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Boston Metropolitan Area Biotechnology Cluster

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Abstract

The biotechnology industry has developed in a number of tight spatial clusters in the US and in other countries. This paper examines the biotechnology cluster in the Boston metropolitan area. Preliminary investigation indicates that firms in this cluster are specialized in technologies related to medical sciences and that they are highly concentrated in one small part of the metropolitan area: the City of Cambridge. In order to better understand the forces that underlie this type of tight clustering, a survey of biotechnology firms was conducted as well as a number of face to face interviews. Results indicate the importance of local universities both as sources of skilled labor and as producers of technological advances with commercial application.

Introduction

Biotechnology is one of the fastest growing industries in the developed world. It is also one of the most spatially clustered industries in the world. In the US, clusters in San Diego, the San Francisco Bay area and the Boston metropolitan area account for a disproportionately high share of total employment and investment. In this paper we will examine the Boston metropolitan area cluster. We will show that there is an exceptionally high degree of clustering *within* this regional cluster – specifically in the city of Cambridge Massachusetts.

We may regard Cambridge as an *industrial district* in the tradition of Marshall (1890). Subsequent research has shown that there are a variety of mechanisms that give rise to industrial districts. In order to shed some light on the underlying mechanisms, we present the results of a survey of biotech firms located in the Cambridge area and in other parts of the Boston metropolitan area. The results will help us eliminate some of the standard explanations for tight agglomeration and identify others that clearly play important roles. We will also suggest some factors that have not been much discussed in the literature to date and that relate to the peculiarities of the biotechnology industry.

The remainder of the paper is organized as follows. The first section is an overview of theoretical and empirical work on industrial districts. This is followed first by an introduction to the biotechnology industry in general and then to the biotechnology industry in Massachusetts. We then present evidence of the extraordinary clustering of Boston Metropolitan Area firms in the City of Cambridge. Following a description of our survey instrument we consider a number of possible explanations for the observed tight clustering. For each explanation we present evidence from our own survey and from

other related research. We conclude by identifying those underlying mechanisms that best explain the clustering and suggesting directions for further research.

Industrial Districts

An industrial district may be defined broadly as a group of related industry located in the same region (Held, 1996). Industries may be “related” in a couple of ways. In the case of the classic industrial complex, industries are related by the transfer of intermediate goods among them. In such cases agglomeration economies arise due to decreased transportation and transactions costs. Of more relevance to our study are groups of firms that are related in the sense that they are in the same general industrial sector. They may be direct competitors or occupy different niches in the same market. Benefits due to clustering of such firms are commonly known as localization economies.

Marshall’s original notion of an industrial district was of the second type. While he made reference to the intangible values of such district, his analysis is principally based on the cost savings of firms drawing from common pools of inputs such as labor, capital and natural resources (Harrison, 1992). As Blaug (1997) has pointed out, the notion of such external scale economies was also appealing to Marshall because his general equilibrium framework could not encompass internal scale economies.

Piore and Sable (1984) emphasize the role of the state and the role of industrial policy as the most important factors for clustering. They claim that the strategies for industrial growth are not pre-determined by the stage of economic development of a particular society, nor is the intra-firm structure determined by the nature of the technology wielded by it.

Markusen (1996), adds new texture to Marshall's work, and Piore and Sable's Italian variant, with their emphasis on government intervention, control of large or small corporations, scale economics, and the role of supplier and buyers, arguing that industrial districts are often dominated by large firms or by large scale state intervention. She adds three additional models: (A) the hub-and-spoke district, dominated by one or several large firms controlling the cooperation in the district; (B) satellite platforms, a congregation of branch facilities of externally based multiplant firms that is controlled by the external large firms in matters of finance, technical expertise, and business services; (C) state-anchored districts, where a public institution like the military or a university is the key player in the district. (Markusen,1985).

Michael Porter (1990) offers four mechanisms that contribute to the success of industrial districts: *factor conditions* including both cost and quality, especially of labor; *demand conditions* such as a specific concentration of buyers; *related and supporting industries* that serve common needs for inputs and services in the cluster; and *firm strategy structure and rivalry*, especially local rivalry that provides constant pressure for improved quality and efficiency.

