Organizational and Institutional Genesis:
The Emergence of High-Tech Clusters in the Life Sciences

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Please note: the figures need to be viewed in color.

Abstract

Most research on the emergence of high-tech clusters samples on successful cases, and works backwards to trace a narrative, often highlighting the role of specific individuals or groups. Our approach begins with the formation of a new field - - biotechnology in the late 1970s and early 1980s, and follows the field to the present. We emphasize the sequence of network formation, and the importance of organizational diversity and catalytic organizations that provide relational and normative glue. We examine eleven regions in the U.S. that were rich in resources - - ideas, money, and skills - - that could have lead to the formation of life science clusters. Three of the communities formed robust groupings, but most did not. Although local details are always relevant, our argument transcends the nuances of history in each community to specify the processes and mechanisms that foster growth. The necessary conditions are a diversity of for-profit, nonprofit, and public organizations, a local anchor tenant, and a dense web of local relationships. These features make possible cross-network transposition, whereby experience, status, and legitimacy in one domain are converted into 'fresh' action in another. The core takeaway is that access to a diversity of partners is more valuable than control over a few. The argument does not hinge on specific types of organizations or ingredients; indeed, it is general enough to accommodate multiple pathways.

1) Introduction: Where Do Organizations and Institutions Come From?

Much of the social science literature on institutions resembles a play that begins with the second act, taking both plot and narrative as an accomplished fact. Very little research asks how a play comes to be performed, or why this particular story is being staged instead of some other one.[1] Young (1998) observed that most social scientists go about their work only after the dust has settled. We thus miss out on seeing where the dust came from or how it settled. Even more important, we may not notice that things are continually moving about, being reshuffled to be used in different ways. The social world is littered, as Meyer and Rowan (1977: 345) remind us, "with the building blocks for organizations", and this 'debris' can be used to assemble and create new combinations.

Individuals construct organizations with the social and technical tools they have at hand, fashioning the future with the available tools of the past and present (Stinchcombe, 1965). A critical challenge, then, is to explain the genesis of organizations and institutions, particularly why specific elements combine to make distinctive configurations possible only at particular points in time and space. Our goal in this chapter is to tackle this question in the context of the development and growth of regional life science clusters in the United States.

Most research on institutions works backward from contemporary cases to develop a story about how institutions were purposefully created or rationally chosen. This analytic strategy unites actor-centered functionalist accounts by rational choice scholars in

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[1] Numerous scholars have lamented that the origins of institutions have been largely opaque to social scientists. Kreps (1990: 530) remarked that whereas the economics literature emphasizes the effects of institutions, it "leaves open the question, where did institutions come from?" In an assessment of the sociological literature, Barley and Tolbert (1997) underscored the neglect of how institutional arrangements are created. More recently, in a comprehensive review of organizations research, Greenwood et al. (2008: 26) conclude that "institutional studies have not been overly concerned with how institutions arise."

economics and political science with organizational and sociological analyses that highlight the social and political skills of institutional entrepreneurs.[2] In both forms of explanation, scholars connect the actions of designers to the functions or interests served by institutions (Pierson, 2004, Ch. 2; Hardy and Maguire, 2008). In these accounts, institutions are often portrayed as a solution to collective action problems that enables participants to realize gains from coordination. The challenge with this inventive work is that the results obtained often seem to be the only possible solution. Unsuccessful efforts are rarely examined, and the necessary functions that are asserted always seem to neatly explain the presence of particular institutional structures or policies.

The limitation of such functional or entrepreneurial accounts is that they generally begin with existing practices and activities. Such a retrospective view largely predetermines the outcomes, rendering social and economic change either inevitable or driven solely by external forces. Moreover, there is an implicit assumption of continuity between those who labored to produce institutional arrangements and those who benefit from them. Stinchcombe (1968) has emphasized, however, that the processes that generate an institution are often different from those responsible for its reproduction. Very different sets of activities and participants are likely to be involved in the creation, reproduction, and disruption of institutions (Lawrence and Suddaby, 2006). We therefore need arguments that attend to both genesis and change and posit similar mechanisms to account for each.

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[2] Leaving aside important concerns about sampling only successful cases, the burgeoning organizational literature on institutional entrepreneurs portrays these people as uncommonly muscular, or endowed with qualities that normal individuals are lacking (R. Meyer, 2006; J. Meyer, 2008). These "champions" are then contrasted with the rule-following rank and file. Powell and Colyvas (2008) have argued that heroes and cultural dopes are a poor representation of the gamut of individuals who populate organizations, and that we need a richer, more relational portrait of individuals and a contextually fuller account of how institutions and fields develop.

To be sure, emergence and transformation are thorny questions. Nonetheless, a number of scholars have begun to tackle these concerns and make progress in accounting for when organizations and institutions arise and how they are transformed (Fligstein, 2001; Pierson, 2004; Thelen, 2004). This chapter utilizes our research on the spatial aspects of the life sciences to join the discussion. Specifically, we seek to explain a critical feature of the emergence and development of the biotech field — geographic propinquity.

Today's pattern of pronounced agglomeration was not at all obvious, given initial founding conditions. Distinctive responses to scientific discoveries developed in particular locales, which in turn became self-reinforcing and resilient. Common expectations and knowledge evolved through on-going contacts, and shared conventions were sustained by members of local technological communities. In this sense we treat a geographic cluster as an entity that became institutionalized. Decisions to locate in particular regions, invest resources, and build a technical community generated increasing returns as a wider number of participants followed suit, developed local norms that guided interaction, and subsequently elaborated on these practices, becoming a community with a common fate. Identities were learned and interests were forged through interaction, producing feedback dynamics that increased interdependence and consensus among the varied participants. Consequently, we argue that the development of a regional technological community offers an apt opportunity to study the origins of institutions. Moreover, this pattern of agglomeration affords comparisons between locales that evolved into productive communities and those that did not.

2) The Puzzle of Space

The pronounced spatial agglomeration of the commercial field of the life sciences in the United States represents an interesting puzzle. Today, roughly 50% of the U.S. companies in this industry are located in only three regions — the San Francisco Bay Area, Cambridge and Boston, Massachusetts, and North San Diego County. As the field developed in the 1970s and 1980s, two resources were critical to fuel the formation of new science-based companies: money and ideas, both of which are highly fungible and arguably very mobile. Yet the new industry developed deep roots in just two locations and then spread to a third, and only these clusters have evolved to become highly interactive centers for biomedical science and commerce.[3]

Timing obviously matters for success; being first out of the gate can confer considerable advantage. The Bay Area took the initial regional lead in the 1970s and 1980s. Boston came later and is today arguably a more intensive and spatially denser cluster, and San Diego came third (Powell et al., 2002; Owen-Smith and Powell, 2004). More important, as illustrated in the previous chapter, companies in the three established clusters have a mix of founding models, suggesting that a simple copying-and-increasing-returns story is insufficient. Different social, political, and economic circumstances typify these three regions, so the learning and coordination effects that helped reproduce the

[3] One might also ask why the early development of the field took place largely in the United States, even though the relevant scientific knowledge was abundant in many leading research centers of Europe and the United Kingdom. Some who have asked this question stress the favorable public policy in the U.S. that supported intellectual property rights for scientific ideas, a financial environment in which equity investments in science and technology companies were encouraged, and private universities interested and engaged in transferring public science into commercial application (Wright, 1994; Coriat and Orsi, 2002; Rhoten and Powell, 2007). To be sure, the U.S. had these endowments to a much more considerable extent than did their European or British counterparts, who came to the field much later. But cross-national comparative analyses still beg the question of why the new field developed in so few areas within the United States, the issue that we consider here.

early successes of these districts stem from divergent origins (for more general reflections on this point, see Mahoney, 2000; Pierson, 2000).

Our analysis reveals that although timing is important to understanding development, clear differences exist between nascent and established regions. Despite divergent origins and founding models, the three established regions display similar patterns of organizational diversity and network configurations that sustained regional activity (Whittington, Owen-Smith and Powell, 2009). But at the dawn of the new industry, it was not obvious that the Bay Area, Boston, and San Diego were necessarily the most or the only propitious venues for the field to emerge.

Although many might think of biotech's development in the Bay Area as a Silicon Valley story, the early location for firms was in South San Francisco and in Emeryville in the East Bay, not in the heart of the information and computer technology world in Santa Clara and Sunnyvale. That early footprint continues today. Biotech blossomed in Cambridge, Massachusetts, in Kendall Square, an area that as late as 1985 was riddled with decaying textile factories. Kendall Square now consists of glass biotech laboratories "as far as the eye can see" (Goldberg, 1999:1). In the 1980s, San Diego was home to retired naval personnel and a haven for tourists and fishermen rather than a beacon for high-tech companies. Torrey Pines Road in La Jolla, the epicenter of "biotech beach" in San Diego County, was more widely known for its golf courses and gorgeous beaches than for its laboratories. Interestingly, at the individual firm level, the odds of success for new entrants in the established clusters do not differ from the life chances of well-connected firms located elsewhere in the U.S. (Whittington et al, 2009). The cluster dynamics are an emergent collective phenomena, as the three regions have become centers where the bar is very high and firms must “run faster just to stay in place.”

The pattern of strong geographic agglomeration is also peculiar in that the basic science discoveries that led to the field’s formation were developed in a number of leading research universities and government institutes in the United States[4] and around the world. To be sure, venture capital firms were concentrated in three regions - - New York City, the San Francisco Bay Area, and, later, Boston (Powell et al., 2002; Chen et al., 2009). But financing for biotech start-ups was available not only from venture capital. Many other financial institutions – investment banks, insurance companies, university endowments, and multinational pharmaceutical and healthcare companies – located throughout the U.S., the U.K., Switzerland, Germany, and Japan joined in bankrolling the industry. The standard explanation for geographic propinquity in high technology sectors stresses spillovers from public science and increasing returns from initial idiosyncratic events (Jaffe, 1986; Krugman, 1991; Arthur, 1994). The path-dependent processes that stem from first moves have a tendency to “lock in”, and thus early advantages become magnified. But spillovers and increasing returns are only a partial answer, as they don’t explain why an event was a catalyst in one setting, but not in another with similar circumstances. Moreover, in the “successful” cases we discuss below, flexibility, switching, and disruption were common, whereas lock-in typified the regions that did not flourish.

[4] Zucker, Darby and Brewer (1998: 293) reported that there were 20 “top quality universities” with very high reputational scores in the biological sciences on the 1982 National Research Council survey of departments. These universities were located on the east coast in Cambridge, Boston, New Haven, New York City, Philadelphia, Baltimore, and Durham; in the Midwest and mountain states in Chicago, Madison, and Denver; and on the west coast in Seattle, San Francisco, Berkeley, Palo Alto, Pasadena, Los Angeles, and La Jolla. Zucker et al (1998:295) also present a U.S. map of active life science ‘star’ researchers in 1990, which shows the heaviest concentrations in the Washington-Boston corridor, the San Francisco Bay Area, Los Angeles, and in the Midwest at Big Ten campuses.

More critical for the theoretical issues we are tackling, numerous nascent clusters formed in the United States, each of them with abundant endowments that could have evolved into a robust regional community. A Brookings Institute study (Cortright and Meyer, 2002) that examined regional patterns in life science intellectual capital, using a count of biological patents by pharmaceutical and biotechnology companies over the period 1975 to 1999, found notable stocks of knowledge in many locations. We summarize this data in Table 1; note that the New York and Philadelphia areas were the initial leaders in number of patents, with the Bay Area third, followed by Boston, Washington, and Los Angeles. San Diego had no stock of patents in the 1970s.

Looked at in terms of organizational resources, the New York City metropolitan area and central New Jersey are both home to leading universities, among them Columbia, NYU, Rockefeller, and Princeton, many wealthy financial institutions, and numerous large multinational pharmaceutical companies. New York City also has an exceptional array of top-tier research institutes and hospitals, such as Sloan Kettering and Cold Spring Harbor. The Philadelphia metropolitan area had the University of Pennsylvania, the Wistar Institute, the Fox Chase Cancer Center, and the Children's Hospital of Philadelphia, all important public research organizations, and a number of major pharmaceutical companies as well. Indeed, Philadelphia was historically "the cradle of pharmacy" in the U.S. (Feldman and Schreuder, 1996:841). In Washington, D.C., and Bethesda, Maryland, the National Institutes of Health (NIH) constitute the world's most comprehensive research center for the life sciences. Johns Hopkins University in Baltimore has *the* preeminent medical school in the nation, and is the leading recipient of NIH funding by a wide margin. Los Angeles, where one of the earliest and most successful biotech companies, Amgen, was founded in 1980, had ample scientific resources at CalTech and UCLA, but a cluster never cohered there. Indeed, by the 21st century, Amgen had relocated some of its research activities to Kendall Square in Massachusetts and to its new subsidiary, Tularik, in South San Francisco.

[Table 1 here]

In areas where there was no strong corpus of intellectual property, other resources could have sparked the emergence of biotech. Houston, Texas had financial wealth, several medical schools and universities, and M.D. Anderson, a path-breaking research hospital. The Research Triangle in North Carolina brought together three major research universities and public provision of land for an incubator that attracted multinational pharmaceutical corporations such as Glaxo. In Seattle, computer technology millionaires tried to combine the research prowess of the University of Washington, with its major medical school, and the Fred Hutchinson Cancer Center to start a biotech cluster there. All of these areas saw the spawning of some new science-based biotech companies in the 1970s and 1980s, and each developed various public-private initiatives to build a biotech community. But none of these areas has yet to develop an interactive community of firms and public research organizations that mirrors the dynamics of the Boston, San Francisco Bay Area, or San Diego regions. We can also look beyond the nascent clusters to other areas rich with endowments that never quite catalyzed. For example, Atlanta, Georgia, has the Centers for Disease Control, research universities Emory and Georgia Tech, a wealthy corporate sector keen to invest in new technology companies, and a well-educated middle-class labor force. Cleveland, Ohio, was an early home to venture capital, and the

Cleveland Clinic is one of the premier research hospitals in the nation. Neither city today has significant activity in biotech.

Thus the questions that animate this chapter: Why do we see so pronounced a pattern of spatial agglomeration in the emergence and formation of new science-based companies and the creation of a new field? Why does one community with a particular set of participants form and not another? Why did very disparate organizations come together to form clusters in these three locales? What was the developmental sequence that lead to the institutionalization of biotech in these three clusters?

3) Theoretical Perspective: Multiple Networks and Transposition

Many narratives describing the emergence of the life sciences stress the scientific and technological revolution ushered in by a series of remarkable breakthroughs in molecular biology. Such arguments highlight the discontinuity between the older tools of drug discovery, based in organic chemistry, and the novel methods of molecular biology and genetics (Gambardella, 1995; Galambos and Sturchio, 1998; Henderson, Orsenigo, and Pisano, 1999). This Schumpeterian portrait of a process of creative destruction captures in broad brushstrokes the changed technological landscape, but this account does not illuminate where the winds of change would be the strongest.

In the previous chapter, our analysis of the links between science and the economy examined the ramifying effects of scientific and technological change, which lead to the creation of new roles and amphibious identities, novel organizational practices, and the invention of the science-based firm. Here we take the next step and argue that changing logics of network affiliation explain both the emergence of organizations and the formation of regional communities. At the core of these developments, we suggest, were new conceptions of both science and finance, which were initially viewed as aberrant but later seen as normal. Central to this transformation was not just statistical reproduction in the sense that something unusual diffused and became widespread, but transposition: the initial participants brought the status and experience they garnered in one realm and converted these assets into energy in another domain.

Two features and one mechanism are central to our argument. The core factors are 1) a diversity of organizational forms and 2) the presence of an anchor tenant, and the mechanism is cross-realm transposition. These two factors increase the possibility and salience of transposition, so that they have consequences that are linked to, but more consequential than, the initial conditions (Abbott, 1990; Mahoney, 2000).

