Research Evaluation, 16(2), June 2007, pages 123–136
DOI: 10.3152/095820207X227510; http://www.ingentaconnect.com/content/beech/reev

Material transfer agreements and collaborative publication activity: the case of a biotechnology network

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Although material transfer agreements may be useful to exchange research materials between laboratories, academics and policymakers have suggested that the trend towards their standardisation might impede the progress of science by constraining one type of research collaboration: the co-publication activity of organisations. For that reason, we examine whether involvement in those agreements affects the pattern of co-publication activity. The construct co-publication activity is thereby operationalised on the basis of a bibliometric approach. The organisations and their collaboration are described with the help of graph theory. According to our interpretation of findings, material transfer agreements might not have interfered in such a way to limit co-publication activity of research organisations in the network.

RATHER THAN AN INDUSTRY *per se*, biotechnology can be seen as a set of technologies that affects existing industries, such as agriculture, food-processing and human health (Pisano, 2002). Fountain (1997) acknowledged that technologies such as biotechnology, which are not only characterised by radical and discontinuous technological advance but also by networks of learning formed through various types of collaboration, reflect an interest to access and exploit knowledge.

Another feature of biotechnology is the high rate of formation and dissolution of linkages among its actors. Universities, government laboratories, non-profit hospitals and research institutes are important players in biotechnology; while on the commercial side, both established pharmaceutical firms and dedicated biotechnology companies are key performers.

Connections are forged with a specific goal in mind, such as transferring research material or complementing expertise. In academia, there is less curtailment of collaboration because there exists a bottom-up approach in scientific co-operation. By contrast, in industry and government the decisions to collaborate are mediated by other mechanisms, such as budget constraints, research findings, business expectations. Thus, if financial support is cut or results are not attained as expected, then the collaboration will end.

Pioneered by industry, material transfer agreements (MTAs) are used in connection with the transfer of materials for safekeeping purposes (for instance, storage in gene banks), research or commercial use, now increasingly being used by public sector laboratories and academia (Rodriguez, 2005). Academics have suggested that the trend toward the standardisation of MTAs might impede the progress of science (Rodriguez *et al,* 2007) by constraining interorganisational collaboration.

While there is a fairly large body of studies related to MTAs (Barton and Siebeck, 1994; Mirowsky and

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 0958-2029/07/020123-14 US$08.00

Van Horn, 2005; Rodriguez, 2005; Rodriguez and Debackere, 2007; Rodriguez *et al,* 2007; Streitz and Bennett, 2003; Streitz *et al,* 2003; Whitaker, 1994), relatively little has been written about the effect of MTAs on collaborative publications (Walsh *et al,* 2003, 2005). Fortunately, there has been a growing interest among scholars in investigating practices that may hamper the development of science (Eisenberg, 2001; Ensenrik, 1999; Kunin *et al,* 2002; Murray, 2006; Murray and Stern, 2006; Van Overwalle *et al,* 2006; Van Zimmeren *et al,* 2006; Verbeure *et al,* 2006). In this context, the question arises whether MTAs negatively affect collaborative publication activity of organisations.

In our study, we consider that some interorganisational collaborative publication activity has taken place if two or more organisations were listed as assignees in patents or as institutional affiliations in articles, letters, notes, or reviews. These documents may be valid indicators of one type of research collaboration since they exemplify sharing of research efforts from at least two individual authors. Those organisations conducted research in biotechnology and belonged to industry, government and academia in Belgium.

In this paper, we assess whether MTAs have an impact on co-publication activity of research organisations. In other words, we examine whether involvement in MTAs positively or negatively affects the pattern of co-publication activity. The construct co-publication activity is thereby operationalised on the basis of a bibliometric approach. The organisations and their collaboration are described with the help of graph theory (Allen, 1985; Krackhart and Hanson, 1993; Nohria and Eccles, 1992; Scott, 1991; Steward *et al,* 1993).

The remainder of this paper is organised as follows. We describe interorganisational collaboration, and then we outline the empirical framework. After that, we detail data and methodology. We present our findings, and then discuss them. Finally, we make some concluding remarks.

Interorganisational collaboration

Biotechnological organisations may improve their learning capacities by interacting with other partners (Freeman, 1995). Collaboration is crucial to the maintenance and development of the biotechnology sector, of organisations within the sector, and of scientists working in these organisations (Liebeskind *et al,* 1996). Furthermore, a need for complementary activities in biotechnology makes co-operation among organisations a strategic transaction mode.

Research collaboration also gives social and community support that may be useful when research becomes politically or intellectually isolating. Collaboration presents opportunities to learn as well. At the level of diffusion of academic research findings, the use of networks of collaborators is valuable as a means of propagating a message and ensuring peer review.

Beaver (2004) has argued that the opportunities provided by collaboration ensure that, regardless of whether or not the research is interdisciplinary, the discussion and interactivity that follows from collaboration guarantees greater peer review and verifiability. Collaboration provides opportunities for the recognition of novelty and the determination of error.

Powell (1990) states that the basic assumption of network relationships is that one party is dependent on resources controlled by another, and there are gains to be made by the pooling of resources. Both resource-dependency approaches (Cook, 1977; Pfeffer and Salancik, 1978; Powell, 1990; Wernerfelt, 1984) and transaction cost economics (Jarillo, 1998; Pisano 1990; Provan, 1993; Thorelli, 1988) postulate that, under conditions of complex, indivisible resources and long-term goal uncertainty, network forms of organisation may be prevalent (Debackere and Clarysse, 1998).

