Experimental Section

Melting points were taken on a Kofler hot stage. IR spectra were obtained on a Perkin-Elmer 137 spectrophotometer. Mass spectra were measured on a CEC 21-110 double-focusing instrument. Where elemental analyses are indicated by symbols of the elements, the analytical results for those elements were within ±0.4% of the theoretical value. Antischistosomal effects in vivo were determined as described previously.[1] Mutagenic activity was assayed according to Ames et al.[3] using *Salmonella typhimurium* strains TA-98 and TA-100 in the presence and absence of a preparation of rat liver microsomes (fraction S_9). The two compounds were dissolved first in Me_2SO, the final Me_2SO concentration of all plates (including that of controls) being adjusted to 0.1 mL per 15 mL of medium. The highest concentrations of each of the two compounds tested were close to the one producing 10% growth inhibition.

4-Amino-4′-nitrodiphenylamine. This compound was synthesized by the method of Morgan and Micklethwait.[8]

4-Isocyano-4′-nitrodiphenylamine (2). A solution of 229 mg (1 mmol) of 4-amino-4′-nitrodiphenylamine in 25 mL of dry ethyl acetate was added dropwise via a syringe over 1 h to an excess of phosgene in 150 mL of dry ethyl acetate. Phosgene was bubbled into the reaction during the addition. The solution was stirred for an additional hour, allowed to stand overnight, then evaporated to 10 mL under nitrogen, and filtered to remove a small amount of dark brown material, and 500 mL of petroleum ether (bp 30–60 °C) was added. The precipitated product (112 mg, 44% yield) was collected: mp 134–135 °C; IR (KBr) 2250 cm^{-1} (NCO); MS, molecular ion at *m/e* 255. Anal. ($C_{13}H_9N_3O_2$) C, H, N.

Acknowledgment. The authors gratefully acknowledge the support of this project by National Institutes of Health Grant GM-16492, Training Grant AI-149, and the Agency for International Development Contract AID/ta-C-1312.

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Book Reviews

Quantitative Structure–Activity Relationships. Edited by Milon Tichy. Birkhauser Verlag, Basel and Stuttgart. 1976. 265 pp. 16 × 24 cm. SwF 58 ($23.50).

The book is a compilation of papers presented at the conference on "Chemical Structure–Biological Activity: Quantitative Approaches" held in Prague, Czechoslovakia, in June 27–29, 1973. The articles cover a wide variety of groups of compounds possessing varied pharmacological activity. The authors have used different physicochemical parameters in estimating the quantitative characteristics of a given biological activity. A total of 35 presentations have been divided under five major portions.

