tion utilizing block copolymers and surfactants in nonaqueous solvents. The volume should find a place in all university and industrial research libraries. Three chapters introduce block copolymer micelles, reversed micelles, and hydrotropes in a manner suitable for newcomers to these areas. Specialists in reversed micelles, microemulsions, and molecular tribology will find valuable reviews of less-accessible bodies of literature.

Harry J. Ploehn
Dept. of Chemical Engineering
Texas A&M University
College Station, TX 77843

Protein Purification Process Engineering

Edited by R. G. Harrison, Marcel Dekker, New York, 1993, $155.

Protein separation operations are expensive. The expanding research and development resources committed to the rational design of protein purification trains by biotech companies reflect the need to minimize manufacturing costs as production scales increase and market pressures mount. Product discovery efforts often result in the development of a small-scale isolation procedure and associated physicochemical property databases for the target protein and major contaminating species. However, the direct scaling of bench isolation biochemistry to production levels won't cut it. The low-cost producer will have a purification process development team with expertise in bioseparation unit operations, comprising an understanding of the design and performance of large-scale protein separation techniques in relation to the properties of the product and impurities. *Protein Purification Process Engineering* should be among the resources consulted by those looking to develop or expand such an expertise.

In this book, Harrison assembled a team of experts, largely from the biotech industry, who discuss current design and scaleup issues for the major unit operations of bioseparations. Each chapter is devoted to a separate unit operation and is self-contained. The operations addressed include cell disruption, membrane filtration, liquid-liquid extraction, precipitation, conventional and affinity chromatography, and lyophilization, as well as associated analytical methods development and validation. The treatment level is introductory and the style is practical. The physical bases for the various techniques and the impact of key process parameters on performance are described qualitatively; detailed quantitative developments are eschewed. Several chapters are rich with examples of industrial applications. Those interested in delving deeper will find that the exhaustive referencing provides multiple entrees into the research literature for each of the operations discussed.

Clear standouts are the chapters on analytical considerations, membrane filtration, precipitation, and conventional chromatography. The chapter on analytical considerations gives a detailed listing of the various assay techniques for purity and bioactivity and describe how assay procedures are integrated with a process. Particularly useful is a discussion of the types of impurities typically encountered during downstream processing and how analytical methods may be tailored to follow their fate throughout a process. It also discusses transforming growth factor beta and recombinant tissue plasminogen activator case studies, as well as the need for assay validation; however, the actual mechanics of validation is vaguely treated just like the FDA has been. This chapter should be required reading for anyone contemplating the development of a commercial protein purification process.

On membrane filtration filtrate flux and solute rejection are discussed concisely with respect to concentration polarization and fouling phenomena as well as operating conditions. Numerous examples are focused on the various applications of microfiltration, from cell harvesting to virus removal. Affinity membrane systems are introduced briefly as an alternative to chromatographic separations.

The chapter on fractional precipitation describes the protein physical properties governing protein solubility and current colloidal solubility theories against an extensive background of the forces governing protein-protein interactions. It includes an encyclopedic catalog of who has precipitated what protein with what reagent. In this regard, the chapter can be overwhelming since so many examples and counterexamples of protein solubility behavior are provided that one is lead, rightly, to question solubility paradigms. General principles of precipitate formation in terms of nucleation, growth and aging phenomena and their relation to the design of precipitation equipment are treated pragmatically with several process flow diagrams. A must-read for protein precipitation operations.

An eminently practical guide to conventional chromatographic separations clearly explains various modes of chromatography, including the powerful, yet oft-neglected displacement mode. Simplified design equations are presented with key procedural and physical details such as column packing, clean-in-place, sterilization, depyrogenation, and inclusion of air traps. These considerations are usually absent from background descriptions of chromatography. Procedures for the identification of the rate-controlling mass-transfer step in a given chromatographic separation are discussed, with which process optimization efforts may be aimed in fruitful directions.

I had a mixed reaction to the chapters on cell breakage, liquid-liquid extraction and lyophilization. The discussion of cell disruption was largely anecdotal and circular in nature. Although important operating parameters for high-pressure homogenizers and bead mills are outlined, little information was given to aid a first-pass design. I would have welcomed a discussion of the close coupling between cell disruption and subsequent centrifugation or microfiltration operations for debris removal. The chapter on liquid-liquid extraction introduces practical process considerations within the context of several case studies, leading to a somewhat scattered presentation. However, in the hepatitis B surface antigen PEG/dextran extraction used as the primary example, key process information such as the temperature, pH and ionic strength were omitted. No discussion of available aqueous two-phase systems and diagrams was given, nor the theory of aqueous two-phase partitioning, the extensive efforts of Blanch's group at Berkeley and Hall's group at N.C. State. Although the author suggests that liquid-liquid extraction should find wider application in industry, it's not clear that this chapter is enabling. The topic of lyophilization is usually and unaccountably omitted from most books on protein separations. This book, however, discusses qualitative freezing, primary and secondary drying processes illustrated with phase diagrams and representative differential scanning calorimetry thermograms of the product. However, the apparently conscious avoidance of even simple mass and heat flux equations made the description of transport phenomena governing this process awkward. No reference at all

was made to the extensive modeling and performance optimization studies of Liapis at the University of Missouri, Rolla. Lyophilizer components and related temperature, pressure, and process monitoring techniques are presented, as well as a case study for the lyophilization of a generic protein formulation. Yet, information or references concerning the critical issues of the selection of excipients and their impact on freeze drying conditions were scant.

