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The Geography of Biotechnology

Gaston Heimeriks
Utrecht University
Innovation Studies
gheimeriks@gmail.com

Ron Boschma

r.boschma@geo.uu.nl

Abstract
In this study, we explore the spatial patterns of knowledge production in Biotechnology. Regions can be shown to have their own specialisation patterns and expand into topics that are related.

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Abstract

In this study, we explored the evolutionary developments of knowledge production in Biotechnology. The aim of the empirical analyses presented here was to gain insight in the localised contributions in knowledge production in Biotechnology and to investigate what changes took place in the geographical distribution of biotechnological developments. The results provide a representation of the evolving status of science. The past decades has seen a remaking of the map of world science and innovation in Biotechnology, as countries including China, India, Brazil, South Korea and South Africa have increased their investment and risen up the league tables of published papers. Our results allow us to elaborate the relationship between locally embedded knowledge in combination with codified and accessible external knowledge in the process of novelty production. We show how at each location, the evolution of knowledge production can be described as a process of branching from existing knowledge embodied in individuals (skills) and in knowledge producing organisations (routines and infrastructures). Additionally, co-occurrence analysis shows that topics originating from cities with a declining growth pattern are on average less related to other topics than cities with a stable growth pattern. Most new topics, are introduced by cities with a stable growth pattern, followed by cities with a high growth rate. Furthermore, the presence of industry in regions can be shown to contribute to distinct patterns of evolutionary development. Concluding, we argue that the evolution of knowledge production can be explained by synergetic interactions among local research practices, the global codified knowledge-base, and the context of application as three relatively independent sources of variance.

Keywords: geography, science, innovation, biotechnology, evolution

1. Introduction

The paper is concerned with spatial clustering of knowledge creation and its relation to the spatiality of economic activity. Knowledge is increasingly recognised as a driver of productivity and economic growth, as well as a vital resource in addressing societal challenges. This results in increased (policy-) attention on the role of knowledge in societal and economic performance. The term “knowledge-based economy” stems from this fuller recognition of the place of knowledge and technology in modern societies (OECD 1996). However, the dynamics and geography of knowledge production are a complex matter. According to Florida, are the locations of scientific discovery very geographically concentrated (more so than economic activity). Most significant contributions to knowledge production occur in a handful of locations, primarily in the USA and Europe (Florida 2002).

A modern knowledge based economy is thus characterized by the growing share of knowledge used in socio-economic processes. In view of this, the study of the mechanisms of knowledge production has received renewed attention in the last decade, while a considerable effort is dedicated to characterise the knowledge base of different sectors in the economy and its relation to economic performance (e.g. (Breschi et al. 2003).

Many studies of geographical distribution in science and innovation have drawn inspiration from evolutionary economics (Nelson and Winter 1982). In this perspective, knowledge is not a public good that is characterized by diminishing returns to scale. On the contrary, knowledge evolves: it is not reduced when it is used, but it accumulates through processes of learning-by-doing (Arrow 1962). Furthermore, existing knowledge provides building blocks for further knowledge production (Arthur 1994). Existing studies suggest that countries and regions tend to expand into sectors that are closely related to their existing activities (Boschma and Frenken 2009). This process of branching is expected to occur primarily at the regional level, because it becomes manifest through a number of path dependent processes that tend to be geographically bounded (Boschma 2005).

Scientific knowledge however, is codified information that is accessible worldwide and as such not bound to a certain location. Can something as elusive as the knowledge base of a system be measured? (Leydesdorff 2001; Foray 2004). Are the knowledge dynamics at the global level indicated with potentially different effects in various world regions and nations?

In this study, we explore the spatial patterns of knowledge production in Biotechnology over a period of time. Biotechnology is characterised by rapid growth, divergent dynamics and new complementarities creating the need for wide-ranging cross-disciplinary competences (Bonaccorsi 2008; Heimeriks and Leydesdorff 2011). Furthermore, fields of techno-science like biotechnology develop in a network mode: disciplinary insights from different backgrounds are recombined and university-industry relations are continuously reshaped (Leydesdorff and Heimeriks 2001). Grasping the fruits of these emerging techno-sciences is an objective of many government priority programs in a knowledge-based and globalizing economy. Consequently, life sciences such as Biotechnology have received extensive investment from both the public and private sectors, because of a growing impact on socio-economic processes. New treatments and drugs, genetically modified foods, biologically controlled production processes, new materials, biologically based computing and many other applications are improving health, the environment, and industrial, agricultural and energy production (OECD 2009).

In a first step, we explore the regional growth paths of knowledge production in Biotechnology. Globalisation and the opening up of numerous economies to market capitalism has lead to significant changes in locations where science is conducted. How do different regions in the world participate in knowledge production in Biotechnology, and what changes took place in the geographical distribution?

In the next step, we measure the evolutionary patterns of branching in Biotechnology knowledge production using title words in Biotechnology papers as an indication of the cognitive developments within the field. Furthermore, we investigate the role extra-regional linkages for regional growth, that is the inflows of knowledge that are related to the existing knowledge base of regions that might be crucial. Co-authorship relations are expected to create more new knowledge when they consist of agents that bring in related competences.

Finally, we wish to contribute to conceptualisations of evolutionary patterns of knowledge dynamics. The geographical setting, the global knowledge-base, and the context of application constitute three relatively independent sources of variance. The three sources of variance may reinforce one another in a co-evolutionary process (Heimeriks and Leydesdorff 2011; Leydesdorff 2006).

2. Knowledge dynamics in an evolutionary perspective

In this study, we explore the spatial patterns of knowledge production in Biotechnology and its relation to economic activity. Boschma and Martin argue that evolutionary economic geography is concerned with how the spatial structures of the economy emerge from the micro-behaviours of novelty creating agents and how, in the absence of central coordination or direction, the knowledge based economic landscape exhibits self-organisation; and with how the processes of path creation and path dependence interact to shape geographies of economic development and transformation, and why and how such processes may themselves be place dependent (Boschma and Martin 2010).

In the knowledge economy, knowledge production provides resources for social and economic developments. In recent years increasing interaction with socio-economic developments in society has been emphasised. Fields of codified knowledge production constantly capture societal phenomena for particular purposes through stakeholder involvement and user-producer interactions (Lundvall 1988). The process by which knowledge or information evolves and spreads through the economy involves changing its nature between tacit and codified forms.

For example, the 'Mode-2' thesis of the new production of scientific knowledge (Gibbons et al. 1994) implies that the knowledge system has recently gained a degree of freedom under the pressure of socio-economic developments reinforced by globalization and the new communication technologies. The perspective of knowledge production, consequently, is changed from interdisciplinary—that is, based on careful translations among different scientific discourses—to transdisciplinary—that is, based on an external societal perspectives (Etzkowitz and Leydesdorff 2000; Heimeriks et al. 2008).

Novelty creating researchers can be considered the nodes that carry the science system in Biotechnology. Knowledge tends to accumulate in space, leading to inter-regional variety of knowledge. Both what constitutes a research opportunity and how it is dealt with, are locally situated. At this research level, researchers compete and collaborate. With the growing specialisation in science and the progressive professionalization (Cronin et al. 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 multiperson 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, with high energy physics as the most extreme example.

Due to its tacit and cumulative nature, research is actor-specific and location-specific and difficult, if not impossible, to copy or imitate by other actors. This cumulative and irreversible nature of knowledge development is embodied in individuals (skills) and in knowledge producing organisations (routines and infrastructures): they develop different cognitive capacities over time (Nelson and Winter 1982). Consequently, knowledge production is expected to be characterised by a path-dependent process of branching; new knowledge is developed from existing knowledge, skills and infrastructures.

New topics, however, rely on a whole series of subsequent topics and insights. Kauffman (1993) has a suggestive name for the set of all those first-order combinations: "the adjacent possible." The phrase captures both the limits and the creative 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, a map of all the ways in which the present can reinvent itself. Each new topic opens up the possibility of other new topics.