After a brief review of different methods used in quantum mechanics in co-relating the structural and electronic features to biological activity, the first part deals with discussions on the possibility of hydrophobic interactions on the receptor protein dominating over the transport system; the importance of the inclusion of the change in charge density values along with the stereochemical changes in the drug molecule; the contributions of dissolution rate; substructural components and the positive inductive effect of the substituents of a drug molecule as a controlling factor in the biologic response; the improvement in the relationship between the partition coefficient and paper chromatographic R_m values after incorporation of pK_a values in the mathematical equation; lipophilicity and the contribution of inorganic cations (Cu, Cd, Mi, Mn) in inhibiting the mobility of Tubifex worms. The second part has one article explaining the advantages of a modified cluster analysis technique in interpreting the chemical structure–activity relationships. The third part deals with calculation methods used in the Soviet Union to determine the toxicohygienic index—the maximum permissible concentration of chemicals in air in industrial areas; the comparative effect of lipophilicity to deacylation rates in co-relating the β-adrenergic blocking activity of Trimepranol; the dominance of steric effects over electronic effects in substituted isonicotinic acid hydrazides as antitubercular agents; substituent effects on the algicidal activity of phenylthiolacetates; the action of foreign compounds with hemiproteins and isolated ferriprotoheme (here an attempt has been made to study the ligand interaction of methemoglobin with a set of foreign compounds to cause a significant spectral change); structure–activity relationships of 1-ethylpiperidine derivatives in which the calculation for the less toxic *N*-oxides in contrast to the *N*-ethyl derivatives is explained; a study of the regression analysis on some 4*H*-pyridopyrimidine analogues wherein a co-relation between toxicity, the hot-plate test, the algolytic test, and the narcotic potentiating effect has been shown; and finally the lipophilicity paralleling the epileptogenic action of aliphatic penicillins is discussed. Part IV reports on the indices obtained from molecular orbital calculations in co-relating the biologic response. The topics discussed and inferences drawn include the preferred conformations of the pharmacophore in β-adrenergic agents, PGE, serotonin, and clofibrate. Some of these studies have appeared in the literature before. In addition, the antiradiation activity of the thiazolidine molecule as a function of an increase in the density on the S and N atoms of the parent molecule is discussed; the antirheumatic activity of hydroxybenzoic acids as influenced by the acidity and dipole moment is explained; the rationalization of the most stable planar form among the tricyclic antidepressants being the most potent; the ionic defect in an α-helical polypeptide causing a change in the geometry in the helix; calculations of electronic characteristics of the indole and the benzofuran nuclei from LCAO-SCF-MO which run parallel to the approximate methods; and the antituberculotic activity of substituted benzenecarboxylic acid thioamides is dependent on the electron density of the thioamide group. The final section deals with the calculation of the absolute values of Henry constants and partition coefficients for a given compound in different solvent as investigated by gas–liquid chromatography. Using water as the stationary phase, Henry constants in the system blood/air have been calculated. In the next paper, a model is presented of Sephadex-G-10 possibly resembling the biologically active macromolecule and the steric effects involved in binding of small molecules to the surface are calculated. The last study describes the dipole moment playing a part in the activity of cardiotonic steroids.

In the light of the increasing interest in rationalizing the use of the quantum-chemical approach in explaining the biological activity of the drug molecule, this certainly is a timely effort on the part of the editor. Even though the topics at the outset give a feeling as a collection of a potpourri, scientists in the field will indeed find the articles very valuable. The majority of the articles are authored by people from Europe; however, the skilled efforts on the part of the editor make it a flawless, readable publication. All the mathematical derivations have been explicitly dealt with so that this book will provide a good reference source for teachers and students involved in instruction of graduate courses in the field.

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Physical Biochemistry. Applications to Biochemistry and Molecular Biology. By David Freifelder. W. H. Freeman, San Francisco, Calif. 1976. 570 pp. 16 × 24 cm. Hardcover, $16.95; softcover, $10.95.

This text might be more appropriately titled "The Techniques of Physical Biochemistry" as it is not, by the author's intent, an exposition of the body of knowledge defined by the discipline, physical biochemistry. The book is divided into six sections, the first describing the simple theory and methods of light and electron microscopy in separate chapters. A multichapter section on general laboratory methods describes measurement of pH, radioactive labeling and counting, autoradiography, and membrane filtration and dialysis. Sedimentation, partial specific volume, and the diffusion coefficient and viscosity are subjects covered in a section on hydrodynamic methods. Chapters on chromatography, electrophoresis, and immunological methods are also grouped as a section. Absorption and fluorescence spectroscopy, ORD, CD, and NMR are considered in a section devoted to spectroscopic methods. The final section describes, among other things, methods of concentration of macromolecules. A nice set of problems concludes each chapter with the answers given at the back of the book. A glossary defines commonly used terms, but I wonder for whom it is necessary to define *peak* (the maximum of a curve). The general level of treatment is appropriate for advanced undergraduates or beginning graduate students, not specialists. The writing is generally clear and there are many excellent figures.

