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LEARNING AT THE BOUNDARIES IN AN “OPEN REGIONAL INNOVATION SYSTEM”: A FOCUS ON FIRMS’ INNOVATION STRATEGIES IN THE EMILIA ROMAGNA LIFE SCIENCE INDUSTRY

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Learning at the boundaries in an "open Regional Innovation System": a focus on firms' innovation strategies in the Emilia Romagna life science industry

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Abstract

The paper investigates the existence of an Open Regional Innovation System (ORIS model). This model is characterised by the firms' adoption of an open innovation strategy, which overcomes not only the boundaries of the firms but also the boundaries of the region.

Using data collected in a sample of life science firms, our research provides the evidence that the Emilia Romagna RIS has evolved towards an ORIS model, where firms' innovation search strategy, despite being still embedded in local nets (involving several regional public research organisations - PROs), is open to external-to-the-region research networks and knowledge sources. It also shows that innovation openness influences significantly the firms' innovative performance.

Keywords: life science sector, learning at the boundaries, Regional Innovation Systems, networks, open innovation model

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1. Introduction

Over the last decades several new concepts have emphasised the systemic character of innovation, which overcomes the old view of innovation being just a specialised activity that depends directly on the amount of resources involved in subsidised science and in internal-to-the firms R&D laboratories (Audretsch et al., 2002; Metcalfe, 2005). This has been elaborated along different directions, looking at innovation as:

- an interactive linked-chain connecting numerous departments (R&D, design and engineering) and activities within a firm (Kline and Rosenberg, 1986);
- a complex modality (Carlsson, 1994) involving private and public actors, through industry-university collaborations, claimed to be fruitful for both the actors involved in the relationship, within a national system of innovation or a triple-helix approach (Etzkowitz, 1998; Freeman, 1987; Lundvall, 1992);
- a specific system characterised by its sectoral dimension, where innovation and technological change show different rates, types, and trajectories, depending on the sector in which they take place, and where agents and institutions of a sector exert a major influence (Malerba, 2002, 2004);
- a distributed process (Coomb and Metcalfe, 2000; Robertson and Smith, 2008) that integrates components, skills and knowledge from several organizations especially in the fields characterised by increasing modularization of complex products (Brusoni and Prencipe, 2001) and decomposability of innovation-related tasks (Jensen and Valentine, 2003);

- a geographically bounded spatial system, whose extension can be either national[2] or regional, or local (Cooke et al., 1997; Cooke, 1998; Lundvall, 1992; Nelson, 1993; Saxenian, 1994). In a globalised (and interconnected) world, the examination of spatial scale seems quite a difficult task, being "compressed" between the existence of overlapping multiple scales and spatial flows. In fact, while contemporary reflections deal with the issue of the internationalisation of national innovation systems (Carlsson, 2006), others reflect upon the local-global connections (Bathelt et al., 2004).

Assuming the complex theorising about the nature, evolution, and impact of the innovation systems, this paper investigates the existence and the performance of an Open Regional Innovation System (ORIS model). This model is characterised by the firms' adoption of an open innovation strategy, which overcomes not only the boundaries of the firms but also the boundaries of the region.

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[2] As argued by Carlson and Stankiewicz (1995), nation-state constitutes a natural boundary of many technological systems, but sometimes, it makes sense to talk about a regional or local system. The elements of a shared culture (including conventions, which are tacit, and rules of the game, which are more codified elements embedded in micro-institutions), common administrative and political dimension are another parameter discussed in Cooke et al. (1997): RISs form a mosaic within a single national system of innovation. A key question with respect to RISs is the extent to which they are systemic. The basic point is that there are a number of discrete elements connected by specific relationships. The RIS can be specified in abstract including organisational element and linkages among them (public actors: like universities, research institutions, skills-development agencies, technology-transfer agencies, science park and incubators, public funding entities, patent offices, etc., and private actors: firms, venture capital organisations, banks, consultants, legal consultants, etc.). Cooke et al. (1997) further hypothesise that there are weak/intense, regular or irregular interactions which shape the system; so we can draw many potential empirically-founded typologies of systems.

Our empirical analysis is grounded on the study of 78 life science firms in Emilia Romagna, which was described as a RIS[3] . Using primary data collected at the firm level, through field interviews, the study explores in detail innovation openness in the life science RIS, focusing on the firms' willingness to overcome both the *organizational boundaries,* through the use of external sources of innovation, and the *regional boundaries,* through long distance research collaborations. The paper applies quantitative research methodologies. In particular, it presents some descriptive analyses on the innovation sources (internal and external) used for innovation and it applies the social network analysis to map the geographical distribution of R&D linkages. The study then offers some indications on the effect of innovation openness, testing the impact of internal and external (regional and global) innovation sources on firms' patenting activity. The paper proceEds. as follows. Section 2 focuses on the theoretical and empirical background and introduces the research issues and objectives. Section 3 describes the method and data used in the analysis. Section 4 gives descriptive results, while Section 5 contains an econometric analysis. Section 6 proposes some concluding remarks and hints for further research.

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[3] In Cooke et al. (1997), "in the Emilia Romagna, the autochthonous emergence of industrial districts, characterised by collaborative and competitive business practices and financed by local banks, led the region, in partnership with banks and other organisations, to support localised innovation centres in promoting systemic interactions around the use of new technologies in traditional industries. In doing so, the region has developed a collective identity and rules of the game which have resulted in "the Emilian model" being exported worldwide. p. 481".

2. Theoretical background and empirical context

*2.1 R*IS and open innovation models

RIS is one of the most influential concepts developed in the context of regional science studies, which has grown rapidly since the middle of the 1990s (Braczyk et al., 1998; Cooke et al., 1997, Iammarino, 2005). The notion of RIS lies on the crossroads of two main bodies of literature: evolutionary theories of economic and technical change, which conceptualise innovation as the result of complex, non-linear social processes, stimulated and nurtured by several actors and factors within and outside the firm (Edquist, 2005), and theories of regionalisation and clustering, which emphasise that economic growth and innovation do not take place in abstract spaces, but are locally rooted, thanks to the advantages of spatial proximity, social embeddedness, interaction with local institutions, and knowledge spillovers (Camagni, 1991; Cooke, 2002; Maskell and Malmberg, 1999; Porter, 1998; Storper 1997; Belussi and Sedita, 2009). According to the RIS approach, regions, especially when they have developed industrial clusters, and an appropriate administrative framework for supporting innovative enterprise, are meaningful loci of innovation, fostered by direct and indirect linkages, co-operation and synergies among local economic actors and institutions. In particular, as regards the evolution of RISs, recent analyses have elucidated the complex relationship that exists between the building of a coherent innovation system and the evolution of innovative local clusters. The undergoing hypothesis is that in fashion-led or engineering-based industry – characterised by the presence of practical knowledge – the development of a competitive regional system is the result of a pre-existing industrial cluster (Belussi, 2002), while in science-based industry – where the role of scientific/analytical knowledge4 is extremely important – the presence of leading

