French Biotech Start-Ups and Biotech Clusters in France. The Importance of Geographic Proximity[1]

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Based on a survey of the French Biotech SMEs (see annex 1), this article examines localisation effects in the biotechnology sector. It consists of two strands of analysis. The first presents a detailed statistical survey of the French biotechnology sector. Among other things, the survey shows that a) localisation effects within France are strong, and b) French firms can be grouped into four general types of firm, ranging from ‘type 1’ growth-oriented product firms, to ‘type 2’ niche market players, ‘type 3’ subsidiaries of larger firms, and ‘type 4’ firms that have been acquired. Localisation effects differ across these firms, especially across type 1 (international) and type 2 (very localised) firms. The second strand of analysis consists of a review of the localisation and related cluster literature, with implications identified for localisation and knowledge spillovers within biotech clusters. The relative effects of the proximity of scientific centres compared to public policy on start-ups is examined.

Introduction

Biotechnology can be defined as a set of techniques and knowledge which are related to the use of living organisms in production processes and are the outcome of recent advances in molecular biology (Ducos and Joly 1988). The division of work is at the centre of research on the economics of innovation which accounts for the dynamics of biotechnological knowledge. Each new breakthrough opens onto new hypotheses and sometimes onto a new sub-discipline with research tools, tests and specific competencies, in a process of cumulative discovery. Within this process, academics perform basic research, SMEs explore these new fields of knowledge, and corporations exploit them industrially and commercially (Orsenigo et al. 1998, Sharp 1999). Our objective is to analyse the role of geographic proximity in the development of those SMEs. The creation and growth of biotech start-ups and, more generally, high-tech firms, has resulted in the formation of clusters in both the US and Europe (Feldman 1994, Prevezer 1998, Swann 1999).

Research on the development of biotechnology, carried out in areas of the economics of innovation and the geography of innovation, is based primarily on cases in the US rather than in Europe. For France, a recent study can be used to draw up a typology of new biotech firms (Lemarié et al. 2000 a), thus completing the overview by Ernst & Young (Ernst & Young, 2000). This study shows that on 1 January 1999 France had just over 400 biotechnology SMEs employing 15,000 people, with an estimated turnover of thirteen billion francs. Estimates based on the survey initiated by the French ministry for education, research and technology are consistent with the information published by Ernst & Young, although they indicate a higher number of firms in France. The average size in terms of the number of employees is nevertheless similar (about forty persons). The majority as founded after 1990 (70 per cent of the sample). Most of the recent firms aim for the pharmaceutical sector. The second sector in terms of the number of firms and employees is agriculture and the agro-food sector. Firms involved in ag-biotech are older than those which aim for the pharmaceutical sector (Lemarié et al. 2000 a).

Most of these new biotech firms were created in the Ile-de-France region, especially at the Evry Génopole, and close to the main French scientific poles (Lyon, Strasbourg, etc.). From this point of view, the French case resembles the US experience. In the US the biotechnology sector has developed around centres of scientific excellence (Zucker and Darby 1996, Zucker, Darby and Armstrong, 1998), since the mobility of researchers from academic research centres towards the private sector is a vehicle for the diffusion of knowledge and a powerful incentive for start-ups. Is the constitution of clusters in France similar to the US? Are the determinants of biotechnology clusters in France the same as those identified for the US? A review of studies on the determinants of the clustering of productive activities and, more specifically, of innovation, will be proposed in the first part of this paper. The second part considers the French case in the light of these approaches. The role of institutions and the importance of the diversity of biotechnology firm models is then discussed in the third part.

How can the clustering of new biotech firms be explained?

Two main categories of analysis are usually applied, based on research conducted in the framework of new economic geography and research on local technological externalities, respectively.

Economic geography and geography of innovation.

The first explanation is the one proposed by new economic geography (Fujita and Thisse 1997), introducing the possibility of conjoint localisation of firms in the same space (a town, for example, but rather a region or area of production in the case under consideration here), at the expense of neighbouring or rival spaces. The suggested causes of this polarisation are multiple but we can identify two particularly important ones leading to the establishment of localised increasing returns (Krugman 1991 a, 1991 b) which maintain a divergent process of localisation of activities: the existence of indivisibilities and the preference for variety. Although the question of indivisibility is hardly relevant for small firms, the instrumentation involved in biotechnology can play a decisive part in the localisation of activities. A start-up cannot in vest in heavy equipment that it will use only occasionally. However, these studies focus only on pecuniary externalities, to the exclusion of technological externalities. For P. Krugman, ‘knowledge flows are invisible, they leave no paper trail by which they may be measured and tracked.’ (Krugman 1991 a: 53) Or else, ‘by focusing on pecuniary externalities, we are able to make the analysis much more concrete than if we allowed external economies to arise in some invisible form. (This is particularly true when location is at issue: how far does a technological spillover spill?)’ (Krugman 1991 b: 485).

