Recovery of Biological Products VI

Engineering Foundation Conference

Co-chairs

Stuart Builder, Genentech, Inc., USA
John Curling, John Curling Consulting AB, Uppsala, Sweden
Maria-Regina Kula, Heinrich-Heine University, Germany

Grand Hotel Victoria-Jungfrau, Interlaken, Switzerland
20-25 September, 1992

Sunday, 20 September

Keynote Address

Biotechnology in Europe: The Role of the Community
Mark F. Cantley, Consertation Unit on Biotechnology in Europe (CUBE), Directorate-General for Science, Research and Development, Commission of the European Communities, Belgium

Monday, 21 September

Protein Design, Folding, and Stability

Session chairs

Rainer Rudolph, Boehringer Mannheim GmbH, Germany
Dennis Lanfear, Amgen, Inc., USA

Protein Design and Mutant Acceptability
George E. Schulz, University of Freiburg, Germany

Mechanism of Protein Folding
Thomas Keifhaber, Stanford University Medical Center, USA

Folding and Oxidation of Recombinant Human Granulocyte Colony Stimulating Factor Produced in Escherichia coli
Hsieng S. Liu, Christi L. Clogston, Linda O. Narhi, Lee Anne Merewether, Wayne R. Pearl and Thomas Boone, Amgen, Inc., USA

Involvement of Molecular Chaperones in Protein Folding and Stabilization
Rainer Rudolph, Boehringer Mannheim GmbH, Germany.

Analytical and Preparative Electrophoretic Separations

Session chairs

Pier Giorgio Righetti, University of Milan, Italy
Barry Karger, Barnett Institute, Northeastern University, USA

Preparative Protein Purification in Multicompartment Electrolyzers with Isoelectric Membranes
Pier Giorgio Righetti, Michel Faupel, Elisabeth Wenisch, University of Milan, Italy

Protein Separation and Purification by Displacement Electrophoresis (Isotachopresis)
Wolfgang Thormann, Petr Gebauer and Jitka Caslavska, University of Bern, Switzerland

Protein and DNA Separations using High Performance Capillary Electrophoresis
Barry Karger, Barnett Institute, Northeastern University, USA

Process Design, Modelling, Economics and Development

Session chairs

Charles L. Cooney, Massachusetts Institute of Technology, USA
Scott M. Wheelwright, Chiron Corp., USA

New Tools for the Design, Optimization, Monitoring, Chiron Corp., USA and Control of Chromatographic Purification Processes
Noubar Afeyan and Scott Fulton, Perseptive Biosystems Inc., USA

Regulated Protein Secretion in Aid of Protein Purification
Gregory Stephanopoulos, Massachusetts Institute of Technology, USA

Rapid Process Development and Technology Transfer within the Corporation
Scott M. Wheelwright, Chiron Corp., USA

The Role of Process Simulation in the Design, Development and Economic Evaluation of Integrated Biochemical Processes
Demetri P. Petrides and Elpida S. Sapidou, New Jersey Institute of Technology, USA

Tuesday, 22 September

Integration of Protein Production, Recovery and Purification

Session chairs

Michael Hoare, University College London, UK
Isao Endo, Institute of Physical and Chemical Research, Japan

Strategies for Proteolysis Control in Production of Recombinant Proteins
Sven-Olof and Andres Veide, Royal Institute of Technology, Sweden

Production of Alkaline Protease by Aspergillus Oryzae Immobilized on Urethane Foam
Isao Endo, Institute of Physical and Chemical Research, Japan

Design of Integrated Downstream Processes using Simulation and Pilot Scale Verification Trials
Nigel J. Titchener-Hooker, University College London, UK
Inclusion Body Processing: Pain or Profit
David Thatcher, ICI Pharmaceuticals Ltd., UK

Adsorptive Separation and Non-Chromatographic Techniques

Session chairs
Edwin N. Lightfoot, Jr., University of Wisconsin, USA
Vipin Garg, DNX Corp., USA

Use of a Scaleable Hollow Fibre Membrane System for Purification of Monoclonal Antibodies
Alan Smith, Baxter Healthcare Corp. USA
Unconventional Adsorptive Separations
Gail Folena-Wasserman, MedImmune Inc., USA
The Potential of Novel Separation Techniques: The View from Academia
Edwin N. Lightfoot, Jr., University of Wisconsin, USA

Product Case Studies

Session chairs
Wolfgang Berthold, Dr. Karl Thomae GmbH, Germany
Stephen Drew, Merck & Co. Inc., USA