By way of other comments, I was surprised that in a section devoted to the identification of peaks in gas chromatograms, no mention is made of the utility of mass spectroscopy. In general, I thought that the utility of gas–liquid chromatography with biological samples (p 185) was grossly understated. Similarly, the section on affinity chromatography (p 204) provides no clue on how the binding molecules are covalently coupled to the column material, although CNBr-activated Sepharose 4B is obliquely mentioned in the reference section. A good general reference on affinity chromatography is also missing.

In the section on NMR, the reader may be confused (p 487) by the statement that there are only two important things to know concerning relaxation ($\Delta\nu_{1/2} = 1/T_2$, and that T_2 depends on molecular motion), while Figure 17-16 (p 502) illustrates relaxation rates in binding studies in terms of $1/T_1$. The apparent discrepancy is resolvable if one appreciates that $T_1 \simeq T_2$ in cases where correlation times are short, as in most proton resonance work in solution. Fourier-transform NMR is mentioned only in terms of its enhancement of sensitivity, but it also offers easy measurement of spin–lattice relaxation times (T_1's).

Also, I was unable to find many of the terms defined in the glossary in the index so was disappointed in not being able to readily find what the text said on these subjects.

These are relatively minor points as, in terms of what the author set out to do, this is a good book. For those interested in having at least a passing acquaintance with the numerous techniques mentioned, the softcover version is a good buy at $10.95 (at least as things go these days).

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Macromolecules in Solution. Second Edition. By Herbert Morawetz. Wiley-Interscience, New York, N.Y. 1975. xix + 549 pp. 16 × 23.5 cm. $27.50.

This new Volume XXI of the High Polymers series of Wiley-Interscience monograph by Professor Herbert Morawetz is an updated and somewhat expanded second edition of the authoritative text by the same title, "Macromolecules in Solution," first published by the author in 1965. The organization of the vast and diverse quantity of material ranging from synthetic polymers in solution to biopolymers such as the immunoglobulins and tRNA has been retained essentially under the same principal chapter headings: The Solubility of Macromolecules; Configuration and Conformation of Chain Molecules; Equilibrium Properties of Dilute Solutions; Spectroscopy; Optical Activity and the Scattering of Light and X-Rays; Frictional Properties of Dissolved Macromolecules; Polyelectrolytes; Molecular Association; and Chemical Kinetics in Macromolecular Solutions.

As stated by the author in his preface, this and the previous edition of the book evolved from a set of lecture notes of his graduate course in "Solution Properties of High Polymers" taught through the years at the Polytechnic Institute of New York (formerly Brooklyn Poly.) and as such it systematically surveys the underlying concepts and theories that govern the behavior of macromolecules in solution, without the artifically imposed barriers that have usually separated the study of synthetic polymers and those of the natural variety—proteins, polysaccharides, and nucleic acids. However, with such an extensive and diverse subject of study the author has necessarily restricted his treatment of some of the very specialized and obtruse theoretical topics, with emphasis on the qualitative comprehension of macromolecular concepts and the application of theoretical results and equations to experimental results. The discerning student and researcher who may wish to gain a deeper understanding of the methods and concepts described is directed to the original literature of the subject or to references with detailed treatment of the topics. Appropriately, the monograph contains some 1600 reference entries and a subject index. The references of the first edition have been updated to include citations through 1973.

Unfortunately, as if often the case with the literature of the most active areas of research, some of the most important developments in a given area appear in print after publications, or at the time of publications their significance is simply overlooked or has not yet been fully explored. Thus, for example, the insights that the recently published x-ray crystallographic results of the immunoglobulins and tRNA afford us could not be included. Nor are the results of x-ray crystallography related to the estimation of α-helical and β-structure content of proteins based on optical rotation and circular dichroism, and the important recent developments based on lazer light scattering and the hydrodynamic behavior of multisubunit systems described. Nevertheless, this authoritative monograph is a recommended addition to the standard texts on polymers and macromolecules. The material presented should be of particular interest to students and researchers with background in organic chemistry and polymer science who would like to gain familiarity with the more physical and exact description of synthetic polymers and natural biopolymers, as well as their literature.

