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## Preface

### Methods for Probing Synaptic Plasticity: Evolution and Revolution

Synapses in the nervous system are capable of a wide range of physiological and structural modifications following both artificially imposed and naturally occurring regimens of chemical and electrical activation. These alterations constitute “synaptic plasticity,” and they are a central focus of modern neuroscience research. Investigations involving incisive mechanistic dissection of various types of synaptic plasticity have revealed that they play key roles in neural development, sensory information processing, cortical remapping following brain injury, perception, and behavioral learning and memory. Conversely, disruptions of synaptic plasticity may underlie neurological and behavioral disorders such as Alzheimer’s disease, Fragile-X syndrome, autism spectrum disorder, and drug addiction. In short, synaptic plasticity underlies the unique ability of the nervous system to adapt itself to cope with internal and external challenges. Not surprisingly, research on the mechanisms of synaptic plasticity holds considerable promise for increasing our understanding of brain function and dysfunction. This research, like much of current neuroscience, embraces methodologies that are truly multidisciplinary. It is now *de rigueur* to use multiple techniques, gleaned from a seemingly disparate range of scientific disciplines, to address key questions in synaptic plasticity.

The substantial advances that we have witnessed in research on synaptic plasticity owe much to technical achievements accomplished mostly in the second half of the twentieth century. In my view, these accomplishments can be grouped under three categories. First, the development of gel electrophoretic separation of proteins [1–2] and the creation of genetically modified (transgenic and knock-out) mice [3–8] have enabled the identification of functions for specific genes and proteins within identifiable brain regions and synaptic circuits. Indeed, a very substantial portion of past and present research on synaptic plasticity has focused on mapping out the intricate molecular signaling components that underlie specific forms of activity-dependent synaptic plasticity, such as long-term potentiation (LTP) and long-term depression (LTD). Second, the invention of confocal microscopy by Marvin Minsky [9] led to the further development and emergence of more advanced optical imaging techniques, such as two-photon laser scanning microscopy [10], that can track the spatial and temporal dynamics of chemical signaling within single dendritic spines and glial processes in *living* brain tissue. Lastly, and from my own perspective as a cellular electrophysiologist, the most critical technical achievement to have influenced the trajectory of research on brain plasticity is the development of *ex vivo* brain slice preparations by Henry McIlwain and his colleagues [11–12]. This innovation, coupled with the use of microelectrode technologies, enabled electrophysiological investigations of synaptic signaling in semi-intact brain circuits that can be extracted from defined subregions of the mammalian brain and kept alive *ex vivo*. Without brain slices, our knowledge of synaptic physiology would have been greatly diminished. It should be noted that by themselves, these



use brain slice preparations. In the first chapter, Tom O'Dell and Erin Gray describe the hippocampal CA1 slice preparation, and highlight the potent utility of this slice for micro-electrode- and biochemically-driven investigations of glutamate receptor signaling during synaptic plasticity. Then Richard Morris and Roger Redondo present their modifications of hippocampal slice maintenance techniques to show how viable recordings of LTP can be accomplished many hours after slice preparation. They present their findings in the context of exploring synaptic and behavioral "tagging," processes believed to contribute to some forms of associative learning in rodents. Richard Robitaille and Aude Panatier then present cellular loading and optical imaging approaches for probing calcium signaling in astrocytes within hippocampal slices. When combined with patch-clamp recording, these techniques provide a very finely resolved window on synaptic transactions occurring between neurons and glial processes in a slice preparation. Melanie Woodin's chapter focuses on probing inhibitory synaptic transmission, an often-neglected area that is overshadowed by research on excitatory synapses. A chapter by Qi Yuan and her colleagues is presented to highlight the use of *in vivo* imaging in a simplified mammalian slice preparation, containing olfactory circuitry, that can be used to probe electrophysiological correlates of olfactory learning in young rat pups. There may now be a rebuttal against those who claim that invertebrates have a monopoly on "simple" nervous systems! Lastly, a chapter by Gregory Funk and Nicholas Mellen describes a rat hindbrain slice preparation that can be used to explore signaling in neural circuits directly relevant for generating respiratory rhythms. It has the potential for revealing forms of synaptic plasticity that may importantly modify respiratory rhythm generation under various physiological and pathological conditions. These six chapters highlight the evolving state of potent research strategies that are centered on the use of brain slice preparations.

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*Edmonton, AB, Canada*

*Peter V. Nguyen*

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