Knowledge, understanding and the dynamics of medical innovation

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ABSTRACT. *This paper investigates the processes by which scientific knowledge is created and legitimized. It focuses on scientific developments in a branch of medicine and explores the pathways through which the growth of knowledge enables advances in medical science and in clinical practice. This work draws conceptually on evolutionary approaches to technological change. The empirical part presents a longitudinal analysis of a database of scientific publications in the field of ophthalmology over a period of 50 years. Such an exercise allows us to identify pathways of shared understanding on a disease area, and to map out distinctive trajectories followed by the ophthalmology research community. The paper also contributes to general understanding of the innovation process by supporting the notion that knowledge coordination is a distributed process that cuts across and connects complementary areas of expertise.*

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1. Introduction

This paper investigates the processes that stimulate and facilitate the creation and legitimization of scientific knowledge. It is focused specifically on the emergence and the diffusion of new medical understanding and of clinical know-how.

The conceptual foundations of this work are located in the vicinity of the Austrian school of economics. In this view individuals' private knowledge can be connected with – but never identical to – the knowledge of others (Loasby, 1991; Metcalfe and Ramlogan, 2005; Shackle, 1992). This puts learning and communication activities at the core of the process of knowledge growth. An important caveat, however, is that both these activities rely on individuals' perceptions and representations of private knowledge and are therefore prone to imperfections. From this it follows that private knowledge contributes to collective action insofar as interactions across individuals are coordinated through rules that stimulate shared understanding.

The paper casts these issues in the context of medicine with a view to exploring the mechanisms through which scientific understanding about human diseases grows over time. It proposes an empirical study of progress in the diagnosis of glaucoma informed by an historical overview and complemented by a longitudinal analysis of scientific publications over a period of 50 years. The observed expansion in the ecology of ophthalmology journals delineates distinctive trajectories followed by the research community and indicates the emergence of pathways of shared understanding on glaucoma. The resulting maps are a novel methodological contribution to innovation studies in that they synthesize the dynamics of generation and use of knowledge. The broader point that emerges from this analysis is that the growth of scientific understanding unfolds along sequences of problems and solutions which draw on and impinge upon an expanding knowledge base. Such a process requires increasing variety not only in the content of scientific knowledge but also in the standards for its dissemination.

The paper contributes also to the field of innovation studies. Our probe of medical research highlights two crucial conditions under which new knowledge stimulates innovative activities, namely variety in the forms of specialization and the coordinating role of institutions (Loasby, 1999; Nelson, 2002). In so doing it supports the notion that knowledge coordination is a distributed process that cuts across and connects complementary realms, namely the organization of scientific research, the design of regulatory rules, the evolution of communities of practitioners, the delivery of services (i.e. patient care) and the creation of new market processes (Metcalfe et al, 2005; Mina et al 2007; Consoli and Mina, 2007).

The paper is organized as follows. Section 2 presents the conceptual background and casts the dynamics of knowledge in the realm of medicine. Section 3 presents the empirical analysis with an overview of the glaucoma disease and the network analysis of relevant scientific work in the ophthalmology community. The last section discusses the main findings and summarizes.

2. Innovation and the growth of knowledge: the building blocks

The first part of this section introduces the conceptual framework and is followed by an articulation of several key themes germane to the empirical domain of medicine.

Scholarly literature on economics of innovation argues that economic development is an evolutionary process driven by the growth of knowledge in historical (real) time (Dosi, 1988; David, 2001; Loasby, 1991; Nelson, 1995; Antonelli, 2001; Metcalfe, 2001). Works in this tradition highlight three general features of economic action: (i) the cyclical emergence of problems – or bottlenecks, or reverse salients; (ii) the concentration of efforts and development of specific expertise towards the formulation of possible solutions; and (iii) the implementation of such solutions, which typically involves mutual adjustments between the micro-behaviours of the agents and the macro-characteristics of their environment.

The evolutionary approach submits that economic agents are boundedly rational, and can therefore generate and exploit new knowledge only within limited domains and circumstances. The primary reference here is the Austrian school of thought which first suggested that individuals' problem-solving ability is circumscribed by natural cognitive constraints (Shackle, 1992; von Hayek, 1945;

Loasby, 1991, 1998; Ziman, 1978). Decision-making in this view is an emerging feature rather than *ex-ante* prerogative, and it reflects how economic agents strive with learning, applying and communicating knowledge. Metcalfe and Ramlogan (2005) emphasise that all such processes are prone to imperfections because knowledge is a characteristic of individuals' states of mind and as such is not accessible by anybody else. Instead, they argue, private knowledge materializes in practical applications and can only be enriched through exposure to others' representations of individual knowledge. In other words private knowledge can be connected with – but never identical to – the knowledge of others. In turn, private knowledge contributes to collective problem-solving through shared rules of interaction. Metcalfe and Ramlogan propose the notion of 'understanding', a socially distributed process that shapes and directs the communication of private knowledge across individuals through languages, rules of behaviour and shared legal and social settings.[1]

