Innovation and competitiveness in European biotechnology

Enterprise Papers - No 7
2002

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Enterprise Directorate-General
European Commission

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This report was prepared as a background report for the Enterprise Directorate-General's *European competitiveness report 2001*. It was written by

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The authors are grateful to Diana Boraschi and Aldo Tagliabue for discussions and background material. Research assistance: Gianluca Baio, Daniela Casula, Antonella Fiori, Chiara Giani, Nicola Lacetera, Francesco La Forgia, Caterina Vollaro, Carmela Pace, Rossana Pammolli, Andrea Paolini.

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Luxembourg: Office for Official Publications of the European Communities, 2002

ISBN 92-894-1805-2

Printed in Belgium

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Executive Summary

Biotechnology has to be understood as a system or network. Innovative activities, as well as production and commercialisation, rest on and involve, either directly or indirectly, a large variety of actors: different types of firms, other research organisations like universities and non-industrial research centers, financial institutions, regulatory authorities, governments, health care systems, consumers, etc.

The competitiveness of innovation and production systems in biotechnology cannot be assessed by looking only at the individual firms, but also at the broader set of institutions, infrastructures, and policies that influence the actions of companies, and – even more important – at the dynamic interactions between these levels of analysis.

The distinctive features of this industry are the strong relationship between innovation and competitiveness, the collaborative basis of research, and the importance of small firms. Biotechnology highlights the importance of firms' "capabilities" – the ability to mobilise and exploit new knowledge and to reach out and exploit collaboration among agents and across stages of product development, scientific disciplines and industry frontiers. The sector is characterised by a new breed of agents, small specialised firms – dedicated biotechnology firms (DBFs) – that have entered the industry with the explicit aim of exploiting the new technologies of life sciences for different industrial purposes. These firms are having a remarkable and radical impact on pharmaceuticals and agriculture.

Patent and collaborative R&D projects data indicate that the US has accumulated and maintains a dominant advantage in innovative activities in biotechnology compared to Europe. Europe in fact lags significantly behind the US in all facets of the commercial development of biotechnology. There is now agreement that this leadership originates essentially in the strength of its DBFs and, more generally, in the development of a deep market for technology. Nevertheless, some of the smaller European countries (Ireland, the Netherlands and the Nordic countries) appear to specialise successfully in biotechnology. Also an intense dynamism has been observed recently in firms' entry – from

1996 to 2000 the population of independent European DBFs almost doubled to close to 2,000 – as well as in clustering of research and production in Europe. In 1999 and 2000, after a 4-year period of intense entry, in which the overall number of EU biotechnology firms almost doubled, the rates of company formation have decreased. This slowdown (not corroborated by Ernst & Young's data) seems to be similar, in nature, to the one observed in the USA at the beginning of the Nineties.

According to the BID data set at the University of Siena, the distribution of biotechnology DBFs in Europe is led by Germany and the UK (with over 500 DBFs) followed by France and Sweden (with at least 200 DBFs). The BID data set indicates that activity is also prominent across the rest of the European nations, ranging from around 30 DBFs in Spain to close to 100 in Switzerland.

It may be argued that Europe's lag behind the US in biotechnology is partly a reflection of its late entry. Innovative activities are generally characterised by increasing returns and being first provides long-lasting leadership. But this may not be the only factor. A fundamental precondition for a successful development of biotechnology is the availability of leading-edge scientific capabilities – without a strong and diversified scientific research base, no technological take–off is possible. Moreover, success in this industry depends on a delicate blend of competencies and incentives and requires decentralisation of efforts, a diversity of approaches, as well as co-ordination of several differentiated agents, capabilities and functions. In particular, new European DBFs are generally smaller than their US counterparts, less active in global networks and collaborative relationships and fewer are present in markets for these technologies. Access to an international scientific community requires direct and active participation in networks of scientists. One finding of the Report is the unattractiveness of the European environment to US research: comparatively little US research is done in Europe.

The European research system in the life sciences and in biotechnology is still too fragmented. To a considerable extent, this fragmentation may be due to regulatory, entrepreneurial, fiscal and financial factors. However, in addition to these factors, the supply of cutting-edge scientific research may be inadequate. If so, this problem could be addressed not only through higher levels of

research funding but also through higher degrees of pluralism in funding sources, lower dependence on closed national systems, and higher integration of research with teaching, clinical research and medical practice. One of the most effective means of achieving this would be through the establishment of a European Research Area. European DBFs are still far too small and too specialised in specific niches and they manifest an insufficient ability to access and make efficient use of networks of collaborative research. Although there has been some success, notably in the promotion of biotechnology start-ups, the growth of DBFs in Europe appears to be hindered.

DBFs exist in a relationship of strong complementarity with large corporations. The latter are not only the fundamental source of demand for the products and services of DBFs but, equally importantly, they also provide the integrative capabilities that transform fragments of knowledge into products and constitute precious reservoirs of technological and managerial competencies. The importance of the relationships between the creation and development of DBFs and the research/absorptive capabilities of the large companies make it clear that policies for biotechnology should be much more strongly linked to policies aiming at raising the competitiveness of “downstream” industries, such as pharmaceuticals and agriculture.

Policies for biotechnology have been in place for several years in Europe, and some important results have been achieved.

The promotion of the creation of DBFs has been central to European biotechnology policies for more than a decade. Still, with the policy emphasis on industry–university relations, on creating the “entrepreneurial university”, on venture capital and on intellectual property rights, the problem of an inadequate supply of cutting–edge scientific research may not have been sufficiently addressed. Increased funding is only a part of the solution.

Higher degrees of pluralism in funding sources, lower dependence on closed national systems, higher integration of research with teaching, clinical research, and medical practice, together with a higher reliance on interdisciplinary research teams in the life sciences, should become priorities of a European research policy biotechnology.

I. Introduction

This Report analyses the current status of innovation and production systems in European biotechnology, and, in particular, the innovative capacity and related factors that are some of the major determinants of the competitiveness of European biotechnology firms.

As such, biotechnology cannot be considered as an industrial sector, but rather a set of technologies. Its applications span a number of industrial and service sectors, as well as agriculture. This direct link with science makes innovative capacity an important determinant of competitiveness.

While large biotechnology firms are undoubtedly important, the emphasis of the chapter is on the role of the small and medium, research-intensive companies, which have emerged from the new opportunities opened up by the life sciences. In the present chapter they are referred to as dedicated biotechnology firms (DBFs).

DBFs are primarily university spin-offs that mobilize scientific and technological knowledge and transform it into potentially commercially useful techniques and products. These firms are usually formed through collaboration between scientists and professional managers, backed by venture capital. Their specific skills reside in the knowledge of new techniques and in research capabilities.

Inevitably, comparisons with the US biotechnology industry are made throughout. In the United States, biotechnology was the motive force behind the first large-scale entry into the pharmaceutical industry since the early post World War II period. Entry rates soared in 1980 and remained at a very high level thereafter, with waves linked to both the stock market performance and to the appearance of successive new technologies. One notable difference between Europe and the US in the 1980s and at the beginning of the Nineties has been that, while in the US a new research–intensive industry in the life sciences has continued to develop, there has been no equivalent specialisation in entrepreneurial biotechnology in Europe (see also Gambardella, Orsenigo, Pammolli, 2001). Partly reflecting this difficulty to develop an industry of DBFs, the perception has emerged that the US has a competitive advantage over Europe in biotechnology.

The US have pioneered the emergence of an effective division of labour between new, small companies, large corporations and other research institutions, which have different comparative advantages in the "exploration" and "exploitation" of new innovation opportunities (March, 1991). Europe has been less effective in facilitating the growth of research-intensive DBFs.

While large multinationals, such as biopharmaceuticals and agro-food, may not need local technology suppliers, the presence of a local industry of research–based firms and technology suppliers is critical. On the one side, despite tendencies towards a wider internationalisation of research, high technological performances tend to be linked to home-based research capabilities. On the other side, the "biotechnology" industry is, by itself, a powerful source of growth and social progress. The US biotechnology industry has generated, over the past two decades, a large number of new jobs and at least a dozen new world-class companies (e.g. Amgen, Chiron, Genzyme, and others), along with several new others in the new general purpose technologies (e.g. Incyte, Human Genome Sciences, Millennium, Celera, and others). It has also produced a stream of revenues, most frequently in the form of royalties from licenses or R&D contracts and collaborations.

Given the impact of biotechnology on social and economic progress, as well as its effects on downstream industries, both national European governments and the European Commission have developed a strong anxiety about European competitiveness in this field and have promoted the birth of a new industry of dedicated biotechnology firms.

Particularly in recent years, the perception has started to diffuse of a new dynamism in European biotechnology.

However, the features and contribution of the new European DBFs have not been the object of systematic comparative investigations, and much of the empirical material on innovation and production systems in biotechnology is based on the American experience.

Moreover, many statistical and methodological problems affect the quality and reliability of the currently available data on European biotechnology. For example,

the lack of standardised survey procedures prevents the existence of comparable indicators on many relevant issues[1]. In some cases, the coverage of biotechnology is incomplete, while other data sources drastically overstate the impact and the expected rates of growth of biotechnology.

In synthesis, any comparison among nations and regions, in terms of biotechnology policies, scientific and technological capabilities, and industrial competitiveness, is severely limited, at present, by currently available data sources and statistics.

Against this background, the first goal of the Report is to expand empirical knowledge on the current state and performance of the new European biotechnology industry. Then, the Report gives an assessment of the institutional, legal, cultural and industrial variables that affect industrial growth and competitiveness in biotechnology.

The Report integrates available statistics and sources of information with an original data set specifically aimed at giving an account of the structure of industrial biotechnology in Europe. BID (the *Biotechnology Industry Database*), developed by the Epris Research Unit at the University of Siena, provides information on location, number of employees, technological and market specialisation, R&D and collaborative activities, of biotechnology firms across Europe, with particular reference to the small Dedicated Biotechnology Firms (DBFs).

Other data for this Report come from OECD, Eurostat, government statistics, from statistics collected by publicly funded organisations such as the US National Science Foundation in the US and NUTEK in Sweden, the most important patent offices, and from commercially available databases such as Windhover, Recombinant Capital, and Bioscan. Reports and data from commercial sources like Ernst&Young, Decision Resources, SRI, McKinsey, the European Venture Capital Association, have also been used.

The Report is organised as follows.

[1] "Many basic indicators are available that are similar in purpose, such as biotechnology employment or the number of 'core' biotechnology firms, but the definition of employment or a 'core' firm varies from country to country. In some countries, we do not even have basic information on the definitions or descriptions of survey methodologies" (van Beuzekom, 2001, p. 4).

Section II presents the main general indicators of European innovative activities in biotechnology. Section III provides a detailed analysis of R&D activities and research collaborations of European biotechnology companies, in the context of the international division of innovative labour within the field. Section IV analyses the structure of the new European biotechnology industry and the new DBFs that entered the industry during the 1990s, while Section V analyses the essential features of biotechnology clusters in Europe. Section VI reviews briefly the institutional, legal, and cultural factors that have an impact on the evolution and performances of the biotechnology industry. The final section summarises the main findings of the Report.

II. Innovative Activities in the European Biotechnology Industry

II.1. Introduction

This section provides an overview of the innovative performance of industrial biotechnology in Europe. It looks first at the general structure and trend in innovative activities, as measured by patent data and patent citations. Second, it examines in more detail the localisation of inventive activities in biotechnology across macro-regions and countries, always relying on patent data.

The use of patents as an indicator of innovative output is largely justified by the peculiarity of the technology and the widespread patenting practices at all levels of the industry. While in other industries patents are a highly imperfect indicator, in biotechnology they closely reflect innovation output (see also the discussion in Gambardella, Orsenigo, Pammolli, 2001).

II.2. General Trends

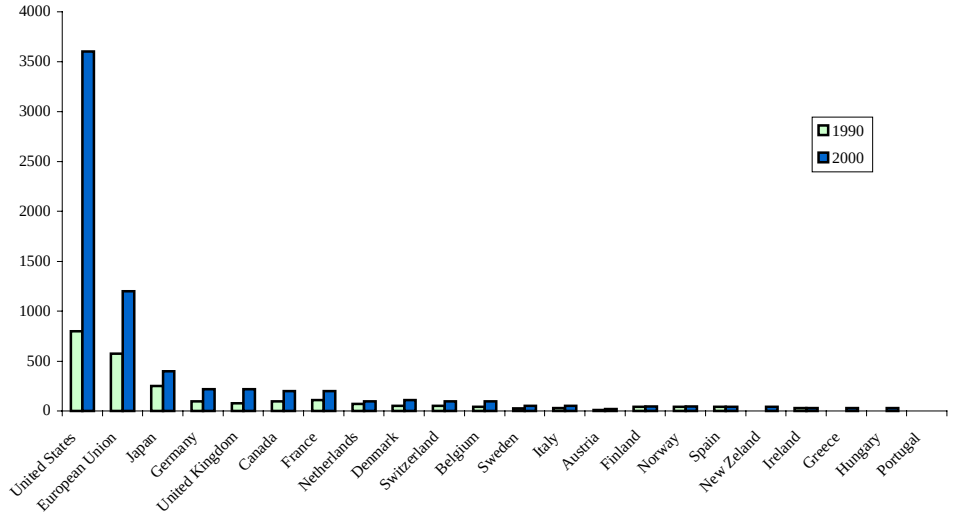
The available empirical evidence shows that the US are and continue to be the most important locus of innovation in biotechnology (see Figure 2.1; Figure 2.2), followed by Japan, Germany, UK, and France.

Figure 2.1 gives an account of the dominance of the US in biotechnology inventions. From 1990 to 2000, the United States increased by 9 percentage points its share of all biotechnology patents granted by the USPTO[2]. The share of Japan declined by 11 %. A modest increase occurred in the case of Denmark (+ 1.1%), while Germany lost a little ground (- 1.2%). The shares of all other European countries have remained relatively stable over the last decade.

[2] Biotechnology patents are covered by class 435 of the USPTO classification system ("molecular biology and microbiology"). For a complete definition of class 435 see http://www.uspto.gov/web/offices/ac/ido/oeip/taf/moc/435.htm.

Between 1990 and 1997, national shares of biotechnology EPO patent applications[3] were relatively stable (see Figure 2.2), with the exception of Japan, which saw a decline of 6%. The UK shows the strongest performance (+ 2.1%). The shares of the other European countries have remained relatively stable over time.

Figure 2.1: Biotechnology patents granted by the USPTO, 1990 and 2000



Source: OECD, calculations based on data from USPTO

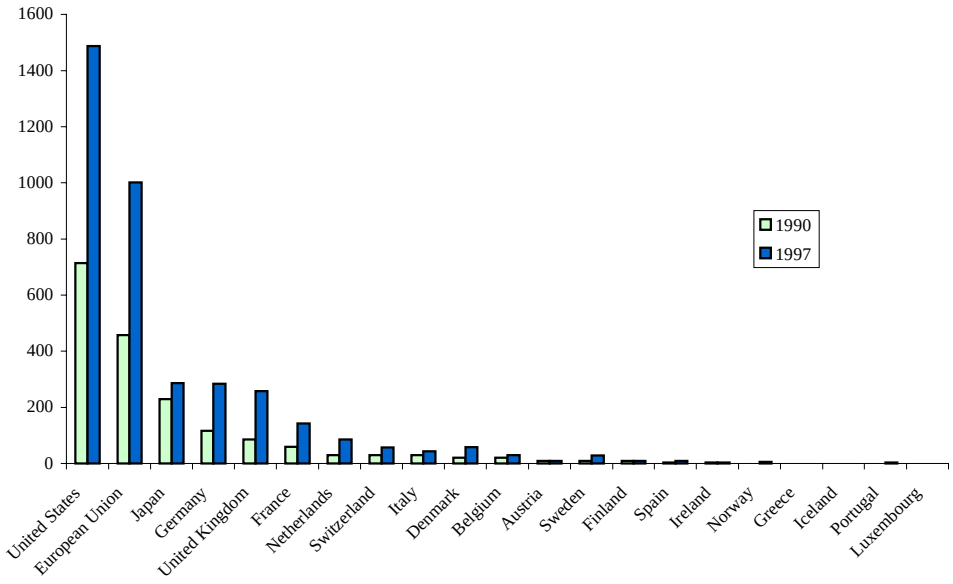
Patent citation data provide a better measure of the technological and economic potential value of innovative activities than patent counts. Citations are a measure of the importance or impact of inventions and a proxy for knowledge flows among patenting institutions. Widely-cited patents tend to be "seminal" patents, i.e. key inventions which further patents must refer to. Moreover, high citation rates have been shown to correlate with the economic value of patents. Thus, a high number of

[3] European biotechnology patents are covered by 5 IPC codes: C12M: Apparatus for enzymology or microbiology; C12N: Micro-Organisms or Enzymes; compositions thereof; C12P: Fermentation or enzyme-using processes to synthesise a desired chemical compound; C12Q: Measuring or testing processes involving enzymes or micro-organisms; C12S: Processes using enzymes or micro-organisms to liberate, separate, or purify a pre-existing compound or composition. For complete definitions of these IPC codes, see http://classifications.wipo.int/fulltext/new_ipc/index.htm.

citations received by a given firm or country can be interpreted as a measure of the quality and relevance of its innovative activities.

Data not reported here for reasons of space (see Lacetera and Orsenigo, 2001), show that the share of citations referring to US patents is substantially higher (around 55%) than the share of simple counts, suggesting that on average US patents are relatively more important. Moreover, among European countries, only UK patents show a higher share for citations than for patent counts.

Figure 2.2: Biotechnology patent applications to the EPO for priority years 1990 and 1997



Source: OECD, calculations based on data from USPTO and EPO

On the basis of a subset of "highly cited" patents (i.e. patents receiving at least 10 citations in the period not counting self-citations) in the period 1978 – 1995 (with citations up to 1997), the US lead increases further to 65.4%.

DBFs hold a disproportionate share of these highly cited patents (48%), and US DBFs account for more than 80% of DBFs' highly cited patents. In Europe (including Switzerland), around 65% of the highly cited patents belong to large incumbent firms and around 20% to DBFs (almost all of them British). Considering the top twenty

institutions in terms of patent citations (i.e. institutions having the higher number of patent citations), 11 are American (4 DBFs, 3 incumbents, 4 universities and other research organisations), 2 are, respectively, German, British and Japanese, while Switzerland, France and Denmark appear with one institution. Almost all of these European institutions are large corporations, with the only exceptions of one British DBF and one French public research organisation. At a more aggregate level, however, it is important to notice that Sweden turned out to have the highest share of highly cited patents in the life sciences filed in 1994-1998 (see US Council on Competitiveness, 2001).

Patent data show also that the USA are relatively more specialised in the pharmaceutical segment of biotechnology. Their share of highly cited agro-food patents is 13.5% as compared to a total of 17%. Only two European countries have highly cited agro-food patents, namely Germany (35%) and the UK (33%) of their total highly cited patents.

The growth and impact of biotechnology is affected, to a certain extent, by the size and the growth of 'downstream' industries, which demand biotechnology products and technologies (see also Gambardella, Orsenigo, Pammolli, 2001).

Table 2.1 shows, over a period of twenty years, the shares on GDP of the most important industries related to biotechnology: food, chemicals, and pharmaceuticals, for the US, Japan, and four major European countries: Germany, France, the UK, and Sweden. The data in Table 2.1 shows a continuous growth of the share of pharmaceuticals, with double-digit growth, while the shares of the food industry on GDP decrease significantly.

The countries that recorded the highest growth in the GNP share of pharmaceuticals are the US and the UK, while Germany and Japan experienced a much slower growth. As for chemicals, UK, Germany and France have the highest share in GNP.

Table 2.1: International Patterns of Specialization in Related Industries: Share of GNP in Food, Pharmaceutical and Chemical[1] Industries, 1978-97, Main Countries

		Average share of GDP		
		1978-1985	1986-1993	1994-1997
United Kingdom	Food	19,11 %	17,97 %	17,00 %
	Chemicals[1]	19,03 %	18,00 %	19,66 %
	Pharmaceuticals	1,50 %	2,14 %	2,78 %
Germany	Food	14,46 %	12,82 %	11,77 %
	Chemicals[1]	20,31 %	17,71 %	18,61 %
	Pharmaceuticals	1,11 %	1,32 %	1,43 %
France	Food	17,79 %	17,01 %	16,68 %
	Chemicals[1]	19,47 %	16,40 %	18,11 %
	Pharmaceuticals	1,65 %	2,24 %	2,65 %
Sweden	Food	4,06 %	2,78 %	2,81 %
	Chemicals[1]	12,87 %	10,69 %	10,25 %
	Pharmaceuticals	0,85 %	1,67 %	2,72 %
USA	Food	14,27 %	14,36 %	13,35 %
	Chemicals[1]	19,42 %	16,69 %	16,59 %
	Pharmaceuticals	1,17 %	1,83 %	2,21 %
Japan	Food	11,07 %	10,90 %	11,11 %
	Chemicals[1]	14,47 %	9,52 %	11,28 %
	Pharmaceuticals	1,26 %	1,42 %	1,56 %

Remark: [1] Except Drugs
Source: OECD, STAN Database (2000)

II.3. R&D Activities and Research Collaborations: Inter-Country and Inter-Regional Comparisons[4]

Patent data provide important information about the geographical distribution of biotechnology research across macro-regions (Europe and the US) and across countries. The extent to which companies locate biotechnology research outside of their home country (internationalisation of research) is also important. To put the analysis in perspective, biotechnology is compared with four other branches of the chemical industry (materials, organic chemistry, pharmaceuticals, and polymers).

The analysis is based on the following data:

[4] This section is based on Mariani, 2001.

The *European Patent Office*. A data base of 97,785 chemical patent applications between 1987-1996, covering five main technological sectors: biotechnology, materials, organic chemistry, pharmaceuticals and polymers[5].

The *European R&D database* (by Reed Elsevier Publisher). This data base provides information on 7,264 laboratories located in Europe that perform research in chemicals, pharmaceuticals, and biotechnology. The laboratories are classified as private if they are firms' labs, or public if they belong to government research institutions, universities, or hospitals.

A *random sample of 10,000 chemical patents* drawn from the original sample of 97,785 patents. The data base includes: the number, name and addresses of the assignees; the number, name and addresses of the inventors; the primary IPC class, and the number and type of supplementary IPC classes; the date of the patent application. Based on *Who Owns Whom* all company assignees have been classified under the name of the ultimate parent company/institution.

Location of research activities

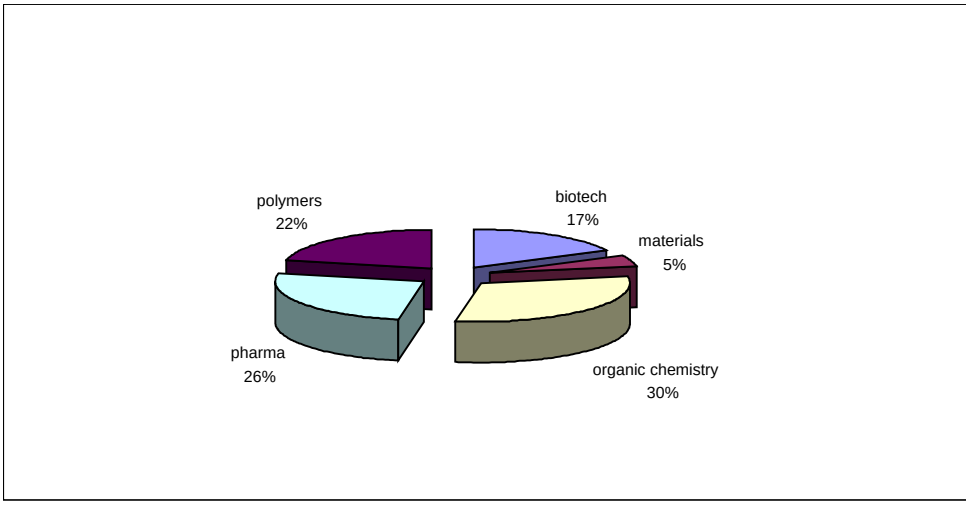
It is assumed that the location of the inventors of the (97,785) patents and the location of the (7,264) chemical R&D laboratories coincide with the location of the inventive activity.

The data suggest that the US are comparatively more specialised in biotechnology innovations, and that some of the smaller European countries show greater specialisation in biotechnology compared to larger European countries.

Figure 2.3 shows the sectoral break down of patents by subsectors. In 1987-1996 biotechnology patents were 17% of the total chemical patents. This ratio has increased over time from 16% in 1987-1991 to 19% in 1992-1996. Clearly, these are EPO patents that include patents developed in Europe and in other countries, like the US and Japan. Figure 2.4 shows the share of patents attributed to each country.

