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Introduction

How can scientists understand the intricate processes that occur inside the tiny cells of a living organism? They tell us about strange-shaped protein molecules that chemically transform foodstuffs to provide the cell with energy, molecules that rotate like propellers, molecules that scan the DNA double helix for structural damage, molecules that turn genes on and off, molecules that pull chromosomes apart when the cell divides, molecules that make the cell crawl around on a surface, and so on. It appears like magic that humans should be able to look inside the cell and unveil all this minuscule clockwork. Yet scientists seem to have found ways of doing exactly that. How is this possible? If scientists are not magicians but people with the ordinary range of human cognitive abilities, how do they deploy these abilities in order to understand life itself?

A traditional answer would be that scientists invent speculative theories or hypotheses, which are then tested by experiments in accordance with the rules of the scientific method. At least this is how an experimental science proceeds according to two major traditions in the philosophy of science: Critical Rationalism and Logical Empiricism. The former approach was championed by Karl Popper, while the latter grew out of the logical positivism of the Vienna Circle. Both Critical Rationalists and Logical Empiricists thought that they could find out about the scientific method on the basis of logical considerations alone. These logical considerations would show what it means to reason scientifically, that is, to reason *rationally*. However, both of these approaches have proven to be inadequate to deal with real science. First, they leave many questions unanswered, for example, questions about how scientists generate new hypotheses (formerly known as the “context of discovery”) and research problems, or questions about the exact conditions under which a theory or theoretical framework is abandoned or retained. Second, a wealth of historical and sociological studies has shown that scientists rarely abide by the prescriptions

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that have been issued from philosophical armchairs. While this could simply mean that scientists fail to act rationally, such a conclusion would be premature. The failure of real science to conform to philosophical accounts is just as likely to be the philosophers' fault and should be taken as a stimulus to doing better epistemology.

If, today, many historians and sociologists of science do not see any rationality in science, a possible reason is that the existing accounts of scientific rationality are too simple.

The great twentieth-century debates on the rationality of science mostly ignored biology. It was assumed that the most advanced science is physics, which was probably true during the first half of the century. However, in the meantime, biology has come of age and it is today at least equal to physics and chemistry in terms of maturity and the reliability of its knowledge claims. Thus, a philosophy of science that cannot deal with experimental biology would be missing some of the best examples of sound scientific knowledge that we have.

This book is partly a result of my conviction that modern science, even though it exhibits a considerable amount of internal diversity, is a well-defined entity from an epistemological point of view. The unity of science may have been exaggerated in the past – especially by the philosophers of the Vienna Circle and their heirs (e.g., Carnap 1938; Oppenheim and Putnam 1958) – but science is not quite as disunified or local as current opinion in science studies (e.g., Galison and Stump 1996; Keller 2002) would have us believe. There are ways of reasoning that can be found in many different scientific disciplines. This, of course, does not mean that there are no differences in the exact ways in which these approaches are applied or that the relative significance of different methods is the same everywhere. What it does mean is that the philosophy of biology should not detach itself from the general debates in philosophy of science to the extent that it has in recent years.¹

When the philosophy of biology began to establish itself as a professional field of inquiry in the 1970s (mainly in North America), its main concern was evolutionary theory. I think there are several reasons for this. First, evolutionary theory has profound philosophical and religious implications for such issues as human origins, the nature of the human mind, love, sex, culture, and morality. Second, parts of evolutionary biology – especially population genetics – are more closely related to physics than areas such as molecular biology. The reason is that there are structural similarities in mathematically formulated theories and models. Until the 1970s, most philosophy of science was philosophy of physics. As a consequence, many philosophers of biology have simply transferred some of the issues concerning the structure of scientific

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theories from physics to biology. Third, several eminent evolutionary biologists have written extensively on historical and philosophical issues in biology, thus challenging philosophers of science to take up these issues. The most important figure in this respect was clearly Ernst Mayr, who has unceasingly defended biology as a science in its own right that is in several ways located between the physical and the social sciences (Mayr 1982, 1997).

