure
Founders' experience				
Scientific experience				
Scientists	28	23	5	*** (P = 0.000)
Scientific researchers	30	13	17	** (P = 0.014)
Famous scientists	11	1	10	*** (P = 0.000)
Managerial experience				
Junior manager	19	16	3	*** (P = 0.004)
Senior manager	20	4	16	*** (P = 0.000)
Firms surveyed (55)		32	23	

The number of founders describes the number of persons involved in the creation of the firm. When available, their initial training and professional experience have been recorded. Two professional experiences are recorded: scientific experience and managerial experience. The scientific experience is ranking in three levels:

.(1) junior scientists are persons who have a scientific background, engineers, or Ph.D.s; (2) senior scientists are at least post doc, and have research experience after the Ph.D. (some of them had a position in an academic team before creating the firm); and

.(3) famous scientists are those who have already published a lot and have a high level of scientific visibility. In our sample, they are those who have published more than 15 papers recorded in the Science Citation Index. Founders are described as having a managerial experience if they have either a managerial training or a scientific background and a managerial experience in a large firm or in the creation of a biotech SME. Those who have little managerial experience are considered junior. Those who have already been in positions of leadership in a major industrial group or banking institution are senior. [Table 5](#) is expressed in terms of presence or absence of each type of founder for a given firm. If a founder has two competencies—scientific and managerial— she/he will be counted twice. By contrast, if the firm has several scientists which similar competencies, they will be counted only once. The founder's experience is determined on the basis of the last job held. The differences in the experiences of founders are significant between types A and B. For each line, a Chi-square test has been performed with the default entries are junior scientist or junior manager, depending on whether the person is from an academic or industrial environment.

presence of a scientist as a founder is not the same when that person is a junior scientist who is able to operate one technique, and when she/he is a famous scientist who brings with her/him a large network of collaboration and relationships. Thus, scientists play different roles, depending on their experience. Junior scientists can run experiments and do the job themselves. Based on a Poperian analysis of scientific production, [Shinn \(1988\)](#) shows that a division of work exists in laboratories. Senior scientists are able to *V. Mangematin et al. / Research Policy 32 (2003) 621–638*

co-ordinate more complex research and divided work and tasks. They are also able to generate new hypotheses and models. Junior scientists have fewer capacities to co-ordinate complex projects and are oriented more towards the implementation of specialised tools.

Moreover, two main types of founder have been distinguished: academics and managers ([Catherine and Corolleur, 2000](#)). In each of these categories a distinction is made on the basis of the person's experience and responsibilities.

The analysis reveals a very clear connection between the founder's characteristics and the type of activity of the firm. Founders with extensive experience are almost systematically involved in the creation of type B firms. By contrast, founders with little experience more often appear in type A firms. This correspondence probably stems from constraints relating to the firm's mode of capitalisation. To be able to raise large amounts of capital the founder has to be able to provide guarantees as to the credibility of the proposed project.

As shown previously, the visibility of the scientist in the academic community plays a key part as regards venture capital. It gives credibility to the scientific project of the firm. A similar conclusion can be drawn for alliances. All biotech SMEs enter into partnerships to gain access to critical resources. But the nature of the critical resources differs in types A and B firms. Type A firms mainly need access to technological platforms and to scientific teams with general knowledge. Thus, scientists in the firm, who are generally the founders, usually maintain contacts with their previous team (from their Ph.D. or post doc) to have

Table 6 General characteristics of the sample

access to certain technological facilities or to scientists in their speciality. They also manage contracts with local or national firms to secure access to markets. By contrast, type B firms are more globalise, even when they are small. They conclude international partnerships with academic teams specialised in a particular field and with large firms which valorise their specific competencies (Table 6).

