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BOOK REVIEW

Chipot, C., Pohorille, A., Eds. Free Energy Calculations: Theory and Applications in Chemistry and Biology

Springer, 2007. 530 + xvii pages. $109.00 in paperback, $199.00 in hardcover

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> "The free energy of a reaction is its single most important thermodynamic property." [1]

It is becoming increasingly widely recognized that interpreting complex reactions in solution or in enzymes is meaningless unless one performs a proper statistical average, which involves a competition of energetic and entropic driving forces and hence a free energy calculation (although one still sees some theoretical and interpretative work that ignores this). Hence, this is a welcome book for computational chemists. The editors have put together a well coordinated series of chapters explaining various aspects of free energy simulations of condensed-phase systems. In addition to the editors and their coworkers, there are chapters by Eric Darve, Gerhard Hummer, Nandou Lu and Thomas B. Woolf, Christoph Dellago, Ioan Andricioaei, Larry Pratt and Dilip Asthagiri, Scott Shell and Athanassios Panagiotopoulos, Tom Beck, and Thomas Simonson, all very knowledgeable and widely recognized experts on the subjects on which they write. These subjects include free energy perturbation theory, umbrella sampling, thermodynamic integration, Jarzynski's identity, Monte Carlo sampling, the Gibbs ensemble, path integrals, the nonhomogeneous Poisson equation, and simplified linear interaction energy methods for ligand–receptor interactions. The chapters are mainly intended to be pedagogical and not conference-like reviews of current work.

For the most part, the book assumes an advanced knowledge of graduate and research-level statistical mechanics. There are 886 displayed equations. The 14 chapters have an average of almost 100 references each, and the references include journal article titles.

I do not have any serious complaints, but a reader interested in calculating reaction rates should be aware that neither transition state theory nor the relationship [2] of free energy of activation to the potential of mean force is covered (however, Darve's chapter provides very useful background for understanding this relation). The limit of small molecules is also not discussed, although some of the techniques used for condensed-phase free energy calculations are also useful for certain calculations of molecular free energies. Except for chapter 13 by Chipot, Mark, Pande, and Simonson, the focus is almost entirely on methods, and not on the results of specific applications. Furthermore, within the focus on methods, the emphasis is on understanding those aspects of the methods related to the extraction of free energy from the simulation or the design of the simulation to allow this. Thus, for example, practical application of these ideas may require running a simulation with a thermostat and periodic or stochastic boundary conditions, but these kinds of aspects of free energy calculations are not the focus here. The promising enveloping distribution sampling method of computing a free energy difference from a single molecular dynamics simulation of a reference state appeared too late [3] to be included in the book.

Readers who enjoy innovative language usage may find it interesting that one author coined the phrase "free-energetically uphill" rather than use the technical term "endergonic."

The book can be highly recommended to serious practitioners who carry out or plan to carry out, proper liquid-phase simulations of free energy changes or equilibrium constants by the molecular dynamics method.

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