Protein Structure and Function

Gregory A. Petsko and Dagmar Ringe.

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Trying to understand protein structure can be a daunting task to life scientists and students not familiar with structural biology. *Protein Structure and Function* by Gregory Petsko and Dagmar Ringe provides much needed help. This book is a treasure trove of information. It is a precious atlas, the usefulness of which is only surpassed by its esthetic value.

The construction and maintenance of three-dimensional organisms from "thread-like" linear proteins several orders of magnitude smaller than the organisms they build is a topic of truly mind-boggling complexity. The book's clarity of organization and presentation go a long way toward facilitating navigation of this complexity. Throughout the book, each double page is consistently structured like an appealing poster, with a catchy heading, short paragraphs highlighted by one sentence subheadings, most inviting graphics, and a box with definitions and references. Many of the poster-like double pages contain very helpful summary tables and graphics (e.g., on types of chemical interactions, domain arrangements in signal transduction proteins, multifunctional proteins, etc., found in living cells).

Despite the phenomenal amount of information their book conveys, the authors have succeeded in keeping a consistently clear and inviting format. Furthermore, each structure presented in the book is given with its Protein Data Bank (PDB) identity code, consistently linking the book with this impressive online resource.

The book contains five chapters: From sequence to structure, from structure to function, control of function, from sequence to function, and structure determination. The authors walk the reader through the most basic aspects of molecular biology, systematically building up familiarity with the basic elements of proteins, their structure, and interactions with other molecules. By introducing the notions of modularity, flexibility, situation-dependent conformation, and posttranslational modification, they prepare the field for discussions of function and its regulation. Petsko and Ringe present an exquisite collection of examples to illustrate the many functional roles of proteins in living cells, including structural elements such as tubulin, catalysis by enzymes, switch mechanisms in G proteins, amplification of signals in various receptor proteins, and control of gene expression in transcription factors.

They present a very up-to-date discussion of comparative genomics, illustrating how DNA sequence similarity can be used to investigate the potential functions of unknown proteins. All this, while pointing out the sobering fact that many proteins with similar structure and function can share

remarkably little sequence identity, effectively limiting the usefulness of homology modeling.

One criticism I have is the exceedingly short treatment of phylogenetic methods. Considering the importance of phylogenetics in comparative genomics, I would have expected the authors to at least mention the different methods of reconstructing evolutionary history (not just distance based, but also maximum-likelihood methods using detailed probabilistic models of sequence evolution).

The last chapter presents a very brief, but equally clear explanation of the methods used for empirically elucidating protein structures, X-ray crystallography, and nuclear magnetic resonance (NMR). The limitations of each method are discussed, as well as factors potentially leading to erroneous structure determination. The book provides a wealth of information and succeeds in keeping the reader's attention through the use of concise text and splendid graphics. Conveniently, the many definitions presented at the bottom of each double page are collated again in a glossary at the end of the book, as are all the references.

This book is likely to generate interest in structural biology in many students. It will also provide much needed guidance to the large number of genome scientists who are starting to investigate events downstream from coding DNA sequences (i.e., how protein structure influences phenotypes). In this era of proteomics, such a clear introduction to structural biology is very precious indeed. At the same time, the book will also serve the increasing number of organismal biologists who have questions about molecular details within their organism of choice. The overview provided by the magnificent tables, be they on various quaternary structures, protein domain interactions, or time and distance scales in functional genomics, will be worth going back to whenever panoramic orientation is needed.

I particularly appreciated that throughout the book, proteins are discussed within an evolutionary perspective, discussing examples of convergent evolution, and addressing gene evolution by domain rearrangement, notions of a past "RNA world" reflected in the persistence of RNA coenzymes, and the differences in complexity between prokaryotes and eukaryotes. Similarly the authors remind us that proteins are part of evolving organisms by repeatedly addressing the complex spatial and temporal relationships between the large number of differently modified proteins in and on living cells.

Much can be learned from viewing functional, properly folded proteins as precarious, "semiliquid" thermodynamic compromises, passed through the generations via their coding DNA sequences. Clearly this excellent book should become electronically available on the bookshelf of the National Center for Biotechnology Information/PubMed as soon as possible.

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