

Technological Regimes and the Growth of Networks An Empirical Analysis

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Abstract

This paper shows how specific technological and relational regimes have shaped the growth of the network of R&D collaborative agreements in pharmaceuticals in the 1990s. Our analysis reveals the existence of a complex set of regimes of firm growth within the network, providing additional evidence supporting prediction that both growth and innovative activities of large and small firms respond, even within a given industry, to considerably different technological and economic factors. Moreover, the paper shows, in the context of a specific industry and by means of a series of preliminary and explorative empirical analyses, that information on the topological properties of a given industrial settings and on roles/positions of organizations within it can be used to disentangle some fundamental generative processes underlying observed processes of growth. This result contributes to the 'old' stochastic approach to firm growth, in the direction of building parsimonious and, at the same time, more realistic, representations of processes of industrial growth.

1 Introduction

Division of innovative labor through networks of contractual exchanges between small firms specialized in the upstream stages of the innovation process (*Originators*) and large firms focused on the downstream stages of development (*Developers*) is recognized as an ever-widening organization form, particularly in high technology, knowledge-intensive fields (Arrow, 1983; Arora, Fosfuri, and Gambardella, 2001).

However, at present, we know little on how these networks of contractual relationships grow, and how their structural evolution is shaped by specific patterns of local interaction and underlying technological conditions.

On the one side, despite recent advances, most formal models of the growth of interfirm networks are largely incomplete when compared to real industrial systems.

On the other side, the literature in applied industrial economics does not provide, at present, any insight as to whether the properties of real-world networks vary across industries, and, if so, to which factors such differences could be attributed. The absence of any such studies appears to be somehow striking, since numerous contributions have shown that industry-specific characteristics play a fundamental role in explaining the structural evolution of specific industries, as well as technological, economic, and growth regimes within them (Dosi, 1982).

Against this background, we analyze the growth of an industry network composed by a set of small firms acting as *Originators* of new technological opportunities (new R&D projects) and a set of large firms acting as *Developers*.

Specifically, we use graph theoretical tools and measures to unravel how the nature and evolution of relevant technological conditions have induced distinguishable patterns of growth in the pharmaceutical innovation system during the Nineties (see also Orsenigo, Pammolli, Riccaboni, 2001). We represent the network and the division of labor within it by means of a *di-graph* (directed graph), in which organizations are associated to nodes and the relationships among them are associated to connections.

Sectoral specificity notwithstanding, we aim at characterizing some general and distinctive properties of the relationships between heterogeneous regimes of firm

growth and the evolution of industry structures. In particular, it is our claim that the topological methods of graph theory deal appropriately with *the evolving nature of industrial networks*: a) First, they encode all relevant information on the *global structure of the network*; b) Second, a graphical analysis of the system at different points in time (*comparative statics*) can enlighten the transition from a global relational regime to a different one. In addition, it provides information on the existence of different roles and types of organizations within the network, contributing to the identification of the generative processes underlying its structural transformation and growth. *Qualitative changes* in the structure of the network are represented by *topologically non equivalent* graphs, while different classes of organizations can be identified in function of their structural positions and, subsequently, accordingly to their role in the growth of the system (see Simon, 1962; Ijiry, Simon, 1977); c) Third, a graph-theoretical approach extracts relevant information on the evolution of the system, disregarding details. As a consequence, it can be both *conceptually simpler* and *computationally cheaper* than any method based on differential equations in finite-dimensional spaces.

In synthesis, we suggest that the graphical toolkit we introduce can capture the essence of industrial transformation when industrial systems are far from stable and unambiguous equilibrium forms. We expect that such an apparatus, if further developed and refined, can deserve insightful applications in other domains relevant for the analysis of processes of industry and firm growth, whenever structural breakthroughs, regime shifts, and technological change are important issues.

The paper is organized as follows. In section 2, we analyze the nature of two major technological regimes that have shaped the formation and growth of an extensive system of division of innovative labor in pharmaceuticals. Then, we provide a description of the growth of the network in the 1990s, based on an inspection of an extensive data set, which covers around 1,300 organizations and more than 3,800 contractual agreements. In section 3, we perform a set of inspections of the topological properties of the network at different points in time, coming to identify two classes of organizations in function of their relational and growth behavior. Moreover, we show the existence of a striking correspondence between the two relational regimes identified by our algorithms and the two technological regimes characterized in section 2. Then, we map the technological and relational regimes

characterized above onto the relative frequencies of local processes and mechanisms of growth that shape the size distribution and the global topological properties of the network. The final section sums up the main findings and implications of our work.

