Foreword

MY COEDITOR, RALPH GREENSPAN, AND I HAVE DECIDED, rather than to coauthor a preface to this book, to act as bookends, with Ralph writing the Afterword and me writing the Foreword. This does not reflect any disagreement in view, but instead, complementary perspectives. Ralph has the point of view of a professional scientist in the field, and I have the point of view of a professional editor who is most definitely not a specialist, but who finds the field fascinating.

Before explaining the rationale and aims of this book, it might be worth giving a bit of background—the views that have informed our approach to the subject. We share the opinion that the molecular revolution which began in the 1950s has over-skewed biology somewhat; the insights into fundamental processes that have been made possible by this revolution are remarkable, but they have tended to foster the view that the main point of biology is to elucidate molecular mechanisms. In the extreme view, a description of any biological phenomenon becomes a mere prelude to analysis by a now well-trod route: Screen for genetic variants where the phenomenon at issue is perturbed; clone the gene; sequence the gene; analyze its product; and so on.

This approach has proved tremendously successful in many areas of biology, particularly cellular and developmental biology. Indeed, when the study of the molecular biology of metazoan organisms began in earnest in the 1970s and early 1980s, it was not clear that it would prove quite so successful—for example, one significant figure expressed the pessimistic view that, when the bithorax complex of homeotic genes of the fruit fly *Drosophila melanogaster* was cloned, it might turn out simply to encode some common enzyme, not in itself shedding great light on developmental mechanisms. This proved to be quite wrong, and the cloning of the bithorax complex and the related antennapedia complex provided the first molecular insights into a set of genes devoted specifically to embryonic patterning.

Molecular biology marched on, casting its bright light on one area of biology after another. In parallel has been a huge focus on those relatively few species that were chosen because of their perceived advantages for genetic and molecular studies: *Drosophila*, of course; the nematode *Caenorhabditis elegans*; the mouse; the yeast *Saccharomyces cerevisiae*; and others. These species were the first in line when it became feasible to sequence entire genomes, something which has become so commonplace that it is now rather taken for granted (I write this in the week that saw publication of the honeybee genome sequence).

Given these great achievements, what is the problem? Our feeling is that this course has led to a mind-set among many biologists which fails to appreciate and give due weight to work done at a higher level than the molecular. The mind-set is somewhat similar to that encouraged by Rutherford's much quoted opinion that science can be divided into "physics and stamp-collecting." We suspect many would take the view that the molecular revolution has turned biology into a kind of physics—made it a hard science that biologists can proudly explain to those in the physical sciences.

We believe this view is flawed, on two main grounds. The first is that, for most biological phenomena, real understanding is a multilayered process. This perhaps is most obviously true in neuroscience. Consider human vision, for example: I would argue that we learn more about this from consideration of a simple visual illusion than from experiments to date involving electrical recordings from single neurons in the brain. Many striking illusions forcefully bring home the understanding that our brain is making inferences about what is out there in the real world on the basis of incomplete data gathered via the eyes, interpreted in the light of assumptions about the character of the real world. This approach, formalized by David Marr with his development of "computational vision," provides an understanding at one level of human vision: It does not explain how the neurons in the brain make the computations, but it suggests what they are doing. In terms of a complete understanding, the psychophysical and computational approaches are at least as important as lower-level neuronal analyses.

The second flaw is a failure to appreciate the wonder and interest of biological diversity. Rutherford's view was held at a time when biology was more dominated by "natural history" and is more understandable in that context. However, it is a mistake to dismiss the specific in biology. A central tenet of physics is that laws are general—they apply anywhere in the universe. It is not especially interesting to describe some specific aspects of the physics of a particular object. I would argue that biology is different, because of its unique historical aspect: The tips of the great Tree of Life that are the extant species on Earth have each a unique history, and each is, in a sense, a unique scientific phenomenon, with intrinsic value and interest.

