Scope, Strategy and Structure: The Dynamics of Knowledge Networks in Medicine

Consoli, Davide and Ramlogan, Ronnie

Manchester Institute of Innovation Research (MIoIR), Manchester Business School, University of Manchester

15 January 2009

Working Paper Series

Scope, Strategy and Structure: The Dynamics of Knowledge Networks in Medicine

Davide Consoli
Ronnie Ramlogan

Manchester Business School Working Paper No 569

Manchester Business School

Manchester Business School
The University of Manchester
Booth Street West
Manchester M15 6PB

+44(0)161 306 1320
http://www.mbs.ac.uk/research/workingpapers/

ISSN 0954-7401

Author(s) and affiliation

Davide Consoli
Manchester Institute of Innovation Research
Manchester Business School
Harold Hankins Building
Booth Street West
Manchester M13 9QH
United Kingdom
davide.consoli@mbs.ac.uk

Ronnie Ramlogan
Manchester Institute of Innovation Research
Manchester Business School
Harold Hankins Building
Booth Street West
Manchester M13 9QH
United Kingdom
ronnie.ramlogan@manchester.ac.uk

Abstract
The objective of this paper is to analyse the dynamics of networks in which new knowledge emerges and through which it is exchanged. Our conjecture is that the structure of a network cannot be divorced from the dynamics of the knowledge underpinning its activities. In so doing we look beyond studies based on the assumption of exogenous networks and delve into the mechanisms that stimulate their creation and transformation. In the first part the paper adopts a functional perspective and views networks as constructs aimed at the coordination of knowledge; accordingly, network structure is an emerging property that reflects the employment of an agreed strategy to achieve a collective scope. In the second part these themes are articulated in relation to the dynamics of medical innovation and enriched by an empirical study on the long-term evolution of medical research in Ophthalmology. This exercise highlights the connection between changes in scientific and practical knowledge and the reconfigurations of the epistemic network over a forty-year period. By mapping different network structures we capture variety in the gateways of knowledge creation – that is, the network participants – as well as in the pathways – that is, the inter-organisational collaborations. Our goal is to analyse how these patterns of interaction emerge and transform over time.

Keywords
Innovation, Network analysis, Inter-organizational Relationships

How to quote or cite this document

Consoli, D and Ramlogan, R (2009). Scope, Strategy and Structure: The Dynamics of Knowledge Networks in Medicine. *Manchester Business School Working Paper, Number 569*, available: http://www.mbs.ac.uk/research/workingpapers/

Scope, strategy and structure:
the dynamics of knowledge networks in medicine

Davide Consoli[*]

Ronnie Ramlogan

Manchester Institute of Innovation Research (MIoIR), Manchester Business School
Harold Hankins Building - Booth Street West; Manchester M13 9QH (United Kingdom)
[davide.consoli@mbs.ac.uk, ronnie.ramlogan@manchester.ac.uk]

The objective of this paper is to analyse the dynamics of networks in which new knowledge emerges and through which it is exchanged. Our conjecture is that the structure of a network cannot be divorced from the dynamics of the knowledge underpinning its activities. In so doing we look beyond studies based on the assumption of exogenous networks and delve into the mechanisms that stimulate their creation and transformation. In the first part the paper adopts a functional perspective and views networks as constructs aimed at the coordination of knowledge; accordingly, network structure is an emerging property that reflects the employment of an agreed strategy to achieve a collective scope. In the second part these themes are articulated in relation to the dynamics of medical innovation and enriched by an empirical study on the long-term evolution of medical research in Ophthalmology. This exercise highlights the connection between changes in scientific and practical knowledge and the reconfigurations of the epistemic network over a forty-year period. By mapping different network structures we capture variety in the gateways of knowledge creation – that is, the network participants – as well as in the pathways – that is, the inter-organisational collaborations. Our goal is to analyse how these patterns of interaction emerge and transform over time.

KEYWORDS: Innovation, Network analysis, Inter-organizational Relationships

(*) = corresponding author

1. Introduction

The objective of this paper is to analyse the dynamics of networks within which new knowledge emerges and through which it is exchanged. Research on networks has grown remarkably in recent years and spanned boundaries across different levels of aggregation. By and large these works focus on the impact that networks' structures bear on their performance while questions such as which processes stimulate the emergence and transformation of networks received less attention. As many observe this view paints an arguably static picture of what is widely understood as a dynamic phenomenon.

Our conjecture is that the structure of a network cannot be divorced from the dynamics of the knowledge underpinning its activities. The paper therefore delves into issues of how and why network structures emerge and change, and addresses the following questions: how does new knowledge grow and diffuse in a community of agents? Which criteria regulate inclusion and exclusion from a network? What drives the emergence and transformation of typologies of relations within them? Such issues are relevant also for network performance and, specifically whether it is possible to detect and learn from patterns of successful coordination.

The paper takes a functional perspective and views networks as constructs aimed at the coordination of knowledge. Accordingly, network structure is an emerging property that reflects the employment of either an implicit or agreed strategy to achieve a collective scope. Networks do not exist outside a context of reference; rather, they are purposive responses to specific problems that no individual can solve in isolation. As will be argued below, the patterns within – e.g. the position of individual agents and the way in which ties are arranged – are path-dependent properties, that is, contingent to the evolution of the network over time.

The framework proposed here contributes the existing literature on two counts. First, it suggests a structural association among three inseparable elements: the scope for which a network exists; the strategy to pursue it; and the structures that emerge as a result of the former two. In so doing the paper moves beyond studies based on the assumption of exogenous networks and delves into the mechanisms which stimulate their creation and transformation. Secondly, it indicates an empirical strategy based on longitudinal data analysis that is better suited to capture the evolution of networks over time. The paper presents an empirical study on the long-term evolution of medical scientific research in ophthalmology using a unique longitudinal dataset of bibliographic information of over 13,000 scientific articles about glaucoma over the period 1945 to 2003. The goal of this empirical exercise is to correlate changes in the scientific knowledge of glaucoma and those observed in the structure of the epistemic network. In particular we show that shifts in understanding of the causes of glaucoma map onto reconfigurations of the scientific network over the forty-year period. By mapping different structures we capture growing variety in the scientific knowledge base by analysing the long-term reorganisation of medical research. Our goal is to understand how these patterns of interaction emerge, take root, and transform.

The paper is structured as follows. Section 2 reviews critically key issues and conceptual approaches to network analysis; Section 3 connects network structures with the dynamics of knowledge. The latter thread is articulated in relation to the specific issue of medical innovation in Section 4 and analysed empirically in Section 5 with a case study on medical research on Glaucoma. The last section summarises and concludes.

2. Network structure and network dynamics

The literatures on business economics and management are replete with theories and empirical studies that, more or less implicitly, concur in claiming that the growth of knowledge is a major thrust of economic development. Therein strong emphasis is placed on the distributed nature of knowledge-related activities and the interdependence between individual and collective action. Innovation scholars, in particular, have repeatedly spelled out the benefits of collaborative agreements that facilitate the incorporation of knowledge from multiple sources (Antonelli, 2001; Langlois, 2001; Nelson, 2003; Garud and Karnoe, 2003). Periodically innovation research has crossed path with studies on the analysis of networks, a body of work that has been developing for more than three decades. A full survey of the literature on networks is clearly beyond the scope of this paper but let us point out a few issues of interest in this expanding area of investigation.

Beginning in the 1970s a number of scholars observed that under specific circumstances the coordination of collective action yields individuals higher benefits than if they operated in isolation. Since the early days the key research question concerned the impact of social relations, in particular their organization, and on knowledge circulation. This has been articulated in a variety of contexts such as weak ties (Granovetter, 1973 and 1983); network centrality (Freeman, 1979); alternative exchange partners (Cook and Emerson, 1978); structural holes (Burt, 1992); the relation between technological location and alliance strategies (Stuart, 1998); and the role of status (Lin et al., 1981), to name but a few. During the 1980s theories on networks surfaced also among economists, the objective being the analysis of incentives and outcomes of strategic interactions among firms (Economides, 1996; Shy, 2001). By and large these models portray networks as operating in a kind of institutional vacuum; as the standard tenet has it, the activities in which they engage – that is the structure of production and the techniques employed– are given and unchanging. This contrasts with the view proffered by organizational scholars who stress the influence of institutional embeddedness and social relationships on the formation of networks and coalitions (Weick 1979; Fleming 2001; Murray and O'Mahony, 2007). A frequent criticism among organizational theorists is that the scope of existing studies is to predict the correspondence between network structures and performance; in so doing, it is claimed, the literature oversees the longitudinal character of network dynamics. As Powell et al (2005) remark, save some exceptions (e.g. Ahuja, 2000; Gulati, 1995; Soda et al 2004; Rosenkopf and Padula, 2008)), few concentrate explicitly on network evolution.

The crucial point is that a large portion of this literature operates under the assumption that knowledge spreads according to the tenet proffered by classic diffusion models; as a result the processes that mould the creation and the exchange of knowledge are ignored, and the implicit conjecture is that networks exist *de ipso facto*. Such research foundations entail two important drawbacks. First, taking relations across actors for granted lead to disregard the existence of search and communication activities. A second important downside is methodological. Put bluntly, the assumption of exogenous network structures does away with history; we may well learn about what a network looks like at a certain point in time but we are no closer to make sense of the processes that mould those structures. Combined together these non-trivial matters lead to the paradox of a static understanding of an essentially dynamic phenomenon. If however one accepts that network structures are endogenous and undergo transformations as the collective scope changes and the strategy to pursue it evolves (Gulati and Gargiulo, 1999; Madhavan et al, 1998; Suitor et al, 1997), the extant view has obvious limitations.