The dissemination of results through scientific journals translates the 'research output' into an emergent 'body of knowledge' where codified claims are utilized (accepted, criticized, rejected) by other scientists. 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 the differences with previous claims (Fujigaki 1998). At the same time, it can lead to a relatively stable, and 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: the new researchers are inclined to position themselves in terms of both the intellectual base, and the research front, and therefore a constant referring to the evolving literature base takes place. This can reinforce the stability and global generalization of the field.

One of the main distinguishing features of spatial clusters of similar and related economic activity is that they provide opportunities for the transmission of sticky, nonarticulated, tacit forms of knowledge between local actors. However, when this locally embedded knowledge is combined in novel ways with codified and accessible external knowledge new value can be created. Consequently, in a knowledge-based system, functions no longer develop exclusively at the local level. For example, Leydesdorff argues that while a political economy can be explained in terms of two subdynamics (e.g., economy and geography), a complex dynamics can be expected when three subdynamics are left free to operate upon one another (Leydesdorff 2010).

A configuration with three possible degrees of freedom—markets, local conditions, and knowledge production—can be modeled in terms of a Triple Helix (e.g., Etzkowitz and Leydesdorff 2000). Geographically positioned units of analysis (e.g., firms, institutions), economic exchange relations, and novelty production cannot be reduced to one another. However, these independent dimensions can be expected to interact to varying extents (Heimeriks and Leydesdorff 2011).

Because of the increase in digitalization and possibilities to transfer information easily over the world, codified knowledge can transfer the globe almost 'frictionless' (David and Foray 2002; Heimeriks and Vasileiadou 2008). This property of codified knowledge in combination with the globalization makes that also building knowledge of this type can be done in collaboration over spatial distances. In contrast to this type of knowledge there is tacit knowledge which got the opposite properties and thereby consequences for the spatial transferability. Tacit knowledge is mostly embedded in the skills of humans or in organizations as a whole (Foray 2004). To transfer this knowledge close and intensive contact between humans or organizations is needed.

Co-author networks are expected to be an important mechanism for providing related variety in local knowledge production. 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. In order to stimulate new ideas, while at the same time enabling effective communication and collaboration, it is likely that an optimal level of cognitive proximity between network partners exists (Boschma and Frenken 2009). Studies on networks suggest that more radically new knowledge is developed when actors bring in different but related competences (Nooteboom 2000). This so-called cognitive proximity has attracted most attention in evolutionary economics. Due to the tacit nature of knowledge, Cohen and Levinthal have argued that researchers and organisations can understand, absorb and implement external knowledge when it is close to their own knowledge base (Cohen and Levinthal 1989).

3. Data and Methods

Ever since evolutionary economists introduced the concept of a 'knowledge-based economy' (Foray and Lundvall 1996), the question of the measurement of this new type of knowledge dynamics in a socio-economic context has come to the fore.

a. Data

In this study, we use the accumulated body of codified knowledge in Biotechnology for the period 1986-2008 as data for our analysis. The field of Biotechnology 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 using a threshold of 1%. For the resulting set of journals we can make the journal- journal citation matrix, with the citing behaviour as the variables. A factor analysis of this matrix results in factors consisting of journals that entertain 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.

Both what constitutes a research opportunity and how it is dealt with, are locally situated. Within the local research context relevant processes include the interdependency that exists among researchers when producing knowledge through shared infrastructures, databases, international collaboration, and the number of contributors to scientific publications. Each publication in the dataset contains one or more addresses that enable us to specify the geographical location of each university and industry and therefore derive information about local path dependent dynamics and collaboration patterns. This geographical information allows us to make a geographic mapping of the institutional addresses and their relations (Leydesdorff and Persson 2010). 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. A co-occurrence matrix among these cities provided input to the further analysis and mapping.

All data from the Web of Science could be organized in a relational database allowing for reorganization of the records as the basis for the spatial analysis. In addition to institutional addresses, the papers provide title-words. In the first step, the dataset can be described in terms of its publications, authors, cities and words. In this paper, cities provide the unit of analysis. The data described above was used to construct matrices of co-occurrences of word per year, of word-city co-occurrences per year and city-city co-occurrences per year (co-authorships) as represented in figure 1 below.

b. City-Word Analysis

The title words in the set of publications in Biotechnology provide a starting point for studying the geographical distributions of topics in Biotechnology. A factor analysis of cities over words (1A) provides us with a first indication of the geography of knowledge production. What pattern can be observed from the clusters (factors) of cities with respect to the (500) most frequently occurring tile words?

The aim of this analysis is to establish the extent to which knowledge production at a number of selected locations is path dependent; is new 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? The series of matrices of cities over words (1986-2008) provide us with detailed information about this process. First we establish what is the correlation between the different years? What cities show a stable pattern? What cities are declining and growing fast. Are there cities that disappear?

In addition to the total set of cities, we use these four different categories of cities to establish whether the observed growth patterns are related to patterns in word use. Are declining cities associated with topics that lose importance? Do fast growing cities contribute new topics? Are stable growth cities using stable title words?

c. Word-Word Analysis

In the next step (1B) we can use these records as the basis for the cognitive analysis of topics. In our case, 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. Recently, a number of scholars have turned to co-occurrence analysis to assess dynamics of branching and relatedness (Hidalgo et al. 2007).

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).

Using the same categories of cities (fast growth, stable growth, decline), the question is whether the growth pattern of cities is reflected in the word patterns. It can be expected that stable growth is associated with strongly related words. Furthermore, related words provide an adjacent set of topics that these cities may branch into. Can we observe this pattern? Likewise, declining cities are expected to use less related words.

d. City-City Analysis

The co-author networks will be mapped on city level in order to see to what extend these collaborations provide a source of related variety. Several analysts have used scientometric data to study patterns of research collaboration. De Solla Price noted increasing collaborative publishing as long ago as 1963 (Price 1963). More recently, scientometric studies have shown an increase in international collaboration (e.g., European Commission 1994). Our data permit detailed assessment of the rate of collaboration among institutions within the fields under study and its growth over time.

Using the same categories of cities (fast growth, stable growth, decline), the question is whether the growth pattern of cities is reflected in the collaboration patterns. It can be expected that stable growth is associated with strongly related networks of collaboration. Furthermore, related cities provide an adjacent set of topics that these cities may branch into. Can we observe this pattern? Likewise, declining cities are expected to maintain a less dense network of collaborations.

