

About Method

Experimenters, Snake Venom, and the History of Writing Scientifically

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"A matter so obscure, so difficult, and likewise so new . . ."

Toward the end of his two-volume *Treatise on the Venom of the Viper*, published in 1781, the Tuscan naturalist Felice Fontana declared: "I have made more than 6000 experiments; I have had more than 4000 animals bit; I have employed upwards of 3000 vipers and may have been deceived; some essential circumstance may have escaped me: I may have neglected some other, not thinking it necessary; my consequences may have been too general, my experiments too few in number. In a word, I may very easily have been mistaken, and it would be almost impossible that I should never have been so in a matter so difficult, so obscure, and likewise so new." When I first encountered Fontana's treatise, it appeared to me as a striking document for many reasons: its peculiar theme, its proportions (more than 700 pages!), the meticulousness with which Fontana described his endeavors, his detailed ideas about proper experimental procedure (and that he carefully laid them out for the reader), his self-deprecating tone, and, of course, the sheer number of experiments that he had performed, which strike the modern reader as rather excessive.

But were Fontana's project and his approach to experimentation really so unusual? I initially thought this question would be easy to answer considering the extensive literature that has resulted from the turn to experiment in history and philosophy of science. I quickly realized that even though we have substantial bodies of literature on scientific methods, experimental practices, scientific rhetoric, and experimental reports, analyses of scientists' conceptions of proper experimental practice are few and far between. Putting Fontana's methodology of experimentation in historical perspective turned out to be much harder than I had expected.

Philosophy of science, for instance, tells us much about scientific methods. For the most part, however, philosophical investigations of scientific methods concern the construction and test of hypotheses or models and the rules and principles of reasoning. Those philosophical analyses that do deal with strategies for assessing experimental outcomes often probe one particular strategy, such as making sure that theories of instruments and theories under test are independent from one another. Even those sets of criteria for the assessment of experimental outcomes that have been provided did not offer what I was looking for. We have a good analytic grasp of epistemological criteria and strategies for the validation of experimental results,² but I wanted to get a sense of how these sets of criteria were interpreted by working scientists and how they developed over time.³

The historical literature on experimentation in the sciences has grown vast, but the rich accounts of past experimental projects and approaches that have been produced since the 1980s focus on research materials, laboratory infrastructure and instrumentation, techniques of visualization, and so forth. Scientists' methodological views are rarely discussed, however.4 Although a great many specific issues have been studied in depth, these bodies of scholarship are largely disconnected from one another, and specific historiographical frameworks are tied to specific periods. There is substantive scholarship on each of a small group of innovators in scientific method, including Bacon, Descartes, Newton perhaps, Herschel, Whewell, Mill, and Duhem. We know quite a bit about experimental reports and the "new method" of experimentation in early modern physical science, both in England and in Italy, as well as about exploratory experimentation in eighteenth- and early nineteenth-century research on electricity. We know about experimental practices in Italian, French, and English medicine and anatomy. We also know a great deal about the rise of physiological experimentation and instrumentation in the nineteenth century and the fierce debates within the medical community (mostly during the nineteenth century) about whether "scientific medicine" would lead to more effective therapies than more traditional clinical approaches had thus far.5 Yet we lack an overarching framework for bringing these analyses together. My motivation for putting together a long-term history of scientists' methodologies is, in part, to connect the islands of knowledge in current scholarship. My overall goal is to understand in more detail how researchers in the life sciences conceptualized their experimental practice, what rules for proper experimental procedure they endorsed, and how these notions changed from the late seventeenth century to the mid-twentieth century.

For a number of reasons, venom research is uniquely suitable for the long-term history of experimentation and the development of methodological thought in the life sciences. First, because experiments with poisonous snakes and venom were tricky, taxing, and often controversial, the experimenters felt compelled to produce quite detailed and graphic accounts of their trials (in every sense of the term). They described their own troubles, discussed and justified their own methods of experimentation, and critiqued other experimenters. Of course, significant developments in venom research and innovations in the methodology of experimentation did not necessarily happen simultaneously, but because venom researchers were generally very explicit about their methods and methodological concerns, an account of how these discussions unfolded can serve as an instructive frame of reference for future study.

