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SPECIAL ISSUE
From Bench to Bed and Back: Laboratories and Biomedical Research

The Table of Alliance

The tapestry (12 metres by 2) is a personal elaboration of the 23 chromosomes present in the map of the human genome. A detail of each chromosome is seen in close-up, a 'zoom' shot of a particular region of interest (in the order of 100 megabytes) that highlights a particular genetic structure and the sequencing of that given chromosomic segment enlarged one billion times. A gene with a particular function and involved in a particular disease has been chosen from each chromosome. In the case of chromosome 15, and its segment q25, for example, the highlighted gene is believed to be responsible for pulmonary cancer. The genome is a bond of communion for the human species, showing how every individual is similar and yet, at the same time, unique. These scientific and cultural premises are the birth-site of the *Table of Alliance* project, a performance involving the realization of a banquet for thirty-six guests seated around a table covered by the tapestry depicting this personal genomic map. The tapestry was hand-sewn, in the early months of 2014, by six women of different nationalities, all of them inmates in the female section of Rome's Rebibbia prison. A first banquet have been realized in the prison the 12th June 2014. A second banquet will take place over the following months in the square of Campidoglio, in Rome. Other performances are planned to take place in other squares around the world. The scientific information used to realize the map was taken from *e!Ensembl* (http://www.ensembl.org/Homo_sapiens/Info/Index), which produces a genome data base and makes the information available free and online. The graphic artist William Greco helped me in co-designing the tapestry and the geneticist Gianni Soldati contributed in identifying the genome (locae) highlighted in it. To the latter, I will now pass the turn.

Daniela Papadia

As a scientist I am involved in many different aspects of scientific research but my main focus is applied research, where the development of clinically useful products is the centre of my work. We look for single nucleotide polymorphisms involved in pathologies. DNA is a very long chain of single small units called nucleotides and each one has billions of these nucleotides chained together in a long spiral molecule called DNA. So, every individual of the human species is similar because of its DNA. Arms, legs, brain, heart, lungs, kidneys: everyone of us has one or a couple of these organs constituting the architecture of the human body, which is exactly written in genes. But if we look a little bit closer to the human being we start to see small variations, like the eye's colour, the pigmentation of the skin, the hair's colour which are due to variations in the sequence of our DNA. More than 4 millions of such small single variations are reported in every DNA molecule of every human being. This indeed represents the source of our biological variability. All human beings are similar and different and this paradox is the central aim of the work of Daniela Papadia. We are all different but still humans, and for scientists like me this is an extraordinary message to be given in a world where we easily tend to forget what we are and where we are coming from. In other words, there is enough scientific evidence to say that uniformity and difference are not a dichotomy anymore.

Gianni Soldati

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From Bench to Bed, Back and Beyond: The Four Bs of Biomedical Research

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Abstract: Contemporary biomedicine is characterized by the ever-closer connection between clinical practice and research. Laboratories become nodes of articulated networks, making it no longer possible to consider them as single entities. In light of these changes, a wide range of actors – researchers, scientific instruments, data-bases, experts in bio-informatics and bio-statistics, pharmaceutical companies, clinicians, drugs, patients, cells, ethical and regulatory issues – are involved. In this Introduction, we address why these processes represent a relevant challenge for social sciences as well.

Keywords: biomedicine; clinical practice; translational research; laboratory studies; networks.

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It might seem banal to suggest that the most recent and radical changes in biomedicine may be summed up by the increasing interconnection between clinical practice and scientific research. From this viewpoint, the development of translational research surely represents the most consolidated example of such an evolution[1].

However, we must not forget that the ever-closer link between bench and bed evolved within the so-called "biomedical paradigm", whose main

[1] Translational research first became a priority at the start of the new millennium. It has given rise to programs, research institutes and scientific journals (such as *Translational Medicine* and the *Journal of Translational Medicine,* for example). In Europe, it has been at the core of the Commission policy: the Horizon 2020 program grants an elevated budget (more than 6 billion Euros) to activities in this field. For a description of the significance of TR in the biomedical field, see Woolf 2008.

characteristics are the separation of mind and body, the prevalence of the analytical aspect within which illness is conceived as the result of an organic lesion (whether at tissue, cell or DNA-portion level) and the extension of the hospital's function to include systematic clinical observation and scientific research, as well as treatment and assistance.

"From bench to bed" is therefore the essence of a union built upon the exaltation of the individual dimension to the detriment of the collective one, the pre-eminence accorded to the body rather than lifestyle, the central role attributed to the hospital as a place of medical practice, and the consequent undervaluation of general practice and healthy living conditions (in homes, the urban territory, air and water quality, the workplace, diet and habitual behavior – in a nutshell, lifestyle). To use a perhaps outdated but still apt expression, medicine centered on the relationship between bed and bench places the cure center-stage, while setting aside prevention[2]. Despite its becoming almost a commonsense statement, we argue the need to reaffirm that contemporary biomedicine is characterized by the ever-closer connection between clinical practice and research.

However, this is merely a starting point: in the first place, the sociological vision highlights the fact that "from bench to bed" not only fails to describe a tension-free relationship, but also indicates the gap between aspiring to a highly desirable future, in which many serious illnesses will finally find a cure, and daily organization of clinical practice and laboratories. Various strategies are adopted in an attempt to overcome this gap and reinforce the connection and continuity between clinical practice and research. Among these strategies are the cultural and political support guaranteed by the "translational imperative" and the idea that doctors and researchers may reciprocally benefit from the greater range of therapeutic resources available to the former and the funding available for research activities to the latter (see the scenarios by Harrington and Hauskeller in this special issue). Secondly, though it is now clear that the expression "from bench to bed" must be completed by adding "and back", many contributions received from Science & Technology Studies (STS), among which also those proposed in this special issue, have highlighted the necessity of further widening the scope to include a heterogeneous and articulated group of actors. Therefore, four "Bs" are to be considered: from Bench to Bed and Back, and Beyond.

The network of actors involved in the relationship between clinical practice and research does not merely include patients and their relatives,

[2] As we know, first-level prevention deals with environmental conditions and lifestyles, while the second level may be considered as "early diagnosis", i.e. an action perspective fully embraced by the biomedical paradigm. Indeed, "early diagnosis" highlights one of the contradictions arising when the discovery of a potential or initial pathological state fails to correspond to a real possibility of therapeutic intervention.

but also the State, pharmaceutical companies, scientific instruments, data and tissue banks, as well as more traditional characters (such as laboratory technicians and medical staff) and new experts (such as biostatisticians and bio-informaticians), together with experimental protocols and diseases. The list then comprises citizens' and patients' associations, which are more and more involved not only in funding research, but also in defining aims and orienting research activities (Callon and Rabeharisoa 2008; Epstein 1996). Thus, what first appeared to be restricted to only two groups of players, doctors and researchers, has rapidly become an issue that involves a growing number of heterogeneous elements moving within temporal and spatial regions in which global visions and local materiality interact (Law and Mol 2001; Law and Singleton 2003).

One of the emerging problems regards the statute and form of such networks: are they cluster or collective, platform or vector, merely the product of interaction among the involved actors or also the result of STS scholars' selection and pre-comprehension processes aimed at extracting, analyzing and representing data? In any case, as it also emerges from the contributions in this special issue, they are hybrid social spheres where elements become mediators and interact and produce a multiplicity of bio-objects (Webster 2012), such as the "triangle DNA origami" studied by Crabu or the umbilical cord, as shown by Beltrame. Notable among the artifacts emerging within these networks are the information infrastructures (Star and Bowker 2002; Mongili and Pellegrino, *forthcoming*) which produce, elaborate and make available ever more abundant and multiform data: genetic sequences, publications, cell lines and tissues. On the other hand, while clearly not all which is deemed "translational research" deserves this definition *strictu sensu*, the opposite is also true: much of what happens outside this definition actually moves within the perspective of an ever-closer interconnection between clinical practice and research, as the contributions by Beltrame and Turrini show.

Together, these changes pose new questions and at the same time reformulate traditional ones, in the attempt not only to understand what bio-medicine is becoming, but also to rethink STS aims and methods. The opening contribution by Cambrosio, Bourret, Rabeharisoa and Callon proposes a deep and sophisticated reflection on this topic. Starting from the results of recent studies on evolution in biomedical research, the authors open a debate on how STS analyze such transformations, especially when adopting tools originally developed for handling the large amounts of data produced in the biomedical research field itself. In this way, STS are linked to a wider debate involving sociology as a discipline which addresses social phenomena departing from the Big Data perspective and by adopting "digital methods" (Rogers 2013) – including visualization tools. Here one of the critical issues is the degree of awareness sociologists may have of the agency of such tools and algorithms, as well as the reliability and accountability of the latter. Cambrosio and colleagues' proposal to see them as "dynamic experimental tools instead of tools for

having/representing static results" is thus of particular interest. Above all, it suggests not to analyze the evolution of networks starting from a stable, pre-determined group of actors, but rather to highlight the emergence of a progressive configuration of collectives made up of human and non-human actors, whose interaction makes the agency of each component reciprocally possible.

Therefore, a dynamic analysis of networks should not only mean observing how configurations of actors' relationships in the same cluster change over time, but also what kind of new actors enter the scene, and which former actors leave it. Both the contributions by Nadine Levine and Conor Douglas reflect on this relationship between Big Data and interpretative processes in translational research.

In Levine's contribution, the diverse concepts researchers and doctors refer to in translational research are explored through an ethnographic investigation in a laboratory working on the development of molecular markers in post genomic studies on metabolism. Due to the ways in which objects, illnesses and data are interpreted, we see the emergence of tensions generated by the interaction of researchers and clinicians. Translational research is therefore a complex and dynamic process, characterized by margins of uncertainty and the hard work involved in transforming this density of data into a greater understanding of illness.

Douglas's contribution too looks at the possibility of translating huge research based data into clinical practice. The case study refers to a vast Canadian scientific network within which two bio-informatics tools – a database (InnateDB) and a suite of analytical visualization tools (Cerebral) – have been developed. Both tools are the result of developers' work on an open source/open access basis in close contact with users in the clinical field.

In various ways and from different perspectives, the contributions in this issue also deal with the theme of standardization as a mix of strategies and combinations, with the scope of aligning the diverse actors involved in the setting up and development of a network. This is what happens in the cases illustrated by Turrini and Beltrame.

Turrini's contribution analyzes how new pre-natal diagnostic technologies are trying to gain a foothold, causing tension in diverse professional traditions and epistemologies. In particular, conflict emerge when an approach based on molecular biomedicine is proposed as a basis for standardization and thus the possible engineering of pre-natal diagnostics, a field still largely dependent on the artful sight of those who observe the chromosomes in order to identify possible anomalies in cytogenetic analysis laboratories.

Beltrame's article, on the other hand, illustrates the complex process through which human waste tissue (such as the umbilical cord) can be transformed into an object of study and innovation in biomedical research. The process of bio-objectification involving this human tissue allows us to observe the interactions between biological research and clini-

cal practice in the development of therapeutic applications for umbilical cord cells, while also highlighting how the emergence of a new class of actors, the bio-banks, produces diverse processes of bio-objectification and economic regimes for their exploitation. The bio-banks have become a hub of particular interest in analyzing the divergent articulations linking biomedicine and society, underlining the tensions which emerge when these actors enter into direct contact with the subjective dimension of social life.

Finally, Crabu's article and the conversation among Burri, Carusi and Aspradaki introduce and examine in depth two further elements which assume particular importance, to both understand the processes connecting heterogeneous actors in biomedical research collectives and analyze their transformations.

According to Crabu the promising scenarios presented by nanomedicine, similarly to what happens in translational research, act as connectors among actors with diverse aims and motivations, on the condition that such a promise might evolve into something concrete, such as in the case of the bio-object denominated "triangle DNA origami". The creation of a nanomedical laboratory, in which research for development of this new nanodevice is carried out, offers the opportunity of observing how this promissory bio-object becomes the terrain for a meeting between the anticipatory narrative level and the materiality of scientific activity.

While raising a series of ethical, economic and legal issues linked to the use of diagnostic images in and around the relationships between clinics and laboratories, Burri, Carusi e Aspradaki clearly show such images are capable of acting as a catalyst among researchers, doctors and patients. At the same time, it is clear that the information overload produced by the flow of Big Data also manifests itself in the form of a huge amount of diagnostic images generated by sophisticated and black boxed apparatuses anything but intelligible and unambiguous[3].

At this stage, it appears clear that both translational and biomedical research move far beyond the laboratory. Laboratories have become nodes of articulated networks, making it no longer possible to consider them as single entities. In light of these changes, a wide range of actors – researchers, scientific instruments, data-bases, experts in bio-informatics and bio-statistics, pharmaceutical companies, clinicians, drugs, patients, cells, ethical and regulatory issues – are involved. Rather than pointing to the end of Laboratory Studies, this awareness promotes their revival. The laboratory becomes one of many actors interacting within a heterogeneous field, giving life to a dynamic network which challenges our possibilities of comprehension, the research tools we use and the theoretical hypotheses we depart from.

[3] For a review, see Perrotta 2012.

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Big Data and the Collective Turn in Biomedicine

How Should We Analyze Post-genomic Practices?

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Abstract: We presently witness a profound transformation of the configuration of biomedical practices, as characterized by an increasingly collective dimension, and by a growing reliance on disruptive technologies that generate large amounts of data. We also witness a proliferation of biomedical databases, often freely accessible on the Web, which can be easily analyzed thanks to network analysis software. In this position paper we discuss how science and technology studies (S&TS) may cope with these developments. In particular, we examine a number of shortcomings of the notion of networks, namely those concerning: (a) the relation between agency and structural analysis; (b) the distinction between network clusters and collectives; (c) the (ac)counting strategies that fuel the networking approach; and (d) the privileged status ascribed to textual documents. This will lead us to reframe the question of the relations between S&TS and biomedical scientists, as big data offer an interesting opportunity for developing new modes of cooperation between the social and the life sciences, while avoiding the dichotomies – between the social and the cognitive, or between texts and practices – that S&TS has successfully managed to discard.

Keywords: big data; network analysis; post-genomic medicine; bio-clinical collectives; actor-network theory.

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1. Introduction

This is a position paper. It discusses how science and technology studies (S&TS), confronted with recent changes in the configuration of biomedical practices – in particular their increasingly collective dimension, and their reliance on disruptive technologies, such as microarrays and next-generation sequencing, that generate large amounts of data – may cope with these developments. Big data represent a (multifaceted) source of information for both S&TS scholars and health care practitioners, while also being the outcome of activities predicated upon the involvement of a large number of heterogeneous actors. As such, they are embedded in biomedical practices and have become key elements of knowledge production, especially in domains such as genomics, where they engender distinctive forms of evidence.

The dual nature of big data – they act as sources of information while also being the outcome of activities that are constitutive of biomedical practices – is not something new. Scientific texts (articles, books, reports) partake in scientific knowledge production, while simultaneously acting as a data repository for the natural scientists who produce and use them. As sources of evidence, they are also of use to social scientists who engage, for instance, in scientometric analyses of the socio-cognitive structure of science, or to historians of ideas investigating the dynamics of a given domain. S&TS scholars have successfully learned how to tame this multi-dimensional nature of scientific texts by displaying the links they entertain with scientific practices, without falling into the dichotomy between the social and cognitive dimensions of science. Big data, however, raise a novel and difficult challenge, for two main reasons. First, because we have only limited evidence concerning their actual use as part of research practices (but see, e.g., Leonelli 2012, 2013, 2014, and Edwards 2010 for noteworthy exceptions), which in turn leaves social scientists wondering how they should understand *and* use them. And second, because the "big" in big data refers not simply to the sheer quantity of data available, but also to their instability, heterogeneity, and proliferation into different domains. In other words, we presently face a dual task: on the one end, we need to better understand the research activities that rely on the production and analysis of big data, and, on the other hand, we need to figure out how science studies scholars can embed big data, and the configurations they generate, into their own practices, and what are the consequences of doing so. In particular, we should be wary of solutions that may end up reintroducing the dichotomies – between the social and the cognitive, or between texts and practices – that S&TS has successfully managed to dispense with. The present text explores a few of the issues and problems involved in such an endeavor.

Big data are everywhere, and thus the issues discussed in this text are not confined to S&TS. Rather, big data represent a more general challenge for the social sciences because they raise the following conundrums:

How should we, as social scientists, use them in our own investigations while taking into account the fact that they also partake in the activities of the actors we investigate, and cannot therefore be considered as unproblematic evidence? How can we revisit, in the light of the growing importance of big data, the traditional tension between qualitative and quantitative approaches, or between local ethnographies and cross-sectional studies? We are particularly interested in those situations in which both the social scientists and the actors they investigate attribute a strategic role to the notion of network, often generically defined. We will center this paper on the theoretical and visualization issues engendered by this notion. In a first section, we will briefly discuss the development of big data in the oncology domain, showing that they have become part and parcel of recent developments in this advanced biomedical domain. This will lead us, in a subsequent section, to examine how the notion of network plays a strategic role in this context. While this notion has, of course, enjoyed a staggering success within S&TS, we will focus on its shortcomings, and in particular on four thorny issues, namely: (a) the relation between agency and structural analysis; (b) the distinction between network clusters and collectives; (c) the (ac)counting strategies that fuel the networking approach; and (d) the privileged status ascribed to textual documents. We will explore how these shortcomings can be overcome, at least tentatively. In turn, this will lead us to reframe the question of the relations between the subjects and objects of observations, i.e., between S&TS and biomedical scientists. Big data, as it turns out, may offer an interesting opportunity for developing new modes of cooperation between social and life scientists.

2. 21st Century Biomedicine: Clinical Wards, Wet Labs, and Bytes

In his address to the 2011 meeting of the American Society of Clinical Oncology – with nearly 35,000 members, most likely the single largest professional organization in its domain – the Society's president, George Sledge, warned fellow oncologists about the upcoming "tsunami" of genomic information that was likely to result from a sharp decrease in the cost of sequencing tumors. He added: "When data are that cheap, every patient's cancer will be informative for tumor biology […] and things will get very, very complicated" (cited in Goldberg 2011). That same year, and along similar lines, in a promotional video for the European Multidisciplinary Cancer Congress, entitled: "Bench, bedside, 'bytes' and back" (also referred to as the three Bs), noted clinical researcher Anne-Lise Børreson Dale explained: "You start with the bed, you have the patients, and then you go to the bench, and then because we create so many […] huge amounts of data, you have bytes, as in gigabytes, and then you

go back to the bench to find out what is the right treatment for that patient, and then you go to the patient again […] it's like a spiral that goes up […] every patient is sort of an experiment for the next who will be coming in"[1]. These two quotations are far from uncommon. They illustrate recent themes and trends in oncology, namely the rise of translational research, closely combining biological and clinical investigations; the search for personalized treatments, whose horizon lies in the singularization (Callon 2012) of patients; and, finally, the premises upon which the previous two items are predicated, namely the availability of large sets of data, whose proliferation, accumulation and heterogeneity raises major interpretative challenges.

We will return in subsequent sections to the collective dimension of contemporary biomedicine, in particular translational research, as exemplified, for instance by large-scale genomic consortia – e.g. the "Breast Cancer Linkage Consortium" that mobilized approximately 100 centres[2], or the "Autism Genome Project" that mobilized "120 scientists from more than 50 institutions across 19 countries" (Szatmari et al. 2007) – or, perhaps more mundanely, the staging of large-scale, national and international clinical trials (Keating and Cambrosio 2012a), although we should hasten to add that, as we will see, the term "collective" does not refer simply to number and size. For now, let us examine the issue of big data that is related to, but not identical to the former topic. The generation and mining of large data sets is by no means an uncontroversial activity. For instance, MIT biologist Michael Yaffe (2013) recently claimed that while "the sequencing of human tumours [has] produced important data sets for the cancer biology community […] these studies have revealed very little new biology", further complaining that scientists were "addicted to the large amounts of data that can be relatively easily obtained [by genome sequencing], even though these data seem unlikely, on their own, to unveil new cancer treatment options or result in the ultimate goal of a cancer cure" (Yaffe 2013, 1). The important point, as far as we are concerned, is of course not whether Yaffe's criticism is warranted. Rather, our claim is that arguments both in favour and against the turn to big data confirm the fact that it has come to occupy a central place in contemporary biomedicine. The relevant issue, thus, is to examine what it involves in terms of rearranging the flow of biomedical practices.

This paper is part of a special issue entitled: *From Bench to Bed and Back*. The synecdoche in the title refers to translational research, as characterized by close relations between laboratory research (bench) and clinical work (bed). The "back" adverb marks a rejection of the unidirectional model of translation, as both the clinic and the laboratory

[1] Video retrieved on Feb 5, 2014 from: http://ecancer.org/conference/101-emcc-2011/video/891/bench--bedside-----bytes----and-back--a-virtuous-cycle-of-knowledge--1-5.php

[2] See http://www.humgen.nl/lab-devilee/bclchome.htm

can be the starting point of a successful translation. We go further and argue that rather than a relation or interface between two poles, translational research corresponds to a new, emerging site, characterized by the presence of distinctive activities. As argued in the previously quoted statement by Børreson Dale, in addition to benches and beds this site includes a third element, "bytes", or, in other words, a new kind of data and a new kind of practice, bioinformatics, needed to make sense of them. Bioinformatics is the "new kid on the block" of biomedical research[3], and, as described elsewhere (Keating and Cambrosio 2012b) has entertained somewhat controversial relations with the older data-processing specialty, biostatistics. For our present purpose the main issue is that by introducing bioinformatics, the rules of the game have changed. For bioinformatics cannot be reduced to the computerization of biology; rather, it involves a rearrangement of biological practices, a redefinition of what counts as valuable biomedical work (Yaffe's aforementioned criticism is a symptom of this process), and it shapes the kind of knowledge emerging from the translational research domain. As a bioinformatician put it: "We're not bioinformaticians who dabble in breast cancer". Instead, he and the members of his lab are "focused on understanding the disease"[4]. Understanding means reframing it, using the "new quantitative methods – the methods of the New Biology"[5].

Let us take as an example the development of a gene expression signature to predict clinical outcome in breast cancer (Finak *et al.* 2008). The researchers collected breast cancer tissue from 73 patients, used painstaking laboratory methods (laser capture micro-dissection) to pre-process the samples, and analyzed them with genomic tools in order to develop a candidate signature. For the subsequent stage, however, which involved the validation of the signature with independent samples, they no longer used local biological samples but, rather, resorted to publicly available data sets downloaded from institutions located in Amsterdam, Oxford, Rotterdam, and Uppsala. The development of the signature, in other words, was made possible by a hybrid approach that combined a "wet lab" analysis of local biospecimens with virtual testing using data sets available for download from the Internet. This is by no means an exceptional situation. If we take, for instance, MINDACT, a very large (several thousand patients), multi-center European breast cancer clinical trial testing another genomic signature, we find two parallel flows of material and data. Participating centres will ship different kinds of biological material (frozen and fixed tissue, RNA, and serum/blood) to central bioreposito-

[3] On the emergence and development of bioinformatics see McMeekin *et al.* (2002, 2004).

[4] Interview, February 14, 2011.

[5] Committee on a New Biology for the 21st Century: "Ensuring the United States Leads the Coming Biology Revolution", *A New Biology for the 21st Century*, (Washington: National Academies Press, 2009).

ries located at cancer institutes in Amsterdam and Milan, and at the biotech company that commercializes the signature. A parallel, web-based circuit will channel clinical and laboratory data from and to the participating centres, and store them in databanks located at the trial sponsor's secretariat, a Swiss bioinformatics institute, and the biotech company (in each case, with different rules for access). As recently forecasted by a leading French oncologist, the databases generated by the first generation of biomarker-driven clinical trials should lead the production of algorithms propelling the design of a second generation of trials, which will in turn generate databases, and so on (André n.d.). In the meantime, this kind of data is becoming increasingly available, as shown, for instance, by the recent announcement that the International Cancer Genome Consortium has made publicly available data from thousands of cancer genomes.

Bioinfomatics is not confined to the handling of data produced by the new genomic technologies: it is constitutive of them. Let us take the example of gene expression profiling (GEP) mentioned in the previous paragraph. One of the key technologies of post-genomic oncology, gene expression profiling, has generated new entities, such as multi-gene "signatures", that have simultaneously been developed in clinical, laboratory and commercial biotech settings (Kohli-Laven *et al.* 2011). Figure 1 reprinted from an article that analyses the development of this field (Cointet *et al.* 2012) uses a modified version of a scientometric technique called "co-citation analysis".

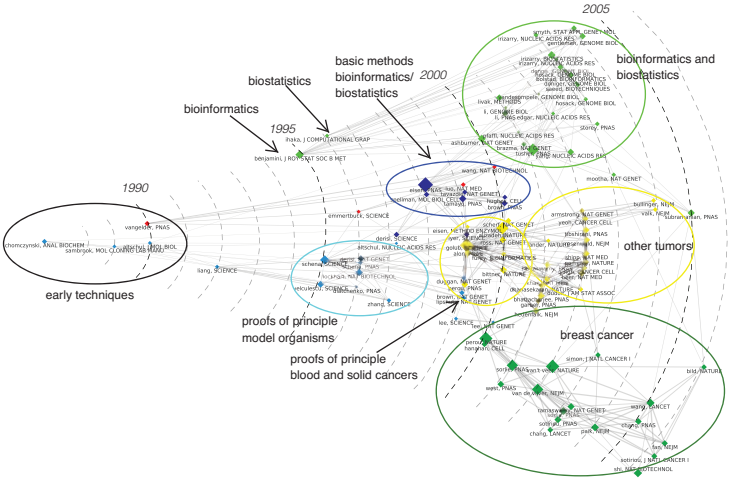

Fig. 1 – Co-citation analysis of the development of gene expression profiling: see text for explanations. Source: modified version of Figure 2 in Cointet *et al.* (2012).

Briefly, two articles are co-cited if they appear together in the list of bibliographic references of another article. Networks of highly co-cited articles display key contributions to a field, and can be equated to its cognitive substructure. After downloading over 16,000 GEP references from the biomedical database *PubMed*, the authors used the software platform *CorTexT* (www.cortetxt.net) to generate a map of the most frequently co-cited references. Each node of the network corresponds to a reference (labeled by the first author's name and journal abbreviation), the size of the node being proportional to the number of citations. The network is arranged chronologically, with time flowing from left to right. Rather than a professional historical narrative, it provides an account of the development of the field as perceived by the authors of articles at a given point in time (in the present case, during the 1990-2010 time window). Using different time windows, the resulting map would be different, as actors will redefine the foundations of their domain: the "historicity" of chronological sequences, in other words, will be displaced by the "historiality" of science reshaping its past (Rheinberger 1997). Clusters of closely associated references organize themselves into specific subdomains that are automatically detected by a clustering algorithm and color-coded accordingly. For further clarification we have added to the original map a number of tags identifying the nature of the activities of each cluster.

Here is a quick summary of the most relevant features of the map (readers can refer to the original article for more information). The oldest references correspond to the basic molecular biology techniques that are held to provide a basis for the subsequent development of GEP. They lead to two clusters of "proof of principle" articles, i.e. demonstrations that GEP did actually work: this was done first with non-medical model organisms, and then with human tumor specimens, thus entering the clinical domain. At approximately the same time we notice a cluster of articles corresponding to biostatistical and bioinformatic methods, in particular heat maps and hierarchical clustering techniques (Wilkinson and Friendly 2009), which are needed to analyze the large data sets produced by GEP. In the case of GEP as with other recent biomedical techniques, there is no such thing as "raw data", strictly speaking, as the data generated by the instruments are already highly processed, while meaningful (i.e., interpretable) results necessitate further statistical and visual manipulations (Cambrosio and Keating 2000). Hence the mutually constitutive relation entertained by wet-lab and data analysis tools. In the most recent period we see the deployment of GEP in the oncology domain, with a strong presence of breast cancer as a distinctive cluster, concurrent with the further development of robust bioinformatic and biostatistical methods. Interestingly enough, references included in this latter cluster refer back to two founding articles, one in biostatistics (on false discovery rates) and one in bioinformatics (on the R language), cor-

responding to the hybrid (and, as previously mentioned, somewhat controversial) nature of this emergent domain.

Mimicking, at a far smaller scale, the collaborative dynamics we saw in the GEP domain between clinical and bioinformatics researchers, the Cointet *et al.* (2012) article exemplifies a collaborative endeavor between social scientists and informatics specialists, in the present case the developers of the *CorTexT* platform. This is why, to cite our own (admittedly anecdotal) evidence, while more traditional social science audiences often experience difficulties in understanding the network slides we present at talks and conferences, natural scientists can readily relate to them, in particular when, as part of our fieldwork, we ask them to comment on the maps corresponding to their activities (Bourret *et al.* 2006). We can now apply Yaffe's aforementioned critical questions to ourselves: are S&TS analysts also becoming addicted to big data? To what extent does the motley of newly available data sources contribute to a renewal of the S&TS research agenda?

3. Problematizing Network Analysis

At this point readers will have noticed that we are entering reflexivity's territory, as the techniques used to produce a map like the one displayed by Figure 1 overlap with those used in the bioinformatics references displayed on the map. While social network analysis has been around for long time, network analysis has been recently transformed by an inflow of mathematical and modeling approaches originating from the physical and life sciences (Watts 2004). Supported by a staggering increase in computer power, these new approaches have found a privileged domain of application in the scientometric analysis of the scientific literature, in particular co-authorship patterns (e.g. Newman 2004), thanks to a parallel development, namely the increasing availability on the Internet of large databases of scientific publications such as Medline (and its search engine *PubMed* freely accessible since 1997), *Web of Science*, *Scopus*, and *Google Scholar*. Traditionally, social network analysis examined social ties between a relatively small number of actors, often derived from *ad hoc* procedures such as interviewing selected actors about their connections or resorting to sampling (Scott 2000). Large-scale bibliographic databases now allow, at the click of a mouse, to obtain information about relational patterns, such as co-authorship, between millions of actors. But these new possibilities come at a price. The fact that a reflexivity loop seems to exist at the level of tools does not necessarily imply that a similar loop should necessarily obtain in terms of conceptual framing. Put otherwise: the fact that scientists can easily relate to maps created by network sociologists can be a positive aspect, but also a symptom of looming problems.

The large databases, the search engines that have been developed to

exploit them, and the data-mining, text-mining, and network-analysis tools that S&TS scholars use to process the resulting data, do indeed give access to unprecedented amounts of information and lead to stunning visuals (Lima 2011). We should not forget, however, that they have not been conceived primarily for sociological analysis. As they emerge from the physical and life sciences – sometimes transiting through the newly established specialty of "information science" (Börner 2010) – they come with built-in epistemological assumptions and models that are seamlessly carried over into the social sciences when they are recycled for use by S&TS scholars. Faced with the sterile alternative of either embracing these new approaches without too many qualms because of their striking effectiveness, or of rejecting them for fear of contamination, we prefer a third alternative, namely to explore the issue of the adequacy between these newly available tools and S&TS research agendas.

The notion of network has provided a key heuristic tool for developing a research program that rejects both technological and sociological determinism, and can thus be put to fruitful use for the analysis of biomedical activities, but this notion is now a victim of its own success. We find it everywhere, within and outside biomedicine, as the term is used for every purpose, from the mundane to the specialized. The expansion of its semantic field, in parallel with the steady increase in the offer of affordable data-mining software and network visualization tools, has resulted in the development of a "network lingo" and of standardized interpretations that are indistinctly applied to substantive, methodological and conceptual issues. To further complicate the situation, the adoption and deployment of network analysis tools have by and large taken place within quantitative domains such as scientometrics and, most recently, information science and informetrics, whose development, in spite of their focus on scientific and technical activities, has only occasionally intersected with conceptual developments in S&TS. Only rarely have these quantitative approaches been interfaced with ethnographic methods (for exceptions see Velden and Lagoze 2013; Navon and Shwed 2012; Bourret *et al.* 2006; Cambrosio *et al.* 2004), but, most often, their production within self-contained professional circles of information specialists has resulted in the offer of tools in search of possible uses (for a recent example, see Skupin *et al.* 2013)[6].

As argued by Michel Callon (2001), thick ethnographic descriptions of individual field sites are ill suited to deal with large-scale collaborative endeavors such as the ones discussed in the previous section. The alternative of reducing such endeavors to a few quantitative indicators is equally unsatisfactory, insofar as it destroys for all practical purposes the very phenomena under investigation. The newly available network analysis tools, in combination with more traditional fieldwork methods, seem to

[6] For earlier examples see the special issue of "Proceedings of the National Academy of Sciences" on "Mapping knowledge domains" (2004; 101, suppl 1).

offer a partial response to this predicament, provided they avoid the limitations of traditional social network analysis. These limitations include an exclusive focus on human actors, and the assumption of the existence of a unified social space within which social ties can be properly measured and described. In a subsequent English version of the 2001 paper, Callon (2006) revisited this issue by postulating that network analysis tools should avoid two pitfalls. First, the aforementioned assumption that actors' interactions take place within a unified space; this assumption belies the existence of a multiplicity of regimes of engagement deployed in different, more or less overlapping spaces (Boltanski and Thévenot 2006; Moreira 2012). A second pitfall lies in the a priori categorization of entities according to a number of pre-set, analyst-defined attributes. In contrast with this approach stands a focus on the emergent categories generated by the relational ties that human and non-human entities establish between each other. By taking into account the heterogeneity of networks (both in the sense of consisting of different entities *and* of corresponding to different regimes of engagement) social scientists can enter in a reflexive relation with the entities they analyze. Such a reflexive relation can itself be of different kinds. It has a substantive dimension, as actor-generated categories and, more generally, the framing they produce, will often question the analyst's assumptions about the proper categories that constitute the world, and his/her epistemological privilege to define them. It also has a methodological dimension, because of the aforementioned, increasing overlap between the network analysis tools developed by natural scientists and those used in the social sciences.

Still, while one should not mistake the co-authorship "network" generated by a few clicks on the Internet for the "network" of actor-network theory (ANT) (Latour 2011), the new tools offer interesting opportunities for the empirical exploration of new techno-scientific configurations, using the conceptual avenues opened-up by ANT. It should be noted, in this respect, that the founders of ANT were among the pioneers of mapping approaches, in particular co-word analysis (Callon *et al.* 1986). These initial attempts have been criticized for their alleged reductionism with regards to the issue of agency, and for lending themselves to structural interpretations. In the meantime, several versions of ANT have been developed that are not always mutually compatible. On the one hand, in response to the aforementioned criticism, there have been attempts to revisit the processes previously analyzed solely in terms of networks by using notions such as regimes and assemblages, or collectives and arrangements. From this perspective, visualization tools can become problematic, and do in fact partake of the emergence of new regimes of innovation that S&TS should investigate rather than adopt blindly (Callon 2012; Rabeharisoa *et al.* 2014). On the other hand, and in spite of their acknowledged limitations and shortcomings, navigational practices that are made possible by the availability of large databases and software tools initially devised to investigate complex systems, are seen as creating

the conditions of possibility for a new kind of generalized social theory, one that could dispense with the opposition between individuals and aggregates (Latour 2011; Latour et al. 2012).

In the present paper we adopt a position closer to the first alternative in order to explore some of the problems raised by the new visualization tools and to discuss, using examples from recent studies of biomedical practices, how we can partly address them. These problems fall in at least four different categories:

- As previously mentioned, while network analysis algorithms are in principle well adapted to the kind of relational sociology embraced, among others, by ANT, they tend to reify the notion of network and to convey structural or strategic interpretations of specific network configurations. Typical examples include analyses in terms of structural holes, obligatory passage points, centrality, etc. The issue thus becomes: Is it possible, and if so how, to interpret maps without resorting to a vocabulary that is derived from structural and strategic analysis? A major obstacle, in this respect, is that 'structure' is embedded into the very production of maps; for instance, the algorithms used to position nodes rely on structural properties, such as symmetry, structural equivalence of points, centrality and 'betweenness' of nodes. Put otherwise: does network analysis allow us to make inferences about the dynamics of a given domain without reducing it to changes in the morphology of the network? Or should we rather opt for a hybrid approach, whereby networks will no longer represent the ultimate analytical horizon, but a tool to better investigate assemblages, or, to use a term that avoids mechanical implications and reintroduces agency, *agencements* (Callon 2013; see also Rheinberger 2009 for the case of biomedicine)? While shifting the conceptual and substantive focus from networks to *agencements*, such a move would still leave room for networks, as they add flexibility, dynamics, but also some amount of ordering to *agencements*.
- In order to make sense of a network, as already hinted in the case of Figure 1, analysts (or the algorithms that replace them) trace boundaries around clusters of closely connected nodes. The sociological relevance of these (formally defined) clusters is itself open to interpretation, as they do not necessarily correspond to taken-for-granted groups or institutions: in fact, if and when they do (which is probably more often the case with homogeneous social networks than with heterogeneous ones), the heuristic interest of tracing a network decreases correspondingly, as it transmutes from being an investigational tool able to produce surprises to a redundant illustration of well-known arrangements. If they do not, we then face the issue of the collective agency of the heterogeneous clusters displayed on maps. When adopting a structural interpretation, this issue is most often swept under the carpet. A closely related issue, similarly overlooked by structural interpretations, has to do with situations in

which the transformation of the entities making up a heterogeneous collective are not the consequence but, rather, the cause of the dynamics of these collectives. Here again, the path forward may necessitate a shift in focus from networks per se to the processes involved in producing specific *agencements* that account for the heterogeneous and distributed nature of collective agency.

- As already mentioned, network analysis, because of its figurational dimension, can be seen as a healthy alternative to the statistical reductionism of quantitative indicators. It also partakes, however, of the quantitative domain, as networks are firmly embedded in a metrological infrastructure. The point is not to contrast qualitative with quantitative analysis, as in the longstanding conflict within professional sociology, but to signal that the modality of action that underlies networks is to "add up", to be "counted in". Other modalities are possible, such as qualifying links instead of accumulating them. The "adding up" strategy, as exemplified most obviously by citation counts, is embedded in a number of databases whose goal is precisely to make things (ac)countable in this specific way. The seamless production of networks derived from these databases brackets the very infrastructure that makes those data, and their relational nature, available and witnessable. From this point of view, networks have no epistemological privilege, as they are one among possible forms of interpretation and enactment of 'the social'. How, then, to integrate this aspect in our analysis? The maps we produce bear the invisible traces of the strategies deployed by data providers: how can we make them visible and, most importantly, take them into consideration when interpreting our results?
- Most often than not, the components of a network are obtained by analyzing bibliographic databases (articles, patents, etc.), repositories of full-text articles, blogs, and other textual documents. While, given its focus on the materiality of practices, non-textual elements, in combination with textual ones, play a key role in ANT analyses, only the latter, or at least entities mediated through inscriptions, end up in the maps. How, then, to convey the heterogeneity of networks when we can only produce and access them via textual inscriptions?

In what follows we revisit these issues – the reductionist understanding of agency resulting from strategic/structural interpretations of networks, their limited capacity to account for the dynamics of collectives, their actuarial nature that privileges quantity over content, and their exclusive reliance on texts. We focus on the first two elements using a few concrete examples.

4. Network Dynamics

Both from a methodological and theoretical point of view, accounting for network dynamics has been one of the major stumbling blocks of this kind of analysis. Change has mostly been interpreted as structural change. A notion such as 'obligatory passage point' equates a given position within a network with processes of circulation, displacement or movement. Dynamics is thus reduced to the distribution of points and their relations in a (virtual) space. The agency of the entities represented in a network is mechanically conflated with their structural/strategic positioning, and since the capacity to act strategically and reflexively is generally ascribed solely to humans, it is not surprising that *social* network analysis still occupies center-stage. Methodologically speaking, attempts to account for dynamical processes often rely on the structural comparison of the 'same' network at different times, pointing to the elements that are held responsible for the observed changes. Algorithms can be used to identify the entities (actors or groups thereof) that are at the origin of structural transformations.

A possible, although not entirely satisfactory way out of this predicament is to opt for interpretations focusing on events, i.e. to 'play' with the content of maps[7] by taking into account the heterogeneous roots of a network's dynamics. A structural reading, when comparing maps corresponding to different periods (say: t1 and t2), focuses on networks characterized by the presence of the same kind or category of entities, e.g., academic researchers, clinicians, biotech or pharmaceutical companies, either individually or as members of homogenous subdomains. To account for change, analysts will for instance point to the role of biotech companies that while only playing a marginal role at t1, have become key intermediaries between public and large private organizations at t2. This kind of account is characterized by the presence of a strong and sophisticated human agency: observers easily acknowledge the key role of biotech companies (or, rather, the entrepreneurial skills of their managers), but are less keen to attribute a similar role to cells and molecules. A non-structural reading will opt for a different approach: to account for the difference between t1 and t2 we should consider the role of entities that were absent from the original t1 and t2 maps, i.e. produce complementary maps that include cells, instruments, molecules or diseases. In other words, the passage from a homogeneous network at t1 to a homogeneous t2 network can in fact be accounted for by the presence of a number of heterogeneous entities that did not appear on the initial maps: the emergence (or disappearance) of connections between two groups of researchers is not reducible to the sole agency of other researchers; it involves the

[7] As the very notion of a 'map' lends itself to structural interpretations, we should opt for a term with different undertones.

simultaneous agency of biomedical entities such as mutations, antibodies, or cells.

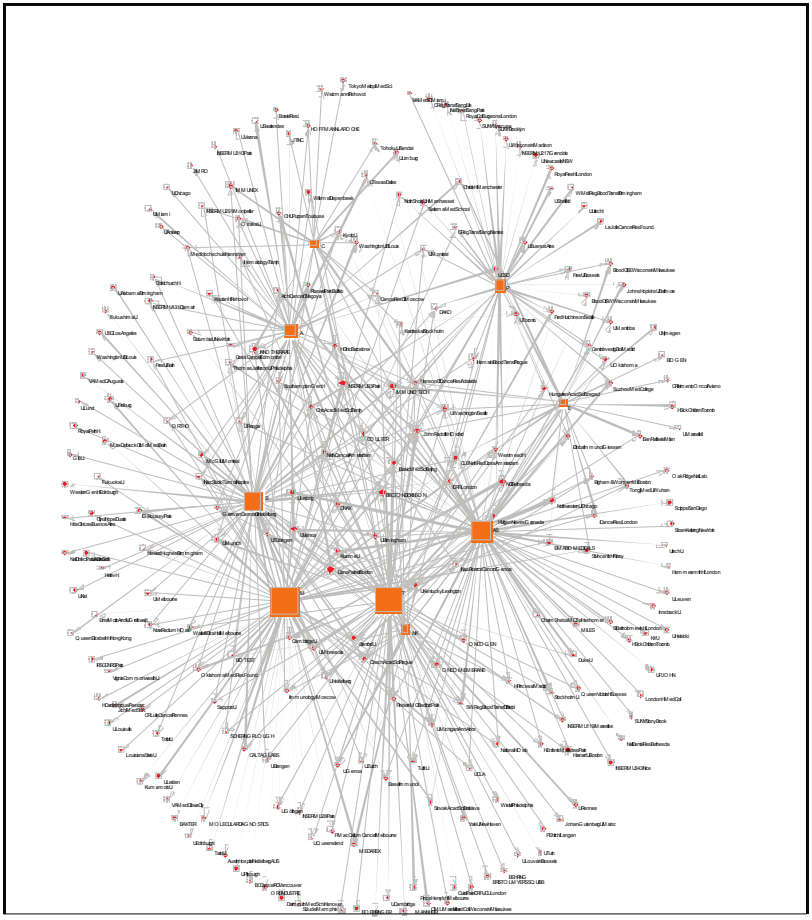

Fig. 2 – Map of laboratories producing monoclonal antibodies targeting different categories of cells: see text for explanations. Source: modified version of Figure 7 in Cambrosio *et al.* (2004)

The following example is taken from a paper (Cambrosio *et al.* 2004) that, in the wake of ethnographic fieldwork on the emergence and circu-

lation of a new kind of reagents known as monoclonal antibodies, attempted to visualize the regulatory infrastructure that resulted in their generalized use. This infrastructure emerge from the establishment of equivalences between individual antibodies produced by different laboratories around the world: antibodies that were held to be the same, in spite of their different institutional or geographical origin, were assigned a same CD (cluster designation) number and could be used interchangeably. In the present case, the authors used an *ad hoc* database of substances and laboratories that they found on the Web, rather than a bibliographic database such as *Medline*. Figure 2 considers two kinds of entities: individual laboratories or companies (round red nodes), and the general category of cells (T-cells, B-cells, etc.) targeted by antibodies (square orange nodes: their size is proportional to the number of antibodies available for that category). A structural interpretation will focus on the positioning of the laboratories vis-à-vis these general cell categories, as the latter correspond to specific biomedical domains (of varying importance as shown by the size of the nodes). The organizations at the center of the map (including all major commercial companies in that field) position themselves strategically, in order to ensure their presence throughout the spectrum of biomedical activities, whereas organizations at the periphery of the map, while aiming to profit from the scientific and/or commercial opportunities offered by this new technology, have adopted a specialization or niche strategy. The original article included maps corresponding to different points in time, thus arguably allowing readers to follow the evolution of these strategies.

Figure 3, in contrast, disaggregates, so to speak, the previous figure by including the same institutions (square orange nodes) and the specific CD antibodies they had developed (round red nodes): the size of the nodes corresponds to the number of antibodies produced by a given organization or included in the same CD. Figure 3 can no doubt also be interpreted structurally (e.g., large vs. specialized producers of widely used vs. esoteric CD antibodies), but a non-structural interpretation will insist on the evolution of the links between researchers and entities in this rapidly unfolding domain. For instance, it appears that some CDs are very robust, as their existence is supported by several laboratories, whereas others are weak, as their existence is ensured by the presence of only one laboratory. Moreover, maps from different periods (not shown here: see original article) document the emergence of novel categories of cells in conjunction with the proliferation of antibodies targeting them, or the transformation (splitting, redefinition, etc.) of individual CDs.

Admittedly, the alternative illustrated by this example still conveys aspects and elements of a structural interpretation, only alleviating its worst shortcomings. This is due in large part to the limits of the database that only listed a limited number of different entities. Moreover, the database did not provide indications about the informational content of the antibodies, i.e. the domains, tests or diseases for which they were deemed to

be relevant. Combining data from different databases could circumvent this difficulty, an approach exemplified in practice (but with a quite different intent) by Boyack *et al.* (2004) who in the case of melanoma research analyzed a data set consisting of papers from *Medline*, genes derived from the *Entrez Gene* database, and proteins from the *UniProt* database. Similarly, but using different techniques and with a different perspective, Mogoutov *et al.* (2008) explored the development of microarrays by combining data derived from *Web of Science* articles, with those from the *CRISP* database of research grants awarded by the US National Institutes of Health (NIH), and patents from the US Patent office and the *Derwent Innovation Index*.

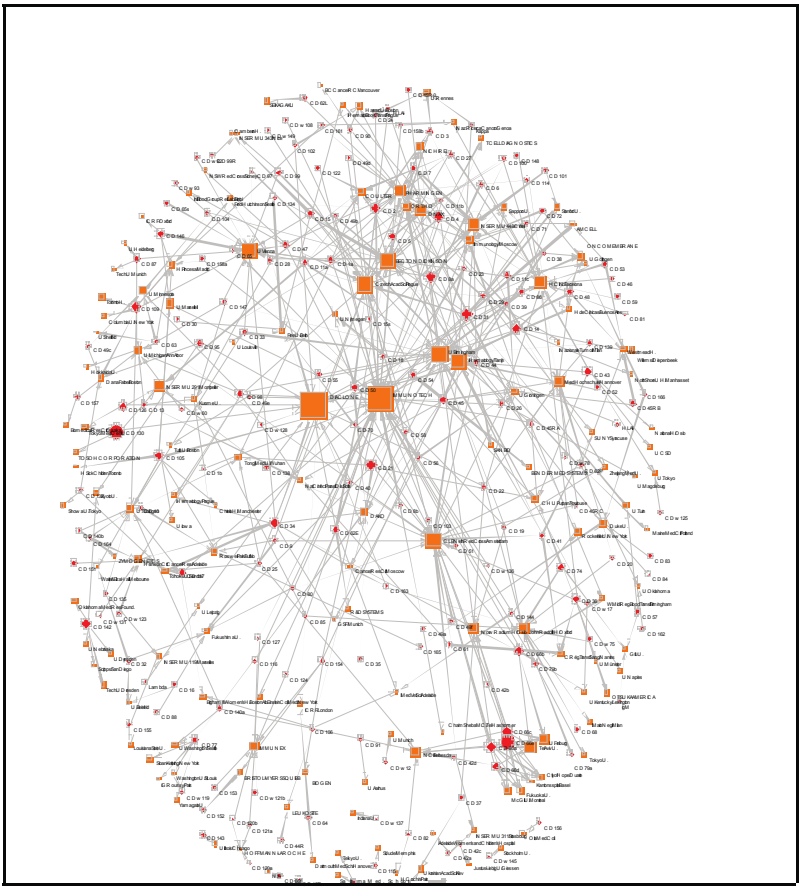

Fig. 3 – Map of laboratories and equivalent categories of monoclonal antibodies. Source: modified version of Figure 12 in Cambrosio *et al.* (2004).

