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RESEARCH ARTICLE

Translating Emergent Technologies into Novel Therapeutics: Tracing Complementarity and Co-evolution in the Cambridge–Boston Innovation Ecosystem

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Abstract

This article traces the history of the life sciences business in the Cambridge–Boston area and explores how it became the global epicenter of the modern therapeutics industry. While business history scholarship on therapeutics is extensive, few have studied recent technological modalities—from therapeutic proteins to cell and gene therapies—or adopted a regional ecosystem perspective. Based on archival materials and oral histories, this research bridges these works and incorporates insights from the innovation ecosystems framework. It considers how dynamic interactions between an evolving network of complementary and interdependent actors, including therapeutics firms, universities, hospitals, and risk capital providers, enhanced innovative capacity. This perspective also illuminates how ecosystem strength derived from the co-evolution of actors—from universities restructuring technology transfer offices to academic scientists becoming entrepreneurs. The research further highlights the nonlinearity of innovation processes. It shows how an extraordinary interplay between structural advantage, serendipitous timing, and strategic actions cultivated an unparalleled capacity to translate emergent technologies into novel therapies.

Keywords: business history; therapeutics; innovation ecosystem; biotechnology

The Cambridge–Boston area has become a world-leading center for innovation in the life sciences business. In recent years, the area has played a disproportionate role in the commercialization of therapeutics, particularly as new technological modalities—such as cell and gene therapies—have come to market. Given that California was home to early biotechnology firms such as Cetus and Genentech in the 1970s, it would not have been surprising if the Golden State had become the global center for novel therapeutics. Yet, in the late 1990s, New England replaced New York as the leading regional biotechnology hub in the Eastern United States.[1] By 2021, Massachusetts had surpassed California in the number of public companies, market capitalization, and research and development (R&D) expenditures in the biotechnology sector.[2] This paper explores how the Cambridge–Boston innovation ecosystem became the epicenter for translating scientific discoveries into ground-breaking therapeutic applications, pioneering the evolution of the field.

This article bridges existing business histories of therapeutics and industrial clusters. Previous scholarship has explored the history of the therapeutics sector, often focusing on pharmaceutical firms and on themes such as intellectual property, regulation, and corporate organization.[3] While studies have increasingly explored the business history of biotechnology-based therapies, few have examined recent technological modalities or have studied the sector from the perspective of geographic concentration.[4] Similarly, while prior business history scholarship has explored the rise—and decline—of industrial clusters on themes such as corporate organization, social networks, and industrial structure, many have focused on traditional manufacturing.[5] While some have examined high technology industries, few include therapeutics.[6]

This article extends existing business history research on regional competitive dynamics by incorporating the concept of innovation ecosystems, defined as the constellation of diverse and interdependent actors required to commercialize new ideas.[7] With a business historical ecosystem perspective, the research reveals how an evolving network of complementary and interdependent actors—including therapeutics firms, universities, hospitals, and risk capital providers—coordinated their

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[1] G. Steven Burrill and Kenneth B. Lee, Jr., *Biotech '97 Alignment: Ernst & Young 11th Industry Annual Report* (Palo Alto, 1996), 45, 46. This and subsequent industry reports by Ernst and Young between 1991 and 2013 were accessed in the Henri A. Termeer Papers, *Baker Library Special Collections and Archives,* Boston, MA.

[2] Ernst and Young, *Beyond Borders: EY Biotechnology Report* (London, 2022), 37.

[3] Tobias Cramer, "Building the 'World's Pharmacy': The Rise of the German Pharmaceutical Industry, 1871–1914," *Business History Review* 89, no. 1 (2015): 43–73; David Schwartzman, *Innovation in the Pharmaceutical Industry* (Baltimore, MD, 1976); Mar Cebrián Villar and Santiago López García, "Assessing the Impact of Field-of-Use Restrictions in Patent Licensing Agreements: The Ethical Pharmaceutical Industry in the United States, 1950–1962," *Enterprise & Society* 18, no. 2 (2017): 282–323; Judy Slinn, "Price Controls or Control through Prices? Regulating the Cost and Consumption of Prescription Pharmaceuticals in the UK, 1948–67," *Business History* 47 no. 3 (2005): 352–366; Alfred D. Chandler Jr., *Shaping the Industrial Century: The Remarkable Story of the Evolution of the Modern Chemical and Pharmaceutical Industries* (Cambridge, MA, 2009).

[4] Lara V. Marks, *The Lock and Key of Medicine: Monoclonal Antibodies and the Transformation of Healthcare* (New Haven, CT, 2015); Nicolas Rasmussen, *Gene Jockeys: Life Science and the Rise of Biotech Enterprise* (Baltimore, MD, 2014).

[5] William Lazonick, *Competitive Advantage on the Shop Floor* (Cambridge, MA, 1990); Philip Scranton, *Endless Novelty: Specialty Production and American Industrialization, 1865–1925* (Princeton, NJ, 1997); Charles Sabel and Jonathan Zeitlin, "Historical Alternatives to Mass Production: Politics, Markets and Technology in Nineteenth-Century Industrialization," *Past & Present* 108 (1985): 133–176; Mary Rose, ed., *The Lancashire Cotton Industry: A History since 1700* (Preston, 1996).

[6] Martin Kenney, ed., *Understanding Silicon Valley: The Anatomy of an Entrepreneurial Region* (Redwood City, CA, 2000).

[7] Ron Adner, "Match Your Innovation Strategy to Your Innovation Ecosystem," *Harvard Business Review* 84, no. 4 (2006): 98–107; Ron Adner, "Ecosystem as Structure: An Actionable Construct for Strategy," *Journal of Management* 43, no. 1 (2017): 39–58.

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activities to commercialize novel therapeutics. It also shows how ecosystem capabilities strengthen over time as these actors co-evolve. The article also contributes to innovation ecosystems scholarship by deepening our understanding of ecosystem development processes and highlighting how structural advantage, serendipitous timing, and strategic actions shape innovation trajectories.

This paper refers to the modern therapeutics sector following the biotechnology revolution in the 1970s. Groundbreaking discoveries such as recombinant DNA and monoclonal antibody technologies generated unprecedented possibilities for novel therapeutics and transformed the industry. The sector encompasses both therapeutic biotechnology firms and conventional pharmaceutical firms. Biotechnology firms refer to firms founded since the 1970s that have taken biological approaches to drug discovery, for example, Genentech and Biogen. While the distinction between biotechnology and pharmaceutical firms has been blurring, the latter refers to the larger, established firms, such as Pfizer and Novartis, that have long used chemistry-based approaches to drug discovery.

This paper is based on archival sources and oral histories. The archival sources enabled an appreciation of the evolving industry context, including scientific advances, regulatory changes, and key players. Archival materials included the Henri A. Termeer Papers in the Baker Library at Harvard Business School (HBS), which provided industry reports and annual reports of Genzyme and affiliated companies. The Walter Gilbert Papers at Harvard University Archives and the Phillip A. Sharp Papers at Massachusetts Institute of Technology (MIT) Libraries' Distinctive Collections offered documentation related to the operations and founding of Biogen, respectively. At Cold Spring Harbor Laboratory Archives, internal company documents were available in the Collections of Walter Gilbert, Charles Weissman (Biogen), and Tom Maniatis (Genetics Institute). Materials consulted at the State Library of Massachusetts included historical, region-specific industry reports. Combined with newspaper and journal articles, for example, from *The Boston Globe* and *Nature*, these sources provided both an industry-wide perspective as well as firm-specific insights into the evolving therapeutics sector.

The oral histories proved invaluable, particularly for understanding the undocumented perspectives and informal relationships between actors that were crucial to building the local ecosystem. The discussions also helped in appreciating the historical context that generated specific actions.[8] The oral histories consisted of 24 semistructured anonymous and non-anonymous interviews with a range of key figures in the local life sciences business, conducted between October 2023 and July 2024 following university ethics approval. The 19 non-anonymous interviewees included (in alphabetical order) Noubar Afeyan, Robert Carpenter, Cristina Csimma, Zoltan Csimma, Walter Gilbert, Bob Higgins, Wilbur Kim, Robert Langer, Harvey Lodish, Lita Nelson, Andrew Plump, Stephen Reeders, Scott Requadt, Jack Reynolds, William Schnoor, Matt Segneri, Phillip Sharp, Josef von Rickenbach, and George Whitesides. The conversations systematically explored similar themes relating to

[8] Geoffrey Jones and Rachael Comunale, "Oral History and the Business History of Emerging Markets," *Enterprise & Society* 20, no. 1 (2019): 19–32; Robert Crawford, "Off the Books: Oral History and Transnational Advertising Agencies in Southeast Asia," *Enterprise & Society* 20, no. 1 (2019): 47–59.

