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The path- and place-dependent nature of scientific knowledge production in biotech 1986-2008

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Abstract

This study explores the worldwide spatial evolution of scientific knowledge production in biotechnology in the period 1986-2008. We employ new methodology that identifies new key topics in biotech on the basis of frequent use of title worlds in major biotech journals as an indication of new cognitive developments within this scientific field. Our analyses show that biotech is subject to a path- and place-dependent process of knowledge production. We observed a high degree of re-occurrences of similar key topics in biotech in consecutive years. Furthermore, slow growth cities in biotech are characterized by topics that are less technologically related to other topics, while high growth cities in biotech contribute to topics that are more related to the entire set of existing topics. Slow growth and stable growth cities in biotech introduced more new topics, while fast growth cities in biotech introduced more promising topics. Slow growth cities also showed low levels of research collaboration, as compared to stable and high growth cities.

Keywords: title words, branching, geography of biotechnology, scientific knowledge production, path dependence, place dependence

JEL codes: o33, r11, l65, d83

1. Introduction

When it comes to the geography of scientific knowledge production, there are opposing views. According to Friedman (2005) and others (e.g. Cairncross 1997), the world is increasingly flat. Scientific knowledge is believed not to be bound to a certain location because it is codified information that is easily transferable across geographical space through the Internet, scientific journals, international conferences and mobility of scientists (David and Foray 2002; Heimeriks and Vasileiadou 2008). This stands in contrast to the view propagated by Storper (1992), Florida (2004) MCann (2008), among others, that the world is spiky, not flat. Knowledge production is geographically concentrated, as shown by the fact that the world's most prolific and influential scientific researchers reside in a relatively small number of cities, primarily in the U.S. and Europe (UNESCO 2010). This is often attributed to the tacit dimension of knowledge, which does not travel easily over large distances (Gertler

2003). As geographical proximity is required to communicate tacit knowledge effectively between individuals and organizations, it tends to accumulate in space.

In such a global-local context, we investigate the nature and geography of scientific knowledge production in biotech over time. From an evolutionary perspective, we argue that existing scientific knowledge provides building blocks for further knowledge production. This cumulative and path-dependent nature of scientific knowledge production is likely to contribute to the spatial concentration of scientific activity in which cities and regions specialize in particular scientific fields. This is further reinforced by the increasing importance of global research linkages, which tends to favour a small number of big scientific hubs (Gertler and Levitte 2005; Laudel 2005; Gittelman 2007; Moodysson 2007; Zucker and Darby 2007; Trippl 2009). At the same time, scientific knowledge production is also subject to dynamics: new scientific fields and topics emerge, and new scientific growth regions appear now and then, while other scientific regions lose their importance, either in absolute or relative terms. The question then is whether new scientific topics are related to, and build upon existing topics, and to what extent new scientific newcomers are more likely to diversify and move into more unrelated scientific topics.

This study explores the dynamics in the geography of scientific knowledge production in biotechnology. We examine the extent to which scientific knowledge production in biotech is subject to a path- and place-dependent process. We use the accumulated body of codified knowledge in biotech as laid down in scientific publications during the period 1986-2008 as data for our analysis. Biotechnology is particularly interesting, because knowledge production is characterised by rapid growth, dynamics in divergent fields ,new complementarities in which knowledge from various disciplines are recombined, and the rise of scientific newcomers, especially in Asia (Bonaccorsi 2008; Heimeriks and Leydesdorff 2012). Grasping the fruits of these emerging biotech fields is an objective of many government programs, because of its high economic growth potential (OECD 2009).

This paper aims to make two contributions. First, we explore new methodology to identify and measure the dynamics in scientific knowledge production (Foray 2004; Leydesdorff 2001). We identify new key topics in biotechnology on the basis of the frequent use of title words in major biotech journals as an indication of new cognitive developments within this scientific field for over a period of 20 years. Second, we test whether dynamics in knowledge production in biotech is a place-dependent process of a path-dependent nature. For that purpose, we use information on the evolution of scientific topics to test whether cities excel in particular topics over time. Then, we develop an indicator of relatedness between major scientific topics in biotech by means of co-occurrence analysis of title words in academic journal publications. We use that information to test whether cities diversify into new topics that are related to existing scientific topics, and whether fast-growing newcomers in biotech science (i.e. new growth cities) expand in more unrelated topics.

The paper is structured as follows. In Section 2, we set out theoretically why we expect that scientific knowledge production is characterized by a path- and place-dependent process. Section 3 identifies the scientific field of biotech on the basis of publication data, and explores regional growth paths of knowledge production in biotechnology worldwide. In Section 4, we present the geography of scientific topics as proxied by title words in biotech papers. We investigate whether differential growth rates of cities in terms of biotech output (i.e. high-growth, stable growth and slow growth) are linked to distinct patterns in the dynamics of biotech topics in cities (as proxied by the rise and fall of title words). In Section 5, we look at the geography of cognitive relatedness between biotech topics based on co-occurrences of title words, and the extent to which the evolution of topics in cities is subject to a path-dependent process. Section 6 examines research collaboration between cities, and investigates whether differential growth rates of cities can be associated with the nature of research collaboration with other cities. Section 7 draws some conclusions.

2. The path- and place-dependent nature of scientific knowledge production

In evolutionary thinking, it is common to describe knowledge production in terms of a cumulative, interactive and path-dependent process. Because of uncertainty and bounded rationality, actors build on knowledge they have acquired and become familiar with in the past. Due to its tacit and cumulative nature, knowledge is actor-specific and difficult to copy by others. Cohen and Levinthal (1990) have argued that researchers and organisations can understand, absorb and implement external knowledge when it is close to their own knowledge base. As a result, actors develop different cognitive capacities over time (Nelson and Winter 1982).

This path-dependent nature of knowledge production often takes place at the regional level, as shown by the extreme spatial concentration of scientific activity (see e.g. Frame, Narin and Carpenter 1977). To transfer tacit knowledge, close and intensive face-to-face contact between humans and organizations is needed, and geographical proximity is a vehicle to accommodate this type of communication (Gertler 2003). The regional innovation system literature has pointed to the importance of local institutions that enable interactions between organizations that sustain learning and innovation (Asheim 1996; Cooke 2001). Knowledge accumulates at the regional level because key mechanisms through which knowledge diffuses across organizations are often spatially bounded (Capello 1999; Boschma and Frenken 2011). This applies to the spinoff process, in which new firms tend to exploit the knowledge acquired at their parent organizations in the same location as their parents (Klepper 2007). Also labour mobility tends to transfer knowledge and skills primarily between local organizations (Eriksson, 2011). There is ample evidence that research collaboration is triggered by geographically and socially proximate partners (Breschi and Lissoni, 2009), as for example in the case of university-industry research collaboration, in which an increase in geographical distance decreases the frequency of research collaboration (see e.g. Katz 1994; Hoekman, Frenken and Van Oort 2009). And even when mobility of researchers is international, this tends to reproduce and reinforce the spatial concentration of scientific activity, as scientific hubs not only retain but also attract leading scientists (Laudel 2005; Zucker and Darby 2007; Trippl 2009).

Consequently, the path-dependent nature of knowledge dynamics is often place-dependent. This explains why regions tend to specialize in knowledge activity, because they provide opportunities for the transmission of sticky, non-articulated, tacit forms of knowledge between local actors. As knowledge accumulates in space and is spatially sticky (Markusen 1996), inter-regional variety of knowledge is a common phenomenon. What constitutes a research opportunity and how it is dealt with, are locally situated. The scope of opportunities for researchers to contribute within the constraints of the existing body of knowledge are different in each location. With the growing specialisation in science and the progressive professionalization (Cronin, Snyder, Rosenbaum, Martinson and Callahan, 1998), it is becoming increasingly difficult for a researcher to possess the necessary skills and knowledge to solve problems alone. The highly durable capital assets and the information channels and codes required by multi-person organizations to function efficiently, provide path-dependent constraints in the evolution of local institutions (David, 1994). Especially established sciences make use of large physical infrastructures.