In general, biotech SMEs have more than two partnerships in average. Partners with whom these alliances are concluded have few distinctive characteristics, except for co-operative agreements with local academic teams for type A firms and with international groups for type B firms. These characteristics confirm the relations between founders and the business model. Junior scientists set-up their firm near the laboratory in which they did their Ph.D. or spent the first years of their scientific career, and maintain close ties with the team in that lab. By contrast, type B firms are founded by senior researchers who often have good international visibility that enables them to convince international groups of the quality of research conducted in their firm. The analysis of the founders of a firm, of the partnership and of the way in which the firm finances its activity reveals that types A and B firms require different resources to run operational activities. Depending on the business model, different indicators are analysed by partners and potential investors. Thus, empirical data supports hypothesis H2. The development of types A and B firms is not based on the same resources. Type A firms have to convince local or national businesses

Number of alliances	155	A	B	Chi-square test
Type of alliances				
With a local academic team	27	19	8	** ($P = 0.055$)
With a national academic team	15	7	8	NS ($P = 0.249$)
With a international academic team	6	2	4	NS ($P = 0.176$)
With a local firm	19	9	10	NS ($P = 0.191$)
With a national firm	21	12	9	NS ($P = 0.845$)
With a international firm	24	9	15	*** ($P = 0.002$)
Other	5	4	1	-
Firms surveyed (46)		27	19	

Table 6 is expressed in terms of the presence or absence of each type of partnership in a given firm. A firm that has two partnerships with an international academic team will be counted only once. By contrast, a partnership in which several types of partner are involved will be counted as many times as there are partners.

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to buy their product or service if they are to generate a turnover enabling them to gradually expand. Their

contacts with local and national teams afford them access to scientific breakthroughs and sometimes also to technological platforms. Capital needs are small, and are often met by local venture capitalists linked to the public authorities. In type A firms, partnerships with firms are alliances for production or commercialisation. The resources that the firm exchanges with other partners are mainly products and services as opposed to turnover, and profits as opposed to investments. These results are consistent with Mansfield's ones (Mansfield, 1995), when he finds that firms draw on local universities for applied research, but for basic research they are connected to the most appropriate labs wherever it is located. Type B firms exchange credibility, signals of excellence, and expectations of potential profit as opposed to capital investments to finance research. Thus, firms are not really competing to convince the same partners, clients or network. The driving force of development is therefore also different. Although, types A and B firms belong to the same sector, the two types of firm do not really compete for resources. Each type is a specific case, with type A firms competing for markets and clients and type B for investors. They are playing the same score, but in different orchestra, and in different theatres. To what extent is a firm locked in a specific business model?

type of evolution. Biotech firms develop an innovative scientific project and explore hypotheses. Some of these hypotheses may prove to be scientific dead-ends, which nullifies investments made and leads to bankruptcy. Other, more conjunctural causes, can also be the cause of bankruptcy, since these firms are highly dependent on venture capital investments. A lack of liquidity of stock markets related to an unfavourable context, as in the first half of 2001, for example, can lead to financial delays or deficiencies that are fatal for firms. Likewise, discussions on intellectual property rights on living organisms, which strongly influence patenting strategies, can lead certain firms to ruin if they have not anticipated new laws. The fall of biotech values following the Blair/Clinton declaration attests to firms' sensitivity to their political and legislative environment. Finally, a discovery made more quickly by another research team in a rival firm can strongly reduce the value of a firm's research. Thus, whether for internal reasons, or reasons related to the environment, certain firms can disappear.

- *Focus on a niche*: The firm's strategy of positioning in international markets may prove fruitless, especially due to the scientific competition to which it is exposed. It may then redeploy its investments, at least partially, in market niches where it valorises specific competencies. This strategy corresponds to a withdrawal to a less ambitious project. Its viability

4.4. Dynamics of the transition from one type of

business to another

firms, the constraints weighing on the founder's pro

file due to the need to raise large amounts of capital.

understand the internal

certain important mechanisms governing each type of

this type of firm involves a transition towards another ⁹ On 16 March 2000, Bill Clinton and Tony Blair advocated free model. Four types of evolution can be identified. access to the human genome, asking for the results of sequencing of the human genome to be put into the public domain and for

- *Disappearance of the firm*: Several reasons of a patents to be limited to their industrial and medical exploitation. structural and conjunctural nature can explain this Le Monde, 15 March 2000.

