APPLICATION OF BIOPROCESS TECHNOLOGY pdf

1: Bioprocess Technology Market By Product Type, Technique, Application, End User â€“ Now India

In this paper, we have provided an overview of the recent advances in understanding and development of bioprocess technology related to petroleum production, refining and remediation, and also highlighted constraints associated with field applications and approaches to overcome those challenges.

Additional Indications for Approved Drugs. Proteins from Recombinant Microorganisms Extensive research on eukaryotic gene expression in bacteria, yeasts, plants, insects, and mammals has resulted in many options for producing proteins in recombinant hosts. In spite of the numerous options, most of the products manufactured today are made either in recombinant E. No other microorganism is used to produce so large a number of products at high level. Rapid progress in the development of E. The body of knowledge that has accumulated has facilitated the adaptation of this bacterium for foreign-protein expression. Sophisticated cloning vectors, tools for regulated gene expression, and knowledge about the process of protein secretion and the physiology of growth were available in E. After translocation, the protein can accumulate within the periplasmic space or might be released to the surrounding medium. If the protein is secreted and accumulated within the cytoplasmic space, it normally aggregates into large inclusion bodies visible with a light microscope. These must be isolated, solubilized, and folded to obtain an active molecule. Isolation and solubilization are routine, but folding to an active form is difficult with present technology. Intracellular accumulation often has the additional disadvantage of producing a substance with an extra amino acid on the N terminus of the protein. Several signal sequences are now available to drive the secretion of eukaryotic proteins across the bacterial cytoplasmic membrane. Occasionally, that results in the formation of properly folded, bioactive proteins. More often, however, the secreted proteins also accumulate as aggregates in the periplasmic space; again, it is necessary to isolate, solubilize, and fold the proteins to their proper conformation. Perhaps the most exciting application for secretion of proteins from E. For both intracellular and secreted eukaryotic proteins, proteolytic degradation in E. Several approaches have been taken to reduce undesirable proteolysis, including the expression of fusion proteins and the elimination of specific proteases by host-cell mutation. The latter approach has been useful, but continued removal of proteases can be expected to affect general cellular metabolism adversely. Mistranslation has also been an occasional problem, but published technology now exists to minimize it. The cells grow and express rDNA proteins rapidly and in high quantities. They also are easily modified genetically and generally require inexpensive growth media. However, the system is often limited by its inability to produce intact, properly folded proteins and by a limited ability to yield posttranslational modifications, such as glycosylation and specific proteolytic modification. Inclusion Bodies High levels of protein synthesis have been obtained with several intracellular expression systems, particularly in E. High expression of a foreign protein in the cytoplasm of E. Isolation of inclusion bodies by centrifugation has become an important first step in the purification and recovery of recombinant proteins. Extensive protein-chemistry studies have revealed substantial fundamental information on the mechanism of inclusion-body formation. Various solubilization agents have been defined strong chaotropes, detergents, and organic solvents for use in recovery of active proteins; the process requires unfolding the protein with strong denaturants and refolding to an active monomer. Studies of the refolding of denatured proteins both in vitro and in vivo indicate that aggregates derive from specific partially folded intermediates and not from mature native or fully unfolded proteins Mitraki and King, Those discoveries focused attention on the properties of intermediates as distinct from native states and the factors interacting with them, such as the intracellular cytoplasmic environment, cofactors, and molecular chaperones. Molecular chaperones were first identified as host proteins needed for phage morphogenesis and have recently been identified as heat-shock proteins Goloubinoff et al. In a recent review Pelham, , it was proposed that heat-shock proteins can act as molecular chaperones and prevent aggregation by binding to hydrophobic regions of partially unfolded polypeptide chains. On the basis of those fundamental discoveries, studies are under way to mimic the mechanics of mammalian protein synthesis compartmentation, interprotein interactions, and posttranslational modifications in bacteria. With rational selection of the characteristics

necessary for correct maturation, it might be possible to direct the fate of the intermediates toward the native conformation. Alternatively, it might be possible to use molecular chaperones to repair and disaggregate proteins outside the cell before releasing them for refolding to the active monomer. Mammalian Host Systems Production of heterologous proteins by mammalian cells has usually used CHO cells or hybridoma cells. Initially, hybridoma cells were the only hosts used for antibody production. More recently, CHO cells and mouse myeloma cells have also been used. CHO cells are generally able to produce bioactive mammalian proteins that are glycosylated and properly folded. As yet, the system is often not able to effect specific proteolytic maturation, except to remove the secretion-signal sequence. Although bioactive molecules are usually formed by CHO cells, the product is a mixture of many subforms that differ in degree of glycosylation, electrostatic charge, the presence of proteolytic clips, and other possible modifications. The modifications do not necessarily compromise the potency or safety of the product, but it is essential that the process be carefully controlled to ensure that the same profile of molecular variants is produced from each batch. Mammalian cells have the advantage of being able to produce complex, bioactive molecules. However, they grow and express proteins at approximately one-twentieth the rate of E. That has the effect of increasing capital and labor costs for protein production. The cells also require expensive media although efforts are under way to reduce these costs and have additional, although tractable, regulatory and safety concerns, such as concern about undetected viral contamination. In spite of those limitations, CHO-cell production of biopharmaceuticals is an established and important technology that has enabled the delivery of such important therapeutics as tissue plasminogen activator and erythropoietin. Other Hosts for Heterologous Gene Expression Several new systems for the production of heterologous proteins are under development. They include such new bacterial systems as Bacillus and Streptomyces, the filamentous fungi, insect cell lines of Drosophila , and systems that rely on the baculovirus expression system, Xenopus oo-cytes, and yeast. Although none of these is as developed or has been studied as extensively as E. In Bacillus, for example, strains that lack most of the usual proteases have been generated. Streptomyces does not compete with E. Filamentous fungi, such as Neurospora crassa and Aspergillus nidulans, can secrete copious quantities of protein and have long been used in the pharmaceutical industry to make natural products. Yeast has been used to produce rDNA proteins, such as IGF-1 and human serum albumin; in spite of substantial effort, it has not been used as extensively as E. Isolation and Purification Isolation generally denotes the separation of the product from the bulk of the producing organism. The disposition and state of the expressed protein affect the isolation procedure. For mammalian cells and some E. If the product has aggregated either in the cytoplasmic or periplasmic space, isolation is more involved. Generally, the cell is first lysed by mechanical, chemical, or enzymatic treatment or a combination. In some cases, the more dense aggregate can be separated by centrifugation from most of the soluble and insoluble cell components; in other cases, the aggregate is first solubilized while still in the soluble protein mixture. Purification of the protein is a critical and often expensive part of the process. Purification has several objectives: In some cases, the first and additional objective is to fold the protein into its desired conformation. Much of the accumulated knowledge about protein purification is the property of individual companies. However, the available information suggests a general consistency in the type and order of process steps. The most common individual operations are centrifugation, filtration, membrane separation, adsorption separation, and chromatography. Regulatory and safety concerns have combined with the desire for stable liquid formulations to motivate the removal of host-organism proteins to a maximal degree. Measurement of those contaminants requires sophisticated assays capable of detecting a spectrum of possible contaminants at a few parts per million of the product protein. The presence of undesired variants of the target protein has motivated the development of techniques to detect and separate on a large scale proteins modified at one of several hundred amino acids. The difficulty of separation can often be decreased by changing the organism or culture conditions to produce a more uniform protein. However, it is still necessary to combine a series of purification steps each of which separates according to a different principle. Ultrafiltration steps are often used between separation steps to concentrate the protein solution or to make the buffer solution compatible with the next separation step. The final steps are designed to place the purified protein in the solution used for the product form. The complexity of the individual purification steps and the need to be able to integrate them into a

