Building Robust Business Clusters: Lessons from Biotech

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- **My aim is to show that three elements are critical to the formation of productive business clusters:**
  - ***Multiple types of organizations*** **- - a rich soup in which diverse practices and rules can emerge. Different criteria for success.**
  - **A *catalytic anchor tenant* that protects the openness of the community and allows multiple views to be heard.**
  - ***Cross-cutting local networks*** **- - ample movement across organizations, job mobility, "rewirings" - - all of which lead to good ideas circulating quickly through a decentralized system.**
- **Much of what makes clusters successful has to do with the character of local networks. The advantages of geography and wealth do not dictate success, but the networks of affiliations among organizations both within and across a region powerfully shape opportunities.**
- **Diversely anchored, multi-connected networks are much less likely to unravel than those reliant on a few powerful organizations.**

Biotech companies in United States, 1978 (n=30)

Potential candidates for formation of biomedical clusters, circa 1980

Ranking in number of biomedical patents, 1980	
1	**New York City** - - extraordinary array of research hospitals, elite universities and medical schools, venture capital and investment banks
1	**Northern New Jersey** - - home of major U.S. and foreign pharmaceutical companies, Princeton University
3	**Philadelphia** - - “the cradle of pharmacy” - - strong pharmaceutical presence, U Penn, Wistar Institute, Fox Chase Cancer Center
4	**Bay Area CA** - - UCSF, Stanford, venture capital…but crowding from ICT industries?
5	**Boston** - - MIT and to lesser extent Harvard (commercial involvement by faculty was initially precluded), numerous research hospitals
6	**Washington DC metro area**- - home of National Institutes of Health, Johns Hopkins University Medical School
7	**Los Angeles CA** - - largest early biotech firm – Amgen, Cal Tech, UCLA, City of Hope Hospital
8	**Research Triangle NC** - - three universities, major state public policy initiative to build a cluster
9	**Houston TX** - - U Texas Medical Center, Rice University, MD Anderson Hospital
10	**Seattle WA** - - Fred Hutchinson Cancer Center, U Washington…large investments by Bill Gates and others in biomedicine in 1990s
10	**San Diego CA** - - sleepy Navy and tourist town, but UCSD, Scripps, Salk, and Burnham Institutes

Biotech companies in United States, 1984 (n=130)

Biotech companies in United States, 1990 (n=253)

Biotech companies in United States, 2002 (n=368)

More than 50% of companies in just three regions

What explains this pronounced pattern of geographic agglomeration?

- The leading sources of knowledge in the life sciences in the late 1970s and early 1980s were widely distributed across U.S. and globally. In the U.S., public policy and political muscle were flexed to support this field's development. But today, nearly 50% of firms and more than 50% of the outcomes (employment, medicines, patents) come from just three regions - - Bay Area, Boston, San Diego.

Data sources:

- Our data cover dedicated biotech firms, large multinational corporations, research universities, government labs and institutes, research hospitals, nonprofit research centers, and venture capital firms and their formal inter-organizational collaborations from 1988-2004. Includes data on earlier years, but is left censored so that we were only able to collect full info on firms alive from1988 to present. In total, 691 dedicated biotech firms, 3,000 plus collaborators, 11,000 plus collaborations - - both local and global ties.

- We also did field work inside companies, examined archival records, interviewed 100s of scientists and managers in DBFs, universities, pharma cos., govt. institutes, technology licensing offices, VC and law firms.

We begin with the Boston Biotech Community

Data: All contractual ties (R&D, finance, clinical trials, manufacturing, marketing, licensing) involving a biotech firm located in Boston and other organizations, either within Boston or outside.

Population:	Within Boston network	Boston "plus" network
Dedicated biotechnology firms	58	212
Public research organizations	19	96
Government agencies	0	24
Venture capital firms	37	240
Pharmaceutical corporations	0	168
Alliances between two Boston area organizations	201	1559

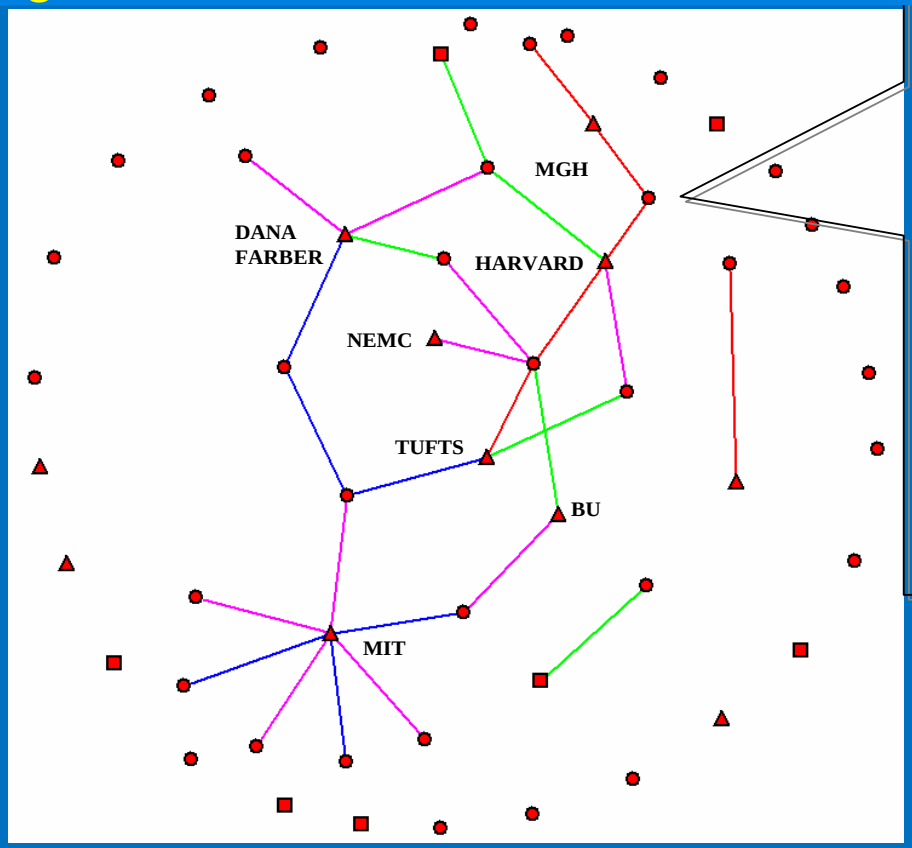
Note the diverse array of organizations – public research organizations, nonprofit institutes, for-profit companies. Recall political scientist Ed Lindblom's (1977) classic quip: Markets are like a hand with only fingers, while states are a hand with only thumbs.

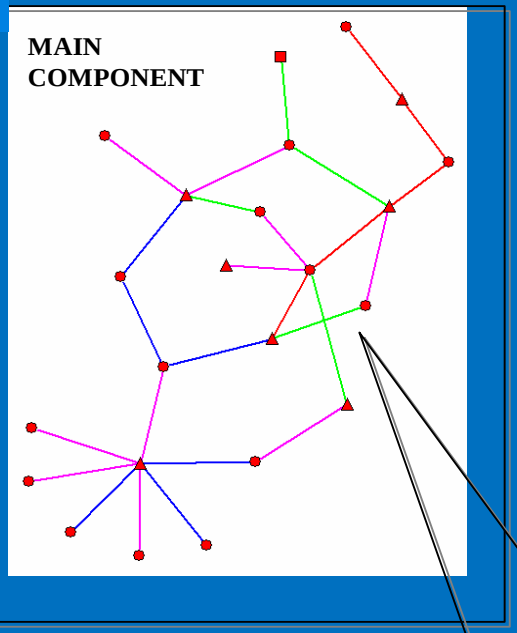
Methods: Visualizing Social Networks With Pajek

- *Pajek* (Slovenian for 'Spider') is a freeware package for the analysis and visualization of large networks created by Vladimir Batagelj and Andrej Mrvar. Available online at http://vlado.fmf.uni-lj.si/pub/networks/pajek/