Readers may wonder why a combination of data from different databases is at all necessary, since one could extract those heterogeneous actants from articles alone. But there are two main reasons for pursuing this strategy. First of all, text-mining article databases for these different kinds of entities runs into a number of technical problems (such as identifying the nature of those entities) that can at least in part be obviated by the combination approach. Second, and most importantly, each database corresponds to different regimes of engagement: the modality of engagement of the 'same' gene in a patent vs. an article or a grant proposal will vary in significant ways. The analytical strategy, then, amounts to diversifying the 'entry points': one can start with a set of human actors, as identified by fieldwork, or, alternatively, with a variety of bio-clinical entities that can be found in publications, but also in specialized databases devoted to genes and mutations, biomarkers and tests, or microarray experiments. Information can also be retrieved from websites, such as medical blogs or patient organization websites. Other (but expensive) opportunities to diversify entry points are offered by databases such as *RECAP* (http://www.recap.com/) that provide information about commercial deals in the biopharmaceutical domain. Multiple maps may destabilize conventional readings, generate a feeling of analytical strangeness, and record unexpected events, in a way similar to how new objects, accounts, and relations redefine and displace the boundaries of emerging domains.

We mentioned these examples as possible, uncertain avenues for further investigation, as they have so far not been exploited in the perspective we are advocating here (but see the next section for steps in this direction). This is partly due to the fact that laborious technical bridges need to be established between the different databases; these calculations and manipulations stand in contrast with the seamless association of heterogeneous entities that underlies translations and mediations between different regimes of engagement, as captured by (multi-site) fieldwork. In the biomedical translational research domain, a promising development is the establishment of the *CinicalTrials.gov* database by the NIH. The creation of this database is itself part of policy initiatives aiming at regulating the controversial domain of clinical research, marred by accusations of conflicts of interest, publication bias, etc. Unsurprisingly, the database itself has run into trouble, due to criticism about its incomplete coverage, failure to include relevant information, and lack of standardization, which in turn has led to additional policy initiatives (compulsory registration of trials if results are to be published, etc.) (Zarin *et al.* 2011). In spite of all these problems that complicate its appropriation for our own purposes, the database offers the advantage of assembling in a single virtual space entities such as clinical researchers, molecules (drugs), the institutions performing the trial, public organizations (oncology networks), commercial organizations (pharmaceutical and biotech companies), diseases, technologies, and publications. Bridges with other databases with a different take on those 'same' entities can then be built. Other databases,

such as *Orphanet* on rare diseases similarly offer opportunities for the kind of heterogeneous analysis we advocate.

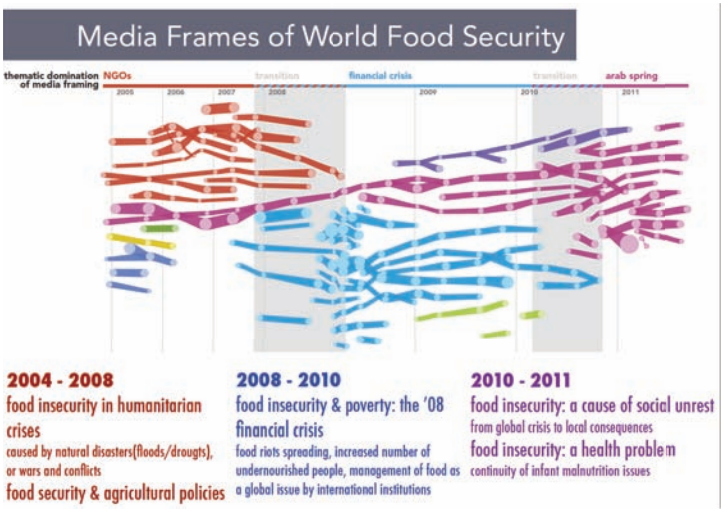

Fig. 4 – Security streams: see text for explanations. Source: Chavalarias *et al.* (2011).

Before closing this section, we would like to briefly introduce a recent attempt to tackle the issue of dynamics. The example below is taken from a report on food security based on the analysis of around 20,000 press articles published between 2004 and 2011 and listed in the database *Factiva* (Chavalarias *et al.* 2011). A somewhat similar approach, albeit with far more primitive tools, was introduced 20 years earlier by the developers of cop-word analysis (Callon *et al.* 1991), and applied to the biomedical domain shortly afterwards (Cambrosio *et al.* 1993). The authors of the 2011 article divided the corpus into 20 subsets, text-mined them, and produced for each of them a semantic network that included clusters of closely associated terms, each corresponding in principle to a topic. Instead of analyzing individual maps separately, they produced a single map with *streams* of clusters, according to the following principle: clusters from a given point in time are linked to previous or subsequent clusters through a stream if they have terms in common. As shown in Figure 4, a stream can split, merge, grow, emerge, decay etc. In spite of a common designation – food security – the domain in 2005 bears little resemblance to the domain in 2011, as new entities have emerged and redefined how

this issue is problematized. Stream analysis amounts to observing the digital traces left by evolving associations in a dynamic landscape, whereby innovation derives from the emergence of new "concerned" entities (Callon and Rabeharisoa 2008), rather than from relational shifts between a predefined list of entities describing a stable state of the world. Parallel instances of "overflows" (Callon 2002) can be associated with these dynamic streams, as indicated on Figure 4.

5. Clusters and Collectives

As previously suggested, the most common interpretation of network maps hinges, first, on the identification of clusters of closely connected entities, and, subsequently, on the analysis of the relations each of these subsets entertains with the others. The tracing of cluster boundaries used to be done manually, by visual inspection of the maps, but cluster detection algorithms, some of which include a fuzzy approach whereby a node can belong to more than one cluster, now increasingly perform this task. Insofar as these algorithms are based on purely structural calculations, they do not necessarily lead to sociologically meaningful units, if by the latter we refer to collective forms of organization and their associated practices, programs, and bodies of knowledge; in short, *agencements* characterized by coordinated (if not homogeneous) ways of problematizing issues. From this point of view, visual inspection, whereby one could deploy his or her sociological imagination, might at first appear as a better alternative, were it not for the following two counter-arguments. First, clustering algorithms are not inflexible tools: one can vary their parameters depending on whether one wants to emphasize, for instance, continuities or discontinuities between clusters, thus playing with variable boundaries. Far from dictating their will, clustering algorithms can thus be used as interactive tools for exploring the associations deployed on a map, the latter becoming an experimental device that can be used to explore alternative configurations in connection to working hypotheses and fieldwork observations. Second, it is far from obvious that the analyst's presuppositions about the proper constitution of the world (which can moreover vary from observer to observer) should have priority over the surprises generated by unexpected network configurations, especially when elicited by interactive tools. Here too maps can function as devices for exploring the variable geometry of the world, rather than as final statements about its ontology. The relevant components of social ontology are in any event open to debate, as shown by the not always mutually consistent attempts to capture them through different notions, such as "communities of practice" (Wenger 1998), "epistemic communities" (Akrich 2010), "collaborative communities" (Adler *et al.* 2008), and the like.

For maps to play an optimal role in this respect we can resort to a trick similar to the one discussed in the previous section, namely to produce a number of maps displaying different categories of actants, i.e. human actors such as researchers and clinicians, infrastructural components such as journals, techniques and models, and notions or concepts. Adding or subtracting some of these components in different combinations could lead to more dense or fragmented situations, helping analysts to put forward hypotheses about the elements that lead to new associations or result in disjunctions. Could, for instance, the densification of a network following the introduction of conceptual components or, alternatively, of certain kinds of tools and techniques be used to differentiate between epistemic communities and communities of practice? While, for a variety of reasons, this seems unlikely, we mention this possibility as a thought experiment to illustrate the kind of analytical approaches we would like to deploy. Actual examples of these approaches do not fully correspond to an ideal translation into practice of this research agenda, but are still worth examining.

Navon and Shwed (2012) analyzed 1400 articles to investigate how a genetic mutation (a microdeletion) transformed biomedical understandings of several rare clinical syndromes, unifying a set of previously independent clinical entities on the basis of molecular analysis. The microdeletion, in other words, was a key actant in "foster[ing] enduring ties between several small, previously disjunct fields of medical research, creating a densely connected literature that brought together an otherwise incoherent set of patients, expertise and clinical observations" (Navon and Shwed 2012, 1640). Their demonstration relies on generating networks derived from citation links between three decades of papers, identifying research communities interested in the older conditions with the help of a modularity algorithm, and showing how the microdeletion progressively unified them, turning a previously invisible collection of conditions into a visible field of coordinated knowledge production. They tell this story by using a set of four maps corresponding to four distinct periods during the last 30 years of the 20th century, and a set of two maps depicting the situation at the beginning of the 21st century.[8] They describe their approach as a way to overcome the limitations of our existing social scientific toolkit that is unable to grapple with non-human entities, such as genetic mutations, that are presently reconfiguring the biomedical field.

Navon and Shwed's (2012) article, which, it should be added, relies on concurrent fieldwork, is a fine-grained investigation of a specific biomedical domain. The reconfiguration of biomedical work by new bioclinical entities can be observed at a higher level of aggregation, where one can examine how translational research has emerged as a distinctive

[8] Given the number of figures, we refer readers to the original publication instead of reprinting them.

site of biomedical activities that cannot be conflated with fundamental and clinical research. These categories are not a priori categories defined by the analyst: they can be derived by the self-organizational properties of maps[9], for instance by observing how journals organize themselves into distinct clusters by spinning a dense web of inter-citations; these clusters can subsequently be qualified by an algorithm that distributes them along a translational continuum on the basis of the terms that appear in the titles of the journals' articles. Cambrosio *et al.* (2006) have adopted this approach to examine a large set of oncology journals: while early periods were characterized by the presence of two major clusters that correspond to activities taking place in either the laboratory or in the clinic, at the turn of the century a third, in-between cluster has become apparent. To further investigate the nature of that cluster, the authors text-mined the titles and abstracts of the articles published by a number of journals in each of the three clusters. Figure 5 shows the resulting map, with the translational space associated with a number of recent bio-clinical entities, such as oncogenes and mutations. Here again, this interpretation was supported by extensive, concurrent fieldwork.

Fig. 5 – Heterogeneous network of journals and bio-clinical entities in the oncology domain: see text for explanations. Source: Cambrosio *et al.* (2006).

[9] Methods have been recently developed for generating maps of biomedicine based on self-organizing algorithms; see Skupin et al. (2013).

As noted at the beginning of this paper, recent biomedical work, in particular translational research, is characterized by a collective turn, which situates it firmly within the scope of inter-laboratory arrangements. This is one of the reasons why local ethnographic observations show their limitations, and the resort to cartography has been suggested as an important complement for investigating contemporary biomedicine, even if ethnography maintains its relevance, in particular for interpreting the maps. As shown by work on French cancer genetics (Bourret 2005) and psychiatric genetics (Rabeharisoa and Bourret 2009), this collective turn is not to be confused with a mere increase in the number of authors co-signing a paper. It is better captured by the notion of "new bio-clinical collective", rather than understood as a network, because it corresponds to a configuration centered on a specific activity, namely the simultaneous development of cancer genetics as a research field and as a domain of clinical intervention. One must start with this activity in order to define the collective. The human components of the collective include a variety of healthcare professionals, whose direct or indirect collaborations and interactions are a *sine qua non* for the development of this hybrid domain. The non-human components include a number of emerging bio-clinical entities, in particular different kinds of mutations, whose uncertain status needs to be managed, re-adjusted, and stabilized as part of the emergence of a "clinic of mutations" (Rabeharisoa and Bourret 2009). The focus of the collective lies precisely in the necessarily temporary qualification of these bio-clinical entities, which explains why the structure and nature of the collective modifies itself on an ongoing basis in relation to the emerging entities that need to be domesticated and mastered for the activity to continue. While the activities of the collective center on building more robust bio-clinical entities, they also involve producing knowledge about what should count as uncertain and unstable: the known unknown. Instead of a passage from local to extended networks, as typically described by early ANT analysts, we face here a situation characterized by the presence of an open-ended list of problematic entities. This is why in order to mobilize these entities they need to be often re-qualified and re-specified. As a result, the collective evolves by incorporating new actors, technologies, entities, and by opening up new fields of investigation.

As an attempt to capture at least a few elements of this dynamics, Bourret *et al.* (2006) collected a comprehensive set of publications by French cancer geneticists over more than three decades[10], and divided them into four periods as defined by major turning points in the history of the field. These data were then used to produce two kinds of maps. First, a set of more traditional co-authorship maps that displayed the progressive constitution of a social network, from an initially fragmented sit-

[10] The procedure involved combining references from *Medline* with those obtained from individual CVs.

uation with a number of local, regional sites, to a fully integrated situation defined by the presence of a single major component. For the second kind of maps the authors opted for an approach displaying the relations between researchers and the bio-clinical entities derived from text-mining titles and abstracts. And here something interesting became visible. Figures 5 and 6 show improved versions (obtained using more sophisticated text-mining software) of the maps used in the original publication. Figure 5 corresponds to the initial period (1970s and early 1980s) of French cancer genetics. As can be seen, the map is organized around a few key researchers: although relations between these researchers are mediated by non-human entities, the distribution of these entities espouses the polarity defined by human actors. Figure 6, corresponding to the turn of the century period, shows a reversal of this situation, as non-human entities, such as mutations, exons, chromosomes, and cell lines, appear to play a key role in organizing the map. The initial maps (not shown here) did not correspond to a given field or specialty, but to the early activities of researchers who subsequently converged on cancer genetics. In other words, the maps do not display structural positions in a scientific field or social world; rather, they follow the movement of researchers and bio-clinical entities leading to the establishment of a collective, even when individual researchers might not conceive of themselves as members of that collective.

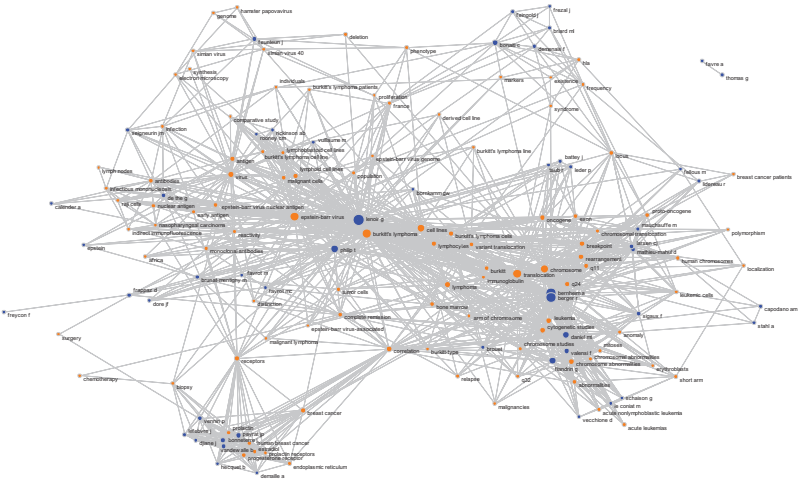

Fig. 6 – Heterogeneous network of early French cancer genetics. Humans: blue nodes; non-humans: orange nodes. Source: revised version of Figure 4 in Bourret *et al.* (2006).

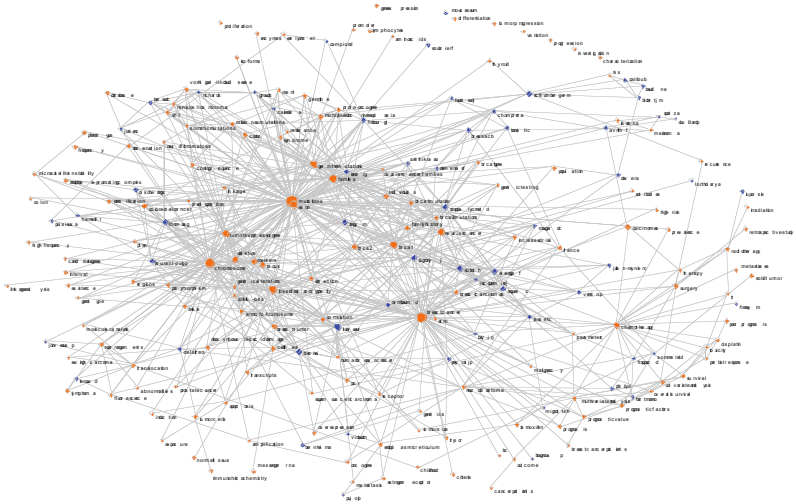

Fig. 7 – Heterogeneous network of turn of the century French cancer genetics. Humans: blue nodes; non-humans: orange nodes. Source: revised version of Figure 9 in Bourret *et al.* (2006).

It can thus be argued, almost paradoxically, that these maps allow one to (pragmatically) distinguish networks from collectives, as the emergence of the collective coincides with the activity of the emerging bio-clinical entities that led to the ongoing readjustment of its internal connections. A collective, thus, amounts not merely to a set of collaborative ties but to a configuration where collaborative work takes place and has been reorganized around these entities – in other words, what we have referred to as an *agencement*. The developmental trajectory of the collective cuts across the initial distinctions between different specialties (cytogenetics, hematology, oncology or medical pediatrics), and reaches a stage where it displays collective agency. The point is not to investigate how networks relate to collectives, but to use network analysis to produce something different from networks. To do so, we need to connect what we see on the maps – the organization of the collective around a number of entities – with what happens in the field, i.e. with the disparate, yet mutually constitutive activities of the collective, including the production, qualification, regulation and circulation of the new entities; in short, all that is needed for these objects to achieve a clinical existence. It is worth repeating that for this to happen actants do not need to be directly acquainted with each other, as long as they work on the same biomedical platforms

(Keating and Cambrosio 2003) that establish transitive relations between, for instance, mutations, diagnostic categories, drugs, and diseases. This also means that in order to capture this dynamics we need to go beyond texts, and take into account wet lab and clinical activities, the circulation of material entities (test kits, samples etc.), and, most recently, the algorithms and codes of bioinformatics.

6. Conclusion: Back to Reflexivity

We presently witness a proliferation of data and databases, often freely accessible on the Web, that can be easily searched and analyzed thanks to a mounting offer of dedicated software platforms, including network analysis software. S&TS scholars, even those with little understanding of quantitative approaches, can now easily perform (semi)quantitative analyses. This is a positive development, but it raises the issue of how S&TS analysts have come to accept these opportunities without asking too many questions about the sociotechnical scripts embedded in the databases they so happily use. Indeed, while S&TS scholars have had much to say about infrastructure, in particular information infrastructure (Star and Ruhleder 1996; Star 1999; Bowker 2006), they have so far not quite succeeded in reflexively incorporating these insights into their own work with (rather than on) information databases. Those of us who work on biomedicine consult almost daily the *Medline* database, and yet we rarely investigate how it has established – thanks to its peculiar structure, format, outreach and universal access – a network-like, worldwide space that multiplies inter-textual relations and favors strategies based on the accumulation of references, citations and co-authorship links. Critical observers have focused their attention on a database like *Web of Science*, holding it responsible for the rise of a whole industry of citation counts and evaluations through controversial tools such as impact factors. Fewer analysts have looked at how *Medline* and its search engine *PubMed*, which are regularly reformatted in response to new information-retrieval needs to whose emergence they contribute, have led to the constitution of a collaborative space by multiplying socio-semantic networks. The aforementioned debates and controversies surrounding the establishment of a database such as *ClinicalTrials.gov* provide a clear indication of how much is at stake in developing this kind of initiatives.

Databases are not restricted to bibliographic databases. Genomics, as noted at the beginning of this text, is generating its own avalanche of big data stored in a number of databases. In order to become "actionable" (Nelson *et al.* 2013) these data need to be interpreted (Leonelli 2014), and part of this interpretation process involves establishing connections between the information provided by the articles and the bio-clinical data stored in the genomics databases. Private companies have invested in this market niche. For instance, *Linguamatics* (http://www.linguamatics.com)

offers text-mining software and services to extract and combine information from the life sciences literature, electronic medical records, clinical pathology documents, clinical trial data and patents. Notice how text- and data-mining tools allow researchers to navigate a seamless web of heterogeneous documents, by the same token moving across the material basis of specialties and disciplines. Nor is this circulation limited to tools: it also involves conceptual transfers, as when information scientists borrow a molecular biology notion – DNA transcriptional bursting – to design and designate algorithms that track word and topic bursts in documents (e.g., Mane and Börner 2004).

As previously noted, in S&TS we are mostly on the receiving end of these processes, both with respect to the tools used to investigate existing databases, and to the establishment of the databases carrying the information that is then retrieved and processed by those tools. We need to investigate these processes in order to understand how these new ways of producing, storing, interpreting, and disseminating data are reframing biomedical activities and configurations. Work by Sabina Leonelli (2012, 2013, 2014) is particularly useful in this respect. But, as just noted, we also need to find ways to reflexively integrate these analyses into our own work with data- and text-mining tools, which in turn means repositioning ourselves both vis-à-vis network analysis approaches and the conceptual and analytical scripts and frames they embed. The point is not simply that we urgently require visualization tools that are better adapted to our theoretical and conceptual framings. A discussion of the shortcomings of existing tools should also lead us to re-examine some key aspects of our conceptual and methodological approaches, especially when they tend to mistake one-click network structures for more complex, rhizome-like arrangements, or to replace agency with structure.

The notion of network is, of course, central to this line of questioning, especially when the actors we investigate reason in terms of networks and extended circulation spaces. But this reflexivity loop, while offering new opportunities for collaboration between S&TS and biomedical researchers, could lead to serious difficulties if insufficiently problematized. As far as opportunities are concerned, we can think of jointly exploring the dynamics (and thus also the forms of agency) characterizing a given domain, or the nature of collectives involved in specific endeavors. Biomedical colleagues are in a good position to replace the few, selective connections displayed on a map with accounts that better correspond to what Strathern (1999) calls the "proliferation of the social", and at the same time our position vis-à-vis their activities is no longer one of externality, as a granting agency such as Genome Canada strongly supports the integration into biomedical projects of ancillary studies on Genomics and its Ethical, Economic, Environmental and Social aspects (GE^{3}LS). As for difficulties, the main one, as we hope to have shown, lies in the notion of network itself, which needs to be theoretically repositioned, because what is relevant in this new context are collective agencies and processes of

agencement, rather than bundles of relations. Such a requirement does not simply express a theoretical preference; it also derives from a close observation of the development of biomedicine in the last half-century (Rheinberger 2009).

As readers who have followed us so far will have realized, we only offer partial solutions, mostly based on tinkering. In fact, we suggested these temporary work-arounds more as a way of exemplifying our questions than as a solution to the conundrums mentioned in this paper. One way of weakening a too strong reliance on structural network interpretations is to multiply the networks, by including different kinds of entities and diversifying entry points. A more intriguing suggestion concerns illegible maps: very often, maps produced in the early stages of a research project do not seem to offer any interpretative handle, as nodes and ties either form a dense, shapeless network, or seem to be randomly distributed. A lot of algorithmic work is then deployed to make those maps legible, to uncover network patterns that were not there at the outset. But what if the lack of a network is indeed the relevant result, and what if instead of using algorithms to turn illegible into legible maps we were to develop tools to explore and account for that illegibility? The point is not to add mess to mess, as some would wish (Law 2004), but to explore the work needed to make maps readable as part of an experimental setting that includes other devices and forms of investigation, not necessarily only interviews, observations, or other traditional forms of fieldwork, but also membership, however temporary, in the collectives we investigate. Beyond what at first we mistook as illegibility we might discover the vanishing points of collective agency.

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Nanomedicine in the Making
Expectations, Scientific Narrations and Materiality

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Abstract: Starting from the theoretical debate about technoscientific expectations, and based on the data collected doing ethnographic research in a laboratory of nanomedicine (in Northern Italy) operating in the field of experimental and clinical pharmacology, the paper explores in detail the relationship between anticipatory knowledge, scientific forward-looking statements and the situated practices of biomedical research in nanomedicine. In particular, I will focus on the processual dimension of scientific narrations on nanomedicine, in order to understand how future-oriented abstractions may represent a fundamental element for the local practices of nanomedical research. In doing so, and referring in particular to a socio-technical artefact called "triangle Dna origami",I develop the notion of *promissory bio-object*, as a conceptual device to improve the understanding of the engagement of anticipatory knowledge in biomedical research.

Keywords: nanomedicine; translational research; anticipatory knowledge; promissory bio-object; ethnography.

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1. Introduction

Nanomedicine as a translational science has the goal to provide cost effective novel therapies and diagnostics using the expanding world of Nanotechnology. To reach this goal the process of translating research results from labs to the clinic has to be greatly improved.
Joint European Commission (2009, 6)

What if doctors could search out and destroy the very first cancer cells that would otherwise have caused a tumour to develop in the body? [...] What if pumps the size of molecules could be implanted to deliver life-saving medicines precisely when and where they are needed? These scenarios may sound unbelievable, but they are the long-term goals of the Nih Roadmap's Nanomedicine initiative that we anticipate will yield medical benefits as early as 10 years from now.
Nih Roadmap for Medical Research

These brief, but sharp, quotations, drawn up by two major regulatory and investment authorities in the field of nanomedicine[1], clearly describe the potential implications of the 'infinitely small' for translational research in life sciences. Nanotechnologies appear to be capable of improving knowledge translation between scientific laboratories and clinical settings, and a number of new treatments and refined diagnostic tools are expected in the very near future.

In recent years, the scientific movement of nanomedicine, which emerged under the aegis of translational research, exemplifying the connection between scientific research and patient care, has become fairly significant in the field of post-genomic sciences (Baird *et al.* 2004; Tsai-hsuan Ku 2012). The proponents of translational research in nanomedicine believe that, within a relatively short time, a new set of 'smart' therapeutic tools incorporating a variety of functions, such as the controlled release and 'real-time' quantification of drugs, will soon be available to doctors and patients, enabling adaptation of therapies to the genetic peculiarities of individuals (Venugopal *et al.* 2008; Tibbals 2011).

Nanomedicine is now being promoted as a potential driver of biomedical innovation, capable of opening a therapeutic scenario in which treatments will become personalised, and individuals will take an increasingly active role in the control and maintenance of their daily well-being. In this sense, the standard view of nanomedicine, supported by the biomedical community and circulating in major scientific journals, appears to be characterised by a 'future-oriented debate' that is to be understood as the complex 'outcome' of scientific narrations, expectations, anticipations and future visions arising from the potential application of nanotechnology in the context of patient care (Grunwald 2004; Lösch 2006; Ach and Lüttenberg 2008).

The ongoing dialogue between nanotechnology and biotechnology is a topic of undoubted importance for Science and Technology Studies

[1] The first excerpt was written by a team of experts from the *European Technology Platforms on Nanomedicine* (Etpn). Etpn is an initiative promoted by the European Commission, together with a strategic alliance of private enterprises, with the aim of pursuing the application of nanotechnology within medical and clinical contexts. The second quotation, appearing in Tibbals (2011), was taken from *Nih's Roadmap Nanomedicine Initiative,* which is a platform founded and financed by the *National Institutes of Health* of the United States.

(STS). In the last decade, numerous contributions within STS have shed light on the ways in which anticipatory expectations and "forward-looking statements" (Fortun 2002) concerning scientific and technological progress may be regarded as rhetorical devices capable of attracting the attention of relevant stakeholders, such as policymakers, investors and directors of research laboratories, together with a number of financial, regulatory and symbolic resources (Brown *et al.* 2000; Holtzman and Marteau 2000; Levidow and Marris 2001; Sturken *et al.* 2004). In this florid debate, one of the most recent developments has been the growing interest in how real-time practices are performed in relation to future-oriented scientific narrations (Borup *et al.* 2006; Horst 2007).

Starting from these theoretical suggestions, and based on the data collected during an ethnographic research conducted in a laboratory of nanomedicine based in Northern Italy and operating in the field of experimental and clinical pharmacology, I explore in detail the relationship between anticipatory knowledge, scientific forward-looking statements and the situated practices of biomedical research in nanomedicine. In particular, I focus on the processual dimension of scientific narrations on nanomedicine, in order to understand how future-oriented abstractions may represent a fundamental element for the local practices of nanomedical research. In doing so, and referring in particular to a socio-technical artifact called "triangle Dna origami", I develop the notion of *promissory bio-object* as a conceptual device to enable improved understanding of the engagement of anticipatory knowledge in biomedical research.

2. Theoretical Tributaries

Anticipatory narrations and expectations regarding science and technology always involve a set of linguistic statements on particular events located within a future-oriented imaginary world, which is still incomplete, but likely to come into effect in certain circumstances (Adam and Groves 2007). Nanomedicine and translational research in general are permeated by rumours and debates outlining future life technologies, future benefits, future patients and future clinical applications (Ioannidis 2004; Thacker 2004; Martin *et al.* 2006; Wainwright *et al.* 2006; Selin 2007).

In accordance with the lively debate on the relationship between anticipatory narrations and technoscientific innovation, the last decade saw the establishment of the so-called "sociology of technoscientific expectations" (Brown and Michael 2003). This approach has been used to investigate the way in which expectations, promises and visions, by means of cultural metaphors, narrative scripts or forecasting policies (Michael 2000; Wyatt 2000; Király *et al.* 2013), are projected and manipulated in

the public sphere as a resource for driving research and development activities and change in the present (Rosenberg 1976; Van Lente 1993; Van Lente and Rip 1998; Brown *et al.* 2000).

In this theoretical framework, the emergence of post-genomic nano/biotechnologies has been interpreted as part of the construction of a new bio-technoscientific regimen, where it may find a number of cultural expectations, biomedical scenarios and promises relating to the potential revolutionary benefits of new treatments or diagnostic and clinical practices (Selin 2006; Hedgecoe and Martin 2007; den Boer *et al.* 2009; Rose and Rose, 2012; Groves 2013). Research has focused on the importance of expectations for the emergence of innovative biomedical fields, such as genomics and biotechnology (Fleising 2001; Fortun 2001, 2002), pharmacogenomics (Hedgecoe and Martin, 2003; Hedgecoe 2006), telemedicine (Rappert and Brown 2000) and information technology (Geels and Smit 2000; Wyatt 2000; Casper 2005). From an analytical perspective, the above contributions have led to a 'top-down' mapping of anticipatory narrations. In particular, the authors have addressed only the temporal cycles of emergence and partial disappearance of anticipatory rhetoric in public spaces, mainstream media or scientific journals.

In this sense, the close relationship between forward-looking statements and the local articulations of scientific research has been neglected. As a consequence, the importance of investigating the way in which scientific expectations of the "future of nanomedicine" may take on a material dimension, becoming variously incorporated into diagnostic procedures, treatment options, and new biomedical technologies, strikingly emerges.

In order to address this issue, it is useful to look at those debates which, focusing on the sociomaterial dimension of technoscientific practices (Law 1987, 1994, 1999; Mol and Law 2002; Orlikowski 2007), suggest that we should pay particular attention to the alignment between human actors, technical objects and discursive representations (Collins and Yearly 1992; Fujimura 1995; Suchman 2000).

Some authors, inspired by these contributions, have recently proposed the notion of bio-objects, in order to conceptualise how new forms of life are designed and materialised into clinically actionable devices (Webster 2011). Such a concept is useful for studying the sociomaterial process by which new biological entities (such as stem cells or synthetic biologically-based devices) are created and, at the same time, how they can shape new clinical, regulatory and commercial issues (Waldby 2006). From an analytical standpoint, bio-objects are embodiments of knowledge in the making that capture the reconstruction of the boundaries between biomedical research and clinical needs. As a consequence, they are characterised by mobility across different techno-scientific domains, such as laboratories and clinical settings (Douglas *et al.* 2012). Furthermore, in a seminal paper, Metzler and Webster (2011) have shown that bio-objects are manifestations not only of material practices, but also of hopes and expectations with regard to the possibility of strengthening the

knowledge that enhances biomedical intervention in health and illness. On the whole, this notion suggests an innovative connection between the sociology of technoscientific expectations and the sociomaterial approach, enabling investigation of the performative dimension of anticipatory knowledge.

In the following sections I will focus on the relationship between scientific narrations and materiality, in order to understand how the expectations of translational nanomedicine can be embedded into biomedical practices and materialised into nanotechnological therapeutic objects. Specifically, in order to show how the dialogue between research and care practices occurs through the mediation of scientific anticipatory narrations and expectations, I will focus on a detailed analysis of the activities involved in the design of a nanodevice, a new biological entity which can be defined as a *promissory bio-object*.

3. Case Study: The Birth of Onco_N@no

Contemporary biomedical science is concerned with the problem of improving the relationship between the laboratories and the bedside. Scientific discourse regarding translational research has recently gained growing importance in shaping imagined futures concerning the application of laboratory research in the clinic (Ioannidis 2004). In particular, as an emerging bio-technoscientific field of translational research (Tsai-hsuan Ku 2012), nanomedicine clearly reveals how scientists, doctors and researchers can occupy a temporality that is strongly biased towards the near future, through the disclosure and declaration of statements and narrations that outline possible developments in biomedicine (Birch 2006).

The articulation between bench and bedside proposed by a translational paradigm may be strongly mediated by expectations and future-oriented scientific statements. Therefore, it becomes necessary to adopt an empirical gaze aimed at understanding how anticipatory scenarios in nanomedicine will break through the walls of research laboratories and contribute to the innovation of biomedical practices. In this sense, the expectations and scientific narrations generated by the supporters of the new technological paradigm in nanomedicine should be understood as productive resources, rather than mere representative statements, which allow to shape and define the conditions for the development of clinical technologies.

Overall, this paper is based on broader ethnographic research that was conducted over a period of 5 months. The empirical material was collected through documentary analysis, in-depth interviews and the ethnographic observation of R&D activities within a laboratory of

nanomedicine called Onco_N@no[2].

Onco_N@no is a newly established laboratory, which, starting in January 2012, has gradually been incorporated within a larger care and research institute in Northern Italy that is engaged in molecular oncology. Doctor Gianni, an internationally recognised oncologist, has been the director since its foundation:

> Nanomedicine provides one of the most exciting and promising paths of research and will help us transfer laboratory discoveries into hospitals – explains Gianni, who deals with translational medicine, the aim of which is to ensure a direct contact between laboratory and patient. [...] Our goal: it's real-time monitoring of the potential side effects of a treatment, be it traditional (chemotherapy) or "smart" (with monoclonal antibodies and other biologics drugs). When I heard that I had been awarded the funding from ***, I have to admit that, after the initial excitement, I was actually quite scared. It was a positive concern though, which had to do with the responsibility of coordinating a project in which I strongly believe and that I have been relentlessly pursuing together with my colleagues. (Gianni)[3]

Gianni's considerations reveal the complexity of what must be accomplished locally to articulate a manifold and composite area of research.

> Nanomedicine, this new current, is my last challenge. What is nanomedicine then? For me, it means designing drugs. It means designing drugs in a different way, in order to make them selective for neoplastic cells, or developing devices that can be useful for treatment. (Gianni)

The utterances of Onco_N@no's director move from an anticipatory narrative level, which includes the expectations and promises involved in the development of new therapeutic nanotechnologies, to the level of everyday research practices, which must be coordinated in such a way as to confer credibility on these expectations. These two levels are, as a whole, the lenses through which Gianni observes the reconfiguration of biomedicine in the near future. He presents a scientific vision of nanomedicine as a tool for the understanding and manipulation of matter, on the nanometer scale, for the benefit of patients and therapeutic planning.

During my ethnographic investigation I followed in detail the early stages of the commissioning of Onco_N@no, which primarily involved two researchers: Beppe and Martino. Beppe, with an academic back-

[2] Persons and locations names are pseudonyms.

[3] Interview given by Gianni in January 2012 for a magazine edited by the institute that co-financed Onco_N@no.

ground in physics, had just returned from the United States to support Gianni's project, suspending his position as *research assistant professor* in the department of biology of an important science and technology institute. Beppe was then joined by Martino, a young PhD student in nanotechnology, who greatly contributed to the local translation of the anticipatory scenario proposed by the director of Onco_N@no.
In what follows, my focus will be in exploring how nanomedical expectations and anticipatory knowledge, such as statements of ideas and scientific facts, can be inscribed and embedded into biomedical practices and diagnostic and therapeutic options (Borup *et al.* 2006). It is a point of particular relevance, which helps to clarify how nanomedicine can contribute to the overall definition of biomedical research in contemporary society, and deepen the notion of promissory bio-objects as a conceptual device for the analysis of the processes that confer materiality, credibility and strength on forward-looking statements.

4. Exploring Nanomedicine through Expectations, Technology and Materiality

Since its inception, Martino and Beppe have been engaged in the *modelling*, *development* and *visualisation* of nanodevices, which are sometimes defined as "Dna origami" (Rothemund 2006) or, more suggestively, as a "Trojan horse to attack cancer" (New Scientist 2012). Technically, Dna origami can be defined as a three-dimensional structure on the nanoscale, the shape of which is arbitrarily decided by the human operator by whom it is created. The peculiarity of biochemical interactions between the molecules that make up Dna[4] makes it extremely useful matter for the construction of new forms of life that do not exist in "nature". Dna origami, developed for the first time by Paul Rothemund at the laboratories of the California Institute of Technology, have rapidly become a "promissory material" for the generation of new biomedical nanotechnologies that are capable of improving drug treatment or "drug delivery"[5]:

[4] The macromolecule of Dna consists of molecules that are called bases. The bases are linked together in an orderly way. This phenomenon is known as complementary base-pairing. The combination of two bases is called a "base pair" and is the unit of measurement used to determine the length of a Dna molecule. The principle of complementary base-pairing was first described by James D. Watson and Francis H. Crick in 1953.
[5] The concept of *drug delivery* refers to a number of approaches and technologies applied on the nanoscale, which are intended for the transport of pharmaceutical compounds to the body in order to improve the efficacy and safety of treatments (Wang and von Recum 2011).

> For drug delivery you need to build an intelligent structure. This will give you better control as compared, for example, to traditional nanotubes. You will also need to characterise this structure. Now, Dna seems to me the most suitable material. Dna is subject to early deterioration. And it is toxic, but for how long? Probably for half an hour. Whereas nanotubes, I mean... they may cause apoptosis of all cells. Nanotubes are toxic, and not only for half an hour. (Beppe)

As Beppe suggested, Onco_N@no research activities were primarily oriented towards the production of a Dna nanostructure that could act as an "intelligent vector" of a specific therapeutic molecule. The clinical rationale derives from the need to identify a number of treatment regimens that are less invasive for the human body and have a relatively low toxicity. Since the early stages of design, Beppe has framed Dna origami within a purely clinical actionability (Nelson *et al.* 2013), expressing a number of therapeutic expectations (for example, the reduction of toxicity level in drug treatments for cancer) as forerunners of his research activities:

> On the basis of this research work, I can say: "Yes, I can use this device and I know how it behaves." And then, I can implement my origami with respect to the clinical needs. That is, for example, the drug delivery. Why could Dna origami be a winning strategy for drug delivery? Because they are biocompatible. They are made with the same biomolecules that you find in our bodies. In doing this new thing, we established a few points to follow. First point, we are in a research and care institute, so we have to do something related to cancer treatment. Second point, our director has always been involved in experimental and clinical pharmacology. Thirdly, we have the patients. Therefore, cancer, patients and medications: these are the ingredients. (Martino)

Through this discursive operation, Beppe and Martino attempted to establish a material-semantic link between the clinical expectations and research activities of Onco_N@no, turning the nanomedicine laboratory into an instrument at the service of the patient. In this respect, researchers' words are pervaded by a sense of moral responsibility, demanding the adoption of explicit and demonstrable procedures, peculiar to a system of 'scientific truth' (Hacking 2009), in order to account for and justify the fact that Onco_N@no's activities move towards clinical application. It is a practice of *accountability* (Garfinkel 1967) which, in conjunction with the modeling, development and visualisation of Dna nanodevices, confers credibility on the future-oriented scientific statements that constitute the global field of nanomedicine.

Moreover, it is important to underline that both quotations elucidate how material expectations regarding translational nanomedicine outcomes enacted by Dna origami are partially shaped by the institutional setting's vision around the potential benefit of the nanodevice. At the

same time, the institutional vision is co-generated by the possibility of successfully constructing the nanodevice as a therapeutic object. In this sense, the articulation between bench and bedside, strongly supported by the translational research paradigm, is mediated by the circulation of expectations between multiple levels and domains.

4.1. Nanomedical Modeling: Centers of Calculation and Molecular Bio-design

According to the researchers' expectations, one of the nanodevices designed and developed at Onco_N@no could significantly enhance the efficacy and safety of a specific drug or therapeutic compound with which it is combined:

> The Dna triangle that I'm preparing, as you can see, is a simple structure. And it is precisely for this reason that I believe that you can have better control when you test it on blood and in patients. We need a structure that can be monitored and aggregated with a drug, that's all. If you create an origami that is too complex, you're back to square one. How do you manage to check it within the body? (Martino)

Designing the nanodevice initially involved the graphic modelling of the intended structure. Martino and Beppe were oriented in the creation of a structure having a triangular shape, hence the name triangle Dna origami (Tdo). By reason of its alleged simplicity and graphic 'abstemiousness', as Martino explained, Tdo would allow improved control by the operators when used in complex biological systems, such as the human body. However, the question of simplicity and visual abstemiousness is not to be understood as a mere technical problem. Describing his Dna molecules in familiar terms, Martino has the ability to make the subject accessible and intelligible, not only for researchers and the confined community of nanotechnologists, but also for clinicians and non-specialists that are simply interested in laboratory scientific activities, such as patients.

While I was conducting my investigation in the laboratory, it often happened to see researchers from other scientific institutes in Northern Italy (who used to visit Onco_N@no to negotiate partnerships and collaborations) showing great interest, and even surprise, with respect to the research activities of Martino and Beppe:

> Martino: So, first of all, I tried to select the best software to design my origami. I tried a few. All of them are CAD [computer-aided design] software and are free [...]. In the end, I found out that the only software I could use was this one. It is called NanoEngineer. In my opinion, it is the best software for this

application, since it also allows 3D design, whereas other software would only support 2D design. Basically, this software allows you to create your own origami.

Engineer (guest): Can you give us an idea of how you create this origami?

Martino: You need to design its structure with NanoEngineer. This way, you will have your assembled structure, also including complementary sequences of DNA. Once you have drawn the structure and you are sure about your project, you need to acquire Dna fragments, mix into solution, and then you can do the rest, that is make your reaction.

Engineer (guest): So you are telling us that the structure is automatically generated? Do you mean that the origami is automatically generated out of this indistinct mixture?

Martino: Basically, yes.

Engineer (guest): It is truly fascinating. It is really incredible how you can create the structure out of this slop. Well, considering that we live thanks to DNA, you can easily figure out why it may react like this. It is a real "wager" when you mix all these things together trying to achieve ordered nanostructures. It is something beautiful and the wager is very powerful for the clinic.

"The wager is very powerful for the clinic": the epilogue of this conversation shows how the research activities in which Martino is engaged require the ability to manage scientific knowledge and technologies, as well as expectations, in the form of the scientific wager, revolving around nanomedicine. From the conversation between Martino and the chemical engineer, we learned that the design and production of the nanodevice implied a composite work of digital and organic, and between clinical expectations and laboratory practices, in order to develop new treatment strategies.

The modelling of Dna origami is articulated through a process of graphic design using an open source; computer-aided design software called *NanoEngineer-1* (Fig. 1).

The software used by Martino conceals a sophisticated corpus of scientific knowledge in the field of molecular biology behind an extremely simple and intuitive user interface. NanoEngineer-1 makes it possible to simulate the biological process of Dna reproduction and synthesis, since the software developers incorporated in the application a codified and formalised knowledge base regarding the complementary pairing of Dna sub-units. This means that the operator can generate 3D images of Dna on a nanoscale, which is potentially achievable in the laboratory.

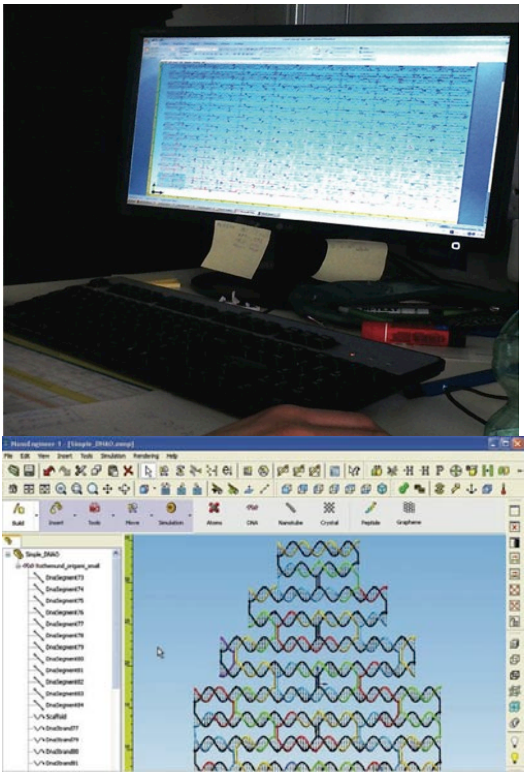

Fig. 1 – Modelling of a nanomedical device with Nano_Engineer-1

However, when modelling the TDO, Martino's activity was not limited to the use of the software. Although it may sound like a highly technical activity, opened by software potential in itself, the modelling required the juxtaposition of other handmade graphic elements, such as drawings, prototypes and proofs (Fig. 2a and 2b).

These were later collated in the laboratory journal and, to some extent, they express Martino's scientific creativity, which confers shape and materiality on the expectations of nanomedical devices.

Such representations, sketches and drawings, may be regarded as central elements of mediation in building Tdo digital images, and constitute the space in which scientific ideas regarding the future are visually refined.

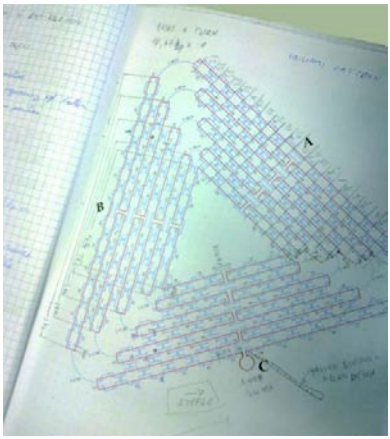

Fig. 2a – Graphic drafts of the nano device

Fig. 2b – Graphic drafts of the nano device

In other words, a specific medical nanotechnology that initially escapes the sensitive perception, becomes present, credible and, above all, achievable, through laboratory practices. In this respect, the goal of the graphic exploration of Dna molecules is not merely theoretical, nor simply attributable to the reconfiguration of new knowledge on Dna properties on the nanoscale. Despite the fact that, to a certain extent, nanomedicine wishes to ascertain the implications of biological processes on an atomic scale, the main goal of Onco_N@no research activities is to make an attempt to actively manipulate organic matter for the design of new therapeutic strategies.

Within this experimental frame, the computer application used by Martino appears to be particularly relevant. While incorporating codified and formalised expert knowledge, the software serves as a "centre of calculation" (Latour 1986, 1987) that is standardized and shared by the international scientific community. The standardization of modelling procedures conveyed by the software and the digital images produced by Martino can meet the approval of the reference scientific community: Tdo digital images do not pertain to the level of imagination, but are self-evident scientific representations of the generative potential of Dna.

Thanks to the knowledge base incorporated in the software and recognized by the international scientific community, the blurred and antithetical boundaries between "imaginary" and "scientific" are reassembled within an epistemologically consolidated regime of disciplinary truth (Knorr-Cetina 1981). In this way, researchers have constructed a "digital object" (Monteiro 2010) as intermediate scientific evidence that helps to recompose the discursive level of future nanomedicine with that which is

experimental. This means that the image can also be shared, displayed, and potentially translated into clinical practice, conferring credibility on the nanomedicine scenario.

