Book Reviews

BASIC Programming for Chemists. By Peter C. Jurs, Thomas L. Isenhour, and Charles L. Wilkins. Wiley, New York. 1987. ix + 313 pp. 16 × 23 cm. ISBN 0-471-85613-4. $34.95.

In their Preface, the authors state that their objectives are to teach the fundamentals of BASIC by description and example; their aim was to develop a text that would permit the reader to acquire the skill of computer programming from a chemist's viewpoint. Indeed, the book is of an introductory nature and intended for the novice. It was very easy to read, and the examples were appropriate; almost every chemist will find several examples of personal interest. By working through the sample programs, one can quickly become rather familiar with BASIC.

BASIC Programming for Chemists begins with a brief introductory chapter on Digital Computers and another on Computer Logic, Programming, and Flowcharts. Chapter 3 describes BASIC. The next 200 pages are devoted to more than 50 example programs. These programs begin with a very simple 5-line program for calculating the molar mass of a hydrocarbon and conclude with several multipage programs on least-squares methods. In between are programs, with increasing degress of complexity, on, for example, gas law calculations, plausible empirical formulas from elemental analysis, pH and titration curves, molecular mass and percent composition, mass spectral fragmentation, theoretical NMR patterns, X-ray diffraction, infrared spectroscopy, thermodynamics, chemical kinetics, and statistical methods. Each of the programs is accompanied by a narrative that outlines various programming problems and describes steps necessary for their solution. (A few of the programs may even be useful in their own right and others can be readily modified for practical application.) By showing the reader the importance of simple programming, and the ease with which BASIC can be learned and applied, the authors have achieved their objectives. Obviously, this book is less than sufficient to make one a "competent programmer"; however, it does a nice job of introducing the basic concepts of BASIC programming and should serve to whet the appetite of those who have previously been somewhat hesitant to explore the subject.

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Advances in Enzymology and Related Areas of Molecular Biology. Volume 59. Edited by Alton Meister. Wiley, New York. 1987. 483 pp. 16 × 23 cm. ISBN 0-471-88012-4. $44.95.

The most recent volume of this well-known series offers seven chapters to the reader on a variety of topics following the long-established tradition of high-quality contributions.

The first chapter Fibronectin by S. K. Akiyama and K. M. Yamada reviews the structure, molecular biology, and functions of the title glycoprotein, an important participant in the complex process of cell adhesion. Recent studies indicate that synthetic peptides containing defined cellular interaction sequences may have potential therapeutic applications in cancer and thromboembolic disease by interfering with metastasis or abnormal platelet activity, respectively. The Synthesis and Degradation of Chitin by E. Cabib (Chapter 2) focuses on the enzymatic aspects of the topic, covering chitin synthetase from fungi and insects, chitin deacetylase, and the chitinases. Inhibitors of fungal chitin synthetase are also discussed. In Chapter 3, K. T. Douglas reviews the Mechanism of Action of Glutathione-Dependent Enzymes: glyoxylase I, glyoxylase II, formaldehyde dehydrogenase, glutathione *S*-transferases, maleyl isomerase, glutathione peroxidase, glutathione reductase, and γ-glutamyl transpeptidase. In Chapter 4, J. A. Duine et al. give an historical account of the discovery of the redox cofactor pyrroloquinoline quinone (PQQ) and discuss its functional role in the mechanisms of the recently recognized family of enzymes, quinoprotein oxidoreductases. In Chapter 5, A. V. Itkes and E. S. Severin give an analysis of the functional link between two regulatory networks, cyclic AMP dependent protein phosphorylation and the 2′,5′-oligoadenylate system. A comprehensive treatment of NMR Studies of the Mechanism of Enzyme Action by A. S. Mildvan and D. C. Fry (Chapter 6) includes the discussion of the most useful parameters of NMR spectroscopy in the study of enzyme–substrate interactions; the application of NMR to elucidate the mechanisms of specific enzyme-catalyzed reactions involving nucleophilic substitutions on phosphorus (adenylate kinase, cyclic AMP dependent protein kinase, DNA polymerase I, staphylococcal nuclease) and carbonyl polarization reactions (glyoxylase I, yeast aldolase), including reactions of biotin. In the last Chapter, E. Van Schaftingen reviews Fructose 2,6-Bisphosphate and the various developments since its discovery in 1980 in relation to its established regulatory role in carbohydrate metabolism.

