The distributed organization of science : with empirical illustrations from the field of diabetes medicine

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Sjoerd Hardeman

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With Empirical Illustrations From the Field of Diabetes Medicine

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1. The distributed organization of science[1]

1.1. Introduction

Many problems confronting contemporary society are of global relevance. People all over the world are implicated by environmental, health and economic crises (Beck 1992). Given that these risks are of global relevance, the current mantra dictates that solutions ought to be provided through the involvement of many different. For example, a recent report of the World Trade Organization is aptly titled "*Global Problems, Global Solutions*" (World Trade Organization 2010), suggesting that tackling current crises requires not just the involvement of the privileged few, rather than the involvement of the many implicated. Likewise, the president of the International Social Science Council Gudmund Hernes recently advocated an integrated approach to science "*where the humanities and the natural and social sciences jointly address natural phenomena, social processes, institutional design, cultural interpretations, ethical norms and mindsets*" (UNESCO 2010 p. ix). Hence, it is argued that given the distributed nature of contemporary problems, the organization of problem solving activities – with science as its hallmark – ought to be distributed as well.

In what follows we will develop an analytical understanding of the distributed organization of science. As a first approximation let us define science to involve both a particular means of production (methods, instruments, and people) as well as a particular outcome (solutions, knowledge, and truth). New technologies, public policies, contemporary art, and today's media all reflect traces of science. In addition, not only is science performed within university laboratories; so do companies and government agencies involve themselves with science. The distributed organization of science is then reflected by its activities being pursued around the globe and its knowledge having implications in all domains of society.

One can describe the main tenet of a distributed organization of science as follows: a distributed organization of science involves a science in which a heterogeneity of actors and their claims are not only to be found in the involvement of many different domains of society, so are these actors and their claims connected in all their heterogeneity. It follows that we take science as constituting an inherently interactive (i.e. collaborative) phenomenon. Interactions then take place within science among those concerning themselves with science as well as between science and society at large in the continuous provision of and demand for solutions to particular problems. That is, actors from different domains of society are in principle 'allowed' to engage with science. The extent to which different actors actually concern themselves with science and in addition are also connected to each other is an empirical issue.

1.2. Modes in the distributed organization of science

Throughout the literature many conceptualizations are proposed to describe the distributed organization of science. Castells (1996 esp. pp. 407-459) for example, in an attempt to describe the means through which physically distant practices become congruent, speaks of "*spaces of flows*". In science, communications among scholars have been institutionalized by its publication system.

[1] To be submitted as: 'Hardeman S. (2012) The distributed organization of science.'

In addition, temporary meetings such as conferences and guest scholarships further facilitate collaboration among distant scholars. Of course, as in other spheres of society, scholars nowadays also maintain extensive communications via internet fora, email, and the like. Hence, the activities of geographically distant actors in science can be described as taking place within "*a circuit of electronic exchanges*" (Castells 1996 p. 441). Alternatively, Leydesdorff and Etzkowitz (1996) and Etzkowitz and Leydesdorff (2000) discuss the emergence of "*a Triple Helix of university-industry-government relations*". They stress the institutionally hybrid arrangements shaping science and innovation in contemporary collaboration networks. Rather than focusing on the geographical aspects to collaborative science and innovation, the Triple Helix concept emphasizes the institutional and functional segmentation and integration in knowledge production activities. Yet another example is provided by the notion of open innovation emphasizing that the crossing of firm boundaries might render innovation activities more fruitful (Chesbrough 2003). While closed innovation follows a philosophy of self-reliance in which each organization individually generates, develops, and commercializes its own ideas, in open innovation organizations generate, develop, and commercialize ideas of their own as well as of other organizations. In an open regime then, collaborative science and innovation more frequently takes place across organizations.

The three examples discussed here focus on respectively the geographical, institutional, and organizational aspects of distributed science. Hence, in focusing on one dimension to a distributed science only, these conceptualizations of knowledge production can be accused of being too restricted in their accounts. A comprehensive account on the multidimensional organization of science is provided by the notion of various modes of knowledge production (Gibbons et al. 1994; Gibbons 2000; Nowotny et al. 2001; Nowotny et al. 2003). The idea of various modes of knowledge production is inclusive in that, instead of focusing on a single aspect of the organization of science such as the physical sites or institutional spheres in and across which science takes place (as for example in the notion of national innovation systems), the idea of modes of knowledge production appeals to an understanding of science as being organized along multiple dimensions (Hessels and Van Lente 2008). Using the notion of various modes of knowledge production, the distributed organization of science is characterized in terms of a collaborative phenomenon in which actors from different organizations, located at different sites, operating under different institutional norms and rules, and from different disciplinary and social backgrounds, jointly produce knowledge in an attempt to solve the problems society is confronted with.

1.2.1 Gibbons et al. (1994): The new production of knowledge

The first book on modes of knowledge production is titled "*The new production of knowledge: the dynamics of science and research in contemporary societies*". This book then is an attempt to provide a description of current trends in the organization of knowledge production. The argument holds that a new (Mode 2) form of knowledge production is unfolding alongside a traditional (Mode 1) form of knowledge production.

Mode 2 knowledge production is characterized along five dimensions and contrasted with Mode 1 knowledge production. First, Mode 2 knowledge production proceeds within a context of application. In other words, knowledge produced under Mode 2 "*is intended to be useful to someone whether in industry or government, or society more generally and this imperative is present from the beginning*" (Gibbons et al. 1994 p. 4). The importance of a context of application under Mode 2 knowledge production resembles the idea of user-inspired research taking place in

Pasteur's quadrant (Stokes 1997). Under Mode 2 knowledge production, research is not just driven by a quest for a fundamental understanding of natural and social phenomena but is also driven by an explicit consideration of societal benefits. The idea of a context of application is contrasted with the disciplinary context of Mode 1 knowledge production whereby "*the context is defined in relation to the cognitive and social norms that govern basic research or academic science*" (Gibbons et al. 1994 p. 4). While under Mode 1 knowledge production is directed at a search for fundamental principles, under Mode 2 knowledge production is directed at the provision of contextualized solutions.

Second, the notion of Mode 2 knowledge production is characterized by transdisciplinarity. Transdisciplinarity is described as a problem-oriented search that transcends disciplinary boundaries (Gibbons et al. 1994). Transdisciplinary research facilitates the successful provision of comprehensive solutions to complex problems (Stokols et al. 2008). In fact, Gibbons et al. (1994 p. 5) argue that under Mode 2 "*the shape of the final solution will normally be beyond that of any single contributing discipline.*" In a way then, transdisciplinarity is taken as the mirror image of societal problems: complex problems require complex problem solving approaches. In addition, the media in which outcomes of Mode 2 knowledge production are expressed are not necessarily those that are traditionally associated with science. Rather, the outcomes of knowledge production under Mode 2 are communicated to those directly implicated by or enacting upon the outcomes. While under Mode 1 knowledge production solutions are communicated within designated disciplinary media such as journals and conference talks, under Mode 2 knowledge production solutions are communicated directly to the audiences implicated. Both in its practices and in its communications then, Mode 2 knowledge production transcends disciplinary boundaries.

Third, under Mode 2, knowledge production is crossing national and cultural boundaries. Here, knowledge production becomes "s*ocially distributed*" across different organizational, institutional, and geographical contexts (Gibbons et al. 1994). That is, Mode 2 knowledge production is marked by "*an increase in the number of potential sites where knowledge can be created; no longer only universities and colleges, but non-university institutes, research centres, government agencies, industrial laboratories, think-tanks, consultancies*" (Gibbons et al. 1994 p. 6). In contrast, Mode 1 knowledge production refers to a traditional view on science. That is, science as taking place within universities and nationally organized university systems. Of course, Mode 1 knowledge production is distributed in the sense that university research takes place across the world. Yet, under Mode 2, not only does knowledge production take place accross a wide range of sites, so are the interactions among these sites no longer hampered by their diverse characteristics. Under Mode 2 knowledge production, collaboration takes frequently place across organizations located in different parts of the world and operating under different institutional norms and rules.

Fourth, Mode 2 knowledge production is socially accountable if not reflexive. Social accountability is related to the heterogeneous composition of teams under Mode 2 knowledge production. Given that Mode 2 knowledge production involves actors from different institutional domains of society, its activities are legitimized in these different domains as well. Likewise, Mode 2 knowledge production thrives on reflexivity. Through involving actors that are affected by the outcomes, actors will anticipate on these outcomes throughout the process of knowledge production. According to Gibbons et al. (1994 p. 7) "*working in the context of application increases the sensitivity of scientists and technologists to the broader implications of what they are doing. (…) This is because the issue on which research is based cannot be answered in scientific and technical terms only.*" In other words, social, ethical, juridical and other considerations are taken into account by definition under Mode 2 knowledge production by virtue of involving different actors.

Fifth, under Mode 2 knowledge production new forms of quality control emerge (Gibbons et al. 1994). As the media in which the outcomes of Mode 2 knowledge production are not restricted to disciplinary outlets, the ways in which the value of these outcomes comes about is not restricted to peer review. As a consequence, the criteria on which outcomes become accepted as solutions broaden as well. That is, not only need solutions stand the test of theoretical and methodological rigor as judged by peer experts, they should also stand the test of social, economic, and political rigor. Quality is not only addressed in terms of the correspondence of particular assertions to 'nature', but also involves considerations of competitiveness, cost-effectiveness, social desirability, and user-friendliness. Under Mode 2 knowledge production the assessment of quality follows from the success of applied solutions.

In all then, Mode 2 knowledge production is defined as "*Knowledge production carried out in the context of application and marked by its: transdisciplinarity; heterogeneity; organisational heterarchy and transience; social accountability and reflexivity; and quality control which emphasises context – and use-dependence. [Mode 2] Results from the parallel expansion of knowledge producers and users in society*" (Gibbons et al. 1994 p. 167). As explained and further illustrated in table 1.1, the five-fold characterization of Mode 2 knowledge can be contrasted with Mode 1 knowledge production (see also Godin 1998 p. 466). While Mode 2 knowledge production is characterized by its context of application, transdisciplinarity, manifold connected sites, social accountability and reflexivity, and new (alternative) forms of quality control; Mode 1 knowledge production is characterized by its academic context, mono-disicplinarity, individual bounded sites, autonomy, and traditional peer review.

Table 1.1. *Mode 1 versus Mode 2 knowledge production*

Mode 1 knowledge production	**Mode 2 knowledge production**
Academic orientation	Orientation of application
Mono-disciplinary	Trans-disciplinary
Restricted number of individual sites	Manifold connected sites
Autonomous and linear	Socially accountable and reflexive
Peer review	Multiple and dynamic quality assessments

In addition Gibbons et al. (1994) discuss a number of developments that give rise to and go along with the new Mode 2 production of knowledge. One such development involves the intensified pressures of international competition among companies. On the one hand then, an ever increasing demand for innovation from society pushes academia towards becoming entrepreneurial (Etzkowitz et al. 2000). In order to legitimize their work, academia continuously has to make clear the societal relevance of their activities (Rip 1997). Knowledge brought about in science needs to be marketable. On the other hand, as science is an important source of innovation (Dosi 1988), not only is academia pushed into the domain of the market, so are non-academic actors such as those in industry and government pulling science into their activities (Rosenberg 1992). For industry, getting involved in science provides absorptive capacity that enables them to keep up with the latest technologies (Gamberdella 1994). In addition, being involved in science enables industry and government to attract talented scholars (Hicks 1995). What is more, scientific knowledge produced by firms can be used to legitimize goods in the market (Azoulay 2002). In all then,

within the current discourse of competitiveness and innovation, the boundaries between academia and non-academia, science and innovation are blurred.

Another development involves the masification of research and education. Here Gibbons et al. (1994) argue that scientific knowledge is no longer confined to the realm of the university laboratory but has spread into other kind of organizations as well. This is not just a rehearsal of the claim that while academia is pursuing activities beyond science, industry and government are also pursuing academic activities. Rather, it is to argue that higher education has opened up to many segments of society. Likewise, scholars are no longer employed by traditional research organizations only but work elsewhere as well. Hence, it is not only expected that the activities of non-academic actors such as those from industry and government have extended into the domain of science; via educated people working in industry and government an academic rationale of performing activities is expected to have entered the domain of the market and the state more generally. In all, we can thus speak of a "*Verwissenschaftligung der Gesellschaft*" (Weingart 1983).

Yet another development involves the role played by the humanities in the constitution of (Mode 2) knowledge. Going from the assertion that apart from technology the marketability of new product innovations is derived from their symbolic value, Gibbons et al. (1994) argue that in this latter part of innovation the humanities play an important role. Given the role played by social and political considerations in the context of application, the humanities are considered important under Mode 2 knowledge production. From the importance of cultural production it is thus argued that the humanities will play an important role alongside engineering and the 'hard' sciences.

A fourth development involves globalization. In light of problems that are of global relevance (environmental risk, health issues and the like), solutions are demanded that span different localities. Under globalization, science and innovation affect people all over the world. However, globalization does not imply that knowledge automatically becomes distributed evenly (Beck 1992). Nevertheless, given a reduction in transport costs and the increase in information and communication technologies, the organized provision of solutions to contemporary problems ought to take place among actors all over the world (Gibbons et al. 1994).

A fifth development involves the blurring of boundaries of organizations and institutional spheres. Again Gibbons et al. (1994) argue that the functions of organizations, and especially universities, are changing if not expanding in the range of activities they perform. In addition, it is argued that different organizations become increasingly linked. These changes then both challenge and change the nature of once stable institutions. The boundaries of organizations involved in knowledge production are hard to define from the outset. Hence, as the institutional and organizational boundaries among those involved in knowledge production become porous, the system of knowledge producing actors are perhaps better described as an organizational field (DiMaggio and Powell 1983). Alternatively, every individual organization can in itself be described in terms of involving multiple value spheres (Stark 2009). What holds then is that the actors involved in knowledge production can be described along multiple dimensions. Organizations are continuously in flux in the kind of activities they perform and the way in which they perform those activities.

A final development involves the ability to steer or manage knowledge production activities. Here the authors become normative in their plea for stimulating Mode 2 knowledge production. To our understanding it is not that Gibbons et al. (1994) favor either a position stressing the potential harm commercialization does to the operative performance of science or a position stressing the

potential benefits of close university-industry interaction for exploiting scientific knowledge commercially. Rather, the authors take a more ambivalent position arguing that given the omnipresence of these pressures, Mode 2 knowledge production should be taken as a logical consequence. Gibbons et al. (1994) thus seem to argue that whether we like it or not Mode 2 knowledge production is here to stay and hence requires to be approached by policy on its own terms (see also Rip 2002).

1.2.2 Nowotny et al. (2001): Re-thinking science

The second book on Mode 2 is titled "*Re-thinking science: knowledge and the public in an age of uncertainty*". Whereas the first book presents a somewhat internalist image of science (or what is then still called knowledge production), the second book sketches a more externalist image of science in focusing on its relation to society at large. The main contribution of this second book then is centered on four main arguments.

First, the emergence of Mode 2 knowledge production – with science as its most vivid exponent – is taken in light of a more general emergence of a Mode 2 society. Not only do the boundaries of science become blurred, so do the boundaries of other societal spheres such as the market, the state, and culture (Giddens 1990). In addition, due to the success of science and the ubiquitous demand for innovation from society at large, uncertainties prevail. As different spheres of society jointly bring about novel goods whose implications are unclear, both the production of solutions and risks become endougenous (Beck 1992). The blurring of boundaries of societal spheres and the endogenous production of new risks and solutions, together create a situation in which the state, the market, the arts, and indeed also science become ever more invasive as well as invaded by each of these other spheres. Hence, the notion of Mode 2 is extended to include a description of society at large in which once separate societal spheres – including science – become ever more blurred.

Second, from recognizing the transgressive nature of society, Nowotny et al. (2001) continue to argue that as a consequence science requires ever more contextualization. One aspect legitimizing science is its relevance to other spheres of society. Whereas under conditions of modernity knowledge production proceeds relatively independent from society in its own "*republic of science*" (Polanyi 1962), it is argued that in contemporary (Mode 2) society science has to connect much more and continuously to society in order to assure its relevance vis-à-vis other domains. Hence, it is argued that under Mode 2 knowledge production not only does science speak to society, so does society speaks back to science (Nowotny et al. 2001). To stress this point, Nowotny et al. (2001) no longer speak of science's context of application rather than of science's context of implication. While the notion of a context of application resonates a linear idea of science being independently produced and subsequently transferred to society at large, the notion of a context of implication resonates the idea of a non-linear relationship between science and society (Nowotny et al. 2003). Under Mode 2, science is neither produced independently from society nor does science instantaneously diffuse into society. Rather, under Mode 2, society is as present in science as science is present in society. Contextualized science then involves the grounding of society in the production and diffusion of scientific knowledge.

Third, in light of the observation that society speaks as much to science as science speaks to society, Nowotny et al. (2001) come up with three forms of contextualization. On the one extreme science is characterized as weakly contextualized when it depends on society in terms of

(financial) resources being allocated to them but is free in its subsequent decisions for using these resources to address particular issues in particular ways. Weakly contextualized science then comes close to the idea of a "*republic of science*" (Polanyi 1962). Weakly contextualized science resonates the idea of Mode 1 knowledge production set out in Gibbons et al. (1994) in which science's prime orientation concerns an understanding of natural and social phenomena without particularly taking into account use considerations.

On the other extreme science is characterized as strongly contextualized when actors outside of science both influence the allocation of resources to science as well as the way and directions in which these resources are used by science. Here, Nowotny et al. (2001 pp. 131-132) argue that "*strong contextualization not only shapes research agendas and priorities, but also influences research topics and methods. It enters into the process of knowledge production and therefore leaves visible traces in 'the science' itself.*" In addition, "*contextualization, therefore, depends on a permanent dialogue between scientists and diverse 'others' in society*" (p. 134). The notion of strong contextualization thus refers to the archetypical idea of Mode 2 knowledge production set out in Gibbons et al. (1994) in which research is use-inspired involving many different actors.

Somewhere in between weak and strong contextualization we find contextualization of the middle range (Nowotny et al. 2001). Here, contextualization takes place in what the authors call transaction spaces; collaborative enterprises in which all actors (from science and elsewhere) bring something to be exchanged with others while keeping their own backgrounds intact. In all, the notion of contextualized science proposed by Nowotny et al. (2001) provides a way out of the idea that the distributed organization of science is to be characterized as either Mode 1 or Mode 2. The notion of contextualization of the middle range then provides a richer understanding of the distributed organization of science. That is, science can be more or less contextualized in terms of being organized in a segregated, disciplinary fashion or in an integrated, transdisciplinary fashion; and science can be more or less contextualized in being restricted to the domain of academia or through involving actors from other domains of society as well. While disciplinary, academic science is typically associated with weak contextualization and Mode 1 knowledge production; transdisciplinary science involving academic, industry and government actors is typically associated with strong contextualization and Mode 2 knowledge production.

Fourth, Nowotny et al. (2001) argue that beyond reliable knowledge, science is moving towards the provision of socially robust knowledge. Socially robust knowledge is knowledge that follows directly from the problems society at large is confronted with and includes a wide diversity of societal actors in the search for solutions. While reliable knowledge is primarily reliable within the confined contours of the laboratory, knowledge is socially robust once it stands to the test of society at large. That is, "*scientific objectivity will have to become localized and contextualized, fitted into the specificities of each case in which it might be and most likely will be challenged"* (Nowotny 1999 p. 16). Not only should knowledge under Mode 2 be reliable; in addition knowledge should be useful (i.e. valuable and applicable) to society at large. It follows that the more science requires contextualization, the more it is in need of socially robust rather than reliable knowledge. As a consequence of both the importance of contextualized science and the demand for socially robust knowledge it is argued that science enters a (new) agora. Here, Nowotny et al. (2001) argue that since science can no longer be discretely distinguished from other spheres of society, it mingles with the state, the market, and the arts in this new public space. The agora then is the space in which problems of societal relevance are defined and solutions become socially robust.

In introducing the notion of Mode 2, Gibbons et al. (1994) and Nowotny et al. (2001) seek to address the distributed organization of science (and to a lesser extent society at large). In both works Mode 2 knowledge production is presented as a new, heterogeneous mode of knowledge production. The differences between the two works on Mode 2 knowledge production are rather small. While in Gibbons et al. (1994) the notion of Mode 2 knowledge production still resonates a linear relationship between science and society involving two distinct spheres, in Nowotny et al. (2001) the notion of Mode 2 knowledge production is addressed in terms of an integral part of society involving feedbacks between science and society. Along similar lines, while the first book is clear on what makes up Mode 2 knowledge production (i.e. context of application, transdisciplinarity, social distributedness, social accountability, and new forms of quality control), the second book provides a more synthetic perspective or what Shinn (2002 p. 604) calls an "*anti-differentiationist*" view on the science-society relationship, dismissing clear boundaries altogether.

Notwithstanding these differences, we notice at least three general similarities (see also Nowotny et al. 2003). First, both works start from the premise that knowledge production and science are inherently interactive phenomena. Interactions then take place within science in the form of collaborative efforts among its main actors (a point especially stressed in the first book). Alternatively, interactions take place between the realms of knowledge production and science on the one hand and other realms of society on the other hand (a point especially stressed in the second book). Either way, the interactive nature of knowledge production and science stand out in both accounts on Mode 2.

Second, as interactive phenomena, knowledge production and science play out on multiple dimensions. The multidimensional nature of knowledge production as an interactive phenomenon is distinctly addressed in the first book. In its fivefold characterization of Mode 2 knowledge production, interactions are characterized along (trans-) disciplinary, (cross-) cultural, and (cross-) institutional lines, among other dimensions. Albeit more implicit perhaps, the second book does also pay attention to the multidimensional nature of the interactions involved in and across science. Especially when discussing contextualization and their notion of the agora; disciplinary, geographical, and social dimensions of science come to the fore. Instead of focusing on one dimension only then, the notion of Mode 2 includes multiple dimensions in its characterization of knowledge production.

Third, both knowledge production and science are taken as self-similar in their production (i.e. organization) and their produce (i.e. outcomes). That is to say, both books stress that under Mode 2 the results of knowledge production and science reflect the interests and cognitive dispositions of those actors that have contributed to problem solving activities. In the first book on Mode 2 knowledge production, the nature of knowledge production as transdisciplinary, socially distributed and oriented at its context of application is a direct reflection of the variety of individuals, organizations, institutions, and sites involved in its production. Likewise, in the second book the extent to which knowledge production is contextualized or socially robust is reflected by the range of different actors involved in the process throughout which that knowledge is brought about. As such, the knowledge produced under Mode 2 is the mirror image of the organization underlying its production.

Beyond these general descriptions, we can formulate a set of seven claims on Mode 2 knowledge production:

1. Mode 2 as an emerging phenomenon since WWII. That is, while in the past science is to be characterized as Mode 1, contemporary science involves ever more Mode 2 characteristics.

2. Mode 2 as existing alongside Mode 1. The claim that Mode 2 is an emerging phenomenon is not to suggest that Mode 1 disappears altogether. Rather, Mode 2 knowledge production is said to exist in conjunction with Mode 1 knowledge production.
3. Mode 2 as prevailing across particular problem solving activities. The more complex and contextualized a problem, the more its science will be Mode 2.
   (Note that these first three claims do not tell much about the nature of Mode 2 itself)
4. Under Mode 2 distinct boundaries among organizations and among institutional domains no longer exist
5. Under Mode 2 diffuse contexts of application and implication require a heterogeneous distributed organization of science
6. Under Mode 2 contexts of application and implication become ever more important for science
7. Under Mode 2 science becomes ever more heterogeneous in its distributed organization

1.2.3 Critiques

Notwithstanding or perhaps due to its success, the notion of modes of knowledge production has rendered much criticism (see for an overview Hessels and Van Lente 2008). First, throughout the two books the central notion of Mode 2 is (arguably) vaguely set. For us this unclarity is reflected by at least two issues. One issue concerns the lack of a clear description of the prime phenomenon of interest. While in the first book the authors are concerned with knowledge production, in the second book the authors are explicitly concerned with science. Both books however leave it in the middle what is meant by knowledge production and science. To make things worse, alongside knowledge production and science the authors also speak of research, innovation, and academia to describe their phenomenon of interest. In all then, it remains rather unclear what defines or constitutes the main phenomenon of interest. The other issue here concerns a lack of conceptual clarity in the characterization of elements deemed important in addressing the main phenomenon of interest. Whatever is meant by knowledge production or science, the (conceptual) terms used to describe it are not clearly spelled out. Especially the second book is vague on what is meant by for example context, contextualization and knowledge that is socially robust. Admittedly, the first book is somewhat more clear (i.e. distinctive) on what constitutes Mode 2 knowledge production. Yet, also here one can question the exact meanings of such notions as the context of application and transdisciplinarity. With respect to the latter, Weingart (1996) criticizes the notion of transdisciplinarity arguing that while on the one hand Mode 2 knowledge production refers to an ever increasing specialization and fragmentation of scientific disciplines, on the other hand Mode 2 takes place outside the realm of scientific disciplines altogether. It remains unclear whether transdisciplinarity refers to a certain characterization of disciplinary scientific structure or whether it goes beyond and has therewith not so much (if anything) to do with scientific disciplines. Part of this conceptual unclarity resides in the absence of a clear theoretical referent (Shinn 2002; Rip 2002). In explicating the notion of Mode 2, the terms used are rather poorly connected to established concepts available in social theory. In addition, presenting the notion of Mode 2 revolves around a complete rejection of clearly demarcating both the phenomenon of interest and the elements deemed important in characterizing this phenomenon. This issue then begs the question of where we are talking about in the first place.

Second, the empirical validity of claims on the emergence, prevalence, and persistence of Mode 2 is debatable. Especially in the first book then Mode 2 is taken as a new and emerging form of organizing knowledge production. Yet, in historical perspective the dominance of universities in

the production of knowledge is preceded by a much wider involvement of industry and government agencies that goes back to the 19th century (Weingart 1996; Godin 1998). It can thus be argued that knowledge production has always been Mode 2 apart from a short period just after the Second World War. However, not only can the emergence of Mode 2 as a new reality be contested, so can the evidence that is provided about its alleged contemporary prevalence. From both the first and the second book on Mode 2 it remains unclear to what extent Mode 2 should be taken as a fact of life. To our opinion, this lack of evidence relates to two issues. One issue concerns the main tenet of the proposed claim on Mode 2. While in the first book it is frequently stressed that Mode 2 emerges alongside Mode 1 knowledge production, a shift seems to have occurred throughout the second book where it is stressed that science needs ever more contextualization suggesting that Mode 1 eventually is to be overthrown by Mode 2. Yet, in introducing the notion of "*contextualization of the middle range*", Nowotny et al. (2001 esp. pp. 143-165) at least also suggests that an alternative to a dichotomous view on science as either Mode 1 or Mode 2 might be viable. For us, the issue then not so much revolves on whether science is either Mode 1 or Mode 2 but much more revolves on the ways in which and the extent to which a distributed organization of science can be characterized as Mode 2. A second issue relates the conceptual unclarity revolving the notion of Mode 2 knowledge production with its empirical validity. As long as the main characteristics of Mode 2 knowledge production are not spelled out clearly, it will be hard to test particular hypotheses on its empirical validity. If the notion of Mode 2 knowledge production is just to suggest that a heterogeneous set of actors concerns themselves with science, then there is indeed empirical evidence that contemporary science can be characterized as Mode 2. Here, using bibliometric data on British science Hicks and Katz (1996) for example find an increase in interdisciplinary, cross-organizational and international science (see also Wuchty et al. 2007; Jones et al. 2008). Hence, actors concerning themselves with science are distributed across various geographical, disciplinary, and institutional contexts. Yet, if the notion of Mode 2 knowledge production is to suggest that a heterogeneous set of actors is not only involved in science but also frequently collaborate with one another, then empirical evidence on Mode 2 knowledge production is much more ambiguous. Godin and Gingras (2000) for example argue that despite the involvement of non-academic actors such as firms and hospitals the central position of universities is not diminishing. On the contrary, although organizations with different institutional backgrounds might be increasingly involved in science, their involvement is still largely accompanied by their collaboration with university partners. In all then, the assertion that a variety of actors involve themselves with science is not to say that this comes at the demise of the university let alone that it renders a science system being organized altogether heterogeneously.

Finally, the two books on Mode 2 are frequently criticized for not being explicit on their aims and implications (see e.g. Godin 1998; Shinn 2002; Hessels and Van Lente 2008). Indeed, it is not completely clear to us either where a Mode 2 organization of science should lead at. As such it is not clear whether Mode 2 should be taken as a descriptive empirical claim, a normative prescriptive claim, or as a conceptual starting point to address the distributed organization of science. As will become clear throughout the remainder of this thesis, our use of the notion of Mode 2 resides in its use as a conceptual starting point. Reading the two books on Mode 2 we take this notion as a rich description of the distributed organization of science. The extent to which Mode 2 is empirically valid is still unclear to us. What is more, while the authors of the two books on Mode 2 are at times favorable to such a Mode 2 state of affairs in science (see e.g. Gibbons et al. 1994 esp. pp. 155-166; Nowotny et al. 2001 esp. pp. 230-244), for us the normative implications of Mode 2 are still unclear. Hence, before making sweeping claims on the desirability of Mode 2 we believe an inquiry into its implications is needed. We will use the notion of Mode 2 in the remainder of this thesis as a meta-concept that requires refinement in order to address the distributed organization of science; including its empirical validity and normative implications.

1.2.4 Research orientations

Despite or perhaps due to its vagueness we believe that the notion of Mode 2 provides an interesting vantage point to start our assessment of science from. The notion of Mode 2 provides enough fruitful ground to assess the distributed organization of science. This thesis has three aims.

1. To problematize, (re)conceptualize and hence come up with a new analytical framework to study the distributed organization of science (chapters 2, 3, 4, and 5).
2. To test existing claims on the distributed organization of science as Mode 2 in light of this newly proposed framework (chapters 3, 4, 6, and 7).
3. To discuss the normative implications of a distributed organization of science as Mode 2 (chapters 6 and 7)

1.3. (Re-) Conceptualizing the distributed organization of science

So far we have addressed the distributed organization of science in terms of conceptualizations proposed by others, that is, in terms of the notion of Mode 2 proposed by Gibbons et al. (1994) and Nowotny et al. (2001). In what follows we will use the notion of Mode 2 knowledge production as a conceptual starting point. However, given that our interest resides in an assessment of the distributed organization of science, first some notes of clarification on the main terms of this thesis: science and its distributed organization.

1.3.1 Science

A critique on the two books on Mode 2 concerns their loose definition of what constitutes the phenomenon of interest. While the first book is concerned with knowledge production and the second book with science, both books lack a description of what constitute respectively knowledge production and science. To our opinion then, we first need to provide a clearer description of what we mean by our phenomenon of interest, that is, science. A concrete definition of science is hard to attain. In fact, science has often been defined in various and sometimes even conflicting ways, therewith leaving its exact boundaries vaguely set depending on the specific purpose at hand (Gieryn 1984). Yet, we do believe that in more abstract terms science can be characterized in terms of at least two distinctive features.

A first distinctive feature of science concerns its produce, namely scientific knowledge. Scientific knowledge is distinct from other forms of knowledge in that it requires recognition from people other than those bringing this knowledge about (Collins 1985). In other words, a knowledge claim is not just considered as scientific by virtue of a particular scholar claiming this to be true. Rather, in order to gain scientificness, a knowledge claim has to be recognized by others as well (Gilbert 1976). This recognition of one's claim by others is a constitutive characteristic of science. However, recognition of knowledge is not enough to warrant knowledge as scientific.

This then brings us to a second distinctive feature of science, namely its system of peer review. The system of peer review facilitates the explicit recognition, rejection, further substantiation or refutation of proposed claims (Merton and Zuckerman 1973). A vivid expression of peer review in science is provided by journal publication. Journal publication is a central means to achieve recognition over ones knowledge claims as scientific. In letting other scholars check the accuracy

and reliability of one's claims, journal publication provides an organized first (and often necessary) step towards certification of one's claims as scientific (Gilbert 1976).

Note then that science, at least how we conceive it, is somewhat different from research (see also e.g. Latour 1998). The notion of research is much more restricted to on-site knowledge production activities as they for example take place within laboratories. Instead, science is concerned with the means by which these local practices are transformed towards (although not necessarily reaching the point of) universal acceptance. To the extent that science and innovation both refer to the provision of acceptable solutions to particular problems at stake, the two notions can be equated. Both science and innovation then refer to the production of knowledge. Yet, in principle we prefer to speak of science when considering the provision of public knowledge and of innovation when considering the commercialization of goods.

It follows from our definition of science that we take the journal publication as our starting point for an assessment of the distributed organization of science. The journal publication is the scholarly medium par excellence facilitating that a certain message is carried from one place to another. In addition, the journal publication assures that the messages contained therein remain stable over time. Taken together, journal publications reflect what Latour (1986; 1987) calls immutable mobiles; journal publication assures that the information contained therein remains stable across both time and space (see also Brown and Duguid, 2000 esp. pp. 173-205). As immutable mobiles, journal publications facilitate the further perpetuation of claims towards extended scientificness (Gilbert 1976). In addition, as the material expression of certified knowledge, not only does the journal publication enable the further substantiation of claims within science, it also enables science to be deployed in society at large. Taken together, the journal publication thus provides the material expression of knowledge enabling the certification, substantiation, and further deployment of claims and hence provides a starting point for an assessment of the distributed organization of science.

Still, one might question what it is that journal publications actually represent. Two interpretations stand out in the literature (see also Luukkonen 1997). On the one hand, some take research as adequately reflected by science. Hence, publications are taken to represent research output (Cole and Cole 1967), co-publications as research collaboration (Price 1963; Katz and Martin 1997), references as valuable inputs to research (Garfield 1962; Lipetz 1965), and citations as research quality or impact (Martin and Irvine 1983). Some do not seem to take issue with the possible mismatch between how and by whom research is performed and how science is represented by journal publications. On the other hand, again Latour (1986; 1987) proposes to think of journal publications as objects used to convince others. Hence, publications are taken as rhetoric technologies, co-publications as coalitions of allies, references as tools to mobilize others, and citations as signaling authority. The inscription of aspects that reflect upon the distributed organization of science do not necessarily have to do with the organization of research but in fact only reflect the successful mobilization of rhetoric elements that make a claim convincing to its audience. Both accounts are somewhat discomforting. While the former idea on journal publication as a truthful representation of research seems to be too naïve (Medawar 1964; Gilbert 1976), the latter idea on journal publications as pure rhetoric devices runs the risk of becoming overly relativistic (Amsterdamska 1990; Van Raan 1998). However, and notwithstanding some important differences, whatever the specific connotations to journal publication it holds that for many disciplines the journal publication is the main standard for the certification of what is taken as scientific.

In addition, many elements inscribed on journal publications can be thought of as involving interactions. Whether one thinks of co-publications as research collaborations or as representations of coalitions of allies; what holds is that co-publications represent interactions among multiple actors. Hence when, throughout this thesis, we speak of collaborative science, as a first approximation we refer to an understanding of collaboration that says something about the support for a particular claim and leave it in the midst whether such a support actually implies an active or total participation in how the claim has been brought about (as in research collaboration) or as a collection of actors enabling the justification of a claim (as in a rhetoric coalition of allies). Likewise, whether one thinks of references and citations as indications of value or as rhetorical tools of persuasion; at a basic level what holds is that both accounts signal an interaction between texts or actors. Again, the reasons for attributing references are left in the midst; we cannot tell whether references are made based on 'pure' quality reasons or 'misplaced' rhetorical reasons. For now we leave it to say that while references are made for some reason as they are actually deemed relevant by those inscribing them on their publications, on aggregate it holds that those texts or actors being frequently cited are apparently deemed highly relevant. What holds in general then is that by zooming in on particular elements inscribed on publications such as organizations and references, we can indeed start to assess the distributed organization of science as an interactive phenomenon.

1.3.2 Heterogeneity in a distributed organization of science

It follows from our discussion of Mode 2 knowledge production that a distributed organization of science can be described in terms of the heterogeneity among actors concerning themselves with science and in terms of the interactions that take place among such heterogeneous actors. In network analytic terms the former notion of heterogeneity involves a description of nodes according to their attributes, while the latter notion of heterogeneity involves a description of dyads connecting any two nodes. We choose to address heterogeneity in the distributed organization of science along five dimensions (Boschma 2005; chapter 2).

First, science systems can be characterized in geographical terms. We define geography as the physical dimension in which interactions among actors take place (Hägerstrand 1970; Giddens 1984; Castells 1996). Here, a group of actors concerning themselves with science is characterized as geographically diverse when the individual actors are located at different locations. Such locations can for example refer to different regions or countries. Obviously, in constituting a global enterprise, the science system at large is inherently characterized by geographical heterogeneity. What is more, in characterizing a national science system and scientific project teams respectively Hicks and Katz (1996) and Wuchty et al. (2007) find evidence for geographical diversity at lower levels of aggregation as well. While groups of actors can be described in terms of their geographical diversity, any two interacting actors in a science system can be described as being more or less distant from each other. The geographical distance separating two interacting actors can be addressed in continuous terms (e.g. in terms of travel time or kilometers) or in categorical terms (e.g. in terms of national versus international collaborations), although the latter can also refer to the notion of institutional distance (see e.g. Hoekman et al. 2009).

Second, science systems can be characterized in institutional terms. Such a characterization of the science system resembles the idea of a Triple Helix of university-industry-government relations (Leydesdorff and Etzkowitz 1996; Etzkowitz and Leydesdorff 2000). An institutional characterization of science thus provides a description of science by the types of organizations

involved therein. Apart from the threefold distinction among universities, private firms, and government agencies one could of course include other type of organizations as well such as hospitals and non-governmental organizations (see e.g. Godin and Gingras 2000; Ponds et al. 2007).

A group of actors concerning themselves with science is institutionally diverse when the individual actors primarily operate within the realm of different institutional spheres. Hence, a scientific project team involving an actor from academia, industry, and government is institutionally diverse. Likewise, the relations between actors can be characterized in terms of institutional distance. However, unlike geographical distance, the institutional distance between actors can only be addressed in categorical terms. That is, an industrial actor is institutionally distant from an academic actor but the extent to which these actors are institutionally distant is unclear as we cannot express the extent to which the norms and rules operating in academia differ from those in industry. Still, we know from sociology and economics of science that the norms and rules operating in academia are different from those in industry (Merton 1973; Dasgupta and David 1994). More in general then, different norms, rules, and goal orientations can be assigned to different types of organizations rendering these actors institutionally distant from each other (Parsons 1956a; Parsons 1956b).

Third, following up on a characterization of science along institutional lines, science can be further described along organizational lines. A characterization of science along organizational lines follows the distinction between a closed and open model of innovation (Chesbrough 2003). Organizational diversity then refers to the involvement of actors from different organizations. Organizational diversity is different from institutional diversity in that while various organizations might be involved these need not be from different institutional domains. Most obviously, different universities can be involved in a single scientific project. Vice versa, different departments of the same organization might in principle appeal to different institutional domains. For example, a university hospital pursues different activities than its corresponding university although both belong to the same organization. As a first approximation then and following a transaction cost economics approach to organizations (Williamson 1981), we thus take science to involve multiple organizations once its activities crosses hierarchical ownership structures (see further chapter 3). Hence, a characterization of science as heterogeneous along organizational lines refers to scientific knowledge production crossing hierarchical boundaries.

Fourth, science can be described in cognitive terms. A characterization of science in cognitive terms resembles the idea of disciplinary science. However, whereas disciplines refer to both the social and intellectual structure of science (Whitley 2000), the cognitive dimension focuses primarily on the intellectual content of science. That is, a characterization of teams, projects, or science systems in terms of the topics it addresses and the methodologies it uses to address these topics. This is not to suggest that the cognitive and social dimensions are easily distinguishable. Yet, as analytical concepts, we can distinguish who concerns themselves with science from what they concern themselves with (see also Leydesdorff 1995). Cognitive heterogeneity then refers to a science comprehending multiple issues and methodologies in novel ways.

Fifth and finally then, science can be addressed in social terms with reference to the particular communities in which scholars are active (Knorr Cetina 1999). The notion of collaborative science suggests that interactions in science are always embedded in a social context and that in turn social relations affect the outcomes of interactions (Granovetter 1985). Social heterogeneity then refers to the involvement of scholars from different closely knit communities. That is, scholars work together with scholars whom they do not know from previous projects.

Table 1.2. *Translation of "Mode 2" knowledge production to collaborative knowledge production along five dimensions of heterogeneity*

Mode 2 knowledge production	**Expressed by Gibbons et al. (1994) as …**	**Related to …**
Transdisciplinarity	"*… a novel environment in which knowledge flows more easily across disciplinary boundaries…*" (p. 20) in which "*integration is not provided by disciplinary structures … but is envisaged and provided from the outset in the context of usage, or application in the broad sense…*" (p. 27) and "*… disciplines are no longer the only locus of the most interesting problems, nor are they the homes to which scientists must return for recognition or rewards*" (p. 30)	Cognitive heterogeneity
Societal contextualization	"*… the organization of research more open and flexible*" (p. 20) "*… with knowledge becoming socially distributed to ever wider segments of society*" (p. 34). Here, "*the previous one-way communication process from scientific experts to the lay public perceived to be scientifically illiterate and in need of education by experts has been supplanted by politically backed demands for accountability of science and technology and new public discussions in which experts have to communicate a more 'vernacular' science than ever before*" (p. 36)	Organizational heterogeneity
Social distributedness	"*… preference given to collaborative rather than individual performance and excellence judged by the ability of individuals to make a sustained contribution in open, flexible types of organization in which they may only work temporarily*" (p. 30)	Social heterogeneity
Institutional hybridization	"*… a closer integration of the process of discovery with that of fabrication*" (p. 19) in which "*… institutional differences between, say, universities and industry, seem to be less and less relevant*" (p. 30). "*Thus while different kinds of institutions are able to maintain their own distinctive character and functions, they continually generate new forms of communication. This partially explains the emergence of hybrid new communities, consisting of people who have been socialized in different subsystems (…), but who subsequently learn different (…) modes of behaviour, knowledge and social competence that originally they did not possess*" (p. 37)	Institutional heterogeneity
A number of different sites	"*… the diffusion over a wide range of potential sites of knowledge production …*" (p. 17)	Geographical heterogeneity

From these five dimensions of heterogeneity a distinction between Mode 1 and Mode 2 knowledge production can now be made analytically. First, cognitive heterogeneity reflects the idea of transdisciplinarity under Mode 2 knowledge production. Second, organizational heterogeneity refers to a widespread contextualization of science in society. Scientific knowledge is produced collaboratively across a wide range of organizations. Third, social heterogeneity refers to the production of scientific knowledge being distributed across different communities. Under Mode 2 knowledge production, collaborative science takes place in temporary projects. Hence, the composition of these projects changes from project to project. Fourth, institutional heterogeneity refers to institutional hybridization under Mode 2 knowledge production. Actors from different institutional backgrounds jointly produce scientific knowledge under Mode 2. Finally,

geographical heterogeneity refers to the involvement of different sites at which scientific knowledge production takes place.

