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Book Reviews

Pharmacogenomics, Werner Kalow, Urs A. Meyer, and Rachel F. Tyndale, Eds., Drugs and the Pharmaceutical Sciences, Volume 113, Marcel Dekker, Inc., New York, NY, 2001. xi, 403 pp., illustrations. $165.00.

Pharmacogenomics can be seen as an extension of Pharmacogenetics, taking advantage of the recent surge in genomic sciences and technology. 'Pharmacogenomics' is one of the first monographs dealing with this topic comprehensively - hence; its publication is timely. It is reassuring to see that the three Editors, Drs. Kalow, Meyer, and Tyndale, have been pioneers or are active participants in the field of pharmacogenetics, bringing long-standing scientific expertise to bear on the subject matter. Wisely, the authors have taken the term 'genomics' seriously by including a broad spectrum of topics that justify the title given to the book.

Appropriately, Werner Kalow covers historical aspects, being one of the earliest pioneers in genetic analysis of drug action. This is followed by a synopsis of pharmacogenomics from an industrial perspective, written by B. Michael Silber from Pfizer Inc., with emphasis on biomarkers to achieve individualized medicine—a main goal of pharmacogenomics. Several chapters deal with the pharmacogenetics of drug metabolism (Leif Bertilsson), receptors (Wendell W. Weber), and transporters (Richard B. Kim and Grant R. Wilkinson). These provide useful overviews even though the format prevents a more detailed and thorough analysis of each area. There is some overlap in the chapters dealing with interethnic differences (Werner Kalow) and clinical viewpoints (Urs A. Meyer), but the information is nevertheless quite up to date and serves as a guide for the novice in pharmacogenetics.

From here on out, the monograph focuses on genomics, and specifically the 'tools of the trade,' introduced by Glenn Miller from Genzyme Corporation. Several chapters deal with genotyping, technologies for SNP analysis, multiplex sequencing strategies, serial analysis of gene expression (SAGE), proteomics, and bioinformatics. Overall, these chapters do cover the technical essentials, but there is some overlap among chapters, and each is limited in depth (even though some chapters cover a specific area in disproportionate detail, such as SAGE). One does learn about the general trends, but one misses a clear guide as to where these technologies are leading us in the area of pharmacogenomics. Maybe fewer chapters with a more comprehensive view would have improved the content value. Nevertheless, each individual chapter is informative.

The remaining two chapters cover mapping of disease loci (Glenys Thomson) and positional cloning and disease identification (M.S. Silverberg *et al.*). These are important but rather short chapters. Again, one obtains a first glimpse of the field, specifically the identification of disease loci. Recently, positional cloning efforts aim at finding QTLs for drug response and toxicity—a better connection to pharmacogenomics by covering these new trends would have helped the reader. Also, haplotype analysis in pharmacogenetic association studies has emerged as a hot topic, which is insufficiently covered.

Conveying a newly emerging field such as pharmacogenomics is clearly a daunting task. Developments are rapid, and by the time the book arrives in print, new ideas have emerged that shape the field. Nevertheless, 'Pharmacogenomics' manages to convey most of the important directions in a concise fashion. It is therefore useful for the novice to get acquainted with the field, and the expert to get a quick reference book in any of the many specialty areas relevant to pharmacogenomics.

Wolfgang Sadée, Ph.D.
University of California-San Francisco
San Francisco, California

The Application of Drug Delivery Systems: Current Practices and Future Strategies, Faiz Kermani and Gordon Findlay, Eds. CMR International, Epsom UK. 2000. iv, 232 pp., illustrations. $2350.00.

This is a coil-bind 237-page book that contains seven articles based on the lectures and discussion given at a workshop on the same title in Surrey, United Kingdom in April 2000. When a book has such a hefty price tag as this, one naturally wonders what new/unique information it may present that are not available in other books. *Pharmaceutical Research* has received numerous books through the years, but there were only a few books that carried such high price tags. All of them were published by firms that specialize business analyses in the pharmaceutical industry. One of the main questions here is whether the book is really worth the price.

The uniqueness of this book is that it also contains different type of information that can be found only in business magazines and journals. Chapter 1 on the usefulness of controlled drug delivery systems is followed by two chapters summarizing the results of the survey on the strategies and practices used by pharmaceutical and drug delivery companies. The results described in the chapters may not be available in any other sources. The survey results show that the majority of drug delivery systems are applied to existing active substances, and big pharmaceutical companies rely heavily on drug delivery companies as outside suppliers of drug delivery technologies. Applications of drug delivery technologies to new active substances have been low, since pharmaceutical companies are extremely reluctant to share information on new drugs in their pipelines with drug delivery companies. Furthermore, as described in Chapter 7, utilizing drug delivery technology would add time to the drug development process when the speed to market is of key importance. Adding to this difficulty is the view in the pharmaceutical companies that the need to use a drug delivery technology implies the "failure" of a particular project.

