Innovation capacity in the healthcare sector and historical anchors: examples from the UK, Switzerland and the US

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Innovation is an integral part of economic development in developed economies. In the post 2008 period, a key policy agenda is that of sustainable development, which calls for innovation in all aspects of value-chains. In this paper, we focus on innovation from the biotech – pharma perspective to see whether or not this will lead to a sustainable future for the regions where there are clusters of firms in this sector. We examine data from a recently completed European Union study of innovation in the Healthcare sector from the UK and Switzerland, countries with an historical base in pharma, to understand how innovation pathways vary at the regional level in the broader life sciences, which incorporate biotech and more. Innovation in the healthcare sector in two regions, Oxfordshire in the UK and Zurich in Switzerland are compared. We contextualize our discussion by drawing on studies that focus on the sector in the United States, specifically Boston. The analytical framework comprises three elements: innovation systems and national and regional economic development theories are the first two, followed by approaches which consider organizational or institutional activity. This framework is used to help explain and understand the complexity of how innovation is organized at the sub-national level. The overall context is that it is increasing becoming a condition for government financing of research that it has more immediate application in industry or have the possibility of commercialisation (e.g., translational research).

Key words

Biotech, innovation, regional development, Oxfordshire, Zurich, Boston

JEL Codes 033 038 R58

1. Introduction

Although innovation is an integral part of economic development in the developed economies of Western Europe and the United States, competitive pressures are now felt from all around the world, especially the East Asian nations, Brazil, India, and Russia. Both the US and the UK went through industrial restructuring in the 1980s, IT revolution in the 1990s, and the biotech craze in the 2000s. In the post 2008 economic downturn, the focus is on sustainable development, which calls for further innovation in all aspects of value-chains. In this paper, we focus on innovation capacity at the regional level from the life sciences sector, which incorporates the biotech/healthcare sector (broadly defined). The goal is to use a series of innovation indicators in specific regions in order to explore cross-national diversity identifying where regions are stronger and weaker in their capacities for sustaining innovation and competitiveness. These indicators include institutional factors, political, legal and cultural; as well as specific advantages for entrepreneurial activities of public research institutes in the case of the biotech/healthcare sector.

Here the indicators are used to examine innovation capacity in Oxfordshire in the UK and Zurich in Switzerland - both locations are places which have strong historical bases in the biomedical research. From this evidence, we argue that not all countries or regions will converge in terms of future innovation paths and outcomes. We contextualize our discussion by drawing on studies that focus on the sector in the United States, specifically Boston, which is one of the three places in the US that are at the forefront of innovation in bio-pharma (Breznitz and Anderson 2006). Boston is far in advance of either Oxfordshire or Zurich.

Several theories inform the interpretation of the data. The analytical framework comprises three elements: innovation systems and national and regional economic development theories are the first two, followed by approaches which consider organizational or institutional activity. A key theoretical theme is that of historical anchor organizations (Feldman 2003). Anchors in this context include major research and industrial organizations, such as universities, hospitals, and big pharmaceutical companies. Their prominence in certain locations relates to the prestige of top universities and their ability to attract the best people as well as research income from public, private and charitable bodies. In the case of the big pharma, factors relating to the reasons why they were established in certain places and why they stay there (national and local factors) are considered. Conceptually, the paper explores how the development of regional specializations in the healthcare sector is associated with historical anchors and how and why they might be linked to sustainable innovation pathways in the future.

This framework is used to help explain and understand the complexity of innovation processes, that is, convergence and divergence in innovation capacity. The overall context is an increasingly made a condition for government finance of research of having more immediate application in industry or possibilities of commercialization (e.g. translational research).

The data are drawn from a recently completed five country European project, HealthTIES (2010-2013)[1], the objective of which was to identify how regions differ

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[1] http://vrr.healthties.eu/ (accessed January 26 2015)

in their strengths and weaknesses in order to inform policy. Four regions were chosen on the basis that that they are four of the top bioscience & technology regions in Europe and combine clinical science with engineering science, businesses, regional authorities, and well-established Bioscience Parks (the others being Leiden-Delft, Netherlands, and Biocat in Spain). The fifth was a developing region in Hungary. The two regions here were chosen to illustrate the value of the methodology in two places with some similar attributes, and to show how innovations arise from geographic specificities of local investors, major research universities, existing companies and highly skilled labor markets.

We show that Zurich performs better on most indicators than Oxfordshire, having elements of both early and late stage biotech and pharmaceutical sector activity. However, a limitation of all of these kinds of study is that they are not able to demonstrate the effects of location with regard to the broader geographical context. For example, Oxfordshire is only one part of the Golden Triangle of Oxford, Cambridge and London universities which collectively have large scale research strengths. Zurich is a major centre of the country's biopharma industry and is not far away from Basel where the headquarters of three of the world's largest companies are located and might be seen as being in competition for resources and firms. We therefore argue that both cases highlight the complexity of speculating on future local growth trajectories in a particular sector in isolation from its broader geography.

2. Explaining the development of innovation capacity

Three geographic scales, the country, the region (locality) and the organization, are considered to understand where spillovers in the form of symbiotic relationships between local firms and other organizations (Agarwal et al. 2007) are found and utilized to create entrepreneurship and innovation. In innovation theory, national innovation systems provide the context – the regulatory system, funding for the science base, and the university sector. However, some countries have very strong regional systems such as Länder in Germany and regions in France that develop their own science policies (Perry and May 2007). Within those two are sectoral systems, which describe the sectoral specifics of non-linear paths from research to commercialization (value chain) within the local geographic context (micro geographies), which are sustained by the macro (country) and meso (region/state) but also sustain the macro and the meso through feedback loops for sustainable policy development. An example is the Massachusetts Biotechnology Council, MassBio[2], and its operations to connect organizations operating at various geographic scales. Within each location reside the specific organizations with variegated cultures of collaboration: firms, universities and industry specific coordination bodies. Within this context, we are interested in what guides institutions to stimulate entrepreneurial activity and commercialization based on their cross-national diversity. In other words, what is national, what is regional and what are the organizational characteristics that matter in understanding pathways of innovation in the broader healthcare sector?

