Developing Adaptive Capability:

The Case of Nottingham's Nascent Biotechnology Sector

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Abstract

A region's adaptive capability describes its ability to respond positively to changes and shocks that affect the regional economy over time and take advantage of new and emerging market opportunities from wherever they arise. Central to this idea is the manner in which historic economic strengths or capabilities can be turned to new purposes. This paper provides a case study that uses the concept of adaptive capability as a lens through which to explore the emergence of a notable bioscience based industrial cluster in a city region of the UK and the part that it played in helping to restructure the economic base of the city.

The local economy of Nottingham faced major structural changes in the late 1990s. These changes saw not only the demise of what had at one time been a key industrial sector, but also the departure of two of the city's three principal employers, and the closure of a major research facility owned by a third. The case explores the manner in which capabilities linked to this constellation of firms were redeployed in order to take advantage of new market opportunities. The case places particular emphasis on the contribution of firms, the restructuring of industry sectors and institutional changes that occurred at this time, to the city's adaptive capability. In the process the case study reveals a notable example of adaptation as the local economy moved away from a previous path of regional and sectoral development, towards a new and yet related trajectory. Central to this process was the purposive re-tasking of physical assets and the mobilization of knowledge assets that were the legacy of one of the city's historic industrial strengths.

The paper concludes with a brief consideration of the wider relevance and applicability of this model of bioscience based regional development.

Introduction

This paper has its origins in a series of research projects undertaken by researchers at Nottingham Business School centred on the development of the UK's largest and arguably most successful bioscience business incubator – BioCity Nottingham. Home to a large and growing concentration of biotechnology companies, the rise of BioCity Nottingham has come to symbolise Nottingham's economic reinvention as a 'knowledge economy' following years of de-industrialisation. From its roots deep in the manufacturing dominated local economy that spawned 'Saturday Night and Sunday Morning'[1], we chart the rise of exactly the kind of knowledge intensive industrial cluster that has been an object of desire for national, regional and local policy makers since the Millennium and before (Swords 2013). Interesting though the tale of BioCity's emergence is in its own right, the principal focus of this paper is on what this case can tell us about the continuing evolutions of Nottingham's economy and the implications that this may have for our understanding of regional economic path creation and adaptive capability more generally.

The local economy of Nottingham faced major structural changes in the late 1990s. These changes saw not only the demise of what had at one time been a key industrial sector (the manufacture of pharmaceuticals), but also the departure of two of the city's three principal employers, and the closure of a major research facility owned by a third. The case explores the manner in which capabilities linked to this constellation of firms were redeployed in order to take advantage of new market opportunities. The case places particular emphasis on the contribution of firms, the restructuring of industry sectors and institutional changes that occurred at this time, to the city's adaptive capability. In the process the case study reveals a notable example of adaptation as the local economy moved away from a previous path of regional and sectoral development, towards a new and yet related trajectory. Central to this process was the purposive re-tasking of physical assets and the mobilization of knowledge assets that were the legacy of one of the city's historic industrial strengths.

The paper concludes by considering the wider relevance and applicability of this model of bioscience based regional development in order to assess the feasibility of replicating the Nottingham model elsewhere. In so doing it endeavours to isolate those factors that are 'place specific' to the city from those that have wider applicability.

[1] Alan Sillitoe's 1958 classic tale of industrial life in Nottingham.

Selective literature review

Recent years have seen growing interest in evolutionary accounts of regional and local economic development – often associated with the New Economic Geography or the 'evolutionary turn in economic geography' (see for example Boschma 2004, Martin & Sunley 2006). Central to these perspectives on economic development are the related concepts of path dependency, lock-in and adaptive capability.

Path dependency is a term that finds application in both economic geography and institutional perspectives in political science. It highlights the manner in which a region's future development trajectory is, to an extent, constrained by history. In other words, the range of possible future paths of development are constrained by the products of social and economic history: accumulations of capital (human and physical), concentrations of expertise, productive infrastructure, institutional architecture etc. This is not to suggest that there is no role for human agency, but that the room for manoeuvre enjoyed by actors in the present is constrained by the products of history and the resources that represent a legacy of this development path.

Closely associated with the concept of path dependency is the idea of lock-in – the manner in which a locality or region gets trapped on a path of relative or absolute decline. Often this is associated with the demise of a key local industry. Prior to the Millennium, Nottingham bore all the hallmarks of a city region trapped on just such a trajectory. Martin and Sunley (2006) identify three forms of lock-in: technological, dynamic institutional returns and institutional hysteresis. They also identify the importance of place specific factors:

"place dependence is an important dimension of path dependence. This implies that forms of co-evolution in which there are mutually constitutive interactions and feedbacks between firms and other institutions are to some degree place-specific, and that these interactions occur simultaneously across several different scales." (Martin and Sunley 2006 page 430)

As these authors also note, the literature devotes far less attention to the means through which lock-in may be avoided. From a policy perspective, this is perhaps the critical question. One response to this question has been to focus on the factors that influence a region's adaptive capability (Martin 2005). Adaptive capability referring here to the ability of a region to respond to shocks and take advantage of new development opportunities from wherever they appear. Central to this attribute is the ability to apply historic accumulations of assets or capabilities to new and emerging opportunities as and when they arise.

The advent of global recession in 2008 saw a shift in focus of research towards the determinants of economic resilience – in part a recognition of the extent to which impact of recession was spatially uneven (e.g. Martin 2012). But also in the belief that exploring the manner in which regions have responded to the shock of recession can generate insight into longer term patterns of change and continuity in regional economic development (Martin, Sunley and Tyler 2015).

More recently there has been widespread recognition of the need to engage more fully with the process of path creation. Martin and Sunley (2006) had noted the problem of the failure to address the problem of path creation. This was a theme to which Martin returned in is Roepke Lecture of 2010, providing a critique of the path dependency model and the central concept of lock-in as privileging continuity over change (Martin 2010). This may be seen as a reaction against the perceived historical determinism implied by many formulations of path dependency. Martin's response was to argue for a more evolutionary account – applying institutionalist insights from political science to the study of economic geography.

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Insert Figure 1, Martin 2010

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In different ways, we can see recent papers by Doussard and Schrock (2015) and Dawley et al (2015) and Bristow and Healy (2015) responding to this challenge. The former's study of North American manufacturing highlights the importance of firm, technological, place and market level contingencies structuring uneven spatial development. In contrast, Dawley at al (2015) present a case study of wind power in the North East of England in which they identify regional policy initiatives and the multi-scalar state as fulfilling mediating functions in the creation of new paths of development. Bristow and Healy (2015) in turn apply a complex adaptive systems approach to explore the nature and scope of agency in regional development. Arguably the key insight that they derive from this perspective is a recognition of the importance of interaction between actors and the sense in which "agents are co-evolving, constantly adapting to each other and to their environment" (Bristow and Healy 2015, 246).

This paper also seeks to understand the process of path creation – with a particular emphasis on the interaction between institutions, agents and place over time. In so doing we seek to identify the sources of a city region's adaptive capability in the co-evolution of institutions, firms and markets. We use a simplified model of path creation that takes inspiration from the

Multiple Streams Framework (MSF) of John Kingdom (1995). MSF is a perspective on the policy process that is notable for the manner in which it conceptualises the process as comprising a number of parallel streams of activity that converge during particular windows of opportunity to effect a change of policy direction. The agency of particular 'policy entrepreneurs' is seen to be critical if a 'policy window' is to be converted into a concrete change of policy.

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Insert Figure 2: Simplified model of path creation loosely based on MSF

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The appeal of MSF as a model of the policy process is the manner in which it eschews simplistic linear or cyclical representations of the process that represents its object of study (Rossiter and Price 2013). Indeed the strength of this approach is its ability to disentangle the often complicated and messy process that is the 'real world' of policy. A world in which parallel streams of activity happen simultaneously, sometimes independent of each other, sometimes interacting. These characteristics make the MSF account of policy change an interesting and relevant analogue for similar processes at work in the phenomenon of regional and local economic path creation. Central to the approach is a recognition of the importance of agency if policy outcomes are to be understood. Following Dawley et al (2015) and Bristow and Healy (2015) we see agency associated with the local implementation of regional policy as an important ingredient in the local 'recipe' that led to the creation of Nottingham's now burgeoning biotech sector.

