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RESEARCH REPORT

An anthropology of the "metabonomics" laboratory?
Conducting ethnographic research at the forefront of personalized medicine

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Abstract

Background: Personalized medicine—most notably in the form of research in genetics and genomics—forms an important area of investigation in social science literature. Social scientific research, however, has failed to account for the range and complexity of research that contributes towards personalized medicine.
Methods: Using a combination of participant observation and semi-structured interviews, this research examines how research in the field of metabonomics is contributing to realizations of personalized medicine in laboratory and clinical settings.
Results: An in-depth examination of the field of metabonomics—the molecular, post-genomic study of metabolism—highlights the ways in which statistical ideas and practices are an emerging and fundamental aspect of research in personalized medicine.
*Conclusion: D*espite the challenges of learning statistical language and observing computational practices, more in-depth ethnographic research is needed to document the ways that personalized medicine is being shaped and impacted by statistical ideas and techniques.

Keywords: Metabonomics, Personalized Medicine, Statistics, Biochemistry, Genomics

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Tracking personalized medicine beyond "the gene"

Since the completion of the Human Genome Project in 2003, social scientists have been fascinated with biological research on "the gene" (Fox Keller, 2002). Following the establishment of the genetic basis of many health conditions, researchers in sociology and anthropology have documented the complex issues that surround the genetic testing and screening of diseases like Huntington's and Alzheimer's, and genetic research on reproduction, ancestry, race, and neuroscience, to name a few (see Lock and Nguyen's An Anthropology of Biomedicine (2010) for an overview).

More recently, social scientists have shifted their focus to the topic of "personalized medicine" (Tutton, 2012), a biomedical paradigm that seeks to provide "the right treatment for the right patient at the right time" (Author's fieldnotes). Personalized medicine focuses on how individual biological information can be used to diagnose, treat, and predict health conditions. Tracking emerging research on personalized medicine, social scientists have examined how genetic information is marketed and popularized as the key to unlocking personalized diets (Harvey, 2009) , drug regimens (Hedgecoe, 2004), and cancer treatments (Gibbon, 2007).

This body of social scientific work, though it has documented the impacts and social aspects of genetic technologies, has provided an overly narrow view of and framework for studying personalized medicine. Social scientists have largely focused on genetic mutations and variations, at the expense of exploring the more varied scientific practices and approaches that make up modern biomedical research. Research on the human body is changing to incorporate systems biology approaches, which examine various levels of biological functioning from genes to metabolism (Figure 1), as well as informational practices (Swedlow et al., 2011). With this shift towards examining not only genes, but the ways that genes interact with the environment, biology is producing more holistic, networked, and relational views of health and disease (Loscalzo et al., 2007).

Given this growing body of post-genomic research, social scientists have left the dense, complex, and varied workings of the science that fuels personalized medicine unexamined. Few researchers have accounted for the ways in which personalized medicine extends beyond the central dogma of the gene, and is entangled with systems biology (Fujimura and Rajagopalan, 2011), statistical practices (Stevens, 2011) or information systems (Leonelli, 2012). Moreover, few