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Innovation and Acceleration in Clinical Drug Development. Louis Lasagna and Alexander G. Bearn, Eds. Raven, New York. 1987. xi + 170 pp. 16 × 24 cm. ISBN 0-88167-346-3. $49.50.

This book results from a workshop sponsored by the Merck Sharp & Dohme International Medical Advisory Council. The purpose of the workshop was to discuss ways of expediting the usually long and expensive process of drug development and registration. In addition to chapters by single authors, there are summaries of five round-table discussions on subjects of general interest. The chapters are written to be very general in nature, and the book will therefore serve as an introductory text on the subject, of value to pharmacologists, pharmaceutical development scientists, and those involved in medical and regulatory aspects of experimental clinical studies. Others in the pharmaceutical industry, such as medicinal chemists or biologists, might also be interested in a broad overview of clinical and regulatory problems faced by their industry.

Chapters are included on improving the drug development process, dealing with regulatory questions both in the U.S. and abroad, alternative clinical strategies, drug level monitoring, biological endpoints, antibiotics, and the transition from clinical studies to marketing. The five round-table discussions cover the pharmaceutical-regulatory interface, Phase I/II clinical trials, Phase II/III clinical trials, postmarketing studies and surveillance, and safety assessment. Most chapters have a bibliography, and there are summaries of each chapter in English, French, German, Spanish, Portuguese, and Italian. A complete subject index to the book is included as well.

The general nature of the various contributions to this book make it valuable for the novice in the field. For those involved with the questions raised on an everyday basis, the book raises some new ideas for approaching answers. However, the reader should be aware that specific answers to questions are not the goal of this book.

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Heme Proteins 7. Edited by G. L. Eichhorn and L. G. Marzilli. Elsevier, New York. 1987. xiv + 271 pp. 15 × 23 cm. ISBN 0-444-00826-8. $75.00

This is the fourth publication of the Advances in Inorganic Biochemistry series devoted strictly to one major subject, i.e. heme proteins. The editors should be complimented for this first-class publication containing articles from established researchers.

The first chapter by Poulos (pp 2–36) gives an overview of the current status of crystallographic structural studies on heme-containing enzymes such as cytochrome *c* peroxidase, catalase, and cytochrome P450. The article contains a critical analysis of the structural differences vis-à-vis their significance on the functions of these enzymes. With regard to the mechanism of action of P450, it has been suggested that the axial thiolate ligand participates in the catalytic cleavage of the O–O bond. Furthermore, the iron-linked oxygen atom, not the peracid or peramide intermediate, is the active hydroxylating specie. The second chapter by Cusanovich et al. (pp 37–91) deals with the oxidation–reduction properties of *c*-type cytochromes. The electron-transfer mechanisms and reaction kinetics are succintly presented. The article provides a rationale to appreciate the role of protein dynamics and biological electron transfer.

Cytochrome oxidase plays a fundamental role in aerobic life; it has been also referred to as a "fascinating playground" for inorganic biochemists (p 95). Its complex-molecular structure and important functional properties form the body of the third chapter by Brunori et al. (pp 93–153). A detailed spectroscopic account of the metal centers is also given. Chapter 4 by Rifkind deals with hemoglobin, a protein contained in the red blood corpuscles which is responsible for the transport of oxygen from the lungs to the tissues. The most fascinating aspects of this protein are the mechanisms which determine the oxygen affinity and the cooperative interactions. The author has done a superb job in tackling these issues. In addition, all the methodologies employed in the study of this heme protein are described in sufficient detail. This is the most extensive article in the book with 89 pages and 571 references. The last chapter by Webster (pp 245–265) focuses on the structure of *Vitreoscilla* hemoglobin (Hb) which is a dimeric protein. Its characteristics have been compared with those of the monomeric heme proteins such as leghemoglobin and myoglobin.

Finally, this book will be a valuable addition to the library of any organization involved in protein research. Considering the high intensity of research in this field, the book will definitely require an updating in due course.

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Transdermal Controlled Systemic Medications. Edited by Yie W. Chien. Marcel Dekker, New York. 1987. xvi + 440 pp. 16 × 23 cm. ISBN 0-8247-7760-3. $79.75.

