Notes and News

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Synchrotron Radiation News

A new magazine with this title has just been published by Gordon & Breach. Volume 1, which will comprise six bimonthly issues, is being distributed free of charge to over 5000 synchrotron users worldwide. The editorial to the first issue states that the backbone of the coverage will be provided by correspondents at each facility who will report regularly on local developments. In addition, issues will include teaching and historical articles, conference reports, book reviews, a calendar of events, and a letters and comments section.

Sample copies of Volume 1 and subscription details for Volume 2 may be obtained from the Editorial Office, Gordon & Breach Science Publishers S.A., PO Box 401, 2130 AK Hoofddorp, The Netherlands.

Book Reviews

Works intended for notice in this column should be sent direct to the Book-Review Editor (R. O. Gould, Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, Scotland). As far as practicable books will be reviewed in a country different from that of publication.

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Protein engineering. Edited by DALE L. OXENDER and C. FRED FOX. Pp. xvii + 365. New York: Alan R. Liss, 1987. Price $36.00 (available in Europe and Africa from John Wiley & Sons, Chichester, England, £22.00).

Over the last ten years molecular biologists have developed an interesting vocabulary to describe the new techniques used to manipulate DNA as a means of producing protein. 'Genetic Engineering' covers the more practical aspects of how to identify, clone, mutate and express the genes which code a particular protein. The ultimate goal is to use this technology to design new properties into proteins by altering the amino-acid sequence: 'Protein Engineering'. For example, the ability to build more stable or more active enzymes which could be turned on or off at a given pH or temperature would have considerable industrial and medicinal value. This sort of molecular tuning, however, requires a detailed understanding of the enzymatic mechanism, of the thermodynamics of protein folding, and last but not least an accurate model of the three-dimensional protein structure.

This book consists of a collection of some 30 'position papers' written by leading biochemists and biophysicists and is based on papers given at a symposium 'Protein Structure, Folding and Design' held in 1985. Overviews of the various methods for determining the three-dimensional structure of proteins are presented in the first section of the book with contributions on protein crystallography by W. A. Hendrickson, on NMR by J. L. Markley and on molecular mechanics and dynamics by M. Karplus. The lion's share of results discussed in the remainder of the book is based on results from protein crystallography. There are only three chapters on the biochemical methods which can be used to prepare and purify site-directed-mutant proteins; just enough to give the reader some feel for the techniques of protein production. Twelve chapters are devoted to the problems of predicting and understanding how the amino-acid sequence relates to the unique active folded conformation. The folding cannot be governed by a random sampling of conformations as this could take some 10^{50} years for a small protein. Site-directed mutagenesis, however, allows us to ask which residues carry the folding instructions, as explained by J. King *et al.* Another feature which most contributors to this section mention is that the free energy of denaturation of a small globular protein is only about 20–60 kJ mol^{-1}; the equivalent of two or three hydrogen bonds. This small energy difference makes the design of mutant properties particularly difficult, as the overall stability of the protein depends on a large enthalpy term (favoured by the formation of strong hydrogen-bonded networks) balanced against a large entropy term (forcing the protein to fold forming a hydrophobic core). Despite such computationally difficult problems, some progress is being made in the computer design of novel proteins, as described by J. Richardson and others, with the development of some design principles explaining, for example, the packing of hydrophobic groups and the formation of amphiphilic helices.

The last section of the book provides a collection of examples of different proteins showing how mutations can affect protein kinetics, thermodynamic stability, biological activity and three-dimensional structure. However, despite the wealth of data, the results are not always easy to interpret. For example, mutations in the active site of DHFR (Howell *et al.*) show the surprising result that substrate binding can be impaired without loss of catalytic activity. Wells *et al.* discuss experiments carried out to modify the activity and stability of the enzyme subtilisin. Here, X-ray refinement shows that although specific site mutations only show slight perturbations in three-dimensional structure, activity is significantly reduced. These results lead the authors to comment that naturally occurring enzymes are already highly optimized and that '... the highest probability of improving the properties of proteins by protein engineering will be to engineer those properties that have not been selected for in Nature'. Another very detailed example of the use of X-ray crystallography to rationalize structure and stability of protein mutants is from T. Alber and B. W. Matthews. Structural analyses of 13 (crystallographically isomorphous) single-site mutants of phage T4 lysozyme have been completed [*Nature* (*London*) (1987), **350**, 41]. All