2 Tools, Experiments, and Theories

An Examination of the Role of Experiment Tools

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1 Introduction

John Bickle (2016, 2018, 2019) offers two frameworks for thinking about the role of experiment tools in neurobiology. First, he argues that "revolutions in neuroscience" do not proceed in a Kuhnian manner such that a dominant paradigm is replaced in response to an accumulation of anomalies. Rather, revolutions in this science begin with *motivating problems* that spur the development of new experiment tools, the importance of which is revealed in *initial-* and *second-phase hook experiments* (2016). The initial-phase hook experiments demonstrate the feasibility of the new tool. The second-phase hook experiments demonstrate its usefulness in a wider range of experimental contexts and bring it to the attention of a much larger audience—both scientific and more general.

Bickle extends this to a second framework, which is grounded in a critique of "theory-centrism" in the philosophy of neuroscience (2018, 2019). As Bickle has it, theory-centrism is the view that neuroscience needs theories—on the model of physics, early modern astronomy, or evolutionary biology—that will drive successful research efforts. One advocate of this view is Patricia Churchland. She writes,

> If neuroscience is to have a shot at explaining—really explaining—how the brain works, then it cannot be theory-shy. It must construct theories. It must have more than anatomy and pharmacology, more than physiology of individual neurons. It must have more than patterns of connectivity between neurons. What we need are small-scale models of subsystems and, above all, grand-scale theories of whole brain function.
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> (1986, p. 406)

And then, more than two decades later, Ian Gold and Adina Roskies say,

> The question remains whether neuroscience is the sort of science that is doomed to be theory-poor, or whether this poverty is due to its relative immaturity as a science. … The brain is an exceedingly

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> complex biological organ which has evolved to perform a variety of sophisticated tasks. It yields its secrets grudgingly. Nonetheless, there is no principled reason why we cannot expect that, in time, we will be able to formulate more general theories about the neural processing that underlies these diverse functions.
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> (2008, p. 353)

Bickle aims to dispel this view that theory should have a central position in our understanding of neuroscience. Rather, he argues that we should appreciate the central role of tool development and use. To the extent that theory has a role in contemporary neuroscience, it is "tertiary" in importance:

> Rather than being the crux point on which everything else depends, … theory turns out to be doubly dependent, and hence of tertiary, not primary, importance. Our best confirmed theory is totally dependent on what our experiment tools allow us to manipulate. And those tools developed by way of solving engineering problems, not by applying theory.
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> (2019, p. 578)

This can be interpreted in two ways. On the one hand, when a theory is proposed, the theory depends on experiments and the tools used in those experiments for its confirmation. Hence, without those tools, the theory would fail to be confirmed. Arguably, though, dependence in this sense doesn't detract from a central role for theory in the scientific process. This sense of dependence, however, doesn't seem to be what Bickle has in mind. For instance, in one place, he writes,

> The molecular mechanisms of cognitive functions rank among contemporary neuroscience's greatest theoretical achievements. And yet this theory is tertiary in dependence. It comes directly from the development and ingenious experimental use of some novel experiment tools, to intervene into specific molecular processes in behaving mammals. And those tools come from a catch-as-catch-can, make-it-work, engineering-first attitude of the sort famously alluded to by Hacking (1983), in his "microscope" argument for the relative independence of "the life of experiment" from theory.
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> (2019, p. 594)

Here it seems that we are meant to understand that the temporal order, as well as the order of importance, is, as Bickle later lays it out, "engineering solutions → new experiment tools → better theory" (2019, p. 595). I will call this the *tools first* (or *anti-theory-centric*) *method* with the idea that, as Bickle stresses, the application of an experiment tool is,

along with other factors, central to the investigation—but one of those other factors is *not* the testing of a theory.

Surprisingly, given the role that it has in his analysis, Bickle is studiously coy about what he means by *theory*. For the most part, rather than use this term, I will use *hypothesis*, defined here as *an explanation for a process or phenomenon that still requires confirmation*. By focusing on hypotheses, I am deliberately setting aside *theory* used in the sense of *understanding*, *knowledge of the discipline,* or *completed explanation*—or, as Churchland says, "this conglomeration of background assumptions, intuitions, and assorted preconceptions" (1986, p. 405). I will take it for granted that *theory* in this latter sense is pervasive at all stages of neurobiological investigations.[1]

Bickle's assertion that the tools first method is *always* used in contemporary neurobiology is a strong claim, and it will be our focus. In Sections 2 and 3, I will look at two cases. The first, gene targeting and investigations of the relationship between memory and long-term potentiation, is extensively discussed by Bickle (2016, 2019). I find, however, that a well-defined hypothesis does have a prominent role in these investigations. In short, a hypothesis was developed and then confirmed by experiments using gene targeting. The second case, however—an optogenetic investigation of neurons in the extended amygdala that were found to drive both anxiety and anxiety-reduction—illustrates the application of Bickle's tools first method.

The takeaway, then, is twofold. First, scientific method in contemporary neurobiology is more varied than Bickle suggests, and sometimes theory does have a central role. But, second, there are important investigations in neurobiology that proceed without a hypothesis or theory as the starting point (and without either coming into play at any point, for that matter). This is, in part, a consequence of, as Bickle argues, experiment tools that allow for ever more precise investigations of cellular and molecular processes. It is also a consequence of the explanatory goals in neurobiology, namely, the description of mechanisms. When these two consequences come together, there is no longer an apparent need for theories of the sort encountered in physics or evolutionary biology.

2 Gene Targeting and LTP

The first case involves two research tracks that intersected with productive results in the 1990s. Long-term potentiation (LTP) is a lasting increase in the efficacy of synaptic transmission following a sufficiently strong stimulation from the pre-synaptic neuron. This phenomenon was first reported by Terje Lømo in 1966 and then in more detail by Lømo and Tim Bliss in 1973 (Lømo 1966; Bliss & Lømo 1973). The idea that changes in the efficacy of synapses would be the neural basis for learning and memory had been proposed before Bliss and Lømo's