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professional experience, historical industry trends, and reasons for the rise of the Cambridge–Boston area as a global epicenter of the therapeutics business.

The next section situates this research within existing scholarship and outlines the nature of the novel therapeutics industry. The article then follows the trajectory of the life sciences business in the Cambridge–Boston area. It shows how an exceptional combination of structural advantage, serendipity, and strategic actions cultivated a locus for translating emergent technologies into therapeutic applications.

Extending the Business Histories of Therapeutics and Industrial Clusters

This research builds upon two strands of business history scholarship: therapeutics and industrial clusters. The business history of therapeutics includes micro-level firm studies and meso-level industry studies around the world.[9] While many have focused on chemistry-based pharmaceutical firms, a growing number of works have studied biotechnology firms founded on biological sciences.[10] Such studies have examined founders of companies such as Biogen and Genzyme, firms such as Genentech and Vertex, and new entrants who diversified into biotechnology-based therapies, such as Kirin.[11] Others have examined the role of institutional context or exogenous factors—such as technological or regulatory change—in reshaping the industry. Some executives have also reflected upon the industry's evolution through their professional experience.[12] A recent book on Kendall Square near MIT offers textured documentation on how the district became a global innovation hub.[13] Augmenting existing business histories with an ecosystem-based perspective, this article considers how the alignment of structure, serendipity, and strategy cultivated conditions that enabled the translation of scientific discoveries into novel therapies in the Cambridge–Boston area.

[9] Richard Davenport-Hines and Judy Slinn, *Glaxo: A History to 1962* (Cambridge, UK, 1992); Carsten Burhop, "Pharmaceutical Research in Wilhelmine Germany: The Case of E. Merck." *Business History Review* 83, no. 3 (2009): 475–503; Hans-Werner Gottinger and Celia L. Umali, "The Evolution of the Pharmaceutical-Biotechnology Industry," *Business History* 50, no. 5 (2008): 583–601; Laurence Monnais and Laurence Monnais-Rousselot, *The Colonial Life of Pharmaceuticals* (Cambridge, UK, 2019); Timothy M. Yang, *A Medicated Empire: The Pharmaceutical Industry and Modern Japan* (Ithaca, NY, 2021).

[10] Jonathan M. Liebenau, "Public Health and the Production and Use of Diphtheria Antitoxin in Philadelphia," *Bulletin of the History of Medicine* 61, no. 2 (1987): 216–236; Charles C. Mann and Mark L. Plummer, *The Aspirin Wars: Money, Medicine, and 100 Years of Rampant Competition* (New York, 1991).

[11] John Hawkins, *Conscience and Courage: How Visionary CEO Henry Termeer Built a Biotech Giant and Pioneered the Rare Disease Industry* (Cold Spring Harbor, 2019); Brian Dick and Mark Jones, "The Commercialization of Molecular Biology: Walter Gilbert and the Biogen Startup," *History and Technology* 33, no. 1 (2017): 126–151; Sally S. Hughes, *Genentech: The Beginnings of Biotech* (Chicago, 2011); Barry Werth, *The Billion-Dollar Molecule: The Quest for the Perfect Drug* (New York, 1995); Michael J. Lynskey, "The Locus of Corporate Entrepreneurship: Kirin Brewery's Diversification into Biopharmaceuticals," *Business History Review* 80, no. 4 (2006): 689–723.

[12] Luigi Orsenigo, *The Emergence of Biotechnology. Institutions and Markets in Industrial Innovation* (New York, 1989); Louis Galambos and Jeffrey L. Sturchio, "Pharmaceutical Firms and the Transition to Biotechnology: A Study in Strategic Innovation," *Business History Review* 72, no. 2 (1998): 250–278; James Geraghty, *Inside the Orphan Drug Revolution: The Promise of Patient-Centered Biotechnology* (Cold Spring Harbor, 2022); Tim Harris, *In Pursuit of Unicorns: A Journey through 50 Years of Biotechnology* (Cold Spring Harbor, 2024).

[13] Robert Buderi, *Where Futures Converge: Kendall Square and the Making of a Global Innovation Hub* (Cambridge, MA, 2022).

Business historians have long examined the importance of geographic concentration and inter-firm relations, well before the seminal work of Michael Porter and industrial clusters.[14] Research on industrial districts illustrated how specialized skills within a network of small firms employing flexible production methods enabled regions to maintain competitiveness.[15] Porter's studies discussed how factor conditions, skilled labor, infrastructure, and supporting industries determined cluster formation and success—as well as the enduring significance of local clusters amidst globalization.[16] Studies of industrial clusters thus focused on innovation, inter-firm relationships, supporting institutions, and competitive advantage. For instance, Annalee Saxenian's work on regional advantage elaborated on how local institutions and corporate forms shaped distinct advantages for the semiconductor and computer industries in Silicon Valley compared with Route 128.[17] A range of business history work has examined the role of key actors in building industrial clusters, such as the state or academia in Silicon Valley.[18] Business historians have also questioned whether institutional path dependence cultivates or undermines subsequent industrial development.[19] For example, the knowledge, skills, and networks from past industries may continue to support subsequent industries, as in the case of the UK outdoor trade around Lancashire during the second half of the twentieth century.[20] This may not be the case when complementary institutions are conducive to supporting a specific technology; small firms are acquired by larger, less innovative firms; or exogenous shocks obliterate supporting institutions. While Cleveland's decline from a center of technological innovation may be attributed to such factors, this article suggests that the Cambridge–Boston area's industrial legacies were largely favorable to the subsequent rise of the therapeutics sector.[21]

Business histories of regional industry development can be enriched by the concept of innovation ecosystems, defined as the configuration of relationships between an interdependent collective of multiple actors that enable the commercialization of new ideas.[22] Prior scholarship on industrial clusters has

[14] Jonathan Zeitlin, "Industrial Districts and Regional Clusters," in *Oxford Handbook of Business History*, ed. Geoffrey Jones and Jonathan Zeitlin (Oxford, 2007), 219–243.

[15] Scranton, *Endless Novelty*; Sabel and Zeitlin, "Historical Alternatives to Mass Production," 133–176.

[16] Michael Porter, *The Competitive Advantage of Nations* (New York, 1990); Michael Porter, "Location, Competition, and Economic Development: Local Clusters in a Global Economy," *Economic Development Quarterly* 14, no. 1 (2000): 15–34.

[17] AnnaLee Saxenian, *Regional Advantage: Culture and Competition in Silicon Valley and Route 128* (Cambridge, MA, 1994).

[18] Stuart W. Leslie and Robert H. Kargon, "Selling Silicon Valley: Frederick Terman's Model for Regional Advantage," *Business History Review* 70, no. 4 (1996): 435–472; Stephen B. Adams, "Arc of Empire: The Federal Telegraph Company, the U.S. Navy, and the Beginnings of Silicon Valley," *Business History Review* 91, no. 2 (2017): 329–359.

[19] Rolv Petter Amdam and Ove Bjarnar, "Globalization and the Development of Industrial Clusters: Comparing Two Norwegian Clusters, 1900–2010," *Business History Review* 89, no. 4 (2015): 693–716.

[20] Mike Parsons and Mary B. Rose, "The Neglected Legacy of Lancashire Cotton: Industrial Clusters and the UK Outdoor Trade, 1960–1990," *Enterprise & Society* 6, no. 4 (2005): 682–709.

[21] Naomi R. Lamoreaux, Margaret Levenstein, and Kenneth L. Sokoloff, "Do Innovative Regions Inevitably Decline? Lessons from Cleveland's Experience in the 1920s," *Business and Economic History On-line* 5 (2007): 1–26, accessed 15 Nov. 2024, https://www.thebhc.org/publications/BEHonline/2007/lls.pdf.

[22] Adner, 98–107; Adner, 39–58. This research incorporates the innovation ecosystem framework, rather than the proximate literature on entrepreneurial ecosystems, given its holistic focus on the

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focused on competitive dynamics, while that on regional systems of innovation (RSI) has emphasized governance and policy interventions within defined administrative regions.[23] By incorporating the ecosystem framework, this article illustrates how multilateral interactions between complementary and interdependent actors were critical for translating scientific discoveries into commercial applications.

Existing scholarship on innovation ecosystems includes longitudinal studies that consider ecosystem emergence, evolution and the coevolution of technologies, actors, and institutions.[24] This research also contributes to these works by illuminating how serendipity and nonlinearity interact in ecosystem development. Here, serendipity refers to "unanticipated, anomalous, and strategic" alignments—such as the timing of scientific discoveries—which are historically contingent and momentary.[25] Nonlinearity refers to the uncertain and unordered process of innovation that challenges deterministic perspectives. The research illustrates how a delicate confluence of structural advantage, serendipity, and deliberate interventions shape the nonlinear trajectory of innovation ecosystems.