Methodology

In developing a case study of the development of the local economy in Nottingham, multiple sources of data were employed. Extensive use was made of documentary and archival materials. The documentary materials included a variety of items from weekly and monthly trade magazines and periodicals, as well as the local and financial press. A number of business histories, industry studies and even biographies and autobiographies were also used to provide background data on the local economy and the development of the pharmaceutical industry in the region. Overall these sources provided a wealth of valuable background and technical

information in relation to the pharmaceutical industry in Nottingham. The study also drew on previous research carried out by the authors exploring the nature of the BioCity incubator and analysing its growth and development, as well as other studies of the biotechnology incubator sector in the UK. The data gathered in this way was complemented by a small number of interviews with 'key informants' (John and Reve, 1982), including staff employed at the facility prior to its closure as an industrial research laboratory, at some of the agencies involved in negotiating and organising the transition to an incubator and at the incubator itself.. Data from the interviews was extremely helpful in understanding and making sense of some of technical aspects surrounding the activities undertaken at the laboratory facility and the key issues that arose in facilitating the transition.

Case study: The development of Nottingham's Bioscience cluster

Adaptive capability and the development of Nottingham' economy

The city of Nottingham has a long history as centre of government and as a market town servicing a wide rural hinterland. However, it was with the establishment of the hosiery industry after 1730 that the town emerged as a major centre of manufacturing industry (Henstock, Dunster & Wallwork, 2006). The physical legacy of this industrial heritage is apparent to anyone strolling through the Lace Market area of Nottingham today – although most of the old textile warehouses and factories have been put to new uses in recent years. Textiles continued to dominate the local economy but as the nineteenth century drew to a close and the twentieth century advanced, new industrial sectors began to emerge. Cycle manufacture, tobacco and pharmaceuticals, having taken root in the closing decades of the nineteenth century, gradually became more significant. Two out of the three owed their location in the city to historical accident, but cycle maker Raleigh, founded by two textile machinery makers and a lace worker (Rosen, 2002), was the product of a process of industrial adaptation that was to re-occur throughout the city's industrial development. In addition the development of the Nottinghamshire coalfield created a demand for labour that in turn provided a considerable stimulus to the economy of Nottingham.

The interwar years were marked by adaptation in the city's textile industry itself. Textiles remained important, but hosiery and knitwear (Chapman, 2002) largely replaced the once dominant lace industry. The latter experienced a dramatic decline in the years after the first World War, while by 1931 there were nearly twice as many hosiery workers in Nottingham as

before the war (Wells, 1966), in both instances as a result of changes in fashion. Meanwhile the new industries, exemplified by retail chemist Boots, cycle maker Raleigh and cigarette manufacturer Players (Wells, 1966), continued to expand and grow. The city's substantial stake in these new industries proved remarkably well adapted to the economic environment of the interwar years, which favoured industries producing branded consumer goods for the home market (Pollard,1992). The result was a significant re-shaping and diversification of employment in the city (Wells, 1966), as the emerging 'big three' employers of the twentieth century expanded, building major new factories in the city and taking on more staff, the sectoral composition of the local economy changed. As a result, while unemployment was severe in the depressions of the early 1920s and 1930s, it was cyclical rather than structural and when conditions improved Nottingham's industrial expansion was resumed (Wells, 1966: p410).

By the middle of the twentieth century, structural change within the local economy had gathered pace. Economists (Wells, 1966, p405) were now able to describe Nottingham as an outstanding example of an economy with 'a well-balanced employment structure'. The early postwar years were golden ones for Raleigh as production doubled in the 1950s to one million cycles a year (Chapman, 2006). Similarly Players' cigarette sales overtook those of rival brand Wills in the late 1950s. At Boots profits from manufacturing, once the Cinderella of the business climbed to 40 per cent of turnover (Chapman, 2006), although the discovery of the painkiller *ibuprofen* by Stewart Adams in the mid-1960s failed to produce the rewards it should because of the company's limited international presence.

Nonetheless by the 1960s Boots, Raleigh and Players had become the mainstays of the local economy (Chapman, 2006). The city's big employers each had nearly 10,000 employees at their height. The early postwar years were also marked by growth in other sectors, most notably engineering. Major employers by the 1960s also included Plessey/GPT in Beeston which employed 5,000 at one point and other major engineering concerns included Royal Ordnance and former textile machinery firms that had diversified into other sectors such as the Jardine Group producing typewriters and Manlove Alliott (Wells, 1966) making hospital equipment.

However the 1960s was to be the zenith for two of Nottingham's 'big three' employers. Increased car ownership combined with stiffer overseas competition saw Raleigh's output and employment steadily decline despite a merger with Tube Investments and attempts at diversification into mopeds and motor scooters both of which proved unsuccessful (Chapman,

2006). Likewise Players, now part of Imperial Tobacco, though it opened a major new factory at Clifton on the outskirts of the city in 1971 (Chapman, 2006), was subject to a similar pattern of declining employment during the course of the 1970s and 1980s. The main factor was increasing public recognition of the health risks associated with tobacco and cigarette smoking. In 1981 five of Players factories were closed and some 3,000 staff made redundant (Chapman, 2006). By the early 2000s both Raleigh and Players had ceased manufacturing operations in Nottingham.

The sustained decline in manufacturing employment in Nottingham (especially in textile related sectors and light engineering) continued in the closing years of the twentieth century. In 1966 the East Midlands Study had identified Nottingham as integral to the 'northern industrial belt' an area within which employment in manufacturing and extractive industries stood at over 60 per cent (EMEPC 1966). By 2014 manufacturing employment in Nottingham stood at around 6 per cent (ESRB 2014). However this decline was largely matched by the growth of service sector employment and specifically business/information services, education and health. This has been sustained and can be said largely to have compensated for the loss of manufacturing employment (in volume terms at least).

This transformation has seen particular growth in the business/information services sector with several large companies now based in Nottingham, including Experian, Capital One and Ikano. Experian is much the largest with more than 2000 employees in the city (Nottingham Post, 2013). Unlike the other two which are the result of inward investment that brought them to Nottingham in the 1990s, Experian originated in Nottingham. It provides a fascinating modern day example of the same process of adaptation that occurred in the late nineteenth century. Experian began life in the early 1970s as the credit checking arm of furniture retailer Cavendish Woodhouse, which was part of Great Universal Stores (GUS). It was commercialised as Commercial Credit Nottingham (CCN) in 1980 (Nottingham Post, 2013). Through a combination of organic growth and acquisitions including many overseas, it grew steadily, continuously adding and developing its portfolio of information service, until it became one of Nottingham's largest employers. Then in 2006 it was demerged from Great Universal Stores as Experian, immediately becoming a FTSE 100 company.

The overall trajectory that has led Nottingham to become a city that is dominated by the service sector, reflects an interesting mix of capabilities that are the product of path dependency and speak to the historic strengths of the local economy in Nottingham (ESRB 2014). A recent

example of this is the city's emerging bioscience cluster. This is a legacy of historic private sector strengths in pharmaceuticals (Boots), a product of the concentration of health related activity in the locality (e.g. the Queens Medical Centre), the growth of two large universities with relevant research capabilities and the uniquely successful BioCity Nottingham, business incubation facility housed in Boots' former research laboratories on Pennyfoot Street in Nottingham.

Boots and the industrial science legacy

One of Nottingham's big three employers by the mid-twentieth century, Boots really began the development of Nottingham's industrial science base. Founded in the mid-nineteenth century, Jesse Boot its founder was a herbalist who lacked any formal scientific training. Despite this he recognized the value of science and from 1884 onwards he began employing trained pharmacists in his shop. But it was the outbreak of war with Germany in 1914 that proved a critical juncture in the firm's development. The war quickly led to crippling shortages of many synthetic and other advanced pharmaceuticals following the cessation of imports from Germany (Corley: 2003). Faced with this Boots established a fine chemical manufacturing facility in 1915, employing a research team poached from Burroughs-Wellcome and over the next three years launched products ranging from antiseptics and anaesthetics to aspirin and saccharin (Corley, 2003). Boots thus placed its self on a par with the longer established pharmaceutical manufacturers.

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Insert Table 1

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During the inter war years Boots recruited a number of leading scientists from universities across Britain, to its research staff and between 1936 and 1941 it had the third highest level of patent filings for a UK-owned pharmaceutical company (Slinn, 2008). In the postwar era Boots built up a formalized research and development (R & D) programme in the 1950s and 1960s, becoming a major force within the UK pharmaceutical industry. Among its major achievements was the discovery of the widely used pain-killer *ibuprofen*, although the company's lack of international marketing expertise meant it never produced the rewards it might.

