What Differentiates Top Regions in the Field of Biotechnology?
An empirical Study of the Texture Characteristics of 101 Biotech Regions in North-America, Europe and Asia-Pacific

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Abstract

Over the last decade, the cluster phenomenon has triggered the attention of researchers and policy makers. While case studies provide valuable insights on the dynamics within (individual) clusters, large-scale quantitative studies addressing the texture characteristics of (biotech) clusters are lacking. Building on patent and publication-based indicators, our analyses encompass the texture characteristics of 101 regions in North-America, Europe and Asia-Pacific that developed substantial technological activities in the field of biotechnology during the rapid growth phase of the biotech industry (period 1992-1997). Our findings signal two distinctive types of biotech regions that are able to obtain the status of “top region” and provide insights into the antecedents of growth in terms of regional texture characteristics. In “concentrated” regions, biotech technology development is mainly situated within private firms with a central role being played by anchor tenant firms (established pharmaceutical firms). In “distributed” regions technology development is more equally distributed between private firms and public knowledge institutes and the entrepreneurial orientation of scientific actors plays an instrumental role for becoming a leading region in biotechnology. Finally, our results indicate that scientific eminence remains important, during growth phases of the industry.

Keywords: biotechnology, high tech cluster, technology development, entrepreneurial universities, industry, regional innovation studies

1. Introduction

Modern biotechnology has generated important breakthroughs in several industries, from food, agriculture to the chemical industry, but most particularly in the pharmaceutical industry (Arora and Gambardella, 1990; Zucker and Darby, 1997), by enabling the creation of entirely new organic materials and profoundly changing the process of (drug) discovery and product development (Powell et al. 1996). Consequently, biotechnology is often considered as a promising technology that will bring economic growth and welfare into a region. Over the last decades, thriving biotech clusters such as the San Francisco Bay Area, San Diego and Boston, but also other emerging biotech regions have therefore been widely studied in order to identify the main factors behind the success of biotech regions.

General consensus exists that well developed biotech regions, so-called clusters or hot spots, are characterized by the presence of world-class scientific research, high levels of entrepreneurial activity (both academic spin-offs and industrial ventures), high labour mobility and dense social networks, the presence of venture capital and a dedicated support infrastructure (e.g. Casper, 2007; Cooke, 2001; Owen-Smith et al., 2002). About the respective role and importance of public knowledge institutes and private firms for the emergence and early development of biotech regions different perspectives are being advanced. Case study research provides evidence that universities and knowledge generating institutes have played a central and active role in the creation of biotech clusters in the region of Boston (Breznitz et al., 2008) and San Francisco Bay area (Chiarone and Chiesa, 2006). In contrast, private firms have played a prominent role in the development of biotech activities in the regions of Milano (Italy) and Uppsala (Sweden) (Chiarone and Chiesa, 2006) as well as in Japan (Bartholomew, 1997). As (industrial) biotechnology is entering a growth phase (Lecocq and Van Looy, 2009), the question whether regions can evolve into leading clusters by relying on a distributed texture or whether the presence and/or emergence of an anchor tenant firm (Agrawal and Cockburn, 2003) is a prerequisite in this respect, becomes pertinent, both for practitioners and policy makers engaged in regional economic development.

While case study research provides valuable insights and detailed information on the characteristics and the dynamics within individual biotech clusters, previous research typically covers only one or a limited number of biotech regions. The results of these studies are difficult to compare since they use different (performance) indicators, relate to different regional units of analysis within different time periods. Large-scale empirical studies addressing the texture characteristics of biotech regions are absent. Building on patent and publication-based indicators, we engage in such a study in the field of biotechnology. Our analyses cover 101 regions from North-America, Europe and Asia-Pacific that developed substantial technological activities in the field of biotechnology over the period 1992-1997, an era characterized by rapid growth of the biotech industry. Our study contributes to the existing literature on biotech clusters by introducing a new typology ("concentrated" versus "distributed" regions) and examining different antecedents of global competitiveness of biotech clusters in terms of regional texture characteristics, according to the type of clusters.

The paper is organized as follows: in the next section the importance of basic science in molecular biology, and the role of knowledge generating institutes, small dedicated biotech firms and large established (pharmaceutical) firms in the development of the field of modern biotechnology are discussed. Next, hypotheses are developed with respect to the distinctive industrial texture characteristics as well as the presence of entrepreneurial-oriented knowledge institutes in top regions during the growth phase of the biotech industry (period 1992-1997). Subsequently, data sources and variables used in the analyses are introduced. In the analyses section, the worldwide leading regions in terms of biotech technology development in the period 1992-1997 are identified. Next, the texture characteristics of those 'top' regions in terms of industrial base and the presence of entrepreneurial-orientated public knowledge institutes are further investigated. In the last part of the analyses, we study which texture characteristics are instrumental to become a top region in the field of biotechnology during the rapid growth phase of biotechnology. The paper concludes with a discussion of the results and some policy implications.

2. The field of modern biotechnology

Modern biotechnology is a complex, knowledge-intensive field that has its origin in academic research in molecular biology. Central for the field of modern biotechnology was the discovery of the double helix structure of DNA (1953) by Watson and Crick in the laboratories of the University of Cambridge (UK). The foundation of the modern biotech industry was laid in 1973, when professors Cohen (Stanford University, US) and Boyer (University of California, US) discovered the recombinant DNA technique, which allowed to transfer the *basic science* of molecular biology into useful knowledge for a wide range of industrial applications (Feldman, 2003).

Following the discovery of the recombinant DNA technique, the second half of the 1970s and the 1980s was marked by the creation of the first companies dedicated to modern biotechnology, the so-called *New Dedicated Biotech Firms* (NDBFs). These new biotech companies were often co-founded by, or maintained strong linkages with academic researchers (Zucker and Darby, 1996). They focused on exploring new technological and scientific research results and translating them into the commercial domain (Acharya, 1999; Galambos, 2006). As new, scientific knowledge is often characterized by a substantial amount of tacit knowledge, developing an idea from science most often requires close links with the academic inventor(s) (Rosenberg and Nelson, 1994; Zucker and Darby, 1996;) and NDBFs were therefore most often established in close vicinity of universities or research centres (Prevezer, 2001).