Others have argued that it is not just rivalry that is important but also cooperation (Lazonick, 1992). For example Piore and Sable (1984) describe how firms in Northern Italy benefit from cooperation through sharing marketing and production assets and participating in active trade associations. Saxenian (1994) stresses networking, technology transfer and organizational learning. In comparing the success of IT firms in Silicon Valley to the eventual decline of similar firms in Massachusetts, she argues that a model of flexibility and cooperation among large and small firms in the former proved

superior to a model whereby large firms tried to internalize all functions and jealously guarded information in the latter.

Of particular relevance to the case of biotechnology is the role of industrial districts as places of high efficiency in the creation, transfer and application of knowledge. Maskell and Malmberg (1999) emphasize the importance of knowledge. Knowledge becomes a valuable commodity that is not simply transferred. The exchange of knowledge is based on trust and ongoing relationships between the seller and the buyer. In a small location most firms and industries will know each other, which promotes trust and exchange of information. Knowledge, in some ways is explicit, that is expressed in words and numbers. In other ways it is tacit, that is “personal, context-specific, and therefore hard to formalize and communicate” (Nonaka and Takeuchi, 1995, p. 8), which demonstrates the importance of regional learning and the clusters. Maskell and Malmberg (1999) argue that tacit knowledge necessitate face-to-face encounters, which provides the competitive advantage of a region or a locality. Thus, in order to achieve new product development in high-tech districts there is a need for cooperation between individuals that share common knowledge and expertise.

Universities play a key role in knowledge intensive industrial districts. In particular they are critical in advancing the human capital of the region (Beck, et al, 1995) and in certain industries (including biotechnology) they create technological innovations that are commercialized by local firms (AICUM, 2003).

The industrial district may be important from a more sociological perspective in industries involving risky ventures. In order to succeed in a risky, knowledge intensive industry a firm has two pressing needs: the need to attract key employees such as

scientists, engineers and experienced managers (usually poached from other firms) and the need to attract venture capital. In both cases, a history of personal relationship is necessary to create the trust needed for people and venture capitalists to come on board. Well established industrial districts produce a wealth of such personal relationships and therefore are the best places to start risky ventures. Stuart and Sorenson (2003) argue, however, that there may be a disadvantage to locating in such districts in the long run because of the prevalence of personnel poaching and the competition for venture capital.

The Biotechnology Industry

Biotechnology may be defined as “any technique that uses living organisms, or substances from those organisms, to make or modify a product, to improve plants or animals, or to develop microorganisms for specific uses.” (Barnum, 1998) By this definition, biotechnology is by no means a new phenomenon. The history of biotechnology can be divided into three phases. The first phase, which predates written history, includes the domestication of plants and animals for human use and the fermentation of foods and beverages such as bread, beer, cheese, wine and yogurt. The second phase, or “classical biotechnology,” includes direct products of science such as the discovery of vaccines and Pasteur’s discovery of the role of microorganisms in fermentation.

Modern or third phase biotechnology is the result of several breakthroughs in molecular biology (Acharya, 1999). In 1953, James Watson and Francis Crick from Cambridge University identified the structure of DNA. This breakthrough was followed by the development of monoclonal antibodies, on which diagnostic kits in the therapeutic industry are based. First developed at Stanford University in 1973, the process of cutting

and rejoining DNA to produce recombinant DNA that could replicate a host cell – known as cloning – revolutionized modern biotechnology.