Organizational diversity provides a rich soup in which practices, strategies, and rules can emerge. The presence of multiple organizational forms suggests diverse selection environments. This heterogeneity may give a community the resiliency to survive downturns in any one population. But more important, a diversity of forms can generate divergent standards and multiple kinds of rules, resulting in competing criteria for gauging success (Grabher and Stark, 1997; Boltanski and Thévenot, 2006). The formation of ties in any one domain becomes influenced by structural position in another, as well as by the categories and cognitive classifications that typify each form. These classifications help define eligibility for participation, but don't dictate participation itself. Field formation in the context of organizational diversity means that relationships are very much entwined with competing status and identity considerations.

During a period of ferment, some organizations have a foot in several doors, and they may develop the ability to sustain themselves by toggling between different evaluative criteria (Brown and Duguid, 2001). Rather than experiencing diversity as flux and confusion, firms can produce new recipes and standards (Lane and Maxfield, 1996; Stark, 2001). Here the categories and classifications familiar to institutional analysis are not yet taken for granted, but are under construction. This emergent process involves search, sense-making, and luck (Weick, 1993; Powell and Colyvas, 2008).

Rather than unleashed, purposive, instrumental behavior of the kind invoked in agentic stories, we draw attention to an assembly process in the context of organizational diversity, one that resembles micro-analyses of "cognition in the wild" (Hutchins, 1995) or "on the hoof category construction" (Clark, 1993). In this context, recipes and standards emerge within a local community, where interaction among participants both refines practices and facilitates their internalization.

A second crucial feature is the presence of an anchor tenant. The anchor becomes a scaffolding that, either intentionally or unexpectedly, assists subsequent connections and field formation. The anchor tenant is not disinterested, in the sense of being neutral, but it neither directly competes with nor dictates to the other organizations that inhabit the community. We think of anchors in relational terms as a well-connected organization – whether a university, nonprofit institute, venture capitalist, or a firm, which mobilizes others and fosters collective growth. But when central organizations insist that others play only by their rules and do not engage in collective problem-solving, they become "800-pound gorillas" rather than anchors.

The organizations that we dub anchor tenants, drawing on the literature in industrial economics (Pashigian and Gould, 1998; Agrawal and Cockburn, 2003; Feldman, 2003), occupy positions that provide them with access to diverse participants and the legitimacy to engage with and catalyze others in ways that facilitate the extension of collective resources. This ability to span disparate domains has proven valuable in high-velocity environments where resources, power, and wealth are constantly shifting (Cohen, 1981; Sabel, 1990; Hedlund, 1993). In the real estate literature, an anchor tenant is typically the large national department store in a shopping mall that pulls in customers who also patronize smaller, more specialized shops (Eppli and Shippling, 1995). In our reformulated use, the anchor tenant sustains multiple principles of evaluation — in this case, world-class science, biomedical discovery, unmet medical need, or financial opportunity, and in so doing continually recombines and repurposes diverse activities.[5] Relational feedback then generates competitive dynamics as more extensive networks of affiliation are formed, and many participants benefit from the productive friction of cross-fertilization that arises from diverse kinds of affiliations with different partners (Powell et al., 1996; Hagel and Brown, 2005). Thus, anchor tenants both mobilize a community and serve as a guardian of diverse organizing principles. In contrast, 800-pound gorillas dominate activity and attempt to control the terms of engagement.

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[5] In bio-ecology, the concept of keystone species is widely used to point out the crucial importance of a specific species in maintaining the organization and diversity of an ecological community (Paine, 1969; Macarthur, 1972). Although the term has been used so broadly it has invited criticism, the core idea that one species can have a disproportionate effect on its many associates has clear parallels with our use of the anchor tenant idea. Specifically, two uses of the concept - - keystone hosts and keystone modifiers - - seem most relevant (Mills, Soulé, and Doak, 1993: 220). The hosts, typically plants and fruits, are pollinators and dispersers. Modifiers, of which the classic case is the beaver, alter hydrology and productivity on a wide scale. Beavers transform temperate forests into wetlands, creating a platform that attracts and supports a diverse web of life. The anchor tenants we analyze are pollinators that create an open platform which others can build on for community-wide benefit.

Brokerage and diversity alone are usually not sufficient to produce institutional transformation, however. Some form of cross-network alignment is needed in which ideas and models are transposed from one domain to another. To be sure, most cross-network transpositions are selected against, because they are likely to fail from at least one perspective, relative to the status quo. The more an idea or activity is multi-purpose, the more perspectives from which it can be judged inferior. Indeed, participation in multiple activities is sometimes viewed as an indication of lack of expertise in each, even when this is not true (Zuckerman et al., 2003). But as we saw in the previous chapter, in those unusual circumstances when a cross-network transposition is absorbed by the social system, it creates a new channel that permits activities from one domain to cascade into others, possibly with reorganizing or tipping potential. Feedback from cross-network efforts generates new potentialities, whether in the form of tipping, converging, or descending into chaos.

When one or more social relations are transposed from one network to another and mix with the relations already present, raw material is created for invention. But recombination and interaction are only the first steps. As new careers, practices, ideas, and organizational models cross significant boundaries, they must congeal to produce novel institutional practices and forms in order to have potent ramifications. The challenge is to understand the feedback mechanisms that reinforce these new combinations. How do links that become routine in a statistical sense cascade into normative understandings in the prescriptive sense, so that participants in a dense network recognize these categorical patterns and start to sustain and reinforce them? As the connective tissue among participants grows, standards develop; even those not involved in their creation aspire to them, and through careers and mobility they transform local standards into more public goals. Cross-realm transposition facilitates the absorption of practices, goals and status into a new domain. This transposition is made possible by a network of affiliations that bridge social worlds, which were formerly not connected. At a basic level, our argument is relational. Our account is sensitive to local characteristics and the details of history that characterized each region, but transcends the cases to make a more general claim that accounts for emergence across multiple particular pathways.

4) Data and Methods

Biotechnology is a field in which all the relevant capabilities were rarely found under a single organizational roof (Powell and Brantley, 1992). The field had its origins in university labs, where research was supported by decades of substantial government investment in R&D. As the new field developed, universities, nonprofit research centers, research hospitals, and startup companies all had a hand in moving discoveries from the lab into clinical development (Audretsch and Stephan, 1996; Zucker and Darby, 1996). Large multinational pharmaceutical corporations moved into the field about a decade after its start, as they came to appreciate the merits of new means of targeted drug discovery (Henderson and Cockburn, 1996; Malerba and Orsenigo, 2002). On the financing side, venture capital firms began to bankroll many start-up companies. Until very recently, however, these diverse types of organizations were not located in physical proximity to one another, so few regional clusters had sufficient access to all of these varied resources; hence there was considerable need for both local and distant affiliations.

This diversity in an emerging field represents more than just novel combinations of organizations. The skills associated with the different parties were distinctive and, as we elaborated in chapter thirteen, different forms of recombining and repurposing helped to generate the first science-based companies with these new capabilities. The participants in the industry became embedded in multiple networks of strategic alliances and gained competitive advantage from continuous scientific, technical, and market innovation (Powell et al., 1996). Access to new knowledge and skills was obtained through both local information spillovers and international alliance networks. Our challenge, then, is to understand the relationship between the scale of activity, the diversity of organizational forms, and the nature and timing of the networks and activities that linked the participants within specific geographic locales.

To explore these and related questions, we built a database that includes 661 dedicated biotechnology firms worldwide, and the more than 3,000 partners with these firms, over the period 1988-2004. The data on firms and their collaborators is drawn from *Bioscan*, an industry publication that reports financial and product information on companies, as well as the formal contractual arrangements that they have with collaborators. *Bioscan* covers a wide range of organizations in the life sciences field.[6]

[6] The first volume of *Bioscan* was released in 1987 by the biotech firm Cetus, but coverage was limited, as many firms were reluctant to share private data with a competitor. Oryx Press issued the first independent directory in 1988, and Oryx eventually sold *Bioscan* to American Health Publishers, which is owned by Thomson. Because the quality of data collection has varied somewhat across years and owners, we supplement *Bioscan* with *Recombinant Capital*, Dun and Bradstreet's *Who Owns Whom?*, and *Standard and Poor's*. For publicly traded companies we use annual reports and Securities and Exchange Commission filings. Many of the firms in our database were founded before 1988. Indeed, there are 253 firms in our sample in the first year (1988). We have extensive data on firm foundings from the early years of the industry, but the larger alliance data set suffers from left censoring. That is, for those firms that were founded *and* disbanded before 1988 we do not have complete network data. We have matched our sample to those developed by other researchers, most notably Steve Barley and John Freeman, Steven Casper, and Martin Kenney and Don Patton. We find one notable early entrant omission in our dataset: Hybritech, founded in 1978 in San Diego and acquired by the pharmaceutical corporation Eli Lilly in 1985. Given the important role of Hybritech in the creation of the San Diego cluster, as detailed in the previous chapter,

Our focus is restricted to dedicated biotechnology firms (DBFs). These companies are independently operated, profit-seeking entities involved in human therapeutic and diagnostic applications of biotechnology. Companies involved in veterinary or agricultural biotech, which draw on distinctive scientific capabilities and operate in very different regulatory climates, are omitted. Our sample of DBFs covers both privately held and publicly traded firms. Organizations that some might consider DBFs that are wholly owned subsidiaries of major pharmaceutical or chemical companies are not coded as biotech firms but are counted as partners. Large corporations, hospitals, universities, research institutes, and government agencies also enter the database as partners that collaborate with DBFs. Our rationale for excluding small subsidiaries and large multinational corporations in the primary database is that subsidiaries seldom make decisions autonomously, and biotechnology may represent only a small portion of the overall activities of international corporations.

Our database includes information on a firm's ownership, formal contractual links to collaborators, founding date, employment, and, for firms that exit, whether they were acquired or failed. Data on interorganizational agreements cover the time frame and purpose of the relationship. We define a collaborative tie or alliance as any contractual arrangement to exchange or pool resources between a DBF and one or more partner organizations. We treat each agreement as a tie and code for both its purpose and duration. A connection exists whenever a DBF and a partner have one or more ties between them. We assign the partner organizations to six categories: public research organizations (PROs, including universities, nonprofit research centers, and hospitals); multinational

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these analyses actually undercount the cohesion in that community. Still, the contrast between San Diego and other clusters will be quite apparent.

pharmaceutical and chemical corporations; government agencies and institutes; financial institutions; other biomedical companies (such as agriculture or veterinary biotech, instrument, or medical device companies); and DBFs that are also partners. We collapse the varied types of ties into four major categories: research, finance, licensing, and commercialization. We did not collect data on the ties among the non-DBF partner organizations. In some cases, such connections would be very sparse (e.g., venture capital financing of universities or major corporations). In other cases, they would be commonplace, for example, pharmaceutical company support of clinical trials at a university medical center. The practical problem is that the complete network affiliations of more than 3,000 disparate organizations, ranging across multinational firms, huge government agencies, venture capital, and research universities, would be very difficult to collect. Thus we focus on the connections that DBFs have to partners and the portfolio of DBFs with whom each partner is affiliated.[7]

In addition to the quantitative database, we have interviewed hundreds of scientists and managers in biotechnology companies, pharmaceutical firms, university labs, and government agencies over the past two decades. We have done participant observations in university technology licensing offices, biotech firms, large pharmaceutical companies, and university labs. Even though the analyses are drawn largely from data derived from industry sources, much of our understanding of the field comes from direct engagement with its participants.

To address the issue of genesis, that is, why certain regions emerged while others grew rather slowly if at all, we undertake longitudinal comparisons of the organizations in

[7] This methodological choice results in a 2-mode network representation, which surely overstates the centrality of some DBFs by virtue of their having many ties to other DBFs and downplays the centrality of some partners that are linked to one another without having connections to a common DBF.

eleven U.S. regions and the links both within and across these clusters, and to partner organizations around the globe. Specifically, we focus on 384 DBFs with headquarters in one of the eleven U.S. regions and their alliances with 1,357 partners, each of whom have two or more agreements with these DBFs.

5) Origins: Geographic Propinquity

The earliest biotechnology companies popped up in a variety of different locales. A precursor of the new field, Alza was established in Palo Alto, California, in 1968, followed by Gamma Biologics in Houston, Texas, in 1970. Cetus Corporation was founded in Emeryville, California, in 1972. In 1976, Enzo Biochem started on Long Island, New York, and Genentech in San Francisco. Genex sprouted in Montgomery, Maryland, in 1977. Biogen appeared in 1978, intended to be based in Cambridge, Massachusetts. Biogen's establishment was contested, however, because of local political opposition to genetic engineering (Watson, 2003: Ch. 4). Public uproar over "Frankenstein factories" led the founders of Biogen to incorporate initially in Switzerland to avoid the controversies in Cambridge, and co-founder and Nobel laureate Walter Gilbert had to take a leave of absence from Harvard University (Hall, 1987: 41-54). Hybritech started in La Jolla, CA in 1978. In 1979 Centocor was founded in Philadelphia, Pennsylvania, and MGI Pharma in Minneapolis. The next year, 1980, saw the advent of Amgen in Los Angeles, Cytogen in northern New Jersey, DNAX in Palo Alto, and Genetic Systems in Seattle. Genentech also had its initial public offering in 1980, fueling interest in the possibilities of this new field (Teitelman, 1989; Robbins-Roth, 2000). Some of these companies lasted but a few years, but several persevered.

Government policies were important to the formation of the industry. Legislation that reduced the capital gains tax and permitted pension funds to invest in venture capital opened the doors for investment in startup companies (Berman, 2007). In 1980, in the *Diamond v. Chakrabarty* case, the Supreme Court, in a close 5-4 ruling, distinguished between a product of nature and a patentable, genetically modified bacterium cell that did not exist in nature, ruling that live, human-made, or genetically modified micro-organisms are patentable. In 1987, the U.S. Patent and Trade Office expanded the domain of patentability to any biological material that required human intervention, thus creating fertile ground for intellectual property rights in genetics and biotechnology (Eisenberg, 1987). The U.S Congress passed the *Bayh-Dole Patent and Trademarks Act* in 1980 (PL 96517), which authorized scientists and universities performing federally funded research to file for patents and grant licenses to others. This legislation replaced what had previously been individual agreements between some universities and companies with a uniform policy, and signaled Congressional support for the negotiation of licenses between universities and firms (Mowery et al., 2004; Rhoten and Powell, 2007). The goal of the legislation was to signal a change in policy, away from fear over possible exploitation of public funds toward acceptance of the transfer of federally funded research results and a regime of strong intellectual property rights.[8] The Orphan Drug Act of 1983 was passed to encourage, through seven years of market exclusivity and tax credits, research on "rare" diseases by biopharmaceutical companies. All of these legislative steps were intended to assist in the commercial exploitation of basic research across the nation.

[8] Analysts debate whether the Bayh-Dole legislation itself prompted greater university commercialization of research, or formalized federal approval of trends that were already well under way (Cole, 1993; Zacks, 2000; Mowery et al., 2004; Powell et al., 2007).

In addition, federal research funding for the life sciences expanded markedly. The National Institutes of Health increased support for recombinant DNA research by 34% per year from 1978 to 1982 (Wright, 1994: 94), and again in the 1990s, research funding burgeoned as the NIH budget went from $8.9 billion in 1992 to $17.08 billion by 2000. Nevertheless, the critical role of the U.S. government in supporting biotechnology tells us very little about why the industry took root in so few places. Indeed, given the capacious scope of the judicial and legislative decisions and the political nature of federal research funding, one might have expected that federal policies would foster a wide distribution of companies across the nation.

Figure 1 plots the geographic location of the 48 U.S. biotech firms in our database that were active in 1980. The size of the dot reflects the number of firms in a city. The initial groupings of firms were in New York, Boston, and the Bay Area, followed by Philadelphia Washington, Houston, Los Angeles, and San Diego. A number of other cities, including Minneapolis, Miami, Memphis, Dallas, and Cincinnati, housed some early firms. Fast-forward to 2002, and the distribution of the 368 firms illustrated in Figure 2 shows very pronounced regional agglomeration. Three clusters — Boston, Bay Area, and San Diego — have grown dramatically. Other areas, such as New York and New Jersey, persisted, and Washington, Los Angeles, and Philadelphia grew modestly as well. Some new areas, such as the Research Triangle in North Carolina, Seattle, Salt Lake City, and Boulder appear as well.

