Development Of A Purification Platform Process For A

The second edition of Comprehensive Organic Synthesis—winner of the 2015 PROSE Award for Multivolume Reference/Science from the Association of American Publishers—builds upon the highly respected first edition in drawing together the new common themes that underlie the many disparate areas of organic chemistry. These themes support effective and efficient synthetic strategies, thus providing a comprehensive overview of this important discipline. Fully revised and updated, this new set forms an essential reference work for all those seeking information on the solution of synthetic problems, whether they are experienced practitioners or chemists whose major interests lie outside organic synthesis. In addition, synthetic chemists requiring the essential facts in new areas, as well as students completely new to the field, will find Comprehensive Organic Synthesis, Second Edition an invaluable source, providing an authoritative overview of core concepts. Winner of the 2015 PROSE Award for Multivolume Reference/Science from the Association of American Publishers Contains more than170 articles across nine volumes, including detailed analysis of core topics such as bonds, oxidation, and reduction Includes more than10,000 schemes and images Fully revised and updated; important growth areas—including combinatorial chemistry, new technological, industrial, and green chemistry developments—are covered extensively

This book will update the original edition published in 1997. Since the publication of the first edition, the biotechnology and biologics industries have gained extensive knowledge and experience in downstream processing using chromatography and other technologies associated with recovery and purification unit operations. This book will tie that experience together for the next generation of readers. Updates include: - sources and productivity - types of products made today - experiences in clinical and licensed products - economics - current status of validation - illustrations and tables - automated column packing - automated systems New topics include: - the use of disposables - multiproduct versus dedicated production - design principles for chromatography media and filters - ultrafiltration principles and optimization - risk assessments - characterization studies - design space - platform technologies - process analytical technologies (PATs) - biogenerics - comparability assessments Key Features: - new approaches to process optimiaztion - use of patform technologies - applying risk assessment to process design

Recombinant therapeutic proteins changed the world over 30 years ago when insulin, the first therapeutic protein, was approved. Since then, over 200 therapeutic proteins have been approved to treat a wide range of diseases from diabetes to immune disorders. Currently, there is no universal platform that can be used to purify any given target protein in a quick and inexpensive manner. The self-cleaving split intein tag technology remedies this issue by creating a universal platform that can purify any traceless, tagless target protein rapidly and economically. Chapter 2 discusses the combination of the split intein purification strategy with cell-free protein synthesis (CFPS) systems to reduce the time it takes to produce therapeutic proteins. With the cell-free systems, proteins can be produced in hours compared to days or even weeks. The combination of CFPS and the split intein tag technology has been utilized in the creation of a device to produce biologics on demand. The BioMOD device aims to produce a single-dose of any therapeutic protein within 24 hours, specifically with a military application in mind. Chapter 3 discusses the use of magnetic beads to mediate the split intein purification. Combining the split intein and magnetic beads creates a more efficient purification process that requires less buffer and set-up time. Four target proteins are used to demonstrate the applicability of the system. Chapter 4 discusses the regeneration of a commercially available resin that has been used to covalently immobilize the N fragment of the split intein using a thioester bond. Due to the commercially available resin having a high price point and the lengthy amount of time it takes to immobilize the N fragment, regeneration of the resin was necessary. A panel of buffers was screened to find the best regeneration buffer. Using the best buffer, a life cycle analysis was done using 20 regeneration cycles to show the resin could be regenerated multiple times. The development of a split intein resin that can be regenerated and reused multiple times makes this platform technology more realistic. Chapter 5 summarizes all the work discussed and goes into future work that can be done on each of the projects including further optimization of CFPS and the creation a split intein that is alkaline stable for regeneration using sodium hydroxide.

With contributions from biotechnologists and bioengineers, this ready reference describes the state of the art in industrial biopharmaceutical production, with a strong focus on continuous processes. Recent advances in single-use technology as well as application guidelines for all types of biopharmaceutical products, from vaccines to antibodies, and from bacterial to insect to mammalian cells are covered. The efficiency, robustness, and quality control of continuous production processes for biopharmaceuticals are reviewed and compared to traditional batch processes for a range of different production systems.

Biopharmaceutical Processing

Integrated Strategies for Drug Discovery Using Mass Spectrometry

Vaccine Development and Manufacturing

Ionic Liquids in Lipid Processing and Analysis

Development and Strategies

Comprehensive Organic Synthesis

Engineered antibodies currently represent over 30% of biopharmaceuticals in clinical trials and their total worldwide sales continue to increase significantly. The importance of antibody applications is reflected in their increasing clinical and industrial applications as well as in the progression of established and emerging production strategies. This volume provides detailed coverage of the generation, optimization, characterization, production and applications of antibody. It provides the necessary theoretical background and description of methods for the expression of antibody in microbial and animal cell cultures and in transgenic animals and plants. There is a strong focus on those issues related to the production of intrabodies, bispecific antibody and antibody fragments and also to novel applications in cancer immunotherapy.