4.2. Development and Visualization of Nanodevices: Seeing Is Believing

As described in the previous section, the concept of Dna, which is the constituent material of the nanodevice, pertained to a computational representation during the modelling phase. It was a computer-based, or *in silico*, simulation of the process of synthesis and aggregation of the subunits forming the Tdo. The graphic design stage was followed by the *in vitro* development of the nanodevice, in the form of a biological sample. The Tdo development path was articulated in a number of experimental activities, which required the manipulation of short sequences of Dna, the so-called oligonucleotides, in order to confer a biological and material status on digital images.

The Dna sequences have the property to aggregate into the ordered and predefined structures that are called Dna origami through a biochemical reaction induced by heat (annealing reaction). After designing the image on NanoEngineer-1, Martino had to "catalogue" the different Dna sequences required for the preparation of the reaction that would lead to the formation of the desired nanodevice. The software incorporates a dedicated tool that automatically generates a list of nucleotides constituting the Tdo. This list is nothing more than a long list of letters indicating nucleotide aggregations in the form of "GATGG" etc. (Fig. 3). This means that the nanodevice, following *in silico* simulation, is translated from a visual and graphic language (the image of the triangle) into a conventional and standardized alphabetic language, taking on a new informational dimension. When preparing the annealing reaction, based on a "trial and error" approach, the researcher defines an experimental protocol providing the instructions, methods, materials and sequences of actions necessary for the *in vitro* development of Tdo.

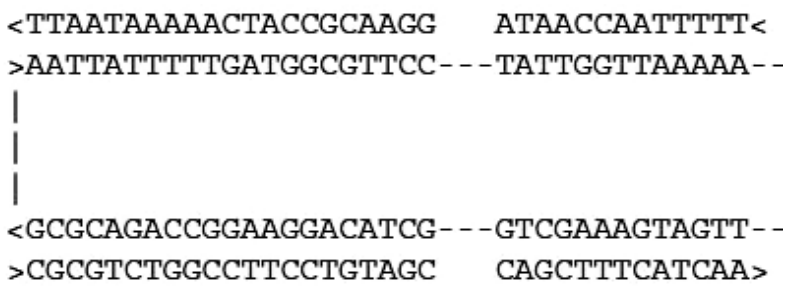

Fig. 3 – Example of nanodevice informational representation

The overall coordination of the reaction for assembling Dna sequences is particularly laborious, and recursively interweaves the subsequent activities of visualization and characterization of TDO. After completion of the annealing reaction, Martino obtained a set of biological samples, in which he may have reasonably expected aggregation of Dna sequences for generation of the nanodevice. At this point, it is necessary to adopt a number of experimental procedures to verify the formation of the desired nanostructures. This verification phase also has a characterization function, since it allows the estimation of some of the biochemical properties of the product obtained from the reaction. The visualization of the nanostructure is achieved through an experimental procedure that is fairly consolidated in molecular biology laboratories: electrophoresis. This technique for the analysis and separation of Dna molecules enables the production of very particular images (Fig. 4), as well as a further graphic and visual representation of the nanodevice.

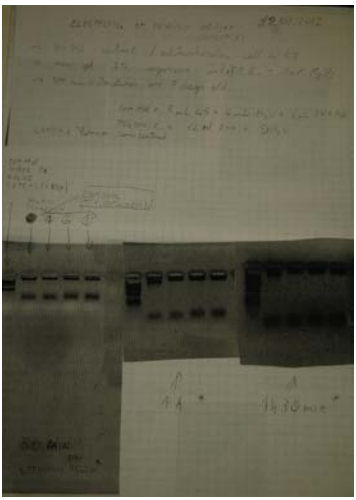

Fig. 4 – View of the nanodevice after electrophoresis

The visual representations of the nanodevice, obtained through electrophoresis and subsequent exposure of Dna inside a photographic device, are configured as 'light/dark bands' and form visual objects of mediation between the computational and purely biological status of Tdo, achieved through experimental laboratory practice. As shown in figure 5, Martino is comparing the image of his nanodevice with one that is standard, or a molecular weight marker, in order to assess whether the resulting "light/dark bands" are compatible with the formation of Tdo. If

the evaluation of the 'bands' does not meet the expected outcome, the protocol should be reviewed, and further development and characterisation activities should be defined.

Beyond the technical aspects, what is interesting is the use of a highly standardised set of technologies within an experimental process that incorporates a potentially high degree of innovation. Although Martino is engaged in an innovative, and therefore unstable and lacking in established standard procedures, field of nanomedicine, it becomes clear how the production of scientific knowledge is connected not only with Onco_N@no-situated purposes and the information obtained from the materials used, but also with a set of knowledge and practices that have been "inherited" from biomolecular scientific culture. In this sense, while

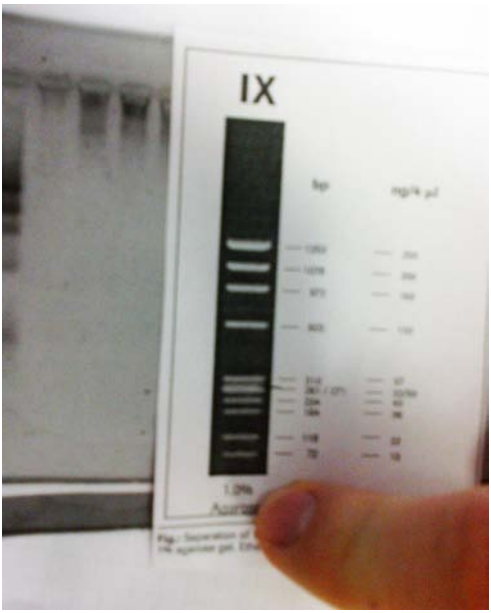

Fig. 5 – Standards for the evaluation of the nanodevice

identifying an ambiguous and opaque biological entity, Tdo calls for the alignment of a set of experimental data and scientifically established technologies in order to manage its controversial and "esoteric" dimension. In other words, in order to assess the outcome of the experimental process for the construction of the nanodevice, and determine whether it also has a material status, in addition to being purely discursive and informational, it is necessary to identify a set of reliable procedures to allow its visualisation. To some extent, Martino implements an established scientific repertoire within an emerging scientific field, in order to give the

procedures a robust epistemological status, and to naturalise a number of emerging scientific practices that still remain opaque and uncertain (Collins 1981; Collins and Pinch 1993).

Overall, the activities of modelling, development and visualisation of Tdo can be understood as explicit scientific procedures that allow the anchoring of the debate on nanomedical future to the local biomedical setting. The outcome of these activities was the production of a new biological entity, a bio-object, which conveys and materialises the set of expectations revolving around the foundation of the laboratory.

This reflection, in accordance with other contributions, documents the central role of visual representation in nanomedicine research (Mestrutti 2011; de Ridder-Vignone and Lynch 2012). We can see how expectations and scientific imaginings are turned into images as a means of construction and communication of objectivity (Daston and Galison 1992, 2007). In particular, the graphic representations of the Tdo enable an important dimension of the scientific images that Burri called *visual persuasiveness* (Burri 2012, 53). This visual dimension emphasises the relevance of images as scientific evidence that make visible the natural world (Frow 2012); or rather, in being considered objective and true, as an emanation of the purity of scientific method (Perrotta 2012). In other words, the scientific images of the bio-object allow us to juxtapose and connect scientific views and practices of biomedical research: this means that anticipatory scientific narrations on translational nanomedicine, which is to be understood as a science lying on the borderline between the clinical world and scientific laboratories, are visualised and translated from a merely discursive level to a level of feasibility and scientific manageability.

5. The Emergence of Promissory Bio-objects

Scientific research in Onco_N@no identifies a broad process in which Martino and Beppe sought to consolidate an experimental procedure for the construction of a new biomedical nanotechnology that is capable of expressing a set of expectations and visions supporting the possibility of translating nanotechnology into patient care devices.

As mentioned above, this process was implemented within a context that extends well beyond the four walls of the laboratory. The technoscientific world of Beppe and Martino is populated not only by human actors "at hand", but also by objects and technologies of various technical complexity that are inherent in scientific practice: Dna (which connects the laboratory with the community of molecular biologists), *NanoEngineer-1* software (which connects Onco_N@no with the community of nanotechnologists), the laboratory journal (which collects all activities and data that will be published and made available to the international community) and expectations regarding the use of nanodevices (which

connect the laboratory with the clinical world). However, when translated from the public sphere to the confines of local laboratories, expectations and scientific visions of nanomedicine become, principally, technical issues that are addressed through the development of experimental standardised procedures.

Through the R&D of Tdo, and the subsequent practices of visualisation and materialisation, that which is exposed to the scientific community is not simply a new life technology, but a broader sequence of events, something far more abstract that concerns the configuration of a new biomedical approach to the body and disease:

> Research in nanomedicine means speculating on treatments that will save you from going to the hospital every day. This is the most powerful aspect. I believe that, otherwise, there would not be enough added value. I mean, what's the point of replacing a treatment with another one, if there is no guarantee of improvement? Therefore, I believe that having something that is not particularly or overly invasive for the patient is paramount. Our goal is not only to increase life expectancy of patients with cancer. What we want to achieve here is defeating cancer. (Beppe)

With clarity and conciseness, Beppe emphasises the scientific challenge undertaken by the director of Onco_N@no: the development and testing of nanodevices operating within the body that are capable of redefining the trajectories of patient bio-medicalization. In this sense, the innovative content of translational nanomedicine lies not so much in the direct manipulation of matter at an atomic level, but in the development of techniques and methods for the creation of devices for molecular intervention, or rather the shaping of "programmable", clinically relevant and promising biological entities.

From a theoretical perspective, Tdo, similar to other nanodevices created in biomedical laboratories, is the product of diverse practices for understanding and improving human life, namely with the creation of tangible objects that can be used in the clinic to govern the development of pathological processes (Webster, 2012). These bio-objects also tend to blur the conventional boundaries between "human" and "non-human", which are traditionally assumed by life sciences in general (Holmberg *et al*. 2011). The use of Dna as 'natural', programmable and bio-compatible material allows the location of the bio-object within a hybrid domain that exceeds the dichotomy between the natural and artificial character of therapeutic intervention.

One last aspect of particular relevance is associated with the knowledge they incorporate. As previously discussed, the practices of construction of the bio-object were triggered by the promissory debate on a nanomedical future that is populated with a number scientific views and expectations regarding the possibility of intervening in therapeutic pathways with new nanodevices. More precisely, expectations and future-

oriented scientific narrations appealed to biomedical experimental activities, so that the continuous reproduction of their meaning by way of practical use bestows their material stability and credibility. In this respect, the emerging biomedical domain is not generated by biomedical expectations and anticipatory narrations. The generative dimension lies, instead, in the relationship between anticipatory narrations and local experimental practices, where the promissory bio-object is a relational and emerging effect of a contingent technoscientific system that is only partially stable.

Therefore, the process of Tdo materialisation should not be understood in finalistic terms, as a scientific fact of linear innovation and development, but as the local and contingent product of an ecology of actions, where expectations and future-oriented biomedical narrations provide a resource to support situated practices. At the same time, the images of the bio-object represent some type of mediators of sense, allowing the communication and actualisation of anticipatory biomedical narrations.

Overall, the theoretical juxtaposition of the material and anticipatory/discursive dimensions allows the definition of an analytical space that is outlined by the concept of promissory bio-objects. This reveals how anticipatory narrations and scientific views shall not remain mere discursive representations, but can return a set of images capable of feeding back on the present, directing the actions and intentions of social actors engaged in the practices of biomedical research.

The analytical potential of the concept of the promissory bio-object lies in the ability to investigate multiple forms of materialisation of expectations and scientific views, which find, in R&D activities and in the materiality of life technology, the ideal conditions for actualisation. This means that expectations are activated as long as they provide an instrument for supporting the local set of contextual elements for the articulation of research practices. Situated practices, in turn, give back credibility and materiality to the discursive dimension that forms the basis of anticipatory statements.

Finally, this concept reveals how contemporary biomedicine and the contextual processes of bio-medicalization are built through a process of alignment of different elements (data, laboratory tests, technologies, scientists, doctors and narrations), whereby the practices of translational research in nanomedicine intertwine with anticipatory knowledge, visions of the future and visual representations, providing an opportunity to investigate the relationships that develop between scientific narrations, situated practices and technologies.

6. Final Remarks

In this paper, nanomedicine has been framed as an emerging field in the cooperation between human actors and technological devices, scien-

tific images, linguistic resources and discursive practices, in order to understand how expectations and scientific narrations can be addressed and coordinated within experimental contexts, where biomedical knowledge and new therapeutic indications are produced and shared. Indeed, the analysis of nanomedicine showed well, as the aspirations and expectations take shape in processes in which researchers are pursuing specific objectives, experiencing what is translational nanomedicine, and representing it as a concrete possibility.

With reference to the daily activities for building a nanodevice, I tried to show how the future can be considered as a discursive arena densely populated with claims, interests, views on medicine and representations of bodies and treatments, which are recursively translated into present courses of action through the situated practices of biomedical research. If, on the one hand, these practices draw on anticipatory visions, on the other hand they confer robustness by attempting to generate new technologies that incorporate planning qualities strongly biased towards the future.

The theoretical perspective outlined in this contribution led to the formulation of the notion of promissory bio-objects as a conceptual device that proves useful for investigating the relationships between the anticipatory narrative level and the materiality of scientific activity. This helps to clarify how an emerging biomedical domain, with blurred and changing boundaries, is legitimised and made scientifically credible, that is, it is capable of generating innovative technologies. Ultimately, promissory bio-objects show a hybrid character that allows joint analysis of human actors, technologies and anticipatory knowledge, as the fundamental and constitutive element of the experimental processes peculiar to contemporary biomedical research. Expectations and scientific views are not mere cognitive issues, but elements materially embedded in the ongoing action and routines.

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The Bio-Objectification of Umbilical Cord Blood: Socio-Economic and Epistemic Implications of Biobanking

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Abstract: In the current biomedical literature Umbilical Cord Blood (UCB) is considered a valid source of hematopoietic stem cells for hemopoiesis reconstitution. The acknowledgment of the potential of UCB for transplants prompted the transformation of this human tissue from a discarded human residuum to a valuable life-saving tissue. Drawing on the notion of bio-objectification (Webster 2012), this paper critically investigates the socio-technical process by which this transformation occurred, and explores the two-way interaction between basic biological research and clinical settings in which the therapeutic use of UCB was developed. Secondly, drawing on the notion of biobanks as forms of governing life, this paper analyzes how different institutional arrangements in UCB biobanking produce different routes in UCB bio-objectifications and different economic regimes of UCB exploitation. UCB biobanking thus entails diverging articulations of the relationship between biomedicine and society, and the co-construction of medical technologies, therapeutic applications, subjectivities and social rationalities.

Keywords: umbilical cord blood; biobank; bio-objectification; bioeconomy.

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1. Introduction

Umbilical Cord Blood (UCB) contains stem and progenitor cells capable of restoring haematopoiesis, i.e. the physiological process by which the organism produces blood cells. It is therefore currently used for

transplantations in patients suffering from haematological malignancies, and immunological and metabolic disorders (Navarrete and Contreras 2009). The discovery that UCB contains haematopoietic stem cells (HSCs) dates back to 1974 (Knudtzon 1974). However, the first successful UCB transplant was performed in 1988 on a paediatric patient with Fanconi anaemia, using UCB from a sibling (Gluckman *et al.* 1989).

Nowadays, UCB is considered a valid alternative to bone marrow (BM) transplantation for reconstituting haematopoiesis in both children and adults also in the case of partial histocompatibility (Kurtzberg *et al.* 1996). The graft/host tissue compatibility in human allotransplant is regulated by the human leukocyte antigen (HLA) complex – i.e. the loci of genes encoding the proteins (antigens) responsible for immune reactions and thus also for organ transplant rejections – so that the more the HLA complex of the donor and recipient match, the less the immune system of the recipient will reject the engrafted tissue. Common in BM transplant is graft-versus-host-disease: the lymphocytes (a particular kind of leukocytes or white blood cells) in the engrafted tissue attack the host's body cells because they recognize them as antigenically foreign. Consequently, there must be histocompatibility between the HLA systems of the BM donor and recipient – which makes the search for a compatible donor a difficult and long procedure. Instead, since UCB lymphocytes have a naive immunophenotype (Han *et al.* 1995), there is a low rate of graft-versus-host disease in UCB transplants (Broxmeyer 1995; Wagner *et al.* 1996) permitting transplantation also between partially mismatched donors and recipients (Kurtzberg *et al.* 1996; Wagner *et al.* 1996; Rubinstein *et al.* 1998).

Moreover, the biomedical literature stresses that, while BM registries are databases of potential donors and BM donation requires hospitalization and general or spinal anaesthesia (a painful and risky procedure), UCB repositories store tissues directly available on-demand, collected with little or no risk for the donors, and with a lower incidence of microbial, fungal and virus infections. Thanks to these features, the use of UCB in transplantation has increased over the years. According to Bone Marrow Donor Worldwide (the organization managing the registries of all HSC sources – BM, UCB and peripheral blood), more than 20,000 UCB transplants were reported worldwide from 1989 to 2009, and more than 560,000 UCB units were stored in more than 100 UCB banks (Bone Marrow Donor Worldwide 2013). Therefore, what "was generally regarded, along with the whole placenta and the attached portion of umbilical cord containing it, as a discarded human residuum" (Fernandez 1998, S84), is now considered a valuable life-saving tissue. The term 'valuable' is of key importance, because it refers not only to UCB's clinical utility in transplants – or as an epistemic thing (Rheinberger 1997) in oncology, haematology and stem cell research – but also to its economic exploitation and the related societal and ethical issues. UCB used in the clinical setting is not what was once discarded; rather, it is a bio-object (Webster 2012) fabricated in a complex, multilayered network of practices, procedures

and institutions that (non-linearly) links the social world of basic biomedical research with that of clinics and, furthermore, with society at large. The key node of this network is the UCB bank: it is the institutional site in which the bio-objectification of UCB takes place. It therefore makes this tissue available for its "mobility across different socio-technical domains…[and] between different sectors or network of society" (Webster 2012, 3), as well as for economic exploitation. Indeed, there are two main institutional arrangements of UCB biobanking: the worldwide network of national public biobanks – which manage the storage and distribution of this tissue for the public healthcare system – and the private sector, where private companies sell to new and prospective parents the opportunity to store the UCB of a newborn child for future familial use by paying a fee. This entails two different forms of (economic) evaluation of UCB: in the public sector UCB is considered a public resource, which is collected through an act of donation and supplied in a redistributive economy; in the private sector, instead, UCB is regarded as a private biological asset, and UCB banking is advertised and sold to parents as a biological insurance against possible future illnesses in a market economy framework, where individuals negotiate with the emerging biomedical industry on exclusive possession of a corporeal commodity.

By drawing on the notion of bio-objectification (Webster 2012), this paper will first explore how UCB was transformed from a waste material to a valuable life-saving tissue. I shall show how the bio-objectification of UCB took place through a two-way interaction between the bench and the bedside. Secondly, by using the analytical framework developed by Gottweis (2008), which considers biobanking as a form of governing life, I shall analyze how the institutional arrangements of UCB biobanks imply different routes to UCB bio-objectification and are thus connected to diverging articulations of the relation between biomedicine and society. According to Martin *et al.* (2008b, 142), UCB biobanking is a crucial site in which there occurs a co-construction of "new promissory technologies, novel therapeutic applications, and new types of consumers motivated by changing moral imperatives". This paper analyzes this co-construction in the two opposing institutional arrangements of UCB biobanking, and thus considers the related social implications.

Finally, I shall show how the focus on institutional arrangements allows the notion of bioeconomy to be rethought in more critical terms.

2. Bio-Objectification, Biobanks and the Bioeconomy

Webster (2012) has developed the concept of bio-objectification as a heuristic device to refer to the technoscientific creation of life forms and "technologically enacted vital materiality" (p. 2) in order to take into ac-

count the biotechnological transformation of life and its biological boundaries.

Developments in biotechnologies and the life sciences have moved the control and manipulation of vital processes to the level of their cellular and molecular mechanisms (Waldby 2002): cells, tissues and biological information (such as gene sequences) are disentangled from their corporeal embodiments and transformed into technologies deployed in biomedicine and, in general, in the biotech industry. Webster (2012, 2), indeed, exemplifies bio-objectification, and the biotechnological reformulation of the living, by showing how aborted foetal tissues, previously regarded as waste matter, "can be re-vitalised as source material for stem cell lines".

This biotechnological reformulation and transformation of biological entities has resulted in new types of "separable, exchangeable and reincorporable body parts" (Rabinow 1999, 95) which flow in international circuits and are exploited for the creation of "biovalue" – i.e. "the yield of vitality produced by the biotechnical reformulation of living processes" (Waldby 2002, 310). A growing body of social science literature has drawn attention to the ways in which the body and its component parts have become a preeminent site of capitalization. Scholars have noted that the biotech field is increasingly "organised as a market" (Birch 2006, 3), and that "the object of bioscience, the practice of bioscience, and the locations of bioscience have all been changing […] toward more corporate forms and context of research" (Sunder Rajan 2006, 4). In other words, biosciences are not only committed to the production of truth, but are increasingly intertwined with the creation and mobilization of venture capital through the "patenting of cell lines, genes and transgenic organisms" and their transformation into "intellectual property and possible sources of profit" (Waldby 2002, 310).

This literature has explored the growing commercialization of life itself and its socio-cultural implications by extending the work of Michel Foucault. Firstly, it draws on his notion of biopolitics (Foucault 1976), i.e. the practice of governance that brought life itself and its mechanisms into the realm of political calculations and rationalities addressing the biological existence of individuals and populations. Secondly, it explores the intertwining between modern biology and political economy – whereby the "organic becomes the living and the living is that which produces, grows and reproduces" (Foucault 1973, 232) – at the molecular and cellular level. In this sense, terms such as bioeconomy or biocapital have been introduced to highlight how biological entities (organs, tissues, cells, and gene sequences) "are increasingly inserted into projects of product-making and profit-seeking" (Helmreich 2008, 464). Consequently, life has become "productive of economic value…[and] the manipulation of life generates a value accorded to the enhancement of health" (Rose and Novas 2005, 455). This "relocation of wealth in the creative forces of human biological

life" (Cooper 2008, 6) means that "life becomes, literally, annexed within capitalist process of accumulation" (Cooper 2008, 19).

Moving from 'molar' level of populations and bodies to cellular and molecular components (Rose 2007) means that the capitalization of life itself and the exploitation of biovalue in the current bioeconomy pass through the bio-objectification of biological entities. UCB represents a paradigmatic example of a bio-object, both because it was transformed from waste to a clinical and epistemic valuable thing, and because it circulates internationally among countries and different social environments (laboratories, hospitals, biotech companies) by virtue of a new medium of technical innovation, namely "biobanks or cord blood banks" (Webster 2012, 3). However, the case of UCB tends to complicate the picture drawn by the literature on bioeconomy. Several scholars define the current bioeconomy as a form of market economy, and they link its birth with the neoliberal turn in national economic policies (Cooper 2008; Birch 2006). The biotech sector organized in a post-Fordist corporate way (Sunder Rajan 2006) is seen as consubstantial with the core neoliberal idea that the human well-being and the social good "will be maximized by maximizing the reach and frequency of market transactions" and by individual entrepreneurial freedoms (Harvey 2005, 3). In this sense, Sunder Rajan (2003, 92) pointed out that, in any institutional arrangement of biomedical research: "it is the very definition of what constitutes market logic that is often most at stake in the strategic articulations of biocapitalism"; and also the relocation of biomedical knowledge and information in the public domain (e.g. in the case of the Human Genome Project) represents "less an attempt to negate market logic as much as it is to redefine the terrain in such a way that 'market logic' is dictated by the strategic interests" of corporate actors (Sunder Rajan 2003, 105).

However, the bio-objectification of UCB does not automatically mean its commodification in a market (bio)economy framework, since the system of public UCB biobanks organizes and supports a global redistributive tissue economy in which UCB is considered a public resource. I shall show in what follows that the bio-objectification of UCB takes place within a particular socio-technical infrastructure, namely a biobank, which connects different areas of biomedical research with society. I shall demonstrate that it is the institutional arrangement of biobanking that determines the route of bio-objectification of UCB and thus both its status as a (bio)economic good and the related implications for the articulation between biomedicine and society. In other words, I shall explore how the co-construction of biomedical technologies, therapeutic applications and subjectivities, rationalities and social solidarities varies according to the institutional arrangements of UCB biobanking. The two main arrangements of UCB biobanking (the public system vs. the private commercial sector) entail:

- two opposing main regimes of UCB biovalue exploitation (i.e. a redistributive tissue economy vs. a market bioeconomy);

- different routes in UCB bio-objectification;
- contrasting meanings of UCB as a clinical object and an epistemic thing (Rheinberger 1997);
- opposing forms of social solidarity and obligation.

This analytical framework is thus based on the notion of biobanks as forms of governing life. Put simply, biobanks are collections of human biological materials combined with information (personal, medical, genealogical, etc.) and are thus crucial sites within contemporary biomedical research, since they provide samples and bio-information for genomics (Gottweis and Lauss 2011) and stem cell research (Waldby and Mitchell 2006).

According to Gottweis and Lauss (2011, 62-65): "Biobanks consist of highly complex and multiconnected networks […] stretching to a variety of nodes such as medical schools, hospitals, and health care provision". Biobanks are not only techno-epistemic technologies linking several sectors of scientific research and healthcare provision, they are also a sort of socio-technical interface between biomedicine and society. As Gottweis and Petersen pointed out, biobanks:

> …constitute a complex process of representing science, bodies, medicine and technology. They are a form of governing life and involve a multitude of actors such as scientists, patients, or industry who actively engage in building, describing and operating biobanks and who contribute to translating particular scientific-technological visions into material practices. They involve the deployment of physical infrastructures, artefacts, machines, tools, instruments and buildings. […] Biobanks always connect with society, culture, the economy and politics. Biobanks incorporate visions for the future of medicine and healthcare, offer resources to medical research and the pharmaceutical industry and embed images of the patient, the citizen, collective identity and society.
>
> (Gottweis and Petersen 2008, 9)

As a form of governing life, the way in which a biobank restructures "the boundaries between the scientific/technological, the social, the cultural, and the political" (Gottweis 2008, 22) depends on the institutional arrangements in which it operates. Gottweis and Lauss identified three different types of biobanks:

> (a) the entrepreneurial biobank model that is often carried out in a public private partnership between a commercially oriented entity and different state institutions; (b) the biosocial model in which patient activist groups promote, fund, and facilitate the creation and operation of a biobank; and (c) the public biobank model in which biobank networks are supported mostly through taxpayers money and nonprofit research funding organizations.
>
> (Gottweis and Lauss 2011, 66)

Each of these types implies a different form of governance: a top-down model in the public biobanks, a bottom-up one in the biosocial and "horizontal exchanges between sellers and buyers, producers and consumers" (Gottweis and Petersen 2008, 8) in the entrepreneurial model based on market logic. This distinction is particularly suitable because UCB biobanking is organized into two main models: the network of public UCB biobanks for allogeneic donation, and the commercial sector of private banks for the autologous or family storage. And, as I shall show in the following sections, the institutional arrangement of UCB biobanking implies different routes to UCB bio-objectification and different ways to articulate the relationship among scientific research, the healthcare system and the market, but also because it exerts effects on the articulations between biomedicine and society.

Therefore, in what follows, first I shall analyze the process of UCB's transformation from a waste material into a valuable tissue. Using the notion of bio-objectification, I shall show how this transformation occurred through a two-way interaction between the social world of basic biological research and that of clinical applications. Second, by drawing on the notion of biobanks as a form of governing life, I shall show how bio-objectification takes place in a particular socio-technical infrastructure whose institutional arrangement defines the articulation of the relation among biomedicine, economy and society. The aim of this paper is to call into question the idea that the modern bioeconomy coincides with the market economy framework and thus means the commodification of life and its cellular and molecular components. On the contrary, I shall show that the economic regime of biovalue exploitation is the outcome of institutional arrangements created by the actors involved, and that these arrangements have implications for the way in which a society is organized.

The paper is based on discourse analysis carried out on articles published in scientific journals – retrieved in PubMed by searching for 'Placental and Cord Blood banking' – and on documents produced by bioethics and medical professional bodies (American Academy of Pediatrics 1999; Royal College of Obstetricians and Gynaecologists 2006; European Group on Ethics in Science and New Technologies 2004; Committee on Obstetric Practice 2008), as well as corporate communications available on the websites of private UCB banking companies. Scientific papers retrieved in PubMed were subsequently selected according to various criteria. The historical analysis of the development of UCB bio-objectification was carried out on the basis of review articles (e.g. Gluckman 2009; Navarrete and Contreras 2009) and therefore considered milestone papers in the evolution of UCB clinical application and UCB-derived stem cell science – retrieved by analyzing bibliographic references. Another set of articles included in the analysis dealt with the establishment of UCB banks and the development of techniques for storing and processing UCB.

Finally, articles concerning ethical issues in UCB biobanking and the debate between public and private UCB banks were collected. In this way, a corpus of 108 papers published in the period 1974-2009 (i.e. from the discovery of the presence of HSC in UCB to the 20th anniversary of the first UCB transplant) was analysed through qualitative discourse analysis aimed at detecting both the construction of UCB-derived stem cells as clinical and epistemic objects and economic goods, and the production of social entities and relations. This approach recovers the constitutive function of discourse – as practice that forms the objects of which it speaks (Foucault 1972, 64) – and is thus constitutive of social identities, social relations and systems of knowledge and belief (Fairclough 1992). But it is less focused on the (re)production of power relations, dominance, ideology and hegemony within discursive practices as in critical discourse analysis (Fairclough 1995; van Dijk 1993), and more on the construction of the image and the role of individuals as citizens and/or consumers in the regimes of economic relations and biopolitics models embedded in the various institutional arrangements of UCB biobanking. This analytical approach was also applied to the analysis of documents produced by bioethics and medical professional bodies, and to the corporate communications of private UCB banking companies retrieved on the Internet by searching for umbilical cord blood banking companies. Analyzing corporate communications and websites was necessary because scientific papers and the documents of medical professional bodies tend to be biased against private biobanking. Following social science analysis of UCB biobanking (Martin *et al.* 2008b; Brown and Kraft 2006) and articles dealing with the controversy between public and private UCB biobanks, I selected the most cited and largest private companies and then analysed their advertising and communications.

3. The Bio-Objectification of UCB from Bedside to Bench

The umbilical cord as a site of haemopoiesis was discovered in the 1970s by Knudtzon (1974), who detected colony-forming cells in human UCB. Unclear at that time was both the nature of these cells and their function, to the point that Knudtzon wrote that "they might merely represent an escape from the bone marrow into the circulation" (Knudtzon 1974, 360). Reported in 1982 was the "identification of a unique class of human hemopoietic colony-forming cells with extensive ability to generate progenitors for secondary colonies" (Nakahata and Ogawa 1982, 1324). However, confirmation that UCB is an effective provider of HSC for haematopoietic reconstitution came only in 1988, when a team led by Eliane Gluckman transplanted UCB into a child in order to cure Fanconi anaemia (Gluckman *et al.* 1989). Interestingly, the laboratory-based confirmation that UCB contains HSCs well within the range of BM stem cells

"that have been associated with successful autologous and major histocompatibility complex-matched allogeneic bone marrow transplantation" (Broxmeyer *et al.* 1989, 3830) was forthcoming only one year later. Indeed, Smith and Thomson recounted the story of UCB science and clinical application in these terms:

> The study of umbilical cord blood began in 1982, when discussions between Broxmeyer and Boyse led to laboratory experiments that suggested that umbilical cord blood contained hematopoietic stem cells that might be suitable for transplantation [...] This laboratory-based research led to the collection and banking at Indiana University in Indianapolis of cord blood from the siblings of children who were in need of transplantation. Gluckman et al in Paris were the first to use a sibling cord blood unit that had been banked by Broxmeyer at Indiana University to transplant a child with Fanconi anemia.
>
> (Smith and Thomson 2000, 127-8)

Similarly, Gluckman (2009) described the clinical application of UCB as the outcome of the collaboration between the laboratory researches of Broxmeyer and her clinical work. The interesting features of this narrative are: (a) the intertwining between laboratory-based research and the clinical setting, and (b) the central role played by the banking of UCB.

The first point testifies to how the clinical application of UCB did not follow the linear model of translational medicine – which postulates a one-way flow from the bench to the bedside – but a two-way interaction between basic biological research and medicine, as described by Keating and Cambrosio (2001) in their study on cytogenetics. In several respects, the history of UCB science and clinical application resembles that of BM, where the first clinical trial was carried out in 1957 before the development of the biological knowledge of HSC (i.e. prior to developing knowledge on the identity of HSC, techniques for its enumeration, and its functioning mechanism). Both BM and UCB clinical applications were developed in a "regime of hope" which proceeded "on the basis of speculative potential therapeutic efficacy, even in the absence of a clear demonstration of underlying principles" (Martin *et al.* 2008a, 32). Authors pointed out that the development of BM transplantation was "characterized by a clinically driven shift from the imagined possibilities of the clinic back into exploratory fundamental research" (Martin *et al.* 2008a, 33). Similarly, in the case of UCB, it was successes in transplantation that prompted the basic research on the features of stem cells contained in it. The clinical application of UCB transplant ran in parallel with laboratory-based research on UCB-derived stem cells. During the 1990s, in fact, clinical applications of UCB transplants were carried out notwithstanding the scant reliability of quantitative assays for HSCs in humans (Gluckman 1996). For example, Broxmeyer *et al.* (1992, 4112) maintained that "the numbers of human repopulating cells cannot yet be calculated". Still to-

day, the suggested minimum quantity of UCB stored is empirically established – it is recommended to store only the largest units of more than 70ml in order to have at least $\geq 2x10^5$ CD34+ cells/kg – even if the optimal cell count and the relation between CD34+ cells and successful engraftment is still not known (Gluckman 2009, 623). CD34+ cells are cells expressing CD34 cell surface protein, which mediates the attachment of stem cells to stromal cells and thus permits haematopoiesis. The CD34 surface marker is thus considered a marker for HSCs, and the assay of CD34+ cells is used to estimate the number of HSCs in a given sample.

However, as Martin *et al.* (2008a, 33) have shown, the identity of HSCs in terms of CD34 surface makers is contested within the bench community, but it is stabilized in practice in clinical protocols (see also Brown *et al.* 2006, 338). In other words, this is another example of the non-linearity between the bench and the bedside in the clinical application of UCB-derived stem cells.

In general, the history of UCB application shows a two-way flow from the bedside to the bench. Indeed, while clinical haematologists transplanted UCB – and demonstrated the therapeutic efficacy of UCB transplant also in HLA mismatching settings (Kurtzberg *et al.* 1996; Rubinstein et al. 1998; Wagner *et al.* 1996) – experimental hematologists were showing that compared with BM, UCB contains a more primitive cell population that has more in vitro and in vivo proliferative potential (Hao *et al.* 1995). Similarly, while clinicians successfully used UCB stored in biobanks, laboratory scientists were developing techniques to reduce the volume of stored UCB units while avoiding the loss of viable HSCs and the use of toxic cryo-preservants (Rubinstein *et al.* 1995; Denning-Kendall *et al.* 1996). More interestingly, the shift of UCB transplant from a "investigational" procedure (American Academy of Pediatrics 1999, 117) to a routine clinical practice (Gluckman 2009) was prompted principally by the publication of statistical analyses on the outcomes of transplant (Rubinstein *et al.* 1998; Eapen *et al.* 2007) and by reviews of follow-up studies (Navarrete and Contreras 2009). This two-way relationship between the bench and the bedside was made possible by a peculiar institutional setting: the university hospital or the close association and proximity between clinical and research institutions. As in the case of BM transplant (Martin *et al.* 2008a), such proximity fostered collaboration between clinicians and scientists and created an international epistemic community of both UCB practitioners and UCB stem cell scientists.

The second point of the narrative quoted above refers to the role of biobanks. In fact, the development of both UCB transplant and UCB stem cell science would not have been possible without the establishment of UCB biobanks. Indeed, in order to be available for both transplantation and experimentation, UCB should be collected, tested, processed, preserved and distributed. The first UCB biobanks were set up in universities and public hospitals (Armitage *et al.* 1999; Lazzari *et al.* 1996; Rubinstein *et al.* 1994), and it was in these infrastructures that knowledge on

UCB stem cells and technologies to improve its clinical use and preservation were developed. Therefore, UCB biobanks are both crucial nodes in the network linking institutions (laboratories, universities, research centres, hospitals and health care providers) and the sites in which the complex and heterogeneous web of knowledge, expertise, devices, technologies and biochemical substances coalesces in the process of UCB bio-objectification. The bio-objectification of UCB takes place mainly in UCB biobanks through a process termed UCB biobanking, that is, the set of "processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution of cord blood units" (NetCord-FACT 2013, 8), since a UCB unit "is the end-product of a series of processes" (NetCord-FACT 2013, 58).

The bio-objectification of UCB starts with the process of collection at the moment of delivery, thanks to an articulation with changes in birthing practices. As Brown (2013) has illustrated, from the late 1960s onwards, obstetric and midwifery manuals and guidelines recommended umbilical cord clamping immediately after the delivery in order to reduce maternal post-partum haemorrhages. This means that the blood in the umbilical cord and placenta is not transferred to the newborn, and thus becomes available to collection, since it has been demonstrated that minimizing the time between infant delivery and cord clamping increases the volume of UCB, and thus of HSCs (Donaldson *et al.* 1999). Moreover, obstetricians or gynaecologists must obtain informed consent from the prospective mothers, and they must also generate a medical record regarding the pregnancy and the medical history of the mother and her family. This is a first step in the process of "informationization" (Gottweis 2008, 27) by which the biological is transformed into information inserted in a computerized database. Similarly, after the umbilical cord has been clamped, the blood contained in it should be drained by gravity (and exploiting placenta pulsation), using a sterilized needle and a catheter, and then gathered in a blood collection bag containing an anticoagulant (NetCord-FACT 2013). Therefore, collecting UCB entails both an articulation of biomedical practices and a network of technologies, devices and substances. In other words, what is sent to a UCB biobank is a tissue partially informationalized and already processed.

The second step of UCB bio-objectification is carried out at a UCB biobank – or a set of UCB processing facilities linked to the biobank – and entails analysis of the UCB units (tests for genetic diseases and microbial contamination, cell count and cell viability assays, and HLA typing), and other UCB processing procedures: volume reduction and cryopreservation. Both procedures involve the use of devices and biochemical substances: centrifuges, Hydroxyethyl Starch to separate HSCs from red cells and plasma, Dimethyl Sulfoxide as cryo-protectant, freezing bags, metal canisters and freezers with a monitoring system (NetCord-FACT 2013). When processed UCB units are stored in a cryopreservation de-

vice, the entire documentation, comprising both biological and technical information, is inserted into a database through a validated system.

The UCB as the end-product of this socio-technical network of processes is something very different from what was once discarded; it is now a biotechnologically manipulated thing available both for clinical application and for biomedical research. In a biobank, UCB has two different ontological statuses: 1) as a processed tissue which is stored in a specific place (a freezer); 2) as a record of medical information inserted in a database which makes it accessible to international electronic search systems (like the international Bone Marrow registry). It thus flows worldwide in a transnational network of computer databases; and when it is identified as suitable for a transplant, also the tissue can flow transnationally in a network of UCB banks, hospitals and transplant centres.

It is worth noting that after the transplantation, the informational ontological status of UCB does not cease existing; not only because the documentation must be conserved, but also because now generated is a new medical record regarding the process of engraftment and the follow-up on the transplant procedure. Again, the UCB unit continues to exist with a double status: as an engrafted tissue in the recipient (in which regenerates haematopoiesis), and as a medical record regarding the transplant and the process of engraftment registered in the biobank's database and thus available to the scientific literature on the outcomes of cord blood transplantations. The bio-objectified UCB is thus an immortal entity.

4. Constructing Communities in the Public UCB Biobanking System

The general process of UCB bio-objectification transforms what was once a discarded material into an usable object, but it does not define the form of its exploitation and valuation. This depends on the institutional arrangement in which the UCB biobanking takes place. The UCB biobank is thus the key node in a network connecting hospitals (where UCB is collected) and universities and transplant centres (where UCB is used as an epistemic and clinical object), and it is also the main site of UCB bio-objectification. However, the institutional arrangement of UCB biobanking determines the specific route to UCB bio-objectification and thus the form of the co-construction of this medical technology and subjectivities and social rationalities.

After the first successful UCB transplantation, researchers and clinicians started to establish biobanks to store UCB units. The first public UCB biobank was set up in New York in 1991 (Rubinstein *et al.* 1994), and at the beginning of the 1990s others were established in Paris (Gluckman *et al.* 1993), London (Armitage *et al.* 1999), Milan (Lazzari *et al.* 1996) and in other Western countries. From the outset, UCB practi-

tioners highlighted the need for forms of international cooperation and coordination among biobanks and clinicians and researchers in the field of UCB transplantation and HSC science. The Eurocord group, an organization aimed at promoting cooperation and developing standards in the field of UCB science, banking and clinical application (Gluckman 1996) established the International NetCord Foundation, a non-profit association of UCB banks which has nearly 35 member banks and registries representing about 51% of the global supply of publicly banked cord blood (NetCord 2013). NetCord manages an integrated database that connects multiple UCB banks registries worldwide. But it operates also for the creation of standards and accreditation criteria for UCB biobanks: together with the US Foundation for the Accreditation of Cellular Therapy (FACT) it publishes a manual defining standards for UCB collection, processing, testing and banking (NetCord-FACT 2013). In this way, along with national and international biobanks' regulations, NetCord and FACT have created an international accreditation system, and thus a set of standards, which applies to UCB biobanks (both public and private) participating in this network. In general, the public UCB biobanking system is organized as an international network (Brown *et al.* 2011), and it is sustained by an institutional architecture consisting of medical professional and governmental organizations.

Within this institutional arrangement, UCB is bio-objectified in such a way that UCB "has gained new status as a natural resource" (Annas 1999, 1521); UCB practitioners, indeed, consider UCB to be a human tissue, so that they apply the rule that "no part of the human body should be commercialized and that donation of organs or cells should be free and anonymous" (Gluckman *et al.* 1996, 108). Defining UCB as a public resource supplied and managed in a redistributive economy framework, means that UCB donation is regarded "as a rare and praiseworthy example of altruism" (Annas 1999, 1522) "for the benefit of society" (Pinch 2001, 59). In this sense, UCB donation is framed "as a gift rather than a commodity" and society can claim ownership "to promote the common good" (Sugarman *et al.* 1995, 1784).

The public UCB biobanking system operates according to the logic of Foucauldian bio-politics of the population: it is a form of governing life that disciplines bodies (and their parts), regulates populations (Gottweis 2008) and creates an identification between "the supply of blood, organs and other bodily fragments and the body politic as contained within the limits of the nation-state [which generates] a relationship between the anonymous solidarity that links donor and recipient and the constitution of a subjecthood that is, simultaneously, biological and national" (Santoro 2009, 18). As Brown (2013, 98) has summarized, public UCB biobanking "is promoted with reference to a solidaristic moral economy of gift and altruistic participation in imagined community and nationhood". For example, when the European Commission asked for an opinion on UCB biobanking from the European Group on Ethics in Science and New

Technologies (2004, 18), the latter stated that public UCB banking "implies an act of solidarity or generosity" and "contributes to the social cohesion", while private companies represent "a more general shift […] from a health system based on solidarity" which has characterized the European social welfare model. In this way, public UCB biobanking also constructs subjectivities and social rationalities: citizens as part of the body politic are requested to contribute actively to the public good by donating UCB, and a redistributive tissue economy operates to sustain this social solidarity and bond.

The subjectivity of citizens is also constructed in the biomedical and bioethical literature on UCB donation. For example, the American Academy of Pediatrics has criticized the advertising of private UCB biobanks, which promise a biological insurance against possible future illness, because "families may be vulnerable to emotional marketing at the time of birth of a child" (American Academy of Pediatrics 1999, 116). Citizens are defined as vulnerable to the mass media advertising and direct-marketing approach of private companies which, through "dramatic, impassioned language" (Pinch 2001, 56), sell a service based on a unrealistic prospects and on a misleading use of the expression 'biological insurance' since the probability that autologously stored UCB will be of use "approaches to zero" (Annas 1999, 1523; Committee on Obstetric Practice 2008). Thus, public UCB practitioners have criticized private biobanking not only because it results in a wastage of resources and damage to public health (Royal College of Obstetricians and Gynaecologists 2006; Perlow 2005), but also because it exploits the vulnerability of prospective parents.

To summarize, in public UCB biobanking, citizens are constructed both as members of the body politic who must participate in the biopolitics of the (national) population for the common good, and as subjects vulnerable to misleading advertising regarding the range of uses of UCB in biomedicine – subjects who must be protected by the state. This framework entails not only the definition of UCB as a public resource for the good of the body politic – and thus a redistributive economy supporting social solidarity – but it more radically affects the ontological and technical status of the bio-objectified UCB.

Martin *et al.* (2008b, 137) have pointed out that public UCB biobanks operate in what they call a "regime of truth": UCB is stored for use in its current applications, and research on UCB is carried out "on the basis of current present-oriented 'evidence-based' support for existing applications" of UCB stem cells. By contrast, private UCB biobanks work in a regime of hope, where the autologous collection is not only aimed at existing applications in oncology and haematology but at the future prospect of regenerative medicine (Brown and Kraft 2006; Martin *et al.* 2008b). It is worth noting that the possible use of UCB-derived stem cells for regenerative medicine is also explored in public research settings – e.g. the study and characterization of mesenchymal stem cells contained

in placenta and umbilical cord tissue, or the possibility to differentiate UCB cells into non-haematopoietic cells for use in organ repair. However, some scholars (Brown and Kraft 2006; Martin *et al.* 2008b) have stressed that public UCB biobanks deal more with the improvement of current UCB applications (e.g. the expansion of HSCs for treating adults as well), while private banks highlight more their possible future use in regenerative medicine. For example, literature reviews of UCB transplantation mention only the current application of UCB-derived stem cells in haematology (e.g. Navarrete and Contreras 2009) while the advertising of private UCB banks or articles explaining the work of research centres linked to private biobanks (e.g. Bardelli 2010) report experiments and clinical trials using UCB-derived stem cells in regenerative medicine.

Hence it seems that there are different expectations in the two institutional settings about the clinical use of UCB-derived stem cells and, accordingly, they are transformed into different epistemic things. Finally, according to Santoro (2009), UCB processing procedures vary between the public and the private sector, and private companies do not perform the quality controls and transformation procedures adopted by public UCB biobanks. Santoro (2009, 16) points out that we find two different bio-objects in the public and private sector.

5. Constructing Citizens as Consumers in the Private UCB Biobanking Sector

Contemporaneously with the establishment of the first public UCB biobanks, also private biobanks were set up in several Western countries (e.g. the Cord Blood Registry in San Bruno, California and ViaCord, Boston). Martin *et al.* (2008b) have counted 112 private UCB banks operating worldwide and which store some 881,000 UCB samples. These biobanks are commercial enterprises which sell the possibility to store UCB for future use by the autologous donor (i.e. the child) or family members. UCB thus acquires a biovalue as a biological asset: it takes the form of economic capital for the private biobank, and of a speculative investment for parents. Accordingly, UCB biobanking is defined by private companies as a "biological insurance" (Wolf 1998, 5) or "a form of property whose value is oriented toward the biological future" (Waldby and Mitchell 2006, 125). By using expressions such as "peace of mind" (CryoSave 2013), "store your child's future" (Smart Cells 2013a) or "put a little something away for a rainy day", private companies try to induce new and prospective parents to invest in a technology that may, in the future, prove to save the life of family members (Brown and Kraft 2006, 314; Brown *et al.* 2006). As Brown and Kraft have pointed out, the language and metaphors of banking, investment and insurance refer not only to commercialization, but also to aspirational emotions, affectivity, expecta-

tions and future health risks: UCB banking promises to offer "a simultaneously metaphorical and material indemnity against some unspecified, though feared, future disease disaster" (Brown and Kraft 2006, 316).

