

Preface

Thanks to enormous progress in sequencing of genomic data, presently we know millions of protein sequences. At the same time the number of experimentally solved protein structures is much smaller, ca. 60,000. This is because of large cost of structure determination. Thus, the theoretical *in silico* prediction of protein structures and dynamics is essential for understanding the molecular basis of drug action, metabolic and signaling pathways in living cells, and designing new technologies in the life science and material sciences. Unfortunately, a “brute force” approach remains impractical. Folding of a typical protein (*in vivo* or *in vitro*) takes milliseconds to minutes, while the state-of-the-art all-atom molecular mechanics simulations of protein systems can cover only a time period of nanoseconds to microseconds. This is the reason for the enormous progress in the development of various multiscale modeling techniques applied to protein structure prediction, modeling of protein dynamics and folding pathways, *in silico* protein engineering, model-aided interpretation of experimental data, modeling of macromolecular assemblies, and theoretical studies of protein thermodynamics. Coarse-graining of the proteins’ conformational space is a common feature of all these approaches, although the details and the underlying physical models span a very broad spectrum.

This book contains comprehensive reviews of the most advanced multiscale modeling methods in protein structure prediction, computational studies of protein dynamics, folding mechanisms, and macromolecular interactions. The presented approaches span a wide range of the levels of coarse-grained representations, various sampling techniques, and a variety of applications to biomedical and biophysical problems. It was our intention to provide a collection of comprehensive reviews that could be used as a reference book for those who just are beginning their adventure with biomacromolecular modeling but also as a valuable source of more detailed information for those who are already experts in the field of biomacromolecular modeling and in related areas of computational biology or biophysics.

Proteins are linear copolymers composed of amino acids. Important ideas of polymer physics inspired the field of protein modeling. Chapter 1 explains some basic concepts of polymer conformational statistics and dynamics of chain molecules in context of simple lattice models. This chapter demonstrates how

these ideas could be employed in protein modeling. Chapter 2 describes application of a lattice-based protein model to the very challenging problem of protein docking. Chapter 3 provides a comprehensive overview of various coarse-grained protein-like and protein models. This chapter describes (among other approaches) probably the most rigorous system of physics-based reduced modeling of proteins. Coarse-grained, multiscale, protein modeling requires specific designs of interaction schemes. Chapters 4–6 provide in-depth overviews of various level force-fields for the reduced representations of protein conformational space, including knowledge-based statistical potentials. Chapters 7 and 8 (but also, in part, Chapters 3–5 and 12) describe a variety of applications of reduced models in the study of protein dynamics, folding pathways, molecular mechanisms of mechanical unfolding, and protein interactions. Chapter 9 gives an overview of the most effective sampling strategies in a reduced, although unrestricted conformational space. Chapters 10 and 11 present a very efficient philosophy of a conformational search, where the target structures are assembled from fragments excised from already known protein structures. These strategies proven to be very effective in the large-scale, automated *in silico* structure prediction. Chapter 12 describes a multiscale method, based on a high-resolution lattice model, for modeling protein folding pathways. Chapters 13 and 14 discuss the most important ideas and techniques of comparative modeling – the most effective and the most popular method for theoretical prediction of protein structures. These chapters provide also reviews of the model-quality assessment methods.

The contributing authors are world-wide recognized experts. Some of them (Bujnicki and Zhang) are leaders in the field of protein structure prediction, as assessed by the recent (CASP6–CASP8) community-wide experiments in a blind structure prediction. Others also developed very successful methods for the protein structure prediction (Scheraga, Liwo, Feig, and Kihara). Several of the authors of this book developed very efficient coarse-grained interaction schemes for protein models based on either an evolutionary knowledge approach (Jernigan and Scheraga have built theoretical foundations of this class of approaches, but others also contributed significantly: Feig and Micheletti) or a physics-based approach (Scheraga, Liwo, Feig, and Irbäck). Among the authors are also the world top leaders of comparative modeling (Bujnicki, Zhang, Tramontano, and Kihara) and automated structure prediction (Zhang and Bujnicki) – the structure prediction server created by Zhang is the best till date. The book presents also the state-of-the-art methods of evaluation of quality of the theoretical protein models (Tramontano and Kihara). Recently, a significant progress has been achieved in multiscale modeling of protein dynamics and folding mechanisms. The authors of the chapters dealing with this class of problems are also world-class leaders (Scheraga, Liwo, Irbäck, Feig, Cieplak, Jernigan, and Micheletti). The conformational search strategies are crucial in protein modeling. Developers of the most efficient computational techniques and strategies are also among the authors (Hansmann, Scheraga, and others).

Multiscale Approaches to Protein Modeling

Kolinski, A. (Ed.)

2011, XII, 355 p., Hardcover

ISBN: 978-1-4419-6888-3