Biotechnology in Massachusetts

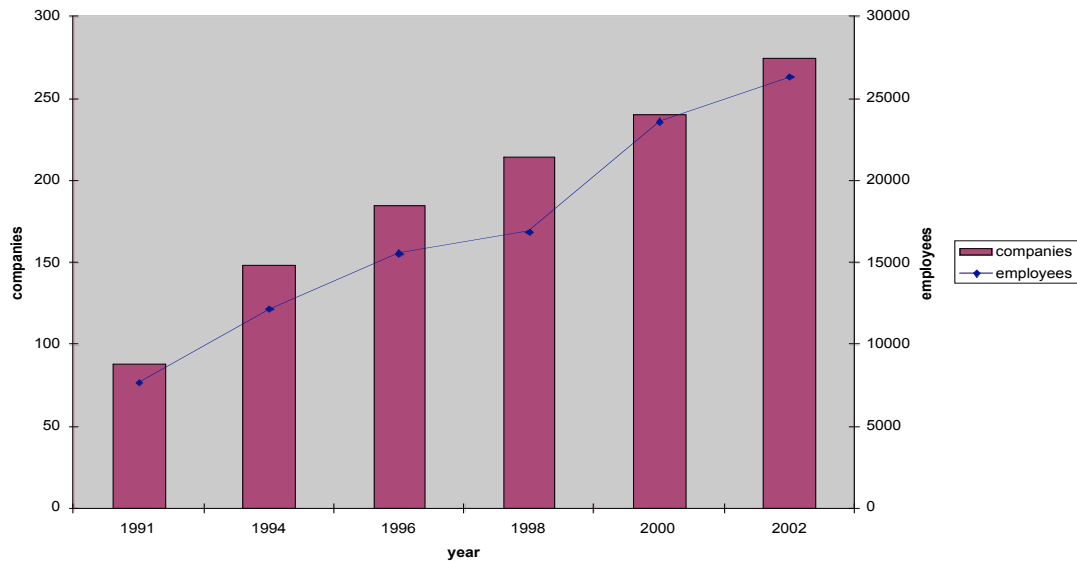
The 1990's were a period of rapid growth in the Massachusetts biotechnology industry and this growth has carried into the new century. Figure 1 is based on membership data for the Massachusetts Biotechnology Council (MBC).¹ By 2002, there were 275 biotechnology firms employing over 26,000 people. Most of these firms were founded in 1996 or later and only 9 were founded before 1980.

Table 1 shows the number of firms reporting significant activity in each of 12 biotechnology market sectors. The total number of reporting firms sums to more than 275 because firms were allowed to report activity in more than one market sector. Also some of the categories, such as contract research and contract manufacturing, describe a type of business arrangement rather than a type of biotechnology product.² It is clear from Table 1, however, that the dominant type of biotechnology activity in Massachusetts is that related to medical science. Relatively few firms work in marine, industrial, environmental or agricultural biotechnology

¹ There are a few firms that are excluded from this figure because they do not belong to the Massachusetts Biotechnology Council.

² Platform Technologies refer to products with applications in two or more of the specific market sectors.

Figure 1: Massachusetts Biotechnology Firms and Employment



225 of the 275 firms reported activity in one or more of biological devices, genomics / proteomics, human diagnostics and human therapeutics. The medical sciences market sectors are defined by the MBC as follows:

- **Genomics/Proteomics:** Focus on the study of defining gene and/or protein functions and interactions through mapping, sequencing and structure analysis (e.g., to develop technologies, therapeutics and diagnostics) comprise this field.
- **Biological Devices:** Use naturally derived materials to make medical appliances, such as those that are used as structural elements in reconstructive surgery (e.g., bone, cartilage or heart valve replacements, skin grafts, etc.)
- **Human Diagnostics** Focus on the identification of the presence or absence of specific chemicals, genes, or proteins within the body which may indicate disease or malfunction of human processes.

- **Human Therapeutics** Focus on the development and/or production of new and unique drugs for the treatment of human diseases and disorders.

The focus on medical science is not surprising, given that medical science has been a staple of the Boston area economy throughout most of the 20th century. Massachusetts General Hospital is the oldest in the US and operates a major research facility and medical school in conjunction with Harvard University. Area hospitals include some of the nation's leaders in cancer (Dana Farber), arthritis (Brigham and Women's), cardiology (Lahey Clinic) and pediatrics (Children's Hospital.) Boston University and Tufts also have medical schools in the Metropolitan area and there is a substantial industry in medical equipment in Eastern Massachusetts.

Table 1: Number of Massachusetts Firms Reporting Activity in Biotechnology

Market Sectors

Market Sector	Firms Working in Sector
Agricultural Biotechnology	12
Bioinformatics Services	20
Biological Devices	30
Contract Manufacturing	24
Contract Research	51
Environmental Biotechnology	4
Genomics / Proteomics	52
Human Diagnostics	44
Human Therapeutics	136
Industrial Biotechnology	5
Marine Biotechnology	6
Platform Technologies	40
Veterinary Diagnostic / Therapeutic	8
Other	37

The Cambridge Massachusetts Industrial Cluster

Biotechnology firms are highly clustered within the Boston Metropolitan Area. The City of Cambridge alone accounts for 30% of the firms and 60% of the employment. Figures 2 and 3 show the number of medical sciences biotechnology firms and employment respectively in 8 cities that collectively account for 72% of the Massachusetts biotechnology firms and 78% of employment. The dominance of Cambridge is especially strong for employment, indicating larger firms are located there. In fact, at 217 the average employment of Cambridge firms is more than twice as high as the overall average. Even the city of Boston has less than 4% as much employment as Cambridge. Other cities with substantial biotechnology activity include Worcester, which is the second largest city in Massachusetts, Watertown, which is adjacent to Cambridge and several towns located along the Route 128 corridor (Waltham, Woburn, Lexington and Bedford.)