The drug delivery industry, as pointed out in Chapter 4, is highly fragmented simply because a huge variety of drug delivery systems are necessary for delivery of drugs with totally different properties by various administration routes. Survey shows that 22 pharmaceutical companies initiated

over 210 collaborations with drug delivery companies between 1997 and 1999. Many collaboration deals between pharmaceutical and drug delivery companies failed to reach agreements mainly due to different expectations on costs, in particular regarding royalties. Chapter 5 details an example of collaborative product development and alliance management using Dura/Eli Lilly Alliance as a "case study." It was pointed out that all too often the reasons for failed alliances are put down to technical problems when the real reasons are due to inadequate alliance management resulting from two different cultures of two different companies.

Chapter 6 deals with the drug delivery companies of the future. While it is difficult to predict what will happen in the next 10 years, the chapter concludes that drug delivery companies may have to develop their own proprietary products to survive, since pharmaceutical companies will need only those technologies that can add values to their products. Although this conclusion seems to be generic and not particularly breathtaking, it has a point in that competition among drug delivery companies will become more intense in time, and the only way to survive is to tailor-make the drug delivery technologies to fit into the drugs by pharmaceutical companies or develop their own products. The latter option, however, is not the one most of the drug delivery companies can afford. Chapter 7 is the summary of discussion and recommendations from industry participants on drug delivery technologies. As mentioned above, each drug delivery company has only one or two technologies and no single drug delivery technology is universally applicable. At the same time, pharmaceutical companies are known to favor dealing with drug delivery companies that have a range of technologies available. These two observations collectively suggest that drug delivery companies will go through a phase of consolidation within drug delivery companies. Thus far, however, no significant acquisitions of smaller drug delivery companies by larger drug delivery companies have happened. Rather, drug delivery companies, large or small, have been acquired by pharmaceutical companies. The best chance for drug delivery companies to survive is to show that its technology can add value to a high profile molecule being developed by a pharmaceutical company as well as blockbuster drugs that will be soon out of patent.

This book describes why many drug delivery companies fail to make deals with pharmaceutical companies. The drug delivery companies should lower their unreasonably high expectations that the pharmaceutical companies have endless resources in the development of drugs, and thus drug delivery systems. Most pharmaceutical companies do not have an existing budget for feasibility studies. Thus, the burden is on the drug delivery companies to present the proof of principle of the technology that will be applied to the drugs in question and the possibility of scaling up the procedure for eventual commercial purposes.

Overall, the book presents unique information on the relationships between pharmaceutical and drug delivery companies. It is rather unfortunate that many of those who would get benefit from the book may not be able to afford it.

Haseun Park, Ph.D.
Purdue University
West Lafayette, Indiana

Protein Structure, Stability, and Folding. Kenneth P. Murphy, Ed., Methods in Molecular Biology, Volume 168, Humana Press, Totowa, NJ. 2001. ix, 252 pp., illustrations. $89.50.

Both theoretical and experimental approaches for studying protein structure, stability, and folding are described in the book. The fundamental concepts are clearly presented. The thermodynamic aspects including the preferential exclusion may seem too elementary, but they may serve as a good introduction for beginners in this field. The topics on modeling and simulation would be useful for protein designers. However, a clear pharmaceutical application of the information presented in each chapter is lacking for pharmaceutical formulation scientists. As the chapters in this book do not follow a specific sequence, I have tried to relate them in a logical structure wherever possible in the review.