manufacturing system translate into a major opportunity for bioprocessing engineering as the process moves from the bench to the plant. Research and development in purification, scaleup integration, and system design will continue to have high priority. Protein Engineering Advances in molecular biology have provided researchers with the opportunity to develop increasingly rational approaches to the design of therapeutic drugs. This technology, when used with computer-assisted molecular modeling, is called protein engineering. Protein engineering combines many techniques, including gene cloning, site-directed mutagenesis, protein expression, structural characterization of the product, and bioactivity analyses; it can be used to modify the primary sequence of a protein at selected sites to improve stability, pharmacokinetics, bioactivity, and serum half-life. A second application of protein engineering is the design of hybrid proteins that contain regions that aid separation and purification. That is achieved by introducing, next to the structural gene for the desired product, a DNA sequence that encodes for a specific polypeptide "tail. Such genetic modifications can be designed to take advantage of affinity, ion-exchange, hydrophobic, metal-chelate, and covalent separations. Examples of affinity tails and the corresponding ligands are given in Table 4. The special properties of fusion proteins allow crude microbial extracts to be passed over an adsorbent that binds specifically to the tail, so that the desired product is retained and contaminants pass through. After elution and treatment to remove the tail, the product is purified further by standard methods, such as size-exclusion chromatography or high-performance liquid chromatography HPLC. Examples of Affinity Tails. Glycobiology Recent studies of receptor biology have resulted in fundamental discoveries about the role of complex oligosaccharides in disease, in modulation of protein function, and as anchors for integral membrane glycoproteins. As additional glycoproteins are identified and cloned, there is an increasing need for more effective chromatographic methods, production systems that mimic mammalian glycosylation patterns, and fast, reproducible analytical methods to minimize microheterogeneity during manufacture. Variability in oligosaccharide biosynthesis has been found to be an important source of heterogeneity for glycoproteins produced by eukaryotic cells Marino, Glycoprotein oligosaccharides are covalently attached to proteins through the amino acid serine O-linked or asparagine N-linked. If a selected carbohydrate type and site are required for bioactivity of a candidate glycoprotein, the expression system must be carefully selected. Bacterial systems cannot glycosylate, many yeast species hyperglycosylate, and glycosylation in mammalian cells has been shown to be specific to tissue and cell type. Future challenges in bioprocess development will parallel research in glycoprotein chemistry. The development of appropriate process controls, analytical methods, and quality-control specifications to control lot-to-lot consistency will be complicated by the inherent microheterogeneity of glycoproteins. Metabolic Engineering A powerful new approach to product development is the creative application of fermentation technology and molecular biology for "metabolic engineering. For protein production on an industrial scale, metabolic engineering could be useful in shifting metabolic flow toward a desired product, creating arrays of enzymatic activities for synthesis of novel structures, and accelerating rate-limiting steps Bailey, Metabolic engineering has recently been used to increase the efficiency of nutrient assimilation increasing the growth rate , improve the efficiency of ATP production decreasing nutrient demands , and reduce the production of inhibitory end products increasing final cell densities. Central to molecular modification of multigene pathways, such as those involved in antibiotic production, is the development of new vectors and transformation procedures and other tools of molecular biology. Another important discovery in metabolic engineering is the isolation of positive-control genes that regulate production of secondary metabolites. Positive regulators have been found in biosynthetic gene clusters for actinorhodin, bialophos, streptomycin, and undecylprodigiosin, all of which are Streptomyces products Bailey,

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

2: Bioprocess Applications | Bioprocess and Cell Culture Products | Corning

Bioprocess Application Library From product selection guides to application notes to validation documents, our online technical library is available anytime you need to facilitate your scale-up and production applications.

Snapshot Bioprocess technology is a vital part of biotechnology that deals with processes combining the complete living matter or its components with nutrients to make specialty chemicals, reagents, and biotherapeutics. The processes form the backbone of translating discoveries of life sciences into useful industrial products. Various stages associated with the bioprocess technology include substrates and media, biocatalysts, volume production, downstream processing, purification, and final processing. Over the past few years, the application of bioprocess technology in the development of a variety of next-generation biopharmaceutical products is gaining traction in the market. One of the rapidly emerging areas of application is in the manufacturing of key oligosaccharides OS â€"galactooligosaccharides and fructooligosaccharides. These OS have promising uses in food ingredients owing to their several health benefits. These are confirmed to possess certain prebiotic functions and will help meet the growing demand for prebiotic for treating various chronic ailments. Recent technological advancements in bioprocessing methods have further expanded the scope of their applications. Conventionally, whole cells or enzymes that are partially purified are used to synthesize both the OS. Enzymes play a vital role in the synthesis process. Fructooligosaccharides can be synthesized by the degrading fructan using the enzyme Inulinase or by the transglycosylation process of sucrose while galactooligosaccharides is produced using lactose. However, the complete conversion poses a challenge, since biocatalysis does not remove digestible carbohydrates found as a result of enrichment processes of oligosaccharides. Various bioengineering techniques for the removal of digestible carbohydrates are being developed. This includes downstream separation technologies, specific fermentation strategies, and further bioconversion using enzymes. Next-generation manufacturing strategies facilitate purification of sucrose-based fructooligosaccharides. Global Bioprocess Technology Market: Overview Bioprocess technology forms the backbone of the biotechnology industry. The process is leveraged to develop industrial products, processes and techniques to fulfill the needs of society. The different stages in bioprocess includes formulating raw materials, substrates and media, the conversion state, biocatalysts, downstream processing, volume production, purification and processing the final product. Bioprocess technology finds application in end use industries for manufacture of biomaterials such as pharmaceutical supplements, antibiotics, food and agricultural products, vaccines, and enzymes. It also finds application in the production of alternative products for treating maladies, the creation and evaluation of safer food materials, and making of biodegradable and environmental-friendly chemicals. As techniques and instrumentation become further sophisticated, bioprocesses may find applications in other domains where chemical processes are now used. A TMR Research report presents a comprehensive evaluation of the global market for bioprocess technology. It does so through qualitative insights and historical data. The report makes verifiable projections about market size. It segments the market based on different parameters and studies the size and potential of each segment. The research report serves as a repository of analysis and information for every aspect of the market, including regional markets, technology, types, and applications. Trends and Opportunities The most prominent growth drivers in the global market for bioprocess technology are the significant expansion in the biopharmaceutical industry, increasing thrust on research and development, higher demand for vaccine, and progress in the field of technology. Besides, bioprocesses steal a march over conventional chemical methods with the use of living materials for production. This is because bioprocesses typically need lower temperature, pressure, and pH, which is a measure of acidity. Second they can use renewable resources as raw materials and consume less energy. Offsetting such benefits is the steep cost of instruments required for bioprocess. Another factor countering the growth in the global market for bioprocess technology is the strict regulations. Depending upon the type, the global bioprocess technology market can be segmented into cell counting, cell culture, cell line development, cell expansion, single-use bioprocessing, virus filtration, flow cytometry, biologics safety testing, tangential flow filtration, and pyrogen testing. Of these, the cell culture segment leads the market with

