The role of policies and the contribution of cluster agency in the development of biotech open innovation ecosystem

Vesna Vlaisavljevica, Carmen Cabello Medina, Bart Van Looy

https://doi.org/10.1016/j.techfore.2020.119987

Running title: Policies in biotech clusters and OI ecosystem

Abstract: Building on the open innovation and cluster literature, our research describes how innovation policies contribute to the development of open innovation dynamics in biotech clusters. Particularly, we address the role and impact of cluster agency by adopting a contextualized perspective. We carry out comparative case studies of the main five Spanish biotech clusters by combining longitudinal data extracted from secondary sources with primary data obtained from relevant stakeholders. Our study shows that clusters policies do not yield uniform effects; the impact in terms of patterns of collaboration and (open) innovation dynamics is path dependent. The characteristics of the local texture significantly contribute to the observed open innovation ecosystems. As such, these findings imply a plea for contextualizing regional policy initiatives.

Keywords: Open innovation ecosystem; Spanish biotech clusters; Cluster agency; Regional public policy; Comparative case study.

1. Introduction

Until recently, dynamics of technological progress have been dominantly modeled by means of linear models of innovation. Nowadays, more complex and multi-layered theoretical frameworks are proposed, emphasizing the interactive nature of innovation and giving prominence to networks and the interaction relationships between social and economic agents. The interactive model of innovation, as its name indicates, includes the ability of all actors to influence others and to directly or indirectly promote technological innovation. In this sense, over the last decades, science-industry relationships have received considerable attention, as can be witnessed in the concept of a national (NIS) or regional (RIS) 'innovation system' (Lundvall, 1992; Nelson 1993; Braczyk, Cooke and Heidenreich, 1998; OECD 1999), the 'Triple Helix' model (Leydesdorff and Etzkowitz, 1996; Etzkowitz and Leydesdorff, 1998; Numprasertchai and Igel, 2005) and 'Quadruple or Quintuple Helix' models (Carayannis, Barth and Campbell, 2012).

All those approaches consider the contribution of different actors such as government institutions, knowledge-generating institutes (including universities), industrial companies, entrepreneurs and supporting institutions (cluster organizations and federations, among others). Collaboration between industry, science and government reveals itself as instrumental for the creation of new knowledge (innovation) and hence economic growth (Cooke, 2001; 2004; Feldman and Francis, 2003; Asheim and Coenen, 2005; Youtie and Shapira, 2008). These collaborative arrangements take place in what is called an innovation ecosystem (Adner and Kapoor, 2010). They work as networks of innovations and communities of people and organizations that interact to produce and use the innovations (Wang 2009), or, simply, as dynamic, interactive networks that breed innovation (Oksanen and Hautamaki, 2014). The concept of an open innovation ecosystem arises as such and can be used to integrate it all under one umbrella (Chesbrough, Kim and Agogino, 2014; West and Bogers 2014; Bogers et al., 2016).

Moreover, high-tech activities tend to concentrate geographically (e.g. over 50% of biotech activity, as measured by patents, are situated in 15 regions (worldwide) and have cluster dynamics (Lecocq and Van Looy, 2016). Marshall (1920) was one of the first scholars responsible for a theoretical treatment of the phenomena of geographic industry clusters. Positive agglomeration externalities are expected to enhance the performance of firms that are located inside an industry cluster (Marshall,1920; Arrow,1962; Romer,1986). In addition, Jacobs (1969) argued that the flow of complementary knowledge across firms from different industries might even play a more important role than within-industry knowledge flows,). She states that a variety and diversity of geographically concentrated industries is most beneficial to stimulate regional innovation and growth. This has spurred empirical research on the relative importance of both kinds of knowledge externalities resulting from the geographical agglomeration of industries: intra-industry spillovers – commonly referred to as MAR (Marshall–Arrow-Romer) externalities and spillovers between industries –called Jacobs externalities. Since then, clusters have been studied using several theoretical perspectives such as an institutional perspective (Cooke, Uranga and Etxebarria, 1997; Lundvall, 1992), a strategy and competitiveness perspective (Enright, 1998; Porter, 1990, 2000), and a knowledge and learning perspective (Bathelt, Malmberg and Maskell, 2004), which are embedded in different research disciplines, among others, business studies, economic geography, and economics (Cruz and Teixeira, 2010). As of today, the notion of 'cluster' remains relevant and figures as an inspiring theme for regional development (e.g. Maskell, 2001; Bathelt et al., 2004; Tallman, Jenkins, Henry and Pinch, 2004; Arikan 2009; Cruz and Teixeira, 2010; Gordon and McCann, 2010; Ingstrup, 2010; 2013, Santos and Mendonça, 2017). The cluster literature provides interesting arguments that the local context may be extremely relevant for knowledge exchanges to take place between different actporterors. Explicitly, regional cluster policies are mainly meant to provide facilitators to its participants, to foster interactions between different organizations in the region, and to promote connections beyond the region, in order to achieve better innovative and entrepreneurial performance. While it is clear that firms benefit from being located in clusters (for an application in biotech, see Lecocq, Leten, Kusters and Van Looy, 2012), Uyarra and Ramlogan (2012) argue that there is no clear evidence that a cluster policy on its own is able to improve and foster innovation outcomes. Furthermore, it is claimed that open innovation can be affected by different types of policy measures (de Jong, Kalvet and Vanhaverbeke, 2010; Bogers, Chesbrough and Moedas, 2018), as well as by a number of internal and external determinants (Santos and Mendonça, 2017). Despite the vast amount of literature on clusters and regional development, since Martin and Sunley (2003) questioned the economic effects of clusters, a concern echoed in a number of recent contributions (Asheim, Boschma and Cooke, 2011; Yu and Jackson, 2011; Trippl, Grillitsch, Isaksen and Sinozic, 2015; Larty, Jack and Lockett, 2016).

In this paper, we bring together open innovation (ecosystem) and cluster perspectives, to describe how innovation ecosystems contribute to the development of different patterns of open innovation in the biotech industry. Particularly, the aim of this paper is twofold: first, to understand the role of specific (cluster) policies and their implementation through cluster agencies in the promotion of open innovation; and second, to explore the effect of other context local variables such as the culture of open innovation in a region and regional innovation system actors on cluster performance. The research is conducted through a multiple, comparative, case study involving the main five Spanish biotech clusters. Open innovation practices are assessed by three indicators: number of alliances for innovation, co-patents and co-publications.

We focus on the Spanish biotechnology sector as one of the most emerging knowledge-intensive industries. Although Spain has experienced growth in the last years in scientific production and the number of biotech firms, it is still far away from the leading countries in the worldwide context in technological developments and innovation performance (Yagüe-Perales, Niosi and March-Chorda, 2015). In line with this, we also provide an in-depth description of the Spanish biotech industry, in order to understand the evolution and structure of the sector as well as the nature/contribution of (regional) policies employed for the development of biotech clusters and their open innovation performance. As far as we are aware, no previous study has been conducted to combine longitudinal data together with different stakeholders' opinions across Spanish biotech clusters.

Our research provides interesting implications for policy makers and contributes to the literature on clusters and open innovation in two ways. On the one hand, while the performance and associated positive externalities of clusters have attracted much attention among researchers at a micro-level (Artz, Kim, and Orazem, 2016; Delgado, Porter and Stern, 2014; Lechner and Leyronas, 2012; Gilbert, McDougall, and Audretsch, 2008; McCann and Folta, 2011), we focus on public cluster policy and the associated meso-perspective which has hardly been raised (Ahlqvist, 2014; Boschma and Fornahl, 2011; Garone, Maffioli, de Negri, Rodriguez and Vázquez-Baré 2015; Nishimura and Okamuro, 2011). On the other hand, open innovation has been mainly studied at the level of companies, and there is a need to assess the impact of regional dynamics (unfolding within the innovation ecosystem) in terms of providing a favorable context for technological developments, open innovation practices and sustainable growth (Chesbrough and Bogers, 2014; West and Bogers, 2014). The study of Santos and Mendonça (2017), in the Portuguese context, concludes that being in a cluster contributes to a more open innovation approach, especially regarding informal networks and formal collaborations, absorption and external transfer of technology and knowledge.

The paper is organized as follows. First, an overview of the literature on (open) innovation ecosystems, clusters and policies for open innovation is provided as the theoretical background. Next, we describe the methodological approach adopted for creating and executing the multiple case study which continues with the presentation of cases. Hereafter, facts and figures comparing longitudinal data are presented, allowing us to evaluate the open innovation performance of studied clusters. Then, the case study findings are discussed, and the main conclusions and policy implications are reflected upon in the final section.

2. Theoretical background

The locus of innovation definitely cannot be considered at the level of the firm in isolation anymore. Due to the dispersed nature of specialized knowledge and the networked nature of technology development, firms cannot successfully pursue R&D and innovation activities by developing knowledge solely in-house (Ritala, Agouridas, Assimakopoulos and Gies, 2013). Likewise, innovation often does not stand alone and usually heavily depends on accompanying changes in the firm's environment. External changes, which require innovation on the part of other actors, place the firm within an ecosystem of interdependent innovations (Adner, 2006). This particular paradigm shift led to the concept of the innovation ecosystem (Adner, 2006; Adner and Kapoor, 2010), which integrates the exploration of knowledge (knowledge ecosystem) and its exploitation for value creation (business ecosystem) (Valkokari, 2015).

The concept of the ecosystem explains the evolutionary nature of interrelations between different actors, their innovative activities and their environment (Papaioannou, Wield and Chataway, 2007). The recent literature (on NIS, RIS, Triple, Quadruple or Quintuple Helix models) confirms the relevance and importance of interaction between a variety of actors and policy initiatives in order to improve competitiveness in knowledge-intensive industries. Thus, rather than focusing on ecosystems as platforms, from a deterministic or linear viewpoint, they should be viewed as structures of, and relationships between, interacting actors, through which they are dynamically evolving (Weber and Hine, 2015; Gomes, Figueiredo, Salerno and Kazuo, 2016). The innovation ecosystem's dynamics benefit from these actors assuming multiple roles — along different stages — when developing particular innovations as well as when building the ecosystem as a whole. Therefore, the sustainable development of knowledge production and diffusion of innovation should be considered as a dynamic, systemic process of co-(r)evolution (Van Looy, Debackere and Andries, 2003; Werker, 2006; Gomes et al., 2016).

In line with this is the open innovation paradigm elaborated by Chesbrough (2003). It refers to a setting where the focal company strives for innovation by purposefully seeking to tap into available knowledge residing outside its boundaries, while simultaneously allowing for its unused knowledge to outflow and be exploited by third parties (Chesbrough, 2003). Open innovation has emerged as an umbrella concept between the macro- and micro-levels of innovation studies (Huizingh, 2011). Open innovation conceptualizes innovation as taking place between companies and other relevant actors who exchange knowledge and co-develop products and services in loosely coupled networks where business models are dynamically created, reshaped, dissolved and recreated in order to continuously enhance innovation competency (Chesbrough, 2003; Chesbrough, 2006; Chesbrough and Bogers, 2014). Therefore, the open innovation approach can serve as a frame of reference to shape actions in the context of an innovation ecosystem (Wallner and Menrad, 2011). In line with this, Chesbrough et al. (2014) introduced the concept of the open innovation ecosystem, presenting the case study of Chez Panisse. Hence, while stressing the collaboration and openness of actors within an innovation ecosystem, the scientific research lacks an understanding of what settings need to be present in the ecosystem in order to create open innovation (Bogers et al., 2016).