Even within the city of Cambridge, there is a high level of local clustering in the Kendall Square area. This is an area of relatively new commercial buildings located adjacent to the MIT campus and directly across the Charles River from Massachusetts General Hospital.

Figure 2: Biotechnology Firms by City

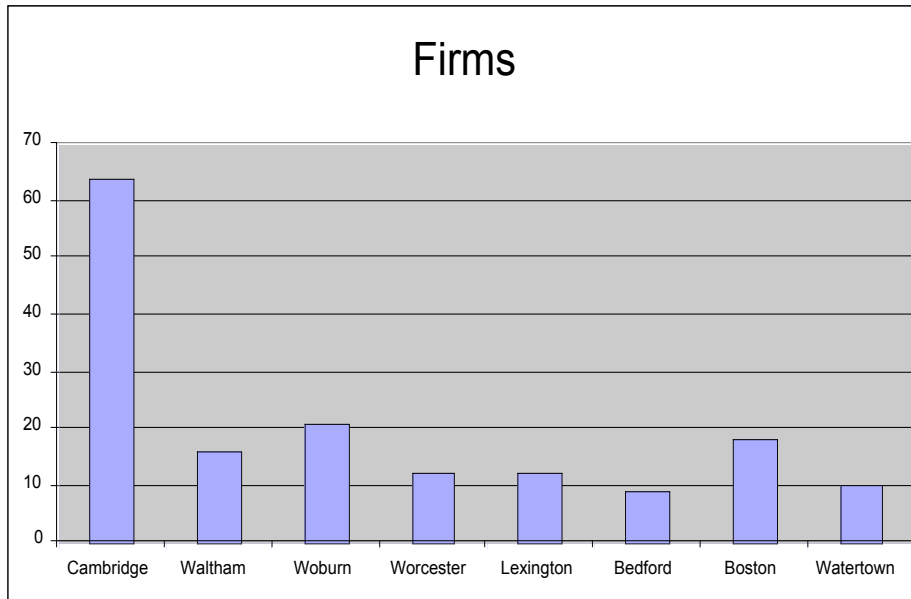
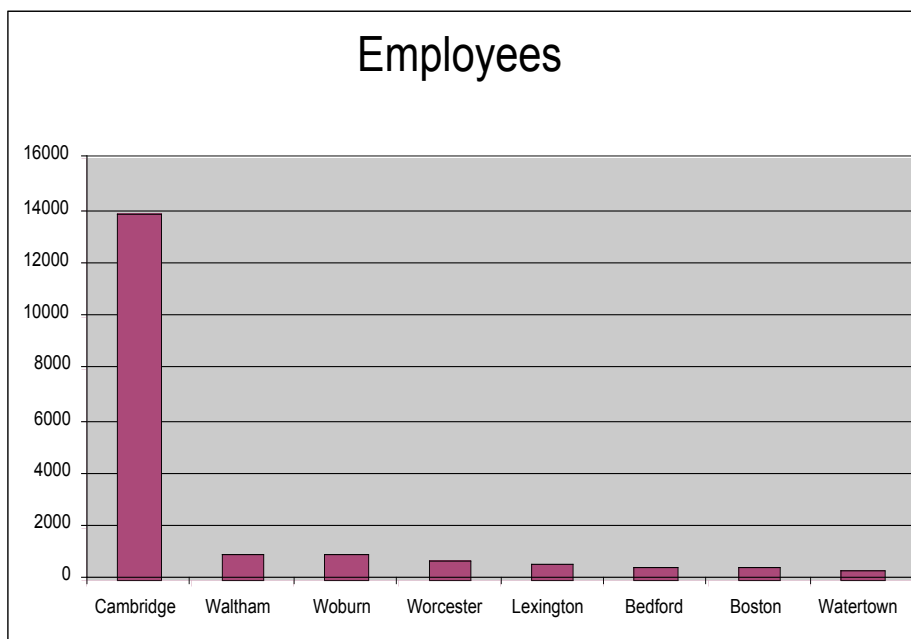


Figure 3: Biotechnology Employment by City



Locational Requirements of Biotechnology Firms

Before considering possible explanations for the tight clustering described above, it is important to consider some unusual characteristics of the medical science biotechnology industry that might affect its location pattern. This industry is substantially different from other “high tech” industries, such as the computer software and hardware industries that were the engine of growth in the 1970’s economy, in a number of important ways.

