This paper contributes to gain a more comprehensive view about the relational dimension of Local Innovation Systems (LIS) by exploring the configuration of the network structure and the variety of inter-organizational relationships in a case of successful LIS. From a methodological perspective the study contributes to meet the challenges related to the adoption of a holistic approach, by capturing the heterogeneous nature of LIS demography, whether most studies limit their analyses to inter-firm relationships and at the node-level. Secondly, the paper provides insights into the network portfolio composition, which has been underexplored in LIS literature, allowing for the identification of those relationships considered more fruitful to enhance innovation processes from a local perspective.

To capture both aspects of LIS’s relational dimension (i.e. network structure and network portfolio of relationships) and our paper adopts an explorative approach, by taking evidence from the empirical study of the Biopharma LIS in Greater Boston Area (GBA), which has been exemplified as a benchmark case in terms of LIS successful performance. Our empirical study combines two methods, namely Social Network Analysis and Expert Interviews. Firstly, we perform a social network analysis to gain insights about the optimal network structure and secondly, we conduct a round of semi-structured interviews with key stakeholders in the system in order explore the characteristics of the desirable network portfolio. Our findings show that a successful LIS presents an open network structure with structural holes, a high level of modularity and a portfolio of relationships that privileges informal and non-
redundant ties within small communities built around specific themes.
ANALYZING THE RELATIONAL DIMENSION OF LOCAL INNOVATION SYSTEMS. AN EXPLORATIVE ANALYSIS OF A SUCCESSFUL CASE STUDY

1. Introduction

In the last decades we assisted to a progressive spatial concentration of innovation activities in specific geographical areas characterized by a vibrant atmosphere due to the synergetic co-location of research centers, innovation–driven enterprises, large corporations and capital providers bound by horizontal and vertical relationships. In many cases, the physical proximity of a diverse community of actors engaged in innovation activities provides the context for new business formation, socio-economical regional growth and knowledge production at the global and local level, with interesting implications in terms of co-evolutionary dynamics at the social, technological and environmental levels. Scholars from both management and economic geography have labelled these environments as Local Innovation Systems (LIS) which stand upon two basic understandings. Firstly, the shift from the linear conception of innovation process towards the idea of innovation as a result of a systemic and interactive process (Chesbrough, 2003) among actors of different nature (Etzkowitz and Leydesdorff, 1995) and secondly, the relevance of the territorial variable in stimulating innovation (Lundvall and Johnson, 1994). Extant literature provides a variety of conceptual definitions of LIS (Cooke et al. 1997; Doloreux 2002; Todtling and Kauffmann 1999; Norton 2007; Morrison 2003; Canzanelli and Loffredo 2008; Rahayu and Zulhamdani 2013; Asheim and Isaksen 1997; Muscio 2006; Hamaguchi 2008; Russell 2011) according to which a LIS’ main elements can be traceable to: (i) a network of innovative firms, bound by horizontal and vertical relationships embedded in a spatially defined area; (ii) a number of large corporations that establish a branch in the area and outsource part of their R&D activities; (iii) a set of research and educational institutions, (e.g. universities and research centers) which generate analytic base knowledge that contributes to innovative processes; (iv) a number of initiatives and programs led by public institutions supporting knowledge exchange and innovation within the region; (v) a community of capital risk providers (e.g. venture capitalists, business angels) involved in activities of innovation scouting to diversify their portfolio of investments; (vi) a series of infrastructure and facilities that incentivize the localization of innovative firms within the given area (e.g. incubator); (vii) a great number of synergetic relationships among all these actors that promote the flow of knowledge, capital, and other vital resources for the growth of the system. The simultaneous presence of all above elements within the LIS refers to an ideal situation where the system is fully developed and
grounds on the observation of benchmark cases of success where all the listed elements are in place, e.g. Silicon Valley or Kendall Square in Boston.

Extant literature tends to appoint the successful performance of systems of innovations to the heterogeneous composition of their actors or to their ability to produce new knowledge and to contribute to the regional economic growth. More specifically, existing contributions on LIS can be divided in two broad groups. The first, which follows an Input-driven approach, mainly focuses on the drivers of LIS performance, as the actors’ heterogeneous composition (e.g. Etzkowitz, 1993 and Etzkowitz and Leydesdorff, 1995; Budden and Murray, 2015; Carayannis et al, 2006-2016); the spatial dimension (e.g. de la Mothe and Paquet 1998; Cooke 2001, 2004; Asheim and Coenen, 2005); the infrastructural endowment and policy incentives (e.g. R&D expenditure; Venture investments; incubators and acceleration programs) and finally, the relational dimension (e.g. Saxenian, 1994; Ahuja, 2000, Owen-Smith and Powell, 2004; Russell et al., 2015), with specific regard to the creation of synergetic connections and cooperative mechanisms existing between the system’s components.

The second group, i.e. Output-driven approach, privileges the focus on the effects of LIS creation in terms of production of new knowledge and contribution to the regional growth (e.g. Bajmocy, 2012; Campanella, 2014; Guan and Chen, 2010; Lerro and Schiuma, 2015).

This work positions itself in the first stream of studies (input-driven approach) and more specifically, within the stream that focuses on the relational dimension of LIS, starting from the assumption that the mere co-location of LIS’s actors per se does not necessarily identify a LIS as such (Russell, 2015) and that the bottom-up creation of synergies and cooperative mechanisms between local actors are the drivers for the well-functioning of a LIS given the advantages in terms of knowledge transfer, access to resources and pooling of complementary capabilities (Ahuja, 2000), thus contributing to both innovation creation and regional economic growth.

In particular, existing studies explore the relational dimension of LIS with respect to two separate aspects of analysis: network structure and network composition, i.e. the level of connectivity among the system’s actors and the portfolio of different types of relationships and forms of cooperation that local actors put in place to produce innovation. Nevertheless, extant studies find contrasting results regarding the characteristics of LIS relational structure and composition, and limit their analysis to the mechanisms driving network emergence and the role of inter-nodal proximity without considering the importance of different kinds of relationships for knowledge transfer. Furthermore, most contributions tend to limit their analyses to the observation of formal and inter-firm relationships, thus failing to
highlight the variety of knowledge channels and the heterogeneous actors’ composition, which are two typical features of LIS. In order to fill these gaps and in an attempt to capture both aspects of LIS’s relational dimension (Network structure and Network Portfolio composition), this work aims to answer to the following research questions: (RQ1) What is the configuration of the network structure of a successful Local Innovation System? And secondly, (RQ2) What is the portfolio of relationships implemented in a successful Local Innovation System?