Preparative Chromatography for Separation of Proteins addresses a wide range of modeling, techniques, strategies, and case studies of industrial separation of proteins and peptides. • Covers broad aspects of preparative chromatography with a unique combination of academic and industrial perspectives • Presents Combines modeling with compliantce useing of Quality-by-Design (QbD) approaches including modeling • Features a variety of chromatographic case studies not readily accessible to the general public • Represents an essential reference resource for academic, industrial, and pharmaceutical researchers

Current Trends and Future Developments on (Bio-) Membranes: Membrane Processes in the Pharmaceutical and Biotechnological field presents the main membrane techniques along with their basic principles, mode of operations, and applications. It covers well-known techniques such as ultrafiltration and membrane chromatography, while also exploring emerging membrane technologies which are finding their way in pharmaceutical and biotechnology industries, including membrane emulsification, membrane bioreactors, and solvent-resistant nanofiltration. State-of-the-art applications of membrane systems in areas such as drug delivery and virus removal are also investigated by leading experts in the field. Current Trends and Future Developments on (Bio-) Membranes: Membrane Processes in the Pharmaceutical and Biotechnological field is a definitive reference for academics, post-graduates, and researchers in the subjects of biochemical engineering, pharmaceutics, and biotechnology. It is also useful to R&D companies and institutions in these areas, specifically those interested in bioseparations, biopurification, bioproduction, and drug delivery. Offers an overview of classical membrane-based separation techniques such as ultrafiltration, microfiltration and virus filtration Discusses emerging membrane-based separation techniques such as nofiltration in the presence of solvent, membrane emulsification and membrane crystallization Outlines their applications to bioseparation, biopurification and bioproduction Includes examples in the production of vaccines, antibiotics, biomolecules, drugs, DNA and cells Lists membranes systems for drug delivery like liposomes, nanocapsules and bilayer membranes

Over the past two decades, inteins have been extensively used in a wide variety of applications in biotechnology. Split inteins are a subset of inteins, which are identified more recently and expressed in two separate segments naturally. They catalyze the splicing reaction in trans upon association of the two halves. Due to their unique features, split inteins offer improved controllability and flexibility in trans-splicing and trans-cleaving over the previous tools based on contiguous inteins. The engineered split inteins would allow the development of efficient self-cleaving affinity tags for purification applications and new methods for protein conjugation. In this work, an engineered split intein derived from Nostoc punciforme (Npu) was applied in a column-free purification strategy in combination with the aggregating tag, elastin-like polypeptide (ELP), as an initial capture step for recombinant proteins expressed in E. coli. Meanwhile, on-column purification strategy using the same engineered split intein was employed for the production of value-added biosimilar target, Granulocyte-colony stimulating factor (G-CSF). To adapt the split intein-based purification platform for the production of protein therapeutics expressed in mammalian cells, multiple leader sequences were designed and screened for optimal expression and secretion of intein-tagged precursor proteins. Moreover, the extein dependency of this engineered Npu split intein was thoroughly characterized by using in solution cleaving kinetics study and Forster Resonance Energy Transfer (FRET) based high-throughput method. The information gathered guides for fast and consistent cleavage reactions among various target proteins and provides insight to the cleavage mechanism. In this work, the trans-splicing properties of split inteins were also exploited for developing novel bioconjugation methods onto fluorescent nanodiamonds. Two split inteins, Gos-TerL and GP41.1, were used for the development of N-terminal and C-terminal oriented bioconjugation schemes, respectively. The new methods would allow rapid and spontaneous immobilization of proteins onto fluorescent nanodiamond surfaces for applications such as biomedical imaging or drug delivery.

Current Trends and Future Developments on (Bio-) Membranes

Approaches to the Purification, Analysis and Characterization of Antibody-Based Therapeutics

Volume II : Applications and Practical Case studies

Developing Molecular Tools for Applications in Metabolic Engineering and Protein Purification

Development of Antibody-Based Therapeutics

Gram-Negative Facultatively Anaerobic Rods—Advances in Research and Application: 2013 Edition

Purification Tools for Monoclonal is an essential book for professionals, educators and advanced students in the field of Biotechnology. It is based on experience gained from purification process development, scale-up, and manufacture of more than 250 monoclonal-based diagnostic and therapeutic products. Ten chapters provide in-depth coverage of major separation mechanisms, process strengths, weaknesses and method development; all fully integrated with the special performance, economic and validation requirements associated with monoclonals. Covered methods include precipitation with inorganic salts, polyethylene glycol, electrolyte depletion, caprylic acid, ethacridine, chromatographic purification by size exclusion, ion exchange, hydroxyapatite, hydrophobic interaction, immobilized metal affinity, hydrophilic interaction, euglobulin adsorption, thiophilic adsorption, protein A, protein G, lectin affinity, and more. 88 figures, 29 tables.