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Annual Reports in Medicinal Chemistry. Volume 11. Edited by F. H. Clarke. Academic Press, New York and London. 1976. ix + 330 pp. $16.50.

The editors and contributors to this volume of the "Annual Reports in Medicinal Chemistry" have done an excellent job of fulfilling the objectives of the series; i.e., providing timely surveys of selected areas of medicinal chemistry in which new aspects of drugs in current use, the chemistry and biology of potential new therapeutic agents, approaches to drug discovery, and basic topics in chemistry and biology are critically and succinctly reviewed. This volume has a good blend of new topics (e.g., the Opiate

Receptor, Membrane Regulators as Potential New Drugs) and updates on areas previously reviewed in other volumes in the series.

Volume 11 consists of six sections each having four to seven topics. The first section is devoted to CNS Agents and consists of reviews on Antidepressant and Antipsychotic Agents; Anti-Anxiety Agents, Anticonvulsants and Sedative-Hypnotics; Narcotic Antagonists and Analgesics; The Opiate Receptor and Biological Factors in Psychiatric Disorders. Pharmacodynamic Agents is the subject of the next section and it is comprised of surveys on Pulmonary and Anti-Allergy Drugs; Antihypertensive Agents; Diuretics and Prostaglandin Structure–Activity Relationships. Section III is dedicated to Chemotherapeutic Agents and describes progress made in Antibiotics; Antifungal Agents; Antineoplastic Agents; Antiparasitic Agents and Antiviral Agents. Immunosuppressive and Immunostimulatory Agents in Rheumatoid Arthritis; Steroids; Peptide Hormones; Diabetes Mellitus; Disorders of Lipid Metabolism: Etiology and Therapy; Drug Metabolism and Agents for the Treatment of Obesity are reviewed in Section IV under the heading Metabolic Diseases and Endocrine Function. Items covered under Topics in Biology (Section V) are Membrane Regulators as Potential New Drugs; Some Features of Solute Active Transport Across Biological Membranes; The Antimetabolite Concept in Drug Design; Comparative Toxicology and Chronopharmacology—Its Implication for Clinical Medicine. The last section, dedicated to Topics in Chemistry, consists of articles on Reactions of Interest in Medicinal Chemistry; Total Synthesis of β-Lactam Antibiotics; Polymeric Reagents in Organic Synthesis; The Chemical Modification of Cyclic AMP and Cyclic GMP; Quantitative Drug Design and Magnetic Resonance Probes of Drug Binding.

This book will be useful to a wide variety of practitioners in the medical sciences (medicinal chemists, pharmacologists, toxicologists, physicians, etc.) who want to learn of progress being made in the selected areas described. In addition to the actual reviews, this book provides a convenient source to important articles on the subject and has a very useful compound name and code number index which facilitates finding the chemical structure of drugs under development. It is well worth the price.

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Evaluations of Drug Interactions. Second Edition. Edited by Drug Interactions Evaluation Program of the American Pharmaceutical Association, Washington, D.C. 1976. xliii + 520 pp. 15 × 23 cm. $12.50 (APhA member rate $8.75)

Adverse drug reactions have been estimated to occur in 18–30% of all hospitalized patients. While many adverse reactions are unpredictable, there are a number which have been documented, particularly those involving drug–drug interactions. Because of the central role played by the pharmacist in providing prescribed and OTC medications, it was natural that he/she function as a monitor to prevent these interactions from occurring. To assist in this function, rapid access to accurate information dealing with drug–drug interactions is required. Unfortunately, many of these information sources available to pharmacists are nothing more than lists, containing interactions only reported in animals or others of anecdotal nature.

In order to bring objectivity into this area of health care, the American Pharmaceutical Association (APhA) organized a program to systematically review the literature available in this area and provide it to the pharmacist so that he/she could properly perform the role of drug therapy monitor. The review, evaluation, and compilation of the data were done by panels of pharmacists, physicians, and scientists. The end product of these evaluations was the First Edition of this book published in 1973. This Second Edition essentially expands and updates that first effort.

