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BOOK REVIEWS

Protein Structure: Determination, Analysis, and Applications for Drug Discovery. Edited by Daniel E. Chasman (Variagenics, Inc., Cambridge, MA). Marcel Dekker, Inc.: New York and Basel. 2003. xi + 606 pp. $195.00. ISBN 0-8247-4032-7.

This book is intended as a reference for the researcher with a basic knowledge of protein structure who would like to understand more about determining, analyzing, and using structural information, especially from a genomics perspective. It emphasizes recent technological advances in high-throughout methods, automation, and computation. Each chapter is self-contained and can be used to organize and initiate an in-depth study.

The book is divided into four parts. Part I is an introduction to structural genomics, while Part II addresses determination of structure, from producing proteins through novel folding to ab initio methods for generating protein structures. Part III deals with structural analysis—identifying errors, comparing structures, and functional annotation—and two major databases: the Protein Data Bank and the European Bioinformatics Institute Macromolecular Structure Base. Part IV is a discussion of the applications to drug discovery, that is, molecular docking, use of pharmacophores in structure-based drug design, and predicting the functional effects of single nucleotide polymorphisms, and includes two case studies: human interferon β-1A and rhodopsin.

This book will be useful both to scientists from other disciplines who wish to undertake structural studies and to experienced structural biochemists needing to stay current with recent developments in this fast-moving field. Many of the chapters are written by scientists working in the biotechnology industry and provide a candid, often insightful view of this frontier. Part II is perhaps the most useful, because these methods are relatively mature so that broad generalizations can be made. Parts III and IV deal with areas under rapid development, where there is much more uncertainty about which approaches will be most useful in the long run. Although each chapter is self-contained, there is some overlap, and thus general statements and caveats tend to be repeated several times in different chapters. The mathematics is occasionally a little heavy for the general reader, but useful to those seeking an understanding of the principles. The methodological discussions in Part IV are well done and very useful; the discussion of specific systems has some value as case studies, but will be of limited interest to the general reader.

This volume is very timely, appearing when there is enormous interest in the potential of postgenomic biology as well as the development of high throughput methods and their applications, particularly in the pharmaceutical industry. All of the chapters have some 2003 references, although some appear to have been written a couple of years earlier. In summary, this is a very readable introduction to topics of broad interest in the chemical community. It will be most useful to those with some knowledge of the subject who are seeking a broader and deeper understanding.

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Chemical Process Research: The Art of Practical Organic Synthesis. Edited by Ahmed F. Abdel-Magid (Johnson and Johnson Pharmaceutical Research and Development) and John A. Ragan (Pfizer Global Research and Development). American Chemical Society (distributed by Oxford University Press): Washington, DC. 2004. xii + 212 pp. $125.00. ISBN 0-8412-3824-3.

This book is based on the symposium "The Role of Organic Synthesis in Early Clinical Drug Development" held in Chicago, IL in August 2001. It opens with a chapter by Grabowski entitled "Reflections on Process Research", and the remaining 10 chapters feature a variety of examples of different styles of chemical process research. A sampling of some of these chapters includes the following: "Process Research and Initial Scale-Up of ABT-839: A Farnesyltransferase Inhibitor"; "Synthetic Approaches to the Retinoids"; and "Solution Phase Synthesis of the Pulmonary Surfactant KL4 : A 21 Amino Acid Synthetic Protein". An author and a subject index complete the book.

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Topics in Stereochemistry, Volume 24: Materials-Chirality. Edited by Mark M. Green (Polytechnic University, Brooklyn), R. J. M. Nolte (University of Nijmegen, the Netherlands), and E. W. Meijer (Eindhoven University of Technology, The Netherlands). Series Edited by Scott E. Denmark and Jay Siegel. John Wiley & Sons, Inc.: Hoboken. 2003. xvi + 608 pp. $175.00. ISBN 0-471-05497-6.

