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The Impact of the Dutch Biopharmaceutical Industry on Regional Economic Development in the Randstad

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“The Impact of the Dutch Biopharmaceutical Industry on Regional Economic
Development in the Randstad”

Submission to European Regional Science Association Conference

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The astounding rate of growth of the biotechnology industry and a general desire to partake of its lucrative economic bounty has led national and regional governments to focus on the development of biotechnology clusters as a catalyst for regional economic development. Indeed, a survey of 77 local and 36 state economic development agencies in the U.S. reported that 83% have listed biotechnology as one of their top two targets for industrial development. Outside the United States, Singapore has launched Biopolis, an 18.5 hectare, \$300 million science park devoted exclusively to biomedical research and development. Thus, this keen focus on biotechnology is increasingly reshaping the physical environment of cities as they seek to become players in a lucrative industry of the future. Recently, continental Europe has also made a bid to become a dynamic player in the biotechnology industry as evidenced by the BioPartner Initiative of the Netherlands. How is this industry affecting the urban milieu? What is the impact of a particular high-technology industry—biotechnology--on regional economic development? This paper will seek to address these issues.

Key Words: Biotechnology, Netherlands, regional economic development

Economic development is a highly mutable process. During the last three centuries, the critical drivers of wealth have shifted from natural resource endowments; to tangible created assets such as buildings, machinery and equipment; to the most intangible created asset, namely knowledge itself.¹ Knowledge refers not only to research and development in the natural sciences and engineering, but also to related scientific activities such as surveys, statistics, mapping, etc. as well as a full range of technical, managerial, and social skills and cultural contexts.² This shift towards the primacy of intellectual capital along with globalization, the growth of collaborations between and within the main wealth-creating institutions such as firms and universities, and the emergence of several new major economic players such as China and India is known as the Knowledge Economy.³ It is an economy in which industries that embody significant intellectual capital and high-value added, in high-manufacturing (high-technology) and knowledge-intensive services play a significant role.⁴ For a small but powerful trading nation like the Netherlands, the transition to a Knowledge Economy has created profound challenges vis a vis economic development as it attempts to compete with larger nations such as the United States and Germany. This is especially true in the field of biotechnology, a rapidly changing industry—scientific knowledge doubles in biology doubles every five years—that is also distinguished by unique characteristics which heighten its impact upon the urban milieu. The central theme of this paper will be to examine the evolution of the Dutch biopharmaceutical industry so as to both assess emerging patterns of urban development and evaluate the impact of this industry on regional economic development.

¹ Dunning, John, ed. Regions, Globalization and the Knowledge-Based Economy. (Oxford University Press: New York, 2000), p.8.

² Cooke, Philip and Piccaluga, Andrea, eds. Regional economies as knowledge laboratories. (Edward Elgar: Northampton, MA, 2004), p.xxii.

³ Dunning John, ed. Regions, Globalization and the Knowledge-Based Economy. (Oxford University Press: New York, 2000), p.8.

⁴ Cooke, Philip and Piccaluga, Andrea, eds. Regional economies as knowledge laboratories. (Edward Elgar: Northampton, MA, 2004), p.xx.

THE CURRENT ECONOMIC CONTEXT

The Knowledge Economy and the process of globalization intrinsic to it has in many respects been catalyzed by the advent of information and communications technologies that have dramatically telescoped distances across the globe—leading some theorists such as Francis Cairncross to herald the “death of distance” and the obsolescence of central cities. Nonetheless, as is evidenced by the propensity of particular industries to concentrate heavily in specific localities, place still matters immensely in the Knowledge Economy. As Saskia Sassen has noted, the global flows of capital intrinsic to globalization has also produced “global cities” that serve as strategic bases for the financial institutions, business service firms, and high-technology start-ups which dominate capitalism in the 21st century. Global flows of capital have produced an economic structure in which the disproportionate share of capital flows to selected areas. For example, according to Peter Hall, as of the early 1990s, in the information-intensive service industries of Europe, London has 93% of the headquarters of service companies in the United Kingdom, Paris 70% of those in France, Rome 67% of those in Italy, and Frankfurt 53% of those in Germany.⁵ In the United States, the financial sector has seen a similar consolidation as investment banking firms in San Francisco and Los Angeles have been bought out by East Coast rivals and New York has emerged as the clear market leader. New York like London and Tokyo benefits from being a key financial center and the hubbing of telecommunications networks has tended to reinforce its position. The same trend is true for the biotechnology industry where, in the United States, 9 metropolitan areas and is increasingly evident on a regional scale as two polynuclear regions—the Northeast Corridor and the San Francisco Bay Area dominate the industry. This has profound consequences for the character of economic development as the sectors of the economy performing global roles dominate the economic base of the affected areas. In turn, these produce similar occupational and earnings hierarchies resulting in similar social outcomes. In Sassen's view, the particular industrial and occupational economic structure of the global city region leads to social polarization and

⁵ Peter Hall, “Moving Information: A Talk of Four Technologies,” Working Paper 515, College of Environmental Design, Berkeley, p.24.

a bifurcated earnings structure due to the prevalence of industries that hire a disproportionate number of high and low wage workers and that in turn creates the outcome of the "disappearing middle."⁶ If the phenomenon of dominant cities is expanding to be evidenced in the dominance of particular regions, then a question arises as to whether the deleterious socio-economic development impacts described by Sassen are also expanding accordingly.

BIOTECHNOLOGY AND EUROPE

The aforementioned trends are stunningly apparent on a regional scale in the quintessentially knowledge-intensive biopharmaceutical industry where the industry tends to agglomerate in certain locales—often intertwined as a regional innovation system—with specific characteristics. Most of those locales are in the United States which dominates revenues from biotechnology companies. However, ironically, the modern biotechnology industry was actually born in Europe in 1953. It was then that Dr. James Watson and Mr. Francis Crick of Cambridge University in the United Kingdom discovered the double helix structure of DNA. Following this discovery, they realized that if the genetic instructions for the manufacture of a desirable protein could be identified and inserted into the DNA of a living cell, then that cell would be able not only to manufacture the protein but also to pass on that ability to future generations of cells.⁷ The practical utility of this discovery was significant in that it allowed for the mass production of rare but desirable proteins, usually drugs, through the use of living organisms as factories; and the “improvement” of the organisms themselves, usually by the addition to their DNA of a new gene which confers a desirable quality on the organism—pest-resistance to crops, for example.⁸ Then in 1973, biotechnology took an important step towards commercialization when a series of patent applications were filed by Professors Stan Cohen of Stanford University and Herb Boyer of the University of

⁶ Sassen, S. (1991). The Global City: New York, London, Tokyo. Princeton, New Jersey. Princeton University Press.