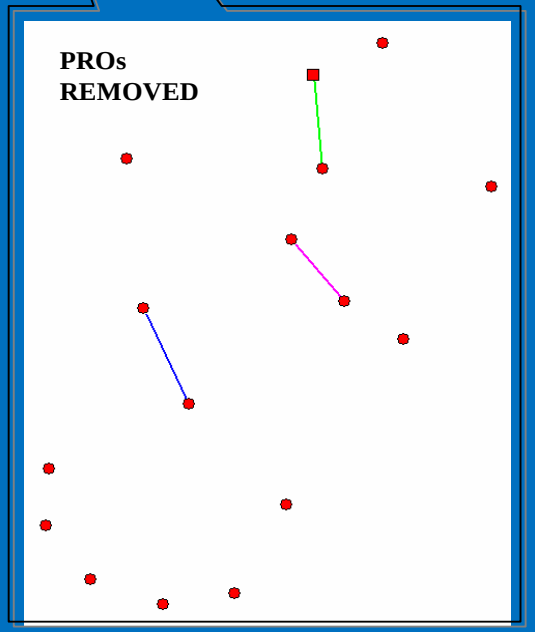
- In Pajek, 'spring-embedded' network drawing algorithms enable meaningful representation of social networks in Euclidean space.
  - 'Particles' repel one another, 'springs' draw attached particles together
  - Drawing algorithms seek a 'solution' where the energy of the entire system is minimized
  - In these representations, the positions of nodes are generated by the pattern of ties connecting the entire system
- We draw on two such algorithms:
  - Fruchterman-Reingold (FR) (1991) optimizes network configurations without reference to graph-theoretic conceptions of distance
  - Kamada-Kawai (KK) (1989) positions connected nodes adjacent to one another and makes Euclidean distances proportional to geodesic path length in the network

Figure 3: Boston Local Network, 1988





42.9% Of Boston DBFs Reachable



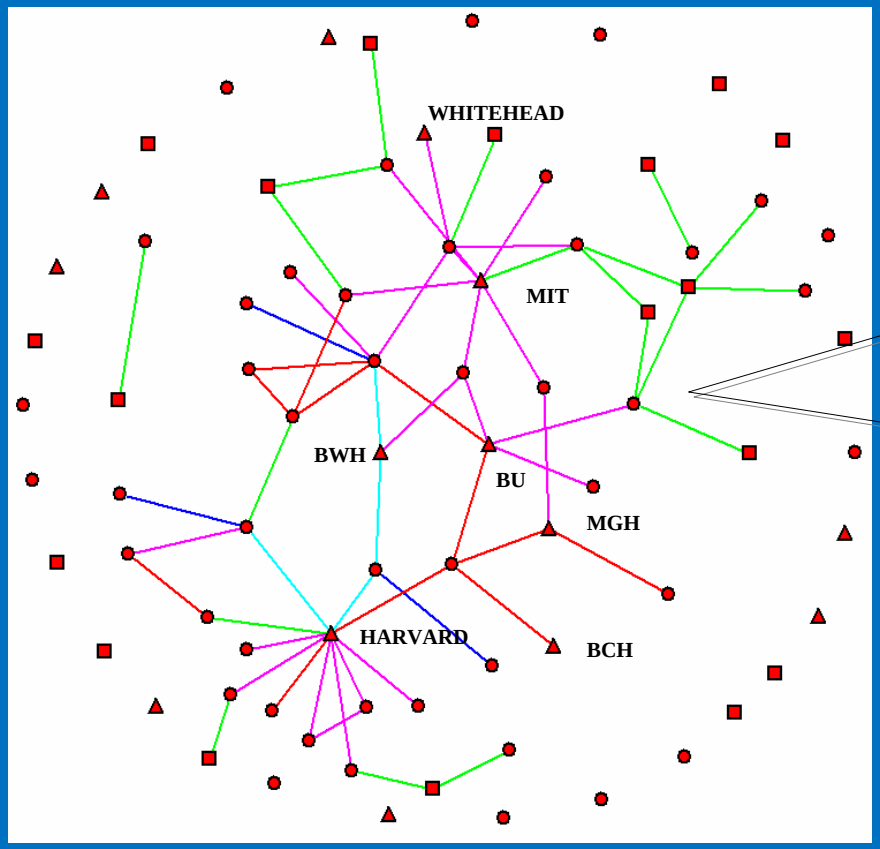
0.0% of Boston DBFs Reachable

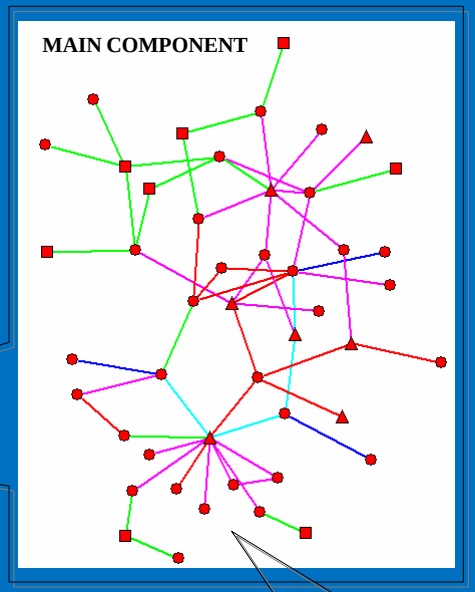
Node Key:
Circles = DBFs
Triangles = PROs
Squares = VCs
Diamonds = Pharma

Tie Key:	
	R&D
	Finance
	Commercialization
	Licensing

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

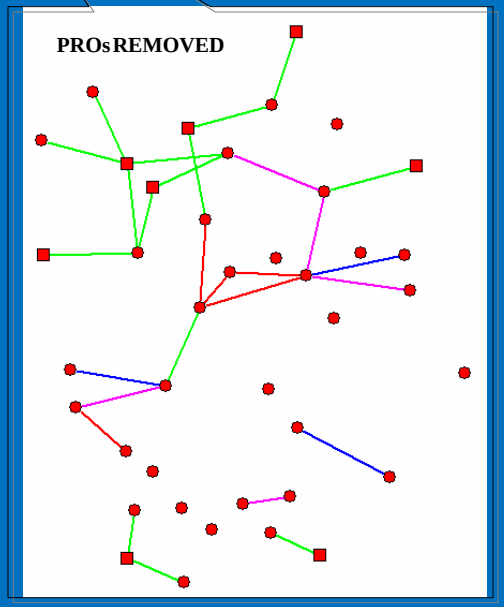
Figure 4: Boston Local Network, 1998





71.1% of Boston DBFs reachable

35.6% of Boston DBFs reachable

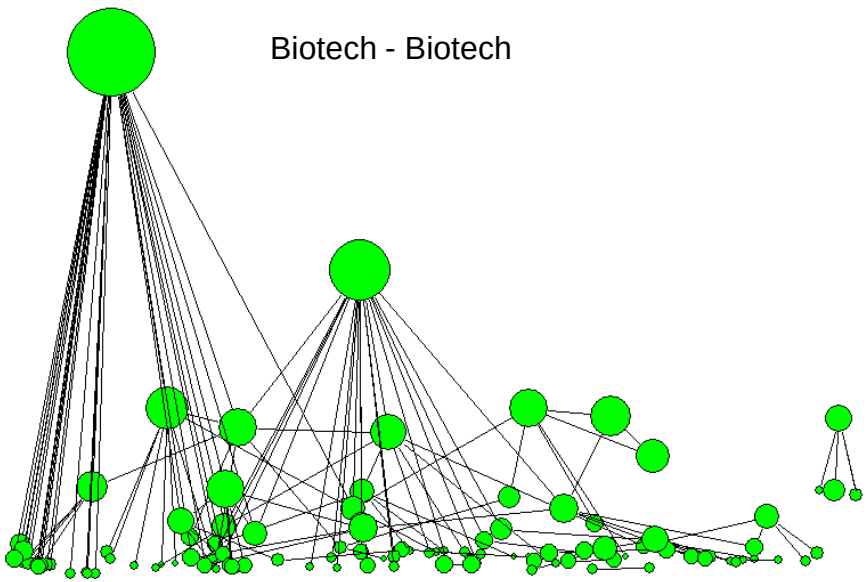


Note: Organizations on the circumference are located in Boston but have no contractual relations with other Boston organizations in 1998.