The book starts with a concise overview on the fundamental thermodynamic concepts and governing forces for protein folding. It is emphasized that since both enthalpy and entropy changes are strongly dependent on temperature and heat capacity, the Gibbs free energy change for unfolding is not a linear function of temperature, leading to a maximum stability at a certain temperature. This point is further developed in Chapter 3. Hence, depending on the actual free energy-temperature profile, having a higher denaturation temperature does not necessarily imply that a protein will be more stable at room or lower temperatures. An implication is that protein stability measured at higher temperatures cannot be used as a predictor of room temperature stability. The temperature effect is particularly important to consider for storage stability of pharmaceutical formulations. To fully specify the temperature stability of a protein, three thermodynamic parameters - enthalpy, entropy and heat capacity changes at the reference temperature - which can be obtained from high sensitivity calorimetry, must be known. Computational analysis of the Gibbs free energy functions is presented in Chapter 3 with discussion on the calculation of enthalpy change, heat capacity change and entropy change as well as calculation of solvent accessibilities. An illustration of the thermodynamic analysis is given using example proteins and mutants. The thermodynamic linkage between the three-dimensional structure of protein, stability and biological functions is also emphasized in Chapter 3. This is particularly important as proteins undergo conformational changes during eliciting physiologic function or biological activity when a ligand is bound. Chapter 3 ends with an interesting discussion on the protein stability and function involving functional cooperativity, i.e., the switching of proteins from one functional state to another by selectively stabilizing some conformations via interaction with ligands. The example emphasizes that strategies aimed at engineering proteins for increased stability must consider the effects of mutations on the redistribution of different conformations, and on the binding affinity of ligands. The concept of cooperativity is recapitulated in Chapter 5 by looking at the effect of perturbing a residue (e.g., by mutation) on the probability of each conformational state in which a protein is unfolded. An important issue is that two residues which behave cooperatively under one set of conditions may not behave cooperatively under a different set of conditions. Modeling the ensemble of different protein conformations can be used to show how perturbations in proteins are propagated through the structure. This may have signifi-

cant implications on designing pharmaceutical proteins for improved stability.

Protein stabilization by naturally occurring osmolytes is described early on in Chapter 2. Naturally occurring osmolytes for protein stabilization fall into three general classes: 1) polyols, 2) amino acids 3) methylamines; each of them is stress-specific. Some of these have already been used for pharmaceutical protein formulations. Using Gibbs free energy diagram for the native and unfolded states, Timasheff's preferential exclusion of the ligand from the vicinity of the protein (i.e., preferential hydration of the protein) is explained. Osmolytes are shown primarily to stabilize protein via destabilizing the unfolded state. The use of the Transfer Model in understanding protein stabilization by osmolytes and effect of denaturants is highlighted with its weakness. The model assumes that the contributions of component parts for both side chain and backbone units of a protein are additive. This assumption is doubtful since the solvent accessibility of each amino acid depends on the specific environment in the protein. Nevertheless, the model is useful as an elementary concept to understand the major components in protein folding.

Chapter 1 also provides a concise discussion on the protein stability as a fine balance between large opposing contributions, with hydrogen bonding and hydrophobic effect being the stabilizing force which is offset by the destabilizing configurational (conformational) entropy. Hence, protein stability can be affected by relatively small changes in the environment. Although hydrogen bonding is enthalpically favorable in stabilizing protein, mutation study using proteins with enhanced hydrogen bondings between side chain and backbone has shown an increased enthalpy of unfolding with a decreased melting temperature, indicating an entropic penalty of forming hydrogen bonds (enthalpy-entropy compensation, i.e., favorable enthalpic changes are coupled to unfavorable entropic changes). The hydrophobic effect may thus contribute less to protein stability than originally believed. Since protein interior is not liquid-like, the inadequacy of the simplistic approach to study hydrophobic effect by transferring model hydrophobic compounds from liquid hydrocarbon to aqueous solution is also pointed out. Conformational entropy is the major force opposing folding, and perhaps a guiding force in the formation of protein secondary structure. In Chapter 1 conformational entropy in protein folding is proposed to be best studied by computational methods and Chapter 6 serves as a guide on the calculation of conformational entropy. As a starting point, the entropy of a molecular system at equilibrium can be calculated using Boltzmann's formalism. The partition of conformational data can be done according to conformation population or energy distribution (such as high-energy/low-population conformations). While conformational distributions can be obtained from known structures, a major limitation is the lack of experimental data. Consequently, simulations have been used to estimate conformational entropy for proteins. Different simulation methods including the advantages and limitations are discussed.

Modelling the native state as an ensemble of conformations involving local unfolding reaction rather than a discrete conformational state is the theme of Chapter 5. The probability of any conformation of a given protein under equilibrium condition can be computed by statistical thermodynamics. Hence the heat capacity, enthalpy and entropy difference between each conformational state and the reference state (from high-resolution structure) can be calculated. The stability of a protein can be expressed as the ratio of the summed probabilities of all folded states to the unfolded states in the ensemble. The same can be applied to a particular residue of a protein and is termed the residue stability or folding constant. Experimental validation of the computed results is carried out by comparison with hydrogen-exchange protection factors. Using hydrogen exchange to measure the conformational stability of a protein is the key focus of Chapters 4 and 9, which together with Chapters 7 and 8 on other techniques, form the experimental core of this book.

