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We analyse the changing contribution of networks to the innovative performance of 30 pharmaceutical companies from 1989 to 1997. Count data models show that collaborations with universities and biotechnology companies are important determinants of the firms' innovative performance, but their respective contributions diverge when industry matures. Larger firms enjoy a significant size advantage and in-house research activities are highly significant. Returns to scale in research are decreasing over time while the size advantage is increasing. The changing contribution of networks to knowledge production suggests that these are phase-specific, which has substantial managerial and policy implications.

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1. Introduction

Networks of collaborative relationships amongst firms and public research institutions have been widely recognised as an important organisational form of innovative activities. Powell *et al.* (1996) argue that in fields of rapid technological change, the locus of innovation is found within networks of inter-organisational relationships, for they sustain fluid and evolving flows of scientific and technical knowledge. Furthermore, the network type of industrial organisation has the advantage of spreading risks and costs amongst members, while postponing the emergence of potential economic leaders.

We argue that the structure of innovation networks is linked to the development of the industry exploring and exploiting a specific set of scientific knowledge and technologies. Central to our argument lies the assumption that since technology and economics interact, the organisational conditions by which knowledge is created, accumulated and exploited must change over time together with firms' strategies and the sources of their innovative performance (Afuah and Utterback, 1997; Utterback and Suarez, 1993).

We analyse the changing contribution of the firms' network to their innovative performance in biotechnology. We argue that behind the apparent complexity of innovation networks in biotechnology, the contribution of different types of partners and of agreements to knowledge creation is linked to the stage of development of the industry and its associated technologies. Therefore, innovation networks should be phase-specific.

Our argument is at odds with the widely accepted idea that networks of innovation are complex because the innovation process is itself complex. The sequential nature of innovation is generally contested by the argument that a successful innovation is one

that has efficiently mixed several knowledge sources such as research activities, production activities, marketing, user relationships, etc (Kline and Rosenberg, 1986). This idea is further proved by the empirical evidence that networks in biotechnology do persist over time and involve a wide variety of actors. Instead, we argue that the complexity of networks stems from two distinct phenomena. First, firms are committed to projects relating to different waves of discoveries, such as gene sequencing, genomics, pharmaco-genomics, etc. These different waves call for a differentiated set of actors with a specific division of innovative labour. Second, within a single wave, firms are engaged in several projects that spread over different phases of research. These two inter-related trends call for a specific mix of actors and collaborative agreements, giving rise to the observed complexity of innovation networks. In this paper, we focus on the effect of the first phenomenon only, i.e. industry and technological development, on the contribution of networks to the innovative performance of firms.

The originality of the paper is to combine industrial organisation variables - such as network characteristics and external knowledge flows - with more traditional production factors - such as firm size and R&D spending between 1989 and 1997. Moreover, the empirical analysis explores the changing contribution of each explanatory variable over time. We combine two datasets: the USPTO dataset accounts for the innovative performance of firms whereas we describe the network structure of 30 US firms in pharmaceuticals using BioScan. These networks are described in terms of types of agreements, from research to commercialisation, and in terms of types of partners, namely large firms, dedicated biotechnology companies and public research institutes.

The paper is structured as follows. Section 2 reviews the theoretical and empirical literature as a background for the elaboration of four hypotheses. In Section 3, we develop respectively the econometric specifications and the construction of the variables

at stake. The statistical results are commented on in Section 4, leading to the discussion and conclusion of section 5.

2. Literature Review and Hypotheses

Industry Life Cycle theories have launched a vigorous research programme studying the forces governing the evolution of industrial structures (Abernathy and Utterback, 1978; Utterback and Abernathy, 1975) and the strategic implications for firm performances (Afuah and Utterback, 1997).

Industry life cycles

Industrial Life Cycle theories underlie the intrinsic changing nature of industry structure based on technological evolution. To sustain competition, technologies and competencies mobilised in a given production process have to adapt. Firms devote additional resources in learning, creating and adapting new knowledge so as to master it. Less efficient actors are not only those that fail in implementing their own production function in the short run. They may equally be those that fail in modifying it in the long run (March, 1991).

Industry Life Cycle theories exhibit two major phases in industry development, each being related to the state of the technological paradigm at stake (Dosi, 1982; Tushman and Anderson, 1986). The first phase is characterised by radical and rapid technical change. The emergence of a new technological paradigm may potentially destroy the traditional barriers to entry, representing a threat to incumbents using the old set of technologies. The second phase reveals some sort of technological consolidation and stabilisation around a dominant design (Anderson and Tushman, 1990). New firms may well be created on the basis of their differentiated knowledge for testing, refining and exploiting such opportunities. In the case of promising scientific results, such entrants

might eventually grow and gain access to preferable positions on new market segments. Large firms must also devote efforts in technology strategies in order to keep up to date with relevant knowledge and techniques and ultimately stay in the industry. Thus the development of knowledge, or say technologies, should not be thought of as provided to either incumbents or entrants of a particular industry. Both must invest in technology exploration and exploitation in order to build their competitive advantage.

As March (1991) pointed out, firms aiming at diversifying their knowledge base might be better fitted in adapting in and to an unstable environment. Yet with the stabilisation of the technological environment, exploitation strategies, *i.e.* the ongoing use of the firm's knowledge base (Vermeulen and Barkema, 2001), helps firms to refine their routines, while allowing them to exploit their competencies more efficiently. Firms focus on the knowledge that allows them to innovate and contributes most to its success, and filters out knowledge and routines that seem less successful. One of the main contributions of these authors is thus to shed light on the effect of the life cycle of the industry. During the exploration phase research and innovation are based on inter-organisational collaborations and alliances. During the exploitation phase, firms should tend to appropriate temporary rents generated through their innovation. Therefore, the type of agreements and of partners with which firms collaborate should target the introduction of new products or processes into the market.

