Ion channels are crucial components of living cells. They are situated in the membranes of the cell, and allow particular ions to pass from one side of the membrane to the other. In recent years the patch clamp technique has allowed the activity of individual channels to be measured, and recombinant DNA technology has revealed fascinating detail on channel structure. Together, these technical advances have produced a great flowering of knowledge and understanding about the subject, itself leading to further breakthroughs in science and medicine. *Ion Channels* provides an introduction to this scientific endeavour. It emphasizes the molecular structure of channels as determined by gene cloning technology. This molecular approach illuminates discussions of the permeability and selectivity of channels, their gating and modulation, their responses to drugs and toxins and the human diseases caused when they do not function properly.

Ion Channels

Ion Channels

Molecules in Action

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Preface

Ion channels are protein molecules containing aqueous pores that can open and shut to permit ion flow through cell membranes. The concept emerged in the 1950s, but the evidence for their existence was at first limited and indirect in nature. It was 1976 before the behaviour of individual channels could be observed, and 1982 before the primary structure of the first channel protein was determined. Since then work on ion channels has burgeoned and blossomed in a most remarkable way. New discoveries about them are now reported in several thousand scientific papers each year.

This book is intended to provide an introduction to this scientific endeavour. It is too short to be comprehensive, so it does not attempt to be. We have tried to emphasize particularly the molecular aspects of the subject, since one of the really exciting aspects of the field is the way in which explanations in terms of molecular structures are beginning to provide some understanding of channel function. We have written it primarily for students and graduate students doing courses in such subjects as pharmacology, physiology, medicine, cell biology, biophysics, neuroscience and molecular biology, but it may also be useful to those just starting research in the area or to those scientists who simply wish to find out what is happening in a field different from their own.

It is important for science students to know not only where we are now but also how we got here. This does not mean that they have to study the history of the subject for its own sake, but they do need to grasp the logic of the accepted views and be aware of some of the evidence behind them. So we have often given details of how particular experiments were done, and many of our illustrations show the results of experiments rather than simply giving their conclusions. It is partly for this reason that we have given literature references for many of our statements. The other reason is that we felt that in a rapidly moving field (60% of the papers in our reference list are from 1990 or

later) it was necessary to let the reader know where our information comes from.

Some biologists like equations, others find that their eyes flick rapidly downward when they meet one on the printed page. We have included a number of equations, but only where they are necessary for the argument. Much of science is concerned with quantitative testing of hypotheses, and in order to make quantitative predictions it is frequently necessary to use a mathematical approach. The precise symbolism of mathematics can also be a considerable aid to clear thinking. But the mathematics in this book, readers will find, is actually pretty easy.

We have benefited greatly from input from our colleagues in Leicester, Norwich and elsewhere, and so it is a pleasure to thank Bill Brammar, Alan Coddington, Peter Croghan, Noel Davies, Alan Dawson, Richard Keynes, Edward Lea, Philip Shelton, Michael Sutcliffe and John Thain for all the help and good advice they have given us in commenting on draft material and discussing particular points with us. It seems appropriate also to acknowledge our long-term indebtedness to Professor Sir Alan Hodgkin, who introduced us to the subject matter of this book and gave each of us considerable encouragement at crucial times. Like most who study channels, our understanding has been greatly helped by Bertil Hille's classic *Ionic Channels of Excitable Membranes*. We are grateful to the many authors and publishers who have given us permission to reproduce diagrams from their works, details of which are included in the reference list at the end of the book. Finally we thank Jessica and Pippa for their tolerance and good humoured support during the writing.

It has been a stimulating and rather enjoyable business writing a book on such a rapidly developing subject, and we have educated ourselves considerably in the process. We hope that our readers will find the result useful.

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Peter Stanfield