Building on such conceptual premises, evolutionary approaches advance two important propositions. First, the growth of knowledge is a path-dependent process which develops along trajectories of technical and procedural understanding (Dosi, 1988; David, 2001). Second, the efficacy of new knowledge depends on the feedbacks generated by its application in relation to specific problems. Social understanding is central both for the accumulation and the recombination of knowledge. In turn, when the growth of knowledge spans different boundaries innovation (viz. effective problem-solving) is characterised like a collective process that draws on and impinges on a variety of sources (Antonelli, 2001; Kogut and Zander, 2003). Let us now cast these themes in the analysis of medical innovation.

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[1] As Metcalfe and Ramlogan (2005: 658) put it: "We can never say two individuals have the same knowledge, nor devise a way of establishing what they know. We can say instead that as individuals they have the same understanding in so far as they provide indistinguishable or at least closely correlated answers to the same question or if they respond in indistinguishable ways to the same instructions".

2.1 – The growth of medical knowledge

The importance of understanding how progress comes about in the field of medicine can hardly be overestimated if one considers the implications on human and social well-being. The archetypal approach in health economics and health-care management is based on a rather simplified model which holds scientific breakthroughs as the key source of new medical technologies, and portrays the route through to adoption and use as a linear process divided into discrete steps, namely Applied Research, Targeted Development, and Manufacturing & Marketing.

Along with recent contributions in this field, we argue that being built on mistaken foundations linear approaches proffer a limited interpretation of medical innovation, especially *vis-à-vis* empirical evidence on the complexities of scientific research and health-care provision (see Gelijns and Rosenberg, 1994; Gelijns et al, 2001). First, by assuming that the link between R&D and technology adoption is one-way, they neglect the instances in which medical devices are modified to accommodate informed feedback generated by end-users (Von Hippel, 1976, 1988). Second, as Rosenberg (1974) makes clear, the development of science and technology is embedded in specific contexts of use that shape the direction and the timing of invention. Unevenness across the pathways of learning in different areas of expertise generates different cost structures and, *a fortiori*, uncertainty in the adoption and development of new technologies (Nelson, 2003). In the medical realm this is especially frequent when General Purpose Technologies, such as lasers and electronics, are transferred into the clinical setting. A third, and more cogent objection is that linear models suggest that scientific developments are primarily the result of deductive methods aimed at the construction of theories or the solution of theory-generated problems. But accepting that theory-building is the prime goal of scientific research implies that applied sciences are derivative and, thus, that they lack distinctive patterns of cognitive development. Neither of these statements seems pertinent to mission-oriented sciences. The history of medicine, in particular, shows that theoretical, methodological but also philosophical constrains may prevent the formulation of some research assumptions or the selection of specific routes of investigation. This is so because the production and legitimation of medical knowledge is embedded in the long-term development of individual disciplines and reflects the social relevance that is attached to health problems at specific points in time (Amsterdamska, 1987; Blume, 1992; Geljins et al, 2001). Equally relevant is the point that the design and implementation of medical solutions involve integration of knowledge via changes in work practices and relationships. Clearly such processes bear upon interest groups – i.e. professional and organizational – which feature, as Rosenberg (1974) reminds us, different cost structures.

This paper takes the view that medical innovation is a long-term learning process, and explores the notion that the diffusion of new scientific conjectures rests on two complementary conditions: growth in the ecology of forms of knowledge and the creation of coordination mechanisms. In so doing it highlights the role of learning pathways across scientific research and clinical practices, a connection which is arguably over-simplified in the context of linear models. The paper argues that the selection and formulation of medical problems is shaped by theoretical conjectures and practical problem-solving alike. In so doing it suggests that problem-finding and problem-solving belong to complementary dimensions, and that their relative contribution to scientific knowledge depends on the efficacy of the institutional conduits that support Health Innovation Systems. While we deem impracticable to establish *a priori* causations in the dialogue between scientific and clinical domains, we propose an analysis that attempts to disentangle the learning pathways that are embedded in scientific problem-choice and problem-solving.

Figure 1 shows a stylised representation of a health system. This is divided in domains of activities, or ‘gateways’, and connected across through channels of interaction, or ‘pathways’ (Consoli and Mina, 2007; Consoli and Ramlogan, 2008).

