Styles of valuation: algorithms and agency in high throughput bioscience

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Introduction

The biosciences are often proclaimed to be going through a data revolution based on high throughput technologies, online data sharing, and algorithmic tools. Sometimes the biosciences are said to be going from *in vivo*, via *in vitro*, to now finally arrive *in silico*, that is, a computer-based bioscientific dream world. In the words of one critical commentary, the dream is that the biosciences will become "Bigger, faster, better" (Davies, Frow, and Leonelli 2013). In response to this enthusiasm, many observers have asked what these technological changes entail for knowledge production in the biosciences.

This article approaches high throughput technologies in the biosciences through actors' valuations in a bioscientific laboratory. More specifically, we examine how different configurations of humans and algorithms are valued in laboratory practices that transform specimens into data. In doing so, we show how these valuations may diverge in ways that are tied to broader struggles about what should count as "good science" or "objectivity" in high throughput bioscience. Concretely, we analyze how actors in a bioscientific laboratory value different configurations of humans and algorithms in relation to two specific algorithms called "normalization" and "randomization."

Our examination shows how different configurations of algorithms and humans are assessed in multiple ways: it is not apparent for our informants which devices are more authoritative than other, nor is it apparent which skills and functions should be redistributed to these algorithms. Thus, for those working in the laboratory, the use of these algorithms evokes many questions: What is a good algorithm? What does it achieve? What distribution of roles between humans and algorithms is good science? Should human know-how or expertise be

central, or should "mechanical objectivity" be the ideal (cf. Daston and Galison 1992)? How should a good cut between signal and noise be made and by whom? Should it be done by an algorithm or a human? In sum, several questions are raised that relate to different configurations of humans and algorithmic automations and the valuation of these configurations.

We treat these questions as being about the valuation of different configurations of humans and algorithms, and *the appropriate distribution of agency between humans and algorithms*. What is striking is that these valuations were not done in a singular manner in the laboratory we examined. What is deemed a good way of configuring agency is a matter of negotiation of the yardsticks that actors' make salient in each situation. Thus, similarly to Knorr Cetina (1999) or Daston & Galison (2007), we are interested in the links between valuations and the machineries of knowledge production—but, rather than studying the disunity of science through comparison of different branches of science (Knorr Cetina 1999), or tracing the instability of a particular scientific value through history (Daston and Galison 2007), *we examine how multiplicities of values are attributed to technologies in situated practices.*

In paying attention to valuations in situated practices, we follow a *valuographic* research program which focuses the practical enactment of values, and stresses how such valuations are an inseparable part of knowledge production (Dussauge, Helgesson, and Lee 2015). Thus, rather than treating the value of an algorithm as a given, we treat these as outcomes. To further highlight the multiplicities of yardsticks and valuations in the biosciences, we propose four different heuristic *styles of valuation* in the biosciences: a *bioinformatic*, a *subjectivist*, an *experimentalist*, and a *trialist* (cf. Fujimura and Chou 1994). We argue that these *styles of valuing* are just like "objectivity," situated in historical and situated continuities and

discontinuities. Thus, we show how different manners of configuring agency are valued differently in practical and situated relations, and how different styles of valuation coexist in one laboratory with varying degrees of dispute.[1] Specifically, with this move, we wish to nuance the tendency to treat *in silico* technologies as having monolithic qualities and pre-given outcomes.

Approaching the data revolution in the biosciences through the concept of styles of valuation, enables us to start to disentangle the multiplicity of yardsticks that coexist in today's high throughput biomedical science. Rather than tying algorithms to one value, such as "speed," "precision," "size," "objectivity" or "subjectivity" this approach allows us to examine in detail what Keating & Cambrosio have referred to as the "hybridization" of the biomedical sciences (Keating and Cambrosio 2012, 37). Thus, rather than tracing how a seemingly static but nebulous set of high throughput technologies affect a seemingly monolithic bioscience, we argue that this approach allows for empirically sensitive accounts of actors' struggles to find good distributions of agency between humans and algorithms.

Technology in the Biosciences

The salience of these issues becomes apparent in relation to STS' long standing interest in the automation and digitalization of the biosciences. Recurring questions of the nature of this change has abounded, ranging from questions on how certain representational devices as constructed as more authoritative than others (Fujimura 1999) to questions about how skills and functions are redistributed between human and machines (Keating, Limoges, and Cambrosio 1999).

Recently we have witnessed an increased interest in how bioscientific research is becoming "big biology" and thus reshaped through "high-throughput" or "data-driven" approaches (cf. Leonelli 2012, Davies, Frow, and Leonelli 2013). Inquiries into these topics have had different research foci: For example, research has inquired into how infrastructures alter how research directions and questions are articulated (Keating and Cambrosio 2012, Calvert 2013, Frow 2013); how organizational and spatial questions are impacted by big biology (Hilgartner 2013, Davies 2013); or how big biology relates to economies (Lezaun 2013) or the postcolonial (Rajan 2013).

Closer to the practices and technologies of knowledge production, questions have been posed about the so-called "omics" fields (e.g. genomics, metabolomics, proteomics), and how they "produce new genres of difference and variation" (McNally and Mackenzie 2013, 75). Here, a number of studies have taken an interest in high throughput technologies: For example, it has been argued that bioinformatics is reshaping the biosciences into a capitalist production machine which emphasizes scale, economy, and surveillance (Stevens 2011). It has furthermore been argued that technologies of knowledge production—in this case multivariate statistics—perform biology in specific ways (Levin 2014, 560). Other studies ask how a new breed of experts without wet-lab experience—such as bioinformaticians and biostatisticians—can lead to new challenges for online data interpretation (Leonelli 2014a, b). One concern being that the data-driven biosciences could lead to an "exaggerated trust in the quality and comparability of the data" as well as a replacement of "subjective judgment" with "statistical kind of objectivity" (Strasser 2012, 87). Another important point being that the fading of singular data points becomes a source of anxiety in the high throughput search for trends and patterns (Leonelli 2014b).

While these lines of research highlight important developments in the biosciences, it is precisely the determinist tendency in such analyses that we wish to address here. Our argument is that there is a propensity to produce monolithic accounts of technology in the biosciences. We maintain that these studies tend to sidestep a tradition of careful research on technology, which has shown the variability and multiplicity of technologies in practice (Pinch and Bijker 1984, Mackenzie 1996, Laet and Mol 2000). Consequently, rather than making wholesale assumptions about the properties and effects of technology—e.g. that bioinformatics is turning biology into a capitalist production machine (Stevens 2011)—we propose to pay attention to situated valuations of technology in the biosciences, *to highlight multiple human-algorithm configurations and the multiple and concurrent values that these are linked to*.