On the one hand, this future and risk-oriented discourse is clearly linked to the neoliberal form of government that produces individuals who "will govern themselves, master themselves, care for themselves" (Rose 1993, 291-296) by acting through "a kind of privatization of risk management […] in which the citizen adds to his or her obligations the need to adopt a calculative and prudent personal relations to risk and danger". In this way, the subject is constructed as a calculative agent who negotiates his/her own health in a market of biological services. This image is mirrored in novel forms of interaction with the field of biomedicine and biomedical research that some authors term 'biological citizenship', a new form of activism related to biological and health conditions which denotes the active engagement in biomedicine by formulating life strategies, developing techniques for the everyday management of physiological conditions, or by actively participating in biomedical research (Rose and Novas 2005).

On the other hand, this discourse is built on notions of kinship responsibilities. Parents are encouraged to do something against some potential future loss or the uncertainties of future disease (Brown 2013); in other words, to take care of the future of their family members. Brown and Kraft (2006, 325) thus define autologous UCB preservation as a "techno-moral entry point into an increasingly private linkage between parenting and biomedicine" with a "set of 'blood ties', reproductive duties and responsibilities connecting private consumers with biological services".

The private UCB banking sector is thus organized according to what Gottweis and Lauss (2011) term the 'entrepreneurial model', which is based on market logic and operates through exchanges between sellers and consumers. It represents a particular articulation of the relationship between biomedicine and society and a form of governing life based on a neoliberal notion of biopolitics. Accordingly, the private UCB banking sector is characterized as "a neoliberal privatised market where individuals or families make an exclusive claim on a […] biological asset that remains private property" (Brown *et al.* 2011, 1115; Santoro 2009). As we have seen, in fact, this arrangement of UCB biobanking is built on, and in turn creates, an ideal of a self-governing citizen who manages his/her own health. Moreover, by using a rhetoric of indemnity, insurance and investment, it also creates a particular subjectivity: the individual is no longer a vulnerable member of the body politic (who has to participate in the common good), but a calculative and prudent consumer under an ethical duty to take care of his/her relatives, who maximizes health and well being by negotiating in a free market of biological services. Therefore, private biobanking creates a different articulation of the co-construction of medical technologies and subjectivities and social ration-

ality.

Moreover, it entails, and in turn enables, a different route to UCB bio-objectification.

Firstly, UCB in private biobanking is not a public resource but a private good, even if it is not properly a commodity. As Brown (2013, 99) has highlighted, parents pay a fee to retain proprietary control over an asset diverted away from the globally distributed public UCB exchange systems (see also Brown *et al.* 2011). For what is sold and bought is not the UCB units, but the storage service. As Waldby and Mitchell (2006, 124) have noted, the private UCB account creates a form of possession which excludes the commodity form, since the value of UCB resides in its not being alienated, in its not having an exchange value.

Secondly, this private good or biological asset has a value which resides in the biological future, and more precisely in "the future-oriented promissory value of regenerative medicine […] embedded largely in future potential rather than present utility" (Martin *et al.* 2008b, 132; Brown 2013; Waldby and Mitchell 2006). Indeed, in their advertising, private UCB biobanks report both the current clinical application of UCB and the experimental setting and clinical trials using UCB for heart, lung and liver diseases (Smart Cells 2013b). Some private biobanks, moreover, operate directly in the field of stem cell research and regenerative medicine (Martin *et al.* 2008b) by promoting and carrying out research on non-hematopoietic stem cells – such as the mesenchymal stem cells – harvested from umbilical cord tissue to repair organs (Bardelli 2010). As mentioned above, UCB in the private sector is thus a different epistemic thing and it is bio-objectified more according to a regime of hope – i.e. the expectations surrounding the future of regenerative medicine – and less according to the regime of truth of established clinical settings in oncology and hematology – in which the public UCB biobanking system operates (Martin *et al.* 2008b). Therefore, in contrast to the public system, the institutional arrangement of the private sector implies a specific route to UCB bio-objectification that defines a different status of UCB, as both a good and an epistemic thing for biomedical research, but also entails a different co-construction of subjectivities and social rationalities.

6. Conclusion

This paper has explored the bio-objectification of UCB as it was transformed from waste material to a valuable life-saving tissue in clinics, and to an epistemic thing in stem cell research. The bio-objectification of UCB has taken place through a two-way interaction between basic biological research and medicine by virtue of a particular institutional arrangement – that of university hospitals – in which different biomedical expertises could cooperate. In this network of institutions and expertises,

a key role is played by biobanks, which are the strategic nodes of interconnection and the material places in which the bio-objectification takes place. Therefore, I have analyzed two opposing articulations of the institutional arrangement of UCB biobanking which give rise to different routes to UCB bio-objectification. These routes are, furthermore, connected to different framings of UCB's status as both a good and an epistemic thing, and therefore to different economic regimes of biovalue exploitation, subjectivities and social rationalities. Indeed, biobanking is a form of governing life. Hence different arrangements in UCB biobanking entail different models of biopolitics.

In the case of the public UCB biobanking system, UCB is bio-objectified as a tissue for its application in established clinical settings (a regime of truth), and it is defined as a public resource managed and exchanged in a redistributive bioeconomy according to a state-led biopolitics of the population, in which the individual body and its component parts are identified with the body politic. Accordingly, citizens are constructed as individuals having responsibilities for the community's good. In this sense, donation is an altruistic act which creates social solidarity and cohesion, and reinforces social bonds. In the case of the private UCB biobanking sector, instead, UCB is bio-objectified as a form of biological insurance, a private corporeal asset, oriented toward the future of regenerative medicine development. It is both a private good and an epistemic thing for the regime of hope of stem cell research. This asset does not have exchange value as a commodity; rather, what is sold and bought is the possibility to store it as an indemnity against possible future risks. In fact, what is exchanged in the market is a biological service, not a material good. In this sense, private biobanking operates according to a neoliberal biopolitics in which the citizen is constructed as a responsible, calculative and prudent consumer under an ethical duty to take care of his/her relatives, and who negotiates the health of his/her relatives in a market of biomedical services.

The case of UCB bio-objectification opens an interesting window on the contemporary bioeconomy because it sheds light on diverging articulations of the process of exploiting biovalue. It shows how different institutional arrangements can give rise to different forms of bioeconomy (a market vs. a redistributive economy) and, thus, how different routes to bio-objectification entail opposing models of governing life, which, in their turn, imply the construction of diverging subjectivities and social solidarities and bonds. The case of UCB invites us to explore how the market logic in the political economy of life itself is not an inevitability, but rather the outcome of strategic articulations of the actors involved and of the institutional arrangements in which both bio-objectification and biovalue exploitation take place. In this sense, an economic regime of biovalue exploitation is not only socially and politically shaping, but it is also socially and politically shaped. Instead of considering bioeconomy in its neoliberal market framework as a given, we should investigate the in-

stitutional arrangements, power relations, and agency of the collective and institutional actors shaping the emerging economic regimes of biovalue exploitation.

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What's Being Translated in Translational Research?

Making and Making Sense of Data between the Laboratory and the Clinic

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Abstract: This paper examines translational or "bench to bedside" research – which is promoted as the application of biomedical knowledge to medical practice – at the interface between the laboratory and the clinic. Referring to the field of "metabolomics", the post-genomic study of metabolism, it argues that efforts to make and make sense of data emerge as one of the key challenges in translational research. Focusing on case studies of translational molecular imaging, clinical databases, and surgery, I explore how metabolomics researchers and clinicians have fundamentally different notions of what data entail. I then argue that metabolomics researchers experience great difficulty not in generating but in interpreting statistical and metabolic data. Finally, I examine the future visions of translational metabolomics research to suggest that data and automation cannot replace judgment and interpretation in clinical practice. Ultimately, the paper problematizes the changing form, role, and value of "data" in post-genomic efforts to carry out translational research.

Keywords: data; metabolomics; translational research; objectivity; statistics.

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1. Introduction

On a warm summer morning, I am standing in a laboratory watching a post-doctoral researcher named Sarah interact with a surgeon-in-training named Joseph. Wearing pristine white laboratory coats that reach down to their knees, they are working on a project to develop molecular markers of cancer within the field of metabolomics, the post-genomic study of metabolism. After completing the clinical component of his surgical train-

ing, Joseph has elected to carry out a PhD on the metabolic properties of cancer, in an attempt to gain insight into the integration of laboratory and clinical approaches to disease diagnosis and treatment. Despite being through more than a decade of surgical training, however, Joseph's laboratory experience is minimal. Having spent the few months of his PhD collecting samples from the surgical operating theatre, Joseph has spent little time in the metabolomics laboratory, and is a self-proclaimed "complete beginner". He is adept with surgical tools, but has none of the skills required to carry out metabolomics laboratory experiments or analyze metabolomics data.

Throughout the morning, Sarah has been reprimanding Joseph for his improper handling of tissues and samples, and her frustration is obvious. Joseph has just exited and re-entered the laboratory while wearing used gloves, and Sarah is upset that this has potentially contaminated the laboratory environment. Joseph, Sarah exclaims, has spread bits of tissue across the computer, freezer, door handle, and anything else he has touched while wearing gloves. Sarah feels that this is a reflection of Joseph's lack of care and concern for the rigor of metabolomics experiments. Joseph's response is to try to defend himself – by explaining that in his clinical work he is not used to changing gloves with such frequency – but Sarah is too flustered to listen to his reasoning.

Several days later, when I speak to Sarah about this incident, she explains her frustration with Joseph's supposed lack of interest and effort in experimental laboratory work. Because Joseph is busy doing surgical training and collecting clinical samples, says Sarah, he is not able to fulfill his duties as a doctoral student-in-training. Problematically, he prioritizes his patients over his experiments, and does not spend enough time learning how to do experiments from Sarah. As a result, Joseph has made critical mistakes handling the tissue samples and machines in the tenth floor laboratory. "He doesn't even know how to pipette" – Sarah says angrily – "and he doesn't actually know what research *is*". She emphasizes, in other words, that laboratory and clinical researchers have divergent notions of how and why to go about biomedical research.

Sarah's comments speak to the fact that clinical researchers and scientists are different not only in their cultures of professional training (Löwy 1996; Knorr-Cetina 1999), but also in their very notions of what constitutes biomedical practice and its objects of investigation. Sarah and Joseph's conflicts over sample handling embodied what other researchers described as a "gulf of understanding" between clinical researchers and scientists. Joseph's struggles with the practicalities of laboratory research – of learning how to use particular pieces of equipment, of attempting to balance the time demands of clinical work and laboratory research – were struggles on a more fundamental level to understand the ideologies and values of molecular, post-genomic research. As one clinical researcher commented, clinicians like Joseph were "not versed in the language of basic science, much less biochemistry and [data analysis]". Joseph was

not expected to have the same skills and knowledge about metabolomics experiments as Sarah, because his everyday clinical work entailed attention to patient needs and disease treatment. Similarly, laboratory researchers like Sarah were not accustomed to "looking beyond [patterns] into the clinical data, and trying to understand what's actually happened to the patient while they were in hospital". Ultimately, and as I discuss throughout this paper, such conflicts and tensions are reflective of the ways in which clinical and metabolomics researchers have different practices and ways of thinking about biology. Issues of communication and collaboration arise from different and overlapping sets of skills and knowledge about experiments, disease, patients and data.

2. Translational Research and Data

This paper begins with a vignette of Sarah and Joseph, because their interaction highlights some of the fundamental and recurring challenges faced within "translational research". Commonly referred to as "bench to bedside" research, translational research has become an increasingly important concept in the biomedical sciences over the past decade (Kohli-Laven *et al.* 2011; Davies 2012; Davies 2013). Often portrayed as the linear movement of knowledge from the laboratory to the clinic, translational research attempts to mobilize biomedical research towards the advancement of human health (O'Connell and Roblin 2006; Wainwright *et al.* 2006; Martin *et al.* 2008; Morgan *et al.* 2011). In such an account of translation, the laboratory and the clinical not only entail different technologies, practices, ideology, cultures, and norms, but are also brought together in unclear and contested ways (Rajan and Leonelli 2013). As this occurs, notions of disease are developed, reinforced, and negotiated at multiple points – and to varying degrees of success – throughout the process of translation (Friese 2013).

Amidst the complexity of these processes and relationships, this paper examines translational research in the context of the post-genomic sciences that seek to examine the combined effects of genes and the environment (Davies 2013). In these fields, research is characterized by the generation and management of data, such that statistical analyses and computation are increasingly central to the production of knowledge (Mackenzie 2003; Stevens 2011; Räsänen and Nyce 2013). Though there are many ways of examining translational research, this paper asks what we might learn from seeing translational research as an informational process: as an often problematic attempt to create, shape, and move data between the realms – conceptual and physical – of laboratory research and clinical practice. It focuses on the practices and negotiations that occur at the laboratory-clinic interface, examining how disease objects are enacted and problematized by researchers in everyday practice. At the in-

terface between the laboratory and the clinic (Fleck [1927] 1986; Löwy 1996; Keating and Cambrosio 2003), how do efforts to make and make sense of data emerge as one of the key challenges in translational research?

This paper examines translational research from the perspective of metabolomics, the post-genomic study of the molecules and processes that make up metabolism. Metabolomics is one of the fastest growing fields of post-genomic research (Dutton 2013), which includes high-throughput genomics, epigenetics, transcriptomics, and proteomics (Blow 2008). It involves efforts to create and analyze metabolic data with biochemistry and statistics, and ultimately to interpret such data in relation to states of health and disease (Nicholson et al. 1999; Nicholson and Lindon 2008). To discuss the challenges inherent in translational laboratory research, I draw from ethnographic fieldwork in the Computational and Systems Medicine (CSM) Laboratory at Imperial College London, one of the leading global metabolomics research centers, as well as interviews with members of the broader metabolomics community within the United Kingdom.

Methodologically, tracking translational metabolomics research in the CSM entailed observations of laboratory-based research on clinical samples, observations of interactions between laboratory researchers and clinical practitioners at meetings, and observations of and interviews with clinical practitioners who had been trained in laboratory methods and were carrying out metabolomics experiments. Because of a variety of efforts to implement molecular metabolic technologies in clinical settings, the CSM represents an ideal site to examine the complexities at the laboratory-clinic interface of translational research. Despite published accounts that allude to "clinical metabolomics" and the use of technologies for disease diagnosis and treatment (Collino *et al.* 2013; Xia *et al.* 2013), translational research and technologies in the CSM are not yet established within clinical settings, and do not yet involve interactions with patients. The research I describe in this paper involves preliminary findings to verify whether and how translational metabolomics technologies might be a possibility. Consequently, my account of translational metabolomics research itself demonstrates the non-linear, hybrid, and complex spaces and temporalities in which translational research occurs more broadly.

Overall, this paper argues that translational research is characterized by different – and at times opposing – articulations of what constitutes data, and of what value data has for biomedicine. Acknowledging that such definitions and values are highly dependent on the context in which data is developed and used, this paper explores how data in translational metabolomics research is something inherently statistical, molecular, moveable, and relational. Here, I define "data" as a series of techniques (Hadolt *et al.* 2012) and practices, which exist in various material and immaterial forms, and also entail constellations of people, technologies, objects, ideas, and values. Thus, the paper argues that translational re-

search is an inherently problematic process because the laboratory and the clinic entail different realms of practice, and thus enact different disease objects (Mol 2002). Metabolomics researchers and clinical practitioners have different notions not only of how disease should be researched and treated, but also of what constitutes disease and the data that relates to it. This creates challenges in assessing what definitions, roles, and values "data" should have in clinical practice, particularly as diseases and individuals are articulated in informational ways (Caduff 2012).

As metabolomics disease objects are translated into clinical practices – or as, in reverse, clinical objects are translated into metabolomics practices – the question becomes: what is and isn't being translated, and why? How might the case of metabolomics allow us to better understand the challenges faced by the implementation of data-intensive approaches in clinical settings? Or, how might the translational efforts of metabolomics help to re-conceptualize translational research, with its emphasis on data rather than clinical technologies and practices, in the first place?

To begin, I argue that translational research involves negotiations about the form and value of "data" at the interface between the laboratory and the clinic. I then argue that, despite invocations to the central role and value of data, metabolomics researchers experience great difficulty not in generating, but in making sense of statistical and molecular data. Finally, I argue that although laboratory researchers pose "data" as the solution to the challenges of translational research, human interpretation and judgment remain indispensable for the alignment of the laboratory and the clinic, signaling the practical limitations inherent in using statistical and molecular data to make sense of disease.

As a final note, in contrasting the laboratory with the clinic, my aim in this paper is not to essentialize different realms of practice, by claiming that there are fundamental differences between laboratory research and clinical work. Nor is my aim to portray translational research as the linear movement of laboratory technologies into clinical settings. My aim, rather, is to examine how the objects of biomedical research are articulated at the interface between the clinic and the laboratory, and how this provides a window onto the changing visions, forms of knowledge, and values inherent in 21st century biomedicine (Rajan and Leonelli 2013). It is, in other words, to examine how the increasing contact and hybridization of the laboratory and clinical sciences is resulting in changing technologies, practices, and approaches to the understanding and treatment of disease.

3. Metabolomics Meets Clinical Practice

In practice, metabolomics consists of a wide variety of techniques and practices for producing, manipulating, and making sense of data. By studying the "raw materials and products of the body's biochemical reactions, molecules that are smaller than most proteins, DNA and other macromolecules" (Pearson 2007), metabolomics provides a snapshot of an organism's "metabolome", the sum of its biochemical compounds and reactions (Hunter 2009). In experiments, metabolomics researchers analyze the composition of urine, blood, and tissue samples with biochemistry technologies like nuclear magnetic resonance and mass spectrometry. They then analyze this biochemical data with a variety of computational techniques, many of which involve multivariate statistics, a domain of statistics involving the observation and analysis of many variables simultaneously, often in large data sets. Such multivariate statistics include forms of analysis such as principal components analysis, cluster analysis, and neural networks, but more generally represent the underlying practices that allow researchers to grapple with large volumes of complex data (Levin 2014).

Throughout my fieldwork, researchers claimed that because metabolomics provided a real-time understanding of the dynamic outcome of the interaction between genes, metabolic pathways, and then environment, it was ideally suited for use in clinical settings (see Bhattacharya 14 December 2009). Researchers worked to develop the technologies in which complex metabolic data could be analyzed to produce molecular ways of diagnosing disease. They envisioned that nuclear magnetic resonance and mass spectrometry machines would exist in surgical operating rooms, allowing clinical practitioners to carry out clinical trials on breast and colon cancer, to generate biomarkers of disease, or to assess –or even predict – adverse reactions to pharmaceutical or surgical interventions (Kinross *et al.* 2011; Nicholson *et al.* 2012).

Such visions of the future of medical treatment and care speak to the kinds of science – and with this the kinds of technologies, ideologies, and values – being created, legitimated, and used during the development of translational research. To this end, many translational metabolomics technologies involved attempts to find a more "objective" alternative or complement to histopathology, a clinical technique involving the visual analysis of stained cells under a microscope. Histopathology plays a central role in the diagnosis of diseases like cancer, and has been the gold-standard of tissue analysis since the early 20th century (Löwy 2009). It is carried out by highly specialized professionals who examine stained cells under a microscope, and who look for morphological differences between normal and abnormal tissues. Through training and individual experience, histopathologists learn recognize abnormal tissues via morphological characteristics like shape, size, and position of cells. Researchers emphasize that such objective practices to can ameliorate or circumvent the

subjective influence of histopathologists and clinical practitioners. They make claims to "digital objectivity" (Beaulieu 2001; Beaulieu 2004), as they attempt to eclipse the manual possibilities of data analysis or reveal the "hidden meanings" of data. Metabolomics and histopathology, therefore, entail different "epistemic virtues" (Daston and Galison 2007: 40) about how knowledge should be produced and how objectivity should be achieved, as metabolomics places value on statistical measurements rather than morphological assessments.

One translational metabolomics project that I observed attempted to develop a molecular technique called matrix-assisted laser desorption/ionization mass spectroscopy imaging (MALDI-MSI), which uses mass spectrometry to develop "molecular maps" of tissues (Moody 2004). It enables researchers to make sense of the quantitative and spatial distribution of hundreds of molecules within a tissue sample, and therefore provides a molecular complement to imaging techniques like histopathology, immunochemistry, and fluorescence microscopy (Stoeckli *et al.* 2001: 493). Alaina, a post-doctoral researcher in the CSM with a background in statistical data analysis techniques, was developing MALDI-MSI as a "clinical platform", as a metabolomics technology that would be used in clinical settings to molecularly measure and diagnosis disease. MALDI-MSI, like many of the other technologies with which metabolomics researchers were working, was a relatively undeveloped and non-standardized technology. Thus, Alaina hoped to carry out a "proof of concept" experiment to determine whether MALDI-MSI data could be correlated with – or could perhaps improve upon – histopathology.

Much of Alaina's work involved efforts to understand the data generated by MALDI-MSI, by implementing and experimenting with a variety of statistical data analysis techniques. I watched her use such techniques to process large data files, and also to make sense of data that was too complex – that held too many data points and patterns – to be interpreted by eye. An analysis of MALDI-MSI data was impossible to do by hand, because each tissue slice contained twenty thousand pixels and tens of thousands of chemical peaks. Alaina used statistical techniques to find patterns and meanings that were "hidden" within biochemical data, and which would otherwise be inaccessible through visual analysis. She asserted that they provided an "objective" and "unbiased" means for researchers to explore those relationships within the data that were not readily apparent. But as researchers like Alaina make choices about sample collection, experimental methods, or data analysis techniques, experiments can never be without the influence of values, world views, or the bias of researchers (Räsänen and Nyce 2013). Data and the techniques through which it is produced are "always structured according to somebody's predispositions…and value choices all the way through" (Brooks 18 February 2013).

By using, experimenting, and playing with statistical data analysis techniques, Alaina produced particular understandings of biology and da-

ta (Levin 2014). Using the computing environment and programming language "MATLAB", she tested how various algorithms and sequences of code could find different patterns and points of comparison in her data. In working with such techniques, Alaina envisioned biological processes and anatomical structures as biochemical similarities and differences, mathematical patterns, and statistical clusters. In using data-intensive approaches to the study of biology, Alaina's concern was not with identifying the biological composition of the tissues, but rather with showing their statistical relationships and meanings.

One day, Alaina presented her MALDI-MSI research to a varied group of clinicians based in St. Mary's Hospital, one of the six research hospitals run by Imperial College London. This meeting of researchers and clinicians occurred under the banner of the National Institute for Health Biomedical Research Council (NIHR-BRC), which – in addition to several industrial partners and other public funders – funded several tens of millions of pounds of translational research activities in the CSM. The Imperial College NIHR-BRC was one of many groups established throughout the UK within outstanding NHS and University partnerships, with the goal of driving innovation and translational research into NHS practice (National Institute for Health Research 2012; Imperial College London 2014). Within the CSM, translational activities funded by the NIHR-BRC involved both the participation of clinically-trained researchers in metabolomics laboratory experiments, and also the application of metabolomics technologies and approaches to clinical issues.

Encouraged to present her work as a tool that could be used by clinicians in everyday research, Alaina contrasted the benefits of "modern" MALDI-MSI technology with "dated" histopathological approaches. She asserted that metabolomics could provide a more "objective" view of biology, because it relied on molecular and statistical technologies rather than the "subjective" decisions of histopathologists. MALDI-MSI would use large quantities of molecular data, which could quantitatively measure the extent and nature of disease, eliminating the reliance on the qualitative judgments of histopathologists. Comparing MALDI-MSI and histopathology, however, was not without its difficulties. At a basic level, researchers struggled to compare the format and resolution of MALDI-MSI data to those of histopathological images. While histopathological slides were analyzed by eye and were therefore not commonly digitized, MALDI-MSI data could only be generated, processed, and analyzed with the aid of computers, due to its size and complexity. The two modes of analyzing tissue, moreover, entailed fundamental issues of scale. While histopathology resolved images of individual cells, MALDI-MSI resolved images with "chunks of cells in each pixel". This presented key problems to the comparative analysis of the two techniques.

Despite these challenges, embedded within Alaina's presentation was the suggestion that MALDI-MSI could one day provide a superior alternative to histopathology. Though most researchers working on transla-

tional projects acknowledged that their work would likely operate in parallel to rather than replace existing clinical practices, Alaina insisted: "You would want to show that you can do *more* than histopathology". Her comments hinted at the notions of "digital objectivity" (Beaulieu 2001) embedded within metabolomics, as researchers made claims to knowledge through statistical data and automation, rather than the "manual possibilities" of clinical judgment and interpretation. In response, the clinicians to whom Alaina was presenting began a heated discussion. They wondered: how could a data-driven approach to biology replace a time-honored practice like histopathology? Would MALDI-MSI be able to inform disease diagnosis and treatment with the same success as histopathology, or would it fall prey to the false promises of other post-genomic technologies?

In their discussion, the clinicians raised concerns that while histopathology visualized biological markers within and between cells, MALDI-MSI visualized tissue as a "molecular signature of anatomy", as a set of statistical signals and patterns. MALDI-MSI, the clinicians acknowledged, could provide a new perspective on the biochemical composition of tissue, but its use in reasoning through the diagnosis and treatment of disease was less clear. As one clinician proclaimed:

> Of course you're going to add a whole lot of information that we simply don't have. But the real thing is to take the information and go back to the tissue, and say: 'What is this telling us about the pathogenesis that we would not know in any other way'?

At stake in this discussion was a challenge to the long-standing, and therefore institutionalized, practice of histopathology. However, also at stake were the different understandings of disease – and of the form and role of data – that metabolomics and histopathological practices espoused. For the clinicians, histopathology was valuable not because it shed light on tissue structures, but rather because it provided morphological markers of vascular invasion or tumor grade and stage, which though visual and qualitative, could be directly linked to disease diagnosis and treatment. Consequently, such an encounter between metabolomics researchers and clinicians hinted at the different notions of "data" and "disease" that existed at the laboratory-clinic interface.

In a similar contrast between metabolomic and clinical data, I spoke to several researchers involved in efforts to apply the data analysis techniques commonly used in metabolomics to clinical databases. These clinical databases consisted of routine physiological measurements, tests, and observations – such as blood glucose, blood oxygen levels, heart rate – with which researchers attempted to. This was an effort to visualize the complexity of clinical data, and to uncover previously hidden patterns or relationships between markers and outcomes of disease. Overall, this work embodied metabolomics' idea that the best way to learn about dis-

ease was to collect as much data as possible, in a process one of the researchers described as "data mining for improved information recovery". Creating more powerful tools to aggregate and look for statistical relationships within large volumes of data, researchers believed, would eventually translate into the improved diagnosis and treatment of disease.

Noah, a research fellow in the CSM who like Alaina had a background in statistical data analysis techniques, commented on the challenges inherent in carrying out such data analysis on a clinical dataset collected from the Intensive Care Unit (ITU) of St. Mary's Hospital. This was part of a translational research initiative within the CSM to integrate existing clinical data with "omics" data derived from metabolomics experiments into a broader database, which would contain a heterogeneous collection of data that could later be correlated with samples stored in bio banks (Mitchell and Waldby 2010). In building such a database, metabolomics researchers attempted to maximize the amount of data – in the statistical sense of the word – that could be made available and used to make diagnoses and predictions about patients. But first, for metabolomics to work in clinical settings, researchers emphasized that statistical and molecular data had to interface with – rather than replace – existing clinical data. Thus, the goal of the research was not only to establish the use of new metabolomics technologies within clinical settings, but also to find new and statistical ways of interpreting existing clinical data.

For Noah working with clinical data would be no different from working with the types of data metabolomics researchers routinely used. Though the type of data contained within the ITU dataset was certainly different, by performing certain steps and methods, it could be analyzed in the same informational way as metabolomics data. This involved building a "data matrix" – a two-dimensional table composed of rows and columns filled with numbers – and looking for patterns with complex statistical methods. "You build a table in a consistent way" – Noah said – "And after that, all of your data is always the same". For Noah, data existed in a specific, multivariate statistical form.

As Noah discussed his attempts to analyze clinical data, he not only revealed the value placed on the collection and analysis of large volumes of data, but also indicated that what counted as "data" was highly specific to metabolomics practices. For Noah, like Alaina, data consisted of statistical patterns and relationships. It relied on computerized algorithms, and ultimately commented on statistical features – referred to with the language of "parameters" or "signals" – rather than disease processes. Thus, as Noah emphasized that the study of disease could be optimized with particular techniques for manipulating data, he highlighted how the translational practice of metabolomics was enabled through large and specially-formatted datasets, and required the practice of particular techniques for generating and manipulating data.

Ultimately, in the examples of metabolomics research on tissues and clinical data, researchers place value on the collection and analysis of

complex statistical data, which they claim has the potential to transform disease diagnosis and treatment. However, what counts as "data" in such cases is highly contextual, and metabolomics researchers only attribute meaning to data once it takes on a particular – quantitative and statistical – form. While histopathological and physiological observations engender certain practices and meanings for medical practitioners, they do not on their own count as "data" within metabolomics research. In this case, translational research at the interface between the laboratory and the clinic entails not only particular types and forms of data, but also different notions of the role and value that data hold within medical practice. As metabolomics researchers attempt to generate and use statistical data, they also attempt to imbue such data with new and "better" meanings.

4. Making Sense of Metabolomic Data

While the previous section explored the form and value engendered by "data" in translational metabolomics research, this section explores the challenges faced by researchers in the interpretation of such data. Throughout my fieldwork, metabolomics researchers emphasized the recurring challenges of making sense of statistical and molecular data in relation to disease processes and outcomes. Despite the overt value they placed on the production and use of multivariate forms of data, they still acknowledged that the interpretation of such data posed a serious challenge to the application of metabolomics technologies to clinical issues. This section explores, therefore, how metabolomics researchers struggle to translate their findings into clinical practice, and to make their results meaningful in relation to clinical epistemologies or understandings of the body, which are oriented around patient care and disease outcomes.

I spoke with a former researcher in the CSM, who after moving to a different research group to work on the statistical analysis of large genomic datasets, had a unique perspective on the strengths and challenges that faced the field of metabolomics. Metabolomics, he emphasized, was very successful at the "analytical side" of experiments, at identifying and quantifying the biochemical components within biological fluids and tissues. The field had discovered a large number of biomarkers, the quantifiable end-products of metabolism that could be correlated with health and disease, and had generated a large number of medium- and high-impact papers. He emphasized, however, that in spite of its research productivity metabolomics struggled to relate statistical data to specific genes, metabolic pathways, or bodily systems. Statistical patterns, like those generated in MALDI-MSI experiments, had no inherent or pre-existing connections to clinical outcomes.

Similarly, another researcher in the CSM suggested that the main challenge faced by metabolomics was not in generating but in interpreting

statistical data. She said:

> It's not necessarily that it's too much information. It's just that it's complicated to put it all together in a meaningful fashion... We're still at a stage where, okay, x metabolite goes up and y metabolite goes down. And we don't really know what that means.

She emphasized that metabolomics was successful at establishing statistical relationships, or at correlating changes in metabolite levels to disease states. It struggled, in contrast, to relate such results to meaningful biological pathways or disease symptoms. She questioned whether the biochemical and statistical methods of metabolomics experiments could be translated, applied to, and used in clinical settings. It was all too easy to "hide behind the numbers" in metabolomics experiments, especially when working with statistical relationships and outputs that were abstract and easy to manipulate.

In general, the interpretation of metabolomics data was made difficult for several reasons. Firstly, the same biochemicals tended to recur across multiple experiments and analyses, making their biological relevance unclear. As a doctoral student commented to me, metabolomics experiments tended to highlight the biological role of the same "common" biochemicals. For example, lactate and hippurate, which play a role in cellular respiration and microbial metabolism respectively, were features of almost every experiment. The recurrence of common biochemicals was due to the fact that many compounds were involved in multiple metabolic pathways, which one researcher described as "metabolic hubs" of activity. The biochemicals commonly detected in experiments were the end result of multiple biological processes occurring simultaneously within an organism. Researchers questioned the spatial, temporal, and environmental relevance of their data (see Rajan and Leonelli 2013, 471-72). They sought to determine if common metabolites were detected because of disruptions of cellular respiration, the use of particular medications, or the ingestion of certain foods. In this way, the complex nature of metabolomics data – the fact that it was the end product of many biological processes – made its interpretation challenging.

The interpretation of metabolomics data was made difficult, secondly, because the biological origins of the biochemicals that metabolomics technologies detected were not always clear. I spoke with a researcher named Thomas about the challenges involved in making sense of the data generated by a technology called the "intelligent knife" (Balog *et al.* 2013). This was a surgical device that used mass spectrometry to analyze the molecular composition of tissues cut during electrocautery, in which the standard surgical blade was replaced by a device that cauterized and cut tissue with an electric current. According to Thomas, one of the main issues with making sense of the data generated by the intelligent knife was in figuring out what exactly the machine was measuring. The intelligent

knife was an incredibly complicated device that attempted to make real-time measurements and statistical analyses about the spatial composition and nature of tissues. Researchers using the technology therefore had difficulty understanding whether the machine detected biochemicals from tissues at the surface of or from deep within the surgical incision. Knowing the origin of the biochemicals was fundamental, because it had implications for the types of molecules, cells, or biological pathways involved in surgical treatment.

The interpretation of metabolomics data was made further difficult by the uncertainty surrounding the range of biochemicals that devices like the intelligent knife were able to detect. The intelligent knife, like other analytical instruments, had inherent capabilities and limitations that made it suitable for the detection of a certain range of biochemicals. This, as Thomas said, raised questions about whether the machine would be able to detect those biochemicals that were implicated in health and disease. Thomas emphasized that the intelligent knife could only detect fat-containing molecules that occurred at the surface of cells, whose importance in surgery and disease diagnosis was unknown. Metabolomics researchers were, as Thomas described, "at the mercy" of the machine's technical capabilities. He said: "There's so much of a metabolome out there, and we're just able to tell tissues apart by lipids because that's what we see". Though they were able to build customized statistical algorithms to analyze the machine's data, they had to operate within the parameters of the machine's commercially-determined settings. Thus, metabolomics researchers struggled to interpret the biological meaning of the intelligent knife data, primarily because they could not always say whether the biochemicals it detected played a key biological role.

In conclusion, this section suggests that the broad challenge facing metabolomics researchers is that of the interpretation – rather than the generation – of data. Researchers continually question how their statistical and biochemical data can be made meaningful or "translated" into metabolic pathways or bodily functions. The links between data and states of health and disease are not pre-given or objective, but rather are enacted through the everyday work of metabolomics research. As such, metabolomics researchers struggle not only to produce situated forms and values of data, but also, and perhaps even more importantly, to make such data meaningful in relation to clinically-relevant understandings of the human body. Such an emphasis and value on the generation and analysis of statistical data therefore side-steps a critical bottleneck in the process of translational research: it is not an easy or trivial question of how metabolomics data can or should be made meaningful in relation to disease treatments and outcomes.

5. Translation and Interpretation

In the previous sections, I explored the processes and challenges associated with the movement of knowledge between the metabolomics laboratory and the clinic. This section steps back slightly from the realm of everyday metabolomics practices, in order to examine how researchers envision the future "translation" of metabolomics technologies into clinical practice. Such future visions tell us about the different forms, uses, and values of data that exist at the laboratory-clinic interface. They portray translational research as an inevitable result of the development of sophisticated technologies and the collection of large volumes of data. But they also implicate, as mentioned in the previous section, fundamental issues of data interpretation. Consequently, this section asks: what role does interpretation and judgment have in translational research, and how does this contrast with metabolomics' emphasis on the value of particular kinds of data?

I spoke at length with William – a surgeon in the NHS who had completed his doctoral training in the CSM – about the future visions and possibilities of metabolomics technologies in clinical settings. William was the clinical coordinator of many of the CSM's translational research projects funded by the NIHR-BRC, and as one of the first clinician-researchers to spend an extended amount of time doing metabolomics research in the CSM, he had developed a concrete vision of the translation of metabolomics technologies to clinical settings. His work was therefore part of the growing impetus to bring academic medicine into contact with laboratory research through the figure of the "clinician-scientist", who would provide input on the development of laboratory technologies which were being translated into clinical practice (Wilson-Kovacs and Hauskeller 2011). It articulated the growing expectation within the UK that research occurs concurrently with clinical practice, and that clinician-researchers are the "essential conduit" for the translation of laboratory research from "bench to bedside and back" (Nature Publishing Group 2004).

For William, metabolomics would form a key platform for developing "surgical metabolomics" technologies, and would give researchers the unique ability to measure, model, and provide data about surgical interventions. William emphasized that surgeons had little knowledge of the metabolic pathways underpinning surgical treatments, or of how patients responded to things like anesthesia, drug treatments, or nutritional interventions. "It's a dense, complex system…and in surgery we have no measure of this system at all, it's totally primitive". William, like other researchers, turned to metabolomics for a way to make surgery more "scientific" and to provide quantitative data about patients before, during, and after surgical interventions. Researchers hoped that metabolomics would transform surgery, like histopathology and other clinical endeavors, from a profession based on subjective human experience to a techno-

logical intervention based on objective data. In asserting that surgical knowledge was subjective, researchers placed value on the data practices and techniques of metabolomics, and in particular on statistical and molecular techniques for diagnosing and treating disease.

As I spoke to William about the development of surgical metabolomics, he painted a vision of the future in which metabolomics technologies would be neatly packaged into self-contained boxes, and would involve easy-to-use, push-button interfaces. Such visions of the future, while they are clearly hypothetical, provide insight into the ideas and values that researchers have about the present and expect for the future (Brown and Michael 2003; Wainwright *et al.* 2006; Martin *et al.* 2008). William valued the use of post-genomic data in clinical practice, and, like other metabolomics researchers, emphasized the importance of generating and using large volumes of statistical data. He said:

> It may take my whole career, so that I can walk into an operating theatre, and there can be a machine there that will be a shoebox sized mass spectrometer. And I'll drop the sample in, and the data will come out [as a] lovely, clear data visualization. And it will tell me the information that I need.

Before this could happen, researchers emphasized that metabolomics data would need to be transformed into a format that made it amenable to clinical use by surgeons. Like Noah's work in clinical database, much of the CSM's translational research involved not only the reformatting of clinical data, but also the development of interfaces that would enable surgeons to combine metabolomics data with existing surgical techniques and procedures. As one clinician-researcher commented:

> With a lot of these, you need an actual surgeon to be able to run it. You're not going to take one of our massive mass spec[trometer]s and shove it in, and expect someone to know how to use it. So you hope eventually it will be…more of a 'yes no' answer to things. Something that's easier to interpret.

There were considerable practical limitations inherent in engaging with metabolomics data – both in its form and visualization – during the diagnosis and treatment of disease. Translational technologies would rely not only on surgeons' ability to use them, but also on surgeons' ability to interpret them, particular in relation to existing clinical data. As another clinician-researcher emphasized:

> Clinicians want simplicity, they crave it in their decision making…They all want a simple test, a simple score, that gets them a yes-no answer…And what's the balance…at what point does complexity become too difficult as a bedside test?

Such comments not only signal the practical limits to engaging with statistical data that does not have an established or obvious meaning, but also signal the challenges inherent in aligning laboratory and clinical practices. Despite assertions that surgery should move away from subjective judgments and towards technological innovations, several clinician-researchers remarked how in their everyday experiences with patients and bodies, they used a combination of medical instruments and bodily know-how (Prentice 2005; Carmel 2012) to "sense" patients' states of health and disease. Clinician-researchers, like histopathologists, relied on trained judgment and interpretation, as well as understandings of disease as something dynamic and normative (Canguilhem 1989), to assess patients and decide a course of treatment. Thus, for clinician-researchers working to apply metabolomics technologies to surgery, the alignment of laboratory and clinical practices did not happen automatically, but instead required active clinical decision making and judgment. Seen in this way, conflicts in the realm of translational research arose not only because of conflicts in the practices used to generate and move data, but also because of the different values and forms placed on data at the laboratory-clinic interface.

In articulating the differences between laboratory and clinical practices, my aim is not to elevate qualitative interpretation and judgment over the quantitative measurements and inferences that characterize metabolomics research. Clinical practitioners themselves rely on quantitative data, and reduce patients to objective and docile bodies (Hirschauer 1991; Foucault 2003). Moreover, as clinicians place value on human intuition and leverage their working knowledge of patients in hospital settings, they attempt to assert their authority and control over certain aspects of medical practice. Clinicians see the influx of medical technologies – which have the potential to "deskill physicians" (Reardon 2011, 104) – as a threat to medical institutions and realms of power. However, amidst such generalizations about the capacities of clinical practitioners to carry out and understand certain types of research, what emerges is the central role that the "human" capacities of interpretation and judgment play in medical practice. Despite technological advances and data-intensive practices, clinical decision-making remains central to patient care, such that medical practitioners are constantly combining technological information with human intuition. Translational research, it becomes clear, relies on the interpretive abilities of medical practitioners just as much as data.

Throughout my fieldwork, it was not only clinicians but also metabolomics researchers themselves who articulated a reliance on human interpretation and judgment, and – to a point – a distrust of statistical automation. As I have discussed throughout this paper, researchers emphasized that multivariate statistics revealed otherwise hidden aspects of biochemical data and allowed them to surpass the limitations of visual analysis. However, researchers also conceded that handling and inspecting their

data manually was critical for assuring the quality of their experimental methods and conclusions. One researcher emphasized that it was important not to completely rely on computers to carry out data analysis, as she said: "I'm not sure how much I really trust the data". Many researchers, she asserted, used statistical analysis as an initial means to explore their data, and then used manual inspection to look for interesting differences. Likewise, another researcher emphasized that it was important not to "let yourself be fooled by the data". For him, statistics were merely a tool, rather than an end-all-be-all for determining if experimental conclusions were obtained by chance. It was necessary to, as a leading metabolomics researcher with a background in engineering described, "keep the human in the loop".

Thus, clinical researchers and metabolomics researchers alike acknowledge the central role that human interpretation and judgment play in the development, interpretation, and implementation of metabolomics technologies within the clinic. Emerging technologies and human capacities are interdependent, such that technologies can serve to rearrange – but never truly replace – human judgment. As Keating and Cambrosio (2003, 59) argue, though technologies attempt to automate biology and transform it into an information science, human judgment is still required to turn "quantitative differences […] into qualitative distinctions".. Thus, this section explores how visions of the technological and data-driven future of translational metabolomics research conflict with the inherent appreciation – among both medical practitioners and metabolomics researchers themselves – of the interpretive practices of clinical medicine. Though technological innovation, through the creation and value of particular types of "data" is posed as a solution to the problem of translation, human interpretation emerges as a fundamental necessity for the alignment of the laboratory and the clinic. Data cannot exist independently of human practices, such that the negotiation of the form and value of data remains one of the main challenges facing translational research.

6. Conclusion

This paper considers how translational research, in attempting to bring metabolomics technologies to the clinic, involves tensions between research practices, disease objects, and data. Processes of translation between laboratories and clinics are fundamentally problematic, because the laboratory and the clinic entail different realms of practice and enact different biological and disease objects. Thus, metabolomics researchers and clinical researchers have fundamentally different notions not only of how disease should be researched and treated, but also of the form and value data about disease should have.

Though translational research is a complex and dynamic process, this paper examines it as an informational practice for generating and making sense of data at the interface between the laboratory and the clinic. Through metabolomics technologies and practices, tissues and diseases come to be understood as statistical patterns and numerical relationships, and value is placed on the production and analysis of particular kinds – large volumes and multivariate statistical forms – of data for the advancement of human health. Despite the fact that data is posed as increasingly central to medical practice, metabolomics researchers struggle to interpret biochemical and statistical data in relation to patient outcomes, presenting fundamental challenges to the "translation" of data into understandings of and treatments for disease. Thus, as metabolomics portrays translation as a technological feat, it raises key questions about the ability of data alone to align the practices and values of the laboratory and clinic. Data and automation cannot triumph or replace trained judgment and interpretation. Such human capacities are still central to the application of metabolomics research to clinical issues, and cannot – at least at this point in time – be overcome with complex types or large volumes of data.

In the end, translation is clearly much more than an informational practice, as it involves a diverse range of actors, materials, locales, disciplines, funding strategies, and ideologies. By showing the practices, values, and ideas at stake in thinking through "data" as something central to translational research, this paper invites us to question the dominant categories, timescales, and dynamics involved in translational research. Though the "translation" of biomedical research to clinical practice is often portrayed as linear and unproblematic, translation is much more messy and complicated in practice. Ultimately, by questioning the challenges involved in alignment of the laboratory and the clinic, this paper addresses the ways in which the very notion of "bench to bedside" becomes a possibility for contemporary biomedicine.

In conclusion, this paper is concerned with how we might think about the act and effect of "translation" in metabolomics research, and even more broadly in the range of post-genomic fields that are attempting to generate knowledge about life with large volumes of data. Of central concern is not the existence of data-intensive sciences per se, but rather the types of knowledge they are able to capture, as well as the values they place on particular ways of understanding and intervening into human health and disease. Data on their own are not neutral or self-evident: they are able to capture and measure some things but not others. At stake in my discussion of translation, therefore, is the question: how do competing practices affect how biomedical research gets done? How does an insistence on the value and use of data promote certain types of medical knowledge and care over others? Returning to the central premise of this paper, how might we use the case of metabolomics to better understand what *kinds* of translation are occurring, or to think through *what is and*

isn't being translated and why? How might we use the notion of "translation" to interrogate the challenges and limits faced by the use of data to understand biology and disease?

In the end – or at least at this point in the evolution of the field of metabolomics – not much is being translated between the metabolomics laboratory and the clinic. This lack of translation emerges because of diverging understandings of what constitutes data, and also because of a failure to relate statistical findings to existing clinical methods for diagnosing and treating disease. While metabolomics researchers think that more data will enhance translational research, clinicians are less optimistic. They overtly recognize, like many metabolomics researchers as well, that the human body is difficult to understand and predict. Based on first-hand experience, clinicians acknowledge that biology is utterly complex, dynamic, and unpredictable: patients respond to pharmaceutical and surgical interventions in different ways, and conditions like obesity and cancer have variable symptoms and etiologies.

Here, what I want to suggest is that as metabolomics ideas and technologies are translated into clinical practices, statistical notions of "data" struggle to capture dynamic and vitalistic (Canguilhem 1989) notions of disease. The utter complexity of biology presents very real challenges to translation in relation to processes of information, quantification, statistics, and biochemistry. Translation entails the movement of some types of knowledge over others, as those carrying out the translation select the meanings and values they wish to convey. Thus, amidst the rhetoric of technological progress, are there aspects of biology, bodies, and health that cannot be captured through statistics? With this in mind, the question becomes not whether statistical and biochemical measures of disease can replace human interpretation and judgment, nor whether the laboratory and the clinic entail different practices and disease objects. The question becomes, rather, if post-genomic ways of engaging with disease can capture the utter complexity of the human body (Levin 2014).

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The Controversial Molecular Turn in Prenatal Diagnosis

CGH-array Clinical Approaches and Biomedical Platforms

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Abstract: How and why are new gene-array techniques, which have been successfully introduced in medical contexts such as "post-natal" genetics, marked by uncertainty and dispute when they change context and are used in prenatal medicine? The so-called "molecular turn" in prenatal diagnosis has created a controversy that still divides the genetic community worldwide. The availability of an increased variety of high resolution-genetic data, including uncertain findings, divides the genetic community regarding production, treatment, and articulation with the older technologies, cytogenetics. Drawing on the methodological and conceptual framework of the "biomedical platform" (Keating and Cambrosio 2003), this paper intends to analyse these new biomedical molecular entities in the space where biology and medicine, science and technology, innovation and routine are intertwined. Empirical data from an ethnographic thick description of the intense debate that took place between Italian geneticists is used to analyze the different ways in which the material and immaterial elements of these platforms are organized. The different positions that emerge from the debate are traced back to two positions regarding the overlapping of biomedical work, technology transfer and research. This case study does not only reconstruct the fast-paced advancements of genetics in prenatal medicine, but also sheds light on the important questions at stake in structuring the expansive movement of molecular biomedicine.

Keywords: genetics and society; prenatal diagnosis; molecular turn; biomedical platform; biomedicine and innovation.