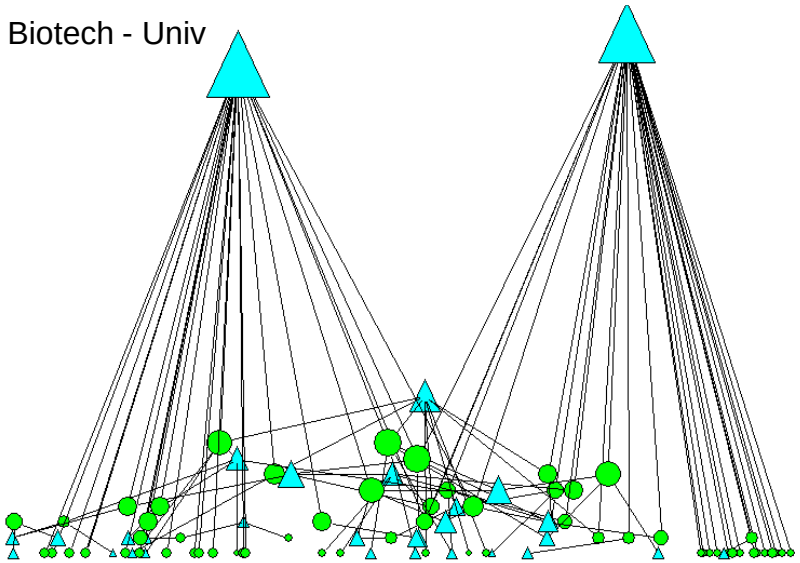
Source: Owen-Smith and Powell, *Organization Science 2004.*

In Boston, organizational diversity drives innovation networks.