Amide hydrogen exchange has become one of the most important tools in analysis of protein folding and unfolding (Chapters 4 and 9). Traditional methods using solvent and thermal denaturation are limited because of 1) the assumption of fully reversible protein transition based on a two-state mechanism without allowing for an intermediate state, 2) the requirement of a long extrapolation from unfolding to ambient conditions, and 3) the assumption that the unfolded states at high temperatures or in denaturants are thermodynamically equivalent to the unfolded states under ambient conditions. The hydrogen exchange method that involves studying the rate of exchange of the amide hydrogen with deuterium by putting the protein in a deuterium oxide environment is hence introduced. Based on a simplistic two-step model, the exchange mechanism (whether monomolecular EX1 or bimolecular EX2 exchange) is determined from the relative magnitudes of the rate constants governing opening and closing of the protein structure in the model. An amide proton exchange mechanism (whether by an EX1 or EX2) can be established by plotting the logarithm of the exchange rate constant versus time, by monitoring the decay of individual proton resonances over time as they exchange with solvent deuterium in NMR experiments, or by comparing the Gibbs free energy values of hydrogen exchange for neighboring amide groups with their corresponding exchange rate constant values. Each of these approaches is described in details.

Chapter 7 draws on both experimental and computational results trying to answer the question of whether turns play an active or passive role in protein folding. Turn scanning is proposed as an experimental method for assessing the role of turns in the folding process. The technique involves systematic replacement or insertion of residues (e.g., proline, glycine, leucine or substitution between hydrophobic and hydrophilic residues, or between residues with large and small side chains) in a turn followed by measuring the effect on the change in the rates of folding or unfolding, stability to denaturing conditions, and structural changes using various biophysical techniques. Both short peptide and protein model systems are discussed, but the importance of turns seems to be case specific.

Many protein systems show more than one rate in the folding process, suggesting the presence of intermediates and the rates are frequently too rapid (time-scales of microseconds or shorter) to measure by normal stopped-flow techniques (time-scales of milliseconds or longer). Laser-temperature jump method for studying folding dynamics is presented in Chapter 8. In this technique, a pulse of laser energy is absorbed by a dye or by the solvent to produce heat within a few nanoseconds to study the kinetics of protein unfolding by the thermal stress. A history of the technique

with physical background is given, followed by description of instruments currently available in major institutes. The use of the technique is illustrated with protein examples.

The book ends with a thorough discussion on molecular dynamic simulation to study protein unfolding and folding. In contrast to experiment studies which report on the average properties of protein ensemble, simulation provides detailed information for a single molecule. Also, simulation can provide molecular structure information that experiments may not be able to generate. However, simulations are meaningless without relating to experiment data. Hence, a necessary first step would require demonstration that the simulation reproduces the native state protein obtained from the crystal or NMR structure. Examples are given in this chapter to illustrate the use of simulation to elucidate protein folding and unfolding pathways at atomic resolution. A potential pharmaceutical application of simulations is to help design faster folding proteins with enhanced stability.

Hak-Kim Chan, Ph.D.
University of Sydney,
Syndney, Australia

Protein Purification Applications. Second Edition. A Practical Approach, Simon Roe, Ed., Oxford University Press, New York, NY. 2001. xvi, 165 pp., $45.00.

This recently published second edition book is part of the Practical Approach series of step-by-step guides to various subjects in molecular biology and biochemistry. The book is not comprehensive, but is a short volume that covers techniques in the separation of proteins from microbial and mammalian cell culture as well as from animal and plant sources. Each chapter begins with an introduction that conveys background information and in some instances directs the reader to previous publications. This section is followed by a description of various purification and process steps. Interspersed in this discussion are helpful protocols that describe a specific step or process in sufficient detail to be reproduced. The book also contains a useful appendix that has an extensive list of suppliers.

A re-occurring theme of the book is the application of both established and new techniques in larger scale isolation processes used in the biotechnology industry. For example, steps specific to the purification of monoclonal antibodies, proteins that have emerged as important therapeutic drugs, are presented in detail. Furthermore, the authors describe the problems of virus and DNA contamination of mammalian cell culture and how these materials may be inactivated or removed in a purification process designed for therapeutic proteins. Finally, the authors discuss how fusion protein technology, a procedure where proteins are modified using genetic engineering to specifically facilitate purification, may be used in a commercial process to solve separation problems and effectively lower the cost of goods.