[Figures 1 and 2 Here]

The number of companies in a cluster is but one measure of its importance. Perhaps more telling indicators are the cumulative accomplishments of companies located in the Bay Area, Boston, and San Diego. To wit, of the thirty-seven new medicines developed by dedicated biotechnology firms and approved by the U.S. Food and Drug Administration through December 31, 2002, twenty-one came from companies in these three regions. Product sales in biotechnology are heavily skewed toward a few winners, and just six companies have developed the ten most widely sold medicines. Five of the six companies come from the three leading clusters. In our database, 49% of the U.S. companies, 60% of the biotechnology patents, and more than 50% of the formal contractual collaborations involve a company from one of the three largest clusters.

This is not to say that firms located in these regions are universally successful. One of the earliest bellwether firms of the industry, Cetus, located in Emeryville, California, next door to Berkeley, suffered a high-profile rejection of its lead drug by the FDA in 1991 and subsequently failed. The Palo-Alto-based Alza, an early pharma-biotech hybrid, was acquired by Johnson and Johnson in 1994 and closed in 2008 in the course of J&J's corporate downsizing. Our analyses reveal that failure rates for companies inside and outside of the three regions show no statistical difference save for San Diego, where firms are actually more likely to fail a bit sooner than in any other locale (Whittington et al., 2009). Stuart and Sorenson (2003) have shown that success in obtaining venture capital and going public is more challenging for companies in the Bay Area than in other parts of the country. Although the three clusters are notable aggregate producers of innovation and populated by a large number of firms, they are also intensively competitive arenas, and certainly not safe havens. Indeed, it is the indissoluble combination of competitiveness and camaraderie that marks these locales (Portera, 2004).

To gain purchase on the pattern of geographic agglomeration, we examine the organizational populations in the early years of the industry in the eleven areas where the earliest firms appeared: Boston, the New York Metropolitan Area, Northern New Jersey, the Philadelphia Metropolitan Area, Washington, D.C.–Baltimore, the Research Triangle in North Carolina, Houston, San Diego County, the Los Angeles region, the San Francisco Bay Area, and Seattle. The comparative analyses begin in 1990, by which time all eleven regions have a cadre of companies located in them. We attend to four points of comparison: 1.) the organizational diversity in the regions, 2.) the effects of anchor tenants, 3.) the role of cross-domain networks, and 4.) the sequence of network formation. We contend that the character of a region is marked by the diversity of its organizations, the ties among these organizations, and the institutional characteristics of the central nodes in the local network, who shape information flows.

The robustness of a regional economy is enhanced when members of the community pursue science under norms of openness. Thus when public research organizations are anchors in a local ecology, we find a greater circulation of knowledge and more fluid labor markets. Public research organizations, such as universities and nonprofit institutes, increasingly conduct research that is both scientifically advanced and immediately valuable to industry. But this class of organizations has historically differed from research-intensive firms on two important dimensions: their disparate approaches to rules for the dissemination and use of scientific findings, and their position in different selection environments (Dasgupta and David, 1987, 1994; Owen-Smith and Powell, 2004). New knowledge spreads out of universities much more readily than it does from commercial organizations (Jaffe et al., 1993). Similarly, sectors in which noncommercial organizations are prominent in early-stage research evince much more open technological trajectories (Dosi, 1982).

The evidence for geographically concentrated knowledge flows in research-intensive industries is compelling. Studies drawing on ethnographic research as well as patent citation data have demonstrated that: 1) ideas travel across organizations more readily when they are co-located; 2) the size and mobility of the scientific labor force increase local information sharing; and 3) strategic alliances among co-located firms augment the stock of common knowledge (Saxenian, 1994; Almeida and Kogut, 1999; Almeida et al., 2003). But it is crucial to recognize that different organizational forms produce varied types of knowledge and resource exchange. Universities and public research organizations contribute to technological advance, whereas research hospitals aid translational applications and clinical evidence. Venture capital investors provide a different channel for information transfer, assist in monitoring companies, and help diffuse managerial practices. Large multinational companies and biomedical supply firms contribute by enhancing regional labor markets for scientists and technicians, attracting a deep pool of industry-specific talent. Thus, diverse sources of knowledge and skills, along with varied channels of communication and exchange, 'irrigate' a local community. But diversity alone is not the whole story. Depth and quality are critical too. In regions that experience 'take off,' internal competition increases quality, so that among those who survive, the best ones persist. Diversity and quality become mutually reinforcing in thriving clusters.[9]

The Boston cluster. We begin by drawing on previous work by Owen-Smith and Powell (2004, 2006) on the Boston biotechnology community, which analyzed how the

[9] We thank Michael Storper for emphasizing this point to us.

institutional form of the most central organizations shaped the practices of this regional community, influencing the nature of spillovers and innovation. We initially studied Boston because of its array of public research organizations (PROs), including universities such as Harvard, MIT, Tufts, and Boston University, independent research institutes such as the Dana Farber Cancer Center and the Whitehead Institute (a vital participant in the Human Genome project), and well-known research hospitals, such as Massachusetts General. In earlier work, Powell et al. (2002) observed that local venture capital firms did not become highly active in biotech in Boston until the 1990s, so they did not play an early catalytic role. In related work, Porter et al. (2005) analyzed the founding teams, scientific advisory boards, and co-patenting relationships of Boston biotech firms, finding that most connections in Boston were local. There were numerous connections among Boston-area universities and institutes and Boston DBFs, but very few founding teams involved faculty from outside of Boston (Porter, 2004). In comparison to the San Francisco Bay Area, the Boston community appeared to be a local "Brahmin" world, whereas the Bay Area was more open to outsiders, a receptivity that has long been a characteristic of California (McWilliams, 1949).

We reproduce several of these Boston analyses, as they serve as the model for our inquiry into other clusters. We use graphical representations of the networks at crucial points in their emergence and evolution. The software we employ, Pajek, uses algorithms that represent centrality in a web of affiliations.[10] The nodes are organizations and the lines are types of connections. Nodes repel one another, and lines pull nodes closer. The

[10] Pajek is a freeware program developed by Vladimir Batagelj and Andrej Mrvar, available on the Web, and in wide use in the biological, physical, and social sciences. Pajek is used to portray meaningful and replicable visual representations of networks. Pajek implements two drawing algorithms based on graph-theoretic conceptions of distance. The images we portray locate isolates on the periphery and situate more connected nodes at the center.

network maps are stable configurations that reflect a local equilibrium — the overall pattern and density of affiliations in a network is captured at rest. Hence the maps are referred to as minimum-energy drawings. We use the visualizations to discern centrality in regional networks.

Figure 3 reprints three images of the Boston biotech community in 1988 (Owen-Smith and Powell, 2004). The shape of the nodes reflects organizational form — triangles represent PROs, circles indicate DBFs, and squares are venture capital firms. The color of the lines reflects the type of activity the relationship involved — red is R&D, green is financial, magenta is licensing, and blue represents commercialization activities. All of these ties are based on formal, contractual interorganizational relationships among Boston-based organizations.

[Figure 3 here]

Look first at the picture in the upper left. The Boston network was relatively sparse in 1988, with the bulk of the organizations located on the outside circle, indicating that they had no formal local connections. Note the critical role of public research organizations (triangles) in connecting the center of the network. Note also the general absence of venture capital firms. Six public research organizations — MIT, Boston University, Tufts, Harvard, Dana Farber Cancer Center, Massachusetts General Hospital, and the New England Medical Center — are located in the most connected cluster. When we extract the main component — the largest minimally connected cluster[11] — from this network, 43% of DBFs in Boston were reachable through connections to this group. But when we remove the public research organizations and their collaborations from the main

[11] For those not versed in network parlance, consider the task of connecting a series of dots. The main component represents only those dots that can be connected without ever lifting a pen.

component, the network collapses. The most striking feature of the 1988 network was the pronounced dependence of the commercial world of biotechnology on public research organizations, which provided coherence to the Boston community.

[Figure 4 here]

We move forward to 1998 and portray the network in Figure 4. The cluster has grown larger and is much more interconnected. Public research organizations continue to be prominent, but now venture capital firms and first-generation companies are also central. When we extract the main component, we find that 71% of the biotech firms in Boston were reachable. When the public research organizations and their ties are removed from the main component, the network no longer dissolves, and 35.6% of the biotech firms remain reachable. These figures capture an important transition in the structure of this regional community, highlighting both the continuing impact of public research organizations and the growing role of for-profit entities, notably the local venture capital firms that became intermediaries for Boston companies. We also examined collaborations with partners outside the Boston area, but do not include those visualizations here. The 'larger' Boston network expanded internationally over time, and the majority of these distant ties were formed with commercial entities. The importance of Boston-based PROs receded, although local centrality remained critical to scientific productivity as it continued to have a positive effect on patenting rates (Owen-Smith and Powell, 2004; Whittington et al., 2009). In sum, basic science acumen was clearly transposed to commercial application in Boston.

As a next step, we compare Boston, the Bay Area, and San Diego at three comparable time points: 1990, 1996, and 2002. The results presented in Figure 5 show several notable differences between the three leading centers of biotech activity. As with Figures 3 and 4, red lines are R&D, green are financial, magenta are licensing, and blue are commercialization activities. But we switch our representation of nodes from shapes to colors and add additional types of partners: blue nodes are DBFs, pink nodes are biomedical supply companies, grey are financial institutions, brown are government institutes, yellow are pharmaceutical corporations, and red are public research organizations.

[Figure 5 here]

The San Francisco Bay Area cluster. The Bay Area is larger, both in the number of organizations – with more biotech companies, several major universities (including Stanford and the Universities of California at San Francisco and Berkeley), and numerous venture capital firms - - and its geographic spread. The Boston network is organizationally smaller and geographically denser, with many more public research organizations and fewer venture capital firms. Whereas the Boston network grew from its early origins with PROs, the Bay Area was heavily influenced by the prospecting and matchmaking efforts of venture capitalists, the multi-disciplinary science of the UCSF medical school, and novel efforts at technology transfer at Stanford (Kenney, 1986; Colyvas, 2007; Jong, 2008).

The biotech community in the Bay Area had its genesis in the partnership of Herbert Boyer, a UCSF scientist, and Robert Swanson, a young, aspiring venture capitalist, who joined together to create Genentech, one of the first biotech companies and long a bellwether of the industry. The organizational model at UCSF fostered by William Rutter, chair of the biosciences there and later a co-founder of Chiron, was interdisciplinary, with a cross-functional approach to medicine and an emphasis on translating basic science into clinical applications (Varmus and Weinberg, 1992; Jong, 2008). Both Genentech and Chiron adopted and refined UCSF's team model, insisting that their scientists publish in academic journals, but added the impatience of venture capital financial backers with their focus on swinging for the fences. Consequently, the Bay Area network had a strong footprint of venture capital backing (note all the green lines for finance ties in Figure 5) and an especially important role for first-generation science-based companies, Genentech and Chiron. The closely spaced nodes at the center of the 1996 figure for the Bay Area represent the multiple ties between Genentech and other Bay Area organizations. The tightly clustered nodes, reflecting multiple affiliations between two organizations, grow in the 2002 figure. A notable aspect of the Bay Area region, present to a smaller extent in Boston, is the considerable inter-firm collaboration among biotech companies that are ostensibly competitors. Here we see the transposition of an invisible college model to the commercial realm, as we detailed in the previous chapter.

Seen broadly, the anchor institutions in Boston and the Bay Area are distinctive, and the type of activity that knits the two regions together also differs. The red lines in the Boston pictures reflect research collaborations, and the blue lines in the 2002 panel typically involve clinical trials. Research hospitals are active participants in Boston. The Bay Area, by contrast, shows a preponderance of green lines, reflecting the imprint of venture capital and the sponsorship role of first-generation companies such as Genentech and Chiron that, over time, became active partners with younger companies. In contrast to Boston, very few local research institutes or hospitals were active in the Bay Area. But the university presence is important in both. The early companies in the Bay Area emerged from academic laboratories, with Chiron started by UCSF and Berkeley faculty and Genentech by a UCSF professor. These companies collaborated intensively with local universities, and they adopted academic norms of publishing and collaboration and repurposed them into the world of commerce through extensive collaborations with other biotech companies and universities.[12]

A striking feature of the Bay Area is the extent to which the commercial entities embraced academic norms, while the universities, particularly Stanford, came to venerate and support academic entrepreneurship (Colyvas and Powell, 2006). Here we see a cross-realm transposition in which the practices common in one domain are imported into another. In the case of Genentech, transposition can be seen as the infusion of a university lab culture into a commercial firm. This is often cast as the commercialization of the university, but the "academization" of for-profit research in the life sciences is also relevant. Consider comments by Genentech co-founder Herbert Boyer that emphasize firm-level engagement with meritocratic rewards, support for publishing in academic journals, and scientific autonomy:

> We set out with a self-imposed mandate that employees would share in anything that came out of the company, in terms of holding stock in the company. I insisted that we have the scientists publish their research in journals…. I felt this was extremely important for attracting the outstanding young scientists in the community that were interested in doing research in an industrial setting. I also wanted to bring in scientists that were outstanding to have them have an opportunity to establish their own reputation, get their own recognition. So we tried to set up an atmosphere which would take the best from industry and the best from the academic community, and put them together (Boyer, 2001: 87).[13]

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[12] Herbert Boyer's research sensibilities are nicely captured in an early interview, where he described his initial motivation to talk with his subsequent co-founder Bob Swanson: "He said he had access to some money, and I thought it would be a good way to fund some post-docs and some work in my laboratory, since we always needed money for that." (Boyer, 2001: 71).

[12]This choice by some early biotech firms to support basic research was consequential, because open-ended exploration by U.S. industry has declined markedly over the past few decades, with venues like Bell Labs and central research units either closed or reoriented toward short-term needs of companies.

The San Diego cluster. Our comparisons of Boston, the Bay Area and San Diego are buttressed by the excellent work of a number of researchers who have studied the development of biotech in San Diego (Lee and Wolshok, 2000; Wolshok et al, 2001; Walcott, 2002; Jones, 2005; Casper, 2007). With our data, we created Pajek images for the San Diego region, which are shown at the bottom of Figure 5. These analyses reveal a different trajectory from either Boston or the Bay Area. The biotech industry emerged slowly in San Diego. Parallel to our network maps of collaborations, Casper's (2007) analysis of inter-firm job mobility among San Diego DBFs between 1978 and 2005 shows that it took about a dozen years for the cluster to take off. Our 2002 representation of local ties in San Diego looks comparable to Boston's and the Bay Area's 1990 clusters.

Interestingly, the trigger for the San Diego cluster was the failed acquisition of an early diagnostics-focused company, Hybritech, by the Indianapolis-based pharmaceutical company Eli Lilly in 1985. Within two years, no Hybritech employees remained with Lilly, but more than 40 San Diego biotech firms were subsequently founded by former Hybritech employees (Walcott, 2002). A senior female scientist at Hybritech quipped that the merger "was like 'Animal House' meets 'The Waltons.'" She also recalls being told by a Lilly scientist that she was young enough to be his daughter (Fikes, 1999: 3). Executives at Eli Lilly have lamented that they are the most successful venture capitalists in San Diego history, only they didn't collect any of the rent.[14]

San Diego is home to numerous first-rate biomedical research centers, including the Salk Institute, Burnham Institute, the Sydney Kimmel Cancer Center, and Scripps Research Institute, all concentrated in the La Jolla area. They are reflected in the multiple

[14] The Lilly Corp. did learn from this unsuccessful $300 million investment; as we shall see in the next chapter, it became one of the first of the large pharmaceutical companies to move away from an acquisition and transaction strategy to a more relational one in its dealings with smaller companies.

red nodes in the bottom row of figure 5. In addition to its rapid rise to scholarly distinction in the biological sciences, the University of California at San Diego developed a very strong medical school. Casper (2007: 443) reports that by the early 2000s, these public research organizations were collectively receiving more than half a billion dollars in federal funding for biomedical research; meanwhile, the DBFs pulled in significant private funding as well. San Diego's combination of former employees of its first startup, who did not want to leave San Diego, and its strong public research community proved to be a lure for venture firms from the Bay Area. These investors set up branch offices in San Diego in the 1990s, and some of the successful VCs became local angel investors.