Patterns of collaboration during the industry life cycle

Firms engage in a wide variety of learning processes (Malerba, 1992) not only to improve their on-going production process or innovate with new products, but also to cope with rapidly changing technological landscapes (Cohen and Levinthal, 1989). In fact, this has quite important implications in knowledge intensive industries, for

mastering a wide range of scientific and technical knowledge often proves unachievable for one isolated organisation. Instead, firms would rely on extra-organisational arrangements, supporting the view that firms are not isolated islands of production (Richardson, 1972).

Empirical facts strongly support the view that firms are embedded in complex networks of alliances and collaborations. Behind the explanation of why firms establish ties lies the assumption that firms naturally benefit from the complementarity of their partners' assets and competencies (Hite and Hesterly, 2001). Empirical analyses show that firms strongly engaged in cooperation tend to achieve higher levels of performance (Powell *et al.*, 1996). In fact, it is not the mere number of alliances that prove important, but rather the firm's central position and the density of its networks that boost innovative performance, market value and operating income (Afuah and Utterback, 1997; Baum *et al.*, 2000; Stuart, 2000; Stuart *et al.*, 1999).

One of the reasons for this is that the expected benefits of alliances and networks are the enrichment of the flow of knowledge amongst partners (Kogut, 1988), the access to complementary assets (Pisano, 1990) as well as access to external legitimacy and status (Baum and Oliver, 1991; Liebeskind *et al.*, 1996). Baum *et al*. (2000) show that at founding, the initial performance of start-ups increases with the size of its alliance network together with the efficiency of the network members. During the creation phase of the firm, the variation in alliance network composition produces significant differences in their performance. The roles of alliance and patterns of collaboration may vary amongst firm age and size. University industry collaborations appear to be one of the sources for capturing new knowledge and know-how (Siegel *et al.*, 2001). Alliances with potential clients and other biotech firms are needed as well (Oliver, 2001; Powell *et al.*, 1996), for they generate new forms of cooperation, from commercial, research or

production agreements to joint ventures and mergers or acquisitions.

Such contributions focus on the firm life cycle. Indeed, several qualitative case studies in biotechnology (McNamara and Baden-Fuller, 1999; Steier and Greenwood, 2000) show that the composition of collaborative networks is changing as firms grow. Commercial and financial alliances become more vital while alliances with other firms or public laboratories gradually decrease. Disappointingly, they do not provide a substantial account of the changing nature of firm patterns of collaborations when the industry matures.

Utterback and Suarez (1993) suggest that as technology evolves, so do industry structures and attractiveness, together with critical factors for firm success. Notably, since firms seek to appropriate knowledge and translate it into private rents, be it higher productive processes or new commercial products, the nature and the partnerships of collaborations in innovative activities ought to change as compared to earlier research phases. During the exploration phase, scientific and technological hypotheses have to be explored. Research and development agreements with universities and with dedicated biotech SMEs are designed to have access to a large diversity of knowledge bodies, to explore a wide variety of hypotheses. When risks and costs of research are high, joint ventures with large firms are designed to make up stream research. Deliberate R&D agreements are important in order to have access to different bodies of knowledge and to design innovative products and processes based on radical innovation. During this phase, firms also benefit from spillovers from other firms and institutions. During the exploration phase, spillovers are all the more important for firms to explore and benefit from knowledge produced by other organisations. During the exploration phase, network relationships are crucial for they provide firms with a higher access to information, external knowledge, goods and services, etc. (Maurer, 2001; Zucker *et al.*,

1998). As the industry matures, products are reaching the market and competition amongst firms is higher and access to market becomes critical. It is reasonable to assume that during the exploitation phase, the pattern of agreements is changing, from R&D to commercialisation. In the same vein, knowledge spillovers should be less important.

The main hypothesis explored in this paper is that the exploitation of a few promising scientific results must have led to corresponding changes in the structure of networks for most of the firms within the industry. As the industry matures, the network structure of a given company not only changes with its size, its age and its growth but also in terms of partnership and alliance purposes (from upstream research to development and commercialisation). At the level of the industry, we might speculate that the changing nature of the technological environment leads to different patterns of collaboration. Thus innovation may be the result of research activities but may be also boosted by development and commercialisation activities. The network structure of inter-organisational alliances governs the exchange of complementary assets among the different actors involved: academic teams, large firms and SMEs.

We investigate such issues in the realm of biotechnology. Biotechnology was not an industry during the period under review 1987-1997, but a set of scientific principles and associated techniques that provides firms with new solutions on research and productive activities in pharmaceuticals, the chemical and the agro-food industries. Biotechnology has traditionally been based on close ties between university and industry (Kenney, 1986) as the nature of biotechnological knowledge blurs the frontier between fundamental and applied knowledge. Discoveries in the former may boost developments in the latter while new applications may well lead to new scientific breakthroughs. As a consequence, public and private laboratories have relied more and more on inter-

organisational arrangements in order to share differentiated yet complementary knowledge.

The biotechnology industry is based on different waves of discoveries. The first wave (under review in this paper) concerns the discovery of monogenetic disease and leads to biotech remediation and gene therapy. This first stage was product-oriented, and it ends with the emergence of bio-informatics that focused on the improvement of process discovery as well as high-speed screening. Post genomic and the generalisation of the use of biotech techniques in life sciences may form the more recent wave. Graph 1 visualises the different waves of discoveries as well as the growing number of collaborations over time resulting in the addition of alliances of the different phases.

