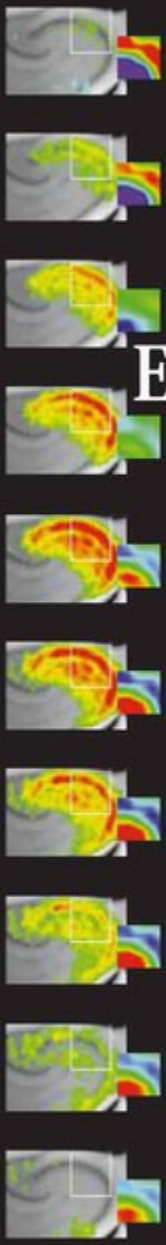

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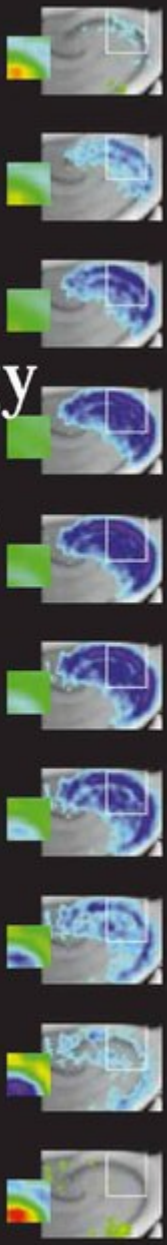

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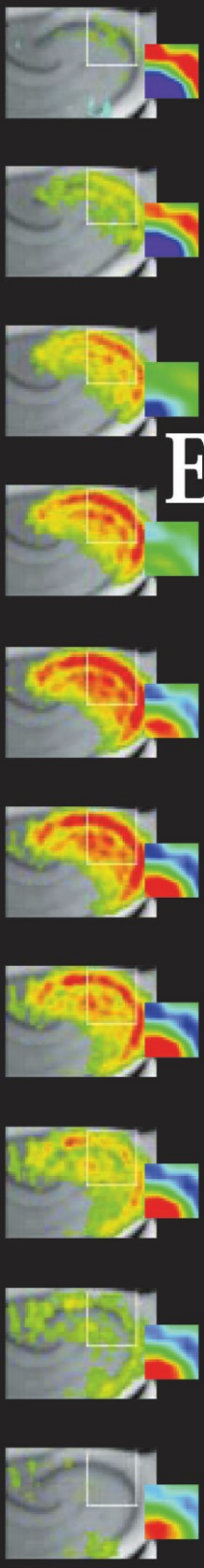

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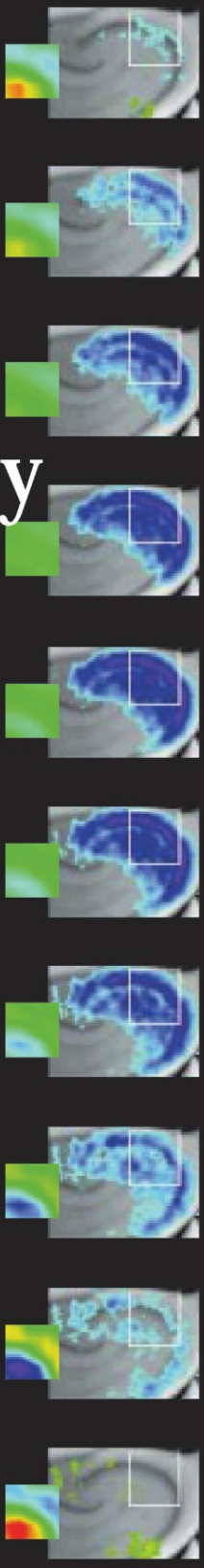

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Using Multi-Electrode Arrays

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Preface

While considerable progress has been made over the last decades in our understanding of electrophysiological processes at the single channel, single synapse and single neuron levels, our understanding of electrophysiological processes at the neuronal network level is still in its infancy. This is in large part due to the technical difficulties of recording electrical activity from large numbers of neurons simultaneously and for prolonged periods of time. Although the first multi-electrode device was built in the mid-1970s, the field of network electrophysiology has only recently started to make significant contribution to our understanding of complex brain operations and functions. These recent advances have been the results of progress in electronic technology, providing for new devices capable of stimulating and recording from large numbers of neurons, as well as advances in the computational methods required to store and analyze the enormous amount of data generated by the new devices. This book is an attempt to review the recent progress in both electronics and computational tools developed to analyze the functional operations of large ensembles of neurons and to provide the readers a sense of the applications made possible by these technological tools. As this field is rapidly growing and evolving, it was difficult to select the contributors and the topics to include in this volume. Instead of being exhaustive, we decided to remain more focus, and to limit the reviews to three general topics.