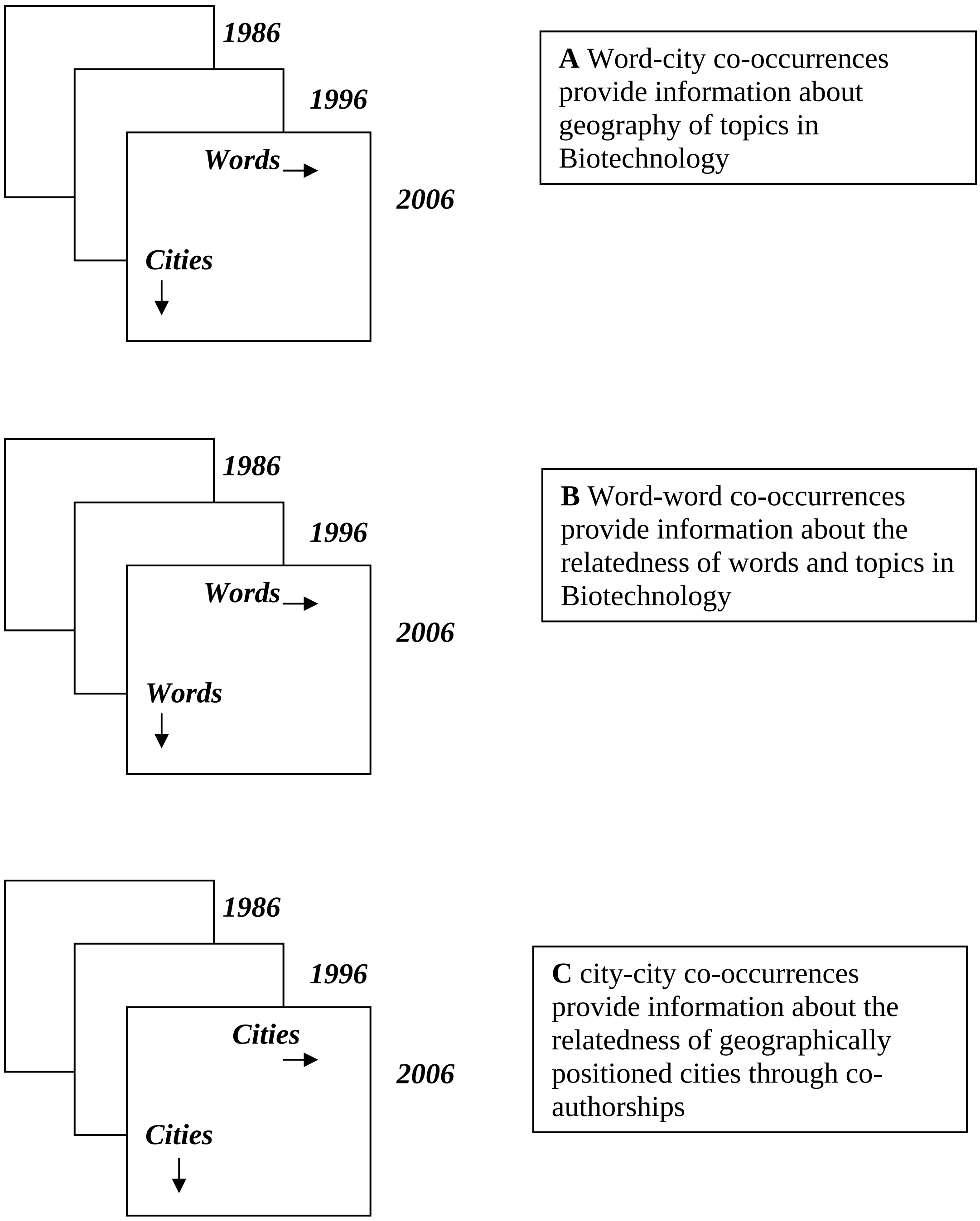

Figure 1. *The organization of the scientometric data for analysis in matrices that are composed of co-occurrences of words and cities.*

e. Context of application: Triple Helix

Furthermore, the socio-economical dynamics of knowledge production in Biotechnology can be made visible by mapping the type of organisations that are involved in knowledge production (academic, governmental or commercial). The Triple Helix model assumes the traditional forms of institutional differentiation among universities, industries, and government as its starting point. The model thus takes account of the expanding role of knowledge in relation to the political and economic infrastructure of the larger society (Etzkowitz and Leydesdorff 2000).

4. Results

a. Development of Biotechnology

Biotechnology is surprisingly stable in terms of its journal structure consisting of the three journals: *Biotechnology Progress*, *Biotechnology Bioengineering*, 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. As hypothesised, the self-organising process of researchers that position themselves in terms of both the intellectual base, and the research front, reinforce the stability and global generalization of the field. This leads to a relatively stable and path-dependent definition of the field.

After obtaining the set of journals, all the publications for the period 1986-2008 were downloaded from the Web of Science. The total set of publications consisted of 13,386 articles. The annual number of publications in Biotechnology shows a steady increase in the period under study (Figure 2).

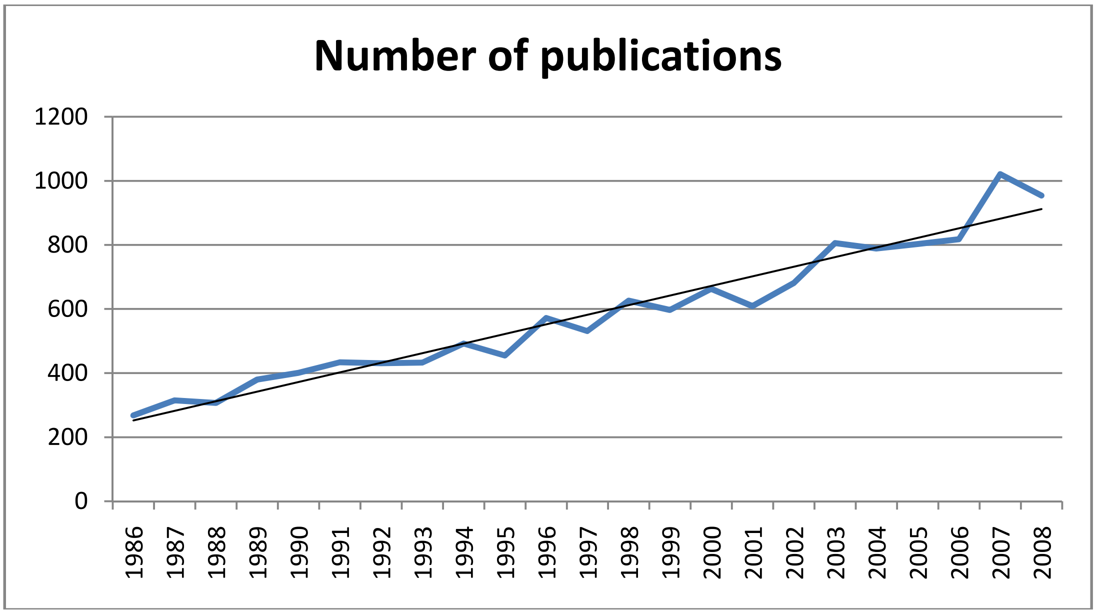

***Figure 2**. Number of publications in the field of Biotechnology (1986-2008).*

Geographical distribution patterns show that the number of countries that contribute to biotechnology grows from 32 in 1986 to 54 in 2008. Furthermore, the contributions from different parts of the world shows a very dynamic development in the period under study. The past decades has seen a remaking of the map of world science and innovation in Biotechnology, as countries including China, India, Brazil, South Korea and South Africa have increased their investment and risen up the league tables of papers published and citation rates.

The process of ongoing globalisation is also reflected in steady increase of the number of countries that contribute to publications in the field of Biotechnology (Figure 3).

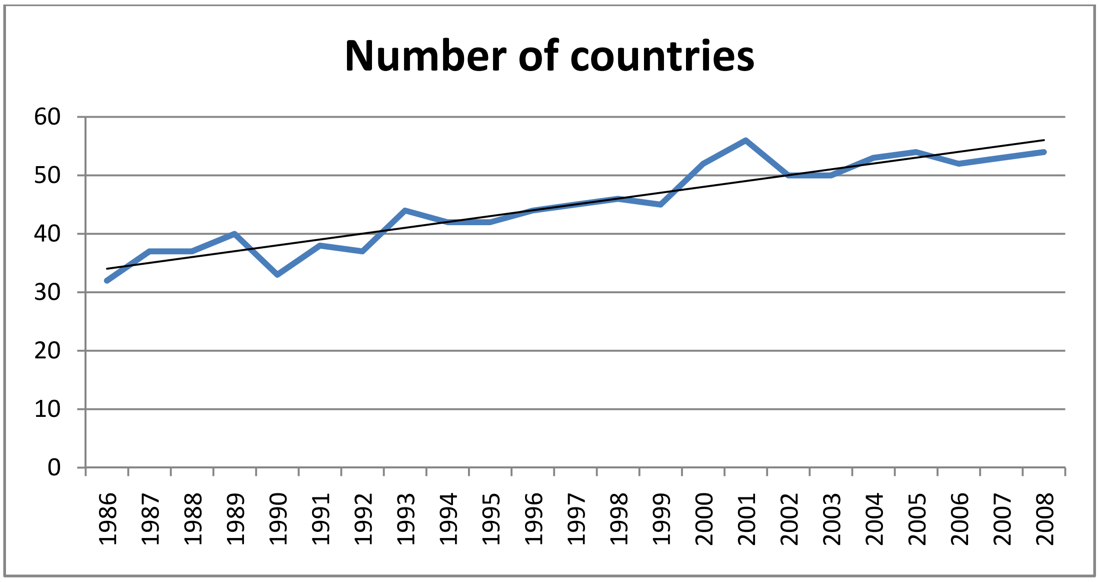

Figure 3. *Number of countries contributing to publications in the field of Biotechnology (1986-2008).*

In general, knowledge production in Biotechnology seems to shift away from the USA towards Asian regions (most importantly Seoul, Tokyo, Beijing and Singapore). European knowledge production in Biotechnology seems to remain rather stable compared to the USA. This means that they keep pace with the increased competition, but are no longer able to improve their marginal return (as they did previously). South Korea, however, shows a steady increase. South Korea shares this pattern with other “Asian Tigers” like Taiwan and Singapore (Zhou & Leydesdorff, 2006). In the most recent years, the growth of the Korean share seems to level off, but this is not yet significant as a trend breach.