*** GRAPH 1 NEAR HERE ***

Graph 1 represents the evolution of the number of alliances by phases of discoveries (dotted lines), e.g. gene sequencing, gene therapy, genomics, etc. The plain line reports the total number of alliances over time, summing over alliances associated with the different phases. One of the main consequences of those waves of discoveries is that firms manage a portfolio of innovation activities that spread over several distinctive phases. Therefore, they manage different collaborations, from research to commercialisation, with universities and other firms. It follows that the alliance strategy of firms is usually considered as complex: for a given year, firms manage a portfolio of alliances referring to different phases. On the contrary, our representation depicts the sequential character of innovation, allowing us to define patterns of collaborations within a given phase. To stress the influence of the industry life cycle, we limit the period under review to the first wave of biotechnology, ending in the second half of the eighties in the USA.

To convincingly grasp changes in technologies and in industry structures, it is necessary

to introduce temporal consideration. Thus, not only the organisation of the industry is changing throughout the life cycle of the industry (Utterback and Suarez, 1993), but also the kinds of capabilities that the firm needs to master vary from one stage to another. As the industry is maturing, rivalry among existing competitors is higher than in the previous phase because products and processes are reasonably developed and enter the market. Firms are investing in capacity, brand name, patents, special licences and distribution channels. Thus barriers to entry within the industry are higher. This suggests that the sources of performance might correspondingly change thoughout the various stages of the industry life cycle. Altogether, we can design the following hypotheses to be explored:

H1. Spillovers as well as collaborations between public and private or amongst private organisations are positively linked with the innovative performance of firms.

However in dynamics:

H2. The contribution of spillovers to firm innovative performance tends to diminish over time.

H3. As the industry matures (within a given wave), the contribution of networks to firm innovative performance changes from upstream research to downstream phases in knowledge production activities.

H4. As the industry matures (within a given wave) and as barriers to entry increase, the size advantage increases.

3. Data and Methods

Hypotheses 1-4 are tested on a sample of firms active in pharmaceutical research. In the pharmaceutical industry, research is different from development as the former deals

with the selection of new molecules while the latter focuses on clinical trials and authority approvals. By way of consequence, the firms' innovative performance can be differently appreciated, whether we concentrate on the discovery phase or on the commercial event. In this paper, we focus on the first phase of innovation, *i.e.* discovery, leading to the patenting of potentially profitable molecules. Since discovery calls for a subsequent appropriation of the knowledge produced by the firms, pharmaceutical firms largely rely on knowledge appropriation through patent applications.

As biotechnology appears to be a vital competence for innovation in life sciences, patents play a central role in firm strategies. From the 1980s onwards, the system of intellectual property rights stabilised and patenting has been included in firm strategy, especially in start-up strategy. Indeed, as pointed out by Afuah and Utterback (1997), patents are one of the central assets needed to succeed in the emerging (fluid) phase. Dodgson (1991) and Rabinow (1996) underline that one of the conditions *sine qua non* for the creation of start-ups is the opportunity to protect their innovation.

Modelling firm innovative performance

The dependent variable focuses exclusively on US biotechnology patent applications as retrieved in the Derwent Biotechnology Abstract database, henceforth DBA. The DBA covers all biotechnology patent applications since 1981. In 2001, more than 96,000 patent applications are reported in the DBA, from 1965 to 2001 and covering 40 intellectual property authorities. Because two years are needed for inventory purposes, the curve drops tremendously after 1998. Therefore, the analysis will be exclusively concerned with patent applications prior to that date.

A particularly attractive feature of the DBA is that it reveals principally the first wave of biotechnology, centred on genetic sequencing and gene manipulation. And indeed,

the observed evolution is well argued by the arrival of a set of stabilising research procedures and instruments, such as PCR, bioinformatics, crystallography, etc. However, recent developments in new promising areas, such as genomics, proteomics, pharmaco-genomics and/or single nucleotide polymorphisms were still in their infancy in 1997. Thus, for the latter part of our study, our dependent variable refers principally to the first phase of biotechnology development.

Patents are a rudimentary measure of discovery success, as they suffer several pitfalls (Archibugi, 1992; Pavitt, 1988). Of notable importance is the extreme volatility of their economic significance: firms may patent in order to consolidate their position in an identified technological space rather than to secure future rents that may potentially come out of new knowledge (Boisot, 1995). We control for this by weighting the patent count with the number of citations received by those patents[1]. The resulting sample is thus composed of 2,324 US patents that account for 6,178 citations. Discarding self-citations led to the withdrawal of 1,448 citations that represent approximately 23% of the original citation count[2].

Non-negative integers call for the use of count data models. As in most previous studies, we assume that patent applications follow a Poisson probability distribution: discovery is the outcome of a large number of trials but with a relatively small probability of success. Let y_i be the dependent variable, *i.e.* the number of patent applications filed by firm *i*, where $i = 1,\ldots,N$. The dependent variable y_i has a Poisson distribution with parameters λ_i:

$$P(Y = y) = exp(-\lambda) \cdot \frac{\lambda^y}{y!} \qquad (1)$$

Parameters λ_i depend on a set of explanatory variables X_i and estimates β_i which are in this case the determinants of the knowledge production function. The expected count of patent application of firm *i* is given by equation (2), the exponential forms guaranteeing the non negativity of the predicted λ_i:

$$E(Y_i) = \lambda_i = exp(X_i, \beta_i) \quad (2)$$

One important peculiarity of the Poisson model lies in the assumption of equality of the mean and the variance of parameters λ_i, while the empirical mean and variance of y_i violates this assumption. We account for this overdispersion by introducing a dispersion parameter ϕ into the equality between the mean and variance. McCullagh and Nelder (1983) suggest estimating parameter ϕ as the ratio of the Pearson Chi Square to its associated degree of freedom. Parameter ϕ provides a correction term for testing the significance of the estimates produced by the Poisson model, but does not introduce a new probability distribution.[3] We also use the negative binomial model (Hausman et al, 1984). This model allows for overdispersion by including a firm unobserved specific effect ε_i into the λ_i parameters so that $\lambda_i = exp(X_i, \lambda_i + \varepsilon_i)$. If $exp(\varepsilon_i)$ is distributed gamma, then the integration leads to the negative binomial model. In this paper, we refer to the Negbin II model as suggested by Cameron and Trivedi (1998), similar to adding a firm random effect to the model.