This paper builds on and expands the notion that network outcomes are endogenous outcomes of changing patterns of relationships (Powell et al, 1996; Soda et al, 2004). Our conjecture is that the structure of a network cannot be divorced from the dynamics of the knowledge that underpins it: the scope of a network and the capabilities necessary to achieve it are therefore inseparable aspects. Accordingly different network structures reflect the combination of specific competences as dictated by the accepted perception of the scope and the strategy. Therefore it is essential to understand not just what collective structures look like but how they got there and, more to the point, which particular problems defined the scope over time; which strategies have been adopted as a consequence; and, finally, which structures emerged as a result of the growth and the application of new knowledge. Compared with previous works, the implications of the proposed approach are twofold: conceptually, a shift of emphasis from the study of given relations to an assessment of the mechanisms that encourage or constrain the creation of relations across actors; methodologically, a call for alternative modeling strategies that capture and make sense of the inherent variety that characterise the changing knowledge bases of networks.

3. Knowledge Networks: scope, strategy and structure over time

Let us offer a definition that straddles theoretical and empirical grounds: networks are structures for the organization of knowledge. Our analysis seeks to articulate three complementary dimensions of networks: the *scope* for which a network exists – which is associated to the emergence of a problem; the definition of a *strategy*, that is, the set of formal and informal rules and practices engaged to achieve the goal; and the *structure* – viz. practical arrangements that regulate the engagement of resources and activities.

A first-order question is: what stimulates the emergence of a network? We adopt a functional approach and argue that networks are purposive responses to specific problems that no individual can solve in isolation. In practice networks imply the achievement of consensus, the implementation of resources and the coordination of activities (Grandori, 2001; Grandori and Soda 2004). This problem-based view fits well the characteristics of networks that are commonly observed across a wide range of contexts. Banking firms adhering to credit card schemes; medical doctors working in hospitals; scholars participating to scientific research: these collective organisations exist because the individuals within them share a common purpose. In pursuit of the latter individuals provide tangible or intangible resources and respond, either formally or informally, to collective rules.

A second-order question is: what drives the transformation of a network structure? The emergence of either limitations in the accepted solution or of new problems challenges the status quo and triggers a search process. Accordingly, new resources are sought and activities are re-organised: our conjecture is that changes in their configuration cannot be divorced from the changes in the knowledge base. More to the point, knowledge is an enabling process as well as a selection mechanism for networks.

The growth of knowledge is rarely, if ever, the outcome of isolated action but rather of collective learning and cumulative interactions. On the one hand, the development of tacit knowledge moulds individuals' responses and is a source for new ideas and solutions; on the other, codified and practical knowledge are crucial to facilitate exchange and interactions across individuals. Contrary to the common view that these dimensions are dichotomic, we stress their complementary aspects: new knowledge grows as a result of coordination across individual experiences and the development of shared understanding. At the same time, however, variety and heterogeneity are not sufficient to replenish the knowledge base, and individual specialization is most effective when coordinated through formal and informal standards (Prahalad and Hamel, 1990; Langlois, 2001; Antonelli, 2008). Accordingly, our conjecture is that an *ecology* of agents, such as that discussed thus far, becomes a *system* only when we account for the creation and evolution of connections across those agents (Metcalfe et al, 2005).

The collective character of knowledge entails two important properties. First, the process is path-dependent in the sense that it is defined and, thus, constrained by specific technical and procedural choices that are adopted as problems emerge and solutions are sought. Secondly, and related to the former, knowledge growth is an essentially uncertain process. Let us recall the foundationalist interpretation of Metcalfe and Ramlogan (2005): economic agents are boundedly rational and generate and exploit new knowledge only within limited domains and circumstances (Hayek, 1945). Learning is a discovery process which is moulded by individual cognitive characteristics as well as codes and rules that allow interpretation and communication. As a result the ability to calculate the outcomes of each individual's decisions as well as the strategies available to others is limited. Clearly the sources of complexity and the associated coordination challenges increase when individual actions are drawn together in collective structures like a network. As Burt (2008) remarks, learning is not an optional attribute of networks – nor it is granted, we would add. In dynamic environments where the scope of collaboration and the operative rules are liable to change, inclusion in a network depends on the ability to remain relevant. That is to say, participation is contingent to learning and adaptation.

Previous literature has sidestepped these hurdles by assuming implicitly that agents learn and adapt swiftly to changes of their environment. If instead we follow the subjective view outlined above, knowledge does not grow on isomorphic spaces but within evolving dimensions – namely individuals' knowledge bases, the routines of communication across them and the criteria that define the collective scope. All these dimensions evolve in a symbiotic, yet uneven, manner (Nelson, 2003). Seen from this perspective the structure of a network, or better its evolution over time, is not a datum but rather a contingent outcome. Likewise, to the extent that problems are the key source of network formation, network performance depends on the ability of achieving successful solutions. If one accepts also the proviso that knowledge growth is an open-ended process, it follows that not all networks are capable of achieving success or sustaining it indefinitely. Again, it is the case to remark that while the literature tends to focus exclusively on successes, network failure is an important, perhaps inevitable outcome of the evolution of shared understanding.[2]

Summing up, the dynamics of networks map closely with those of individual cognitive processes. As argued above knowledge both enables and constraints and, in relation to the latter, it exerts a two-fold selection: it determines the criteria for inclusion – i.e. the capabilities that are relevant and the conditions of access to, membership of or exit from a network; once the structure is defined on the basis of the foregoing criteria, it determines the ability of a collaborative undertaking to achieve or not its scope.

4. Knowledge Networks in medicine

In the previous section we argued that the structure of a network is an endogenous outcome of individual decisions to partake in collaborative activities; the configurations they adopt reflect the criteria of inclusion, the competences that participants bring in and the relations they engage. In this section we articulate these concepts by focusing on medical scientific epistemic communities.

---

[2] For examples of failure in network alliances see Ulset (2008) and Consoli (2009)

4.1 – Medical innovation: conceptual foundations

A broad purpose of the study of medical innovation is to map and replicate the processes that facilitate the discovery or improvement of diagnosis and therapy. Recent works refuted the orthodox linear model that emerged in the 1960s and argued instead that medical innovation is a long-term learning process driven by variety, specialization and coordination within and across the component domains of health systems (Gelijns and Rosenberg, 1994; Gelijns et al, 2001; Consoli and Mina, 2009). Two aspects emerge with clarity from this approach. First, as medical jargon would have it, there are multiple pathways between bench and the bedside. Put another way, the notion that breakthroughs in medicine stem primarily from basic scientific research disregards the importance of know-how generated in the context of practice. As Nelson (2007: 8) puts it, "[the former view] misses the important interactions between learning in research and learning in practice". A second, and related, issue is that medical innovation processes are embedded in specific contexts of use. As a consequence the production and legitimization of medical knowledge reflect the social relevance that health problems acquire at specific points in time, and the latter can either stimulate or constrain by long-term development of individual disciplines (Rosenberg, 1989).

Members of any scientific community operate according to specific standards and respond to specific professional routines. Knowledge sharing is central to their operation: the commitment to disseminate results by publishing scientific papers, among others, is a key requirement for inclusion. This is what Hull (1988) advocated when commenting on the interdependence between explorative discovery and dissemination: as his evolutionary metaphor has it, knowledge sharing is to scientific communities what transmission is to populations. Along broadly similar tracks Dasgupta and David (1994) pinpoint disclosure and reward as basic institutional conditions for the cumulation of scientific knowledge. More recently Murray and Mahony (2007) and Antonelli (2008) pick up the thread and articulate it in relation to knowledge recombination and integration and conditions of access to external knowledge. Specifically in the context of medical innovation, various studies document the pivotal role of networks for the creation and diffusion of new medical knowledge (Ramlogan et al, 2007; Cambrosio et al, 2006).

The ontological question is why do networks of professionals emerge in the realm of medicine? Let us propose that medical scientists and practitioners share the goal of understanding and solving medical problems (Langlois and Savage, 2001). The key question, then, is: how do their communities operate to define and address those problems?

The problem-based view offers a good starting point to reflect on the open-ended nature of knowledge growth and the challenges associated to it. The emergence of new knowledge in epistemic communities is both a consequence and a source of change: at times when a research strategy that was committed to an agreed specification of the problem – say the development of a therapy according to a particular understanding of a disease – fails, or is refuted, the community initiates a search process which stimulates the emergence alternative strategies; accordingly, new actors come into play, scientific collaborations are forged or reorganised, new resources are employed, and activities are recombined or substituted. On the whole as the prevailing set of medical practices proves ineffective, the epistemic community undergoes structural transformations. Novel ideas or discoveries shift the nature of the problem at hand but at the same time they can grind to a halt in front of hurdles that prove to be beyond the remit of the extant knowledge. This is the case of medical fields where uncertainty or insufficient agreement among scientists and practitioners prevent successful diagnosis and therapy. Complex diseases generally stimulate cross-fertilization of disciplines and heterogeneity in the scientific and clinical knowledge bases (Ramlogan and Consoli, 2007).

Given the increasing importance of combining knowledge inputs, sourcing knowledge for a scope, and keeping sourcing options open, we hold knowledge networks as key unit of analysis to understand the organization of health innovation systems (Consoli et al, 2008; Consoli and Mina, 2009). Our focus is on the matrix of knowledge-generating activities that stem from such networks and, in particular, the knowledge flows and pathways through which medical research and clinical practices evolve over time.

4.2 – Citation Networks: methodological implications

A staple in the argument proposed so far is that the *scope*, the *strategy* and the *structure* of networks are intertwined elements within the dynamics of knowledge. Thereby changes in the configuration of relations within a network indicate complementary quantitative and qualitative aspects of knowledge growth. On the one hand the cumulative character of knowledge entails that network growth is due to either higher contributions from existing agents, or an increase in the number of contributors. On the other hand, as the agreed perceptions about the scope trigger reconfigurations in the structure of the network in that, it will change the criteria for inclusion and the relative importance of the activities that agents undertake. The question is: how to capture empirically these processes?