A valuography of algorithms

As we stated above, this article is about the valuations of two algorithms in a bioscientific laboratory. Historically, the word *algorithm* is said to be derived from the name of the Persian mathematician al-Khwārizmī (c. 780—850) (Knuth 1997). A current dictionary definition of algorithm is: "a process or set of rules to be followed in calculations or other problem-solving operations, especially by a computer."[2] In the social sciences, algorithms have recently received an upsurge of interest (e.g., Kitchin 2014, Dourish 2016). Some researchers employing the strategy of '*going under the hood'* of the algorithm, to understand what algorithmic calculations do, and the values embodied in their operations and calculations. For example, this type of study has shown how machine gambling algorithms produce fake "near misses" to entice gamblers to bet again (Schüll 2012), or how algorithms embody a utilitarian moral philosophy for allocating organs in the UK health service (Roscoe

2015). In still other research, algorithms have been productively analyzed as being performative, showing how they perform and transform the objects that they are brought to bear on, like in spam filtering (Kockelman 2013) or plagiarism (Introna 2013).

This article is positioned closer to research on algorithms which argues for an ethnomethodological or emic perspective that pays attention to the practices of designing, interpreting, and using algorithms, rather than going under the hood to understand what they *really, really* do (cf. Neyland 2015, Ziewitz 2017, Seaver 2017). As stated above, it employs a *valuographic* research strategy (Dussauge, Helgesson, and Lee 2015) to analyze the multiplicity of values attached to and enacted by algorithms in the biosciences.[3] A particular facet of algorithms—which makes them intriguing as objects of inquiry in this *valuographic* sense—is their multivalence. This implies that their characteristics as well as their effects and values—just as bikes, missiles, bush pumps, or tomatoes—are difficult to fully stabilize (Pinch and Bijker 1984, Mackenzie 1996, Laet and Mol 2000, Heuts and Mol 2013). *As a consequence, we do not treat algorithms nor the values that are ascribed to them as stabilized or pre-given entities.*

As hinted at above, we here analyze actors' valuations of different human-machine configurations through the notion of *styles of valuation.*[4] We introduce this concept to shine light on the multiplicities of problems, values, and yardsticks that are articulated in situated practices—in this case around bioscientific algorithms. In this, we draw on Fujimura & Chou's (1994) concept *styles of practice*, which is defined as "historically located and collectively produced work processes, methods and rules for verifying theory" (Fujimura and Chou 1994, 1020). While Fujimura and Chou "examine the co-production of facts and the rules for verifying facts over time" (1994, 1017), *styles of valuation* brings attention to

distinct differences in the valuations of scientific work processes, methods, and their relation to "good science." Thus, the concept styles of valuation highlights how technologies are intertwined with multiple concurrent sets of values, such as objectivity or universality (Fujimura 1999). In the words of Fujimura, what is at stake here is that:

> Scientific technologies are highly elaborated symbolic systems, not neutral media for "knowing" nature. For example, neutrality, or the idea that one can eliminate "noise" versus "signal" to reach a tabula rasa from which one can then produce "reproducible effects," is part of a set of "values" historically located in so-called "Western traditions of thought." These values include realist, objectivist, and empiricist rhetorics, which form the basis for establishing factness and the universality of findings. (Fujimura 1999, 75)

In line with this, we are interested in the different values that actors articulate in the laboratory. With Fujimura (1999, 76) we ask how some "technologies and practices of representation […] are constructed as more authoritative than others."

An important feature of the notion *styles of valuation* is that it centers on actors' articulations of problems, solutions, devices, and configurations of agency. We analyze these articulations in sets that are identifiable in a *style for assessing what is appropriate, valuable and worthy*. For example, the style of valuation which we heuristically dub *the trialist* centers around the actors' problematization of undue human influence on experiments. Here, algorithms are deemed valuable for their ability to blind experimenters, so they do not introduce unwanted bias in the experiment. Using these heuristic *styles of valuation*, we wish to stress how actors' valuations of different configurations of human-machine agencies are not constrained by

inherent technological properties, professional identities, or laboratory specialties. The notion instead opens for the possibility of multiple styles being present in a situated practice.[5] It therefore provides a means for examining frictions between articulations of problems and what are seen as appropriate and valuable means to address these problems. A *style of valuation* is hence recognized by a particular problematization and is tied to a particular valuation of what solutions, devices, and configurations of agency are appropriate and valuable.

By introducing the concept of *styles of valuation* to analyze how actors value algorithms, and different configurations of human-machine agency, we can examine several tensions, inversions, and coordinations. These include tensions that arise in how to value "raw" and "cooked" data as well as different problematizations of what algorithms might do to the data. More broadly then, styles of valuation open up for examining the negotiation and enactment of a multitude of values tied to algorithms in the biosciences.[6]

Our argument is that algorithms are cultural artifacts that have multiple meanings and meander through different social practices in the laboratory. At one time and place an algorithm might be considered a device for dealing with non-biological variation. At another, the very same algorithm might be seen as problem that introduces precisely the dreaded variations that it was seen as solving earlier.

Fieldwork

The article draws on the first author's longitudinal and polymorphous engagement with an anonymous research group working with high throughput biomedical mapping. The empirical

work started in 2010, and was concluded in spring 2014, with a return visit to present results in 2016. The data collection consisted of interviews, meeting observations, demonstration sessions, as well as analysis of both published and unpublished laboratory documents (such as articles, protocols, screenshots, and unpublished papers). Interviews were done at the laboratory, and were audio recorded and subsequently transcribed. The laboratory demonstrations entailed sessions where different laboratory and software practices were demonstrated and explained—often in conjunction with scheduled interviews. Demonstration sessions were documented in field notes. In total, 34 interviews or demonstration sessions were conducted with researchers, lab technicians, doctoral students, and other actors related to the laboratory. Articles from the group and elsewhere, as well as unpublished laboratory protocols, screenshots from laboratory management systems, and analysis software, as well as textbooks on research design were analyzed. All interviews and documents were coded and analyzed by the first author using software for coding and retrieval, *Atlas.ti*. To preserve the anonymity of the laboratory, the country, language, publications, and names are kept unstated.

Entering the laboratory

The studied lab is situated at a research university in a European country. It consists of about 20 individuals which are divided into two research groups with specific methodological competencies. The laboratory has been running for roughly 10 years. It is focused on biomedical mapping of protein biomarkers, or more simply put, identifying links between protein "signatures" and different diseases. That is, protein patterns which can be linked to specific conditions. The identified protein signatures, it is hoped, are to provide leads for developing novel methods of diagnosis, and perhaps, in the longer term, to new treatments.