Innovation clusters are geographically localized agglomerations of collaborating firms and organizations, which enjoy a highly developed pattern of collaboration, associated with a triple helix model, i.e., an interactive pairwise collaboration between three types of networked institutional actors, namely companies, knowledge-generating institutes and government (Etzkowitz and Leydesdorff, 2000). Previous research has highlighted why regional clusters are favorable for the application of open innovation as close geographical proximity within the region provides positive and significant enhancements to open innovation practices (Cooke, 2005; Simard and West, 2006; Vanhaverbeke, 2006; West, Vanhaverbeke and Chesbrough, 2006). Explicitly, Simard and West (2006) recognized regional clusters as an ideal setting for the analysis of open innovation, in which networking with multiple actors and agents and the presence of knowledge spillovers and flows are two key elements. Therefore, clusters can be observed from the perspective of open innovation ecosystems (Valkoraki, 2015). In fact, the cluster literature (Porter and Ketels, 2009) suggests that innovation clusters constitute a special variety of innovation ecosystems, in which triple helix interactions enable unique economic effects of innovation synergy or co-creation of innovative goods and services on a continual basis. These ecosystems are shaped by collaborative partners of various profiles, who are free to join and leave the open cluster network (Porter, 1990). In this sense, the biotech innovation ecosystem consists of the organizations active in biotech technology development, such as entrepreneurs, companies, knowledge-generating institutes, as well as the organizations supporting biotech activities, such as regional development agencies and/or cluster organizations. Open innovation clusters could be considered as the most convenient ecosystem model both for continuous co-creation of innovations and for disseminating them across an economy. Findings from Delgado et al. (2014) confirm that a successful innovation cluster can function as a pole of growth for a given region. All this suggests that the advantages arising from the open innovation approach can be enhanced in the context of regional clusters. However, there has been limited research around this issue so far.

Clusters can also be viewed as an additional way of influencing and achieving economic policy objectives by policy makers, stimulating innovation and growth through the development of policies directed at them (Santos and Mendonça, 2017). However, not all clusters are equally effective. As shown in our conceptual model (Fig. 1), this may depend on the implementation of cluster policies through cluster agencies, among others. The active role of a cluster agency, as the organization responsible for implementing the regional policies (Okamuro and Nishimura, 2015), offers services and other mechanisms that augment the inter-linkages between actors and provides a platform to better leverage existing assets in the cluster's business environment (Huxham, Vangen and Eden, 2000). Moreover, there is no consensus on the degree of intervention and influence of public policies in the development of clusters, the context factors and the maturity of the clusters being relevant in the definition of public instruments and incentives (Vicente, 2014). Regarding the contextual factors, the effectiveness of open innovation strategies is believed to be strongly related to the presence of regional innovation system actors (Vanhaverbeke, 2006), thus governments may initiate development programs to support geographically bounded innovation networking within the context of knowledge-based clusters (Maskell, 2001). The culture of open innovation in the region (Tödtling, van Reine, Homme and Dörhöfer, 2011) may act as another relevant contextual factor that will determine the open innovation practices in the cluster.

We propose that policies, contextual factors and the characteristics of the clusters may enable different patterns of open innovation.

Fig. 1 summarizes the elements from the innovation ecosystem proposed for the analysis in our qualitative research that enable different open innovation practices.

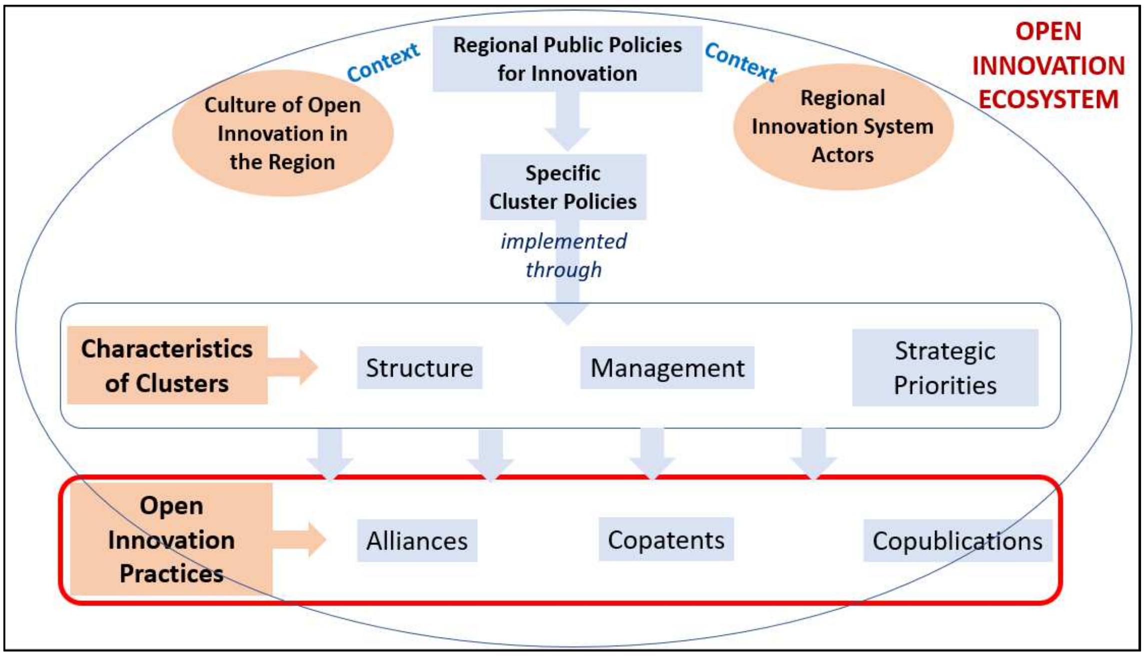

Fig. 1. Theoretical framework: Elements of the open innovation ecosystem in a regional cluster. Source: Own elaboration.

3. The comparative case study of Spanish biotech clusters

3.1. Design of the multiple case study analysis

Multiple case study, as the research strategy, is effective because it enables collection of comparative data and so it is likely used in the quest for both analytical depth and comparability (Yin, 1994). Moreover, Acs and Vargas (2002) claimed that case studies are preferable and are the suitable approach for examining clusters and cluster-based phenomena.

The setting for our study was the Spanish biotechnology industry and the implemented cluster policies, which was appropriate for several reasons. First, the Spanish biotechnology sector has been growing over the last decades. Though this industry is relatively new in Spain, the strong scientific environment has provided a rich medium for the rapid growth of biotechnology, which has seen intensive investment and development in the past years. National and local governments have increased funding for research, created new research centers, and provided mechanisms to advance technology transfer. Second, after the founding of the Spanish Association of Biotechnology Companies (ASEBIO) in 1999, various business associations have been established, both on the national and regional level. Afterwards, five biotechnology clusters have been created, as shown in Fig. 2 together with some basic information about them. These are: BioBasque (Basque Country), BioCat (Catalonia), BioVal (Valencia), Madrid Biocluster and

Andalusia BioRegion. They still represent the vast majority of biotechnological activity in Spain (80% of total internal expenditures in R&D and 77% of the total employment in biotech), whether technological, industrial or commercial (Genoma España Report, 2011). However, they vary widely in evolution, structure, management and goals. Performances of these clusters also differ from each other, hence there is a need for their deeper examination to understand the facilitators of open innovation.

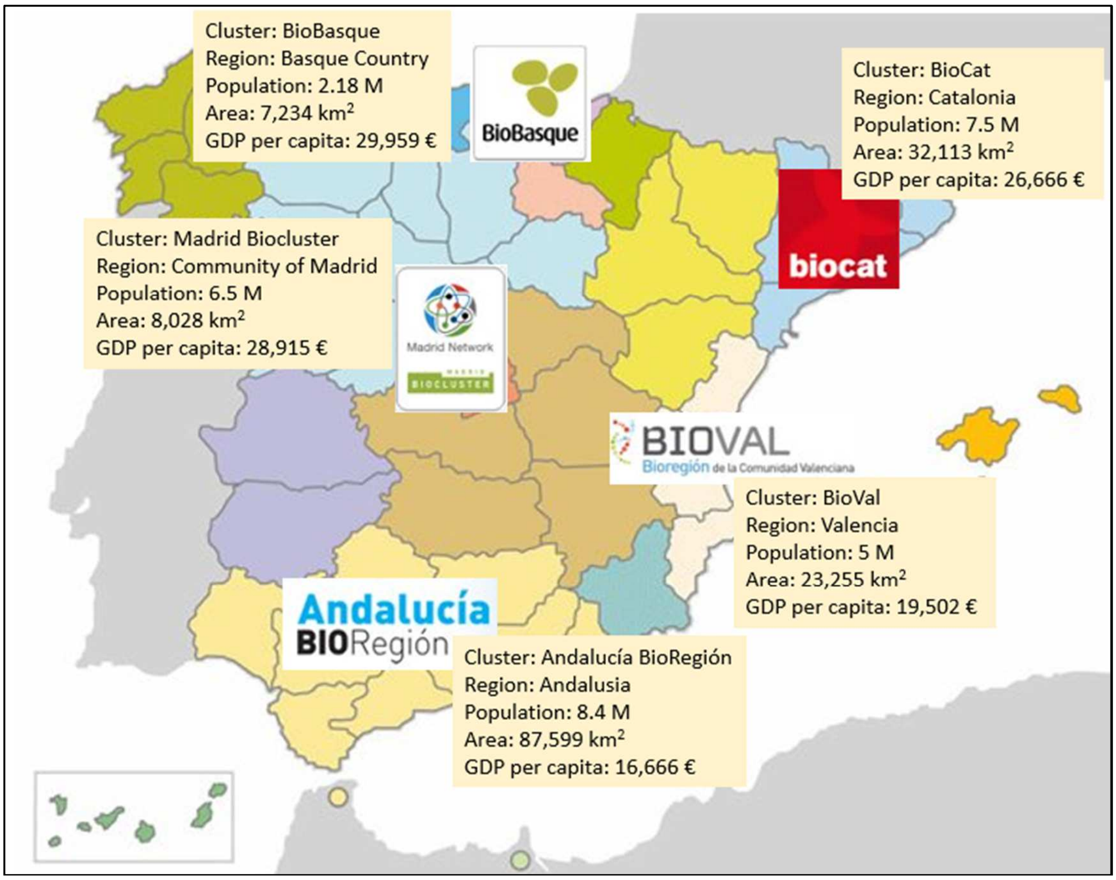

Fig. 2. Map of Spanish biotech clusters and some basic facts. Source: Own elaboration, data from National Statistics Institute (INE) 2013.

The data used for the multiple case study stem from several data sources: 1) extensive archives, including business publications, Internet sources, corporate materials and annual reports (ASEBIO, Genoma España); 2) other documents and literature studies; 3) secondary available databases for science, technology and economic data (WoS, PATSTAT, INE); 4) interviews with different groups of stakeholders (15 actors from the five clusters and two experts in the topic). These interviews have been conducted in a semi-structured way, aimed to better understand the observed 'growth' patterns and their antecedents. The interviews were conducted between the months of April and September of 2015 and lasted between 30 minutes and one hour. All interviews have been recorded via Skype Recorder with the intention of later transcription. Whereas we used an open approach to obtain explanations of different stakeholders of cluster evolutions and success factors for innovation, the analysis was guided by some sub-questions in order to compare the data and align the interviews (Table 7 contains some of the answers).

Table 1 characterizes the regions under study by means of different classifications advanced in the literature.

