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# PRINCIPLES OF NEURAL SCIENCE

SECOND EDITION

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and

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## Preface

Four major advances have occurred since the appearance of the first edition of *Principles of Neural Science*, and they have stimulated us to undertake this revision earlier than we had planned. The *first* advance has been an application of recombinant DNA and monoclonal antibody techniques to the nervous system. These methods have made accessible the solution of many neurobiological problems; for example, it is now possible to study the genome of the nerve cell fruitfully and to determine the complete structure of several membrane proteins important for signaling. Many new neuropeptides and their precursors have also been identified. The organization of the genes that encode them is being rapidly mapped. In addition, these techniques are beginning to elucidate the molecular details that distinguish different neuronal cell types. The *second* important advance is patch clamping, which has allowed investigators to explore in intact membranes the conformational changes that occur in single ion channels. This advance is bringing our understanding of the precise molecular changes underlying synaptic transmission to a new level. It also has important implications for the future development of pharmacological agents used to treat a wide range of clinical disorders. The *third* advance, the revolution in nerve cell labeling and cell tracing methods, has clarified many previously poorly understood relationships between brain structure, and behavior. *Fourth*, new, noninvasive methods of imaging have made it possible to study anatomical structures in the living human brain. Because of these last two advances, neuroanatomy can now be taught in an integrated manner with other segments of neural science.

In addition to major developments in methodology and technique, an important conceptual advance is that neural scientists have recognized that cell and molecular biology are crucial to their field. Although half a decade ago few neural scientists would have denied the importance of regarding the neuron in cell-biological terms, this approach to studying the nervous system was, until very recently, by no means central to the field, nor was it particularly useful for dealing with most day-to-day

problems, either in the experimental laboratory or in the clinic. Today the view that neural science is a special—and important—part of cell biology has become commonplace. Only when neuronal function is viewed as a consequence of the activities of specific molecular components within nerve cells can the great importance of the new advances in neural science be appreciated. As the boundaries of neural science expand, and with them our understanding of the mechanisms of perception, behavior, and learning, so must the way in which neural science is taught.

The modern era in neural science began about 35 years ago. In 1953, John Eccles reviewed results based on the first intracellular recordings from single nerve and muscle cells in a book he modestly entitled *The Neurophysiological Basis of Mind*. At that time, this title seemed overly bold because so little was then known about the mechanisms of behavior. What could be learned by sticking cells with microelectrodes that could possibly help in understanding the mind? As time passed, many of us have read this marvelous book again, and each time we are more impressed with its author's prophetic insight. Eccles' book pointed the field in the right direction: its major message is the necessity to study the brain in terms of its elementary units—individual nerve cells. Only by applying analytical techniques that can resolve neural processes at a cellular level can we develop a realistic and coherent understanding of how the brain works. Studying nerve cells with analytical techniques, however, is necessary but not sufficient for understanding how the brain works (how we think, behave, feel, act, and interact with one another). It is also essential to relate cellular function to behavior.

In the years since *The Neurophysiological Basis of Mind* was published, neural science clearly has not yet fulfilled the promise implied in Eccles' title. We hope to show, however, that neural science is beginning to give insight into some of the most difficult problems of cellular differentiation on the one hand, and some of the most profound problems of behavior on the other. For

example, considering that the brain is made up of a million million ( $10^{12}$ ) cells, it is remarkable how much has been learned about the functioning of the nervous system as a whole by looking at nerve cells one at a time. It has become apparent from cellular studies that the building blocks of different regions of the vertebrate nervous system, and indeed of the nervous systems of all animals, are quite similar. What distinguishes one brain region from another and one brain from the next are the number of building blocks and the ways they are interconnected. Moreover, by applying a cellular approach to different sensory systems of the brain, it is possible to gain insight into how visual and other sensory stimuli are sorted out and transformed at various brain levels and how these regions contribute to perception. These cellular studies show that the brain does not simply replicate the external world or project it onto a tabula rasa, but begins at the lowest levels of the sensory system to abstract and represent reality according to its own rules by encoding it into informational signals. These developments in neural science press upon the borders of experimental psychology. We hope that the merger of neural science and experimental psychology, which we encourage in this text, will in turn lead to further advances in understanding behavior and learning.

The second edition is again designed as an introductory text for students of biology, behavior, and medicine. A major change in this edition is a more extensive treatment of neuroanatomy. The growth of functional neuroanatomy has made it possible both to describe the principles that underlie the anatomical structure of each system of the brain and to discuss each structure in terms of its physiology on the one hand, and its role in behavior and disease on the other.

Our goal in this textbook is to convey the interest and excitement surrounding the application of cell- and molecular-biological techniques to the study of the nervous system, how the brain develops, and how it controls behavior. This text also emphasizes those neurological and behavioral disorders that are both instructive scientifically and important clinically. We have again attempted to be selective and to stress the major principles that emerge from the study of the nervous system without becoming lost in detail. Toward this end we have divided the book into eleven parts, covering the following topics:

1. An overall view of the brain,
2. The cell and molecular biology of the neuron,
3. The mechanisms of synaptic transmission,
4. The anatomical organization of the nervous system,
5. The cellular basis of perception,
6. The control of movement,
7. The brain stem and reticular core,
8. Motivation and homeostasis,
9. Localization of higher cognitive functions, and the disorders of language, thought, and affect,
10. Development and the emergence of behavior, and
11. Genes, experience, and the mechanisms behavior.

In addition, we include an appendix on brain fluids, neuroophthalmology, and a discussion of current flow in neurons together with some practice problems for self study.

Our ultimate aim is to integrate information from experimental studies with practical areas of interest. For the general student, it will be important to see how basic information about the nervous system can be applied to psychology. For the student of medicine, integration with the clinical fields of neurology and psychiatry is of prime importance. Integration with neurology is relatively easy; neurology and neural science have long been interdependent. The bridge to psychiatry is more difficult. Thus far, neural science has taken only rudimentary steps toward understanding the mind. We have therefore tried to provide a systematic introduction to the biological basis of behavior and higher functions. Behavior is one of the last frontiers in biology at which we still stand in relative ignorance. We hope that this text will encourage the student to view behavior with the same combined social and biological perspective that serves so well in other areas of biology and medicine.

The past 35 years have seen splendid progress in the techniques and practice of neurology and psychiatry, but we believe that this textbook would be inadequate if it were only to summarize the information now accumulated that is directly pertinent to clinical practice. We also consider it our responsibility to impart a sense of direction for future developments by introducing students to the most important advances of our times, so that they will be able to evaluate the progress of this field in years to come. For this reason we are not content to consider only those aspects of neural science immediately relevant to neurology and psychiatry, but shall also discuss important scientific developments from current studies of animals that promise to provide a foundation for more effective understanding of normal and abnormal human behavior.

Engraved at the entrance to the Temple of Apollo at Delphi was the famous maxim "Know thyself." Central to enlightened Western culture from ancient times has been the idea that it is wise to understand oneself and one's behavior. Needed not only for clinical application, neural science is required for understanding human behavior, because all behavior is an expression of neural activity. Beyond medicine, in society at large, the problems of crowding, addiction, violence, and war are rooted in the nature of human beings. Any intelligent attempts at solving the enormous problems of human behavior, both individual and collective, must benefit from greater knowledge of neural function. Many of these problems are not yet in the domain of neural science, but progress is rapid and we can hope that neural scientists will soon be able to contribute directly to understand them.

Eric R. Kandel

James H. Schwartz

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