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in 1988 and bought out by Sandoz in 1992), and Agrogene (founded in 1989, gradually bought out by Limagrain and then taken over by Perkin-Elmer). These firms differ from subsidiaries created ex nihilo, in so far as they started off independently. This evolution is not specific to type B firms. The event must be considered as a stage in the development of the SME and not as a sign of failure. The buy-out may be explained by problems experienced by the SME (problems securing access to markets, incomplete technology base) but also by the group's wish to acquire it. The buyer's aim is either to complete its technology base with the patent portfolio or technical competencies of the SME, or to use the SME to gain a foothold in the country. In the latter case, the acquirer is often a foreign group. The firm then

depends on the state of the competition and investments made. Some firms, whose shareholders in-

clude venture capital companies that have remained present for many years despite the business not tak-Characterisation of types of business has made it

ing off, seem to be in this case. Such firms are not possible to explain the financial constraints weighing

as successful as anticipated, and venture capitalists on a firm's development and, in the case of type B

have difficulty withdrawing their capital since the

firms concerned are not quoted on the stock market.

Business models enable us to

• *Buy-outs*: Some firms are bought out by industrial

groups after proving themselves. In this category we coherence of firms and to characterise the resources they mobilise. This representation also helps to explain find companies such as Appligene (founded in 1985,

with an 80% buy-out by the US Oncor in 1995 and

then by the Canadian Quantum), Systemix (founded activity. The emergent business model characterising type B firms can only be temporary. The longevity of

acts as a bridgehead in France to transfer technologies or products developed by the parent company. The buy-out is followed by changes in the SME. Its research may be concentrated with that of the group to avoid duplication.

seen that it is not easy for founders with limited experience to directly set-up a type B firm. Some entrepreneurs interviewed in the survey, nevertheless, clearly planned to progressively move towards a type B business. In other words, going through type A firms is a way of building up additional experience and credibility in the biotech business. This experience will not, however, be equivalent to that of the founders of type B firms because it will have been acquired in very different organisations. Moreover, the founder will have to agree to concessions regarding control of the company. Thus, the question is to study how type B businesses can be developed when they have a past that differs substantially from that previously observed. The sample studied did not include that type of case except for Kappa biotech which was created by the founders of Biovector-Therapeutics and Genome Express, two persons formerly employed by a large firm which sells biotech equipment. Kappa has chosen to valorise its innovations in cosmetics and

- *Coming out on top*: For some firms the gamble pays off. They market radical innovations that generate huge cash flows and make them unavoidable actors. These firms, most of which are in the human health sector, are the ones that, either alone or in partnership with a pharmaceutical firm, produce active principles or new drugs that capture a large slice of the market (what in the pharmaceutical industry are known as blockbusters). If the firm chooses to commercialise its product itself, it will have to acquire the competencies of pharmaceutical firms and act like a firm in that sector. If it sells its innovation to a pharmaceutical firm, it will remain in the biotechnology sector to valorise its research in other directions.

The emergent business model is temporary and is developing research capabilities to move into pharmaceutical markets. It is clearly a type A firm, but the ambition of the founders is to set-up a type B firms as soon as possible. Genome Express began by doing sequencing and functionalisation. It is now setting up large research programmes involving international teams to develop new sequencing and functionalisation techniques.

- *Geographic expansion to conquer new markets*: Founded on the basis of a local or national market, firms with recognised competencies in a market niche can expand by conquering new markets, either in sectors neighbouring those in which their competencies are recognised (application to animals or plants of competencies acquired in human health, as in the case of genomics or bio-computing, for example), or in countries which lack their specific the evolution

of firms corresponding to this development model vary widely. Possible trajectories of type A ^{biotech} firms are more classic. Three possibilities can be identified in the sector, as in eastern Europe and southern Europe. This strategy often implies external growth

identified.

- *Development of an ambitious project based on the firm's competencies:* With a scientific and technological base valorised in existing products and services, some firms can run ambitious projects that take them closer to the type B model. Transition from types A to B is probably rare. We have of local partners. It can also take the form of direct investments abroad in the form of creation of subsidiaries.

operations, such as joint ventures or the buy-out

- *Maintaining the "craft" character of the business:* Some firms have no growth strategy and generate a business enabling them to live.

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The analysis of business models enables us to highlight the development prospects of biotech firms. It shows the eminently labile character of the emergent business model that represents only a stage in the firm's development. While it is legitimate for investors and actors in the sector to have their eyes fixed on the short-term evolution of firms, it is legitimate for the public authorities to support the middle-term development of these firms.

