TIGER

TRANSFORMATION, INTEGRATION and GLOBALIZATION ECONOMIC RESEARCH

CENTRUM BADAWCZE TRANSFORMACJI, INTEGRACJI I GLOBALIZACJI

TIGER **Working Paper Series**

No. 135

Universities, social capital formation and biotechnology clusters in the EU

Małgorzata Runiewicz-Wardyn

Warsaw, December 2016

1. Introduction

Biotechnology is among today's most innovative technologies and is a significant driver of economic growth within the EU. Decades of research and technological development have led to solutions to some of the most pressing social challenges: reducing environmental pressures, mitigating climate change and maintaining the sustainable growth. Biotechnology is gaining pace as an economic driver, for which research, innovation and economic development go hand in hand. In fact, biotechnology phenomenon today has the same effect on productivity and innovation as Internet had few decades ago.

The role of social capital and collaboration networks seem to be even more important in the case of the complex and dynamic industries. These, so called soft factors of growth, became the accelerators of the growth processes in the biotechnology. For example, Silicon Valley grew up in the proximity of the top universities like Stanford and UC Berkley.

However, the research studies show that there is no straight forward correlation between investments in R&D at universities and successful business innovations (Runiewicz-Wardyn 2013; Runiewicz-Wardyn & Lopez-Rodriguez 2013). This relationship is a bit more complex and rather circular and therefore requires more in-depth analysis, especially of the linkages between university R&D faculty and industry clustering. The scale and scope of these linkages are certainly related to the social capital formation and the level of technological maturity of the industry.

The following paper attempts to contribute to the existing empirical findings and theoretical discussion on the interlinkages between determined knowledge spillovers, social networks and cluster dynamic externalities. The paper ends with relative conclusions and policy recommendations.

2. **Measuring Social Capital**

One of the first attempts to define the social capital was taken by Bourdieu (1985), who used the term as an attempt to understand the production of classes and class divisions. Social capital, being constituted by social relationships, is referred as both economic and a set of power relations. Bourdieu and Coleman (1988) claimed that social capital is embedded in people`s social relationships, that are realized by individuals. Putnam, on the other hand, perceived social capital as a resource that individuals or groups possess or fail to possess. In his article Putnam wrote "Working together is easier in a community blessed with a substantial stock of social capital. For Putnam social capital is a public good representing a set of social norms and civic attitudes supporting common actions and sharing interpersonal trust. Similarly, OECD defines social capital as "networks together with shared norms, values and understanding that facilitate cooperation within or among groups (OECD 2001). Furthermore, Bourdieu (1985) and Coleman (1988) all argued that social capital is not embodied in any particular person, but rather is embedded in people`s social relationships, but realized by individuals. Whereas, Fukuyama identified social capital as a set of informal norms and rules as well as ethical values shared by individuals and social groups that enable them to cooperate effectively (2002). Wolfe (2002) notes that "The strength of the cluster and its supporting infrastructure of quasi-public goods and public institutions create a mutually reinforcing positive feedback loop". For example, The high levels of social capital present along Route 128 and Silicon Valley results in a lower barrier to entry as facilities are close together and shared between firms to make the best use of them. This low barrier to entry is also reflected in Vancouver's biotechnology industry as research within labs locations serves the needs of many parties.

The position of the World Bank is that social capital is linked to "institutions, relationships, attitudes and values that govern interactions among people and contribute to economic and social development" (Grootaert & van Bestelaer 2002). Finally, for Rosenfeld social capital embodied in a statement leading from "know-who" to building "know-how". He furthermore distinguishes positive social capital from negative (Rosenfeld 2007). The first one creates economic

advantages, whereas the second one can occur when efforts to limit membership in clusters and may lead to "lock-in".
Some more formal measures of innovation prominent in regional systems of innovation include measuring the return on money invested in bonuses for employee referrals. The employees may be able to provide very good information about those in their work-related networks (both within and outside of the organization), especially if they are members of work-related groups such as unions or professional associations (Marsden, 200 1, p. 1 19). Relationships reach social capital beyond the local cluster and leverage social capital across distances. Cultural capital is the cumulative sum of human capital within the organization (Jones, 2001, p. 1).

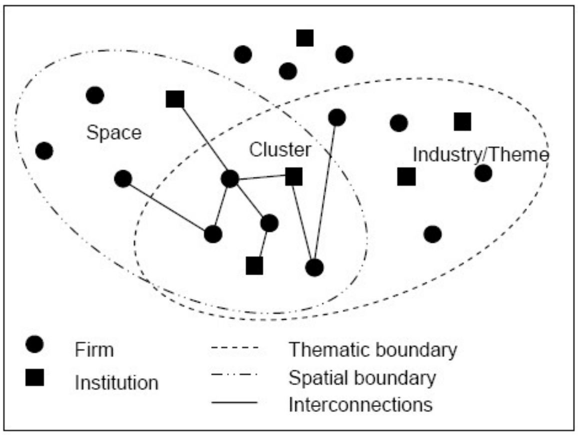
In short, there is no one particular measure of social capital. Overall social capital measures are collapsed into indicators for measuring competition, cooperation and size of barrier to entry in a particular market, and should be considered adequately in the research analysis.