To answer to our research questions our paper adopts an explorative approach, by deriving propositions from the empirical study of the Biopharma LIS in Greater Boston Area (GBA), which has been exemplified as a benchmark case in terms of LIS successful performance. Our empirical study combines two methods, namely Social Network Analysis (SNA) and Expert Interviews. More specifically, firstly, we perform a SNA to gain insights about the optimal network structure (RQ1), and secondly, we conduct a round of semi-structured interviews with key stakeholders in the system in order explore the characteristics of the desirable network portfolio (RQ2). The remainder of the paper is organized as follows: section two reviews extant contributions on LIS relational dimension, identifies the literature gaps and formulates the research questions. Section three illustrates the research strategy adopted for addressing the theoretical gap and the research techniques implemented for the empirical case study of Greater Boston Area Biopharma LIS. Main results are reported and discussed in section four, before concluding.

2. Theoretical Background

Extant studies on innovation systems have started to analyze the network dimension as a further variable of LIS performance. In particular, studies focus on two aspects: the structure of the network of relationships within a LIS, and the types of relationships implemented by the different LIS actors. While the first aspect is generally framed within the traditional debate characterized by two contrasting visions about the desirable structure of networks, namely the Coleman’s Network closure (Coleman 1988) and the Burt’s Structural hole arguments (Burt 1992), the latter refers to the nature of ties (strong vs. weak; formal vs. informal) that the network’s actors choose to establish with their partners in their innovation practices. Contrasting visions characterize the debate on which relational structure ensures a better performance and main arguments relate to the trade-off existing between the potential for innovation deriving from weak and informal ties and the trust-based exchange of information resulting from strong ones.
The seminal work of Saxenian (1994) represents a first attempt to relate the structure of networks to the performance of regional clusters: the more decentralized and horizontal industrial system of Silicon Valley seemed to outperform Route 128, which, conversely, was recognized as a network dominated by a few large firms, with a high degree of vertical integration that privileges practices of secrecy and corporate hierarchies.

Later on, scholars from innovation systems literature started to empirically study the relational dimension of LIS by adopting a social network approach. With the aim of relating the network structure to firms’ innovation output, Ahuja (2000) developed a comparative empirical study of collaborative linkages (financial and R&D cooperation) in Japan, United States and Western Europe in the chemical industry, emphasizing the importance of indirect ties in a firm’s ego-network for its innovation performance. From a similar regional standpoint, Kajikawa et al. (2010) focused on a more traditional set of customer-supply relationships to conduct a comparative analysis on eight regional Clusters in Japan to explore the role of bridging organizations across different industries and provide a framework to analyze multiscale structure of inter-firm networks from a Small World perspective. Small World properties (i.e. average path length and clustering coefficient) typically combine both Burt’s and Coleman’s rents and the authors found out that in networks with high small world properties, the number of connector firms is larger than those networks presenting lower small world properties. From a more sectorial perspective, Balland et al. (2013) explored the emergence of inter-firm networks in the video game industry by investigating product co-development relationships among firms, suggesting that – as the industry matures – firms tend to prefer to partner over short distances and with more cognitively similar organizations.

More recent studies have started to consider a wider portfolio of formal inter-firm relationships as in the case of Russell et al. (2015) and Still et al. (2013) who gathered relational data on R&D, finance, commercial, custom-supply, IP transfer and manufacturing links to explore and describe the network infrastructure of spatially defined innovation systems in the three metropolitan areas of Austin, (Texas, US); Minneapolis, (Minnesota, US); Paris (France) and in the Finnish ecosystem, respectively. The authors provided an evidenced based approach to illustrate how network metrics can be valuable resources to analyze the complexities of “engagement, agility, vitality, linking and embeddedness in innovation ecosystems” and suggest their usefulness for network orchestration and evidence-based policies.
Shifting the focus to the individuals, Cassi and Plunket (2015) analyzed co-patenting relationships among French researchers in the field of genomics to investigate the impact of proximity on the dynamics of network formation. The findings suggest that geographical, technological and organizational proximities strongly determine the likelihood of network formation but that, once the network is established social proximity prevails. Similarly, Ter Wal (2014) analyzed the evolution of co-inventor networks’ structure in German biotechnology, arguing that the role of geographical proximity decreases as the technological regime experiences a shift from tacit to more codified knowledge.

While the above-mentioned studies limit their analysis to inter-firm networks, Owen-Smith and Powell (2004) are among the first to consider the organizational heterogeneity in innovation networks by analyzing contractual linkages among dedicated biotech firms, public research organizations, VC firms, government agencies and biopharma companies in the Boston biotechnology innovation system, suggesting that the node’s organizational form alter the flow of information through a network. More specifically, they found that the extent to which information is transmitted in a network is function of whether the key nodes that anchor a networks pursue private or public goals suggesting that institutional and legal arrangements that secure direct information transmission are a result of participant commitment and effort. Balland et al (2012) explored network evolution dynamics in the technological innovation system of global navigation satellite system (GNNS) by analyzing formal collaboration within EU R&D partnerships among large companies, SMEs, Research institutes, Public Agencies and Non-profit, showing that geographical, organizational and institutional proximity favor collaborations, while cognitive and social proximity do not play a significant role. More recently, Broekel and Mueller (2017) studied the characteristics of critical links in technology-specific subsidized knowledge networks in Germany by empirically analyzing links among universities, firms, research institutes and other types of organizations and showed that first, critical links tend to be formed among regional gatekeepers that offer related knowledge resources and that secondly, the links bridge institutional distances by exploiting the benefits of geographic and social proximity.

