Book Reviews

Amino Acids, Peptides, and Proteins. Volume 5 (Specialist Periodical Reports). Edited by R. C. Sheppard with 21 contributors. The Chemical Society, London. 1974. xviii + 515 pp. 14 × 22 cm. £8.00.

The latest volume in the outstanding specialist report series issued under the auspices of The Chemical Society reviews the progress of the amino acid, peptide, and protein field during 1972. Attesting to the continuing expansion of this field is the fact that the book contains 35% more pages than its predecessor, which was reviewed in these pages 2 years ago [J. M. Stewart, *J. Med. Chem.*, 15, 1002 (1972)]. Moreover, there are now 21 specialist reporters instead of 15, and the total number of references is well over 2000.

The opening chapter presents structures of newly discovered natural amino acids, describes advances in the art of amino acid synthesis and optical resolution, reports a number of new chemical reactions of amino acids which are of general interest, and summarizes important aspects of the physical and analytical chemistry of amino acids. Chapter Two, which comprises nearly half the book, summarizes the latest advances in methodology in the area of peptide and protein structural investigation and then details specific developments relating to enzymes, structural proteins, immunoglobulins, membrane proteins, hormones, toxins, ribosomal proteins, chromosomal proteins, and so on. Included also is a useful section on reagents capable of altering chemical and biological properties in peptides or proteins. Part Two of this chapter is devoted to X-ray diffraction studies, and Part Three deals with other physical techniques such as spin labeling, fluorescence probes, Mössbauer spectroscopy, nuclear magnetic resonance, circular dichroism, and optical rotatory dispersion in studies of peptide and protein interactions in solution, as well as in the construction of theoretical models for the folding of protein chains.

Chapter Three reports new developments in synthetic methodology with respect to protection, activation, coupling, deprotection, and racemization in peptide synthesis. Special attention is given to the solid-phase technique and its growing importance in oligopeptide synthesis. A useful compilation is also given of natural peptides and proteins whose synthesis was reported during 1972. Chapter Four focuses on special types of peptides and on those containing unusual structural features. Included in this category are various kinds of cyclic peptides, peptide alkaloids, penicillins and cephalosporins, glycopeptides, and peptide-containing nucleosides.

Chapter Five is concerned with progress in the area of structure–activity correlation, primarily with respect to peptide hormone action, which seems to be receiving the greatest amount of attention at the present time. Chapter Six reports advances in the field of metal derivatives of peptides and proteins, and Chapter Seven is devoted to the latest status of peptide and protein nomenclature. This includes revised IUPAC–IUB rules for definitive as well as abbreviated naming and also a new system of one-letter notation which is coming into vogue. The latter will be of special interest to computer-based information storage experts.

The strongest points in this book (as they have been in earlier volumes) are superb organization, conciseness, and price economy. It unquestionably belongs on the desk of every amino acid, peptide, and protein chemist who wishes to remain informed of the latest developments in his field.

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Glutathione. Edited by L. Flohé, H. Ch. Benöhr, H. Sies, H. D. Waller, and A. Wendel with 47 contributors. Georg Thieme Verlag, Stuttgart. 1974. 15.4 × 22.9 cm. paperback. x + 316 pp. 64 DM, *ca.* $25.00.

This book represents an interdisciplinary symposium in which clinical, biophysical, and biological approaches to the significance of glutathione are presented.

The study of glutathione (usually referred to as an "ubiquitous tripeptide") has reached the exciting stage of development at which models are being blocked out. During the next few years these models can be expected to coalesce into an overall model and places will be found for the details that past years of research have provided. This book provides a good background to this coming intellectual adventure.

Papers on the clinical aspects of glutathione metabolism deal with the long-known involvement of glutathione in hematologic disorders, particularly susceptibility to drug-induced hemolytic anemias. Clinical manifestations of reduced-glutathione deficiency, including fragility of red blood cells and experimentally induced cataracts, are related to the part this compound plays in protecting cell membranes from oxidative damage. Discussion here centers on hereditary deficiencies of glucose-6-phosphate dehydrogenase, glutathione reductase, enzymes of glutathione synthesis, and glutathione peroxidase. These enzyme deficiencies are discussed with emphasis on the light they shed on glutathione utilizing pathways in the cell.