⁷“The Genetic Alternative: A Survey of Biotechnology.” *The Economist*, April 30, 1988, p.5.

⁸Ibid.

California at San Francisco.⁹ These patents provided a technique for moving genes between organisms and transformed the basic science of molecular biology into commercially useful knowledge. Importantly, the timing of these discoveries coincided with a new era of active technology transfer by American research universities that relied on patenting scientific discoveries and then licensing the right to use these patents to firms to increase the commercialization of academic research.¹⁰ This era of technology transfer was inaugurated by the Bayh-Dole University and Small Business Patent Act of 1980 that permitted small businesses, universities and not-for-profit institutions to retain title to inventions resulting from federally funded grants and contracts. Interestingly, many of the original scientific discoveries that drove biotechnology were not made in the United States but rather in Europe, specifically Great Britain. However, the U.S., because of its well-developed venture capital system and a greater acceptance of entrepreneurial endeavor has been much more adept at commercializing those discoveries.

	Europe	USA
Life sciences companies (total)	1570	1273
Public companies	105	300
Market cap sector (euro bln.)	75	376
Employees (industry total)	61,104	162,000

Figure 1: U.S. European Life Science Market 2000¹¹

In recent years as the immense wealth to be created by biotechnology has become increasingly evident, European countries such as the Netherlands with its BioPartner Initiative and Asian countries such as Singapore with its Biopolis Science Park have sought to catch up by reforming their domestic contexts to support innovation in this critical field. As is reflected in Figure 1, Europe has become increasingly successful in establishing life science companies although the market capitalization of those companies is significantly less than those in the United States.

⁹Feldman, Maryann. "The Locational Dynamics of the U.S. Biotechnology Industry: Knowledge Externalities and the Anchor Hypothesis." Prepared for the Dutch interuniversity research group *Technology and Economic Growth* conference on August 26-27, 2002, p.3.

¹⁰Ibid.

¹¹Regions of the Future: Life Sciences. Ernst & Young. May 2002.

THE SIGNIFICANCE OF BIOTECHNOLOGY

The emergence of the biotechnology industry is one of the most significant products of the Knowledge Economy. However, what is routinely referred to as the biotechnology industry is not really a distinct industry at all but rather a collection of techniques, the most important of which is genetic engineering.¹² Specifically, biotechnology itself is the application of biological knowledge and techniques pertaining to molecular, cellular, and genetic processes to develop products and services.¹³ These techniques may be applied to a broad array of industries including agriculture (genetic engineering of plants and animals for food and fiber); manufacturing (food processing and chemical engineering); and even computing (bio-computers).¹⁴ Biotechnology blurs many of the distinctions between the health, food, chemicals, and agricultural industries, uniting them by means of a common group of techniques.¹⁵ However, at present, the largest category of biotechnology applications is in health and medicine: the diagnosis, treatment, and prevention of disease.¹⁶ According to estimates by Standard and Poors, human diagnostics (15%) and therapeutics (80%) account for 95% of biotechnology revenues.¹⁷ But given the importance of agricultural applications of biotechnology and genomics to the Dutch economy, those will also be considered herein. The terms biotechnology and biopharmaceuticals will be used interchangeably.

Aside from its status as an exemplar of the Knowledge Economy, biotechnology is highly significant because it is the most urban of high technologies. It is a very space intensive enterprise that requires a sustained physical presence in the urban core and face to face relationships with the universities, hospitals, and governmental entities that still reside in the urban core. In that sense, biotechnology is indicative of the concept of

¹²Feldman, Maryann. "The Locational Dynamics of the U.S. Biotechnology Industry: Knowledge Externalities and the Anchor Hypothesis." Prepared for the Dutch interuniversity research group *Technology and Economic Growth* conference on August 26-27, 2002, p.1 and "The Genetic Alternative: A Survey of Biotechnology." *The Economist*, April 30, 1988, p.10.

¹³Cortright, Joseph and Mayer, Heike. *Signs of Life: The Growth of Biotechnology Centers in the U.S.* The Brookings Institution Center on Urban and Metropolitan Policy, (2002), p.6.

¹⁴Ibid.

¹⁵"The Genetic Alternative: A Survey of Biotechnology." *The Economist*, April 30, 1988, p.18.

¹⁶Cortright, Joseph and Mayer, Heike. *Signs of Life: The Growth of Biotechnology Centers in the U.S.* The Brookings Institution Center on Urban and Metropolitan Policy, (2002), p.6.

¹⁷Ibid.

industrial filtering¹⁸ which refers to the tendency of establishments to locate in metropolitan areas when they are new because proximity to the higher skilled, higher cost labor associated with metropolitan locations is relatively important; and because of the imperative of entrepreneurs retaining close ties with research centers and hospitals. Moreover, because biotechnology deals with fundamental research into the application of new scientific knowledge, that knowledge is highly tacit and non-codifiable so it is very difficult to transfer it abroad.

The significance of biotechnology vis a vis urban dynamics is also due to the unique process through which biotechnology products come to market. This process is evidenced in the biotechnology value chain:

Phase	Tasks	Time	Actors
1) Research	Product discovery; identification of product for commercialization	0-3 Years	Research Universities and Start-Ups
2) Development	Clinical Trials; Involves animal and human testing for the product's safety and efficacy; Government Review and Approval	3-4 Years	Governmental Regulatory Agencies; Research Universities and Start-Ups
3) Manufacturing	Mass Production	Variable	Large Pharmaceutical Firms
4) Commercialization	Marketing and Selling	5 Years	Large Pharmaceutical Firms

Figure 2: The Biotechnology Value Chain¹⁹

Unlike another knowledge-intensive industry such as software, biotechnology has a long production phase.²⁰ These phases are greatly influenced by both the political dynamics of the regulatory process which in the Netherlands is based in the Hague. The process of

¹⁸Bingham, Richard, and Mier, Robert, eds. Theories of local economic development. (Newbury Park: Sage Publications, 1993), p.12.

¹⁹November 25th 2002 interview with Mr. Glen Camiso, Biotechnology Project Leader, The Boston Consulting Group and Lourdes Pagaran. Determinants of Location and Competitiveness in the Biotechnology Industry: The Case of Massachusetts, MCP Thesis, MIT DUSP, 1993, p.21.