An important contribution to the philosophy of biology that is due to Mayr (1961) is the distinction between *proximate* and *ultimate* causes (cf. Ariew 2003). On Mayr's view, evolutionary biology is concerned with ultimate causes or historical explanations of an organism's properties. Evolutionary biology explains how species of organisms came to have the properties they do. It is concerned with *phylogeny*. By contrast, areas such as genetics, neurobiology, and biochemistry are concerned with proximate causes, in other words, with the processes that occur within an individual organism. Proximate causes explain how an individual organism develops during its own lifetime, that is, by virtue of its physiological makeup, its genes, and its environment. This kind of biology is interested mainly in *ontogeny*. It is the biology of proximate causes that this book is concerned with.

It will become clear in the course of this study that, by and large, to make sense of the practice of experimental biology, it is not necessary to refer to evolutionary theory. Thus, I want to counter a certain tendency in recent philosophy of biology to see evolutionary theory as some sort of master theory of biology. This is not to question the scientific status or importance of evolutionary theory. What I want to claim is that there is a certain conceptual, explanatory, and foundational independence of experimental biology from evolutionary theory, which mirrors its institutional independence.² However, this independence is not complete, as I show (see Chapter 6).

Apart from evolutionary biology, a predominant concern in the philosophy of biology has been the issue of reduction and reductionism, mainly in the context of genetics. Because the relationship between classical, Mendelian genetics and molecular biology has been widely viewed as a paradigm case of reduction in biology, philosophers of science have taken it as an important test case for the theory of reduction developed by logical empiricist philosophers, in particular Ernest Nagel (1961). A student of Nagel's, Kenneth Schaffner (1969), has claimed that a slightly modified account of reduction can accommodate this case. This claim was subsequently challenged by David Hull (1972, 1974, 1976), which sparked a voluminous debate. Eventually, a consensus formed that classical genetics is not reducible to molecular biology – in either Nagel's or any other sense. Only a few authors have opposed this consensus, most forcefully Kenneth Waters (1990, 1994, 2000). Both reductionists

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Excerpt

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and antireductionists have given little attention to the possibility that genetics may be a special case within experimental biology.

Since the 1980s, the field has opened up considerably. Many authors have directed their attention to other areas of experimental biology, as well as to issues other than reduction. Important monographs in this respect include Lindley Darden's *Theory Change in Science* (1991), Kenneth Schaffner's *Discovery and Explanation in Biology and Medicine* (1993), and William Bechtel and Robert Richardson's *Discovering Complexity* (1993). In addition, there is now a considerable body of individual articles dealing with diverse philosophical issues in various areas of experimental biology, including molecular biology, biochemistry, cell biology, immunology, neurobiology, and developmental biology. However, apart from Schaffner's *Discovery and Explanation in Biology and Medicine*, there is (to my knowledge) currently no monograph available that treats the central problems of philosophy of science in connection with these experimental disciplines. Hence the present book.

As I mentioned previously, the philosophy of biology has shown a strong tendency to detach itself from general philosophy of science as well as from the philosophy of the physical sciences. Thus, philosophers of biology have mostly kept themselves busy with philosophical issues that arise from within biology or from areas where biology engages social and political issues (e.g., issues related to race or gender). And indeed, this development has been fruitful and has advanced the debates beyond the initial attempts to simply apply logical empiricist philosophy of science to biology. However, the time is now ripe to reconnect some of the issues to more general philosophical problems and to other areas of the history and philosophy of science. This is one of the main goals of this book.

The historical literature on experimental biology has really exploded in recent years. Historians of biology have produced a considerable number of detailed studies, especially of twentieth-century developments in genetics, biochemistry, molecular biology, and immunology. Even though it is generally accepted today that good philosophy of science should take the history of science very seriously, there have not been many attempts by philosophers of biology to assess the philosophical implications of recent developments in historical scholarship. One of the most important such developments is clearly the increasing emphasis that historians have placed on experimental practice, especially the "material culture" of biology, such as experimental systems and model organisms. Thus, the "New Experimentalism" has found an especially strong resonance in the history of biology. This work raises a number of challenges for philosophers of science that must be addressed.

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Therefore, I want to critically assess the implications of some of this work for the philosophy of science. This is another goal of this book.

In the following chapters, I address a series of central epistemological and metaphysical issues, some of which also arise in other sciences, while others are specific to experimental biology. These issues concern the ways in which scientific knowledge is structured, how it explains natural phenomena, how it is generated and evaluated, and how it connects to the world. All of these issues are dealt with in the present book, roughly in this order. The book is thus organized according to the philosophical issues, not according to biological disciplines or historical epochs.

