Book Reviews

Molecular Modeling: Basic Principles and Applications. 2nd Edition. By Hans-Dieter Höltje, Wolfgang Sippl, Didier Rognan, and Gerd Folkers. Wiley-VCH, Weinheim, Germany. 2003. xii + 228 pp. 17 × 24 cm. ISBN 3527305890 (Paperback). $50.00.

The explosive growth in the interest in, and application of, computational drug design strategies by the industry a few years ago is now being followed by a wave of students who are eager to learn the tools and techniques of molecular modeling. While the earliest books on molecular modeling were little more than collections of loosely related chapters by panels of contributing authors, the most recent books on modeling are more focused and now are potentially useful as classroom texts. Such is the case with this revised second edition of Höltje, Sippl, Rognan, and Folker's *Molecular Modeling: Basic Principles and Applications.* It quite nicely presents both theory and applications to give a beginning student of molecular modeling a balanced overview of the methods. Also (correctly!) emphasized is the necessity for real critical thinking and even skepticism by users of modeling software packages.

The book is organized in a very pragmatic way. After a short chapter introducing the concepts of models and modeling, the book continues with a chapter detailing the underlying principles of tools for modeling small molecules (ligand, inhibitor, drug, etc.). This covers topics of building, geometry optimization, conformational analysis, three-dimensional field properties, pharmacophore mapping, and 3D QSAR. Chapter 3 presents a case study of modeling dopamine D_3 receptor antagonists. While it is somewhat directed toward obtaining the ultimate 3D QSAR result, this study illustrates many of the concepts from Chapter 2.

Chapter 4 is a good introduction to comparative protein modeling, with sections on finding model data on the Web, an overview of protein structure elements, building of models with homology tools, optimization and validation of models, and properties of proteins. I especially liked the section on model validation because this information is generally available only from scattered references and Web sites. Chapter 5 brings together the protein and small-molecule models with a description of "virtual screening". The key technologies, docking and scoring, are discussed in considerable detail. In Chapter 6, the potential pitfalls of docking, such as incorporating cofactors, water, and metals, at the active site and the difficulties in properly modeling the ionization states of acids and bases at the active site are illuminated, hopefully to forestall undue exuberance by inexperienced users. Finally, Chapter 7 presents a very interesting and rather thorough case example of modeling protein−ligand complexes: the antigenic complex between a viral peptide and a class I major histocompatibility glycoprotein. In this example, homology modeling (from a structurally known protein with 70% homology), ligand docking of the peptides, molecular dynamics of the protein−ligand complex, and analysis of the resulting complex molecules are described. From these results, SAR and design of new ligands follow.

In summary, this is an excellent introductory text for the rapidly evolving field of molecular modeling and computer-aided drug design. It includes numerous up-to-date and useful references. However, a complementary workbook for commonly used software packages would be a nice addition to fully exploit this book as an educational tool in academic settings.

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Chiral Separations. Methods and Protocols. Edited by Gerald Gübitz and Martin G. Schmid. Humana Press, Totowa, NJ. 2004. xiii + 432 pp. 15 × 24 cm. ISBN 1-58829-150-2. $99.50.

Chiral Separations is a multiauthored volume describing thin-layer, HPLC, and capillary electrophoresis methods for separating isomers of chiral compounds. Thus, it describes mainly analytical scale and small preparative scale methods.

This book is part of Humana's Methods in Molecular Biology series. One of the features of this series is that the Methods section of each chapter includes detailed, step-by-step examples. Often these are accompanied by useful Notes describing common pitfalls and critical parameters. The Methods are usually detailed enough to enable one to reproduce the results described, and the Notes give the reader a reasonable chance to adapt a method to his/her particular problem. On a practical level, the book is undoubtedly useful.

There are a few problems. The book was not carefully proofread for typographical and grammatical errors; the publisher should ensure that this is done. And the editors should have imposed some sort of limit on the use of acronyms. For example, one fairly typical page had acronyms on 29 of 39 lines. The reader must constantly stop to translate the less familiar ones, making each page far too difficult to read. Chapter 4 includes a table that goes on for 12 pages, cataloging cyclodextrin-based separations from the chemical literature. This seems unnecessary with the availability of modern literature-searching tools. Finally, the indexing is very uneven. Nevertheless, the book will undoubtedly be of value to those who need to find useful ways to carry out such separations.

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