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An Assessment of the Technological Performance of Biopharmaceutical Firms.

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Abstract

Firms active in knowledge-intensive fields are increasingly organizing their R&D activities on an international scale. This paper investigates whether firms active in biotechnology can improve their technological performance by developing R&D activities in multiple technology clusters. Regions in the US, Japan and Europe, that host a concentration of biotechnology activity are identified as clusters. Fixed-effect panel data analyses with 59 biopharmaceutical firms (period 1995-2002) provides evidence for a positive, albeit diminishing (inverted-U shape) relationship between the number of technology clusters in which a firm is present and its overall technological performance. This effect is distinct from a mere multi-location effect.

Introduction

Corporate activities, especially in knowledge-intensive industries, display a tendency to cluster geographically (AUDRETSCH and FELDMAN, 1996; FELDMAN and FLORIDA, 1994). Following MARSHALL (1920), presence in clusters enhances the innovative capacity of firms through the presence of localized knowledge spillovers, and the access to a pool of highly-skilled labor and specialized suppliers that agglomerate in such regions. Innovation dynamics in clusters are further stimulated by the presence of local competition and peer pressure among firms (PORTER, 1990). Empirical studies stemming from the economic geography literature indeed provide evidence that firms located in clusters are more innovative than counterparts located elsewhere (BAPTISTA and SWANN, 1998; BATEN et al., 2007; BEAUDRY and BRESCHI, 2003; DEEDS, DECAROLIS and COOMBS, 1999; VAN GEENHUIZEN and REYER-GONZALES, 2007). At the same time, little is known about the relationship between presence in multiple clusters and the overall technological performance of firms. Exploring this relationship is relevant because firms increasingly organize R&D activities on an international scale whereby knowledge from different regions is being accessed. (GASSMAN AND VON ZEDTWITZ, 1999; KUEMMERLE, 1997; GRANSTRAND, 1999). In this paper, we engage in such analysis by means of a panel dataset of 59 biopharmaceutical firms (period 1995-2002). The focus of the paper is on the relationship between the technological performance of consolidated firms (i.e. the parent firm and its subsidiaries) and the number of technology clusters in which they engage in R&D activities. Clusters are identified as regions within the United States, Europe and Japan with a critical mass of technological activities in the field of biotechnology. Whereas previous economic geography studies controlled only to a limited extent[1] for the heterogeneity of firms in terms of innovative efforts and capabilities, this study uses fixed effect panel data techniques and includes controls for time-varying firm differences in R&D expenditures and past experience. This allows to distinguish cluster presence from firm-specific performance effects (BEUGELSDIJK, 2007). The analyses provide evidence of an inverted-U shape relationship between the number of technology clusters in which a firm is present and its overall technological performance. This effect is distinct from a mere multi-location effect.

The remainder of the paper is organized as follows. First, an overview of prior research on clusters and firm performance is provided, resulting in hypotheses on the relationship between cluster presence and firm's technological performance. Next, the data sources and variables used in this study are presented, followed by the empirical results. Conclusions, limitations and directions for further research are discussed in the final section.

Industry and technology clusters

The clustering of *industrial* activity in well-defined and relatively small geographic areas has been observed for a long time by economic geographers and regional scholars (e.g. MARSHALL 1920; KRUGMAN 1991; PORTER 1990). Famous examples of industrial clusters include Detroit's car manufacturing industry, the entertainment industry of Hollywood and the fashion industry in northern Italy. Clustering remains a striking feature of national and regional economies, despite the availability of better transportation and communication infrastructure and the presence of global markets from which capital, talent and technology can be sourced (PORTER, 1998; 2000). Following the success of Silicon Valley in California and Route 128 in Boston (SAXENIAN, 1994), there has been a wide interest of researchers and policy makers in the innovative and economic potential of *technology* clusters. Unlike industry-focused clusters, where inter-firm connections are predominantly vertical, technology clusters exhibit a more lateral structure consisting of direct and indirect competitors developing diversified applications of the same core technology within different markets or industries (ST. JOHN and POUDER, 2006). Value dynamics in technology clusters or "technology districts" build on unique technological resources - the technological infrastructure - which supports firms' innovation activities (FELDMAN et al, 1994; STORPER, 1992). Sources of knowledge in technology clusters are diverse, ranging from universities and public research institutes to firms, suppliers and customers.