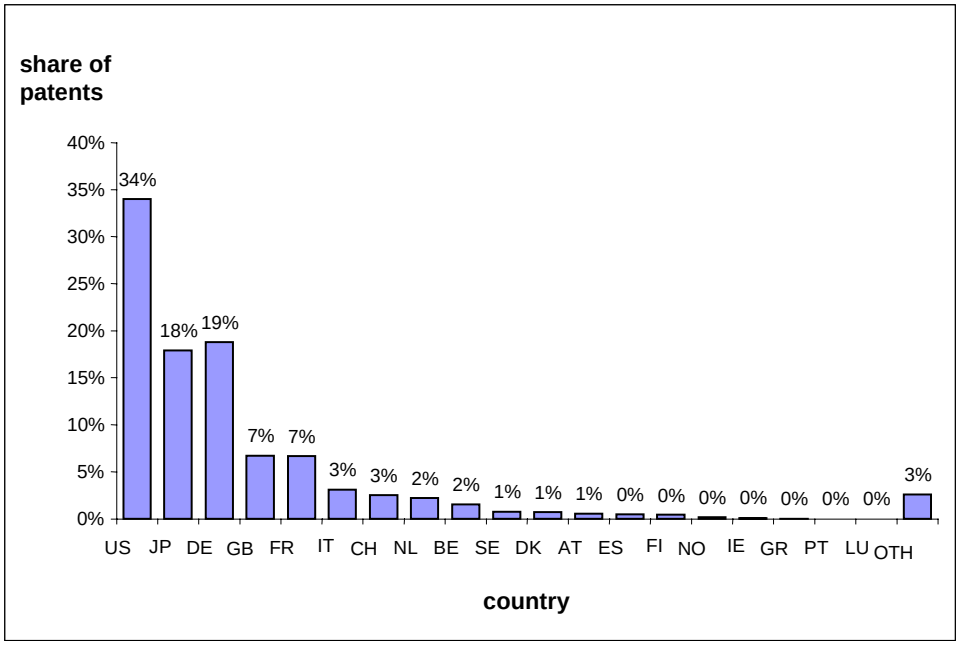
[5] The classification was developed by a research unit coordinated by R. Pammolli, a pharmacologist, who assigned the 3-digit IPC (International Patent Classification) classes in chemicals (and in chemical related technologies) to one of the five sectors above. We attributed each patent to one of these five sectors according to whether its main IPC class belonged to that sector. Since our expert did not feel comfortable with assigning all 3-

Figure 2.3: Share of Patents by Chemical Class (1987-1996)



Source: Elaboration on European Patent Office (1998)

Figure 2.4: Share of 1987-1996 EPO Patents in Chemicals by Country of Invention



Source: Elaboration on European Patent Office (1998)

digit IPC classes in chemicals and especially in chemical related technologies to one of the five sectors, the concordance could be safely done only for 97, 785 patents rather than the whole set of 201,531 patents.

The biotechnology patents invented in Europe represent 14.4% of the total number of chemical patents invented in Europe, compared to 22.5% of the EPO biotechnology patents invented in the US over the total number of chemical EPO patents invented in the US. This suggests that the US chemical companies are relatively more focused than European ones on biotechnology. To examine this issue further, the Revealed Technological Advantage Index (RTA) was computed for different countries. RTA is a country's share of all patenting in a given technology/sector relative to the share of patents in that technology/sector over all technologies/sectors, and it gives an account of the specialisation of a country or region in a technological field (Soete, 1989; Archibugi and Pianta, 1992; Caniels, 1999). The index is defined as $(P_{ij} / \sum_J P_{ij}) / (\sum_i P_{ij} / \sum_i \sum_J P_{ij})$, where P denotes the number of patents in country/region *i* and sector *j*. Table 2.2 shows the Standardised Revealed Technological Advantage Index (SRTA) = (RTA-1)/(RTA+1), for Europe, the USA and Japan. The standardised index varies between –1 (non-specialisation) and 1 (specialisation). The evidence in Table 2.2 suggests that the US has a stronger specialisation in biotechnology than Europe (and Japan). The SRTA index for the US in biotechnology is 0.13 compared to –0.09 for Europe, and –0.12 for Japan.

Table 2.2: Standardised Revealed Technological Advantages of Europe, USA, and Japan in biotechnology, materials, organic chemistry, pharmaceuticals and polymers (97,785 patents in 1987-1996).

(RTA-1) / (RTA+1)					
Country	**Biotech.**	**Materials**	**Organic chemistry**	**Pharma**	**Polymers**
EU total (*)	-0,09	0,01	0,06	0,02	-0,05
US	0,13	-0,06	-0,08	0,01	-0,01
JP	-0,12	0,08	0,01	-0,11	0,15
OTHERS	0,22	0,02	-0,08	0,11	-0,39

(*) This is EU-15 plus Switzerland (CH) and Norway (NO)

Source: Elaboration on European Patent Office (1998)

Table 2.3: Standardised Revealed Technological Advantages of European countries in biotechnology, materials, organic chemistry, pharmaceuticals and polymers (97,785 patents in 1987-1996) (*)

(RTA-1)/(RTA+1)					
Country	**Biotech.**	**Materials**	**Organic chemistry**	**Pharma**	**Polymers**
D	-0,31	0,05	0,12	-0,08	0,07
F	-0,03	0,08	0,01	0,12	-0,22
UK	0,01	-0,14	0,04	0,16	-0,37
I	-0,24	-0,07	0,00	0,09	0,05
CH	-0,17	-0,40	0,25	-0,06	-0,27
NL	0,15	0,16	-0,14	-0,18	0,15
IRL	0,23	0,02	-0,30	0,19	-0,24
B	0,02	0,14	-0,23	0,06	0,12
S	0,25	-0,07	-0,28	0,26	-0,55
DK	0,41	-0,29	-0,12	0,06	-0,80
E	-0,02	-0,21	0,19	0,05	-0,54
A	0,34	0,19	-0,19	-0,10	-0,16
FIN	0,12	-0,08	-0,29	0,01	0,18
N	0,45	0,42	-0,30	-0,14	-0,54
GR	0,39	0,02	-0,31	0,03	-0,28
L	-1,00	0,31	-0,24	-0,14	0,42

Remark: (*) Portugal is excluded because it had too few patents
Source: Elaboration on European Patent Office (1998)

Table 2.3 reports the standardised RTA by individual European country. It shows that it is the larger European countries that show no specialisation in biotechnology compared to the other branches of the chemical industry. The standardised biotechnology RTA for Germany (–0.31), Italy (–0.24), France (–0.03) and the UK (0.01) are negative or very close to zero. By contrast, the standardised biotechnology RTA for the smaller European countries – Denmark (0.41), Ireland (0.23), the Netherlands (0.15), Sweden (0.25), Finland (0.12) and Norway (0.45) – is positive and has a large value. Germany and the UK have dominated the traditional chemicals industry for many years while Italy and France have also been important worldwide. The RTA results indicate that whereas the latter countries continue to focus their activities in traditional chemicals, smaller European nations do not. Thus, the traditional dominance of the larger European nations in chemicals seems to lead them to do a higher proportion of their research in traditional areas of biotechnology.

The results shown by Tables 2.2 and 2.3 are confirmed by simple ratios of total biotechnology patents over the total number of patents by country of invention. Table 2.4 shows that 45.4% of the total biotechnology patents in the sample were invented

in the US and 36.5% biotechnology patents invented in Europe. However, in all chemical sectors the US share is 34.5% while Europe's share is 44.8%.

As for individual countries, the share of biotechnology patents invented in Germany over the total number of biotechnology patents in the sample is 9.9%. The shares of organic chemistry and polymer patents invented in Germany over the total number of patents in each of these two sectors are respectively 23.7% and 21.8%. The differences are less striking for the other large European countries. In particular, the share of pharmaceutical patents invented in France over the total number of pharmaceutical patents is 8.5%, and the share of French patents in materials is 7.8%. The same percentages for biotechnology, organic chemistry, and polymers are respectively 6,3%, 6,8%, and 4,3%. The UK is specialised in organic chemistry and pharmaceuticals: 7.4% and 9.3% of the total patents in each of the two sectors. The percentages for the other three technological sectors are smaller. Consistently with the results shown in Table 2.3, there is a higher percentage of biotechnology patents invented in the smaller European countries, notably the Netherlands, Sweden, Denmark, Ireland, and Austria, than the share of patents in the other classes that were invented in these countries.

The data on the R&D laboratories also shed light on the comparative specialisation of European countries in biotechnology. Of the 7,264 chemical R&D labs in the sample, 32% perform biotechnology research[6]. Smaller countries (Denmark, Finland, Ireland, and the Netherlands) are more focused on biotechnology than the larger countries (Italy, Germany, and France), thus confirming the results seen earlier[7].

Finally, about 72% of the biotechnology laboratories in the sample are public (i.e. government research institutions, universities, and hospitals). The evidence across countries is mixed. In Finland and in Ireland, 82.9% and 80.6% of the biotechnology labs are public. This percentage drops to 67.7% in Denmark, and to 56.8% in the

[6] Each R&D lab in our sample can perform more than one activity. For example, only one third of the 32% of labs carrying out biotechnology research perform only biotechnology research. The other two thirds perform research in biotechnology and in one or more other chemical sectors.

[7] For example, in Denmark, Finland, Ireland, and the Netherlands, the percentage of chemical R&D labs doing biotechnology research is respectively 48.5%, 49.4%, 40.4%, and 42.0%. By contrast, the percentage for Italy, Germany, and France, is 21.0%, 25.1%, 30.7%. In the UK, the percentage is 39.5%. This confirms that biotechnology offers an opportunity for entry in the broadly defined chemical industry to countries that were not

Netherlands. The former two countries are above, while the latter are below the sample average. It appears, therefore, that the entry of Finland and Ireland is related to public funding and public research in biotechnology. By contrast, in the Netherlands, and partly in Denmark, the share of activities in biotechnology is to a greater extent associated with private research. No single model emerges. Either private or public research can be the means by which newcomer countries can focus on biotechnology.

Home vs. foreign locations of the inventive activity in biotechnology

The data provide information on the extent to which patent assignees locate research activity in their home country. It is assumed that the locus of the innovative activity is the location of the inventors of the patent and that the location of the patent assignee is given by the nationality of the ultimate owner of the assignee[8]. The results show that, in general, the home country is the preferred location of inventive activities in all countries and sectors, and that biotechnology is a partial exception, with the European countries locating a significant share of their inventive activity in the US.

leaders in traditional chemicals. The long standing dominance of Germany and the UK, and partly of Italy and France, in chemicals does not seem to provide a critical advantage in the new biotechnology industry.

[8] The need to control for the ultimate owner of the assignees was the reason why the smaller sample of 10,000 patents was used here. It would be very difficult to examine the complete sample of 97,785 patents for the purpose of this Report.

Table 2.4: Share of patents by region of the assignee, region of the inventor and by sector (10,000 sample patents).

Country of the assignee			
Country of the inventor	**EU**	**US**	**Total**
All chemical sectors			
EU	86.3 %	9.0 %	44.8 %
US	11.9 %	87.8 %	34.5 %
Total	98.2 %	96.8 %	79.3 %
Biotechnology			
EU	82.1 %	4.9 %	36.5 %
US	14.6 %	92.7 %	45.4 %
Total	96.7 %	96.6 %	81.9 %
Materials			
EU	90.7 %	8.0 %	44.9 %
US	7.8 %	90.1 %	30.9 %
Total	98.5 %	98.1 %	75.8 %
Organic chemistry			
EU	89.1 %	10.8 %	50.8 %
US	9.5 %	87.4 %	28.4 %
Total	98.6 %	98.2 %	79.2 %
Pharmaceuticals			
EU	85.0 %	11.5 %	47.3 %
US	13.3 %	86.2 %	36.0 %
Total	98.3 %	97.7 %	83.3 %
Polymers			
EU	85.4 %	8.3 %	40.1 %
US	12.9 %	84.6 %	33.5 %
Total	98.3 %	92.9 %	73.6 %

Source: European Patent Office (1998)

Table 2.4 shows that European assignees invent 86.3% of their chemical patents in Europe and US assignees 87.8% of their patents in the US.

When European companies locate their patenting activity outside Europe, they develop almost all of their "foreign" chemical patents in the US – the total share of patents by European assignees invented either in Europe or in the US is 98.2%. Thus, the US is the favourite foreign location of the European assignees. Finally, there seems to be a fairly balanced interchange of research between the two continents in chemicals since the share of EPO patents by European assignees invented in the US (11.9%) is very close to that of the EPO patents by US assignees invented in Europe (9.0%).

As shown also in Table 2.4, this pattern of cross-location between Europe and the US is also similar across the chemical subsectors, with biotechnology being the only exception. The result that really stands out is the share of biotechnology patents by US assignees invented in Europe, which is only 4.9%, while the share in the other

direction is 14.6%, suggesting that the US is an attractive location for biotechnology research by European assignees.

Therefore, the data do not show that European assignees perform a disproportionately large amount of biotechnology research in the US – they do almost as much biotechnology research in the US as they do in the other chemical sectors – but that Europe is not attracting similar levels of biotechnology research performed by US assignees. Even in pharmaceuticals, which is the closest to biotechnology, Europe attracts 11.5% of the patents applied for by US assignees. The apparent European lack of attractiveness to US research seems to be specific to biotechnology.

Table 2.5 shows the shares of biotechnology patents invented by European assignees in their home country, in the US, and in European countries other than the home country. The Table shows that the assignees locate research largely in their home-country, although inter-country differences exist. The most important difference is that Swiss assignees invent almost half of their biotechnology patents in the US, while assignees from all the other countries in Table 2.5 (Germany, France, Italy, the Netherlands, and the UK) invent over 70% of their biotechnology patents at home. Apart from the US, the latter countries have a sizeable share of biotechnology patents invented in other European countries and, moreover, these patents are not concentrated in the leading nations – Germany or the UK – but are spread across European countries. When Swiss multinationals are excluded from the sample, the share of biotechnology patents by European assignees invented in the US declines from 14.6% to 11.3%. This is more aligned with the analogous share for the other chemical sectors presented in Table 2.4.

Table 2.5: Share of biotechnology patents invented by European assignees in the home country, in the US and in other European countries (10 000 patents in 1987-1996)

	Country of the assignee					
	Switzerland	**Germany**	**France**	*Italy*	**Netherlands**	**UK**
Patents invented in the home country	30,6	76,2	81,5	73,3	70,7	76,9
Patents invented in the US	48,2	7,6	11,0	4,9	4,4	8,1
Patents invented in the other EU countries	18,4	11,2	4,2	21,8	24,8	12,8

Source: European Patent Office (1998)

II. 4 Summary of Results

The main findings of this section can be summarised as follows:

The USA have accumulated and maintain a large absolute advantage in innovative activities in biotechnology vis-à-vis Europe.

The USA are more specialised in biotechnology research compared to Europe and Japan. However, some of the smaller European countries (particularly Ireland, Denmark, the Netherlands and the Scandinavian countries) are also focused on biotechnology.

Either private or public research can be the means by which newcomer countries can enter biotechnology research, and no single mode has emerged.

The share of biotechnology patents invented in the US and assigned to European organisations is higher than that of the other chemical sectors. This suggests that the US are an attractive location for biotechnology research conducted by European organisations.

The share of biotechnology patents invented in Europe and assigned to US organisations is particularly small, and much smaller than the analogous share for the other chemical sectors.

A key finding of the Report is therefore the lack of attraction of US biotechnology research by Europe rather than the European research investments in the US.

III. Division of Innovative Labour and Markets for Technology

III.1 Introduction

The growth of technological opportunities and the relevance of scientific research for innovative activities associated with molecular biology and biotechnology has promoted the emergence of a vibrant market for technology (see Arora, Fosfuri, and Gambardella, 2001; Arora, Gambardella, Pammolli, Riccaboni, 2001).

The ability of firms to access and make efficient use of markets for technology and networks of collaborative relations has become a crucial source of competitiveness. As a consequence, in the last 25 years collaborations in biotechnology have increased dramatically, worldwide (Orsenigo, Pammolli, Riccaboni, 2001).

Most DBFs exploit their basic competences and act primarily as research companies and specialised suppliers of high technology intermediate products, performing contract research for, and in collaboration with, established corporations in downstream sectors. Collaboration allows DBFs to survive and – in some cases – to pave the way for subsequent growth. First, clearly, collaboration with large companies provides the financial resources necessary to fund R&D. Second, it provides the access to organisational capabilities in product development and marketing.

The latest generations of DBFs (and the new "stars" like Affymax, Incyte and Celera) were created on the basis of specialisation into radically different new technologies like genomics, combinatorial chemistry, bioinformatics and what is now called "platform technologies". These technologies are essentially research tools and their developers do not aim to become producers but rather providers of tools and services to corporations involved in drug discovery and development. They may thus be able to sell customised services to a wider range of potential buyers.

Established companies face the opposite problem. While they need to explore, acquire and develop new knowledge, they have the experience and the structures necessary to control testing, production and marketing. Faced with an explosion of the space of innovative opportunities, no individual company, irrespective of its size,

can even think to be able to successfully originate and control all the relevant knowledge. Thus, participation in the network of collaboration and in markets for technology becomes a crucial ingredient for sustained technological and economic performances.

Assessing the involvement of European firms and institutions in these networks is therefore a crucial exercise for an evaluation of the status of the European biotechnology industry.

III.2 Research Teams in Biotechnology Patents: Geographical vs. Organisational Proximity as Coordination Mechanisms

Collaborations across assignees

A review of the patents with multiple assignees shows that in biotechnology the share of patents assigned to multiple assignees is higher than in the other sectors. On the basis of the 10,000 patent sample, there are 11.2% biotechnology patents with multiple assignees as against 8.9% in pharmaceuticals, 5.4% in organic chemistry, 3.8% in polymers, and 3.1% in materials[9]. Biotechnology appears to be more open to collaboration. This is so even when it is compared to pharmaceuticals, which is technologically closer to biotechnology and is a more collaborative field (8.9% multiple assignee patents) than the other fields in traditional chemicals. Furthermore, the evidence suggests that there are no country–specific factors that could account for this.

Collaborations among inventors

Single inventors develop only 18.3% of the sample's 97,785 chemical patents, while the remainder (81.7%) are developed by two or more inventors. Hence, while there are few patents with multiple assignees, there is a great deal of collaboration among individuals. These teams of inventors are mostly national. Overall, 90.8% of the

[9] Overall in our sample of 10,000 patents, the share of single assignees is 93.2%, for the same as in the 97,785 sample. This is suggestive of the comparability of the statistics computed by using either of the two samples. In this case, we are using the 10,000 sample because, as we shall see below, we need to use the information on the country of origins of the ultimate parent of the assignees.

patents in the sample developed by multiple inventors are among individuals from the same country.

To review further the question of the nature and characteristics of research teams in biotechnology patents a sub–sample of 4,649 patents from the EPO sample of 10,000 patents was selected on the basis of having at least one inventor located in Europe. The focus on inventions carried out in Europe is related to the finding that Europe does not appear to be a very attractive location for biotechnology research. It is therefore interesting to understand in greater depth the characteristics of the research located in it.

The data show that single inventors develop 788 patents (16.9%) and multiple inventors the remainder (83.1)%. In addition, there is no major difference across countries or sectors in the size of the research team.

Table 3.1 reports the average number of supplementary classes of these patents. Again, this is broken down by sectors and by some leading countries. As is evident, biotechnology patents by US assignees that were invented in Europe have a significantly higher degree of interdisciplinarity compared to biotechnology patents by the other countries in the table (Germany, France, and the UK). This suggests that the US assignees patent in Europe research outputs with a greater degree of generality compared to the others, the difference being particularly striking with Germany. The average number of IPC classes in German biotechnology patents invented in Europe is 1.8, compared to 2.7 for the US. The figures for France and the UK are respectively 2.4 and 2.5.

Table 3.1: Mean number of supplementary classes by patent. Inter-country (country of the assignee) and inter-sectoral differences

Sectors	DE	FR	UK	US	TOT
Biotech	1.8 (0.17)	2.5 (0.18)	2.4 (0.18)	2.7 (0.3)	2.1 (0.08)
Materials	1.02 (0.19)	1.2 (0.31)	1.5 (0.38)	1.5 (0.54)	1.3 (0.13)
Organic chemistry	2.4 (0.07)	2.4 (0.13)	2.7 (0.15)	2.9 (0.21)	2.5 (0.05)
Pharma	1.7 (0.09)	1.2 (0.13)	1.5 (0.14)	1.2 (0.2)	1.6 (0.06)
Polymers	1.8 (0.09)	1.5 (0.19)	1.7 (0.23)	1.6 (0.26)	1.7 (0.07)
Average by country	2.0 (0.05)	1.8 (0.09)	2.0 (0.09)	2.3 (0.12)	2.0 (0.03)

Standard errors in parentheses.
Source: Our elaboration from the EPO data.

The higher interdisciplinarity of the US biotechnology patents might reflect the fact that for the US assignees, patents in Europe are inventions patented abroad. Since patenting abroad is more costly, one may patent abroad only the more important patents, which are likely to be the more interdisciplinary ones. But Table 3.1 shows that US biotechnology patents are relatively more interdisciplinary compared to other countries than the US patents in the other chemical sectors. For example, even in pharmaceuticals, which is the sector closest to biotechnology, the average number of IPC classes of the US patents is 1.2 *vs* 1.7 for Germany, 1.2 for France, and 1.5 for the UK. This suggests that the US biotechnology patents invented in Europe may indeed be more general. If so, this would indicate that US biotechnology research in Europe plays a beneficial role, as US assignees are more likely to perform interdisciplinary research that tends to lead to more valuable inventions than European assignees (see Trajtenberg, 1990).

As for geographical proximity of inventors, data show that the share of Delocalised biotechnology patents (DL)[10] over the total number of biotechnology patents in the

[10] The address of the inventors listed in each patent was used to attribute its location to a given NUTS1 or NUTS2 European region. A patent is defined to be Colocalised (CL) if all the inventors are located in the same region. If at least one of them is located in a different region, the patent is classified as Delocalised (DL).

sample of European inventions is 40.9%. Colocalised patents (CL) are 59.1%[11]. The relatively high share of CL patents suggests the importance of geographical proximity among inventors. Moreover, the research teams of DL patents involve a significantly higher number of inventors than CL patents. The size of the teams in DL patents is on average 4.1, while for CL patents it is smaller by 1.7 units[12]. That is, DL patents involve larger teams.

However, DL patents do not imply a significantly higher number of IPC classes per patent. Biotechnology patents that list inventors located in different regions entail larger teams, but they are not more general than those developed by inventors who are all located in the same region.

Moreover, the share of the DL patents developed by US assignees is higher than the share of the DL patents of any other country[13]. According to the data, the share of DL biotechnology patents in the total sample of US biotechnology patents is 70.4%. This figure is higher than that of the US in all the other chemical sectors. Moreover, DL biotechnology patents with US assignees mainly correspond to collaborations across European regions. This suggests that US assignees doing biotechnology research in Europe are an important vehicle for inter-regional collaboration, doing more of it than the assignees by the European countries, and more than the US assignees themselves do in other chemical sectors.

Finally, there is evidence that large firms are less involved in interdisciplinary biotechnology[14]. The analyses reveal that compared to the other four chemical sectors, biotechnology patents exhibit a much higher share of patents by smaller firms (Non Fortune 500). About 75.5% of the biotechnology patents go to such firms, while the share for the other sectors ranges between 44.7% and 58.2%. This finding is consistent with the existing literature on the industry, which has stressed

[11] These include 18% patents with only one inventor. We included the single inventor patents in CL because we are interested in the search for competencies outside of the region or cluster. Individual inventors did not team up with others, and hence they seemed to have no need (or opportunity) to reach outside of their region.

[12] The teams in the CL patents might be smaller because they include the single inventor patents. However, when excluding the latter, the CL patents were still significantly smaller than the DL patents by 1.3 units.

[13] This is not surprising, since the sample includes only US patents with at least one inventor located in Europe. Hence, it does not consider the CL patents developed by the US assignees in the US.

that competencies for producing innovations with greater breadth (and value) tend to be associated with smaller academic labs and research-intensive firms (e.g. see Gambardella, 1995). In other words, it is the quality of the team, rather than the size of the organisation, that matters in this case. Moreover, research in biotechnology appears to be internationalised, with its knowledge foundations being developed on a "global" basis.

[14] A distinction between Fortune 500 and Non Fortune 500 firms was made. Overall, these firms cover a very large fraction of the patents in the sample (4,320 out of our 4,649).

III. 3. The Network of Collaborative Relations

Table 3.2 shows the nationality of origin and development of collaborative agreements (CA) in biotechnology for selected years. A crucial difference between Europe and the US becomes immediately apparent. The overwhelming majority of the biotechnology collaborative projects originates (70,07%) and is developed (66,12%) in the US. However, European biotechnology organisations have progressively increased their role both as originators (from about 14% in 1990-94 to about 20% in 1998-00) and as developers (from 12.46 to 21.61%) of new projects.

Table 3.2: Number of Organizations and Number of Originated and Developed Collaborative Agreements (CAs) in Biopharmaceuticals, by Nationality:1990-1994, 1995-1997, 1998-2000

Nationality	Total	Number of Organizations						Number of CAs			
		EFs		DBF s		PRO s		as Originators		as Developers	
		Num.	(%)	Num.	(%)	Num.	(%)	Num.	(%)	Num.	(%)
1990-1994											
EU15	112	41	36,61	36	32,14	35	31,25	274	14,05	243	12,46
USA	496	154	31,05	241	48,59	101	20,36	1 463	75,03	1459	74,82
Japan	25	23	92,00	1	4,00	1	4,00	65	3,33	84	4,31
Other	93	31	33,33	36	38,71	26	27,96	148	7,59	164	8,41
Total	726	249	34,30	314	43,25	163	22,45	1950	100,00	1950	100,00
1995-1997											
EU15	226	89	39,38	95	42,04	42	18,58	510	17,90	553	19,41
USA	652	196	30,06	338	51,84	118	18,10	1989	69,81	1830	64,23
Japan	47	41	87,23	6	12,77	0	0,00	61	2,14	173	6,07
Other	195	59	30,26	73	37,44	63	32,31	289	10,14	293	10,28
Total	1120	385	34,38	512	45,71	223	19,91	2849	100,00	2849	100,00
1998-2000											
EU15	447	117	26,17	223	49,89	107	23,94	838	20,19	897	21,61
USA	1124	334	29,72	587	52,22	203	18,06	2819	67,91	2629	63,33
Japan	81	64	79,01	8	9,88	9	11,11	119	2,87	212	5,11
Others*	313	78	24,92	151	48,24	84	26,84	375	9,03	413	9,95
Total	1965	593	30,18	969	49,31	403	20,51	4151	100,00	4151	100,00
1990-2000											
EU15	785	247	31,46	354	45,10	184	23,44	1622	18,12	1693	18,92
USA	2272	684	30,11	1166	51,32	422	18,57	6271	70,07	5918	66,12
Japan	153	128	83,66	15	9,80	10	6,54	245	2,74	469	5,24
Others*	601	168	27,95	260	43,26	173	28,79	812	9,07	870	9,72
Total	3811	1227	32,20	1795	47,10	789	20,70	8950	100,00	8950	100,00

*Argentina, Australia, Bermuda, Brazil, Canada, China, Costa Rica, Croatia, Cuba, Czech Republic, Egypt, Hong Kong, Hungary, Iceland, India, Indonesia, Israel, Malaysia, Mexico, New Zealand, Norway, Philippines, Poland, Puerto Rico, Russia, Singapore, Slovenia, South Africa, South Korea, Switzerland, Taiwan, Thailand, Yugoslavia.

