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Mapping the De Facto Governance in the Case of Emerging Science and Technologies

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Abstract

In this study, we discuss the use of novel scientometric mapping techniques as informative and interpretative tools about the rapid dynamics and uncertainties featuring in Emerging Science and Technologies (ESTs). We show how these techniques can provide perspectives on and crosscuts of the geographical, social, and cognitive spaces of the complex emergence process. Shedding light on these spaces the set of, both intentional and un-intentional, institutional arrangements that are established in the emergence of novel science and technologies - that is, as de facto governance - can be revealed. The informative and interpretative power of these tools resides in their transversal flexibility within and across databases, which themselves are characterized by longitudinal and institutional rigidities. Changing informed perspectives can play a crucial role in supporting the design of governance that is ?tentative?, i.e. forms of governance

aiming to address the complexity, interdependencies, and contingencies featuring in ESTs. We discuss the contribution of these mapping techniques to the understanding of the phenomenon of tentative governance of ESTs across three case studies, namely RNA interference (RNAi), Human Papilloma Virus (HPV) and Thiopurine Methyltransferase (TPMT) testing technologies.

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MAPPING THE *DE FACTO* GOVERNANCE IN THE CASE OF EMERGING SCIENCE AND TECHNOLOGIES

ABSTRACT

In this study, we discuss the use of novel scientometric mapping techniques as informative and interpretative tools about the rapid dynamics and uncertainties featuring in Emerging Science and Technologies (ESTs). We show how these techniques can provide perspectives on and crosscuts of the geographical, social, and cognitive spaces of the complex emergence process. Shedding light on these spaces the set of, both intentional and un-intentional, institutional arrangements that are established in the emergence of novel science and technologies - that is, as *de facto* governance - can be revealed. The informative and interpretative power of these tools resides in their transversal flexibility within and across databases, which themselves are characterized by longitudinal and institutional rigidities. Changing informed perspectives can play a crucial role in supporting the design of governance that is 'tentative', i.e. forms of governance aiming to address the complexity, interdependencies, and contingencies featuring in ESTs. We discuss the contribution of these mapping techniques to the understanding of the phenomenon of tentative governance of ESTs across three case studies, namely RNA interference (RNAi), Human Papilloma Virus (HPV) and Thiopurine Methyltransferase (TPMT) testing technologies.

Key words: maps and overlays; *de facto* governance; emerging science and technology; scientometrics; case study.

1. INTRODUCTION

Emerging Science and Technologies (ESTs) have the potential to generate profound - both positive and negative - social changes such as creating new industries as well as dramatically reconfiguring or destroying existing ones. The context of this phenomenon is the knowledge-based economy where the systematic production of novelty in science and technology is added as a social coordination mechanism to markets and policy making. Whereas both markets and institutions tend to (quasi-)equilibria (Aoki, 2001), knowledge-based science and technology outputs continuously upset equilibria (Nelson and Winter, 1982). For this reason the governance of ESTs has assumed an increasing relevance.

Identifying and defining governing arrangements for ESTs is a complex activity for policy makers. Uncertainties and rapid dynamics feature in the emergence process. The development of ESTs may follow some directions rather than others as a result of a variety of factors. These include the visions, goals, and expectations of the actors involved (e.g. Geels, 2002; Wiek et al., 2007; Stirling, 2009). These actors are at the same time regulated by and regulating the emergence process. While their explicit attempts to shape government arrangements are only one part of this process (Braithwaite and Drahos, 2000), un-intentional influences also matter as they also constitute part of *de facto* governance (Rip, 2010).

Traditional forms of governance, which may find legitimacy in times of more incremental changes, are unsuitable for ESTs. Novel governance approaches that are 'tentative' have indeed started to appear (e.g. Hagendijk and Irwin, 2006; Stirling, 2006; Wiek et al., 2007; Boon et al., 2011). These forms of governance aim to flexibly address the complexity, interdependencies, and contingencies featuring in the process of emergence of ESTs by creating a space where the generation of a number of options for the development is desired and supported. The definition of tentative government arrangements requires decision and policy makers to be informed, in a timely manner, on the dynamics of the emergence process across a number of spaces.

The rapid growth of the Internet over the last decade has provided scientometricians with access to a large number of novel sources of data in parallel. This has stimulated the development of user-driven and interactive techniques, i.e. base maps combined with projections (overlays) (e.g. Leydesdorff and Persson, 2010; Rafols et al., 2010), that can inform on *de facto* governance of ESTs with more granularity. These new techniques have the potential to relate the evolutionary dynamics of the institutional arrangements across three spaces of the emergence process, namely the geographical, social, and cognitive spaces, thus providing informative and interpretative perspectives on ESTs. These techniques are relatively flexible since they are not constrained by the institutional rigidities of individual databases. Their informative and

interpretative power crosscuts multiple databases thus providing flexible monitoring of ESTs. This may in turn increase our understanding of the phenomenon of ESTs as well as support the definition of forms of governance that can be considered tentative.

Despite the large number of scientometric techniques developed in the last decades - this includes co-citation (Small, 1973) and bibliographic coupling (Kessler, 1963), and co-words analysis (e.g. Callon et al., 1983; Cambrosio et al., 2006) - only with these recent portfolio-oriented developments of the mapping approaches one can trace the *de facto* governance of ESTs across time in terms of different configurations among a multitude of dimensions. For example, these techniques allow projecting an entity's (e.g., individual, organisation, community, research field) publishing activity on maps of science or Google maps (e.g. Klavans and Boyack, 2009; Rafols et al., 2010) across different levels such as disciplines (Leydesdorff et al., 2013), or research topics (e.g. Waltman and van Eck, 2012). Overlays can be also animated including the time dimension and thus providing evolutionary perspectives on the *de facto* governance. It is worth noting that we do not wish to claim that the data and data-driven representations can guide the theorizing. The representations provide heuristics by confronting the respective theoretical debates with puzzles in the relevant data as well as inform governance by specifying uncertainties in considerable detail.

We discuss the use of mapping and overlay techniques as tool to reveal the institutional arrangements of the *de facto* governance across three illustrative case studies of ESTs: (i) RNA interferences (RNAi), (ii) Human Papillomavirus (HPV) and (iii) Thiopurine Methyltransferase (TPMT) testing technologies. While the uncertainty and rapid dynamics featuring in the three case studies make them suitable examples for our discussion, they also provide an opportunity to enrich the analysis by crossing different phases and contexts of the emergence process. Results show how these novel scientometrics techniques capture the different dynamics in these three ESTs such as the evolutionary structure of the web of relationship among the involved actors, pace and directions of diffusion.

The paper is structured as follows. In the next section (§2), we introduce the methodologies, the three case studies, and the data sources. We also discuss the issues related to the identification of the boundaries of ESTs. We then present the results on how mapping and overlay techniques can inform analysts on the *de facto* governance (§3). We conclude by elaborating on the contributions of these techniques and the relative implications for the research investigating the phenomenon of the tentative governance of ESTs (§4, §5). Given that the many of the methods presented are interactive visualisations, the article is supported by

supplementary figures (some with interactive features), which are available at: http://www.interdisciplinaryscience.net/defactogov

2. METHODS

2.1. Mapping and overlay techniques

The scientometric community has made great efforts in developing a number of techniques to trace the dynamics in science and technology domains since the seminal works by Small (1973) and Kessler (1963). Yet, only recent technical developments with the mapping and overlay techniques allows one investigating the *de facto* governance of ESTs with an macro-evolutionary perspectives involving several dimensions of the emergence process. The basic idea underlying these novel approaches is the projection of publication and patent data, which constitute the overlay, over a basemap. Publication and patent data may refer to the knowledge production of individuals, organisations, communities, or, especially for this paper, entire emerging fields in science and technology - the choice depends on the specific research question(s) one is pursuing. A number of basemaps can be identified. These include geographical maps, maps of science representing the entire structure of science at multiple levels of analysis such as disciplines, journals or topics, and maps of technological areas as identified by patent technological classes. With a specific focus on ESTs, the animation over time of these overlays over basemaps provides evolutionary perspectives that inform in an accessible manner on the dynamics of the *de facto* governance.

The present paper summarizes and applies a number of mapping and overlay techniques that were previously developed in studies published in the domain of information science and scientometrics for reasons of quality control. The purpose of these tools was to generate a set of visualisations that allows integrating different perspectives. For this study, several in-between steps were further developed and made available on the Internet. We methodologically build on Leydesdorff & Persson (2010) for mapping co-authorship relations in publications as overlay to Google Maps; Rafols et al. (2010) for mapping publications in terms of subject categories; Bornmann & Leydesdorff (2011) for the mapping of excellence in publications and Leydesdorff & Bornmann (2012) for the equivalent mapping of patents; Leydesdorff, Rotolo & Rafols (2012) for mapping medical innovations in terms of Medical Subject Headings. Several other studies with further elaborations will be mentioned as they are used. The reader is referred to these studies and the corresponding webpages for technical details.

2.2. Background on the case studies

The selection of the case studies is driven by their diversity in terms of context and position in the innovation chain. RNAi is a technology positioned close to basic research while screening tests for HPV and TPMT have emerged as applications of basic research. HPV is relevant in the clinic, whereas TPMT is still in the development stage. This variety of areas of development and use provides us with the opportunity to test the tools, to enrich the discussion on the use of scientometric mapping and overlay techniques, and to build informative and interpretative perspectives on *de facto* governance of these ESTs.

Firstly, RNAi, which is a technique for gene silencing, can be conceived as a general purpose technology for research in labs (Fire et al., 1998; Youtie et al., 2008). Genes play a critical role in the progression of cancers, genetic diseases, and infection agents. Theoretically, by silencing specific genes one can stop the progression of a given disease. This small RNA silencing mechanism was discovered in 1998 (Fire et al., 1998) and its discovery reshaped the landscape of research on gene expression creating important expectations especially for the therapeutic applications (Sung and Hopkins, 2006; Lundin, 2011).