MARSHALL (1920) highlighted three incentives for firms to cluster geographically: (i) broader access to specialized, highly-skilled labor; (ii) access to specialized suppliers; and (iii) the presence of inter-organizational knowledge spillovers among similar firms[2]. The broad concept of knowledge spillovers is probably the most frequently invoked source of agglomeration economies (HEAD et al, 1995) and has been widely investigated in the literature (e.g. DÖRING and SCHNELLENBACH, 2006; BRESCHI and LISSONI, 2001). Knowledge spillovers arise through labor mobility (ALMEIDA and KOGUT, 1999) and exchange processes involving competitors, suppliers, customers and providers of professional services (VON HIPPEL, 1988; ROSENKOPF and ALMEIDA, 2003). They allow firms to achieve similar R&D results faster and/or with fewer resources. Empirical work has shown the existence and geographically bounded nature of knowledge spillovers (JAFFE et al., 1993; ALMEIDA and KOGUT, 1999; VARGA, 2000; RODRÍGUEZ-POSE and CRESCENZI, 2008). Spillovers are more local to the extent that the relevant knowledge base is tacit (POLANYI, 1966; NONAKA, 1994; VON HIPPEL, 1994). This is particularly true for emerging, complex technologies like biotechnology. PORTER (1990; 1998) provided two additional reasons why firms located in clusters are more innovative than firms located outside clusters. First, opportunities for innovation (both new buyer needs and new technological opportunities) are more visible in clusters. Next, competitive and/or peer pressure among local firms stimulates firms to be more innovative and increases the efficiency of their operations.

While clusters are often associated with positive effects on firm performance, potential disadvantages can be noticed as well. First, resources (e.g. labor, real estate, professional services) might be significantly more expensive in clusters due to congestion effects (BEAUDRY & BRESCHI, 2003). Second, cluster membership might lead to an inward orientation whereby relevant developments situated outside the cluster are neglected (PORTER, 1998). Firms located in clusters might also be confronted with higher levels of unintended (outward) knowledge spillovers, affecting the firm's competitive advantage in a negative way (SHAVER and FLYER, 2000). While such disadvantages might occur, they are not directly relevant for the research questions addressed in this paper as the focus is on the firm's technological performance (as opposed to the overall competitive position of the firm or the efficiency implications of being present in clusters).

Clusters and Firm Performance

The capacity of firms to innovate is not limited to the boundaries of the firm but increasingly depends on external resources that agglomerate in specific places (FELDMAN and FLORIDA, 1994; STORPER, 1992). If knowledge spillovers are an essential characteristic of clusters, the beneficial effects from being present in a cluster should manifest themselves in the first place on the innovative output of firms rather than on the firm's financial or growth performance (BAPTISTA and SWANN, 1998). Studies in the *economic geography* literature have investigated whether firms (plant level) located in an industrial or technology cluster are more innovative than firms outside clusters[3]. These studies can be classified in two groups based on the methodologies used to measure clusters.

A first set of studies investigated whether firms located in industrial clusters are more innovative. The concentration of industrial activity in a region is measured by sector level employment data. BAPTISTA and SWANN (1998) found a positive effect of own sector employment in the region, on the likelihood of manufacturing firms in the United Kingdom to innovate. In contrast, BEAUDRY and BRESCHI (2003) found no effect of own sector employment on firms' innovative performance for a sample of UK and Italian firms. Only the concentration of innovative firms (and the size of their accumulated knowledge base) in the own industry had a positive impact on the technological performance of firms. Similar results were found in the study of BATEN et al. (2007) for firms trading in the state of Baden (Germany) around 1900. These findings suggest that for firms' innovative performance, the presence of critical mass in terms of knowledge creation activities in a region is more important than the overall industrial activity per se.

A second set of studies classified regions in clusters and non-clusters based on the amount of technological activity observed in the region, and examined whether firms located in technology clusters are more innovative than firms located elsewhere. DEEDS et al. (1999) classified eight regions in the United States (MSA level) that host the largest number of biotechnology firms, as clusters and found that biotechnology firms located in clusters are more innovative than firms located outside the clusters.

For the Netherlands, VAN GEENHUIZEN and REYER-GONZALES (2007) defined clusters as regions with at least one knowledge institute and 10 young entrepreneurial biotechnology firms. Their analyses showed no significant effect from cluster location on the innovativeness of biotechnology firms. However, when only the largest and oldest biotechnology cluster in the Netherlands - the Leiden region - is considered, cluster presence had a significant positive effect on firm performance. These results, again, suggest that a critical mass of technological activity is needed before positive cluster effects can be observed at level of the firm.

Aforementioned economic geography studies use cross-sectional data at the level of single plants to investigate whether clusters are supportive to firms' innovation activities. While the results indicate that firms in clusters are more innovative than firms located elsewhere, they do not provide evidence whether firms can improve their technological performance by extending their presence within multiple clusters. This research question is addressed in this paper. More specifically, the relationship between the number of technology clusters in which a firm is present and its overall technological performance is studied. Exploring this relationship is relevant because firms increasingly organize R&D activities within multiple units - located in different regions - to benefit from agglomeration externalities (GASSMAN and VON ZEDTWITZ, 1999; KUEMMERLE, 1997; GRANSTRAND, 1999; CANTWELL and PISCITELLO, 2005). In so doing, R&D location choices are not confined to national borders, but increasingly take place on a global scale. As such, empirical analyses assessing the impact of cluster presence should not be limited to one particular country or region, but should consider technology clusters on a more global scale. Likewise, on the firm level, studying the impact of cluster presence requires taking into account the location of all firms' R&D facilities (headquarters and subsidiaries).