Our methodological proposition is to apply network analysis techniques to visualise and study patterns of institutional collaborations that can be extracted from bibliometric data. Conceptually a collaborative undertaking, such as co-authorship of scholarly work, signals a direct and intentional association between two or more (or groups of) authors in a field of research; the most frequent connections generate links between nodes which, taken all together and over time, generate network configurations. Methodologically such connections are reliable unit of analysis to the effect of validating background information on the development of a research area through measurable and observable results (Leydesdorff, 1994; 2003). Mapped onto the underpinning knowledge domain the connection across organisations in a scientific network indicates the emergence of pathways for the creation and diffusion of new knowledge. Stretching Hull's metaphor, co-authorships are instrumental to recombine and transmit emerging knowledge.[3]

---

[3] Interestingly the characteristics of articulation and creation *per se* have fundamental effects on the evolution of networks. For example, the emergence of specific professional standards such as a specific type of journal bears important implication on the path of knowledge cumulation (see Ramlogan and Consoli, 2007).

The analysis of knowledge flows within and across areas of scientific research informs on the process by which solutions to medical problems are searched for and, at times, achieved rather than merely pinpointing punctual discoveries. When applied to specific disease areas this technique uncovers the structure of relations underpinning patterns of referencing in the field of research; such long-term trajectories are likely to display clustering behaviour corresponding to highly debated – thus scientifically relevant – problems. Coupled with historical background of the medical area at hand, the study of citation patterns elucidates on the strategies that have been pursued in search of solutions, and on the evolution of the associated network structures.

The technique is amenable to different variations depending on the unit of observation; thus far two types of analysis have been proposed. The first focuses on networks of *individual articles* to capture the emergence, development, and occasionally the demise, of scientific paradigms (see Ramlogan et al, 2007; Consoli and Ramlogan, 2008). A second option is to analyse networks of *professional standards* (such as scientific journals) to record the evolution of the infrastructure underpinning the operation of medical and clinical communities. Ramlogan and Consoli (2007) employ this technique to illustrate the increase of specialisation and heterogeneity of knowledge as inadequate medical understanding stimulates cross-fertilisation of medical disciplines. A third, yet unexplored, variant consists in looking at the emergence and transformation of networks of *organisations* that can be extracted from the affiliations of the authors. Such an exercise provides a measure of the extent of division of scientific labour within a community; this is especially interesting in relation to research on complex, viz. partially unsolved, medical problems which are likely to stimulate growing *variety* in the knowledge base and progressively richer *ecologies* of organisations. As new scientific and clinical conjectures originate at the interface of different institutional settings – such as university departments, academic medical centres, general hospitals, firms and regulators – inter-organizational linkages are created or transformed. The next section will present a case study on the network structures emerging in the field of Ophthalmology research.

5. Knowledge Networks in action: Glaucoma research

Glaucoma is a chronic disease of the optic nerve which, if untreated, causes blindness. Global prevalence is estimated at 50-70 million, of which 7-8 million finally suffer total blindness (Source: Glaucoma Foundation). Damage caused by the disease can be slowed or arrested, but not reversed: patients affected by glaucoma experience progressive impairment of visual field as damage to the optic nerve advances. Despite abundance of theories in the textbooks and in the specialized literature the pathogenesis of the disease remains elusive. Glaucoma provides a quite interesting perspective on the nature of medical innovation in that the problem has not as yet proved amenable to a solution sequence but, at the same time, has spearheaded a series of innovations of considerable importance like, for example, the embedment of lasers and electronics upon diagnostic procedures and devices.

In what follows we provide a brief outline of major advances in both ophthalmologic research and practice drawing on previous work (Quigley, 2004; Consoli and Ramlogan, 2008). The fist subsection will outline a background overview of the glaucoma problem and of the key discoveries that marked advances in scientific understanding and clinical practice; the remaining subsections will stress the complementary role of (i) institutionally-bound interactions among participating agents – 'gateways' of innovation – and (ii) path-dependent trajectories of change – 'pathways' of innovation.

5.1 – Shifting paradigms of scientific understanding on Glaucoma

The key scientific paradigms of glaucoma research can be broadly divided into two phases, the first between mid-1870s and the late 1950s and the second between the mid-1960s and the early 2000s. In the early days the aetiology of glaucoma was associated to the Intra Ocular Pressure (IOP), that is, the pressure of a fluid that regulates the nourishment of the optic nerve. The prevailing conjecture was that elevated pressure levels obstruct the microcirculation of blood and impede the nourishment of the optic nerve. As a result of this degenerative process eyesight would deteriorate. Ever since the late 1800s this understanding directed the research strategy of the ophthalmic scientific community towards IOP-based symptomatology and, accordingly, towards specific diagnostic techniques and therapeutic treatments, such as incisional surgery or drugs (Quigley, 2004).

Unfortunately the ethos of detecting and lowering eye pressure proved only partially successful among patients, and often to a different degree. In turn, such mixed fortunes revealed crucial drawbacks which undermined both the established scientific knowledge base as well as the research strategy on glaucoma. Two key discoveries, both in the 1960s, changed the course: the disease manifested itself differently across populations; and the degenerative process observed in the optic nerve had neurological nature (Albert and Edwards, 1996). It is important to highlight that such crucial insights emerged in the context of medical practice (e.g. population studies) rather than theory; this, de facto, contradicts the linear model of scientific research outlined above. As a result the research strategies pursued by the community of ophthalmology scientists and practitioners grew diverse and accelerated the shift towards evidence-based approaches which, later, would be at heart of new diagnostic tools based on lasers and computers (Consoli and Ramlogan, 2008).

In the 1970s new advances stemming from the clinical realm drew more attention to the diversity of the disease, in particular the changing degree of intensity that could be observed across patients of different age and ethnic origin (Albert and Edwards, 1996). In the 1980s the increasing relevance of new scientific disciplines previously unrelated to ophthalmology, like biology and pharmacology, borne significant changes on the understanding of the disease and, accordingly, on the configuration of the scientific network. The growing variety of outlets used by the community, for example, is a testimony to this cross-fertilisation (Ramlogan and Consoli, 2007). A number of successful experiments aided by newly developed diagnostic techniques in the late 1980s pushed glaucoma research further in uncharted territories such as molecular biology and genetic studies. Later, in 1994, the discovery of the glaucoma gene has set off the third research paradigm which to this day dominates the discipline (Ray et al, 2003).

Nowadays it is widely accepted that glaucomas – increasingly referred to in the plural form – are a heterogeneous if complex group of eye conditions with variable manifestations attributable to differences in genetic causes as well as in lifestyles. Despite the unitary association between ocular pressure and glaucoma has been challenged for some fifty years, elevated intraocular pressure remains the most easily identifiable and treatable factor and both primary diagnosis and treatment are still largely based on IOP detection and reduction (Zeyen, 2004). As Nelson (2003) remarks, successful medical solutions frequently fall outside the boundaries of theoretical knowledge; in those times practical and scientific understanding proceed unevenly.

This long, if cursory, journey over the long-term development of ophthalmology scientific knowledge and clinical practices suggests that the uncertainty triggered by the demise of the IOP paradigm stimulated significant transformation in the scope, the strategy and, a fortiori, the structure of the research network. In turn, the involvement of a variety of different disciplines called for the implementation of specific institutional and organisational processes to coordinate the growing diversity of the knowledge base. Key questions about whether glaucoma can be detected with certainty or can be cured still loom large. Such, we surmise, is the nature of progress when the problem is inaccurately specified, or too complex to understand given the prevailing knowledge base. Let us now articulate the outlined pattern of medical innovation in the context of emerging networks of medical scientific research in ophthalmology.

5.2 – Network Analysis: the gateways of change

The next two sections will employ social network methods to construct and analyse the collaborative networks that developed during the more recent phase of scientific research on glaucoma. This is a two-fold exercise that seeks to bring out the gateways of innovation, that is, institutional components that can be identified from the author addresses associated with each paper, and the pathways, that is, the patterns of collaborations across them. The primary source is a longitudinal database of over 13,000 scientific articles over the period 1945 to 2003 extracted from the ISI Thompson online resources. Affiliations are identified in the dataset from the period 1968 thus restricting our analysis largely to the 45 year period up to 2003 which comprises around 9000 publication records.

Over the period under consideration, published glaucoma research was undertaken across the world in 111 countries. Table 1 presents an overview of the main countries that populate our network by country and type of organisation involved. For the purpose of this analysis we have identified 7 organisational types playing a role in glaucoma research. We have also included an eighth type, Miscellaneous, for those addresses which we are unable to assign. The 20 countries featured in the table are selected on the basis of total number of organisations within each and all together these account for 80 % of all organisations publishing research over the entire period. As can be observed from the table American organisations dominate glaucoma research with over 25% of the total; European representation is significant, 12 out of the 20 countries with Germany occupying second place overall; Japan is in third place with other countries in Asia or/and the Far East also represented. The table also indicates that University Departments, General Hospitals and Teaching Hospitals – besides Miscellaneous – retain the lion share.

Interesting variety emerges within each of the countries in terms of the relative contribution of each type whereby, for example, in the United States the relatively less skewed distribution indicates that no single institution dominates over others as opposed to the USSR, where Public Research Institutes account for 66%; India features a different model of research organisation that revolves around University Hospitals and Public Research Institutes, accounting for well over 50% of glaucoma research; in Israel the two leading research organisations are General Hospitals and Eye Clinics; General Hospitals and University Hospitals are most prominent in a number of European Countries such as Netherlands, Denmark, Finland and Italy. Conversely, among European countries England is the only in which one type – General Hospitals – accounts for almost half of the whole research contributions on Glaucoma. Despite not being able to classify around 18% of addresses, the table provides a clear indication of the extent of institutional diversity across countries and, in particular, of the heterogeneity of research organisations in Ophthalmology.