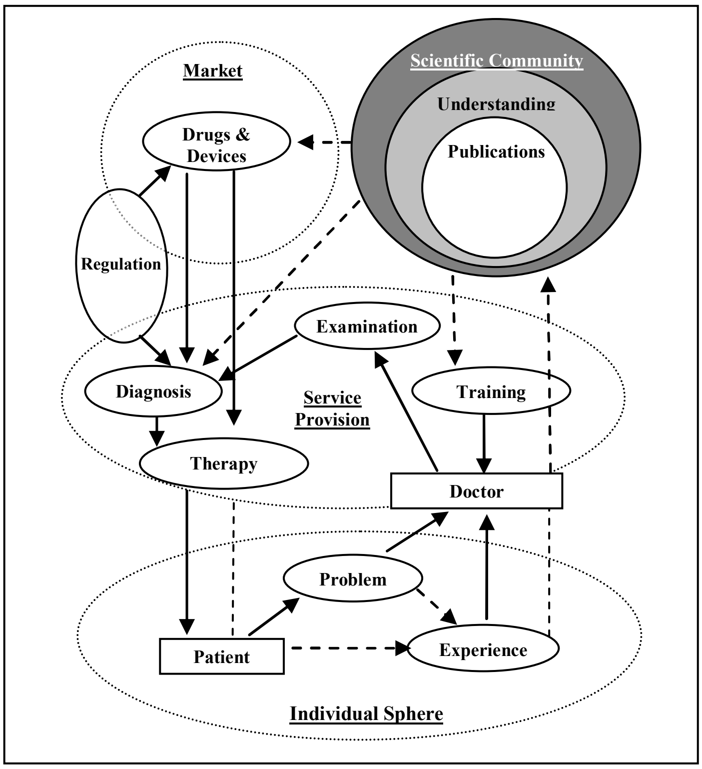

Figure 1. *Gateways and Pathways in a Health System*

The hypothesis that such systems feature different ecologies of expertise and domains of influence is useful to the effect of accounting for the diversity of knowledge involved in health-care. Thereby, gateways correspond to sub-components domains such as the patient-practitioner relation; the system for the provision of patient services (i.e. consultation, diagnosing, choice and therapy) and of medical training; the system of production for medical devices and drugs; the supervisory role of regulation. At the same time the evolution of medical practice involves interactions both within and among the foregoing domains: their instituted coordination through pathways marks the transition from *ecology* of agents to *system* (Metcalfe et al., 2005). The emergence of pathways in a system reflects both the application of knowledge into specific activities, and the exchange of information across the gateways (Consoli and Mina, 2007). Different from linear models of medical innovation, the directionality of pathways does not confine the potential of innovation only to scientific breakthroughs but calls for appreciation of multiple sources across all domains.

It is worth mentioning that the importance of variety in a system of innovation thus defined draws attention on the coordinating task of institutions. Following Loasby (2001) we take the view that scientific progress requires a clearly defined system of understanding to circumscribe the space in which solutions are searched. The notion of pathways presented here accounts for a purposefully broad view of institutions, one that includes formal and informal processes aimed at facilitating the coordination of learning across a variety of interest groups – i.e. gateways – within a health-system. Pathways are, we argue, prime drivers for the growth of medical knowledge and innovation. The synthesis of the dynamics of Health Innovation Systems based on such heuristic notions opens up promising methodological avenues. This view draws primarily on empirically-informed observations and seeks to disentangle how health problems come to the attention of the medical community; how their scientific understanding evolves over time; and how they are ultimately translated into clinical solutions. The empirical part of the paper will cast these themes in the context of a specific area of medical research.

2.2 – Health Systems and Problem Sequences

Reflecting back on the opening statement, that medical innovation involves long-term learning, we focus on the processes that contribute to the growth of scientific understanding and the complementary role of institutional pathways for the diffusion of scientific ideas. Echoing the evolutionary approach outlined earlier, we take the view that innovation represents a systemic response to the emergence of problems in a set of prevailing practices. This process begins with the search for alternatives and experimentation and, if successful, leads to the emergence of novel ideas that challenge existing knowledge and the prevailing system of understanding. Innovations, however, can be rarely if ever pinpointed to a single point in time, or ascribed to isolated sources of knowledge. Innovation comes about through trajectories of improvement *sequences* in which procedures are progressively refined and extended in their scope of application. This process is incremental, it unfolds over time and it implies that as old problems are solved new ones range into view. The latter, in turn, form new foci for innovative effort within the broad objective to improve the efficacy of the extant procedure. Furthermore, by extending the range of application and improving practice, solutions to medical problems challenge the boundaries of scientific understanding and contribute to reshape them.

Our conjecture is that a process thus defined consists in the exploration of a *design space*, unfolding in a largely path-dependent fashion within bounds set by the perception of the problem (Metcalfe et al. 2005). Accordingly, the accumulation of medical knowledge occurs along *trajectories of change* that emerge over time in the search for better and better solutions to clinical problems (Metcalfe et al. 2005; Mina et al. 2007; Consoli and Ramlogan, 2008). Such trajectories emerge in the form of sequences of innovative ideas, reflect coherent directions of change and signal the cumulativeness of research activities whose results build on previous knowledge. These involve also the creation of formal and informal standards (Utterback, 1994) to support the search for novel solutions.