Table 1. Classification of regions by previous literature taxonomies

Region	Type of region by innovation barriers (Tödtling & Trippl, 2005)	Approaches to innovation policy by regional governments the period 1980– 1990 (Sanz-Menéndez & Cruz-Castro, 2005)	Approaches to innovation policy by regional governments the period 2001–2014 (Borras & Jordan, 2016)	Classification according to knowledge and innovation performance (Capello & Lenzi 2013)
Andalusia	Peripheral region with problems of organizational thinness	Academic approach or public-oriented innovation policy	Significant institutional and budgetary efforts to advance the innovation strategy but no substantially transformation of the academic approach	Imitative innovation region
Basque Country	Old industrial region having lack of knowledge diversity	Business approach or investment in industrial innovation	Balance between business and academic approach	External knowledge-based innovative region
Catalonia	Metropolitan region with problems of fragmentation in their capabilities	Academic approach	Academic approach	External knowledge-based innovative region
Madrid	Metropolitan region	Academic approach	Academic approach	Knowledge-based innovative region
Valencia	Peripheral region	Academic approach	Academic approach	Imitative innovation region

Source: Own elaboration from the previous literature and Internet sources.

As can be observed in Table 1, our study deals with different types of regions in relation to innovation barriers, approaches to innovation policy and performance indicators on science and technology. All possible cases are covered by our research sample. The first typology (Column 1) comes from Tödtling and Trippl (2005), who claimed that identifying regional system problems aims to define more fine-tuned and specific regional innovation policy, avoiding a "one size fits all" approach. Three main innovation barriers are organizational thinness in peripheral regions (Andalusia, Valencia), fragmentation of existing capabilities in metropolitan regions (Madrid, Catalonia) and lock-in and lack of knowledge diversity in old industrial regions (Basque Country).

The second typology (Column 2) was set by Sanz-Menéndez and Cruz-Castro (2005) and updated by Borras and Jordan (2016) who aimed to observe the transformations in regional innovation policies since 2001 in terms of institutional framework and budgetary priorities (Column 3). They developed the framework to study the extent to which regional innovation policies have changed. The earlier study (Sanz-Menéndez and Cruz-Castro, 2005) distinguished between two approaches to innovation policy by regional governments: the academic approach (mainly universities and public research centers) and the business approach (mainly technology centers and innovative firms). Basically, this is the focus of investment in principal actors of the innovation system. Considering the period 1980–1990, these authors found a predominance of the public-oriented innovation policy in most Spanish regions, with only one case clearly related to investment in industrial innovation (Basque Country). In the recent studied period (Borras and Jordan, 2016), from 2001–2014, most regions (Catalonia, Madrid, Valencia) remained with the same policy priorities or overall did not transform substantially the innovation strategy (Andalusia), which kept their regional innovation system problems unresolved. Only the Basque Country succeeded to introduce a policy transformation; from 2007, the regional government created series of institutional developments addressing the traditional weakness of the innovation system and achieved the trade-off between academic and business sectors.

The last typology (Column 4) is established in Capello and Lenzi (2013), who classified European regions into four groups according to their knowledge and innovation performances with respect to the European average. Our study shows only three groups of innovative regions, according to the existence of internal or external sources of knowledge. Only one Spanish region (Madrid) is characterized as a knowledge-based innovative region, performing above average in both, knowledge and innovation performance. The Basque Country and Catalonia are considered as external knowledge-based innovative regions as they are very successful and efficient in the use of local knowledge (whose endowment is below the average) and in accessing external knowledge sources to achieve above average innovation performance. Finally, Valencia and Andalusia are considered imitative innovative regions as their knowledge and innovation intensity is below the European average.

3.2. Regional public policies for innovation

Following the logic of our research model, we analyzed implemented innovation policy in five studied regions. The RIM Plus[1] repository was consulted to count existing regional innovation support measures from 2005 to 2014.

Table 2. Number of regional innovation support measures

Policy Priority	Andalusia	Basque Country	Catalonia	Madrid	Valencia
1. Competitive funding to foster public research	3	10	3	2	1
2. Science-industry cooperation	12	17	8	9	7
3. Human resources for science, technology and innovation	2	4	2	2	1
4. Business R&D and innovation	6	5	2	2	4
5. Innovation climate and business ecosystem	0	2	2	3	0

Source: RIM Plus Repository, European Commission, 2014.

[1] Regional Innovation Monitor Plus (RIM Plus) provides a unique platform for sharing knowledge and know-how on major innovation and industrial policy trends in the EU regions.

The analysis of values from Table 2 shows that the focus of regional innovation policy measures has been placed on providing support for science-industry cooperation, principally through investments in public research, research infrastructure and R&D cooperation (joint projects, public-private partnerships with research institutes). Among the leading regions with the highest number of measures in this form of support are the Basque Country (17) and Andalusia (12). At the same time, the most active region in implementing supporting measures for innovation is the Basque Country, followed by Andalusia. Of particular interest for our research, coming from this analysis, is that all regions have some measures related to cluster framework policies that have been launched for cluster dynamization. Some of them are more developed than others, but that will be discussed in more detail further on. Nonetheless, there are only few measures in support of innovation climate and business ecosystem.

3.3. Regional innovation system actors

Table 3 shows the regional institutions active in R&D (all fields). Huge differences in absolute terms are found between studied regions. As expected, Madrid, as a capital region, leads with the highest number of universities, R&D centers and TTOs (technology and transfer offices). However, Catalonia is closely following with a very developed infrastructure of research centers and science and technology parks. It is not surprising for Andalusia to have an institutional system as illustrated due to its huge regional extension and recent policy priorities to invest in research infrastructure. The Basque Country and Valencia seem as two less developed regions, but knowing that these two are also quite small regions, we can assume that, in fact, all cases have enough actors to shoulder their innovation systems. Specific differences related to biotech are further addressed in the description of the clusters.

Table 3. RIS actors

Region	Universities	Research Centers	Innovation and Technology Centers	TTOs	Science and Technology Parks
Andalusia	**10**	**37**	**37**	22	10
Basque Country	3	14	4	18	3
Catalonia	**12**	**90**	**22**	34	**25**
Madrid	**14**	**64**	**53**	**40**	8
Valencia	5	14	4	27	5

Source: Various reports and Internet sources, 2011.

3.4. Culture of open innovation

To characterize the studied regions regarding the culture of open innovation in them, we used three RIS indicators: international co-publications, public-private co-publications and innovative small- and medium-sized enterprises (SMEs) collaborations which are summarized in Table 4 (from 2011 to 2017). On one side, we can observe that in relation to two co-publication indicators, no big differences are found, although two metropolitan regions, Catalonia and Madrid have slightly more publications with international co-authors and public-private collaborations than the others do. On other side, it is important to highlight that within the Basque Country SME's are relatively more present in terms of collaboration for innovation.

Table 4. Regional potential regarding open innovation culture

Region	International Co-publications	Public-Private Co-publications	Innovative SMEs Collaborations
Andalusia	0.280	0.167	0.132
Basque Country	0.355	0.251	**0.392**
Catalonia	**0.433**	**0.332**	0.182
Madrid	**0.445**	**0.337**	0.180
Valencia	0.316	0.205	0.177

Source: RIM reports and RIS indicators, European Commission, average value 2011–2017.

3.5. Specific cluster policies

Let us now turn our attention to the sector of interest for this research, biotechnology. Spanish biotech has developed from being mainly diversified of existing traditional industries to have a large number of spin-off companies originating in the knowledge-generating system. Fig. 3 shows the cumulative evolution, from 2003, of the number of small companies, mainly in the biopharma sector, whose business is completely dedicated to biotechnology (DBFs: dedicated biotechnology firms).

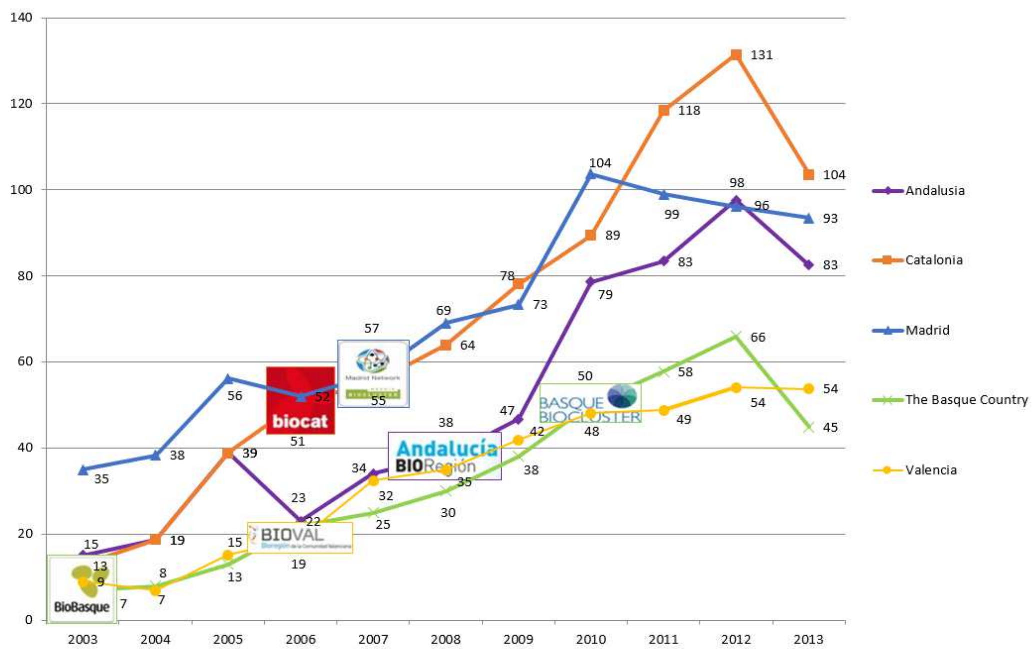

Fig. 3. Number of (DBFs) (2003–2013). Source: Own elaboration from annual ASEBIO reports and INE.

As illustrated in Fig. 3, in 2013 Catalonia ranks first (with 27%), followed by Madrid (25%), Andalusia (22%), followed by Valencia (14%) and the Basque Country (12%). However, here we can see similar trends as the overall trend in the number of DBFs has been very positive; it has experienced growth of 478% for the period 2003–2013, going from 79 to 378 companies). Indeed, in a decade, the number of fully dedicated biotech firms in Spain has been multiplied by almost 5. However, we observe a net decrease (of 5.3%) of the number of DBFs in 2013 compared to 2012. ASEBIO explains the first decline after 10 years by the difficulty of access to public and private funding (resulting in exits and bankruptcies in that time period) and appeals to public policies to accompany the industry consolidation.

The distribution of public funding for R&D&I and infrastructure is very similar throughout the decade 2000–2010. As shown in Table 5, Madrid and Catalonia account for over 57% of available funding, followed by Andalusia with just over 22% in 2010. Up to 2010, the Basque Country and Valencia absorb around 10% of public subsidy each.

Table 5. Evolution of distribution of public subsidies (national and regional) for R&D and innovation projects and infrastructure in biotechnology

Region	Amount in 2000 (millions of euros)	Amount in 2010 (millions of euros)	Annual growth rate (%)
Andalusia	15.84	83.89	23%
Basque Country	2.1	39.37	48%
Catalonia	13.38	92.47	24%
Madrid	22.32	125.61	23%
Valencia	9.51	37.25	17%

Source: Own elaboration from Genoma España 2011 Report.

With respect to the amount provided by the local governments, all of the regions have contributed additional funds to those received from the central administration for R&D&I and infrastructure in biotechnology. The Basque Country and Andalusia stand out here with contributions exceeding 100 million euros, Madrid and Catalonia have between 50 and 100 million euros, and Valencia has below 50 million euros. From the relative point of view, the Basque Country is the one that makes the biggest effort by its own government, as shown in Table 6.

