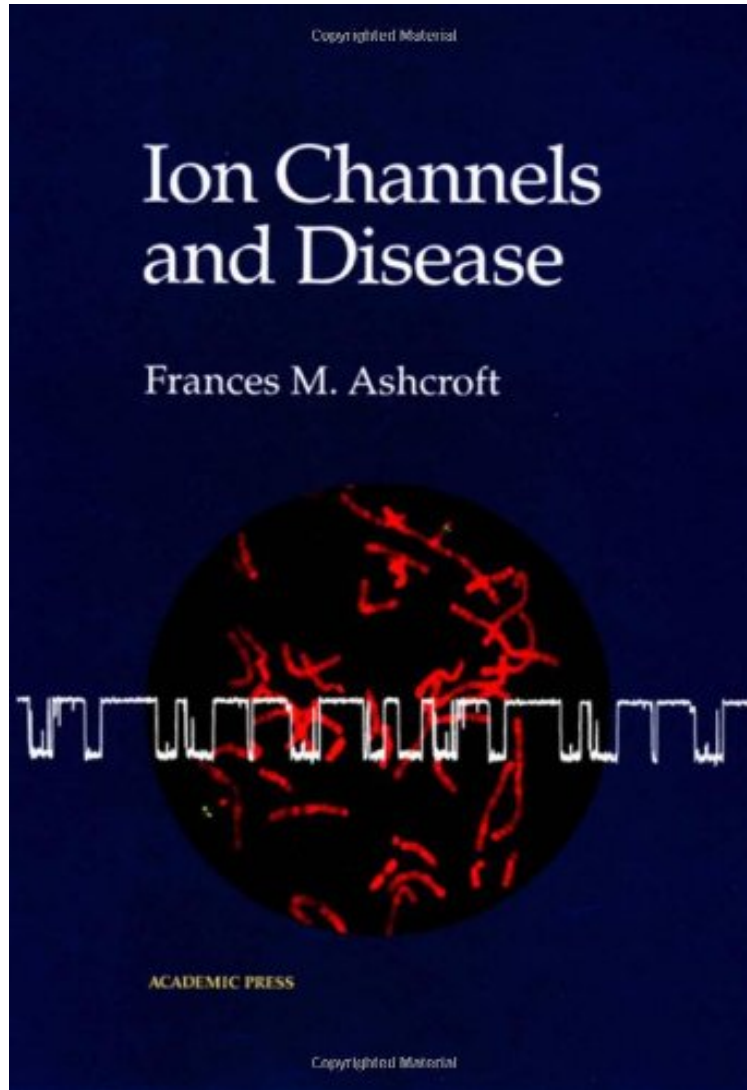


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Ion Channels and Disease (Quantitative Finance)

Frances M. Ashcroft

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Frances M. Ashcroft : Ion Channels and Disease (Quantitative Finance) before purchasing it in order to gauge whether or not it would be worth my time, and all praised Ion Channels and Disease (Quantitative Finance):

1 of 1 people found the following review helpful. Good companion to Hille's By schneider1004 Good overview of the various ion channels. Ashcroft is well respected in the biophysics and writes in an accessible manner. 0 of 0 people found the following review helpful. The Ion book By Professor Dr Jafri A much needed textbook is now available for all neurologist and neuroscientist doing experiments in this field. 4 of 5 people found the following review helpful. The answer is in here ...and here is the question: By A Customer The author has a splendid writing gift, and she has

produced a broad and wonderfully clear survey of the state of the art in this vigorous field. For a detailed summary of what you will find in the book, check the editorial review (above) from the New England Journal of Medicine. It seems to me the book might well be read in the context of two other important books in this field: One is Bertil Hille's classic, "Ionic Channels of Excitable Membranes." As a science gathers momentum (and this one is certainly surging) we tend to lose track of what is known and what is simply assumed. Hille's book will fill in some blanks at the fundamental level - and show you exactly where the underlying assumptions are in this science. If you are at all skeptical, and of course you should be, you will like Hille's calm precision and care. The other background book is Spikes, by Rieke et al. The implication of Spikes is that Adrian was wrong and that, therefore, all of us have been wrong about what nerves actually do - and wrong since 1926. The authors put this rather more diplomatically than I have, but there it is: Adrian wrong. Spikes summarize evidence accumulated since about 1993 that a single nerve impulse, all by itself, can somehow convey information to the brain. This shocking news will have to be either explained or explained away in terms of the biochemical machinery of the neuron. The current explanation (which is based on precise arrival timing) would seem to rely upon the physiological equivalent of a quartz crystal, um, a device we don't often come across in biochemistry. It would be my guess that a better understanding of ion channels will point to a more biologically realistic solution. And a new and better picture of how the neuron works. Ion Channels and Disease is the most current and broadest survey of the subject. The key to the problem is probably in here somewhere, or is referenced here, and is waiting to be discovered. I would pay particular attention to any type of evidence for linkage, structure or signaling between "individual" channels. Linkage between discrete trans-membrane ion channels could create a longitudinal channel running the length of the nerve, probably many of them. A multi-channel axon - a cable rather than a wire -- would be one possible solution to the new mystery of how a single impulse can be freighted with graded information.