This practical guide for advanced students and decision-makers in the pharma and biotech industry presents key success factors in R&D along with value creators in pharmaceutical innovation. A team of editors and authors with extensive experience in academia and industry and at some of the most prestigious business schools in Europe discusses in detail the innovation process in pharma as well as common and new research and innovation strategies. In doing so, they cover collaboration and partnerships, open innovation, biopharmaceuticals, translational medicine, good manufacturing practice, regulatory affairs, and portfolio management. Each chapter covers controversial aspects of recent developments in the pharmaceutical industry, with the aim of stimulating productive debates on the most effective and efficient innovation processes. A must-have for young professionals and MBA students preparing to enter R&D in pharma or biotech as well as for students on a combined BA/biomedical and natural sciences program.

This book introduces fundamental principles and practical application of techniques used in the scalable production of biopharmaceuticals with animal cell cultures. A broad spectrum of subjects relevant to biologics production and manufacturing are reviewed, including the generation of robust cell lines, a survey of functional genomics for a better understanding of cell lines and processes, as well as advances in regulatory compliant upstream and downstream development. The book is an essential reference for all those interested in translational animal cell-based pharmaceutical biotechnology.

Developing a bioprocess model can not only reduce cost and time in process development, but now also assist the routine manufacturing and guarantee the quality of the final products through Quality by Design (QbD) and Process Analytical Technology (PAT). However, these activities require a model based process design to efficiently direct, identify and execute optimal experiments for the best bioprocess understanding and optimisation. Thus an integrated model based process design methodology is desirable to significantly accelerate bioprocess development. This will help meet current urgent clinical demands and also lower the cost and time required. This thesis examines the feasibility of a model based process design for bioprocess optimisation. A new process design approach has been proposed to achieve such optimal design solutions quickly, and provide an accurate process model to speed up process understanding. The model based process design approach includes bioprocess modelling, model based experimental design and high throughput microwell experimentation. The bioprocess design is based on experimental data and a computational framework with optimisation algorithm. Innovative model based experimental design is a core part in this approach. Directed by the design objectives, the method uses D-optimal design to identify the most information rich experiments. It also employs Random design and Simplex to identify extra experiments to increase the accuracy, and will iteratively improve the process design solutions. The modelling and implementation method by high throughput experimentation was first achieved and applied to an antibody fragment (Fab') precipitation case study. A new precipitation model based on phase equilibrium has been developed using the data from microwell experimentation, which was further validated by statistical tests to provide high confidence. The precipitation model based on good data accurately describes not only the Fab' solubility but also the solubility of impurities treated as a pseudo-single protein, whilst changing two critical process conditions: salt concentration and pH. The comparison study has shown the model was superior to other published models. The new precipitation model and the Fab' microwell data provided the basis to test the efficiency and robustness of the algorithms in model based process design approach. The optimal design solution with the maximum objective value was found by only 5 iterations (24 designed experimental points). Two parameterised models were obtained in the end of the optimisation, which gave a quantitative understanding of the processes involved. The benefit of this approach was well demonstrated by comparing it with the traditional design of experiments (DoE). The whole model based process design methodology was then applied to the second case study: a monoclonal antibody (mAb) precipitation process. The precipitation model was modified according to experimental results following modelling procedures. The optimal precipitation conditions were successfully found through only 4 iterations, which led to an alternative process design to protein A chromatography in the general mAb purification platform. The optimal precipitation conditions were then investigated at lab scale by incorporating a depth filtration process. The final precipitation based separation process achieved 93.6% (w/w) mAb yield and 98.2 % (w/w) purity, which was comparable to protein A chromatography. Polishing steps after precipitation were investigated in microwell chromatographic experimentation to rapidly select the following chromatography steps and facilitate the whole mAb purification process design. The data generated were also used to evaluate the process cost through process simulations. Both precipitation based and protein A chromatography based processes were analysed by the process model in the commercial software BioSolve under several relevant titre and scale assumptions. The results showed the designed precipitation based processes was superior in terms of process time and cost when facing future process challenges.