In the US, small research-intensive biotech firms set up to further explore and commercialise the results of scientific research, have significantly contributed to the development of biotech clusters. In the Greater Boston area for example, one of the first biotech clusters in the US, more than 50 biotech companies spun off from the Massachusetts Institute of Technology (MIT) and an additional 50 start-ups were founded by academic inventors of the university (Breznitz et al., 2008). The first mover advantage in the US in the growth of small research-intensive biotech firms has been facilitated by supportive institutional arrangements such as the presence of venture capital specialised in high technology and the Bayh-Dole Act[1] that facilitated technology transfer between academia and industry (Owen-Smith et al., 2002, Prevezer, 2001). Furthermore, scientists in the US were able to be involved in the creation of start-ups while retaining their academic position (Prevezer, 2001). Owen-Smith et al. (2002) also point to the diversity in the organizations involved in research activities (universities, research institutes, hospitals, and small firms) and the support of the National Institutes of Health (NIH) enabling the integration between basic science and clinical development.

[1] The Bayh-Dole Act (1980) allows - and even encourages - US universities to appropriate the results of publicly funded research through patenting.

By the mid 1980's, *large established firm*s in the chemical, and in particular the pharmaceutical industry, increasingly started to display interest in the field of biotechnology. However, as the main knowledge base (organic chemistry) of these incumbent firms differed significantly from the science base of biotechnology (molecular biology), large firms had difficulties to internalize this new knowledge (Zucker and Darby, 1997). From the late 1980s onwards, they entered into the field by setting up strategic alliances with and/or acquiring small biotech firms (Arora and Gambardella, 1990; Dominguez-Lacasa, 2006; Roijakkers and Hagedoorn, 2006; Rothaermel 2001; Rothaermel and Hess, 2007). Most of these research and/or joint development agreements with small biotech firms were product-specific, more market-oriented alliances focussed on clinical trials, FDA regulatory management and marketing and sales activities (Arora and Gambardella, 1990; Rothaermel 2001), while acquisitions mostly aimed at acquiring NDBF's specialised knowledge in particular areas of biotechnology research (Arora and Gambardella, 1990).

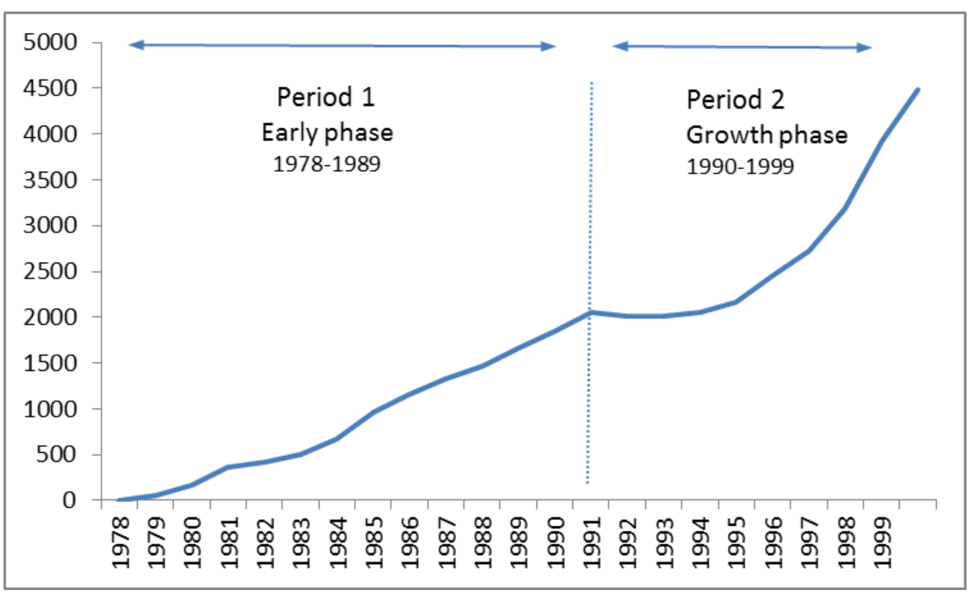
Several case studies provide evidence that large established firms have played an important role in developing regional activities in the field of biotechnology: in the region of Basel (Switzerland), the strong presence of a pharmaceutical industry with firms like Novartis and Roche, has contributed to the growth of biotech activities in the region (Houston, 2003); equally, in the Bioregion Rhineland in Germany, the presence of a chemical and pharmaceutical industry is considered to be "an advantage for the creation of an integrated biotech sector from research to production" (Zeller, 2001). Around the 1990's, mergers and acquisitions by large established players resulted in an upsurge of *entrepreneurial activities* in the field of biotechnology in the regions of Milan (Italy), Uppsala (Sweden) and San Diego (South California), leading to the emergence of totally new business structures in the region (Chiaroni and Chiesa, 2006). In the San Diego cluster for example, nearly 50 industrial spin-offs were created by former employees / scientists of the biotech company Hybritech that left the company after Hybritech was acquired by the pharmaceutical company Eli Lilly.

A large strand of literature shows that further technology advances in the biotech industry relies to a large extent on interorganisational collaborations between organizations with complementary resources, with universities and public research centres at the basis of new scientific knowledge, large pharmaceutical and chemical firms having the capabilities to market products (including experience with clinical testing, engineering know-how about manufacturing and access to commercial market), and new dedicated biotech firms often considered as the nexus between academia and large established firms (Arora & Gambardella 1990; Gambardella et al. 2000, Gertler & Vinodrai, 1996; Mangematin et al. 2003; Powell et al. 1996). Collaboration on an international scale appears to be of particular relevance for technology development since it introduces new knowledge and skills to a region (Cooke, 2001; Lecocq et al. 2009; Zeller, 2001). Over the period 1975-1999, Roijakers and Hagedoorn (2006) found evidence for changing patterns in the networks of inter-firm R&D partnering in the pharmaceutical biotechnology: from a few, isolated clusters of cooperating firms in the early years (1975-1979) into increasingly dense research networks in the 1980's with small dedicated biotech firms playing important bridging roles between different networks. By the 1990s, interfirm R&D networks became very large and densely interrelated and some large, incumbent firms developed into important network players.