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I. Introduction: The Establishment of a Biomedical Platform

The development of biomedicine seems to be reflected in an increased interaction of biological research, technological innovation and medical work (Gaudillière 2002; Clarke *et al.* 2010; Keating and Cambrosio 2012). The recent introduction of Comparative Genomic Hybridization array (CGH-array henceforth) technology has intensified these exchanges even in medical areas such as prenatal diagnosis, i.e. the detection of congenital molecular anomalies in the foetus. Prenatal diagnosis used to adopt a different technique, cytogenetics, disconnected from the rapid advancements that molecular genetics has seen the last three decades. Dating back to the beginning of the 20th century, and developed without substantial successive changes in the seventies, cytogenetic procedures are based on the analysis of the most visible cellular elements that carry genetic information, the chromosomes. This technique was the disciplinary standard until recently, and is still used in many settings for prenatal diagnosis. Only recently has cytogenetics been partially or even totally replaced by new molecular procedures, which allow for a much more sensitive investigation of Dna sequences. This shift is part of a larger trend, due to the rapid advancement of molecular genetic techniques and knowledge, usually defined as the "molecular turn". Several research projects have tracked the effects of this shift in clinics, in terms of the expansion of care-subjects (from individuals to families), and the shift from symptomatic disease to a-symptomatic risk, and so forth (see e.g. Conrad and Gabe 1999; Cunningham-Barley and Boulton 1999). Although these observations parallel our case study, they tend to revolve around the "diffusion model", according to which technological transfer is a linear and universal process articulated from a scientific discovery to its industrial application and, eventually, to the impact on society, deemed as an empty space endowed only with a variable capacity to resist or accept technology (Latour 1987; Bijker 1995; Akrich and Callon 1988a; 1988b). Other more recent approaches from Science and Technology Studies have recently criticized the monolithic conception of the evolution of genetics. Some authors have shown that genetic tests are not immutable and self-confined tools, but are moving entities with no "pre-defined" content (Palladino 2002; Parthasarathy 2005). In a similar manner, the socio-historical narrative of the introduction of molecular techniques in the medical domain is presented here not as part of the general evolution of biomedicine, but rather as an overall reconfiguration of biomedicine characterised by multiple and tiny imbrications between laboratories and clinics produced at the intersection of innovation, work and research.

The theoretical and methodological framework of "biomedical platforms" (Keating and Cambrosio 2003) addresses the contemporary cross-fertilization that has occurred between medicine and biology since the

Second World War, by focusing on its epistemological and organizational shifts. Drawing on the French original meaning of *platte-fourme* (literally "flat-form"), a "biomedical platform" is defined as the material support on which the new regime of production and regulation of biomedicine can be arranged and connected. In so doing, these theorists provide a pragmatic perspective on biomedicine as a new space where new biomedical entities bridge the gap between the qualitative, synthetic clinical evaluation of the pathology, and the quantification of biological variables:

> biomedical platforms [are] material and discursive arrangements that act as a bench upon which conventions concerning the biological or normal are connected with conventions concerning the medical or pathological.
>
> (Keating and Cambrosio 2003, 4)

Instead of assuming a paradigm-ordered or theory-driven analysis of biomedicine, this pragmatic stance resorts to the constitution of laboratory-clinic relations as enabled by the mediation of material and discursive objects, such as protocols, reagents, instruments, procedures, representational spaces, clinical indications, etiologic accounts and scientific categories. These elements constitute the material and discursive infrastructures where new biomedical entities are mobilized. The material organisation of their various parts, which "do not need shared understanding in order to operate, but just consistency" (Keating and Cambrosio 2003, 15), are thus intertwined with the epistemological production of knowledge. At this point a second significant aspect of biomedicine emerges: the continuous monitoring of patients' physiological variables in relation to environmental stresses on the human body. This trend towards the increased production of health-data implies new connections with the industrial production of instruments that "move the problem of automation out of the sphere of pathology and human judgment into the sphere of biology and quantification" (Keating and Cambrosio 2003, 60-61). In synthesis, this perspective insists on dissecting the well-accepted oppositions not only between biology and medicine, but also between science and technology, innovation and routine.

These are some of the reasons why investigating the development of new genetics seems so pertinent. Studying the expansion of predictive genetic diagnosis and testing for cancer after the discovery of the two susceptibility genes for breast and ovarian cancer, Brca1 and Brca2, Pascale Bourret (2005) investigated the implications for clinical work. New forms of collaborative, multidisciplinary activities cross professional skills and specialties as well as laboratory and clinical data and tools, and they constitute what she terms "bio-clinical collectives". Recently, this concept was expanded and more specifically applied to investigating how both genetics and clinics work together to give clinical meaning to new syndromes and pathologies. Accordingly, their interactions shape the very

content of work, which consists in "simultaneously producing the clinical relevance and the biological significance of mutations" (Rabeharisoa and Bourret 2009). The endogenous elaboration of these new bio-clinical entities results from the production of evidence derived by their mobilization in a clinical context. In some cases, the nosological explanation of a pathology is derived from a genomic anomaly, and not from clinical symptoms. Daniel Navon (2011) has recently established the concept of "genomic designation" to indicate syndromes and diseases that did not exist before molecular analysis. An even clearer example of this trend is the attempt to isolate genetic entities that are considered "actionable", i.e. that can be articulated through current protocols, procedures, treatments and clinical interventions (Nelson *et al.* 2013).

In this sense, the molecular turn of prenatal diagnosis provides a valuable fieldwork, in that it offers the possibility to scrutinize the establishment of a biomedical platform marked by uncertainty and controversy. Even if the CGH-array technique has already been set as the gold standard of other clinical practices, such as in the post-natal diagnosis of psychiatric impairment or other congenital syndromes, its application to prenatal diagnosis has raised issues that have not yet been settled. This dispute, which divided the medico-scientific community over the world, as well as, remarkably, the two most important medico-scientific societies on the opposite shores of the Atlantic (Eca 2012; Acog 2013), is multifaceted and shifts according to the perspective assumed.

In the scientific literature, the quarrel is presented in a rather abstract fashion. Not accidentally, the main issues that emerge concern the war of numbers instead of the actual increased detection rate in molecular procedures as compared to cytogenetic ones. An exact evaluation is also complicated by two factors. The first regards the uncertain clinical meaning that characterizes the new biomedical entities mobilised by CGH-arrays, i.e. the "sub-microscopic anomalies". The sensitivity of CGH-arrays is so high that not all of the detected genetic data is necessarily clinically encoded. Technically they can be called "variants of uncertain significance" (Vous). The second factor regards CGH-arrays limitations, as compared with traditional cytogenetics. While producing more quantitative genomic data, CGH-arrays are blind to so-called "structural or balanced anomalies", which are however very rare and usually not related to a genetic disease or syndrome. Amazingly, if we turn our attention to the exchanges within the geneticists' community, we find totally different arguments. The different positions refer not so much to scientific justifications, rather to matters that are strictly organizational and professional. The Italian controversy provides a good framework with which to analyse the process of organizing and fine-tuning this new biomedical platform, because it provides a case study that is, both representative of many other settings and specific. On one hand, the final statement of the Italian Society of Human Genetics (Sigu, Società Italiana di Genetica Umana) reflects, as we will see later in detail, the position that was also assumed by

the European Cytogeneticists Association (Eca). On the other, the Italian debate assumed decidedly heated tones and drew widely on arguments of extra-scientific nature, as each side implied that opposite party position lied about economic and professional interests. This situation, thus, gave a symmetrically opposite perspective than that provided by scientific literature.

This paper intends to reject both positions as two different reductionist versions, based respectively either on a purely epistemological evaluation of a technique, or on economic or professional interests. Building on the conceptual framework of biomedical platforms, the epistemological status of the "sub-microscopic anomalies" produced by CGH-arrays is strictly connected to organisational arrangements. In other words, the production, circulation and interpretation of these new biomedical entities requires a multi-layered biomedical platform which involves intimate and dynamic connections between equipment, tools, concepts, medico-scientific guidelines, biotech companies, databases, health services, and so forth.

So far, interdisciplinary collaboration and bio-clinical collectives have not particularly addressed prenatal diagnosis, even if it is one of the first, and still remains one of the most important, applications of genetics in the medical routine. In prenatal medicine, the cytogeneticist works in isolation, without the possibility to triangulating genetic findings with "non-genetic" information of the same level of reliability, and at best handles the diagnosis communication (Turrini 2011). This clear division between the laboratory and the clinic is partially comprehensible due to the nature of the test-subject, the fetus. The subject is in a movement of rapid change, not fully developed or organically autonomous (i.e. healthy in the common sense). In addition the subject is located in the womb, where the clinical observation is clearly difficult. The only obtainable phenotypic information is anatomical measurements obtained by ultrasound visualization technology. Given that the clinical observation provides little and uncertain data on the fetus, cytogenetic analysis has to and actually does provide solid data, on which important clinical decisions are made. Aside from the rare cases of surgery on a fetus (Casper 1998), the only available practice after the diagnosis is the voluntary interruption of the pregnancy. Genetic counseling is offered only in case of a positive result that indicates the presence of a given pathology, and, since the most common anomaly that this technique detects is the well-known Down syndrome, even physicians without a specialty in genetics may communicate the diagnosis. Afterwards, the pregnant woman or couple is then often left to their own resources regarding their decision.

The advent of a molecular technique such as the CGH-array has dramatically changed the practices of prenatal diagnosis under many respects. The doctor-patient relationship explodes into a complex constellation of elements. Genetic counselling becomes mandatory before any examination due to possible uncertain outcomes. Likewise, any referral of

the anomaly requires a consultation with international databases, and, therefore promotes a tighter interface between pre-natal and post-natal diagnosis by collecting and correlating genetic anomalies detected in individuals before and after birth. Further, the relationship with research as well as with biotech companies grows more dynamic, as equipment is constantly advancing to keep pace with the ever-increasing amount of new diseases and the ever-higher sensibility needed to detect them. The last point, indeed, emerges from our analysis as the crucial bone of contention, in that it affects the way in which to locate and organize submicroscopic abnormalities.

After an introductory section on materials and methods, and a brief explication of the aforementioned process, we will expand the description of this emerging biomedical platform through a discussion of the scientific controversy. First, we will indicate the general terms in which the technology is presented in scientific literature, and, second, we will look closer at the Italian debate. In the final section, we will analyse the controversy in terms of two different ways to conceive and organise the biomedical platforms, by focusing in particular on the important relationship with technological transfer and biomedical research.

2. Materials and Methods

The methodology adopted combines the analysis of scientific literature with the more traditional methods of qualitative research, like in-depth interviews and ethnographic observation of laboratory practices. More precisely, we collected all of the relevant literature on PubMed that had a title and abstract related to "array comparative genomic hybridization" and "prenatal diagnosis". After reading the abstracts of the 143 results, we have selected those that have been considered the most relevant articles from a clinical point of view. They include, for example, two special issues that two important journals, "Human Mutation" and "Prenatal Diagnosis", devoted to this topic in 2012, entitled respectively "Focus on Cnv detection with diagnostic arrays" and "New Cytogenetic Technologies in Prenatal Diagnosis".

Beyond the scientific literature, we also gathered the position statements and guidelines of the most important US, EU and Italian medical-scientific societies: The American College of Obstetricians and Gynaecologists, Acog, and the already mentioned Eca and Sigu. We conducted extended, and in some cases multiple, interviews with 16 geneticists (either biologists or physicians) from nine different clinics (all Italians apart from one, in Austria). In order to reconstruct the development of this technique in Italy, we addressed both the "core group" involved in the Italian debate, and those involved in the research aimed at the establishment and validation of CGH-array technology. Regarding the Italian controversy, I

was able to reconstruct parts of the Cytogenetic Working Group of Sigu meeting in which the dispute broke out, as well as the criticism that followed, through the testimony of individuals present at the event. We also gathered the opinions of those who, after having worked for several decades in cytogenetics, saw their expertise (and therefore jobs) threatened by the molecular turn. In this case, the intergenerational separation between older practitioners, and those who started their career in the mid-2000s with CGH-array research, is clear. We selected three different groups of professionals: first, young researchers who have worked at least for several years of research in Italian health service as Ph.D. students, post-docs or with other forms of research funding; second, directors and managers of genetics departments, or big laboratories who handle the process of clinical genetics; and third, older cytogeneticists. We supplemented this aspect with the direct observation of genetic laboratories in order to unpack how CGH-array works.

3. The Molecularization of Clinical Genetics

The introduction of molecular instruments in clinical genetics represented a radical alternative to traditional methods encompassed by the family of cytogenetic practices. Up until a few years ago, these two kinds of genetic methods were complementary. Whereas the older cytogenetic techniques gave a broad overview of the entire set of chromosomes, the molecular techniques, like Pcr, were used to detect specific targets with a higher sensibility. In the 21st century, this distinction became obsolete with the development of new molecular, high-throughput (hyper-fast) techniques like CGH-arrays and Next generation sequencers, which can produce an overview analysis of the whole genome at a high-resolution.
Cytogenetics was the only technique able to obtain an overview of the whole chromosomal set and therefore the most used technique in clinical genetics. However, it is a rudimentary and artisan discipline, essentially based on manual manipulation and microscopic diagnosis. It is a residual exception on the verge of extinction in an era when most clinical testing has become more and more automated or "high tech". It is not by chance that its craft-like practices have recently captured the attention of several social scientists (Rapp 1999, 193-222; Martin 2004; Turrini 2012). It is a long and articulated procedure that consists in arresting the cell cycle during the metaphase, just before the process of division, when the chromosomes are most visible, and then fixing them on a slide and banding them. In addition to being more time-consuming, this procedure requires the counting and analysis of the chromosomes under the microscope. The width, brightness, and the arrangement of the stripes – *bands* according to the laboratory vernacular – constitute the specific appearance by which each chromosome can be recognized by peering into microscope.

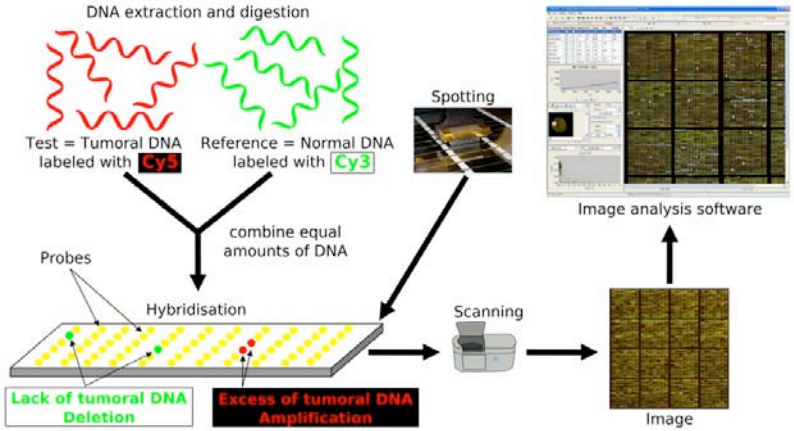

Fig. 1 – CGH-array protocol (source: Emmanuel Barillot, Laurence Calzone, Philippe Hupé, Jean-Philippe Vert, Andrei Zinovyev, *Computational Systems Biology of Cancer,* Chapman & Hall/CRC Mathematical & Computational Biology, 2012).

Comparative genomic hybridization is a technique that was developed at the beginning of the 1990s in the field of clinical research on cancer. Its principle action is to compare small fragments of a genome sample to the same fragments of a "reference sample" deemed "normal" and, thus, see if there are extra or missing pieces of genetic material. At the end of the 1990s this technique was conducted by Dna microarrays. The arrays allowed for a visualization beyond the "metaphase plate", in the "digital space" of a matrix, in which each square corresponds to a specific chromosomal region, according to the library of cloned Dna fragments with known locations throughout the human genome that was produced by the Human Genome Project. In practical terms, in CGH-arrays, Dna is chopped into thousands of shorts sequences (called "probes") that are then labelled, coloured, arranged on a slide with a precise grid (it is called a "biochip" for that reason), and finally compared with probes of a different colour from a reference sample. The resulting gains and losses of chromosomal material are read by a scanner, which provides an analysis as broad as cytogenetics but with a definitely higher resolution that is automated and fast.

While cytogenetics produces chromosomes analysed by the human eye under the microscope (fluorescent or not), the CGH-array produces signals that are automatically read by an electronic scanner. In describing this innovation some geneticists use a telling geographical analogy. If the images of chromosomes produced and analysed by cytogenetics are com-

pared to a traditional map of any given country level, then the maps produced by the biochips are a sort of Google Earth that permit us to zoom-in down to street level. To make things still clearer, the image in figure 2 compares a *conventional chromosome* as it appears through microscope and a *digital chromosome* image from an array.

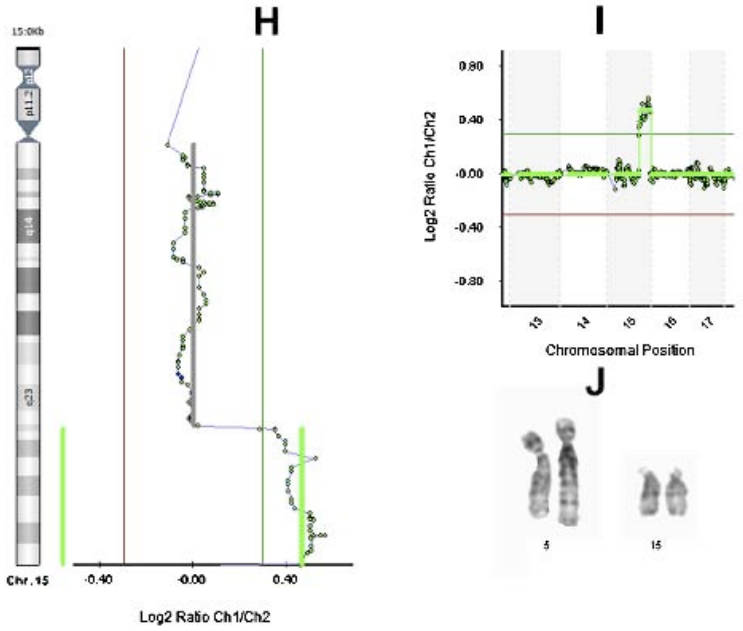

Fig 2 – Digital and conventional chromosomes (Fiorentino *et al.* 2011)

The molecularization and digitization of genetic analysis has several advantages over traditional karyotyping, in that it allows for the detection of thousands of genetic variations, up to one hundred times smaller than those that can be detected by peering into the microscope, in an automatized procedure. Thanks to the detection of these *sub*-microscopic alterations (technically called micro-deletions, micro-duplications, and so forth), new syndromes have been coded, or genetically re-coded.

This is one of the primary reasons why genome-wide arrays have quickly become the primary tool of chromosomal evaluation in certain medical areas, such as oncology. They have also significantly improved "post-natal" diagnostics with respect to conventional karyotyping for children with developmental delays, intellectual disabilities, multiple congenital anomalies, and autism. This led to an international consensus statement according to which gene arrays technologies *should* be used in

the diagnostic workup of such patients (Miller *et al.* 2010), and, as a result, more laboratories are now introducing biochips as the first-tier testing technique. Although this has had a deep impact in the classification of syndromes (Navon 2011), it has raised no controversy within the genetic community.

Due to the reasons we briefly summarised in the introductory paragraph, things are more slippery in prenatal settings, where questions regarding certain aspects of clinical implementation still remain unanswered.

4. A Special Challenge. The Scientific Debate On CGH-array

Biochips were first applied to a clinical practice in the US in 2006 (Shuster 2007). In the same period, genetic laboratories all over the world were experimenting with this technique in clinical practice. Yet, after almost ten years of practice and experiments, the usage of biochips in prenatal diagnosis still raises many issues. In 2011, when array technologies had already replaced conventional karyotypes as the standard for genetic diagnosis after birth, the International Congress of Prenatal Medicine of Amsterdam at "a very well-attended debate" discussed whether CGH-array could be considered as a replacement for this routine testing in the near future (Bui *et al.* 2011, 235). This article intends to look at the reasons for which the use of arrays in prenatal diagnosis is still considered "a special challenge" (Vetro *et al.* 2012), to paraphrase the title of an article written for the Genetic Services Quality Committee of the European Society of Human Genetics by a large group of geneticists working in six different clinics.

In the scientific literature this controversy revolves around *the war of numbers* over the effective rise of detection rates brought about by the passage from cytogenetics to the CGH-array. Findings vary, but in general there is agreement regarding the advantages of biochips over traditional cytogenetic techniques (see. e.g., Wapner *et al.* 2012). What make the assessment of the actual gain provided by the CGH-array so difficult to assess, is, first and foremost, the issues that the increased quantity of results produced by CGH-arrays pose in terms of clinical interpretation. Even if cytogenetic procedures also produce some uncertain results, molecular instruments drive this uncertainty to an extreme, in that some of these results are beyond the current comprehension of genomes. The different methods for organizing the introduction of CGH-arrays for prenatal diagnosis depend on the different approaches to the so-called "variants of uncertain significance" (Vous). The assessment of the actual limitation of CGH-arrays, as compared with traditional cytogenetics clinical definition of the anomaly, also contributes to rendering the assessment of

effective gain provided by the CGH-array even more difficult. While producing more quantitative genomic data, CGH-arrays are blind to some kinds of anomalies. These anomalies may be defined as out of place Dna fragments, derived from the movement of a filament piece from a chromosomal region to another. Since arrays read genomes resulting from a cut and copy process, they cannot detect those anomalies, but only those due to either a gain or a loss of Dna. Similar problems can be found regarding another kind of genetic abnormalities, mosaicism, i.e. the presence of two or more populations of cells with different genotypes in one individual.

Some papers on the debate tend to polarise these different positions into two practical options regarding the introduction of CGH-array in prenatal diagnosis. For some, the use of molecular instruments should be restricted to pregnancies that are considered "high risk" based on observed ultrasound abnormalities, or as a second-tier test to confirm and characterise those chromosomal anomalies that resulted from conventional cytogenetic analysis. For others, this type of test should be provided indiscriminately to all pregnant women who seek invasive prenatal testing, as the universal, primary tool of genomic evaluation of the foetus. Besides the war of numbers, ethical and regulatory issues are mentioned in these debates. They refer first and foremost to the elaboration of new strategies to inform pregnant women or couples about such a test that produces a vast and sometimes incomprehensible amount of information. In any case, beyond this debate, what is really at stake in practical terms is two different ways of arranging the biomedical platform of one of the most important clinical genetic practices in quantitative terms.

In this regard it is important to recall the socio-economic dimension of this phenomenon. The first medical practice to bring genetics to the public, prenatal diagnosis is still nowadays one of the genetic practices with the most experience in the clinics[1], used on over one hundred thousand pregnant women a year in Italy alone. These different approaches, which can be summarized as either indiscriminate use or the use as a second-tier test, have a deep economic implication and are dividing the genetic communities all over the globe. The strong discrepancy between the last guidelines of the American College of Obstetricians Committee on Genetics (Acog 2013), which changed its position from the previous ones (Acog 2009), and the Europeans Cytogenetic Association (2012) lies just in that choice. The former is in favour of a total replacement of cytogenetics with gene array technologies, which would then be used as a first-tier test, while the latter is in favour of partial use only, just for at-risk cases. The Italian controversy tellingly counters this perspective on the debate by providing a diametrically different one.

[1] Nowadays, genetics techniques as applied to the study and treatment of cancer are rapidly expanding, and are undoubtedly the most promising sector of genomics both from a clinical and economic point of view.

5. The Italian Controversy: Socio-economic Interests and Technology Transfer

While scientific literature has focused on the technicalities of gene array technologies in terms of diagnostic sensitivity, in the Italian scientific community this dispute has taken a decidedly animated tone, which is more focused on socio-economic aspects. There are undoubtedly structural reasons behind this controversy. It suffices to mention here that genetic laboratories are fragmented, often of small or even tiny dimensions. A recent survey counted over 160 laboratories (Dallapiccola *et al.* 2006). This number includes private laboratories, many of which operate on a larger scale (including Toma in Busto Arsizio (Va), Genome in Rome), and also respond to the demand of public structures, mostly of small dimensions.

In any case, the controversy arose almost by accident, after a meeting of the Sigu (the Italian Society of Human Genetics) Working Group on Cytogenetics, in which they attempted to re-elaborate the guidelines for the use of the CGH-array. During the meeting that took place on April 7 2011, a clear majority position emerged which desired to limit these techniques to subsequent diagnostic investigation, and consequently, to discourage the hasty replacement of traditional procedures. Dissenting voices were raised. In particular a private laboratory that was betting on CGH-arrays, involved in research aimed at evaluating its benefits among other things, railed against this measure. The aim was to produce empirical results regarding the usefulness and reliability of the CGH-array-technique in prenatal diagnosis. In practical terms, this would mean switching to an analysis procedure that examined biological samples "in parallel", making use of both the traditional cytogenetic techniques and those of molecular genetics, so as to be able to compare the results of the two. The research had by then reached a conclusive stage and the results, which would be submitted one month later to an international scientific journal (Fiorentino *et al.* 2011), seemed encouraging. The representatives of this facility rejected this prudent attitude, and proposed a chromosomal array approach as first-tier approach for all pregnancies. During an animated correspondence that took place immediately after this meeting in the mailing list of Sigu Working Group between these two positions, an advocate of the immediate and indiscriminate application proposed to initiate a large-scale multi-centred study involving the most important Italian centres, and thus creating prestige for Sigu.

The position that was agreed upon, however, was decidedly more cautious. The introduction of gene array technologies for prenatal diagnosis thus became the central issue of a bitter dispute that seemed to divide critics and advocates of this innovation. On one hand, Sigu reiterated its

cautious attitude first in a public document in Italian, distributed amongst its members, and then in a position statement, that is the public stance of a scientific society, published in an international scientific journal. As from this last document: "we recommend the use of Cma [*chromosomal microarray analysis*] in prenatal testing: 1) never as a substitute for conventional karyotyping; 2) for specific diagnostic purposes in selected pregnancies and not for general screening in all pregnancies" (Novelli *et al.* 2012, 386). This approach echoes the European Association of Cytogenetics guidelines, which were published in those same months (Eca 2012).

On the other hand, the private Italian laboratory's adverse position did not subside, if anything, it intensified. In addition, in virtue of the positive results obtained by the previously mentioned research, the company definitively abandoned cytogenetics in favour of chromosomal array analysis, which was then used as the only first-tier test for all women undergoing invasive prenatal tests. Their dissent was then expressed in an official manner through a "correspondence" (e.g. letters sent to a scientific journal to distance oneself from one of its articles) in which the Sigu position statement is described as anachronistic and ignorant of the most recent results that have emerged from research. A group of geneticists from the National Taiwan University Hospital intervened in support of this critical position, signing a second "correspondence" in the columns of the same magazine. In these letters, we find a discussion that rests on arguments that are quite similar to those mentioned in the previous section on scientific literature. The subject of discussion is the manner through which to objectively evaluate the actual detection-rate increase of the array techniques in light of the loss of certain types of data and, above all, the uncertainty of some of the results. However, as we have mentioned, what is at stake in practical terms is the way in which to arrange the biomedical platform of one of the most important arenas in quantitative terms.

If we turn our attention to the exchanges between the more prominent members of this controversy, we find not only decidedly heated tones, but also reasoning of entirely different nature. The different positions refer not so much a scientific justification, as to matters that are strictly organizational and professional. It created a situation in which a constructivist agenda, committed to exposing those contingencies that are usually deleted or forgotten in scientific literature, was adopted outside of social science research. The Italian debate on the molecular turn in prenatal diagnosis activated "a sociology of knowledge machine" (Lynch, 1996) which promoted a passage from scientific arguments to others grounded on social interests that lay behind the adversaries' position[2]. The following

[2]Deconstructivist efforts conducted within scientific controversies to discard adversaries' arguments have been widely analysed within STS. See, for example, Collins and Pinch (1979) and Lynch (1996).

opinion stated by a protagonist of the controversy has been reiterated by others interviewed, especially by experienced geneticists:

> The reasons why the scientific community takes a certain path can be understood through many different factors. Science was not what was mainly used in this circumstance.

The extra-scientific interests referenced here are of a purely socio-economic nature. On one hand, the National Health Service (Servizio Sanitario Nazionale – Ssn) is essentially accused of adopting a conservative position. The reasons for this reside in an inability to keep up with innovations due to the slowness of bureaucracy and, above all, the desire to defend a particularly important national scientific tradition as advanced as cytogenetics. By scientific tradition we intend to refer here to a series of "scientific styles" developed over the years (Turrini 2012). These "styles" involve both skills and job positions that are framed in the context of clinical laboratories and universities. In the event of a radical technological substitution, these components would be put at serious risk. Using once again the words of a protagonist in this controversy:

> There is a shift from cytogenetics to molecular genetics. What does that entail? Where will this situation bring us? When we no longer perform cytogenetic karyotyping, the cytogeneticists will no longer have power or a role, meaning they will no longer have work. (Francesco Fiorentino, Director of Laboratory Genoma of Rome)

In this regard, it is important to clarify the importance of prenatal diagnosis in terms of employment. Just to give an idea, in 2004, out of 283601 cytogenetic tests done in Italy, 51.7% were prenatal (Dallapiccola *et al.* 2006). The prevalence of prenatal diagnosis touches not only the number of workers employed in various capacities (technical, biologists or doctors) in this area, but also an economic volume that is extremely relevant in the context of genetics.

On the other hand, CGH-array enthusiasm is mainly attributed to the purely commercial private laboratories:

> Everything that is introduced into clinical practice, and therefore in its routines, has to be assessed and developed by disease control centres, a system that provides a record of safety and effectiveness. [...] What I pose as a problem is that it shouldn't be the market to decide, it should be a relaxed scientific community that does not have other interests in the decision regarding what you can and can't do. (Antonio Novelli, Chair of Cytogenetics Laboratory of Istituto Mendel of Rome and Chair of the Working Group "cytogenetics" of Sigu)

The interests at stake are many. Antonio Novelli balances the reduction of personnel costs related to procedures with a level of automation with a prudent attitude towards innovations that are quickly commercialized by biotech and pharmaceutical companies. According to this perspective, the presentation of any given procedure as the most effective and rapid, which reduces waiting times from an average of two weeks to a handful of days, seems to respond more to economic interests than a substantial improvement in the service of care. Not surprisingly, the private Roman genetic laboratory's report, along with the previously mentioned Taiwanese's study, appear in a brochure in which a British biotech company introduces biochips for clinical diagnosis to the market – CytoChip Focus produced by BlueGnome[3].

The controversy "heats up" when these two divergent attitudes lock horns, caution versus enthusiasm, towards the innovative proposals that biomedical companies put on the market. However, describing the two factions as simply private and public would be inaccurate. The cautious attitude seems to depend on the desire to both better protect the patient from illusions generated by the medical industrial complex, and ensure greater sustainability of medical services. This position is criticized as medical paternalism. Supporters of the introduction of CGH-array techniques also add that a conservative and "directive" strategy is a rhetorical means used to justify an economic and technological inability to keep up with the pace of current technological transfer.

While this article adopts the analytical-perspective of biomedical platforms, it also attempts to examine the political aspects that the analysed dispute presents in the first place. As it has already been pointed out, the opposition between advocates and critics is deliberately simplistic. The controversy does not divide those in favour of the use of this technique from those who oppose it. Instead, the variety of stances and positions developed inside the different choices reflects the relationships of the invested parties to the issue. In this regard, this debate provides insight onto complexity involved in gene array technologies, new procedures, other existing procedures, medical and scientific associations, biotech companies, work groups, publications, and so forth. It also points out the relationship between the "biomedical collectives" (Rabeharisoa and Bourret 2009) and the biomedical industry. However, we do not intend to explain the differences of these position with a causal model based on economic and professional interests. Even if they undoubtedly play a crucial role, we would like to grasp the epistemological and organisational difference of the "biomedical platform", articulated around the molecular genetic diagnosis of the foetus, in greater detail.

[3] BlueGnome, *Delivering decisions from DNA*, "CytoChip", (http://www. cambridgebluegnome.com/products/cytochip-isca/product-information/cytochip - oligo-spike-in-controls/, last visited on the 3rd of May 2014).

6. A "Lab-on-a-Chip"

"It's the platform that makes the difference."
A geneticist interviewed

The notion of biomedical platform is used in this article with a semantic ambiguity much like the synecdoche rhetorical figure. Biomedical platform does not refer only to a specific conceptual framework. In the fieldwork the term "platform", without the adjective "biomedical", was used quite frequently to mean the slide, the matrix on which the analysis is physically carried out. This meaning is more limited and specific, basically indicating the glass slide on whose grid the thousands of short sequences of Dna are arranged.

The two meanings, despite their apparent differences, are actually contiguous under different aspects. The first meaning comes from a reflection on a tendency towards biologization and automation in contemporary medicine, and the second comes straight from the biomedical field in which this transformation has already reached a very advanced stage. These objects share not only a historical and technological proximity, but also some functional/operational elements. The biochip incorporates a wide range of tasks that were previously conducted by hand. Thanks to the chip, even the reading of the results themselves is performed by a computer scanner. In other words, biochips are the result of scaling several laboratory procedures down to a chip-format. This is the reason for which they are generally referred to as "lab-on-a-chip" (Loc), which, curiously, is another synecdoche widely used for this kind of miniaturization processes. All of these considerations indicate the extraordinary closeness of the two semantic levels of platforms. Through sociological reflection "biomedical platforms" are defined as criteria for the arrangement of the various discursive elements and materials. In molecular genetics, "platforms" are defined as extremely flexible and encompassing variables in much the same way, on which however, the entire material and epistemological data production cycle depends on. This correspondence is not an accident, but is rather understood through ethnomethodological reflection on "perspicuous phenomena", i.e. overlapping areas where concerns of particular groups resonate with social science categories or issues (Lynch 1993). Indeed, the arrangement of the slide where the analysis is carried out reflects on the broader regime of production and regulation of the new biomedical entities analysed by CGH-arrays. If one were to play with the multiple meanings of this category, one could argue that the physical type of platform chosen for the lab predominantly influences the articulation of the overall biomedical platform. Returning to the debate in the light of this perspective, the type of array that will be used emerges as one of the primary obstacles upon which the controversy was built. As the researcher seen at the beginning of this section states, "it's the platform that makes the difference!"

One of the most meaningful differences among the number of array platforms that have been commercially offered by a wide range of companies in recent years regards the optimal resolution of these arrays. Increasing the resolution has the advantage of detecting a larger number of anomalies; however, the number of benign or uncertain significance increases exponentially. Although there are publications that indicate a specific level of sensitivity, each laboratory practically chooses its own in-house detection-rate resolution (Vermeesch *et al.* 2012). At the same time, the two most common families of technologies used for biochips, namely "targeted array" and "whole-genome array", represent the general difference between low and high resolution. Targeted arrays, also known by the technical name of Bac arrays or Bobs, have a lower sensitivity, while whole-genome arrays, or oligonucleotide arrays, have higher sensitivity.

Those who are in favour of immediately replacing the conventional cytogenetics with gene array technologies adopt targeted array biochips. As the name says, these chips target "hot spots", the gene-dense regions where the most common genetic anomalies are located, yet have low resolution for the rest of genome. This mixed resolution responds to the need to facilitate data interpretation by keeping uncertain and unsolicited results to a minimum. The rationale underlying this technology is a strategy that seeks to balance technological innovation with the needs of pregnant women who want the maximum amount of information currently obtainable by prenatal diagnosis. For this reason, the supporters of this platform consider it the only option that is genuinely respectful of the patient, as it allows for "a more accurate test", and the right to have the most accurate analysis of the foetus. Depriving patients of the most advanced medical techniques is therefore considered the effect of a paternalistic medical culture, and a resistance to change, typical of some clinical facilities:

> And what does it involve [the decision of using conventional karyotype, even when the molecular one is available]? It really means medical malpractice, going against everything that should be a goal of a doctor, a biologist, to give the patient at least an option other than the test that has been used for more than forty years, the cytogenetic karyotype. (Francesco Fiorentino, Director of Laboratory Genoma of Rome)

Others, however, do not take kindly to these products. In their eyes the immediate availability of these techniques, especially in an area as sensitive as prenatal diagnosis, would primarily respond to economic interests instead of clinical ones. Of course, the targeted platforms are specifically designed for an indiscriminate and exclusive use at prenatal diagnosis, while whole-genome arrays, although used as a second-tier analysis in prenatal medicine, are also used for the diagnosis of rare diseases and intellectual impairment. Instead of being considered the gold standard, tar-

geted platforms are seen as backward compared to oligonucleotide or genome-wide platforms, which detect even smaller anomalies throughout the whole genome. Here, for example, is the opinion of a researcher specialized in CGH-arrays:

> Making a new technology available is also right, making it available to the patient, and therefore the pregnant woman [...]. Using low-resolution platforms, however it shouldn't mean closing your eyes and saying, "yes, I used a low-resolution platform, I'm at ease because I have no doubts about the interpretation." I don't think that's how it is, because even a low-resolution platform leaves you with interpretative doubts, plus it also leaves you with something you haven't seen. I am very puzzled about this platform, although I realize that from the commercial point of view it makes a lot of sense.

Another researcher, states more concisely: "I'm not crazy about targeted platforms because they limit the *openness* of the array". As emerges from these testimonies, the type of platform one uses is a choice, that is not only related to the commercial volume of extremely sophisticated platforms, but also to epistemological choices that once again involve a reorganization of the medical work. In this regard, the whole-genome platform option provokes closer interaction between prenatal diagnosis and post-natal diagnosis, which is confirmed by the role played by biobanks.

7. Biobanks, the Molecular Body and the Prenatal Medicine to Come

In order to understand how the molecular breakthrough is transforming and complicating clinical genetics, it is worth mentioning the epistemological change produced by it. This advance is not only due to the increased number of coded diseases created by increasingly precise information. It is also a logical step. Up until a few years ago, clinical genetics mainly utilized Mendelian "one gene-one trait" or the "gene for x-disease" logic. This model tied each genetic abnormality to a given condition. The molecular turn promotes the establishment of multiple and flexible relationships. In the diagnosis of intellectual disability, autism, and multiple congenital diseases in the prenatal and postnatal field, the new approach is seen primarily in the evaluation of "penetrance", and interactions between genes (see e.g. Lock, 2005).

The categories and practice of clinical genetics are subverted and rewritten by submicroscopic reality, beginning with assumptions regarding heredity. The first assumption that is subverted is the idea that a genetic variance not present in the parents (technically a *de novo* anomaly) should

always be considered pathological. This principle is still considered valid for anomalies detected with cytogenetics techniques. However, not all microanomalies necessarily have negative health consequences. Therefore, one cannot consider them pathological based on the mere fact that they were not present in either parent.

In a manner symmetrical to the first example, the second principle of clinical genetics to be challenged by molecular techniques is considering an abnormality inherited from the parents benign in the case they do not manifest a genetic condition. This reality does not necessarily protect from the development of a disease, because some microanomalies are activated under particular conditions. It is easy to understand, therefore, that the quantitative difference brings with it a basic qualitative difference regarding interpretation, so much so that the clinical use of these technologies necessitates many years of data interpretation experience.

If, therefore, gene array technologies have automated the long cytogenetics laboratory procedures, they have instead made the clinical interpretation of the data extremely complex and indeterminate. In the words of one researcher:

> Technically, it has become much easier than it was to prepare a chromosome. Technically it has really become much easier to produce the data. What has become difficult is to interpret the data.

We could describe this complexity in terms of the loss of the phenotype-genotype correlation that was established in the first period of clinical genetics. Restoring such a connection is a far from easy undertaking, and requires the development of genetic data databases from both healthy subjects and those with intellectual disabilities, developmental disorders, autism and multiple congenital diseases at both global and local levels. The reconfiguration of what is normal and what is pathological occurs through the mediation of these institutions, biobanks, which collect, collate, and compare the vast amount of data produced by clinical laboratories around the world. Biobanks have become a fundamental element of molecular genetic biomedical platforms, establishing a link between anomalies detected in prenatal and post-natal diagnosis, which did not yet exist with cytogenetics. What is most significant is that the relationships between biobanks and laboratories are regulated by the type of platform that is used. Oligonucleotides platforms (those with higher resolution) require a continuous relationship with biobanks. Each result has to be confronted with those stored in several genetic databases, and these references are a mandatory section of the bio-clinical report. In case the result has not been perfectly codified, research for the scientific state of art regarding that anomaly should be conducted and interpreted, and then explained to the pregnant woman or the couple accompanied by other members of the medical team specialized in genetic counselling. In practice, to quote a junior researcher who works with gene array technol-

ogies, it means that:

> we must study the genes that are involved in the relevant region, and see, for example, if there are animal models, or cases partly described in scientific literature on the subject.

At the same time, each new case enriches the database, and helps establish a link between genetic information and disease. Since knowledge in this field is rapidly expanding, new syndromes associated with micro-anomalies are continuously being reported. As a result, a good example of "translational medicine" emerges, where clinical results are used to build a dynamic and ever-changing model of the "genetic molecular body".

The same genetic molecular body is instead incorporated in fixed form by Bac platforms, where the analysis is roughly limited (never fully) to known areas of the genome. In this case, the work of interpretation is largely (but not completely) embedded in the technology itself. There is still a relationship with genetic databases, but that is limited to the few uncertain cases that emerge in the analysis, and to updates that such platforms with targeted designs requires now and again. In essence, the continuous mutation of the molecular body is frozen by these technologies into a series of still images, which serve to lighten the task of interpretation and, therefore, to implement a higher level of automation. Clearly, once again, increased automation, while minimizing the number of uncertain cases and lowering unit costs, potentially extends these tests to a greater number of people and therefore plays into the hands of the companies that manufacture these devices. At the same time, to a lesser extent, increased automation contributes to the codification of the "molecular body".

The platforms build a relationship with the future of prenatal medicine in a second and equally important sector, in relation to other tests that seem to redefine the practice of prenatal diagnosis. A particular comparison can be made with non-invasive prenatal diagnosis (Nipd), which is based on cell-free foetal Dna in maternal serum. Although this is not yet widely available in Europe, it is already widely practiced in North-America. It is possible that in the near future this technique will replace all other current techniques of prenatal screening and diagnosis. Even if, at the moment, it addresses only a handful of anomalies, such like trisomies 21 (Down's Syndrome), 18 and 13, it may be extended to wide set of genetic anomalies, including genes of susceptibility like Brca1 or Brca2. As part of the molecular turn, they will pose again similar issues about how to organise materially and clinically new biomedical entities, which in this latter case are not only molecular/submicroscopic, but also non-invasive.

8. Conclusions

Defined as the biomedical platform, the introduction of molecular genetic techniques in the field of prenatal diagnosis is a far from concluded process based on a stronger interaction between techno-scientific innovation and research and clinical routines. In a recent public speech, Eric D. Green (2013), the Director of the National Human Genome Research Institute at the National Institute of Health, stated that prenatal diagnosis is one of the "hot areas" of genomic research. With the advent of Nipd, genetic analysis seems to have lost one of the main obstacles to its diffusion, that is the inherent risk of miscarriage that the process of foetal biological material extraction carries. The possibility to analyse foetal Dna present in maternal blood opens even new possibilities. Dna sequencing may provide a genetic analysis still more accurate than CGH-arrays, and its clinical application seems not so far. The *Mit Technology Review* mentioned it as among the ten breakthrough technologies of 2013, namely, the possibility for a pregnant woman to obtain the complete Dna sequence of her foetus through a simple, non-invasive blood draw (Regalado 2013). Bioethics approaches the phenomenon with a prescriptive approach regarding the ethical norms that should be applied to the new techniques of prenatal diagnosis and screening. This paper tries to deal with these transformations from a different approach, focusing instead on the pragmatic changes that such innovations bring, and the various methods with which geneticists articulate these new technologies. In this sense, the concept of biomedical platform proves useful as a perspicuous conceptual framework that allows us to grasp the crucial role played by the ever increasing intersection of activities between not only the laboratory and clinics, but also among biomedical routines, innovation and research. The *platform* is not only the complex network of heterogeneous actors involved in the production and reproduction of new submicroscopic anomalies detectable by gene array technologies, but also indicates the central element on which the other elements revolve, namely the biochip.

Consequently, we have analysed the controversy over this embryonic biomedical platform as a multi-layered debate. The selection of submicroscopic anomalies that will be detected depends on the kind of arrays chosen for prenatal diagnosis. At the same time, the differences in the way these biomedical entities are produced affects the arrangement of the platform in which they are mobilised. In other words, this dispute shows the multiple possibilities in which it is possible to mediate relations among procedures, instruments, the representational space of Dna, clinical indications, etiological classification and scientific categories. Through the investigation of the correlations between routines, innovation and research, the organisational and epistemological way in which these material and immaterial entities are collectively arranged appears to impact connections between biotechnology companies, genetic database,

healthcare institutions and practice, the human body, and the normal/pathological divide. The controversy, therefore, drew attention to the important stakes involved in the material and discursive arrangement of the biomedical platform. Geneticists manage the prenatal diagnosis of the present, and prepare the future by playing with the organizational flexibility of the platform. We can identify the political sense of the biomedical platform as the manner in which the material and discursive intertwinement of biology and medicine, the normal and the pathological, is arranged. In synthesis, the framing and structuring of the extension movement of the medicine to come.

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The Role of Bioinformatics in Facilitating Translational Science and Medicine

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Abstract: Significant challenges exist around the translation of the enormous amounts of data generated from large-scale gene and genome sequencing that has been facilitated by the Human Genome Project into tangible medical. Widespread acceptance exists within the biomedical research community about the role that bioinformatics will play in that translational process. While the goal of moving research from "the bench" into socially beneficially applications "at the patient's bedside" has long driven science and technology policy, the picture is now more likely to resemble interactions between very powerful computers, and lab benches. Given the importance of bioinformatics, work presented here reports on a case study of a large Canadian scientific network that has developed a bioinformatics tool designed to facilitate investigations into gene-gene and gene-protein interactions and pathogenomics pathways. By focusing on this kind of bioinformatics system that facilitates a project's own internal biomedical research and simultaneously serves as a free and open resource for a wider group of academic nonpeers, we advocated for a broadening of what translational science and medicine can and should entail. Furthermore, by highlighting the importance of movements between developers and a host of prospective users (and back again) we show how translational bioinformatics systems can be more effectively advanced.

Key words: bioinformatics; translational science; translational medicine; user-configuration; infovis; systems biology.

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1. Introduction

Biomedical research and development (R&D) is undergoing major transformations as it attempts to achieve translational goals of moving research into the clinic, and deliver on earlier health-related promises issued alongside the Human Genome Project (HGP). One of the components of that transformation has been the development of bioinformatics systems and tools necessary to make sense of enormous amounts of data generated from large-scale gene and genome sequencing that has been facilitated by the HGP and the subsequent (next generation) sequencing activities. There is widespread acceptance within biomedicine that the development of medical interventions derived from that data will only be possible with such bioinformatics systems and tools (Zerhouni 2005; Yang *et al.* 2008; Ostrowski and Wyrwicz 2009; Szalma *et al.* 2010), which has even culminated in an emergent subfield in-and-of itself: translational bioinformatics (Butte 2008; Altman 2012). While biomedical R&D may have once been understood as processes that involve movements between the lab bench and the clinical bed, the picture is now more likely to resemble complex interactions between very powerful computers, lab benches, and maybe some place down the road a clinical bed. That said, bioinformatics systems and tools on their own are not sufficient to facilitate developments in biomedicine. In the interest of understanding the role that bioinformatics systems play in the process of translation, social science research has been conducted on a database and suite of analytical tools called InnateDB (Lynn *et al.* 2008; Breuer *et al.* 2012), which has been developed for the systems-level analysis of the innate immune system as a part of the Pathogenomics of Innate Immunity project (PI2)[1]. This bioinformatics case study was a component of a broader social science endeavor located within the PI2 project that asked which cultural and socio-technical factors constrained and/or enabled the translation of pathogenomics research into medical applications. The argument forwarded here is that bioinformatics systems and tools must be designed with keeping the larger (biological) research community in mind so that biomedical advances can be made more broadly. On top of the need for this particular design mindset, it is argued here that particular design processes and features can also facilitate the development of bioinformatics systems and tools that can be of tangible and far-reaching use in translational science and medicine.

Work in Science and Technology Studies (STS) and beyond has explored the history of bioinformatics (Suárez-Díaz 2010) as well as definitional issues important to understanding these novel systems (Leonelli 2010). Still other work has outlined some of the socio-culture aspects af-

[1] Pathogenomics of Innate Immunity (PI2) project website, *About the project,* http://www.pathogenomics.ca/, accessed 17 December 2009.

fecting the usability of bioinformatics systems (Douglas *et al.* 2011), and the corporeal implications for data that bioinformatics facilitates (Mackenzie 2003). Despite this recent interest, the production processes of bioinformatics systems – such as it is taken up here- has received relatively little attention from a social science perspective.