However while Raleigh and Players went into decline from the 1970s Boots continued to prosper. Through acquisitions, including rival chemist Timothy Whites with its 600 branches, Boots' retail chemist business continued to expand in the 1970s. It was a similar pattern for Boots' pharmaceutical business which saw a number of important acquisitions in the 1970s including Crookes Laboratories and Rucker Pharmacol, and in the 1980s the Flint division of Baxter Tavernol (Chapman, 2006). Flint was a US company that owned *synthroid*, a big selling treatment for thyroid conditions. Thus by the mid-1980s Boots was not only the UK's largest retail chemist, it was also the fifth largest pharmaceutical company in the UK (see table 1). But it lacked the international marketing capability of rivals like Glaxo, Wellcome and Beecham.

In the late 1980s under a new chief executive James Blyth, who had formerly worked for the confectionary firm Mars, Boots attempted to diversify into other areas of retailing, in particular larger stores in out-of-town locations. This included the launching of the abortive Children's World stores in 1987 and the acquisition for £900million in 1989 of the Ward White group which included the Halfords automotive parts chain, the Payless home improvement chain and A G Stanley's FADS home decorating chain. At the same time Blyth engineered a re-structuring which saw the emergence of four divisions that included Boots the Chemist, a retail division and Boots Pharmaceuticals. The acquisitions proved disastrous as they were followed by a five year depression in the UK housing market which severely cut DIY sales turning Boots' Do-It-All chain (which now included Payless) and FADS into loss making operations. The company was also hurt by the high debt incurred in making the Ward White acquisition.

In 1991 two new units were split off from Boots Pharmaceuticals. Thus while Boots Pharmaceuticals retained responsibility for prescription only drugs, Boots Healthcare International (BHI) assumed the over-the-counter (OTC) business and Boots Contract Manufacturing (BCM) became the company's producer of mostly private label health and beauty products (Smith, 1996). By now Boots Pharmaceuticals was facing difficulties. These reflected its relatively small size internationally (see table 1) and problems surrounding the development of new drugs. In 1993, having spent 14 years and £150 million on research and development (Hoskings, 1993), Boots withdrew its heart drug *manoplax*, when new research showed that while it was effective in relieving the symptoms of congestive heart failure (CHF) it could in certain circumstances shorten life slightly.

It had been back in 1979 that biochemists at Boots laboratories in Nottingham first synthesized *flosequinan*, the active ingredient in *manoplax*. It showed early promise as a means of relieving congestive heart failure. By 1990 after 10 years of trials commentators were bullish about the prospects for *manoplax*. It was a crucial development for Boots, as none of its other prescription drugs was still under patent in the UK. Even *synthroid*, Boots highly profitable thyroid replacement therapy was out of patent and margins on it and other drugs like *ibuprofen* were shrinking (Hoskings, 1993). By the time *manoplax* was finally granted a licence in the UK in August 1992 (see table 2) it had come to be seen as 'great white hope not only for Boots Pharmaceuticals, but for the wider group' (Hoskings, 1993). Hence the impact when it finally flopped was all the greater.

Faced with this setback, and with other parts of Boots such as Do-It-All and FADS in trouble and the new Children's World chain taking much longer than expected to come good, this placed the future of Boots Pharmaceutical division in doubt. There were those who argued that Boots, ranked in 50th place in the world by size, was simply too small.

With its ambitious plans for expansion into new areas of retailing having largely failed, and its drug development portfolio in tatters, Boots board took the decision to divest itself of the prescription only drug business. Thus early in 1995 the business was sold to the German chemical conglomerate BASF for £850 million (Green, 1994). Although Boots retained the over-the-counter pharmaceutical business along with contract manufacturing, the deal ended the company's 80 years in the prescription drugs sector.

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Insert Table 2

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The attraction for BASF was that its core business of agrochemicals was highly cyclical, whereas pharmaceuticals were almost untouched by the business cycle. In addition BASF already had a modest pharmaceutical business which traded under the Knoll brand and a worldwide marketing network. Another attraction for BASF was that Boots had an anti-obesity drug, 'at a fairly advanced stage' (Hoskings, 1993), and this held the promise of large sales in the US where BASF already had a presence. However BASF's ownership of the Boots research laboratories in Nottingham was to prove relatively short-lived.

Within four years, BASF was conducting a strategic review of its entire pharmaceutical operation worldwide. There were those within the company who had always found it difficult to see BASF as anything other than a chemical company. This was not helped by regulatory concerns limiting the use of *reductil* the anti-obesity drug developed by Boots. In any event the 1990s were a tumultuous decade for the worldwide pharmaceutical industry which saw significant re-structuring (Owen, 1999).

As a result Lehman Brothers were called in to prepare the unit for sale. While there was considerable interest from prospective purchasers, they tended to be more interested in the IPR rather than the site. Then out of the blue it was announced in December 2000 that the American pharmaceutical company Abbott Laboratories was to purchase the worldwide business of Knoll Pharmaceuticals for $6.9 billion (thepharmaletter, 2000). However there was a problem. While Abbott was keen to acquire the Nottingham site's IPR which included the anti-obesity drug *reductil,* it did not want either the site itself or the staff, since its own research facilities were distinctly home-based and not multinational. As a result BASF was forced to make 450 highly qualified scientific staff in Nottingham redundant and try and find a buyer for the site itself. The loss of some 450 highly skilled science jobs was a major blow to the local economy. The redundancies came at a point when the closure of the last Raleigh manufacturing plant in Nottingham had recently been announced and not long after another big manufacturing plant in the city, Royal Ordnance owned by British Aerospace, had also closed.

However disposal of the former Boots research laboratories on Pennyfoot Street in Nottingham was to prove somewhat problematic. Although the site was quickly put up for sale, there was little interest from buyers. The laboratories were modern and purpose built so were not easily converted to alternative uses and the site itself had limited scope for development.

While BASF were casting around what to do with the site, a specialist consultancy firm, Angle Technologies Ltd, was commissioned to undertake a study into the feasibility of using the facility as a bioincubator. The impetus for this move may well have been that a number of small biotechnology firms including RenaSci in Nottingham and a Cambridge based SME did approach BASF about the possibility of renting laboratory facilities.

When it became clear that there was little prospect of selling the site without demolishing the buildings and writing off the equipment, BASF took the unusual step of giving the facility

away. It gifted the site and the laboratory facilities to one of Nottingham's two universities. Surprisingly BASF chose to gift the laboratories not to the University of Nottingham, the more research intensive of Nottingham's two universities and the one that historically had stronger links to Boots, but to the city's former polytechnic, Nottingham Trent University. The choice surprised many. However the site was much nearer to Nottingham Trent University's city centre campus and many of its technical staff had been trained there over the years. It is also possible that BASF wanted to be seen to be even handed since Boots had over the years been very generous to Nottingham University, having given the university its 300 acre University Park campus in the 1929. Interviews with participants in this process suggest that it was precisely this difference between the nature of the two universities that led key decision makers within BASF conclude that a gift to NTU would have the 'greatest impact'[2].

Whatever the motives, in August 2001 it was formally announced that BASF had gifted the facility, which comprised three buildings valued at some £4 million, comprising more than 100,000 square feet (THES, 2001) of laboratory space, to one of Nottingham Trent University. Spread across three buildings, the facility comprised world class laboratories and state-of-the-art equipment. The buildings comprised a manufacturing facility for early stage clinical trials, together with a total of 16 medical chemistry laboratories. The facility would have cost close to £50 million to build and equip at current prices (Hansard, 2008).

The move on BASF's part was unprecedented. At the time it was the largest corporate donation ever to have been made to a post-1992 university (Hansard, 2008). The offer of the Pennyfoot Street laboratories when it was made in 2001 even came as a surprise to Nottingham Trent University's vice chancellor, Professor Ray Cowell.

Having acquired the former BASF laboratories, Nottingham Trent University had to consider just how to establish it and manage it as a bioincubator, especially since it was significantly larger than existing biotechnology incubators, bigger even than the Babraham bioincubator outside Cambridge.

As the consultants brought in to advise observed, when it came to developing the facility, *'Nottingham Trent University wisely decided it needed it needed to work with partners*'

[2] Interview with senior research scientist employed first by Boots and then BASF on the Pennyfoot Street site.