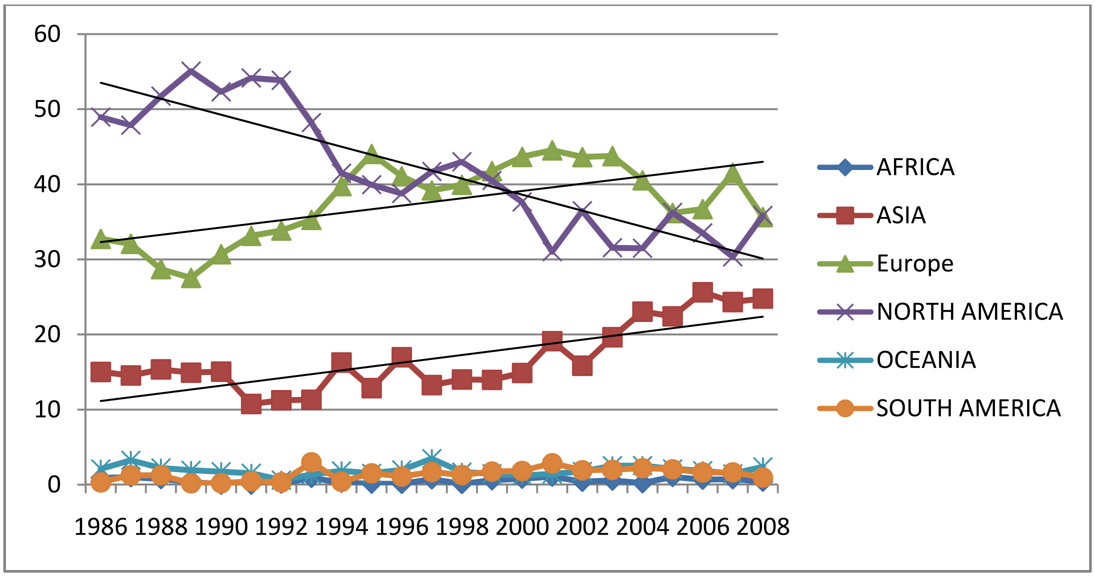

Figure 4*. Share of publications of different continents in the field of Biotechnology (1986-2008).*

The development shown here reflects the process of ongoing globalisation and the consequent escalation in scientific competition. The increasing number of publications and the rising number of contributing countries indicate a growing emphasis on science and innovation in industrialised countries as a response to the increasing competition from the rest of the world; governments, both nationally and regionally, need to ensure that the local knowledge base is strong and therefore attractive to the rest of the world. Note that China showed 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 & Leydesdorff, 2007).

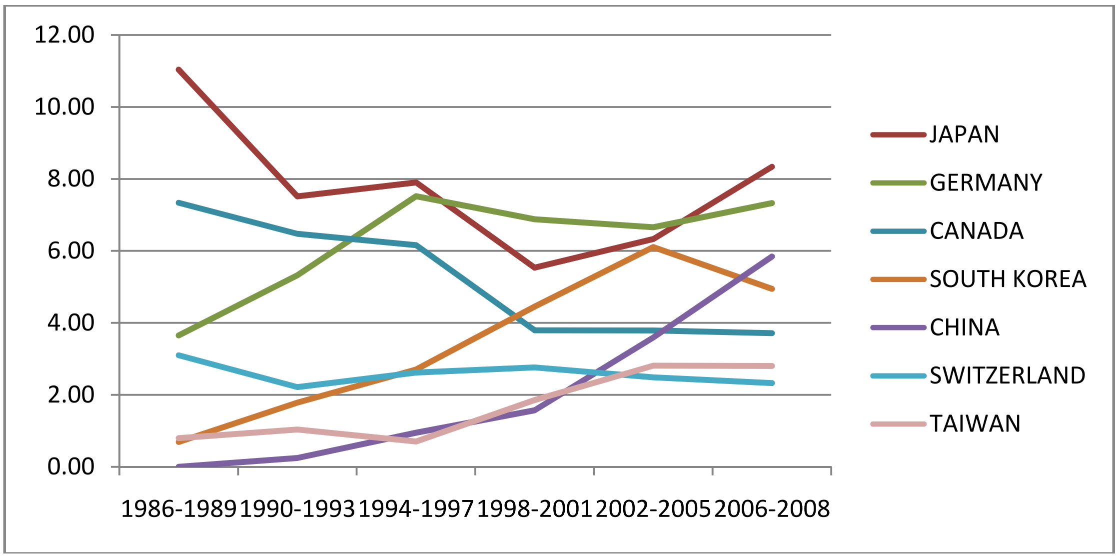

Figure 5*. Relative contributions in percentages of selected countries between 1986-2008.*

The author addresses included in the 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 2027 unique cities contributed to publications in Biotechnology. Of these, only 1243 cities were involved in more than 1 publication. Sixty cities contributed more than 100 publication between 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 than on the country level. Especially Asian cities such as Seoul and Beijing exhibit very fast growth rates (Figure 5).

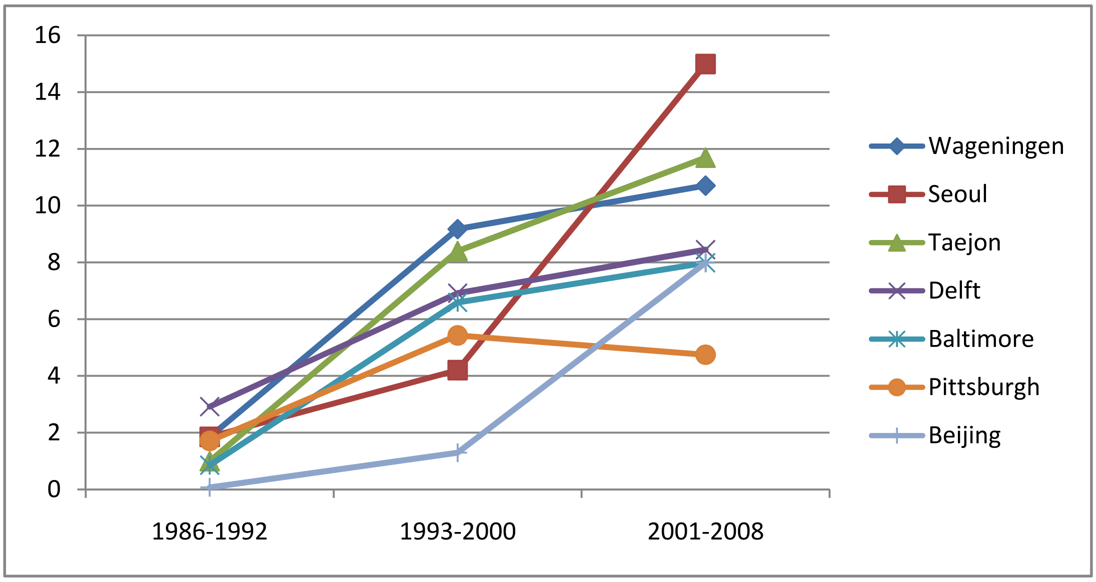

Figure 6. *Relative contributions in percentages of selected cities between 1986-2008.*

b. The geography of topics

The previous analyses showed that locations of scientific discovery are indeed very geographically concentrated. One of the main distinguishing features of spatial clusters of similar and related knowledge-based activities is that they provide opportunities for the transmission of sticky, nonarticulated, tacit forms of knowledge between local actors. In the next step, we focus on the geographical distribution of topics in Biotechnology. The use of title words in Biotechnology provides us with an indication of the cognitive developments within the field. A factor analysis of cities over title words provides us with an indication of similarities in word-use in different cities. The analysis of reveals a strong correlation between geography and topics of research (table 2). Cities that exhibit similar patterns of word use are often in geographical proximity of each other, and mostly located in the same country.