A more limited number of scholars have chosen to address the empirical challenges of considering informal, rather than contractual, relationships in their empirical studies, with the exception of Dahl and Pedersen (2004), who investigated the regional cluster of wireless communication firms in Northern Denmark to study the effect of informal networks among engineers on innovation system growth dynamics, suggesting their key role in knowledge diffusion within the system.
Finally, one of the only attempts to provide a more comprehensive picture of innovation systems’ relational dimension was provided by Salavisa et al (2012) who explored networking variety in biotechnology and software innovation systems by considering - at the same time - the different role of both formal and informal relationships among firms to access both knowledge and complementary assets, suggesting that their effect is mediated by different knowledge bases. More precisely, the authors found that, as far as biotechnology is concerned, the informal knowledge network tend to be structured in sub-groups with frequent inner connections, i.e. *knowledge epistemic communities* and that universities play a key role of informal knowledge provider since they have a bridging position among communities. From the review of above literature, it emerges that most contributions employing a network approach for the study of innovation systems’ performance limit their analysis to the mechanisms driving network emergence and the role of inter-nodal proximity in knowledge transfer, without providing insights about the network structure itself. Also, these studies mainly focus on inter-firm relationships, thus overlooking the heterogeneous nature of a system’s components, which is an important driver for the production of new knowledge and rather privilege the analysis of strong and formal ties, overlooking the potential of informal and weaker ties. Finally, extant literature, with a few exceptions, does not address the variety of inter-organizational relationships, thus failing to gain insights into the optimal network portfolio composition.

3. Methodology

3.1. The methodological approach and research design

In order to answer to our research questions, this work conducts an exploratory, data-driven and qualitative empirical case study. Case study research allows for the exploration and understanding of complex issues and its robustness as a research strategy it is particularly appreciated when an in-depth and holistic approach is required. More specifically, this study conducts an exploratory critical single case study. Compared to multiple or collective case studies, a single case study is more adequate when the case itself is either a representative or typical case, as in the current research. Also, in our case, a critical case study would allow for formulating propositions to be tested in future research, starting from the selection of a case study that meets all conditions that we are willing to explore (Yin, 2003; Streb, 2010).

We decided to perform our empirical study in the case of the Greater Boston Area (GBA) Biopharma system. Due to its high ranking position among U.S. Biotech Clusters rankings (JJL U.S. Life Science,
The Greater Boston Area (GBA) is renowned as the leading US Life Science cluster for the number of patent ownership per capita, venture capital funding and number of IPOs. The region is home to many of the leaders in tech and life science as well as world-class academic and research institutions as Harvard and the Massachusetts Institute of Technology (MIT). The area hosts approximately 250,000 students across 52 higher education institutions and can rely on the largest concentration of life science researchers in the country, as well as world-class medical facilities, including the top three NIH-funded hospitals. As a result of direct access to top talent, the GBA system has attracted a dynamic community of investors. More precisely, VC funding is of 2,580 million of dollars, which represents the 38% of the total funding of United States in GBA, which in turn, makes the area particularly attractive to innovative entrepreneurs (JJL U.S. Life Science, 2016)

The empirical case study in this paper is articulated in two phases. Firstly, in order to define the network structure, we developed a network analysis of the cluster to explore the number and the nature of the formal relationships among business, academic, corporate, start-up and government entities. The results of the SNA suggest insights about the optimal network structure (RQ1), as SNA has been widely used and proved its efficacy for representing the features of the network structure configurations by providing visual and quantitative information on the level of openness and closure through a variety of specific indicators. However, the exclusive use of this methodology does not allow capturing the whole variety of relationships occurring within an innovation system. More specifically, the relational data available in databases are usually indicators of formal relationships (financial, commercial and R&D). However, it is widely accepted that one of the main advantages deriving from geographical propinquity is the opportunity to exchange information through informal channels resulting from the establishment of personal relationships among co-located actors. These informal ties are generally excluded from quantitative relational data and to overcome this limitation and gain insights about network portfolio, SNA technique is complemented with qualitative expert interviews. For these reasons, we conducted a round of semi-structured interviews with key stakeholders in the system in order to gain insights into the desirable network portfolio mix by also including the informal relationships, for the transfer of knowledge. The conversation with opinion leaders allow for insights on the advantages of being in spatial proximity with partners and on the specific types of relationships that best contribute to the knowledge transfer and to the innovation process (RQ2).

3.2 Social Network Analysis
**Sample description.** To explore data-driven network analytics by taking into account the diversity of the LIS’ community, we selected the sample based on their memberships to MassBio, the freely available membership directory of the Massachusetts Biotechnology Council. MassBio counts more than 975 members dedicated to advancing cutting-edge research in life science industry in Massachusetts and provides information on their location, typology and area of specialization. Members range from academic hospitals and non-profit organizations to pharmaceutical biotech companies and capital providers. We selected those organizations with headquarters or branch offices having mailing addresses in the metropolitan areas of Greater Boston. The spatial identification of each area included the suburban city names associated with respective identification of that metropolitan area, counting more than 50,000 inhabitants (U.S. Census Bureau, 2015). Additionally, we included in the sample only those members belonging to the Biopharma industry mainly specialized in drug development. The final sample counts 450 organizations distributed as follows: 85 Academic Hospitals & Non-Profit Organizations (Universities, Research Institutes, Hospitals, Government Agencies, Incubators); 61 Capital Risk Providers (VC, CVC, Hedge Funds, PE Firms); 304 Pharma-Biotech firms (62 Large firms, 198 SMEs, 44 Start-ups). Figures 1 and 2 report the geographical distribution of our sample and main areas of specialization of nodes’ activities.

**Data Collection.** To reveal insights about the overall innovation system’s structure and create the final dataset, we relied on two sources of relational data. More precisely, to collect data on venture deals, we used Preqin Dataset (Prequin Ltd. 2017), which is a comprehensive and historical database on the private equity industry offering detailed information and analytics on firms, funds, deals and portfolio companies dating back to 1999 on over 5,000 funds and 11,000 hedge funds. We selected venture deals (i.e. Series A-E/Round 1-5; Grant; Seed; PIPE; Add-on; Venture Debt) between portfolio companies and investors located in Massachusetts (U.S.) completed within the last five years (2012-2017) in Biotechnology and Pharmaceutical Industries and matched with our sample. To gather information on the other kinds of formal relationships: R&D cooperation partnerships (including Trial Collaboration); Licensing agreements (including Reverse licensing); Purchase of Intellectual Property (including Product or Technology Swap; Spin-Out and Spin-Off; Joint Ventures, we collected data from the Strategic Transactions Database (Pharma & MedTech Business Intelligence) that summarizes deals by type, industry and sector from 1995 to date. We collected this information within 2012 – 2017-time frame.
We have finally integrated these two databases into a single dataset on networks consisting of 450 nodes and 323 links. The links are non-directed in order to measure small world properties (Kajikawata, 2010). We observed 148 Venture deals and 141 Strategic Alliances (Figure 3).