For the people working in the lab, the dream is to repeat other laboratories' successes in finding genomic biomarkers for—for instance—the diagnosis of breast cancer (the BRCA genes) or biomarkers for prostate cancer (the PSA test).

In this lab, the identification of protein signatures entails attempting to find differences between signatures from "cases"—people understood as having a specific condition—and samples from "controls"—people considered to not have the condition.[7] In order to find these coveted protein signatures, the lab analyzes samples from patients in the form of various bodily fluids: such as blood, urine, and spinal fluid. The samples are supplied by different collaborators around the world, and have often been gathered in different places, using different techniques, and for different purposes. In the analysis of these samples, the scientists utilize a technique called suspension bead array to map protein levels in the body fluids. This entails mapping how much of a range of proteins exists in a sample. For each sample the levels of multiple proteins are measured—often hundreds of different proteins for each patient sample.

The high-throughput methods employed are also designed to analyze hundreds of patient samples in one run. In general, the laboratory's process entails: First, transferring body fluid samples from different collaborators to so-called micro titer plates (square plastic "plates" with small indentations—"wells"—for body fluids ordered in a grid formation). Each plate contains a number of wells (up to 384 wells per plate in their fastest machine), and each well contains a body fluid sample from a single patient. Second, the plates are fed through so-called multiplex machines that analyzes the protein levels of all the samples on a plate.[8] The fastest machine can analyze the levels of 500 proteins in one well in one pass. The third and last step, involves comparing the protein levels of different samples to find patterns linked to

different conditions. This involves comparing "cases" and "controls" through different types of statistical software, scripts, and algorithms.

The high throughput methods make automation through algorithms, scripting, and robotics crucial in the studied lab. The laboratory workflow included machines to automate the handling of plates and samples, computer scripts that controlled the machines, as well as scripts that cleaned the data. As stated in the introduction, the focus of this article are two algorithms in use in the lab: randomization and normalization. The *randomization algorithm* was used in the first step of the process outlined above and generated instructions for sample-handling robots. These robots were used to transfer body fluid samples from the test tubes they were stored in, to the plates that were fed into the multiplex machines.[9] The *normalization algorithm* was used (in step three above) to separate—as one of our informants expressed it—"biological variation" from "non-biological variation." That is, to separate noise from signal when the data from the multiplex machines was analyzed. We will return to the valuations of these algorithms in detail below.

The two algorithms in focus here are thus tied to a central matter of concern for our informants—separating signal from noise, patterns from static, protein signatures from trash. We are thus interested in, to return to our initial question: How do actors in the lab value different configurations algorithms and humans—different configurations of human/machine agency?

Randomization: ignorance and tinkering

As described above, randomization algorithms were used to place body fluid samples on

plates.[10] However, achieving a good randomization was not straightforward for our informants and included a multitude of devices and practices throughout the lab: It was sometimes introduced manually (literally by hand) by putting samples into cardboard boxes and shaking them—which an informant jokingly called "the box method of randomization." Sometimes the randomization was brought about using a very simple algorithm in the R scripting language that took a "vector" and scrambled it. That is, the algorithm took an orderly list of numbers—1, 2, 3, 4—and randomly re-ordered the sequence into for example 2, 4, 1, 3. This new sequence of numbers was then used to guide the researcher's hand when manually sorting samples onto a plate. Our informant's argument was that the vector method ensured random placement without the researchers having to "think about it"—without mental energy being expended on producing a randomization. However, when large numbers of samples had to be randomized—when the lab ran their signature high throughput analyses—another algorithm in R produced by the lab's resident bioinformatician could be used. This bespoke "plate layout algorithm" produced instructions for a sample handling robot, which automatically randomized the samples on a micro titer plate according to a specific "plate layout."

The experimentalist style of valuation: machine noise and human tinkering

Paradoxically, the randomization algorithm used in the laboratory was not random—it produced what our informants called "a balanced randomization." This was by design, since a complete randomization was understood as problematic. Thus, alongside the argument *for* randomization, our informants contended that the randomization algorithm needed to produce a balanced distribution of samples according to several parameters.

The reasons for introducing this balanced randomization was a concern that the machines and

processes used to analyze the samples—the multiplex machines—could introduce non-biological variation in the resulting data. The first source of concern was that samples that were located on different plates when they were fed through the multiplex machines could yield different results due to them being on different plates. The researchers' fear was that a comparison of samples located on different plates would point to differences stemming from differences between the plate runs, rather than biological differences between samples. Hence, the appropriate randomization was considered to be one which located samples to be compared on *the same* plate in the multiplex machine. By placing them on the same plate they could, our informants argued, neutralize differences in the analysis resulting from differences in plate runs.

The second source of concern was that samples of a certain kind (for example cases/controls or male/female) could become clustered in one location on *one* micro titer plate. If, for instance, all control samples happened to be grouped in the top left corner, this could then produce data-patterns that could be picked up in the subsequent analysis of the data. According to this way of thinking, the plate layout algorithm should not (not even by chance) place all samples of one type in one cluster on the plates. Thus, to counter these two problems our informants wanted to place samples randomly—but not haphazardly—on the plates:

> There are several different methods to do it [the randomization]. But, the important part is to check if all control samples happen to be placed at the start—and all with the condition at the end of the plate.
>
> (Excerpt from interview, Biotechnologist 2, 2013)

Thus, while randomization was considered beneficial, a concern was that certain random patterns in how samples were placed could introduce noise. That is, non-biological

differences in the data would be read as a signal—as biological variation. The fear that such random arrangements could produce a false signal was thus countered by introducing the notion of balanced randomization.

A common way to algorithmically counter the problems that could arise from a complete randomization was to decide which parameters were to be distributed evenly on the plate, and feed these parameters into the randomization algorithm. Three parameters that were frequently seen as being in need of balancing were age, sex, and diagnosis of the patients. One informant told us how their algorithm worked to balance the samples:

> I can note the information I have about age, gender and diagnosis, and that I want these characteristics to be evenly distributed. Then—say I have four initial plates that are to be combined into a 348 well plate—I want to be sure that the samples are distributed in a balanced way across the four plates.
>
> (Excerpt from interview, Biotechnologist 2, 2013)

Another biomedical researcher at the laboratory developed her thoughts on confounders, balance, and knowledgeable comparison of samples:

> It's well-known that, for many diseases, there's a link between age and when you start to develop the condition. We can see this, for example in different kinds of cancer where this link is strong. Some of those known links—you could call them confounders, or information, or factors about people—are important and you really want to have them in balance when comparing different groups of samples…
>
> (Excerpt from interview, Biotechnologist 1, 2013)

Thus, to counter the fear of the algorithm inadvertently randomizing the samples in a bad way, the researchers utilized different means to create a balanced randomization. Knowledge about certain sample characteristics—such as sex, age, and diagnosis—was seen as an important input for the randomization algorithm since this knowledge allowed for countering patterns emerging from plate differences.

