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Book review

P. Deuflhard, J. Hermans, B. Leimkuhler, A.E. Mark, S. Reich, R.D. Skeel (eds): Computational molecular dynamics: challenges, methods, ideas. (Lecture Notes in Computational Science and Engineering, Vol. 4)

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The *Lecture Notes in Computational Science and Engineering* is an infrequently published series that currently consists of 21 volumes http://www.springer.de/math/series/lncse.html. This fourth volume of the series presents the proceedings of the second international symposium on algorithms for macromolecular modelling, which was held at the Konrad Zuse Zentrum in Berlin, Germany, on 21–24 May, 1997.

The symposium brought together more than 120 computational scientists from diverse disciplines. The proceedings contain a total of 29 refereed articles, including both original research and review-type papers. In accordance with the main topics of the symposium, the volume is divided into five chapters: conformational dynamics, thermodynamic modelling, enhanced time-stepping algorithms, quantum–classical simulations, and parallel force field evaluation.

It is certainly not a trivial task to keep up with all the developments in the molecular dynamics (MD) arena. Herman Berendsen's excellent introduction to this volume provides a review of the entire MD field and is perhaps the article most accessible to a nonexpert. It attempts to illustrate the complex details of numerous essential approximations and their incumbent pitfalls. The traditional distinction is made between the treatment of molecular phase space and the fields in which molecules are embedded. For the latter, Berendsen anticipates increasing focus on Poisson–Boltzmann fields and smoothing functions between different ranges of these fields. Berendsen states that two major problem areas MD faces are the development of effective models for long-range forces and of algorithms for the simulation of time periods of microseconds and beyond. We are now a third of the way nearer to Berendsen's 15-year extrapolation that we will be capable of performing simulations over microseconds, yet this goal, often echoed in articles in this volume, remains a challenge for MD simulations to this date.

An in-depth discussion of all 29 papers in this volume is beyond the scope of this review but some selected and representative contributions are highlighted. In the "conformational dynamics" chapter, proteins take center stage. Helms and McCammon, for example, present a study based upon cAMP-dependent kinase, which represents perhaps the most common implementation of protein MD in this collection. Using the CHARMM22 force field for free energy calculations, adaptive time steps, and the Poisson–Boltzmann approach to reduce electrostatic interactions to forces, the authors make use of normal-mode and principal component analysis to predict concerted protein domain motions.

Izrailev et al. model protein–ligand complexes along with an external force to pull the ligand away from its receptor site. Although this presents an irreversible process, averaging multiple events permits the calculation of thermodynamic factors that are reconcilable with atomic force microscopy experiments. Several examples are presented, ranging from the popular avidin–biotin test case to studies designed to "pull out" lipids from membranes.

In the chapter "enhanced time-stepping algorithms", Skeel and Izaguirre demonstrate how a little numerical finesse can be applied to reduce the threshold effect in MD sampling wherein time stepping in the region of half the fastest normal mode results in large deviations in calculated energies. As is often the case for biopolymer simulations, the phase space is divided into "fast" and "slow" terms. In this case, it was discovered that a time-averaged slow force term, when applied in impulses,

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allowed the so-called 5fs barrier to be overcome. This technique was implemented in a program titled MOLLY.

"Parallel" in the title of the final chapter refers to parallel processing computation. The current trend towards "economical computing" by clustering low cost computers makes this chapter perhaps the most topical of all. In order to investigate the possible increase in calculation speed via parallel processing, Okunbor and Murty distribute MD pairwise force matrices over 4, 8, and 16 processors using a variety of schemes. By contrast, Phillips et al. introduce a system (NAMD) that uses a hybrid of spatial grid distribution and interleaved interaction forces. NAMD makes use of common computer memory and messaging; however, this hardware implementation has generally not experienced significant interest in the years following this report, which ought to be reconsidered.

Even 5 years after the symposium was held, the articles of the proceedings remain an excellent survey of the topic. In general, the contributions are well written and illustrated, although there are some minor typographical and grammatical errors. Any computational scientist wishing to read a limited number of articles to become familiar with this complex subject matter and the diversity of concepts in this research area would be well advised to consider this collection. However, without doubt, these articles make significant assumptions about a reader's prior general knowledge of theoretical and computational chemistry and may thus not be suitable as an introduction for a more general audience, with the exception of Berendsen's review, as mentioned earlier. Particularly the "quantum–classical simulations" chapter is rich in bewildering acronyms and formulations. Also, a glossary index and a summary bibliography, including some related review articles, would have further improved this nevertheless important volume.