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International Journal of Engineering Business Management
Special Issue: Innovations in Pharmaceutical Industry

Innovating Through Clusters

Regular Paper

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Received 26 Jun 2014; Accepted 26 Aug 2014

DOI: 10.5772/59028

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Abstract This paper focuses on innovation performance and investigates the impact of clusters, or localized networks involving industrial, academic and institutional players, in the pharmaceutical setting; we aim 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. By analysing the U.S. pharmaceutical context, we show the structural and nodal network characteristics of the clusters and we shed some light on the "small-world" effects of the structural holes.

Keywords Cluster, Innovation, Networks, Pharmaceutical Industry.

1. Introduction

With the growth of cooperative forms of management, positive perspectives on cooperation have, over the last decade, enjoyed a notable revival, especially when compared to the dominant strength of the competitive model as a paradigm of resource allocation efficiency [1]. The high level of competition in the business environment pushes firms towards new learning models based on the high value of relationship patterns: firms interact to successfully learn from one another [2]. Moreover, innovation is increasingly recognized as requiring the convergence of many sources of knowledge and skills, usually linked through a network [3].

Therefore, since the late 1980s, the rate of inter-organizational alliances, or voluntary agreements between firms involving the exchange, sharing, or codevelopment of products, technologies, or services, has accelerated in multiple industries [4].

This situation is particularly true in an R&D intensive sector such as the pharmaceutical industry, where innovation is perhaps the most relevant performance driver. The pharmaceutical industry is characterized by the growing phenomenon of alliances and mergers and acquisitions (M&A)—both of which are strategic paths to increased reliance on external sources in a vertical de-integration process—due to some remarkable tendencies. These are mainly connected to R&D activities and reflected in increased regulatory constraints and technological complexity.

Some authors have suggested that the industry is facing a crisis that threatens the established model [5] and some tensions in the business model have begun to emerge.

In fact the dynamic and uncertain scenarios that economic organizations have to face force them to deeply rethink themselves and their structure through an internal innovation process aimed at making them more reactive and proactive, often through networks of informal relationships [6].

Several factors are contributing to a crisis in the R&D area, such as the continuous change in the process of drug discovery and development, the cost containment policies of institutions, the increasingly stringent requirements for the approval of new drugs resulting in more costly, long, internationally-based R&D activities [7], the growing number of patent expirations on blockbuster drugs, the enhanced competition from generic drugs, the growing importance of emergent countries [5], and an increase in the percentage of failures or non-completions in the R&D process.

At the same time, the crisis in the productivity of pharmaceutical R&D organizations, as opposed to the positive results produced by biotechnology R&D, is leading to the development of bio-pharmaceutical firms [8], in which biotechnological opportunities are integrated with pharmaceutical ones.

All these elements are forcing the industry to make adjustments to established patterns: pharmaceutical companies are searching for new, more efficient ways of managing the drug development process, while maintaining the process's ethical integrity through M&A, in-licensing, alliances, new organizational and decisional structures of R&D, and outsourcing that are changing the traditional model of vertical integration of the pharmaceutical industry.

Outsourcing practices, widely applied and boosted by the rush of corporate downsizing as an alternative to divestiture [9], have varied over the years, covering a diverse range of services from support activities to core managerial processes and from service-based activities to productive processes, such as modular production [10]. In knowledge-intensive industries (e.g., pharmaceutics, biochemistry, and healthcare), selective outsourcing usually occurs in favour of specialized and focused suppliers [11]. In fact, contract research organizations have become a fundamental component of R&D.

In the end, a pharmaceutical firm cannot exist without networking in the scientific community: the amount of resources and knowledge needed for R&D has become overwhelming for a single organization; technological and market uncertainties foster the search for new opportunities; and performing R&D activities in networks can produce extra value for the participants and for innovation outcomes [12]. 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 stages of R&D [8].

2. Research Problem

Starting from these premises, the aim of the paper is to investigate a specific form of alliance, the *cluster*, in the setting of the pharmaceutical industry and its impact on innovation. 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 work tries to enrich the line of inquiry into cluster-based innovation by studying the effects of networks on clinical research.

Clusters are localized networks [13], territorial aggregations of different players, that usually arise when business segments require high levels of specialization from multiple contributors [14]. They can have a more or less formalized structure, and, in any case, they assume a network configuration through contractual mechanisms.

The cluster we analyse involves a public, an industrial and an academic player, which, in the pharmaceutical industry, typically comprise pharmaceutical firms, biotech firms, universities, research centres, and healthcare organizations such as hospitals, clinics, and healthcare institutions.

