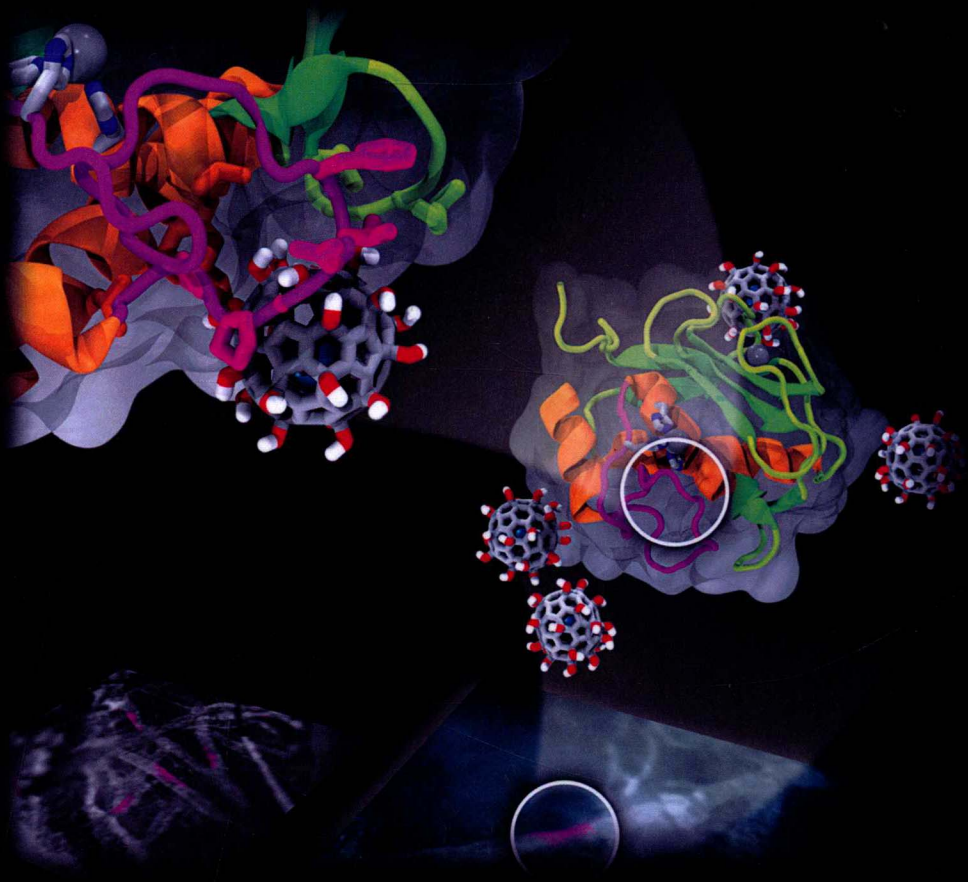
SERIES IN COMPUTATIONAL BIOPHYSICS
Nikolay V. Dokolyan, Series Editor

Molecular Modeling at the Atomic Scale

Methods and Applications in Quantitative Biology



Edited by
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Molecular Modeling at the Atomic Scale

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Molecular Modeling at the Atomic Scale: Methods and Applications in Quantitative Biology
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To my father Guomei and my mother Hanqing

To my wife Grace for her everlasting support

Series Preface

The 2013 Nobel Prize in Chemistry was awarded for the "development of multiscale models for complex chemical systems." This prize was particularly special to the whole computational community as the role that computation has played since the pioneering works of Lifson, Warshel, Levitt, Karplus, and many others was finally recognized.

This Series in Computational Biophysics has been conceived to reflect the tremendous impact of computational tools in the study and practice of biophysics and biochemistry today. The goal is to offer a collection of books that will introduce the principles and methods for computer simulation and modeling of biologically important macromolecules. The titles cover both fundamental concepts and state-of-the-art approaches, with specific examples highlighted to illustrate cutting-edge methodology. The series is designed to cover modeling approaches spanning multiple scales: atoms, molecules, cells, organs, organisms, and populations.

The series publishes advanced-level textbooks, laboratory manuals, and reference handbooks that meet the needs of students, researchers, and practitioners working at the interface of biophysics/biochemistry and computer science. The most important methodological aspects of molecular modeling and simulations as well as actual biological problems that have been addressed using these methods are presented throughout the series. Prominent leaders have been invited to edit each of the books, and in turn those editors select contributions from a roster of outstanding scientists.

The Series in Computational Biophysics would not be possible without the drive and support of the Taylor & Francis Group series manager Luna Han. All the editors, authors, and I are greatly appreciative of her support and grateful for the success of the series.