Some empirical studies have highlighted the importance of knowledge communities and networks of collaboration in the production of scientific knowledge (Hagstrom, 1965; Crane, 1972; Frame and Carpenter, 1979; Goffman and Warren, 1980; Narin, Stevens and Whitlow, 1991). As new organisations join the network, there will be a preferential attachment to an organisation that already has ties (Price, 1965). Preferential attachment leads to a dynamic of rich-get-richer. Power law tails of degree distributions are present in various kinds of networks. For example, in science, new publications cite well-known papers.

Preferential attachment in network formation bears a strong similarity to the more general phenomenon of cumulative advantage (Merton, 1973), in which those who experience early success capture a larger share of subsequent rewards. A Matthew Effect[1] can be observed in network configuration. So, the more collaborative are the nodes, the more new nodes will be attached to them. Hence, understanding network formation and growth is relevant and necessary. Network growth is not a random phenomenon. Preference for the most collaborative organisations does indeed develop.

Network structures in biotechnology are highly dynamic and dense. The objectives of those structures are multivocal in and of themselves. More

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precisely, research material and the tacit knowledge embedded in it become crucial in biotechnological research when they do not belong to the research laboratory. Collaboration is characterised by strong pragmatism — when there is something to be gained, such as access to research material, then a particular collaboration will occur; otherwise it will not (Melin, 2000). Once the task is completed, the relationship is ended and successful collaborators depart gracefully.

Empirical framework

Network position describes the pattern of research collaboration in which an organisation is involved and characterises its location relative to other nodes in the network. A useful method to describe and measure properties of node location in a network is centrality. Being centrally located refers to the position of a node in a network and represents the extent to which the focal node occupies a strategic position in the network by virtue of being involved in many significant ties (Salman and Saives, 2005).

In the literature, we find explanations of why ties form between two nodes as well as the consequences of their particular positions in a network. Powell *et al* (1996) reported a liability of disconnectedness in biotechnology, in which older, less-linked organisations were the most likely to fail. The pathway to centrality in biotechnological networks was through collaboration in research and development (R&D). Furthermore, organisations that do not expand or renew their R&D ties lose their central positions. In particular, resource-rich participants are more capable of altering their positions by reconfiguring their ties. Persson *et al* (2004) observed increasing collaboration and its interaction with publication activity and citation impact. Collaboration has been noticed for all fields and at all levels of aggregations — for countries (Glänzel and De Lange, 1997; Glänzel, 2001); for organisations (Gómez *et al*, 1995); and for individuals (Glänzel, 2002).

Local and global characteristics of networks help to define network topologies such as small worlds (Milgram, 1967). A small world is a network structure that both is highly locally clustered and has a relatively short global distance between nodes (Watts, 1999). Newman (2001) has applied the small world concept to scientific collaboration. He examined scientific co-authoring in seven diverse scientific fields and found that each had a small world structure, leading to a conclusion that small worlds might account for how quickly ideas flow through disciplines. A similar conclusion echoed the small world of scientific patents (Fleming *et al*, 2004).

Degree distribution is a diagnostic indicator of whether tie formation in a network — growth or replacement — is equiprobable — simply random — for all pairs of nodes, or biased proportionally to existing ties of potential partners. The degree of each node is measured as the number of other nodes directly connected to the focal node. Preferential attachment to already connected nodes is referred to as popularity bias. A distribution generated by a popularity bias has a fat tail for the relatively smaller number of nodes that are highly connected. The fat tail contains the hubs of the network with unusually high connectivity. Different types of degree distributions can be distinguished when plotted on a log-log scale, with a logarithm of degree on the x-axis and logarithm of the number of nodes with this degree on the y-axis.

The actual attachment probability of new nodes with incumbents, $P(k)$, is proportional to k where (k) is the degree of the incumbent. The preferential attachment probability generates a degree distribution in which the frequency of nodes with a given degree k is a function of k, namely $f(k) = 1/k^a$, where a is the power-law coefficient and can be calculated from the slope of the linear regression line on a log-log plot of k and $f(k)$. Thus, newcomers attach to well-connected nodes (Barabási and Albert, 1999; Barabási, 2002).

The rate at which new nodes appear in the network is partly determined by the success that existing nodes have in making progress on a technological frontier. Many of the network participants are multivocal, that is they are capable of performing multiple activities with a variety of constituents (Burt, 1992; White, 1985). But multivocality is not distributed evenly; those organisations that are more centrally located in the industry have access to more sophisticated and diverse collaborators and have developed richer protocols of collaboration (Powell *et al*, 1996).

As the combinations of collaborators and research agendas unfold, dynamics emerge. Organisational research choices may turn into similar topics. Or research trends may cluster and find coherence only in small, densely connected groups. Research agenda choices made early may strongly affect subsequent opportunities, but path dependence might be offset by a constant flow of new arrivals and departures. The challenge to understanding MTAs and research collaboration is to detect whether MTAs negatively affect the relationship between collaborators.

Data

Using the above definitions for nodes and links, we constructed the network. Organisations were directly linked to each other when they collaborated on the same publication. Thus, in our study *interorganisational co-publication activity* existed when organisations either co-applied for patents at the European Patent Office or co-authored articles, letters, notes and reviews in scientific journals. The nodes in our network were the organisations that appear as collaborators in those disclosed research results. Specifically, an edge or tie is a relationship between two nodes in a particular publication, and collaboration between two nodes may refer to one or more edges or ties.