On a global scale, the number of contractual R&D partnerships between firms has grown over time, especially since the 1980's, with a clear dominance of the pharmaceutical sector (including pharmaceutical biology) and other high-tech industries (information technology, and aerospace and defence) from the mid-1980's onwards (Hagedoorn, 2002). The need for learning and flexibility in a highly competitive landscape are put forward by Hagedoorn (2002) as major reasons for the increase in the joint R&D projects in high tech industries. Powel et al. (1996) point to the specific skills and know-how required to translate scientific advances into commercial applications which in an industry characterized by a regime of rapid technology development and a complex knowledge base such as biotechnology, most often does not reside within a single organization but has to be acquired through networks of learning.

Figure 1 presents the (worldwide) evolution of biotech technology development over the period 1978-1999, measured by the number of EPO patent applications. The figure shows a steady, linear increase in the number of patent applications in the early phase of the biotech industry (period 1978-1990), followed by an exponential growth in the number of patent applications from the early 1990s onwards (Lecocq and Van Looy, 2009). This study focusses on the period 1992-1997, characterized by rapid growth of biotech technology development.

Figure 1. Evolution of patenting in the field of biotechnology
(EPO Patents, period 1978-1999, worldwide)



3. The regional clustering of biotech activities: towards hypotheses

Aforementioned studies (e.g. Bartholomew, 1997, Breznitz et al., 2008; Chiarone and Chiesa, 2006; Houlton, 2003; Owen-Smith et al, 2002, Prevezer, 2001; Zeller 2001) suggest the existence of different pathways of regional cluster formation with different types of actors leading the process of cluster emergence in the field of biotechnology. Part of these differences in texture may also be related to life cycle dynamics with universities playing a main role in the early stages of the industry (period 1978-1989), while industrial capabilities are becoming more important after a "dominant design" sets in (Utterback, 1994) and technologies (products) are being commercialized (period 1990-1999). In order to profit from the take-off of economic activities in the growth phase of biotech, regions may benefit from a different configuration in terms of presence of (entrepreneurial) research universities and industry composition (presence of new dedicated biotech firms and more established firms) than in the early days of the industry. The question whether regions can evolve into leading clusters in the growth phase of the biotech industry by relying on a distributed texture where both private firms and public knowledge institutes contribute significantly to regional biotech technology development or whether the presence and/or emergence of an anchor tenant firm is a prerequisite, becomes a pertinent question.

3.1 Industrial texture characteristics

By their nature and core raison d'être, firms are best placed to identify market needs, translate technological opportunities into prototypes and commercial products, and bring these new products to the market. Even in science-intensive fields such as biotechnology, private firms remain the major player on the market place. When industries are evolving and technologies are becoming more mature, relations are evidently becoming more market-based and the competition amongst firms intensifies (Baglieri et al., 2012). In regions with a critical mass of activities directed towards market exploitation and commercialization, firms have more opportunities to interact and learn from high-quality suppliers, demanding (industrial) customers and other innovative firms producing similar or complementary goods and services (Porter, 2000) resulting in enhanced innovation dynamics in the region.

The concentration of innovative activities within larger, R&D intensive firms might be of particular relevance for the development of a new industry because of their scale and access to larger financial resources as compared to new and / or small firms (Gray and Parker, 1998). By creating local niches and/or intermediary markets, larger firms may also encourage entrepreneurial activity in the region and attract high-quality suppliers which would not be present or of lower quality in the absence of the anchor firm (Agrawal and Cockburn, 2003). Therefore, we propose that:

Hypothesis 1a: Regions in which technology development activities are to a larger extent situated within firms, are more likely to become a leading biotech region in the growth phase of biotech.

Hypothesis 1b: Regions with higher levels of concentration of regional biotech technology development activities (by private firms) within an anchor tenant firm, are more likely to become a leading biotech region in the growth phase of biotech.

3.2 Entrepreneurial-orientated knowledge institutes

For firms active in complex, science-intensive fields such as biotechnology searching for and acquiring highly-specialized scientific knowledge from outside the boundaries of the organization is essential (Powell et al., 1996). As the field of biotech further develops, knowledge becomes codified in routine procedures or commercially available equipment such as the automatic DNA sequencer (Rothaermel and Thursby, 2007) and the relevant scientific knowledge is spreading on a more global scale. The diffusion of knowledge is further enhanced by the numerous international collaborations between public knowledge institutes and private firms (e.g. Cooke, 2001; Lecocq and Van Looy 2009; Zeller, 2001). Therefore, geographical proximity of a strong science-base and the presence of entrepreneurial-oriented knowledge institutes in the region may become less important in later stages of the technology life cycle. This leads to the following two hypotheses:

Hypothesis 2a: The science-intensity of a region, measured by the number of publications per population, is no longer instrumental for becoming a leading biotech region during the growth phase of biotech.

Hypothesis 2b: The entrepreneurial orientation of scientific actors, measured by their involvement in technology, is no longer instrumental for becoming a leading biotech region during the growth phase of biotech.

4. Data

To identify the worldwide leading clusters in terms of biotech technology development and study the texture characteristics of biotech regions in a quantitative way, we draw on the dataset with EPO patent applications and Web of Science publications in the field of biotechnology created by Glänzel et al. (2004).