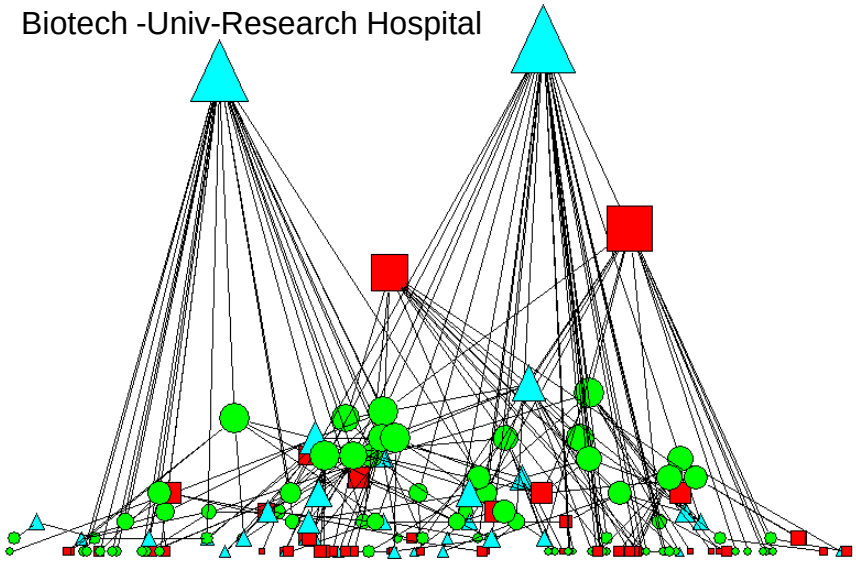
Biotech - Biotech



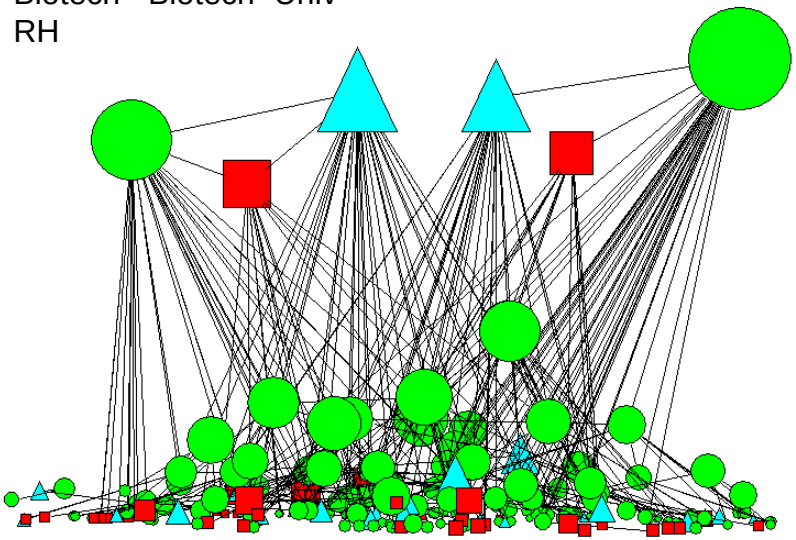
Biotech - Univ



Biotech -Univ-Research Hospital



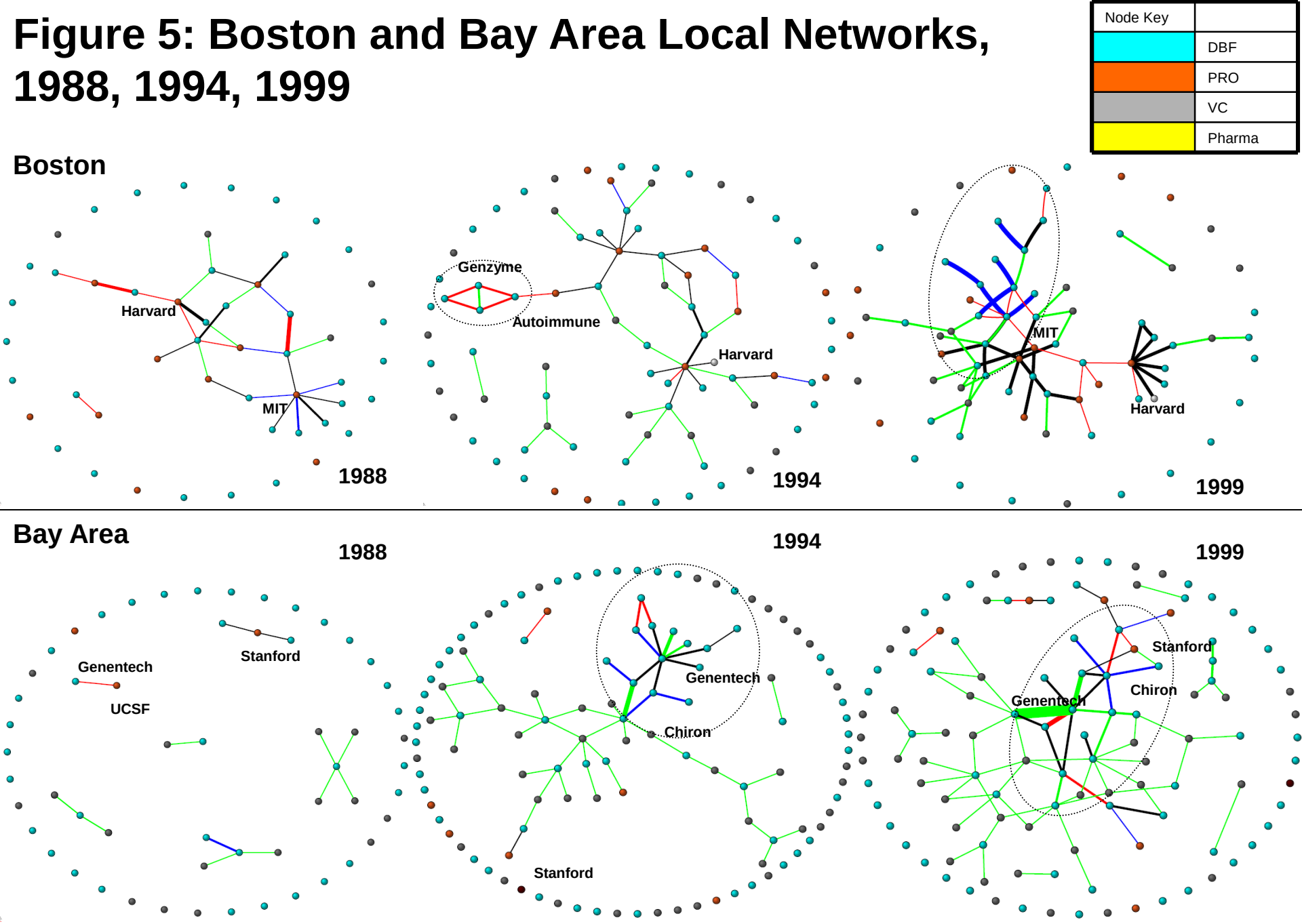
Biotech - Biotech -Univ-RH



Results from Analysis of Boston Biotechnology Community

- Local public research organizations (PROs) were the foundation on which the Boston commercial biotech community was built. Ties to local PROs increased rates of patenting by companies.
- Over time, the Boston network changed to become more anchored by for-profit firms. Ties to organizations outside of Boston grew rapidly. As the network expanded, the majority of ties became commercial. The importance of local PROs receded, but their footprint remained. Centrality in the Boston network continued to have a large impact on patenting.
- Ties to local PROs are leaky (spillovers), while external commercial ties are closed and contractually restricted.
- Public research organizations contribute to industry innovation *precisely because* they perform commercially important research under academic institutional arrangements.
- Active commercial participation by PROs catalyzes life science innovation, but may carry the danger of 'capture' by industrial interests.

Figure 5: Boston and Bay Area Local Networks, 1988, 1994, 1999



Note: Thickness of line indicates multiple ties. **Source**: Owen-Smith and Powell, 2006.

We turned to study other successful clusters and found there is no one recipe for successful cluster formation. The initial endowments in the successful clusters were quite different.

Bay Area:

- First-generation companies collaborated with one another – Genentech, Chiron – acting like an academic invisible college
- Active engagement of venture capitalists as executives
- Relational model of technology transfer developed at Stanford
- Interdisciplinary science at UCSF
- Blending of public and private science

How do transactional and relational ties differ? Consider the Cohen-Boyer patent, jointly held by Stanford and UCSF, administered by Stanford

- Patent held from 1980-97, 467 licensees, $194,319,000 in revenues. Cohen and Boyer had to be persuaded to patent the invention. They were initially opposed to the idea.

- Open, not an exclusive, license. Patent never challenged in court.

Tell me about negotiating the Institutional Patent Agreement (prior to Bayh-Dole).

Reimers, then director of OTL: So we got the inter-institutional agreement with UC worked out. The research at Stanford had been sponsored by NIH [National Institutes of Health], and at UC by NSF [National Science Foundation] and the American Cancer Society. The American Cancer Society had never released rights on an invention before. So I contacted them and explained the situation. I said that what I'd like to do is have it managed under our institutional patent agreement with NIH. And I explained the patent system and how *the net returns would go back into research*. They eventually agreed.

Why were you convinced that this invention could be something big?

Reimers: I wasn't convinced. I didn't know that much about it. Because a great excitement developed regarding this area, I maintained from the beginning that the work of Cohen and Boyer would underlie the whole field of biotechnology. And I repeated it and repeated it. When I first went to the companies, the business people didn't understand the technology. They had just been reading about its potential. So we had to go through a tutorial as well.

How are decisions about patenting made at Stanford?

***Kathy Ku, current Director, Office of Technology Transfer, Stanford University*: The lack of attorneys was a totally conscious decision. We think of ourselves as a business office. We think that lawyers are trained to be risk averse and so [our founding director] felt strongly against hiring them and I fundamentally agree. *We feel that our agreements represent business relationships rather than legalistic ones*. Even the good licenses and relationships are going to require modification along the way. We take a much more 'Japanese' attitude, which is to say that the license is the beginning of an ongoing relationship and the situation changes we can always renegotiate. *We renegotiate a lot*.**

How are rewards shared?

10% off the top goes to OTL or admin. charges, 1/3rd to university, 1/3rd to dept., 1/3rd to inventor(s). (Peer-based monitoring).

San Diego - - A sleepy Navy and tourist town became a high tech cluster in biotech and wireless in the 1990s.

1978 - - Hybritech founded by Ivor Royston, an asst prof. at UCSD and former Stanford postdoc, and Howard Birndorf, a lab tech. They secured backing from Kleiner, Perkins and got Brook Byers as their manager.

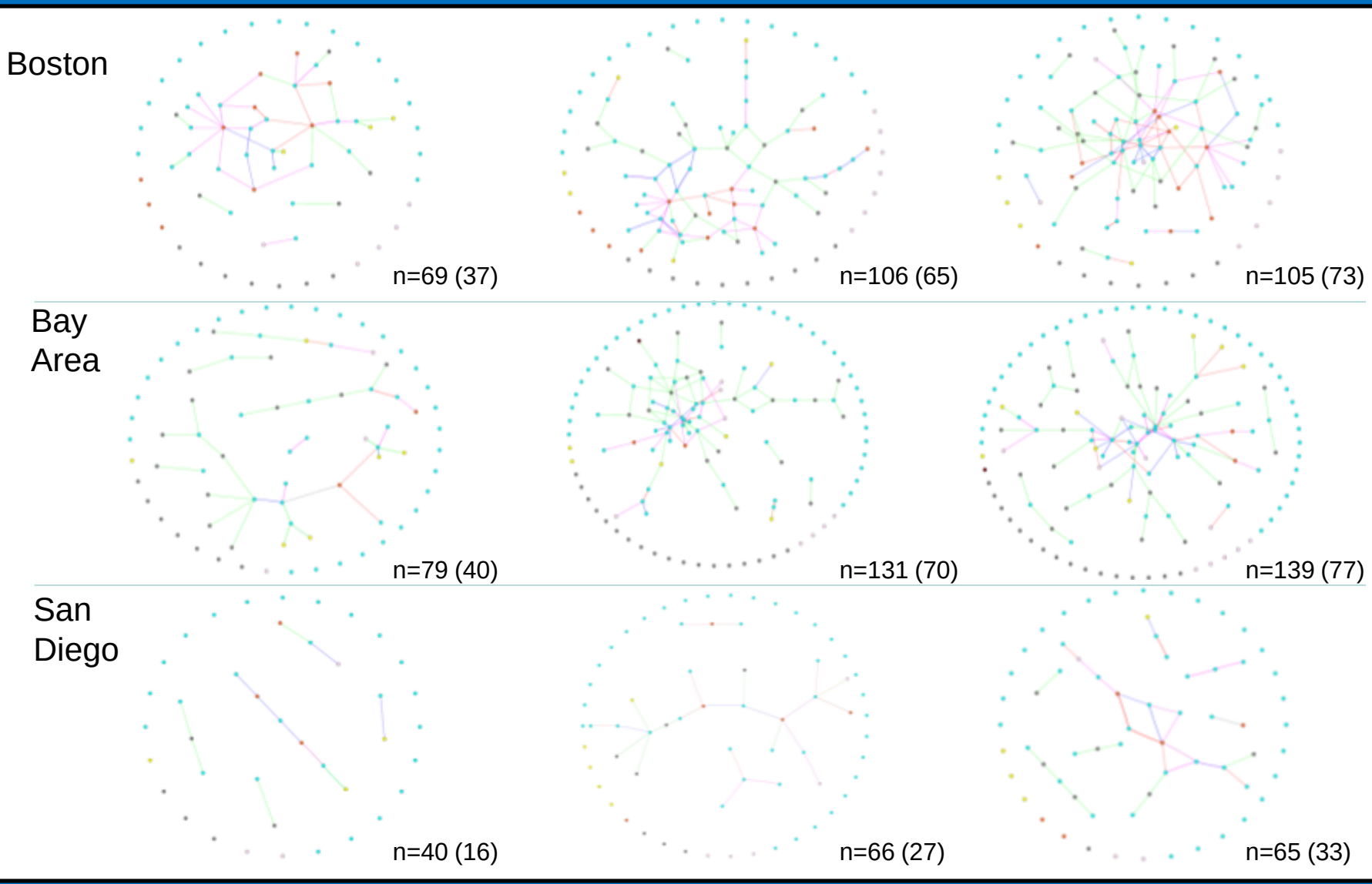
Developed diagnostic tests based on monoclonal antibody technology, no need for lengthy clinical trials or FDA approval, generated revenue within months of invention…one of few firms to become profitable early, had a successful IPO in 1981.