As for the relevance of the topic, it is grounded in reality because the *cluster* meets two specificities of the pharmaceutical industry: (1) it is a highly regulated R&D setting. The pharmaceutical R&D process is organized as a strict sequence of different stages that are better performed through the involvement of different players assuming different roles in the healthcare value chain (e.g., research, manufacturing, provision of care, and regulation). In such a context, organizations often decide to work on a multiplayer basis in order to speed up the multistage process of pharmaceutical research through the sharing of scientific knowledge and the division of labour and the inclusion of patients in clinical trials to foster enrolment and the fulfilment of protocols.

(2) Interactions between complementary players are needed for innovation. Firms must deal with the new systemic dimensions of technology and research. The strength of the cluster in the pharmaceutical industry can be said to rest upon the fact that research is built on three

pillars: basic academic research, corporate R&D, and clinical R&D. Diverse actors contribute together to these three crucial elements.

Since pharmaceutical clusters are composed of players who have different roles in the value chain, operating in a pharmaceutical R&D process, we can presume that it is very likely that each player in the cluster has ties with similar organizations (with the same role in the value chain) that are however involved in other clusters. This assumption has driven us to the *small world* concept - highly dense clusters or hubs randomly connected to other clusters or hubs by weak ties in a sparse structure. The reference to this kind of structure allows us to enrich the literature on clusters and networks theoretically in many respects.

As for the literature on clusters, we can analyse simultaneously *intra-cluster* and *inter-cluster network characteristics* and their impact on the cluster's innovative performance, overcoming the limits of the absence of significant contributions examining clusters of clusters, and we do this by using constructs and concepts derived from SNA.

As for the literature on networks, we contribute to the debate on the network structure most beneficial for innovation. A *small world network* structure could provide an intermediate solution between sparse and dense structures that are complementary, through the distinction between intra-cluster and inter-cluster dynamics, and trying to establish its connection to innovation output would be a useful contribution to the abovementioned debate.

The paper examines the impact of *small world* characteristics in the network structure on the network's innovative performance. The aim is to analyse some principles of *small world networks* as conceptualized by reference [15] applying them in the context of U.S. pharmaceutical clusters and trying to identify their connection with network innovative outcomes.

Finally we go further and enrich the *small world network* model by considering not just the *structural* components, but by introducing and analysing other attributes of the nodes composing the *small world network*, which are *knowledge heterogeneity* and *geography*. These are contingencies that affect knowledge sharing dynamics besides network structure.

The research questions are the following: *what is the impact of small world network structural characteristics on the cluster's innovative performance in the pharmaceutical sector*? *How do contingencies, such as knowledge heterogeneity and geography, moderate the impact of a small world network structure on the cluster's innovation performance?*

3. Literature review

3.1 Networks

Studies that examine the consequences of networks[1] typically follow the structuralist perspective. This line of inquiry focuses on the configuration of ties, analysing how actors in networks influence each other's attitudes and behaviours, and concluding that an actor's payoff is a function of the 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 [16-18], 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) [16]. The greater the social capital possessed by the firm, the greater its knowledge will be, and therefore, the faster its innovation process [19].

Scholars supported competing schools of thoughts and two trade-offs are still in place: the first one is between the benefits of strong [20-21] versus weak [22] ties (that are likely to be bridges), the second one is between the benefits of disconnected network structures [23] versus dense network structures [24-25]. 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 structures 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 [26]. Contingencies need to be introduced, such as nodal heterogeneity [27].

3.2 Clusters and small world networks

The concept of a network is more general than that of a cluster and does not necessarily entail local embedding, a shared objective, or a specific market [28]. The cluster concept has been defined in ambiguous ways. The full range of cluster definitions falls under two main lines of conception: (a) definition in reference [29]: "a geographically proximate group of inter-connected companies and associated institutions in a particular field, linked by commonalities and complementarities", (b) definition in reference [30]: "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 clusters. Contrary to the definition in reference [29], the approach of reference [30] is

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

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 localized 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.

A cluster - an aggregation of different players in a localized network [13] - has been better characterized by reference [31] in this way: *"it comprises an ensemble of various organizations and institutions that are defined by respective geographic localizations occurring at variable spatial scales; that interact formally and/or informally through inter-organizational and/or interpersonal regular or more occasional relationships and networks; 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"*. As we can see, the concept involves a wide range of variation and even starting from this, it is possible to build around the type of organizations, the best spatial scale for geographical localization, the focus on a single domain, and the configuration of the network, as we do in this paper.

In particular, we consider the impact of *small world network* structures, nodes' heterogeneity and nodes' geography on the innovation of clusters.

The *small world network phenomenon* - i.e., the principle that we are all linked by short chains of acquaintances (commonly known as "six degrees of separation") - was introduced in the context of experimental studies in social sciences by reference [32] and since then it has been studied analytically in several network models. Among the most refined models there is the one by reference [15], the one we refer to. In this construction there is a local structure with a high density of integration in a wider random network and the coexistence of short-range and long-range connections (something that happens in many realistic networks, such as that of U.S. pharmaceutical clusters that we analyse).