The use of patent and publication data has several advantages (Griliches, 1990; Jaffe, 1989; Pavitt 1985). They are an important source of information about the time and location of technological and scientific inventions, as well as the organizations and institutions involved. Furthermore, patent and publication data have a global coverage and allow adopting a (technology) field-specific perspective. Prior research has established patent counts as a valid indicator of novel technological activities at the level of regions (Acs et al. 2002) and firms (Hagedoorn and Cloodt, 2003; Narin and Noma, 1987), and this is certainly true for the field of biotechnology which is characterised by a high propensity to patent (Arundel and Kabla, 1998). Some research points out that patented inventions may vary in technical and economic value (Mansfield 1986, Gambardella et al. 2008) and therefore suggest to weight patent counts by the number of forward citations received (Hall et al., 2005; Harhoff et al., 1999; Trajtenberg, 1990). Recent research by Hagedoorn and Cloodt (2003) indeed indicates that patents counts and patent citations represent somewhat different aspects of innovation performance with patent counts more strongly related to R&D input, while patent citations showing a stronger link with new product development. Hagedoorn and Cloodt (2003), nonetheless, provide evidence for the presence of a large degree of overlap between patent counts and citation-weighted patent measures in high-tech industries[2].

For the purpose of this study, all biotech patents and publications with applicant or author addresses in Australia, Canada, Europe (EU-15), Japan, the US and Switserland have been withhold. Together, these countries represent more than 97% of all patents in the field of biotechnology. We focus on the time frame 1992-1997, the period of rapid growth of the biotech industry.

In a first step, all patents and publications have been allocated to their respective regions based on the address information of applicants (patents) and authors (publications) following the "*patent allocation methodology*" developed by Lecocq et al. (2011). Table 1 shows, for every country, the regional level of analysis selected in this study in order to provide comparable units of analysis in terms of population[3]. Only those regions that developed a substantial amount of biotech activity over the time period 1992-1997 (minimum 18 EPO patent applications, i.e. on average three patents/year) are retained for the analyses.

[2] For the pharmaceutical industry, Hagedoorn and Cloodt (2003) found a 0,777 correlation between patent counts and patent citations at the firm level.
[3] The state of California (US) was split in North and South California as the state covers 2 large and distinct biotech clusters. Three outlier regions have been removed.

Table 1. Regional level of analysis

North America	Canada: states (n=6) and major mainland territories (n=2);
	US: states (n=50) and Washington D.C.
Europe	EU-15 and Switzerland: NUTS1/2 regions[4] (n=197)
Asia-Pacific	Australia: states (n=6) and major mainland territories (n=3);
	Japan prefectures (n=47)

The "*sector allocation methodology*" developed by Du Plessis et al. (2011) allows to identify which type of actor (private firms, public universities and research centres, research hospitals and/or persons) applied for the patent. Based on the "*name harmonizing method*" of Magerman et al. (2011), we identify the firm and/or other actor with the largest number of biotech patents in the region. In the study, we refer to those firms and other actors as respectively the "lead company" and the "lead actor" in the region. The "lead company" in the region is further classified as "New, Dedicated Biotech Firm" (NDBF), "Established Firm (EF) or "Other firm" according to the definitions in Table 2. This classification of firms relies on information on the industry(ies) in which the firm is (primarily) active, it's year of establishment and the location of the headquarter[5] retrieved from company websites and other sources[6] such as reports on merger and acquisition activities, reports on new products and technologies in the field of life science, market research reports and company profiles.

Table 2. Refinement of the typology of firms

New Dedicated Biotech Firms (NDBF)	Firm primarily active in the field of biotechnology and established after 1974.
Established Firm (EF)	Firm primarily active in other fields than biotechnology (e.g. pharmaceutical, chemical, food and other industries) and established before 1974.
Other Firm	Firm active in the field of biotechnology but not as a product or research company (e.g. regional technology transfer offices, venture capitalist, regional industrial agency)

[4] Nuts1 level was selected for the smaller countries (Austria, Belgium, Greece, and Ireland), while nuts2 level is used for the other European countries.

[5] Information on the (headquarter) location was matched with the address information on the patent to ensure the information retrieved via web sources corresponds with the assignee (company) of the patent application.

[6] Since the 1990s have been characterized by a lot of merger and acquisition activities in the field of biotechnology, but also because of the high failure rates of new (biotech) companies, we had to rely on exhaustive web searches to find company information, especially for the companies that no longer exist today, exist under a different name or have been acquired in the meantime.

Table 3 provides an overview of the texture variables used in the analyses of the paper. Patent counts at the level of regions are used as performance measure in terms of novel biotech technology development activities (*"technological performance"*), whereby the 15 regions with the highest count of biotech patents (based on assignee addresses) are considered as worldwide leading regions in biotech ("*top 15 region"*). The industrial texture characteristics of regions imply the share of patents in the region owned by companies ("*share of company patents"*), the count of firms in the region that are active in biotech technology development (*"Number of firms"*) as well the degree of concentration of industrial biotech technology development within the leading firm in the region (measured by the concentration ratio, "*Company concentration index"*). As a measure for the scientific capabilities of regions, the number of publications normalised by population ("*Science-intensity of the region"*) is used. This measure includes both publications from scientific actors and company publications. The ratio of the total number of patents owned by knowledge institutes and total number of publications in the region ("*Entrepreneurial orientation of knowledge institutes"*) is used as an indicator for the entrepreneurial attitude of the knowledge institutes in the region. Finally, given the importance of inter-organisational collaboration in the field of biotechnology (e.g. Arora and Gambardella, 1990; Gertler and Vinodrai, 1996; Powel et al., 1996; Roijakers and Hagedoorn, 2006), measures for international R&D collaboration based on co-patenting between assignees from different countries will be included in our analyses: based on the type of the foreign assignee, we distinguish between a) international technology collaborations with firms ("*International collaboration with firms"*) and, b) international technology collaborations with knowledge institutes ("*International collaboration with knowledge institutes"*).