²⁰ A more detailed version of the specific steps in the biotechnology value chain is provided in Figure 3.

bringing a product to market is also lengthy—it can take anywhere from 10 to 15 years—and the costs of bringing it to market can get as high as 800 million dollars.²¹ This makes biotech even more urban because it is rooted for long periods during the R&D and testing phases. As the industry has become more science-intensive and innovation-driven, it has become harder to pick winners so a peculiar relationship has developed between small startups who do the R&D during the first 5-7 years and the large pharmaceutical firms who commercialize and manufacture the viable products. The startups identify those scientific breakthroughs that are most commercializable and seek to create enough value to be bought out by a large pharmaceutical firm that is able to leverage its ability to identify, access, harness, and effectively coordinate and deploy resources and capabilities from across the globe so as to bring the product to market.

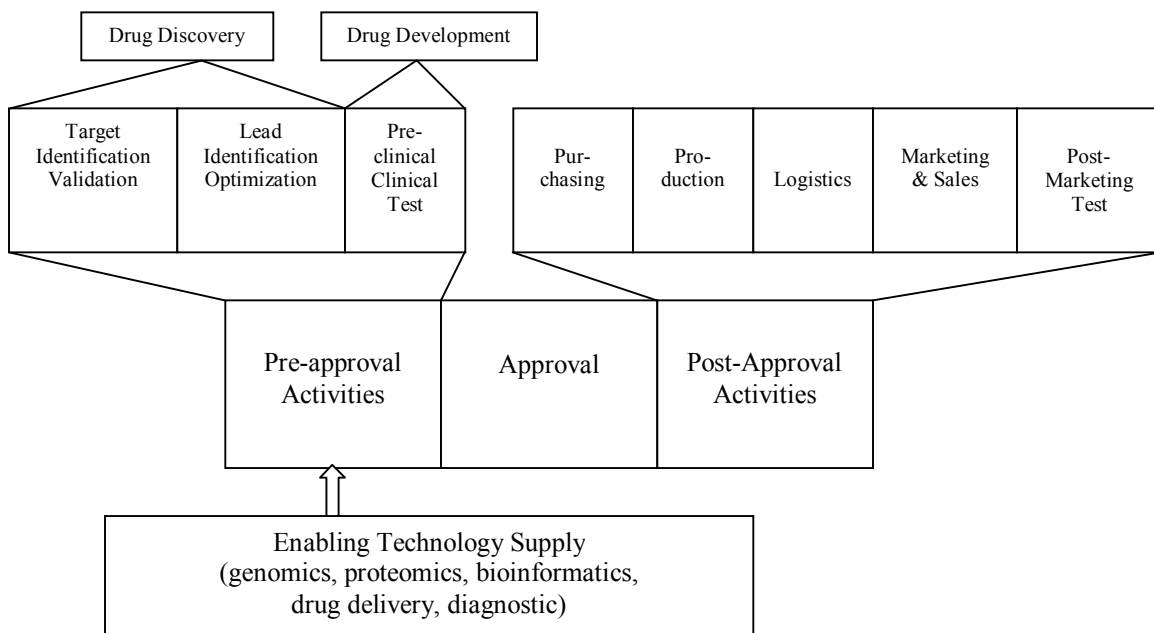


Figure 3: Detailed Biotechnology Value Chain²²

In the United States, both the startups and the large firms tend to cluster in distinct locales in the regional innovation system of the Northeast Corridor. For example, 80% of large pharmaceutical employment is in the New York-New Jersey metropolitan area while the Boston-Cambridge metropolitan area is the second largest biotechnology cluster in the

²¹ Bill Fair. "Chasing Science: Can bioscience drive economic development? It depends." *The Scientist*, vol. 19, issue 8, April 25, 2005.

²² Chiesa, Vittorio. *Industrial Clusters in Biotechnology*. (World Scientific: Hackensack, NJ, 2005), p.20.

United States.²³ Three of the ten largest U.S. biotech companies—Biogen, Genzyme, and Charles River Laboratories—in terms of sales are located in the Boston metropolitan area and seven of the ten largest U.S. pharmaceutical companies by sales rank are located New York-New Jersey metropolitan area including Merck, Bristol-Myers-Squibb, Pfizer, American Home Products, Warner Lambert, Schering Plough and Pharmacia & Upjohn, Inc.²⁴ However, in the Netherlands, the polynuclear region known as the Randstad is emerging as the focal point for a biopharmaceutical *regional innovation system* with key nodes including the Hague (regulation); Leiden (R&D and startups); Amsterdam (cancer research); and Utrecht (proteomics). As a regional innovation system in a nation that is trying to catch up through a concentrated approach, the nodes of the Randstad's biotechnology regional innovation system are defined more explicitly by disciplinary specialization with an emphasis on entrepreneurship and commercialization; and governmental intervention than by functional specialization as is the case with the Northeast Corridor where Boston is a center for research and startups; Washington, DC acts as a center for regulatory oversight and research; and New York-New Jersey is a center for managerial expertise and pharmaceutical companies.

Another significant factor vis a vis the character of regional economic development and biotechnology is the dynamic between large firms and biotechnology startups. The Netherlands is one of the most open economies in the world but it has two large indigenous pharmaceutical firms—DSM and Akzopharma—while the US have several. Ironically, the U.S. advantage in biopharmaceuticals has been strengthened by the exorbitant costs of its inefficient health care system. In Europe, the shift to innovation through biotechnology has been complicated by government interventions such as cost control measures, cut-backs on state-reimbursed pharmaceutical purchases, health care reform, and pressures on physicians to limit prescribing that have greatly decreased profit margins.²⁵ For example, in 1993, the German government imposed a 5% price cut on prescription drugs and a 2% price reduction on 'over-the-counter' (OTC) medicines.²⁶ As

²³“Life Science--Hot Job Spots.” *The Scientist*, July 14, 2000.

²⁴ Cortright, Joseph and Mayer, Heike. Signs of Life: The Growth of Biotechnology Centers in the U.S. The Brookings Institution Center on Urban and Metropolitan Policy, p.8.

²⁵Williams, Gwilym. “Biotechnology market development in Ireland: Issues of strategy, risk, and partnership.” *Irish Marketing Review*, 1998.