3. Clusters and their role in social networking

The cluster or agglomeration approach to innovation considers the interrelated nature of innovation process. Because the process of innovation and technological change takes place in space, it is bounded to the local productive system therefore it is defined by the interrelated activity of firms, suppliers, service providers, coordinating intermediaries, and institutions such as universities or community colleges. According to Porter's cluster-based theory of externalities (1990, 1998), the specialization of a local industrial structure, with many firms competing in the same industry or collaborating across related industries, tends to trigger innovation and learning processes. As Malmberg and Maskell (2002, p. 433) point out, "in such environment, chances are greater that an individual firm will get in touch with actors that have developed or been early adapters of new technology. The flow of industry-related information and knowledge is generally more abundant, to the advantage of all firms involved." According to Van der Berg, Braun, and van Winden (2001), most definitions of the cluster "share the notion of clusters as localized networks of specialized organizations, whose production processes are closely linked through the exchange of goods, services and/or knowledge."[1]

Furthemore, as Audresch (1998, p. 23) suggests, the local knowledge spillovers and propensity for innovative activity to cluster spatially "will be the greatest in industries where tacit knowledge plays an important role (…) it is tacit knowledge, as opposed to information, which can only be transmitted informally and typically demands direct and repeated contacts." As Feldman (1994) argues, innovation-driven industries, in which tacit knowledge and innovative activity play an important role, show a higher tendency to spatially cluster. However, there have been only a few attempts to empirically investigate the role of spatial proximity for explicit knowledge spillovers, because from the methodological point of view, tacit knowledge flows are hard to track, especially when pure technological externalities are concerned (Johansson, 2005).

Figure 1. Interconnections between firms and institutions in a cluster



Source: Menzel and Fornahl, 2007

[1] Even though Porter's (1998, 2008) cluster approach has been vastly popularized at the regional and local level in the US, there are still problems with the definition of clusters. One of the simplest ways to define cluster is suggested by Doeringer and Terkla, according to whom industry clusters are "the geographical concentrations of industries that gain performance advantages through co-location" (1995, p. 225). Other authors, Barkley and Henry, define cluster as "a loose, geographically bounded collection of similar and/or related firms that together create competitive advantages for Memberfirms and the regional economy" (2002). Gibbs and Bernat (1997) further add to these definitions by identifying shared input needs and inter-relationships with suppliers and buyers. On the other hand, Swann and Prevezer put it very simply – they say that "geographical cluster is a collection of related companies located in a small geographical area. (...) Companies group together to take advantage of strong demand in the location, a large supply of scientific manpower and the network of complementary strengths in neighboring firms" (1998, p. 3).

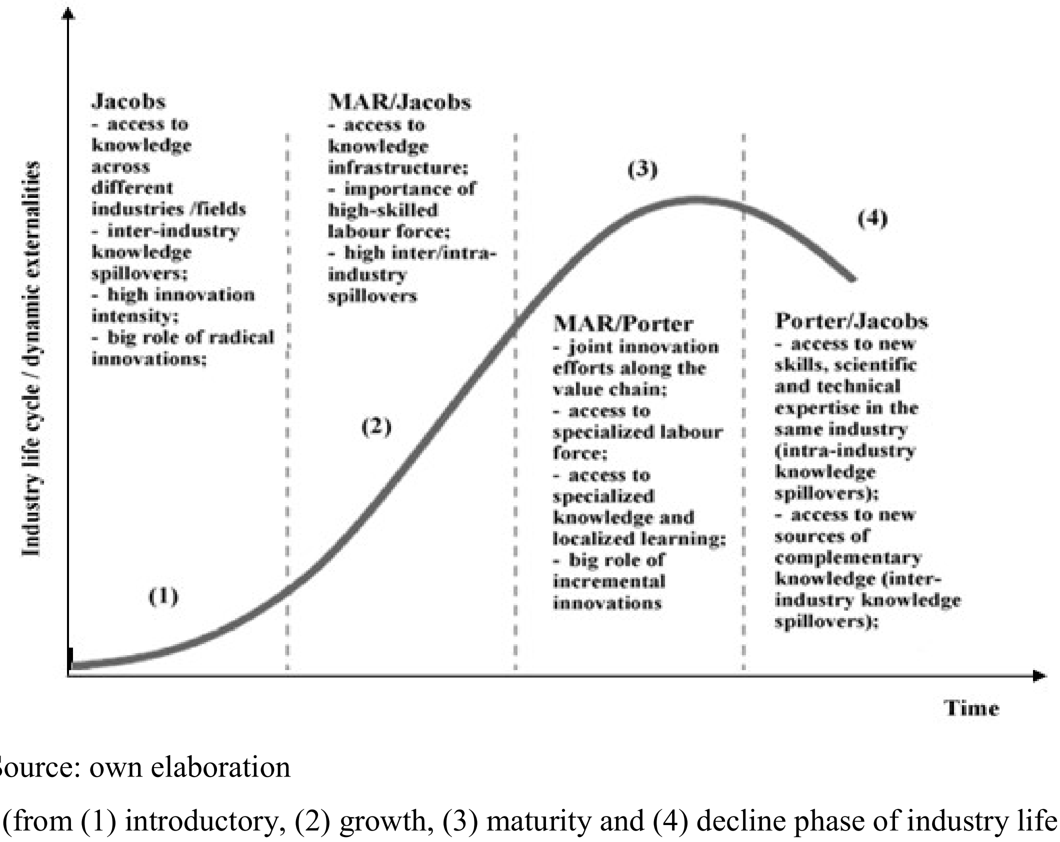
There are interesting dynamics in cluster development, based on their integration from functional clusters through clumps to working clusters described by Derik Andreoli (Bochniarz, Andreoli 2008). *Functional clusters* are spatial networks of like and functionally-linked industries, which enjoy basic positive externalities from geographic proximity (co-location), known in economic literature as Marshallian externalities (Runiewicz-Wardyn 2013). Technological boundary of a cluster "implies that only certain firms and institutions 'in a particular field' belong to the cluster." In other words, a certain "technological proximity" serves as the basis for various exchange processes and synergies. Thus, the cluster forms only a part of the regional production system. The geographic scope of a cluster (spatial boundary) can range from a single city or state to a country or even a group of neighboring countries. The spatial boundary delimits the firms of a cluster from firms located elsewhere. Figure 1 shows that the shape of the cluster depends on the interface between industrial and local dynamics (Menzel and Fornahl, 2007; Albino *et al.*, 1999).