Unlike Krugman, Jaffe, Trajenberg and Henderson analyse pecuniary externalities and their relation to geographic proximity. ‘Despite the invisibility of knowledge spillovers, they do leave a paper trail in the form of citations' (Jaffe et al. 1993: 26). These three authors, as well as Almeida and Kogut, use patent citations to identify knowledge spillovers and their geographical dimension (Jaffe et al. 1993, Almdeida and Kogut 1997). Two types of research can be differentiated in the latter type of approach (Feldman 1999).

The first is to try to measure directly the impact of geographic proximity on technological spillovers, which are themselves supposed to enhance innovation performance. Proximity is modelled in terms of distance or geographical coincidence of research units inside the boundaries of a state or a metropolitan area. Despite differences in the modelling and identification of technological spillovers (the patent or innovation identified in the market), the econometric results of Feldman (1994), Audretsch and Feldman (1996a), Jaffe (1989) and Acs et al. (1994) all indicate that spillovers are favoured by geographic proximity (for a critical analysis, see Autant-Bernard and Massard 1999).

In the US, biotech start-ups are localised near poles of academic excellence (Prevezer 1998). More generally, innovation in a given region is closely related to public and private research spending in the region (Feldman 1994). There are no substitution effects between public and private R&D spending. They enhance each other to create areas of expertise (Jaffe et al. 1993). Venture capital companies also contribute to the growth of biotechnology clusters. Lerner shows that growth in the number of employees and the sales of start-ups is greater when they are located near venture capital companies. These start-ups also benefit from capital inputs needed for their development of a flow of superior information (Lerner 1996). It is primarily regional public venture capitalists and above all ‘business angels’ that finance the early stages of SMEs. The main characteristics of these actors is that they are essentially local, they invest small sums and they establish very informal relationships with SMEs (Mason and Harrison 1995).

The second strand of analysis focuses on the role of interactions as sources of knowledge transfers (Zucker et al. 1996, 1998; Almeida and Kogut 1997, Autant-Bernard and Massard 2000). For Zucker et al., ideas are embodied in individuals who have the skills, knowledge and know-how to engage in technological progress. Their papers analyse the human capital of key individuals rather than the average human capital of the local labour market. Biotech start-ups are localised in regions in which this intellectual capital resides. These star scientists embody knowledge breakthrough techniques that are initially available only at the scientists’ laboratory, making it costly for other to obtain and use. These results suggest that the localisation of biotech start-ups and their performance cannot be explained by the presence of universities but by the relationship between renowned academic researchers and biotech firms (Zucker et al. 1998). Technological spillovers are no longer abstract, they can be traded (research contracts, licences, etc.). Consequently, the formal institutions that link inventors, capital and markets are important factors explaining the localisation of high-tech firms (Lamoureaux and Sokoloff 1997).

The importance of geographic proximity in question

But if geographic proximity is important for firms' innovation, what are we actually talking about? For economic geography, geographic proximity is a physical distance between actors and is accompanied by transport costs. For the geography of innovation, it is related to the creation of tacit knowledge that firms assimilate. Geographic distance is not the only significant factor here. In order to understand it, it is useful to distinguish and define two concepts: geographic proximity and organisational proximity (Torre and Gilly 2000).

Geographic proximity concerns spatial separation and relations in terms of distance. It consists of more than the reference to natural and physical constraints, clearly inscribed in its definition, since it also encompasses aspects of social construction, such as transport infrastructure, which impact on access time, or financial resources allowing for the use of certain communication technologies. Organisational proximity is based on two types of logic that can be qualified as similitude and affiliation, respectively. With the logic of affiliation, actors belonging to the same area of relations (firm, network, etc.), in which different kinds of interaction take place (e.g. co-operation or circulation of knowledge), are close in organisational terms. With the logic of similitude, actors who resemble one another, i. e. who possess the same area of reference and share the same knowledge, so that the institutional dimension is important, are close in organisational terms. In the first case, membership of the same set is conditioned by the effective nature of co-ordination; in the second, proximity is related to the ‘resemblance’ of representations and modes of functioning. Far from being antinomic, these two aspects can sometimes be reconciled, particularly when affiliation initially based on horizontal relations of an intra-industrial nature are subsequently concretised in an increase in interdependence between organisations, signifying greater similarity (or institutional proximity) between the players. In the case of biotechnology and many high-tech activities, it is the logic of affiliation that plays an important part, particularly in the circulation of knowledge between organisations – a circulation based on a mode of functioning similar to that of inter-individual relations.