This reconciles the local properties of a regular network with the global properties of a random one, by introducing a certain amount of random long-range connections into an initially regular network [33], therefore the edges of the network are divided into "local" and "long-range" contacts. The authors argued that such a model captures two crucial parameters of social networks: there is a simple underlying structure that explains the presence of most edges, but a few edges are produced by a random process that does not respect this structure.

This is useful in reconciling competing views in the literature on networks: the benefits of strong vs weak ties and of disconnected [23] vs dense [24] structures.

The main characteristics of *a small world network* are the following: the overall network is numerically large; it is sparse in the sense that each node is connected to an average of only k other nodes n; it is decentralized in that there is no dominant central vertex to which most other networks are directly connected (not only the average degree k is much less that n but the maximum degree k_{max} over all the vertices must also be much less that n); it is highly clustered [34].

Since we are interested in the impact of *small world networks* on innovation, we refer to studies that analysed the effect of networks, and in particular of clusters, on innovation.

Reference [35] 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) multidisciplinarity and spillovers, with interactions and synergies among disciplines; (f) development of fiscal and financial conditions supporting innovation.

Clusters reflect the systemic character of modern interactive innovation, and therefore they are related to several conceptual frameworks and models developed under the literature on innovation systems. In this field, which emphasizes interactions among actors and innovation as a process embedded in a given social context, research has been carried out on sectoral systems [36], technology systems [37] 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 "mode 3" of knowledge production, which advocates a system, consisting of innovation networks and knowledge clusters for knowledge creation, diffusion, and use [38]. This is a multilayered, multimodal, multinodal, and multilateral system, encompassing and reinforcing mutually complementary innovation networks and knowledge clusters characterized by the coexistence, coevolution, and cospecialization of different knowledge paradigms and different modes of knowledge production.

This recall also the "Triple Helix" (TH) model of knowledge, developed by references [35-36], focused on three helices that intertwine and thus generate a national innovation system: academia/universities, industry, and

state/government. References [39-40] spoke of "university-industry-government relations" and networks, also placing a particular emphasis on "tri-lateral networks" where those helices overlap and create synergies that result in product and process innovations. Strong, enterprise-supporting infrastructures complement strong, local science bases [41] challenging the conventional, linear model of interaction. Universities provide advanced research and a ready supply of human capital in the form of skilled graduates and basic research; companies provide real-world problems, commercialization opportunities, and funding. Innovative dedicated biotechnology firms (DBFs) seek to commercialize the results of the basic research; large pharmaceuticals provide funding, downstream marketing and distribution capabilities [42]); and governmental organizations provide user feedback and regulatory support.

Many studies analysed the role of university–industry relationships in triggering new industrial R&D innovative projects [43] and found a positive impact [44-45].

4. Hypotheses development

The aim of this paper is to study the concepts used to characterize the *small world network*, identify their connection with the cluster's innovation output, and complete the model with contingencies related to the nodes' characteristics.

4.1 Small world network structure

We refer to the *small world network* structure, a community of actors structured into well-defined clusters that are only sparsely connected to each other.

We can deconstruct the *small world network* concept in the following elements: each cluster's density[2]; the presence of structural holes[3] between one cluster and other clusters; and we can analyse its impact on innovation in the pharmaceutical industry.

A dense innovative cluster provides benefits both from the learning and the governance perspective, favouring the *exploitation*[4] of knowledge.

From the learning perspective, it facilitates the local transmission of information by providing numerous communication channels and pathways among actors, so that information introduced into a cluster will quickly reach other actors in it; it assures the future existence and relevance of different multiple sources of information; allows triangulation (i.e., by utilizing third parties to aid the judgment of knowledge and its absorption) [16,24]; facilitates intense interactions and knowledge integration [47]; improves the transfer of tacit, embedded knowledge [48-49]; enhances interfirm cooperation [47]; favours mutual understanding based on common norms or behaviours; increases the potential to build knowledge through intensive, repeated interactions and the exchange of ideas; and allows coordinated action.

From a governance (TCE) perspective, it reduces transaction costs, allowing easier interactions between partners; reduces barriers to resource mobilization; reduces competitive practices; discourages misbehaviour, due to the so-called "shadow of the others" and "shadow of the future"; fosters a normative environment against opportunism; reduces risks; and engenders mutual trust, reciprocity norms, and shared identity, thus facilitating collaborative efforts by making the actors more willing to exchange information [16, 50].

On the other hand, 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, new opportunities, diverse experiences, and new understandings; the preservation of variety and heterogeneity, through the access to resources that are different from those found in an actor's more immediate social network [22]; interfirm resource pooling [47]; flexibility; arbitrage opportunities for the brokering actors [51-53]; and novel combinations and re-combinations of ideas. These conditions favour the *exploration* component of innovation.