(Hansard, 2008). These partners included a range of supporting institutions based or operating in the region. As the consultants were later to report, the partners represented,

> *'a unique example of strong collaboration between a Regional Development Agency (East Midlands Development Agency), two universities (the Nottingham Trent University and the University of Nottingham) and a major science–based company (BASF plc).*' (Hansard, 2008).

Each was able to contribute to the development of a distinctive 'local recipe'. This recipe was designed to facilitate academic-industry links and putting the facility to constructive use in supporting local economic development.

Given its size it was capable of providing a home not just for start-up firms, but for firms providing related support services as well. In utilizing the facility in this way the aim, according to Alan Meers, Nottingham Trent University's director of business development, was to have,

> *'a mixture of units coming in, including mature research and development companies, emerging biotechnology companies that might be at the first phase of development, and incubator units which will either come from universities or will want to work with universities'* (THES, 2001).

Thus was borne 'BioCity Nottingham' a bioscience incubator designed to facilitate the biomedical research of universities in the region, especially at the technology-transfer stage.

Quite apart from providing the facility, BASF's contribution extended to underwriting the running costs of the facility until the other partners had had an opportunity to, '*develop a robust business plan and secure the necessary funding*' (Hansard, 2008). By now EMDA had the capability to assess possible uses for the redundant laboratories. It was also sufficiently well established to be able to ensure that Nottingham's two universities, who often found themselves in competition both for students and academic staff, worked together for common goals. Its particular contribution was,

> *'a well designed and well developed regional strategy that ensured public funding could be made available to help BioCity get established*' (Hansard, 2008).

The University of Nottingham was able to contribute a very strong bioscience and healthcare research base.

The project also benefited from the use of specialist consultants, Oxford Innovation Ltd, with first-hand experience of managing incubator facilities. One such incubator was DiagnOx, at Upper Heyford near Oxford, was housed in re-furbished rather than purpose-built premises and focused on biotechnology and medical technology applications. Given their prior experience, the consultants were able to manage the initial operation of the BioCity facility, providing time for the careful recruitment and selection of a manager for the incubator with just the right mix of skills and experience.

Thus a joint venture in which the two universities were partners along with EMDA, was set up with the very specific aim namely to 're-purpose' the Pennyfoot Street laboratories. Under EMDA's guidance it was agreed that the Pennyfoot Street laboratories should become an 'incubator' specializing in embryonic life science companies. They would be housed in small laboratory based units and sharing common facilities and services. Some £9 million was spent over the next ten years to extensively refurbish and modernize the facilities. The facility was re-named as 'BioCity Nottingham' to reflect its city centre location. The first phase of the development was opened by the science minister, Lord Sainsbury in September 2003 (Connon, 2003). This facility provides generic laboratory space for small biotechnology start-ups together with an administrative hub comprising, office space, meeting rooms, café and a conference room.

Phase two of the incubator was launched in July 2006 with the opening of the adjacent Stewart Adams building, named after the Boots scientist who led the team that discovered the painkiller *ibuprofen* on the site. The development was part funded by EMDA and the Greater Nottingham Partnership. This additional facility provided a particular focus on medicinal chemistry and pharmaceutical applications, with larger laboratories. The third phase which opened in 2009 saw the opening of the adjacent Laurus Building, provided an additional 48,000 square feet of space.

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Insert Figure 3

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At 129,000 square feet BioCity is now the largest biotechnology incubator in the UK. With the inclusion of 'grow-on' space in the Laurus Building it is able to accommodate a unique range of enterprises that includes not merely for small start-up companies larger and more mature ones as well.

The BioCity incubator and the development of Nottingham's bioscience cluster

Figure 3 shows that the BioCity incubator attracted a steady stream of new tenants every year between 2003 and 2009. Within months of opening, the incubator had attracted five new tenants. In the following year, this swelled to 11 new arrivals. After peaking in 2004, the number of new tenants dipped markedly the following year. But as phase two came on stream in 2006 there was a resurgence of new arrivals. New tenants then dipped again in 2007 and 2008, possibly reflecting the worsening financial climate, before rising with the opening of phase three of the incubator in September 2008.

By 2009 BioCity was home to some 60 companies, covering a range of bioscience applications. Unlike the situation in the golden triangle regions of the East and South East, where new life science companies are predominantly ones focusing on purely biotechnology applications (e.g. new drug therapies and diagnostics), BioCity's tenants were almost equally divided between biotechnology and medical technology applications. This is a pattern found in other 'peripheral' regions like the North West, North East and Yorkshire and Humberside (strangely Scotland is alone in following the pattern found in the South East and East). This appears to be a function of spatial dynamics in that the golden triangle is home to the leading research universities (i.e. Cambridge and Oxford) and nearest the principal source of capital (i.e. London). In the East Midlands it also seems likely that this reflects the location of major medical institutions such as the Queens Medical Centre in Nottingham. A similar pattern is evident in the United States where Feldman and Francis (2003) found medical technology applications were important outside the leading biotechnology regions like California and Massachusetts.

Many of the new tenants arriving in the early years were existing biotechnology companies. Figure 4 shows that in the first couple of years, there was little additionality in terms of new jobs created. However this quickly changed. In 2005 some 30 new jobs were created in the

incubator, rising to 70 in 2006 and almost 150 in 2007. Although the recession slowed employment growth (see figure 4), nonetheless by 2008 employment within the facility had risen to almost 400.

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Insert Figure 4

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Clearly these weren't all new jobs as some tenant companies weren't newly created and were already employing staff when they moved into the incubator. The arrival of tenants who were already employing staff meant that jobs were effectively being displaced from elsewhere. In all 118 jobs were displaced in this way. Nonetheless, over the period to 2008 additional job creation amounted to 278 out of a total of 396, an average of 46.3 per year. Hence during its first six years of operation the incubator had a significant direct impact on the city of Nottingham in terms of job creation, especially since the majority of new jobs created were science based. What is also apparent from figure 4 is that job creation, took time to get going. In the early period employment growth through displacement greatly outweighed growth through new job creation. There was a distinct lag between firms setting up in the incubator and new jobs being created. This lag would appear to be a function of the new venture creation process with a 'settling in' period following formation or transfer to the incubator, during which firms organise and establish their activities.

Of the 60 companies located at BioCity by 2009, 39 were generic biotechnology companies (the remainder provided a range of support services such as patent agents, that would otherwise have been missing in a nascent cluster). Just over one third (38.5 per cent) of the generic biotechnology companies, comprising 15 companies, were utilising a 'product' (i.e. drug discovery) business model, based on what Pisano (2006) terms 'the monetization of intellectual property' (IP). With this business model the company aims to capitalise on a scientific breakthrough by patenting it and then either licencing it or selling it to a third party with the resources to commercialise it. This requires the company to bear significant risks because of potential problems in the development process. It is also expensive because large investments in R & D may be required before there is any kind of financial return. An example of a BioCity tenant company utilizing this model is Regentec Ltd, a spin-out company from the School of Pharmacy at the University of Nottingham that is working in the field of regenerative medicine

(Smith and Ehret, 2013). Regentec specializes in orthopaedic applications and has grown to the point where it has 15 employees and has filed 4 patents.

In contrast, nearly two thirds (61.5 per cent) comprising 24 companies at BioCity, were using a 'service' business model. With this business model companies are not seeking to commercialise IP but instead focus on the provision of a range of specialised research services that typically facilitate the new product development process of third parties (Kasabov and Delbridge, 2008). These research services, often based on the possession of specialised tacit knowledge or cumulative experience and expertise, include: outsourced R & D services, quality management and testing, and data handling and storage. The service business model offers a very different risk reward profile. It typically requires a much smaller upfront investment and revenues begin much earlier and are more predictable. The downside is that the chances of a big breakthrough leading to a huge capital gain are much less. Sygnature Chemical Services Ltd is an example of a BioCity company using a service business model. It was founded at BioCity in 2004 by a medicinal chemist with extensive pharmaceutical industry experience. Sygnature undertakes specific elements of the drug discovery process and is able to offer expertise in medicinal chemistry, synthetic chemistry, arrays/focused libraries and computational chemistry. Outsourcing for pharmaceutical companies forms a major feature of its work. Sygnature has grown rapidly and now employs 31 staff.