2.1 National systems of innovation

The national context has one major element often overlooked, that is, wealth creation through industrial development in the 20th century. Then, pharmaceutical companies

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[2] http://www.massbio.org/ (accessed February 22nd 2015)

emerged in Europe and the United States. In the post World War II period, universities and institutes forged ahead with R&D in various science, technology, engineering and medical disciplines. These trends created centers of high technology and geographic clusters of high tech industries, which are well documented by Porter (1998), Feldman (2000, 2003) and others. Within these clusters, studies have shown that various trajectories have developed indicating that, even if the initial input is more or less the same, clusters or regions can take different paths, grow, die, remain closed or become open (see for example Asheim et al. 2006).

In the mid 20th century, the role of government emerged as Keynesian views received broader acceptance. This has continued with many ups and downs. Science and technology policy at various scales have created anchor institutions that lead to possibilities for innovation at the local level with far reaching impacts for collaboration and human development (e.g., National Institutes of Health (NIH) in the United States).

National innovation systems' (Freeman 1995, Lundvall 1988 & 1992, Nelson 1988 and 1993) analysis of inputs and outputs into an innovation system includes industries and firms (the central elements of the system) but also actors and organizations including the research base in science and technology as well as innovation/technology policy (Carlsson et al. 1999). The national innovation system essentially consists of three sectors: industry, universities, and the government, with each sector interacting with the other, while at the same time having an independent existence (Goto 2000) - the Triple Helix model describes these relationships in greater detail (Etzkowitz and Leydesdorff 1995).

Within national contexts, we can trace such institutions from the Fordist era, the information technology revolution, the biotech revolution to the current life sciences focus with a goal toward sustaining and improving health and human development. However, the specific difference between life sciences and other clusters is the specific requirements relating to the capital infrastructure, including lab facilities (e.g., wet labs), health and safety regulations, people with formal scientific qualifications and the realization that many innovations come directly out of university labs to patients/hospitals. Typically, a biological agent is discovered in a university lab and is patented. Then, a licensing agreement with a company is reached for commercialization (Breznitz and Anderson 2006).

The research base or universities are central players in national systems of innovation, having broadened their scope to be noted for their societal role of creating wealth through making the applications of their research accessible for commercialization (Etkzowitz 1983, Shane 2004, Clarysse et al. 2011). Switzerland and the UK are renowned for their strengths in the pharmaceutical sector as well as their science base in biomedical science and now also for their national biotech chain[3].

The US national innovation system (Atkinson 2014) includes the business environment, the regulatory environment and the innovation policy environment. In the business environment, key factors are managerial talent, adoption of ICT across the value chain in most industries and venture capital. Atkinson finds that the US is

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[3] http://www.swissbiotech.org/Php5/aa2/UserFiles/File/pdf/swissbiotechreport/SBR_2014.pdf accessed November 26 2014)

the world leader in all three. While most venture capital placements are concentrated in a few states e.g. California and Massachusetts, there is some venture funding in almost every state. There is also a robust business angel system in the US. However, Atkinson finds that, although university is supported through a number of agencies such as the Department of Defense and the NIH, university research income has fallen behind competitor countries. This is because of cuts at state and at Federal government levels. This decline in investment has potential consequences for the future of university research (Atkinson 2014).

National R&D spending is often attributed to cross-country differences in innovation and high technology productivity (Fagerberg et al. 2014). In Europe, the 2000 Lisbon strategy of setting a target of increasing member states' R&D investment to 3% was influenced by the observation that the US share of R&D to GDP is almost double the European level. However, the authors argue that social, institutional and economic factors need to be in place to absorb R&D investments. Moreover, Fagerberg et al. (2014) suggest that comparisons between European countries and the US are unrealistic and a better comparison would be between individual US states and European countries or between European nations. For example, Massachusetts invests nearly 4% of its GDP on R&D, which is the same as Sweden. It is also the case that different sectors have different levels of R&D intensity. Although R&D intensity is a commonly recognized indicator, the relationship between R&D intensity and innovation is not clear cut in biotechnology given the lag in translating research into commercializable products.

Indicators at national level seem to be important for small European countries. However, almost every country has a particular city or a region that has captured the value chain activities (from research to production), which is indicative of agglomeration economies or historic development of anchor institutions, policy, related infrastructures, and labour markets. Some dispersal is present, but the recent phenomenon of intense clustering cannot be ignored in places such as Zurich and Oxford. In each, as we will show later, they are underpinned by healthcare infrastructure, research systems and to varying extent the commercial components of the sectoral innovation system (big pharma, subsidiaries and biotech firms). In turn these regional characteristics define the localities' positions within national (and international) systems of innovation.

2.2 The regional level

In recent literature on high technology and biopharma, the focus has been on understanding what differentiates the high performing regions from the periphery or ordinary regions. The evolutionary economic geography literature discusses regional pathways (see for example Boschma and Frenken 2011). In this context, these pathways in translational research point to outputs that indicate what the innovation chain looks like in the broader healthcare sector, that is, the directions it is taking and the specialisations in research. They also raise the question of why some are more effective than others in translating into commercial products. Big pharma and its subsidiaries, biotech firms, universities of which parts of the innovation system are present in each region, are significant in determining pathways - or indicate how regions are differentiated in terms of resources, networks, outputs and so on.

