this book is well worth reading—and may even be enjoyed—by a broad spectrum of scientists and engineers, thoughtful bureaucrats, and politicians.

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Advances in Neurochemistry

Monitoring Neurotransmitter Release during Behavior. M. H. JOSEPH, M. FILLENZ, I. A. MACDONALD, and C. A. MARSDEN, Eds. VCH, Deerfield Beach, FL, and Horwood, Chichester, U.K., 1986. 270 pp., illus. $57. Ellis Horwood Health Science Series. Based on a meeting, Oxford, U.K., Sept. 1984.

Neurochemical Analysis of the Conscious Brain. Voltammetry and Push-Pull Perfusion. ROBERT D. MYERS and PETER J. KNOTT, Eds. New York Academy of Science, New York, 1986. xii, 560 pp., illus. $40. Annals of the New York Academy of Sciences, vol. 473. From a symposium, New York, April 1985.

These two volumes focus on methodological advances that open up new opportunities for neurochemistry: the development of new methods of collecting extracellular fluid from brain and the application of electrochemistry to the detection of neurotransmitters.

Traditional neurochemical methods applied to postmortem tissues have been extremely useful in characterizing the static condition of the nervous system. However, because such measurements can be made at only a single time point per animal, they have been of limited use for relating neurochemical events to functional changes in physiology and behavior. Measurements of metabolite concentrations and turnover provide some insight into dynamic changes, but many animals have been needed to provide a time course, and individual differences in time courses are lost. Furthermore, measurements of biogenic amines in tissues cannot give a direct indication of neurotransmitter release, the variable often the most relevant with respect to function. Measurement of biogenic amines in plasma, urine, and cerebrospinal fluid has been of some assistance in these regards, but such measures are, at best, indirect indicators of neurotransmitter availability at target cells. Moreover, biochemical methods generally have been too insensitive for direct measurements on extracellular fluid. Although measurements of changes in electrical potential can provide the necessary time resolution, the neurochemical bases of electrophysiological changes often are difficult to determine, and release and neuronal firing rate may not always covary.

The problem, then, has been a technical one—how to measure the relevant variables with sufficient sensitivity and in freely moving animals. These monographs deal with both issues.

At the heart of the matter is the application of electrochemistry to the measurement of biogenic amines and their metabolites. When exposed to carbon electrodes poised at the appropriate voltages, these compounds undergo an oxidation to the quinones or quinone-imines. The number of electrons passed at the electrode surface during such an oxidation provides an index of the concentration of the biogenic amine. Such carbon electrodes can be used to detect and quantify these oxidizable compounds as they elute from a high-performance liquid chromatographic (HPLC) column. With the right conditions, detection in the low picomole range is possible.

The application of electrochemistry to measurements of biogenic amines has developed largely from work of Ralph Adams at the University of Kansas. Over the past several years, the work of Adams and others has led to three additional developments: analysis of ever smaller samples of tissue and plasma, analysis of extracellular fluid collected from brain regions by perfusion or dialysis probes, and direct monitoring of transmitter release via intracranial microelectrodes. We will comment briefly on the second and third of these.

The idea of brain perfusion was introduced nearly 30 years ago by Feldberg, Gaddum, and others. This approach has reached its most advanced state with extremely small push-pull perfusion systems and with the development of intracerebral dialysis. In the latter technique, tiny sections of dialysis tubing are implanted in specific brain regions and a solution is slowly infused. This perfusate equilibrates with extracellular fluid, and analysis of its contents can then provide an index of the concentration of specific substances in extracellular fluid. The development of this approach owes much to Urban Ungerstedt at the Karolinska Institute, whose innovative work in histology, pharmacology, and behavior had already left its mark on the field.

The alternative to perfusion is the use of miniature carbon electrodes that can be implanted directly into the brain. In theory this should permit the direct monitoring of extracellular fluid. The problem, however, has been that, in the absence of the chromatographic separation, all the specificity must be provided by the electrode. At first many of the electrodes that were used responded to a multitude of compounds, leading to much debate about the exact nature of the species being detected. During the past few years, however, there has been considerable progress in the development of more specific electrodes, including electrodes coated with anion-suppressing substances (Adams; Blaha and Lane), carbon fiber microelectrodes and the application of special scanning techniques (Wightman; Kruk), and electrolytic pretreatment of microelectrodes (Ganon).

All the principal researchers mentioned above are represented in these two valuable volumes. In *Monitoring Neurotransmitter Release during Behavior* the section on investigations of the central nervous system, which occupies almost half of the book, contains a number of particularly interesting contributions from groups that have pioneered the use of these techniques, among them those of Bradford, Curzon, Fillenz, Freed, Marsden, and Ungerstedt. The initial chapter of this section, by Maidment *et al.*, serves as an introduction to intracerebral dialysis and voltammetry, and a final commentary by Korf provides a useful summary of the various approaches currently being used.

A separate section contains papers dealing with the sympathoadrenal system. Hjemdahl provides a review of the variables involved in HPLC measurements for assessing sympathetic activity through measurements of adrenergic activity, and Landsberg and Young discuss measurements of catecholamine turnover. The volume concludes with reports from workshops on recent developments in HPLC analysis and in vivo monitoring techniques. Of particular interest is the description by Kruk of fast-scan cyclic voltammetry, which is becoming an important technique for use with in vivo electrochemistry.

Neurochemical Analysis of the Conscious Brain focuses exclusively on the analysis of the extracellular fluid. The introductory section includes a plenary lecture by one of the "fathers" of perfusion techniques, Feldberg, as well as several overviews: push-pull perfusion systems in awake animals by Meyers, voltammetry in the brain by Adams, application of voltammetry to central nervous system pharmacology by Lane and Blaha, and electrophysiological recordings made in freely moving animals by Jacobs.

The second section of the book focuses on analysis of the brain's catecholaminergic systems. In addition to several papers on voltammetry and push-pull perfusion, there is a paper by Marsden *et al.* on intracerebral dialysis. Later sections focus on factors influencing the release of catecholamines, serotonin, peptides, and amino acids. Bio-

chemical, pharmacological, and behavioral issues are included. Papers representing posters presented at the meeting from which the book derives conclude this excellent summary of voltammetry and perfusion systems and their limitations.

As described in both volumes, voltammetry and perfusion techniques coupled with HPLC and electrochemical detection have developed significantly over the last five years and, as predicted, are providing information on the dynamics of transmitter systems that was not previously available. Many issues remain to be resolved, including electrode specificity, perturbation of brain tissue by the probes, the relationship between probe sensitivity in brain tissue and beaker calibration, and the isolation of probes by encapsulation of glia cells. However, these matters are receiving considerable attention, and congruence among results obtained is beginning to emerge. The technology is coming of age.

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