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Book Review

“Patch Clamp Electrophysiology Methods and Protocols,” Editors Mark Dallas and Damian Bell

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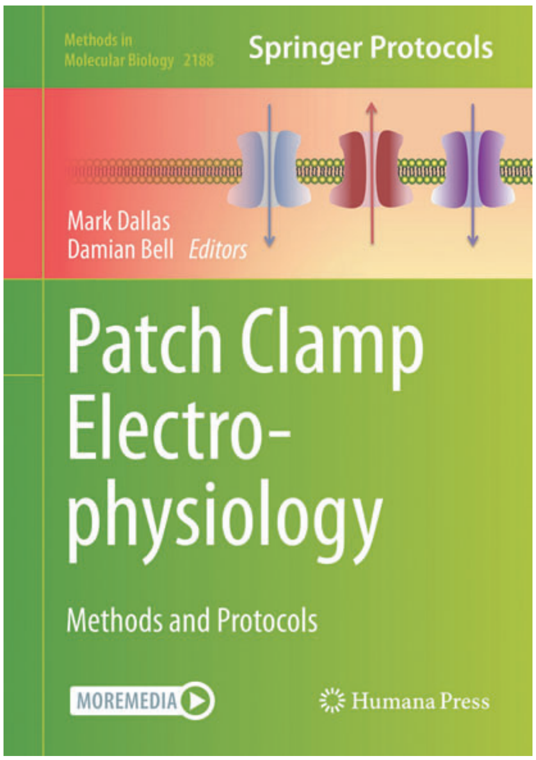

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In their seminal work in the 1950s, Alan Hodgkin and Andrew Huxley used glass electrodes to record intracellularly from the squid giant axon and provided the first prediction of the key ionic conductances underlying the action potential in excitable cells. However, it was not until the early 1980s that Bert Sakmann and Erwin Neher developed the patch clamp technique, which enabled, for the first time, direct and real-time measurement of ion channel function, even at the level of single proteins, as well as exquisite characterization of pharmacological and biophysical properties. In recognition of this pivotal achievement, Neher and Sakmann in 1991, like Hodgkin and Huxley earlier, were awarded the Nobel Prize in Physiology or Medicine. Forty years have now passed since the patch clamp technique was first developed. Over this period, building on these prior successes, our understanding of the multiplicity of ion channels and their structural and functional diversity has grown almost beyond recognition. The patch clamp technique has since been further developed and refined, scaled up and automated for high-throughput analysis, and combined with other powerful electrophysiological, imaging, and genetic approaches.

The gold standard go-to textbooks for young physiologists embarking on patch clamping and electrical signaling for the first time continue to include, among others, Bertil Hille’s *Ion Channels of Excitable Membranes* (now in its third edition), Neher and Sakman’s own edited volume on *Single-Channel Recording* (in its third edition), The Plymouth Workshop Handbook, *Microelectrode Techniques*, as well as the venerable *Axon Guide*. Although all of these are as indispensable and relevant today as when they were originally written, as the field of cellular and subcellular bioelectricity has continued to grow conceptually, some kind of a technical update has been keenly awaited. The purpose of this important new technical textbook is to provide such a timely update to the field, complementing and extending the original volumes. The focus has been to bring the reader up to speed regarding critical advances in the field as well as to introduce new methodologies. For new electrophysiologists and more experienced ion channel researchers alike, this new book provides a refreshingly accessible and much needed update.

One of the key advances of the past 20 years has been the development of high-throughput patch clamp systems and associated automation of the recordings. Of course, this cannot fully replace the low-throughput high-fidelity single-cell patch clamp approach for certain key applications, for example, for interrogating ion channel function in specific subcellular domains and organelles. Nonetheless, multiwell planar patch clamp systems have become critically important as platforms for high-throughput screening of large compound libraries, an important topic covered in this book. In contrast, pioneering updates to glass microelectrode approaches have enabled researchers to now record from distinct microdomains, including presynaptic terminals and dendrites, for example. Another important example covered in the book is the exciting and rapid development of optogenetic tools to manipulate ionic conductance and membrane potential, together with how this can be combined with patch clamp recording both *in vitro* and *in vivo*.

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In this methods in molecular biology series volume, ''Patch Clamp Electrophysiology Methods and Protocols,'' the editors Mark Dallas and Damian Bell have assembled an impressive anthology of 45 authors, who have themselves produced an outstanding set of 16 chapters introducing and updating the patch clamp electrophysiology field. The composition of the volume nicely reflects the paradigm shift since the 1990s to turnkey systems that no longer require detailed knowledge of electronic circuitry underpinning the approach. Indeed, the emphasis has shifted somewhat toward patch clamping being a tool integrated into a wider suite of techniques used to investigate a specific biological problem.

Each chapter, with its own list of references, consists of a helpful introduction providing background and context to the method for the nonexpert, followed by detailed step-by-step protocols (including equipment and reagent lists) to enable the readers to set up each technique in their own laboratory. Example experiments and real-world data are also provided, facilitating understanding of the data acquisition and analytical approaches required for each technique. The volume covers a useful array of core and emerging techniques—too many to do full justice to here—including, in addition to the approaches already mentioned, patch-seq (combining patch clamp recording and single cell RNAseq), macropatch recordings, bilayer recordings, dynamic clamp, organotypic slice culture, combined *in vivo* patch clamp recording and optogenetics, and multielectrode arrays. Refreshingly, the notable challenges that electrophysiologists face in implementing some of these approaches are not ignored: glassware destruction arising from such frustrations, and even voodoo rituals get a mention!

Methodological challenges aside, this volume provides an optimistic and helpful addition to the patch clamper's bookshelf. This book should become a well-thumbed reference guide for new and experienced ion channel physiologists both now and into the future.

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