1986 - - Hybritech acquired by pharma giant Eli Lilly for $300 million and 100 million in shares. "Animal House meets the Waltons." Huge failure!

UCSD began CONNECT program to help networking and teach financial and business skills missing in local community.

But ex-Hybritech scientists and managers stayed in San Diego and started more than 40 biotech firms (Idec, GenProbe, Ligand, Gensia, Genta, Nanogen, Amylin, etc.) and several VC firms (Biovest, Forward Ventures, Kingsbury Partners). They partnered with scientists at the Salk Institute, Scripps, and UCSD. Bay Area VCs moved to SD. This failed merger seeded the San Diego biotech cluster.

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

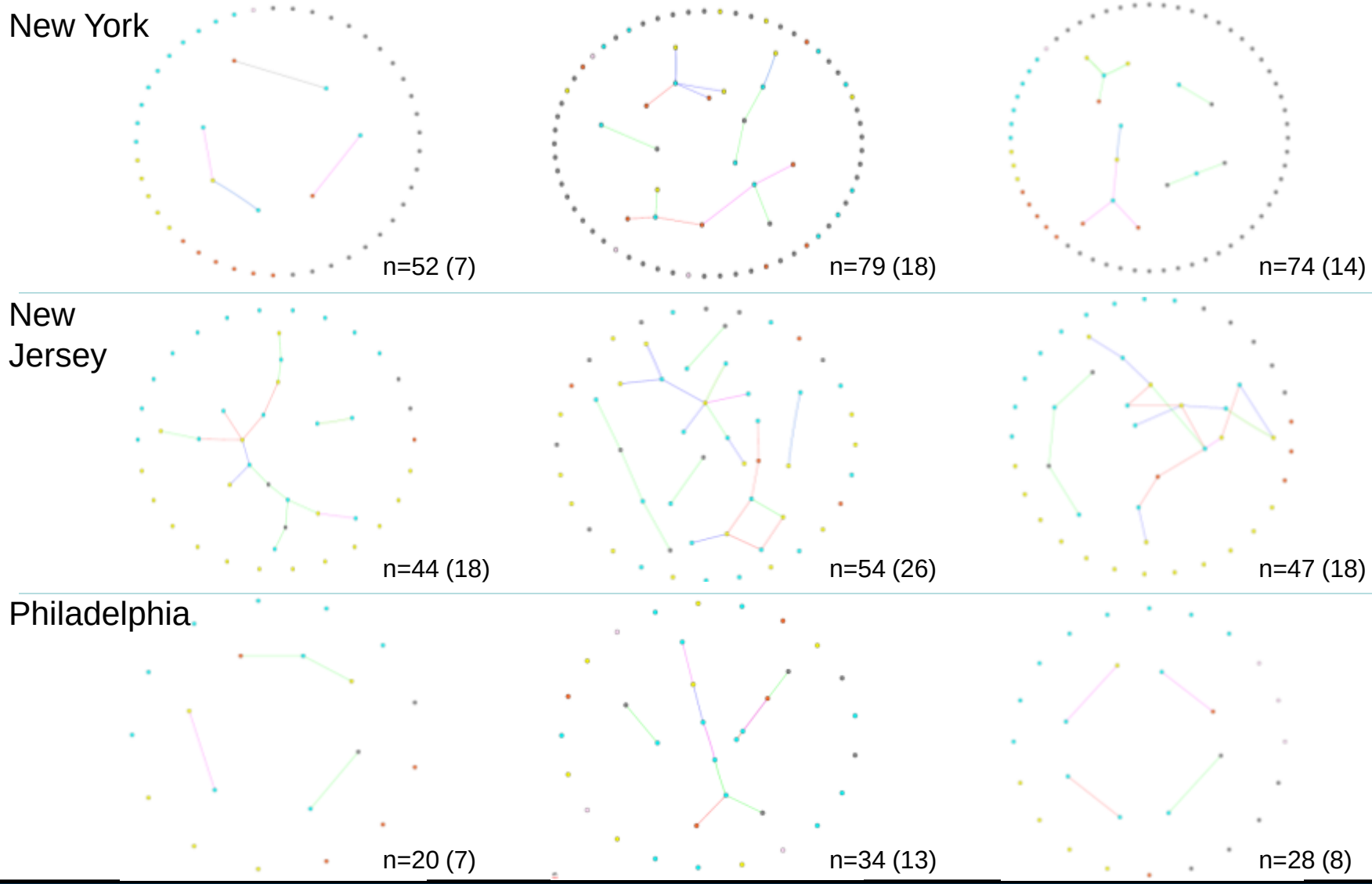
Tie Key: R&D Finance Commercialization Licensing **Note:** n = all nodes, number in brackets = connected nodes

Comparison of Boston, Bay Area, and San Diego:

- Different organizations serve as anchor tenants, but each operates to foster interaction among disparate parties and provide means for local information sharing. These organizations spark the mixing of practices across domains. No standard solution, *instead a topology of the possible*.
- Boston: Public Research Organizations
- Bay Area: Venture Capital, multidisciplinary model of UCSF, technology transfer office at Stanford focused on relationships with startups, first-generation companies pursued invisible college model.
- San Diego: Spinoffs from failed acquisition of Hybritech by Eli Lilly ("Animal House meets the Waltons"), Salk, Scripps, Burnham, UCSD, and Connect, a local nonprofit incubator.
- Common processes in all three regions: considerable job mobility, ostensible local competitors collaborated, public and private science interwoven, all independent from overweening control of a dominant organization.