TABLE ONE ABOUT HERE

Let us now elaborate a primary sketch of the changing configurations of this scientific network over time. To this end we utilise over 28,000 separate addresses which were parsed with Perl scripts and, finally, cleaned manually. These were subsequently converted to networks of collaborations and implemented within the Pajek software[4]. We opted to capture network evolution by constructing four cross-institutional networks based on overlapping periods: 1968-1975, 1968-1985, 1968-1999, 1968-2003. These were chosen on the basis of a qualitative criterion – namely by taking key discoveries in the field of glaucoma research and practice as reference points.[5] Table 2 shows the essential characteristics of these networks: the number of nodes increased almost twentyfold over time from 218 to 3955 and, as the network grew, so did the average connections per node which increased from 0.3 to 2.7. Although we observe the aforementioned growth in the network its connectivity, measured by the density – the proportion of connections (edges) relative to the total possible, declined. Next we consider the degree centralisation, that is, a measure of the network structure (de Nooy et al, 2005)[6] : In particular, a network with high degree centralization is one in which the connections concentrate around a few nodes while many nodes have few ties. We observe this to be the case in our network whose degree centralization increases from 0.02 to 0.05 as its size grows. The relatively low clustering coefficient tells essentially a similar story: this measure compares the number of connections in the neighbourhood of a node relative to the number of

[4] Pajek is software developed for network analysis provided freely for academic use at http://vlado.fmf.uni-lj.si/pub/networks/pajek/.

[5] This clarifies why the time intervals differ in length and is coherent with the notion discussed before that the growth of knowledge is uneven and non-uniform.

[6] Various measures for centrality are available in the social network literature (see also the discussion of their limitations in Borgatti, 2005). For the purpose of this exercise the normalised degree centrality available in the software program Pajek was used.

connections if the neighbourhood was fully connected. Finally we consider the average path length which is the average of distances between all pairs of nodes in the network and another measure of structure. This variable changes over time and is indicative of changes in network structure.

TABLE TWO ABOUT HERE

Figures 1a to 1d show 4 configurations of the network at different time intervals. The shapes of the nodes in the diagrams correspond to the eight categories of organisations we identified in the database, namely University Departments (circle), General Hospitals (box), Firms (vertical ellipse), Eye Clinics (diamond), Health Centres (triangle), Teaching Hospitals (horizontal ellipse), Public Research Institutions (rectangle) and Miscellaneous – such as private addresses remain blank; we also colour-coded addresses by broad geographical region, thereby the Americas except the US (orange), US (red), Europe (green), Africa (grey), South East Asia (brown), Western Pacific countries (violet) and Easter Mediterranean countries (yellow). The difference in node sizes in the first two diagrams, determined on the basis of the standardised degree centrality, is indicative of individuals' relative importance. In Figure 1a we show the 95 nodes among which collaborations took place. The remaining nodes were isolates and deleted for matters of convenience.

FIGURES 1.a TO 1.d ABOUT HERE

Clearly in this early period the network is loosely connected and Canadian organizations are among the leaders in the field. Figure 1b, show a more complicated picture as the network starts to develop. On this occasion we were more parsimonious in the labelling but retained the isolates. The top 20 organisations are identified. Relative to the University of British Columbia which was the leading institution in the earlier period, other American universities and other organizations began to assume greater prominence. Indeed the University of British Columbia had slipped down the ranking to 11th place, with CUNY Mt Sinai School of Medicine, Harvard University, the Wills Eye Hospital, (Philadelphia) and Johns Hopkins University being the top four ranked organisations. Figures 1c and 1d show the more recent network configurations. In terms of structural characteristics, these two networks are quite similar, probably because the time difference is just a few years. The latter diagram shows the whole network less isolates and we use the former to illustrate some aspects of the internal structure. For this we restricted the diagram to those nodes with five or more connections within the network and we observe some interesting behaviours. Clearly we can see some clusters attached to the periphery of the main cluster which is dominated by collaborations from American organisations while some peripheral clusters are easily identifiable as national collaborations. For example, in the upper left of the diagram is visible a French cluster comprising hospitals that is connected to the main body of the network by INSERN; to the right of this is a cluster of organisations based in Italy made up mainly of universities as well as a Japanese cluster comprising hospitals and universities. As before, the latter groups are connected to the main network by just a few gatekeepers. Another distinguishable cluster to the bottom right indicates a cross-country venture with organisations from North American, Japan and Europe co-operating.

One of the disadvantages of constructing these overlapping networks is that we preclude by definition exit of any institution however we can still observe dynamic behaviours within our networks reflected in changing composition as new individuals enter and the relative importance of each network participant changes. Therefore one organisation which was important in the early period may become a peripheral player over time as a result of relatively lower relevance vis-à-vis the development of new knowledge. As a whole this method provides an opportunity to capture the redistribution of players between core and periphery of the changing network.

To better comprehend the dynamic of the networks we narrow the focus on the top 10 institutions in the first period (1968-1975) and over the whole period (1968-2003) in Table 3. The upper part lists the key individual players in the earlier period and their subsequent performance in terms of ranking as the network expanded. Here we detect a prime indication of network evolution associated to both size increases (219 to 3955) as well as structural changes in the configuration as a result of the changing relative importance of its members. Let us pick out two cases: the University of British Columbia (Canada), the top research institution in period 1, manages to remain in the upper echelons throughout the time span (No. 35 in period 4); conversely the British Columbia Institute of Technology (Canada) which started in tenth position plummeted to the bottom half of the large final network. The lower portion of Table 2 shows a backward view of the performance, indicated by the ranking by degree centrality, of the top 10 organisations. Among those, seven out of ten of those that feature in the most recent top ranking were also part of the early networks. Johns Hopkins University (USA) ranked 60th at the beginning but moved to a dominant position since 1975; other recent top players such as the Universities of Illinois, Washington and Michigan (5th, 6th and 7th respectively) started from initial low rankings (108, 121, 181 respectively). The only two European institutions in this list are based in London (England): the Moorfields Eye Hospital, which moved to 66th position up to 3rd, and even more noticeable the Institute of Ophthalmology, which currently ranks 9th but was not initially present in the network.

TABLE THREE ABOUT HERE

We conclude our composite profile of the ophthalmology community with a summary of the institutional types of the population showed in Figure 2. This shows the decreasing participation of authors based at General Hospitals, down to 21% from the initial 37%; a marginal increase of participation of firms over time; a relative decline of Public Research Institutes, from 17% to 5%; and a doubling of University Departments, from 17% to 33%. As the latter group is likely to feature significant variety we break down university departments according to their field of specialisation and summarise the relative importance in percentage terms in Table 4. This provides an interesting insight on the degree of variety that characterised the forms of scientific specialisation that became relevant to glaucoma research as the understanding of the disease evolved. As one might expect Ophthalmology and Optometry departments hold the lion share with an aggregate value between 66% and 80% over the four periods; the same might be said for the second place of General Medical

Department, such as Oncology and Cardiology. Further down the list of the remaining department types one can observe higher dispersion of specialization and increasing variety over the time span. Neurology together with Community studies are the next two most important departments at the beginning, and decline towards the end; this is consistent with the general background above, more precisely the emergence of two important research trajectories between the 1960s and the 1970s – respectively on the neurologic nature of Glaucoma and on the impact on the quality of life among patients. Further we note a paradigm shift from the second period onwards confirmed by a relatively higher contribution of departments such as Pharmacology, Genetics and Biology. Once again, this is consistent with the broad picture of the previous section. Yet one more noticeable feature is the relatively steady contribution by Epidemiology and Immunology Departments, as a confirmation that once the diversity of Glaucoma had been accepted by the community, research on the observed impact of the disease across different populations flourished.

FIGURE TWO ABOUT HERE

TABLE FOUR ABOUT HERE

This subsection has overviewed the institutional gateways observed in the glaucoma research network, that is, the component organisations who contributed to medical scientific research. Let us now turn to analyse pathways of knowledge diffusion and, specifically, the instituted connections that drive the evolution of the network's structure.

5.3 – Patterns of Cross-Institutional Collaborations: the pathways of development

In this final part of the paper we seek to analyse how patterns of cross-institutional collaborations emerge, develop and decline over time. As we have recognized before each paper potentially emerges out of a collaboration across the eight different types (seven plus a Miscellaneous category) which we coded individually and ordered as follows: Miscellaneous; University Departments; General Hospitals; Firms; Eye Clinics; Health Centres; University Hospitals; Public Research Institutes. From our initial data set of 13,000 we subsequently dropped around 4,000 papers that were authored by single institutions. Next we computed the distribution of organisational collaborations for each paper across the eight types. From this we can observe different patterns across types (inter-organisational) and within types (intra-organisational) or within and between collaborations. We are primarily interested in the inter-organisational patterns and therefore classify each record in terms of a binary code: if an organizational type is present, we assigned "1, "0" otherwise. This exercise allowed us to generate a unique string of eight characters for each record and produced a final group of 165 unique combinations of cross-institutional collaborations, which form the unit of analysis for our empirical analysis.[7] We focus on 27 specific types whose total observations over time were above the population average, and Figure 3 shows their changing shares.

