The Dynamics of Industrial Clustering in Biotechnology

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ABSTRACT. This paper is a study of the process by which industrial clusters form. It identifies the forces of attraction to new companies to a cluster in biotechnology in the U.S. as it grows. It uses a model of entry of new firms into the industry to measure the degree of attraction to those new firms of the presence of an existing cluster at a particular location.[1] The paper finds that the main agent of attraction to new firms to enter the biotechnology industry is the presence of a strong science base at that location. This provides a greater magnet than the strength of any particular sector of the industry. In terms of attraction between different sectors within the industry, the paper finds that there is positive attraction and feedback between a group of sectors in the biotechnology industry – namely the therapeutics, diagnostics and the equipment/research tools sector. However in other sectors of the industry – chemicals, food and to some extent agriculture – there is much less attraction and interaction between them. This implies that clusters of firms tend to develop only in particular sectors of the industry and positive feedback mechanisms do not extend to other parts of the industry.

Introduction

What are industrial clusters? Clusters as defined here are groups of firms within one industry based in one geographical area. This is different from the groups of firms in different industries based in one area, looked at by Porter (1990). Geographical industrial concentration – the concentration of firms in one industry at a particular location – has been and continues to be high (Krugman, 1991). Krugman gives examples from a monograph in the 1900 U.S. census entitled "The Localization of Industries" which includes:

> collars and cuffs localized in Troy, New York; leather gloves localized in two New York towns of Gloversville (sic) and Johnstown; shoes in several cities in the north-eastern part of Massachusetts; silk goods in Patterson, New Jersey; jewelry in and around Providence, Rhode Island; and agricultural machinery in Chicago. (Krugman, *op. cit.*, p. 61)

What Krugman stresses is that whereas much attention has been focused recently on high technology clusters, concentration and localization of industries has been typical of many not particularly highly technological industries. They were founded through particular circumstances and these initial small events had large and long-lasting effects through the cumulative process of growth of the industry drawn by a particular feature of that industry. This may be a new process or specialized inputs, or a pool of labour with skills related to that process, aside from the more recent emphasis on technological or knowledge spillovers from high technology sectors of industry.

The phenomeon of such concentration and localization of industries, which we now call clusters is not therefore a recent one. Clustering includes both the phenomeon of a critical mass of one sector of an industry developing in one place such that other firms in that sector are attracted to that location, and the force of attraction that a core sector of an industry has on auxiliary sectors of that same industry to that location. Thus one can distinguish between the production of cars being centred in Detroit and the production of tyres and other components of cars being drawn to Detroit as the location of the core activities of the industry.

However, our focus here is on a high technology industry, the biotechnology industry and in looking at the factors that have been specific to that industry in its development at particular locations and how those factors compare with

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those that affected the formation of previous clusters such as that in computing in Silicon Valley. There has been interest in the initial ingredients of a location that started off the process of building the new semiconductor industry in a predominantly agricultural area (Saxenian, 1985). Silicon Valley was started by a mixture of serendipitous events combined with some watershed changes: World War II and the Korean War gave military stimulus to the nascent electronics industry in California (Swann, 1993); Frederick Terman's tuberculosis made the California climate preferable to that on the East coast and so a more congenial place to settle; William Shockley's hometown was Palo Alto (Larsen and Rogers, 1984). Underlying these events there were also more systematic influences on the location decisions of pioneering firms in the industry: the policy to build up the electrical engineering department at Stanford by Vice President Frederick Terman and to cultivate the application of its work to industry; the creation of the Stanford Research Institute and Stanford Industrial Park to stimulate research and encourage start-ups and established companies to settle in the area. These all contributed to the initial momentum that founded Silicon Valley as the centre of the new electronics industry. Swann (1993) looks in particular at this growth of the computing industry from its initial roots in the new semiconductor technology.

Some of the reasons why the biotechnology industry took root in California, around San Francisco initially, are owing to the heritage of the computing industry and Silicon Valley. Particularly important were the presence there of venture capital with expertise in starting and growing high technology companies, the communications networks and high job mobility that meant that new ideas spread rapidly in the area, the experience of Stanford and its Research Institute and Industrial Park which could be used as a model for the biotechnology industry. However, the focus of the biotechnology industry has been different from that of computing. Whereas computing links were inter-industrial with important communication flowing between engineers within the industry, in biotechnology the important links to foster and sustain have been between the science base and companies. (Zucker, Darby and Brewer, 1994).

The science was the external stimulus to the founding of the industry, in some ways parallel to the stimulus that the various wars and military needs had on the semiconductor industry. The industry originated from a series of scientific discoveries, starting in 1953 with Watson and Crick's discovery of the double helix structure of DNA, the discovery of interferon in 1957, the classification and identification of various important enzymes and plasmids, the development of immobilisation techniques. The two most prominent scientific events occurred in 1973, with the development of the recombinant DNA technique by Cohen and Boyer at Stanford, and in 1975 with Kohler and Milstein's production of monoclonal antibodies in Cambridge, U.K. The earliest companies in the 1970s, such as Cetus (CA), Genentech (CA), Biogen (MA), Hybritech (CA), were based near important research centres on the west and east coasts and were started by prominent academic scientists from those universities. The area around San Francisco became the focus for the early industry in the main for its collection of important research bases at University of California at San Francisco (UCSF), Stanford, City of Hope and CalTech.

The closeness of commercial biotechnologies to the science and therefore the importance of the science base have ensured that the science base has remained a critical source of innovation. Whereas with computing, interactions within the commercial sector between different parts of the industry were important in fostering the dynamic whereby new firms entered the industry, in biotechnology the early companies came out of the science base.

Another important feature to biotechnology has been the stock market's role in raising new money for start-up companies making initial public offerings. Although not exclusive to California, centres of expertise in how to promote new companies by the venture capitalists there started with the spectacularly successful flotation of Genentech in 1980 which led the way for many other companies to raise capital during the various windows of opportunity during the 1980s and also to receive publicity and put themselves on the map. The stock market has operated in a more influential way than in the case of nascent computing companies.

The role of the large companies in the emerging industry has been different for biotechnology as well. Whereas in computing the presence of IBM and Fairchild in California opened up many opportunities, in biotechnology pharmaceutical and chemical companies have been involved in the creation of the new industry without having to have their own research facilities in California or Massachusetts. Thus Eli Lilly sponsored the insulin conference in 1976 designed to stimulate research into alternative methods of producing the seemingly scarce protein, backed the creation of Genentech and helped finance research into recombinant methods which benefitted the large company. Collaboration occurred through alliances and networks over large distances between the research community and the small and large company. In the chemicals area Monsanto occupied a similar leading role in the early 1980s, and other leading chemical and drug companies have followed in their efforts to become involved in the new technology and absorb the new techniques into their companies. The biotechnology community has therefore been more diffuse, even in its relatively early stages, with clear clusters of small firms developing near centres of research on the west and east coasts, but without the equivalent interaction between companies of different types that has been so important in the computing industry.