EFs: established firms; DBFs: dedicated biotechnology firms; PROs: public research organisations

Source: BID, University of Siena.

In the second part of the 1990s the number of DBFs rose in Europe but remained substantially unchanged in the US (see below). European DBFs are still proportionately less integrated than US DBFs in the networks of division of innovative labour: 68% of all collaborative agreements originate in the US, compared with only 20% that originate in the EU (see Table 3.2). Age is not the only factor underlying the lower participation of European DBFs in markets for technology. Some structural differences between Europe and the US affect the collaborative capabilities of DBFs.

American DBFs develop a larger share of projects originated by domestic public research organisations (PROs) and DBFs and by European DBFs than European counterparts. In Europe, DBFs tend to be substituted as developers by established companies. Interestingly enough, the only exception is for projects originated by European PROs, which are developed mainly by co-localised DBFs or by European PROs.

European PROs have increased their relationships with both European and American DBFs in 1996-2000. On the contrary, US-based PROs collaborate more and more directly with established companies and act more frequently as developers of projects originated by DBFs. In general, universities and research institutes increasingly reach out and collaborate with delocalised partners both as originators and as developers. European DBFs do not seem to be able to attract US established pharmaceutical companies as developers of projects originated in Europe, and they turn preferentially to European partners.

Only a minority of European DBFs in Europe participates as developers in collaborative projects originated by other organisations. Established companies have the lion's share of bio-pharmaceutical products in Europe.

Moreover, (see Arora, Gambardella, Pammolli, Riccaboni, 2001), European companies tend to access markets for technologies later on during product development (clinical research and marketing), and are less active in the early stages of research. Product innovation in therapeutic biotechnology is highly dependent on both the originator and developer capabilities of US companies. European DBFs, still young and small, do not take part in the division of innovative labour in product development, particularly with American PROs and established companies.

Finally, PROs in Europe tend to be focused on the generation of new research opportunities, while they tend to be absent from the downstream stages of product development.

III.4. Summary and Conclusions

The main findings of this section can be summarised as follows:

First, markets for technology and networks of collaborative agreements are important in biotechnology.

Second, the biotechnology patents by US assignees invented in Europe are more interdisciplinary than those of the European assignees. This finding is specific to biotechnology and suggests that they are also potentially more valuable.

Third, US biotechnology patents developed in Europe are the outcome of teams of inventors located in different regions, whether different NUTS European regions, or Europe and the US. This suggests that US biotechnology patents enhance international and inter-regional collaboration in Europe.

Fourth, small firms produce a large amount of inventions in biotechnology.

Fifth, the network of the biotechnology collaborative projects is largely US based, despite a recent increase in the participation of European biotechnology organisations. European DBFs tend to be less active in the networks and they do not seem to be able to attract US established pharmaceutical companies as developers of projects originated in Europe. Rather, they turn preferentially to European partners.

Sixth, PROs in Europe tend to be focused on the generation of new research opportunities, while they tend to be absent from the downstream stages of product development. Moreover, European companies tend to access markets for technologies in biopharmaceuticals later on during product development (clinical research and marketing), and they are less active in the early stages of research. In synthesis, product innovation in biopharmaceuticals is highly dependent on the capabilities of US companies.

IV. The New European Biotechnology Industry[15]

IV. 1. Introduction

It was suggested in the previous section that European biotechnology is lagging significantly behind the US. However, encouraging signals related mainly to the good performance of some small (mainly northern) European nations and to an impressive recent increase in the number of DBFs was also stressed. This section examines the characteristics of European DBFs.

DBFs are widely considered to be the most efficient available organisational solution for the development of innovative activities in biotechnology.

First, DBFs are fundamental organisational devices for exploring an enormous, quickly expanding and incredibly complex space of new innovative opportunities. In a context of rapid and tumultuous technological advance, where knowledge is still fragmented and dispersed, no single institution is able to generate and develop all the necessary ingredients for discovering and bringing new products to the marketplace (see Powell, Koput, Smith-Doerr, 1996; Orsenigo, Pammolli, Riccaboni, 2001).

Second, the DBFs perform a crucial function by transforming scientific knowledge into technological and commercial applications. They intermediate in the transfer of knowledge from universities to established large corporations that cannot be always at the forefront of scientific discovery but have the downstream capabilities needed for commercialisation (Orsenigo, 1989; Henderson, Orsenigo and Pisano, 1999).

Third, DBFs promote and are crucial agents in markets for technology and division of innovative labour (Arora, Gambardella, 1994; Gambardella, 1995; Arora, Gambardella, Pammolli, Riccaboni, 2001), in the context of a system in which control rights can be allocated to maximise innovative output in conditions of incomplete contracting (Lerner and Merges, 1998).

[15] This section is based on Pammolli and Riccaboni, 2001.

IV. 2 The Database

The analysis in this section is based on the Biotechnology Industry Database (BID) built up by the EPRIS Group at the University of Siena[16]. BID includes a wide range of information concerning European organizations active in biotechnology innovation and production systems. BID provides a full-fledged set of information on the state of the industry, up to the end of year 2000. In particular, it integrates a comprehensive set of sources of information to provide an articulated representation of the variegated factors and players that take part in European biotechnology. Organizations have been identified by referring to:

1) *Descriptions of core business, technological background, and fields of applications*. Such information is voluntarily provided by biotechnology organizations through Internet sites, specialized press, venture capitalists, and participation in public surveys or biotechnology and regional associations. Furthermore, the analysis builds upon information from commercial directories (i.e. Pharmaventure, Bioscan, BioCommerce, Windhover, Recap, Scrip) and by means of an Internet survey (www.eprisproject.com/eubio);

2) *Records of research and production activities*. Even though small biotechnology companies might sometimes be secretive about their innovative efforts, information on R&D activities tends to leak out in the public domain. In particular, publications, patents, collaborative alliances, pharmaceutical and agricultural trials, participation in national and EU biotechnology programs, and quotation on public stock markets provide an unequivocal trace of active biotechnology companies. Research and industrial activities have been monitored by accessing and integrating multiple (both public and proprietary) sources of information. In addition, members of European and national biotechnology associations and, moreover, all the companies that monitored in BID,

[16] The Epris Group at the University of Siena includes: Fabio Pammolli (Director), Massimo Riccaboni (Coordinator), Gianluca Baio, Rossana Pammolli, Daniela Casula, Carmela Pace and Antonella Fiore (Research Assistants). Alberto D'Amico, Chiara Giani, Andrea Paolini and Pietro Bubba Bello, (Industrial Liaison Office, University of Siena) provided a generous organisational support.

were asked to provide information on their in-house R&D projects and on collaborative agreements.

The analysis of the structure and evolution of innovation and production systems in biotechnology is particularly complex, for the following reasons:

(a) The lack of a general and commonly accepted definition of biotechnology affects the reliability and the comparability of official analyses and statistics, making any measurement extremely difficult. Historically, the definition criteria adopted from different national and international sources have been heterogeneous. The report adopts the definition of biotechnology developed by the OECD (see van Beuzekom, 2001). This definition focuses on techniques (tools, manipulation and know-how) that either modify existing living organisms/part of them, or transform material, of living origin or not, by the use of processes involving living organisms, for the purpose of producing new (scientific) knowledge or developing new products or new processes.

The following classification is referred to:

- DNA (the coding): genomics, pharmaco-genetics, gene probes, DNA sequencing/synthesis/amplification, genetic engineering;
- Proteins and molecules (the functional blocks): protein/peptide sequencing/synthesis, lipid/protein engineering, proteomics, hormones, and growth factors, cell receptors/signalling/pheromones;
- Cell and tissue culture and engineering: cell/tissue culture, tissue engineering, hybridisation, cellular fusion, vaccine/immune stimulants, embryo manipulation;
- Process biotechnology: Bioreactors, fermentation, bioprocessing, bioleaching, bio-pulping, bio-bleaching, biodesulphurisation, bioremediation, and biofiltration;
- Sub-cellular organisms: gene therapy, viral vectors.

In addition to ‘core’ biotechnology organisations identified according to the OECD definition, the report takes into account those firms which are focused on the development of tools, instruments, and devices that apply directly and prevalently to

biotechnology product development, such as bioinformatics, highthroughput screening, combinatorial and chiral chemistry.

(b) Most of the dedicated biotechnology organizations, especially in Europe, are so young and small that they do not show up in any survey. They are deeply involved in set up and early-stage R&D activities that do not provide any externally visible signal, be it a scientific board, a deal, or a first-round of financing. Aware of that, both strategy 1 and 2 were implemented for all the European countries, trying to reduce the black area of unobserved biotechnology activity.

(c) A third limitation of currently available statistics is a consequence of the fact that organisations active in biotechnology are typically heterogeneous and embedded in complex proprietary and collaborative networks. They range from public research organisations (universities, hospitals, research labs, foundations, and institutes), to large pharmaceutical, agro-chemicals, food and chemical companies (typically, highly diversified multinationals with several divisions and intricate proprietary and control links). Dedicated biotechnology firms (DBFs) play a pivotal role in connecting heterogeneous components and actors. As a result, boundaries among different organizations are often evanescent and it becomes hard to count the number of independent units. In order to take into account the existence of these complex systems of innovation, production, and control, the organisations monitored in the survey have been classified according to four main categories:

Independent dedicated biotechnology firms (DBFs): i) core biotechnology firms: European private and public firms specialised in biotechnology product and process development; ii) specialised suppliers, e.g. firms active in combinatorial chemistry, bioinformatics, DNA sequencing instrumentation, and in the production of tools and techniques which are used by 'core' biotechnology companies.

Established companies active in related fields (ECs): large companies that do have a sound research position in modern biotechnology. Although the core business of firms in this category is not in biotechnology, they are actively involved in biotechnology research and development;

Biotechnology divisions: units that operate in biotechnology and are controlled either by established companies or by DBFs;

Public Research Organizations (PROs): research institutes, universities, hospitals and other public organizations with relevant scientific results in molecular biology and in fields and disciplines related to biotechnology.

IV. 3. The Structure of the Industry

This section uses data from the Biotechnology Information Databank (BID), maintained at the University of Siena, which includes 3669 organisations active in biotechnology (see also Pammolli and Riccaboni, 2001).

Among them, there are 2092 independent dedicated biotechnology firms (DBFs). More specifically, there are 1730 core biotechnology firms (according to the OECD classification) and 362 specialised suppliers. Detailed data for each of these has been collected[17].

Localisation of European DBFs

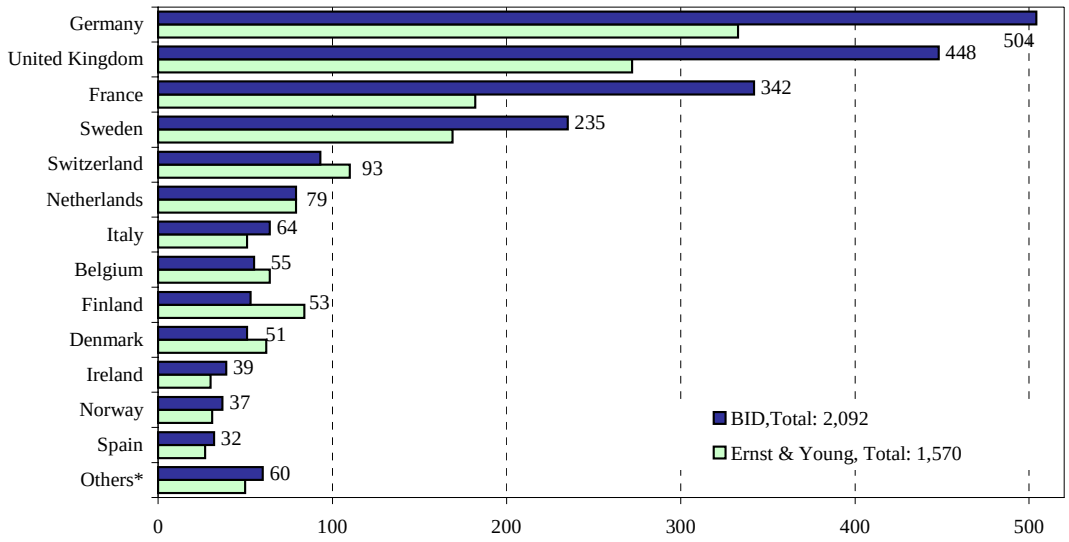
Figure 4.1 shows the number of independent dedicated biotechnology firms in major European countries at the end of year 2000. Figure 4.1 does not consider public research organisations, companies whose main activities are in fields other than biotechnology, or biotechnology divisions of larger firms. They represent the 'inner core' of the European national systems of innovation in biotechnology. According to the data collected in BID, Germany leads the league with more than 500 small independent dedicated biotechnology firms (DBFs), followed closely by the UK. Taken together, Germany and the UK account for about one half of the total number of DBFs in Europe. France ranks third with 343 biotechnology companies, followed by Sweden.

If one calibrates the number of DBFs using population or GDP numbers (Table 4.1), a clear representation emerges, with Sweden ranked first according to both measures,

[17] For each firm, the following information was collected: name, type of organization, business description, location, year of establishment, major historical events (such as date of starting of biotechnology activities and M&As), main financial data (when available), employees, fields of activity, technological background, patents, collaborations, R&D projects

followed by Switzerland, Ireland, Finland, and Denmark. The UK, Germany and France have similar values while Italy and Spain have the lowest ratios.

Figure 4.1: Number of Independent DBFs, Main European Countries (Dec. 2000)



Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

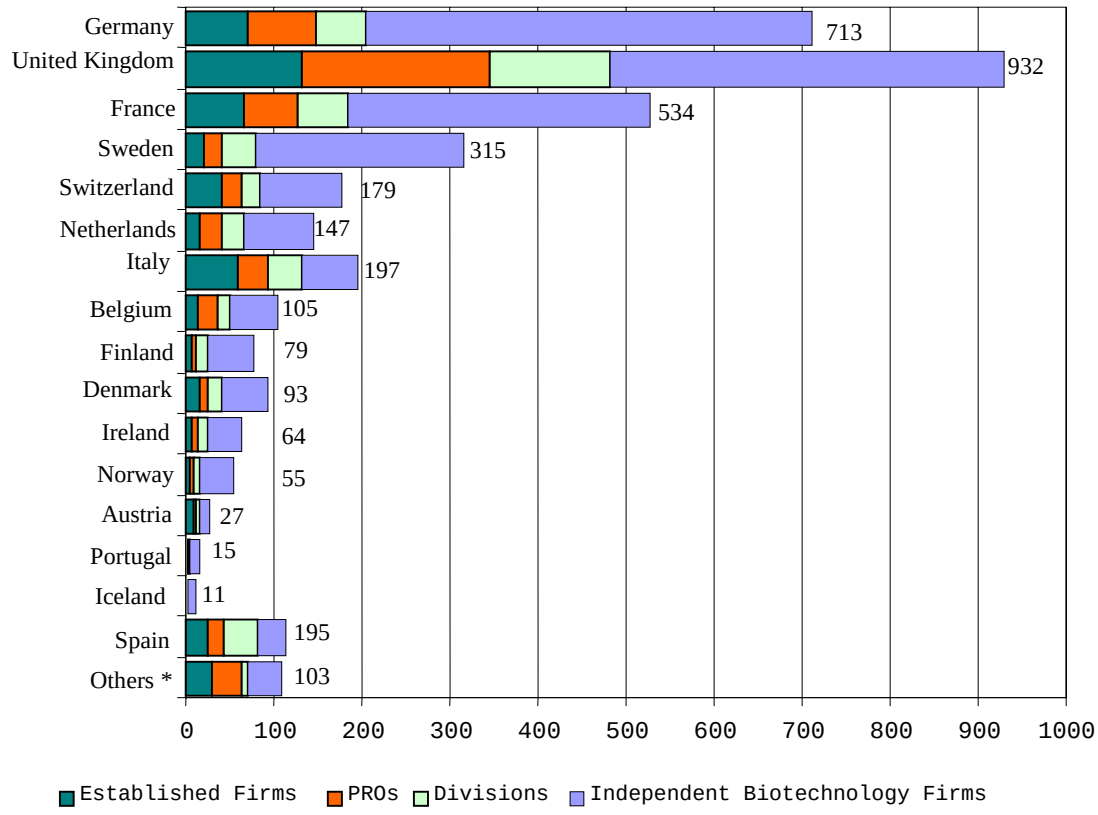
Figure 4.2 characterises European biotechnology innovation and production systems in terms of the types of active organizations. There are important differences in the composition of the industry across European countries. In particular, the UK and, to a lesser extent, France, differ from Germany, both because of the high number of divisions of companies focused on biotechnology, and because of the higher number of large firms. Moreover, in the UK one can observe a higher number of non-industrial research institutes in the fields of molecular biology and biotechnology. In Italy and Spain the number of DBFs is particularly low when compared to the number of large firms or of divisions of large firms.

Table 4.1. Number of DBFs per Inhabitant and National GDP (Dec.2000)

Country	Number of DBFs (1)	Inhabitants/1000 (2)	GDP (EURO Thousands) (3)	DBFs per Inhabitants (1/2)	DBFs/GDP (1/3)
Sweden	235	9052	37750127	0,02596	0,006225
Switzerland	93	7374	12444024	0,01261	0,007473
Ireland	39	3493	19875805	0,01117	0,001962
Finland	53	5115	42337212	0,01036	0,001252
Denmark	51	5320	213290714	0,00959	0,000239
Norway	37	4461	28201643	0,00829	0,001312
United Kingdom	448	59247	230860181	0,00756	0,001941
France	342	58816	346953663	0,00581	0,000986
Germany	504	85684	25433691	0,00588	0,019816
Belgium	55	10286	40219969	0,00535	0,001367
Netherlands	79	15893	59744161	0,00497	0,001322
Austria	11	8124	88226106	0,00135	0,000125
Italy	64	57807	189869364	0,00111	0,000337
Spain	32	39545	34198374	0,00081	0,000936

Source: BID, University of Siena

Figure 4.2 Number of Organizations Active in Biotechnology, by Type (Dec. 2000)

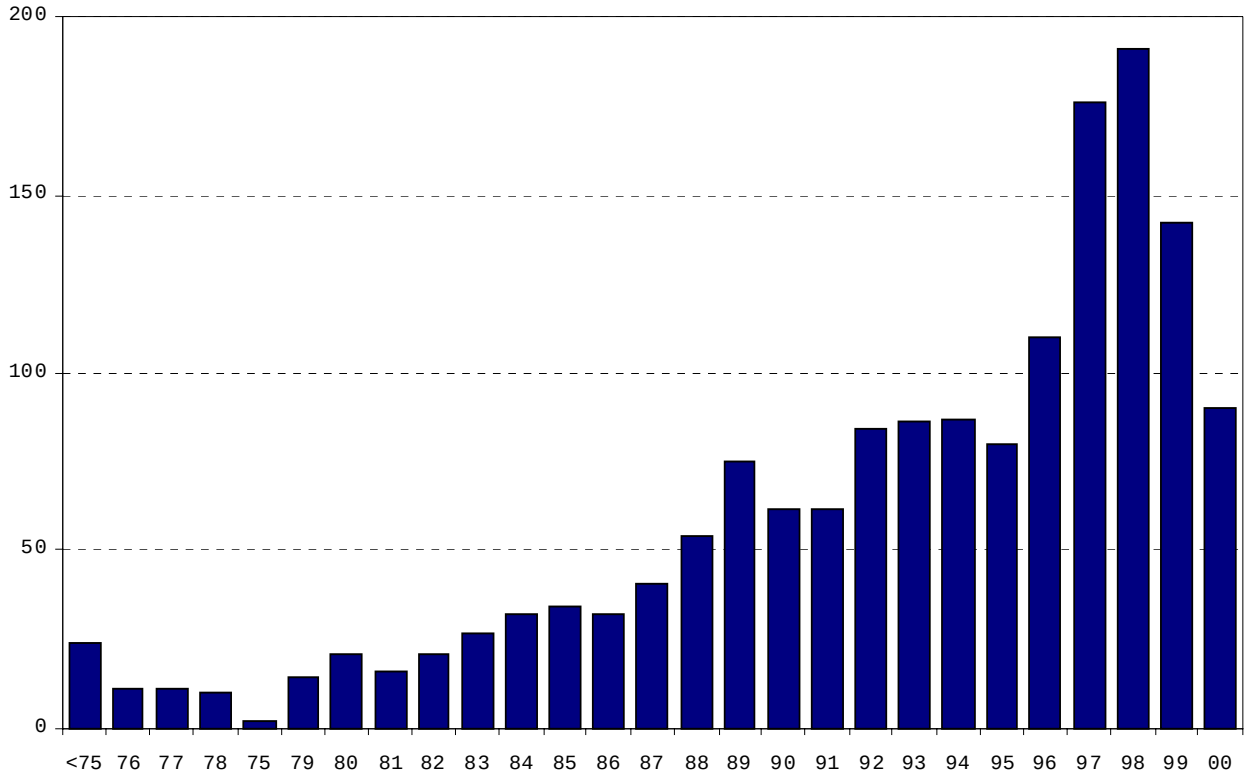


* Others: Czech Republic, Estonia, Hungary, Lithuania, Luxembourg, Poland, Romania, Russia, Slovakia. Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

The dynamics of entry

Figure 4.3 shows the distribution of European DBFs by year of foundation. Peak years of entry were 1997 and 1998. In 1999 and 2000, after a 4-year period of intense entry, in which the overall number of EU biotechnology firms almost doubled, the rates of company formation decreased. This slowdown (not corroborated by Ernst & Young's data) seems to be similar, in nature, to the one observed in the USA at the beginning of the Nineties and it could anticipate a period of stabilisation, consolidation, and selection, with mergers, acquisitions, and exit offsetting new company formation. As a consequence, the impact of the intense entry on the long-term evolution of the industry is not known, and the industry seems to be far from any equilibrium configuration.

Figure 4.3. European Dedicated Biotechnology Firms: Distribution by Year of Foundation (firms per year)



Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

Table 4.2 and Figure 4.4 show the distribution of dedicated biotechnology companies in Europe, by cohorts of entrants. It is clear that there are important differences in terms of the generational composition of DBFs in major European countries. Nordic countries like Sweden have experienced a relatively stable pace of entry of new firms, while in other countries, particularly Germany, the upsurge of the number of new firms has occurred in the last five years. At present, Germany accounts for a third of the total number of new European firms (i.e. those which entered the industry after 1995), followed by UK and France. The three countries, taken together, account for more than ¾ of the new biotechnology firms that entered the industry between 1996 and 2000, with numbers well above the EU–15 average.

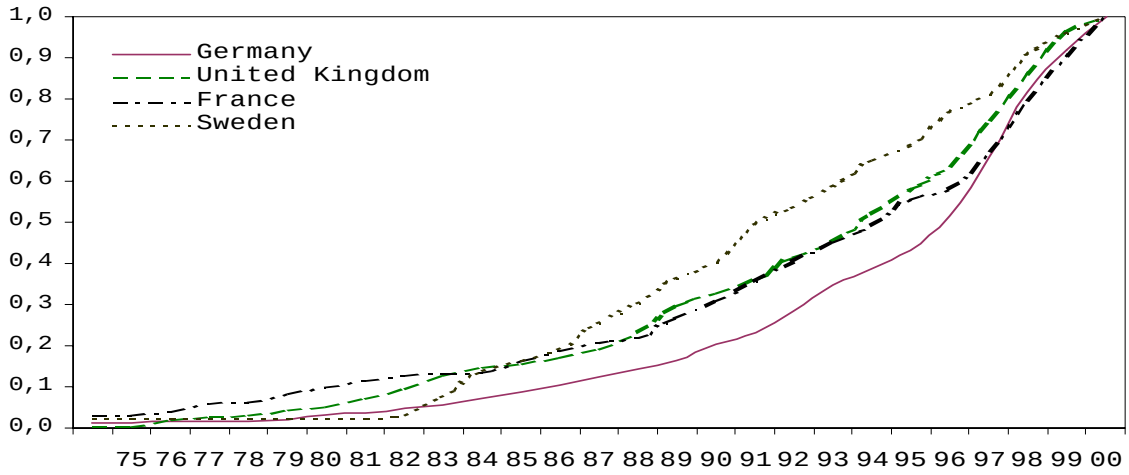
Table 4.2 European Dedicated Biotechnology Firms: Distribution by Cohorts of Entrants

	EU15		United Kingdom		Germany		France		Sweden		Others*	
	Nr	**%**	**Nr**	**%**	**Nr**	**%**	**Nr**	**%**	**Nr**	**%**	**Nr**	**%**
<=90	600	31,09	147	32,81	102	20,24	112	32,18	89	37,87	150	37,9
91-95	487	25,23	113	25,22	114	22,62	86	24,71	61	25,96	113	28,6
>=96	843	43,68	188	41,96	288	57,14	150	43,10	85	36,17	132	33,4
Total	1930	100,00	448	100,00	504	100,00	348	100,00	235	100,00	395	100,0

*Others: Austria, Belgium, Denmark, Finland, Ireland, Italy, Luxembourg, Netherlands, Portugal, and Spain

Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena.

