NEUROBIOLOGY

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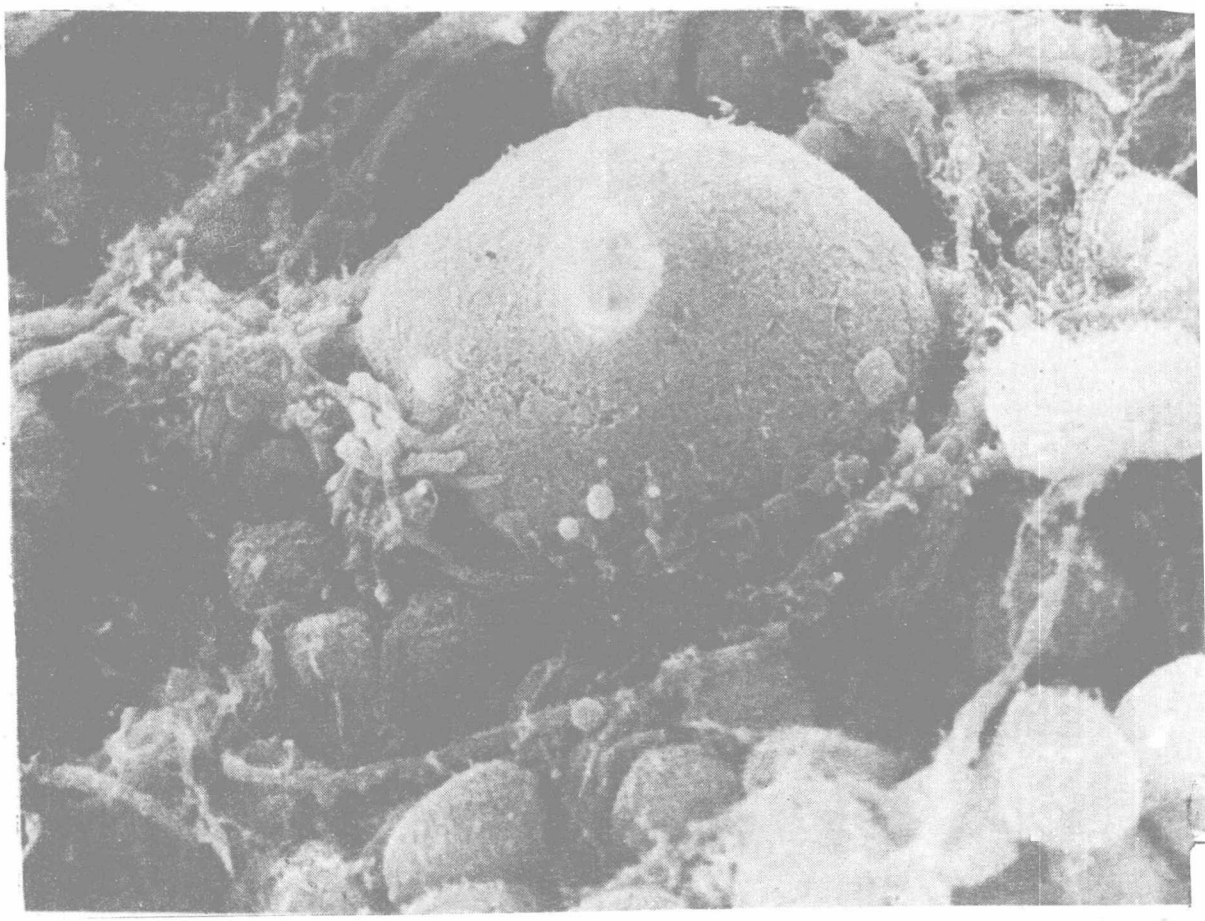

Scanning electronmicrograph of a large egg-shaped Purkinje cell body in the rat cerebellum. On its surface are small button-like synaptic terminals from basket cell axons; surrounding it are several long nerve fibers, and numerous small spherical cell bodies of granule cells. The tissue was prepared by chemical digestion in osmium and drying, after which the slices were gently pulled apart to expose the nerve cells and fibers. Magnification × 4030. (Courtesy of Bonnie Reese, Dennis Landis, and Thomas Reese, National Institutes of Health and Harvard Medical School)

Preface

This book is written as an introduction to the field of neurobiology. It aims to summarize modern knowledge about nerve cells and their organization into functional circuits, and show how this relates to animal behavior.