Another difference which has shaped the two industries has been the type of markets that the new technologies have created. The computing industry has developed in terms of specialization within it along technological lines into sectors with different technologies; markets for applications of the end product are spread diffusely across many other industries and home users. Biotechnology has segmented into sectors according to its application to a particular industry; thus the new therapeutics and diagnostics firms address their applications to the pharmaceuticals industry; the agricultural and chemical firms see their technologies as applying to the agro-chemical market; new enzymes or food products address the food industry. This division into existing sectors of industry is not completely clear-cut. Some new diagnostic firms address not just the health care industry but water and food testing services; the research tools and equipment sectors supply both industry and research establishments; and environmental applications create a largely new sector without an existing market although with obvious potential for one. Nevertheless this structure broadly applies, whereby biotechnology start-ups are dependent to a substantial extent on existing companies in their own sector for their market and for help in jointly developing technologies. This has contributed to more rapid development of sectors where those links have been strong and to a slower diffusion of techniques in sectors where links have been weaker.

We make use of these observations in setting up a model to gauge the relative strengths of the main forces of attraction to particular locations for new firms into the biotechnology industry. This model is based on that of Swann (1993) which applies to the computing industry. There is a variety of types of attraction. Sophisticated buyers attract suppliers of products that the buyer needs. This is attraction via demand for new products and is likely to have been a significant force in the creation of new equipment and research tools companies. On the supply side, firms are created close to the origin of a new technology. Many of the new therapeutic and diagnostic technologies have stemmed either directly from the science base, through an academic wishing to commercialize research, or with close contact with academic researchers who have contributed to a company's technology and serve as scientific advisers to the company. This contact requires proximity to the research centre from which the technology originated. Much of the knowledge needed to develop the technologies requires continuing contact with academic researchers. In these circumstances companies drawing on such knowledge settle close by in order to be able to absorb these spillovers from research.

This study finds a complex mixture of types of attraction: of the need to have close contact with the science base from which much of the new technology has and continues to be developed; of new companies providing specialist research equipment and tools both to strongly growing sectors in the industry and to research laboratories with expanding research needs. There is also encouragement to entry of new firms by the presence of clusters in certain sectors closely related to each other: therapeutic firms attract diagnostics and equipment firms where new types of testing and genetic probes and drug delivery systems provide an adjunct to new therapeutics that are being commercialised. The paper finds relatively little impetus for new firms to enter into another group of sectors: food, chemicals, waste and energy. This may be due to the relative underdevelopment of the new ‘environmental’ technologies in the waste and biomass energy areas; in the case of the food and chemicals industries it may be due to large incumbent companies absorbing most of the research spillovers.

The benefits and costs of clusters

Why do firms locate in clusters? We may distinguish between benefits on both the supply side, in making the supply of particular products easier, and on the demand side, through access to customer specification and to markets.

Supply side benefits

Krugman (1991) and Marshall (1920) before him highlight three factors that attract firms to a particular location: specialized labour, specialized intermediate inputs, and spillovers of knowledge. The third is thought to be particularly important for high technology industries. **Specialized labour** has several facets to it. Labour is specialized in particular technical or scientific skills. For biotechnology this means scientific expertise in a collection of disciplines: microbiology, biochemical engineering, biochemistry, genetics; expertise necessary to start companies: venture capital, management skills, sales and marketing skills. Specialized labour for biotechnology exists therefore in the science base, where leading edge science is developed, and in companies. Many of the companies interested in absorbing the new technologies are large pharmaceutical, agrochemical or food companies, and expertise exists in the process of drug development, knowledge of regulatory issues, and of marketing and distribution networks. Management expertise is found both in large companies, used to handling the panoply of issues in bringing a new compound to the marketplace, and in small companies, often more innovative in perceiving new niches and market opportunities and more adaptable to the requirements of new scientific development.

Labour is also specialized within a cluster in being part of a network and possessing knowledge about people and their work. It will have specialized knowledge about the network of people in that technical or business community, which will be valuable to incoming firms. Employees’ networks are a chief mechanism of information exchange. Specialized labour within a cluster may also be an advantage in particular job markets. A noticeable feature of the Silicon Valley job market has been very high turnover of jobs, as a way of employees advancing their careers (Larsen and Rogers, 1984). This has both advantages and disadvantages to employers. Training is more costly but employers benefit from access to a ready supply of new specialized labour, from other firms or from the research centres and universities.

Specialized inputs means any inputs of equipment, research tools, related technologies that need to be tailored and developed for a particular new market. Locating near a pool of those inputs may provide some advantages to a new firm. For early stage biotechnology, reagents as chemical precursors, biosensors, separation and purification equipment, testing devices, plus a range of bioprocessing equipment for scale-up and manufacture, constitute specialized inputs for companies commercialising research. Have such companies been attracted by the presence of equipment firms?

Knowledge spillovers are harder to trace. Some evidence for their existence and that they are tied to particular locations is provided by the work of Jaffe *et al.* (1993). They find a linkage between the place of a patent and citation of that patent. This suggests that knowledge available in patents is more frequently used by firms within the same locality. They find that knowledge spillovers are localised, that the effects are large and that they fade only slowly with time. For clusters to be the result of knowledge spillovers there must be information exchange that is easier to accomplish within the same location. This exchange may be of a technical nature, of tacit information which is not encoded, or of a business or social nature resulting from local networks of people. There is anecdotal evidence that such local networks are important. However we are also aware of the way in which networks, formal and informal, transcend local boundaries and are a method of absorbing information spillovers without having to be situated in the same location. Alliances and collaboration are an example of this and there have been many different types of alliance and collaboration in this industry, between research centres and companies and between companies of different types. The tendency and ease of forming such alliances may act as either a centripetal force towards greater clustering through the greater facility of close communication, or as a centrifugal force, collaboration being a substitute to physical proximity as a method of forming ties. Further work needs to be done on the location of alliances to see whether they occur more between firms close to each other, or cover long distances.

Demand side benefits

The benefits or causes of clusters discussed so far have been supply-side benefits – supply of specialized labour, specialized inputs and knowledge spillovers. We may also think of demand side benefits that come from locating in a cluster. These may be divided into benefits to the industry from locating near users (von Hippel, 1988) and benefits from sectoral (inter-industry) demand. In the case of biotechnology, location near end-users would refer to close contact with hospitals for therapeutic or diagnostic firms for instance. Such contact may have acted as an attracting factor to some therapeutics and diagnostics firms, in order to be able to test and develop new drugs and kits in consort with a typical end-user. Or it might refer to the benefits to equipment and research tool makers or diagnostic companies of being situated close to a ready market in other sectors of the industry and in research establishments.

Other demand side benefits include those along the lines of Hotelling, where firms within one sector gain market share from locating close to other established firms. There are also agglomeration economies which are due to lower search costs for users from locating in a cluster. Clusters of firms allow customers to assess and compare firms more easily. Information externalities also exist on the demand side, where entrants can assess the market more easily from perceiving successful firms in a particular cluster.