The Nature of the Industry

The features of the modern therapeutics industry should be noted in exploring its history. Comparisons have been made between the Cambridge–Boston therapeutics sector and Silicon Valley's high technology sectors, as there are several shared features. These include rapid technological advances, requirements for risk capital, interdisciplinary collaboration, and entrepreneurial spirit. Yet, closer inspection reveals that the two areas are not entirely comparable. The modern therapeutics sector features much longer lead times along with higher levels of uncertainty, risk, technological complexity, regulatory intervention, and cost.[26]

Even in pharmaceutical firms, where chemistry was the dominant technology until the 1980s, therapeutic R&D had been subject to much higher costs, longer lead times, and significant risk of failure compared with most industries. Until outsourcing to contract research organizations (CROs) became more commonplace in the 1990s, pharmaceutical R&D was usually based in large firms and involved the large-scale scanning of chemical substances that might safely and effectively remedy certain

network of organizations and their collaboration that enable the introduction of new products, rather than on the environment that specifically fosters the creation and growth of new firms.

[23] Porter, *The Competitive Advantage of Nations*; Porter, "Location, Competition, and Economic Development," 15–34; Philip Cooke, Mikel Gomez Uranga, and Goio Etxebarria, "Regional Innovation Systems: Institutional and Organisational Dimensions," *Research Policy* 26, nos. 4–5 (1997): 475–491.

[24] Ozgur Dedehayir, Saku J. Mäkinen, and J. Roland Ortt, "Roles during Innovation Ecosystem Genesis: A Literature Review," *Technological Forecasting and Social Change* 136 (2018): 18–29; Leena Aarikka-Stenroos and Paavo Ritala, "Network Management in the Era of Ecosystems: Systematic Review and Management Framework," *Industrial Marketing Management* 67 (2017): 23–36; Ethan Gifford, Maureen McKelvey and Rögnvaldur Saemundsson, "The Evolution of Knowledge-Intensive Innovation Ecosystems: Co-evolving Entrepreneurial Activity and Innovation Policy in the West Swedish Maritime System," *Industry and Innovation* 28, no. 5 (2021): 651–676.

[25] Robert K. Merton and Elinor Barber, *The Travels and Adventures of Serendipity: A Study in Sociological Semantics and the Sociology of Science* (Princeton, NJ, 2004), 197; Saxenian, *Regional Advantage*.

[26] Gary P. Pisano, *Science Business: The Promise, the Reality, and the Future of Biotech* (Cambridge, MA, 2006); Andrew Plump (President of R&D at Cambridge-based Takeda), interview by author, 17 Jan. 2024.

symptoms of disease. The discovery of a potential therapy was therefore based on considerable serendipity. Given requirements to gain regulatory approval across several phases of clinical trials, many firms developed therapies for ailments shared across a large patient population or chronic ailments, to maximize revenue and recoup the cost of R&D. For medicines approved in the 1980s, for example, the average cost of development was estimated at US$231 million (in 1987 dollars), with a lead time of 12 years, and an average success rate of 23%.[27] By comparison, Moore's Law—which observed that the number of transistors on a microchip doubled biennially—revealed a more rapid rate of development and significantly shorter lead times for semiconductors.[28]

The risks involving uncertainty and cost in therapeutic development increased with advances in biotechnology. Since the early 1970s, recombinant DNA technology—developed by Paul Berg, Herbert Boyer, Stanley Cohen, and others—enabled scientists to engineer genetic material to produce proteins as therapeutic agents (e.g., insulin, hormones, and enzymes) in host cells (e.g., bacteria and yeast).[29] The discovery of hybridoma technology by Köhler and Milstein in 1975 enabled scientists to create an immortal cell that could produce large amounts of identical/monoclonal antibodies to interact with disease-specific proteins.[30] Therapeutics increasingly originated in university laboratories and were developed by academic scientists, who began to launch small startups, which, for example, began making human proteins in bacteria for medical treatment.[31] From the 1980s until the early 2000s, recombinant proteins and monoclonal antibodies were at the frontier of therapeutic innovation. These included recombinant human insulin by Genentech (*Humulin*, 1982), which treated diabetes, and the first-approved monoclonal antibody by Ortho Pharmaceutical (*OKT3*, 1986), which was used for transplant rejection despite substantive side effects.[32] Over time, the larger and longer clinical trials required to demonstrate incremental clinical efficacy also raised drug development costs, which increased from US$802 million (2000 dollars) in the 1990s to US$1.8 billion dollars by 2010, with a success rate of 6.8%.[33]

[27] Joseph A. DiMasi, Ronald W. Hansen, Henry G. Grabowski and Louis Lasagna, "Cost of Innovation in the Pharmaceutical Industry," *Journal of Health Economics* 10, no. 2 (1991): 107–142.

[28] Robert R. Schaller, "Moore's Law: Past, Present and Future," *IEEE Spectrum* 34, no. 6 (1997): 52–59.

[29] David A. Jackson, Robert H. Symons, and Paul Berg, "Biochemical Method for Inserting New Genetic Information into DNA of Simian Virus 40: Circular SV40 DNA Molecules Containing Lambda Phage Genes and the Galactose Operon of *Escherichia coli*," *Proceedings of the National Academy of Sciences* 69, no. 10 (Oct. 1972): 2904–2909; Stanley N. Cohen, Annie CY Chang, Herbert W. Boyer, and Robert B. Helling, "Construction of Biologically Functional Bacterial Plasmids In Vitro," *Proceedings of the National Academy of Sciences* 70, no. 11 (1973): 3240–3244.

[30] Georges Köhler and Cesar Milstein, "Continuous Cultures of Fused Cells Secreting Antibody of Predefined Specificity," *Nature* 256, no. 5517 (1975): 495–497.

[31] Walter Gilbert, "Harvard Medical School Symposium Address," 16 Nov. 1982, Walter Gilbert Papers, Box 8, Harvard University Archives, Cambridge, MA.

[32] Arthur D. Levinson, "For Success, Focus Your Strengths," *Nature Biotechnology* 16, Supplement 1(1998): 45–46; Thomas A. Waldmann, "Immunotherapy: Past, Present and Future," *Nature Medicine* 9, no. 3 (2003): 269–277.

[33] Joseph A. DiMasi, Ronald W. Hansen, and Henry G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22, no. 2 (2003): 151–185; Steven M. Paul, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy

As products, therapeutics depend upon strong intellectual property protection and market exclusivity for an extended period. Given the association with academic research and human health, proximity to universities—particularly those with clinical infrastructure—has also been important. Furthermore, the sector has featured cycles of hype and disappointment, owing to the extraordinary risk and returns for companies and the promise of a cure for patients.[34] These features illuminate how the Cambridge–Boston innovation ecosystem became a premier locus for translating emergent technologies into medicines.

Location, Declining Sectors, and the Imprint of Past Clusters

A remarkable combination of structural advantage and serendipity contributed to the area's rise as the global center of the therapeutics industry. One structural advantage was location. Boston is a port city that has prospered as a center of trade through its harbor for centuries, and through its public transportation networks since the nineteenth century. The area had evolved as a regional center of various industries, from textile and shoes in the nineteenth century to defense and electronics in the mid-twentieth century.[35] The institutional and organizational legacies following the decline of earlier industries—whether from overseas competition or technological advances—facilitated the rise of subsequent industries.[36]

The legacy of past industries was not inconsequential. The decline of local manufacturing—from textiles in the broader region to soap in Cambridge (e.g., Lever Brothers, Fig. 1)—left behind skilled workers and physical infrastructure.[37] There was low-cost real estate that provided invaluable access to leading universities nearby. Furthermore, the clearing of 29 acres around the Kendall Square area in 1964 to create the National Aeronautics and Space Administration (NASA)'s Electronic Research Center (Fig. 2) not only displaced many businesses but NASA's 1970 withdrawal also left a large space available for use.[38] Such space enabled the concentrated construction of new facilities associated with biotechnology. These included, for example, the Whitehead Institute, a biomedical research organization specializing in genomics, known for its contributions to the Human Genome Project. As co-founder and MIT professor Harvey Lodish stated, "The fact that there was land that was cleared, old industrial land, made a

R. Lindborg, and Aaron L. Schacht, "How to Improve R&D Productivity: The Pharmaceutical Industry's Grand Challenge," *Nature Reviews Drug Discovery* 9, no. 3 (2010): 203–214; Chi Heem Wong, Kien Wei Siah, and Andrew W. Lo, "Estimation of Clinical Trial Success Rates and Related Parameters," *Biostatistics*, 20, no. 2 (2019): 273–286.