2 Technological Regimes and Division of Innovative Labor in Pharmaceutical Innovation

2.1. Technological Regimes in the Recent Evolution of Pharmaceutical R&D

The last thirty years have witnessed a revolution in biological sciences, with significant basic advances in molecular biology, cell biology, biochemistry, protein and peptide chemistry, physiology, pharmacology, and other relevant scientific disciplines.

These new bodies of knowledge have generated a plethora of scientific and technological opportunities, with an enormous impact on the nature of pharmaceutical innovation and on patterns of industry evolution. They have nurtured a continuous flow of entry of new firms, as well as an extensive division of innovative labor between firms that act mainly as *Originators* of R&D projects that are then licensed to firms that act as *Developers*.

In synthesis, the emergence of a dense set of collaborative relationships among firms and other research institutions has been a major feature of the recent evolution of the industry (Powell, Koput and Smith-Doerr, 1996).

In a previous paper, we have shown that the recent evolution of research strategies and technologies in pharmaceutical R&D can be characterized by referring to two main *technological regimes*, which coexist and complement each other (see Orsenigo, Pammolli, Riccaboni, 2001).

The first regime, which has started in the mid Seventies, is based on the advances in molecular biology. According to the so-called molecularization of physiology, pathology, and pharmacology, the development of new drugs rests on the ability to generate more fundamental biological theories, towards deeper explanations (i.e. molecular and infra-molecular levels) of pathological processes that take place at higher levels of organization inside the human organism. Following this approach, new technological opportunities have been generated in the form of new therapeutic

targets and research techniques, along a *hierarchy* of increasingly specific sub-hypotheses. The first regime relies upon research techniques which tend to be originated by new entrants and stay *co-specialized* with specific research hypotheses and fields of application. The *hierarchization* and *co-specialization* of the first regime have dominated the evolution of industry structure in pharmaceutical R&D until the beginning of the Nineties, promoting a division of labor among organizations and research labs, which is hierarchical in nature. In this context, older firms, particularly *Developers*, capture new technological opportunities and increase their connectivity more than proportionally than younger ones, benefiting from a significant first mover advantage. Therefore, in the analyses that follow we refer to the first regime as the *cumulative regime*.

The second regime has started to coexist with the cumulative one beginning from the beginning of the Nineties. It consists of *generic research tools and techniques* for the classification, generation, sampling, and screening of thousands upon thousands of genetic and molecular structures. *General-purpose technologies* (GPTs) such as bio-informatics, polymerase chain reaction (PCR), large-scale screening techniques, combinatorial chemistry, and (post-)genomics achieve a high breadth of applications and map onto multiple biological targets and diseases. At the level of the industry, the *general purposiveness* of the second regime has induced a division of labor across different fields of application. As compared to the cumulative one, the regime based on GPTs does not sustain any first mover advantage for *Developers*, since *Originators* specialized in GPTs tend to establish new links irrespectively of their partners' connectivity. Thereby, we refer to the second regime as the *random regime*.

In other words, the features of the cumulative and random technological regimes lead to different patterns of local interaction, as well as to different topological structures of the network. In synthesis (see Orsenigo, Pammolli, Riccaboni for a detailed analysis): i) *Originators* enter the industry by introducing successive waves of new research technologies and hypotheses, which shape the growth of the network; ii) Firms already active within the network do not play a major role as *Originators* in the new technological trajectories that emerge after their entry; iii) Earlier entrants gain access to the new technological trajectories mainly capturing the new opportunities acting as *Developers* of projects started by younger firms; iv) As times goes by, the rate of entry of specialized technology *Originators* in any given technological

trajectory tends to slow down as far as *Developers* succeed in developing internal capabilities in the new fields. Correspondingly, relational intensity, as well as of entry, shift forward to new technologies and firms; v) Since the beginning of the Nineties, the emergence of *new General Purpose Research Technologies* has affected the structure of the network, with entrants based on new general purpose technologies acting as *Originators* of projects that are licensed to different types of *Developers*, irrespectively of age.

Based on this background knowledge, in this paper we focus on the growth of the network during the Nineties and, in particular, we establish an explicit connection between the existence of organizations playing different relational roles and the generative processes that drive the growth of the network over time.

