

Recovery of Biological Products V

Engineering Foundation Conference

Co-chairs

Clark K. Colton, Massachusetts Institute of Technology, USA

Louis Fries, Collagen Corp., USA

Arnold Hershman, Monsanto Company, USA

Maria-Regina Kula, Heinrich-Heine University, Germany

Don CeSar Registry Resort, St. Petersburg Beach, Florida, USA

13-18 May, 1990

Sunday, 13 May

Keynote Address

The Biotech Revolution - Status report 1990

George Rathmann, Amgen Corp., USA

Monday, 14 May

Techniques to Enhance Purification and Refolding Properties of Recombinant DNA Proteins

Session chairs

Steve Brewer, Monsanto Co, USA

Mathias Uhlen, Royal Institute of Technology, Sweden

Facile Metal-affinity Purifications of Recombinant Proteins which Contain Strong Metal-binding Sites

Barry Haymore, Monsanto Company, USA

Enhanced Selectivity in Bulk Separations Using Charged-peptide Fusions

Ilari Suominen, Craig Forney, John Luther, Mark Niederauer and Charles Glantz, Iowa State University, USA

An Approach to Achieving High Protein Refolding Yields

Steven M. Vicik, Randall W. Swartz and Eliana De Bernardez-Clark, Tufts University, USA

Oxidation and Naturation of Recombinant Bovine Somatotropin

S. Bradley Storrs and Todd M. Przybycien, Monsanto Company, USA

A Rational Approach to Protein Refolding using Quasi-elastic Light Scattering

H. M. Sassenfeld, R. Klinke, H. Madani and M. Deeley, Immunex, USA

Gene Fusions to Facilitate Protein Recovery and Folding

Björn Nilsson, Thomas Moks and Mathias Uhlen, Royal Institute of Technology, Sweden

Separations of Commercially Relevant Proteins

Session chairs

Dennis Fenton, Amgen Corp., USA

Robert Herschberg, Genentech, Inc., USA

Preparative Immunoaffinity Chromatographic Purification of Recombinant Factor VIII

G.Mitra and P.Ng, Cutter Biological, Miles Pharmaceutical, Inc., USA

Development of a Process for Commercial Production of Bovine and Porcine Somatotropins

G.L. Bachman, D. S. Inloes, and J. R. Ryland, Monsanto Company, USA

Relationship of Ultrafiltration and Downstream Processing in the Production of Recombinant Human Erythropoietin

Thomas W. Strickland, Kenneth H. Aoki, and David Bengston, Amgen, Inc., USA

Fluid Dynamic Optimisation of Tangential Flow Filtration for Mammalian Cell-Protein Separation

Robbie Van Reis and Stuart E. Builder, Genentech, Inc., and Lee C. Leonard, Millipore Corp., USA

Tuesday, 15 May

Solid/Liquid Separations

Session chairs

Charles Glatz, Iowa State University, USA

Michael Hoare, University College of London, UK

Biospecific Precipitation of Enzymes

E.A. Miranda, P. Pan, S. T. Summerfeldt, and K. A. Berglund, Michigan Biotechnology Institute, USA

Continuous Precipitation of an Industrial Enzyme

R. S. Hamstra, Royal Gist-Brocades, The Netherlands

The Monitoring and Control of Protein Purification Processes Application to Fractional Precipitation

M. Niktari, S. Chard, M. T. Flanagan, and M. Hoare, University College London, and J. Molloy, Fisons Scientific Instruments Ltd., UK

Recovery and Characterisation of Inclusion Bodies of Bovine Somatotropin

Steve Baladan, J. F. Kane, J. B. Striebel, and G. Bogosian, Monsanto Company, Inc., USA

Fluidized Bed Adsorption for Whole Broth Extraction

F.P. Gailliot, C. Gleason, J. J. Wilson, and J. Zwarick, Merck & Company, Inc., USA

Wednesday, 16 May

Membrane Separations

Session chairs

Robert Bratzler, Sepracor, Inc., USA
Andrew L. Zydney, University of Delaware, USA

An Improved Ultrafiltration System Capable of High Resolution Removal of Viruses from Protein Solutions

Anthony J. DiLeo, Anthony E. Allegranza, Jr., Millipore Corp., and Stuart E. Builder, Genentech, Inc., USA

Membrane-Based Affinity Chromatography

Stephen E. Zale, O. Dile Holton III and Vipin K. Garg, Sepracor, Inc., USA

Effect of Protein Deposition on Flux and Sieving during Ultrafiltration and Microfiltration

Andrew L. Zydney, University of Delaware, USA

Cross-Flow Microfiltration of Biosuspensions - Tangential Flow versus Shear Filtration

K. H. Kroner and H. Hustedt, Gesellschaft für Biotechnologische Forschung, USA

Ion Exchange Hollow Fiber Systems for Protein Purification

K. H. Milby, D. E. Steinmeyer, and M. K. Tripodi, Kinetek Systems Inc., USA

Isoporous Membranes and Supports for the Immobilization of Macromolecules and Langmuir Blodgett Films from Two-Dimensional Protein Crystals

Uwe B. Sleytr, Margit Sara, University of Bodenkultur, Austria

Thursday, 17 May

Adsorption and Chromatography.