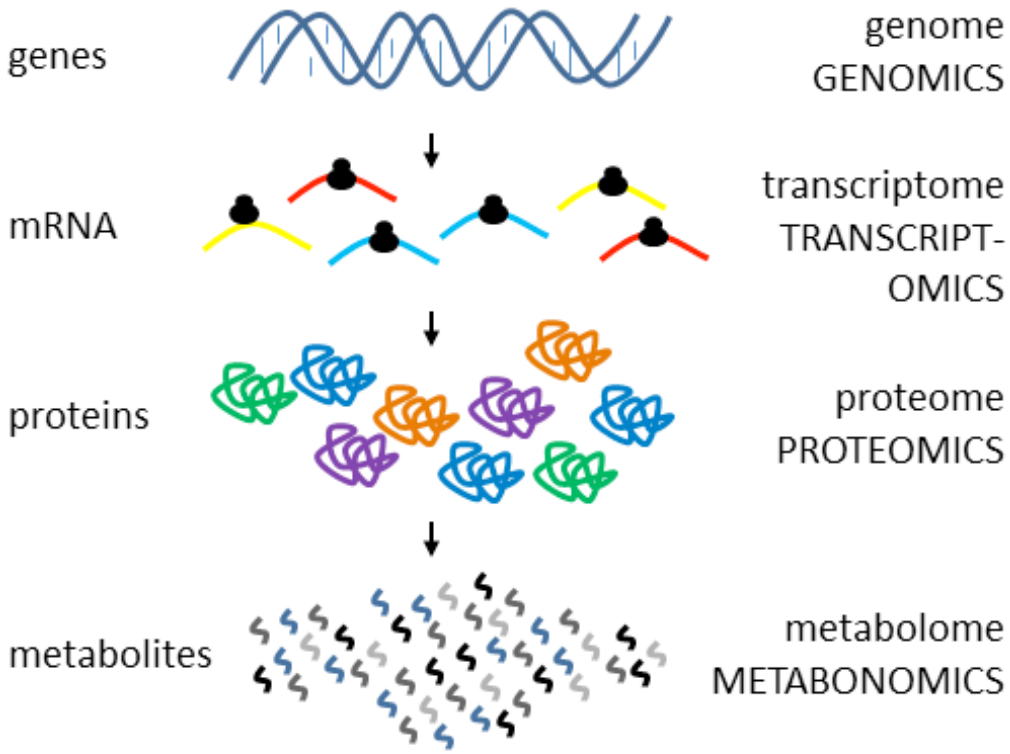

Figure 1. An overview of several fields of research that make up systems biology, which includes genomics (the study of the genome), transcriptiomics (the study of RNA transcipts), proteomics (the study of proteins), and metabonomics (the study of metabolism).

researchers have accounted for the material practices¬¬—the actions that scientists carry out in everyday laboratory research—that make up post-genomic research, focusing instead on published documents, policy and ethics implications, and or popular media accounts.

Ultimately, my research seeks to diversify social scientific perspectives on personalized medicine by documenting the diverse fields that make up post-genomic research. Following recent works on epigenetics (Landecker, 2011, Niewöhner, 2011) and metagonomics (Benezra et al., 2012), my research explores the lesser-known field of metabonomics, the post-genomic study of metabolism, which is the combined output of genes and environment.

The metabonomics laboratory

My DPhil research, which is being carried out at the Institute of Social and Cultural Anthropology at Oxford University, investigates how personalized

medicine is being conceptualized and enacted in relation to metabonomics. This emerging area of research uses systems biology, statistics, and biochemistry to investigate dynamic changes in the metabolism of organisms, and to identify the key "metabolites"—biochemical molecules—involved in metabolism. My research, which was supported by a Biosocial Bursary Small Research Grant , involved one year of ethnographic fieldwork in the Biomolecular Medicine Department (BMM) of Imperial College London. Through this research, I sought to understand the predominant themes, discourses, and practices occurring in everyday personalized medicine laboratory research.

The BMM is situated in a large building in the South Kensington area of London. It encompasses a multi-sited and multi-disciplinary laboratory that involves the collaboration of more than 50 biologists, statisticians, biochemists, clinicians, surgeons, and technicians. Overseen by Professor Elaine Holmes, the BMM was founded in 1999 by Professor Jeremy Nicholson, one of the founders of the field of metabonomics, and the head of the Department of Surgery & Cancer at Imperial College London. Known for its flagship projects in pharmacometabonomics (Clayton et al., 2009) and more recently the surgical "patient journey" (Kinross et al., 2011), the BMM investigates how metabolic information can be used to understand personalized medicine. Within metabonomics, organisms are envisioned as complex, dynamic systems of biochemical reactions and pathways, while specific biomarkers of metabolism are seen as the means of predicting and diagnosing health and disease. Collaborations are held with pharmaceutical companies and medical departments through Imperial College to enhance the BMM's potential to do "translational medicine," the application of laboratory research to clinical settings within the arena of personalized medicine.

