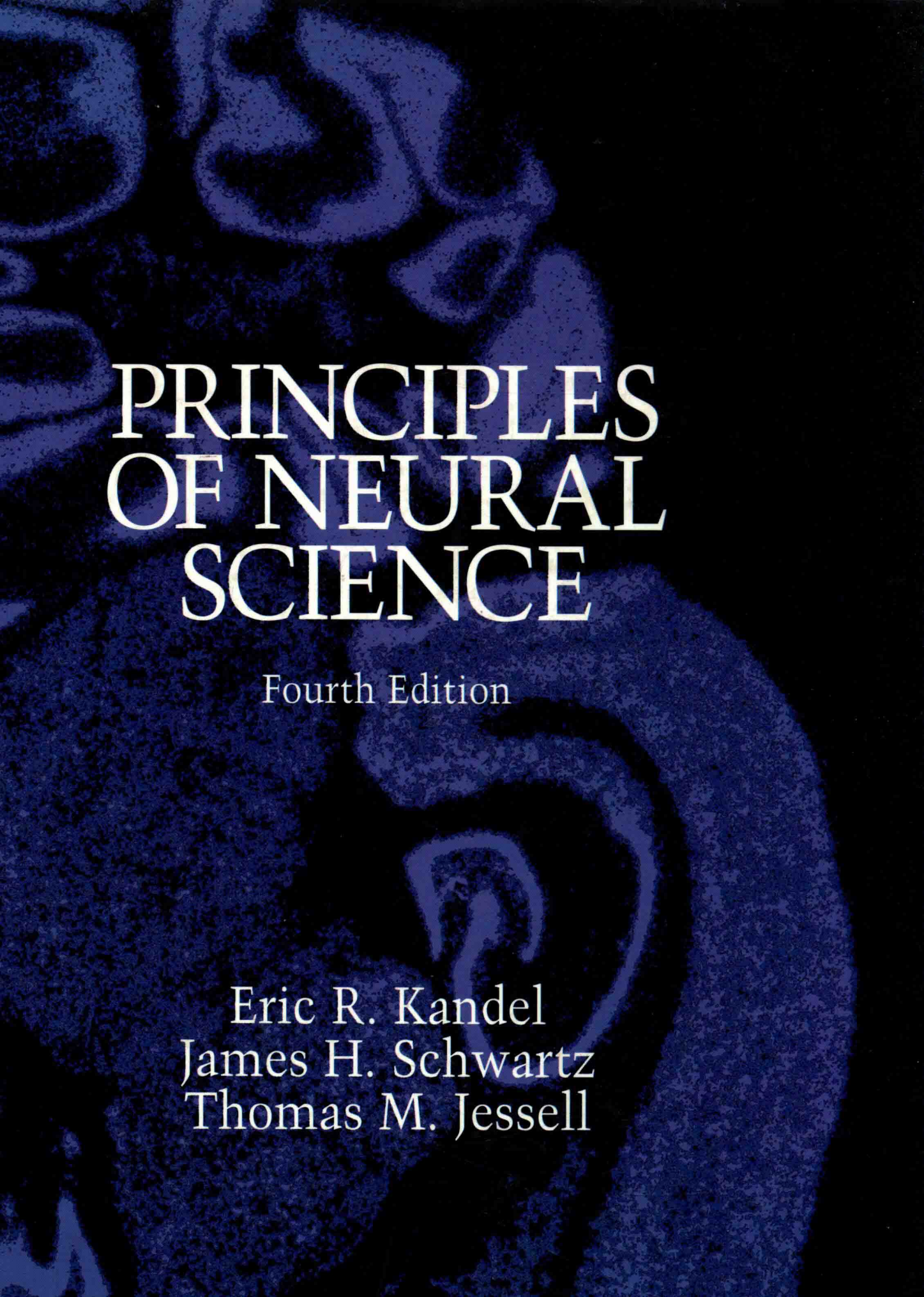

PRINCIPLES OF NEURAL SCIENCE

Fourth Edition

Eric R. Kandel
James H. Schwartz
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Cover image: The autoradiograph illustrates the widespread localization of mRNA encoding the NMDA-R1 receptor subtype determined by in situ hybridization. Areas of high NMDA receptor expression are shown as light regions in this horizontal section of an adult rat brain.

From Moriyoshi K, Masu M, Ishi T, Shigemoto R, Mizuno N, Nakanishi S. 1991. Molecular cloning and characterization of the rat NMDA receptor. Nature 354:31–37.