Figure 4.4. European Dedicated Biotechnology Firms: Patterns of Entry, Main Countries



Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

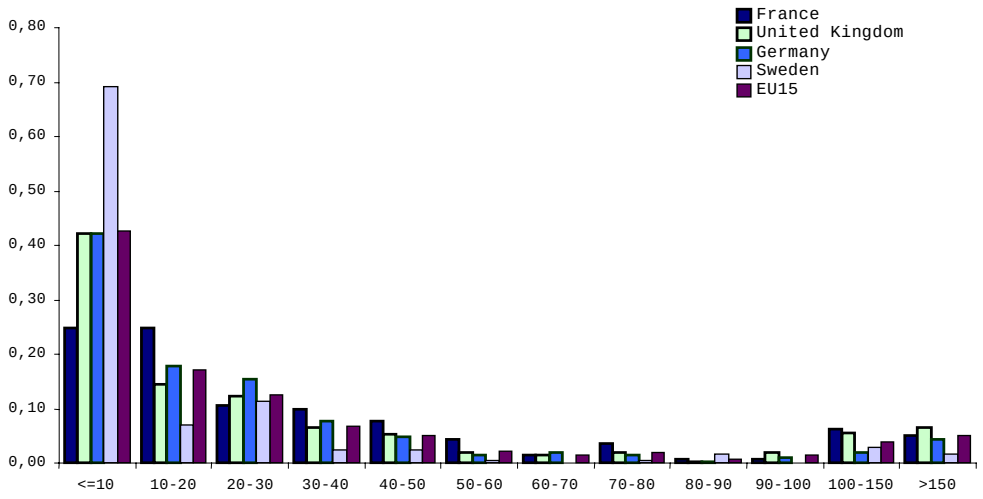
Size

Figure 4.5 shows the size distribution of European DBFs, in December 2000, divided into classes according to the number of employees. As is evident, most European DBFs are either micro or small, research-intensive firms. Only approximately 10 percent of active European DBFs have more than 50 employees, while the vast majority (about 57 per cent) have fewer than 20 employees. It is worth noting that despite general similarities in the shape of business size distributions, European national systems of innovation in biotechnology rely on quite different mixtures of small and medium biotechnology companies. Surprisingly enough, if compared with general figures about firm size in manufacturing, the size of French DBFs is well above the mean for EU-15, while the opposite it is true for Sweden. Moreover, while UK and Germany look similar in terms of shares of micro business units over the total number of firms active in biotechnology, Germany has a higher proportion of firms in the middle size range (10 to 50 employees) than the UK, which relies upon a higher number of medium and large DBFs.

Sectoral composition and areas of specialisation

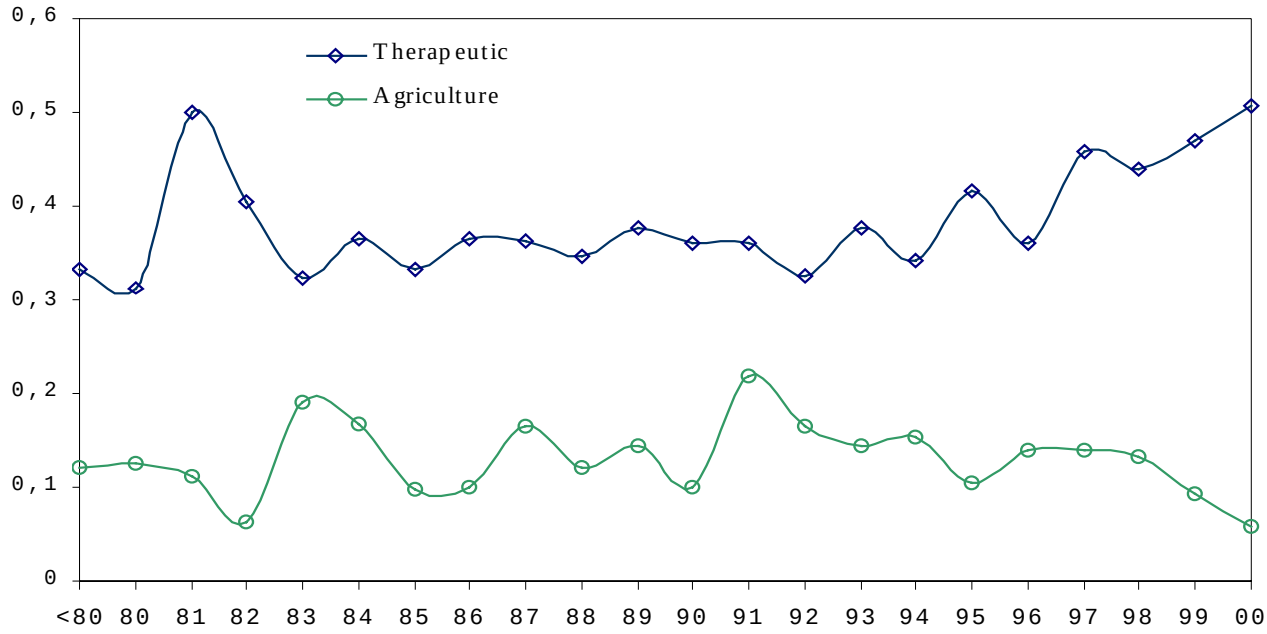
The sustained flow of entry shown above has changed the relative importance of agro–food and pharmaceuticals as areas of application (see Figure 4.6). The proportion of new DBFs that entered the agro-food industries declined from 1995, from about 15% to less than 5% in the year 2000; this fall probably reflects regulatory factors and growing public opposition to genetically-modified crops. During this time, the number of dedicated bio-pharmaceutical companies rose from 35% to more than 50 % of the total number of new firms. Thus, the dramatic increase in the number of European DBFs from 1996 to 2000 reflects, to a large extent, a flow of new DBFs that entered the industry to exploit the therapeutic applications of genomics and new techniques, such as combinatorial chemistry and bio-informatics, which can be used to improve and speed up the development of new therapeutic treatments (see Pammolli and Riccaboni, 2001).

Figure 4.5. European Dedicated Biotechnology Firms: Distribution of Employment by Size Classes



Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

Figure 4.6. Proportion of European DBFs Active in Human Therapeutics and Agriculture, by Year of Foundation



Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

Table 4.3 summarises the technological profiles of EU DBFs according to broad areas of interest in biology, chemistry and medicine. It shows the existence of differences among European countries concerning the areas of specialisation of national DBFs in main fields of application. German biotechnology companies are active mainly in human health care (therapeutics and diagnostics), Swedish firms concentrate on human and animal therapeutics, while France, Italy, and Switzerland have a higher proportion of companies active in agro-food. A large proportion of French and German DBFs entered the industry, both in pharmaceuticals and agro-food, to explore the commercial value of recent technological advances at the lowest levels of organisation of living organisms in genomics, proteomics and bioinformatics. The UK keeps a strong technological basis in cell and tissue engineering, process biotechnology, instrumentation, and devices. Moreover, new UK DBFs are more active in combinatorial chemistry and in other general–purpose research techniques applied to drug discovery and development. Italy's specialisation is in targeting sub–cellular organisms, while Swedish companies tend to focus mainly on manufacturing biomaterials and on innovative technologies in drug discovery, such as combinatorial chemistry and chiral synthesis.

Finally, Table 4.4 shows the extent to which biotechnology applications and research technologies are integrated at the firm level, in key European countries. French and British companies have the highest degree of integration between technologies and applications. The higher level of integration of UK firms could well reflect a difference in the composition of industry in terms of cohorts of entrants, since the UK has a higher fraction of early entrant DBFs, which had sufficient time to implement their technologies in specific domains of application. On the contrary, German and, particularly, a significant fraction of Swedish firms, tend to be vertically specialised either in terms of technologies or domains of application.

Table 4.4. European Dedicated Biotechnology Firms: Distribution by Technological Fields

Country	Cell and Tissue Culture and Engineering		Subcellular Organisms		DNA		Proteins and Molecules		Process Biotechnology		Chemical Synthesis[1]		Bioinformatics		Other Devices[2]		Analysis[3]		Total	
	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%
EU 15	*436*	*18,72*	*189*	*8,12*	*349*	*14,98*	*504*	*21,64*	*218*	*9,36*	*177*	*7,60*	*126*	*5,41*	*233*	*10,00*	*97*	*4,16*	2329	92,53
Germany	93	*14,03*	60	*9,05*	114	*17,19*	170	*25,64*	38	*5,73*	62	*9,35*	44	*6,64*	50	*7,54*	32	*4,83*	663	26,34
United Kingdom	117	*22,90*	30	*5,87*	60	*11,74*	87	*17,03*	53	*10,37*	34	*6,65*	25	*4,89*	88	*17,22*	17	*3,33*	511	20,30
France	82	*16,94*	41	*8,47*	85	*17,56*	107	*22,11*	61	*12,60*	36	*7,44*	30	*6,20*	24	*4,96*	18	*3,72*	484	19,23
Sweden	47	*26,26*	7	*3,91*	20	*11,17*	24	*13,41*	14	*7,82*	20	*11,17*	12	*6,70*	19	*10,61*	16	*8,94*	179	7,11
Switzerland	25	*22,32*	5	*4,46*	11	*9,82*	17	*15,18*	11	*9,82*	4	*3,57*	7	*6,25*	27	*24,11*	5	*4,46*	112	4,45
Italy	24	*21,24*	16	*14,16*	13	*11,50*	18	*15,93*	16	*14,16*	8	*7,08*	3	*2,65*	14	*12,39*	1	*0,88*	113	4,49
Others[4]	16	*21,05*	4	*5,26*	13	*17,11*	19	*25,00*	8	*10,53*	4	*5,26*	5	*6,58*	5	*6,58*	2	*2,63*	76	3,02
Total	*477*	*18,95*	198	*7,87*	373	*14,82*	540	*21,45*	237	*9,42*	185	*7,35*	138	*5,48*	265	*10,53*	104	*4,13*	2517	

1 Chemical Synthesis: Includes Combinatorial Chemistry, Chiral Chemistry, Molecular Synthesis

2 Others Devices: Includes Medical Equipments, PCR

3 Analysis: Environmental and Agro-Food Test

4 Others:Czech Republic, Estonia, Hungary, Iceland, Lithuania, Norway, Poland, Portugal, Romania, Russia, Slovakia

Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

Figure 4.7 shows the effects of patterns of technological change on national profiles of specialisation. In the second half of the Nineties, new technologies have emerged, particularly in the field of DNA coding, which have promoted the application of advanced computational methods and technologies (such as bio-informatics, and high throughput screening) to R&D. Proteins, monoclonal antibodies, and enzymes continue to characterise the technological background of many European DBFs, especially in France, where the application of enzymes to agro-food also plays an important role, and in Nordic countries, where the wool, pulp, and paper industries have increased the use of enzymes and bacteria to develop new products and

processes. First-generation process biotechnology (such as fermentation and bioremediation) appears to be less and less relevant in the characterisation of firms profiles and core technological capabilities.

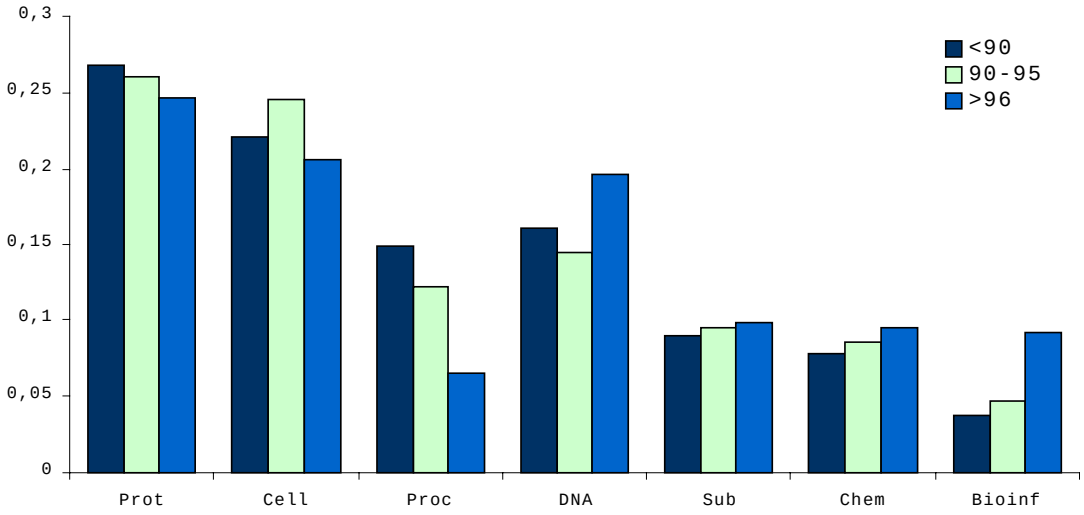
Diversification and integration

Tables 4.5 and 4.6 give an account of the extent of diversification of DBFs in Europe, in terms of fields of application and research technologies. Companies monitored in the survey were classified according to the characterisation that they provide of their own business and technological background. In Table 4.5, DBFs that identify their activity exclusively in terms of technological background are labelled as 'basic' companies. Analogously, DBFs that are characterised only by field of application, and do not refer to any specific technological background, are classified as 'applied' in Table 4.5. In both cases, DBFs that refer to a given area of specialisation are labelled as 'specialised', while firms with at least two fields of interest are labelled as 'diversified'[18].

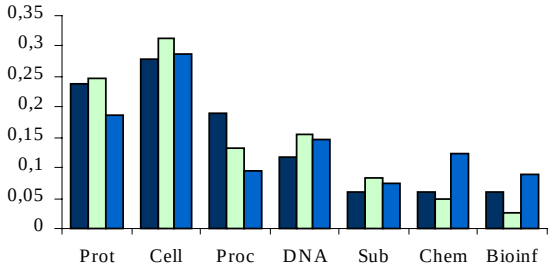
Tables 4.5 and 4.6 show that European DBFs tend to be either technologically specialised in given fields of application or active in baseline research and technology development. Almost 50% of European DBFs are specialised in one specific domain in terms of technological background or field of application. Notably, a high share of Swedish and German firms are specialised in general-purpose technologies (GPTs). Italian firms have, on average, the highest degree of diversification, followed by French DBFs.

[18] Sub categories have been identified according to the number of fields the company operates in: Low (2 fields), Medium (3) and High (more than 3) levels of diversification are reported.

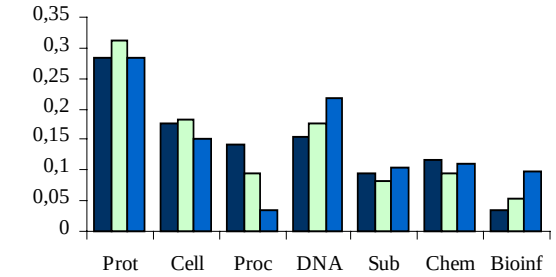
Figure 4.7. European DBFs: Cohorts of Entrants by Technological Background



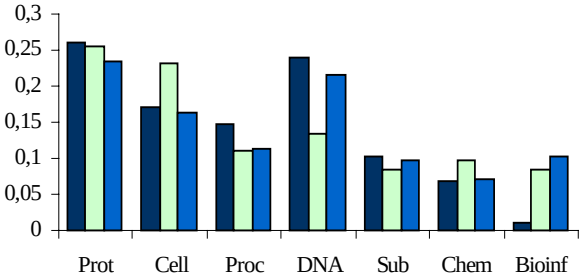
EU15



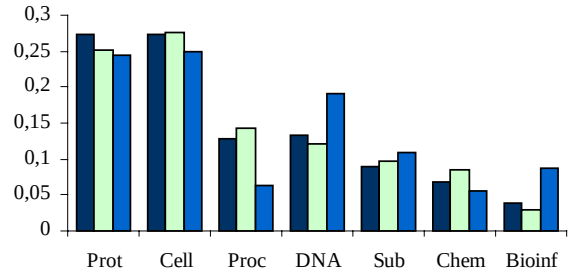
United Kingdom



Germany



France



Others*

Legend: Prot – Proteins and Molecules; Cell - Cell and Tissue Culture and Engineering; Proc - Process Biotechnology; DNA - Genomics and Genetic Engineering; Sub - Subcellular Organisms; Chem - Chemical Synthesis (including Combinatorial); Bioinf – Bioinformatics

*Others: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, Hungary, Iceland, Ireland, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Russia, Slovakia, Sweden, Switzerland and Spain

Source: Pammolli and Riccaboni, 2001, based on BID, University of Siena

Table 4.5. Diversification Profiles of European DBFs: Areas of Application

Degree of Diversification		Germany		United Kingdom		France		Sweden		Switzerland		Italy		EU 15		Other	
		Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%
Basic		127	27,08	30	8,17	30	10,56	44	23,78	16	19,28	3	5,08	260	15,86	32	9,76
Specialized		200	42,64	198	53,95	129	45,42	109	58,92	48	57,83	18	30,51	799	48,75	169	51,52
Diversification	Low	97	20,68	85	23,16	72	25,35	24	12,97	15	18,07	20	33,90	373	22,76	86	26,22
	Medium	30	6,40	35	9,54	36	12,68	8	4,32	3	3,61	10	16,95	137	8,36	28	8,54
	High	15	3,20	19	5,18	17	5,99	0	0,00	1	1,20	8	13,56	70	4,27	13	3,96
Total		469	100,00	367	100,00	284	100,00	185	100,00	83	100,00	59	100,00	1639	100,00	328	100,00

Source: BID, University of Siena

Table 4.6. Diversification Profiles of European DBFs: Technological Background

Degree of Diversification		Germany		United Kingdom		France		Sweden		Switzerland		Italy		EU 15		Other	
		Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%	Num.	%
Basic		93	19,83	109	29,70	57	20,07	65	35,14	30	36,14	9	15,25	405	24,71	83	25,30
Specialized		227	48,40	153	41,69	113	39,79	100	54,05	32	38,55	23	38,98	732	44,66	141	42,99
Diversification	Low	111	23,67	74	20,16	55	19,37	16	8,65	17	20,48	13	22,03	327	19,95	68	20,73
	Medium	25	5,33	22	5,99	33	11,62	4	2,16	2	2,41	9	15,25	114	6,96	25	7,62
	High	13	2,77	9	2,45	26	9,15	0	0,00	2	2,41	5	8,47	61	3,72	11	3,35
Total		469	100,00	367	100,00	284	100,00	185	100,00	83	100,00	59	100,00	1639	100,00	328	100,00

Source: BID, University of Siena

IV. 4 Summary of Main Results

The entry of European DBFs is a recent phenomenon. From 1996 to 2000 the overall number of EU biotechnology firms almost doubled and the growth has been particularly strong in Germany. More recently, the rates of company formation have decreased.

European DBFs are typically extremely small, much smaller than their American equivalents.

Germany leads the league in terms of number of dedicated companies, with more than 500 small independent dedicated biotechnology firms (DBFs), followed closely by the UK. Taken together, Germany and the UK account for about one half of the total number of DBFs in Europe. France ranks third and Sweden follows.

If one calibrates the number of DBFs using population or GDP numbers, a clear representation emerges, with Sweden ranked first according to both measures, followed by Switzerland, Ireland, Finland, and Denmark. The UK, Germany and France have similar values while Italy and Spain have the lowest ratios. In sum, these data confirm the good performance of the small (Northern European) countries.

The new European DBFs are active mainly in the so-called “platform technologies”, e.g. genomics, combinatorial chemistry and bio-informatics. The proportion of DBFs active in the agro-food sector has declined sharply.

European DBFs tend to be specialised either in narrow fields of application or in baseline research technologies.

French and British companies show the highest degree of integration between technologies and applications. On the contrary, German and, particularly, a significant fraction of Swedish firms, tend to be specialised either in terms of technologies or domains of application.

V Geographical Clusters in European Biotechnology

V.1. Introduction

In the US, biotechnology has been characterised, historically, by a relatively high concentration of firms, employment, and activities in a restricted number of regions, mainly in the US (San Diego, the Bay Area, Boston, New Jersey, New York metropolitan area, Maryland (between Baltimore and Washington DC), and the Houston area in Texas) (see Owen Smith, Riccaboni, Pammolli, Powell, 2001; Zucker, Darby, 2001).

Based on this, economists, analysts and policy-makers have argued that spatial concentration of innovative and industrial activities is indeed a pre-requisite for the successful development of biotechnology and policies have been devised (e.g. the German BioRegio Program) with the explicit aim to support not so much the birth of new DBFs but rather the development of clusters of biotechnology activities.

Why is such concentration observed? As this is fundamentally a science-based technology, involving abstract and codified knowledge, it should in principle be available to everybody. What forces lead to the agglomeration of biotechnology activities in specific clusters? Different explanations have been suggested:

- the (partially) tacit nature of knowledge implies that personal contacts, imitation and frequent interactions are necessary for knowledge transmission. These are clearly possible at lower costs for firms located within the same city or region. The transmission of tacit knowledge requires mutual trust, a sharing of language and culture and intense non-business relations that co-location in areas of homogeneous social background makes easier (Jaffe, Trajtenberg and Henderson, 1993; Audretsch and Feldman 1996; Swann and Prevezer, 1998);

- discoveries in this technological area are characterised by high degrees of natural excludability, i.e. techniques for their replication are not widely known and anyone wishing to build on new knowledge must gain access to

the research team or laboratory setting having that know–how (Zucker, Darby and Brewer, 1997, Zucker, Darby and Armstrong, 1998; Audretsch, 2001). In these circumstances, inventor–scientists tend to enter into contractual arrangements with existing firms or start their own firm in order to extract the supranormal returns from the fruits of their intellectual contribution. And they tend to do so within commuting distance from their laboratories[19];

- however, empirical evidence suggests that there might be a threshold effect (Echeverri-Carroll and Brennan, 1999): local sources of knowledge are key in determining success in the development of new products and processes only in areas with a large accumulation of knowledge (Silicon Valley). Innovations by firms located in other areas depend on distant relationships with universities, and other high–technology firms (suppliers and customers) located elsewhere, especially in urban centres. In this perspective, local boundaries play a fundamental role for the recruitment of skilled workforce and technical personnel. However, the most dynamic and innovative firms look for knowledge embodied in engineers and scientists wherever they are available, and are not necessarily constrained in this by geographical barriers. *Local* knowledge sources are relatively less important for firms located in lower-order regions. For these firms, local universities are viewed as suppliers of skilled workforce, rather than loci of innovations or sources of product ideas or spillover effects. In order to sustain high rates of innovation they must develop linkages with actors (universities and other high-tech firms) located in higher-order regions (see also Lyons, 1995).

Trying to draw some conclusions from this discussion, it would appear that clustering may be the outcome of different factors, but mainly:

[19] Zucker, Darby, and colleagues have shown that the innovative performance of biotechnology firms is positively associated with the *total* number of articles by local university 'star' scientists. However, when the number of articles written by university stars is broken down into those written in collaboration with firm scientists ('linked') and the remaining ('untied'), the coefficient on articles written by local university stars *not in collaboration* with the firm loses its significance and nearly vanishes in magnitude. Previous evidence on the existence of localised knowledge spillovers seems therefore to have resulted from a specification error, i.e. the inability to control for the actual relationships linking *individual scientists* to *individual firms.*

– the existence of a strong critical mass of scientific knowledge, in absolute terms: in other words, excellence in scientific research is a basic precondition for attracting innovative activities. In its absence, firms (incumbents and/or prospective entrepreneurs) might look for other locations to tap the relevant knowledge. Moreover, diversity is also important. Insofar as innovation rests on the integration of different fragments of knowledge, the presence of a diversified scientific base becomes a key issue;

– the existence of a strong and diversified industrial base, with accumulated capabilities and organisational structures enabling them to actually participate in the network of cognitive and social relationships that are necessary to get access to, to absorb, integrate the new knowledge and, on these bases, to engage in successful innovative activities;

– the existence of specific and often formal organisational devices (including markets for know-how) that allow flows of knowledge to take place.

V. 2 Regional Distribution of Biotechnology Patents in Europe

Geographical concentration of biotechnology in Europe: Evidence from patent data

Table 5.1 shows the regional distribution of the 4,649 patents invented in Europe from the sample of 10,000 chemical patents. The table lists the top 20 regions in which patenting activity in chemicals concentrates among the 146 European regions as classified by Eurostat at the NUTS1 and NUTS2 level. (See Mariani, 2001, for further details).

The top 20 regions (13,7% of the total number of regions) account for 77.5% of the sample of chemical patents invented in Europe. The top 10 regions (6.8% of the total) host 59.5% of these patents. The distribution of chemical patents across European regions is highly concentrated.

There are many German regions among the top 20, ranging from 5 in biotechnology to 9 in pharmaceuticals. This is consistent with the well–known leadership of Germany in chemicals, although the lower number of German regions among the top

20 regions in biotechnology confirms earlier remarks about its lower specialisation in this field. Other studies show that, in general, many of the most innovative European regions are in Germany (Paci and Usai, 1998). Overall, 52% of the patents invented in the top 20 regions were invented in Germany. Germany is followed by France (with 13.8% of the patents in the top 20 regions), the UK (13.8%), the Netherlands (5.3%) and Italy (4.6%).

Although the data in Table 5.1 show that patenting concentrates geographically in all five chemical branches, biotechnology shows the least geographic concentration. In the sample, the top 20 regions account for 68.6% of the biotechnology patents invented in Europe. There are some regions that appear in all five listings in the top 20 positions. These are South–East England, Île de France, Bayern, Hessen, West-Netherland, Nordrhein-Westfalen, Baden-Württemberg, Vlaams Gewest and Rhône-Alpes. There are other regions, such as Rheinland-Pfalz and Sachsen, which are in the top 20 positions in all the chemical sectors, except in biotechnology.

There are also regions that are ranked in the top 20 positions in biotechnology, but that are not among the top 20 in any of the other four chemical fields. This suggests a peculiarity of biotechnology within the overall chemical sector, especially that biotechnology is a technology that facilitates the entry of new actors. Specifically, it is opening up opportunities for regions that have not been active in developing innovations in the traditional branches of the chemical sector, including pharmaceuticals. The new regions in the top 20 for biotechnology are Københavns in Denmark, Uusimaa in Finland, Stockholm in Sweden, and the area around Madrid in Spain. This suggests that biotechnology offers opportunities for new entries in technologically dynamic fields.