The previous models normally assume that an increase from zero to one is not qualitatively different from an increase from one to two. In fact, there may be quite a deal of difference, for patenting one or several times strengthens the competitiveness of the firms as compared to those which do not patent at all. Thus, zero values represent a special outcome in the firm's innovative performance. We account for this by experimenting with additional estimation methods, namely the Zero-Inflated Poisson

and negative binomial (ZIP and ZINB) models (Lambert, 1992). ZIP models deal with two sources of overdispersion by partitioning the observed variable *y* into a qualitative and quantitative part. The qualitative part estimates specific covariates that explain the decision not to patent, using a logit type of link function. The quantitative part explains the positive patent outcome for those firms, which actively patent. Thus a mixture distribution arises when a proportion ω of firms do not patent, so that the dependent variable *y* has a zero-inflated distribution given by:

$$\begin{cases} P(Y=0) = \varpi + (1-\varpi)\cdot exp(-\lambda) & if\ y=0 \quad (3) \\ P(Y=y) = (1-\varpi)\cdot exp(-\lambda)\cdot \dfrac{\lambda^{y}}{y!} & if\ y>0 \quad (4) \end{cases}$$

Since we are essentially interested in the determinants of the firm's innovative performances, zero-inflated results will exclusively report its Poisson part (equation 4). The ZIP model can easily be extended to the negative binomial distribution, yielding the so-called Zero-Inflated Negative Binomial model (ZINB).

The independent variables

Hypotheses 1-4 posit relationships between the firms' portfolio of collaborative agreements and their innovative performance. The data on collaborative agreements were found in the 1999 edition of BioScan, gathering information on the type of agreements and the names of organisations involved in the alliances. Altogether, our sample is composed of 1,048 collaborative agreements between 1985 and 1997, involving 425 different actors: 95 large firms, 278 biotechnology companies and 52 universities. Graph 2 reports the evolution of collaborative agreements by type of institutions involved, agreements with large firms (AWL), agreements with

biotechnology companies (*AWB*) and agreements with universities and public research institutes (*AWU*) since 1985. Graph 2 also reports the type of agreements, research agreements (*RA*), development agreements (*DA*) and commercial agreements (*CA*).[4]

Firms learn from collaborative agreements by assimilating, integrating and then exploiting some of the partners' knowledge into their own competencies. This may be time-consuming; therefore we must introduce a lag structure in all variables on collaborative agreements. Similar to Stuart (2000), we account for this by computing the weighted sum of alliances over the past five years:

$$A_{i,t} = \sum_{i=1}^{i=5} \varpi_i \cdot a_{t-i} \qquad (5)$$

where $A_{i,t}$ is the weighted number of collaborative agreements of firm *i* at time *t*, accumulated during the previous five years, a_{t-i} is the number of a given type of agreement, such that $a \in \{AWL; AWB; AWU; RA; DA; CA\}$, and ϖ_i is the linearly depreciated weight such that $\varpi_1 = 0.2$ if $t = 5$, $\varpi_1 = 0.4$ if $t = 4$ and so on until the lagged year which received a weight of 1.

The intrinsic characteristics of the firm are described according to two complementary dimensions: R&D expenditures (*RD*) and assets (*ASSETS*), by year and by firm. These financial data were collected through *World Scope Global Researcher*. R&D expenditures reveal the effort dedicated to the renewal of its own knowledge base as well as the development of an absorptive capacity of external scientific and technological advances (Cohen and Levinthal, 1990). The variable *ASSETS* represents the current real assets of the firm for each year. It is a proxy of the size of the firm. The advantages of a larger size are usually (1) the repartition of fixed costs on a larger variety of activities, (2) the reduction of the uncertainty on the cash flows linked to R&D activity and (3) economies of scale when research activity becomes routinised.

Thus, *ASSETS* and *RD* are two proxies of firm size (Henderson and Cockburn, 1996), though they reveal two different types of advantages, namely those concerning risk and cost spreading and those regarding firm effort in R&D activities. We account for this by measuring the R&D intensity (*RDI*) of the firm, computed as the ratio of firm R&D expenditures on real assets.

*** GRAPH 2 NEAR HERE ***

External flows of knowledge as well as the firm absorptive capacity play an important role in the firm's innovative performance. Notably, firms may identify, assimilate and exploit formerly external flows of knowledge so as to translate it in its own production function. External flows of knowledge are described following Jaffe's methodology (Jaffe, 1986). For a specific year, we define the variable *SPILLOVERS* as an external knowledge pool:

$$SPILLOVERS_{i,t} = \sum_{j \neq i} SF_{ij} \cdot RD_i \qquad (6)$$

The variable *SPILLOVERS* of firm *i* is higher when the effort of research of other firms *j* is high and when the knowledge base of those firms is close to that of firm *i*. Using the cosine index, SF_{ij} is a measure of the similarity between firm *i* and firm *j* based on the technology classes provided by the DBA for every year between 1989 and 1997. Finally, we use two additional variables to control time and specialisation effects. *TREND* depicts a linear time effect on patent applications. Firms may well apply for patents for various reasons, some of which reveal a general evolution accounting for changes in regulation, the adaptation of the patent systems, etc. *BIOTECH* is a dummy variable, which takes the value 1 if the firm is a Dedicated Biotech Firm (DBF), 0 otherwise. These additional variables control for various aspects that may influence firm

activity in knowledge production.

