Reasoning in Biological Discoveries

Reasoning in Biological Discoveries brings together a series of essays written and cowritten by Lindley Darden that focus on one of the most heavily debated topics of scientific discovery today. Collected, and richly illustrated for the first time in this edition, Darden's essays represent a ground-breaking foray into one of the major problems – biological mechanisms – facing scientists and philosophers of science alike. Divided into three sections, the essays focus on broad themes, notably historical and philosophical issues at play in discussions of biological mechanism; and the problem of developing and refining reasoning strategies, including interfield relations and anomaly resolution. In a group of essays published here for the first time, Darden summarizes the philosophy of discovery and elaborates the role that mechanisms play in biological discovery. Throughout the book, she uses historical case studies to extract advisory reasoning strategies for discovery. Examples in genetics, molecular biology, biochemistry, immunology, neuroscience, and evolutionary biology reveal the process of discovery in action.

Lindley Darden is Professor of Philosophy and in the Committee for Philosophy and the Sciences at the University of Maryland, College Park. She is the author of *Theory Change in Science: Strategies from Mendelian Genetics*, as well as numerous articles in history and philosophy of science journals. Elected a Fellow of the American Association for the Advancement of Science in 1995, she served as President of the International Society for History, Philosophy, and Social Studies of Biology from 2001 to 2003.

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Reasoning in Biological Discoveries

Essays on Mechanisms, Interfield Relations, and Anomaly Resolution

LINDLEY DARDEN
University of Maryland, College Park

Illustrated by
Darren Hudson Hick

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For my family: Tom, David, and Morgan

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one stage of the mechanism and then detecting effects at a different stage, either later or up/down in a hierarchy. Incompleteness and anomalies drive refinements during discovery.

Chapter 3: Strategies in the Interfield Discovery of the Mechanism of Protein Synthesis with Carl F. Craver

In the 1950s and 1960s, an interfield interaction between molecular biologists and biochemists integrated important discoveries about the mechanism of protein synthesis. This extended discovery episode reveals two general reasoning strategies for eliminating gaps in descriptions of the productive continuity of mechanisms: schema instantiation and forward/backward chaining. Schema instantiation involves filling roles in an overall framework for the mechanism. Forward and backward chaining eliminates gaps using knowledge about types of entities and their activities. Attention to mechanisms highlights salient features of this historical episode while providing general reasoning strategies for mechanism discovery.

Chapter 4: Relations Among Fields: Mendelian, Cytological, and Molecular Mechanisms

Philosophers have proposed various kinds of relations between Mendelian genetics and molecular biology: reduction, replacement, explanatory extension. This chapter argues that the two fields are best characterized as investigating different, serially integrated, hereditary *mechanisms*. The mechanisms operate at different times and contain different working entities. The working entities of the mechanisms of Mendelian heredity are chromosomes, whose movements serve to segregate alleles and independently assort genes in different linkage groups. The working entities of numerous mechanisms of molecular biology are larger and smaller segments of DNA plus related molecules. Discovery of molecular DNA mechanisms filled black boxes that were noted, but unilluminated, by Mendelian genetics.

PART II: REASONING STRATEGIES: RELATING FIELDS, RESOLVING ANOMALIES

Chapter 5: Interfield Theories with Nancy Maull

This chapter analyzes the generation and function of *interfield theories*, theories which bridge two fields of science. Interfield theories are likely to be

of natural selection. Once constructed, this abstraction provides a useful tool for analyzing the nature of other selection theories and may be of use in new instances of theory construction. This suggests the potential fruitfulness of research to find other theory types and construct their abstractions.

Chapter 9: Strategies for Anomaly Resolution: Diagnosis and Redesign

Anomaly resolution entails both diagnosis and redesign tasks. Steps and strategies for localizing and fixing anomalies for scientific theories are outlined. The resolution of a monster anomaly in genetics resulted in the discovery of lethal gene combinations. A simulation model for genetic processes is systematically debugged as an illustration of anomaly localization in a computational philosophy of science experiment.