The book had its origins several years ago in conversations with Jeffrey House of Oxford University Press, and our mutual feeling that although there were a number of excellent texts covering many parts of neurobiology, there was none that adequately covered the whole field in a systematic way. An informal survey of a dozen or so undergraduate courses in neurobiology was accordingly carried out, and the response of course directors at colleges and universities throughout the United States very much confirmed our feeling. I studied and collated the course outlines provided by this survey, and used this as a basis for organizing the material. I should like to record my thanks to all the course directors who responded to this survey and discussed their particular needs and generously offered detailed comments and suggestions on our proposal.

The format of the book is meant to be adaptable to several learning modes. The primary aim of the book is to serve the needs of the undergraduate student who is meeting the subject for the first time. Modern studies of the nervous system now touch on so much of animal life that some colleges are beginning to offer a broadly based course in neurobiology and behavior in parallel with the traditional sequence of introductory biology followed by upper level neurobiology. The present book can be adapted to both situations. The beginning student will focus mainly on the narrative account, whereas the upper level student will want to study details of the text, figures, and figure legends, and pursue the references to more specialized subjects. The 31 chapters can be taken in weekly steps for a full year course; the pace may be quickened, or a selection made of certain chapters, for shorter courses lasting a quarter or a semester. Although the book is not primarily aimed at medical school or graduate school students, it does cover a good deal of material, much of it very recent, not available at present in textbooks at those levels, and it may be useful therefore in those settings as a core or supplemental text.

In addition to being organized for effective learning and teaching, the material builds on some fundamental concepts

about the ways that nervous systems themselves are organized. One of these concepts is the idea that any given region or system contains successive levels of organization, beginning with ions and molecules, and building up through cells and their circuits to behavior. Although the work of identifying these different levels and their specific functions is at an early stage, it seems to me important that we begin to think about organization in these terms, and try to correlate the different levels within a region in a coherent way. A related concept is the idea that different regions contain more or less corresponding levels, and that a full understanding of one region rests to a certain extent on our ability to relate its levels of organization to those of other regions. These concepts seem to me crucial to the task of developing common principles that apply to all nervous systems. Colleagues in the field will recognize that these are concerns that have been coming to the fore in recent years. There is a growing realization that we are in an era in which experimental results are pouring in much faster than we can fashion concepts that give them meaning. I hope the present effort will serve to some extent as a contribution toward the goal of synthesizing a body of basic principles for the functional organization of all nervous systems.

With regard to the main sections of the book, I felt it important to begin with an overview of invertebrate and vertebrate animals, as a basis for the comparative approach which underlies the later accounts of different systems. It helps to emphasize the evolutionary context within which nervous systems and the behaviors they mediate need to be evaluated. It also, incidentally, introduces some of the terms relating to the classification of different species which many students—myself included—find difficult to remember! The section on cellular mechanisms reflects the widely shared view of the cell as the fundamental building block of the nervous system. The sections on sensory and motor systems reflect a logical division of these subjects. However, the more centrally one proceeds, the more artificial is this division, and the present simplified accounts do not do justice to the extent of descending, motor, or centrifugal control of sensory systems; or of ascending, sensory, or internal feedback control of motor systems. Beyond sensory and motor systems, most textbooks tend to roam over a landscape populated by miscellaneous "higher functions." I decided to group all of these together in a section on Central Systems. As will be seen, this forces a definition of central systems, as specifically concerned with mediating global behavior patterns, that sets them apart from specific sensory and motor systems. This definition is heuristically useful for the teacher and the student, and I believe also reflects crucial distinctions between these types of systems and their levels of organization in relation to behavior. These distinctions are necessary, as will be shown, in defining and discussing global behaviors such as waking, emotion, learning, and memory.

Because the entire book is written as one continuous narrative, I have had an opportunity to attempt a wider integration of many aspects of neurobiology than is usually the case. One of my discoveries as the writing progressed was the extent to which a given subject is never isolated, but needs to be discussed in many contexts. The sensory hair of insects may be cited as an example. Its development is discussed in Chap. 10, the chemosensory types mediating taste and smell in Chap. 12, the tactile variety in Chap. 13, the type subserving the sense of balance in Chap. 15, the role in sensorimotor control of the proboscis of the fly in Chap. 24, and the role in control of feeding behavior in Chap. 27. Similarly, synaptic plasticity, in its molecular and cellular aspects, is discussed in the early chapters on basic cellular mechanisms; it is referred to in several subsequent chapters on specific sensory and motor systems; it is at the core

of the discussion of learning and memory in Chap. 30, and it is also important in the cellular basis of human cortical function in Chap. 31. I have made a particular effort to cross-reference related aspects of subjects such as these as they arise in the text, so that the reader can follow through on specific topics. The importance of understanding a given neuronal property or type of circuit in all its functional and behavioral contexts is one of the key messages I hope to convey to the student of neurobiology by this means.