Consequently, our informants use of a particular randomization algorithm was closely tied to handling what they call "confounders" or "confounding factors." For our informants, a balanced randomization algorithm which breaks up patterns, distributes samples evenly, or balances samples to be compared was seen as an appropriate solution to the problems of clustering and comparison. We call this the *experimentalist style of valuation* as it emphasizes how the randomization algorithm makes it possible for the experimenters in the laboratory to handle noise, thus facilitating comparison between samples.

Ignorance for objectivity: the trialist style of valuation

However, the value of having a balanced randomization was not self-evident to all collaborators. As we outlined initially, the lab depended on partners around the world for the supply of samples to be analyzed. These collaborators were an essential part of the high-throughput set-up. In a particular misunderstanding between the lab and a collaborator, different ideas about randomization came head to head. Several of our informants touched on the incident and discussed how their collaborators had had a different idea about randomization. The person working in the collaboration recalled:

> Then they [the partner] randomized the samples and sent them to us, and I didn't know they were going to randomize them for us. That's something we usually do ourselves.

> We weren't happy with their randomization […] So we had to have a meeting. They wanted us to be blinded. We shouldn't know which [samples] were [from] healthy and ill [patients].
>
> (Excerpt from interview, Biotechnologist 3, 2013)

In this situation, the collaborators tied the idea of randomization to the production of ignorance and blindness (see, e.g. Kaptchuk 1998). The collaborators stressed that the recipient laboratory needed to be blind to the characteristics of the samples. The people doing the analysis should not know which samples came from patients with a condition and which samples came from those without. However, as our informants stressed above, such information about the samples was crucial to achieve the "balanced randomization" that they valued so highly. Their argument was that having certain data about the samples, like sex, age, or sampling hospital was crucial information for achieving a good analysis. In contrast to the experimentalist style of valuation the emphasis of the collaborators lay on removing the researchers' influence on data interpretation.

Tensions: the experimentalist and trialist styles of valuation

We argue that the episode above shows how the practice of randomization is articulated differently by the actors around the lab. We heuristically group their valuations in two different styles of valuation: an experimentalist and a trialist. One where actors emphasize the human handling of machine noise, the other where they emphasize mechanical objectivity and the ignorance of the experimenter. The different kinds of randomization point to epistemic tensions in contemporary biomedical research. What is a good distribution of agency between humans and algorithms? What is the value of human knowledge and tinkering? What is the value of automation through algorithms?

On the one hand, what was at stake for our informants was the tinkering to produce epistemic comparability. These experimental practices of comparison are reminiscent of the balanced planning of plots of land in classic agricultural experiments in the UK (Hall 2007). Just as our informants attempt to create a balance on their micro well plates—early agricultural researchers aimed to compare plots that were similar in terms of rainfall, sunshine, soil, etc. The goal of both the agricultural researchers and our informants being to facilitate comparison by matching the characteristics of agricultural plots—or body fluid samples.[11]

On the other hand, the balanced randomization ran against the practice of randomization favored by a partner supplying samples to the lab. This partner wanted to perform a blinded randomization to render the introduction of bias through human intervention impossible. For them, *randomization* aimed to protect against the specter of *human intentionality*: the biased experiment that is so feared in medical research (See for example Hacking 1988, Kaptchuk 1998). These valuations seem to echo a medical and pharmaceutical understanding of randomization where keeping clinical personnel ignorant is a key component for producing "unbiased" results. In short, it is similar to a key trait in the so-called "gold standard" for medical research, the double-blind randomized controlled trial (RCT). In a textbook on medical research design the blindness of the clinical team is stressed:

> If the allocation is predictable, then the investigating physician has knowledge that he or she may subconsciously use to influence their decision to include (or exclude) certain patients from the trial… […] As a consequence, any prior knowledge by the clinical team or the patient of the allocation can therefore introduce bias into the allocation process, and hence lead to bias in the final estimate of the parameter β1 at the close of the trial. (Machin and Campbell 2005, 70)

This highlights the common conceptualization of blinding in RCTs to ensure that experimenters consciously or subconsciously can influence the results (cf.Vineis 2002, Helgesson, Lee, and Lindén 2016). In contrast, in the high-throughput practices in the laboratory studied here, the balanced randomization necessitated certain knowledge about the samples. For this lab, a blinding randomization ran counter to their inclinations to value knowledgeable and "balanced" randomization to facilitate comparison. Here, it seems that an algorithmic and "mechanical objectivity" stands against a style of valuation stressing the benefits that arise from non-blinded tinkering, and sorting in order to achieve balance (cf. Daston and Galison 2007, 1992).[12]

There are tensions in how actors assess different configurations of humans and algorithms, and in particular the value that actors ascribe to different distributions of agency. On the one hand, human knowledge and agency were seen as crucial for achieving a balanced randomization. Here, the value of informed tinkering of human experimenters stood front and center. On the other hand, unblinded humans were also articulated as problematic as they could introduce an undesirable bias. Here the algorithmic randomization was seen as protecting from biased human intervention. Randomization was subjected to two different *styles of valuation* which each favored a particular randomization procedure. Each style articulating the problems and the appropriate means to address these problems in particular ways.

Normalization: the cooked and the raw

Another common operation in the studied lab was algorithmic normalization. This is a

frequent operation in different types of signal processing which is used to make datasets more similar. A normalization entails treating data computationally through different algorithms. In everyday life, normalization algorithms are, for example, used to make similar the volume of different music tracks. The driving idea being that normalization can minimize unwanted differences between sets of data (like the volume of songs, or the measured protein levels of body fluid samples) by making them have similar amplitudes. A key aspect of algorithmic normalization is that it can *automate* the bringing data into the same dynamic range. You don't need to constantly fiddle with the stereo volume or sample amplitudes. The algorithm does it for you. Hence, in the studied laboratory, normalization brought protein levels from different samples—the data that resulted from the analyzing the body fluid samples in the multiplex machines—into the same dynamic range.

The dream of a smooth biology: the bioinformatic style of valuation

Early on in the data collection, normalization was introduced by a medical epidemiologist working as a bioinformatician in the lab. Most projects ran through his normalization algorithms at one time or another. In a sense he functioned as a bioinformatics hub for most of the lab's projects. In answer to our questions on what normalization was, he turned to the practical value of normalization, which according to him was to "minimize non-biological variation" and thus, extract the "biological variation":

> **Lee**: What is normalization?
>
> **Bioinformatician 1**: There is an expression: minimizing non-biological variation. Because we are interested in biological variation, but there's always some non-biological variation. Which we should try to remove. But there is no way to remove it, so we try to minimize it.