Table 3. Texture variables

Variable	Description
Top 15 region	Variable taking the value 1 if a region is among the top 15 regions worldwide based on the number of biotech patents in the region
Technological performance	Total number of biotech patents in the region
Share of company patents	Share of company-owned biotech patents over the total number of biotech patents in the region
Company concentration index	Ratio of the number of biotech patents of the leading firm in the region and the total number of company biotech patents in the region
Science-intensity of the region	Number of biotech publications in the region per 1000 inhabitants
Entrepreneurial orientation of knowledge institutes	Ratio of the total number of biotech patents applied by public knowledge generating institutes in the region and the total number of biotech publications in the region
Number of firms	Number of companies in the region active in biotech patenting
International collaborations with knowledge institutes	Number of biotech co-patents in the region with a knowledge generating institute from outside the country
International collaborations with knowledge firms	Number of biotech co-patents in the region with a firm from outside the country

Table 4 provides descriptive statistics and correlation coefficients for the variables of the study. In general, the large standard deviation in relation to the mean value of the variables indicates the presence of large differences between the regions under study in terms of technological performance, industrial texture characteristics, science-intensity as well as the entrepreneurial orientation of the knowledge institutes in the regions. The technological performance of regions, and being a top region in biotech, is mainly correlated with the number of firms in the region active in biotech technology development. None of the indicators used as explanatory variables in the regression analyses show excessively high correlations.

Table 4. Descriptive statistics

		Mean	Std. Dev.	1	2	3	4	5	6	7	8	9
1	Top 15 region	0.15	0.36	1								
2	Technological performance	24.06	35.72	0.828	1							
3	Share of company patents	0.66	0.28	0.109	0.098	1						
4	Company concentration index	0.55	0.29	-0.315	-0.379	0.083	1					
5	Science-intensity of the region	0.19	0.13	0.253	0.238	0.004	-0.152	1				
6	Entrepreneurial orientation of knowledge institutes	0.005	0.006	0.294	0.387	-0.565	-0.186	0.109	1			
7	Number of firms	6.23	9.36	0.707	0.895	0.160	-0.482	0.182	0.245	1		
8	International collaboration with knowledge institutes	0.26	0.82	0.380	0.386	0.185	-0.104	0.086	0.026	0.303	1	
9	International collaboration with knowledge firms	0.26	0.74	0.362	0.464	0.159	-0.160	0.156	0.060	0.419	0.276	1

5. Analyses

5.1 Top regions in biotech

Biotechnology development activities are highly concentrated in a few regions or clusters worldwide (Audretsch and Feldman, 1996; Feldman and Florida, 1994). Our data provides evidence that, in the rapid growth phase of the biotech industry (period 1992-1997), the 15 worldwide leading biotech regions in terms of biotech technology development, measured by the count of biotech patents, account for 56% of all biotech patent activity. Table 5 shows that most top regions are located in the US, e.g. North-California (San Francisco region), Massachusetts (Boston) and South-California (San Diego region). Japan has two top regions in biotech: Tokyo and Osaka. The three largest biotech regions in Europe are Île de France (Paris region, France), Denmark and London (United Kingdom). For the 101 biotech regions under study, we find further evidence of a high correlation (r= 0.90) between the number of patents in early phase (period 1978-1990) and the number of patents in the growth stage (period 1992-1997) of biotech. Likewise, a high correlation is found between the ranking of regions in terms of biotech patents in both periods (r= 0.83), suggesting the presence of important early mover advantages at the regional level for the development of biotech activities.

Table 5. Leading biotech regions

EPO patents, period 1992-1999, based on assignee addresses

Rank	Region, country	Patents 1992-1997 (rank)	Patents 1978-1990 (rank)
1	North California, US	1,083 (1)	781 (2)
2	Tokyo-TO, Japan	921 (2)	1,204 (1)
3	Massachusetts, US	824 (3)	651 (4)
4	South California, US	711 (4)	413 (9)
5	New Jersey, US	650 (5)	562 (6)
6	New York, US	626 (6)	565 (5)
7	Maryland, US	576 (7)	146 (20)
8	Île-de-France, France	563 (8)	543 (7)
9	Osaka-FU, Japan	477 (9)	760 (3)
10	Pennsylvania, US	449 (10)	214 (15)
11	Denmark, Denmark	376 (11)	188 (16)
12	Inner London, UK	328 (12)	428 (8)
13	Illinois, US	305 (13)	261 (14)
14	Karlsruhe, Germany	288 (14)	293 (12)
15	Nordwest Schweiz, Switzerland	280 (15)	290 (13)

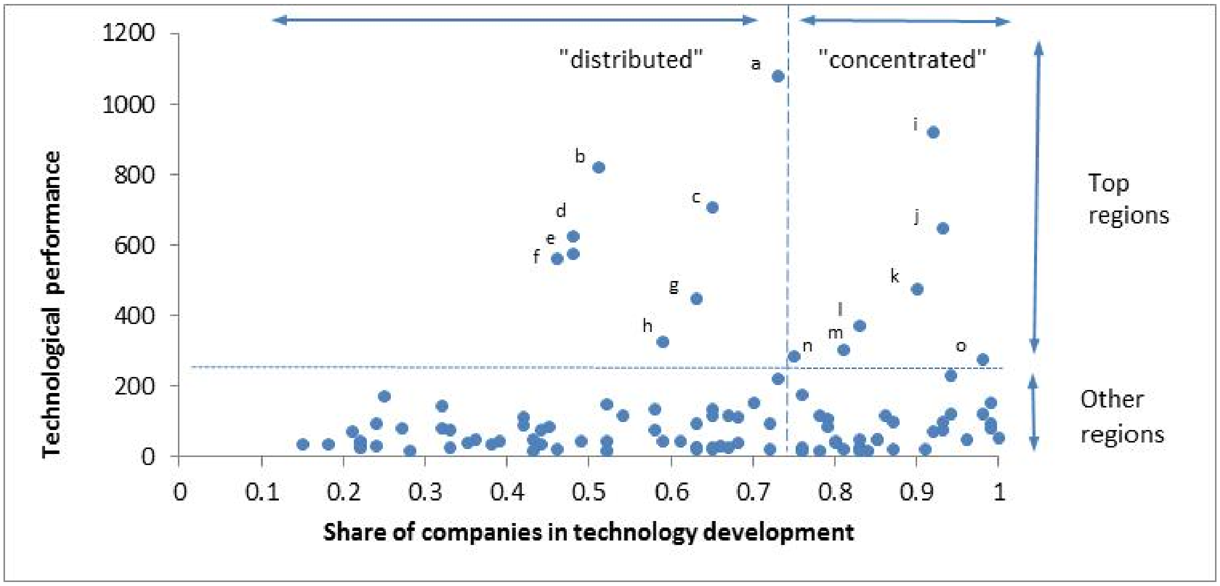
5.2 Towards a typology of (leading) biotech regions

The history of the biotech industry illustrates that different types of actors ranging from private firms (new dedicated biotech firms and established firms) to public knowledge institutes (universities and public research centers) and research hospitals, are involved in biotech technology development. In this part of the analyses, we investigate whether during the growth phase of biotech, technology development activities in 'top' regions are to a larger extent driven by firms as compared to the other biotech regions (hypothesis 1a).