On a more general level, there are reviews of the involvement of glutathione in amino acid transport across the membranes of the renal tubule, choroid plexus, intestinal mucosa, and red blood cell by way of the γ-glutamyl cycle (Meister) and a valuable summary of the glutathione *S*-transferases which represent another aspect of cell protection, the detoxification of foreign compounds (Chasseaud). Recent work [Habig, *et al.*, *Proc. Nat. Acad. Sci. U.S.*, 71, 3879 (1974)] which reports that one of the glutathione *S*-transferases is identical with the cytoplasmic liver protein, ligandin, which plays a major role in controlling the flow of organic anions from the plasma to the liver suggests that the transferases will have increasing attention focused on them and should be of particular interest to medicinal chemists.

Discussions of the overall mechanism of thiol functions in the cell include the role of thiols in protecting cells from radiation damage. Radiation affects are interpreted as alterations of the redox equilibrium of cells manifested as decreases in the ratio of reduced to oxidized glutathione. These decreases are linked to inhibition of a number of enzymes, interferences with growth, changes of surface charges on cell membranes, and changes in the permeability of membranes to electrolytes. Reduced glutathione, however, appears to be linked to lipid peroxidation in mitochondrial membranes which shows that this compound is not an antioxidant *per se* but acts as part of an enzyme process.

Increases in oxidized glutathione are shown to decrease protein synthesis in the cell (Kosower) and, for a grand finale, changes in the ratio of reduced to oxidized glutathione are linked to neurotransmission and memory formation by way of acetylcholine release at the synapse. This symposium runs the full gamut of model building from the biophysical to the evolutionary. A considerable background in biochemistry (especially with reference to thiol compounds) is assumed, but, given that, this book presents a useful cross section of the present state of thinking about glutathione.

Publication was unusually prompt. The symposium took place in October 1973 and publication was the following February. The book is well edited and has very complete bibliographies.

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DNA Synthesis. By Arthur Kornberg. W. H. Freeman, San Francisco, Calif. 1974. 399 pp. 18.5 × 25.3 cm. $18.00.

A compelling model for DNA replication was proposed by Watson and Crick in 1953. It was based entirely on the structure of their famous DNA double helix; no biochemical experiments bearing on this problem were available at that time. Implicit in this model is a mode of replication, now termed semiconservative, in which the precursors for the daughter strand are correctly aligned by complementary base pairing with a strand of parental DNA. Within a few years, Meselson and Stahl had demonstrated that DNA replication *in vivo* is indeed semiconservative, and A. Kornberg and his coworkers had discovered an enzyme of *Escherichia coli* which appeared to synthesize a DNA strand complementary to a DNA template. Additional research on the biochemical mechanism of DNA replication during the past 15 years, a re-

markable portion emerging from the laboratories of Kornberg or of his former associates, is revealing an apparatus of unpredicted subtlety and complexity but which nevertheless operates according to the basic tenets proposed during the 1950's.

With the model for DNA replication now well established in general outline, but with many details remaining to be learned, it is an appropriate time to summarize the biochemical information now known. The book "DNA Synthesis" is intended to provide this summary; it is also an unusually attractive work which provides a substantial picture of the way of thinking, the interests, and the concerns of its distinguished author.

The first chapter summarizes the structure and function of DNA. Topics ranging from nucleotide structure to recent evidence on the folding of the bacterial chromosome are presented in 27 pages of text and illustrations. The second chapter outlines the biosynthesis of DNA precursors. It stresses that this subject, still not thoroughly studied or appreciated, is of profound importance for understanding the control of the rate of synthesis and the structure of DNA. Four chapters are devoted to DNA polymerases; the many tables and diagrams admirably summarize the conclusions embodied in a voluminous and complex literature spanning more than 15 years. The next two chapters on DNA replication comprise one-third of the total text. Of particular value in these chapters is the equal stress on the properties of the biological systems studied and the conclusions drawn from each system. Two chapters discuss biological functions of DNA other than replication including repair, recombination, restriction, and transcription. In a final chapter, recent strategies are presented for elucidating the structure of genes and for their synthesis. Throughout the text, an abundance of excellent diagrams, photographs, and tables summarizes experimental results, and carefully selected references lead serious readers to the original literature. The direct, lucid style of the author coupled with the attractive production of the abundant illustrative material makes this book a pleasure to read. Its timeliness is attested by the Feb 1974 dateline for the preface and the inclusion of references to 1974 publications. My only criticism of the text is the superficiality and lack of content in places where the author attempts to give a really broad overview of a subject. The summary paragraph on page 221 entitled "DNA Replication in General," and the potentially misleading diagram accompanying it, is a particularly unfortunate example.