Secondly, the HPV testing technology is positioned within a specific domain of application, i.e. the screening of cervical cancer. Cervical cancer has a significant disease burden - about 500,000 new cervical cancers occur and cause about 250,000 deaths each year. This has led to the development of a large screening program (especially in the US) with 100+ million tests performed annually. While the screening has been conducted for years by using the Pap test (cytology-based test), in the 1980s, the discovery of the strong association of the HPV, especially the HPV types 16 and 18, with cervical cancer opened the space for the development of a competing and more sensitive technology test based on molecular diagnostics (Casper and Clarke, 1998; Hogarth et al., 2012).

Thirdly, similarly to HPV test, the TPMT testing technology is positioned close to the applied-research domain. Yet, its application for clinical utility is contested across medical fields (e.g. different clinical guidelines supporting and discouraging the use of the test). TPMT testing is specifically focused on an emerging class of Pharmacogenetic tests (which predict adverse events affecting patient's health) (Hopkins et al., 2006). TPMT is an enzyme in the human body responsible for metabolising thiopurine drugs. Cytotoxic Thiopurine drugs such as Azathioprine are used to treat a range of conditions including leukaemia, and autoimmune diseases (such as Lupus, or rheumatoid arthritis). However, when a patient has mutations in the gene encoding TPMT, she/he is at increased risk of toxicity from a build-up of thiopurines. Therefore, several

types of TPMT test began to emerge across a number of clinical fields of use such as transplantation, gastroenterology, rheumatology, and paediatric oncology.

2.3. Data sources

Data were collected from multiple databases. We relied on ISI Web of Science (WoS) and MEDLINE/PubMed for publication data and on the United States Patent and Trademark Office (USPTO) database for patent data. These databases were queried by using a specific set of keywords we identified combining multiple knowledge sources such as interviews with experts and previous research works on these ESTs (see Table A1 in the Appendix). For scientific articles, we limited the search of the keywords and their combinations in titles. While abstracts may represent an additional source to identify records related to the given EST, they often contains technical and methodological terms not representing the core of knowledge the given article claims (Leydesdroff, 1989). Therefore, a search that extends to articles' abstract may retrieve many additional records, yet with the risk of including many records not closely related to the research activity of the given EST - it increases 'recall' at the expenses of losing 'precision', in bibliometric technical terms.

On the other hand, identifying patents for an EST requires a different approach. The incentives to patent are indeed different from those underlying the publication of scientific articles (e.g. Dasgupta and David, 1994; Murray, 2002). The primary purpose of the patent system is to reward patentees by providing them a temporary monopoly to commercially exploit the patented inventions. Yet, this requires patentees to disclose the technical knowledge of the inventions. In this regard, patent attorneys are very careful in including valuable information in the appropriate sections of the patent. Among these sections, claims are the most relevant source informing on the scope of the technical knowledge (Hunt et al., 2007). Claims "define the invention and are what aspects are legally enforceable" (USPTO Glossary).[1] We therefore focus the search of keywords in patent's claims. Issues related to the definition and delineation of the boundaries of ESTs will be further discussed in the next section.

The number of publications and patents from 1982 to 2011 are reported in Table 1 - data for RNAi are available since 1998 when this silencing mechanism was discovered (Fire et al., 1998). Publication data from ISI WoS and MEDLINE/PubMed report a rapid emergence of these three ESTs in terms of published scientific articles. Yet, the pace of this growth as well as the

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[1] The USPTO Glossary is available at http://www.uspto.gov/main/glossary

[2] The search string used to retrieve scientific articles in ISI WoS related to miRNA is reported in the followings: (TI=microRNA* or TI=miRNA*).

[3] The *z-test* for two independent proportions is used - the null hypothesis is the randomness in the selection of papers for a city (see Bornmann and Leydesdorff, 2011).

scale of this emergence is significantly different from one case to another in two respects. First, the growth in the number of publications for RNAi is stepper than the other two case studies. Second, RNAi and HPV testing technology show an increasing number of publications for the entire observation period. Conversely, the testing technology for TPTM enzyme seems to have reached the mature phase. Patent data (both granted patents and patent applications) reveal similar distinctive features. The production of patents related to RNAi, for instance, is much greater than HPV and TPMT testing technologies. Yet, the trends in patenting activity show also a declining phase for RNAi in the last two years of observation. This decreasing trend is possibly related to the decision of some large pharmaceutical companies, specifically Roche and Pfizer, to shut down their R&D units on RNAi (Lundin, 2011). The R&D productivity crisis in the pharmaceutical sector may have been a strong determinant of those decisions (Pammolli et al., 2011). The patenting activity around HPV testing technology grows from 2002 to 2004 in terms of patent applications and then stabilises in the subsequent years with a peak of applications in 2009. On the other hand, the low number of granted patents and patent applications for TPMT testing technology does not allow identifying clear trends in the production of technical knowledge. As discussed, we believe the diversity - position in the innovation chains, scale, and phase of development - that characterizes the selected case studies enriching the discussion on the potential mapping and overlay techniques have in informing about the *de facto* governance of different ESTs.

Insert Table 1 about here.

2.4. Definition and Delineations Issues

Identifying the boundary of ESTs is more ambiguous than one may initially expect (Arthur, 2009). The study of an emergent science and technology suffers from this ambiguity: it can be defined as the knowledge underpinning method or processes to fulfil a purpose (e.g. understanding of gene silencing) or as a network of practices and components (e.g. the molecules and techniques that result in gene silencing). The case of RNA interference is apt to highlight the ambiguity inherent in the delineation of the boundary of ESTs. RNA interference is the naturally occurring process in which gene expression is reduced as a result of the destruction of messenger RNAs. This process can be triggered by naturally occurring (endogenous) molecules, called microRNAs (miRNAs), or by externally inserted (exogenous) molecules, called small interfering RNAs (siRNAs). Soon after the discovery of RNA interference by Fire et al. (1998), siRNAs were recognised as valuable for gene silencing, both as tools for research and for

therapeutic purposes, which lead to a boom in public and private R&D investments. In parallel, but with some significant delay, it was realised that miRNAs were not a marginal phenomenon, but played a major role in gene regulation, including abnormal down or up regulation in certain diseases caused or earmarked by anomalous gene expression, such as many cancers.

In principle, then, research on the science and technology of RNA interference should include both siRNAs and miRNAs. However, it turns out that 'RNA interference' as a technology (not as phenomenon) became mainly known as the human-induced, exogenous interference which was developed mainly for therapeutic purposes. We have then two potential definitions of RNAi, one covering the entire field - used, for example to classify articles in the journal *Molecular Therapy–Nucleic Acids* - and one excluding miRNA - commonly adopted for the discussion of therapeutic applications. In this regards, Figure 1 illustrates that the observed dynamics are very different. Whereas miRNA research is still booming due to new finding suggesting their potential use as biomarkers in disease, publications focused on siRNA have reached a plateau of about a thousand publications per year. The latter is possibly related to the challenges encountered in delivering siRNA in therapeutic applications that resulted in a retreat of pharmaceutical investment (Haussecker, 2012). These differences in trends support the views that the use of miRNAs and siRNAs follow separate trajectories, which it is best to differentiate. In this study, we focus on RNAi as research tool and for therapeutic applications, i.e. not including miRNA.[2]

Insert Figure 1 about here.

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3. RESULTS

We apply and discuss the overlay and mapping techniques across three spaces of emergence process - the geographical, social, and cognitive ones. To do so, we rely on the aforementioned three case studies of ESTs. Due to space limitations, we discuss and report in the paper a sample of the results obtained by applying the aforementioned overlay and mapping techniques. The entire set of maps and overlays, which includes also interactive features, across the three case studies, is available at http://www.interdisciplinaryscience.net/defactogov.

[2] The search string used to retrieve scientific articles in ISI WoS related to miRNA is reported in the followings: (TI=microRNA* or TI=miRNA*).

3.1. *De Facto* Governance in the Geographical Space

Novel scientometrics mapping techniques combine the use of overlays with geographical maps to visualise the emergence process in the geographical space. Efforts in this direction have been made to map - across cities, regions, and nations - the distribution of publications and citation data from the WoS or Scopus databases (e.g. Bornmann and Leydesdorff, 2011) as well as patent data from USPTO (e.g. Leydesdorff and Bornmann, 2012). One can, for instance, identify the centres of excellence for a given ESTs as revealed by those cities where highly cited scientific articles were published more frequently than expected - this deviation is reported in terms of the size of nodes. In addition, a node's is coloured dark green when the observed number of top-cited publications is higher then the expected one and this difference is statistically significant ($p < 0.05$), light green when the difference is positive but not statistically significant.[3] On the other hand, when the difference is negative the given node is coloured red and orange, respectively. The lime green is used to indicate those cases where the z-test cannot be evaluated. A threshold of top 10% cited scientific articles is selected (Bornmann and Leydesdorff, 2011).