This book is Volume 31 in *Drugs and the Pharmaceutical Sciences*, A series of Textbooks and Monographs edited by James Swarbrick. It consists of 18 chapters; 13 of these were part of the 1985 International Pharmaceutical R & D Symposium, "Advances in Transdermal Controlled Drug Administration for Systemic Medications". The other five chapters were contributed by selected specialists to provide a coherent presentation of the science and technology of transdermal rate-controlled drug delivery systems. Development of such systems requires the utilization of various physical and biomedical sciences, e.g., pharmaceutics, pharmacokinetics, and pharmacodynamics. The objective of the book is to concisely present the fundamentals of transdermal controlled administration of drugs, i.e., the basics of skin permeation as well as other principles essential for attainment of optimum bioavailability and maximum therapeutic efficacy. To achieve this goal the book describes the historical background and recent advances in transdermal systemic medication, development, preclinical and clinical evaluation of these systems, engineering and manufacturing aspects, as well as regulatory requirements for approval of administration of drugs by this route.

In all likelihood this book will be of principal interest to industrial pharmacists. Medicinal chemists will certainly appreciate this clearly presented pharmaceutical technique, but will probably find it of only marginal relevance.

Staff

Steroid Hormones. A Practical Approach. Edited by B. Green and R. E. Leake. IRL, Oxford. 1987. xvi + 261 pp. 15 × 23 cm. ISBN 0-947946-53-5. $32.00.

This volume is a compilation of seven chapters devoted to the practical aspects of steroid study. The book is based on a set of techniques used commonly in biochemistry, molecular biology, and endocrinology which are applied to the steroid field. Procedures covered try to strike a balance between methods used in semiroutine clinical analysis and those aimed at basic research.

Chapters 1 and 2 deal with the analysis of steroid hormones and their receptors, respectively. Steroid nomenclature and metabolism are covered in the first chapter along with a history of steroid analysis. Radioimmunoassay (RIA) is now used almost exclusively in the analysis of steroids and their receptors. The basic principles of RIA including production of antisera by both animal immunization and monoclonal antibodies are described in some detail. These chapters account for almost half the volume of the book.

Chapters 3 and 4 describe the techniques involved for cloning of steroid-responsive genes and the analysis of these cloned genes by gene transfer. The chapters outline an overall strategy for cloning and analyzing eukaryotic genes much of which can be generalized to steroid responsive genes. Both chapters contain referenced tables describing steroid-responsive genes to which these techniques have been applied.

Chapters 5, 6, and 7 are among the shortest chapters of the book and examine topics of less generalized interest to researchers. Steroid receptor binding to DNA sequences is covered in Chapter 5. Steroid hormone action is mediated by soluble proteins (receptors) that exhibit DNA-binding properties. This chapter specifically discusses techniques involved in analysis of receptor binding to DNA sequences when using either a crude receptor preparation or when purified receptors are available. Chapter 6 is a description of how steroid responses can be measured in primary and established cell cultures. Much of the chapter is devoted to a general description of the growth of cells in primary culture. Anti-hormones and other steroid analogues are discussed in Chapter 7. This chapter is of particular value to medicinal chemists since it discusses a screening strategy for steroid hormones. The chapter's author Alan E. Wakeling points out that the discovery and purification of cytoplasmic receptors for steroid hormones has opened up in vitro alternatives to in vivo screening. It is now possible to test large numbers of compounds quickly and efficiently. The chapter includes the structures of many anti-hormones which have been discovered.

The primary value of this book is the practical information which it imparts. Many of the procedures which it describes are written in table form so that they are easy to follow in stepwise fashion. The text is filled with pragmatic "do's and don'ts". The individual chapters of this book are authored by eleven different contributors, but the volume is well-organized and the chapters flow smoothly from one topic to the next. There is little redundancy between chapters and the book has been well edited by Green and Leake so that it is very readable. References are as recent as 1986. This book should prove an invaluable source of information to both the novice and more experienced steroid investigator.

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Parkinson's Disease. Clinical and Experimental Advances. Current Problems in Neurology: 6. Edited by F. Clifford Rose. John Libbey. London. 1987. viii + 212 pp. 17 × 25 cm. ISBN 0-86-196-1102. $49.00.