But of course, scientific knowledge production is not developing exclusively at the local level. Successful knowledge regimes require synergetic interactions among local research practices and the emergent scientific landscape. Large numbers of researchers around the world interact in both competitive and collaborative relations which are characterized by heterogeneity, and with no overall direction. Science is a global, collective and distributed system where the sequence of knowledge claims constitutes the research front of a field, and brings the field further by emphasizing differences with previous claims (Fujigaki 1998). Science is adaptive and co-evolving because both the science system and its constituent researchers respond to changing environmental conditions such as shifts in research priorities of granting organisations as well as new discoveries and changing contexts of (commercial) application. Science is recognisably a system, a collection of individuals and institutions contributing to a common body of knowledge (Wagner 2008). This gives rise to an emergent science system with limited predictability. It can lead to a relatively stable, path-dependent definition of the field, in as far as the knowledge claims remain referring to a common literature, which constitutes the intellectual foundation of the field. When a field is stabilized in this way, the process of circular causality may lead to further stabilization and even globalization: researchers are inclined to position themselves in this intellectual base and research front.

However, new scientific fields also emerge, and new growth regions also appear now and then. When locally embedded knowledge is combined in novel ways with codified and accessible external knowledge, new knowledge and ideas are created. The evolutionary approach to knowledge creation has put a lot of emphasis on incremental knowledge production, and has not always been keen on describing discontinuities and regional dynamics (Hollingsworth 2009). However, we believe that processes of new path creation and path dependence interact to shape geographies of transformation, in which such processes are themselves place-dependent (Boschma and Martin 2010). Consequently, new knowledge creation is expected to be characterised by a path-dependent process of branching in which new knowledge is developed from existing knowledge, skills and infrastructures.

We claim that new scientific topics rely on a whole series of subsequent topics and insights. Kauffman (1995) has coined a name for the set of all those first-order combinations; "the adjacent possible". The phrase captures both the limits and the potential of change and innovation in research topics. The adjacent possible defines all those new topics that are directly achievable from an existing set of skills and insights. The adjacent possible is a kind of shadow future, hovering on the edges of the present state of knowledge. It provides a map of all the ways in which the present can reinvent itself form a current set of topics.

Recent studies in economic geography suggest that regions diversify and expand into industries that are closely related to their existing activities (Neffke, Henning and Boschma 2011). This process of branching is expected to occur primarily at the regional level, because it becomes manifest through mechanisms that tend to be geographically bounded. But this branching process might also need a degree of unrelatedness to diversify in completely new directions. There is indeed some evidence that the bridging of research collaborators that are cognitively distant from each other might lead to more radical breakthroughs (Gilsing et al. 2007; Lambiote and Panzarasa 2009) and new scientific fields (Lucio-Aria and Leydesdorff 2009). Therefore, we expect that regions diversify into new topics that are related to existing scientific topics, whereas new fast-growing science regions (i.e. scientific newcomers) are more likely to move into more unrelated fields of science.

3. Data, methods and some descriptives

In Section 3.1, we set out how we determined the field of biotechnology by means of journal-to-journal citations patterns, and which scientific publications will be selected to conduct the analyses. In Section 3.2, we describe the geography of biotech on the basis of the spatial pattern of scientific publications in biotech for the period 1986-2008. This will give a glimpse of the stability and dynamics of the geography of biotech worldwide. In addition, we will select a category of three types of cities (high growth, stable growth and relative decline in biotech output), which we will use in the analysis of the evolution of the geography of biotech topics in Section 4.

3.1 Identification of scientific field of biotechnology

Scientific communications are extremely well archived, and therefore, we have a wealth of data at our disposal. In this study, we use the accumulated body of codified knowledge in biotechnology for the period 1986-2008, as put down in scientific publications. We could have used patent data instead, but licensing and patent practices are expected to differ among national innovation systems (Nelson 1993).

The field of biotech is delineated using journal-journal citation patterns (Leydesdorff and Cozzens 1993). This method is based on a factor analysis of the journal-journal citations matrix of the core journal of a specialty, in this case *Biotechnology and Bioengineering* (Leydesdorff and Heimeriks 2001). The relational citation environment of that journal can be determined by using a threshold of 1%. For the resulting set of journals, we can make a journal-journal citation matrix, with citing behaviour as the variables. A factor analysis of this matrix results in factors consisting of journals that show similar citation patterns. The factor on which the core journal has it highest loading represents the field under study. The other factors represent a set of research fields that are related to the field under study.

The outcome shows that biotechnology is surprisingly stable in terms of its journal structure, consisting of three main journals: *Biotechnology and Bioengineering, Biotechnology Progress* and the *Journal of Biotechnology*. In the entire period, among the journals that together define the field of biotechnology, *Biotechnology and Bioengineering* not only has the highest impact factor of the set, it also has the highest factor loading on the factor indicating biotechnology. Around the field of biotechnology, the neighbouring fields of microbiology, water research (including environmental sciences in later years), biochemistry and chemical engineering are to be found in all years. Consequently, the self-organising process of researchers that position themselves in terms of the intellectual base and the research front reinforce the stability and global generalization of the field. This has led to a relatively stable and path-dependent definition of the scientific field of biotech.

After obtaining this set of journals, all publications for the period 1986-2008 were downloaded from the Web of Science. The total set of publications consisted of 13,386 articles. As shown in Figure 1, the annual number of scientific publications in biotechnology shows a steady increase in the period under study.

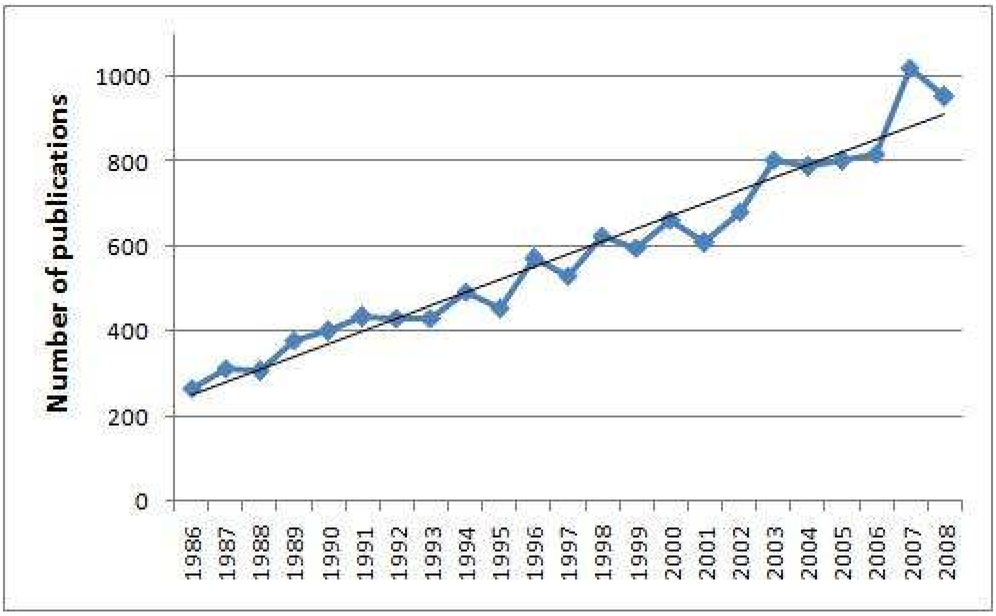

Figure 1. *Number of scientific publications in the field of biotechnology (1986-2008)*

3.2 The spatial evolution of biotechnology

Each publication in our dataset contains one or more institutional addresses that enable us to specify the location of the university and the company authors are affiliated to. All addresses in the publication set could be provided with geo-coordinates at http://www.gpsvisualizer.com/geocoder/. Yahoo! was used for obtaining the coordinates. From this geographical information, we can derive information about local path-dependent dynamics and collaboration patterns based on co-authorships (Leydesdorff and Persson, 2010).

Our study confirms the finding of other studies (see e.g. Cooke 2006b) that there is a process of ongoing globalisation in biotech research, as reflected in the increasing number of countries that contribute to scientific publications in the field of biotech in the period 1986-2008 (see Figure 2). While the number of countries that contributed to the field of biotech was 32 in 1986, this number had risen to 54 in 2008.