How can this distinction help us to understand high-tech clusters and, more specifically, those of biotechnology and their growth? First, incubators and facilities for assisting and supporting business creation play an essential role in the geography of localisation as presented in spatial economic models. The actors may be geographically close without any relations between them. They will take as much advantage as possible of pecuniary externalities. The localisation of R&D is then the result not of spillovers but of the localisation of production factors. For Simmie, the presence of skilled workers is the only local determinant of the innovative capacity of firms in the Herefordshire region (Simmie 1997). Another example is the numerous cases of failure of technology parks, technopoles, etc. which, it was hoped, would create ex nihilo a dynamic of collective innovation. Secondly, is this collective dynamic, if it does exist, strengthened or not by the specialisation of the cluster? Not all studies agree on this point. Yet for high-tech activities, unlike traditional activities, it seems that Jacobs-type externalities (diversity) and not Marchal-type externalities (specialisation) have a specific impact on the growth of towns (Paci and Usai 2000). Swann distinguishes the effects of localisation on the entry of new firms and on the growth of incumbents (Swann 1999, see also Prevezer 1998). It appears that while the effect of own-sector strength on growth is positive, the effect on entry can be negative. The effect of other sectors on incumbent growth is negative (though often statistically insignificant), but (in contrast) the effect of other sectors on entry can be positive and fairly significant. But in biotechnology it is the strength of the science base in a cluster that is particularly important in influencing the amount of new entry, although there are a limited number of cross-sectoral effects attracting entry (Swann 1999: 116).

While most of the studies cited highlight the correlation between the R&D efforts of firms or universities situated in the same area, this does not mean that location plays a particular part. Firms’ innovation can be affected as much by the R&D of firms or universities located in other regions (Autant-Bernard and Massard 1999). A study by Audretsch and Stephan (1996) on biotechnology in the US is illuminating in this respect. It shows that employment of local scientists varies considerably from town to town and from firm to firm. This seems to argue for a more detailed analysis of the characteristics of regions and firms. Their study also concludes that while the founders of firms set up near the university from which they graduated, the companies for which they work as scientific advisors are not essentially local. Finally, it shows that 70 per cent of formal relations between scientists and biotech firms are inter-city relations (Audretsch and Stephan 1996).

Studies on relations between biotech firms and universities are not, however, transposable to the choice of location when firms set up. The analysis is very different at the time of start up, when the survival and development of the firm depend on the founder's close network of relations, and later when the firm is established and builds sound relations in the same scientific, productive and commercial network. A number of studies illustrate the theory of decreasing importance of geographic proximity in the course of time. The localised character of externalities is explained by the tacit dimension of knowledge and its embodiment in certain persons (not all). Almeida and Kogut share this theory with Zucker et al. in a study of patents, their citation and the mobility of patent holders (Almeida and Kogut 1997, Jaffe et al. 1993, Audretsch and Feldman1996b). They claim that there is a substitution of geographic proximity by an organisational proximity detached from the locality. This theory of a natural tendency for knowledge to be codified must nevertheless be qualified. First, it is impossible to codify everything. Codification of existing knowledge paves the way for new combinations of knowledge and hence for new tacit knowledge (Senker 1995). Moreover, if the creation process is quick (thus, if the rate of technological obsolescence is high), it is not profitable to invest in codification. Lastly, expertise at the cutting edge of knowledge is not always mobilised in the same way by firms. Catherine and Corolleur, by analysing business models of biotech firms, show that, depending on their scientific ambition, SMEs will or will not mobilise scientific resources in their geographic environment (Catherine and Corolleur 2000).

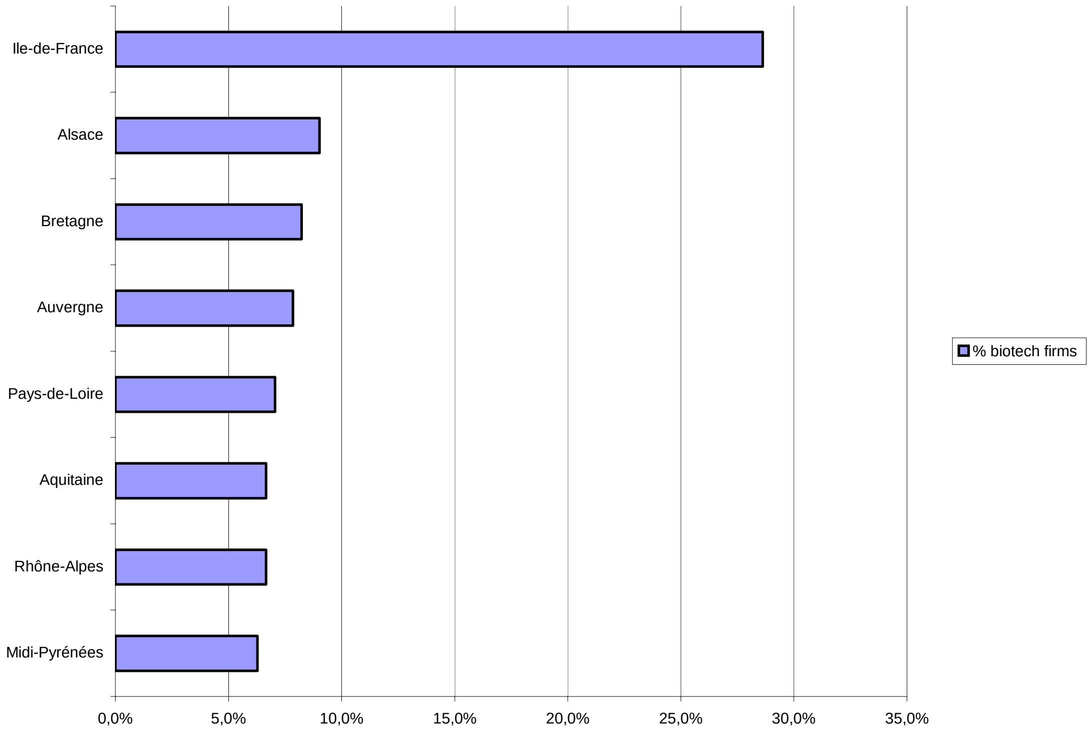
Biotechnology clusters and biotech start-ups in France.

