Textbook of Structural Biology

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The purpose of this letter is to briefly comment on the recently published "Textbook of Structural Biology". This review does not attempt to be balanced, but is a personal view biased by my interest in disentangling the evolutionary and physicochemical determinants of biomolecular structure.

Modern Structural Biology (SB) started in the 1950s with the determination of the structure of DNA and the proteins myoglobin and hemoglobin. Knowledge of biomolecular structures resulted in a deeper understanding of the molecular mechanisms of biological processes. The success of the SB program in illuminating the structural basis of the biological function of biomolecules is, in my opinion, the main reason behind the development of this research field; a field which, year after year, continues to gain momentum.

In contrast with the accelerated development of SB as a research field, there are relatively few SB textbooks. The magnitude of SB research results in a flood of information, which makes writing a textbook on structural biology a very difficult task. It demands that the authors be at the same time comprehensive, to make sure that the textbook is up to date with current SB knowledge, and selective, so that the book is comprehensible. The book under review here accomplishes the comprehensiveness-comprehensibility balance nicely.

This book is a quite thorough account of what is currently known and deemed important in SB. After a general introductory chapter, the book devotes three chapters to describe the structure of biomolecules: proteins (Chapter 2), DNA and RNA (Chapter 3), and lipids (Chapter 4). The protein-structure chapter is complemented by a series of appendices which deal with the physicochemical basis of protein structure and with computational methods related to protein research. Following this first part, most of the rest of the book consists of descriptions of central biological processes from the perspective of structural biology. The structural features of proteins, DNA, RNA, lipids, and their interactions are presented in the context of their natural functional role. In this way, we learn about protein-DNA interactions in relationship to replication, protein-RNA interactions in the chapters on transcription and translation, protein-lipid interactions in the chapter on membranes, and so on.

The first point to be made is that the authors have managed to keep an adequate balance between nucleic acids, proteins, and lipids. This contrasts with most books on Structural Biology which either consider only one type of biomolecule, or are heavily biased towards one type, often proteins. In the present book, there is one chapter to discuss the basics of each type of biomolecule, and the functional roles of all of them are described in the context of the processes in which they participate. This is one of the main strengths of this work.

Regarding perspective, the book emphasizes the structure-function relationship over the physicochemical basis of biomolecular structures. Rather than a drawback, this just makes it clear that Structural Biology is not concerned with structure per se but rather in how structure is related to biological function. The book also leaves out most of the methods used in SB research, including X-ray crystallography and NMR. I found this somewhat unsettling at first, but I later came to the opinion that this may well be considered one of the strengths of the book, which boldly focuses on Structural Biology as a body of knowledge, rather than as a research field.

An interesting and noteworthy feature of this book is that it includes a chapter on molecular evolution. This should not surprise us, since biomolecular structures are not only determined by physical chemistry but also by evolution. However, most books on structural biology do not consider evolution in great depth so this is a refreshing approach. This chapter starts with a brief account of the historical origin of evolutionary theory. Then it moves to explaining evolution at the molecular level, mentioning briefly key terms of molecular evolution theory: fitness, mutations, neutral theory, molecular clock, etc. The book then goes on to discuss in some detail two specific examples: first, that of enzymes involved in the metabolism of nucleic acid precursors, which is useful to understand subfunctionalization and neofunctionalization, and second, the evolution of globins, with nice accounts of the origin of cooperativity in (vertebrate) hemoglobin and the independent emergence (parallel evolution) of cooperativity in the dimeric Scapharca hemoglobin. I think the main weakness of this chapter is a bias towards an adaptationist view of molecular evolution: even though the Neutral Theory is mentioned, an adaptationist perspective, summarized in the statement "all present proteins have had or still have a beneficial influence on the host organism", underlies most of the chapter.

In spite of its drawbacks, the strength of the chapter on evolution is its very existence. Biomolecular structures are determined by evolution as much as by physical chemistry. However, for many years evolutionary studies were left out of SB mainstream research. It is only in the last 10-15 years that SB has again become concerned with evolution, recognizing that evolutionary theory is needed if one is to understand the meaning of current classifications of biomolecular sequences and structures, and assume they convey something more than mere similarity or dissimilarity. Therefore, it is encouraging that this textbook on Structural Biology includes a whole chapter on molecular evolution, a chapter that we hope will be improved and expanded in further editions.

To sum up, I think this book is a very good introduction to Structural Biology. It is comprehensive, balanced, clear, and up to date. The main strength of the book is that it describes biomolecular structures in the context of the biological processes in which they participate. I found it interesting that the book includes a whole chapter on evolution, which is usually not given so much weight in Structural Biology accounts, despite its importance. Since in my view biomolecular structures are as much determined by evolution as by physical chemistry, I hope the chapter on evolution will evolve towards the more central position it deserves in further editions of this fine book.

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