Introduction

In 1952, Alan Hodgkin and Andrew Huxley argued that sodium ions carry the initial inward current of the action potential. Historians and philosophers of science will want an account of what it is for sodium ions to carry the initial inward current and what Hodgkin and Huxley's arguments were. In recent years, the gist of an answer to the ontological question – what it is for sodium ions to carry the initial inward current – has emerged. Hodgkin and Huxley meant that an influx of sodium ions into the axon noncausally determines the inward current. There are multiple variations of this answer and, of course, challenges to it. Still, the ontological question has been the subject of active debate in the philosophy of science.

In contrast to the ontological question, there has yet to be any serious philosophical effort to address the methodological question of Hodgkin and Huxley's arguments for the sodium hypothesis. What reasons did they offer for believing that sodium carries the initial inward current of the action potential? For a serious effort, one must at least review Hodgkin and Huxley's experimental work. One of these experiments involved depolarizing an axon by 65 mV and then measuring the change in current across the membrane, first in a sodium-containing medium (seawater), then in a sodium-free medium, then again in a sodium-containing medium[1] (see Figure 0.1). When the axon is depolarized in the sodium-free medium, the initial inward current (represented by the initial rise at the left of the curve) disappears.

How did Hodgkin and Huxley interpret the results shown in figure 0.1? Results do not simply speak for themselves. More concretely, how did Hodgkin and Huxley link the manipulation of an axon membrane potential and a measurement of the subsequent axonal currents to unmeasured movements of ions? Part of the story is that Hodgkin and Huxley realized that an influx of sodium after voltage clamping in seawater would explain

[1] Hodgkin and Huxley (1952a, pp. 450–451).

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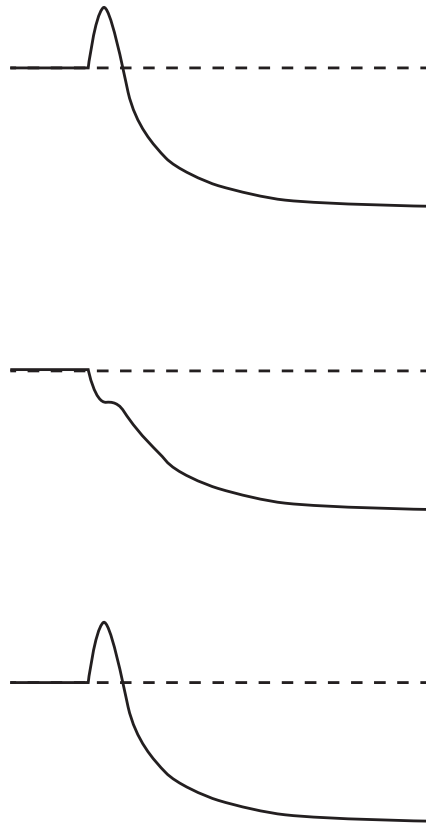


Figure 0.1 Currents in axon no. 15 depolarized by 65 mV in a sodium-containing medium (top panel), sodium-free medium (middle panel), and sodium-containing medium (bottom panel). Redrawn from Hodgkin and Huxley (1952a, p. 451, figure 1).

the currents. Further, they assumed that this explanation provides evidence supporting the hypothesis that sodium carries the initial inward current. They supported the sodium hypothesis based on the idea that this hypothesis would explain their experimental results. In brief, Hodgkin and Huxley were engaged in abductive reasoning.

0.1 Singular Compositional Abduction

The methodological starting point of this book is a specific take on the idea that the history and philosophy of science should be scientifically engaged.

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The take is that one important method for a historian and philosopher of science who wishes to understand how scientists confirm hypotheses about noncausal dependence relations is to closely attend to how scientists do this in the experimental literature. Focus on how, in the scientific literature, scientists interpret experimental results for their peers. Focus, for example, on Hodgkin and Huxley's interpretation of the results shown in figure 0.1. This is what William Wimsatt might have accepted as looking at "actual inferences from actual data" (Wimsatt, 1994, p. 207).

I propose that Hodgkin and Huxley interpreted their results using "singular compositional abduction." So, what is singular compositional abduction? Abductive reasoning, in general, is often taken to be a matter of inferring some hypothesis, because that hypothesis explains something.[2] It is also sometimes proposed that abductive inferences may be individuated, at least partly, by reference to the explanations they invoke.[3] Thus, etiological explanations figure into etiological abductions. Compositional explanations figure into compositional abductions. Just so, singular compositional explanations figure into singular compositional abductions.