The authors also cover the purification of smaller amounts of protein in a research laboratory. For example, chapters are dedicated to the isolation of protein from tissue sources that contain a significant level of contaminant proteins and plant sources, where the major contaminants are non-protein material. Furthermore, the purification of proteins from milk, a source that contains a high lipid content, and the preparation of protein crystals to facilitate structural studies are also discussed. Finally, the authors describe how genomics and fusion protein technology may be combined to obtain a screening process where proteins are rapidly expressed, isolated and may be further subjected to a functional analysis.

Protein purification is a significant subject and I was initially skeptical as to what could be conveyed in such a small volume. However, I found this book serves as a good reference to those who are not purification specialist, but require a working knowledge of current techniques used in the isolation of proteins from a variety of sources in both a large scale commercial process and at a smaller scale for research purposes.

James D. Andya, Ph.D.
Genetech Inc.
South San Francisco, California

Star and Hyperbranched Polymers, Munmaya K. Mishra and Shiro Kobayashi,Eds., Marcel Dekker, Inc., New York, NY 1999. ix, 350 pp., illustrations. $175.00.

The opportunity of macromolecular substrates to be used in pharmaceutical fields has been increased significantly ever since the field of macromolecular chemistry began a few decades ago. In particular, supramolecular-structured polymers have been well received for their potential applications in controlled drug delivery. The book presents a concise summary on the chemistry of star and hyperbranched polymers, representatives of the newly-generated supramolecular polymers. One could expect that star-shaped polymeric architectures perform multivalent interactions with various biological systems via their multi-armed structures. All the chapters in the book focus on specific research interests of the contributors as chemists, and thus the book may not cover other interesting areas of the supramolecular polymers ranging from the basis to the application. It is clear, however, that the contents of the book are very fresh with many new references. This makes the book highly helpful to researchers in the pharmaceutical and biomedical fields for considering the future potentials of star and hyperbranched polymers in drug delivery and biomedical applications. Of special interest in this book is a variety of chemistry for preparing unique star and hyperbranched polymers with a wide range of properties. Understanding those synthetic schemes may require advanced organic chemistry. Although the book is lacking in some topics on the biological and pharmaceutical applications of commercially available dendrimers and related polymers, it can certainly provide more than adequate information for those interested in utilization of tailor-made supramolecular polymers in the future.

Nobuhiko Yui, Ph.D.
Japan Advanced Institute of Science and Technology
Ishikawa, Japan

Cells, Gels and the Engines of Life. A New, Unifying Approach to Cell Function, Gerald H. Pollack, Ebner and

Sons Publishers, Seattle, WA. 2001. xiv, 305 pp., illustrations. $27.95 (paper).

The basic premise of this book is that the cell can be treated as a polymer gel (or hydrogel) with a lipid bilayer (that does not have to be intact) surrounding the gel. When a cellular body is treated as a polymer gel, all cellular functions become physicochemical phenomena that can be explained by physicochemical principles. This book tries to explain much (if not all) of cellular functions by a single unifying mechanism, known as the phase transition between the sol and gel states of polymer chains. The phase transition can also occur between swollen and shrunken gel states, if the polymer chains are crosslinked. It is rather remarkable that the author, using just the polymer gel phase transition theory, made successful arguments against well-accepted concepts, such as ion channels and pumps. In fact, Chapter 1 is devoted to debunking myths on channels and pumps. The main question that the author asks is that how the cell might isolate a certain solute it has never seen before. This is an interesting question that can also be extended to a recently found pump system known as P-glycoprotein, which is supposed to spew out absorbed anticancer drugs in the name of protecting the cells. How is the cell prepared for the molecule it has never seen before? Well, evolution and/or adaptation may explain this, but if the cell keeps on adding new pumps on top of the existing ones, the cell will not have enough space and energy required to power all of its pumps.

One of the nice features of this book is that it starts with the basic information so that the readers without proper background can easily follow the development of the story. For the subject as diverse as this one ranging from biology (e.g., cell division, muscle contraction, and cell secretion) to polymer chemistry (e.g., diffusion through polymer network and phase transition), the book is incredibly easy to read. Chapter 4 explains different states of water in the presence of polymers (natural or synthetic), and how different water states affect solubility and transport of solutes. Other chapters describe examples showing that ion selectivity between sodium and potassium can be done without invoking sodium pumps. Diffusion of the two ions through polyanionic hydrogels results in the same ion selectivity. Chapter 8 on the phase transition of polymer gels is an excellent summary of smart hydrogels, which in itself is a huge scientific discipline.

