Bioseparation Engineering

Progress in Biotechnology 16

BIOSEPARATION ENGINEERING

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Preface

Bioseparation process systems are most influential upon quality and quantity of the products of the bioindustry. The process systems, therefore, determine stability, safety and cost of the bioproduct.

The process systems consist of various unit operations like centrifugation, precipitation, chromatography, membrane separation, crystallization and so on. These operations are executed in special order according to the product. The characteristic features of this process system are summarized as follows:

1)The product is contained in the culture broth at a low concentration and in a complete mixture with many other compounds.

2) The product material is very sensitive to temperature, pressure, pH and to other operation variables.

3) The bioproduct is required to be of high quality in activity and / or in purity. The production is restricted by certain laws and regulations. Hereby, the bioseparation process should often be operated under mild condition in the clean room which is determined by regulation.

Recently, regulations in terms of environment protection became common in the world. Bioindustries in any countries can not neglect this social pressure. In other words, close to zero emission from factory is strongly requested particularly in advanced countries like U.S.A., the EC countries and Japan. Thus, bioseparation engineering of today is going to include downstream process engineering such as waste water, material and gas treatment. Taking into account this tendency in the world, we, bioseparation process engineers in Japan who gathered to the special research group on bioseparation engineering in the Society of Chemical Engineers, Japan planned the international conference on bioseparation engineering at Nikko, Japan during July 4th to 7th under the main theme of "Recovery and Recycle of Resources to Protect the Global Environment".

The scope of this book, is based on the conference, and deals with not only the recent advances in bioseparation engineering in a narrow sense but also the environmental engineering which includes waste water treatment and bioremediation The contributors of this book cover many disciplines, including such as chemical engineering, analytical chemistry, biochemistry, microbiology and so on.

This book contains the following 5 chapters:

Chapter 1: Adsorption, Chromatography, and Membrane Separations

Chapter 2: Refolding Processes for Protein

Chapter 3: Partitioning and Extraction

Chapter 4: Bioseparation Engineering for Global Environment

Chapter 5: Industrial Separation Processes and Validations

The editors do hope strongly that the content of this book would stimulate young engineers and scientists who will develop the bioseparation engineering further in 21C. and contribute to a world-wide attention to the global environment.

We thank Professors Sven-Olof Enfors (Royal Institute of Technology, Sweden), Michael R. Ladish (Purdue University, U.S.A.) and Rainer Rudolph (Martin-Luther University, Germany), for their valuable contribution to the review of manuscripts in this book.

The Editors, I. Endo, T. Nagamune, S. Katoh and T. Yonemoto

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Contents

Preface v

Acknowledgments vii

Chapter 1. Adsorption, Chromatography and Membrane Separations 1

Recent Advances in Membrane Technology that Could Improve Resource Recovery and Recycle : Fluid Mechanics, Surface Science and Bioaffinity 3
BELFORT, G.

Stabilization of Target Protein during Bioseparation 9
FENG, X.-L., JIN, Y.-T., SU, Z.-G.

Bioseparation of Natural Products 15
KEIM, C., LADISCH, M. R.

On-line Recovery of Large Molecules from Mixture Solution Using Semi-continuous Size Exclusion Chromatography 21
KIM, Y.-M., CHANG, W.-J., KOO, Y.-M.

Dye Adsorption by Activated Carbon in Centrifugal Field 25
LIN, C.-C., LIU, H.-S.

Formation and Structural Change of Cake during Crossflow Microfiltration of Microbial Cell Suspension Containing Fine Particles 29
TANAKA, T., YAMAGIWA, N., NAGANO, T., TANIGUCHI, M., NAKANISHI, K.

Continuous Separation of Ternary Mixture of Amino Acids Using Rotating Annular Chromatography with Partial Recycle of Effluent 35
FUKUMURA, T., BHANDARI, V. M., KITAKAWA, A., YONEMOTO, T.

Mass Transfer Characteristics of a Perfusion-type Gel Analyzed by Shallow Bed Method 41
TERASHIMA, M., NISHIMURA, S., YOSHIDA, H.