FIGURE THREE ABOUT HERE

In it we observe three dominant types of collaborations, namely 01011000 = University Departments, Firms, Eye Clinics (Tot. Freq. 782); 00101100 = General Hospitals, Eye Clinic, Firms (Tot. Freq. 420); and 10000100 = Miscellaneous, Health Centres (Tot. Freq. 350). Over the course of the four decades we observe three striking patterns that correlate with the background story of Glaucoma research outlined above. Early on the 'Miscellaneous-Health Centres' and the 'General Hospitals-Eye Clinic-Firms' combinations dominate and up until the early 1980s together account for at least 50% of all collaborations. Reflecting on the nature of the component organisations we observe that the first type 'Miscellaneous-Health Centres' declines due to a relative faster fall of the former, which we connect to the increasing institutionalisation of the ophthalmology community (Langlois and Savage, 2001; Albert and Edwards, 1996). As far as the other type of collaborative endeavours (General Hospitals- Eye Clinic-Firms') the decline is relatively slower after the late 1980s and it is attributed to the diminishing importance of General Hospitals, which resonates with the increasing specialisation of the ophthalmology community as the understanding of the problem evolved.

[7] To make matters clear, type 01010100, for example, represents the collaboration between University Departments, Firms and Health Centres.

Over time, however, parallel to the increase in variety of the knowledge base discussed before, we observe that their combined share declines steadily and this contrasts with the rising contribution of the soon-to-be dominant 'University Departments-Firms-Eye Clinics' collaboration. This has arguably been a major driver for the second paradigm of glaucoma research, characterised by the integration of basic scientific knowledge, business knowledge and experimental/practice-based knowledge. It is worthwhile to recall briefly that as the shared understanding of the glaucoma problem evolved, the research strategies took different directions between the 1970s up to the early 1990s. These diverse strategies led to the discovery of neurological factors; of new diagnostic avenues in conjunction with the emergence of complementary general purpose technologies, such as lasers; and the diversity of glaucoma manifestations across patients. In turn, these discoveries reflect how individual specialisations embedded in of each of the component organisations contributes to the joint achievements of this dominant collaboration trajectory. Innovation scholars attentive to long-term institutional processes would find commonalities between this finding and the Triple Helix concept (Leydesdorff and Meyer, 2003). It should be observed also that firms feature as a key component in this fabric of collaborations. Indeed expert users in medicine need not be restricted to practitioners and scientists, especially in the face of complex diseases like glaucoma. Entrepreneurs and large corporations learn to know the need and articulate plausible ways to satisfy them. In this sense, it should not be surprising that firms are genuine sources of invention and capable of generating innovation driven by those entrepreneurial motivation and skills that are necessary to turn new ideas into business (Roberts, 1989).

Figure 4 narrows the focus on implicit collaboration strategies undertaken by the top ten organisations on the basis of degree centrality within the glaucoma research network. This is constructed by comparing the number of collaborations over two macro periods (P1: 1968-1985 and P2: 1968-2003)[8] disaggregated by organisational type.

FIGURE FOUR ABOUT HERE

[8] The latter is consistent with the cumulative logic that was mentioned earlier in relation to the construction of the networks.

Here we notice a generalised trend across all the key players whereby a relatively high concentration of partnering in the earlier period with few organisations was followed by the diversification of the portfolio of collaborations. A pattern observed in the first period almost unique to University Departments is the engagement with other university departments which, however, dilutes in the second period as partnering becomes more widely diffused. For example, 43% of Johns Hopkins University collaborations in P1 were with other university departments but this declines to 24% later; even more striking, is the case of Washington University where the share with university departments decreased from 55% to 32%. The University of Michigan (7^{th} in the overall ranking) is distinctive among the top ten in that there were no external collaborations in the first period. Specialist eye organisations such as the New York Eye and Ear Infirmary and the Institute of Ophthalmology in London feature the highest individual concentration of partnering in the first period – 60% with University Hospitals and 67% with General Hospitals respectively. The only two non-American institutions in the top ten, the Moorfields Eye Hospital and the Institute of Ophthalmology, both based in London, feature a dominance of partnering with General Hospitals in the earlier period. Yet one more striking feature, consistent with the wider picture provided above, is the non-engagement with firms which only picked up, albeit relatively small, after 1985.

6. Discussion and conclusions

In this paper we set out to understand multi-level dynamics of collaborative interactions among network participants, and relate these to the search for new knowledge. This endeavour is cast against the backdrop of medical innovation, in particular the search for effective diagnosis and therapy for glaucoma. Until the 1950s this most elusive disease was thought to be monocausal and both scientific understanding and clinical practices were focused on a single major aetiology; subsequently, major breakthroughs during the 1960s brought about significant developments and understandings, some of which unintended, and a great deal of churn in the knowledge base. The paper has sought to capture some of these developments at the organisational level by analysing a longitudinal dataset of scientific publications on glaucoma. The resulting network structures, we suggest, proxy for the search space in the quest of effective answers to the glaucoma problem.

This paper builds on and expands the notion that network outcomes are the endogenous outcomes of changing patterns of relationships. The basic conjecture is that the structure of a network cannot be divorced from the dynamics of the knowledge that underpins it: the scope of a network and the capabilities necessary to achieve it are inseparable aspects. As the nature of the problem changes, the criteria of inclusion in the network change accordingly; indeed, as we move along in time we find that the reconfigurations between the core and the periphery of the network reflect the changing relative importance of individual contributions. Accordingly different network structures reflect the combination of specific competences as dictated by the accepted perception of the scope and the strategy. The analysis proposed here highlights complementary aspects between the creation of knowledge that is attributable to the gateways, that is, individual organisations, and the pathways of collaborations that are central to its wider diffusion. As each level search, discovery, uncertainty and problem-solving are essential aspects of the dynamics and the performance of this network.

The analysis proposed here connects the long-term changes in the configuration of this scientific community to the development occurring in the scientific, institutional and clinical realms. The resulting maps synthesise both the changing boundaries of a search space as well as the evolution of the structure of relationships within it. The more specific analysis of the most important components speaks to the variety of the emerging and restless nature of the knowledge base; the diversity of University departments confirms the tendency towards growing multidisciplinary of specialisations. In turn, the analysis of the patterns of organisational collaborations show that as new research directions emerge, develop and/or decline different types of expertise are combined in ways that are contingent and specific to the changing perception of the problem. Our focus on the cross-organisational collaborations provides a measure of the extent of division of scientific labour within that scientific community. This is interesting in relation to research on complex, viz. partially unsolved, medical problems like glaucoma which are likely to be characterised by growing *variety* in the knowledge base and progressively richer *ecologies* of organisations. As new scientific and clinical conjectures originate at the interface of different institutional settings – such as university departments, academic medical centres, general hospitals, firms and regulators – inter-organizational linkages are created or transformed.

The proposed approach is multi-dimensional just as its object of analysis: the growth of knowledge and its component processes - creation, legitimization, application, and refutation – reflect the shifting balance between global search and locally constrained choices. In particular we argue that 'know-what', as in knowledge embodied in scientific disciplines is the outcome of codification and diffusion processes, has a global character. Conversely 'know-how', as in the implementation of tacit knowledge for problem-solving, has a local flavour. The upshot of this is that the continual reconfiguration between the core and the periphery driven by both global and local constraints impact on the nature and structure of networks. It is not only about variety in the forms of specialisation embedded in individuals but also in the instituted relations that regulate their interactions. Future research on network dynamics should integrate the growing attention towards topologies with a deeper understanding of how structures come about as a result of underlying historical processes. The latter informs about the causal connections between incentives, the capabilities and the collective behaviours that ultimately define the scope, the strategy and the structure of networks as they evolve over time.

References

Ahuja, G. (2000) Collaboration networks, structural holes, and innovation: A longitudinal study. *Administrative Science Quarterly*, **45** 425-455.

Albert, M.D., Edwards, D.D. (1996) *The History of Ophthalmology*. Cambridge: Blackwell Science.

Antonelli, C. (2001) *The Microeconomics of Technological Systems*. Oxford: Oxford University Press.

Antonelli, C. (2008) *Localized Technological Change: Towards the Economics of Complexity*. London: Routledge.

Borgatti, S. P. (1995) Centrality and AIDS. *Connections*, **18**(1) 112-114.

Burt RS. (1992) *Structural Holes*. Boston: Harvard University Press.

Burt, R.S. (2008) Information and structural holes: comment on Reagans and Zuckerman. *Industrial and Corporate Change* **17** 953-969.

Cambrosio, A., P. Keating, S. Mercier, G. Lewison, A. Mogoutov (2006) Mapping the emergence and development of translational cancer research. *European Journal of Cancer* **42** 3140–3148.

Consoli, D. (2009) Systems of innovation and industry evolution: the case of retail banking in the UK. *Industry and Innovation* (forthcoming).

Consoli, D., R. Ramlogan (2008) Out of sight: problem sequences and epistemic boundaries of medical know-how on glaucoma. *Journal of Evolutionary Economics* **18**(1) 31-56.

Consoli, D., A. McMeekin, J.S. Metcalfe, A. Mina, R. Ramlogan (2009) The Process of Innovation: Incentives, Behaviour and Organization. J. Costa-i-Font, C. Courbag, A. McGuire ed. *The Economics of New Health Technologies: Incentives, Organisation and Financing*, Oxford University Press. Forthcoming.

Consoli, D., A. Mina (2009) An evolutionary perspective on the dynamics of Health Innovation Systems. *Journal of Evolutionary Economics* (forthcoming).

Cook K.S., R.M. Emerson (1978) Power, equity and commitment in exchange networks. *American Sociological Review* **43** 712–739.

Dasgupta, P., P.A. David (1994) Towards a new economics of science. *Research Policy* **23** 487-521.

de Nooy, W., A. Mrvar, V. Batagelj (2005) *Exploratory Social Network Analysis with Pajek*. Cambridge University Press.

Economides, N. (1996) The economics of networks. *International Journal of Industrial Organization* **14**(6) 673-699.

