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Patch-Clamp Analysis

NEUROMETHODS

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Advanced Techniques

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Preface to the Series

When the President of Humana Press first suggested that a series on methods in the neurosciences might be useful, one of us (AAB) was quite skeptical; only after discussions with GBB and some searching both of memory and library shelves did it seem that perhaps the publisher was right. Although some excellent methods books had recently appeared, notably in neuroanatomy, it was a fact that there was a dearth in this particular field, a fact attested to by the alacrity and enthusiasm with which most of the contributors to this series accepted our invitations and suggested additional topics and areas. After a somewhat hesitant start, essentially in the neurochemistry section, the series has grown and will encompass neurochemistry, neuropsychiatry, neurology, neuropathology, neurogenetics, neuroethology, molecular neurobiology, animal models of nervous disease, and no doubt many more "neuros." Although we have tried to include adequate methodological detail and in many cases detailed protocols, we have also tried to include wherever possible a short introductory review of the methods and/or related substances, comparisons with other methods, and the relationship of the substances being analyzed to neurological and psychiatric disorders. Recognizing our own limitations, we have invited a guest editor to join with us on most volumes in order to ensure complete coverage of the field. These editors will add their specialized knowledge and competencies. We anticipate that this series will fill a gap; we can only hope that it will be filled appropriately and with the right amount of expertise with respect to each method, substance or group of substances, and area treated.

Alan A. Boulton
Glen B. Baker

Preface

Neher and Sakmann were the first to monitor the opening and closing of single ion channels in the membranes of cells by conductance measurements. In 1976, they used firepolished micropipets with a tip diameter of 3–5 μm to record currents from a small patch of the membrane of skeletal muscles, thereby decreasing background membrane noise. In order to reduce the dominant source of background noise, the leakage shunt under the pipet rim between membrane and glass, the muscle membrane had to be treated enzymatically. Despite these early limitations, a new technique was born—the patch-clamp. The final breakthrough came in 1981 when the same workers, in collaboration with Hamill, Marty, and Sigworth, developed the gigaohm seal. Not only did this improve the quality of recordings, it was now possible to gently pull the membrane patch with the attached pipet off the cell and study its trapped ion channels in isolation. Another offshoot of the gigaohm seal technique was the whole-cell patch-clamp technique, in which the path is ruptured without breaking the seal. This technique is really a sophisticated voltage-clamp technique and also allows for the altering of cytoplasmic constituents if the experimenter so wishes.

The first part of this treatise on *Patch-Clamp Analysis: Advanced Techniques* presents modern developments associated with the basic patch-clamp techniques outlined above. These chapters are supplemented with information on the newest developments in fast external solution switching to study fast inactivating responses as well as the switching of the pipet solution during recordings. The application of the patch pipet technique not only to clean membrane preparations, but also to brain or other tissue slices, was an important development in the last decade. Other offshoots of the patch pipet technique are the loose patch, the perforated patch, as well as the recording from macropatches and the patch-cram detection technique. These are all introduced and described in detail. Perhaps the recent developments in the patch-clamp field with the biggest impact are the combination of two of the most powerful life science technologies: molecular biology and imaging. This led to the intertwining of the patch pipet with RT-PCR and fluorometric techniques.

The methods associated with the patch pipet are certain to become even more refined in the future, as new applications involving genomics, proteomics, and sophisticated imaging techniques emerge.

Wolfgang Walz
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