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[4] For a definition see Cooke (2005).

research institutions (and research funds) represents the sine-qua-non precondition (Asheim and Coenen, 2006).The influence of the RIS has grown rapidly since the middle of the 1990s (Asheim et al., 2003; Braczyk et al., 1998; De la Mothe and Paquet, 1998; Doloreux, 2002; Howells, 1999). Autio (1998) illustrates RIS as composed by two interdependent sub-systems embedded in a common regional socioeconomic and cultural setting. The industry sub-system, which includes the companies, their clients, suppliers and competitors, and the institutional sub-system, which consists of various institutions that are engaged in the production and diffusion of knowledge and skills such as public research organisations (PROs), technology mediating organisations, universities and other educational organisations. In high-performing regions, these two sub-systems are expected to share strong interactions sustaining a continuous and virtuous process of knowledge generation, diffusion, application and exploitation.

As pointed out by Tödtling and Trippl (2005), RISs should not be understood as internally homogeneous systems since they can encompass – and usually do – several industries, clusters and/or industrial districts. Further, RISs should not be conceived as isolated entities, since they are encapsulated in national and supra-national innovation systems. RISs can also have various linkages with external actors and the importance of these external ties has been increasingly recognised as crucial in accelerating technological change (Coenen et al., 2004) and innovation processes also in many SMEs (Asheim and Isaksen, 2002). Many studies have tackled this issue referring to the role of multinational corporations (Zander, 1999; Cantwell and Iammarino, 2003). While the traditional RIS approach has above all emphasised the importance of local sources of innovation, more recent studies have underlined the crucial role of accessing knowledge and innovation from the outside (Bathelt et al., 2004; Boschma and ter Wal, 2007; Gertler and Levitte, 2005). Actually, the structure of some high-tech industries seems to conceal globalisation and regionalisation through a small world pattern of connections: some local firms – often the leading enterprises – play the role of “knowledge gatekeepers” (Owen-Smith and Powell, 2004), which search for and absorb non-local knowledge, and transmit it to other actors within the RIS.

The RIS approach draws on the view that innovative dynamics are not held within organisational borders or single firms’ research units. Similarly to RIS, other recent research approaches have contributed to affirm a new model of open innovation that overcomes the single firms’ boundaries. Chesbrough (2003) observed that organisations increasingly resort to open innovation strategies to augment the variety and speed of knowledge flows essential to innovation. According to Chesbrough (2003), the old closed innovation model, which dominated most of the 20th century, is becoming obsolete today. The increasing importance recognised to external sources of knowledge and innovation is threatening the closed model, which postulates the effectiveness of vertically integrated R&D departments, aimed to develop technology in-house for their sole use. Chesbrough claims that also modern technology powerhouses, like Cisco and Microsoft, have dropped the "do-it-all-yourself" approach, and pioneered a new model of open innovation, in which companies import ideas from outside, and let their own innovations enter the wider marketplace. Today, the largest firms spread around the world their R&D laboratories around new poles of excellence (Chiesa, 1995).

In the closed innovation model, small firms, which clearly are not able to afford large investments in R&D, are at a disadvantage. These types of firms cannot be innovative only counting on internal knowledge, but they have to build fruitful relationships with other organisations, in a network perspective. Firm size in the emergent open innovation model is no more an obstacle or unique driver to increase innovative productivity (Belussi and Gottardi, 2000). Relational and co-ordination capabilities of firms and research labs allow the establishment of a positive spiral of learning at the boundaries (Belussi, Sedita and Pilotti, 2008), which appear to be the crucial variable to look at when determining the degree of innovativeness (Boari and Lipparini, 1999; Lipparini and Sobrero, 1994; Lorenzoni and Lipparini, 1999; Giuliani, 2007).

Crossing the boundaries of the firm and co-operating with external actors (research labs or institutions) is an opportunity to multiply the learning occasions, mostly in knowledge intensive sectors (Baba et al., 2009). These industries have witnessed the wide spread diffusion of distributed forms of innovation driven by the necessity to integrate specialised and complementary knowledge (Coombs and Metcalfe, 2000). Recent studies on modularity and system integration (Brusoni and Prencipe, 2001; Hobday, Davies and Prencipe) have pointed out that increasing modularisation of complex products has favoured firms' R&D disintegration and knowledge specialisation although raising the need and complexity of inter-organisational coordination.

External sources represent a form of "learning at the boundaries", which is rooted in the capability to enrich the firm knowledge with a network of interactions including external partners (suppliers, customers, research and market institutes). Knowledge flows are easier, thanks to the increasing adoption of international-shared languages and ICT infrastructures (Castells, 2000). Consequently the number of innovation sources for the creation of new processes and productive inputs increases, favouring economies of variety, and enhancing the heterogeneity of firms.

2.2 Innovation trajectories in the life science industry

The life science concept emerged in the mid-1980s along with a novel emphasis on biotechnology, to provide a rationale for the new technological trajectory with strengthened links between the agrochemical and pharmaceutical divisions of multinational chemical companies (Tait et al., 1990). The growth of biotech gave rise to a novel technological regime with specific characteristics of appropriability (very high), opportunity (very high), cumulativeness (very low at the beginning), and differentiated knowledge base (with the shift from the chemical paradigm to the bio-molecular technology). The organisation of R&D activities in the high-tech sectors of life science firms (biomedical, biotech, pharmaceutics and computer science applied to the medical fields), typically based on the exploitation of scientific knowledge, represents one of the main components of the innovative activity of the enterprises. However, at the same time, life science firms show a systematic access to external knowledge sources. Not all of the useful knowledge for the innovative activity of the enterprises originates "inside" the firm, and the absorbing activity of external knowledge from outside appears equally fundamental (Cohen and Levinthal, 1989, 1990). Science-based firms produce and absorb knowledge in a continuous game of interactions that generate a hybridisation of the possessed knowledge, and give rise to a cumulative process of acquisition of knowledge and competences, becoming the quintessence of a new model of firm (Antonelli, 1999; Dasgupta and David, 1987; Winter, 1987).