Session chairs

Per Hedman, Pharmacia LKB Biotechnology AB, Sweden
Robert Sitrin, Merck Sharp & Dohme Research Laboratories, USA

The Assessment of Chromatographic Procedures for Protein Purification

M. Hoare, University College London, UK

Perfusion Chromatography

Fred Regnier, Purdue University, and Noubar Afeyan, PerSeptive Biosystems, Inc., USA

Production Scale Purification of Biosynthetic Human Insulin using High Performance Liquid Chromatography

Eugene P. Kroeff, Rebecca A. Owens, Eddie L. Campbell, Ronald D. Johnson, and Harlene I. Marks, Eli Lilly and Company, USA

Industrial-Scale Ion Exchange Chromatography for Purification of Proteins

Thomas A. Keuer and James R. Ryland, Monsanto Company, USA

Validation of Chromatographic Purification Methods used for the Manufacture of Therapeutic Proteins

Christopher R. Hill, Celltech Ltd., UK

Protein Adsorption in Liquid Fluidized Beds

Howard A. Chase and N. M. Draeger, University of Cambridge, UK

Process Chromatography - Where do we go from here? Discussion

Workshop Session

Process Changes - Insuring Safety and Efficacy during Development and Manufacturing of Biological Products or How to make (or not make) Process Changes without Shooting Yourself in the Foot

Session chairs

Michael L. King, Merck Sharp & Dohme Research Laboratories, USA
Kathryn C. Zoon, Center for Biologics Evaluation and Research, USA

Introduction

Michael L. King, Merck Sharp & Dohme Research Laboratories, USA

Scientific Issues Regarding Process Changes

Kathryn C. Zoon, Center for Biologics Evaluation and Research, FDA, and Michael L. King, Merck Sharp & Dohme Research Laboratories, USA

Environmental Effects on Protein Glycosylation

C.F. Goochee, Thomas Monica and Timothy J. Hahn, Stanford University, USA

Case History - Agency Perspective (EPO)

Ken Seamon, Division of Chemistry and Biophysics, FDA, USA

Case History - Industrial Perspective (TPA)

Stuart Builder, Genentech, Inc., USA

Panel Discussion

Michael Beatrice, Division of Product Certification, FDA, USA
Michael L. King, Merck Sharp & Dohme Research Laboratories, USA
Kathryn C. Zoon, Center for Biologics Evaluation and Research, USA

Friday, 18 May

Extraction, Affinity, and Packed Bed Processes

Session chairs

T. Alan Hatton, Massachusetts Institute of Technology, USA

M.-R. Kula, Heinrich-Heine University, Germany

Systematic Studies of Protein Partitioning in Polyethyleneglycol/Dextran/Water Systems

D. Forcinti, C. K. Hall, North Carolina State University, Raleigh, NC, and M.-R. Kula, Heinrich-Heine University, Germany

Purification of Calf Chymosin Free *Aspergillus Niger* var. *Awamori* using Two-Phase Liquid-Liquid Extraction

Kirk Hayenga, Matt Murphy, Ray Arnold, Jeff Lorch and Henry Heinsohn, Genencor, Inc., USA

Microstructured Solvents for Recovery of Biologicals Solvent Extraction

T. Alan Hatton, Massachusetts Institute of Technology, USA

Diffusion of Proteins Inside Macroporous Resins: Visualization and Mathematical Studies

Edward Firouztale, Heidi Wald, Amie Scott, Marybeth Wall, Rohm and Haas Company, and Jarrett Burton, Lehigh University, USA

Displacement Effects in Preparative and Large Scale Chromatography

Alois Jungbauer, Karola Uhl, and Christa Tauer, Institute of Applied Microbiology, Austria

Affinity Interactions in Free Solution as an Initial Step in Down Stream Processing

Bo Matthiasson, University of Lund, Sweden

Poster Sessions

Session chair

M.-R. Kula, Heinrich-Heine University, Germany

Perfusion Chromatography: The Next Generation in Biomolecule Separations

Noubar Afeyan, Scott Fulton, Neal Gordon, Laszlo Varady Perseptive Biosystems, Inc., and Fred Regnier, Purdue University, USA

