

## book reviews

observed. There are many other reasons why what little remains of the tropical forests should be cherished, but what Plotkin laments here is that the annihilation of species by the thousand deprives us of untold opportunities to discover new medicines and other valuable classes of compounds — strong materials, process chemicals and many more.

He also denounces the profligacy with which existing therapeutic resources are being degraded: antibiotics are still fed to cattle and federal law is content to allow trace amounts of no fewer than 80 antibiotics to enter the milk that Americans drink. And finally, Plotkin notes, a large proportion of the most important medicinal substances were brought to us by research driven only by curiosity about the natural world and mocked by Senator William Proxmire and his allies as a waste of the taxpayers' money. Let us hope that Plotkin's voice is heard in the quarters that count, those in which economic and not moral interests prevail. Dr Johnson put it pithily: "Sir, I have found you an argument, but I am not obliged to find you an understanding." ■

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## A function for dysfunction

### Ion Channels and Disease

by Frances M. Ashcroft  
*Academic: 1999. 352 pp. £46.95, \$75*

Thomas J. Jentsch

The importance of many things in our lives becomes apparent only when we lose them, or when they malfunction. In genetic disease, mutations in a gene may lead to interesting and sometimes unexpected insights into the physiological importance of their product. Detailed comparison of the properties of both the normal and mutant gene products can reveal deep insights into the physiological role of the protein encoded by the gene and how it goes awry in disease.

This combination frequently occurs in ion-channel diseases (or 'channelopathies'). Over the past 15 years, genes encoding ion channels have been isolated at ever-increasing rates. Their number exceeds estimates obtained from biophysical studies, and one might wonder why there are so many different channels. In many cases, mutations in ion-channel genes, in both humans and animals, have provided clues or answers. Some ion-channel genes were even cloned on the basis of the effects of their disruption. For example, positional cloning in the fruitfly

## Channelling other energies

The Kongo peoples inhabit the River Congo region in west-central Africa, and are divided into many subgroups, all of which have many different cults. Their strong belief in a wide spectrum of spiritual forces catalysed the development of a wealth of sculptural forms dedicated to containing and harnessing these forces. The statue shown here, called *nkisi nkonde*, represents a power figure generally associated with vengeance and aggression, but it could also be involved in the sealing of pacts between individuals — each nail or point driven into the statue reinforces the pact. Failure to keep the pact would provoke retribution from *nkisi nkonde's* particularly ferocious spirit. From *Spirits Embodied: Art of the Congo* by Evan M. Maurer and Niangi Batulukisi (University of Minnesota Press, \$34.95, £24.50).



*Drosophila* led to the isolation of the *shaker* potassium channel, and the CFTR chloride channel was found because its gene is mutated in cystic fibrosis.

The large number of ion-channel diseases provides an impressive illustration of the many functions of channels. These range from signal transduction to ionic homeostasis, cell-volume regulation, trans-epithelial transport, vesicle acidification and trafficking, and cytotoxic effects, to name just a few. As a result, ion-channel diseases are clinically very diverse, ranging from cystic fibrosis to inherited forms of kidney stones, periodic paralysis, high blood pressure, epilepsy and hyperinsulinaemia.

Ion channels can be studied in great detail using biophysical methods. One such method is the patch-clamp technique, which investigates the properties of single molecules in real time. The *in vitro* analysis of channel mutations found in patients has contributed considerably to our understanding of the relationships between channel structure and function. Compared with most other genetic diseases, this provides an unrivalled level of understanding of how mutations cause disease.

Frances Ashcroft's book is a fascinating and accessible account of ion-channel

diseases. But it does not stop there — it is also an up-to-date description of the different classes of cloned ion channels, their structure and function, and how the disease characteristics resulting from their dysfunction are used to elucidate their physiological roles. For completeness, channels not (yet) known to cause human disease are also covered, and the chapter "Ion channels as lethal agents" even discusses the pore-forming peptides of bacteria and fungi.

Ashcroft begins with a short introduction on the essentials of molecular biology, human genetics, electrophysiology and ion-channel design. Although necessarily superficial, this section will be useful for students from different backgrounds. Beginning with voltage-dependent sodium channels, the author goes on to discuss the different classes of ion channels individually. Only cloned ion channels are included, thereby omitting several classes of ion channels (such as calcium-activated chloride channels) whose molecular correlate has not been firmly established.