Chapter 10: Exemplars, Abstractions, and Anomalies: Representations and Theory Change in Mendelian and Molecular Genetics

Representations of scientific theories are closely tied to reasoning strategies for theory change. A scientific theory may be represented by a set of concrete exemplary problem solutions. Alternatively, a theory may be depicted in an abstract pattern, which, when its variables are filled with constants, becomes a particular explanation. The exemplars and abstractions may be depicted diagrammatically, as they are in the cases from Mendelian genetics and molecular biology. One way that a theory grows is by adding new types of exemplars to its explanatory repertoire. Model anomalies show the need for a new exemplar; they turn out to be examples of a typical, normal pattern that had not been included in the previous stage of theory development. A special-case anomaly indicates the need for a new exemplar or abstraction, but it has a small scope of applicability. Thus, ideas discussed here are exemplars, abstractions, diagrammatic representations, and anomalies and the roles they play in the representation of explanatory theories and in the change of such theories. Examples come from Mendelian genetics and molecular biology, including a special-case anomaly for the central dogma of molecular biology, namely, the discovery of the enzyme, reverse transcriptase, that copies RNA into DNA.

Chapter 11: Strategies for Anomaly Resolution in the Case of Adaptive Mutation

The phenomenon of adaptive mutation is an anomaly that has received many diverse responses. These range from radical challenges to the theory of natural selection and the central dogma of molecular biology to the claim that adaptive mutations are produced via operation of previously known mechanisms. Examination of this anomaly provides a range of responses, from viewing the anomaly as a monster, a special case, or a model for all mutations. The case suggests refinements of strategies for anomaly resolution.

PART III: DISCOVERING MECHANISMS: CONSTRUCTION, EVALUATION, REVISION

Chapter 12: Strategies for Discovering Mechanisms: Construction, Evaluation, Revision

This chapter brings together the discussions of Part I on mechanisms and Part II on reasoning strategies. It summarizes the view of discovery via iterative refinement and elaborates the way that the characterization and features of mechanisms aid their discovery. In Section 12.2, the MDC (Machamer, Darden, Craver) discussion of mechanisms from Chapter 1 is refined and defended against recent criticisms. Subsequent sections of the chapter summarize and expand earlier discussions of reasoning strategies for construction, evaluation, and refinement. Construction strategies include schema instantiation, modular subassembly, and forward/backward chaining. Evaluation strategies serve to assess adequacy. They detect incompleteness and aid in moving from how possibly, to how plausibly, to how actually the mechanism works. Anomaly resolution strategies guide diagnosis and repair during revision. Examples come from molecular biology, biochemistry, immunology, neuroscience, and evolutionary biology discussed in more detail in earlier chapters.

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My visit to the hospitable Center for Philosophy of Science at the University of Pittsburgh led to my collaboration with Peter Machamer and Carl Craver on "Thinking About Mechanisms." Peter and I had been in graduate school together at the University of Chicago and revived shared perspectives in our collaboration. It was a pleasure to work with him and enjoy his legendary hospitality in Pittsburgh. While Carl was a post-doc at the University of Maryland (for which I thank the Committee on Cognitive Studies), he drafted "Discovering Mechanisms in Neurobiology" (Chapter 2), and I drafted "Strategies in the Interfield Discovery of the Mechanisms of Protein Synthesis" (Chapter 3). Then, with much lively conversation producing new insights, we rewrote both together. Carl probably talked more about discovery as a result of my influence, and Carl saw more general ideas about mechanisms than I did as I reveled in the particular details of the protein case study. Peter contributed vociferous comments. It was a pleasure working with Carl again as we edited and wrote the introduction for the special issue on mechanisms of *Studies in History and Philosophy of Biological and Biomedical Sciences* (June 2005). Chapter 12 makes use of several excellent articles from that issue. Carl influenced my ideas in Parts I and III more than citations to his work can indicate. Most recently, his comments on Section 12.2, where I respond to some critiques of MDC, greatly improved it, even though I didn't always take his advice. I look forward to reading the new book he is writing on mechanisms in neuroscience, which I have purposely not read until I finished Part III.

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Lindley Darden
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