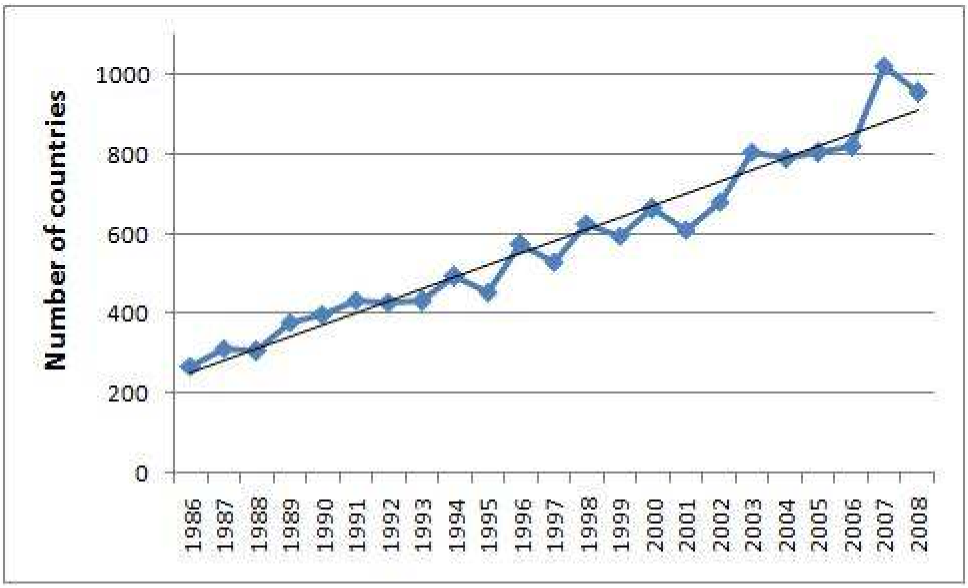

Figure 2 *Number of countries contributing to scientific publications in the field of biotechnology (1986-2008)*

Furthermore, the past decades have seen a remaking of the global map of world science in biotech in the period under study, as depicted in Figure 3. A bipolar world in which biotech science is dominated by the EU, Japan and the US is gradually giving way to a multi-polar world, with an increasing number of public and private research hubs spreading across North and South. In general, knowledge production in biotech seems to shift away in relative terms from the US towards Asian regions, most importantly Seoul, Tokyo, Beijing and Singapore. The contribution of American scientific institutions to publications in biotech has continued to rise in sheer numbers over the past decades. The US and other scientifically advanced countries have maintained slow growth. European knowledge production in biotechnology shows a rather stable pattern, especially since the mid 1990s. This means that Europe seems to keep pace with increased competition, but is no longer able to improve its global share in biotech. The development shown here reflects the process of ongoing globalisation and the consequent escalation in scientific competition (UNESCO, 2010). The increasing number of publications and the rising number of contributing countries indicate a growing emphasis on science and innovation in many countries worldwide. As this happens, the US and the EU drop as a percentage share of all publications. The drop in percentage share is however not an absolute loss of ground.

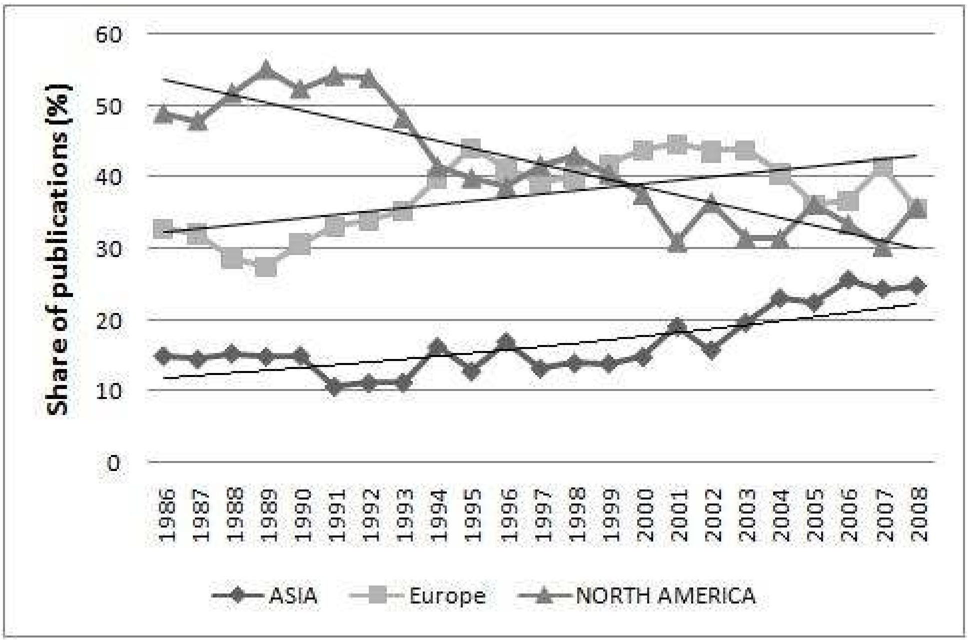

Figure 3. *Share of scientific publications of different continents in the field of biotechnology (1986-2008)*

In Figure 4, we show the relative importance of a few selected countries. China shows exponential growth. This spectacular and hitherto sustained pattern of growth may be due to the increasing availability of human capital at Chinese universities and research institutions for publishing in ISI-listed journals, as well as to incentives within China to publish in refereed journals (Zhou and Leydesdorff, 2007). South Korea also shows a steady increase. In most recent years, the growth of the Korean share seems to level off, but this is not yet significant as a trend breach.

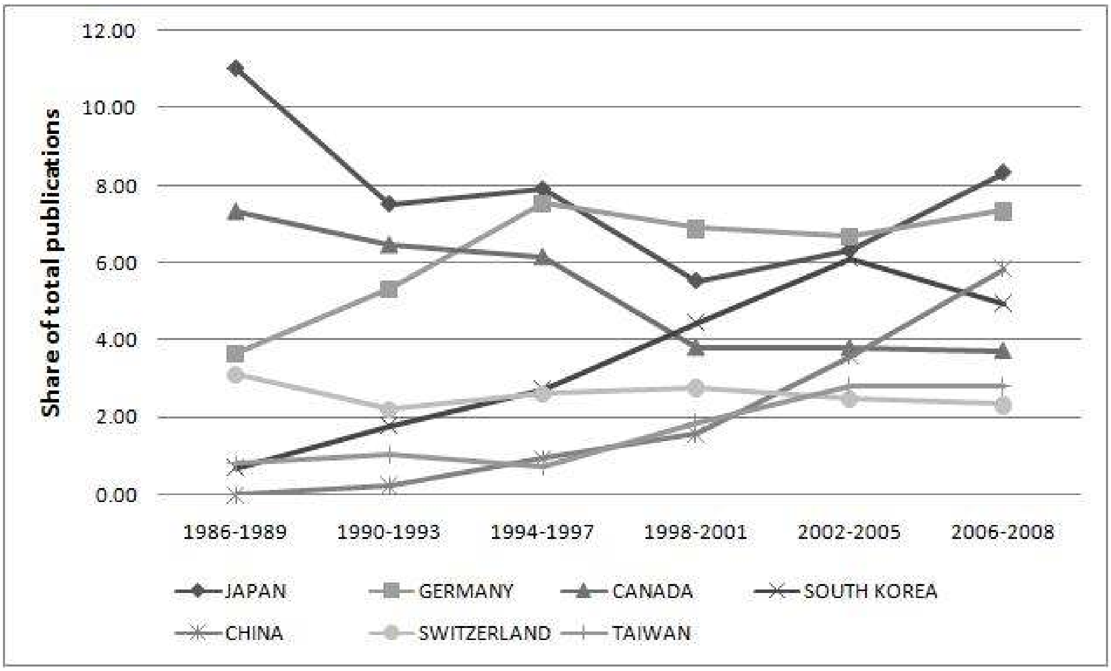

Figure 4*. Shares of selected countries with respect to scientific publications in biotech in percentages for period 1986-2008*

The author addresses included in ISI Web of Science allow us to specify the geographical location of each research organisation on the city level as provided by the Yahoo! geo-coordinate tool. The distribution of publications per city shows a skewed pattern. In the period under study, research organisations from 2,027 unique cities contributed to publications in biotech. Of these, 1,243 cities were involved in more than 1 publication. Sixty cities contributed to more than 100 publications in the period 1986-2008. Cambridge, USA (431), Wageningen, Netherlands (353), London, UK (352) and Seoul, South Korea (350) are the most important cities in biotechnology knowledge production. However, the growth patterns are even more pronounced and turbulent than on the country level. Especially Asian cities such as Seoul and Beijing exhibit very fast growth rates (Table 1).