The dynamic approach to clusters requires considering the changes in the spatial and technological boundaries of a cluster . One of the factors and processes that influence the spatial and technological boundaries of a cluster is the ongoing process of globalization and increasing competition in knowledge-intensive sectors. Hence, important knowledge sources of the innovation of local firms stem from both local and global knowledge linkages. These linkages consist the base on which social capital is flourishing enabling all cluster participants to efficiently cooperate with one another, which leads to the increased generation of positive externalities coming from co-location and building collaborative synergy within the cluster, as well as openness for cooperation with other clusters, which leads to knowledge spillovers among them and increasing innovations (Bochniarz-Faoro 2016).

4. Dynamic externalities and technological life cycle

Knowledge spillovers and positive externalities from co-location play a larger role in knowledge-intensive industries and high-tech industries, such as biotechnology, as well as industries that are undergoing rapid technological change or are in a growing stage of their economic life cycle. There are three types of dynamic externalities: the MAR, Porter's, and Jacobs', that allow tracking the role of knowledge flows throughout industry's life cycle. The industry life-cycle model is based on a stylized description of the evolution of an industry and follows the logistics of an S curve, starting with the introduction of new products, followed by a period of strong expansion of production, which then levels off and eventually leads to a decline. It is possible to assume that certain types of dynamic externalities assist the industry as it moves from a young to a more mature stage (Figure 2). Fuerthermore, new industries – or industries at the introductory stage of their development – benefit mostly from diverse knowledge infrastructure and inter-industry knowledge spillovers. Therefore, Jacobs' externalities will be more important at this stage. The birth of a new industry typically follows radical innovations, which may originate outside of the particular industry or sector. Innovation intensity is high, as there are many unexplored technological opportunities (Neffke *et al.*, 2009).

Figure 2. Technological life cycle* and dynamic externalities



Source: own elaboration

*(from (1) introductory, (2) growth, (3) maturity and (4) decline phase of industry life cycle).

At the growth stage of industry development, production becomes more standardized, which opens up possibilities for firms to exploit their divisions of labor and economies of scale, companies produce more or less similar products and get increasingly involved in price competition. This leads typically to a sharp drop in prices and a growth in production volumes. Both MAR's and Jacobs's externalities may be important at this stage.

At the stage of maturity, firms typically face vigorous price competition. Profit margins are reduced and technological opportunities get exhausted. In terms of innovation, longer jumps in technology are less likely and innovations are more of Arrow's nature (radical innovations are all but infeasible, as the industry has invested heavily in machinery and skill development that would become obsolete by dramatic discontinuities in technology). Major emphasis of R&D efforts is directed towards efficiency gains, which requires very specialized, industry-specific knowledge and skills (Gort and Klepper, 1982). Such know-how is often of a strong tacit nature and is best acquired through processes of learning by doing and imitation. The focus on local possibilities to tailor education and training systems increases (Grabher, 1993). Both tendencies lead to a lowering of Jacobs' and an increase of MAR/Porter's externalities.

If the industry is unable to reinvent itself, it approaches a late state of maturity and will start declining if no radical changes are introduced, e.g. industries can rejuvenate after radical innovation with far-reaching consequences for the industry, which may take the industry back to a more infant stage. The latter requires concentrating on either upgrading the current knowledge sources or looking for new sources of innovations. Acquiring external sources of complementary knowledge is likely to have positive effects in terms of Jacobs' knowledge externalities. This depends, however, on the extent to which external knowledge can be efficiently absorbed and used. When the technological distance between different knowledge bases is too high, and these are divergent and unrelated, acquiring external knowledge is difficult. Consequently, new skills and scientific and technical expertise in the same industry can boost technological innovations and Porter's externalities.

Since the creation of MAR's, Jacobs's, and lately Porter's externalities, no consensus has been achieved in the literature concerning the role of externalities in explaining knowledge spillovers and innovations within particular industry and cluster context. Therefore, it is important to carry out further tests for such dynamic externalities in case the selected industries have more specified environments.

5. Biotechnology technological life cycle and drivers of development

The process of technological change in the *Biotechnology industry* represents technological evolutions in the biopharmaceutical industry, as a whole. Biotechnology is a relatively young branch of bioscience, developed by the biopharmaceutical industry in the late 2000s. According to the literature the biotechnology industry started to form its shape in the early 1980s. when improved the regulatory and patenting and licensing systems and launch government-lead research initiatives, especially in the US. The innovation process shows that there is not just one S-curve but a succession of S-curves from organic chemistry/pharmacology to biochemistry and molecular biology (Figure 3). It can be seen that the waves of molecular biology overlap the waves of biochemistry and are about to leap upwards, according to Utterback and Abernathy (1975). Currently, scientists and researchers are attempting to exploit basic molecular research to identify new drugs, the production of which will be based on recent advances in genomics technology. Scientific breakthroughs such as genetic engineering, the ability to create monoclonal antibodies, and the mapping of the human genome have opened up new areas of research, and the pace of discovery in basic biomedical science has accelerated dramatically over the past few decades. The emergence of biotechnology is changing the pharmaceutical industry in terms of requiring a convergence of science and technologies and a multi-disciplinary approach to produce new technological discoveries (biological sciences, chemical engineering, bioprocess engineering, information technology, biorobotics). Increasing competition drives the specialization of firms in specific products; however, so far this has been somewhat limited due to the few experts in the specific biotechnology fields, e.g. cancer diseases.

