

Localized networks and innovation in the life-science sector. Inter-cluster and intra-cluster dynamics

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Localized networks and innovation in the life-science sector.

Inter-cluster and intra-cluster dynamics

Abstract- The paper investigates the impact of clusters, or localized networks involving industrial, academic and institutional players, in the life-science setting and aims to enrich the line of inquiry into cluster-based innovation by applying a social network analysis (SNA) approach. The cluster concept has been defined in ambiguous ways, corresponding to a large variety of spatial and organizational concrete configurations. We try to understand which of these configurations - i.e. what structural and nodal network characteristics of the cluster - are best suited to maximize the likelihood of clusters' innovation, from an intra-cluster and inter-cluster perspective. Quantitative methods are applied to relational and nodal data, using SNA and a regression model. The work sheds light on the factors that give rise to differential innovative outcomes across different clusters.

1. Introduction

Innovation has been proven to be an interactive, cumulative, and cooperative phenomenon (Ahuja, 2000; Burt, 2004; Powell et al., 1996; Zaheer & Bell, 2005), requiring the convergence of many sources of knowledge and skills, usually linked through a network (Pyka & Koppers, 2002). Research has highlighted the importance of a network including various types of organizations as the locus of innovation, because the stock of knowledge itself is located in a complex system of interactions among different organizations. Arora and Gambardella (1990), analyzing the biotechnology industry, emphasized the difficulty in identifying a single innovator in a context of increasing multidisciplinary. In fact as the product becomes increasingly modular and knowledge is distributed among organizations (Baldwin & Clark, 2000), collaboration becomes a necessity for new product development, individual organizations do not possess all the knowledge needed to undertake innovation internally and mobilize external actors, with different knowledge bases. R&D networks are typically driven by different incentives: the amount of resources and knowledge needed for

R&D has become overwhelming for a solitary organization; technological and market uncertainties foster the search for new opportunities; performing R&D activities in networks can produce extra value for the participants and for innovation outcomes (DeBresson & Amesse, 1991). From an organizational point of view, not only the managerial components of R&D but also patent, regulatory, and commercial aspects are involved in all R&D stages and spur cooperation among firms (Gianfrate, 2004).

The starting point for the analysis is the assumption that strong links between the production structure and the knowledge and institutional infrastructure in science-based industries are necessary to overcome innovation challenges: innovations could result directly from ongoing interactions among scientific, commercial, educational, and public institutions, in a context of bridging between different worldviews. When business segments require high levels of specialization from multiple contributors (Ghadar et al, 2012), clusters arise.

The aim of the paper is to investigate the impact of the cluster - an aggregation of different players in a localized network (Curzio & Fortis, 2003) - on innovation in the life-science setting. The work tries to enrich the line of inquiry into cluster-based innovation by analyzing which cluster configuration in terms of structure and partner characteristics is most conducive to innovation.

The cluster we analyze involves an industrial player, an academic player and a public player belonging to the government sphere, which, in the life-science sector, typically are comprised of pharmaceutical firms, biotech firms, universities, research centers, and healthcare organizations such as hospitals, clinics, and healthcare institutions linked through an informal or formal arrangement. It can be thought of as a reduced National Innovation System (NIS), in which the functional system's elements help stimulate the emergence of innovations (OECD, 2002). Cluster organizations are extended organizations in the sense that, being part of a broad learning circuit involving the supply chain and local society, they optimize the use of internal intellectual and financial resources and specialize in the performance of narrowly defined functions that cannot be performed in the absence of cluster-type learning (Varaldo & Ferrucci, 1997).

2. Research problem and Research questions

The cluster concept has been defined in ambiguous ways, it is rather flexible, corresponding to a large variety of spatial and organizational concrete configurations. Trying to understand which of them drives to a higher cluster's innovative outcome, we address the following

research question: *What is the impact of intra-cluster and inter-cluster network characteristics on the cluster's innovative performance in the life-science sector?*

More specifically we analyze what **structural** and **nodal characteristics** are best suited to maximize clusters' innovation, from an intra-cluster and an inter-cluster perspective: we focus on network size and density/spanning of structural holes as main explanatory variables; on nodal vertical heterogeneity and geographical distance among the nodes, as contingency factors.

The paper can make a theoretical contribution by enriching the literature on cluster dynamics and filling some gaps of the previous works.

There are *no significant contributions that analyze clusters of clusters*, meaning groups of clusters. The study of *inter-cluster dynamics* is an interesting field to explore. Inter-cluster ties are *weak ties*, and the strength of weak ties has been often advocated in the network literature. Despite the vast literature on clusters, *the notion of a cluster remains rather indefinite in its theoretical contours*: a chaotic concept (Martin & Sunley, 2003). This *lack of clarity and conceptualization raises many research questions*. There are no consensual views among scholars on several key issues (e.g., the spatial/geographical boundaries or the properties of the players).

There has been only occasional use of constructs and concepts derived from SNA in analyses on clusters, we try to introduce the social network analysis approach.

Regarding network theory, scholars have been *unable to agree on the form of structures most beneficial for innovation*. There is a fundamental tradeoff between a sparse network (rich in structural holes) and a cohesive network. Whereas the first structure facilitates the generation of ideas and hampers implementation and action, the second one favors implementation but not the generation of ideas. The complementarity of these two structures is clear. We try to solve this tradeoff problem by finding an intermediate solution through the distinction between internal and external networks, that is, intra-cluster and inter-cluster dynamics. Firms in networks benefit from inter-firm resource pooling and cooperation (Uzzi, 1996). The former is achieved through open networks; the latter is achieved through closed networks.

Researchers have stressed the importance of *network structure, thereby undervaluing other dimensions that affect knowledge sharing*. We try to overcome this limit by adopting a contingent approach. The *contingency factors* analyzed are the network knowledge base (expressed by the range of diverse nodes composing the network, meaning a heterogeneous knowledge base) and the network nodes localization (expressed by the geographic distance among the network nodes).

The existing literature has focused on the impact of collaborations on the innovative performance of focal firms, but scarce attention has been paid to the overall network performance (Zollo et al., 2002). It would be interesting to consider in our predictions the *network's overall performance* as a dependent, aggregated variable to analyze the efficacy of the research network as a whole.

The paper's topic is relevant and grounded in reality because the cooperative options are widespread¹ and the new systemic dimensions of technology and research, the interdisciplinary knowledge and the interdependence of productive processes led to cooperation and division of labor in R&D (Goransson & Palsson, 2011).

2. Conceptual framework and Literature

To examine the research problem, we can refer to literature on strategic alliances, networks, and especially clusters, on the Triple Helix model for innovation and on system innovation perspectives.

A. Strategic Alliances

Strategic alliances are considered an integral component of a firm's strategy to shorten the development time while spreading the risks and costs associated with product development (Powell, 1990). One perspective explaining the benefits of strategic alliances for innovation, which is also the impetus of our contribution, is the resource dependence theory (RDT), which proposes that the key to organizational survival is the ability to acquire and maintain resources rather than to make profit. RDT treats the environment as a source of scarce resources and therefore views the firm as dependent on other firms in the same environment. When organizations have similar objectives but different kinds of resources, the exchange of resources will often be mutually beneficial to the organizations in the pursuit of their goals.