Supercritical Fluid Chromatography

Comprehensive Biotechnology, 4th Revised Edition

Protein Therapeutics

In Biologics Production

Creating an Efficient Biopharmaceutical Factory

Biological Drug Products

Promoting a continued and much-needed renaissance in biopharmaceutical manufacturing, this book covers the different strategies and assembles top-tier technology experts to address the challenges of antibody purification. • Updates existing topics and adds new ones that include purification of antibodies produced in novel production systems, novel separation technologies, novel antibody formats and alternative scaffolds, and strategies for ton-scale manufacturing • Presents new and updated discussions of different purification technologies, focusing on how they can address the capacity crunch in antibody purification • Emphasizes antibodies and innovative chromatography methods for processing

Gram-Negative Facultatively Anaerobic Rods—Advances in Research and Application: 2013 Edition is a ScholarlyEditions™ book that delivers timely, authoritative, and comprehensive information about Shewanella. The editors have built Gram-Negative Facultatively Anaerobic Rods—Advances in Research and Application: 2013 Edition on the vast information databases of ScholarlyNews.™ You can expect the information about Shewanella in this book to be deeper than what you can access anywhere else, as well as consistently reliable, authoritative, informed, and relevant. The content of Gram-Negative Facultatively Anaerobic Rods—Advances in Research and Application: 2013 Edition has been produced by the world ' s leading scientists, engineers, analysts, research institutions, and companies. All of the content is from peer-reviewed sources, and all of it is written, assembled, and edited by the editors at ScholarlyEditions™ and available exclusively from us. You now have a source you can cite with authority, confidence, and credibility. More information is available at http://www.ScholarlyEditions.com/.

Biopharmaceutical Processing: Development, Design, and Implementation of Manufacturing Processes covers bioprocessing from cell line development to bulk drug substances. The methods and strategies described are essential learning for every scientist, engineer or manager in the biopharmaceutical and vaccines industry. The integrity of the bioprocess ultimately determines the quality of the product in the biotherapeutics arena, and this book covers every stage including all technologies related to downstream purification and upstream processing fields. Economic considerations are included throughout, with recommendations for lowering costs and improving efficiencies. Designed for quick reference and easy accessibility of facts, calculations and guidelines, this book is an essential tool for industrial scientists and managers in the biopharmaceutical industry. Offers a comprehensive, go-to reference for daily work decisions Covers both upstream and downstream processes Includes case studies that emphasize financial outcomes Presents summaries, decision grids, graphs and overviews for quick reference

Approaches to the Purification, Analysis and Characterization of Antibody-Based Therapeutics provides the interested and informed reader with an overview of current approaches, strategies and considerations relating to the purification, analytics and characterization of therapeutic antibodies and related molecules. While there are obviously other books published in and around this subject area, they seem to be either older (c.a. year 2000 publication date) or are more limited in scope. The book will include an extensive bibliography of the published literature in the respective areas covered. It is not, however, intended to be a how-to methods book. Covers the vital new area of R&D on therapeutic antibodies Written by leading scientists and researchers Up-to-date coverage and includes a detailed bibliography

Development of an Integrated Precipitation-filtration Process for Initial Purification of Recombinant Proteins

Value Creation in the Pharmaceutical Industry

Model Based Process Design for Bioprocess Optimisation

Antibody Drug Discovery

New Bioprocessing Strategies: Development and Manufacturing of Recombinant Antibodies and Proteins

Comparative Approaches to Retardation, Learning Disabilities, and Giftedness

This volume address the similarities and differences in the cognitive processes that characterize children at the extremes of human talent. Its purpose is to assess the adequacy with which theories derived for normal children also account for performance and processes variability among retarded, learning disabled, and gifted children; and to advance the analaysis of quantative versus qualitative

differences in cognition by focusing on more extreme contrasts than have traditionally been examined in the developmental literature.

There is growing interest in the use of precipitation for the initial purification (capture) of monoclonal antibody (mAb) products due to the significant increase in product titer that have been achieved over the past two decades. Soluble impurities can be removed from the precipitated protein using a wash step, with the solid-liquid separation accomplished using either centrifugation or membrane microfiltration (MF). The objective of this thesis was to explore the development of a platform process using precipitation and tangential flow microfiltration for continuous protein capture. High yield precipitation of bovine serum albumin, human serum immunoglobulin G (IgG), and two commercial monoclonal antibody products were successfully achieved using a combination of a cross-linking agent (zinc chloride - ZnCl2) and a volume exclusion agent (polyethylene glycol - PEG). A high throughput method was developed to determine the solubility, precipitation, and re-dissolution behaviors of two monoclonal antibodies in both HEPES buffer and in their respective harvested cell culture fluid (HCCF) by systematically varying the PEG and zinc chloride concentrations. These results were used to narrow down the appropriate precipitation conditions for subsequent exploration in an integrated continuous precipitation-filtration system. Tangential flow microfiltration systems were successfully developed for dewatering and washing the precipitated protein. Continuous (long-time) operation of these membrane processes could be accomplished by maintaining the filtrate flux below the critical flux for the protein precipitate, where the critical flux was defined as the highest value of the filtrate flux below which the transmembrane pressure remained stable during operation at constant flux. The critical flux was found to be a function of both the filtration conditions, most significantly the effective shear rate in the hollow fiber membrane modules, and the properties of the precipitate, including the viscosity and particle size distribution. Correlations were developed to predict the performance of the tangential flow filtration over a range of conditions, enabling the design of optimized microfiltration processes. This included the use of a feed-and-bleed configuration to increase the effective conversion (ratio of permeate to feed flow rates) in the hollow fiber module to enable more effective washing. These results were used to design and successfully demonstrate a fully integrated continuous process for precipitation, dewatering, washing, and re-solubilizing a monoclonal antibody without any intervening hold steps. The process provided 10-fold reduction in host cell protein (HCP) levels with good yield of the antibody product. Model calculations showed that the impurity removal could be increased to nearly 1000-fold by increasing the conversion in the hollow fiber membrane modules, which is similar to, if not better than, the impurity reduction currently obtained with commercial applications of a platform Protein A chromatography capture step. These results provide important insights for the development of fully continuous precipitation-filtration processes for initial capture and purification of high value biotherapeutics.