In this paper, such an analysis is performed by means of a panel dataset on the technological activities of 59 biopharmaceutical firms (1995-2002). In line with economic geography studies, locations of firms' R&D activities (including cluster presence) are analyzed at the regional level. Technology clusters are defined as worldwide leading regions in technology development. The models in this study control for firm-level heterogeneity in innovative efforts and capabilities by employing fixed effects panel data techniques and including time-varying, firm-level controls on R&D expenditures and innovation experience. This allows to clearly distinguish between cluster presence and firm-specific performance effects (BEUGELSDIJK, 2007).

A positive effect on a firm's overall technological performance is expected from being present in multiple clusters, as this coincides with an increased access to state-of-the-art knowledge available within each of these regions. At the same time, the more one is already involved in different clusters, the smaller the additional effects in terms of access to new, relevant knowledge might become. In addition, the costs of coordinating multiple R&D units and leveraging and integrating knowledge from multiple locations will increase with the number of locations in which a firm is present. The more a firm is present in clusters, the more it is also exposed to potential negative effects from clusters, resulting in diminishing technological performance effects. Building on the aforementioned research, it is expected that location benefits principally stems from presence in technology clusters with a critical mass of relevant knowledge, as opposed to other regions. Therefore, the effects of cluster membership on the overall technological performance of firms should be distinctive from a mere multiple location effect. Taken together, these arguments lead to the following set of hypotheses:

Hypothesis 1: Firms improve their technological performance when extending their presence in technology clusters.

Hypothesis 2: Firms extending their presence in technology clusters will gain additional benefits in terms of technological performance, albeit of a diminishing nature (inverted U-shape relationship).

Hypothesis 3: The relationship between cluster membership and overall technological performance is distinct from a mere multi-location effect.

Data and methodology

Panel data on the technological activities of 59 biopharmaceutical firms with parent firms located in the United States, Europe and Japan, have been collected to study the relationship between the location of R&D activities in multiple clusters and regions and the overall technological performance of firms. Patent data are used to create indicators of firms' technological activities (location and performance) and to identify biotechnology clusters within the United States, Europe and Japan . The use of patent data has several advantages (PAVITT, 1985; GRILICHES, 1990). They are easy to access, cover long time series and contain detailed information on the technological content, owners and inventors of patented inventions. This allows to mark out biotechnology patents, construct indicators of the technological performance of firms and regions, and identify the locations where inventions took place. At the same time, patent indicators also have some deficits: not all inventions are patented, patent propensities vary across industries and firms, and patented inventions vary in technical and economic value (MANSFIELD, 1986; GAMBARDELLA et al, 2008). One can lessen these problems by restricting patent analyses to technologies with high propensities to patent such as biotechnology (ARUNDEL and KABLA, 1998), and by weighting patent counts (technological performance indicator) by the number of forward citations received (HALL et al, 2005; TRAJTENBERG, 1990; HARHOFF et al., 1999). Despite their shortcomings, there is simply no other indicator that provides the same level of detail on firms' technological activities as patents do (GRILICHES, 1990). Further, studies have found a strong correlation between patent counts and other technology indicators (e.g. new product announcements and expert opinions) on the level of firms (HAGEDOORN and CLOODT, 2003; NARIN and NOMA, 1987) and regions (ACS et al, 2002), establishing patents as a valid indicator of novel technological activity.

In this study, patent indicators are based on data from the European Patent Office (EPO). Patent application data rather than patent grants are used because of the extensive time periods observed between application and granting decisions at the European Patent Office (especially for biotech)[4]. The geographic location of inventions is identified via inventor address information (LECOCQ et al., 2008). Allocation based on inventor addresses is the most commonly used approach in patent studies since – especially for large firms - allocation based on assignee addresses might signal the location of corporate headquarters rather than the research laboratory where the invention took place (DEYLE and GRUPP, 2005; KHAN and DERNIS, 2006). The use of inventor addresses may however also introduce some bias since inventors may not live in the same region as they work. LANDONI et al. (2008) performed a validation exercise where both allocation methods (inventor and applicant addresses) are compared with the real R&D locations of inventions. This work confirmed the superiority of the inventor's address criterion, for patent statistics at a fine-grained geographical level.

Sample of Biopharmaceutical Firms

Parent firms with a large biotech patent portfolio are identified from a dataset with all EPO patent applications in the field of biotechnology (time period 1978-2001). This dataset is the result of a study by GLÄNZEL et al. (2004) that delineates technological activity in the field of biotechnology[5]. The selected firms are active in different sectors: mostly in biotechnology, the pharmaceutical or chemical industry, but the list of parent firms also includes producers of consumer products, energy concerns and breweries. For consistency of the sample, only the biopharmaceutical firms (75 largest patenting firms) were retained. Due to missing data on firm R&D expenditures or incomplete information on the group structure of parent firms, the list of firms was further reduced to 59 biopharmaceutical firms. All these firms have headquarters in the United States, Japan or Europe (EU-15 and Switzerland). Appendix 1 contains a complete list of the firms under study.