Table 5.1: Distribution of patents across European regions (region of the inventor): cumulative frequencies and Herfindahl index. top 20 regions (10 000 patent sample in 1987-1996)

Biotechnology		Materials		Organic chemicals		Pharmaceuticals		Polymers	
Regions	**Cum. Freq.**	**Regions**	**Cum. Freq.**	**Regions**	**Cum. Freq.**	**Regions**	**Cum. Freq.**	**Regions**	**Cum. Freq.**
South East Engl. (UK)	8,6	Nordrhein-Westfalen (DE)	14,3	Nordrhein-Westfalen (DE)	15,3	Nordrhein-Westfalen (DE)	12,9	Nordrhein-Westfalen (DE)	20,8
Île de France (FR)	15,9	Hessen (DE)	22,3	Hessen (DE)	24,9	Île de France (FR)	23,7	Rheinland-Pfalz (DE)	33,9
Bayern (DE)	21,5	Île de France (FR)	29,0	Rheinland-Pfalz (DE)	34,4	South East Engl. (UK)	31,5	Hessen (DE)	40,5
Hessen (DE)	26,9	Rheinland-Pfalz (DE)	34,4	Switzerland	42,2	Hessen (DE)	37,0	Switzerland	44,2
West-Nederland (NL)	31,5	West-Nederland (NL)	39,3	South East Engl. (UK)	49,5	North West Eng. (UK)	41,7	Rhône-Alpes (FR)	47,9
Switzerland	35,6	North West Eng. (UK)	43,8	Île de France (FR)	55,7	Switzerland	46,2	Lombardia (IT)	51,5
Eastern (UK)	39,5	Vlaams Gewest (BE)	47,8	Lombardia (IT)	59,8	Lombardia (IT)	50,5	Île de France (FR)	54,8
Nordrhein-Westfalen (DE)	42,9	Baden-Württemberg (DE)	51,8	Sachsen-Anhalt (DE)	62,6	Rheinland-Pfalz (DE)	54,6	Sachsen (DE)	57,6
Københavns amt (DK)	46,2	Sachsen (DE)	55,4	Rhône-Alpes (FR)	65,5	West-Nederland (NL)	57,7	West-Nederland (NL)	60,4
Baden-Württemberg (DE)	49,2	Zuid-Nederland (NL)	58,5	Sachsen (DE)	68,2	Baden-Württemberg (DE)	60,4	Zuid-Nederland (NL)	62,9
Niedersachsen (DE)	52,0	North East Eng. (UK)	61,6	Baden-Württemberg (DE)	70,9	Sachsen-Anhalt (DE)	62,7	Sachsen-Anhalt (DE)	65,4
Vlaams Gewest (BE)	54,5	Bayern (DE)	64,3	Bayern (DE)	73,0	Bayern (DE)	65,1	North West Eng. (UK)	67,9
Ostösterreich (AT)	56,6	Niedersachsen (DE)	67,0	West-Nederland (NL)	75,1	Berlin (DE)	67,3	Vlaams Gewest (BE)	70,1
Rhône-Alpes (FR)	58,6	Sachsen-Anhalt (DE)	69,2	Vlaams Gewest (BE)	77,2	Vlaams Gewest (BE)	69,3	Bayern (DE)	72,3
Berlin (DE)	60,4	Rhône-Alpes (FR)	71,4	Sachsen (DE)	78,7	Eastern (UK)	71,2	Région Wallonne (BE)	74,4
Lombardia (IT)	62,2	South East Engl. (UK)	73,7	Alsace (FR)	80,2	Lazio (IT)	73,0	Emilia-Romagna (IT)	76,4
Alsace (FR)	63,8	Ostösterreich (AT)	75,0	Eastern Eng. (UK)	81,5	FR71 Rhône-Alpes	74,7	Baden-Württemberg (DE)	78,3
Uusimaa (FI)	65,5	Bruxelles (BE)	76,3	Berlin (DE)	82,9	Hamburg (DE)	75,9	South East Engl. (UK)	80,1
Stockholm (SE)	67,1	Région Wallonne (BE)	77,7	Scotland (UK)	83,9	North East Eng. (UK)	77,1	Niedersachsen (DE)	81,5
Comunidad de Madrid (ES)	68,6	Haute-Normandie (FR)	79,0	Cataluña (ES)	84,7	Sachsen (DE)	78,2	Bruxelles (BE)	82,9
Herfindahl index	**0,03**		**0,05**		**0,07**		**0,05**		**0,08**

Source: Mariani, 2001.

Clusters of biotechnology activities in Europe

In this section, which is an extract from Pammolli and Riccaboni, 2001, the main biotechnology clusters in Europe are identified, by looking directly at firms and research centres, based on BID. Figures 5.1 to 5.5 show that a process of clustering is taking place in Europe where a relatively small number of local clusters are capturing a dominant majority of biotechnology firms and of public research organisations. Some of these clusters (i.e. Oxford, Cambridge, and Stockholm) are more consolidated and can rely upon a sound research background and high international reputation, coupled with a critical mass of both young and established spin-off companies and international contacts. Other biotechnology clusters, like the German Bio-Regions (Munich, Rhine/Neckar and Rhineland), some French districts and, to a lesser extent, the Medicon Valley between Copenhagen and Lund, are younger. They they took off during the Nineties mainly thanks to a supportive policy environment, availability of public and private finance, new infrastructures, the presence of large companies active in related industries and institutes of research in biomolecular biology, biomedical sciences and biochemistry. Biotechnology activities in Germany, UK, France, Sweden, and Switzerland (Figure 5.1a) are concentrated in a handful of clusters (Figure 5.1b).

Figure 5.1 (a). European Dedicated Biotechnology Firms: Employment by Country

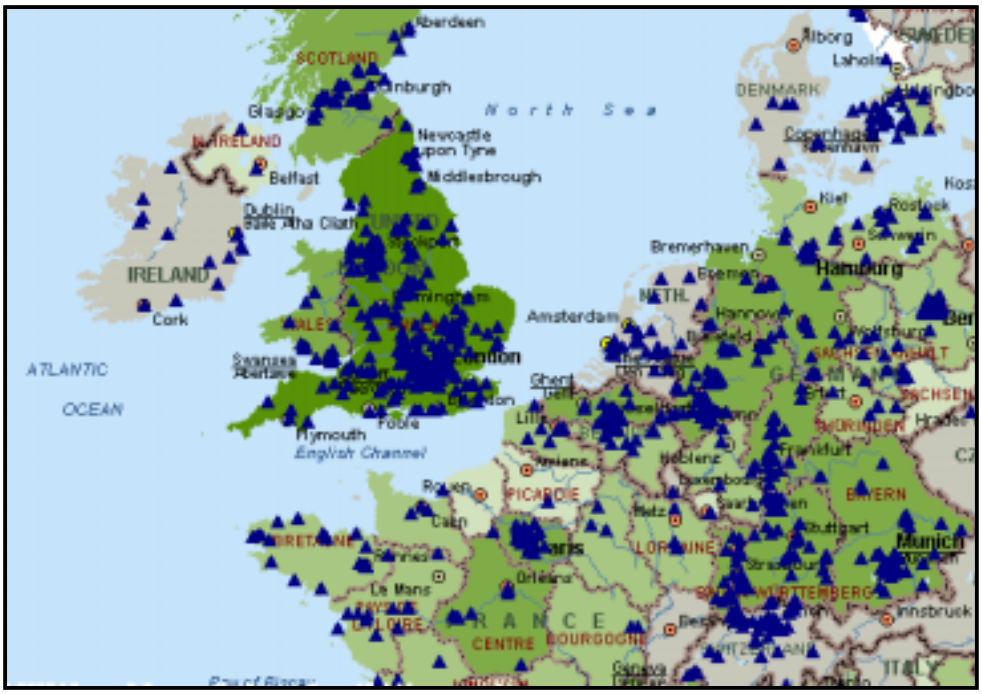
Source: BID, University of Siena

Apparently, most of the factors that contribute to the growth of the national systems of biotechnology innovation and production are local in nature. Figures 5.2 to 5.5 provide a descriptive atlas of biotechnology regions in Europe.

In the UK, British DBFs are clustered in East Anglia (Cambridge), South East England (Oxfordshire, Great London, Surrey), and Central Scotland (see Figure 5.2; see also DTI, 1999 and 2001). A circle of 10 kilometres includes most of the activities around the Oxford and Cambridge campuses, as well as within the City of London. Each of these regions encompasses a variegated set of public and private research organisations. In addition to the university, Oxford includes other prestigious research organisations and hospitals (John Radcliffe Hospital, AEA Technology, MRC Radiobiology Institute, and Wellcome Trust Human Genetics Center). Also, a number of well-known Oxford spin–offs are located along the A34 corridor from Oxford to Didcot (i.e. Oxford GlycoSciences, Oxford Asymmetry, Powderject Pharmaceuticals). Around the University Campus in Cambridge, one can find other leading institutes (Laboratory of Molecular Biology, the Babraham Institute, the Sanger Centre, and the European Bioinformatics Institute), as well as 27% of UK DBFs, with a vast variety of technological and business profiles. Finally, a large variety of actors – public research organisations (Imperial College, Medical Research Council, University College), research hospitals (Guy's and St Thomas' Hospital), venture capitalists, headquarters of the main pharmaceutical and chemical enterprises and new biotechnology firms – are located in London.

Most of the firms active in the London area are active in biopharmaceuticals, with particular reference to decoding/transformation of DNA material or functions of sub-cellular organisms.

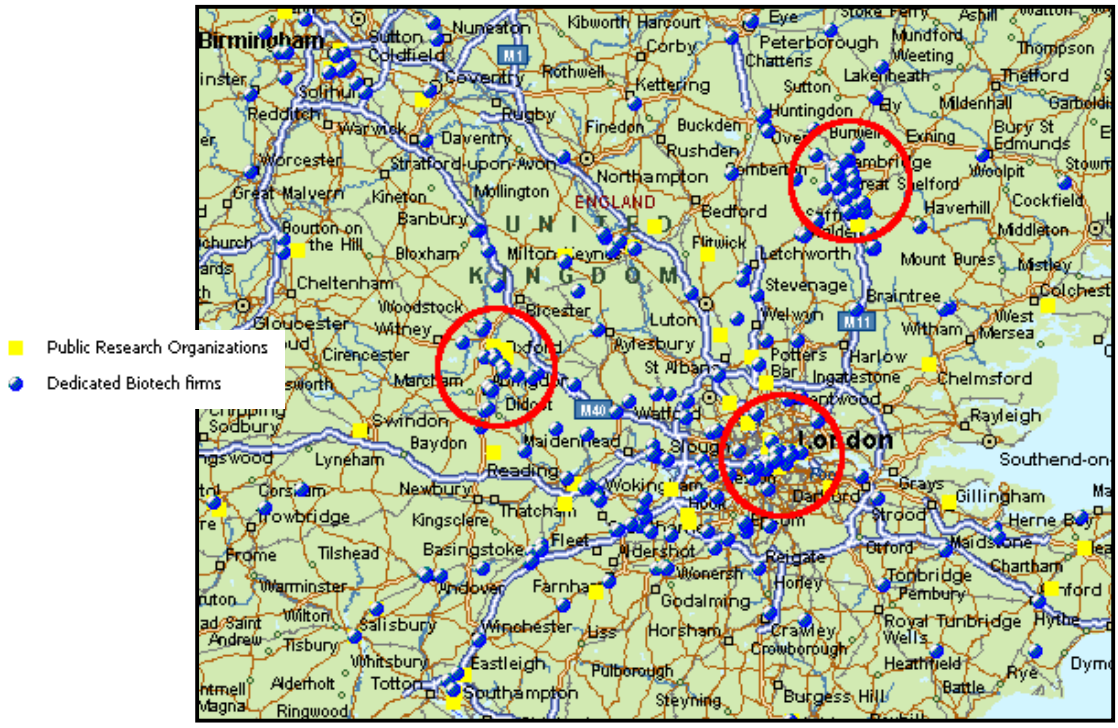
Figure 5.1 (b). European Dedicated Biotechnology Firms:
Main Geographical Clusters



Source: BID, University of Siena

Companies specialised in functional genomics, the production of vaccines and biomaterials, and drug delivery systems are also located in London. In the East Anglia Cluster (Cambridgeshire), biopharmaceuticals are by far the most important segment, with a variety of profiles, ranging from large first generation biotechnology companies, to drug discovery companies specialised in the fields of genomics, proteomics, bioinformatics, combinatorial chemistry, to firms specialised in the development of techniques of protein/rDNA sequencing/engineering and, finally, to firms specialised in the production of biomaterials. In Surrey one can observe a higher proportion of firms active in agricultural biotechnology and, moreover, in the production of reagents and of cell and tissue cultures. On the contrary, in Oxfordshire almost all DBFs tend to be specialised in biopharmaceuticals, with particular reference to proteomics, genomics, the development of chemical libraries, and the production of vaccines and monoclonal antibodies. Finally, 25-30 DBFs are located in Scotland, with competencies in human and animal healthcare, as well as in environmental biotechnology, covering technological fields such as gene therapy, protein engineering, and combinatorial chemistry.

Figure 5.2. Main UK Biotechnology Clusters



Source: BID, University of Siena

On 20 November 1996, the German Federal Ministry for Education, Science, Research and Technology announced the three winners of the BioRegio competition (see Dohse, 2000). Munich, Rhine/Neckar and Rhineland received an extra DM 50 million of federal funding over the next five years and at least the same amount from industry. Also as a consequence of this program, German DBFs tend to be localised in Bayern, Baden-Württenberg, Rheinland-Pfalz, Nordrhein-Westfalen, and Berlin (see Figure 5.3). Many of the new DBFs benefited from the BioRegio program and located their activities close to leading institutes of research. As an example, Figure 5.3 focuses on the Munich and Freiburg clusters and reveals the presence of a high number of early-stage platform biotechnology companies closely connected to local PROs. All these clusters emerged in the last 5 years, thanks to both strong public and private support and world–class local research institutes, particularly in small molecule discovery and computational chemistry.

In the Berlin area, one can observe a high number of diagnostic firms and, moreover, DBFs specialised in the fields of genomics and proteomics. Freiburg (Baden-Württemberg) is characterised by a remarkable degree of technological diversity, both in biopharmaceuticals and agricultural biotechnology. The cluster around Hamburg is populated mainly by DBFs specialised in the analysis of nucleic acid, in

the production of in vitro diagnostics and in drug discovery, with particular reference to the development of target molecules or target genes for specific diseases, while the platform technologies of genomics and proteomics are diffused among DBFs located in Bayern (Munich, Martinsried), where one can find also firms specialised in the provision of software tools and know-how for bioinformatics and functional genomics.

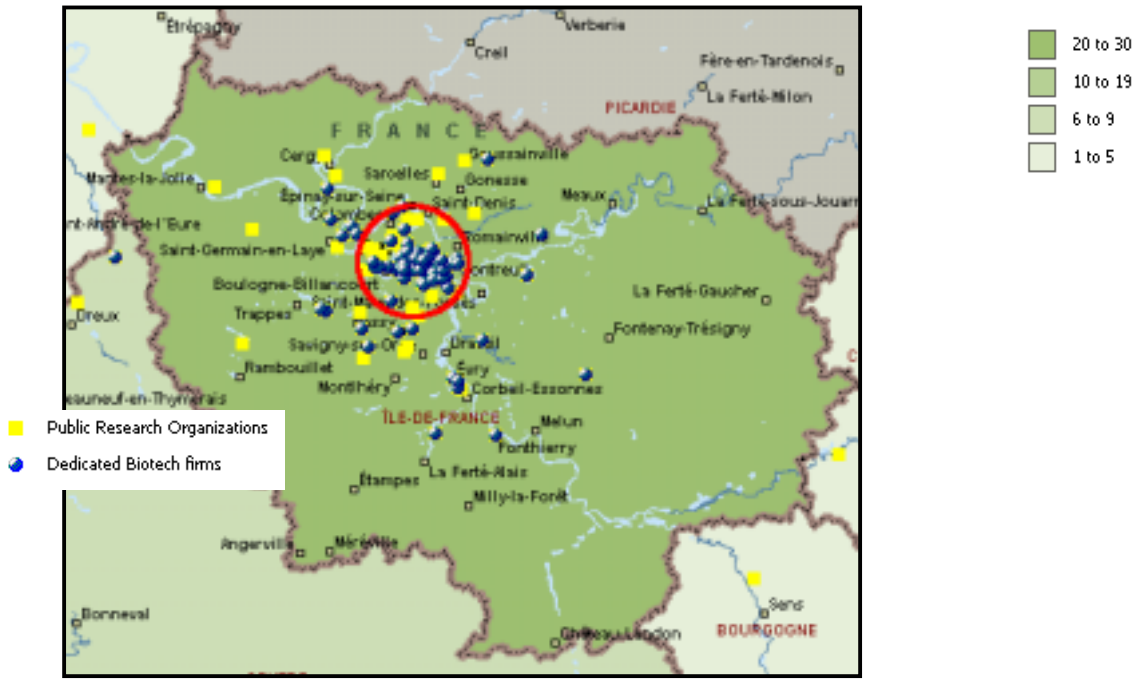
Figure 5.3. German Biotechnology Clusters: Bayern and Baden-Württenberg

Source: BID, University of Siena

Figure 5.4 shows the high concentration of French biotechnology firms in Paris, the second largest cluster in terms of number of DBFs in Europe after Cambridge (Mytehlka, Pellegrin, 2001). According to BID data, about 30% of French biotechnology firms are located in Paris trailed by a group of French regions (Auvergne, Loire, Rhone-Alpes and Midi Pyrennees) that have been catching up in the last five years (see France Biotech, 2000). Here again, in a 10 km2 area one can find a heterogeneous set of both public and private biotechnology organisations. More than 100 DBFs are located around Paris, many specialising in diagnostics and therapeutics (genetic engineering, cell and tissue culture). In Alsace, out of 36 companies monitored in BID, 12 are active in agro-food, 5 in environmental biotechnology, and 19 in biopharmaceuticals, with particular strengths in proteomics and gene delivery technologies. Agro-food is important also in the Rhone-Alpes area,

with relatively large DBFs using both traditional fermentation techniques and more innovative techniques derived from genomics and proteomics.

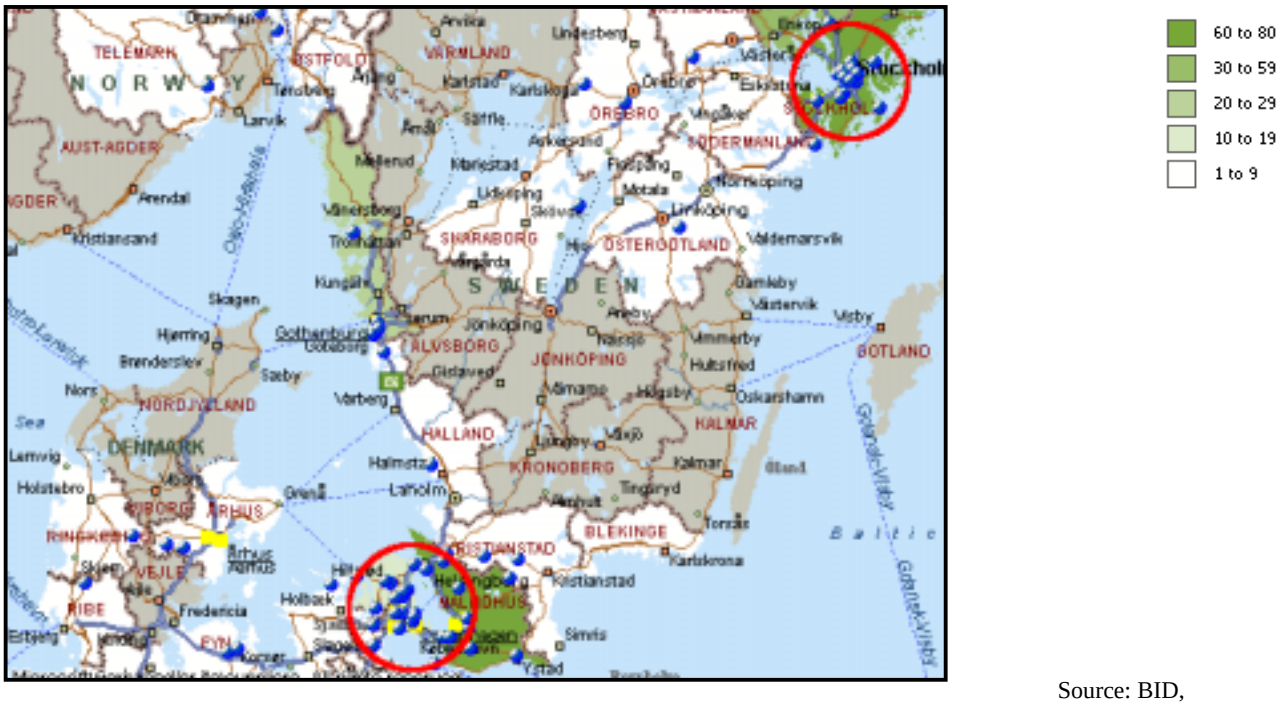
Figure 5.4. French Biotechnology Companies: Île-de-France



Source: BID, University of Siena

Figure 5.5 shows two large Nordic clusters. The Novum Biopark in Stockholm is closely related to the Karolinska Institute Complex, which has a long tradition of excellence in medical and biological fields. The southern region (Øresund), is known as *Medicon Valley* (Horton, 1999). Medicon Valley has grown up between Copenhagen and Lund–Malmö, especially after the construction of the bridge between Denmark and Sweden. Almost all biotechnology firms in Sweden are located in four major regions: Stockholm-Uppsala, Skåne, which is the southern region including Lund and Malmö, Gothenburg and Umeå (Vinnova, 2000), while in Denmark they are highly concentrated in the Sjælland Island. The Stockholm area is populated by DBFs active in biopharmaceuticals, with a focus on vaccine research and production and the technologies of cell-therapy, proteomics, and genomics. The region around Uppsala is populated by DBFs specialised in biopharmaceuticals (mainly in cell culture), while the Sydsverige cluster is more differentiated.

Figure 5.5. Main Nordic Biotechnology Clusters



Source: BID, University of Siena

Other fast-growing clusters are in Finland (Helsinki, Turku, Tampere, Kuopio, Oulu)[20], in the Netherlands (Zuid-Holland Region), and in Lombardia (Milan).

This data review suggests two remarks. First, clustering would seem to be strongly related to the presence of heterogeneous and interconnected prestigious research institutions. And, second, the main clusters are not simply characterised by dense internal or local relations but also by the ability to establish strong and varied external ties with other clusters.

European clusters such as Cambridge, Oxford and Karolinska show a remarkable degree of organisational heterogeneity and internal interconnectivity, comparable to the one characterising the most important clusters in the US. The Swedish collaborative network

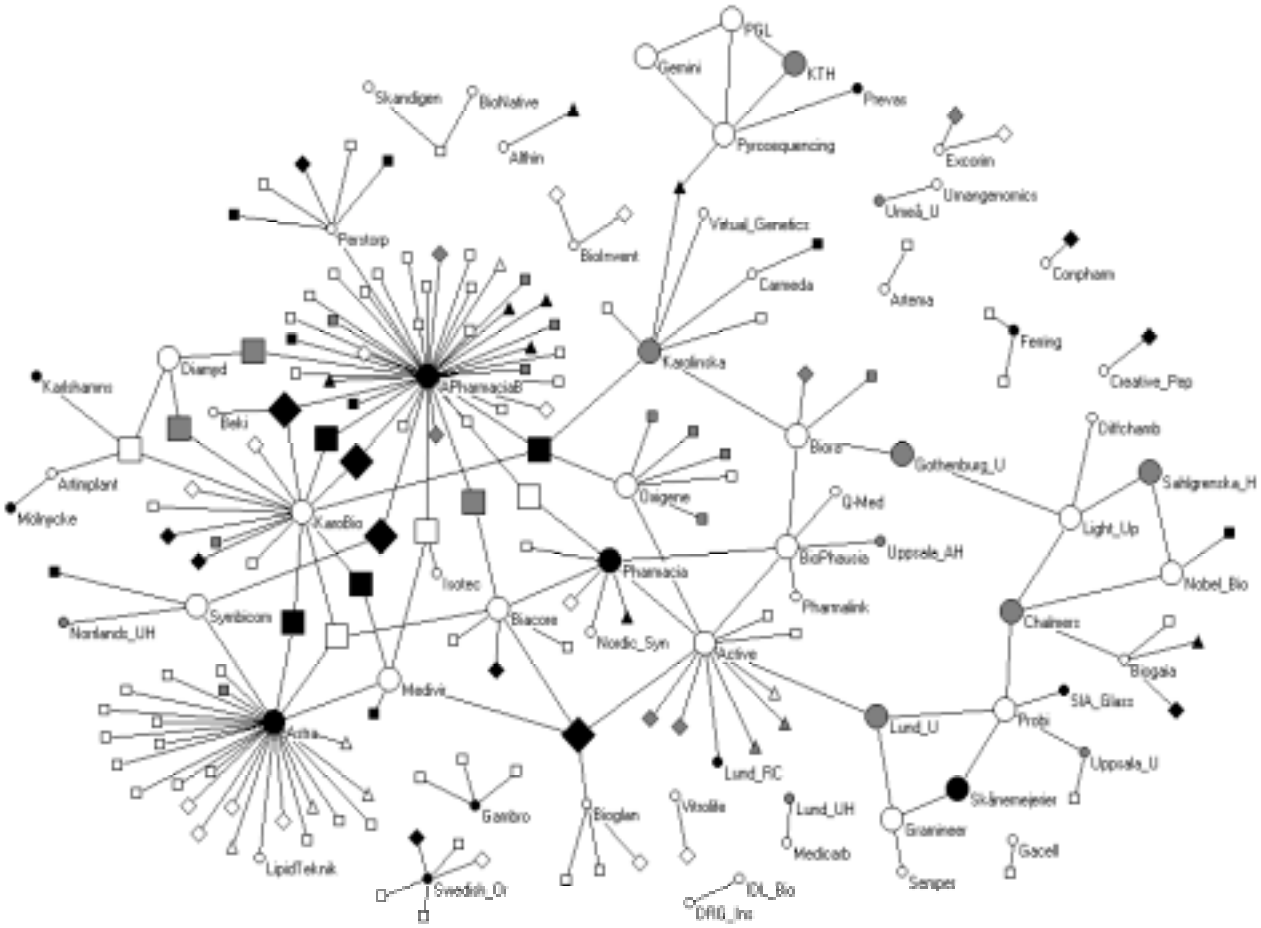
[20] The main Finnish biotechnology centers are located in the Helsinki Metropolitan Area (Uusimaa) and in the Etelae-Suomi region (mainly in Turku and Tampere) (see Kuusi, 2001). Local relationship with public research organizations appear to be crucial for the success of there regions. Finland ranks first in Europe in terms of proportion of innovative firms having cooperative agreements with universities. More than a half of Finnish high-tech companies collaborate with universities vs. a European mean of only 12% (Eurostat, 2000), and these contacts are particularly intense in life sciences. The Helsinki Science Park and Biomedicum are initiatives designedt around top-level Finnish research institutes in Helsinki: the University of Helsinki, the Viikki Biocentre, the National Public Health Institute and the Helsinki University of Technology. Other important centres of expertise are located in Tampere and Turku.

presented in Figure 5.6 shows the central role of the Karolinska complex (Karolinska Institute and KaroBio) in the middle between the Astra and Pharmacia stars of international contacts. The most important cluster of Swedish biotechnology firms around Karolinska is brought into closer connection by diverse organisations located outside Sweden. As in the case of the most important US clusters (see Owen-Smith, Riccaboni, Pammolli, Powell, 2001), the density of the Swedish national innovation network is greatly increased by the inclusion of diverse organisations from other geographic locations. Moreover, the Swedish picture emphasises the central role that small science–based firms can play in reaching out to other areas.