Figure 2 shows the technological performance of regions and the share of biotechnology development activity undertaken by private firms for the 101 regions under study. The figure again confirms the strong geographical concentration of biotech technology development. Overall, no obvious, linear relationship can be discerned between the performance of regions and the share of technology development undertaken by private firms. On the one hand, one observes no 'top regions' when the share of companies (in terms of technology development) is situated below 40%. On the other hand, when looking at the leading regions only, we notice that in some regions technology development activities are highly concentrated within firms (share of company patents above 75%), while in other regions technology development is much more distributed over private firms and other types of actors (with the share of company-owned patent situated around 50%). These results indicate that to become a leading biotech region in the growth phase of biotech, regional technology development activities do not need to be primarily driven by private firms, so that hypothesis 1a only partly holds.

Figure 2. The technological performance of regions and the share of biotech technology development activities undertaken by private firms

(EPO Patents, period 1992-1997, 101 biotech regions)



The top 15 leading regions in biotech technology development over the period 1992-1997 are a. North California, US; b. Massachusetts, US; c. South California, US; d. New York, US; e. Maryland, US; f. Île de France, France; g. Pennsylvania, US; h. Inner London, UK ; i. Tokyo-TO, Japan; j. New Jersey, US; k. Osaka-FU, Japan; l. Denmark, Denmark; m. Illinois, US; n. Karlsruhe, Germany; and o. Nordwestschweiz, Switzerland.

The Table 6 shows for each of the 15 main biotech regions, the "lead actor(s)" in the region, where "lead actor" is defined as the organization with largest number of biotech patent applications in the years 1992 to 1997. For the leading biotech regions where technology development is highly concentrated within private firms, the leading organization in the region is always an established firm, mostly primarily active in pharmaceuticals. In the leading biotech regions where technological activity is much more distributed over private firms and other actors, the leading organizations in the region imply a combination of public research institutes (university, research center or research hospital) and private firms (new dedicated biotech firm or established firm).

Table 6. Leading organizations in the top biotech regions
(lead actor based on biotech patent count, yearly figures, period 1992-1997)

Region	Organisation name	Organisation type
1. North California, US	Genentech Inc.	New Dedicated Biotech Firm
	Incyte	New Dedicated Biotech Firm
	University of California	University
2. Tokyo-TO, Japan	Ajinomoto Co., Inc.	Established Pharmaceutical Firm
	Kyowa Hakko Kogyo Co., Ltd.	Established Firm
3. Massachusetts, US	General Hospital Coporation	Hospital
	Genetics Institute	New Dedicated Biotech Firm
4. South California, US	Amgen	New Dedicated Biotech Firm
	Gen-Probe Incorporated	New Dedicated Biotech Firm
	Scripps Research Institute	Research Center
5. New Jersey, US	Becton Dickinson & Co.	Established Pharmaceutical Firm
	Merck	Established Pharmaceutical Firm
6. New York, US	Bristol Myers Squibb Co.	Established Pharmaceutical Firm
	Johnson & Johnson	Established Pharmaceutical Firm
	Ludwig Institute for Cancer Research	Research Center
	New York University	University
7. Maryland, US	Department of Health and Human Services	Research Center
	Human Genome Sciences, Inc.	New Dedicated Biotech Firm
8. Île de France, France	Institut National de la Sante et de la Recherche Medicale (INSERM)	Research Center
	Institut Pasteur	Research Center
	Rhone-Poulenc AG	Established Firm
9. Osaka-FU, Japan	Ono Pharmaceutical Co., Ltd.	Established Pharmaceutical Firm
	Sumitomo Electric Industries, Ltd.	Established Firm
	Suntory Limited	Established Firm
	Takeda Chemical Industries, Ltd.	Established Firm
10. Pennsylvania, US	BAYER AG	Established Firm
	Smithkline Beecham	Established Pharmaceutical Firm
	University of Pennsylvania	University
11. Denmark	Novo Group	Established Pharmaceutical Firm
12. Inner London, UK	Cancer Research Campaign Technology Limited	Other Firm
	Medical Research Council	Research Center
	Unilever	Established Firm
	Zeneca	Established Pharmaceutical Firm
13. Illinois, US	Abbott Laboratories	Established Pharmaceutical Firm
14. Karlsruhe, Germany	Roche Diagnostics	Established Pharmaceutical Firm
15.Nordwestschweiz, Switzerland	F. Hoffmann-La Roche AG	Established Pharmaceutical Firm
	Novartis	Established Pharmaceutical Firm

The analysis of the texture characteristics of the top biotech regions thus provides evidence for the presence of two types of regions: regions in which technology development is mainly situated or concentrated within private firms – hereafter called “***concentrated regions***” - and regions where technology development is more equally distributed between private firms and entrepreneurial universities and/or research centres/hospitals, hereafter referred to as “***distributed regions***”. Figure 2 shows that both a distributed and a concentrated texture can give rise to a leading technology cluster in biotech.

The Wilcoxon-Mann-Whitney test statistics on the refined texture variables in Table 7, further reveal some distinct features of leading “distributed” versus leading “concentrated” biotech regions. Leading “concentrated” regions are characterized by a higher share of technology development activities by private firms. Technology development activities by private firms is also much more concentrated into the leading firm in the region than in the leading “distributed” regions. Leading “distributed” regions are characterized by a higher science-intensity of the region, measured by the number of publications per population, as well as the presence of universities and research centres with a more entrepreneurial orientation. On average, the leading “distributed” region count more firms than the leading “concentrated” regions. In terms of collaborations, leading “concentrated” regions engage more into international collaboration with knowledge institutes than the leading “distributed” regions. No statistical significant difference is found with respect to the international collaboration variable with firms.