Ever since the discovery of chirality and its origins, these topics have been central issues in science, especially the life sciences. Although there has been much debate and disagreement about chirality in terms of its origins and role in the origin of life, there is no disagreement about the impact it has at the building-block level on supramolecular assemblies, for example, biomembranes, and macromolecular conformations of proteins, nucleic acids, and carbohydrates. Although chiral induction and the conservation of chirality are very challenging aspects of chemical synthesis, scientists have been making regular technical gains in these areas. In living systems, chirality pervades form and function, and materials science brings chemistry into our daily lives, where form and function are everything. How far we have come in understanding the role of chirality in materials

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science and where we go from here are timely questions that this book attempts to address.

This volume of the *Topics in Stereochemistry* series covers chirality in materials from several perspectives, including synthesis, mechanism, structure, and application. It looks beyond the utility of materials such as high-density polypropylene and polyethylene column packings and liquid crystals to the essential science behind such materials. Utility in materials science has traditionally trumped theory because to the everyday user what a material *does* is more important than what it *is*.

The book is prefaced with an interesting historical look at the discovery of the phenomenon of chirality and a discussion of the important visionary roles played by Biot, Fresnel, Pasteur, Le Bel, and van't Hoff in articulating their original observations and formulating their concepts of chirality. It ends on the very modern topic of nonlinear optics and chirality. Throughout, the book is well referenced and the citations are quite timely.

The launching pad for the work is a discussion of the real first triumph in the application of chirality to macromolecular synthesis, that is, the development by Ziegler et al. of transition metal catalysts that effect olefin polymerization and their application to the production of stereoregular polymers by Natta et al. The discussion, fittingly presented by groups from Salerno and Naples, focuses on the elements of chirality at the end of the polymer chain and at the center of the catalytic complex. The authors explore the interplay between the roles played by these elements and use them to elaborate a very comprehensive mechanistic picture. Unfortunately, the discussion does not probe deeply the origins of these chiral consituents themselves. The focus here is on their utility in defining the overall stereochemical outcome.

The overall structure and conformational properties of stereoregular polymers are treated by De Rosa in Chapter 2. Here, various rules that define the relationship between chemical connectivity and overall structure and properties are detailed in a very comprehensive and informative fashion. Thus, much information has been derived from in-depth studies of the conformational properties of isotactic and syndiotactic polymers. However, despite years of theoretical studies and model building and recent advancements in computer technology, predicting conformation and properties from basic structures remains nontrivial. This makes the general rules that support helix formation over extended chains or that anticipate crystallinity over disorder invaluable. Newer concepts of symmetry-breaking, frustration, and spontaneous order are covered, as are the usual molecular mechanics grid search and potential energy surfaces.

Various traditional chemical systems are presented in other chapters of this book, including one from authors at several Japanese institutions on chiral polysilanes that was especially good reading. A compelling case is made for advancing synthetic chemistry in this area because of its potential in materials science.

The material presented in this book is decidedly "big picture" because the contributors generally make an effort to connect molecular chiral elements to the macroscopic level. Chapters on the amplification of chirality in discotic systems, the packing and organization of ferroelectric liquid crystalline systems, and the manifestation of chirality at the molecular level in helical polymers and biaryls in the behavior of cholesteric handedness are examples of this. A very good attempt at the difficult challenge of relating chirality at the molecular level to supramolecular structure is made by the group from the U.S. Naval Research Labs. They give an especially comprehensive and very interesting treatment of self-assembly in biological and hybrid systems. Theoretical models that integrate spectroscopic arguments are also presented.

Although spectroscopic and computational methods are treated throughout the book, there is no separate chapter on relating physical measurement to theory. The prediction of optical activity using computational tools is still in its infancy, but advances have been made. Techniques such as vibrational Raman optical activity and vibrational circular dichroism are becoming more common. FTIR spectroscopy using polarized light or reflectance modes, where the reflected beam is polarized from metal substrates, has been used very successfully. A chapter (or two) in this area would certainly add a lot to an otherwise gallant and successful attempt to put chirality in matter into such a sharp focus.

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