In all, Mode 1 stands for scientific knowledge production in which actors are homogenous, while Mode 2 knowledge production stands for distributed knowledge production processes in which actors are heterogeneous. The proposed definition of Mode 1 coincides with the ivory tower image of scientific knowledge production, which is said to be disciplinary, within university departments, in personal networks, under a strict set of academic norms and co-present within the walls of the laboratory site. Mode 2, by contrast, is characterized by as transdisciplinary, cross-organizational, in temporary and open networks, with various, possibly conflicting, goals, and crossing national borders and physical space. A close reading of the book by Gibbons et al. (1994) provides further support for this interpretation of the Mode 2 concept. For each of the dimensions, quotes from Gibbons et al. (1994) can be found that express the nature of Mode 2 knowledge production, as reported in table 1.2.

1.3.3 Distance, diversity, and coordination

The fivefold notion of heterogeneity in science's distributed organization can be conceptualized in terms of distance and in terms of diversity. While distance refers to a characterization of heterogeneity at the dyadic level, diversity refers to a characterization of heterogeneity at the group level. Geographical distance reflects the extent to which any two actors are separated from each other in physical terms (e.g. in terms of kilometers). Geographical diversity then reflects the extent to which the individuals comprising a group of actors operate in various geographical contexts (e.g. in different countries or regions). Likewise, all four other dimensions of heterogeneity can be operationalized in terms of distance and diversity. The more collaborations in a science system take place among distant actors along all five dimensions, the more that science system conforms to a characterization of science as Mode 2. Similarly, the more a science system can be characterized as diverse along all five dimensions, the more that science system conforms to a characterization of science as Mode 2. While both the notion of distance and the notion of diversity reflect instances of heterogeneity in the distributed organization of science, both provide a more analytical understanding of a distinction between Mode 1 and Mode 2 knowledge production. While the notion of diversity primarily refers to an understanding of Mode 2 knowledge production as involving multiple different actors, the notion of distance allows us to address the extent to which actors collaborate despite being distant from each other.

Heterogeneity in a distributed organization of science can be described along five dimensions in terms of both distance and diversity. Yet, this is not to say that heterogeneity in the distributed organization of science is easily established. On the contrary, distance and diversity among actors easily leads to friction and conflicts in the coordination of activities. Alternatively then, coordination in collaborative science is facilitated by the opposites of distance and diversity, that is, proximity and uniformity (Boschma 2005; chapter 2).

First, actors that operate in different geographical contexts have to communicate over longer distances. Nowadays, long distance communications can be easily established via information and communication technologies and fast transportation. Yet, to the extent that knowledge production still requires frequent face-to-face interaction among actors, geographical distance and diversity hamper communication and hence coordination in science (Olsen and Olsen 2000; Amin and Roberts 2008). Despite the secular rise in long distance collaborations (Waltman et al. 2011),

collaborative science is still facilitated by geographical proximity and uniformity among actors (Hoekman et al. 2009; Hoekman et al. 2010).[2]

Second, differences in norms and rules – in terms of either institutional distance or institutional diversity – easily lead to incentive incompatibility problems at the relational or team level. For example the interests of academia and industry need not be the same. While the former has an incentive to disclose the outcomes of research publicly as to gain recognition for its activities (Merton 1973), the latter has an incentive to keep its research outcomes secret as to prevent unwanted knowledge spillovers to competitors (Arrow 1962; Dasgupta and David 1994). Consequently, collaborations among academic and industry actors need not be established and maintained easily. More in general then, institutional proximity and uniformity still facilitate collaborative science. Note that our notion of institutional heterogeneity differs from Boschma's (2005) notion of institutional proximity. Although norms and rules can be taken to operate on the territorial level (see e.g. Hoekman et al. 2009), we follow Ponds et al. (2007) and Ponds (2008) in their notion of institutions as differing across different spheres of society.

Third, collaborative science crossing organizational boundaries are not easily established as these also come with a risk of opportunistic behavior (Williamson 1981). For example, in making investments that are specific to a particular collaborative effort, a partner organization might take advantage without making these investments themselves. Organizational proximity and uniformity then facilitate the establishment and maintenance of collaboration networks as they reduce uncertainty and opportunism through collegiality and shared goal orientations.

Fourth, cognitive heterogeneity might lead to incommensurability problems among actors with different cognitive backgrounds. Incommensurability then refers to a situation in which scholars have different ideas about the importance of particular problems, standards of solving problems, and use different vocabularies to describe problems and solutions (Polanyi 1958; Kuhn 1962). As a consequence, actors with different cognitive backgrounds find difficulty in collaborating with each other. Alternatively, the knowledge bases of actors should be similar enough in order to communicate, understand and process scientific knowledge successfully (Cohen and Levinthal 1990; Nooteboom 1999).

Fifth, in line with institutional and organizational heterogeneity, social heterogeneity increases the risk of opportunistic behavior. Hence, scientific actors are inclined to collaborate with those they can trust and rely upon. As social proximity and uniformity boost trust and commitment (Granovetter 1985; Uzzi 1996), collaborative science is expected to take place within stable social networks. Again our notion of social heterogeneity differs from Boschma's (2005) notion of social proximity. While Boschma's (2005) social proximity is about friendly relationships, our notion of social heterogeneity is about actors frequently tapping into different social communities. Our notion of social heterogeneity is in line with the idea of Mode 2 knowledge production in which it is stressed that actors, in collaborating with others, frequently switch partners (see also table 1.2).

[2] Some contributions stress the role played by temporary geographical proximity (Torre 2008). These contributions argue that actors need not be geographically proximate at all time. In the context of Mode 2 knowledge production, actors might be located at sites that are very distant from each other but occasionally meet at conferences and seminars to discuss their joint research efforts and plan to perform new ones. Here however, we do not discuss how collaboration takes place (i.e. at a single or multiple research sites). Rather, we discuss the patterns among those collaborating. What holds is that actors who are geographically proximate are also more likely to meet on a temporary basis than actors who are geographically distant (Van Dijk and Maier 2006).

Yet, whereas coordination is facilitated by proximity and uniformity among actors, distance and diversity might render scientific outcomes more relevant. On the one hand, distance and diversity among actors might render the knowledge that they jointly produce more comprehensive. Here, Bonaccorsi (2008; 2010) argues that scholars have to operate beyond their own cognitive domain if they are to comprehensively address a particular problem at stake. With reference to the notion of Mode 2, science has to be transdisciplinary if it is to tackle complex societal problems (Gibbons et al. 1994; Nowotny et al. 2001). Likewise, including actors from different geographical contexts, institutional domains, and organizations is more responsive to the different interests at stake in solving a particular problem. More in general then, in introducing different insights, distance and diversity can be a source of creativity rendering a distributed organization of science more valuable (Page 2007; Stark 2009). On the other hand, distance and diversity among actors need not just lead to 'better' knowledge but also makes a wider diffusion of that knowledge more likely (Frenken et al. 2005; Singh 2008). Hence, as various geographical contexts, organizations, institutional domains, and disciplines are involved in the production of knowledge, its outcomes are likely to diffuse across a wide range of contexts. Whether heterogeneity in the distributed organization of science leads to (intrinsically) 'better' knowledge or to a wider diffusion of that knowledge is unclear, what holds is that heterogeneity in the distributed organization of science renders relevant outcomes more likely.

Taken together, heterogeneity in a distributed organization of science leads to two opposing effects. One effect is that heterogeneity hampers coordination among collaborating actors. Hence, we expect that collaborative science takes place along lines of proximity and uniformity rather than distance and diversity. The other effect is that heterogeneity renders relevant outcomes more likely. Hence, we expect that collaborative science that renders relevant outcomes takes place along lines of distance and diversity. With respect to the notion of proximity Boschma and Frenken (2009) aptly refer to these opposing outcomes as the proximity paradox. That is, while proximity has a positive effect on the establishment of collaboration networks, too much proximity has a negative effect on the performance of actors. The extent to which the proximity paradox holds along all five dimensions is unclear (see also Broekel and Boschma 2012). What holds is that – at least in theory – heterogeneity in a distributed organization of science is likely to hamper coordination and hence collaboration while at the same time it renders relevant outcomes more likely. In economic terms, heterogeneity in a distributed organization of science can be described in terms of both costs and benefits. While heterogeneity raises the costs of coordinating collaborative science, it is also expected to increase its benefits. What we expect then is that the science system at large is more likely to be characterized as Mode 1 in a descriptive sense. The extent to which the distributed organization of science is characterized as enough heterogeneous by rendering collaborative science most beneficial remains open for normative debate.

1.4. Empirical illustrations: the case of diabetes medicine

The choice for diabetes as a case to illustrate our main points empirically, resides first and foremost in the reality of the problem. Whatever one thinks about the causes, appearances, and consequences of diabetes, its prevalence as a societal and scientific problem cannot be denied. Diabetes affects millions of people around the globe and is expected to do ever more so in the near future (Danaei et al. 2011; Hurley 2011). It is clear that diabetes not only affects many people as a problematic disease, but also affects many people as they work on solving this problem in their daily lives as scholars. In other words, diabetes is a real problem.

The fact that diabetes is a chronic disease further problematizes its prevalence. Diabetes not only affects many people, as a chronic disease it also affects many people for longer periods of time and possibly with major consequences. The prime medical issue of diabetes is described as hyperglycemia, that is, the bodily condition in which an excessive amount of glucose circulates the blood. A state of hyperglycemia is problematic in that it is indicative of the blood delivering to little energy for the organs to function properly. When this state continues for longer periods of time, this may lead to severe complications. Among the complications of hyperglycemia, diabetic coma can be most acute. Other, more common complications involve a loss of sight and severe foot ulcers. Although largely similar in their complications, we can grossly distinguish two most prevalent types of diabetes (type 1 diabetes and type 2 diabetes). On the one hand, type 1 diabetes is generally taken to reflect a state in which the body is insufficiently capable of producing hormones that enable the transformation of glucose into energy (Tattersall 2009). The hormone of interest here has become known as insulin. The discovery of insulin has been a major breakthrough in the treatment of type 1 diabetes patients (Bliss 2007). That is, the discovery of insulin has made type 1 diabetes "manageable", yet the root problem is far from being definitely solved (Mol 2008). On the other hand, type 2 diabetes is generally taken to reflect a state in which the body is insufficiently capable of metabolizing (i.e. transforming) insulin properly therewith leading to an inadequate bodily uptake of energy (Tattersall 2009). Regardless of the bodily capacity to produce insulin (characteristic of type 1 diabetes), type 2 diabetes is primarily characterized by a resistance or deficiency of the body to use insulin. As compared to type 1 diabetes, type 2 diabetes can be said to be even less intermediately solved. That is, to our knowledge no treatment has been proposed for type 2 diabetes so far that is fully capable of improving the bodily capacity to metabolize insulin on a continuous basis, in a similar fashion as insulin itself has been proposed as a continuous treatment option for patients with type 1 diabetes.

Diabetes, and especially its type 2 variant, constitutes a complex disease involving many interacting factors such as genetics, lifestyle, and the (industrialized) environment (Zimmet et al. 2001). However, not only are the aspects involved in the constitution of this disease varied, as a consequence so are the people and organizations occupying themselves with finding solutions to this problem. What medical professionals call translational medicine (Woolf 2008) seems to be especially accurate for diabetes, that is, as a description of medical science that concerns itself with diabetes duly takes into account the whole process from the laboratory bench to the patient bedside involving different actors (see e.g. National Institutes of Health 2004). Hence, the nature of diabetes as a scientific problem is immediately enmeshed with societal undertones whose provision of solutions is expected to be organized heterogeneously. Hence, as diabetes reflects a hard, complex and key societal issue, we can expect its organization to be charactterised by Mode 2 rather than Mode 1 knowledge production.[3]

1.5. Outline

This thesis consists of four parts. First, chapters 1 and 2 provide a general introduction. Second, in chapters 3 and 4 we take the organization as the basic unit of analysis to assess collaborative science. While chapter 3 discusses the nature of the organization conceptually, chapter 4 addresses inter-organizational collaboration empirically. Third, in chapters 5 and 6 we discuss the determinants of scientific and societal relevance as measured by citation. Again we start with a

[3] In order to avoid overlap we will not discuss our particular case further here. In each individual chapter we will discuss the relevance of this case more in detail.

conceptual paper (chapter 5) and continue with an empirical assessment (chapter 6). Finally, chapter 7 discusses the determinants of scientific publication by pharmaceutical companies.

Before exploring heterogeneity in the distributed organization of science further, chapter 2 provides an overview of past studies that addresses this issue. Labeling these studies "*spatial scientometrics*" we propose a research program to analyze spatial aspects of the science system. Here, we draw on insights from economic geography (esp. from the literature on the geography of innovation) to discuss existing contributions dealing with spatial aspects of the science system. From this overview we conclude that although a number of studies explicitly take into account the geographical dimension as a determinant of collaborative science and its impact, few studies simultaneously take into account multiple dimensions of heterogeneity.

Chapters 3 and 4 take up this issue and address the extent to which the science system – conceived of as a set of collaborating organizations – can be characterized as Mode 2 on all five dimensions of heterogeneity. First, in chapter 3 we problematize the notion of the organization as it is used in scientometrics. On the one hand, throughout the scientometric literature the idea of what constitutes an organization is not taken as controversial. That Although it is widely acknowledged that taking the organization as the basic unit of analysis in scientometrics requires lots of cumbersome work (see e.g. Van Raan 2005a; Van Raan 2005b), the actual nature and boundaries of the organization are taken for granted. It appears that researchers in scientometrics using the organization as a basic unit of analyses take little issue in how to conceive of the organization in the first place. On the other hand, within contributions on Mode 2 knowledge production, the whole idea of what constitutes an organization is unclear as the boundaries of universities, firms, and government agencies get increasingly blurred (Gibbons et al. 1994; Nowotny et al. 2001). From the perspective of Mode 2 knowledge production, the whole idea of what constitutes an organization is contested. Chapter 3 then makes an attempt to comprehend both perspectives on the nature and boundaries of the organization. We make an attempt to enrich the scientometric literature dealing with the organization as a basic unit of analysis. The main argument of this paper holds that performing organization level research in scientometrics should proceed by taking an explicit pragmatic stance on the constitution of the organization. We argue that performing organization level research in scientometrics (i) requires both authoritive 'objective" and non-authoritive "subjective" background knowledge, (ii) involves non-logic practices that can be more or less theoretically informed, and (iii) depends crucially upon the general aim of the research endeavor in which the organization is taken as a basic unit of analysis. To our opinion an explicit pragmatic stance on organization level research in scientometrics is a viable alternative to both overly positivist and overly relativist approaches as well as that it renders the relation between scientometrics and science policy more productive.

Having qualified our understanding of the organization in chapter 3, chapter 4 addresses the extent to which collaborations among organizations active in diabetes medicine can be characterized as Mode 2 along five dimensions as discussed in section 1.3.3. We define Mode 2 knowledge production as knowledge production resulting from a collaboration between distant organizations, and Mode 1 knowledge production as knowledge production resulting from a collaboration between proximate organizations. Here, we define Mode 2 knowledge production at the level of dyads as a characterization of collaborating organizations. It turns out that proximity shapes collaborative science on all five dimensions. Hence, there seems to be little evidence for Mode 2 knowledge production at the system level. In addition we compare the European science system of collaborating organizations with that of North America. From a policy perspective such a comparison is interesting as differences in their relative performances are attributed to differences in the characteristics of their science and innovation systems (Dosi et al. 2006). Here, our main

results hold that both for North-America and Europe geographical proximity is the prime determinant of research collaboration while institutional boundaries between university, industry, government, and hospitals are more blurred. Interestingly, despite policy discourse suggesting otherwise, no significant differences were found regarding cross-institutional collaboration between North-America and Europe. Chapter 4 then contributes to the literature on science and innovation systems by providing an analytical approach to the subject using bibliometric data.

From chapter 5 onwards we address the implications of a distributed organization of science. First, in chapter 5 we address the notion of scientific – or Mode 1 – impact as measured by citations. Here we turn to the literature on information retrieval to reconceptualize the whole idea of scientific impact in terms of relevance. In the information retrieval literature the notion of relevance is traditionally taken to reside either at the side of the information system or at the side of the information user. Recently an attempt has been made to get rid of the duality in the notion of relevance (Hjørland 2010). Likewise, we propose to conceptualize scientific impact and especially the notion of citation relationally to involve both quality characteristics residing at the cited end and personal characteristics residing at the citing end. Following up on this third perspective on relevance, we propose a theoretical approach to citation focusing on the notion of embeddedness. Here, we combine theoretical insights from the sociology of networks with existing citation theories in the field of scientometrics and come up with an interpretation of citation that both provides enough ground to comprehend the existing conflicting interpretations of citation and at the same time provides for a renewed interest in theoretical and empirical research on citation.

Second, in chapter 6 we move beyond the notion of scientific relevance to empirically assess science's societal relevance. In other words, while chapter 5 focuses on the establishment of relevance in the context of Mode 1 knowledge production, chapter 6 focuses on the establishment of relevance in the context of Mode 2 knowledge production. Focusing again on the case of type 2 diabetes, we assess the effect of diversity (as explained in section 1.3.3) in the organization of scientific project teams on the likelihood of such projects rendering impact in a clinical practice guideline. Hence, we take the NCC-CC (2008) clinical practice guideline on managing type 2 diabetes as a context of implication in diabetes medicine. We test whether diversity along five dimensions has an effect on rendering the outcomes of scientific projects societal relevant whilst controlling for quality characteristics. As it turns out only geographical diversity has a positive effect on the likelihood of scientific projects gaining societal relevance. In addition we find that the pharmaceutical industry has a prominent role in rendering the outcomes of medical science societal relevant. Although this result in itself does not discredit industry's involvement in science, it does warrant further research into the nature of this involvement.

Finally, in chapter 7 we turn to the normative implications of a distributed organization of science as Mode 2. Here we focus particularly on industry's involvement in science. We assess the publication behavior of firms in a context of complete information disclosure where firms face the choice of publishing study outcomes either in scientific publications or in web publications. Due to recent institutional reforms it is now mandated to register clinical trial protocols before onset and publish basic results after study completion. For a sample of clinical trials on diabetes, we link clinical trial protocols to result publications and classify those publications based on the type of evidence they disclose. The results indicate that under conditions of complete information disclosure, firms do indeed not publish less than not-for-profit research. However, firms strategically publish in scientific journals where they highlight favorable outcomes to their therapies and clinically relevant studies, since regulators value evidence published in peer-reviewed journals much more than evidence published on web sites without peer-review. Thus, despite institutional reforms, pharmaceutical firms still find a way to strategically highlight

particular pieces of evidence in scientific journals. We conclude that concerns about publication based on the nature of evidence have shifted rather than disappeared. The presented results in this paper thus signal a problem of persistent publication bias of a more fundamental nature which is not easily solved by regulatory reform alone.

1.6. Concluding remarks

Throughout this thesis we propose an analytical understanding of a distributed organization of science along five dimensions of heterogeneity. We reconceptualize the notion of Mode 2 knowledge production in terms of geographical, institutional, organizational, cognitive and social heterogeneity in the distributed organization of science. In addition we make a distinction between scientific (Mode 1) relevance and societal (Mode 2) relevance. From these distinctions we assess the distributed organization of science both theoretically (chapters 3 and 5) and empirically (chapters 4, 6, and 7). The general conclusion of this dissertation is threefold.

First, the framework of proximity (distance) and diversity (uniformity) along five dimensions provides a useful analytical tool to address the distributed organization of science. Using this framework, two important critiques on the idea of Mode 2 knowledge production, namely its lacking conceptual clarity and empirical validity, can be tackled. Characterizing scientific actors and their relations along lines of geographical, social, cognitive, institutional, and organizational heterogeneity, renders a more distinct picture of the distributed organization of science.

Second, the idea of Mode 2 knowledge production as conceptualized along five dimensions of heterogeneity takes different forms depending on the level of aggregation. On the level of individual organizations we argue that since the boundaries of the organizations are inherently blurred, many organizations can in principle be characterized as Mode 2. Yet, our empirical analysis shows that on an aggregate level the science system as a whole is not characterized as Mode 2. Rather, proximity plays an important role in shaping collaboration among organizations. What is more, in comparing the European science system with the North-American science system we show that the extent to which proximity plays a role in shaping collaborative science differs between territorial science systems. In general then one cannot say that science is either Mode 1 or Mode 2. Rather, depending on the level of aggregation science can be characterized as more or less Mode 2 along different dimensions of heterogeneity.

Third, the implications of heterogeneity or Mode 2-ness in the distributed organization of science are ambiguous. On the one hand, heterogeneity in the distributed organization of (medical) science does not render societal relevant knowledge more likely per se. While distance hampers collaboration on all five dimensions, we only find evidence of an increase in the likelihood of societal relevant outcomes under geographical diversity and not for the other four dimensions of heterogeneity. This does not imply that more heterogeneity in the distributed organization of science is bad per se. Rather, and contrary to the Mode 2 thesis, heterogeneity does not seem to render science societal relevant. On the other hand, the involvement of industrial actors does render societal relevant knowledge more likely. However, the extent to which such involvement is desirable from a normative perspective is unclear. What holds is that pharmaceutical companies publish their study outcomes strategically. In order to circumvent the possible downturns of such strategic publication behavior of pharmaceutical companies, public policy should not only mandate public disclosure of study outcomes but might also reconsider the operation of the peer review system internal to science itself.

In all, the findings of this thesis indicate that Mode 2 knowledge production as a positive and normative description of the current state of affairs in science is ambiguous. The framework of proximity and diversity helps to conceptualize the distributed organization of science and hence renders the idea of Mode 2 knowledge production analytically tractable. As a positive description of science, heterogeneity in the distributed organization of science is neither obvious as it introduces problems of coordination nor does it render societal relevant knowledge more likely per se. As a normative description of science, more heterogeneity in the distributed organization of science need not be desirable per se considering that the interests of individual actors need not be in line with the general interest of public science.

This thesis contributes to an understanding of a distributed organization of science, yet some limitations remain. Some of these limitations can be taken up in further research. Above all, the empirical results of this thesis are restricted to the case of diabetes medicine. Therefore, the extent to which the results can be generalized across the sciences at large is unclear. To the extent that other sciences can be expected to be even less Mode 2 than diabetes medicine due to the inherent complexities involved in this particular problem, one can expect that heterogeneity is even less apparent in these other sciences. Still, it is unclear to what extent different dimensions of heterogeneity play a role across the sciences. Here again however the proximity framework provides a useful analytical tool to address differences in the distributed organization of science across topics. Just as we compared territorial science systems, science systems that concern themselves with different problems can be compared in their heterogeneity along five dimensions.

In addition, although we stress that the organization is not a fixed unit of analysis in quantitative studies of science, we made little attempt to perform analyses using different operationalizations of the organization. What is more, since we focused on the issue of diabetes, we did not include the cognitive dimension as delineating the boundaries of the organization. As a more general note then, we propose to perform analyses using different operationalizations of the organization. Not only can we compare the results of analyses assessing the distributed organization of science systems along lines of heterogeneity; we can also compare different rankings using different operationalizations of the organization.

All empirical chapters in this thesis are based on a static research design. That is, we used cross-sectional regression analyses to address the issues at stake. We were able to compare different territorial science systems in terms of proximity, address the effect of diversity on rendering societal relevance, and estimate the determinants of scientific publication by pharmaceutical companies. In addition however, a dynamic perspective might also render valuable insights on the distributed organization of science. In fact, as Mode 2 knowledge production is said to be an emerging phenomenon, a dynamic network approach on the evolution of scientific collaboration is most welcome. Not only might the role of different proximity dimensions in shaping collaborative science differ across territories and problem solving activities, they might also differ over time (see e.g. Balland et al. 2011). For example, as knowledge on a particular solution to a problem becomes more accepted (i.e. less controversial) the role of geographical proximity might become less important (Frenken 2010).

In a different vein a dynamic perspective is much needed in assessing the process through which research is transformed into science and ultimately enters the societal domain. As of recent such analysis has been difficult, if not impossible. This has rendered most studies to take a rather fragmented approach. With respect to medicine, while Fisher (2009) addresses the practices within the operation of clinical trials, Timmermans and Berg (2002) address the use of clinical practice

guidelines by medical practitioners. Chapters 6 and 7 of this thesis cover some of the space in between. That is, we address decisions to publish study outcomes once they have been generated (chapter 7) and the likelihood of being cited as evidence in a clinical practice guideline once the results have been published (chapter 6). However, now that registration of clinical trials before study onset has become mandatory (see www.clinicaltrials.gov) and the inscription of recommendations becomes ever more standardized (see e.g. www.guideline.gov), more data has become available to address the whole sequence from research via science to implication. More in general, quantitative studies of science might improve our understanding of knowledge production by not only taking into account journal publication data but also considering alternative data sets reflecting upon research and science's context of implication.

Finally, let us briefly address some policy implications of this thesis. Our analytical framework of heterogeneity stresses the different dimensions to collaborative science. As argued in the opening section of this introduction, contemporary science policy discourse takes collaborative science as a condicio sine qua non found on the promise that it renders solutions to the most pressing societal problems more viable. The notion of Mode 2 knowledge production in this respect provides an extreme configuration of a distributed organization of science. Our explicit framework along five dimensions of heterogeneity allows policy makers to address the distributed organization of science more carefully. Particular kinds of collaborative science can be more explicitly targeted ex ante. For example, in a context where transdisciplinarity is expected to raise societal relevance, science policy should focus on supporting collaborative science crossing cognitive boundaries in particular rather than replying on a broad notion of Mode 2 knowledge production along all five dimensions. Likewise, the effects of a particular form of distributed science can be evaluated ex post. That is, using scientometric techniques we can measure the extent to which collaborative science is organized heterogeneously along different dimensions and to what extent such heterogeneous collaborative also renders its outcomes relevant more likely. As heterogeneity in a distributed organization of science is neither self-evident from a coordination perspective nor necessarily good in both a positive and a normative sense, policy makers on the one hand ought to make clear what kind of heterogeneity is most wished for and on the other hand make sure that possible downturns to heterogeneity are ruled out. It is this debate, on what kind and the extent to which we want Mode 2 knowledge production, that policy makers should be engaged in.

2. Spatial scientometrics: towards a cumulative research program[4]

2.1. Introduction

During the past five years, we witness a surge in studies that address spatial aspects of science. Though research on national differences in publication output and international collaboration goes back a long time, it is only recently that the spatial analysis of science is broadened to include the regional[5] unit of analysis and the effects of geographical distance on the scientific interaction. Doing so, scientometrics follows the increased interest in science and technology studies in the globalization of knowledge production on the one hand (Ziman 1994; Stichweh 1996) and the location of such activities in specific places on the other hand (Shapin 1998; Cronin 2008). We suggest to group these contributions under the heading of spatial scientometrics.

We present a review of the quantitative science studies that explicitly address spatial aspects of scientific research activities. Here, we limit ourselves to classic papers and recent contributions, and only to those studies that made use of information as it can be retrieved from publication data.[6] For analytical purposes we treat space in our framework as a Euclidian surface. This perspective renders the three related concepts of direction, distance and connection central for understanding scientific knowledge production and diffusion in terms of nodes, networks and movements. In geography, such an approach falls under the heading of regional science or spatial analysis (for overviews and critiques see Martin 1999; Barnes 2001).[7]

From the review it will become apparent that key activities in scientific interaction (co-publication, citation, labor mobility) display clear spatial patterns. The review also makes clear that spatial analyses of science are generally done without taking into account other dimensions in terms of which scientific interaction can be characterized. It is for this reason that we turn to an analytical framework in the second part of the paper based on the proximity concept (Rallet 1993; Rallet and Torre 1999; Boschma 2005). In short, the proximity concept allows one to integrate the analysis of the spatial organization of scientific research with cognitive, organizational, institutional and social dimensions in scientific research. Such a framework provides researchers with a platform to combine hypotheses from different theoretical perspectives into a single scientometric framework.

2.2. A review of spatial scientometrics

The spatial scientometric literature is multifaceted in terms of the topics addressed and methodologies used. We choose to organize our review in this section under three headings: (i)

[4] Published as: 'Frenken K., Hardeman S., Hoekman J. (2009) Spatial scientometrics: towards a cumulative research program. *Journal of Informetrics*, 3: 222-232.' Hardeman contributed to all sections of the chapter.
[5] In the remainder, we mean by region a sub-national region.
[6] Other large datasets that have been used for spatial analysis of science include Framework Programme data for the European Union (Autant-Bernard et al. 2007; Magionni and Uberti 2007; Scherngell and Barber 2008), student mobility flows (Maggioni and Uberti 2007), editorial boards (Gutierrez and Lopez-Nieva 2001) and biographies of famous scientists (Catell 1906, 1910; Taylor et al. 2007). Some authors collected own data using surveys (Duque et al. 2005; Jöns 2007; Marceau et al. 2008).
[7] We refrain from using the terms 'geography' and 'geographical', as most contemporary geographers no longer use these terms to refer to Euclidean space (Lefebvre 1991; Massey 2004).

spatial distribution, (ii) spatial biases, and (iii) citation impact. The following section will go into specific methodological issues.

2.2.1. Spatial distribution

Probably the first comprehensive study discussing the spatial distribution of science is performed by Frame et al. (1977).[8] Here, the ISI Science Citation Index is assessed for 117 countries and 2,300 journals divided into 92 disciplines for the year 1973. This study found that publications are highly concentrated at the country level. The world's 10 most productive countries accounted for almost 84 percent of all ISI publications. More recent studies showed that the spatial concentration has remained high with OECD countries still dominant in world output (May 1997, Adams 1998; Cole and Phelan 1999; Glänzel et al. 2002; King 2004; Dosi et al. 2006; Horta and Veloso 2007).

The US typically ranks first and the UK second with respect to their share in the world's papers and citations. It remains unclear, however, to what extent the exceptional performance of the US and the UK can be attributed to an English-language advantage, an English-language bias in ISI data, or to the alleged better functioning of Anglo-Saxon institutional structures. A recent phenomenon worth noting in these descriptive studies is the rapid increase in scientific publications coming from China, which is likely to affect the top rankings in the near future (Leydesdorff and Zhou 2005; Zhou and Leydesdorff 2006).

Moving from the national to the regional unit of analysis, we find only few scientometric studies. The lack of regional research is probably due to the fact that the address information in many scientific publications does not contain the postal code information, which implies that regional information must be derived indirectly from address information. An early study on regions concerns the study by Matthiessen and Schwarz (1999), who addressed aggregated publication records of 1994-96 for European regions. They found a leading group in terms of publications of only four regions (London, Paris, Moscow, and the Amsterdam-The Hague-Rotterdam-Utrecht region) publishing more than 30,000 publications each with London as the absolute number one (64,742 publications). Normalizing for population size produced a somewhat different picture boosting the rank of city regions that rely heavily on science and have relatively small populations (e.g. Cambridge, Oxford-Reading, and Geneva-Lausanne). Differentiating among scientific fields did not alter group constellations and the four regions are present in almost every list of top 10 regions per discipline.

Only a few studies address the spatial distribution of citations. Bonitz et al. (1997) develop a Matthew index for countries. It turns out that both for science at large and for particular scientific fields only a few countries receive more citations than expected whereas a large majority of countries receive fewer citations than expected. Though the Matthew effect for countries is said to be rather stable over time, its magnitude is said to be rather small: only five percent of all citations account for the redistribution effect of citation winning countries and citation losing countries.

More recently, Batty (2003) assessed the concentration of scientific citations at the national, regional and organizational level. His study was limited to highly cited individuals in 12 scientific fields. He found that only a few countries (especially the United States), a few regions (especially

[8] Note that most studies until then either make use of publication data without taking space into account (for instance Merton 1937; Price 1963) or take space into account without making use of publication data (Catell 1906; 1910).

the south-west coast and the north-east coast in the United States), and a few organizations (especially Harvard University, Stanford University and University of California San Diego) are populated by highly cited researchers. At all different units of analysis there is considerate concentration of highly cited individual researchers.

Whether concentration of research also brings advantages is another relevant issue in spatial scientometrics. The notion of agglomeration advantages is useful here. These are efficiency gains for a researcher or research institute stemming from co-locating in a geographical cluster, that is, in the vicinity of many other researchers or research institutes, respectively. Advantages stem primarily from cost advantages in search costs for partners and new personnel, sharing of infrastructure, and the availability of supporting services. Furthermore, the cost of collaboration is lower as travel costs increase with physical distance.

We know of only two studies that have been specifically focused on the measurement of agglomeration advantages in scientific knowledge production. From an economic point of view, agglomeration advantages are best measured by the effects of spatial concentration on efficiency. In the context of scientific knowledge production, Bonaccorsi and Daraio (2005) analyzed the effect of spatial concentration of research on the publications per researcher. Looking at CNR researchers in Italy and INSERM researchers in France, they found agglomeration effects to be present indeed, though the evidence has found not to be very strong. Carvalho and Batty (2006) use a technique in which they are able to detect whether research productivity is spatially concentrated in the US after controlling for investments in Research and Development and for population. They also find agglomeration effects to be present though again the evidence is thin.

2.2.2. Spatial biases

The extreme spatial concentration of scientific activity is quite remarkable. There may exist systematic spatial biases in the interactions of researchers favoring those located in the vicinity of many fellow researchers. At least three mechanisms may explain why interactions in science are spatially biased towards physically proximate actors. First, serendipitous encounters are more likely when two actors are in close vicinity of each other. Second, the need for face-to-face interaction when engaging in interactions comes at a cost which increases as a function of travel time. Third, 'the rules of the game' that matter for scientific knowledge production (e.g. funding, labor market regimes, intellectual property right regimes, languages) are spatially differentiated and constrain mobility within particular institutional frameworks, in particular, within national boundaries.

One particular bias that has received a lot of attention within scientometrics is the bias to collaborate domestically rather than internationally. It is commonly assumed that the bias to collaborate nationally has decreased over time due to globalization of the science system. The classic study by Narin et al. (1991) looked at publications in 28 scientific fields in the period 1977-1986 and found that that the share of papers that are internationally co-authored increased from around ten percent in 1977-1979 to around 13 percent in 1983-1985. A number of studies have used the same definition of internationalization (Hicks and Katz 1996; Georghiou 1998; Glänzel 2001) with the most recent one showing that the share of internationally coauthored papers in all ISI publication increased from 10 percent in 1990 to 23 percent in 2005 (Leydesdorff and Wagner 2008). Liang et al. (2006) show in this respect that internationalization has also occurred at a

higher level of spatial aggregation, as the share of collaborations within the EU has decreased, while the share of papers that list both an EU-country and a non-EU country has increased.

Yet, the conclusion of 'internationalization' or 'globalization' in research collaboration is not undisputed. If one does not measure internationalization by the share of internationally co-authored papers, but by the share of international collaborations over national collaborations counting each co-occurrence of two addresses as one research collaboration, other results have been obtained. Using this alternative methodology, Frenken (2002) observed for EU collaborations in the period 1993-2000 that the strong bias toward domestic collaboration persists over time. Similarly, looking at eight disciplines, Ponds (2008) found for papers involving at least one address from the Netherlands that the internationalization of research seemed to have come to a halt in the Dutch case.

The tendency to collaborate domestically may also be related to the number of researchers in a country. An early study by Frame and Carpenter (1979) found that larger countries are less prone to collaborate internationally. Their analysis, however, did not control for the fact that if researchers would choose their partner randomly, researchers in countries with many researchers will automatically have a stronger domestic bias than researchers in smaller countries. Controlling for this effect, Frenken (2002) found that the countries with most researchers actually display the weakest bias to collaborate domestically.

Apart from analyzing biases towards domestic collaboration, studies have also focused on biases in the country of origin of the collaboration partner. Frame and Carpenter (1979) observed that the strongest collaboration patterns exist among nearby countries sharing socio-political characteristics. Frenken's (2002) study on the EU also found a bias toward collaboration with neighboring countries, while Frenken et al. (2008), in a study on the 36 most productive countries in the world, showed that the propensity to collaborate was negatively affected by the flight distance between capitals. Liang et al. (2006) drew similar conclusions for the countries of the European Union.

Studies on collaboration patterns among regions or cities are rare. The first study has been Katz's (1994) analysis of the effect of physical distance for university-university collaboration in the UK, Canada and Australia. Distance was computed from the physical distance ('as the crow flies') between the cities in which two universities are located. The main conclusion was that an increase in distance significantly decreases the frequency of research collaboration pointing toward the importance of face-to-face communication for collaboration. A subsequent study by Liang and Zhu (2002) for Chinese regions confirmed Katz's earlier study. At the city-level, Havemann et al. (2006) came to a different conclusion. They found that German immunological institutes are more likely to collaborate with partners in the same city, but in collaborations with institutes outside the city distance was found not to affect the probability of collaboration.

More recent studies applied the gravity model, which determines the collaboration frequency between two regions from their physical distance and their respective sizes, where size is measured by the total number of publications in a region. For Dutch NUTS3[9] regions, a gravity analysis by Ponds et al. (2007) used travel time as a distance indicator and concluded that a longer travel time decreases collaboration frequency, but less so for university-university collaborations than for

[9] The *Nomenclature of Territorial Units for Statistics* (NUTS) is a uniform breakdown of spatial units in the European Union which follows a four-level hierarchy that ranges from NUTS0 to NUTS3. The NUTS0 level corresponds to the territory of individual member states, whereas NUTS3 roughly corresponds to labor market regions in most countries.

university-industry-government collaborations. In a study on NUTS3 regions in the EU27, a gravity analysis by Hoekman et al. (2008) found that both physical distance (as measured 'as the crow flies') and country borders render collaboration between regions less likely. This study also found that the most producing regions and the regions hosting a capital city are collaborating more than proportionally. Such observations suggest that there are 'elite structures' consisting of well-off regions with excessive number of collaborations among them.

Concerning the analysis of spatial bias in citations, only few examples can be mentioned. Matthiessen et al. (2002) identified the 40 most publishing regions in the world in terms of publication output in 1997-1999 and compared collaboration with citation patterns among these regions. Though not using any systematic statistical methodology, they concluded from their data that (i) both citation and collaboration relations occur most frequently domestically, (ii) citations are much less affected by distance than collaboration, and (iii) that the domestic bias in citation and collaboration increase with the size of the country. Recently, Börner et al. (2006) assessed the kilometric distance decay of the 500 most cited research institutions in the United States between 1982 and 2001 statistically. As opposed to Matthiessen et al. (2002) the results suggest that there is a distance-decay in citation relations between research organizations: articles from nearby research organizations are more likely to be cited than articles from research organizations further away. Over time, the effect of physical distance on the probability of citation relations to occur did not decrease, which suggest that the Internet did not affect the distance effects in citation.

Spatial biases may also exist in the labor mobility patterns of researchers. Stephan and Levin (2001) selected a group of researchers based on highly cited papers in ISI and complemented the data with biographical information on their countries of birth. The main result held that the international mobility balances of researchers are highly skewed across countries, resulting in brain drain of researchers in some countries and exceptionally high contributions of the foreign-born to the science system in others, in particular, the United States. This result qualifies the finding of U.S. dominance in science as being partially an effect of migration. A more comprehensive scientometric framework to study movements of researchers is provided by Laudel (2003). The author asserts that longitudinal bibliometric data open up the possibility of tracking down changes in affiliation addresses of individuals over time. An application to elite researchers in two small research fields confirms the magnetic forces that draw researchers to the United States, but also points towards disciplinary specificities of the phenomenon (Laudel 2005). In this study, however, it remains rather unclear whether we should speak about mobility or migration of researchers as the extent to which movements have a permanent character cannot be observed from the data.

A final topic has been addressed by Van Dijk and Maier (2006) and concerns conference attendance patterns. Looking at papers presented at the annual European conferences of the Regional Science Association (ERSA), the authors analyzed the effect of physical distance on conference attendance. Using conference dummies to control for city-specific effects, they found that the physical distance to a conference venue indeed affects participation.

2.2.3. Citation impact

A particular question in scientometric research concerns the citation impact of different types of collaboration. In particular, several studies have compared the citation impact of internationally co-authored papers with domestically co-authored papers in the light of investigating the rationale

for internationalization policies. Such an effect is expected since more resources are invested in international collaboration and more diffusion channels are activated once results are published.

Among the first to assess this issue has been the study by Narin et al. (1991) on a subset of papers covering biomedical research published in 1977. They found that international co-publications are cited on average more often than domestic co-publications, while no differences were found for international co-publications among EU countries, between EU and non-EU countries and among non-EU countries. Katz and Hicks (1997) posed the same question for all publications from the UK in 1981-1991. Controlling for the number of authors, organizations and countries, they also found that the average citation rate of papers increases more by adding an author from a foreign organization as compared to adding an author from a domestic organization. Frenken et al. (2005) assessed the citation impact of international research collaboration in European biotechnology for the period 1988-2002, while controlling for number of authors and organizations as well as country dummies. They found only evidence of a higher citation impact of international co-publications for EU publications, while publications between an EU country and a country outside the EU did not receive more citations than a domestic collaboration. Using a similar methodology, but adding author-fixed effects to control for the observation that more successful authors tend to collaborate more internationally than less successful authors, Singh (2007) and He (2008) still found a significant and positive effect of international collaboration on citation impact compared to domestic co-publications. In all, these studies suggest that international research has more impact, on average, than domestic research

2.2.4. Summary

In quantitative science studies that explicitly take into account space, we distinguished between three major topics. First, there are descriptive studies on differences between countries and between regions in terms of their publication output and citations. Second, a range of studies found systematic evidence on spatial biases in collaboration, citation, labor mobility and conference attendance. Third, the citation impact for international co-publications is higher than for national co-publications. Table 2.1 provides a summary table.