The basic conclusion from strategic alliance literature is that the *causal relationship between alliances and new product development depends on the type of alliances*, in which *type* refers both to the alliance's organizational form and the partners' characteristics. In fact, *partner selection* emerges as one of the most influential factors affecting an alliance's success (Shah & Swaminathan, 2008). Several contributions have built on the organizational learning literature to examine the factors that facilitate knowledge transfer among partner firms and have identified partner-specific variables, the characteristics of the collaborating firms, such

¹ Cases of common knowledge are the UK, where there are 56 innovative clusters but particularly important are those of Cambridge (with 28 colleges, 370 hi-tech firms) and Edinburgh; Route 128 in Boston around MIT; Silicon Valley. Clusters diffusion is above the average in Finland, Germany, Sweden, Uk, US, Japan.

as absorptive capacity, prior experience, and cultural and geographical distance (Cohen & Levinthal, 1990; Malmberg & Maskell, 2005; Pisano et al., 1988).

B. Networks

Studies that examine the consequences of networks² typically follow the structuralist perspective. It focuses on the configuration of the ties, analysing how actors in networks influence each other's attitudes and behaviors and concluding that an actor's payoff is a function of network structure and of its position in the network.

The literature suggests that a firm's network of relationships influences its rate of innovation and R&D (Ahuja, 2000; Podolny, 2001; Shan et al., 1994), often highlighting the benefits of networking. Networks allow knowledge sharing (knowledge, skills, physical assets) and knowledge flows (information conduits about technical breakthroughs and new insights) (Ahuja, 2000).

Scholars supported competing school of thoughts and 2 trade-offs are still in place: the first one is between the benefits of *strong* (Krackhardt, 1992; Nelson, 1989) versus *weak* (Granovetter, 1973) ties (that are likely to be bridges), the second one is between the benefits of *disconnected* network structure (Burt, 1992) versus *dense* network structure (Coleman, 1988; Walker et al., 1997). The question is whether network positions associated with the highest economic return lie between or within dense regions of relationships.

Despite the considerable focus on the role of network structure in explaining firm performance outcomes, some researchers have acknowledged that a network of ties merely gives the focal firm the potential to access the resources of its contacts (Portes, 1998). Contingencies need to be introduced, such as nodal heterogeneity (Galaskiewicz & Zaheer, 1990).

C. Clusters

The concept of a network is more general than that of cluster and does not necessarily entail local embedding, a shared objective, or a specific market (Nooteboom, 2004). The cluster concept has been defined in ambiguous ways. The full range of cluster definitions falls under two main lines of conception: (a) Porter's (2000) definition: "*a geographically proximate group of inter-connected companies and associated institutions in a particular field, linked by commonalities and complementarities*", (b) OECD (2002) definition: "*networks of production of strongly interdependent firms, knowledge producing agents (universities, research institutes, engineering companies), bridging institutions (brokers, consultants) and customers, linked to each other in a value-adding production chain*", a mainly reticular conception of

² A form of organized economic activity that involves a set of nodes (e.g., individuals or organizations) linked by a set of relationships.

clusters. Contrary to Porter's definition, the OECD approach is not very explicit on the issue of proximity, and it stresses the frequently localized but open nature of clusters: "in most cases they operate within localised geographical areas and interact within larger innovation systems at the regional, national and international level". In the end there is no clarity on the geographical as well as on the sectoral characterization of clusters.

As for the impact of clusters on innovation, Owen-Smith et al. (2002) showed that innovative research in biomedicine has its origins in regional clusters in the United States and in European nations. The success factors of a cluster have been identified with reference to the life-science industry as (a) proximity between university and research institutes and industry, with cross-fertilization and know-how sharing; (b) access to human capital; (c) availability of infrastructures such as facilities and transportation; (d) cultural openness; (e) multidisciplinary and spillovers, with interactions and synergies among disciplines; (f) development of fiscal and financial conditions supporting innovation (Gianfrate, 2004).

Clusters reflect the systemic character of modern interactive innovation and therefore they are related to several conceptual frameworks and models developed under the *Innovation System literature*. In this field, that emphasizes interactions among actors and innovation as a process embedded in a given social context, research has been carried out on sectoral systems (Malerba, 2001), technology systems (Carlsson & Jacobsson, 1997) and regional systems. The frameworks "Mode 1, 2 and 3" of knowledge production trace the evolution from the linear model of innovation to the interactive, non-linear model. We refer to the "Mode 3" of knowledge production, that advocates a system, consisting of innovation networks and knowledge clusters for knowledge creation, diffusion, and use (Carayannis & Campbell, 2006). This is a *multilayered, multimodal, multi-nodal, and multilateral system*, encompassing and reinforcing mutually complementary innovation networks and knowledge clusters characterized by the *coexistence, co-evolution, and co-specialization* of different knowledge paradigms and different knowledge modes of knowledge production.

Another framework is the "Triple Helix" (TH) Model of knowledge, developed by references (Etzkowitz & Leydesdorff, 1998, 2000) that will be theoretically investigated in this paper. It is focused on three helices that intertwine and thus generate a national innovation system: academia/universities, industry, and state/government. Etzkowitz & Leydesdorff spoke of "university-industry-government relations" and networks, also placing a particular emphasis on "tri-lateral networks and hybrid organizations," where those helices overlap and create synergies that result in product and process innovations. This model allows the linking of basic and applied research to the market, via technology transfer and commercialization, in a

setting in which strong, enterprise-supporting infrastructures complement strong, local science bases (Cooke, 2002), challenging the conventional, linear model of interaction. The TH model is based on: (a) the internal transformation in each one of the helices; (b) the influence of one helix upon another.

Universities provide advanced research and a ready supply of human capital in the form of skilled graduates; companies provide real-world problems, commercialization opportunities, and funding; and governmental organizations provide user feedback and regulatory support. In particular the life-science clusters are characterized by: the presence of basic biomedical research by universities and public research institutes; the emergence of entrepreneurial, innovative dedicated biotechnology firms (DBFs) seeking to commercialize the results of the basic research; and the provision of funding, downstream marketing and distribution capabilities from large pharmaceuticals (Wong, 2007).

Many studies analyzed the role of university–industry relationships in triggering new industrial R&D innovative projects (Cohen et al., 2002) and found a positive impact (Cockburn & Henderson, 1998; Lim, 2000).