Where are biotech start-ups located in France and why? How can biotech clusters be explained in the French case? What part have public institutions played in their emergence? Do all these firms mobilise the resources of their close geographical environment to the same extent?

Biotech clusters in France, the importance of public institutions

In France, the development of the biotechnology sector remains concentrated on a few leading regions, as shown in Graph 7.1. While Ile-de-France remains dominant, especially as regards firms created around universities and Genopole Evry, Alsace, Auvergne, Aquitaine, Bretagne, Rhône-Alpes and Midi-Pyrénées are also regions in which biotech firms set up. Firms specialising in genome and drug-development technologies are situated primarily in Ile-de-France, while firms in Aquitaine, Brittany and Auvergne focus more on agri-food related markets.

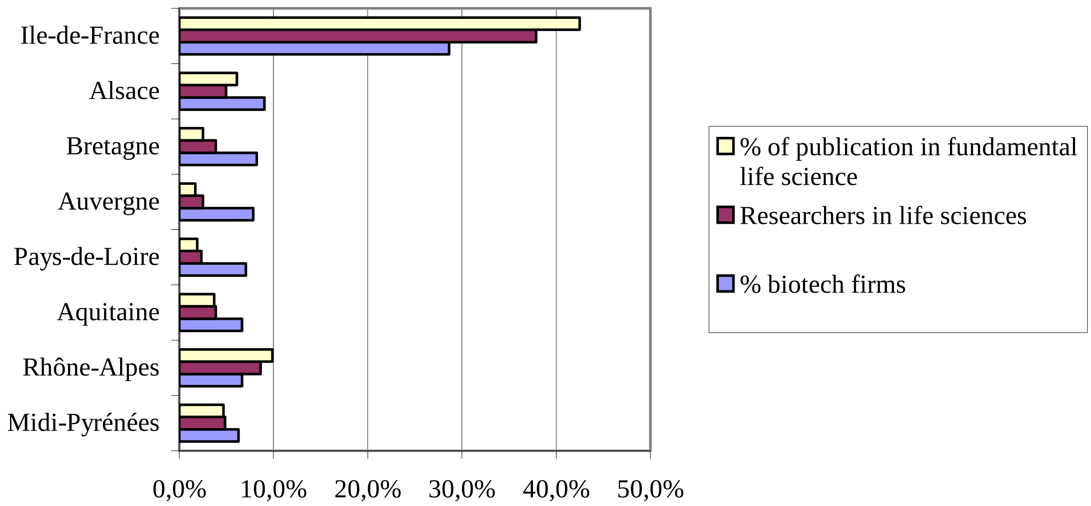
Graph 7.1: Percentage of biotech firms in each area (main regions)



Source: Author’s Calculation

Is the geography of new biotech firms related to public R&D externalities (are biotech SMEs set up in regions in which many researchers are present)? Graph 7.2 shows that the localisation of biotech start-ups is neither proportional to the number of researchers in academia in the region nor proportional to the global number of publications in the same area. A first explanation can be found in the specific nature of the French public research system compared to the US one. Unlike the US system, where relations between universities and local firms are particularly strong (Mansfield 1995), the intensity of relations appears weak in France. Public research in France is very often situated high upstream and the Paris-Province structure is dominant (Grossetti and Bès 2000). Research contracts between the public and private sectors and business creation by researchers are in the minority. When they are present, public research externalities appear far more localised in the research phase and less in the innovation phase (Autant-Bernard 2001).[4] Yet over 90 per cent of firms created by researchers are set up in the immediate environment of the laboratory for which they used to work (Grossetti and Bès 2000; and for biotechnology in France: Catherine and Corolleur 2000). Do clusters show a critical mass at which entry starts to take off rapidly? Swann considers that the take-off point for entry in most computer industry sectors is reached when total computer industry employment in the cluster is about 10,000 (Swann 1999). By 1985 Ile-de-France had already grown beyond the critical mass but the other regions had not (Swann 1999.). A priori, one would expect the same to apply to biotechnology. But the regions with the highest proportion of new firms are Auvergne, Rhône-Alpes and Ile-de-France, while firms in Alsace, Brittany and Centre are generally older. While Ile-de-France attracts new firms, it is not the only one. How can this geography be explained?