From the bibliographic database of core biotechnology created by Glänzel *et al*. (2003) for Belgium, we have selected those documents that contained more than one institutional affiliation and more than one author between 1992 and 2000. There were two types of retrieved documents. The first type was formed by articles, letters, notes or reviews published in journals retrieved from the following subject categories of ISI Web of Science: biochemical research methods, biochemistry and molecular biology, biophysics, biotechnology and applied microbiology, cell biology, developmental biology, genetics and heredity, microbiology, and plant sciences.

The second type of retrieved documents was formed by European patent applications in the following patent classes of the International Patent Classification: C12M (apparatus for enzymology or microbiology); C12N (micro-organisms or enzymes; propagating, preserving or maintaining micro-organisms; mutation or genetic engineering; culture media); C12P (fermentation or enzyme-using processes to synthesise a desired chemical compound or composition or to separate optical isomers from a racemic mixture); C12Q (measuring or testing processes involving enzymes or micro-organisms; compositions or test papers therefore; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes); C12S (processes using enzymes or micro-organisms to liberate, separate or purify a pre-existing compound or composition; processes using enzymes or micro-organisms to treat textiles or to clean solid surfaces of materials); C07G (compounds of unknown constitution); and C12R (indexing scheme related to subclasses C12C to C12Q or C12S, related to micro-organisms).

Thus, the selected publications totalled 817 collaborative documents. As our analysis was conducted at the meso level, we used institutional affiliation information to operationalise variables. As a result, 58 organisations from industry, government and academia became the nodes of the network. Those biotechnology entities were involved in human therapeutic and diagnostic, veterinary, environmental, or agricultural biotechnology applications. In particular, there were 166 bilateral interorganisational relations or links that occurred only once in the nine-year period.

It was necessary to determine whether or not the documents were related to MTAs in order to study the effect of MTAs on co-publication activity. For that purpose, we asked organisations' representatives to indicate whether or not the documents were related to MTAs. In this manner, we obtained 16 collaborative publications using external research materials received through MTAs published by 13 organisations. Specifically, in industry and government, every sampled article, letter, note and review related to MTAs was co-authored and almost 19% of the sampled patents related to MTAs were applied for by co-assignees.

We coded the dominant forms of partner organisations into three categories, representing those that populate the field: industry, government and academia. In our sample, industry was formed by for-profit corporations; government was composed of public research institutes; and academia was constituted by universities and colleges. The dataset is summarised in Table 1.

Regarding the impact of MTAs in the co-publication activity, a caveat should be interposed here. It is not the quantity of MTAs or the number of co-publications related to them that should matter but whether and to what extent MTAs affected the collaborative publication pattern of research organisations in the biotechnology network.

Methodology

We utilised Pajek (Batagelj and Mrvar, 2006), a freeware package for the analysis and visualisation of networks, to present a series of discrete-time images of the evolution of the biotechnology network. Pajek employs two powerful minimum energy or spring-embedded network-drawing algorithms to represent network data in two- or three-dimensional Euclidian space.

These algorithms simulate the network of collaboration as a system of interacting particles, in which organisational nodes repel one another unless network ties act as springs to draw connected nodes closer together. Spring-embedded algorithms iteratively locate a representation of the network that minimises the overall energy of the system, by reducing the distance between connected nodes and maximising the distance between unconnected nodes.

Regarding network topology, global separation could be quantified by the average path length (*PL*), which measures the average number of intermediaries between all pairs of collaborators in the network (Feld, 1981). In our work, the term cluster coefficient (*CC*) has been used to refer to two different

Table 1. Dataset

Data	MTA-related	Non-MTA-related	Total
Collaborative patents	6	9	15
Collaborative articles, letters, notes and reviews	10	792	802
Total collaborative documents	16	801	817
Government nodes	0	13	13
Industry nodes	6	16	22
Academia nodes	7	16	23
Total nodes	13	45	58

concepts. Let $deg(v)$ denote the degree of vertex v, $|E(G_1(v))|$ the number of lines among vertices in the 1-neighborhood of vertex v, $MaxDeg$ the maximum degree of vertex in a network, and $|E(G_2(v))|$, number of lines among vertices in the 1- and 2-neighborhoods of vertex v. Coefficients considering the 1-neighborhood (CC_1) or the 2-neighborhood (CC_2) are computed by Batagelj and Mrvar (2006) as follows:

$$CC_1(v) = 2|E(G_1(v))| / [deg(v) \cdot (deg(v) - 1)] \text{ and}$$

$$CC_2(v) = |E(G_1(v))| / |E(G_2(v))|.$$

As we needed a control group, we examined whether or not the selected variables significantly differed between the nodes that were related to MTA (group 1) and the nodes that were not related to MTAs (group 2). The first empirical strategy was to perform a two-group discriminant analysis using SPSS. The variables considered in the analysis were betweenness centrality, degree, local and global clustering coefficient scores and frequency of collaborative documents. These variables were denoted in Table 2 as: Betweenness, Degree, CC_1, CC_2, and Co-publication. The value of the variables for each node was calculated from the 817 collaborative documents.

Second, as far popularity bias in the network, we used graphical tools. Thus, we plotted the degree distribution of the network on the log-log graph to detect popularity bias in Figure 1. For such representation, we used 88 collaborative documents; all of them were articles letters, notes or reviews. The formation of edges is governed by a popularity bias when nodes with more connections have a higher probability of receiving new attachments.