On the one hand, life science firms' innovation strategy develops within open models, characterised by their participation in inventive and innovative activity on an international scale. The life science field shares a strong interface with research activities placed on the frontier of scientific knowledge discovery. The innovative activities introduced are therefore strongly tied to the public research (R&D projects on basic research) developed within the scientific institutions, and collectively shared (Arrow, 1994). In this field the importance of non-profit, public and semi-public research institutions is significant. They are a crucial source of public knowledge and they contribute to the sponsoring of the most promising firms' projects (Cooke, 2002; Nelson, 1992; Nelson and Levin, 1986). On the other hand, life science firms' strategy is planned within closed systems, in order to protect their "dedicated technological knowledge" (tacit or codified), building intangible reservoirs for creative activity of invention and innovation (Arora and Gambardella, 1994). Science-based firms protect their capability (Penrose, 1959; Kougt and Zander, 1992) and proprietary knowledge especially through the maintenance of the industrial secret (Levin et al., 1987) and patenting activity (Foray and Hargreaves, 2002). However, the necessity of acquiring complementary knowledge, in order to guarantee the progress of the research projects, tends to stretch them towards a more open model. Complementary production abilities, technological interdependences, interactions with customers and end users, and the ability to recombine different, distant, but equally necessary, sources of knowledge militate in this direction (Penner-Hahn and Shaver, 2005).

Successful firms are those which invest in “strategic resources”, not just in in-house R&D, but in effective relations with suppliers, sub-contractors, and service firms (Teece et al., 1997; Wernerfelt, 1984). A crucial element for accumulating strategic resources is to develop numerous channels to absorb information (meetings, participation in international fairs), codified technical knowledge or know-how (university R&D, consultants, reverse engineering techniques, strategic alliances with knowledgeable suppliers, etc.). The emergence of a complex network of cooperation, as Richardson pointed out long ago (1972: 888) is explained by the need to combine closely complementary but dissimilar activities (from R&D to marketing) that in certain circumstances cannot be allocated either straightforwardly to the market (because of the existing complementarities with firm assets), or to the firm itself (because it lacks the required capabilities). The literature on system integrators (Hobday, Davies, and Prencipe, 2005) discusses in detail the relationship between the division of cognitive labour and organisational structures, providing significant insights on the role of innovative assemblers, the latter being considered repositories of architectural knowledge (Henderson and Clark, 1990),

These arguments all together tend to support the motion for an open innovation model, because “The process of innovation is becoming more distributed across firm boundaries” (Coombs and Metcalfe, 2002: 263). Following Chesbrough (2003), West and Gallagher define open innovation as “(…) systematically encouraging and exploring a wide range of internal and external sources of innovation opportunities, consciously integrating that exploration with firm capabilities and resources, and broadly exploiting those opportunities through multiple channels” (West and Gallagher, 2006: 82).

In life science firms, then, technological spillovers appear to be extremely frequent. They take place both inside the relationship between firms and public research centres, or in localised networks of enterprises, or again, in global international networks of enterprises (Owen-Smith and Powell, 2004). This happens in all life science clusters (or technological districts) like in the area of Cambridge and Oxford in the UK, or in Boston and Minneapolis in the US, or in the life science scientific parks, like Sophia Antipolis, in France (Longhi, 2002). The degree of decomposability of complex problems, introduced by Simon, represents another way to underline the cooperative nature of inter-organisational relations. This concept has been further applied by Valentin and Jensen (2003), in the realm of biotech in food processing.

In order to investigate the role of research collaborations on firm innovativeness, performance and growth, many theoretical and empirical studies have focused on the type and location of external partners (Dahlander and McKelvey, 2005; McKelvey et al., 2003). With respect to type of partners, the literature on innovation systems (Cooke, 2001; Lundvall, 1992; Nelson, 1993) and the triple helix model (Etzkowitz and Leydesdorff, 1997) have both stressed the fundamental role in boosting innovativeness of close interactions among heterogeneous actors such as large firms and SMEs, venture capitalists, end users, universities and other public and private research institutions. With respect to the spatial distribution of partners, some authors suggest that external research collaborations should be more frequent and effective among co-located partners, while others emphasise the importance of research links with geographically distant partners in order to get access to global circuits of knowledge creation and diffusion. The former argument is based on the idea that the complexity of the innovation process requires direct contacts between partners for the success of research collaborations (Pisano et al., 1988). Spatial proximity should enable the transfer of tacit knowledge and facilitate the exploitation of knowledge spillovers (Malmberg and Maskell, 2005; Maskell 2001). The geography of spillovers has been also analysed in the context of patent citation. Comparing the geographical location of patent citations with that of the cited patents, Jaffe et al. (1993) found evidence that knowledge spillovers are geographically localised. In opposition with this view, the latter theoretical perspective sustained the importance of global sources of external knowledge, claiming that, in high-tech industries, innovation requires knowledge that is both “global best” and “diverse” (Dahalander and McKelvey, 2005).

2.3 Research issues and objectives

The theoretical overview presented above underlines that in many sectors, and especially in the life sciences, two intertwined phenomena are modifying the traditional model of innovation: i) the increasing relevance of external to the firm knowledge sources, which foster the adoption of a new open/distributed innovation model; ii) the need of exploiting the advantages of local knowledge spillovers while getting access to non-local sources of knowledge and information. Whereas the first phenomenon is perfectly consistent with the traditional RIS model – typically based on the view of innovation as an interactive process – the second phenomenon implies the evolution towards a new model of open RIS (ORIS).

On the basis of this consideration, the objective of the present paper is to examine the empirical existence and the performance of the ORIS model in the Emilia Romagna life science industry. In order to do so the study focuses on three research questions:

i) *External sources of innovation:* To what extent do firms within the RIS rely on external innovation sources? What are the most important sources according to firms' evaluation?

ii) *Geographical scale of innovation relationships:* Do firms prefer to engage in collaborative research relationships with proximate partners (within the RIS) or external ones (national, European or extra-European)?

iii) *Effectiveness of open innovation model*: Is the open innovation model more effective than the closed one in terms of patenting activity? Which is the impact of internal sources (R&D efforts) and external sources (variety of external channels and number of research ties) on firms' innovativeness?

The first two issues aim to assess the openness of the life science RIS (towards an ORIS model). In order to do so, the study examines which are the external channels more frequently activated by the interviewed firms, and the importance they attribute to each source for innovation. The study also provides a descriptive analysis of research collaborations, useful to capture the geographical scale of the inter-organisational division of innovative tasks in the life science RIS. This analytical framework is designed to provide a comprehensive and bottom-up understanding of the existence of the ORIS model. When local firms are strongly oriented towards the use of a breadth search strategy, cultivating multiple channels for innovation (both institutional and market-based) and are engaged not only in local research collaborations, but also in extra-regional ones, the RIS fits what we have here called the ORIS model. The dominant mode of innovation here is largely influenced by the firms' capability of learning at the boundaries.