*** TABLE 1 NEAR HERE ***

The final sample is an unbalanced panel dataset composed of 30 firms from the period 1989 to 1997, which leads to 238 observations. Table 1 presents the variables entering into firm knowledge production function. We chose all variables in logs so as to estimate the elasticities of patent applications, weighted by their citation count, with respect to research efforts, firm size, networking portfolio and external knowledge flows. All explanatory variables are lagged one year in order to avoid spurious correlations with the dependent variable.

4. Results

Table 2 reports the results of various regressions and computations entering into the knowledge production function. Models (1)-(5) analyse the determinants of firm innovative performance, approximated through individual patent applications. We note the following:

- Though positive, *RDI* remains substantially below unity, indicating decreasing returns to scale in pharmaceutical research. Thus, a 1% increase in R&D leads to a less than proportionate increase, *i.e.* about 0.5%, in the expected number of patent applications. These results corroborate those of Henderson and Cockburn (1996) when they observe decreasing returns to R&D spending in the pharmaceutical industry.
- *ASSETS* seem to positively correlate with knowledge generation, leading us to conclude that larger firms have a significant size advantage in pharmaceutical

research. However, this size effect is half of that induced by firm research effort. Innovation depends primarily on R&D expenditures.

*** TABLE 2 NEAR HERE ***

- External Knowledge flows (*SPILLOVERS*) have a large, significant and positive influence (Model 2). Looking at the McFadden Pseudo R^2, the introduction of this additional variable increases significantly the explanatory power of the knowledge production function. Thus, firms assimilate initially external knowledge flows and exploit them within their own knowledge production function. The significant and positive sign of *BIOTECH* suggests that DBFs have a significant advantage in generating highly cited patents. The negative effect of *TREND* suggests that prior research has focused on simpler problems, such as monogenetic diseases, shifting future discoveries into more complex therapeutic areas, *i.e.* polygenetic diseases.
- In models 3, 4 and 5, we introduce the firm's portfolio of collaborations, that is, the network structure in terms of types of collaborations and types of partners. In model 3, we introduce the weighted sum of all agreements (*TA*) signed by a firm over the previous five years. We observe that the number of agreements has a positive and significant effect on firm innovative performance. This suggests that firms not only benefit from spillovers, that is, from what we could label passive activities of assimilating knowledge flows, but they enter into more interactive activities of knowledge creation.
- In model 4, we distinguish between research (*RA*), development (*DA*) and commercialisation agreements (*CA*). Only development agreements have a significant and positive impact on the innovative performance of firms. Research

agreements do not impact on the number of patent applications, weighted by the number of citations received by those patents.

- Discriminating amongst the type of partners involved in firm collaborations significantly improves our estimations (model 5). Agreements with either biotechnology firms or universities enter the knowledge production function significantly and positively, while agreements with larger firms are negatively linked with the number of citation-weighted patent applications. These results suggest that all kinds of partners bring differentiated complementary assets and competencies to the firms in the sample.

All in all, hypothesis 1 is thus generally corroborated. The firms' connection to external flows of knowledge and partners is consistent with the view that firms translate such knowledge into their own production function. However, only collaborations with universities and DBF increase significantly the quality of the knowledge produced by pharmaceutical firms. Collaborations with large firms correlate negatively with our measure of innovation, suggesting collaborations with large companies concern later phases of the innovation stages, rather than the mere invention phase.

*** TABLE 3 NEAR HERE ***

In Table 3, models 6 to 9 explore the robustness of the results. The familiar approaches to accommodating heterogeneity in panel data have fairly straightforward extensions in the count data setting. The negative binomial model takes into account some firm unobserved random effects, while the Zero-Inflated Poisson model is another model in which the zero outcome of the data generating process is qualitatively different from the positive ones.

The McCullagh and Nelder model (6) inflates all standard errors while producing the same Poisson parameter estimates. We note that only the firms' internal research effort (*RDI*), external knowledge flows (*SPILLOVERS*), *BIOTECH* and *TREND* remain significant at the 5% level. Although in the negative binomial model (7), all variables loose their significance, the sign of the parameter estimates are consistent with our prior estimates. The Zero-Inflated models produce similar results with different significance levels. All things considered, the results show some sign of volatility regarding their significance level, but not regarding their sign.

To test hypotheses 2-4, we explore structural changes in the knowledge production function throughout time. To do so, the pooled sample was split into two sub-periods running between 1989-92 and 1993-97 respectively. Such a method allows us to grasp some structural change in the conditions of knowledge production through time. With the relatively short time span at hand, we are actually assessing directions (positive or negative) rather than the actual magnitude of parameter changes throughout time. The changing effects of network structure from 1989-92 to 1993-97 are presented in Table 4. Models (10) and (11) present the results using the variables on the types of agreements (*RA*, *DA*, *CA*). Models (12) and (13) display the results for using the variables on the types of partners (*AWL*, *AWB*, *AWU*)

*** TABLE 4 NEAR HERE ***

- The contribution of research effort (*RDI*) to the production of knowledge decreases over time. In the first period, our estimate is above unity, while it goes below unity in the second period. This suggests that over time, returns to scale in R&D are decreasing in such a way that in the most recent period, an increase in R&D spending

implies a less than proportionate increase in citation-weighted patent output. In the meantime, the contribution of the variable *ASSETS* to the production of knowledge increases, suggesting that the size advantage increases over time. This does conform to our appreciative knowledge of the industry: the current concentration in pharmaceuticals suggests that firms increase the size of their activities in order to reach a minimum critical mass in research. Likewise, Henderson and Cockburn (1996) observed that research efforts made by larger firms tend to be more productive, although they witnessed decreasing returns to scale in research.