In the 1980s, the San Diego community had a notable lack of financial services and well-connected business networks. To compensate for this, a few business leaders and UCSD officials created a program called CONNECT in 1985, intended as a venue to link academic researchers, budding entrepreneurs, and business support services (Walshok et al., 2001). CONNECT proved to be a highly successful public-private springboard (Lee and Walshok, 2000). The blend of the Hybritech spinoffs, the anchor of public research organizations, and the entry of investors from the Bay Area stimulated cluster formation. By the mid-1990s, a number of companies were founded by former Hybritech alums, including Amylin, Gensia, Genta, Idec, Ligand, and Vical. In particular, our data show that Ligand and Neurocrine Biosciences, a spin-off from the Salk Institute, were central in linking San Diego firms (blue) and local PROs (red).

On the surface, the origins of the three robust regions are different, suggesting there is no standard recipe. Rather than a common story of genesis, we see a topology of the possible in which the participants appear to have made do with what they have at hand, following opportunistic, sequential moves, aided by the presence of anchor organizations that fostered the sharing of information, dampened cut-throat rivalry, and enabled cooperative competition. In Boston, PROs played this role. In the Bay Area, venture capital firms were critical. Skilled VCs are very adept at networking, spreading best practices, and gracefully exiting from relationships (Powell et al., 2005). The technology licensing policies developed at Stanford, which focused on relationship building with start-ups rather than maximizing revenue, and the interdisciplinary orientation of UCSF combined to give the Bay Area several anchor organizations, which helped institutionalize a community of like-minded participants. In San Diego, the mismatch between young scientists at Hybritech and senior staff twice their age at Eli Lilly had the unexpected effect of creating a pool of alumni who went on to establish numerous new companies while staying in close touch with one another. Hybritech's failure, unexpectedly, seeded the job market and created a context in which job mobility and information sharing took place. These former employees collaborated with scientists at the numerous research institutes in the La Jolla area and with UCSD faculty.

Nascent clusters - - Lessons from negative cases. We turn now to the eight nascent clusters, with the goal of trying to isolate processes and mechanisms that make a cluster self-reinforcing. Earlier, we suggested that in number of participants and available endowments, the broader New York metropolitan area, Northern New Jersey, the Philadelphia metropolitan area, the Washington, D.C. metro area, the Research Triangle in North Carolina, Houston, Seattle, and the Los Angeles metro area were plausible candidates for the development of a regional biotechnology cluster. To be sure, each of these areas had a large number of existing industries, and perhaps incumbent sectors acted in some fashion to preclude the formation of new fields. But that explanation doesn't seem to apply to Boston, where insurance and computers preceded biotech, or the Bay Area, where computers and information technology came before biotech, or San Diego, where a large military presence and a tourism industry predated both biotech and an emergent wireless cluster (Simard, 2004).

Moreover, each of these nascent regions had strong potential magnets for biomedical research. New Jersey has many major pharmaceutical companies – including Johnson & Johnson and Merck, as well as Princeton University. The New York City metropolitan area has many world-class research hospitals, numerous top-tier universities, leading biomedical research institutes, and, at that time, the world's largest financial sector. Philadelphia also has a major pharmaceutical presence, public research institutes, and universities. Washington, D.C., and its suburb of Bethesda, Maryland, house the National Institutes of Health, and Northern Virginia has seen the rapid development of an information technology cluster. Houston, Seattle, and Los Angeles all had major research hospitals and medical institutes, as well as leading research universities. The Research Triangle had two state universities and the notable private Duke University, a research park with a major corporate presence in the British pharmaceutical firm Glaxo, and a state government keen to support high tech. Clearly, there were many possible candidates that might have spawned the creation of a biotech cluster in each of these locales.

When we map the local networks in these eight regions, however, we see a marked contrast with the clusters that formed in Boston, the Bay Area, and San Diego. Although there is a diversity of participants, few of the nascent regions developed an extensive pattern of interorganizational affiliations. In contrast to the successful clusters, local ties are rather sparse. The bulk of collaboration occurs with partners outside the regions, suggesting that local knowledge exchange and inter-organizational labor mobility are rather limited. Figures 6 through 8 show the patterns of regional collaboration at six year intervals, in 1990, 1996, and 2002. The number of organizations in each cluster is listed in the lower right corner of each figure, with the number with local affiliations in parentheses. The eight nascent clusters in 1990 are quite varied. New York has by far the most organizations, but very little local activity. New Jersey, Washington, Houston, and Los Angeles are populated by a diverse set of organizations, and some regional links have formed. Philadelphia and Seattle have scant local activity; the Research Triangle cluster has not really formed. In comparison to Boston, the Bay Area, and San Diego (Figure 5), much less biotech activity is going on *within* these regions.

[Figures 6, 7, and 8 here]

Moving forward to 1996, Houston and Los Angeles regress, showing even less local activity. More organizations appear in the Research Triangle, New York, Northern New Jersey, Washington, D.C., and Seattle, and some signs of cluster formation are apparent. The promise does not pan out, however. All the regions, save for the Research Triangle, are less regionally linked in 2002. Even though organizational diversity was present in each locale, there was no apparent stimulus for creating a regional cluster. Instead, the organizations developed connections to outside parties and largely eschewed local linkages. In sharp contrast, the panels in Figure 5 show that the three "successful" clusters multiplied. The Boston biotech community became densely interwoven and burgeoned in numbers as well. A similar process characterized the Bay Area, where there are even more regional participants and dense collaborations. San Diego, as the most recent arrival, was not as initially linked locally through formal alliances, but the number of participants and the density of the network increased. Moreover, in related work we have shown that the organizations in the main component of these three high-growth regions are rich in both local *and* global ties, which enable them to recombine well-vetted local ideas with more distant knowledge flows and thus avoid lock-in or myopia (Whittington et al., 2009).

A comparison of the role of anchor tenants across the different regions affords further insight into their divergent trajectories. Figure 9 portrays the percentage of ties from DBFs (located anywhere in the world) to regional partner organizations in each cluster, by type of organizational form. In every case, one party to the formal tie is a dedicated biotech firm, and the other is either another biotech firm, a biomedical supply company, a financial institution, a government institute or agency, a pharmaceutical company, or a public research organization. On the left are the three clusters that became institutionalized; on the right are the eight nascent clusters. Two features stand out.

[Figure 9 here]

First, note that the three regions on the left had a mix of different types of organizations in 1990. Finance led in the Bay Area and public research organizations in Boston and San Diego, but there is a considerable variety of types of organizations in each. On the right side, however, with the exception of Los Angeles, a single type of organization dominated in each nascent cluster, responsible for 50-80% of all ties. In New Jersey, it was pharmaceutical corporations; in the D.C. area, government institutes; in New York and Houston, financial institutions; in Philadelphia, pharmaceutical corporations; and in the Research Triangle, research universities. In Seattle, DBFs were partners with other biotechs. Although there was an array of different signature organizations in each nascent region, a dominant local presence controlled the bulk of collaborative activity. This hegemony, we suggest, precluded the chance to recombine diverse evaluative criteria and blend practices across different domains.

The second feature is the lack of dynamism in the nascent clusters, compared to the transitions underway in the growing regions. Move down the figure to the panel for 1996. In the three regions on the left side, the anchor tenant spurred activity and passed the baton (reflected by the arrows) to other types of organizations: in the Bay Area to DBFs, in Boston to VCs, and in San Diego to DBFs. In 2002 in Boston there was another hand-off, from VCs to biotech firms. In these three areas, the organizations that initially anchored the community helped create enduring collaborations with other types of organizations, who in turn continued this pattern. In contrast, in 1996, in New Jersey, Washington, Los Angeles, New York, Philadelphia, Seattle, the Research Triangle, and Houston there was no change; the same organizations remained in charge. Pharmaceuticals continued to reign in New Jersey, the NIH in D.C., financial institutions in New York and Houston, research organizations in LA and the Research Triangle, and biotech firms in Seattle. In 2002, Los Angeles and Houston shifted and there was some reshuffling in Philadelphia, but all three regions also experienced a decline in overall activity. In the other regions, the dominant parties persisted. Rather than acting as a catalyst, the most active partners appear to have operated as 800-lb. gorillas rather than anchor tenants.

Digging deeper, Figure 10 offers a different perspective on the organizational ecologies of these different regions, and the diversity of organizations involved in each. Here we focus only on ties within a region and look at the percentage of ties by form of organization. We have dropped Houston and the Research Triangle because there were simply too few local ties to analyze. Note first the range of firms that are involved. In 1990, San Francisco, Boston, and Washington are the only locales with five different types of organizations, while San Diego has four. The rest have but three, except for New York and Seattle with only two. Looking down the page, we see that San Diego gains a fifth in 1996 and DC drops to four in 2002. New Jersey and New York stay the same with three, but Philadelphia and Seattle expand, suggesting some signs of local vitality.

[Figure 10 here]

We turn now to regional variation in the role of anchor tenants. Our interest is in examining whether anchors facilitated expansion, drawing in other organizations for mutual benefit. In 1990, venture capital dominated in the Bay Area and public research organizations in Boston and San Diego. In New Jersey, New York, and Philadelphia, pharmaceutical companies were the most active on the local scene, with New York's many financial institutions (apparent in Figure 9) heavily engaged globally, but not regionally. Washington bears the imprint of the NIH, whereas LA has an unusual number of equipment and supply companies and Seattle a local biotech presence. Move down to 1996. In the Bay Area, biotech firms emerge as the community leaders; in Boston, venture capital grows. In San Diego, biotech firms almost reach equivalence with PROs, and in Boston, a further shift occurs to biotech firms assume relational leadership in 2002. But note that in none of these growing clusters does the original catalyst disappear. Instead of a contest for control, we see multiple types of organizations involved, and over time, public research organizations, venture capital, and biotech firms are all deeply involved locally.

In the nascent clusters, very different patterns are apparent. In New Jersey, DC, and New York, the same type of organization dominates the local scene for all three time periods. Transitions occur via shrinkage in LA, due to the departure of the supply companies, and in Philadelphia, where the local role of pharma companies recedes. New Jersey, Los Angeles, and New York do not have collaborations among local biotech firms, perhaps the most telltale sign of the absence of a regional community. Philadelphia and Seattle, however, show some signs of emergence, with transitions among their dominant parties and some balancing of engagement, especially in Philadelphia. Although figures 6 and 8 illustrate that there are only a modest number of participants in these clusters, they do show some indication of the early features that characterized the successful regions back in 1990.

As a check on our assessment of the nascent clusters, we looked to see whether the organizations in these locales eschewed collaboration in favor of internal development. Put differently, this is the issue of unobserved heterogeneity. Are we biasing our arguments by focusing only on collaboration? Perhaps the established organizations chose a different model of drug development in which they focused on vertical integration. Figure 11 compares the eleven regions over the same time periods (1990, 1996, and 2002), looking at the number of ties in a region to: 1) biotech firms within the same geographic locale; 2) biotech firms in the Bay Area, Boston, and San Diego clusters; 3) biotech firms in the eight nascent clusters; and 4) biotech firms located elsewhere in the world. Here we simply use a count of the number of ties. The results are striking. In 1990 the most active region in terms of number of ties was D.C., reflecting the expansive national reach of the NIH. New Jersey and New York were also highly engaged, on a relational par with the Bay Area and Boston. Los Angeles, Philadelphia, and San Diego were roughly comparable in volume of collaborations. Note, however, that in New Jersey, D.C., Los Angeles, New York, Philadelphia, Seattle, and the Research Triangle, the local organizations forged more ties externally than within their own clusters. That trend becomes even more pronounced in NJ, DC, LA, NY, and Philadelphia in 1996 and 2002. Far from foregoing collaboration, the organizations in the nascent clusters were very active partners, *but* with outsiders. Moreover, the bulk of those extra-local connections were to DBFs in the three established regions.

[Figure 11 here]

The comparison of San Diego with Philadelphia, Los Angeles, and Seattle is intriguing, as all four had sparse connectivity in 1990, but San Diego grew rapidly over the next decade while the latter three did not. In addition to San Diego, the Bay Area and Boston also expanded markedly, and local ties drove the growth, complemented by ties to one another that further fueled the burst of activity. Although collaboration in the nascent clusters grew to varying degrees, it did so by forging alliances to firms in either the successful clusters or around the world, and rarely locally or to one of the other nascent clusters. Only Seattle, with its limited activity, shows signs of a regional cluster.

More work is needed to specify carefully the sequence and dynamics of collaboration, but clearly there is no preference for internal development over collaborative production. Moreover, we find an intriguing suggestion of a “virtuous cycle” in the successful clusters: local ties were formed first, then connections were made to the other established clusters, then global linkages were created. In the Bay Area, Boston, and San Diego, local connectivity became the linchpin for global centrality. In contrast, in the nascent clusters external ties came first and connectivity developed outside the region, which appears to dampen local growth. We want to be careful that our argument is not perceived as a recipe for success.[15] The account we are giving is very much a process story: starting points and sequences matter, what types of organizations are involved and where you begin shapes where you can go. Moreover, the windows of locational opportunity may be brief, and catalysis may only occur at specific stages in a cluster's evolution (Scott and Storper, 2003). Nevertheless, the three burgeoning clusters created local ecologies initially, then expanded globally; whereas the nascent clusters had many more external linkages in their early years.

The three clusters that became institutionalized are characterized by high rates of firm formation *and* dissolution. Unlike the nascent clusters, which never took off and even shrank, organizational formation in the successful clusters occurred at a greater rate than dissolution. This ferment had several consequences. One, labor market mobility became easy. For example, the involvement of early employees of Genentech and Hybritech in starting new companies was quite notable. One report traces eighteen companies founded in the 1990s by scientists and managers who had worked at Genentech during its first

[15] Indeed, an ingredient that many might consider as essential for any successful recipe - - federal research dollars - - were as or more abundant in the nascent clusters as the successful regions. The list of the top recipients of NIH awards in 1996 has Johns Hopkins first by a wide margin, the University of Washington and UCSF tied for second, and the University of Pennsylvania fourth. The nascent clusters have strong representation throughout the top 50 recipients: UCLA (9th), Duke (11th), Univ. of North Carolina (12th), Columbia (13th), USC (24th), Baylor College of Medicine in Houston (26th), Fred Hutchinson Cancer Center (33rd), Yeshiva Medical Center in NYC (34th), NYU (35th), Univ. of Texas Health Center in Houston (40th), Univ. of Maryland (42nd), and Mt. Sinai in NY (43rd). In contrast, from the successful clusters, Harvard is 8th, Stanford 10th, UCSD 15th, but UC – Berkeley is 41st and MIT 47th. Clearly, differential access to federal research funding is not the explanation.

decade (Van Brunt, 2000). Similarly, MIT faculty and alumni played a big role in the creation of the Boston biotech community (Roberts and Eesley, 2009). Two, these personnel flows suggest that the creation of a regional community and the presence of catalytic anchors greatly lessened the risks of starting a new firm. Three, the high rates of founding and turnover point to experimentation with new scientific ideas and business models, which further sustains a cluster.

In sum, several factors distinguish the geographic locales where biotech emerged and grew into an interactive, robust community. All regions possessed some diversity in types of organizations, but the clusters where a local community became institutionalized had anchor tenant organizations that fostered interaction among disparate parties. PROs and VCs appear to have functioned as organization-forming organizations (Stinchcombe, 1965). And rather than recede as new entrants joined the scene, these organizations remained active participants.