Table 2.1. *Notions of space in spatial scientometrics*

Topic	Author	Geographical scope	Spatial unit	Notion of distance
Spatial distribution of publications	Frame et al. (1977)	World (117 countries, 7 sub-continental regions)	Country and sub-continental region	--
Spatial distribution of publications and citations	May (1997)	World (15 countries)	Country	--
Spatial distribution of publications and citations	Bonitz et al. (1997)	World (50 countries)	Country	--
Spatial distribution of publications and citations	Adams (1998)	World (7 countries)	Country	--
Spatial distribution of citations	Cole and Phelan (1999)	World (95 countries)	Country	--
Spatial distribution of publications	Matthiessen and Schwarz (1999)	Europe (39 regions)	Region	--
Spatial distribution of publications and citations	Glänzel et al (2002)	World (32 countries)	Country	--
Spatial distribution of citations	Batty (2003)	World (multiple countries and regions)	Country and region	--
Spatial distribution of publications and citations	King (2004)	World (31 countries)	Country	--
Spatial distribution of publications and citations	Leydesdorff and Zhou (2005)	World (31 countries)	Country	--
Spatial distribution of publications and citations	Dosi et al. (2006)	World (multiple countries)	Country and sub-national region	--
Spatial distribution of publications and citations	Zhou and Leydesdorff (2006)	World (6 countries, EU 15 and EU 25)	Country and sub-continental region	--
Spatial distribution of publications	Carvalho and Batty (2006)	USA	Region	Continuous
Spatial distribution of publications	Bonaccorsi and Daraio (2006)	France and Italy	Region	Categorical

Table 2.1. *Continued*

Topic	Author	Geographical scope	Spatial unit	Notion of distance
Spatial distribution of publications and citations	Horta and Veloso (2007)	World (EU 15 and USA)	Country and sub-continental region	--
Spatial bias in research collaborations	Frame and Carpenter (1979)	World (15 countries, 8 sub-continental regions)	Country and region	Categorical
Spatial bias in research collaborations	Narin et al (1991)	World (5 countries and EU 9)	Country	Categorical
Spatial bias in research collaborations	Katz (1994)	UK, Canada, Australia	Region	Continuous
Spatial bias in research collaborations	Hicks and Katz (1996)	UK	Country	Categorical
Spatial bias in research collaborations	Georghiou (1998)	World (EU – Economic zone, North-America, Japan, the Republic of Korea and Australasia)	Sub-continental regions	Categorical
Spatial bias in research collaborations	Glänzel (2001)	World (multiple countries)	Country	Categorical
Spatial bias in labor mobility of scientists	Stephan and Levin (2001)	USA	Country	Categorical
Spatial bias in research collaborations	Frenken (2002)	Europe (15 countries)	Country	Categorical
Spatial bias in research collaborations and citations	Matthiessen et al (2002)	World (40 regions)	Region	Categorical
Spatial bias in labor mobility of scientists	Laudel (2005)	USA	Country	Categorical
Spatial bias in research collaborations	Wagner and Leydesdorff (2005)	World	Country	Categorical
Spatial bias in research collaborations	Havemann et al. (2006)	Germany (multiple cities)	City	Continuous
Spatial bias in citations	Börner et al. (2006)	USA	Region	Continuous

Table 2.1. *Continued*

Topic	Author	Geographical scope	Spatial unit	Notion of distance
Spatial biases in research collaborations	Liang et al. (2006)	Europe (EU 15)	Region	Continuous and categorical
Spatial bias in conference attendance	Van Dijk and Maier (2006)	Europe (6 cities)	City	Continuous
Spatial bias in research collaboration	Ponds et al (2007)	Netherlands	Region	Continuous
Spatial bias in research collaboration	Tijssen (2007)	Europe (EU 15 and EU 27)	Region	Categorical
Spatial bias in research collaboration	Frenken et al. (2008)	World (36 countries), Europe (1316 regions), the Netherlands (40 regions)	Country and region	Continuous and categorical
Spatial bias in research collaboration	Hoekman et al. (2008)	Europe (27 countries)	Region	Continuous and categorical
Spatial bias in research collaboration	Leydesdorff and Wagner (2008)	World (multiple countries)	Country	Categorical
Spatial bias in research collaboration	Ponds (2008)	Netherlands	Region	Categorical
Citation impact	Narin et al. (1991)	World	Country	Categorical
Citation impact	Katz and Hicks (1997)	UK	Country	Categorical
Citation impact	Frenken et al (2005)	Europe (15 countries)	Country	Categorical
Citation impact	Singh (2007)	Europe (15 countries)	Country	Categorical
Citation impact	He (2008)	New Zealand	Country	Categorical

2.3. Methodological issues

Spatial scientometrics relies on the address information on publications to locate the places where knowledge is created or diffused to. Using such data is not without problems and a number of methodological issues are recurrent. Here, only those methodological issues are discussed that are of particular interest to spatial scientometrics rather than of scientometrics at large.[10] First, the use of address information is based on the assumption that addresses listed on publications tell something about the location where the actual research was conducted. In general, there are no reasons to believe that this assumption is unreasonable. Yet, we know that publication data exhibit noise and we do not yet have clear estimates of the amount and nature of this noise. For example, researchers on temporary visit may choose to list their home institute and researchers may sometimes list the grant organization rather than the institute where the research was being done. Concerning research institutes, headquarters are sometimes listed instead of the subsidiary where the research was carried out.

Second, address information refers to research institutes and not to authors. Only recently, information is available linking authors to addresses. In the absence of information on author-address links, multiple address publications may actually refer to a single author with multiple affiliations or an author who conducted research at one institute and subsequently moved to another institute. Even though someone with multiple affiliations can be said to establish collaboration between multiple organizations, its meaning is clearly different from a project where multiple researchers from different organizations are involved. It was estimated that within the UK on app. 2.5% of all articles the number of organizations exceeds the number of articles (Hicks and Katz 1996).

Third, constructing aggregated data at the level of spatial units also poses some methodological problems. The fundamental problem in spatial research is to decide what spatial unit is a relevant unit of analysis. Most studies aggregate addresses to predefined administrative areas (e.g. countries, states, provinces, municipalities, etc.). Yet, there is generally no reason to believe that such administrative boundaries coincide with relevant boundaries as perceived by researchers. In geography this problem is known as the Modifiable Areal Unit Problem (Openshaw 1984). It is well known that this problem has a significant effect on results in spatial analysis and caution when aggregating is therefore necessary. Ideally, one would like to analyze individual authors or institutes with a specific address and the effects of physical distance between each pair of authors or institutes. Effects of higher order spatial units can then be addressed in a multi-level framework. Yet, collecting and treating such detailed data is very time-consuming. Aggregating authors or organizations to a spatial unit is often more practical. In that case, labor market areas consisting of one major city and its commuting area can be considered the most relevant unit of analysis as such areas facilitate face-to-face interaction at a daily bases (Hoekman et al. 2008).[11]

Finally, from the relational nature of the data on research collaboration, citations, labor mobility and conference attendance raises the problem of measurement of physical distance. Distance can be measured in a categorical way (domestic vs. foreign) or in a continuous way. In the latter case, most studies rely on physical distance ('as the crow flies') as such information is readily available from Geographical Information System software. When dealing with regions or countries, distances are generally taken as those between capitals. However, more appropriate measures of

[10] For an account on methodological issues in scientometrics at large see for example Schubert et al. (1989).
[11] In the EU context, labor market regions are best covered by the NUTS3 level of analysis.

distance would be travel time or travel cost as these measures indicate more directly the real burden people have to overcome while travelling from A to B.

2.4. Towards a proximity approach

From our review it has become clear that, thus far, research in spatial scientometrics is rather fragmented and is lacking an analytical core. Studies differ in methodologies, units of analysis, notions of distance, and explanatory frameworks. What is more, spatial analyses of science are generally done without taking into account other dimensions in terms of which scientific interaction can be characterized. Following the analytical notion of proximity as introduced in the field of economic geography, we propose a framework that can function as one possible conceptual core allowing to link research in spatial scientometrics with other endeavors in scientometrics.

The proximity concept has been developed by a group of French economists interested in the spatial evolution of economic activities (Rallet 1993; Rallet and Torre 1999; Carrincazeaux et al. 2008). The main contribution of their approach lies in disentangling physical proximity from other forms of proximity. Like physical proximity, other forms of proximity structure interactions. To mention one prominent example, the presence of social relationships among employees of two firms may create trust and lower transaction costs in future interactions (Uzzi 1997).

In a review of the various literatures on the role of proximity on collaborative innovation, Boschma (2005) distinguished between five forms of proximity: physical[12], cognitive, social, organizational and institutional. All five dimensions can be expected to play a role in scientific interaction.

- Physical proximity, as already discussed, is generally taken as the kilometric distance (Liang et al. 2006; Hoekman et al. 2008), travel time (Ponds et al. 2008) or in a binary fashion contrasting domestic versus foreign relations (Frenken et al. 2005; Liang et al. 2006; Singh 2007; He 2008; Hoekman et al. 2008; Ponds et al. 2008). From the review provided above, we conclude that physical proximity indeed affects scientific interaction patterns.
- Cognitive proximity can be defined as the extent to which two researchers share the same knowledge base. Cognitive proximity among researchers is fundamental as to engage in meaningful interaction. As sociologists of scientific knowledge have been arguing, the establishment of a knowledge claim as a scientific fact is not exclusively determined by observation, but also requires that researchers have a shared understanding of the meaning of an observation (Shapin 1984; Collins 1985). Previous statistical studies have shown that cognitive proximity has a strong impact on citation (Baldi 1998; White et al. 2004). Similarly, one expects collaboration patterns to be primarily present among researchers who already share disciplinary knowledge, which is evident from the disciplinary focus of most journals and research departments.
- Social proximity can be defined as the extent to which researchers have friendly relationships. Social relationships facilitate interaction by creating trust among researchers. Trust is important in carrying out complex research projects, but also plays a

[12] Boschma (2005) calls this form of proximity 'geographical proximity' but for reasons of consistency we use the term physical proximity.

role in judging the validity of claims written down in papers (Shapin 1984). Social relations can stem from private life or professional life and have been measured as such in statistical studies addressing citation patterns between researchers (Baldi 1998; White et al. 2004).[13]

- Organizational proximity can be defined as the extent to which two researchers are under common hierarchical control, which is important to coordinate research activities. Such a variable can be constructed as a dichotomous variables indicating whether two people work for the same or for different organization as done in studies on the citation impact of research collaboration (Singh 2007; He 2008).
- Institutional proximity can be defined as the extent to which researchers operate under the same incentive structures, which aligns the objectives of researchers. In the context of spatial scientometrics, the main institutional spheres that are generally distinguished are universities, industry and government (Frenken et al. 2005; Ponds et al. 2007; Singh 2007). University researchers primarily aim at transforming research into publication, corporate researchers at transforming research into commercializing knowledge and government researchers at transforming knowledge into policies. This conflict of interest has been a central topic in the economics of science literature (Dasgupta and David 1994; Stephan 1996). The lack of institutional proximity in university-industry-government relationships reflects the complexity of such projects and the difficulty to design policies aimed at fostering projects (Gibbons et al. 1994; Etzkowitz and Leydesdorff 2000).[14]

The list of proximity dimensions presented here is by no means exhaustive. For example, lingual proximity (Liang et al. 2006), ethnic proximity, ideological proximity or proximity in terms of age may also play a role in scientific interaction. Analytically, the proximity approach as further outlined below allows for the inclusion of any number of proximity dimensions.

Any two entities (researchers, research institutes, regions, countries) can now be conceptualized as having a relational distance in five dimensions. Thus, for a study comprising of n entities, we have $\frac{1}{2}(n^2-n)$ pair wise relationships, which constitute the observations in a proximity analysis. For each observation, the distance between the two entities involved is then described in all proximity dimensions. Once the data are constructed in the manner, one can start to combine proximity dimensions in a single research design. Table 2.2 summarizes the analyses done so far in quantitative science studies that both take the spatial dimension into account and at the same time make use of one other proximity dimension.

The importance of explicitly including a proximity dimensions varies across research designs. Often, by focusing the study on a specific subset of publications one can already control for proximity dimensions in an implicit manner, albeit imperfectly. For example, analyzing the effect of physical proximity on collaboration between universities (Katz 1994), implicitly controls for effects of institutional proximity. Similarly, focusing the analysis on a particular discipline (Frenken et al. 2005; Singh 2007; Ponds et al. 2007; Hoekman et al. 2008; Ponds 2008) renders the inclusion of an explicit cognitive proximity less important.

[13] White et al. (2004) also speak of socio-cognitive proximity structures, which they defined as whether two researchers have collaborated in the past. In our framework, this form of proximity would be treated as social proximity following Singh (2007).

[14] Note that Hoekman et al. (2008) defined institutional proximity as a collaboration that takes place under the same set of territorially bounded institutions as in domestic collaboration. However, for reasons of consistency, we define domestic relations here under geographical proximity and position this study in table 2.2 in the column of geographical proximity.

Table 2.2. *Spatial scientometric papers using the proximity framework*

Author	Topic	Unit of analysis	Proximity dimensions				
			Physical	Cognitive	Social	Organizational	Institutional
Frenken et al. (2005)	Citation impact of collaboration	Papers	Categorical: domestic vs. foreign	-	-	-	Categorical : university vs. other
Ponds et al. (2007)	Collaboration bias	Organizations	Continuous: travel time	-	-	-	Categorical: university-industry-government
Singh (2007)	Citation impact of collaboration	Papers	Categorical: domestic vs. foreign	-	Categorical: past collaboration	-	Categorical: firms vs. other
He (2008)	Citation impact of collaboration	Papers	Categorical: domestic vs. foreign	-	-	Categorical: intra-university vs. extra-university	-
Ponds (2008)	Collaboration bias	Organizations	Categorical: domestic vs. foreign	-	-	-	Categorical: university vs. other

There are at least four types of analyses that can be done within the proposed proximity framework. In such analyses, several hypotheses can be developed and tested, and separate studies can be compared more easily in terms of their mutual consistency. First, taking these distances as independent variables, the strength of scientific interaction as the dependent variables can then be predicted. As a dependent variable one can take collaboration frequency, citation frequency or labor mobility flows.[15] This is essentially what is done when applying the gravity model (Ponds et al. 2007; Hoekman et al. 2008; Frenken et al. 2008), whether addressing collaboration, citations or labor mobility flows. The main advantage of the proximity approach as described here is that scientific interaction is assessed in a multivariate framework. Taking into account multiple proximity dimensions simultaneously is important since proximity dimensions are generally significantly correlated. That means that the effect of a particular form of proximity (e.g., physical proximity) can only be properly assessed when controlling for other proximity dimensions. For example, in general, one expects cognitive proximity to be much more important in structuring scientific interaction than physical proximity.

Second, within a proximity framework one can analyze whether proximities are substitutes. The proximity concept includes the idea that being proximate in one dimension allows distance in another dimension. For example, physical proximity is helpful in many forms of scientific interaction, but it is expected to be less important if two researchers are proximate in, say, the cognitive dimension. In the latter case, interaction through the Internet is expected to be very effective (Amin and Cohendet 2004). Another example concerns the relation between physical and institutional proximity. In university-industry-government collaboration institutional proximity is lacking, which might reflect why such collaborations are often realized within the boundaries of a region (Ponds et al. 2007).

Third, in the case of research collaboration, one can relate the proximity in each dimension to citation impact. For example, one can ask the question whether physical distance between collaborating actors contribute to the citation impact of the joint paper, while controlling for cognitive, organizational, social *and* institutional distance. Controlling for all proximity di mensions other than physical proximity is important to analyze whether physical proximity, or its absence, truly affects citation impact.

Finally, concerning research collaboration specifically, the notion of temporary geographical (i.e. physical) proximity is useful as to extend the proximity framework from mere static to dynamic analysis (Rallet and Torre 1999; Rychen and Zimmermann 2008; Torre 2008). For example, one can analyze whether different proximity dimensions matter throughout the 'life-cycle' of a scientific field. A new field may emerge from a single research institute where researchers develop a cognitive proximity in over time. When these researchers subsequently move to other organizations, geographical and organizational proximity vanishes, but the cognitive proximity built up in the past allows them to continue to collaborate effectively. On a shorter time-scale, one can analyze the evolution of a single collaborative project in terms of project stages. In this context, Torre (2008) developed the hypothesis that temporary geographical proximity through face-to-face meetings is most important at the start of such projects as to create a common understanding (cognitive proximity) and to agree upon coordination rules and management practices (institutional proximity). Once established, the need for face-to-face interaction falls and interaction can takes place effectively over long distance.

[15] Another dependent variable can be the similarities among science systems. Using co-structure cluster analysis Bonitz et al. (1993) argue that some countries are similar in their publication patterns to other countries. They suggest that these similarities might be due to geographical proximity as in the case of the Scandinavian countries or institutional proximity as in the case of the commonwealth countries.

Note that the concept of temporary geographical proximity can also be transferred to other forms of proximity. Cognitively, two researchers can become temporarily proximate through the intervention of a third researcher who translates knowledge from one domain to another domain. Such translators can be important in carrying our multi-disciplinary research. Socially, distant researchers can be brought together temporarily by someone they know in common. This mechanism is known as closure in network sociology. One study found that closure structures a significant part of co-authorships (Goyal et al. 2006). Organizationally, a temporal organizational form can bring together researchers under common hierarchical control. This is especially common in R&D collaboration between firms in the form of joint ventures. And, institutional distance can be overcome by allowing researchers to align their objectives on a temporal basis. For example, in university-industry collaborations corporate researchers may be allowed to co-author scientific papers with university researchers, or university researchers may be given a bonus if a research leads to a corporate patent application.

2.5. Concluding remarks

Our objective was to provide an analytic framework for spatial scientometric research. In our review of the literature, we extracted collaboration, citation and mobility as the main research topics. To analyze these forms of scientific interaction we then proposed to use the concept of proximity, which distinguishes physical proximity from other forms of proximity as determinants of scientific interaction. The framework provides researchers with a platform to combine hypotheses from different theoretical perspectives into a single scientometric framework.

3. Organization level research in scientometrics: a plea for an explicit pragmatic approach[16]

3.1. Introduction

The main aim of this paper is to come to terms with the organization and organization level research in scientometrics. Whatever the exact unit of analysis, by virtue of using bibliometric data, scientometric research is bound to run into data quality issues (Sher et al. 1966; Smith 1981; Moed 1988; Ingwersen and Christensen 1997; Hood and Wilson 2003; Moed 2005). These issues involve among others the completeness, correctness, and interpretability of the data (Galvez and Moya-Anegón 2007). Data quality issues are especially pertinent once we take the organization as the basic unit of analysis (De Bruin and Moed 1990; Bourke and Butler 1996; Bourke and Butler 1998; Van Raan 2005a; Van Raan 2005b; Galvez and Moya-Anegón 2006; Galvez and Moya-Anegón 2007). One notable exception aside (McGrath 1996), most of the debate on this matter is fairly technical (see e.g. Galvez and Moya-Anegón 2007). As such, most contributions presume a clear understanding of what constitutes the basic unit of analysis (i.e. the organization) in the first place (see e.g. Van Raan 2005a). To our opinion however, such "a-priorism" is at least awkward, given that even in such specialist fields as economics, economic sociology, and organization and management science there is no clear cut understanding of what constitutes the organization.[17] This then warrants a discussion on how to conceive of organizations in scientometrics.

The general argument of this paper holds that performing organization level research in scientometrics should proceed by taking an explicit pragmatic stance on the nature and boundaries of the organization. The nature and boundaries of the organization cannot be set purely objective; hence organization level research in scientometrics can only proceed pragmatically. As many "isms" in philosophy, pragmatism has been interpreted differently across the many contributions (Bernstein 2010). Notwithstanding the diversity in interpretations of pragmatism, we center our argument on three main assertions that support our main claim (see also Hjørland and Nissen Pedersen 2005; Hjørland 2008).

The first assertion holds that in order to perform organization level research in scientometrics one is always in need of and indeed always uses some kind of background knowledge on what constitutes an organization. This assertion then is a reformulation of the more general pragmatic claim made already by Peirce (1868) that every cognition is determined by previous cognitions. Perhaps we do not have and in fact even cannot come to a definite understanding of what constitutes an organization; let alone that we are and can be fully explicit about this understanding. Yet this does not mean that we do not have some understanding of the organization on which we might be more explicit. Section 3.2 then discusses the need for background knowledge in organization level scientometric research with reference to existing studies available from the literature.

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[17] The classic contribution to this debate is probably Coase's (1937) "The nature of the firm". Theories of the firm have been formulated ever since; ranging from transaction costs (Williamson 1981) to knowledge based theories (Grant 1996) and from a resource based view (Wernerfelt 1984) to a capabilities approach (Teece et al. 1997). Some of these approaches will be discussed in section 3.2. of this paper.

The second assertion holds that performing organization level research involves a balancing between on the one hand classifying the named entities we are confronted with from the bibliometric data as organizations and on the other hand conceptualizing the nature and boundaries of organizations on the basis of our informed intuitions. Performing organization level research then is not just the logic and immediate application of our background knowledge on organizations to the bibliometric data at hand, but also involves an alteration of this background knowledge and hence readjustments in classifying named entities from the data along the way. Comprehending organization level information from bibliometric data then is neither a purely theoretical nor a mere practical job, but reflects a practice which can be more or less theoretically informed. Hence, the more general pragmatic assertion alluded to here is taken from Dewey (1929) and holds that rather than seeking a dichotomy between theory and practice we would rather speak of less informed versus more informed practices in taking the organization as the basic unit of analysis in scientometric research. By drawing upon the discussions on the nature of classificatory work and the nature of the organization, section 3.3 discusses why comprehending organization level information from bibliometric data is never a purely logic activity.

The third and final assertion holds that the treatment of organizations within scientometrics depends on the goals, purposes, values, and interests of those pursuing organization level scientometric research. In other words, the way scientometricians make use of bibliometric data for organization level research is thoroughly inflicted with the orientation of the particular studies at stake. This assertion then resonates the idea set out by Putnam (2002) that fact and value are thoroughly entangled. That is, in stressing some aspects and not others in the description or explanation of phenomena lies an inherent attachment to particular normative positions. In section 3.4 then we continue to discuss our personal experience in using bibliometric data for organization level scientometric research. In so doing we try to make clear how the goals, purposes, and interests of our own study fed into our classification of organizations. Finally, section 3.5 concludes with some general remarks on some of the implications of this paper.

3.2. Comprehending organization level information from bibliometric data: the need for background knowledge

It is often stressed that using the organization as a basic unit of analysis in scientometrics requires a lot of cumbersome work in cleaning the bibliometric data (Moed 1988; De Bruin and Moed 1990; Moed et al. 1995; Bourke and Butler 1996; Bourke and Butler 1998; Van Raan 2005a; Van Raan 2005b). Part of this cumbersome work not only applies to the organization as a basic unit of analysis, but applies to other units of analysis in scientometrics as well. In general then, whatever the particular unit of analysis, bibliometric data suffer from many inconsistencies across records (Sher et al. 1966; Smith 1981; Moed 1988; Ingwersen and Christensen 1997; Hood and Wilson 2003; Moed 2005).

One of the main problems associated with extracting organization level information from bibliometric data is called the unification problem (see e.g. Moed 2005 pp. 183-187). That is, the problem that information of a single organization is scattered across multiple records in different forms. The problem of unification is basically twofold (Galvez and Moya-Anegón 2007). First, there is a lack of consistency in naming organizations across entities. Thus, the same organization is named differently across entities; i.e. bibliometric data contain organizational synonyms. Alternatively, not only do bibliometric data contain synonyms, they also contain homonyms; across records the same named entity can refer to different organizations. Second, there is a lack of

consistency in the amount of and the order in which named entities occur across records. That is, while some records contain a host of named entities containing information on all kinds of organizational aspects (e.g. "University of California at San Diego; School of Medicine; Department of Epidemiology; Division of Cardiovascular diseases; San Diego CA; United States"), other records make mention of a restricted number of named entities only (e.g. "University of California; San Diego"). What is more, the order in which these named entities occur across the data need not be standardized. That is, while some records might mention named entities belonging to the main organization first (e.g. "University of California; …; etc."), other records might mention named entities belonging to the sub organization first (e.g. "School of Medicine; …; etc.").

Whatever the specific causes of this twofold unification problem, what holds is that one cannot proceed in solving it without the use of background knowledge on what constitutes an organization. The need for background knowledge is readily acknowledged in the literature discussing the problem of unification. Moed (2005 p. 185) even explicitly states that "*[b]ackground knowledge about the institutions is essential*". However, most of the – implicit or explicit – references made to the need for background knowledge seem to refer to a particular kind of background knowledge. That is, most accounts on the need for background knowledge seem to refer to a need for a dictionary or other authoritive communications making sure that the named entities on organizations being scattered in different forms across multiple bibliometric records are justly unified. Moed (2005 pp. 185-186) goes as far as to argue that "*an appropriate identification scheme of an organisation's publication output must involve detailed background knowledge provided, or at least thoroughly checked by, the organisations themselves. Verification by representatives of the organisations is indispensable for obtaining outcomes that are sufficiently accurate and hence can be properly used in policy analysis and the public domain.*" The point is however that rather than solving the problem of justly unifying named entities, most contributions seem to merely circumvent the problem with reference to authority.

In fact, in referring to a need for authority as a kind of background knowledge, at least three additional problems are being introduced. One problem concerns the constitution of authority in the first place. In other words, which dictionary or communication counts as an authority and which not? Related, another problem concerns ascertaining the basis of the authority diverted to. Now, without having the pretention to solve these problems here, what holds is that they all point at the need for additional background knowledge that precedes our use of authoritive background knowledge such as dictionaries and communications with knowledgeable people. Obviously, these three problems cannot be completely solved by introducing more authoritive background knowledge, for these authorities would in turn require additional background knowledge to be interpreted and hence would eventually leave us being stuck in an infinite regress (see e.g. Collins 1985).

To make our point clear, consider an example from our own research in which bibliometric data records mention "Steno Diabetes Center; Copenhagen; Denmark". From its name "Steno Diabetes Center" alone it is not clear at all what kind of organization this is. Hence, a priori we cannot know whether this named entity should be treated as a single organization or whether it belongs to another main organization. In order to solve this ambiguity we turned to the website of this entity. That is, we made use of what we consider to be an authoritive source on the nature and boundaries of this named entity. From their website we read among others the following (Steno Diabetes Center 2011): "*Steno Diabetes Center is a world leading institution within diabetes care and prevention. Steno is owned by Novo Nordisk A/S and is a not for profit organisation working in partnership with the Danish healthcare system. … Steno Diabetes Center is associated with the*

University of Copenhagen through the university's hospitals management forum … Our vision is to become leaders in diabetes care and translational research with focus on early disease and prevention." In itself however, these excerpts do not provide a conclusive idea on the objective status of "Steno Diabetes Center" as an organization. In order to provide such a conclusive idea then we need to make additional judgments grounded in some kind of background knowledge that goes beyond these statements alone. The point we would like to stress then is not that the rules that have been used throughout the literature so far are necessarily wrong, but rather, and more modestly, that we need such rules in the first place if we are to perform organization level research using bibliometric.

The nature and boundaries of the organization do not follow immediately from the bibliometric data itself. Rather, the nature and boundaries of the organization have to be imposed on the data by the researcher using it. Indeed, we cannot filter out organization level information from bibliometric data alone but need additional background knowledge. However, the point we would like to raise is that the particular background knowledge that we need relates but cannot be restricted to the use of authoritive sources because these sources would require additional background knowledge to be understood and further applied in turn. Non-authoritive background knowledge then remains a prerequisite for any idea on organizations one starts of with and continuous to be necessary in further substantiating and adapting one's idea on the nature and boundaries of organizations as they are represented within bibliometric data.

3.3. The boundaries of logic in classification and the logics on the boundary of organizations

3.3.1. Classification and the boundaries of logic

The previous section of this paper discussed why background knowledge is always necessary if we are to comprehend organization level information from bibliometric data. Hence, we always need and indeed always use background knowledge on what constitutes an organization in order to comprehend organization level information from bibliometric data. As a first approximation then let us define the organization as follows: an organization is a group of people and their resources together performing tasks to achieve a common goal (e.g. Parsons 1956a). The task of comprehending organization level information from bibliometric data can then be characterized as on the one hand involving classificatory work and on the other hand involving conceptual work. In what follows we will discuss both in turn.

The idea of classification involves at least three aspects (Spärck Jones 2005). First, by implication, any classification is supposed to divide the universe of entities into a smaller number of objects. If we would keep the range and number of entities as they appear we cannot speak of a classification in the first place. With respect to our concern here we are concerned with a reduction of all named entities in to sensible organizations. The underlying rationale of every classification then is to provide a simplification for the complete range of different entities. Second, any classification is based on the premise that any two entities that appear within the same class can be said to be similar in one way or another. That is, entities that belong to the same class (i.e. organization) share characteristics that make them distinct from other classes (i.e. organizations). Third, any classification is meant to attribute meaning to the classes thus derived. That is to say, by virtue of assigning an object to one class and not to another this object gets a particular interpretation and not another. Without such meaning classifications can be said to reflect mere groupings of objects and can readily be conflated with statistical techniques such as clustering. Such statistical

techniques however in itself never provide an interpretation of these groupings, something that classifications do strive for. More formally then, we can describe classifications as meaningful groupings of objects that resemble each other (see also Hjørland and Nissen Pedersen 2005).

Ideally then, we would like to come up with a classification system in which all entities can be consistently and meaningfully assigned to mutually exclusive classes (Bowker and Star 1999). Developing such an ideal type classification is however constrained by issues of logic, issues associated with meaning, and the interaction between these issues of logic and meaning (Hjørland and Nissen Pedersen 2005). First, logical issues revolve around the extent to which entities can be systematically, exhaustively, and non-discriminatory assigned to classes on the basis of their properties. Depending on the number of properties characterizing each entity and the number of organizations we are to deduce from these objects it can be readily shown that a logic classification need not be possible. Consider for example 3 entities (I, II, III) with each two properties (A and B) that can be of two types (A1 versus A2 and B1 versus B2).[18] If element I is characterized by properties A1 and B1, element II is characterized by properties A1 and B2, and element III is characterized by properties A2 and B1 we cannot logically deduce 2 organizations from these three elements. Either we favor property A over property B and we consider elements I and II as one organization leaving element III as a second individual organization or we favor property B over property A and we consider elements I and III together as one organization leaving element II as a second individual organization. Again Spärck Jones (2005 [1970]) argues that the more a classification can be characterized as polythetic, overlapping, and unordered, the less feasible a logic classification becomes.

Second, issues of meaning revolve around the interpretation of different classes in terms of their representative function. Consider the possibility that the organization itself might be thought of in different terms by different people. Consider again 3 different entities (I, II, III) but now each with four properties (A, B, C, D). Obviously, if some only take properties A and B as constitutive characteristics of organizations therewith disregarding properties C and D while others conceive of properties C and D as constitutive characteristics of organizations therewith disregarding properties A and B we end up with different organizations if properties A, B, C and D are distributed differently (i.e. do not come in pairs) across entities. If for example entity I is characterized by properties A1, B1, C2, and D2; entity II is characterized by properties A1, B1, C1, D1; and entity III is characterized by properties A2, B2, C1, and D1; it follows that these entities will form different organizations depending on which properties are deemed important in constituting an organization. Here, Mai (2004) rightly argues that any characterization of units (i.e. organizations) in terms of properties depends crucially upon what counts as a constitutive property and hence how organizations ought to be thought of in the first place.

Third, the interaction between issues of logic and meaning revolve around situations in which these two issues might be in conflict. On the one hand, based on a given set of properties a logic classification might be deductible whose classes can be said to have little meaning. For example if properties A1 and A2 are distributed evenly across a large amount of entities, classifying on the basis of this property only might render large chunks of objects we would hardly call organizations. In other words, a particular property might be a necessary but not a sufficient condition (i.e. a defining characteristic) to call a group of entities an organization. Such properties then are not considered distinctive enough to base a meaningful classification scheme on.

[18] The examples considered here are drawn from Hjørland and Nissen Pedersen (2005) comparison of objects with different shapes and colours.

On the other hand, a meaningful identification of classes need not be logically deducible due the possible transgressive nature of the properties involved. That is, while the boundaries of the prime unit of interest may be vaguely set, so can the properties that are said to make up this main unit. With respect to comprehending organization level information from bibliometric data, and anticipating our discussion of the boundaries of the organization in the next section, we argue that many of the characteristics defining the organization are fluid rather than fixed. That is, many properties characterizing the organization gradually flow into its surroundings.

To conclude on classificatory issues, we stress that although in principle we might be able to come up with a logic classification of organizations from information entities available in bibliometric data, this classification might not make sense in terms of our general idea on what constitutes an organization. Hence, in classifying objects from a set of elements often we have to find a middle way between interpretative richness (i.e. including all possible properties in their variegated appearances) and logical robustness (i.e. relating elements systematically to form coherent objects). This then brings us at discussing our basic idea on what constitute the nature and boundaries of the organization beyond our first approximation given at the beginning of this section.

3.3.2 The logics of the boundary of the organization

Let us first qualify the classification issue at hand a bit more formally. Strictly when we speak of classifying named entities that refer to organization level information from bibliometric data we do not necessarily talk about the classification of organizations around us. That is to say that we only speak about the organizations as they are represented by particular information entities in bibliometric data. In principle we are interested in classifying these named entities into meaningful groups that we call organizations instead of being interested in classifying organizations. To the extent that we concordate named entities from bibliometric data that refer to organization level information with a given set of organizations that we see around us, one might even argue then that we are concerned with matching information rather than classifying organizations. Yet, to the extent that we don't know what it is that we call organizations as we see them around us we are not just matching organizations as they exist but also classifying them at the same time. This then immediately brings into focus classifying organization level information from bibliometric data as problematic given its non-straightforward interpretation as a basic unit of analysis in the first place.

Already from an intuitive understanding on the nature and boundaries of the organization we can come up with numerous aspects that can be considered as belonging to the organization. That is, defining the organization as constituting a group of people and their resources together performing tasks to achieve a common goal, immediately brings to the fore a number of images on the organization (Morgan 1986). We can link the nature and boundaries of the organization to a particular name (e.g. Eli Lilly and Company), a particular good (e.g. the drug Prozac) or abbreviation (e.g. its ticker symbol LLY), but also to an exemplary building and its location (e.g. the Lilly Corporate Center in Indianapolis, Indiana), a particular subsidiary (e.g. Elanco Animal Health), an even finer grained organization level (e.g. Lilly Research Laboratories) or just an individual (e.g. its CEO John C. Lechleiter).

Although all important in their own right, these images together do not immediately provide a comprehensive picture of the organization as a whole. Yet they do provide some insights on the

constitutive characteristics of the organization. One such characteristic defines the organization in terms of legal ownership structures. The ILL ticker symbol, Elanco Animal Health as a subsidiary of Eli Lilly and Company, and John C. Lechleiter being its CEO all resonate an idea of the organization as a formal legal entity and relates to descriptions of organizations as hierarchical, bureaucracies, and involving employment relationships controlled by managers. In a strict sense, organizations ought to be distinguishable from one another through clearly identifiable distinct hierarchical control systems (i.e. ownership and employment relationships). This idea is particularly salient within transaction costs economics approaches to organizations (see e.g. Williamson 1981). The argument from the classic contribution of Coase (1937) holds that the existence, size and boundaries of the organization (firms in his account) are determined by its relative efficiency to coordinate exchanges as compared to the market. As long as hierarchical/managerial control is more efficient (i.e. less costly) in coordinating exchanges than prices, the formal organization will be the dominant mode of coordinating economic activities. In the context of drawing organization level information from bibliometric data here, this would imply taking into account the legal ownership status of every organizational constellation vis-à-vis other organizational constellations.

Another constitutive characteristic of the organization revolves around the kind of activities performed by the organization. Producing pharmaceutical drugs is thus taken as a constitutive characteristic of Eli Lilly and Company. The good or range of goods that are produced often contrasts one organization from another organization. As such, the goods produced by a commercial firm are often taken as different from the goods produced by a university. Not only then, are the goods taken as different but also the means by which these goods come about are very much constitutive of the organizations producing them. For that matter, commercial firms are said to operate by a different set of norms and values than universities. The idea of organizations as delineated by the kind of and way they produce goods, resembles the idea of Parsons (1956a) on organizations as functionally and institutionally differentiated subsystems of society. As such, Parsons (1956b) identifies four such subsystems which can in principle be further differentiated: (i) organizations with an economic goal orientation, (ii) organizations with a political goal orientation, (iii) integrative organizations, and (iv) pattern-maintenance organizations. Apart from taking into account the legal ownership status of organizational constellations then, a view on organizations as constituting functionally and institutionally differentiated subsystems of society, implies that in cleaning up organization level bibliometric data we should also take into account what and how these organizational constellations produce goods.

A final characteristic discussed here refers to the organization as a particular place or space. This place can be a concrete building such as the Lilly Corporate Center or a more abstract space as for example Lilly Research Laboratories. This place can be fairly concentrated such as in the city of Indianapolis (Indiana) or distributed as is inherent to the idea of Eli Lilly and Company as a multinational. What holds then is that the idea of organization has a clear geographical connotation (see also Dicken and Malmberg 2001). As such, a geographical connotation to organizations refers to co-presence as a constituting characteristic of as organizations defined earlier as groups of people and resources jointly performing tasks to achieve a common goal. More in general then, geography provides a means to set the boundaries of the organization; i.e. a means to bundle labor, resources, and markets (to the extent that these are locally constituted). What is more, many named entities in bibliometric data contain information on the locality of organizations and hence provide the means to actually nail down organizations on the global map (Leydesdorff and Persson 2010).

So far, our understanding of the nature of the organization is directed at the organization as a multidimensional study object. Apart from the already discussed dimensions legal ownership, type

of activities involved, and geographical scope, other dimensions can be easily added such as the knowledge base.[19] However, whatever the exact dimensions involved, this multidimensional nature in itself does not tell much about the scope of these dimensions, that is, their boundaries. For some dimensions the exact boundaries of the organization seem to be easily set in theoretical terms. With respect to legal ownership for example it can be readily argued that the boundaries of the organization can be drawn at the point where its power to execute formal control stops. Likewise, the boundaries of the organization can be drawn at the point where different goals are pursued.

These theoretical ideals are however hardly systematically tenable once we need to comprehend organization level information from bibliometric data empirically. First, the idea that organizations can be distinguished on the basis of legal ownership and employment relationships make organizations that are intuitively taken as distinct (e.g. Eli Lilly and Company and Pfizer, Inc.) potentially to be considered as one organization by virtue of their boards being interlocked (see e.g. Mizruchi and Schwartz 1992). What is more, organizations that are intuitively taken as distinct might also be linked via formal partnerships (e.g. via alliances) and cross-ownership (see e.g. Shleifer and Vishny 1997). Second, the idea that organizations can be distinguished on the basis of their activities only shifts the issue to identifying mutually exclusive activity categories, that is, to answering such questions as does "university X" perform the same activities as "Research Institute X"? In addition, ascertaining the geographical scope of an organization need not be straightforward as well. That is, many organizations, as we intuitively understand them, are scattered across a larger industrial site, a city, regions, and even countries. Hence the idea of the organizations as belonging to a particular point on a geographical map does not necessarily hold.

In all then, and despite an understanding of the nature of the organization as revolving multiple dimensions, we are not able to fix the boundaries of the organization unambiguously. Rather, what we are left with is an understanding of the organization as in itself reflecting a multi-dimensional network among a dense web of relationships (Badaracco Jr., 1991). The task of comprehending organization level information from bibliometric data as on the one hand involving classificatory work and on the other hand involving conceptual work is hence problematic for at least three reasons. First, the nature of the organization can be characterized along multiple dimensions. Although not problematic in itself, this makes ideal type classificatory work in organization level scientometric research highly unlikely. Second, and more problematic, is that the scope of the dimensions defining the nature of the organization cannot be objectively fixed. That is, at some point we might speak of some entities as belonging more or less to any particular organization; however the exact point at which the one organization ends and the other begins cannot be set completely unambiguously. As such, the nature of the organization can be characterized as thoroughly transgressive leaving an unambiguous assessment of organizations in scientometrics virtually impossible. All this does not imply that we cannot perform organization level research in scientometrics altogether. Rather, and without falling into a trap of mere subjectivism, it is to suggest that we should abandon the sometimes salient idea in scientometrics that organizational level research herein can be completely objective.

[19] For example the knowledge base as delineating organizational boundaries (Nonaka 1994; Grant 1996; Teece et al. 1997).

3.4. How goals and interests feed into organization level research in scientometrics

The previous section of this paper discussed the practice of performing organization level research in scientometrics as involving a balancing act between on the one hand classifying the named entities we are confronted with from the bibliometric data as organizations and on the other hand conceptualizing the nature and boundaries of organizations on the basis of our informed intuitions. Both classification and conceptualization then run into the limits of logic; along the way of comprehending organization level information from bibliometric data we have to make ad hoc decisions at some point. This section pursues this argument further and addresses how views upon the organization reflect the goals and interests of organization level research in scientometrics. In order to make this argument clear we will draw primarily upon our own organization level research.

In the study for which we use organization level information from bibliometric data we are interested in a characterization of territorial science systems (see chapter 4). Following the notion of innovation systems (Carlsson et al. 2002; Lundvall 2007), we first defined science systems as a set of interacting organizations. A characterization of territorial science systems then involves typifying these organizations and their interactions. Different contributions to the literature on science and innovation systems stress different aspects in the characterization of organizations and their interactions (see among others Lundvall 1988; Gibbons et al. 1994; Etzkowitz and Leydesdorff 2000; Bonaccorsi 2008). Of all these contributions we believe that the notion of Mode 2 knowledge production (Gibbons et al. 1994; Nowotny et al. 2001) provides a fairly inclusive account in that it addresses an extensive number of dimensions at once (see also Hessels and Van Lente 2008). Hence we sought to characterize territorial science systems along five dimensions they pay attention to; i.e. the geographical, cognitive, social, institutional, and organizational dimension to knowledge production (see also chapter 2). As such we had to characterize every organization in our data as a point in multidimensional space.

In order to comprehend organization level information from the bibliometric data and assign to a point in multidimensional space we followed a five-step procedure (see also appendix A). First we collected the data of our science system of interest, that is, we collected all bibliometric records that represent publications concerned with tackling the problem of type 2 diabetes. Second, from the data thus retrieved we extracted all named entities we deem important as possibly reflecting information on the organizations of interest. Third, in order to make sure that unique organization IDs are consistently attributed across publication records and can thus be used as a starting point for our classification work, we manually checked a random set of organization id's for internal consistency. Fourth, we formulated a set of three rules that can be used to comprehend organization level information from bibliometric data. Fifth and finally, we applied these rules accordingly using two extra sources (i.e. the organizations' websites and an online tool for attributing geographical coordinates to the organizations).

The way goals and interests feed into the classification of organizations is best illustrated through a more in-depth discussion of the rules we applied in comparison to those applied by others in their classification work. Note however that the requirement of background knowledge discussed in section 2 of this paper already comes in when for example manually checking organization IDs on their internal consistency in step two and three. This consistency can only be checked against the background of some kind of baseline and thus requires considerable interpretation which in turn can only be performed with some kind of background knowledge. Likewise, the application of the rules set in step five requires considerable interpretation and as such can again only be performed

with the use of background knowledge. It is however in the actual formulation of classification rules and its underlying rationale that our goals and interests come most to the fore.

In order to comprehend organization level information for purposes of assessing territorial science systems we applied a set of three rules (see section 4 of appendix A). The first rule sets the hierarchical boundaries of the organization; the second rule sets the institutional boundaries of the organization; and the third rule sets the geographical boundaries of the organization. Together then we take the organization as a bundle of boundaries revolving on hierarchy, institutional domain, and geography (see also Carlile 2004 on the organization as a bundle of boundaries).

The geographical rule is perhaps a most obvious instance in which our study concern feeds into our classification of organizations. That is, if we are to assess interactions between any two organizations in terms of their geographical proximity (or distance), we have to locate every organization (as we define them) on the world map. This is not to say that assigning organizations to a particular location is a straightforward job to do. For one thing, a single organization can be substantively geographically distributed. While some organizations are located in a single building, other organizations are spread across a city, country or even the entire world. Second, the way the location of an organization is inscribed on publications and subsequently represented within publication records might vary considerably across publication records for the same organization. In order to still be able to assign every organization to a single location, part of our classification depends on restricting the geographical scope of any organization by a maximum of 50 kilometers separation between any two elements belonging to the same organization id.[20] Whereas in assessing territorial science systems every organization has to be attributed to a particular geographical location, in ranking organizations no such reference to the location of the organizations involved. That is, in ranking for example companies' productivity in terms of publication output it does not matter whether a particular company has branches on multiple locations across the world or is located at one particular site only. Hence while in some studies the geographical dimension need not be taken into account per se, for purposes of assessing territorial science systems the geographical dimension of the nature and boundaries of the organization have to be taken into account by implication.