5. Conclusion

Based on a study of the development of the biotechnology sector and of biotech SMEs in France, this paper underlines the diversity of firms involved in this sector even if the two main business models share common characteristics: science base, leading role of SMEs, and resource acquisitions through alliances. Our analysis is based on the construction of two business models, each corresponding to a viable position for SMEs in the industrial environment. Within a SIS, firms do not form a homogeneous group. Development of the different types of firm is based on different dynamics, and different actors play a role in those dynamics. The main differences appeared between models A and B. When an SME focuses on a market niche and conducts small research programmes, it will experience steady growth if it is able to reach financial equilibrium fairly quickly. By contrast, when SMEs embark on large research programmes in partnership or competition with major companies in the sector, development is possible only with outside capital and the participation of venture capital firms. The founding members' experience is then a key factor if the SME is to enter into certain partnerships. On the basis of these results, we were able to see how certain business models that are less risky, but probably make less use of the founders' knowledge, can appear as gateways in the establishment of a final business model.

The heterogeneity of the firms studied here affords a different view compared to existing studies of biotechnology SMEs. We mentioned, for instance, some results of the study of factors favouring the growth of biotechnology SMEs, but which do not differentiate the characteristics of these firms. For example, [Audretsch and Stephan \(1996\)](#) highlight the importance of scientific networks in the capacity of firms to raise capital at the IPO stage. This result is totally consistent with results obtained here for model B, but does not apply to model A. This confirms the more general idea that it is necessary to develop appropriate economic indicators when the firms studied have different characteristics.¹⁰

Finally, this research provides important elements for an analysis of the advantages of public policies focused on the development of biotech SMEs. The differentiation of business models helps to explain the sometimes very variable effects of certain public policies, and can facilitate the definition of appropriate instruments for each type of business. It finally underlines the crucial role of public policy in funding, basing science (through subsidies, venture capital, or other ways) developed in type B firms.

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References

- Arora, A., Gambardella, A., 1990. Complementarities and external linkages: the strategies of the large firms in biotechnology. *Journal of Industrial Economics* 4, 361–379.
- Arundel, A., Rose, A., 1998. Finding the substance behind the smoke: who is using biotechnology? *Nature Biotechnology* 16 (7), 596–597.
- Audretsch, D., Stephan, P., 1996. Company scientist locational links: the case of biotechnology. *American Economic Review* 86 (3), 641–652.
- ¹⁰ See Paranque et al. (1997) for a more in-depth study of problems relating to business indicators in varied sectors. V. Mangematin et al. / *Research Policy* 32 (2003) 621–638
- Barley, S.R., Freeman, J., Hybels, R.C., 1992. Strategic alliances in commercial biotechnology. In: Nohria, N., Eccles, R. (Eds.), *Networks and Organizations*. Harvard University Press, Boston, MA, pp. 311–348.
- Barney, J.B., 1991. Firm resources and sustained competitive advantage. *Journal of Management* 17, 99–120.
- Barney, J.B., Spender, J.C., Reve, T., 1994. Does Management Matter? On Competencies and Competitive Advantage. Lund University Press, Lund Bromley, UK.
- Boissin, J.P., Trommetter, M., 2001. Contextes Et Pratiques Du Gouvernement Des Entreprises De Biotechnologie. Troisième forum de la moyenne entreprise, Caen, IAE.
- Breschi, S., Malerba, F., 1997. Sectoral innovation systems: technological regimes, schumpeterian dynamics, and spatial boundaries. In: Edquist, C. (Ed.), *Systems of Innovation*. Pinter Press, London.
- Catherine, D., Corolleur, F., 2000. Pme Biotech Et Géographie De L'innovation, Des Fondateurs À Leur Modèle D'entreprise. XXXVIe colloque de l'Association de Science Régionale de Langue Française, Trans Montana (CHE). INRA/SERD/IREPD, Grenoble.
- Dodgson, M., 1991. The Management of Technological Learning: Lessons from a Biotechnology Company. Walter de Gruyter, Berlin.
- Estades, J., Ramani, S., 1998. Technological competence and the influence of networks: a comparative analysis of new biotechnology firms in France and Britain. *Technology Analysis and Strategic Management* 10 (4), 483–495.
- Feldman, M., 1999. The new economics of innovation, spillover and agglomeration: review of empirical studies. *Economics of Innovation and New Technology* 8 (1), 5–25.
- Grant, R., 1991. The resource-based theory of competitive advantage: implications for strategy formulation. *California Management Review* 33 (3), 114–135.
- Hamel, G., 1991. Competition for competence and inter-partner learning within international strategic alliances. *Strategic Management Journal* 12, 83–103.
- Klavans, R., Deeds, D.L., 1997. Competence building in biotechnology start-ups: the role of scientific discovery, technological development and absorptive capacity. In: Sanchez, R., Heene, A. (Eds.), *Strategic Learning and Knowledge Management*. Wiley, New York.
- Lemarie, S., Mangematin, V., 2000. Biotech firms in France. *Biofutur* 32–42 (special issue).
- Lemarie, S., Mangematin, V., Torre, A., 2001. Is the creation and development of biotech SMEs localised? Conclusions drawn from the French case. *Small Business Economics* 17 (1/2), 61–76.