Table 6. Funding for R&D&I projects in biotechnology

Region	Amount received from National Government (2000–2010) (millions of euros)	Amount received from Local Government (2000–2010) (millions of euros)	Local vs. National Amount Received in %
Andalusia	314.95	173.81	55%
Basque Country	82.29	204.53	249%
Catalonia	660.62	51.63	8%
Madrid	698.19	99.17	14%
Valencia	220.49	38.47	17%

Source: Own elaboration from Genoma España 2011 Report.

The implementation of cluster policies determined the characteristics of each cluster. Following our theoretical model, those characteristics could be reflected in differences in their structure, management and strategic priorities toward cooperation. The general overview that contains all this information of the five studied clusters is shown in Table 7. Besides, in the next sections we describe the historical background, policy characteristics and the status of the five clusters as well as the main activities performed by their respective cluster agencies.

3.5.1. Andalusia BioRegion (Andalusia)

Andalusia BioRegion is the strategic booster unit of the Andalusia Biotech Cluster, which depends 100% on IDEA, the regional government agency for innovation and development of Andalusia. Andalusia BioRegion is based at the health science technology park in Granada. Most of the firms belonging to the cluster are SMEs. The mission of Andalusia BioRegion is to link together firms, research teams, hospitals and other bioregions through strengthening the knowledge generation stages and its transfer to the industry. The main objectives are to develop the industrial sector and promote research and transfer of knowledge in the sector to become globally competitive and to increase the size and quality of job creation. There is no formal strategic plan. Mostly, the funds of the agency have been allocated to activities and initiatives such as participation in fairs, actions to awareness-raising and revitalization of projects, representing expansion projects or R&D performed by companies.

3.5.2. BioBasque (Basque Country)

BioBasque is small but vibrant biotech cluster from the Basque Country. It represents the first cluster policy in Spain, and its strategic mission is to establish international competitiveness. The BioBasque agency belongs to the SPRI (Basque Development Agency), a public company dependent on the Basque Government. BioBasque provides to its members financial support and other expertise and also helps start-ups to accelerate growth through networking and access to strategic partners. Strong regional and political supports are involved in the development of the biosciences sector. Despite the fact that the Basque Country was first to implement the strategy, from the very beginning the region did not have critical mass of biotechnology companies. In the beginning, they counted on two small multinational pharmaceutical companies and some competencies in bioscience at universities. By trying to take advantage of this situation, the government set a radical diversification strategy (2000–2010) and decided to invest more in knowledge-intensive sectors. As the result of this strategy, the cluster achieved 20% growth in the sector until 2010. In 2012, it had more than 55% of its employees in dedicated biotech firms, compared to total biotechnology employees in the region, indicating that the business sector was getting more and more relevance. Their main objective was to foster development of critical mass, but the sector still has many weaknesses, such as the lack of quality scientific production and the absence of international collaborations. Thus, the great efforts of the cluster agency remain in carrying out three main areas of activity: knowledge creation, development of the companies and dynamization (more interactions) of the cluster. Moreover, supported by an extensive network of infrastructure and a favorable public administration for business, the cluster agency actively promotes collaboration between academia, the healthcare system and industry.

3.5.3. BioCat (Catalonia)

The BioRegion of Catalonia is an emerging biotechnology, biomedicine and medical technology cluster concentrated around the University of Barcelona Scientific Park and the Pompeu Fabra University. It has become one of the main biotechnology cores in Spain, with the highest level of patents in the application process. This cluster is also starting to be competitive with other European bioregions, with its high ranking of entrepreneurs/start-up firms. The Barcelona Science Park (PCB), established by the University of Barcelona in 1997, was the first science park in Spain. The European Observatory for Biotechnology is located at the Barcelona Science Park.

The cluster is driven by a cluster organization called BioCat that coordinates all activities from research to market, fostered by various governmental funds and political support. BioCat promotes, stimulates and coordinates actions to promote biotechnology and biomedicine as an economic engine. The mission of BioCat is to help the creation of the right environment to add value to bioscience in the region with an active, efficient and dynamic knowledge-transfer system. BioCat structures its activities around five major strategic areas: cluster consolidation, business competitiveness, internationalization, training and talent and social perception of biotechnology. The cluster's consolidation as a network of knowledge and collaboration is considered essential to achieve goals related to both scientific and business growth and improvement. Featuring the high quality of research institutions and successful organization of international networks, this cluster attracts more and more scientific talent.

3.5.4. Madrid Biocluster (Community of Madrid)

Madrid Biocluster was created to support the common interests of its members and promote the development of biotechnology in the Madrid region. Since biotechnology is considered as a high-technology activity which requires mostly a short distance for tacit knowledge exchange, sustained physical presence and face-to-face relationships with the universities, hospitals, and governmental entities, Madrid region is very well suited for the development of the sector. Until 2013, in the Madrid region there were 93 fully dedicated biotechnology firms, mostly SMEs but only 42 formally belonged to the cluster. Madrid Biocluster has five major areas of activities for its participants: business cooperation, internationalization, training and talent-attracting, financing of projects and everything related to infrastructure, since biotechnology companies tend to settle in common platforms to foster synergies and complementarities. The principal objective sought is to become an international cluster, supported by the potential in the region, embodied in researchers, public institutions and business development initiatives. Moreover, the cluster agency mostly aims to help increase the supply of funds for R&D, and thus the majority of the efforts and agency budgets are dedicated to the presentation in international projects which will provide the required funding for the research projects of its participants.

3.5.5. BioVal (Valencian Community)

BioVal is an emerging biotechnology cluster. Its scientific base represents a combination of the long-established University of Valencia, several quite young research centers and knowledge institutions. The cluster is relatively young and small in terms of its industrial base. Most of the firms present in the cluster are SMEs. BioVal aims to promote the development and competitiveness of the business in bioscience in order to position its participants on the international map. The most important activities carried out by the cluster agency refer to networking, lobbying and training. Science parks where biotechnology companies are located are well represented in the cluster. However, the cluster does not have a sufficient base of various types of consultants including financial, legal, property and marketing services necessary for its development. Besides, the cluster agency is lacking funds and regional government support (as could be seen previously in Tables 5 and 6). The cluster agency used primarily its website as a communication tool, providing new contents to improve its positioning and visibility; allowing associated companies to have an active platform about their research and services, facilitating in that way the creation of synergies, and the promotion and sale of their products. It also organizes various activities of information/formation for its participants, such as 'Biobreakfast', workshops, conferences and visits to trade fairs to enhance the promotion of cluster actors.

Table 7 summarizes the overview of the clusters, in terms of origin, structure, management and implemented policies. The relevant information for its elaboration is extracted from both secondary sources and interviews with policy makers. Although we tried to provide homogeneous information for all studied regions, in some cases we were able to find more details and in others we lack some data.

Table 7. Basic characteristics of the five clusters and overview of their policies

Name of Regional Cluster	Andalusia Bioregion	Biobasque	Biocat	Madrid Biocluster	Bioval
Origin of the cluster (initiated by government, by industry, or equally by both?)	The germ comes from Andalusian **government**, although there is a business association that is involved in the cluster creation.	The strategy was designed and implemented at the behest of the Basque **Government** to develop bioscience and to create biocluster.	Initiated by Catalan **Government**, although there existed already a fairly strong entrepreneurial base.	Initiative of the six most representative **biotechnology companies** and three regional public entities.	Emerged as an initiative of the **industry** initiated by several companies.
Year of cluster policy implementation	2008	2002	2006	2007	2006
Core Management Organization	As such **there is none**. IDEA, public agency, dedicated to promote entrepreneurship. Cluster doesn't have a differentiated structure.	SPRI is 100% **public** the Basque Business Development Agency until 2010 when biocluster was created as **independent** organization.	Biocat. It is a **private organization** that has its own governance.	Madrid Biocluster. It's a **private non-profit association**.	Bioval. More than cluster is an **association of biotechnology companies**.
Number of Employees of Cluster Organization	**No employees** specifically dedicated to this. Depending on the project, but overall 4 people from IDEA are part time engaged in biotech cluster activities.	**3** (2 in Spri but only 1 fully dedicated which is responsible to align all horizontal services available and 1 in Biocluster).	**15 fulltime dedicated** permanent employees, + subcontracts for almost all activities performed by the organization.	**3 fulltime dedicated**, depending on the project subcontracting of additional employees.	**1 fully dedicated**. Before it was 3 when they had more budgets.
Selection of the cluster participants	It's an **open approach**, voluntary membership of both DBF and users firms.	Any firm with activities in bioscience belongs to bioregion. But for new cluster there is a **membership fee**.	**Any firm** in the cluster region which is somehow related to biotechnology R&D is a cluster firm.	**Membership fee** is required and obligatory for all members including Government.	**Membership fee** is required. From the beginning it was just DBF and recently it includes other organizations related to biotechnology R&D.
Regional potential (2015)	Approx. 100 DBF. 10 universities, but 2 are more dedicated to biotechnology related areas. **No direct leader** firms, some from related industries.	50 DBF, 3 universities, 4 R&D centres (2 specific for bioscience). **Four leader firms** but comparing on international level quite small.	110 DBF 11 universities that offers biosciences; 15 research centres; **Several leader firms** from pharmaceutical and chemical sector.	70 DBF but not all of them are participating in the cluster; 6 universities (4 active in biotechnology), more than 20 research centres. **Several leader firms** and multinationals.	Almost 50 DBF, 5 universities, 14 research centres. Some potential related industries and end users of biotechnology, but **not real leader firm** oriented to collaboration.
Total nº (in DBF) of employees (2012)	2509 (769)	1270 (777)	6551 (1830)	6421 (1531)	1917 (435)
Total nº (in DBF) of researchers (2012)	1629 (431)	970 (531)	4422 (1099)	3354 (1045)	1338 (247)
Coordination with other cluster projects	**None**. Limited to cooperation (partnerships) with few local entities.	Coordination of **interregional relationship** with Aquitania and very informal relationships within region, but still no concrete organizational cooperation.	Promotion of exchanges with **other Catalan clusters**; Interest but no concrete interregional cooperation in Spain. Very active in **worldwide** cooperation.	Active informal exchanges with **domestic and foreign organizations** and clusters. Partnerships based on the call for projects as cluster organization participate in the EU consortia projects.	No concrete organizational cooperation, **only informal relationship with some regional** associations.

Source: Own elaboration from interviews, policy documents and Internet sources.

To sum up, the analysis of all information presented in this section suggests that there are still imbalances between public and private spending in R&D in a number of regions and a relatively dominant role of the government at different levels in all studied regions. Most of them suffer from a lack of dynamism a low level of applied R&D and innovation due to the predominance of SMEs sectors and different types of 'lock-ins' presented in some of regions (Andalusia and Valencia especially).

3.6. Open innovation indicators

Following the rationale of this study and within the methodological framework above, we next illustrate a comparison of various longitudinal data of five Spanish biotech clusters to assess their performances and other characteristics regarding open innovation. Three indicators will be discussed in detail: alliances, co-patents and co-publications. For all of them, we followed the same logic: we only considered the data from the year of cluster policy implementation to 2012. Moreover, we looked at three different types of collaborations, intraregional, meaning the connections between only members of the determined cluster; national, where at least one member of the cluster has to collaborate with some national organization; and international, where at least one partner was from outside Spain. Nevertheless, in the case of publications, we did not find it relevant to look at publications between cluster members only, as scientific collaboration by its nature is regionally favorable and also in many cases a scientist may sign as a member of various regional institutions. Additionally and more interesting for our research, we looked at the percentage of industrial collaborations, which are the publications with at least one author from industry.

