Re-introducing protein structure

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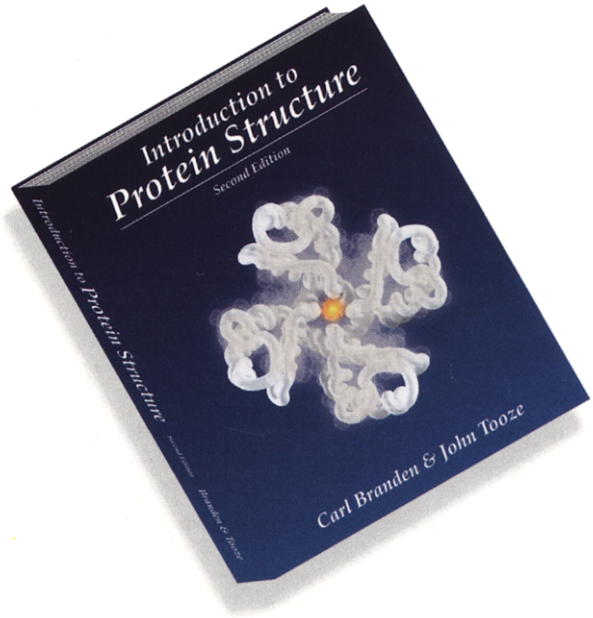
Introduction to Protein Structure (2nd edition) by Carl Branden and John Tooze, Garland Publishing, New York, 1999, 410 pp. £29.95, $47.95 ISBN 0-8153-2305-0 (paperback); £55.00, $72.95 ISBN 0-8153-2304-2 (hard cover).



We live in interesting times. The notion underlying molecular biology—that a full understanding of biology requires us to know the structures of the participating molecules in atomic detail—has evolved from a plausible premise to a conspicuous reality. Most of us use atomic structures of biological molecules on a daily basis. But as a Chinese proverb makes clear, living in interesting times may not be a blessing. As I began examining the second edition of *Introduction to Protein Structure*, the ten thousandth structure appeared in the Protein Data Bank. Every four hours, 24 hours a day and seven days a week, yet another three-dimensional structure is deposited. How can so much information be grasped? Understanding the common structural features of proteins and the relation between these structural features and biological function would be a great beginning, and Carl Branden and John Tooze have updated their classic text to do just that. Both authors are likely to be known to readers of *Chemistry & Biology*. Carl Branden recently stepped down as Research Director of the European Synchrotron Radiation Facility (ESRF) in Grenoble to return to Sweden and the Microbiology and Tumor Biology Center at the Karolinska Institute. While at the ESRF he developed one of the world's leading facilities for structural biology and continued his important original contributions to protein structure and function. He is an editor of *Structure* with *Folding & Design*, a sister publication of *Chemistry & Biology*. John Tooze is currently editor of the *EMBO Journal* and co-author of *Molecular Biology of Tumor Viruses*, *The DNA Story*, and *Recombinant DNA: A Short Course*. Many researchers keep the first edition of *Introduction to Protein Structure* handy, and the completely updated and slightly expanded second edition will soon displace its predecessor from this location.

The book is divided into two parts; the first seven chapters discuss basic structural principles, and the next eleven chapters deal with the relation of structure to function. The authors adopt the didactic approach of successful modern texts: tell the readers what you're going to tell them, tell them, and tell them what you told them. Each chapter has a short introductory statement, frequent topic headings, and a conclusion. The authors include strategically placed stories to keep the reader focused. In what could be a rather dry recital of structural motifs, one finds the story of sickle cell hemoglobin and malaria resistance in the chapter on α-helical structures and an introduction to the influenza virus, neuraminidase and hemagluttinin in the chapter on β structures. The authors also select key features and return to them in different contexts. For example, the β-α-β motif is introduced early and referred to often. It first appears briefly in Chapter 2 on protein motifs and then forms the organizing principle of Chapter 4 on α/β structures. The reader becomes so used to recognizing right-handed β-α-β motifs, that the left-handed β-α-β motif of subtilisin acquires immediate significance. The authors, along with illustrator Nigel Orme and a team of consultants, have prepared a beautifully illustrated book. The point of each figure is readily apparent with extraneous detail stripped away and the effective use of colors enhancing the point.