As a consequence, the norms that characterized inter-organizational relations in the three clusters bear the signatures of the anchor tenants. DBFs collaborated with other DBFs in biomedical product development; older DBFs joined in as investors in new startups. The older companies took on some of the features of both the PROs and VCs, while the PROs and VCs in these areas became intensively involved in starting companies. Universities took equity positions in startup biotech companies and facilitated the licensing of university science. Employees at VCs moved to biotech firms to take on founder or executive roles, and biotech company veterans moved on to found VC firms. Whatever one may think of this outcome (with respect to its consequences for corporate governance or public science), in the three regions where cross-network transposition occurred, we see a thorough mixing of participants from formerly separate domains.

In contrast, the regions that did not develop local clusters were dominated by one type of organization that may have been more inclined to "call the shots," asserting its own primacy and dictating the rules of the game. In some cases, these 800-pound gorillas were giant pharmaceutical companies; in others, the local leader was either a large government institute or local university or research hospital. In Los Angeles and Seattle, first-generation biotechs did not spawn subsequent companies. Our aim is not to point a finger at particular organizations for not being generative, but to emphasize that the continuing predominance of a single type of organization hinders community emergence.

7) Summary and Implications

The genesis of the life sciences field offers an opportunity to reflect on the process of institutionalization. The core question in studies of field formation concerns how a collection of organizations coheres into a community, engaged in common activities and subject to similar reputational and regulatory processes (DiMaggio and Powell, 1983; Bourdieu and Wacquant, 1992; Hoffman, 1999). To be sure, the origins of biotech have some idiosyncratic features. The crucial role of university research in creating and sustaining the science, the importance of intellectual property and patent law, and large-scale public financing of R&D all render biotechnology distinctive, at least in comparison to many twentieth-century manufacturing industries. It remains to be seen whether these factors prove to be more typical building blocks for twenty-first-century science-based fields. Nonetheless, the processes we have analyzed can shed light on invention and institutionalization more generally.

Our argument hinges on two main factors: one, the presence of a diversity of organizations, and two, connections mediated through anchor tenants, some of which prompted the boundary crossing we have termed transposition. This combination produced relational density in a very small number of geographic locales, and not in other venues that also had an enviable set of initial endowments. Relational density in the context of geographic proximity generated shared expectations. Local norms for collaboration and knowledge exchange developed. Both competition and cooperation co-existed, through repeated exchanges and fluid labor markets. The three clusters became institutionalized as intense incubators for scientific ideas and business models, so that jockeying for success occurred on more meritocratic (or at least publicly transparent) grounds.

The diversity of organizations provided multiple means for information exchange, varied organizational strategies, and divergent criteria for success. In each of the three communities, a distinctive model of information diffusion developed to enable relational contracting (Macneil, 1985; Powell, 1990). Public research organizations were most influential in Boston, but they were clearly important in the Bay Area and San Diego too. PROs are unusual because they are very "leaky" institutions, as information flows out of them readily. But they are also venues for the rapid dissemination of standards and evaluative criteria, as well as high-speed gossip networks to carry stories of malfeasance.

Venture capital was a spark plug in the Bay Area, most notably because it provided the bridge to transport basic science into the commercial realm. To be sure, academic biological science had become “big,” and running a successful lab at a top-tier university had taken on many elements of managing a small business. But as we showed in chapter 13, few faculty members were prepared back then to be biotech executives — or even wanted to. VCs functioned as stand-in executives and advisors to new biotech firms, and they translated practices from the semiconductor and computer worlds to biotech.

San Diego saw the unusual case of a failed merger that generated numerous spinoffs. There are many historical cases of spinoffs driving industry evolution, in such areas as autos in Detroit and the tire industry in Akron (Klepper, 2008), and in the footwear industry as well (Sorenson and Audia, 2000). Many of the more famous examples, such as Olds in cars and Fairchild in semiconductors, led to disgruntled employees who exited and formed competitors. The Hybritech example seems to have a different twist. The many alumni appear to have treated the unsuccessful acquisition of their young firm as a signal that they could collectively build a biotech industry in San Diego. Rather than becoming competitors with one another, they cooperated, and a number of alums went on to become serial entrepreneurs. Meanwhile, the acquiring multinational, Eli Lilly, eventually became one of the first big companies to be an engaged collaborator with startups and PROs, after writing off the losses from the Hybritech acquisition in 1994.

The role of first-generation biotech companies in partnering with smaller companies changed the model of competitive spinoffs to a more relational one. The scientists who moved from university to firm, or from firm to nonprofit (dubbed “sector switchers” by Whittington, 2007, in her analysis of Boston life scientists) transferred research ideas and business blueprints. In sum, inter-firm job mobility was crucial to the cross-network transfer of knowledge in all three locales.

Extending beyond these cases of genesis, the sequence of network ties may significantly affect the practices and relationships that become institutionalized (Stark and Vedres, 2006). Starting points matter a great deal in institutional formation. We have emphasized that the industry's origins were characterized by an asymmetric distribution of resources and capabilities. This initial variation may have been one of the drivers for change, as startup firms and research organizations looked to alter the status quo. We also see an apparent sequence of tie formation. For organizations in the three clusters, the creation of a local community, as well as affiliations with organizations in the other "successful" regions, led to a more diverse portfolio of distant partnerships. In the successful clusters, biotech firms occupy a dual position: both as a member of a cluster and as a conduit to external activity.[16] In contrast, in all of the nascent regions, save for Seattle, which remains small, local DBFs have to make do with distant ties.

Some might contend that the analysis we have offered is 'just' a case of brokerage, albeit one in which the brokers (i.e., the anchor tenants) acted to coordinate and distribute resources rather than benefit from arbitrage.[17] Certainly, as the field developed, the distribution of resources and benefits shifted to privilege different groups over others. But the transition from somewhat sparse local networks to a densely connected field reflected not just the brokerage role of PROs, VCs, and DBFs. Cross-network feedback is an

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[16] Multivocality can be a risky strategy early in a career or in a field's formation (Zuckerman, 1999). Put differently, a multi-vocal categorization may pose obstacles at certain moments in a field's evolution. But as cross-network transpositions occur and ramify, a multi-vocal persona may become venerated, as the ability to tap a wider pool of resources is translated as richness and generativity.

[17] Ron Burt has commented to us that this process of managing diversity could be regarded as sponsored "collateral brokerage."

essential part of the story. The catalyzing effects of combining the tools of one sector with those of another transformed the life science business in ways that no strategic broker or entrepreneur could ever have anticipated. Brokerage certainly forged contacts among a diverse collection of organizations, but the ramifications of these collaborations led to an important institutional transformation. To be sure, the prior experiences of the founders of DBFs (university researchers, venture capitalists, or refugees from established companies) shaped the way in which they thought about how a science-based company could be organized, and how organizations in the same field might interact with one another.[18] But, the outcome of this recombinatory process generated a landscape that was unanticipated by all — and not necessarily in any one group's interest. Moreover, in the successful clusters, spillovers extended further, into the architectural, financial, legal, medical device, and biomedical supply fields that supported the burgeoning life sciences community.

Cross-network transpositions operated as the means by which ideas and skills were transferred into new domains, where they recombined with existing practices. This mixing created new possibilities in organizational practice and strategy, to be sure, but in identity as well. These new clothes may fit somewhat awkwardly, however. Identities change as individuals and organizations move from one domain to another, and as they do, original meanings can be lost (White, 1992). Consider how the blurring of basic and applied

[18] The first CEO of Amgen, George Rathman, had three decades of experience as a manager at 3M, Litton Industries, and Abbott Laboratories, all of which left him discouraged at the ability of most large firms to pursue R&D: "Deciding to decompartmentalize and fragment R&D is just plain wrong! The whole tenor of Abbott was grind it out, grind it out, make sure you have all your details right. Make sure you execute it properly. I hated the word execution; I liked the word innovation that I had brought from 3M…. But at 3M, just about the time when things started to move, the marketing guys would move in, and they would take over to run the business." With Amgen, Rathman was determined that: "If you're going to be a science-based business, for gosh sakes recognize who's essential to that business! It's the scientists" (Rathman, 2004: 6, 20).

research, or public and private science, has subtly transformed the identities of the public institutions that carry out basic research.

Thoughtful current discussions of the innovation process emphasize the need for "collaborative public spaces" to facilitate creativity and search (Lester and Piore, 2004). Sometimes, however, such admonitions can be couched in a language that vastly overstates the ability of public research organizations to contribute to new product development. Recall that the PROs in this field were critical for successful cluster formation precisely because they acted as research organizations contributing to the continuing advance of science and technology, rather than as commercial entrepreneurs (Owen-Smith and Powell, 2004). Today, many U.S. research universities are burdened with the demands of regional job creation and economic development, sometimes at the expense of scientific advance. Moreover, the tendency for many large corporations to wait until technologies are vetted by public science before investing in them does not necessarily bode well for continuing technological advance.

It is important not to view the transformations we have outlined as the necessary or desirable route for the trajectory of science and industry. Our goal was not to offer a recipe for how a science-based industry develops. Instead, our aim is to illuminate how institutions emerge from the interactions of organizations with divergent skills and resources, and explain how transpositions across a multiplicity of networks triggered change in the organizing logic of this field.

Multiple-network combinations can be regarded as legitimate, as a compromise, or as deviant. Four decades ago, the interface of public science and private finance was highly contested. The challenge of meeting evaluative standards in distinct domains is considerable, but this threshold is lessened when practices in one domain satisfy the standards of those in others. In this field, practices sculpted for the use of science and medicine turned out to have unexpected utility in a new domain. In these unusual circumstances, cross-talk generates innovation through new models of behavior (academic scientist as entrepreneur, venture capital tycoon as public policy activist), new organizational practices (proprietary firm rewarding publication of public science, public research organizations pursuing licensing deals and equity shares, venture capital firms creating entrepreneurs in residence programs), and new modes of financing (venture capital funds and research grants combine to fund startup companies). These varied innovations reverberated to transform all the participants and concatenated to produce novel institutions. Such cascades are quite unusual. When they do occur and are reinforced by the most central organizations and authorized by law and public policy, the potential for systemic change — either positive or negative — is considerable.

REFERENCES

Abbott, Andrew. 1990. "Conceptions of Time and Events in Social Science Methods." *Historical Methods* 23(4): 140-50.

Agrawal, Ajay and Iain Cockburn. 2003. "The anchor tenant hypothesis." *International Journal of Industrial Organization* 21: 1227-53.

Almeida, Paul and Bruce Kogut. 1999. "Localization of knowledge and the mobility of engineers in regional networks." *Management Science* 45:905-917.

Almeida, Paul, Gina Dokko, and Lori Rosenkopf. 2003. "Startup size and the mechanisms of external learning: increasing opportunity and decreasing ability?" *Research Policy* 32(2):301-315.

Arthur, W. Brian. 1994. *Increasing Returns and Path Dependency in the Economy*. Ann Arbor, MI: University of Michigan Press.

Audretsch, David B. and Paula Stephan. 1996. "Company-scientist locational links: The case of biotechnology." *American Economic Review* 86(3):641-52.

Barley, Stephen R. and Pamela S. Tolbert. 1997. "Institutionalization and Structuration: Studying the Links between Action and Institution." *Organization Studies* 18(1): 93-117.

Berman, Elizabeth Popp. 2007. "Creating the Market University: Science, the State, and the Economy, 1965-85." PhD dissertation, UC – Berkeley Sociology.

Boltanski, Luc, and Laurent Thévenot. 2006. *On Justification: The Economies of Worth*. Princeton, NJ: Princeton University Press.

Bourdieu, Pierre and Loic Wacquant. 1992. *An Invitation to Reflexive Sociology*. Chicago: University of Chicago Press.

Boyer, Herbert W. 2001. "Recombinant DNA Research at UCSF and Commercial Application at Genentech," an oral history conducted in 1994 by Sally Smith Hughes, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, CA.

Brown, John Seely and Paul Duguid. 2001. "Creativity versus structure: a useful tension." *MIT Sloan Management Review* 42: 93-95.

Casper, Steven. 2007. "How do technology clusters emerge and become sustainable? Social network formation within the San Diego biotechnology cluster." *Research Policy* 36(4):438-55.

Chen, Henry, Paul Gompers, Anna Kovner, and Josh Lerner. 2009. "Buy Local? The Geography of Successful and Unsuccessful Venture Capital Expansion." NBER working paper #15102.

Clark, Andy. 1993. *Associative Engines: Connectionism, Concepts, and Representational Change*. Cambridge, MA: MIT Press.

Cohen, Michael D. 1981. "The Power of Parallel Thinking." *Journal of Economic Behavior and Organization* 2(4):285-306.

Cole, Jonathan. 1993. "Balancing Acts: Dilemmas of Choice Facing Research Universities." *Daedalus* 122(4):1-36.

Colyvas, Jeannette. 2007. "From Divergent Meanings to Common Practices: The Early Institutionalization of Technology Transfer at Stanford University." *Research Policy* 36(4):456-76.

Colyvas, Jeannette and W. W. Powell. 2006. "Roads to Institutionalization: The Remaking of Boundaries Between Public and Private Science." *Research in Organizational Behavior* 27: 305-53.

Coriat, Benjamin and Orsi F. 2002. "Establishing a new intellectual property rights regime in the United States: Origins, content and problems." *Research Policy* 31(8-9):1491-507.

Cortright, Joseph and Heike Mayer. 2002. "Signs of Life: The Growth of Biotechnology Centers in the United States." Washington, D.C.: Brookings Institute.

Dasgupta, Partha and Paul A. David. 1987. "Information disclosure and the economics of science and technology." Pp. 519-542 in *Kenneth Arrow and the Ascent of Economic Theory*, G. R. Feiwel (ed.), New York: New York University Press.

____________. 1994. "Toward a New Economics of Science." *Research Policy* 23(5):487-521.

DiMaggio, Paul J. and Walter W. Powell. 1983. "The Iron Cage Revisited: Institutional isomorphism and collectivity rationality in organizational fields." *American Sociological Review* 48(2): 147-60.

Dosi, Giovanni. 1982. "Technological Paradigms and Technological Trajectories." *Research Policy* 11(3):147-162.

Eisenberg, Rebecca. 1987. "Proprietary Rights and the Norms of Science in Biotechnology Research." *The Yale Law Journal* 97(2): 177-231.

Eppli, M.J. and J.D. Shilling. 1995. “Large-scale Shopping Center Development Opportunities.” *Land-Economics* 71(1):35-41.

Feldman, Maryann. 2003. “The Locational Dynamics of the U.S. Biotech Industry: Knowledge Externalities and the Anchor Hypothesis.” *Industry and Innovation* 10: 311-28.

Feldman, Maryann and Yda Schreuder. 1996. “Initial Advantage: The Origins and Geographic Concentration of the Pharmaceutical Industry in the Mid-Atlantic Region.” *Industrial and Corporate Change* 5(3):839-62.

Fikes, Bradley J. 1999. “Why San Diego Has Biotech.” *San Diego Metropolitan*. March: 1-7.

Fligstein, Neil. 2001. *The Architecture of Markets: An Economic Sociology of Capitalist Societies.* Princeton, NJ: Princeton University Press.

Galambos, Louis and J. Sturchio. 1998. "Pharmaceutical Firms and the Transition to Biotechnology." *Business History Review* 72(2):250-82.

Gambardella, Alfonso. 1995. *Science and Innovation: The U.S. Pharmaceutical Industry during the 1980s*. Cambridge, UK: Cambridge University Press.

Goldberg, Carey. 1999. “Across the Country, Universities Generate a High-Tech Economic Boom.” *New York Times* Oct. 1: 1, 22.

Grabher, Gernot, and David Stark. 1997. “Organizing diversity: evolutionary theory, network analysis, and the postsocialist transformations.” Pp. 1-32 in *Restructuring Networks: Legacies, Linkages, and Localities in Postsocialism*, Gernot Grabher and David Stark, (eds.). London and New York: Oxford University Press.

Greenwood, Royston, Christine Oliver, Kersten Sahlin, and Roy Suddaby. 2008. “Introduction.” Pp. 1-47 in *The Sage Handbook of Organizational Institutionalism*, R. Greenwood et al. (eds.). London: Sage.