To position our case study some of the literature and current models of translational science and medicine are first overviewed, along with the acknowledgment of the importance of users in the translation of successful innovation. After detailing the methods through which we have collected and analysed our social science data on this bioinformatics system, we will then outline the functions of InnateDB and the Pathogenomics of Innate Immunity project (PI2) project in more detail. In the body of the text we use the classical sociological concept of *verstehen* to describe the particular mindset that bioinformaticians within the PI2 project adopted when designing a system for translational biomedical work. Further, we will show how specific design processes such as limited release strategy and a particular peer-review system facilitated the development of this translational bioinformatics tool. We will also describe the particular information visualization design features that were integrated into InnateDB so that it would be of use to researchers beyond those with computational backgrounds.

It is our position that resources and systems that are being designed both for internal project-specific use and as platforms that the broader biomedical community of academic non-peers can use for biotechnological development might be conceptualized as form of translational science (TS) that is distinct from other forms of commercial and/or clinical TS. While the iterative movements between bedside and bench (and back again) can be shown in cases of clinical translation, which are mirrored by bench-to-bedside (and back again) movements in the technology transfer and cases of commercial translation, this case of the development of bioinformatics tools suggests that TS needs to be more broadly understood. By including activities that involve movements between developers of research and analysis resources and a host of prospective users (and back again) we not only account for diverse forms of TS, but in doing so we also contribute to the larger goal of translating the masses of genomic data into usable information for health improvements.

2. Translational Science/Medicine and the Role of Users in Innovation

There has long been policy pressure to translate investments in a variety of research into socially beneficial applications (Bush 1945), and more recent demands for medical genetics research activities to deliver health benefits is no exception. The novel journal *Translational Medicine*

– published by American Association for the Advancement of Science (AAAS), who produces *Science* among other journals – outlines the need for a specific sub-field to facilitate this process:

> A profound transition is required for the science of translational medicine. Despite 50 years of advances in our fundamental understanding of human biology and the emergence of powerful new technologies, the rapid transformation of this knowledge into effective health measures continues to elude biomedical scientists. This paradox illustrates the daunting complexity of the challenges faced by translational researchers as they apply the basic discoveries and experimental approaches of modern science to the alleviation of human disease. Studies in humans often highlight deep gaps in our fundamental understanding of biology, but the linkages back to basic research to fill these gaps have not been as effective as they could be. Clearly, creative experimental approaches, novel technologies and new ways of conducting scientific explorations at the interface of established and emerging disciplines are now required to an unprecedented degree if real progress is to be made. Nothing short of a true reinvention of the science of translational medicine is likely to suffice.
>
> (*Science Translational Medicine* Mission Statement)[2]

Alongside academic journals, models of translational medicine have also been developed to try and steer translational work. For instance, common models describe the movement of biomedical research into diagnosis or treatment (i.e. phase 1 translation, or T1), which then moves to subsequent development into evidence-based protocols (T2) (Kerner 2006, 73), and their deployment into clinical practice (T3) (Westfall, Mold and Fagnan 2007), and ultimately the verification and evaluation for 'real world' impacts on health (T4) (Khoury *et al.* 2007). Specific areas of research (e.g. autoimmunity) have adapted their work and concurrent challenges to such models for translational medical research (Blumberg *et al.* 2012).

Work in the area of technology transfer and cooperative research centers (CRCs) suggests that advances in medicine need not be restricted to the kind clinical translation described above. A considerable amount of scholarship exists in the area of management sciences and science policy that have sought to facilitate the flow of knowledge and technology between universities and industry (Bozeman 2000). In this way we can come to think of commercial translation in medicine when health technologies or research on medicinal products are transferred to private companies or spun-off into their own market venture.

While it may be the case that these areas of scholarship have some traction with forms of clinical and commercial translation, they are argu-

[2] http://stm.sciencemag.org/site/about/mission.xhtml, accessed March 20, 2014.

ably less well equipped to handle dynamics related to the production of open access bioinformatics research and analysis infrastructures that are being discussed here. What the case presented here shows is that a particular design mindset and specific design processes and design features stand to play a significant role in the production of bioinformatics systems that are critical for the translation of gene and protein data into actionable medical information. As the body of the text shows, what these design mindset, processes, and features share is their attention to –if not direction integration of- system users in the development and production process. To be sure our work is not the first to acknowledge that a reliance on users is beneficial for the innovation processes with considerable attention being given to "user-driven research" (De More *et al.* 2010), customer-active innovation (von Hippel 1978), or "user-producer interactions" (Laursen 2011). Our case marks a slight departure from this perspective and instead suggests a bi-directional flow of innovation between users and creators of technology. Attention to such dynamics has been made in innovation studies (von Hippel 2005), science and technology studies (Oudshoorn and Pinch 2003), and e-commerce and computer programming (Klein and Totz 2004); however, it has yet to be applied in the area of translational science and medicine as is the case here.

3. Methods

The examination of InnateDB was a part of a broader social science project that sought to understand the social, political, economic, cultural, and technological factors that constrain and enable translational biomedical science. As such our team was an integrated component of the PI2 network from 2006 through 2009, and we conducted three translation cases studies within the PI2 network related to the clinical translation in the university hospital (Lander and Atkinson-Grosjean 2011), commercial translation associated with a pharmaceutical spin-off company, and the bioinformatics case presented here. While these three cases do not form an exhaustive list of translational pathways, we selected them because of their respective success in the translational process, their heterogeneity, and because of their connections with the PI2 network.

Given our integration within the PI2 network we knew that the bioinformatics database (InnateDB) and suite of analytical visualizations tools (Cerebral) would play a central role in the development and success of the PI2 project. Not only was clear that InnateDB and Cerebral were critical to the PI2 project, but as it is described in more detail below, these systems and tools were also being developed as a platform technology for those within and outside of the PI2 project to build knowledge, facilitate future discoveries, and assist in the early development of future medical prophylactics and/or therapeutics. Given our research goal of describing

the constraining and enabling factors in translational science, and in light of our recognition of the role that the bioinformatics system and tools were playing in the translational process of PI2 and beyond, we chose to conduct in-depth social science research on the production, maintenance, and use of InnateDB and its associated tools. As a result, from July 2007 to December 2007 we conducted ethnographic participant research and qualitative semi-structured interviews with one part of the bioinformatics collaboration responsible for the design and construction of InnateDB, and in November and December of 2008 we conducted a series of follow-up interviews across the two institutions involved in InnateDB (total n=25). Our interviews included the heads of the bioinformatics lab, the leaders of the PI2 network, the bioinformaticians designing the front-end and logic of the system, the computer scientist writing the programming code, and the curators who were manually inputting and managing the data submitted to the system. Given the relatively small number of researchers involved with InnateDB we choose to interview practically everybody who was significantly involved in the design, production, and maintenance of the system. Our integration within the PI2 network meant we were able to contact and arrange interviews directly with participants who were ready and willing to contribute to the social science component of the project.

Interviews were audio recorded, and transcribed by members of the research team and private transcriptionists. Interviews were then analyzed using a grounded theory approach to guide our exploration of the material (Charmaz 2006). This approach does not assume a theoretical position *a priori* to analysis, but instead allows a theory to grow out of the data in a developmental movement from code to concept to category to theory. In our case this was accomplished by the team constructing a coding matrix containing terms that highlighted important aspects related to the social, political, economic, cultural, and technological factors that constrained and enabled translational biomedical science. Codes were then attached to segments of interviews using qualitative software ATLAS.ti. Some codes were applied across the three cases (e.g. 'role of teaching and learning', 'impact of disciplinary background', or 'patents and intellectual property'), and some specific to the bioinformatics case (e.g. 'limited release strategy', 'manual database curation', or 'problems with database maintenance'). To improve the reliability in applying the coding matrix between team members, several interviews were coded by multiple members. Variations in coding application were discussed and consistent definitions agreed upon. A lead researcher for each case study then coded all remaining transcripts. The software was then used to produce reports on specific codes, which is similar to the 'concept' development phase within the grounded theory method. These reports were then examined for the most salient factors involved in the diverse forms of translation within the PI2 network, which were worked into concepts. It is here that we identified the importance of users, and consequently developed categories that

described the difference facets through which users were included in the translational process. These categories consisted of the importance of the end-user in the design process, the integration of users in developmental processes, and the creation of a system that includes features to enhance the user experience and enlarge the user-community. These categories have formed the core sections in the body of the text presented here. Within qualitative methodologies interview excerpts have been used to illustrate the above mentioned categories. In doing so the code reports that were used to develop our concepts were re-examined, and the most clear and succinct interview responses have been used as quotations in the body of the text to illustrate the specific category.

The final step in the grounded theory approach is to use identified categories, and the associated quotations, as the basis for a theory of the phenomenon in question. In our case that theoretical supposition is that if bioinformatics systems are going be of use to those beyond the development team for the translation data into useable health information, then they need to be constructed with a particular a mindset (i.e. *verstehen*) that take users into account, and they need to integrate users in the design process (i.e. through the peer review and a limited release strategy), and design the system with tools that facilitate systems-level analysis for those without a computational background.

4. InnateDB Case Study and the PI2 Project

The PI2 project/network was funded largely by Genome Canada to improve the systems-level understanding of the innate immune system. The human immune system has two general components: the adaptive immune system that response defensively against microbial infection and is stimulated by medical interventions like vaccination, and the innate immune system which acts as the first line defense against all foreign pathogens. According to the project's webpage, innate immunity can be understood as a:

> …part of our natural biological makeup – [and because of it] we are able to withstand a daily onslaught of tens of thousands of potentially pathogenic microbes in air, food and water, and in our interactions with other people and animals. But our innate immunity can sometimes get over-stimulated, leading to inflammation of tissue and even sepsis – a deadly infection of blood or tissue. Understanding the balance between infection resolution and inflammation is the goal of the new Pathogenomics of Innate Immunity Genome Canada Competition III project.
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> (PI2 2006) [3]

[3] Pathogenomics of Innate Immunity (PI2) project website (2006) *About the project,* http://www.pathogenomics.ca/, accessed 17 December 2009.

If the goal of the PI2 project is to understand "the balance between infection resolution and inflammation", then InnateDB's role in that project was to create a roadmap of the immune system. The metaphor of the roadmap is apt for non-scientific writers and audiences to deploy when trying to make sense of InnateDB, and was also a guiding metaphor for members of the InnateDB development team. It is worthwhile for one of bioinformaticians to explain themselves how this metaphor of the roadmap can facilitate an understanding of InnateDB:

> We just kind of want to make a roadmap to the immune system that, you know, when people… If you just look at a list - say you go to an atlas and you look at the index. Oh, very exciting; it's just a list of places. You can't really picture that. But then when you open things, when you open your atlas to a map page, you say, "Oh, this city is connected to this city by this road. Oh, these cities are in the same country. Oh, these cities are in a different country". And it's just like that. In the past, people have been analyzing their array data by just looking at a list. And they've never really put that list into biological context. So we are giving them a map. And we are giving them a map that's laid out well... But once you lay things out in their proper context - this goes here, this goes there, this goes there, this is in this part of the cell, this is in this part cell- then it makes it so much clearer, and people can start to follow relationships and trace pathways [and think]: "Oh, this receptor up here is being activated. And all these genes down here are getting turned on. Maybe that receptor is linked to this set of genes somehow".

While the broader PI2 project had numerous goals, one of the distinct objectives was to identify the key molecules involved in infectious disease response, which might ultimately give rise to new prophylactics or treatments. According to one of the InnateDB Project Leaders, "if you can target those key central molecules, perhaps you can predict therapeutic effects on the outcome of disease or the outcome of information". As a result when genes are identified to have an association to disease response InnateDB can be used to model the pathways and networks of those genes and proteins across different datasets. If the concurrent systems-level analysis does identify mechanisms within the pathway, then lab biologists will conduct wet experiments for the confirmation or dismissal of the mechanisms within the identified pathway.

Importantly, InnateDB also boasts supplementary interactions that innate immunity genes participate in, and because it has been created as resource to include all human and mouse pathways of interactions at systems biology level its relevance is not limited to innate immunity. Further, unlike bioinformatics resources that contain large amounts of annotated data, InnateDB comes equipped with a suite of tools through which re-

searchers can conduct analysis directly in the InnateDB website. What is more InnateDB is an open source and open access database and analysis environment. While there is a tradition (or even convention) in computer science (and perhaps even in bioinformatics) to design databases to be open access and open sources, the bioinformatics Primary Investigator describes the importance of open source and open access characteristics in some length:

> Yeah, so for open source it's important that you realize that open source doesn't mean "free", you know, so it just means that when you make software you can actually… the way you make software you write a program, and you can release that program to somebody and then they can run that program. Or you can package it up into an executable - a wxe file - and so that it's actually just in this binary code that you can actually see what the original program was, and you can release that…The open source model is where you just keep that package open so…you still have the ability to see that code, see that program, see how it works, know exactly how it works so you can either modify it for your own uses, or…redistribute it as some other version, or you just might want to see how it works to understand why it's doing… and so there's definitely been a growing movement of people that really want that, because they're frustrated with the sort of closed black box kind of software and for example in our pathogenomics project we found it very useful because there was definitely some microarrays software that was black box like that…

While the open source characteristic of InnateDB refers to the process of keeping lids lifted on black boxes so that users can see the computational processes that have gone into making the database function the way that it does, the open access refers to a similar characteristic of transparency. Within the open access model all users are provided free right of entry into the database, and the data contained within the database is free to access, download, and use for one's own research purposes.

Part of the data contained within InnateDB is itself an amalgamation of three or four different types of data that come from four or five different categories of open access data. This data that is present within the database is mostly "gene, proteins, and interactions and signalling responses involved in the mammalian innate immune response"[4]. These different kinds of data are collected from gene lists, external interaction databases, and external pathway databases, which are all integrated within InnateDB, and all open access. There are also links to external databases containing immunology-relevant data, but it is not clear if this information is integrated within InnateDB. As new data is compiled in these external

[4] InnateDB website *Home page*, www.innatedb.ca/index.jsp, accessed 1 March 2014.

databases it is regularly uploaded into InnateDB by website administrators. Keeping abreast of novel pathway and interaction data can be achieved in part by those with computer science backgrounds as they amalgamate existing databases into InnateDB; however, one of the distinct characteristics of this tool for translational biomedicine is that it is also manually curated - a point which we will return to as a key design feature of the system.

Alongside the massive amounts of curated and standardized interaction data that is accessible through InnateDB there is also a multitude of search mechanism available to mine the data. A researcher can make use of the search functions included in the suite of tools provided by InnateDB to investigate genes and proteins of interest, or view statistics for manually-curated molecular interactions that are relevant to innate immunity and submitted weekly by curators. Further searches can be conducted for "experimentally-verified molecular interactions by gene/protein name, interaction type, cell type, etc." as well as searches for 147,240+ interactions & 4,400+ pathways[5].

Not only can a researcher mine the gene, protein, and interaction data that is provided through InnateDB, but because it has been concurrently constructed as a suite of tools researchers can also upload their own data and conduct particular kinds of analysis immediately on the InnateDB website. Gene expression data can be uploaded by anyone, and then through the use of a piece of software called Cerebral researchers are "able to interactively visualize interaction networks with expression data overlaid; carry out Pathway, Gene Ontology and Transcription Factor Binding Site over-representation analysis, construct orthologous interaction networks in other species and much more"[6]. Not only are these tools provided as an integral part of InnateDB, but video tutorials also exist on the website so to help users familiarize themselves with how these tools can be most effectively used. In light of the central role that is played by Cerebral in the InnateDB analysis environment, it will receive more attention later when we more directly describe the particular design features of the system that can facilitate the translation of data into valuable biomedical information.

5. Designing Bioinformatics Systems for Translational Science and Medicine

[5] InnateDB website *Home page,* www.innatedb.ca/index.jsp, accessed 1 March 2014.

[6] InnateDB website *Home page*, www.innatedb.ca/index.jsp, accessed 1 March 2014.

5.1. Particular Design Mindset

In order for InnateDB to be usable tool for translational science to both those inside the PI2 network and to those outside of it who may or may not have a computational background, the researchers building the system had to adopt a particular design mindset. Classical German sociologist Max Weber used the word "*verstehen*" to describe the process through which the social researcher would develop an interpretive understanding of meaning and human activity (Ritzer 2007). By approaching a human's actions from their point of view Weber hoped to gain an appreciation of the way in which they constructed and gave meaning to their own world. In doing so the social actor is not seen as the mere object of investigation, but rather as a subject. Here we can adapt this concept to the social study of science and technology to explore the case of InnateDB and the particular mindset the bioinformatics system designers deployed in making a tool that would be broadly usable for translational activities. The system architects -whom were largely computer programmers coming from a computer science background- needed to develop a level of interpretive understanding (or *verstehen*) of diverse prospective users of InnateDB, so that it could be appropriately configured to their needs. While the system architects and designers had a general understanding of what members of the PI2 team would be using the system for, they had to develop a more nuanced understanding of systems biology so that InnateDB would be equipped for the kinds of translational work that such researchers would be undertaking. One of the developers described this learning process in these words:

> I didn't anticipate that people would be uploading entire GeneChips of data. I thought it would probably be 100 or 200 queries at a time. And so I sort of…the way it was designed, it was sort of a design in the manner to handle these many pieces of data. But when you get into, sometimes…like 25,000 or 30,000 genes being uploaded is quite a load on the server. And it sort of brought it to a crawl at first until we said: "Okay. I've got to step back and rewrite this". So, it was a few extra months, but it definitely paid off.

InnateDB also boasts a team of curators that manually keep gene, pathway, and interaction data current. Their training in biologically-relevant disciplines means that they can sift through individual pieces of published data – as opposed to already curated data that is found in the other interaction and pathway databases. They are then able to make decisions with regards to the accuracy and relevance of that data to InnateDB, and submit it to the system. Without this curation the database becomes a rather static entity, and its practical value concurrently decreases to the PI2 project team as well as those interested in innate immunity and

systems biology more broadly. Curating originally began as an examination of data concerning single genes, and if the quality of that data could be confirmed then it would be uploaded into InnateDB for subsequent use. However as InnateDB grew, curating extended towards the examination of specific pathways with curators themselves playing an increasing role in deciphering the balance between infection resolution and inflammation. While these curators are not the analytical bioinformaticians who conduct the systems-level analyses that identify mechanisms within the pathway, nor are they the lab biologist that produce experimental confirmation or refutation of the mechanisms within the pathway, they are key players in the pathway identification process. Having a level of interpretive understanding of how systems-level bioinformaticians go about assembling these pathways greatly facilitates the work of the curators by sensitizing them to the kind of data that they should be on the look-out for. In turn, systems-level bioinformaticians increasingly grow to trust the data within InnateDB when they know its character, quality, and standards, which then facilitates their analytical work. One of the curators explains this dynamic when asked about the potential for training to increase her analytical role in the project:

> But from a bioinformatics point of view, to understand how it kind of is related to this database, like that's the whole point right, is to analyze data basically. So from me, I think it would be more interesting to kind of learn the aspects of that [analysis], but our job description is to look for particular protein-protein, or protein-gene interactions. So you don't necessarily need [added understanding of the analytical processes], it's just kind of an added thing that might actually increase the analysis, or maybe things that you kind of pick-up on that other people may need later on. Because I think [the project leader] also kind of looks at it with the perspective of: "How he would analyze his data", but when it comes to curating, I ask for certain things that maybe weren't on the website, but might help us later on to do the pathway curation. But over all, it's supposed to help out data analysis.

By demonstrating a level of end-user *verstehen*, manual curators also affect the development of the data that goes into InnateDB, which influences the analytical applications that the data is used for. Seeing the relationship between curators and system-level analysts in this way conforms to the colloquialism of 'garbage-in-garbage-out' which is well worn within database and bioinformatics cultures. The PI2 analysis emergent from InnateDB will only be as good as the interaction and pathway data that is boxed-up inside of it, so it is clear why high quality curated data is central to the project. Part of the process of obtaining high quality curated data is to equip curators with a bigger picture of what the data would be used for in bioinformatics terms. Therefore it seems useful -if not necessary- for each member of the project team to have an appreciation of what oth-

er team members are doing and what their job entails so that they can do their own job better. For analysts to do their job well they need to know that they have good interaction or pathway data to conduct their analysis with, and for curators to do their job well it is good to know the larger analytical picture (i.e. the purpose of the databases is about, what it is meant for and what it is meant to accomplish) so that they can input the right kind of data with the right kind of annotations. This suggests that understanding the roles and goals of other project team members is highly relevant to the success of multidisciplinary research, and ultimately to the achievement of translational goals. While we have seen here how a particular design mindset that takes into account the prospective user of the technology is critical in the construction of a useful translational tool, the following section explores how particular design processes are similarly important in achieving this goal.

5.2. Particular Design Processes

InnateDB was first released for public use in May of 2008. However, before it could effectively "go live" a number of design processes were undertaken that included a limited release strategy and a rigorous peer review, which helped it to become a useful tool to the PI2 network and beyond. In his work *Democratizing Innovation*, Eric von Hippel shows that "much of the information needed by product and service designers is 'sticky'" (von Hippel 2005, 67). Different users have diverse needs and capabilities that require inscription into a system so that its' utility can be maximized. As a result, unsticking those needs and capabilities and getting them to the designers is of paramount importance in the development of useful technologies such as bioinformatics systems. One of the ways through which this was accomplished with InnateDB was by releasing drafts of the system prior to its public release to select colleagues in the innate immunity community and to the PI2 project team. The role of the limited release strategy should not be underestimated, as prospective users of a technology are proving to play an increasingly central role in up-stream innovation processes. With a working version of the database in place, and with some data now loaded in, PI2 team members from other components of the project were invited to access the system and experiment with its uses while the database was still in its developmental stages. Incorporating project team members outside of the database development team at this stage was important for a number of reasons. First, the development of any system is bound to have bugs, and identifying problems with the operations of InnateDB would be crucial before it was to be released to the public. More importantly PI2 project team members were brought into the development process so that their needs could be readily identified and configured into the design of the technology. While the developers of InnateDB would certainly consider themselves bioin-

formaticians their familiarity with biological sciences varied. As a result experimental biologists were consulted to provide feedback on the system. One of the InnateDB's designers explained the content and function of that feedback:

> [Biologists provided feedback on] all sorts of levels to, you know, to broadly… kinds of things you want to do, you know, feedback to the extent of what are the biological questions that they want to be able to use the system to use, down to pretty nitty-gritty questions of, you know, in our visualization system, you know: "Do you want to see broad spectrums of colours or do you just want to keep it pretty simple? Yes/No, kind of colours? [up-down] kind of thing?" Yeah, so from quite a broad spectrum of very nitty-gritty stuff to big picture types of big questions they want answered.

Two bioinformaticians who conducted system-level research and who were familiar with the challenges of databases and tools were also a part of the process through which InnateDB would be improved upon. Both of these bioinformaticians were members of the PI2 project, and involved with the construction of InnateDB, but were not the developers responsible for the schema, submission system, or search mechanisms. As one of these key figures point out:

> The other thing that I think was kind of critical is that, although I've worked in bioinformatics for about 10 years now, my background and interest is on the biological sciences side of things. I think having someone with that background making the key decisions on the direction of the thing was very beneficial to ensuring that it was relevant to a biologist, and a lot of these things are developed by people with computer science backgrounds who, you know, can come up with great algorithms or whatever but don't have the same insight into how a biologist wants to see things.

As the above excerpt demonstrates, these two bioinformaticians were of a particular ilk which made them crucial to the development of InnateDB. Not only did these two actors have more familiarity with the computer science end of databases, which allowed them to engage with the developers on a deep level that the average experimental biologist was unable to do, but more importantly they were prime examples of the kinds systems-level end-users of InnateDB. Problem areas of InnateDB were identified through the early deployment of the suite of tools for high-level analysis and future improvements were also prospected.

Another important aspect of the design process that has facilitated the construction of a translational bioinformatics system was the peer-review process, and subsequent publication of both the article that describes InnateDB (i.e. Lynn et al. 2008) and the actual database system itself. While

it may seem obvious that a journal would access the functionality of a system like InnateDB in the peer-review process, this strategy seems to represent a departure from traditional articles in bioinformatics. One of the members of the PI2 network described it this way:

> I mean bioinformatics when it started, and bioinformatics really only started to become big ten to fifteen years ago. And for the longest time, it was such a specialized field that people were doing it for sort of discovery sake, and not really making tools that were ideally suited to an end-user. Even when I was doing my PhD [2001-2005], I'd say half of the papers I read that reported sort of a relevant method to what I was doing were just algorithm papers. There was no software; there was no website to go along with it. It was just telling you the method, "We did this, and he's our paper with some math showing how we did it, but you can't actually do this unless you create this entire system and do this entire training dataset". So that was the prevailing mindset in bioinformatics, and I think that was probably, I don't know maybe it was sort of a cultural thing. The scientists that first got there, they were these specialized scientists. They didn't really care; they were just doing this for discovery sake. But then the people that have gotten into bioinformatics more recently, people of sort of my generation, or a couple of years older and sometimes younger realized the importance of the user community. Because we had to do our Master's and our PhD's seeing these methods that looked really interesting, and not being able to use them anywhere. So I think to our generation of bioinformaticians the notion of open source is a big thing. Making your work available to people. And people realize that your tool can be open source, and available to the world, but if it's not designed well people aren't going to use it.

In light of transformations within bioinformatics to publish functional tools rather than a theoretical algorithms and methods, InnateDB had to be up and running before the review process could get under way. In this respect the publication process that the InnateDB paper had to navigate – before it could be deployed to grow its user community – had to pass a kind of usability test in the form of peer review. While peer reviewers may not have embodied the traditional notion of 'user' that is conjured up in one's mind when technologies are discussed, and nor does the publication process meet conventional understandings of technological 'use', both would prove to be an essential hurdle that the team had to overcome in their attempt to manifest InnateDB's translational potential:

> Writing any paper takes a while to complete, a big paper like this. The reviewer comments were probably the most positive comments I've got on anything I've ever been involved in before. They were hugely positive comments and the suggestions that they wanted to do were very relevant and things that we would have wanted to do and that we just, we did it for them. For example, we

> used to allow users to upload just four gene expression datasets at one time and they wanted to increase the capacity to be able to do more datasets in one go, so we increased it so that you can now do up to 10 different conditions at any one time. We had some other limits to do with computational power in terms of the number of interactions you could return in any one search, and they felt that if we could find a way around that it would be better not to have any limits. Our original thinking was that, you know, we had pretty generous limits - like we're talking you could return up to 10,000 data points kind of - and if you really wanted to do any more than that you were probably at a fairly advanced bioinformatics level and you can just download the entire database including all the data and then analyse it, but they would have preferred that the limits be removed. So we came up with a computational approach to mean that we could do that. And so now we don't have limits in our searches now, you can return all the data in any search.

What this section shows is that there is a clear link between the publication process, the role of users in the design and development stage of bioinformatics tools, and potentialities of translation.

5.3. Particular Design Features

For InnateDB to be a useful tool for making sense of vast amounts of sequence data it also had to include a suite of tools to aid researchers conducting analyses into problems of systems biology. One of the analytical tools that can be found within InnateDB is called Cerebral. This tool was created as a Postdoc project by researcher within the PI2 network to facilitate the research into innate immunity by the team, but also to act as a tool for the wider biological community in general. As she explains herself:

> Sure, well I was always sort of peripheral to the InnateDB project, I was brought on to work on Cerebral, which is a spin-off, you know it's a component of InnateDB, but in and of itself it's, its own project. And so I really, you know when I was doing the Cerebral work; I tried to develop it for the larger community.
>
> [Researcher]: Which larger community, sorry?
>
> Biology in general, anybody interested in visualizing networks in a pathway like fashion. So you know, it's all basically, its creation was inspired by InnateDB, and sort of went along with InnateDB, but I always kept my eye towards a larger audience when developing it. So, I was always sort of on the periphery. I'd be included in some of the InnateDB meetings, and things, just to provide guidance as one of the ultimate users of the database.

Cerebral – or CEll REgion-Based Rendering And Layout – is a tool that allows analysts to visualize biological information in traditional sig-

naling pathway/system diagrams. It is not a stand-alone tool, but rather a plug-in for one of the most widely used bioinformatics tools called Cytoscape, which: "is an open source bioinformatics software platform for visualizing molecular interaction networks and biological pathways and integrating these networks with annotations, gene expression profiles and other state data" (Cytoscape 2012). As a plug-in, Cerebral brings many features useful for pathway and interaction analysis that Cytoscape lacks, and seeks to supplement -rather than supplant- the existing visualization tool: "Cerebral is a plug-in that enhances Cytoscape's functionality by using extra annotation provided by the user to both automatically generate a more pathway-like representation of a network and to provide an environment for the visualization, comparison, and clustering of expression data from multiple conditions" (Barsky *et al.* 2007; Cerebral 2012). While Cerebral could have been developed as a standalone tool, Cytoscape has created a certain degree of technological lock-in within the bioinformatics user community that has been facilitated by its open source and open access character. Releasing a tool outside of Cytoscape software platform would undoubtedly reduce the numbers of users accessing Cerebral thereby diminishing its capacity as a piece of translational science. One of the developers of Cerebral explained it this way:

> "By piggybacking on a big endeavour like that, there's two main advantages to the plug-in developer both of which are entirely selfish. 1) Is its way less work…if you're looking at it [Cytoscape] from an infovis perspective, you're kind of like: "Oh, why did they decide to do this?". And the rendering engine is goofy, and all that stuff. So initially [our collaborators] looked at Cytoscape, and they're like, "Oh gees this is a piece of crap, can we please just build our own version". And I was pretty adamant that, "No we gotta do it in Cytoscape", I mean there's so many functions beyond the visualization that we would have to code into one of these bits of software that would take years, and years, and years to do something that even did a tenth of what Cytoscape does. So it's saving you a pile of work by piggybacking on something, and 2) it's also giving a huge user community too.

One of the ways that Cerebral enhances Cytoscape's functionality is by integrating ideas and lessons from the emergent interdisciplinary fields of information visualization and visual analytics. Information visualization – or infovis – is "the use of computer supported, interactive, visual representations of abstract data to amplify cognition" (Card *et al.* 1999). Data can take both numerical and non-numerical form, such as genes and proteins. Visualization can aide users from various disciplines to address a variety systems-level problems in biology because "visual representations and interaction techniques take advantage of the human eye's broad bandwidth pathway into the mind to allow users to see, explore, and understand large amounts of information at once. Information visualization

focused on the creation of approaches for conveying abstract information in intuitive ways" (Thomas and Cook 2005). Visual analytics (VA) on the other hand is an outgrowth of infovis, which "combines automated analysis techniques with interactive visualizations for an effective understanding, reasoning and decision making on the basis of very large and complex data sets" (Keim *et al.* 2008). Whereas infovis is concerned with principles, ideas, and assumptions concerning how users see and use information, VA is more about the development of tools resultant from these visualizations to facilitate analytical reasoning.

In the case of InnateDB infovis principles were used in the development stages of Cerebral and the tool can boast of both infovis and VA characteristics in its most recent incarnation. When asked what role infovis would play in developing bioinformatics systems that are useful tools in the translation process and resolving biological problems, one of the developers of Cerebral responded this way:

> Infovis is going to be huge, huge, huge. And Cerebral and a few other sort of similar type tools are really the first ones to bring visualization to bioinformatics. I think Cerebral was probably the first one to bring principles from information visualization to bioinformatics. You know tools like Cytoscape were obviously around for a while that would create a visual representation of data so you could interact with it easily. But they didn't really do any research into infovis principles and ideas when they built Cytoscape. But when we built Cerebral, we had our two infovis collaborators so they brought in all these things that we sort of never heard of before and never considered in biology that just made Cerebral that much better. Because all this research into a how a user looks at screen or where do they look, what colours do they respond to, what shapes do they respond to all of that went into Cerebral, and it really was the first instance of that happening. But, I think visual analytics are going to be huge…So if you can make things as simple and as universal as possible, then you're well on your way forward to satisfying as many people and getting a huge user community as you possibly can. So I think as bioinformatics professionals recognize this, they're going to be making their tools more usable by adopting visual methods.

Through their integration of Cerebral into the construction of InnateDB the project team was not simply coupling a suite of analytical tools with a database; rather, they were creating a research resource that would be as widely usable as possible. Further, it is important to note that this was not required by their funders, and they were under no obligation to create their own project tool this way; rather, it was an initiative they took of their own volition. Not only would their choices of particular design features allow them to tap into a larger research community associated with Cytoscape, but by designing a visual analytics tool like Cerebral with infovis principles the PI2 team were purposefully creating a research re-

source that would extend beyond their own project and into the wider biological research community without a hardcore computational background.

6. Conclusion

We have argued here that a number of features of InnateDB have functioned to make it a research and development resources both for internal use of the PI2 team and as platforms for the broader biomedical community to engage in translational work. Specifically we have shown how the development team took on a particular design mindset throughout the construction process in which they constantly envisaged who their diverse users might be, and how they might use the system. By deploying a level of interpretive understanding – or *verstehen* – of their users the InnateDB team was able to construct a tool more suitable to diverse user needs. Furthermore, through an appreciation of how systems biologists would use InnateDB the architects of database were able to make important alterations to the amount of gene data that could be uploaded by users, and the curators were able to improve the data that they were inputting into the database so as to minimize the 'garbage-in-garbage-out' phenomenon. Both of these changes stand to have an impact on the ability of systems biologists to move their work along in the translational process. We have also shown how particular design processes related to the limited release strategy and peer review worked to not only debug the system, but to construct a tool that was more useful for the kinds of system-level analyses needed to advance translation in innate immunity and beyond. Finally, work here has made clear how design features related to information visualization and visual analytics make InnateDB a resource and tool increasingly usable to those who may not have a computational background. By designing a system that is more usable, the potential users of the system expand, and then so too does the potential to make sense of data contained within the database.

By creating resources and tools for the broader biological community to use, activities like the construction of InnateDB could be considered a particular form of translational science, or what we have referred to elsewhere as 'civic translational science' (CTS) (Atkinson-Grosjean and Douglas 2010; Lander and Atkinson-Grosjean 2011). The motivation behind the labelling of CTS practices is not to construct a hard and fast definition that will be true for a specific set of activities, but rather to call attention to a broader set translational dynamics that exist beyond the clinic or the market. Iterative movements between bedside and bench (and back again) can characterize clinical TS (see Lander and Atkinson-Grosjean 2011 for e.g. within PI2 network), which are mirrored by bench to bedside (and back again) movements in the commercial TS and tech-

nology transfer. However, the development of an open source and open access resource like InnateDB that facilitates the translation of massive amounts of gene and protein data into usable health information for clinical and commercial developments is not well suited to such clinical or commercial representations of TS. What InnateDB shows is the importance of movements between developers and a host of prospective users (and back again) in the production of research and analysis tools. In the case presented here those users were the wider scientific polis or academic non-peers who would use InnateDB, but the concept needn't be applied strictly to such users. For instance, in other cases users might also include factions of the public, as "civic science" has elsewhere been "used interchangeably with participatory, citizen, stakeholder and democratic science, which are all catch words that signify various attempts to increase public participation in the production and use of scientific knowledge" (Bäckstrand 2003). Rather than exacerbating ambiguities that already exists around the notion of "civic science" or "civic scientist" (Clark and Illman 2001), our intention here has been to broaden what counts as translation science and medicine to include the construction of bioinformatics systems, and to show how such systems can be more beneficially constructed to fulfil translational tasks.

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Visualising Bodies Within and Beyond Laboratories and Clinics

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Abstract: As a response to the spread of biomedical imaging, this conversation explores crucial aspects related to the production, interpretation and use of body images within and beyond laboratories and clinics. Regula Valérie Burri's contribution raises questions about the implications of medical imaging technologies and practices for both medical treatments and patients' identities. Annamaria Carusi explores the intertwined epistemic and ontological roles of visualizations in the field of personalized medicine within two contexts of mediation: that of basic research and biomedical application; and and that of biomedical research and health care systems. Finally, Aikaterini A. Aspradaki discusses the use of body images from a bioethics perspective, focusing on the autonomy of persons and the ethical, economic, legal and social issues raised by the visualizations of bodies.

Keywords: visualisation; bodies; biomedical imaging; personalised medicine; bioethics.

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Pictures, Practices, Paradoxes: Medical Imaging and Modernity

Regula Valérie Burri

In this contribution, I argue that medical imaging technologies and practices imply several paradoxes. While, on the one hand, medical imaging opens up a set of new options and possible choices for patients and physicians, it narrows down, on the other hand, the scope of perceptions, agency, and alternatives in certain situations. The new freedom of (diag-

nostic) choice is contrasted, for example, by the power of the diagnostic facts and the rhetorics of the images on self-perceptions, or the lack of an adequate treatment for several indications. Paradoxes are implied all along the imaging trajectory – from the construction of the images and their interpretion to the ways they are used and deployed in (biomedical) practices within and beyond the labs and clinics. Paradoxes are thus implied in the whole process, which should be studied in the context of social studies of scientific imaging and visualization (SIV): production, engagement, and deployment (Burri and Dumit 2008), in other words, the production, interpretation, and use of images (Burri 2008, 2012).

This contribution explores the paradoxes and unintended dilemmas related to medical imaging. It raises questions about their implications for medical treatments and patients' identities, and finally discusses the findings in the context of the modern societies we live in.

1. Blackboxing the Apparatus: The Technology Paradox

The first paradox relates to medical technology. Imaging apparatuses such as computed tomography (CT) and magnetic resonance imaging (MRI) scanners are very complex machines. However, their output – the image – does not reveal the complexity of the apparatus that was used to produce it. The technology is blackboxed and made invisible in a body scan. A medical image thus appears to be a photorealistic depiction of nature instead of a sociotechnically constructed representation in many situations. "It's almost a photograph of the brain", said a neuroscientist during my fieldwork in imaging centers of large university hospitals, and a professor of neuroradiology held that through these pictures, you can look directly into someone's head (see also Dumit 2004; Joyce 2005; Burri 2008, 2013).

Whereas in the early days of imaging technology, CT and MRI body scans were not able to display any clear contours of body parts, today's images are high in resolution and contrast, thus making the sophisticated technology 'transparent' and able to disappear behind the image (Borck 2001; Burri 2008). The technology paradox thus implies that the better developed and more complex an imaging technology is, the more likely people are to forget about it once they look at the images.

2. Flood of Images: The Selection Paradox

Once images are interpreted, a further antagonism comes into play. The process of understanding the images and making up a diagnosis includes a selection paradox. Physicians appreciate the advantage of images to provide information on the inside of the body in a noninvasive manner. Visual screening makes surgery often unnecessary. Physicians also say

that images allow them to perceive information at once, just by looking at one image, whereas it would take them much more time to read the information provided by an accompanying report. Such "visual value" (Burri 2012, 49) allows people to perceive visual information simultaneously.

In order to make this one glance possible, a lot of images have to be produced. Even if the number of images constructed depends on the patient, the examination, the physician, and the local routines, there are usually several dozens of images produced in one imaging examination. An MRI examination of a person's head, for example, may include two series of 24 images each with a contrast agent (which enables the visualization of the blood vessels) and three series of 24 images each without applying a contrast agent, thus fabricating 120 brain scans in total. In some centers, these images are printed out on film and the whole examination results in several films, each of them containing 12-20 images. Other centers do not print out digital scans at all.

To make sense of an imaging examination, a radiologist does not consider all fabricated images. Usually, the medical technologist in charge picks a selection of a few images, which she or he presents to the radiologist for interpretation. The final diagnosis is thus based on only one or a few images, although a large amount of images had to be produced to make this one glance possible.

3. Increasing Uncertainty: The Epistemic Paradox

After their production, the images have to be interpreted to get more insight into the human body. The increased knowledge that is gained through the new digital possibilities of looking inside a patient's body, however, is often accompanied with an epistemologically nondefined situation. In other words, the certainty gained through the visualization of the body may at the same time imply an increase of uncertain knowledge. For example, when someone is examined with MRI because she or he suffers from a headache, diffuse changes of brain regions may accidentally be detected on a scan. In some cases it is not clear what such changes mean – they may be a symptom of a tumor or may not be pathological at all. The further course of a detected change often remains unclear. The interpretation of such images may thus increase both the unknowns and the epistemic uncertainty of a situation instead of gaining in-depth medical knowledge and achieving certainty about the course of an illness.

4. Lack of Treatments: The Option Paradox

Although in most cases the interpretation of images does contribute to

the diagnosis of an illness (or helps to exclude the existence of such), such stabilized medical knowledge may include an option paradox. While, on the one hand, the diagnostic advantages of MRI are widely recognized today, and diagnostic skills have increased in recent decades, there is not always an adequate therapy at hand to treat the diagnosed illness. The gap between the diagnostic possibilities and the available treatment for certain indications is growing.

For example, medical imaging is widely used in the evaluation of Alzheimer's disease. This debilitating disease affects approximately 5 million, mostly elderly people in the United States, and 50-70 percent of an estimated 7.3 million Europeans who suffer from different types of dementias[1]. Although Alzheimer's disease was first described 100 years ago, the causes of the disease are complex and not yet fully understood. Up to this day, there is no adequate treatment to heal Alzheimer's but only treatments aimed primarily at slowing progression of the disease rather than halting it completely or reversing its progression. This produces the paradoxical situation that, on the one hand, the diagnostic tools (including MRI) are very advanced but, on the other hand, this new freedom of diagnostic choice contrasts with the limitations of available treatments.

Another example is the diagnosis of brain aneuyrisms. By the use of imaging technologies such as magnetic resonance angiography, a brain aneurysm, which is a localized, blood-filled bulge in a blood vessel of a brain, can be quite easily detected. Today, elaborated techniques for treatment called *surgical clipping* and *coiling* are available, and less invasive methods such as endovascular management have been developed in recent years. Nevertheless, there is a lack of adequate treatments for some patients. In several online forums, patients report that because of the size or location of their aneurysm, it can't be treated. A user called newtons63, for example, recounts that: "doctors are watching and waiting as it is in a [too] dangerous area for coiling procedure"[2] and another patient with two aneurysms holds: "The smaller one could not be operated on because they didn't have anything small enough to stint it"[3]. Similarly, the user peaches217 claims that: "the surgeons say that my aneurysm is inoperable"[4]. In cases when aneurysms have not yet ruptured – and may never do so – physicians are very cautious about invasive procedures. While treatments of brain aneurysms have advanced over recent years, the gap between diagnostic and available therapeutic methods is thus increasing.

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[1] US National Institutes of Health (2012) and http://ec.europa.eu/health/major_chronic_diseases/diseases/alzheimer/index_en.htm#fragment1 (retrieved May 10, 2014). The data refer to the year 2006; see also introduction section.

[2] See http://neurotalk.psychcentral.com/thread52715.html (retrieved March 18, 2014).

[3] See http://www.bafound.org/survivor-stories-2 (retrieved March 18, 2014).

[4] See http://neurotalk.psychcentral.com/thread52715-2.html (retrieved March 18, 2014).

5. Forcing Decisions: The Agency Paradox

Once medical images are interpreted, they force physicians and patients into decision situations that may be difficult to cope with. Despite the uncertainty of the further course of a detected and only potentially dangerous disease, patients have to decide whether to get special treatments such as surgery or not. A discovered aneurysm may remain stable and not rupture at all during a patient's life course. This is recalled in patient forums, for example, by a neurosurgery physician assistant called Mike: "Remember, most people with aneurysms die with them… unruptured"[5]. It is thus a mere potential risk that a patient is confronted with. Nevertheless, once an unruptured aneurysm is diagnosed, patients and doctors have to deal with the situation and are forced to decide whether to opt for an intervention (i.e. to clip or coil the aneurysm, or treat it by endovascular management) or refrain from taking any activities and just monitor the cerebral abnormality.

Taking a decision may be especially difficult in cases of accidental diagnostic findings when the detected abnormality is not causing any pain, like in the case of a patient called Raglet, who reports that she or he did not have any symptoms and thus did not know about having any medical problems at all.[6] Patient Anna's story illustrates the difficulties of decision making regarding choice of treatment. Being concerned about a pain in the side of her face, the 40-year-old schoolteacher went to see a doctor who sent her for a CT scan and an MRI. She was diagnosed with two brain aneurysms. Anna reports: "As a family, we had to make very serious decisions… Should we do nothing and hope [the aneurysms] never burst or should we risk two invasive operations?"[7]. After having several consultations with a top neurosurgeon, weighing all the factors, and calculating the odds, Anna and her family finally opted to go for the clipping surgeries.

Within families, such decisions may be controversial, as a female patient recounts, who agreed to the surgery but whose husband "was totally against" her decision[8]. In such situations, patients have to trade off two forms of risks – the risk that the aneurysms may rupture, and the risk of a complex neurosurgical intervention. These decisions are very difficult to make, given the uncertainty of the situation: "They said I could live to be 70 or die in my sleep tonight", peaches217 notes in her forum contribution, and seeks advice from other patients by asking them: "Did you get it

[5] See http://neurotalk.psychcentral.com/thread152664-2.html (retrieved April 4, 2014).
[6] See http://neurotalk.psychcentral.com/thread52715.html (retrieved April 4, 2014).
[7] See http://www.bafound.org/annas-story (retrieved March 18, 2014).
[8] See http://www.bafound.org/survivor-stories-2 (retrieved March 18, 2014).

fixed?"[9].

Mostly, decisions are not the result of mere medical assessments or simple rational calculations but rather the outcomes of complex considerations that include psychological and social aspects. For some patients, it is simply no option to live with the knowledge of having a bulge in their brain that may rupture at any time. Mike, the above-mentioned forum user, explains: "What may eat [yo]u up psychologically is thinking you have a 'ticking time bomb' in your head"[10]. Such patients may take the risk of surgery even if there is a certain chance that their aneurysm will never burst.

Medical imaging thus forces patients and doctors into situations to decide for or against certain activities. The new options and possibilities that imaging technologies and practices open up – the new freedom of choice – go along with the obligation to indeed make a choice. Other medical technologies and diagnostic methods, such as genetic testing, result in a similar agency paradox. Nevertheless, medical images allow people to see abnormalties with their own eyes. Images are thus visually more persuasive than genetic testing results, as patients confirmed during my fieldwork, and may thus make a greater imposition on one's self-perception (Burri 2008).

6. Shaping Self-Perception: The Identity Paradox

Such "visual persuasiveness" (Burri 2012, 52) involves the next antagonism: the identity paradox. The new freedom of diagnostic choice enabled by medical imaging is in contrast to the shaping power of the images regarding self-perception. If a person, for example, gets a brain scan that shows no abnormality in medical terms, this person knows that this finding is evaluated as a biological fact, and that she or he will thus be considered as normal by both physicians and society. A 'normal' finding – in which a neurologist can't see any major differences when comparing a brain scan with a so-called normal or average brain image – is considered as a confirmation that this person legitimately feels good. If, however, she or he rather experiences being ill, a 'normal' finding makes an imposition on him or her: because of the lack of any medical indications, this person is expected to feel well. A normal finding, and thus the absence of any medically classifiable disease, can otherwise be a great relief to persons who suffer, for instance, from an enduring headache. Based on an imaging examination, an illness such as brain tumor can be excluded. On the contrary, if the finding is abnormal, the person is assigned a legitimation

[9] See http://neurotalk.psychcentral.com/thread52715-2.html (retrieved March 18, 2014).

[10] See http://neurotalk.psychcentral.com/thread152664-2.html (retrieved April 4, 2014).

for his or her possible pain and is thus stigmatized as being in a problematic condition even if she or he subjectively feels healthy.

Although historians have shown that boundaries of what is socially considered normal and abnormal (Canguilhem [1966] 2007; Foucault [1963] 1973, [1975] 1995), or objective and non-objective (Daston and Galison 1992), are contingent and change over time, patients know that images are mostly considered as evidence by both physicians and the public. Any knowledge based on a person's medical images will thus shape the way this person perceives him or herself (Dumit 2004). The evidence of medical images thus includes an identity paradox, that is, an antagonism between the new freedom of choice and the shaping power of the images for people's self-perception and identities.

7. Conclusions

The paradoxes related to medical imaging correspond to the ambiguous feature of contemporary societies described by Beck *et al.* (1994, 76), who have pointed out the characteristic of reflexive modernity to offer new choices to individuals: "choice has become obligatory. This is a substantive thesis about everyday life today," the authors note. At the same time, they state that people constantly have to opt for one of the offered choices. Drawing on this analysis of the contemporary modern society, medical imaging can be interpreted in a wider context. On the one hand, it offers a set of new diagnostic choices for physicians and patients, yet, on the other hand, it limits the agency and alternatives in certain situations, for example through fashioning the ways people feel and see themselves. Medical imaging technologies and practices open up spaces while at the same time restricting them. They offer new choices but force people into steady processes of decision making – a situation that is enforced by cutting-edge biomedical and other emerging technologies. Just like these complex technologies, medical imaging may increase unknowns and non-knowledge, which have been termed by Ulrich Beck and Peter Wehling (2012) as further characteristics of contemporary society. In this understanding, medical imaging technologies and practices can be seen as a characteristic feature and expression of modern technosocieties.