Table 2*. Rotated Component Matrix result of factor analysis of 100 most important cities and 500 most used title-words. Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.*

	1	2	3	4	5	6	7	8
Boston USA	.795							
Piscataway USA	.671							
Cambridge USA	.528							
Chiba Japan		.668						
Tokyo Japan		.666						
Ibaraki Japan		.471						
Minneapolis USA			.816					
Paul USA			.781					
Amsterdam Netherlands				.767				
Wageningen Netherlands				.755				
Cambridge UK					.778			
London UK					.774			
Taipei Taiwan						-.675		
Taichung Taiwan						-.630		
Hsinchu Taiwan						-.619		
Morelos Mexico							.755	
Mexico City Mexico							.752	
Zurich Switzerland								.752
Pasadena USA								.552
Basel Switzerland								.510

The cumulative nature of local knowledge development is expected to be embodied in individuals who develop skills and in organisations that develop durable infrastructures. Consequently, locations of knowledge production are expected to develop different capacities over time. These local path dependencies can be expected to contribute to a recursive pattern of topics. Once a research organisation contributes to a topic, it is expected to work on the same topic again. From the reverse perspective, it holds that topics that “die out” are often associated with research location with a declining contribution to knowledge production in a field. Can we quantify these evolutionary patterns of branching in Biotechnology knowledge production?

As was shown in Figure 5, the cities contributing to knowledge production in Biotechnology exhibit different growth patterns. The most important cities can be catagorised as fast growth, stable growth and relative decline (table 3).

***Table 3**. Categorisation of selected cities in terms of growth patterns between 1986-2008.*

Fast growth	**Stable growth**	**Relative decline**
Seoul South Korea	Wageningen Netherlands	Cambridge USA
Lyngby Denmark	London UK	Lafayette USA
Madrid Spain	Tokyo Japan	Ann Arbor USA
Vienna Austria	Braunschweig Germany	Atlanta USA
Bielefeld Germany	Houston USA	Toulouse France
Vancouver Canada	Cambridge UK	Newark USA
Singapore Singapore	Lausanne Switzerland	Pasadena USA
Beijing China	Taipei Taiwan	Raleigh USA
Milan Italy		Baltimore USA
Shanghai China		
Ankara Turkey		

The topics of study show a dynamic development. The fastest growing cities (in terms of scientific output) contribute to the most turbulent (rapidly growing) topics in the field. In dynamic (emerging) fields, with high growth rates, entrance barriers may be low for new researcher to contribute (Bonaccorsi 2008). This developed can be made visible by the recursiveness of title words at different locations representative of the different catagories; Seoul (fast growth), Wageningen (stable growth) and Baltimore (relative decline).

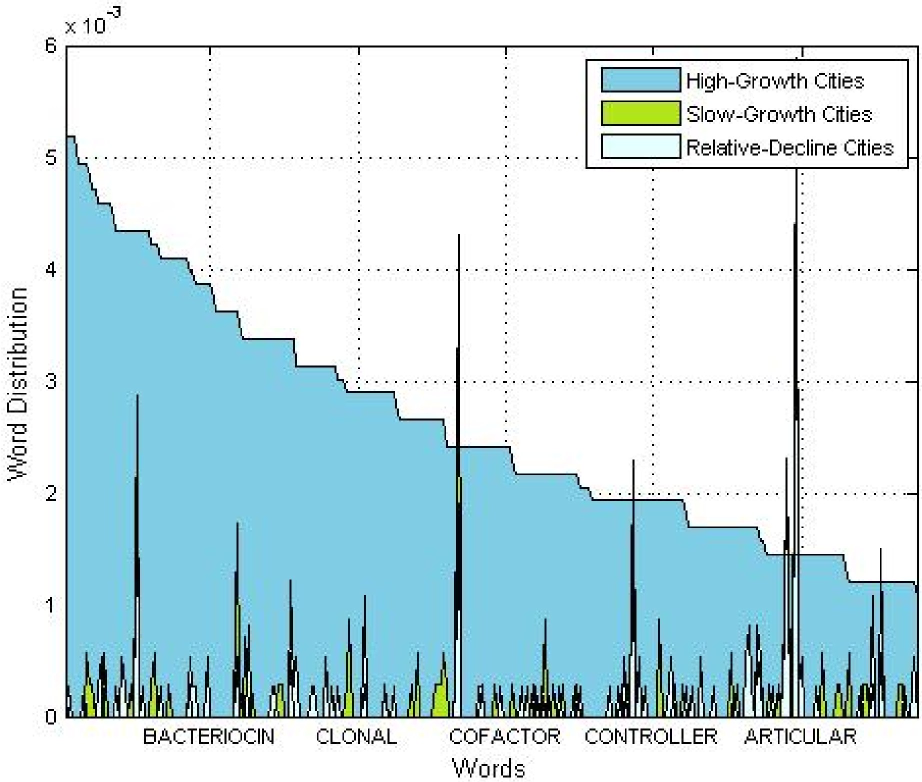

***Figure 7**. Distinct patterns of words can be observed among the different categories of cities. The word frequency distributions of cities with a declining and a stable growth pattern deviates from the word frequency distributions of cities with a high growth pattern.*

Correlation patterns show that newcomers (fast growth) build on the existing knowledge base only to a limited extend. Within group correlation is relatively ‘high’.

The underlying document set contains 6613 unique title words with an occurrence of more than 1, that provide a starting point for studying the geographical distributions of topics in Biotechnology.

In three consecutive periods, the word use in Wageningen shows a relatively modest overlap, in line with the previous observation of the dynamic cognitive development of the field. However, the unique words used in the second period (1993-2000) and third period (2001-2008), are to a great extend related through co-occurrences with the words used in the previous period. In both cases, 83% of the tile words are related to the tile words in the previous period (Figure 8).

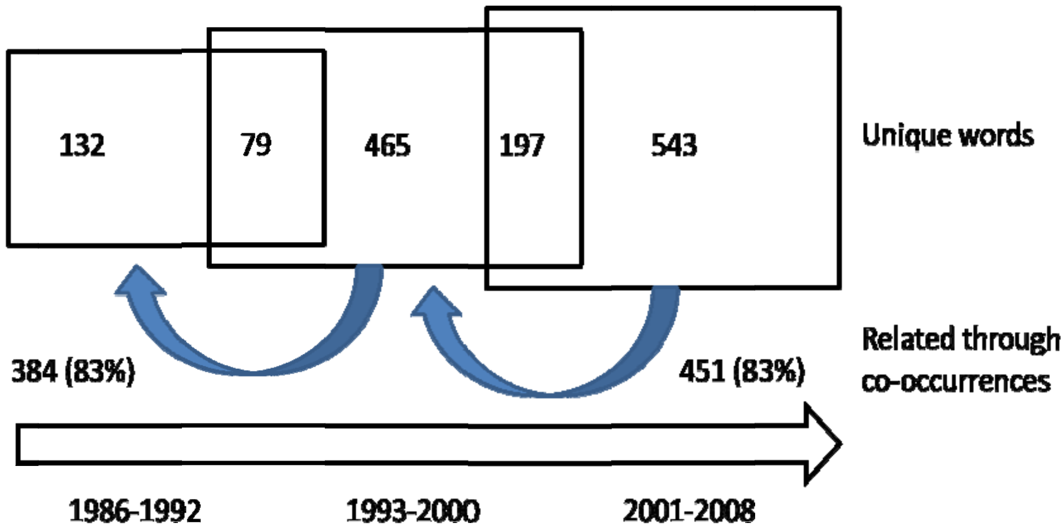

Figure 8. *Related variety of word use in Wageningen between 1986-2008.*

Baltimore and Seoul are, like Wageningen, important locations of research in Biotechnology. However, the relatedness through co-occurrences in title words is lower in these cities than in Wageningen. The relatedness ranges between 53% and 64% (Table 4).