The most important cities in biotech knowledge production all host several organizations (companies, universities and public research organizations) that contribute to biotech publications in the period under study. However, since the names of these organizations are not standardized, it is impossible to determine the precise numbers of organizations. Furthermore, some organizations change names, others merge, and sometimes spin-offs are established. Consequently, cities are a more appropriate unit of analysis, in line with the expectation that knowledge transfer mechanisms like labour mobility and spin-offs tend to be geographically bounded.

The cities contributing to scientific knowledge production in biotechnology exhibit different growth patterns. Although some cities exhibit fluctuating rates of knowledge production, some general patterns can be observed. As Table 1 shows, the most important cities (in number of publications in biotech) can be categorised as fast growth cities, slow growth cities and stable growth cities. To the 29 most important cities, we added Ankara as an additional example of a fast growth city in order to arrive at 10 slow growth cities (2,454 publications in total), 10 stable growth cities (2,095 publications) and 10 fast growth cities (2,239 publications) for further analyses. Together, these cities produce more than 40% of all publications in biotech.

Table 1*. Most important cities in Biotechnology can be categorised as fast growth cities, slow growth cities and stable growth cities.*

City, country	rank 1986-1992	(number of publications)	rank 2001-2008	(number of publications)	Total number of publications	Growth catagory
Cambridge+USA	1	(126)	10	(153)	431	slow
Wageningen+Netherlands	27	(26)	5	(185)	353	stable

London+UK	15	(32)	4	(191)	352	stable
Seoul+South Korea	28	(26)	1	(259)	350	fast
Taejon+South Korea	65	(14)	2	(202)	346	fast
Zurich+Switzerland	5	(56)	6	(180)	346	slow
Tokyo+Japan	6	(55)	7	(175)	325	slow
Delft+Netherlands	9	(41)	13	(146)	294	slow
Lund+Sweden	16	(32)	9	(162)	273	stable
Montreal+Canada	3	(72)	23	(102)	255	slow
Lyngby+Denmark	103	(7)	3	(201)	254	fast
Baltimore+USA	75	(12)	14	(138)	252	stable
Braunschweig+Germany	30	(24)	18	(121)	247	stable
Lafayette+USA	2	(89)	26	(97)	233	slow
Osaka+Japan	10	(41)	21	(109)	221	slow
Ithaca+USA	12	(39)	27	(97)	216	slow
Stockholm+Sweden	29	(15)	49	(97)	160	slow
Berkeley+USA	13	(33)	19	(119)	214	slow
Madrid+Spain	104	(7)	11	(149)	206	fast
Houston+USA	19	(30)	17	(126)	205	stable
Vienna+Austria	90	(9)	16	(127)	200	fast
Pittsburgh+USA	32	(24)	39	(82)	190	slow
Bielefeld+Germany		(0)	8	(167)	180	fast
Singapore+Singapore	136	(4)	12	(147)	175	fast
Boston+USA	45	(18)	44	(77)	164	stable
Beijing+Peoples R China	175	(1)	15	(138)	159	fast
Lausanne+Switzerland	84	(10)	22	(105)	148	stable
Graz+Austria	63	(15)	34	(90)	132	stable
Shanghai+Peoples R China	159	(2)	33	(91)	120	fast
Berlin+Germany	86	(10)	54	(69)	113	stable
Ankara+Turkey	161	(2)	20	(82)	105	fast

Slow growth cities typically exhibit a steady growth in their publication output in the period under study, but lose as a percentage share of all biotech publications. Overall, these results indicate that there are only limited advantages to first movers in biotech. All slow growth cities were important contributors in biotechnology in the early years (1986-1992), but they dropped in the ranking in later years (2001-2008). On average, these cities dropped 10 places in the rankings of most important contributors comparing the first and the last period. The slow growth cities are all located in Japan, Europe and especially the US.

Like slow growth cities, stable growth cities were typically early contributors to knowledge production in biotechnology. However, stable growth cities managed to increase their relative share of publications and rise in the ranking of the most important biotechnology knowledge producers. Most of these stable growth cities are located in Europe, while a smaller number is found in the US (Baltimore, Houston and Boston).

In contrast, fast growth cities in biotech were relatively minor or non-existent contributors to biotech publications in the early period under study, but managed to achieve a dominant role in biotechnology in later years. This is reflected in an average jump of more than 100 positions in the rankings between the first and the last period. Many of these fast growing cities are found in Europe and Asia, especially in South Korea and China.

A small number of cities can be classified as 'declining'. As shown in Table 2, these cities typically exhibit a steady decline in their publication output in the period under study, losing their position as important contributors to biotechnology. Most of these declining cities are located in the US. This category of cities has not been included in our analyses, because they represent only a very small number of publications in the dataset.

Table 2. *The declining cities in biotechnology during period 1986-2008*

City	rank 1986-1992	(number of publications)	rank 2001-2008	(number of publications)	Total number of publications	Growth catagory
Ann Arbor+USA	8	(44)	>200	(27)	120	decline
Pasadena+USA	4	(59)	>200	(20)	99	decline
Raleigh+USA	14	(33)	>200	(24)	95	decline
Irvine+USA	73	(13)	>200	(12)	56	decline
Ottawa+Canada	34	(24)	>200	(23)	54	decline
Durham+USA	60	(16)	>200	(15)	43	decline
Vandoeuvre Nancy+France	119	(6)	>200	(0)	42	decline
Compiegne+France	54	(17)	>200	(9)	39	decline
New Brunswick+USA	61	(16)	>200	(3)	31	decline
Buffalo+USA	55	(17)	>200	(6)	29	decline

4. The geography of topics in biotech

The previous analyses showed that scientific discovery in biotech is geographically concentrated. But to what extent is scientific knowledge production in cities subject to a path-dependent process? As discussed before, we expect spatial clusters of similar and related knowledge-based activities to provide opportunities for the transmission of sticky, non-articulated forms of knowledge between local actors. In that respect, we expect cities to specialize in certain fields in biotech. Is new knowledge at a given location related to previous knowledge production? In other words, can the research dynamics in cities be described as a process of branching?

A major challenge is to identify the most important cognitive developments in biotech science. During the 1980s and 1990s, the biotechnological knowledge base underwent a structural change (Krafft et al., 2011). The events that catalysed the first industrial applications in biotechnology occurred in the early to mid 1970s (1972 recombinant DNA, 1975 monoclonal antibodies), but only in the mid 1980s the new knowledge started to be adequately integrated into the knowledge base of biotechnology firms. This transition meant a shift from exploration to exploitation. A declining rate of growth of technological variety occurred in the second half of the 1990s.

The structure of the knowledge base in biotech has been characterized by the existence of a strong core, with some older topics becoming extinct or losing importance (related to food preservation and organic chemistry) and with some new ones emerging and becoming important components of the knowledge network (related to molecular biology and physical measurements). The use of title words in the set of biotech publications provides us with an indication of the cognitive developments within the field. Our publication records provide title words, in addition to institutional addresses. Several scientometric indicators have been develop based on title words to trace the development of science (e.g. Leydesdorff 1989). These quantitative methods rely on measuring relations between different pieces of information, for example, words in sentences (Leydesdorff 2006). The information is thus positioned in a network with an emerging (and continuously reconstructed) structure (Leydesdorff 2010). In this way an evolving discourse of scientific knowledge can be measured by using words and their co-occurrences as the observable variation.

In a first step, we looked at the most frequently used title words in the field of biotechnology in the period under study, which are presented in Table 3. Some topics seem to lose some of their relevance in the field and move down the ranking of important keywords, like ‘fermentation’, ‘enzyme’ and ‘reactor’. Other topics become more prominent, such as ‘recombinant’, ‘expression’ and ‘gene’.