For the three case studies of this article, we used overlays projecting the publication data of three case studies according to a 5-year time window.[4] ISI WoS publication data were used. Figure 2 depicts the results of this approach applied to the HPV and TPMT testing technologies for the 2002-2006 period - see the supplementary materials for the interactive maps of the three case studies. We specifically reported in the paper a focus on US and Europe. For HPV testing technology these maps identify European centres of excellence in the areas of London, Paris, and Amsterdam over the entire observation period. New centres have also started to appear both in the North (areas of Copenhagen, Helsinki, and Jena) and South (nearby Barcelona, Bologna, and Turin) of Europe since the mid 1990s. The US excellences in the scientific knowledge production for this EST are mainly located on the coasts, specifically in the area of Washington D.C., Baltimore, New York, and Boston, for the East Coast, and nearby San Francisco and San Diego for the West Coast. Georgetown University and the private company Digene Corp. in the area of Washington D.C. have played a key role for the development and the adoption of the HPV testing technology (Hogarth et al., 2012). The maps also reveal the rise of new centres of excellence in South America (e.g. nearby Sao Paulo, Buenos Aires) in the last

[3] The *z-test* for two independent proportions is used - the null hypothesis is the randomness in the selection of papers for a city (see Bornmann and Leydesdorff, 2011).

[4] Similar dynamics are observed by using narrower/broader time windows (e.g. 3-year, 7-year). It is worth noting that having started to observe the dynamics of RNAi since its discovery in 1998 the first time window for this EST is the 1998-2001 period, i.e. four years of observations.

ten years of observation. The geographical mapping of the highly cited scientific articles related to TPTM testing technology locates, at the beginning of the observation period, centres of excellence in the area of Rochester and Memphis (US) as well as Sheffield (UK). However, as for HPV testing technology, new centres have started to appear since 1997 nearby the US coasts (e.g. areas of Washington D.C., Boston, San Diego, San Francisco), across UK (e.g. near London, Glasgow, Edinburgh) and Europe (e.g. Berlin, Madrid, Seville).

A similar approach can be used to geo-localise highly cited patents. Figure 3, for example, geo-localises the sample of patents related to RNAi by using the inventors' addresses - the technique can also be extended to the assignees' address. While for publication data we selected the threshold of the top 10% cited scientific articles, we decreased this threshold to the top 25% cited patents. This is to take into account that number of publications is an order of magnitude higher than the number of patents (Leydesdorff and Bornmann, 2012). In addition, the geographical overlays for RNAi are provided for the 2002-2011 period. The first time window (1998-2001) indeed includes only 11 patents which constitute a too small sample for the statistical analysis. Results in Figure 3 reveal the area of Denver as the area with the most cited patents, which were related to patenting of reagents used in RNAi (small interfering RNAs). Yet, new centres also have appeared in the last five years nearby New York and Philadelphia, which were mainly related to therapeutic applications. The analysis does not identify any centre in Europe or Asia. The supplementary materials provide these maps across the three case studies when the number of observed patents was sufficient for the statistical significance.

In summary this mapping approach may reveal 'unexpected' - as compared to expected number of top-cited scientific articles or patents - geographical areas of excellence for the given EST, thus suggesting patterns to investigate the emergence process as well as positing additional questions that may guide through the understanding of this phenomenon - such as which actors produced these high quality knowledge outputs? What aspects of the EST this knowledge refers to? For instance, the maps for HPV and TPMT testing technologies show, across the observation period, centres of excellences also located in developing countries (see supplementary materials). A further analysis on the collaboration networks (see below) revealed strong linkages between these areas and areas leading the advancements of the given EST in the developed countries. These collaborations have provided developing countries with the access to critical knowledge and resources to produce novel and high quality knowhow on the given ESTs thus *de facto* contributing to the shaping of the development of the ESTs. It is important however recognising the limitations of the above-discussed and similar approaches. First, the geographical information reported in publication and patent data may not reflect the locations where the

research was conducted. Second, while the overlays built at city-level provides granularity to the visualisation, they represent two or more cities located in the same urban area as two different nodes - e.g., in the case of HPV testing, Silver Spring was considered as a different node from Washington D.C. Third, publications and patents are only one form of research outputs.

Insert Figure 2 and 3 about here.

3.2. *De Facto* Governance in the Social Space

The structure of the relationships among the actors surrounding ESTs and its dynamics play a critical role in the emergence process (e.g. Latour, 1993). These connections are channels through which actors gain access to and mobilise knowledge, resources, and power. Networks of agents therefore affect and are affected by ESTs (e.g. Klijn and Koppenjan, 2000). By using co-authorship data (e.g. Crane, 1972; Wagner, 2008), the dynamics across this relevant space of emergence can be traced. Novel techniques allow specifically building perspectives crosscutting both the social and geographical spaces (Leydesdorff and Rafols, 2011).

For instance, Figure 4 shows the 2002-2006 co-authorship networks at city-level for the HPV and TPMT testing technologies - see the supplementary materials for the interactive maps of the three case studies. In this map, nodes are cities and the linkages between nodes are traced by using co-authorship data. The size of each node is proportional to the logarithm of the number of scientific articles (plus one)[5] that the organisations in the given city (node) published in the relative time window.[6] Investigating the evolutionary dynamics across these maps may provide informative perspectives that are derived by combining the geographical and social spaces (see the supplementary materials) - examples of empirical questions that can be addressed are: where does the given EST emerge? Does the collaboration network cluster in specific areas? Does the given EST spread across cities, regions, and countries and, if yes, through which (collaboration) channels?

The collaborative network of HPV testing technology, for instance, discloses three relevant dynamics of the emergence process. First, a strong collaborative activity between the US (especially the areas of Washington and New York) and Europe (initially Germany) can be observed. This technology has indeed started to emerge after a German scientist, Harald zur

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[5] We added one to the number of scientific articles in order to avoid the evaluation of log(1).

[6] Similar maps can be also built with the top-cited publications approach we described in the previous section. This provides additional perspectives on the structural position cities producing highly cited knowledge occupy in the web of collaborative relationships (co-authorships). We made these maps available for the three case studies as supplementary materials at http://www.interdisciplinaryscience.net/defactogov.

Hausen, at German Cancer Research Centre proved the HPV infections to be strongly associated with the development of the cervical cancer (Zur Hausen, 1987) - Zur Hausen won the Nobel Prize in "Physiology or Medicine" in 2008. This discovery subsequently found important applications in US where an extensive screening program on cervical cancer was already in place. Specifically, a small biotech company, namely Digene Corp., marketed, in 1999, the first FDA-approved HPV test to use as adjunct to the widely diffused Pap test. Second, the last ten years of observation show an increasing involvement of developing countries (e.g. Brazil, India) in the research networks. The cervical cancer in these countries is a significant social burden. HPV is sexually transmitted and the costs associated with the screening of the population are not always affordable the lower classes of the population. This has led to an intense scientific collaboration among the developed and developing countries. Third, a globalisation of research on HPV testing technology can be observed across the entire period as revealed by the density of the network of relationships across cities. The co-authorship network for TPMT testing technology overlaid on the geographical map reveals a strong collaboration between Rochester (US) and Sheffield (UK) since the early observations. This collaboration intensifies over the entire period while collaborative networks within the UK and US national boundary were forming only since the 1990s. Subsequently, from 1997, we observed also the rise of the European network of collaborations initially involving Germany, France, The Netherlands, and UK and then including other countries such as Italy and Spain.

Building on these crosscuttings on the geographical and social spaces, one can focus more attention on the social dynamics by looking at the structure of the web of relationships composing the network at a lower level of analysis as the organisation-level. The network can be explored with algorithms that identify cohesive groups of organisations as well as public and private players occupying key positions (e.g. the Kamada & Kawai (1989) algorithm) – in this regard, the network analysis provides a broad range of measures (e.g. centrality, constraint, k-core) (Wassermann and Faust, 1994). For example, the lower part of Figure 4 depicts the organisational collaborative networks corresponding to the aforementioned collaborative networks overlaid on the geographical space.[7] While for HPV testing technology a giant component can be identified, the organisational network for the TPMT testing technology is

[7] Organisations' names included in publication data of ISI WoS present a number of variations, i.e. the same organisation may be spelled in different manners. We use The Vantage Point software to clean the data. This software specifically analyses and suggests groups of names that may refer to the same organisation by using a fuzzy algorithm that exploits also the information included in other fields of the publication data. We checked those suggestions for our sample of publications and confirmed those matches for which the manual desktop search over the Internet provided further support. Freeware routines for using institutional addresses but without this cleaning process can be retrieved at http://www.leydesdorff.maps.

highly fragmented, as revealed by the different separated groups of organisations (components), until the last five years of observation (see Table 2). For clarity of the representation, Figure 4 depicts the largest component for HPV testing technology for 2002-2006 period. We instead represented for the TPMT testing technology the strong components - i.e. groups of at least four organisations - for the same period of observation. We reported labels for the top 5% central organisations in those networks - we used the degree centrality measure (Freeman, 1979). As for the previously discussed maps, the size of each node is proportional to the logarithm of the number of scientific articles (plus one) that a given organisation published in the given time window.[8]

The evolutionary dynamics of the collaborative network surrounding the research activity on HPV testing technology show Digene occupying a strong and influential position within this network by collaborating with the main institutions in the field involved in the regulation of the cervical cancer screening (e.g. National Cancer Institute, Kaiser Permanente). This eventually allowed Digene to influence the regulation process, as the definition of medical guideline, for the adoption of the HPV test in adjunct to the Pap test for the screening program (Hogarth et al., 2012). In other words, while Digene's activity was 'regulated', Digene was affecting the developments and dynamics in cervical cancer screening. As discussed, the co-authorship network for TPMT testing technology is characterized by the presence of several separate components for a large part of the observation period. The network seems to develop around two distinct relationships, i.e. the collaborations between Mayo Clinic and University of Sheffield as well as between St. Jude Children's Research Hospital and University of Tennessee. These relationships are established since the initial observed years and, especially the latter, reinforces over time as revealed by the number of co-authored publications. These two key relationships seem to act as catalysers for the further development of the network. A variety of actors started to collaborate with the aforementioned four organisations creating two distinct components in the network. In the last five of observation (2007-2011), these two component however merged in a larger component involving other key players in the TPMT domain such as University of Manchester, Stanford University, and Dr Margarete Fischer Bosch Institute - a large research foundation working on the customization and improvement of drug therapy.