Fouling of Cheese Whey during Reverse Osmosis and Precipitation of Calcium Phosphate 47
TSUGE, H., TANAKA, Y., HISAMATSU, N.

Separation of Dead Cells from Culture Broth by Using Dielectrophoresis 53
HAKODA, M., SHIRAGAMI, N.

Microcalorimetric Studies of Interactions between Proteins and Hydrophobic Ligands in Hydrophobic Interaction Chromatography : Effects of Ligand Chain Length, Density, and the Amount of Bound Protein 59
LIN, F.-Y., CHEN, W.-Y., RUAAN, R.-C., HUANG, H.-M.

Membrane Phase Separation of Aqueous/Alcohol Biphase Mixture and Its Application for Enzyme Bioreactor 63
ISONO, Y., NAKAJIMA, M.

Microfabricated Structures for Bioseparation 69
HONG, J. W., HOSOKAWA, K., FUJII, T., SEKI, M., ENDO, I.

Production of a Human IgM-type Antibody and Preparation of Combinatorial Library by Recombinant *Saccharomyces cerevisiae* 75
SHIOMI, N., MURAO, K., KOGA, H., KATOH, S.

Dynamic Binding Performance of Large Biomolecules such as γ-globulin, Viruses and Virus-like Particles on Various Chromatographic Supports 81
YAMAMOTO, S., MIYAGAWA, E.

Effects of Swelling Pressure of Resin and Complex Formation with a Counter-ion on the Apparent Distribution Coefficient of a Saccharide onto a Cation-exchange Resin 87
ADACHI, S., MATSUNO, R.

Separation Behavior of Proteins near the Isoelectric Points in Electrostatic Interaction (Ion Exchange) Chromatography 93
ISHIHARA, T., YAMAMOTO, S.

Chapter 2. Refolding Processes for Protein 99

Large-scale Refolding of Therapeutic Proteins 101
HONDA, J., ANDOU, H., MANNEN, T., SUGIMOTO, S.

Novel Method for Continuous Refolding of Protein with High Efficiency 107
KATOH, S., KATOH, Y.

Novel Protein Refolding by Reversed Micelles 113
GOTO, M., FUJITA, T., SAKONO, M., FURUSAKI, S.

Development of Efficient Protein Refolding Systems Using Chaperonins 119
KOHDA, J., KONDO, A., TESHIMA, T., FUKUDA, H.

Monitoring Structural Changes of Proteins on Solid Phase Using Surface Plasmon Resonance Sensor 125
MANNEN, T., YAMAGUCHI, S., HONDA, J., SUGIMOTO, S., KITAYAMA, A., NAGAMUNE, T.

Chapter 3. Partitioning and Extraction 131

Recent Advances in Reversed Micellar Techniques for Bioseparation 133
FURUSAKI, S., ICHIKAWA, S., GOTO, M.

A Novel Method of Determining the Aggregation Behavior of Microemulsion Droplets 137
CHEN, W.-Y., KUO, C.-S., LIU, D.-Z.

Preparation of Temperature-sensitive Antibody Fragments 143
KAMIHIRA, M., IIJIMA, S.

Stability Enhancement of α-amylase by Supercritical Carbon Dioxide Pretreatment 149
LIU, H.-S., CHENG, Y.-C.

Behavior of Monodispersed Oil-in Water Microsphere Formation Using Microchannel Emulsification Technique 155
TONG, J., NAKAJIMA, M., NABETANI, H., KIKUCHI, Y.

Chapter 4. Bioseparation Engineering for Global Environment 161

Domestic Wastewater Treatment Using a Submerget Membrane Bioreactor 163
HUANG, X., GUI, P., QIAN, Y.

Biosorption of Heavy Metal Ion with Penicillin Biomass 169
TAN, T., CHENG, P.

Removal of Cadmium Ion by the Moss *Pholia flexuosa* 175
AZUMA, M., OBAYASHI, A., KONDOH, M., KAWASAKI, C.
IGARASHI, K., KATO, J., OOSHIMA, H.

The Effects of Additives on Hydrolysis of Cellulose with Water under Pressures 181
FUNAZUKURI, T., HIROTA, M., NAGATAKE, T., GOTO, M.