The third research question is concerned with testing the effectiveness of the open innovation model. In order to do so, the study applies multivariate analysis to test the impact of internal sources (R&D investments) and external sources (variety of external channels and number of research ties) on firms' innovativeness. The statistical test presented in the study is a negative binomial regression, where the dependent variable is innovative performance (measured as the number of patents registered in the period 2000-2004), which is explained by R&D expenditure, number of external research collaborations, and variety of external sources used for innovation search. The model also includes a number of control variables, such as size, age, and firms' sub-sector.

3. Empirical setting, data source, and sampling procedure

The empirical context of this study is the life science industry in Emilia Romagna[5]. Our definition of the sector includes the following specialisations: biomedical, biotechnology, pharmaceutics and computer science industry applied to the medical fields. Therefore, our study does not focus only on dedicated biotech enterprises, including all firms active in the knowledge areas of the modern life science industry.

Several data sources were used to build a systematic database of the population of firms involved in the Emilia Romagna life science sector. Our research work started

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[5] An extended work related to our empirical survey is published in Belussi (2005).

with the inspection of the CERVED archive, an existing database provided by the Italian Chamber of Commerce, which includes all the registered firms – not only legally founded but also operative. We updated and completed this archive using information gathered through other sources: websites inspection, interviews with regional experts and queries of firm associations' archives, like Consobiomed, the association of small firms belonging to the biomedical district of Modena.

We identified 3 productive segments:

1) biomedical firms, which produce medical appliances and disposables for diagnosis and therapeutic aims;

2) pharmaceutical and biotech firms, even if the latter are little developed in the Emilia Romagna region and in Italy at large;

3) information science firms that have developed specific medical applications, mainly in the field of distance telemedicine.

In turn, the biomedical segment has been divided into 4 sub-areas of specialisation: (i) diagnostics, (ii) therapeutics (complex machinery), (iii) disposable, and (iv) other electro-medical or non therapeutic machinery (other apparatus and appliances)[6].

---------- Insert table 1 about here ------------

Table 1 provides the distribution of firms and employees for the population of life science firms identified. Overall, the Emilia Romagna life science sector appears quite significant – more than 500 firms and about 11 600 employees (data refer to all productive and commercial firms). The main sectors are, respectively, therapeutic and

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[6] See Appendix 1 for a short description of the sub-sectors of activity of the enterprises inserted in the sample.

rehabilitation, other appliances, pharmaceutical and biotech. From a spatial point of view, the regional life science system is composed of a clear-cut industrial district, centred in the province of Modena, and a mosaic of niches of dispersed producers, mainly localised along the Modena-Bologna axis, where there are also numerous regional clinical institutions and universities (important university centres and medical clinics are also in the nearby cities of Ferrara and Parma).

A simple random sampling technique was applied, and 78 firms entered the sample[7]. We assigned the sampled firms to each sub-sector using the information obtained directly during the interview, or using the Cerved archive (which describes the sector of activity in some dedicated records). From a spatial point of view, the interviewed enterprises are mainly concentrated in the province of Modena (42 cases corresponding to 53.8% of the firms, and 84% of the employees), where the only Italian biomedical industrial district is located[8]. 22 firms are based in Bologna, while the others are dispersed within the region.

Semi-structured interviews were conducted in the period March-September 2005 by a group of four researchers (Alessia Sammarra, Massimo Gastaldon, Alberto Corazza and Tito Casali) directed by Fiorenza Belussi. Interviews were mainly organised with the entrepreneur, owner of the firm, or with the manager delegated to deal with innovation activities. Interviews lasted 1-2 hours and were focused on the

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[7] During the sampling procedure we excluded firms involved only in assistance services, because they are not firms endowed with innovation and technological capabilities.

[8] The district enterprises are located in a small bunch of municipalities which show high spatial contiguity, like Camposanto, Cavezzo, Concordia, Finale Emiliano, Medolla, Mirandola, S. Felice, S. Possidonio and S. Prospero. The biomedical district of Modena counts about 80 firms and 5,000 employees, quite a small cluster if compared with the Medicon Valley, localised between Lund and Copenhagen with 1,000 firms and 34,000 employees.

history of the firm, products, innovation capability, R&D investments, patents, markets, number of competitors, recent growth trend, external R&D cooperation, and the relationships with the regional supporting institutions. Interview data on the number of employees, firm sales, and number of international patents registered by the firms were controlled through the inspection of firms' web sites and on-line official sources (Chamber of Commerce, European Patent Office). The utilisation of multiple sources to collect data allowed us to reduce the risk of the variables used for descriptive and multivariate analyses being affected by single-source bias.

4. Descriptive results

4.1 Innovative search strategy

In order to assess the degree of openness of firms' search strategy, firms were asked to indicate which external sources they use for their innovation activities, and evaluate the importance of each source on a scale from 1 to 10. The interview questionnaire contained a list of 16 possible sources (see table 2), grouped together under three different headings (market-based, institutional-based, and semi-public). Overall, our findings indicate that firms use on average about 5 external knowledge sources out of the total of 16. The most frequently used source is "clients and customers" (or "end users"). Indeed, 65% of respondents gathered some information useful for innovation activities from their clients. Among all the market sources, "clients and customers" is also considered the most relevant, receiving an average score of 8.57. This result is consistent with the Innovation Systems approach, which emphasises the importance of interactions among actors in the industry sub-system as crucial driver of innovation, especially with regards to close relationships with customers and end users.

The other most frequently used sources are the semi-public ones, which are – in order – the Internet (56%), scientific publications (51%) and fairs and exhibition (47%). The important role played by semi-public sources can be explained by taking into account their relative greater accessibility and lower cost compared to the other external sources of knowledge or information. It is interesting to notice that scientific publication (a form of indirect interaction with PROs) is, in absolute terms, the most relevant source according to firms' evaluation, receiving the highest average score in the list (9.20). This result clearly indicates the strategic importance of keeping pace with scientific discoveries for firms operating in the life science sector, which is typically more dependent on the exploitation of scientific knowledge in comparison to other industries.

The number of firms relying on direct interactions with PROs (institutional sources) is also quite relevant, although with some degree of variation within the category (which includes not mutually exclusive options). Indeed, this percentage rises up to 24% for regional universities, while it decreases to only 9% for the National Research Council (CNR). These sources are generally ranked as highly important, with an average score of 8.19.

Finally, quite an interesting result concerns the use for innovation activities of research agreements with other firms. A very small percentage of respondents (10%) draw on this external source, which is also considered not very relevant, with an average score of 4.89. This finding indicates a clear divide between firm-to-PRO and firm-to-firm research collaborations, the latter being a concern of a small minority of firms in our sample. This finding is further confirmed by the descriptive analysis of the occurrence of research collaborations presented in the following section.