Concerning the selection of examples and historical case studies, I chose a middle path between two different approaches. One approach would have been to present a single case study in great detail and then treat all the philosophical issues on the basis of this example. Something could be said for such an approach; however, experimental biology shows considerable internal diversity and probably no single example instantiates all the main philosophical problems equally well. The alternative approach is to treat each philosophical issue using a different example that seems especially well suited. This approach is somewhat uneconomical in terms of the amount of technical discussion that has to be presented and digested. Furthermore, this approach threatens to paint an overly disunified picture of experimental biology. For these reasons, I have chosen to focus on a few different examples, but not to introduce a new one for every issue addressed. The cases I ended up with are derived from neurobiology (Chapter 2), genetics and molecular biology (Chapters 3, 6, 7, 9), biochemistry (Chapters 3, 4, 5), developmental biology (Chapter 8), and microbiology (Chapter 9).

Chapters 2, 3, 4, 5, 7, and 9 address issues that also arise in other sciences (e.g., the physical sciences or the earth sciences). By contrast, Chapters 6 and 8 deal with philosophical issues that are specific to modern experimental biology and where (to my knowledge) no corresponding problems exist in other sciences.

Chapter 2 examines the reductionistic explanations of biological phenomena given by modern experimental biologists. As already mentioned, a consensus has developed among philosophers of biology that reductionism fails even in those areas of biology that are generally considered to be successes of reductionism, such as molecular genetics. However, this consensus is based on too restrictive an account of reduction, namely the logical empiricist account. The time is ripe to develop an alternative account that captures the main sense in which much of modern experimental biology is truly reductionistic (for better or for worse).

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My approach is to first present an example from the area of neurobiology. This example is the mechanism of nerve signal propagation (action potentials), which has been known in its basic outlines since the 1950s. The mechanism is fundamental to the entire discipline of neurobiology, as it explains how nerve fibers conduct signals. This is the basis of information processing in the nervous system.

I begin by investigating what kind of theoretical structure is instantiated by this example. I suggest that the most salient question is whether we should look at the case as a self-contained biological *theory* – as most philosophers of biology do – or, instead, as an *explanation* that applies theories from physical chemistry to a certain type of biological system. To affirm the latter defines a strongly reductionistic position. It is this position that I try to defend, at least for parts of experimental biology (but not for evolutionary theory or population biology). This defense involves a discussion of the nature of the *laws* that carry the explanatory burden in such examples.

A number of philosophers of physics have argued that the traditional concept of natural law should be dropped altogether (Cartwright 1989, 1999; van Fraassen 1989; Giere 1995). The idea that there are natural laws could be a relic from the theistic worldview that was popular during the formative years of modern science in the seventeenth century. In this worldview, God acted as a lawgiver in both the moral and natural realms. However, God has been banned from the explanations of natural science, and perhaps the concept of natural law should go with Him. I examine whether experimental biology is ready for this, in other words, whether its explanations can dispense with laws of nature.

I also address the issue of whether there are genuinely *biological* laws of nature. It has been suggested that all distinctly biological generalizations are contingent and therefore not laws of nature. This claim is known as the Evolutionary Contingency Thesis (Beatty 1995). I assess the validity of this thesis in the context of experimental biology. In addition, I want to exhibit its strong affinity to the kind of reductionism that I defend. Furthermore, I discuss the status of natural kinds in experimental biology. As it turns out, this issue is also strongly connected both to the existence of laws and to reductionism.

Functional explanations are viewed as a hallmark of biology, a feature that seems to distinguish it from the physical sciences. In giving functional explanations of some organismic traits, biology – even molecular biology – seems to be closer to psychology and the social sciences than to physics and chemistry. Thus, functional explanations pose a challenge for reductionism. Functional explanation is *teleological* in that it shows that some structure or capacity is a means to some end. Aristotle thought that each organism has an intrinsic

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end or *telos*, and his entire biology (as well as his general metaphysics) was permeated by this idea. However, modern science rejects intrinsic *tele* in the realm of nature. This raises the question of whether functional explanation should be eliminated. Most twentieth-century philosophers have been reluctant to issue such a radical recommendation and have instead tried to explicate functions in a metaphysically unproblematic way by somehow relating them to causal explanations (though some have argued that functional analysis is at best of heuristic value in science). In the literature, we find two different kinds of accounts, known as *etioloical functions* and *causal role functions*. The main difference between the two is that the former attempts to explain why function bearers are present in a system, whereas the latter only states the specific contribution that function bearers make toward some system capacity.