In the end, while the presence of structural holes is suited to idea generation and invention, as it favours exploration and hampers implementation/action, a dense network structure is suited for idea implementation (coordinated action to implement ideas), as it favours exploitation but could potentially have an idea problem.

The application of this debate to the pharmaceutical context and to the clusters can result in the following arguments.

Some arguments suggest that *the higher the density in the pharmaceutical cluster, the higher the cluster's innovative performance*.

In fact, density is especially useful in the pharmaceutical industry because the innovation process, which is a complex sequence of stages, is a trial-and-error process,

[2] Actual number of direct ties between nodes as a ratio of the maximum possible number of ties.

[3] A structural hole exists between the brokered actors, two nodes in a network, if the nodes share a tie with an individual but are not connected to each other [23]. Bridges between groups of nodes span structural holes with weak ties.

[4] *Exploitation* (efficient employment of current asset and capabilities, implementation of the ideas discovered through exploration) and *Exploration* (discovery and development of novel ideas) and are both needed for the innovation outcome [46].

with a lot of feedback loops and continuous shifts from exploration to exploitation as well as the opposite, which requires interaction.

We could argue that in the specific context of the pharmaceutical industry, inside a single cluster the processes of *exploration* and *exploitation* are both in place. This is evident considering that biotech firms play an intermediary position, establishing exploration networks with universities and exploitation networks with pharmaceutical companies for commercialization [54]. However, in an exploration network of universities–biotech, reference [55] found high network density, high frequency of interaction, and high specific investment in mutual understanding. This is because we maintain that there is a fundamental difference between *intra-cluster exploration* and *inter-cluster exploration*. In the former, there is the involvement of the players in a common project that must have a specific innovative outcome, and not just the suggestions of ideas. So it is a finalized exploration process that will shortly result in exploitation and it is an exploration process that occurs in a prearranged systemic way.

Therefore, inside a pharmaceutical cluster, in the cluster there is a finalized and structured exploration, a concept that is more similar to exploitation for certain characteristics, and for this reason the dense structure seems to accomplish both *exploration and exploitation* aims. In this way, we try to solve the debate between the two divergent views, that of reference [28] and that of references [22, 23] about the network structure more suitable for exploration and exploitation.

Since we have varied players both inside and outside the clusters and usually exploration comes from variety, we have considered innovation as comprising *inter-cluster exploration* and *intra-cluster exploration*. Density is suitable for *intra-cluster exploration* while structural holes are good for *inter-cluster exploration.* Therefore, in order to spur inter-cluster exploration we could assert that *the more the nodes in the pharmaceutical cluster span structural holes between the cluster and other clusters, the higher the cluster's innovative performance.*

Due to different formation conditions and causes, clusters typically own heterogeneous knowledge that can migrate and be fruitfully recombined through links that span those clusters.

Therefore, the presence of structural holes spanning between a cluster and other clusters (a configuration based on semi-isolated subgroups) determines the extent to which the cluster's knowledge base is continuously rejuvenated through knowledge inputs from outside the cluster [56] and novel combinations of ideas.

While authors studying *small world networks* have usually focused on single organizations, suggesting that they can be broken into subgroups, semiautonomous subunits[5], we focus instead on inter-cluster dynamics, where the subgroups are the single clusters and the organization can be all the clusters considered together.

Therefore, we are considering an open cluster, where some members are engaged in relations with organizations belonging to other clusters, playing the role of the bridge [58]. This is a solution that tries to also join the conceptions of clusters of reference [29] and of reference [30], as explained in the literature review.

Combining the organizational learning arguments with the small-world networks concept, we conclude that networks that have both clustering and some amount of linking between them, cluster-spanning bridges, spur each cluster innovation, striking the balance of *exploration* and *exploitation*.

The bridging ties with other clusters allow for outside exploration through the possibility for any point in the network to benefit indirectly from the information or the knowledge received by his neighbour in other clusters [57], with the access to heterogeneous and novel ideas, while the high density of clusters allows for effective exploitation of ideas and inside cluster exploration. The benefits of local transmission and the information scope of cross-cluster connections can be simultaneously achieved.

Dense and sparse configurations coexist at different scales and levels of the network, in a multiscaled cluster. Density comes from intra-cluster dynamics, while sparseness comes from inter-cluster dynamics, to assure the cluster life in the short as well as in the long term with the capability of catching new ideas from outside and of effectively implementing them inside the cluster in wider innovation oriented networks.

Closure allows us to realize the value buried in a structural hole, effectively implementing the new ideas obtained from outside inside the cluster [59].

This means that *the more the nodes in the pharmaceutical cluster span* ***structural holes*** *between the cluster and other clusters, the higher the positive impact of* ***density*** *will be in the life-science cluster on the cluster's innovative performance.*

Therefore, in sum, we can formulate the following hypothesis:

[5] The whole firm could be studied as a smallworld network and the workgroups could be considered as clusters interacting with one another [57].