²⁶ Ibid.

monopoly purchasers of pharmaceuticals, Europe's government-run health care systems have pushed drug prices down 40% to 60% of U.S. levels, thereby making the American market far more profitable.²⁷ In contrast, in the United States, the cost of prescription drugs is higher, doctors are more willing to prescribe innovative treatments, and direct-to-consumer advertising is not banned as it is in Europe.²⁸ Since most large European pharmaceutical firms now generate most of their profits in the United States, they have been moving more and more of their R&D to the U.S. as well. While Europe has made significant gains in the biopharmaceutical industry, this commercial logic will play a key role in the dynamism of the industry unless two factors intercede: 1) the political context in the U.S. shifts such that there is greater government intervention to produce lower prices; and/or 2) the politically-motivated U.S. reluctance to engage in stem cell research allows European biotechnology firms to vault ahead of their U.S. counterparts which would negate the imperative of conducting research in the U.S.

²⁷ The Novartis Warning.. *Wall Street Journal*, May 8, 2002.

²⁸ Capell, Kerry. .Novartis.. *BusinessWeek*, May 26, 2003.

POLYNUCLEAR REGIONS AS REGIONAL INNOVATION SYSTEMS

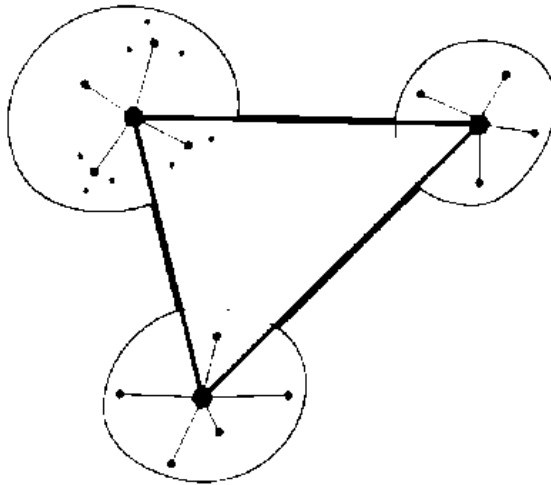


Figure 4: Polynuclear Region²⁹

“A small but growing number of modern urban agglomerations consist of an intricate web of corridor cities whose functional and locational relationships can provide them with holistic competitive advantages over some of their monocentric rivals.”

--D. F. Batten, “Network Cities: Creative Urban Agglomerations for the 21st Century”

A polynuclear region such as the Randstad³⁰ of the Netherlands is an urban network of cities/nodes connected by facilities (links, arcs, ties, relationships) through which entities such as goods and services pass.³¹ The Randstad, where most of the Dutch biopharmaceutical industry is located, is a polynuclear regional agglomeration of 3,200 square miles in the western Netherlands with 7.1 million inhabitants (45% of the population). As defined within this study, the Randstad consists of Utrecht, Amsterdam, Wageningen, Rotterdam, Leiden, Dordrecht, Haarlem, and Flevoland, The Hague, and Delft. Just like the Northeast Corridor, the Randstad is a center for health care in the Netherlands with ten university hospitals in close proximity to each other. Overall, it ranks 6th in Europe but due to the small size of the Dutch market and the general character of the Dutch economy is much more export-oriented. The most significant area

²⁹ Batten, D. F. (1995) Network cities: creative urban agglomerations for the 21st century, *Urban Studies*, 32, pp. 313–327.

³⁰ See Figure 5.

³¹ Business Plan RISNET: ‘Spatial Investment in Urban Networks Background Paper.’

is Leiden which has a substantial science park that is serving as an anchor for the growth of the biotechnology industry in the region.



Figure 5: Location of Key Cities in the Randstad³²

Polynuclear regions are characterized by territorial concentration and networked interrelations between clusters of firms, services, and research institutes; relations of trust; and formal and informal institutional networks.³³ They tend to develop into functionally coherent metropolitan systems.³⁴ The cities in the network are historically and spatially distinct; located within feasible commuting distance; politically independent entities; and complementary to each other.³⁵ Increasingly it is evident that there are distinct advantages to this pattern of organization as it facilitates the networking essential to success function as a regional innovation system in the Knowledge Economy. Polynuclear regions act as regional innovation systems in that they optimize collective learning by giving knowledge-intensive industries rapid access to different labor markets,

³²Robert Kloosterman and Bart Lambregts. "Clustering of Economic Activities in Polycentric Urban Regions: The Case of the Randstad." *Urban Studies*, vol. 38, 2001, no. 4.

³³Meijers, E.J., Romein, A., Hoppenbrouwer, E.C. Planning polycentric urban regions in North West Europe, OTB Research Institute for Housing, Urban and Mobility Studies, Delft University of Technology, p.11.

³⁴Romein, Arie. Spatial planning in competitive polycentric regions. Paper submitted to City Futures Conference, Chicago IL, 8 – 10 July 2004, p.1.

³⁵Kloosterman, R.C. and B. Lambregts. "Clustering of Economic Activities in Polycentric Urban Regions: The Case of the Randstad." *Urban Studies*, 38 (4), 2001.

embedded knowledge, milieus of innovation, and networks of customers.³⁶ They also provide highly skilled professionals and their spouses with a greater array of employment opportunities across a region. In effect, the assets—including infrastructure facilities and specialized services such as higher education—of the separate but networked cities within the region are pooled together to provide greater agglomeration or external economies for businesses within the region.³⁷ Secondly, polynuclear regions promote innovation in that geographical proximity and interaction amongst each of the nodes reduces transactions costs and fosters the development of business networks that promote interfirm trading linkages and facilitate the exchange of knowledge and expertise.³⁸ Finally, the networks intrinsic to polynuclear regions allow cities to develop and exploit complementarities or synergies between different locations. By encouraging interaction between neighboring locations, each will develop specializations in areas in which it has a competitive advantage which will leave individual firms and the region as a whole in a stronger competitive position.³⁹ The character of the Randstad as a biopharmaceutical regional innovation system has influenced the dynamics of regional economic development in the area.

THE ANCHOR TENANT HYPOTHESIS AND THE URBAN DYNAMICS OF THE RANDSTAD

In many respects, each geographical node in the Randstad has a dominant specialization that acts as an “anchor tenant” and influences urban dynamics. The author’s notion of the “anchor tenant” is built upon the version of the anchor tenant hypothesis posited by Prof. Maryann Feldman in “The Locational Dynamics of the U.S. Biotech Industry: Knowledge Externalities and the Anchor Hypothesis.” Therein Dr. Feldman uses shopping malls as an example and argues that an anchor tenant’s brand

³⁶ Stam, Erik and Egbert Wever. “Propinquity with Community: Spatial transfer of knowledge in the Netherlands—a national and international comparison of collective learning in high-tech manufacturing and services” in Knowledge: The Spatial Dimension.