[34] Pisano, *Science Business*.

[35] David Koistinen, *Confronting Decline: The Political Economy of Deindustrialization in Twentieth-Century New England* (Gainesville, 2013). Barry Bluestone and Bennett Harrison, *Deindustrialization in America: Plant Closings, Community Abandonment, and the Dismantling of Basic Industry* (New York, 1982).

[36] Edward L. Glaeser, "Reinventing Boston: 1630–2003," *Journal of Economic Geography* 5, no. 2 (2005): 119–153.

[37] Ian Menzies, "New England's Industry Is Enjoying a Rebirth Because It Has … the Greatest Brains in the World," *The Boston Globe*, 5 July 1959, B3–B4.

[38] Urban Land Institute, "Appendix: Background of the Kendall Square Renewal Area," in *Cambridge Center: An Evaluation of the Redevelopment Potential of Cambridge Center in the Kendall Square Renewal Area for the Cambridge Redevelopment Authority, Cambridge, Massachusetts, 15–19 November 1976: A Panel Service Report* (Washington, DC, 1977).

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Figure 1. Advertisement for Lever Bros. Co. site, 1950.
Source: Cambridge Historical Commission, Boston Herald Photo Collection

huge difference … There was a place to put all of this, and that is not often noticed." Moreover, local officials at both state and municipal levels (e.g., state governors, Cambridge Redevelopment Authority) collaborated with academics and private investors to support urban redevelopment. "The fact that everybody is on the same page working together makes a huge difference," he added.[39]

[39] Harvey Lodish, interview by author, 21 Dec. 2024.

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Figure 2. Kendall Square NASA site, 1965.
Source: Cambridge Historical Commission, Survey Files

Coincidentally, the institutions supportive of past industries were compatible with those of the oncoming sector. The emergent cluster benefited from the structural advantages of world-class universities such as Harvard and MIT as a source of human capital and repository of knowledge, along with networks of collaboration between academia and industry. MIT had particularly close relationships with the industry as an engineering school emphasizing the practical application of knowledge. In the shadow of industrial legacies, entrepreneurial initiative as well as a professional community—including venture capitalists, lawyers, and consultants—supported startups in the nascent biotechnology sector.

From National to Local Institutional Change

The biotechnology revolution prompted regulatory change at both national and local levels. As a heavily regulated industry, major legal changes at the national level, including the *Diamond v. Chakrabarty* ruling and the Orphan Drug Act, altered the rules of the game. The co-occurrence of local industrial decline with concurrent institutional change was remarkably well timed.

The *Diamond v. Chakrabarty* ruling in 1980 was a landmark decision confirming that genetically modified organisms could be patented—if they were novel, original, and not obvious.[40] While the biotechnology revolution offered the possibility of creating medicines with genetically modified organisms, it remained unclear whether organisms created out of human genetic manipulation could be patented. While prevailing US regulation indicated that living organisms could not be patented, the ruling clarified and expanded the scope of patentability, catalyzing the

[40] *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

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commercialization of biotechnology-based drugs.[41] Another turning point was the passage of the Bayh–Dole Act in the same year, which had a profound impact on the commercialization of federally funded—often through the National Institutes of Health (NIH)—life sciences research. Indeed, university patenting in life sciences increased substantially after Bayh–Dole.[42]

One of the other significant regulatory changes at the national level was the Orphan Drug Act introduced in 1983. A result of patient advocacy, the Act created incentives for firms to conduct R&D in therapeutics for rare diseases, defined as ailments affecting fewer than 200,000 patients in the US.[43] By granting a period of market exclusivity, tax incentives, and a waiver of certain Food and Drug Administration (FDA) fees, the Act reoriented the model of therapeutic development away from blockbuster drugs and toward smaller patient populations—facilitating the rise of academic startups.[44] Furthermore, the Economic Recovery Tax Act of 1981 not only introduced R&D tax credits but also reduced capital gains tax, which encouraged greater investments into startups.[45]

While national regulations concerning safety and efficacy for marketing approval were influential, local regulations—including those relating to planning and research permissions—were also impactful in shaping the sector. In fact, local restrictions introduced in the city of Cambridge delayed industry activity in the short term but supported local growth in the long term. In the 1970s, public health concerns over the safety of recombinant DNA research conducted at Harvard prompted the city of Cambridge to impose a moratorium on recombinant research. Between July 1976 and February 1977, the municipal Cambridge Experimental Review Board held public hearings with experts from Harvard, MIT, and the NIH over concerns that new organisms could cause unknown diseases. While some actors expressed frustration that the Cambridge City Council delayed research activities, the eventual vote for regulations more stringent than NIH guidelines enabled local actors to operate under clear and predictable rules.[46] One reason that a leading biotechnology company, Biogen, decided to locate its operations in Cambridge was for this reason.[47] Institutional changes at both national and local levels altered drug development models and transformed the competitive environment.

[41] Stacy V. Jones, "Patents; Creating Life Forms in the Lab," *The New York Times*, 4 Apr. 1981, 38.

[42] Bayh–Dole Act of 1980, 35 U.S.C. § 200–212; Rebecca S. Eisenberg, "Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research," *Virginia Law Review* 82 (1996): 1663–1727.

[43] Orphan Drug Act of 1983, 21 U.S.C. § 360aa–360ff.

[44] Geraghty, *Orphan Drug Revolution*.

[45] Economic Recovery Tax Act of 1981, Pub. L. 97-34. Consideration of the 1981 Tax Act noted in Genetics Institute, "Meeting of Directors," 12 Nov. 1981, Box 1, Folder 2, Tom Maniatis Collection, Cold Spring Harbor Laboratory Archives, Cold Spring Harbor, New York.

[46] Cambridge City Council, Correspondence, June 1976 to April 1977, Massachusetts Institute of Technology, Oral History Program, Oral History Collection on the Recombinant DNA Controversy, accessed 15 Nov. 2024, https://hdl.handle.net/1721.3/200724; Laura L. Lindsey and Massachusetts General Court Science Resource Office, *Recombinant DNA and the Cambridge City Council* (Boston: Science Resource Office, Massachusetts General Court, 1976), accessed 15 Nov. 2024, https://www.biodiversitylibrary.org/page/41433399; Peter Feinstein Inc., *An Assessment of the Massachusetts Biotechnology Industry* (Cambridge, MA, 1990), 14.

[47] Phillip Sharp, interview by author, 18 July 2024. Philip Sharp was a co-founder of Biogen.

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Structural Transformations and Eastward Shifts in Therapeutic Innovation

While the early therapeutic biotechnology firms were often represented by West Coast firms such as Cetus (1971) and Genentech (1976), a sequence of serendipitous timings shifted the center of therapeutic innovation toward the East Coast in the 1990s. The first was the decline of large pharmaceutical firms. The second was the rise of biopharmaceutical services, such as contract research organizations (CROs). The third was the rise of lean biotechnology firms.

As the millennium neared, large pharmaceutical firms began to outsource their R&D. To begin with, there were pressures to generate new therapies. By the 1990s, many drugs were still generating significant revenue, but their patent lives were nearing an end. There was a sense that, unless firms outsourced the development process, they would be operating inefficiently by peak-loading staff. As firm performance was cyclical, dependent on the success of a given discovery, companies opted to outsource to adjust employment and use labor more effectively.[48] Pharmaceutical firms were also becoming increasingly sensitive to short-term returns amidst growing financialization in America.

These pressures to enhance efficiency accelerated the rise of CROs. Since the 1980s, entrepreneurs had launched firms that offered a range of research and development services on a contract basis, such as preclinical research and clinical trials management. In 1982, Harvard Business School (HBS) graduate Josef von Rickenbach and organic chemist Anne Sayigh established Parexel, which grew into a leading local CRO, rivalling contemporaries such as Quintiles and Pharmaco. CROs catered to the demands of clinical trials, which, with increasingly complex data requirements, were distinct from academic research. Von Rickenbach, who led Paraxel for over two decades explained, “To run a big clinical trial is like a small business. I mean, it is a huge undertaking. You have probably dedicated, several hundred people who work on that trial for multiple years, in highly complex, highly dynamic environments.”[49] By exposing the respective activities across the value chain to market forces, the growth of biopharmaceutical service companies such as CROs enhanced the dynamism of the local innovation ecosystem and altered the competitive landscape. They did so by enabling established firms to achieve greater efficiencies and enabling less established and foreign firms to build their foothold in the market.