2.2. *Data and Notation*

The dataset used throughout this study was compiled from Windhover's databases¹. Windhover is a well-known source of information on deal-making, financing, and merger and acquisition activities² in pharmaceuticals. As a whole, Windhover monitors 1583 organizations and 5353 collaborative agreements. In this paper – given our focus on division of innovative labor – we have selected 3807 R&D collaborative transactions. As a result, our sample includes 349 pharmaceutical companies, 808 biotechnology firms, and 292 non-industrial research institutes. For each of organization, we have collected additional information on location, size, main areas of activity, age, and type.

For each R&D contract, we have recorded the following *transaction-specific attributes*:

Date of signing (from January 1991 to December 2000);

¹ See www.windhoverinfo.com for further details about Windhover's databases and information services.

² Windhover monitors 989 Mergers & Acquisitions (M&As) that took place over the decade. For the 445 firms that stay as legal distinct entities after M&A, our data base continues to keep trace of their external relational activities. In many cases pharmaceutical companies acquired biotech firms not to incorporate their expertise but to add mass to the total R&D effort. As an example, after Roche acquired Genentech, the latter stayed separate geographically, financially and managerially, and Roche executives "hardly visited it".

Deal value (the preliminary deal value is available for 1229 transactions)³;

Stage of development at signing (i.e. discovery, preclinical, clinical);

Technological content (i.e. gene therapy, genomics, molecular diversity...);

Targeted disease (i.e. AIDS, Alzheimer, Cancer...);

Typology (viz. license, joint venture, co-development...).

For 3171 contracts (83.3%) we were able to distinguish an *Originator* (Licensor) of a specific R&D project from one or more *Developers* (Licensees). The remaining 636 R&D agreements have been classified as *mutual* (two-ways) relationships.

In our empirical analysis, we establish an association between research opportunities/techniques and R&D projects. Every organization is defined by the collection of its research projects over time, while contractual agreements are conceived as organizational devices through which opportunities and development capabilities meet.

The set of relationships is analyzed throughout this work as a *directed graph*. Formally, the structure of the network is represented by $N(E,V)$, where V is the set of vertices (organizations), and every edge e (deal) within the graph (industry) is an oriented link defined by a couple *Originator/Developer* (o, d) ⁴. The directed graph N can be represented by an *adjacency matrix* $N \Leftrightarrow A(N) = [a_{do}]$. Matrix entry a_{do} equals 1 if an edge $e(d,o)$ does exist, and 0 otherwise. Furthermore, we label each connection with the date of signing, and the overall graph $N(E,V)$ is decomposed in time specific subgraphs $N_t(E,V)$, which include only the agreements signed in period t .

In the rest of this section, *Originators* are distinguished from *Developers*, while the graph is decomposed according to multiple criteria (deal value, date of signing, technological content), in order to highlight some of the key determinants of its structural evolution.

³ Preliminary value equals the sum of all pre-commercialization payments including equity, up-front licensing, R&D and milestone payments.

⁴ We refer the reader to Harary et al., 1975 and Diersel, 1997 for a deep discussion on directed graphs.

2.3. A Description of the Recent Evolution of the Network

From 1991 to 2000, the size of the R&D network in pharmaceuticals has increased substantially. Table 1 shows the number of collaborations, by partners' type, for the first (*a*) and the second (*b*) half of the Nineties. As it is evident, non industrial research institutes and new biotechnology firms have sustained the growth of the network acting as *Originators* of projects developed by large pharmaceutical companies and leading biotech firms. Over time, the biotech-biotech network has increased significantly, in correspondence with the raise of a set of agreements based on the new general purpose research technologies.

[INSERT TABLE 1 ABOUT HERE]

Figure 1 shows the number and the value of R&D collaborative agreements and M&As during the Nineties. The number of organizations active in the R&D network has stabilized around 500, more than twice as many as in 1991, while the number of research alliances subscribed has grown fourfold, and the value of collaborations in the period 1997-2000 was five times greater as compared to the beginning of the nineties. At the same time, the number of M&A events has been steadily high, culminating with a few mega-mergers in the last years⁵.

[INSERT FIGURE 1 ABOUT HERE]

The sustained growth of the network in the last decade reflects the opening up of new technological opportunities driven by the evolution of relevant scientific and technological knowledge bases, especially through advances in the fields of genomics, proteomics, molecular diversity, and high throughput screening. As shown in Figure 2, the proportion of collaborations devoted to *general purpose technologies* took off starting from the early Nineties, up to about 35% of the total in 1997-2000. The new technologies have bolstered the expansion of the network, somehow blurring the distinction between *Originators* and *Developers*. In fact, in the second half of the 1990s, organizations have increasingly tended to play both roles (see Figure 3) and, as we have noticed, the number of collaborations among biotech firms has increased significantly (see Table 1 above).

