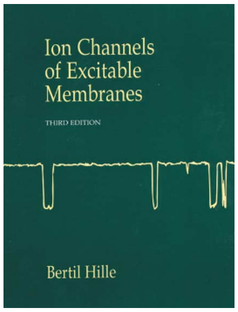
Defining the field of ion channels



Ion Channels of Excitable Membranes, Third Edition

by Bertil Hille

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Reviewed by Charles F. Stevens

Ever once in a while, a book comes along that not onl summari es a field but actuall defines it. Bertil Hille, professor of ph siolog and bioph sics at the Universit of Washington, wrote such a book with *Ion Channels of Excitable Membranes*, now in its third edition. The new edition of this modern classic brings the reader up to date in the important and rapidl growing field of ion channel research.

The modern era of ion channel studies began about two decades ago with two technical advances, the development of single-channel recording and the cloning of ion channels. The electroph siological revolution dates from the publication (in 1980) b Sigworth and Neher of the first single-channel recordings made with what is now just called the 'patch clamp'. When a glass micropipette is pressed against a cell's surface, the glass seals onto the cell's membrane (forming a 'gigaseal') and permits the measurement of the tin currents, fractions of a picoamp, that flow through the pore of a single channel. The molecular revolution, initiated with the cloning of acet lcholine receptor subunits b the Patrick and Heinemann and Numa laboratories in 1983, gave a molecular realit to the ion channel which onl a few ears before had been a purel h pothetical entit   and permitted the primar structure of the channel to be determined and manipulated. The first edition of Hille's book appeared just after the start of the modern era; it summari ed knowledge from the 'classical period' (1950 1980) and captured the e citement generated b the new methods that were just beginning to be applied. As the field grew and matured, the first and second editions of the book guided graduate students, postdoctoral fellows and researchers through the latest developments, both e perimental and conceptual.

The third edition continues to be the authoritative source for information about ion channels. The writing is crisp and clear, the organi ation is logical and importantl in a fast-moving field the content is up to date. Although thoroughl modern, the book has consistentl adopted an historical point of view, so one not onl learns the latest information but also can follow the development of ideas. After an introductor chapter that provides motivation, nomenclature and essential bioph sical concepts (for e amples, Ohm's law, the concept of equilibrium potential and the beloved and ever-popular I V curves), the remainder of the book is divided into two main parts. Part One covers the classical Hodgkin Hu le theor and the basic descriptive facts about various channel t pes. The main emphasis is on the voltage-gated channels responsible for the electrical e citabilit of cells, but ligand-gated channels used in s naptic transmission, and other channel t pes that have special roles (in, for e ample, phototransduction and the release of intracellular calcium) are covered briefl , as is the important topic of neuromodulation and second-messenger signaling. In Part Two, the general principles and mechanisms that appl across channel t pes are e plained. Here Hille reviews the relevant ph sical chemistr and bioph sics (in a ver readable form), the structure of ion channels and the mechanisms of gating and of ion permeation and selectivit .

The book concludes with two interesting chapters, the first of which places ion channels in their modern cell biological conte t. Because ion channels are not distributed evenl over the cell surface, their targeting to the right place (the 'trafficking problem') has provided an important model s stem for cell biologists stud ing the general question of how the right protein gets delivered to the right place at the right time. Ion channels with their PDZ domains and other t pes of molecular 'Velcro' have also provided an important s stem for cell biologists to stud to determine how protein 'machines' are placed and maintained relative to other proteins for proper function.

The final chapter presents as it has since the first edition, when the topic was completel new a discussion of evolutionar relationships between channels. The attractivel biomorphic ph logenetic trees, conceived and drawn b Hille himself, have alwa s been an important feature of this final chapter, and their evolution parallels the changes that have occurred in thinking about evolutionar biolog and reflects the increased knowledge provided b the man primar sequences that have recentl become available.

For those who have depended on the earlier editions as a reference, this new version is a must. The third edition has e panded b over 200 pages. (The fifth edition will presumabl be 1,600 pages, as the doubling time appears to be two editions.) Whereas the first edition was a combination of a long review article and an introduction to channel bioph sics, as the field has e panded, the character of the book has evolved toward a more enc clopedic coverage. In the new edition, Hille has updated and e panded the treatment of channel structure, structure function studies of permeation and gating, and the cell biolog of ion channels, and he has added a new chapter on the role of channels in epithelial transport, intracellular signaling and intercellular coupling. Inside the front and back covers, Hille includes particularl useful data on the classification of ion channels and some relevant facts (such as values of constants and central equations).

This book is a model of monograph writing, and has been central in the development of ion channel studies, b both presenting the facts and providing a conceptual organi ation for the data. The new edition is even more important because it covers the dramatic advances of the past several ears, including the first cr stal structure of an ion channel and an increasingl refined picture of channel mechanisms derived b combining insights from the atomic-level structure with new information from clever structure function studies.

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