In other words, these mapping approaches allow exploring the evolutionary dynamics of ESTs by combining the geographical and social spaces of emergences and by moving across

[8] The network analysis and visualizations were produced by using Pajek 3.10 (De Nooy et al., 2005)

units of analysis, in this case from the city- to the organisation-level.[9] The mapping can therefore inform on *de facto* governance in terms of the constellation of actors involved in the emergence process as well as on the structure of relationship among these actors and - for instance, key actors and collaborations shaping the emergence or main channels connecting critical geographical clusters for the given ESTs can be revealed. As discussed, these approaches provide perspectives that can both answer to and posit additional questions, which in turn may drive the investigation of the tentative governance of ESTs.

Insert Figure 4 and Table 2 about here.

3.3. *De Facto* Governance in the Cognitive Space

As a new science and technology emerges, epistemic developments occur in terms of discoveries, novel theories, or changes in technical developments such as experimental systems, materials, methods and instrumentation (Rheinberger, 1997; Joerges and Shinn, 2002). As discussed, these dynamics can be traced across the cognitive space by creating overlays of publications on basemaps of science that can be defined at different levels of analysis (e.g. Klavans and Boyack, 2009; Waltman and van Eck, 2012; Leydesdorff et al., 2013). The publishing activity related to three case studies can be, for instance, projected across the map of science defined by the 225 WoS Categories (WCs) (Leydesdorff et al., 2013). In this map, each node is a WCs and its size is proportional to the number of publications assigned to the given WC the node represents. The different colours of nodes represent different clusters of disciplines - Leydesdorff et al. (2013) identified 19 macro-disciplinary areas. Figure 5 depicts the projections of publications related to the three case studies. We reported the map representing the structure of science (left) - the strength of each linkage is proportional to the extent to which the two WCs cite each other - and the heatmap version (right).[10] This combination provides an intuitive visualisation of the diffusion process of ESTs.[11]

As for the previous analyses, we used overlays projecting the publishing activity according to 5-year time windows. While these maps show the rapid diffusion of RNAi technology across many disciplines such as molecular biology, oncology, biomedical research, and chemistry, the overlays of the HPV and TPMT testing technologies reveal different directions of diffusion. The

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[9] Additional interactions across this space can be traced at different level of analysis - e.g. individual researchers, communities, disciplines - and by using additional databases - e.g. co-invention, inter-organisational alliances data.
[10] The visualizations of cognitive maps were produced by using VOSviewer 1.5.4 (Eck and Waltman, 2010).
[11] The animations of the different cognitive maps are available on the Internet as supplementary materials http://www.interdisciplinaryscience.net/defactogov.

HPV testing technology diffuses from basic research in oncology, pathology, and virology disciplines towards issues related to the public health. We interpret this evolutionary dynamic as a representation of the extensive and ongoing debate on the practices adopted for the screening of population. The debate has been specifically focused on the adoption of the HPV testing technology as adjunct/substitute of the widely adopted Pap test (Hogarth et al., 2012). TPMP testing technology diffuses from the basic research in pharmacology towards gastroenterology and dermatology disciplines. The research activity seems to equally spread in gastroenterology and dermatology disciplines during the 1992-1996 period. Yet, in the subsequent years, it shrinks from dermatology area while continuing to grow in gastroenterology. This can be interpreted as the results of the contested use of TPMT testing technology between the communities of gastroenterologists and dermatologists.

A similar cognitive perspective can be built by using a map of which nodes represent academic journals (Leydesdorff, Rafols, et al., in press). The map is specifically composed by 10,330 journals (nodes) - the different colours of nodes represent different cluster of journals, i.e. groups of journals of which the cross-citation patterns are similar. Figure 6, for instance, illustrates the rapid diffusion of RNAi across this map. The Rao-Stirling diversity index (Stirling, 2007), measured on the set of journals of the map, provides further evidence of this rapid diffusion, especially when the index is compared with the other two ESTs on which we focused our analysis - see the supplementary materials for the overlays of the HPV and TPTM testing technologies.

Insert Figure 5 and 6 about here.

Perspectives on the cognitive dynamics can be also built by using MeSH terms - terms used to characterise the content of scientific articles in life science. These terms are assigned to articles in MEDLINE/PubMed through an intensive indexing process that is performed by examiners at the National Institute of Health (NIH). The terms are organised in a 16-branch tree which can reach up to 12 levels of depth.[12] Drawing from this classification, Leydesdorff et al. (2012) developed a MeSH map on three branches - i.e. "Diseases", "Chemicals and Drugs", and "Analytical, Diagnostics and Therapeutic Techniques and Equipment" - and on the first two levels of tree. The map is specifically composed by 822 MeSH terms (nodes) of which linkages

[12] The 16 branches of the MeSH tree are: "Anatomy", "Organisms", "Diseases", "Chemical and Drugs", "Analytical, Diagnostics and Therapeutic Techniques and Equipment", "Psychiatry and Psychology", "Phenomena and Processes", "Disciplines and Occupations", "Anthropology, Education, Sociology and Social Phenomena", "Technology, Industry and Agriculture", "Humanities", "Information Science", "Named Groups", "Health Care", "Publication Characteristics", and "Geographicals".

reflect the (cosine) similarity according to co-occurrence of these terms in scientific articles. Each branch is marked on the map with a different colour – "Disease" is red, "Chemicals and Drug" is green, and "Analytical, Diagnostics and Therapeutic Techniques and Equipment" is blue (see Figure 7). Similarly to previous approaches, the publishing activity characterising a given EST can be projected on this map - the size of the nodes is proportional to number of publications assigned to the given MeSH term - to trace dynamics across three branches of the MeSH tree.

This approach, applied to the three case studies, revealed different evolutionary dynamics in this cognitive space. RNAi, in line with previous results, rapidly globalizes across the set of the MeSH terms thus affecting many areas of the three represented branches. On the contrary, HPV testing technology diffuses from "Diseases" branch, specifically from "Tumor Virus Infections", in the "Analytical, Diagnostics and Therapeutic Techniques and Equipment" branch and eventually across the "Chemicals and Drugs" area. Yet, interestingly, in the last time window (2007-2011 period) scientific articles on HPV testing technologies concentrate in the techniques and equipment area. This may reflect the efforts in developing competing HPV testing technologies. On the other hand, results show a specialisation of the TPMT case study in specific areas of the maps. This result is in line with the scale of TPMT testing technology that is limited to a narrow domain of application.

Mapping the patenting activity of ESTs provides additional and different perspectives on the cognitive dynamics of the emergence process given the diverse incentives featuring in the creation process of scientific articles and patents (Dasgupta and David, 1994; Murray, 2002). Scientometricians have developed techniques also to trace the dynamics of the patenting activities (e.g. Newman et al., 2011; Schoen et al., 2012). The nodes of these maps are technological classes that, as for previously maps, are linked by cross-citation (cosine) similarity (Leydesdorff, Kushnir, et al., in press). Figure 8, for example, depicts the overlays of RNAi patenting activity on the patent map based on technological areas as defined by the International Patent Classification (IPC). One can trace the dynamics in this space by moving across different levels of the classification (e.g. 3-digit, 4-digit). Contrarily from the perspectives built by using publication data, the patent map visualisation revealed a different dynamics for the RNAi. While this EST seems to spread in many technological areas between 2002 and 2006, the last five years of patenting activity show an increase specialisation in certain areas of the technological space as biochemistry, organic chemistry, and medical science. We provided the patents maps for HPV and TPMT testing technologies in the supplementary materials. It is worth noting that small samples of patent data tend to weaken the consistency of this map since the nature - see for

instance the first time windows for of the two case studies. We therefore advice to interpret the results of the mapping in this conditions carefully.

In summary mapping and overlay techniques applied to the cognitive space of the emergence may inform on several facets of the *de facto* governance. One can trace the directions of diffusion of the given EST across a number of domains - as identified, for instance, by the different classification systems. This, for example, may support the investigation process by identifying the key knowledge areas involved in the emergence process as well as how these areas integrate or misalign. Key actors in the knowledge creation process can be also revealed, traced, and investigated in their behaviour. This may enrich the information and details on the process of emergence to support policy analysts and makers in the designing of forms of governed that are tentative.

Insert Figure 7 and 8 about here.

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4. DISCUSSION

In a tentative governance approach, the actors that engage in technology development are aware of being in a situation of very incomplete knowledge: it is unclear what the technology is, in which direction it is moving, and how it should move forward. In the face of uncertainty, ambiguity, and ignorance (Stirling and Scoones, 2009), the emergence process should be investigated and analysed from various perspectives. In this article, we have presented at a variety of mapping approaches that may guide in the understanding of the complexity of the emergence process in terms of (geographical, social, and cognitive) positions and relations among various aspects of the technology. Yet, the informative and interpretative power of the mapping and overlay techniques discussed relies on the set of choices one makes - some choices that may seem eminently technical (e.g. level of aggregation) have also important implications for the type of patterns one can observe.

As discussed previously, a key preliminary choice is to identify the boundary of ESTs - i.e., the delineation of the corpus. Deciding what to include and what to exclude in the analysis is always a problematic exercise in the case of emergent sciences and technologies. In the case of RNA interference, for example, one delineation portrayed this technology as already having achieved the mature phase, whereas a broader definition portrayed it as still quickly growing (Figure 1).

