

Neuroanatomical Tract-Tracing 3

Molecules, Neurons, and Systems

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Cover illustration: Reconstruction of functional connectivity between neurons based on the temporal coherence of spiking activity recorded extracellularly from the somatosensory cortex of a rat. See Fig. 20.8 on page 666.

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To Sarah Z for her 18th birthday

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Preface

Between the first edition of *Neuroanatomical Tract-Tracing Methods* in 1981 and the current, third edition, neuroscience has witnessed a total transition into the information age. Scientists, whether they wanted it or not, have turned digital. Today, everyone is linked up with worldwide computer communication networks, with local and worldwide digital environments offering vastly increased speed and accuracy of data acquisition and processing. Communication and exchange of information between scientists worldwide is a matter of seconds. The electronic dissemination of research data has become routine. Publication of scientific results has changed from the typewritten manuscript to electronic online submission. Search engines, PubMed-like services, and electronic notification and delivery services are making life more convenient for scientists. *What is not on the Web does not exist.* Do we still need books?

We think positively about books. In the first place, it is common sense to have at hand a printed technical protocol in the setting of a laboratory engaged in experimental neuroscience. Although the workbench protocol does not necessarily have to be a book, it is nonetheless helpful to have a book at hand that not only provides the technical protocol, but also explains why the protocol is designed as it is, what the alternatives are, and what their consequences are. The Web is a wonderful yet particularly fluid medium in which things change very quickly. Data that were here today are gone tomorrow. A book has a longer time constant, which sometimes is beneficial.

The first two editions of the book (Heimer and Robards, 1981; Heimer and Zaborszky, 1989—both published by Plenum Press) had a tremendous impact on neuroscience. They are still among the frequently consulted books in the laboratory. We feel that the moment has arrived to pursue a third, thoroughly updated version of this landmark book, in order to continue the line originated by *Neuroanatomical Tract-Tracing Methods*. The target audience remains the graduate students and young investigators working in the laboratory, seeking fast, complete, up-to-date, and immediately applicable information about techniques, written by acknowledged experts in the field.

Since the last edition, several methods that were in their infancy 15 years ago have become routine, older methods have experienced a renaissance, and newly emerging techniques need validation. Molecular techniques, such as genomics and proteomics, have become established methods, which allow for the study of gene expression of recorded and traced neurons (chapters by Ginsberg, Griffith, Stornetta, and their colleagues). The simultaneous

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development of new fluorescence probes, single- and multiphoton confocal laser scanning microscopes, and vastly increased computer processing power have contributed to a renaissance of fluorescence methods (chapters by Lanciego, Molnar, Reiner, and Wouterlood). In vivo tractography as well as structural and functional imaging techniques allow for the study of the living human brain with a degree of detail never dreamed possible (chapter by Amunts and Zilles). Immunocytochemistry using pre- and postembedding electron microscopy for identifying neuroactive substances still remains an art which has to be tailored to one's needs (chapters by Sesack, Ottersen, and their coworkers). Viral tracers for the analysis of neural circuits have become established in some laboratories (chapter by Geerling and his colleagues). Several chapters briefly discuss how databases help in acquisition, analysis, modeling, and integration of complex cross-scale data sets (chapters by Zilles, Bjaalie, and Nadasdy). Readers interested in these topics are referred to a recently published textbook edited by Koslow and Subramaniam (2005) that summarizes efforts in this field led by the Human Brain Project of the National Institutes of Health.

As neuroscience research progresses, we witness drastic changes in how methods are used. The previous editions of this series reflected the reductionist approach to study neuroscience which was characteristic for the previous century. Even in the second edition, only 2 out of 13 chapters combined techniques that crossed the traditional borders of anatomy and physiology. In the present edition, most of the chapters describe methods, which allow for the integration of molecular, cellular, and system level data, reflecting a holistic-integrative approach to neuroscience in the twenty-first century. Specifically, using sophisticated combinations of tracing methods, the molecular and genetic identity of a neuron (chapters by Ginsberg and his colleagues), as well as the synaptology of any circuitry can be accurately determined (chapter by Sesack and her coworkers). Using extracellular, juxtacellular, and intracellular recordings (chapters by Duque and Zaborszky, and Sik), anatomical features can be correlated with electroencephalographic (EEG), multiunit activity (MUA), local field potentials, and intrinsic membrane characteristics. Recent advances in voltage-sensitive dye imaging (chapter by Petersen) and two-photon calcium imaging (chapter by Goldberg et al.) are promising techniques for studying the spatiotemporal dynamics of hundreds of neurons in the living brain. Sophisticated statistical designs (Avendaño) and expanding computational approaches have the potential to capture full three-dimensional (3D) relations of neuronal and architectonic features of entire brain systems (chapters by Ascoli, Bjaalie, and their colleagues). The last chapter (by Nadasdy *et al.*) predicts that within the next 10 years the complete 3D vectorial database of the rat brain will be available to address specific questions about hidden organization principles of the nervous system. However, these authors also address the gap that exists in our understanding between "structural" and "functional" connectivity (e.g., Friston *et al.*, 1993). We hope that students of this book will bridge this gap eventually, leading to a better understanding of

how the human brain functions in health, aging, and disease. This is our ultimate goal.

ACKNOWLEDGMENT

It has been an honor as well as a pleasure to select contributors for the current edition of *Neuroanatomical Tract-Tracing Methods* and to produce with them this book. However, this book would never have been written without several generations of scientists designing and optimizing the methods discussed in the chapters. Among all those whose shared legacy is the current technological standard, we would like to specially mention the recently deceased **Sanford Palay** (Sandy) (1992), who saw the first synapse using electron microscopy and **Theodor Blackstad** (see, e.g., Blackstad and Bjaalie, 1988) whose contribution was instrumental to computational neuroanatomy as we understand it today. We had the great privilege to work or interact with them. However, we learned the most from our mentors, **Lennart Heimer** and **Enrico Mugnaini**, pioneers in tract-tracing and cellular neuroscience. They were not only mentors and teachers, but friends as well. We dedicate this book to them.

We thank the authors for their contributions and patience during the somewhat lengthy editorial process. They exerted great effort in writing their chapters, and also provided essential feedback by cross-reviewing each manuscript. We are also indebted to Drs. James Tepper (Rutgers University), Harry Uylings (The Netherlands Brain Research Institute), and Rolf Kötter (C. and O. Vogt Brain Research Institute, Düsseldorf) who as external reviewers read earlier versions of some of the chapters. We have the fortune to have on our side Kathleen Lyon, Senior Biosciences Editor of Springer, who spearheaded this edition with great enthusiasm. Last, but not least, we would like to acknowledge Professors Ian Creese and Paula Tallal, codirectors of the Center for Molecular and Behavioral Neuroscience, Rutgers University, for encouragement. The National Institutes of Health (L.Z.) gave generous financial support over many years. Elizabeth Hur, helping the editorial process at Rutgers University, was the first Graduate Student who read and benefited from this book. We hope many will follow.

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