The emergence of such trajectories also implies that the evolution of knowledge is not random but rather driven by guided search within defined design spaces (see Dosi, 1988; Loasby, 1991). In other words, the direction of progress can very rarely be seen *ex ante* meaning that there is little room for determinism in the emergence of trajectories. Research paradigms thus understood are complex processes shaped by the experiences, the competences and the visions nurtured within communities of practitioners.

As already anticipated, the power of theoretical understanding is severely circumscribed in those areas of medicine in which practice and experience come to play a bigger role. The notion of problem sequence captures the idea that the search for solutions in a design space spans a variety of areas of expertise be they clinical, medical, organizational or entrepreneurial. In this view each innovation implies the embodiment of individual knowledge in the design of medical solutions. For the very same reason innovation sequences can halt when the problems are beyond knowledge and imagination and await some breakthrough, possibly in an unrelated body of knowledge.

The overarching proposition that emerges from these observations is that the growth of medical knowledge and its application into changing design spaces fuel the evolution of open systems of scientific understanding. To show this, and taking our cue from the conceptual points discussed before, we focus the empirical analysis on the activity of the scientific community. In terms of Figure 1 we will thus concentrate on the learning pathways in the upper part of the diagram. Scientific and medical communities are important to the effect of catalyzing experiences, exploring alternatives, and designing new clinical solutions. As Langlois and Savage (2001) show, their organization relies on professional networks that are coordinated by means of formal and informal standards. In the next section we will focus specifically on scientific publications whose function is to provide a standard for the dissemination of ideas both within research communities and between the latter and other domains such as clinical practice or the market (Shryock, 1974; Weisse, 1991).

3. Empirical case study: Glaucoma

This section presents an empirical study on the dynamics of medical knowledge in a specific disease area, namely Glaucoma, and is organized in two subsections. The first introduces the nature of the medical problem and highlights the changing boundaries of scientific understanding of the disease. The following subsection integrates this overview with a network analysis of a database of publications in scientific journals with a view to disentangle the pathways of learning observed in the context of the ophthalmology research community.[2]

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[2] For a more detailed version of the case study on glaucoma see Consoli and Ramlogan (2007).

3.1 – Background and overview

Glaucoma is a chronic disease of the optic nerve which, if untreated, eventually causes blindness. Global prevalence of the disease is estimated at 50-70 million, of which 7-8 million finally suffer total blindness (Source: Glaucoma Foundation[3]). Damage caused by glaucoma 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.[4] Despite abundance of theories the pathogenesis and the development of this disease have not been clearly identified yet.[5] Progress in diagnostics has brought about various techniques to detect the onset of glaucoma, but the connection between the degenerative process in the structure of the eye and loss of vision has not been fully clarified. If anything, more accurate research has reinforced the notion that glaucoma is a complex disease, and that ophthalmology has still a limited grasp of the connections among causes and symptoms.

A quick look at the history of ophthalmologic research and practice highlights two phases of scientific exploration. The first (1880s-1960s) is characterized by the dominance of the Intra-Ocular Pressure paradigm which has shaped research efforts and the creation of important diagnostic techniques but has also led to blind avenues. Refutation of the latter conjecture is the thrust of the second phase (1970s-2000s) in which the research community has explored increasingly diverse routes of investigation.

The clinical diagnosis of glaucoma in the early days was based on the interpretation of symptoms of the glaucomatous eye, usually swollen and congested. Accordingly, the prevailing diagnostic techniques were based on the observation of the iris, which regulates the entry of light in the eye similar to the aperture of a camera. In this area is found an aqueous humor which has the important role of

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[3] http://www.glaucomafoundation.org/

[4] The optic nerve plays a fundamental role as it connects the eye to the brain.

[5] A comprehensive, yet accessible also to non-practitioners, overview of the state-of-the-art in research on glaucoma can be found in the authoritative article by Quigley (2004).

bathing the lens and the cornea. The pressure of this fluid, Intra Ocular Pressure (IOP), regulates the nourishment of the optic nerve which is in the inner part of the eye. It is well known that elevated pressure can obstruct the microcirculation of blood and, in turn, if blood does not properly nourish the optic nerve some of its tissues die causing an excavation, known as 'cupping'. The prevailing scientific understanding of glaucoma until the mid-1950s was based on the notion that glaucoma is solely associated to abnormal levels of IOP.