Having defined the technology, a second choice is about the type of databases selected. It is clear that using bibliographic data from publications and patents or firm alliance data yields

different types of information. A third choice is about the elements to be analysed from the records of the databases. From a patent record, for instance, one can extract information about inventors, firms, technology classes, or location, which, as discussed, provide insights on the social, cognitive or geographical spaces of emergence, respectively. A fourth choice is about the categories into which the elements are assigned. In the case of categories one needs to decide the level of aggregation (the granularity of the description) as well as the type of classification - i.e., whether a predetermined, top-down typology or an emerging, bottom-up taxonomy.

The choices of database, elements and categories ought to be informed by conceptual and theoretical frameworks that suggest why taking some perspective can be more fruitful than others for the understanding of tentative governance of ESTs. However, from a policy analyst's standpoint, it may be also critical to monitor the technology emergence in the lack of an explicit understanding of conceptual framework used. In these cases, the analytical perspective is implicitly building a conceptual framework, since the choice of certain elements and categories is privileging certain understanding over others. For example, looking at collaborative networks of individual scientists may place more attention on the social capital as a key factor in the emergence process (Nahapiet and Ghoshal, 1998; Adler and Kwon, 2002). If one looks at the disciplinary position of the technology it is likely to be assuming that integration of disparate knowledge is relevant as, for instance, it has been perceived to be the case of nanotechnologies (e.g. Schummer, 2004; Porter and Youtie, 2009) and in RNA interference (Leydesdorff and Rafols, 2011), but not necessarily in HPV or TPMT.

However, it is worth noting that in the lack of a clear understanding associated with tentative governance, it is wise to investigate the phenomenon by using several perspectives, because one does not know in advance which one may turn out to be useful for understanding the relations of the emergence in place, or because the area in which the action is occurring is shifting over time. Since many emerging technologies do not conform to established bodies of knowledge, they cut across pre-existing organisational and institutional units, challenging established managerial and policy practices. As a result, one key demand from policy-makers is a description of the types of interdisciplinarity or convergence in the emergence (Schmidt, 2007), often related with specific visions and expectations (Roco and Bainbridge, 2002; Beckert et al., 2007).

5. CONCLUSIONS

Our contribution to the theme of 'tentative governance' of ESTs is based on new scientometric techniques of using overlays to basemaps that can provide both overview and the possibility to focus by zooming in on specific developments and phenomena. These techniques function as a flexible toolbox that allows users to move from one database to another using the

same or a highly similar search string, and thus to generate surplus value in the recombination of different sources. A single representation of a highly non-linear process such as ESTs would be misleading since relevant contexts are then necessarily black-boxed.

In this article, we combined the various tools to map the emergence process in terms of two main baselines: the geographical and socio-cognitive diffusion. These baselines were specified as the main dimensions early in the scientometric project by Narin (1976) and Small & Garfield (1985). The geographical component was identified with nations and the socio-cognitive with journals and their classifications. The national dimension of this matrix enabled national S&T policies to compare and evaluate differentiating among disciplines (e.g. Martin and Irvine, 1983; Irvine et al., 1985; Moed et al., 1985). More recently, the perspective of social network analysis has added co-authorship/co-invention relations - or more generally, affiliations of co-occurrences - as a third source to the mapping (Otte and Rousseau, 2002; Newman, 2004; Persson et al., 2004; Wagner and Leydesdorff, 2005). Co-occurrence relations can be used to show structures (such as densities) on the geographical and socio-cognitive maps.

An analogous program of studies has been pursued in the case of patent analysis (Pavit, 1984; Jaffe, 1986). In this context, the geographical dimension is specified in terms of possible 'spill overs' and the cognitive classifiers are not the journals, but the patent classifications (Jaffe, 1989). Jaffe & Trajtenberg (2002) elaborated a full schema for analysing the patent system as a source for mapping the knowledge-based economy. A third major (and publicly available) database is provided by MEDLINE/PubMed of the NIH as the result of a yearly investment of approximately 100 MUS$/year to disclose information about R&D in the medical field. Both patents and publications allow for using citation rates as impact indicators; as discussed, the MEDLINE/PubMed database organizes data in terms of an elaborate system of MeSH terms that allow mapping innovations in terms of affiliations and recombination among "supply," "demand," and "infrastructural" factors (Leydesdorff et al., 2012).

The research efforts on the discussed mapping and overlay techniques in the last years can be considered as an attempt to help solving what Grilliches (1994) identified - even before the advent of the Internet - as the 'Computer Paradox' in the increasingly available 'big data': Measurement problems have become worse despite the increased availability of data and statistics because "the current statistical structure is badly spit, there is no central direction, and the funding is heavily politicized" (p. 14). Relating patents to publications in terms of "non-patent literature references," for example, requires professional skills and cannot be done on a large scale without substantive investments. For instance, while MEDLINE/PubMed was integrated with the *Science Citation Index* in the WoS, this interface does not allow for citation

analysis at a large scale (Leydesdorff and Opthof, in press). One is able to make cross-connections among these relevant databases, but case-wise - that is, in-depth and over time - and hitherto not transversally at the level of the files.

Tentative governance requires a functional instead of institutionally organized perspective. ESTs 'tumble' through the databases in terms of their representations with different attributes such as geographical addresses, patent classes, etc., retained and organized in different contexts. A multi-perspective approach is needed that adds flexibility to the institutionalized perspectives of the databases. The possibility of such a multi-perspective approach is intended and anticipated by the MeSH tree structure that allows for hierarchical searching from different (orthogonal) perspectives, but does not provide the oversight of a map. The map enables the user to compare different technologies and alternatives in terms of strengths and weaknesses at the portfolio level. For example, when the exploitation of a technology is oligopolistic and concentrated at a few places with major players entertaining sets of co-authorship and co-inventor relationships with specific university centres, then the road of access for newcomers who may be able to publish and patent about alternative technologies or variants of existing technologies is predictably different at the publishing or the patenting end. In the case of RNAi, for example, two research centres in the UK and Israel launched the EST, but one can follow how the latter moves to metropolitan cities such as Boston, London, and Seoul during the 1980s. These 'centres of excellence' become the preferential loci of attachment for newcomers to the field. Despite the structure of intellectual property control that two of these oligopolistic centres (Boston and Munich) attempt to organize, the economic dimension evolves during the 1990s and early 2000s increasingly in monopolistic centres such as in Denver, Colorado. On this journey of the EST, the epistemology of the science-technology also changes, first from an explorative and science-based innovation into a 'movable immutable' (Latour, 1987) that can be imported as a laboratory asset in other specialties and disciplines, and then also exported from science into the economy.

Mergers and acquisitions add another dimension that was not yet sufficiently explored in this study. Mergers and acquisitions, however, are not specific to the 'knowledge-based' economy. Governments have instruments (such as Statistics Offices) that organize this data from the perspective of a political economy. The long-term program is to endogenise the diffusion of knowledge produced in the techno-sciences into these statistics using relational database management. For the purpose of tentative government, however, relational database tables are too abstract, whereas their representations in terms of maps do not overload the user with information. Informed base maps have to be stabilized so that one can animate overlays over

time. The maps and animations do not provide answers, but instruments to inform the political discourse about stumbling blocks ahead and possible openings in the landscape.

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FIGURES

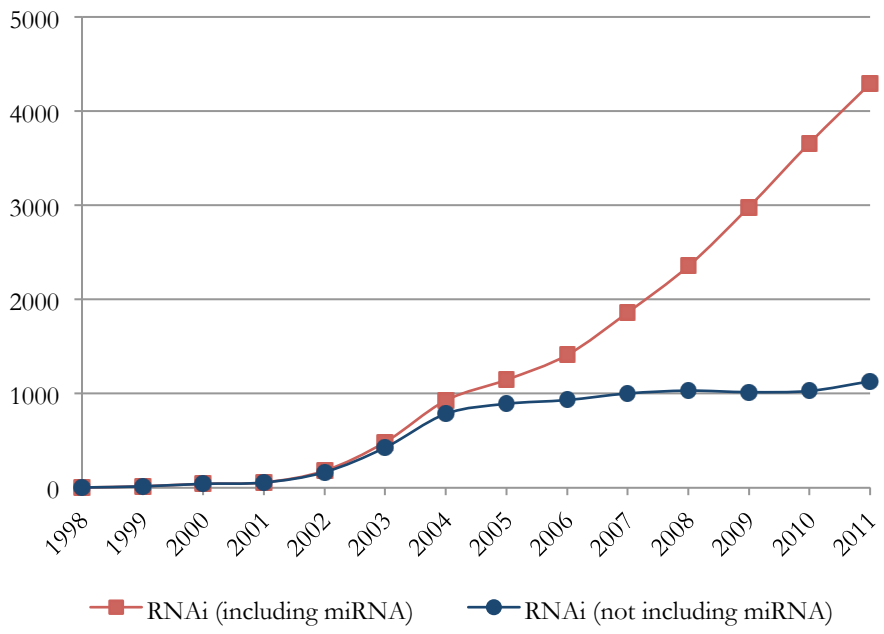


Figure 1. The delineation issues of RNAi.

Figure 2. Centres of excellence (based on top 10% cited scientific articles).