3.6.1. Alliances for innovation

As we have argued throughout this paper, the relevance of clusters comes from their consideration as an ideal environment for the exchange of knowledge and information. In this sense, the success of the cluster would be given by the networks and agreements established between the companies. For this purpose, alliance data were extracted from the ASEBIO database. The number of agreements in which the companies of each cluster participate is shown in the small rectangles in each respective column in Fig. 4. However, if we wanted to make an assessment of the most active clusters, the number of agreements should be put in relation to the size of the cluster itself (Fig. 4). In this regard, the most efficient clusters in terms of exchanges of knowledge materialized in agreements between companies are BioCat and BioBasque.

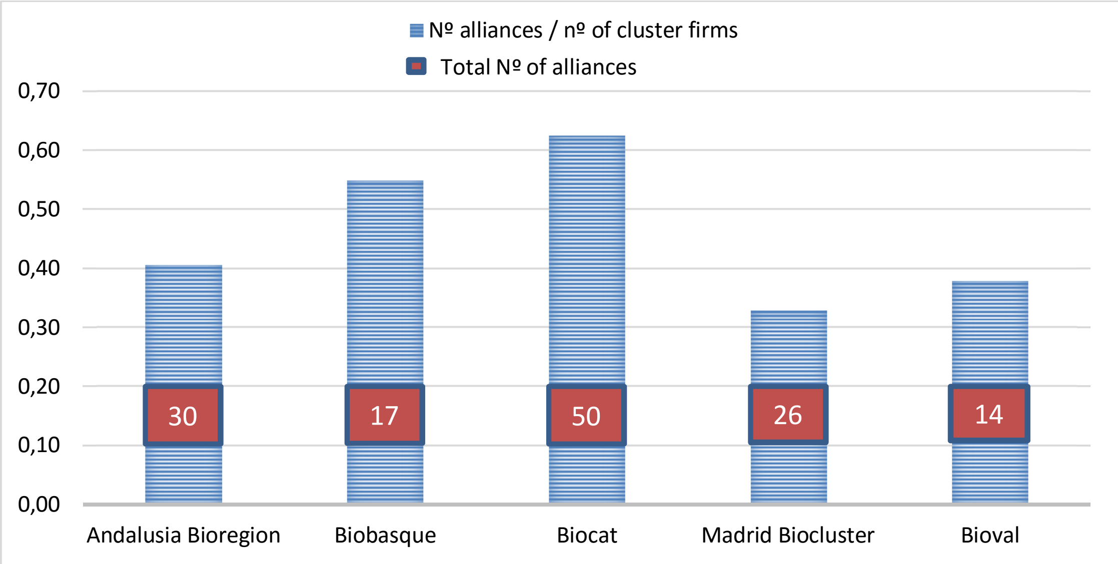

Fig. 4. Alliances as open innovation indicator. Source: ASEBIO, 2013.

Although it is essential that such relationships are stable enough to build the necessary trust to help the sharing of valuable knowledge, the effectiveness of such exchanges could be reduced if such agreements are made repeatedly with companies belonging to the same network of relationships. In this sense, the stock of knowledge available in the agreements needs to be continually rejuvenated. For this, it is important to establish alliances with companies outside the cluster itself, as a way to facilitate the creation of new knowledge. Fig. 5 shows, for each cluster, the percentage of alliances established exclusively between companies belonging to respective cluster together with the percentage of alliances in which other companies and external organizations participate. BioBasque, BioVal and BioCat are the clusters in which a greater proportion of agreements with external companies are made.

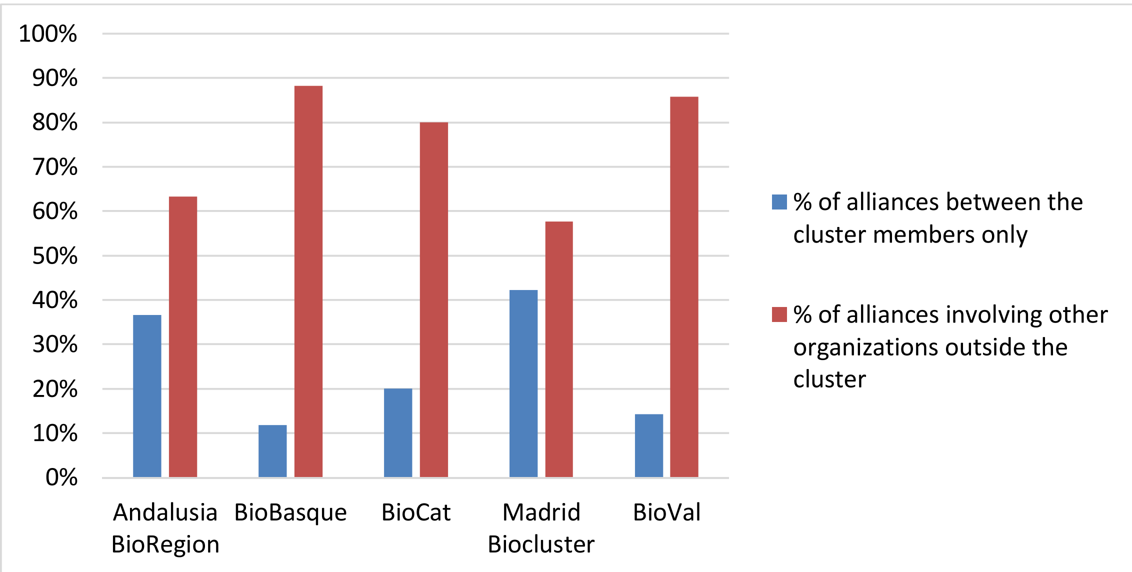

Fig. 5. Proportion of non-cluster alliances. Source: ASEBIO, 2013.

Moreover, the international dimension is considered to be very important for knowledge-intensive industries as an emerging industry probably has enough critical groups all over the world currently. A concentration of expertise to supply this thinking definitely may not be found in one place, thus the biotechnology firms are forced to look outside their locality. The collaboration on an international scale is required because of the particular relevance that the introduction of new knowledge and skills has for the technological development of a region (Cooke, 2001; Lecocq and Van Looy, 2009). Fig. 6 shows that BioVal and BioCat are internationally active clusters as their members maintain the highest proportion of partnerships with entities outside Spain.

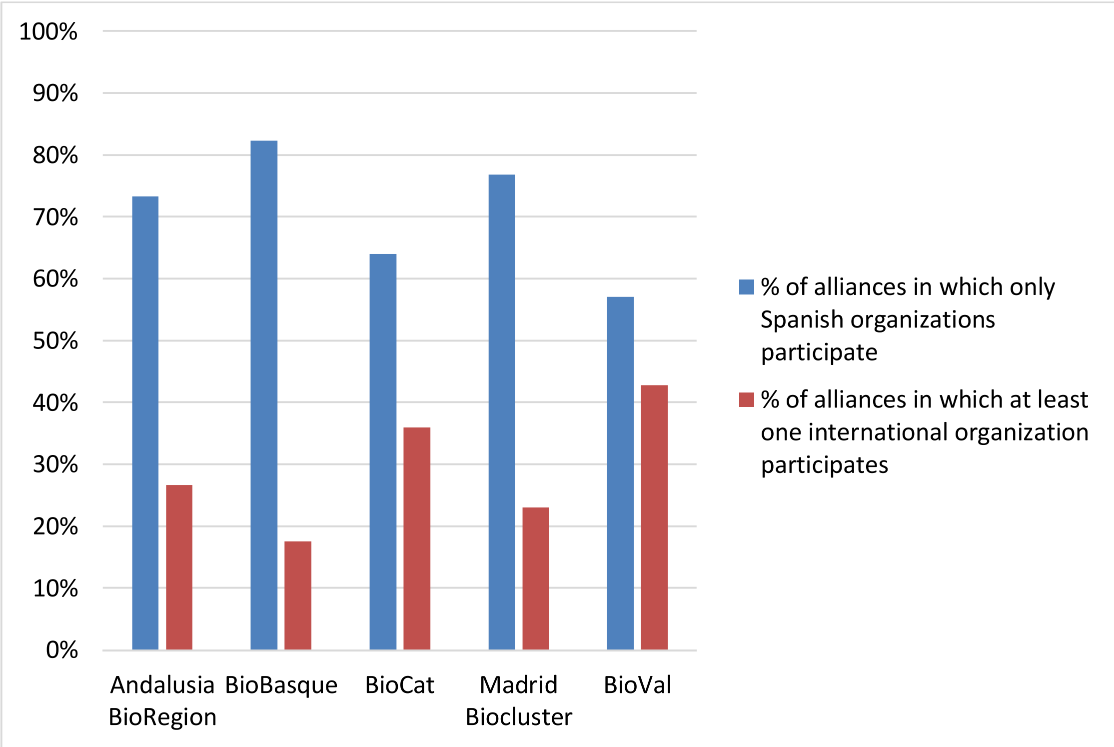

Fig. 6. Proportion of international alliances. Source: ASEBIO, 2013.

3.6.2. Co-patents

In order to compare Spanish biotech clusters, we have derived patent applications from the PATSTAT database (version October 2013) on the NUTS2 regional level, and we have used OECD IPC classes to identify biotechnology patents. Since NUTS2 levels are only available for patents applied by the European Patent Office (EPO), our data are limited to them. However, we assume that similar trends and distributions among studied regions are present in other patent offices. As we can observe in Table 8, there are differences in technological performance measured by patent applications among studied regions. Two groups can be identified. Catalonia and Madrid have started before others, and since then they have continued positive trends (70% of all Spanish biotech technological activities come from these two regions). Other regions are still performing modestly; the only difference may be noticed in the Basque Country which, since 2008, has succeeded to surpass more than 10 patents per year. Besides, Table 8 indicates that co-patenting is similarly distributed among all clusters, except BioBasque where it seems that co-patenting is less developed, especially in the international scale. It is worthwhile to notice that BioCat is the only cluster whose co-applicants mostly come from its own region while the rest ones are mostly relying on other national collaborations to apply for patents. Andalusia is the region with the relatively highest proportion of international co-patents.

Table 8. Co-patents as open innovation indicator

Cluster	Total patents	% of co-patents	Total co-patents	% of intra cluster co-patents	% of national co-patents	% of international co-patents	% of industry patents	% of public patents
Andalusia BioRegion	26	50%	13	31%	46%	23%	46%	54%
BioBasque	66	27%	18	39%	56%	6%	68%	32%
BioCat	212	43%	91	57%	32%	11%	63%	37%
Madrid Biocluster	145	39%	56	23%	61%	16%	40%	60%
BioVal	35	54%	19	21%	68%	11%	38%	62%

Source: PATSTAT database, 2013.

Moreover, if we take a look at the texture characteristics of the clusters under study we observe that there are other differences between them, in terms of the type of actors responsible for the technological development of cluster (business versus public sector). The two last columns of Table 8 show EPO patent applicants by sector. In Catalonia (63%) and the Basque Country (68%) the majority of patent applications belong to business, indicating that the industrial sector is playing a dominant role in developing technological innovations. These two regions are also considered among the majority of informants as more entrepreneurial with a strong business-minded orientation and a clear focus on markets. Both, in Valencia and Andalusia the public sector is predominant, accounting for more than 50% of public patent applications. The case of Madrid is special. The vast majority of stakeholders from our sample pointed out that Madrid benefits from a 'centralization' (capital) effect. For instance, the administrative headquarter of the most relevant national research institution (CSIC - the third largest in Europe) is located in this region. CSIC is accounting for 32% of EPO patent applications for Madrid region in biotech.