The guiding heuristic for the design of early diagnostic techniques sought to enhance visualization of the inner part of the eye and to achieve reliable measurement of IOP. The standard instrumentation in an ophthalmologist studio in the first half of the 1900s included direct and indirect techniques (Consoli et al, 2005). Among the former were visualization tools such as the *ophthalmoscope*, to observe the optic nerve; the *funduscopy* to examine the back of the retina through a dilated pupil; and the *gonioscope*, a variation of the former two techniques used to scrutiny the anterior chamber of the eye. These were used together with the *tonometer*, an instrument to measure the eye pressure which featured two basic variants (e.g. indentation and applanation). Direct techniques seek to provide an objective assessment of the structural feature of the eye. Indirect ones, such as *perimetry*, instead are based on the collaboration of the patients who is required to report on perceived alterations of the visual field. This particular technique which was originally developed in the context of patient care and later used for laboratory research, offers a clear example of the flawed logic of linear models. In fact, the design of most of such instruments went through significant changes as a result of the interplay between scientific research and clinical care, also aided by the assimilation of new sophisticated technologies for digital imaging (i.e. Scanning Laser Ophthalmoscope, Scanning Laser Polarimetry) and digital measurement (i.e. Electronic Indentation Tonometer).

Beginning the 1960s the notion that glaucoma manifests itself homogeneously had been abandoned following empirical evidence that pointed to three major forms of the disease: primary open angle glaucoma (POAG), primary acute closed angle glaucoma (PACG) and primary congenital glaucoma (PCG), as well as a few others associated with developmental abnormalities (Duke Elder, 1959). The discovery of POAG is particularly important for the future of ophthalmologic research because it showed that disease is not always related to abnormal IOP levels. Interestingly, this new conjecture started in the clinical setting and not in theory-based work, and fuelled several epidemiological (i.e. population-based) studies which confirmed that glaucoma is a demographically-selective disease. The Collaborative Glaucoma Study, the Beaver Dam Study and the Baltimore Study among others, collectively contributed to a detailed picture of the incidence of glaucoma according to age, racial background, existence of glaucoma in family history or the co-presence of heart diseases. These studies also revealed important differences between the Open Angle Glaucoma (OAG) and Angle Closure Glaucoma (ACG), although the majority of studies have been concerned with 'definite cases' of Primary OAG.

Such a broader understanding of the disease coupled with the only partial success of existing techniques led the scientific community to explore new routes and to intensify clinical-based work. As Nelson (2005) has often noted, this kind of turn of events is typical of practice-based sciences, for the ability to provide effective solutions to medical problems does not always imply synchronism between scientific understanding and the prevailing forms of clinical practice. Rather, these will probably advance at an uneven pace.

The following phase of scientific research in the 1970s followed the conjecture that glaucoma can be assimilated to some form of neuropathy, and tested through diagnostic scanning of physical changes in the optic disc (see discussion in the following section). Subsequently as the notion that disc changes are always a factor in glaucoma patients was undermined, attention shifted to the diverse manifestations of the disease, and its changing degrees of intensity across patients. Other than reaffirming once more the partial inadequacy of existing diagnostics, it became clear that the correct interpretation of individual features of each patient may lead to early detection of glaucoma, even before any damage occurs. To this novel direction of research are associated novel diagnostic techniques – like the Retinal Nerve Fibre Layer (RNFL) assessment – based on the examination of factors that are independent from changes in the optic disc. These issues mark a clear step in the direction of modern genetic investigation. The discovery of the genetic cause associated to glaucoma in 1994 has radically altered the course of research and stimulated cross-fertilization of ophthalmology with specialist areas like molecular biology and genetics.

It is now clear that glaucomas (now commonly used in the plural form) are a heterogeneous group of eye conditions with manifestation from early in life to late age and with different genetic bases. Interestingly enough, though the unitary association between IOP and glaucoma has been challenged for some fifty years, treatment is still largely based on the variants of the IOP-lowering axiom with the recent addition of laser surgery. This is so because elevated intraocular pressure remains the most easily treatable factor. In fact, greater specialization in pharmacotherapy has brought about a spur of alternatives like selective and nonselective β-blockers and inhibitors. As a consequence, prescribed regimens have now evolved into patient-specific combinations of these medications. New research is seeking to operationalize improved understanding on the aetiology of glaucoma and to generate therapies for those cases that cannot be treated with IOP-lowering techniques. The field of gene therapy holds great promises and is expected to trigger significant advances, though the practical implementation of this type of treatment is still at its infancy. Again, it seems clear that advancements in basic research (i.e. genetics) proceed unevenly with respect to practical applications that may be implemented.

Summing up, scientific progress in glaucoma indicates that despite many advances key questions about this disease still loom large: can glaucoma be detected with certainty? Can it be cured? If so, how? Such, we surmise, is the nature of progress when the problem is inaccurately specified, or too complex to understand given the prevailing knowledge base.