Table 7. Texture characteristics of leading “distributed” versus “concentrated” regions
(Mean value, Wilcoxon-Mann-Whitney test, based on yearly figures, period 1992-1997)

	“distributed” Regions (n=8)	**“concentrated” regions** (n=7)	**z-value** wmw test	
Share of company patents	0.581	0.913	-7.938	***
Company concentration index	0.273	0.419	-2.447	**
Science-intensity of the region	0.314	0.215	3.453	***
Entrepreneurial orientation of knowledge institutes	0.014	0.004	7.312	***
Number of firms	23.813	20.071	2.481	**
International collaboration with knowledge institutes	0.646	1.429	-2.192	**
International collaboration with firms	0.875	0.929	-0.707	

***, **, * represents statistically significance at respectively 1%, 5% and 10% level

5.3 What differentiates leading regions from other biotech regions?

During the growth phase of biotech, some biotech regions are catching up while other regions are falling back in the ranking of (leading) biotech regions. Changes in the top 15 leading regions over the period 1992-1999 are used to analyze which texture characteristics differentiates leading regions from other biotech regions by means of logit regression models with the following functional form:

$$P(y_{it} = 1 \ / \ x_{it}) \text{ with } t = 1\text{-}7, \ x_{it} \text{ contains the explanatory and the control variables}$$

The analyses comprise all 101 biotech regions in our study, with the dependent variable taking the value 1 if the region is among the top 15 regions in year t, and the value 0 for all other biotech regions in year t. Random effects are used to control for the unobserved heterogeneity of regions. The explanatory variables are the refined texture variables presented in the data section (Table 3). We further include the size of the region (measured by its population) and time-specific effects in the regression models. A US dummy variable is used to control for a possible “first mover”-effect of US regions in the field of biotechnology.

Table 8 shows the results of the logit regression models. First, the regression is run for all 101 biotech regions (Model 1). As prior results in this paper showed that leading regions have different texture characteristics, separate analyses are also run for the regions with a “distributed” texture (n= 64, Model 2) and the regions with a “concentrated” texture (n=37, Model 3), where the latter have been defined as those regions in which technology development activities is predominantly situated within private firms (share of company patents >= 0.75) and the leading player in the region (period 1992-1997) is an established firm.

Table 8. Random Effect Logit models
(101 biotech regions, yearly figures, period 1992-1997)

	Model 1 **All regions**	**Model 2** **“Distributed” regions**	**Model 3** **“Concentrated’ regions**
Science-intensity of the region	17.5619**	86.1780***	52.3908***
	(7.8916)	(25.0164)	(17.3365)
Number of firms	0.6920***	2.1685**	0.9249**
	(0.1799)	(0.8742)	(0.4070)
Company concentration index	6.1367**	-22.7696	25.3441***
	(3.0207)	(23.4079)	(9.5590)
Entrepreneurial orientation of knowledge institutes	201.1364**	1479.3749***	504.0695
	(102.2134)	(557.6798)	(329.2293)
International collaboration with knowledge institutes	1.2805**	3.3563	4.3152***
	(0.5952)	(5.2437)	(1.2478)
International collaboration with firms	-0.4101	-1.9755	-0.3095
	(0.5655)	(3.0821)	(0.9891)
Population	0.0005	0.0007	0.0032***
	(0.0003)	(0.0006)	(0.0012)
US dummy	-0.2342	14.2357*	-6.0670
	(1.9595)	(7.5663)	(6.3827)
Time	-0.7769***	-0.8702	-2.5191***
	(0.2881)	(1.1603)	(0.7597)
Constant	-19.0575***	-75.4876***	-51.6588***
	(5.0345)	(18.3475)	(10.3443)
Observations	606	384	222
Loglikelihood	-52.5065	-9.8587	-27.2306
P	0.0086	0.0021	0.0004

***, **, * represents statistically significance at respectively 1%, 5% and 10% level

The regression results in Table 8 (Model 1) reveal that higher levels of science-intensity as well as increasing numbers of firms active in biotech technology development contribute to becoming a ‘top region’ in biotech. These results hold for both “distributed” (Model 2) and “concentrated” regions (Model 3) and indicate that in science-intensive industries such as biotechnology, in contrast to hypothesis 2a, the continuous development of a strong science base remains instrumental, also in the growth phase of the technology. At the same time, the results indicate that the creation or attraction of companies active in biotech technology development is instrumental as well in this respect.

The analyses (Model 3) further reveal that leading biotech regions with a “concentrated” texture not only benefit from increasing numbers of firms active in biotech technology development; higher levels of concentration within an ‘anchor tenant’ firm are instrumental for a leading position as well. These results confirm that for regions with a “concentrated” texture, hypothesis 1b holds: regions with higher levels of concentration of regional biotech technology development activities within an anchor tenant firm are more likely to become a leading biotech region in the growth phase of biotech.

Next, the regressions also show that “distributed” regions (Model 2) benefit from a stronger entrepreneurial orientation of the knowledge institutes in the region, while no significant impact is found for the “concentrated” regions (Model 3). The results thus indicate that hypothesis 2b does not hold for “distributed” regions: despite the more global diffusion of scientific knowledge, the entrepreneurial-orientation of scientific actors in regions with a “distributed” texture remains important for becoming a leading region during the growth phase of biotech.

Finally, the analyses provide evidence that “concentrated” regions (Model 3), in which a positive impact of entrepreneurial-oriented institutes is largely absent, do benefit from international technology collaborations with knowledge institutes. For the “distributed” regions (Model 2), no similar effect is found in terms of international collaboration. The results also reveal no significant impact from international technology collaborations with firms.