Pressures to enhance efficiency also encouraged pharmaceutical firms to connect with and acquire biotechnology firms with promising therapies that would secure robust returns. The limits of traditional pharmaceutical companies—with chemistry-based expertise—enabled biotechnology firms to gain prominence by adopting novel therapeutic approaches to treat complex diseases. Academic startups, such as Genetics Institute (Harvard), Repligen (MIT), and Alkermes (Harvard Medical School), emerged in the 1980s.[50] As pharmaceutical firms became less interested in conducting their own research and considered academic science too early stage and risky for

[48] William Schnoor, interview by author, 6 Dec. 2023.

[49] Josef von Rickenbach, interview by author, 25 June 2024.

[50] Growing actors in the local ecosystem can be identified in Massachusetts Office of International Trade and Investment, *Massachusetts International Biomed Directory* (Boston, MA, 1990).

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commitment, biotechnology companies became the carrier that would bring academic science into the real world.

Biotechnology entrepreneurship was also unfolding amidst a backdrop of changes in American corporate culture. While workers in large American companies expected a job for life in the 1960s, many American workers had experienced a layoff at least once in their career by the 1990s. This shift altered employer–employee relations and made entrepreneurship in America feel less risky.[51]

Coincidentally, many of the world-leading pharmaceutical companies in the 1980s and 1990s were situated in the Northeastern US. In 1985 and 1990, for example, most of the top 10 prescription drug companies in the world by sales were headquartered in the northeast. These included Merck & Co (New Jersey), American Home Products (New York), Pfizer (New York), SmithKline Beckman (Pennsylvania), Bristol-Myers (New York), and Johnson & Johnson (New Jersey).[52] Geographically, the leading centers of the US biotechnology industry were in three regions (Tables 1a and 1b). For example, in 1991, the areas of New York, San Francisco, and Boston accounted for 17%, 14%, and 13% of public biotechnology companies, or 12%, 14%, and 10% of all biotechnology companies, respectively.[53] As East Coast pharmaceutical companies realized the possibility of biologicals, they sought strategic alliances with biotechnology companies nearby.

The co-location and alliances between biotechnology and pharmaceutical firms eventuated in a more durable eastward shift of the life sciences sector. As the East Coast was closer to Europe than the West Coast, European pharmaceutical firms also began to establish their global R&D headquarters in the area. Novartis's 2002 establishment of its primary research arm—the Novartis Institutes for BioMedical Research—in Cambridge marked the area as a central location for therapeutic R&D.[54]

With the new technological modalities, drug development evolved toward a collaborative model across interdependent actors. Biotechnology firms often developed scientific discoveries from academic laboratories into "proof of concept," or a potential therapeutic product for pharmaceutical firms, which could be integrated into their pipeline. As innovative activity moved from pharmaceutical companies to university laboratories and biotechnology firms, the locus of innovation gravitated toward world-leading universities in the Cambridge–Boston area.

Universities and the Powering of Scientific and Entrepreneurial Talent

The Cambridge–Boston universities were deeply entwined with the development of the local therapeutics sector and were core to its strength. Not only were these universities the source of a highly skilled pool of human capital, but they were also the source of world-leading scientific research, star scientists, and early academic entrepreneurship.

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[51] Lita Nelson, interview by author, 9 Jan. 2024.

[52] Scrip, *Yearbook* (Richmond, 1986), 36; Scrip, *Pharmaceutical Company League Tables* (Richmond, 1991), 2.

[53] G. Steven Burrill and Kenneth B. Lee, Jr. *Biotech '92: Promise to Reality: An Industry Annual Report* (San Francisco, 1991), 46.

[54] Paul Smaglik, "Boston: A Magnetic Hub," *Nature* 417 (2002): 4–5.

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Table 1a. Leading Centers of the US Biotechnology Industry, Industry Scale and R&D Investment by Region, in Millions of US Dollars

	Market Capitalization				*Total Revenue*				*R&D*			
	1991	2001	2011	2021	1991	2001	2011	2021	1991	2001	2011	2021
New York	281	9,403	7,607	86,496	205	279	1,164	17,359	110	397	770	4,475
San Francisco	2,074	61,435	61,108	278,598	1,618	7,439	14,376	42,428	524	3,307	3,954	18,121
Boston / New England	670	38,273	64,994	344,979	326	3,934	10,326	44,236	229	2,676	3,473	20,466

Table 1b. Leading Centers of the US Biotechnology Industry, Public Companies by Region

	Public Companies			
	Percentage of Industry	Number of Companies		
	1991	2001	2011	2021
New York	17%	18	23	45
San Francisco	14%	67	68	107
Boston / New England	13%	53	46	152

Notes:
1. Figures for 1991 show the percentage of public companies by region while subsequent years show the total number of public companies by region.
2. Geographic scope varies across years in the source publication. 1991 figures refer to New York Tri-State Area, San Francisco Bay Area, and Boston Area. 2001 and 2011 figures refer to New York State, San Francisco Bay Area, and New England; 2021 figures refer to New York, Northern California, and Massachusetts.
Source: Burrill and Lee, *Biotech '92*, 46, 47; Ernst and Young, *Beyond Borders: The Global Biotechnology Report* (2002), 67; Ernst and Young, *Beyond Borders: Global Biotechnology Report 2012* (2012), 31; Ernst and Young (2022), 37.

The local universities supplied vital human capital for emerging firms, particularly by producing graduates with advanced degrees in biology who eagerly sought opportunities in industry. After the biotechnology revolution, biochemists and molecular biologists suddenly found job opportunities—beyond teaching and academic research—that had not existed before. As former Harvard professor and Biogen CEO Walter Gilbert explained of such graduates, "If you have another turn of mind, you want something immediate in terms of human good … creating drugs that are going to influence somebody in your lifetime … Everybody with that sort of mind suddenly finds … there are jobs available and even well-paying jobs … "[55] The local biotechnology sector capitalized upon not only a strong pool of human capital but also university (e.g., HBS) and company (e.g., Genetics Institute, Genzyme) alumni networks that facilitated talent mobility and entrepreneurship.[56]

Local universities had also been at the forefront of scientific research, providing an exceptional source of scientific knowledge with a high concentration of star scientists. The latter refers to highly research-productive scientists who have delivered significant social impact—through research collaborations and the commercialization of academic discoveries via entrepreneurship.[57] MIT scientists' founding of the defense contractor Raytheon and the computer company Digital Equipment Corporation illustrate the historical significance of universities and MIT's strengths in the application of research.

[55] Walter Gilbert, interview by author, 19 July 2024.

[56] Robert Carpenter, interview by author, 16 July 2024; Monica C. Higgins, *Career Imprints: Creating Leaders across an Industry* (San Francisco, 2005); Scott Requadt, interview by author, 8 Dec. 2023; Robert Weisman, "How Genzyme Became a Source of Biotech Executives," *The Boston Globe*, 11 July 2015; Zoltan Csimma, interview by author, 15 Dec. 2023. Zoltan Csimma, former chief human resources officer at Genzyme, observed that the collaborative nature of developing therapeutics also facilitated enduring relationships.

[57] Alexander Oettl, "Reconceptualizing Stars: Scientist Helpfulness and Peer Performance," *Management Science* 58, no. 6 (2012): 1122–1140.

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Indeed, MIT played a pioneering role in the commercialization of academic science.[58] Not only did its scientists have statutory privileges to engage in consulting activities one day of the week, but substantial reforms to facilitate technology transfers were also made at the university, particularly after Bayh–Dole.

More specifically, the MIT technology licensing office (TLO) began to reorganize its office from a largely legal, administrative office staffed by patent attorneys to a more technology- and marketing-savvy office oriented toward business. In the 1980s, MIT invited colleagues such as Neils Reimers from Stanford's TLO to facilitate the translation of academic science into the market, allow faculty to bring their science into the real world as consultants or entrepreneurs, and support government aims to bring federally funded scientific research into public use. By the late 1990s, MIT's TLO advised start-ups and connected them to local venture capitalists, earning a reputation for speaking the language of both industry and academia.[59]

Area universities also began to launch entrepreneurship education and interdisciplinary research centers that would help translate scientific discoveries into therapeutic applications. For instance, MIT professor Edward Roberts, who founded the university's Entrepreneurship Center (1990) and related programs, was credited for cultivating the university's entrepreneurial culture.[60] As MIT attracted family foundations that established research centers supportive of commercialization, such as the Broad Institute (2004) and the Koch Center for Integrative Cancer Research (2007), similar centers were established at Harvard, such as the Harvard Stem Cell Institute (2004) and the Paglucia Life Lab (2016).