Questions concerning national and regional factors that facilitate coordinating functions among various actors involved in the innovation process and create spillovers, are the basis of many studies in the field of innovation studies (Agrawal et al. 2007). A region's diffusion (or spillover) capacity works alongside its capability to absorb knowledge external and internal to the region (firms and research organisations), its level of skills, as well as its institutional quality (number and quality of knowledge institutions, R&D and innovation activities and networks) (Wintjes and Hollanders 2011). Developing and sustaining technologies may be affected by location, for example the size of the local market, activity of proximate actors, regional specialization that allows for economies of scale, and technological capabilities (Fagerberg et al. 2014). Technology spillovers in which universities are active participants in various ways as the case in the Boston area biotech sector are another type of context (Breznitz and Anderson 2006). Autant-Bernard et al. (2006) found that high levels of scientific activity within a region are necessary to sustain a continuous flow of new business creation in the biotech sector

Typically, such clusters have vertical (customers and suppliers) and horizontal (producers of complementary products and specialist infrastructure) dimensions. Depending upon their sophistication, they might include other public and private institutions as well as trade associations and regulatory agencies that provide specialized training, information and technical support (Tracey et al. 2004). How regional trends, trajectories or pathways are developed varies with the local context (Lawton Smith and Bagchi-Sen 2010, Casper 2013). A factor in this variety is the role of local stakeholders (e.g., entrepreneurs, intermediaries) who have been argued to be key in the creation of networks which build capacity and sustain regional economic development (Feldman 2014).

The regional systems of innovation (RIS) concept (Cooke et al. 1992, 1998) captures the importance of location-specific inputs, system elements and outcomes in geographies of innovation. However, it neither focuses on technology nor on sectors but on the growth trajectories of regions taking into account broader industrial/sectoral, institutional and research contexts. A RIS consists of “interacting knowledge generation and exploitation subsystems linked to global, national and other regional systems” that may stretch across several sectors in the regional economy (Asheim and Coenen 2005, 1174). Regional government and innovation infrastructure are main agents of a RIS - the geographical dimension is the element of distinctiveness. Important elements are the spillovers associated with clustering effects. The indicators – specialized labor markets, clustering of firms in the supply chain giving rise to knowledge spillovers, infrastructure – show that the whole is greater than the sum of parts (Spencer 2013). Context conditions include resources of the area before building of a cluster or a pathway – local scientific and technological resources in academia and industry, industry specificities, specific composition of local firms in the sector, their origins and linkages, specifically presence of large global firms, infrastructure, existing partnerships and institutions facilitating cooperation (Weil et al. 2010).

A main characteristic of the regional geography of the broader healthcare sector is the clustering of biotech firms around the research universities with large engineering and medical schools. The RIS approach takes into account a much wider set of knowledge transfer mechanisms which account for this clustering. These include contract research, formal R&D co-operations and forms of knowledge transmission that are indirect such as knowledge spillovers (through the provision of graduates to the local labour market), and informal contacts with firms.

Capabilities of institutions are seen as a bundle of knowledge. Both firm and university level capabilities can include patents, while university equivalents of business R&D and financing of innovation (Fagerberg et al. 2014) could be research income and expenditure. On their three indicators of technological capability (patents, business R&D and venture capital) Massachusetts topped the rankings (2008) with Switzerland 10th, with only Sweden above it in the top 10 rankings, the others being US states. This ranking shows that on average technological capability is higher on average at state level in the US when compared to whole countries in Europe. Fagerberg et al. also examined social capabilities – social, institutional dynamics and political characteristics. They found that when these are taken into consideration in the form of knowledge infrastructure indicators of the science system (scientific publishing), university R&D expenditures, government R&D expenditures and tertiary education, the US led except in the area of university R&D, whereas government R&D was much higher. Overall, the knowledge infrastructure benefitted high-tech regions in the US disproportionately. However, Fagerberg et al. (2014) concluded that most European countries, particularly the top performers, are just as

2.3 The organizational level

The effects of anchor institutions including firms and universities in local development have been found to be stronger when they are located in close proximity with enterprising firms and other stakeholders such as firms providing professional services and local public policy organizations. The theory of the Anchor Firm originally applied to the development of shopping malls. Since then it has been applied to a both low and high tech sectors shopping malls (Konishi and Sandfort, 2003), R&D intensive firms (Agrawal & Cockburn, 2003), the aircraft industry (Niosi and Zhegu, 2010) and the biotech industry (Feldman, 2003). Existing firms can serve as anchors that attract skilled labor pools, specialized intermediate industries and provide knowledge spillovers that benefit new technology intensive firms in the region. This can positively affect firm survival and growth and subsequently the viability of the regional clusters (Feldman, 2003).

The presence of large global firms within a local economy under some circumstances can act as catalysts for innovation, labor force development and trade (Spencer 2013, see also Markusen 1996). An anchor, in the form of a large, established firm therefore may create externalities that benefit agglomerations. These can create local advantages such as pools of skilled labor and demand for specialized products, which may benefit smaller start-up firms (Feldman, 2003). They can produce positive agglomeration effects on a region by spinning off new local innovative firms and by attracting other innovative firms to the region (Niosi and Zhegu, 2010). FRIDA (2014) also concluded that anchor firms and the networks they create constitute ‘key drivers’ of the European Union’s 2020 growth strategy. The anchor firms have the capacity to upgrade local economies and thereby contribute to a more dynamic economy in Europe overall.[4]

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[4] http://www.scoopproject.org.uk/1frida-anchor-firms-contribute-to-regional-development.aspx (accessed December 29 2014)

Feldman (2003) considered the locational dynamics of the US biotech industry in relation to the anchor firm hypothesis. For the US biotech industry, the geographic location of the industry appears to be anchored by some large institutions, related firms and successful early entrants to the industry. More generally, regional anchors may encompass other institutions such as universities, government labs, research institutes and other entities (Feldman, 2003). What is important is the extent to which they work with other parts of the value chain to enable their locations to function as places of high efficiency in the creation, transfer and application of knowledge (Breznitz and Anderson 2006).

More recently, Spencer (2013) set out to test whether proximity delivers superior advantages for smaller businesses and entrepreneurial activity in four sectors in Canada, including bio-pharma. This sector in Canada, as in the US, is mainly clustered in large urban areas, with educated populations and top-rate research institutions, and relies less on material inputs and more on knowledge for competitiveness. He found, however, that there was not enough strong evidence to suggest that close proximity to anchor firms made a significant difference to firm performance. This finding is relevant to the regions in this study.