With respect to our institutional identity of organizations we deliberately decide not to assign publications to organizations that are not mentioned on the publication record itself. Compare this with Van Raan (2005a) who argues from his concern with ranking universities that for some organizations (like CNRS in France) the publications should be assigned to a university. Likewise, in ranking universities the publications of hospitals neighboring the universities should also be assigned to the latter (especially university hospitals). Our concern however specifically resides in an assessment of the heterogeneous nature of interactions between organizations. As such it would be questionable to assign publications of for example political agencies or hospitals to universities especially given that claims on "Mode 2 knowledge production" (Gibbons et al. 1994; Nowotny et al. 2001) and a "post-modern research system" (Rip and Van der Meulen 1996) emphasize the role played by organizations other than universities. If we are to include these non-traditional scientific knowledge producing organizations into our analysis we cannot assign publication records of them to universities. All this is not to suggest that the method advocated by Van Raan (2005a) and others is misguided per se. On the contrary, given the "*fiercely debated*", "*sometimes controversial*", and "*politically highly sensitive*" nature of university rankings (Moed 2005 p. 185), it is perhaps applaudable to go for a strategy that reduces type 2 errors to a minimum (i.e. not

[20] It could be argued that instead of organizations our study is about the system of organization branches. Although we are appreciative to this point we do not think it alters our argument.

ascribing some publications to an organization while in fact they should have been). What holds however is that there is nothing natural or logical in attributing for example the output of university hospitals to a particular university.

We do not claim that our approach in classifying organizations is the best, let alone that our approach is most suitable for different kind of uses of organization level scientometric research. On the contrary, what we like to stress is that our classification of organizations has to be seen in light of the general orientation of our study. Given that both science systems and organizations can be described in similar terms along multiple dimensions we have to set boundaries on where the organization stops and the outer system begins. These boundaries then can be set reasonably, but not pure logically. Here we choose to set the boundaries of the organization along three dimensions (institutional, hierarchical, and geographical). In principle however one could add other dimensions as well. That is, one could set the boundaries of the organization on the basis of particular (related versus unrelated) activities or social relations as well. As our study is concerned with a fairly specialized field already (i.e. type 2 diabetes) and since we do not have data on relationships among employees we choose not to take these extra dimensions into account. To generalize on this point, we believe that every classification of organizations used in scientometric studies has to be seen in light of the goals, purposes, and interests of these studies. That is, throughout classificatory work in organization level scientometric research, scholars have to make choices. This does not mean that these choices are made arbitrary; most scholars have good reasons to go for one particular way of comprehending organization level information and not another. Yet, the choices that we make cannot be qualified as either "best" or "thoroughly wrong"; rather the choices that we make are biased, fallible (not wrong per se!), and hence always open to debate.

3.5. Concluding remarks

The main aim of this paper was to come to terms with the organization and organization level research in scientometrics. We deem this a pertinent issue, given that organization level research in scientometrics is abound although the whole notion of what constitutes an organization is rather vaguely set. It seems that in identifying unique organizations most scientometric studies thus far apply a set of mostly implicit rules only that appear to be objectively set. As argued throughout this paper however, rather than being objectively set, the boundaries of the organization in scientometrics can only be set pragmatically.

Our discussion of the pragmatic nature of organization level research in scientometrics might give the impression that we think of pragmatism as a theory instead of a philosophy, that is, as a way in which scientometrics actually proceeds rather than how scientometrics ought to proceed. Indeed, to our opinion, and as we have tried to show throughout this paper, organization level research in scientometrics can only proceed pragmatically. This claim of course leaves open the issue whether this situation is applaudable or not.

Let us then, by way of conclusion, briefly reflect on the normative implications of our main claim. For at least two reasons an explicit pragmatic approach to organization level research in scientometrics need not be lamentable. First, pragmatism opens the door to theoretical and methodological pluralism in scientometrics. An explicit recognition of the non-foundationalist (section 2) and fallible (section 3) nature of research might render non-positivist approaches more viable. This is certainly not to propose a relativist approach to scientometrics (see also Mäki 1997;

Collins 2009). Rather, it is an appeal on taking the provisional nature of all knowledge claims seriously. This means amongst others that scientometric studies have to open up on its conceptual, theoretical, and methodological proceedings (see also Opthof and Leydesdorff 2010). To our opinion then, explicitly recognizing the non-foundationalist and fallible nature of (social) scientific knowledge claims increases the likelihood that scientometrics comes up with a range of viable solutions to the issues at stake.

Second, an explicit pragmatic stance on organization level research in scientometrics might also help scientometrics to come to terms with those using its outcomes. As a specialist field of research, scientometrics easily runs the risk of being used uncritically by science policy makers and the lay public (Van Raan 2005a; Weingart 2005). Rather than seeking the solution to this problem only at the side of those using scientometric research, we believe there is much to gain once scientometrics itself becomes more open about its proceedings and practices (see also Shapin 1992). Given that organization level research in scientometrics can never be purely objective, scientometrics might consider being more explicit on its fallibility possibly rendering awareness at the side of science policy makers that scientometrics can indeed not be used uncritically. In all then, we not only believe that much of organization level research in scientometrics actually proceeds pragmatically; we also believe that an explicit pragmatic stance in scientometrics is a viable alternative to both overly positivist and overly relativist approaches as well as that it might render the relation between scientometrics and science policy more constructive.

Appendix A.

A.1. Extracting bibliometric records representing publications on type 2 diabetes

Extracting bibliometric information about a particular research field or discipline is in itself far from straightforward. Just as the organization is a highly transgressive entity, so are disciplines, research fields, and even – as in our case – particular research topics. The particular issue at hand involves coming up with a set of search terms that are both general enough to extract all records reflecting upon research on type 2 diabetes and still specific enough in order not to extract records that are not concerned with type 2 diabetes at all. The issue is especially complicated given that the arsenal of terms that is used to describe diseases (like type 2 diabetes) changes over time and across contexts (for a discussion on this matter see Bowker and Star 1999)). As such, the whole term type 2 diabetes as a particular form of diabetes for example did not even exist 70 years ago (Tattersall 2009). However, in restricting ourselves to a specific and fairly narrow time frame (1996-2008), we believe we are still able to come up with a comprehensive set of terms that capture type 2 diabetes during that period.

We used Elsevier's Scopus database to extract bibliometric records concerned with type 2 diabetes. In order to identify and extract all bibliometric records representing documents that are concerned with research on type 2 diabetes we constructed a search query based on a list of tags that capture the different names used to address this health problem (see table 3.1). The list that we used is adapted from discussions that we had with experts from this field of research and is complemented by terms denoting type 2 diabetes as they are provided by medical classification systems of the International Classification of Diseases (World Health Organization 2011), the Medical Subject Headings (MeSH) (U.S. National Library of Medicine 2011), and EMTREE (Elsevier Pharma Development Group 2009). Using the search query thus defined, we extracted

72,725 uniquely coded bibliometric records that represent scientific publications concerned with type 2 diabetes for the period 1996 – 2008.

Table 3.1. *Search query to extract publication records on type 2 diabetes*

1. The source of our bibliometric data is the offline version of Elsevier's Scopus which we acquired in June 2009.

2. In order to retrieve records representing evidence from research on type 2 diabetes we searched for records mentioning in one way or another the following terms in their abstract, title or (indexed or author) keywords: "non insulin dependent diabetes", "adult onset diabetes", "mason type diabetes", "maturity onset diabetes", "insulin independent diabetes", "non ketotic diabetes", "stable diabetes", "type 2 diabetes", "type ii diabetes", "ketosis resistant diabetes", "slow onset diabetes", "mody", "lipoatrophic diabetes", "insulin independent diabetes", "dm2", and "niddm".

3. Note that some terms denoting type 2 diabetes research are rather general, that is, some terms are suspect of having meanings not referring to type 2 diabetes in specific (e.g. "dm2"). Hence, we first performed a more general search for diabetes research using "diabetes" and "diabetic" as search terms only.

4. More formally then we used the following search query:
{{{diabetes OR diabetic} AND {{adult onset} OR {adultonset} OR {adult-onset} OR {auto somal dominant} OR {autosomal dominant} OR {auto-somal dominant} OR {autosomaldominant} OR {autosomal-dominant} OR {auto-somal-dominant} OR {insulin independent} OR {insulinindependent} OR {insulin-independent} OR {ketosis resistant} OR {ketosisresistant} OR {ketosis-resistant} OR {late onset} OR {lateonset} OR {late-onset} OR {mason type} OR {masontype} OR {mason-type} OR {maturity onset} OR {maturityonset} OR {maturity-onset} OR {non insulin dependent} OR {non insulindependent} OR {non insulin-dependent} OR {non ketotic} OR {noninsulin dependent} OR {non-insulin dependent} OR {noninsulindependent} OR {non-insulindependent} OR {noninsulin-dependent} OR {non-insulin-dependent} OR {nonketotic} OR {non-ketotic} OR {slow onset} OR {slowonset} OR {slow-onset} OR {type 02} OR {type 2} OR {type ii} OR {type-02} OR {type-2} OR {type-ii} OR {aodm } OR {dm 2 } OR {dm2 } OR {dm-2 } OR {mod } OR {mody } OR {ncdmm } OR {niddm } OR {niddy } OR {aodm,} OR {dm 2,} OR {dm2,} OR {dm-2,} OR {mod,} OR {mody,} OR {ncdmm,} OR {niddm,} OR {niddy,} OR {aodm:} OR {dm 2:} OR {dm2:} OR {dm-2:} OR {mod:} OR {mody:} OR {ncdmm:} OR {niddm:} OR {niddy:} OR {aodm;} OR {dm 2;} OR {dm2;} OR {dm-2;} OR {mod;} OR {mody;} OR {ncdmm;} OR {niddm;} OR {niddy;}} OR {{stable diabetes} OR {stable diabetic} OR {diabetes, stable} OR {diabetic, stable} OR {stable-diebetes} OR {stable-diabetic}} OR {{diabetes in young} OR {diabetes in youth} OR {diabetes mellitus in young} OR {diabetes mellitus in youth} OR {diabetes mellitus of the young} OR {diabetes mellitus-in-young} OR {diabetes mellitus-in-youth} OR {diabetes mellitus-of-the-young} OR {diabetes of the young} OR {diabetes-in-young} OR {diabetes-in-youth} OR {diabetes-mellitus in young} OR {diabetes-mellitus in youth} OR {diabetes-mellitus of the young} OR {diabetes-mellitus-in-young} OR {diabetes-mellitus-in-youth} OR {diabetes-mellitus-of-the-young} OR {diabetes-of-the-young} OR {diabetic in young} OR {diabetic in youth} OR {diabetic of the young} OR {diabetic-in-young} OR {diabetic-in-youth} OR {diabetic-of-the-young} OR {diabetics in young} OR {diabetics in youth} OR {diabetics of the young} OR {diabetics-in-young} OR {diabetics-in-youth} OR {diabetics-of-the-young}} AND {{maturity onset} OR {maturityonset} OR {maturity-onset} OR {non insulin dependent} OR {non insulindependent} OR {non insulin-dependent} OR {noninsulin dependent} OR {non-insulin dependent} OR {noninsulindependent} OR {non-insulindependent} OR {noninsulin-dependent} OR {non-insulin-dependent}}}

A.2. Extracting information on organizations from bibliometric records

Every record represents one or more strings of information. These strings are divided by 8 named entities containing organization level information (see table 3.2). The different named entities contain information on (i) the main name, (ii) a main organization ID, (iii) a sub-name, (iv) a sub-ID, (v) a country location, (vi) a city and/or region location, (vii) a more fine grained description of the location of an organization (e.g. a street, zip-code or post box; we call this the address), and (iix) additional organization level information not attributed to any of the other six named entities (we call this rest information). If we record wise split these strings of named entities we identify 186,719 such publication-record/organization-information combinations.

Table 3.2. *Strings with named entities (186,719 strings in total; 8 named entities per string)*

Main name	Main ID	Sub name	Sub ID	Country	City	Address	Rest

A.3. Classifying organizations (I): Scopus' main organization IDs as a starting point

In comprehending organization level information from our bibliometric dataset we choose to start from the main IDs. Given that within 96% of all strings the named entity on the main ID contains information at all and that the total number of different main IDs is relatively small (i.e. 22,647 main organization IDs); our unification problem would be considerably reduced if these main IDs are consistently attributed across all strings. In order to make sure that Scopus assigned the main IDs consistently, we randomly checked 105 such id's which occur across 18,390 strings (9.8% of all strings). This manual checking involved making sure that the different main names attributed to each unique ID are enough similar to conclude that they indeed represent the same organization. We performed this checking manually and conclude that, whereas only 1.8% of all ID-name combinations represent deviating main names, in general Scopus' main organization IDs are consistent across strings. This then lends support to taking Scopus' main organization IDs as our starting point in comprehending organization level information from the bibliometric data at hand.

Note however that the assertion that the main organization IDs within our dataset are internally consistent does not imply that they immediately leave us with a coherent set of entities which can reasonably be said to represent information on unique organizations. First, multiple main organization IDs might refer to the same organization entity. Most straightforward then, there might be two IDs that are both about "Harvard University". Likewise, there might be two IDs that concern the same organizations; e.g. one referring to "Leiden University" and the other referring to "University Leiden". Second, a single main organization ID might also (consistently) refer to multiple organizations (or organizational entities). For example, the name "Harvard Medical School Boston Brigham and Women's Hospital" refers consistently to a single main organization ID but can be reasonably considered to belong to two different organizations; i.e. Harvard Medical School and Boston Brigham and Women's Hospital. Hence, we still need to comprehend (unify and split) the main organization IDs to render unique organization level information that makes sense.

In addition there are two other issues to take into consideration. One is that locational information is attributed inconsistently across strings of the same main organization ID. As such, the named

entity reflecting the city name of an organization might refer to different cities for the same main organization ID. For example, the main organization ID referring to the University of California might sometimes refer to Los Angeles as its city location while in other cases it refers to San Diego. Likewise, the main organization ID of a multinational organization might report on locations across multiple countries. What is more, the detailed description of locational information differs across cases belonging to the same main organization ID. Thus, while it is possible to locate some cases at the address level, for other cases of the same main organization ID we only have locational information at the city level. Second, the hierarchical level to which a main organization ID belongs differs across main organization IDs. As such, "Harvard University" belongs to a particular main organization ID while "Harvard University Medical School" belongs to another main organization ID. Hence, main organization IDs can in principle refer to different levels of the same organization.

Table 3.3. *Problems of unification with Elsevier's Scopus' main IDs as a starting point*

Main name	Main ID	Country	City	Address	Rest
X	1				
X	2				
X/Y	3				
	4		A		
	4		B		
	4	i			
	4	ii			
	4			a	
	4			b	

Table 3.3 summarizes the main problems of unification: (i) a main name (X) can be scattered across multiple IDs (1 and 2); (ii) a main ID (3) can refer to multiple organizations (X and Y); (iii) a main ID (4) can be scattered across multiple cities (A and B), multiple countries (i and ii), and multiple addresses (a and b). Note that we choose not to take the named entities sub name, sub ID, and rest information to comprehend organization level information. Of these named entities, the sub ID had a coverage of only 72%. Yet for those instances for which we do not have a main ID at our disposal (i.e. 4%) we manually attribute a main ID judged on the basis of information contained by other named entities including these three.

A.4. Conceptualizing organizations: formulating rules to unify strings

In unifying the main organization IDs we introduce a threefold rule. Organization id "X" and organization id "Y" belong to the same unique organization:

1. if both belong to the same meta-organization (we call this the hierarchical rule) and,
2. if both belong to the same institutional sphere and the same institutional sphere as the meta-organization (we call this the institutional rule) and,

3. if both belong to the same geographical region in which they are not further apart from each other than 50 kilometers (we call this the geographical rule).

Note that this threefold rule only applies to unifying the different main organization IDs. However, in assigning every main name to a particular hierarchy we will split those strings. In the example from table 3.3 given above we will split main ID 3 (referring to both X and Y) into main ID 3.1 (X) and main ID 3.2 (Y). Hence, with respect to the main names, the resulting list of strings will only involve a problem of unification (although on the basis of the geographical rule main IDs might still be split!).

A.5. Classifying organizations (II): applying the classification rules

In order to apply the rules thus defined we made use of two additional sources. One source is the organizations' websites that we found using the text of the longest main name of every unique main ID. Searching for these websites we could first of all assess whether the text of a main name refers to a single organization (e.g. X) or to multiple organizations (e.g. X and Y). As argued earlier, once a single name refers to multiple organizations we split the string (3) into multiple strings (3.1 and 3.2). Second, from each website we assessed whether the organization thus addressed is part of a larger (meta) organization. If so, we noted the website of hierarchical levels. For example, "Harvard Medical School" is part of "Harvard University; hence we noted both http://hms.harvard.edu/hms/home.asp and http://www.harvard.edu/. Third, from each website we noted the institutional domain of the particular (meta) organization. We looked for the mission statements mentioned on the organizations' websites. On the basis of these mission statements we assigned every (meta) organization to a particular institutional domain. Similar to Parsons' (1956a; 1956b) idea of bracketing up society into sub-domains we distinguish among four such institutional domains: industry, care, academia, and political.

Table 3.4. *Assigning organization level names to institutional domains*

Institutional domain	Mission	Examples
Industry	Prime objective of generating income or profit for its owners	pharmaceutical companies; consultants; insurance companies
Care	Prime objective of providing medical care	Hospitals; medical centers (both private and public; including university medical centers)
Academia	Prime objective of producing medical scientific knowledge without profit orientation	Universities; schools; research institutes (both private and public; not-for-profit or non-profit)
Political	Prime objective proposing medical policy and its enforcement	NIH; ministries (public); WHO; NHS; patient representative groups

Table 3.4 summarizes the rationale for assigning organizations to a particular institutional domain. Whenever an organization does not mention a mission statement on their website (as e.g. Harvard University!), we assigned them an institutional domain on the basis of their names (hence Harvard University has been assigned to academia). Note that we assigned university hospitals to the institutional domain of care rather than academia. In light of our concern with new modes of

knowledge production in which the involvement of non-academic organizations is stressed, we believe that taking university hospitals as performing different activities than universities is legitimate. Finally, we merged those main IDs that belong to both the same meta-organization and the same institutional sphere.

The other source that we used in applying the rules defined previously (section 4 of this appendix), is an online tool to geocode information on the location of organizations (http://www.gpsvisualizer.com/geocoding.html; see also Leydesdorff and Persson 2010). First, from every string we group all three named entities that contain information of the location of the organization level information string. As such, we created a new named entity containing information like "address, city/region, country" and geocoded these new named entities accordingly. For every pair of strings that belong to the same hierarchy and the same institutional domain but have been assigned different geographical coordinates we calculated the kilometer distance separating them. From these distances and using K-means clustering we grouped all strings that are within a range of 50 kilometers from each other and attributed a new coordinate (longitude, latitude) to this organization. We use 50 kilometers as a reasonable range whereas figures on labor commuting areas revolve on this number (see e.g. Karlsson and Olsson 2006). Apart from taking 50 kilometers we also experimented with 30 and 70 kilometers as our geographical boundary of the organization. These alternative geographical boundaries did not alter the results of our analyses. In all then, following this threefold procedure we unified all main IDs that occur more than 9 times in our data set and on a global level eventually end up with 1,218 distinct organizations that can be characterized as a coordinate in five-dimensional space.

4. A proximity approach to the comparative analysis of innovation systems[21]

4.1. Introduction

Few doubt that the organization of scientific knowledge production has changed substantially over the past few decades. Universities now interact more closely with industry and other societal stakeholders to legitimate public funding on the one hand and to valorize their research findings on the other hand. Though, historically, these hybrid collaborations were already quite common in some fields of science, it has been argued that only recently these forms of collaboration have become ubiquitous. Indeed, this trend has been evidenced by publication data showing that universities increasingly co-publish with other institutional actors including firms, governments, and hospitals (Hicks and Katz 1996; Adams et al. 2005).

From a geographical perspective, one can expect that the nature and extent of such cross-institutional interactions differ across territories to the extent that territories control the institutions that structure such hybrid collaborations. A national innovation system (Freeman 1987; Lundvall 1988), then, can be defined as a country whose organizations interact across institutional spheres for the purpose of knowledge production and innovation. *Mutatis mutandis*, one can also speak of a regional innovation system (Cooke et al. 1998) or an international innovation system (Carlsson 2006). More generally, one can speak of territorial innovation systems with its boundaries defined by geographical areas that have some degree of institutional specificity (Morgan 2004).

A comprehensive assessment of the distributed nature of knowledge production has been proposed by Gibbons et al. (1994). They considered the increased interaction across institutional spheres as just one aspect out of many more aspects that characterize today's knowledge production processes. They introduced the distinction between the traditional university mode of knowledge production termed "Mode 1", and the emerging distributed mode of knowledge production termed "Mode 2". Gibbons et al. (1994 p. 34) summarized their central thesis concerning Mode 2 knowledge production as follows:

"*not only is the average number of authors per paper increasing, but much more significantly, so are the diversity of specialisms and disciplines involved in the writing of a single paper and the range of institutions and organizations from which the authors originate. In addition, the geographical distribution of these institutions continue to broaden. In mode 2, not only are more actors involved in the genesis of knowledge, but they remain socially distributed.*"

Thus, their thesis does not only emphasize university-industry-government collaboration similar to the territorial innovation system concepts, but it also highlights a trend towards globalization (Castells 1996) and interdisciplinarity (Barry et al. 2008) in collaborative knowledge production.

Though the concepts of innovation systems and Mode 2 knowledge production have become very influential in academic research and policymaking circles alike (Lundvall 2007; Hessels and Van Lente 2008), their use have been limited to qualitative research. We argue that the lack of quantitative empirical research emerges from a lack of operational concepts that capture the various characteristics of Mode 2, as a result of which there is a lack of methodological

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standardization and empirical understanding of the innovation system and Mode 2 concepts. We believe that, ultimately, operational difficulties are rooted in the a-theoretical notions underlying the two concepts. What is more, the proliferation of alternative concepts that aim to capture the changing nature of scientific knowledge production – the network society (Castells 1996), the triple helix of university-industry-government relations (Leydesdorff and Etzkowitz 1996; Etzkowitz and Leydesdorff 2000), academic capitalism (Slaughter and Leslie 1997), open innovation (Chesbrough 2003), global pipelines (Bathelt et al. 2004), logics of interdisciplinarity (Barry et al. 2008), and search regimes (Bonaccorsi 2008) – further complicates the quest for a common understanding and more cumulative research programs.

What is lacking is an analytical approach that allows for a systematic understanding of the nature and extent to which organizations interact in innovation systems, and how such systems can be compared across territories. As innovation system and Mode 2 knowledge production are essentially concepts that refer to 'interactive learning' (Lundvall 1988) and 'distributed' knowledge production (Gibbons et al. 1994), one can base an analytic approach on network theory and apply network-analytic techniques to quantitative data on collaboration. Below, we propose such a framework based on the proximity concept (Rallet 1993), which has also been applied to explain the drivers of network formation in scientific collaboration (for a review see chapter 2). The proximity dimensions we adopt are taken from Boschma (2005) and Balland (2011) who distinguish between cognitive, organizational, social, institutional and geographical proximity. As will be shown, these dimensions map almost one-to-one to various aspects headed under the Mode 2 knowledge production concept. That is, actors engaged in collaborative knowledge production can be positioned along the several Mode 2 dimensions as being more or less proximate, where proximity corresponds to Mode 1 and its opposite (distance) to Mode 2 knowledge production. In doing so, we develop an analytical framework for the study of territorial innovation systems based on the various dimensions of collaboration.

We apply our framework to the case of knowledge production in the field of type 2 diabetes, analyzing the worldwide patterns of collaboration in this field as well as providing a comparative analysis of the North-American (U.S. and Canada) and European (EU15 and Switzerland) innovation systems in the field of type 2 diabetes. Our system delineation is akin to the notion of a technological system (Carlsson et al. 2002) in that we delineate our innovation system in terms of the actors that work on solutions to a common problem (here, type 2 diabetes). We use co-publication data to indicate the collaborations between actors in the innovation system. As such the problem at stake concerns type 2 diabetes as addressed throughout the scientific literature; the actors involved are the organizations that concern themselves with providing evidence on solutions to this problem; and their interactions are reflected by collaborations among organizations as measured by co-publication.[22]

Our main results hold that: 1. geographical proximity is the prime determinant of research collaboration suggesting the geographical focus inherent to the concept of territorial innovation system is still warranted, notwithstanding the secular rise in international collaborations *per se*, and 2. institutional proximity is the least important in explaining research collaboration reflecting that, indeed, the 'triple helix' boundaries between university, industry, government and other stakeholders as the single most important mode of collaboration in innovation systems, are indeed blurred. On the specific comparison between North-American and European innovation systems,

[22] When looking at collaboration as captured by co-publication data, some may prefer to speak of science systems rather than innovation systems (see chapter 1). We choose to use the more common term of innovation system here, as scientific research is an integral component of medical innovation.

we find that social and organizational proximity play a relatively smaller role in Europe while cognitive and institutional proximity are equally important in Europe and North America.

4.2. Theoretical framework

If anything characterized the change in scientific knowledge production over the past century, it has been its increasing distributed nature. This trend was noted already by Price (1963) who noticed an increase in the number of authors on scientific papers. He described this trend at the time as a transformation from 'little science to big science'. Since then, the number of authors per paper has steadily increased with the mean number of authors per paper currently exceeding 3.5 in science and engineering and 2.0 in social sciences (Wuchty et al. 2007).[23] The secular trend in increasing levels of collaboration is accompanied by an increase in the share of university-industry-government relations (Hicks and Katz 1996; Adams et al. 2005) and increasing internationalization (Adams et al. 2005; chapter 2).

Interaction patterns between actors engaged in scientific knowledge production can be extracted from co-authorship data, or any other relational data such as grant data, acknowledgements, conference attendance, email exchange, et cetera. Such data allow for a systematic statistical analysis of the structure and evolution of research collaboration. To explain the pattern of interaction, the proximity approach is useful as it emerged from research in innovation networks (Rallet 1993; Rallet and Torre 1999). The proximity concept can be applied to interaction in science using the same five dimensions as distinguished in the study of innovation networks: cognitive, organizational, social, institutional and geographical proximity (Boschma 2005; chapter 2).

Cognitive proximity. The effective transfer of knowledge in research collaboration requires absorptive capacity to identify, interpret and exploit the new knowledge (Cohen and Levinthal 1990; Nooteboom 1999). In effect, the ease of knowledge transfer and mutual learning between actors may depend on the similarity of their knowledge bases (Lane and Lubatkin 1998). The capacity of actors to exchange and combine their knowledge requires cognitive proximity. That is, the knowledge bases of actors should be similar enough in order to communicate, understand and process scientific knowledge successfully. The importance of cognitive proximity is evident from the disciplinary nature of most scientific research, publishing and teaching.

Organizational proximity. Organizational proximity has been defined as the extent to which networks occur within the context of an organizational arrangement (Boschma 2005). Typically, organizational proximity thus refers to the extent to which any two actors are under shared hierarchical control. Historically, universities have emerged as the prime organizational vehicle to organize interaction between actors in science, where hierarchy is typically delegated to a *primus inter paris*. Yet, other organizational forms have emerged in science including public research agencies and industrial laboratories. Organizational proximity is argued to facilitate the establishing of collaboration networks, because it reduces uncertainty and opportunism in collaboration projects through collegiality and shared goal orientations.

[23] In humanities, by contrast, this trend is rather weak (Wuchty et al. 2007).

S**ocial proximity.** The notion of social proximity has its roots in the embeddedness literature (Granovetter 1985). This literature indicates that interactions are always embedded in a social context and that, in turn, social relations affect the outcomes of interactions. In the context of science, social proximity may refer to the extent that two actors have established a friendly relation in the past (in previous projects, as colleagues, as friends, or otherwise). As for organizational proximity, social proximity reduces the uncertainty and opportunism in collaboration, as opportunistic behavior will lead to reputational loss within an actor's social network (Dasgupta and David 1994). In addition, social proximity between actors may stimulate commitment and mutual trust, which both may trigger the initiation and continuation of collaborative engagements.

Institutional proximity. Whereas social proximity is defined in terms of socially embedded relations between actors at the micro-level, institutional proximity is associated with institutions at the macro-level. As such, actors are institutionally proximate once they operate under the same set of norms and values. Both formal and informal institutions structure behavior by providing particular incentives. In science, universities, industries, governments, and hospitals all operate under different institutional regimes, hence giving rise to incentive incompatibility problems (Dasgupta and David 1994). For example, firms have an incentive to appropriate knowledge, while universities have an incentive to publish research as quickly as possible. Collaboration thus benefits from institutional proximity as fewer conflicts are expected to arise when collaborators have similar incentives. This explains why cross-institutional collaborations (viz. 'triple helix interactions') are difficult to organize.

Geographical proximity. The final dimension to be distinguished is geographical proximity. There is a strong claim that geographical proximity is still an important driver of network formation despite the tendency for innovation systems to internationalize globalization (Castells 1996; Carlsson 2006). Indeed, the majority of scientific collaborations take place between actors that are geographically proximate, and generally, within the same country (Katz 1994; Hoekman et al. 2009). Geographical proximity is beneficial for research as effective learning requires face-to-face interaction to transfer tacit knowledge (Collins 1985). Such interaction is easier (and cheaper) to organize when agents are co-located in space. Once having defined the four other forms of proximity, geographical proximity can be defined in a restricted manner as the inverse of physical distance between actors in absolute (e.g. kilometers) or relative terms (e.g. travel time) (Boschma 2005).[24] For analytical purposes, it is essential to define geographical proximity in such a restricted manner, in order to isolate it from the other dimensions of proximity.

As proximity is an analytical concept, it offers some specific advantages in empirical work explaining the (spatial) structure of networks. First, by incorporating multiple proximity dimensions in a single explanatory framework, one can test what forms of proximity are determining patterns in collaboration networks. When including only one proximity dimension in the analysis, findings typically show strong explanatory power of that dimension. However, due to correlation between proximities, one can only assess the effect of a dimension if other dimensions are controlled for (Boschma 2005; chapter 2). Second, one can extend the list of relevant proximity dimensions from Boschma's (2005) five dimensions to any number of dimensions without changing the meaning of each dimension. For example, linguistic and cultural proximity dimensions may be introduced. Thus, the proximity dimensions are analytically orthogonal even though many dimensions of proximity may empirically turn out to be correlated.

[24] Some prefer to speak of physical proximity in this context (see e.g. chapter 2).

Although each form of proximity facilitates collaborative science and interactive learning, one expects a reduced impact of proximity in one particular dimension if proximity is already present in other dimensions. That is to say, to establish a (productive) relation, proximity in at least some dimension(s) is required to manage the inherent uncertainties involved in collaborative science. High levels of proximity in one dimension reduce the need for high levels of proximity in other dimensions. For example, Ponds et al. (2007) found that university-industry-government collaboration take place relatively often at regional levels. Here, geographical proximity compensates for the lack of institutional proximity in university-industry-government collaboration.

Following the proximity concept, the distinction between Mode 1 and Mode 2 knowledge production can now be made analytically. Mode 1 stands for scientific knowledge production in which actors are distributed, yet proximate, while Mode 2 knowledge production stands for distributed knowledge production processes, in which actors are distant. The proposed definition of Mode 1 coincides with the ivory tower image of scientific knowledge production, which is said to be disciplinary (cognitive proximity), within university departments (organizational proximity), in personal networks (social proximity), under a strict set of academic norms (institutional proximity) and co-present within the walls of the laboratory site (geographical proximity). Mode 2, by contrast, is characterized by Gibbons et al. (1994) as transdisciplinary (cognitive distance), cross-organizational (organizational distance), in temporary and open networks (social distance), with various, possibly conflicting, goals (institutional distance), and crossing national borders and physical space (geographical distance).

From a proximity perspective, one can further qualify the Mode 2 concept as proposed by Gibbons and colleagues. If one were to define Mode 2 knowledge production in a strict sense as collaborations in which actors are distant in *all* dimensions, one can expect to observe very few instances of such modes of collaboration. More often, one would expect to observe that actors are proximate in one dimension as a means to manage the difficulties and conflicts that arise from being distant in the other four dimensions. Accordingly, one could develop a more refined typology of Mode 2 knowledge production. For example, Mode 2 knowledge production within geographic clusters would make use of geographical proximity as an organizing principle, while Mode 2 knowledge production within a dedicated organization would make use of organizational proximity as organizing principle.

The proximity framework also aptly highlights the differences between the Mode 2 concept on the one hand and the more specific terminology proposed by other scholars. The innovation system concept stressed inter-organizational learning, cross-institutional interaction and proximity within a particular territory. As such, the innovation system concept (Freeman 1987; Lundvall 1988) emphasizes the importance of bridging organizational and institutional distances while benefiting from geographical proximity. Thus, while rich in scope, the innovation system concept does *not* explicitly include the cognitive and social dimensions of collaborative knowledge production.

Other concepts have been even more strongly focused on a single dimension. For example, the network society concept (Castells 1996) emphasizes geographical distance, the triple helix concept (Leydesdorff and Etzkowitz 1996; Etzkowitz and Leydesdorff 2000) and the academic capitalism concept (Slaughter and Leslie 1997) focus on institutional distance, the open innovation concept (Chesbrough 2003) is essentially addressing organizational distance, and the logics of interdisciplinarity concept (Barry et al. 2008) obviously deals with the role of cognitive distance. More encompassing are the notions of global pipelines (Bathelt et al. 2004) stressing geographical, organizational and cognitive distance and the notion of search regimes (Bonaccorsi 2008;

Bonaccorsi 2010) focusing on the role of cognitive and institutional distances in different disciplines and changes herein over time.

The main advantage of conceptualizing an innovation system in terms of collaborative knowledge production among proximate (Mode 1) or distant actors (Mode 2) holds that each single actor can be characterized as a coordinate in five-dimensional space using only the information on the actors involved. What is required is to operationalize the cognitive, organizational, institutional, social and geographical attributes of each actor such that their mutual distance can be established in five-dimensional space. This renders the empirical operationalization of the Mode 2 concept straightforward (obviously at the expense of the richness of the qualitative descriptions put forward by Gibbons and colleagues).

In our empirical analysis below, we will explain the intensity of collaboration between organizations as measured by co-publications in the scientific field concerned with type 2 diabetes by simultaneously incorporating all five proximity dimensions in the analysis. To our knowledge such a five-dimensional proximity analysis has only been performed empirically once by Balland (2011), yet on data limited to collaboration in EU funded projects rather than worldwide co-publications (see also Autant-Bernard et al. 2007). There has been previous work on co-publication networks, but these distinguished fewer proximity dimensions and analyzed inter-regional networks rather than inter-organizational networks (Ponds et al. 2007; Hoekman et al. 2009; Hoekman et al. 2010; Hoekman et al. 2011; Maggioni and Uberti 2009; Scherngell and Barber 2009, Scherngell and Barber 2011; Scherngell and Hu 2011). A second empirical contribution we make holds that we apply the proximity framework in a comparative perspective. In particular, we analyze to what extent the innovation systems of Europe and North-America can be said to be differently organized in terms of the relative importance of proximity dimensions in facilitating collaborative science.

4.3. Data and methods

Case. The choice for diabetes as a case to illustrate our framework empirically, resides first and foremost in the reality of the problem. Diabetes affects millions of people around the globe and is expected to do ever more so in the near future (Danaei et al. 2011; Hurley 2011). Within the scientific literature then, contributions to solving this problem have grown tremendously. The fact that diabetes is a chronic disease further underlines its importance. Diabetes not only affects many people, as a chronic disease it also affects many people for longer periods of time and possibly with major consequences.

The prime medical issue of diabetes is described as hyperglycemia, that is, the bodily condition in which an excessive amount of glucose circulates the blood. A state of hyperglycemia is problematic in that it is indicative of the blood delivering to little energy for the organs to function properly. When this state continues for longer periods of time, this may lead to severe complications. Among the complications of hyperglycemia, diabetic coma can be most acute. Other, more common complications involve a loss of sight and severe foot ulcers. Although largely similar in their complications, we can grossly distinguish two most prevalent types of diabetes (type 1 diabetes and type 2 diabetes). On the one hand, type 1 diabetes is generally taken to reflect a state in which the body is insufficiently capable of producing hormones that enable the transformation of glucose into energy (Tattersall 2009). The hormone of interest here has become known as insulin. As such, the discovery of insulin has been a major breakthrough in the treatment

of type 1 diabetes patients (Bliss 2007). That is, the discovery of insulin has made type 1 diabetes "manageable", yet the problem as such is far from being definitely solved (Mol 2008). On the other hand, type 2 diabetes is generally taken to reflect a state in which the body is insufficiently capable of metabolizing (i.e. transforming) insulin properly therewith leading to an inadequate bodily uptake of energy (Tattersall 2009). Regardless of the bodily capacity to produce insulin (characteristic of type 1 diabetes), type 2 diabetes is primarily characterized by a resistance or deficiency of the body to use insulin. As compared to type 1 diabetes, type 2 diabetes can be said to be even less intermediately solved. That is, to our knowledge no treatment has been proposed for type 2 diabetes so far that is fully capable of improving the bodily capacity to metabolize insulin on a continuous basis, in a similar fashion as insulin itself has been proposed as a continuous treatment option for patients with type 1 diabetes.

Diabetes, and especially its type 2 variant, constitutes a very complex disease involving many interacting factors such as genetics, lifestyle, and the (industrialized) environment (Zimmet et al. 2001). However, not only are the aspects involved in the constitution of this disease varied, as a consequence so are the people and organizations occupying themselves with finding solutions to this problem. What medical professionals call translational medicine (Woolf 2008) seems to be especially accurate for diabetes, that is, as a description of medical science that concerns itself with diabetes duly takes into account the whole process from the laboratory bench to the patient bedside involving different actors (see e.g. National Institutes of Health 2004). As such, the nature of diabetes as a scientific problem is immediately enmeshed with societal undertones whose provision of solutions can thus expected to be organized along various modes (Gibbons et al. 1994; Nowotny et al. 2003).

Dependent variable. The dependent variable in the analysis is the intensity of collaborative science between each pair of organizations. Co-publications are scientific papers that are produced by multiple organizations and are often used as indicator of collaborations in science (Katz and Martin 1997; chapter 2). Generally, co-publications concern co-authored papers by scholars each working for different organizations. In fewer cases, co-publications concern single-authored papers by scholars with multiple affiliations. In both cases, multiple organizations can be said to have been involved in the production of scientific knowledge.

It must further be noted that co-publications representing collaborative science are only a proxy of research collaboration, since not all research collaborations may end up in a scientific publication, and, *vice versa*, not all organizations mentioned on a paper may have had an active role in the production of that particular knowledge. Yet, as long as large sets of data are used, these exceptions are no longer expected to influence the conclusions that can be drawn from the data analysis. For this reason, co-publications have been an accepted indicator of collaborative science (Lundberg et al. 2006).

We used Elsevier's Scopus database to construct our dependent variable. We proceeded in a number of steps. First, in order to identify and extract all bibliometric records representing documents that are concerned with research on type 2 diabetes we constructed a search query based on a list of tags that capture the different names used to address this health problem (see appendix A to chapter 3). Extracting bibliometric information about a particular research field or discipline is in itself far from straightforward. The list that we used is adapted from discussions that we had with experts from this field of research and is complemented by terms denoting type 2 diabetes as they are provided by medical classification systems of the International Classification of Diseases (World Health Organization 2011), the Medical Subject Headings (MeSH) (U.S. National Library of Medicine 2011), and EMTREE (Elsevier Pharma Development Group 2009).

Using the search query defined, we extracted 72,725 uniquely coded bibliometric records that represent scientific publications concerned with type 2 diabetes for the period 1996 – 2008.

Second, every record lists one or more organizations as author affiliations. For each publication record, the information elements can include (i) the name of an organization, (ii) an organization ID, (iii) a sub-organization ID, (iv) the country in which the organization is located, (v) the city and/or region in which the organization is located, and (vi) a more fine grained description of the location of an organization (e.g. a street, zip-code or post box). If we split the publications record-wise for every organization represented thereon we identified 186,719 publication-organization pairs.

In addition, to identify unique organizations we made use of the ID Scopus assigns to an organization listed as an affiliation of an author of a document. To assess Scopus' consistency in assigning unique IDs to unique organizations, we randomly checked 105 such IDs across 18,390 records (9.8% of all information elements). This check involved making sure that the different names attributed to each unique ID are indeed representing the same organization. We performed this check manually and conclude that as only 1.8% of all records represent a deviating name, in general Scopus' affiliation IDs are consistent across records (at least in our case). This lends support to our approach to take Scopus' affiliation IDs as our starting point to identify organizations.

However, although the affiliation IDs assigned by Scopus are internally consistent, this does not imply that different affiliation IDs cannot refer to the same (overarching) organization. In order to make sure that different IDs indeed reflect different organizations we thus had to unify our organizational level data (see also Van Raan 2005a). We used a set of three rules to unify our organization level data. If any two affiliation IDs belong (i) to the same institutional sphere, (ii) the same hierarchical meta-structure, and (iii) the same geographical area; then these organization IDs are taken to reflect the same organization. Institutional spheres were assigned on the basis of the mission statements taken from the websites of the organizations representing the affiliation IDs. Similar to Parsons' (1956a; 1956b) idea of bracketing up society into sub-spheres we distinguish among four such institutional spheres: industry, care, academia, and government. Likewise, from their websites we assign all affiliation IDs to their overarching hierarchical structure. Given that a single (overarching) organization can be located at different physical sites we define the organization at the branch level. That is, every set of unique institutional-hierarchical entities were clustered according to their geographical location (see Leydesdorff and Persson (2010) for a discussion on using bibliometric data to map the geography of science). Here we took 50 kilometers of separation to delineate one branch from another.[25] Following this threefold procedure we unified all affiliation IDs that occur more than 9 times in our data set and eventually end up with 1,218 distinct organizations that can be characterized as a coordinate in five-dimensional space.[26]

[25] Apart from taking 50 kilometres we also experimented with 30 and 70 kilometres as our geographical boundary of the organization. These alternative geographical boundaries did not alter the results of our analyses.

[26] Note that our delineation of organization branches depends crucially upon our ideas on what constitutes an organization branch in the first place. A definite and 'objective' delineation of organization branches is hard if not impossible to achieve. We take the organization branch within innovation systems as constituting "*a dense network at the center of a web of relationships*" (Badaracco Jr. 1991 p. 314). Hence, our treatment of the organization closely follows a relational perspective on organizations as they are embedded in territories (Dicken and Malmberg 2001). As such we believe it fits perfectly within the larger multi-dimensional proximity framework.