These views are reflected in this book. Indeed, the rationale of the book resides very much in the conflicting views of biology touched on above. Thus, those working on the neurobiology of the two key invertebrate "model species," the fly and the worm, are becoming increasingly interested in the more complex perceptual and behavioral phenomena, such as vision, olfaction, and sexual behavior. These species have already made notable contributions to neurobiology in general, with Seymour Benzer's pioneering work on the behavioral genetics of *Drosophila* leading to identification of genes involved in memory, circadian behavior, and so on, and with the complete elucidation of the nervous system of the nematode. *Drosophila* molecular neurobiologists are pioneering methods which allow increasingly precise perturbations to neuronal circuits, even to the level of being able to increase or decrease the activity of specific, identified neurons "at will."

Indeed, this is one argument for the timeliness of this book: At one level, work on invertebrate species is well ahead of anything that can be done in vertebrate neurobiology. This may be history repeating itself—*Drosophila* studies heralded huge progress in developmental biology in the 1980s and 1990s, to the extent that most developmental biologists of whatever stripe are working on homologs of genes initially identified in *Drosophila*.

As the focus moves increasingly to behavior, the neurogeneticists working on these model species are beginning to share interests and problems with those in more "classical" areas of invertebrate neurobiology, where there is a rather different tradition. This is a second argument for this book: We believe there is a need to bring together these two slightly disparate groups of invertebrate neurobiologists.

The classical areas I am referring to here—neurophysiology, where the need for an accessible preparation is greater than that for easy genetics; and neuroethology, with an emphasis on behavior in the "wild" and the natural ecology of a species—themselves have a very fine history. It was work on an invertebrate preparation, the squid giant axon, which provided the basic data that led to Hodgkin and Huxley's Nobel Prize-winning modeling of the action potential. Work over decades on central pattern generators has provided perhaps our best understanding of how neurons function in circuits. Analysis of synaptic plasticity in *Aplysia* has played a great part in the understanding we have of how nervous systems can learn and remember, leading to another Nobel Prize, for Eric Kandel. Studies of how insects fly must be one of the great examples of real "systems biology," showing how an understanding of the system depends on analyses at many levels, from mechanics and aerodynamics to metabolism to neural systems control.

The chapters in this book have been commissioned to illustrate these diverse strands of the subject, with the hope of stimulating communication between those working on genetic model species and those working on the more diverse subjects of neuroethology. There is a great deal of emphasis on behavior, which we justify by the argument given above in relation to human vision: We need to know what an organism does, what it can learn, and what it "knows" so that appropriate questions can be framed for neurophysiologists to address. We hope the chapters also illustrate the great diversity of invertebrates. Anyone who has seen David Attenborough's wonderful recent television documentary series "Life in the Undergrowth" must have been struck by the extraordinary diversity of behaviors seen among invertebrates, complex hard-wired behaviors (for example, an orb spider spinning its web) as well as a remarkable capacity for learning and transmitting information (for example, a honeybee dancing on return to the nest).

This great diversity is one reason that invertebrates are so interesting; it makes them particularly promising subjects for studying how nervous systems evolve—an evo-neuro is surely emerging to match the evo-devo of developmental biology. Invertebrates range from species that lack any kind of nervous system to species such as cephalopods with their large eyes and sophisticated behaviors. To what extent do they exhibit cognitive features associated with higher vertebrates? Are any of them sentient, with conscious awareness? Presumably, this is not true of the sponges, which lack true nerves; but if the most complex invertebrates are conscious, the question naturally emerges: What is the simplest nervous system to support consciousness? It is not obvious at this point whether this question will ever be amenable to experiment, but in a way, I think it is good that there are questions about which this can still be said.

We hope that this book will demonstrate the interest of the field and justify our excitement about the way it will develop, and that it will inspire students, inform specialists of what is happening in other branches of the field, and perhaps—by illustrating the common areas of interest—go some way toward bridging the gap between vertebrate and invertebrate neurobiology.

Finally, Ralph and I thank the excellent staff at Cold Spring Harbor Laboratory Press for all their efforts in making this book possible, in particular, Mary Cozza, Cher Mattes, Pat Barker, Denise Weiss, Lauren Heller, and Alex Gann, whose idea the book was and who persuaded the two of us to take on the joint editorship.

GEOFFREY NORTH