⁵ 1996: Ciba-Geigy – Sandoz (*Novartis*); 1997: Roche – Boehringer Mannheim; 1998: Hoechst Marion Roussel – Rhône-Poulenc Rorer (*Aventis*); Sanofi – Syntélabo; Astra – Zeneca (*AstraZeneca*); 1999:

[INSERT FIGURE 2 ABOUT HERE]

[INSERT FIGURE 3 ABOUT HERE]

In a nutshell, the evolution of the network during the Nineties can be synthesized as follows. First, the size and connectivity of the network has increased significantly over time. Second, non industrial research institutes and biotech firms have continued to originate new technological opportunities. Third, large pharmaceutical companies have played a pivotal role in structuring the division of innovative labor within the industry, acting as *Developers* of R&D projects started by a set of smaller specialized *Originators*. Fourth, the new Originators which have entered the industry based on *General Purpose Research Technologies* have tended to establish new links irrespectively of their partners' age (and connectivity).

3 Relational Regimes and the Growth of the Network

In this section, we analyze the topological properties of the network and characterize, in a preliminary way, the generative processes underlying its growth in the last decade. In particular, we show how the combination of the cumulative and the random relational regimes sketched above has increased the frequency of new interconnections among firms and fields of activities, inducing dramatic changes in the global structure of the network.

In order to come to a better understanding of how different combinations of actors and relational roles have shaped the growth and the structure of the network, we have performed a decomposition procedure (Dulmage-Mendelsohn (DM) Procedure: see Dulmage and Mendelsohn, 1967), sorting the nodes of the network in different classes based on their relational properties.

The DM decomposition procedure isolates a set of vertex covering separators of minimum size, i.e. the smallest set of firms able to reach out to every network components which, if removed, would dissect the overall graph into the highest number of isolated subgraphs. In the DM decomposition the vertex set V of a graph N is partitioned into two sets O and D , in such a way that no two vertices from the same

Pharmacia & Upjohn – Monsanto (Pharmacia Corp.); 2000: Glaxo Wellcome – SmithKline Beecham (*Glaxo SmithKline*); Warner Lambert – Pfizer.

set are related (see Asratian et al., 1998). In the case of the network under investigation, the two vertex sets correspond to *Originators* and *Developers*, respectively⁶. A *matching* of N is defined as a set of edges (and hence a subset of E), no two of which are incident on a common vertex (see Lovasz, Plummer, 1986; Diersel, 1997)⁷. An example is reported in Figure 4. The graph in Figure 4 (a) has two color classes – black and white vertices – corresponding to its bipartition. The bold lines represent a possible matching of the bipartite graph. A *vertex covering* of a graph N is defined as the subset of vertices $C \subseteq V$, such that each edge e is incident to some vertex in C . The lines that belong to a matching are said to be admissible, while the remaining ones are called inadmissible⁸.

Figure 4 synthesizes the logic (a) and the outcomes (b) of the Dulmage-Mendelsohn Decomposition, in graph (a) and matrix (b) terms. The graph presented in Figure 4 (a) refers to a stylized network, while the matrix of Figure 4 (b) provides a representation of the network as for the year 2000.

[INSERT FIGURE 4 ABOUT HERE]

In Figure 4, O_M denotes *matched Originators*, while, O_U identifies *unmatched Originators*. Moreover, $O(D)$ means that there is a matching alternating path from d to o , for some $o \in O$ ⁹. The same notation holds for *Developers*. As a result, the following components are singled out:

- | | | |
|-----|--------------------------------|----------------------------------|
| (1) | $O_1 \equiv O_M(D_U)$ | $D_1 \equiv D_U \cup D_M(D_U)$; |
| (2) | $O_2 \equiv O_{MM}$ | $D_2 \equiv D_{MM}$; |
| (3) | $O_3 \equiv O_U \cup O_M(O_U)$ | $D_3 \equiv D_M(O_U)$; |

Firms classified either in O_1 or in D_3 *cannot be assigned an unambiguous relational role* within the network, i.e. *they play a transversal role*, attracting most of the

⁶ The reader might find it helpful to recall the adjacency matrix representation discussed in section 2.2. In those terms, the two vertex sets are associated with rows and columns respectively. For further details on this point see Orsenigo, Pammolli and Riccaboni (2001).