I found, however, a dearth of books on venom research. A number of historical works focus on the rich cultural history of poisons and on the cultural imagery of serpents, and some historians have examined specific medical topics such as theriac or snake stones. 6 Moreover, a few herpetologists have written popular books on snakes and snake venom poisoning.⁷ But no book-length study specifically traces the history of venom experiments. This, too, is surprising, for venom research has been significant for many fields in the life sciences—among others, therapeutics, pathology, physiology, bacteriology, and immunology. Over time, the aims of venom research have included—besides finding antidotes—clarifying key chemical concepts such as "fermentation," elucidating nerve functions, understanding the circulation of blood and pathological changes of blood, explaining cardiovascular functions, and illuminating immune reactions and the structure of biological building blocks. Even though the topic "venom research" might seem narrow and exotic at first, it can tell us a great deal about more general issues in the history of the life sciences: Venom research was shaped by, and in turn informed, the concepts of life, disease. and body functions that were available to venom researchers. Those concepts also influenced views about how to make experiments reliable and instructive. If, for instance, a living body is regarded as extraordinarily complex, establishing the exact effects of an intervention in the working of a living body will seem next to impossible for an investigator. As this book will show, late nineteenth-century investigators developed specific methodological strategies to address precisely this problem.

The key episodes in venom research were closely linked—another reason why this topic is so suitable for a long-term history of methodologies of experimentation. For more than 250 years, venom research was imbued with a strong sense of tradition both in terms of techniques and results and in terms of the methodology of experimentation. Indeed, as late as 1962, toxicologists praised the eighteenth-century scholar Fontana for having been the first to use "adequate controls" in his venom experiments. Fontana, in turn, announced his own work as "new" but at the same time presented it as a continuation of an endeavor that had begun in the mid-seventeenth century. Venom researchers saw their works as contributions to an ongoing endeavor, engaging with and explicitly building on the work of their predecessors.

Of course, as analysts of conceptual developments in the sciences, we cannot simply take at face value the historical actors' sense of tradition. their "origin stories," and their narratives of steady progress. This book seeks to account for both continuity and change in venom researchers' endeavors to analyze the nature of venom and to find out what venom does to the human and animal body. Similarly, it accounts for both continuity and change in venom researchers' views about how experiments should be performed, how results should be checked and secured, what standards of precision should be applied, and how—and exactly what—one can learn from experiments. The tradition of venom studies that venom researchers themselves have construed and continued to evoke can be only one aspect of a multifaceted analysis. If we turn our attention to the institutional and intellectual contexts for venom research, the protocols that were applied, or the material resources the researchers had available, we find that venom researchers' projects owed much more to contemporaneous practices than those researchers' talk of tradition would lead us to expect.

My focus on snake venom research is a compromise of sorts. The topic of the history of methodologies of experimentation in the life sciences is dauntingly broad—much too broad for one book—so I must be selective. Perhaps my most controversial choice (at least to historians of early modern science) will be to dissociate throughout the book the study of snake venom from that of poisons in general. Prior to the late eighteenth century, snake venom research was an integral part of more general research into how living bodies were affected by small amounts of certain substances. My choice of focus helps limit a potentially overwhelming mass of materials so as to produce a book of tolerable length. Because venom research is situated at the intersections of so many different fields in the life sciences, methodological discussions pertaining to experiments with

venom are indicative of methodological concerns in those other fields as well. My selection of examples makes it possible to produce a narrative that is thematically coherent yet cross-disciplinary in perspective. The focus on venom can thus be viewed as a strategic choice that allows the bringing together of these different subfields.

There is, of course, one considerable challenge both to the writer and to readers of this book. Many of the experiments that are described in the sources are extremely cruel and will strike readers as impermissible. For the most part, however, I have decided not to place the ethical aspects of this research center stage in my analysis: neither the—admittedly sparse—comments by past experimenters nor contemporary concerns about ethics of animal experimentation. 10

Methods Discourse

The turn to experiments that history and philosophy of science took in the 1980s was a turn away from the analysis of scientific ideas and the dynamics of theory change. This book takes another turn, shifting the attention from materials, practices, and tools back to scientific texts: their content and their organization. But this is not a shift back to the development of scientific concepts, models, and theories. Instead, the book examines specifically how questions about proper experimental procedure were dealt with in scientific texts.

Historians have long warned that the study of scientific publications alone cannot give us an adequate picture of the activities involved in scientific research: Experimental reports are not a reliable source of information about what researchers really do in the laboratory. They are not transparent windows on the day-to-day research practice in which they originated. This is undoubtedly correct. Indeed, the same caveat applies to methodological thought: scientists often do not explicitly express their methodological convictions, and if they do, the expressed convictions might not capture the methodological rules and strategies that were actually applied and pursued in the project described in the report.

Arguably, however, methods-related concepts, statements, and reflections as they are presented in experimental reports are significant because they reflect the authors' understanding of the structure and organization of good experimental research. This is what makes these reports valuable resources for the history of methodology. If an approach, a methodological strategy, or a methodological concept is explicitly appealed to, one

may assume that it is endorsed. It if is explicitly defended, discussed, or justified, we can at the very least state that it was of concern for the author or authors of the report. Methodological concepts, statements, and reflections are important indicators of scientists' views about proper experimental procedure in this sense.