Lee: So, how do you know what non-biological variation is?

Bioinformatician 1: Actually, we don't know. It's a really tricky question. […] if we make a plot of the signal and […] plate one generally has a higher signal than plate two, it's visualized in the plot. Then [we can see that] there's a big difference between the plates and we try to adjust them, for them to have the same or similar values. That's normalization.

(Excerpt from interview, Bioinformatician 1, 2013)

In the exchange above, the bioinformatician valued normalization for its power to "minimize non-biological variation." The ideal was to use normalization algorithms to remove noise stemming from variations in samples, machines and laboratory processes so that biological variations were highlighted.

Here we deal with the valuation of one of the normalization algorithms employed in the studied laboratory, Probabilistic Quotient Normalization (PQN), which originated outside the studied lab. However, in order to preserve anonymity, we deal here with an article published by the outside lab that originated the PQN algorithm. The PQN algorithm's creators argued that its value lay in its ability "to reduce variances and influences, which might interfere with data analysis" (Dieterle et al. 2006, 4281). This power was illustrated with an image that compared un-normalized data, to the left, and normalized data, to the right (see figure 1).

<insert figure 1 here>

Both the diagrams and the text in the article highlight the similarity of the different datasets after normalization: "it's obvious that only very few differences […] between both spectra exist" (Dieterle et al. 2006, 4282). Just as with the bioinformatician we interviewed, the PQN

originators' argument was that normalization removed "non-biological variations" to make datasets more similar. The value of the algorithm lay in its power to make an *automatic separation between biological and non-biological variation*.

An important part of showcasing this value, was the demonstration of its power to produce smoother sets of data. In the above cited article on PQN, three different normalization methods are compared visually. The argumentation and visualization in the article focusing on the power of the algorithm to produce "optimal normalization" results. A diagram shows four different simulated datasets that vary the "non-biological variation" in different ways. The optimal normalization being represented as a flat line—which only PQN achieves in three of the dataset visualizations (data set 4 shows a marked "shelf" drop-off for PQN):

<insert figure 2 here>

An interesting facet of this valuation of the PQN algorithm, is that it supposedly automates the work of smoothing out of non-biological differences. It is the algorithm that automatically decides (based on a set of predetermined calculations) if a sample varies because of biological or non-biological differences. The normalization algorithm is thus valued for its ability to produce smooth datasets—*but also for its ability to produce an automatic separation between biology and non-biology—data and noise.* Hence, the PQN algorithm is assessed in a style of valuation which emphasize the benefits of automatic smoothing of variations in the data. We call this *a bioinformatics style of valuation*, where high value is attached to the reduction of noise while retaining the signal unchanged.

The allure of the raw: the subjectivist style of valuation

However, as alluring as the idea of an automatically flattened biology is, the normalized biology was constantly questioned by our informants. The smooth, algorithmically produced data provoked serious doubts about what really constituted biological difference. For example, one informant highlighted the difficulty of delineating biological and non-biological differences:

> And then you get stuck in a kind of argument about whether it is age or disease. And if we normalize away the age—which is something you can compensate for in an analysis—then one loses those differences. And are they then biological or are they somehow…
>
> (Excerpt from interview, Biotechnologist 2, 2013)

In the quote above the tensions and challenges of data normalization are self-reflexively brought to the fore. Are the identified differences due to normal aging or the progression of a disease? Is age to be treated as a biological difference or should it be "normalized away?" For our informants the algorithmic cut between biological difference and noise not only became a solution to variable data sets, but also a source of concern. What should the normalization classify as noise?

The trust in the smooth biology produced through algorithmic normalization was at times also contrasted with "destroying the data through normalization." In these situations, it was argued that non-biological variation could be introduced by the very algorithmic normalization practices that were used to remove them:

> I'm not a trained statistician or mathematician. I don't have the proper understanding or feel for all the effects of throwing a massive number of variables into models. This is

> also something I hear from others, that you can tweak your data to the point of breaking it. You can destroy the data through normalization.
>
> (Excerpt from interview, Biotechnologist 1, 2013)

Here our informant pointed out her lack of training and "understanding or feel" for the algorithmic methods used in the normalization procedures. She voiced a concern that the "tweaking" of the data could at some point break it, and that algorithms of normalization were a potential danger for her work. Thus, rather than being seen as a solution, the normalization algorithms were seen as the source of problems.

This skepticism against algorithmic data processing was also expressed by another informant who argued that patterns observed using normalized data, should be visible also in "raw data," thus protecting against the normalization introducing non-biological variations. Here, looking at the un-normalized "raw data"—straight from the multiplex machine—was seen as a safe-guard against seeing non-biological variation introduced by the normalization as biological variations:

> When you're working to normalize and trying to get rid of certain things in the data, a helpful rule can be that things should also be visible in the raw data. A difference that you want to point out in a publication shouldn't be something that has been introduced through normalization.
>
> (Excerpt from interview, Biotechnologist 3, 2013)

Our informant put forward the notion that "things should also be visible in raw data" as a criterion for both analysis and publishing results. Thus, for all the effort put into normalization algorithms in the laboratory, it was highly prized to find "biological variation"

in “raw data.” That is, to find noteworthy differences in non-normalized data. “Raw data” that contained a marked correlation between a biomarker and a disease was thus seen as a stronger indicator that this was a “signal” representing a biological variation.

The practices of normalization seemed to stick the researchers between a rock and a hard place. On one hand they articulated a concern that they might accept non-biological variations stemming from procedures as a signal, and on the other hand they voiced a worry of introducing non-biological variation due to practices of normalization. For one informant, getting a feel for how the “raw data” varied was crucial, but the crux of the matter was that this “hands-on disposition” also precluded a high-throughput approach.

> I’m such a nerd. I like to print out the raw data on paper and have it in a paper table since it can be nice to highlight certain things by hand. I’m pretty hands-on. Of course, I do all my analyses in R with the latest statistical software packages and all that jazz, but I think it’s reassuring to be able to go back and actually check if I have done something quick and dirty. It’s way too easy to drop lines and get lost in the normalization. But that’s not possible if you’re working with 10,000 antibodies.
>
> (Excerpt from interview, Biotechnologist 4, 2014)

Here, the high-throughput methodology staked out as the lab’s specialty brought normalization up as a necessary evil in doing high throughput analyses. The traditional know-how and feeling for the data that the biologist could use as an epistemic base-line can in our view represent a *subjectivist style of valuation.* This style of valuation devalues normalization—as well as the distribution of agency between humans and algorithms entailed in it. Normalization was subject of two different *styles of valuation* that we have labelled the bioinformatics and subjectivist respectively.[13] They each represent a different articulation of

the problem of signal and noise and what are appropriate means to address these problems. They also entail distinctly different assessments of the merits and problems of normalization procedures. The simultaneous articulation of these two styles of valuation provides a way to highlight how bioscientific researchers struggle with multiple concurrent yardsticks for valuing high-throughput analyses.