Another feature of the profile of BioCity companies is that the proportion of companies using a service business model seems to be increasing. Figure 3 shows the mix of new tenants arriving in the incubator on a year by year basis, in terms of their business model. Although one cannot be precise, the general pattern seems to show that in later years the proportion of companies coming into the incubator with a service business model has increased. This may well reflect significant changes in the commercial environment in particular greater use of outsourcing and open innovation.

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Insert Table 3

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The significance of the BioCity incubator in terms of the development of bioscience in Nottingham can be gauged from a recent survey which looked at new bioscience companies

formed between 2005 and 2011. The results compare the distribution of new companies formed in an incubator with those formed outside such a facility. In the case of the East Midlands only a tiny proportion were formed outside an incubator with a very much bigger proportion within an incubator. Since BioCity in Nottingham is the only bioincubator in the region one may conclude that its opening in 2003 has had a powerful impact on the growth and development sector of this sector and the emergence of a bioscience cluster in Nottingham. Many of these firms were the product of the region's research base, specifically the universities located in the region. Table 3 shows that about a third of the new firms located in the incubator were university spin-outs. Not unsurprisingly the chief source of these spin-outs was Nottingham University which was the source of seven of the thirteen companies shown in table one, although Nottingham Trent University contributed as did Leicester University. What is perhaps surprising is that the incubator was even able to draw in a small number of spin-offs from as far afield as Cambridge and Oxford universities.

Case Analysis: A new development path emerges in Nottingham

From the case study it is evident that a new development path, based on bioscience and health, has emerged in Nottingham in the last couples of decades. The most obvious symbol of this new development path is the bioscience cluster centred on the BioCity incubator and comprising more than 70 bioscience related companies established in Nottingham since 2000. Another symbol was the designation of Nottingham by the UK government in May 2005, as one of six 'Science Cities' (Charles, 2015). The designation of these cities was based on the presence of 'high performing universities and research establishments' that can contribute to attracting 'a critical mass of knowledge-based businesses' (HM Treasury, 2004). Nottingham's designation reflected the city's scientific achievements (i.e. the discovery of the painkiller *ibuprofen* at Boots in the 1960s), the quantity and quality of its scientific institutions and the strength of science-based sectors within the local economy. It also reflected increasing recognition of the BioCity incubator's success as one of the largest biotechnology incubators in the UK. Another symbol was the East Midland Development Agency's (EMDA) selection in its Regional Economic Strategy, entitled 'A flourishing region' (EMDA, 2006), of bioscience/health as one of four priority sectors predicted to, 'make the greatest contribution to the East Midlands economy over the lifetime of the strategy'. Similarly when in 2012 Nottingham City Council published its contribution to local economic development in the form of the *Nottingham Growth Plan* (Nottingham City Council, 2012), this explicitly recognized recent changes in the city's economy by specifically identifying life sciences as a 'growth

sector' in which the city had a 'competitive advantage' and including it as one of just three sectors prioritized in terms of their potential contribution to the development and growth of the city economy.

Given that bioscience has emerged as a new development path in Nottingham, this raises the important question of just how this has come about. On the basis of this case study, it is tempting to suggest that it is simply a matter of serendipity, that is the product of a series of chance events of which perhaps the most notable were Abbott Laboratories wish to purchase Knoll Pharmaceuticals' IPR but not the Nottingham site where it was developed, and the decision by Knoll's parent company BASF, to gift the Nottingham site to one of the city's universities. However putting it down to serendipity is highly simplistic and ignores strong elements of path dependency revealed when we consider the wider economic and institutional context within which this development occurred.

Using the model of path creation developed earlier (figure 2), there appear in this case to be three parallel yet inter-acting and co-evolving strands of development that ultimately brought about a unique 'window of opportunity' for Nottingham at the beginning of the twenty-first century. Importantly these strands also interacted to provide the capability necessary to take advantage of an opportunity that they were implicated in creating.

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Insert Figure 6: The development of biotech in Nottingham

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The first stream of activity operated at the industry level, where the 1990s saw a decade of industry concentration fuelled by successive mergers (See table 4). Underlying this process of concentration were a number of factors. Foremost was the rising cost of drug development, with leading firms spending 15%-18% of their turnover on research and development (R & D), with a new drug taking at least 10 years to develop at a cost of $250-$350 to develop (Collett, 2000). Other factors included an over-dependence in some companies on a single blockbuster drug and the need for critical mass in both R & D and marketing.

At the same time as concentration was taking place, changes were occurring in the model of R & D used by many pharmaceutical companies. With the rise of the biotechnology sector

(Pisano (2006), small firms were increasingly able to provide both potential new drugs and a range of research services. Across the UK the number of small specialist biotechnology companies doubled beween 1994 and 1999 (DTI, 1999). As a result there was a gradual move away from what Chesbrough (2006: p51) describes as, 'the traditional paradigm of R & D', as pharmaceutical companies increasingly embraced open innovation. Hence the industry landscape evolved rapidly during the 1990s. Boots was in no way isolated from these changes to the structure of the global pharmaceuticals industry. The concentration of the global pharmaceuticals sector and intensified competition for Boots created a problem to which the Boots leadership had to respond. The industry wide shift towards 'open innovation' in the development of new treatments also created a market opportunity for exactly the kinds of biotech firms that would later come to occupy BioCity.

The second stream operated at the firm level and in this case centred on Boots and its pharmaceutical division. As the case study has outlined Boots evolved from a retail chemist to a national player in pharmaceuticals and ultimately one with international ambitions, over the course of 80 years. In research terms by the 1990s it had a potentially valuable drug development pipeline. Its most notable success had been the discovery of the painkiller *ibuprofen*, but there were others including *synthroid* and *sibutramine*, though the company's lack of international marketing skills, meant none realised their full potential as a blockbuster drug. Consequently Boots had remained a national rather than an international player. Then a combination of regulatory problems surrounding its heart drug *manoplax*, combined with leadership changes that brought in a strong retail focus, led to the company divesting its pharmaceutical division. The purchaser, BASF, then ran into regulatory problems with a new drug itself and with a wave of mergers driving many pharmaceutical companies to seek further acquisitions, it too took the decision to divest. However this time the purchaser wanted the IPR but not the Nottingham site or its research staff. Unable to sell the site, BASF chose instead to gift it to one of the city's universities, thereby creating a unique window of opportunity. This development both freed a key economic asset for redeployment (the Pennyfoot Street laboratory site) and created a pool of highly specialised research scientists who were displaced. The question was, to what new purpose could the site and this pool of related human capital be put?

The third strand comprised the development of local institutions, including particular scientific ones. Chief among these public sector anchor institutions was the Queens Medical Centre

(QMC) opened in 1977 following the creation of a new Medical School at the University of Nottingham in 1970. The QMC was the first purpose-built teaching hospital to be constructed in the UK. As such it constituted a significant addition to the City's science base. Currently the main acute hospital for the East Midlands region QMC employs nearly 6,000 staff and until very recently was the largest hospital in the UK and the largest teaching hospital in Europe. The advent of the QMC helped the City to generate 'critical mass' in health related biosciences. It also created a ready market for the kind of health related bioscience companies adopting the services business model that is such a notable feature of the companies resident at BioCity.

Other important public sector anchor institutions that form part of the city's science base included its two universities. From their earliest years both had close contact with local industry. Nottingham's University College finally gained its charter to become a full university in 1948 having acquired a large new 300 acre campus two miles south west of the city in the interwar years, through the generosity of Boots founder, who had originally planned to use the site for a Cadbury-style model community (Chapman, 1974). From this point onwards Nottingham University developed into one of the UK's leading research intensive universities, with major departments in bioscience and healthcare (see figure 5) and rated a, 'leading biotechnology research university' in terms of funding support from the relevant UK research councils. A measure of the university's rise among the scientific community was its first Nobel prize in 2003 awarded to Sir Peter Mansfield for his work on Magnetic Resonance Imaging (Ehret et al., 2012). The city's polytechnic, which had for a long time played an important role in training technicians and laboratory staff working in local companies like Boots, merged with the city's college of education in 1975 and gained independence from local authority control in 1992 when it became Nottingham Trent University (NTU).

The development of Nottingham's two universities and their relation to local industry is itself noteworthy and provides evidence of co-evolution. Indeed, in different ways the development of both universities may be seen as directly stimulated by local industry. The philanthropy of Jesse Boot played a key role in the development of the University of Nottingham, just as the needs of local manufacturing firms had stimulated the creation of NTU's earliest antecedent – a college of arts in the 1840s. To this extent both universities can be regarded as products of a particular industrial milieu. That both universities later came to play significant roles in the creation of a new biotech development path is suggestive of an intriguing symmetry. In

different ways the development of both universities can be seen as having been 'seeded' by local industries and industrialists.