Continuous Fermentation of *Nitrosomonas* Spec. with Concentration by Centrifugal Separation

Angela Ante, Institute of Biotechnology, Nuclear Research Centre Julich GmbH, Rolf Wichmann, Universität Dortmund, Germany

Aqueous Phase Systems: New Applications in the Extraction and Purification of Proteins

Michael J. Boland, Biochemical Processing Centre, New Zealand, Jens Paulsen, Gesellschaft für Biotechnologische Forschung mbH, Germany

Liquid/Liquid Extraction in a Novel Multistage Extractor: Batchwise Purification of a Synthetic Undecapeptide

Max Brenner, University of Basel, Switzerland, John L. Hughes, David Stevenson, Martin Edelstein, and Ken Tubman, Smith Kline Beecham Pharmaceuticals, USA

Fast Recovery of Pyruvate-Decarboxylase by Membrane Processes

K-G. Briefs and M.-R. Kula, Heinrich-Heine University, Germany

Cross-Flow Electrofiltration of Microbial Suspensions

A. Brors, K. H. Kroner, and H. Hustedt, Gesellschaft für Biotechnologische Forschung, Germany

The Role of Porous Polymeric Reversed Phase Packings in the Large Scale Purification of Peptides, Proteins and Antibiotics

P. G. Cartier, K. C. Deissler, J. J. Maikner, Rohm and Haas Research Laboratory, W.G. Schwartz, TosoHaas, USA

On-Line Detection of Molecular Size and Purity

Paul Claes, Paul Griew, Penny Vardy, Sue Fowell and Andrew Kenney, Oros Instruments Ltd., UK

Electropartitioning: Two-Phase Electrophoresis for Protein Recovery

William M. Clark, Worcester Polytechnic Institute, USA

Solid-Liquid Separation Using Rotary Annular Filtration Technology

Rajiv Datar, Pall Corporation, USA

Endotoxin Elimination from Immunoaffinity Media by Acticlean™ Solution

Peter Grandics, Susan Szathmary and Toby O'Neill, Sterogene Bioseparations, Inc., USA

The Integration of Cell Culture/Fermentation with Continuous, On-Line, Aseptic Product Recovery

Peter Grandics, Susan Szathmary, Zsolt Szathmary and Toby O'Neill, Sterogene Bioseparations, Inc., USA

Ultrafiltration Studies of Recombinant Porcine Somatotropin-Producing *Escherichia coli* and of Inclusion Bodies

J.-F. P. Hamel, U.B. Holeschovsky and C.L. Cooney, Massachusetts Institute of Technology, B.R. Breslau, Romicon, Inc., Separation Technologies, USA, M. Snoswell, Bresatec Ltd., Australia

Bacterial Cell Rupture by High Pressure

Homogenisation: The Influence of the Cell Parameters
Susan T. Harrison and Howard A. Chase, University of Cambridge, UK, and John S. Dennis, UK

Impact of Mass Transfer Resistances of Proteins in Ion Exchange and Dye Affinity Chromatography During Process Scaleup

Milton T. W. Hearn and Anna Johnston, Monash University, Australia

Adsorption of Proteins onto Ion-Exchange Gels

E.A. James, D. D. Do, and M. Johns, University of Queensland, Australia

Stability Assessment of Monoclonal Antibodies

Wim Jiskott and Dean J. A. Crommelin, University of Utrecht, The Netherlands, E. Coen Beuvery, National Institute of Public Health and Environmental Protection (RIVM), The Netherlands

Recovery of Hyaluronic Acid by Ultrafiltration

M. R. Johns, University of Queensland, and D. E. McManus, Qlone, Ltd., Australia

Rapid Quantitation of Contaminants During Purification of Biopharmaceuticals

Paul D. Johnston, Robert S. King, and Vartan Ghazrossian, Molecular Devices Corporation, Catherine Lucas, Genentech, Inc. USA

Release of Intracellular Bioproducts by Means of High Pressure Homogenization or Counter Current Impingement Jets: A Comparison

P. Kraemer, A. Bomberg, and B. Godelmann, Dechema-Institut, Germany

Recovery and Purification of Proteins by Means of Dye-Ligand Membranes

S. Krause and K.H. Kroner, Gesellschaft für Biotechnologische Forschung, mbH, Germany

A Sterilizable Centrifugal Separator System for Aseptic and Contained Cell Harvest and Recycle
Göran Krook and Hans Axelsson, Alfa-Laval Separation AB, Sweden**Crystallization of L-Cystine Harmonized to Enzyme Reaction**