***Table 3**. Most important title words in biotechnology in the period 1986-2008*

Word	**rank 1986-1992**	**rank 2001-2008**	**Total number of publications**
cell	1	1	2529
production	2	2	1894
protein	8	3	1441
culture	3	4	1411
effect	5	5	1097
coli	13	8	948
recombinant	**18**	**7**	**929**
system	11	9	902
Escherichia	14	10	861
growth	6	16	832
Expression	**27**	**6**	**795**
Kinetic	10	17	708
analysis	21	12	697
acid	19	13	693
fermentation	**4**	**20**	**691**
Bioreactor	17	14	682
model	16	15	622
Gene	**39**	**11**	**589**
enzyme	**15**	**26**	**537**
reactor	**12**	**32**	**516**
human	**51**	**21**	**449**
Membrane	**24**	**34**	**430**
aqueous	**82**	**138**	**204**
biosynthesis	**410**	**234**	**85**
genome		**295**	**51**

Then, we investigated whether the observed growth patterns in the three categories of cities in terms of scientific output (high-growth, stable growth, slow growth) are related to distinct patterns in biotech topics in terms of the rise, stabilization and fall of title words. As explained earlier, we expect cities to specialize and develop different cognitive capacities over time. We envisage that these local path dependencies can be associated with differential growth rates of cities because cities specialize in topics that are rising, dominant or declining in relative terms within the scientific domain of biotech. That is, are slow growth cities associated with biotech topics that lose importance? In other words, do topics that "die out" occur mainly in cities with a declining contribution to knowledge production in biotech? And do fast-growing cities contribute to new influential topics in biotech? And are stable growth cities mainly using leading, stable title words in biotech? As shown in Figures 5 and 6, we do indeed find such distinctive patterns across the three types of cities.

In Figure 5, we show on the X-axis several title words that have lost importance and have become more marginal in biotech over time, as shown on the Y-axis by means of the total number of publications in which these title words occur. As shown, these title words are used much more frequently in slow growth biotech cities, as expected, as compared to the two other more successful categories of biotech cities.

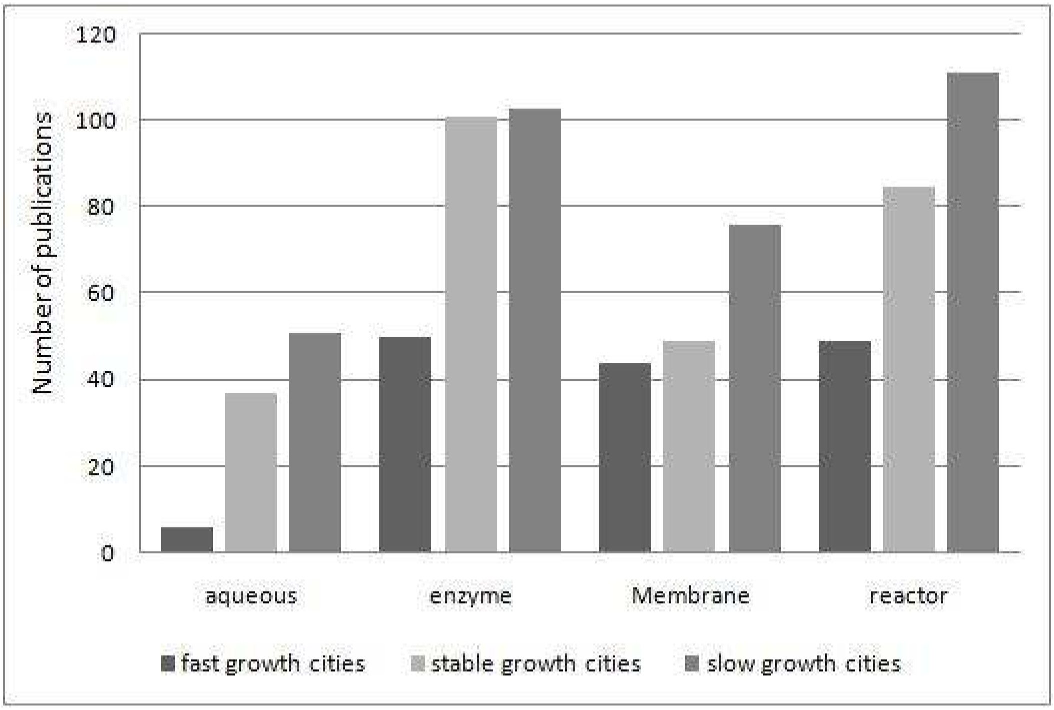

Figure 5 *Distinct patterns of declining title words across the three categories of cities*

In Figure 6, we show the use of title words that are relatively new and growing rapidly in biotech. As expected, the fastest growing cities (in terms of scientific output in biotech) contribute much more to the most turbulent (rapidly growing) topics in the field of biotech, leaving behind the two other categories of cities.

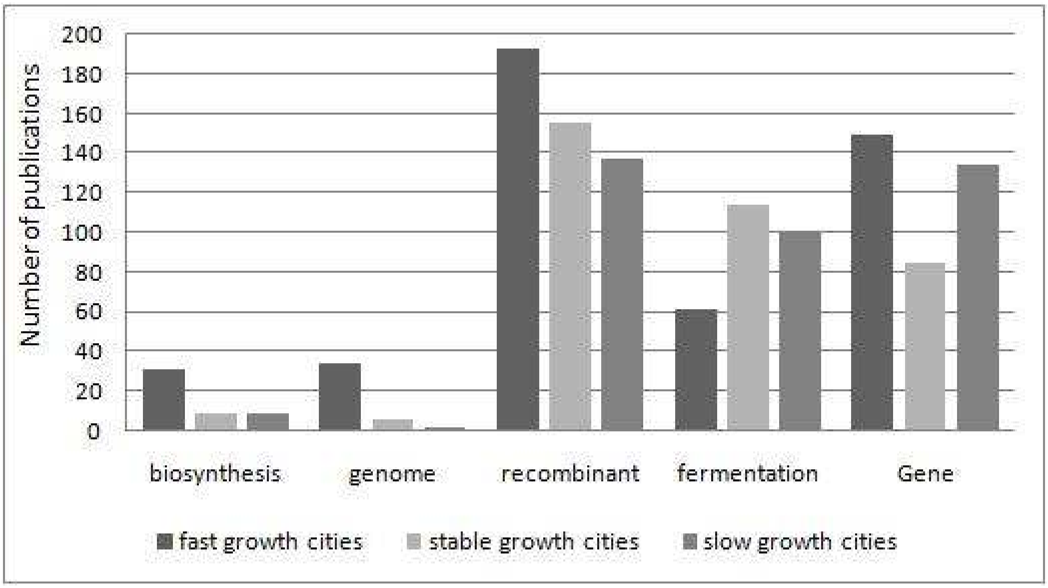

Figure 6. *Distinct patterns of new and rapidly growing title words across the three categories of cities*

The development of topics is in line with the observations of Krafft et al. (2011) with a declining role of organic chemistry and an increasing role of molecular biology and genomics. The rise and fall of cities in the ranking of biotechnology knowledge production seems to coincide especially with the rise of genomics in biotechnology. According to Saviotti and Catherine (2008), the transition to genomics based technologies led to a discontinuity in the pattern of knowledge production because the competencies required in the new practices differed as bioinformatics acquired a key role in the sequencing of genomes.

In addition to the important topics discussed above (featuring in a large number of publications), many smaller topics have appeared in the period under study. Many of these topics only originate from a small number of locations. Table 4 gives examples of 7 selected title words and their re-occurrence in selected cities. For example, 39 out of a total of 63 publications with “fluorescent’ in its title originate from Baltimore, USA. The results indicate strong local path dependencies that contribute to a recursive pattern of topics. Once a research organization contributes to a topic, it can be expected to work on the same topic again. These examples provide further indication of the pattern of path dependent specialization over time.