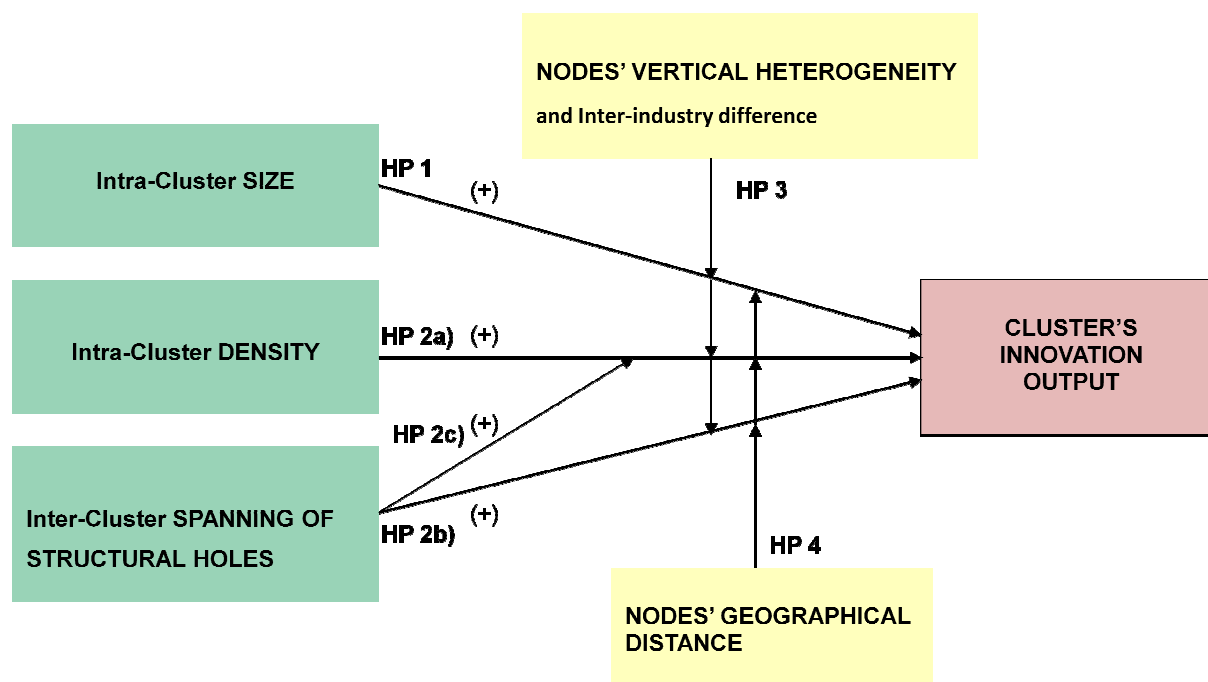
3. Hypotheses development

From the literature review, we can conclude that in the cluster field, two interesting aspects that can be further investigated are network structure and the partners' characteristics. The concept of cluster could correspond to a large variety of spatial, institutional, and organizational concrete configurations, as proposed by reference (Hamdouch, 2007): an innovation cluster *"comprises an ensemble of various organizations and institutions (a) that are defined by respective geographic localizations occurring at variable spatial scales, (b) that interact formally and/or informally through inter-organizational and/or interpersonal regular or more occasional relationships and networks (c) that contribute collectively to the achievement of all kind of innovations within a given industry or domain of activity, i.e. within a domain defined by specific fields of knowledge, competences and technologies."* It involves a wide range of variation and even starting from this definition, it is possible to build around the type of organizations involved, the best spatial scale for geographical localization, the focus on a single industry or domain, and the configuration of the network, as we do in the paper.

Moreover, the literature review shows that for an adequate understanding of clusters, contrasting perspectives and concepts should be combined: (a) the perspectives of learning (theory of knowledge and innovation) and governance (Transaction Costs Economics) (Williamson, 1975) and the concepts of exploration (the discovery and development of novel

ideas) and exploitation (efficient employment of current asset and capabilities, the implementation of the ideas discovered through exploration) (Holland, 1975; March, 1991), both needed for the innovation outcome. These are the general principles to follow in the hypotheses development. As for the specific constructs, we can consider that a fundamental prerequisite for innovation is variety of resources and knowledge (Nelson & Winter, 1982). From a learning perspective, cognitive diversity in a cluster can be summarized in three dimensions: the number of cognitive entities involved in the learning process (size) and connections (density) and the cognitive distances among the nodes, here expressed by partner vertical diversity and geographical distance (Nooteboom, 1999). We will focus on intra-cluster and inter-cluster (i.e., cluster of clusters) dynamics and characteristics. The comprehensive model is shown in figure 1.

Figure 1 - The Model



A. Structural Characteristics

The first aim of the paper is to investigate what structural characteristics of the cluster maximize the cluster's innovations, from an intra-cluster as well as an inter-cluster perspective. We focus on size and density/spanning of structural holes.

1) Size

Size is the basic structural feature of networks (Nooteboom, 2004), it determines the amount of knowledge circulating and spilling over between firms located in a cluster. In a Resource Dependence view, this can be an important predictor of firm performance, leading to reliance

on a higher volume of flows of information and opportunities and a wider pool of product and process technologies during the innovation process.

As shown in Nobeoka et al. (2002), there is a positive relationship between the number of contacts of a node and a node's knowledge, if the innovative performance of each node increases, the overall cluster innovative performance will increase too.

Wider networks promote innovation indirectly by facilitating (a) increased specialization and division of labor which leads to more focused expertise development (Saxenian, 1991), (b) the scale effect (increases in inputs are rewarded with more than proportionate increases in output) that affects the transformation function f of the innovation function, and (c) a leverage effect, given that each node in a cluster is part of other networks of different kinds.

Therefore, we can formulate the following hypothesis.

HP1: *The larger the size³ of the life-science cluster, the higher the cluster's innovative performance.*

2) *Density/Structural Holes*

Despite the growing awareness that networks matter, the effects of specific elements of network structure on innovation remain ambiguous. This is the case of density (the number of the effective ties divided by the number of possible ties). There is a tension between two schools of thought about which network structure creates innovation: one supporting dense network structure (Coleman, 1988), the other sustaining sparse network structure (Burt, 1992). The absence of density results in the presence of many structural holes⁴.

A dense innovative cluster provides benefits both from the learning perspective (quick transmission of information, communication channels and pathways among actors, triangulation, intense interaction and integration, transfer of tacit, embedded knowledge, mutual understanding, coordinated action) (Zander & Kogut, 1995) and from the governance perspective (lower transaction costs and barriers to resource mobilization, competitive practices, opportunism, risks; higher trust, reciprocity norms, shared identity). These conditions favour the *exploitation* component of innovation.

However in a dense cluster over time, the knowledge overlap between cluster organizations will increase (Pouder & St.John, 1996), the only way to compensate for this trend is to increase the cluster firms' knowledge exchanges with outside entities. The presence of structural holes spanned between a cluster and other clusters determines the extent to which

³ number of nodes

⁴ A structural hole exists between the brokered actors, if the actors share a tie with ego but are not connected to each other (Burt, 1992).

the cluster's knowledge base is continuously rejuvenated through knowledge inputs from outside the cluster (Dandi et al, 2006).

In fact, brokerage - the presence of structural holes - allows the detection and the development of new ideas from remote parts of the network synthesized across disconnected pools of information, diverse experiences, and novel combinations and re-combinations of ideas. These conditions favour the *exploration* component of innovation.

The question of **how firms can better maintain the balance of exploration and exploitation** remains unresolved (Fang et al., 2010). Recent research has suggested the possibility of using organizations structure to meet this aim (Jacobides, 2007). In different fields, from evolutionary biology to organization literature and network theory, we can find hints suggesting a configuration based on semi-isolated subgroups as a solution that may help strike the balance. In particular, we can combine the organizational learning arguments (March, 2004) with the small-world networks concept. The latter states that when a community of actors is structured into well-defined clusters that are only sparsely connected to each other, this structure can help to create and preserve the requisite variety of knowledge in the broader community (Fang et al., 2010; Uzzi & Spiro, 2005; Yayavaram & Ahuja, 2008). Usually, authors have focused on a single organization, suggesting that it can be broken into subgroups, semiautonomous subunits, we focus instead on inter-cluster dynamics, where the subgroups are the single clusters and the organization can be all the clusters considered together.

In the end, the bridging ties with other clusters allow for outside exploration, with the access to heterogeneous and novel ideas while the high density of clusters allows for effective exploitation of ideas and inside cluster exploration. In fact intra-cluster exploration is a “finalized exploration process”, with a specific innovation outcome, that will shortly result in exploitation and is an exploration process that occurs in a “prearranged systemic way”, a concept that is more similar to exploitation for certain characteristics. Therefore, inside the cluster, the dense structure seems to accomplish both exploration and exploitation aims. This is even more true in the life-science industry considering that the innovation process, is a complex sequence of stages, is a trial-and-error process, with a lot of feedback loops, where continuous shifts from exploration to exploitation as well as the opposite take place.