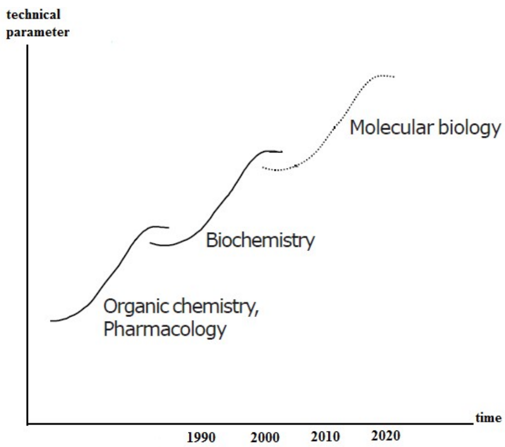
Biotechnology is firmly rooted in the growth stage, with heavy reliance on science and R&D investments. Patenting has increased sharply over the past few decades[2], with biotechnology patenting applications far outpacing the general rise in patenting applications. The biggest number of patents in biotechnology grew from the late 90s up to early 2000. For example, in 1977, there were only 12 biotechnology patents filed globally under the PCT. By 2009 this number had increased up to 9,339 patents (this is substantially more than a 77% increase). Almost 70% of these patents were filed by an inventor resident in either the EU-27 or US (Patent statistics, OECD 2012). However, while the biotechnology sector shows a strong growth stage, the degree of diffusion and adoption of biotechnology products and processes has been slowed down for several reasons. Although product innovations enabled by biotechnology have increased the quality and variety of goods and opened up new markets, integrating product innovations into modelling frameworks is difficult according to Pianta (2005). Furthermore, the substitution of traditional techniques for producing products with the use of biotechnology is related to the costs of transformation of existing production processes, e.g. substituting diesel extracted from petroleum with biodiesel made from feedstock or canola oil (McNiven, 2007). Moreover, in the present case of biopharmaceuticals, the demand side is largely influenced by regulations. It is strongly regulated and therefore excludes many inventions due to morality (based on Art. 53(b) of EPC). The latter may have an impact on further intensity in biotechnology. These influence the financing of new products and the degree to which markets may grow. As a result, industrial biotechnology is still in its relatively early stage of growth, and many potential products are not yet on the market.

The level of activity in the biotechnology industry among the EU countries depends largely on the research field. For example, Europe's competitive edge lies mainly in healthcare applications and in industrial biotechnology, including the chemical industry. Some Member States have developed advanced biotech sectors whereas others have stayed behind (Denmark, Germany, UK). New Member States of the EU are generally the early movers in the biotechnology sector.

[2] Still, this is not to say that biotechnology patenting outside the OECD did not experience significant growth. In fact, in the BRIC economies, as well as a number of other Asian and Latin American 'tigers,' biotechnology patenting increased substantially over the same time period.

Thus, the identification of the stage of life cycle of the biotechnology industry must be treated with necessary caution.

Figure 3. Industry life cycle maturity and technology diffusion in high-tech industries



Source: Own elaboration based on Wunderlich and Khalil 2002; biotechnology based on Utterback and Abernathy (1975) and Fisher and Pry (1971).

Note: Technology Life Cycle Maturity Level Score: Solid concept/idea conceived 1; Rapid growth enabled 15 Peak growth; 50 percent diffusion 50; Rapid growth slows, market-saturating 85; Market saturated, technology mature 100.

In summary, the analysis of the growth stage of biotechnology shows that the industry is still in the initial stage of growth in its life cycle. This requires huge amounts of R&D funding, whereas R&D projects often involve high risk of failure. Biotech firms that are active in the biopharmaceutical sector and do not have alliances with large pharmaceutical firms, tend to rely more heavily on domestic sources in their innovative activities, including universities and public research organizations[3]. Thus, in order to stimulate positive technological externalities in the biotech industry, the local productive structure must be determined by the presence of diversified local technological capability centers (clustered near universities). Furthermore, the rate of innovation in biotechnology depends on the strong interaction with science-based university

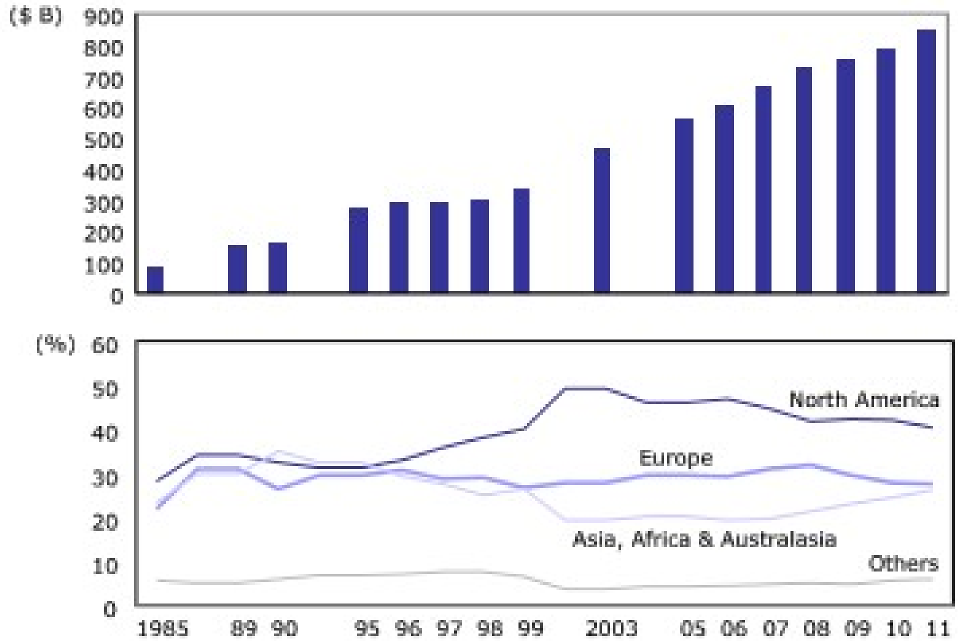
[3] www.ndu.edu/icaf/programs/academic/industry/reports/2011.

research and on the presence of other industries, such as pharmaceutical, chemical, health care, food, etc. Therefore, the innovative activity of biotechnology firms is determined by a combination of both innovative specialization, industry diversity, and competition externalities. The diversity is the measurement of social capital within a biotechnology cluster (Porter 2008).