Fleming, L. (2001) Recombinant uncertainty in technological search. *Management Science* **47**(1) 117-132.

Freeman L.C. (1979) Centrality in social networks: conceptual clarification. *Social Networks* **1** 215–239.

Garud, R., K. Peter (2003) Bricolage versus Breakthrough: Distributed and Embedded Agency in Technology and Entrepreneurship. *Research Policy* **32**(2) 277-301.

Gelijns A.C., J. Zivin, R.R. Nelson (2001) Uncertainty and Technological Change in Medicine. *Journal of Health Politics, Policy and Law* **26** 913-924.

Gelijns, A.C., N. Rosenberg (1994) The Dynamics of Technological Change in Medicine. *Health Affairs* **13**(3) 28-46.

Grandori, A. (2001) *Organization and Economic Behavior*. London: Routledge.

Grandori, A., G. Soda (2004) A Relational Approach to Organization Design. *Industry and Innovation* **13**(2) 151–172.

Granovetter, M.S. (1973) The strength of weak ties. *American Journal of Sociology* **78**(6) 1360–1380.

Granovetter M.S. (1983) The strength of weak ties: a network theory revisited. *Sociological Theory* **1** 201–233.

Gulati, R. (1995) Social Structure and Alliance Formation Patterns: A Longitudinal Analysis. *Administrative Science Quarterly* **40**(4) 619-652.

Gulati, R., M. Gargiulo (1999) Where do interorganizational networks come from? *The American Journal of Sociology* **104**(5) 1439-93.

Hayek, F. (1945) The Use of Knowledge in Society. *American Economic Review* **35** 519-530.

Hull, D. (1988) *Science as a Process*. Chicago: University of Chicago Press.

Langlois, R.N. (2001) Knowledge, Consumption, and Endogenous Growth. *Journal of Evolutionary Economics* **11**(1) 77-93.

Langlois, R.N., D.A. Savage (2001) Standards, Modularity, and Innovation: The Case of Medical Practice. R. Garud, P. Karnøe (eds.) *Path Dependence and Path Creation*. Hillsdale, NJ: Lawrence Erlbaum.

Leydesdorff, L. (1994) The Generation of Aggregated Journal-Journal Citation Maps on the basis of The Cd-Rom Version of the Science Citation Index". *Scientometrics* **31**(1) 59-84.

Leydesdorff, L. (2003) Can Networks of Journal-Journal Citations be used as Indicators of Change in the Social Sciences? *Journal of Documentation* **59**(1) 84-104.

Leydesdorff, L., M. Meyer (2003) The Triple Helix of university-industry- government relations. *Scientometrics* **58**(2) 191-203.

Lin, N., W.M. Ensel, J.C. Vaughn (1981) Social resources and strength of ties: structural factors in occupational status attainment. *American Sociology Review* **46**(4) 393-405

Madhavan, R., B.R. Koka, J.E. Prescott (1998) Networks in transition: How industry events (re)shape interfirm relationships. *Strategic Management Journal* **19** 439–459.

Metcalfe, J.S., R. Ramlogan (2005) Limits to the Economy of Knowledge and Knowledge of the Economy. *Futures* **37**: 655-674.

Metcalfe, J.S., A. James, A. Mina (2005) Emergent Innovation Systems and the Delivery of Clinical Services: the Case of Intra-Ocular Lenses. *Research Policy* **34**(9) 1283-1304.

Murray, F., S. O'Mahony (2007) Exploring the Foundations of Cumulative Innovation: Implications for Organization Science. *Organization Science* **18**(6) 1006–1021.

Nelson, R.R. (2003) On the uneven evolution of human know-how. *Research Policy* **32** 909-922.

Nelson, R.R. (2007) How Medical Know-how Progresses. Mimeo, Manchester University.

Powell, W.W., K.W. Koput, L. Smith-Doerr (1996) Interorganizational Collaboration and the Locus of Innovation: Networks of Learning in Biotechnology. *Administrative Science Quarterly* **41** 116-45.

Prahalad, C.K., G. Hamel (1990) The Core Competence of the Corporation. *Harvard Business Review* May-June 79-91.

Quigley, H.A. (2004) New paradigms in the mechanisms and management of glaucoma. Eye (The Doyne Lecture). Available online at http://dx.doi.org/10.1038/sj.eye.6701746

Ramlogan, R., D. Consoli (2007) Knowledge, understanding and the dynamics of medical innovation. *European Journal of Economic and Social Systems* **20**(2) 231-249.

Ramlogan, R., A. Mina., G. Tampubolon, J.S. Metcalfe (2007) Networks of Knowledge: the distributed nature of Medical Innovation. *Scientometrics* **70**(2) 459-489.

Ray, K., A. Mukhopadhyay, M. Acharya (2003) Recent advances in molecular genetics of glaucoma. *Molecular and Cellular Biochemistry* **253**(1-2) 223-31.

Roberts, E.B. (1989) The personality and motivations of technological entrepreneurs. *Journal of Engineering and Technology Management* **6** 5-23.

Rosenberg, C.E. (1989) Disease in History: Frames and Framers. *The Milbank Quarterly* **67**(1) 1-15.

Rosenkopf, L., G. Padula (2008) Investigating the Microstructure of Network Evolution: Alliance Formation in the Mobile Communications Industry. *Organization Science* **19**(5) 669–687.

Shy, O. (2001) *The economics of network industries*. Cambridge: Cambridge University Press.

Soda, G, A. Usai, A. Zaheer (2004) Network Memory: The Influence of Past and Current Networks on Performance. *Academy of Management Journal* **4**(6) 893-906.

Stuart T.E. (1998) Network positions and propensities to collaborate: an investigation of strategic alliance formulation in a high-technology industry. *Administrative Science Quarterly* **43** 668–698.

Suitor, J.J., B. Welman, D.L. Morgan (1997) It's about time: How, why, and when networks change. *Social Networks* **19** 1–7.

Ulset, S. (2008) The rise and fall of global network alliances. *Industrial and Corporate Change* **17**(2) 267–300.

Weick, K.E. (1979) *The Social Psychology of Organizing*. Addison, Wesley, Reading, MA.

Zeyen, T. (2004) Early Surgical Treatment of Glaucoma. Shaarawy,T., J. Flammer (eds) *Glaucoma Therapy: Current Issues and Controversies*, Informa Health Care.

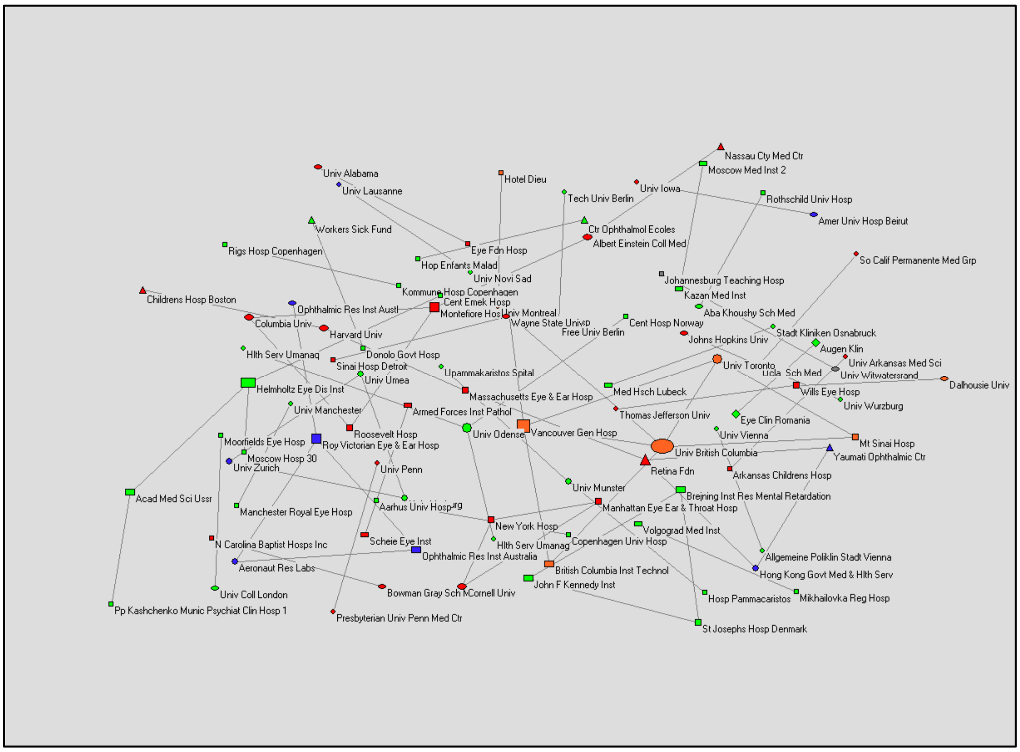
	Miscellaneous	University Departments	General Hospitals	Firms	Eye Clinics	Health Centres	University Hospitals	Publ. Res. Institutes	Total Types
US	260	140	151	98	100	198	167	111	*1225*
Germany	90	86	27	6	33	12	38	22	*314*
Japan	14	56	92	20	12	7	79	26	*306*
England	33	36	132	11	8	20	52	9	*301*
France	70	24	76	8	1	22	48	12	*261*
Italy	53	47	57	1	4	18	18	14	*212*
Canada	20	27	40	5	6	16	28	9	*151*
Turkey	50	35	19			5	33	1	*143*
Spain	29	20	27			9	26	6	*117*
Australia	22	17	38	1	7	6	16	10	*117*
USSR	3	3	17		6	3		63	*95*
Switzerland	21	10	16	7	8	3	17	9	*91*
Sweden	16	14	26	3	1	7	19	3	*89*
India	14	4	6		6	8	22	25	*85*
Israel	5	5	17	1	5	25	12	6	*76*
PR China	1	17	21		2	3	23	7	*74*
Netherlands	10	15	15	2		9	14	6	*71*
Denmark	5	6	15	3	7	8	14	3	*61*
Greece	15	7	21		1	3	11	2	*60*
Finland	7	11	10	2		4	13	2	*49*
	738	**580**	**823**	**168**	**207**	**386**	**650**	**346**	***3898***