Ion channels are membrane proteins that act as gated pathways for the movement of ions across cell membranes. They play essential roles in the physiology of all cells. In recent years, an ever-increasing number of human and animal diseases have been found to result from defects in ion channel function. Most of these diseases arise from mutations in the genes encoding ion channel proteins, and they are now referred to as the channelopathies. Ion Channels and Disease provides an informative and up-to-date account of our present understanding of ion channels and the molecular basis of ion channel diseases. It includes a basic introduction to the relevant aspects of molecular biology and biophysics and a brief description of the principal methods used to study channelopathies. For each channel, the relationship between its molecular structure and its functional properties is discussed and ways in which genetic mutations produce the disease phenotype are considered. This book is intended for research workers and clinicians, as well as graduates and advanced undergraduates. The text is clear and lively and assumes little knowledge, yet it takes the reader to frontiers of what is currently known about this most exciting and medically important area of physiology. Introduces the relevant aspects of molecular biology and biophysics Describes the principal methods used to study channelopathies Considers single classes of ion channels with summaries of the physiological role, subunit composition, molecular structure and chromosomal location, plus the relationship between channel structure and function Looks at those diseases associated with defective channel structures and regulation, including mutations affecting channel function and to what extent this change in channel function can account for the clinical phenotype

From The New England Journal of Medicine This book reviews a wide variety of congenital and acquired conditions caused by abnormalities in ion-transport mechanisms. It starts with a description of relatively simple channels that respond to voltage changes or certain cellular metabolites by a conformational change that opens the pore. These channels are closed by a cytosolic loop that plugs the pore. The book continues with more complex channels composed of multiple subunits of the same composition and controlled by other subunits with a different composition. The complexity increases in a last group of ion channels that regulate more than one type of ion passage and form an intrinsic part of certain receptors or combine ion-channel activity with a transport function for more complex molecules. The last few chapters describe interesting roles of ion channels in cell-cell communication by mediating electrical impulses or exchange of nutrients or regulatory signals. There are examples of autoantibodies that interfere with the function of channels, cells that transport channels from one site to another, and cells that excrete ion channels to kill their target cells by ruining their membrane resistance. These discussions are preceded by a comprehensive and up-to-date summary of molecular biology, biochemistry, electrophysiology, and molecular genetics. This might be superfluous for some readers, whereas others might prefer more extensive textbooks, but in any case, this survey clearly defines the basis for understanding subsequent chapters. The strength of this very readable overview is that its focus is disease. There is a uniform style throughout the book. Starting with descriptions of a few disease states related to a particular ion channel, the authors provide a model of the channel based on protein composition and structure derived from molecular biologic, biochemical, and crystallographic data. The often complex channel responses to depolarization and hyperpolarization, binding of regulatory ligands, and certain toxins are then explained on the basis of the model. Mutations that cause abnormal channel control are discussed and form the basis of the description of the