Table 4. *Selected title words in biotechnology in the period 1986-2008 and their (re-) occurrence in selected cities.*

fluorescent																								**63**
Baltimore, USA												7	4	1	6	2	12		2	5				39
fiber																								**71**
Cambridge, USA		1	1	5	1	3		1		1														13
Tokyo, Japan					2	1	1	1	1					1			1							8
fermentation																								**307**
Lund, Sweden		3	1		3				1	2	1	2			2	1	4		1		2		5	28
Cambridge, USA			3	1	9	5	2	1		2	1	1												25
Lafayette, USA	2	1	1	6	5	3	1		1	3												1		24
Wageningen, Netherlands															2	6	8	4	3					23
Membrane																								**185**
Tokyo, Japan		2		3	4	1	1		2	2		1		1	1		2	1	1	4	2	1	3	32
London, UK	2		1					2	2	3	2	1	3	1	1			2		1	1			22
Seoul, South Korea		1			1		1				2			2		2				5	2			16
Gene																								**403**
Seoul, South Korea			1			1		1	2		2				2		1	6	5	8	4	10		43
Tokyo, Japan				1	1				5	1	4	1	1	1				3	3	2	1	3	6	33
Bielefeld, Germany														1			1	13			5	2	7	29
Osaka, Japan		1						1	1		1				1	3			2	5	3	2	7	27
Taejon, South Korea						1				1	2		5	3	1	2	3	1	1		2			22
recombinant																								**526**
Taejon, South Korea									6	1	7	1	6	9	3	10	3	4	7	6	2	3	6	74
Braunschweig, Germany					1		1		4	5	2	1	3	6	2	1	8		6	7		6		53
Seoul, South Korea			1		1						2	4	2	2		2	3	2	1	9	6	3	3	41
London, UK									5	2	2		3		2	2	3	3	3				8	33
Osaka, Japan		2	1	2	1				3		1	1	1		1	1					4		11	29
Vienna, Austria											1		1		2	1	2	2	3	1		6	7	26
Bioreactor																								**323**
Wageningen, Netherlands		1					2		3	2		3	3	1	2	3	4	3	4	2	2	2	2	39
Cambridge, USA			1	2	1	3	1	3		3	3			1		1	4		2		3	2		30
Montreal, Canada			1		4	2	1		2		2			2	2		1			1	3		7	28
Houston, USA			2	1	5	1					1				3	1	4		4		1	1		24
London, UK						1		3	2	1	1		3	1	4			1		2	1		3	23

5. Geography of cognitive relatedness between topics in biotech

In the next step, we conduct more systematic cognitive analyses of biotech topics to find out the level of path dependency in knowledge production, to what extent title words are related, to what extent new topics build on existing topics, and how these knowledge dynamics in biotech science may be characterized in the three types of cities. In Section 5.2, we conduct co-occurrence analysis to measure the relatedness between research topics in biotech by assessing whether title words are often found together in one and the same paper. In Section 5.3, we investigate the extent to which new scientific topics rely on the existing set of topics, to provide evidence for the 'adjacent possible', and how this differs in the three types of cities.

5.1 Re-occurrence analysis: path and place dependency in biotech

Topics of the past—embodied in skills, infrastructures and specific competencies—are expected to influence subsequent choices of method, designs, and practices. This logic of path dependence applies to locations of knowledge production as well, and can be made visible by the re-occurrence of topics at each location. In Section 4, we already found indications that scientific knowledge dynamics in biotech is indeed a path-dependent process with a place-dependent dimension. Further indication of this pattern of path dependency in research topics at different locations is provided by the re-occurrence of words in consecutive years. This way, we can quantify how often a location of research in biotech contributes again to the same topic in the next year, thus providing evidence for the path and place dependent pattern of knowledge production.

In Table 5, we present the average number of re-occurrences of title words for the period 1986-2008. The results show that for each type of city the extent to which the same topics re-occur differs. Slow growth cities are most path dependent in the use of title words, closely followed by stable growth cities, while fast growth cities show the lowest degree of path dependence in terms of re-occurrences of topics in biotech.

Table 5*. Average number of re-occurrences of title words in biotechnology in the period 1986-2008*

	average number of re-occurring words per publication
Fast Growth	1.33
Slow Growth	1.45
Stable Growth	1.43

5.2 Co-occurrence analysis: relatedness between title words in biotech

Systematic evidence is becoming available that shows that territories are more likely to branch into activities that are closely related to their existing activities (Hidalgo, Klinger, Barabasi and Hausmann 2007; Neffke et al., 2011; Boschma et al., 2012). Scholars have turned to co-occurrence analysis to assess these dynamics of branching and relatedness. Co-occurrence analysis measures the relatedness between two events by assessing whether they are often found together in one and the same economic entity. Hidalgo et al. (2007) counted the number of times that two industries showed a revealed comparative advantage (the co-occurrence) in the same country (the economic entity). Similarly, Teece, Rumelt, Dosi, and Winter (1994) and Bryce and Winter (2009) counted the number of times one firm (the economic entity) owned plants in two different industries (the co-occurrence).

In our case, co-occurrence analysis measures the relatedness between research topics by assessing whether title words are often found together in one and the same scientific publication. The aim of this analysis is to determine the extent to which knowledge production at a number of selected locations is path dependent; is new scientific knowledge at a given location related to previous knowledge production? In other words, can the local research dynamics be described as a process of branching?

We constructed matrices of word-word co-occurrences to provide information about the relatedness of words and topics in biotech science. Callon *et al.* (1983) proposed developing co-word maps to the study of semantic relations in scientific and technology literatures. Based on the co-occurrence of words, co-word analysis has been used to discover linkages among subjects in research fields and describe the development of science. These techniques for co-word analyses have been developed further (Callon, Law and Rip 1986; Leydesdorff 1989), for example, into "Latent Semantic Analysis" (Leydesdorff 1997). These methods operate on a word-document matrix in which the documents are treated as cases (rows) to which the words are attributed as variables (columns).

The words and their co-occurrences will be considered as the observable variation. By using words and their co-occurrences, one observes the intellectual space as represented in the textual domain in the widest of its ramifications (Leydesdorff 2001). Stegmann and Grohmann (2003) emphasized that co-words are particularly suited for the study of 'weak links': the co-words relate otherwise unconnected topics. Our techniques are based on commonly available software programs, which generate word frequency lists (excluding common stop words and the plural *s*). For practical purposes, we limit ourselves to counting the occurrences and co-occurrences without taking into account the frequencies of word (co-) occurrences. We investigated 6,613 unique title words with an occurrence of more than 1.

Because of the very skewed distribution of words, co-occurrence matrices are typically large and sparse. In our case, this results in a matrix of all title words in which only two words (cell and production) are related to over a thousand other words. Most words however, maintain very few co-occurrence relationships. As a consequence, these small clusters of related words are often unrelated to other topics. In other words, co-occurrence analysis measures the relatedness between topics of research by assessing whether title words are often found together in one and the same paper in the entire set of publications.

In section 4, we demonstrated that specific topics are associated with particular growth patterns of cities in terms of biotech output. Research topics tend to occur at the same locations because these topics requires similar local capabilities (tacit knowledge, skills and infrastructures). We found indeed that many words that are strongly related through co-occurrences (like ‘aqueous’, ‘biochemical ‘and ‘enzyme’) originate often in slow growth cities, while they are very marginal topics in fast growth cities. Likewise, important related topics in fast growth cities (‘genome’, ‘recombinant’ and ‘strain’), hardly occur in slow growth cities.

In Table 6, we present the average number of co-occurrences of words in the three categories of cities for the period 1986-2008. The results show that topics in cities with a slow growth pattern are on average less related to other topics than cities with a stable growth pattern. High growth cities contribute to topics that show high levels of relatedness to the entire set of topics.

Table 6*. Average number of co-occurrences of title words in biotechnology in the period 1986-2008*

	average number of words per year	average number of co-occurrences per year	average number of co-occurrences per word

Fast Growth	740.65	29008.00	83.00
Slow Growth	1071.83	40825.61	41.75
Stable Growth	841.52	35754.78	55.42

We argued that the opportunity to explore new scientific topics relies on a whole series of subsequent topics and insights, that is "the adjacent possible." The analysis presented here shows that there is a strong relationship between the growth rate of cities in biotech and the number of adjacently possible research topics in biotech. High growth cities have a large number of potential new topics available that are directly achievable from an existing set of topics, while slow growth cities have a smaller set of adjacent possibilities.

5.3 The degree of cognitive relatedness in cities

The question is whether we can establish the evolution of word patterns into the adjacent possible. Do cities indeed branch into topics of related words? Can we establish different patterns among the different categories of cities?