Therefore, networks that have both clustering and some amount of random linking between them, cluster-spanning bridges, seem the best solution to spur each cluster innovation: the benefits of local transmission and the information scope of cross-cluster connections can be simultaneously achieved.

Since we are focusing on the single cluster's innovation outcome and not on the innovation outcome of the network including all the clusters together, a concern may arise: cross-cluster connections are able to engender an outflow of knowledge and a competition to appropriate the innovation outcomes. However, this seems to be not very relevant: at the exploration stage, the possibilities of exact imitation are reduced; the firm would have to know the exact way to implement the idea, which is difficult; the implementation process is very long and complex, and there would certainly be a first-mover problem.

The hypotheses provide a solution in which dense and sparse configurations co-exist at different scales and levels of the network, this can be defined as a multi-scaled cluster, where at the same time the logic of exploitation may prevail at some spatial scale but the logic of exploration may entail the commitment of some actors in open-ended networks (Hamdouch, 2007).

This is a solution that tries to join also the conception of clusters expressed by Porter (2000) and OECD (2002), as explained in the literature review.

The interaction of the two effects (density and spanning of structural holes) will have the greatest effect on innovation considering that, as stated by reference (Burt, 2000), closure can be a significant factor in realizing the value buried in a structural hole: catching new ideas from outside and effectively implementing them inside the cluster.

We can formulate the following hypotheses, distinguishing between intra-cluster and inter-cluster characteristics.

a) *Intra-cluster characteristic*

HP2a): *The higher the density in the life-science cluster, the higher the cluster's innovative performance.*

b) *Inter-cluster characteristic*

HP2b): *The more the nodes in the life-science cluster span structural holes between the cluster and other clusters, the higher the cluster's innovative performance.*

c) *Intra-cluster and inter-cluster characteristics*

HP2c): *The more the nodes in the life-science cluster span structural holes between the cluster and other clusters, the higher will be the positive impact of density in the life-science cluster on the cluster's innovative performance.*

B. Nodes' Characteristics

The second aim of the paper is to investigate what characteristics of nodes in a cluster maximize the cluster's innovations, from an intra-cluster and an inter-cluster perspective. We focus on nodal vertical heterogeneity, sectoral difference, geographical distance.

1) *Nodal vertical heterogeneity*

Vertical diversity means differences in the nodes' operational contexts in the value chain, it implies the distinction among three categories: horizontal, upstream, or downstream (Bruyaka, 2008). In the specific case of the life-science cluster, the different players that occupy the different roles from downstream to upstream are: pharmaceutical company, biotech firm, university, research institute, institutions. Much of the existing literature on strategic alliances implicitly say that biotechnology firms act as value-added intermediaries between universities and downstream alliance partners. Their role is to facilitate transactions in a number of distinct ways. Here we consider for instance a biotech and a pharmaceutical firms as diverse and two pharmaceutical firms as equal. This kind of diversity seems to be a quite comprehensive measure, since in most cases it implies also resource-based diversity, industry-based diversity, technological diversity, and strategic fit. *Inter-industry difference* is included in that concept of partner vertical diversity (according to our definition). In fact, the definitions of "cluster" in the literature do not establish in a definite way whether the concept of cluster refers to a single or multiple industries; it could be both. In fact, Isaksen & Hauge (2002) defined a cluster as: "*a concentration of interdependent firms within the same or adjacent industrial sectors*".

Alliances between the different organizations could be horizontal (pharma-pharma, biotech-biotech), vertical downstream, vertical upstream. In this sense, we also distinguish between the effects of two forms of alliances: scale (two competitors come together to achieve scale economies) and link (two companies at different points in the value chain link up, thus obtaining synergies).

Referring to the *learning* and the *governance* theoretical perspectives, cognitive distance can represent both an opportunity (i.e., the novelty value of a relation), and a problem (i.e., mutual understanding or absorptive capacity that decreases with diversity, higher transaction costs, coordination difficulties, moral hazard risk) (Nooteboom, 2004; Goerzen & Beamish, 2005). In the end, we can make a distinction between *knowledge development* and *knowledge transfer*. Partner diversity probably favors the first one and disfavors the second one, because it increases the possible number of new recombinations, but adds difficulties to the transfer process. This resembles the exploration/exploitation trade-off: knowledge transfer is more related to exploitation and knowledge development to exploration.

Looking at the empirical works, we can assert that few studies reject the notion that there can be benefits associated with diversity but that these come with a cost; in any case, the findings are mixed. The main empirical findings are the following: reference (Rodan & Galunic, 2004)

found that knowledge heterogeneity in the network was a significant predictor of the node's innovation performance; reference (Nieto & Santamaria, 2007) maintained that innovation can only be achieved by collaborating with enterprises that have different knowledge bases; reference (Watson, 2007) did not find a positive impact of partner diversity on small and medium enterprises' survival. Given the contrasting nature of the previous contributions, it is an interesting subject to investigate; we aim to analyze the effect of diversity in the intra-cluster and inter-cluster context.

In the **intra-cluster setting**, with reference to the context drawn in hypothesis **HP2a**, vertical diversity in the cluster has a positive moderation effect, strengthening the positive impact. This is because it will enhance the *internal exploration* process, favoring Schumpeterian “novel combinations,” while the problem of the absorptive capacity will be counterbalanced by the presence of high connectivity in the cluster. Vertical diversity will also allow the effectiveness of the *exploitation process* that in the life-science industry requires the possession of complementary skills and experience, favoring a division of labor. Moreover, redundancy in a dense network is something that structurally discourages idea generation; this redundancy will be reduced in the presence of nodes' vertical diversity.

As for the **specificities of the life-science industry**, we can point out some important remarks. (a) First, partner diversity is really important to answer the **regulatory requirements**. The life-science R&D process is scheduled as a strict sequence of different stages that will be better performed if they involve different specialized players, covering different roles and responsibilities. Moreover, diversity will better allow feedback loops and support a trial-and-error sequence, typical of life-science industry R&D (Maier & Sedlacek, 2006). (b) Second, vertical diversity in this industry means also **complementarity**. Therefore, a cluster high in vertical diversity implies that firms may specialize in either exploitation or exploration, and seek the other in relations with other organizations with complementary specialization. Also, in the literature, arguments have been made that when firms combine complementary skills, greater innovation results (Glaister, 1996). If partners' vertical diversity implies complementarity, which in turn implies innovation, partners' vertical diversity drives innovation. (c) Third, partner diversity in the life-science industry involves a **related knowledge background**: players act in subsequent phases of the same macro-process, and thus it is possible to suppose that they own the same background in terms of basic skills, shared language, and knowledge of the most recent scientific or technological developments; techno-organizational systems (TOS), molecules, and drugs (Okba & Figueiredo, 2007). This reduces the concern of absence of absorptive capacity.

In the **Inter-cluster setting**, with reference to hypothesis **HP2b**, there is a node of the cluster that is spanning a structural hole between the cluster and other clusters. The link connecting cluster to cluster should be a weak tie, in a sparse configuration, and **the problem of absorptive capacity is higher than in the intra-cluster case** because the two extreme nodes are gatekeepers. If learning performance from interaction is the mathematical product of novelty value and understandability, the result is an inverted-U shape relation with cognitive distance. Optimal cognitive distance lies at the maximum of the curve (Nooteboom, 2004).

