Book Reviews

Reviews in Computational Chemistry, Volume 10. Edited by Kenny B. Lipkowitz and Donald B. Boyd. VCH Publishers, Inc., New York. 1997. xxiii + 334 pp. 16 × 24 cm. ISBN 1-56081-957-X. $120.00.

As with previous volumes in this series, several topics of recent interest in computational chemistry are reviewed at a fundamental level, and in addition the reader is given a perspective on current and historical trends and developments in the field. The volume consists of five chapters: Genetic Algorithms and Their Use in Chemistry by Richard Judson at Sandia National Laboratories; Does Combinatorial Chemistry Obviate Computer-Aided Design? by Eric J. Martin, David C. Spellmeyer, Roger E. Critchlow, Jr., and Jeffrey M. Blaney at Chiron Corporation; Visualizing Molecular Phase Space: Nonstatistical Effects in Reaction Dynamics by Robert Q. Topper at the Albert Nerken School of Engineering; Computational Studies in Nonlinear Dynamics by Raima Larter and Kenneth Showalter at IUPUI and West Virginia University; and The Development of Computational Chemistry in the United Kingdom by Stephen J. Smith and Brian T. Sutcliffe at the University of York.

Emphasis is placed on structuring the chapters as tutorials for those unfamiliar with the topic. Some of the chapters particularly excel at this aim, e.g., the first chapter on genetic algorithms (GAs), which describes the development and design of GAs as well as their application to problems of interest in chemistry. The latter include conformational searches for small molecules, proteins, and DNA/RNA; molecular docking; molecular similarity; protein NMR data analysis; protein X-ray data analysis; spectral curve fitting; QSAR; data clustering; de novo molecular design; DNA and protein sequence analysis; optimization of potential energy functions; and general model fitting. GAs are also compared/contrasted with other available global search methods, and several sources of information concerning GAs, as well as public domain GA codes, are listed in the appendices.

The second chapter on combinatorial chemistry surveys the approaches to rational design of combinatorial libraries. Several important issues are discussed, e.g., the use of whole molecule vs fragment descriptors, the relevant measure of similarity, the appropriate molecular descriptor(s), and the nature of the experimental design (to maximize diversity or to focus on a particular area of property space). Thus, coverage of the topic is good and certainly a propos but would be aided by additional concrete examples of how combinatorial libraries are designed and how they have been used to identify and optimize lead compounds.

The third and fourth chapters are complementary treatises on the nonlinear dynamics of energy-conservative and energy-dissipative systems, respectively. Chapter 3 focuses primarily on visualizing the molecular phase space which is used to describe such nonstatistical effects in reaction dynamics and molecular dynamics simulations. The reader is led, via extensive examples, from a simple isomerization system that simultaneously experiences uncoupled twofold torsional oscillation and anharmonic vibration, visualized as a torus, to a complex isomerization system in many coupled degrees of freedom, which leads to a hyperbolic manifold representation. This visualization of simpler conservative systems sets the stage for Chapter 4 that outlines more complicated examples of nonlinear dynamical behavior in dissipative systems, e.g., multiple stationary states, periodic oscillations, and chaos. Specific chemical examples illustrating these behaviors are described in detail, e.g., the iodate−arsenite reaction which exhibits bistability, the chlorite−iodide−malonic acid reaction which exhibits oscillation, and the horseradish peroxidase reaction which exhibits chaotic behavior. Both the mathematics and graphics visualization of these more complicated systems are discussed in detail, including illustrations of the major difference between the conservative and dissipative systems, i.e., the presence of an attractive force such as a steady-state attractor, a limit-cycle attractor, or, in the case of chaos, a strange attractor. Additionally, the basic concepts and tools used in the study of complex chemical phenomena are related to the understanding of other scientific behaviors, e.g., population biology.

The last chapter is an interesting survey of the development of computational chemistry in the United Kingdom, which begins with the development of COLOSSUS, the first digital computer in the U.K. which was used to break secret codes during World War II, continues through the period when all research had to be performed on U.K. computers, and finishes with the introduction of outside machines, e.g., IBM, CDC, and Cray computers. Along the way, the authors outline the contributions from such pioneers as Alan Turing, Douglas Hartree, John Lennard-Jones, Charles Coulson, and Frank Boys, among others. While the other chapters in this volume tell the science behind their respective topics, this chapter conveys the personalities, day-to-day developments, and political and bureaucratic forces that comprise the real life of scientists in general and computational chemists in particular. It makes for entertaining reading, and as the editors remark, "it might be regarded as the 'dessert' for the readers who have navigated the mathematics" of Chapters 3 and 4.