Finally, for each pair of unique organizations, we counted the number of times they are co-occurring on a paper during the period 2003 – 2008. Given that we have a total of 1,218 organization branches, we have 741,153 observations of organization pairs. Since collaborations are undirected interactions (i.e. the number of collaborations between organization i and organization j is the same as the number of collaborations between organization j and organization i), we only use half of the total collaboration matrix. What is more, we only take into account inter-organizational collaborations and thus dispense with the diagonal of the full matrix (i.e. those instances in which organization i is the same as organization j). Hence, given $N = \frac{(n^2-n)}{2}$ where N is the number of organization pairs and n the number of organizations, we end up with 741,153 observations at the global level. It must be noted that most observations are zero implying that most organization pairs that could, in principle collaborate, did not actually collaborate at all during the period under investigation.

Independent variables. In order to explain collaboration intensity between each pair of organizations, we propose five independent variables covering the five proximity dimensions described (see table 4.1 for a formal description of the independent variables). First, geographical proximity is operationalized as the inverse of the distance in kilometers separating two organizations. Apart from measuring geographical proximity in terms of the inverse of kilometric distance, we also include a dummy variable measuring whether any two organizations are from the same country or not. While the former operationalization of geographical proximity comes closest to the idea put forward by Boschma (2005), the latter operationalization of geographical proximity captures the role of national boundaries deemed important within the concept of national systems of innovation.

Second, social proximity is operationalized as the number of prior ties between any two organizations, measured as the log of the number of co-publications in the period 1996–2002. We acknowledge that one would ideally have more fine-grained data on social ties between organizations, for example about labor mobility flows, friendship relations or ties among former colleagues (Breschi and Lissoni 2009). In absence of such data, we take social proximity as approximated by past collaboration activities, as this operationalization comes very close to the idea of flexible networks deemed important within Mode 2 knowledge production (Gibbons et al. 1994). That is, if social proximity as operationalized here explains collaboration, one would rather speak of inflexible networks and hence Mode 1 knowledge production. Note that as such social proximity as a determinant of collaboration does not necessarily reflect social relations as they occur at the time of collaborations but much more the persistence of past social relations.

Third, starting from the premise that organizations are more cognitively proximate when they often publish in the same academic journals, we measure cognitive proximity as the cosine of the overlap in journals in which any two organizations published in the period 1996-2002. Let X_i be a vector of length N=1995, where N is the number of all journals where type 2 diabetes research is published. The K^{th} element of X_i indicates the number of papers published by institute i in journal K. For a dyad comprising institute i and j, cognitive proximity is simply the cosine of the angle between vectors X_i and X_j. Using journal source information instead of patent class information this measure of cognitive proximity very much resembles existing measures of technological (Jaffe 1986) or knowledge relatedness (Breschi et al. 2003).

Fourth, institutional proximity is represented by a dummy variable denoting whether any two organizations belong to the same institutional sphere. In delineating organizations we collected data on the mission statements of the organizations involved. From the websites of organizations

we were thus able to assign every organization to a unique institutional sphere. It follows that any pair of organizations can be readily characterized in terms of institutional proximity once the two organizations belong to the same institutional sphere of either academia, industry, government or care (see also Ponds et al. 2007).

Table 4.1. *Description of variables*

Variable	Description
# Co-publications$_{ij}$	The number of papers between 2003 and 2008 on which both organization i and organization j both appear
Intra country dummy$_{ij}$	Dummy equals 1 if both organization i and organization j are from the same country
Geographical proximity$_{ij}$	The inverse of the distance in kilometers (plus 1) between organization i and organization j
Social Proximity$_{ij}$	The log of the number of papers between 1996 and 2002 on which both organization i and organization j appear
Cognitive proximity$_{ij}$	Cosine of the overlap in journals in which both organization i and organization j publish between 1996 and 2002
Institutional proximity$_{ij}$	Dummy equals 1 if both organization i and organization j are from the same institutional sphere (i.e. academia, industry, government or care)
Organizational proximity$_{ij}$	Dummy equals 1 if both organization i and organization j belong to the same hierarchical meta-structure
Mass$_{ij}$	The log of the total nuber of publications of organization i times the total number of publications of organization j between 2003 and 2008
Transitivity$_{ij}$	The number of organizations with which both organization i and organization j co-publish between 2003 and 2008
EU dummy$_{ij}$	Dummy equals 1 if both organizations are from the European Union
Expected collaboration propensity$_{ij}$	The square root of the number of dyads formed by organization i between 2003 and 2008 times the number of dyads formed by organization j between 2003 and 2008

Finally, organizational proximity is measured as a dummy variable indicating whether two organizations belong to the same overarching hierarchical meta-structure. In the context of our study organizational proximity can be of two kinds. It involves either a characterization of the relation between a university (assigned to the institutional sphere of academia) and its associated university hospital (assigned to the institutional sphere of care) or a characterization of the relation between two organizations of the same overarching hierarchical meta-structure but located at different physical sites. As such, our operationalization comes very close to a transaction cost interpretation of organizational proximity along hierarchical lines (Williamson 1981).[27]

Methods. To analyze the determinants of co-publication activity between any two organizations, we apply a gravity equation specification of the kind proposed by Ponds et al. (2007) and later adopted by Hoekman et al. (2009), Maggioni et al. (2009), among others. In a gravity model, the gravitational force between two objects is assumed to be positively dependent on the mass of the objects and negatively (positively) on the distance (proximity) between them. In our case this

[27] Note that, as for other proximity dimensions, institutional and organizational proximity are orthogonal. That is, any two organizations (defined at the branch level) might be organizationally proximate yet institutionally distant and vice versa.

means that the collaboration intensity between two organizations is dependent on their size (as approximated by their total number of publications) and the various proximity measures.

As in other gravity equation specifications to model collaborative science, we apply a zero-inflated negative binomial regression model since we deal with count data characterized by over-dispersion (see also Burger et al. 2009). In the zero-inflated part of our regression models we include one variable only that captures the expectation on any two organizations collaborating (i.e. "Expected collaboration propensity") (see table 4.2). As such we assume that in principle any two organizations should be able to collaborate provided both organizations have collaborative capacity in the first place. The negative binomial part of our regression models then explains the extent to which the collaboration intensity between any two organizations can be explained by proximity provided that the organizations involved can in principle collaborate.[28]

Given that our observations are at the dyadic level, each organization affects multiple observations. Known as Galton's problem (Tylor 1889), it can thus be argued that observations are not statistically independent therewith potentially leading to an underestimation of standard errors (Lincoln 1984). On top of this, co-publication networks generally show a high degree of clustering (Newman 2001). Consequently, collaboration as measured by co-publication need not necessarily be driven by a strict mutual (or dyadic) proximity rationale only rather by a rationale in which any two organizations are primarily connected by both being connected to a third organization. To correct for these issues we include a structural variable (i.e. "Transitivity") that accounts for the number of collaborators that any two organizations have in common (Lincoln 1984; Stuart 1998) (see table 4.1). In addition all models are performed reporting on robust standard errors.

4.4. Analysis

Table 4.2 shows the descriptive statistics of the variables included in the analysis. A first observation that can be made holds that organizational proximity is very rare. From the mean of this dummy variable, one can read that only 0.1 percent of organization pairs are organizationally proximate. Concerning correlations, the intra-country dummy is obviously correlated with geographical proximity as both reflect proximity in physical space, albeit in fundamentally different ways. More interesting, the highest positive correlations are found between some of the other proximity variables. Geographical proximity is correlated with social and organizational proximity. The first correlation seems to suggest that social proximity is more easily maintained when actors are geographically proximate. The second correlation reflects the fact that organizations belonging to the same parent organization are often co-located. This holds true in

[28] Zero-inflated negative binomial regression modeling is used when the dependent variable reflects count data with an excessive number of zeros (Long 1997). Zero-inflated negative binomial regression models allow for a separate modeling of the process generating excessive zeros vis-à-vis the process generating the counts of the dependent variable. In addition, while the zero-inflated part models the process generating excessive zeros independent from the process generating the counts of the dependent variable, the negative binomial part models the counts of the dependent variable conditional on the likelihood that the dependent variable can be non-zero. Theoretically, proximity is neither a necessary nor a sufficient condition for collaborative science to take place. Likewise, distance – on whatever dimension – is not an absolute barrier to collaborative science. Rather, proximity (distance) only facilitates (hampers) the establishment and recurrence of collaborative science but cannot make sure that collaborative science indeed does (not) take place. As such, the process generating excessive zeros in collaborative science should be modeled differently from the process generating the counts of our dependent variable. While in the former zero-inflated part we thus do not include proximity variables but only a variable that captures the likelihood that any two organizations collaborate, in the latter negative binomial part we specify a gravity model that includes variables on multiple proximity dimensions.

particular for academic hospitals and their corresponding universities. Further, social proximity is correlated with cognitive proximity, which seems to suggest that repeated ties occur more often within disciplines than across disciplinary boundaries. This is in line with the Mode 1 vs. Mode 2 distinction of Gibbons et al. (1994) who emphasized that transdisciplinary projects often occur in one-off projects.

Model 1 and 2 in Table 4.3 show the results for the global analysis taking into account all organizations worldwide that publish on type 2 diabetes. Model 1 shows the results when only taking into account the geographical variables 'intra-country' and 'geographical proximity', while model 2 takes all five proximity dimensions into account.

From model 1 we read that all determinants have the expected sign and that, looking at the z-scores, the intra-country dummy is most important. Thus, being located in the same country is the single most important variable explaining research collaboration reflecting the (continued) importance of national systems in the collective production of knowledge, at least in this particular field.[29]

In model 2 it is clear that all five proximity dimensions are positive and significant reflecting that all five dimensions contribute to facilitating the establishment of research collaboration leading to a co-publication. This result suggests that on the aggregate level, evidence of a Mode 2 type of pattern of collaborative science is absent. That is, distant organizations are not attracted to collaborate. This does not mean that for each individual organization particular forms of distance may not motivate a particular research collaboration. Rather, when aggregating all collaborations, the effect of such motivations disappears given that in most of collaborations proximity rather than distance is driving the formation of research partnerships.

Adding more proximity variables in model 2, we observe that the relative importance of national collaboration remains robust, yet the relative importance of geographical proximity becomes weaker. This reflects the correlation between geographical proximity on the one hand and social and organizational proximity on the other hand (table 4.3). That is, the importance of geographical proximity is generally over-estimated when other forms of proximity are not taken into account (Boschma 2005).

What can be further derived from model 2 by looking at the z-scores concerns the relative importance of each proximity dimension (see footnote 7). Institutional proximity is least important reflecting the relative importance of cross-institutional collaboration in this scientific field. Interestingly, after geographical proximity, social proximity as a driver of collaboration is most robust, reflecting that many organizations prefer 'repeated ties' thus profiting from the trust and experience from past collaborations.

[29] Note that our interpretation of some proximity dimensions being more important than others is not to suggest that the estimated coefficient of one proximity dimension lends itself to be easily compared with the estimated coefficient of another proximity dimension. Given that different proximity dimensions do not involve a common unit of measurement we cannot easily compare the size of the coefficient estimates of different proximity dimension (King 1986). Instead, what we suggest then is that the result of the estimated coefficient of one proximity dimension is more likely to hold across larger samples and when including more explanatory variables than the estimated coefficient of another proximity dimension. As such, the relative importance of proximity dimensions should be interpreted here in terms of the estimated effect of one proximity dimension being more or less robust than the estimated effect of another proximity dimension.

Table 4.2. *Descriptive statistics of the global type 2 diabetes innovation system (n = 741,153)*

	Variable	Mean	S. D.	Min.	Max.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1.	# Co-publications$_{ij}$	0.052	0.602	0.000	161.000	1.000									
2.	Intra country dummy$_{ij}$	0.095	0.294	0.000	1.000	0.159	1.000								
3.	Geogra-phical proximity$_{ij}$	0.001	0.022	0.000	1.000	0.255	0.163	1.000							
4.	Social proximity$_{ij}$	0.007	0.084	0.000	3.761	0.440	0.155	0.227	1.000						
5.	Cognitive proximity$_{ij}$	0.072	0.134	0.000	1.000	0.146	0.160	0.052	0.203	1.000					
6.	Institutional proximity$_{ij}$	0.407	0.491	0.000	1.000	0.012	-0.008	-0.007	0.013	0.008	1.000				
7.	Organiza-tional proximity$_{ij}$	0.001	0.036	0.000	1.000	0.124	0.103	0.191	0.117	0.039	0.027	1.000			
8.	Mass$_{ij}$	6.498	1.087	4.605	12.180	0.136	0.047	0.013	0.132	0.380	0.075	-0.009	1.000		
9.	Transitivity$_{ij}$	0.259	1.101	0.000	45.000	0.332	0.236	0.093	0.530	0.393	0.026	0.041	0.357	1.000	
10.	Expected collaboration propensity$_{ij}$	26.888	21.167	0.000	289.239	0.196	0.122	0.022	0.178	0.429	0.025	0.003	0.792	0.482	1.000

Table 4.3. *Zero inflated negative binomial regression results (dependent variable: # Co-publicationsij)*

	Model 1: Global – geographical proximity				**Model 2: Global – five proximities**			
Negative binomial part	Coef.	Std. Err.	Z score	P value	Coef.	Std. Err.	Z score	P value
Intra country dummy	1.95	0.02	80.63	0.000	1.87	0.02	78.92	0.000
Geographical proximity	4.65	0.16	29.66	0.000	3.27	0.16	20.90	0.000
Social Proximity					1.09	0.04	27.70	0.000
Cognitive proximity					0.65	0.06	10.13	0.000
Institutional proximity					0.15	0.02	8.16	0.000
Organizational proximity					1.16	0.11	10.81	0.000
Mass	0.38	0.01	26.43	0.000	0.39	0.02	25.69	0.000
Transitivity	0.11	0.00	25.01	0.000	0.03	0.00	6.19	0.000
Constant	-5.43	0.13	-42.49	0.000	-5.65	0.13	-42.61	0.000
Zero inflated part								
Expected collaboration prop.	-0.06	0.00	-60.00	0.000	-0.06	0.00	-58.78	0.000
Constant	3.12	0.05	60.43	0.000	3.04	0.05	56.28	0.000
lnalpha	0.85	0.03	29.92	0.000	0.72	0.03	23.50	0.000
Pseudo log likelihood	-86806.5				-85876.8			
Observations	741153				741153			
Non zero observations	19601				19601			
McFadden's Adj. R^2	0.25				0.25			

Table 4.3. *Continued*

	Model 3: EU versus North America			
Negative binomial part	Coef.	Std. Err.	Z score	P value
Intra country dummy	1.03	0.05	18.84	0.000
Geographical proximity	4.45	0.31	14.47	0.000
Social Proximity	0.87	0.05	18.39	0.000
Cognitive proximity	0.20	0.09	2.25	0.024
Institutional proximity	1.56	0.15	10.67	0.000
Organizational proximity	0.17	0.03	5.54	0.000
Intra country dummy*EU	1.22	0.07	18.15	0.000
Geographical proximity*EU	-2.72	0.34	-8.11	0.000
Social Proximity*EU	-0.14	0.07	-2.16	0.031
Cognitive proximity*EU	0.14	0.12	1.17	0.243
Institutional proximity*EU	-0.02	0.05	-0.43	0.664
Organizational proximity*EU	-1.15	0.18	-6.34	0.000
EU dummy	0.13	0.07	1.95	0.051
Mass	0.53	0.02	32.30	0.000
Transitivity	0.02	0.00	5.48	0.000
Constant	-6.44	0.15	-42.28	0.000
Zero inflated part				
Expected collaboration prop.	-0.06	0.00	-41.29	0.000
Constant	2.56	0.07	39.10	0.000
lnalpha	0.26	0.04	6.97	0.000
Pseudo log likelihood	-43168.0			
Observations	163051			
Non zero observations	11393			
McFadden's Adj. R^2	0.25			

In order to compare different territorial innovation systems, we took the example of North-America (United States and Canada) and Europe (E.U. 15 and Switzerland). This comparison is relevant in light of the ongoing debate regarding the alleged superior performance of the North-American innovation system (Dosi et al. 2006), often attributed to better cross-institutional partnerships. In model 3 we included only organizations located in North-America and Europe and included interaction terms to analyze whether proximity dimensions had a differential effect on establishing collaborations within the EU as compared to within North-America.

These results reveal three major differences between the European and North American innovation systems. First, the intra-country interaction effect highlights that the bias towards national rather than international collaboration is much stronger in the EU than in North-America (read US-Canada collaboration). Second, geographical, organizational, and social proximity play less of a role in Europe than in North-America. Third, cognitive and institutional proximity are equally

important in Europe as in North-America. Taken together, and apart from some similarities, the comparative analysis thus shows that there are indeed significant differences between the two territorial innovation systems.

The interpretation of the results warrants a fine-grained analysis in its own right. However, some suggestive interpretation can be given already. The first result regarding the bias towards national collaboration in Europe may well reflect larger linguistic and cultural variety within Europe as compared to North-America (see also Crescenzi et al. 2007). Perhaps more interestingly in light of science policy debates, a second result holds that no differences are found between the two innovation systems where it concerns the roles played by institutional and cognitive proximity. Although both forms of proximity are of importance in shaping interactions in European and North American science, it does not seem the case that institutional or disciplinary differences are more easily bridged in either one of these two systems. As such the widely held conviction that Europe is worse in translating basic research into commercial innovation seems not to be supported by our findings (Dosi et al. 2006). Finally, the result of social and organizational proximity being of less importance in Europe as compared to North-America suggests that in North-America science structures are more stratified than in Europe in the sense that North-American collaboration patterns are more responsive to avoiding opportunism. Although warranting much more research, this tentative conclusion seems to be supported by claims on the United States innovation system as very much stratified (Jones et al. 2008) and the European innovation system as fairly cohesive (Hoekman et al. 2009).

4.5. Concluding remarks

We proposed an analytical framework based on the proximity concept to analyze and compare territorial innovation systems in the field concerned with type 2 diabetes. Where innovation system analysis tends to focus on inter-organizational and cross-institutional dimensions of collaboration, we propose a richer framework based on five dimensions taken from the work by Boschma (2005) on proximity and collaboration. We have been able to show how the five proximity dimensions map almost one-to-one to various aspects of distributed 'Mode 2' knowledge production (Gibbons et al. 1994). The proximity framework thus allows for an analytical operationalization of the Mode 2 concept. In the empirical analysis we assessed the extent to which each proximity dimension affected the intensity of collaboration between organizations working on type 2 diabetes.

Our main results hold that: 1. geographical proximity is the prime determinant of collaboration suggesting the geographical focus inherent in the concepts of territorial science and innovation system concepts is still warranted, notwithstanding the secular rise in international collaborations *per se*, and 2. institutional proximity is the least important in explaining collaborative science reflecting that, indeed, cross-institutional collaboration is the most prevalent mode of heterogeneous collaboration as described in the innovation systems concept. Our main contributions thus lie in enriching the concept of innovation systems to include cognitive and social dimensions of knowledge production and in showing that the main foci underlying territorial innovation systems analysis on institutional distance and geographical proximity are supported empirically.

With respect to various modes of knowledge production it seems that at the systems level there is little evidence of Mode 2. This is not to say that at the project level all proximity dimensions are important in shaping innovation. In many individual innovation projects actors are distant in

multiple dimensions at the same time. Yet, at an aggregate level all proximity dimensions play their role in shaping collaborative innovation.

Our framework allows for systematic comparisons between different territorial innovations. In our analysis we compared the North-American and the European innovation systems on type 2 diabetes. This analysis showed that while there are some marked differences between both territorial innovation systems, Europe and North America do not seem to differ with respect to the roles played by institutional proximity as it has been often suggested. The next step in applying our framework would be to do comparative analysis in combination with a performance analysis in the form of a 'benchmarking exercise'. By comparing different systems in terms of their modes of knowledge production and relating these modes to differences in performance, hypotheses regarding the functioning of different territorial innovation systems can be analyzed (Carlsson et al. 2002); for example, in terms global market shares in research output, inventions and innovations (cf. Bonaccorsi 2008). A simple hypothesis would posit that the higher the level of 'Mode-2-ness', the better the performance of a particular system. This claim seems to be inherent to the Mode 2 concept as introduced by Gibbons et al. (1994) as their description of Mode 2 knowledge production suggests that Mode 2 is better able to solve complex societal problems than Mode 1. It is for this implicit normative reasoning that the Mode 2 concept has been criticized (Godin 1998). Alternatively, one could argue that proximity along at least some dimensions is required to reduce uncertainties and avoid conflicts in research collaboration (Boschma 2005; Balland 2011). Yet, as long as empirical research is not carried out in a systematic way such that evidence can be compared and accumulated across different units of comparison, the debate remains empirically ill-informed. We hope that as a first step our proximity approach can also serve as a framework to assess the performance of different varieties of innovation systems.

5. Elements of a relational theory of citation[30]

5.1. Introduction

Citation analysis as a tool to assess the sciences has become popular among academic scholars and policymakers alike. For academics, the Science Citation Index (SCI) and other citation database like Elsevier's Scopus provide rich sources of data on scientific communication and allow for the quantitative study of all kinds of aspects of science including the growth of scientific knowledge (Price 1963), the reward structure of science (Cole and Cole 1973), geographical biases in scientific communication (chapter 2), and interdisciplinarity (Wagner et al. 2011). In striving to make informed science policy decisions and at the same time making science funding better accountable to society, policy makers can apply citation analysis as a useful tool to achieve both (Wade 1975; Moed 2005). As compared to more traditional science assessment tools such as peer review, citation analysis provides a relatively cheap and seemingly objective tool to assess the sciences on a large scale.

The interest in citation analysis in the two communities has not developed independently. For one thing, academic scholars have been actively promoting the use of citation analysis for science evaluation purposes (see e.g. Garfield 1979). More fundamentally, most academic scholars and science policymakers seem to share a common understanding of the meaning of science citation. Albeit sometimes expressed in different terms, both groups tend to take the science citation as an expression of some kind of value attributed to the cited object by a citing object.

Today, citation analysis is an established science assessment tool within circles of science policy. Although it is recognized that citation analysis is an imperfect science assessment tool and should therefore always be complemented with more traditional science assessment tools (see e.g. Zuckerman 1987), its use has become widespread among science policymakers worldwide. Within academic circles, the situation is somewhat different. Here, scholars seem to be divided by proponents and opponents of the use of citation analysis as a tool in analyzing science. In academia, as we will argue, this has led to an intellectual dead-end in debates on the interpretation of science citation and the (mis)use of citation analysis. Proponents of citation analysis in principle take citation as an scholarly act following the Mertonian norm of "giving credit where credit is due" (Merton 1957), while opponents to citation analysis stress that citation occurs for all kinds of reasons besides reward and hence should not be used to assess science.

Despite the wide interest in citations as data to analyze science as well as to evaluate research and researchers, and the vivid debates regarding the appropriate use of such data, theorizing about citation as a phenomenon has been scarce (Leydesdorff 1998; Nicolaisen 2007). One possible reason for the lack of interest in theorizing about citation may be exactly the polarization into two extreme positions: one Mertonian view that regards citations primarily as pointing to the value of the contents of the cited text and another more critical view that considers citations first and foremost as following from the personal interest of the citing author (see also Wouters 1998). We propose an alternative 'relational' theory of citation where the occurrence (and absence) of citations in one text to another text is explained by the relations that exist between a pair of texts. Following this perspective, we can still maintain the main arguments of the two conflicting views,

[30] To be submitted as: Hardeman S., Frenken K. (2012) Elements of a relational theory of citation. Hardeman contributed to all sections of the chapter.

while at the same time we are able to derive network-theoretic propositions as a basis for future hypothesis-driven research about citations.

The remainder of this paper is organized as follows. We first summarize the two dominant positions in theorizing about citations in section 5.2. Then, we discuss in section 5.3 a very similar theoretical divide that exists in the field of information retrieval, and go into a recent attempt to reconcile the two positions in this field. In section 5.4 we develop our own relational framework for understanding citation practices building on the concept of relevance from information retrieval on the one hand and network sociology on the other hand. In section 5.5 we discuss some further remarks on the role of geography in citation. Section 5.6 concludes.

5.2. The current status quo on the interpretation of citation

In abstract terms a science citation can be represented as a directional link going from a citing object to a cited object. On an aggregate level, the complete set of links connecting citing objects with cited objects forms a citation network whose structural characteristics can be analyzed using network analytic techniques (see e.g. Price 1976; Karrer and Newman 2009). Although such structures are interesting in themselves, the abstract treatment of citation leaves the meaning of citation and therewith a clear interpretation of the meaning of these networks unspecified.

Debates on the proper interpretation of science citation are most often concerned with science citation as an indicator of some other (more fundamental) phenomenon of interest (Leydesdorff 1998). Many early citation studies took citation as reflecting an indication that the cited object is of some kind of value. As such, citation has been labeled as reflecting amongst others eminence (Clark 1957), recognition (Hagstrom 1965), reward (Cole and Cole 1973), and impact (Martin and Irvine 1983). Crucial to an interpretation of citation-as-value is the assumption that from science's Mertonian normative structure scholars are to "give credit where credit is due" and hence are forced by their peers to cite previous contributions that have been influential for laying down their own (Kaplan 1965; Merton 1979; Merton 1988).

Empirically, there is indeed evidence for an interpretation of citation as value.[31] Clark (1957), comparing a group of psychology scholars considered as eminent by field experts with non-eminent psychology scholars, finds that the former group scores significantly higher on all indicators of evidence including the citation score of each individual scholar. What is more, of these various indicators of eminence, citation counts showed the highest correlation with the number of votes a scholar received by the group of field experts. Likewise, but on the level of university departments in biochemistry, Bayer and Folger (1966) correlate the number of received citations by the departments with the quality of those departments as judged by a group of experts while controlling for the variation in I.Q. scores across departments. They find that citation counts are highly correlated with research quality.

Extending this line of research, Cole and Cole (1967) for a group of 120 university physicists address the question to what extent recognition in science is a function of either quantity as measured by publication output as measured by the number of articles published or publication

[31] We stress to note that we do not intend to provide a comprehensive review of citation studies. Rather, what we try to do here is to place the contemporary debate on science citation in a historical context. For comprehensive recent reviews on science citation see: Moed (2005), Nicolaisen (2007), Bornmann and Daniel (2008), and De Bellis (2009).

quality as measured by the number of citations received. They correlate publication counts and citation counts with the number of honorific rewards, positions at top-ranked departments and reputational visibility. Again it turns out that differences in rewards among individual scholars are merely reflected by scholars' research quality as measured by their citation counts instead of scholars' research quantity as measured by the number of papers they publish.

However, notwithstanding the empirical evidence, the validity of interpreting citation as value is very much contested (Wouters 1998). The extent to which the attribution of citations fully conforms to the scientific norm of giving credit where credit is due is at least debatable (Porter 1977). As such, the idea of citation fully conforming to the norm of "giving credit where credit is due" reflects an over-socialized idea of behavior (Granovetter 1985). That is, scholars are assumed both to be fully aware of what to cite and indeed also actually follow the norm instantaneously. Alternatively, it has been argued that rather than directly following the value of cited objects, citation should be taken as primarily following from personal motivations of the author of the citing object (MacRoberts and MacRoberts 1996). As an alternative to the Mertonian interpretation of citation as value, others have thus come up with interpretations of citation as reflecting rhetoric tools to persuade readers of the credibility of a knowledge claim (Gilbert 1977) or to mobilize authority in defense of an argument (Latour 1987).

As it is the case for interpretations of citation as value, there is also considerable empirical evidence supporting these alternative interpretations of citation.[32] In performing citation context analysis, Moravcsik and Murugesan (1975) classified citations from 30 articles published in the journal *Physical Review*. Amongst other things, they find that citations are (at least to some extent) negational, that is, attributed out of a concern with the cited text being wrong rather than of value. Being more explicitly concerned with citer motivations, Brooks (1986) surveys 20 scholars from 15 different fields about their reasons for attributing citations. As it turns out, citer motivations are complex involving apart from normative considerations (i.e. those favored by an interpretation of citation as value) also personal considerations (i.e. invoked to persuade the reader). More recently, Harwood (2009) uses semi-structured interview techniques to trace reasons of scholars to cite papers. Again it turns out that scholars cite for reasons of positioning and supporting own claims (both personal reasons) alongside giving credit to others (a clear normative reason). Thus, it seems clear that citation is not just a normative act. While normative considerations certainly cannot be denied, citing motivations are at least in part personal.

In an attempt to conclude this long-standing debate between citation-as-value and citation-as-personal, some studies empirically test both assertions simultaneously (Stewart 1983; Baldi 1998; White et al. 2004). Although all three studies conclude that citation primarily stems from normative considerations, none of these studies deny that personal considerations play a role in citation. While normative considerations certainly cannot be denied, citing motivations are at least in part personal. As such, some argue that personal considerations precede normative standards (Cozzens 1989). Alternatively, others argue that the norms of citation form the basis of personal citation acts (Camacho-Miñano and Núñez-Nickel 2009). In all it seems clear that citation is neither just a normative act nor just personal.

Summarizing, neither an interpretation of citation as value nor an interpretation of citation as personal fully capture the complex practice of citation. While an interpretation of citation as value tends to be overly optimistic regarding the functioning of the Mertonian norm in science, an interpretation of citation as personal tends to be overly naive in taking citation as to reside at the

[32] For a complete overview of the literature on citing behaviour see Bornmann and Daniel (2008).

side of the citer as an individual only (Bornmann and Daniel 2008). Hence, while an interpretation of citation-as-value tends to provide an over-socialized account where scholars instantaneously and perfectly follow the norm, an interpretation of citation-as-personal tends to provide an under-socialized account where scholars randomly cite in their own best interest.

Judging from the few theoretical contributions in recent times, the debate on science citation seems to have come to a dead end. While in the 1980s and 1990s the debate on interpretations of citation was very lively as for example reflected by various special issues on this matter (Scientometrics 1987; Scientometrics 1998) this debate seems to be much more quite in recent years (for some notable exceptions see e.g. Nicolaisen 2007; De Bellis 2009). This is not to say that citation analysis has not progressed methodologically.[33] Rather, it seems that those attracted to a personal interpretation of citation are left abandoning the use of citation analysis for assessing science altogether (Luukkonen 1997), while those who are (at least sufficient) content with an interpretation of citation as value do not seem to be concerned with alternative interpretations therewith applying citation analysis for the study of science seemingly uncritical (Van Raan 1998).

We believe that this current status quo is regrettable for at least two reasons. One is that, from an academic perspective, in sticking to a position of interpreting citation either as value or as personal, we do not seem to get to a deeper understanding of the phenomenon itself. Second, given the increasing use of citation based indicators in the science policy domain, the construction of citation based indicators is too important to be left to statisticians alone. Put different, citation analysis – both for purposes of scholarly science assessments as well as for purposes of informing science policy making – might well be served by paying explicit attention to considerations beyond an *assumed* conformity to academic norms. In this, we follow Cronin arguing that (1984 p. 84): "*We cannot say that citation is an activity governed by adherence to a specific and universally recognised set of norms. By the same token, the evidence does not permit us to conclude that the practice is characterised by randomness and inconsistency. The interplay between institutional norms (even if only vaguely grasped by authors) and personal considerations is extremely complicated. We may not be able to champion the normative view, but by the same token we are under no obligation to subscribe wholly and uniquely to the literalism of the interpretative approach.*" As such, he advocated a middle ground in arguing that "*it is to be hoped that future studies of citation will at least take note of the microsociological viewpoint, and use it to enrich our appreciation of what citation signifies in the knowledge construction and dissemination process*" (p. 84). Likewise, Gläser and Laudel (2007 footnote 1 p. 104) argue that personal motivations and norms are inherently enmeshed in the act of citation. That is, persuading one's peers is best served by citing those texts that meet the standard of citation. Instead of assessing whether citation stems from either normative or personal considerations, these suggestions shift our discussion to considering how norms feed into scholarly citation practices.

A first challenge then would be to come up with an interpretation of citation which in principle provides room for both theoretical positions on citation. In addition, and apart from coming up with "yet another" interpretation of citation, the new interpretation should also provide further leads for gaining a richer theoretical understanding of citation. We believe that in interpreting citation in terms of the concept of relevance, and more specifically socio-cognitive relevance, we meet both of these challenges. Using this concept, an alternative 'relational' theory of citations can be developed to derive network-theoretic propositions as a basis for future hypothesis-driven research about citation.

[33] Think, for example, about the development of new citation based indicators (see e.g. Hirsch 2005; Van Raan 2006; Opthof and Leydesdorff 2010) or the maps of science (Bollen et al. 2009; Leydesdorff and Rafols 2009).

5.3. On the notion of relevance in information retrieval

According to Mooers (1951 quoted in Saracevic 1999 p. 1057), research on information science and retrieval concerns itself with "*the intellectual aspects of the description of information and its specification for search, and also whatever systems, techniques or machines that are employed to carry out the operation.*" From an engineering perspective the aim of information retrieval research resides in designing systems to obtain a best possible match between an information need on the one hand and information elements available in a given population of information elements on the other hand. Alternatively, from an academic perspective the aim of information retrieval research resides in specifying, qualifying, and explaining the nature of the relation between an information need and information element in a given population of information elements as best. In all then, information retrieval research is concerned with answering the question "When is an information element relevant to an information need?" for the construction of better information retrieval systems.

In addressing this issue, the concept of relevance is a central conceptual building block in most (if not all) information retrieval research (Mizzaro 1998; Saracevic 2007). That is, in being concerned with the relation between an information need and information elements, this relation has generally been qualified as involving a relation of relevance. As such, the concept of relevance has often been paraphrased in terms of a source-destination model of communication as a property of the relation between an information need on the one hand and a set of information elements available on the other hand.[34]

Apart from a commonality in taking relevance in terms of a source-destination model of communication, two opposite positions regarding information retrieval have been developed (Saracevic 2007; Hjørland 2010). Some contributions focus on relevance as residing on the source-end of communication (see e.g. Cooper 1971; Wilson 1973). These systems approaches to relevance stress that given any explicit information need, relevance is primarily an attribute of the information elements themselves. Other contributions stress that relevance is much more determined by the destination-end of communication (see e.g. Schamber et al. 1990; Harter 1992). These user approaches to relevance stress that both the timing of the information need as well as the situation in which the information need comes about are crucial for determining what information elements are relevant to what information needs.

Alternatively, Hjørland & Albrechtsen (1995) propose to take relevance as involving a historically and socially contingent relation between information needs and information elements. This social-cognitive view on relevance (Hjørland 2002) thus takes relevance as an emerging and evolving relation between an information element and an information need as embedded and 'encultured' in collective human practices. In this view, relevance is taken as the best available match between information elements available and information needs at hand given the goals, interests and values to which people are subdued in their group or community (Hjørland 2010).

The three perspectives on relevance differ with respect to a number of aspects (see also Hjørland 2010 table 3 p. 232). A first distinction among the various perspectives on relevance can be made on the basis of the elements deemed important in each perspective. Within the systems perspective

[34] Different contributions on the concept of relevance have framed this source-destination model of communication differently. While some have extensively added different aspects (e.g. Saracevic 1975), others are in principle very close to a simple source-destination model of communication (Hjørland 2010). What holds across these various contributions is the underpinning of the concept of relevance as basically involving an act of communication between source and destination that is mediated by some other property.

on relevance, central emphasis is put on information in its syntaxed form. It is from the match between an information need syntax and an available information element that the relation between the two becomes qualified as relevant. User perspectives stress the role of individual perceptions in steering the qualification of any relation between information need and available information elements as relevant. The socio-cognitive perspective then stresses the role played by the broader community in which individuals in need of information are embedded. The qualification of a relation between an individual's information need and the available information elements as relevant is relative to accepted views on what counts as relevant within the wider group of people in which an individual participates given the task of the individual at hand.

It follows that within systems perspectives on relevance the qualification of a relation between information need and information elements available as relevant can be logically derived from their syntaxes. At the one extreme then, systems perspectives on relevance promote an objective interpretation of relevance, that is, an interpretation of relevance without the interference of personal characteristics of users. At the other extreme, user perspectives on relevance take relevance essentially as residing in the eye of the beholder, that is, as subjective to the individuals in need of information. From a socio-cognitive perspective relevance is neither purely objective nor completely subjective. Rather, the qualification of a relation between an information need and the information available as relevant is said to be constituted inter-subjectively.

The three perspectives on relevance also differ with respect to their treatment of time and context. For system perspectives on relevance both time and context do not seem to play a large role. Algorithms proposed to retrieve relevant information should in principle be capable of dealing with new syntaxes once formulations of new information needs and new information elements enter. Alternatively, user perspectives stress the volatility of individual relevance assessments. It is argued that as individuals move from one situation into another their idea of what counts as relevant changes. The socio-cognitive perspective on relevance is most explicit about the role attributed to time and especially context in the constitution of relevance. In positioning information users in their wider context of tasks and other information users, the socio-cognitive perspective on relevance very much problematizes the ways in which context enters the constitution of relevance. As such, the socio-cognitive perspective on relevance opens up empirical questions about the extent to which individual relevance assessments can be explained by their position in socio-cognitive networks, that is, in their disciplinary context.

Taken together, the field of information retrieval as concerned with determining the relation between information needs and information elements as relevant for the construction of better information systems seems to be best served by a fruitful and continuing interaction among these different perspectives. With respect to the systems perspective on relevance we feel that this perspective – in starting to reason from information needs in their syntaxed form only – is somewhat narrow in its orientation. Likewise, the user perspective on relevance seems to disregard the qualification of relevance by users as (at least partially) constituted by the wider context in which a user acts. In problematizing the constitution of relevance further we believe that the socio-cognitive perspective provides a fuller (albeit perhaps only additional) understanding of relevance. Most importantly, in further problematizing the constitution of relevance, we believe that a socio-cognitive perspective on relevance might provide some interesting leads to a renewed interpretation of science citation and a basis for further theorizing about citation practices in science.

5.4. Towards a relational theory of citation

5.4.1. Mirroring relevance and citation

In its most abstract form a citation – defined as the relation between a cited and a citing object – is very much similar to operationalizations of relevance in terms of an abstract source-destination model of communication. As such, the source of a citation reflects the cited object and the destination of a citation reflects the citing object.[35] The two extremes within the debate on interpretations of citation mirror two of the three perspectives on relevance: while interpretations of citation as value resonate a systems perspective on relevance, interpretations of citation as personal resonate a user perspective on relevance (see table 5.1).

First, both a systems perspective on relevance and an interpretation of citation as value stress that relevance and citation primarily reside at the source end of communication. In counting citations – and whatever the specific interpretation attributed to these counts – citation is meant to say something about the cited objects rather than about the citing objects or the citation relation itself. Alternatively, both a user perspective on relevance and an interpretation of citation as personal stress that respectively relevance and citation primarily reside at the destination end. Instead of focusing on what a citation means to the cited object, interpretations of citation as personal focus on what a citation means to the object citing.

Table 5.1. *Two different interpretations of citation*

Interpretation of citation	Citation-as-value	Citation-as-personal
Main object	Cited object	Citing object
Epistemology	Objectivist	Subjectivist
Perspective on relevance	Systems	User
Explanans	Value of contents	Personal motivations
Methodology	Positivist	Hermeneutic

Second, the epistemological backgrounds between a systems and a user perspective on relevance differ considerably (Hjørland 2010). Likewise, there are important differences between the epistemological backgrounds of interpreting citation as value or as personal (Luukkonen 1997). Although the epistemological backgrounds of systems versus user perspectives on relevance do not completely mirror the epistemological backgrounds of the distinction between respectively value and personal interpretations of citation, there are some notable aspects on which they resemble.

Both the systems perspective on relevance and the interpretation of citation as value tend to stress the inherent logic of the phenomena of interest. That is, while within a systems perspective the relevance of an information element logically follows from the characteristics of the information element itself, those adhered to an interpretation of citation as value stress that citation logically

[35] Taking the cited object as the source of citation might appear counter-intuitive. Yet, source in this respect does not refer to the origin of a citation (i.e. the citing object), but refers to the pool of objects that can potentially be cited. Likewise, destination in this respect does not refer to the attribution of citation to a cited object, but refers to the incorporation of another object by a citing object.

and instantaneously follows from the characteristics of objects that can be cited, in particular, its contents and the time it has been published (because of the priority rule). It follows that the systems perspective on relevance and an interpretation of citation as value both take an epistemological stance on knowledge as primarily being of an objective kind. Like the qualification of an information element as relevant does not depend on the cognitive dispositions of specific users, qualification of an object as a "must cite" does not depend on the interests of specific citing objects. The sole difference is that while for interpretations of citation-as-value the objective logic stems from normative pressures, for information retrieval the logic stems from objective computer algorithms. Yet, what holds is that for both the systems perspective on relevance and the interpretation of citation-as-value it is assumed that the personal characteristics of the user respectively the citing object do not interfere with the actual constitution of relevance respectively citation.

In contrast, both the user perspective on relevance and an interpretation of citation-as-personal tend to stress the volatility involved in the constitution of relevance and citation. This volatility then is primarily ascribed to the user respectively the citing object. Whereas relevance is primarily taken as stemming from the cognitive (pre) dispositions of users, citation is taken as primarily stemming from citing objects pursuing their own interest. Instead of following some kind of inherent logic then, both the qualification of an information element as relevant and the attribution of citations are thus considered highly subjective and contingent. The difference between user perspectives on relevance and interpretations of citation-as-personal lies in the *type* of aspects causing subjectivity. While user perspectives on relevance especially focus on cognitive aspects of the user (see e.g. Harter 1992), interpretations of citation as personal tend to stress the social interests of citing objects for citing or not citing another object (see e.g. Latour 1987).

Third, apart from both taking an objectivist stance on knowledge, the systems perspective of relevance and an interpretation of citation-as-value also share a more methodological orientation, that is, both are grounded in a positivist research tradition. With positivist we mean here that the research strategies used are familiar to research designs common in the (natural) sciences.[36] With respect to an interpretation of citation as value, Van Raan (1998) for example explicitly proposes a "bibliometric chemistry" approach to citation. Alternatively, both user perspectives on relevance and interpretations of citation as personal use a much more hermeneutic methodological approach in their studies. Whilst not abandoning the use of statistics altogether, these studies often apply an interpretative approach, that is, using for example case studies in which they apply interview techniques (see e.g. Wang and Soergel 1998; Wang and White 1999; Harwood 2008; Harwood 2009).