Large Scale Production of Recombinant Factor VIII from Mammalian Cell Culture: Purification Issues
Berthold Boedeker, Miles Inc., USA
Rational Approaches to Maximization of Capacity and Resolution in Large Scale Ion Exchange Chromatography
David Naveh, Centocor BV, The Netherlands

Production of Clinical Grade Recombinant Exotoxin A from E. coli
A. M. Tsai, J. B. Kaufman, J. Shiloach, M. Gallo and Susan Fass, National Institute of Health, USA

Recovery of High Purity Recombinant Platelet Factor 4
Peter Kellaris, Laura Dickert, Linda Rich, Jonathan Stenbuck, Michael Purple, T. Ransohoff, H. Levine and Jill A. Myers, Repligen Corp., USA

Wednesday, 23 September

Chromatography

Session chairs
Jan-Christer Janson, Pharmacia BioProcess Technology AB and Uppsala University, Sweden
Michael Ladisch, Purdue University, USA

Towards High-Column Performance at High-Flow Velocities
Shuichi Yamamoto, Yamaguchi University, Japan

Displacement, Zonal or Step Elution in the Chromatography of Proteins: Which way to go?
Milton T. Hearn, Monash University, Australia

Affinity Chromatography in Industrial Plasma Protein Fractionation
Rainer Eketorp, Pharmacia AB, Sweden

Automation of Chromatography Processes in a GMP Environment
V. Saxena and R. Kupferschmidt, Sepragen Corp., USA

Bioprocess Factors Affecting Glycoprotein Oligosaccharides

Session chairs
Raj B. Parekh, Oxford GlycoSystems Limited, UK
Charles F. Goochee, Stanford University, USA

Potential for Degradation of Glycoprotein Oligosaccharides by Extracellular Glycosidases
Michael Gramer and Charles F. Goochee, Stanford University, USA

Effect of Cell Culture Conditions on Glycosylation of Recombinant Proteins
Mary B. Slikowski, Jane V. Gunson, Edward T. Cox, Michael W. Spellman and Thomas G. Warner, Genentech, Inc., USA

Effects of Glycoprotein Oligosaccharides on Protein Purification
Larry Bush and Godfrey Amphlett, Genetics Institute, USA

Thursday, 24 September

Membrane Separations

Session chairs
Clark K. Colton, Massachusetts Institute of Technology, USA
John A. Howell, University of Bath, UK

High Performance Tangential Flow Filtration
Robert van Reis, E. M. Clapp, J. W. Caspari and S. E. Builder, Genentech, Inc., USA.

Virus Removal from Fluids by Membrane Filtration
Jerold Martin, Pall Corp., USA

Protein Fouling during Membrane Microfiltration
Andrew L. Zydney, University of Delaware, USA

The Performance of Microporous Hollow Fiber Immunoaffinity Membranes for Protein Purification
Clark K. Colton, Massachusetts Institute of Technology, USA

Raw Materials, End-Product and In-Process Analysis

Session chairs
William S. Hancock, Genentech Inc., USA
Inger Mollerup, Novo Nordisk A/S, Denmark

Separation, Isolation and Identification of Recombinant Proteins
K. R. Hejnaes, H. H. Soerensen and Benny S. Welinder, Novo Nordisk A/S, Denmark

Analytical Chemistry of rDNA Derived Proteins
William S. Hancock, Genentech Inc., USA

Metal Chelate Affinity Chromatography can Damage Recombinant Proteins during Purification
Paula J. Shadle, K. Silverness, J. Cundy, L. C. Wallace, T. Scheuermann, S. Joseph Tarkowski, Scios Inc., Mountain View, USA

Keynote Adress

The Uneasy Alliance: Biotechnology and the European Public
John Durant, Imperial College and The Science Museum, London, UK

Friday, 25 September

Regulatory and Approval Issues

Session chairs

Gail Sofer, Pharmacia Bioprocess Technology, USA
Florian Horaud, Institute Pasteur, France

Validation of Process Scale-Up. Purification of Therapeutic Grade Monoclonal Antibody from 100 L and 2,000 L Fermenters
Julian Bonnerjea and Chris Hill, Celltech Ltd, UK

Process Changes and their Impact on Product Quality
Rolf Werner, Dr. Karl Thomae GmbH, Germany

FDA Perspective on Multi-Product Facilities
Susan Vargo, Food and Drug Administration, USA