The second half of the book, using only physicochemical principles, explains a variety of biological phenomena, such as cellular secretory discharge, cell action potential, cellular transport, cell migration, cell division, ciliary bending strokes, and muscle contraction. For example, cellular secretory discharge is explained by phase-transition of the vesicle matrix (which is a polyanionic gel). The polyanion gel shrinks into a tight packet in the presence of divalent cations, such as calcium ions. Once this packet is shipped to the cell periphery, monovalent cations, such as sodium ions, displace divalent cations which are bound to the polyanion chains. (Displacement of the bound divalent cations by abundant monovalent cations is in fact how a water softener recharges itself). The expansion, or swelling, of the compact vesicle can also release any other contents present inside the vesicle. Whether this phase transition is really the underlying principle in the cell remains to be seen, but there is no reason why the cells would adapt unnecessarily more complex mechanism. While the phase transition theory may not be perfect yet, it is extraordinary that it can explain so much of cellular functions with ease. Considering that this new phase transition theory is just beginning, I have no doubt that it will be refined to perfection in time.

This is a science book that is as interesting as any nonfiction novels that are listed in the best seller list in The New York Times. At last, we have a book which clearly shows that the science book does not have to be boring. The author did an outstanding job in introducing a new theory, new insights, and a new way of thinking by combining biology with known polymer principles, in a way that almost everyone can afford.

Kinam Park, Ph.D.
Purdue University
West Lafayette, Indiana

Endotoxins, Pyrogens, LAL Testing, and Depyrogenation, Second Edition, Revised and Expanded, Drugs and the Pharmaceutical Sciences, Volume 111, Kevin L. Williams, Ed., Marcel Dekker, Inc., New York, NY. 2001, x, 372 pp., illustrations. $150.00.

This book is a significant update and expansion of the original edition published in 1985. Knowledge in this complex field has increased substantially over the past 15 years, and the author, Kevin Williams has assembled an excellent fifteen-chapter text. The chapters are well referenced and documented. Special attention is focused on practical aspects of laboratory technique, quality documentation systems, and current regulatory expectations. Examples include: How are endotoxin release limits established? What approaches are used to validate the *Limulus* Amebocyte Lysate (LAL) test? How might QA/QC manage excipient quality (pyroburden) for a parenteral product?

Chapters 1 and 2 present the historical context of fever and the early therapeutic strategy of inducing fever to fight disease. Development of the rabbit pyrogen test and later inclusion in the 1942 U.S. Pharmacopeia is introduced. The rabbit pyrogen test is discussed at length by Karen Roberts in Chapter 9. Chapter 3 is an excellent review of the structural aspects of endotoxins, including location in the cell membrane, potential aggregation states, and relative potency of subunits. A further review is provided on pyrogen classification (endogenous pyrogen versus exogenous pyrogen), including an interesting discussion on pyrogens of nonmicrobial origin. Chapter 5 discusses nonendotoxin microbial pyrogens. The chapter concludes with a discussion of the difficultly in validating removal of nonendotoxin pyrogens from classic biological products, proteins of microbial origin, and proteins of mammalian expression. The reviewer had not seen this information presented in historical context in previous publications, and found this section valuable.

The host response to endotoxin insult is discussed in Chapter 4 "The Host Response to Endotoxin", Chapter 9, and in Chapter 15 (written by N. Anthony Nnalue) in a discussion of therapeutic considerations for combating gram-negative sepsis. All of this information could have been provided in a single chapter. A discussion of drugs that produce fevers is found in Chapter 6. An interesting review of antibiotic mediated endotoxin liberation is also included.

Chapters 10–12 present the LAL assay discovery, development, test methodologies, regulatory status, validation, and current practices. Topics include assay interference/enhancement testing and automation. Chapter 13 presents both factual information and forward thinking regarding the next generation analytical techniques for detecting endotoxins and other residual cellular components. The discussion includes methods such as GC-MS used to detect 3-hydroxy fatty acids in lipid A, the silk worm larvae plasma test, PCR testing for specific foreign DNA fragments, and as well as bioassay techniques using human mononuclear cells. Chapter 14 discusses depyrogenation processes used to inactivate, exclude, or remove endotoxin from equipment, components, excipients and products.

In conclusion, the reviewer believes this well written, in-depth book will become a standard reference used by those working in this challenging, rapidly changing field.

John Ludwig, Ph.D.
Pharmacia Corporation
St. Louis, Missouri

Pharmaceutical Process Engineering, Drugs and the Pharmaceutical Sciences Volume 112, Anthony J. Hickey and David Ganderton, Eds., Marcel Dekker, Inc., New York, NY. 2001, x, 268 pp., illustrations. $135.00.