⁷ A matching of maximum cardinality is a *maximum matching*. If it covers all vertices is called *perfect*.

⁸ Incidentally, is useful to notice that an edge e is inadmissible if and only if there exists a *minimum vertex cover* — i.e., a cover consisting of as few elements as possible — such that e belongs to that cover (see Lovasz, Plummer, 1986; Asratian et al., 1998).

⁹ A path is alternating relative to a matching if its edges are alternately in the set of matched and unmatched edges.

agreements at any given point in time (they are present in all the intersections among minimum coverage vertex sets).

In the case of the network in pharmaceuticals, the leading *Developers* have tended to establish multiple relationships with a wide variety of *Originators*. As for *Originators*, a clear distinction can be drawn between a set of firms that are co-specialized in their relational behavior, i.e. they are matched, and a set of firms that play a transversal role within the network.

Through the comparison of the output of the procedure at different points in time we are able to show that a variety of generative processes and corresponding relationships has characterized the evolution of the graph.

In particular, during the period of observation, a dramatic increase of the overall degree of interdependence within the network can be detected. Figure 4 (b) shows the results of the Canonical Decomposition performed on the set of collaborative agreements signed in the year 2000. As it is evident, the region (O_1, D_3) of the matrix, which contains relationships that are transversal within the network, is highly populated, while it was almost empty at the beginning of the Nineties.

An analysis on the identity and the technological background of the nodes classified as O_1 has revealed that relational roles within the network correspond to organizations embodying different types of technologies (see also Orsenigo, Pammolli, and Riccaboni, 2001). Our controls have shown that *Originators* specialized in general purpose research technologies belong with high probability to O_1 and play a transversal role within the network. Almost all the firms which are active in general purpose research technologies (i.e. genomics, proteomics, bioinformatics and molecular diversity), turned out to be *transversal Originators* in the graph at different points in time. Conversely, and most important, all the organizations classified as O_1 by means of the DM permutation of the matrix act as *Originators* of general purpose research technologies. Finally, all the most connected *Developers* have been located by the algorithm in D_3 , as they have been able to integrate, through collaborative agreements, the new general purpose technologies with more “conventional” research opportunities and techniques, originated by firms acting as *Co-specialized technology suppliers*.

This last result is confirmed, in a synthetic way, by the evidences produced in Figure 5, in which we plot the probability of having a new agreement (probability of relinking) for different categories of firms classified according to the technological content of their previous agreements. As it is evident, the probability of relinking is highest for firms that are able to act integrating both Co-specialized and General Purpose Technologies. Interestingly enough, different generative processes seem to be in place for Originators vs. Developers, as confirmed by available empirical evidences on the existence of measurable differences in their connectivity distributions (see Riccaboni, 2000; Riccaboni and Pammolli, 2001).

[INSERT FIGURE 5 ABOUT HERE]

4 Conclusion

In this paper we have shown how specific technological and relational regimes have shaped the growth of the R&D network in pharmaceuticals during the Nineties.

First, our analysis has revealed the existence of a differentiated set of regimes of firm growth within the network, so providing additional evidence supporting prediction that both growth and innovative activities of large and small firms respond, even within a given industry, to considerably different technological and economic factors (see Winter, 1984; Acs and Audretsch, 1988).

Second, we have shown, in the context of a specific industry and by means of a series of preliminary and explorative empirical analyses, that information on the topological properties of a given industrial settings and on roles/positions of organizations within it can be used to disentangle some fundamental generative processes underlying observed processes of growth. This result is interesting, since it constitutes an important contribution to the ‘old’ stochastic approach to firm growth (see Ijiri and Simon, 1977; Sutton, 1997), in the direction of building parsimonious and, at the same time, more realistic, representations of processes of industrial growth (Riccaboni, 2000; Riccaboni and Pammolli, 2001).

In conclusion, we want to state that the graphical toolkit we have introduced is an useful complement to more traditional econometric and analytical techniques to capture the essence of industrial dynamics when systems are far from stable and unambiguous equilibrium configurations. We expect that such an apparatus can deserve insightful applications in future research, whenever regime shifts and

technological change are important issues in explaining the growth of firms and industries.