Virus safety of Biologicals
Florian Horaud, Institute Pasteur, France

Regulatory Panel Discussion

Session chair

Stuart E. Builder, Genentech, Inc., USA

Panelists
Susan Vargo, Center for Biologics Evaluation and Research, FDA, USA
Geoffrey Schild, National Institute of Biologics Standards and Control, UK
Florian Horaud, Institute Pasteur, France
Yuan-Yuan Chiu, FDA, USA

Poster Sessions

Session chair

Juan A. Asenjo, Biochemical Engineering Laboratories., University of Reading, UK

Early stages and process integration

Use of Decanters with very High Speed in Downstream Processing
Hans Axelsson, Theodore J. De Loggio, Jörgen Kolby Nielsen, Alfa-Laval Separation AB, Sweden

Integrated Recovery
Kirsten Biedermann, The Technical University of Denmark, Denmark

Recovery with Polyelectrolyte Precipitation of Glucoamylase from Yeast Supernatants
Heikki Heimo and Ilari Suominen, University of Turku, Finland

Perfusion Culture of Mammalian Cells in Stirred Tank Bioreactors Using a Novel Continuous Flow Centrifuge
Volker Jäger, Gesellschaft für Biotechnologische Forschung mbH, Germany

Large Scale Separation of Recombinant Proteins from Prokaryotic Cells Using Alginate Beads
P. Wikstrom, H. Sassenfeld, J.T. Dunn, Immunex Corporation, USA

Adsorptive processes

Recovery of a Recombinant Protein from an E. coli Homogenate Using Expanded Bed Adsorption
Ann-Kristin Barnfield Frej, Stefan Johansson and Rolf Hjorth, Pharmacia Bioprocess Technology AB, Sweden

Adsorptive Recovery of Proteins from Whole Broths Employing a Three-Phase Fluidized Bed Technique
M. R. Grote, Ursula B. Finger, M. -R. Kula, Heinrich-Heine University, Germany

Simultaneous Extraction and Adsorption from Whole Broth in a Fluidized Bed Column
Patrick Gailliot, James Corry, Barry Buckland and Robert Sitrin, Merck Research Laboratories, USA

Characterization of the Internal Flow Hydrodynamics in an Expanded Bed Adsorption Column
Annika Lindgren, Piotr Wnukowski, Pharmacia Bioprocess Technology, Sweden

Cross-flow Application of Affinity Membranes
Karl H. Kroner, Gesellschaft für Biotechnologische Forschung, Germany

Membrane Chromatography for Rapid and Automatic Concentration of Proteins from Cell Culture Supernatant in a High Flux System
Dirk Lütkemeyer and J. Lehmann, University of Bielefeld, Germany.

Affinity Purification of Biotin Tagged Proteins
F. Carl Haase, Dean E. Cress, Lisa Fellmeth, Kathleen Fletcher, Rohm & Haas Company, USA

Microporous Poly(caprolactum) Hollow Fibers for Therapeutic Affinity Adsorption
Elias Klein, Amy Mosley, George Harding, University Of Louisville School of Medicine, USA

A New Super Bioabsorbent
Ryuichiro Kurane, Yasuhiro Nohata and Noboru Tomizuka, Fermentation Research Institute, Agency of Industrial Science and Technology, MITI, Japan

New Thiophilic Ligands for the One-step Purification of Antibodies
Alexander Schwarz, Fortuna Cohen and Meir Wilchek, Weizmann Institute of Science, Israel

Chromatography

Functional, Chemical and Physical Characterization of a new BioProcess Medium for Hydrophobic Interaction Chromatography- Butyl Sepharose® 4 Fast Flow
Anna Berggrund, I. Drevin, K.-G. Knuutila, J. Wardhammar and B.-L. Johansson, Pharmacia Bioprocess Technology AB, Sweden

Stereochemical Optimisation of Affinity Adsorbents
Kami Beyzavi and Frank Roberts, Bioprocessing Limited, UK

Theoretical and Experimental Study of the Use of Polymeric Reversed Phase Media for the Purification of Pharmaceuticals
E. Firouztale, Peter G. Cartier, J. J. Maikner, K. C. Deissler, J. T. McNulty, and A. P. Scott, Rohm and Haas Company, USA

Purification of Recombinant Proteins by Immunoaffinity
Shigeo Katoh, Masaaki Terashima and Elizo Sada, Kyoto University, Japan

Continuous Stationary Phases for Chromatographic Filtration of Proteins
Michael R. Ladisch, Ajoy Velayudhan, Richard Hendrickson and Karen Kohlmann, Purdue University, USA