3.2 – A network analysis on Glaucoma research

In this section we use network analysis to highlight the pathways of learning within the glaucoma scientific community. The primary source is a database of bibliographic information of over 13,000 scientific articles about glaucoma over the period 1945 to 2003 drawn by the authors from the ISI Thompson online resources. To parse the data we developed a Perl script and implemented it within the Pajek software.[6] In particular, we employ the idea of the main path algorithm that is incorporated into Pajek (Batagelj, 2002). This method was first proposed by Hummon and Doreian (1989) in their analysis of the development of DNA theory. In that paper and in a subsequent study of the literature on measures of centrality in social networks research (Hummon and Carley, 1993) distinctive pathways through the respective citation networks were found to be related to the key intellectual developments that defined the respective fields (see also Carley et al., 1993).[7]

The main path captures a structural feature of a network that contrasts with the orthodox approaches such as bibliometric coupling or co-citation, used for studying structure, in that these latter approaches focus on the clustering of nodes. The novelty Hummon and Doreian proposed is to make use of the links of the network rather than the nodes, that is, on the network's connectivity. Thus the algorithm captures what is referred to the 'structurally determined most-used path' in a network; it is the path with the *highest traversal counts* (Batagelj and Mrvar, 1998), measured by the number of times that a tie or link between articles is involved in connecting other articles in a citation network (Hummon and Doreian, 1989). The main path analysis thus analyses all possible search paths through the network starting with an origin article through to endpoint articles, and calculates the traversal counts of each link in the network.

Figure 2 shows the main path emerging from our network of over 300,000 nodes made up of the primary references and their citations. The algorithm selected the connections between these 43 nodes as being the most important in the network and interestingly, as we discuss below, they synthesise the brief journey in the history of glaucoma research outlined previously.[8]

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

[7] Besides the authors' cited works, other innovation scholars have recently employed this method to analyze patent citations on fuel cell research, e.g. Verspagen (2007), and data communication standards, e.g. Fontana et al (2008).

[8] It is not possible to visualize the entire network. For our purposes we capture and display essential aspects of it. In this respect although main path connections are

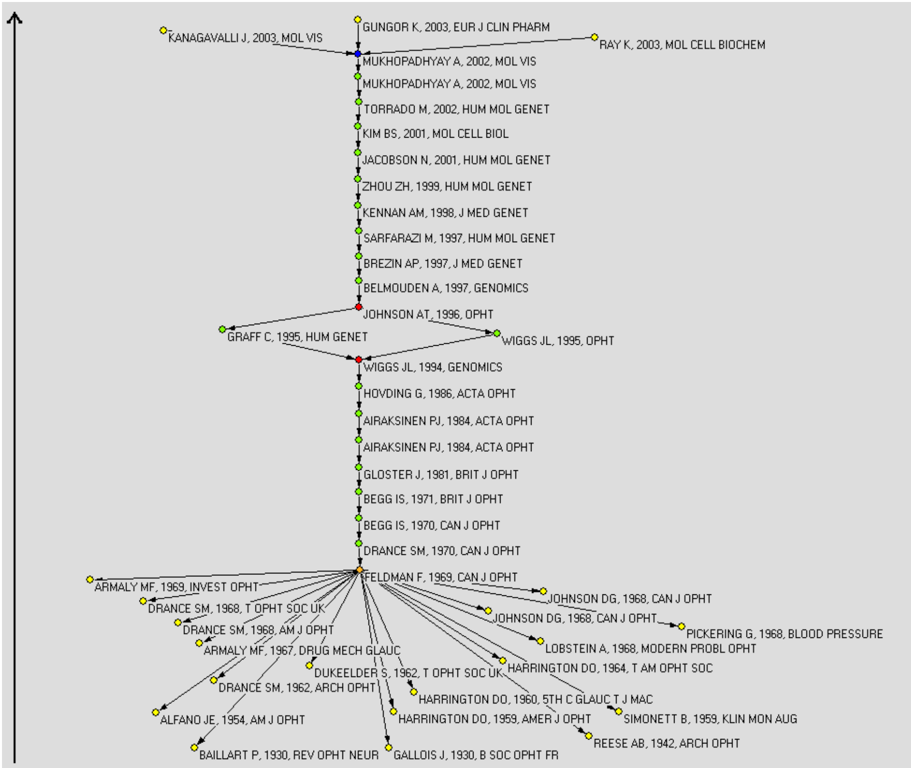

Figure 2. *The main path of Glaucoma research*

The graph is organized temporally starting with some of the earliest citations in the 1930s and finishing at three papers which represent the end point of the study. The nodes connected to Feldman (1969) at the bottom of the diagram represent the IOP paradigm discussed earlier. Subsequently, Drance and Begg (1970) and Begg et al (1971) put forward the hypothesis that glaucoma is a neuropathy. In the following decade the path-breaking work by Airaksinen and Tuulonen (1984) finally refuted the idea that optic disc changes are always a factor in glaucoma, and highlighted that the pathogenesis of the disease differs to a substantial degree. Finally, Høvding and Aasved (1986) established the impact of family history on glaucoma patients.