This finding provides further justification for study of how the presence of a university as an anchor institution in a locality affects the behavior of its academics and the potential for fostering network activities in the broader healthcare sector, which includes bio-pharma. While this implies that such networks occur spontaneously, often the process of making networks requires facilitation. A facilitating process can include academic engagement - which represents an important way by which academic knowledge is transferred – or translated – into the industrial domain (Perkmann et al. 2014). These authors that show the forms that it takes is related to the characteristics of individuals as well as the organizational and institutional contexts in which they work. The motives and outcomes for university and industry interactions in the UK are also examined by Ankrah et al. (2013). They found a match of motives and beneficial outcomes for university and industry actors, in spite of differing work environments. Thus government funding for collaboration was justified by the benefits to individual organisations (rather than societal benefits).

However, organizational behavior and academic links with industry vary by academic experience and by place (Jong 2008, 2012 & Jong and Slavova 2014). Jong (2008) finds differences in the behavior of therapeutic biotech firms in Cambridge and Munich that have relied on their institutional environments differently to develop their capabilities. Differences include for example in accessing investment finance (public funding is present in Munich but not in Cambridge), finding CEOs – Cambridge but not Munich firms recruited mostly from the national pharmaceutical industry, and in networking - Cambridge firms less likely to be part of academic knowledge networks in their local region than those in Munich, and are less likely to publish with academics. Later, Jong and Slavova (2014) found that a firm's involvement in academic communities enhances its innovation performance, and that co-publishing and collaboration positively affects firm innovation. Therefore it can be concluded from both Perkmann et al. (2013), and Jong and Slavona (2014) that there are gains to both firms and academia in 'open science' activities but that organizational and institutional characteristics have been found to have an effect on the extent and nature of universities as anchor institutions in particular places.

The section below presents the description of the data used to compare the two example regions: Oxfordshire and Zurich. First, the data source is described. Second, each of the two regions are characterized based on a discussion of their national and regional system of innovation as well as specific local characteristics. Third, regional comparisons of inputs, innovation system/structure, and outputs are presented for the broader life sciences. Fourth, these two regions are set against one of the leaders in bio-pharma innovation – Boston. A discussion of the regional characteristics of Boston is followed by a comparison of the three regions across several areas of specialization in life sciences to show possibilities for collaboration or lack thereof.

3. Methodology, Data, and Findings

3.1 Methodology and Data

One of the key problems in comparing regions is the availability of comparable data as reliable indicators of a particular phenomenon. In this study, the Innovation Indicators illustrating the three regions are based on those developed by the Healthcare, Technology, Innovation and Economic Success (HealthTIES) project. This was an EU FP7 funded study (2010-2013) which aimed to identify key elements in the functioning of healthcare technology innovation systems with a view to speeding up these systems. The project included bioscience regions in four core countries centred around the following cities: Leiden, Rotterdam and Delft (Medical Delta; Netherlands), Oxford, (UK), Barcelona (Spain) and Zurich (Switzerland) along with an emerging region in Eastern Hungary, Debrecen.

The Innovation Indicators were specific to the disciplines of biotech, medtech, life sciences and medical sciences. Data relevant to inputs, innovation system and outputs were collected on universities, research institutes, intermediate vocational education, care providers, public and private funding, industry, technology transfer and science parks. Additionally, publications and citations (combined in the h-index; Hirsch, 2005) were used to describe the disease and technology platform indicators (data for Boston were collected for disease and technology platforms out of interest as a comparator as Boston was not included in the HealthTIES project). These data were quantitative, discriminatory and primarily in the public domain. A further intention of developing the indicators was their application to similar clusters in other countries so that comparisons could be made using a variety of statistical and graphical techniques[5]. The data presented here were primarily collected for 2010: other time periods are indicated in the tables. We include the data for the three stages of the innovation cycle (Tables 1-3) and h-indices for diseases and technology platforms (Table 4).

3.2 Regional Contexts

3.2.1 Oxfordshire/UK

Oxfordshire's population is approximately 2.7 million. It is the leading component of the South East of England research, educational, health and life science cluster (population 8.3 million), that continues to be the fastest growing region in the UK. Oxfordshire is one of the UK's leading clusters. The others are Cambridgeshire in

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[5] Data are available at http://vrr.healthties.eu/(accessed June 3 2013)

East Anglia, London and Eastern/central Scotland (Edinburgh, Dundee). Its path of development has been influenced by national policy which reinforces clustering in a few regions which have hospitals as well as leading universities and a biotech infrastructure. This effectively means that Oxfordshire (along with London, Cambridge and Central Scotland) will continue to be leading biomedical regions (Minshall and Wicksteed 2005).

According to the UK BioIndustry Association, the UK's strength in life sciences lies in it having "4 of the top 10 universities in the world, 19 of the top 100 universities, a stable of quality service providers, world class charitable supporters of the industry and a rich heritage of globally recognized medical research"[6]. The pharmaceutical industry has a long history in the UK dating back to the 1840s. Major UK pharmaceutical companies now include GlaxoSmithKline and AstraZeneca, and smaller ones such Kent Pharmaceuticals. Consolidation in the form of mergers and acquisitions has reduced the number of big pharma and biotech companies. For example Celltech was bought out by the Belgian firm UCB in 2004. In 2011, the government launched its strategy for UK Life Sciences designed to support companies through every stage of the product life cycle. This is of interest because it highlighted weaknesses in the UK healthcare innovation cycle for R&D funding for translational activities or the "translational funding gap"[7]. A more recent report (HM Government 2014)[8] identified two particular measures to support the industry. The

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[6] http://www.bioindustry.org/home/ (accessed November 26 2014)

[7] https://www.gov.uk/government/organisations/office-for-life-sciences (accessed June 7 2014)

[8] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/427769/BIS-15-224-BIS-strength-opp-2014.pdf (accessed July 14 2015)

first is the Accelerated Access Review into Innovative Medicines and Medical Technology for which work has begun on mapping the UK landscape and international benchmarking. The second is the creation of "test beds" for the assessment and adoption of 21st Century life science innovation in the real time patient population as set out in the NHS's five year forward view. These sit alongside improving the business environment in order to attract life sciences companies to set up and expand in the UK.