Hagel, John III and John Seely Brown. 2005. “Productive Friction: How difficult business partnerships can accelerate innovation.” *Harvard Business Review* 83(2): 82-91, 148.

Hall, Stephen S. 1987. *Invisible Frontiers: The Race to Synthesize a Human Gene*. Atlantic Monthly Press.

Hardy, Cynthia and Steve Maguire. 2008. “Institutional Entrepreneurship.” Pp. 198-217 in *The Sage Handbook of Organizational Institutionalism*, R. Greenwood et al. (eds.). London: Sage.

Hedlund, Gunnar. 1993. “Assumptions of Hierarchy and Heterarchy, with Applications to the Management of the Multinational Corporation.” Pp. 211-36 in *Organization Theory and the Multinational Enterprise,* S. Ghoshal and E. Westney (eds.). London: Macmillan.

Henderson, Rebecca and Iain Cockburn. 1996. “Scale, Scope, and Spillovers: The Determinants of Research Productivity in Drug Discovery.” *Rand Journal of Economics* 27(1): 32-59.

Henderson Rebecca, Luigi Orsenigo, and Gary Pisano. 1999. “The Pharmaceutical Industry and the Revolution in Molecular Biology: Interactions among Scientific, Institutional, and Organizational Change.” Pp. 267-311 in *Sources of Industrial Leadership*, D.C. Mowery and R.R. Nelson (eds.). New York: Cambridge University Press.

Hoffman, Andrew. 1999. “Institutional Evolution and Change: Environmentalism and the U.S. Chemical Industry.” *Academy of Management Journal* 42(4): 351-71.

Hutchins, Edwin. 1995. *Cognition in the Wild*. Cambridge, MA: MIT Press.

Jaffe, Adam B. 1986. "Technological opportunity and spillovers of research-and-development - evidence from firm patents, profits, and market value." *American Economic Review* 76(5):984-1001.

Jaffe, Adam B., Manual Trajtenberg, Rebecca Henderson. 1993. “Geographic localization of knowledge spillovers as evidenced by patent citations.” *Quarterly Journal of Economics* 108(3):577–598.

Jones, Mark Peter. 2005. *Biotech’s Perfect Climate: The Hybritech Story*. PhD dissertation, Sociology, University of California – San Diego.

Jong, Simcha. 2006. “How organizational structures in science shape spin-off firms: the biochemistry departments of Berkeley, Stanford, and UCSF and the birth of the biotech industry.” *Industrial and Corporate Change* 15(2): 251-283.

Jong, Simcha. 2008. “Academic organizations and new industrial fields: Berkeley and Stanford after the rise of biotechnology.” *Research Policy* 37(8):1267-1282.

Kenney, Martin. 1986. *Biotechnology: the University-Industrial Complex*. New Haven, CT: Yale University Press.

Klepper, Steven. 2008. “Silicon Valley: A Chip Off the Old Detroit Bloc.” Paper presented at the DRUID Conference, Copenhagen Business School, Copenhagen, Denmark.

Kreps, David. 1990. *A Course in Microeconomic Theory*. Princeton, NJ: Princeton University Press.

Krugman, Paul. 1991. "Increasing returns and economic geography." *Journal of Political Economy* 99(3):483-99.

Lane, David, and Robert Maxfield. 1996. "Strategy under complexity: fostering generative relationships." *Long Range Planning* 29(2): 215-231.

Lawrence, Thomas B. and Roy Suddaby. 2006. "Institutions and Institutional Work." Pp. 215-54 in *Handbook of Organizational Studies*, S. Clegg et al. (eds.). London: Sage.

Lee, Carolyn and Mary Walshok. 2000. *Making Connections: The Evolution of Links Between UCSD Researchers and San Diego's Biotech Industry*. A report for the University of California's Industry-University Cooperative Research Program.

Lester, Richard K. and Michael J. Piore. 2004. *Innovation: The Missing Dimension*. Cambridge, MA and London: Harvard University Press.

Macarthur, R. 1972. "Strong, or weak, interactions?" *Transactions of the Connecticut Academy of Arts and Sciences* 44: 177-88.

Macneil, Ian. 1985. "Relational contract: what we do and do not know." *Wisconsin Law Review* 3:483-526.

Mahoney, James. 2000. "Path Dependence in Historical Sociology." *Theory and Society* 29(4): 507-48.

Malerba, Franco and Luigi Orsenigo. 2002. "Innovation and market structure in the dynamics of the pharmaceutical industry and biotechnology: towards a history-friendly model." *Industrial and Corporate Change* 11(4):667-703.

McWilliams, Carey. 1949. *California, the great exception*. New York: Current Books.

Meyer, John W. 2008. "Reflections on Institutional Theories of Organizations." Pp. 790-812 in *The Sage Handbook of Organizational Institutionalism*, R. Greenwood et al. (eds.). London: Sage.

Meyer, John W. and Brian Rowan. 1977. "Institutionalized Organizations: Formal Structure as Myth and Ceremony." *American Journal of Sociology* 83(2):340-63.

Meyer, Renate. 2006. "Visiting relatives: Current developments in the new sociology of organization." *Organization* 13(5): 725-38.

Mills, L. Scott, Michael E. Soulé, and David F. Doak. 1993. "The Keystone Species Concept in Ecology and Conservation." *BioScience* 43(4): 219-24.

Mowery, David C., Richard R. Nelson, Bhaven Sampat, and Arvids Ziedonis. 2004. *Ivory Tower and Industrial Innovation*. Stanford, CA: Stanford University Press.

Owen-Smith, Jason and W. W. Powell. 2004. "Knowledge Networks as Channels and Conduits: The Effect of Spillovers in the Boston Biotechnology Community." *Organization Science* 15(1):5-21.

____________. 2006. "Accounting for Emergence and Novelty in Boston and Bay Area Biotechnology." Pp. 61-83 in *Cluster Genesis: The Emergence of Technology Clusters and Their Implication for Government Policy,* P. Braunerhjelm and M. Feldman (eds.), Oxford: Oxford University Press.

Paine, R.T. 1969. "A note on trophic complexity and community stability." *American Naturalist* 103: 91-93.

Pashigian, B. Peter and Eric D. Gould. 1998. "Internalizing externalities: the pricing of space in shopping malls." *Journal of Law and Economics* XLI: 115-42.

Pierson, Paul. 2000. "The Limits of Design: Explaining Institutional Origins and Change." *Governance* 13(4): 475-99.

Pierson, Paul. 2004. *Politics in Time.* Princeton, NJ: Princeton University Press.

Porter, Kelley. 2004. *You Can't Leave Your Past Behind: The Influence of Founders' Career Histories on their Firms*. PhD dissertation, Department of Management Science and Engineering, Stanford University.

Porter, Kelley, Kjersten Whittington, and W. W. Powell. 2005. "The Institutional Embeddedness of High-Tech Regions." Pp. 261-96 in *Clusters, Networks, and Innovation*, S. Breschi and F. Malerba (eds.), Oxford: Oxford University Press.

Portera, Carol. 2004. "Serious Research in Biotech Beach Corridor." *Genetic Engineering News* 24, 1 (Jan. 1): 46.

Powell, W.W. 1990. "Neither Market nor Hierarchy: Network Forms of Organization." *Research in Organizational Behavior* 12: 295-336.

Powell, W. W. 1996. "Inter-organizational collaboration in the biotechnology industry." *Journal of Institutional and Theoretical Economics* 120(1):197-215.

Powell, W. W. and Peter Brantley. 1992. "Competitive Cooperation in Biotechnology: Learning Through Networks?" Pp. 366-394 in *Networks and Organizations,* R. Eccles and N. Nohria (eds.), Boston: Harvard University Press.

Powell, W. W. and J. A. Colyvas. 2008. “Microfoundations of Institutional Theory.” Pp. 276-98 in *Handbook of Organizational Institutionalism*, R. Greenwood et al. (eds.), London: Sage Publishers.

Powell, W. W., K. W. Koput, and L. Smith-Doerr. 1996. "Interorganizational collaboration and the locus of innovation: Networks of learning in biotechnology." *Administrative Science Quarterly* 41(1):116-45.

Powell, W. W., K.W. Koput, J.I. Bowie, and L. Smith-Doerr. 2002. “The Spatial Clustering of Science and Capital: Accounting for Biotech Firm-Venture Capital Relationships.” *Regional Studies* 36(3): 291-306.

Powell, W. W., J. Owen-Smith, and J. A. Colyvas. 2007. “Innovation and Emulation: Lessons from American universities in selling private rights to public knowledge.” *Minerva* 45:121-42.

Powell, W. W., D. R. White, K.W. Koput, and J. Owen-Smith. 2005. "Network dynamics and field evolution: The growth of inter-organizational collaboration in the life sciences." *American Journal of Sociology* 110(4):1132-1205.

Regional Oral History Office, The University of California Berkeley Bancroft Library. 1997. Available from the online archive. Interviews by Sally Smith Hughes with: Herbert Boyer, 1994, George B. Rathman, 2003, Robert A. Swanson, 2000.

Roberts, Edward B. and Charles Eesley. 2009. “Entrepreneurial Impact: The Role of MIT.” Report to the Kauffman Foundation.

Rhoten, Diana and Powell, W. W. 2007. “The Frontiers of Intellectual Property: Expanded Protection vs. New Models of Open Science.” *Annual Review of Law and Social Science* 3:345-373.

Robbins-Roth, Cynthia. 2000. *From Alchemy to IPO*. Cambridge, MA: Perseus Publishing.

Sabel, Charles. 1990. “Moebius-strip organizations and open labor markets: some consequences of the reintegration of conception and execution in a volatile economy”. Pp. 23-54 in *Social Theory for a Changing Society*, Pierre Bourdieu and James Coleman (eds.), Boulder, CO and New York: Westview Press.

Saxenian, Annalee. 1994. *Regional Advantage: Culture and Competition in Silicon Valley and Route 128*. Cambridge, MA: Harvard University Press.

Scott, Allen J. and Michael Storper. 2003. “Regions, Globalization, and Development.” *Regional Studies* 37: 579-93.

Simard, Caroline. 2004. “From weapons to cell phones: knowledge networks in San Diego's wireless valley.” PhD Thesis, Stanford University, Department of Communication.

Sorenson, Olav and Pino Audia. 2000. “The social structure of entrepreneurial activity: Geographic concentration of footwear production in the US, 1940-1989.” *American Journal of Sociology* 106(2):424-61.

Stark, David. 1996. “Recombinant property in East European capitalism.” *American Journal of Sociology* 101(4): 993-1027.

____________. 2001. “Ambiguous assets for uncertain environments: heterarchy in postsocialist firms.” Pp. 69-104 in *The twenty-first century firm: changing economic organization in international perspective,* Paul DiMaggio (ed.). Princeton, NJ: Princeton University Press.

Stark, David and Balazs Vedres. 2006. “Social Times of Network Spaces: Network Sequences and Foreign Investment in Hungary” *American Journal of Sociology* 11(5): 1367-1411.

Stinchcombe, Arthur. 1965. "Social structure and organizations." Pp.142-193 in *Handbook of Organizations*, James G. March (ed.), Chicago, IL: Rand McNally.

____________. 1968. *Constructing Social Theories*. New York: Harcourt, Brace World.

Stuart. Toby E. and Olav Sorenson. 2003. “The geography of opportunity: Spatial heterogeneity in founding rates and the performance of biotechnology firms” *Research Policy* 32:229-53.

Teitelman, Robert. 1989. *Gene Dreams: Wall Street, Academia, and the Rise of Biotechnology*. New York: Basic Books.

Thelen, Kathleen. 2004. *How Institutions Evolve*. New York: Cambridge University Press.

Van Brunt, Jennifer. 2000. “Biotech’s Impeccable Lineage.” *Signals Magazine* March 22: 1-10.

Varmus, Harold E. and Robert A. Weinberg. 1992. *Genes and the Biology of Cancer*. New York: Scientific American Press.

Walcott, Susan M. 2002. “Analyzing an Innovative Environment: San Diego as a Bioscience Beachhead.” *Economic Development Quarterly* 16(2): 99-114.

Walshok, Mary L., Carolyn Lee, Ed Furtek, and Pat Windham. 2001. *Networks of Innovation: Contributions to San Diego’s Telecommunications and Biotechnology*

Clusters. A report for the University of California's Industry-University Cooperative Research Program.

Watson, James D. 2003. *DNA: The Secret of Life*. New York: Knopf.

Weick, Karl. 1993. "The collapse of sensemaking in organizations: the Mann Gulch disaster." *Administrative Science Quarterly* 38(4): 628-652.

White, Harrison C. 1992. *Identity and Control.* Princeton, NJ: Princeton University Press.

Whittington, Kjersten Bunker. 2007. "Employment Sectors as Opportunity Structures: Male and Female: The Effects of Location on Male and Female Scientific Dissemination". PhD Dissertation, Stanford University.

Whittington, Kjersten Bunker, Jason Owen-Smith, and W. W. Powell. 2009. "Networks, Propinquity and Innovation in Knowledge-Intensive Industries." *Administrative Science Quarterly,* 54(1): 90-122.

Wright, Susan B. 1994. *Molecular Politics Developing American and British Regulatory Policy for Genetic Engineering, 1972 – 1982.* Chicago: University of Chicago Press.

Young, Peyton. 1998. *Individual Strategy and Social Structure*. Princeton, NJ: Princeton University Press.

Zacks, Rebecca. 2000. "The Technology Review University Research Scorecard 2000." *Technology Review* 103(4):88-90.

Zucker, Lynne G. and Michael R. Darby. 1996. "Star scientists and institutional transformation: patterns of invention and innovation in the formation of the U.S. biotechnology industry." *Proceedings of National Academy of Science* 93:709-16.

Zucker, Lynne G., Michael R. Darby, and Marilyn Brewer. 1998. "Intellectual Human Capital and the Birth of U.S. Biotechnology Enterprises." *American Economic Review* 88(1): 290-306.

Zuckerman, Ezra. 1999. "The Categorical Imperative: Securities Analysts and the Illegitimacy Discount." *American Journal of Sociology* 104(5):1398-1438.

Zuckerman, Ezra, Tai Kim, Kalinda Ukanwa, and James von Rittman. 2003. "Robust Identities or Non-entities? Typecasting in the Feature Film Labor Market." *American Journal of Sociology* 108(5):1018-74.