Sociologists of science often read scientists' writings as a means with which to persuade relevant audiences (within the scientific community and beyond) of the value of the claims that are made in those writings. 12 Publications are treated as artifacts of "literary technologies" through which the outcomes of events and activities in the laboratory are articulated and brought into publishable form.¹³ A number of scholars, most notably Steven Shapin, Simon Schaffer, Larry Holmes, and Paula Findlen, have argued that if we pay attention to the social organization of the community of experimenters and its place in society, we will become aware that several features of experimental reports are attempts to appeal to others within and outside the community. These features include the reference to witnesses (Shapin and Schaffer), the amount of procedural detail that is related in an experimental report and the proportion of narrative and argument (Holmes), and the narrative style of the writing (Findlen).¹⁴ Scientists' methodological views may also become part and parcel of literary strategies to situate one's work within a community of, say, Newtonians, Baconians, or Popperians.15

Persuasion and positioning are certainly important goals of text production (as of any form of communication, scientific or otherwise). But even if there is general agreement on this point, other questions regarding the content, organization, and historical development of methodological views are still wide open: What methodological concepts and strategies were referred to, described, and discussed in different periods? What challenges were perceived as being the most severe? How was "proper [experimental] procedure" established in experimental reports?

General recourse to social factors does not fully explain the content, organization, and history of methodological discussions concerning experimentation. This book shows, among other things, how the development of methodological views about experimentation resonates with the history of broader ideas about life, body, and body functions. As we will see in more detail, these notions affected the content of scientists' methodological conceptions. Even the very practice of experimenting might generate novel methodological thought.

Moreover, experimental reports are shaped by certain historically changing conventions of textual organization. In his studies of the development of scientific writing, Charles Bazerman once warned that we should not overestimate the freedom that experimenter—authors have to bend rules and take advantage of local resources as they see fit for their purposes. Bazerman thus urged that we must recognize the role of "accepted genre and style" in defining current work.¹⁷ Heeding Bazerman's admonition about the formative and constraining role of available literature for methods discourse, the following chapters consider books on scientific methodology, manuals on writing scientifically, and emerging editorial guidelines, along with the experimental reports themselves. Even though we cannot assume that scientists actually followed these guidelines, these writings on scientific writing are telling, indicating the kinds of constraints and rules that confronted scientists at a given time.

In the twentieth and twenty-first centuries, experimental reports are highly standardized and typically follow the same scheme—sometimes called the IMRD (introduction, methods, results, discussion) scheme—and the methods sections are typically completely devoid of details and of justifications of techniques and procedures. Sociologist Karin Knorr-Cetina described the methods sections in these reports as highly decontextualized: "full of brand names of instruments, lists of materials, and descriptions of procedures tied together by nothing but sequence"; methods become "a catalogue of sequential manipulations stripped of both context and rationale." It is still not clear, however, when and how these methods sections came into being. Of course, even early modern researchers told their readers—often at great length—how they had proceeded. In their writings, accounts of methods were integral parts of the narrations of experiments. But as late as 1950, the IMRD scheme was not always strictly and consistently applied.

Prior to the mid-twentieth century, accounts of methods were often rich in detail; descriptions of procedures were usually tied together by narratives of experimental procedures, and the rationale for using specific techniques and approaches was discussed as well. For my analysis, I thus prefer the broader term *methods discourse* to *methods sections*. I use the term *discourse* in a nontechnical sense to refer to all kinds of methods-related statements in scientific writing about experimentation, including explicit commitments to experimentalism, descriptions of protocols, explanations of methodological concepts, and justifications of strategies of experimentation.¹⁹

Precisely because scientists are often silent about methodological views and commitments, the long-term perspective is especially important for the history of methods discourse. If we find that a particular procedure or

methodological conception is described and justified in a textual source, we can conclude that the procedure or conception is novel, unusual, or perhaps contested; hence, the methods-related statements and discussions that are provided in scientific writings become all the more significant.²⁰ Because extended coverage of methodological issues indicates what is not yet, or what is no longer, taken for granted, putting methods accounts and methodologies in historical context and perspective is crucial. Studying the history of experimental reports with an eye to innovations in their structure, the emergence of new concepts, and changes in how arguments were framed, evidence presented, methods described, and methodological approaches justified and defended can give the analyst a sense of what later reports tacitly presuppose.

