SPATIAL CLUSTERING OF VENTURE CAPITAL-FINANCED BIOTECHNOLOGY FIRMS IN THE U.S.

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ABSTRACT

Biotechnology is a knowledge-intensive industry that requires a large amount of capital for research and development. The Biotechnology Industry Organization indicates that approximately one fourth of the industry financing comes from venture capital, which provides not only money but also managerial guidance to biotechnology firms. This paper focuses on biotechnology businesses that are financed by venture capital and examines their geographic distribution pattern across United States metropolitan areas. Based on data from 2006, we found that there is a highly concentrated pattern of these biotechnology firms in a few metropolitan areas. Using Poisson regression, we found that, these biotechnology venture activities are highly clustered in urban centers where there is socio-economic diversity. Such firms are also located in close proximity to research universities, institutes and/or hospitals, where there is a strong life science research base and a large pool of life scientists. These firms also cluster in areas where there are large pharmaceutical companies, venture capital providers and entrepreneurial spirit as well.

Key words: biotechnology, venture capital, cluster

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INTRODUCTION

Biotechnology is the subfield of biological science that is linked to such research areas as genetic engineering and recombinant DNA technology; thus it is applied in a wide range of industries. According to a survey by the United States Department of Commerce (2003), firms that label themselves as "biotechnology" fall into over 60 North American Industry Classification System (NAICS) codes. Due to this wide application and especially its success in pharmaceutical production (United States Department of Commerce 2003), biotechnology is becoming more commercialized. According to the Biotechnology Industry Organization (2007), by the year 2005, there were 1,415 biotechnology companies in the United States, most of which were highly concentrated in a few geographic areas. This pattern has raised great interest in location analysis for the biotechnology industry (Kenney 1986; Audretsch and Stephan 1996; Feldman 2000; Audretsch 2001; Cortright and Mayer 2002).

As a knowledge-intensive industry, biotechnology commercial activities need a large infusion of capital dedicated to research and development (United States Department of Commerce 2003). One important way that biotechnology firms get funded is through venture capital financing (Biotechnology Industry Organization, 2007), which is specialized in high-growth, high-risk and high-technology firms in the form of equity rather than debt (Black and Gilson 1998). In 2005, almost one fourth of biotechnology industry financing came from venture capital (Biotechnology Industry Organization 2007). In general, although venture capital accounts for a small fraction of total corporate finance in the United States, it plays a crucial role in technology innovation and economic growth in the national economy (Global Insight 2007). Major public technology firms, such as Microsoft, Genetech and Google, all received venture capital financing at their start-up stages (Gompers and Lerner 2006; Global Insight 2007; Neis 2007). In the biotechnology industry, commercial activities are claimed to have emerged out of university labs because of venture capital (Kenney 1986; Boehm and Schuehsler 2003). As venture capital is an equity investment until the company matures, the investors' fate is bound to the firms in which they invest. As experienced entrepreneurs, venture capitalists are usually actively involved in a biotechnology firm's development during the early critical stage by becoming board members and advisers on potential strategic partnerships (Kenney 1986; Munroe et al. 2002). They can also act as a "coach" to help a company establish a business plan (Boehm and Schuehsler 2003). Very often, a venture capitalist provides not only cash but also contacts, information, advice and a set of networks in the region that prove to be very important to the success of the ventures they fund (Rind 1981; Saxenian 1996). These resources, therefore, provide venture capital backed firms advantages over non-venture capital backed firms. Furthermore, when compared to non-venture capital backed firms, venture capital backed firms are usually newer; more focused to new technologies and thus more likely to make technology breakthroughs and to boost economic growth (Black and Gilson 1998; Kortum and Lerner 2000; Neis 2007). The relationship between these firms and venture capitalists is also a circular process, as the greater the innovation, the greater venture capital investment to come in the future (Gompers and Lerner 2006). From an economic perspective, evidence has shown that venture backed companies outperformed their non-ventured counterparts in both job creation and revenue growth (Global Insight 2007). For instance, between 2003 and 2005, the annual growth rate of jobs among venture capital backed companies was 4.1 percent, more than three times faster than the 1.3 percent for total private sector employment for the same time period; similarly, the annual sales growth rate was 11.3 percent for venture capital backed companies, compared to 8.5 percent for all U.S. companies (Global Insight 2007). At the regional level, venture capital is viewed as an important economic infrastructure for regional economic development (Florida and Smith 1993).

The purpose of this study is to investigate the spatial clustering of biotechnology firms that are financed by venture capital. For convenience, these firms are referred to as biotechnology ventures or venture firms / activities / businesses in this study. We aim to establish theoretically-informed statistical models to explain the geography of these biotechnology venture firms. Despite the interest in the biotechnology industry as a whole, very few studies have focused on biotechnology firms that are financed by venture capital. We believe that our study will add insights applicable to the fields of location analysis and regional economic development.