Affinity Chromatography of Biopolymers on Immunosorbents
Levon A. Nakhapetyan, L. I. Motina, F. Svec, J. Hradil, V. P. Kuznetsov, Institute of Biotechnology, Russia

Towards Prediction of Chromatographic Retention: Molecular Modelling of Protein Adsorption
C.M. Roth and Abraham M. Lenhoff, University of Delaware, USA

Influence of Column Design on Chromatographic Performance of Ion-exchange Media
Peter R. Levison, Stephen E. Badger, David W. Toome, Edward T. Butts, Mark L. Koscielny and Linda Lane, Whatman Specialty Products Division, UK

A New Hydrophobic BioProcess Medium with Defined Performance Characteristics
Tua Lindblom, A. Berggrund, I. Drevin, K.-G. Knuttila and J. Wardhammar, Pharmacia BioProcess Technology AB, Sweden

Separation and Quantitation of Monoclonal Antibody Aggregates by Asymmetrical flow Field-flow Fractionation. Comparison to Gel Permeation Chromatography
Anne Litzen, Joachim K. Walter, Heike Krischollek, and Karl-Gustav Wahlund, University of Lund, Sweden

Metal Chelate Affinity Chromatography can Damage Recombinant Proteins during Purification
Paula J. Shadle, Kate Silverness, John Cundy, Lynn C. Wallace, Trina Scheuermann, S. Joseph Tarnowski, Scios Inc., USA

Modelling and Experimental Verification of Gradient Elution Chromatography
Yung-Huoy Truei, Tingyue Gu, Gow-Jen Tsai and George Tsao, Purdue University USA

Modelling of MulticOmponent Diffusion in Protein Separations by Chromatography
Pieter Vonk, Hans Wesslingh, University of Groningen, The Netherlands

Separation of Amino Acids on Strong Acidic Cation Exchanger Resins with Displacement Chromatography
Marcus Barwe and Rolf Wichmann, Universität Dortmund, Germany

Bioprocess Monitoring Using Ultrafast HPLC
Kenneth C. Olson and Richard Gehant, Genentech Inc., USA

Membrane processes

Recovery of Penicillin Using Membrane Extraction
Y. S. Park and H. N Chang, BioProcess Engineering Research Center, KAIST, Korea

Electrokinetic Transport of Amino Acids Through a Cation Exchange Membrane
Kisay Lee and Juan Hong, University of California, USA

Local flux and Wall Cocentrations in Unsteady Membrane Filtration
John A. Howell, Ian Wang and Robert Field, University of Bath, UK

Air Slugs Entrapped Cross-flow Filtration of Microbial Suspensions
Cheng-Kang Lee, and Y.-H. Ju, National Taiwan Institute of Technology, China

The Application of Ultrafiltration Membrane for the Purification of Microbial Peroxidase
Masamitsu Takaya, Motoo Sumida, Hideo Tsujimura, Nobuya Matsumoto, Suntory Ltd., Japan

Change of State of Solute for Improving Characteristics of Ultrafiltration.
Hideharu Yagi, Kansai University, Japan

Virus Removal and Inactivation

Size Exclusion Removal of Model Mammalian Viruses Using a Unique Membrane System
Anthony J. Dileo, Dominick A. Vacante, Edward F. Deane, Millipore Corporation, USA

Virus Inactivation at Low pH With a Variety of Organic Compounds
Milton B. Dobkin, Michael A. Shearer, and George B. Dove, Cutter Biological, Miles, Inc., USA

Virus Removal and Inactivation- Concept and Data for Process Validation of Downstream Processing
Joachim Walter, Wolfgang Berthold, William Werz, Dr. Karl Thomae GmbH, Germany

Reverse micelles and two-phase systems

Recovery of Proteins from Reversed Micelles Using Novel Ion-exchange Material
Julian B. Chaudhuri, Gordana Spirovska and Fang Ming, University of Bath, UK

Selective Separation and Concentration of Biochemicals Using Emulsion Liquid Membranes
Julian B. Chaudhuri, Paul Pickering and Leo Pyle, University of Bath, UK

New Water-soluble Polymers for Separation of Biological Molecules by Two-phase Aqueous Systems
Edward M. Davis, Kathryn M. Matera Pramod Z. Rao and Robert W. Coughlin, University of Connecticut, USA