This model suggests that successful systems of innovation in biotechnology appear to grow from "old" regional clusters, developed around the strength of scientific expertise, the integrative capabilities of established pharmaceutical companies, and the dynamic role of small firms. These clusters have become over time both internally denser and much more outward–oriented.

In the second model of EU clusters (many French and German regions) networking is not yet developed to the same extent. . They seem to lack interdisciplinary teams and the connections across stages of the R&D process that dense webs of local relations among hospitals, university labs, and firms make possible. These difficulties, together with the centralisation and bureaucratisation of some of the relevant evaluation and selection processes, could constitute an inherent element of fragility for some of the younger clusters in continental Europe.

Figure 5.6. The Swedish Network of R&D Collaborations in Biopharmaceuticals



Source: BID, University of Siena

Legend:

Shape: Nationality
Circles – Swedish organizations
Boxes – US partners
Diamonds – European partners
Triangles – Other partners

Colour: Organization Type
White – New Biotechnology Firms
Gray – Public Research Organizations
Black – Large Established Companies

Size: Critical points for network connectivity
Large nodes – Articulation points
Small nodes – Peripheral nodes

These result would seem to lend some support to the notion that biotechnology is indeed characterised by a strong tendency towards clustering and that it derives to a large extent from the availability of a strong, heterogeneous but integrated research base that facilitates the transfer and the integration of knowledge, as well as the development of skilled labour, the mobility of such labour and – presumably – also the development of other supporting institutions like venture capital.

However, the tendency towards clustering is accompanied by a parallel process of increasing openness of the original clusters, a process also noted in the US. Recent trends suggest a combination of an increasing number of collaborations and a decreasing proportion of local connections. In the USA too, local ties moved from a high of 40% in 1988 to a low of 8% in 1998 (Owen-Smith, Riccaboni, Pammolli, Powell, 2001), in the context of a rising volume of collaborations (the number of ties active in 1998 was more than double the number a decade before).

In general, the recent evolution of the biotechnology industry has sustained a combination of an increasing number of collaborations and a decreasing proportion of local connections. This tendency might derive from different factors. One of the most likely resides in the need to get access to state-of-the art knowledge, wherever it might be located. Sustained performances are based on leading-edge research, which cannot be exclusively local. Second, the tendency towards clustering and subsequent de-localisation might also derive from the very properties of the evolution of knowledge in biotechnology (Orsenigo, Pammolli, Riccaboni, 2001), in relation to the diffusion of "platform", general purpose technologies (see also Pammolli and Riccaboni, 2001).

VI. Institutional Factors that Affect Industrial Competitiveness in Biotechnology

VI. I. Introduction

The commercial development of European biotechnology, as already indicated previously, is lagging significantly behind the USA. Despite encouraging signals of dynamism – especially from the small Northern European countries – and a wave of entry of new DBFs – especially in Germany – innovative activities remain far below US levels. European companies make significant use of American research while US firms do not seem to make as much use of the European research. The new European DBFs are much smaller than their American counterparts, much less active in the global network of collaborative relations and in the markets for technology, and mainly present in platform technologies.

One explanation for this may be that US firms enjoy first–mover advantages. In technologies where innovative activities are often characterised by increasing returns, first–mover advantages are an important phenomenon and are likely to provide long–lasting and difficult to erode leadership. European DBFs may have simply been pre-empted by their American counterparts, while the excellence of the American scientific research system has attracted financial and human resources from all parts of the world, further strengthening US leadership in biotechnology. However, other variables have likely played a role. With biotechnology being fundamentally science–based, and characterised by rapid innovation, it is possible that, at least partially, first–mover advantages may not be sustainable. Under these circumstances, catching–up and forging ahead – at the firm and country level – might be possible.

This section reviews some major institutional determinants of industrial competitiveness in biotechnology that might have hindered its development in Europe.

VI.2 The Structure of the Research System

Funding

Biomedical research is expensive and public money always played an important role in supporting this field. With the takeoff of biotechnology the cost of research increased further, thus making a strong support even more necessary in maintaining high-quality competitive research.

Molecular biology was developed predominantly in the USA and in the UK even though significant research groups were active in many other European countries (Morange, 1998). After World War II, US support for research in life sciences literally exploded. Public funding of biomedical research in the post–war period increased dramatically in Europe too, but total spending remained significantly lower than in the USA. The sheer size of resources devoted to biomedical research in the US in the post–war era explains much of the American leadership in life sciences.

In the US, the funding of biomedical research has been designed around the National Institutes of Health (Stokes, 1997). In 1998 the budget for funding extramural research was of $ 8 billion. Biomedical research is expensive and public money always played an important role in supporting this field. With the advent of biotechnology the cost of research increased further, thus making a strong support even more necessary in maintaining high-quality competitive research.

As a contrast, the total budget of the 5th Framework Programme (1998-2002) is about € 15 billion[21]. The first prevision for the total budget of the 6th Framework Programme (2002-2006) is of € 17.5 billion, equal to the NIH budget for the year 2003 at current exchange rates.

Table 6.1 provides an indication on the relative importance of public funding for biotechnology in different OECD member countries other than the US. In absolute PPP$ terms Germany spends the most on biotechnology, followed by the United Kingdom and France. The median contribution of government budgets dedicated to biotechnology is 3.5%, with a quite large spread, ranging from 0.4% in Italy to 13.8% in Belgium, 10.1% in Canada, and 8.1% in Finland.

[21] In addition, the Quality of Life Programme budget, only partially devoted to biotechnology, is € 2.4 billion.

Table 6.1: Public funding of Research and Development in biotechnology (1997)

	Biotechnology R&D	Total Government Budget Appropriations or Outlays for R&D (GBOARD)	R&D Biotech/R&D Overall
	Millions PPP$		Percent
Austria	16.8	1.146.5	1.5%
Belgium	181.7	1.314.0	13.8%
Canada	261.4	2.581.0	10.1%
Denmark	45.2	945.6	4.8%
Finland	94.5	1.165.0	8.1%
France	560.0	12.683.1	4.4%
Germany	1.048.2	15.595.7	6.7%
Greece	6.5	430.9	1.5%
Iceland	0.9	68.5	1.3%
Ireland	15.0	229.9	6.5%
Italy	32.1	7.329.6	0.4%
Netherlands	78.0	3.069.9	2.5%
Norway[1]	26.8 - 32.2	880.3	3%-3.7%
Portugal	19.2	781.9	2.5%
Spain	15.5	3.202.6	0.5%
Sweden[2]	65.6	1.795.2	3.7%
Switzerland[2]	16.4	1.379.7	1.2%
United Kingdom	705.1	9.055.7	7.8%

Remarks:
1. These data are national estimates, hence the range.
2. GBOARD has been estimated.
Source: OECD, based on data from the European Commission (*Inventory of public biotechnology R&D programmes in Europe*, 2000), Eurostat, Statistics Canada, and national sources.

The institutional structure of research

The institutional structure of biomedical evolved quite differently in continental Europe as opposed to the USA (and partly to the UK).

There is substantial integration between the production of biological knowledge concerning the nature and mechanisms of human diseases, clinical research, medical practice, and the discovery and development of new therapeutic treatments; and significant support for fundamental science in universities and public research centres, widely disseminated through publication in the refereed literature. Moreover, the US system is characterised by a variety of sources of funding and selection mechanisms, which complement the role of the NIH and act according to different allocative principles (see Stokes, 1997; Braun, 1994; Owen-Smith, Riccaboni, Pammolli, Powell, 2001). Overall, the US research system achieves efficiency

through competition among research units providing room, at the same time, for diversity and institutional flexibility.

In Europe, funding has tended to be administered mainly at the national level, with strongly differentiated approaches and wide differences across countries. In many cases, resources have either been spread among a large number of "small" laboratories, or they have been excessively concentrated in the few available centres of excellence. Funding coming from the various European programmes has only partially changed the situation. However, recently the EU Commission has introduced the new European Research Area concept, proposing huge multicentric projects for the next 6th Framework Programme, such as Integrated Projects, Centres of Excellence, and a Clinical Trial Platform.

At present, the absolute size and the higher degree of integration of the American research system, as opposed to the fragmented collection of national systems in Europe, constitutes a fundamental difference. Moreover, one claim of the Report is that there is a structural alignment between the features of the US biomedical research system and the intrinsic features of the biotechnology scientific and technological paradigm, or search regime. The structural coupling between competition at all levels of the system and variety of institutions involved in research satisfies the intrinsic tension between the need to explore a large number of alternative hypotheses and the need to integrate heterogeneous stages of the exploration and development process.

The organisation and structure of universities

The US research system in the life sciences is highly decentralised. Even public universities rely on diverse funding sources, including state and national governments, foundations and corporate supporters, tuition revenues, and alumni gifts. Private universities, especially elite ones, are also supported by generous endowments.

The organization of research and teaching has characteristics that facilitate the flexibility and decentralisation, but also the integration, of research. In the US and the UK, academic departments have long been the main organisational entities while in Europe a single professor dominates. The departmental structure makes it easier to

respond to the emergence of new disciplines, like computer sciences and biotechnology, both by integrating them in curricula in conventional programs and/or by creating new departments and programs.

Thus, blurring boundaries between basic and goal-oriented research and increased competition for research support and funding enable greater mixing of disciplines in the US (Galambos and Sturchio, 1998; Morange, 1998). Elite research institutes in the US, such as Cold Spring Harbor, Salk, or Scripps, routinely bring together faculty from multiple disciplines.

It is possible to argue that, the European model is characterised a high degrees of division of labour and specialisation between teaching and research institutions, whereas in the US the dominant model of post-graduate students being exposed and trained to scientific research within teams composed by students and professors within departments has been a more integrated one. In Europe, this separation might have had negative effects on both the quality of research and on the ability of academic institutions to interact with industry.

Despite national distinguishing characteristics, the structure of research systems in Europe is profoundly different from the Anglo–Saxon model.

First, in Europe financing is considerably more centralised and, consequently, it entails more hierarchical control.

Second, research institutions are far less interdisciplinary and flexible. In Germany, for example, a number of the highly prestigious Max Planck institutes are organised hierarchically around a single field, such as biochemistry, genetics, or immunology.

Third, the integration of teaching with research has progressed far less than in the US (and to some extent than in the UK). Ph.Ds are a relatively recent innovation in many continental European countries and they remain far less professionally orientated than in the US. Thus, for example, the diffusion of molecular biology into the general training in many European countries is a relatively recent phenomenon as compared to the USA and it has become only recently a standard part of the curricula of pharmacologists, pathologists, medical consultants, and plant biologists.

Diversity and integration among publicly funded research organisations (PROs)[22]

The research systems in the US and Europe are organized in qualitatively different ways; hence any comparison must be sensitive to variation on multiple dimensions.

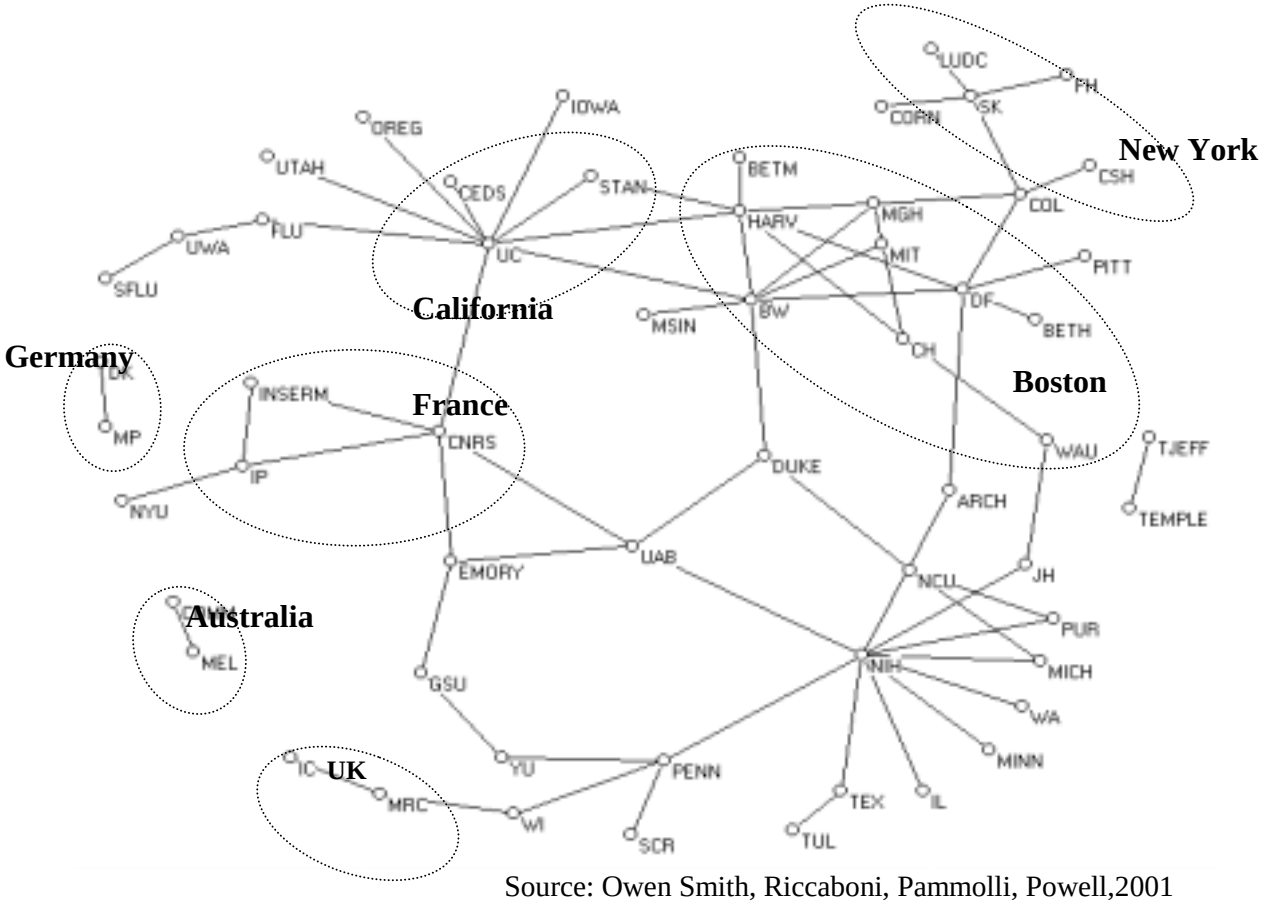
The analysis is based on 8,031 patents for therapeutically useful compounds or processes issued by major world patent offices (US, UK, Germany, France, Japan, European, and the Patent Cooperation Treaty legal office), and assigned to the 98 most prolific non-industrial research organisations, worldwide[23].

Figure 6.1 examines the upstream collaborative network among individual PROs to analyse relationships among organizations. Figure 6.1 is based on patent co-assignment networks among public research organizations. Each node is a university, research institute or hospital, and each tie represents two or more patent co-assignments between the organisations. Several features stand out in this image.

[22] This section is an extract from Owen Smith, Riccaboni, Pammolli and Powell, 2001.

[23] These 98 institutions represent more than 70% of all non-industrial patents in this sample. Thus, there is a natural cut-off point at 98, as the remainder of the distribution is very widely dispersed across hundreds of organisations. Information on the patents is found in *Patent Fast Alert*, published by Current Drugs, Ltd., London, U.K.

Figure 6.1. Organization Level Patent Co-Assignment Network for PROs, 1990-99



Source: Owen Smith, Riccaboni, Pammolli, Powell,2001

ARCH	Arch Dev. Corp., Univ. of Chicago (IL)
BETH	Beth Israel Hospital (MA)
BETM	Beth Israel Medical Center (MA)
BW	Brigham and Women's Hospital (MA)
CEDS	Cedars-Sinai Medical Center (CA)
CH	Children's Hospital Medical Center (MA)
CNRS	Centre Nat. de la Recherche Sc. (France)
COL	Columbia University (NY)
COMM	Commonwealth Sc. and Ind. Res. Org. (Australia)
CORN	Cornell Research Foundation (NY)
CSH	Cold Spring Harbor Lab. (NY)
DF	Dana-Farber Cancer Institute (MA)
DK	German Cancer Institute (Germany)
DUKE	Duke University (NC)
EMORY	Emory University (GA)
FH	Fred Hutchinson Cancer Res. Center (WA)
FLU	University of Florida (FL)
GSU	Georgia State University (GA)
HARV	Harvard University (MA)
IC	Imperial Cancer Research Fund. (UK)
IL	University of Illinois (IL)
INSERM	Institut National de la Santé et de la Rech. Médicale (France)
IOWA	University of Iowa (IA)
IP	Institut Pasteur (France)
JH	Johns Hopkins University (MD)
LUDC	Ludwig Inst. for Cancer Res. (Switzerland)
MEL	University of Melbourne (Australia)
MGH	Massachusetts General Hospital (MA)
MICH	University of Michigan (MI)
MINN	University of Minnesota (MN)
MIT	Massachusetts Institute of Tech. (MA)
MP	Max Planck Institut (Germany)
MRC	Medical Research Council (UK)
MSIN	Mount Sinai Hospital (Canada)
NCU	University of North Carolina (NC)
NIH	National Institutes of Health (MD)
NYU	New York University (NY)
OREG	University of Oregon (OR)
PENN	University of Pennsylvania (PA)
PITT	University of Pittsburgh (PA)
PUR	Purdue University (IN)
SCR	Scripps Research Institute (CA)
SFLU	University of South Florida (FL)
SK	Sloan Kettering (NY)
STAN	Stanford University (CA)
TEMPLE	Temple University (PA)
TEX	University of Texas System (TX)
TJEFF	Thomas Jefferson University (PA)
TUL	Tulane University (LA)
UAB	University of Alabama (AL)
UC	University of California System (CA)
UTAH	University of Utah (UT)
UWA	University of Washington (WA)
WA	Washington University (MO)
WAU	Wisconsin Alumni Research Found. (WI)
WI	Wistar Institute (PA)
YU	Yale University (CT)

The tightly clustered French, German and British research organizations on the left side of the figure and the densely connected US regions in the image's upper right hand quadrant are the result of minimum-energy network drawing techniques and not of arbitrary placement. In addition to demonstrating the coherence of national and regional R&D systems, close inspection of the patterns of patent co-assignment help explain the causes of the US leadership in division of innovative labour in biopharmaceuticals. Note the organizational homogeneity of the French and German national clusters, which do not include hospitals and have no identified universities[24]. The United Kingdom has a somewhat higher degree of organizational diversity, reflected by the presence of both government and non-profit research and funding agencies. Contrast these relatively isolated and homogeneous national clusters with the large and densely interconnected Boston region in the upper quadrant of the figure, which is composed of tight, repeated interconnections among a diverse set of PROs. Elite universities (Harvard, MIT), research institutes (the Dana-Farber Cancer Center), and hospitals (Brigham and Women's and Massachusetts General) play central roles in innovative collaborations both within Boston and across US regions.

Closely-knit regional networks such as those found in Boston help account for the global centrality of American PROs. But connections across US regions (note for instance the ties between Harvard, Stanford, and the UC system, connections from Dana Farber to the University of Chicago, and from Brigham and Women's hospital to Duke University) and co-assignment ties linking geographically dispersed universities to the National Institutes of Health illustrate a public research system that also reaches across regions and organizational forms. These systemic cross-national variations in the organization of early-stage research collaborations can explain national differences in biomedical commercialisation above and beyond variations in policies or later-stage technology transfer infrastructures.

Relatedly, additional empirical evidence produced by Owen Smith, Riccaboni, Pammolli, Powell, 2001, show the existence of substantial differences between leading US and European research institutions in terms of scientific specialisation. In other words, national specialisation in Europe falls along scientific lines. Points of

[24] Scientists at the CNRS or Max Plancks may well have university laboratories, but the government institute is identified as their primary affiliation on the patents.

excellence develop in both the US and European systems, but in continental Europe those clusters tend to be limited to narrower specialities and specific nations. The US are characterised by diverse, substantively generalist research organisations connected both within and across key regional clusters, though the prevalence of Boston and California-based research organizations in the core suggests the importance of regional agglomeration (see Owen-Smith, Riccaboni, Pammolli, Powell, 2001). British institutions, e.g. Cancer Research Campaign (CRC), Medical Research Council (MRC), and the British Technology Group (BT) are somewhat broader in focus but still cluster in therapeutic classes largely related to cancer research. The greater breadth of the British research system, and its higher degree of diversity compared to France and Germany, may explain the higher centrality of UK research institutes in international R&D networks.

These differences in the science base seem to be critical, implying that increases in scale alone will not alter the focus of R&D efforts because organizations typically engage in local search, and would continue to patent in those areas in which they are most skilled. In essence, one reason for greater integration across and within US regions can be found in the scientific overlap among generalist patentees. Alterations in the scale of patenting activity without corresponding shifts in this division of labour will not make the European system resemble its American counterpart. Instead, mere increases in scale might deepen specialisation and, perhaps, heighten fragmentation among European national research systems.

University-industry relations

A further set of factors that explain the US advantage relate to the ability and willingness of the American academic system to interact with the industrial and commercial world. The key role acquired by scientific knowledge for technological innovation manifested itself in an unprecedented intensification of both industry–university ties and in the direct involvement of academic institutions and scientists in commercial activities. While both phenomena are not new, since the mid-1970s the drive towards an increasing commercialisation of the results of research accelerated dramatically, and patenting and licensing activities on the part of universities started to soar. The number of universities having established Offices for Technology Management also increased from 25 in 1980 to 200 in 1990. The creation of spin-

offs became a distinct and crucial phenomenon of the American academic system. Increasingly, universities were assuming and were asked to assume the role of direct engines of (local) economic growth.

The emergence of the entrepreneurial university and the specific forms this process took in the USA depend strongly on some general characteristics of the social, institutional and legal context of the USA, including the attitudes towards intellectual property rights and the availability of venture capital. There is high mobility between academia and the commercial world – and, more generally, there exists an active labour market for scientists, technicians, and managerial experts – to a much more developed extent than in Europe. American university professors often participate in various forms in commercial activities either retaining their academic affiliation or migrating back and forth between different affiliations. An alliance between scientific, organisational and entrepreneurial capabilities (together with a favourable attitude towards the establishment and enforcement of robust intellectual property rights) constitutes an essential precondition for growth in industry–university relations. It is possible to argue that high degree of integration between research and teaching tends to favour further linkages, easier communication and more intense flows of knowledge and people between academia and the business world.

Conversely, the ties, bureaucracy, and hierarchies of its scientific institutions, both at the national and the European levels, strongly discourage labour mobility across academia and industry. As discussed by Soskice (1997) and Zucker, Darby and Brewer (1997), the organisation of labour and company law in Europe, combined with the organisational strategies of most large companies and with the structure of the academic labour market, constrains the development of US–style active labour markets, and make it harder for companies to “hire and fire” personnel or rapidly cut non–performing assets. Moreover, though there is often some lateral movement across firms very early in a person’s career, the vast majority of European employees build their own careers within one firm and university.

Correspondingly, the structure of decision–making, remuneration, and career paths within firms and universities differ fundamentally from the US or UK model. Career paths, especially in universities, tend to be well specified, incremental, and based on rank hierarchies. This structure works quite well in industries dependent on long–term investment strategies in relatively stable technologies, characterised by the

diffusion of deep skills throughout the firm, but it creates fundamental obstacles to the creation of high–risk technology firms.

To the extent that innovation depends on the flow of knowledge between university labs, start–up research firms and large firms, joint research projects and strategic alliances facilitate this exchange of knowledge. Conversely, if the labour market does not support extensive lateral career mobility across academia and firms, these network externalities would be difficult to sustain (Soskice, 1997)[25].

In continental Europe, university–industry relationships have developed much more slowly[26] and still now – despite considerable progress – the situation remains unsatisfactory. Integration of research and teaching and collaboration with industry has been more frequent in the case of engineering schools and in selected disciplines in particular countries (chemistry in Germany). Differently from the US, where universities have gradually extended their functions (an integrated model centred on universities), continental Europe has leaned towards the development of various types of specialised institutions for technology transfer who act as intermediaries between research and industry (the institutional specialisation model).

Thus, there have been a large number of initiatives all across Europe aimed at establishing stronger links between industry and universities and at encouraging a more entrepreneurial attitude by universities. In practice, policies have been targeted mainly towards the setting up of specific devices to manage technology transfer, like science and technology parks or other such agencies, but their performance has so far been mixed.