For this sample of 59 biopharmaceutical firms, patent data were collected at the consolidated parent level, i.e. comprising headquarters and all majority-owned (share > 50%) subsidiaries of the parent firm. This consolidation process implied the mapping of all changes in the group structure of the parent firms due to acquisitions, mergers, green-field investments and spin-offs during the period 1995 to 2002. For this purpose, yearly lists of subsidiaries included in annual reports were used, as well as yearly 10-K reports filed with the SEC in the United States and, for Japanese firms, information on foreign subsidiaries published by Toyo Keizai in the yearly Directories of Japanese Overseas Investments. Using consolidated patent data is important to get a complete picture of firms' technological activities as a significant part of large firms' patents are not filed under the parent firm name (LETEN et al, 2007). Firm financial data are also collected at the consolidated firm level via corporate annual reports, Worldscope and Compustat financial databases.

Biotechnology Clusters

Biotechnology is a knowledge-intensive technology field, which from its origin has developed within a limited number of regions, such as California and the Boston area in the United States, and Cambridge in the United Kingdom. To identify biotechnology clusters worldwide, the aforementioned dataset with all EPO patent applications in the field of biotechnology created by Glänzel et al. (2004) is used. The dataset shows that, for the period 1990-1999, almost all patenting activity in the domain of biotechnology (94%) takes place in the United States, Europe (EU-15 and Switzerland) and Japan. No other region has sufficient patent applications to qualify as a cluster.

In this study, the focus is on regions in the United States, Europe and Japan. It is important to select a spatial level of analysis which is comparable across continents in terms of size (population). Regions are therefore defined at the level of following national subdivisions: European NUTS 1 regions (n=73), US states (n=50), and Japanese prefectures (n=47)[6]. Cluster boundaries do not necessarily coincide with the boundaries of such administrative regions. Clusters may well spread over more than one region (e.g. the tri-state cluster in the states of New York, New Jersey and Pennsylvania and the cluster covering the prefectures of Tokyo and Kanagawa). Alternatively, regions may enclose more than one cluster (e.g. the triangle San Francisco - San Jose - Sacramento, better known as Silicon Valley, and the region between Los Angeles and San Diego in the state of California). Despite these concerns, an analysis of regions coinciding with the boundaries of the administrative subdivisions was chosen, as it is believed that they provide comparable regional units of analysis.

The amount of biotechnological R&D activities in a region is measured by the number of EPO patents in that region during the period 1990-1999. Patent applications are allocated to regions based on inventor addresses. When a patent contains multiple inventors in different regions, the patent is fully counted in each region. Table 1 shows the 50 regions with the highest technological performance in the field of biotechnology. A region is defined as a biotechnology cluster if it contains at least 2.5% of the total number of EPO patent applications in the field of biotechnology. Twelve regions satisfy this condition. Together they account for 50% of biotechnology patents worldwide. Most biotechnology clusters are located in the United States, with a clear supremacy of the state of California which account for almost 15% of all biotechnology patents. Other US regions with a substantial amount of activity in biotechnology are Massachusetts, Maryland, Pennsylvania, New York and New Jersey. Europe has three top regions: the region of Paris (France) , the region of Cambridge, Bedfordshire, Hertfordshire and Essex (East Anglia. United Kingdom) and the region of Munich (Bayern, Germany). With Tokyo, Kanagawa and Osaka, Japan counts three top regions in biotechnology.

Insert Table 1 about here

Firm Variables and Model

Dependent Variable

The dependent variable in the study is the technological performance of firms in biotechnology. This is measured by the number of biotech patent applications of a firm in a certain year, weighted by the number of forward patent citations received over a fixed four year time window[7]. The 'weighting' is done to account for variation in the technological and economic importance of patented inventions (ALBERT et al., 1991,HARHOFF et al., 1999; TRAJTENBERG, 1990; HALL et al, 2005)[8].

The dependent variable is a count variable with only non-negative integer values. In this case, non-linear count data models are preferred to standard linear regression models as the former explicitly take into account the non-negativity and discreteness of the dependent variable (CAMERON and TRIVEDI, 1998). Negative binomial models used in the study allow for overdispersion in the dependent variable. To control for the presence of unobserved firm-specific effects (which may correlate with, and bias the effect of explanatory variables in the models, if not controlled for), fixed effects panel data estimators are used. This estimation technique removes (time constant) unobserved firm-specific factors by time-demeaning all variables (dependent and explanatory) before performing regressions (WOOLDRIDGE, 2001).