Recovery Conditions for Living Enzymes in Reverse Micellar Extraction Processes
Kazumitsu Naoe, Masanao Imai and Masaru Shimizu, The Tokyo Univeristy of Agriculture & Technology, Japan

Protein Purification in Aqueous Two-phase Systems Containing Solid Phase Adsorbents
Ryoichi Kuboi, Tetsuya Ohta, Wei-Hong Wang and Isao Komasawa, Osaka University, Japan

Electrophoresis

Plasma Protein Fractionation by Recycling Isotachophoresis
Jitka Caslavska, Petr Gebauer and Wolfgang Thormann, University of Bern, Switzerland

Two-phase Electrophoresis for Protein Recovery
William M. Clark, Michael A. Marando and Charles W. Theos, Worcester Polytechnic Institute, USA

A New Method of Scaling up Free Flow Electrophoresis
Prabha Painuly, Mark C. Roman and Paul S. Schauer, Separations Technology, Division of EM Industries, USA

Protein folding

Refolding of Cytochrome b562 and its Single Disulfide Mutant
Yukio Kobayashi, T. Nagamune, H. Sasabe and N. Saito, The Institute of Physical & Chemical Research, Japan

Effect of Glycosylation on the In Vitro Refolding of Human Interleukin 4 Receptor
Hassan Madani, T. Granston, J. McGourty, K. Brasher, P. Baum, M. Deeley, J. Thomas, L. Clark, H. Sassenfeld, Immunex Corp., USA

Thermal Stability of Cytochrome b562 and its Mutants from Site-Directed Mutations
Teruyuki Nagamune, K. H. Kim, K. Kobayashi, Y. Kobayashi, H. Uedaira, H. Morii, I. Endo and H. Sasabe, The Institute of Physical & Chemical Research, Japan

Thermostabilization of the Clostridial Celloxylanase and Endoglucanase by Gene Modification
Kunio Ohmiya, Masayuki Fukumura, Kazuo Sakka, Shuichi Karita and Kyo Shimada, Applied Microbiology, Mie University, Japan

Product case studies

Production of Novel Analogues of Insulin-like Growth factor-II as Fusion Proteins Expressed in Escherichia coli
Geffrey L. Francis, S. Milner, F. J. Ballard, S. Aplin, and J. Wallace, Cooperative Research Centre for Tissue Growth & Repair, Australia

Integrated Process for Monoclonal Antibody Production and Purification
Hugues Graf, J. N. Rabaud, J. M. Egly, Setric Genie Industriel, France

Process Development for Production of a Yeast-Derived HBsAg Vaccine Carrying the pre-S2 Region
Makoto Kobayashi, Tsuneo Asano, Yukio Fujisawa, Koichi Kato and Atsushi Kakinuma, Takeda Chemical Industries, Ltd. Japan

Downstream Processing of a Labile Live Virus Varicella Vaccine: Challenges in Modifying existing Process
Douglas Seifert, Frank Leu, Scott Reynolds, Merck & Co., USA

Mouse-human Chimeric Antibody Fragments Secreted from E. coli: Purification and Recovery for Therapeutic Use
Joachim L. Weickmann, Xoma Corporation, USA

Historical Perspective on Human Growth Hormone Processing

Kenneth C. Olson, Genentech Inc., USA

Miscellaneous Topics

Foam separation of two component protein mixtures
Sarah M. Ball and Juliet Varley, University of Reading, UK

The rational Design of Large Scale Protein Separation Sequences: Development of an Expert System
Eduardo W. Leser and J. A. Asenjo, University of Reading, UK

Recovery of PHB from Gram-negative Alcaligenes eutrophus and Alcaligenes latus Using Fatty Acyl Carnitine
Kyung Mi Lee, Yong Kuen Chang, BioProcess Engineering Research Center, KAIST, Korea

Extractive Synthesis of Oligopeptide Accompanied with Optical Resolution
Makoto Hirata and Akira Hirata, Waseda University, Japan

Selective Release of Enzymes and Protein from Yeast by an Agitator Bead Mill
Kanji Matsumoto, Yokohama National University, Japan

Phage Display of Protein A for Isolation of Novel Forms
Richard Willson, Baby Djojonegoro and Michael Benedik, University of Houston, USA

Extraction and Purification of Trehalose from Baker's Yeast
Yumi Yoshikawa, and Kanji Matsumoto, Yokohama National University, Japan

Study on the Recovery of L-malic Acid
Lian-wan Yang and Jian-Xin Chen, Institute of Microbiology, Academia Sinica, China