Costs of clusters

Costs on the supply side include congestion costs and competition in input markets which drive up the prices of labour and land. Indeed reports of Silicon Valley stress soaring real estate prices, high wages, shortages of housing, length of commuting times, all of which may deter companies from settling there (Larsen and Rogers, 1984). On the demand side, there might also be saturation costs and costs from competition in output markets. Competition between firms within a sector in producing the same product will reduce per firm profits, sales etc. Or, as is often the case in some biotechnology markets, if there is a race to produce the same product between firms, more competitors decreases the likelihood of any one firm winning the race and securing monopoly (if patented) profits. If success in a race depends on access to scarce research resources at a particular location, then competition may be more acute in particular clusters and congestion may occur.

Whereas these congestion effects are thought to be quite strong in some of the older clusters, it is less likely that in biotechnology, being relatively young, there will have been saturation in clusters. However, as several of the biotechnology clusters overlap with or are built close to previous clusters in earlier technologies such as computing in California, saturation from those earlier technologies may well affect the location decisions of new biotechnology firms.

Our model (described below) distinguishes between attraction of a new firm to research centres and attraction to particular sectors within the industry. In so far as the type of knowledge that exists in research centres may be distinguished from that within companies, research centres may be thought to possess more generalised and basic knowledge which is more associated with particular people within the science base. By contrast knowledge within companies may be more closely tied to the company itself, and relate to networks, strategies or products associated with that company rather than with particular people in the company. If such a distinction is true, it may be fair to say that attraction towards a cluster of research centres is evidence of attraction towards specialized labour whereas attraction towards particular sectors of the industry may be an indication of attraction towards the specialized inputs that that industrial structure offers.

What have been the strongest attractors to new firms in biotechnology in the formation of clusters? In this science-based industry has it been more important to have a science base which is strong in the relevant sciences to attract entry of new firms? This might be entry of subsidiaries of existing firms or the creation of new firms near the science base. Or have particular sectors of the industry, the new therapeutics for instance, exercised a pull to the creation of firms into that sector or auxiliary to that sector? Can we distinguish a core activity to biotechnology that attracts the creation of new companies into its periphery? Using this model we gauge the extent to which a strong cluster attracts new entrants and what part of that existing cluster is exerting the attraction.

Preliminary view of clustering

The phenomenon of clustering is illustrated by looking at the map of biotechnology companies in the United States for 1993 (Figure 1). There are six main groupings of firms: in the San Francisco Bay Area, the New York Tri-State region and the Boston area which contain about 45% of public companies; there are also significant populations of companies in San Diego, Los Angeles, around Washington DC and Maryland and in the Philadelphia/Southern New Jersey region. The San Francisco, Boston and Philadelphia/Southern New Jersey areas contain the highest proportion of large companies, whereas the companies in the San Diego region for instance are mainly small and medium sized (Ernst and Young, 1993).

The following data are drawn from our database which is described in more detail below. Just less than a quarter of all firms in 1991 were located in California (Table 1 and Figure 2), and the proportion has risen slightly since then (Ernst and Young, 1993). The impetus to cluster within California had not yet been saturated in the early 1990s.

This is a 'survival' data set, of firms which have entered or been present and have adopted the new technologies, and have survived until 1991. It does not capture those firms that entered or were present and exited from the relevant industries.

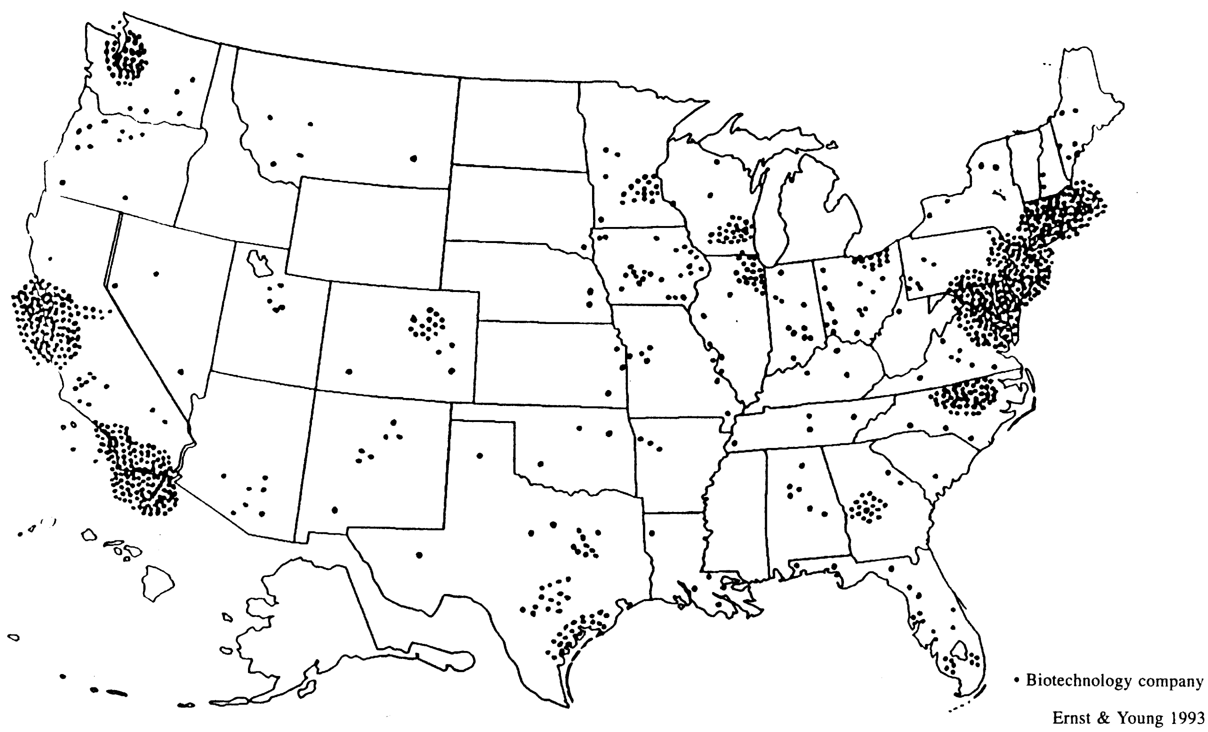

Fig. 1. Location of biotechnology companies in the U.S.A. in 1993.

TABLE I
Proportion of biotechnology companies in different states, 1991

State	Number of companies	Proportion of companies per cent
California	197	23.2
Massachusetts	68	8.0
New Jersey	58	6.8
Maryland	57	6.7
Texas	41	4.8
New York	39	4.6
North Carolina	39	4.6
Pennsylvania	37	4.4
Total above	536	63.1
Out of	849	100

Source: Dibner.

However survival is the feature which we want to capture, as we want the cluster pattern to reflect stable clusters of firms that have entered and survived rather than ephemeral firms that entered and exited. It is also thought that the exit rate among dedicated biotechnology firms has been low. Barley, Freeman and Hybels found that 6 per cent of dedicated biotechnology firms in their data set had ceased operating since 1975. This was thought to be "exceptionally low when compared to other populations studied by population ecologists."(Barley, Freeman and Hybels in Nohria and Eccles, 1992, p. 324). This suggests that our 'survival' data set may be sufficiently accurate to capture the presence of those firms that have contributed most to the growth and stability of cluster formation.