Presence in Technology Clusters

To identify the regions in which firms are present, inventor address information on the biotechnology patents of the firms is used. More specifically, a firm is considered to engage in biotechnology R&D activities in a region if the firm owns patents with at least two inventors residing in that region during the last two years. Given the fact that

R&D collaboration is quite widespread in the field of biotechnology (LECOCQ and VAN LOOY, 2009)[9], it was decided to consider presence in a region only on the firm's *fully owned patents*, thus reflecting the number of regions (clusters and other regions) in which a firm is present through its fully owned or single parent patents. For co-owned patents, i.e. patents with multiple assignees from different parent organizations, it is not possible to identify to which assignee an inventor belongs. Therefore using inventor address information on such patents may not only pick up a firm's own R&D locations, but also the R&D locations of co-assignees. It should be noted that our R&D location variable, even after correcting for co-assigneeship, might contain additional locations through the location of co-inventors not belonging to the firm. This is for instance the case when a firm engages in collaboration with a university or other organization, while retaining full ownership of the IP. The location variable will then be overestimated, however, only to the extent that the firm is collaborating with at least two inventors that are located outside the firm's own region. Despite this shortcoming, patent data are the best available public source to systematically map the biotech R&D locations of global firms. Other sources of information such as corporate annual reports also show some limitations: they often do not specify the exact location (region) of firm facilities and the type of activities (e.g. research, production, administration, sales) undertaken at different locations. Corporate annual reports also do not provide information on the type of research activities (biotechnology versus other research fields) in R&D establishments. This is however important information, as we study the locations where firms engage in biotech R&D activities.

Three indicators related to the location of the biotechnology R&D activities of a firm are created: (i) *clusters*, reflecting the number of R&D biotechnology clusters in which a firm is present, (ii) *other regions*, reflecting the number of other regions, not defined as clusters, in which a firm undertakes R&D activities, and (iii) *countries*, the number of countries in which a firm is present[10]. To test for non-linear relationships between the R&D location variables and the firm's overall technological performance, both linear and squared terms of the location variables are included in the empirical models. Applying fixed effect panel data models require that there is enough within-firm variation in the number of R&D locations over time. This is the case for the sample firms, as they all engaged in M&A activities, opened new laboratories and/or close down existing ones over the time period 1995-2002.

Control Variables

Several (time varying) variables that might affect the technological performance of firms are included as control variables in the analyses. First, an indicator for the size of a firm's existing *technology portfolio in biotech* is included, measured by the number of biotech patents applied for by the firm in the last 5 years. In analogy to the dependent variable, this variable is weighted by the number of forward patent citations received over a fixed four year time window to account for differences in patent quality. Firms with large technology portfolios are more experienced in innovation, and may be better positioned to develop new technological competences (NESTA and SAVIOTTI, 2005). In previous studies, a time period of 5 years has been considered as appropriate for assessing the validity of knowledge bases in a given technology (STUART and PODOLNY, 1996; AHUJA and LAMPERT, 2001; LETEN et al., 2007). Second, differences in the *size* of firms' *R&D effort* are included, measured by one-year lagged R&D expenditures[11]. Firms that have more R&D resources, are expected to have a higher technological performance. Third, *year dummies* are included in the models to control for changes over time in the propensity of firms to patent.

Descriptive statistics and correlation coefficients for the dependent and explanatory variables are reported in table 2. The mean (yearly) number of citation-weighted patents for the firms in the sample is 21, and firms' average R&D expenditures amount to 452 million US dollars a year. The sample firms are, on average, present in 1.8 biotechnology clusters and 2.4 other regions, spread over 2 countries. None of the reported correlations are excessively high.

Insert Table 2 about here

Empirical results

The results of the fixed effects negative binomial models on the relation between cluster membership and firms' overall technological performance are presented in Table 3. Model 1 includes only the control variables. Both the lagged biotech patent portfolio and the R&D expenditure variable are positive and significant. In model 2, the clusters variable is introduced, which indicates the number of *clusters* in which a firm is involved when developing R&D activities. The cluster variable is positive and significant, indicating that firms can enhance their technological performance by extending their R&D activities in multiple technology clusters (confirming hypothesis 1). In model 3, the *other regions* variable is added to the set of control variables, reflecting the number of regions, outside clusters, in which a firm develops R&D

activities. This variable is not significant. The log likelihood ratio test reveals that including the other regions variable does not add significantly to the explanatory power of the model (Chi2 LR test = 1.89, p=0.17). Model 4 includes both the clusters and other regions variables. A positive and significant coefficient is found for the clusters variable, while the coefficient for the other regions variable remains insignificant. Together, the findings from models 2 to 4 suggest that presence in technology clusters, and not in other regions, influences the technological performance of firms.

Insert Table 3 about here

Model 5 is the most complete model and includes, besides the linear terms, also the quadratic terms of the clusters and the other regions variables. Including quadratic terms allows to check for non-linear relationships between the location variables and firm performance. The log likelihood ratio test indicates that model 5 significantly adds to model 4 in terms of explanatory power (Chi2 LR test =.7.43, p=0.02). The cluster variable has a positive and significant linear term, and a negative and significant quadratic term. This confirms hypothesis 2: there is an inverted U-shape relationship between the number of technology clusters in which a firm engage in R&D activities and the firm's total technological performance. The coefficients of the clusters variables in model 5 further indicate that biopharmaceutical firms should – ideally – be present in 4 biotechnology clusters. Since the average biopharmaceutical firm in the sample is present in less than 2 biotech clusters, most firms can still improve their technological performance by setting up R&D activities in additional biotechnology clusters[12]. In line with previous models, no significant effects are found for the other regions variables in model 5 (confirming hypothesis 3).

