Book Reviews

Sodium Channels, Pain and Analgesia. Edited by Kevin Howard and Mark D. Baker. Birkhauser Verlag, Basel, Switzerland. 2005. x + 199 pp. 17 × 24 cm. ISBN 10-3-7643-7062-9. 126 euro.

Ion channels make up a significant fraction of the human genome, and nature, as befits its status as the best medicinal chemist, has made significant use of this in the design of a large number of peptide and non-peptide toxins. Such agents often act with both exquisite potency and selectivity; we need to be able to more effectively mimic nature's success. Indeed, many therapeutically available agents, including local anesthetics, antiarrhythmics, and antidiabetic and antihypertensive drugs, do interact with voltage-gated ion channels as their principal site of action.

However, ion channel drug discovery is an area where dialogue between the chemist and biologist is of particular significance. The existence of state-dependent interactions between a drug and its channel binding site(s) renders complex the interpretation of structure−function relationships, and the chemist must have at least some understanding of channel structure, function and gating mechanisms, and the underlying physiological functions.

Sodium Channels, Pain and Analgesia is an edited volume of some 10 chapters covering the role of voltage-gated sodium channels in pain and analgesia, including neuropathic pain. Neuropathic pain is an area of active research for ion channel workers, with current emphasis on sodium channels, calcium channels, and excitatory amino acid gated channels.

The volume is strong on underlying electrophysiology and the role of sodium channels in a variety of pain states. It will be very useful for the pharmacologists and electrophysiologists but less useful for the medicinal chemists. There are no chemical formulas in the entire volume, and while this is not a drawback for some of the chapters, for others it is a problem. For example, in the chapter discussing sodium channel gating and drug blockade a few pictures depicting local anesthetic structures and their proposed binding sites would have been immensely useful.

Nonetheless, this is a useful biologically based volume in an important research area.

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Molecular Interaction Fields. Edited by Gabriele Cruciani. Wiley-VCH Verlag, Weinheim, Germany. 2006. xviii + 307 pp. 17.5 × 25.5 cm. ISBN 3527310873. $185.00.

Molecular Interaction Fields is the 27th volume in a series of valuable specialized monographs on topics pertaining to drug discovery. The book continues the tradition and provides comprehensive coverage of computational modeling and its progress and applications in pharmacophore development and other areas of drug discovery. The basic message that the book delivers is that although a tremendous amount of progress has been made, there is still a long way to go because, despite a plethora of models that are available, the challenge is to select the one that agrees best with the experimental data—not always the simplest of tasks.

The book has 12 chapters contributed by specialists from academia and pharmaceutical companies, and it includes a CD-ROM containing some software packages used in the book. The chapters are conveniently divided into three sections. Chapters 1 and 2 provide a good introduction to the basic principles of GRID force fields and the calculation and application of MIFs.

Chapters 3−7 describe the use of GRID-MIFs in a diverse range of applications. Chapter 3 illustrates the approach with a number of excellent examples in different families of proteins. This is a very instructive chapter, but it could be improved, particularly for the medicinal chemist, by the inclusion of more chemical structures to illustrate the textual material. Chapters 4 and 5 focus on the development of four-point pharmacophores and molecular shape fingerprints, while Chapter 6 describes an approach (GRIND) to extract the most relevant information from MIFs, together with the limitations and problems of this approach. Chapter 7 advocates the use of GRID in the development of 3D-QSAR as a supplement to the widely used CoMFA approach, and it is well-illustrated by examples in the estrogen receptor and acetylcholinesterase inhibitor areas.

Section III (Chapters 8−12) is devoted to the application of the method to problems of pharmacokinetics and physicochemical parameters and the prediction of ADME properties. The book is replete with software acronyms that are the specialized language of computer modelers but to relatively few medicinal chemists who are primarily interested in the validity of the results from their computer colleagues rather than the particular model used. Chapter 11 attempts to provide an additional set of filters to address ADME properties that supplement the Lipinski rules, to offer a comprehensive picture of understanding ADME models.

Overall, the book provides a great deal of useful information; it has ample references, and it is a worthy volume in this series of monographs. It will become a good addition to the libraries of computational/modeling chemists rather than to the traditional synthetic medicinal chemists.

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