The book contains 144 monographs on specific drug–drug interactions. These monographs summarize the mechanism of action and clinical data available on the interactions, specific recommendations for action, and supporting bibliography. Supplemental chapters dealing with the mechanism of action of specific drug classes, a discussion of possible interactions based on these mechanisms, and tables of normal clinical lab test values are also included. A complete and usable index permits rapid access to the specific drug–drug interaction monographs as well as drug–drug interactions which could result due to similarity of mechanism of action with documented interactions.

Like other publications of the APhA such as the Handbook of Non-Prescription Drugs and the Pediatric Dosing Handbook, Evaluations of Drug Interactions provides the pharmacy student, instructor, and practitioner an easy to read and practical reference. Apart from its supplemental value in courses such as pharmacology and clinical pharmacy, this reference should be found behind the counter of every pharmacy.

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Enzyme Structure and Function. Volume 3. By S. Blackburn. Marcel Dekker, New York, N.Y. 1976. viii + 528 pp. 15.5 × 23.5 cm. $39.50.

In the past decade, a tremendous wealth of basic information has become available about both the structure and catalytic function of enzymes. Through the combined efforts of enzymologists, physical biochemists, and x-ray crystallographers, our spectrum of knowledge about enzymes has expanded to the point where relationships can be made between the protein's structure and its catalytic function. This book discusses in great detail the structure–function relationships for a select group of enzymes for which sufficient structural and mechanistic data are available. The enzymes covered in detail include chymotrypsin, trypsin, elastase, carboxypeptidase A, carboxypeptidase B, subtilisin, papain, streptococcal proteinase, ribonuclease, staphylococcal nuclease, and lysozyme. For each of these enzymes sufficient information is available about their primary sequence, three-dimensional structure, active site, substrate specificity, inhibitor specificity, and mechanism to permit conclusions to be drawn about the relationship between their structure and function. The author provides a fairly up-to-date and extensive review of the literature for each of these enzymes, attempting to correlate this information in a form suitable to draw conclusions concerning how an enzyme structure is related to its ability to catalyze a specific chemical reaction.

The book has an adequate subject and author index. Each essay is well referenced, giving the reader easy access to very extensive literature. This book would not, however, be recommended for a personal library unless the individual is interested in an up-to-date review of the literature on one or more of the enzymes discussed. It would be worthy of purchase by an institutional library, since it does provide a fairly concise review of an ever expanding volume of literature in this area of biochemistry.

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Enzyme Reactions and Enzyme Systems. Volume 4. By C. Walter. Marcel Dekker, New York, N.Y. 1976. ix + 204 pp. 15.5 × 23.5 cm. $19.50.

This book describes how the kinetic properties of enzymes can be translated into mathematical models and how these models can be used to design experiments that will aid in the elucidation of the mechanism of enzyme catalysis. The first five chapters deal with the kinetic properties of single enzymes with particular emphasis on the assumption made in deriving steady-state rate equations, the use of computers to derive and simulate kinetic models, and the techniques for on-line data collection and analysis. Chapters 6–8 describe multienzyme systems with particular emphasis on the chemical kinetics of multicomponent systems with and without feedback control.

The book is directed toward "practicing experimental enzymologists" who wish to construct enzyme models so as to be able to design worthwhile kinetic experiments. For an enzymologist specifically interested in such modeling experiments,

the book is probably worthy of purchase. As a general introduction to enzyme kinetics the book would not be recommended, since other more easily understood texts are available. This book would be of interest to only a very limited audience. However, its purchase by an institutional library would be recommended, since it does provide a worthwhile introduction to both the theoretical and practical aspects of modeling of enzyme kinetics.

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Crystals, X-rays and Proteins. By Dennis Sherwood. Wiley, New York, N.Y. 1976. 702 pp. 17 × 25 cm. $35.00.