These chapters begin with a concise description of what is known about the structure and function of the channels, and a discussion of the key experiments that led to these insights. The physiological role of the

channels is then described. These short sections introduce the reader to the cellular physiology of such diverse systems as the  $\beta$ -cells of the pancreas, photoreceptors, kidney tubules, the neuromuscular junction and even the complement system.

Ashcroft then discusses diseases that are caused by mutations in these channels. The main focus is on human disease, but mouse models of disease, channel mutations in goats and horses, and in *Drosophila* and the roundworm *Caenorhabditis elegans* are also covered. The perspective is broadened by the inclusion of such aspects as the modulation of inositol phosphate metabolism by lithium in the treatment of manic depression, and a discussion of how glutamate-receptor ion channels are affected by the ingestion of excitotoxins (from shellfish, Nutrasweet or glutamate in the Chinese restaurant syndrome).

Not only are these sections interesting, they are also fun to read. We learn what to pay attention to when preparing a meal from the pufferfish *Fugu*, or how to differentiate clinically between myotonia and paramyotonia (give the patient ice-cream!). Each chapter is illustrated with useful figures and diagrams, and remaining problems are highlighted. For instance, the pathophysiological mechanisms underlying some important channelopathies (such as cystic fibrosis) are still not completely understood many years after the gene was identified.

*Ion Channels and Disease* is a very good introduction to the whole field of ion channels, and will be useful for researchers, clinicians and students. Although Bertil Hille's *Ionic Channels of Excitable Membranes* (Sinauer, 1992) remains the standard textbook on the biophysical aspects of ion channels, and *Ion Channels* (Cambridge University Press, 1996) by David Aidley and Peter Stanfield is a very good, balanced overview of the structure and function of such channels, Ashcroft's book combines a short review of individual ion-channel classes with an excellent discussion of their physiological and pathophysiological roles. It is the favourite of several of my colleagues. Although the book is as up-to-date as it can reasonably be, I hope that frequent new editions will keep pace with this rapidly developing and fascinating area. ■

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**More molecular biology**  
**Biology of Sensory Systems**  
 by C. U. M. Smith  
 Wiley, £39.95, \$80 (pbk)

**Molecular and Cellular Physiology of Neurons**  
 by Gordon L. Fain  
 Harvard University Press, \$65, £40.50



Feathered flagships: kagus, endemic to the biodiversity hotspot New Caledonia.

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**Conservation gets heavy**

**Hotspots: Earth's Biologically Richest and Most Endangered Terrestrial Ecoregions**  
 by Russell A. Mittermeier, Norman Myers & Cristina Goettsch Mittermeier  
 University of Chicago Press: 2000. 432 pp.  
 \$65, £45.50

Rory Howlett

Beautifully illustrated, *Hotspots* represents the second volume resulting from a three-way collaboration between the non-profit organization Conservation International, the Mexican conservation organization Agrupación Sierra Madre and, believe it or not, Cemex, the world's third-largest cement company. Judging from the book's weight, one would be forgiven for musing that Cemex contributed more than just corporate support to its production. That aside, the company's environmental credentials are now no doubt set in concrete.

The first volume in the series, *Megadiversity: Earth's Biologically Wealthiest Nations*, published in 1997, dealt with the so-called B-17, the 17 biologically richest nations. The present volume focuses on 'biodiversity hotspots'. The hotspots concept, conceived of and promulgated by ecologist Norman Myers, is nebulous, but, roughly speaking, highlights the importance of those regions of

the world that have disproportionately high levels of species richness and, in particular, endemism.

Defining the thresholds of biodiversity and endemism above which a region qualifies for 'hotspot' status is arbitrary. Indeed, as the first chapter makes clear, hotspots have been subject to 'reanalysis and reassessment', with areas being added or removed as criteria for what constitutes a hotspot have evolved. The basic message, though, is that an estimated 60% to 70% of all terrestrial plants and non-fish vertebrates occur within just 1.44% of the Earth's land surface, providing a rationale for what Myers has advocated as a 'silver bullet' approach to biological conservation.

The following 25 chapters document separate terrestrial ecoregions, each chapter authored by specialists. The organization is formulaic. Overviews of the regions, their diversity of habitats and global importance are followed by subheaded sections on 'Flagship species', 'Threats' and 'Conservation'. This makes it easy to access information, despite the absence of an index. For example, the chapter on New Caledonia starts by pointing out that, although the region has a land surface area roughly equivalent only to that of Wales or New Jersey, it is remarkably species rich, with high levels of endemism. In this it is like Madagascar, once also part of the ancient continent of Gondwana. Flagship taxa include a rainforest-dwelling bird, the