Other important institutional developments locally included the award unitary status to Nottingham City Council in 1998. The significance of this was to increase the authority's influence over and resources devoted to strategic planning, transport and economic development. The following year saw another important institutional development, the establishment of regional development agencies (RDAs) across the UK, including the East Midlands Development Agency (EMDA) based in Nottingham. EMDA was part of the actor network associated with attempts to implement cluster policies under the then New Labour government (Swords, 2013). However they were also important actors in economic development at the local level, especially since they had substantial funds at their disposal. By accident of location, it is also noteworthy that EMDA's main offices in Nottingham overlooked the Pennyfoot Street laboratory site – meaning that the site and its potential future use could hardly fail to be prominent in the minds of key EMDA executives.

Even so while the opportunity might have emerged, the path itself was far from clear at the time. But into this space came a relatively new but important institutional actor (or institutional enabler in figures 2 & 6), namely the local RDA. EMDA's distinctive contribution to the local recipe was to facilitate the establishment of a collaborative joint venture comprising the two universities and EMDA. This entailed encouraging two often competing universities to work together for their mutual benefit. EMDA also had a remit from the then Department for Trade and Industry to implement regional cluster policies. To this the Agency could also add a level of financial resources commensurate with the task of re-purposing the Pennyfoot Street laboratories.

Hence when BASF took the decision to sell Knoll Pharmaceuticals to Abbott Laboratories in 2000, in a deal that included the Nottingham site's intellectual capital (i.e. its IPR), but not its physical assets or the human capital , all three of the strands in figure 2 converged. By so doing they created what was potentially a unique window of opportunity. Had the site become available ten years earlier or ten years later it is much less certain that local institutions would have had the capability or resources required to take advantage of the opportunity. Through these three co-evolving strands a new window of opportunity emerged alongside the institutional capability required to take advantage.

Concluding Discussion – of agency and agencies

The case of Nottingham and the creation of a new bioscience development path in this way raises a number of important questions. In particular is it place specific or is it capable of wider replication? Aspects of the Nottingham recipe would seem to be present elsewhere. It is notable that similar biotechnology incubators have now been developed at other locations where pharmaceutical companies have closed research laboratories – often explicitly based on the BioCity Nottingham model. Examples include BioPark Herts developed at laboratories vacated by Roche and BioCity Glasgow developed from laboratories once owned and operated by Merck. This should be no surprise given the character of the concentration, intensification of competition and shift to 'open innovation' that marked the global pharmaceuticals sector in the closing decades of the twentieth century. This was a global phenomenon that impacted on many firms and the localities in which they were based.

It is however at the firm and the institutional levels that we start to see the emergence of a more place specific set of contingencies that, with the considerable benefit of hindsight, we can say led to the creation of a unique window of opportunity in Nottingham circa 2000/2001. It is here too that we see the evolution, in the interplay between firms, administrative and scientific institutions, of the capabilities necessary to take advantage of the opportunity. We also see the emergence of specialised and localised markets for scientific labour and services of direct relevance to the kinds of biotech businesses attracted to Nottingham and BioCity after 2001.

Equally important is the role of agency – individual, corporate and institutional. From Jesse Boot's philanthropy to the extraordinary gift of a fully equipped industrial laboratory and trial drug manufacturing facility by BASF– key decisions by individuals and company boards shaped both the problem faced by Nottingham (losing pharmaceuticals manufacture) and the availability of specific assets that could be redeployed to take advantage of a new local and global opportunity.

Finally we must note the key role played by EMDA – itself a product of national Government's regional policy – as both a new institutional player on the ground in Nottingham and a source of resources and expertise that would prove critical in establishing the new biotech related development path. This was rooted in Nottingham's history of industrial science and centred on the Pennyfoot Street laboratory.

References

Boschma RA (2004) *Competitiveness of regions from an evolutionary perspective*, Regional Studies 38, 993-1006.

Bristow, G. and Healy, A. (2015) *Crisis response, choice and resilience: insights from complexity thinking* Cambridge Journal of Regions Economy and Society 8 (2): 241-256.

Chapman, S.D. (1974). *Jesse Boot of Boots the Chemists: A study in business history*, Hodder and Stoughton, London.

Chapman, S.D. (2002). *Hosiery and Knitwear: Four Centuries of Small Scale Industry in Britain, c.1584-2000*, Oxford University Press, Oxford.

Chapman, S.D. (2006) Economy, industry and employment, in J.V. Beckett (ed.) *A Centenary History of Nottingham*, Phillimore, Chichester, pp480-512.

Chesbrough, H.W. (2006) *Open Innovation: The New Imperative for Creating Profit from Technology*, Harvard Business School Press, Boston, MA.

Connon, H. (2003). Incubatorcity bids to hatch golden egg, *The Observer*, Business section, 19th October 2003.

Corley, T.A.B. (2003). The British pharmaceutical industry since 1851, in Richmond, L., Stevenson, J. & Turton, A. (eds.) *The Pharmaceutical Industry: A Guide to Historical Records*, Ashgate, Aldershot.

Crocker, G. (2010) *Opportunity: UK Life Science Start-up Report 2010*, Mobius Life Science Fund, Nottingham.

DTI (1999) *Biotechnology Clusters: report of a team led by Lord Sainsbury*, Minister of Science, Department of Trade and Industry, London.

Ehret, M., McDonald-Junor, D. and Smith, D J. (2012) 'High technology and economic development: the BioCity Nottingham technology incubator', *International Journal of Entrepreneurship and Innovation*, 13 (4) pp301-309.

East Midlands Development Agency (2006) *A flourishing region: Regional Economic Strategy for the East Midlands 2006-2020*, East Midlands Development Agency, Nottingham.

East Midlands Economic Planning Council (1966) *The East Midlands Study*, published by HMSO for the Department of Economic Affairs.

Feldman, M.P. and Francis, J.L. (2003) 'Fortune favours the prepared región: The case of entrepreneurship in the capitol región biotechnology cluster, *European Planning Studies*, 11 (7) pp765-788.

Green, D. (1994) BASF in £850m Deal to Acquire Boots, *Financial Times*, 15th November 1994, p1,20.

Hansard (2008) Memorandum submitted by Oxford Innovation Ltd, *Hansard*, 1st October 2008. Available at: Source: http://www.parliament.the-stationery-office.co.uk/pa/cm200809/cmselect/cmberr/89/89we120.htm.

Henstock,A. Dunster, S. and Wallwork, S. (2006), Decline and regeneration: Social and economic life, in J.V. Beckett (ed.) *A Centenary History of Nottingham*, Phillimore, Chichester, pp132-164.

HM Treasury (2004). *Pre-budget report opportunity for all: The strength to take long term decisions for Britain,* The Stationary Office, London.

Hoskings, P. (1993) Manoplax: from heart to heartbreak, *The Independent*, 24th July 1993.

John, G. and Reve, T. (1982) The reliability and validity of key informant data from dydadic relationships in marketing channels, *Journal of Marketing Research*, 19 (4): 517-524.

Kingdon, J.W. (1995) *Agendas, Alternatives and Public Policies*, HarperCollins, New York.

Martin R.J. (2010) *Roepke Lecture in Economic Geography Rethinking Regional Path Dependence: Beyond Lock-in to Evolution* Economic Geography 86 (1).

Martin & Sunley (2006) *Path dependence and regional economic evolution* Journal of Economic Geography 6 (4):395-437.

Martin, Sunley & Tyler (2015) *Local growth evolutions: recession, resilience and recovery* Cambridge Journal of Regions Economy and Society 8 (2): 141-148.

Nottingham City Council (2012) *The Nottingham Growth Plan*, Nottingham.

Nottingham Post (2013) Experian continues to deliver jobs and growth, *Nottingham Post* 12th February 2013. Available at: http://www.nottinghampost.com/Experian-continuers-deliver-jobs-growth/story-18125776-detail/story.html

Owen, G. (1999) *From Empire to Europe: The Decline and Revival of British Industry since the Second World War*, Harper Collins, London.

Pisano, G. p. (2006) *The Business of Science: The Promise, The Reality and The Future of Biotech,* , Harvard University Press, Cambridge, MA., New York.