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presented in a linear fashion, the reader is warned not to represent the process as linear. In fact the trajectory of the main path meanders across the glaucoma search space and the layout of the map is just a convenient way to compact the journey.

This confirms the historical background discussed in the previous section, and points to the emergence of new scientific understanding which later paved the way to genetic-oriented studies on glaucoma, located in the upper part of the main path diagram. The works of Sarfarazi (1997) and Ray et al (2003), in particular, inform on the recent spur of techniques seeking to map various types of glaucoma in relation to specific genetic mutations.

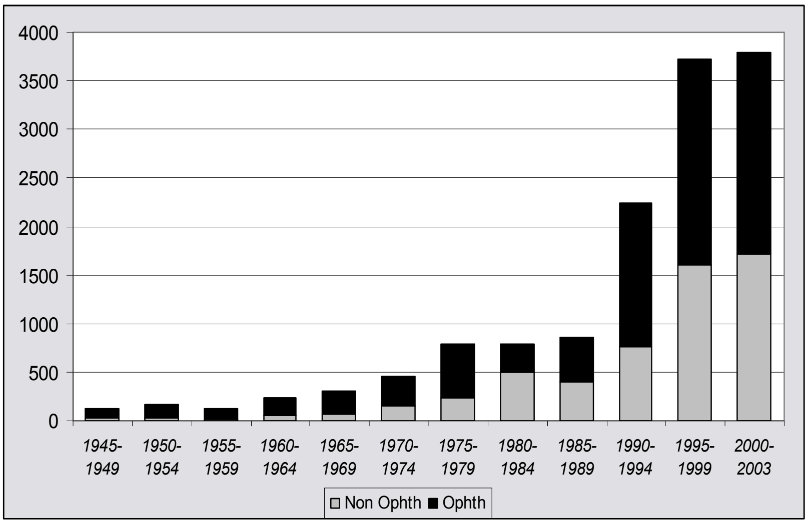

Figure 3. *Glaucoma Journal Population*

So far individual papers have been used as unit of analysis. Let us now shift the focus slightly. Figure 3 provides a breakdown of the ecology of scientific journals in our dataset and confirms the tendency towards greater variety: beginning the 1970s almost half of the articles on glaucoma have been published on journals whose scientific scope falls outside the traditional boundaries of Ophthalmology, and span diverse areas of medicine.

Subsequently, if we use a variation of the main path algorithm and focus on journals as the unit of analysis, can we capture the changing pathways from a network perspective? To answer this question we recoded our data to illustrate the significance of the non-traditional journals. Figure 4 shows the journal-journal citation network obtained.[9]