a dominant share. Among them, North America accounts for maximum share. The stellar growth in the North America market has been brought about by a strong demand for good quality biologics, and a very strong emphasis on research and development by prominent players in the region. The market in the region will likely be propelled by the expansion in the biopharmaceutical industry, rising government initiatives, development in research and development, higher investments by key market players, and the trend of outsourcing production to Asia Pacific countries full of cheaper, high skilled manpower. Companies Mentioned in Report To present a detailed assessment of the competition prevailing in the global market for bioprocess technology, the report profiles companies such as Abbott Laboratories, Philips Healthcare, Becton, Thermo Fisher Scientific Inc. The study presents reliable qualitative and quantitative insights into:

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

3: Bioprocess Applications

A perhaps-attractive application of biotechnology and bioprocess engineering is in point-of-origin control of pollutants before they disperse into the environment. Many industriesâ€"such as the medical industry, electronics, and polymersâ€"are important sources of waste solvents.

Request Report Methodology Global Bioprocess Technology Market â€" Snapshot Bioprocess is defined as a technique that is used to produce biological materials such as genetic microbial strains and commercially useful chemicals through biological processes. Applications of bioprocess technology include antibiotics, recombinant proteins, biosimilars, cell culture, cellular analysis, etc.. Expansion in the biopharmaceutical industry is anticipated to boost the bioprocess technology market. The global biopharma sector continued its positive momentum in Sustained patient demand for innovative drugs is expected to continue to play a key role in the growth of the biopharma sector. The bioprocess technology market is being positively impacted by rise in flexibility in terms of customization. Demand for bioprocess technology has increased from both greenfield facilities as well as brown field facilities due to advancements in technology and the momentum is likely to continue. Thus, innovations in product offerings are likely to boost sales of bioprocess technology equipment. Increased demand for vaccine development and increased prevalence rate of several acute and chronic diseases is also driving demand for bioprocess technology. The global bioprocess technology market is in the growth stage. Major players such as F. In the past few years, the global bioprocess technology market has witnessed high investments by various multinational manufacturers such as Nova Biomedical, Siemens Healthineers and Becton, and Dickinson and Company. The global market is driven by increase in demand for vaccines, expansion in the biopharmaceutical industry, and rise in number of new drug launches. For example, in July , Advanced Instruments introduced OsmoPRO, which is able to analyze several types of samples, such as, blood, urine, cell culture, biological cell, etc.. In February , Advanced Instruments launched Osmo 1 Single Sample Micro-Osmometer, which is expected to increase efficiency, decrease sample turnaround time, and reduce the risk of loss of sample. The global bioprocess technology market has been segmented based on product, application, end-user, and region. High rate of adoption of cell culture media globally for several research and development studies is driving the segment. Bioreactors was a major sub-segment of the instruments segment in In terms of application, the recombinant proteins segment is expected to expand at a rapid CAGR from to Recombinant proteins was a leading segment in and is likely to account for a major market share during the forecast period. North America constituted a dominant share of the global bioprocess technology market in The predominance of the bioprocessing technology market in the U. The market share of Asia Pacific is projected to rise during the forecast period. The region is likely to be significant in terms of revenue in the next few years. Development of health care infrastructure; rise in population; growth of the biotechnology industry; and increase in burden of diseases necessitating diagnostics in Brazil, South Africa, Saudi Arabia, etc. Key companies operating in the global bioprocess technology market and profiled in the report include F. These players are adopting advanced techniques in the development of bioprocess technology to expand product offerings, strengthen geographical reach, increase customer base, and garner market share. In April , F. Global Bioprocess Technology Market: Overview Bioprocess is defined as a technique that is used to produce biological materials such as genetically microbial strain, and commercially useful chemicals through biological processes. However, limited adherence of biological product development and shift toward stratified medicine are likely to hamper the market during the forecast period. The global bioprocess technology market report comprises an elaborate executive summary, which includes a snapshot that provides information about various segments of the market. It also provides information and data analysis of the global market with respect to the segments based on product, application, end-user, and region. A detailed qualitative analysis of drivers and restraints of the market and opportunities has been provided in the overview section. Additionally, the section comprises a competitive matrix and company profiles along with business overview to understand the competitive landscape in the market. This section of the report also provides market attractiveness analysis by geography and market share analysis by key players, thereby presenting a thorough

analysis of the overall competitive scenario in the global bioprocess technology market. In terms of application, the global bioprocess technology market has been classified into antibiotics, recombinant proteins, monoclonal antibodies, and biosimilars. The market has been analyzed based on price variations, technology trend, and presence of key players. The market size and forecast for each of these segments have been provided for the period from to , along with their respective CAGRs for the forecast period from to , considering as the base year. Regional Outlook In terms of region, the global bioprocess technology market has been segmented into five major regions and the key countries in the respective regions: North America the U. The market size and forecast for each of these regions and the mentioned countries have been provided for the period from to , along with their respective CAGRs for the forecast period from to , considering as the base year. The research study also covers the competitive scenario in these regions. Companies Mentioned in Report The report also profiles the major players in the market in terms of various attributes such as company overview, financial overview, product portfolio, business strategies, and recent developments. The global bioprocess technology market has been segmented as follows:

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

4: Bioprocess Technology

Read chapter 4 Current Bioprocess Technology, Products, and Opportunities: The ability of the United States to sustain a dominant global position in biote.