Unlike computer hardware and software firms, some of which were famously started in garages, biotechnology firms have specific capital infrastructure requirements. Many of them have lab facilities and therefore require the same sort of specialized space required by university labs: individually vented hoods, special electrical and plumbing services, *etc.* Furthermore, there are a number of special precautions that must be taken to protect public safety. In the early 1990’s there was active opposition to biotechnology development in Cambridge based on the fear that biological agents would escape into the environment. The city enacted special “recombinant DNA ordinance” that is more stringent than federal codes and that requires special design elements for buildings.

Also unlike the IT industry, where some leaders like Bill Gates were college dropouts, biotechnology requires people with formal educational credentials. The organizational charts of many firms indicate that founders, chief scientists and a very large proportion of research staff hold doctorates, especially in molecular biology. Securing these people may require not only access to but an intimate knowledge of leading graduate programs.

The link with universities goes much deeper than just hiring their graduates. Especially in the medical science field of biotechnology a large proportion of innovations come directly from the university labs. Typically a biological agent is discovered in a university lab and is patented. The university then enters into a licensing agreement with a private firm for commercialization. This generally requires complex, face-to-face interaction between university researchers and the staff of the firm, both before and after the licensing agreement is struck.

Biotechnology industry is of the high risk / high reward variety. Take for example the case of developing a therapeutic drug. The “discovery phase” where the biological agent is identified often occurs in a university lab. The biotechnology firm is responsible for the following

- Pre-clinical studies (includes animal studies)
- Clinical trials
 - Phase 1: safety
 - Phase 2: safety and efficacy
 - Phase 3: controlled safety and efficacy
- New drug application
- Manufacturing with post approval monitoring

According to the US Food and Drug Administration (FDA), of new drugs that enter this process, 70% fail to survive from preclinical studies to Phase 2 trials. Of those that do 33% fail to make it from Phase 2 to Phase 3 and an additional 25% fail to make it from Phase 3 to the application stage. Of the applications that are made 25% fail. Overall, fewer than 1 in 200 drugs that enter the pre-clinical stage make it to approval. For those

that make it, the cost is in excess of \$500 million and the entire process takes over 8 years on average.

Even after approval, drug manufacturers may be subject to substantial liability risk. Thus medical biotechnology is certainly one of the most risky businesses in the modern economy. This high level of all-or-nothing risk means that most firms will eventually fail and that many venture capital investments will have zero return. This is critical to understanding all aspects of the industry, including its location pattern.

Massachusetts Biotechnology Survey

A survey was conducted in 2000 to gather information specifically related to the question of why Massachusetts biotechnology firms cluster in the City of Cambridge (Breznitz, 2000.) 244 questionnaires were sent to firms with a letter of support from the Massachusetts Biotechnology Council. 58 complete responses were received. The brief survey asked a number of questions to identify the factors that contributed to the firm's location decision, characteristics of its labor force, its main forms of information acquisition, its relationship to local hospitals and whether or not it currently engaged in manufacturing.³

In order to determine whether the completed surveys were a representative sample, chi-square tests were conducted comparing the sample to the population on the basis of producing vs. non-producing companies, members vs. non-members of the Massachusetts Biotechnology Council and Cambridge firms vs. firms located elsewhere. In no case did the test indicate a significant difference between the sample and the population at the 5% level.

³ Details of the survey and a more detailed presentations of results are found in Breznitz (2000).

To acquire more detailed information, 15 face-to-face interviews were conducted with people from the technology transfer and liaison programs at Harvard and MIT, from the Cambridge Development Department, the Massachusetts Business Development Office, the Massachusetts Biotechnology Council, Massachusetts General Hospital (including two clinical investigators), a consultancy to the biotechnology industry and executives from five biotechnology firms.

Reasons for Tight Clustering

Table 2 presents average responses to the question in the survey that asked firms to rate various factors in terms of the importance they had on the location decision. The ratings are on a scale of 1 (most important) to 5 (least important). A few results are clear at the outset. The pool of skilled labor is the most important factor, followed by the access to university research labs. This is not surprising, given the information intensive nature of the industry. What is perhaps more surprising is that access to hospitals is much lower than access to university labs. Tax incentive is the least important factor followed by access to suppliers. In what follows, we use information from this table, from other questions in the survey and from the face to face interviews to address a number of factors in more detail.