CLUSTERING OF BIOTECHNOLOGY VENTURE ACTIVITIES

This study investigates the spatial distribution of biotechnology venture firms that are financed by venture capital investment. Biotechnology firm data came from the MoneyTree survey in 2006. The MoneyTree survey is a quarterly study of venture capital investment activity in the United States. It has been used in other studies on venture capital (Green 2004). In this database, the phrase "biotechnology companies" refers to developers of technology promoting drug development, disease treatment, and a deeper understanding of living organisms (PricewaterhouseCoopers 2007). All these venture capital recipient companies are private and new. Venture capitalists in this database come from a variety sources, including professional venture capital firms, small business investment companies (SBICs), venture arms of corporations, institutions and investment banks (PricewaterhouseCoopers 2007). PricewaterhouseCoopers database also includes other investors, such as angels, corporations, and governments, as long as their financing rounds are qualified and verified. This database has been widely used in venture capital studies (Zook 2002; Green 2004; Wonglimpiyarat, 2005)

All biotechnology firms that received venture capital investment in 2006 were investigated in our study. Therefore, our sample does not include biotechnology firms that have received venture capital in years other than 2006. Using zip code centroids, biotechnology ventures were integrated into the geographic information system (Figure 1). Overall, three hundred biotechnology companies in the United States received venture capital investment during the time frame under study. This figure represents slightly more than twenty percent of all biotechnology firms (Biotechnology Industry Organization 2007). As indicated in Figure 1, there is a strong pattern of clustering in the Bay Area and the northeastern part of the U.S.

Biotechnology venture businesses were then aggregated according to metropolitan boundaries, where there is more homogeneity and economic connectivity than for individual municipal boundaries (Cortright and Mayer 2002). Among all biotechnology venture firms studied, 292 (97%) were located inside 370 metropolitan areas. Table 1 presents the top ten metropolitan areas, ranked by the number of biotechnology ventures. San Francisco, the home of biotechnology industry, ranked number one. In 2006, 48 (16%) firms in San Francisco received venture capital investment. San Francisco was followed by Boston, with 37 venture capital funded firms. In third place was San Diego, a fast growing and well recognized biotechnology