Data analysis. To present the data and its metrics in a visual form we used NodeXL, an interactive network analysis software that implements a set of key functionalities for visual network analytics and metrics computation. We used a force-driven algorithm where nodes repel each other and edges pull the connected nodes together to gain insights on the spatial structure of relationships (Russell et al., 2015). In graph theory, force-driven layout reveals the macro-level structure of the network including the key clusters, the key brokers in the network, as well as possible structural holes (Burt, 1992). Also, color-coding was added to provide information about the frequency of the tie (measured by counting the number of interaction in the timeframe), nodes’ localization within GBA and to differentiate the types of edges. Tie data allowed us to calculate measures of network structure that we used to evaluate the level of embeddedness of the network and to classify individual ties by their type: (i) R&D strategic alliances (i.e. R&D co-development and clinical trials), (ii) Venture Deals, (iii) Joint Ventures, (iv) IP transfer (which includes licensing agreements, product purchase, technology swap and acquisition of intellectual property rights); (v) Spin-Off/Spin-Out.

3.3 Interviews with Key informants

In order to gain insights about the most desirable network portfolio mix, a round of semi-structured expert interviews was organized and carried out with 9 key informants who have been chosen as representatives of the different categories of stakeholders in the Biopharma innovation system of Greater Boston Area (3 start-ups, 1 university, 1 large biopharmaceutical, 2 biotech firms, 1 spin-off, 1 public agency). The interviews have been conducted directly by the authors. The list of participants who took part in each interview is reported in Table 3. Assuming that the conditions that distinguish LISs from other forms of territorial aggregations (e.g. Industrial Districts) and a-spatial innovation systems (e.g. technological/sectorial systems of innovation) are: (i) the existence of knowledge-intensive relationships for the combination of non-existing knowledge (analytic base of knowledge), and (ii) the embeddedness of the LIS’ actors found in spatial proximity, which in turns allows easier access to information (Ferretti and Parmentola 2015), insights on the LIS successful network composition have been gained by exploring: (i) which relationships have a greater impact on knowledge transfer, and (ii) for which relationships being in spatial proximity with the partners was more valuable. The experts were asked to discuss those types of relationships that were more frequently
implemented in their practices of innovation processes and provide insights on those that best contribute to knowledge transfer and about the importance of being in spatial proximity with the partners for each specific type of relationship.

Figure 1. Geographical distribution – MassBio members in GBA (2012-2017)

Source: authors’ own elaboration from MassBio

Figure 2. Areas of specialization- MassBio members in GBA (2012-2017)

Source: authors’ own elaboration from MassBio

Figure 3. Data sources
<table>
<thead>
<tr>
<th>Source of Data</th>
</tr>
</thead>
</table>
| **Preqin dataset**  
Preqin Ltd. 2017 |
| **Strategic Transactions Database**  
(Pharma & MedTech Business Intelligence) |
| Source: authors’ own elaboration |

<table>
<thead>
<tr>
<th>Ecosystem entities</th>
</tr>
</thead>
<tbody>
<tr>
<td>BigPharmas, Biotech firms, Start-ups; Risk Capital providers</td>
</tr>
<tr>
<td>BigPharmas, Biotech firms, Start-ups; Risk Capital providers; Academic, Hospital and non-profit institutions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Types of relationships</th>
</tr>
</thead>
</table>
| **Venture deals** (148)  
between firms and investors co-located in the GBA |
| **Strategic Alliances** (141)  
R&D and Marketing – Licensing; Purchase of Intellectual Property; Spin-Out; Spin-Off; Trial Collaboration; Reverse licensing; Product purchase; Product or Technology Swap; Joint Venture; Intra Biotech Deals; Marketing-Licensing |

Source: authors’ own elaboration

**Table 3.5. Expert interviews – List of participants**

<table>
<thead>
<tr>
<th>Position</th>
<th>Organization</th>
<th>Stakeholder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Professor</td>
<td><em>MIT Dept. of Chemical Engineering</em></td>
<td>University and Research institutes</td>
</tr>
<tr>
<td>General Counsel and Vice-President for Academic and Workforce Program</td>
<td><em>Massachusetts Life Science Center</em></td>
<td>Government</td>
</tr>
<tr>
<td>Chief Executive Officer</td>
<td><em>Obsidian</em></td>
<td>Entrepreneurship – Biotech</td>
</tr>
<tr>
<td>Chief Executive Officer</td>
<td><em>Angiex</em></td>
<td>Entrepreneurship – Start-up</td>
</tr>
<tr>
<td>Chief Executive Officer</td>
<td><em>Kymera Therapeutics</em></td>
<td>Entrepreneurship – Start-up</td>
</tr>
<tr>
<td>Chief Executive Officer</td>
<td><em>Revive-med</em></td>
<td>Entrepreneurship – Spin-off</td>
</tr>
</tbody>
</table>
4. Findings

4.1 Social Network Analysis

The network resulting from the sample of organizations consists of 166 connected nodes and 323 edges, with a diameter of 13. From the analysis of network composition, it emerges that venture deals represent the most frequent type of interaction in our sample (56%), followed by R&D strategic alliances (21%) and IP transfer (21%). Finally, joint ventures and academic spin-offs / corporate spinouts represent only the 2% of the network portfolio, each (Figure 4.1).

Figure 4. Network portfolio composition – Greater Boston Area (2012-2017)