- External knowledge flows (*SPILLOVERS*) play an important role in the first sub-period. This suggests that firms tend to benefit from knowledge spillovers in early phases of the industry and the technological paradigm.
- We observe a fundamental switch in the contribution of the firm network portfolio over time, whether we look at the types of agreements or the types of partner involved in the collaborations. In the first phase (1989-93), the number of research agreements in which the firm is involved is significantly linked to knowledge production (model 10). This first phase involves mainly universities and public research institutes (model 12), which contributes positively to the citation-weighted patent count. In the second sub-period (1993-97), development agreements contribute significantly to knowledge production (model 11), involving mainly biotechnology firms (model 13). Note that commercialisation agreements, which involve mainly large firms, contribute negatively and significantly over the whole period. This suggests a rather sequential model of innovation, which is mainly science and technology driven. The characteristics of the market are likely to concern the very introduction of new products and services into the market (the innovation stage), which is not grasped by our dependent variables.

Table 4 supports hypotheses 2-4. The contribution of spillovers decreases over time (hypothesis 2), the size advantage increases as the technology matures (hypothesis 4), and the type of agreements and partners changes over time to downstream phases in knowledge production (hypothesis 3).

The evolution from emergence to maturity reveals the changing nature of networks over time. During the exploration phase, collaborations and co-patenting amongst different partners are linked to the innovative performance of the firm. Novelty is based on the transformation of scientific breakthrough to potential innovation. This phase was largely supported by the growth of scientific collaborations between academia and private firms as revealed here. The transitional and maturing phase is based on the transformation of potential innovation onto effective innovation, *i.e.* application of generic patents to product and process patents within given technological trajectories. When the technologies stabilise, they develop more traditional forms of organisation in research activities. They internalise research activities along their business lines, as has been suggested by increase in the contribution of *ASSETS* and by decrease in the contribution of both *RDI* and *SPILLOVERS*.

The above results do not deny the role of collaborations. Quite the contrary, they tend to emphasise the fact that both networks and in-house R&D are phase specific. Basic research naturally associates with research productivity when the technological environment is characterised by high uncertainty. When the technological environment stabilises, firms have a higher predictive power so as to bet on a given set of technologies. This phase is characterised by the development of research hypotheses that have proven fruitful through contracts with DBFs. In this case, DBFs play the role of knowledge developers for other firms.

5. Discussion and Conclusions

Our analysis highlights the relative influence of alliances, according to their aim (research, development and commercialisation) and types of partner (large firms, DBF, universities), on the innovative performance of the firm for a given phase. Based on the analysis of a specific wave of innovations, we show that the efficiency of collaboration on innovative performance is phase-specific. This has both managerial and policy implications.

Managerial implications

This paper goes beyond the raw picture that networking is profitable. Networks are not profitable *per se*, for they do not represent a sole moral or accounting entity. Though clusters of firms do exist, the boundaries of networks remain to a large extent blurred both geographically and over time. This suggests that the performance of networks should relate to the individual performance of the companies embedded in collaborations. At best, networks contribute to the activities of individual members, the performance of which may in turn be positively or negatively affected. Correspondingly, this paper has analysed the contribution of collaboration networks in the research activities of individual pharmaceutical companies.

We found that industrial organisation, networking activities and the intensity of in-house research are phase-specific. Our empirical findings support the hypothesis of Hite and Hesterly (2001): the emergence phase is characterised by a high degree of uncertainty regarding resources, routines, products and the technological environment. Given the lack of necessary capital and legitimacy to exchange on the basis of market transactions (Baum *et al.*, 2000), firms develop external collaboration networks to access capabilities without committing too large a share of firm resources. Research

collaborations with academic laboratories remain a preferable solution to reach new scientific developments. During the maturation phase, efficient development is mainly based on collaborations with DBFs. The appropriation process for both pharmaceutical firms and DBFs is based on a clearer division of labour between partners. Internal R&D also changes from large and broad R&D projects for generating a high absorptive capacity to market-oriented product and process developments.

The presence of waves of innovations implies that firms must manage a portfolio of collaborations that focus on different waves, according to the development of the technology. It implies that firms must *phase* their portfolio of collaborations, which includes both research agreements (to explore new scientific solutions) and development collaborations (to better exploit their existing knowledge base). The observed evolution is well argued by the arrival of a set of stabilising research procedures and tools, such as PCR, bioinformatics, crystallography, etc.

However, the observed decline in the contribution of research agreements does not amount to denying the persistent role of collaborations. Additional scientific collaborations came up in the second half of the 1990s to explore recent developments in new promising areas such as genomics, proteomics, pharmaco-genomics and/or single nucleotide polymorphisms. Thus, our contention is that networks may reflect the changing nature of the technological landscape not in the mere number of ties, but rather in their types. Networks are not dead; their nature is simply changing together with the industry life cycle.

Implications for Public policy

This paper carries important managerial implications for policy makers. As the emergence, development and maturation of an industry follow successive waves of

innovations, public policy makers must also *phase* their support to innovation in biotechnology. With the presence of several generations of biotechnological development, public policies must both support a constant effort in research in order to ensure the renewal of the industrial knowledge base, simultaneously with a continuous support for development activities, to ensure the profitability of the biotech-related industries.

Support for start–ups is suitable during the emerging phase while growth of firms must be carefully analysed when barriers to entry are high. Industry life cycle approaches also question benchmarking activities, which tend to integrate different phases in summary statistics rather than identify and support specific phases of development of industries. In turn, this implies that replicating public policies that were successful in other settings can prove extremely counter productive.

