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Book Review: *A Practical Introduction to the Simulation of Molecular Systems*

A Practical Introduction to the Simulation of Molecular Systems. M. J. Field, Cambridge University Press, Cambridge, 1999.

The author begins this fine book with the comment "The reason that I have written this book is simple. It is the book that I would have liked to have had when I was learning how to carry out simulations of complex molecular systems." Anyone who simulates proteins or other polymers knows exactly what the author is talking about: the huge gap between monographs on computer simulations of atomic and small molecule systems, and those of biopolymers. Astute beginning graduate students might read the former and then readily simulate liquid argon. Likewise, they might read the latter and be able to understand a research paper on the normal modes of myoglobin. But it is very unlikely that any student would be able to generate those modes without access to a large molecular simulation package such as CHARMM, AMBER or GROMOS, and a local expert for help with the input parameters. This book and the accompanying FORTRAN modules (DYNAMO) systematically walk the reader through the maze of operations required to simulate a complex molecule.

Chapters 1 through 5 describe how to set up a simulation. After preliminaries in Chapter 1, Chapter 2 introduces the "hydrogen atom" of biomolecules, N-methyl-alanyl-acetamide, sometimes referred to as the alanine dipeptide, or blocked alanine (bALA). Three different residues (N-methyl, a central alanyl, and terminal acetyl) are defined for bALA, thereby initiating the reader into the complicated bookkeeping required for proteins. Chapter 3 defines the internal coordinates (bonds, angles, and dihedral angles) and the transformations required to superimpose structures. The energy function is introduced in Chapters 4 and 5. The underlying quantum mechanical basis for molecular interaction and the Born–Oppenheimer approximation are discussed, though the main emphasis is on the empirical (and classical) potential energy functions presently used in biopolymer simulations. Details essential to the calculation of derivatives of

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the energy function, polarization, and truncation of interactions at long distances, as well as programming issues are carefully explained.

Chapters 6 and 7 describe molecular mechanics, which is to be distinguished from molecular dynamics (MD) or Monte Carlo (MC). While MD and MC are the methods of choice for simulating simple and organic liquids, molecular mechanics is in many ways the "heart and soul" of protein simulation. This is because the time scale of protein motion is too long and the potential energy surfaces too complex for MD and MC to explore much of the interesting behavior. These chapters describe ways of calculating energy minima, saddle points, reaction paths and normal modes, as well as how to estimate equilibrium and rate constants from them. The techniques are illustrated using a Muller–Brown two parameter potential energy surface, argon clusters, cyclohexane, and bALA. These chapters are among the best in the book. They take the reader from the elementary to the advanced in an extremely clear fashion, and even experts in simulation should gain new insights.

Molecular dynamics is described in Chapters 8 through 10. First, elementary algorithms (Verlet and its minor permutations) and trajectory analysis are illustrated with a short trajectory of bALA in a vacuum, and then simulated annealing is shown to accelerate conformational sampling (Chapter 8). Periodic boundary conditions, Ewald summation, multipole expansions, and implicit solvent models are introduced (Chapter 9), followed by correlation functions, temperature and pressure control, and estimation of free energy differences using umbrella sampling (Chapter 10). This is a lot to cover, and some might find the treatment too cursory (statistical mechanics is de-emphasized, and quantum mechanical methods are not discussed). The ambitious novice, however, should be able to simulate a peptide in water after going through these chapters, which invariably will be very satisfying.

The Metropolis Monte Carlo method is introduced in Chapter 11, and the exposition of free energy techniques is continued. A very clear formal explanation of thermodynamic integration and statistical perturbation methods is followed by an example of computer age alchemy: turning a water molecule into methane in order to calculate the free energy of methane solvation. This application of what appears to be a liquid state physics problem is not an accident. The methane/water system illustrates hydrophobic interaction, a cornerstone of protein structure, and has been used to parameterize potentials for protein simulations.

Chapter 12 contains useful details on *z*-matrices, constraints, and solvation that are needed to carry out some of the exercises and examples. The annotated bibliography provides an excellent background, although it lacks the most current literature (e.g., the more advanced MC methods). At

the time of this writing, readers attempting to get the programs online will find that the internet site listed in Appendix A is not correct. The downloadable software is available from the book's catalogue page, http://www.cup.cam.ac.uk/scripts/webbook.asp?isbn = 052158129X or directly from the DYNAMO web site, http://www.ibs.fr/ext/labos/LDM/projet6/welcome_fr.htm. It is noted on the latter site that modules for quantum molecular mechanics will soon be made available.

In summary, this book provides a very useful introduction to the simulation of complex molecules, particularly peptides and proteins, and nicely fills the gap in monographs noted at the beginning of this review. It could be used as a text for an advanced undergraduate course in molecular modeling. Instructors could add theoretical details knowing that the practical ones are covered (including a free and well documented program), and will be able to build on the carefully thought out examples and exercises. Anyone who wants to learn how to simulate biopolymers from the ground up will find this book an excellent resource.

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