It has been estimated that £1.2bn has been invested in the Oxford biotech sector in the period between 2010 and 2013. Hence Oxfordshire is a growing focal point of the UK national innovation system (Lundvall 1992, Nelson 1992) in biomedical research, and as we show below, of a local, national and international sectoral system of innovation, comprising firms and a rapidly growing and important sector specific network (Romeo and Lawton Smith 2014).

Oxfordshire's place–specific trajectory in biotech/healthcare lies in the dominance of University of Oxford, one of the top five of universities in the world. During the first part of the 2000s, continuous long term government investment supported university and biotech research centers making the University of Oxford one of the largest biotech environments in Europe with more than 2500 members of staff and 800 postgraduate students in medical sciences, pharmaceutical studies and biotechnology degrees (Lawton Smith, 2014). This key component of the system (national but working sectorally at the local level, Carlsson et al. 1999) has promoted a world leading cluster of biotech research and biotech firms (as in the US and Canada, Spencer 2013).

The research base has undergone institutional change due to the search for greater efficiency and effectiveness in translational research. For example, the partnership between the University of Oxford and its clinical partners in the form of the NIHR Oxford Biomedical Research Centre (BRC) focuses upon 14 research themes, incorporating 11 disease themes and 3 cross-cutting themes providing technology and innovation platforms and infrastructure with broad application across the clinical themes (clinical imaging, molecular genetics including high throughput sequencing and bioengineering). At the regional level, the Thames Valley Comprehensive Local Research Network (TVCLRN) brings together 6 universities and 15 NHS organizations and provides support for the dissemination of clinical trials and other well designed studies in all areas of disease and clinical need. A major theme is translational research involving the rapid early-stage development and assessment of new vaccines in clinical trials, including new influenza strains.

During the period 2000-2009, the cluster became a recognized worldwide biotech hub, comprising over 200 mostly small local firms. Although Oxford University, since 1997 Isis Innovation, Oxford University's technology transfer company, has incubated several biotech companies in Oxfordshire, other biotech companies started in Oxfordshire were independent of the university (Lawton Smith 2005, Lawton Smith et al. 2008). A number of local firms have been acquired by international companies such as Novartis (Switzerland) and Siemens (Germany). In the case of the former, the Oxfordshire operations were largely closed down. In the case of the latter, in 2003 Siemens acquired the 49% remaining shares in a company making magnets for medical technologies (OMT). This formerly local company, is still to some extent an anchor firm (Feldman 2003), being a world centre for design and R&D in magnet technology.

The Life Science group accounts for 56% of all companies. The Medical Technology group accounts for the remaining 44%. Looking at the evolution of these two groups over time in terms of company formation, it is also noteworthy that the Life Science group, initially the largest one, has become progressively less dominant. This also indicates how the characteristics or attributes of the system are changing (Carlsson et al. 1999). However, the industry mix does not include either the research or production activities of big pharma anchor firms – which are represented to a greater extent in Cambridgeshire. For example in 2013, AstraZeneca announced the move of its headquarters from London to Cambridge[9].

In spite of the strong focus on R&D, the region lacks capabilities in commercialization as indicated by the much smaller number of biotech companies than in Zurich. This shows that the basic conditions in Oxfordshire are very different from Zurich. While Oxford University dominates and its translational trajectory is predicated on its very strong science base, the institutional support system is limited. Moreover, the lack of large R&D intensive firms in the life sciences sector is particularly distinctive of how the overall biomedical sectoral system of innovation (Malerba 2002) functions in this location. However, at the sectoral level, a bioscience network, OBN, a membership organization – has grown as the sector as expanded. OBN is the main body which coordinates industry actors (firms, professional service

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[9] http://www.telegraph.co.uk/finance/newsbysector/industry/9966414/Cambridge-home-of-Britains-biotech-boom-offers-relief-to-UK-economic-ills.html (accessed January 26 2015).

providers and so on) supporting and bringing together the UK's emerging life sciences companies, corporate partners and investors[10]. Although there are elements of cluster activity relating to the knowledge base, there is therefore evidence of incomplete knowledge chains and infrastructure which are more developed in Zurich and Massachusetts (below). What is also missing is an integrated regional innovation system that brings together other local actors such as the county's local authorities and the universities in which there is collective leverage to bring about greater levels of investment across the board (Asheim and Coenen 2005).

3.2.2 Zurich/Switzerland

Switzerland is the most competitive business location in the world according to the 'Global Competitiveness Report 2013'. Switzerland even more than the UK is renowned for its strengths in the pharmaceutical sector as well as its science base in biomedical science and its developing national biotech chain.

However, the chemical and pharmaceutical sector has a very small Swiss domestic market: Europe (35%), America (40 %) and Asia (23 %) account for the majority of the sales destinations[11]. Rather different to other countries, 90 % of the Swiss chemical industry's overall product portfolio are specialties and cover some seven main areas including Pharmaceuticals and diagnostics (56% of product markets). This is a considerable proportion compared to international averages. Since 1990, the pharmaceutical sector has increased its exports by a factor of seven (in terms of

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[10] http://www.obn.org.uk/ (accessed January 21 2015)

[11] http://www.en.scienceindustries.ch/_file/9257/branchenportrait-e.pdf (accessed January 26 2015)

value), and it now contributes more than 30% of Switzerland's total exports[12]. Major companies with R&D and manufacturing operations include Roche, Novartis, Pfizer and Merck Serono. The chemical and pharmaceutical industry is composed of companies of different size. In addition to the well-known large companies, the sector consists of around 1000 smaller and medium-sized enterprises, geographically spread over the whole of Switzerland, though with a concentration in the north-western region. 95% of all companies in Switzerland employ less than 250 persons; only around a dozen companies have a workforce of more than 1000.