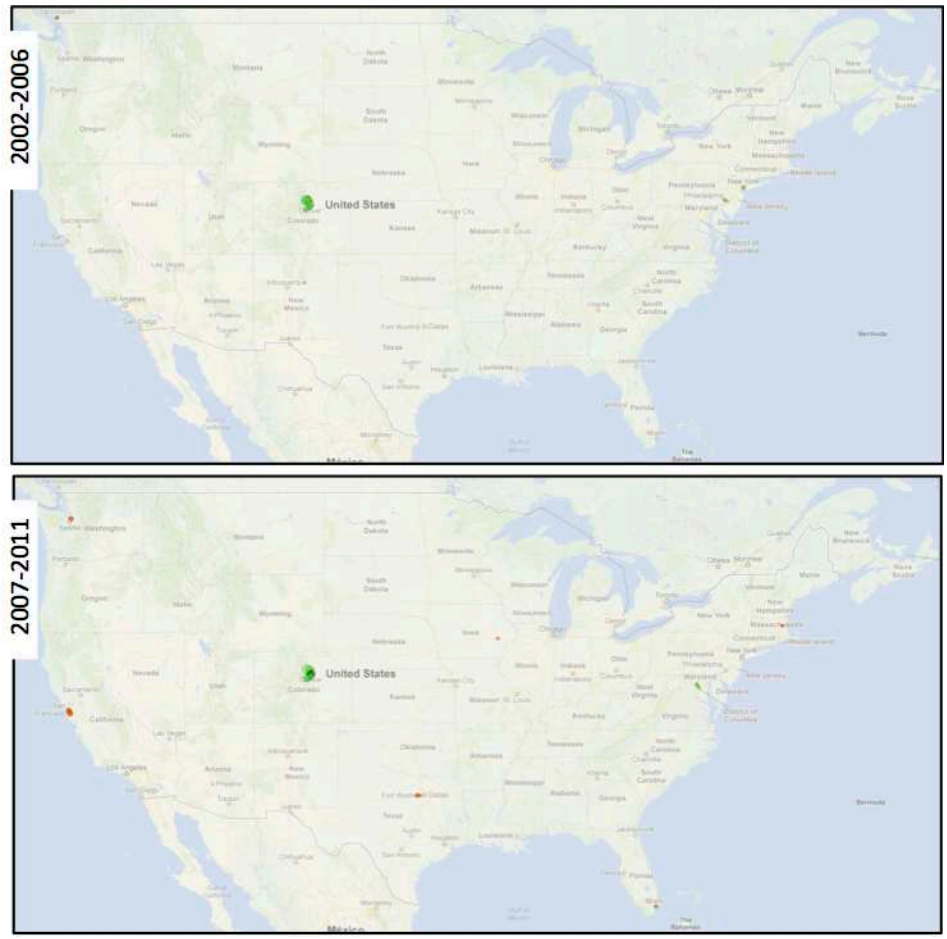


Figure 3. Centres of excellence for RNAi (based on top 25% cited patents).

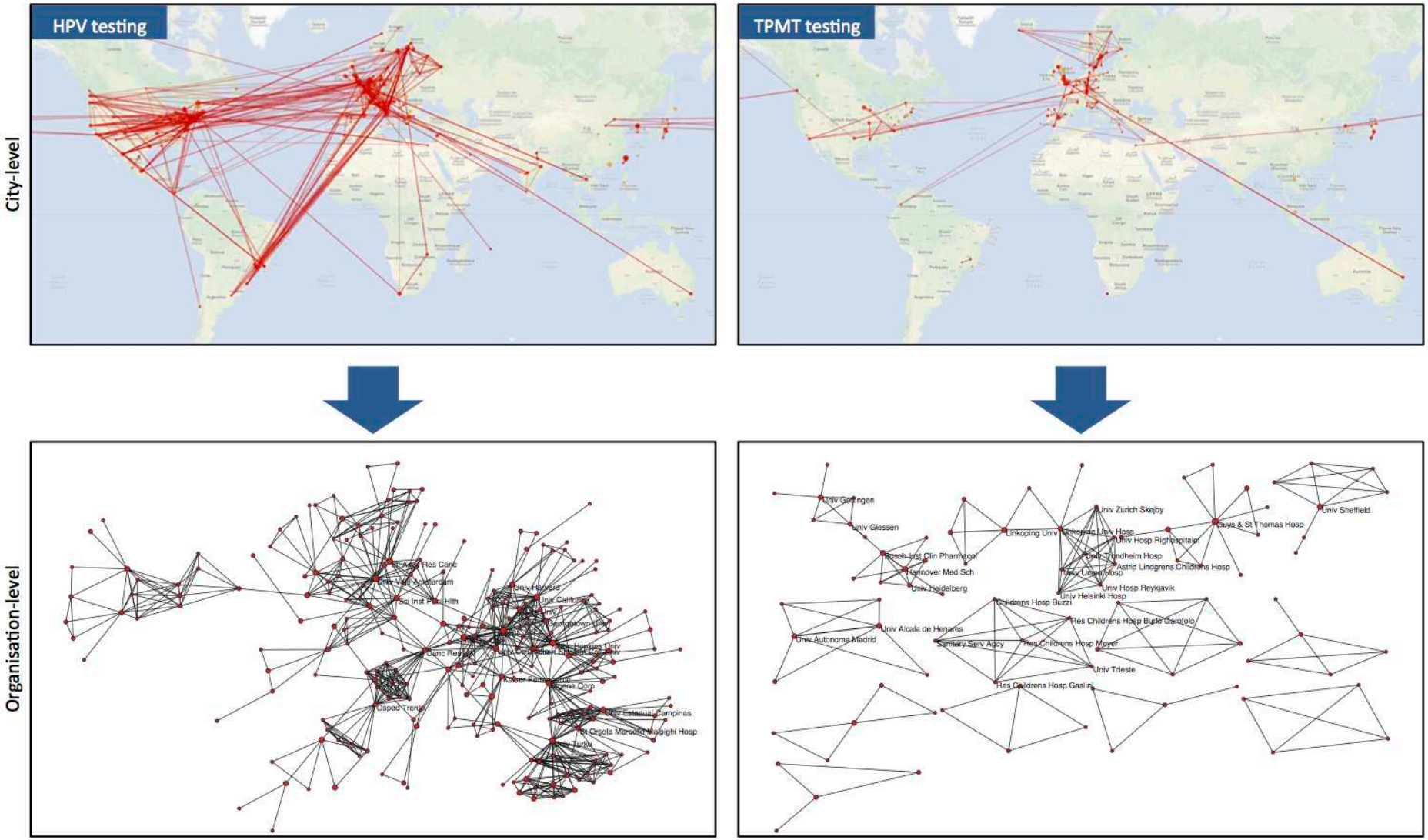


Figure 4. Crosscuttings on the geographical and social spaces of the emergence process (2002-2006 period).

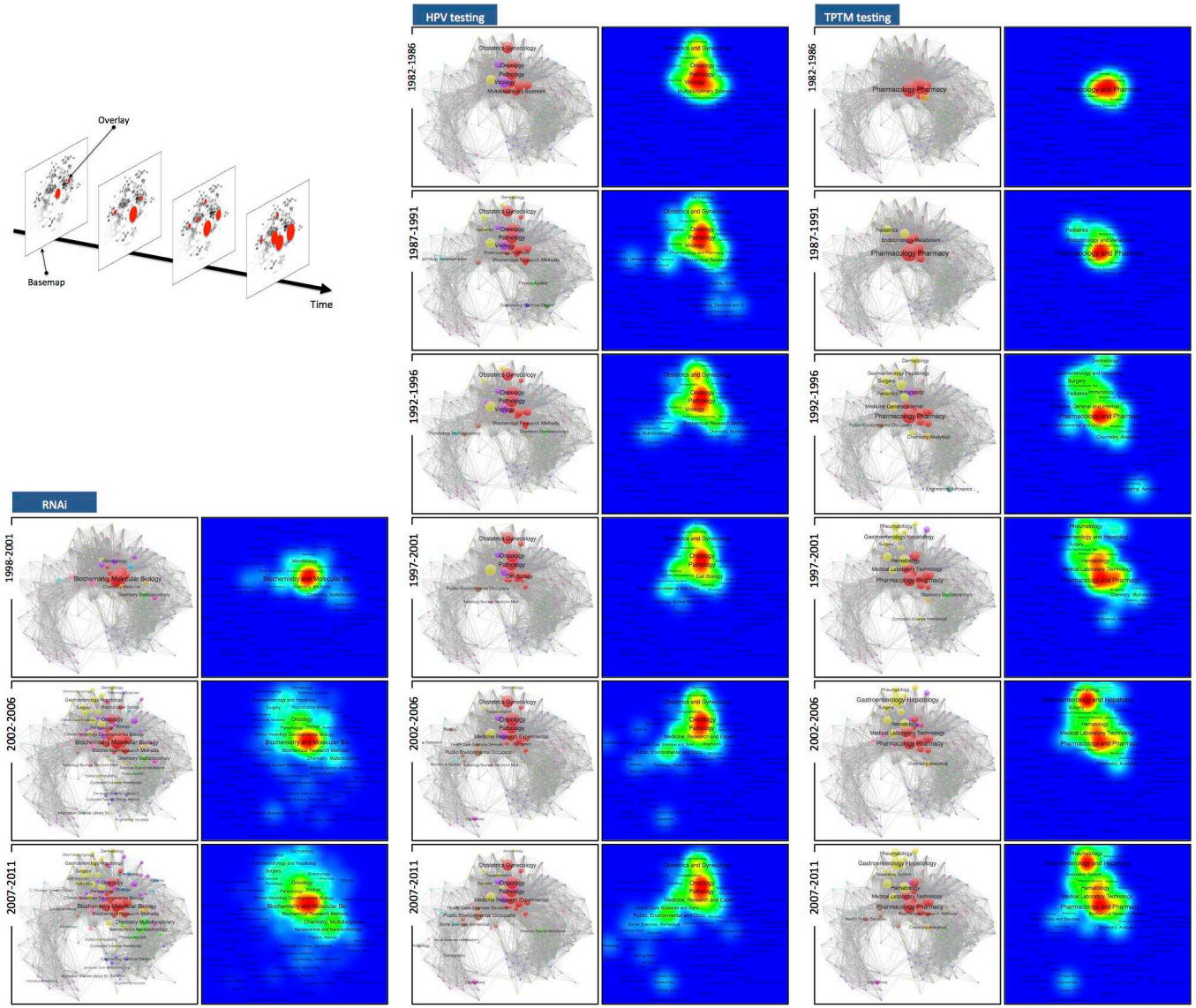


Figure 5. Case studies: overlay of publishing activity across the map of science.