Graph 7.2: Comparison between the number of biotech firms and the academic research potential, by region (main regions)



Source: Author's Calculation

Since geographic proximity seems important in the early phases of research (theory of the link between geographic proximity and the nature of the knowledge involved) and the growth of new start-ups does not strictly follow the ranking of regions, should an explanation for the dynamics of biotech clusters not be sought in the intervention of public actors (laws, innovation incentives, etc.)? P. Monsan (Monsan 2000) proposes an up-dated analysis of the recent history of government policy to support biotechnology. At the beginning of the 1980s the aim of French public support for biotechnology was to encourage a number of industrial sectors such as agro-food and seeds. In this way, public funding was used to revitalise groups working in the life sciences and to bring them together, at the same time assisting them to rapidly integrate molecular biology and genetic engineering methodologies. To strengthen relations between public research and industry, biotechnology transfer centres were set up, for example in public sector research (PSR): Institut Pasteur, CNRS (Conseil National de la Recherche Scientifique), INRA (National Institute of Agronomic Research) etc. Subsequently, several of them became research innovation and technological centres (CRITTs, Centre Régional d' Innovation et de Transfert de Technologie)). Lastly, national public policy in favour of biotech was also designed to support start-ups. A number of companies were created using venture capital. These include Transgene (founded in Strasbourg in 1979), Immunotech (Marseille 1982) and BioEurope (Toulouse 1984).

After this initial phase, the major concern of public policy as it was redesigned in 1985 was to preserve the transversal nature of biotechnology while concentrating funds on four priority domains: the food industry, health, IT and international relations. With a budget of 16.5 million Euros over three years, the 'Expansion' biotechnology programme largely funded small biotech companies created during the eighties, enabling them to boost their own research activity (most often within a close partnership with French state research establishments), and to accelerate the development of innovative products. But despite all these efforts, the biotechnology revolution announced at the beginning of the eighties was slow in coming, and the results of research already engaged, in terms of turnover and job creation, remained erratic. At the beginning of the 1990s the authorities decided to directly support the big industrial groups' research and development programmes, so as to accelerate the commercialisation of research through concrete action. This was the objective of the BioAvenir programme launched in 1991. In bringing together Rhône Poulenc and various public research establishments, BioAvenir constituted an innovative partnership between the private and public sectors. In the mid-90s national and regional public authorities launched new biotechnology programmes. Their aims were to reinforce the partnership between private and public research, and to encourage the creation of new growth companies by facilitating research scientists' mobility between sectors and by creating facilities (technology platforms and incubators). This was a strong incentive to business creation, and at the time was backed up by renewed interest in biotechnology from the finance community, in particular for gene therapy, neuro-degenerative disease treatment and genomics. 1996 saw the arrival of the EASDAQ (European Association of Securities Dealers Automated Quotation), the European financial market for high growth high-tech companies, along with that of the Paris Bourse's 'Nouveau Marché'. Both factors contributed to the development of numerous biotech company creation projects.

Different public policy tools have been mobilised at national and regional level. The effects of local public policy can be seen in very dynamic regions such as Auvergne, Alsace and Aquitaine where the science base appears to be weaker than in other regions (like Rhone Alpes, for example). As shown by Genet (1997), these regions have all invested in a technopole as an incentive for start-ups. The main public structures founded in 1999 - 2000 (in addition to the Ivry Génopole) are the genopoles in

Montpellier, Strasbourg, Paris (Institut Pasteur), Toulouse, Lille, Lyon-Grenoble, Aix-Marseille and Bordeaux, with an annual budget of 10 million francs. To these can be added the incubators financed by the state and regions. The regional distribution of innovation incentives from ANVAR (Agence National de Valorisation de la Recherche) can be used as a (partial) indicator of differences in regional growth (Table 7.1). At this stage the public structures set up have been defined in such a way as to promote specialisation and complementarity on a national scale. Competition between public actors in clusters, to accommodate as many biotech start-ups as possible, is therefore likely to concern a territory-specific offering rather than an undifferentiated public offering (Corolleur and Pecqueur 1996). But while the strategy of public actors is to anchor as many firms as possible in the territory (i. e. to limit firms' nomadism), some firms' interest in a territory is limited to the availability of skilled workers at a low cost, while others seek local partners (laboratories, consultants in intellectual property rights, other biotech firms, etc.).

