PREFACE

The seminal work by Ralph Adams and co-workers in the early 1970s applying microelectrodes to the electrochemical detection of neuroactive substances made possible their monitoring in real time in the rodent brain. Thus, along with oxygen and ascorbate, catecholamines such as dopamine, norepinephrine, and serotonin were detected by employing an implantable electrode. The invention of the carbon fiber microelectrode by François Gonon and coworkers in the 1970s, the introduction of fast-scan cyclic voltammetry by Julian Millar and coworkers in the 1980s, and their combination and ceaseless refinement by Mark Wightman and coworkers to the present day has enhanced the sensitivity, selectivity, and temporal and spatial resolution of the *in vivo* voltammetric approach.

The repertoire of target analytes was expanded by the development of biosensors in the 1990s and early 2000s compatible with real time measurements in the brain. These include biosensors for glucose, lactate, glutamate, acetylcholine/choline, ATP, and adenosine. In addition, reactive oxygen and nitrogen species such as $\bullet O_2^-$, H_2O_2, NO, and $ONOO^-$ are electroactive and can be detected, although reliable measurements are challenged by low concentrations and transient existence.

In this volume the authors have consistently addressed the question, "Now that we have a series of monitoring tools, what can we learn using them?" Answering the question of the role of a particular analyte immediately raises the issue of how to account for time-dependent changes in concentration in response to a stimulus, the application of a pharmacological agent, changes in behavior, or in various animal models of disease. A challenge is to be able to measure more than one parameter at a time: concentrations of two different analytes, physiological parameters such as EEG activity or the frequency of cell firing. Increasingly, behavioral parameters are also correlated with changes in neurotransmitter concentration fluctuations. With the recent contributions of Kendall Lee, Paul Garris, Charles Blaha, and others, translation of electrochemical measurements to the human brain is under way.

As usual, research generates more questions than answers. More information acquired simultaneously is needed and the role of neuroactive peptides has been

scarcely scratched. While implanting a sensor in brain tissue has the obvious advantage of good time and spatial resolution and provides species-specific information, it is an invasive process and we are just beginning to understand the effects of tissue alteration in the vicinity of the implant due to tissue disruption and inflammatory response. To understand chronic effects, it will be necessary to have sensors that can survive for extended periods of time in tissue. New opportunities continue to appear on the horizon: the coupling of *in vivo* monitoring to optogenetic stimulation, for example, has already cast new light on the regulation of dopamine release by cholinergic interneurons of the striatum. This is illustrated graphically on the book cover with a drawing taken from Chapter 9 by Cragg and co-workers.

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