Preface

The goal of neural science is to understand the mind—how we perceive, move, think, and remember. As in the earlier editions of this book, in this fourth edition we emphasize that behavior can be examined at the level of individual nerve cells by seeking answers to five basic questions: How does the brain develop? How do nerve cells in the brain communicate with one another? How do different patterns of interconnections give rise to different perceptions and motor acts? How is communication between neurons modified by experience? How is that communication altered by diseases?

When we published the first edition of this book in 1981, these questions could be addressed only in cell biological terms. By the time of the third edition in 1991, however, these same problems were being explored effectively at the molecular level.

In the eight years intervening between the third and the present edition, molecular biology has continued to facilitate the analysis of neurobiological problems. Initially molecular biology enriched our understanding of ion channels and receptors important for signaling. We now have obtained the first molecular structure of an ion channel, providing us with a three-dimensional understanding of the ion channel pore. Structural studies also have deepened our understanding of the membrane receptors coupled to intracellular second-messenger systems and of the role of these systems in modulating the physiological responses of nerve cells.

Molecular biology also has greatly expanded our understanding of how the brain develops and how it generates behavior. Characterizations of the genes encoding growth factors and their receptors, transcriptional regulatory factors, and cell and substrate adhesion molecules have changed the study of neural development from a descriptive discipline into a mechanistic one. We have even begun to define the molecular mechanisms underlying the developmental processes responsible for assembling functional neural circuits. These processes include the specification of cell fate, cell migration, axon growth, target recognition, and synapse formation.

In addition, the ability to develop genetically modified mice has allowed us to relate single genes to signaling in nerve cells and to relate both of these to an organism's behavior. Ultimately, these experiments will make it possible to study emotion, perception, learning, memory, and other cognitive processes on both a cellular and a molecular level. Molecular biology has also made it possible to probe the pathogenesis of many diseases that affect neural function, including several devastating genetic disorders: muscular dystrophy, retinoblastoma, neurofibromatosis, Huntington disease, and certain forms of Alzheimer disease.

Finally, the 80,000 genes of the human genome are nearly sequenced. With the possible exception of trauma, every disease that affects the nervous system has some inherited component. Information about the human genome is making it possible to identify which genes contribute to these disorders and thus to predict an individual's susceptibility to particular illnesses. In the long term, finding these genes will radically transform the practice of medicine. Thus we again stress vigorously our view, advocated since the first edition of this book, that the future of clinical neurology and psychiatry depends on the progress of molecular neural science.

Advances in molecular neural science have been matched by advances in our understanding of the biology of higher brain functions. The present-day study of visual perception, emotion, motivation, thought, language, and memory owes much to the collaboration of cognitive psychology and neural science, a collaboration at the core of the new cognitive neural science. Not long ago, ascribing a particular aspect of behavior to an unobservable mental process—such as planning a movement or remembering an event—was thought to be reason for removing the problem from experimental analysis. Today our ability to visualize functional

changes in the brain during normal and abnormal mental activity permits even complex cognitive processes to be studied directly. No longer are we constrained simply to infer mental functions from observable behavior. As a result, neural science during the next several decades may develop the tools needed to probe the deepest of biological mysteries—the biological basis of mind and consciousness.

Despite the growing richness of neural science, we have striven to write a coherent introduction to the nervous system for students of behavior, biology, and medicine. Indeed, we think this information is even more necessary now than it was two decades ago. Today neurobiology is central to the biological sciences—students of biology increasingly want to become familiar with neural science, and more students of psychology are interested in the biological basis of behavior. At the same time, progress in neural science is providing clearer guidance to clinicians, particularly in the treatment of behavioral disorders. Therefore we believe it is particularly important to clarify the major principles and mechanisms governing the functions of the nervous system without becoming lost in details. Thus this book provides the detail necessary to meet the interests of students in particular fields. It is organized in such a way, however, that excursions into special topics are not necessary for grasping the major principles of neural science. Toward that end, we have completely redesigned the illustrations in the book to provide accurate, yet vividly graphic, diagrams that allow the reader to understand the fundamental concepts of neural science.

With this fourth and millennial edition, we hope to encourage the next generation of undergraduate, graduate, and medical students to approach the study of behavior in a way that unites its social and its biological dimensions. From ancient times, understanding human behavior has been central to civilized cultures. Engraved at the entrance to the Temple of Apollo at Delphi was the famous maxim "Know thyself." For us, the study of the mind and consciousness defines the frontier of biology. Throughout this book we both document the central principle that all behavior is an expression of neural activity and illustrate the insights into behavior that neural science provides.

Eric R. Kandel
James H. Schwartz
Thomas M. Jessell

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