Table 4*. Related variety of word use in Wageningen, Baltimore and Seoul between 1986-2008*.

City	indicator	period 1	overlap	period 2	overlap	period 3
Wageningen	unique words	132	79	465	197	543
	related to previous period			384		451
	%		16.99	82.58	36.28	83.06
Baltimore	unique words	619	329	503	132	638
	related to previous period			296		367
	%		65.41	58.85	20.69	57.52
Seoul	unique words	205	167	349	126	1004
	related to previous period			223		547
	%		47.85	63.90	12.55	54.48

These analyses provide a quantative indication of path dependency in knowledge production due to local skills, competences and infrastructures. Path dependency is highest in case of a stable growth pattern. Furthermore, the combination of this locally embedded knowledge with codified external knowledge is stronger in case of stable growth.

We argued that in many important aspects, path dependence is a place-dependent process, and as such requires geographical explanation. Further indication of this pattern of path dependency in topics of research at different geographical locations is provided by the re-occurrence of words in consecutive years. Looking at the selected cities mentioned above, we observe that the re-occurrence of topics is strongly related to different growth patterns (Figure 9).

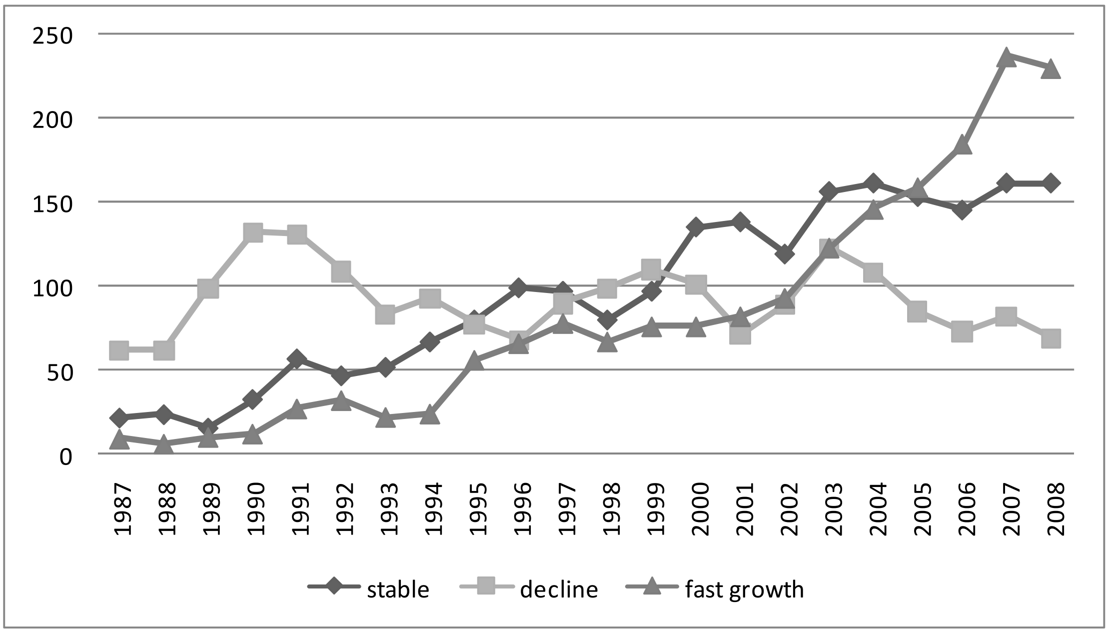

Figure 9*. Path dependency as indicated by the number of re-occurrences of words in consecutive years in selected cities between 1986-2008.*

Above, we showed how fast-growing newcomers build on the existing knowledge base only to a limited extend. In the next step, we measure the evolutionary patterns of knowledge production in Biotechnology in terms of the relatedness of topics. 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. The results show that topics originating from cities with a declining growth pattern are on average less related to other topics than cities with a stable growth pattern. High growth cities contribute topics that show relatively little relatedness to the entire set of topics, providing further evidence for the observation that new entrants contribute to new and unrelated topics in the field of Biotechnology.

Interesting is the pattern that that is visible in the ratio of word occurrences to co-occurrences. Declining cities contribute to a relatively small number of topics as indicated by the word occurrences. The number of co-occurrences associated with these words is lower on average than in stable growth cities, but also lower than in high growth cities (Table 5).

Table 5. *Average number of occurrences, co-occurrences and re-occurrences per year in word use in selected cities between 1986-2008.*

	occurrences	co-occurrences	occurrence/co-occurrence
Decline	279.13	33148.52	8.38
High Growth	308.13	30982.39	8.54
Stable Growth	356.96	36029.78	9.34

Further evidence of this relationship between evolutionary development and the availability of a new topics is provided by the appearances and disappearances of topics in the selected cities under study. As mentioned, new topics rely on a whole series of related topics and insights that constitute the adjacent possible. The adjacent possible defines all those new topics that are directly achievable from an existing set of skills and insights. The average number of new topics at certain locations is related to this availability space as indicated by the co-occurrences above. Most new topics are introduced by cities with a stable growth pattern, followed by cities with a high growth rate. Locations of declining importance contribute only small numbers of new topics. Furthermore, the disappearance of topics seems related to the rate of appearance of new topics (Table 6).

Table 6. *Average number of new words and disappearing words per year in selected cities between 1986-2008.*

	exit words	new words	exit words/publicati	new words/publicat
Decline	7.39	5.52	0.13	0.07
High Growth	11.74	10.65	0.16	0.09
Stable Growth	12.91	13.87	0.11	0.11

c. City-City Collaborations

Co-authorship relations are expected to create more new knowledge when they consist of agents that bring in related competences. The next question is whether relatedness plays a role in extra-regional linkages through co-author relationships. Co-author relationships indicate a declining importance of national boundaries; the share of internationally co-authored papers increases significantly. There is a clear correlation between the topics under study in regions and the likelihood of establishing co-author relations. Furthermore, the role extra-regional linkages for knowledge developments show that the inflows of knowledge through co-authorships are related to the existing knowledge base.

The network of co-author relationships is very sparse and predominantly nationally oriented in 1986. However, the average number of authors per paper showed a steady increase in the period under study from 2.89 to 4.61. Biotechnology shows a pronounced pattern of international collaboration as indicated by the number of articles with authors from more than one country (Figure 10).

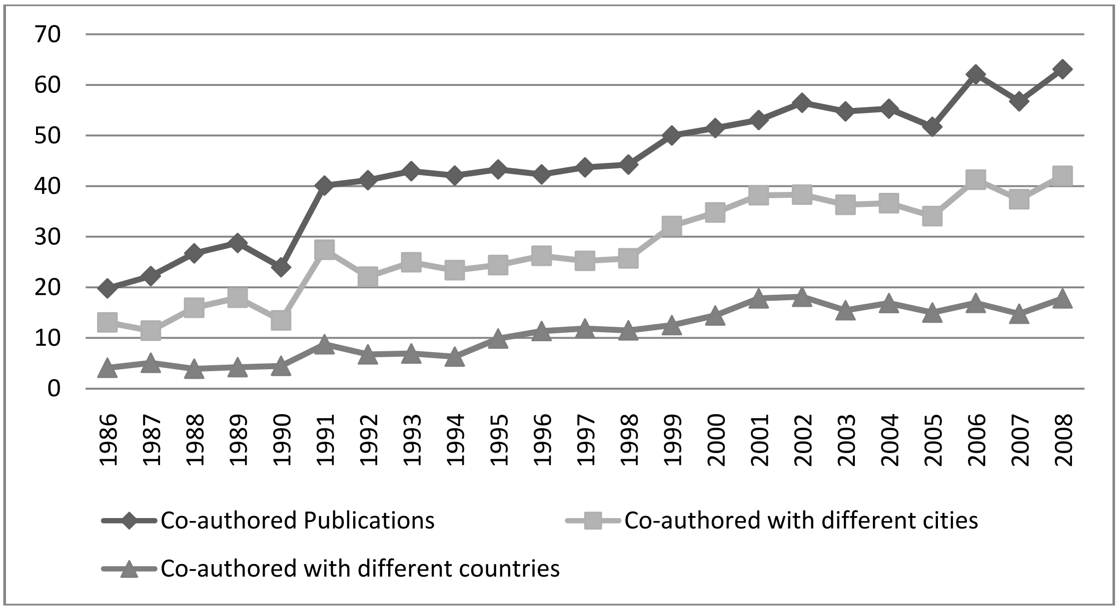

Figure 10. *Share of (internationally) co-authored papers in the field of Biotechnology (1986-2008).*