Table 2. Tests of equality of group means

Variable	Wilks' Lambda	F	df1	df2	Sig.
Betweenness	0.823	12.016	1	56	0.001
Degree	0.848	10.003	1	56	0.003
CC_1	0.861	9.016	1	56	0.004
CC_2	0.770	16.758	1	56	0.000
Co-publication	0.849	9.975	1	56	0.003

Third, regarding skewness in the degree distribution, we plotted the aggregate degree distributions of collaborative organisations on log-log scale for the three types of partners: government (Figure 2), industry (Figure 3), and academia (Figure 4). For the construction of the degree distribution of governmental collaborators in Figure 2, we used 98 collaborative documents (three patents and 95 articles, letters, notes and reviews). For the construction of the degree distribution of industrial collaborators in Figure 3, we used 74 collaborative documents (13 patents and 61 articles, letters, notes and reviews). For the construction of the degree distribution of academic collaborators in Figure 4, we used 786 collaborative documents (eight patents and 778 articles, letters, notes and reviews). For each of the three plots, the x-axis reflects log-degree (aggregated over all time periods) and the y-axis the log of the number of respective organisations having a given network degree (also aggregated over all time periods).

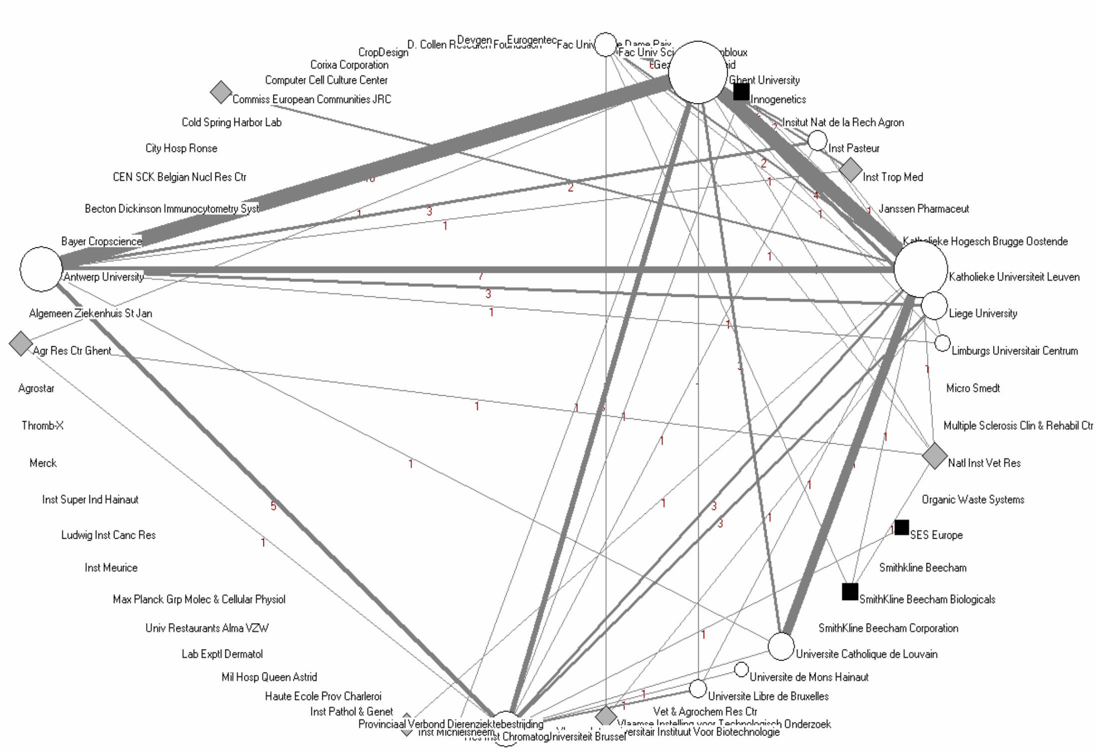

Figure 1. Co-publication in 1998

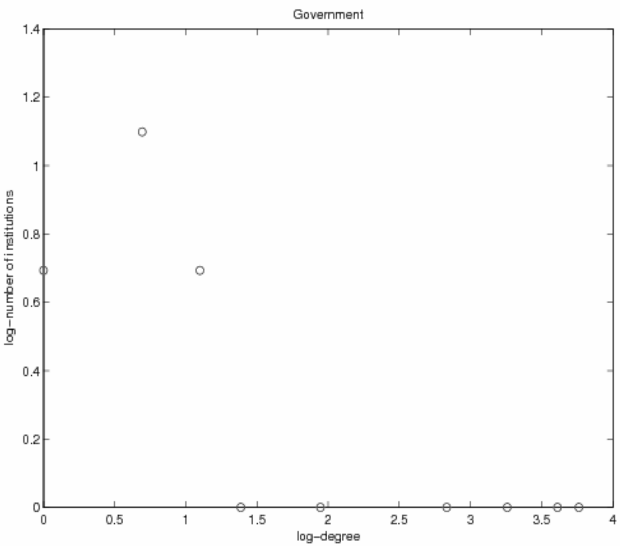

Figure 2. Government degree distribution between 1992 and 2000

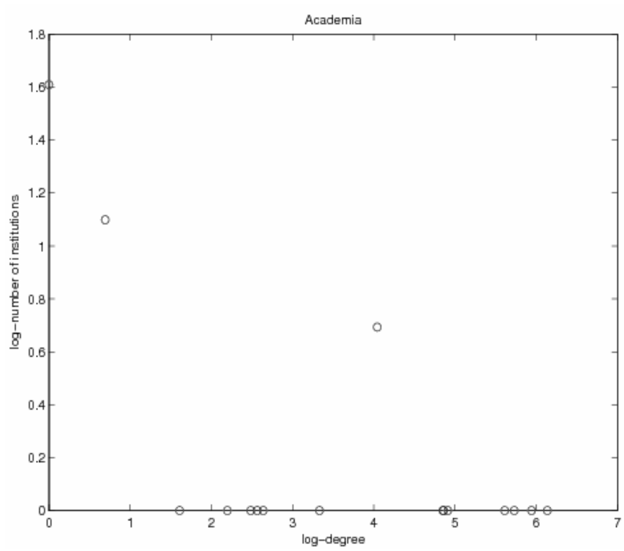

Figure 4. Academia degree distribution between 1992 and 2000

Fourth, for exploring the dynamics of the field and the changing impact of different organisations, we represented a series of network visualisations, followed by descriptive statistics of the actual attachment processes. In the construction of the co-publication network for the period 1992–2000 (Figure 5), we used the 817 collaborative documents. For depicting the 1998 ties (Figure 6), we used 88 documents co-published in 1998. Node size represented number of publications (the larger the node, the more productive). Link length denoted the amount of collaboration (the closer, the more collaborative). The node shape corresponded to the type of sector (rounded nodes stood for academia, square nodes symbolised industry, and rhomboidal nodes referred to government).

Finally, for validating the effect of MTAs on co-publication activity we implemented two strategies. The first was to find out discontinuities of the collaborative publication pattern caused by MTA. To do so, we carried out the following steps. To begin with, we listed the pairs of research organisations that published documents related to MTAs between 1992 and 2000 following a bilateral commutative approach. Thus, when the nodes A, B, and C co-authored articles, we had three unique pairs of institutions: A–B, B–C and A–C. Then, we checked whether those pairs had obtained collaborative publications not related to MTAs between 1992 and 2000 after their MTA-related co-publication for an inclusive approach (that is, at least the two nodes should appear in the assignee list of patents or