Medicinal chemistry is both science and art. The science of medicinal chemistry offers mankind one of its best hopes for improving the quality of life. The art of medicinal chemistry continues to challenge its practitioners with the need for both intuition and experience to discover new drugs. Hence sharing the experience of drug research is uniquely beneficial to the field of medicinal chemistry. Drug research requires interdisciplinary team-work at the interface between chemistry, biology and medicine. Therefore, the topic-related series Topics in Medicinal Chemistry covers all relevant aspects of drug research, e.g. pathobiochemistry of diseases, identification and validation of (emerging) drug targets, structural biology, drugability of targets, drug design approaches, chemogenomics, synthetic chemistry including combinatorial methods, bioorganic chemistry, natural compounds, high-throughput screening, pharmacological in vitro and in vivo investigations, drug-receptor interactions on the molecular level, structure-activity relationships, drug absorption, distribution, metabolism, elimination, toxicology and pharmacogenomics. In general, special volumes are edited by well known guest editors

The conventional large-scale, centralized, single-product manufacturing model for biologic drugs does not allow for the economical production of drugs for small patient populations or for the distribution of these drugs in developing countries. A decentralized model featuring small-scale, fully automated, multi-product manufacturing of biologics at the point-of-care could address some of these issues. To truly realize the benefits of such a manufacturing paradigm, it must also be paired with rapid process development methods for the production of new molecules. In this thesis, we describe the development of a bench-scale, automated, multi-product manufacturing system for the end-to-end production of hundreds to thousands of doses of clinical quality protein medicines in about three days. We then demonstrate the application of this platform to the manufacture of a trivalent vaccine in a single campaign through co-expression and co-purification. We further demonstrate new methodologies for the accelerated development of manufacturing processes to produce new molecules on the system including a strategy for the development and optimization of fully integrated, multi-column processes for straight-through chromatographic purification, and the development of a platform process for the production and purification of single-domain antibodies. We then propose a workflow for the collection of a dataset relating the chromatographic behavior of host-cell proteins to their biophysical characteristics with the goal of building an in silico tool for the prediction of purification processes for any new molecule. Finally, we propose a platform approach, as opposed to a platform process, for the development of manufacturing processes for new biologics which is based on gaining a deeper understanding of process development challenges with regard to the host and to the molecule itself. Ultimately, we believe that the combination of a small-scale, automated manufacturing platform and accelerated strategies for developing processes to manufacture new products on the platform could enable time- and cost-efficient manufacturing of a wide variety of biologic drugs, increasing access to medicines throughout the world.

Protein Expression and Purification Using a Self-cleaving Split Intein

Translational Considerations

Design of Experiments for Pharmaceutical Product Development

Membrane Processes in the Pharmaceutical and Biotechnological Field

Continuous Processing in Pharmaceutical Manufacturing

Animal Cell Biotechnology

Monoclonal antibodies represent one of the fastest growing areas of new drug development within the pharmaceutical industry. Several blockbuster products have been approved over the past several years including Rituxan, Remicade, Avastin, Humira, and Herceptin. In addition, over 300 new drugs are currently in clinical trials. With both large, established biotechnology companies and small start-ups involved in the development of this important class of molecules, monoclonal antibodies products will become increasingly prevalent over the next decade. Recently the regulatory review of monoclonal antibodies has been moved from Center for Biologics and Research to the Center for Drug Evaluation and Research (CDER) division of the US Food and Drug Administration. It is anticipated that CDER will expect a certain minimal amount of data to be provided as more of these products move through the regulatory pipeline. Current Trends in Monoclonal Antibody Development and Manufacturing will provide readers with an understanding of what is currently being done in the industry to develop, manufacture, and release monoclonal antibody products and what will be required for a successful regulatory submission.