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ENDNOTES

[1] The USPTO patent number was matched with the Metrics Group Database, providing received citations for each US patent. The choice of this database was based on the fact that citations are updated weekly, thus moving the citation truncation substantially later in time. We first intended to use the NBER US Patent Citation Database. But because the database runs until 1999, the time truncation proved too severe to be effective for this study.

[2] While self-citations do carry information on internalised knowledge transfer (Hall et al., 2001), they inevitably embody firms' specific effects on organisational and technological practices that may not reflect the quality of patents as perceived by external users of the technology.

[3] Therefore, when $\phi = 1$, the parameter estimates and their associated p-values strictly correspond to the standard Poisson model.

[4] BioScan lists 11 types of agreements which we have gathered in three groups: research agreements, gathering mainly upstream research; development and innovation agreements, including licensing; production agreements and commercial agreements gathering distribution, and marketing. Thus the three groups created aim at reproducing the sequential chain for one given research project.

TABLE 1
Descriptive Statistics. Pooled Sample (1989-1997)

Variable			Obs	Mean	Std. Dev.	Min	Max
Citation weighted patent application count	Y	t	238	19.874	30.490	0.000	164.000
R&D spending (log of)	RDI	t_{-1}	238	0.024	0.590	-2.383	1.349
Firm size measured as Assets (log of)	$ASSETS$	t_{-1}	238	13.483	2.230	8.394	16.822
Knowledge Spillover Pool (log of)	$SPILLOVERS$	t_{-1}	238	16.816	0.229	15.821	17.155
Total number of Agreements (log of)	TA	$\sum_{i=1}^{i=5} \varpi_i \cdot TA_{t-i}$	238	1.713	1.041	0.000	4.067
Research Agreements (log of)	RA	$\sum_{i=1}^{i=5} \varpi_i \cdot RA_{t-i}$	238	0.675	0.755	0.000	3.025
Development Agreements (log of)	DA	$\sum_{i=1}^{i=5} \varpi_i \cdot DA_{t-i}$	238	1.302	0.887	0.000	3.484
Commercialisation Agreements (log of)	CA	$\sum_{i=1}^{i=5} \varpi_i \cdot CA_{t-i}$	238	0.784	0.710	0.000	2.501
Agreements with Large Firms (log of)	AWL	$\sum_{i=1}^{i=5} \varpi_i \cdot AWL_{t-i}$	238	1.039	0.803	0.000	2.986
Agreements with Biotech Firms (log of)	AWB	$\sum_{i=1}^{i=5} \varpi_i \cdot AWB_{t-i}$	238	1.171	1.058	0.000	3.932
Agreements with Universities (log of)	AWU	$\sum_{i=1}^{i=5} \varpi_i \cdot AWU_{t-i}$	238	0.277	0.498	0.000	2.197

TABLE 2

The Network Determinants of Patent Output. Pooled Sample. Poisson Regressions. Dependent Variable: Number of Citation Weighted Patents (N=238).

	Equations				
	Model (1)	Model (2)	Model (3)	Model (4)	Model (5)
Constant	1.999 ** (0.91)	-32.31 *** (4.39)	-30.85 *** (4.42)	-32.20 *** (4.49)	-33.49 *** (4.53)
RDI	0.430 *** (0.08)	0.509 *** (0.08)	0.501 *** (0.08)	0.494 *** (0.08)	0.555 *** (0.09)
ASSETS	0.141 ** (0.06)	0.294 *** (0.06)	0.275 *** (0.06)	0.283 *** (0.06)	0.243 *** (0.07)
SPILLOVERS		1.969 *** (0.24)	1.888 *** (0.25)	1.963 *** (0.25)	2.099 *** (0.25)
Total Agreements (*TA*)			0.078 ** (0.03)		
Research Agreements (*RA*)				-0.012 (0.05)	
Development Agreements (*DA*)				0.117 ** (0.05)	
Commercialisation Agreements (*CA*)				-0.071 (0.05)	
Agreements w/ large firms (*AWL*)					-0.249 *** (0.04)
Agreements w/ Biotech firms (*AWB*)					0.196 *** (0.02)
Agreements w/ universities (*AWU*)					0.150 ** (0.06)
BIOTECH		0.843 *** (0.11)	0.799 *** (0.11)	0.851 *** (0.12)	0.794 *** (0.13)
TREND		-0.572 *** (0.03)	-0.578 *** (0.03)	-0.578 *** (0.03)	-0.614 *** (0.03)
Log-likelihood	-1,352.05	-1,317.92	-1,315.75	-1,315.40	-1,293.95
McFadden Pseudo R^2	0.704	0.712	0.712	0.712	0.717

Standard errors in parentheses.

Firm Fixed Effect Poisson Regressions. Year dummies included in all regressions.

*** ** * Significant at 1, 5 and 10 % levels respectively.

TABLE 3
The Network Determinants of Patent Output. Pooled Sample.
Exploring the Robustness of the Results Using Model (5).
Dependent Variable: Number of Citation Weighted Patents (N=238).