affiliation list of articles, even if other institutions are included). After that, we listed the pairs that produced non-MTA-related co-publications indicating the bibliographic data. For instance, when A, B, and C co-authored in 1992 an MTA-related article, the number of non-MTA ties or edges from 1993 to 2000 between A and B, A and C, and B and C was counted and institutional authors, sector of activity and publication year supplied. Apart from that, we listed the pairs that did not produce non-MTA-related co-publications indicating the last year that they produced together a co-publication. In order to understand the discontinuity of co-publications in the non-MTA sphere we looked for an explanation in the documents, but no reason was found. Therefore, we contacted directly the organisations to know the reasons for stopping co-publication till 2000.

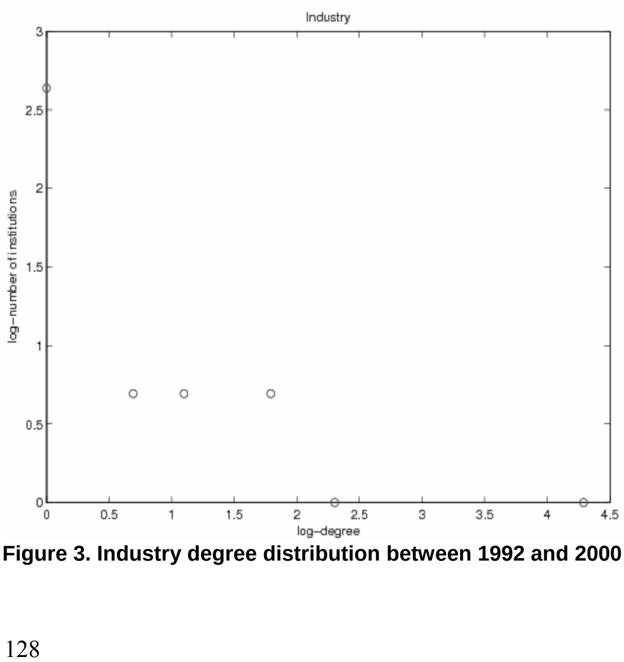

Figure 3. Industry degree distribution between 1992 and 2000

If MTAs were harmful to co-publication activity, research topics of publications that used MTAs would not overlap with those that did not use MTAs. To test this, we launched a second validating strategy: a search of common terms stemming from publications that used MTAs and from collaborative publications that did not used MTAs by means of a co-word analysis. The terms of the research topics were derived from the titles and abstracts of the publications using the same co-word technique as Rodriguez *et al* (2007).

Figure 5. Network topology of co-publications between 1992 and 2000

Results

For identifying the variables that discriminated best between the nodes that used MTAs and those that did not, a discriminant analysis was necessary. The null and the alternative hypotheses were $H_0 : \mu_1 = \mu_2$ and $H_a : \mu_1 \neq \mu_2$ for each variable respectively. As the significance level was 5%, the p-values allowed us to reject the null hypothesis (Table 2). The selected variables — betweenness centrality, degree, local and global clustering coefficient scores and number of collaborative documents — significantly differentiate between the group 1 formed by nodes that were related to MTA and group 2 constituted by nodes that were not related to MTAs.

As for popularity bias, we examined whether the nodes with more connections were receiving new attachments. For instance, in Figure 1 we depicted the

Figure 6. Ties present in 1998

Table 3. Number of nodes and new entrants into the MTA network

Year	Government		Industry		Academia		Total Nodes
	In network	New entrants	In network	New entrants	In network	New entrants	
1992	0		1		6		7
1993	0	0	1	0	6	0	7
1994	0	0	3	2	6	0	9
1995	0	0	4	2	7	1	11
1996	0	0	2	0	7	0	9
1997	0	0	1	0	6	0	7
1998	0	0	1	0	6	0	7
1999	0	0	3	1	7	1	10
2000	0	0	2	0	6	1	8
All years	0		6		7		13

Note: The 13 nodes, which used at least one MTA, collaborated in 705 publications (nine patents and 696 articles, letters, notes and reviews).

co-publication activity of 1998 in a circle of edge or tie patterns where the popularity of the nodes was depicted by their sizes and the links by the thickness of their connecting lines.