³⁷ Bailey, N., Turok, I., 2001, Central Scotland as a polycentric urban region: useful planning concept or chimera? Urban Studies, vol. 38, no. 4 and Priemus, H. (1994) Planning the Randstad: between economic growth and sustainability, Urban Studies, pp.509-534.

³⁸ Bailey, N., Turok, I., 2001, Central Scotland as a polycentric urban region: useful planning concept or chimera? Urban Studies, vol. 38, no. 4.

³⁹ Ibid.

recognition creates an externality for smaller stores who realize a benefit—a greater sales volume than they would in other locations. The value of this externality is reflected in higher rents the average tenant pays in comparison to the rent paid by the anchor tenant. This form of price discrimination reflects a willingness of the average tenants to pay a premium for location near the anchor tenant. It is through the role that each dominant institution in the value chain plays as an anchor tenant in this particularly urban high-technology that the biotechnology industry's regional innovation system influences economic development in the Randstad.

The urban dynamics of the Randstad have been greatly influenced by the policies of the Dutch government, particularly in the realm of housing. Although the Randstad is the most highly urbanized part of the Netherlands, the region's population geography is characterized by both *urban deconcentration* and *compact city* policies that are a response by planning authorities to the process of suburbanization that, beginning in the 1960s, had caused population decline in the four largest cities of the Randstad until the mid-1980s.⁴⁰ The former policy attempted to guide this process into a limited number of designated new towns and growth centers, while the latter policy tried to slow suburbanization down.⁴¹ Since the implementation of these policies, in contrast with the largest cities, rather high population growth rates have been witnessed by new towns and, to a lesser extent, by intermediate and small towns and rural municipalities, particularly at the fringes of the Randstad and in the Green Heart.⁴² A key instrument in these strategies has been subsidized housing. Until recently, the national government subsidized 60% of newly built homes.⁴³ This policy is changing but large subsidies still support the urban renewal process and rent subsidies are given to low income households which has resulted in a quite diverse population composition for most districts at significant expense to the government. As a result of subsidies, the Netherlands has a

⁴⁰ Meijers, E.J., Romein, A., Hoppenbrouwer, E.C. Planning polycentric urban regions in North West Europe, OTB Research Institute for Housing, Urban and Mobility Studies, Delft University of Technology, p.35.

⁴¹ Ibid.

⁴² Ibid.

⁴³ "Inequality in Global City Regions." Paper for presentation at the Conference on Global City Regions. UCLA. October 21-23, 1999. (revised version was published in Allen, J. Scott, ed. *Global City-Regions*. New York: Oxford University Press 2001, pp. 285-98. Reprinted in *DISP* (Zurich), 144 (1) Spring 2001, 20-25.

large, differentiated stock of social rented dwellings that forms more than 40% of the total housing stock.⁴⁴ Generally speaking these policies reflect the Dutch commitment to a social market model in which there is a high degree of centralization of tax collection and social contributions combined with a high degree of decentralization of expenditure on welfare. It is similar to the German social market economy in that there are extensive social welfare provisions, influential workers' councils at plant or company level, and an important role for trade unions in national policymaking. However, the emphasis in policymaking and industrial relations is on consensus and a pragmatic approach to dealing with most issues and the labor market has become much more flexible than in Germany.

During the 1980s, as was the case globally, the composition of production in the Randstad began to change. Manufacturing employment declined twice as fast as in the rest of the country and the service sector grew strongly (especially banking, insurance, commercial and public services) - but not as strongly as in the rest of the country.⁴⁵ Housing policy has also been shifting from the national to the regional level as housing markets have increasingly become regional in scope and cities lost population to new single-family housing in the municipalities surrounding the cities.⁴⁶ These trends and the financial strains of subsidized housing lead to a 1990s shift in housing policy towards the privatization of the social housing sector and the sponsorship of more expensive dwellings, which are virtually inaccessible to low-income households, and to a reliance on market mechanisms. The aim of these new policies was to increase the rate of home ownership and diminish the socially rented sector so as bring more middle class families back to the cities while reducing the financial strains on the government.⁴⁷ Politicians feared that the loss of the middle class to the suburbs would lead to a loss of tax base. In

⁴⁴ Sigstedt, Johan (1997): *En bostadspolitik i förändring. En historisk överblick hur bostadspolitiken har förändrats i Nederländerna och Amsterdam under 1900-talet.* [A change housing policy. A historical view of the change in the Netherlands and the city of Amsterdam housing policy during the twentieth century.]

⁴⁵ Ibid.

⁴⁶ Ronald van Kempen and Jan van Weesep. "Gentrification and the Urban Poor: Urban Restructuring and Housing Policy in Utrecht." *Urban Studies*, vol. 31, no.7, 1994, pp.1043-1056.

⁴⁷ Sigstedt, Johan (1997): *En bostadspolitik i förändring. En historisk överblick hur bostadspolitiken har förändrats i Nederländerna och Amsterdam under 1900-talet.* [A change housing policy. A historical view of the change in the Netherlands and the city of Amsterdam housing policy during the twentieth century.]

that sense, in the Netherlands, gentrification—the physical, social, economic, and cultural process whereby inner-city/urban core neighborhoods receive an influx of more affluent neighbors—is regarded in a positive light in the Dutch socio-political context. Moreover, as the economy began to change, a desire emerged to attract more lucrative enterprises to the urban core so as develop them as sources of both attractive middle class employment and tax revenue for city services. This is especially true as it became evident that the competitiveness of the Randstad as a production location was declining due to the interactions between labor markets and housing markets. Indeed, the original success of the Randstad was to a great extent based on port activities—through the port of Rotterdam and Amsterdam’s Schiphol Airport, it served as a gateway to the rest of the country and beyond—but aside from distribution services, metropolitan functions were not so well developed in contrast with other European centers such as Paris and London.⁴⁸ Moreover, firms, when choosing a location, prefer to be near a pool of well-trained labor but the shift of those workers to residences on the urban fringes outside of major municipalities; and the danger of the less skilled being segregated in neighborhoods where employment is not growing posed an economic development quandary.⁴⁹ Increasingly, this private sector quandary and the public sector’s aforementioned quandaries are being resolved by the Netherlands success in harnessing the biotechnology industry as an anchor tenant to drive economic development in metropolitan areas.