- Mahoney, J., Rajendran Pandrian, J., 1992. The resource-based view within the conversion of strategic management. *Strategic Management Journal* 13, 363–380.
- Mangematin, V., 2000a. Competing business models in the French biotech industry. In: de la Motte, J., Niosi, J. (Eds.), *The Economic and Social Dynamics of Biotechnology*. Kluwer Academic Publishers, Boston, pp. 181–204.
- Mangematin, V., 2000b. What Business Model for Biotech SMEs. Statcan, Ottawa, Canada. INRA/SERD, Grenoble.
- Mansfield, E., 1995. Academic research underlying industrial innovations: sources, characteristics and financing. *Review of Economics and Statistics* 75 (1), 55–65.
- McKelvey, M., 1996. *Evolutionary Innovations—The Business of Biotechnology*. Oxford University Press, Oxford.
- Nilsson, A., 2001. Biotechnology firms in Sweden. *Small Business Economics* 17 (1/2), 93–103.
- Penrose, E., 1959. *The Theory of the Growth of the Firm*. Basil Blackwell, Oxford.
- Peteraf, M., 1993. The cornerstones of the competitive advantage: a resource-based view. *Strategic Management Journal* 14, 179–191.
- Pfeffer, J., Salancik, G.R., 1978. *The External Control of Organizations: A Resource Dependence Perspective*. Harper & Row, New York.
- Porter, M., 1980. *Competitive Strategy*. Free Press, New York.
- Powell, W.W., Koput, K.W., Smith-Doerr, L., 1996. Interorganisational collaboration and the locus of innovation: networks of learning in biotechnology. *Administrative Science Quarterly* 41, 116–145.
- Rabinow, P., 1996. *Making PCR: A Story of Biotechnology*. University of Chicago Press, Chicago.
- Russo, M.V., Fouts, P.A., 1997. A resource-based perspective on corporate environmental performance and profitability. *Academy of Management Journal* 40 (3), 534–559.
- Saviotti, P.P., Joly, P.B., Estades, J., Ramani, S., De Looze, M.A., 1998. The creation of European dedicated biotechnology firms. In: Senker, J.V.V., Cheltenham, R. (Eds.), *Biotechnology and Competitive Advantage: Europe's Firms and the US Challenge*. E. Elgar, pp. 68–88.
- Shinn, T., 1988. Hiérarchies des chercheurs et formes de recherche. *Actes de la Recherche en Sciences Sociales* 74, 2–22.
- Shrivastava, P., Huff, A.S., Dutton, J.E. (Eds.), 1994. *Resource-Based Views of the Firm: Advances in Strategic Management*, Vol. 10a. JAI Press, Greenwich, CT.
- Stephan, P., Everahrt, S., 1995. *The Changing Rewards to Science: The Case of Biotechnology*. Department of Economics and Policy Research Center, Atlanta.
- Teece, D., 1986. Profiting from technological innovation: implications for integration, collaboration, licensing and public policy. *Research Policy* 15, 285–305.
- Teece, D., Rumelt, R., Dosi, G., Winter, S., 1993. Understanding corporate coherence: theory and evidence. *Journal of Economic Behaviour and Organization* 22.
- Zucker, L., Darby, M.R., Armstrong, J., 1994. Intellectual Capital and the Firm: The Technology of Geographically Localized Knowledge Spillovers. NBER, p. 4946.