This volume summarizes the presentations made at a conference held in December 1986. As is the case for any symposium volume, there is a wide spread in the topics covered. Thus, one article asks the question "Can music help people with parkinson's disease" while at the other extreme there are discussions of new therapeutic agents for the treatment of parkinson's disease as well as the relative importance of the D-1 and the D-2 dopamine receptors as therapeutic targets. The readers of the *Journal of*

Medicinal Chemistry will, no doubt, be more interested in the latter topics. Many of the papers contain material that was previously published, although it may be convenient for the interested reader to have a recent overview to an author's approach towards a topic.

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Compendium of Organic Synthetic Methods. Volume VI. By Michael B. Smith. Wiley, New York. 1988. xix + 534 pp. 16 × 23 cm. ISBN 0-471-84896-4. $39.95.

The *Compendium of Organic Synthetic Methods*, first published in 1971, was an attempt by Ian and Shuyen Harrison to provide "a comprehensive one-volume listing of synthetic methods as an intermediary between the chemist and the literature". It was of value for quickly locating references to methods for the preparation of a variety of functional groups and became a widely used reference by the practicing organic chemist. Subsequent volumes updated and also expanded the original concept to include difunctional compounds. This, the sixth volume in the series, presents an additional 1100 examples of methods for preparing monofunctional compounds and 900 examples of difunctional compounds published during the years 1983–1986. The original format has been retained and expanded to include a new chapter on the oxides of nitrogen, sulfur, and selenium which include nitrones, nitro derivatives, *N*-oxides, nitrile oxides, sulfoxides, sulfones, and selenoxides. This chapter which contains only 23 references is remarkably brief in view of the synthetic importance of these functional groups. A listing of all authors for each reference and a complete author index are welcome additions to this volume.

While the Compendium remains a useful reference for the organic chemist, several aspects concerning this volume deserve comment. To this novice reader some of the terminology and classifications are confusing. Section 34B, for example, is titled Alkylation of Aldehydes, forming Alcohols but includes mainly addition reactions of aldehydes with organometallic reagents to give alcohols. Some very similar reactions and products are also found in the difunctional compound section 332: Alcohol, Thiol–Olefin. In this case the reader must, therefore, search at least two sections to be sure that all appropriate references have been reviewed. Interesting classifications are sometimes found. A reference to a Baeyer–Villiger *oxidation* of a benzaldehyde to a phenol is located in section 34A: Reductions of Aldehydes to Alcohols. There are also occasional noteworthy omissions: A reference to the reaction of a carboxylic acid with an amine to form an amide in refluxing *p*-xylene omitted the condensing agent, 1,1′-dimethylstannocene. Since there are now other available surveys of the current literature, it was of interest to compare this volume with one of them. It was found that this volume contained only seven of over 27 references to the reduction of aldehydes and ketones to alcohols listed in the 1986 volume of *Annual Reports in Organic Synthesis* edited by E. F. V. Scriven and K. Turnbull. This volume of the compendium can thus *not* be considered to be a *comprehensive* survey of the literature for the period indicated. With the current literature explosion it would be desirable for literature surveys to provide some indication of the generality of reactions and the experimental detail provided by the reference. This series makes no attempt to address these questions.

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Organic Photochemistry. Volumes 8 and 9. Edited by Albert Padwa. Marcel Dekker, Monticello, New York. 1987. xi + 373 pp. xi + 353 pp. 15 × 23 cm. ISBN 0-8247-7702-6; 0-8247-7775-1. $99.75 each.

Volumes 8 and 9 continue the good taste and high level of reviews of various aspects of organic photochemistry that have been typical of this series. In Volume 8 the first three reviews deal with similar subjects, the photochemistry of simple molecules, but from very different points of view. Chapter 1, by J. P. Ferris, discusses the photochemical transformations on the primitive earth and other planets, whereas Chapter 2, by M. G. Steinmetz, deals with photochemistry with short wavelength UV light. Chapter 3, by R. Sheridan, involves a very different topic, matrix isolation photochemistry. Chapter 4, by J. R. Scheffer and his students, reviews an area of growing interest, the influence of organized environments on the course of photochemical reactions. In this case the influence of the molecular crystalline environment on organic photorearrangements is comprehensively summarized.