As applications now span from cell banking to drug product, that in turn is raising interest in the interaction of extractables with proteins and cells. The conference was well attended by representatives from end-user organizations; academia; and suppliers of resin, film, single-use components, and gamma irradiation solutions. They participated in positive, scientific, collaborative discussions among different functional areas. The program included six workshops and six main sessions. Representatives from other industries e. It is imperative that all groups work together collaboratively for SU technology implementation to reach its full potential. A keynote presentation by Jay Kunzler research fellow at Dentsply Sirona demonstrated similarities between the medical device and biopharmaceutical industries and how to leverage lessons learned from use of plastics in other industries. In another keynote presentation, Manuel Carrondo director of the Institute of Experimental Biology and Technology in Portugal painted a picture of how industry and technology have evolved. He also discussed choosing between single-use and stainless steel equipment for applications such as antibodyâ€"drug conjugates ADCs and for small- or large-volume products. Preconference Workshops Polymers and Sterilization: Diane Hahm technical consultant at DuPont and Trishna Ray-Chaudhuri senior associate II in corporate quality product supply administration at Genentech chaired this preconference workshop. He detailed the polymers that are most likely to come into direct contact with biopharmaceutical solutions: Finally, he covered additives and their potential migration or interactions with bag contents. Tiffani Burt global process platform leader at Sealed Air Corporation overviewed the extrusion processes used to create films that go into bioprocessing. She provided a clear explanation of extrusion and how subsequent blown or cast processing methods differ. She also addressed mechanical properties of polymer films and their influence on handling. Olivier Vrain e-beam technical operations manager at Steris AST gave an excellent overview of sterilization, covering basics such as radiation measurement units and comparing methods. He described three radiation sterilization methods in detail: An important consideration is dose distribution for a product in its packaging. Determining the minimum and maximum doses is an important part of validating such processes, which also includes process parameters and temperature both important factors that can influence sterilization. Vrain concluded by highlighting the effects of sterilization on polymers: One particularly memorable point is that three polymeric materials are apt to fail: Basics of Biotechnology and Bioprocessing: Gary Lye professor at University College London and Qasim Rafiq senior lecturer and associate professor in bioprocessing of regenerative, cellular, and gene therapies at UCL University College London chaired this preconference workshop. Depending on the product of interest, different expression systems have been used. Traditionally microbes such as Escherichia coli have been used to produce insulin and growth hormones; however, such systems cannot produce more complex proteins that require posttranslational modifications and other expression systems such as mammalian cells. Each expression system offers advantages and disadvantages, and selecting an appropriate system depends on the product protein of interest. Lye overviewed production processes for therapeutic proteins and identified bioreactor fermentor platforms for cell expansion with different modes of operation: Bioreactor design and engineering are important to cell and protein production, particularly in performance and scale-up considerations. Lye discussed key factors for engineering characterization: He also highlighted key bioprocess parameters such as product titer and impurities as well as environmental and operational conditions e. Finally, he reviewed downstream processes for product recovery and purification, featuring the complexity, expense, and loss of yield that come with each recovery and purification step. Veronica Caravalhal principal engineer and group leader at Genentech followed with a presentation that focused on manufacturing therapeutic antibodies and how SU technologies are helping to advance the field. Next she outlined the seed and inoculum train process and demonstrated major challenges with three case studies highlighting the impact of raw materials, equipment, and scale. Finally, she compared stainless steel and SU bioreactors, with major advantages of the

latter being flexibility, fast set-up, and reduced cleaning validation requirements. Caravalhal concluded with examples of how Genentech has integrated SU technologies for certain applications, particularly bioreactors and disposable downstream equipment such as tangential-flow filtration TFF and chromatography systems. Qasim Rafiq delivered the final presentation of this session. He began by outlining how the emerging area of cell and gene therapies CGTs is developing into a fully fledged industry with recent product approvals, clinical successes, and increasing commercial investment. Rafiq outlined differences between traditional bioprocessing of proteins and of living cells as therapies; namely, the challenges of maintaining cell quality throughout, the anchorage-dependent nature of many CGT candidates, and the challenge of variation particularly for patient-specific therapies. Next, he segued into the two main manufacturing paradigms of CGTs: The final form, fit, and function of a plastic part is determined by the polymer family and formulation including additive packages , the polymer processing equipment, and the sterilization method. All three must be considered in design and qualification of a plastic component. The most thorough validation of polymers makes sense only with the appropriate control of variability through all processing steps. That makes openness, transparency, trust, and partnerships among all stakeholders from polymer supplier to converters, SU system manufacturers, sterilizers, and end users mandatory for disposables adoption in biopharmaceutical applications. Continuing to share knowledge about polymers, processing, and sterilization methods, this session integrated an example of practices in other industries. Talks, posters, and open discussions confirmed the willingness of all key players to collaborate, and some of their key learnings follow. The multiple polymers in a single film often are adhered in a melted state using tie layers typically made of a matrix resin that has been functionalized to optimize bonding at the interfaces of noncompatible materials. Tie layers often are miscible with one film layer and can form chemical bonds with the adjacent layer. As critical film components, tie-layer materials must be considered along with other polymers that constitute multilayer films when designing and testing the film structure. A knowledge gap exists between supplier and end-user specifications and standards regarding gels in films for SU systems. Attendees discussed the mechanisms of gel formation and black specks, focusing on how to minimize their presence in films. Before specifications are set, the impact of gels and other film imperfections must be assessed â€” especially because a trade-off has to be made between additives content and gel formation. Specifications should take into account the risks that gels and other imperfections impose on a process the possibility of leaks and product potential introduction of impurities. Recent experimental data obtained using different techniques and scrutinized by chemometrics have showed that within the dose range of 30â€”50 kGy, gamma irradiation has almost no impact on the structural, surface, and core properties of a commercially available film S Interaction between gamma irradiation and plastic materials remains a topic of interest for further investigation. Rapid prototyping technology widely used in the plastic industry can be applied to SU bioreactors for faster time to market and reduced cost. This technology is perfectly adapted to process development, but implementation is limited by the availability of materials suitable for bioprocess applications for regulatory compliance and stability after gamma irradiation. Overengineering this new approach provides a false sense of advanced understanding. The most thorough validation of polymers makes sense only with appropriate variability control in formulation and processing conditions. Although this session focused on common SU system applications e. Collaborative partnerships and lessons learned by makers of SU systems can help to overcome these future challenges. Xueyuan Wang principal project specialist at Bayer Healthcare and Isabelle Uettwiller regulatory affairs director and head of the validation laboratory at Sartorius Stedim Biotech chaired this session. He focused on testing results of filter capsules and lessons learned when adopting the BPOG protocol. He presented extractables study results of three different resins and how their profiles change according to test parameters and sterilization methods. Christian Julien director of pharma process solutions at Meissner Filtration Products presented extractables results from a biocontainer film based on BPOG protocols and compared them with previous results. The outcomes of this study could promote understanding of extractable profiles and different testing protocols. Martina Micheletti senior lecturer at University College London and Torsten Mayr associate professor of analytical chemistry at Graz University of Technology chaired this session. They sought discussion of the potential for traditional sensor technologies to be converted into reliable and robust SU