At the organizational and the individual level, we have calculated centrality metrics, which generally indicate the number of connections, the frequency of occurrence on paths between others and the diversity of connections. These indicators are generally used to identify those nodes that are well positioned to influence the network or to channel information (Freeman, 1979). Table 4 reports the top
twenty actors in terms of degree centrality, betweenness centrality and closeness centrality. Degree Centrality is typically an indicator of engagement as it exemplifies the number of connections for a given vertex, providing information on its immediate connectivity, popularity and influence in the networks. Indeed, nodes in a position of high centrality are of particular attractiveness within the network which, in turn, leads new entering nodes to partner with them (Barabasi and Albert, 1999). In our sample, top positions are occupied mainly by large pharmaceutical companies with a venture arm (e.g. Astrazeneca Pharmaceutical, LP; Pfizer, Inc.; Celgene) and large venture capital firms (e.g. New Enterprises Associates; Third Rock Ventures; Polaris Partners), suggesting their propulsive role in the system’s development since, especially for venture firms, the relationships may be key for partners’ survival or for market access. Similar results are obtained by identifying the top 20 actors for betweeness centrality (Freeman, 1979), which, by providing information about the number of times that a given node appears in the shortest path from all nodes in the network to all others, is an indicator of the extent to which a node brokers indirect connections among all other nodes in the network. The holes in social structure, i.e. structural holes, thus provide a competitive advantage for those actors whose connections span the holes, which in turn, act as buffers by separating non-redundant sources of information (Burt, 2002). Additionally, firms who are positioned in structural holes may have more opportunity of brokerage activities, by serving as bridges among relatively unconnected parts of the network. As a consequence, high betweenness centrality shows the importance of a node in bridging the different parts or components of the network together. Interestingly, differently from degree centrality’s top positions, the list of actors with the greatest level of betweenness centrality includes, apart from big pharmas and venture capital firms, also smaller biotech firms and startups (e.g. Catabasis Pharmaceuticals; Syndax Pharmaceuticals; Unum Therapeutics; Neon Therapeutics) suggesting that brokering positions are not necessarily undertaken by those actors that are greater in seize and with a more influential position. A completely different hierarchy is achieved by computing metrics of closeness centrality, which calculates the mean length of all shortest paths from a vertex to all the other ones in the network. It is a measure of reach in the sense that it indicates the speed with which information can reach other nodes from a given starting vertex. As consequence, nodes with the highest closeness centrality hold a position where they have the quickest access to emerging information, e.g. pulse-taker (Brass, 1981). Top positions are in this case occupied by smaller manufacturing biotech firms (e.g. Gen9, Inc.; Ginkgo BioWorks; GreenLight Biosciences) and to a lesser extent by big pharmas and venture capital firms (e.g. Pfizer, Inc., Moderna, AstraZeneca Pharmaceuticals LP, Rhythm Pharmaceuticals, Inc., Merck & Co., Inc., Wellington management).
unveiling that an important source of informational advantage may derive from a position of receiver of externalization of R&D activities.

Table 4. Top 20 actors for centrality scores – Greater Boston Area (2012-2017)