Within this sample which includes both small and large companies involved in biotechnology, there are differences in composition of small and large companies between sectors (Table 2, Figure 3). Companies specialising in diagnostics are mainly small. Therapeutics, agricultural and equipment companies comprise a mixture of small start-ups alongside large pharmaceutical, agrochemical and equipment manufacturers. There are very few small food or energy companies, with those sectors and the chemicals sector dominated by large multinational companies.

California ranks first in almost all sectors (Table 3), and Massachusetts, New Jersey, Maryland and North Carolina are consistently amongst the leading states in those sectors where biotechnology has developed earliest (namely therapeutics, diagnostics, and equipment). In sectors which have been developing more recently

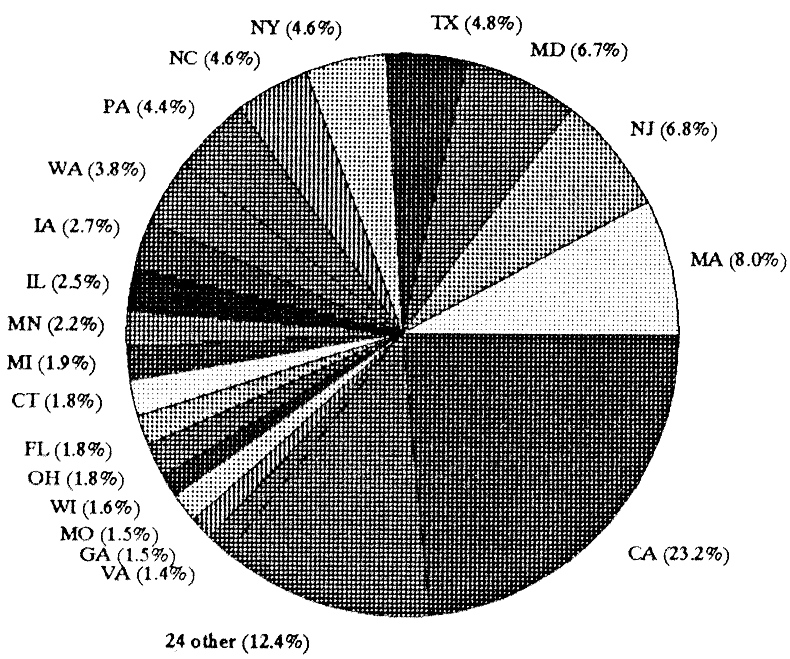

Fig. 2. Distribution of biotechnology companies by U.S. state (1991).

TABLE II
Classification of firms in sample

	Number of firms small and large in 1991	of which small firm	Employment in firms small and large 000s
All companies	849	742	1850.7
Therapeutics	293	265	624.5
Diagnostics	158	151	84.5
Equipment	186	156	189.5
Agriculture	107	87	444.3
Chemicals	52	41	369.4
Food	10	7	37.0
Waste	30	28	42.1
Energy	11	7	65.3

Source: Dibner.

TABLE III
Ranking of top 4 states; Numbers of firms per state
(including large companies)

Ranked	1	2	3	4
All sectors	CA	MA	NJ	MD
Therapeutics	CA	MA	NJ	PA
Diagnostics	CA	NJ	MD	MA
Equipment	CA	MD	MA	NC
Agriculture	CA	IA	NC=NJ	TX
Chemicals	CA	NJ	NY=IL	MD,PA,TX,WI
Food	PA	–	–	–
Waste	CA	TX	–	–
Energy	–	–	–	–

(– denotes only one company per state)
CA = California; MA = Massachusetts; NJ = New Jersey; MD = Maryland; TX = Texas; PA = Pennsylvania; NC = North Carolina; IA = Iowa; IL = Illinois; WI = Wisconsin

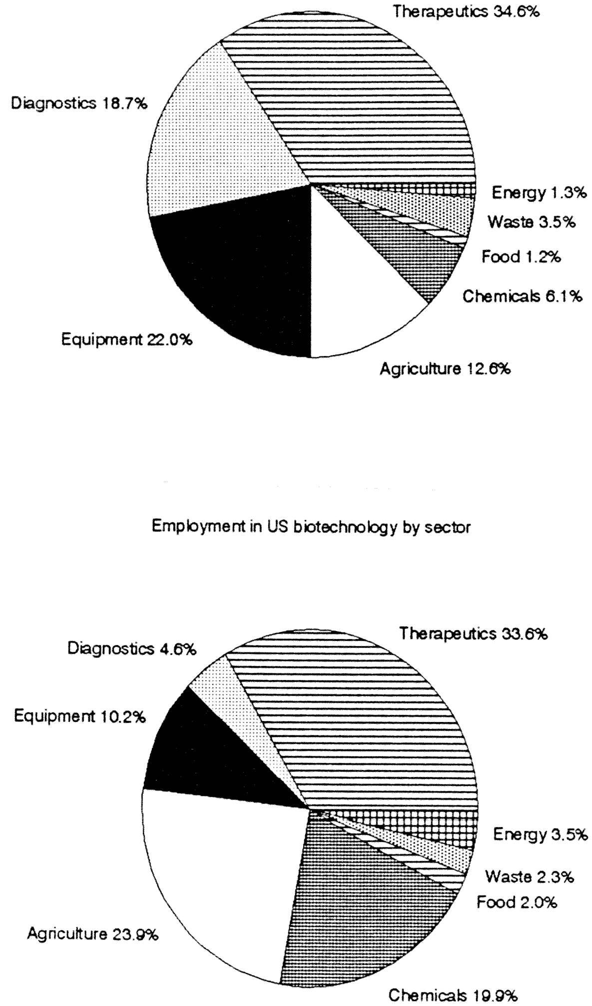

Fig. 3. Proportion of firms in U.S. biotechnology by sector.

(agriculture, chemicals and waste) California is still the state with most activity, but other states such as Iowa, Texas and Illinois begin to rank highly as well, suggesting some diffusion of activity to other states. The predominance of California and Massachusetts in a variety of sectors which are most developed suggests that clusters are created in states with a mix of type of company and not through specialization by each state in one sector.

Entry of new firms over the period and geographic concentration

Table 4 shows total entry of new firms into the industry in our sample between 1979 and 1990, along with the four-state concentration ratio for each year and the ranking of states for entry in each year. There were 609 'surviving' entrants between 1979 and 1990 recorded in our database. Entry during the 1980s, when the industry was in the main created, was variable, with peaks occurring in 1981, 1984 and 1986–1987. There was consistently more entry into the therapeutics sector than into any other sector, but also fairly steady

TABLE IV
Number of new firms in our sample and the four state concentration ratio of entry by new biotechnology firms across the U.S.