The main features of the area are its anchor institutions (universities, R&D centers and major firms), and more recently a system of coordination - Life Science Zurich (LSZ). Zurich hosts more than 90 internationally well-positioned R&D institutes and 26 clinics and has about 1.3 million people. ETHZ, University of Zurich has the highest university ranking in continental Europe. Zurich University of Applied Sciences, life science division is placed within the top 20 globally. The University Hospital of Zurich (USZ) is the most important of about 25 major hospitals in the Canton of Zurich, and the Paul Scherrer Institute (PSI) has a third-generation synchrotron light source facility for research in materials science, biology and chemistry.

There are some 4800 healthcare companies in the Canton. In addition, most universities have their own internal incubation programs, allowing young companies to develop business ideas whilst using the scientific infrastructure in the initial stages

[12] http://www.interpharma.ch/sites/default/files/polynomics-2011_bedeutung-der-pharmaindustrie-fuer-die-schweiz_e.pdf (accessed January 26 2015)

and finally to profit from supportive technology transfer circumstances. Life sciences, especially the pharmaceutical industry in Switzerland, play an important role in this development. LSZ is a virtual region with a small physical co-ordination base. It was established in 2001 by University of Zurich and the Federal Institute of Technology Zurich (ETHZ). It aims to establish co-operation networks bringing together academia, industry and the public sector, and support science education. Approximately 80 % of the cluster activities are related to human health. It is the headquarters of the anchor firm Pfizer AG and is the location of the Roche Innovation Center Zurich, which has a multinational team of some 140 employees – 95% of whom are research scientists[13].

3.3 Comparative Inputs, Infrastructure, and Outputs in Oxfordshire and Zurich

Generally the data show a snapshots of each location at 2010, or periods leading up to 2010. Without repeated measures, we cannot infer how stable, typical on average, or dynamic any of the regions are for any of the indicators, but the results are directly comparable, detailed and objective. Knowledge and research funding patterns (see Table 1) show that for professors with an h-index equal to or greater than 30, the Oxford (238) and Zurich (231) numbers are comparable. In contrast, in the total number of publications in high impact journals (2001-2010), Oxford significantly exceeds Zurich (2264 versus 1190). This reflects Oxford's position in the world rankings of Universities for the Life Sciences compared with Zurich (Oxford: 4th against ETHZ: 14th and UoZ: 44th. However, Harvard and MIT – both Boston

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[13] http://www.roche.ch/en/standorte/schlieren.htm (accessed January 26 2015)

addresses - are ranked 1st and 2nd[14]). However, Oxford's ranking in high impact journals is based on a lower level of research funding whereas the total value of Zurich exceeds Oxford (1042 over 632 mio Euro). The pressure on UK academics is extremely high due to public sources of funding based on periodic national assessments of UK Higher Institutions' research in which publication in top journals is a key component (Research Excellence Framework, 2014)[15] which is not as clearly present in Switzerland. Therefore, in principle, both have the high levels of scientific activity necessary to sustain flows of new business activities (Autant-Bernard et al. 2006), even though outcomes are different (see below).

Table 1 here

With respect to human capital in the life sciences, Zurich exceeds the total number for Oxford in graduate students, particularly for international students. This may just reflect the capacity of support in Zurich. Moreover, in terms of senior ERC grants, Zurich is a long way ahead of Oxford while the amount of grants for junior scientists is comparable. This shows that early career support is competitive in Oxford. This demonstrates a difference in spillover capacity in relation to the quantity (supply) and characteristics of the skill base (Agrawal et al. 2007, Spencer 2013, Feldman 2014) in the two locations.

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[14] http://www.timeshighereducation.co.uk/world-university-rankings/2014-15/subject-ranking/subject/life-sciences) (accessed February 22 2015)

[15] http://www.ref.ac.uk/ (accessed July 28 2015)

In terms of healthcare infrastructure, the data show that Oxford has the lead in clinical trials, but the areas available for research in universities and research beds in hospitals are larger in Zurich, whereas Oxford has a more general facility. Indictors of innovation systems, patents, spinoffs, private projects and TTO are shown in Table 2. The overall science park space and personnel support is greater in Oxford, reflecting the presence of the Oxford Science Park in Oxford, Oxford University's own science park at Begbroke and two major sites to the south of the county at Milton Park (privately owned) and the Harwell Science and Innovation Campus, located on part of what was United Kingdom Atomic Energy land. With respect to technology transfer personnel, Oxford leads Zurich. However, patent and spin off numbers are not drastically different with Oxford having a slight lead. More tellingly Zurich has the lead in public-private collaboration indicating that there is a more effective knowledge diffusion process through interaction with industry (Agrawal et al. 2007).

Table 2 here

Consistent with the input data in Table 1, the picture on output shows that Oxford is ahead at the exploration phase while Zurich is ahead in the exploitation phase (see Table 3). Zurich has more biotech companies and products on the market while Oxford leads in clinical trials, discovery phase products, investments especially series A investments etc. Oxford fits our understanding (see Cooke 2001) of a place/institution with early phase focus while Zurich fits the late phase focus. Zurich has the advantage of having the knowledge to take products to market and it is not far behind in discovery phase numbers, patents etc. Zurich has better opportunities for benefitting from more industrial engagement leading to innovation within its system.