The low level of vertical diversity implies redundancy in resources (Burt, 1992) and knowledge, turning core capabilities in core rigidities (the addition of similar capabilities does not increase innovation, since possible new combinations of existing capabilities quickly become exhausted). It may involve inter-firm rivalry, as the partners may compete in the same industry. This implies that the partners may not be willing to transfer knowledge and also there will be a higher risk for negative spillovers.

With a high level of vertical diversity exposure to diverse industries and technologies may provide firms with valuable learning opportunities (Teece et al., 1997). However, beyond a point there will be decreasing returns to learning (March, 1991). Too-high diversity may suggest that firms will have too little in common to offer each other cooperative benefits; the collaborative opportunities may be difficult to pursue, because the partners will experience high costs of sharing and transferring knowledge (Kogut & Zander, 1992; Lane & Lubatkin, 1998) and low absorptive capacity.

Based on the previous framework, we can desume that a moderate level of partner diversity (e.g., between biotech and pharmaceutical firms) is ideal: it contributes more to firm innovation than does a very low or very high level of diversity, partners have a sustainable level of transaction costs and competition and a good level of complementarity and absorptive capacity. Partner capabilities are diverse, creating a large number of possible combinations, but not so diverse so as to prevent efficient assimilation.

We can formulate the following hypotheses.

a) *Intra-cluster characteristic*

HP3a): The nodes' vertical diversity in the life-science cluster positively moderates the impact of size and density on the cluster's innovative performance.

The higher the level of nodes' vertical diversity in the cluster, the higher the positive impact of size and density on the cluster's innovative performance.

b) *Inter-cluster characteristic*

HP3b): *The vertical diversity between the two nodes spanning an inter-cluster structural hole moderates the impact of the inter-cluster spanning of structural hole on the cluster's innovative performance with an inverted U-shaped pattern.*

A too-low level and a too-high level of vertical diversity between the two nodes spanning the inter-cluster structural hole reduce the positive impact of the inter-cluster spanning of structural hole on the cluster's innovative performance.

A moderate level of vertical diversity between the two nodes spanning the inter-cluster structural hole enhances the positive impact of the inter-cluster spanning of structural hole on the cluster's innovative performance.

2) *Geographical distance*

The second contingency analyzed is nodes' geographical distance in the cluster and in the inter-cluster setting.

With the theory of clustering and the new "economic geography" (Krugman & Venables, 1996), economic theory took a closer look at the territory. However, as mentioned in the literature review section, there is still a significant lack of clarity about the spatial definition of clusters, on whether local embedding and geographical proximity should be retained as defining characteristics of clusters. Should the cluster be local or can it be trans-local?

Apart from the ambiguity in the definition of the concept, we will investigate whether geography matters and determine the impact of nodes' geographical distance in favoring a cluster's innovation process. We are trying to apply what in the firm context would be the definitions of the optimal boundaries of a firm, in the cluster context. The question is motivated by the consideration that there are some elements or theories that support localization and proximity and others that are in favor of a wider geographical extension, all related to the *learning or governance* approach.

As for the factors supporting geography proximity, we can mention the following: (a) geographical concentration reduces transaction costs and favors the development of the relational dimension between different players; (b) sometimes the process of drug development is location-specific because the drugs are differentiated from country to country, for the epidemiological characteristics of the population; (c) often each geographical area has its own regulatory framework, imposing specific rules to the R&D process and therefore many knowledge exchanges could be unfruitful because ideas cannot be implemented through exploitation in another context; (d) knowledge spillovers often have significant tacit component that remains geographically local, requiring direct interaction (Agrawal, 2001); (e)

regions and agglomerated economies are positive “externality arenas” where long path-dependent histories produce location-specific assets (Maier & Sedlacek, 2006); (f) a regional skills base is cumulative; (g) local specificities (agglomeration economies, sticky knowledge, increases in the local pool of skilled labor, scientific, technical, and commercial spillovers) and local favorable conditions (regulatory opportunities, causes of manufacturing efficiency) can be exploited; (h) wide scope of communication, frequency of interaction, and trust are greatly facilitated by proximity and local embedding (Nooteboom, 2004); and (i) the theory of proximity in the network theory identifies proximity as the main facilitator of knowledge flow (Giustiniano & Bolici, 2012).

On the contrary, the factors supporting geographical distance are next listed: (a) an escape from local embedding may be needed for innovation. Oinas & Malecki (2002) in the study of regional systems of innovation, recognizes the need for linkages outside a region and suggests that it may be better to speak of “spatial systems of innovation,” leaving an open boundary of the concept. (b) Embedding needs not always be tied to location, and may also occur in communities that are to some extent virtual, with communication at a distance. (c) Geographical distance can be fruitfully complemented by frequent meetings to build and maintain a shared focus (Nooteboom, 2004). (d) Too durable, local embedding, particularly when it is cut off from outside contacts, may reduce cognitive distance too much (Nooteboom, 2004). (e) Lock-in can easily arise implying social legitimacy, location-specific investments like facilities, physical asset specificity, institutional embedding: local obligations of loyalty and conformity. (f) The Internet effect weakens the geography effect due to reductions in transaction costs. (g) Recent trends show an increasing tension toward trans-local, disembedded clusters, in the real world as well as in the institutional recommendations, perhaps deriving also from the globalization effect. In the European Commission documents, the need of promoting the cluster of transnational dimension is underlined as a means to increase the level of competitiveness of Europe and to overcome the fragmentation of traditional districts. According to the European Cluster Observatory the bio-pharmaceutical clusters show a high degree of international openness. Recent studies, show that the famous Italian industrial districts are becoming locally disembedded, and are shifting some activities, especially in production, to emerging countries (Boschma & Lambooy, 2002; Zuchella, 2003) drug companies are beginning to invest in Chinese R&D. (h) Finally, trans-local collaboration could provide some arbitrage opportunities with respect to regulatory framework. The performance of R&D networks can be positively or negatively moderated by constraints and opportunities provided by the institutional framework.

In the end, as shown by most cases, clusters may transcend geographical levels (OECD, 2002), they are economic phenomena that operate at various geographical levels. Moreover, during the last decade, there seems to be a widespread perception that if success is to be attained, the THM (Triple Helix Model) is the ideal referential, encompassing the territorial scale. Although localized in a specific space, the activities carried out in a territory, not necessarily originate from that space or have their effects just inside that area.

Inter-cluster relations enrich the range of possibilities. Even within a single cluster, clear international as well as regional or even localized elements can be identified, as was shown in many of the case studies on ICT clusters. Increasingly, national and regional cluster performances are linked to and form part of international value chains (OECD, 2002). Several factors can make advantageous or necessary, to carry out activities of the value chain in other places. Clusters of which all individual elements are to be found in a confined area are the exception rather than the rule. Especially in some industries, it might even be counterintuitive to expect “complete” clusters at the regional or national level, as the relevant knowledge base is strongly internationalized, as in the life-science industry. The life-science industry is in fact an industry with a high degree of international research collaboration. A final element to take into consideration is that we are dealing with a cluster composed of diverse players: universities, firms, public organizations. This means a certain degree of variety is introduced. For instance, while co-location in firm-to-firm collaboration is not found to be an important factor (large pharmaceutical firms have an international orientation), for universities’ and firms’ agreements, the picture is slightly different, as they are likely to engage in local and national collaborations too (McKelvey et al., 2003).