HP1: ***The more the pharmaceutical cluster is integrated in a small world network structure, the higher the cluster's innovative performance.***

4.2 Contingencies

Although the solution of combining density in the intra-cluster dimension and brokerage in the inter-cluster dimension is undoubtedly conceptually attractive, it appears likely that its impact on innovation will be contingent on several elements. We focus on two relative properties of the nodes as contingencies: partner heterogeneity and geography.

4.2.1 Heterogeneity

Pharmaceutical clusters comprise different actors, which occupy different positions in the supply value chain, from downstream to upstream: pharmaceutical, biotech firms, universities, research institutes, institutions. From the "Triple Helix" Model of knowledge [39-40], we know that when three helices (universities, industry, and government) intertwine, through relations and networks, they overlap and create synergies that result in product and process innovations. Universities provide advanced research and human capital; companies, real-world problems, commercialization opportunities; institutions, user feedback and regulatory support.

This system provides a broader view of the value chain and interaction between private and public actors in innovative R&D activities [60].

However, diversity can represent both an opportunity (novelty value), favouring knowledge development, and a problem (reduced absorptive capacity, higher transaction costs), disfavouring knowledge transfer [28].

The impact of heterogeneity on innovation appears different in the local (intra-cluster) and long-range (inter-cluster) setting of the *small world network*.

On one side, in the **local,** intra-cluster setting of the *small world network*, vertical diversity[6] has a positive moderation effect. It enhances the *internal exploration* process, favouring Schumpeterian "novel combinations", while the problem of the absorptive capacity[7] is counterbalanced by the presence of high connectivity in the cluster.

Reference [62] argued that it is the *preservation of diverse ideas within sub-groups* (i.e., single clusters) that increases the information scope of the overall network and consequently the innovation output of the single cluster.

Moreover, vertical diversity allows the effectiveness of the *exploitation process* that in the life-science industry requires complementary skills and the appropriate division of labour. A final argument is that redundancy in a dense network discourages idea generation; this redundancy will be reduced in the presence of the vertical diversity of nodes.

Considering the context of the pharmaceutical industry, we can point out some additional remarks. First, partner diversity is really important to answering 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 [63]. 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 through relations with other organizations with complementary specialization. Furthermore, in the literature, arguments have been made that when firms combine complementary skills, greater innovation results [64]. If partners' vertical diversity implies complementarity, which in turn implies innovation, partners' vertical diversity drives innovation.

Therefore, *the nodes' vertical diversity in the pharmaceutical cluster positively moderates the impact of density on the cluster's innovative performance.* The higher the level of nodes' vertical diversity in the cluster, the higher the positive impact of density on the cluster's innovative performance.

On the other side, in the **long-range,** inter-cluster setting of the *small world network***,** the link connecting cluster to cluster should be a weak tie in a sparse configuration, and the problem of absorptive capacity between the two extreme nodes is higher than in the intra-cluster case.

It is true that partner diversity in the pharmaceutical industry involves a related knowledge background: players act in subsequent phases of the same macro-

[6] Vertical diversity can be defined as the cognitive distance and differences in alliance partners' operational contexts in the value chain, it implies a distinction among three categories: horizontal, upstream, or downstream [61]. For instance a biotech and a pharmaceutical firm are diverse, two pharmaceutical firms are equal. Vertical diversity in **the intra-cluster setting** is the range of diverse partners - number of diverse partners inside the cluster. In the **inter-cluster setting** it is measured for pairs of nodes (the extremes of the structural hole).

[7] The ability to recognize, assimilate, and apply external knowledge.

process, and thus it is possible to suppose that they have 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 [65]. This reduces the concern of an absence of absorptive capacity.

However, in any case, if learning performance from interaction is the mathematical product of novelty value and understandability, the result is an inverted-U shaped relation with cognitive distance. Optimal cognitive distance lies at the maximum of the curve where there is a sustainable level of transaction costs and competition, and a good level of complementarity and absorptive capacity.

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

A moderate level of vertical diversity between the two nodes spanning the inter-cluster structural hole enhances the positive impact of the inter-cluster structural hole on the cluster's innovative performance; while a level that is too low or too high reduces this impact.

Finally, we can state the following hypothesis:

HP2: ***The nodal vertical diversity moderates the impact of the integration of the cluster in a small world network structure on the cluster's innovative performance.***

4.2.2 Geography

In the literature some elements support localization and proximity for innovation, others a wider geographical extension.