X-Ray crystallography has had great impact in elucidating the three-dimensional structures of biologically important molecules, large and small. The techniques of crystallography have improved to the point where large protein and nucleic acid structures can now be determined, providing detailed information at the atomic level of these important macromolecular structures and a deeper understanding of their function. Although there are a number of books that treat various aspects of crystallography, few give a full account of the fundamental principles and practical aspects of x-ray diffraction in a clear and understandable way. Sherwood succeeds in presenting a thorough explanation of the theory of x-ray diffraction, developing at the same time the relevant mathematical, crystallographic, and wave theory principles. The basic concepts of x-ray crystallography are developed, explained, and clearly illustrated in a comprehensive manner.

The book consists of 16 chapters plus an appendix and is divided into four parts. Part I which is comprised of the first six chapters deals with fundamental crystallographic principles and relevant mathematical description of waves. This section closes with an illustrative explanation of Fourier theory and its significance to understanding the diffraction phenomenon. The heart of the book is presented in chapters 7–9 of Part II where the theory of diffraction is developed from first principles. The significance of the diffraction pattern of a simple one-dimensional object is investigated and then expanded to a three-dimensional lattice. In chapter 8 the relationship between the Ewald sphere and Bragg's law is clearly demonstrated, and the importance of this geometrical construction for the interpretation of the reciprocal lattice and the diffraction pattern of a crysal lattice is emphasized. The author also explains how information concerning the lattice, the shape of the crystal, and the structure of the unit cell is contained in the diffraction pattern of a crystal. The mathematical form of the diffraction pattern of a crystal is derived and the relationship between diffraction symmetry and the crystal symmetry is described in chapters 8 and 9.

Part III deals with practical applications of the theory of diffraction developed earlier in the book. Chapters 10 and 14, the first and last chapters of Part III, cover different aspects of intensity measurement. The rules by which intensity data are corrected and the principles behind each correction are discussed in the former and the more common procedures of data collection are described briefly in the latter. Chapters 11–13 deal with the techniques necessary for structure determination. First, in chapter 11 the Patterson function and its utility in locating heavy atom positions in the unit cell are described. This information can serve as an important beginning in solving the phase problem. The nature of the phase problem as well as the two principal approaches used to solve it is then detailed in chapter 12. The chemical modification methods involve introduction of heavy atoms and anomalous scatterers which in turn provide phase information that can be developed sufficiently to determine the structure of the molecule under study. These methods are used primarily in the analysis of macromolecular structures. The important application of anomalous scattering not only to phase determination but also to absolute configuration assignment is covered here in lucid detail. A brief description of the direct method of phase determination, used primarily for small molecule analysis, is also presented in this chapter. In chapter 13 the various techniques of structure refinement used to obtain a more accurate model of the molecular structure are discussed.

The two chapters of Part IV deal with aspects of crystallography which are particularly applicable to macromolecules. In chapter 15 the disorder phenomenon is explored, including its possible causes and the effect it has on the diffraction patterns of biopolymer crystals. The chapter concludes with a discussion of various difficulties encountered in protein crystallography from data collection and phase determination to interpretation of electron density maps and structure refinement. In chapter 16 the theory of diffraction by helical structures is presented. While the presentation of this material is quite mathematical, the author also offers the reader adequate qualitative descriptions of various features of the diffraction patterns of helical structures.

As an important adjunct to the text, especially to the chapters in Part III, the author has included an appendix in which the step by step procedures of solving a structure are presented. In this way the techniques described in chapters 8–13 are put into practice, thus helping to clarify the concepts covered in the text. A simple structure is followed through all the steps from the diffraction pattern to solution of the phase problem to structure refinement.