Removal of Volatile Organic Compounds from Waste Gas in Packed Column with Immobilized Activated Sludge Gel Beads 187
NAKAO, K., IBRAHIM, M. A., YASUDA, Y., FUKUNAGA, K.

Chapter 5. Industrial Separation Processes and Validations 193

Validation of Bioprocess Chromatography : Principles and Practices 195
LEE, E. K., AHN, S. J.

Column Qualification in Process Ion-exchange Chromatography 201
KALTENBRUNNER, O., WATLER, P. K. YAMAMOTO, S.

Characterization of Phage Encoded Lysis Proteins and Its Applications for Cell Disruption 207
TANJI, Y., HORI, K., YAMAMOTO, S., UNNO, H.

Recovery of Poly-β-hydroxybutyrate from Recombinant *Escherichia coli* by a Combined Biologi-chemical Method 213
YIN, J., XU, Y., YU, H.-M., ZHOU, P.-J., SHEN, Z.-Y.

Cleaning Liquid Consumption and Recycle of Biopharmaceutical Plant 219
MURAKAMI, S., HAGA, R., YAMAMOTO, S.

Index of authors 225

Chapter 1

Adsorption, Chromatography and Membrane Separations

Bioseparation Engineering
I. Endo, T. Nagamune, S. Katoh and T. Yonemoto (Editors)

Recent Advances in Membrane Technology that Could Improve Resource Recovery and Recycle: Fluid Mechanics, Surface Science and Bioaffinity

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THE GLOBAL ENVIRONMENT

With the realization that enormous investments will be needed to balance economic activity with environmental protection (called sustainable development), new clean and cleaning technologies will be needed to address the global conditions of excessive pollution, increasing population and increasing industrialization[1]. Of these technologies,

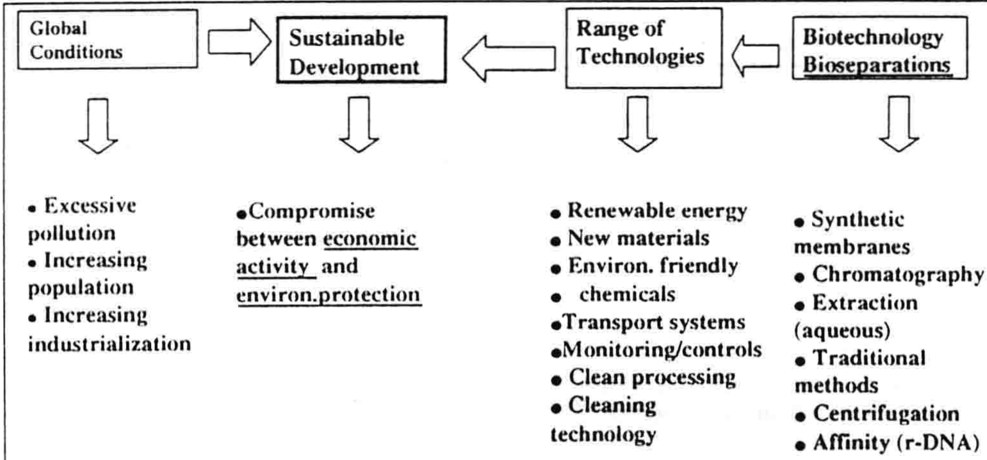

Fig. 1 Sustainable development how can synthetic membrane technology contribute? Ref: B. Zechendorf, TIBTECH 17, 219 (1999)

synthetic membrane technology is expected to be a major player. See Fig. 1. The reasons for this are that pressure-driven membrane processes are very attractive because they do not involve a phase change (i.e. do not consume large amounts of energy), are often linearly scalable, do not need additives, are relatively fast (rate governed rather than equilibrium processes), operate in a continuous mode, are easily combined with other processes, and are completely contained. However, several limitations, still need to be addressed. Foremost among these are concentration polarization (CP) and fouling phenomena which can substantially reduce performance through osmotic effects and solute adsorption and deposition on the membrane surface. These limitations can readily result in additional energy requirements and larger capital and maintenance costs, thus