----------- Insert table 2 about here ------------

4.2 The role of external research collaborations

Given the relevance of research collaborations in the modern life science industry, we investigated in further detail the role played by this particular external source of knowledge and information for innovation. Following Dahlander and McKelvey (2005), we gathered relational data on the occurrence and spatial distribution of research collaborations among the sampled firms. Specifically, respondents were asked to list the number of research collaborations they have established with other firms and PROs in the period 2000-04 and to indicate the geographical location of each partner. Figure 1 illustrates the research network established by the respondent firms with regional, national and foreign partners[9].

----------- Insert figure 1 about here ------------

Table 3 shows that 58% of firms in the sample are involved in external research collaborations. Indeed, out of the 78 respondents, 45 have established external ties, reaching a total number of 170 collaborations. Table 3 clearly indicates that firm-to-firm relationships have a marginal diffusion, being only 17 out of the 170 total collaborations. Indeed, only 10% of the sampled firms have established research collaborations with other enterprises. This result is quite remarkable, since it indicates a lower number of firm-to-firm relationships than could be expected, given the emphasis assigned by the literature on this type of collaborations in the life science industry. The low frequency of firm-to-firm relationships in the Emilia Romagna sample appears quite striking also with respect to the empirical findings reported by Dahlander and McKelvey (2005) for the Gothenburg population of biotech enterprises. Indeed, in terms of occurrence, the authors found that 43% of the firms were involved in firm-to-firm relations, measured through formal arrangements. One possible reason for the difference

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[9] The software used to analyse relational date is Ucinet 6 (Borgatti et al., 2002).

may lie in the fact that we focused exclusively on research collaborations, while the results obtained by Dahlander and McKelvey are based on a broader set of inter-organisational relations, which include also marketing and distribution alliances. Further, compared to the typical biotech model, our results may testify a specific form of distributed innovation in the Emilia Romagna life science RIS, whose main peculiarity resides in the prominent role of PROs in R&D collaborations. Overall, our analysis shows that firms in the Emilia Romagna life science RIS are much more strongly linked to public research organisations. Indeed, in terms of occurrence, 56% have established collaborative relationships with research organisations, reaching a total number of 153 ties.

---------- Insert table 3 about here ------------

In terms of the spatial distribution of research collaborations, tab. 4 shows some interesting variations across the two sets of relationships analysed. Firm-to-firm collaborations occur primarily with European enterprises (41% of the ties), followed by national (29%) and extra-European (18%), while collaborations with enterprises localised in the Emilia Romagna region are the least frequent (12% of the whole ties). The analysis of the spatial distribution of collaborations with PROs offers a quite different picture. Firms in the sample establish half of their external ties with regional PROs, and another half with trans-regional PROs. Our data partially align with Dahlander and McKelvey (2005), because, despite indicating that geographical location matters, they also reveal that distant research collaborations with PROs heavily characterise the firms' behaviour.

---------- Insert table 4 about here ------------

Overall, our results show that firms in the Emilia Romagna life science sector establish the largest part of their research collaborations with PROs localised outside the region, supporting the shift towards an ORIS model. The majority of these ties are national (31%); local firms have shown a lower propensity or capability to establish transnational research collaborations (23%).

Several studies have provided empirical evidence on the positive correlation between collaborative ties and company performance measures (Ahuja, 2000; Powell et al. 1999; Stuart and Podolny, 1999). We conducted a correlation analysis between research collaborations with both PROs and firms and companies' innovativeness, measured as the number of patents registered in the period 2000-04. The total number of external research relations shows a significant correlation at the 0.05 level (2-tailed) with the number of patents owned by the firm, suggesting that innovativeness is positively correlated with the firm's capacity to be engaged in multiple external relationships. In terms of type of actors involved, both firm-to-firm and firm-to-PROs relationships are significant and positively correlated with firms' innovativeness. Finally, and what is most relevant for the present study, when geographical location is taken into account, only the relationships established with foreign partners appears significant and positively related to the firm's patenting activity.

5. Econometric analysis

The econometric analysis presented here investigates the role and relevance for firms' innovativeness of the various components of the open innovation strategy that are respectively: a) the internal innovative efforts (R&D investments), b) the external sources of knowledge used for innovation and, last but not least, c) the capabilities of building innovative networks. The statistical method applied is a negative binomial regression. The variables entered in the model and the regression results are described in the following sections.

5.1 Measures

Since we are interested in the evaluation of the determinants of firms' innovative capabilities, our dependent variable (N_PATENTS) is a measure of the firms' patenting activity. N_PATENTS measures the number of patents owned by the single firm in the sample. Data were gathered from the European Patent Office Database and field interviews[10]. Earlier studies have suggested, and assumed, that patents are a fairly good indicator of the inventive output of a firm's research department and a measure of the "output" or "success" of R&D (Bound et al., 1982; Hausman et al., 1984), although they have only been able to prove a simultaneous effect of R&D on patents, without considering any lagged effect (Hall et al., 1986).

The regression model includes three explanatory variables, which are listed and briefly described in tab. 5.

---------- Insert table 5 about here ------------

The first variable (RD_EXP) measures the amount of investments in R&D allocated by the firm during the year 2004. In the innovation literature, this variable is usually used to capture two intertwined although distinct phenomena. On the one hand, the amount of internal R&D investments is considered as a proxy to measure firms' internal innovation effort. On the other hand, it is used as an indicator of the firm's absorptive capacity (Cohen & Levinthal, 1989). In this view, doing R&D internally should increase firms' ability to integrate internally the knowledge gathered from the outside with the prior knowledge base.

We used two variables, N_SOURCE and N_REL, to measure external innovation efforts. Specifically, N_SOURCE is a proxy variable similar to the one used

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[10] We decided to integrate the information derived from the European Patent Office Database with the entrepreneurs' declarations, to avoid the risk of not considering the patents not signed by the firm, but by the individual researcher regularly employed by the firm.

by Laursen & Salter (2004, 2006), which indicates the number of different external sources of knowledge and information normally used by the firm for innovation activities. This indicator is calculated from the list of 16 external sources reported in tab. 3. The external sources listed in the questionnaire were not mutually exclusive. They have been coded as binary variables (0=not used; 1=used) and then added up to create the proxy variable N-SOURCE, which varies from 0 if none of the sources is used to 16 if all knowledge sources are used by the respondent firm. Therefore, this indicator reflects the firm's external search breadth.

The variable N_REL is a proxy which measures the intensity of firms' networking activity for research purposes. This indicator corresponds to the total number of external collaborative relationships established for research purposes with both firms and PROs within and across the RIS boundaries. This indicator is used to assess the impact of research relationships on the firm's capability to produce innovations. It is a proxy of the firms' propensity to invest in research activities through the establishment of inter-organisational networks.