In model 6, an additional regression is ran to check whether the cluster effect is distinctive from a mere R&D internationalization effect. Therefore, the linear and quadratic term of the *countries* variable, reflecting the number of countries in which a firm is present, are added to the initial model. The "countries" variables are not significant, and the model does not significantly improve compared to the model containing only the control variables (Chi2 LR test =1.57, p=0.46). This again confirms that presence in multiple technology clusters and not the mere presence in multiple locations, is contributing to the firms' technological performance.

Conclusions

Firms active in knowledge-intensive fields such as biotechnology, are increasingly developing global R&D activities with location choices for an important degree being determined by the presence of local technological capabilities. Studies in the economic geography literature have shown that firms located in regions where technological activities agglomerate (technology clusters), are more innovative than firms located elsewhere (BAPTISTA and SWANN, 1998; BEAUDRY and BRESCHI, 2003; DEEDS, DECAROLIS and COOMBS, 1999; VAN GEENHUIZEN and REYER-GONZALES, 2007; BATEN et al., 2007). However, so far, little is known about the impact of presence in multiple clusters and regions on the technological performance of multi-location firms.

In this study, such an analysis is performed, based on a panel dataset of the largest biopharmaceutical firms in terms of technological output - in biotechnology. The companies have headquarters in the United States, Europe or Japan, and engage in biotech R&D activities in different locations worldwide. Biotechnology clusters are defined as worldwide leading regions in terms of technology development in the field of biotechnology. Over the time period under study (period 1995-2002), most of the firms in our sample extended and/or contracted their presence in technology clusters and other regions. In the analyses, firm-fixed effect regression techniques and controls on time-varying changes in R&D efforts and past innovation experience of firms are used to account for firm-level differences in size and innovative capabilities. The findings suggest that biopharmaceutical firms can enhance their technological performance by developing R&D activities in multiple technology clusters. The results also reveal that boundaries exist in terms of the net beneficial effects of spreading R&D activities over multiple locations. When the number of clusters in which a firm is engaged becomes too large, increasing costs in terms of coordinating and integrating geographically dispersed R&D units might start to prevail over the marginal benefits from getting access to new, relevant knowledge. At the same time, the observed diminishing effects might also be caused by insufficient critical mass in terms of technological activity (economies of scale and scope) when R&D activities are over-dispersed.

The analyses provide evidence that the cluster effect is distinctive from a mere multi-location effect: the presence in technology clusters, and not the presence in multiple regions and countries, is contributing to a better technological performance of firms. As such, the study provides interesting insights for the R&D internationalisation literature. Recently, this stream of literature started to investigate the relationship between the geographical dispersion of firms' R&D activities and firm performance. Some studies (SINGH, 2008; FURMAN et al, 2006) found negative effects, while other studies (CRISCUOLO and AUTIO, 2008; IWASA and ODAGIRI, 2004; PENNER-HAHN and SHAVER, 2005; TODO and SHIMIZUTANI, 2008) found positive effects of geographical dispersion on firms' performance. These studies did not take into account the technological characteristics of regions in which R&D activities are deployed (clusters or non-cluster regions). This may be one factor explaining the mixed results reported so far.

At the same time, the observed findings imply limitations as well. First, our sample consists of firms with large biotech patent portfolio's and, consequently, the results apply to this type of technology-active biopharmaceutical firms only. Further research could investigate whether smaller firms in terms of biotech technology development activities – e.g. entrepreneurial ventures -, also benefit from being present in (multiple) technology clusters. Next, to retrieve the locations in which firms develop biotechnology research activities, inventor addresses on the firms' fully owned patents are used. While we corrected for co-assigneeship, the derived R&D location variables might still reflect locations of co-inventors not belonging to the firm. This is notably the case when a firm engages in collaboration with a university or other organization, while retaining full ownership of the IP. Ideally, the locations where firms have R&D establishments (R&D labs) should be distinguished from locations where firms are present through other modes, such as R&D collaborations or sponsoring of research at universities and public labs. This requires conducting a firm survey since corporate annual reports do not provide sufficiently detailed information on the type and exact location of the research activities (biotechnology versus other fields) performed by firms.