The general plan of this book has been well conceived. Each chapter concludes with a summary of the significant points covered and at the end of the first three major sections brief reviews of the most important concepts developed therein are presented. In addition to the general bibliography, index, and glossary of crystallographic terms at the end of the text, most chapters contain specific bibliographies. These features allow the reader to use the book more easily and more effectively. Overall, this reviewer recommends the book as a good introductory text to x-ray crystallography. While many aspects of crystallography must be put into practice for proper understanding, this book will serve well as an aid in learning the many facets of this important field of science.

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The Merck Index. 9th Edition. Merck & Co., Rahway, N.J. 1976. xv + 2547 pp. 18 × 25.5 cm. $18.00.

The new edition of the Merck Index contains descriptive monographs of some 10 000 chemicals, drugs, and biologicals arranged alphabetically by generic or nonproprietary name. In addition, the volume cmprises 500 organic name reactions, a cross index of names, formula index, Chemical Abstracts registry numbers, and a variety of tabular information of value to chemists, biochemists, botanists, physicists, chemical engineers, and others interested in the life sciences.

The cross index of names of over 50 000 synonyms represents chemical, trivial, generic, and trademark names of the compounds listed in the monograph section. More than half of the monographs are illustrated with modern, stereochemical structural formulas and 7500 offer information on general, medical, or veterinary uses as well as toxicity. Monographs also embrace data such as molecular weight, percentage composition, literature references, physical data, derivation, and trademark owner. In the 9th Edition almost 1000 monographs are new and more than 5500 have been revised and updated with titles conforming to latest USAN and WHO nomenclature.

Thumb-indexed for the first time to facilitate location of encyclopedic information, the new Merck Index is printed on high-quality bible paper and bound in green, moisture-resistant, gold-stamped, plastic-coated cloth over board.

Staff Review

Biochemical Fluorescence: Concepts. Volume II. Edited by Raymond F. Chen and Harold Edelhoch. Marcel Dekker, New York, N.Y. 1976. xv + 536 pp. 16.5 × 23.5 cm. $38.00.

This volume is a continuation of Volume I of the same title and authors. It contains 16 chapters and gives an overall review on wide-ranging topics from intrinsic protein fluorescence and flavine fluorescence to fluorescent probes for biological membrane and antibody-active sites. There are lucid chapters on drug–

protein interaction and cationic fluorescent probes of polynucleotides.

The volume puts great emphasis on techniques of fluorescence in the physical chemistry and biochemistry of proteins and in membrane structure and on the role of fluorescence in the determination of conformation and active site of antibody. Some of the subjects span several chapters. In addition, there are single chapters on cationic fluorescent probes of polynucleotides which are very good reading.

The chapters on protein and fluorescence provide a group of very interesting contributions that probe the limitations of steady-state fluorescence measurements and suggest ways in which this technique can be extended to obtain more detailed information on trans-conformation transitions in proteins. Of these chapters, Chapter 8 provides an excellent summary of what is known about the heterogeneity of tryptophan emitters in various proteins, and Chapter 9 puts emphasis on tryptophan emission as a technique for evaluating conformational changes in proteins. The authors, who have made substantial contributions in this area, carefully review the problem of separating tyrosine and tryptophan fluorescence, as well as considering the problems of emitter heterogeneity. Chapter 10 discusses several ingenious attempts to extend the usefulness of steady-state fluorescence measurements in providing detailed information about trans-conformational changes in proteins. In Chapter 11, the author has contributed to the ability to physically locate tryptophan emitters within proteins by studying the quenching of their fluorescence with oxygen, with iodide ion, and with other substances. Chapter 12 describes the role of fluorescence and polarization on structures of polypeptide hormones, and Chapter 13 enumerates the uses of various metal cations for probing the structure of proteins and how metal cations can extend the usefulness of intrinsic fluorescence as a parameter of conformation. These chapters constitute a collection of important information. The reviewer is unaware of any other source which deals as succinctly and critically with these complex matters. Chapter 14 is a treatise on synthetic substrate analogues, which can act as enzyme substrates, and fluorogenic substrates are most useful for kinetic or analytical studies with enzymes. Chapters 15 and 16 are on free and bound flavine fluorescence and intrinsic and extrinsic fluorescence in the study of structure transitions in glutamine dehydrogenase, respectively. Chapters 17 and 18 are two well-written chapters concerning two techniques widely used in modern pharmacology and cell biology. Chapter 17 deals with the most versatile techniques currently available for the study of drug interactions with proteins. Chapter 18, on the other hand, discusses the cationic fluorescent probes of polynucleotides that find prevalent use in chromosome karyotyping.