In addition to the three explanatory variables discussed above, we included three variables to take into account the structural dimension of the firms in the sample, controlling for size, age and sub-sector. Specifically, we used the number of employees (expressed in logarithms) as the measure of size (SIZE), and 5 sub-sector dummies (SECi) to control for different propensities to produce innovations across the life science sub-sectors identified[11].

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[11] We are aware of the limitation given by the sample size on the regression analysis estimation (Green, 1991), nevertheless, since we do not want to infer heavily on the generalisability of the results to the population, and we are working in the field of the social science, we adopted the simplest rule of thumb for determining the minimum number of subjects required to conduct multiple regression analyses, that is N>50+m, where m is the number of predictors (Harris, 1975).

Tab. 6 provides descriptive statistics and simple correlations for our variables. In particular, we can notice the significant and positive correlation between the dependent variable (N_PATENTS) and the selected explanatory variables (N_REL, N_SOURCE, RD_EXP). As a preliminary comment, we can claim that the patent activity is positively related to the main components of an open innovation model: the internal efforts - absorptive capacity (in terms of R&D expenditure), the breadth of innovation search (in terms of number of sources for innovation) and the intensity of networking activities (as number of external research collaborations).

---------- Insert table 6 about here ------------

5.2 Statistical method and results

Since the dependent variable (number of patents – N_PATENTS) is a count of scores (nonnegative integers), ranging from zero to many, rather than continuous, a negative binomial model is applied as the means of estimation (Bound, Cummins, Griliches, Hall and Jaffe, 1982; Hausman, Hall and Griliches, 1984; Zimmermann and Schwalbach, 1991; Crépon and Duguet, 1997; Licht and Zoz, 1998)[12]. This type of regression analysis is applied to deepen our understanding of open innovation models, assessing the relative importance of internal R&D investments, search activities and networking abilities, on the innovative firms' performance. The results of the models estimation are reported in tab. 7. To interpret the negative binomial regression estimated coefficients, we must take in account the logarithmic transformation of the dependent

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[12] The Poisson regression model assumes that the variance of the counts is equal to the mean, which appears not to hold in our situation, where we witness an overdispersion phenomenon. The negative binomial succeEds. in accommodating this problem. The negative binomial model is an extension of the standard Poisson model where the Poisson parameter for each firm has an additional random component, accounting for (unobserved) heterogeneity, not yet accounted for by the regressors that determine the individual mean function.

variable that is the count of patents (Liao, 1994). The estimated model (1), which is representative of the closed innovation model, reveals the significant positive impact of R&D expenditures on the patenting activity of firms. A doubling of the R&D investment, in fact, is associated with a 11% increase in the number of patents[13].

---------- Insert table 7 about here ------------

The estimated model (2) tests exactly what we have called the open innovation model. Here R&D expenditure and networking activities are taken into account, together with the search breadth strategy and the interaction between R&D expenditure and networking activity, the latter explaining how the impact on patents of the external relationships is dependent on the internal R&D. The model, which shows the highest fitness (R-square of 0.28), capturing 30% of the variability of the dependent variable, indicates that engaging in external research relationships has a positive and significant impact on the firm's innovative output (a 10% increase in the number of relations is associated with a 40% increase in the number of patents[14]), as well as the breadth strategy does (a 10% increase in the number of sources is associated with a 14% increase in the number of patents). Similarly R&D investments significantly and positively affect the number of patents owned by the firm (a doubling of the R&D investment is associated with a 18% increase in the number of patents[15]). Interestingly, the interaction term is significant and negative, informing on the costs of the joint management of networks and internal R&D. As the complexity of the innovation

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[13] Given the coefficient of 0.145 for the R&D investment, a doubling of the R&D investment would multiply the rate by exp (0.145*log(2)), which is 1.11.

[14] Given the coefficient of 0.337 for the number of external relationships, a 10% increase in the number of external relationships would multiply the rate by exp (0.337), which is 1.40.

[15] Given the coefficient of 0.245 for the R&D investment, a doubling of the R&D investment would multiply the rate by exp (0.245*log(2), which is 1.18.

strategy increases, the individual positive effect of networks and R&D is mitigated. Besides, creating and maintaining networks could lead to knowledge leaking and thus diminish the returns on R&D investment efforts. Moreover, the number of relations seems to influence positively the innovative output in a non linear way, suggesting the existence of an inverse U-shaped relationship. The size of the firm is significant for the determination of the innovative output, showing a higher innovative capability of larger firms, while the age of the firm seems not to be relevant. We controlled also for the sub-sectors that the firms belong to, which appear to influence the results. Model 2 estimation suggests that an open innovation strategy, which combines an investment in internal efforts - absorptive capacity (by means of R&D expenditure), a breadth innovation search, and a networking activity, is better performing, in terms of patenting activity, despite the costs of managing multiple innovative inputs.

6. Conclusions

The aim of this paper was to provide some empirical evidence on a new model of ‘open RIS’ (ORIS). The empirical evidence presented focused on a representative sample of life science firms operating in the Emilia Romagna RIS.

The innovation system approach describes innovation as a systemic and interactive process that crosses the firm’s boundaries to include several external sources of knowledge and information available in both the industry and institutional sub-systems. In order to explore this aspect, our analysis focused on the breadth of firms’ external search with respect to an ample list of possible external sources of knowledge and information, distinguished in market-based, institutional-based, and semi-public. Our results showed that several firms in our sample do not follow the closed innovation model as they employ various external sources of innovation. The most frequently used are clients and customers and semi-public sources (51.7%) while the most relevant are the institutional ones.

In the ORIS model, innovation is not only a systemic and open process which crosses the firm's boundaries but also a trans-local phenomenon which overcomes the regional border. In order to explore this aspect in the Emilia Romagna life science RIS, the study presented a detailed analysis of the spatial distribution of R&D collaborations.

Our results showed that firms in our sample establish the largest part of their research collaborations with actors localised outside the region (54%). These ties link local firms with national, European and extra-European circuits of knowledge creation and diffusion. Interestingly, the propensity of establishing research collaborations outside the region is not confined to a small minority of leading enterprises.

This evidence is particularly relevant because it testifies a shift towards the "ORIS" model, where firms innovation search strategy, despite being still embedded in local nets (involving several regional PRO), is open to external-to-the-region research networks and knowledge sources.