3.6.3. Co-publications

Scientific relevance is measured primarily by the number of articles published in prestigious international journals. For this aim, we retrieved bibliographic records from the articles in the database ISI Web of Knowledge, the principal collection of Web of Science (WoS), in the research area Biotechnology/Applied Microbiology by year. The procedure of search followed was this: in the address field, we wrote the name of each region with all possible variations in the names; subsequently, the results were refined by country (Spain), and only articles and reviews have been considered as document types. Thus, we have a global view of the evolution of the scientific relevance in biotechnology. The first column of Table 9 indicates the number of scientific publications of the studied regions. Later, we used the WoS tool for the evaluation of scientific production, InCites, to analyze in more detail these publications, and we extracted data on national, international and industry collaborations.

Several differences among regions are presented. On one side, we can see that Andalusia, Catalonia and Madrid account for 84% of the total number of scientific publications. Although Valencia is displaying growth during this period, it is not able to catch up with other regions. On the other side, the level of scientific production of the Basque Country is low, and it is not making any leap in this perspective. Besides, it is the region which is co-publishing more than others are, and it has the relatively highest proportion of national co-publications. Moreover, in Table 9 we can see clearly that Catalonia is the region with the relatively highest number of international co-publications, meaning that their scientists are collaborating mostly with international co-authors.

What is very interesting to notice is that Madrid is very much outperforming the others in industry collaborations as 3.46% of its co-publications are signed with authors from the business sector.

Table 9. Co-publications as open innovation indicator

Cluster	Total publications (PUB)	Total COPUB (NAT+INT)	% of total COPUB	% of national COPUB	% of international COPUB	Industry collaborations
Andalusia BioRegion	869	465	53.51%	25.19%	37.86%	1.50%
BioBasque	156	102	65.38%	49.53%	31.41%	1.28%
BioCat	1566	874	55.81%	22.20%	43.17%	1.79%
Madrid Biocluster	1270	814	64.09%	42.70%	37.40%	3.46%
BioVal	757	476	62.88%	41.09%	36.99%	1.98%

Source: WoS, InCites, 2012.

To summarize, as we can notice, there are clear differences between the three considered indicators of open innovation in this research. In some cases, organizations are collaborating more for alliance purposes, and these partnerships are also different in their nature (BioBasque mainly, then BioCat and BioVal). In other cases, cluster members are more active in co-patenting with partners from their own region, like BioCat. And, in terms of scientific collaborations, the distribution between studied cases is more or less comparable but still with obvious texture differences.

4. Discussion and conclusions

By bringing together open innovation ecosystem and cluster approaches, our research has examined how a number of elements making up the innovation ecosystems contribute to different patterns of open innovation (OI) in five Spanish biotech clusters.

We opted for a systemic view on biotech clusters, acknowledging the potential contribution of a variety of actors towards knowledge creation and open innovation dynamics within the cluster.

In order to create such a more encompassing picture, we relied on longitudinal data and indicators stemming from a variety of sources (Publications, Patents, Firm level data, Government Expenditures,…) and complemented these quantitative data with insights obtained from expert interviews. As such the adopted methodology results in a more enriched understanding of the unfolding innovation dynamics of clusters.

In our research, we assume that the implementation of both regional public policies for innovation and specific cluster policies results in different features of clusters, in terms of genesis, evolution, structure, management and strategic priorities toward collaboration. Besides, a culture of open innovation in the region as well as the presence of relevant actors (universities and science and technology parks, among others) also act as important contextual factors in the innovation ecosystem. The conjunction of all these elements enables different trends of technological development and open innovation in the cluster.

An overview of these elements for each of the five analyzed clusters is shown in Table 10.

Table 10. An overview of the elements of innovation ecosystem present in studied clusters

THE CONTEXT	Andalusia Bioregion	Biobasque	Biocat	Madrid Biocluster	Bioval
PROACTIVITY IN REGIONAL POLICIES FOR INNOVATION	medium	Very high	medium	medium	low
CULTURE OF OPEN INNOVATION IN THE REGION	low	high	high	high	medium
VOLUME OF REGIONAL INNOVATION SYSTEM ACTORS	medium	low	high	high	medium
SPECIFIC CLUSTER POLICIES	**Andalusia Bioregion**	**Biobasque**	**Biocat**	**Madrid Biocluster**	**Bioval**
EVOLUTION OF PUBLIC SUBSIDIES IN BIOTECHNOLOGY	Medium growth	High growth	Medium growth	Medium growth	Low growth
RELATIVE INVESTMENT OF LOCAL GOVERNMENT	Medium	Very high	Very low	Very low	Medium
STRUCTURE, MANAGEMENT AND PRIORITIES OF THE CLUSTER	**Andalusia Bioregion**	**Biobasque**	**Biocat**	**Madrid Biocluster**	**Bioval**
CORE MANAGEMENT INDEPENDENT ORGANIZATION	None	Yes	Yes	Yes	None
NUMBER OF EMPLOYEES FULLTIME DEDICATED TO THE CLUSTER AGENCY	None	Very low	High	Very low	Very low
NUMBER OF LEADER BIOTECH FIRMS IN THE CLUSTER	None	Medium	High	High	Very low
ORIENTATION TO COLLABORATION	Only local	Interregional	Regional and International	Local and international	Only local
ORIENTATION TO OPEN INNOVATION	**Andalusia Bioregion**	**Biobasque**	**Biocat**	**Madrid Biocluster**	**Bioval**
NUMBER OF ALLIANCES	Medium	High	High	Low	Medium
DEGREE OF COOPERATION WITH ORGANIZATIONS OUTSIDE THE CLUSTER	Medium	High	Medium	Low	High
DEGREE OF INTERNATIONAL COOPERATION	Low	Low	Medium	Low	Medium
COOPERATION FOR DEVELOPING NEW TECHNOLOGIES (COPATENTS)	Mainly national	Mainly national	Mainly intracluster	Mainly national	Mainly national
COOPERATION FOR KNOWLEDGE GENERATION (COPUBLICATIONS)	Mainly international	Mainly national	Mainly international	Mainly national	Mainly national

Source: Own elaboration.

From Table 10, different patterns in the orientation to open innovation can be observed, in terms of: 1) level of openness; 2) geographic localization of cooperation; and 3) type of output from cooperation. The level of openness comes not only from the number of alliances (Lazzarotti and Manzini, 2009) but can also be considered in terms of the degree of cooperation with organizations outside the cluster (Belussi, Sammarra, and Sedita, 2010). Depending on these two variables, the level of openness can be high, medium or low. The geographic location of cooperation also determines a certain pattern of open innovation. In this sense, some clusters may show a prevalence of local/national vs. international collaboration. Although research on how the geographic distribution of partners determines innovativeness provides contradictory results (Belussi et al., 2010), Dahlander and Mckelvey (2005) state that knowledge involved in biotech must be 'global best'. Finally, the type of output from cooperation is the third element that shapes the pattern of open innovation in the cluster. In this sense, Wanzenböck, Scherngell and Brenner (2014) highlight co-patents and co-publications, as different modes of knowledge creation, which implies different requirements from innovation systems and regions.

As shown in Table 10 and Figure 7, the resulting patterns in each of the five clusters analyzed are the following:

Andalusia BioRegion shows a *medium level of OI*, with a *diversified geographic orientation*, i.e., cooperation in the national context for developing new technologies (co-patents), and international cooperation for generating scientific knowledge (co-publications).

BioBasque presents a *high level of OI*, mainly in a *national context*, with a remarkable orientation to scientific knowledge co-production.

BioCat also shows a *high level of OI* with a *diversified geographic orientation*, i.e., local (intracluster) cooperation for developing new technologies (co-patents), and international cooperation for generating scientific knowledge (co-publications).

Madrid Biocluster shows a *low level of OI*, through cooperation mainly in a *national scope* for both the development of new technologies (co-patents) and the generation of scientific knowledge (co-publications).

BioVal presents a *medium level of OI*, mainly in the *national context*, for both the development of new technologies (co-patents) and the generation of scientific knowledge (co-publications).

Figure 7 shows the intensity of OI in the five studied clusters depending on their geographic orientation. The size of the circles reflects the total amount of patent activity observed within each cluster (see table 8).

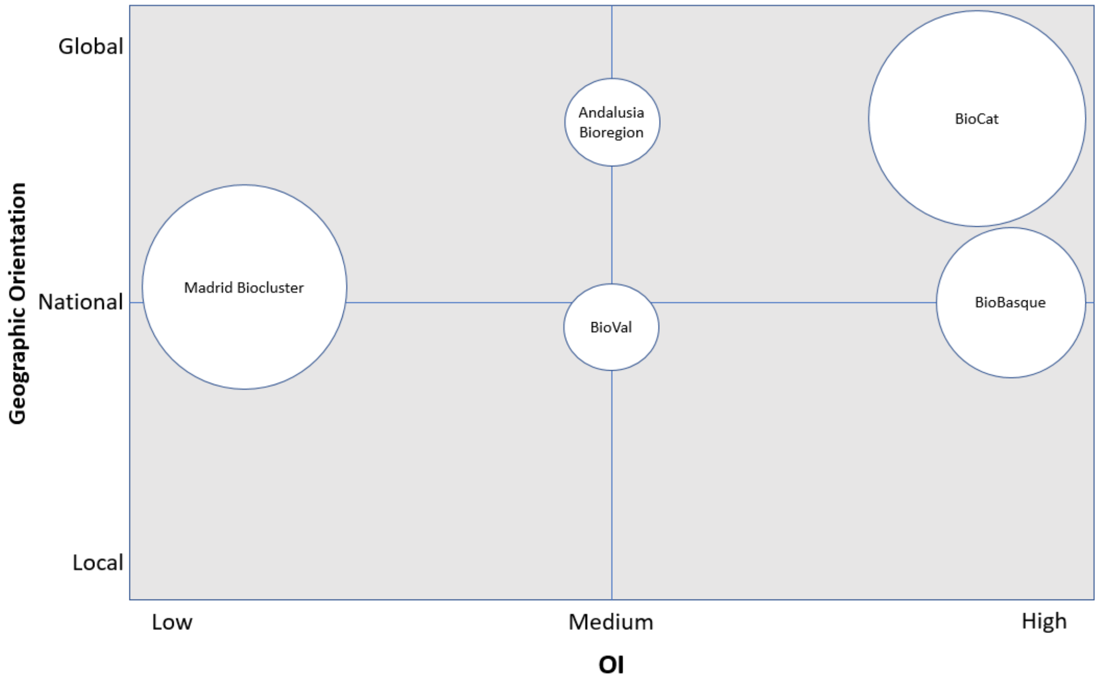

Fig. 7. Patterns of OI in the five biotech Spanish clusters. Source: Own elaboration.

From our case studies on five open innovation ecosystems in the Spanish biotech industry, we can draw a number of conclusions/propositions which enrich the field of cluster analysis and might inform the development of relevant cluster policies.

First, the more *systemic and contextual view* adopted in this study, reveals that open innovation dynamics at the level of the cluster (ecosystem), vary considerable across clusters. This variety becomes visible in terms of scale, texture (public, business actors), orientation (local – international) and scope (science, technology, alliances). These open innovation ecosystems benefit from *regional public policies* promoting cooperation for innovation, but not all the regions are affected by the same policies, and not all the policies are equally effective. Besides, the *implementation of specific cluster policies* is closely connected to the genesis of the cluster and its constituents. The cluster agency is, at the same time, the outcome and the nexus of these cluster policies. Although the specific cluster policies and their implementation through the cluster agency are expected to be the main determinants of the development of the open innovation ecosystem, their contribution may become diluted by other constituents of the regional ecosystem. In this sense, *path dependency processes* seem to play a key role as well, translating into a variety of OI practices across clusters. In fact, different patterns in the *orientation to open innovation* are the result of the conjunction of the elements involved in an innovation ecosystem. We did not observe a single and ideal model of open innovation that applies to all the regions under study.