Factors supporting geographical proximity are: transaction costs reduction and development of relational dimensions; location-specific drug development for epidemiological reasons; location-specific regulatory framework; tacit knowledge transfer, frequency of interaction, trust; location-specific assets (agglomeration economies, pool of skilled labour; scientific, commercial spillovers) in positive *externality arenas*. Moreover, the theory of proximity in the network theory identifies proximity as the main facilitator of knowledge flows [66]. Factors supporting geographical distance are: the need for an escape from local embedding for innovation; embedding in virtual communities, with internet use reducing transaction costs; the substitutive role of frequent meetings; the avoidance of the lock-in effect (social legitimacy; institutional embedding: local obligations); tension toward trans-local, disembedded clusters, in the real world and in institutional recommendations (e.g., the European Commission) to enhance competitiveness.

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 dispersed, as in the pharmaceutical industry.

For instance, drug companies are beginning to invest in Chinese R&D; in fact, the Chinese market may become the second-biggest pharmaceuticals market in the world by 2020. Recent studies show that the famous Italian industrial districts are facing a crisis [67]. In order to survive they are becoming locally disembedded, shifting some activities, especially in production, outside the local environment [68].

Therefore, a better solution for innovation would be a balance between local and non-local players in the *small world network,* both inside the cluster and in the inter-cluster connections: the shared context of a local circuit and of remote cooperation will be complementary resources [13], favouring the combination of *exploration* and *exploitation*. A moderate level of geographical distance will enhance the positive impact of density and structural holes on a cluster's innovative performance.

Therefore, we can presume that *the geographical distance between the nodes in the pharmaceutical cluster moderates the impact of density on the cluster's innovative performance with an inverted U-shaped pattern* and similarly *the geographical distance between the two nodes spanning an inter-cluster structural hole moderates the impact of the inter-cluster structural hole on the cluster's innovative performance with an inverted U-shaped pattern.*

This means that a moderate level of geographic distance between the nodes in the life-science cluster enhances the positive impact of density; while a level that is too low or too high reduces this impact. Similarly, a moderate level of geographic distance between two nodes spanning an inter-cluster structural hole enhances the positive impact of the inter-cluster structural hole on the cluster's innovative performance; while a level that is too low or too high reduces this impact.

Finally, we can state the following hypothesis:

HP3: ***The nodal geographical distance moderates the impact of the integration of the cluster in a small world network structure on the cluster's innovative performance.***

5. Analysis

5.1 Sample and data collection

We explored the arguments mentioned in the previous sections by using a social network approach and a regression model applied to the U.S. pharmaceutical industry.

We built a sample including eight pharmaceutical 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 pharmaceutical clusters established in the U.S. was drawn up using the *U.S. Cluster Mapping Database*[8].

We retrieved the list of clusters 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 minimum number of nodes in the clusters is 92, the maximum 645. The final sample includes the following eight clusters (CL): CL1: Life Science 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 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.

In order to build our dependent variable, we collected patent data for each cluster from the *U.S. Cluster Mapping Database*. We filtered the patent data according to the year 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) the 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 sources 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 short-range intra-cluster from long-range inter-cluster ties.

Intra-cluster ties are ties between 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 an inter-cluster tie (even if the tie will occur between two divisions of the same firm).

To retrieve these data we combined the sources mentioned before with the *SDC Platinum* database, produced 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 [69-70]. 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 and manufacturing agreements. Thus, we built the networks using the UCINET VI program [71]: the network of each cluster and the inter-cluster network.

In figure 1, the long-range, inter-cluster ties are summarized: each of the eight clusters 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 a function of the number of ties.

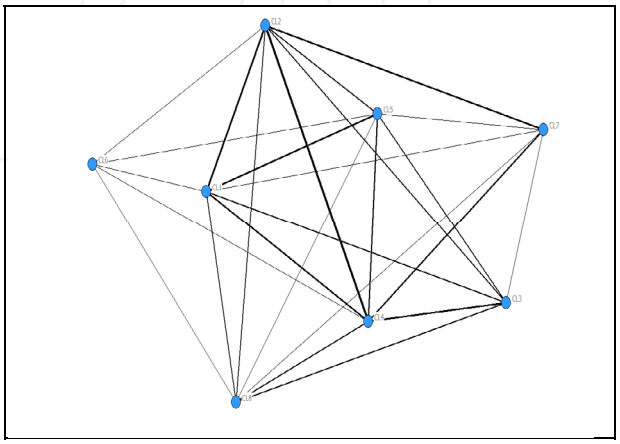

Figure 1. Long-range, inter-cluster ties

In this way we reconstructed both the whole network and the single sub-units of the network, which are clusters.

[8] From Harvard Business School, a project funded by the U.S. Department of Commerce, Economic Development Administration.

Finally, we adopted a *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 of many types of organizations. The results show that, in general, clusters have a high density inside the cluster, and many structural holes between different clusters. Therefore, the setting is suitable for testing the *small world network* impact.