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Personalised Medicine: Visions and Visualisations

Annamaria Carusi

The new generation of computational life sciences that is bound up with 'big data' and all its associated forms of data gathering, processing, modelling, simulating and visualising are currently positioning themselves for 'translation' into personalised medicine, or what has become known as P4 medicine (preventive, predictive, personalised and participatory medicine). Currently the ground is being prepared for this 'translation' in a raft of position papers, funding calls and medical science and health care strategies[11]. No doubt social, cultural and political actors will play a role alongside science, and will be co-responsible for the forms of personalised medicine that may be actualised.

The notion of translation is not an especially good one to describe the process of bringing science to application as it does not capture the extent to which both science and application shift and mutate along the way (Löwy 1996). The formation of a personalised medicine informed by systems biology (which from now on I'll refer to as systems personalised medicine) will occur through the co-evolution of the technoscience of computational systems biology with experiences and understandings of personalised medicine. While 'personalised medicine' is generally understood as 'tailoring diagnosis and treatment to particular individual patients', the meaning of each of the terms in that statement ('diagnosis', 'treatment', 'individual patients') is still indeterminate in many ways. Scholars have raised questions about the definition of individuality in a genomically informed personalised medicine, which is closer to a statistical ensemble than to anything in which a particular person may recognise themselves (Jones 2013). Even though proposing a different approach[12], a systems biology informed mode of personalised medicine will come up against similar issues: how will the personal be carved out of the systems of the science and research?

In the process of forming the systems personalised medicine, the various visualisations that permeate computational systems biology (as they do any form of computational science) will play a key role. Information visualisations (for example, that visualise large quantities of data so that patterns become evident in them), network visualisations (that visualise the output of network modelling) and computational science visualisa-

[11] See for example Auffray *et al.* (2010); Wolkenhauer *et al.* (2013); Kyriakopoulou and Mulligan (2010); Hunter *et al.* (2013); Hood and Flores (2012); European Commission (2011).

[12] See Carusi *et al.* (2013) for an in-depth discussion of an example of computational systems biology, and Wolkenhauer (2014) for an overview of different modes of systems biology.

tions (that are the material output of the computational simulation of a dynamical process), are just some of the variants used. In computational science (as in many other forms of science), they are hybrid visual artefacts, with complex causal-computational etiologies (Carusi 2012). These visualisations are an integral part of the scientific process, playing a central role in the construction of the experimental phenomenon: that is, what is observed as the outcome of the experiment, and what this can be taken to be evidence for. They play a crucial role in materialising the biological process under investigation as a system, and in making that system something that can be considered real, or something that can engage with as real. By 'the real' I do not mean anything particularly philosophically burdensome. In using it, I am echoing the practices of the scientists in the domain, for whom what is real in their own and others' experimental practices is a constant preoccupation. My use of it indicates what experimenters, researchers, and ultimately individuals who will encounter personalised medicine in the health care systems, take to be real, experience as real, and interact with as real. This might be the experimental phenomenon or research context, or the way people, individual and collective, experience the personal as real in the personalised health care system. This use of 'real' does not imply a pre-existing, pre-formed real, but precisely something that is negotiated over, struggled over, formed and transformed.

Visualisations do not do this on their own but as part of a experimental system where, however, they play a role that cannot be reduced simply to showing the output of the prior computation (Carusi 2011 and 2012; Spencer 2012; Chandrasekharan and Nersessian 2011). In their role of making the outputs of simulations and other forms of computations materially available for observation, manipulation and interaction, they have intertwined epistemic and ontological roles: the mode in which they provide evidence for the process as a system also has ontological consequences for defining both what is 'realistic' in the visualisation and what is real in the experimental system. They also have ontological consequences for the disciplinary and other social groupings that are brought into contact, and need to cooperate or participate in order to realise the vision of systems personalised medicine. Because they have this epistemo-ontological role in virtue of being material artefacts, that can be shown, displayed, interacted with, discussed, and so on, they are also sites of mediation between the different spaces of systems biology research, and the different modes of collaboration that are required for it. Elsewhere I have discussed the role of visualisations in mediating the context of forging new collaborations between wetlab and drylab (Carusi 2008, 2011). Here I shall discuss two other contexts of mediation: between basic and applied biomedical research, and between research and health care each of these in turn. As in Carusi (2011), I continue here the approach of tracking visualisations that are emerging, are not entrenched and over which there is disagreement, as in these cases it becomes more evident what

might be ontologically at stake in contexts of mediation[13].

1. Between Basic and Applied Biomedical Research[14]

This context of mediation can occur in places where academic researchers interact with clinicians, or in other contexts such as pharmaceutical companies or drug regulatory institutes. The example I discuss is taken from an initiative to show that computational cardiac modelling can be useful for clinical research, in that it can propose new hypotheses that are not readily available using widespread clinical cardiological techniques. It is an example of the mode of systems biology that constructs models of dynamic processes in order to investigate the mechanisms that give rise to them. Obtaining data that are relevant for modelling and simulation is a driver for establishing collaborations in this context too; however, the shift to the clinic or other biomedical context also brings an engagement with experimental systems geared towards clinical research questions and concerns. There are many routes to showing the role of the visualisations in making this crossover into applied biomedical contexts such as the clinic. Here I shall discuss just one example episode involving the work of a computational systems biologist, a mathematician by background, who – in a collaborative team that included a 'converted' clinician who had contributed clinical data from in vivo human hearts – had used modelling and simulation to show that there may be factors that give rise to arrhythmias (irregular heartbeat) that have not yet been considered by clinicians. Getting clinicians' interest more broadly would be beneficial because it may result in access to more clinicians' data, or even to experiments targeted to the hypothesis explored by the model, and therefore to a contribution to the development of the model. The particular research reported on focused on the tissue level of electrical activity in the heart; in this case, the systems approach is evident in the interest in the interactions between sub-cellular, cellular and tissue levels, and ultimately with other electro-physiological levels of the 'whole heart'. In our conversations the researcher stressed that in the simulations, the aim is to achieve *a correspondence with what happens in the real heart*. Since the pattern of electrical activity is a dynamic process, the only way it can be seen is through a movie as the visualised output of the simulation. This visible pattern is a crucial aspect of the evidence for the claim being made. However, the production of the visible pattern necessitates a change in the parameter space of the data (fast speeds are made faster and slow speeds are made slower) – and in this respect, there is not an

[13] For a discussion of the mediating role of images see also Carusi and Hoel (2014); and Hoel and Lindseth (2014).

[14] 'Basic' is of course always relative. By 'basic' here I mean science that is not targeting a specific application.

exact correspondence with the 'real heart'. The researcher was very concerned to make this clear to viewers of the visualisations.

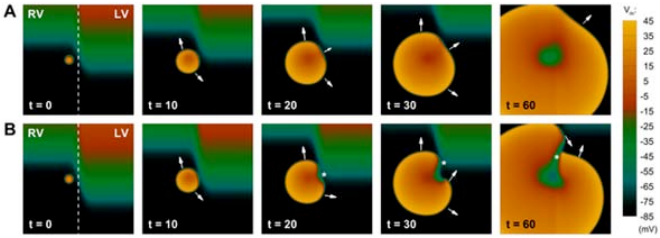

Figure 1 – The visualisation of mathematically modelled and computationally simulated action potential re-entry at tissue level[15]

The work was presented at conferences through presentation and posters, particularly targeting clinicians. Presentations included figures that were similar to the electrocardiagrams that clinicians are used to, as well as an extremely striking visualisation in the form of a flow of swirls of colours to show patterns of Action Potential Duration Reentry (the form in which electrical activity of the heart is salient to experiment) [see Figure 1]. However, clinicians tended to respond sceptically to that visualisation. Their response, as reported by the researcher, was: *"this is not what is happening in real hearts"*[16] – not because they object to the distortion of parameter space of the data (which they do not remark upon). Rather there is a lack of correspondence between what is shown in the visualisation of these mathematically modelled and simulated patterns of arrhythmia at tissue level, and what they see in their own research. The computational visualisation is of a localised bit of *mathematically modelled* tissue showing up relationships between ion channels; it is not of a whole heart and it is not generated by an automated connection with physical hearts. Clinicians, instead, deal in visualisations with a very different logic, that is visual output in the form of tracings made by automated connections via electrocardiagrams, catheters and needles, attached to or inserted into human research subjects. The visual output of these experimental settings – an example of which is found in Figure 2 – is interpreted as being of 'real hearts' against the background of these settings. Their reservations about the visualisation are not elicited by distortions of the parameter space, but by the fact that the visualisation does not map onto these experimental settings. Not only is its smooth, swirling pattern formally (or we could say aesthetically) very different from the jagged tracings of an electrocardiogram, but how these visual features are

[15] Availble at http://www.plosone.org/article/info:doi/10.1371/journal.pone.0052234 (retrieved May 14, 2014).
[16] Fieldwork notes.

related to 'real hearts' is not evident to them; they have no implicit setting against which to interpret these mathematical visual objects.

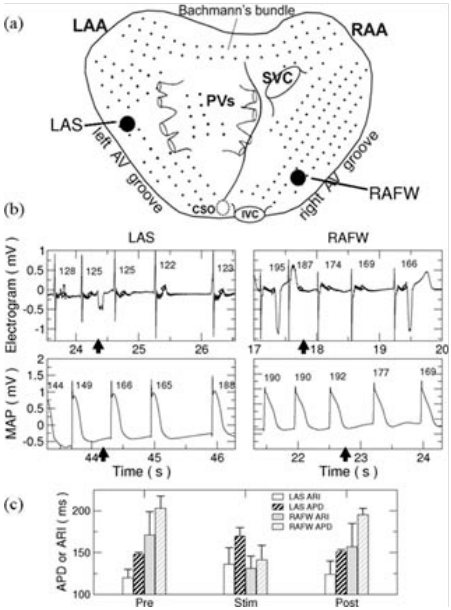

Figure 2: Typical visualisations used for cardiac electrophysiology using electrograms[17]

Considering that these cardiac clinicians consider ECGs in the context of 'whole hearts', the researcher reflected that perhaps if he had tried visually to contextualise the tissue in the whole heart, "maybe then they would see it happening in real hearts, but then it would look as though this is a 3D model, and this is not a 3D model"[18]. However, the context that seems to be missing is the link to the experimental setting that makes it, for clinicians, of a real heart. What is at issue in the ability to see the visualisations as evidence providing is a tension over what counts as a 'real heart'. For the systems biologists, reality depends upon the way that data are obtained (from which experiments) and from the ability of the mathematical model to fit the data thus derived. It is this fitting that makes the model 'realistic'. But clinicians fail to recognise these patterns

[17] Reprinted with permission from Vigmond and colleagues (2009). Available at http://ieeexplore.ieee.org/xpl/login.jsp?tp=&arnumber=4785512&url=http%3A%2F%2Fieeexplore.ieee.org%2Fxpls%2Fabs_all.jsp%3Farnumber%3D4785512 (retrieved May 14, 2014).

[18] Fieldwork notes.

as occurring in real hearts: the mathematical model with which they are presented cannot be contextualised in anything they recognise as a 'real heart' – and the modeller's attempts to contextualise it for them runs the risk of misleading them as to the nature of the model.

2. Between Research and Health Care System

Big data approaches to systems biology are predicated upon technological capabilities to collect and process large quantities of data, yet those data do not always already exist. In the case of the vision of personalised medicine that issues from the big data mode of systems biology, there is a reliance on users of the health care system to be data producers, and many of its rhetorical efforts are geared to this end. Because this part of the vision of personalised medicine is still programmatic and future oriented, my research has focused on the documents and other public engagement output that attempt to gain support for this vision, or to show what concrete form it could take. This vision of systems personalised medicine stresses the participatory aspect of P4 medicine. For example:

> "Patients and consumers will be a major driver in the realizaton of P4 medicine through their participation in medically oriented social networks directed at improving their own healthcare."
> (Hood and Flores 2012)

The 'big data' mode of systems personalised medicine in fact depends on data acquired from large populations. Scientists in this domain talk of a 'data cloud' for any individual of trillions of data points, from the genomic to the social level and everything in between (Hood and Flores 2012). Data can be acquired through a myriad different encounters with the health care system; but importantly, to be really effective, it needs active participation from health care users, for example, through self-monitoring via social media and through their willingness to use a whole new range of devices to gather data. This kind of participation entails non-trivial social, economic and political transformations of health care, which are impossible to broach in this article (see Prainsack 2014). I shall focus on a representational issue. Like vaccination programmes, the benefits to any particular individual of this mode of personalised medicine, depend on the participation of very large numbers of people. There are different rhetorical arguments that can be made for participation, but one is to appeal to the stake that any individual has in this massive data gathering exercise. This is the tactic that is sometimes used. For example, 'The Digital Patient' is a project funded under the auspices of the Virtual Physiological Human Network of Excellence, with the aim of describing how computational systems biology can be transformed into personalised medicine. Computational systems biology aims to construct models of the

organs and physiological processes of the human body and the digital patient is envisaged as a model of each individual patient:

> "The Digital Patient is a vision of a coherent digital representation of each patient that is used to provide an integrative framework for personalized, predictive, and integrative medicine."
>
> (Hunter *et al.* 2013)

The website of the project has a more patient directed version of this:

> "The Digital Patient is an envisaged super-sophisticated computer program that will be capable of generating a virtual living version of yourself. When this is achieved, it will be possible to run 'simulations' of health and disease processes on the virtual or 'digital' you, and use the results to make predictions about your real health. It will also be possible to determine the best treatment specifically for you. This is termed 'personalised medicine', and is intended to be the future of healthcare."[19]

The project's exploration of the digital patient includes an in-depth consideration of the visualisations that would be used in the patient-doctor encounter. The highly detailed account of what would be required of these visualisations is in itself a good indicator of how significant they are in the interface between the patient and the systems mode of personalised medicine. There is much to say about this, but here too, for the sake of brevity I shall focus on just one detail. From the patient's perspective, their 'corresponding' digital patient will be an avatar. Included in a draft of the Digital Patient roadmap is the following statement:

> Avatar lookalike.
>
> Develop rapid, automatic and low-cost strategies to individualise the physical appearance of the Avatar to that of the patient. This provides emotional intensification, as used in Microsoft's Xbox Live Service or Nintendo's Mii, which can affect individual behaviour, including healthy behaviour.
>
> (Digital Patient Project, undated)

In a short animated movie,[20] that is a kind of scenario of what such a consultation might be like, a patient is shown an avatar, which is at first of a generic human that (in the patient's voice) is described as "breathing and moving its eyes", and when made to jog, "started to sweat". We hear the patient say that he does not understand what this has to do with his check up, but he is then asked to stand on a platform and is scanned by a

[19] Available at http://www.digital-patient.net (retrieved May 10, 2014).
[20] Available at http://www.youtube.com/watch?v=JijSCaVrYhw (retrieved May 10, 2014).

laser, and "suddenly the model on the screen changed and it was me... it even had my face", down to "all my skin blemishes". Two of these blemishes are picked out on the avatar, and "a robotic arm came and found them on me". The movie then goes on to describe other forms of interaction between this highly personalised avatar and the patient. In this whole consultation scenario, the line between what is personal to the patient, via those trillions of data in 'his' data cloud, and what is personal to him, via the avatar, is blurred: in fact the 'emotional involvement' depends on this blurring.

It must be stressed that this has not been developed, and interestingly, this visual strategy does not appear as such in the final roadmap. However, it is telling that this visual strategy of getting patients to recognise themselves in the generic mass of data that systems personalised medicine actually is, could even be considered as part of the roadmap. It points to a fissure in this vision of otherwise seamless all inclusive data, a fissure between data for systems biology and the personal in any way that 'personal' is actually experienced. It will take work to knit together the ends of this fissure, a work that we might expect, will result in a new form of personal, bridging experience and data. For this very reason, it is of social, cultural and political importance how this new personal is forged.

3. Conclusions

Just as in contexts of mediation between wetlab and drylab, visualisations figure in multiple ways in mediations between basic research and biomedical application, and between biomedical application and health care system. They are part of observation and evidence of experimental systems; but they are also depended upon to communicate with researchers who do not share the same experimental system, to policy makers who must be convinced of the viability of this vision of personalised medicine, and eventually, to act as an interface between the personalised health care system, doctors and patients. At each of these junctures, the visualisations show slippages in what is taken to be 'real'. These examples have in common that they are not, or not yet, entrenched. They are visualisations that are questioned, of which the communicative intent is not smoothly accepted, or which are programmatic and futuristic rather than actualised. At these points, before the gaps are closed, we have the opportunity to see the slippages, misunderstandings, and struggles over how to realise systems personalised medicine. The visualisations that are deployed and crafted in this process are crucial to the formation of these new realities. As such, they are also sites around which participation and activism can occur in the emerging modes of personalised medicine.

* * *

Bioethical Issues on Autonomy of Persons in Visualizing Bodies

Aikaterini A. Aspradaki

1. Introduction

The research on the "increasingly sophisticated visualization tools" (Perrotta 2012) in science and technology and their implications – with emphasis on visualizing bodies by biomedical imaging and body picturing in a broader sense – is an area of growing interest at the intersection of the fields of science and technology studies (STS) and bioethics.

In this context, scholars in the social studies of scientific imaging and visualization (SIV), for example, have emphasized on a research agenda including the epistemic status of images in the knowledge generation process and the impacts that images and imaging technologies have on social organization and research communities (Burri and Dumit 2008, 307-308). Special research interest has been drawn to the "labor- and capital- intensive" nature of imaging and visualization and the related identification of "hype" in bioinformatics, computer-generated imaging and nanotechnologies. This hype has been partly attributed to the visual persuasiveness of scientific imaging, as "a crucial part of contemporary scientific authority" (ivi, 308-309). Moreover, scientific images of humans have been highly correlated to issues on the deployment of persuasion because of their special character of being images of "our own bodies and lives", our "educated" bodies as well as our thoughts and actions regarding an "ideal and fit person" (ivi, 306). In addition, due to the deeply personal character that medical images have in picturing ourselves, scientific images of humans are considered to be not only persuasive but also "entangling", many times in a special relation with our human personhood (ivi, 307).

At the same time, scholars in bioethics have emphasized on the research work required on the epistemological status of results from imaging studies in sciences. As an example, epistemological considerations on neuroimaging as a "prerequisite" for the neuroethics have been strongly discussed (Huber and Huber 2009). The discussion has been illustrated by the widely used method of functional magnetic resonance imaging (fMRI) for analyzing brain structure. More concretely, in a common framing for neuroimaging methods in neuroscience, philosophy of science and sociology of science into the elaboration of neuroethics discourse, the concept of objectivity has been challenged in its use to guarantee methodological quality in current neuroscience (ivi, 341-343). Two arguments have been mainly discussed. The first develops the hypothesis of technological construction of scientific objects detected by neuroimaging and concludes that: "the artificial environment of the laboratory situation will remain an epistemological problem" (ivi, 344). The second considers the

interdependence of theories and data (hypothesis-driven/data-driven approaches) in neuroimaging research and highlights the problems in the interpretation of controversially defined cultural and philosophical concepts such as the concepts of self, well-being, and empathy. Finally, a probability of hypotheses to generate their own phenomena as objects of research in neuroscience is supported (ivi, 345). Something like that would be extremely crucial and would raise ethical, legal and social implications in the case of extremely debated concepts such as the concepts of racism and proneness to mental illness. In particular, neuroimaging research, especially racism research, is referred to have the possibility to create new diagnostic entities, such as the pertaining to unconscious attitudes and, to provide the potential for discrimination and for legal, financial and privacy issues (ivi, 347).

In parallel, scholars in sociological studies of health and illness have emphasized on a number of problems raised by body picturing visual methods, including video and photography, in the research methodology of social life, health and health care (Harrison 2002). More specifically, four considerations have been suggested to social researchers (ivi, 859-860). The first is the relationship of visual data with the research questions and the need of visual data to be used, since it would possible that the same data would be provided through words or/and that the visual dimension would be provided without visual display. The second consideration is the "conventionality" of visual methods, such as everyday photographic practices, if, for example, the responders would be asked to produce a visual diary of their illness progress, since such photographic records would encompass only selected social occasions, particular people and places and would be framed by particular aesthetic principles. The third is about the technologies of visual production, since the developments in camera technologies, audio/video recording, multi-media software and internet have crucially determined, by also opening new questions, the provided opportunities for both the access to resources of visual data and the development of skills required by researchers and participants to use them. Finally, the fourth consideration is the ethical issues of anonymity, confidentiality and privacy raised by the use of health-related visual materials, since, due to their very nature, much more personal information can be available to a "public gaze" during investigation process.

Taking into consideration all the aforementioned issues raised by visualizing bodies, a very central area of bioethics, namely the issues regarding the bioethical principle of the respect for the autonomy of persons, is coming to the fore. It is widely accepted that autonomy has gained a prominent thesis as a key principle in the field of bioethics. Already in the ancient Greek philosophy, the term "prohairesis" in the Aristotelian ethics has usually been translated as choice, decision, purpose, will, intentional choice, free choice and, in Epicteus' Discourses, as moral purpose, choice and free will (Dragona-Monachou 1978-1979, 309). The word "au-

tonomy" derived from the Greek words "*autos*" ("self") and "*nomos*" ("rule", "governance", "law"). Referring originally to the self-rule or self-governance of independent city-states, it has been extended to individuals acquiring a great number of "diverse" meanings, such as "self-governance, liberty rights, privacy, individual choice, freedom of the will, causing one's own behavior, and being one's own person" (Beauchamp and Childress 2001, 57-58). In contemporary moral and political philosophy, the concept of autonomy has been used in an "exceedingly broad fashion" (Dworkin 1988). In particular, autonomy has been equated with "dignity, integrity, individuality, independence, responsibility, and self-knowledge", and identified "with qualities of self-assertion, with critical reflection, with freedom of obligation, with absence of external causation, with knowledge of one's own interests" and also to be related to "actions, to beliefs, to reasons for acting, to rules, to the will of other persons, to thoughts and to principles" (ivi, 6).

In this paper I aim to open a discussion on this principle in the field of the applications of the visualizing bodies technologies in biomedical imaging and body picturing in a broader sense, by posing three questions. First, could the applications of these technologies enable individuals to take a more proactive role in the maintenance of their health and help society improve health and reduce health costs? Second, what about public participation in scientific and technological developments in contemporary democracies? Third, what about the understanding and interpretation of the principle of the autonomy of persons in contemporary applications of these visualizing bodies' technologies? I will answer to these questions and discuss the related bioethical concerns in the next three sections.

2. Individuality, Resource Allocation and Regulation Issues in Biomedical Imaging

Researchers in bioethics have worked on the ethical implications for the "autonomous and relational dimensions of the person" raised by the use of home-based self-testing diagnostic devices, including biomedical imaging like computer assisted tomography (Kearns *et al.* 2010). It is worth mentioning that these ethical implications have been considered to be fully understandable long after their initial applications, due to the "pace of discovery within the biomedical world and its subsequent interface with technological developments" (ivi, 200). Moreover, despite the suggested potential for such biomedical diagnostic self-testing technologies to benefit both individuals in taking a more proactive role for their health and society in improving health and reducing health costs, the possibility to "push health care away from its relational basis and further into an individualistic paradigm" has been importantly heightened (ivi, 207). Then, in a climate of "new pressures" by such offered diagnostic tools,

"isolated individuals" are considered to be forced to decide on their own whether to use them, how to interpret their results and how to face with difficult situations coming from the resulting health knowledge for themselves and their families (Kearns *et al*. 2010).

Furthermore, there is an emphasis in bioethics on the ethical and social implications of the fostering a "consumerist" approach to healthcare and health-related services by the use of direct-to-consumer body imaging services, including computerized tomography (CT), magnetic resonance imaging (MRI) and ultrasound (Nuffield Council on Bioethics 2010). In particular, in such a consumerist approach, which puts individuals in the position of a customer in the marketplace, conflicts have been importantly reported. These conflicts are considered to arise between the ethical values of individuals "being able to pursue their own interests" and those of state actions in order to "reduce harm, safeguarding private information, fair and efficient use of public resources and possibly social solidarity" (ivi, 166). At the same time, body imaging services have been widely advertised and sold directly to asymptomatic individuals by commercial companies as a form of their "health check-up" in a highly suggested health "responsible behavior". However, the lack of regulatory frameworks for these private providers to "ensure services are meeting established standards of quality and safety" has been importantly pointed out (ivi, 174-178). Appropriate legally constituted regulator schemes have been then highly recommended (ivi, 178).

3. Health-related Bioethics Oriented Social Movements and Body Picturing

While it is widely accepted that the fetus' ultrasound photos are coming to be crucial in discussing issues of women's autonomy (Seavilleklein 2009), there has been a tremendous influence of coma patients' photos, as body picturing in a broader sense, in discussing issues of dying patients' autonomy too. The latter could be interestingly illustrated by the world-famous Quinlan Case and the subsequent constitution of a right to privacy (liberty) in "letting die".

In particular, in January 1976, after 2 months of deliberation, the New Jersey Supreme Court in the United States ruled unanimously in favor of Karen Quinlan's parents allowing "the family of a dying incompetent patient to decide to let that patient die by disconnecting her life support" (Pence 2004, 38). Doing so, the New Jersey Court was the first to apply the right to privacy in a case of "letting die", as the Supreme Court of the United States had not made a comparable decision until that time (ivi, 38).

Taking coma Karen's photos, with the "new" "oppressive" medical technologies of nasogastric feeding tube and big respirator "unnaturally"

prolonging her dying, has been importantly determined by the respect for her autonomy and dignity in the reported her parents' refusal for their coma daughter having a photography taken to be published in a tabloid. More specifically, it has been written that:

> A hired security force vigilantly kept Karen from being photographed, thus never allowing her condition to penetrate public consciousness. During the wait for the later court verdict, a national tabloid offered the Quinlans $10,000 for just one picture. They refused because they wanted their daughter to be remembered as she had lived rather than as a coma patient. Ignorant artists even portrayed her in newspapers and magazines as a normal girl resting peacefully so that most people never understood the horrible nature of her deterioration.
>
> (Pence 2004, 32)

Furthermore, on the basis of concerns regarding the justification of the bioethical principles of autonomy and dignity in cases such as that of the Quinlan Case, scholars in social movements in bioethics have emphasized on the constitution of the end-of-life social movements as health-related bioethics oriented social movements (Aspradaki 2008). It is well accepted that "contentious politics consists of a wide range of portrayals of concerted social actions aiming to overcome deeply rooted structural obstacles" (Kousis 2004, 275). In such a context, end-of-life social movements, going beyond the typologies of health social movements (Brown *et al.* 2004; Brown and Zavestoski 2004; Epstein 2008), demand institutional (public) support for legal reforms supporting the "right to die" while simultaneously changing the relationships between patients, doctors and the state. They also play a crucial role in the development and strengthening of the public in view of the omnipotence of biotechnologies, the negotiability of death and more generally the medicalization of life and death (Aspradaki 2008). More generally, issues of public participation in scientific and technological developments in contemporary democracies have been highly correlated to deliberative procedural arrangements based on substantive commitments to autonomy "for the essential establishment of the equal moral and political value of collectively acting individuals" (Aspradaki 2013, 13).

4. On the Understanding and Interpretation of the Principle of Autonomy of Persons

A minimalist interpretation of individual or personal autonomy often amounts simply to a right to choose or refuse medical treatments on offer and to the corresponding obligations of practitioners not proceeding without patients' consent. This interpretation has been in accordance

with an extremely ethically problematic "consumer view of autonomy" and a highly problematic consumeristic view of justification in bioethics and beyond (O' Neill 2002). Alternatively, autonomy, against such "atomistic reductions to individual preferential choice" (Tsinorema 2006), should be interpreted as a "principled autonomy" that is "expressed in action whose principle could be adopted by all others" (O' Neill 2002, 85).

Moreover, in the aforementioned case of coma patients, the bioethical principle of autonomy is extremely difficult to enact in the sense of individual self-determination and self-expression, if it is not grounded on the Kantian approach, in other words, on human obligations to respect human persons and protect their inviolability and integrity (Aspradaki 2008). In this way autonomy is interpreted in terms of human dignity.

5. Conclusions

Respect for the autonomy of persons seems to be in high relevance to visualizing bodies. A further investigation in biomedical imaging and body picturing in both the fields of science and technology studies and bioethics normative inquiry of moral, social and political challenges resulting from the rapid developments in the life sciences and biotechnologies, would be very valuable. At the same time, evolving global economic, social and political crisis makes this need extremely urgent.

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Translational Research: An Imperative Shaping the Spaces in Biomedicine

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Abstract In this paper we recapitulate the history of the conceptual entwinement of biomedicine and translation and argue that a translational imperative (still peripheral to the practices that order the fields unified under the term biomedicine) has come to dominate public and institutional perceptions of biomedical research. We show this by first delineating a brief history of the conceptual developments in the sociology of science and technology, in particular in relation to translation and the complex multi-agent social interactions contributing to the structure of this field. We then report the findings from our studies of translational spaces and how the actors in them conceive of the imperatives. At least in the field of cell therapy research, the push toward translational research from funding and science policy institutions seems not to have altered greatly the established practices of validation and merit that organise the disciplinary complexes that form cell therapy biomedical research today.

Keywords: translational research; biomedicine; translational space; translational imperative; cell therapy.

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1. Introduction

We were invited to contribute a discussion of the concept of translational research and its emergence in biomedicine on the basis of our work on this topic. The history of the intersection of biomedicine and translational research is complicated, and therefore we discuss in this article the changing relationship between both, how they influence and grow together in what is a current translational imperative in which biological

and medical research give direction and set restrictions for one another. We use examples from cell therapy research, an area we conducted extensive empirical research on, assuming that whilst the configuration of biomedicine through translation may play out differently in detail in different fields of biomedicine, the degree and influence of the translational imperative has similar structural effects.

2. Concepts of Biomedicine and Translational Research

That medicine relates to biology is a trivial notion. That increasingly medical diagnosis has come to rely on biological/tissue tests, and that therapies intervene into biochemically well-defined physiological or metabolic processes, is a product of the 20th century. In this context the emergence of the concept of biomedicine has occurred. Biomedicine has changed medicine and constitutes a whole set of new practices and localities of research, including multidisciplinary laboratories, new journals and the grammar of research ethics and clinical trials. Viviane Quirke and Jean-Paul Gaudillière date the rise of biomedicine to after the Second Word War and characterize it as a: "step change in the scale of investment in research, a new role for the state as scientific entrepreneur, an increasingly fundamental level of investigation in biology and medicine, and a closer relationship between the laboratory and the clinic", accompanied by the idea of "the therapeutic miracle" and the "search for magic bullets against tuberculosis, cancer, and cardiovascular disease" (Quirke and Gaudillière 2008, 442-443). Cell therapy research developed in this period as studies into the effects of nuclear radiation on the body and how destroyed cell systems could be repaired. The stem cell in the bone marrow and its regenerative function for the blood system, and with it the leukaemia patient, were determined as biomedical cell therapy research (Kraft 2009).

2.1. The Translational Imperative

Translation between the laboratory and the clinic may seem to be at the core of the activity we call biomedicine. In its Funding guide the UK's largest medical research funder, the Wellcome Trust, explains that: "*Translational research helps turn early-stage innovations into new health products, advancing the innovation to the point where it becomes attractive for further development by the medical industry or healthcare agencies*"[1]. This present-day definition suggests a one-directional flow of information, from the laboratory into general medical care, identifying the en-

[1] http://www.wellcome.ac.uk/funding/Innovations/wtd027704.htm.

visioned gaps between the different stages of such innovation. The imperative, therefore, of what funding bodies and science policy managers have introduced as *translational research* lies on the concept of 'pulling through'; the problem is how to effectively turn new biological knowledge into widely used medical treatments. The 2014 overview for the UK NIHR Biomedical Research Centres (BRC) stresses that all projects and project leaders must have a track record "*in translating advances in basic biomedical research into clinical research, and pulling through basic biomedical research findings into benefits for patients, the public and the NHS*"[2].

2.2. Biomedicine and Translation in Sociology

The one-directional model stressed in the above notions of translation is simplistic compared to the ways in which the sociology of science and technology has been using this same concept since the 1960s. The scientists' use of the metaphor *translation* for flows of knowledge and information across disciplines and their peculiar languages and practices was followed by the emergence of the *sociology of translation*. A name commonly attributed to Bruno Latour (1979), Michel Callon (1986) and others who worked in this field in the 1980s. Translation is a key concept in actor-network theory. Applied to the field of biomedicine it presents its main actors as attempting to create a central network of interactions that each actor has an interest in building and defending.

> The first is that of the reduction of the big world (the macrocosm) to the small world (the microcosm) of the laboratory. The second stage is that of the formation and setting to work of a restricted research group that, relying on a strong concentration of instruments and abilities, devises and explores simplified objects. The third stage is that of the always perilous return to the big world [...].
>
> (Callon *et al.* 2009, 48)

This description points out that the flow of information and what is needed to achieve biomedical innovation is not from the bench to the bedside but a more complex interweaving of stages in which complexity is reduced and then reintroduced again. The emphasis is on *interactive practices* that produce translation as a reconfiguration of the macrocosm (Callon *et al.* 2009, 68).

[2] http://www.nihr.ac.uk/files/pdfs/Briefing%20documents/4.2%20Biomedical%20Research%20Centres.pdf.

2.3. Science as Social Practice

This focus on the performance of science also dates back to the 1960s when the knowledge practices of science became a study object for sociologists and they began to perform science on science, a turn of attention aimed at rational policy decisions on science and technology innovation in the future. Proponents of the Sociology of Scientific Knowledge (SSK) studied science as a social practice and consequently scientific knowledge as a social product (Barnes 1974; 1977; Bloor 1976, Collins 1985; Shapin 1982). In policy contexts this was taken up as a new imperative to understand the developments in the sciences in their relationship to technology and economic growth and, above all, how "to get returns on the money we spend on science" (Edge 1995, 6).

SSK and its precursors, especially Ludwik Fleck ([1935] 1979) and Thomas Kuhn ([1962] 1970), began to understand science as the product of social processes and negotiations, which mediate scientists' accounts of the natural world, raising fundamental questions about taken-for-granted divisions between "social versus cognitive, or natural, factors" (Shapin 1995, 289). The 'truth' or 'falsity' of scientific claims derives from the interpretations, actions and practices of scientists rather than residing in nature as a separate world of facts that exists objectively for the scientists, independent of the methods and practices they employ to study it. Understanding science as a social practice includes not only studying its methods but also its social structures and the vested interests and social objectives that operate on and within the activity of making scientific knowledge.

This perspective presents translation as a process in which the knowledge practices of different fields in the macro-and-microcosms in biomedicine cooperate with social practices that influence the epistemic and internal stratification processes in complex webs of interactions. Scientists and clinicians balance many and often conflicting expectations of what counts as achievement as set out by funding organisations, the scientific community, publics, patients, industries and policy makers. The art of translation is to balance these expectations across disciplines and turn them into individual and institutional successes and desirable medical innovations. Biomedicine and translation thus is multi-layered, an interweaving of interests and activities. From 2000s onward, the concept was further expanded in sociological studies on cell therapy research to different concepts of intersecting social spheres.

3. Cell Therapy Research: New Understandings of Translation

From its beginnings in bone marrow repair, research on cell therapies

has taken several forms over the past decades, diversifying into many expert areas. Thus the term cell therapy research now ties together a range of types of specialist expertise in both biology and medicine, strongly influenced by cultural and political factors (Hauskeller 2004). Paul Martin, Nik Brown and Alison Kraft (2008) chart the development of haematopoietic stem cell research over a fifty-year period and describe the relationship between basic science and clinical research communities as a two-way flow of knowledge in which clinical innovation has played a key role. They emphasize the *communities of promise* that form around emerging cell therapies and that national governments incentivize the exploitation of basic research and the creation of new policies and institutions to ensure that scientific findings can be applied in the clinic.

The large body of social science work on the external societal influences on cell therapy research from the past 15 years is accompanied by a number of studies on the translational processes within scientific communities. For example, Steven Wainwright, Clare Williams, Mike Michael, Bobbie Farsides and Alan Cribb describe a distinction between the "warp of discourses which enact the improbability of collaborations between 'bench' and 'bedside', and the weft of other discursive strategies which enact the possibility of collaboration between the lab and the clinic" (2006, 2062). Steven Wainwright and Clare Williams (2008) draw on Livingstone's metaphor of *geographies of science*, which he described as "sites of speech and locations of locution" (2003, 23) to explore the spatial shaping of science and the scientific shaping of conceptual, social and political spaces.

3.1. Platforms and Trading Zones

The metaphor of the platform is moved from being applied to biomedicine to being used to characterize processes of translation. Peter Keating and Alberto Cambrosio describe biomedicine as a 'hybrid-practice' and their notion of the *biomedical platform* draws together panoply of diverse actors (technicians, physicians, researchers, policy makers, regulators) with material objects (Keating and Cambrosio 2003). They argue that in the 1990s biomedicine itself had become an independent actor in cancer research, alongside basic and clinical research (Cambrosio *et al.* 2006). Joelle M. Abi-Rached, Nikolas Rose and Andrei Mogoutov re-configure the *translational platform* as an array of heterogeneous actors including technologies, practices and techniques and enabling multiple transactions between the clinic, the laboratory and society. They stress that the products of translational research, be they specific applications (drugs, neurodevices, etc.) or practical guidelines (systematic reviews, meta-analyses etc.) allow a change in both clinical practice and population behaviour, as identified by Steven Woolf (2008). In the context of their study on the new brain sciences, Abi-Rached *et al.*

(2010) distinguish areas of research that act as vectors between the laboratory, the clinic and society, arguing that each specialized community is centred around its own journals, institutes and organizations. These are connected in *trading zones*, a notion they develop following Peter Galison (1997), to capture not merely zones of passive exchange and flow of information but:

> Zones which facilitate the active transactions and transmutations of diverse devices, practices, techniques, and perhaps above all styles of thought. They are platforms which allow the emergence of new disciplines and discursive practices and along with them a reorganization of their objects of study.
> (Abi-Rached *et al.* 2010, 13)

This notion of trading zones where translational activity is enacted is helpful to identify agency. However, engagement in the translational trading zone is not always deliberate, but affected by targeted policy decisions. Whether we prefer the image of interconnected platforms or of the webs woven through multiple centers of agency, a social and political imperative to be translational acts upon biomedicine as shown across the range of social science studies. To illustrate this we provide a brief summary of findings from empirical research concerning the scientists' view of, and practical engagement with, this imperative.

3.2. The Utility Imperative in the Translational Space of Cell Therapy Research

Between 2006 and 2011 the authors carried out ethnographic studies on stem cell research for the heart in laboratories, clinical environments and at networking events. Analysis drew on observation and semi-structured interviews with laboratory scientists, clinicians and focused on the regulatory, disciplinary and ethical tensions that shape the "translational space" (Harrington 2011). In addition, we studied from its inception in 2004 the *British Cardiovascular Collaborative for Stem Cell Repair of the Heart* (Collaborative), a clinician-led multi-disciplinary group of top UK biomedical researchers who aimed at developing stem cell treatments together (instead of competitively) in order to achieve fast clinical implementation. One of the aims of our research was to explore the motivations and attitudes of the stakeholders working in this field. The data on practices, networks of interactions and interdisciplinary exchanges show that differently positioned participants in the field employed different strategies to negotiate the translational imperative. The quotes below exemplify opposite views on *translational research* and what we call the *translational imperative*. First a molecular biologist working in a laboratory funded for translational research:

> So I have to play the game, I have to play the rules of the game because in the end what I want is to be funded and to be in a lab working and doing research. [...] There are many things you can do with the cells I work on. They are not necessarily going to translate into something useful, but you can do the research and that research will be useful anyway. It may not be translated, but the point is, in a paper when I send my project to the funders, it's like, yeah, stem cells, a disease, a cure! So… it's more about, [pause] giving the people what they want to read, even if inside you know it's not necessarily achievable, or it's not your first priority, but again you have to combine all these things, basic research with translational research and get the money.

The scientist states that conforming to the translational imperative is necessary in order to get funded. Translational research is performed as an adjunct to the biological inquiry. The opposite perspective is presented by a clinical–scientist who states that biological research should be driven by medical needs and requirements, describing the purpose of the Collaborative and the view of the multidisciplinary group that met several times a year over a period of 7 years, as:

> All agreed that clinical researchers had first to define which problems they would attempt to treat with transplanted cells (e.g. heart failure, dilated cardiomyopathy, or myocardial infarction) and by what route (e.g. intravenous, percutaneous, or surgical). Then the groups working on animal models would adapt their models to that clinical need […] The group working on cells and gene transfer to cells would define the best cells to transplant, or the best way of stimulating endogenous cells to activity.

The clinicians participated in the Collaborative in order to find new methods to change the function of the ailing heart and expected the scientists to provide them with the biological knowledge and cells to aid that goal without necessarily fully understanding the mechanisms by which the cells regenerate heart tissue. The clinical focus is on whether procedures are safe[3] and in the long term prove to be efficacious[4].

[3] The Clinical Trials observed in this research were Phase 1 that is designed to 'assess safety' although often the conversations between clinicians were centred on 'efficacy'. This dilemma raises questions concerning the 'focus' of a clinical trial and the ethics surrounding this position.

[4] When discussing this divide between the scientist and the practicing clinician reference was made to 'Aspirin' [acetylsalicylic acid (ASA)] and the fact that it's functioning mechanisms have only relatively recently been discovered although it has been in use since 1500BC when an infusion of dried myrtle leaves (which contain salicylic acid) was used to relieve back pain and since 1899 under the trade name 'Aspirin'.

Innovation pathways for new cell therapies from the laboratory into the clinic have been promoted and pre-planned by both funding organisations such as the Wellcome Trust and regulatory institutions such as the UK Human Tissue Authority[5] and the scientific interest currently focuses on new ways of creating cells with regenerative potential. Some of the clinicians involved in the Collaborative have formed a significant European Network that won funding in 2011 for a large clinical trial with established stem cells, which they perceive as the ultimate test. The Collaborative as a group however ceased meeting in 2012. This may be interpreted as a case in which the tensions between biological and medical research could not be resolved and the translational imperative failed to pull through the new treatments originally envisaged.

The heteronomy of success indicators in the different fields of biomedicine seems still stronger than the commitment to translation, which is not directly one of them. Scientists and clinicians need to publish papers in top journals and the criteria which the translational imperative aims to introduce and add to the success stories of a particular biological or medical laboratory's achievements, are not aligned with the internal workings of the sciences that contribute to biomedicine. The platforms are not aligned and thus the difference between publicly accountable research and research excellence still overshadow compliance with this imperative of social and commercial utility.

This case of stem cell research for the heart offers a valuation of the imperative for translational research that so far has not been very successful. Research in other fields within biomedicine is likely to show equal levels of complexity, in which the justifications, initiatives, rhetoric, funding support, and other strategic mechanisms of facilitating translation may more successfully create the normative basis for science that translates into improved health.

4. Conclusion

Biomedicine and translational research as concepts have different historical origins, yet, the necessity for multidirectional and multi-actor engagement is inherent in both. Sociology has been analysing and reflecting on the social practices which shape the developments of translation and its penetration of more and more areas of biology and medicine which draws in a growing number of social sectors and agents. That research has to be oriented toward therapeutic application to deserve public funding and be of societal value is an imperative that contradicts and challenges to the point of denial the complexity of

[5] http://www.hta.gov.uk/_db/_documents/Role_of_regulators_in_regenerative_medicine.pdf

successful interactions and transfers between multiple agencies. Biomedicine is pregnant with translation. Implied in the use of the metaphor of translation is that exchanges are transformations in which the meaning, however well captured, shifts slightly between original text – be it the clinical or the laboratory's – and the new text. With narrow reins regulators try to predetermine with simplistic notions of translation and to-do-lists the outcome of the science yet to be conducted and how its results ought to be implemented. They negate the potential that lies in biomedicine as an evolving project for many kinds of therapeutic innovations and understandings of biology.

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Nina Möllers and Karin Zachmann (eds.)

Past and Present Energy Societies: How Energy Connects Politics, Technologies and Cultures
Bielefeld: Transcript Verlag, 2012, pp. 340

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There is much focus today on the "next big energy transition", mostly defined as a transition away from the prevailing fossil fuel base of most energy systems in the world. This potential transformation can imply a more sustainable resource base, or the change from a high-energy society to a low- (or just less high) energy society. The concept of an energy transition is in itself nothing new; it has been used to describe earlier changes from for example wood to coal and in connection to the nuclear debate. However, the contemporary discussion often fails to historicize the concept in itself and its different meanings over time. Historical knowledge is also seldom used to unpack the complex processes, politics and artefacts that make up the diverse energy systems globally in the framework of the contemporary discussion.

The book *Past and Present Energy Societies: How Energy Connects Politics, Technologies and Cultures* edited by Nina Möllers and Karin Zachmann, brings history into this discussion. It gathers authors from the humanities and social sciences to investigate how "energy concatenates politics, technologies and cultures", providing a basis for reflection on the complex relationships between energy and society in relation to possible future transitions. The volume gathers ten chapters into three themes: 1) Cultural Representations of Energy, 2) Energy Consumption Practices and 3) Societal Perceptions of Energy Resources.

In the first chapter, Nina Möllers analyses energy-related displays at world's fairs, showing the changing views of energy (predominantly electricity) in society. She highlights how a prevailing energy narrative of abundance and connection to economic growth has been perpetuated at these world's fairs. Even when this narrative was challenged in relation to the energy crises through the 1970s, the displays did not question the overall narrative, nor did they urge a change in consumption patterns. Instead they prolonged a technocratic narrative concentrated on a "technological fix".

Sophie Gerber follows with an analysis of marketing strategies of power companies in Germany throughout the 20th century, describing how these strategies became a "crucial element and condition of the electrification and mechanization of households". The advertisements show discourses and conflicts that arose around electrification, making it clear that the introduction of this new technology was not in any way a smooth and predictable process.

Electricity advertisements are also the focus of Yves Bouvier, in his study of promotional films from the French electricity company Électricité de France (EDF). He shows how electrical appliances went from being central characters in these films during the 1950s and 1960s, to being replaced by a more consumer based narrative of energy saving during the 1970s and 1980s, only to return in the 1990s. In addition to showing how prevailing narratives of energy during different time periods are played out in the films, he also concludes that they both reproduce dominant energy narratives and partakes in the social construction of the relationships between consumers and electricity itself. This conclusion is valid for all the contributions in this first section, which provides an interesting comparison of energy narratives reproduced through cultural representations. Especially important is the contribution to visual representations of energy cultures, as these representations tend to be left aside in many analyses.

Although the first section is preoccupied with consumers and consumerism, it deals mainly with representations of consumers from the side of companies and exhibit constructors. The second part of the book delves more deeply into the practices of energy consumption, starting with Nina Lorkowskis study of the rental business of storage water heaters in Berlin in the 1920s-1960s, and how it led to changes in electricity consumption patterns. Lorkowski brings to attention both the "projected consumer", imagined by engineers at the electricity company Bewag, and the actual practices of the consumers. She shows how the installation of water heaters connected directly to ideals of hygiene by making it possible to take baths more often, and how new hygiene patterns were co-created by consumers and engineers. The water heater is described as a "Trojan horse" into the households, making it possible for companies to change electricity consumption patterns. Lorkowski draws an interesting parallel to today's household introduction of smart meters.

Mathias Mutz focuses on the introduction of Daylight savings time (DST) in East and West Germany, and its connection to discourses of energy saving. He concludes that although the passage to DST has been framed as an effort to save energy, this framing is simplified. Issues connected to leisure, quality of life and individualization were central in the debate, while the energy issue served as a background to discuss these matters. Mutz thereby shows the complex way that energy problems are integrated in broader societal and political discourses.

A different political perspective is given by Karl-Michael Brunner, Anja Christanell and Markus Spitzer, dealing more specifically with social inequality and consumer practices in a contemporary setting. Starting from the notion that energy consumption patterns can put a spotlight on social inequalities, not only on a global scale but also within countries, they present a case study based on in-depth interviews with members of poverty-stricken households in Vienna about their energy consumption patterns. This study stands out in the volume due to its contemporary and anthropological rather than historic nature. While the subject matter is

pressing and the political intent is laudable, its place in the volume is not completely clear.