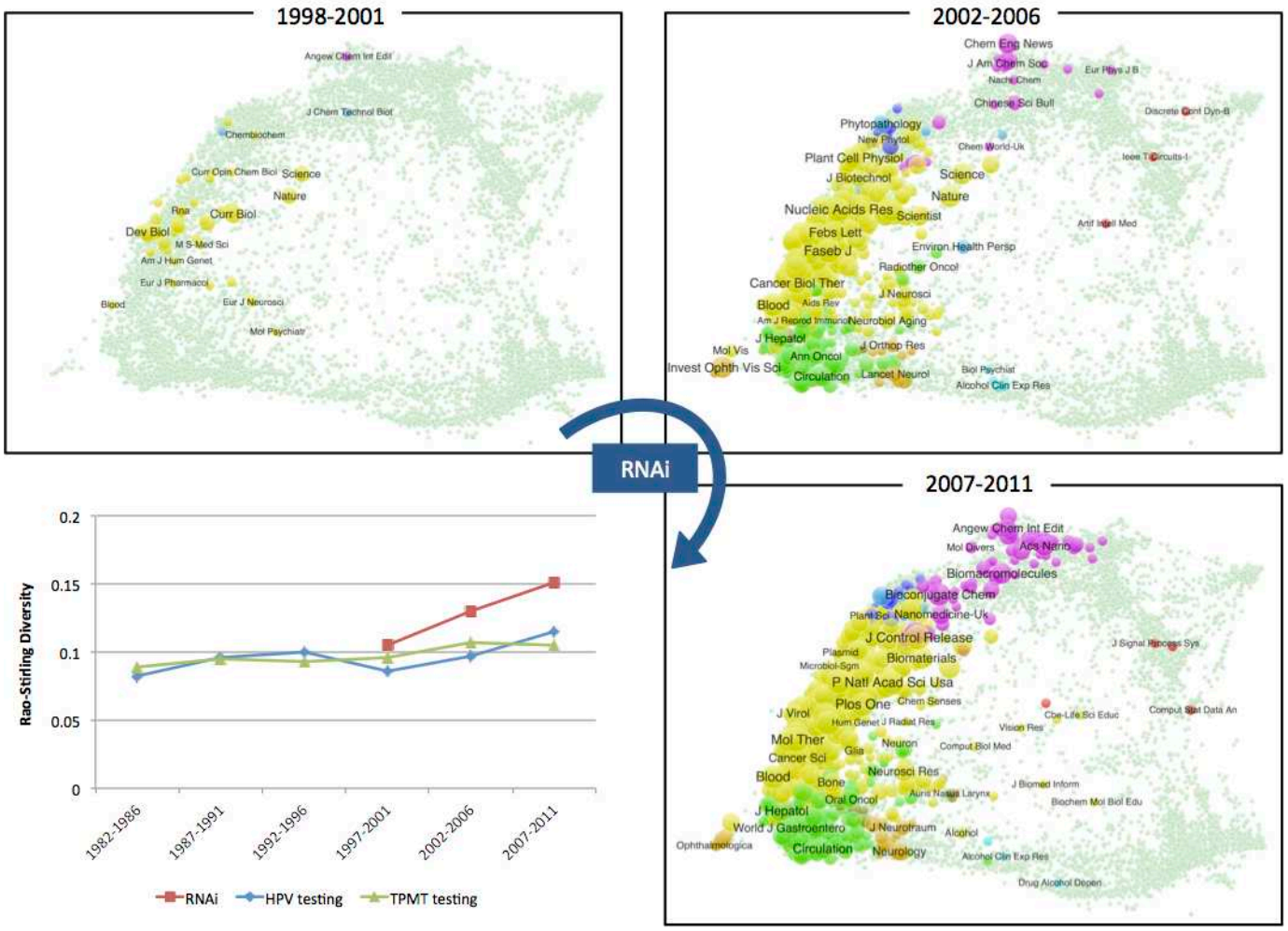


Figure 6. Journal map for RNAi and diversity index (Rao-Stirling diversity).

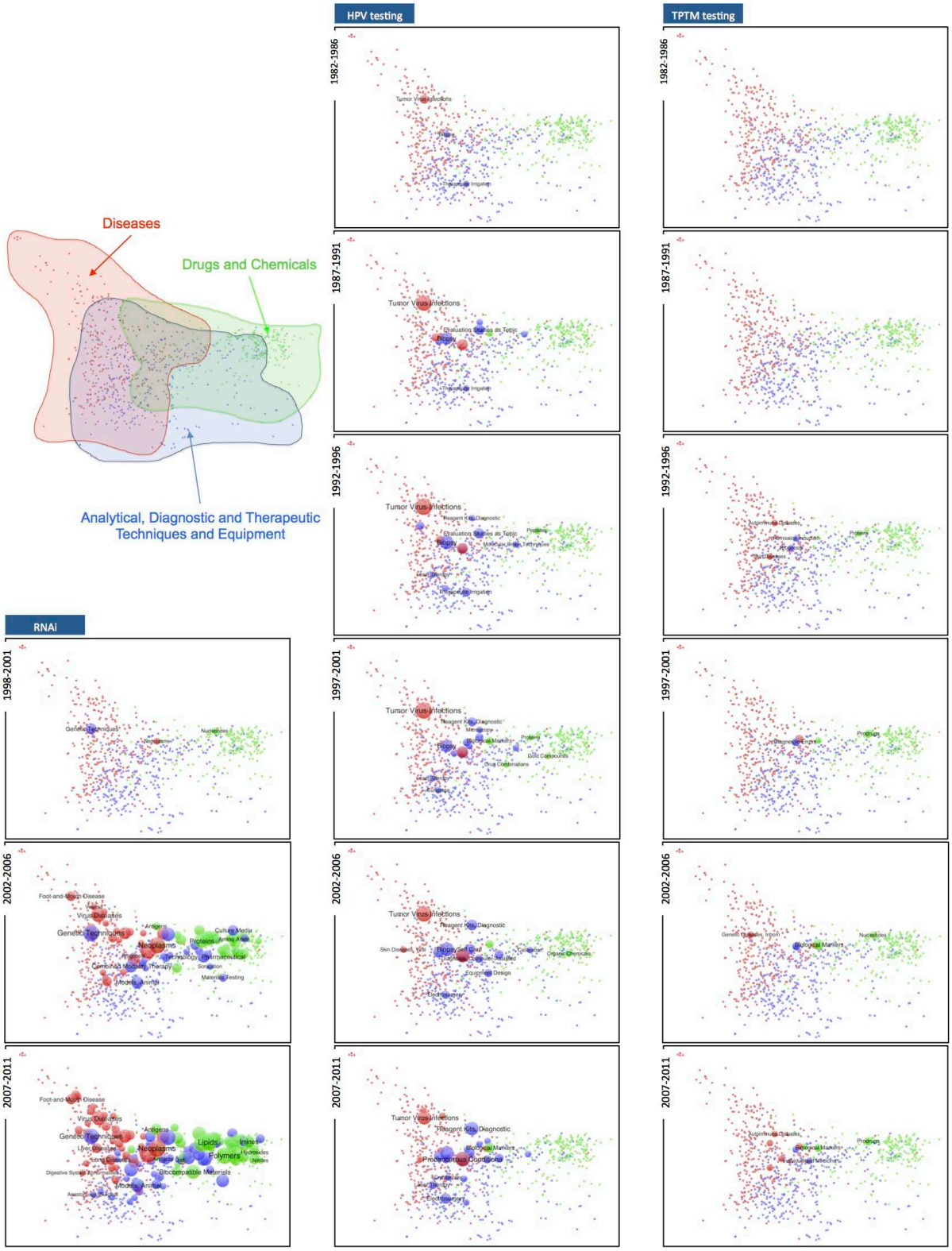


Figure 7. Case studies: overlay of publishing activity across the map of MeSH terms.