Concerning skewness, in government (Figure 2) and academia (Figure 4), the degree distribution has a highly skewed form. In industry (Figure 3), the distribution is much less skewed, having a sharp peak and a fast decay in the tail. Regarding sectoral hubs behind the sectoral degree distributions, the industry plot (Figure 3) displayed the central function of Innogenetics. This company essentially carries out studies on human health. The government plot (Figure 2) presented the highly pivotal role of the Flemish Institute for Technological Research, which specialises in industrial research on energy, waste disposal, biotechnologies, and advanced materials (Lawton Smith, 1997). The academia plot (Figure 4) showed the central positions of the University of Ghent and the Katholieke Universiteit Leuven. The former is mainly investigating plant genetics and the latter is primarily devoted to human health genetics.

For exploring the dynamics of the field and the changing impact of different organisations, we represented a series of network visualisations in two types of images. The co-publication network for the nine-year period 1992–2000 is shown in Figure 5, while the ties or edges for 1998 are depicted in Figure 6.

As a supplement to the graphics, count data on patterns of entry and exit into the network for nodes that used at least one MTA in their publications are shown in Table 3. The counts for nodes that did not use MTAs at all are presented in Table 4. Only those organisations that actively collaborated in publications were counted for the yearly columns titled “In network”. However, in the columns “New entrants” only organisations that have never been in the network before were counted. It can be seen in Table 3 that the yearly pattern of academia nodes that used MTAs is more stable than that of industry, where entrances and exits occurred more often. By contrast,

Table 4. Number of nodes and new entrants into the non-MTA network

Year	Government		Industry		Academia		Total Nodes
	In network	New entrants	In network	New entrants	In network	New entrants	
1992	2		2		4		8
1993	2	1	1	1	6	3	9
1994	3	1	0	0	3	0	6
1995	5	3	1	0	6	0	12
1996	4	0	1	1	5	1	10
1997	3	0	0	0	5	0	8
1998	4	0	2	1	5	0	11
1999	2	0	6	5	6	1	14
2000	5	2	5	4	6	1	16
All years	13		16		16		45

Note: The 45 nodes, which did not use MTAs at all, collaborated in 556 publications (9 patents and 547 articles, letters, notes, and reviews).

Table 5. Collaboration patterns in publications for the MTA network

Year	Total number of edges (e_i)	Unique pairs of collaborating organisations	Completely new collaboration (unique pairs of organisations)	New collaboration (unique pairs of organisations)	Sum of additional edges per organisation pair (a_i)
				With regard to the previous year	
1992	40	15			
1993	34	14	2	2	6
1994	33	12	1	3	11
1995	59	22	9	11	30
1996	28	11	1	3	7
1997	58	18	2	9	36
1998	44	11	0	3	8
1999	43	16	2	6	13
2000	61	19	1	7	26
All years	400	33			

Note: The MTA network is formed by 13 nodes, which published 705 collaborative documents (nine patents and 696 articles, letters, notes and reviews).

the number of nodes that did not use MTAs in their collaborative publications followed an erratic yearly pattern as shown in Table 4.

The patterns of collaboration in publications are shown in Table 5 for those organisations that used MTAs and in Table 6 for those that did not. In both tables, the "Total number of edges" in a specific year equals the total amount of mutual collaboration between any pair of organisations. Then, each collaborative publication by N organisations always accounts for $N \cdot (N - 1)/2$ edges. Second, the column "Unique pairs of collaborating organisations" considers, in each year, multiple collaboration between the same two organisations only as one. Third, "Completely new collaboration (unique pairs of organisations)" denotes that the two involved organisations had never collaborated before. Fourth, in column "New collaboration (unique pairs of organisations) with regard to the previous year", one mark is added for each pair of collaborating organisations that had not collaborated in the year before. Finally, the last column adds up, for each pair of organisations, the amount of additional collaboration with regard to the previous year (that is, how many papers there are more, with regard to the previous year, that have at least both affiliations).

The expansion rate of collaboration and new collaboration in publications, whether or not using MTAs (Tables 5 and 6, respectively), outpaced the entry of organisations (Tables 3 and 4, respectively), suggesting a more connected field or a denser network. The visualisations afford the opportunity to see the diverse types of organisations that are driving this connectivity.

Table 6. Collaboration patterns in publications for the non-MTA network

Year	Total number of edges (e_i)	Unique pairs of collaborating organisations	Completely new collaboration (unique pairs of organisations)	New collaboration (unique pairs of organisations)	Sum of additional edges per organisation pair (a_i)
				With regard to the previous year	
1992	11	8			
1993	14	9	7	7	9
1994	12	6	2	3	8
1995	27	14	7	10	21
1996	16	9	2	3	7
1997	22	9	1	4	16
1998	15	11	6	7	7
1999	14	11	5	7	8
2000	21	14	8	12	17
All years	152	46			

Note: The non-MTA network is formed by 45 nodes, which published 556 collaborative documents (nine patents and 547 articles, letters, notes and reviews).