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Table 1. Number of Collaborations, by Partners' Types. First (a) and Second (b) Half of the Nineties

(a)

| 1991-1995 | | Developers | | | | | Total |
|-------------|------------------------|------------|-----|-----|-----|-----|-------|
| | | (1) | (2) | (3) | (4) | (5) | |
| Originators | (1) Lead Pharma | 73 | 47 | 20 | 75 | 16 | 231 |
| | (2) Pharma | 82 | 63 | 15 | 65 | 11 | 236 |
| | (3) 1 Tier Biotech | 74 | 27 | 15 | 40 | 4 | 160 |
| | (4) Biotech | 279 | 135 | 58 | 87 | 39 | 598 |
| | (5) Univ. - Res. Inst. | 52 | 35 | 28 | 204 | - | 319 |
| | Total | 560 | 307 | 136 | 471 | 70 | 1544 |

(b)

| 1996-2000 | | Developers | | | | | Total |
|-------------|------------------------|------------|-----|-----|------|-----|-------|
| | | (1) | (2) | (3) | (4) | (5) | |
| Originators | (1) Lead Pharma | 70 | 40 | 28 | 88 | 9 | 235 |
| | (2) Pharma | 112 | 105 | 29 | 114 | 11 | 371 |
| | (3) 1 Tier Biotech | 125 | 57 | 38 | 81 | 7 | 308 |
| | (4) Biotech | 542 | 278 | 125 | 385 | 79 | 1409 |
| | (5) Univ. - Res. Inst. | 39 | 41 | 34 | 382 | - | 496 |
| | Total | 888 | 521 | 254 | 1050 | 110 | 2823 |

Figure 1. Number (a) and Value (b) of Mergers and Acquisitions (full lines) and R&D Collaborations (dotted lines) per Month. One-Year Moving Averages