As such, the presence of this *variety resonates equifinality*; as regions differ in terms of initial textures, different pathways to innovative growth - resulting from localized cluster policies - become a logical consequence.

Second, whereas the above implies a strong plea for a contextualized view on innovation dynamics, the question arises whether and to what extent it is feasible to distill 'best practices' from these five case studies. With Biotech moving into a growth phase, it is still difficult to predict to what extent different regions in Spain will be playing a significant role in terms of biotech on a European/global scale. Besides 'contextualizing' growth paths, additional concerns emerge from our analysis. Chesbrough, Vanhaverbeke, Lopez-Vega and Bakici (2011) suggest that innovation policies have to adapt to increasing globalization and rapid proliferation of open innovation. In addition, the findings of Lecocq and Van Looy (2016) signal positive growth effects of an international orientation (of clusters); as such our findings signal the relevance of paying more attention to cluster policies that enable and stimulate *collaboration beyond the boundaries* of the cluster (national, international).

Third, *the role of universities and public research institutions*, as relevant actors in the regional innovation system, deserves to be highlighted. These actors, as fundamental source of knowledge, can contribute to open innovation dynamics in the ecosystem by acting as a catalyst for private sector development through licensing of technology to the biotechnology industry and promoting the creation of spin-offs. Indeed, the development of the biotechnology industry largely depends on exploiting research results generated in, and transferred from, the public sector. As such, the entrepreneurial orientation of these actors becomes a critical ingredient of cluster dynamics.

Fourth, without contradicting the aforementioned, an exclusive focus on the public part of the innovation system might be detrimental for innovation dynamics once a field enters the growth phase (which is the case for Biotechnology, see a.o. Lecocq and Van Looy, 2016). Our findings reveal that a number of Spanish biotech clusters are still 'dominated' by the public sector (universities and research centers), while the contribution of business and industry remains limited. It is important to recognize the necessity to take the technology to market and to increase the role and contribution of firms and entrepreneurs. Developing initiatives to *foster public-private partnerships* can be an effective stepping stone in this respect; the same applies for sustained, adequate public and private budgets for R&D as well as an improved uptake of European funds. Fostering relationships between university, industry and administration is not only justified theoretically but also economically, favoring allocation of budget items, developing driving initiatives and strengthening commitments. In this respect, the concept of 'innovation systems' has gained widespread acceptance and has been used as a general framework for designing innovation policies and adequate institutional arrangements in order to support growth objectives in new, knowledge-intensive economic activities (OECD, 1999). Although it is assumed that open innovation contributes to sustainable regional development, (local) *efforts are equally required* by biotech entrepreneurial firms, larger incumbents, universities and research institutions as well as regional governments. These efforts should be oriented *to facilitate interactions*, to build knowledge capabilities and a strong infrastructure, to attract human capital, and to develop a socio-cultural environment by combining a strong regional identity with openness for external developments (Tödtling et al, 2011). Therefore, initiatives of policy makers for developing biotech regions should be consistent with this approach. The Spanish regional governments have to be aware of the important role they can play in the development of their regions, and the promotion of interconnections between all actors must be based on real market needs resulting in a higher level of innovation performance and progress in technological achievements.

Whereas these reflections have implications for policy makers across regions, our analysis especially reveals that regions are characterized by divergent conditions. As such, cluster development will always be a path dependent (He, Rayman-Bacchus and Wu, 2011) and contextualized process. Thus, region-specific solutions and policies are required that account for differences and reflect the local texture. Besides, the impact of these policies in every context should be evaluated. This message is conveyed in a number of studies (Tödtling and Trippl, 2005; Gertler and Vinodrai 2009; Asheim et al., 2011; Ahonen and Hamalainen, 2012; Mastroeni, Tait and Rosiello, 2013; Lecocq and Van Looy, 2016): there is no one-size-fits-all approach to regional economic development, including the policy part thereof. Policy instruments should be coherent with the chosen objectives, appropriate for the regional actors and capabilities, and flexible enough to evolve over time (implying ongoing monitoring, feedback and policy learning).

In conclusion, under the umbrella of the open innovation ecosystem approach, our discussion speaks to the research on biotechnology clusters including its policies addressed to foster knowledge creation and transfer in knowledge-intensive industries in a contextualized, path dependent manner. Our research reveals that local, path dependent dynamics, result in different patterns of open innovation (practices) in biotech regions.

References

Acs, Z.J., and Varga, A. (2002). Introduction to the special issue on regional innovation systems. Int. Reg. Sci. Rev. 25 (1), 3-7.

Adner, Ron. (2006). Match your innovation strategy to your innovation ecosystem. Harv. Bus. Rev. 84 (4), 98-107.

Adner, R. and Kapoor, R. (2010). Value Creation in Innovation Ecosystems: How the Structure of Technological Interdependence Affects Firm Performance in New Technology Generations. Strateg. Manag. J. 31 (3), 306–333.

Ahlqvist, T. (2014). Building Innovation Excellence of World Class: The Cluster as an Instrument of Spatial Governance in the European Union. Int. J. Urban. Reg. Res. 38 (5), 1712-1731.

Ahonen, L. and Hamalainen, T. 2012. CLIQ: A practical approach to the quadruple helix and more open innovation. In: Macgregor and Carleton, T. Sustaining innovation. Collaboration models in a complex world. Springer.

Arikan, Andaç T. (2009). Interfirm Knowledge Exchanges and the Knowledge Creation Capability of Clusters. Acad. Manage. Rev. 34 (4), 658-676.

Arrow, K.J. (1962). The implications of Learning by Doing. Review of economic studies 29, 155-173.

Artz, G.M., Y. Kim, and P.F. Orazem. (2016). Does agglomeration matter everywhere?: New firm location decisions in rural and urban markets. J. Reg. Sci. 56 (1), 72-95.

ASEBIO. Informe Anual 2013. Situación y tendencias del sector de la biotecnología en España.

Asheim, B.T. and Coenen, L. (2005). Knowledge bases and regional innovation systems: Comparing Nordic clusters. Res. Policy 34, 1173–1190.

Asheim, B.T., Boschma, R. and Cooke, P. (2011). Constructing Regional Advantage: Platform Policies Based on Related Variety and Differentiated Knowledge Bases. Reg. Stud. 45 (7), 893-904.

Bathelt, H., Malmberg, A., and Maskell, P. (2004). Clusters and knowledge: local buzz, global pipelines and the process of knowledge creation. Prog. Hum. Geogr. 28 (1), 31-56.

Belussi, F., Sammarra, A., and Sedita, S. R. (2010). Learning at the boundaries in an “Open Regional Innovation System”: A focus on firms’ innovation strategies in the Emilia Romagna life science industry. Res. Policy 39, 710–721.

Bogers, M., Zobel, A., Afuah, A., Almirall, E., Brunswicker, S., Dahlander, L., Frederiksen, L., Gawer, A., Gruber, M., Haefliger, S., Hagedoorn, J., Hilgers, D., Laursen, K., Magnusson, M.G., Majchrzak, A., McCarthy, I.P., Moeslein, K.M., Nambisan, S., Piller, F.T., Radziwon, A., Rossi-Lamastra, C., Sims, J. and Ter Wal, A.L.J. (2016). The open innovation research landscape: established perspectives and emerging themes across different levels of analysis. Ind. Innov. 24 (1), 8-40.

Bogers, M., Chesbrough, H. and Moedas, C. (2018). Open Innovation: Research, Practices, and Policies. Calif. Manage. Rev. 60 (2), 5-16.

Borras, S. & Jordan, J. (2016.) When regional innovation policies meet policy rationales and evidence: a plea for policy analysis. Eur. Plan. Stud. 24 (12), 2133-2153.

Boschma, R., and D. Fornahl. (2011). Cluster evolution and a roadmap for future research. Reg. Stud. 45 (10), 1295-1298.

Braczyk, H.J., Cooke, P., Heidenreich, M. (Eds.), 1998. Regional Innovation Systems. University College London (UCL Press), London.

Capello, R., & Lenzi, C. (Eds.) 2013. Territorial patterns of innovation. An inquiry on the knowledge economy of European regions (pp. 70–92). London: Routledge.

Carayannis, E.G., Barth, T.D. and Campbell, D. F. (2012). The Quintuple Helix innovation model: global warming as a challenge and driver for innovation. J. Innov. Entrep. 1(1), 1-12.

Chesbrough, Henry W. 2003. Open innovation: The new imperative for creating and profiting from technology: Harvard Business Press.

Chesbrough, Henry W. 2006. Open innovation: The new imperative for creating and profiting from technology: Harvard Business Press.

Chesbrough, H., Vanhaverbeke, W., Lopez-Vega, H. and Bakici, T. 2011. Open innovation and public policy in Europe. A research report commissioned by: ESADE Business School & the Science I Business Innovation Board AISBL. Science-Business Publishing Ltd.

Chesbrough, H. and Bogers, M. 2014. Explicating open innovation: clarifying an emerging paradigm for understanding innovation. In: Chesbrough, H., Vanhaverbeke, W., West, J. (Eds.), New Frontiers in Open Innovation. Oxford University Press, Oxford.

Chesbrough, H., Kim, S., Agogino, A., (2014). Chez Panisse: building an open innovation ecosystem. Calif. Manage. Rev. 56 (4), 144–171.

Cooke, P., Uranga, M., and Etxebarria, G. (1997). Regional innovation systems: Institutional and organizational dimensions. Res. Policy 26 (4-5), 475-491.

Cooke, P. (2001). Regional innovation systems, clusters, and the knowledge economy. Ind. Corp. Change 10 (4), 945-974.

Cooke, Philip (2004). Life Sciences Clusters and Regional Science Policy. Urban Stud. 41 (5/6), 1113-1131.

Cooke, P. (2005). Regional knowledge capabilities and open innovation: Regional innovation systems and clusters in the asymmetric knowledge economy. In S. Breschi, & F. Malerba (Eds.), Clusters, Networks & Innovation: 80–112. Oxford University Press Inc, New York.

Cruz, S.C.S. and Teixeira, A.A.C. (2010). The evolution of the cluster literature: Shedding light on the regional studies-regional science debate. Reg. Stud. 44 (9), 1263-1288.

Dahlander, L. and Mckelvey, M. (2005). The occurrence and spatial distribution of collaboration: Biotech firms in Gothenburg, Sweden. Technol. Anal. Strateg. 17, 409-431.

Delgado, M., M.E. Porter, and S. Stern. (2014). Clusters, convergence, and economic performance. Res. Policy 43 (10), 1785-1799.

Enright, M.J. (1998). Regional clusters and firm strategy. In A.D. Chandler Jr., P. Hagström & Ö. Sölvell (eds.), The dynamic firm: The role of technology, strategy, organization, and regions (pp. 315-342). Oxford: Oxford University Press.

Etzkowitz, H. and L. Leydesdorff (2000). The Dynamics of Innovation: From National Systems and 'Mode 2' to a Triple Helix of University-Industry-Government Relations. Res. Policy 29 (2), 109-123.

Etzkowitz, H., and Leydesdorff, L. (1998). The endless transition: A 'triple helix' of university-industry-government relations. Minerva 36, 203-208.