2. The emergence, growth and development of pharmaceutical and biotechnology clusters

The European Union (EU) represents approximately 25-30% of the global pharmaceutical market. In the mid 1990s, Europe and the US each had shares of about 30% in the markets worldwide. The US since then has grown to approximately 50% in the early 2000s and slightly reduced its share down to around 40%.

Figure 4. The global pharmaceutical market compared



Source: Mizuho Corporate Bank analysis on IMS World Review, www.mizuhobank.co.jp/

Factors underlying the EU lead in pharmaceutical industry are observed especially in the high level of healthcare and pharmaceutical industry. The EU pharmaceutical market is the second largest globally next to the US. The US has also developed the unified pharmaceutical regulatory system across its members. For example, EU established the European Medicines Agency (EMA) responsible for evaluation and supervision of EU centralized procedure for marketing authorizations.

In the EU, many of biotechnology clusters and regions started to form around in the mid 1990s, typically in regions and countries with prominent university centres, with a long tradition of life sciences and biotechnology research base and activities in contributing industries such as pharmaceuticals and chemicals (Figure 5).

Figure 5. Major biotechnology clusters/concentration in Europe

Source: www.mbbnet.umn.edu/scmap/hotspots.html

Today, biotechnology clusters are concentrated in Belgium, Denmark, France, Germany, Italy, Spain, Sweden, Switzerland and the UK. Almost half of EU biotechnology patenting is located in Iˆle de France (France), Oberbayern (Germany), and Denmark (Eurostat, 2008). This trend repeats itself on a global scale. For example, slightly more than half of the biotechnology firms in the United States are clustered in just three areas – Cambridge (Massachusetts), San Diego County, and the San Francisco Bay Area in California.

These regions were much more successful in providing a "critical mass" for encouraging research and enhancing networking between business, higher educa-tion institutions, research centers, and technology parks. As a result, they follow the virtuous circle of growth – innovations and technological change are fueling economic growth, which is being fed back into higher earnings and greater invest-ment in education and R&D.

Biotechnology clusters are composed of diverse mix of participants. The healthcare biotechnology clusters are typically structured with cluster organisations, policy makers (e.g., national and local authorities), research institutions and universities, companies (e.g., pharmaceutical, biotechnology, medical technology companies and specialist services providers), clinical networks (e.g., hospitals, contract/clinical research organisations) and investors.

Table 1. Selected biotechnology clusters and cluster organizations in the EU

Cluster	Region	Country	Key Strengths
Regional & Trans-Regional Clusters			
One Nucleus	Cambridge London	UK	• Established research base and pharmaceutical industry
OBN	Oxford	UK	• Established research base • Investor-focused approach (OBN Investment Network)
Bio[M]	Munich	Germany	• Portfolio of successful biotechnology firms • Business-centric organizational structure (Bio[M] AG and Bio[M] Biotech Cluster Development GmbH)
BioTOP	Berlin Brandenburg	Germany	• Focus on regenerative medicine R&D • Partnerships with research institutions and clinical networks
Genopole	Evry (Paris)	France	• Partnership with Essonne Development Agency • Business-centric support provided by Genopole Entreprises
FlandersBio	Ghent	Belgium	• Portfolio of successful biotechnology firms • Partnership with VIB (Flanders Institute for Biotechnology)
Trans-National Clusters			
BioValley	Basel South-Baden Alsace	Switzerland Germany France	• Established chemical and pharmaceutical industries with tri-national market access
Medicon Valley	Copenhagen Skåne	Denmark Sweden	• Established pharmaceutical industry • Active branding development in international markets • Mobility of knowledge and capital
Pan-European Networks			
The European Association of BioIndustries (EuropaBio) **Council of European BioRegions (CEBR)** **European Biotechnology Network** *(all based in Brussels, Belgium)*			

(Source) Mizuho Corporate Bank analysis on public information

In the EU, biotechnology clusters and initiatives are managed by specialized institutions, known as cluster organizations, which take various forms, ranging from non-profit associations, public agencies to companies (Table 1). Often lead by highly experienced and entrepreneurial-minded leaders, cluster organizations offer one-stop support system designed to foster entrepreneurial business environment for both science and industry participants.

Initiatives and activities vary, but what leading biotechnology clusters have in common is the ability to adapt and evolve with the strategic vision in tune with the changing business environment and market demands. Examples include providing specialist support for spin-off companies and SMEs, access to premises and infrastructure (incubator, accelerator and shared services), access to partnership events (match making, show-case, promotion and networking), thematic projects (e.g., personalized medicine), technology transfer programs and information-sharing platforms (e.g., online database of drug pipelines, company profiles, research papers and others).

Additionally and importantly, biotechnology clusters and cluster organizations function as the first introduction and contact point enabling national and international partners and investors to explore cluster potentials and new business opportunities with innovative life science companies.

One of the key and unique characteristics of biotechnology clusters in Europe is the importance of unified and united approach to cluster development as demonstrated in the establishment of trans-regional, trans-national clusters and pan-European networks (Figure 5). For example, a pan-European network Council of European BioRegions (CEBR) was established in 2006 as a network linking clusters, with an aim to promote collaborations, provide policy support and share best practices between clusters.

3. Dynamic externalities in the biotechnology clusters. The research study results

One of the ways to identify the type of externalities dominant in the biotechnology clusters in the EU is to take from the literature on Marshallian agglomeration externalities, Porter`s cluster theories as well as Jacobs's externalities (Runiewicz-Wardyn, 2013). Based on the latter literature three measures to track the potential externalities were introduced: specialization measure (calculated on the basis of employment data), diversity measure (production and innovation diversity, measured by the reciprocal of the Gini coefficient varying inside the interval of (0, 1) and increases together with production and patent diversities) as well as competition measures (measuring the number of establishments per employee (COMP) in the site-industry, relative to establishments per employee in the biotechnology industry on the overall industrial area of the region).