Nikolay V. Dokholyan
Series Editor
Chapel Hill, North Carolina

Preface

Molecular modeling has seen great progress in a wide range of biological applications in recent years due to the advancement of novel algorithms and high-performance computing. The gap between the timescales achievable by experiments and by computer simulations has been significantly reduced due to the concurrent advances in both experimental and theoretical techniques. Scientists can nowadays access microsecond-to-millisecond timescales with atomic detail, which is sufficient to characterize many important biological processes, such as the folding dynamics of some key proteins. This book captures the perspectives of leading experts on this transformation in theoretical molecular biology and illustrates how molecular modeling approaches are being applied to change our understanding of many important aspects of structural and molecular biology. Together, I hope these chapters provide a comprehensive overview of the fundamentals of molecular modeling and its applications in modern quantitative biology.

Although molecular modeling has been around for a while, the groundbreaking advancement of massively parallel supercomputers and novel algorithms for parallelization is shaping this field into an exciting new area. There is an increased interest in molecular modeling, as witnessed by many new conferences and newcomers, particularly from the emerging world. Until now progresses, particularly the development of novel algorithms and massively parallel computing techniques, have been led by a small group of risk-takers. With the maturation of these algorithms and simulation techniques, a broadly accessible book that lays out the fundamentals of molecular modeling will helpfully broaden these techniques to a much larger community.

This book covers both the advanced techniques of molecular modeling and the latest research advancements in biomolecular applications from leading experts, so the content should be of interest to academic and industry professionals in addition to graduate students. The book begins with a brief introduction (preface) of the major methods and applications that are presented in the chapters for molecular modeling and its applications in structural and molecular biology. Section I: Advanced Simulation Techniques (Chapters 1 through 3) covers the development of cutting-edge methods/algorithms, new polarizable force fields, and massively parallel computing techniques. Chapters 4 through 12 will describe how these novel techniques can be applied in various

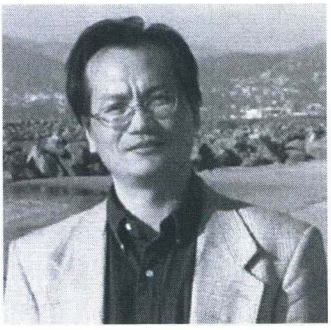
research areas in molecular biology. Section II: Self-Assembly of Biomolecules (Chapters 4 through 7) covers topics related to the self-assembly of biomacromolecules, including protein folding, RNA folding, amyloid peptide aggregation, and membrane lipid bilayer formation. Section III: Biomolecular Interactions (Chapters 8 through 10) focuses on the important biomolecular interactions, including protein interactions with DNA/RNA, membrane, ligands, and nanoparticles. Section IV: More Applications in Molecular Biology (Chapters 11 and 12) covers other emerging topics in biomolecular modeling, such as DNA sequencing with solid-state nanopores, biological water under nanoconfinement, and so on.

This book provides advanced techniques and real-world examples, which should be useful to senior undergraduate and graduate students, as well as established researchers in chemistry, molecular biology, computer science, and bioengineering. I hope courses such as computational chemistry, biophysical chemistry, biophysics, statistical mechanics, and computational molecular biology might find some of the contents useful as textbook or supplementary material. In addition, it might be of interest to academic and industry professionals in drug discovery and other biotechnologies.

Finally, I thank all the contributing authors for their excellent work and fruitful collaboration on this project. The very helpful and efficient technical assistance of Luna Han in putting together this book in a timely manner is greatly appreciated.

Ruhong Zhou

Editor



Ruhong Zhou is a research staff scientist and manager of Soft Matter Theory and Simulation Group at IBM Thomas J. Watson Research Center, as well as an adjunct professor in the Department of Chemistry, Columbia University. He is an elected fellow of the American Association of Advancement of Science (AAAS) and American Physical Society (APS). He received his PhD under the guidance of Prof. Bruce Berne in chemistry from Columbia University in 1997. Dr. Zhou joined IBM Research in 2000 after spending two and a half years working with Prof. Richard Friesner (Columbia University) and Prof. William Jorgensen (Yale University) on polarizable force fields. He has authored or coauthored more than 150 journal publications and 20 patents, delivered more than 150+ invited talks at major conferences and universities internationally, and chaired or cochaired many conferences in the fields of computational biology, computational chemistry, and biophysics. He is part of the IBM BlueGene team that won the 2009 National Medal on Technology and Innovation. He has also won the IBM Outstanding Technical Achievement Award (the highest technical award within IBM) in 2014, 2008 and 2005, the IBM Outstanding Innovation Award (OIA) in 2012, the IBM Research Division Award in 2005, the Columbia University Hammett Award in 1997 (for best graduates), and the American Chemical Society DEC Award on Computational Chemistry in 1995. His current research interests include the development of novel methods and algorithms for computational biology and bioinformatics, as well as large-scale simulations for protein folding, ligand–receptor binding, protein–protein interaction, and protein–nanoparticle interaction.

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Contents

SECTION II Self-Assembly of Biomolecules

SECTION III Biomolecular Interactions

SECTION IV More Applications in Molecular Biology

Section I

Advanced Simulation Techniques