Feldman, M. P., and J. L. Francis. (2003). Fortune Favours the Prepared Region: The Case of Entrepreneurship and the Capitol Region Biotechnology Cluster. Eur. Plan. Stud. 11(7), 765-788.

Fundación Genoma España. Relevancia de la Biotecnología en España 2011.

Garone, L.F., A. Maffioli, J.A. de Negri, C.M. Rodriguez, and G. Vázquez-Baré. (2015). Cluster development policy, SME's performance, and spillovers: evidence from Brazil. Small Bus. Econ. 44 (4), 925-948.

Gertler, M.S. and Vinodrai, T. (2009). Life Sciences and Regional Innovation: One Path or Many? Eur. Plan. Stud. 17 (2), 235-261.

Gilbert, B.A., P.P. McDougall, and D.B. Audretsch. (2008). Clusters, knowledge spillovers and new venture performance: An empirical examination." J. Bus. Ventur 23 (4), 405-422.

Gomes, L.A.V., Figueiredo Facin, A.L., Salerno, M.S. and Kazuo Ikenami, R. (2016). Unpacking the innovation ecosystem construct: Evolution, gaps and trends, Technol. Forecast. Soc. Change, in press, 1-19.

Gordon, I.R. and McCann, P. (2010). Industrial clusters: Complexes, agglomeration and/or social networks? Urban Stud. 37 (3), 513-532.

de Jong, J.P.J., Kalvet, T. and Vanhaverbeke, W. (2010). Exploring a theoretical framework to structure the public policy implications of open innovation. Technol. Anal. Strateg. Manag. 22 (8), 877-896.

He, Z., Rayman-Bacchus, L., & Wu, Y. (2011). Self-organization of industrial clustering in a transition economy: A proposed framework and case study evidence from China. Res. Policy 40(9), 1280–1294.

Huizingh, E.K.R.E. (2011). Open innovation: State of the art and future perspectives. Technovation 31 (1), 2-9.

Huxham, Chris, Vangen, S. and C. Eden. (2000). The challenge of collaborative governance. Public Manag. Rev. 2, 337–58.

Ingstrup, M.B. (2010). The role of cluster facilitators. International Journal of Globalisation and Small Business 4 (1), 25-40.

Ingstrup, Mads Bruun (2013). Facilitating Different Types of Clusters. Management Revue 24 (2), 133-150.

Jacobs, J. (1969). The economies of cities. New York: Vintage.

Larty, J. Jack, S. and Lockett, N. (2016). Building regions: a resource-based view of a policy-led knowledge exchange network. Reg. Stud. 51 (7), 994-1007.

Lazzarotti, V., Manzini, R. (2009). Different modes of open innovation: a theoretical framework and an empirical study, Int. J. of Innov. Manag. 13 (4), 615–636.

Lechner, C., and C. Leyronas. (2012). The competitive advantage of cluster firms: the priority of regional network position over extra-regional networks–a study of a French high-tech cluster. Entrep. Region. Dev. 24 (5-6), 457-473.

Lecocq, C. and Van Looy, B. (2009). The impact of collaboration on the technological performance of regions: time invariant or driven by life cycle dynamics? An explorative investigation of European regions in the field of biotechnology. Scientometrics 80 (3), 845-865.

Lecocq C., Leten B., Kusters J. and Van Looy B. (2012). Do firms benefit from being present in multiple technology clusters? An assessment of the technological performance of biopharmaceutical firms. Reg. Stud. 46 (9), 1107-1119.

Lecocq C. and Van Looy B. (2016). What Differentiates Top Regions in the Field of Biotechnology? An empirical Study of the Texture Characteristics of 101 Biotech Regions in North-America, Europe and Asia-Pacific. Ind. Corp. Change 25 (4), 671–688.

Leydesdorff, L. and Etzkowitz, H. (1996). Emergence of a triple helix of university-industry-government relations. Sci. Public Policy 23, 279-286.

Lundvall, B.A. (Eds), (1992). National Systems of Innovation. F. Pinter, London.

Marshall, A. (1920). Industry and trade. London: Macmillan.

Martin, R. and Sunley, P. (2003). Deconstructing Clusters: Chaotic Concept or Policy Panacea. J. Econ. Geogr. 3, 5-35.

Maskell, P. (2001). Towards a Knowledge-based Theory of the Geographical Cluster. Ind. Corp. Change 10 (4), 921–943.

Mastroeni, M., Tait, J. and Rosiello, A. (2013). Regional innovation policies in a globally connected environment. Sci. Public Policy 40 (1), 8–16.

McCann, Brian T. and Folta, Timothy B. (2011). Performance differentials within geographic clusters. J. Bus. Ventur. 26, 104-123.

Nelson, R. 1993: National Systems of Innovation. Oxford University Press, UK.

Nishimura, J., and H. Okamuro. (2011). R&D productivity and the organization of cluster policy: An empirical evaluation of the Industrial Cluster Project in Japan. J. Technol. Transf. 36 (2), 117-144.

Numprasertchai, S., and B. Igel (2005). Managing Knowledge trough collaboration: multiple case studies of managing research in university laboratories in Thailand. Technovation 25, 1173-1182.

OECD 1999. Managing National Systems of Innovation.

Okamuro, H. and Nishimura, J. (2015). Local Management of National Cluster Policies: Comparative Case Studies of Japanese, German, and French Biotechnology Clusters. Adm. Sci. 5, 213-239.

Oksanen, K., and Hautamaki, A., (2014). “Transforming regions into innovation ecosystems : A model for renewing local industrial structures.” The Innovation Journal: The Public Sector Innovation Journal 19 (2): 1–16.

Papaioannou, T., Wield, D., and Chataway, J. (2007). “Knowledge ecologies and ecosystems? An empirically grounded reflection on recent developments in innovation systems theory.” In 6th International Triple Helix Conference on University-Government-Industry Relations.

Porter. M. E. 1990. The competitive advantage of nations. London: Macmillan.

Porter. M. E. (2000). Location, Competition, and Economic Development: Local Clusters in a Global Economy. Econ. Dev. Q. 14 (1), 15-34.

Porter, M. and Ketels, C. 2009. "Clusters and Industrial Districts: Common Roots, Different Perspectives," Chapters in: A Handbook of Industrial Districts, chapter 14 Edward Elgar Publishing.

RIM Plus Repository, European Commission, 2014

Ritala, P., Agouridas, V., Assimakopoulos, D., and Gies, O. (2013). Value creation and capture mechanisms in innovation ecosystems: a comparative case study. Int. J. Technol. Manag. 63 (3/4), 244–267.

Romer, P.M. (1986). Increasing returns and long-run growth. Journal of Political Economy 94 (5), 1002-1037.

Santos, A.B., and Mendonça, S. 2017. Open innovation in clusters: The Portuguese case, In S. Monteiro & E. Carayannis, The Quadruple Innovation Helix Nexus: A Smart Growth Model, Quantitative Empirical Validation and Operationalization for OECD Countries: 245-264. Palgrave MacMillan.

Sanz-Menéndez, L. & Cruz-Castro, L. (2005). Explaining the science and technology policies of regional governments. Reg. Stud. 39 (7), 939–954.

Simard, C. and West, J. (2006).Knowledge network and geographic locus of innovation. In H. Chesbrough, W. Vanhaverbeke, & J. West (Eds.), Open Innovation: Researching a New Paradigm. Oxford University Press, Oxford.

Tallman, S., Jenkins, M., Henry, N. and Pinch, S. (2004). Knowledge, clusters and competitive advantage. Acad. Manage. Rev. 29, 258-271.

Tödtling, F. and Trippl, M. (2005). One size fits all? Towards a differentiated regional innovation policy research? Res. Policy 34(8), 1203–1219.

Tödtling, F., van Reine, P. P. Homme, and Dörhöfer, S. (2011). Open Innovation and Regional Culture-Findings from Different Industrial and Regional Settings. Eur. Plan. Stud. 19 (11), 1885–1907.

Trippl, M., Grillitsch, M., Isaksen, A. and Sinozic, T. (2015) Perspectives on Cluster Evolution: Critical Review and Future Research Issues, Eur. Plan. Stud. 23 (10), 2028-2044.

Uyarra, E. and Ramlogan, R. (2012). The Effects of Cluster Policy on Innovation: Compendium of Evidence on the Effectiveness of Innovation Policy Intervention. Manchester. University of Manchester, http://www.fteval.at/upload/The_Effects_of_Cluster_Polidy_on_Innovation.pdf.

Valkokari, K. (2015). Business, Innovation, and Knowledge Ecosystems: How They Differ and How to Survive and Thrive within Them. Technol. Innov. Manag. Rev. 5 (8), 17–24.

Van Looy, B, Debackere, K. and Andries, P. (2003). Policies to stimulate regional innovation capabilities via university-industry collaboration: an analysis and an assessment. R&D Management 33 (2): 209-229.

Vanhaverbeke, W. (2006), The Interorganizational Context of Open Innovation, In: Chesbrough, H., W. Vanhaverbeke & J. West (eds), Open Innovation: Research a new paradigm, Oxford: Oxford University Press, p. 205-219.

Vicente, J. 2014. “Don’t throw the baby out with the bath water”. Network failures and policy challenges for cluster long run dynamics. Papers in Evolutionary Economic Geography (PEEG) 1420, Utrecht University, Department of Human Geography and Spatial Planning, Group Economic Geography.

Wallner, T., and Menrad, M. 2011. “Extending the Innovation Ecosystem Framework.” Proceedings of the XXII ISPIM Conference, 12.-15. Juni, Hamburg, Hamburg, Germany.

Wang, P. 2009. “An Integrative Framework for Understanding the Innovation Ecosystem.” In Proceedings of the Conference on Advancing the Study of Innovation and Globalization in Organizations, Nuremberg, Germany.

Wanzenböck, I., Scherngell, T. and Brenner, T. (2014). Embeddedness of regions in European knowledge networks: a comparative analysis of inter-regional R&D collaborations, co-patents and co-publications. Ann. Reg. Sci. 53 (2), 337–368.

Weber, M.L., and Hine, M.J. (2015). Who Inhabits a Business Ecosystem? The Technospecies as a Unifying Concept. Technol. Innov. Manag. Rev. 5 (5), 31–44.

Werker, C. (2006). An Assessment of the Regional Innovation Policy by the European Union based on Bibliometrical Analysis. Max Planck Institute of Economics, Evolutionary Economics Group, http://EconPapers.repec.org/RePEc:esi:evopap:2006-11.

West, J. and Bogers, M. (2014). Leveraging External Sources of Innovation: A Review of Research on Open Innovation. J. Prod. Innov. Manage. 31 (4), 814–831.

West, J., Vanhaverbeke, W. and Chesbrough, H. (2006).Open innovation: A research agenda. In H. Chesbrough, W. Vanhaverbeke, & J. West (Eds.), Open Innovation: Researching a New Paradigm. Oxford University Press, Oxford.

Yagüe-Perales, RM, Niosi, J and March-Chorda, I (2015) Benchmarking biotechnology industries: A comparative perspective. Int. Entrep. and Manag. J. 11: 19-38.

Yin, R.K. 1994. Case study research: Designs and methods. London: Sage Publications.

Youtie, J. and Shapira, P. (2008). Building an Innovation Hub: A Case Study of the Transformation of University Roles in Regional Technological and Economic Development. Res. Policy 37, 1188-1204.

Yu, J. and Jackson, R. (2011). Regional Innovation Clusters: A Critical Review. Growth Change 42, 111–124.