Within this study, the focus was on regional technological capabilities within the same field (biotechnology); as such, a natural extension of the research reported here implies an examination of 'Jacobs' externalities as well. Regions do not only differ in terms of biotechnology capabilities but also with respect to the presence of technological activities within other, related and unrelated, fields. Studying the impact of technological variety in regions on the technological performance of firms, as well as the number of regions needed to access such variety, is an interesting avenue for further research. In addition, one could study the relative importance of field-specific regional capabilities (MAR externalities) and technological variety (Jacobs externalities) in regions for the technological performance of firms. A final suggestion for further research is to study the micro-dynamics underlying the observed positive performance effects from presence in multiple technology clusters. While the findings are interesting within the framework of R&D location decisions, identifying the most effective mechanisms (e.g. collaboration with local firms and/or research institutes, technology acquisition, researcher mobility, establishment of local research labs) through which firms can benefit from agglomeration externalities in technology clusters might be highly relevant to ensure that firms yield results once location decisions have been made. We do hope that our analyses and findings inspire colleagues in the fields of economic geography and R&D internationalisation to engage in such endeavours.

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Appendix 1: List of biopharmaceutical firms

Abbott Laboratories
Affymetrix Inc.
Ajinomoto
Amgen
Applera
Astrazeneca
Aventis
Beckman Coulter
Becton Dickinson And Company
Biogen Idec
Boehringer Ingelheim
Bristol Myers Squibb
Cell Genesys Inc
Chiron
Diversa Corp
Eli Lilly
Fujisawa Pharmaceutical
Gen Probe Inc
Genelabs
Genencor
Genentech Inc
Genzyme
Geron Corp
Gilead Sciences
Heska Ag
Human Genome Sciences
Hybridon
Icos Corporation
Idexx Laboratories
Incyte Corporation
Innogenetics
Invitrogen
Isis Pharmaceuticals Inc
Johnson Johnson
Kyowa Hakko Kogyo
Lonza Ag
Martek Biosciences
Maxygen Inc
Merck Co
Merck Kgaa
Millennium Pharmaceuticals
Mochida Pharmaceutical
Myriad Genetics Inc
Nanogen Inc
Novartis
Novo Nordisk As
Pfizer
Regeneron Pharmaceuticals
Ribozyme Pharmaceuticals
Schering
Schering Plough
Scios Inc
Seikagaku
Sequenom Inc
Shionogi
Solexa
Tanox Inc
Transgene
Wyeth

[1] Prior studies used cross-sectional data analysis techniques, and did not control for differences in firms' innovation efforts (absolute level of R&D expenses) when studying the impact of cluster membership on firms' technological performance.

[2] MARSHALL (1920), ARROW (1962) and ROMER (1986) (henceforth M-A-R) suggest that knowledge spillovers mainly arise among firms in the same industry. On the contrary, JACOBS (1969) believes that the most important knowledge spillovers occur across industries. Empirical results on the relative importance of both types of knowledge externalities are mixed (see for example GLAESER et al, 1992; FELDMAN and AUDRETSCH, 1999; HENDERSON et al, 1995; BEAUDRY and SCHIFFAUEROVA, 2009; FRENKEN et al, 2007).

[3] Other studies (ex. HILL and NAROFF, 1984; SWANN and PREVEZER, 1996 and HENDRY and BROWN, 2006) have studied the impact of cluster location on the financial performance and growth of firms.

[4] We calculated that for EPO biotechnology patents applied for in 1995 and granted by 2006, only 40% of the patents were granted within 6 years after application.

[5] GLÄNZEL et al. (2004) defined and validated a search key to retrieve all EPO patents in the biotechnology domain in the period 1978-2001.

[6] The NUTS (Nomenclature of Territorial Units for Statistics) classification, established by Eurostat, provides a breakdown of European countries into regions, primarily based on institutional divisions currently in force in the country. The average population size for NUTS 1 regions in Europe (n=73) is 5.3 million . The United States of America consist of 50 sub-national entities called states, having their own state government with substantial state responsibilities. The average population in the US states is 5.5 million. The prefectures of Japan consists of 47 sub-national jurisdictions with an own governor and parliament. The average size of prefectures is 2.7 million inhabitants.

[7] Forward patent citations are calculated on the EPO patent citation database described in Webb et al. (2005). They are calculated for all citing EPO patents and national patents with EPO patent equivalents.

[8] In addition to citation-weighted patent counts, we have also used the number of triadic patents as an alternative measure to control for differences in the quality of patents. Triadic patents are patents simultaneously applied at the patent offices of the US, Europe and Japan. Analyses with triadic patents lead to similar results as the analyses presented in table 3.

[9] In Europe, 12% of biotech patents have multiple assignees (LECOCQ and VAN LOOY, 2009).

[10] Analogous to the cluster and other regions variables, we only count countries from Europe (EU-15 and Switzerland), US and Japan.

[11] Firm level R&D expenses specifically related to biotechnology activities are not available.

[12] Only in 7.35% of the observations (firm-year), firms develop biotech activities in more than 4 technology clusters.