Considering what explained, a better solution for innovation would be a balance between local and non-local players inside the cluster, as well as in the inter-cluster connections. In this configuration, the shared context of a local circuit and the shared context of remote cooperation will be complementary resources (Curzio & Fortis, 2003). This would help in combining exploration and exploitation needs. Therefore, a moderate level of geographical distance will enhance the positive impact of size, density, and structural holes on a cluster’s innovative performance, as stated in the following two hypotheses.

a) *Intra-cluster characteristic*

HP4a): *The geographical distance between the nodes in the life-science cluster moderates the impact of size and density on the cluster’s innovative performance with an inverted U-shaped pattern.*

A too-low level and a too-high level of geographic distance between the nodes in the life-science cluster reduce the positive impact of size and density on the cluster's innovative performance.

A moderate level of geographic distance between the nodes in the life-science cluster enhances the positive impact of size and density on the cluster's innovative performance

b) *Inter-cluster characteristic*

HP4b): *The geographical distance between the two nodes spanning an inter-cluster structural hole moderates the impact of the inter-cluster spanning of structural hole on the cluster's innovative performance with an inverted U-shaped pattern.*

A too-low level and a too-high level of geographic distance between two nodes spanning an inter-cluster structural hole reduce the positive impact of the inter-cluster spanning of structural hole on the cluster's innovative performance

A moderate level of geographic distance between two nodes spanning an inter-cluster structural hole enhances the positive impact of the inter-cluster spanning of structural hole on the cluster's innovative performance.

4. Methods

The sample. The empirical analysis is carried out in the U.S. Life Science Industry. The sample includes 8 Biopharmaceutical Clusters in the U.S. and their firms, which are industrial, academic and institutional organizations. To obtain the final sample the following procedure was followed.

First, a list of all the Biopharmaceutical clusters established in the U.S. was drawn up using the *U.S. Cluster Mapping Database* (from Harvard Business School, a project funded by the U.S. Department of Commerce, Economic Development Administration).

We retrieved the clusters' list for four years: 2007, 2008, 2009, 2010. Second, we identified the nodes composing each cluster (firms, institutions etc) through complementary sources: *U.S. Cluster Mapping Database*, websites, online libraries, newspapers, archival data (official documents, previous studies on clusters). Then, we executed a standardization of the names.

Subsequently, we excluded from the sample a few clusters for which data were not available.

The final sample includes the following 8 clusters (CL): CL1: LifeScience Alley; CL2: Massachusetts Biotechnology Council; CL3: Oregon Bioscience Association, CL4: BIOCOM; CL5: Arizona Bioindustry Association; CL6: Nashville Health Care Council; CL7: North Carolina Biotechnology Center; CL8: Connecticut United for Research Excellence, Inc.

The maximum number of nodes composing each cluster is respectively: 645 in CL1, 590 in CL2, 167 in CL3, 546 in CL4, 232 in CL5, 257 in CL6, 595 in CL7, 92 in CL8.

Data collection. In order to build our dependent variable, we collected patent data for each cluster from the U.S. Cluster Mapping Database. We filtered patent data according to the years and the industry of interest. Afterwards, for the independent and control variables we collected attribute and relational data.

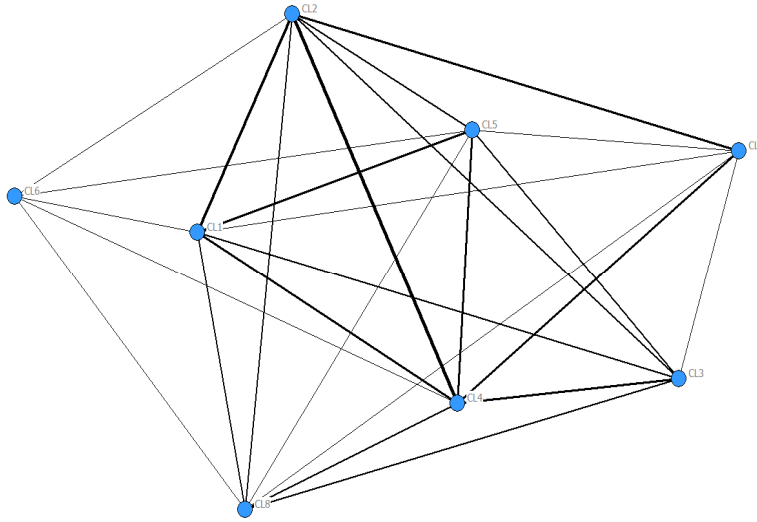
As for the attributes we considered: a) nodal characteristics: for each node in the clusters we identified the type of organization, i.e. the role in the vertical chain, and the geographical location. We obtained different categories for the firm type (e.g. biotechnology, pharmaceutical, academic institution etc.) and the states in which the firms are located. We used the sourced mentioned above; b) the cluster's characteristics: the number of employees and the cluster's specialization (from U.S. Cluster Mapping Database).

As for the relational data, we collected all the transactions and agreements between the nodes of the cluster related to research and development and distinguished intra-cluster from inter-cluster ties. Intra-cluster ties are ties among the nodes belonging to the same cluster, while inter-cluster ties are ties between nodes belonging to different clusters. One node can be simultaneously in different clusters and this is another case of inter-cluster tie (even if the tie will occur between two division of the same firm). To retrieve these data we combined the sources mentioned before with the *SDC Platinum* database, by Thomson Reuters, specifically the *Joint Venture/Strategic Alliances* section that provides substantial archival information on inter-firm agreements and represents one of the most comprehensive and reliable sources used in alliance research (e.g., Anand & Khanna, 2000; Li, Boulding, & Staelin, 2010). Since the focus is on the impact of the ties on a firm's innovative performance, we filtered the output to keep just the alliances of selected types, namely R&D agreements, manufacturing agreements. In figure 2 the inter-cluster ties are summarized.

Therefore we built the networks using UCINET VI program (Borgatti et al. 2002): the network of each cluster and the inter-cluster network.

Figure 2 shows the inter-cluster network: each cluster is connected to external clusters through the linkages of its nodes to other clusters' nodes; the thickness of the segment represents the strength of the connection as function of the number of ties.

Figure 2. Inter-cluster ties



Following the data collection, we adopted *social network analysis* (SNA) and we computed the network variables with a full network method aimed at identifying network characteristics and actors' positions. We applied procedures which can be used to study networks of networks, composed by many types of organizations.

The model. Traditional estimations of the effects that network variables have on cluster's innovation are carried out with a regression model. The regression equation can be written as follows, using a pooled cross-sectional notation⁵:

$C_Patents_{it} =$

$$\begin{aligned} & \beta_0 + \beta_1(C_Size)_{it-n} + \beta_2(C_Density)_{it-n} + \beta_3(Inter-C_Spann.SH)_{it-n} + \beta_4(C_Density) * (Inter- \\ & C_Spann.SH)_{it-n} + \beta_5(N_Vert.Diversity_Intra-C)_{it-n} + \beta_6(N_Vert.Diversity_Intra-C) * (C_Size)_{it- \\ & n} + \beta_7(N_Vert.Diversity_Intra-C) * (C_Density)_{it-n} + \beta_8(N_Vert.Diversity_Inter-C) \\ & + \beta_9(N_Vert.Diversity_Inter-C) * (Inter-C_Spann.SH)_{it-n} + \beta_{10}(N_Geogr.Dist_Intra- \\ & C) + \beta_{11}(N_Geogr.Dist_Intra-C) * (C_Size)_{it-n} + \beta_{12}(N_Geogr.Dist_Intra-C) * (C_Density)_{it- \\ & n} + \beta_{13}(N_Geogr.Dist_Inter-C) + \beta_{14}(N_Geogr.Dist_Inter-C) * (Inter-C_Spann.SH)_{it-n} + \\ & \beta_{15}(controls)_{it-n} + \varepsilon_{it} \end{aligned}$$

where C: Cluster's, N: nodes', SH: structural holes.