While the first two parts of the volume focus on electricity, the third part is more diverse, including other energy carriers and sources. This part suffers from a certain lack of coherency, but nonetheless includes interesting cases, starting with Helena Ekerholm's study of the use of wood gas as automobile fuel in Sweden around the time of the Second World War. She highlights how promoting actors did not manage to make wood gas an alternative to petrol in the minds of the consumers. This was partly due to technical problems, but even more to the view of the fuel as non-progressive and a necessity during the war more than a viable choice for the future. Petrol, on the other hand embodied the ideal of modernity connected to the automobile expansion, and soon regained its place on the market after the end of the war.

Valentina Roxo adds an explicit environmental perspective when she demonstrates the lack of environmental discourse surrounding the oil extraction in Western Siberia. She shows how environmental problems have been blindsided by the discourse of economic profit and technological progress in the Russian debate about resource extraction. Even when critical voices have been raised in the political discussion and institutions for the protection of nature have been created, this has had practically no consequences for policy practice in the extraction areas. The complex relations between extractors and the people living in the area are also brought to the fore.

Thomas Moe Skjøldsvold turns our attention back to Northern Europe in his chapter on the Swedish and Norwegian discussion on bioenergy use. He focuses on how promoting actors within the field have imagined their "public's" view of bioenergy. The discussion is an interesting theoretical complement to the discussion on marketing and images of the consumer projected by energy companies. Sjøldsvold shows that the imagined responses of different publics on bioenergy have had real effects in the strategies of public engagement from the side of the bioenergy actors. This shows the importance of imaginaries for the practices of energy producers as well as consumers, adding an important dimension to the earlier studies in the volume dealing with cultural representations of energy and energy practices.

As a final contribution, Silvana Bartoletto writes an overview of the connection between energy and economic growth in a long-term perspective, showing four general phases of different relationships between energy and growth.

The introduction states that the book is meant to "contribute to the current scholarly energy debate by shedding light on the political, technological and cultural premises of the high-energy society and its capacities of transitions". As it stands, the book focuses more on the premises of the high-energy society and changing perceptions and uses of energy over time than on practical capacities for transition. Several contributions un-

derline and show the social construction of energy societies, but we are left with very little in terms of alternatives in the end, especially with regard to different political or market organization. However, this is perhaps not surprising considering the predominantly historical perspective.

Nevertheless, this volume is a great contribution to the field of energy history and provides the reader with many useful and enlightening case studies. I especially want to underline that certain contributions will be excellent as readings for university education dealing with social and historical perspectives on energy discourses in production, consumption and culture.

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Ronald Leenes and Eleni Kosta (eds.)
Bridging Distances in Technology and Regulation
Oisterwijk: Wolf Legal Publishers, 2013, pp. 204

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The recent history of technology is characterized by a significant degree of regulatory pluralism. As a rough approximation, this growing pluralization is the consequence of two intersecting processes. Firstly, the fundamental transformation induced by globalization affects the previously unchallenged role of the nation state in setting regulations domestically through traditional command-and-control mechanisms and internationally through the forms of international public law (Ferrarese 2000; Malsch 2013, with a reference to S&T) and opens up the regulatory space to non-state actors. Secondly, in emerging technological fields that are characterized by a high degree of uncertainty regulators lack the resources or information needed to develop sound "discretion-limiting rules" of mandatory nature (Dorbeck-Jung and Shelley-Egan 2013). As a consequence, new regulatory instruments complement traditional hard, mandatory regulation. Soft regulation is typical of this context and it constitutes a tool for leveraging the information advantages of those actors to be regulated. In this broad picture, space opens for other forms of normativity. Such normative but extra-legal aspects enter regulation especially through the science advisory system (Tallacchini 2010), and instruments and mechanisms such as ethics advisory committees (Tallacchini 2009, Mali *et al.* 2012) and technology assessment (Rip *et al.* 1995).

As far as high scientific uncertainty pushes "regulatory decision-making into a more political direction" and thus requires "the weighing up of sometimes competing values" (Falkner and Jaspers 2012), the reli-

ance on these policy advising instruments intersected the rapidly consolidating consensus that early involvement of both stakeholders and the broader public is extremely important for effective and sustainable science policy (von Schomberg 2010). This convergence opens up regulation and contributes to build, in turn, a diversified and plural regulatory and policy space.

The book by Ronald Leenes and Eleni Kosta collects twelve chapters that provide several interesting entry points into regulatory pluralism and new technologies. The papers in the book are grouped in four different parts. The first one examines how the fast scientific and technological development and scientific uncertainty (Gregory Mandel and Gary Marchant; Hans Ebbers, Huub Schellekens, Hubert Leufkens and Toine Pieters; Johan Söderberg) challenge the capacity of regulation to adapt and cope with its changing object. This first part is completed by a comparison of the European and Australian approaches to innovate regulation for dealing with new technologies (Lyria Bennett Moses). The second part discusses the scope of law in technology regulation. The two chapters in this section of the book explore the plurality of legal, social and technical rules, their interplay and their effects in a networked society (Michael Anthony C. Dizon; Robin Hoenkamp, Adrienne de Moor-van Vugt and Gorge Huitema). The third part presents four case studies on how technology affects moral judgement (Mark Coeckelbergh), trust (Esther Keymolen; Federica Lucivero and Lucie Dalibert) and healthcare relations (Anton Vedder). The fourth part includes two chapters on the technical and legal instruments to regulate access to data stored either by the owner of a website or, in a more general fashion, to data about the users of online services (Maurice Schellekens; Gergely Alpár and Bart Jacobs). The chapters of the book present a variety of case studies, ranging from synthetic biology (Mandel and Marchant), to pharmaceuticals (Ebbers, Schellekens, Leufkens and Pieters; Söderberg), smart grids (Hoenkamp, de Moor-van Vugt and Huitema), nanomedicine (Lucivero and Dalibert), and a various set of cases from the internet and ICT (Keymolen on online collaborative consumption, Vedder on e-health, Schellekens on internet robots and privacy issues, Alpár and Jacobs on the design of credentials in user identity management, Dizon on hacking).

Collectively, these chapters are a fascinating journey into regulatory pluralism, well beyond law. For example, Dizon explores the interplay of legal and social norms with technical codes and instructions in the building of a regulatory framework; Hoenkamp, de Moor-van Vugt and Huitema examines how technical standards obtain legal effects; Lyria Bennett Moses compares the experiences of the law reform commissions in Australia and of technology assessment in Europe to assess their respective strengths and weaknesses in informing regulation to cope with technological development.

As from the title, "bridging" conceptual and empirical distances in technology and regulation is the overall goal of the book and this meta-

phor of the "bridge" provides its unifying logic. Sometimes, the Authors of the chapters straightforwardly interpret the "bridge metaphor" and examine what can overcome such distances in technology or (and) regulation. With regard to this, bridging temporal distances between technology and regulation through soft law (Mandel and Marchant) or building trust between consumers through the technological infrastructure supporting online collaborative consumption (Keymolen) are examples of relevant themes that are covered by the book. Some other times, technology ambiguously relates with distance. For example, technologies and the related human practices simultaneously create both physical distance and relational proximity as Coeckelbergh illustrates by referring to the links between the target and the operator in drone fighting. On the contrary, other technologies work precisely because they unrelate data and properties, as it happens in attribute-based credential data management (Alpár and Jacobs).

In general, although many bridges are built, the book provides only a few road signs to travel the distances in technology and regulation. Indeed, the reader is left with the feeling that little dialogue exists in between the chapters and the absence either of a thematic introduction or of a section dedicated to digest and frame the individual contributions in a broader, comprehensive perspective may be puzzling, as one has to figure out such a framework and the links between the chapters on his own. This is particularly evident for the whole section on ethics (Part III) with regard to the rest of the book and for the last chapter on credentials design and identity management (Chapter 12).

Notwithstanding this aspect, the book is undoubtedly rich and provides a broad and diverse review of the connections between technology and regulation.

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Paul Rabinow and Gaymon Bennett

Designing Human Practices: An Experiment with Synthetic Biology
Chicago: The University of Chicago Press, 2012, pp. 200

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Kate Bulpin *University of Sheffield*

Rabinow and Bennett's book addresses their experiments in what they term the design of human practices, which they conducted whilst working within the Synthetic Biology Engineering Research Centre (SynBERC) in the USA. Their work sits alongside a number of other projects internationally that have sought to develop new forms of collaboration between the natural, engineering and social sciences in the context of synthetic biology. They outline the phases through which their experiments in collaboration proceeded, describing their conceptual and methodological approach and reflecting on the various factors that eventually contributed to what appears to have been a rather acrimonious end to the collaboration and parting of ways.

The book has so far proven controversial in some communities, particularly perhaps within the synthetic biology community itself. Some in this field have characterised it as an intractable and intentionally abstruse description of the events that took place at SynBERC whereas others have labelled it an undignified airing of dirty laundry. For our part, being admirers of conceptual developments in human practices so far, we find ourselves wishing the book could update itself as its own reception unfolded, further detailing the ways in which the struggle to develop new

forms of collaboration continues today. But alas not.

Before describing some of the book's merits let us first make two comments on why it has been branded obscurantist by some. It is a book that poses a number of challenges for the reader. First, it is misleadingly slim, suggesting if not a light then at least a swift read. Not so. Certainly, the text is broken down into short sections and sensibly organised according to the various transitions in experimentation and subsequent reorientations through which human practices at SynBERC developed. However, it is a conceptually rich and often complex work, so that periodically the reader must juggle not only a detailed knowledge of this particular case but also a number of rather difficult and multifaceted terms, drawn from various canonical thinkers, and here uniquely deployed alongside and reflected through each other. Second, and relatedly, to access the significant theoretical and methodological riches that this book has to offer, it is necessary for the reader to be familiar/well-versed with the works that precede, contextualise and inform it, in addition to the numerous working papers produced during the lifespan of the SynBERC collaboration. So the volume perhaps assumes too much of those readers who might approach chiefly out of interest in the development and implications of synthetic biology. Indeed this is, if anything, a book that laughs in the face of 'implications', scorns the language of 'downstream engagement' and simply will not tolerate anything that looks even vaguely like 'consequences'. Whilst it is clear that the authors have sought to make this a lighter read than some of their working papers and have tried to explicate the conceptual framework in as transparent a fashion as possible, they still struggle to chart a navigable course between their own understanding and that of a multidisciplinary and sometimes uncharitable audience. Moreover, as has already been lamented (quite rightly) by critics from STS dispositions, Rabinow and Bennett ignore much of the work that has been conducted in STS on the issues with which they deal, and are perhaps themselves guilty of an uncharitable reading of the literature. A more hospitable relationship with the STS tradition and contemporary developments might have helped to open a dialogue with a broader audience. Putting that issue aside, however, their findings and analysis remains of interest to those of us who are engaged in the study of scientific innovation and particularly those interested in collaboration.

So now on to some of the virtues. Presenting their research as a series of experiments is a fair description of what Rabinow and Bennett's work comprised since it undoubtedly involved many of the rhythms and practices that we take to be constitutive of experimental work. Moreover, against the backdrop of the struggles at SynBERC and the still fragile relations being established between humanities and science scholars in synthetic biology, the choice to present the work as experimental has to be understood as a political statement and as one response to the ongoing problematization of these relations. The question of what exactly collaboration might be, what it might do and what we might learn from it very

much remains open to question. Experimentation with the forms that collaborations might take, what they might aspire towards, and how they might orient themselves to questions of knowledge, technology and ethics is vital. Such experimentation is exactly what is at the heart of this book and although it can be conceptually dense it is often a refreshingly practical and down-to-earth account of people trying to innovate together.

In pursuing experimental forms of collaboration human practices work moves away from the more Foucauldian archaeology of the present, through which the past is interrogated in order to understand the present's contingency. Instead, Rabinow and others associated with the 'anthropology of the contemporary' have sought to entangle themselves with the near future. If Foucault examined problematizations (of the self, punishment, therapy and so forth) from the past to chart the formation of the present then Rabinow and Bennett have designed their anthropological enquiry so as to work from within an ongoing problematization.

Early on in their experimentation Rabinow and Bennett identified three principles to guide the design of human practices for synthetic biology: emergence, flourishing and remediation. Emergence is intended to capture the ways in which human practices must be attuned to the ongoing problematizations and innovations of synthetic biology from within the collaborative enterprise, so that it is able to adapt in real-time to ongoing reconfigurations of relations, materials and practices. Flourishing is a broad approach to ethics, so that the emphasis is not on the ethical consequences of innovations but instead extends throughout the project and into life more generally. As they say, it should range over: "physical and spiritual well-being, courage, dignity, friendship, and justice" (p. 42). Flourishing, in their view, should be both the mode and *telos* of scientific and ethical practice. It is clear then, that for these authors the collaborative enterprise is intended to help reflexively to constitute practices that are organised through these ethical imperatives, so that what happens in a scientific collaboration should be open to scrutiny as regards justice, dignity and so forth. In attending to these kinds of ethical dimensions in all levels of scientific work, the knowledge, technologies and styles of governance that emerge should help to secure the foundational principles of human practice in the world more broadly. Ultimately, the ambition for human practices is nothing short of a significant if not complete recalibration of the way in which scientists (and social scientists) view themselves and their work, practice research and work towards the implementation of industrially-relevant innovations.

Their attempts to begin such a recalibration were – perhaps predictably – thwarted. It is here that one of the book's most engaging contributions emerges. They describe how discordancy at SynBERC was importantly connected to a mismatch between the ethical equipment that they wanted to develop in human practices and the adoption of "ethical, legal and social implications" (or ELSI) by other actors in the research groups (p. 85-90). That Rabinow and Bennett find the ELSI-paradigm to

be obstinate even in the face of its open refusal should be no surprise to the readership of Tecnoscienza since it is well documented in the field. However, the elaboration of the factors involved in ELSI's obstinacy does prove for interesting and illuminating reading. They argue that the individual dispositions and affects displayed by actors at SynBERC were instrumental in sustaining these established modes of equipment but that these forms of resistance were also deeply embedded in activity at all levels of social organisation. In this regard they connect behaviour at the everyday individual level (for example, stubbornness and learned incapacity) to group dynamics and practices (the distribution of funding within the research group) and to larger sequences of collective action (the contestation around ontologies of standards and parts and the National Science Foundation's management of the funding). As such, their experiments in human practices draw attention to the significance of mundane daily micro-interactions in the continuation of more long-lasting structures of power, research organisation and scientific work and how those structures inform everyday practice. This reciprocal, co-productive relation between the general and the specific is familiar territory for anthropologists and sociologists of science. Nonetheless, it is a vitally important lesson to be learned as we, in Europe and elsewhere, seek to transform the relations between the natural and social sciences. As such, the book makes for good reading if given time and a little hospitality.

It is important to note, in concluding, that the book itself has begun to play a role in the negotiation, upkeep and closure of collaborations. As SynBERC has been so central to the ramification of synthetic biology the (at least partial) failure of the human practices enterprise has had consequences for those of us working to develop such collaborations elsewhere. The book, and more acutely Rabinow himself, has come to stand in for – and is sometimes used in conversation as a shorthand for – a series of anxieties that natural and engineering scientists feel as regards the place and purpose of the human sciences in synthetic biology. The book contains a wealth of information that is of use to those of us confronted with negotiating relationships in light of such anxieties and will be of interest to many currently engaged in the important work of experimenting with new ways of working together.

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Jon Agar

Science in the Twentieth Century and Beyond
Cambridge: Polity Press, 2012, pp. 614

Massimo Mazzotti *University of California Berkeley*

Jon Agar's latest book is ambitious, thought provoking, and a veritable tour de force. For one thing, it far exceeds what is currently considered the standard scope for a study in the history of science. Since the felicitous interaction with science studies and the practice turn, historians of science have indeed tended to concentrate their attention on relatively narrow settings, steering away from grand narratives and great heroes. This move, among other things, facilitated the control of relevant parameters and the empirical reconstruction of scientific knowledge as the outcome of social processes. Hence the wealth of microhistorical narratives, and their paradigmatic status for the history of science of the last three decades. Well-crafted microhistories have certainly brought delight, but also raised some important issues. Has the field become too specialized and less open to interdisciplinary dialogue? Is the fragmentation of the historiographical landscape irreversible? Does it mean that we have lost the ability to discern and write about large-scale features of scientific life? For example: does it still make sense to talk about the "scientific revolution" as if it were some kind of unitary phenomenon? In short, historians of science have found themselves wrangling with a version of the micro-macro problem. We need to leave behind the comfort zone of small-scale case studies, some have argued, and search for larger patterns, especially if we want to open up conversations with emerging fields such as the history of capitalism and globalization.

Agar's book addresses the question head-on: how can one write about "science in the twentieth century and beyond" in our post-Kuhnian world? The logical structure of scientific theories has long lost its appeal as an analytic tool set, while narratives of major ruptures and revolutions have always been too otherworldly for historians. Steven Shapin offered an intriguing model of large-scale social constructivist narrative in his concise history of the scientific revolution, a book about something that, as he says, didn't quite happen – and yet is worth writing about. Shapin's anti-essentialist approach looks explicitly at microsociology (e.g., Barnesian performativity) for strategies to write about the changes in the way knowledge was produced and legitimated between the sixteenth and eighteenth centuries. Agar, by contrast, filters the rich social constructivist repertoire through the interpretive notion of "working worlds". Drawing on authors such as Thomas Hughes – who certainly did not shy away from tackling large-scale systems – Agar uses the notion of working worlds to refer to: "arenas of human projects that generate problems" (p. 3). These problems can hardly be solved directly but, once they are fully

articulated, they can be treated scientifically. That is to say, science can build simplified, abstract models that can be represented and manipulated through an array of techniques. The outcomes of these manipulations are possible solutions to the original problems. Such is the sophistication of the techniques involved that, in the course of this process, the very actors might become oblivious to the fact that the models and theories they are manipulating and deploying originated from concrete working worlds. This notion is thus designed to do some heavy lifting, including connecting the most esoteric theoretical knowledge to the material dimension of scientific practice. Yet Agar leaves his own articulation of social constructivism via working worlds rather open and flexible, more of a gesture in a certain direction than a fully developed analytic concept. Note, for example, how he does not elaborate it further in the concluding section.

The working worlds give Agar a handle on crafting a narrative of the history of twentieth-century science. He recognizes four partially overlapping working worlds that have dominated the century: the construction and maintenance of technological systems, the mobilization of fighting forces, civil administration, and the maintenance of the human body. The book, however, is not organized around a thematic structure, but follows a fairly traditional chronological one. The first part focuses on continuities and discontinuities between nineteenth- and twentieth-century science, focusing on the emergence of the new physics and the new life sciences. The laboratory is introduced as the distinctive site of these news sciences, while their practices are related to the modes of emerging mass production industry. Here Agar deals also with the new sciences of the self. In this case the relevant working world is the administration of institutions such as the asylum, the school, and the army. The second part of the book examines what we might call the co-production of science and warfare, a well-trodden area in the historiography of recent science. Agar discusses the effects of mass mobilization in the First World War, the American scientist-entrepreneurs of the interwar period, Weimar science and the Forman thesis, Nazi science, and science in the Soviet Union. This part ends with the dawn of a new generation of large-scale scientific instruments, especially in California. The third part is indeed devoted to Big Science, from its emergence and institutionalization during the Second World War to the ways in which it transformed the sciences during the Cold War period. Typical Cold War sciences such as electronic computing, cybernetics, particle physics, information theory, systems ecology, and molecular biology are examined in some detail. Finally, in part four, Agar focuses on "our world", identifying the forces and factors that are re-shaping scientific life at the opening of the twenty-first century. De-regulated markets, social movements, informatization processes, and the Internet are the main protagonists of these last few chapters. In his concluding remarks Agar fleshes out four main cross-cutting themes that run through the book: the extraordinary importance

of warfare, the rise of the United States as scientific superpower, the shift of funding from physics to biology in the second half of the century, and what Agar calls the "missing stories". This term refers to the historiographical gaps that characterize the existing historiography, from the many connections that are not pursued, to the scientific ideas that are not mentioned because they died out quickly, to neglected analytical tools such as those that reveal the specificities of national research systems. But missing are also those stories that did not break through post-war regimes of secrecy, what Peter Galison called the: "classified universe…[which] very probably is much larger than…[the] unclassified one" (p. 508).

While always effective and highly readable, Agar's narrative is, perhaps inevitably, uneven in terms of originality and depth. This has to do with expertise as well as the current status of historiography – which is very sketchy for some areas, e.g., the most recent trends. Agar is at his best when discussing post-war digital computing and the many paths not taken – which is hardly surprisingly given his own groundbreaking work in this area. But the specialist reader will find other insightful and though provoking sections, such as the discussion on science and social movements in the 1960s.

Agar has produced a truly impressive piece of scholarship, synthetizing a vast amount of secondary literature – this alone would make for an invaluable contribution to the history of science. But this book is not just interesting and useful as a survey. Most intriguing is the way it provokes the reader into reflecting on the possible modes and implications of scaling up the level of our analyses to identify larger patterns in contemporary scientific life.

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Felipe Ortega and Joaquín Rodríguez

El Potlatch Digital: Wikipedia y el Triunfo del Procomún y el Conocimiento Compartido [The Digital Potlatch: Wikipedia and the Triumph of Commons and Shared Knowledge]
Madrid: Ediciones Cátedra, 2011, pp. 212

Lucía Liste Muñoz *Norwegian University of Science and Technology*

Wikipedia is an unexpected miracle. The contemporary experiment of management by the common has turned into a very efficient and success-

ful socio-technical venture. This book investigates the collaborative endeavors and practices around Wikipedia. It aims to understand the particular logics behind one of the greatest and most interesting examples of collective action, creation and free dissemination of knowledge. In concrete terms, the authors intend to shed light on the motivations of Wikipedia editors. In order to do so, they combine qualitative perspectives with quantitative approaches.

The book begins with an introductory chapter in which Ortega and Rodríguez present some of the central notions and arguments of their work. The departure point is their concern over the reasons why people engage in digital collaborative projects. The authors argue that no single motivation can account for the variety of economic practices and behaviours that take place in the Internet, not even within the subset of those who form and sustain the Wikipedia community. Rather, there are multiple, and even contradictory, causes behind such efforts; for instance, altruism, entertainment, obsession, addiction, quest for recognition and, even, vandalism – which is frequently counteracted by digital patrols aimed at detecting attacks and restoring originals. Yet, among this diversity and heterogeneity, Ortega and Rodríguez aim to identify a homogeneous ground or underlying explanation that will allow us to understand the reasons for practices that exclude immediate material or monetary reward, and are therefore alien to our universe of everyday and one-dimensional economic performances. At this point, the potlatch notion enters the scene as a useful example of an economic practice that contradicts the pervasive capitalist logics of accumulation and distribution. This notion is further explored in the next section.

What are the necessary conditions for collaboration and cooperation to be not only possible and recursive, but also interesting, appealing and desirable? In their pursuit of a theoretical framework to help us understand the different economies of practices that can be observed in the Internet, the authors guide us through untenable theories and sites of altruism and cooperation. In the second chapter, "The Digital Potlatch", Ortega and Rodríguez review several contributions from the scholarly literature. The authors argue that some existing theoretical resources – such as the prisoner's dilemma, the drama of the commons, etiologic perspectives and classic postulates of liberalism – provide unsatisfactory explanations of the phenomena, due to their excessive focus on monetary-based logics and their lack of attention to individual factors and the contexts in which cooperation is enacted. The authors draw on the notion of potlatch to overcome these insufficient accounts of altruism.

Ortega and Rodríguez describe the general features of the original potlatch ritual, a complex behavioural ceremony practiced in various forms by many North American tribes, in which distribution of property and gifts allows persons to affirm or reaffirm their social status. This example illustrates how, in certain contexts, gifts of material and/or intangible capital allow persons to gain acknowledgment, recognition and re-

nown from the community. This form of generosity brings enormous social prestige. Thus, the sacrifice of economic capital results in symbolic capital gains, which opens the possibility of effective power over the tribe.

Wikipedia is a collaborative venture that aims to create and disseminate knowledge. In this vein, the project shares its commitments with scientific practice. In the third section, "The Genesis of the Field of Scientific Production or an Example of Instituted Collaboration", the authors explore the relationship between science and the Web 2.0. The authors reflect on the similarities and differences, as well as the opportunities and emerging constraints and challenges, enabled by the interplay. Science works as a resistant collaborative network, although pressures and challenges form both inside and outside. Reputation, impact and diffusion are the main characteristics of the logic of symbolic capital accumulation in science.

In the fourth section, "An Ethnography of Wikipedia", the authors report the findings of their qualitative and quantitative analyses of practices around Wikipedia. The investigation thoroughly examines organizational, managerial and operational patterns, and the data point out the parallelisms between Wikipedia behaviour and the potlatch model. The phrase "digital potlatch" refers to practices through which assets (e.g. knowledge) must be given away in order for more valuable capital (namely recognition and popularity) to be obtained. Wikipedia offers a prototypical example of a community that develops common policies, articulates its internal recognition and monitoring mechanisms and coordinates its controls, without monetary flow. What is more, it illustrates how valuable capital in a certain habitat is not necessarily material, but can be symbolic. Arguably, the main argument of the book is that meritocracy and effort recognition are the main driving forces of those who participate in collaborative ventures such as Wikipedia. Although the example is not generalizable for all Internet communities, the authors argue that the success of Wikipedia exemplifies the triumph of shared knowledge and collaborative practices over individualistic strategies.

Ortega and Rodríguez summarize the main findings from their quantitative and qualitative analyses in the fifth section, "The Digital Social Contract." The initial disinterest – the generation of freely accessible shared knowledge – is rewarded with some kind of recognition, and the accumulation of this symbolic capital is the fundamental principle for the acquisition of status in the community. However, Wikipedia is not a tension-free project. For instance, there is ongoing debate over the organization of a system of acknowledgment. Furthermore, meaningful participation seems incompatible with long-term involvement. In the sixth section, "Notes on the Political Dimension of the Shared Knowledge. Towards a Politic Anthropology of the Future More Participatory and Open Democratic Governance", the authors briefly reflect on the democratic opportunities that this kind of collaborative undertaking might entail for governance.

In the last section, "Twelve Ideas to Avoid the Tragedy of the Shared Knowledge", Ortega and Rodríguez outline some ideas for tackling what seems to be an inevitable and progressive abandonment of participation in collaborative ventures. The authors point towards several potential initiatives, such as: redefining the notion of work in our societies and reducing the time devoted to it; dedicating released time to the common, such as by creating shared knowledge; thinking differently and challenging the dominant ideas of production and economic growth; facilitating universal free accessibility to the Internet; encouraging, acknowledging and rewarding collaboration with symbolic capital that can be converted into other forms of capital; and organizing self-managed governance agencies to promote, monitor and evaluate the involvement. Finally, the authors include an appendix in which they provide an account of the methodology employed in the investigation.

Ortega and Rodríguez do an admirable job of attempting to understand how a collaborative endeavour like Wikipedia operates. This book could be very interesting for anyone aiming to understand the logics of collective action and those concerned with new ways to manage the public. Furthermore, it introduces new questions and touches upon issues of interest in different fields. This investigation of the hybrid assemblage known as Wikipedia could be a thought-provoking contribution not only to STS scholars, but also to historians wondering about the origins of practices, economists studying economic practices, sociologists dealing with communities of practice, legal scientists examining questions of property, anthropologists enquiring about the persistence of gift culture and even political scientists captivated with the rebirth of the public space. Lastly, the book is well documented and a valuable contribution to the scarce scholarly literature on Wikipedia in Spanish.

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Claire Waterton, Rebecca Ellis and Brian Wynne

Barcoding Nature. Shifting Cultures of Taxonomy in an Age of Biodiversity Loss

London: Routledge, 2013, pp. 212

Giuseppina Pellegrino *University of Calabria*

Making visible the density of the ongoing changes which articulate the relationship between (techno)science and society is not an obvious task. The three authors of *Barcoding Nature. Shifting cultures of taxonomy in an age of biodiversity loss* succeed in such an enterprise, being participant observers and engaged witnesses of a complex turning point in one of the En-

lightenment natural sciences, commonly perceived as a 'dusty' and old fashioned discipline (taxonomy). Waterton, Ellis and Wynne drive the reader into the crisis of reputation and identity of a scientific community and *episteme* in face of the encounter with the most promising and threatening of the life sciences (genomics). Such encounter produces and shapes the establishment of few interconnected projects aimed at extending the DNA barcoding to all animal life forms constituting nature, forms put at risk by the emergent and publicly alarming phenomenon of biodiversity loss.

However, *Barcoding Nature* is not only an accurate ethnographic account of the research fieldwork carried out at the Natural History Museum in London over a period of six years, which comprised a research on contemporary taxonomy as well as the dawning and development of the DNA barcoding for biodiversity, a project led by the University of Guelph (Ontario). The book is also, and especially, a multifaceted, sophisticated travel across ambivalences, ambiguities, (dis)continuities, and contradictions of a powerful and ambitious knowledge infrastructure, aimed at matching the quest for a new, more robust identity of the taxonomic discipline with the universalistic promises of classification and recording enabled by the DNA barcoding technique.

Drawing on both STS – especially the infrastructural approach of Bowker and Star as well as ANT and Fujimura's do-able science – and anthropology of science – in light of Toulmin's and Helmreich's work – Waterton and colleagues investigate the controversies which from 2000 onwards shook the taxonomists' scientific community with the model of a genomic taxonomy. This model was based on harnessing and enhancing indexes of the morphological Linnean tradition, through the construction of a "barcode library" organized "around the identity-differentiation exhibited by a single gene segment held constant across all species" (p. 34).

Both simplicity and complexity, recording and forgetting, detachment and re-attachment of information characterize the DNA barcoding project investigated by authors, known as BOLI (Barcoding of Life Initiative) and its main archiving infrastructure, BOLD (Barcoding of Life Data Systems). All of the above categories constitute the poles of a continuous oscillation, which conducts the project of genomic (or genomicized) taxonomy to go beyond the promise of a revolution and the practice of a conciliation (cf. chapter 2) inside the scientific community. Therefore, BOLI and BOLD also embody and adhere to the endeavor of a therapeutic and salvationary vision of science, what authors name as "redemptive technoscientific innovation" (cf. chapter 7). Again, such a turn is neither univocal nor free from ambivalences.

While embodying the tension towards a new cosmology of connection between mankind and nature to confront with the uncertainty due to biodiversity loss and the intangibility of an appeased future, genomic taxonomy has been transformed through more local, user-oriented and commercial applications (e.g. environmental bio-monitoring) enabled by bioinformat-

ics. Such applications, however, seem to put at risk the primacy of taxonomy as *the* discipline devoted to investigating and archiving diversity of life forms.

Indeed, ambitions of a universalistic approach to classify nature via a technology imagined and designed as ubiquitous, pocketable and freely accessible (p. 66) represent a recurrent discursive frame in sociotechnical innovation – the so called 'ubiquitous computing paradigm' is a clear example of such a frame in the design of information infrastructures, which are very much part of the DNA barcoding project. In this project, the pursued universalism of a global access to all forms of life though a micro fragment of the DNA code materializes itself into technological artifacts shaped by the mission of archiving diversity, which as usual, "enacts a very particular kind of memory and indeed a particular kind of forgetting in making data available and accessible for its potential users" (p. 109).

While analyzing negotiations and conflicts, translations and misunderstandings in the making of these technological artifacts, authors trace a fascinating path to the expert reader – clarity of language stands out, but the book is undoubtedly targeted to a specialized audience. They depart from the microsequence of DNA barcoding which materially mobilizes and purifies knowledge through extraction and amplification of a short fragment of the genetic code (chapters 1-2). The path goes on detecting reactions, uncertainties and aspirations of a relatively small, greatly disoriented, scientific community (chapters 2-3), then deepening the redesign of taxonomic culture via the BOLI/BOLD projects (chapters 4-5) as well as their care and support to biodiversity archiving (chapter 6).

As the ethnographic account proceeds depicting the multiple and diverse – often contradictory – faces of the encounter between 'the old' (taxonomy) and 'the new' (genomics), the sight and the focus of the narrative broaden, embracing the issue of the public role of science and the ambivalent motives and tensions of a universalistic cosmologic mission (chapter 7), though sensitive to more mundane and utilitarian values (chapter 8 – again, a detachment and re-attachment of reach to the barcoding nature project).

This path ties together the very small to the very big, articulating the micro and the macro as dimensions of a *continuum*, drawing on a STS perspective which combines, borrows and recounts philosophy (Benjamin and Foucault), anthropology (Strathern and Verran), history of science (Bowker). Such an integration constitutes the hallmark of Waterton and colleagues' STS vision and ethnography.

As a final note, the STS reader could be surprised by a missing reference in the bibliography. Given that the research carried out by Waterton and colleagues took place at the Natural History Museum in London, the connection with Star and Griesemer' analysis of Berkeley's Museum of Vertebrate Zoology which baptized the concept of Boundary Object is not extravagant. Ideally, a *fil rouge* ties the historical analysis of translation and cooperation among Berkeley Museum's scientists carried out by Star and

Griesemer to the taxonomists, bioinformaticians and molecular biologists followed by Waterton, Ellis and Wynne at London Natural History Museum.

In the end, the need for classification and standardization of knowledge is a *master* or *grand narrative* of science and goes hand in hand with the resilience of infrastructures of and for science. Forms and networks which comply with this need can be very diverse. This diversity is vital for knowledge infrastructures, as much as biodiversity for life survival and development. But more often than not, "what are really continuities in practice can appear and be claimed as dramatic innovations" (p. 39).

This infrastructural inversion a la Bowker goes straight to the book final concerns about knowledge ethics and politics. These concerns substantiate the call for a modest, responsible and relational thinking on technoscience, based on the awareness that the shifting boundaries and apparent inconsistencies of genomic taxonomy can serve - and become - different technoscientific articulations. These can functionally enroll scientists and their disciplinary scientific communities, but also embrace and enable public "poetic sensibilities" (p. 177) towards the crucial and ambivalent relevance of 'treating' and 'caring' about global biodiversity.

Indeed, the book final reflections go far beyond taxonomy and genomics, or genomic taxonomy: the current hype on 'Big Data' infrastructures 'in an age of consistency and coherence loss' (to suggest an echo of the book subtitle) makes even more urgent the quest for new sensibilities, to see contradictions embedded in the making, use and maintenance of emergent sociotechnical arrays devoted to archiving and using myriad of sensitive information set.

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Jonas Löwgren and Bo Reimer

Collaborative Media. Production, Consumption, and Design Interventions
Cambridge MA: The Mit Press, 2013, pp. 198

Federica Timeto *'Carlo Bo' University of Urbino*

This book is based on the fifteen-year collaboration between an interaction designer (Löwgren) and a media scholar (Reimer) at the School of Arts and Communication and the Medea Collaborative Media initiative at Malmö University in Sweden. Combining interaction design with media and communication studies, Löwgren and Reimer's approach draws connections back to the main assumptions of cultural studies about cultural artifacts, and to Stuart Hall in particular, while showing an affinity with the recent materialist turn of social sciences and its interest in the generativity

of matter and the materiality of information.

All media are social media. However, collaborative media can be defined as action-oriented social media, or mediated cultural forms, that enhance collaboration in the first instance. Here, action is intended as the particular form of mediated interaction that links human and humans but also humans and machines inside a mediated environment. If the notion of affordance proposed by Gibson and extended by Norman partially addresses this concept, action, so intended, is more similar to the notion of inscription proposed by Actor-Network Theory (ANT). In fact this theoretical framework not only foregrounds the ways in which artifacts can be encoded with context-specific meanings, i.e. 'inscripted'; it also brings forth the links that relate human and non-human actors in ways that produce action and change at the social level, while also making the social context 'happen', so to speak (thus overcoming the system-actor distinction).

The recurrent aspects of collaborative media that Löwgren and Reimer identify are: collaborative media are above all forms of practice; they make possible three forms of practice, production, consumption and design; such forms of practice "prioritize collaboration"; collaborative media should be read like frameworks rather than containers or vehicles in which the elements can be differently appropriated and combined; infrastructures and texts are always interlinked in collaborative media; this is also what makes collaborative media more and more 'material' as well as cross-medial.

As it has already been highlighted in media and communication studies, with the emergence, diffusion and increasing availability of new media technologies, the relationship between production and consumption has radically changed: while acknowledging the importance of concepts like pro-am (professional-amateur), produsage (production and usage) or prosumption (production and consumption), however, the authors prefer to maintain the distinction between production and consumption. Actually, if these practices can happen simultaneously, it does not mean that they completely overlap, and a third important moment, that of the design of the infrastructure, clearly characterizes collaborative media practices, according to the authors. Löwgren and Reimer specifically attribute the latter to the characteristics of those media in which the producer/consumer distinction is becoming less clear than it was in mass media like television, since collaborative media are decisively more open to modification and sharing than other media, thanks, for example, to open source software and platforms as well as easily mixable components. Additionally, the three moments of production, consumption and design are not only not necessarily sequential, according to the authors, since the process of collaboration can be initiated at any moment; each moment is also linked to the others and also contains them, so that, for instance, there can be moments of design-in-production or design-in-consumption, an aspect which is valid for each part of the process. Paramount to understanding such interchanges is the concept of infrastructuring, which, as Löwgren and Reimer explain, stresses the socio-material linkages between different social actors and the role of the design-

er as facilitator (what in ANT terms would be called a 'mediator').

Actually, focusing on the importance of participatory design, a term with which the authors "do not mean the design of an artifact or an infrastructure, but the design of the situation making practices and collaborations possible", they prefer to speak of interventions rather than actions, combining the particular situation that requires that certain conditions of interventions are designed (metadesign) with more conventional forms of design aimed at producing things, but always according to a participatory approach that prioritizes expression and communication rather than the mere resolution of problems.

The first part of the book focuses on what characterizes collaborative media as a cultural form that enables new practices, and on the possibility of adopting a trans-disciplinary approach that, following the approach initiated in the recent field of digital humanities, combines the study of technologies and societies and includes the practice-based approach assumed in the field of interaction design inside collaborative media research: this involves non-academic actors and relies on real-life experiments (the Living Lab) to support theoretical assumptions and to take action at a social level. The second part collects the examples of ten case studies that have personally involved the authors as researchers in the past years, and takes into account collaborative media practices at a social, institutional and "tribal" level.

The "Social Section" includes examples that show how collaborative media contain the potential for (which does not mean that always lead to) social change that relies on grassroots activism and bottom-up governance. The Avatopia project, an attempt by Swedish Television (SVT) to experiment with cross-media formats brings together different social actors, from students and activists to researchers; Bambuser, a mobile-first live video stream service based in Sweden also linked with an online archive, massively downloaded and accessed by worldwide users and also remediated by broadcast media for the coverage of critical events such as, the Arab spring in 2011; Parapolis, a project of participatory urban planning of Malmö's city administration that asks citizens with the collaboration of architects and graphic designers, among others, to envision future urban developments by means of an augmented reality device, the Parascope, that overlays imagined cityscapes on existing ones.

The institutional case studies account for the ways in which collaborative media engage with institutionalized media or other institutional sectors of society. So, for example, in MyNewsMyWay, whose long term effects are taken into account in the following section, with the analysis of the complementary OurNewsOurWay project, the innovative aspects of on-demand media are experimentally assumed by Swedish institutional television to take advantage of the increasing collaborative merging of the producer and the consumer; Substrate is a collaborative platform showing the positive effects of collaborative media on the production and diffusion of technical information, particularly business-to-consumer (B2C) technical

information, that are the instructions traditionally contained in a manual and increasingly replaced by Internet searches and peer advice today; Kliv is a sort of video-tagging of medical equipment made by the intensive care unit of the Malmö Hospital, in order to share one's practical knowledge so as to enable others to be familiar with the work environment; Hacktivism, explores fashion as a form of social activism according to Otto von Busch, a fashion designer whose work is an example of the way fashion can also be used as a form of collaborative media to facilitate collaboration through the horizontal distribution of skills and tools and through practices of re-combination.

In the end, focusing on "tribes", Löwgren and Reimer analyze what happens with collaborative media in small communities characterized by a very high level of cohesion and reciprocity, using them as a magnifier to better highlight some specific traits of collaborative media practices. After opening with the OurNewsOurWay project, the central part of the section analyzes the renowned Arduino project, focusing on the potentialities of open source hardware and software for their design-in-consumption aspects in particular, and its connections with the principles of hacker culture, play, hobbyism and artistic as well as amateurish creativity. The last case discussed is the Malmö City Symphony, carried out at the School of Arts and Communication in Malmö to put together a landscape of video clips of the city with the collaboration of both professionals and amateurs, and the aid of a P2P platform (The Pirate Bay) for their open archiving, distribution and further modification.

The book ends with a section of insights and conclusions, which is by far the most interesting, since the authors, after summarizing the specificities of collaborative media in what they devise as six major "recurrent themes", already introduced at the beginning of this review, nonetheless maintain their focus on the differences among practices. They restate the importance of situated methodologies and practical interventions at the level of research. At the same time, they deal with the most common critiques advanced against collaborative media, trying all the while to escape the binarism between what they call "bright-side" and the "dark-side" perspectives. In fact, even when they recognize that some open issues actually exist in collaborative media, for example the blurring between professionalism and amateurism and the loss of competencies, the question of intellectual property, the difficulty of using traditional categories such as quality or originality to assess the value of collaborative media products, or the risk of exploitation of free labour and corporate control, they problematize each conceptual node, indicating the importance of adopting specific, situated, nontrivial perspectives for each criticality that they examine.

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Yves Gingras

Sociologie des Sciences [Sociology of Sciences]
Paris: PUF, 2013, pp 127

Thomas Vangeebergen *Liège University*

According to the author, sociologists of science have an unfortunate tendency to favour a polemic attitude in their field of study by excessively multiplying the theoretical currents and methods, and by being almost systematically opposed to their colleagues. This book intends to offer a synthesis of these various works, in a cumulative and integrative vision of the knowledge accumulated in this field. It comes in four parts, namely: (1) the socio-cultural foundations of science; (2) the institutions of science; (3) the social system of science; and (4) the social determinants of scientific knowledge.

In the first chapter, Yves Gingras succinctly addresses the developments of scientific activities in relation to the religious context, the emerging democracies and the growing importance of the expert's role, and finally regarding the redefinition of the contract between science and society. The approach consists in profiling the contexts that allow science to flourish fully, and in attempting to go beyond the simplistic shortcut stating that religions are systematically opposed to science, while (in contrast) the political organization of liberal democracies is systematically the best soil for science. We notice that the predominant historicist vein, dear to the author, leads him along two complicated paths. To begin with, the framing he chooses is reductive. Religious issues are primarily treated on a 17th century basis, relations to democracy in sight of the 19th, and the social contract from the prevailing point of view in the post-war period. Assigning a central and specific standpoint to each era and according a dominating role to the historical context make the analytical framework unnecessarily rigid, whereas these themes are rather key threads beyond times and places. Besides, and this is undoubtedly more fundamental, this diachronic approach assumes the idea that some contexts favour the emergence of scientific activities more than others. Though he mentions nuances and counter-examples, the author always choses to explain rather than understand the events. However, it is not offensive to Comte nor to Merton to say that their work has been continued after them, and that there are alternatives to the causal and/or internalist analyses of scientific phenomena.

In the second chapter, we discover a panorama of scientific institutions. Academies and universities, or the learned societies, the organization of laboratories, the disciplinary constitutions, the dissemination and training organizations, are structures that display the organizational framework of science. Here again the approach is largely historical, but it extends the argument to pre-modern contexts. By unfolding a series of

facts that, the other way around, seems necessarily inevitable, this rationalist approach has a strong deterministic tinge. Apart from the fact that the sociological approach of the title is refuted, we hesitate between a scientist macro-history and anachronistic interpretations.

The third part deals with the "social system". Regarding the increasing and constant autonomisation of science in the 19th and 20th centuries, Gingras focuses on how order is established in the area of science, whith its specific standards, logic, setting and conflicts. This chapter, which deeply engages in the functionalist analysis of scientific values and standards, is probably the most mertonian. Further, the analyses dealing with the issues of production, peer recognition, stratification and hierarchy take a more critical turn. Remarkably, while today science is generally treated in conjunction with techniques (an approach summed up under the STS banner), the author focuses here on science for he considers that it belongs to an autonomous field of study, with its own actors and logic, its history, and a particular literature. One of the reasons for this choice is probably the decidedly internalist approach, rooted in a scholarship heavily impregnated with epistemic issues.

The fourth and final part takes shape around the "nebula" of social constructivism in science, and seeks to establish an inventory of the different recent approaches in social studies of science. There again, the presentation, from the beginning of the 20th century until the 1980s, is too easily chronological. Sociology of translation can be found in this chapter entitled: "Social determinants of scientific knowledge", which brings together ethnomethodology, cognitivism, SSK and the strong program (among others). The author does not really linger on these theoretical and methodological renewals but places them in a category of more descriptive than explanatory work – which is supposed to be the goal of the sociology of science. In this chapter, the author also proposes a very popperian version of scientific controversies, boiling down to argument contests, the outcomes of which are determined by the cognitive (theoretical and experimental) contingencies of the time. It is probably is a little more complex, insofar as controversies are a good way of questioning the scientific autonomy and the relations to actors of a different nature.

The book closes with a disconcerting conclusion: it shows us, with statistics to back up the demonstration, that today increasingly costly and instrumented science is essentially collective and largely globalized. This would force a comeback to normative concerns, necessarily treated on meso or macro scales. In the introduction, Y. Gingras explains the need to combine the different levels of analysis, based on the principle that the focus depends on the objects the researcher is interested in. Rather than seeing a contradiction or a competition between these scales, it would be best to reserve a suitable framework for each object and, if necessary, articulate it. If we can fully subscribe to the will of interpretative pluralism recommended by the author (of which, to be true, he does not give us here a very convincing demonstration), we find once again a profund *dis-*

sensus in his approach of sociology. Not only is the macro level not the analysis framework of 'lower' frameworks, in the Matrioshka dolls fashion, but this *a priori* division between phenomena break their interactions and singularities, terribly impoverishing them. It seems much more judicious to stay tuned to phenomena and to the actors themselves, in order to carve a made-to-measure framework as the investigation progresses[1].

It would not be fair to put the blame of the shortcuts, of the omissions, of the choice of themes found in this short book only on the author. Indeed, some editorial responsibility is engaged here in the sense that the issue of the readership is questionable. Considering the tone as well as the "factual" contents, I wonder who would benefit from this type of reading.

Undergraduate students would find here a partial and biased introduction to something much more complex and branched out than it seems in these pages. The discrepancy between the level of generality suitable to an introduction and the concern to give empirical landmarks contributes to the perception of bias. Professionals in the field of social sciences wishing to approach themes more or less remote from their own practice would probably be battling with methodological issues, discussed elsewhere but presented here as evidences (see above). Finally, the general public wishing an accessible approach of a learned domain would not necessarily be satisfied with this approach, for here pedagogy amounts to swotting up on issues the scope of which is still to be to demonstrated. Through this booklet, the question may actually be that of popularization, of opportunities it offers and prohibits, of effectiveness, of its relevance[2].

It must be said that it is difficult to locate this dense set of issues related to sciences among other lines of research in such a restricted space. Inevitably, what the author can do is pass over many important issues in silence: the political meaning of research, its relation to techniques and to their study, the parallel evolution of other issues that have shaped them (colonialism, feminism, social emancipation, education and mass knowledge), the marginality of the links with other disciplines dealing with scientific activities (philosophy, anthropology, economics and management). Ironically, it could be said that history has been overshadowed by this very historicist vision. Here the author's approach seems to take

[1] This question has been treated by sociologists of science, including: Callon (1991) and Knorr-Cetina and Cicourel (1981). For arguments in favour of an emergentist approach of analytical frameworks see also: Boltanski *et al.* (1984) and Ragin and Becker (1992).

[2] For purposes of comparison, here are two other introductory books in French that address the subject in a different vein: Pestre, D. (2006) *Introduction aux Science Studies*, Paris, La Découverte; Vinck, D. (2007) *Sciences et société. Sociologie du travail scientifique*, Paris, Armand Colin.

advantage of all these limits and to offer a highly personal reading of the sociology of science. Admittedly, on this point, he has been very successful.

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