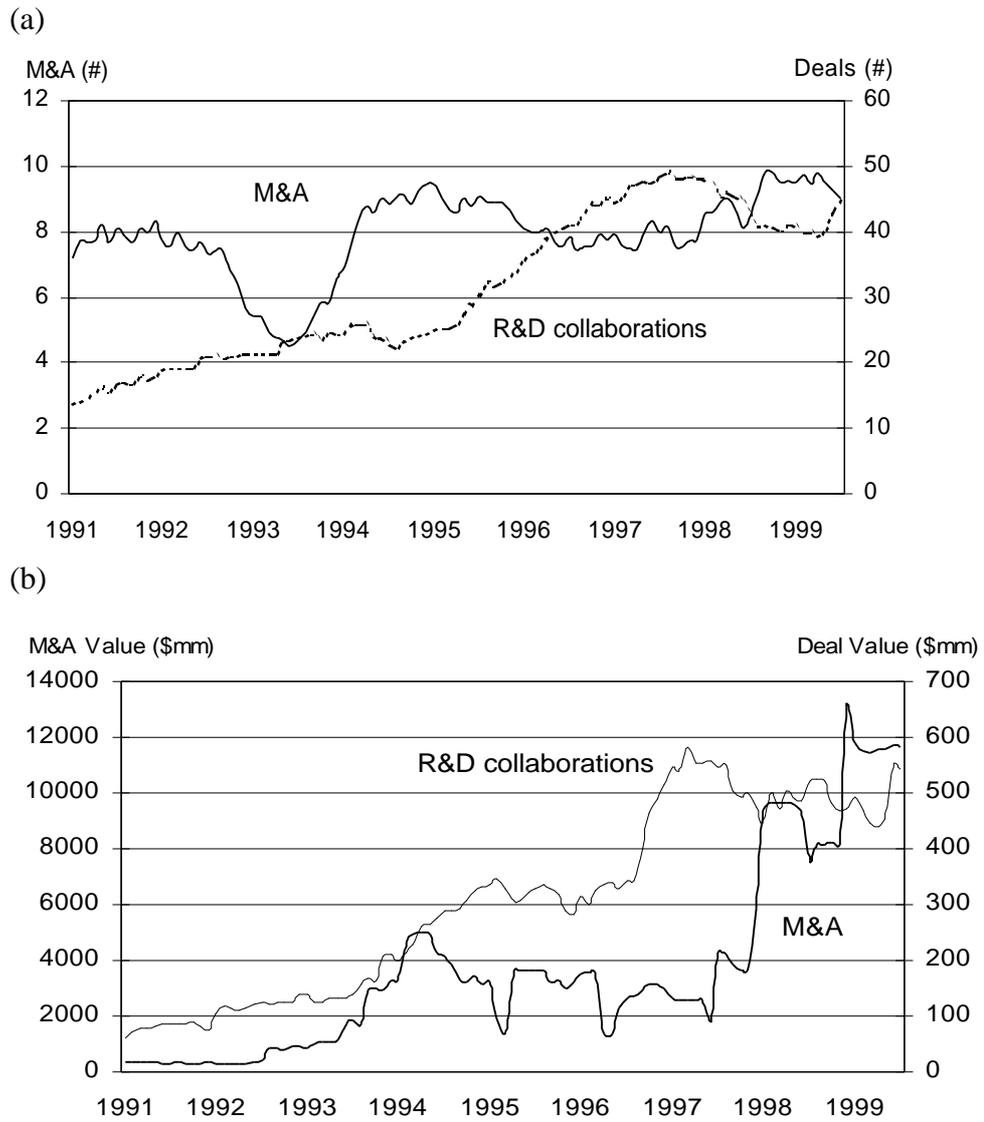
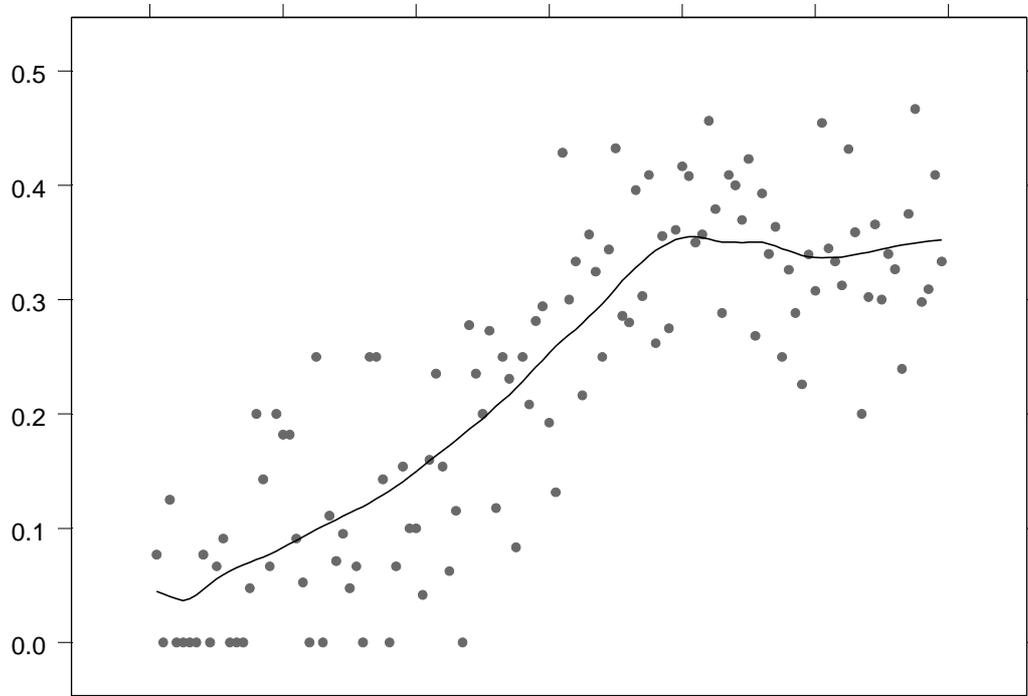


Figure 2. Proportion of alliances based on general purpose technologies (genomics, proteomics, bioinformatics, molecular diversity). Monthly values and Freeman smoothing fit¹⁰



¹⁰ See Friedman, 1984.

Figure 3. Number of firms/institutions, by relational role

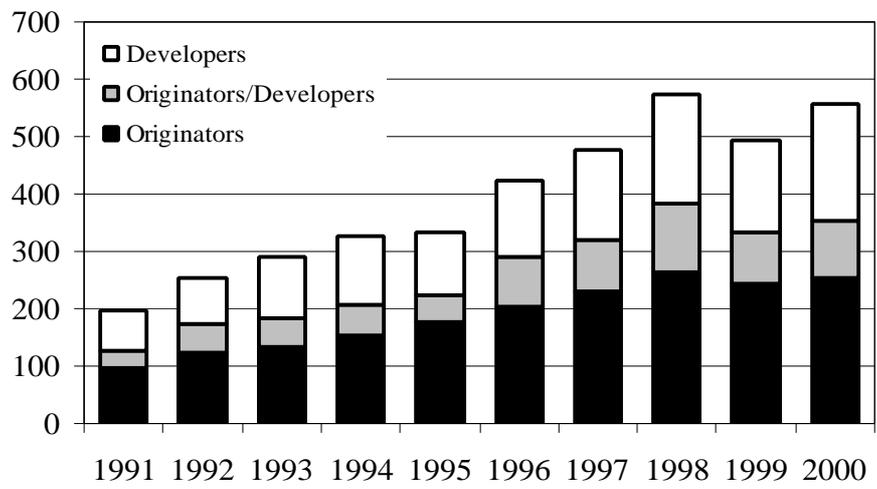


Figure 4. Classification of the Nodes of a Graph According to the Dulmage-Mendelsohn Decomposition Procedure (a); Dulmage-Mendelsohn Decomposition of the R&D Network in Pharmaceuticals, Year 2000 (b)