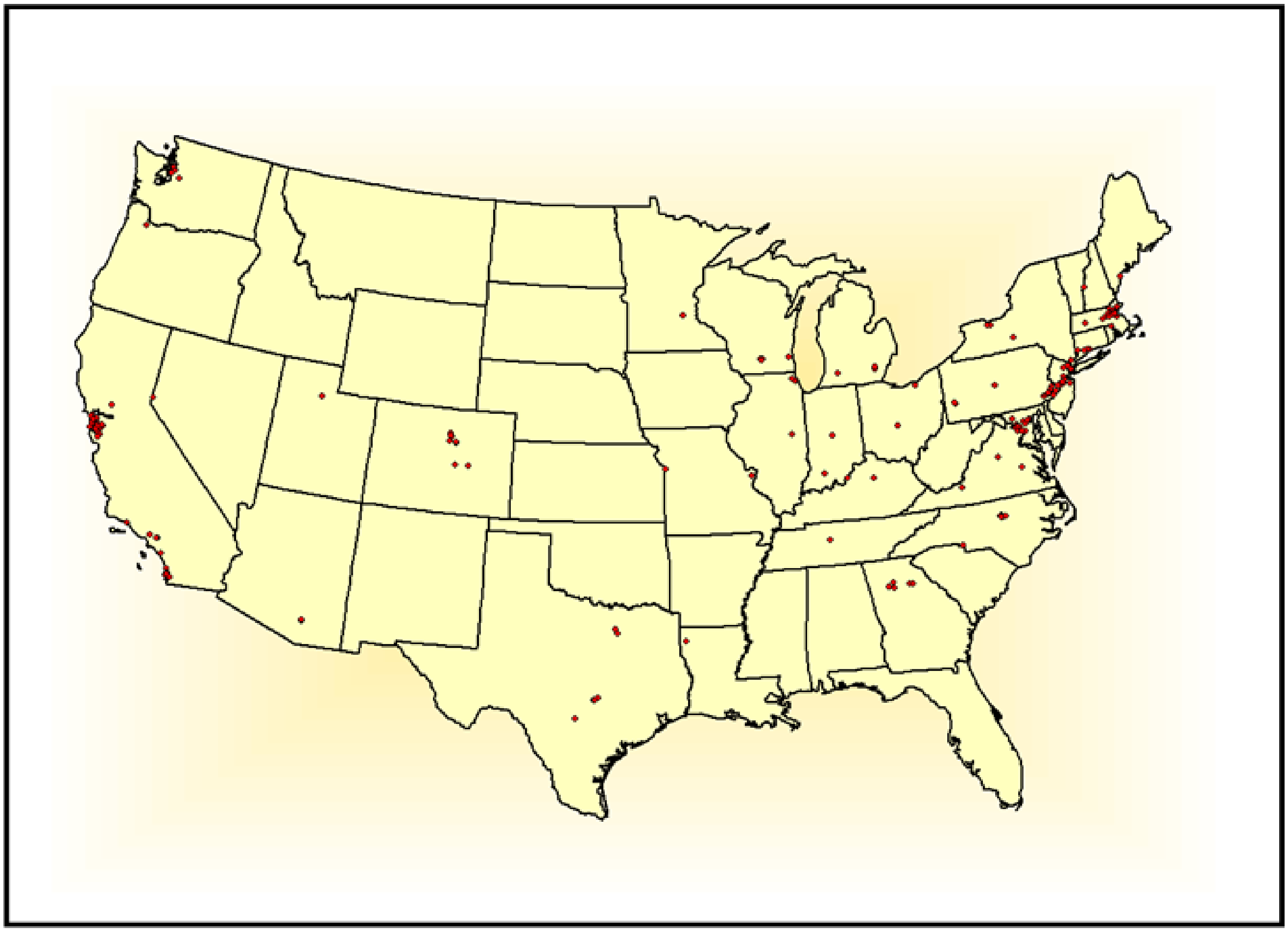

Figure 1: Location of venture capital financed biotechnology firms in 2006

center. Washington D.C. was fourth and Philadelphia ranked fifth. These top five metropolitan areas accounted for 45 percent of all biotechnology venture businesses.

LOCATION FORCES IN BIOTECHNOLOGY INDUSTRY

We assume that the geographic clustering of venture capital financed biotechnology businesses follows a similar geographic pattern as the overall biotechnology industry. In the following section, we first review cluster theory and then the location forces for biotechnology business clustering.

Why Cluster?

Geographers have always been eager to explain the uneven spatial distribution of industries and the regional disparity of economic development. One popular explanation of industrial concentration in space is the industrial cluster model, offered by Porter (1990, 1998). In his model, Porter (1990, 1998) defines industrial clusters as "geographic concentrations of inter-connected companies and institutions in a particular field, linked by commonalities and complementarities". Porter states that innovation is enhanced through close contact between various players in a cluster, including businesses, universities, infrastructures and government agencies.

Table 1: Biotechnology Ventures for the Top Ten Metropolitan Areas

Rank	Metropolitan areas	# of Ventures	Share of Total %
1	San Francisco-Oakland-Fremont, CA	48	16.4%
2	Boston-Cambridge-Quincy, MA-NH	37	12.7%
3	San Diego-Carlsbad-San Marcos, CA	21	7.2%
4	Washington-Arlington-Alexandria, DC-VA-MD-WV	20	6.8%
5	Philadelphia-Camden-Wilmington, PA-NJ-DE-MD	19	6.5%
6	San Jose-Sunnyvale-Santa Clara, CA	17	5.8%
7	New York-Newark-Edison, NY-NJ-PA	15	5.1%
8	Baltimore-Towson, MD	12	4.1%
9	Seattle-Tacoma-Bellevue, WA	11	3.8%
10	Los Angeles-Long Beach-Santa Ana, CA	8	2.7%

Industrial clusters are especially linked to the concepts of innovation process, innovative milieu, regional innovation systems and learning regions, knowledge economy, and learning economy etc (Antonelli 2000; Martin and Sunley 2003; Coenen et al. 2004). As indicated by Marshall in the late 19th century, the benefits for businesses to cluster can be explained through scale economy, specialized labor pooling, knowledge and technology spillover, and decreased transaction costs (Marshall 1890; Hotelling 1929; Czamanski and Ablas 1979; O'hUallachain 1984; Porter 1990; Feser and Bergman 2000; Feser and Lugar 2003). In our study, we focus more on the latter two aspects, technology spillover and transaction costs.

High labor mobility is one important reason for knowledge and technology spillover within an industrial cluster (Saxenian 1994; Fosfuri and Ronde 2003). The clustering of firms in a similar industry makes it easy for workers to change jobs for higher salary or promotion, as they do not have to travel long distances for job interviews and may not need to relocate homes after job transfer. Labor mobility then facilitates the exchange of information, technology and knowledge among different firms or organizations, raising the likelihood that newer ideas and products will be developed (Fosfuri and Ronde 2003). The high turnover rate in the Silicon Valley is one good example of technology spillover through labor mobility within industries (Saxenian 1994). This spillover effect, however, is argued to occur in circumscribed geographic areas and decays with increasing physical distance (Almeida and Kogut 1999).

Antonelli (2000) states that clustering of technological changes is attributable to the decreased transaction costs among economic agents. He argues that technological knowledge is fragmented among different institutions, and that more economic institutions bring out higher degrees of productivity. This process is facilitated by geographic proximity (Antonelli 2000). The benefits of decreased transaction costs could be further understood through the concepts of tacit knowledge communication and face-to-face contact (Antonelli 2000; Martin and Sunley 2003; Coenen et al. 2004; Zook 2004). In contrast to codified knowledge that could be learned through textbooks, learning of tacit knowledge often needs regular face-to-face interactions (Almeida and Kogut 1999; Sainsbury 1999; Desrochers 2001; Pinch et al. 2003). It is even argued that effective communication can only be transmitted via personal contact in limited spaces (Lawson and Lorenz 1999). There are several ways that face-to-face contact creates an economic advantage (Almeida and Kogut 1999; Sainsbury 1999; Desrochers 2001; Pinch et al. 2003). First of all, it allows more in-depth and speedy feedback among economic agents and facilitates collective learning (Lawson and Lorenz 1999). It also helps build trust and incentives in economic relationships, which further decreases transaction costs. Furthermore, it facilitates socialization within a professional network, where participants share a pool of technological knowledge, which further stimulates cooperation, competition or innovation (Storper and Venables 2004); therefore, Storper and Venables (2004) argue that face-to-face contact is central to the coordination of the economy, even in modern society that is experiencing tremendous reduction in transportation costs and more efficient communication.