versions. Can recent developments in accuracy of small-scale sensors and microfluidics be adapted to work with SU bags, and for which operations would they be suitable? The session started with Martin Smolka materials scientist at the Joanneum Research Institute for Surface Technologies and Photonics presenting on roll-to-roll manufacturing methods of large-scale sheets of polymer film with precise characteristics. He presented two applications of the technology: Torsten Mayr offered an example of optical chemical sensors and described how they can be developed to measure oxygen concentration and pH. He showed results from cell culture applications and ended with a snapshot of a new luminescent-nanobead technology for rapid pH measurements. Thomas Nacke of the Institute for Bioprocessing and Analytical Measurement Techniques in Germany presented sensor technology based on the change of dielectric properties such as conductivity at microwave frequencies. Used to measure conductivity during E. John Carvell director of Aber Instruments presented an impedance probe for online detection of viable biomass concentration. He also discussed challenges encountered in integrating the probe within stirred and rocked SU bioreactors and described the journey to commercialization. Dan Nicolau professor and chair of the bioengineering department at McGill University described factors affecting the compatibility of proteins with plastic surfaces. His team has established a database of biomolecular adsorption information that can be used to assess potential interactions. To understand the potential for changes in the solution concentration of proteins, it is important to evaluate how they interact with plastic components in SU systems. Nicolau also discussed the impact of extractable compounds on protein structure and the health of cell cultures. As SU adoption grows, we continue to learn about the impact of such materials on biopharmaceutical systems. Matthew Hammond principal materials and polymer scientist at Amgen presented a case study on protein degradation found to occur with storage in a SU bioprocess container. Studies led to the conclusion that hyperperoxide extractables from the plastic film were responsible for protein cleavage. Those compounds are formed by gamma irradiation of the container. So concerns regarding extractables are not limited to SU bags and assemblies. Growth was hindered by an extractable compound 3,5-dinitro bisphenol A formed during a high-temperature molding process in combination with gamma irradiation. Andre Pastor senior expert at Bayer and Simone Biel field marketer for single-use technology at Merck chaired this session focused on challenges encountered during scale-up of SU systems. Case studies presented here investigated the rheology of different types of SU bioreactors. Key questions were addressed: What is the best mixing type to ensure the best supply of nutrients including oxygen in a homogenous cell culture without creating detrimental shear or other stress factors? Once established at small scale, how do we best translate a process to manufacturing scale? Phase-resolved PIV and high-frequency visual fluid tracking were used to investigate mixing characteristics. Cell culture performance effects were investigated using a GS-CHO cell line and measurement of recombinant protein productivity. Micheletti discussed how the results could be used to improve scaling methodologies. Many SU container shapes and mixing technologies have been developed. However, all CFD and experimental data presented showed that more flexibility in the geometry of SU bioreactors is needed to optimize cell culture performance. SU system suppliers should investigate further using such data to develop new bioreactors best fit for their intended purpose. Advances in Application of Single-Use Technology:

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

5: Bioprocess Technology Market Size, Share & Trends | Industry Analysis Report,

Bioprocess engineering is the discipline that puts biotechnology to work. Biotechnology involves using organisms, tissues, cells, or their molecular components (1) to act on living things and (2) to intervene in the workings of cells or the molecular components of cells, including their genetic material (NRC,).

Biotechnology-derived products already affect human health, nutrition, and environmental improvement and will grow to provide new products and employment in new industries. Bioprocess engineering is the subdiscipline within biotechnology that is responsible for translating life-science discoveries into practical products, processes, or systems capable of serving the needs of society. It is critical in moving newly discovered bioproducts into the hands of the consuming public. Although the United States has nurtured the discovery phase of biotechnology, it has not been aggressive in developing bioprocess engineering. Bioprocess Engineering and Global Competitiveness The importance of engineering capability in achieving and maintaining global competitiveness is compelling; witness the growth of the pharmaceutical industry after the development of penicillin production during World War II and of the computer and electronics industry after the discovery of the transistor. But the situation is changing. The emerging families of food, agricultural products, and industrial chemicals to be generated by biological routes, as well as the biopharmaceutical products now in development, will have markets measured in thousands of kilograms, or more, and will require innovative manufacturing techniques. The participation of the United States in the expanding bioproducts markets will necessitate world-class bioprocess engineering. Comparison of the global competitive position of the United States with that of other technologically advanced nations in biotechnology and bioprocess engineering reveals that The United States continues to be the world leader in basic health-science and life-science elements of biotechnology. Japan leads in applied microbiology and biocatalysis and is effectively coordinating government, industrial, and academic resources in biotechnology and bioprocess-engineering development. Europe matches Japan in progress in applied biocatalysis and is establishing a strong, government-supported technology-transfer infrastructure between industry and academe with emphasis on bioprocess engineering. World competition in biotechnology and other industries that depend on bioprocess engineering will be keen because of the notable capabilities in and commitments to biologically relevant manufacturing and bioprocess development among industrially developed nations. It is debatable whether the United States can be dominant or even competitive in bioprocessing: That will require that the existing resources of government, industry, and academe collaborate in Rapidly translating scientific discoveries into marketable products and processes. Promoting cross-disciplinary research and education and thereby fostering innovative, multidisciplinary solutions to important bioprocessing problems. Providing a growing cadre of bioprocess engineers to meet the needs of an expanding bioprocess-industry. Opportunities The committee addressed trends in biotechnology that are likely to have important worldwide social and financial impact within the next 10 years. In this context, current commercial activities related to biotechnology and biotechnology products are dominated by biopharmaceutical biologics, such as insulin, tissue plasminogen activator, and erythropoietin. Innovative bioprocess engineering in the manufacture of these products can lead to improvements in product recovery, product purity, process safety, and reduced manufacturing and quality-control costs. The need for such process innovation will intensify as patent protection for these products expires, global competition for international markets increases, and regulatory procedures that would otherwise slow introduction of new bioprocess technologies are streamlined. Health-care products emerging from biotechnology will be consumed in much larger quantities around the world than they are now examples include recombinant hemoglobin, recombinant albumin, and conjugate vaccines. These second-generation products will require large-scale manufacturing facilities that handle biological systems; and bioprocess engineering will be a sine qua non for successful commercialization of the products. Bioprocess engineers will be employed in applying the new biology to producing smaller molecules and specialty bioproducts. These are in a category where the challenge is to apply bioprocessing to obtain value-added products and to engineer large-scale, integrated processes that use agricultural and forestry-based