Let's take a fast look at the places that didn't take off →

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



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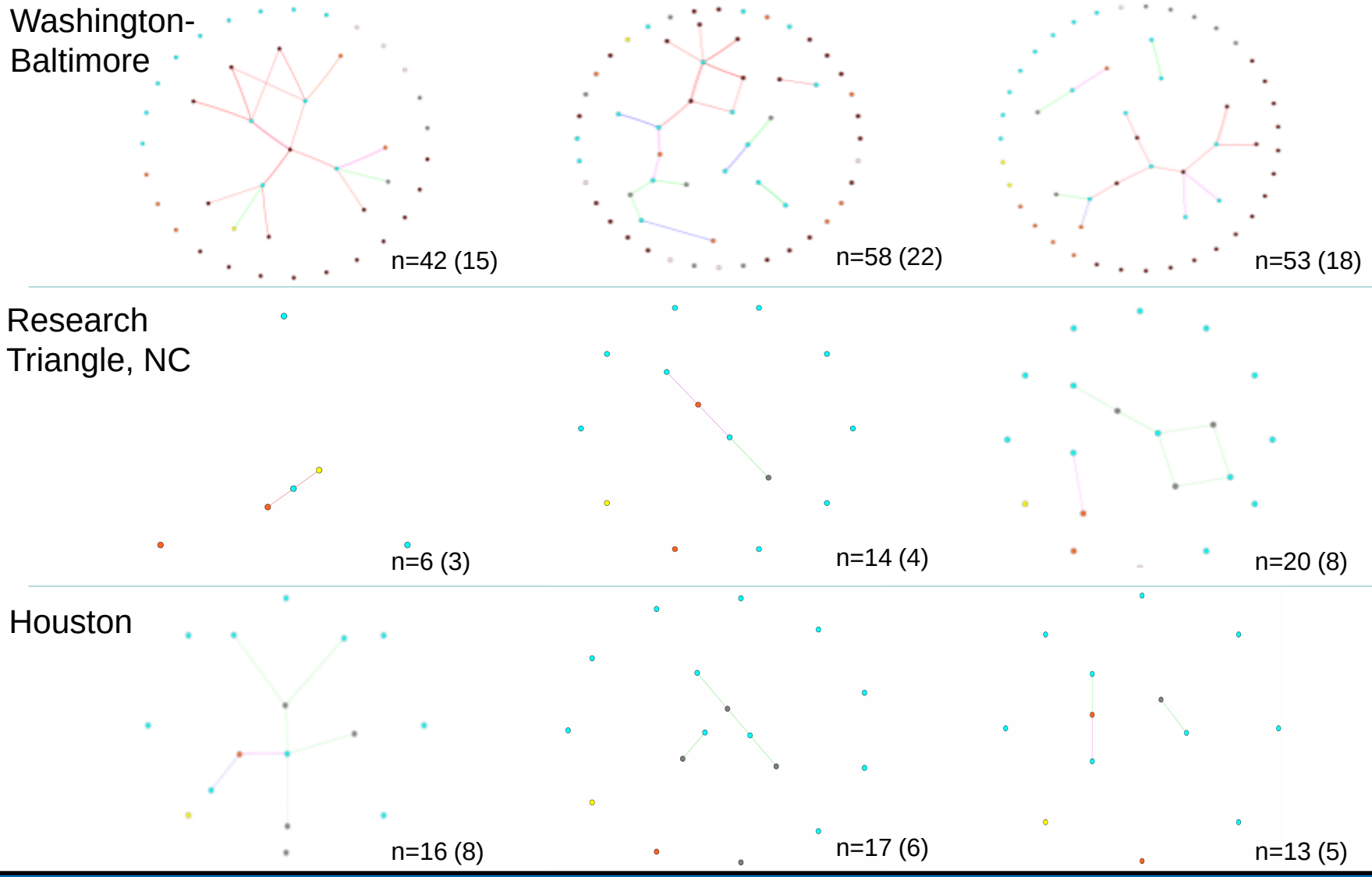
Washington-Baltimore, Research Triangle, NC, and Houston, 1990, 1996, and 2002



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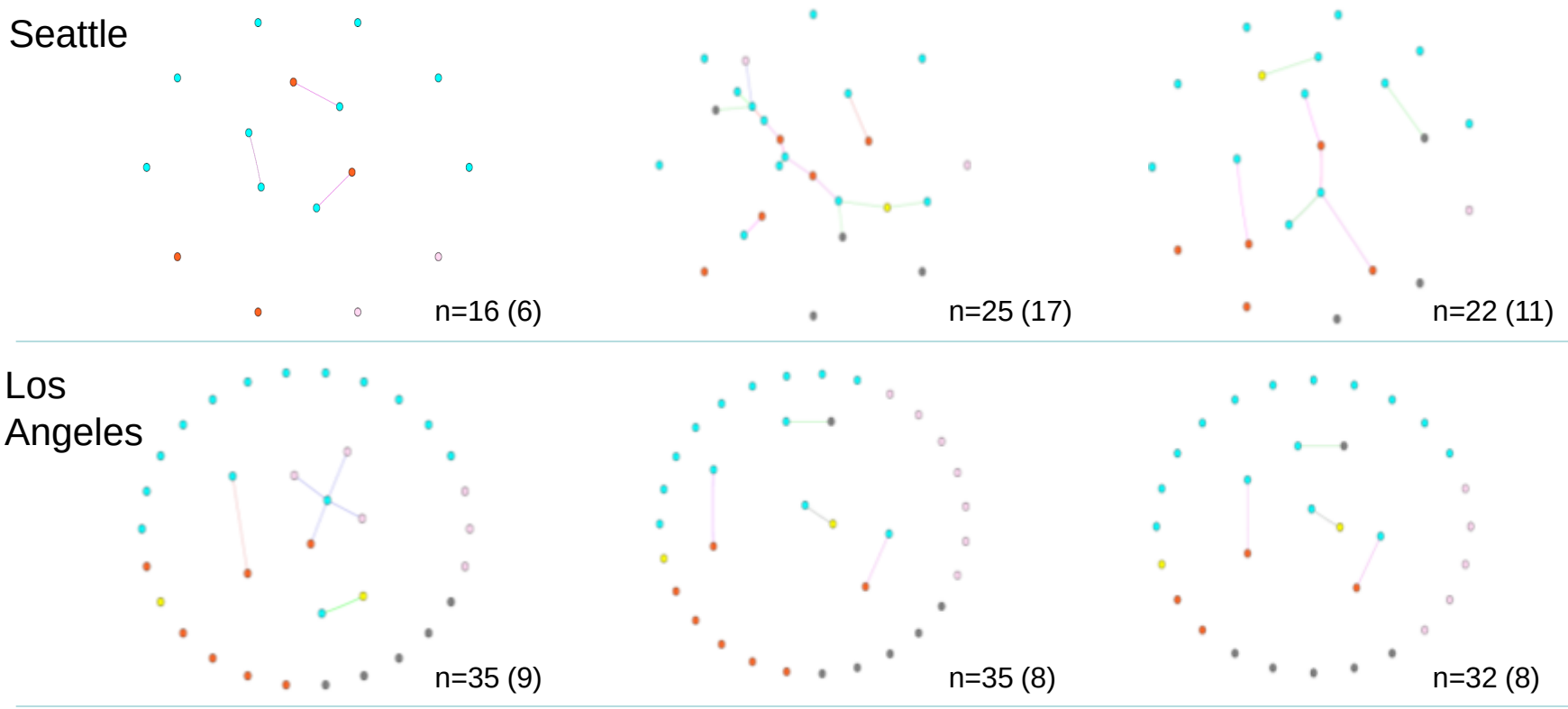
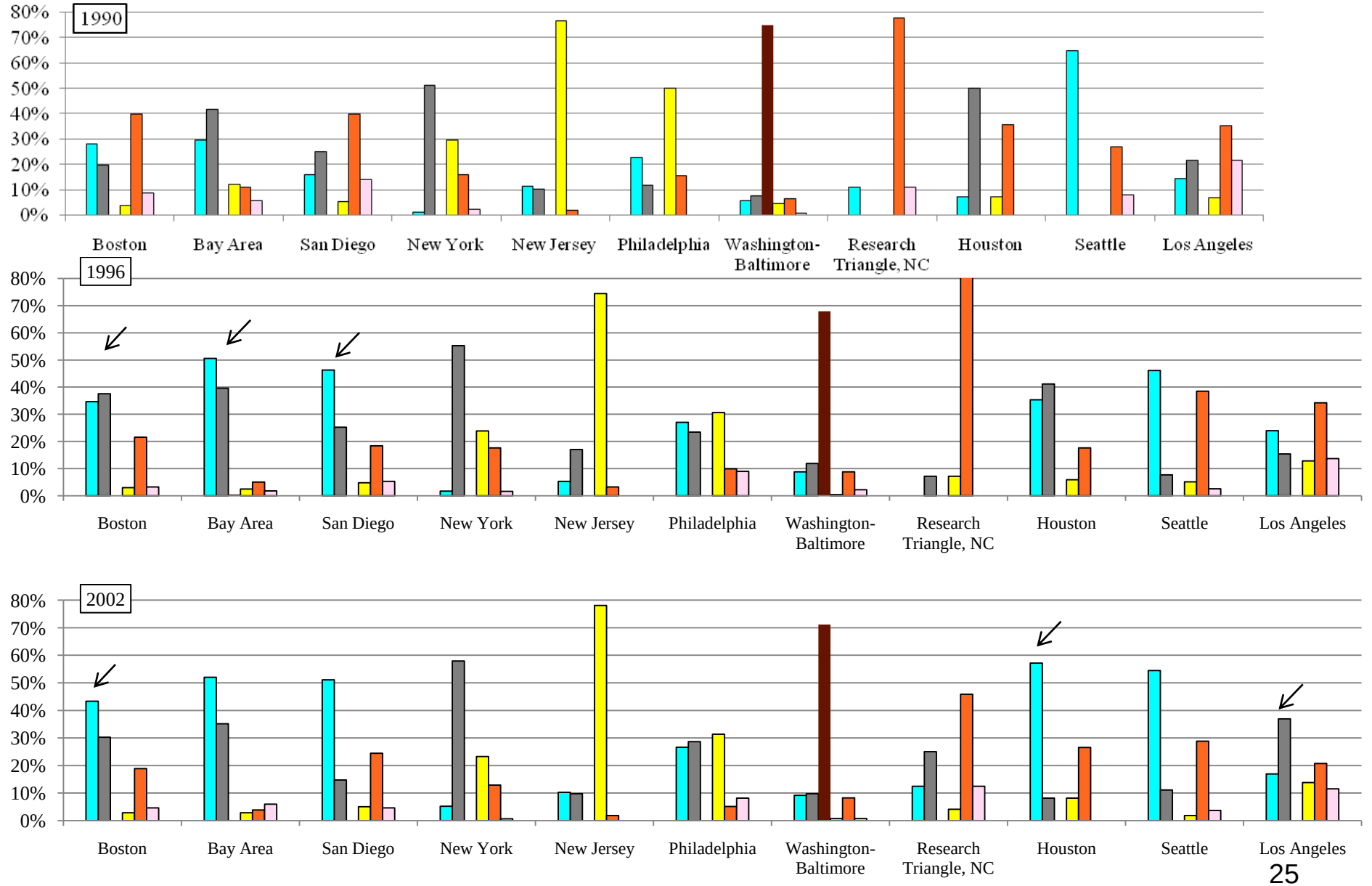
Seattle and Los Angeles, 1990, 1996, and 2002