The first section places the emphasis on the technological development of multi-electrode arrays (MEAs) and related electronics and software. In the first Chapter, Jerome Pine reviews the relatively brief history of MEAs. Chapters 2 and 3 are written by two groups of scientists who have been and continue to be involved in developing commercially available MEA instruments. While Fejtl, Stett, Nisch, Boven, and Möller describe mostly the hardware and software of their instruments in Chapter 2, Whitson, Kubota, Shimono, Jia, and Taketani focus more on the MEA applications and discuss why researchers use MEAs (Chapter 3). This section also includes more recent developments of new MEA devices. Heuschkel (Chapter 4) describes an array of spiky 3D microelectrodes which should improve recording in acute slices by reducing the distance between the cells and the recording electrodes, and should allow better measurement and stimulation conditions than with planar electrode arrays. Hakkoum, Muller and Stoppini (Chapter 5) describe a MEA built

on a porous membrane or onto a permeable support that can be used to conduct long-term electrophysiological studies applied specifically to 3-D interface-type organotypic cultures. Soussou et al. (Chapter 6) illustrate the utility and advantages of MEAs in electrophysiological investigations with acute hippocampal slices, while introducing a new generation of conformally designed higher-density MEAs as an adjuvant approach to facilitate and enhance MEA-based research. Finally, Chang and Wheeler (Chapter 7) discuss their attempt to build neuronal networks on MEAs.

The second section of the book reviews a number of applications of the MEA technology to dissociated cell cultures. Dissociated cultures have been favorite specimens for MEAs since the early days of the technology and recent studies using these preparations have provided a much deeper understanding of the properties of neuronal networks. The ability to record and stimulate neuronal activity for long periods of time in cultured neurons and myocytes has provided a unique tool for testing chronic effects of drugs on network physiology. First, Gross and Gopal (Chapter 8) provide evidence that networks prepared from different tissues from the murine CNS have different native activity states and may also differ quantitatively in their pharmacological responses, although these responses remain similar to what is observed in vivo. Potter and colleagues (Chapter 9) describe their interesting technologies that allow recording and stimulation on every electrode of an MEA, and a new closed-loop paradigm that brings in vitro research into the behavioral realm, as they embody their networks in Neurally-Controlled Animats. The whole system of MEA culture plus embodiment thus becomes a "hybrot," because it is a hybrid robot with both living and artificial components. Finally, Guigliano and his collaborators (Chapter 10) review their work related to the analysis and the modeling of the development of neuronal activity in cultured cortical neurons. They make the remarkable observation that it is relatively easy to mathematically capture the essential features of the synaptic interactions in the network and to model the behavior of these networks. Chapter11 is the only non-CNS chapter of this book, where Egert, Banach and Meyer discuss the use of MEAs with cardiac myocytes to understand the dynamics of these special types of networks.

Brain tissues, on the other hand, used to be difficult targets for MEA observation despite the fact that the tissues preserve intact structural relationships between groups of cells and should thus provide fruitful information of brain networks. The third section proves that this is no longer true. The first four chapters of the section review the use of MEAs to identify or classify drugs based on the pattern of modifications of spontaneous or evoked electrical responses elicited in various networks. Gholmieh and colleagues (Chapter 12) summarize their successful efforts to build a hippocampal-based biosensor for neurotoxin detection and classification. They combine the use of MEAs with a mathematical analysis of the input/output functions performed by hippocampal networks while classification is performed by an artificial neural network. Guenther et al. describe a preparation of the vertebrate retina on microelectrode arrays they use to record local electroretinograms in vitro (Chapter 13). They then show that this so-called retinasensor is a suitable in vitro