Spatial clustering within the biotechnology industry, it is argued, results from the concentration of specific location factors, such as life science knowledge, venture capital availability, large pharmaceutical firms, entrepreneurship and urban diversity (Kenney 1986; Florida 2003; Audretsch and Stephan 1996; Feldman 2000). In the following sections, we will review the importance of these location forces.

Public Research Base

One highlighted characteristic of the biotechnology industry is its reliance upon public life science research base (Kenney 1986; Audretsch and Stephan 1996; McMillan et al. 2000; Dalpe 2003; Oliver 2004). Before the first biotechnology firm, Genetech, was established in San Francisco in 1977, practitioners of genetic engineering were almost without exception located around universities and research institutes (Kenney 1986). Since then many new biotechnology firms have formed and maintained strong ties with academic researchers. For example, the founding scientists of Genetech, Biogen and Immulogic all retained their university affiliations (Powell et al. 2002). In most cases, a university faculty's involvement in biotechnology businesses can only occur when their biotechnology firms are physically close to universities due to the tacit nature of knowledge (Audretsch and Stephan 1996; Feldman 2000).

Life science universities or institutions also provide a quality labor force (Kenney 1986; Lawson and Lorenz 1999; Feldman 2000). According to a survey of biotechnology industries in 2003, 55 percent of their labor force is comprised of life scientists, who usually hold a Ph.D. degree (United States Department of Commerce 2003). Apparently, areas that are geographically close to life science research institutions enjoy an advantage with better access to trained graduates or post-doctorate students. In reality, it has been reported that a large portion of biotechnology firms recruited their employees from the local labor market. In Boston, for instance, it was reported that 50 percent of biotechnology scientists in the industry came from local universities (Audretsch and Stephan 1996). University scientists often prefer to work locally after school or training because of family situations and local connections (Feldman 2000).

One important characteristic of life science research universities is that, as non-profit institutions, they are highly dependent on public funding, the largest amount being from the National Institute of Health (NIH) (Cooke 2003). Without substantive funding from NIH, it may not be possible for universities and institutions to make breakthroughs in the research of genetics and cellular processes (Cortright and Mayer 2002). However, NIH funding is highly competitive. Only those proposals that stand out in the evaluation of significance, approach, innovation, investigator, and environment will be funded. As a result, the amount of NIH funding has also been used to measure the strength of life science research capability (Cortright and Mayer, 2002).

Venture Capital

In the introduction section, we discussed the importance of venture capital for biotechnology firms. The focus here is on the geography of venture capital. Geographically, venture capital investments have been highly concentrated in space for decades (Green 2004; Gompers and Lerner 2006). Leinbach and Amrhein (1987) found that the Pacific Southwest, New England and Gulf Coast/Southwest regions attract the largest volumes of venture capital. In the late 1990s, more than one-third of venture capital was invested in the state of California (Gompers and Lerner 2001). In the biotechnology industry particularly, heavy investment of venture capital has been infused into California and Massachusetts, including San Francisco, San Diego and Boston (Cortright and Mayer 2002; Green 2004; Gompers and Lerner 2006).

Demand for venture capital from high technology firms has greatly shaped this spatial pattern (Florida and Smith 1993; Mason and Harrison 2003; Gompers and Lerner 2006). As discussed earlier, high technology firms prefer to locate close to each other to reap the benefits of clustering, including scale economy, specialized labor pooling, knowledge and technology spillover, and decreased transaction costs (Marshall 1890; Hotelling 1929; Czamanski and Ablas 1979; O'hUallachain 1984; Porter 1990; Feser and Bergman 2000; Feser and Lugar 2003). Geographic proximity between venture capital investors to biotechnology firms then are beneficial to both parties for the following reasons. First, the process of venture capital investment is highly selective and it is not uncommon for a single venture capital firm to receive thousands of funding requests (Jeng and Wells 2000). Besides firm-specific characteristics (Boehm and Schuehsler 2003), geographic proximity between firms and venture capitalists decreases information asymmetry and, thus, enhances the possibility of receiving funding (Gifford 1998). Second, when funding decisions are made, venture capitalists are usually engaged in their portfolio companies' management operations. Geographic proximity, or face-to-face contact, then reduces transportation and opportunity costs and facilitates transfer of technical skills and managerial experience between investors and investees (Mason and Harrison 2003). Studies have shown that venture capital firms favor investees close to their offices (Powell et al. 2002; Mason and Harrison 2003). The following is a quotation from an interview conducted by Zook (2002) that illustrates the importance of geographic proximity between investors and investees from an entrepreneur's perspective:

> *You can't be anywhere. To start companies you need to raise capital and investors would prefer to make investments locally because they have to spend time with the companies. I know some venture firms that say, 'if I can't drive there within an hour, I don't make the investment.' Especially in an early stage company, you want to have regular contact with the company, so access to capital drives a lot of decisions.*

This spatial concentration pattern may change over time. Myrdal (1957) proposed that capital investment is cumulative and that spatial unevenness deepens. Thompson (1989), however, provides a contrasting perspective. He argues that there might be a spatial diffusion or the trickle down effect in venture capital investment over time to peripheral areas to seek new investment opportunities. For instance, Green (2004) found a short period of venture capital diffusion after the dotcom bubble burst.

Entrepreneurship

Broadly speaking, entrepreneurial spirit is especially important for innovation and a knowledge-based economy. Schumpeter (1942) states that innovation and technological change of an economy comes from entrepreneurs. Following Schumpeter, it is argued that entrepreneurial spirit is vital to the effectiveness of markets and the increased productivity of the economy (Kirzner 1997; Jenner 1998). The finding that entrepreneurial spirit leads to greater economic growth has been well-established for technology innovations at not only the national level, but at local levels as well (Kreft and Sobel 2005).

In the biotechnology industry, securing funds from venture capitalists is not an easy task. Findings or brilliant ideas in university labs will not attract money and turn into products without a clear and thorough business plan. For a biotechnology firm, especially during its early stage of development, entrepreneurial skill and knowledge are needed to convince investors that a given proposal will be profitable (Witriol 2004). When the company gets started, entrepreneurs are mostly responsible for recruitment and management (Witriol 2004). Without talented entrepreneurs, life science findings may not be able to move out of university labs and survive in the competitive business environment.

In biotechnology, entrepreneurial spirit exists not only in venture capitalists and business managers, but also among academicians. University scientists can reap monetary benefits from intellectual property by starting businesses (Feldman 2000). One measurement of entrepreneurship in both academics and industry is patents, which are widely used to protect intellectual properties (Besen and Raskind 1991; Oliver 2004). The protection of scientific inventions through patents not only indicates interest in product commercialization but also signals involvement of scientists in commercial activities (Feldman 2000; McMillan et al. 2000; Dalpe 2003; Oliver 2004). For small firms, patenting is especially important, as they develop their intellectual property and often sell the technology to larger firms (Cortright and Mayer 2002). There have been some concerns over the use of patent data, for instance, in the way they are structured and collected (Desrochers 1998). It was also found that patents are often granted to venture backed companies early in their development and there might be multiple filings (Kortum and Lerner 2000; Neis 2007). Therefore, patents may not provide an accurate picture regarding innovative activities, but represent for innovation potentials (Desrochers 1998). Despite these concerns, the ability to patent is still perceived as a reflection of the most direct and visible outcome of the entrepreneurial process in innovation (Feldman 2000; McMillan et al. 2000; Dalpe 2003; Oliver 2004; Kreft and Sobel 2005).

Anchoring Effects from Large Pharmaceutical Firms

A large proportion of biotechnology firms are engaged in pharmaceutical research and development (United States Department of Commerce 2003). Many of them can move quickly during drug discovery, but when it comes to development, preclinical work, and human trials, they may not have sufficient financial or human resources to complete these tasks (Boehm and Schuehsler 2003). Alternatively, if they align themselves with large pharmaceutical firms that are regarded as anchors in a regional economy (Feldman 2002), they can get not only monetary supports, but also gain access to experienced executives in pharmaceuticals regarding product commercialization applications and procedures (Gwynne and

Page 2004); therefore, there is a recognized one-way technology and knowledge spillover from large pharmaceutical anchors to small biotechnology firms (Westlund 2000; Audretsch 2001).

This technology spillover exists even if there is no direct alliance between small biotechnology firms and large pharmaceutical companies (Westlund 2000; Audretsch 2001; Feldman 2002). Anchor firms usually provide a large pool of skilled labor and possess an established customer and supplier base (Feldman 2002). These may bring beneficial externality effects to small biotechnology firms if they are located close to anchor firms. Furthermore, when there is a regional anchor with a sophisticated expertise in new drugs, start-up firms may be more likely to specialize in that direction (Feldman 2002). Over time, a cluster may develop around a specialized expertise. Anchor firms may be beneficial to the regional innovative system as well, since large pharmaceutical firms are found to be more capable of establishing collaborations with research universities, fund their research projects and exploit their research results (Dalpe 2003). Consequently, innovation in science is encouraged and supported, and the knowledge and technology transfer from science to industry is facilitated. In empirical studies, the Milken Institute (2004) suggests that San Diego, for example, needs more biotechnology anchor firms to stabilize biotechnology industry development in the region.