The negative and significant time coefficients in Model 3 can be explained by the fact that over the time period 1992-1997, the number of top regions with a “concentrated” decrease in favor of regions with “distributed” texture characteristics. The presence of a positive and significant population variable in Model 3, indicates that regions with a “concentrated” texture are more likely to become top when their population is larger. For the “distributed” regions, being located in the US, seems to favor regions in terms of likelihood to become a leading region, although the result is not very strong (significant only at the 10% level). Results are robust for an alternative specification of the dependent variable, being a top region is year t, where top regions are defined as regions with 50 or more patents in year t.

6. Discussion and conclusions

In this paper, the texture characteristics of regions (industry composition, presence of entrepreneurial-orientated scientific actors) are studied in relation to their technological performance in the field of biotechnology. Our analyses comprise 101 regions in North-America, Europe and Asia-Pacific that developed a substantial amount of biotech activity over the time period 1992-1997. The period under study corresponds with an era of rapid growth in the biotech industry in which industrial capabilities are evidently becoming more important.

Our results confirm that biotech technology development activities are highly concentrated in a limited number of top regions worldwide (Audretsch and Feldman, 1996; Feldman and Florida, 1994). Evidence is provided for the presence of *two* types of leading biotech regions: "concentrated" regions in which technology development is mainly situated within private firms and "distributed" regions where technology development is more equally shouldered by private firms, entrepreneurial universities and/or research centres/hospitals. The high rank order correlation in terms of technological performance of regions in biotech in the early and the growth phase of biotech, suggests the presence of important early mover advantages at the level of regions in new emerging, science-based fields.

Using random effect logit models, we further analyse which texture variables differentiate leading regions from other biotech regions. The empirical analyses indicate that regions with "concentrated" texture characteristics benefit, in terms of overall technological activity, from increased levels of concentration of technology development activities within a leading firm, thereby supporting the anchor-tenant hypothesis proposed by Agrawal and Cockburn (2003). Further research reveals that the "anchor" firm(s) in the leading "concentrated" biotech regions are large, R&D intensive firms primarily active in the pharmaceutical, chemical, food and other industries, and established well before the creation of the first dedicated biotech firms in the second half of the 1970s. Our analyses suggest that these large established firms, which have extensive industry experience and important access to (internal) financial resources, have been of particular importance for the development of regional biotech technology activities in the growth phase of the biotech industry. Following Agrawal and Cockburn (2003), such large, R&D intensive firms, by creating local niche and/or intermediary markets, may have played an important role in breeding regional entrepreneurial initiatives in the field of biotechnology and attracting high-quality suppliers to the region. Our results also indicate that in science-based industries such as biotechnology, developing relevant and highly-specialized scientific knowledge within the region remains essential (see also Anselin et al., 2000; Dosi et al., 2006; Jaffe, 1989; Leten et al., 2011). Regions with a "concentrated" texture also benefit from engaging in international technology collaborations with scientific actors.

While the role of science and entrepreneurial-orientated universities and research centres is widely acknowledged for the early incubation phase of new, science-based technologies, our study shows that in the growth phase of the biotech industry, the orientation and contribution of scientific actors in terms of technology development is positively influencing whether or not regions with more “distributed” texture characteristics evolve to become leading regions in biotech. Indeed, our results show that top “distributed” regions benefit, along with an excellent science base, from a more entrepreneurial orientation of their knowledge institutes. To become a leading region, regions with a “distributed” texture also have to create sufficient industrial activities in the field of biotechnology by generating new entrepreneurial activities or attracting new firms in the region active in biotech. Also the continuous investment in a strong science base remains important in the growth phase of science-based industries.

Our results have important implications for policy makers who wants to foster regional economic activities in science-based technology fields. While previous research have shown the importance of institutional settings such as the legal environment, the presence of venture capital and a dedicated support infrastructure for the development of regional biotech activities, our results point to the importance of the existing texture characteristics of regions in terms of the presence of entrepreneurial-oriented knowledge institutes and/or large established firms. Our analyses show that large, established firms have been able to adopt the new technological opportunities offered by a disruptive technology, and in several leading regions, dominant anchor firms have been playing a key role in the development of the new technology, similarly as in the fields of nanotechnology (Rothaermel and Thursby, 2007; Baglieri et al., 2012; Genet et al., 2012) and microelectronics (Genet et al., 2012). To become a leading biotech region in the growth phase of biotech, regional technology development activities do however not necessarily need to be primarily driven by private firms: also entrepreneurial-oriented knowledge institutes continue to play a major role. In those regions, large incumbent firms do not seem to play a central and dominant role in technology development, as they did in the nanotech and microelectronics industries where they formed an important bridge between public research and the industry (Genet et al., 2012).

The presence of two different avenues for becoming a leading region in biotech, calls for public policies consistent with the existing texture characteristics of the region. At the same time, our results demonstrates that both a strong science base and a strong industrial texture consisting of many competing firms is of crucial importance for sustaining innovation and growth within regions during the rapid growth phase of science-based industries. Indeed, as technologies are maturing and getting more specialized and the industry as a whole is moving through its life cycle and becoming more standardized, further technology development activities in technology clusters tend to become more homogeneous and increasingly co-aligned, thereby affecting the innovative potential of firms inside the cluster (Pouder and St. John, 1996). To prevent regional lock-in (Baglieri et al., 2012; Gertler and Vinodrai, 2009; Porter 1998), academic research and intense technology competition between local firms are essential to stimulate new knowledge creation and the opening of new technological trajectories and to sustain the innovation dynamics in science-based technology clusters.

Further research in the regional development paths during the more mature stages of the biotech industry seems highly relevant to better understand the processes of path dependence and regional lock-in as place-dependent processes (Martin and Sunley, 2006). Within this study, the focus is on regional technological development within the field of biotechnology. As biotechnology is a very broad field with applications in many industries, further refinement of our results could take into account the extent to which regions are specializing in one or more specific niches in biotech or alternatively, developing a wide range of biotech activities, and investigate how different levels of specialization are related to cluster development (see e.g. Gertler and Vinodrai, 2009; Owen-Smith et al., 2002).

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