

not have given proofs of many results, with such a self-imposed restriction of avoiding technical details. Nevertheless, the author has done a very good job, the only exception being chapter 8, in which the author attempts to outline aspects which are more topological in nature such as the Dehn's surgery, branched coverings, etc. A typical exercise in this chapter asks the reader to show that the torus is not a covering space of a 2-dimensional sphere. One fails to understand the kind of audience the author may have in mind, in including such exercises immediately after giving the definition of a covering space. The book can do well without these eighteen pages. This book is translation of the original Japanese version. Even though I do not know Japanese, I feel that there is a lot of scope for an improvement in the translation.

Although this book may not impart any lasting education in knot theory to the reader, it will not fail to inspire and inform substantially. With so many results in one single place, it may be used as a good reference book also.

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**Lysozymes: Model Enzymes in Biochemistry and Biology.** P. Jolles, ed. Birkhäuser Verlag, Basel, Switzerland. 1996. 449 pages.

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Fleming's discovery of lysozyme preceded his discovery of penicillin and both are part of scientific folklore. It was in 1922 that Alexander Fleming reported his discovery of lysozyme in the nasal mucous to the Royal Society. However, when the word lysozyme is currently used, it generally means the enzyme from hen egg white (HEW). Pierre Jolles, who sequenced the HEW enzyme in the early sixties, has been working with lysozymes from various sources and has now put together this comprehensive book on this enzymatic activity.

Lysozyme is widespread in nature. By definition, lysozyme activity consists of hydrolysis of a  $\beta$ -glycosidic

bond between the C-1 of *N*-acetylmuramic acid and the C-4 of *N*-acetylglucosamine of the bacterial peptidoglycan. Analysis of known 75 complete and 13 partial amino acid sequences shows that there are 20 invariant residues. In addition to conventional lysozyme (called lysozyme c for chicken type or conventional type), other distinct types of lysozymes also occur. Lysozyme g (after the Embden goose, the specie in whose egg white it was first discovered) is also widespread, though in bird egg white only. Some lysozyme c, notably from pigeon egg and horse milk have few aspartic acid residues critically positioned, enabling them to bind calcium and are called calcium-binding lysozyme c. The two lysozyme c families along with  $\alpha$ -lactalbumin form a lysozyme c superfamily. Evolutionary analysis points to a common ancestor and places the divergence event prior to 400 million years. The question whether lysozyme g also shares the common ancestor is still debatable. However, v-type lysozymes (viral type from phage infecting both gram-positive and gram-negative bacteria), on the basis of similarities between their three-dimensional structures with lysozyme c, are believed to share this remote common ancestor.

Several other phage lysozymes encoded by phages infecting gram-positive bacteria called CH-type lysozyme (first investigated in Chaloropsis) belong to a totally unrelated family. A striking observation which emerges out of these evolutionary studies is that only acid catalysis seems to be essential, the rest of the catalytic process is based upon 'broadly scattered interactions (electrostatic, H-bonding, . . .) and substrate distortions' (p. 58).

The role of lysozyme in bacterial cell wall lysis was elucidated only in 1964. 'An intriguing question, not yet answered, is how the cell controls this dangerous enzyme from premature or unbalanced action. . . although it is clear that they are involved in the metabolism of bacterial cell wall' (p. 63). Equally fascinating is their presence in plants. 'All lysozymes also have chitinase activity but not all plant chitinases are lysozymes. However, for many chitinases, it is not known whether they also possess lysozyme activity' (p. 75). As fungal cell walls contain chitin, it is believed that chitinase activity is used by

plants to combat fungal pathogen.

Lysozyme (c-type) is ubiquitous in insects, normally present in blood. In this context, the role of lysozyme as an active defence molecule has been questioned, since in most bacteria, the peptidoglycan layer is not directly accessible to this enzyme. It may be that the main role of the enzyme is in cell wall lysis after the bacterium has been killed.

Both in flies and cows, lysozyme also has a digestive role. Whereas typical lysozymes are basic, ruminant enzymes are neutral and *Drosophila* midgut lysozymes are even acidic.

Thus this book, consisting of twenty-two chapters, looks at lysozymes from the perspective of protein chemistry, enzymology, protein crystallography, molecular biology, immunology and pharmacological and therapeutic applications. The authors, drawn from various parts of the world, represent a unique wealth of experience.

An attractive feature of this book is that it also captures a sense of history of the growth of ideas. McKenzie's recall of editorial opposition to Campbell's opinion that ' $\alpha$ -lactalbumin may have evolved by gradual modification from lysozyme' is a case in point (p. 365). The lucid discussion on the catalytic mechanism by Karplus and Post nicely illustrates the usefulness of theoretical methods in establishing enzyme mechanism. As few biochemists are familiar with the area of molecular dynamics, the inclusion of this chapter is welcome.

Analysis of formation of disulfide bonds in this enzyme shows that there exists a restricted search of structures and a nucleation in the folding pathway. 'Folding of both denatured and denatured/reduced lysozyme is characterized by transient folding species possessing structural properties of the molten globule state: high content of secondary structure, no tertiary fold and appearance of hydrophobic structures' (p. 144). Imoto has described protein engineering work on c-type lysozyme (p. 163 onwards). Although references to the work on T4 lysozyme by Mathew's group have been provided, a little more extensive discussion on the latter would have been welcome. Also missing is the early chemical modification with the enzyme.

HEW lysozyme was the first enzyme

in which case the three-dimensional structure was available from X-ray crystallography. It is interesting to recall that X-ray crystallography of lysozyme gave the first view of  $\beta$ -sheet in a globular protein. The X-ray diffraction studies on binding of substrate analogs, transition state mimics and oligosaccharide products to various lysozymes have provided considerable insight into binding of sugars to proteins.

Evolutionary variants of bird lysozyme played a major role in the development of correlation between immunological and sequence differences. 'The

anti-hen egg lysozyme monoclonal ab DI.3 is perhaps the best characterized immunoglobulin to date' (p. 303). The chapter by Prager on adaptive evolution of the enzyme focuses on lysozyme c turning into a digestive enzyme and in a subsequent chapter, Irwin discusses this as a link between molecular evolution and evolution at the level of organisms.

The last chapter by Sava outlines the underexploited potential of therapeutic applications of lysozymes. However, a very important warning of general importance is given by Imoto (p. 177), 'Engineered proteins might be some-

times harmful to human bodies; only one amino acid substitution (He 55 Thr or Asp 66 His) turned human lysozyme to an amyloid fibril protein'.

In a way, this book also reflects the state of the art in the area of enzymes in general. Pierre Jolles has yet again made a tremendous contribution to biochemistry.

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