Table 3 here

Zurich also benefits from its relatively close proximity to Basel (c50 miles) – home of some of the largest big pharma companies in the world. Oxford and the Thames Valley do not have a pharma cluster with headquarter and R&D centers nearby. This performance of Oxfordshire's commercialization activity reflects national problems. In 2007, the UK was ranked as the fifth or sixth nation in the worldwide pharmaceutical market. By 2013 it had fallen to 10th position. Moreover, the share of the market attributable to products launched in the previous five years is lower than most comparable countries[16] (interestingly Switzerland does not appear in the top ten). Therefore, Oxfordshire's research base necessarily has to collaborate with institutions outside of the region, especially the United States, by keeping historic ties that have been built up over the 20th century in terms of mutual foreign direct investment (Dicken, 2015).

3.4 Comparison with US/Boston/Massachusetts

By way of contrast, we consider the scale and scope of activities in Boston which is the world's leading biotech cluster, one which is tightly clustered (Breznitz and Anderson 2006), and has a mix of types of firms. It is also one that has strong anchors (universities and big firms), attracts major amounts of money from public and

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[16] http://www.abpi.org.uk/industry-info/knowledge-hub/global-industry/Pages/industry-market-.aspx (accessed February 26 2015).

private sector organisations, has a very highly skilled labour force, and has developed a very strong infrastructural support system.

The biotech cluster grew rapidly in the 1990s. By 2002 there were 275 biotech firms employing over 26,000. The dominant type of biotechnology activity is medical sciences, particularly human therapeutics (Breznitz and Anderson 2006). By 2011, there were are more than 550 biotech and pharma companies located in Massachusetts (MassBio, 2011); 284 of these companies are drug development companies *(Evaluate Pharma, 2014).* As of July 2014, there were 1,384 drugs in development by then in Massachusetts, from research project to pending approval stage. These figures do not include the substantial number of drugs being developed in Massachusetts by companies with headquarters outside of the state.[17] In 2013 there were 57,642 biopharma employees in Massachusetts (2013) and the companies employing those workers are responsible for over $7.2 million of in-state payroll. The Massachusetts biopharma industry grew by 41% between 2004 and 2013.

The Boston area has a number of key anchor institutions. For example, the Massachusetts General Hospital is the oldest in the US. In conjunction with Harvard University it operates a major research facility and medical school. In the area are also a number of hospitals including some of the nation's leaders in cancer (Dana Farber), arthritis (Brigham and Women's), cardiology (Lahey Clinic) and pediatrics (Children's Hospital). Boston University and Tufts also have medical schools in the Metropolitan area and there is a substantial industry in medical equipment in Eastern

[17] http://www.massbio.org/economic_development/the_massachusetts_supercluster (accessed January 21 2015)

Massachusetts (Breznitz and Anderson 2006). Massachusetts has 122 colleges and universities - over 40 of which offer advanced degrees in the life sciences, the top five National Institutes of Health-funded hospitals in the nation, and the highest educated workforce in the US.

Funding for the sector in the state and Boston area from the national public sector is massive and underpins scientific and translational research. Massachusetts received $2.3 billion in National Institutes of Health funding for basic research in Fiscal Year 2013. Massachusetts researchers receive over 11% of all NIH research funds. On a per capita basis, Massachusetts receives over twice as much NIH funding (FY 2012) as the next closest state. Massachusetts biotechnology companies received $984 million in Venture Capital financings in 2013. Massachusetts biotech companies received 21% of all US venture capital for biotech in 2013. It ranks 1st in the nation in percentage of residents with a bachelors degree or higher. Its elementary and secondary students outperform the rest of the nation in national assessments.

The mix of firms is important (Malerba 2002). There are a growing number of manufacturing assets in Massachusetts because of a workforce highly skilled in biologics process development. In addition to a number of contract manufacturers, Massachusetts is also home to commercial manufacturing for Genzyme, Biogen-Idec, AbbVie, Shire, and Pfizer. This makes it different to other bio-pharma clusters in North America (Spencer 2013) because it includes material inputs and outputs. Hence, as more of the innovation value chain is located in state, the potential for a greater range of spillovers is increased (Agarwal et al. 2007).

Breznitz and Anderson (2006) in a survey of why biotech firms cluster in the Cambridge Massachusetts area found that the pool of skilled labor was the most important factor, followed by access to university labs (many of the founders came from university labs). The former is linked to the universities which supply qualified people. Access to hospitals was much lower. However, as in other surveys e.g. Mckelvey et al. (2003) found that in Sweden, firms did not rate access to other firms as important, nor the availability of venture capital. A study of the sector in Oxfordshire (Lawton Smith and Bagchi-Sen 2012) found that while the industry respondents did not rank the presence of universities as their top locational factor, they emphasized the presence of talent in science and technology as critically important to their operation. Local talent, appears therefore to be the primary locational attribute in this sector, enabling firms to get the job done (see also McKelvey 2004, Gertler and Levitte 2005). Thus what appears to be important from the literature – the mix of firms, universities labor markets need the addition of but not yet present – are systems of coordination.

Table 4 about here

There are two technology platforms where Oxford and Zurich show relative strengths i.e. research based on synchrotrons and microscopy. All three appear to be developing newer technology platforms to a similar extent – those of genomics, proteomics and imaging. Interestingly the disease platforms show similar patterns of past and present research/investment cancer greater than cardiovascular disease which is greater than immunology and infectious diseases which in turn is greater than neurodegenerative diseases. There is likely to be vastly increased research/investment into neurodegenerative diseases (e.g. dementia) with global population ageing.

The h-index is a convenient way of combining publications and citations. However there is a temporal influence such that older publications have been exposed longer for potential citations. As these findings are based on h-indices, it is not surprising that Boston shows higher results generally, but particularly where it reflects research investment in cardiovascular disease and cancer together with their associated clinical trials and life science related structural research. Oxford follows this pattern to a lesser extent compared with Boston, but to a greater extent than Zurich. The exceptions to Boston's dominance are microscopy and research using a synchrotron where both European regions have greater access to these or one is available locally. Oxford and Zurich are similar for the most part on other measures. However, Zurich leads both Oxford and Boston in medicinal chemistry, which is typically low as this is likely dominated by pharmaceutical companies, of which there are many in Switzerland, rather than being based on university research.