The analysis of R&D collaborations also offered some interesting indications on the form of distributed innovation in the Emilia Romagna life science ORIS. We indeed found that firms in the Emilia Romagna life sciences are more likely to establish research collaborations with PROs than with other firms, suggesting a different form of inter-organisational division of innovative tasks compared to the typical biotech model. This finding is consistent with the study conducted by Valentin and Jensen (2003) on R&D collaborations in food biotechnology, which showed a prominent role of PROs compared to other firms specialised in biotech research. Considering that firms in our sample belongs to several sub-sectors of the life science industry, our findings corroborates the argument made by Valentin and Jensen (2003): it is misleading to expect that all fields in the life sciences or in high-tech sectors in whatever country should emulate or reflect the typical biotech model of distributed innovation. In this respect, our study provides new empirical evidence useful to challenge some taken-for-granted assumptions about the life science industry.

Finally, our study tested the effectiveness of the open innovation model. The open innovation model better explains firms' innovative performance compared to the closed one, which is based on the sole use of internal R&D. We also found that research collaborations contribute significantly to the determination of firms' innovative output. In our sample, internal R&D investment is significant, but the use of research collaborations can compensate low levels of internal investment. This result indicates a substitution effect between these two sources of innovation. A similar effect was found in the study of Laursen and Salter (2006), concerning the interaction between the openness to external search activities and the internal R&D investments. The authors explained this substitution effect as a manifestation of the "Not Invented Here" syndrome. One likely interpretation of the substitution effect is related to the costs of simultaneous network building and internal R&D investment.

This paper has some limitations that should be acknowledged. The first one is connected to the choice of the specific empirical setting. To what extent the Emilia Romagna life science ORIS can be elected as representative of a new model? Further empirical evidence from different contexts (in other countries or industries) is necessary to fully understand the implications of the open innovation approach for RIS evolution. While the present study examined RIS openness in one period, another future research challenge is to investigate the evolution towards a model of 'open RIS' using a longitudinal research design. Still, our methodological choice allowed gathering fine-grained information on the role played by research collaborations in firms' external search processes, strengthening the importance of the "learning at the boundaries" mechanism in a new ORIS model.

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APPENDIX 1

Description of the business model of the sampled enterprises

We describe here in greater detail some characteristics of the sampled firms working in the life science field. 50 interviewed enterprises are exclusively productive, 23 are mainly commercial (but they have developed on order large quantities of specific products) and 5 have a fifty/fifty mixed activity, as we can see in the following table.

Classification of the Emilia Romagna life science sector firms based on their main product

Manufacturing enterprises in the life science field (production and commercialisation)	**Firms in the sample**
Diagnostic	**5**
Bio-image	
Clinical Diagnosis	5
Functional evaluation	
Therapy and rehabilitation	**11**
Machinery for dialysis and respiration	4
Artificial organs	1
Rehabilitation and Support	1
Surgical Therapy	1
Orthopaedics and prostheses	2
Other	2
Non durable materials	**28**
Dental materials	1
Firms Hospital Materials	27
Other equipment	**21**

Aesthetic and stimulators	3
Dental equipment	
Hospital equipment	3
Electromedical equipment.	12
Various machinery	3
Pharmaceutical and biotech firms	**3**
Pharmaceutical enterprises	2
Biotech enterprises	1
Computer science enterprises applied to telemedicine	**10**

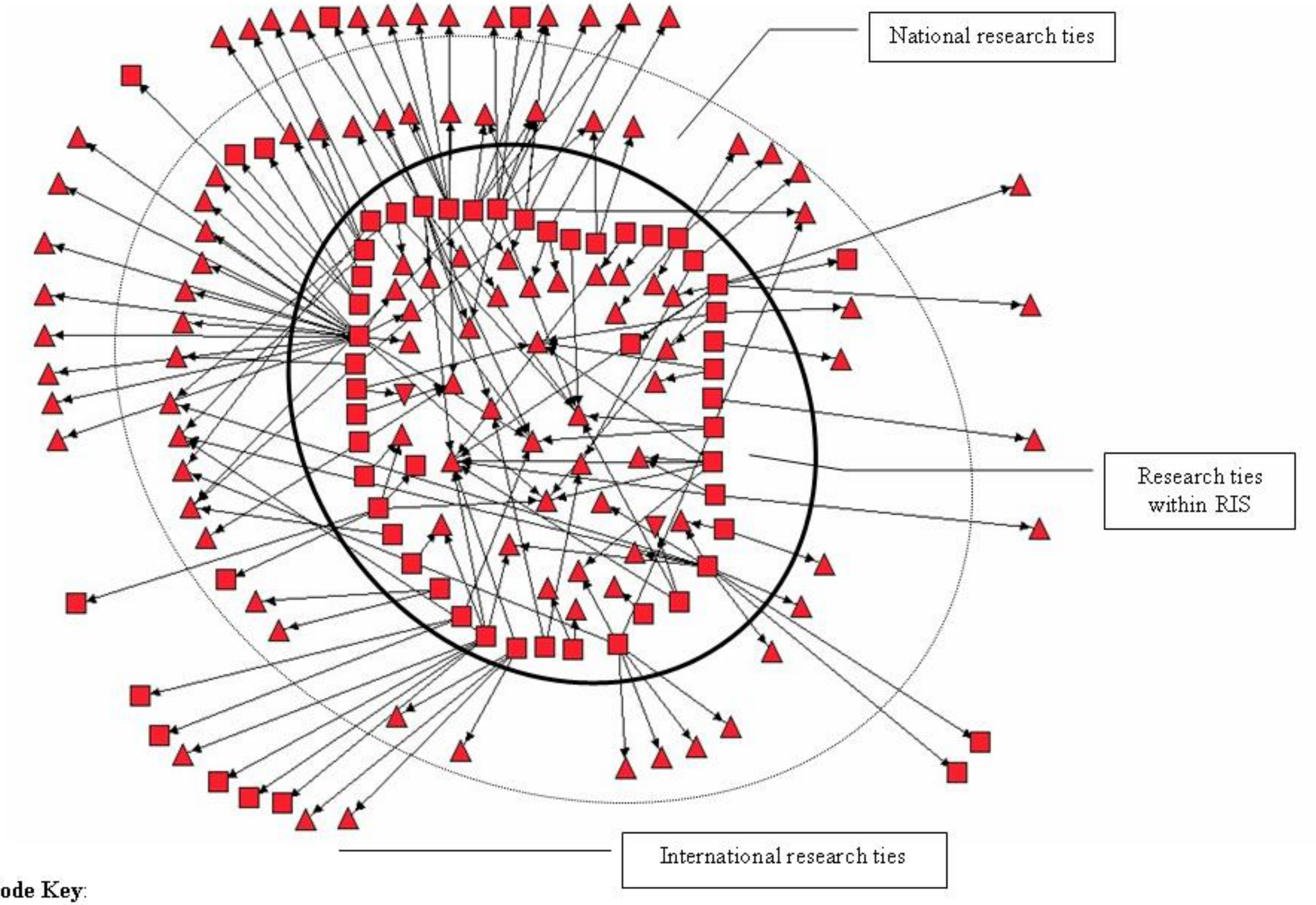
Source: our elaborations on 78 interviews