Pharmaceutical Process Engineering contains 15 chapters, which are divided into two sections, Fundamentals and Processes. The Fundamentals section contains four chapters on fluid flow, heat transfer, mass transfer and powders. The second section contains eleven chapters on air conditioning and humidification, drying, solid-liquid extraction, crystallization, evaporation and distillation, filtration, size reduction and classification, mixing, solid dosage forms, sterilization and bioprocessing. This book is a re-release of the out-of-print book *Unit Processes in Pharmacy* written by David Ganderton and published by William Heinemann Medical Books LTD of London in 1968. The new volume is essentially the same, but some chapters have been rearranged, combined or deleted, and three new chapters on solid dosage forms, sterilization and bioprocessing were added. Also, in the revised book the photographs and some of the detailed drawings of equipment have been removed; in general, there is an overall decrease in the illustration quality.

In the book's preface, the authors state " . . . this text should again find a role as a reference and review book . . . " to this end the book succeeds admirably. Thus, it should be emphasized that this book is not intended to be a textbook or a comprehensive treatise on the subject of unit operations, and there are few worked examples and no homework problems given. The level of the book would be appropriate for an advanced undergraduate student or first year graduate student in the pharmaceutical sciences; engineering students would consider this book to be an elementary review of unit operations. The book assumes a basic knowledge of differential and integral calculus, physical chemistry and basic engineering concepts like stress, strain, heat, work and some background in unit operations.

The authors' strategy is to begin with a discussion of the theoretical basis behind the unit operations and then apply this theory to the discussion of the different unit operations and processes. The first chapter covers key concepts in fluid mechanics including hydrostatics, measurement of pressure and flow, Bernoulli's Theorem, laminar and turbulent flow, pumps, dimensional analysis and Reynolds' number. The second chapter on heat transfer covers conduction, convection, radiation, heat transfer in and between fluids, heat exchange and heat transfer associated with phase change, e.g., boiling and condensation. The third chapter on mass transfer covers diffusion in gases and liquids, equimolecular counter diffusion, mass transfer in turbulent and laminar flows and interfacial mass transfer. I found the discussion on convective mass transfer to be very informative and valuable especially given the fact that this is an often overlooked but important subject in pharmaceutics. Also, I thought it was unfortunate that the non-steady state problem was omitted from both the heat transfer and the mass transfer chapters. The Powders chapter had a qualitative discussion that included powder bed packing, particle interactions, basic measurement of powder cohesion and adhesion, granulation and mixing. The important issues of stress distribution in a powder bed, Mohr's circle and shear cell analysis were not covered. Unfortunately, space precludes a detailed discussion on the Processes section of the book, but most of these chapters followed a similar format, that being, introduction, significance, theory, methods, equipment and equipment operation. Like the Fundamentals section, these discussions were very brief and readable.

Despite some criticism I have about the depth of coverage, the concept and outline of the book are excellent, and it would be difficult to find another book that packs so much information into such a brief and readable volume. In summary, this book is not intended to be a self-contained comprehensive treatise or textbook but a quick reference for the reader who already has some familiarity with the subject of unit operations.

Stephen W. Hoag, Ph.D.
University of Maryland, Baltimore
Baltimore, Maryland

Books Received

Biochemistry & Immunochemistry

Enzymes in Nonaqueous Solvents Methods and Protocols, Evgeny N. Vulfson, Peter J. Halling, and Herbert L. Holland, Eds., Human Press, Totowa, NJ. 2001, xix, 679 pp., illustrations. $139.50.

This book, composed of 49 chapters, is divided into three parts. Part I is on the control of enzyme activity in nonaqueous solvents. This section includes topics on molecular imprinting for locking the enzyme conformation favorable for catalysis during lyophilization, enzyme loading methods into microcapsules and hydrogels, PEGylation, water activity control, and others. Part II on Synthetic Applications focuses on the use of suitable catalyst to the application of nonaqueous enzyme technology for chemical production and on the optimization of water activity in low-water sys-

tems. Examples are use of hydrolytic enzymes for formation of esters and amides, enantioselective reactions, preparation of chiral alcohols, and whole-cell applications. Part III. Reaction Systems and Bioreactor Design deals with solvent-free systems where the reaction takes place in a neat mixture of substrate in the absence of added solvent for the synthesis and modification of lipids and numerous other products. This section also deals with biotransformation involving solid substrates as well as reverse micelles and microemulsions.