Pollard, S. (1992) *The Development of the British Economy 1914-1990*, 4th edition, Edward Arnold, London.

Rosen, P. (2002) *Framing Production: Technology, Culture and Change in the British Bicycle Industry,* MIT Press, Cambridge, MA.

Rossiter, W. and Price, L. (2013) Local economic development strategy under Regional Development Agencies and Local Enterprise Partnerships: Applying the lessons of the multiple stream framework, *Local Economy*, 28 (7-8) pp852-867

Slinn, J. (2008) 'Patents and the UK pharmaceutical industry between 1945 and the 1970s', *History and Technology*, 24 (2) pp191-205.

Smith, D.J. (1996) Set-up Reduction in Pharmaceutical Manufacturing: An Action Research Study, *International Journal of Operations and Production Management*, 16 (3) pp4-17.

Smith, D. J. & Ehret, M. (2013): 'Beyond the golden triangle': Biotechnology incubation in the East Midlands region of the UK. *Local Economy*, 28, (1), pp. 66-84.

Swords, J. (2013) Michael Porter's cluster theory as a local and regional development tool: The rise and fall of cluster policy in the UK, *Local Economy*, 28, (4), pp. 369-383.

Thepharmaletter (2000) BASF sells pharma business to Abbott Labs for $6.9 billion in cash, *thepharmaletter*, 15th December 2000.

THES (2001), £4m gift for innovation centre, *Times Higher Education Supplemen*t, 31st August 2001.

Wells, F.A. (1966) Industrial Structure, in K.C. Edwards (ed.) *Nottingham and Its Region*, British Association for the Advancement of Science, Nottingham, pp405- 415.

Table 1

UK-owned Pharmaceutical companies, 1982

UK Ranking	*Company*	*Pharmaceutical sales (£m)*	*Pharmaceuticals % Total sales*	*World ranking*
1.	Glaxo	990.0	88.0%	18th
2.	ICI	839.0	7.0%	23rd
3.	Wellcome	837.0	80.0%	24th
4.	Beacham	782.0	31.3%	25th
5.	Boots	399.0	16.0%	42nd
6.	Fisons	206.0	36.0%	66th

Source: Owen (1999)

Table 2

Chronology of Manoplax development

Year	*Month*	*Action*
1979	July	Synthesis of BTS49465
1980	March	Animal tests start
1982	September	Tested on volunteers
1983	October	Clinical trial certificate
1983	November	Used in heart failures
1984	December	Approval inquiry starts
1985	May	UK Phase 2 dosage trials
1990	July	Phase 3 safety trials
1991	October	US heart panel approval
1992	August	License granted in UK
1992	September	Sent to UK doctors
1992	December	Licence granted in USA
1993	March	Launched in USA
1993	April	Warning on dosages
1993	July	Manoplax withdrawn

Source: Hoskings (1993)

Table 3
University spin-off companies at BioCity

	Company	Description	Start	University	Business model
1.	*CellAura Ltd*	Produces fluorescent agonists and antagonists for use in molecular pharmacology and imaging at the single cell level	2003	Nottingham	Service
2.	*CompanDX Ltd*	Utilizeses a range of proteomic genomic bioinformatics technologies to enable the discovery of novel biomarkers	2008	Nottingham Trent	Service
3.	*Critical Pharmaceuticals Ltd*	Developing proprietary drug delivery technologies for injectable sustained release drugs	2004	Nottingham	Product
4.	*CrossGen Ltd*	Developing microarrays using genome hybridization technology for species without sequenced genomes	2005	Nottingham	Service
5.	*Eminate Ltd*	Designs commercial applications of micro and nano particles, coatings and powders	2006	Nottingham	Product
6.	*Haemostatix Ltd*	Developing a protein based products to prevent or control different forms of bleeding	2003	Leicester	Product
7.	*Monica Healthcare Ltd*	Developing wearable devices utilizing wireless technologies for use in obstetric applications	2005	Nottingham	Product
8.	*Oxtox Ltd*	Developing a drug sensor that uses a novel technology to detect whether a person is under the influence of drugs	2006	Nottingham	Product
9.	*Pharminox Ltd*	Developing novel small molecule drugs for use in the treatment of cancer	2002	Oxford	Product
10.	*Promethean Particles Ltd*	Develops and manufactures bespoke nanoparticles for use in a range of industries	2008	Oxford	Service
11.	*q-flo Ltd*	Commercialising a continuous process to manufacture yarns of carbon nanotubes	n/a	Cambridge	Product
12.	*RegenTec Ltd*	Produces injectable scaffolds for use in regenerative medicine	2001	Nottingham	Product
13.	*X-Link Ltd*	Developing applications of the transglutaminase family of enzymes for wound healing and scar management	2000	Nottingham Trent	Product

Source: Ehret, McDonald-Junor and Smith (2012)

Table 4

Mergers and acquisitions in pharmaceuticals, 1989-2000

Year	Companies	Countries
1989	Dow/Marion	US/US
	Bristol-Myers/Squibb	US/US
	SmithKline/Beecham	US/UK
1990	Rhône-Poulenc/Rorer	France/US
	Roche/Genentech	Switzerland/US
1994	SmithKline Beecham/Sterling Health	UK/US
	BASF/Boots	Germany/UK
	American Home Products/ American Cynamid	US/US
	El Sanofi/Sterling Drug	France/US
	Roche/Syntex	Switzerland/US
1995	Glaxo/Wellcome	UK/UK
	Hoescht/Marion Merrell Dow	Germany/US
	Pharmacia/Upjohn	Sweden/US
	Rhône-Poulenc/Fisons	France/UK
1996	Ciba-Geigy/Sandoz	Switzerland/Switzerland
1997	Roche/Boehringer	Switzerland/Germany
1999	Hoescht/ Rhône-Poulenc	Germany/France
	Astra/Zeneca	Sweden/UK
2000	Glaxo Wellcome/SmithKline Beecham	UK/UK
	Pfizer/Warner-Lambert	US/US

Source: Owen (1999)

Figure 1: Towards an alternative path dependence model of local industrial evolution (Martin 2010, 21)