Peter Tordoir has argued that the challenges confronting the Randstad can best be addressed through a process known as *metropolitanization*,⁵⁰ whereby the high costs of sustainable, high-density and high-quality urban development are matched by high productivity and the value added by the urban economy. This involves innovation, spiraling agglomeration economies, widening and diversifying markets, subsequent increases in quality, the specialization of productive resources and business activities, and the reinvestment of resulting profits in the capacity and quality of local resources—all of which are characteristic of a knowledge-intensive industry that clusters in the urban core

⁴⁸ Rein Jobse and Barrie Needham. “The Economic Future of the Randstad, Holland.” *Urban Studies*, vol.25, 1988, pp.282-296.

⁴⁹ Ibid.

⁵⁰ Peter Tordoir. The Randstad: The Creation of a Metropolitan Economy.

as part of a regional innovation system and has broad applicability to myriad lucrative markets. Biotechnology is such an industry. Those ideas have become embodied in Dutch policy through the 4th Memorandum on Spatial Planning in 1988 and many local plans from the 1990s.⁵¹ Broadly, these plans focused on:

- 1) The realization of high-quality environments for living, working and recreation
- 2) The development of high-quality amenities and facilities of international allure
- 3) The strengthening of functioning coherence between Amsterdam, Rotterdam and The Hague on the one side, and between these three cities, Schiphol Airport, the Port of Rotterdam and the Green Heart on the other side
- 4) Marketing of this metropolitan business environment
- 5) The development of a functional division of tasks and specialties between Amsterdam, Rotterdam and The Hague on the one side and the city of Utrecht in its function as a national centre on the other side⁵²

The effort to develop the biotechnology industry in the Netherlands has emerged as the embodiment of this process of metropolitanization through the establishment of the industry as an anchor tenant in the Randstad.

DUTCH BIOTECHNOLOGY POLICY

The Dutch government has emphasized biotechnology since the 1980s with its Innovation Oriented Research Program Biotechnology (IOPb) and Programmatic Industry Related Stimulation on Biotech (PBTS), which received approximately 178 million euros (\$240 million dollars) in public investment between 1981 and 1993.⁵³ The country's Research and Development Promotion Act provides for up to 40% deductions of wage tax and social insurance for employees engaged in R&D and market viability studies while the Technical Development Project Act issues interest free loans for technically innovative projects that can cover up to 35% of project costs.⁵⁴ Of particular importance has been the Technological Cooperation Act which offers subsidies of up to 2.5 million euros for R&D projects in which companies or research institutions in the

⁵¹ Meijers, E.J., Romein, A., Hoppenbrouwer, E.C. Planning polycentric urban regions in North West Europe, OTB Research Institute for Housing, Urban and Mobility Studies, Delft University of Technology, p.50.

⁵² Ibid.

⁵³ TNO Report. STB-04-12. *OECD Case Study on Innovation: The Dutch Pharmaceutical and Food Biotechnology Innovation Systems*.

⁵⁴ "A Fertile Ground For Life Sciences," Ministry of Economic Affairs.

Netherlands work with other Dutch or foreign entities. As a result of the latter policy and the open character of the Dutch economy—there are more than 5,000 foreign-based companies in the Netherlands with 1,626 U.S. firms employing nearly 200,000 people in the Netherlands including leading biotechnology companies such as Amgen, Biogen, and Genzyme—since 1997, 37.5% of European framework programs in the life sciences have included Dutch researchers and 90% of Dutch life sciences companies have a global perspective and client base.⁵⁵

After a period of general focus on technology and innovation, a specific commitment to the biotechnology sector was initiated in 1998 when the Ministry of Economic Affairs, prompted by the results of a government-sponsored benchmark study that compared the Dutch entrepreneurial bioscience industry with six other regions in the world discovered that many conditions for growth such as financing and incubator facilities were missing in the Netherlands. Thus, in 1999, the Ministry of Economic Affairs presented the *Life Sciences Action Plan 2000-2004* which devoted 45.3 million euros to the establishment of the BioPartner program (see below) whose goal was to establish at least 75 new life science start-ups in the period 2000-2004.⁵⁶ Then, in 2000, the Dutch industry and public sector research organizations presented the ‘*Strategic Action Plan Genomics*’ for building a strong research infrastructure in the field of genomics. A Temporary Advisory Committee for the Genomics Knowledge Infrastructure advised the Dutch government to invest heavily in genomics research and infrastructure; and to adopt an integrated approach that emphasized commercialization (a critical U.S. advantage) and the social and ethical aspects of genomics. Based on this advice, the Dutch government presented in 2001 its view in the policy report ‘*Genomics Knowledge Infrastructure*’. This resulted in the Netherlands Genomics Initiative (NGI), which is responsible for the execution and management of a national genomics strategy, with a budget of 189 million euros for the period 2002-2007.⁵⁷

⁵⁵ Foreign-Based Companies in the Netherlands Generate 7 Percent of Dutch Employment,” at NFIA web site: <http://usa.nfia.nl/index.php?openpage=/newsitem.php&id=51>

⁵⁶ TNO Report. STB-04-12. *OECD Case Study on Innovation: The Dutch Pharmaceutical and Food Biotechnology Innovation Systems*.

⁵⁷ Ibid.

The Netherlands has an excellent public research infrastructure in the biomolecular and biomedical fields with a well-developed health care system.⁵⁸ However, the growth of the Dutch biotech industry has until recently been inhibited by the low popularity of entrepreneurship and a flawed policy that focused on the top innovative start-ups.⁵⁹ In order to address this problem, for the past five years, the government has focused on the establishment of two programs as major pillars of Dutch biotechnology policy. These include the BioPartner program and the National Genomics Initiative. BioPartner, which is run by the Ministry of Economic Affairs, has supported the development of biotechnology startups in several ways. It has established six incubators known as BioPartner Centers in Amsterdam, Leiden, Groningen, Maastricht, Utrecht, and Wageningen. At these centers which are located near universities, new life science companies can rent office space and laboratories. The companies also receive the support to obtain the necessary permits and funds. In addition, the BioPartner Facility Support initiative provides young biotech start-ups with the opportunity to use advanced and oftentimes expensive equipment at universities and other research institutes. The BioPartner program also offers grants to potential biotech start-ups to allow them to develop an idea into a viable business proposal which they can present to a bank or venture capital firm. In addition to financial capital, the BioPartner Network provides social capital as it operates as a central point of contact for both new and established life sciences entrepreneurs. It helps to broker relationships between life sciences entrepreneurs and useful contacts, such as potential investors and government representatives. The economic development results have been impressive as the BioPartner program realized its objective of the establishment of 75 new life science companies in 2003 instead of 2004.