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Table 1 Top Biotechnology regions (period 1990-1999)

	Region	Country	Patents	%	Cum %
1	California	United States	4,162	15.4%	15.4%
2	Massachusetts	United States	1,853	6.8%	21.6%
3	Maryland	United States	1,285	4.7%	25.5%
4	Pennsylvania	United States	1,264	4.7%	29.6%
5	New York	United States	1,072	4.0%	32.8%
6	New Jersey	United States	1,005	3.7%	34.9%
7	Tokyo	Japan	916	3.4%	38.2%
8	Île De France	France	873	3.2%	41.1%
9	East Of England	United Kingdom	766	2.8%	43.5%
10	Kanagawa	Japan	724	2.7%	45.2%
11	Bayern	Germany	716	2.6%	47.6%
12	Osaka	Japan	672	2.5%	49.7%
13	Baden-Württemberg	Germany	654	2.4%	51.7%
14	Danmark	Danmark	643	2.4%	53.7%
15	Switserland	Switserland	626	2.3%	55.4%
16	Washington	United States	619	2.3%	57.1%
17	South East	United Kingdom	614	2.3%	58.8%
18	Hessen	Germany	607	2.2%	60.3%
19	West-Nederland	Netherlands	601	2.2%	62.1%
20	Nordrhein-Westfalen	Germany	534	2.0%	63.4%
21	Illinois	United States	473	1.7%	64.7%
22	Texas	United States	446	1.6%	65.8%
23	London	United Kingdom	444	1.6%	66.6%
24	North Carolina	United States	416	1.5%	67.5%
25	Indiana	United States	406	1.5%	68.7%
26	Ibaraki	Japan	394	1.5%	69.6%
27	Hyogo	Japan	394	1.5%	70.1%
28	Vlaams Gewest	Belgium	389	1.4%	71.2%
29	Connecticut	United States	385	1.4%	71.9%
30	Kyoto	Japan	377	1.4%	72.5%
31	Sverige	Sweden	376	1.4%	73.5%
32	Centre-Est	France	373	1.4%	74.4%
33	Wisconsin	United States	320	1.2%	75.1%
34	Saitama	Japan	317	1.2%	75.5%
35	Ohio	United States	308	1.1%	76.2%
36	Niedersachsen	Germany	283	1.0%	76.8%
37	Missouri	United States	280	1.0%	77.4%
38	Chiba	Japan	276	1.0%	77.7%
39	Michigan	United States	265	1.0%	78.3%
40	Iowa	United States	261	1.0%	79.0%
41	Berlin	Germany	258	1.0%	79.6%
42	Colorado	United States	251	0.9%	80.2%
43	Shizuoka	Japan	245	0.9%	80.6%
44	Scotland	United Kingdom	237	0.9%	81.1%
45	Delaware	United States	232	0.9%	81.4%
46	Nord-Ovest	Italy	220	0.8%	82.1%
47	Minnesota	United States	213	0.8%	82.6%
48	Est	France	213	0.8%	82.9%
49	Virginia	United States	211	0.8%	83.1%
50	Rheinland-Pfalz	Germany	210	0.8%	83.4%

[1] Cumulative % excludes double counts due to co-patenting in multiple regions

Table 2 Descriptive statistics

	Obs	Mean	Std. Dev.	Biotech patents	Biotech portfolio	R&D	Clusters	Other regions	Countries
Weighted number of Biotech patents	422	21.1	36.2	1					
Size of Biotech Patent Portfolio (5year, weighted)	422	106.1	131.1	0.5673	1				
R&D Expenditures (in thousands USD)	422	452.4	760.3	0.0681	0.2164	1			
Number of clusters	422	1.8	1.6	0.3082	0.5024	0.4427	1		
Number of other regions	422	2.4	2.7	0.1471	0.3253	0.5401	0.4453	1	
Number of countries	422	2.0	1.5	0.0930	0.2435	0.5579	0.4348	0.7685	1

Table 3 Fixed Effect Negative Binomial Regressions:

Weighted Number of Biotech Patents Acting as Dependent Variable

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Biotech portfolio	0.0014***	0.0011***	0.0012***	0.0011***	0.0012***	0.0013***
	(0.0003)	(0.0004)	(0.0004)	(0.0004)	(0.0004)	(0.0003)
R&D expenditures	0.0005***	0.0004***	0.0005***	0.0004***	0.0005***	0.0005***
	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)
Clusters		0.0948**		0.0864**	0.2945***	
		(0.0402)		(0.0440)	(0.0924)	
Clusters²					-0.0339**	
					(0.0132)	
Other regions			0.0325	0.0123	-0.0634	
			(0.0231)	(0.0256)	(0.0540)	
Other regions²					0.0066	
					(0.0042)	
Countries						-0.0095
						(0.0974)
Countries²						0.0075
						(0.0113)
Time dummies	yes	yes	yes	yes	yes	yes
Constant	0.2229	0.0954	0.1566	0.0802	0.0052	0.207
	(0.1541)	(0.1641)	(0.1620)	(0.1675)	(0.1879)	(0.2100)
Number Obs	422	422	422	422	422	422
Wald Chi²	122.00***	131.01***	127.15***	132.13***	141.03***	127.85***

Standard errors are reported between parentheses; *, **, *** indicate significance at the 10% 5% and 1% levels