	Specification			
	McCullagh and Nelder	Negative Binomial	ZIP	ZINB
	Model (6)	Model (7)	Model (8)	Model (9)
Constant	-33.49 ** (14.04)	-21.13 (19.66)	-32.58 *** (4.65)	-16.86 (18.93)
RDI	0.555 ** (0.27)	0.199 (0.32)	0.651 *** (0.08)	0.296 (0.30)
ASSETS	0.243 (0.20)	0.206 (0.22)	0.273 *** (0.07)	0.241 (0.20)
SPILLOVERS	2.099 *** (0.77)	1.394 (1.12)	2.013 *** (0.26)	1.097 (1.09)
Agreements w/ large firms (*AWL*)	-0.249 * (0.13)	-0.124 (0.176)	-0.218 *** (0.04)	-0.106 (0.161)
Agreements w/ Biotech firms (*AWB*)	0.196 (0.13)	0.276 * (0.158)	0.161 *** (0.04)	0.287 ** (0.147)
Agreements w/ universities (*AWU*)	0.150 (0.20)	0.301 (0.234)	0.114 ** (0.06)	0.278 (0.21)
BIOTECH	0.794 ** (0.39)	0.520 (0.53)	0.816 *** (0.13)	0.570 (0.46)
TREND	-0.614 *** (0.10)	-0.648 *** (0.11)	-0.574 *** (0.03)	-0.621 ** (0.11) *
Overdispersion coefficient	9.62	0.651	N/A	0.448
Log-likelihood.	1,293.95[a]	-736.42	-1,174.43	-733.74

Standard errors in parentheses.
Firm Fixed Effect Poisson Regressions. Year dummies included in all regressions.

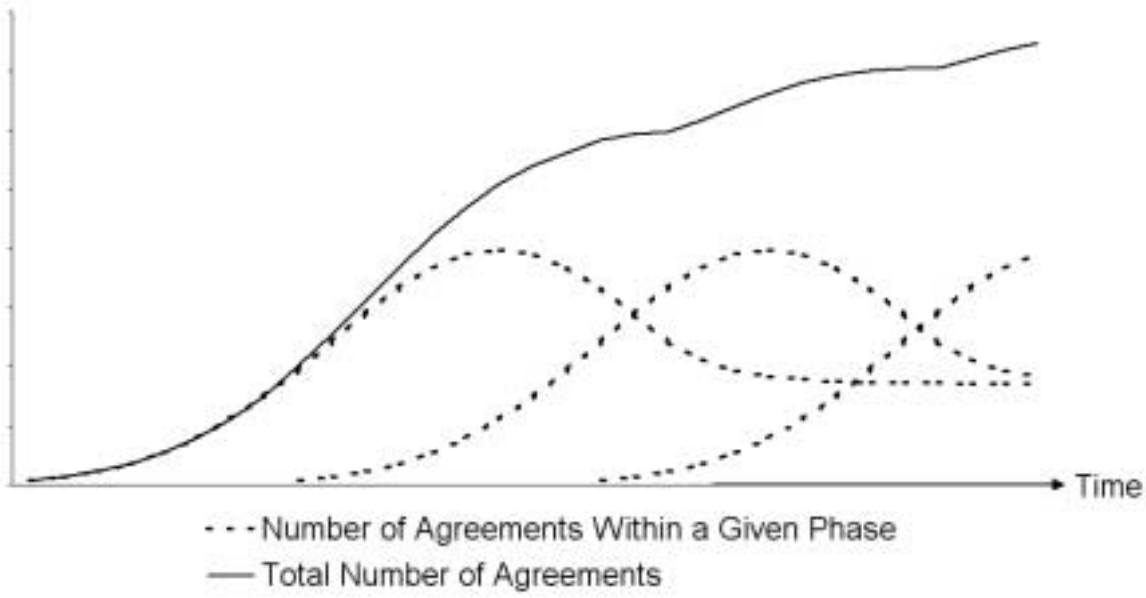
*** ** * Significant at 1, 5 and 10 % levels respectively.

TABLE 4
Determinants of Patent Output. Poisson Regressions.
Exploring the Dynamics of Innovation Networks.
Dependent Variable: Number of Citation Weighted Patents.

	Type of Agreements		Type of Partners	
	1989-92	1993-97	1989-92	1993-97
	Model (10)	Model (11)	Model (12)	Model (13)
Constant	-55.16 *** (6.33)	29.91 (20.81)	-39.33 *** (6.50)	-6.56 *** (20.94)
RDI	1.231 *** (0.20)	0.129 (0.18)	1.241 *** (0.20)	0.658 *** (0.19)
ASSETS	0.638 *** (0.11)	0.899 ** (0.16) *	0.417 *** (0.13)	1.507 *** (0.17)
SPILLOVERS	3.027 *** (0.34)	-2.140 * (1.20)	2.30 *** (0.34)	-0.462 (1.20)
Research Agreements (*RA*)	0.462 *** (0.09)	-0.075 (0.09)		
Development Agreements (*DA*)	-0.198 * (0.10)	0.498 ** (0.11) *		
Commercialisation Agreements (*CA*)	-0.000 (0.12)	-0.233 ** (0.09) *		
Agreements w/ large firms (*AWL*)			-0.550 *** (0.09)	-0.465 *** (0.09)
Agreements w/ Biotech firms (*AWB*)			0.115 (0.07)	0.660 *** (0.09)
Agreements w/ universities (*AWU*)			0.475 *** (0.14)	-0.648 *** (0.13)
BIOTECH	1.463 *** (0.20)	1.652 ** (0.35) *	0.982 *** (0.24)	2.025 *** (0.44)
TREND	-0.552 *** (0.06)	-0.813 ** (0.08) *	-0.388 *** (0.06)	-1.087 *** (0.09)
N	91	147	91	147
Log-likelihood.	-503.30	-533.23	-501.12	-502.51
McFadden Pseudo R^2	0.738	0.780	0.739	0.793

Standard errors in parentheses.
Firm Fixed Effect Poisson Regressions. Year dummies included in all regressions.
*** ** * Significant at 1, 5 and 10 % levels respectively.

GRAPH 1. Hypothetic waves of discoveries and alliances



GRAPH2. Agreements by type of partner and type of collaboration
(Source: Bioscan, 1999)