Since the biotechnology industry is still in its early phase of growth, increasing competition in biotechnology has a significant positive influence on the acceleration of innovations. This would suggest the existence of Porter externalities. However, since production and innovation diversities determine patenting performance in biotechnology, these externalities could also suggest Jacobs's externalities. Except for the fact that Jacobs (1969) and Porter (1990) argue the opposite, Porter considers that competition is more conducive to knowledge externalities than a local monopoly would be. It should be emphasized that by local competition, Jacobs refers to the competition for new ideas embodied in economic agents. An increased number of firms provide greater competition for new ideas, but greater competition across firms facilitates the entry of new firms specializing in some new product niche. This is because the necessary complementary inputs and services are likely to be available from small, specialist niche-oriented firms but not necessarily from large, vertically integrated producers. Most European companies specializing in biotechnology are small or medium-sized enterprises (SMEs). Therefore, rivalry is extremely intense. High research costs, the need to fully exploit patent protections before they expire, and the expenses of costly marketing induce close alliances and co-operation among biotech firms and R&D institutions. In fact, the study by Runiewicz-Wardyn (2013) show that both agglomeration economies (dummies) and the proximity to a qualified labor pool (ekc) as well as other biotechnology firms have a positive and significant impact on biotech patents. Other researchers have reached a similar conclusion. In fact, Prevenzer (1997) and Zucker *et al*.(1994) show that in biotechnology firms tend to cluster together in just a handful of locations.

Furthermore, the results of Runiewicz-Wardyn study (2013) indicate that diversity across complementary economic activities is very conducive to innovation in the biotechnology industry. In fact, a one percent increase of production diversity of an average EU region increases the number of patents by about 5.593 percent (with 99% significance), whereas, an increase in the innovation diversity indicator by 1% decreases the number of patents by approximately -2,246 (with 95% significance). The above results may simply mean pursuing many innovative goals across various high-tech fields will not stimulate new knowledge creation in the biotech industry. Although biotechnology is a very interdisciplinary science and draws on the experience of a number of different disciplines, the result of the model suggests the need to permanently adapt R&D efforts to changing technological and market priorities within the same industry.

Overall, the analysis suggests that biotechnology in the EU still remains a clustered economic activity and relies strongly on interaction with science-based university research. Biotech companies – especially those whose success depends on staying on top of new technologies and processes, increasingly want to be where new, hot ideas are percolating. This suggests patenting in biotechnology requires combining innovative specialization with industry diversity. The rate of innovation in biotechnology depends on the availability of a highly skilled and well-educated workforce.

3.1. Knowledge and social networking in biotechnology industries

The capacity of regional agents for R&D collaborations and knowledge creation depends on their absorptive and diffusive capacities as well as the extent of technological similarity between the regional agents in the knowledge network. Furthermore, Feldman (1994) argues, innovation-driven industries, in which tacit knowledge and innovative activity play an important role, show a higher tendency to spatially cluster. However, there have been only a few attempts to empirically investigate the role of spatial proximity for explicit knowledge spillovers, because from the methodological point of view, tacit knowledge flows are hard to track, especially when pure technological externalities are concerned (Johansson 2005). On the other hand, innovation plays a larger role in knowledge-intensive industries and high-tech industries, such as biotechnology, as well as industries that are undergoing rapid technological change or are in a growing stage of their economic life cycle. More recent developments in the literature of knowledge spillovers bring important evidence to this observation. Jaffe and Trajtenberg (1996) and Johnson et al. (2002) record the application year of cited patents and investigate changes in the locations of citing patents over time. They find that, in the early years after the patent is approved, citations are made disproportionately by inventors in the same country (a localization effect). However, in later years, the proportion of foreign citations increases (an internalization effect). This suggests that knowledge becomes available to people across long distances only after some time, thereby confirming the benefits of proximity in the production and timely acquisition of cutting-edge technology knowledge. A similar conclusion could be drawn from results of Patel and Pavitt (1991), which show that multinational firms are strong in patenting in the areas in which their home national economies are generally strong in innovation, showing strong dependencies between the organizational capacities of multinational firms and the national systems of innovation of their home countries.

Bearinginmindthe studies ofJaffe and Trajtenberg(1996), Johnson etal. (2002b), and Patel and Pavitt (1991), one could assume that the role of geographical proximity in knowledge spillovers is further determined by the importance of scientific, techno-logical, market-related, and managerial types of knowledge in the process of innovation. Despite the fact that technological knowledge has become significantly more global in recent decades, knowledge associated with new scientific discoveries can have a high tacit, and therefore local, component (Zucker et al. 1998). Thus, scientific entrepreneurs are likely to have some advantages in identifying and exploiting new business opportunities. Likewise, relationships with research organizations, namely those conducting frontier research, can be critical for their development (Murray 2004; Bagchi-Sen 2007; Witt and Zellner 2007). On the other hand, the growing variety of fields necessary for biotechnology development suggests a more distributed nature of knowledge production; firms and R&D units may need to resort to a variety of organizations in diverse locations (McKelvey et al. 2003; Owen-Smith and Powell 2004). Managerial and organizational knowledge may come from

3.2. Networks and collaborations

In terms of the character of networks the case study based on Irish biotech industry (Egeraat and Curran, 2010) showed that networks do exist in the Irish biotech industry and that both the formal networks, connected through patents, and the informal networks, connected through directorship. However the formal network is noticeably less clustered than the informal network, which suggests knowledge in the formal network will flow and diffuse in a different, slower manner. The complex and interdisciplinary nature of relevant knowledge bases in pharmaceutical R&D tends to make technological innovations the outcome of interactions and cooperation among different types of agents commanding complementary resources and competencies. Formal network is noticeably less clustered than the informal network, which suggests that the informal networks are far more conducive to knowledge flow than the formal networks. Owen-Smith et al. (2002) compare the structure of the American and European networks in biomedical research. They show that the US network is characterised by extensive relationships between U.S. public research organizations and firms located in dense regional clusters that span therapeutic areas, cross multiple stages of the development process, and involve diverse collaborators. In contrast, European innovative networks are characterized by sparser, more specialized and upstream relationships among a more limited set of organizational participants located in national clusters. Both U.S. and European networks are geographically clustered, then, but in quite different manners.