These universities had a high concentration of star scientists whose role expanded over the years—from conducting groundbreaking research to establishing startups, to participating in wider industry engagement. Early star scientists such as Walter Gilbert (Harvard), Phillip Sharp (MIT), Mark Ptashne (Harvard), and Tom Maniatis (Harvard) were world-renowned scientists who established companies such as Biogen and Genetics Institute based on university research, situated these firms near their universities; and spearheaded the academic–industry collaboration model at a time of significant skepticism toward academic entrepreneurship.[61] The second generation of star scientists, such as Robert Langer (MIT) and George Church (Harvard), were esteemed scholars with considerable publications and research grants who solidified the academia–industry collaboration model. They not only worked with companies but also established multiple companies—often based on a platform technology—with strong patent protection.[62] Furthermore, star scientists attracted star students and star postdocs and trained the next generation of academic entrepreneurs. Local universities—and affiliated hospitals—helped establish the area as the center of the

[58] Noted by numerous interviewees.

[59] Nelson, interview. Lita Nelson led MIT's TLO between 1986 and 2016. Interviewees commented upon the office's efficiency and speed.

[60] Edward B. Roberts, interview by Infinite MIT, accessed 6 Nov. 2024, https://infinite.mit.edu/video/edward-b-roberts-58-sm-58-sm-60-phd-62.

[61] Biogen N.V., "Private Placing Memorandum," 28 Sep. 1981, 3, Walter Gilbert Papers, Box 8, Harvard University Archives, Cambridge, Massachusetts; deliberation between scientists and Harvard administration on patent use are noted, for example, in Genetics Institute, "Meeting of Directors."

[62] Carolyn Y. Johnson, "Building a Better Bacteria," *The Boston Globe*, 29 Aug. 2011; Carolyn Y. Johnson, "MIT Bioengineer to Share Medical Prize," *The Boston Globe*, 15 Sep. 2011.

therapeutics industry, creating a self-reinforcing ecosystem that attracted more firms. As MIT institute professor and entrepreneur Robert Langer explained:

> If I thought the number one thing that was critical was ... that you have two of the greatest universities in the world, two miles from each other in Cambridge: MIT and Harvard. You have Harvard Medical School, all the great hospitals here ... and you have a lot of other colleges that are excellent, too, like BU, BC, Tufts, Brandeis. I think that to me, and then you had some companies that got started like Biogen and Repligen and then more just kept coming and coming ...[63]

The Clinical Infrastructure

The prominence of the Cambridge–Boston area as a center for novel therapeutics also owed much to the local clinical infrastructure, such as that of the Longwood area. Harvard Medical School moved closer to its affiliated teaching hospitals in the early twentieth century, and these hospitals were leaders in education, research, and clinical delivery. Over the years, the proximity of these specialist hospitals—including the Boston Children's Hospital and the Dana–Farber Cancer Institute—facilitated the training of clinicians across specialisms as well as interdisciplinary and translational research.

The hospitals' research focus was evidenced as major recipients of NIH funding, which placed Boston—over San Francisco (Fig. 3)—as the highest recipient city of NIH funds since 1992.[64] Four were also among the seven largest recipients of industry-sponsored hospital research in the mid-1990s.[65] As MIT institute professor and Biogen co-founder Phillip Sharp elaborated, the working relationships between hospitals, firms, and universities were significant:

> One of the things—there were many things that made Cambridge and Boston so powerful in biotech—one is there are great universities here ... the other thing that's really striking is there are great hospitals and medical schools in nearby Boston ... and we have had relationships with them, working relationships for over 50 years before recombinant DNA, where we collaborate, individual faculty collaborated to take technology, radiology, other technologies into medical care. So, this whole engagement with the expertise of clinical medicine, working with the basic scientists, working with the private sector was important. We understood each other. We understood who to talk to ... and this includes a whole generation of MD PhD students and others, who can talk both languages, have experience in medical care, clinical medicine and laboratories ...[66]

[63] Robert Langer, interview by author, 17 July 2024.

[64] Boston Planning & Development Agency, Research Division, *Boston: Most NIH Funds for 24 Consecutive Years* (Boston, MA, 2019).

[65] Association of University Technology Managers, "AUTM Licensing Survey," in Biotechnology Industry Organisation, *Economic Importance of Technology, Medical Research and Improved Healthcare: Forum of the Task Force on Science, Healthcare and the Economy, 23 June 1998*. Henri A. Termeer Papers, Box 69, Folder 22, Baker Library Special Collections and Archives, Harvard Business School, Boston, MA.

[66] Sharp, interview.

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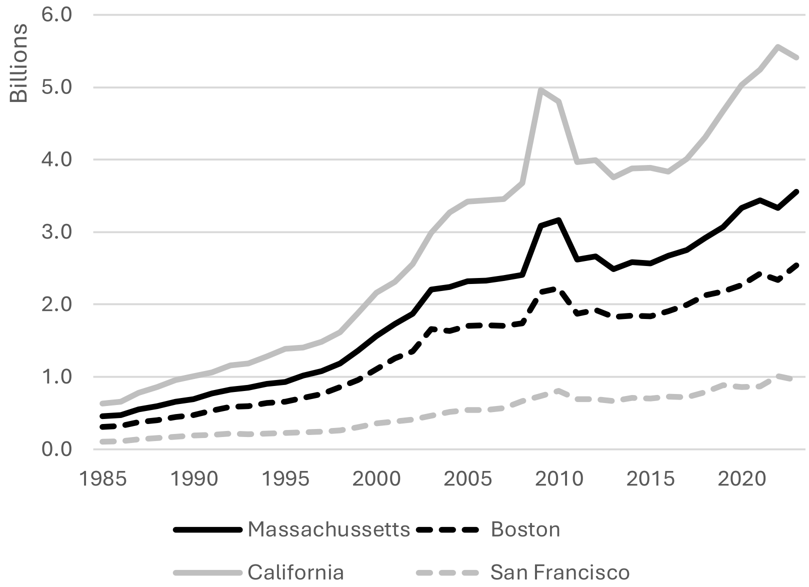

Figure 3. Total NIH funding in Massachusetts, Boston, California and San Francisco.
Source: National Institutes of Health, NIH RePORTER

The area's strengths in collaborative R&D drew from the complementary capacities of local universities and clinical infrastructure. For example, many MIT scientists had expertise in platform technologies—for example, drug delivery systems, tissue engineering, and genome editing—that had a wide range of applications, rather than therapeutic compounds per se. Such technologies were often essential to developing therapies involving new technological modalities.[67] As MIT did not have a medical school, its academics often developed close collaborations with Harvard Medical School and affiliated hospitals.[68] These networks facilitated knowledge exchange and the translation of fundamental discoveries from bench to bedside.

Venture Capitalists, Foundations, and Alternative Forms of Funding

If universities and the clinical infrastructure were the engine, risk capital was the fuel that propelled growth of the life sciences business. Yet in the 1970s, there was limited venture capital and few biotechnology startups. Most investors would realize the potential gains from biotechnology following Genentech's initial public offering (IPO) in 1980.[69] Indeed, from a sector-wide perspective, venture capital funding increased from roughly US$50 million in 1984 to over US$300 million in 1988.[70]

[67] Robert Langer, "New Methods of Drug Delivery," *Science* 249, no. 4976 (1990): 1527–1533.

[68] Robert Langer and Judah Folkman, "Polymers for the Sustained Release of Proteins and Other Macromolecules," *Nature* 263, no. 5580 (1976): 797–800.

[69] Karen Arenson, "A 'Hot' Offering Retrospective," *The New York Times*, 30 Dec. 1980, 1.

[70] Burrill and Lee, *Biotech '92*.

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Risk Capital for Biotechnology Firms in the 1970s and 1980s

The area's early biotechnology firms attracted venture capital financing from within and outside of Massachusetts, such as Kleiner Perkins (California) and Venrock Associates (New York)—the venture arm of established companies—and private investors. For example, Biogen, founded by a collective of scientists, was financed by the local venture capital firm TA Associates, the venture arm of the Canadian nickel mining company Inco, the US pharmaceutical firm Schering Plough, the agricultural biotechnology company Monsanto, and private investors such as Moshe Alafi.[71] Funding amounts in those years were modest compared with later decades. For instance, Genetics Institute, founded by Harvard scientists Mark Ptashne and Tom Maniatis, to develop therapeutic proteins, was initially offered US$6 million by a venture capital consortium. The group comprised the locally founded Greylock; New York-based Venrock and J.H. Whitney; the private investor William Paley, founder of the television company CBS; and firms such as Baxter and Pfizer. Despite its origins in university laboratories and initial support from the Harvard Management Group, which managed university endowments, faculty opposition led to the withdrawal of that support.[72] Concerned over potential conflicts of interest, Harvard remained ambivalent toward academic entrepreneurship.[73]

In the 1970s and 1980s, venture capital firms in the Boston area were generalists with limited funding.[74] When Cambridge-based Highland Capital Partners was established in 1988, it was the first among specialist venture firms that developed deep, industry-specific expertise; focused on early-stage companies; and invested substantial capital with smaller syndicates.[75] As co-founder Bob Higgins reflected, "We thought focusing by technology sector would be an interesting idea … we chose software, medical and telecom as our … three foci … It doesn't sound like it's a focus, but at the time it was considered unusual, if not radical."[76]

The large investment banks such as Goldman Sachs and JP Morgan were not interested in life sciences for much of the 1990s. Life science investments were covered by four boutique banks, three of which were on the West Coast. These were Robertson Stephens, Hambrecht & Quist, and Montgomery Securities (all San Francisco), and Alex Brown (Baltimore).[77] Hambrecht & Quist, for example, was an

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[71] Letter to Shareholders of Biogen N.V., 20 May 1980, Series 2: Board of Director Documents, Box 18, Charles Weissmann Collection, Cold Spring Harbor Laboratory Archives, Cold Spring Harbor, New York.