Table 7. Other patterns of collaboration in publications for the MTA network

Year	Repeated collaboration (unique pairs of organisations)	Sum of renewed edges per organisation pair (r_i)	Discontinued collaboration (unique pairs of organisations)	Sum of edges less per organisation pair (d_i)
	With regard to the previous year			
1992				
1993	12	28	3	12
1994	9	22	5	12
1995	11	29	1	4
1996	8	21	14	38
1997	9	22	2	6
1998	8	21	14	38
1999	10	30	1	14
2000	12	35	4	8

Note: The MTA network is formed by 13 nodes, which published 705 collaborative documents (nine patents and 696 articles, letters, notes and reviews).

Tables 7 and 8 show other collaborative patterns in publications with respect to the previous year for the MTA and non-MTA networks, respectively. The first column gives the number of unique pairs of organisations that had renewed their existing mutual collaboration of the year before. The second column counts, for each organisation pair, the minimal number of collaborative documents that were produced in a specific year but did so in the year before. The third column counts the number of organisation pairs that did not collaborate in a specific year but did collaborate in the year before. The last column counts, for each pair of organisations, the decrease in the amount of collaboration with respect to the year before (that is, how many fewer papers there are having at least both affiliations). In other terms,

$$e_i = a_i + r_i,$$

$$e_i - e_{i-1} = a_i - d_i,$$

$$d_i = a_i + e_{i-1} - e_i,$$

where e is the number of edges, a is the number of additional edges per organisation pair, r is the number of renewed edges per organisation pair, d is the decrease of edges per organisation pair, i is a given year, and i–1 represents the year before i. For instance, in Table 7 for the year 1993 the last column shows d = 12, which can be computed applying the last formula in Table 5 (6 + 40 – 34). In both tables, the rate of collaboration dissolution waned and grew, in a to-ing and fro-ing pattern, so there is considerable turnover in interorganisational relations.

Table 8. Other patterns of collaboration in publications for the non-MTA network

Year	Repeated collaboration (unique pairs of organisations)	Sum of renewed edges per organisation pair (r_i)	Discontinued collaboration (unique pairs of organisations)	Sum of edges less per organisation pair (d_i)
	With regard to the previous year			
1992				
1993	2	5	6	6
1994	3	4	6	10
1995	4	6	2	6
1996	6	9	8	18
1997	5	6	4	10
1998	4	8	5	14
1999	4	6	7	9
2000	2	4	9	10

Note: The non-MTA network is formed by 45 nodes, which published 556 collaborative documents (9 patents and 547 articles, letters, notes, and reviews).

Overall, the general picture was one of a continuing flow of new entrants into the field, alongside forging new collaborations, making for an increasingly dense network. New attachments expanded the structure of the network, whereas repeat collaboration thickened relations between existing nodes. Because the network is social, it is inherently unstable (Law, 1990).

Discussion

Our study addressed the crucial question of whether MTAs hamper research freedom by constraining one type of research collaboration, that of co-publication activity. A caveat must be stated at the outset; we must be cautious interpreting or explaining findings because of the small sample size or sample selection bias. One of the major obstacles to conducting empirical studies on collaboration is that the really important outcome under discussion, research freedom, is an abstract construct. Research freedom suggests the freedom to choose research methods or questions, the freedom to communicate research results, and the freedom to interpret research results (Bailyn, 1985), but it also indicates the freedom to collaborate in research projects that will be published in co-authored articles or co-assigned patents.

Hicks and Katz (1997) found that research in general is increasingly conducted in networks, both domestic and international. As biotechnology is a science-based domain (that is, with frequent references to scientific publications and inventions from academia), research is the vehicle that drives the knowledge forward (Grupp and Schmoch, 1992). Because of this feature of biotechnology, research needs various kinds of non-human resources (equipment, materials, among others). Thus, an actor network is an association of unstable elements that influence and redefine each other continuously (Callon, 1990).

Learning and knowledge creation play a decisive role in the emergence of interorganisational networks. According to the absorptive capacity (Cohen and Levinthal, 1990), nodes that are more centrally located accumulate greater knowledge and, thus, will be in a better position to convert this knowledge into further knowledge. Powell *et al* (1996) show that a network provides access to knowledge and resources that are otherwise unobtainable. In a knowledge network, members offer various kinds of resources. Different projects could be pursued combining some members' resources on a timely basis. Thus, specific assets of the network are flexibility and ability to handle complex projects and access to pivotal partners.

One of the major obstacles to conducting empirical studies on collaboration is that the really important outcome under discussion, research freedom, is an abstract construct

The literature on national systems of innovation depicts intensive scientific collaboration between industrial, governmental and academic organisations (Etzkowitz and Leydesdorff, 2000). Given the differentiation of organisational forms, we treated the each sector and organisation as equally important. The benefit of this assumption is that it permits comparisons across time periods. The advantages of nine years of fine-grained data reside in capturing the length of relationships, the dissolution of ties to particular partners and the forging of ties to others, as well as the deepening of some ties.

In the Pajek visualisations (Figures 1, 5 and 6), we did not indicate the organisations that used MTAs in their collaborative publications because of confidentiality provisions included in the contracts. We only displayed the information that is available in the public domain, without any prejudice to the rights embedded in MTAs. These graphics provided evidence of collaboration patterns.

Although the degree distributions (Figures 2, 3 and 4) are aggregate measures over all time periods, they give some hint of growth processes in attachment. The shape of the distributions mimics what would be expected for tie formation in biotechnology networks from a process of preferential attachment to degree. The static snapshots of the degree distributions indicate sectoral patterns of affiliation. One possible reason for the different degree distribution of government and academia from that of industry is that the maintenance of ties in industry has strategic goals and a substantial cost associated with it. Apart from that, industry tends to publish more patents than articles. These differences may put a sharper limit on the number of research partners an organisation can hold.

