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book reviews

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Protein structure, stability and folding. Edited by Kenneth P. Murphy. Totowa: The Humana Press, 2001. Pp. ix + 252. Price US$89.50. ISBN 0-89603-682-0.

Virtually all aspects of structure and function of living things derive from the marvelous and intricate structures of proteins, and every protein's structure is tailored specifically to its biological function. Recent advances in X-ray crystallography and NMR spectroscopy have led to unprecedented progress in protein structure determination, with more than 98% of all protein structures known solved in just the last 10 y. Progress in our understanding of the stability and folding of proteins over that same period has been more modest, but there have still been significant advances in both theory and experiment.

This volume, No. 168 in the Humana Press series *Methods in Molecular Biology*, summarizes several of these recent advances in clear and concise fashion. This volume follows on from two related works from that publisher: *Protein Stability and Folding: Theory and Practice*, edited by Bret A. Shirley and published in 1995, and *Protein Structure Prediction: Methods and Protocols*, edited by David M. Webster and published last year as No. 143 in the same series. The Shirley volume dealt mainly with the practical aspects of the stability and folding of proteins. The two more recent volumes are both a mix of theoretical and practical aspects of protein structural study, with the Webster collection dealing primarily with protein structure predictive methods [see *Acta Cryst.* (2001), D**57**, 766].

Kenneth Murphy's book presents ten chapters that encapsulate many of the recent advances in the study of protein structure, stability and folding. His own opening chapter briefly discusses the thermodynamics of protein folding, the importance of hydrogen bonding and hydrophobic effects for protein stability and the loss of configurational entropy that must be overcome to achieve a folded stable state. This is followed by an excellent quantitative discussion of protein stabilization by naturally occurring osmolytes, by Wayne Bolen. The third chapter, by Ernesto Friere, summarizes recent work on structure-based prediction of protein stability and functional cooperativity. His application of structural parameterization to the global stability of a protein is illustrated with the SH3 domain of α-spectrin, in which he shows that atomic packing densities must be explicitly considered in enthalpy calculations.

Chapter 4 describes a relatively new amide-exchange NMR method that can provide direct estimates of the conformational stability of a protein without having to drive the protein through unfolding transitions. The following chapter, by Vincent Hilser, shows how ensemble-based models of protein native states can reconcile cooperative behavior observed in folding/unfolding events with non-cooperative behavior seen under native conditions. Trevor Creamer follows with a chapter that describes calculational and modeling methods for estimation of conformational entropy loss in protein folding. Chapter 7, by Carl Frieden and colleagues, presents both theoretical and experimental evidence assessing the roles that turns play in the folding and stability of proteins and proposes a method called 'turn scanning' as a general method for evaluating the importance of turns in the folding process.

James Hofrichter presents a thorough account of laser temperature-jump methods for exploring fast kinetics in protein folding systems, including peptides and model systems as well as larger proteins such as myoglobin. Chapter 9, a comprehensive evaluation of amide hydrogen exchange as a probe of kinetics of conformational fluctuations in native proteins, is a nice counterpoint to Chapter 4. As noted in the earlier chapter, the exchange process for a globally exchanging residue must occur by an EX2 (bimolecular exchange) mechanism in order to determine the conformational stability of the protein by amide hydrogen exchange. On the other hand, EX1 (monomolecular) exchange, which has received less attention over the years, can provide useful information on the kinetics of conformational interconversions. Finally, in Chapter 10, Valerie Daggett presents an update on molecular-mechanics simulations of protein unfolding and folding. This fascinating topic might have filled a volume by itself, but Daggett does the next best thing, providing 97 references that nicely summarize the relevant recent developments.

Like the predecessor volumes, this book is full of valuable insights. The selected topics are both timely and compelling, and this collection should be of interest to any researcher who is concerned about the structure, stability and folding of proteins. This reviewer would like to have seen a chapter on the statistical mechanics of protein folding (perhaps by Ken Dill), but this is a minor omission in an otherwise outstanding collection of essays.

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