

Preface

Computational structural biology aims primarily at establishing sequence-structure-function relationships for biological molecules using *in silico* techniques. This discipline emerged about 40 years ago (Levitt M. (2001). *Nature Struct Biol* 8:392–393) and has made much progress in the past decade. The purpose of this book is to provide an overview of the progress in the field and to articulate some of the key challenges for the coming years. By no means could we cover the field comprehensively in just one book, and we thus focused on the structure and function of proteins and RNAs.

The advent of large genome sequencing reinforced the observation that structural information is needed to understand the detailed function and mechanism of biological molecules such as enzyme reactions and molecular recognition events. Furthermore, structures are obviously key to the design of molecules with new or improved functions. In this context, computational structural biology emerged as a discipline to develop computational tools to analyze and predict molecular structures and simulate their dynamical behavior. These theoretical approaches provide valuable insights into the detailed basis of molecular function and enable the effective design of experimental approaches to functional genomics. Major research topics include protein and RNA structure prediction, protein folding, protein and RNA dynamics with emphasis on large complexes and assemblies, molecular recognition, drug discovery and protein engineering.

A key motivation for putting together this book came from our own experience, as 15 years ago we established the Swiss-Model, the first Web-based server for protein structure modeling. One major driver behind our vision was to mask much of the complexity associated with protein modeling behind a simple interface, thereby providing the scientific community with the possibility to gain insights

into the 3D structures of proteins of interest, without the need to learn and purchase complex and expensive software. There are probably three major factors contributing to the success of the Swiss-Model. First, the server is easy to use, as the Web-interface removes most of the complexity normally associated with protein modeling. Second, DeepView (also known as the Swiss-PdbViewer), which is available for most relevant computer platforms, has many powerful and easy-to-use features developed by modelers for modelers. Third, the uninterrupted operations for 15 years has allowed us to develop a robust and stable system. Today, well over 60,000 users build in excess of 400,000 models every single year and can access over a million pre-computed models available in the Swiss-Model Repository. Our objective is to continuously improve the performance of the server and the quality of the models it generates.

We are particularly thankful to Nicolas Guex for his many crucial contributions to the development efforts of the Swiss-Model and the DeepView and to Gale Rhodes of the University of Southern Maine for coordinating the active DeepView user community. We also thank Alexander Diemand, Konstantin Arnold, Jürgen Kopp and Lorenza Bordoli for their many contributions to the development and operations for the modeling platform. Furthermore, we are deeply indebted to Jake V. Maizel Jr, Timothy N.C. Wells, Jonathan C.K. Knowles, and Allan Baxter who have provided the necessary environment and resources during the various phases of this project. Finally, we thank Stanley K. Burt, Robert W. Leberer III, Karol Miaskiewicz and Jack R. Collins of the Advanced Biomedical Computing Center at the National Cancer Institute in Frederick Maryland for their support in operating the US mirror of the Swiss-Model server. We gratefully acknowledge the financial support by GlaxoSmithKline, Novartis, the Swiss National Science Foundation, the Biozentrum of the University of Basel and the Swiss Institute of Bioinformatics.

T. Schwede and M.C. Peitsch