Urban Attraction

Spatially the biotechnology industry is also found to be located near large population centers (Schweitzer et al. 2006). Numerous studies indicate that large urban centers are, in general, favorable places for industry development (Hoover 1948; Isard 1956; Isard et al. 1959; Swann and Prevezer 1996). Urban advantages include easier access to infrastructure, value chain linked industries, accounting and legal services, urban amenities, large pool of workers, and a population with high purchasing power (Hoover 1948; Vernon 1966).

In a modern society, the importance of backward and forward linkages and transportation costs in urban areas is fading (Gordon and McCann 2000; Storper and Venables 2004). However, the diverse social, economic and intellectual environment in large urban settlements still makes them centers of innovation and creativity (Florida 2003). In the creativity class argument, for example, Florida (2003) states that the emerging geography of the creative class is dramatically affecting the competitive advantage of regions across the United States. The core creative class includes scientists, engineers, architects, educators, writers, artists, and entertainers. The creative class also includes a broader group of creative professionals in business, finance, law, health care and related fields. The more diverse the urban center is, the greater the advantages it enjoys in economic development.

Storper and Venables (2004) offer further explanations on how highly populated areas possess an economic advantage in a modern society. They argue that, urban areas, with higher population densities, enjoy an advantage from geographical proximity, or face-to-face contact among the different agents in the economic production. Face-to-face contact facilitates socializing, learning, and communication between workers; it also helps build trust in economic relationships and provides psychological motivation (Storper and Venables 2004).

HYPOTHESIS

Informed by literature, we expect that biotechnology venture businesses that are financed by venture capital investment have similar demands for specific locations as the biotechnology industry as a whole. Therefore, we developed the following hypotheses regarding the spatial clustering of biotechnology venture businesses. We hypothesize that there are more biotechnology venture businesses in metropolitan areas where there is 1) a concentration of life-science research 2) proximity to venture capital providers 3) entrepreneurial spirit 4) closeness to large pharmaceutical companies and 5) an urban agglomeration economy.

DATA AND VARIABLES

The number of biotechnology venture businesses for each of 370 metropolitan areas in the U.S. is the dependent variable in this study. Ten independent variables are used as proxies for non-commercial life science research base, venture capital providers, entrepreneurial spirit, anchor impact from large pharmaceutical companies, and urbanization economies.

Life science research base is measured through five variables: the number of research universities with active life science research, the number of life science research institutes, the number of hospitals that are active in life science research, the amount of NIH funding grants between 2003 and 2005, and the number of life scientists in 2006. Data came from NIH website and the Bureau of Labor Statistics. Data on the number of venture capital providers came from the MoneyTree survey database in 2006. The majority of venture capital providers are professional venture capital companies and the rest are investment banks, large pharmaceutical companies, government agencies, universities, and even individuals. Entrepreneurial spirit is measured by patents and patent holders. These data were collected through a keyword search of "biotechnology" in the abstract section between 1995 and 2005 from the U.S. Patent and Trademark Office. Although our search does not exhaust all patents related to biotechnology, it provides a good representation of the patents that are directly applied in biotechnology industry. Large pharmaceutical firms or anchor establishments refer to those companies with 500 or more employees. This number comes from the United States Small Business Administration, where the standard size for small business in manufacturing is less than 500. Data came from the 2005 County Business Patterns. The last variable is metropolitan population. Data for metropolitan areas came from the 2000 census. All data were integrated into the geographic information system and aggregated into 370 metropolitan areas according to the 2003 Census definition. For convenience, definitions of all variables are provided in Table 2.

METHODS

This research employs several methods to investigate the importance of various location forces on the geographic clustering of venture capital financed biotechnology firms. Examination of the extensive literature on the subject of biotechnology firms provides hypotheses and supports for conclusions. New empirical analyses add to this knowledge base.

Statistical descriptions and tests were performed on the dependent and independent variables. Correlation analyses among all variables were applied and a principal component analysis (PCA) was conducted to reduce data redundancy. Location factors generated from PCA results then became the new independent variables for further regression analysis. A Poisson regression was then performed to estimate the counts of biotechnology venture companies in each metropolitan area. The same technique is used by Schweitzer et al. (2006). We assume that the probability (p) of having a certain number of biotechnology companies (k) in each metropolitan area is

$$p(Y = k \mid X_1, X_2, ..X_n) = \frac{e^{-\mu(X)}\mu(X)^k}{k!},$$

$k = 0, 1, 2, 3, \ldots$

For the expectation μ, $\log(\mu) = b_0 + b_1 * X_1 + b_2 * X_2 + \ldots + b_n * X_n$

and $\mu = \exp(b_0 + b_1 * X_1 + b_2 * X_2 + \ldots + b_n * X_n)$.

In the above equation, $X_1, X_2, \ldots$ and X_n refer to the location factors from PCA results. K refers to the number of biotechnology ventures each metropolitan area hosts and e is the constant in a natural logarithm. The maximum likelihood method was used to estimate the parameters of the regression model for $\log(\mu)$.

RESULTS

Descriptive Statistics

Table 3 provides some descriptive statistics of dependent and independent variables in the study. All but the metropolitan population variable are highly skewed. This suggests that both biotechnology venture activities and biotechnology related location factors are highly concentrated in very few metropolitan areas.