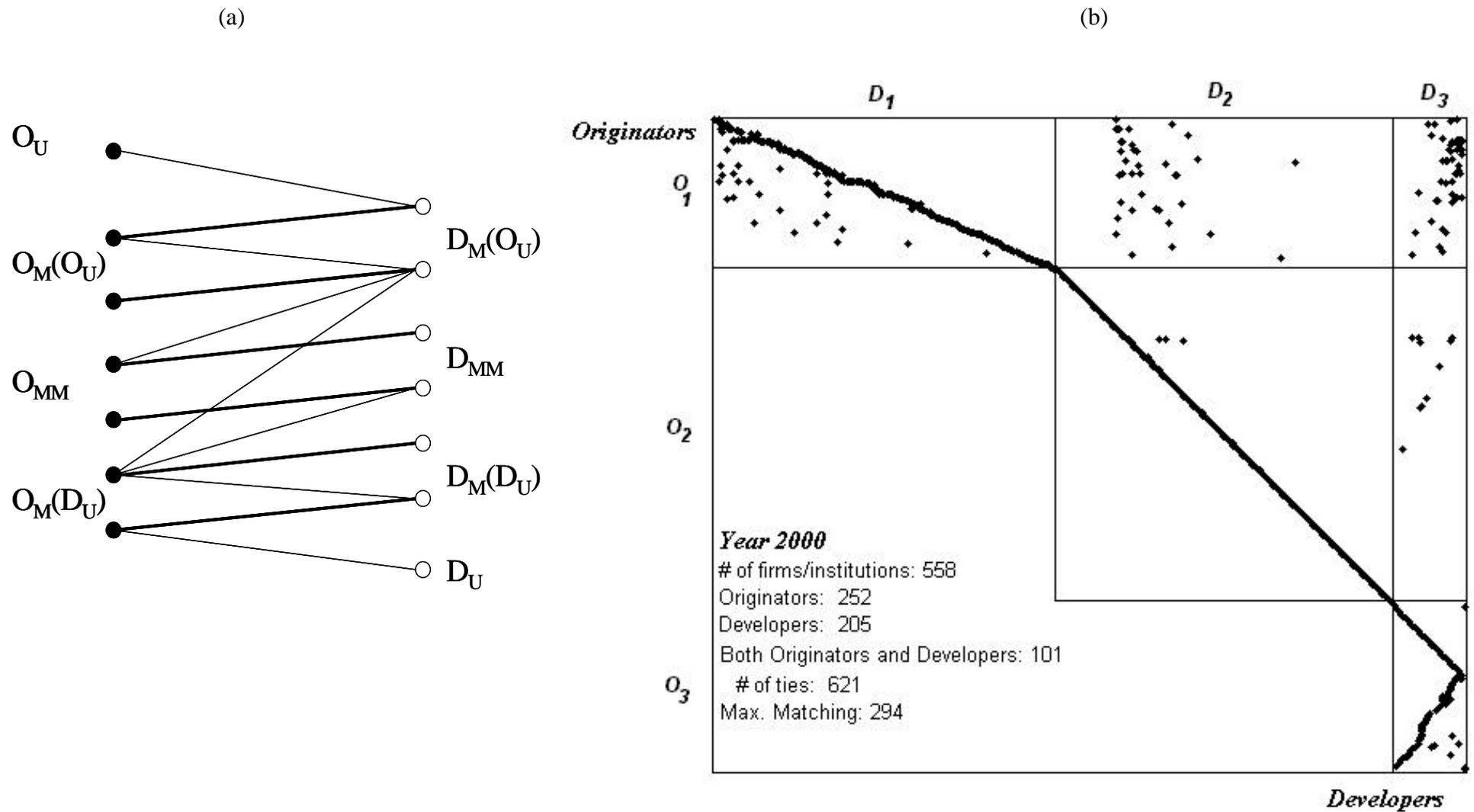


Figure 5. Complementarities Among Relational Roles in the Evolution of the Network