This book should be required reading for all professional biologists. For students, it can serve both as an introduction to this important subject and as a model for a style for summarizing research results far removed from the multi-authored compilations of specialized papers. For many biologists, it may dramatize how sophisticated biochemical methodology and knowledge have recently become. For specialists in nucleic acid research, it will provide a logical basis for developing papers or lectures covering more detailed or new information.

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Metal Ions in Biological Systems. Volume 4. Metal Ions as Probes. Edited by H. Sigel. Marcel Dekker, New York, N.Y. 1974. 240 pp. $24.75.

The editor's objective in this carefully outlined series of six volumes is "to focus attention on the connection between the chemistry of metal ions and their role for life" and "to break down the barriers between the historically independent spheres of chemistry, biochemistry, biology, medicine, and physics."

Chapter I describes the phenomenon of magnetic circular dichroism (MCD) and how it can be used to detect possible similarities in coordination geometries between simple inorganic complexes and metalloproteins. Many figures are included showing MCD spectra of complexes and enzymes, but because this application of MCD is relatively new, the actual list is rather short. In general, the qualitative agreement of MCD spectra of metalloproteins and model compounds of similar geometry is good, and with a broader data base behind it this method might prove to be a better indicator of complex geometry than uv–visible spectroscopy. An interesting development is the conclusion, based on MCD, that the Co(II) in cobalt–carbonic anhydrase is five-coordinate in alkaline solution.

Chapter II is concerned with ternary complexes of enzymes, metals, and substrates. It begins with a review of esr, nmr, ENDOR, and Mössbauer spectroscopies and the kinds of studies that they are used for. However, the review is very superficial and, therefore, not very useful. Several different enzymes have been studied using these spectroscopic techniques, and the results are discussed for pyruvate kinase, creatine kinase, aconitase, and carbonic anhydrase. Unfortunately, little work by other approaches is mentioned, but the paramagnetic probe studies are critically reviewed and their limitations are carefully pointed out. The discussions of aconitase and carbonic anhydrase are particularly interesting, and the chapter concludes on the optimistic note that "the future outlook for studies of enzyme structures by physical techniques could not be brighter."

Chapter III (all 160 pages of it!) contains the real meat of this volume. It is a very thorough discussion of the use of paramagnetic probes to elucidate the structures of ligand–metal or enzyme–metal–substrate complexes in solution. Mathematical equations permeate every paragraph and make the reading tedious until one is thoroughly familiar with the symbolism used. Most of the chapter is devoted to discussing paramagnetic *relaxation* probes in a variety of enzymes and other proteins. Manganese(II) is used as the prime example, but spin labels and chemical *shift* probes, such as molecules with ring currents and lanthanide ions, are also discussed. A nonspecialist will probably regard this chapter with mixed emotion: bewilderment at the theory and equations but great excitement at the potential power of the method, which hopes eventually to provide for dynamic systems the equivalent of what X-ray diffraction can show for static crystalline systems.

Chapter IV, "The Thermochemistry of Bioinorganic Systems," mentions the various uses of calorimetry in studying intact living organisms as well as their molecular constituents. A concise explanation is given for the functions ΔG, ΔH, ΔS, and ΔCp (heat capacity) and how they may be measured. The remainder of the chapter is rather jumpy. After relating the thermodynamics of bond formation between two centers to their relative hardness or softness and to accompanying changes in their solvation, the chapter concludes with a collection of examples intended to show how "microcalorimetry is not just an alternative instrument for the biologist, but one that can improve upon existing technique." Enzyme or substrate assays are one example as shown by flow-calorimetric assays for acetylcholine using acetylcholinesterase and Tris buffer, the protonation of which by acetic acid produces heat. Although not discussed in this chapter, the possibilities for measuring directly the enthalpy of binding of a drug or hormone to a receptor on a cell in culture should be of considerable interest to medicinal chemists from a drug design point of view.