<table>
<thead>
<tr>
<th>Vertices</th>
<th>Degree Centrality</th>
<th>Vertices</th>
<th>Betweenness Centrality</th>
<th>Vertices</th>
<th>Closeness Centrality</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca Pharmaceuticals LP</td>
<td>12</td>
<td>AstraZeneca Pharmaceuticals LP</td>
<td>1640,518111</td>
<td>Gen9, Inc.</td>
<td>1</td>
</tr>
<tr>
<td>Third Rock Ventures</td>
<td>12</td>
<td>Moderna</td>
<td>1559,506416</td>
<td>Ginkgo BioWorks</td>
<td>1</td>
</tr>
<tr>
<td>Pfizer, Inc.</td>
<td>12</td>
<td>RA Capital</td>
<td>1481,039692</td>
<td>GreenLight Biosciences</td>
<td>1</td>
</tr>
<tr>
<td>Celgene</td>
<td>11</td>
<td>Ra Pharma</td>
<td>1391,164228</td>
<td>Kodiak Venture Partners</td>
<td>1</td>
</tr>
<tr>
<td>Moderna</td>
<td>9</td>
<td>Third Rock Ventures</td>
<td>1348,30687</td>
<td>Rapid Micro Biosystems, Inc.</td>
<td>1</td>
</tr>
<tr>
<td>New Enterprise Associates</td>
<td>9</td>
<td>Pfizer, Inc.</td>
<td>1324,328027</td>
<td>TPG Biotech</td>
<td>1</td>
</tr>
<tr>
<td>Fidelity Management &amp; Research Company</td>
<td>9</td>
<td>Rhythm Pharmaceuticals, Inc.</td>
<td>1204,029593</td>
<td>INVERSCO Asset Management</td>
<td>0,166667</td>
</tr>
<tr>
<td>CRISPR</td>
<td>9</td>
<td>Celgene</td>
<td>1197,555191</td>
<td>SciFluor Life Sciences, LLC</td>
<td>0,142857</td>
</tr>
<tr>
<td>Unum Therapeutics</td>
<td>8</td>
<td>New Enterprise Associates</td>
<td>1140,367992</td>
<td>Vedanta Biosciences</td>
<td>0,142857</td>
</tr>
<tr>
<td>Novartis</td>
<td>8</td>
<td>MPM Capital</td>
<td>1139,845167</td>
<td>Allied Minds</td>
<td>0,1</td>
</tr>
<tr>
<td>AbbVie Biotech Ventures</td>
<td>8</td>
<td>Lightstone Ventures</td>
<td>1029</td>
<td>PureTech Ventures</td>
<td>0,1</td>
</tr>
<tr>
<td>Merck &amp; Co., Inc.</td>
<td>8</td>
<td>Fidelity Management &amp; Research Company</td>
<td>990,360021</td>
<td>Pfizer, Inc.</td>
<td>0,002123</td>
</tr>
<tr>
<td>MPM Capital</td>
<td>7</td>
<td>Wellington management</td>
<td>965,928655</td>
<td>Moderna</td>
<td>0,002012</td>
</tr>
<tr>
<td>Wellington management</td>
<td>7</td>
<td>CRISPR</td>
<td>958,276947</td>
<td>AstraZeneca Pharmaceuticals LP</td>
<td>0,002</td>
</tr>
<tr>
<td>Syndax Pharmaceuticals</td>
<td>7</td>
<td>Catabasis Pharmaceuticals</td>
<td>899</td>
<td>Rhythm Pharmaceuticals, Inc.</td>
<td>0,001984</td>
</tr>
<tr>
<td>Alexandria Venture Investments</td>
<td>7</td>
<td>Syndax Pharmaceuticals</td>
<td>838,574509</td>
<td>Merck &amp; Co., Inc.</td>
<td>0,001984</td>
</tr>
<tr>
<td>Atlas Venture</td>
<td>7</td>
<td>Unum Therapeutics</td>
<td>792,342353</td>
<td>Wellington management</td>
<td>0,001972</td>
</tr>
<tr>
<td>Sanofi Genzyme</td>
<td>7</td>
<td>Neon Therapeutics</td>
<td>720,947721</td>
<td>Novartis</td>
<td>0,001946</td>
</tr>
<tr>
<td>Polaris Partners</td>
<td>7</td>
<td>Novartis</td>
<td>685,485807</td>
<td>WaVe Life Sciences</td>
<td>0,001927</td>
</tr>
<tr>
<td>RA Capital</td>
<td>6</td>
<td>Alexandria Venture Investments</td>
<td>671,879417</td>
<td>Syndax Pharmaceuticals</td>
<td>0,001923</td>
</tr>
</tbody>
</table>
At the *structural level*, metrics of density, average degree, modularity and small worlds properties have been computed to gain insights about the overall configuration of the network (Table 5). Values of density close to 0 indicate that the network is poorly connected, and conversely, when these are proximate to 1, they exemplify a high level of connectivity in the network. In the case of GBA Biopharma LIS, the graph shows a low value of density (0.0026), suggesting that the network is relatively sparse (Balland et al., 2012) and characterized by the presence of structural holes (Ahuja, 2000). The average degree, i.e. the average number of available connections per entity, reveals insights about the relational potential and expresses, on average, the number of organizations’ partners. In the case of GBA Biopharma LIS, the average degree value (1.178) indicates a low-medium level of engagement by the network’s actors with partners in spatial propinquity (Kajikawata et al., 2010; Still et al., 2010 and Salavisa et al., 2012). At the meso-structural level, modularity scores (0.510) and the high number of connected components (289) suggest a high tendency of network’s actors to form small sub-groups where interactions occur more easily. In fact, a connected component of an undirected graph is a maximal set of nodes, in a way that a path connects each pair of nodes. Connected components constitute a partition of the set of graph nodes, which means that connected components are non-empty, but rather pairwise disjoints, and the union of connected components constitutes the set of all nodes. Additionally, we analyzed the network from a *small world* perspective, by calculating the average path length and the average clustering coefficient (Watts and Strogatz, 1998). Following Kajikawata (2010), the average path length, i.e. the average graph-distance between all pairs of nodes, is fundamental for the assessment of the network performance as it indicates that a node can have an easier and quicker access to other actors with less efforts, thus accessing to a larger amount of knowledge or information. Generally speaking, a small value of average path length indicates a small diameter of the network, which in turns suggests that organizations in the network can pool resources through a smaller number of paths and structural holes are buried. Clustering coefficient represents the extent to which nodes connected to *i* are also linked to each other and the average cluster coefficient shows the system’s overall connectivity based on local relationships, suggesting a greater accumulation of social capital. It is argued that small world configuration allows achieving both advantages of closed and open networks. In fact, while, a network with a small path length sustains network closure (as it allows information to circulate more easily and quickly through a less number of paths and structural holes) a network with high clustering coefficient suggests that a larger social capital is accumulated, which is a benefit of open and sparser networks. The GBA innovation system presents relatively high values for the first small world property, i.e. average geodesic distance (4.428), and
relatively low for the second one, i.e. clustering coefficient score (0.014) (Kajikawa et al., 2010), thus confirming its structural tendency toward a more open configuration, with specific implications in terms of a more diversified relational capital through less redundant and weaker ties. Visualisation of the GBA network is provided in Figure 4 that highlights the tendency of forming dyadic and triplets forms of interactions and includes labels for the most central actors. In conclusion, the GBA Biopharma LIS appears to be characterized by an open structure with structural holes and the tendency of vertices to form small groups where interactions are more frequent. Finally, most influential position and bridging functions appear to be mainly undertaken by large venture capital firms and pharmaceutical companies with a venture arm. However, due to the lack of exact benchmark parameters for network structural metrics in the network literature, these results mean to be taken as a reference for future comparative analysis.
**Table 5. Social Network Analysis Metrics - Greater Boston Area (2012-2017)**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td># nodes</td>
<td>444</td>
</tr>
<tr>
<td># edges</td>
<td>323</td>
</tr>
<tr>
<td>Ratio edge-to-node</td>
<td>1.41</td>
</tr>
<tr>
<td>Network Diameter</td>
<td>13</td>
</tr>
<tr>
<td>Average Degree</td>
<td>1,178</td>
</tr>
<tr>
<td>Graph Density</td>
<td>0,0026</td>
</tr>
<tr>
<td>Modularity</td>
<td>0.510</td>
</tr>
<tr>
<td>Connected components</td>
<td>289</td>
</tr>
<tr>
<td>Avg. Clustering Coefficient</td>
<td>0.014</td>
</tr>
<tr>
<td>Average Geodesic Distance</td>
<td>4,428</td>
</tr>
<tr>
<td>Average Betweenness Centrality</td>
<td>91,827</td>
</tr>
<tr>
<td>Average Closeness Centrality</td>
<td>0.015</td>
</tr>
<tr>
<td>Average Eigenvector Centrality</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Source: author’s own elaboration
Figure 5. The GBA Biopharma LIS

Social media network connections

Created with NodeXL Basic (http://nodexl.codeplex.com) from the Social Media Research Foundation (http://www.smrfoundation.org)
4.2 Expert interviews

From the results of expert interviews, it emerged that the most frequent practices of innovation-driven interactions, including informal relationships, with the actors in the area are: (i) Value Added Supply agreements (ii) Venture Capital and Seed investments (iii) Agreements for the access and use of infrastructure (iv) Co-participation in thematic associations and symposia (v) Board interlocks (vi) Formal and informal industry-university agreements for the mobility of human resources (vi) Sponsored research (vii) Intellectual Property transfer and (viii) R&D strategic alliances.

Figure 6 reports the extent to which, according to the experts, above types of interactions contribute to the knowledge transfer and their degree of formalization. Most formal types of relationships report low scores for knowledge transfer (i.e. Value Added Supply, R&D Strategic Alliances, IP transfer and Sponsored research) while all low-formal relationships report a relative high score for knowledge transfer except in one case, i.e. Board interlocks. The relationships that contribute more to the knowledge transfer are two informal (i.e. Co-participation in thematic associations and symposia; industry-university mobility of human resources) and two formal (Agreements for the Access and Use of Infrastructure and Venture Capital and Seed investments).