Table 1

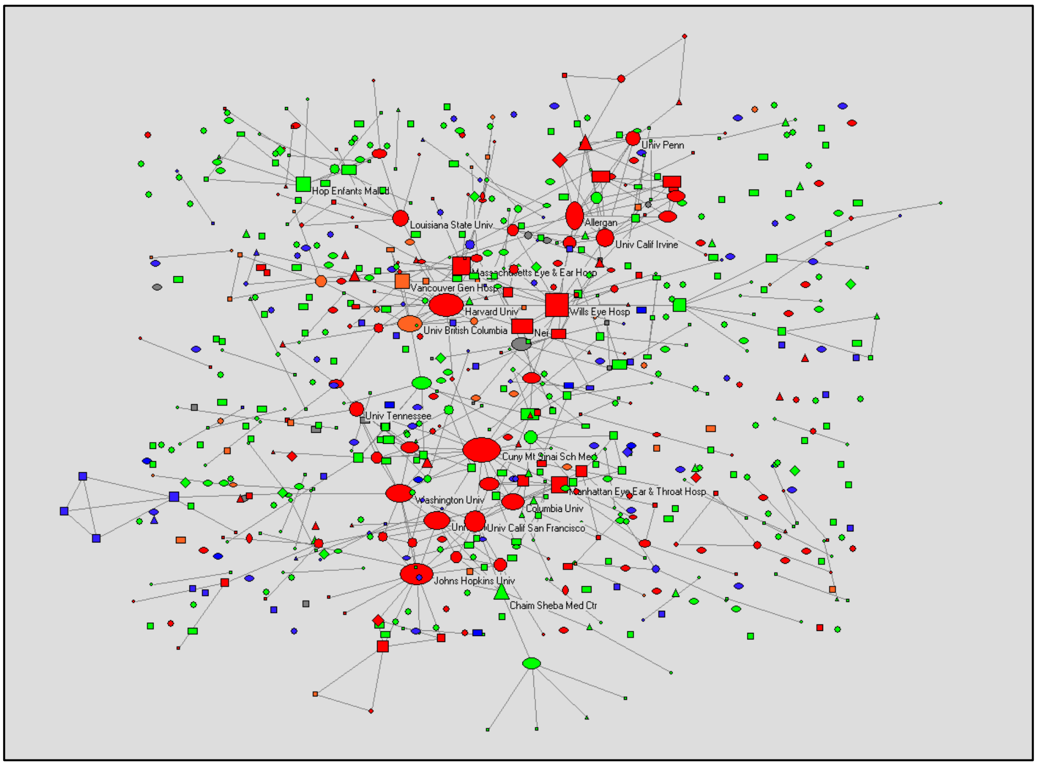
Network	**1968-1975**	**1968-1985**	**1968-1999**	**1968-2003**
Nodes	218	729	2695	3955
Total Edges	69	432	6754	10721
Density	0.0030	0.0016	0.0019	0.0014
Degree centralization	0.0230	0.0232	0.0505	0.0505
Clustering Coefficient	0.4280	0.3620	0.3955	0.4100
Avg. Path Length	1.43	4.65	4.12	4.65

Table 2

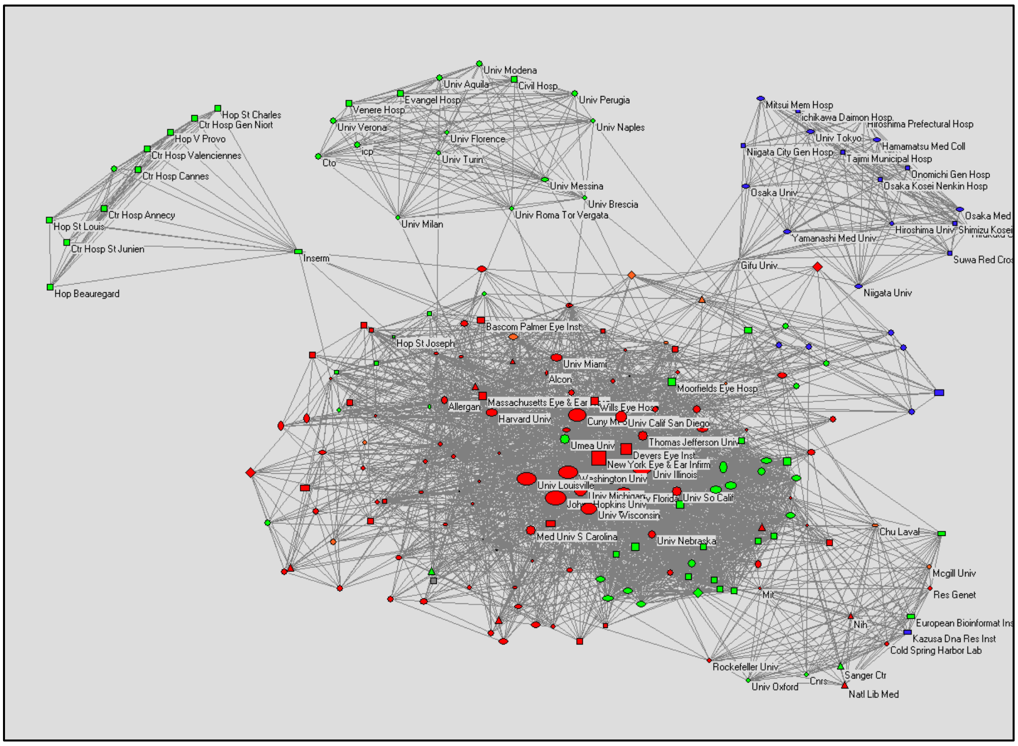
1a: Network 1968 -1975



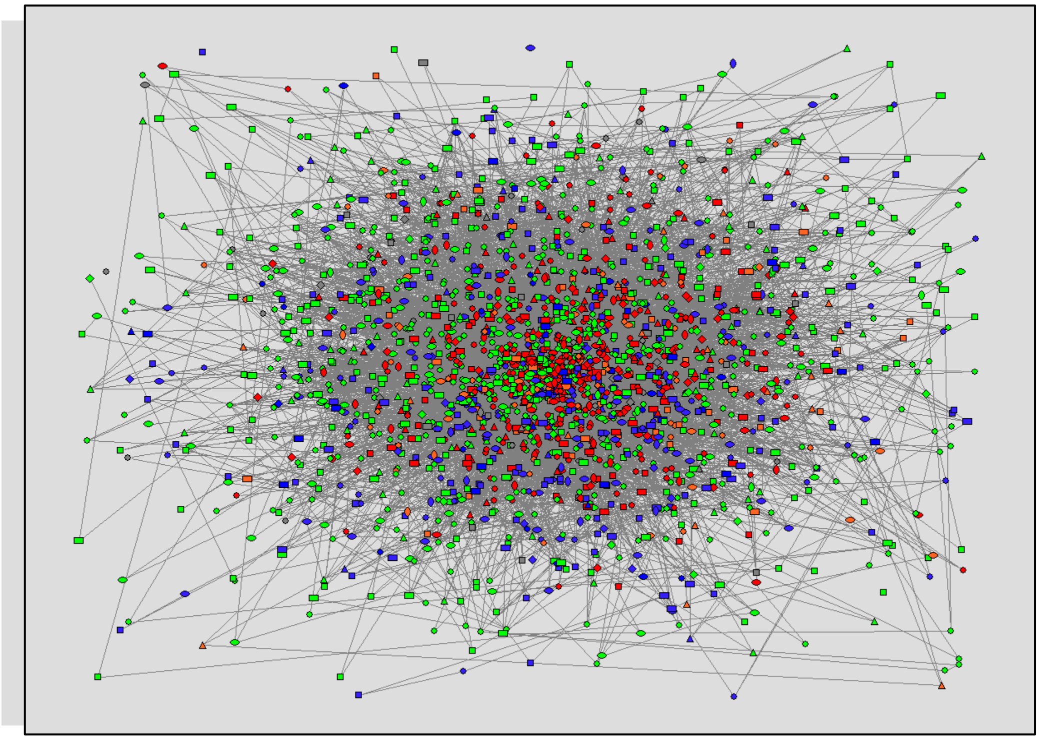
1b: Network 1968-1985



1c: Network 1968-1999 (selected area)



1d: Network 1968 -2003



	T1	T2	T3	T4
Univ. British Columbia	1	11	46	35
Vancouver Gen Hosp	2	20	306	434
Univ. Toronto	3	72	25	17
Retina Fdn	4	51	592	987
Helmholtz Eye Disease Inst.	5	32	294	415
Roy Victorian Eye & Ear Hosp	6	85	904	1524
Montefiore Hosp & Med Ctr	7	41	189	269
Univ. Odense	8	97	991	1612
Univ. Munster	9	101	730	664
British Columbia Inst. Technol.	10	113	1079	1729
Tot. Size of Network	**219**	**729**	**2695**	**3955**

	T4	T3	T2	T1
Johns Hopkins Univ.	1	1	4	60
New York Eye & Ear Infirm	2	2	39	
Moorfields Eye Hosp	3	3	26	66
Harvard Univ.	4	4	2	18
Univ. Illinois	5	5	9	108
Washington Univ.	6	7	6	121
Univ. Michigan	7	6	542	181
Univ. Iowa	8	20	92	86
Inst. Ophthalmology	9	19	95	
Univ. Wisconsin	10	11	29	