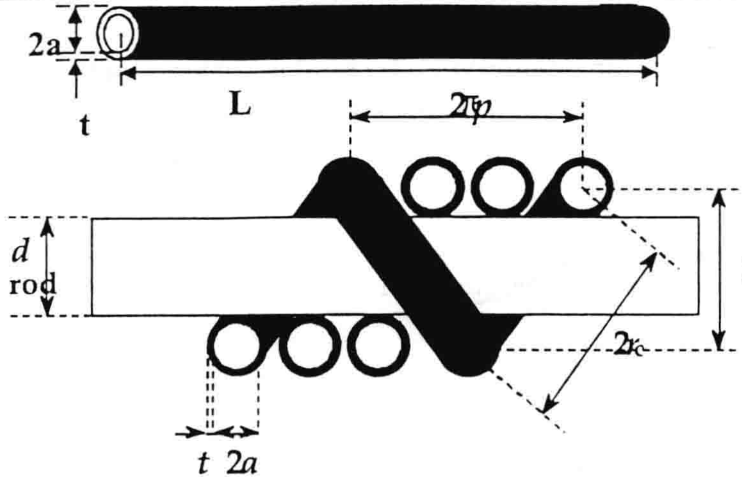

Fig. 2. Schematic of (a) the current commercial linear hollow fiber and (b) a new helical hollow fiber in which centrifugal vortices are produces that clean the membrane surface.

reducing the attractiveness of pressure-driven membrane technology. Various approaches have been used to address these limitations including improved methods of operation through the use of positive displacement pumps for controlling permeation rate and minimizing transmembrane pressure drop, operating at or below a prescribed protein wall concentration, modifying the chemical properties of the membrane surface so as to minimize solute-membrane interactions, and improved fluid mechanics and module design for reducing solute concentration and deposition on the membrane.

SYNTHETIC MEMBRANE TECHNOLOGY

The success of synthetic membrane technology has depended on a collaboration between polymer and surface scientists, who have developed suitable commercial membranes, and chemical engineers with an expertise in mass transfer and fluid mechanics, who have designed modules for optimizing filtration performance. Recent developments in these two fields will be emphasized in this presentation with a particular focus on biotechnology and the need to recover valuable proteins from solution. We argue that the need to understand the behavior of fluid flow with imposed centrifugal vortices can assist in designing optimal flow paths with minimal fouling and reduced concentration polarization[2,3]. Similarly, the connection between a fundamental understanding of intermolecular forces between a model protein, hen egg lysozyme (Lz), and polymeric membranes is crucial for the development of new and improved membrane materials for this application[4,5].

THREE FUNDAMENTAL EXAMPLES

An example of the first module design without moving parts especially designed for suspensions commonly found in the biotechnology industry is our new "Da Vinci" module. By flowing sufficiently fast along a helical twisted membrane tube, counter rotating Dean vortices can be used to clean the membrane surface and reduce particulate build-up and fouling. See Fig. 2.