materials and other renewable resources. Bioproducts for use in food production and in foods animal health-care biologics, biological plant-growth promoters and pesticides, nutritional supplements, and food additives present large-tonnage product opportunities that can be tapped in the coming decade, provided that suitably efficient and economical manufacturing facilities can be designed and built. Such capabilities do not exist, and their creation is a major challenge for bioprocess engineering. The use of biomass for the production of industrial chemicals and of liquid and gaseous fuels represents a major hope for reducing U. The processing of renewable resources must have high national priority in the coming decade, so that the necessary know-how and production infrastructure for its practical implementation can be developed. Bioprocessing in space presents unique opportunities, particularly in bioregenerative life support and as a research platform for the study of new types of manufacturing processes. Bioprocessing for protection and beneficiation of the environment represents another large and important opportunity. Biological processes could offer alternatives to environmentally polluting or fossil-fuel-consuming manufacturing processes and could help to remove toxic pollutants from industrial and municipal wastes. Needs Generic applied research is critical to the optimal exploitation of bioprocess engineering by industry, in that it addresses technologies that are too risky for companies or that require too long a period for results. This category of research bridges the gap between basic biological science that is carried out by university and government laboratories and the industrial applied research that assists in converting biotechnology into products and services. For biopharmaceuticals, needs identified by the committee are to Improve analytical methods that facilitate rapid testing of products for purity and activity. Develop high-resolution protein-purification methods for scaleup and application in the industrial manufacture of ultrapure products. Develop process-control technology for integrating biological production sequences into stable and robust automated manufacturing systems. Enhance biological and biochemical technology for increasing the efficiency of protein folding and improving the expression of recombinant proteins. For specialty bioproducts and industrial chemicals, key needs are to Develop separation and purification technologies that are specially adapted to the recovery of products from dilute aqueous streams characteristic of materials derived from microbial fermentation, plant cell culture, or whole plant material. Develop processing technologies that will facilitate the economical conversion of cellulose-based materials into industrial chemicals and fuels. Develop specially adapted or genetically altered microorganisms that can transform biomass materials into industrial chemicals and other products. Develop bioproduct manufacturing processes that are controlled and regulated and have predictable performance. Appropriate bioreactor design and operating conditions must be implemented on scaleup to ensure that product characteristics are maintained, regardless of the type of product. Bioprocess engineers are particularly well suited to integrate bioreaction engineering concepts with the subtleties of cellular metabolism to achieve the necessary product qualities. Bioprocess engineering input is important for environmental applications of biotechnology, where the needs are to Study the role of microbial interactions in degrading of toxic wastes in the environment and detoxifying industrial wastes at the plant site. Define standards by which the effects of bioprocessing in detoxifying wastes will be measured. Implement bioprocess-engineering methods in the design of waste-processing technologies. Recommendations To meet the global challenges of competition in industrialization of biotechnology and to address national needs, the committee recommends A coordinated, long-term plan of research, development, training, and education in bioprocess engineering, with well-defined goals that involve participation of industry, academe, and the federal government. A research and educational program in bioprocess engineering that emphasizes cross-disciplinary interactions between scientists and engineers and a multidisciplinary team approach to problem-solving, which has historically been the keystone of success in American industrial development. Increased cooperation between industry and the Food and Drug Administration for the express purpose of developing quality-control methods and standards and good manufacturing practices for the manufacture of biotechnology products. Sustained funding by the federal government is essential to the success of research and education programs for training bioprocess engineers, as is the participation of industryâ€”in planning, training, and supply of physical and financial resources. The ability of the United States to sustain a dominant global position in biotechnology lies in developing a strong resource base for bioprocess engineering and bioproduct manufacturing and maintaining its primacy in basic

life-science research. The United States has made an enormous, and enormously successful, investment in basic biological science. To protect the investment and to capitalize on it, there must now also be an investment in bioprocess engineering. A Plan for Action The discoveries emanating from the basic life sciences provide the knowledge that supports new concepts for biologically based products and manufacturing systems. The committee strongly recommends that federal funding of research in biotechnology be extended to support efforts that provide the science and technology base for producing and manufacturing products from biology. Targeted long-term research support would speed the development of commercial products, provide the trained personnel needed to support industrial activities, protect entry-level U. The Committee on Bioprocess Engineering recommends these actions to improve U. Human-Resources Development The committee recommends a major commitment to developing the human-resources base through funding of research programs in universities, continuing-education programs, and research directed toward industrial problems applied-engineering research by the cognizant government agencies, including the National Science Foundation NSF , the National Institutes of Health NIH , the Department of Energy DOE , and the Department of Agriculture USDA. New resources must be provided to strengthen the infrastructure for bioprocess engineering and biotechnology in this context. A major commitment is needed to educate personnel skilled in bioprocess engineering. These are the individuals who will develop bioprocesses and support biologically based manufacturing technologies if the U. Assessing Developments Abroad The committee recommends vigorous efforts in technology assessment in Japan and Europe and support for exchange-scholar, exchange-student, and collaborative research programs. For bioprocess engineering, particular emphasis should be placed on tracking developments in process technology for manufacture of new bioproducts. Germany, Switzerland, Austria, the United Kingdom, France, Scandinavia, Italy, the Netherlands, and other European nations have a strong base serving biotechnology in products and services. Given the upcoming economic unification of Europe, we recommend a separate study on bioprocessing in Europe. Cross-disciplinary research should be part of the training of the bioprocess engineer and include activities at the postgraduate level. For example, a postdoctoral scholarship program for biological scientists to gain exposure to engineering activities should be considered. Promoting Awareness of Importance of Manufacturing Technology The committee strongly recommends formulating a federal strategy for fostering increased awareness of the importance of manufacturing technology in the research and university communities through education and training. Postdoctoral and graduate students should have contact with issues in manufacturing through research, course work, teaching laboratories, and industrial experiences. Continuing education is also critical for bioprocess engineering because of the rapidity of advances in the biological sciences and should be part of the training offered by universities to leaders in the bioproduct industry. Such programs should be created by industry, universities, and government in a cooperative fashion. Teaching laboratories for bioprocess engineering should be upgraded so that they can provide a high-quality training experience for a larger number of students. Competitive-Grants Program The committee recommends that research funding be allocated to topics listed in this report through a competitive-grants program for bioprocesses in the manufacture of biopharmaceuticals and other bioproducts that cover a wide range of biological, chemical, and engineering disciplines. We believe that structuring the research in a manner that requires an industry-university or industry-government interaction would catalyze further research. Role of National Laboratories and Research Centers Industry involvement and the special facilities and capabilities of government laboratories, such as those under the auspices of USDA and DOE, could help to speed adaptation of some types of new bioprocesses on a commercial scale. Similarly, the NSF Engineering Research Centers program and more recently the National Aeronautics and Space Administration Scientific Centers for research and training provide cross-disciplinary environments for research related to manufacturing or large-scale systems. The committee recommends that these laboratories and centers be examined as models and applied, in a suitably modified form, to the processing of renewable resources. Bioprocessing for Cleanup of Environmental Hazards The committee recommends an analysis of the costs of biological treatment compared with other technologies. Bioremediation promises lower costs than other types of technology for cleaning up certain environmental hazards.

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

6: Applications: Bioprocessing | Kaiser Optical Systems, Inc. | An Endress+Hauser Company

In terms of application, the global bioprocess technology market has been classified into antibiotics, recombinant proteins, monoclonal antibodies, and biosimilars. In terms of end-user, the global bioprocess technology market has been classified into biopharmaceutical companies, contract manufacturing organizations, academic research.