Solid introductory and affinity chromatography chapters compose the balance of the book. The first chapter provides an overview of purification process considerations including typical facilities and equipment, current good manufacturing practices (cGMP), teams, process synthesis, and scaleup. The number of topics necessarily limits the discussion to a cursory level. I particularly appreciated a brief introduction of cGMP and the associated literature. Regulatory issues often delimit the design and operating parameter space available to the purification process development team; for a team to proceed in ignorance of cGMP will result in costly delays in bringing product to the market. Process synthesis is of major importance, but this book adds little beyond a recounting of the heuristics that Asenjo of the University of Reading has enunciated; this topic would have been much more effective if expanded into a summary chapter.

The chapter on affinity chromatography offers an extensive listing of available affinity resins and modes of operation. The discussion is slanted toward the materials of Pharmacia Corporation, even though it is a major player in the field. The myriad potential affinity ligands including dyes, immobilized metals, antibodies, receptors, lectins, and thiophilic interactions as well as a directory to the available immobilization chemistries are provided with numerous examples of the use of affinity chromatography at the bench scale. The available descriptions of process-scale applications are, however, few in number. This perhaps reflects the reluctance of the biotech industry to use unconventional separations techniques or to divulge details of the successful application of such techniques. The discussions of the economics of using often expensive affinity resins, the development of both elution and eluent removal strategies, and the consequences of ligand leaching were limited. However, the incredible referencing more than compensates for any slight these issues may have been dealt in this chapter.

This book, as the genesis of a handbook in many respects on bioseparations unit operations provides a centralized resource for introductory material and a guide to the literature for all of the major unit operations of protein purification. As such, *Protein Purification Process Engineering* should be an important reference for those involved with protein purification process development. The book is touted as being useful for ". . . all upper-level undergraduate, graduate, and continuing-education courses in biochemical engineering, bioseparations, and biochemical separations," in addition to industrial practitioners. I suspect that this book will not gather any dust on the library shelf.

Todd M. Przybycien
Dept. of Chemical Engineering
University of South Carolina
Columbia, SC 29208

Biotreatment of Industrial and Hazardous Waste

Edited by Morris A. Levin and Michael A. Gealt, McGraw-Hill, New York, 1993, 331 pp.

This is yet another volume edited for a comprehensive overview of this high-profile subject area, but leaves chemical engineers anxious about the lack of useful technical details. At bare minimum, process analysis or design requires information on product characterization, stoichiometry, and kinetics. This book has none of this, and unfortunately that is keeping within the norm for literature in this field.

The editors intend the book to approach biodegradation of hazardous wastes in a holistic fashion. Issues of science, engineering and regulation are all addressed. Chapter authorship or titles do not reveal a clear indication of the balance among these issues, but they are not presented evenly. Chapters 2 and 3 deal with the microbiology of biodegradative activities as effected by augmentation of nutrient concentrations, molecular oxygen, redox potential, or moisture, or genetic manipulation. These chapters are rich in scientific content, but are not very well illustrated. Chapter 2 contains not a single table or figure, and the figures of Chapter 3 do not add much to the written communication.

Chapters 4 and 5 address engineering aspects of bioremediation. Chapter 4 is an encyclopedic treatment of bioreactor configurations and design relationships. Analysis of bioreactor performance is restricted to conventional wastewater applications and therefore is limited in its applicability to the subject of bioremediation. Chapter 5 strives to present conceptual foundations for modeling biodegradation of hazardous organic compounds by classifying microbial substrates as primary or secondary, and as electron donor or acceptor. The hazardous compound targeted for degradation may be any of these. Unfortunately, the quantitative aspects of the models are incomplete or unnecessarily complicated, and the utility of this framework is never illustrated by modeling actual data. Unsteady mass balances of perfectly mixed bioreactors are presented with no application in mind. Rate equations for electron acceptor and donor lack stoichiometric coefficients. Real biodegradation systems will contain multiple compounds, and each one may have multiple roles (electron acceptors, donors).

Chapter 6 presents the federal statutes and regulations which apply to the use of bioremediation. The chapter stands alone, and its relevance to the subjects covered in other chapters of the book is not described.

Chapter 7 describes experiences with *in-situ* bioremediation. Conditions which favor or disfavor this method of site renovation are described. Engineering aspects, such as oxygen or nutrient delivery, are illustrated through specific examples of petrochemical remediation. These examples and the 15 case studies summarized in tabular form provide the best backdrop for thinking about engineering details as can be found anywhere in the book.

Four of the remaining six chapters are further illustrations or examples of practices previously described. Chapter 8 on the use of altered microorganisms adds little new information to what has already been described in Chapter 3 and should have been incorporated into the previous chapter. Chapter 9 on the biotreatment of phthalate-laden soils near the site of a train derailment is a very interesting tale about a specific bioremediation success story wherein the effects of background environmental variables had to be carefully assessed to find the optimum remediation strategy. Chapter 10 deals with the anaerobic bioremediation of the nitroaromatic herbicide Dinoseb (2-sec-butyl-4,6-dinitrophenol). Biocatalytic pathways for degrading these compounds are reviewed, and bench- and pilot-scale data presented on the kinetics of degradation by anaerobic incuba-