Despite its entanglement with biomedical and clinical issues, the BMM is fundamentally a biochemistry laboratory and statistical powerhouse. Its sixth floor facility is similar to many other laboratories: it contains desks for research, a room for the processing of human and animal samples, a small coffee lounge, a meeting room, and a freight elevator with access to the basement freezers. But more uniquely, it houses millions of pounds worth of equipment in the form of nuclear magnetic resonance spectrometers and mass spectrometers, technologies whose creation and use dates back to the 1950s. Inundated by bright fluorescent lighting and peppered with color-coded signs for health and safety hazards, its open floor plan hums with the constant ticking and white noise of machinery. Large metallic containers of liquid nitrogen sit next to six-foot tall machines, encircled by yellow dotted lines indicating the presence of powerful magnetic fields.

In contrast to the sixth floor laboratory, the bulk of the BMM forms a massive, multi-floor arena that houses the workspace for staff and students. Rows of desks form a circular ring around the open central space, which spans four stories and is flanked by smaller laboratories. The space is filled by the tapping of keyboards, the rustling of papers, and the constant low-level chatter of students. Overall, these spaces of the BMM stand in stark contrast to typical social science visions of laboratory work, which portray scientists wearing white lab coats and gloves, and pipetting liquid in and out of test tubes. Moreover, the nature of these spaces is indicative of the kinds of work that characterize research in the BMM: the processing and interpretation of huge amounts of biochemical data through the design and implementation of multivariate statistical algorithms.

Detailing statistical practices in metabonomics research

One of the main tasks of my ethnographic fieldwork at the BMM was to understand and detail the ideas and practices of statistical analysis: to explore how, why, and to what end statistics were being used in metabonomics research. To do so, I helped conduct metabonomics experiments, carried out interviews with more than 30 members of the BMM, and observed numerous training sessions and seminars. Doing so required observations of scientists at computers, as well as discussions of highly-technical mathematics and computer-programming concepts.

Statistical practices, in essence, demarcate and define the differences between experimental groups of chemicals, cells, tissues, animals, or humans. Metabonomics research, and consequently research on personalized medicine, revolves around the classification of biological materials into states of health and disease. To do so, metabonomics researchers use a variety of multivariate statistical techniques—methods that make sense of combinations of variables—to make sense of biochemical data, which is derived from nuclear magnetic resonance (NMR) spectroscopy or mass spectroscopy (MS). Multivariate statistics, researchers assert, allow them to capture the complexity of their data, which is the result of multiple pathways and biological processes. In using multivariate statistics, researchers generate "biomarkers"—measurable and quantifiable biological entities—to discriminate between and classify healthy versus diseased samples.

As an example, researchers commonly use Principal Component Analysis (PCA) as a preliminary multivariate statistical technique for exploring their data. PCA generates a two-dimensional graph—a visual representation—of metabonomics data (Figure 2). This method takes the sum of biochemical information that is contained in each biological sample and collapses it into a single data point on a

graph, and then summarizes the main biochemical similarities and differences of the samples along the two axes of a graph. PCA as one of many multivariate statistical techniques, therefore, allows researchers to compare those aspects of their data—the chemical compounds and their corresponding biochemical pathways—that are responsible for the main differences in metabolic states of health and disease.