	Number of new firms in sample (four state concentration ratio)	Ranking of top four states by entry of new firms (% of new firms entering into that state)			
1979	19 (64%)	NC (21%)	CA (16%)	MD (16%)	MA (11%)
1980	33 (51%)	CA (33%)	NC (6%)	TX=NJ=MA (6%)	
1981	81 (55%)	CA (31%)	MA (12%)	NJ (7%)	MD=WA (5%)
1982	40 (48%)	CA (24%)	MD (10%)	NJ=NY (7%)	
1983	57 (46%)	CA (18%)	MD (14%)	NJ (9%)	NY=NC=MO (5%)
1984	69 (46%)	CA (24%)	WA (9%)	TX (7%)	MD=NJ (6%)
1985	54 (52%)	MD (17%)	CA=MA (15%)		MN=NC (6%)
1986	64 (50%)	CA (25%)	MA (13%)	NC (8%)	PA=TX (5%)
1987	88 (47%)	CA (24%)	MA (9%)	MD (8%)	TX=NC (7%)
1988	56 (55%)	CA (30%)	MD (9%)	NC (9%)	NJ=NY=PA (7%)
1989	35 (60%)	CA (26%)	TX (17%)	MA (11%)	NC=WA=PA (6%)
1990	13 (69%)	CA (38%)	MA (15%)	CO=NY=MD=NJ=PA=WA (8%)	

CA = California; MA = Massachusetts; NJ= New Jersey; MD = Maryland; TX = Texas; PA = Pennsylvania; NC = North Carolina; IA = Iowa; IL = Illinois; WI = Wisconsin; WA = Washington; NY = New York; MO = Montana; CO = Connecticut; MN = Minnesota.

net entry of new firms into the diagnostics and equipment sectors. The surges of entry were encouraged by the financing 'windows of opportunity' in the early 1980s and around 1987 in particular when 'waves of biomania' or enthusiasm for new biotechnology stocks was strong. There was less entry in the late 1980s. Over fifty per cent of entry was concentrated in 6 states. Almost a quarter was into California but entry was also concentrated into Massachusetts, Maryland, New Jersey, North Carolina and Texas.

Geographic concentration of entry fell in the first half of the 1980s, as measured by the four-state concentration ratio of entry of new firms into the industry, rising again in the second half of the decade to its previous levels. Most entry is into the same group of states for most of the period – California, Massachusetts, New Jersey, and North Carolina. In the second half of the decade California consolidated its position attracting most entry, with some diversification into other states such as Texas, Maryland and Pennsylvania.

Data and classification of the industry for the model

Unit of location

The individual state was taken as the unit of location for this study of clusters. Although clusters may not be confined to one state, or there may be more than one cluster in for instance California, using the state as the area over which clusters may form does have some justification.

Individual states have their own tax regimes, utility pricing, policies towards nascent industries and in particular towards biotechnology. However distinctions between states especially on the East coast are not always clear-cut and clusters of companies have developed in Maryland and North Carolina which are likely to be part of the same cluster, encouraged by factors such as the location of the National Institutes of Health which are relevant to several states.

Company data

Our model uses a company data base. Data on companies are taken from Mark D. Dibner's *Biotechnology Guide U.S.A*. Our database has 849 companies, which includes both small companies dedicated to biotechnology and large companies such as pharmaceutical and chemical companies with interests in biotechnology. This gives data on: date of foundation, location by state and address, numbers employed and main field of application. The main field of application defines the sector in which the company operates. Biotechnology companies are divided into sectors not by technologies, which in the first generation of companies at least have been similar between companies operating in different sectors (recombinant DNA technology; hybridoma technology; fermentation; cell and tissue cultures). They are divided according to the industrial sector to which they are applying the technologies: therapeutics; diagnostics; equipment and research tools such as reagents; chemicals; agriculture; food processing; environmental; energy applications. Dibner gives 33 industrial categories and we have amalgamated them into the eight given above. Each company may be active in more than one sector, but is assigned a main field of operation by Dibner, and we use this unique designation to put each company into only one sector. This will have led to some errors where a company is active across industrial boundaries. However, the eight categories chosen are fairly broad, and most companies in their early stages have fallen squarely into one of those categories.

Companies may be divided into small companies dedicated to biotechnology and large corporations with an involvement in biotechnology. The same data are given for both types of company. We treat both categories identically; they are distinguishable in the database by the earlier foundation of the large companies and that they employ more people. The problem of identifying how much of a large corporation is dedicated to biotechnology is ignored. This is because in biotechnology, unlike in computing, one of the main attracting characteristics of the large corporation in for instance the pharmaceutical sector is not just that some of its research may be given over to using biotechnology; more important is the complementary nature of the assets possessed by the large pharmaceutical company to the small biotechnology company. The assets of the large company that attract the small include: finance, development ability, marketing and distribution departments and expertise with regulation. In some ways these are more important to the small company than the degree of use of biotechnology within the large company. It seems legitimate therefore to use numbers employed in the large company as a proxy for the extent or weight of expertise and ability in these various areas, without which the biotechnology research and products of the small company could not be scaled up and commercialised.

The science base

We also created a database on research expertise in biotechnology in the U.S.A. We wish to identify where the strongest bases for research in areas relevant to biotechnology are in the U.S.A. Data on research institutes are taken from *Research Centers Directory U.S.A., 1991*. We focus on life science research centres and ignore other sciences. The centres include universities and any establishment with research specialization in the life sciences. This fits our purpose neatly, as we focus on research expertise rather than teaching centres. Within the life sciences the centres are divided into: agricultural, food and veterinary sciences; biological and environmental sciences; and medical and health sciences. Each centre is given a brief description of its activities and the area in which it works. We have picked out those centres relating to biotechnology. This was defined to include a wide range of disciplines including all types of microbiology, genetic engineering, biochemical engineering, cancer genetics, plant breeding and genetics, fermentation research, biological instrumentation research, medical applications research from molecular or cellular approaches but excluding clinical or epidemiological approaches, and a variety of other closely related categories. We have tried to include all those areas of research which have taken a molecular, cellular, or genetic approach as opposed to clinical or epidemiological approaches. This is a fairly broad-brush distinction, but at least in the early stages of the development of biotechnology, the main impetus has come from an understanding of microbiology and it is from this type of research that the biotechnology industry has been formed. This database, like that of the companies, is a 'survival' dataset, not recording exits of research centres from the dataset; however the exit rate amongst research centres is thought to be even lower than for companies, and we have therefore ignored this problem.

Each research centre has an address with state and post code, the date of foundation and the number of staff. We have aggregated the different categories of staff to give a crude figure of numbers employed in each research centre. The model of entry requires estimates of the level of employment in each sector, by state for the period 1979–1990. We have estimates of employment levels in each firm in 1991 and the date of foundation. We do not have employment data at the company or state level by sector for any earlier year. We have therefore estimated a profile of the history of each firm's employment by interpolation (assuming an exponential growth path, calibrated individually for each firm from the starting date, and employment in 1991). This is not an accurate picture of each firm's employment history, but when aggregated over all firms in the cluster, we believe the overall measure of cluster size may not be too bad.