4. Conclusions

This study considers two exemplar regions Oxfordshire and Zurich to illustrate similarities and differences in inputs, infrastructure and outputs. These depict innovation capacity in the broader life sciences which includes academics, industry, as well healthcare and/or clinical facilities. In addition, the study contrasts these two regions with one of the leaders in this broad sector, Boston/Cambridge Massachusetts. It has taken three geographical scales - national, regional and organizational - to reflect on what makes them unique and therefore how they differ in their development to others with some similarities in research and industry characteristics.

The results show each location's position as leaders in their national as well as international systems of innovation. Oxford excels in terms of inputs (e.g., science base). In particular, at the organizational level, Oxford has academic excellence as indicated by the very high level of publications in leading journals. This in part is related to the necessity of Oxford University's academics maintaining its leading world rankings thus enabling it to attract the best staff and students as well as research income.

However, at the regional level, Oxford's performance as a diffuser of innovation through the formation and growth of spin-off firms (Agrawal et al. 2007) appears to be focused on generating startups/small companies that are later bought out by bigger players thus removing the potential for the growth of anchor firms (Feldman 2003, Spencer 2013). Oxford University does not appear to be an anchor institution other than in research (see Autant-Bernard et al. 2006), and therefore is not as a leader of innovation, and its contribution to regional innovation capacity is limited except in specific respects. Here Oxford is similar to Boston as it follows the same pattern of focus on cardiovascular disease, cancer and clinical trials but to a lesser extent. Moreover, there is a smaller pool of graduates in the healthcare disciplines than in Zurich which also limits feed into translational research.

However, parts of an innovation support system are in place – such as the space on science and business parks, while the lack of a bioincubator is being addressed.

However, some of the more structural problems include an absence of R&D intensive big pharma anchor firms (Agrawal and Cockburn 2003) and the kind of public sector support which is needed for a RIS (Cooke 1992 & 1998, Asheim and Coenen 2005) which is present in Massachusetts.

Zurich and Switzerland which has a generally healthier population, appears to have better funding than Oxford generally and possibly its academics have less pressure to publish in top journals. Zurich appears to have greater innovation capacity being better at growing companies than Oxfordshire and also benefits from of the presence of big pharma (see Feldman 2003, Spencer 2013). With respect to diffusion of innovation (Agrawal et al. 2007), Zurich is similar to Boston as it appears to invest comparatively more in technologies.

There is evidence here, therefore, to support Jong (2008) and Jong and Slavova (2014) that organizational behavior and academics' links with industry vary by academic experience and by place. In Oxfordshire and Zurich, this is also related to varying levels of research funding and supply of graduates. This is reflected in Oxfordshire's position in the national sectoral system of innovation (Malerba 2002, 2005) as being at the exploration stage compared to Zurich's greater capacity for innovation at the exploitation stage. That said, both regions have the base to become bigger and better in discovery, therapeutics, diagnostics, clinical research etc.

However, this does not make generalizations with respect to policy easy. Each region follows its own pathway in which individuals make their own choices about collaboration in the light of funding opportunities. Therefore in this complex industry, specific policies necessarily relate to what each cluster has done so far and what it could do in the future based on current assets.

Moreover, it is difficult to quantify micro-geographies, that is, the location of departments within a campus, the culture of collaboration in universities, the tradition and practice of reaching out to scientists in institutes and industry for furthering translational research, and finally, the tolerance of funding agencies to lag times and failures. While a field trip to Stanford, Berkeley, and MIT would show how various types of proximity can work, in other places, this is not as apparent. This lack of transparency may be the “unquantifiable” that cannot be captured and operationalized by one agent (e.g., policymaker) or by one firm.

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Tables Innovation pathways

Table 1: Innovation Indicators for Inputs in Oxford and Zurich

	Oxford	**Zurich**
Profs H-factor >30	238	231
Publications	2264	1190
Research spending/funding (mio Euro)	633	1042
International graduated MSc students	148	348
International PhD students	345	2762
National graduated MSc students	193	1212
National PhD students	805	2167
Junior ERC grants	16	17
Senior ERC grants	19	33
Research m2	98,249	315,000
Research hospital beds	4727	2258
Clinical trials	8	2

Source: HealthTIES

Table 2: Innovation Indicators for the Innovation System in Oxford and Zurich

	Oxford	**Zurich**
Spin-offs	36	33
Granted US patents	50	40
W.A.I.T. indicator (Oxford *estimated in chart)	n/a	140
Joint research projects	59	41
TTO FTEs	89	37.6
Governmental innovation support (Government procurement of advanced technology products) WEF GCR	3.8	4.4
Regional attractiveness, WEF GCR index	5.25	5.63
Science parks m2	312,528	88,700
Science parks FTEs	49	17.75

Source: HealthTIES

Table 3: Innovation Indicators for Outputs in Oxford and Zurich

	Oxford	Zurich
FTEs working in HT disciplines	13,563	34,440
Companies <20 FTEs	154	1,449
Companies >20 FTEs	46	262
Big trade sales	4	2
Products on market	122	282
Products phase I-III + NDA	66	43
Products in discovery phase	49	37
Medicines available in countries	n/a	37
Total investments (Mio Euro)	420.75	130.30
# investments	20	16
Average Series A investments (Mio Euro)	9.10	3.97

Source: HealthTIES

Table 4: Scientific indicators for disease and technology platforms

	Oxford	Zurich	Boston
Cardiovascular	102	58	229
Cancer	167	111	430
Neurodegeneration	52	38	88
Immunology and Infection	70	55	117
Proteomics	31	58	73
Genomics	45	35	77
Structure	130	127	280
Microscopy	114	126	111
Synchrotron	52	38	29
Imaging	58	52	112
Medicinal Chemistry	9	18	12
Clinical Trials	124	73	380
Drug Delivery	34	43	84
Drug Development	65	65	125

Source: HealthTIES