Table 1: Regional Agglomeration Was Not Based on Initial Advantage in Patents

Biotechnology Patents, by Metropolitan Region

Metro Area	*1975-1979*	*1980-1989*	*1990-1999*
Boston, MA	126	592	3,007
Houston, TX	18	144	634
Los Angeles, CA	106	330	1,399
New York, NY, and Northern New Jersey	1,420	3,590	6,800
Philadelphia, PA	679	1,309	3,214
Research Triangle, NC	27	204	796
San Diego, CA	23	210	1,632
San Francisco Bay Area, CA	414	1,173	3,991
Seattle, WA	9	93	770
Washington, DC, and Baltimore, MD	121	470	2,162

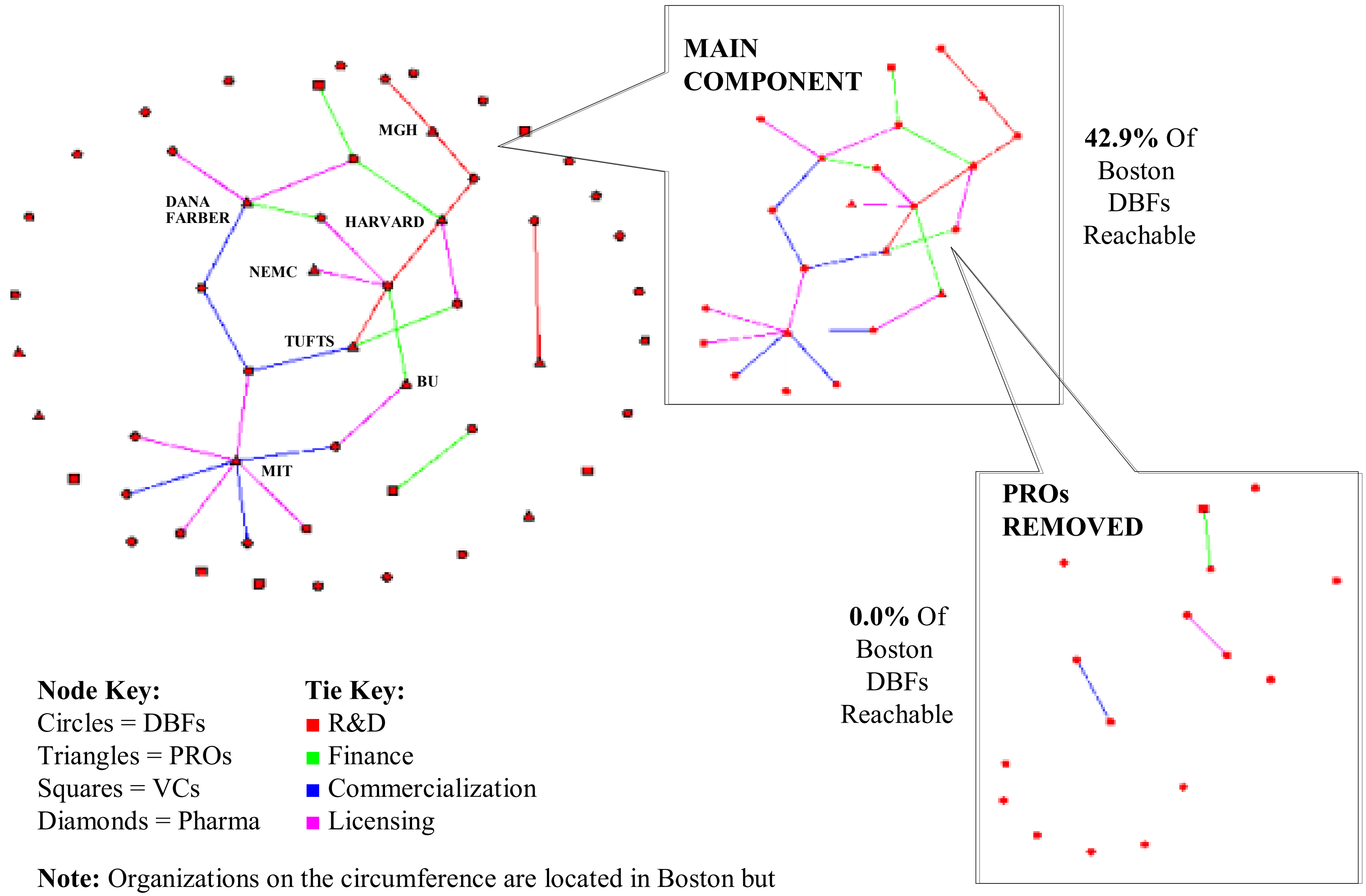
Source: Drawn from J. Cortright and H. Mayer, "Signs of Life: The Growth of Biotechnology Centers in the U.S.," Brookings, 2002.

Biological and chemical patents held by pharmaceutical and biotechnology companies

Figure 1: Location of U.S. Biotechnology Companies, 1980 (n=48)

Figure 2: Location of U.S. Biotechnology Companies, 2002 (n=368)

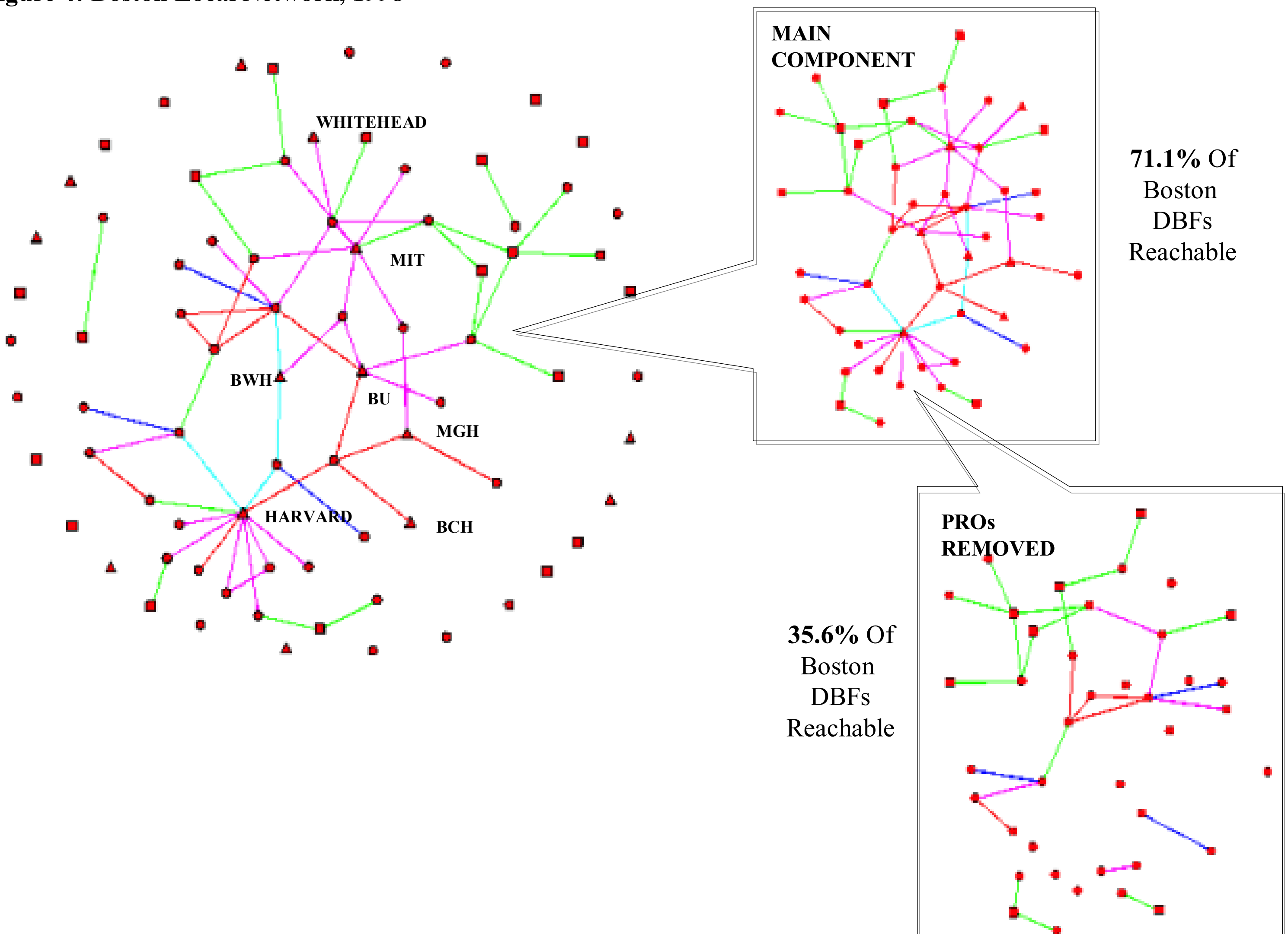
Figure 3: Boston Local Network, 1988



Note: Organizations on the circumference are located in Boston but have no contractual relations with other Boston organizations in 1988

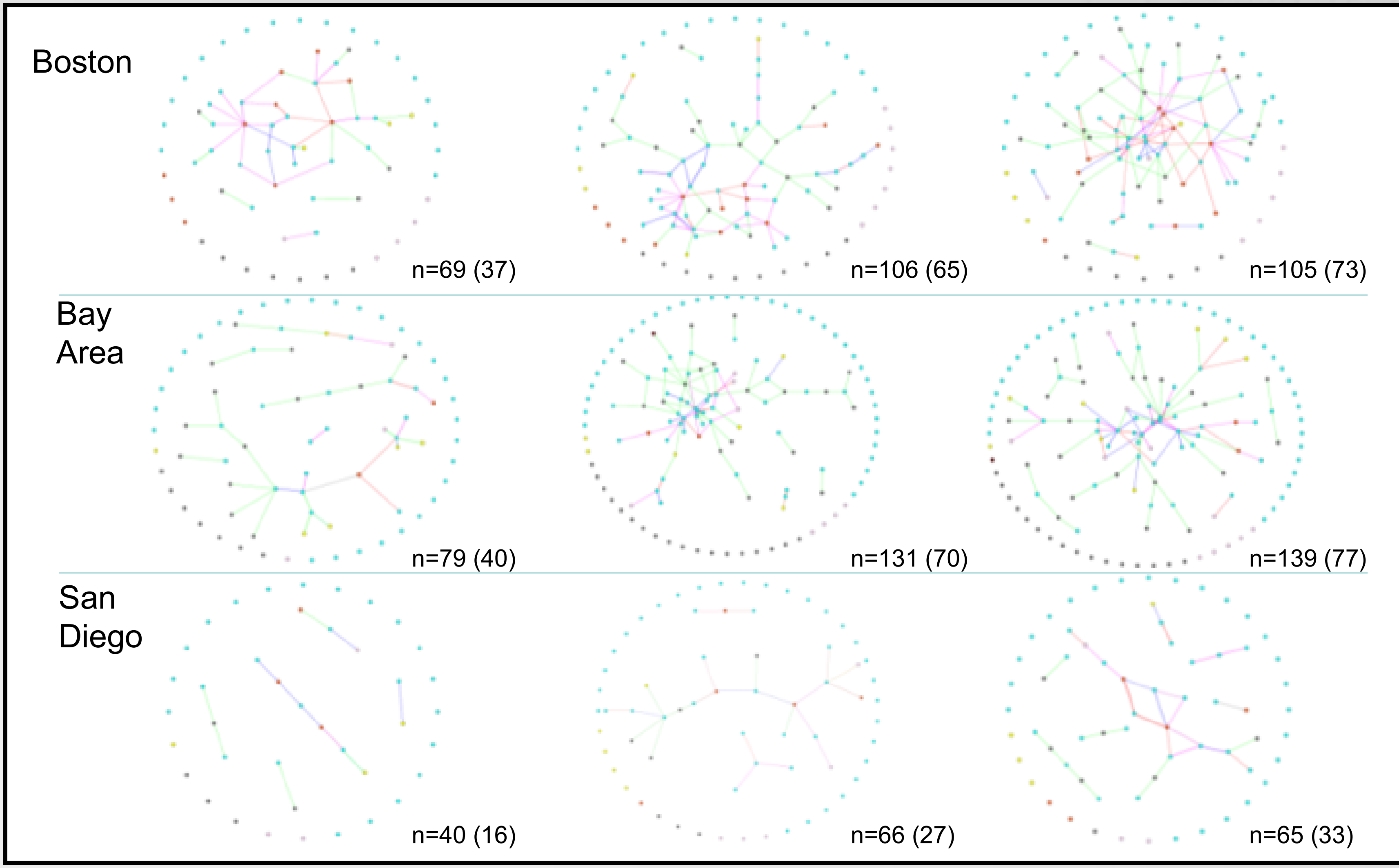
Source: Owen-Smith and Powell, *Organization Science* 2004.

Figure 4: Boston Local Network, 1998



Source: Owen-Smith and Powell, *Organization Science* 2004.

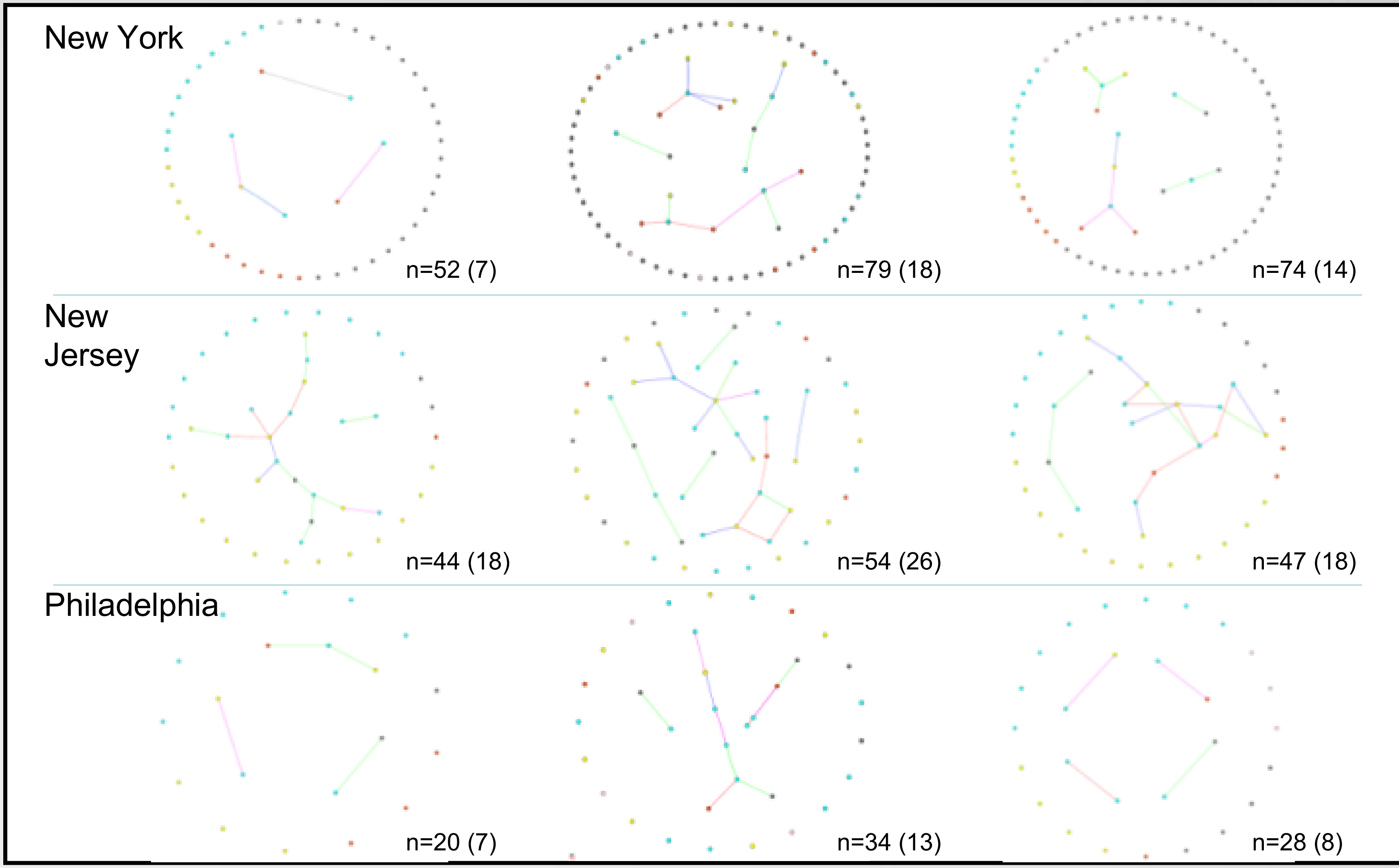
Boston, Bay Area and San Diego, 1990, 1996, and 2002



Node Key: DBFs, Fin. Institutions, Gov't Institutes, Pharma Corps, Public Research Orgs, Biomed Suppliers