Translational strategies for development of antibody-based therapeutics should allow understanding of the relationship between the ‘unit dose’ and ‘unit effect’ with respect to both beneficial and deleterious effects from early stages of development. The flow of information from later to earlier stages of development should provide opportunities to facilitate selection of more effective novel and next-generation drug candidates. Selection and evaluation of relevant biomarkers in early preclinical development in "relevant" animal models should allow for identifying potential risks to humans and establishing safe First-In-Human (FIH) dosing strategies. Hence, integration of knowledge with respect to target antigen properties such as antigen distribution, expression profile, kinetic properties, target pharmacology, antigen isoforms and pharmacological redundancy in health and disease, as well as antibody design criteria, such as antibody isotype, affinity, PK/PD and safety is a critical necessity for the design of effective translational strategies. Additionally, these factors will further offer critical differentiating characteristics for next-generation antibodies, and novel technologies prove instrumental in generation of biosuperior antibody candidates for market entry. This book will examine many important considerations necessary for the design of effective translational strategies during the development of antibody-based therapeutics.

Separation Methods in Drug Synthesis and Purification, Second Edition, Volume Eight, provides an updated on the analytical techniques used in drug synthesis and purification. Unlike other books on either separation science or drug synthesis, this volume combines the two to explain the basic principles and comparisons of each separation technique. New sections to this volume include enantiomer separation using capillary electrophoresis (CE) and capillary electro- chromatography, the computer simulation of chromatographic separation for accelerating method development, the application of chromatography and capillary electrophoresis used as surrogates for biological processes, and new developments in the established techniques of chromatography and preparative methods. Features descriptions and applications of all separation methods used in the pharmaceutical industry Written by the leading scientists in their respective fields, providing solutions for a wide range of industrial separation problems encountered within the pharmaceutical industry Thoroughly updated with brand new separation science techniques and the latest developments in the established techniques of chromatography

Chapter 4 discusses the development of a self-cleaving affinity tag for the purification of recombinant proteins and has applications in medical biotechnology. Process development of new recombinant biotherapeutic proteins involves complex optimization and scale up based on the characteristics of each protein. There is no simple, low-cost platform that can be utilized to purify these diverse proteins. Thus, it is desirable to create an affinity tag-based platform for purification of any recombinant protein, but with the requirement that the purified protein be tagless and traceless. Consequently, our lab has developed a pH-controllable self-cleaving tag based on the Npu DnaE intein from Nostoc punctiforme for affinity-based purification of recombinant proteins. Previous work done with self-cleaving inteins has shown that the target protein residues (extein residues) at the cleavage junction can strongly affect cleavage kinetics of the tag. Therefore, in Chapter 4, the extein dependence of this tag is characterized using model (eGFP) and biotherapeutic (streptokinase (SK) and granulocyte colony stimulating factor (GCSF)) proteins. Through these studies, N-terminal extein residues that result in accelerated or diminished cleavage kinetics were identified. An eGFP model system was also established to predict the effect of the primary extein sequence on the cleavage kinetics of this tag. Finally, the information from this study was utilized to improve cleavage kinetics of the tag with GCSF.

Selective-membrane Platforms

DEVELOPMENT AND CHARACTERIZATION OF HISTIDINE-TAGGED HPV16 L2 AND MS2-ARGININE-TAGGED RECOMBINANT PROTEINS FOR DOWNSTREAM PROCESSES

Opportunities and Challenges

Development of Microfluidic-Based Valve Controlling Platform for Continuous Protein Purification

Separation Methods in Drug Synthesis and Purification

Process Scale Purification of Antibodies

Vaccine Manufacturing and Production is an invaluable reference on how to produce a vaccine - from beginning to end - addressing all classes of vaccines from a processing, production, and regulatory viewpoint. It will provide comprehensive information on the various fields involved in the production of vaccines, from fermentation, purification, formulation, to regulatory filing and facility designs. In recent years, there have been tremendous advances in all aspects of vaccine manufacturing. Improved technology and growth media have been developed for the production of cell culture with high cell density or fermentation. Vaccine Manufacturing and Production will serve as a reference on all aspects of vaccine production by providing an in-depth description of the available technologies for making different types of vaccines and the current thinking in facility designs and supply issues. This book will provide insight to the issues scientists face when producing a vaccine, the steps that are involved, and will serve as a reference tool regarding state-of-the-art vaccine manufacturing technologies and facility set-up. Highlights include: Comprehensive coverage of vaccine production : from a process point of view- fermentation to purification to formulation developments; from a production point of view - from facility design to manufacturing; and from a regulatory point of view - requirements from government agencies Authors from different major pharmaceutical and biotechnology companies Describes the challenges and issues involved in vaccine production and manufacturing of the different classes of vaccines, an area not covered by other books currently on the market

Antibody-based therapeutics are a central driver of the success of biopharmaceuticals. The discovery technology of this field is isolated to a limited number of centers of excellence in industry and academia. The objective of this volume is to provide a series of guides to those evaluating and preparing to enter particular areas within the field. Each chapter is written with a historical perspective that sets into context the significance of the key developments, and with the provision of “points to consider” for the reader as a value-added feature of the volume. All contributors are experts in their fields and have played pivotal roles in the creation of the technology.