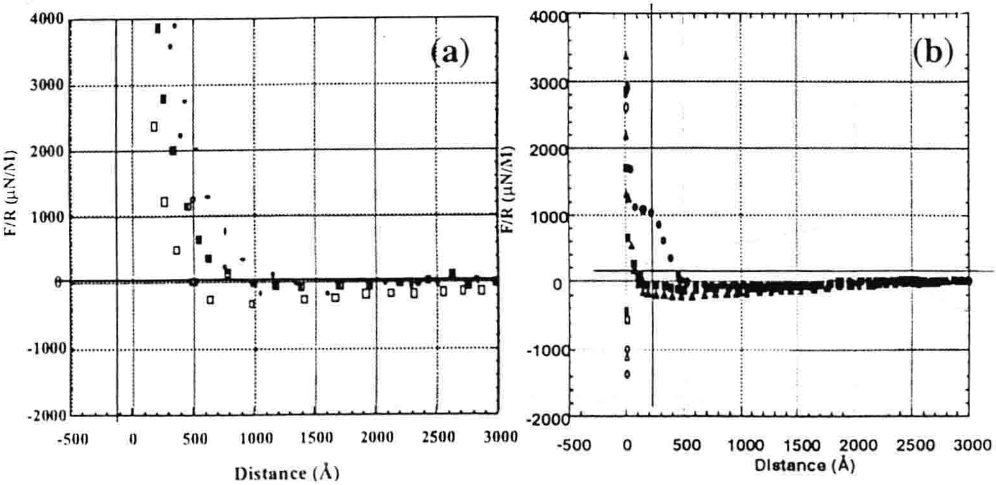

Fig. 3 Protein-membrane force-distance curves for (a) a HEMA-modified poly(ethersulfone) membrane and (b) an unmodified poly(ethersulfone) membrane. The feed contained hen egg white lysozyme at 50 mg/l and pH 6.6

Koehler et al.[4,5] have explained the well-known phenomenon of increased protein fouling on hydrophobic (poly(sulfone), PES) as compared to hydrophilic (hydroxyethyl methacrylate-PES, HEMA/PES) surfaces by using a correlation between adhesion forces and filtration fluxes. See Fig. 3. They show that protein-protein and protein-polymer interactions are about equally important for the PES-Lz system, while only protein-polymer interactions are important for the HEMA/PES-Lz system. How these two surfaces effect the stability of Lz and the fouling of membranes is discussed in detail.

Synthetic membranes or porous chromatographic beads are attractive binding media for affinity separations of fusion proteins because they overcome diffusion limitations with convective flow. In our final example, we illustrate the development and application of a new linker with controllable cleavage activity between the binding domain and the desired protein[6]. See Fig. 4. Both batch and column examples of the resulting one-step purification using temperature and pH excursions to induce cleavage are presented. Excellent purity and yield are obtained in all cases.

CONCLUSIONS

Cost estimates for achieving sustainable development up to the year 2,000 are about twice the current world pharmaceutical market of US$308 billion![7,8]. Whether the advanced societies will be prepared to spend such a large amount without a crisis or environmental disaster, is open to question. Clearly, attractive technologies that utilize less energy and produce less waste such as biotechnology and synthetic membrane processes are prime candidates for such an effort.

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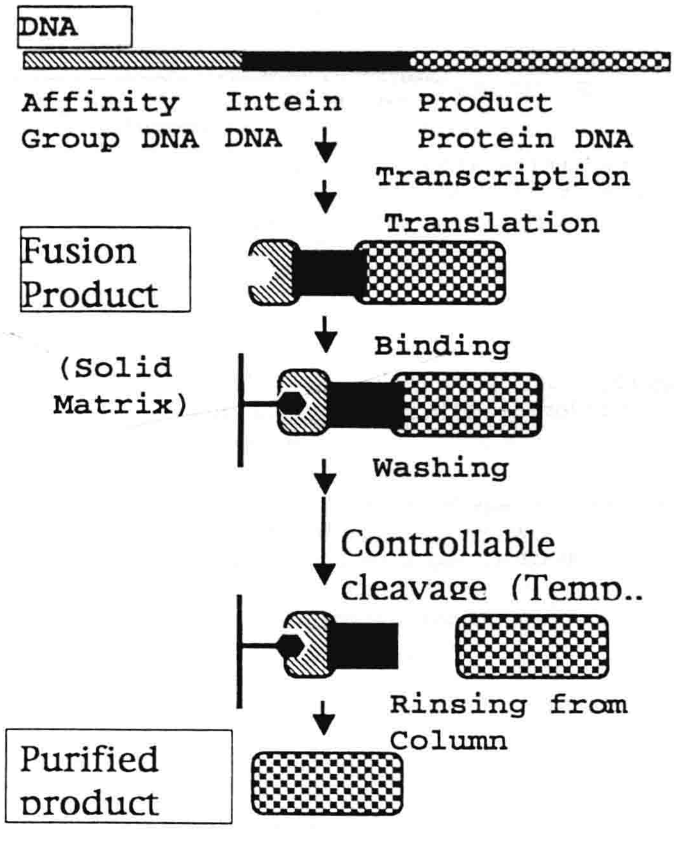

Fig. 5 Development of a new controllable linker for fusion protein

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