Despite the enormous growth in international collaboration, co-authorships still have a strong local dimensions. All research locations in the dataset collaborate most intensively with location within the same country. Being exposed to extra-regional knowledge is considered crucial, because it brings new variety into the region. So, researchers with tight relationships that focus too much on their own region may not easily adapt to external changes. Non-local relations as such, however, do not guarantee effective knowledge transfer either: a certain level of social and cognitive proximity is needed to make effective connections over large distances (Boschma 2005). The table below provides an example of the locations of all co-authors of Wageningen in the period under study (Wageningen itself excluded).

***Table 7**. Cities of origin of the most important co-authors of Wageningen 1986-2008.*

Amsterdam (NL)	21		Geleen (NL)	5
Enschede (NL)	18		Groningen (NL)	5
Zeist (NL)	15		Basel	4
Bilthoven (NL)	13		Heidelberg	4
Delft (NL)	11		Louvain	4
Ede (NL)	10		Vienna	4
Galway	7		Vlaardingen (NL)	4
Grenoble	7		Ankara	3
Leiden (NL)	7		Frankfurt	3
Naples	6		Ghent	3
Sonora	6		Oss (NL)	3
Balk (NL)	5			

We hypothesised 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. 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.

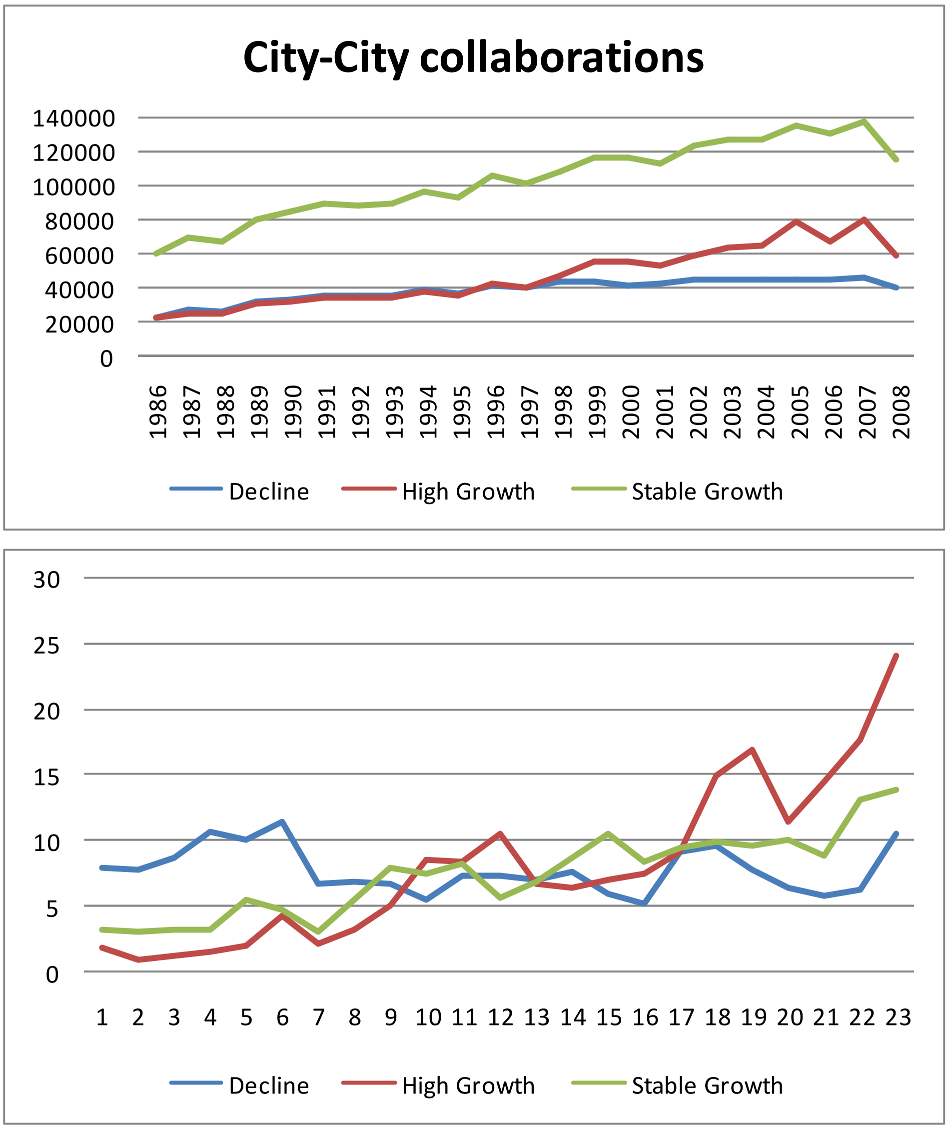

Figure 11. *Number of city-city collaborations (in absolute numbers above, relative to the number of publication *100 below) in selected cities in the field of Biotechnology (1986-2008).*

The result provide a strong indication of the importance of co-authorship relations as a source of related competences. Declining cities show a much lower level of relatedness than cities with a growing share of publications.

In the next step, the co-author networks of Wageningen were mapped in order to see to what extend these collaborations provide a source of related variety. The word-frequencies of all publications in Wageningen, all publications of co-authors of Wageningen and the total word frequency of the entire dataset were correlated. The results indicate a small but significant difference in the correlation pattern (Table 6). In other words, 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 8. *Pearson Correlation of word frequencies 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

d. Triple Helix Interactions

Finally, the role of non-academic organisations, most notably industry, in knowledge production was investigated. In a knowledge-based society, most socio-economic developments require new knowledge developments (Webster 2006), and thus 'problem-based' R&D will become increasingly important and encompassing. These societal dynamics were made visible by the contribution of researchers outside universities to knowledge production. Biotechnology shows a fairly stable pattern in company participation and governmental participation in the period under study.

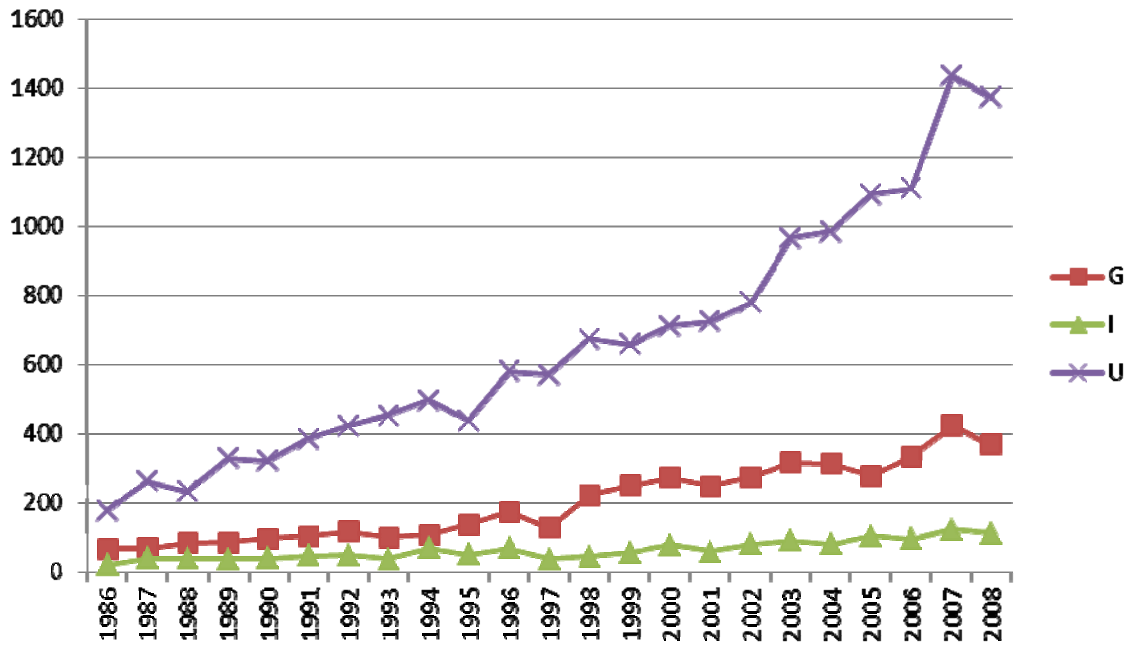

Figure 7. *Number of Academic (U), Public (G) and Commercial (I) organisations in the field of Biotechnology (1986-2008).*