[72] Gabriel Schmergel, interview by Arnold Thackray, Cassandra Stokes, and Mark Jones, 15 Dec. 2011, accessed 5 Nov. 2024, https://digital.sciencehistory.org/works/lutrzki; Genetics Institute, Inc. Annual Report 1983, Tom Maniatis Collection, Box 1, Folder 1, Cold Spring Harbor Laboratory Archives, Cold Spring Harbor, New York.

[73] Harvard President's Report to the Members of the Board of Overseers 3 Sep. 1981, Tom Maniatis Collection, Box 1, Folder 9, Cold Spring Harbor Laboratory Archives, Cold Spring Harbor, New York.

[74] "Venture Capital in Boston, 1971–1974," Patrick R. Liles papers, Box 6, Folder 7, Baker Library Special Collections and Archives, Harvard Business School, Boston, MA.

[75] Bob Higgins, interviewed by Amy Blitz, July 2001, HBS Entrepreneurs Oral History Collection, Baker Library Special Collections, Harvard Business School, Boston, MA.

[76] Bob Higgins, interview by author, 15 July 2024.

[77] Schnoor, interview; Arthur Klausner, "Demand Increasing for Biotech Analysts on Wall Street," *Bio/Technology* 1, no. 9 (1983): 740–741.

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underwriter for the IPOs of Genentech and Cetus in 1980 and 1981, respectively.[78] Following successful IPOs and therapy launches, along with advisory experience of mergers and acquisitions between pharmaceutical and biotechnology firms, larger investment banks came to form dedicated healthcare and biotechnology divisions.

Growing Interest among Local Venture Firms

As biotechnology companies from Biogen to Genzyme achieved considerable success—completing public offerings and developing effective therapies—further venture capital firms such as Morgenthaler opened offices in Boston. Existing firms such as Schroder Ventures and Atlas Ventures also became more interested in biotechnology, just as specialist firms such as Polaris Partners (1996) and Flagship Pioneering (1999) were founded. Local venture companies began to take a heightened interest in biotechnology just as West Coast contemporaries began to doubt its potential.

Doubts among West Coast investors intensified in the 1990s with several high-profile failures of antibody drugs. The first monoclonal antibody drug, OKT3, encountered clinical complications, while the therapies of Xoma and Centocor—monoclonal antibody drug companies—struggled to gain FDA approval. These failures led to a decline in investment, despite strong intellectual property.[79] Contemporary West Coast venture firms opted to invest in thriving tech companies with shorter lead times, clearer paths to market, and significant returns from IPOs—such as those of Yahoo (1995), Amazon (1997), and eBay (1998).

Diversification of Funding Sources

Venture capital in the biotechnology industry grew significantly after the millennium (Table 2), supporting early-stage biotechnology companies. Startups benefited from local venture capitalists who considered companies in their earliest stages to be a local business, where the ability to walk the halls of universities and understand ongoing activities was crucial.[80] Moreover, pulling a company together required conversations that were difficult to conduct at a distance.

Meanwhile, funding sources diversified, particularly for companies in later stages of development. Corporate investment became important as pharmaceutical companies turned to biotechnology firms for the seeds of discovery and created venture arms, such as Novartis Venture Fund (1996) and Pfizer Ventures (2004). Investment banks also became more interested in the life sciences business, as reflected by JP Morgan's sponsorship of the industry's premier conference: the JP Morgan Healthcare Conference. Additionally, patient organizations became funders

[78] Genentech, Inc., "New Issue: 1,000,000 Shares Common Stock," [Announcement], *The Economist*, 1 Nov. 1980, 25; Susie Gharib, "The Folks Who Brought You Apple," *Fortune*, 12 Jan. 1981.

[79] Lara Marks, "The Birth Pangs of Monoclonal Antibody Therapeutics: The Failure and Legacy of Centoxin," *Mabs* 4, no. 3 (2012): 403–412; Lawrence M. Fisher, "Market Place; Price of Failure in Biotechnology," *The New York Times*, 17 Apr. 1992; Stephen Reeders, interview by author, MVM Partners, 22 Dec. 2024.

[80] Reeders, interview.

Table 2. Venture Capital in the Biotechnology Industry

	Company count	*Deal count*	*Capital invested (millions of US dollars)*
2000	75	80	1,440.98
2005	175	184	2,316.29
2010	325	333	4,131.67
2015	617	646	11,190.97
2020	1,004	1,056	31,400.91

Source: PitchBook Data, Inc., venture capital data, 2000–2020.

for firms focused on rare diseases. For example, in 2000, the Cystic Fibrosis Foundation offered Vertex a US$150 million investment in exchange for future therapy revenues.[81] As Vertex launched cystic fibrosis drugs, the Foundation's venture philanthropy model spread to other organizations such as CureDuchenne, which funded area firms including Sarepta Therapeutics.[82]

Boston's long association with multigenerational wealth was also an important source of capital. While New York was regarded as a city where transactions were short term and deal-focused, Boston was regarded as an investment city with more patient, relationship-based capital conducive to building biotechnology companies.[83] As biotechnology attracted attention from the wider investment community, family offices such as the local Kraft Group further supported biotechnology firms.[84]

Over time, the Cambridge–Boston area attracted a community of investors who could identify and fund emerging opportunities with significant potential. As limited partners of venture capital firms were often universities, venture firms were also familiar with promising technologies from academic laboratories. Financing sources also came to involve sophisticated combinations, including venture capital, corporate investment, patient organizations, family offices, and public markets.[85]

The Global Origins of Local Talent

Finally, the greater Boston area benefited from a foreign-born population above the national average, which increased in the last decades of the twentieth century—from 13.1% in 1970 to 25.8% in 2000.[86] The relocation of Novartis' R&D headquarters to

[81] Werth, *The Billion-Dollar Molecule.*

[82] CureDuchenne, CureDuchenne Ventures, accessed 15 Nov. 2024, https://cureduchenne.org/ventures/.

[83] Higgins, interview.

[84] Melanie Senior, "Family Offices Bolster Early-Stage Financing," *Nature Biotechnology* 31 (2013): 473–474; Jessica Bartlett, "Kraft Group Participates in $30m Funding for Cambridge Biotech," *Boston Business Journal*, 9 June 2015. It was noted that family offices that engage in such investments tend to be those that have billions or tens of billions, rather than hundreds of million or a billion dollars. Jack Reynolds, interview by author, 7 Dec. 2023.

[85] See also, Dennis Ford and Barbara Nelsen, "The View Beyond Venture Capital," *Nature Biotechnology* 32 (2014): 15–23.

[86] US Census Bureau 2010–22 American Community Surveys (ACS), and 1970, 1990, and 2000 decennial census; Campbell J. Gibson and Emily Lennon, "Historical Census Statistics on the Foreign-Born

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Table 3. Number of International Students at Harvard and MIT 2004–2024

	Number of international students		*Percentage of total enrollment*	
	Harvard	*MIT*	*Harvard*	*MIT*
2004–2005	3,546	2,724	18.0%	24.6%
2014–2015	4,822	3,625	22.5%	29.1%
2023–2024	6,713	4,130	26.8%	28.8%

Source: MIT International Students Office, "Statistics," accessed 8 May 2024, https://iso.mit.edu/about-iso/statistics/; Office of the Vice Provost for International Affairs, "One Harvard", accessed 8 May 2024, https://oneworld.worldwide.harvard.edu/; Harvard University Office of Budgets, Financial Planning and Institutional Research. *Harvard University Fact Book 2004-2005* (Cambridge, MA, 2005), 6, 14.