Table 2. Overview of the research outcomes of knowledge spillovers and networks based on the literature mentioned in the text (the case of the EU member countries for the period 1997-2013)

Knowledge spillovers	Networks and collaborations		
	Character of networks	Degree of diversity	Geographical dimension of networks
1) proximity to universities is important for tacit knowledge, sharing R&D opportunities and personal acquaintance. 2) superstars enter into contractual arrangements with existing firms (contract or ownership) or start their own firm (to gain supra-normal returns); 3)scientist work with or create a new firm within commuting distance of home or university (of affiliation) creating localised effects of research.	1) cooperation among different types of agents of complementary resources and competencies. 2) links between distinct clusters in the network. 3) networking and informal contacts more important at the early stage of R&D process whereas further knowledge sharing is determined by the importance of IP protection and secrecy. 4)formal network is noticeably less clustered than the informal network.	1)networks are characterized by sparser, more specialized and upstream relationships among a limited set of organizational participants located in national clusters.	1) strong geographical dimension spanning well beyond the boundaries of the location. 2) openness to geographical distant nodes: increasing number of collaborations and a decreasing proportion of local connections. 3)better performing and growing firms rely less on local sources of knowledge. 4) inter-organizational collaboration follows the accumulative advantage based on the overlapping specialisation, and multi-connectivity. 5)network tends to

			consolidate around a rather stable core of companies, composed by large incumbents and early entrants in the network.

Source: own elaboration.

Networks span well beyond the boundaries of the geographical location, but the performance of the individual nodes within the network is strongly associated to high degrees of openness to geographical distant nodes (Owen-Smith at al. 2002; Pammolli & Riccaboni, 2001). Moreover, in a dynamic perspective, the growth of geographical networks and the tendency towards towards clustering is accompanied by a parallel process of increasing openness of the original clusters. In Europe, recent trends suggest a combination of an increasing number of collaborations and a decreasing proportion of local connections (Pammolli & Riccaboni, 2001). Similarly, in the USA biotechnology clusters rely increasingly less on local sources of knowledge (Corolleur et al., 2004). In similar way, Powell et al (2005) conclude that biotechnology clusters in the EU follow the accumulative advantage based on the overlapping specialisation, and multi-connectivity.

3.3. Local knowledge spillovers and universities-industry collaborations

Research collaborations between universities and industry are considered to be an important channel of potential localized knowledge transfer and spillovers in case of biotechnology field. Most of the knowledge universities produce may flow and spill over to the local economy by means of university-industry transfer projects, university spin-offs, and the mobility of university graduates and researchers to industry and social networks. Trained science and technology (S&T) graduates look for their first jobs in an area of the university. In fact, Bekkers and Freitas (2008) conclude that labor mobility is very important for the transfer of academic technological 'breakthroughs' into the biotechnology industry in Dutch universities (PhDs and academic staff). Zucker et al. (2002) report that biotechnology firms that collaborate with 'star' scientists are more likely to be productive in terms of number of patents. On the one hand, doctoral S&T graduates of pharmaceutical or engineering industries employ their academic knowledge in industry; on the other hand, they learn from their training in laboratories in large corporations.

Audretsch and Stephan (1996) points that the discovering scientists ('superstars') tend to enter into contractual arrangements with existing firms (contract or ownership) or start their own firm in order to extract the supra-normal returns from the fruits of their intellectual human capital. Moreover, the scientist work with or create a new firm within commuting distance of home or university (where they tend to retain affiliation) thus creating localised effects of university research. Similarly, in terms of R&D collaborations and knowledge networking in the biotechnology local knowledge spillovers and nationally based R&D institutions and business entities seem to play significant role and thus confirms the general features of a strong spatial concentration of the biotechnology industry.

Biotechnology field experts have emphasized the importance of IP protection and secrecy in R&D projects and suggested that all the results are to be published, but not however discussed in public or in an informal way (Runiewicz-Wardyn 2013).

Aharonson, Baum and Feldman (2004) emphasise consistently that proximity to universities and/or other local sources of knowledge is important for the circulation of tacit knowledge and that personal acquaintance with the scientists, continuous monitoring of companies are fundamental aspects of venture capital and this knowledge is much easier to be acquired at the local level. The discovering scientists ('superstars') tend to enter into contractual arrangements with local firms (contract or ownership) or start their own firm in order to extract the supra-normal returns from the fruits of their intellectual human capital. Moreover, the scientist work with or create a new firm within commuting distance of home or university (where they tend to retain affiliation) thus creating localized knowledge spillovers. Access and ability to use (and integrate) external knowledge becomes increasingly important for growth and diversification (Lemariè et al. 2001, Corelleur at al. 2003).

Furthermore, in other terms of a secrecy of knowledge sharing localised effects of university and industry research are most likely to result primarily from a combination of appropriability of tacit non-replicable knowledge and low geographical as well as organisational mobility of researchers

(Breschi and Lissoni (2001). Some knowledge tends to remain sticky and limited in its circulation. Naturally excludable and rivalrous knowledge does not spill over, it is rather people embodying knowledge move (locally) across organisations in order to exploit the value of their knowledge.