Overall, this volume fits nicely in the series, especially if one looks ahead to forthcoming volumes. It has both author and subject indexes, but they are not cumulative of other volumes. Hopefully, this deficiency will be corrected in the final volume; otherwise some continuity and breadth will be lost to the effort of searching six indexes instead of one.

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Affinity Chromatography. By C. R. Lowe and P. D. G. Dean. Wiley, New York, N.Y. 1974. xi + 272 pp. 15.5 × 23 cm.

The book by Lowe and Dean provides a lucid description of the technique of affinity chromatography. Since the modern description of this technique a relatively few years ago, affinity chromatography has emerged as a method that is applicable to almost every area of biochemistry. Indeed, over the past few years, the literature describing this approach has grown at an exceedingly fast rate. For the individual who is only casually or peripherally interested in this technique, it is almost impossible to learn the salient points of the method without conducting an extensive literature search. This book serves to bring together this mass of literature and present it to the research worker in a compact, readable form.

There are five chapters in the book. The first presents a brief review of protein structure and describes some of the classical procedures of protein purification.

Chapter 2 discusses the principles of affinity chromatography. This chapter will be tremendous value to the individual who seeks to use affinity chromatography for the first time. Upon reading

this chapter, an individual should have an excellent grasp of the concepts involved in all aspects of affinity chromatography. Included in this chapter is a description of the matrix, factors involved in the selection of a ligand, and a discussion of the principles of absorption of proteins to affinity chromatography columns. Factors that affect this absorption are discussed along with an excellent description of the theory of elution of absorbed macromolecules. This chapter finishes with a number of examples of the technique of affinity chromatography that have been carefully chosen so as to offer the reader a description of a number of variations in the technique. It should be emphasized that chapter 2 is extremely useful in providing an understanding of the basis of the technique.

The third chapter discusses group specific absorbants. The authors point out that, due to difficulties that may be encountered in choosing an ideal ligand, it is possible in some cases to prepare group specific absorbants which are capable of interacting with a wide range of proteins. This, of course, reduces the process of screening a large number of ligands in an attempt to find that which is best suited for the separation in question. This potentially powerful variation on affinity chromatography is clearly described and a liberal number of examples are given.

The fourth chapter discusses some special applications and techniques of affinity chromatography. While the technique is most widely employed for the purification of either individual enzymes or a group of enzymes, the authors point out that the technique can be extended to the purification of other biologically important compounds, such as antibodies and antigens, receptor proteins, cells, viruses, and others. In addition, the authors discuss analytical applications of the method in this chapter. The section dealing with the use of affinity chromatography in exploring enzyme mechanisms is particularly interesting.

The fifth and last chapter is entitled: "The Chemistry of Affinity Chromatography." Here the authors discuss the various types of support matrices that are available for use in affinity chromatography and the advantages and disadvantages of each. They next approach the subject of activation and functionalization of support matrices. The topic of spacer arms is again discussed, after having given the theoretical basis in the second chapter, as well as some techniques for the preparation of high capacity absorbants. The authors also discuss reactions available for coupling ligands to spacer arms and go on to discuss methods for quantifying the immobilized ligands. They complete the chapter with a practical description of laboratory techniques for preparation of affinity chromatography columns.

This book is a welcome addition to the biochemical literature. In the first place, it is a pleasure to read; it is written in an easy style and the material clearly presented. The liberal use of illustrations of the technique, in both practical and theoretical discussions, contributes very substantially to the book's clarity. The book is well documented with some 642 references being cited; these extend to the middle of 1973. The book is remarkably free of errors.

The authors state that their objective in writing this book was to guide the student through the maze of literature. This reviewer concludes that the authors have achieved this objective and have done so in a most admirable fashion.