Furthermore, industry involvement can be shown to contribute to distinct topics in the field of Biotechnology, adding to the cognitive turbulence. In Biotechnology the correlation between geographical location and word-use are relatively high and indicates a strong relationship between the geography of knowledge production and the research topics under study. Consequently, Biotechnology seems strongly rooted in local socio-economical context of application.

5. Discussion

Before we proceed to draw conclusions and consider policy implications, we should emphasize that this effort was motivated by methodological considerations as well as conceptual ones. Can the knowledge base of Biotechnology be measured? For this purpose, we combine the perspective of the path dependent research practices with the development of the global science system and the role of socio-economic dynamics.

In our conceptualisation, large numbers of researchers around the world interact in both competitive and collaborative relations which are characterized by heterogeneity, and with no overall direction. These local processes give rise to an emergent science system with limited predictability (Arthur 1989; Kauffman 1993; Holland and Miller 1991). 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 conceptualisation provides a starting point for measuring and modelling the evolutionary patterns of knowledge dynamics. The geographical setting, the global knowledge-base, and the context of application constitute three relatively independent sources of variance. The three sources of variance may reinforce one another in a co-evolutionary process. The evolutionary perspective is obtained by focussing on the local path dependencies in terms of word use in scientific publications.

Scientific communications are extremely well archived, and therefore, we have a wealth of data at our disposal when we study the dynamics of the sciences and science-based technologies. We could have used patent data instead of scientific publications. However, licensing and patent practices are expected to differ among national innovation systems (Nelson, 1993).

Words, however, are a complicated indicator. Firstly, we assume that words and their co-occurrences are representative of topics under study. 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 field differences exist in terms of local path dependencies (Heimeriks and Leydesdorff 2011).

6. Conclusions

In this study, we explored the evolutionary developments of knowledge production in Biotechnology. The aim of the empirical analyses presented here was to gain insight in the localised contributions in knowledge production in Biotechnology and to investigate what changes took place in the geographical distribution of biotechnological developments.

The results provide a representation of the evolving status of science. It shows in particular how, while the disparities between countries and regions remain huge, the proliferation of digital information and communication technologies is increasingly modifying the global picture. By making codified information accessible worldwide, it is having a dramatic effect on the creation, accumulation and dissemination of knowledge, while at the same time providing specialized platforms for networking by scientific communities operating at a global level.

The distribution of research efforts in Biotechnology between North and South has changed with the emergence of new players in the global economy. A bipolar world in which Biotechnology is dominated by the European Union, Japan and the USA is gradually giving way to a multipolar world, with an increasing number of public and private research hubs spreading across North and South. Early and more recent newcomers to the Biotechnology knowledge producers, including South Korea, Brazil, China and India, are creating a more competitive global environment by developing their capacities in the industrial, scientific and technological spheres.

The contribution of United States scientific institutions to publications in Biotechnology has continued to rise in sheer numbers over the past decades, as have most countries. At the same time that the USA and other scientifically advanced countries have maintained slow growth, some countries that are newly developing their own scientific systems are making spectacular gains in numbers of publications contributed to Biotechnology journals. As this happens, the USA and the EU drop as a percentage share of all publications. The drop in percentage share is not an absolute loss of ground.

However, the data shows that the scientific system as a whole is growing, and new members are contributing to the pool of knowledge. As they do, the system as a whole benefits. Science is codified and networked at the global level, so it would be difficult to argue that any nationally defined contribution can “lose” in relation to any other part through the addition of new knowledge (Wagner 2008). Far from losing ground in science to new entrants, the USA and other scientifically-advanced countries are gaining new colleagues and partners as well as access to new resources as other countries develop their scientific capacities. New sources of variety are being introduced in the Biotechnology system, thus increasing the innovative potential of the system as a whole.

We hypothesised that at each location, the evolution of knowledge production can be described as a process of branching from existing knowledge embodied in individuals (skills) and in knowledge producing organisations (routines and infrastructures). Our results allow us to elaborate the relationship between locally embedded knowledge in combination with codified and accessible external knowledge in the process of novelty production.

In three consecutive periods between 1986 and 2008, the word use in geographical locations with a stable growth pattern, shows a relatively modest overlap, in line with the observation of the dynamic cognitive development of the field. However, the unique words used in the second period (1993-2000) and third period (2001-2008), are to a great extend related through co-occurrences with the words used in the previous period. In these cases, around 83% of the tile words are related to the tile words in the previous period. In locations of relative decline (such as Baltimore) and strong growth (such as Seoul), there are lower levels of relatedness of between 53% and 64%.

Further indication of this pattern of path dependency in topics of research at different geographical locations is provided by the re-occurrence of words in consecutive years; re-occurrence of topics is strongly related to the evolutionary success of different locations in Biotechnology research.

Additionally, co-occurrence analysis shows that topics originating from cities with a declining growth pattern are on average less related to other topics than cities with a stable growth pattern. High growth cities contribute topics that show relatively little relatedness to the entire set of topics, providing further evidence for the observation that new entrants contribute to new and unrelated topics in the field of Biotechnology.

Further evidence of this relationship between evolutionary development and the availability of a new topics is provided by the appearances and disappearances of topics in the selected cities under study. The average number of new topics at certain locations is related to the availability space as indicated by the co-occurrences. Most new topics are introduced by cities with a stable growth pattern, followed by cities with a high growth rate. Locations of declining importance contribute only small numbers of new topics. Furthermore, the disappearance of topics seems related to the rate of appearance of new topics.

Interaction between knowledge producing regions is increasing rapidly, as indicated by co-author relationships. Co-author networks are expected to be an important mechanism for providing related variety in local knowledge production. The word-frequencies of all publications in Wageningen, all publications of co-authors of Wageningen and the total word frequency of the entire dataset were correlated and the results indicate a small but significant conformation of co-authors as a source of related variety in knowledge production.

Furthermore, industry involvement can be shown to contribute to distinct topics in the field of Biotechnology, adding to the cognitive turbulence. In Biotechnology the correlation between country and word-use is relatively high and indicates a strong relationship between the geography of knowledge production and the research topics under study. Biotechnology seems more rooted in local contexts, related to socio-economical context of application.

Interactions among the local research practices, global scientific fields, and the context of (industrial) application are multidirectional and involve positive and negative feedback loops. In other words, local research practices, codified knowledge, and economy interact and shape one another in processes of co-evolution (Whitley 2000).

More precisely, three dynamics can generate a stable regime if these dynamics are compatible with one another. Successful regimes require synergetic interactions among local research practices, emergent scientific landscapes, and the field's relationship to its societal context. The limitations of Nelson and Winter's (and similar) models of evolutionary-economic processes are most clearly seen when they are confronted with the question of "What evolves?" We argue that rather than routines, 'regimes' are the unit of evolutionary analyses. Regimes differ in terms of self-organization among these three sources of variance. The scope of opportunities for researchers to contribute within the constraints of the existing body of knowledge are different in each field and at each location.

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