Model of entry

Prior to developing the full entry model, we tested some of its assumptions with two preliminary steps. We generated a time series of surviving entry for each sector and state (cluster). From this we created a sector by sector covariance matrix, and taking principal components of this matrix, looked at its eigenvalues and eigenvectors. The size of each eigenvalue indicates how much variation in entry into all eight sectors is accounted for by some underlying latent variable. The eigenvector associated with each eigenvalue shows into which sectors that entry is occurring. This step is therefore a way of identifying whether there are any significant common attractors of entry of firms into particular sectors.

In this case there was one highly significant eigenvalue, accounting for 69% of the variation in entry. A second eigenvalue accounted for a further 13% of the variation. The others were not significant. The eigenvector for the principal eigenvalue indicated that most of the entry driven by the first latent variable was into therapeutics, with some entry into the diagnostics and equipment sectors. The second latent variable had a strong positive effect on entry into equipment and diagnostics and a negative effect on entry into therapeutics. The other eigenvalues did not explain any of the variation in entry, and of their eigenvectors, there tended to be one significant coefficient indicating a factor specific to that sector.

We wish to identify these latent variables that act as powerful attractors of entry into some sectors. Our next step was to estimate cluster/sector fixed effects and see how these correlated for each sector with employment in the science base in that cluster and employment in the relevant biotechnology industries in that cluster. We constructed mean entry across all years into each sector into each state and we ran a regression to see how mean entry is correlated with employment in the science base and employment in the biotechnology industry. Results are summarised in Table 5. Employment effects account for about half of the variation in entry, suggesting that fixed effects are likely to be important alongside employment in attracting entry. Nevertheless, these regressions do suggest a well determined pull to entry by the science base into certain sectors. Employment in the industries associated with biotechnology on the other hand was only very weakly correlated with entry into each sector. Looking at variation in entry between specific states, we constructed plots for each sector of mean entry into each state against total employment in both the science base and industry. They showed that for certain sectors and states such as California, Massachusetts,

TABLE V
Correlation of mean entry in each sector into each state with science base employment and biotechnology industry employment

Sector	Therapeutics	Diagnostics	Equipment	Agriculture	Chemicals	Food	Waste	Energy
Science base employment	0.00005 (5.76)	0.000024 (5.86)	0.000025 (6.03)	8.06e-06 (3.75)	6.51e-06 (4.52)	5.5e-06 (1.66)	4.29e-06 (4.34)	4.59e-07 (1.16)
Industry employment	7.36e-08 (0.18)	1.51e-07 (0.77)	–1.75e-07 (–0.88)	1.08e-07 (1.06)	1.46e-07 (2.15)	–1.36e-08 (–0.87)	7.7e-08 (1.61)	–2.96e-08 (–1.59)
R^2	0.49	0.52	0.48	0.34	0.47	0.07	0.43	0.07
Prob > F(2, 41)	0.0000	0.0000	0.0000	0.0002	0.0000	0.2523	0.0000	0.2426

Maryland and North Carolina, particularly in therapeutics, diagnostics and equipment, entry was correlated with employment. However, for other sectors high employment in the state did not generate new entry. Notably these are states such as New York and New Jersey associated with the older and larger established companies in sectors such as pharmaceuticals and chemicals.

These results imply that employment in the science base of 10,000 accounted for entry into a cluster of half a firm per annum into therapeutics, and a quarter of a firm per annum into each of the diagnostics and equipment sectors.

The 'full' entry model attempts to identify more fully the main attracting forces for entry of new firms into each sector. It is a more complex model and requires more stringent assumptions in generating time series of employment data in each sector. Swann (1993) developed this model to examine the extent that new entrants to the computer industry are drawn towards existing clusters of computing firms, identifying the strength of attraction by each sector within computing to entry of new firms into particular sectors of the industry. This paper does the same for the biotechnology industry but includes as possible attractors to new firms employment in various parts of the science base. This means that research strength reflected in large research institutes in biotechnology at particular locations may also serve as magnets to the creation or entry into the state of new firms in biotechnology. The variable we use to measure this attraction is employment in companies in particular sectors and employment in different parts of the science base that relate to biotechnology. We measure whether entry is stimulated more by employment at a particular location in the science base or in a specific sector of the industry.

Entry of firms to clusters

This model treats the entry of firms into sector k at location c (each state) in year t as a function of the extent of total entry in sector k (across all locations) in period t, and a function of the current size of the cluster (at the end of year $t-1$) at location c. The size of the cluster is measured by employment in companies at that cluster at $t-1$ and employment in research centres at that cluster at $t-1$.

Number n of entrants to sector k (sector k, state c, time t) = F(Entry into Sector; Employment in sectors (1, . . . , 8) in state c in $t-1$; Employment in Science base (1, . . . , 3) in state c in $t-1$; State Fixed Effects)

$$n_{ckt} = a_k N_{.kt} + \sum_{i=1}^{8} b_{ki} \ln E_{cit-1} + \sum_{j=1}^{3} d_{kj} \ln S_{cjt-1} + m_{ck} + u$$

where N is the total extent of entry in sector k across all locations c, E is employment in each of the i sectors 1–8 and S is employment in each part of the science base j = 1–3, and m are the state fixed effects. There is also a random error term u.

The sectors 1, . . . , 8 are: therapeutics, diagnostics, equipment and research tools, agriculture, chemicals, food, waste and energy. The first employment term shows the effect of employment in sector k and location c at the end of period $t-1$ on the extent of entry to sector k and cluster c in period t. We can therefore distinguish between the effect of own sector employment (e.g. attraction to new therapeutics firms by employment in the therapeutics sector at a particular location) and the effect of other sector employment (attraction to therapeutics firms by employment in each of the other sectors). The employment in the science base variable allows for the attracting effect of the three types of research centre in biotechnology (agricultural, biological and medical) via the strength of employment in those centres. And the state fixed effects pick up whatever is not captured by the employment variables that is specific to each state.

Different trial models

1) Full model (56 parameters): total entry coefficient, employment in each of the 8 sectors, employment in each of the 3 types of science base, 44 state fixed effects.
2) (9 parameters): total entry coefficient, employment in 8 sectors, no fixed effects, no science base.
3) (12 parameters): total entry coefficient, employment in 8 sectors, employment in 3 types of science base, no fixed effects.

We report the F tests, of model 1) against 2), 1) against 3) and 3) against 2).

Sector	1) against 2) $F_{47,472}$	1) against 3) $F_{44,472}$	3) against 2) $F_{3,516}$
1	9.3041 (0.000)	9.5776 (0.000)	3.057 (0.028)
2	4.3835 (0.000)	4.5301 (0.000)	1.7165 (0.161)
3	4.1316 (0.000)	4.1176 (0.000)	3.4264 (0.017)
4	3.0031 (0.000)	3.0548 (0.000)	1.9104 (0.000)
5	2.2167 (0.000)	2.2679 (0.000)	1.3228 (0.265)
6	1.646 (0.006)	1.7352 (0.003)	0.3182 (0.814)
7	1.3487 (0.067)	1.4113 (0.046)	0.4156 (0.745)
8	1.7122 (0.003)	1.5954 (0.011)	3.2609 (0.021)

The preferred model is 1) which includes parameters for employment in each sector, employment in the three types of science base, and the fixed effects. The restrictions (of no science base, and no fixed effects) are all rejected in all 8 sectors. Between models 3) and 2), without fixed effects, but including the science base in 3), model 2) is an acceptably parsimonious representation of model 3) in most cases, but neither is an acceptable simplification of model 1). The parameter estimates for model 1) are given in the matrix below.