The tables 2 and 3 present the research conclusions based on the review of over 30 different research papers and case studies, applying case study and econometric analysis methods, aiming to identify the knowledge spillovers, the role of newtorks and collaborations and dynamic externalities in the biotechnology clusters in the EU.

3.3.Cluster and agglomeration externalities

Agglomeration externalities in the sense of Jacobs's resulting from inter-industry knowledge spillovers turned out to be predominant in the biotechnology industry, at least in its early growth phase. The rate of innovation in the EU biotechnology sector depends on the strong R&D interaction with science-based university research and on the presence of other industries, such as pharmaceutical, chemical, health care, food, etc. Therefore, the innovative activity of biotechnology firms is determined by a combination of both innovative specialization, industry diversity, and competition (Runiewicz-Wardyn, 2013). The study results by Prevezer (2003) and Aharonson et al. (2004) show that Marshallian externalities related to the availability of skilled labour and intra-industry specialisation play indeed an important role in generating externalities in biotech clusters. Access and ability to use (and integrate) external and local knowledge becomes increasingly important for growth and diversification (Prevezer, 2003; Corelleur at al. 2003; Lemariè et al. 2001; and Swann and Prevezer, 1996).

Similarly, Pammolli and Riccaboni (2001) and Allansdottir et al (2001) conclude, in their analysis of the European biotechnology clusters, that clustering derives to a large extent by the availability of a strong, heterogeneous but integrated research base that facilitates the transfer and the integration of knowledge, as well as the development of skilled labour, the mobility of such labour and – presumably – also the development of other supporting institutions like venture capital. Furthermore, the network tend to consolidate around a rather stable core of companies, composed by large incumbents and early entrants in the network. This suggests the existence of first-mover advantages in the network of collaborations, which point to difficulty in entering as time goes by and can be perturbed only and temporarily by new major technological discontinuities (Orsenigo et al. 2001).

Table 3. Overview of the research outcomes of biotechnology cluster development based on the literature mentioned in the text (the case of the EU member countries for the period 1997-2013)

Clusters/agglomeration externalities	
Role of university spin-offs	Local research base
1) many new biotechnology firms in the EU15 are university spin-offs (which are at the initial stage of development of New Member states). 2)successful clusters exhibit high rates of internal firms formation, whereas weaker clusters are characterized by lower domestic productivity and higher propensity to migrate. 3) process of spinoff from local institutions originates and sustains the cluster. 4)spinoffs and startups tend to locate close to their "parents" and region-specific practices/ways of doing things.	1)local sources of knowledge appear to be fundamental in the early stages of cluster development and for new, highly specialized firms. 2) access to external and inter- regional knowledge becomes important for growth and diversification. 3) firms collaborate with 'star' scientists, PhDs and academic staff, especially in case of very specific, narrow fields. 4) strong, heterogeneous but integrated research base facilitates knowledge/technology transfer. 5)pharmaceutical firms, which perform basic research in close co-operation with academia produce more patents.

Source: own evaluation.

Many new biotechnology firms in the EU15 are university spin-offs, in the New Member states spin-offs are at the initial stage of development. Consequently, successful clusters continue to exhibit high rates of internal firms formation, whereas weaker clusters are characterized by both lower domestic productivity and higher propensity to migrate. Moreover, spinoffs and startups tend to locate close to their "parents, therefore the process of spinoff from local institutions originates and sustains the cluster.

Furthermore, local sources of knowledge appear to be especially important in the early stages of the development of a cluster and for new, highly specialized firms. Wheeras access and ability to use (and integrate) external/pan European/globa knowledge becomes increasingly important for growth and diversification (Lemariè et al. 2001; Corelleur et al. 2003; Prevezer; 2003; Swann & Prevezer, 1996).

4. Conclusions

The results of the study show that the biotechnology industry relies very much on university-business R&D partnerships and research mobility as knowledge-diffusion channels (e.g.pharmaceutical firms that performed basic research in close co-operation with academia produced more patents). Whereas social networking and informal contacts seem to be a more important at the beginning of R&D process, as

Biotechnology cluster is one of the key driving forces behind biotechnology industry/company growth. the interaction and collaboration are of particular importance to the biotechnology companies, especially for the SMEs, for securing financial resource, business platforms and infrastructure required for biotechnology research or business development.

The results of the study show that biotechnology cluster is one of the key driving forces behind biotechnology industry/company growth. The interaction and collaboration are of particular importance to the biotechnology companies, especially for the SMEs, for securing financial resource, business platforms and infrastructure required for biotechnology research or business development. The EU biotechnology industry relies very much on university-business R&D partnerships and research mobility as knowledge-diffusion channels.

The results confirm the general features of a strong spatial concentration of the biotechnology industry. Social networking and informal contacts seem to be a more important at the early stage of R&D process, whereas in terms of further knowledge sharing experts emphasized the importance of IP protection and secrecy in R&D process; and therefore the importance to publish all the results, prior discussing them in public or in an informal way. The R&D collaborations and knowledge networking in the home region and nationally based R&D institutions and business entities seem to play a more significant role for the newer EU member states. For many R&D units EU ERA-NET-based R&D funding play only a secondary role. The latter fact shows that the actual ability of regional R&D units to participate and take advantage of knowledge networks (locally or/and globally) depends largely on their own stock of knowledge and absorptive capacities.

In terms of policy recommendations it is essential to encourage EU Member States to consider the role of universities and social capital in their regional/local innovation systems, especially when drafting smart specialisation strategies. Furthermore, analyse how universities are being involved in smart specialisations, including sharing experiences and best practices of university-regional engagement across the EU; match the technical and academic profiles of local universities with the economic priorities of the region as well as study the existing relationships between the university, individual academics and other regional actors to 'nourish' the partnerships. Last, but not least, understand the specific obstacles and challenges that inhibit a greater level of engagement of local universities in the region.

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