A European Paradox?

Despite the presence of centres of absolute excellence, scientific research in Europe seems to lag behind the US. This could have created a significant drain of human and

[25] There is interesting evidence in this respect that mobility of researchers across different institutional settings enhances both scientific research and commercial performance, not only in the US but also in European countries (Gittelman 2000).

[26] More detailed information on the modalities and practices characterising industry-science relations in Europe can be found in the forthcoming report "Benchmarking Industry-Science relations – the role of framework conditions" cosponsored by the Austrian Federal Ministry of Economy and Labour and the European Commission.

financial resources from Europe to the US that contributes to further strengthen the American advantage.

There is now significant qualitative and quantitative evidence indicating that the R&D productivity of large firms as well as the rates of formation of new firms are highly correlated with the strength of universities and other research institutions in the underlying sciences (Ward and Dranove, 1995; Cockburn and Henderson 1996; Zucker, Darby and Brewer, 1997; Swann and Prevezer, 1996).

However, there is less agreement about the existence of a direct link between the strength of the local science base and industrial and commercial performance. For example, the UK was a leading location for a disproportionate share of the main research breakthroughs in biotechnology in the second half of 1900s, but much less so in the industrial application of such discoveries (Cooke, 2001). More generally, it is widely believed that scientific, but not industrial, research in Europe fares much better compared to the US – the so-called European paradox. On this view, competitive advantages cannot be explained by the strength of the local scientific base since academic science is rapidly published and thus rapidly available across the world. Differential performance in industrial biotechnology is more likely explained by different institutional mechanisms favouring the rapid translation of scientific research into industrial R&D.

The empirical evidence on the existence and relevance of the European paradox is mixed. However, the formation of university spin–offs and the emergence of biotechnology clusters seems to depend less on the existence of academic research as such than on the presence of "star scientists" and cutting edge research (Zucker, Darby and Brewer 1997). Similarly, there is substantial – albeit largely anecdotal – evidence suggesting that successful experiences in industry–university ties in Europe take place in areas where concentration of world class research in different fields of biotechnology is available (and where the need for explicit supporting policies is, as a consequence, less severe).

These observations support the notion that the absolute quality and "quantity" of scientific research and the coupling of scientific and organisational capabilities constitute essential preconditions for subsequent developments in industry–university

relations. Indeed, the development of an entrepreneurial function within universities in the US has not substituted for their traditional functions.

Rather, the entrepreneurial function appears to be strongly complementary to and integrated with the other functions, primarily teaching. The US experience would seem to suggest, in this respect, that linkages with industry simply cannot develop without the constant mediation of teaching, as a stimulator of demand for relationships and an important source of absorptive capabilities within firms. In Europe, the presence of intermediary institutions might in some cases have paradoxically increased the distance between university and industry, introducing an additional layer in the relationship instead of favouring the development of organisational and integrative capabilities within firms and within academic institutions.

VI. 3 Financial Markets and Venture Capital

The availability of venture capital is commonly invoked as a fundamental ingredient of American leadership in biotechnology. Clearly, venture capital played an enormous role in fuelling the growth of the new biotechnology firms. Venture capital is a long–standing institution in the US financial and innovative system. It was already active in the beginning of the 20th century and emerged as a vibrant industry with the electronic revolution in the 1960s. On the contrary, in many European countries, the lack of developed capital markets for technology firms creates important barriers for prospective venture capitalists. Here it is worth recalling how venture capital plays a crucial role of bridging and complementing different constituents and roles within the system of biotechnological innovation.

Venture capital provides first of all finance to prospective academic entrepreneurs. Second, venture capital not only provides finance but also and perhaps more importantly managerial advice, organisational capabilities and "signals" to prospective investors about the potential of the new company. Contrary to the conventional stereotype of the American financial institutions, venture capitalists are characterised by an extremely strong "hands-on" and "long-run" approach towards the companies they are financing. A significant number of doctorate holders in

biology end up working in venture capital firms and venture capitalists have to be part of the same network of conferences, literature, scientists, etc. Thus, venture capital mixes technology, academia and finance.

Lack of a developed venture capital market has restricted the start–up of biotechnology firms outside the US. In Europe, and despite various forms of intervention at the national and even local level aiming at fostering its formation, venture capital has only very recently began to develop.

Nevertheless, in Europe there have been many other sources of funds (usually through government programs) available to prospective start–ups. Moreover, survey results suggest that financial constraints did not constitute the main obstacle to establishing new biotechnology firms in Europe (Senker, 1998). Although venture capital played a critical role in the founding of US biotechnology firms, collaborations between the new firms and the larger established firms provided a potentially even more important source of capital. This raises the question why couldn't prospective European start–ups turn to established pharmaceutical firms as a source of capital? A speculative but plausible answer could be that European companies tended to collaborate more with US biotechnology rather than European firms[27]. Even in the absence of other institutional barriers to entrepreneurial ventures, start–ups in Europe might have been crowded out by the large number of US–based firms anxious to trade non–US marketing rights for capital (Henderson, Orsenigo, Pisano, 1999). Given the number of American DBFs in search of capital, European firms interested in commercialising biotechnology had alternatives to investing in local biotechnology firms.

Finally, the slow development of European venture capital for biotechnology could reflect less inability or unwillingness of European financial institutions to fund new ventures and more a scarcity of “good” projects on the part of the industry. Partially supporting this interpretation, it is worth recalling that several initiatives by both domestic and foreign investors to launch venture capital funds were attempted in Europe during the 1990s. Many of these funds, if anything, ended up investing in new biotechnology companies outside Europe. Conversely, foreign venture capital

firms have funded some of the few experiences of successful European DBFs. Thus, the delayed development of venture capital in Europe seems to depend less on the lack of investors and funds than on the limited supply of promising start–ups.

The role of venture capital markets in sustaining small, young high–tech firms that do not meet strict creditworthiness institutional criteria for funding new projects remains crucial in Europe. Recent evidence suggests that European venture capital markets are increasingly active in supporting small biotechnology companies in their innovative efforts. Yet, some potential drawbacks still persist at the interface between public and private financial markets and institutions, which need to be better co-ordinated for defining coherent incentive schemes for risk–taking innovative entrepreneurs.

Table 6.2 shows that, during the period of unprecedented expansion of the European biotechnology industry (1996-2000), venture capitalists did not change their capital allocation from less research–intensive sectors toward biotechnology.

While total investment rose from about € 6900 million to € 35000 million, most of it is devoted to traditional sectors (industrial machinery and equipment, fashion, leisure products) and to expansion and leveraged buyouts. The main recipient of higher early–stage investment (seed and start–up financing, about 12% more in 1996-2000) has been the ICT sectors. US data (Science and Engineering Indicators, 2000) for 1996-1998 show that the share of venture capital devoted to US biotechnology was more than double, ranging from 6.1% to 8.1% as has the share of seed investments which varied between 3.8% (1996) and 4.6% (1997)[28]. Moreover, unlike in Europe, the period 1996-98 was one of stability for the US biotechnology industry and the proportion of venture capital disbursements to DBFs was far from its historical 1992 peak. As a result, despite recent growth, European DBFs have continued to attract only ¼ of the global venture capital investments in biotechnology during the last five years (Ernst & Young, 2001).

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[27] Indeed, most NBFs' strategies emphasized licensing product rights outside the US to foreign partners. Thus to an even greater extent than many established US pharmaceutical firms, European firms were well positioned as partners for US NBFs.

[28] Original data provided by the Venture Economics Investor Service, Newark, NJ. Since data on US and European venture capital come from different sources, they are not strictly comparable (for a tentative comparison see National Science Foundation, 1998).

The unique exception to this general trend within the EU appears to be Germany. Germany's financial support has favoured biotechnology and start-up investments. France ranks second both in terms of total investment in biotechnology and of its share in early–stage financing, followed by the UK. French and German venture capitalists are playing an important role in supporting the rapid growth of their national systems of innovation in biotechnology. They are likely to start a phase of selection and buyouts among the vast population of new European biotechnology firms and to complement public start–up initiatives by providing financing to selected growing biotechnology companies. But the unbalanced distribution of venture capital investments toward American early–stage biotechnology companies could represent a structural weakness in Europe for a considerable length of time.

Table 6.2: European venture capital disbursements, by sector and financing stage, 1996–2000 (€1000)

	1996	**1997**	**1998**	**1999**	**2000**
By sector					
Biotech	182.355	250.348	346.354	643.838	1.017.185
	2,70 %	2,60 %	2,40 %	2,60 %	2,90 %
Hi-Tech	1.347.926	2.306.820	4.026.917	6.418.215	10.976.494
	19,60 %	23,90 %	27,80 %	25,60 %	31,40 %
Total	**6.878.646**	**9.654.942**	**14.460.781**	**25.115.694**	**34.985.753**
By stage					
Seed	68.992	85.137	169.271	467.536	819.680
	1,0 %	0,9 %	1,2 %	1,9 %	2,3 %
Start-up	375.430	625.953	1.468.511	2.771.872	5.843.723
	5,5 %	6,5 %	10,2 %	11,0 %	16,7 %
Expansion	2.712.015	3.375.956	4.334.539	7.432.678	12.986.306
	40,0 %	35,0 %	30,0 %	29,6 %	37,1 %
Replacement Capital	481.014	733.017	1.078.675	1.186.228	930.092
	7,1 %	7,6 %	7,5 %	4,7 %	2,7 %
Buyout	3.150.195	4.834.879	7.409.785	13.257.380	14.405.952
	46,4 %	50,1 %	51,2 %	52,8 %	41,2 %
Total	**6.787.646**	**9.654.942**	**14.460.781**	**25.115.694**	**34.985.753**

Source: EVCA (2001).

VI. 4. The Regulation of Intellectual Property Rights in Biotechnology

Introduction

One important factor contributing to the growth of biotechnology in the US has been the recognition and enforcement of strong intellectual property rights. The establishment of clearly defined property rights has played an important role in the explosion of new firms since, by definition, few firms had complementary assets that enabled them to appropriate returns from the new science in the absence of strong patent rights. In the early years of biotechnology, considerable confusion surrounded the conditions under which patents could be obtained. Research in genetic engineering was on the borderline between basic and applied science, conducted primarily in universities or otherwise publicly funded, and the degree to which it was appropriate to patent results of such research became almost immediately the subject of controversy[29].

IPRs in European biotechnology

By adopting Directive 98/44/EC of the European Parliament and Council on the Legal Protection of Biotechnology Inventions[30], after intensive and lengthy discussions, the EU equipped itself with a common set of principles regarding the granting of biotechnology patents. However, in spite of this political commitment, only four of the fifteen Member States have adopted the necessary legislation.

Most European national legislation did not explicitly address some of the most controversial problems in the regulation of IPRs in biotech. The dominant situation

[29] Millstein and Kohler's groundbreaking discovery -- hybridoma technology -- was never patented, while Stanford University filed a patent for Boyer and Cohen's process in 1974. Boyer and Cohen renounced their own rights to the patent but nevertheless were strongly criticized for having being instrumental in patenting what was considered to be a basic technology. Similarly, growing tension emerged between publishing research results versus patenting them. Whilst the norms of the scientific community and the search for professional recognition had long stressed rapid publication, patent laws prohibited the granting of a patent to an already published discovery. In the second place the law surrounding the possibility of patenting life-formats and procedures relating to the modification of life forms was not defined. This issue involved a variety of problems, but essentially boiled down, first, to whether living entities could be patented at all; and, second, to the scope of the claims that could be granted to such a patent (Merges and Nelson, 1994). The Bayh–Dole act of 1980 greatly facilitated university patenting and licensing, but the emergence of the industry–university connection depended very greatly on the revolutionary developments in micro–electronics and biotechnology in the second half of the 20th century.

[30] J.O. - L 213 of 30.7.98

was one in which national legislation did not include, in general, legal principles that prohibit the granting of patents on living matter, but at the same time it did not offer definitions and general principles, much less specific guidelines, to manage the most controversial problems. At the same time, biotechnological inventions were de facto patented in most countries.

According to an OECD study on patenting practice in 22 member countries[31], all reporting countries allowed patentability without exceptions for a large variety of objects. National differences concern the patentability of plants per se, parts of plants or vegetal varieties; and of animals per se, animal organs or animal varieties. All countries excluded the patentability of human beings, human organs or derived products of human origin, including cell lines, genes and sequences of nucleic acids or amino-acids. However, an isolated element of the human body, or obtained through a technical process, including the sequence or partial sequence of a gene, might be patentable, even though its structure may be identical to the naturally occurring one.

It is clear that national legislation does not include, in general, any legal principles that prohibit the patentability of biotechnological inventions. At the same time, however, the implementation of patentability is subject to a number of specific norms that require explicit treatment by national legislators.

Directive 98/44 is based on the principle that biotechnological inventions can be patented but there may be specific exclusions depending on the nature of the invention. These exclusions clearly address the ethical concern expressed in the European Parliament and by the public opinion for the possibility of granting patents on processes that may modify human genetic identity or utilise human genetic materials in the organised form of embryos. However, the Directive is clear that an invention cannot be excluded for the sole reason that it concerns living matter.

A separate and relevant issue is the protection to intellectual property rights in academic research. On the one side, it is argued that property rights would favour the creation of markets for technology and hence a faster and more ordered diffusion and

[31] These include Germany, Australia, Austria, Belgium, Canada, Korea, Denmark, Spain, United States, Finland, France, Hungary, Italy, Japon, Norway, New Zealand, Netherlands, Czech Republic, United Kingdom, Sweden, Switzerland, Turkey.

use of knowledge. On the other side, some authors emphasise that strong protection for intellectual property in academic research might ultimately hinder the search for diversity which is intrinsic to the scientific activity. Scientists might be motivated more by the need to reach a patentable result than by intrinsic interest of discovery. In sum, a world of private science might be a world of poorer science. Clearly, these arguments require closer scrutiny.

The concession of very broad claims on patents might also have a detrimental effect on the rate of technical change, because they might preclude the exploration of alternative applications of the patented invention. To the extent that such techniques and knowledge are critical for further research that proceeds cumulatively on the basis of the original invention, the attribution of broad property rights might hamper further developments.

In general, the rationale of the establishment of strong IPRs as a means for the development of markets for technology rests critically on the assumption of competition among inventors. Thus, excessive concentration of patents might constitute a legitimate source of concern, calling for a systematic connection between IPR policy and antritrust.

Another line of criticism refers to the problem of sequential patents and blocking patents. In biotechnology, many developments require the utilization of several patents, which may be owned by different players. Particularly with gene sequences, industrial utilization may require the licensing of several patents in sequence. In other words, a market for technologies should be put in place, where rights over several pieces of knowledge are contracted for. If this is the case, then the owner of the first patent in a row might behave opportunistically. The argument is in line with the well known 'tragedy of anti-commons' raised by Heller and Eisenberg (1998): while in the commons the lack of proprietary rights leads to over-utilization and depletion of common goods, in biotechnology the risk may be that too many rights, creating a barrier to use of otherwise public knowledge, lead to under-utilisation. High transaction costs are expected, with an upsurge of litigation and legal costs. The effect can clearly be more negative in the case of cumulative technological change and, moreover, for publicly-funded academic research. However, there several remedies can be designed for this problem, such as cross-licensing, patent pools, mergers or side payments (see also Shapiro, 2001).

In synthesis, the debate about IPRs in biotechnology is still highly controversial and problematic. The emergence of a regime where property rights can be precisely defined and appropriated has been favourable to the development of the biotechnology industry in the USA, especially as an incentive for the creation of DBFs. At the same time, however, there is growing concern that the current US system might not be sustainable in the long run. In Europe, the IPR situation is less extreme and there is opposition to the Directive as well as problems of harmonisation across national legislation. The issues raised clearly go much beyond biotechnology and will continue to be controversial over the next decade(s). Within this environment, the key concerns raised at the frontier of science and technology can only be resolved through informed discussion, careful economic analysis, sound policy debate, and finally and most importantly, democratic consensus.

VI. 5 Biotechnology Policies in Europe

It was suggested earlier that the slow pace of development of biotechnology in Europe has been due to lack of the basic preconditions for innovative activities in this field. These concern the scientific and industrial base, the organisational structures linking science to industry, venture capital and intellectual property rights.

However, in recent years European biotechnology appears to have found new dynamism. One possible reason for this might be that policies have begun to exert some impact. Many European countries began to initiate policies supporting biotechnology in the 1980s. These included measures to introduce some typical US institutional features that have been crucial to the development of new biotechnology start–ups (such as fostering venture capital, developing financial markets tailored for new high risk companies, promoting the commercialisation of academic research and the mobility between academia and commercial activities) but primarily aimed at strengthening technology transfer and new firms formation. Efforts were also directed towards supporting basic research in universities and national research laboratories and, in some countries, firms (France). Furthermore, in the UK and France the government has been instrumental in the foundation of some of the oldest European biotechnology firms, namely Celltech in Britain and Transgene in France.

The forms and rationale of public intervention have been quite different across countries and regions. The experiences discussed below reflect such different patterns.

The experience of the United Kingdom has been well documented by several studies, like the Diebold Institute Entrepreneurship and Public Policy Project (moreover, see DTI, 1999, 2001). Consequently, it is not covered in a specific section in this Report.

France

Starting in early 1980s, with the "mobilisation (later "expansion") program", public effort has been directed in France to stimulate both private and public research in biotechnology (see Lemariè, Mangematin, Torre, 2001). The majority of basic research was actually conducted by public structures such as the Centre National de la Recherche Scientifique (CNSR) and the Institute National de la Recherche Medicale (INSERM). These institutes have also transferred funds to private institutions like the Institute Pasteur. Several initiatives were then taken: beyond supporting start-ups by venture capital and stimulating the creation of science and technology transfer centres within the major universities and research institutes, public funding was used to revitalise large established groups operating in the life sciences. In the 1990s, with the launch of the BioAvenir program, the latter form of intervention became more pronounced, as suggested by the joint support to Rhône Poulenc and several public research centers, aimed at creating public–private partnerships.

The improvement of some indicators of biotechnology activity in France, and then the creation of a more solid scientific and technological base, became more evident during the implementation of this "latent" national champion policy, in which a large part of the public research system was made available to one private group. This approach has been frequently blamed for the slowdown in the birth of new firms in the early nineties. However, this period was one of scarce interest of investors towards biotechnology in general. In recent years, a renewal of interest towards start-ups has characterised the French policy, with new initiatives aimed at promoting knowledge transfer, mobility of scientists, and more generally, at increasing co-ordination between different agents and at improving the control of funded projects.

Moreover, the opening of the "Nouveau Marché" is a relevant channel to collect financial resources.

Germany

Publicly funded research has been the primary source of biotechnology knowledge also in Germany. The "Applied Biology and Biotechnology Program", launched in 1986 by the Federal Ministry of Research and Technology, was intended to stimulate biotechnology research in universities (by the creation, for example, of "Gene Centers" at universities of Munich, Cologne, Heidelberg and Berlin) and knowledge transfer to firms. Established chemical and pharmaceutical corporations were, in this phase, the main subjects of such interventions.

Characteristics of recent public policies in Germany, such as support for an environment encouraging new start–ups, and the "regional" focus in the development of some high–tech industries, have also been evident especially in the US but also elswhere in Europe. Local labour markets, specialised inputs and knowledge spillovers are suggested to be the main factors contributing to such phenomena. The Ministry of Research launched the BioRegio program in 1996 to create a competition between 18 German regions, each of which expected to define research projects based on biotechnology networks. Three of them (München, Rheinland and Rhein-Neckar) "won" the competition and received extrafunding, and one, Jena, received a special vote by the jury. This type of intervention is seen as one of the crucial factors contributing to growth in the number of new biotechnology firms, after a decade during which Germany had been losing its leading European position in life sciences.

However, such intervention has worked differently in different regions. In most of them, firm and job creation has been limited, both in terms of number and size of new firms, and then of new jobs. A review of the leading regions shows that the new start–ups have been able to rely on a pre–existing, and quite diffused, knowledge base, as represented by universities, research institutes, and even the chemical and pharmaceutical industry. The case of the Rhine-Neckar is characteristic. The majority of life science firms are located in the Heidelberg Technology Park (that is, very close to University clinics and the German Cancer Research Centre), and, furthermore, chemical and pharmaceutical companies have long been present in the area. One can only speculate how the future will unfold once public support is over.

Clearly, it is difficult to evaluate the effectiveness of different policy approaches and arrive at one that might be preferable to others[32]. What emerges clearly, however, is that forward-oriented policies can have an impact, but that the presence of other factors – principally an established and developed knowledge and competence base – are necessary to attain a "critical mass" for the growth of the sector. Even if policies have played an important role in the recent dynamism of European biotechnology, it is not easy to isolate the contribution of any particular intervention. As already noted, the simultaneous presence of various factors appears to have played a determinant role. In many countries, indeed, policies have often been criticised for the lack of co–ordination between different measures and also the lack of a "strategic" vision.

In general, it is true that several member states have had policies to promote biotechnology in place for several years. Although there has been some success, notably in the promotion of biotechnology start-ups, the growth of DBFs in Europe appears to be hindered. To a considerable extent, this may be due to regulatory, entrepreneurial, fiscal and financial factors. However, in addition to these factors the supply of cutting-edge scientific research may be inadequate. If so, this problem could be addressed not only through higher levels of research funding but also through higher degrees of pluralism in funding sources, lower dependence on closed national systems, and higher integration of research with teaching, clinical research and medical practice. One of the most effective means of achieving this would be through the establishment of a European Research Area, starting from the constitution of a single market for human capital in academic and non industrial research.

[32] Another interesting case is Denmark, where the development of biotechnology firms is in different ways linked, according to many observers, to their relationship with large and established companies like Novo Nordisk and Heineken. On the other hand, creating a favorable framework for foreign investment by providing fiscal incentives has been central to Ireland's biotechnology policy. The birth of new firms is mainly concentrated in areas such as Dublin where, again, a solid knowledge base and a scientific community were already present.

VI. 6 Other Institutional Factors: Public Perceptions and Overall Regulatory Stance

Public perceptions and attitudes can affect the economic and regulatory conditions under which an industry operates. Their impact can be felt through supply channels (attraction towards young graduates and scientists, perceived social utility of related research, perceived risk factors with respect to financial conditions), the economics of the production or on the demand for the products and techniques that this industry puts on the market.

Regulation tends to be specific to the field of application and the technology. Generally, there cannot be any unequivocal judgement over its role as its short-term effects may differ from its longer term ones. However, there is little doubt that the regulatory framework can have a major impact on the competitiveness of biotechnology in Europe.

Available research (Gaskell et al., 2000) seems to suggest that the European public discriminate quite clearly among the fields of application of biotechnology. Europeans are neutral about agricultural biotechnology and opposed to both genetically modified food and the cloning of animals. By contrast, perceptions of medical and environmental biotechnology are very positive.

In the EU, no new genetically modified organisms (GMOs) have been authorised to be placed on the market for the past 3 years (since October 1998). Though the EU has one of the strictest pre-market risk assessment systems in the form of Directive 90/220/EEC, revised this year (see Directive 2001/18/EC), Member States have refused to authorise GMOs. As a consequence, genetically modified food products have not been authorised under the sector-based legislation and the entry of new genetically modified plant varieties onto the common catalogues was not possible, despite positive assessments from the EU's scientific bodies.

The above situation and the uncertainty as to when authorisation of GMOs and derived products may restart, has led the biotechnology industry to focus most of its investments – especially concerning R&D and the basis for new start-ups and SMEs, – in non-plant related areas, where mechanisms for product approval are in place and functioning.

This situation is in stark contrast with the one in the US, where markets for all areas of biotechnology are in place.

VI.7. Adoption of Biotechnology Among Large European Firms

An important aspect of the development of European biotechnology is the considerable lag, compared to American (and to some extent to British) companies, in the adoption of new techniques, notably molecular biology, by many large established companies. The relevance of this factor is crucial. During the Seventies and the Eighties, given the low rate of creation of new firms, development of biotechnology in Europe rested on the activities of large companies. Moreover, in the absence of vibrant research activity by large firms, prospective start-ups lacked an essential source of survival and growth through the establishment of collaborative agreements. As claimed previously, in the absence of such competencies, large companies have turned to the American scientific and technological base to tap and absorb the new requisite competencies during their catching-up process. Thus, in Europe a vicious circle between the relative backwardness of large firms and low rate of formation of new start-ups has been created.

The rate of adoption of biotechnology by established companies varied widely across the world and across firms. Within Europe some large British and Swiss firms were able to adopt the technology rather quickly. Other firms, with smaller research functions, more local in scope or more orientated towards the exploitation of established research, found the transition more difficult. Thus, almost all of the established French, Italian, German and Japanese companies appear to have been slow to adopt the new technologies. To be sure, some German companies (e.g. Hoechst) were among the first to establish connections with the American research base in biotechnology (as early as 1982 Hoechst signed a multi-million, ten-year agreement with Massachusetts General Hospital). Nevertheless, the actual absorption of the new technologies progresses on average more slowly in Europe as compared to the USA. What factors have possibly contributed to this?

- The relative strength of the local science base again appears to be relevant. For example, Swiss firms have established strong connections with the US scientific system, suggesting that geographic proximity as such has played a much less important role in the diffusion of molecular biology.

- Second, it is possible that size and structure of the various national pharmaceutical industries determines diffusion. The existence of a strong national pharmaceutical industry, with some large internationalised companies, may have been a fundamental factor in the rapid adoption of biotechnology. In many European countries, the industry was highly fragmented into small companies engaged essentially in the marketing of licensed products and the development of minor products for the domestic markets. However, while size or global reach may have been a necessary condition, the delay of the largest German firms in adopting these techniques suggests that it was not sufficient. The largest German firms were undoubtedly among the most internationalised and largest companies in the world.