Tab. 1: Sectoral classification of life science firms: universe and sample of firms

Manufacturing firms of the Emilia Romagna life science sector	**Revised Cerved population**				**Sampled firms**			
	Firms		**Employees**		**Firms**		**Employees**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Diagnostic	12	2.34	31	0.27	5	6.41	28	0.62
Therapy and rehabilitation	106	20.66	3,306	28.42	11	14.10	2,535	56.73
Disposables	157	30.60	1,917	16.48	28	35.90	892	19.97
Other appliances	211	41.13	1,947	16,74	21	26.92	680	15.21
Pharmaceutical and biotech	14	2.73	4,264	36.65	3	3.85	165	3.69
Computer science applied to medicine	13	2.53	169	1.45	10	12.82	169	3.78
Total	513	100.00	11,643	100.0	78	100.00	4,469	100.0

Source: our elaboration on Cerved data, website and interviews with sector experts.

Figure 1 The research network within and across the RIS boundaries



Node Key:
Squares = firms; Triangles = PROs

Tab. 2: Sources of information and knowledge for innovation activities, year 2004 (N=78)

Type	**Knowledge source**	**Occurrence**		**Importance (score: 1-10)**
		N	**%**	**Mean**
Market-based	External R&D labs	23	29.5	7.91
	Regional firms imitation	9	11.5	5.22
	National firms imitation	10	12.8	5.40
	Foreign firms imitation	17	21.8	6.35
	Research agreements with other firms	8	10.2	4.89
	Clients and customers	51	65.4	8.57
	Suppliers of intermediary goods	15	19.2	7.47
	Patent acquisitions	8	10.2	7.87
	Distribution network	27	34.6	7.74
	Average – Market sources	**18.78**	**24.00**	**6.82**
Institutional	CNR (National Research Centre)	7	9.0	8.29

	R&D Regional Universities	24	30.8	8.25
	R&D National Universities	23	29.5	8.09
	R&D Foreign Universities	15	19.2	8.13
	Average – Institutional sources	**17.25**	**22.12**	**8.19**
Semi-public	Fairs, exhibitions	37	47.4	6.95
	Internet	44	56.4	7.25
	Scientific publications	40	51.3	9.20
	Average – Other sources	**40.33**	**51.70**	**7.80**

Source: Elaboration from our survey

Table 3: Occurrence of external research collaborations within the 78 sampled firms and total number of ties; absolute value (row percentage in brackets)

Type of relation	**Occurrence**			**Total number of ties**
	Yes	**No**	**Total**	
Total external relationships	45 (58%)	33 (42%)	78 (100%)	170
of which:				
Firm-to-firm relations	8 (10%)	70 (90%)	78 (100%)	17
Firm-to-PRO relations	44 (56%)	34 (44%)	78 (100%)	153

Source: Our survey

Tab. 4: Spatial distribution of the overall relations of the 78 sampled firms; absolute value (row percentage in brackets)

Type of relation	**Spatial distribution**				
	Regional	**National (Italy)**	**Foreign**		
			EU	**Extra-EU**	
Firm-to-firm relations	2 (12 %)	5 (29%)	7 (41%)	3 (18%)	17 (100%)
Firm-to-PRO relations	76 (50%)	48 (31%)	24 (16%)	5 (3%)	153 (100%)
All	78 (46%)	53 (31%)	31 (18%)	8 (5%)	170 (100%)

Source: Our survey

Tab. 5: Variables description, year of analysis: 2004

Role	Phenomenon	Variable	Description
Explanatory variables	Internal innovation effort - absorptive capacity	RD_EXP	R&D expenditure – log
	Openness of firm's innovation strategy	N_SOURCE	*External search breadth* (number of external sources used for innovation activities)
		N_REL	*Research networking* (number of collaborations established with PROs and firms for research purposes)
Control variables		SIZE	Firm size (number of employees – log)
		AGE	Firm age
		SECi	Sectoral dummies (diagnostic, therapy and rehabilitation, disposables, other appliances, pharmaceutical and biotech, information science applied to medicine – i =1, 2, 3, 4, 5, 6)
Dependent variables	Innovative capacity	N_PATENTS	Number of patents owned by the firm

Tab. 6: Descriptive statistics, year of analysis: 2004

Variable	N	Mean	Std.Dev.	Min	Max	1.	2.	3.	5.	6.
1. N_PATENTS	78	2.10	4.30	0	22					
2. N_REL	78	2.18	3.21	0	19	0.273*				
3. N_SOURCE	78	4.67	3.25	0	16	0.309*	0.341**			
5. RD_EXP (log)	78	7.68	6.03	0	15.12	0.261*	.346**	0.434***		
6. SIZE (log)	78	2.88	1.46	0	6.68	0.508***	0.213†	0.277*	0.270*	
7. AGE	78	16.04	12.20	1	73	0.374**	0.109	0.096	0.008	0.344**

† $p < .10$; *$p < .05$; ** $p < .01$; ***$p < .001$

Note: The R&D expenditure varies from 0 to 3,700,000 €, the mean value being 290,437 €. The size of the firm varies from 1 to 800 employees, the mean value being 57.29 employees.

Tab. 7: Negative binomial regression, firm analysis (dependent variable = N_PATENTS)

	Model 1			**Model 2**		
	Coeff.		Std. Err.	Coeff.		Std. Err.
RD_EXP (log)	.145	***	.033	.245	***	.050
N_REL				.337	*	.163
N_REL (squared)				-.001		.006
N_SOURCE				.128	*	.053
RD_REL				-.030	**	.010
AGE	.022	†	.013	.023		.011
SIZE (log)	.441	**	.133	.239	*	.117
SEC$_1$ - Diagnostic	3.340	**	1.014	3.717	***	1.011
SEC$_2$ - Therapy & rehab.	2.817	**	.896	3.343	***	.903
SEC$_3$ - Disposables	2.053	*	.839	2.764	**	.867
SEC$_4$ - Other appliances	2.420	**	.823	3.085	***	.852
SEC$_5$ - Pharm. & biotech	.607		1.251	1.526		1.130
SEC$_6$ – Informatics	Benchmark					
Constant	-4.976	***	.970	-6.757	***	1.130
No. of observations	78			78		
Log likelihood	-110.799			-138.857		
Chi-square	56.117	***		77.876	***	
McFadden’s R-square	.202			.280		

$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$