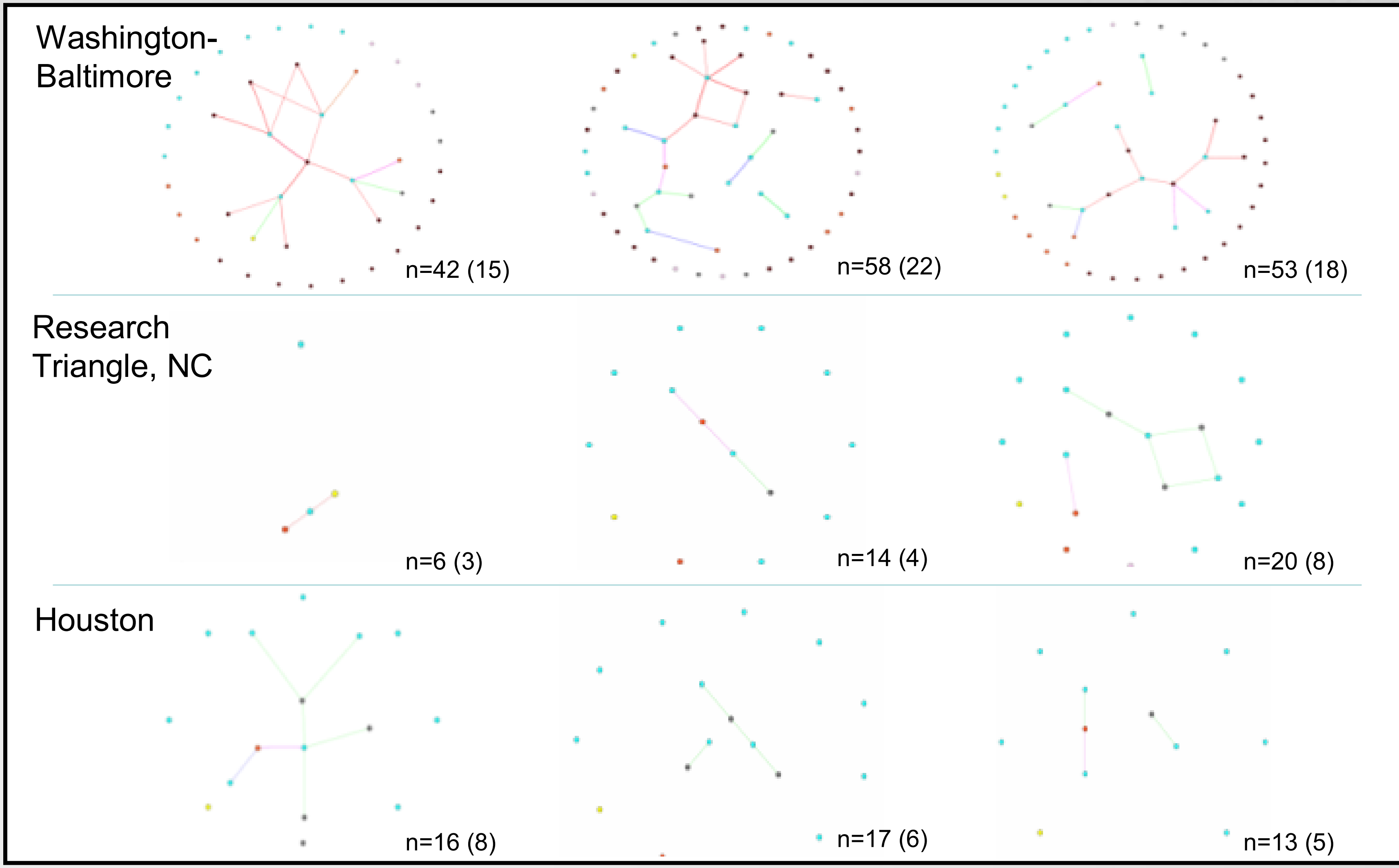
Tie Key: R&D, Finance, Commercialization, Licensing **Note:** n = all nodes, number in brackets = connected nodes

New York, New Jersey, and Philadelphia, 1990, 1996, and 2002



Node Key: DBFs, Fin. Institutions, Gov't Institutes, Pharma Corps, Public Research Orgs, Biomed Suppliers
Tie Key: R&D, Finance, Commercialization, Licensing **Note:** n = all nodes, number in brackets = connected nodes

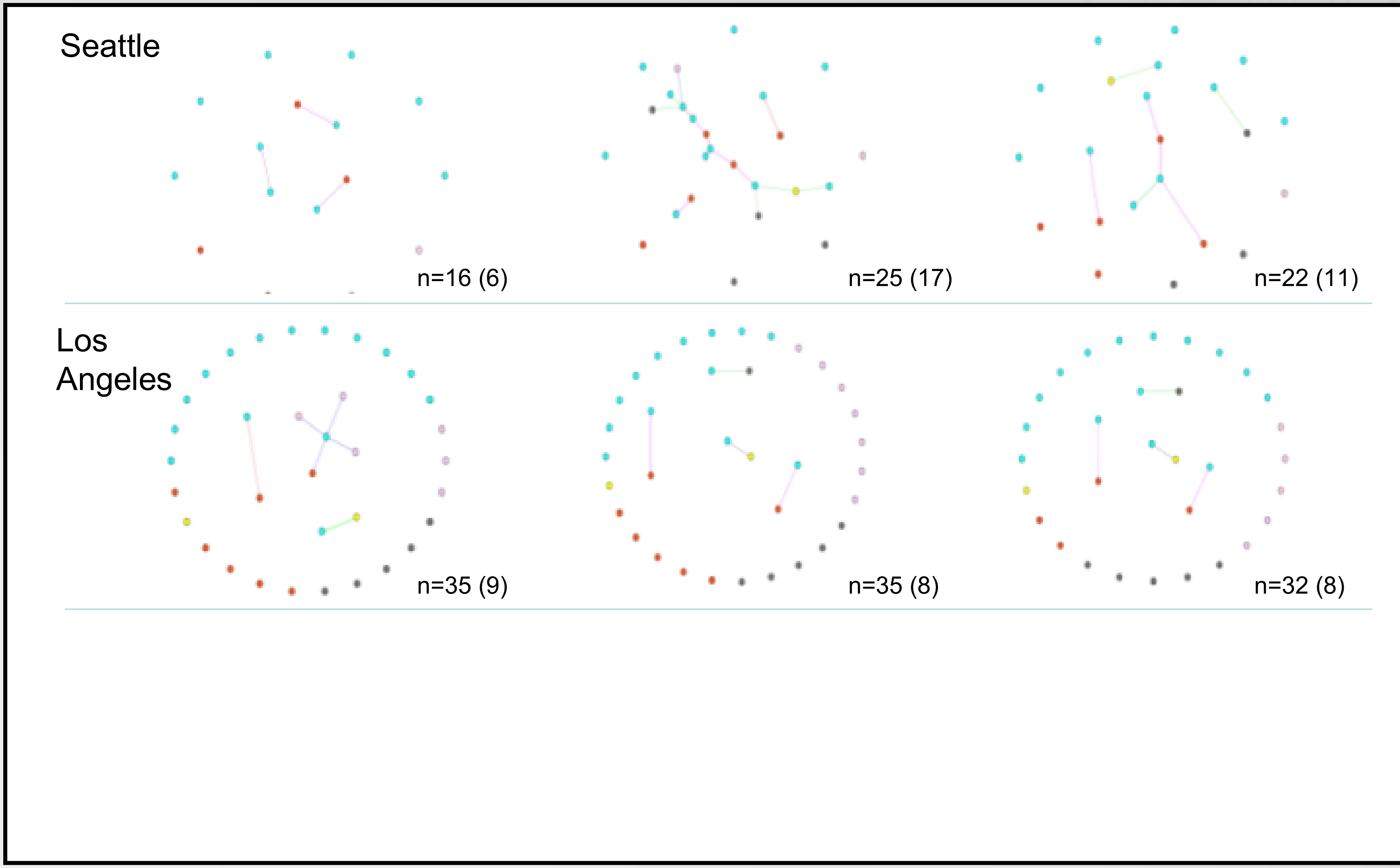
Washington-Baltimore, Research Triangle, NC, and Houston, 1990, 1996, and 2002



Node Key: DBFs, Fin. Institutions, Gov't Institutes, Pharma Corps, Public Research Orgs, Biomed Suppliers

Tie Key: R&D, Finance, Commercialization, Licensing **Note:** n = all nodes, number in brackets = connected nodes

Seattle and Los Angeles, 1990, 1996, and 2002



Node Key: DBFs Fin. Institutions Gov't Institutes Pharma Corps Public Research Orgs Biomed Suppliers
Tie Key: R&D Finance Commercialization Licensing **Note:** n = all nodes, number in brackets = connected nodes

Figure 9:Anchor tenant vs. 800 lb. gorilla: % of all ties by organizational form of partners, 1990, 1996, and 2002

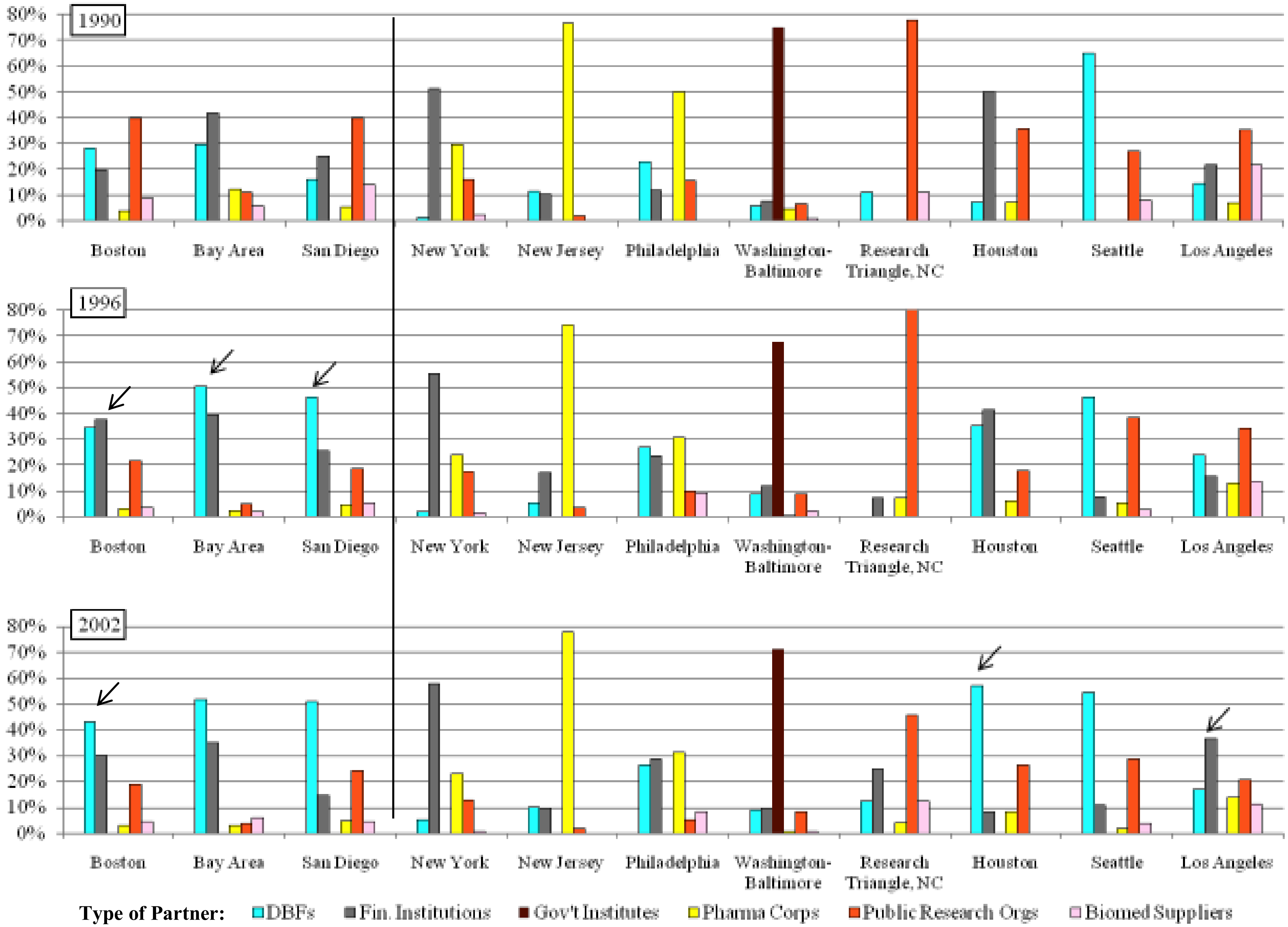


Figure 10: Transposition: % of local ties by organizational form of partners, 1990, 1996, and 2002

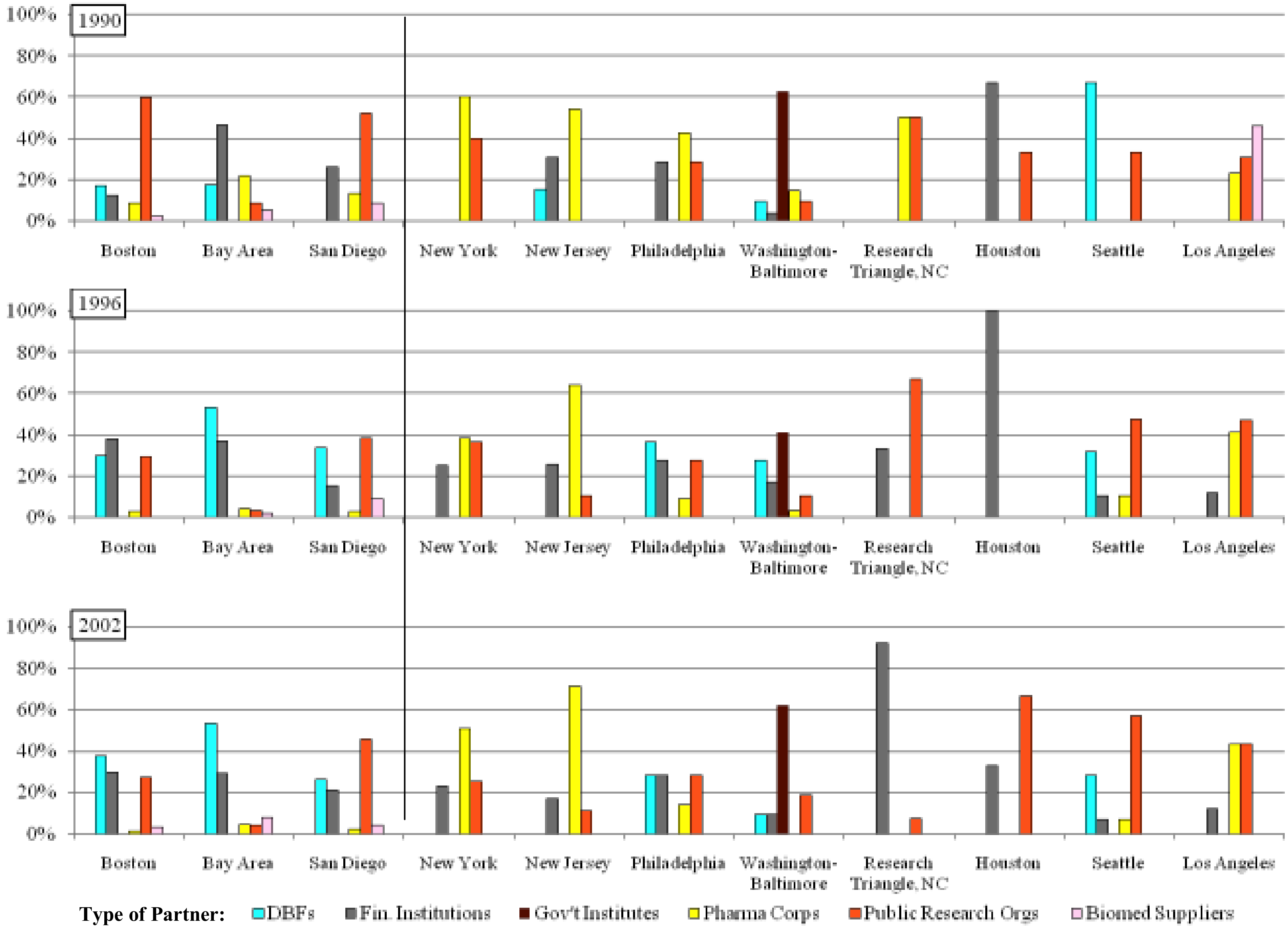


Figure 11: Sample selection on networks? Count of partner ties by location, 1990, 1996, and 2002