The approximately \$200 million dollar National Genomics Initiative (NGI) was established in 2001 as an independent organization affiliated with the Netherlands Organization for Scientific Research. In contrast to the BioPartner program which focuses on commercialization and the business side of biotechnology, the NGI aims to

⁵⁸ Ibid.

⁵⁹ How can we reap the fruits of academic research in biotechnology? In search of critical success factors in policies for new-firm formation” van Geenhuizen, M. *Environment and Planning C: Government and Policy* 2003, vol. 21.

promote research and development by encouraging scientific excellence in genomics and related fields. The NGI operates with a high degree of autonomy but is funded by five Dutch ministries: Education, Culture and Science; Economic Affairs; Agriculture, Nature and Food Quality; Health, Welfare and Sport; and Housing, Spatial Planning and the Environment. It is an interdisciplinary taskforce dedicated to strengthening genomics-based research and business in the Netherlands by promoting a clearly focused research strategy on the origins of multifactorial diseases; the functioning of ecosystems, focused on sustainable, environmentally safe and healthy vegetable and animal products; the mechanisms of infectious diseases; and the relationship between food and health, including food safety. The NGI approach emphasizes collaboration and coordinated efforts amongst companies, public research institutes and universities. As is the case with the BioPartner Program, several (4) centers of excellence have been established to carry out this work.

ECONOMIC DEVELOPMENT IMPACTS

These policies have yielded benefits as the biotechnology industry in the Netherlands has become particularly strong with special regard to medical devices, regenerative medicine, agricultural applications, and disease treatments. To support these efforts, the country has 18 graduate research schools that are active in biopharmaceutical research. Between 1994 and 2001, the number of dedicated biopharmaceutical firms increased from only 18 to approximately 80:

Type of life Sciences company Sector:	Dedicated	Diversified	Followers	Totals
Pharmacy (incl. fine chemicals)	76	7	21	104
Agro-food	15	17	248	280
Machines & Instruments	8	1	3	12
Environment	9	-	2	11
Other	16	-	-	16
Total	124	25	274	423

Figure 6: Life sciences companies in the Netherlands⁶⁰

⁶⁰ TNO-STB (2002), adaption of Biopartner data.

In terms of percentages, this breaks down approximately as follows:

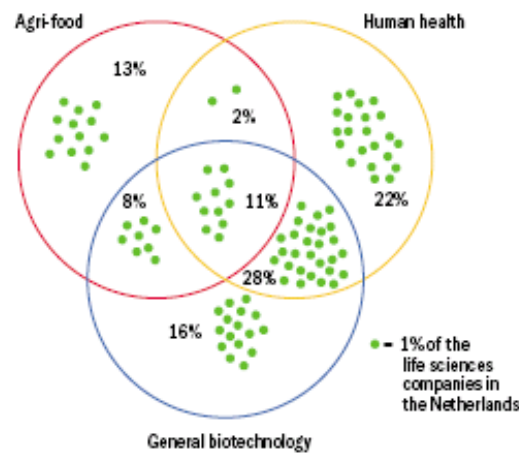


Figure 7: Percentage of Dutch Life Sciences Companies by Sector⁶¹

The Dutch life sciences sector has continued to develop at a rapid pace. Almost a hundred new life science ventures were launched over the past ten years. For example, the pharmaceutical and fine chemicals industries both expect that a third of their turnover will be biotech-related in 2010, compared to just 5% in 1999.⁶² In the agro-food sector around 20% of the turnover is expected to be biotech-related in 2010; and in addition, a fourfold increase of biotech-related products and services related to environmental protection is predicted.⁶³ The recent successful initial public offerings of two firms—Crucell and Isotis—founded by Leiden University academics demonstrates how the country has become more receptive to entrepreneurship. Overall, the Netherlands currently ranks 6th in Europe and 5th in continental Europe in terms of the number of entrepreneurial biotechnology firms:

⁶¹ Regions of the Future: Life Sciences. Ernst & Young, 2002.

⁶² “A Fertile Ground For Life Sciences,” Ministry of Economic Affairs.

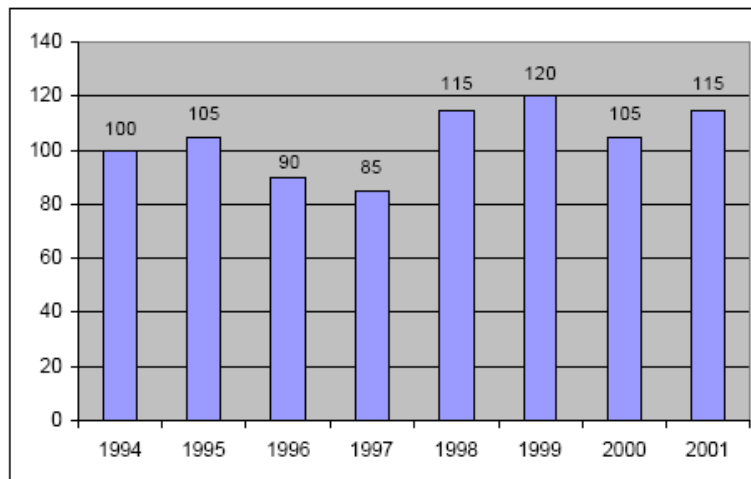
⁶³ Ibid.

Country	Number of firms
Germany	335
United Kingdom	265
France	180
Sweden	165
Switzerland	115
The Netherlands	80
Belgium	65
Denmark	60
Norway	35
Ireland	35

Figure 8: Number of Entrepreneurial Biotechnology Firms in Europe (2002)⁶⁴

The Dutch pharmaceutical industry, which is a driver of the biotech industry, consists of 115 companies that employ over 15,000 individuals:

Figure 9: Size of the Dutch Pharmaceutical Industry in Number of Firms⁶⁵

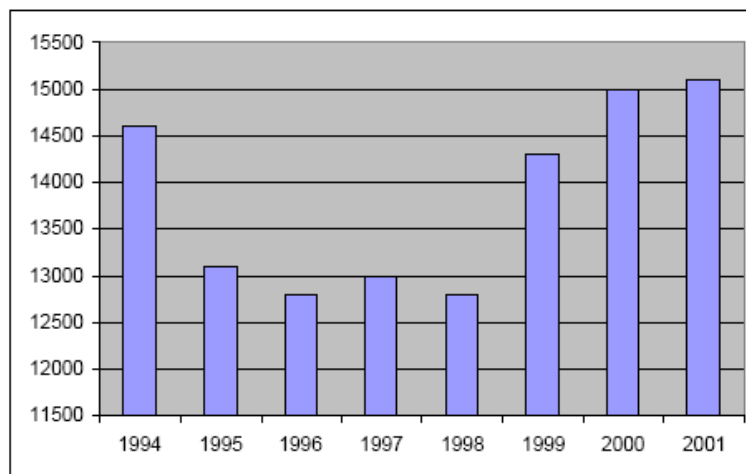


Source: Central Bureau for Statistics / StatLine database 2003

⁶⁴ Ernst & Young in "How can we reap the fruits of academic research in biotechnology? In search of critical success factors in policies for new-firm formation" van Geenhuizen, M. *Environment and Planning C: Government and Policy* 2003, vol. 21.

