Book Reviews

Thrombin Structure and Function by Lawrence J. Berliner, Editor

Plenum, New York, 1992. 438 pages. $95.00.

Reviewed by Gary Nelsestuen, Department of Biochemistry, University of Minnesota

Every research area is characterized by certain seminal points where it is appropriate to evaluate the past and outline the future. In areas of protein science, the solution of an x-ray crystal structure almost invariably creates such a point. This book is well timed and its stated purpose is to "serve as a desk reference on almost any thrombin-related problem": The book is quite attractive. It is a handy size, and the mixture of text and figures welcomes the reader. Unfortunately, the attractive aspects of readability may have forced some selectivity or narrowing of topics.

Three major parts of the book deal with the extremely broad research areas of thrombin: Structure, Biochemistry, and Physiology. Chapter 1 presents the x-ray structure of thrombin in a manner designed for a general biochemical audience. It walks the reader through the molecule and should be of great value to anyone interested in thrombin or other serine proteases. The Structure section is rounded out with chapters on NMR and ESR. Perhaps it is more an observation than a criticism to point out that chapters dealing with the latter techniques seem to always include an explanation of the method or presentation of actual data. Unfortunately, the explanations or data presentation must often be so brief that they are not very useful to the uninitiated and contain only information that is obvious to an expert. In contrast, chapters dealing with an x-ray crystal structure often do not attempt to explain the technique but only give conclusions. Perhaps this difference arises because the scientific audience understands or trusts the information obtained by x-ray crystal structure, but is still unclear about the value of the other methods. Anyway, NMR and ESR are contributors to our knowledge of thrombin structure and they should become more important in the future.

Parts II and III on Biochemistry and Physiology provide valuable additions to round out a desk-top reference on thrombin and are generally quite good. However, two matters arose that appeared less than optimum. The chapters in Biochemistry include a collection that seemed less than comprehensive. For example, chapters dealing with the Biochemistry of physiological interactions (inhibition by antithrombin, activation of factor XIII) are mixed with the properties of substrates or inhibitors and properties of hirudin inhibition. This combination seemed incomplete. For example, the role of thrombin in the inhibition of blood coagulation via thrombomodulin plus protein C is not given much attention even though the biochemistry of this area has enjoyed recent advances and there is much potential for application. The latter area does receive some coverage in the section on Physiology but this still seems incomplete. Actually, the various biochemical functions of thrombin in procoagulation also have no separate chapter(s), but are covered as incidental parts of many chapters. An inconsistency in style is that some of the chapters in these sections are written in a standard review format, while others concentrate on presentation of actual data.

Overall, it seems possible that this book would have benefitted from an introductory chapter tying together the various independent chapters and filling in the gaps that are invariably left when authorship is by committee. While some problems distracted somewhat from my enjoyment of the book, as well as my evaluation of its all-encompassing nature, the fact remains that *Thrombin: Structure and Function* fulfills many roles of a desk reference. I am pleased to have received a review copy and anticipate that this volume will have value for many years.

Binding and Linkage: Functional Chemistry of Biological Macromolecules by Jeffries Wyman and Stanley J. Gill

University Science Books, Mill Valley, CA. 1990. 330 pages.

Reviewed by Timothy M. Lohman, Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine, St. Louis, Missouri 63110 USA

Interactions between macromolecules (e.g., proteins, nucleic acids) and their ligands as well as among macromolecules are essential for the proper function and regulation of all biological processes. One is hard-pressed to think of a biological process that is not absolutely dependent upon a number of such interactions. However, to understand *how* these biological processes function and are regulated it is essential to understand the equilibrium binding energetics (stabilities and specificities) and kinetics of the interactions among the macromolecules and their ligands. All biological macromolecules bind ligands, hence the energetics of the interactions and conformational transitions of these macromolecules will generally be influenced by the concentration of the ligand. Furthermore, since all biological macromolecules also bind

multiple ligands, the effects of one ligand are generally influenced by or "linked" to the binding of other ligands. For example, all proteins and nucleic acids bind ions as well as protons, hence the effects of pH and ion concentration on a protein-nucleic acid interaction are generally linked. Such heterotropic effects of ligand binding are ubiquitous in biological systems and provide the basis for important levels of regulation, thus an understanding of the energetics of macromolecular interactions requires an understanding of linkage effects.

Unfortunately, there are not many monographs available that provide a useful introduction to the concepts and approaches of the thermodynamics of macromolecule-ligand binding that can be used by graduate students or advanced researchers who have not been trained in this area. *Binding and Linkage*, by Jeffries Wyman and Stanley J. Gill fills much of this gap by providing a comprehensive, yet understandable introduction to the power and utility of the concepts of equilibrium binding and thermodynamic linkage as applied to macromolecule-ligand interactions. *Binding and Linkage* is an excellent book by two of the foremost researchers in the field of the thermodynamics of macromolecular-ligand interactions. Jeffries Wyman has been the major developer of the theoretical foundations for linked function analysis of macromolecular-ligand interactions over the past 50 years. His ideas have had a major influence on most current approaches to studies of the thermodynamics of these interactions. Wyman's linked function theories provide the essential thermodynamic framework for understanding the influences of ligand binding on macromolecular conformational transitions or the binding of other ligands (heterotropic effects) or the binding of the same ligand (homotropic effects). Wyman's logic of linked function analysis provided the basis for an explanation of allosteric effects. The late Stanley J. Gill spent most of the last part of his scientific career using and refining such approaches in experimental studies of a range of interacting systems, including cytochromes and oxygen carrier proteins such as hemoglobin. Hence, the fundamental concepts in *Binding and Linkage* are made clear by two of the major figures in this discipline.

Binding and Linkage provides a basic guide for the analysis and interpretation of ligand-linked equilibria that facilitates its use by beginners; however, it also discusses more advanced topics. The first three chapters provide excellent introductions to the basic concepts and nomenclature with good experimental examples. Discussions of the properties of binding curves, methods for plotting binding curves, and the Binding Polynomial (partition function for a macromolecular system) provide a good introduction for the following chapters. Examples are given for how to construct expressions for the Binding Polynomials for more complex cases of ligand binding to multi-site macromolecules, including both homotropic and heterotropic effects and the concepts of cooperative ligand binding. Allosteric systems are discussed in Chapter 4, which also includes Wyman's first-hand historical perspective of the development of these ideas. Physical Linkages (e.g., effects of temperature and pressure) are treated in Chapter 5, with most examples being drawn from calorimetric approaches. The treatments of ligand-linked assembly of macromolecules provided in Chapter 6 and ligand linkage to macromolecular phase transitions in Chapter 7 are excellent. These are subjects that are often neglected in discussions of ligand binding, yet examples of these phenomena abound and are particularly important in a variety of biological systems.

Binding and Linkage is appropriate for both beginners and experts since it provides a general introduction to the subject as well as discussions of more advanced topics. Furthermore, the concepts of binding and thermodynamic linkage are discussed without dealing explicitly with many concepts of statistical thermodynamics, hence it can be readily used by students with a wide variety of backgrounds. The ability to analyze quantitatively and understand the implications of linkage effects, both homotropic and heterotropic, on the thermodynamics of macromolecular interactions is fundamental to all areas of biochemistry and molecular biology. As such, *Binding and Linkage* is required reading for anyone studying interacting systems at any level.