In Volume 9 the three reviews are quite different in flavor from those in Volume 8 and deal with conventional organic photochemistry. Chapter 1, by P. S. Mariano, reviews the photochemistry of the C=N bond, with emphasis on electron-transfer processes. Chapter 2, W. H. Laarhoven, outlines one of the areas responsible for the establishment of organic photochemistry as an exciting discipline in he 1960s, namely photocyclization and intramolecular cycloadditions of conjugated olefins. Chapter 3, by V. N. R. Pillai, is of considerable synthetic interest and considers the use of photochemistry for deprotection and activation of functional groups.

In spite of the continuing expansion of the scientific literature and the proliferation of specialized journals, well-written, comprehensive, and critical review articles on topics of broad appeal to experts and students are still welcome. These two volumes fall into the latter category.

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The Pharmacology and Toxicology of Proteins. Edited by J. S. Holcenberg and J. L. Winkelhake. Alan R. Liss, New York. 1987. xvii + 381 pp. 16 × 24 cm. ISBN 0-8451-2664-4. $70.00.

This book is based on the proceedings of a Cetus–UCLA Symposium on Molecular and Cellular Biology that was held in Lake Tahoe, CA, in February 1987 to focus attention on the therapeutic benefits as well as toxic side effects of peptides and proteins when these are used as drugs. Because of their large size in comparison with "classical" pharmaceuticals, proteins are in some instance more likely to act at the cell surface than by direct binding to drug receptors inside the cell. One obviously would not need to be concerned about problems of cellular uptake if the effect of a drug were restricted to the cell surface. Unfortunately things are never as simple as one might wish them to be, as it is well known now that many proteins are "internalized" after becoming bound to cell surface receptors, and are eventually released inside the cell. The protential of peptides and proteins to modulate the action of "native" hormones and growth factors in the body is attracting much attention in the research community because the technology now exists for producing such materials in quantity by genetic engineering (e.g., by site-directed mutagenesis). This book therefore represents a very timely contribution to what is clearly an emerging, if not yet commercially mature, area of pharmaceutical research.

The editors have divided some two dozen papers making up the symposium into six groups dealing with (1) conceptual problems associated with the design and chemical synthesis of structurally modified peptides for use as biochemical probes or drugs, (2) the question of how peptides interact with cell surface receptors, and are subsequently internalized and degraded in the cell, (3) strategies that may be used to modulate the pharmacokinetics of peptides and proteins (e.g., osmotic pumps and liposomes), (4) possible toxicities associated with the use of proteins as drugs, (5) the potential that exists to alter deleterious immunological properties of proteins (e.g., attachment of polyethylene glycol chains to specific antigenic sites), and (6) the current status and future prospects of protein therapeutics in the clinic. Among the peptides/proteins for which valuable clinical pharmacological data are presented in the book are monoclonal antibodies (and their drug conjugates), interferons, interleukins, "second-generation" plaminogen activators such as atriopeptin, and other potentially important antithrombotic agents such as protein C.

This is a highly diverse collection of papers and clearly one that reflects a desire by the symposium organizers to offer a broad perspective of the field rather than one which is highly technical

or narrowly focused. The papers are concise, clearly written, and supported by an appropriate (i.e., not overwhelming) number of tables and charts. It is a book that any medicinal chemist who does not yet share the "peptidologist's" view of the world would do well to read and enjoy.

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Modern Spectroscopy. Edited by J. Michael Hollas. Wiley, New York. 1986. xx + 388 pp. 15 × 23 cm. ISBN 0-471-91121-6. $59.95.

This book is an introductory text which covers pure spectroscopic methods. It begins with a brief survey of the results of quantum mechanics needed for the remaining chapters. This is followed by chapters dealing with the theory of interactions of electromagnetic radiation with matter, experimental methods, and some elementary group theory. The remainder of the book deals with specific types of spectroscopy, viz. rotational, vibrational, electronic, and photoelectron spectroscopy. Finally, there is a chapter on Lasers and Laser Spectroscopy which includes sections on Raman spectroscopy and CARS.

There will, of course, be few medicinal chemists who will have need of the material presented. For those who do, however, this book can be highly recommended. The material is very clearly presented and each chapter contains questions which allow the reader to establish his degree of understanding. The level is that of an introduction to principles of spectroscopy, and each chapter concludes with a bibliography of more advanced treatises.

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