

## Preface

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Since the pioneering discoveries of Hodgkin, Huxley, and Katz, it has been clear that specific ion conductance pathways underlie electrical activity. Over the ensuing 50 years, there has been ever increasing, and occasionally explosive, changes in the scope of efforts to understand ion channel behavior. The introduction of patch clamp technology by Erwin Neher and Bert Sakmann about 20 years ago led to the realization of the great variety of novel ion channel species, and the subsequent revolution in cloning has revealed an even greater diversity of the underlying molecular entities.

Today, advances in the study of ion channel structure and function continue at a high pace, from angstrom resolution imaging of crystallized channels to their genetic manipulations in animals. In this regard, the field is a balanced one that inquires not only *what* ion channel entities are there, or how they operate, but also *where* are these molecular electronic switches? However, this balance is not particularly well presented to the general scientific audience or to specialists in the field. There are plenty of wonderful and useful books and monographs, as well as conferences and meetings on virtually every aspect of ion channel structure and function. However, we are unaware that the channel localization theme has been considered in a unified forum. In *Ion Channel Localization: Methods and Protocols*, therefore, we have invited leading specialists to contribute to a comprehensive review of methods in ion channel localization, to bring together in a single collection different aspects of the versatile potentials of today's technologies.

Pharmacological tools for ion channel localization are the core topics of the book. They have offered, and will continue to offer, probably the most specific way of localizing channels and receptors beyond and in addition to what can be accomplished by immunochemical and other technologies. Part I of the book deals with both fluorescent and radioligand applications of pharmacological tools. In Part II readers will find a detailed description of methods employing green fluorescent protein (GFP), a novel tool that is now facilitating an explosion of research in many areas, including the mapping of ion channels and receptors. We hope readers will find here the "exciting" part of the technology as well as warnings of pitfalls and data misinterpretation. In Part III of the book we have attempted to pull together

assays in ion channel localization that utilize their functional properties, i.e., ion conduction, as a marker of their localization. Though channel function can only be found where there is underlying channel protein, the reciprocal is not necessarily true. The search for where active channels are to be found is the true goal of many localization studies, and this ultimately requires a function-based assay. Atomic force microscopy is a potentially revolutionary tool for understanding localization and organization in virtually every field of biological research, including ion channels. Detailed description of this technology and its application to ion channel localization, as well as discussion of some pioneering studies and perspectives, are considered in Part IV.

The potential scope of *Ion Channel Localization: Methods and Protocols* is enormous, and various aspects relevant to the issue of channel localization are not considered in detail. Standard techniques of molecular biology and protein biochemistry, including descriptions of immunochemical technology of antibody labeling, epitope tagging, biotinylation, in both fluorescent and radiolabeled versions, and electron microscopy are discussed elsewhere in detail (*see Immunochemical Protocols*, J. Pound, ed. and *Electron Microscopy Methods and Protocols*, M. A. N. Hajibagheri, ed. *Methods in Molecular Biology* series).

We would like to give our sincere thanks to all of the specialists who have contributed chapters to the book. It has been a pleasure and a privilege to work with them. We hope that the outcome will be useful to researchers interested in the localization of ion channels in cells, tissues, and organisms.

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