So, what are singular compositional explanations? They are representations of compositional many-one ontological dependence relations between spatially and temporally localizable particulars. For concreteness, consider further the Hodgkin–Huxley example. A scientific result is a spatially and temporally localized particular. One day, in the late summer of 1949, Hodgkin and Huxley depolarized axon no. 15 by 65 mV and measured the subsequent currents, twice in a sodium-containing solution and once in a sodium-free solution. Figure 0.1 graphically represents three currents – three spatiotemporal particulars – generated in the same lab not too many minutes apart. Hodgkin and Huxley treated these results – each of these particulars – as an explanandum, that is, something to be explained. That which does the explaining – the explanans – in each of the cases is the movement of many sodium ions across the membrane. A singular compositional explanation, in this case, explains an instance of an activity of axon no. 15 in terms of instances of activities of individual sodium ions.[4] The ontological dependence relation is many-one since

[2] See, for example, Peirce (1992), Bird (2005), and Aliseda (2006).

[3] Psillos (2007), Schurz (2008), Schupbach (2017).

[4] The "New Mechanists" in the philosophy of science might take these to be cases of "singular mechanistic constitutive explanations" by embracing the "singular" aspect of the explanation. See, for example, Machamer et al. (2000), Craver (2007), Bechtel and Richardson (2010), and Craver and Darden (2013).

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there are many activity instances of sodium ions standing in an ontological dependence relation to an activity instance of axon no. 15.

As brilliant as Hodgkin and Huxley were and as transformative as was their development of their theory of the action potential, among their innovations was not the use of singular compositional abduction. Indeed, singular compositional abduction is, on the one hand, widely used in chemistry, biology, and psychology, but largely unexamined by historians and philosophers of science, on the other. This, despite the widespread commitment among historians and philosophers of science to look closely at actual scientific practice. This, despite the widespread presupposition that scientists make pervasive use of abduction.

Enormous tracts of research in animal behavior, chemistry, child development, generative linguistics, and psychology would not exist were it not for singular compositional abduction. However, consider just one concrete illustration. In a much-discussed *Psychological Review* paper published in 1948, Edward Tolman argued that rats sometimes navigate mazes using a cognitive map, rather than simpler "stimulus-response" strategies.[5] Such maps, he proposed, indicate "routes and paths and environmental relationships, which finally [determine] what responses, if any, the animal will finally release" (Tolman, 1948, p. 192). Consider one of the simplest experiments Tolman discussed, performed by Kenneth Spence and Ronald Lippitt in the Psychological Laboratory at the State University of Iowa sometime between 1939 and 1942.[6] The experiment involved a Y-maze with food in one goal arm and water in the other. During the training period, each of the twenty rats in the experiment was allowed to roam the maze freely four times per day, neither thirsty nor hungry. During the test phase, ten of the rats were hungry, whereas the other ten were thirsty. Unsurprisingly to most contemporary philosophers and psychologists, the thirsty rats were more likely to go to the water, but the hungry rats were more likely to go to the food. Tolman interpreted these results in terms of a cognitive map. He proposed that the thirsty rats had formed a cognitive map of the maze that specified that food was in one arm and water in the other and they wanted water. He also proposed that the hungry rats had formed a cognitive map of the maze that specified that food was in one arm and water in the other and they wanted food. Given manipulations of the rats and measurements of their behavior, Tolman postulated an unseen and unmeasured cognitive map. Why? Because

[5] Tolman (1948).
[6] Tolman cites an unpublished manuscript that subsequently appeared as Spence and Lippitt (1946).

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instances of the activity of a cognitive map in those rats would explain the behavior (the instances of the activities) of those rats in the Iowa Psychological Laboratory sometime in 1939–1942.