clinical phenotype. The result is a fascinating voyage through the human and, in a few cases, animal body, showing the molecular defects in ion channels in diseases ranging from diabetes mellitus, deafness, and myotonia to cystic fibrosis and migraine, and all placed by the author under the common denominator "channelopathy." A nice illustration of the foregoing is the voltage-gated sodium channel in muscle fibers. This channel is activated by positively charged residues in the channel that sense a voltage change and respond by triggering a conformational change described as a "helical screw model," which opens the channel. Binding of an intracellular inactivation "ball" connected to the channel binds to the pore, blocks further passage of ions, and closes the channel. It is clear that mutations that change the composition of the voltage-sensing domains, the structure of the inactivation ball, or the size of the acceptor domain for the inactivation ball will interfere with channel function. The results of such mutations are changes in voltage dependence or the time course of channel inactivation, resulting in enhanced muscle excitability or paralysis; both conditions sometimes occur in a single patient. The often complex material in this book is illuminated by pleasing examples of channel malfunction in everyday life. Eating too much of the Japanese delicacy fugu (puffer fish) increases the intake of tetrodotoxin, which plugs the voltage-gated sodium channel and can be fatal. Charybdotoxin in scorpion venom blocks the voltage-gated potassium channel. Certain goats with a defect in a skeletal-muscle chloride channel fall over every time a train passes their field. The gene that causes certain mutant fruit flies to shake their legs when anesthetized with ether codes for a voltage-gated potassium channel and is called "ether-a-go-go." The book is richly illustrated with single-channel-current recordings of the relevant ion channels; hierarchical classification schemes for the relevant genes; tables listing locations of chromosomes, the distribution of various ion channels in tissue, mutations, and related protein abnormalities; and colored models based on crystal structures. There are a few tracings and listings meant for the insider, but in general, the illustrations contribute greatly to the clarity of the chapters. An extensive index helps readers locate all this information, and the bibliography is up to date, with references as recent as 1998. This book will help readers to review basic knowledge regarding muscle and neuronal activity, the functions of the kidney and the eye, and the intracellular events that make cells excrete water, activate signaling pathways, and prevent apoptosis. J.W.N. Akkerman, Ph.D. Copyright 2000 Massachusetts Medical Society. All rights reserved. The New England Journal of Medicine is a registered trademark of the MMS. "...this volume is a gem of large proportion. The clear writing style, comprehensive coverage, up to date information and low cost mandate a most enthusiastic recommendation to any physician interested in the mechanisms of epilepsy." -- EPILEPSY RESEARCH, February 2001 "The book is self-contained in the sense that it provides all the background knowledge necessary to understand the field. ...It manages to communicate complex ideas with clarity, precision and efficiency, and I personally enjoyed the sense of history that pervades the book, as well as the lucid style in which it is written." --Blanche Schwappach, Universitate Heidelberg, in NATURE CELL BIOLOGY, September 2000 "...a fascinating and accessible account of ion-channel diseases. Each chapter is illustrated with useful figures and diagrams...a very good introduction to the whole field of ion channels, and will be useful for researchers, clinicians and students. ...It is the favourite of several of my colleagues." --Thomas J. Jentsch in NATURE, July 2000 "This is a well documented and informative treatise on ion channels and associated pathologies. Experimental details are omitted without compromising clarity and understanding, making this an easy to read reference source... The audience is broad, ranging from advanced undergraduates to clinicians and researchers. The author reaches this large group with a balance among introductory scientific details, relevance, and completeness... Researchers will appreciate the full range of topics and extensive bibliography. Clinicians will find molecular explanations of pathologies such as retinitis pigmentosa, cystic fibrosis, and Charcot-Marie-Tooth Disease enlightening... This much needed book is informative, readable, and worth having."--DOODY'S PUBLISHING REVIEWS, 2000 "This relevant and timely book provides an extensive and excellent overview of membrane channels and their potential involvement in disease. ...The book is well written and enjoyable to read. Given the rapid advance of knowledge in this field, the content is amazingly up-to-date. This book is an excellent overview text for the advanced undergraduate or beginning graduate student and would be beneficial to the ion channel researcher as well as established scientists whose expertise is in unrelated areas. ... I believe that this text also provides an excellent and essential source of information for clinicians wishing to better understand the relevance of "channelopathies" to the presentation of disease. Dr. Ashcroft has certainly hit the mark." --Rodney L. Parsons, University of Vermont, in CELL

From the Back Cover Ion channels are membrane proteins that act as gated pathways for the movement of ions across cell membranes. They play essential roles in the physiology of all cells. In recent years, an ever increasing number of human and animal diseases have been found to result from defects in ion channel function. Most of these diseases arise from mutations in the genes encoding ion channel proteins, and they are now referred to as the channelopathies. This book provides an informative and up-to-date account of our present understanding of ion channels and the molecular basis of ion channel diseases. It includes a basic introduction to the relevant aspects of molecular biology and biophysics and a brief description of the principal methods used to study channelopathies. For each channel, the relationship between its molecular structure and its functional properties is discussed and ways in which genetic mutations produce the disease phenotype are considered. This book is intended for research workers and clinicians, as well as for graduates and advanced undergraduates. The text is clear and lively and assumes little knowledge, yet it takes the reader to the frontiers of what is currently known

about this most exciting and medically important area of physiology.