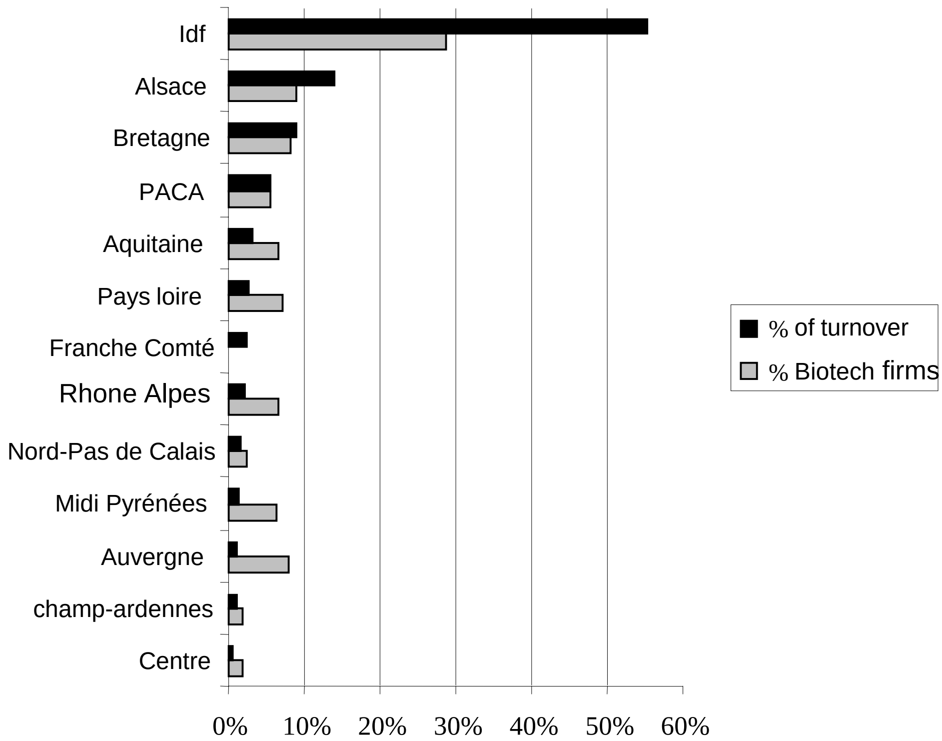
Table 7.1 : Distribution of ANVAR aid by region in 1999

	Number of projets		Total amount of ANVAR grants	
Ile-De-France	42	20%	20,4	23%
Provence-Alpes-Côte-D'Azur	32	15%	13,2	15%
Rhône-Alpes	23	11%	9,4	11%
Auvergne	19	9%	9,2	10%
Midi-Pyrénées	13	6%	5,1	6%
Aquitaine	10	5%	2	2%
Bretagne	8	4%	1,6	2%
Languedoc-Rousillon	9	4%	4,4	5%
Nord-Pas-De-Calais	8	4%	2,4	3%
Pays de la Loire	8	4%	1,3	1%
Alsace	7	3%	7,7	9%
Limousin	6	3%	1,4	2%
Picardie	7	3%	1,1	1%
Centre	5	2%	2,2	2%
Haute-Normandie	4	2%	1,8	2%
Poitou-Charentes	5	2%	2,7	3%
Basse-Normandie	2	1%	1,3	1%
Bourgogne	3	1%	0,4	0%
Lorraine	3	1%	1,3	1%
Champagne-Ardenne	1	0%	0,2	0%
		100%		100%

Source: ANVAR 2000 Bilan sectoriel 1999, Pharmacie Biotechnologie, Paris, Direction de la Technologie ANVAR.

Recently public policy supports business creation in the regions is recent. It has stimulated new business creation. However, the creation of economic wealth remains strongly localised in Ile-de-France, as shown in Graph 7.3.

Graph 7.3: Comparison of the number of firms and the turnover of those firms, by region



Source: Author's Calculation

Different trajectories on which geographic and organisational proximity have a differing impact

Our study (Lemarié and Mangematin 2000) reveals one successful trajectory (Type 1), representing a minority of cases, and three more disparate trajectories. Some firms have a regular but non-exponential growth of employee numbers and turnover, although they have existed for over ten years (Type 2); others are affiliated to a parent company (Type 3); and, lastly, large industrial corporations (Type 4) have bought others out. These different business models do not mobilise local technico-economic resources equally.

Type 1: Successful start-ups – a small minority of firms

Twenty-eight firms in our sample (14.4 per cent of the 194 respondents), considered to be the flagships of the French biotechnology industry, have grown very fast. Active primarily in the fields of genome research and drug development, their main outlet is the pharmaceuticals market. Whether they were founded about ten years ago (eleven of them) or before 1980 (twelve of them – close to half), all of them have over fifty employees. Yet these firms employ less than a quarter of all employees in the biotechnology sector. Moreover, only eight of them (i.e. 4.1 per cent) have a turnover of more than 100MF (fifteen million Euros) and only six of those are listed on the stock exchange (Biodome, Cerep, Chemunex, Genset, Quantum Appligene, Transgène).

Their development is based primarily on the presence of investors in national and international capital. Venture capital companies, present from the start, have been active in orientating these companies, setting them on a course of rapid growth. By extending the number of subscribers beyond the inner circle, firms are able to benefit from advice, contacts, human capital and an introduction into networks with which they are unfamiliar or which require too much effort to explore. (Fewer than 30 per cent of the 194 respondent firms have a venture capital company among their shareholders.)

Moreover, quoting of the firm on the stock exchange enables venture-capital firms to sell their shares and withdraw their capital, an indispensable condition for the perpetuation of venture capital financing of biotechnology firms. The presence of venture-capital firms in these companies favours the development from essentially domestic organisational proximity (family capital, network of entrepreneurs) to organisational proximity with networks comprising all actors on the biotech scene.