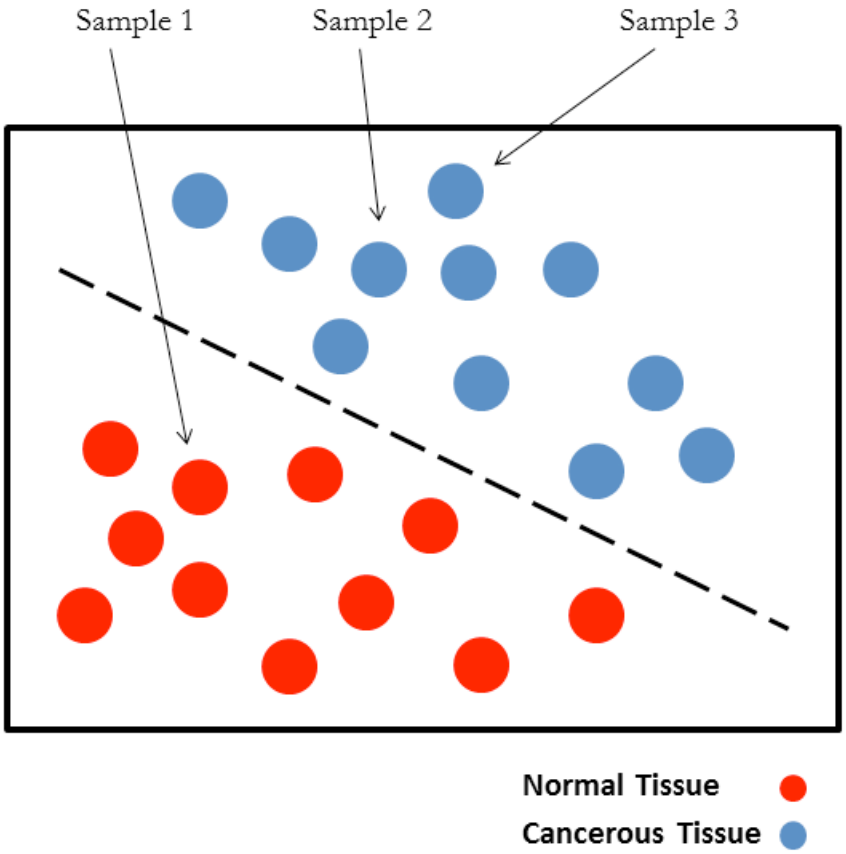

Figure 2. A graphical representation of Principal Component Analysis (PCA), showing the ways in which samples correspond to the information on multidimensional statistical graphs.

Multivariate statistical analyses like the PCA described above are a routine part of metabonomics laboratory practice. They are taught to PhD students and new members of the laboratory as a "right of initiation" during the twice-a-year Metabonomics Shortcourse, in which academic staff and industry leaders provide comprehensive lectures on metabonomics methods. Throughout their time in the BMM, metabonomics researchers learn to read multivariate statistical plots as a skill, as they encounter them in metabonomics publications and build

and rebuild them through their own research. As a result, the BMM encompasses particular technologies, methods, and practices for carrying out "correct" forms of statistics, which implicitly value the use of multivariate approaches over univariate ones.

The processes of creating, reading, and working with statistical plots form the core practices for dealing with metabolic data and "doing" metabonomics. By exploring the everyday material practices of the metabonomics laboratory, my DPhil research examines the ideas and practices that researchers use to apply statistics to the investigation of personalized approaches to disease diagnosis, treatment, and prediction. In their use of multivariate statistics, metabonomics researchers see personalized medicine as something that can best be measured through combinations of multiple biomarkers, and in which metabolism is inherently interconnected and complex. Thus, my research explores how multivariate statistical practices and ideas do not exist as objective, pre-defined things, but rather come into being through particular practices, people and technologies. It explores, moreover, how visions of personalized medicine in the metabonomics laboratory are embedded within networks of values and ideologies, and create increasingly molecular and statistical conceptions of organisms, life, and disease.

Conclusions

As biomedicine in the United Kingdom and other Western societies becomes an increasingly complex and varied endeavor, social scientists must engage with the multitude of research practices and approaches that make up research on personalized medicine. Moreover, as this research becomes increasingly characterized by data practices and informational structures, social scientists must critically explore how statistics forms a fundamental—and to this point, under-researched—undercurrent of personalized medicine research. Scholarship at the forefront of anthropology, sociology, and the interdisciplinary field of science and technology studies (STS) has only just begun to engage with the complex role that statistics plays in biomedical research (Stevens, 2011, Fujimura and Rajagopalan, 2011, Keating and Cambrosio, 2012, Leonelli, 2012, Chow-White and Garcia-Sancho, 2011). Despite the challenges of learning statistical language and observing computational practices, more in-depth ethnographic research is needed to document the ways that personalized medicine is being enacted through and impacted by statistical ideas and techniques.

Ultimately, statistical concepts and practices constitute a difficult but fundamental area for conceptual and ethnographic analysis, and are central to understanding modern cultures of biomedical research. Statistics represents a

unique area of focus, because numbers and probabilities are fundamental but also immaterial things. Statistics, though they revolve around physical occurrences such as diseases or family relations, occur primarily in the abstract realm of numbers and digital data. As such, biological and disease concepts based on statistics are slippery things: the statistical boundaries that demarcate the differences between states of health and disease are seen as "objective," but in reality are influenced by distinct practices, technologies, and idealogies. Consequently, my research endeavors to examine not only the findings produced through statistical analysis, but also the processes by which these findings are produced and made culturally salient.

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