Tensions in valuing normalization: bioinformatics vs. subjectivist styles of valuation

What we have called the *subjectivist style of valuation,* is well documented in research on the cultures of the biosciences. It can be connected to a long series of studies done on the biomedical sciences, emphasizing the hands-on work, the tinkering, or openness of biological experimentation (e.g. Keller 1983, Jordan and Lynch 1998, Lynch 1985K, Cambrosio and Keating 1992). An early example in this vein is Evelyn Fox Keller's book *A feeling for the organism* (1983) which documents, among other things, the geneticist Barbara McClintock's resistance to the increasing quantification of genetics in the 1930's and 40's, who "rejected the wholesale fascination with numbers and the reductionism of modern genetics" (Hein 1984).[14] A classic quote from McClintock documents her passion for knowing the organism:

> I start with the seedling, and I don't want to leave it. I don't feel I really know the story if I don't watch the plant all the way along. So, I know every plant in the field. I know them intimately, and I find it a great pleasure to know them.
> (Keller 1983, 198)

McClintock's words resonate with how our informants problematize normalization algorithms. The "rawness" of the data—the lack of algorithmic signal processing—is

described using the same type of words that McClintock uses: a feeling for the data. Knowing your specimens, intimately.[15]

What we called the subjectivist style of valuation put a high value on intimate knowledge of data, and it seems that it also includes a skepticism toward high throughput approaches and algorithms. The value of human agency and tacit knowledge are central. The bioinformatic style of valuation, in contrast, ascribes a high value to the power of algorithmic filtering. For our informants, the practices of algorithmic normalization to smooth data stood in many instances front and center. For the resident bioinformatician and the biotechnological researchers minimizing non-biological variation through algorithmic normalization was seen as central. It was deemed impossible to know your data in the traditional manner.

However, the tension between the bioinformatic and the subjectivist styles of valuation was a constant issue for our informants. For example—at a revisit to the lab presenting our results after the conclusion of the fieldwork—we were told, by one of our informants, that she had discussed normalization, and their lab's criterion to see patterns in *non*-normalized data, with an outside biostatistician. The biostatistician's comment was:

—"But why normalize at all then?!"[16]

This exchange highlights how different yardsticks for value ascribed different values to algorithms in high throughput work. Different styles of valuation co-exist in the same laboratory, and surface regularly as disagreements about how to define a problem and what are the proper means to address them. What distribution of agency between algorithms and humans is the right one? There seems to exist no single yardstick for valuing different

human/machine configurations in this laboratory. Concerns about human influence, machine noise, objectivity, and smoothness intermingle and create situations of which can, and are, addressed differently with different styles of valuation—and different yardsticks for value.

Styles of valuation: algorithms and distribution of agency

We have examined how different valuations are brought to bear on algorithms in a bioscientific laboratory. In this, our emphasis has been on how researchers problematize and assess different configurations of humans and algorithms, and in effect, how they assess different distributions of agency. Thus, we pay attention to how actors struggle with the questions "What is a good algorithm?" and "How should competencies and roles be assigned between humans and machines?"

We have heuristically identified the researchers' different problematizations and valuations as being done in four different *styles*. These *styles of valuation* center on actors' articulations of problems, solutions, devices, and configurations of agency. Each style is characterized by a particular problematization as well as a particular assessment of what is appropriate, valuable and worthy solutions to the problem.[17] We argue that *styles of valuation* is a helpful heuristic analytic for examining the ambiguous role of algorithms in the examined lab as well as for appreciating broader tensions in current high-throughput biomedical research. Table 1 provides a summary of key characteristics of each style of valuation identified in this case study.

<insert table 1 here>

First, we attended to the actors' valuations of randomization algorithms, and the tension between what we dubbed the *experimentalist* and *trialist styles of valuation*. In, the *experimentalist style*, the actors problematize noise stemming from laboratory machinery—and see it appropriate to use algorithms to remove it. It is through human know-how and tinkering that good data can be achieved. In contrast, in the *trialist style*, researchers problematize human biases, and see blinding through randomization algorithms as the appropriate means to alleviate this problem. This style articulates human agency as potentially problematic.[18] Second, we considered normalization algorithms, and the conflict between the *bioinformatic* and *subjectivist styles of valuation*. In the *bioinformatic style* actors value algorithms for their ability to automatically smooth out differences between datasets, placing the responsibility for making a cut between data and noise in the domain of the algorithm. Here, the possibility of normalization algorithms is articulated as the solution to high throughput analysis. Clashing with this, is the *subjectivist style of valuation*, with which normalization algorithms are seen as able to destroy data. Here the intimate knowledge of "raw data"—an oxymoron to be sure—is articulated as a remedy against algorithmic destruction (cf. Gitelman 2013).[19]

Our observations summarized along these four different styles of valuation should be understood against the backdrop of an ongoing technological shift towards high throughput bioscience, which has led observers to ask if subjective judgment will be replaced with statistical objectivity and an exaggerated trust in data (Strasser 2012), and if singular data points will fade away from high throughput work (Leonelli 2014b). Our observations, however, both support and contradict these arguments: the tension between subjective judgment and statistical objectivity did not fade away for the actors. Rather tensions were heightened. Individual data points were understood as impossible to know as intimately as

desired, but the drive to intimacy and subjective judgment seemed to persist.

We propose that by paying attention to different styles of valuation—with their distinct articulations of problems, solutions, devices, and configurations of agency—we can create a more multifaceted and nuanced understanding of technology in the biosciences. The point being that an analysis of styles of valuation—with an emphasis on articulations of what is problematic, as well as the appropriate and valuable means to address these problems—can shine light on tensions in how actors in the biosciences relate to high throughput technology. Our argument has been that, if the biosciences are becoming data driven, and we are swimming in a tide of data, we might—as Adrian Mackenzie has suggested—attend to "different ways of swimming in this tide" (Mackenzie 2014).

In certain laboratories high throughput technologies might be valued in line with a capitalist logic of production (Stevens 2011), in other places technology might be valued for its ability to capture complexity (Levin 2014), yet at other junctions technology might be valued for its ability to enable "data journeys" (Leonelli 2016). But surely, tensions and instabilities persist within these practices!? Our suggestion has been to analyze these different ways of swimming in the high throughput tide of data by paying attention to actors' valuations of scientific devices and technologies. This approach allows us, as Fujimura proposes, to understand these scientific devices as part of elaborate symbolic systems, with links to different ideas about what good science should be (Fujimura 1999, 75).