Table 2: Definition of Variables (spatial unit: metropolitan)

Variables	Definition
Dependent Variable	
Biotechnology Ventures	Number of biotechnology firms that received venture capital investments in 2006
Independent Variables	
Life science research universities	Number of universities active in life science research between 2003 and 2005
Life science research institutes	Number of institutes active in life science research between 2003 and 2005
Hospitals with life science research	Number of hospitals active in life science research between 2003 and 2005
NIH	Amount of NIH grants between 2003 and 2005
Life scientists	Number of life scientists in 2006
Venture capital providers	Number of venture capital providers to biotechnology firms in 2006
Patent	Number of patents between 1995 and 2005
Patents inventors	Number of patent holders between 1995 and 2005
Pharmaceutical Anchors	Number of large pharmaceutical firms with over 500 employees in 2005
Population	Metropolitan population in 2000

Correlation Results

The results of correlation analyses among dependent and independent variables are presented in Table 4. The dependent variable, number of biotechnology ventures, is most highly correlated with the number of venture capital providers (r=0.84), the amount of life science research institutes (r=0.80) and the amount of life scientists (r=0.79). Its relationship with other variables is positive and significant.

The independent variables are correlated within themselves as well. The life science research university variable is highly related to the metropolitan population variable (r=0.90), the pharmaceutical anchor variable (r=0.81), the venture capital provider variable (r=0.79), and the hospital variable (r=0.78). The life science research institutes variable is highly correlated with the life scientist variable (r=0.84) and venture capital provider variable (r=0.76). The hospital variable is also highly correlated with the population variable (r=0.76). There is high positive correlation coefficient between the venture capital providers variable and the pharmaceutical anchor variable (r=0.74) as well. Furthermore, there is no surprise that patent variable is highly correlated with the patent inventor variable (r=0.84). High correlation coefficients among all variables further suggest that there is a network of resources in biotechnology innovative activities.

Table 3: Descriptive Statistics

	Mean	Median	St. dev	Kurtosis	Skewness	Mini	Max
Biotechnology Ventures	0.78	0	3.93	81.01	8.30	0	48
life science research universities	1.33	0	3.47	95.48	8.33	0	48
life science research institutes	0.60	0	2.68	67.38	7.62	0	31
Hospitals with life science research	0.26	0	1.04	90.11	8.14	0	14
NIH (in millions)	194.97	0	722.82	53.68	6.38	0	8375
Life scientists	256.86	0	988.20	54.03	6.75	0	10700
Venture capital providers	0.68	0	3.14	72.64	7.88	0	36
Patent	0.10	0	0.61	193.24	12.52	0	10
Patents inventors	0.26	0	1.34	76.74	8.02	0	16
Pharmaceutical Anchors	0.20	0	0.83	108.50	8.89	0	12
Population (in thousands)	5797	4162	6529	8.84	2.64	502	35874

Table 4: Correlation Results

		1	2	3	4	5	6	7	8	9	10	11
Biotechnology Ventures	1	1	0.55	0.81	0.40	0.66	0.79	0.84	0.54	0.69	0.51	0.46
Life science research universities	2		1	0.68	0.78	0.56	0.44	0.79	0.35	0.32	0.81	0.90
Life science research institutes	3			1	0.51	0.69	0.84	0.76	0.44	0.48	0.55	0.65
Hospitals with life science research	4				1	0.38	0.31	0.62	0.25	0.22	0.71	0.76
NIH	5					1	0.68	0.56	0.31	0.38	0.41	0.50
Life scientists	6						1	0.60	0.38	0.49	0.32	0.48
Venture capital providers	7							1	0.61	0.66	0.74	0.73
Patent	8								1	0.84	0.37	0.37
Patents inventors	9									1	0.39	0.33
Pharmaceutical Anchors	10										1	0.76
Population	11											1

Note: all significant at 0.01 level

PCA Results

Due to the high correlation among independent variables, a principal component analysis (PCA) was conducted to overcome the multicollinearity problem and to reduce data redundancy. PCA produced three rotated factors, which represented 92 percent of all variance in the original ten independent variables. Factor loading of each independent variable on the new factor are presented in Table 5. In the first factor, which captures 70 percent of all the variance among the independent variables, the highest loading comes from the life science research universities variable. Three other variables, hospitals with life science research variable, metropolitan population variable and pharmaceutical anchors, also have large contributions. Therefore, the first factor represents an urban factor with strong life science education, hospital research and pharmaceutical anchoring effect. In the second factor, the highest loading comes from the life scientists variable, science research institutes variable and NIH variable. This factor represents a strong life science research base. In the third factor, highest loading comes from the patent inventor variable and patent variable. It also has a contribution from the venture capital provider variable. This factor could be interpreted as an entrepreneurship and venture capital factor.