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Annual Reports in Medicinal Chemistry. Volume 9. Edited by R. V. Heinzelman. Academic Press, New York and London. 1974. xi + 318 pp. 17.5 × 25 cm. $13.50.

Aided by six section editors Dr. Heinzelman reports on the state of the art of medicinal chemistry for the past year. This overview of the areas, CNS agents (M. Gordon), pharmacodynamic agents (F. H. Clarke), chemotherapeutic agents (G. H. Warren), metabolic diseases and endocrine function (W. T. Moreland), topics in biology (W. J. Wechter), topics in chemistry (R. A. Wiley), is a boon to anyone involved in one or the other aspects of medicinal chemistry research.

As in past volumes, the individual chapter authors are recognized authorities in their fields. The predominant number of papers cited are of 1972 and 1973 vintage. Hence, the reader can readily update bibliographies and play the favorite guessing games as to which compound made it to the clinic and which fell by the wayside.

This reviewer finds much more interesting meat in the four discipline-oriented sections (chapters 1–21), in contrast to the methodologically oriented "topics." In fact, the topics sections in essence are afterthoughts of a miscellaneous nature, nice by themselves for study, but lacking the coherence of the disease- or syndrome-based common denominators.

Paraphrasing a latin proverb "sic tempora–sic pretia," the publishers list price of this volume is 50% greater than that of its predecessors! Hence, all those who subscribe to it as an inducement to membership in the medicinal chemistry division are getting a great bargain!

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Subunits in Biological Systems. Part B. Edited by Gerald D. Fasman and Serge N. Timasheff with five contributors. Marcel Dekker, New York, N.Y. 1973. 369 pp. $27.50.

A recent book on the techniques of molecular biology starts out with cheerful arrogance by suggesting to the reader that "if he finds the contents adequate, he should know he is already out of date" ("Molecular Techniques and Approaches in Developmental Biology," Maarten J. Chispeels, Ed., 1973). In fact, molecular biology, which is what this book is about, suffers from a lack of reviews which are neither breathlessly current nor awesomely sweeping and metaphysical.

One chapter in this book, that by academician A. S. Spirin on Principals of Ribosome Structure, represents this rare middle ground and gives a coherent and well-organized account of the state of knowledge concerning ribosome structure at the end of 1970. An addendum bringing coverage up to 1972 is, unfortunately, very brief. This chapter, which is very well done, possibly because translation from the Russian forces a certain logic and lucidity upon the material, is an example of the difficulties inherent in the publisher's original concept. Written in 1971, up-dated in 1972, and published in June of 1973, this book was no longer really current when it was published. With the exception of the ribosome chapter and, to some extent, the chapter by Pardon and Richards on the Structure of Nucleoprotein Systems, the material included in this book does not represent a synthesis making order out of divergent points of view either.

The actual editing and printing of this book do not appear to really justify the time involved, since the comments of the editors are confined to one page, the translations of the Russian and French contributors are nonidiomatic ("disobedience" for "disagreement" in the Spirin chapter, "incoming" for "entering" in the chapter by Witz and Strazielle), and the typing for photo-offset seems to have been done on nonjustifying typewriters.

This book includes, in addition to the chapters on ribosomes and nucleoprotein structures, a chapter on Viral RNAs (Witz and Strazielle), a chapter on Probing Subunit Systems by John R. Cann, J. L. Bethune, and Gerson Kegeles, and one on Bacterial Cell Walls by D. J. Tipper.

Of interest to medicinal chemists would be the discussion of bacterial cell walls because of their role in antibiotic resistance and antigenicity and the discussion of transport techniques and errors which can take place in readings of electrophoresis, velocity sedimentation, and gel filtration experiments through failure to allow for macromolecular interactions. The remainder is straight molecular biology and for those who take an interest in macromolecular macramé, the spotlight has moved onto the effects of restriction endonucleases, enzymes which cleave DNA at a limited number of specified points, or to a current hypothesis that DNA wraps itself around histones rather than vice versa. If you find this new and exciting, however, you are, of course, already out of date.

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