According to one version of the etioloical account, the presence of the function bearers can be explained with the help of evolution by natural selection. This view faces considerable difficulties. A more recent and more viable version of the etioloical account (McLaughlin 2001) states that functions explain the presence of function bearers via the latter's contribution to self-reproduction, that is, the continuous self-regeneration of individual organisms. I argue that the etioloical view does not capture the use of the term "function" in experimental biology. Instead, I adopt a causal role account. The main difficulty of the causal role account lies in the selection criteria for the significant system capacities to which the function bearers are supposed to contribute. Based on my neurobiological example, I suggest a way of solving this problem of the causal role account of biological functions.

In the final part of the chapter, I examine how the basic mechanism of action potentials is embedded in higher-level mechanisms that explain animal behavior. A strategy like this is often involved when experimental biologists explain some complex property of organisms. The specific question I discuss is whether a well-known argument against reductionism known as the "multiple realization" argument is relevant to this example. This argument is quite powerful for showing that theories like classical Mendelian genetics or Darwinian evolutionary theory are irreducible. However, these theories could be special in this respect, while multiple realization may not be an obstacle to reductionism in other areas.

Chapter 3 turns to an issue that is generally known as "scientific discovery." Clearly a misnomer, this term is widely used to refer to the reasoning processes by which scientists construct or generate new theories, hypotheses, or explanations. There is a long tradition of rejecting this as a legitimate subject for philosophical inquiry. Most twentieth-century philosophers thought that the proper domain for epistemology is only the justification or validity of

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scientific explanations, not their genesis. The reason behind this was the idea that only justification is subject to the constraints of rationality, such as the rules of deductive and (perhaps) inductive logic. The process of generating ideas was viewed as a psychological process not subject to normative considerations. Since the 1970s, this view has increasingly come under attack. A number of philosophers, together with some cognitive scientists, have argued that “discovery” is a rational process after all and that it can be analyzed as such. Since then, the search has been on for a “logic of discovery.”

Some participants in this quest took the term “logic” quite literally and started to design computer programs that generated hypotheses after being fed experimental data (Gillies 1996). The goal of these attempts was both to design expert systems that might assist working scientists and to remove some of the mystery surrounding scientific creativity. Initial attempts at simulating discovery were hardly more than computer-aided curve-fitting; however, more advanced programs are also capable of introducing theoretical entities and suggesting experiments. Of course, all this research in artificial intelligence cannot show that human scientists *actually* reason like these computer programs. Thus, the most that computer simulations could show is that some machine-implementable rules or heuristics are *sufficient* for generating plausible theories or hypotheses from some given inputs. There is no denying that such proofs of sufficiency would be interesting, provided that the rules implemented do not already contain the solution in some way. However, it seems to me that the computer programs in existence today suffer from exactly this drawback. In spite of this, artificial intelligence research on scientific discovery may have its applications. At any rate, it is not my goal to provide a systematic appraisal of this work. I am concerned mainly with flesh-and-blood attempts to understand the genesis of scientific ideas.

I critically examine three different attempts to use the historical record in order to draw conclusions concerning generative reasoning in experimental biology. The first is Kenneth Schaffner’s (1974a) early attempt to reconstruct the reasoning behind the genesis of François Jacob and Jacques Monod’s repressor model of enzyme induction in bacteria. Schaffner argued that this model was basically deduced from experimental results with the help of theoretical background assumptions. Schaffner suggested that this is indicative of an identity of generative and justificatory reasoning. Even though Schaffner has since revised these conclusions, a critical examination of his thesis is quite revealing.

The second attempt I examine is Lindley Darden’s (1991) account of the genesis of the “classical theory of the gene” due to Thomas Hunt Morgan and his students. Like most biological theories, the theory of classical genetics

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was not created by a single stroke of genius. Instead, it originated from a very simple precursor by a series of modifications triggered by experimental anomalies. Darden is concerned mainly with the way in which these anomalies necessitated revisions in genetic theory. Based on the published record, Darden inferred some heuristics or “strategies” that could have generated a number of the anomaly-driven revisions that occurred between 1900 and 1926. I critically examine in particular Darden’s claim that her strategies are both sufficient *and* general.