Satoshi Kumon, Ajinomoto Co., Ltd., Japan

Factors Affecting the Removal of Nucleic Acid from Hybridoma Cell Culture Fluid

Howard L. Levine, Xoma Corporation, USA

Seeking Alternatives to Differential Chromatography

E. N. Lightfoot, University of Wisconsin, USA

The Effect of Temperature and Pressure on the Supercritical Carbon Dioxide Extraction of Biosurfactants

A. Margaritis, The University of Western Ontario, Canada

Factors Affecting the Kinetics of Solvent Extraction of Cyclosporin A from the Fungus Beauveria Nivea

A. Margaritis, The University of Western Ontario, Canada

Affinity Sensors for Monitoring and Control of Downstream Processes

Bo Mattiasson and Håkan Håkanson, University of Lund, Sweden

Azalactone-Functional Polymer Beads, Supports for Affinity Separations

D.S. Milbrath, D. M. Stauffer, M. M. Walker, P. L. Coleman, J. K. Rasmussen, S. M. Heilmann, and L. R. Krepski, 3M Center, USA

Isolation of Virus-Safe Transferrin by Ion Exchange Chromatography and its Application for the Production of Monoclonal Antibodies in Defined Culture Media

W. Moeller, D. Rudnick, U. Bethke, N. Kothe, and M. Kloft, Biotest Pharma GmbH, Germany

A Novel Role for Ion-Exchange Chromatography in the Large Scale Production of a High Quality Human Albumin Product from Cohn Fraction V

J. E. More, J. Rott, and G. E. Chapman, Blood Products Laboratory, UK

Continuous Separation of Proteins by Free-Flow Zone Electrophoresis

Sunil Nath, Horst Schutte, Helmut Hustedt and Wolf-Dieter Deckwer, Gesellschaft für Biotechnologische Forschung mbH, Germany

Protein Separation and Recovery from Cell Lysate Mixtures Using a Magnetically Stabilized Fluidized Bed

L.Nixon, C. A. Koval and R. D. Noble, University of Colorado and G. Slaff, Synergen, Inc., USA

Cell Disruption in Pilot Scale

H.Ojamo and M. Siika-aho, Technical Research Centre of Finland, Finland

Adsorptive Recovery of Intracellular Enzymes Using Expanded Beds

N. Papamichael and H. Hustedt, Gesellschaft für Biotechnologische Forschung, Germany

A Method for the Recovery of Monoclonal Antibodies (MAb) from a Hollow-Fiber Bioreactor System

Torbjörn Petterson, Ingemar Daniels, Pharmacia LKB Biotechnology AB, Lena Söderström and Gunnilla Westin, Pharmacia Diagnostics AB, Sweden

Continuous Perfusion of Animal Cell Cultures

M.C. Philippi, C. A. M. van der Valden-de Grott, and E. C. Beuvery, National Institute of Public Health and Environmental Protection (RIVM), The Netherlands

Radial Flow Chromatography - A New Approach to Rapid Large-Scale Separations

Vinit Saxena, Sepragen Corporation, USA

An Automated System for Optimization of High Performance Process Chromatography

Robert D. Sitrin and Peter A. DePhillips, Merck Sharp and Dohme Research Laboratories, USA

An Integrated Process of Cell Disruption and Aqueous Two-Phase Extraction

Zhiguo Su, Dalian University of Technology, China

Sample Displacement Mode Chromatography - A Tool for Final Protein Purification

K. Veeraragavan, A. Bernier and E. Braendli, Biotechnology Research Institute, Canada

Affinity Partitioning of Proteins

A. Walsdorf, L. Elling, and M. -R. Kula, Heinrich-Heine University, Germany

Design and Application of Affinity Adsorbents for Antibiotic Production

Henry Y. Wang, The University of Michigan, USA

A Development of the Liquid-Liquid Two Phase Extraction for Enzyme Purification

Zhenping Xiong, Shanghai Institute of Pharmaceutical Industry, China, Zuning Bian, United Biomedical, Inc., USA

Separation of a Glucose-Fructose Mixture and Amino Acid Mixtures by Using an Intermittent Moving Bed Adsorber

Muneki Yama, Yoshiharu Okamoto, Katsumichi Osaki, and Takeshi Akao, Kikkoman Corporation, Japan

Separation of Proteins by Preparative Scale Continuous Flow Electrophoresis - Theoretical and Experimental Approach

Toshikuno Yonemoto, Shuang Ning Zheng, and Teiriki Tadaki, Tohoku University, Japan