These results are reported in Table 6 and are summarised by the two flow diagrams (Figures 4 and 5) which highlight the direction of attraction (attractor → attracted) and the strength of attraction (shown by width and darkness of line). We look here only at attractor effects above an arbitrary cut-off point of 0.02. There are three degrees of strength of attraction: weak (coefficients between 0.02 up to 0.04), medium (coefficients between 0.04 up to 0.06) and strong (coefficients of 0.06 and above).

We can distinguish between two main types of attraction: links between the science base and industrial sectors; and links between industrial sectors. Coefficients on the science base as attractors are larger than those for most sectors (see Table 6). Strong links occur between the

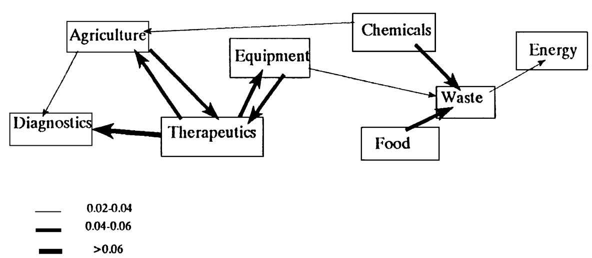

Fig. 4. Principal new entry attractors in U.S. biotechnology: sectors.

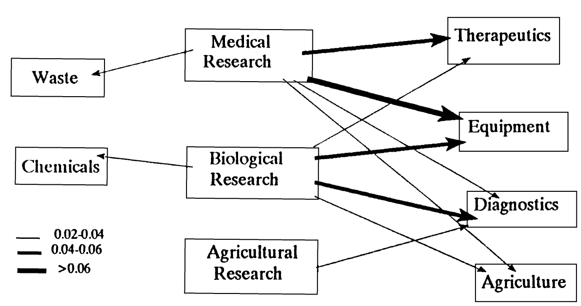

Fig. 5. Principal new entry attractors in U.S. biotechnology: science base.

TABLE VI
Attractor effects on entry into biotechnology: mean change in the number of entrants for given percentage increase in employment in each sector

Entry into	Therapeutics	Diagnostics	Equipment	Agriculture	Chemicals	Food	Waste	Energy
R^2	0.103	0.102	0.101	0.129	0.058	0.111	0.084	0.108
Std error	0.696	0.52	0.56	0.395	0.234	0.083	0.223	0.102
Attracted by:								
Total entry into sector (all states)	0.022 (0.004)	0.021 (0.005)	0.02 (0.004)	0.022 (0.004)	0.023 (0.006)	0.021 (0.007)	0.021 (0.006)	0.022 (0.007)
Therapeutics	–0.01 (0.048)	0.091 (0.036)	0.043 (0.039)	0.048 (0.02)	0.017 (0.016)	0.005 (0.006)	0.0002 (0.015)	–0.000 (0.007)
Diagnostics	0.006 (0.057)	–0.089 (0.042)	–0.026 (0.046)	0.006 (0.024)	–0.002 (0.019)	0.003 (0.007)	–0.003 (0.018)	–0.008 (0.008)
Equipment	0.037 (0.061)	–0.022 (0.045)	–0.064 (0.049)	0.019 (0.026)	0.01 (0.02)	–0.005 (0.007)	0.021 (0.019)	0.017 (0.009)
Agriculture	0.054 (0.068)	0.026 (0.05)	–0.007 (0.055)	–0.084 (0.029)	0.017 (0.023)	–0.012 (0.008)	–0.017 (0.022)	0.011 (0.01)
Chemicals	–0.019 (0.065)	–0.075 (0.048)	–0.022 (0.052)	0.025 (0.028)	–0.048 (0.022)	0.011 (0.008)	0.056 (0.021)	0.012 (0.01)
Food	–0.052 (0.084)	–0.057 (0.062)	0.014 (0.068)	–0.045 (0.036)	0.017 (0.028)	–0.061 (0.01)	0.042 (0.027)	–0.002 (0.012)
Waste	–0.157 (0.089)	–0.06 (0.066)	–0.098 (0.072)	–0.13 (0.038)	–0.026 (0.03)	–0.009 (0.011)	–0.141 (0.029)	0.022 (0.013)
Energy	–0.14 (0.124)	–0.136 (0.092)	–0.317 (0.099)	–0.066 (0.052)	–0.019 (0.042)	–0.012 (0.015)	0.019 (0.04)	–0.11 (0.018)
Science base								
Agriculture	–0.023 (0.157)	0.025 (0.117)	–0.006 (0.127)	–0.003 (0.067)	–0.019 (0.053)	0.003 (0.019)	–0.032 (0.05)	–0.015 (0.023)
Biology	0.021 (0.09)	0.052 (0.067)	0.057 (0.073)	0.034 (0.038)	0.02 (0.03)	0.004 (0.011)	0.002 (0.029)	–0.018 (0.013)
Medical	0.029 (0.104)	0.03 (0.077)	0.119 (0.084)	0.029 (0.044)	–0.011 (0.035)	0.017 (0.012)	0.029 (0.033)	0.008 (0.015)

medical research base in attracting companies into the equipment sector in particular with a coefficient of 0.12, and from the biological research base to equipment and diagnostics sectors, with coefficients of 0.06 and 0.05. There is only one strong link between industrial sectors, which is the therapeutics sector attracting diagnostics companies with a coefficient of 0.09 attracting entry into diagnostics. Both medical and biological parts of the research base exert a weak pull on companies into therapeutics, agriculture, chemicals and waste. Between sectors there are weaker attractor links, running in both directions between therapeutics and equipment and between therapeutics and agriculture. This gives some positive feedback effects of cumulative growth feeding from entry in one sector affecting entry into the other. We can therefore divide the sectors into two groups: one is the more closely interrelated group centred around the therapeutics sector, comprising also diagnostics, equipment and agriculture. The other group is more loosely linked: chemicals attract companies into the agricultural and waste sectors but entry into chemicals is not itself stimulated. The food sector attracts waste companies but there is little attraction into the food sector. And the waste sector attracts energy companies. All these links are weak ones.

Interpretation

The science base – in particular the biological and medical research centres – exerted the strongest pull to the creation of companies. This attraction may have worked in two ways. First, leading edge research at scientific institutions has been the origin of much of the commercial potential of this industry, in particular in its early days. For instance the creation of therapeutic companies, such as Genentech or Cetus, came out of the research expertise in the cluster of universities and research hospitals in California. The close links between people within the science base and those setting up the companies was vital to that process. The second form of attraction recognises research centres as a market for specialized research equipment. It is mainly diagnostic and equipment companies which have been attracted into this market in research tools and diagnostic kits for research in the science base. The coefficients of attraction by the science base for entry into the equipment and diagnostic sectors reflect this. The development of DNA sequencers, reagents and different types of antibodies needed in research has led to the creation of companies which specialized in providing those research products close to their research markets. In distinguishing between demand attractors and supply side attractors, this second type illustrates the strength of demand that the research bases have exerted in the formation of new companies to cater for their needs. The first type of attraction is supply side driven, with companies created to absorb spillovers in the form of commercial potential of academic research. Although it is this type of process that has received most publicity, the supply side spillovers from research do in fact seem slightly weaker than those on the demand side.