- Another important factor may be the degree of diversification. Most European firms have been large chemical firms, largely diversified into different technologies and markets, ranging from chemicals and pharmaceuticals to agricultural applications. US firms have been more specialised in narrowly defined areas. In other words, even if chemistry was the fundamental technological base for all firms, the European corporations have been essentially defined by their chemical culture, whereas US firms have been focused on more specific products and markets and, as a consequence, perhaps, more ready to explore new and alternative research. Moreover, in the early stage of development, biotechnology was often perceived as an opportunity for synergies. Over time, however, pharmaceutical, agro-food and chemical applications tended progressively to diverge and to progress along distinct paths.

- An additional factor is the stringency of the regulatory environment. There is now widespread recognition that the introduction of the 1962 Kefauver - Harris Amendments had a significant impact in inducing a deep transformation of the US pharmaceutical industry. Similarly, it has been suggested that the European country whose leading firms did move more rapidly to adopt the new techniques - Britain – also appears to have actively encouraged a "harsher" competitive environment. This induced British firms to pursue strategies aimed less at fragmentation of innovative efforts into

numerous minor products than to the concentration on few important products that could be diffused widely into the global market. By the 1970s, the ensuing transformations of British firms had led to their increasing expansion in world markets.

The diffusion of the new technologies has varied also across firms. Most of the firms that rapidly adopted the new techniques have been large multinational or global companies, with a strong research presence in the US and in international markets. These firms had developed early a "taste" for science and were able to integrate the new knowledge within the firms. This, in turn, was accomplished through organisational changes directed towards building and sustaining close links with the public research community through successful adoption academic-like forms of organisation of research. Other institutional factors have also been necessary, albeit not sufficient.

- First, it is possible that the Anglo-Saxon forms of corporate governance made it easier for firms to “hire and fire” personnel or cut non-performing assets; European companies seem to have hesitated giving long–term employment to biologists before biology was proven to be successful over the long run.
- Second, it is possible that the American advantage in the use of biotechnology within large corporations, as well as in new biotechnology companies, relates to the proximity and availability of first rate scientific research in universities and in the closer integration between industry and the academic community. One might also speculate that this has been the result of the strong scientific base of the American medical culture and of the adoption of strict scientific procedures in clinical trials. Through this mechanism, American companies might have to develop earlier and stronger relationships with the biomedical community and with molecular biologists in particular.

VII. Industrial Competitiveness in Biotechnology. An Interpretative Framework

The commercial development of European biotechnology is still lagging significantly behind the US. Despite encouraging signals of dynamism – especially in the small Northern European countries – and a wave of entry of new DBFs – especially in Germany – innovative activities remain far below the American levels. European companies rely partially on American research while, more worryingly, US firms do not seem to consider European research equally attractive. The new European DBFs, furthermore, are much smaller than their American counterparts, much less active in the global network of collaborative relations and in the markets for technology and are mainly present in platform technologies.

To some extent, the European performance deficit in biotechnology is the result of its late entry. Even in such a strongly science–based industry, innovative activities are characterised by various forms of increasing returns and early entrants acquire long-lasting leadership. This is a crucial point since it implies that catchingup is inherently difficult. Yet, catchingup is possible, but it requires determined efforts to generate the appropriate competencies, market signals and incentives.

Europe has had policies promoting biotechnology in place for several years and some important results have already been achieved. It is possible that recent developments suggest that the policies might have eventually begun to produce effects. Thus, it could be that European biotechnology might takeoff suddenly and sooner than expected.

However, the results of this chapter suggest that late entry is only part of the problem and that the take–off of European biotechnology is still hindered by a variety of structural factors. This leads to some general implications.

A systemic approach seems necessary

First, it is important to recognise that the lagging behind of European biotechnology has also systemic causes, rather than being simply the result of specific market or institutional failures. Successful innovative and commercial activities in this industry depend on a delicate blend of competencies and incentives and require the

integration and co-ordination of several differentiated agents, capabilities and functions. Focusing on some specific aspects of the puzzle is not likely to yield the desired outcomes but a co–ordinated strategy appears to be necessary.

Biotechnology involves the exploration of an enormous, imprecisely defined and rapidly changing space of unknown opportunities. This requires both decentralisation of efforts and a variety of approaches as well as an ability to integrate and co-ordinate them. Clearly, this is a challenge where no unique optimal solution may exist but in fact alternative strategies may be appropriate. For example, in the de-codification of the human genome the Human Genome Project was achieved by extreme decentralisation of tasks and approaches among a large number of institutions while Celera Genomics approached it through strong centralisation of resources and efforts. Both approaches have been partially successful and each benefited from the existence of the other.

US leadership in biotechnology derives from a unique blend of capabilities and institutional arrangements. These include a strong scientific, technological and industrial base; mechanisms that favour communication and transfer of knowledge between academia and industry; a financial system that promotes the starting up of new, risky ventures; strong intellectual property protection; and a favourable climate in terms of public perception and regulation that does not restrict genetic experimentation. European biotechnology should not blindly follow the US model. Some aspects of the development of biotechnology in the US cause concern, such the government's reluctance to labelling genetically modified food. Europe has different institutional settings, histories, traditions and competencies. On them, it might be possible to develop a different, but equally successful road to competitiveness. Yet, some basic lessons can be learned from the US case and serve as a source of inspiration for European policy.

Strengthening basic scientific research and building a European research system

Second, it is clear that the availability of leading–edge scientific capabilities is one of the fundamental preconditions for successful development of biotechnology. Without a strong and diversified scientific research base, no technological take–off is possible. Nor can the European industry simply tap American scientific knowledge. At the very least, acquiring knowledge implies the ability to produce knowledge.

Access to the scientific community requires direct and active participation in the networks of scientists. The dynamics (and the economics and sociology) of scientific research is characterized by strong path–dependence and first–mover advantages.

Europe is lagging behind in this respect too. While centres of excellence exist, Europe does not attract comparable levels of foreign resources, and European biotechnology in the large companies relies significantly on American research. Increased funding is certainly necessary, but it is only a part of the solution. An important finding is that the European research system is weak in terms of organisational diversity, it is specialised in rather narrow areas and is insufficiently interconnected across different research areas, types of organisations and stages of the research process. Thus, higher degrees of pluralism in funding sources, lower dependence on closed national systems, and higher integration of research with teaching, clinical research, and medical practice, should become priorities of a European research policy in this area, allowing more efficient exploitation of available resources.

Finally, the European research system appears to be still too rigid, bureaucratic and segregated. While important advances have been achieved in recent years, further progress needs to be made in this respect.

Integration of research and industry

The European research system may still be insufficiently integrated with industrial research. This is most likely a reflection of several factors, possibly that that European industry does not fully exploit the potential offered by European science, as well as institutional and organizational obstacles, which could be more directly relevant here, such as low mobility of researchers and bureaucratic obstacles to collaboration.

Policies in this area have focused on introducing incentives for academic researchers to become involved in industrial research and building bridges between university and industry as well as developing financial and infrastructure facilities like venture capital, science parks, etc. In practice, these measures, important as they are, appear to reflect an understanding of the innovation process as based on the transfer of knowledge. However, because innovation is primarily an interactive process, more

emphasis is necessary instead on how to integrate more directly different agents and fragments of knowledge. To a considerable extent these difficulties derive from some long–standing characteristics of the European academic systems, particularly the integration of research and teaching and the structure of career paths in universities. In fact, universities often lack the necessary organisational capabilities to sustain intense interchange with industry. Again, considerable progress has been achieved in this area in recent years, but science and industry continue to encounter difficulties in their interactions. Thus, measures are necessary to favour the development of more direct linkages between universities and industry, through the integration of research and teaching and the development of markets for technology. These observations apply both to the creation of university spin–offs and to the relationships between universities and large corporations.

Sustaining the creation and development of dedicated biotechnology firms

The creation and development of a strong DBFs sector is a crucial priority. DBFs constitute an important organizational device allowing the exploration of the new opportunities. In Europe, this sector remains underdeveloped and is concentrated in few areas. Moreover, the European DBFs are hardly comparable with the American biotechnology firms. Many are far too small, possibly because they are too specialized in specific niches.

Once again, interventions aiming at promoting the birth of DBFs have been at the center of European biotechnology policies for more than a decade. Still, the emphasis is on strengthening of industry–university relations, the creation of the "entrepreneurial university", the development of venture capital and, to a lesser extent, on intellectual property rights. Although these are important, the problem of an inadequate supply of cutting–edge scientific research may not have been sufficiently addressed. Moreover, venture capital may not necessarily be always a solution considering that it might make the growth of DBFs hostage to stock market fluctuations. While venture capital remains an essential instrument for supporting the process of formation and early growth of the new firms, it ought to be understood as one instrument within a wider array of sources of funding (including public research funding) and managerial capabilities.

Finally, it is important to recognize that DBFs exist in a relationship of strong complementarity with the large corporations. The latter are fundamental sources of demand for products and services of DBFs and provide crucial integration capabilities for transforming different fragments of knowledge into products. Large firms constitute reservoirs of technological and managerial competence. In general, given the relationships between the creation and development of DBFs and the research/absorptive capabilities of the large companies, policies for biotechnology should be much more strongly linked to interventions aiming at raising the competitiveness of "downstream" industries, mainly pharmaceutical (see also Gambardella, Orsenigo, Pammolli, 2001).

Intellectual property rights

Intellectual property rights constitute one of the most delicate and important issues for biotechnology. While problems of clarification and harmonization of the legislation on these matters remain, the emerging European approach is on the whole balanced and flexible enough to accommodate diverging requirements. The creation of the Community Patent and the implementation of the Biotechnology Patent Directive will provide a useful addition in this area, by making EU-wide protection easier.

It is useful to recall that rigorous regulation is not always an impediment to scientific and technological progress. On the contrary, it can be beneficial, both by providing reassurance to society and by forcing industry to adopt higher quality standards which, if combined with more streamlined administrative procedures, can lead it to become more competitive and efficient. In this respect, the example of the regulatory reforms concerning product approval in the pharmaceutical industry might be instructive (see Thomas, 1994; Gambardella, Orsenigo, Pammolli, 2001). However, unnecessarily onerous regulation can severely undermine competitiveness by placing unnecessary constraints on innovation that may encourage individuals and companies to relocate to other markets.

References

Archibugi D., Pianta M., 1992, *The Technological Specialisation of Advanced Countries. A Report to the EEC on International Science and Technological Activities,* Kluwer; Heidelberg.

Arora A., Fosfuri A., Gambardella, A., 2001, *Markets for Technology*, MIT Press, forthcoming.

Arora A., Gambardella A., 1994, The Changing Technology of Technical Change: General and Abstract Knowledge and the Division of Innovative Labor, *Research Policy*, 23, 5, pp. 523-532.

Arora A., Gambardella A., Pammolli F., Riccaboni M, 2001, *The Nature and the Extent of the Market for Technology in Biopharmaceuticals*, NBER Summer Institute, Cambridge, Ma.

Arrow K.J., 1983, Innovation in Large and Small Firms, in Ronen J., ed., *Entrepreneurship*, Lexington Books, Lexington, Ma.

Arundel A, Hocke M, Tait J., 2000, How Important is Genetic Engineering to European Seed Firms?, *Nature Biotechnology 18:578.*

Audretsch D. B., Stephan P., 1996, Company-Scientist Locational Linkages: The Case of Biotechnology, *American Economic Review*, vol. 86, pp. 641-652.

Audretsch D., 1989, Agglomeration and the Location of Innovative Activity, *Oxford Review of Economic Policy*, Vol.14, No. 2.

Audretsch D., M. Feldman, 1996, R&D Spillovers and the Geography of Innovation and production, *American Economic Review*, 86, 3, 630-40.

Audretsch D.B., 2001, The Role of Small Firms in U.S. Biotechnology Clusters, *Small Business Economics*, vol. 17, pp. 3-15.

Barnett R., et al., 1998, *Biotechnology in Germany. Report of an ITS Expert Mission*, British Embassy, Bonn.

Bauer M., Gaskell G., Durant J., 2001, *Biotechnology in the Public Eye*, Cambridge: Cambridge University Press.

Ben-David J., 1977, *Centers of Learning: Britain, France, Germany and the United States*, New York, McGraw-Hill.

BioWorld, 2001, *Biotechnology State of the Industry Report.*

Braun D., 1994, *Structure and Dynamics of Health research and Public Funding: An International Institutional Comparison*, Kluwer Academic Publishers, Amsterdam, The Netherlands.

Breschi S., Lissoni F., Orsenigo L., 2001, *Success and Failure in the Development of Biotechnology Clusters: The Case of Lombardy*, Cespri, Bocconi University, Milan, mimeo.

BVK, 1994-2000, *Venture Capital in Europe*, BVK Nachrichten Special Report.

Casper S., Kettler H., 2000, The Road to Sustainability in the UK and German Biotechnology Industries, ESSY project, mimeo.

Clark B.R., 1995, *Places of Inquiry. Research and Advanced Education in Modern Universities*, Berkeley, University of California Press.

Cockburn I., Henderson R., 1996, Public-Private Interaction in Pharmaceutical Research, *Proceedings of the National Academy of Sciences*, 93/23, November, pp.12725-12730.

Cohen W., Florida R. and Goe R., 1994, University-Industry Research Centers in the United States, Technical Report, Center for Economic Development, Carnegie-Mellon University.

Cooke P., 2001, Biotechnology Clusters in the U. K.: Lessons from Localisation in the Commercialisation of Science, *Small Business Economics*, vol. 17, pp. 43-59.

David P., 2000, A tragedy of the public knowledge "commons"? Global science, intellectual property and the digital technology boomerang, *Stanford Institute for Economic Policy Research*, SIEPR Discussion Paper No. 00-02, October 2000.

Deutsche Bank Research, 1999, *German Biotech: New Stars in the Universe*, Deutsche Bank Research German Equities Biotechnology Group, April 27.

Dohse D., 2000, Technology Policy and the Regions. The case of the BioRegio Contest, *Research Policy*, vol. 29, pp. 1111-1133.

DTI, 1999, *Biotechnology Clusters*, Department of Trade and Commerce, London, UK.

DTI, 2001, *Genome Valley Report. The Economic Potential and Strategic Importance of Biotechnology in the UK*, Department of Trade and Industry, London.

Echeverri-Carroll E.L., Brennan W., 1999, *Are Innovation Networks Bounded by Proximity?*, in Manfred Fischer, Luis Suarez-Villa, and Michael Steiner eds., *Innovation, Networks and Localities*, Springer Verlag, Berlin.

Eisenberg R., 1996, Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research, *Virginia Law Review*, vol. 82, pp. 1663-1727.

Ernst & Young, 1993-2001, *Biotech Biotechnology Reports*, Ernst&Young, London.

European Private Equity & Venture Capital Association, 2000, *EVCA Yearbook*, European Private Equity & Venture Capital Association, Zaventem, Belgium.

Faulkner J., Senker J., 1995, *Knowledge Frontiers: Public Sector Research and Industrial Innovation in Biotechnology, Engineering, Ceramics and Parallel Computing*, Oxford: Clarendon Press.

Financial Times, 2000, 'One Continent, Two Experiences', Life Sciences: Biotechnology, October 13, 2000.

Fuchs G., 2001, Introduction. Biotechnology in Comparative Perspective: Regional Concentration and Industrial Dynamics, *Small Business Economics*, vol. 17, pp. 1-2.

Galambos, L., Sturchio, J., 1998, Pharmaceutical Firms and the Transition to Biotechnology: A Study in Strategic Innovation, *Business History Review*, LXXII, pp. 250-278.

Gambardella A., 1995, *Science and Innovation in the US Pharmaceutical Industry*, Cambridge, Cambridge University Press.

Gambardella A., Orsenigo L., Pammolli F., 2001, *Industrial Competitiveness in Pharmaceuticals. A European Perspective*, DG Enterprise, European Commission, Working Paper n. 1, Brussels (http://dg3.eudra.org/pharmacos/comdoc_doc.htm).

Gaskell G. et al., 2000, Biotechnology and the European Public, *Nature Biotechnology*, Vol. 18, September 2000, pp. 935-936.

Gaskell G., Bauer M., Durant J. eds., 2001, *The Years of Controversy: Biotechnology 1996-2000*, London: Science Museum.

Gieseke S., 2000, The Contrasting Roles of Government In The Development of Biotechnology Industry in the US and Germany, *Research Policy*, n. 29, pp. 205-223.

Gittelman M., 2000, *Mapping National Knowledge Networks: Scientists, Firms and Institutions in Biotechnology in the United States and France*, Ph.D. Dissertation, New York University.

Gompers P., Lerner J., 1999, *The Venture Capital Cycle*, MIT Press, Cambridge, Ma.

Grabowski H., Vernon J., 1994, Innovation and Structural Change in Pharmaceuticals and Biotechnology, *Industrial and Corporate Change*, vol.3, n.2.

Griliches Z., 1990, Patent Statistics as Economic Indicators: A Survey, *Journal of Economic Literature*, vol. 28, pp. 1661-1707.

Hagedoorn J., Schakenraad J., 1990, Strategic Partnering and Technological Cooperation, *in New Explorations in the Economics of Technical Change*, Printer, London.

Heller M.A. and R.S. Eisenberg, 1998, Can Patents Deter Innovation? The Anticommons in Biomedical Research, *Science*, 280, 698-701.

Henderson R., Cockburn I., 1996, Scale, Scope and Spillovers: The Determinants of Research Productivity in Drug Discovery, *Rand Journal of Economics*, Spring, 27(1), pp. 32-59.

Henderson R., Orsenigo L. and Pisano G., 1999, The Pharmaceutical Industry and the Revolution in Molecular Biology, pp. 267-311 in *Sources of Industrial Leadership*, Mowery D., Nelson R.R., eds. New York: Cambridge University Press.

Horton B., 1999, Medicon Valley: A Bridge to Collaboration, *Nature*, 395, pp. 412-413

Jaffe A., Trajtenberg M., Henderson R., 1993, "Geographic Localisation of Knowledge Spillovers as Evidenced by Patent Citations", *Quarterly Journal of Economics*, n. 108, pp. 577-598.

Jorgenson D. W., Griliches Z., 1967, The Explanation of Productivity Change: *Review of Economic Studies*, Vol. 34, n. 3, July, pp. 249-283.

Kenney, 1986, *The University-Industry Complex*, Cornell University Press, Ithaca, 1986.

Krauss G., Stahlecker T., 2001, New Biotechnology Firms in Germany: Heidelberg and the Bio Region Rhine-Neckar Triangle, *Small Business Economics*, vol. 17, pp. 143-153.

Kuusi H., 2001, 'Finland: A European Leader in Biotechnology', *Kemia-Kemi*, 28(6), 432-437.

Lacetera N., Orsenigo L., 2001, *Political Regimes, Technological Regimes and Innovation in the Evolution of the Pharmaceutical Industry in the USA and in Europe*, Paper prepared for the "Conference on Evolutionary Economics", Johns Hopkins University, Baltimore, March 30-31, 2001.

Lemarié S., Mangematin V., Torre A., 2001, Is the Creation and Development of Biotech Biotechnology SMEs Localised? Conclusions Drawn from the French Case, *Small Business Economics*, vol. 17, pp. 61-76.

Lerner J., Merges R., 1998, The Control of Technology Alliances: An Empirical Analysis of the Biotechnology Industry, Journal of Industrial Economics, vol.46, pp. 125-156.

Lyons D., 1995, Agglomeration Economies Among High Technology Firms in Advanced Production Areas: The Case of Denver/Boulder, *Regional Studies*, 29, 3, pp. 265-78.

March J., 1991, Exploration and Exploitation in Organizational Learning, *Organization Science*, vol. 1, n. 2, pp. 71-87.

Mariani M., 2001, The Location of R&D and the Networks of Inventors in the Chemical and Biopharmaceutical Sectors, EPRIS Project, working paper.

McMillan G.S., Narin F., Deeds L., 2000, An Analysis of the Critical Role of Public Science in Innovation: The Case of Biotechnology, *Research Policy*, vol. 29, pp. 1-8.

Merges R., Nelson R.R., 1994, On Limiting or Encouraging rivalry in Technical Progress: The Effect of Patent Scope Decisions, *Journal of Economic Behavior and Organization*, Vol. 25, 1-24.

Morange M., 1998, *A History of Molecular Biology*, Cambridge, Ma, Harvard University Press.

Mowery D., 1997, *Market Failure or Market Magic? Structural Change in the U.S. National Innovation System*, OECD meeting on "Best Practices in Technology and Innovation Policy", Paris.

Mowery D., Nelson R.R., Sampat B.N., Ziedonis A.A., 2001, The Growth of Patenting and Licensing by U.S. Universities: An Assessment of the Effects of the Bayh-Dole Act of 1980, *Research Policy*, 30 99-119.

Mytelka L. K., Pellegrin J., 2001, *Can SME Survive? Static vs Dynamic Externalities in the French Biotechnology Industry*, Paper to be presented at the DRUID Summer Conference, Aalborg June 12-15,2001.

Nilsson A., 2001, Biotechnology Firms in Sweden, *Small Business Economics*, vol. 17, pp. 93-103.

OECD, 2001, *Biotechnology Statistics in OECD Member Countries: Compendium of Existing National statistics*, Second ad Hoc meeting on biotechnology statistics, OECD, Paris.

Orsenigo L., 1989, *The Emergence of Biotechnology*, St. Martin Press, London.

Orsenigo L., F. Pammolli, M. Riccaboni, 2001, Technological Change and Network Dynamics, *Research Policy*, 30 pp. 485-508.

Paci R. and Usai S., 1998, Technological Enclaves and Industrial Districts: An Analysis of the Regional Distribution of Innovative Activity in Europe, *Regional Studies*, vol. 34.2 pp.97-114.

Pammolli F., Riccaboni M., 2001, Geographical Clusters in the Biotechnology Industry, *EPRIS working paper, University of Siena*.

Pavitt K., 1998, The Inevitable Limits of EU R&D funding, *Research Policy*, vol. 27, pp. 559-568.

Peterson J., Sharp M., 1998, *Technology Policy in the European Union*. Basingstoke, MacMillan.

Powell W. W., Doput K. W., Smith-Doerr L., 1996, Interorganizational Collaboration and the Locus of Innovation: Networks of Learning in Biotechnology, *Administrative Science Quarterly*, 41, pp. 116-145.

Prevezer M., 2001, Ingredients in the Early Development of the U.S. Biotechnology Industry, *Small Business Economics*, vol. 17, pp. 17-29.

Prevezer, 1997, The Dynamics of Industrial Clustering in Biotechnology, *Small Business Economic*s, n.9.

Rai A.K., 1999, Regulating Scientific Research: Intellectual Property Rights and the Norms of Science, *Northwestern University Law Review*, Vol. 94, No.1.

Schienstock G., Tukki P., The Fourth Pillar? An Assessment of the Situation of the Finnish Biotechnology, *Small Business Economics*, vol. 17, pp.105-122.

Scriabine A., 1999, The Role of Biotechnology in Drug Development, in Landau R., Achilladelis B., Scriabine A. eds., *Pharmaceutical Innovation*, Chemical Heritage Foundation, Philadephia.

Senker J., ed, 1998, *Biotechnology and Competitive Advantage*, Edward Elgar.

Shapiro C., 2001, *Navigating the Patent Thicket: Cross-Licenses, Patent Pools, and Standard-Setting*, in Jaffe A., Lerner J., and Stern S., eds., *Innovation Policy and the Economy*, Vol. 1, MIT Press.

Sharp M., 1985, *The New Biotechnology: European Governments in search of A Strategy*, Brighton, Sussex European Papers, University of Sussex.

Soete L., 1989, The Impact of Technological Innovation on International Trade Patterns: The Evidence Reconsidered, *Research Policy*, 16.

Soskice D., 1997, German Technology Policy, Innovation and National Institutional Frameworks, *Industry and Innovation*, 4, pp. 75-96.

Stokes D.E., 1997, Pasteur's Quadrant: Basic Science and Technological Innovation, *The Brookings Institution*, Washington DC, USA.

Swann P., M. Prevezer and D. Stout eds., 1998, *The Dynamics of Industrial Clustering*, Oxford: Oxford University Press.

Swann P., Prevezer M., 1996, A Comparison of the Dynamics of Industrial Clustering in Computing and Biotechnology, *Research Policy*, vol. 25, pp. 1139-1157.

Thomas L. G., 1994, Implicit Industrial Policy: The Triumph of Britain and the Failure of France in Global Pharmaceuticals, *Industrial and Corporate Change*, Vol.3, n.2.

Trajtenberg M., 1990, A Penny for Your Quotes: Patent Citations and the Value of Innovations, *Rand Journal of Economics vol. 21.1 pp.172-187.*

UK Department of Trade and Industry, 1999, *Genome Valley: The Economic Potential and Strategic Importance of Biotechnology in the UK*, DTI, London.

US Council on Competitiveness, 2001, *U.S. Competitiveness 2001: Strengths, Vulnerabilities and Long-Term Priorities*, Council on Competitiveness, Washington DC.

Van Beuzekom B., 2001, *Biotechnology Statistics in OECD Member Countries: Compendium of Existing National Statistics*, Ad Hoc Meeting on Biotechnology Statistics, OECD, Paris, 3-4 May.

Vinnova, 2000, *The Swedish Biotechnology Innovation System*, by A. Backlund, H. Häggblad, N. Markusson, L. Norgren, and A. Sandström.

Ward M., Dranove D., 1995, The Vertical Chain of R&D in the Pharmaceutical Industry, *Economic Inquiry*, Vol. 33, January 1995, p 1-18.

Zeller C., 2001, Clustering Biotech: A Recipe for Success? Spatial Patterns of Growth of Biotechnology in Munich, Rhineland and Hamburg, *Small Business Economics*, vol. 17, pp. 123-141.

Zucker L., Darby M., Armstrong J., 1998, Geographically Localized Knowledge: Spillovers or Markets?, *Economic Inquiry*, vol. 36, pp. 65-86.

Zucker L., Darby M., Brewer M., 1997, Intellectual Human Capital and the Birth of U.S. Biotechnology Enterprises, *American Economic Review*, June 1997, v. 87, n. 3.

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