The systematic nature of this account brings in material that may be unfamiliar to some readers. For example, the chemical senses—taste and smell—are regarded as minor senses in most accounts, and are even left out completely in some textbooks. However, cell biologists know that chemosensitivity involves molecular interactions that are of great interest with regard to basic membrane mechanisms, and ethologists know that these senses have dominant roles in the behavioral and social organization of most animal life. I have tried to show how this chemical sensitivity may be integrated into the principles of neurobiology. Another subject that is almost completely ignored in modern textbooks is the vocal mechanism of human speech. This puzzling neglect of one of our highest and most important faculties seems no longer supportable to me, and I have tried to rectify it by including an account that describes this function from a perspective of sound production in both invertebrates and vertebrates. These are just two among a number of subjects which are included in this book, and which I believe must be incorporated into our thinking from the start of our studies if we are to build a truly valid and coherent view of neurobiology based on first principles.

The present account, though extensive, is by no means exhaustive, and there are many subjects which are absent or covered only skimpily. Any account of this vast field must be selective, and I hope that this attempt can serve as a framework so that the student or teacher can add other material or explore other subjects in a logical way.

My interest in writing a book of this nature has evolved out of my own work in two main areas: the principles of organization of synaptic circuits, and the mapping of activity in those circuits in the awake behaving animal. The idea that these two levels—synaptic circuits and natural behavior—could be joined in a way that would allow one to begin to build the neural basis of behavior was first instilled in me by Niko Tinbergen, through his early writings and through a conversation we had while I was a graduate student at Oxford in 1960. This goal seemed remote to my own work until the early 1970s, when James Sprague at Philadelphia encouraged me to start thinking again of synaptic organization in terms of its behavioral significance. In the synthesis of ideas that has ensued, I was stimulated by Eric Kandel to include invertebrates equally with vertebrates, and by Tomas Hökfelt to incorporate the new findings of neurochemistry.

The neural basis of behavior is a central concern of modern neurobiology and of this book, and deserves further comment. Many workers in recent years have studied synaptic properties and circuits and their correlations with simple behaviors; what is still needed is an understanding of how, beginning at the single synapse, one builds up successive levels of synaptic circuits of increasing extent to mediate complex naturally occurring behaviors. The synaptic circuits within different regions have only been revealed in their correct details in recent years; surprisingly, it is at these intermediate levels of circuit organization that common principles are emerging very clearly, as is documented in many chapters of this book. From all this work one can see that complex naturally occurring behaviors, such as feeding and mating, are just what nervous circuits are primarily designed for. One can summarize this in a proposition, paraphrasing the

well-known aphorism of Theodosius Dobzhansky about biology and evolution, that "Nothing in neurobiology makes sense except in the light of behavior."

In view of these considerations, it was important in this book not to describe neural circuits and mechanisms in isolation from the kinds of behavior that they mediate. What is accomplished if the student is asked to learn the neural mechanisms that control manipulation, for example, without a clear picture of what the organs of manipulation look like, how they function, and how they compare with other organs of similar or related function? I have therefore extended the usual scope of a neurobiology text, and have included treatment of anatomical structure, comparative physiology, and different kinds of social behavior, wherever it seemed to help illuminate the text or simply bring out the precision or beauty (too often forgotten) of the behavior involved. This extension of scope should help the student pursue further, using the references provided, those topics that overlap with other fields.

Many parts of the text have grown directly out of my teaching experiences here at Yale and at other institutions. In addition to medical and graduate courses, they include a Pierson College seminar course for undergraduates on "Man and his Brain" at Yale. I am indebted to Kurt Schlesinger and Herb Alpern for their kind invitation to give a mini-course on synaptic organization in the Department of Psychology at the University of Colorado in 1981, and for stimulating discussions there which helped in formulating some of the ideas relating to Central Systems in Section V. Chapter 24 includes material I have used as a guest lecturer in the Master Class for Vocal Music, under Blake Stern, the noted tenor, at the Yale Music Festival in Norfolk, Connecticut; I thank Mr. Stern and George Shepherd for stimulating discussions about the singing voice. Parts of the book draw on material from the second edition of my book, *The Synaptic Organization of the Brain,* published by Oxford University Press in 1979. These include especially Chaps. 8 and 9, as well as excerpts and figures scattered in Chaps. 4–7, 9, 12, and 17. Much of this material is concerned with basic principles of cells and synapses, and is more appropriate now in the present context.