We see this move as a remedy to an unfortunate tendency to treat "high throughput" or "big data" technologies as monolithic and deterministic phenomena that are reshaping the biosciences. An unfortunate consequence being how "new technology" can become a

featureless placeholder that allows reifying conclusions about how "big data," "infrastructures," and "biomedicine" are reshaping each other. Perhaps the quintessence of this simplifying move can be found in Anderson's much criticized article *The End of Theory: The Data Deluge Makes the Scientific Method Obsolete* (2008).

What we wish to point out, is that there is a troubling tendency to reproduce "Algorithms," "Big Science," "Big Data," or "Data driven science" as monolithic phenomena. And that it is all too easy to fall into the current "algorithmic drama" (cf. Ziewitz 2015) which highlights either a dystopian future where human agency is curtailed, or a utopian dream world of "bigger, faster, better" (Davies, Frow, and Leonelli 2013). We contend that this dualistic take on new technologies in the biosciences—in its seductive simplicity—risks undoing a lot of careful work on the complexities of laboratory practices in STS and elsewhere, and reproducing bioscientists as "cultural dopes," who act within preconceived notions of how technology in the biosciences has worked and will work in the future (cf. Garfinkel 1967, 68).

Approaching the data revolution in the biosciences through the concept of styles of valuation, enables us to start to disentangle the multiplicity of valuations that coexist in today's high throughput biomedical science. To understand how new technologies interface with bioscience we need to be open to actors' articulations of these challenges and how they assess different distributions of agency between humans and algorithms. Our argument is that if we fail to acknowledge the distinctly different ways this might be done in a particular setting, we risk becoming blind to actors' struggles to work with automation and algorithms. "What is good technology?" will always be an open question, and we want to highlight that tension, to bring out the multiplicities, dilemmas, and trade-offs over deterministic accounts of

science. As Donna Haraway (2010) phrases it, we wish to provide tools for "sticking with the trouble."

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[1] We are indebted to one of our anonymous reviewers for this observation.

[2] New Oxford American Dictionary, 2016.

[3] It is worth noting, that styles of valuation share an interest in values with other broadly pragmatist approaches to the study of valuations. For example Boltanski and Thévenot (Boltanski and Thévenot 2006) have introduced the concept worlds of worth, to describe how actors justify and reach compromise in French organizational life. An analytical frame that could be also be productively applied also in the biosciences: How do scientists justify their way doing things? How are the right yardsticks for valorizing algorithms arrived at? However, we argue that applying an analytical frame that emphasizes tensions between different "worlds of worth," would risk playing into precisely the monolithic descriptions of the in silico biosciences that we wish to unsettle. Thus, rather than analyzing how actors' reach agreements on the justified use of technology, we wish to show how multiple concurrent sets of values can coexist in one situated practice. As should be apparent, we want to avoid reifying technology in the biosciences by succumbing to ready-made categorizations of technologies, actors, or values. To paraphrase Donna Haraway: we wish to stick with the trouble (Haraway 2010).

[4] A similar concept being for example Hauge's *modes of valuation* (2016), which emphasizes devices' "relationship to prevailing tools and practices of valuation at play in the organization" (Hauge 2016, 128). In our

view, Hauge's approach is a productive avenue to explore in that it refocuses the analytical lens from how devices reshape an organization's values, to how valuation devices exist in more complex ecologies of values (See also Zuiderent-Jerak and Egmond 2015). Our goals in introducing the concept *styles of valuation* are similar to Hauge's. However, in difference to Hauge's modes of valuation, we wish to stress the continuity with classic laboratory studies, drawing primarily on the work of Fujimura & Chou. Thus, by using styles of valuation we wish to emphasize not only the complex interplay between valuations and devices, but also the links between valuations, devices, and the production of scientific knowledge.

[5] Fujimura and Chou (1994) emphasize with reference to Hacking (1992) that working with such styles "assume no one-to-one mapping of group membership to a particular world of practice" (Fujimura and Chou 1994, 1021). Scientists of sharing a particular training may very well in a setting participate in processes tied to different styles of valuation.

[6] As we have alluded to above, what we do here stands in direct relation to the contributions that Daston & Galison (2007) have done with objectivity. However, while they traced the multiplicity of objectivity and its concomitant virtues through a number of utterances, practices, and devices that vary over time, we investigate two algorithmic devices in high throughput bioscience—normalization and randomization—and the multiplicity of ways in which these are valued in one place. They emphasize one value that changes over time, while we emphasize multiple values in one situation (cf. the strategies outlined in Dussauge, Helgesson, and Lee 2015).

[7] The control samples were sometimes harder to come by, as most body fluids that they had available came from investigations of specific patients and diseases. Therefore, they sometimes used "controls" that were "cases" from other studies.

[8] Different machines in the lab accepted plates with different numbers of wells, and could analyze varying numbers of proteins concurrently. The output from an analysis was a set of numbers that indicated the level of the many different proteins found in each well. The newest machine in the lab was the Luminex Flexmap 3D.

[9] According to the protocol randomization was to be done through programming a robot familiarly called Tecan (it's full name was TECAN Freedom EVO®).

[10] Randomization is a well-known practice and concept in biomedicine and elsewhere. Randomness, plays a large role in a multitude of scientific and social practices. It is used in games of chance like slot machines. It is used in encryption of networks and computers. It is used in statistics to select samples. In pharmaceutical development it is used together with blinding to safeguard against staff and patients from knowing who receives what treatment, which is understood as potentially influencing the results of the trial.

[11] However, this style of experimentation underwent a momentous but gradual shift as RA Fisher introduced a statistically oriented randomness—which emphasized randomness to produce statistical significance—to experimental design (Hacking 1988, Dehue 1997, Hall 2007). Perhaps then a statistical style of valuation?

[12] In other fields of research—such as in medical research based on clinical trials—randomness has also been

tied to multiple styles of valuation. The historian Harry Marks has commented on the value ascribed to randomness in randomized clinical trials: "Two epistemological claims underwrite the randomized clinical trial (RCT). The first, associated with Austin Bradford Hill, asserts that randomization prevents biased estimates of the value of new therapies. The second, associated with RA Fisher, maintains that randomization is necessary for the valid interpretation of statistical significance." (Marks 2003, 932) One style of valuation—tied to Austin Bradford Hill—emphasized blindness and ignorance to "prevent physicians from cream skimming—selectively assigning healthier patients to the experimental drug". While RA Fisher valued randomness for its power to infer statistical significance.