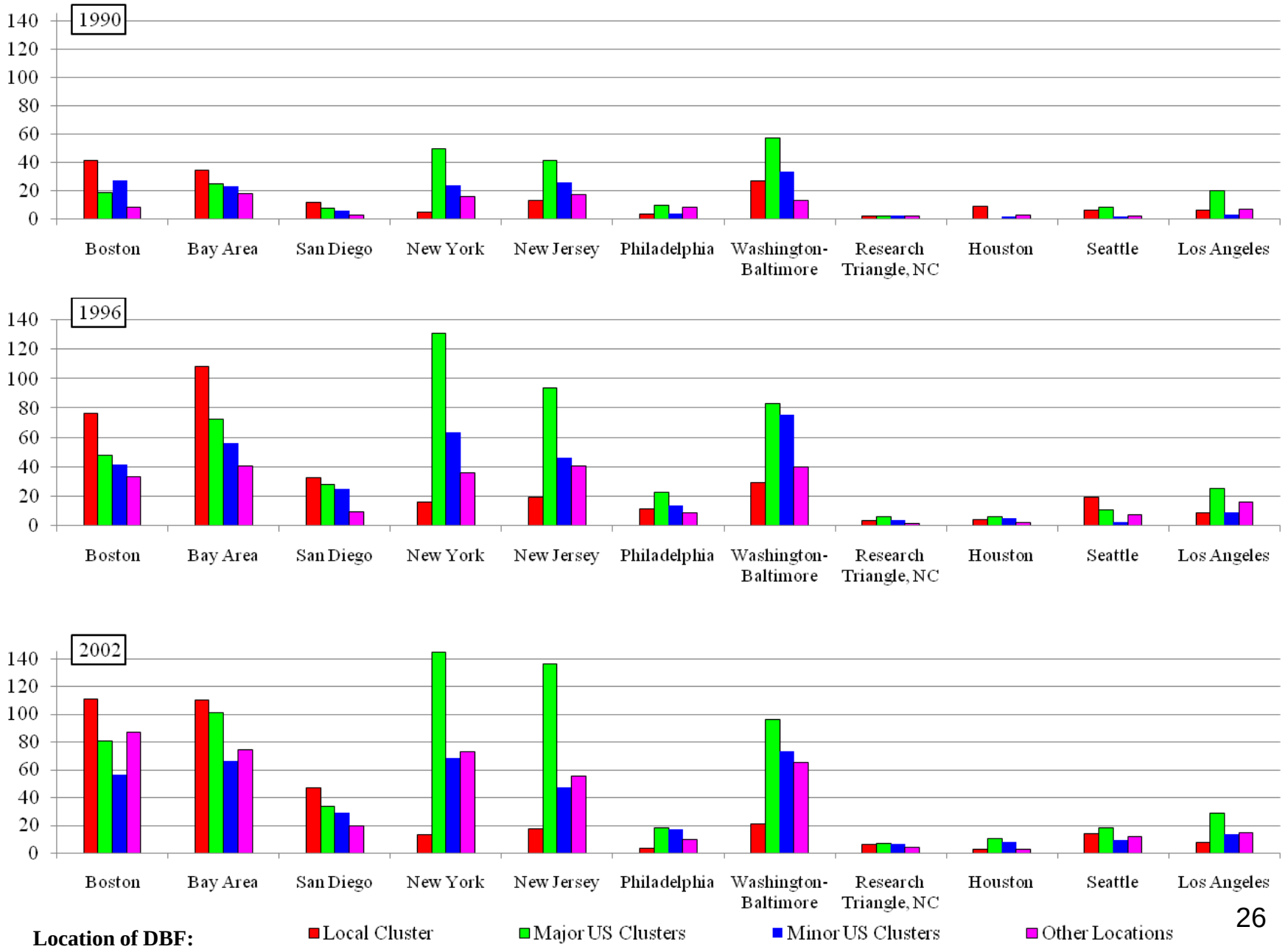
In all the nascent regions, initial opportunities did not translate into local growth. Most areas plateaued, a few grew but through external affiliations. Individual firms survived and a few prospered, but no clusters formed.