We used a lag of one year between the dependent variable and the regressor values: the dependent variable is computed at time t, while all the regressors are computed at time t-1.

The dependent variable, cluster's innovation performance measured through patents count, is a variable that takes only non-negative integer values. Since the assumption of the linear regression model of homoskedastic normally distributed errors is violated, a count model should be used.

⁵ We use a longitudinal research design and therefore all variables are indexed over firms (i) and over time (t).

Poisson regression is the standard or base count response regression model (Hilbe, 2007).

We considered six statistical specifications, following Cameron and Trivedi (2010) who explained panel models for count data, mentioning four panel Poisson estimators - pooled Poisson with cluster-robust errors, population-averaged Poisson, Poisson random effects (RE), and fixed effects (FE) and Negative binomial models RE and FE. We finally choose *pooled Poisson with cluster-robust errors* following Cameron and Trivedi (2010) who asserted that in the use of pooled Poisson model, getting cluster-robust standard errors with cluster on individuals (i) has the effect to control for both overdispersion and correlation overtime for given i. The authors provided an example, showing that with respect to the default non-cluster-robust, the default standard errors are one-fourth as large and that the default t-statistics are four times as large. We checked also for the need of using Negative binomial models, but this was not supported by the value of the dispersion parameter α .

Variables and measures. The **dependent variable** is the *cluster's innovation output*, measured through *patents counts*: the number of patents granted for a cluster *i* in a given year *t*.

The **independent variables** are the following: (1) *Size intra-cluster*: number of nodes in the cluster; (2) *Density intra-cluster*: number of the effective ties divided by the number of possible ties in the cluster, i.e. $L/[n(n-1)/2]$, where *L* is the number of the effective ties; (3) *Spanning of Structural Holes (SH) inter-cluster*: number of linkages of a cluster with external clusters, through its nodes that span structural holes between clusters; (4) *Vertical Heterogeneity intra-cluster*: number of different firm types for each cluster. It is measured using an index similar to the Berry–Herfindahl Index. It is calculated by squaring the weight of each firm type in a cluster (in terms of number of firm of that category on the total number of firms in the cluster) and then summing the resulting numbers. The index is equal to 1 minus this sum. The index takes into account the relative size distribution of the firm types in a cluster. It approaches zero when a cluster is controlled by a single firm type and reaches its maximum when a cluster is occupied by a large number of firm types of relatively equal size (number of firms). The effect of the measure is to not take into account the firm types that are marginal. (5) *Vertical Heterogeneity inter-cluster*: ratio of the firm types in the external clusters different from the firm types inside the cluster (that the cluster reaches through inter-cluster ties) to the internal firm types. Firm types are weighted by the number of firms in each firm type; (6) *Geographical Distance intra-cluster*: weighted sum of all the distances of the node's locations from the cluster's main area (the majority of the nodes composing a cluster are located in the same state). The weight is given by the number of firms in a same location; (7) *Geographical Distance inter-cluster*: weighted sum of the distances of a cluster from all

the external clusters to which it is connected through inter-cluster ties. The weight is given by the number of inter-cluster ties; (8) Interaction terms: mathematical products of the above mentioned variables.

The **control variables** are: *Empshare*: share of national employment for each cluster, and *Cluster specialization*: level of concentration of employment in specific clusters. These are retrieved from the U.S. Cluster Mapping Database. We should add also financial variables regarding the nodes composing the cluster. This is a time consuming task that we will carry out in the future to improve this work.

5. Results

Descriptive statistics and Correlation Matrix. The regression has been implemented on 8 clusters, with 32 observations over the four years analyzed. As a general remark, the results of the correlation matrix are in line with what one would expect (Table 1). The correlation between the independent variables amongst themselves is not particularly high, except for the correlation between the interaction variables and the variables of the main effects.

Table1-Correlation Matrix

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1.patents	1.000																				
2.empshare	-0.362	1.000																			
3.specializ.	-0.426	0.542	1.000																		
4.size	0.048	-0.394	0.180	1.000																	
5.dns	0.848	-0.339	-0.430	0.134	1.000																
6.ssh	0.473	-0.207	-0.205	0.623	0.544	1.000															
7.dnssh	0.771	-0.320	-0.356	0.332	0.919	0.761	1.000														
8.divintra	0.576	-0.412	0.073	0.289	0.538	0.465	0.522	1.000													
9.divinter	-0.366	0.849	0.204	-0.693	-0.376	-0.511	-0.439	-0.690	1.000												
10.size*divintra	0.138	-0.390	0.263	0.974	0.217	0.650	0.411	0.468	-0.743	1.000											
11.dns*divintra	0.853	-0.345	-0.413	0.114	0.998	0.521	0.913	0.565	-0.381	0.206	1.000										
12.ssh*divinter	-0.210	0.897	0.187	-0.555	-0.215	-0.204	-0.251	-0.506	0.919	-0.591	-0.227	1.000									
13.12 squared	-0.277	0.955	0.345	-0.536	-0.272	-0.253	-0.296	-0.476	0.928	-0.550	-0.280	0.982	1.000								
14.gdistintra	0.966	-0.383	-0.449	0.059	0.863	0.526	0.803	0.612	-0.402	0.155	0.871	-0.239	-0.308	1.000							
15.14*size	0.736	-0.377	-0.274	0.532	0.754	0.865	0.917	0.534	-0.558	0.596	0.747	-0.351	-0.393	0.788	1.000						
16.14*dns	0.858	-0.307	-0.396	0.004	0.971	0.376	0.832	0.510	-0.291	0.096	0.978	-0.176	-0.228	0.878	0.662	1.000					
17.15squared	0.642	-0.267	-0.197	0.419	0.691	0.790	0.899	0.464	-0.420	0.498	0.690	-0.254	-0.279	0.703	0.955	0.607	1.000				
18.16squared	0.766	-0.246	-0.353	-0.120	0.886	0.155	0.658	0.412	-0.179	-0.042	0.895	-0.110	-0.157	0.759	0.443	0.955	0.375	1.000			
19.gdistinter	0.342	0.019	0.034	0.375	0.444	0.865	0.692	0.547	-0.336	0.479	0.439	-0.077	-0.064	0.416	0.736	0.292	0.776	0.065	1.000		
20.19*ssh	0.454	-0.184	-0.170	0.583	0.541	0.985	0.787	0.464	-0.485	0.628	0.522	-0.211	-0.243	0.517	0.882	0.374	0.848	0.136	0.918	1.000	
21.20squared	0.427	-0.199	-0.168	0.566	0.526	0.934	0.801	0.386	-0.458	0.609	0.510	-0.245	-0.266	0.494	0.895	0.368	0.899	0.120	0.898	0.977	1.000

Hypotheses Testing. As Table 2 shows, the results support the hypotheses, and the mechanisms referring to the structural and nodal characteristics are confirmed.