The third attempt I examine concerns what should be one of the best understood episodes in the history of science, namely, the discovery of the urea cycle by the biochemist Hans Krebs. In comparison to the two other examples, this case offers a very rich historical record. Not only have most of Krebs’s laboratory notebooks and his letters been preserved, but the historian Frederic Holmes was also able to conduct extensive interviews with Krebs in the late 1970s. A true master of his trade, Holmes has assembled one of the most detailed accounts of any episode in the history of science, tracing Krebs’s activities from day to day (Holmes 1991, 1993a). In spite of this, it has been remarkably difficult to reconstruct how Krebs generated some of his more important ideas. The problem is that the historical record reveals in great detail what Krebs was *doing*, but not much of what he was *thinking*. Thus, the exact sequence of mental steps that Krebs took remains a matter of historical debate. Nevertheless, Holmes thinks that it is possible to make Krebs’s discovery “intelligible to reason.” I consider in particular the questions of what this means and whether the case supports the idea that there are general and domain-unspecific problem-solving heuristics operative in science.

Chapter 4 turns to the question of how hypotheses are subjected to experimental test. After reviewing some extant accounts of scientific inference, I present a detailed case study of a historical episode. This episode is known as the “oxidative phosphorylation controversy” in biochemistry (ca. 1961–1977). It involved two competing hypotheses that explain how cells generate biological energy. Several years of experimental research and theoretical debate failed to resolve this controversy. Finally, the development of novel experimental techniques allowed biochemists to stage a crucial test that provided definitive reasons for choosing one of the two theories. This account is somewhat simplified, and I point out some complicating factors.

I then examine whether this case instantiates a philosophical conundrum known as the “Duhem–Quine thesis” or underdetermination. Actually, this “thesis” needs to be differentiated into Duhem’s problem, which is the problem of allocating praise and blame between a theory and the auxiliary assumptions needed for connecting the theory to observable consequences, and the

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problem of underdetermination, which concerns the possibility that two theories are empirically equivalent. I examine whether the two competing theories involved in the ox-phos controversy instantiate any of these problems.

Next, I critically examine whether a currently popular account of scientific inference and theory comparison does a good job of explicating this case. This account is known as “Bayesian confirmation theory” and is thought to provide some sort of an inductive logic. More precisely, Bayesian confirmation theory claims that rational cognitive agents ought to attach a probability value to empirical statements. These probability values should reflect the agent’s personal probability, which measures how much the agent is willing to bet on the truth of the statement. Then the theory says that rational agents ought to update these subjective probabilities under the impact of incoming evidence according to Bayes’s theorem. This theory is riddled with difficulties, and Bayesians have been quite ingenious in their attempts to fix these difficulties. I examine whether the scientists involved in the ox-phos controversy qualify as rational agents in the sense of Bayesian confirmation theory. Of course, any discrepancies will be blamed on the Bayesians, not on my biochemists. I give a justification for this reversal of the traditional order of things.

Another theory of scientific inference I critically examine on the basis of my case study is Deborah Mayo’s (1996) error statistical approach. Mayo has attempted to provide an alternative to Bayesianism. She also advocates the use of probabilities in scientific inference, but not the standard Bayesian personal probabilities. Mayo’s probabilities are objective and measure the relative frequency with which an experimental test procedure passes a hypothesis given that the hypothesis is false. If this *error probability* is very low, then the test earns the label “severe” from Mayo. I examine in particular to what extent this account of scientific inference can be applied to a case such as ox-phos, where the experimental test procedures were not of a statistical nature.

Having found fault with all these accounts of theory testing, I then try to develop my own account. I take on board some valuable insights from Mayo, especially the central role she accords to the control of errors. However, “error” should not be interpreted in a formal, statistical sense. I place particular emphasis on the practice of controlled experiments in biochemistry, which I think holds the key to understanding experimental reasoning.

Chapter 5 critically examines a perspective on experimentation that radically differs from the perspective of Chapter 4. The historian of biology Hans-Jörg Rheinberger (1997) has presented a novel account of the role of experimental systems in biological research. His notion of experimental system is very broad, as it includes a constellation of various material and cognitive resources needed to do research in biology. Based on his detailed historical