Our results suggest that between the research centres, biological and medical research centres created a stronger pull to new companies than agricultural centres. The distinction between type of research centre may be that those classified as biological and medical are conducting more general types of microbiological research whereas those in the agricultural domain have a somewhat more applied stance. The results also suggest that research in the biological and medical areas are transferable to a variety of sectors and that the most obvious linkages – between medical research and therapeutics companies for instance or agricultural research and the agricultural sector – may not be the strongest. Instead research transcends these company sectoral boundaries and a stronger pull to new companies may come out of a quite general biological research result.

Companies have been more attracted by proximity to centres of research than to other companies. However looking at inter-industry linkages we may divide this matrix into two parts: those sectors into which there has been entry, namely therapeutics, diagnostics, equipment and agriculture. These four sectors accounted for 88 per cent of the entrants over our period, 1979–1990. There was much less entry into the other four sectors: chemicals, food, waste and energy. In the ‘entry’ sectors, there has been positive feedback between some sectors, with therapeutics attracting equipment companies and equipment companies attracting therapeutics. The same two-way process applied between therapeutics and agricultural companies. Therapeutics strongly attracts diagnostics companies, although the reverse is not true.

It is noticeable from the matrix that activity in one’s own sector consistently acts as a mild repellent to new firm entry. In other words the extent of a cluster in therapeutics deters further therapeutics firms from entering, a cluster in diagnostics deters new diagnostics firms etc. This effect is not terribly strong, but is mildly negative; ie a repelling one rather than an attracting one. This may be termed a Cournot effect,[2] where the prospect of competition at a location within its own sector is a deterrent to a new firm from setting up at that location. Cournot effects also exist between diagnostics and equipment companies, ie they compete with each other. There is in fact considerable overlap in terms of the use of various new monoclonal antibody diagnostic tests, DNA probes and new types of biosensors, which may be classified in either the diagnostics sector or equipment sector but are used for similar purposes in enhancing sensitivity to detection of disease or presence of particular chemicals for instance. Competition between these two sectors might well be a relevant factor in location decisions for new firms.

The pattern that emerges from this is that the process of attraction between companies has been self-reinforcing within one block of the matrix: companies entering were attracted by other companies entering, except in their own sectors. This suggests that feedback, the reinforcing mechanism that prompts clusters to grow once entry of new companies is underway and visible, has been limited to one block of industries. There has been interrelation in particular within the different parts of the health care sector and a process of specialisation in the provision of research tools and equipment to service other sectors. Agricultural companies have sprung out of the transfer of genetic research generally into the plant area in particular. Spillovers from research are likely to have been from research in the genetic area generally rather than in agricultural research.

The other sectors are either dominated by large companies – in food processing, chemicals and energy – or are as yet underdeveloped novel sectors in waste and environmental applications. One question that arises with regard to the sectors where no entry has occurred and which are dominated by large companies is whether these large companies absorb the spillovers in particular from research centres and in the process deter entry of potential competitors. A related question is whether such large companies benefit from spillovers in the form of faster growth. This is explored in another paper (Prevezer and Swann, 1994).

An alternative explanation for the lack of entry in these other four sectors, food processing, chemicals, waste and energy, is a much slower take-up of the new technologies. In the last two sectors – waste technologies and biomass energy technologies – the technologies themselves are relatively underdeveloped and although some small companies are being created, they are relatively few and recent. In food processing and chemicals, the industries are dominated by large companies. These companies in themselves are not attractive to the creation of new companies in their own sectors developing new technologies. This stands in contrast to the pharmaceuticals area where the large drug companies have recognised the value and have needed the development of new technologies by small companies within their own therapeutics and diagnostics sectors. This symbiotic process, which has resulted in many alliances in the pharmaceutical area, has not operated to the same degree in chemicals or food (Prevezer and Toker, 1995). One possible explanation for the absence of symbiosis between large and small companies in food processing and chemicals may be a perception of competence destruction of large company skills, a threat to their own core business skills and technologies from these new alternative technologies (Tushman and Anderson, 1986). In the pharmaceuticals area on the other hand, the perception of pharmaceuticals companies is that the new techniques developed by the small companies are valuable to them and enhance their own capabilities; and hence a large number of partnerships of various sorts have resulted. Organisational explanations looking at the absorptive capacity of companies might be relevant (Cohen and Levinthal, 1990), with pharmaceutical companies being more outward looking and geared towards absorbing external research, and chemical, energy and food companies preferring to rely more exclusively on in-house research.

Our results do show however some symbiosis between chemical companies in attracting the entry of agricultural companies. This arises from the chemical companies' interest in plant breeding research which offers alternative routes to plant resistance to disease, and affects the chemical companies' markets in pesticides and herbicides generally. There are also spillovers from the chemicals and food sectors in the creation of new technologies dealing with waste which has resulted in some new companies in the waste sector. However, there has been relatively little entry of small companies into the chemicals and food sectors themselves; the absorption of the new technologies, in so far as it is happening, is doing so inside the large companies. In terms of cluster formation, these sectors where activity occurs within existing large companies, insulated from local research and industrial communities, do not stimulate entry of new firms. Feedback between large and small firms and between small firms and research centres is therefore more limited in these sectors, and slower development and diffusion of techniques might be the outcome of the absence of feedback and spillovers.

Conclusion

Our model looks at the forces that make firms in the biotechnology industry cluster around existing firms in particular sectors or around research institutes in the science base relating to biotechnology. It finds that clustering forces from particular parts of the science base are stronger than those between most sectors. However, there is a group of sectors – in health care around the therapeutics sector – where positive feedback occurs and entry of new firms is encouraged. The creation of new markets in research centres and therapeutics for specialist equipment and diagnostic kits encourages entry of new firms into those sectors. This suggests that there are spillovers from research and therapeutics which are absorbed by the creation of new firms. Another group of sectors is more insulated from these attracting forces and there is not much entry of new firms into the food processing, chemicals or energy sectors. Spillovers from research may be absorbed by large incumbent companies in these sectors.

Notes

[1] I would like to thank Peter Swann for his extensive help and guidance through the work on clustering. I would also like to thank Chris Walters for his valuable computing assistance. This paper is part of a wider study of clustering in computing and biotechnology. The model is based on Swann (1993). Acknowledgment also goes to the Gatsby Foundation for funding the work and to participants of the International Schumpeter Conference, Munster 1994. The author remains responsible for errors.

[2] In Cournot models profit margins decrease as the number of firms increases. The attractiveness of entry might therefore fall as the number of firms in that sector rises.

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