0.2 Some Philosophical Context

My "science-first" approach to actual inferences from actual results reveals details often unnoticed by philosophers of science. C. S. Peirce, for example, proposed that abductive inference does not support hypotheses, but merely introduces them or suggests them as worthy of further examination by other methods.[7] However, I will argue that Hodgkin and Huxley, among others, tried to use a series of compositional abductive inferences to confirm hypotheses. One might defend Peirce by noting that he could not have foreseen how mid twentieth-century scientists would use abductive reasoning. Nevertheless, many later philosophers have followed Peirce's understanding of the role of abductive reasoning in science.[8]

Gilbert Harman proposed that warranted abductive inference is a matter of inference to the best explanation (IBE), where what determines the best explanation is a matter of, among other things, what is simpler, more plausible, and has broader scope.[9] Further, he mentioned that IBE is used in science. This account has been extremely influential among philosophers of science who study abduction, but Harman says nothing about how IBE might apply, if at all, to local scientific arguments, such as Hodgkin and Huxley's interpretation of their experimental results. Harman was engaged in an epistemological project of trying to show that enumerative induction is merely a special case of IBE. He was, therefore, noncommittal about exactly how his picture might apply, if at all, to specific scientific arguments.

Peter Lipton developed what is widely recognized to be the most advanced version of Harman's idea of IBE and its application to scientific reasoning.[10] Unlike in Harman, the preponderance of the evidence shows that Lipton intended his account of IBE to be applicable in many contexts, including the scientific interpretation of experimental results. In the context of interpreting experiments, Lipton proposed that explanatory questions have a contrastive structure, such as "Why did the women in Clinic 1 have a high rate of mortality from childbed fever, but those in Clinic

[7] Peirce (1992).
[8] For example, Hanson (1960), Magnani (2001), and Gabbay and Woods (2005).
[9] Harman (1965). [10] Lipton (2003).

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2 did not?" Further, he proposed that these contrastive questions align with controlled experiments as he illustrates with Ignaz Semmelweis's interpretation of experimental results concerning childbed fever.

Close attention to scientific experiments and arguments also reveals details unexamined in the New Mechanist philosophy of science literature. Although the Hodgkin–Huxley model is something of a fixture in this literature, there has been no attention to Hodgkin and Huxley's use of experimental work to support the sodium hypothesis.[11] Part of the story is that in Hodgkin and Huxley's first experiment, an axon is voltage-clamped and a current is measured. This is an experiment with an intervention at the level of the axon and a measurement at that same level. This is what might be called an "intralevel experiment."[12] (The Tolman example also relied on an intralevel experiment.) Based on this, Hodgkin and Huxley advanced a hypothesis about sodium ion fluxes. New Mechanists have never discussed the possibility that intralevel experiments might be used to confirm relations of noncausal dependence.[13] New Mechanists have never considered an abductive account of Hodgkin and Huxley's reasoning.[14]

The overarching methodological point of this book is that if historians and philosophers of science are interested in how scientists confirm compositional hypotheses, then one important resource is the examination of the primary experimental literature. If they take this science-first approach – one that involves asking new questions – they will find that existing answers to other questions are unsatisfactory. Existing views need to be reconsidered in the light of new questions.

0.3 Roadmap

The book is divided into three parts. The first part presents the theory of singular compositional abduction and the portions of scientific reasoning that it is meant to describe. Chapter 1 will articulate and defend the

[11] See, for example, Craver (2007, 2008), Weber (2008), Craver and Darden (2013), Levy (2014), and Bickle (2023).

[12] Another important part of the story is the variation in the external sodium concentration. This will be discussed in Chapter 3.

[13] See, for example, the discussions in Craver (2007), Craver and Darden (2013), Baumgartner and Gebharter (2016), Baumgartner and Casini (2017), Craver et al. (2021), and Prychitko (2021).

[14] Baumgartner and Casini (2017) have an account of "constitutive abduction," but they do not discuss any scientific cases. Further, their model assigns no role for intralevel experiments. Still further, their account provides an abductive interpretation of the results of multiple scientific experiments, whereas mine provides an abductive interpretation of a single experiment.

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Table 0.1 *Entities, their composition, and their use in explanation*

Type of entity	Compositional relation	Compositional explanation
Individuals	Lower level individuals together *constitute* a higher level individual	Singular Analytic Compositional Explanation
Activity instance	Lower level activity instances together *implement* a higher level activity instance	Singular Dynamic Compositional Explanation
Property instance	Lower level property instance together *realize* a higher level property instance	Singular Standing Compositional Explanation

metatheoretic presuppositions of this work, most notably the commitment to developing a theory that provides a descriptively adequate account of some of the reasoning scientists offer in the recent primary experimental literature in support of compositional hypotheses. Having a descriptively adequate theory is more than merely describing or reporting what scientists themselves say they are doing. It is more than describing or characterizing reasoning in laboratory life or reasoning that appears in review articles or textbooks. The primary experimental literature has a distinctive role in science and it is the focus of attention here.