Table 2: Factors affecting the location decision

Factor	Average Rating
Other biotechnology companies	3.25
Pool of skilled labor force	2.29
Venture capital	3.80
Research labs (not university)	3.22
University research labs	2.54
Hospitals (for clinical trials)	3.89
Tax Incentives	4.23
Rent	3.39
Recombinant DNA ordinance	3.59
Suppliers	4.27
Others	2.86

Location relative to other firms: In considering a clustering of firms in a narrow industrial sector one should ask whether they are there to be close to each other or whether they have other things in common that they want to be close to. In this case, it is largely the latter; firms do not rate access to other companies especially highly. This is consistent with recent research in Sweden (McKelvey, Alm, Riccaboni, 2003) which found that firms in the Uppsala biotechnology cluster were no more likely to interact in formal ways (joint ventures, licensing agreements, etc.) with firms within the cluster than with other firms.

But other questions in the survey and results from the face-to-face interviews indicate that in more subtle ways, co-location is important. There is frequent reference to a “halo effect” that successful firms have created in the Boston area and especially in Cambridge. An address in Cambridge is seen as a valuable asset in part because of the firms that are there. Also, there are both formal and informal ways in which firms impart information to one another. (We discuss this further below.)

Skilled labor force: As noted earlier, in the biotechnology industry “skilled” generally means holding an advanced scientific degree. With at least three universities with commercially oriented graduate programs in molecular biology (MIT, Harvard and Boston University), the Boston area (and again, especially Cambridge) is a world class supplier of such people. Information from the interviews and from other recent studies (Eaton, 2000; Eaton and Bailyn, 1999) indicate that community, cultural and lifestyle characteristics of the region contribute to retention of skilled people. While Boston’s climate is hardly an attraction, its cultural and social institutions and general ambiance have proved one of its greatest assets.

An important question is whether labor poaching occurs. Firms crowding into a market to exploit the labor of incumbent firms, driving up labor costs and causing high turnover, can over time turn into a disadvantage of locating in clusters of knowledge intensive firms (Stuart and Sorenson, 2003). The survey results indicated that local universities were the main source of labor. Also, none of the people interviewed expressed concern with this issue.

Universities: Local universities contribute to the success of the cluster in three ways. The first, which we have already discussed, is by providing the highly specialized, skilled people who are indispensable for biotechnology firms. The second is that many of the founders and chief scientists of the firms come from the universities, often from the faculties. As in many industries, one of the chief factors affecting location is the place of residence of the firm's founder or owner. Audretsch and Steven (1996) found that, compared with all other US cities, scientists in the Boston area are more likely to remain in their current location.

The third way that universities support the cluster is by directly providing technological innovation. The Bayh-Dole Act of 1980 radically changed the role of universities by allowing the patenting and commercialization of technological innovation produced using federal funds, such as from the National Science Foundation and the National Institutes for Health. Patenting and licensing is now a source of income for research-oriented universities. MIT, Harvard, Boston University and others now have offices specifically devoted to technology transfer and licensing. Since such relationships with commercial firms require complex interaction both before and after the agreement, close proximity is a great advantage.

It is interesting to note that Saxenian (1994) concluded that one of the main advantages that Silicon Valley had over Boston (Rte 128) in the IT industry was that MIT and other local universities were not as adept and proactive in working with commercial firms as were Stanford and other California universities. The history of biotechnology suggests that the regional universities have improved their capabilities for commercial cooperation.

Hospitals: As table three indicates, access to hospitals for clinical trials is not nearly as important as access to universities. This is because a relatively small proportion of clinical trials are ultimately carried on in the Boston area. In order to get a sufficient mix of subjects it is generally necessary to conduct such trials in a variety of locations involving several hospitals or firms that specialize in conducting trials. This does not, however, diminish the importance of hospital research labs as potential sources of new biological agents or as pools of skilled labor.

Suppliers and Services: The surveyed firms ranked access to suppliers of very minor importance. This makes sense from a classical location theory perspective because most capital and material inputs in this industry would have very high value to weight ratios, so transportation is a small proportion of total costs. There may be additional advantages of locating close to producers of complex capital goods, such as rapid repairs and consultation, but the survey does not provide evidence of this.