Taken together these mirroring aspects lead to a similar research orientation of systems perspectives on relevance and interpretations of citation as value. Both are concerned with assessing some kind of performance. In case of information retrieval studies this performance hinges on the performance of the information retrieval systems themselves while for citation studies it is directed at how well a text, individual scholar, research group or even country performs. Not only do these studies assess the performance of systems or cited objects in terms of respectively relevance or citation (or citation based indicators) themselves, in an attempt to prove that their measure is superior to other measures they often also compare their measurements or

[36] For only due the fact that different interpretations exist on notions such as positivism, we have to admit that ours is fairly (perhaps even too) narrow. What is more, some would even deny that positivism implies an approach akin to the natural sciences (see e.g. Hjørland 2005). Still, and lacking a better term to capture what we mean here, we use positivism to denote those approaches (especially in citation analysis) that use research designs that mirror research designs commonly used in the natural sciences.

indicators with alternative measures such as expert judgments.[37] In contrast, both information retrieval studies taking a user perspective on relevance and citation studies interpreting citation as personal are primarily concerned with the motivational aspects as for why subjects judge information elements relevant respectively judge certain objects worthwhile to be cited. Not accidently perhaps, it is often stressed in these studies that the motivations of judging an information element or cited object as relevant respectively worthwhile citing are not reflected by only one single motivation rather than by a complex set of motivations.[38]

5.4.2. Interpreting citation as relational: a socio-cognitive perspective on citation

The approach to citation analysis we advocate here takes citation as relational, that is, as a relationship established by the citing text with the cited text as well as between the citing author and the cited author.[39] A relational perspective implies that citations should be understood as the joint outcome of properties of the cited and citing text, in that the *content* of cited text must be deemed relevant in the *context* of the citing text (Small 2004). It also implies that the citing author must deem it relevant to cite the authors of particular texts. Put differently, citation practices involve both cognitive and social aspects (Nicolaisen 2003). For a text to be cited or not, an author has to assess the relevance of potentially citable texts and authors. Following the socio-cognitive view on relevance (Hjørland 2002), such an assessment is made within the socio-cognitive context in which an author communicates his/her research findings. In general, an author will cite texts from fellow members of the same disciplinary sub-community in which the author is operating.

Citation as relational follows two different logics of proximity. One dimension is cognitive and concerns the relation between texts; a citing text is more likely to cite a text when the content of the former is relevant to the content of the latter. Thus, the probability that text A cites text B and not text C will be high when text A is cognitively proximate to B and not to C, ceteris paribus. That is, the more two texts are similar in content (be it, topical, theoretical, methodological, etc.) the higher the probability of citation.[40] If the set of similar texts is very large, citations will be biased towards the older original texts because reward is based on priority. The extent to which citation actually follows from cognitive proximity among texts is, however, mediated by the social proximity of authors where social proximity means that a relation between two authors involves trust based on friendship or experience (Boschma 2005) (often, but not necessarily, former colleagues or co-authors). Two deviations from the cognitive norm of citation as value are then possible. First, an author may cite a text that is cognitive distant. This is the case when a text cites another text despite their contents being dissimilar. One expects that socially proximate authors are *more* likely to engage in such practices, since social proximity supports reciprocity in that the cited author will cite the citing author again in the future (Nowak 2006) cited in return.[41] In this context, others have aptly referred to such practices as intellectual back scratching (White et al. 2004). A

[37] For examples on such studies in the domain of citation analysis see e.g. Norris and Oppenheim (2003) and Van Raan (2006).
[38] Probably the best example of this argument is provided by the studies of Brooks (1985; 1986).
[39] The terms citing author and cited author may also refer to citing authors and cited authors, in case a text is co-authored.
[40] Similarly, Small (2004) speaks of literalness as an important dimension to citation.
[41] Empirical studies indeed suggest that social proximity has a positive effect on the likelihood of citation (Baldi 1998; White et al. 2004; Johnson and Oppenheim 2007; Wallace et al. 2012). Few studies however simultaneously take into account the effect of social proximity and cognitive proximity. Given that cognitive proximity and social proximity might well be positively correlated, the role of social proximity in steering citation might instead be driven by an underlying effect of cognitive proximity. Hence, in assessing the effect of social proximity in steering citation one should always control for the effect of cognitive proximity (chapter 2).

second deviation from the cognitive norm is a text that omits a citation to a very similar text. Authors are indeed incentivized to omit citations to similar texts as to suggest priority, or at least, originality. Again, social proximity is likely to play a role in that socially proximate authors are *less* likely to omit citations, since a one-time omission will break down the reciprocal citation relationship supported by social proximity. Hence it seems that the choice of citations indeed does not only follow from cognitive proximity, but also from social proximity.

Although occurring on different levels (respectively between texts and between authors), the rationale of both proximity dimensions is similar. In general then, both cognitive and social proximity increases the likelihood of citation between two texts. As such, the notion of proximity substantiates a phenomenological understanding of citation, that is, an understanding of why text A cites B and not C (Cronin 1998). However, proximity refers to the dyadic relation between citing and cited texts or authors. As a dyadic concept, the notion of proximity ignores the wider socio-cognitive context of the disciplinary sub-community in which authors operate. It is at the level of such sub-communities that citations norms operate and are being enforced.

In dense socio-cognitive networks, the Mertonian norm of "giving credit where credit is due" is generally well established, since those who would deviate from this norm are easily detected. Even though socially proximate authors have an incentive to cite each other and socially distant authors not to cite each other, the risk of a reviewer, or reader, to detect omitted or superfluous citations is very high within a disciplinary context (see e.g. Dasgupta and David 1994). Understanding citation as a strategic act, the logic of "embeddedness" can be used to explain the conditions that incentivize an author of text A to cite an author of text B. Embeddedness here refers to the extent to which a relation between two authors is embedded in a wider social network. One can measure the level of embeddedness simply by the number of fellow scientists the authors of text A and text B know in common. This interpretation then is similar to Granovetter's older concept of tie strength as the degree of overlap of two individuals' friendship networks (Granovetter 1973 p. 1362). The higher this number, the higher the reputational consequences once the word gets out that A does not behave according to the norm, given that B will warn those that A and B know in common about A's norm-conforming behavior. Thus, the more authors of any two texts are embedded in the same community, the higher the likelihood that the citing text will cite appropriate texts and will not cite inappropriate texts.

We can now illustrate our relational theory of citation graphically (figures 5.1-5.3b). First, figure 5.1 illustrates the situation in which there is perfect norm adherence. That is, the higher the cognitive proximity between texts, the more likely a citation occurs between texts. In other words, the Mertonian norm of "giving credit where credit is due" is provided by the similarity in cognitive content between any two texts. Second however, deviations from the cognitive norm of citation occur due to social proximity among authors. As illustrated in figure 5.2, citation is more (less) likely between socially proximate (distant) authors. In other words, the more any two authors are socially proximate, the steeper the slope of the curve representing the relation between cognitive proximity and the likelihood of citation. Third, social embeddedness puts a limit on the extent to which citation can deviate from the norm. Provided that authors are socially proximate (figure 5.3a), high social embeddedness brings citation in line with the cognitive norm of citation while low social embeddedness allows for an increase in deviations from the cognitive norm of citation. Likewise, provided that authors are socially distant (figure 5.3b), high social embeddedness again brings citation in line with the cognitive norm of citation while low social embeddedness allows for an increase in deviations from the cognitive norm of citation. Note then that social embeddedness increases the likelihood of citation regardless of whether authors are socially proximate.

Figure 5.1. *Citation likelihood under the Mertonian norm of citation*

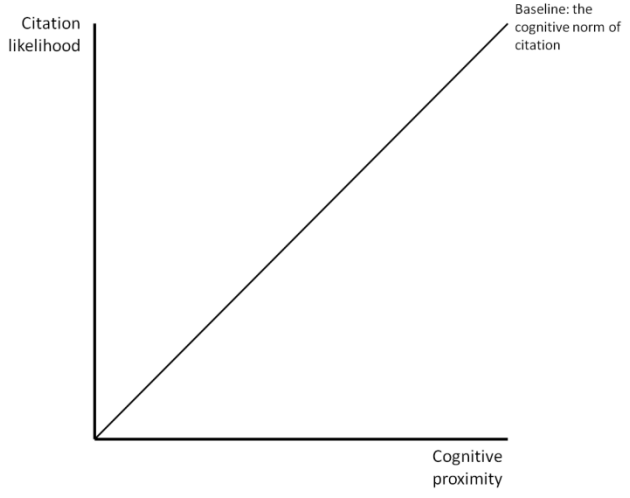


Figure 5.2. *Citation likelihood under different degrees of social proximity*

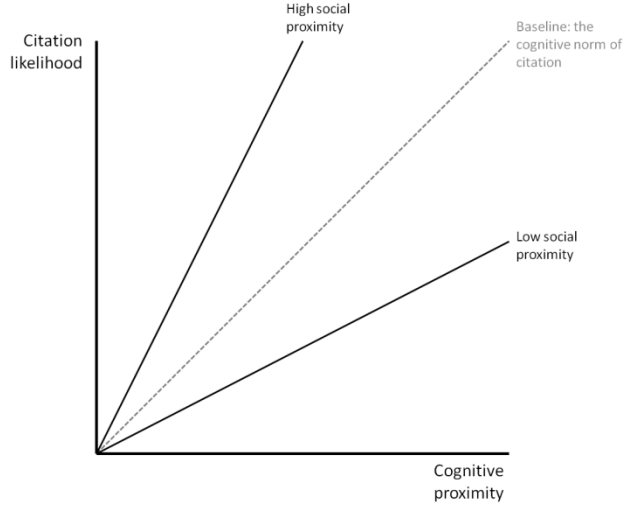


Figure 5.3a. *The effect of social embeddedness on citation under high social proximity*

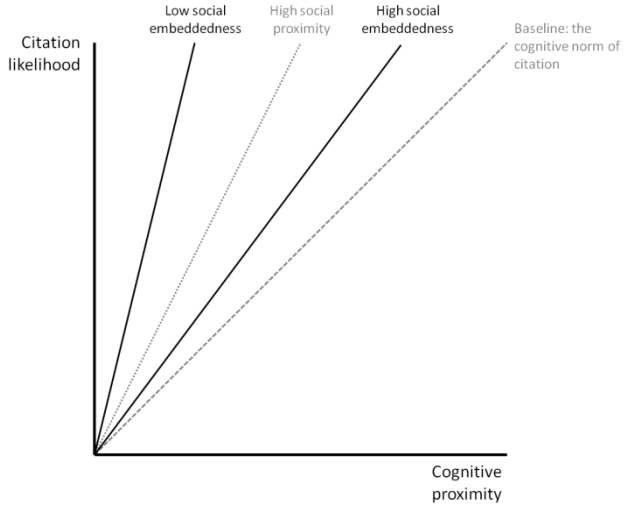
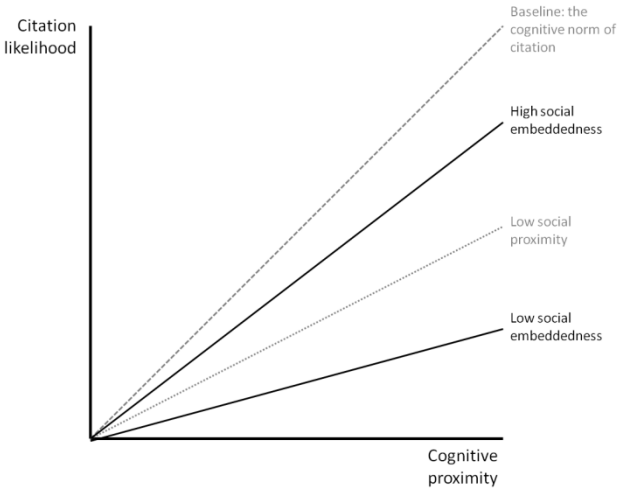
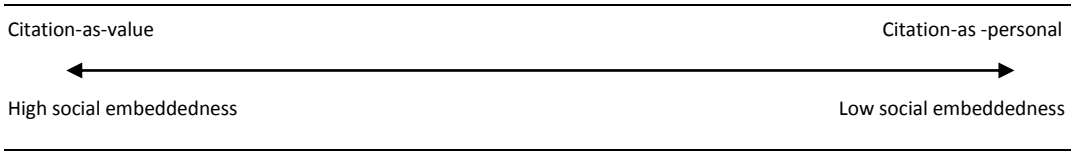


Figure 5.3b. *The effect of social embeddedness on citation under low social proximity*



The degree to which authors are socially embedded increases (decresases) the extent to which citation follows a value (personal) perspective on citation. As such, a relational theory based on the socio-cognitive context of specialized disciplines in which authors operate, puts both the interpretation of citation-as-value and the interpretation of citation-as-personal into a new perspective. The extent to which the Mertonian norm operates is *contingent* upon the degree of social embeddedness among authors. If social embeddedness is high, authors face higher risks of reputational loss than if such embeddedness is low. Hence, in context of high social embeddedness, citations are expected to follow from cognitive proximity. Note that in some contexts, the assumption of high degrees of social embeddedness can be justified, yet as a general theory it ignores the fact that in many instances the level of embeddedness may be rather weak. It is precisely in these contexts of low degrees of embeddedness that citation practices can become more personal as authors are less bounded by communal norms held by particular closely knit sub-communities. Figure 5.4 illustrates our framework. Depending on the degree to which authors are socially embedded, citation follows from Mertonian considerations rendering a value perspective on citation viable or from Latourian considerations rendering a personal perspective on citation more viable.

Figure 5.4. *Conceptual representation of a relational theory of citation*



A relational perspective thus provides a more general theory of citation, which includes the citation-as-value logic in contexts of high levels of proximity and embeddedness and the citation-as-personal logic in context of low levels of proximity and embeddedness. Table 5.2 summarizes the relational perspective to citation as compared to the other theories of citation.

Table 5.2. *Three different interpretations of citation*

Interpretation of citation	Citation-as-value	Citation-as-personal	Citation-as-relational
Main object	Cited object	Citing object	Citation dyad
Epistemology	Objectivist	Subjectivist	Inter-subjective
Perspective on relevance	Systems	User	Socio-cognitive
Explanans	Value of contents	Personal motivations	Network of relations
Methodology	Positivist	Hermeneutic	Both

5.5. Geography

A final note on the implications of our relational theory of citation for the understanding of geographical patterns in citation. It has been observed that citations display a geographical bias (for a review, see chapter 2). This pattern can now be understood as resulting from the

geographical patterns in social networks. One can safely assume that the probability that a scientist knows a fellow scientist declines with geographical distance. For example, several empirical studies have shown that geographical proximity is one of the main determinants of collaboration between scientists (chapter 2). This assumption is based on the common idea that face-to-face interaction is supportive of research collaboration and maintaining social relations, and that such face-to-face interaction is more likely to place when authors are geographically close. Given that social and geographical proximity are highly correlated, three implications follow for the understanding of the geography of citation patterns.

First, authors may simply not be aware of all relevant texts on a certain topic, despite the increased access to scientific papers through ICT and search engines. In particular, geographically remote authors are more likely to be unaware of each other's works than geographically proximate authors, since such information percolates within social networks that are geographically localized, as stressed before. Second, and following from our relational theory of citation, the average level of embeddedness between authors will decrease with geographical distance between authors, even if they are part of the same global disciplinary sub-community. It follows that omitted citations are less likely to occur between authors that are geographical proximate. Hence, citations should display a geographical bias. Third, one can assume that on average the level of social proximity between authors decreases with geographical distance between authors. It follows that the practice of reciprocal citation is expected to be often geographical localized.

5.6. Summary and conclusion

Over the last decade or so the science citation became surrounded by an intriguing paradox. On the one hand, from taking citation as its main study object, the use of citation analysis as a tool for science evaluation and management is by now a fact of scientific life. Not only do science policy administrators use the outcomes of citation analysis to make informed policy decisions, so are scholars themselves keeping track of the relevance of their work and the work of their peers by looking at citation scores that are easily on-line accessible via for example Google Scholar, Thomson Reuters Web of Knowledge, and Scopus Elsevier. In light of this, the role of the science citation as an active ingredient in the operation of scientific life cannot be denied (Wouters 1999).

At the same time, however, the scholarly debate on how to interpret the very phenomenon of citation seems to be more quite than ever. While those perfectly comfortable with an interpretation of citation as some kind of value proceed with the everyday business of producing citation (based) indicators, those rejecting such an interpretation and instead take citation as a personal phenomenon very much refrain from participating in any attempt whatsoever to improve on citation (based) indicators. In our opinion, the construction of citation based indicators would benefit from renewed efforts in theorizing citation practices.

The aim of this paper has been to come up with an interpretation of citation that both provides enough ground to comprehend the existing conflicting interpretations of citation and, in so doing, get advance theoretical and empirical research on citation. As a source of inspiration we turned to the field of information retrieval and its core concept of relevance. In discussing this concept we encountered a similar debate among perspectives on relevance as we saw in the debate on interpretations of citation. However, while the debate on citation is stuck in a conflict between two such interpretations, the debate on relevance has recently been injected by an alternative third socio-cognitive perspective. In mirroring the socio-cognitive perspective on relevance with an

interpretation of citation as relational we believe to have come up with an interpretation of citation that is capable of both comprehending older interpretations and at the same time provide for a renewed interest in theoretical and empirical research on citation.

Our proposed relational theory is based on the socio-cognitive context of specialized disciplines in which authors operate. This socio-cognitive context is taken as following a logic of proximity and a logic of embeddedness. The logic of proximity is twofold. While cognitive proximity substantiates the norm of citation for an interpretation of citation-as-value, social proximity substantiates the extent to which personal motivations under an interpretation of citation-as-personal are informed by scholars' immediate peers. The extent to which the Mertonian norm – giving credit where credit is due – operates is contingent upon the degree of social embeddedness among authors. If authors are part of the same disciplinary sub-community, the risk of reputational loss is high and, hence, authors are expected to adhere to the Mertonian norm. In contexts of low degrees of social embeddedness, citation practices can become more personal as authors are less bounded by communal norms held by particular closely knit sub-communities. As long as citation indicators are insensitive for the social context in which citation practices operate, important sources of bias in citation data will remain. Hence, the use of citation data for evaluative purposes can be improved by controlling for such social contexts, be it with complementary qualitative research or through the use of quantitative controls.

6. Mode 2 knowledge production and societal impact: the case of diabetes medicine[42]

6.1. Introduction

Science is a collaborative enterprise (Price 1963; Wuchty et al. 2007). The benefits of collaborative science can be summarized by the basic assertion that actors collaborating in problem solving activities such as science provide more viable solutions than each actor could have done individually (Katz and Martin 1997). As such, not only is science a collaborative enterprise; as a collaborative enterprise science is allegedly also more successful in providing solutions to the most pressing societal problems (Nowotny et al. 2001; Stokols et al. 2008).

The notion of Mode 2 knowledge production (Gibbons et al. 1994; Nowotny et al. 2001) provides a useful first starting point to address the relation between the organization of science and its relevance (see also Hessels and Van Lente 2008). The main premise of Mode 2 knowledge production holds that the organization of science having societal impact constitutes a mirror image of the domain of society to which its knowledge applies. The organization of science ought to reflect the complexity of the problems at stake. As such scientific projects should include various disciplinary backgrounds and interests. Two elements that shape the notion of Mode 2 knowledge production are of particular importance. One is the role attributed to the context in which science has impact. That is, science's context of application (Gibbons et al. 1994) or implication (Nowotny et al. 2001). Here it is argued that while under Mode 1 knowledge production science is primarily directed at a search for fundamental principles, under Mode 2 knowledge production science is directed at the provision of contextualized solutions (Gibbons et al. 1994; Nowotny et al. 2001). A second element crucial to an understanding of Mode 2 knowledge production is their description of context itself. Here, an important role is attributed to a distributed organization of science. In characterizing Mode 2, especially Gibbons et al. (1994) envision a new form of knowledge production in which scholars, practitioners and lay people with multiple disciplinary and institutional backgrounds jointly attempt to solve today's most pressing problems. In addition, Gibbons et al. (1994) and Nowotny et al. (2001) very much present Mode 2 knowledge production as a positive phenomenon in a normative sense. That is, the notion of Mode 2 knowledge production is presented with reference to its benefits without due attention to possible negative implications.

This paper is a first attempt to analyze the patterns of distributed organization underlying science in its context of implication, that is, as science becomes societal relevant. Assessing the determinants of science rendering societal relevance is by no means straightforward. First, as most of quantitative science studies focuses on the impact of science within the context of science itself (see e.g. Moed 2005), few contributions assess the determinants of science's relevance outside its own domain, that is, on society. Second, collaborative science takes place along multiple dimensions. Following Boschma (2005) (see also chapter 2), modes of collaboration can be distinguished along geographical, cognitive, social, institutional and organizational dimensions. However, so far different empirical contributions stress different and only a limited number of aspects to collaborative science. Though some take into account a subset of the five aforementioned dimensions (e.g., Frenken et al. 2005; Singh 2007; Valentin et al. 2008), what is

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missing then is an assessment of the impact of collaborative science that takes into account all relevant dimensions. Finally, all kinds of biases might occur by which some contributions are favoured over others in becoming societal relevant. Such biases then possibly signal the negative implications of heterogeneity in the distributed organization of science.

We make our contribution with respect to medical science, in particular type 2 diabetes research, where the question of societal relevance is evident. Section 2 discusses the main premises of a distributed organization of science in the context of medicine. Here, the distributed organization of medical science is characterized along five dimensions with its context of implication reflected by clinical practice guidelines (see also Lewison 2002; Lewison 2003). Section 3 addresses the data and variables that we use in our analysis of the role of a distributed organization of science in steering societal impact. Specifically, we look whether a more distributed organization of science indeed leads to more societal impact, where impact is measured as scientific papers cited in clinical guidelines. Section 4 presents the results which are further discussed in section 5. Section 6 concludes.

6.2. Mode 2 knowledge production in diabetes medicine: evidence based medicine, translational medicine, and the problem of conflicts of interest

Evidence based medicine arguably constitutes the dominant paradigm in contemporary medical science (Montori and Guyatt 2008; Hjørland 2011). Evidence based medicine advocates "*the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients*" (Sacket et al.1996 p.71). Hence, evidence based medicine aims at systematically strengthening the link between medical science on the one hand and clinical decision making on the other hand in providing the latter with best evidence brought about by the former (Timmermans and Berg 2003). As such, two aspects are deemed particularly important within evidence based medicine.

First, underlying much of evidence based medicine is the idea that the quality of evidence set out in publications can be graded (Atkins et al. 2004; Glasziou et al. 2008). As such, evidence based medicine relies on a ranking of research output based on scientific quality. The assumption underlying such quality structures is that the evidence obtained from medical studies provides varying degrees of certainty about the true effects of medical treatments (see e.g. Montori and Guyatt 2008). The idea of best evidence in evidence based medicine is closely related to the design characteristics of medical studies. Of all possible study designs, the randomized controlled trial is considered the gold standard in evidence based medicine (Timmermans and Berg 2003). A randomized controlled trial is a controlled experiment in which investigators compare the effects of two or more intervention treatments on a predefined state of human subjects who receive either intervention randomly. The underlying rationale of favoring randomized controlled trials over other study designs is that the former provide greater certainty over the accuracy of the study outcomes than the latter. Pushing this argument further, it is also argued that bigger trials (i.e. involving more patients over longer periods) provide the most reliable outcomes and hence are considered as best evidence (Moher et al. 1994).

Second, apart from providing a ranking of evidence, evidence based medicine also makes use of pre-processed evidence (Guyatt and Busse 2006). As such evidence based medicine provides the means to make sense of the masses of evidence available. Due to the problem of information overload, best clinical evidence does not immediately let alone necessarily end up at clinical

practitioners. To remedy this issue, evidence based medicine provides a peer review system of critically appraising and filtering current best evidence in medicine. As Mulrow (1994 p. 596) puts it: "*the vast amount of available information underscores the value of systematic reviews … [D]ecision makers of various types are inundated with unmanageable amounts of information. They have great need for systematic reviews that separate the known from the unknown and that save them from the position of knowing less than has been proved.*" Thus after the outcomes of randomized controlled trials (and other studies) are published they are scrutinized in light of other pieces of evidence available and comprehensively reported in systematic reviews. The clinical practice guideline can be considered the hallmark of this review system (Timmermans and Berg 2003). As such, clinical practice guidelines provide "*statements that include recommendations intended to optimize patient care. They are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options*" (Institute of Medicine 2011 pp. 25-26). In other words, through the formulation of clinical practice guidelines, evidence based medicine provides clinical practitioners and other implicated actors the filtered evidence that supports their decisions and behavior.

Notwithstanding its success in constituting the dominant paradigm, evidence based medicine has also been heavily criticized. One critique questions the implications evidence based medicine in general and clinical practice guidelines in particular have on actual clinical practices (Timmermans and Berg 2003). That is, although evidence based medicine might be aiming at informing clinical practice with the best clinical evidence available, its actual success in reaching and hence influencing clinical practices might be limited or at least unclear (Solberg 2000). Likewise, others criticize evidence based medicine and especially its clinical practice guidelines for being insufficient in providing effective guidance for the best possible care. That is, clinical practice guidelines are never enough to ground clinical practice decision making in; one always needs additional knowledge to interpret and apply evidence on best medical care in practice (Henry et al. 2007).

Translational medicine has been proposed as an extension of evidence based medicine to align scientific merit with practical needs (Narayan et al. 2004). Translational medicine can be defined as "*the "bench-to-bedside" enterprise of harnessing knowledge from basic sciences to produce new drugs, devices, and treatment options for patients*" (Woolf 2008 p. 211). However, not only is translational medicine concerned with the mere provision of health care options, so is translational medicine concerned with "*ensuring that new treatments and research knowledge actually reach the patients or populations for whom they are intended and are implemented*" (Woolf 2008 p. 211). Note that translational medicine is generally not taken as an alternative to evidence based medicine, but rather as a complement of evidence based medicine (Lean et al. 2008; Montory and Guyatt 2008). In all, translational medicine can thus be defined as the multifaceted process enabling the translation of scientific outcomes into clinical practice.

The main claim of the proponents of translational medicine holds that in order to assure that the best evidence available actually reaches the patient, science should immediately integrate all aspects deemed relevant in the provision of comprehensive solutions to the most pressing problems (Lean et al. 2008; Ledford 2008). In other words, the organization of medical science ought to be responsive to the nature of the problem at stake and actors involved in clinical practice. Hence it is argued that "*the scale and complexity of current science requires novel team approaches, including: interdisciplinary research teams; public-private partnerships; and programs to fund high-risk, high-impact research*" (Kington 2004 p. 65). Such an interpretation of translational medicine then closely resembles the idea of Mode 2 knowledge production (Gibbons et al. 1994; Nowotny et al. 2001; Smits and Boon 2008; see also chapter 1). That is, an

interpretation of Mode 2 knowledge production in which social, institutional, organizational, disciplinary, and geographical boundaries are very much blurred. Accordingly, like Mode 2 knowledge production, the integration of medical science as translational can be characterized along multiple dimensions as well.[43]

First, almost by implication, the notion of translational medicine defined as a bench-to-bedside enterprise, includes other than academic actors. As such translational medicine is often described as involving both actors primarily occupied with the provision of scientific knowledge (as those in academia) and actors primarily concerned with public health and the provision of care (as those in government and hospitals) (Marincola 2003; Ledford 2008). With respect to problem solving activities in the context of medicine it is hence argued that "*we should take more of an engineering approach to the problem, designing for dissemination from the discovery phase, working at the outset in partnership with potential adopters for reality testing*" (Rimer 2004 p. 40). The importance of involving non-academic actors in scientific problem-solving resembles the idea that under Mode 2 knowledge production the boundaries between academia and non-academia become blurred (Gibbons et al. 1994; Nowotny et al. 2001). Apart from including actors affiliated to hospitals and government then, translational medicine is also said to be best served when combining the efforts of academia with the efforts of industry. As such, Schwartz and Vilquin (2003 p. 493) argue that "*at the crossroads of academia and industry, translational research provides the vehicle for the application of medical discoveries and developments. A productive and expended relationship between these two sectors is essential for the continued success in translating basic research findings to the clinic*". More in general then, translational medicine can thus be said to involve a triple helix of university-industry-government relations (Leydesdorff and Etzkowitz 1996; Etzkowitz and Leydesdorff 2000).

Second, the notion of translational medicine encompasses the involvement of the community in the provision of solutions to health care problems (Green and Mercer 2001). Here, community "*should be interpreted broadly as all who will be affected by the research results, including lay residents of a local arena, practitioners, service agencies, and policymakers … [W]hen results are to be used for, in, and by communities, those communities should collaborate not only in applying findings but also in determining the ways in which the findings are produced and interpreted*" (Green and Mercer 2001 p. 1926). In part, the emphasis put on communities again stresses the importance of involving different types of institutional actors (i.e. care providers and government agencies alongside academic actors) or a number of organizations more in general. However, in pointing at a role for "*lay residents of a local arena*", the community not only has an institutional connotation but also a social and geographical connotation. When Nowotny et al. (2001) stress that "*not only does science speak to society, but society also speaks back at science*", what is argued for then is that within a distributed organization of medical science actors from different organizations, social communities, and geographical locations should be represented in the production of knowledge. However, not only should these different settings be represented as such; they should also be represented in balanced terms. That is, the organization of projects should involve the different kind of actors equally.

Third, support for inter-, multi-, or transdisciplinary team science is often grounded in a belief that it provides the best means to tackle multifaceted problems comprehensively. As such, Stokols et al. (2008 p. S77) argue that "*considering the enormous complexity and multifactorial causation of*

[43] Throughout the medical literature the notion of translational medicine is interpreted differently. One such interpretation focuses on the organizational aspects of medical science. It is this interpretation on which we will focus here. Other interpretations are less concerned with the organization of medical science rather than with the design characteristics of studies (see e.g. Tunis et al. 2003).

the most vexing social, environmental, and public health problems (e.g., terrorism and inter-ethnic violence; global warming; cancer, heart disease, diabetes, and AIDS; health disparities among minority populations), efforts to foster greater collaboration among scientists trained in different fields are not only a useful but also an essential strategy for ameliorating these problems." Hence, bringing together actors with various disciplinary backgrounds is said to bring about more fruitful solutions than mono-disciplinary science. Whether addressed in terms of interdisciplinary, multidisciplinary, or even transdisciplinary science (see e.g. Wagner et al. 2011); all these concepts point at the potential of solving complex problems by including multiple cognitive perspectives. In a way, the proponents of involving multiple cognitive perspectives take this as a necessary strategy for it ought to better reflect the ontological complexity involved in the constitution of particular problems.[44]

In stressing the potential benefits of a distributed organization, however, few contributions on Mode 2 knowledge production pay attention to the possible downsides of a distributed organization of science. Nowotny et al. (2001 esp. pp. 174-175) for example, while recognizing that Mode 2 knowledge production need not be favorable per se, stress that overall Mode 2 knowledge production is not likely to harm the integrity of science. Yet, especially in medicine a distributed organization of science is not taken as reflecting a positive development per se. The involvement of particular (non-academic) actors in medicine might imply that conflicts of interest arise. Conflicts of interest are defined as "*a set of conditions in which professional judgment concerning a primary interest … tends to be unduly influenced by a secondary interest*" (Thompson 1993 p. 576). As such, conflicts of interest potentially endanger the proper operation of evidence based medicine. That is, judgments made throughout the process of medical science are prone to be biased into certain directions.

One obvious conflict of interest is financial (Norris et al. 2011). That is, financial interests might among others corrupt the impartial judgment of one's own study outcomes, the work of others, and allocation of resources (e.g. funding) by virtue of striving after one's own best financial interest. Financial conflicts of interest are often associated with industry's involvement in medical science. Here, not only judgments made by industry itself are taken as suspect of being interest driven but also the judgments made by those who have or had ties to industry. Here it is often argued that the relation between industry and academia is characterized as a reciprocal gift-giving economy; industry actors provide academic actors with funding in exchange of the latter judging positively on the former's goods (Sismondo 2008). In the context of the formulation of clinical practice guidelines, financial conflicts of interest, and especially those attributed to industry's involvement in medicine, might thus lead to recommendations that are in the interest of those possessing financial resources (Norris et al. 2011).

Note however that the occurrence of conflicts of interest does not mean by implication that the judgments made by particular actors are indeed also serving some individual interests at the cost of not serving the public interest. Hence, having a conflict of interest does not necessarily imply the conflicting interest is enacted upon in a detrimental way. What we do know however is that many

[44] Alternatively, Bonaccorsi (2008; 2010) uses the notion of cognitive complementarities to characterize problem solving activities in some branches of science as crossing disciplinary boundaries. Rather than seeking the occurrence of such complementarities outside the domain of science itself (i.e. in the complexity of the problems at stake), he takes cross-disicplinarity as an (inevitable) outcome of failed reductionism. That is, in order to comprehensively solve problems in one domain scholars are said to be forced to enter other domains. Notwithstanding the difference between transdisciplinarity as residing within the nature of complex problems (Gibbons et al. 1994; Nowotny et al. 2001) and cognitive complementarities as residing within the nature of epistemics in science itself (Bonaccorsi 2008; Bonaccorsi 2010); what holds is that both accounts characterize the nature of problem solving activities in terms of crossing disciplinary boundaries.

of the judgments made in medical science do present at least traces of bias. As such, industry sponsored studies are less likely to be disclosed than non-industry sponsored studies (Bekelman et al. 2003; Lexchin et al. 2003), industry sponsored studies disproportionately more often report on positive results (Dwan et al. 2008), and studies reporting on positive outcomes are disproportionately more often cited (Gøtzsche 1987). What is more, there are sound theoretical arguments that provide a rationale for the occurrence of some biases and not others. For example the relative non-disclosure of industry sponsored studies can be explained from an economics of science perspective holding that given the nature of scientific knowledge as a public good, industry actors will be less inclined to disclose their knowledge (Arrow 1962; Dasgupta and David 1994). In all, and whatever the particular behavioral causes and normative implications to be attributed, what holds is that different kind of biases are likely to occur during the clinical practice guideline development process (Cohen 2004). However, what kind and the extent to which biases also apply for clinical practice guidelines are unclear as of now.

To summarize, we consider three aspects important as possible determinants increasing the likelihood that science becomes societal relevant. First, under an evidence based medicine paradigm, study quality aspects are most likely to have a positive effect on the likelihood that studies are societal relevant. As such, medical studies that are considered scientifically relevant are also more likely to be considered societal relevant. Second, the importance of translational medicine – as a natural extension of evidence based medicine – implies that those studies whose organization is characterized by diversity along multiple dimensions are most likely to render societal relevant outcomes. Hence, geographical, cognitive, social, institutional, and organizational diversity in the organization of medical projects are expected to have a positive effect on the likelihood of projects to become societal relevant. Finally, given that conflicts of interest are considered a serious issue within the medical literature, biases are likely to occur in the transformation of study results into evidence of societal relevance. That is, the establishment of studies as societal relevant might be steered by different kind of biases. Especially the involvement of industry in medical projects can be expected to have a positive effect on the likelihood of medical projects rendering societal relevant outcomes. In what follows then, we will address these three premises on the role played by study quality, diversity, and biases in the determination of societal relevance empirically using a clinical practice guideline on managing type 2 diabetes as an example.

6.3. Data and variables

Diabetes affects millions of people around the globe and is expected to do ever more so in the near future (Danaei et al. 2011; Hurley 2011). The fact that diabetes is a chronic disease further underlines its importance. Diabetes not only affects many people, as a chronic disease it also affects many people for longer periods of time and possibly with major consequences. The prime issue revolving diabetes is described as hyperglycemia, that is, the bodily condition in which a too high amount of glucose circulates the blood. A state of hyperglycemia is problematic in that it is indicative of the blood delivering too little energy for organs to function. When this state continues for longer periods of time then this may lead to severe complications such as a loss of sight and severe foot ulcers (Tattersall 2009).

Although largely similar in their complications, we can grossly distinguish two most prevalent types of diabetes (type 1 diabetes and type 2 diabetes). One the one hand, type 1 diabetes is generally taken to reflect a state in which the body is insufficiently capable of producing hormones

that enable the transformation of into energy (Tattersall 2009). The hormone of interest here has become known as insulin. As such, the discovery of insulin has been a major breakthrough in the treatment of type 1 diabetes patients (Bliss, 2007). That is, the discovery of insulin has made type 1 diabetes very much "manageable", yet the problem as such is far from definitely solved (Mol 2008).

On the other hand, type 2 diabetes is generally taken to reflect a state in which the body is insufficiently capable of metabolizing (i.e. transforming) insulin properly therewith leading to an inadequate bodily uptake of energy (Tattersall 2009). Regardless of the bodily capacity to produce insulin (characteristic of type 1 diabetes), type 2 diabetes is primarily characterized by a resistance or deficiency of the body to use insulin. As compared to type 1 diabetes, type 2 diabetes can be said to be even less intermediately solved. That is, to our knowledge no treatment has been proposed for type 2 diabetes so far that is fully capable of continuously improving the bodily capacity to metabolize insulin, like insulin itself has been proposed as a treatment option to produce that relatively absent hormone so characteristic of type 1 diabetes. Diabetes, and especially in its type 2 variant, then constitutes a very complex disease involving many interacting factors such as genetics, lifestyle, and the (industrialized) environment (Zimmet et al. 2001).

In 1999 the National Institute for Clinical Excellence (NICE) was established as a special health authority of the British National Health Service. Its main aim has been "*to provide health professionals in the UK National Health Service (NHS) with the tools to enable them to give high-quality clinical care and cost-effective care to their patients*" (Rawlins 1999 p. 1079). As such, NICE serves three functions; appraising health technologies, developing clinical practice guidelines, and promoting clinical audits. Although its name changed in 2005 into the National Institute for Health and Clinical Excellence, its main aims pursued remain largely the same as did its abbreviation.

Since 2001 the National Collaborating Centre for Chronic Conditions (NCC-CC) provides clinical practice guidelines on chronic diseases on behalf of NICE. As such, the NCC-CC also provides clinical practice guidelines on managing type 2 diabetes. The aim of the NCC-CC (2008) clinical practice guideline is "*to provide a user-friendly, clinical, evidence-based guideline*" (p. 7). As such, the guideline is meant to address a broad audience including among others healthcare professionals, patients and their family, and patient support groups. Together with recommendations made by the American Diabetes Association (see e.g. Diabetes Care 2012), the NCC-CC (2008) clinical practice guideline on type 2 diabetes can be considered most influential around the world.

As other guidelines supported by NICE, the NCC-CC (2008) guideline on managing type 2 diabetes has been developed in a number of steps (see also National Institute for Health and Clinical Excellence 2006). First, a number of questions have been formulated to be addressed by the guideline. These questions thus define the scope of the topics addressed throughout the guideline. Second, a search has been formulated enabling the systematic collection of all available publications possibly containing evidence on the specific topics deemed relevant. Third, all publications possibly presenting evidence on relevant topics are then critically assessed by the members of the guideline development group. Finally, after agreeing upon interpretations of the evidence the guideline development group proposes a number of recommendations to be included in the eventual clinical practice guideline.

The guideline development group is chaired by an academic scholar and involves 23 other individuals affiliated to universities, the NCC-CC, clinics, hospitals, and patient organizations.

Apart from the formal guideline development groups 18 other individuals have been involved as advisors or peer reviewers. The extent to which members of the guideline development group potentially have a conflict of interest is unclear. In the guidelines manual it is stressed that guideline development members are to be excluded from being involved in providing recommendations on topics for which they possibly have a conflicts of interest (National Institute for Health and Clinical Excellence 2006 p. 28). Of course this does not imply that the members of the guideline development group cannot be affected in their decisions by industry interests. Rather, if at all, these conflicts of interests might be much more subtle than involving direct industry relations per se (Sismondo 2007).

The tasks of the guideline development group are threefold. One task is to develop questions to be addressed on relevant topics. A second task is to formulate a search query enabling them to assess all publications that potentially contain evidence on these topics. A third task is assessing the set of publications that potentially contain evidence on the topics to be addressed and to propose recommendations on the inclusion of these publications as evidence in the clinical practice guideline itself. Our interest primarily resides in an assessment of this third task. That is, we will assess the extent to which the final decision of the guideline development group to include some and exclude other publications as evidence in the clinical practice guideline is mediated by particular organizational characteristics of medical science. As argued, the central hypothesis holds that the more distributed organization of science, the more likely its research output will have societal impact as measured by a citation in the guideline.

Dependent variable. The dependent variable in the analysis is the citation of a clinical trial outcome publication in sections of the clinical practice guideline that discus evidence on managing type 2 diabetes. As such, we take citation as indicating that the outcomes of the study are considered to reflect societal relevant evidence in the context of properly managing a particular issue of type 2 diabetes. Alternatively, non-citation indicates that the outcomes of the study not cited are not deemed relevant. To construct our dependent variable we proceeded in a number of steps (see figure 6.1).

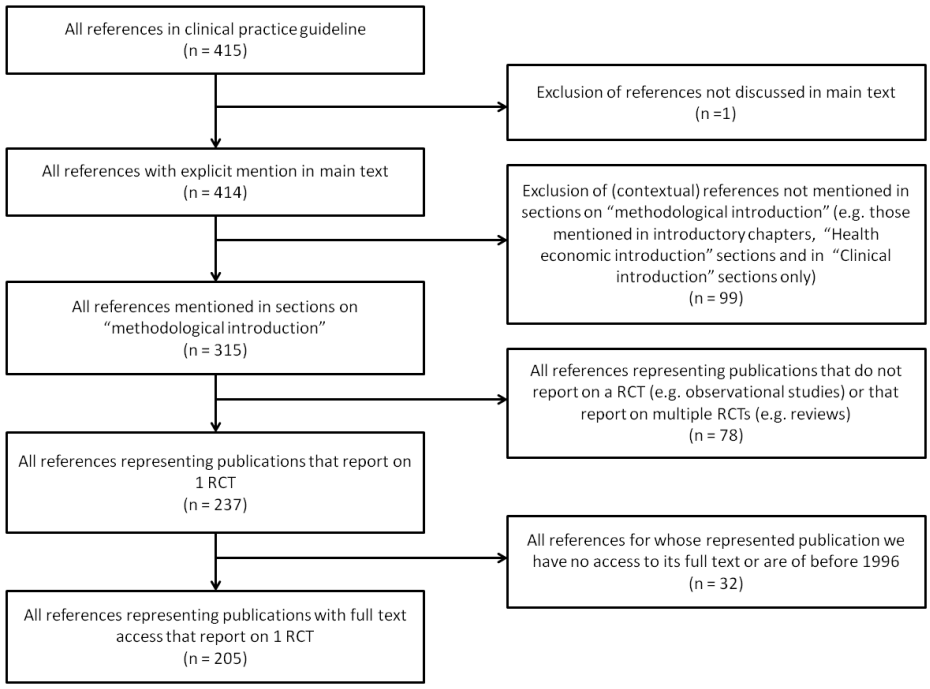
First, we collected all references from the NCC-CC (2008) clinical practice guideline on type 2 diabetes. As such we collected 415 references listed in the clinical practice guideline. Given that one of these references is not discussed at all throughout the main text, we only include 414 references representing studies suspect of providing evidence on managing type 2 diabetes.

Second, from the 414 references suspect of providing evidence on managing type 2 diabetes we exclude all references that are not mentioned in methodological sections of the clinical practice guideline. As explained, methodological sections present the studies that are eligible of providing evidence on managing type 2 diabetes. That is, these are the studies that came out of the search for studies performed by the guideline development committee. Here, we exclude all 99 references made to publications discussed in introductory sections and sections discussing health economics. As such we further restrict our set of references to include 315 publications only.