Registration will close by July 1, Participant Takeaways: Recognize the fundamentals of fermentation technology. Describe current knowledge in biological and biochemical technology, with a focus on industrial practices. Comprehend growth and metabolism, genetics and metabolic engineering in the age of genomics, the biological basis for monitoring bioprocesses including process analytical technology, and applications of the modern biological concepts in bioprocess developments. Examine eukaryotic and prokaryotic protein expression relevant to industrial practice, including post-translational modifications esp. Assess power requirements in bioreactors, modeling of bioprocesses, traditional and new concepts in bioprocess monitoring, and the biological basis for industrial fermentations and cell cultures. Distinguish bioreactor operations in bacteria and mammalian cell systems, oxygen transfer and shear in bioreactors, process improvement through metabolic manipulations, and scale-up of bioreactors such as bacterial, yeast, and mammalian cells. Analyze the bioprocess paradigm: Scale-down, bioprocess simulation and economics, sterilization, and bioburden in biological manufacturing. Examine considerations in bioprocess simulation and economics, sterilization in biological manufacturing, and clinical implications of bioprocesses. The course is intended for engineers, biologists, chemists, microbiologists, and biochemists who are interested in the areas of biological systems in prokaryotic and eukaryotic hosts. It is desirable that individuals enrolled be familiar with some of the general aspects of modern biology, genetics, biochemical engineering, and biochemistry. Some general knowledge of mathematics is also desirable for dealing with the engineering aspects of the course. Lectures will cover the following topics: Growth and metabolism Molecular biology in bioprocess developments Bioprocess concepts in mammalian cell culture technology Protein expression in bacterial and mammalian cells: Electrical power is available in the lecture hall. The program is under the direction of Professor Daniel I. Lectures will be presented by: San Francisco, CA Dr. View Course Schedule pdf Class begins at 8: Class runs until 5: Special events include a reception for course participants and faculty on Monday night and a dinner on Thursday evening. All evening activities are included in the tuition. ARMY "I would definitely recommend this course to colleagues. In fact, I already have. I would recommend it because of its prominence in the pharmaceutical community The presenters are all top-notch and knew how to keep their presentation interesting and engaging. I believe all were able to take something away from the course and directly apply it to their daily roles, as well as learn something new about applications of fermentation technologies. Went beyond the curriculum and provided real-world examples. Gained new knowledge and appreciation for cell fermentation that directly applies to the work I perform each day. With my new knowledge, I will be able to take on more duties and help ease the load of our current fermentation engineers, as well as bridging the gap between the genetic engineering and strain development side of things with the aspects of scaling up fermentations from shake flasks to bio-reactors. Because of the broad range of topics and coverage of new technology, a higher level unit manager esp. This will also allow me to predict concerns from when products are transitioned to our site for the first time. He is the recipient of numerous awards from the American Chemical Society, the American Institute of Chemical Engineers, and from schools here and abroad. This course was developed under the leadership of Prof. While he no longer takes an active role in instruction, he does continue to stay involved in the role of course co-director. Jones Prather Kristala L. She received an S. She has been recognized for excellence in teaching with the C. Professor Prather has co-authored more than 75 manuscripts and two book chapters, and has five issued patents with several additional applications pending. Neal Connors Neal Connors Dr. He has worked at all experimental scales, from well-plate and shake flask to lab and pilot fermentor scales. He also serves on the editorial boards of two peer-reviewed journals: Cooney is Robert T.

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

7: Executive Summary - Putting Biotechnology to Work - NCBI Bookshelf

Like other applications of biotechnology, modern bioprocess technology is an extension of ancient techniques for developing useful products by taking advantage of natural biological activities.

Cell bioprocessing[edit] Cell therapy bioprocessing is a discipline that bridges the fields of cell therapy and bioprocessing i. The goals of cell therapy bioprocessing are to establish reproducible and robust manufacturing processes for the production of therapeutic cells. Produce products that maintain all of the quality standards of biopharmaceutical drugs [3] Supply both clinical and commercial quantities of therapeutic cells throughout the various stages of development. The processes and production technologies must be scalable, [2] and Control the cost of goods CoGs of the final drug product. This aspect is critical to building the foundation for a commercially viable industry. Upstream bioprocessing[edit] Therapeutic cell manufacturing processes can be separated into upstream processes and downstream processes. The upstream process is defined as the entire process from early cell isolation and cultivation, to cell banking and culture expansion of the cells until final harvest termination of the culture and collection of the live cell batch. Aside from technology challenges, concerning the scalability of culture apparatus, a number of raw material supply risks have emerged in recent years[when? Upstream processing involves all the steps related to inoculum development, media development, improvement of inoculum by genetic engineering process, optimization of growth kinetics so that product development can improve tremendously. Fermentation has two parts: After product development, the next step is the purification of product for desired quality. When they reach the desired density for batch and fed-batch cultures they are harvested and moved to the downstream section of the bioprocess. Downstream bioprocessing[edit] The downstream part of a bioprocess refers to the part where the cell mass from the upstream are processed to meet purity and quality requirements. Downstream processing is usually divided into three main sections: The volatile products can be separated by distillation of the harvested culture without pre-treatment. Distillation is done at reduced pressure at continuous stills. At reduced pressure distillation of product directly from fermentor may be possible. The steps of downstream processing are: If the product is biomass, then it is recovered for processing and spent medium is discarded. If the product is extra cellular the biomass will be discarded. Ultra filtration is an alternative to the centrifugation. If the desired product is intra cellular the cell biomass can be disrupted so that the product should be released. The solid-liquid is separated by centrifugation or filtration and cell debris is discarded. The spent medium is concentrated if the product is extracellular. Initial purification of metabolites: According to the physico-chemical nature of the product molecule several methods for recovery of product from the clarified fermented broth were used precipitation, etc. If low amount of product is found in very large volume of spent medium, the volume is reduced by removing water to concentrate the product. It is done by vacuum drying or reverse osmosis. The purified product is mixed with several inert ingredients called excipients. The formulated product is packed and sent to the market for the consumers.

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

8: Bioprocess Technology Market - Scope, Size, Share, Analysis by

*Best Technology Application - DOWNSTREAM. WINNER: Pall Life Sciences * Cadence Acoustic Separator The Cadence Acoustic Separator is a scalable single-use technology for cell culture clarification using acoustophoretic separation from process development through to large-scale drug manufacturing.*