Table 3

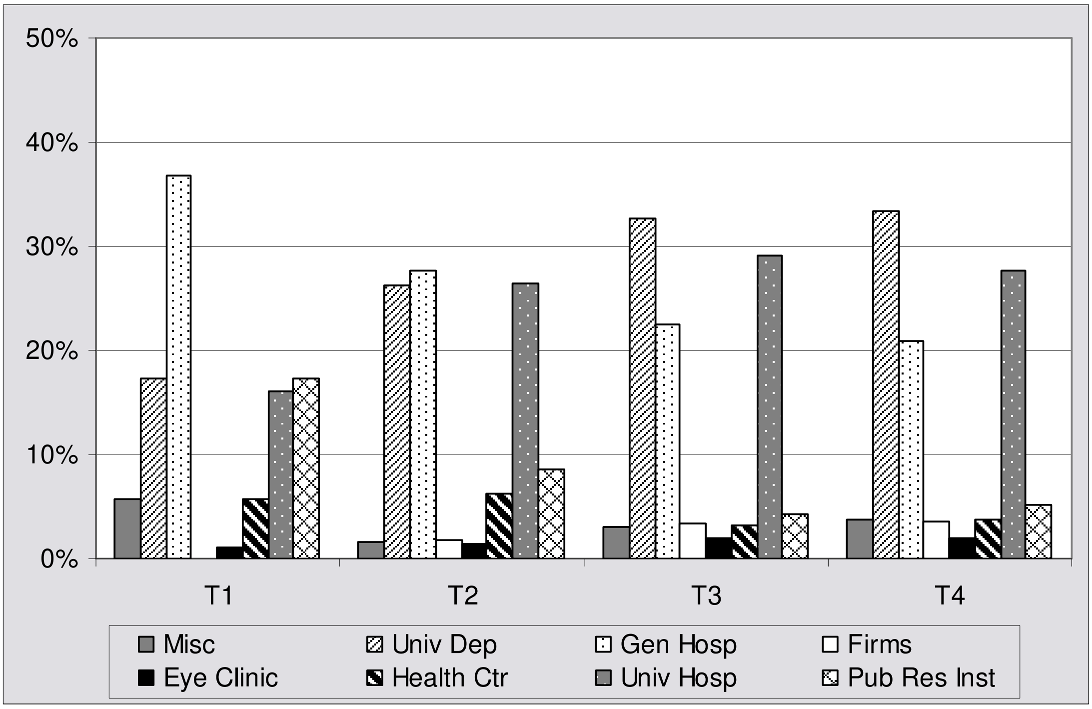

50%
40%
30%
20%
10%
0%
T1
T2
T3
T4
Misc
Univ Dep
Gen Hosp
Firms
Eye Clinic
Health Ctr
Univ Hosp
Pub Res Inst

Figure 2

	T1	T2	T3	T4
Anatomy	1.0%	0.5%	1.1%	1.8%
Animal Studies	1.0%	0.8%	1.4%	1.3%
Basic Science	0.0%	0.0%	0.0%	0.0%
Biology	0.0%	0.3%	3.0%	4.3%
Chemistry	1.0%	0.0%	1.0%	0.8%
Community Stud.	3.9%	1.6%	1.2%	1.5%
Epidemiol/Immunol	1.0%	0.8%	1.6%	1.5%
Genetics	0.0%	0.8%	0.9%	1.8%
Informatics/Statistics	2.0%	1.1%	2.0%	1.5%
Medicine	6.9%	7.6%	9.8%	10.0%
Miscellaneous	0.0%	1.1%	1.0%	1.4%
Neurology	3.9%	2.5%	1.6%	2.8%
Ophthalm & Optom	79.4%	80.0%	70.2%	66.4%
Pharmacology	0.0%	2.0%	2.1%	2.7%
Physics/Engineering	0.0%	0.0%	0.7%	0.4%
Radiology	0.0%	0.2%	0.9%	0.5%

Table 4

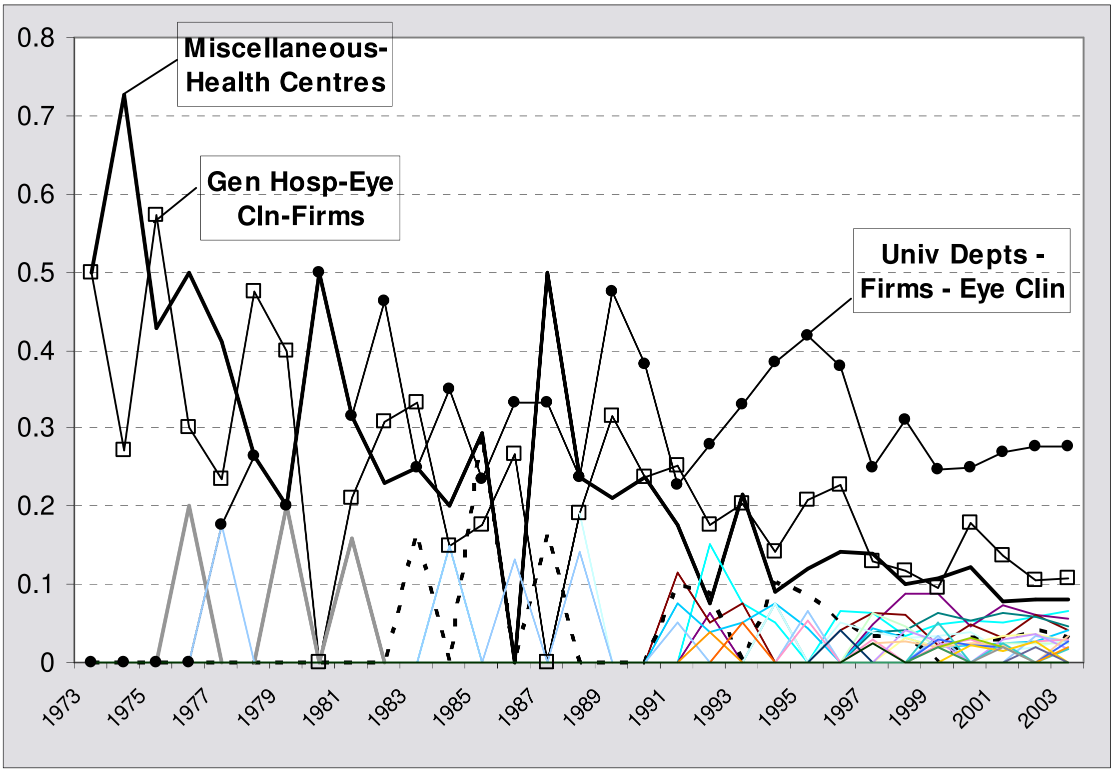

Miscellaneous-
Health Centres
Gen Hosp-Eye
Cln-Firms
Univ Depts -
Firms - Eye Clin
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1973
1975
1977
1979
1981
1983
1985
1987
1989
1991
1993
1995
1997
1999
2001
2003

Figure 3

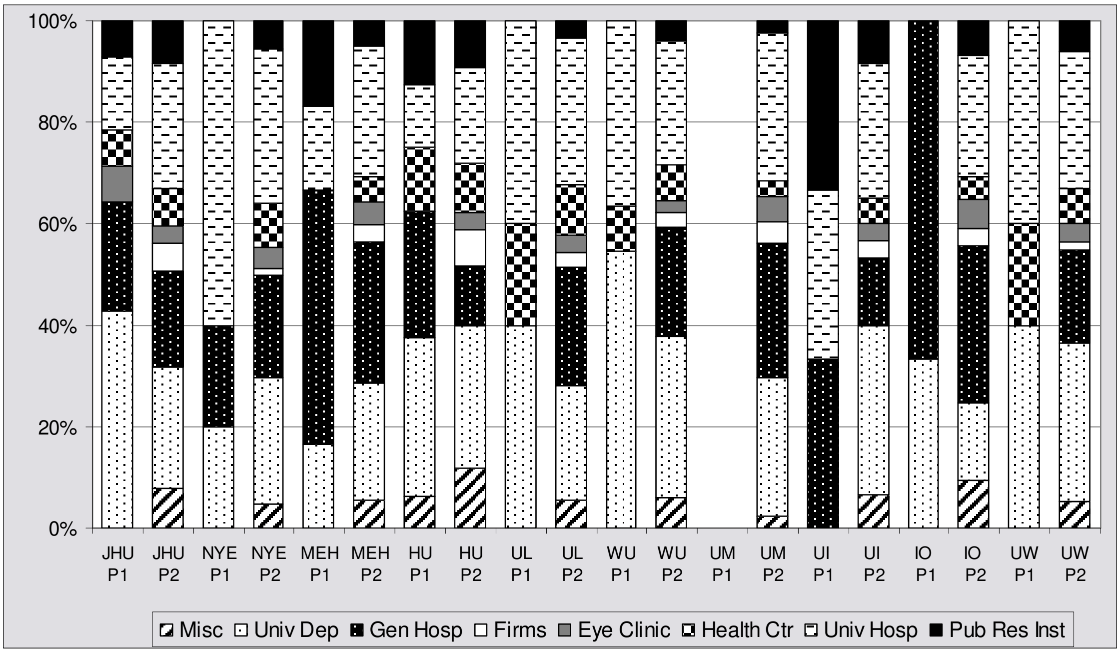


Figure 4*

*** Legenda:** P1 = Period 1 (1968-1985); P2 = Period 2 (1968-2003); Johns Hopkins University = JHU; New York Eye & Ear Infirmary = NYE; Moorfields Eye Hospital = MEH; Harvard University = HU; University of Illinois = UL; Washington University = WU; University of Michigan = UM; University of Iowa = UI; Institute of Ophthalmology = IO; University of Wisconsin = UW.