The Immunoassay Handbook, Second Edition. David Wild, Ed., Nature Publishing Group, 2001, 345 Park Avenue South, New York, NY 0010-1707, www.naturereference-.com, 2001, xxix, 906 pp., $185.00.

Micro- and Nano-Materials

Nanophase and Nanocomposite Materials III, Materials Research Society Symposium Proceedings Volume 581, Sridhar Komarneni, John C. Parker and Horst Hahn, Eds., Marcel Dekker, Inc., New York, NY. 2000, xviiii, 688 pp., illustrations. $99.00.

Fine Particles: Synthesis, Characterization and Mechanisms of Growth, Surfactant Science Series, Volume 92, Tadao Sugimoto, Ed., Marcel Dekker, Inc., New York, 2000. xi, 738 pp., illustrations. $235.00.

Fullerenes: Chemistry, Physics, and Technology, Karl M. Kadish and Rodney S. Ruoff, Eds., John Wiley & Sons, Inc., New York, NY. 2000, ix, 968 pp., illustrations. $195.00.

Pharmacy Practice

Research in Health Care Concepts, Designs and Methods, Julius Sim and Christine Wright, Stanley Thornes (Publishers) Ltd., United Kingdom, 2000, ix, 402 pp., $37.50.

A Primer of Drug Action. A Concise, Nontechnical Guide to the Actions, Uses, and Side Effects of Psychoactive Drugs, Robert M. Julien, Ed., W. H. Freeman and Company, New York, NY. 2001, xiii, 498 pp., illustrations. $19.95.

The NDA Pipeline - 1999. 18th Edition, Melissa Carlson, Betsy Goodfellow, Eds., F-D-C Reports, Inc., Chevy Chase, MD. 2000, xxx, 1418 pp., illustrations. $1295.00.

Polymer Chemistry

Advanced Polymer Chemistry. A Problem Solving Guide, Manas Chanda, Ed., Marcel Dekker, Inc., New York, NY. 2000, xiii, 852 pp., illustrations. $225.00.

This book is written as a text book for a one-year course in polymer chemistry. The presence of many illustrative, worked-out problems makes it easier for beginners to grasp many difficult concepts rather easily. Each chapter has a large number of problems with detailed explanation, and many exercise questions also have answers. The first four chapters deal with fundamentals in polymer chemistry, such as introductory concepts, polymer characterization, thermodynamics of polymer solutions, and measurements of polymer molecular weights. The last six chapters are devoted to polymerization reactions: step, chain, ionic, coordination, and ring-opening polymerizations, and copolymerization. This book will undoubtedly help students who want to reach a fairly advanced level of proficiency in polymer chemistry in a relatively short period of time.

Polymer Blends and Alloys, Gabriel O. Shonaike and George P. Simon, Eds., Marcel Dekker, Inc., New York, NY. 1999, xiv, 745 pp., illustrations. $225.00.

Reactive Processing of Polymers, V. P. Begishev and A. Ya Malkin, Eds., ChemTec Publishing, Toronto, Canada. 1999, viii, 253 pp., illustrations, $145.00.

Solvents

Handbook of Solvents, George Wypych, Ed., ChemTec Publishing, Toronto, Canada, 2001, xxv, illustrations. 1675 pp., $285.00.

This handbook provides a comprehensive and extensive analysis of all current information on solvents. The exhaustive information on a variety of solvents helps readers to identify the risks and benefits associated with specific solvents and classes of solvents. This handbook is different from other handbooks in that general information, physical & chemical properties, health & safety information on each solvent are presented in a companion CD-ROM, *Solvent Database* (see below). This book utilizes its space to provide the background, explanations, and clarifications needed to convert data to information. A significant portion of the book is devoted to physical chemistry, polymer chemistry, and transport phenomena. Also described extensively in this book are solvent production applications, solvent detection and testing, environmental impact of solvents, solvent recycling, regulatory aspects, toxic effects, and contamination cleanup. This book may be essential for many pharmaceutical scientists who utilize solvents in their research.

Solvent Database. The World's most comprehensive database on solvents. CD-ROM ChemTec Publishing, Toronto, Canada. 2000, $295.00.

This CD-ROM is a companion database to the above book, Handbook of Solvents. It contains a searchable database on 1141 solvents. The vast amounts of comprehensive data necessary for solvent evaluation are presented in a CD-ROM format, since it allows frequent updates.

Kinam Park, Ph.D.
Book Review Editor
Purdue University
West Lafayette, Indiana