Suppliers of specialized services such as waste disposal, contract manufacturing and specialized legal services are certainly important to the biotechnology industry and there is a concentration of such suppliers in the Boston area. It is possible that respondents did not interpret “suppliers” as including such firms.

Commercial Space: The availability of commercial space in some circumstances may produce an artificial sort of clustering. For example, it is plausible that as the biotechnology industry developed in Boston’s tight office space market, firms had little

choice but to locate in areas where new space was being developed. Kendall Square in Cambridge was the most concentrated area of office space development in the late 1980's and early 1990's. One might argue therefore that the cluster in Cambridge simply reflects that the fastest growing industry took up space in the area with the fastest expansion of commercial space.

This argument is almost certainly too simplistic, however, as history suggests that the growth of biotechnology and the growth of commercial space in Cambridge were mutually supportive. As recently as the early 1980s the East Cambridge neighborhood around Kendall Square was an area of low rise warehouse and other commercial activity. As biotechnology firms were founded there were abundant opportunities to retrofit warehouse space for use as biotechnology laboratories. The industry was already well established in the area before the commercial building boom occurred and it is reasonable to assume that the growth of biotechnology was one of the main spurs to the boom. Once a few large buildings were established and successful in finding clients new projects were developed including some that were specifically designed with the industry's needs in mind.

Information exchange: The questionnaire asked firms to identify those mechanisms by which information is transferred among firms. Five options (plus "other") were offered and the respondent was asked to indicate all that apply. The results are most interesting when broken out for those firms located in Cambridge and those located outside Cambridge (Table 3). While the largest number of firms in both groups identified newsletters and the internet as an important information channel, the number of firms

who indicated informal gatherings and meetings was second highest within the Cambridge group and lowest within the outside Cambridge group. Interviews reinforces this, with respondents stressing the importance of meeting other scientists at lunch or in other social environments as a good way of gaining information. The fact that this does not appear to be very important to the outside Cambridge group is a clear indication that there is a professional / social milieu that is only present in Cambridge.

Table 3: Important Channels of Information Exchange Among Firms

	Outside Cambridge	Cambridge
Movement of employees from one firm to another	43.2%	52.9%
Informal gatherings and social meetings	24.3%	64.71%
Formal meetings organized by the MBC	48.65%	52.9%
Formal meetings in universities	29.7%	23.5%
Newsletters and internet	70.3%	82.3%
Others	35.1%	23.5%

Research vs. Production: Only a minority of biotechnology firms in the Boston area are engaged in production. Most firms are small and are built around one or two core products. After a long research phase, if clinical trials and applications are successful these firms go into production (or they may license the product to a large firm for production and marketing.) The survey indicated that firms located outside Cambridge are more likely to be in the production stage. Some of them were originally based in

Cambridge but moved out at the production stage. Still other Cambridge-based firms that are undertaking both research and production have transferred production activity to suburban location.

For the questions shown in Table 2, producing firms rated university access as less important and both rent and the Cambridge DNA ordinance more important when compared to research-only firms. While these differences are too small to be statistically significant, they, along with comments from the interviews, suggest that in general it is research activities that benefit most from location in Cambridge.

Concluding Remarks

The Boston Metropolitan area biotechnology cluster exhibits many attributes of economic agglomerations studied elsewhere. Factor conditions, especially labor force characteristics, comparable to those in Boston are to be found in very few other locations. Also, Boston has demonstrated a capacity for retaining its skilled people. The Radcliff 1999 study of the labor force in biotechnology observed that many people in this industry came from the region, and chose to work in this area because of family connections and the dense network of biotech and university communities (Eaton, 2000).

Rivalry is no doubt important in terms of competition for the best scientists but less so with respect to production. For a successful and sustainable cluster, there is a need for cooperation and information flows between all the parties of the cluster—the companies, the universities, the trade associations and the government. The cluster's levels of cooperation and information flows distinguish the level of innovation and flexibility to change. The fact that a number of large pharmaceutical and out-of-town

biotechnology firms have recently located research facilities within the cluster supports this point.

Perhaps the most interesting characteristic of the cluster is the central role of universities. Traditional ideas of technological “spillovers” must give over in this case to a model whereby the universities are active participants in a variety of ways. The notion of a “spillover” applies external economies, but in this case the universities gain rewards in the form of research finance, practical experience for students, and access to expensive equipment for their technological contributions.

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