Third, in order to make sure that all references represent studies that can in principle be compared; we further restricted our set to include only those references that represent studies reporting on the outcomes of a clinical trial. As such, we exclude references that represent publications that report on outcomes of observational studies, epidemiological studies, and case studies. Likewise, we also exclude references that represent publications that report on outcomes of multiple randomized controlled trials such as (systematic) reviews and meta-analyses. As such we exclude 78 additional

references and are left with 237 references representing publications that report on the outcomes of one randomized controlled clinical trial.

Figure 6.1. *Sample selection flow chart*



Fourth, in collecting on the organization and design of these studies we are restricted to those studies whose publications we have full text access to and for which we are also able to collect bibliometric data. With respect to the latter we could only include studies published from 1996 onwards as these are included Elsevier's Scopus offline bibliometric data set. From the remaining 237 references we thus had to exclude an additional 32 references leaving us with 205 references to be assessed.

Finally, we split the 205 remaining references accordingly based on their being cited as evidence in sections reporting on the outcomes of studies or not being cited therein. Note then that all publications included in our analysis appear as references in the NCC-CC (2008) clinical practice guideline on type 2 diabetes. Yet, of these references only 167 are actually cited in "evidence statements" sections discussing evidence on how to manage type 2 diabetes and its complications properly. The reasons for citing or not citing studies that in principle could be cited are not made explicit. That is, although all studies report on the outcomes of a randomized controlled trial and were deemed topically relevant at forehand, for unspecified "methodological reasons" still some studies are excluded from being discussed as evidence on the proper management of type 2 diabetes.

Independent variables. In order to explain evidence citation in the NCC-CC (2008) clinical practice guideline on type 2 diabetes we include three sets of in total twelve independent variables (see table 6.2). Unless noted otherwise we use Elsevier's Scopus database on bibliometric records on scientific publications (1996-2008) to construct these variables. For each reference extracted from the NCC-CC (2008) clinical practice guideline we searched for the corresponding bibliometric record. Accordingly we extracted all bibliometric data on the bibliometric records such as author information, citation counts, references, and the like.

The first set of independent variables indicates quality aspects of the publications. First, we measure the quality of a publication by the number of citations a publication has received throughout the scientific literature up until January 2008. Citation counts are an imperfect and incomplete measure of scientific quality (Moed 2005). Yet, as they are attributed by scholars as references in attempt to develop their own claims, they do at least reflect on instances of perceived (scientific) relevance (see also chapter 5).[45] Second, as in other studies (see De Bellis 2009), we use the number of references attributed by a publication as an indicator of the quality of a publication. As an indication of the number of different claims it combines in laying down a new claim, this variable indicates the scope of the publication (Lovaglia 1991). Third, we measure the quality of a publication by the number of patients included in the study. From an evidence based medicine perspective it has been argued that studies involving larger patient samples are more likely to render results that are representative for the whole patient population (Moher et al. 1994). Likewise we measure the quality of the publication by the duration of the study in weeks. Here the argument goes that studies that take longer are more likely to render reliable results. Note then that while the first two variables measure scientific quality in general, the latter two variables are specifically designed to capture evidence based medicine's notion of best evidence. What holds for all these indicators of publication quality is that we hypothesize that the higher the quality of the publication, the more likely it is that the study is cited as evidence in the clinical practice guideline.

The second set of independent variables operationalizes the notion of a distributed organization of science. Apart from the social dimension – measured in terms of the number of authors listed on the publication – we measure the distributed organization of science using Shannon's entropy (Shannon 1948; Stirling 2007) along four dimensions. The basic formula of Shannon entropy is as follows: $H = -\sum_{i=1}^{R} p_i \log p_i$, where p_i is the share of actors belonging to category i over all categories R. Hence, the more actors are involved and the more equal their contribution, the higher the diversity. International, organizational, and institutional diversity are all measured author-wise. When authors are affiliated to multiple organizations we first take a weighted share of these organizations over all authors and then calculate diversity. Accordingly, international diversity is measured from the country in which the authors' organizations are located and institutional diversity is measured from the institutional domains assigned to the organizations authors are affiliated with (academia, industry, government and care).[46]

For example, the publication "Duloxetine vs. placebo in patients with painful diabetic neuropathy" (Goldstein et al. 2005) lists 5 authors (D.J. Goldstein, Y. Lu, M.J. Detke, T.C. Lee, and S.

[45] One of the critiques on using citation counts as an indicator of quality is that publications with different publication years have different citation time windows, i.e. have different opportunity to become cited by other publications. To account for these different citation time windows we also experimented with taking into account citations received in the first full year after publication only. This alternative citation count measure did not alter the main results of the analysis.

[46] Apart from measuring institutional diversity on the basis of four categories (i.e. academia, industry, government, and care) we also experimented with using two categories only (i.e. public versus private organizations). This approach however did not alter the results of our analysis.

Iyengar) from 4 different organizations that are all located in one country (see table 6.1). One author (M.J. Detke) is affiliated with 3 organizations, one author (D.J. Goldstein) is affiliated with 2 organizations, and four authors (Y. Lu, M.J. Detke, T.C. Lee, and S Iyengar) are all affiliated with the same company (Eli Lilly and Company). First, all organizations are divided over all authors individually. For example, D.J. Goldstein is affiliated with two organizations. Given that D.J. Goldstein is one out of five authors each of his affiliations has a share of 0.10 over all author-organization combinations. Second, all author-organization combination shares are summed over all organizations. This renders a value p for all organizations from which we calculate organizational diversity ($H_{organizational}$ = 0.48). Likewise we calculate the values of p for the institutions and countries involved and obtain the values of respectively institutional diversity ($H_{institutional}$ = 0.30) and international diversity ($H_{international}$ = 0).

Table 6.1. *Calculating organizational, institutional, and international diversity: an example*

Author	Organization(s)	Institution(s)	Country
D.J. Goldstein	PRN Consulting (share = 0.10; p = 0.10)	Industry (share = 0.10; p = 0.75)	United States (share = 0.10; p = 1.00)
	Indiana University (share = 0.10; p = 0.15)	Academia (share = 0.10; p = 0.20)	United States (share = 0.10; p = 1.00)
Y. Lu	Eli Lilly and Company (share = 0.20; p = 0.65)	Industry (share = 0.20; p = 0.75)	United States (share = 0.20; p = 1.00)
M.J. Detke	Eli Lilly and Company (share = 0.05; p = 0.65)	Industry (share = 0.05; p = 0.75	United States (share = 0.05; p = 1.00)
	Indiana University (share = 0.05; p = 0.15)	Academia (share = 0.05; p = 0.20)	United States (share = 0.05; p = 1.00)
	McLean Hospital (share = 0.05; p = 0.05)	Care (share = 0.05; p = 0.05)	United States (share = 0.05; p = 1.00)
	Harvard University (share = 0.05; p = 0.05)	Academia (share = 0.05; p = 0.20)	United States (share = 0.05; p = 1.00)
T.C. Lee	Eli Lilly and Company (share = 0.20; p = 0.65)	Industry (share = 0.20; p = 0.75)	United States (share = 0.20; p = 1.00)
S. Iyengar	Eli Lilly and Company (share = 0.20; p = 0.65)	Industry (share = 0.20; p = 0.75)	United States (share = 0.20; p = 1.00)

$$H_{organizational} = -(0.10 * \log(0.10) + 0.15 * \log(0.15) + 0.65 * \log(0.65) + 0.05 * \log(0.05) + 0.05 * \log(0.05)) = 0.48$$

$$H_{institutional} = -(0.75 * \log(0.75) + 0.20 * \log(0.20) + 0.05 * \log(0.05)) = 0.30$$

$$H_{international} = -(1 * \log(1)) = 0$$

Cognitive diversity is measured using references (see also Porter et al. 2007). All references listed in the set of publications represent other documents. Accordingly, we use Elsevier's Scopus disciplinary classification to determine how many different disciplines are referred to by the references listed in each publication.[47] Given that 93% of all references in our set represent publications whose journals can be assigned to disciplines, we thus calculated for every publication its disciplinary composition in terms of cognitive diversity. Again with reference to the above given example, the publication "Duloxetine vs. placebo in patients with painful diabetic neuropathy" (Goldstein et al. 2005) lists 25 references of which 19 represent publications that are part of Elsevier's Scopus. On average every reference has been attributed 2.1 disciplines; yet in total the set of 19 references refer to only 5 different disciplines (biochemistry, genetics and molecular biology (4 references); medicine (18 references); neuroscience (8 references); pharmacology, toxicology and pharmaceutics (7 references); and psychology (3 references)). As opposed to organizational, institutional, and international diversity we used a full counting method to calculate cognitive diversity. That is, a single reference whose journal has been attributed to more than one discipline is taken to belong completely instead of fractionally to every single discipline.[48] Hence the values of p for biochemistry, genetics and molecular biology (p = 4/40 = 0.10); medicine (p = 18/40 = 0.45); neuroscience (p = 8/40 = 0.20); pharmacology, toxicology and pharmaceutics (p = 7/40 = 0.18); and psychology (p = 3/40 = 0.08); and cognitive diversity renders $H_{cognitive} = -(0.10 * \log(0.10) + 0.45 * \log(0.45) + 0.20 * \log(0.20) + 0.18 * \log(0.18) + 0.08 * \log(0.08) = 0.61$.

The final set of independent variables measure the possibility of particular biases in evidence citation in the clinical practice guideline. That is, whereas indicators of publication quality are attributes of the references themselves, this second set of variables reflect the possible interests of those citing (i.e. the guideline development committee). Here, we include three such variables. The first variable is a dummy variable measuring whether or not a member of the guideline development committee has also been involved in the study that is cited or not as evidence. In citation studies self-citations are sometimes considered as instances of egotism (Lawani 1982; Glänzel et al. 2006). Hence, this variable is included to estimate the extent to which members of the guideline development committee are prone to cite their own studies as evidence in the clinical practice guideline. The second variable is also a dummy variable and measures whether an author from the United Kingdom has been involved in the publication. Here the argument goes that as NICE is an institute based in the United Kingdom its consideration of studies as evidence might be biased towards studies produced by someone from the United Kingdom (Brittain 1985; Börner et al. 2006; chapter 5). The third variable that we include here is an industry dummy variable and measures whether one or more authors are affiliated to a commercial organization. Unlike the previous two variables, as no one of the guideline development committee is explicitly said to be affiliated to industry in a direct way, this industry dummy does not directly or necessarily reflect the interests of the guideline development committee. Yet, given the widespread concerns over industry's alleged thorough involvement in all branches of medicine (Angell 2004; Sismondo 2007), this variable is meant to measure the extent to which this concern is legitimate with respect to the evidence presented in clinical practice guidelines.

[47] Elsevier's Scopus disciplinary classification attributes every journal to one or more core disciplines. In total there are 27 such core disciplines. In addition, most of these core disciplines are divided into sub-disciplines. For our calculations we only make use of the 27 core-disciplines.

[48] Nevertheless we also experimented with fractional counting. The correlation between cognitive diversity using full and fractional counting is 0.88.

Table 6.2. *Variables and descriptive statistics (N = 205)*

Variable	Description	Mean	Std. Dev.	Min.	Max.
1. Evidence citation	Citation of a publication as evidence in the guideline	0.81		0.00	1.00
2. # Science citations	Number of citations a publication has received until publication of the guideline	73.64	175.93	0.00	1972.00
3. # References	Number of references listed on the publication	27.69	11.31	0.00	71.00
4. # Patients	Number of patients enrolled in the study presented by the publication	1437.18	3990.06	16.00	31512.00
5. # Weeks	Study duration in weeks of the study presented by the publication	55.54	71.69	4.00	390.00
6. # Authors	Number of authors listed on the publication	7.03	6.00	1.00	69.00
7. Organizational diversity	Shannon entropy of the organizations listed on the publication	3.60	5.50	0.00	39.26
8. International diversity	Shannon entropy of the countries listed on the publication	0.17	0.27	0.00	1.19
9. Institutional diversity	Shannon entropy of the institutions listed on the publication	0.28	0.15	0.00	0.59
10. Disciplinary diversity	Shannon entropy of the disciplines represented by the references listed on the publication	0.49	0.13	0.00	0.77
11. Self-citation dummy	Involvement of a guideline committee member as author on the publication	0.03		0.00	1.00
12. UK dummy	Involvement of an organization located in the United Kingdom on the publication	0.19		0.00	1.00
13. Industry dummy	Involvement of an industrial organization on the publication	0.59		0.00	1.00

6.4. Analysis

Table 6.2 summarizes the definitions of all variables and the descriptive statistics. Table 6.3 presents the correlations of the variables included in the analysis. A first observation we make is that the size of projects in terms of number of authors correlates much more with the number of science citations received than with being cited as evidence in the clinical practice guideline. As a first approximation, and if we think of science citation and guideline evidence citation in terms of respectively Mode 1 and Mode 2 impact, it thus seems that – unexpectedly – involving many

actors goes hand in hand with Mode 1 impact but less so with Mode 2 impact. This tentative observation obviously requires more thorough investigation. For one thing, all publications assessed here have at least some societal impact as they are considered as potentially representing evidence.

Second, few independent variables correlate positively and significantly with evidence citation. Self-citation, though not significantly, even correlates negatively with evidence citation. Of all variables capturing quality aspects of the publications, only the number of references included correlates positively and significantly with evidence citation.

Third, of all variables measuring distributedness in the organization of medical science, international and cognitive diversity correlate positively and significantly with evidence citation. Although number of authors, organizational diversity, and institutional diversity also correlate positively with evidence citation these correlations are not statistically significant.

In addition, except for institutional and cognitive diversity, all variables on the distributed organization of medical science correlate positively and significantly with each other. Hence, distributedness in one dimension seems to go hand in hand with distributedness in another dimension. This result then further support our concern for including multiple dimensions at once as to single out the effect of each dimension individually.

Finally, the dummy variables indicating biases in the assessment of evidence in the clinical practice guideline show mixed results. The U.K. dummy correlates positively but not significantly with evidence citation. Remarkably, self-citation does not correlate positively but negatively with evidence citation (though not significant). The only bias in evidence selection in this clinical practice guideline seems to be reflected by the positive and significant correlation between the involvement of industry actors and evidence citation. Judging from these first results a concern with industry's involvement in medicine indeed seems to be warranted.

To analyze the determinants of guideline evidence citation, we used logit regression modeling (see table 6.4). In model 1 we only include the first set of independent variables capturing publications' quality aspects. As it turns out neither 'pure' scientific quality as measured by science citations nor characteristics that head under evidence based medicine's indicators of 'best evidence' turn out to have a positive and significant effect on publications to become cited as evidence in the clinical practice guideline. Of course this is not to suggest that quality aspects do not play any role in medicine's context of implication. As argued before, quality aspects play an important role for publications to become considered as potentially containing evidence in an earlier stage of the guideline development process. What holds then is that once publications are selected as potential evidence, these quality aspects do not seem to play an additional role in the ultimate selection of actual evidence.Instead, what is left is a positive and significant effect of the number of references listed by the publications. Hence, only the scope of the claim(s) discussed in a publication increases the likelihood of publications eventually being cited as evidence.

Table 6.3. *Correlations (N = 205)*

	Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.
1.	Evidence citation	1.000												
2.	# Science citations	0.034	1.000											
3.	# References	0.222#	0.037	1.000										
4.	# Patients	0.001	0.121*	-0.017	1.000									
5.	# Weeks	0.046	0.213#	0.012	0.438#	1.000								
6.	# Authors	0.087	0.157†	0.086	0.292#	0.178†	1.000							
7.	Organizational diversity	0.087	0.277#	-0.001	0.365#	0.251#	0.520#	1.000						
8.	International diversity	0.207#	0.111	0.010	0.142†	0.140†	0.237#	0.486#	1.000					
9.	Institutional diversity	0.014	0.105	-0.033	0.054	0.038	0.052	0.283#	0.305#	1.000				
10.	Disciplinary diversity	0.125*	0.182#	0.180#	0.156†	0.247#	0.200#	0.196#	0.157†	-0.079	1.000			
11.	Self-citation dummy	-0.049	-0.050	-0.031	-0.024	0.023	-0.051	-0.009	0.131*	0.066	0.047	1.000		
12.	UK dummy	0.071	0.041	0.007	0.178†	0.277#	0.164†	0.306#	0.498#	0.158†	0.073	0.388#	1.000	
13.	Industry dummy	0.210#	-0.045	0.026	-0.063	-0.197#	0.066	0.096	0.179†	0.418#	-0.008	0.104	0.030	1.000

* Significant at the 10% level; † significant at the 5% level, # significant at the 1% level

Table 6.4. *Logit regression results (binary dependent variable: citation as evidence; N = 205)*

	Model 1			Model 2			Model 3		
	Coef.	Robust S. E.	P value	Coef.	Robust S. E.	P value	Coef.	Robust S. E.	P value
# Science citations	0.00	0.00	0.764	-0.00	0.00	0.982	0.00	0.00	0.862
# References	0.06	0.02	0.001	0.06	0.02	0.003	0.06	0.02	0.002
# Patients	-0.00	0.00	0.767	-0.00	0.00	0.468	-0.00	0.00	0.481
# Weeks	0.00	0.00	0.507	0.00	0.00	0.938	0.00	0.00	0.433
# Authors				0.04	0.06	0.563	0.04	0.07	0.573
Organizational diversity				-0.02	0.06	0.760	-0.04	0.05	0.408
International diversity				3.25	1.04	0.002	3.18	1.24	0.010
Institutional diversity				-0.82	1.27	0.521	-3.05	1.81	0.091
Disciplinary diversity				0.82	1.31	0.530	0.83	1.40	0.552
Self-citation dummy							-2.05	1.07	0.055
UK dummy							0.32	0.73	0.659
Industry dummy							1.56	0.57	0.006
Constant	-0.10	0.48	0.842	-0.61	0.81	0.452	-0.96	0.91	0.289
Log pseudo likelihood	-92.54			-86.50			-80.15		
Prob. > Chi square	0.018			0.005			0.003		
Pseudo R^2	0.06			0.12			0.18		

Model 2 shows the results for the variables on the distributed organization of science. As it turns out only international diversity has a positive and significant impact on publications to become cited as evidence in the clinical practice guideline. Apparently, the two dimensions most often stressed within notions of Mode 2 knowledge production – namely institutional and disciplinary diversity – does not render such publications to become cited as evidence more likely. Also, involving more authors does in itself not render evidence citation to become more likely. Instead, international diversity does render evidence citation to becomemore likely. Hence, a balanced involvement of authors from various national contexts has a positive impact on steering evidence to become societal relevant more likely.

In model 3 we add the final set of independent variables capturing the interests of those citing. No evidence is found for self-citation bias or for a bias for research carried out in the United Kingdom. However, a positive and strong effect of the industry dummy is found. Hence, the involvement of industry actors as author on a publication increases the likelihood of that publication being included as evidence in the clinical practice guideline.

In all we interpret the results of our analysis to reveal three patterns. First, notwithstanding the systematic nature of evidence collection throughout the development of a clinical practice guideline, aspects unrelated to the quality of published studies still play a role in the eventual selection of evidence. Striking in this respect is our first result that beyond 'pure' quality aspects evidence eventually also seems to become selected on the basis of the scope of claims as well. Second, direct personal interests do not seem to play a decisive role in the selection of publications for inclusion as evidence in a clinical practice guideline. Rather, the role of interests seems to be much more subtle (Sismondo 2007). That is, in its orientation towards including evidence of publications that involve industry, the widespread concern over industry's involvement in all domains of medicine seems indeed to be warranted. Industry seems to be particularly acquainted with the requirements of publications that are eventually considered as clinically relevant evidence. Third, a geographically distributed organization of medical science renders societal relevant outcomes more likely as authors from different countries are involved.

6.5. Concluding remarks

This paper attempted to provide insights into the effect of science's distributed organization on its impact in contexts of implication, here, in the context of medical science concerned with type 2 diabetes. As such, we made a first attempt to empirically address the relation between science's distributed organization and its societal relevance. The relation between the distributed organization of science and its societal relevance is far from straightforward. The outcomes presented here only capture a small part of a larger sequence through which medical study outcomes are transformed into sound medical evidence to be applicable in medical practices. That is, we only considered the final step in the selection process transforming study outcomes into evidence. For example, from our analysis we cannot say that quality considerations do not play a role in the process leading to the presentation of evidence in clinical practice guidelines at all. On the contrary, we know from the guideline development process that in earlier stages of the selection of evidence (at least as defined within the contours of the evidence based medicine paradigm itself), quality plays an important role in the selection of evidence. The outcomes of this study thus have to be interpreted conditional on the process preceding the final selection of evidence addressed here.

Ideally then we would like to address the complete sequence from the decision to publish study outcomes to the inclusion of evidence in clinical practice guidelines (Scargle 2000). However, given the time lags involved from the initiation of studies to publication and eventual inclusion in clinical practice guidelines such an analysis is not straightforward. What is more, until recently data on the initiation of studies was lacking altogether. Given the availability of such data nowadays future work could address the whole sequence in full. Future work can also pay more attention to the relation between the organization of clinical trial research, its representation on publications, and its impact in clinical practice guidelines. Therewith we could for example also assess whether practical clinical trials render more societal impact than effectiveness clinical trials (Tunis et al. 2003). In all, such an assessment would allow for a more rich understanding of the role of a Mode 2 organization of (medical) science in steering its societal impact (in clinical practice guidelines).

Our results are by no means meant to attach normative implications to how medical science is organized in a distributed way. Rather, we make a first attempt to describe the current distributed organization of medical science that is taken as societal relevant (i.e. that is cited in a clinical practice guideline). Two important results were found. First, there is little evidence that more heterogeneity in the distributed organization of science leads to societal relevance to become more likely, as the mode 2 thesis would predict. We only found such evidence for international research projects, while disciplinary, organizational and institutional diversity did not raise the probability of publications being cited in the guideline. Second, industry involvement raises the probability of publications being cited in the guideline. Although this result in itself does not discredit industry's prominent involvement, it does warrant further research in whether this involvement indeed improves the societal quality of research, or whether other mechanisms are in play. If anything, the results do point at the need for a more thorough empirical understanding of the up and downsides of a distributed organization of science. Our framework provides a straightforward operationalization of the Mode 2 concept and its impact on society, and hence, an avenue for future systematic empirical research.

7. Persistent bias in the publication of evidence by pharmaceutical companies[49]

7.1. Introduction

The changing relation between science and the marketplace has raised new questions about the nature of knowledge production (Gibbons et al. 1994; Nelson 2004; Shapin 2008). Although firms are active producers of scientific knowledge, they do not necessarily conform to the norms held by the academic community (Dasgupta and David 1994; Vallas and Kleinman 2008). Numerous scholars have therefore expressed concerns over strategic publication behavior of firms in which they disclose research findings that support their market strategies and suppress negative findings (Lexchin et al. 2003; Sismondo 2008). This behavior seems above all significant in close-to-the-market settings where appropriation of the underlying technology has already taken place and scientific signals are primarily intended to inform regulators and to support the diffusion of the new technology.

Biomedicine is a prime example in this context. Historically, this is one of the fields where the role of industry in the production and publication of scientific research has been extensive (Swann 1988; Furman and MacGarvie 2007). Despite this established position, the academic community and the public have raised concerns over the scientific integrity of research conducted by pharmaceutical companies (see for instance: Angell 2004; Smith 2006). This situation can be best understood by making reference to the hegemonic status of evidence-based medicine which is an attempt to directly ground clinical decision making in the available scientific evidence on medical therapies (Timmermans and Berg 2003). An important condition for the functioning of this system is that firms both produce evidence by conducting clinical trials on the safety and efficacy of their innovations and that they disclose this evidence as to inform regulators and practitioners. However, for a long time firms have been forced to contribute to evidence making (in order to gain market approval for their innovations), but not to evidence disclosure *per se.* This has provided them the opportunity to conceal the outcomes of research that failed to detect a hypothesized effect as the dissemination of such evidence can hamper the successful introduction of a new drug on the market. This phenomenon is known as publication bias and holds that scientific publication takes place based on the direction or strength of the observed effects of a study (Rosenthal 1979; Dickersin 1990, Lexchin et al. 2003; Bekelman et al. 2003; Dwan et al. 2008).[50]

To remedy the situation the Food and Drug Administration (FDA 2007) and the International Committee of Medical Journal Editors (De Angelis et al. 2004) have recently mandated both registration of clinical research in a public database before study onset and publication of research results after study completion. These institutional reforms provide us a unique opportunity to unravel the publication decision of firms by studying their considerations to disclose their research findings either in scientific publications or in web-based repositories. We will argue that the decision to submit research results to scientific journals rather than publishing these results on the web remains a strategic choice as scientific articles, unlike web reports provide certification by

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[50] Recent examples are controversies surrounding the diabetes drug Avandia (Bloomgarden 2007), the nonsteroidal anti-inflammatory drug Vioxx (Horton 2004) and SSRI anti-depressants agents (Turner et al. 2008). Note also that the phenomenon of study publication bias is not restricted to medicine and has also been detected in other fields including animal experiments (Sena et al. 2010), ecology (Murtaugh 2002), sociology (Gerber and Mahotra 2008) and economics (Stanley 2005).

experts that the research is scientifically sound, methodologically rigorous and thus credible (Merton and Zuckerman 1973; Crane 1976). Our results suggest that even under conditions of complete information disclosure, firms still have an interest to carefully construct and mobilize scientific publications resulting in a persistent bias in the scientific publication of evidence.

We make our contribution in the context of research on diabetes mellitus which is one of the fastest growing diseases in the world. At a global scale the number of adult diabetics has doubled within the past three decades and one in four U.S. adults now suffers from diabetes (Daneai et al. 2011). The promising market prospects have attracted large investments from pharmaceutical companies and many insulins and compounds are currently in the development stage. We focus in this study on a very homogenous group of research projects that all test whether the experimental therapy is effective in controlling blood glucose values which is the prime marker for all current diabetes research (Tattersall, 2009). This implies that the clinical trials in our sample all answer the same research question and only differ in terms of research design (e.g. control group, size), the therapy being tested, project organization and the results of the study. The homogeneity of our sample allows us to address many issues that are considered important in evidence-based medicine including definitions of scientific quality and clinical relevance.

The remainder of this paper is organized as follows. In section 2 we provide a theoretical framework to understand the decision of firms to publish their results in scientific journals against the background of evidence-based medicine. Section 3 introduces the data and methods. We then proceed in section 4 with the empirical analysis which consists of a comparison between publication practices in industry-funded research and publicly-funded research, followed by the main analysis in which we explain the decision of industry to publish in scientific journals as compared to web-based repositories. Section 5 concludes.

7.2. Theory Development

In the contemporary context of corporate drug testing firms are mandated to publish the evidence that results from the conduct of clinical trials. In doing so, they now face the choice of publishing clinical trial evidence either in the scientific literature or in web-based repositories. Publication of evidence in scientific journals fulfils a specific function in this context. Both the specific 'inscription practices' used in scientific publications and critical peer-evaluation of the outcomes before, during, and after publication contribute to the establishment of credibility in the truth value of the results (Collins 1985; Latour 1987; Shapin 1995). Scientific publications are subject to review by peers who certify that the conducted evidence has been obtained by methods that are scientifically sound (Merton and Zuckerman 1973; Crane 1976). Reviewers and overseeing editors also make sure that clinical trial results are reported in a standardized way and that all relevant information to interpret the results and replicate the study design becomes available. Peer-review thus facilitates both consistent interpretation of clinical trial evidence by readers and readily made comparison of treatment effects of different therapies communicated in different publications (Polidoro and Theeke 2011).

Web-reports do as of yet not have these components and it also not likely that they will become more authoritative sources in the near future. The published data in web-reports is not reported in standardized formats *per se* and there is no quality control on the evidence. Although penalties for non-compliance to mandatory disclosure are high (up to $10,000 per day), it is unlikely that strict quality control of the content will be performed in the near future as this would be time-consuming

and therefore too costly (Wager 2008). The absence of independent scrutiny and peer review implies that quality-control is only ensured by firms themselves which is likely to hinder the construction of credibility in the results of web-reports, as compared to scientific publications.[51]

Given the differences between scientific publications and web-reports, we expect the persistence of bias in publication practices where firms continue to strategically certify research findings in the scientific literature following their commercial interests. Firms consider scientific publications not merely as objects that signal information, but as devices that need to be carefully constructed and mobilized to anticipate on impact on practitioners and regulators (Gøtzche, et al. 2007; Sismondo 2009). In the search for impact, firms need to conform to the epistemologies of the academic community and its associated norms (DiMaggio and Powell 1983). In case of clinical trial research these norms are defined by the evidence-based medicine. Our main argument thus holds that firms make scientific publishing simultaneously dependent upon their commercial interests and the quality standards defined within evidence-based medicine.

The rise of evidence-based medicine can be best understood against the background of the increased use of randomized clinical trials as a means to legitimate medical treatments on the market. Strict regulatory oversight of corporate drug testing became mandated in the sixties but its use for producing evidence did not eradicate geographical variations in medical practice. Over the years, new treatment options also emerged and this rendered medical decision making increasingly complex for practitioners (Timmermans and Berg 2003; Elstein 2004). Proponents of evidence-based medicine provided a solution by de-emphasizing *"intuition, un-systematic clinical experience and pathophysiologic rationale as sufficient grounds for clinical decision making"* (Evidence Based Working Group 1992, p. 2420) and advocating instead "*the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients*" (Sacket et al.1996, p.71). Following this definition, evidence-based medicine is an attempt to strengthen the link between scientific research and clinical decision making, by explicitly formulating standards on what is considered best evidence (Timmermans and Berg 2003).[52] Firms consider these standards when pursuing scientific publication of their studies, because this is a necessary condition for having impact. Two elements that shape definitions of 'best evidence' are of particular importance in this respect.

First, the idea of best evidence has become closely related to the design characteristics of research. Evidence-based medicine relies on hierarchical grading systems of research quality and results derived from randomized clinical trials are consistently ranked on top of this hierarchy (Atkins et al. 2004; Glasziou et al. 2008). The assumption underlying hierarchical quality ratings is that the evidence obtained from medical studies provides regulators and practitioners with varying degrees of certainty about the true effects of medical treatments (see for instance: Montori and Guyatt 2008). Quality ratings standardize this certainty by providing a probability that the estimates of a treatment effect will be falsified or adjusted in future studies (Balshem et al. 2011). The uncertainty about possible changes in effect estimates is reduced when studies with superior research designs are performed as these studies are more likely to approximate the unknown true

[51] Now web-reporting is becoming a standard practice, more practical questions are also warranted including how to cite this evidence in the scientific literature and how and when to acknowledge study teams and writing groups for their contributions (see for instance: Wager 2006).

[52] Indeed, evidence-based medicine has also been criticized for many reasons (see for instance: Goldenberg 2005, Lambert 2006), including for being too positivist and empiricist (Hjørland 2011) and for its limited impact on changing physicians actual decisions (Timmermans and Berg 2003; Armstrong and Ogden 2006; Greenhalgh et al. 2008).

effect of a treatment.[53] Due to this expression of mechanical objectivity (Porter 1995), it is rather the research design that is important for the quality of the study than the outcomes of the study as such. In its most apparent form this has led to a situation where prestigious journals issue a provisional commitment to publish research findings purely on the base of research designs (Horton 1997; McNamee et al. 2007).

The nature of graded quality standards and its direct association with experimental designs provides firms with explicit guidance to conform to the norms of the academic community. Although the conduct of clinical trials is costly[54], investments in high-quality research designs are instrumental in mitigating the risks of critical peer evaluation by academic experts both before, during and after publication. The possibility of actual replication is very low in clinical research, yet firms are still anxious to publish knowledge of low quality standards as it is more likely that in these cases the estimates are subject to change in future studies.

One of the main factors affecting the quality of studies in this respect is the size of the clinical trials and its associated statistical power to detect treatment effects. Ideally, clinical trials should be large enough to detect reliable effects of the intervention on the primary outcome measure, and it is not uncommon that studies fail to do so simply because they are too small (Moher et al. 1994; Halpern et al. 2002). Larger studies have the benefit that - next to an analysis of the primary outcome measure - relevant secondary questions can be answered and subgroup analyses can be conducted to test whether the effects of a treatment differ between patient groups. Moreover, larger studies are more likely to detect adverse events of treatments, especially if those adverse events are rare.

In addition to sheer number of patients, size also refers to the study locations where the clinical trial is conducted. It can be expected that the effects of an intervention will differ between population groups with varying genetic and cultural backgrounds. Clinical trials that are conducted in many countries can factor out these 'contaminating' effects by controlling for differences between study locations. Hence, the authority of clinical trial results tends to increase when clinical trials are conducted in multiple countries.

A second element that is key to the idea of 'best evidence' in evidence-based medicine relates to the clinical relevance of the research. Evidence-based medicine emphasizes critical appraisal of the scientific literature by clinical decision makers in order to match available evidence with the needs and values of individual patients (Evidence-based medicine Working Group 1992). This implies that clinical trials explicitly designed to assist health care decision makers are considered to be of higher quality than clinical trials that are merely designed to understand the effectiveness of an intervention. This prioritizes clinical trials that resemble in their experimental set-up practical choices facing patients and practitioners such as head-to-head comparisons between multiple therapies and testing particular treatments against viable alternative clinical strategies (Tunis et al. 2003; Angell 2004). In contrast, comparisons between an experimental therapy and a placebo do not provide practitioners with knowledge on the trade-offs between alternative treatment options.

[53] This view on uncertainty cannot deal with unknown unknowns which are bound to be present in a knowledge activity where the full spectrum of a treatments' effect is inherently uncertain (Knight 1921). However, it is believed that large enough clinical trials will eventually signal such effects after which regulatory agencies mandate additional studies or gather advisory committees to assess its relevance.

[54] The exact costs of conducting clinical trials is an area of contestation itself with estimates ranging from $802 million at the high end (DiMasi et al. 2003) to well under $100 million at the low end (Angell 2004).

In sum, evidence-based medicine defines quality of evidence largely on the base of research designs and its value for clinical decision making. Clinical trials that score high on these elements are therefore more likely to have impact within evidence-based medicine. Firms anticipate on impact and devote resources to scientific publishing when the perceived quality of their clinical trials is high as expressed both in the statistical power of the project and the clinical relevance of the research design. Our first hypothesis thus holds:

Hypothesis 1: The likelihood that clinical trials conducted by pharmaceutical companies are scientifically published increases with the quality of the evidence according to evidence-based medicine standards.

An associated outcome of the rise of evidence-based medicine is that clinical decision making on therapies and associated pharmaceutical sales have become directly dependent upon signals in the scientific literature (Azoulay 2002). The rise of evidence-based medicine has thus created an incentive for firms to carefully construct and mobilize scientific publications in order to strengthen their market position (Sismondo 2009). In contrast to publishing in basic research, this incentive is further facilitated by the fact that appropriation of the underlying technology has already taken place during corporate drug testing which makes scooping risks associated with scientific publication a relatively minor concern (Nelson 1959; Arrow 1962; David and Dasgupta 1994).

It follows that firms select clinical trial results to create a consistent drug profile in the literature (Henry 2009; Sismondo 2009). The publication bias literature has in this context confirmed over and over again that publications funded by companies are disproportionally more often favorable to the tested therapy (Bekelman et al. 2003; Lexchin et al. 2003; Dwan et al. 2008; Sismondo 2008). Importantly, this empirical result is neither driven by a lower quality of industry-funded research designs which is at least perceived to be similar if not higher (Djulbegovic et al. 1999; Clifford et al. 2002) nor by higher rejection rates of either industry-funded trials or trials with negative results (Olson et al. 2002; Lee et al. 2006).

Even experiments with therapies that are ultimately assessed as being safe and efficacious can render negative results due to incorrect clinical trial design or simply by chance. Negative findings may interfere with the approval process and is less likely to result in scientific and clinical impact because these results cast doubt on the efficacy and safety of the experimental therapy and may contradict other findings that are already published. Thus, research that fails to detect a hypothesized effect of a firms' technology can seriously lower the chances of commercial success of the drug. Hence, firms are expected to publish these results as a web report rather than submit it to scientific journals, despite the fact that the research design is sophisticated enough to warrant publication. Our second hypothesis holds:

Hypothesis 2: The likelihood that clinical trials conducted by pharmaceutical companies are scientifically published increases when the evidence is favorable to the compound that is being tested.

One can argue that evidence-based medicine has augmented the fear of negative impact as clinical decision making responds directly to scientific signals in the literature. It is ironic, however, that this incentive runs counter to evidence-based medicine which crucially relies on the public availability of all evidence, irrespective of the actors involved or the direction or strength of the observed effects (Scargle 2000; Guyatt et al. 2011). Evidence from multiple clinical trials accumulate in meta-analysis, systematic reviews and clinical guidelines which have become reputable sources to disseminate proven diagnostic and therapeutic knowledge among peers and

practitioners (Timmermans and Berg 2003). Publication bias is especially problematic in light of this accumulated evidence which can be severely distorted due to the absence of negative findings. In its most extreme manifestations it is the 5% of studies with positive findings simply due to statistical fluctuations that are published, whereas the 95% with negative findings remains hidden in "file drawers" (Rosenthal 1979; Scargle 2000). The institutional reforms that mandate disclosure have opened the "file drawers" but have not changed scientific publication behavior per se.

7.3. Data and methods

Sample definition. The starting point for the empirical analysis in this paper is registrations of clinical trials on diabetes mellitus in the public database www.clinicaltrials.gov. This internet based registry managed by the US National Library of Medicine was established in response to the enactment of Section 113 of the 1997 FDA Modernization Act that called for the establishment of a public resource for information on ongoing clinical studies that target serious or life threatening diseases (including diabetes mellitus). In 2004, the editors of the most prestigious medical journals (i.e. the International Committee of Medical Journal Editors) acted upon this law by announcing that they would only consider for publication manuscripts that were properly registered in this database (de Angelis et al. 2004). As a result, registration of clinical trials soared between May and October, 2005 (Zarin et al. 2005), in the years afterwards (Zarin and Tse 2008), and www.clinicaltrials.gov now contains information on more than 100,000 clinical studies (Zarin et al. 2011).

The representatives of all major pharmaceutical companies changed their policy accordingly by announcing that "*the pharmaceutical industry has committed to registering information about all new and ongoing clinical trials"* (PhRMA 2004). In the same press release PhrMa also announced that they established a clinical trial result database (www.clinicaltrialstudyresults.org) and several large companies (e.g. Elli Lilly, GlaxoSmithKline, Merck) immediately committed to this initiative by disclosing the research results of all clinical trials going back to 2000. Section 801 of the FDA Amendment Act 2007 further mandated the disclosure of research results (FDA 2007), although web-reporting of research results had already become common practice before the act was implemented.

The registered clinical trials provide us with information about research projects well before the research results are disclosed in scientific publications or web reports. We limit ourselves to studies for which registration has become mandated before onset in order to avoid the selection problem that research projects simply may be registered because the researchers want to publish the results in scientific journals. To further prevent selection bias due to the possible exemption of individual clinical trials from mandatory disclosure we only focus in the main analysis on research projects that are disclosed in scientific publications or on the web. In this way, we avoid the well-known file drawer problem which holds that the results of studies that are not published in the scientific literature cannot be known (Rosenthal 1979; Scargle 2000). It follows that we do not have to rely on surrogate measures such as funnel plots or meta-regression analysis (Sutton et al. 2000; Stanley 2005) to study publication bias.

Construction of our sample closely follows the registration specifications enforced by the ICMJE and the FDA which resulted in the inclusion of 329 research projects. In short, we consider

completed or terminated[55] clinical trials that were specifically designed to test whether a drug or insulin intervention is effective in controlling blood glucose values as a primary endpoint. This implies that our sample is very homogenous and that the research projects only differ according to the therapy being tested, the research design (e.g. control group, size) and project organization. All tested experimental treatments in the sample are in later stage development (i.e. Phase II or Phase III) or already on the market. Details of inclusion criteria pertaining to the relevant fields in www.clinicaltrials.gov are found in figure 7.1.

Important in this study is that we equal industry-funding with the production and intentional publication of evidence by pharmaceutical companies. This is a realistic assumption given the focus on an efficacy endpoint and the observation that most of the therapies in our sample are in the development stage. Certain tasks and responsibilities in these clinical trials may be outsourced to academic centers, contract research organizations or for profit clinics but this does not shield pharmaceutical firms from responsibility for the scientific integrity of the study (Azoulay 2003). The active involvement of pharmaceutical companies in the production and publication of evidence is also indicated by the observation that all registrations are posted and maintained by firms. In addition, the web-reports in our sample are almost always published on the websites of pharmaceutical firms (Merck being an exception as they post all their results on www.clinicaltrials.gov), whereas all but four scientific publications have at least one author from a pharmaceutical company. Exclusion of these four cases did not change the reported results.

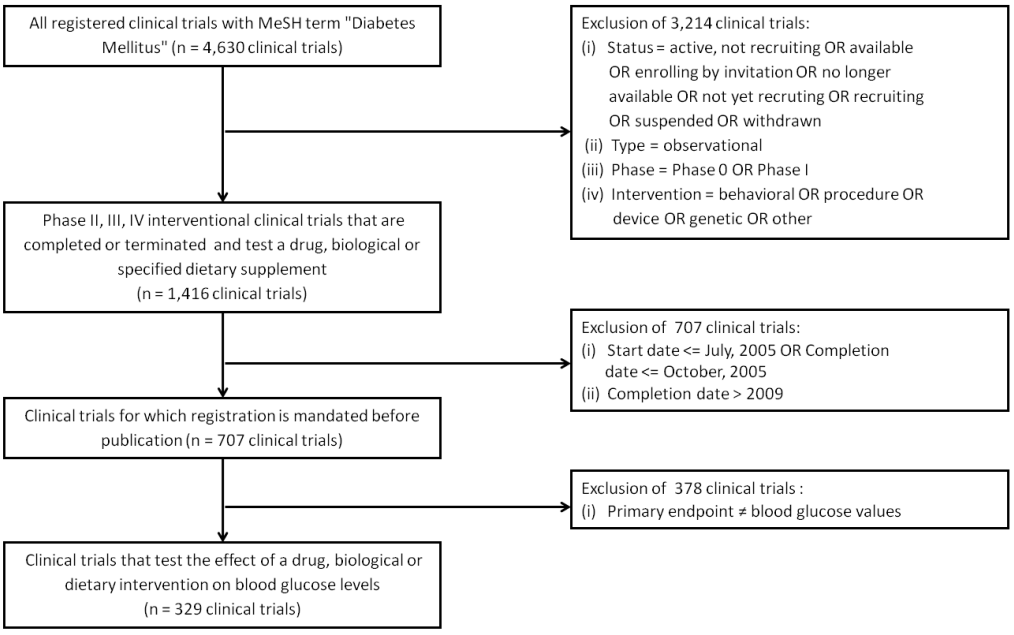
Assessment of registrations and publications. An extensive data collection effort was made (i) to code the research design characteristics of the 329 research projects, (ii) to link the registration to subsequent publication in the scientific literature or on the web and (iii) to assess the results of the clinical trial as being positive or negative. In all these three steps most data was independently collected and coded by the two authors, after which differences were resolved by consensus. We provide a short description of this effort below and refer to the appendix for a more elaborate description and an overview of all collected variables.