We worked with a control group consisting of nodes that were not involved in MTAs, whose variables significantly differed from the nodes that used MTAs. We detected a popularity bias and skewness and preferential attachment for the hubs of the network.

If MTAs were harmful to co-publication activity of research organisations, the patterns of entry and exit nodes would remain unaltered and the expansion rate of collaboration and new collaboration would be zero. The findings showed the opposite. Thus we construe that MTAs might not have interfered in such a way as to limit co-publication activity of research organisations in the network.

For validating the results that an MTA did not affect negatively co-publication pattern we implemented two strategies. First, we checked whether the

MTA unique pairs of institutions have published non-MTA-related documents between the publication that used MTAs and 2000. We detected 85 post-MTA co-publications done by eight pairs of organisations. Nevertheless, ten pairs of organisations discontinued their co-publication activity after using MTAs up to 2000. Among those ten unique pairs, three of them should be ignored because the MTA-related papers were published in 2000 and we found other co-publications after 2000. As no explanations of such discontinuations where found in the documents, we contacted directly those organisations. Of the reasons given by the representatives, three were due to the ending of financial support, one because of the lack of research results, two because the research projects arrived at their end, and one was discontinued before 2000 and resumed afterwards. Consequently, they explained that none of those discontinuations were due to MTAs.

Another issue arises when non-MTA ties or edges are non-existent after using MTAs. Why did the organisations discontinue co-authoring papers or co-applying patents? We did not check if non-MTA collaboration was discontinued afterwards or if negotiations for collaboration did not succeed because of MTAs.

As we found in our sample some non-MTA ties or edges after using MTAs, does this mean that MTAs did not interfere in co-publication activity patterns? It is possible that MTAs did not hinder the progress of science by limiting co-publication activity. If this were the case, research topics of publications that used MTAs would overlap with those that did not. To test this, we launched a second validating strategy: a search of common terms stemming from publications that used MTAs and from collaborative publications that did not used MTAs. The common terms in Table 9 might be interpreted as related to MTAs and collaborative publications not related to MTAs.

Table 9. Common terms between publications related to MTAs and collaborative publications not related to MTAs derived from co-word analysis

Overlapping number of terms	Collaborative non-MTA-related publications		
MTA-related publications	**1992–1994**	**1995–1997**	**1998–2000**
1992–1994	N/A	9	30
1995–1997	–	13	66
1998–2000	–	–	94

Notes: N/A means not analysed because there was only one cluster.
For the co-word analysis, the number of publications related to MTAs totalled 496. These publications included not only the 16 collaborative documents used in this paper but also documents with single authorship or single assignment.

Concluding remarks

Despite the multiple topics related to MTAs on research freedom, we have only focused on one type of research collaboration: co-publication activity of organisations. The present study examined whether or not co-publication activity was hindered by MTAs. This required examining the research organisations involved and their collaborative pattern of publication. We were able to incorporate bibliometric data and graph theory in our study as variables that help us to detect the effect of MTAs on co-publication activity of organisations in a biotechnology research network.

We worked with a control group, nodes that were not involved in MTAs, whose variables significantly differed from the nodes that used MTAs. We detected a popularity bias and skewness and preferential attachment for the hubs of the network. As far the network patterns of entry and exit, the pattern of academia nodes that used MTAs was more stable than that of industry, where entrances and departures occurred more often. In contrast, the pattern of nodes that did not use MTAs in their collaborative publications was erratic. The expansion rate of collaboration and new collaboration in publications, whether or not using MTAs, outpaced the entry of nodes, suggesting a more connected field or a denser network.

In general, the network was characterised by a continuing flow of new entrants into the field, alongside forging new collaboration in publications, making for an increasingly dense network. New attachments expanded the structure of the network, whereas repeat collaboration thickened relations between existing nodes. The findings passed two validation tests. According to our interpretation of findings, it is possible that MTAs might not have interfered in such a way as to limit co-publication activity.

Organisations that want to strengthen or have to defend their leading positions in research thus appear to partially give up their autonomy, develop and implement co-authorship or co-assignment strategies with other organisations, and use the results of these strategies to reinforce their research capabilities. Organisational collaboration entails tying the activities of one organisation to those of others. One explanation is that such collaboration is assumed to facilitate the acquisition of research materials from other organisations.

Acknowledgements

We extend our gratitude to *Steunpunt O&O Statistieken* for providing the venue where these ideas were initially discussed and much of the work was done. We would like to thank John Nye, Sebastián Galiani, Claude Ménard, and Manuk Ghazanchian for their comments at the Workshop on Institutional Analysis of the Ronald Coase Institute in Boulder in September 2006. We appreciate the valuable remarks of the anonymous referees of

Research Evaluation. During the edition of the manuscript, we received suggestions from Kristin Blanpain, Li Wan, Wolf Vanpaemel, Bart Ons, Tuan Bui, and Tom Howes. We are grateful for the assistance of Mariëtte Du Plessis, Xiaoyan Song, and Rebecca Crabbé. We acknowledge very much the support from the KUL Research Council (GOA AMBiorics), the FWO (G.0499.04), the IWT (GBOU-McKnow-E) and the Belgian Federal Science Policy Office (IUAP P5/22).

Note

1. The name of the Matthew Effect is taken from the Gospel of Matthew 25:29, which reads: ‘For to all those who have, more will be given, and they will have an abundance; but from those who have nothing, even what they have will be taken away.’

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