Table2 - Results - Full model

Variable	
Size Intra-cluster	0,049*** (0,002)
Density Intra-cluster	4,819* (2,050)
Spanning of SH Inter-cluster	0,020* (0,010)
Density intra-cluster* Spanning of SH Inter-cluster	0,023** (0,008)
Vertical heterogeneity Intra-cluster	0,422** (0,155)
Vertical heterogeneity Intra-cluster* Size Intra-cluster	0,002*** (0,000)
Vertical heterogeneity Intra-cluster* Density Intra-cluster	0,203** (0,073)
Vertical heterogeneity Inter-cluster	0,048*** (0,002)
Vertical heterogeneity Inter-cluster* Spanning of SH Inter-cluster	0,002*** (0,000)
Squared Vertical heterogeneity Inter-cluster* Spanning of SH Inter-cluster	-2,52e-07*** (1,06e-08)
Geographical Distance Intra-cluster	-0,006*** (0,001)
Geographical Distance Intra-cluster* Size Intra-cluster	0,001*** (3,79e-06)
Geographical Distance Intra-cluster* Density Intra-cluster	0,026*** (0,001)
Squared Geographical Distance Intra-cluster* Size Intra-cluster	-2,95e-10*** (1,70e-11)
Squared Geographical Distance Intra-cluster* Density Intra-cluster	-0,001*** (2,98e-07)
Geographical Distance Inter-cluster	-0,006*** (0,000)
Geographical Distance Inter-cluster* Spanning of SH Inter-cluster	0,001*** (5,23e-06)
Squared Geographical Distance Inter-cluster* Spanning of SH Inter-cluster	-3,84e-10*** (1,43e-11)
Constant	-5,904*** (1,098)
Empshare	-0,057*** (0,004)
Cluster specialization (Iq)	0,257 (0,024)
N, obs	32
Log Likelihood	-113,048
Prob > chi2	0,000
Pseudo R2	0,9642

* p<0,05 ; ** p<0,01; *** p<0,001. Standard errors are in parenthesis

Hypotheses 1, and 2 investigated the impact of the network structural characteristics on the cluster's innovation output. Hypothesis 1 and 2a) referred to the **intra-cluster** setting (variables *Size* and *Density Intra-cluster*) and predicted that the cluster size and density would be associated to superior cluster's innovative output. These two main effects are supported by the statistical analysis, being the resulting coefficients positive and significant at level $p < 0,001$ for size and $p < 0,05$ for density. Hypothesis 2b) referred to the **inter-cluster** setting (variable *Spanning of SH Inter-cluster*) and predicted that the inter-cluster spanning of structural holes would be associated to a greater cluster's innovative output. This hypothesis was supported, being the resulting coefficient positive and significant at level $p < 0,05$. Hypothesis 2c) integrated the **intra-cluster** and **inter-cluster** dimensions (variable *Density intra-cluster*Spanning of SH Inter-cluster*) and predicted that the combination of intra-cluster density and inter-cluster spanning of structural holes (interaction term) would have a positive impact on the cluster's innovative output. The hypothesis is supported, being the resulting coefficient positive and significant at level $p < 0,01$.

Two moderation effects, related to nodal characteristics were predicted to intervene in this process.

The first effect involves nodes' vertical heterogeneity and corresponds to Hypothesis 3. Hypothesis 3a) predicted that the **intra-cluster** vertical heterogeneity would positively moderate the main effects preseted in Hypotheses 1 and 2a). The hypothesis is tested with interaction terms (*Vertical heterogeneity Intra-cluster*Size Intra-cluster*; *Vertical heterogeneity Intra-cluster*Density Intra-cluster*) and is supported with a coefficients that is negative and significant at level $p < 0,001$ for size and $p < 0,01$ for density. Therefore, the higher the intra-cluster vertical heterogeneity, the higher the positive impact of the intra-cluster size and density on the cluster's innovation output. Hypothesis 3b) predicted that the **intra-cluster** vertical heterogeneity would moderate the main effects preseted in Hypotheses 2b) with an inverted U-shaped pattern. The hypothesis is tested with an interaction term and with its square (*Vertical heterogeneity Inter-cluster*Spanning of SH Inter-cluster*; *Squared*). The hypothesis found strong support, with a positive coefficient for the interaction term and a negative coefficient for the square, that are both highly significant at level $p < 0.001$. Therefore, a moderate level of inter-cluster vertical heterogeneity, would emphasize the positive impact of inter-cluster spanning of structural holes on the cluster's innovation output.

The second effect involves nodes' geographical distance and corresponds to Hypothesis 4.

Hypothesis 4a) predicted that the **intra-cluster** geographical distance would moderate the the main effects preseted in Hypotheses 1 and 2a) with an inverted U-shaped pattern. The

hypothesis found strong support, with a positive coefficient for the interaction term (variable *Geographical Distance Intra-cluster*Size Intra-cluster*; *Geographical Distance Intra-cluster*Density Intra-cluster*) and a negative coefficient for the square, that are highly significant at level $p < 0.001$, for both size and density. Hypothesis 4b) predicted that the **inter-cluster** geographical distance would moderate the the main effects preseted in Hypotheses 2b) with an inverted U-shaped pattern. The hypothesis found strong support, with a positive coefficient for the interaction term (*Geographical Distance Inter-cluster* Spanning of SH Inter-cluster*) and a negative coefficient for the square, that are highly significant at level $p < 0.001$. In sum, a moderate level of geographical distance, would emphasize the positive impact of size and density on the cluster's innovation output, in the intra-cluster setting, and of inter-cluster spanning of structural holes on the cluster's innovation output, in the inter-cluster setting. In conclusion, the theoretical framework is supported by the data. As for the control variables in the full model, *Empshare* is negative and significant at level $p < 0.001$ and *Cluster specialization* is not significant.

6. Discussion and conclusions

Clusters have become a prevalent form of industrial organization and their innovativeness is considered to be a key source of regional and national competitive advantage.

The primary contribution of the study is a framework and results that suggest an understanding of the factors that give rise to differential innovative outcomes across different clusters. Other contributions have been explained in the research problem and research question section. We tried to identify the impact of cluster's structural as well as nodal characteristics on the cluster's innovative performance. The potential moderation effect of contingency factors on the relations between network structure and cluster innovative performance have been underlined. More importantly we tried to distinguish between intra-cluster and inter-cluster dynamics in line with the OECD (2002) conception of cluster as mainly open and reticular.

To the extent that cluster may be thought of as a specific type of inter-firm network, some of the conceptual categories offered here may be considered valid also for a wider theory of network innovativeness, contributing to the literature on alliances and inter-firm networks. Moreover, despite the numerous contributions on topic of alliances, the effects of alliances on highly regulated settings, are unexplored; this can open a novel research path.

However one limitation of the study is the low level of *external validity* with respect to the setting. We articulated our conceptual framework with respect to the life-science industry

clusters in which trends of increased specialization, enhanced regulatory hurdles, growing systemic complexity have clearly emerged over the last decades. The advent of molecular biology and genetic engineering yielded a profound transformation of the life-science industry and induced a new division of labour that required a new organizational form made up of new networks of scientists, specialized new entrants and large pharma firms. The historical data on inter-firm R&D partnering in the pharmaceutical biotechnology industry reveal, despite some irregularities, an overall growth pattern in the number of newly established R&D partnerships since the mid-1970s.

Therefore, we want to underline the scope conditions of our predictions. The hypotheses are valid for a specific context that is a highly regulated setting, such as the life science industry, having some specificities: a process involving different, strict stages that must follow definite rules, as in clinical trials, and to which the contribution of diverse players - healthcare organizations or governmental organizations such as the technical and scientific public bodies of the National Health Service - are fundamental.

The work could be further improved from the empirical point of view by enriching the model with more control variables, like financials of the nodes composing the clusters (e.g. R&D intensity, ROA, Current ratio, Debt to equity etc.).

The conclusions of the work can significant for the world of the practice in that they could drive the choice of the best structural configuration and the best partner mix, thus increasing the managerial capabilities with reference to clusters' formation.

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