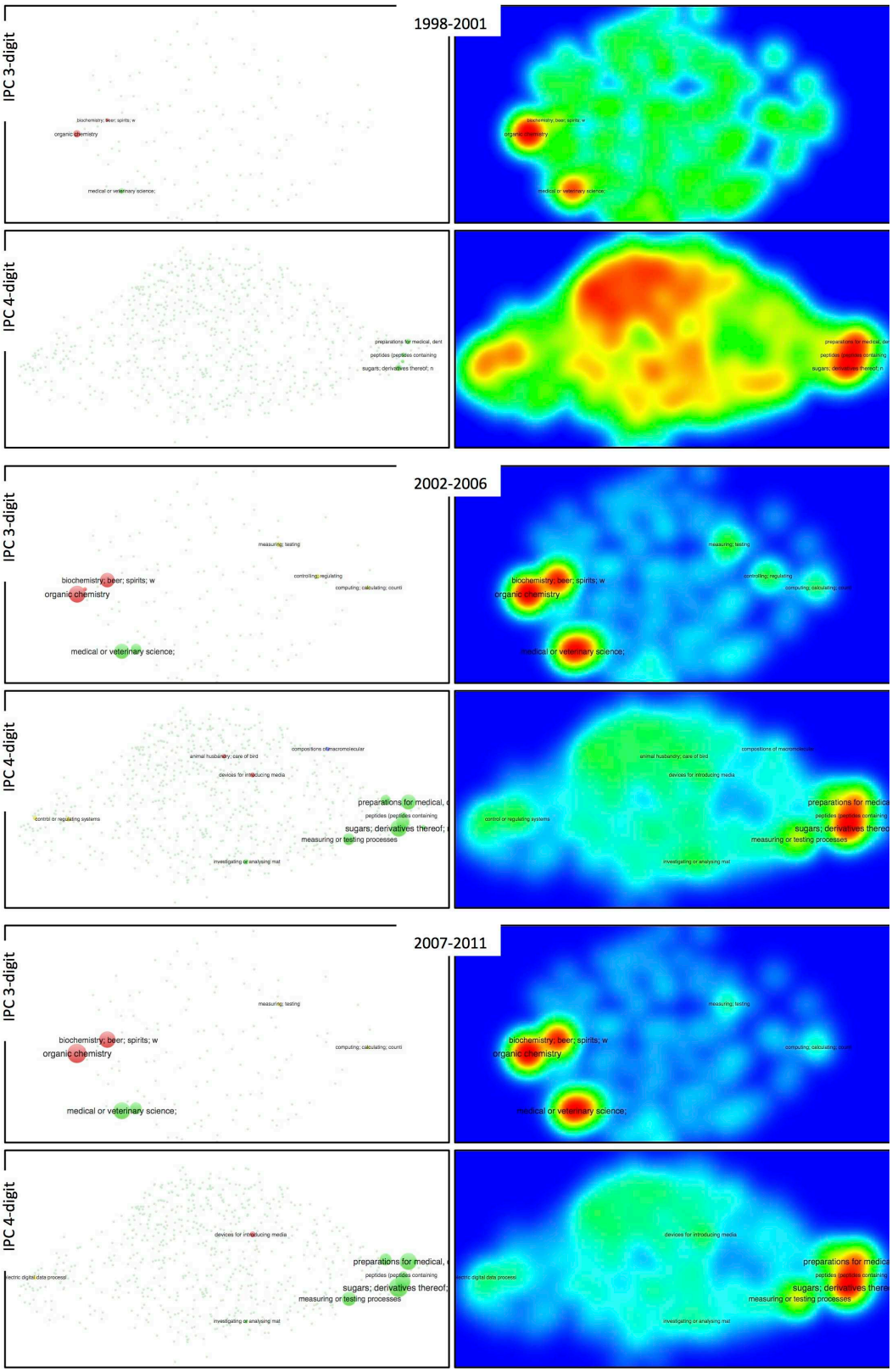


Figure 8. Patent map for RNAi (IPC–based).

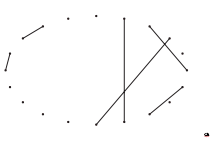
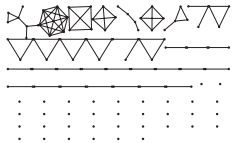
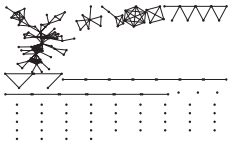
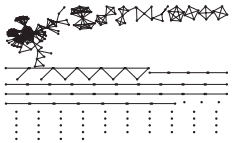
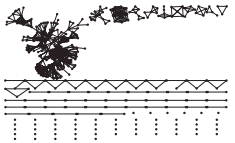
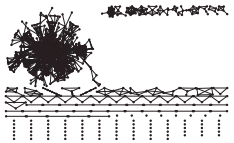
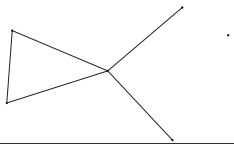
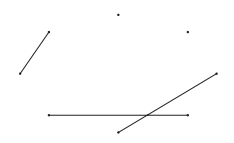
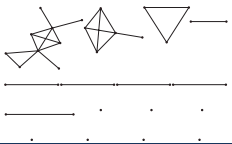
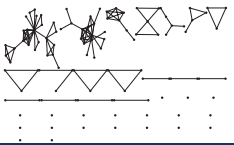
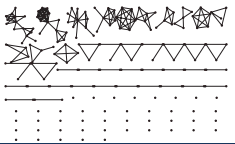
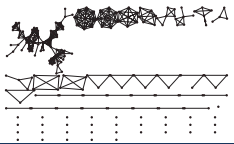
TABLES

Table 1. Publication and patent data (1982-2011).

Year	RNAi				HPV testing				TPMT testing			
	ISI WoS	MEDLINE PubMed	USPTO (granted)	USPTO (applications)	ISI WoS	MEDLINE PubMed	USPTO (granted)	USPTO (applications)	ISI WoS	MEDLINE PubMed	USPTO (granted)	USPTO (applications)
1982	-	-	-	-	0	0	0	0	3	2	0	0
1983	-	-	-	-	2	1	0	0	2	0	0	0
1984	-	-	-	-	0	0	0	0	0	2	0	0
1985	-	-	-	-	4	2	0	0	3	2	0	0
1986	-	-	-	-	12	10	0	0	5	1	0	0
1987	-	-	-	-	22	14	4	0	5	4	0	0
1988	-	-	-	-	17	16	0	0	2	0	0	0
1989	-	-	-	-	30	24	3	0	1	1	0	0
1990	-	-	-	-	32	28	0	0	2	2	0	0
1991	-	-	-	-	36	31	1	0	6	5	0	0
1992	-	-	-	-	41	49	2	0	5	5	0	0
1993	-	-	-	-	18	27	1	0	11	9	0	0
1994	-	-	-	-	29	30	4	0	8	5	1	0
1995	-	-	-	-	24	28	5	0	17	14	1	0
1996	-	-	-	-	35	32	1	0	11	8	0	0
1997	-	-	-	-	33	28	2	0	15	10	0	0
1998	3	2	1	0	37	33	1	0	20	15	1	0
1999	15	10	1	1	41	35	4	0	21	11	0	0
2000	42	33	4	1	43	41	4	0	24	15	0	0
2001	56	52	5	22	50	52	1	5	28	19	3	6
2002	166	126	25	113	54	43	2	13	43	25	1	2
2003	427	280	45	400	69	59	9	29	42	30	1	3
2004	785	523	83	685	59	59	8	19	36	23	1	2
2005	892	681	86	583	105	95	6	21	40	19	1	4
2006	932	782	124	684	94	86	3	24	39	28	2	6
2007	1002	737	131	752	121	91	6	16	30	15	0	1
2008	1032	827	106	772	134	106	5	21	26	15	4	9
2009	1016	837	118	767	154	120	5	33	43	30	0	1
2010	1029	904	89	761	121	99	0	18	24	19	0	2
2011	1131	969	35	410	143	118	0	11	28	16	0	5
Total	8528	6763	853	5951	1560	1357	77	210	540	350	16	41

Notes. Data were collected in January 2013. The data of USPTO patent applications are accessible since year 2001. The filing year of patents was considered.

Table 2. Structural properties of the co-authorship network at organisation-level.

	Time window					
	1982-1986	1987-1991	1992-1996	1997-2001	2002-2006	2007-2011
HPV testing technology						
Scientific articles	18	137	147	204	381	673
Nodes	20	130	173	265	471	816
Ties	6	88	223	476	980	2075
Components	0	7	5	10	10	25
Nodes in the giant component	0	7	62	83	239	504
	(0.00%)	(5.38%)	(35.83%)	(31.32%)	(50.74%)	(61.75%)
Isolated nodes	8	35	43	47	55	83
	(4.00%)	(26.92%)	(24.85%)	(17.73%)	(11.68%)	(10.17%)
						
TPTM testing technology						
Scientific articles	13	16	52	108	200	151
Nodes	6	8	36	111	200	232
Ties	5	3	28	123	203	413
Components	1	0	2	6	13	12
Nodes in the giant component	5	0	9	25	15	82
	(83.33%)	(0.00%)	(25.00%)	(22.52%)	(7.50%)	(35.34%)
Isolated nodes	1	2	7	19	43	33
	(16.67%)	(25.00%)	(19.44%)	(17.12%)	(21.50%)	(14.22%)
						

Notes. The minimum size of a component is set to four nodes. Percentage values are reported in parentheses. The networks were energized by using the Kamada Kawei algorithm.

APPENDIX

Table A1. Data sources and search strings.

Case Study	Data	Database	Search string
RNAi	Publications	ISI WoS	TI=siRNA or TI=RNAi or TI="RNA interference" or TI="interference RNA"
		MEDLINE/PubMed	siRNA[Title] or RNAi[Title] or "RNA interference"[Title] or "interference RNA" [Title]
	Patents	USPTO	ACLM/(siRNA or RNAi or "RNA interference" or "interference RNA")
HPV testing	Publications	ISI WoS	(TI=HPV* or TI="Human Papilloma Virus*" or TI="Human Papillomavirus*" or TI="Human Papilloma*virus*") and (TI=Cervical or TI=Cervix) and (TI=diagnos* or TI=test* or TI=assay or TI=detect* or TI=screen* or TI=predict*)
		MEDLINE/PubMed	(HPV*[Title] or "Human Papilloma Virus*"[Title] or "Human Papillomavirus*"[Title]) and (Cervical[Title] or Cervix[Title]) and (diagnos*[Title] or test*[Title] or assay[Title] or detect*[Title] or screen*[Title] or predict*[Title])
	Patents	USPTO	ACLM/((HPV or "Human Papilloma Virus$" or "Human Papillomavirus$") and (Cervical or Cervix) and (diagnos$ or test$ or assay or detect$ or screen$ or predict$))
TPMT testing	Publications	ISI WoS	TI=TPMT or TI= "Thiopurine Methyltransferase"
		MEDLINE/PubMed	TPMT[Title] or "Thiopurine Methyltransferase"[Title]
	Patents	USPTO	ACLM/(TPMT or "Thiopurine Methyltransferase")