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

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



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



A Virtuous Cycle

Expansive local clusters matter not only because they generate a pool of high-tech companies. The spillover effects are, in some respects, even more consequential:

- **Growing labor markets for the well educated; attraction of highly skilled human capital**
- **Suppliers - - research tools, equipment…**
- **Services - - law (intellectual property), finance (venture capital, angel investors, investment banking), accounting (intangible assets), architecture (green buildings), universities (technology transfer and endowment managers)**

Red Queen Effect **– High rates of foundings and disbandings raise the bar!**

Some of you may think the story is about differential access to money. No, research funding was abundant in nascent clusters

1	JOHNS HOPKINS UNIV	BALTIMORE, MD	$ 279,185,690.00
2	UNIV OF CALIFORNIA SAN FRANCISCO	SAN FRANCISCO, CA	212,877,232.00
3	UNIV OF WASHINGTON	SEATTLE, WA	212,281,915.00
4	UNIV OF PENNSYLVANIA	PHILADELPHIA, PA	186,727,955.00
5	UNIV OF MICHIGAN	ANN ARBOR, MI	179,651,361.00
6	YALE UNIV	NEW HAVEN, CT	174,741,782.00
7	WASHINGTON UNIV	ST. LOUIS, MO	172,774,071.00
8	HARVARD UNIV	CAMBRIDGE, MA	166,727,904.00
9	UNIV OF CALIFORNIA LOS ANGELES	LOS ANGELES, CA	156,574,520.00
10	STANFORD UNIV	STANFORD, CA	153,205,664.00
11	DUKE UNIV	DURHAM, NC	143,358,921.00
12	UNIV OF NORTH CAROLINA	CHAPEL HILL, NC	140,140,193.00
13	COLUMBIA UNIV	NEW YORK, NY	137,815,335.00
14	UNIV OF PITTSBURGH	PITTSBURGH, PA	136,204,607.00
15	UNIV OF CALIFORNIA SAN DIEGO	SAN DIEGO, CA	135,469,556.00
16	UNIV OF MINNESOTA	MINNEAPOLIS, MN	131,077,595.00
17	CASE WESTERN RESERVE	CLEVELAND, OH	124,180,639.00
18	UNIV OF WISCONSIN	MADISON, WI	121,990,782.00
19	UNIV OF ALABAMA-BIRMINGHAM	BIRMINGHAM, AL	118,292,038.00
20	SCIENCE APPLICATION INTERNATL CORP	SAN DIEGO, CA	114,109,079.00
21	MASSACHUSETTS GENERAL HOSPITAL	BOSTON, MA	109,955,960.00
22	BRIGHAM AND WOMEN'S HOSPITAL	BOSTON, MA	99,967,195.00
23	CORNELL UNIV	ITHACA, NY	94,291,478.00
24	UNIV OF SOUTHERN CALIFORNIA	LOS ANGELES, CA	91,642,586.00
25	SCRIPPS RESEARCH INSTITUTE	SAN DIEGO, CA	91,249,662.00

National Institutes of Health Extramural Awards, 1996, Top 50 Recipients

KEY: **BLUE**: established clusters **GREEN**: nascent clusters **BLACK**: other locales

Top 50 NIH Awardees, cont.

26	BAYLOR COLLEGE OF MEDICINE	HOUSTON, TX	$ 90,895,535.00
27	UNIV OF CHICAGO	CHICAGO, IL	89,200,036.00
28	VANDERBILT UNIV	NASHVILLE, TN	87,150,662.00
29	UNIV OF IOWA	IOWA CITY, IA	83,480,815.00
30	UNIV OF COLORADO-HEALTH SCI CTR	DENVER, CO	83,423,416.00
31	UNIV OF TEXAS SW MED CTR	DALLAS, TX	82,900,672.00
32	EMORY UNIV	ATLANTA, GA	78,300,389.00
33	FRED HUTCHINSON CANCER RESEARCH CTR	SEATTLE, WA	78,133,179.00
34	YESHIVA UNIV	NEW YORK, NY	76,639,587.00
35	NEW YORK UNIV MEDICAL CTR	NEW YORK, NY	71,294,949.00
36	UNIV OF ROCHESTER	ROCHESTER, NY	70,978,006.00
37	BOSTON UNIV	BOSTON, MA	69,918,952.00
38	NORTHWESTERN UNIV	EVANSTON, IL	68,165,506.00
39	INDIANA UNIV	BLOOMINGTON, IN	67,131,615.00
40	UNIV OF TEXAS HEALTH SCIENCES CTR	HOUSTON, TX	63,809,470.00
41	UNIV OF CALIFORNIA BERKELEY	BERKELEY, CA	63,345,228.00
42	UNIV OF MARYLAND BALT	BALTIMORE, MD	63,312,861.00
43	MOUNT SINAI SCHOOL OF MEDICINE	NEW YORK, NY	62,127,860.00
44	UNIV OF UTAH	SALT LAKE CITY, UT	61,933,250.00
45	MAYO FOUNDATION	ROCHESTER, MN	60,604,497.00
46	UNIV OF VIRGINIA	CHARLOTTESVILLE, VA	59,289,524.00
47	MASSACHUSETTS INSTITUTE OF TECHNOLOGY	CAMBRIDGE, MA	59,167,175.00
48	UNIV OF MIAMI	CORAL GABLES, FL	57,665,548.00
49	UNIV OF CALIFORNIA DAVIS	DAVIS, CA	57,047,488.00
50	DANA-FARBER CANCER INST	BOSTON, MA	56,620,062.00

KEY: BLUE: established clusters GREEN: nascent clusters **BLACK**: other locales

Why did clusters form communities in some locales but not others?

- All of the regions had considerable local endowments, but these alone were not sufficient.
- The anchor tenants in three ‘successful’ regions catalyzed further org. and network formation, rather than acting as a ‘hegemonic’ power. The norms that characterized inter-org. relations in the three clusters bore the institutional stamp of the anchors.
- Cross-network transposition:
  - DBFs collaborated with other local DBFs; DBF scientists published in scientific journals
  - PROs became active in commercialization and licensing
  - VCs became executives in DBFs and donors to universities
  - Serial founders of DBFs became VCs
  - In sum, a distributed network led to a thorough mixing of practices from multiple domains

Organizational Diversity and Innovation

Heterogeneity is a critical feature of innovation process

→ Multiple organizational forms entail: diverse selection environments and varied strategies; different regimes of information use and disclosure; more opportunities for recombination.

→ Diverse portfolios of collaboration allow firms to learn from a wider stock of experience. Mix of strong and weak ties:

***Strong ties* - - deep relationships allow for greater commitment and more thorough knowledge sharing. Partners with a broader bandwidth for communication are more capable of transferring complex (tacit or sticky) knowledge.**

***Weak ties* - - longer reach, introduce more novelty, but less cohesive relations, narrower bandwidth.**

How do clusters develop and evolve?

Starting points and sequences matter - - what types of organizations are involved and where you begin shapes where you can go. Local ties embody a firm's initial core knowledge and form its social capital base. Distant ties reflect cosmopolitan status, but when they come first, they hinder building a local cluster. (A process story not a recipe!)

Windows of opening can be brief - - locational opportunities are ephemeral in science-based fields, and institutionalization may depend on catalyzing those ingredients at specific moments. (This is *not* a linear story!)

Multiple logics always present - - but how you work, whom you work with, and what you work on are conditioned by micro patterns of partner choice and local norms that sustain the evolving field structure. Particular types of ties (R&D) can be repurposed in ways that others cannot.

Multivocality - - actions can be interpreted from diverse perspectives simultaneously; multivocal actions are moves in multiple games at once.

Change does not necessarily entail uprooting of incumbents and replacement by challengers. Elements of the old guard may find new tools to retain position, or forge alliances with new entrants, or co-opt them. Multiple network transposition does insure reshuffling of relations and identities, and altering of criteria of evaluation. For ex., Pharma corps. move R&D labs to Kendall Square and La Jolla; Novartis creates nonprofit Genomic Institute in La Jolla; Harvard endowment fund invests as VC, etc.

Successful clusters are:

- emergent, not planned or dictated
- cooperative, have strong local norms of collaboration and knowledge sharing and rules for revenue sharing
- information-rich locales for labor, technology, and services
- skilled at forbearance and relational contracting
- include critical roles for university tech transfer office, IP law firms, and venture capital in orchestrating, counseling, and sustaining relationships.
- BUT it is not a recipe that is easily emulated: ENTREPRENEURIAL and COMPETITIVE within a community that shares a common FATE, sustained by strong consensus on local values

Implications

- Anchor tenant is host of the party, *not* the loudest person at the party.
- Important roles for public research organizations and small firms.
- Relational vs. Transactional ties
- Institutional diversity - - public, nonprofit organizations, small and large private firms, key supportive infrastructure of tech transfer, IP law, and VCs.
- Transposition - - using the coin of the realm in one network in a new one.
- Cross-cutting multiple networks; fluid labor markets.