Tested and proven solutions to the challenges of biologicaldrug product development Biological drug products play a central role in combating humandiseases; however, developing new successful biological drugspresents many challenges, including labor intensive productionprocesses, tighter regulatory controls, and increased marketcompetition. This book reviews the current state of the science,offering readers a single resource that sets forth the fundamentalsas well as tested and proven development strategies for biologicaldrugs. Moreover, the book prepares readers for the challenges thattypically arise during drug development, offering straightforwardsolutions to improve their ability to pass through all theregulatory hurdles and deliver new drug products to the market. Biological Drug Products begins with generalconsiderations for the development of any biological drug productand then explores the strategies and challenges involved in thedevelopment of specific types of biologics. Divided into fiveparts, the book examines: Part 1: General Aspects Part 2: Proteins and Peptides Part 3: Vaccines Part 4: Novel Biologics Part 5: Product Administration/Delivery Each chapter has been prepared by one or more leading experts inbiological drug development. Contributions are based on acomprehensive review and analysis of the current literature as wellas the authors' first-hand experience developing and testing newdrugs. References at the end of each chapter serve as a gateway tooriginal research papers and reviews in the field. By incorporating lessons learned and future directions forresearch, Biological Drug Products enables pharmaceuticalscientists and students to improve their success rate in developingnew biologics to treat a broad range of human diseases.

Comprehensive Medicinal Chemistry III provides a contemporary and forward-looking critical analysis and summary of recent developments, emerging trends, and recently identified new areas where medicinal chemistry is having an impact. The discipline of medicinal chemistry continues to evolve as it adapts to new opportunities and strives to solve new challenges. These include drug targeting, biomolecular therapeutics, development of chemical biology tools, data collection and analysis, in silico models as predictors for biological properties, identification and validation of new targets, approaches to quantify target engagement, new methods for synthesis of drug candidates such as green chemistry, development of novel scaffolds for drug discovery, and the role of regulatory agencies in drug discovery. Reviews the strategies, technologies, principles, and applications of modern medicinal chemistry Provides a global and current perspective of today's drug discovery process and discusses the major therapeutic classes and targets Includes a unique collection of case studies and personal assays reviewing the discovery and development of key drugs

A Practical Guide to Manufacturing, Preclinical, and Clinical Development

Biosimilars of Monoclonal Antibodies

The Critical Path to Innovation

Handbook of Process Chromatography

Preparative Chromatography for Separation of Proteins

Purification Tools for Monoclonal Antibodies

*New strategies and techniques for today's fast-paced discoveryprocess Today, the pressure is on for high-throughput approaches toaccelerate the generation, identification, and optimization ofmolecules with desirable drug properties. As traditional methods ofanalysis become antiquated, new analytical strategies andtechniques are necessary to meet sample throughput requirements andmanpower constraints. Among them, mass spectrometry has grown to bea front-line tool throughout drug discovery. Integrated Strategies for Drug Discovery Using Mass Spectrometryprovides a thorough review of current analytical approaches,industry practices, and strategies in drug discovery. The topicsrepresent current industry benchmarks in specific drug discoveryactivities that deal with proteomics, biomarker discovery,metabonomic approaches for toxicity screening, lead identification,compound libraries, quantitative bioanalytical support,biotransformation, reactive metabolite characterization, leadoptimization, pharmaceutical property profiling, sample preparationstrategies, and automation. THIS BOOK: * Clearly explains how drug discovery and mass spectrometry areinterconnected * Discusses the uses and limitations of various types of massspectrometry in various aspects of drug discovery * Prominently features analytical applications that requiretrace-mixture analysis * Provides industry applications and real-world examples * Shares historical background information on various techniques toaid in the understanding of how and why new methods are now beingemployed to analyze samples*

This book volume provides complete and updated information on the applications of Design of Experiments (DoE) and related multivariate techniques at various stages of pharmaceutical product development. It discusses the applications of experimental designs that shall include oral, topical, transdermal, injectables preparations, and beyond for nanopharmaceutical product development, leading to dedicated case studies on various pharmaceutical experiments through illustrations, art-works, tables and figures. This book is a valuable guide for all academic and industrial researchers, pharmaceutical and biomedical scientists, undergraduate and postgraduate research scholars, pharmacists, biostatisticians, biotechnologists, formulations and process engineers, regulatory affairs and quality assurance personnel.