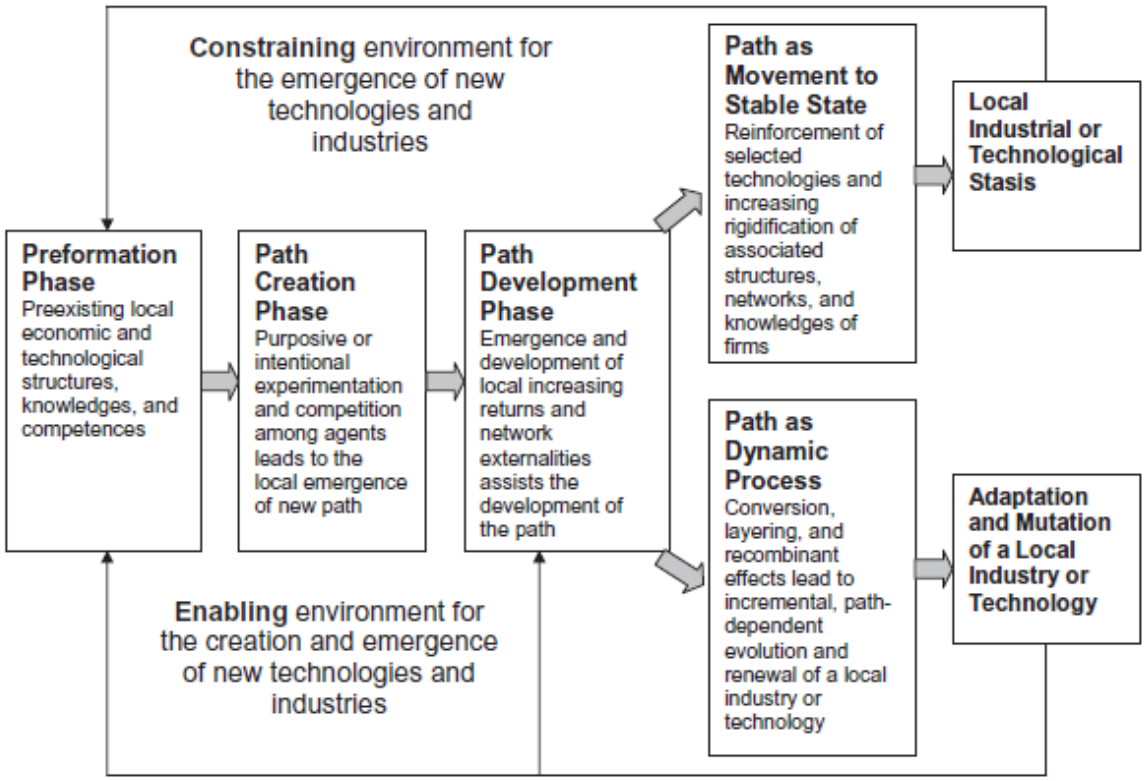


Figure 2 Simplified model of path creation loosely based on MSF

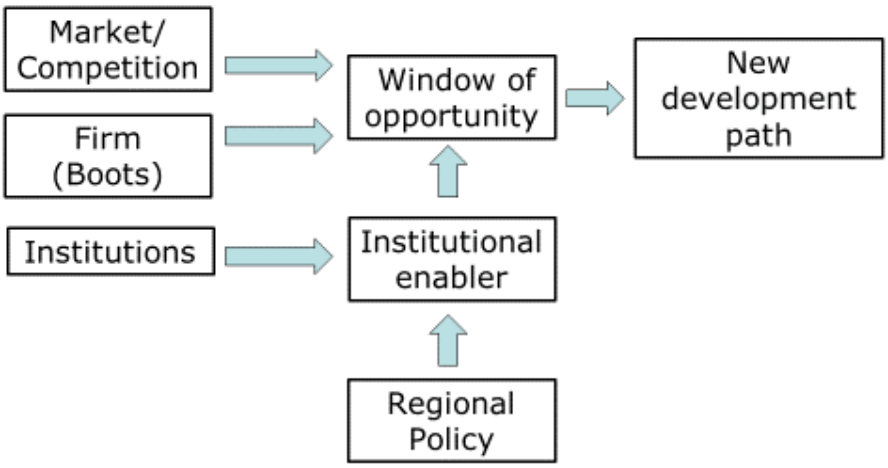
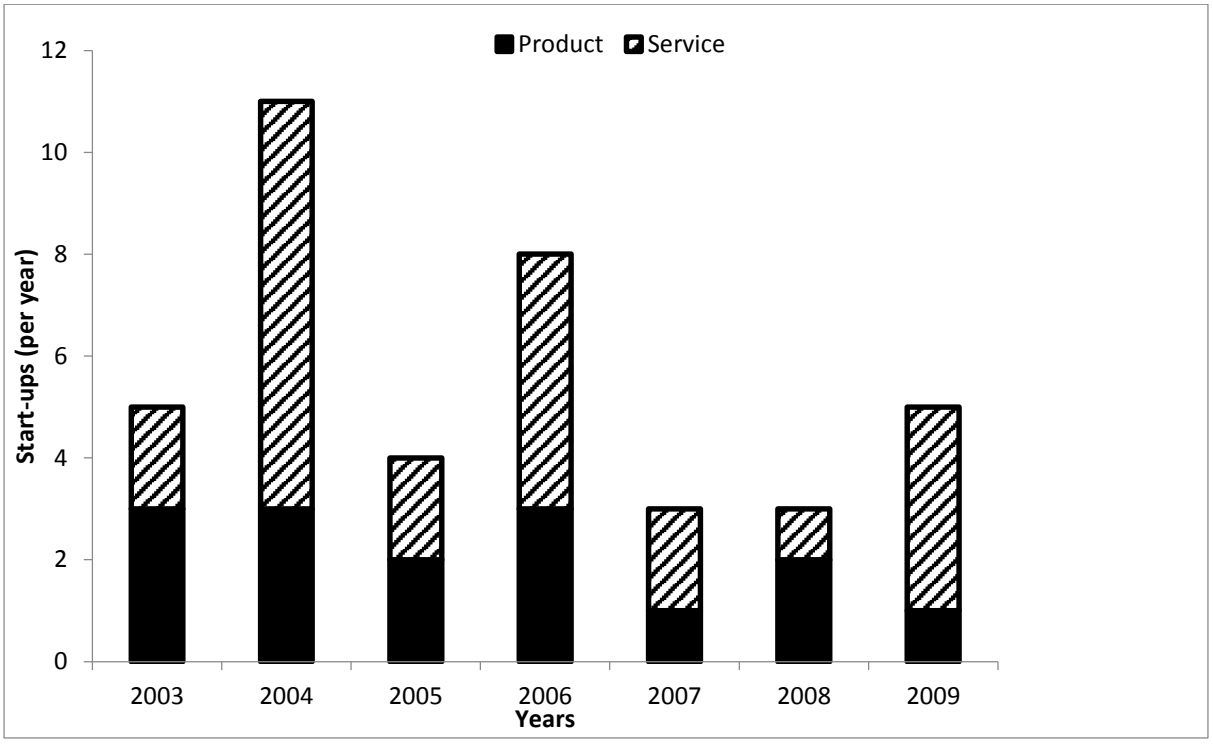
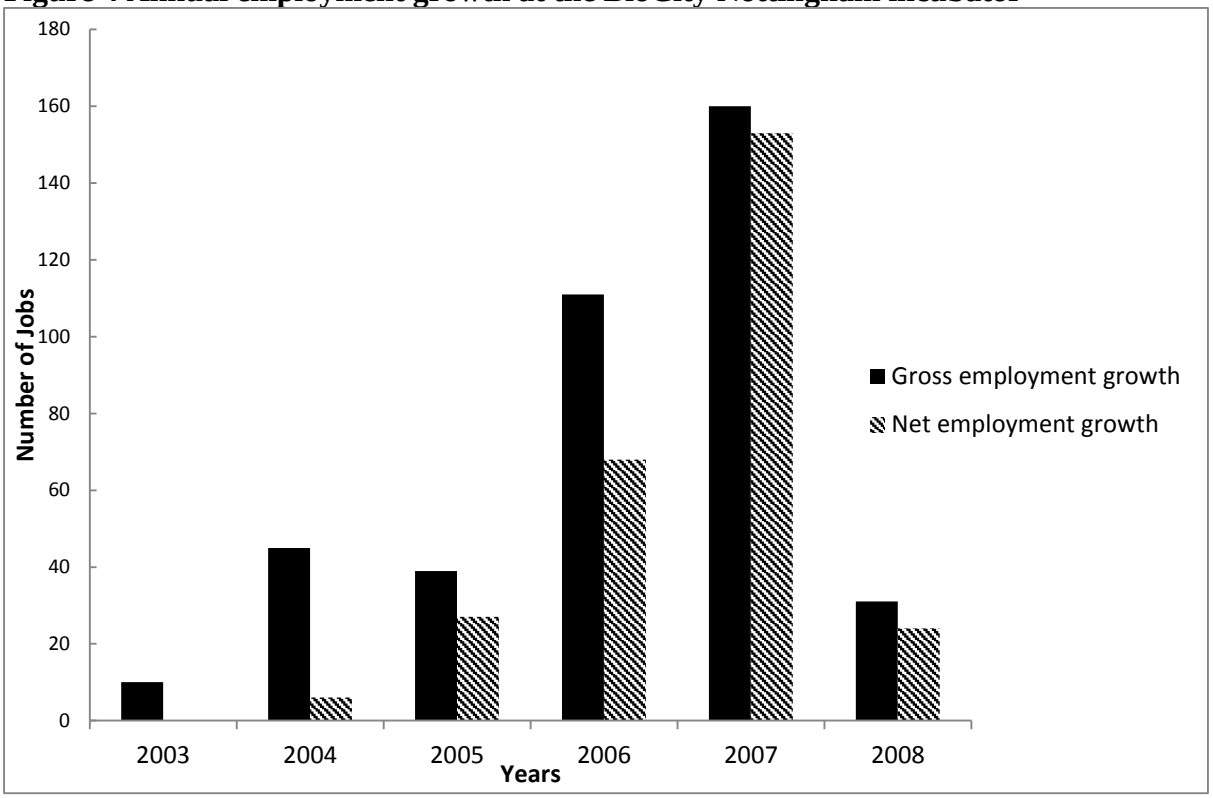


Figure 3 New Tenants at the BioCity Nottingham incubator (per year)



Source: Smith and Ehret (2013)

Figure 4 Annual employment growth at the BioCity Nottingham incubator



Source: Smith and Ehret (2013)

Figure 5
Location of research centres of excellence relating to biotechnology

DTI (1999)

Figure 6

The development of biotech in Nottingham