Chapter 2 will present the principal features of a theory of singular compositional explanation. One could, of course, write an entire book on singular compositional explanation; however, this is not such a book. So, there will be many issues that do not receive the attention they would deserve in a book entirely devoted to scientific explanation. In brief, the theory is this. Singular compositional explanations are representations of natural ontological dependence relations among spatiotemporally localizable explanandum and explanans entities. Further, there is a plurality of singular compositional explanations corresponding to a plurality of singular compositional relations among explanandum and explanans entities. (See Table 0.1 for a summary.) There are the relatively familiar explanations of instances of activities of wholes in terms of instances of activities of the associated parts of the whole. These are "singular dynamic compositional explanations." Such explanations implicate a natural ontological dependence relation of "implementation." In addition, there are explanations of instances of properties of wholes in terms of instances of properties of their associated parts. These are "singular standing compositional explanations." Finally, there are explanations of individual wholes in terms

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of their individual associated parts. These are "singular analytic compositional explanations."

Whereas Chapter 2 outlines a relatively coherent body of theory regarding singular compositional explanation, Chapter 3 draws attention to a more motley collection of features of singular compositional explanations as found in the scientific experimental literature. So, for one thing, scientists sometimes explain the rate of an activity of a whole. As Hodgkin and Bernard Katz comment, "Our hypothesis therefore suggests that the rate of rise of the action potential should be determined by the rate of entry of sodium" (Hodgkin & Katz, 1949a, p. 55).[15] Second, scientists sometimes explain scientific results. They are not "mysterians" about how results come about. The theory of singular compositional explanation is part of a story about explaining scientific results. Finally, scientists often try to explain the results of controlled experiments. With closer attention to Hodgkin and Huxley's experiment introduced above, one sees that they are trying to explain why axon no. 15 *in seawater* displays an initial *inward* current when depolarized by 65 mV, whereas *in a sodium-free medium* it displays an initial *outward* current when depolarized by 65 mV. The "control" assumption is that there is only one difference between the conditions in which there is an inward current and the conditions in which there is an outward current. Further, however we might explain axon no. 15's behavior in the two contexts, the explanation is not simply a singular compositional explanation.

Chapter 4 will introduce the theory of singular compositional abduction built around the work on singular compositional explanation in Chapters 2 and 3. It begins by identifying features that singular compositional abduction shares with many other abductive inferences. It also provides an account of why some scientists would take abductive reasoning to be truth-conducive. Further, it explains how abductive confirmation offers a successor to the logical positivist theory of hypothetico-deductive (HD) confirmation. Hypothetically, if sodium ions were to move across the axonal membrane after a 65 mV depolarization, then that would make for an experimentally detectable initial inward current.[16] Given the experimentally detected current, scientists take themselves to have a good reason

[15] In one autobiographical account, Hodgkin (1994, p. 274) comments, "Another strong argument for the sodium theory was that the maximum rate of rise of the action potential was approximately proportional to the sodium concentration."

[16] In the abduction/IBE literature, it is common to suppose that possible explanations lead to actual explanations. See, for example, Lipton (2003), McCain (2015, 2019), Fumerton (2017), and Lange (2022).

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to think that there are sodium ions moving inward across the axonal membrane soon after a 65 mV depolarization. For much of the twentieth century, empiricist philosophers would have interpreted this scientific practice as illustrating HD confirmation. I propose that it is an instance of singular compositional abductive confirmation. The broader conclusion is that some, but not all, scientific hypothetical reasoning that philosophers of science would have once taken to be HD confirmation is in fact singular compositional abductive confirmation.

The second part of the book, Chapters 5 and 6, will provide detailed case studies showing how the theory from the first part provides a descriptively adequate account of some of the scientific reasoning in some of the twentieth- and twenty-first-century scientific experimental literature. Chapter 5 will describe more of the scientific reasoning involved in developing the Hodgkin–Huxley theory of the action potential. Chapter 6 will review the ongoing debate regarding the neurophysiological basis of the Hermann grid illusion.

Although compositional abductive reasoning plays a part in both historical episodes, there are variations in how experimental work figures into that reasoning. Hodgkin and Huxley's research focused on the manipulation of axons and the subsequent measure of axonal voltages or currents. The results of these experiments were, often in combination with further assumptions and mathematical reasoning, used to develop compositional hypotheses about ion fluxes and membrane permeabilities. Sometimes, these inferences led Hodgkin and Huxley to hypotheses they found convincing. At other times, they did not.