The next two chapters, 19 and 20, summarize the ever-increasing role of fluorescence in membranes. Emphasis is placed on the use of fluorescent probes in the study of membrane structure and function and on fluorescent probes for the energized state in biological membranes; and these will provide readers with up-to-date information on cytochrome c binding to artificial and mitochondrial membranes, as well as an introduction to and references on the anionic and cationic "energy probes" for mitochondrial membranes. The last three chapters, Chapters 21–23, are devoted to the use of fluorescence techniques in studies involving antibodies. Chapter 21 deals with quenching and enhancement of hapten fluorescence by the antibody IgG and with the quenching of antibody fluorescence by haptens. Chapter 22 constitutes an introduction to the use of fluorescence in measurement of resonance energy transfer between the bound chromophore and the conformational and structural features of IgG and, in the opinion of the authors, the result of the work, with regard to rabbit IgG, has been gratifying.

Chapter 23 represents a clear narration of the studies of fluorescent probes for antibody-active sites. The fluorescent enhancement method is an efficient means of measuring antibody hapten reactions and will likely find wide applications in studies on various immunoglobulins. The future of the techniques seems promising.

The authors deserve credit for doing an excellent job in this volume in bringing together and expanding both knowledge and techniques of fluorescent spectroscopy with regard to the application of measurements of important physicochemical parameters of biological macromolecules. This volume is, however, largely devoted to the prospect of wider applicability of the techniques of biochemical fluorescence, rather than to the presentation of the fundamental knowledge and concepts, as the title implies. Persons interested in pursuing studies in the field of biochemical fluorescence will find this work an important contribution to their library and an adequate contribution to the literature.

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Biology of Cholinergic Function. By Alan M. Goldberg and Israel Hanin. Raven Press, New York, N.Y. 1976. xiv + 716 pp. $35.00.

The "Biology of Cholinergic Function" by A. M. Goldberg and I. Hanin is a unique test in the sense that it presents exactly what its authors intended, i.e., "an integrated overview of cholinergic biology". There has been a long overdue need for a book of this caliber and type. The material is presented in a very logical sequence beginning with the basic anatomy, biochemistry, and physiology of peripheral, as well as central, cholinergic systems. This is followed by a section on pharmacology, which, unfortunately, is rather limited in scope.

Recent studies of cholinergic function in cell culture and in invertebrate systems are included, in addition to an excellent chapter on behavioral and environmental aspects of the cholinergic system. Clinical relevance is also presented with an extensive section on cholinergically linked disorders, including peripheral (myasthenia gravis), as well as central (Parkinson's disease, Huntington's chorea, tardive dyskinesia, and psychiatric), diseases.

An outstanding feature of the book is the inclusion of four appendixes which are extremely useful. The first basically outlines assays available for determinations of acetylcholine, choline, choline acetyltransferase, and cholinesterase. The second is a brief discussion with a table on the distribution of acetylcholine and choline acetyltransferase in the central nervous system. The latter two appendixes are quite extensive and include the concentrations of acetylcholine and choline in various tissues from numerous species, in addition to the effects of drugs on these parameters.

A major advantage of this book, unlike recent symposia publications on this topic, is the integration of the material. The individual authors presented a well-rounded treatise on the topics, not merely data obtained from their laboratories. This book may find use in graduate courses and is a definite must for anyone involved in studies of cholinergic function.

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