This book serves as a reference for those interested in state-of-the-art research on the science and technology of ionic liquids (ILs), particularly in relation to lipids processing and analysis. Topics include a review of the chemistry and physics of ILs as well as a quantitative understanding of structure-activity relationships at the molecular level. Further, chapter authors examine the molecular basis of the toxicity of ILs, the prediction of the properties of ILs, and the rationale and steps toward a priori design of ionic liquids for task-defined applications. Emerging research in developing lipid-inspired ILs and their prospective use in drug formulation is described. Among the highlights are the latest advances in IL-mediated biocatalysis and biotransformation, along with lipase production, purification, and activation. Reviews the state-of-the-art applications of ionic liquids in lipid processing and relevant areas from a variety of perspectives Summarizes the latest advances in the measurement of the physical and chemical properties of ionic liquids and available databases of thermodynamic property datapoints Presents the tremendous opportunities provided and challenges faced from ionic liquids as a newly emerging technology for lipids processing area

Abstract : Human papillomaviruses (HPVs) are the most common sexually transmitted infections. Persistent infection with HPV can lead to anogenital cancers including head and neck cancers. Three prophylactic vaccines have been approved to prevent against some types of HPV infection. However, the vaccines are HPV-type specific and protect mostly against the HPV types included in the vaccines. To offer broader protection against more HPV types, studies in the field are developing candidate vaccines targeting a conserved minor capsid protein, L2. Nevertheless, reagents for developing and assessing L2 vaccines are limited. For example, antibodies to assess the antigenicity of some L2 epitopes are not available commercially and multivalent platforms to develop and purify clinical grade L2 antigens are limited. In this study, I developed and characterized the immunogenicity of a recombinant Histidine-tagged HPV16 L2 (amino acid 1-130) antigen. In addition to this, I explored the development of a multivalent display platform, a recombinant MS2-bacteriophage coat protein, with a C-terminal Arginine-tag for downstream purification using cation exchange chromatography. All Recombinant proteins (Histidine-tagged L2 and MS2-Arg tagged) were successfully expressed in bacteria. However, only Histidine-tagged L2 proteins were successfully purified in large quantity to homogeneity. Mice immunized with the Histidine-tagged L2 protein elicited anti-L2 IgG antibody titers greater than 103. The anti-L2 antibodies generated in this study will be valuable to researchers, in the field, developing L2 vaccines.

Strategies for the Development of Integrated Purification Processes for Non-platform Biologic Therapeutics

Development, Manufacturing, Validation and Economics

Antibody Expression and Production

Current Trends in Monoclonal Antibody Development and Manufacturing

Cognition in Special Children

Development, Design, and Implementation of Manufacturing Processes

This book review series presents current trends in modern biotechnology. The aim is to cover all aspects of this interdisciplinary technology where knowledge, methods and expertise are required from chemistry, biochemistry, microbiology, genetics,

chemical engineering and computer science. Volumes are organized topically and provide a comprehensive discussion of developments in the respective field over the past 3-5 years. The series also discusses new discoveries and applications. Special volumes are dedicated to selected topics which focus on new biotechnological products and new processes for their synthesis and purification. In general, special volumes are edited by well-known guest editors. The series editor and publisher will however always be pleased to receive suggestions and supplementary information. Manuscripts are accepted in English.

Addressing a significant need by describing the science and process involved to develop biosimilars of monoclonal antibody (mAb) drugs, this book covers all aspects of biosimilar development: preclinical, clinical, regulatory, manufacturing. • Guides readers through the complex landscape involved with developing biosimilar versions of monoclonal antibody (mAb) drugs • Features flow charts, tables, and figures that clearly illustrate processes and makes the book comprehensible and accessible • Includes a review of FDA-approved mAb drugs as a quick reference to facts and useful information • Examines new technologies and strategies for improving biosimilar mAbs

For B.Sc. and M.Sc. Students of Different Indian Universities as per UGC Model Curriculum. This is revised edition of the book "Plant Biotechnology". Several new topics such as Aquporins, Artificial intelligence Automation in Micropropagation, Biochips, Green House, Hydroponic, Inteins, Nanotechnology, Space Biotechnology, Supercritical Fluid extraction, etc. have been included in this revised. This edition provides latest information on the frontier area of biotechnology.

Supercritical Fluid Chromatography (SFC) provides a timely overview of SFC application areas which were unimaginable just a decade ago. This two-volume series opens with an overview of the history and expectant future of SFC and continues with recent applications in the pharmaceutical industry and other fascinating areas of science. SFC has found its place in the pharmaceutical industry with an increasing body of applications for chiral and achiral molecules in both the research and development phases of the drug discovery process. As illustrated in this two-volume series, the current interest in SFC extends well beyond the pharmaceutical industry. Chapters encompassing applications for polar and non-polar mixtures of importance are covering widely disparate areas in substance abuse, natural products including cannabinoids, bioactive lipids, flavor and fragrance. With its broad balance and coverage, this two-volume book constitutes a unique educational platform to students and scientists for many years to come. The major objective of this book editions is to inspire and stimulate readers to continue exploring the possibilities of exploiting supercritical fluids as a particular media for analysis, purifications and synthesis

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