In the previous section, we showed the average number of adjacent possibilities that are potentially available at each moment in time (Table 6). This section focuses on the observed patterns of branching into related topics. In Table 7, we present the average number of related title words in biotech for the three categories of cities. For all cities, we found that more than 40% of the words is related through the set of co-occurrences of the title words in the previous year. Looking at the selected cities mentioned above, we observe that the branching of topics into the adjacent possible is strongly related to differential growth patterns. That is, slow growth cities (which have the smallest number of branching opportunities) show indeed the lowest level of branching into related topics. This level of cognitive relatedness is higher for stable growth cities, but in the case of fast-growing cities (with the highest number of potential branching opportunities), the degree of observed cognitive relatedness between title words is the highest by far.

***Table** 7. Average number of related title words in biotechnology in the period 1986-2008*

	average number of related words
Fast Growth	49.26%
Slow Growth	40.27%
Stable Growth	44.87%

Further evidence of the relationship between evolutionary development and the availability of new topics is provided by the appearances and disappearances of topics in the entire set of publications in each year compared to the previous year. Where do new topics in the global set of biotechnology publications emerge?

As Table 8 demonstrates, most new topics are introduced by cities with a stable growth pattern, followed by cities with a slow growth rate and a fast growth rate. Furthermore, the disappearance of topics is more or less similar between the three categories of cities.

***Table 8**. Average number of new words and disappearing words per year in selected cities between 1986-2008*

	average number of new words per publication	average number of exit words per publication
Fast Growth	0.98	0.12
Slow Growth	1.07	0.12
Stable Growth	1.17	0.13

The results confirm our hypothesis that research activities are to an extent location-specific due to its (partly) tacit and cumulative nature. This cumulative and irreversible nature of knowledge development is embodied in individuals (tacit skills) and in knowledge producing organizations (routines and infrastructures): they develop different cognitive capacities over time. Because these local capabilities (tacit and codified) accumulate over time, they are difficult to copy by others.

In sum, we found strong path dependencies in knowledge dynamics in biotech science, but the degree and nature differed between the three types of cities. Slow growth cities are a particular case, with the highest degree of path dependency. These cities show the highest levels of re-occurrence of words. Furthermore, these cities suffer from a lower degree of consistency in their scientific knowledge production, which is also shown in their relatively low level of co-occurrences, meaning that their topics are on average less related to other topics. Consequently, the new topics at these locations are relatively unrelated to the set of co-occurrences in each previous year.

The other interesting category is fast-growing cities. They have a relatively low degree of re-occurrences of similar words, but they have a relatively high degree of relatedness among the topics. This implies that they rely less on existing topics and tend to move more towards new topics that are related to existing topics. Stable growth cities have relatively high levels of entry and exit, and high degrees of relatedness (co-occurrences) and similarity (re-occurrences).

6. Research collaborations between cities

Till so far, we assumed that knowledge dynamics in biotech occur mainly within cities, but in reality, there is an increasing tendency of international research collaboration, and the scientific field of biotech is no exception to that rule (see e.g. Frenken and Van Oort, 2004; Cooke 2006a; Cooke 2006b). Our data permit assessment of the rate of research collaboration among organizations in biotech and its growth over time by means of co-authored papers. Based on this information, we constructed matrices of city-city co-occurrences per year.

Figure 7 shows the share of co-authored papers in biotech is rapidly increasing in the period 1986-2008, and this applies to research collaboration both at the national and international scale. Whereas biotechnology shows a pronounced pattern of international collaboration, as indicated by the number of articles with authors from more than one country, the data also show that the network of co-author relationships is still predominantly nationally oriented. Thus, despite the growth in international collaboration, co-authorships still have a strong local dimension. All research locations in the dataset collaborate most intensively with locations within the same country.

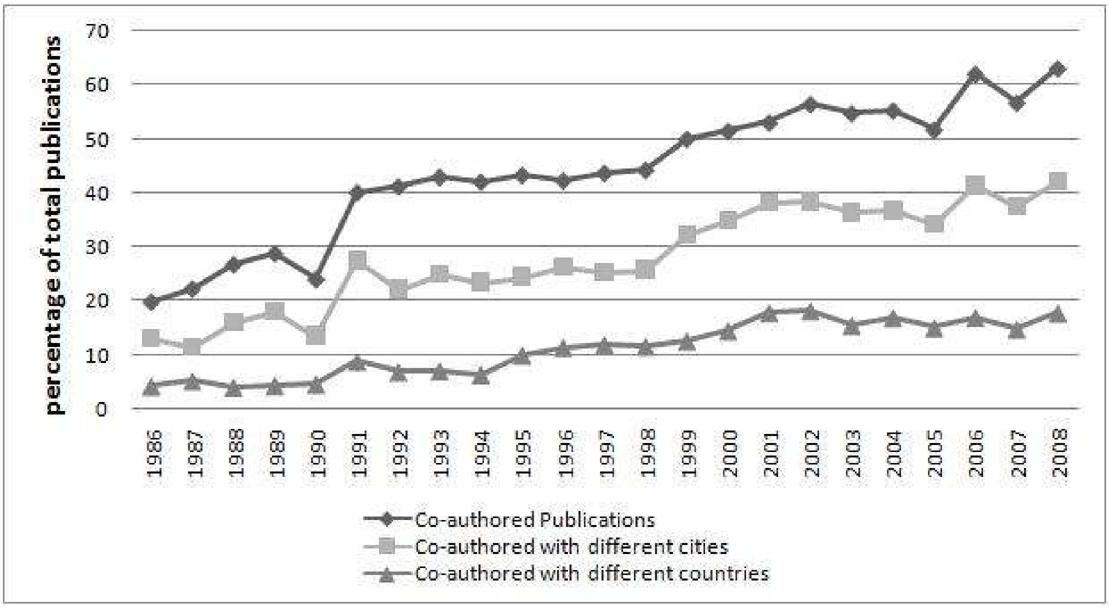

***Figure** 7 Share of co-authored papers in the field of biotechnology (1986-2008)*

Table 9 provides an example of the locations of co-authors of Wageningen, Pittsburgh and Seoul in the period under study. Table 9 confirms the predominantly national bias in research collaboration in biotechnology. Interestingly, these data also show that by far most collaborations happen within the same region.

***Table 9**. Cities of origin of the most important co-authors of Wageningen, Pittsburgh and Seoul in the period 1986-2008.*

	Wageningen, Netherlands		**Pittsburgh, USA**		**Seoul, South Korea**
Wageningen, Netherlands	525	Pittsburgh, USA	492	Seoul, South Korea	710
Amsterdam, Netherlands	21	Moscow, Russia	8	Taejon, South Korea	75
Enschede, Netherlands	18	Cambridge, USA	6	Pusan, South Korea	28
Zeist, Netherlands	15	Groton, USA	5	Inchon, South Korea	12
Bilthoven, Netherlands	13	Frankfurt, Germany	4	Suwon, South Korea	11
Delft, Netherlands	11	Manhattan, USA	4	Ansan, South Korea	11

Ede, Netherlands	10	York, Canada	3	Chunchon, South Korea	8
Leiden, Netherlands	7	Manchester, UK	2	Ithaca, USA	6
Grenoble, France	7	Huntsville, USA	2	Jinju, South Korea	6
Galway, Ireland	7	Maharashtra, India	2	Kwangju, South Korea	6
Naples, Italy	6	Palo Alto, USA	2	Gyonggi, South Korea	6
Sonora, Mexico	6	Bozeman, USA	2	Osaka, Japan	5
Geleen, Netherlands	5	Aberdeen Proving Ground, USA	2	Yongin, South Korea	5
Groningen, Netherlands	5	Res Triangle Pk, USA	2	Princeton, USA	5
Balk, Netherlands	5	Tokyo, Japan	1	Chinju, South Korea	5
Vienna, Austria	4	Montreal, Canada	1	College Stn, USA	4
Basel, Switzerland	4	College, USA	1	Zurich, Switzerland	4
Heidelberg, Germany	4	College Stn, USA	1	Houston, USA	4
Vlaardingen, Netherlands	4	Charlottesville, USA	1	Asan, South Korea	4
Louvain, Belgium	4	Newark, USA	1	Kyonggi, South Korea	4
Ankara, Turkey	3	Raleigh, USA	1	Kyoto, Japan	3
Ghent, Belgium	3	Edinburgh, UK	1	Pohang, South Korea	3
Frankfurt, Germany	3	Santiago, Chile	1	Stanford, USA	3
Oss, Netherlands	3	Champaign, USA	1	Ansung, South Korea	3
Zurich, Switzerland	2	Fayetteville, USA	1	Kimhae, South Korea	3
Braunschweig, Germany	2	Midland, USA	1	Puchon, South Korea	3

Being exposed to extra-regional knowledge is often considered crucial in the literature, because it brings new variety into the region (Asheim and Isaksen, 2002; Boschma and Iammarino, 2009). So, researchers with tight relationships that focus too much on their own region may not easily adapt to external changes. We used the same three categories of cities, and examined whether the nature of their growth patterns is somehow reflected in their collaboration pattern. It can be expected that stable growth is associated with strong networks of collaboration. Likewise, declining cities are expected to maintain a less dense network of collaborations.