With regards to Co-participation in thematic associations and symposia, as in the case of the Neuroscience Consortium, which was created by Mass Life Science with the aim of filling the gaps in research funds through the organization of periodical operative meetings between different stakeholders in the field of neurodegenerative diseases, it emerged that this practice was particularly important for knowledge transfer as it allows the sharing of experiences in the pre-commercial phase, i.e. target identification and validation. One of the main issues is that failures in the industry are not generally published and therefore, bringing around the table different stakeholders allows avoiding the duplication of efforts, including mistakes, thus avoiding redundancy of information and enhancing innovation potential. Other indirect benefits to knowledge transfer deriving from this type of practice, regard primarily the achievement of time and cost efficiencies in relationship-seeking activities, and secondly, the alignment of visions and missions of the different epistemic communities by promoting dialogue among them and leading to a collective resolution of problems. Proximity is also particularly important, as it enables to enhance interactions outside the association’s meetings and building trust mechanisms, which are particularly valuable if we consider that many of the members are competitors and their frequent interactions contribute to align their vision.
As for the *Agreements for the access and use of infrastructure*, the advantages in terms of knowledge transfer reside in the spillover effect of the environment provided by hosting organizations. Apart from the well-known advantages in terms of visibility and costs efficiencies deriving from renting a space within an innovation center, it is also the opportunity of casual encounters with industry operators that enhances the chance of knowledge exchange. Also, incubators and accelerators generally offer services of business consultancy to scientists and engineers that lack capabilities in this field. As for geographical proximity, this is at the core of the innovation centers concept, some of the experts that we interviewed have operations in different of these centers and therefore, it is clear that operating in the same area of the hosting structure is fundamental. According to the experts, embeddedness itself is favored by the presence of incubators and co-working spaces that multiply the networking opportunities thanks to their strategic design that promotes casual encounters.

*Venture Capital and Seed investments* relationships turn out to be ground for the transfer of new knowledge due to the complementarity of the skills between innovative firms’ scientific know-how and investors’ support for business operations. As reported by Kymera’s CEO, especially in the case of funding VC, the start-up is usually provided with support regarding every aspect of the business management, including assistance for hiring the right people and for seeking potential partnerships to exploit the developed innovation at its best. In this case, the importance of spatial proximity is mainly explained by the frequency of interactions required –especially at the seed stage - and the need of establishing trust mechanisms with the partners. Proximity allows to have more frequent interactions with a network of operators in the area that may eventually function as a talent validation device, which turns out to be particularly useful for risky operations as in the case of VC and seed funds. While exploring the relationship between Kymera and Atlas Venture – a VC company headquartered in Kendall Square (Cambridge, MA) - it emerged that it is not uncommon for VC to host their portfolio companies in their office spaces. Also, especially in the case of VC founders, relationships tend to be long-term, thus implying an investment not only in money but also in time, which – as reported by Alnylam’s CEO – allows for a more efficient corporate resource management.

*Formal and informal industry-university agreements for the mobility of human resources* are deemed by the experts to be one of the most fruitful relationships in terms of knowledge transfer. The Massachusetts Life Science Internship Challenge and the Northeastern Co-Op (Cooperative Education and Career Development) are some of the examples appointed as best practices in promoting knowledge transfer between industry and academia. The former provides a platform to facilitate the
placement of college students in Life Science by subsidizing paid internships hosted by companies in the area, while the latter constitutes a powerful learning model that promotes intellectual and professional growth by integrating classroom learning with practical experience. In so doing, to the one hand, real-world experience enhances the potential for innovation of academic human capital and on the other, the employer partners pursue a cost-effective strategy for hiring and training talented workforce.

Figure 6. Network portfolio in Biopharma LIS in Greater Boston Area

Source: author’s own elaboration

5. Discussion

From the results of the analyses reported in section 4.1 and 4.2, it emerges that the GBA Biopharma LIS is an open network with structural holes where influential positions and bridging functions are mostly undertaken by large venture capital firms and pharmaceutical companies with a venture arm, and in which vertices tend to form small groups where interactions are more frequent. Also, the network portfolio of relationships that enhance knowledge are traceable to those that foster cross-
disciplinary interaction and match complementary resources (financial and technical) and skills (business support and scientific capabilities), i.e. Co-participation in thematic associations and symposia; Agreements for the Access and Use of Infrastructure; Venture Capital and Seed investments and industry-university agreements for the mobility of human resources. These results are in contrast with that strand of reviewed literature whose empirical results suggest the tendency of innovation systems’ actors to partner more with organizations which are cognitively similar (Balland et al. 2013). Conversely, these results are in line with those studies that demonstrate that informal contacts represent an important channel of knowledge diffusion (Dahl and Pedersen 2004; Ter Wal 2014) and that show how critical links and organizations with brokering positions compensate the negative effects of network dispersion for the system’s innovation performance by spanning structural holes and ensuring the exchange of non-redundant information (Casanueva et al. 2013; Broekel and Mueller (2017). In this regard, it is worth mentioning how the closed network structure was appointed by Saxenian (1996) as one of the determining causes of the decline of the Boston innovation system on semiconductor industry - known as Route 128 – in favor of the more open and horizontal network of Silicon Valley.

While comparing the results deriving from both analyses, findings from SNA are coherent with the outcome of expert interviews that suggest that an open network with non-redundant ties is preferable in terms of positive impact on innovation system performance. More specifically, informal relationships as the co-participation in thematic associations and symposia, the agreements for the access and use of infrastructure and the HR mobility from industry and university are the best relationships to contribute to the exchange of academic knowledge.

Similarly, Venture Capital and Seed investments represent an important vehicle for the transfer of complementary assets and represent a key player for the development of innovative products along the whole innovation process. In general terms, it is possible to argue that the innovation system performance is enhanced by those types of partnerships that promote connectivity among different kinds of actors as these contribute to smooth knowledge disabilities and the know-how trading. This network portfolio is coherent also with the tendency, at the structural level, of being divided in small groups where interactions occur more easily, as in the case of specific thematic associations (e.g. the Neuroscience Consortium or the Massachusetts Biotechnology Council) or sector specific innovation centers (e.g. Lab Central), so as to form local innovation communities that focus their joint effort on specific R&D targets within the LIS. These local innovation communities are
therefore characterized by a high intensity knowledge transfer through organizations of different nature and a high frequency of interactions, yet with a low degree of formalization, co-localized in the same geographical area. These results support those studies that suggest the key role of informal networks in knowledge diffusion (Dahl and Pedersen 2004) and those suggesting the tendency of science-based innovation systems’ networks (as Biotech) to form small sub-groups, i.e. knowledge epistemic communities characterized by frequent inner connection and informal channels of knowledge diffusion (Salavisa et al 2012).

