Protein denaturation

Physicochemical Aspects of Protein Denaturation. By S. Lapanje. Pp 331. (Wiley: Chichester, UK, and New York, 1978.) £19.50.

THERE has been no significant, full-length review of protein denaturation since 1970. Although many fundamental principles had been laid at the time, there has been a steady advance in the detailed understanding of denaturation in the intervening years. Further, the biological and industrial significance of conformational change and stability is more widely appreciated today, and more chemists, biochemists and physicists are ready to devote time and energy to rigorous studies of the dynamics of protein structure. The field of protein denaturation has a distinguished history, starting with Ramsden's observation in 1902 that "a dead frog placed in saturated urea solution becomes translucent and falls to pieces in a few hours". Anfinsen's thermodynamic hypothesis of folding, the concept of limited pathways, quantification of protein stability, the hydrophobic interation and prediction of tertiary structure all owe something to denaturation studies, and many of these areas are still under active study.

This monograph sets out to survey the physicochemical basis of denaturation and therefore leaves the reader to apply the fruits of this approach to his own field of work and interest. Methods appropriate for studying denaturation are described; in each case a self-contained account of the fundamentals is given, with examples taken from conformational studies on proteins and polypeptides and references to recent reviews for further detail. Techniques include hydrodynamic, optical, light scattering, NMR and hydrogen exchange, although calorimetry, surprisingly, considering the author's interest, is given only passing mention.

The largest section of the book comprises a survey of experimental results obtained with a range of perturbants including heat, *p*H change, urea and guanidine, inorganic salts, organic solvents, and detergents. This draws together a wealth of detail from the literature and enables the reader to compare the different and frequently rather specific effects of these modes of denaturation. The results are well illustrated with data from original papers. It is useful to have the literature presented objectively and without the constraint of a particular theoretical viewpoint.

The chapter on the thermodynamics of denaturation, an aspect to which the author has made significant contributions, contains a good discussion of the two-state hypothesis and an up to date account of calorimetric studies and of the thermodynamics of thermal denaturation. Although it is mentioned in several places that the denatured states may differ depending on the mode of perturbation, I could find no discussion of the dependence of derived thermodynamic parameters on the definition of the denatured state. Also, the values of n in the relationship $K^1_D = Ac^n$ surely range wider than 12 to 20 — probably a misprint. The interpretation of biphasic kinetics of unfolding and refolding of proteins in terms of the proline isomerisation model is a particularly hot issue at the present moment and the short chapter on kinetics of denaturation provides a useful background to the various ways in which such experiments have been treated. This leads into a final chapter dealing more with interpretation of kinetic and thermodynamic experiments, particularly with respect to the mechanism of folding of globular proteins and the nature of the interactions of denaturants with proteins. As regards the latter, the author seems to favour the direct binding of urea molecules to a protein as a driving force in denaturation, and it is an interesting exercise to try and fit an alternative explanation to the results he quotes purely in terms of change in water structure.

This monograph is valuable as an unusually well organised survey of a massive literature. I found it stimulating, not because of strongly argued personal ideas, but because of the creative apposition of the different experimental approaches and interpretations which have been used in this field. It is, however, encouraging to find that his thermodynamic hackles are capable of being roused when his basic convictions are challenged (see p295). This review is valuable also in that the author emphasises the complexity of deriving and assigning thermodynamic parameters from systems as complex as proteins in multicomponent solvents.

The book is well produced and well illustrated. The index contains the reviewer's favourite enzyme but omits "two state transition". One is enormously impressed by the feat of writing (over 300 pages) in what is, to the author, his third language. Only occasionally is there a misplaced and, very occasionally, a misleading nuance. Most of these are so obvious that in more happy and responsible days one might have expected the publisher to have brought them to the author's attention. The duplication of equation 2-26 and the confusing layout of Table 4.4 also fall into this category. Nevertheless, this is a monograph that will be an essential reference work for all those concerned with the stability and dynamics of proteins and provides excellent value for money.

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