To maintain technological skills, fast-growing firms rely on collaboration with French or foreign universities and with public institutions such as the CNRS or INRA, rather than basing their development on a product–specific market combination. Collaboration with other firms, especially pharmaceutical companies, enables them to extract value from their technologies. Geographic proximity is clearly of little importance for this type of firm which is situated in an international market for the diffusion of its products, and maintains relations with laboratories situated elsewhere. On the other hand, the need to be connected to major communication axes shows the full importance of relations of organisational proximity and the crucial nature of introduction into networks of strong relations. Note, however, that these firms need to be close to centres of excellence to benefit from public research spillovers through interpersonal relations and international exchange maintained by academic laboratories. The quality of a firm’s interaction with players in the same geographic area will depend on scientific life in that environment. To attract the best researchers, PhDs and post-doctoral researchers – all potential collaborators –, firms are well advised to take advantage of neighbouring centres of academic excellence. This applies to their creation as well as their development.

Type 2: Stable businesses in niches

More than half (53.3 per cent) of biotech employees work in firms that have followed a different development trajectory to that of Type 1 firms. Founded in some instances in the 1970s, generally as limited liability companies (SARL) or limited companies (SA) with private persons only as shareholders, their turnover today is between ten MF (1.5 million Euros) and 100MF (fifteen million Euros). These firms (e.g. Cayla and Anda Biologicals) employ between 10 and 50 people, derive a large share of their turnover from export and invest close to 25 per cent of their turnover in research. Active mainly in the pharmaceuticals market, they have a relatively broad technological base maintained both by internal research and by relations with French and foreign universities. These firms, which have been in existence for several years, do not seem to have the intention of becoming leaders in their field on a world wide scale; they nevertheless represent an alternative development trend for biotech companies.

These companies are characterised by a strong reference to geographic proximity when they seek research or market resources in their immediate environment. In this case, relations with users of products and services are formed on the basis of geographic proximity. Yet they do not, for all that, neglect resources from organisational proximity, as attested by their membership of networks.

Type 3: Firms affiliated to a parent company

One of the strategies of pharmaceutical or seed companies is to create biotechnology firms, either alone or as a joint venture. Biotechnology is in fact a high-risk business whose development requires specific skills. Moreover, small structures are more flexible and easier to adapt to major changes triggered by the production of new scientific knowledge. Finally, investing in a biotechnology enterprise also enables firms to set up in a country with a view to taking advantage of its research "externalities" and of new markets.

Thus, major French or foreign companies (e.g. Limagrain or Rhône Poulenc, and Monsanto, respectively) have invested in subsidiaries specialised in biotechnology, either to secure a foothold in France (e.g. BioSepra, Bachem Biochimie and Diagnostica Stago) or to separate biotechnology from the firm’s main business (e.g. Syral, Biosem and Limagrain Genetics). These firms, which benefit from the captive market represented by the parent company and from the network of markets to which the latter provides access, have a faster-increasing turnover than that of independent firms. It seems here that geographic proximity plays a relatively minor part in this type of strategy, based above all on the parent company’s internal network. Organisational proximity is the most important factor, for geographic incidence is related to location of the parent company.

Type 4: Firms which are sold

In the latter type of trajectory, firms are bought out by industrial groups after proving themselves. Included in this category are firms such as Appligene (founded in 1985, with an 80 per cent takeover by the US company Oncor in 1995, and Appligene Oncor then bought out in 1999 by the Canadian Quantum), Systemix (founded in 1988, bought out by Sandoz in 1992) and Agrogene (founded in 1989 and progressively bought out by Limagrain before takeover by Perking Elmer), which differ from subsidiaries created ex nihilo (Type 3) in so far as they are initially independent. Takeovers can be explained by problems encountered by some SMEs (difficulty in gaining access to the market, incomplete technological base) and by the purchaser's intentions. The takeover must be considered as a step in the development of the SME and not as a sign of failure. The purchaser's intention is either to complete its technological base by adding the SME's portfolio of patents or technological competency, or to use the SME to facilitate its commercial growth. In the latter case, seldom mentioned, the purchaser is often a foreign group. The SME then acts as a bridgehead in France to transfer technologies or products developed by the parent company.

A takeover generally leads to significant changes in biotech SMEs, for these firms were initially created to support an independent activity that ends up having to serve the interests of its main shareholder. If the SME was bought to be a bridgehead in Europe or France (e.g. Oncor's takeover of Appligene or Perkin Elmer's buy-out of Agrogene), its research activities will probably be scaled down to ensure there is no duplication with the parent company's R&D effort. In some cases problems arise due to a culture shock between different companies or sectors, necessitating a sufficiently long period of transition before the benefits of such restructuring can be reaped.

We cannot talk here of proximity, whether geographic or organisational, for the aim is of a totally different nature. On the other hand, the location of the firm plays an important role since it is often a Trojan horse enabling a bigger firm to penetrate a geographic market to which it does not otherwise have access.