One of the major concerns of this book is a comparison between the circuits of invertebrates and vertebrates for each major functional system, and one of the major themes is the extraordinary degree to which the circuits appear to be built on similar organizational principles. In pursuing these comparisons I have been led into many areas of invertebrate neurobiology with which I have no first-hand experimental knowledge. Many colleagues have helped me, with stimulating discussions and criticisms, and clarification of innumerable items of detail. Among them I am especially indebted to Jurgen Boeckh, John Hildebrand, Steve Matsumoto, Malcolm Burrows, Keir Pearson, Brian Bush, Alan Roberts, Jeffrey Wine, Simon Laughlin, John Miller, Robert Wyman, Melvin Cohen, and John Nicholls.

A great number of colleagues have helped with parts of the text and with specific illustrations. Those to whom I am most indebted include Marilyn Farquhar, Amiram Grinvald, Raymond Murray, Linda Bartoshuk, Robert LaMotte, Carole LaMotte, Melvin Cohen, Daniel Alkon, Simon Laughlin, Pasko Rakic, Patricia Goldman-Rakic, Stephen Smith, Rich Aldrich, Lynn Landmesser, Robert Wyman, Jeffrey Wine, Richard Day, Charles Bradford, Albert Beveridge, Ralph Norgren, Alan Peters, Bonnie Reese, Tom Reese, Stephen Kitai, Dennis Lincoln, William Schwartz, Kent Morest, Mahlon DeLong, Aage Moller, Fred Naftolin, Tom Thach, Peter Strick, Edmund Crelin, Damien Kuffler, William Miller, and Victor Wilson.

The parts of the book that are drawn from my own research reflect the results of the combined efforts of many students

and co-workers with whom it has been my privilege to be associated in recent years. It is a pleasure to record my special indebtedness in this respect to Lewis Haberly, Lanay Land, Thomas Getchell, John Kauer, Frank Sharp, William Stewart, Martha Nowycky, Neil Krieger, Ulrich Waldow, Kensaku Mori, Charles Greer, Doron Lancet, Norbert Halasz, Burton Slotnick, Patricia Pedersen, Thane Benson, Leona Masukawa, Paul Greengard, and Tomas Hökfelt. Our work has been generously supported by research grants from the National Institute of Neurological and Communicative Disorders and Stroke, and from the National Science Foundation.

Several colleagues graciously consented to take time from their busy schedules to read entire sections of the book while it was at the manuscript stage. These were Sol Erulkar (Section II), Albert Hudspeth (Section III), Keir Pearson (Section IV), and Alan Epstein (Section V). They have corrected many errors of detail, and made a number of valuable suggestions about organization and emphasis. The faults which remain are mine, not theirs.

Particular care has been taken with the illustrations. A number of these are composites of several figures, which help the student to correlate different levels of organization or function. Many are original illustrations, which constitute new interpretations of recent findings. I apologize to colleagues whose work in this regard has been oversimplified in the interests of clarity or meaning for the introductory student. For these, my pencil drawings have been put into final form by Virginia Simon, of the Medical Illustration Department at Yale, and her associates, Linda Seigneur, Wendolyn Hill, and Beverly Pope. I am grateful to them for their beautiful artwork, to Thomas Coughlan for expert photography, and to all of them for their considerable efforts in seeing over 400 illustrations to completion in a limited period of time.

Each author of an original illustration is credited in the figure legend, and is cited under References at the end of that Chapter. The citation is either to the original publication, or, in some cases, to a later publication which would be more accessible or relevant to an introductory student, or in which the original illustration has been updated or otherwise modified. Authors referred to in the text are also cited in the References. In resolutely keeping the account at an introductory level, I have held the number of references to an absolute minimum, which has meant leaving out much work that deserves equal mention; I hope my colleagues will be understanding in this regard. Even at that, there are some 500 references, many of them within the past several years. I thank the many authors and publishers who have kindly granted permission to reproduce copyrighted material.

The writing has been done on evenings, weekends, and holidays, and this has placed great burdens on my family. I am not only deeply grateful to my wife, Grethe, and to Gordon, Kirsten, and Lisbet, for their understanding and support, but also for their assistance in typing, editing, copying, and reading the text, and helping with several of the illustrations.

From first to last, Jeffrey House has given unstinting support. He has maintained his belief in a single-author text during the hard times when my faith was wavering, and he deserves much of the credit for seeing the project through to completion. The editing of text and figures within the time available was a demanding job, which Brenda Jones has performed with efficiency, and a tactful indulgence in my idiosyncracies.

I dedicate this book to my parents, Eleanor and Geoff Shepherd, who have taught me by word and deed to explore life carefully, write about it as clearly as possible—and retain a gentle sense of humor.

Hamden, Connecticut G. M. S.
June 1982

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