[13] We are reluctant to attribute these different styles to different disciplines or areas of expertise. Our informants fluidly move between different ways of problematizing or assessing algorithms. It seems here that is quite possible for and individual researcher to navigate competently between different styles of valuation of algorithms.

[14] Sabina Leonelli (Leonelli 2016, 100) also pays attention to this "feeling for the organism" to the data deluge in the biosciences, by pointing to how metadata facilitates transportability, and attempts to verbalize "embodied, non-propositional knowledge in scientific research".

[15] This ideal of intimate knowledge can also be tied to Knorr Cetina's analysis of the epistemic culture of biotechnology in the 1990's (Knorr Cetina 1999). Her argument being that microbiology was a bench-centered science that dealt with small objects in small laboratories. She argued that microbiology has an epistemic culture of object orientation and experimental intervention.

[16] Lee's field notes 2016-11-18.

[17] We have used four labels as a heuristic to describe four different styles of valuing algorithms in our laboratory. An important point is that the different styles of valuation are shorthand and we would expect styles of valuation to vary over time and space. The particular configuration of styles of valuation in the high throughput biosciences will constantly vary and evolve.

[18] It is in this respect a style of valuation close to what has been termed "mechanical objectivity" (cf. Daston and Galison 1992).

[19] Just as Tom Boellstorf (2015) has observed in relation to big data and Levi Strauss' "culinary triangle"—different valorizations of the "raw" and the "cooked" produce tensions in how actors approach algorithms in high throughput laboratories.

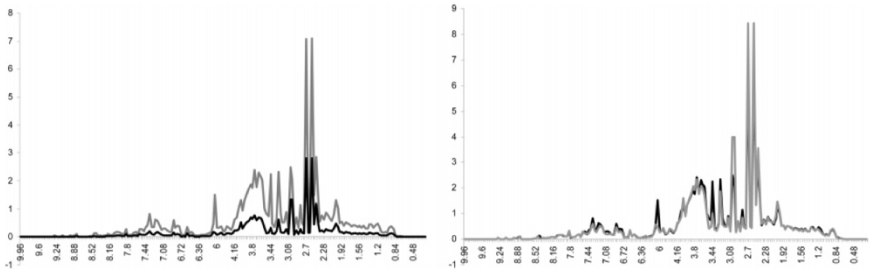

Figure 1. Two binned NMR urine spectra before normalization (left side) and after normalization (right side). The black spectrum is diluted by a factor of 3 compared to the gray spectrum. After normalization, it is obvious that only very few differences of the relative concentrations of metabolites between both spectra exist.

Figure 1 *An illustration of the effect of normalization from Dieterle et al.* (2006, 4282)*. The image shows two diagrams. Both diagrams show the same two sets of data (presented in grey and black). The left diagram shows the datasets before normalization, the right diagram after normalization. The grey and black datasets diverge significantly on the left, while they are nearly aligned on the right.*

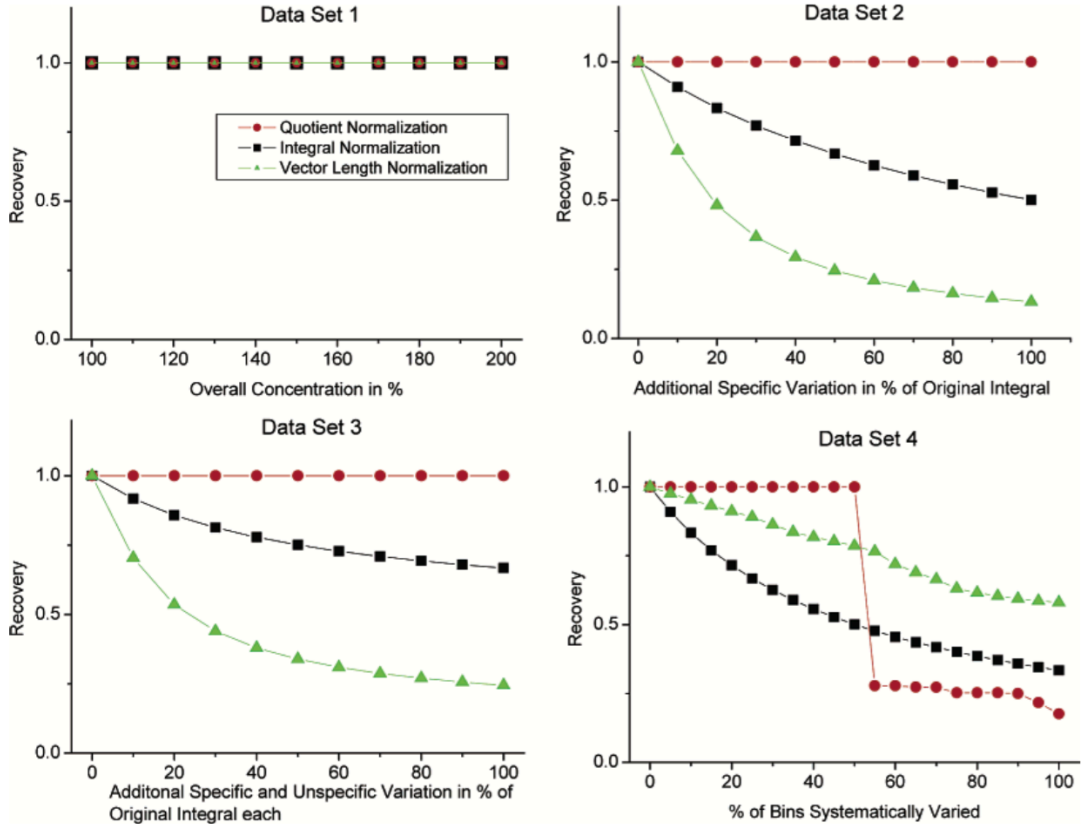

Figure 2. A comparison of different normalization methods, with PQN as the clear "winner" (Dieterle et al. 2006, 4286).

Table 1. A summary of key characteristics of each style of valuation identified in this case study.

	Experimentalist	**Trialist**	**Bioinformatic**	**Subjectivist**
Problematization: the problem to be addressed	Machine noise	Biased human intervention	Data variations (ex. amplitude)	Algorithmic data destruction
Solution: that addresses the problematization	Matching of samples	Blind researchers	Automatic smoothing of data	Observing “raw” data
Devicing: the favored device for realizing the solution	Balanced randomization	Randomization for blinding	Normalization	Human assessment
Agencing: favored distribution of agency	Human tinkering central	Algorithmic objectivity central	Algorithmic automation central	Human judgment central
The achievement that is considered valuable	Sample comparability	Objective analysis	High throughput analyses	Trust in data