Methods discourse is multifaceted. It comprises the description of actual, localized research techniques and experimental designs, more general experimental strategies and criteria to assess proper procedure, and broader, even more general commitments, such as the commitment to experimentation as the principal means of knowledge acquisition. This book examines methods discourse on all three of these levels, albeit with an emphasis on "middle-term" methodological concepts and strategies.²¹ Are experimental procedures and techniques described in detail, or are they reduced to a list of brand names and acronyms? What methodological strategies and criteria are mentioned? Are they discussed—or even defended? Are methods-related topics presented in separate sections, or are they integrated in an overall narrative? Questions like these guide my analysis of experimental reports.

Actors' Terms and Reconstructions

This book is, in a sense, an extended commentary on Fontana's statement quoted at the beginning of this introduction—an attempt to situate his rather astounding methodological pronouncement in historical perspective. The attempt to make sense of a striking methodological statement by an eighteenth-century scholar has resulted in a book that traces the entwined histories of venom research, of scientists' methodological views about experimentation, and of the organization of methods discourse in experimental reports. The geographical and chronological span of this account is vast. My story ranges over continental Europe, Britain, and the Americas and spans three centuries. Obviously, since the early modern

period, the practices and tools of biomedical experimentation have as profoundly changed as have the conceptions of life, disease, poison, and the body. Also, the institutional contexts of research in different countries were sometimes radically different even within the same time period. Many more episodes could have been included in this book. Each episode I selected for inclusion could be probed more deeply and could be presented in much richer detail.

What insights can be expected of such a selective long-term history? Will it not simply show that with the advancement of experimentation over the centuries, the methodology of experimentation progressed as well—that methods and methodologies became more sophisticated, more rigorous, and more complex? In a sense, this book does tell a story about progress: scientists are "getting better" at experimenting, and their methodologies are becoming more complex and more sophisticated over time. But, more important, this book discusses in what sense specifically experimentation and the methodology of experimentation advanced, as well as what factors contributed to the development of experimental approaches and methodologies. There is a surprising twist to the story of progress, because, as we will see, methodological advancement really means developing strategies for managing and perhaps overcoming ever new difficulties of biological and medical experimentation.

My own analytic approach sits somewhere in between the history and the philosophy of science. I offer a history, but historians of science might find my analysis mainly driven by current philosophical issues. After all, I analyze the historical development of methodological concepts and strategies such as variation, replication, independent confirmation, and so forth, which are usually discussed in philosophy papers.

Philosophers of science, conversely, might find my approach mainly historical, both because I do not subject the methodological arguments and concepts of past scientists to formal analysis and because I do not measure the distance between past methodological notions and ideal epistemic conditions of successful confirmation and test. Moreover, several of the figures who populate my account were not luminaries, leading figures, or innovators of methodologies but merely representatives of their time. Their writings exemplify "normal methods discourse," as it were. In contrast to my approach, philosophers' analyses of experimental reasoning strategies often consider cases—generic situations, plausible scenarios that might or might not be inspired by actual scientific episodes and that can be used as conceptual tools to think through philosophical issues.

Changing the features of such scenarios demonstrates the epistemic significance of certain conditions, showing that such conditions must obtain for an argument to have epistemic force. Turning to actual scientific episodes can then show the philosopher whether, and by how much, an actual argument falls short of the epistemic ideal.

Because my analysis of past methods discourse draws on discussions in current philosophy of science, I make occasional reference to "ideal" epistemic situations. This is not to measure past scientists' methodologies against standards that were not theirs, nor to suggest that their methodologies were somehow lacking. To me, current philosophical terminology and philosophical reconstructions are helpful for the purpose of characterizing past scientists' concepts and strategies. But in my account, philosophically informed reconstructions are complemented by an analysis of the changing meaning and use of actors' terms and conceptions.

Generally speaking, the historical study of methodologies of experimentation requires a combination of reconstructions of experimental designs and strategies in current analytic terms and sensitivity to actors' terms. If we try to ground our histories of experimentation just in reconstructions of experimental designs and strategies based on interpretations of experimental reports, experimental practices now and then would often appear quite similar. It would be easy to find "forerunners" of, say, John Stuart Mill's "method of difference" or modern control experiments in seventeenth-century experimental practice. Only if we bring our reconstructions of experimental designs together with a careful study of the experimenters' own conceptualizations of their experimental practices do we get a sense of their own ideas about what aspects of their practices were indicative of proper procedure—and do we realize, for instance, that the method of difference did not play such a key role in seventeenth-century experimentation as it did in the mid-nineteenth century. Both actors' terms and interpretative reconstructions of experimental designs and methodologies in present-day terminology are important, and together they tell us something about the epistemic force that past scientists attached to specific strategies of experimentation—and thus something about the historical development of methods discourse.