The first part of the book, roughly one-third of the material, is a masterful introduction to the structural principles of molecular biology. Not surprisingly, most of this material has been updated but little altered from the first edition. It remains one of the most concise, insightful and useful introductions to protein structure available.

A new Chapter 6 on folding and flexibility introduces the fascinating subject of how proteins adopt and adapt the

wonderful shapes that form the basis of the book. As usual, the chapter brings the reader from basic principles—the striking fact that globular proteins are only marginally stable—through the latest developments in chaperonin-assisted folding by the GroEL–GroES complex. The chapter also highlights the importance, at least for a protein, of being flexible, with illustrations from cyclin-dependent kinases, serpins, and the allosterism of phosphofructokinase. Each chapter ends with thoughtful lists of suggested readings, and the 18 general readings for this chapter have all appeared since the publication of the first edition. The book is not strictly limited to protein structures, and Chapter 7 on DNA structures is an excellent, if brief, introduction to this important area.

Part 1, the first seven chapters on the structural principles of biological macromolecules, sets up part 2 on the relation of structure to function. These chapters are so full of useful information and illustrative examples that only a brief summary of highlights can be given here. Part 2 begins with three chapters on protein–DNA interactions. Chapter 8 focuses on the helix–turn–helix protein motif used by prokaryotes to bind DNA, and Chapter 9 discusses DNA recognition by eukaryotic transcription factors. Chapter 10 amplifies the discussion of the preceding two chapters by covering several families of transcription factors, including zinc fingers, retinoid X receptors, GAL4, leucine zippers, GCN4 and b/HLH. Much of the material in these chapters is new to this edition, and the authors' desire not to greatly expand the length has led to some losses. A chapter on enzymes that bind nucleotides is one of the casualties. One traditional topic that survived the winnowing is Chapter 11 on serine proteinases.

The remaining chapters have been extensively, if not completely, rewritten. Chapter 12 on membrane proteins has been greatly expanded to represent the important advances in this area. The bacterial rhodopsin photosynthetic reaction center is now joined by porin channels, the potassium channel and light-harvesting complexes. Chapter 13 on signal transduction has an extensive discussion of G proteins, human growth hormone receptor, and SH2 and SH3 modules as adaptors for signaling networks. Chapter 14 deals with fibrous proteins and includes topics ranging from amyloid fibrils to spider silk. A thoughtful discussion of myosin and actin in muscle fibers finishes the chapter. Chapter 15 selects topics from the immune system and covers the immunoglobulin fold and the hypervariable regions, class I and class II major histocompatibility complex (MHC) molecules and their peptide complexes, and T-cell receptors among other topics. Chapter 16, on spherical viruses, begins with a clear discussion of icosahedral symmetry, which is used to organize the presentation of plant viruses and picornaviruses, especially human rhinovirus. A notable addition on the polyomavirus SV40 ends the chapter. The final two chapters, Chapter 17 on the prediction and design of protein structures, and Chapter 18 on the X-ray and nuclear magnetic resonance (NMR) experimental techniques used to determine structures, close out this whirlwind tour of structural biology at the close of the century.

When the first edition of *Introduction to Protein Structure* was written almost a decade ago, the authors had roughly 300 three-dimensional protein structures to consider. When the second edition was being composed, that number had grown to 6500, and when it appeared, the number was close to 10,000. We're still in an exponential growth phase, and when high-throughput structural proteo-nomics initiatives kick in, the numbers that seem so awesome today will become modest. This growth in numbers shouldn't disguise the regularity of nature, and the way in which some themes reappear in many slightly different guises. Readers of this book will understand that profound lesson for proteins.