Table 10 depicts the number of city-city collaborations, both in absolute and relative terms. Our analyses indicate there is a strong correlation between growth patterns and the level of connectivity, as indicated by the number of collaborations at different locations of knowledge production. As expected, slow growth cities show low levels of collaboration with other cities, as compared to stable and high growth cities.

Table 10. *Number of city-city collaborations (in absolute numbers) in the three categories of cities in the field of biotechnology (1986-2008)*

	number of unique partners per publication	number of partners per publication
Fast Growth	0.19	2.48
Slow Growth	0.14	2.23
Stable Growth	0.20	2.41

However, city-city collaborations are expected to create more new knowledge when they consist of agents that bring in similar and related competences. Does relatedness play a role in extra-regional linkages through co-author relationships? We expect a clear correlation between the topics under study in cities and the likelihood of establishing co-author relations. And we hypothesise that the extent to which networks will matter for novelty production, and thus for developing new topics of research, may depend on the degree of relatedness among the network partners. Due to the tacit nature of knowledge production at a geographical location, we expect researchers and organisations to understand, absorb, and implement external knowledge when it is close to their own knowledge base.

As a first indication, we mapped the co-author networks of the city of Wageningen in order to see the extent to which these collaborations provide a source of related variety. To investigate this, we correlated the word-frequencies of all publications in Wageningen, all publications of co-authors of Wageningen, and the total word frequency of the entire dataset. The results in Table 11 indicate a small but significant difference in the correlation pattern. That is, the topics of study of co-authors are more related to the research taking place in Wageningen than the average profile of topics in the entire set.

***Table 11**. Pearson Correlation of word frequencies (WF) in Wageningen, its co-authors and the total set. All correlations are significant at the 0.01 level (2-tailed)*

Pearson Correlation	Total WF	Wageningen	Co-authors WF
Total WF	1.00	0.42	0.85
Wageningen WF	0.42	1.00	0.58
Co-authors WF	0.85	0.58	1.00

7. Conclusions

In this study, we explored the evolutionary developments of scientific knowledge production in biotech in the period 1986-2008. Our aim was to identify the extent to which scientific knowledge production in biotech is subject to a path- and place-dependent process. We employed a new methodology based on the analysis of title words in key scientific publications in biotech as a proxy for the dynamics of knowledge production in this scientific field, in order to gain more insight in the cognitively and geographically localised nature of scientific knowledge production.

Our first finding was that scientific discovery in biotech is geographically concentrated. But we also showed that the geography of knowledge production in biotech science is subject to changes worldwide, with many newcomers mainly in Asia. This made us to distinguish between three types of cities that show differential growths rates in terms of scientific output in biotech: high growth cities like Seoul, stable growth cities like London, and slow growth cities like Cambridge in the US.

By analyzing the use of key words in our set of biotech publications, we made an attempt to identify major cognitive developments within the field of biotech in the period 1986-2008. We found evidence that knowledge dynamics in biotech is indeed a path- and place-dependent process. We could observe a high degree of re-occurrences of similar key topics in biotech in consecutive years, which points to the importance of a persistent and durable nature of scientific knowledge production in biotech. Interestingly, we found that this re-occurrence of topics is strongly related to the growth of cities in biotech: we observed higher level of re-occurrences in slow growth cities and stable growth cities, than in high growth cities.

We also measured the evolutionary patterns of knowledge production in biotech in terms of the relatedness of key research topics by means of co-occurrence analysis. We found that unique words used in consecutive years were to a great extent related through co-occurrences with the words used in the previous period. We also found that slow growth cities are characterized by topics that are on average less related to other topics, than cities with a stable growth pattern. High growth cities contribute to research topics that show relatively the highest degree of relatedness to the entire set of topics in biotech, which implies they evolve in more related topics. Stable growth cities showed a high degree of path dependency, with high co-occurrence levels. In sum, the emergence of novelty in science is subject to a path-dependent and place-dependent process of branching; new knowledge is developed from existing knowledge, skills and infrastructures.

As far as the rise and fall of key topics in biotech is concerned, we found that slow growth and stable growth cities introduce more new topics, in contrast to high growth cities that show lower entry levels. However, we could also observe that high growth cities tend to develop new topics that are rapidly growing and more promising, in contrast to slow growth cities, which were more associated with topics that lost importance in the scientific field of biotech. However, levels of disappearing biotech topics hardly differed between the three types of cities.

This paper is explorative, making a first attempt to delineate the spatial evolution of scientific knowledge production based on a new methodology that examines dynamics in key title words in scientific publications. For that reason, the findings of this study raise many new questions that need more careful attention in further research. We briefly mention three of those research challenges.

First, it deals with the methods of using title words to identify key cognitive developments in science. The use of title words is not unproblematic. It is difficult to distinguish empirically how much of the observable variation in words is dependent on change in terms of the changing positions of individual words against a more stable background vocabulary, or on change in the vocabulary itself, i.e. in the way it attaches to the description of reality. At the set level, one finds change both in terms of how words are used and in terms of what words stand for conceptually. In other words, the line of research presented in this paper looks promising, but further research remains necessary to understand the robustness of this approach. For example, we expect that enormous differences exist between fields of science in terms of local path dependencies (Heimeriks and Leydesdorff 2012).

Second, we have identified the rise and fall of topics in three types of cities, and we have investigated the extent to which new and disappearing topics in those cities are related to the existing set of topics that is available worldwide. Taking the global set of research topics as reference, we provided evidence for the process of branching and the adjacent possible at the global scale, and how that works out at the local level (i.e. in different city contexts). This enabled us to describe the evolution of scientific knowledge as a dynamic interplay between the global and the local, in which codified and accessible knowledge available in leading international journals interacts with geographically localized processes of scientific knowledge production to which researchers that operate mainly in a local context contribute. The next step is to further investigate the extent to which the emergence of new topics and the disappearance of existing topics in cities are dependent on their degree of relatedness with existing topics available in those cities. This is similar to the main question raised in a recent paper on regional diversification (Neffke, Henning and Boschma 2011), which investigated the extent to which the rise of new industries and the disappearance of old industries in regions is dependent on the degree of technological relatedness with existing industries in those regions. Such kind of study would provide evidence for the branching process at the city scale, in which the adjacent possible in scientific knowledge production is defined at the city scale instead of the global scale, and thus different for each city.

Third, we showed that research collaborations between knowledge producing cities, as indicated by city-city co-author relationships, are rapidly increasing in biotech. Author networks are considered a major channel of knowledge diffusion and learning among researchers (Wagner 2008). However, the extent to which networks will matter for novelty production, and thus for developing new topics of research, may depend on the degree of relatedness among the network partners (Phene and Tallman 2002). In order to stimulate new ideas, while at the same time enabling effective communication and collaboration, an optimal level of cognitive proximity between network partners may exist (Boschma and Frenken 2010). Studies on networks suggest that more radically new knowledge is developed when actors bring in different but related competences (Nooteboom, 2000). Thus, co-author networks are expected to provide a crucial source of related variety in local scientific knowledge production but we did not provide substantial evidence for that claim. Thus, (local and non-local) networks may provide relational access to the adjacent set of possible topics cities may branch into, next to the global and local context that provide access to the adjacent possible in science. Are cities with related profiles more connected indeed? Is there indication of the importance of co-authorship relations as a source of related competences? This topic remains to be studied, but is crucial to increase our understanding of the path and place-dependent nature of scientific knowledge production, of which we found some evidence in this study.

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