5.2 The model

Traditional estimations of the effects that network variables have on the innovation of a cluster are carried out with a regression model. The regression equation can be written as follows, using a pooled cross-sectional notation[9]:

$$C\ Patents_{it} = \beta_0+\beta_1(C\_Density)_{it-n}+\beta_2(Inter\text{-}C\_SH)_{it-n}+\beta_3(C\_Density)*(Inter\text{-}C\_SH)_{it-n}+\beta_4(N\_Vertical\_Heterogeneity)_{it-n}+\beta_5(N\_Vertical\_Heterogeneity)*(C\_Density)_{it-n}+\beta_6(N\_Vertical\_Heterogeneity)*(Inter\text{-}C\_SH)_{it-n}+\beta_7(N\_Geogr.Dist)+\beta_8(N\_Geogr.Dist)*(C\_Density)_{it-n}+\beta_9(N\_Geogr.Dist)*(Inter\text{-}C\_SH)_{it-n}+\beta_{10}(controls)_{it-n}+\varepsilon_{it-n}$$

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

We used a time-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 the number of patents, 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. Poisson regression is the standard or base count response regression model [72]. We considered six statistical specifications, following reference [73] who explained panel models for counting 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 reference [73] who asserted that in the use of the pooled Poisson model, getting cluster-robust standard errors with clusters on individuals (i) has the effect of controlling for both overdispersion and correlation overtime for a 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 also checked the need to use negative binomial models, but this was not supported by the value of the dispersion parameter α.

5.3 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) *small world network characteristics*, which are expressed by (1.1) *intra-cluster density:* the 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; (1.2) *inter-cluster spanning of structural holes (SH):* number of linkages of a cluster with external clusters, through its nodes that span structural holes between clusters; (2) *intra-cluster vertical heterogeneity:* number of different firm types for each cluster. This 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 the number of firms of that category by 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. (3) *Inter-cluster vertical heterogeneity:* the ratio of the firm types in the external clusters are different from the firm types inside the cluster (which 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; (4) *intra-cluster geographical distance:* the 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 the same location; (5) *inter-cluster geographical distance:* the 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; *cluster specialization:* level of concentration of employment in specific clusters; *intra-cluster size*: number of nodes in the cluster; *R&D ratio:* R&D expenses / Operating revenue. These are retrieved from the U.S. Cluster Mapping Database.

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

Empshare, *cluster specialization* and *intra-cluster size* were retrieved from the U.S. Cluster Mapping Database; *R&D ratio*, was found by collecting data from the *Osiris* Database from the balance sheets of the companies composing the clusters (compatibly with their availability) and computing the mean inside each cluster.

5.4 Results

The regression was implemented on eight clusters, with 32 observations over the four years analysed.

As Table 1 shows, the results support the hypotheses, and the mechanisms referring to the impact of *small world network* characteristics and contingencies on innovation are confirmed.

Hypothesis 1 investigated the impact of the *small world network* structural characteristics on the cluster's innovation output. Hypothesis 1 referred to the combination (interaction) of the two main components of *small worlds*: density and the spanning of structural holes, and predicted that the integration of the short-range clustering and the long-range reach would have a positive impact on the cluster's innovative output. The hypothesis is supported, being the resulting coefficient positive and significant at level $p < 0,01$.

The effect of each of the components taken individually is the same as the effect of the interaction term. As for the short-range intra-cluster ties, the cluster density is associated with the superior cluster's innovative output. In fact, the resulting coefficient of the variable *intra-cluster density* is positive and significant at a level of $p < 0,05$.

As for the long-range, inter-cluster setting the inter-cluster spanning of structural holes is associated to a greater cluster's innovative output. In fact the resulting coefficient of the variable *inter-cluster spanning of SH* is positive and significant at a level of $p < 0,05$.

Two moderation effects, related to nodal characteristics, were predicted as being likely to intervene in this process, introducing a contingent approach in the *small world network* setting.

The first effect involves nodes' vertical heterogeneity and corresponds to Hypothesis 2.

Hypothesis 2 predicted two effects.

First, that the **intra-cluster** vertical heterogeneity would positively moderate the main effects presented in Hypotheses 1 regarding density. The hypothesis is tested with the interaction terms (*intra-cluster vertical heterogeneity * intra-cluster density)* and is supported by a coefficient that is positive and significant at a level of $p < 0,001$. Therefore, the higher the intra-cluster vertical heterogeneity, the higher the positive impact of the intra-cluster density on the cluster's innovation output.

Second, it predicted that the **inter-cluster** vertical heterogeneity would moderate the main effects presented in Hypothesis 1 regarding the spanning of structural holes, with an inverted U-shaped pattern. The hypothesis is tested with an interaction term and with its square (*inter-cluster vertical heterogeneity* inter-cluster spanning of SH; squared*). The hypothesis found strong support, with a positive coefficient for the interaction term and a negative coefficient for the square, which are both highly significant at a level of $p < 0.001$. Therefore, a moderate level of inter-cluster vertical heterogeneity would emphasize the positive impact of the inter-cluster spanning of structural holes on the cluster's innovation output.

