Preface

As computational hardware continues to develop at a rapid pace, quantitative computations are playing increasingly important roles in studying biomolecular systems. One of the eminent challenges that the field faces is to develop the next generation of computational models that strike the proper balance of computational efficiency and accuracy, so that problems of increasing complexity can be tackled in a systematic and physically robust manner. In particular, properly treating intermolecular interactions is fundamentally important to the reliability of all computational studies. In this book, we have invited leading experts in the area of biomolecular simulations to discuss cutting-edge ideas regarding effective strategies to describe many-body effects and electrostatics at quantum, classical and coarse-grained levels.

The first section covers recent developments of quantum mechanical (QM) models for biomolecular applications. We start with two chapters that discuss quantum mechanics–based force fields, i.e., linear-scaling quantum mechanical models that divide a macromolecule into smaller QM fragments that interact with each other through approximate intermolecular forces. The model of York and co-workers is built on an approximate density functional tight binding model for the fragments but multipolar interactions between the fragments. The Xpol framework of Gao and Truhlar is general with respect to the QM level and inter-fragment interactions can be treated with different levels of approximations. The next few chapters discuss the physical origins of intermolecular interactions using different energy decomposition schemes, and the insights provide guidance to the development of the next generation of force field models. Sherrill and Merz discuss the symmetry adapted perturbation theory in great depth, while Zhang

examines intermolecular interactions using a different density-based energy decomposition scheme; Slipchenko reviews the recent developments of the effective fragment potential approach, in which all terms have clear physical connection to an underlying QM model.

The second section focuses on recent advances in atomistic force fields for biomolecules. Mackerell and Roux summarize the recent development of polarizable force fields, especially the Drude-oscillator based model. This is complemented by chapters by Meuwly et al., and Cisneros and Piquemal, who discuss the importance of multipole-based electrostatic models in development of highly accurate atomic force fields. These discussions are then followed by the contribution of Ichiye, who clearly highlights the importance of multipoles in describing water, arguably the most important molecule of all time. Zhang and co-workers then discuss the treatment of polarization using a framework that couples linear-scaling QM calculations with classical simulations. Finally, we have two chapters on the treatment of solvent using a continuum model; although this topic has a long history, progress is needed to make such models numerically robust and efficient for very large solutes, treated either quantum mechanically or classically. Herbert et al. and Wei and Baker have attacked these issues from complementary angles.

In the final section, we have several chapters that discuss the treatment of electrostatics and many-body effects in the context of coarse-grained (CG) models. CG models are required to extend the temporal and spatial scales of molecular simulations, although the development of physically robust and transferrable CG models represents a major challenge as well. The chapters of Li, Grossfield and Ren emphasize the importance of including multipolar effects in developing CG models for proteins, lipids and RNA systems, respectively. The contribution from Papoian and co-workers nicely demonstrates how electrostatic interactions can be treated effectively at the CG level for highly charged systems such as DNA and protein-DNA complexes.

With this book, our goal is to not only provide an up-to-date snapshot of the current molecular simulation field but also stimulate the exchange of ideas across different sub-fields of modern computational (bio)chemistry. We hope that the book will

become a broadly adopted reference for the biomolecular simulation community and help attract talented young students into this exciting frontier of research.

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