Table 5: Principal Component Analysis Results

	Factor1	Factor2	Factor3
Life science research universities	0.742	0.079	-0.055
Hospitals with life science research	0.704	-0.030	-0.068
Population	0.693	0.083	-0.028
Pharmaceutical Anchors	0.692	-0.078	0.099
Life scientists	-0.114	0.736	0.027
life science research institutes	0.164	0.596	0.016
NIH	0.105	0.519	-0.026
Patents inventors	-0.064	0.060	0.767
Patents	0.027	-0.048	0.752
Venture capital providers	0.424	0.156	0.313

Poisson Regression Results

As the dependent variable in this study is highly skewed and most metropolitan areas possess little or no biotechnology venture activities (Table 3), the use of Ordinary Least Square regression on such a distribution will produce biased estimates and invalid inferences (Maddala 1983). Alternatively, a Poisson regression was performed (Schweitzer et al. 2006). Results from Poisson regression are presented in Table 6. With no surprise, all three factors have significant and positive impacts upon the dependent variable. This result leads to the conclusion that biotechnology venture activities are located where there are large urban centers with strong life science education, hospital research and pharmaceutical anchoring effect, where there is a strong life science research base, and where there is strong entrepreneurship and a large number of venture capital providers.

CONCLUSIONS AND DISCUSSIONS

This study investigated the spatial clustering of biotechnology firms that are financed by venture capital. All proposed hypotheses are supported through statistical analysis, indicating that biotechnology venture activities are clustered in urban centers, where there is a strong life science research base, a large pool of life scientists, large pharmaceutical firms, many venture capital providers and a strong entrepreneurial spirit. This conclusion on the biotechnology venture firms is consistent with studies on the biotechnology industry as a whole (Schweitzer et al. 2006).

There is no surprise that biotechnology venture activities are located in urban centers. This finding is consistent with Schweitzer et al. (2006) and gives further support for the creative class argument (Florida 2003). With a large concentration of talent, technology, and tolerance, a favorable environment exists for new ideas and technological breakthroughs (Florida 2003). An urban environment also provides more geographic proximity between various economic agents (Storper and Venables 2004), facilitating the communication of tacit knowledge in biotechnology industry (Dalpe 2003).

Biotechnology venture activities are also found to be located close to a strong life science research base with a large pool of life scientists. While previous studies have focused on the attraction of research universities (Schweitzer et al. 2006), we also included life science research institutes and hospitals. Besides the strong statistical evidence of co-location between life science research universities and biotechnology firms at metropolitan level, detailed examination of firm locations and firm founders provide additional insights. For instance, within 5 miles, there are 19 biotechnology venture companies around Stanford University, 32 companies around MIT and Harvard, and 33 companies around California State University at San Diego. This geographic proximity enables university faculties to be directly involved in biotechnology businesses.

Our hypothesis that proximity to venture capital providers increases the number of biotechnology venture businesses is supported by statistical results as well. Venture capital is not only important in terms of financial support, but also important in the sense that venture capitalists provide insights, managerial skills and entrepreneurial spirit to newly established biotechnology companies. This proximity encourages people with ideas to communicate and collaborate with people with fiscal resources and business expertise. It is important to note that, in reality, most biotechnology venture firms receive investment from multiple sources. In such cases, there is almost always one local venture capital firm involved in the new biotechnology business. One biotechnology firm, Microbia, Inc., for instance, located in Cambridge, received 75 million venture capital investments from six investors in the first quarter of 2006. Among five identified investors, one is located in Cambridge, one in Dallas, one in Waltham, MA, one in Boca Raton, FL, and the other one in New York. The finding is also consistent with the co-investment argument in the studies on venture capital, where it is found that if a firm secures investment from a lead investor, other investors would follow and infuse more money into the investee company, resulting in an accumulated money influx (Timmons and Bygrave 1986; Powell et al. 2002).

The hypothesis that entrepreneurial spirit is important for biotechnology venture activities is also supported. Using patents and patent holders as proxies for entrepreneurial spirit, this study finds that when there are more patents filed in biotechnology and/or more patents holders in biotechnology, there are more biotechnology venture firms. Entrepreneurial spirit is one key link to attract venture capital

Table 6: Poisson Regression Results

Dependent variables	Estimates	Chi-square	Pr > ChiSq
Factor1 - urban factor	0.139	59.72	<0.0001
Factor2 - life science research factor	0.401	479.65	<0.0001
Factor3 - entrepreneurship factor	0.243	215.46	<0.0001

investment and lead the scientific findings into commercial activities.

This study also finds strong support for the anchor effect from large pharmaceutical companies. Large pharmaceutical companies have more insights regarding the direction of the industry in the long run, provide a large pool of skilled labor, subcontract research to small biotechnology firms, and even provide venture capitals to firms or fund university research projects (Westlund 2000; Audretsch 2001; Feldman 2002). Furthermore, large pharmaceutical companies provide training for employees who become potential entrepreneurs in biotechnology companies.

We hope that our research has helped to elucidate the geographic location of biotechnology firms that are highly dependent on venture capital investment and the role that life science research base, proximity to venture capital providers, large pharmaceutical firms, entrepreneurial spirit, and urban diversity play. It remains for future research to investigate how the spatial distribution pattern has changed over time and whether venture capital backed firms behave differently from non-venture capital backed firms.

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