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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