Conclusion

Based on a statistical analysis of the regional location and growth of biotech SMEs in France, this article considers the dynamics of localisation of firms when they set up, and the influence of geographic environment on their development. At the time of creation, geographic proximity with the initial networks of the entrepreneur (often from the public or private research community) impacts strongly on the firm's location. Geographic proximity enables the firm to establish itself soundly in its local environment, and organisational and geographic proximity overlap. This is one of the reasons why the impact of regional public policy in favour of business creation is so strong. As the firm grows, organisational proximity dominates and the firm moves away from geographic proximity since its market and field of reference are often international.

As in traditional sectors, certain elements influence biotech firms' choice of locality. Local infrastructure (incubators, support activities, innovation missions, etc.) plays a key part in firms' location. For some firms with technological needs that they cannot meet on their own, the existence of a technology platform is essential. For these firms, whose development is science-based, proximity with high-quality academic research is important. Such research provides a favourable cultural and scientific environment to attract able researchers likely to cooperate with the firm and thus enhance its scientific potential and reputation.

Even if, in high-tech sectors with an international profile, the importance of geographic proximity decreases as the firm grows, localisation in a dynamic scientific environment suited to the emergence of new activities is essential at the time of creation. Regional policies thus have a strong impact on a firm's initial location, simultaneously creating self-reinforcing effects on a given geographic area and clusters of firms.

While policies in favour of business creation seem to combine harmoniously on the different levels of public intervention (municipal, regional and national), the problem of firms' survival after two or three years is a very real one in an industry characterised by rapid technological change. Further studies will need to examine the development of firms in each region, in order to evaluate the impact of each factor (public policy in favour of start-ups and geographic spillovers). Others will also need to examine the linkages between the scientific reputation and the development of firms, by region.

In France there is diversity in the modes of development of biotech SMEs, adapted to the projects of their directors and shareholders. The path of ‘success’, where the firm tries to grow as fast as possible and aims at becoming world leader in its sector and in the stock market, is not the only possible one for biotech firms. It is probable, however, that from their creation firms in the biotech sector prepare their future and growth trajectory which will depend on the amount of initial investments, the networks to which they have access, the partnerships they form and whether or not they choose to appeal to outside investors. Policies supporting innovation and high-tech SMEs have to take this into account, or they could set viable firms on paths that prove to be nothing more than a lure.

Box 7.1: Data collected by means of the questionnaire

- Identity of the firm and the top managers, with position
- Main technologies developed and implemented by the firm (to be ticked off on a list of 33 technologies)
- Main areas of activity (markets) in which the firm is active (to be ticked off on a list of 28 markets)
- Turnover, R&D spending, net and effective income for past three years
- Patents owned and exploited by the firm
- Quality control in the firm
- Effective and hoped for partnerships for research, production and commercialisation.

On the initiative of the MENRT Technology Division (Biotechnology group)[5] a survey was made of firms performing biotechnology research. Biotechnology firms were considered to be those that develop or use industrial technologies derived from life science and technology (and sometimes materials) using the properties of living organisms for producing goods and services (definition proposed by the Industry Ministry, 'Les 100 technologies clés à l'horizon 2000').

The survey consisted of several stages:

1. Compilation of list of organisations (firms, economic interest groups, and associations) engaged in biotechnology research), from available sources.

2. Validation of list and addition of information, by local experts.

3. Definition of list of 478 target organisations, irrespective of size or status (SA, not for profit organisations).

4. Administration of the questionnaire.

5. Processing of data and compilation of a directory.

221 answers were registered but remained largely incomplete. In order to obtain a representative sample, the data base thus obtained was enhanced with various other available data bases: base constituted by the INRA/SERD team, the France Biotech base, the Genetic Engineering Directory, Infogreffe and Diane. Missing information was thus obtained and certain firms were added to the base when all the required information was available.

In order to standardise the answers, only registered companies (SA (Société Anonyme), SARL (Société Anonyme à Responsabilité Limitée), SNC (Société en Nom Collectif)) were selected. To ensure the relevance of comparisons with information published by Ernst & Young (1999 Report), we analysed only those firms with under 500 employees. Finally, we excluded the rare biotech firms created before 1960. The base used in our analysis consisted of 194 firms, for which full information was available. Several indications allow us to consider the analysed sample as representative: over 60 per cent of the firms in the France Biotech directory and 90 per cent of the firms present in the Genetic Engineering Directory answered the questionnaire. When we analyse the base of 600 firms to which the questionnaire was sent, fewer than 450 corresponded to the selected criteria. We can therefore consider that the sample analysed corresponds to roughly half of the biotech firms active in France

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Notes

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[4] This result was obtained for the 1990s by measuring the geography of public R&D spillovers over the R&D and patents of firms (Autant-Bernard, 2000). It is contradictory to the results of Mansfield for the US, where geographic proximity is equally important for applied research and for basic research (Mansfield, 1995).

[5] A steering committee consisting of Pascale Auroy (ARD), Christine Bagnaro (ANVAR), Patrice Blanchet (DTA/2, MENRT), Marie José Dudézert (DTA/2, MENRT), Anne Sophie Godon (Arthur Andersen) and Vincent Mangematin (INRA/SERD) met under the chairmanship of Jean Alexis Grimaud in 1998-99 to plan and conduct the survey.