Book Reviews

Molecular Design. Concepts and Applications. By Gisbert Schneider and Karl-Heinz Baringhaus. Wiley-VCH Verlag, Weinheim, Germany. 2008. xv + 262 pp. 17 × 24 cm. ISBN 978-3-527-31432-4. $70.00.

Since 1996, the number of new chemical entities approved yearly by the U.S. Food and Drug Administration has precipitously declined, even as pharmaceutical R&D spending spirals ever upward. Although an impatient pharmaceutical industry is not prepared to abandon traditional methods of drug discovery altogether, it is clear that rational drug design has captured its imagination, resources, and expectations. However, with so many diverse drug targets, so much data and software, and so many strategies to select from, the actual practice of molecular modeling can be daunting. Molecular Design successfully explains and demystifies this important field, providing sound recommendations for successful drug construction.

The authors, Schneider and Baringhaus, are recognized authorities with significant experience in drug discovery at prominent European pharmaceutical firms. They are therefore well aware of the deadline driven, resource prioritized environment in which this emerging technology is most often employed. The book includes five large chapters, each with specific well developed subsections. After a foreward by medicinal chemist colleague, Hugo Kubinyi, the book begins with a preface by the authors, pointing out the truly transdisciplinary nature of this complex field. The first chapter provides key background information, definitions, and vocabulary for the topic along with a discussion of the graphical and mathematical ways to represent a molecule. It also explores the concepts of "druglikeness" and bioactive conformations of drugs. Chapter 2 discusses the critical issue of receptor−ligand interaction from both a thermodynamic and entropic perspective and addresses the subjects of QSAR, pharmacophore modeling, and ligand docking and scoring.

After this introductory material, Chapter 3 outlines the strategies for systematic in silico modeling, highlighting structure-based and de novo design methods. Also, given their profound pharmacological effects, the influence of natural products on drug design is discussed in this section. Virtual screening, perhaps the signature tool in rational molecular design, is the main topic of Chapter 4. Emphasis is placed on the use of both negative and positive selection techniques to quickly eliminate compounds with liabilities and to engineer highly desired properties into drug candidates. The final chapter reviews the parameters in molecular design that effect drug absorption, distribution, metabolism, elimination, and very importantly, toxicity. Chapter 5 also includes a discussion of prodrugs, data scaling, and several successful drug design case studies. Each of the chapters includes numerous pertinent references to the original literature with some citations as recent as 2007. The book concludes with a comprehensive subject index.

Molecular Design is very easy to read and contains many useful illustrations. The authors have done an admirable job of simply explaining a complex and rapidly evolving field to a wide and varied audience. For that reason this timely volume will be valuable to chemistry and life science graduate students, experienced medicinal chemists, and bioinformaticians for both an introductory entry point and a useful reference work.

Crist N. Filer

PerkinElmer Life and Analytical Sciences, Inc.
940 Winter Street
Waltham, Massachusetts 02451

JM8010433

10.1021/jm8010433