PREFACE

For biomolecular systems as big as solvated proteins, the combined quantum mechanics/molecular mechanics (QM/MM) method has proved its role as a potent computational technique. This method synergizes the advantages of both the quantum mechanical (QM) and the molecular mechanical (MM) methods. The QM method is needed for modeling of electronic processes including reaction mechanisms and is applicable to systems as big as a few hundreds of atoms. For biomolecular interactions, however, we need to be able to model systems as big as several thousands of atoms which are doable by applying MM methods. The QM/MM method uses the advantages of both the QM and the MM methods, and hence, its accuracy is due to the QM method and the speedup is due to the MM method. In a QM/MM scheme, a QM method is applied to the species of interest for a chemical transformation and the MM method is used for the treatment of the rest of the protein and the solvent.

Warshel and Levitt published the first paper on the QM/MM method and the two authors together with Martin Karplus were awarded the 2013 Nobel Prize in Chemistry (http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2013/) for the development of this method for modeling of complex biomolecular systems.

This thematic volume of *Advances in Protein Chemistry and Structural Biology* is a collection of some of the most recent advancements in both QM/MM method developments and applications to biomolecular systems. In Chapter 1 by Juan Torras et al., the development and application of a new program—PUPIL—for simultaneous treatment of more than one active site in complex biological systems is reviewed. In Chapter 2 by Marcelo Marti et al., the application of HyDRA—a hybrid differential relaxation algorithm—for calculation of an enzymatic reaction free energy is presented. In Chapter 3 by José Ortega et al. is reviewed the application of a new QM/MM method—FIREBALL/AMBER, synergizing a density functional theory method—FIREBALL—and the molecular dynamics package—AMBER—for studying biomolecular interactions. Chapter 4 by Poonam Singh et al. focuses on QM/MM-based approaches for the prediction of novel drug–target interactions. Chapter 5 by Sam de Visser et al. introduces a review of mechanistic computational studies on metal-containing haloperoxidases and halogenases. Chapter 6 by Russell

Boyd et al. focuses on explanation of the effect of the protein environment and the choice of the quantum mechanics method on the reaction mechanism in QM/MM simulations. Chapter 7 by Maciej Szaleniec et al. represents on comparative study of metalloenzymes by QM and QM/MM methods. Important findings of glycosyltransferase reaction mechanisms modeled by QM/MM methods are reviewed in Chapter 8 by Laura Masgrau et al. The application of QM/MM methods in modeling of the excited states of significant for the biology photoactive proteins is represented in Chapter 9 by Wei-Hai Fang.

I would like to thank all authors of this volume of *Advances in Protein Chemistry and Structural Biology* for their excellent contributions to the volume and for their work. I would like also to thank the *APCSB* Editor-in-Chief Dr. Rossen Donev and Helene Kabes, Mary Ann Zimmerman from Elsevier (Oxford, UK), and Surya Narayanan from Elsevier (Chennai, India) for their work on this volume.

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