rats but not for obese humans, because the compounds failed in clinical trials. Subsequent cloning of the human β_3 receptor showed that the original compounds were not as active against the human as the rodent β_3 receptor. Re-screening of the compounds against the human β_3 receptor led to the identification of a new series of closely related beta-blocker-like structures. We must now wait to see how the story unfolds.

In summary, in spite of the β_3 agonist 'hoopla', no significant breakthroughs were reported during the week, just reminders of the difficulties associated with drug discovery and development and the fact that only hard work and the data that result from it will allow us to chemically disrupt biological processes.

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Book review

Molecular Modeling: Basic Principles and Applications

by H-D. Höltje and G. Folkers, VCH, 1996. DM 168 (xii + 194 pages) ISBN 3 527 29384 1

This is the fifth book in the series *Methods and Principles in Medicinal Chemistry* published by VCH. The authors state their intention is 'to provide support for the beginner', and indeed this book provides a fine introduction to many of the techniques used in biomolecular modeling.

The authors begin in Chapter 2 by considering small molecules: issues such as how to generate 3D coordinates and optimize geometries are discussed. Along the way, they interweave discussions of force fields, minimizers, solvent models, charge models and many other 'basic topics' that are a prerequisite for understanding modeling. They then switch to a discussion of somewhat more advanced topics, including electrostatic potentials, grids, comparative molecular field analysis (CoMFA), pharmacophores and superposition. This is a lot of material, but it is well laid out, clearly presented and well supported by figures and tables. Each subchapter reads as a distinct unit, making it easy to read the book in easily digestible instalments. References are given at the end of each section: a very helpful, but sadly uncommon practice.

In Chapter 3, the design of serotonin receptor antagonists is used to exemplify much of the material on small molecule modeling. Chapter 4 then moves on to a different scale and discusses protein modeling, including homology modeling, secondary structure, sequence alignment, distance geometry, etc. Geometry optimization and molecular dynamics are presented, as well as solvent models. Again, many topics are included, and are covered well. A very nice point – often overlooked – that is brought up in this chapter is the validation of protein models: how accurate are they and how can you tell? Chapter 5 illustrates the modeling of protein–ligand complexes with an analysis of antigen presentation by major histocompatibility complex (MHC).

Any introductory text has to avoid two great sins: putting in too much material and not putting in enough. This book tends towards omission (admittedly, the more venial of the two). The meat of the book, ignoring the introduction and the appendices, is only around 150 pages. One might have hoped for somewhat more coverage of certain topics such as docking, *de novo* design, conformational searching for small molecules, and the prediction of ligand–receptor binding affinity. However, the book does cover many current topics in biomolecular modeling.

The one flaw of the book is an advertisement for Tripos software, thinly disguised as a scientific article but with no authors and no references, included at the back (after the appendices and the index). I have never seen such an 'advertorial' in a computational chemistry book before. On the title page is an acknowledgement thanking Tripos for financial assistance. Such advertising, clearly marked as such, is not a problem; book publishers need to make money like everyone else. However, the 'advertorial' is quite another matter; an inexperienced end-user (the target audience for this book) may not be able to discern 'fact from fiction'. This practice raises red flags in many directions; it should be made clear whether other software companies were offered the chance to advertise, whether the content of the book was in any other way influenced by Tripos (there is no evidence for this) and what form the 'sponsorship' took. Book-buyers should be wary of such practices.

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