The second moderation effect involves nodes' geographical distance and corresponds to Hypothesis 3.

Hypothesis 3 predicted two effects.

First, that the **intra-cluster** geographical distance would moderate the main effects presented in Hypotheses 1 with an inverted U-shaped pattern. The hypothesis found strong support, with a positive coefficient for the interaction term (*Intra-cluster Geographical Distance * Intra-cluster Density)* and a negative coefficient for the square, that are highly significant at a level of $p < 0.001$.

Second, it was hypothesized that the **inter-cluster** geographical distance would moderate the main effects presented in Hypotheses 1 with an inverted U-shaped pattern. The hypothesis found strong support, with a positive coefficient for the interaction term (*inter-cluster geographical distance * inter-cluster spanning of SH*) and a negative coefficient for the square, which are highly significant at a level of $p < 0.001$. In sum, a moderate level of geographical distance, would emphasize the positive impact of density on the cluster's innovation output, in the intra-cluster setting, and of the 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 a level of $p<0,001$, *size intra-cluster* is positive and significant at a level of $p<0,001$, *cluster specialization* and *R&D ratio* are not significant.

6. Discussion and conclusions

The main contribution and results of the study are a framework that suggests an understanding of the factors that give rise to differential innovative outcomes across different clusters, by using a network approach. In particular we tried to hypothesize the impact of a cluster's *small world network* structural characteristics as well as of nodal characteristics on the cluster's innovative performance.

By using the concept of *small worlds*, we tried to distinguish between intra-cluster and inter-cluster dynamics in line with the conception of cluster in reference [30] as mainly open and reticular. Then, the potential moderation effect of contingency factors on the relations between *small world network* structure and cluster innovative performance were underlined.

Type of variable - HP tested	Variable	
Small world characteristic HP1	Density Intra-cluster	4,560* (1,950)
Small world characteristic HP1	Spanning of SH Inter-cluster	0,020* (0,010)
Small world characteristic HP1	Density intra-cluster* Spanning of SH Inter-cluster	0,021** (0,006)
Contingency 1 - Heterogeneity	Vertical heterogeneity Intra-cluster	0,407** (0,157)
Contingency 1 - Heterogeneity HP2	Vertical heterogeneity Intra-cluster* Density Intra-cluster	0,217*** (0,060)
Contingency 1 - Heterogeneity	Vertical heterogeneity Inter-cluster	0,047*** (0,002)
Contingency 1 - Heterogeneity HP2	Vertical heterogeneity Inter-cluster* Spanning of SH Inter-cluster	0,002*** (0,000)
Contingency 1 - Heterogeneity HP2	Squared Vertical heterogeneity Inter-cluster* Spanning of SH Inter-cluster	-2,49e-07*** (8,37e-09)
Contingency 2 - Geography	Geographical Distance Intra-cluster	-0,006*** (0,001)
Contingency 2 - Geography HP3	Geographical Distance Intra-cluster* Density Intra-cluster	0,026*** (0,001)
Contingency 2 - Geography HP3	Squared Geographical Distance Intra-cluster* Density Intra-cluster	-0,001*** (3,23e-07)
Contingency 2 - Geography	Geographical Distance Inter-cluster	-0,006*** (0,000)
Contingency 2 - Geography HP3	Geographical Distance Inter-cluster* Spanning of SH Inter-cluster	0,001*** (5,23e-06)
Contingency 2 - Geography HP3	Squared Geographical Distance Inter-cluster* Spanning of SH Inter-cluster	-3,84e-10*** (1,43e-11)
Control	Empshare	-0,053*** (0,004)
Control	Cluster specialization (Iq)	0,057 (0,034)
Control	Size Intra-cluster	0,048*** (0,001)
Control	R&D Ratio	-0,004 (0,003)
	N, obs	32
	Log Likelihood	-112,875
	Prob > chi2	0,000
	Pseudo R2	0,9643

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

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 clusters in the pharmaceutical industry in which trends of increased specialization, enhanced regulatory hurdles, and growing systemic complexity have clearly emerged over the last decades. The advent of molecular biology and genetic engineering yielded a profound transformation of the 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 predictions could be hardly applied to other contexts.

Finally, the work could be further improved from an empirical point of view by enriching the model with more control variables, like the financials of the nodes composing the clusters (e.g., ROA, current ratio, debt to equity etc.).

The results provide a test of the impact of a *small world network* structure on innovation outcomes, thus increasing the managerial capabilities with reference to the choice of the best structural configuration and partner mix in cluster formation.

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