Cambridge in 2002 also signaled the increasing presence of international pharmaceutical firms in the region—with foreign personnel. This influx of human capital featuring diverse ideas, perspectives, and connections supported the growth of the sector.

The Cambridge–Boston universities had long attracted global talent. By the 1980s, this trend led Gabriel Schmergel, then CEO of Genetics Institute, to remark that access to international talent, along with foreign capital and markets, were key to the strengths of the field.[87] The inflow of international students and researchers at flagship universities (Table 3) enhanced research caliber, cultivated an international workforce, and seeded immigrant entrepreneurs.

International talent had been integral to building the leading local biotechnology firms, such as Biogen (1978) and Genzyme (1981).[88] Admittedly, there was still limited entrepreneurship in the 1980s and much less so by immigrants. While the 1990 introduction of the H1-B visa program facilitated the hiring of foreign skilled workers who might become company founders, most entrepreneurs were mid-career, middle-aged white men who had experience in senior-level management in large, established companies. As biotechnology firms came to play an integral role in therapeutic development, foreign-born managers and entrepreneurs assumed an increasingly prominent role in the sector, fueled by ideas, ambitions, and tolerance for risk.[89] Noubar Afeyan, co-founder and CEO of Flagship Pioneering (established 1999), suggested that immigrants were more inclined toward innovation and entrepreneurship, as it constitutes "intellectual immigration."[90] Just as immigrant entrepreneurs made an outsized contribution to Silicon Valley high technology firms in the 1980s and 1990s, by 2006, 25.7% of founders in Massachusetts biotechnology firms were

Population of the United States: 1850 to 1990," (Working Paper no. 29, US Census Bureau, Washington, DC, 1999), Table 23.

87 Gabriel Schmergel, "Technology Transfer: Biotechnology Industry Perspectives," *Technology and Society* 8 (1986): 233–236.

88 Inco Europe Limited, "Report of Proceedings at the European Microbiology Conference II," 25 Mar. 1978, Phillip A. Sharp Papers, Box 3, MIT Libraries Distinctive Collections, Cambridge, MA.

89 Cristina Csimma, interview by author, 16 Jan. 2024.

90 Don Seiffert, "Immigrant Entrepreneurs: They Get the Job Done," *Boston Business Journal,* 2 Dec. 2016, accessed 29 Sep. 2025, https://www.bizjournals.com/boston/news/2016/12/02/immigrant-businesses-they-get-the-job-done.html.

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foreign-born, with companies producing over US$7.6 billion dollars and employing over 4,000 people.[91]

Immigrant entrepreneurs not only founded firms but also founded enduring institutions that reshaped the local innovation ecosystem. Genzyme's Henri Termeer, for example, pioneered the business model for orphan drug development during his decades at the firm's helm.[92] Flagship's Noubar Afeyan introduced a business model of "institutional professional entrepreneuring," engaging in parallel—as compared with serial—entrepreneurship, based on platform technologies. Flagship also cultivated a "network insurgency," a network architecture of interconnected companies that share novel biotechnology platforms, provide access to capital and talent, and have pushed the technological frontier.[93] While the industry workforce remained less diverse than that of higher education into the late 2010s, diversity was regarded as a driver of strength in the local therapeutics business.[94]

Conclusion

This research traces how the Cambridge–Boston area evolved as the global center of the therapeutics industry. Adopting insights from the innovation ecosystem perspective, it examines how dynamic, multilateral interactions between complementary and co-evolving actors enhanced innovative capacity. This approach also illuminates how an extraordinary confluence of structural advantages, serendipitous timing, and strategic actions fostered an exceptional capacity to translate emergent technologies into novel therapies.

In fact, the rise of the Cambridge–Boston ecosystem occurred at the intersection of such structural, temporal, and strategic dynamics. For instance, the local therapeutics sector was built upon the institutional legacies of past innovation ecosystems, partly owing to ongoing industrial decline over the twentieth century. These legacies included the resources of world-leading universities as well as networks of collaboration (e.g., alumni, industry–academia). Local biotechnology firms were also proximate to pharmaceutical headquarters on the East Coast and Europe. Cambridge–Boston firms also benefited from the cross-fertilization of knowledge arising from social and professional interactions or changing jobs within a contained geographical location.

Fortuitously, scientific breakthroughs, institutional change, and the development of risk capital unfolded in parallel. For instance, the biotechnology revolution unfolded as regulatory reforms, including the *Diamond v. Chakrabarty* ruling, the Bayh–

[91] AnnaLee Saxenian, "Silicon Valley's New Immigrant High-Growth Entrepreneurs," *Economic Development Quarterly* 16, no. 1 (2002): 20–31; Immigrant Learning Center, *Immigrant Entrepreneurs in the Massachusetts Biotechnology Industry* (Malden, 2007). The 2005–2007 American Community Survey indicated that the foreign-born population of Massachusetts was 14.2%. Alan Clayton-Matthews, John McCormack, and Paul Watanabe, *Massachusetts Immigrants by the Numbers: Demographic Characteristics and Economic Footprint* (Malden, 2019).

[92] Annual reports such as Genzyme Corporation, *Annual Report* (Cambridge, MA, 1995).

[93] Noubar Afeyan, interview by author, 4 Jan. 2024.

[94] Brady Huggett, "Biotech's Pale Shadow," *Nature Biotechnology* 36, no. 1 (2018): 20–30; Jeremy M. Levin, Steven H. Holtzman, John Maraganore, Paul J. Hastings, Ron Cohen, Bassil Dahiyat, Julian Adams et al., "US Immigration Order Strikes against Biotech," *Nature Biotechnology* 35, no. 3 (2017): 204–206.

Dole Act, the 1981 tax cuts, to the Orphan Drug Act, were introduced in the 1980s. Such changes took effect alongside the emergence of research services firms as well as specialized and alternative forms of risk capital.

The convergence of structural advantages, historical serendipity, and strategic actions generated a talent pool of globally sourced, highly skilled human capital as well as star scientists. The area had a high concentration of these star scientists, who not only secured large grants, authored many publications, and pushed the technological frontier in interdisciplinary areas but also founded multiple companies and mentored the next generation of star scientists.

The ecosystem perspective helps illustrate how therapeutic innovation resulted from complementary and co-evolving actors. Biotechnology firms not only altered the structure of the therapeutics industry but also created new networks of academic–industry collaboration. Universities enhanced technology transfer activities by restructuring TLOs. MIT's commercial orientation led academics to capitalize upon long-standing ties to industry or engage in entrepreneurship as well as form complementary collaborations with local universities and hospitals in pursuing the application of new technologies. Providers of risk capital also diversified over the years, encompassing a community of specialist venture capital firms, pharmaceutical firms, patient organizations, and family offices.

While the Cambridge–Boston area became an epicenter for novel therapeutics, business historians have shown that location-specific industrial prowess is impermanent and subject to change—whether from newer technologies, market shifts, or policy changes. Future research may consider how social challenges—from socioeconomic inequalities to the displacement of long-standing residents and businesses—generated by ecosystem development may recursively reshape their evolution. Such studies could be enriched by cross-sectoral and comparative approaches.

The adoption of the innovation ecosystem framework helped deepen a system-level appreciation of industry development. Additional micro-level studies may provide further insights. Building upon our understanding of how actors' capabilities co-evolve, expanded archival work could also deepen insights into the mutual shaping of technologies, actors, and institutions.

Moreover, future research may engage in debates on the state's role in fostering innovation and knowledge-intensive industries.[95] Ecosystem actors regarded federal government as significant for basic research and approving therapeutics and local government as important for enhancing livability—improving public infrastructure, including transportation and education. They did not regard government as central to commercialization, despite state funding initiatives or municipal research restrictions—as with recombinant DNA—that had affected business. Massachusetts, after all, was more an enabler of organic collaboration between geographically proximate actors: therapeutics firms, universities, hospitals, and risk capital providers. While California was similar, collaborative innovation centered less around hospitals, which were fewer and more geographically dispersed. Actors often

[95] Marianna Mazzucato, *The Entrepreneurial State: Debunking Public vs. Private Sector Myths* (London, 2013); Deirdre N. McCloskey and Alberto Mingardi, *The Myth of the Entrepreneurial State* (Great Barrington, MA, 2021).

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indicated that other states—such as North Carolina or Texas—intervened more actively to foster industry development by creating research parks or generous incentives to attract companies via tax breaks, grants, and business-friendly regulation. Yet, governments cannot forecast or orchestrate the development of emergent technologies, such as safe and effective cell or gene therapies. Future research may also consider how the relative significance of different levels of government, from sub-national to national to supranational (e.g., European Union), have evolved in shaping the history of the therapeutic sector.

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