⁶⁵ TNO report STB-04-012; OECD Case Study Innovation: The Dutch Pharmaceutical and Food Biotechnology Innovation Systems.

Figure 10: Employment in the Dutch Pharmaceutical Industry in Number of Jobs⁶⁶



Source: Nefarma Annual Report 2002, based on CBS figures

The market for biopharmaceuticals is growing and pharmaceuticals based on biotechnology are expected to account for 15-20% of the total pharmaceutical expenditures in the Netherlands in the near future.⁶⁷

Geographically, the biotech industry itself is concentrated in the Randstad, most notably in Amsterdam, Leiden and Delft, and Wageningen which have science parks that are readily accessible to major research universities.⁶⁸ Leiden is a key center of innovative life sciences research and supplies business in the Netherlands in the area of biomedical life sciences. Half of all dedicated Dutch biotechnology companies are located in Leiden. The Leiden BioSciences Park is one of the largest life sciences clusters in Western Europe, and home to 50 companies that employ over 2300 employees. Many of these companies have been established with the assistance of the Business Incubator of BioPartner Center Leiden. The park is in close proximity to the Leiden University Medical Center and eight other knowledge institutions. The emphasis is on biopharmaceuticals. Likewise, the impact of the biotechnology sector can be felt in the agro-food industry which is one of the main industrial sectors in the Netherlands where

⁶⁶ Ibid.

⁶⁷ TNO Report. STB-04-12. *OECD Case Study on Innovation: The Dutch Pharmaceutical and Food Biotechnology Innovation Systems*.

⁶⁸ During, W. "Co-operation between Technology-Based Firms in Business and Science Parks: An Exploratory Study into the Situation in The Netherlands" in *New Technology-Based Firms in the 1990s*, vol. V, (Paul Chapman Publishing, 1998).

there are over 5000 companies in the food sector including such brand names as Unilever and Numico.⁶⁹ However, this figure represents a decrease of over 17% since 1994.⁷⁰ The area around Wageningen is known as the Dutch “Food Valley” as with 10,000 biotechnology employees it is the largest agro-food cluster in the world. It is there at the Wageningen University and Research Center that biotechnology is being utilized to revitalize the industry. Investments in food R&D (including tobacco) have increased considerably: from 182 million euros in 1994 to 269 million euros in 2001; and employment in R&D in the food industry has expanded from 2,989 full-time employees in 2001, compared to 2,523 full-time employees in 1994.⁷¹ On average 60% of the employees of established food companies are performing biotechnology R&D and for half of these companies more than 80% of their personnel is active in R&D activities.⁷² Areas of emphasis and strength include: food development, processing and safety; the development of functional foods and nutraceuticals; plant genomics and breeding; agro-product technology used in crop production and protection; and optimized microorganisms and enzymes (e.g., fungal cultures, yeasts).⁷³

In Amsterdam, another cluster of biomedical activity is yielding exciting results in the field of oncology. The Netherlands Cancer Institute, one of Europe's top centers of cancer research, has combined forces with a neighboring hospital to integrate R&D with clinical practice. The integrated institutions' cutting-edge oncology research has been repeatedly featured in *Science*. Also, in Amsterdam, is the Dutch Central Laboratory for Blood Research, which develops blood-related products and diagnostic services. These institutes jointly opened incubator space for biotechnology companies in 2004. Finally, the city of Utrecht in the Randstad is best known for its expertise in the fields of genomics and proteomics which involves the systematic analysis of protein sequences and expression patterns responsible for carrying out the instructions of genes. Utrecht's top-notch research in this area is anchored by the Utrecht Institute for Pharmaceutical

⁶⁹ TNO Report. STB-04-12. *OECD Case Study on Innovation: The Dutch Pharmaceutical and Food Biotechnology Innovation Systems*.

⁷⁰ Ibid.

⁷¹ Ibid.

⁷² Ibid.

⁷³ Ibid.

Studies and the Bijvoet Graduate School for Immunology and Infectious Diseases, as well as industry leaders such as Glauco Proteomics. In January 2002, the Center for Proteomics opened in Utrecht, providing infrastructure for both structural and functional proteomics work. Nine internationally recognized research teams based in Utrecht are working with six research institutions and graduate schools, as well as teams of industrial partners, affiliated research organizations and academic collaborators. The Center represents the first time that Utrecht has sought to formally combine its significant proteomics resources.

Since the Netherlands only has a population of 15 million people—1/20th of the U.S. and 1/6th of Germany, the size of the biotechnology industry—while at a different scale and less mature level of development than the U.S.—is actually surprising. However, the country's size has profound implications for the character of both its biotechnology industry and the attendant shape of economic development impacts. The Netherlands is much more focused on the efficient utilization of scarce resources. Thus, biotechnology is much more geographically focused—Wageningen (agri-food); Amsterdam (oncology); Utrecht (genomics and proteomics); and Leiden (biopharmaceuticals). Each of these clusters of innovation serves as an anchor tenant that is influencing the real estate and labor dynamics of that particular node in the broader regional innovation system. Real estate prices in the Netherlands have risen 75% between 1997 and 2004, which is 40% higher than the U.S. which has had a 53% price increase in the midst of an unprecedented boom.⁷⁴ Low interest rates and an emergence from recession deserve some credit for the boom but factors such as housing deregulation and a desire to use knowledge-intensive industries such as biotechnology as an anchor tenant to shape the dynamics of the city have also had a profound impact.

⁷⁴Sarah Max. "Global Housing Boom." *CNN Money*, November 11, 2004.