In a first step, research design characteristics of the clinical trial were extracted from the registrations and classified. Among these characteristics are the name of the sponsor, the sponsor-type (i.e. industry or public), the name of the treatment that is being tested (i.e. the experimental arm), the type of diabetes that the experimental therapy targets and the nature of the control group (i.e. active, placebo, uncontrolled etc.). The status and history of all experimental therapies was tracked down to determine whether and when the therapy was approved on the market.

In a second step, a search protocol was used to determine the publication status of the 329 clinical trials by categorizing them as belonging to one of three mutual exclusive categories: scientific publication, web report or no disclosure. We only considered original reports of clinical trials that provide information on the results of the primary endpoint of the project as defined in the registration (i.e. blood glucose values). The search protocol was elaborate and included searches of the medical literature (PubMed and Embase), publications indexed in a citation database (Scopus) and manuscripts and citations in clinical trial result databases (www.clinicalstudyresults.org and firm databases). Abstracts and full texts of all potential matches where manually screened in order to prevent both false positives to be included and false negatives to be excluded. Our final match of disclosed research projects is 74.4% which is comparable to, or even somewhat higher than, previous efforts (Lee et al. 2008; Ross et al. 2009; Bourgeois et al. 2010).

[55] Terminated clinical trials are defined as projects for which the recruitment or enrolment of patients halted prematurely but definitive (National Institutes of Health 2008).

Figure 7.1. *Sample selection flow chart*



In a third step, we determined for all publications whether the reported results were favorable or unfavorable to the experimental therapy being tested. Results were considered favorable if they were statistically significant (judged from p-values or confidence intervals) and confirmed the hypothesis on the primary endpoint as stated in the registration or publication. The assessment of manuscripts was classified as unclear in case no significance analysis was performed on the primary endpoint of the study.

Dependent variable. Our research is concerned with the factors that explain the scientific publication of research projects. To understand these factors we first analyze differences in publication practices between publicly-funded and industry-funded clinical trials. In doing so, we implicitly evaluate the effects of the new disclosure policies and follow the traditional publication bias literature that has analyzed differences in the results of scientific publications according to funding sources.

However, we also show that traditional publication bias analysis cannot distinguish between the reasons why pharmaceutical companies produce and the reasons why they publish more positive evidence (which both turns out to be the case in our sample). We consider this distinction between production and publication pertinent and this draws attention in the empirical strategy to the construction of a very precise control group.

Without trivializing the importance of publication bias, there are many reasons why companies obtain more often positive results in clinical trials compared to non-industry funded trials. Given the high costs of clinical development they only advance innovations in clinical trials that are

technologically promising and they reconsider their decision every time evidence from a clinical trial becomes available (DiMasi et al. 2003). Part of observed publication bias between industry-funded and publicly-funded research might therefore be driven by a selection process where only those clinical trials are conducted that have a high likelihood of obtaining positive results. The same reasoning also applies to the termination of clinical trials which is more likely when firms are involved than other actors (Lexchin 2005).

From an empirical perspective this necessitates a within-group comparison of industry-funded trials that all focus on the same research question. By employing this strategy we rule out many alternative explanations that are bound to be present in the publication process. Our main dependent variable is therefore the choice of pharmaceutical companies to publish their research findings in scientific publications as compared to reporting in web-based repositories.

Independent variables.

Result variables. To test the influence of clinical trial outcomes on the likelihood that the study is published in a scientific journal, we created a dummy variable that is set to 1 if the hypothesis on the primary outcome of the study is confirmed (i.e. positive outcome) and to 0 if the hypothesis is rejected (i.e. negative outcome). In order to prevent that our assessment was influenced by selective presentation of research results in the publications such as a change of hypothesis from superiority to non-inferiority to obtain positive results (Boutron et al. 2010), we also test a model in which all outcomes are assessed on the base of a superiority hypothesis.

Research design variables. The influence of quality standards in evidence-based medicine on scientific publishing is captured by including variables on the statistical power of clinical trials and the clinical relevance of the evidence. With respect to the statistical power we include as a variable both the number of patients and whether patients from multiple countries are enrolled in the clinical trial. With respect to the clinical relevance of the evidence, we focus on the control group in the clinical trial that is used to compare the relative safety and efficacy of the experimental arm. We create a dummy variable which is set to one, in case a clinical trial makes a head-to-head comparison with another therapy or compares alternative clinical strategies for administrating the same or similar therapies (e.g. difference in the times of administration, different titration schemes). These control groups reflect actual clinical decision choices facing patients and practitioners. The reference group in this case becomes placebo-controlled studies and therapies that are tested as an add-on to existing treatments.

Controls. We control for several potential sources of heterogeneity across observations that may influence both the design and outcome of research projects and their subsequent reporting in scientific publications or on the web. More specifically, the interest in this paper is in understanding the type of evidence that firms disclose in scientific publications and as such we want to control for other factors that influence their publication strategies. In order to do so we start by excluding all 23 disclosed but terminated clinical trials in our sample which are always disclosed in web-reports and often do not provide enough information to make an assessment of their results.

We take into account in all models the possibility that publication decisions are driven by unobserved heterogeneity at the level of the firm and at the level of a therapy's development program. At the level of the firm, disclosure decisions may be influenced by explicit policies or the presence of (internal or external) staff that have a taste for science (see for instance: Sauermann and Stephan 2011). We capture this effect by including firm-level dummies.

At the level of development programs, unobserved characteristics of a therapy may drive our results as some experimental therapies may be intrinsically better which influences both the likelihood that positive results are obtained and the willingness to highlight these results in the scientific literature. Disclosure policies may also be decided on the therapy level instead of the firm-level. To account for these potential factors we include a set of dummies for the therapies that are being tested in multiple clinical trials.

We also consider the possible effect of time-lags on scientific publication by including dummies for completion years of the clinical trial. Although all clinical trials are completed before 2009 and disclosure of most research results is mandated within 12 months after completion date, firms might have a strategy of disclosing initially on the web after which the evidence appears in scientific publications.

In addition to these variables we control for an additional set of factors that may influence the decision to disclose scientifically. *First*, firms often conduct clinically relevant studies after their therapies are already approved on the market (i.e. Phase IV), although not necessarily so. To make sure that publication is driven by clinical relevance and not by the market conditions of the therapy we include a dummy set to 1 for all experimental arms that are already on the market when the clinical trial is completed. *Second,* we include a dummy variable set to 1 if a clinical trial targets diabetes, type 2 and to 0 otherwise, because market prospects and associated publishing may differ between diabetes types. *Third*, we control for the duration of the study by including the number of weeks the experimental treatment is administered to patients as the costs of clinical trials tend to increase with the length of the study. *Fourth,* we control for the observation that studies mainly conducted in major pharmaceutical markets are considered more convincing to regulators and better resemble the actual situations in which practitioners work. To test this we include the percentage of recruitment in traditional research countries in North America (i.e. United States and Canada), Western Europe (i.e. EU15+Switzerland+Norway), Japan, Australia and New Zealand.

Model estimation. We estimate the probability that the evidence of a research projects becomes disclosed in a scientific publication. This implies that our dependent variable either takes on a value of *one* in case the evidence from a research project is scientifically published, or zero in case the evidence of a research project is published on the web. Because of the binary categorical nature of this variable we estimate logistic regression models and report the coefficients of the independent variables which are equal to the log-odds ratios (Long and Freese 2006). We estimate our model using robust standard errors, as decisions on several components of the research design of a clinical trial may not be completely independent.

7.4. Results

Funding source comparison. Table 7.1 presents the results of a comparison in publication practices between industry-funded trials and publicly funded trials. Publication rates between industry (75.3%) and publicly-funded trials (71.2%) are similar (p=0.498) suggesting that institutional reforms indeed have eradicated disclosure differences between funding sources. Publicly sponsored trials are almost by default published in scientific journals, whereas firms choose to publish clinical trial reports either in scientific journals or on the web. It follows that industry-funded trials are significantly less likely to be published in scientific journals (p<0.001). The results also strongly confirm that scientific publishing of industry-funded trials still depends on the observed outcomes of clinical trials. The percentage of positive results observed in all clinical trial

reports is already higher in industry-sponsored research (72.7% versus 59.6%), but these differences are augmented when focusing only on publications in the scientific literature (87.6% versus 58.7%).

Although our narrowly defined sample only includes trials that are designed to test the effect of an experimental treatment on controlling blood glucose values, we observe striking differences in the nature of the tested therapies between industry and publicly funded trials. The fast growing market of diabetes, type 2 attracts many resources from industry whereas diabetes, type 1 is especially being studied in publicly funded clinical research. Publicly funded research also tends to be more explorative and often studies new causal associations of therapies that are not explicitly designed to control blood glucose values. As a final note Table 7.1 shows that industry funded studies are more often terminated, probably because the financial risks associated with those trials are larger.

We conclude from these results that publication bias according to funding source persists in the scientific literature despite institutional reform. Yet, we also show that the tested treatments are significantly different between funding sources rendering comparisons problematic, even when focusing on a single primary endpoint. To control for these factors, we study in the next section the decision of industry to disclose their research results either in web-reports or in scientific publications.

Table 7.1. *Differences in disclosure and treatment according to funding source*

Characteristic	Industry funded (n=263)		Publicly funded (n=66)		p value
Disclosure type					
All	198	75.29%	47	71.21%	0.498
Scientific	121	46.01%	46	69.70%	0.001
Positive outcomes					
All	154	77.78%	30	63.83%	0.047
Scientific	111	91.74%	29	63.04%	0.000
Terminated	34	12.93%	2	3.03%	0.021
Experimental therapy					
Diabetes treatment	253	96.20%	35	53.03%	
Non-diabetes treatment	8	3.04%	12	18.18%	
Foods and supplements	2	0.76%	19	28.79%	0.000‡
Diabetes Type					
Diabetes Mellitus	7	2.66%	14	21.21%	
Only Type 1†	26	9.89%	12	18.18%	
Only Type 2†	230	87.45%	40	60.61%	0.000‡

P-values are based on two-tailed proportional t-tests; † A clinical trial can test both on patients with diabetes type 1 and type 2; ‡ Chi-square test

Design comparisons. A concern of our analysis is that industry-funded trials are simply less interesting to publish in scientific journals and have higher rejection rates when considered for publication. We test this proposition in table 7.2 by comparing the research designs of industry-funded clinical trials that are published on the web with publicly-funded research projects that are published in the scientific literature. We focus specifically on the quality of the studies according to evidence-based medicine that can be derived from the statistical power of studies as indicated by project size and the clinical relevance of the research as captured by the control groups used.

The results indicate that – according to evidence-based medicine standards – web-disclosed industry-funded studies are of statistical similar or higher quality as publicly funded clinical trials that are published in the scientific literature. More specifically, industry-funded trials are larger in size and the strength of their control treatments does not differ between funding sources. The former outcome probably reflects the financial resources and infrastructure of pharmaceutical companies which are able to finance much larger research projects than public science.

Table 7.2. *Differences in research design according to funding source*

Characteristic	Publicly funded Scientific (n=46)		Industry funded Scientific (n=121)		*p*-value	Industry funded Web (n=77)		*p*-value
Project Size								
# Patients†	72.35	76.53	540.83	632.10	0.000	279.19	226.46	0.000
International	2	4.35%	87	71.90%	0.000	32	41.56%	0.000
Design								
Active	18	39.13%	52	42.98%		33	42.86%	
Placebo	17	36.96%	50	41.32%		21	27.27%	
Uncontrolled	4	8.70%	2	1.65%		12	15.58%	
Alternative Control	6	13.04%	9	7.44%		6	7.79%	
Other	1	2.17%	8	6.61%	0.123	5	6.49%	0.415

Data represents number, percentage and associated two-tailed proportional t-tests compared with publicly funded; † mean, standard deviation and associated two-tailed mean sample t-test compared with publicly funded.

These empirical observations demonstrate that web reports of industry-funded clinical trials are of high enough quality to warrant publication in the scientific literature. The regulatory nature of corporate drug testing ensures that the late-stage clinical trials in our sample (i.e. Phase 2 and Phase 3) conform to basic evidence-based medicine standards. In addition, there are ample initiatives within the academic community to create specific outlets for publishing 'deviant' results and for publishing as many results as possible (due to open-access which is not limited by space-constraints).[56] This means that the decision of firms to publish clinical trial results in scientific journals or on the web is a deliberate choice rather than an outcome of the peer-review process.

[56] For instance, there are now journals that publish studies only based on technical standards and not on the base of relevance or impact (e.g. PloS One), and there are journals that publish only studies with negative results (e.g. Journal of Negative Results in Biomedicine).

Reports published on the web are most likely not papers that were initially rejected by scientific journals. Rather, firms deliberately choice to publish particular results in scientific journals and other results as reports on the web.

Main analysis. Table 7.3 reports the correlation matrix for the included variables. Table 7.4 presents the estimates of the logistic regression on the likelihood of scientific publication. All models include firm-level dummies, therapy-level dummies and publication year dummies. Model 4-5 also include additional control variables. Estimation of the model with firm-level dummies results in the exclusion of 12 clinical trials from one firm (Elli Lilly) which are all published in the scientific literature. In addition, therapy-dummies render the exclusion of 8 additional clinical trials on the compound Alogliptin (developed by Takeda) which are also all scientifically published. This implies that our sample for estimation consists of 157 clinical trials.

Table 7.3. *Correlation matrix*

	Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.
1.	Scientific publication	1.000								
2.	Positive result	0.334	1.000							
3.	# Patients	0.357	0.166	1.000						
4.	International	0.380	0.070	0.431	1.000					
5.	Clinical Relevance	0.099	-0.110	0.043	-0.097	1.000				
6.	Diabetes Type	-0.040	0.019	0.143	-0.020	-0.302	1.000			
7.	Trial duration	0.001	-0.135	0.373	0.227	0.166	-0.062	1.000		
8.	Therapy on Market	-0.221	-0.133	-0.221	-0.260	0.284	-0.151	0.081	1.000	
9.	% Traditional locations	-0.021	0.083	-0.187	-0.352	0.131	-0.126	-0.112	0.025	1.000

Hypothesis 1 predicts that scientific publication by pharmaceutical companies depends on the explicit quality standards of evidence-based medicine. Consistent with this prediction, we observe a positive and significant coefficient for the project size of clinical trials as captured by the number of patients and by a dummy that indicates whether the trial enrolls patients from multiple countries. In Model 3, the number of patients is only significant at the 10% level ($p = 0.090$) which is probably due to the correlation between the two project size variables ($r = 0.431$). We also find a positive coefficient for clinical trials with clinically relevant study designs. These results are simultaneously significant whilst controlling for a number of possible alternative explanations.

Hypothesis 2 states that firms are more likely to report evidence in scientific publications when they obtain positive results. Model 2-5 confirm this hypothesis by showing positive and highly significant ($p < 0.007$) coefficients for this variable. The results hold independent of the introduction of a number of additional control variables in Model 4 and a uniform definition of positive results based on a superiority hypothesis in Model 5.

Table 7.4. *Logistic regression results*

	Model 1		Model 2		Model 3		Model 4		Model 5	
	coef.	*p*-value	coef.	*p*-value	coef.	*p*-value	coef.	*p*-value	coef.	*p*-value
Results										
Positive			2.298	0.002	2.604	0.000	2.005	0.007	2.404	0.002
									Positive to superiority	
Research Design										
# Patients	0.585	0.040			0.535	0.090	0.702	0.035	0.863	0.013
International	2.141	0.000			2.279	0.000	2.587	0.000	3.196	0.000
Clinical Relevance	2.069	0.005			2.120	0.005	2.173	0.012	3.601	0.000
Control Variables										
Diabetes Type							-0.063	0.947	-0.753	0.431
Trial duration							-0.499	0.169	-0.834	0.055
Therapy on Market							-0.765	0.282	-1.541	0.057
% Traditional locations							0.996	0.090	1.300	0.047
Therapy Dummies		YES		YES		YES		YES		YES
Firm Dummies		YES		YES		YES		YES		YES
Completion Year Dummies		YES		YES		YES		YES		YES
Constant	-4.049	0.022	-1.557	0.164	-6.296	0.003	-5.954	0.015	-5.632	0.015
N	157		157		157		157		157	
Log Likelihood	-55.582		-67.247		-50.350		-48.945		-46.089	

Several control variables show some influence on the decision of firms to highlight evidence in scientific publications. Particularly noteworthy in this case is the proportion of traditional research countries in the clinical trial. The coefficient of this variable is positive and significant ($p < 0.05$) in Model 5. In addition, tests on the joint significance of the included dummy variables indicate that the three groups of dummies are significant ($p < 0.016$) in all models.

7.5. Conclusion

Firms' leeway in marketing their products is often limited by legislative and normative standards. This raises the issue to what extent firms can still pursue their market interest when they have to conform to institutional norms. We address this issue by focusing on pharmaceutical companies who in order to convince regulators and practitioners of the relevance of their drugs need to produce evidence on the safety and efficacy of their innovations. The publication bias literature has made clear that pharmaceutical companies are prone to highlight only positive evidence, but recent regulatory reforms have mandated pharmaceutical companies to report the evidence of almost all the studies they perform. The key question then becomes how firms strategically operate within a context of complete information disclosure.

We address this issue by comparing the reporting of evidence between industry-funded and publicly-funded diabetes trials. Our initial results indicate that pharmaceutical companies do indeed not report less evidence than other researchers in the new institutional context. However, although firms can no longer conceal evidence, they now make a deliberate choice to report their evidence either in scientific publications or in web-based repositories. This stands in stark contrast to the research of non-industry sponsored projects which by default is published in scientific journals.

These initial empirical outcomes call for an understanding of the decision by pharmaceutical companies to highlight their evidence in the scientific domain. We argue that publication in scientific journals consists of a continuous scrutiny of the evidence before, during and after publication which increases the truth value of the evidence and establishes trust in the results. Pharmaceutical companies are aware of this function of science and therefore carefully select the evidence they wish to certify. In order to anticipate on impact, firms also need to conform to particular standards that are deemed relevant by the academic community. In case of clinical research these standards are defined by the emphasis of evidence-based medicine on the quality of research designs. We therefore hypothesize that the decision of firms to publish in scientific journals is simultaneously dependent on the direction of the obtained evidence and the quality of research designs.

Our main analysis confirms our argument and rules out alternative explanations at the level of the firm, development program and clinical trial. Publication bias thus persists as positive findings are more likely to be published in scientific publications, whereas negative findings are more often filed in web-repositories. In addition, we also a find a bias of scientific publications towards studies that are of higher quality according to evidence-based medicine standards.

We conclude from these empirical observations that pharmaceutical firms still find a way to strategically highlight particular pieces of evidence in scientific journals despite the recent institutional reforms. This implies that concerns about publication based on the nature of evidence have shifted rather than disappeared. The presented results in this paper thus signal a problem of

persistent publication bias of a more fundamental nature which is not easily solved by regulatory reform alone.

To better understand this issue we suggest focusing the attention on the science system itself which allows for differential media exposure of individual research findings. Evidence on the meaning of a particular research object (such as the effectiveness of a drug) is preferably reviewed in light of the whole body of evidence of a research object (and related objects). Current publication practices however only make sure that a single piece of evidence is certified on its own merit. It follows that pharmaceutical firms can 'buy' certainty by conducting a number of clinical trials that attain to the highest quality standards while only highlighting the one which has the most favorable evidence components. In addition, firms can also decide to publish multiple pieces of evidence at the same time if they want to draw particular attention to a new therapy.[57] However, the submission of individual pieces of clinical trial evidence does not give an overview of the whole body of evidence in these situations which hinders an integrated evaluation of the qualities of a therapy and prevents critical reflection on the internal validity of development programs.

This focus stands in contrast to earlier studies on publication bias which merely question the scientific integrity of pharmaceutical firms, but do not acknowledge the limits of the science system and evidence-based medicine in dealing with the problem. We show that the organization of science has not prevented pharmaceutical companies from responding timely and in their own interest to recent regulatory reforms that mandate ever more transparency on their behalf. It seems therefore especially important to build institutions that enforce scientific integrity irrespective of firms' intentions, rather than mandating any further change in the behavior of pharmaceutical companies.

Appendix B.

In this appendix we describe in detail the three steps involved in classifying registrations, linking those registrations to disclosed manuscripts and assessing the outcomes of the disclosed manuscripts.

B.1. Assessing registrations and classifying drugs

We extracted the 329 research projects from the XML version of www.clinicaltrials.gov on October 21, 2010. Each registration contains information on the lead sponsor of the study and research design characteristics of the clinical trial. However, information about the latter is not consistently indexed in pre-defined fields. In order to obtain consistent research design information across all trials we manually assessed clinical trial registrations on the following dimensions:

- Type of diabetes: Diabetes Type 1, Diabetes Type 2, Diabetes Gestational
- Name of experimental arm: The experimental arm is defined as a single drug that is being tested on efficacy against a comparator treatment. The experimental drug is most often explicitly mentioned as such in the registration, although in a small number of cases we

[57] For instance, we observe in our sample that when the diabetes drug Sitagliptin was under review by the FDA, Merck submitted at the same day three papers on the same drug to prestigious scientific journals which were all accepted for publications a couple of months before the final decision on market approval was made.

determined the experimental arm based on a match between the producers of the therapy and the sponsor of the clinical trial. In 5 publicly funded clinical trials the experimental arm could not be determined because more than one drug was being tested and no explicit hypothesis was stated about the drug that should have favorable effects *vis a vis* control groups.

- Control group (see also Figure 7.2): In controlled experiments such as clinical trials, the effect of the experimental arm is compared with a control group keeping other baseline characteristics of patients (e.g. age, sex, weight) as identical as possible. We classified the control group as one of five types: (i) no intervention control (ii) placebo control (iii) active control (iv) dose control or (iv) alternative control. In case a clinical trial has more than one comparator arm we turn to the stated hypothesis to determine the main comparator (see A3). All encountered examples are mentioned in Figure 7.2.

We searched the FDA catalogue of approved drug products (www.accessdata.fda.gov/scripts/cder/drugsatfda) to determine whether the experimental arm was approved on the market. For all approved drugs we collected the approval year.

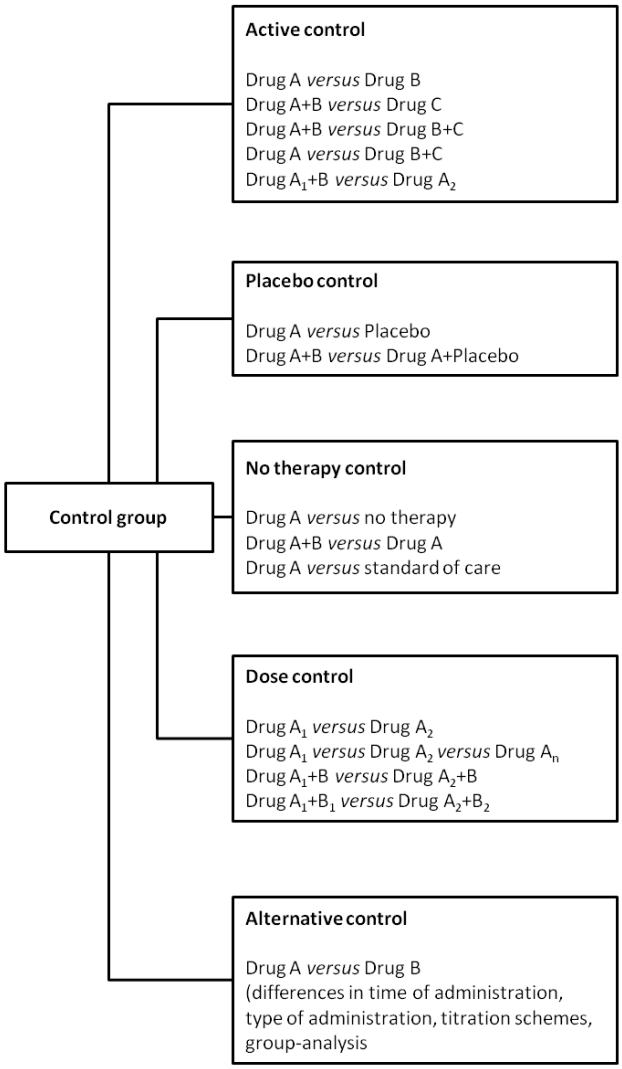
B.2. Linking registrations to disclosed manuscripts

A search protocol was used to determine whether the results of the 329 clinical trials were disclosed. Publications were defined as original manuscripts of clinical trial results that reported on the primary endpoint of the project as defined in the registration (i.e. blood glucose values). The search protocol to identify such disclosed manuscripts consisted of five steps that were independently executed by both authors. After each step, the authors compared the results of their search and any differences in findings were resolved by reading (again) abstract and full text of the publication. We searched for disclosed manuscripts for each clinical trial registration until we found a scientific publication. In a last step we complemented the set of all scientific publications with web reports for those clinical trial projects that were not scientifically disclosed. Part of the procedure is an adjustment of recent work in the medical literature (Ross et al. 2009; Bourgeois et al. 2011).

The five steps in the search process were as follows:

1. Examination of abstract and if necessary full text of scientific publications that are listed in the publication field of www.clinicaltrials.gov. This field is used to list citations of trial results or other relevant 'background' research as provided by the researchers.
2. Search of the medical literature (PubMed and Embase) using the national clinical trial identifier (NCTID) which is the unique identifier of each clinical trial registration. Many journals that follow ICMJE requirements (including the ICMJE member journals) publish this identifier in the abstract or acknowledgement of the scientific publication. The number is also indexed in PubMed as 'secondary ID' and in Embase as 'clinical trial numbers' and these fields can be searched as such.
3. Internet search (Google) using other clinical trial identification numbers mentioned in the field 'other study ID numbers' in www.clincialtrials.gov. Firms assign their own identification number to a particular project and clinical trials may also be indexed in other registries with relevant citations. Note that this search already resulted in a set of web reports that were only included in step 5. In this step we only screened those reports to assess whether they contained references to scientific publications.

Figure 7.2. *Definition of control group*



4. Free search of the medical literature (PubMed and Embase) and of a citation database (Scopus) using various search combinations of the name of the experimental arm, name of the comparator arm, name of the sponsor, name of the principal investigator (if mentioned), diabetes type, treatment period, recruitment countries and approximate patient enrolment. It turned out that in this free search not yet found scientific publications were easily identified. We therefore decided to stop searching for a scientific publication of a project if a relevant publication was not found within ten minutes.
5. Search of web reports by screening the web repositories maintained by all pharmaceutical companies that sponsor clinical trials in our sample. In addition, we also searched the result pages maintained in www.clinicaltrials.gov and an online registry,

www.clinicalstudyresults.org, which is consistently fed by some firms. As a final search action, we again screened all web reports for any additional references to the scientific literature which had remained unnoticed until that point, but we did not find any additional scientific publications.

All searches were updated and finalized as of June 1, 2011.

B.3. Outcome assessment of publications

We determined for all published manuscripts (web and scientific) whether the reported results were favorable or unfavorable to the experimental drugs being tested. In doing so we compared the effect of the experimental arm to the main control group that was mentioned in a stated hypothesis in the registration or publication. Before we made an assessment of the result of the publication, we stated the hypothesis of the clinical trial as either superiority or non-inferiority of the experimental arm to the control group. In a small number of cases no explicit hypothesis was stated in registration or publication. We solved this issue by taking superiority as our default hypothesis for all control groups except for active comparisons for which we stated a non-inferiority hypothesis.

The outcome assessment was made on the base of significant statistical differences in primary endpoint between the experimental arm and the control group. Results were considered favorable if the experimental arm demonstrated significant greater improvement in primary endpoint (in case of superiority hypothesis) or statistically similar improvement in primary endpoint (in case of non-inferiority hypothesis). Statistical significance was judged based on *p*-values or confidence intervals. If significance levels were not reported the outcome assessment remained unclear.

In case of active control groups we also made assessments that were not based on the stated hypothesis in the registration or publication but on both a non-inferiority hypothesis and a superiority hypothesis. This was done for consistency reasons and in order to prevent that our assessment was influenced by selective presentation of research results in the publications such as a change of hypothesis from superiority to non-inferiority to highlight that the experimental treatment was beneficial despite nonsignificant differences in primary endpoint (Boutron et al. 2010).

Next to an assessment of research results in the publications, we also noted for all publications the exact number of patients that were enrolled in the study and the countries were patients were recruited. Although these data elements are also available in www.clinicaltrials.gov they are sometimes missing or classified as ‘anticipated numbers’ (Sekeres et al. 2009; Ross et al. 2009).

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The Distributed Organization of Science: With Empirical Illustrations From the Field of Diabetes Medicine

Summary

The premise of this thesis holds that the organization of science is distributed in nature. That is, science takes place all over the world and within different spheres of society. Within the literature, the distributed organization of science is characterized in different ways. While some focus primarily on the substantive aspects of science such as the increasing importance of interdisciplinarity, others emphasize processes of de-institutionalization as seen in the cooperation between companies, universities and government agencies. Other contributions combine several aspects of science and as such for example speak of both the social and intellectual organization of science. More in general, then, the distributed organization of science can be characterized along different dimensions.

The aim of this thesis is to provide insight into the nature and consequences of a distributed organization of science. We take the distinction between Mode 1 and Mode 2 knowledge production as a starting point to describe the distributed organization of science. Mode 1 knowledge production conforms in many respects to the traditional image of scientific knowledge production that takes place primarily within the university; under Mode 1 knowledge production science takes place within strongly defined disciplines and focuses on the fundamental comprehension of natural and social phenomena. In contrast, the idea of Mode 2 knowledge production is characterized by its heterogeneity along all dimensions. That is, besides universities, actors from industry and government are also involved in science; science takes place across disciplines rather than within disciplines only; and under Mode 2 knowledge production science involves not only a quest for fundamental laws and regularities, but has a clear public interest.

Despite, or perhaps because of its rich description of science, the distinction between Mode 1 and Mode 2 knowledge production is much criticized. This criticism can be summarized in terms of three main points. First, the notion of Mode 2 knowledge production is conceptually vague. For example, it is unclear what exactly is meant by the notion of transdisciplinarity. Second, the empirical validity of claims on the emergence, prevalence, and persistence of Mode 2 knowledge production is debatable. Although at the project level there is evidence on an increase in the diversity of actors involved in science, it is unclear to what extent this also holds at the level of science systems at large. Finally, it is unclear to what extent Mode 2 knowledge production should be interpreted as a positive phenomenon in a normative sense. The normative implications of the idea of Mode 2 knowledge production have at least two sides. On the one hand the question arises to what extent and how diversity in the organization of distributed science indeed leads to more relevant knowledge. On the other hand, it could also be asked to what extent a development of science towards Mode 2 would prejudice the public interest of scientific knowledge.

Within this thesis, the criticisms of the notion of Mode 2 knowledge production are picked up. As such, this thesis addresses (i) an analytical approach to the notion of Mode 2 knowledge production, (ii) the empirical validity of the notion of Mode 2 knowledge production, (iii) the establishment of relevance in a distributed organization of science, and (iv) the normative implications of Mode 2 knowledge production. To strengthen our arguments empirically, we use the case of diabetes medicine. Diabetes medicine is an interesting case for at least three reasons. First, diabetes is a socially relevant problem in the sense that a large group of people around the world are faced with this disease. Consequently, research on diabetes is also widespread. Second,

diabetes constitutes a complex disease involving interacting factors such as genetics, lifestyle, and the environment. However, not only are the aspects involved in the constitution of this disease varied, as a consequence so are the people and organizations occupying themselves with finding solutions to this problem. What medical professionals call translational medicine seems to be especially accurate for diabetes, that is, as a description of medical science that concerns itself with diabetes duly takes into account the whole process from the laboratory bench to the patient bedside involving different actors. As such, the nature of diabetes as a scientific problem is immediately enmeshed with societal undertones whose provision of solutions is expected to be organized along various modes. Hence, we expect the organization of diabetes medicine to be characterized by Mode 2 rather than Mode 1 knowledge production.

The patterns of a distributed organization of science are addressed empirically using bibliometric data. The choice for a quantitative approach in our empirical research is pragmatic; bibliometrics allows me to address the science system on a large (i.e. global) scale. More fundamentally, we take the scientific publication as a useful starting point to assess science. Here we make a distinction between research and science. Whereas research is about local knowledge production practices, science is first and foremost about the transformation of knowledge towards universal acceptance. As such, the scientific publication is taken as a first and necessary step towards the certification of knowledge as scientific. It follows that the organizational aspects of science that are displayed on the scientific publication such as authorships, affiliations and references provide an input to investigate the patterns underlying the distributed organization of science.

Chapter 1 provides a first outline of an analytical approach to Mode 2 knowledge production. To substantiate the notion of Mode 2 knowledge production analytically we distinguish and define five forms of heterogeneity. First, institutional heterogeneity refers to the different value orientations and norms the different actors involved in science adhere to. Second, organizational heterogeneity refers to the different organizations involved in science. Third, geographical heterogeneity refers to science taking place in different countries, regions and cities. Fourth, cognitive heterogeneity refers to the various disciplinary backgrounds of actors. Finally, social heterogeneity refers to the different communities in which actors are active. While some descriptions of science focus on only one dimension of heterogeneity in the distributed organization of science, the notion of Mode 2 knowledge production provides a description of science along all of these five dimensions. The great advantage of studying science along these five dimensions is that we can now analytically address the distributed organization of science along multiple dimensions simultaneously.

Then, chapter 2 provides an overview of the recent empirical literature on the distributed organization of science. Of central concern here is the relationship between proximity on the one hand and impact and collaboration on the other hand. At the relational level, the concept of proximity is taken as the counterpart of the concept of heterogeneity. That is to say, where cooperation takes place between operators who are in close proximity to each other, the relationships between these actors are described as homogenous rather than heterogeneous. The main conclusion of this literature review holds that most studies that examine the role of proximity in collaborative science look only at a limited number of proximity dimensions. It follows that to gain a complete understanding of the distributed organization of science we need to include multiple proximity dimensions simultaneously.

Chapter 3 forms the prelude to the study of collaboration patterns between organizations in chapter 4. To come to such an analysis, first the idea of 'the organization' is discussed in chapter 3. While in quantitative science studies the nature of the organization is assumed to be unproblematic,

within discussions of Mode 2 knowledge production precisely the opposite is true. That is, within the notion of Mode 2 knowledge production, the boundaries between, say, the university and the commercial enterprise have faded. As such, the organization is not an unambiguous unit of analysis in quantitative science studies. However, this does not mean that the organization cannot be used to study science at a higher level of aggregation. Rather, in taking the organization as the basic unit of analysis in quantitative science studies choices must be made in conceptualizing the organization in the first place. These choices are not completely value-free, but must be viewed in light of the research in which the organization as the unit of analysis is used. On the basis of various organization theories, chapter 3 shows how the organization can be conceptualized along several dimensions.

Given our conceptualization of the organization that we proposed in chapter 3, chapter 4 analyzes collaboration patterns between organizations. Whereas in the literature on Mode 2 knowledge production the diversity of backgrounds of scientific actors is taken to form no obstacle for collaboration to take place, within the literature on proximity and innovation emphasis is put on the role of proximity in facilitating collaborative innovation. The latter does not mean that proximity needs to play a role along all five dimensions. On the contrary, there may be substitution between different forms of proximity. As such, differences may exist among science systems in how various proximity dimensions shape collaboration between organizations therein.

Chapter 4 examines (i) to what extent proximity in all five dimensions plays a role in scientific collaboration in the field of type 2 diabetes and (ii) to what extent the European science system differs from the North American system of science in terms of the comparative importance of the five proximity dimensions. Regarding the role of proximity in scientific collaboration, the main conclusion of this chapter holds that in general all proximity dimensions play their role in shaping collaboration between organizations. In particular, geographical proximity plays an important role in scientific collaboration which suggests that a regional or national focus in the study of science and innovation systems is legitimate. On the other hand, the focus on a "Triple Helix" of university-industry-government relations is no less legitimate because of the relative importance of this type of collaboration, both in North America and in Europe. Regarding the comparison between the European and North American science system, a difference is observed in the role of geographical, social and organizational proximity in shaping scientific collaboration. Where geographical proximity plays a larger role within the European science system, social and organizational proximity play a larger role within the North American science system. The relative importance of geographical proximity within the European science system can be traced to the greater differences in terms of language and culture in Europe. On the other hand the relative importance of organizational and social proximity in North America suggests a more hierarchical system there. It is notable that with regard to the role of institutional proximity the two science systems do not differ. In other words, the attention paid in policy discussions to a relative absence of relationships between academic and non-academic actors in Europe as compared to North America is not justified.

The last three chapters of this thesis discuss the implications of a distributed organization of science. First, chapter 5 addresses the citation as a measure of scientific (Mode 1) impact. Within science studies the citation is a contested measure of scientific impact. While some take little issue in using citation indicators, others completely dispense with the use of citation analysis as a tool for scientific evaluation. In order to get out of this impasse we turn to information science studies (in particular, "information retrieval" studies), in which the concept of relevance is important. Parallel to the debate on citation theories, where a distinction is made between a Mertonian perspective on citation as value and a rhetorical perspective on citation as personal, within the

information science literature a distinction is made between relevance as system-oriented and relevance as user-oriented. Recently, however, a third perspective on relevance emerged within the information retrieval literature. This socio-cognitive perspective on relevance connects the system approach to the user approach on relevance by paying explicit attention to the context in which relevance is established. On the basis of this socio-cognitive perspective on relevance, we develop a supplement to existing citation theories on the basis of the notion of social embeddedness. The most important conclusion is that, on the basis of the concept of social embeddedness, the two opposite perspectives on citation can be connected. In all we argue that, in the context of Mode 1 knowledge production, the establishment of scientific relevance is contingent upon the structure of social networks and the position of scientists therein.

Chapter 6 addresses the role of heterogeneity in relation to the societal relevance (Mode 2 impact) of science. Again we use the case of science in the field of type 2 diabetes. As in Chapter 4, we operationalize the distributed organization of science through five forms of heterogeneity. However, instead of talking about the role of distance (proximity) in the distributed organization of science we speak of the impact that diversity (singularity) in the organization of science has on in its societal relevance. To assess societal relevance, we use the references listed in a clinical practice guideline. Two types of references are distinguished: (i) references that are included in the clinical practice guideline but not as evidence for the treatment of type 2 diabetes and (ii) references that are included in the medical manual and also reflect evidence for the treatment of type 2 diabetes. In comparing the organizational aspects related to the publications associated with these two types of references, we assess the determinants of societal relevance in medical science in the field of type 2 diabetes. The main conclusion holds that, controlling for the scientific relevance of publications, only geographical diversity increases the likelihood of societal relevance. In all it seems that heterogeneity in the distributed organization of science does not naturally lead to a greater chance of societally relevant knowledge. Interesting fact is that publications in which industry is involved have a greater chance of becoming societally relevant. This suggests that the influence of industry in the creation of societally relevant knowledge is large.

Finally, chapter 7 elaborates further on the position of industry in medicine. We assess the publication behavior of firms in a context of complete information disclosure where firms face the choice of publishing study outcomes either in scientific publications or in web publications. Due to recent institutional reforms it is now mandated to register clinical trial protocols before onset and publish basic results after study completion. For a sample of clinical trials on diabetes, we link clinical trial protocols to result publications and classify those publications based on the type of evidence they disclose. The results indicate that under conditions of complete information disclosure, firms do indeed not publish less than not-for-profit organizations. However, firms strategically publish in scientific journals where they highlight favorable outcomes to their therapies and clinically relevant studies, since regulators value evidence published in peer-reviewed journals much more than evidence published on web sites without peer-review. Thus, despite institutional reforms, pharmaceutical firms still find a way to strategically highlight particular pieces of evidence in scientific journals. We conclude that concerns about publication based on the nature of evidence have shifted rather than disappeared. The presented results in this chapter thus signal a problem of persistent publication bias of a more fundamental nature which is not easily solved by regulatory reform alone.

The general conclusion of this thesis is threefold. First, the framework of proximity (distance) and diversity (uniformity) along five dimensions provides a useful analytical tool to address the distributed organization of science. Using this framework, two important critiques on the idea of

Mode 2 knowledge production, namely its lacking conceptual clarity and empirical validity, can be tackled. Characterizing scientific actors and their relations along lines of geographical, social, cognitive, institutional, and organizational heterogeneity, renders a more distinct picture of the distributed organization of science.

Second, the idea of Mode 2 knowledge production as conceptualized along five dimensions of heterogeneity takes different shapes depending on the level of aggregation. On the level of individual organizations we argue that since the boundaries of the organizations are inherently blurred, many organizations can in principle be characterized as Mode 2. Yet, our empirical analysis shows that on an aggregate level the science system as a whole is not likely to be characterized as Mode 2. Rather, proximity plays an important role in shaping collaboration among organizations.

Third, the implications of heterogeneity or Mode 2-ness in the distributed organization of science are ambiguous. On the one hand, heterogeneity in the distributed organization of (medical) science does not render societal relevant knowledge more likely per se. We only find evidence of an increase in the likelihood of societal relevant outcomes under geographical diversity and not for the other four dimensions of heterogeneity. On the other hand, the involvement of industrial actors does render societal relevant knowledge more likely. However, the extent to which such involvement is desirable from a normative perspective is unclear. What holds is that pharmaceutical companies publish their study outcomes strategically.

This study has two important implications for further research on the distributed organization of science. First, the framework of proximity and diversity along several dimensions provides an input for further research on the distributed organization of science. Not only can local science systems in this way be compared; in principle one can also compare different disciplinary systems in the same way. In addition, the dynamics of scientific collaboration can be addressed using social network analysis techniques. Second, the relationship between scientific and societal relevance warrants further research. Some exceptions aside, much of quantitative science studies focuses primarily on the development of scientific relevance leaving societal relevance often unaddressed. Ultimately, such data sets enable us to get a better description and explanation of the whole sequence from research via publication towards science becoming societally relevant. More in general, quantitative studies of science might bring together our understanding of knowledge production by not only taking into account journal publication data but also considering alternative data sets reflecting upon research and science's societal relevance.

Finally, with regard to science policy, the question holds what kind of heterogeneity should be targeted given the particular scientific and societal problems at stake. In addition, science policy makers should take into account the institutional requirements of a heterogeneous science system. Non-traditional scientific actors such as companies have interests that are not necessarily in line with the public provision of scientific knowledge. This does not mean that these actors by definition should be excluded from science. Rather, this raises the question whether the way that science is traditionally organized still adequately serves the general interest of public knowledge provision.

Curriculum Vitae

Sjoerd Hardeman was born on 17 May 1983 in Eindhoven, the Netherlands. He studied Economics & Geography at the Utrecht School of Economics at Utrecht University and graduated in 2008 as MSc. Subsequently, he started working on his doctoral thesis at the the Department of Economic Geography, Utrecht University. In 2009 he moved to the School of Innovation Sciences at Eindhoven University of Technology where he finished his thesis.

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