From the results of the study conducted on the GBA Biopharma LIS it is possible to derive a set of propositions, which are intended to be tested in future studies and to develop practical implications for those regions whose innovation system is at its early stage of development. Our study suggests that a successful LIS is positively impacted by a sparse network (+ distance among the actors, - network density) where bridging roles are mostly undertaken by venture firms or large biopharmaceutical companies with a venture arm. Therefore, a proposition may be derived:

**P1. A successful LIS is characterized by an open network structure with structural holes**

Also, indicators at the meso-structural level suggest that a successful LIS characterized by network’s division into modules (i.e. groups, clusters or communities) in which nodes have dense connections with those belonging to the same module but sparse connections with nodes in different modules (+ connected components). Therefore,

**P2 A successful LIS is characterized by a high level of division of a network into modules**

As a second step, network portfolio composition has been analyzed according two dimensions, namely the impact for knowledge transfer, considered as a precondition of innovation creation and secondly, the importance of spatial proximity which, in turn, is a precondition for the frequency of the interactions and for the emergence of trust mechanisms that favor the emergence of informal ties (Granovetter, 1985). Weak ties result from the existence of informal relationships favored by the embeddedness of actors within a certain spatial configuration. Figure 4.4 shows the relationships with high scores for knowledge transfer, i.e. *venture capital and seed investments, co-participation in thematic associations and symposia and agreements for the access and use of infrastructure* and *HR mobility between industry and academia*. With reference to *VC and seed investment*, despite the
formalization that characterize this form of tie, it emerged that it is mainly the exchange of complementary skills (business support and scientific capabilities) and the advantages in terms of reputation for the startups within VC portfolio, that play a major role. The relationships that are established between VC and start-ups allow the latter to access to VC’s network with large pharmaceutical companies and give them credibility and talent validation for further partnerships and future growth. The way through which these relationships emerge and grow is considered to be highly enhanced by the spatial proximity that multiply the chances of casual encounters and visibility for those start-ups willing to receive funds. Additionally, the spatial propinquity allows VC to achieve a more effective monitoring and continuous support to their start-up partners. With regards to co-participation in thematic associations and symposia, spatial proximity of the partners ensures the frequency of the interaction between members, who can establish relationships outside the periodical meetings and form further partnerships based on trust mechanisms resulting from the common affiliation and mission toward specific target research areas.

More specifically, the form of the observed types of relationships, with specific reference to the way through which transfer of information occurs and future partnerships arise, appears to be mainly based on trust and reputation effects without the necessity of contractual bounds (- formalization) whose existence is stimulated by spatial proximity (+ spatial proximity). This, in turn, suggests that the composition of a network portfolio is predominated by the presence of weak ties. Therefore:

**P2.1 A successful LIS is characterized by a network portfolio dominated by weak ties**

Also, these relationships involve actors of different nature and disciplines, which ensures the non-redundancy of the exchanged information and the transfer of different (and complementary) practices to tackle with specific research challenges (+ heterogeneity of actors)

Additionally, the content of the observed types of relationships, with specific reference to the diversity of the nature of engaged partners and the complementarity of the resource exchanged (+ complementarity of resources), suggests that:

**P2.2 A successful LIS is characterized by a network portfolio dominated by non-redundant ties**

Finally, by combining the results deriving from both the analysis of the structure and the portfolio of the network, it is possible to observe the tendency of actors from different epistemic communities to convene in small groups around specific thematic areas where knowledge transfer occurs through loose ties whose frequency is ensured by their spatial proximity, that are able to span the structural
holes typical of the open structure of the network, i.e. local innovation communities. Therefore,

P3. A successful LIS is characterized by the presence of local innovation communities

Conclusively, this work suggests that a successful Local Innovation System is characterized by the openness of its network structure, the weakness of the relationships between its actors and the tendency of the actors to form local innovation communities (Figure 7).

Figure 7. Analytical framework for the study of LIS performance from a relational perspective

Source: author’s own elaboration

6. Conclusion

In this paper we have explored the characteristics of network’s structure and network portfolio composition in a successful LIS, by conducting a social network analysis of relational data and interviewing key stakeholders in the Biopharma LIS in Greater Boston Area. Our analysis reveals that a successful Local Innovation System presents an open network structure with structural holes, a high level of modularity and a portfolio of relationships that privileges informal and non-redundant ties
within small communities around specific themes. The results provide some support to the Burt’s argument within the debate about the optimal configuration of network structure suggesting that an open structure is typical for a successful LIS. Also, this study is in line with those scholars that argue that informal contacts represent an important channel of knowledge diffusion. In spite of its exploratory nature and the specificity of the regional context to which it has been applied, this research contributes to fill a gap in the network literature as well as that of innovation systems. More precisely, this study offers a more comprehensive view about the relational dimension of local innovation systems by taking into account both network structure and the quality of its relationships. Additionally, from a methodological perspective the study contributes to meet the challenges related to the adoption of a holistic approach, by capturing the heterogeneous nature of LIS demography when most studies limit their analyses to inter-firm relationships and at the node-level. Finally, the study provides insights into the network portfolio composition, which has been underexplored in LIS literature, allowing for the identification of those relationships considered more fruitful to enhance innovation processes from a local perspective. Our study has many practical implications both for the companies that can define which kinds of relationships are more important for knowledge transfer and for policy makers and those actors willing to undertake an active role in the development of a LIS in their own regions suggesting the relational configuration that a successful LIS should have. However, this study is not free from limitations. As a start, the sample could be expanded to include a greater number of organizations in the expert interviews. Also, new databases could be included in the social network analysis for extending the analysis on a greater number of typologies of partnerships and in order to achieve less biased results regarding the nature of bridging actors deriving from their centrality score. Finally, a comparative study with other LIS in different stages of development would contribute to a greater extent of validation of the propositions. Therefore, future studies can be developed to fill these limitations and test the propositions in different geographical and industrial contexts and operationalize the dimensions alongside with measuring the LIS performance from a relational perspective.

References


Doloreux, D. (2002). What we should know about regional systems of innovation. Technology in society, 24(3), 243-263.


Sampson, 2004


Watts and Strogatz (1998)