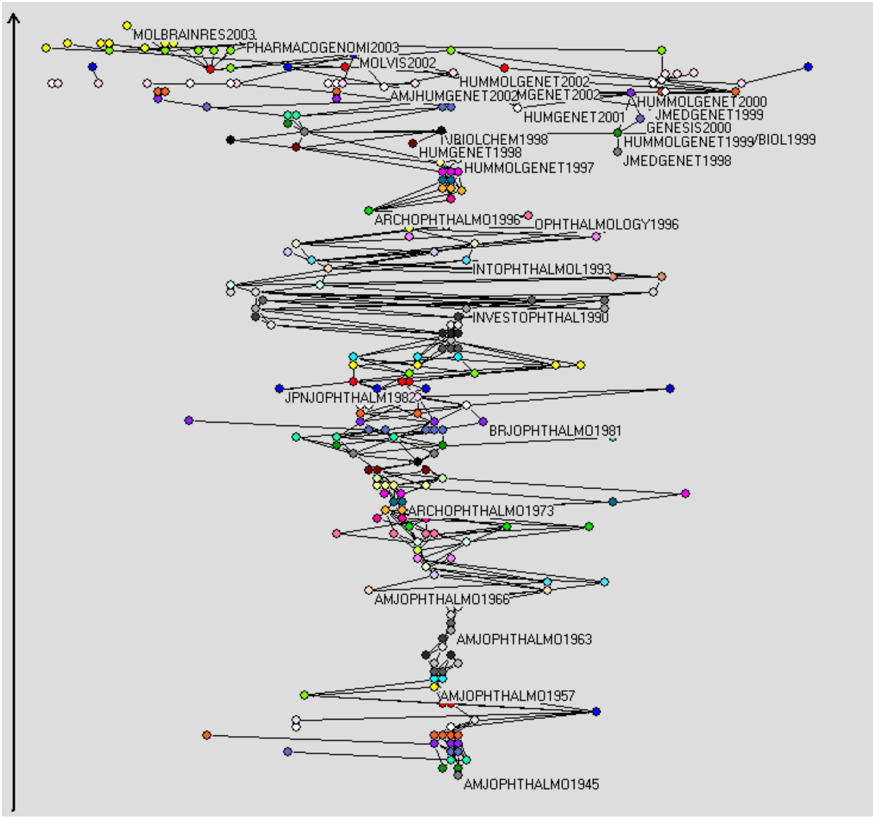

Figure 4. *Longitudinal Analysis of the Network*

This diagram provides two overriding indications. First, there is a clear pathway from the early period, 1945, through to 2003. Second, and more importantly, the network of citations features a 'broadening' in the upper part with several non-traditional journals that now make up the ophthalmology ecology. These include Pharmacogenomics, Molecular Brain Research, Molecular Vision, Journal of Biological Chemistry, Human Molecular Genetics, Journal of Medical Genetics. This development roughly corresponds to what had been observed in

[9] We limit the amount of nodes in this diagram to 235 and label only selected journals to improve the readability of the map.

the main path of the papers in Figure 2. Interestingly, these branch out from the main path of traditional journals such as British Journal of Ophthalmology, American Journal of Ophthalmology and Archives of Ophthalmology.[10]

Recall that earlier we raised the point that scientific publications represent a *de facto* standard for the coordination of information exchange within and across scientific communities. Professional scientific journals have long been recognised as being a vital channel in the communication system of contemporary science (Ziman, 1968). In the field of Scientometrics, journal-journal citations are widely used to indicate changes in science. Such networks provide a rich domain to observe the emergence and death of individual units and clusters of journals at various levels of aggregation, that is, journal mappings can be used to indicate changes in science (Leydesdorff, 1994, 2003). Taking technological breakthroughs in natural sciences as empirical probes, Leydesdorff and various coauthors (Leydesdorff & Gauthier, 1996; Van den Besselaar & Leydesdorff, 1996) concluded that new developments can be traced in terms of the being cited patterns of journals. New developments attract attention by scholars in neighboring fields and therefore journals reporting on these new developments are cited to a significantly larger extent than in a previous year.

In sum, taking journals as a unit of analysis enables us to reflect on the observation that as knowledge grows the design space expands qualitatively in that it involves the cross-fertilization of different areas of scientific expertise. In turn, we see the expression of this in the form of additions to the ecology of journals related to a specific problem, such as glaucoma. We argue that the proliferation of this particular professional standard is one of the signatures of the emergence of new branches of sub-specialization. Tracking journals helps us to capture emerging pathways among the different research communities to a greater degree than individual papers (see Metcalfe et al, 2005; Mina et al 2007; Consoli and Mina, 2007; Consoli and Ramlogan, 2008; Ramlogan et al, 2007).

[10] Journals were classified as tradition or non traditional according to whether the word ophthalmology (in English or otherwise) appeared in their title.

4. Concluding Remarks

This paper has investigated the processes by which scientific knowledge is created and legitimized. More specifically, it has focused on a branch of medicine with a view to exploring the pathways which enable the emergence and the diffusion of new medical understanding and its translation into effective clinical practice.

The paper explored the idea that medical innovation is a long-term learning process, and that the diffusion of new scientific conjectures is driven by two complementary processes: growth in the ecology of forms of knowledge and the emergence of coordination mechanisms. Accordingly, it proposed the notion that the selection and formulation of medical problems is shaped by theoretical conjectures and practical problem-solving alike. It delved on the directionality of learning pathways across scientific and clinical practices by applying network analytical methods to a dataset of Glaucoma publications. Through the application of the Main Path algorithm we have mapped a cross section of important papers in this scientific medical community. The selection of papers captures and confirms the changing trajectory that has occurred in Glaucoma research over the past fifty years. We have been able to document the transition from a single cause paradigm (i.e. Intra Ocular Pressure) to a multi causal explanation of the disease and reflect on the fact that problem-finding and problem-solving are complementary processes. Therefore, while we claim that it is not possible to establish *a priori* any directionality in the dialogue between scientific and clinical domains, we propose an analytical route to disentangle the pathways of learning embedded in scientific problem-choice and problem-solving activities.

The longitudinal analysis undertaken also enabled us to highlight the expansion of the ecology of scientific journals, and connect this to the growth of knowledge. In so doing it interprets the evolution of a *de facto* standard, namely the journal, which facilitates information exchange within and across scientific communities. We have also argued that their proliferation is one of the signatures of the emergence of new sub-specialization.

Overall the paper contributes to the general understanding of the medical innovation process. It supports the notion that knowledge coordination is a distributed process that cuts across and connects complementary realms encompassing the organization of scientific research, the design of regulatory rules, the evolution of communities of practitioners, the organization of patient care and the creation of new market processes.

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