Research on the Hermann grid has relied extensively on psychophysical methods wherein vision scientists present participants with one or another physical stimulus – some version of a Hermann grid – and then measure the participant's response. These intralevel results are generally combined with independent neurophysiological experiments that involve stimulating photoreceptor cells, sometimes one at a time, and then measuring downstream cellular responses. Both psychophysicists and neurophysiologists have their own interpretations, but my interest lies in the compositional interpretation of psychophysical results in terms of neurophysiological individuals, activity instances, and property/relation instances.[17] This is where scientists often rely on compositional abduction.

The first two parts of the book form the "primary project" of articulating and defending a positive account of several important instances of

[17] Hereafter I will typically simplify "property/relation instances" to "property instances."

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scientific reasoning. The third part carries out a "secondary project" of describing possible rival accounts, how the rival accounts differ from my account, and some reasons for taking my positive account seriously. It probably cannot be emphasized too strongly that my project is *not* a matter of taking "off the shelf" ideas, such as Peirce's conception of abduction, Harman's concept of IBE, or some version of Carl Craver's manipulationism, and showing how scientific work fits into those preconceptions. My science-first approach looks closely at actual scientific reasoning, and then develops a theory that yields a descriptively adequate account of that reasoning. It should not be surprising that my version of a science-first approach leads to distinct ideas about confirming compositional hypotheses.

Chapter 7 will review how my account differs from that offered by Peirce and various "Neo-Peirceans." The key difference is that, whereas Peirce and the Neo-Peirceans assume that scientists use abduction to introduce new hypotheses, I propose that scientists use it to confirm hypotheses. Chapter 8 will illustrate respects in which the compositional abductive account differs from an application of the Harman picture of abduction to local scientific reasoning. Here I emphasize a distinction between abduction and warranted abduction, so that one can have abductive inferences that do not rule out rival hypotheses. The distinction facilitates the recognition that the results of individual scientific experiments, such as Hodgkin and Huxley's, do not typically warrant the adoption of some hypothesis. Instead, the results of a single experiment are only part of a more extended process of establishing a hypothesis. Chapter 9 will contrast the compositional abductive account of the scientific interpretation of controlled experiments with the account in Lipton (2003). The most significant difference between the views surveyed in Chapters 7–9 and the current view is the development of a specific theory of explanation and the use of extended case studies.

Chapter 10 will contrast the abductive approach with Carl Craver, Stuart Glennan, and Mark Povich's "matched interlevel experiments" (MIE) approach.[18] MIE is the latest iteration of a manipulability account of the testing of compositional hypotheses.[19] One of the most significant differences between the compositional abductive approach and MIE is that the former recognizes the use of intralevel experiments to confirm compositional hypotheses, whereas the latter does not. Chapter 10 also broaches an abductive approach to the interpretation of the results of some

[18] Craver et al. (2021).
[19] See, for example, Craver (2007), Kaplan (2012), Craver and Darden (2013), and Prychitko (2021).

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interlevel experiments, wherein something at one level is manipulated and then something at another level is measured. One descriptive advantage of the abductive approach is that it recognizes that scientists sometimes confirm compositional hypotheses using a combination of intralevel and interlevel experiments.

Chapter 11 will summarize some of the principal conclusions of the book but also draw attention to a limitation of my account. In reading carefully through the primary experimental literature, one quickly finds that scientific practice is much more complicated than Peircean abduction, IBE, and manipulationism may have led one to believe. The practice of explaining rates of activity instances is an illustration. Further, once one recognizes a scientific practice, the historian and philosopher of science will want a theory of that practice. Yet, the recognition of practices is much easier than the development of a theory of those practices. In Chapter 4, I propose explanations of some rates, but leave open the possibility that there are other explanations of other rates. In this example, we see that the science-first methodology adopted here readily paves the way for philosophical theory revision. A more serious example involves functional magnetic resonance imaging (fMRI). The blood-oxygen-level-dependent (BOLD) signal in fMRI indicates changes in amounts of deoxyhemoglobin. Yet, the deoxygenation of hemoglobin is not typically taken to explain any cognitive processes. Deoxygenation is, instead, somehow "coupled" to the neurophysiological processes that implement cognitive processes. As familiar as this practice is, neither the abductive approach nor the MIE approach as they stand provides a theory of this practice.

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