Preface

The application of neurophysiological methods to the study of the brain–behavior relationships represented a major advance to the field of neuroscience when it was in its infancy. Modern neuroscientists now have a great deal more technology available to them than ever before; and consequently the field of neurophysiology has grown considerably. Following a tradition set by the original *Neuromethods* series, this book presents a current view of the widespread application of electrophysiological methods to the study of the brain and to the problem of brain–behavior relationships. The book has been organized to display the research topics to which modern neurophysiological methods have been applied. Such applications range from recordings of single neurons and ensembles of neurons to recordings of field potentials within discrete brain regions to field potential recordings across multiple brain areas.

In the interest of continuity, the present volume begins with a chapter by Stan Leung who contributed to an earlier volume (Volume 15) of the series. The present chapter by Leung describes the basic principles of field potential recording/analysis and current source density (CSD) analysis. Using experimental data as well as model systems of hippocampal pyramidal cells, Leung nicely illustrates the differential patterns of current flow (sources/sinks) along pyramidal cell dendrites and soma to the activation of different segments of the neuron (basal dendrites, soma, proximal or distal regions of apical dendrites), depicting averaged evoked potentials and their derived CSD profiles. Complementing Leung's chapter, Ding, Schroeder, and colleagues (Chen, Dhamala, Bollimunta, Schroeder, Ding) describe an *in vivo* procedure for CSD analysis of ongong, non-triggered, neural activity. The method termed 'phase realigned averaging technique (PRAT)' extracts generally low amplitude signals from continuous streams of activity. The procedure involves parceling, phase realigning, and averaging ongoing activity at select frequencies to determine spatiotemporal properties, such as peak current flow within defined cortical fields from awake animals. Among other things, the method allows for a determination of the relationship of endogenous activity (e.g., alpha rhythm) to behaviorally relevant events, such as sensory or motor responses to external stimuli.

The chapter by Pinault describes a technique that permits the discrete labeling of individual neurons during simultaneous extracellular recording, an important tool for defining the discrete connectivity of neurons whose physiological properties have been identified. Four chapters, those from Fenton, Jeffery and Donnett; Kuang and Tsien; Hampson, Simeral, Berger, Song, Chan and Deadwyler; and Stackman provide details of new strategies that apply to *in vivo* single-unit recording from freely moving rodents. Fenton, Jeffery, and Donnett present the challenges that face the design of wireless recording systems. They describe the advantages of their new digital telemetry (DT) system over other analog wireless systems and outline two applications for DT – tetherless recordings from freely moving rodents during truly unrestricted behavioral performance and an epilepsy monitoring system for use in humans. Kuang and Tsien's chapter addresses two of the exciting challenges emerging in the field, that of how to acquire high-density ensemble neuronal activity from wild type and genetically engineered mice, and second, how to analyze these data. The chapter by Stackman addresses the inherent challenges of relating neuronal firing patterns of limbic neurons to distinct behavioral sequences. The chapter focuses on the rodent head direction cell as a model system to delineate the degree to which directional correlates of single-unit activity relate to spatial navigation.

In a computational vein, the chapter by Bressler is devoted to event-related potentials (ERPs) while that by Albo and colleagues (Albo, Viana Di Prisco, Vertes) examines spike–field interactions. As Bressler points out, local field potentials (LFPs) recorded with depth electrodes (intracortical) are 1–2 mV in amplitude, whereas those recorded from the scalp (e.g., EEG recordings in humans) are 10–50 mV in amplitude. The latter generally requires special procedures for detection and analysis, particularly if internally or endogenously generated. The chapter by Bressler, then, provides an in-depth description of various procedures for characterizing event related potentials (triggered and non-triggered), with special attention to state of the art time and frequency domain analytical methods that are particularly useful in situations in which standard ensemble averaging techniques may be inappropriate. The chapter by Albo et al. describes current methods for unit-field (and field-field) analysis, or the application of spike-field coherence techniques to the study of unit-field oscillations. The chapter provides a nice overview of the advantages/disadvantages of various approaches to assessing functional interactions among synchronously occurring signals (spike trains and field potentials) across the brain. As a direct application of some of the techniques, they describe their findings showing a three way interaction (coherence) between theta rhythmic units in the anterior thalamus and theta oscillations in the hippocampus and retrosplenial cortex, suggesting that hippocampus may drive the anterior thalamus, which in turn rhythmically paces the retrosplenial cortex, with implications for the role of theta in limbic functions.

Recording from ensembles of hippocampal neurons (15-35 cells of CA1/CA3), Deadwyler, Berger, and colleagues (Hampson, Simeral, Berger, Song, Chan, Deadwyler) describe a "closed loop system" which distinguishes among the separate behavioral components of a two choice delayed nonmatch to sample (DNMS) task, and then uses ensemble activity at phases of the task to both predict choice behavior and modify it during task performance. In effect, ensemble activity (or codes) was used to adjust delay times (between sample and choice) during ongoing trials to improve performance *on those trials.* Specifically, depending on the relative strength (or efficacy) of the ensemble code in the sample phase of the task, the delay between sample and nonmatch task phases could be shortened or lengthened, thereby improving performance. It is well recognized that the septum and hippocampus are strongly interconnected and together serve as a functional unit generating the hippocampal theta rhythm. Theta serves a well-recognized role in mnemonic functions. In a major advance in examining septo-hippocampal interactions, Williams and colleagues (Goutagny, Jackson, Williams) have developed a remarkable *in vitro* preparation in which the septum and hippocampus are simultaneously dissected (with connections between them intact) and kept viable for at least 8 h. In addition, with a barrier placed between them, the two structures can be independently manipulated to assess the effects of one on the other. Using this preparation, Williams and colleagues have confirmed the pronounced septal influence on the hippocampus in the modulation of theta, and further showed that hippocampal theta activity, in turn, exerts a strong driving influence on the septum. Helen Mayberg is a pioneer in the use of deep brain stimulation (DBS) to treat depression. The chapter by Mayberg and Holtzheimer begins with a review of background material (mainly imaging studies) that led to the use of DBS for major depressive disorders (MDD). In effect, they (and others) found that certain regions of the frontal cortex, such as the subcallosal cingulate cortex (SCC) were hyperactive in MDD, whereas other areas such as dorsolateral prefrontal or posterior cingulate cortices were hypoactive in MDD, and that successful antidepressant treatment normalized activity in these regions. This suggested a critical role for the frontal/prefrontal cortex (particularly the SCC) in MDD. Mayberg and Holtzheimer proceed to describe in detail the specific procedures used for DBS of the SCC and summarize the extremely promising results that have been obtained to date with the technique with two groups of patients with treatment resistant depression. DBS is not only a cutting edge procedure for the treatment of depression, but also used in conjunction with other methods and has the potential to define an extended circuitry responsible for MDD.

It is daunting to take on the challenge of describing the "current" state of any field of science. This is especially the case for neurophysiological techniques since this area is in a near constant state of improvement. This collection of chapters provides a clear indication of how modern technological advances have influenced the study of the neurophysiological substrates for behavior. As one will find in reviewing this volume, current challenges in electrophysiological techniques will most certainly be conquered by the next generation of improvements in technology and analysis.

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