Book Reviews

Computer Modeling of Chemical Reactions in Enzymes and Solutions. By Arieh Warshel. John Wiley & Sons, Inc., New York, NY. 1997. xiv + 236 pp. 15.5 × 23.5 cm. ISBN 0-471-18440-3. $49.95.

The late physical chemist Bright Wilson attributed the post-WW-II success of American science to a generation of high-school kids who had worked on cars and machinery and to basement tinkerers who built their own radios. This practical, hands-on approach is one important element of success in education which is often overlooked in present-day pedagogy. However, it is apparent from listening to talks at professional meetings that most of the superstars of the molecular modeling profession are hands-on types. They have prepared or modified their own software code, in addition to being sophisticated users of a range of modeling techniques.

Warshel, whose work is the intellectual predecessor of a whole branch of molecular modeling which became the CHARMM and AMBER force fields, aims to foster just such a hands-on learning approach with this book. In the nine chapters, the author emphasizes learning by doing. Starting with Chapter 1 on Chemical Bonding and culminating with Chapter 9 on How Enzymes Really Work, the author works through a series of interesting examples which emphasize the step-by-step development of the theory, from a hydrogen molecule to enzymatic reactions. The author's aim is "to simplify the key concepts of chemical bonding so that they can be used to correlate the structure and function of proteins. The reader is encouraged to define enzyme mechanisms in terms of well-defined chemical statements about bonding and charge distribution so that they can be analyzed by computer simulation approaches. The general philosophy of the book reflects the opinion that, while we may still be arguing about the way that different enzymes work, we have clearly reached the state where key mechanistic problems should be addressed in terms of the underlying energetics, and where some incorrect mechanisms can be excluded."

In each chapter, the book provides a clear and engaging discussion of the relevant theory, with excellent diagrams and clearly written text and equations. The real *pièce de résistance* is the listing of computer code, which the reader can execute on his own computer and follow along with the exercises that are keyed to the chapters. The code is concise and annotated and includes a listing of relevant input files. The approach provides a practical software template for learning the theory and techniques of computational chemistry.

The choice of topics is excellent. After the fundamentals of Hückel and SCF calculations, the author considers the relationship of the calculated results to thermodynamics, solvent effects, and free-energy perturbation techniques. Chapter 4 considers force-field methods and the calculation of normal modes. There is a discussion of minimization methods, which gives practical exercises and source code for the steepest descent and Newton−Raphson methods. This is vital background information for a generation of individuals who tend to look no further than the "minimize" button on their PC modeling program. It is nice to know how it works.

The latter half of the book concentrates systematically on enzyme structure and function. These are exemplified beginning with the proton-transfer reaction in papain. This example introduces enzyme molecule components, such as imidazole, as participants in the reaction. Subsequent examples and input files explore electrostatic effects and alkali metal cations, in the context of enzymatic reactions.

Software examples follow the development of theory in each chapter. Implementation of the software provides the means to do the exercises. Source code is written in FORTRAN. This choice makes it very readable and comprehensible to people who are not heavy-duty programmers but who want to browse the code for understanding. It is well-structured, so that it would be easy to convert the subroutines to C or BASIC to suit your own computer, with a minimum of bother. In that regard, it would be convenient to have a file with the code listing, to avoid retyping. Perhaps this could be accomplished in the future through a web site.

The volume includes a comprehensive table of contents; the index is complete and thorough. Each chapter concludes with a bibliography. Given the book's focus on learning by examples, the choice of topics and the literature meet the purpose very well.

The book is designed for a one-semester course for advanced undergraduate or graduate students in biophysical chemistry and computer modeling of macromolecules, and also for self-study. I wish that I had had such a course 25 years ago. The book is highly readable and is strongly recommended to scientists and to students who want to advance beyond the menu screen and graphic user interface of their computer.

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The Merck Index. Twelfth Edition on CD-ROM and User Guide. By Janet E. Ash. Chapman-Hall, London, 1996. ISBN 0-412-75650-1. $299.95.

To most practitioners of medicinal chemistry, the utility of the *Merck Index* is self-evident. The current 12th edition lists over 10 000 compounds that have demonstrable biologic effects and additionally lists common solvents, reagents, and many chemical building blocks. The *Merck Index* now meets the challenge of the contemporary, on-going information explosion by providing computer access via CD-ROM.

A keyword search of the *Merck Index* will locate many additional citations where the keyword is mentioned,

as well as higher levels of aggregation, beyond what has been traditionally supplied in a simple paper index. The CD-ROM index can be searched for various categories of text strings, using a very simple query input format. The power of this is clear: the text of the entries can be searched for an author's name, to reveal what else the author has invented; other useful categories (such as "herbicide" or "flame retardant") can be searched.

Perhaps the most important single feature of the computer version is its ability to do structure and substructure searches. Thus, it is possible to rapidly search for such topics as, e.g., all benzyl-containing carboxylic acids or all primary amines attached by a two-carbon chain to any substituted or unsubstituted imidazole ring. The substructure query can be narrowed as much as desired, by explicitly attaching hydrogen atoms or other relevant substituents. The cited literature should quickly provide synthetic methods and toxicology of the subjects compounds; patent citations will reveal the extent and state of prior art. All of this is accomplished efficiently by the Hampden Data Services structure drawing and search engine which are embedded in the program. This is the same as in the STN Express and the Sigma-Aldrich Catalog on CD-ROM. It is easy and user-friendly.

Beyond the obvious scientific utility of the exact structure and substructure search, all of the usual catalog entries (line name, empirical formula, physical properties, and text) are searchable from the program main menu. Various search strategies can be chained together using Boolean constructs, leading to lists of compounds which meet several criteria simultaneously. The program runs on an IBM-compatible PC, using Windows 3.1 or Windows 95. My colleagues and I have tested it on a 200-MHz Pentium-Pro, with Windows 95 environment. A Macintosh version is also available. Queries such as those mentioned above can be processed in minutes, and output may be viewed and browsed on the screen or printed. Structural results of the search may be printed with up to 18 chemical drawings per page. Graphical output may also be copied and imported to word-processing programs.

This product is not a direct substitute for a search of the scientific literature. But, the information gleaned from the *Merck Index* on CD-ROM can assist in defining a search strategy for STN on-line, for example, and can lead to establishing what key words or substructures are important, prior to committing to the expense of the on-line search.

The *Merck Index* on CD-ROM is highly recommended, in addition to the traditional hard copy.

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