Overall, this volume lives up to the reputation of its predecessors as an excellent reference, both to current developments and to past history in the field of computational chemistry. It should be valuable to both computational chemists and to others interested in the field. In particular, Chapters 1 and 2 will be of interest to those working in the medicinal/pharmaceutical area, as genetic algorithms and combinatorial library design have made their way into the mainstream of current drug design research, while Chapter 4 may be of interest to those scaling up reactions to pilot plant or production scale where nonlinear dynamical behavior may be

observed, for example, in a continuous-flow stirred tank reactor system.

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The Impact of Stereochemistry on Drug Development and Use. Volume 142 in Chemical Analysis. Edited by H. Y. Aboul-Enein and I. W. Wainer. John Wiley & Sons, New York. 1997. xxvii + 695 pp. 16 × 23.5 cm. ISBN 0-471-59644-2. $99.00

This book is Volume 142 in the Wiley-Interscience Chemical Analysis series of monographs. The multiauthor work contains 23 chapters that have a focus on some aspect related to drug stereochemistry and also contains contributions from some outstanding scientists. The topic is timely and important as drug companies make decisions about whether to bring to market a racemic or enantiomeric drug entity and as the FDA increasingly focuses attention on the same question.

I'm not quite sure what I initially expected to find in a book with this title. What I did find was a *lot* of information, but the sequencing of the chapters seemed somewhat illogical. Late in the book, for example, one moves from a chapter on chiral derivatization reagents, to two chapters on circular dichroism, then to two chapters on regulatory guidelines for stereoisomers, followed by a chapter on first pass phenomena and then one on gastrointestinal transport, and finally to a chapter on chromatographic resolution on chiral stationary phases. Because I read the chapters in order, this sequence of presentation was perplexing, to say the least. In Chapter 9, after many examples of differences in the metabolism of stereoisomers have already been presented in preceding chapters, I found a section entitled "Chirality and Optical Isomerism: A Brief Overview", which begins a basic discussion and definitions of stereogenic centers, molecular dissymmetry, and resolution methods. Such fundamental information should have been presented early in the book.

The book also has a degree of redundancy that is perhaps not surprising in view of the fact that many of the chapter authors work in the same or closely related areas. Nevertheless, more editing effort could have eliminated much overlap. For example, many of the chapters have general introductory material about stereochemistry that could have been covered in one early chapter for later chapters to reference.

The chapters seem to fall into two general categories. The first broad area comprises analytical theory, techniques, and technologies (e.g., HPLC applications of various chiral stationary phases, chiral derivatizing agents, capillary electrophoresis, detection methods, ORD, etc.). The second category seems to include what might be called case studies of drug metabolism, wherein numerous examples of stereospecific or stereoselective metabolism of drug isomers or racemates are discussed, along with the pharmacological consequences and discussions of the analytical methods that were used. There's a lot of good material here.

Although I did not attempt to give the index a thorough workout, it does not appear quite extensive or detailed enough for the amount of information contained in the book. For example, the book contains one chapter with material on in vivo "chiral inversion" but another with a discussion of in vivo "stereochemical interconversion". The index contains both terms, as well as the term "stereochemical inversion" which occurs in yet a third chapter, but none of these apparently synonymous terms are cross-indexed.

Despite its perceived shortcomings with respect to overall organization, information flow, and redundancy, the book does contain a lot of information and will be a worthwhile addition for many libraries. I would envision the major audience to be pharmaceutical scientists who are particularly concerned with the in vivo metabolism and pharmacokinetics of racemates versus stereoisomers. A number of pharmaceutical companies no doubt have pharmaceutics groups that would be included there. The book provides a good and reasonably comprehensive starting point for someone trained in analytical methods who is about to embark on projects involving the biological activity and metabolism of chiral drugs. A complete read of the book would quickly bring one up to speed on current technology and thinking regarding the issue of racemic versus enantiomeric drugs.

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