After translocation, the protein can accumulate within the periplasmic space or might be released to the surrounding medium. If the protein is secreted and accumulated within the cytoplasmic space, it normally aggregates into large inclusion bodies visible with a light microscope. These must be isolated, solubilized, and folded to obtain an active molecule. Isolation and solubilization are routine, but folding to an active form is difficult with present technology. Intracellular accumulation often has the additional disadvantage of producing a substance with an extra amino acid on the N terminus of the protein. Several signal sequences are now available to drive the secretion of eukaryotic proteins across the bacterial cytoplasmic membrane. Occasionally, that results in the formation of properly folded, bioactive proteins. More often, however, the secreted proteins also accumulate as aggregates in Page 56 Share Cite Suggested Citation: Putting Biotechnology to Work: The National Academies Press. Perhaps the most exciting application for secretion of proteins from E. For both intracellular and secreted eukaryotic proteins, proteolytic degradation in E. Several approaches have been taken to reduce undesirable proteolysis, including the expression of fusion proteins and the elimination of specific proteases by host-cell mutation. The latter approach has been useful, but continued removal of proteases can be expected to affect general cellular metabolism adversely. Mistranslation has also been an occasional problem, but published technology now exists to minimize it. The cells grow and express rDNA proteins rapidly and in high quantities. They also are easily modified genetically and generally require inexpensive growth media. However, the system is often limited by its inability to produce intact, properly folded proteins and by a limited ability to yield posttranslational modifications, such as glycosylation and specific proteolytic modification. High expression of a foreign protein in the cytoplasm of E. Isolation of inclusion bodies by centrifugation has become an important first step in the purification and recovery of recombinant proteins. Extensive protein-chemistry studies have revealed substantial fundamental information on the mechanism of inclusion-body formation. Various solubilization agents have been defined strong chaotropes, detergents, and organic solvents for use in recovery of active proteins; the process requires unfolding the protein with strong denaturants and refolding to an active monomer. Studies of the refolding of denatured proteins both in vitro and in vivo indicate that aggregates derive from specific partially folded intermediates and not from mature native or fully unfolded proteins Mitraki and King, Those discoveries focused attention on the properties of intermedi- Page 57 Share Cite Suggested Citation: Molecular chaperones were first identified as host proteins needed for phage morphogenesis and have recently been identified as heat-shock proteins Goloubinoff et al. In a recent review Pelham, , it was proposed that heat-shock proteins can act as molecular chaperones and prevent aggregation by binding to hydrophobic regions of partially unfolded polypeptide chains. On the basis of those fundamental discoveries, studies are under way to mimic the mechanics of mammalian protein synthesis compartmentation, interprotein interactions, and posttranslational modifications in bacteria. With rational selection of the characteristics necessary for correct maturation, it might be possible to direct the fate of the intermediates toward the native conformation. Alternatively, it might be possible to use molecular chaperones to repair and disaggregate proteins outside the cell before releasing them for refolding to the active monomer. Initially, hybridoma cells were the only hosts used for antibody production. More recently, CHO cells and mouse myeloma cells have also been used. CHO cells are generally able to produce bioactive mammalian proteins that are glycosylated and properly folded. As yet, the system is often not able to effect specific proteolytic maturation, except to remove the secretion-signal sequence. Although bioactive molecules are usually formed by CHO cells, the product is a mixture of many subforms that differ in degree of glycosylation, electrostatic charge, the presence of proteolytic clips, and other possible modifications. The modifications do not necessarily compromise the potency or safety of the product, but it is essential that the process be carefully controlled to ensure that the

same profile of molecular variants is produced from each batch. Mammalian cells have the advantage of being able to produce complex, bioactive molecules. However, they grow and express proteins at approximately one-twentieth the rate of E. That has the effect of increasing capital and labor costs for protein production. The cells also require expensive media although efforts are under way to reduce these costs and have additional, although tractable, regulatory and safety concerns, such as concern about undetected viral contamination. In spite of those limitations, CHO-cell production of biopharmaceuticals is an established and important technology that has enabled the delivery of such important therapeutics as tissue plasminogen activator and erythropoietin. Page 58 Share Cite Suggested Citation: They include such new bacterial systems as Bacillus and Streptomyces, the filamentous fungi, insect cell lines of Drosophila , and systems that rely on the baculovirus expression system, Xenopus oo-cytes, and yeast. Although none of these is as developed or has been studied as extensively as E. In Bacillus, for example, strains that lack most of the usual proteases have been generated. Streptomyces does not compete with E. Filamentous fungi, such as Neurospora crassa and Aspergillus nidulans, can secrete copious quantities of protein and have long been used in the pharmaceutical industry to make natural products. Yeast has been used to produce rDNA proteins, such as IGF-1 and human serum albumin; in spite of substantial effort, it has not been used as extensively as E. The disposition and state of the expressed protein affect the isolation procedure. For mammalian cells and some E. If the product has aggregated either in the cytoplasmic or periplasmic space, isolation is more involved. Generally, the cell is first lysed by mechanical, chemical, or enzymatic treatment or a combination. In some cases, the more dense aggregate can be separated by centrifugation from most of the soluble and insoluble cell components; in other cases, the aggregate is first solubilized while still in the soluble protein mixture. Purification of the protein is a critical and often expensive part of the process. Purification has several objectives: In some cases, the first and additional objective is to fold the protein into its desired conformation. Much of the accumulated knowledge about protein purification is the Page 59 Share Cite Suggested Citation: However, the available information suggests a general consistency in the type and order of process steps. The most common individual operations are centrifugation, filtration, membrane separation, adsorption separation, and chromatography. Regulatory and safety concerns have combined with the desire for stable liquid formulations to motivate the removal of host-organism proteins to a maximal degree. Measurement of those contaminants requires sophisticated assays capable of detecting a spectrum of possible contaminants at a few parts per million of the product protein. The presence of undesired variants of the target protein has motivated the development of techniques to detect and separate on a large scale proteins modified at one of several hundred amino acids. The difficulty of separation can often be decreased by changing the organism or culture conditions to produce a more uniform protein. However, it is still necessary to combine a series of purification steps each of which separates according to a different principle. Ultrafiltration steps are often used between separation steps to concentrate the protein solution or to make the buffer solution compatible with the next separation step. The final steps are designed to place the purified protein in the solution used for the product form. The complexity of the individual purification steps and the need to be able to integrate them into a manufacturing system translate into a major opportunity for bioprocessing engineering as the process moves from the bench to the plant. Research and development in purification, scaleup integration, and system design will continue to have high priority. This technology, when used with computer-assisted molecular modeling, is called protein engineering. Protein engineering combines many techniques, including gene cloning, site-directed mutagenesis, protein expression, structural characterization of the product, and bioactivity analyses; it can be used to modify the primary sequence of a protein at selected sites to improve stability, pharmacokinetics, bioactivity, and serum half-life. A second application of protein engineering is the design of hybrid proteins that contain regions that aid separation and purification. That is achieved by introducing, next to the structural gene for the desired product, a DNA sequence that encodes for a specific polypeptide "tail. Examples of affinity tails and the corresponding ligands are given in Table 4. The special properties of fusion proteins allow crude microbial extracts to be passed over an adsorbent that binds specifically to the tail, so that the desired product is retained and contaminants pass through. After elution and treatment to remove the tail, the product is purified further by standard methods, such as size-exclusion chromatography or high-performance liquid chromatography HPLC.

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

As additional glycoproteins are identified and cloned, there is an increasing need for more effective chromatographic methods, production systems that mimic mammalian glycosylation patterns, and fast, reproducible analytical methods to minimize microheterogeneity during manufacture. Variability in oligosaccharide biosynthesis has been found to be an important source of heterogeneity for glycoproteins produced by eukaryotic cells Marino, Glycoprotein oligosaccharides are covalently attached to proteins through the amino acid serine O-linked or asparagine N-linked. If a selected carbohydrate type and site are required for bioactivity of a candidate glycoprotein, the expression system must be carefully selected.

9: Fermentation Technology

Bioprocess engineering, also biochemical engineering, is a specialization of chemical engineering or Biological engineering, It deals with the design and development of equipment and processes for the manufacturing of products such as agriculture, food, feed, pharmaceuticals, nutraceuticals, chemicals, and polymers and paper from biological.

APPLICATION OF BIOPROCESS TECHNOLOGY pdf

Introduction Peter Rand Book II. The qualities of style. 1919. Ten Timid Ghosts On A Christmas Night (Read With Me (New York, N.Y.).) History of Govenment Volume Ancient Monarc Blood rites book 2 Mary Higgins Clark presents Malice domestic 2 A Spanish inheritance Inside City Schools An introduction to public and community health evaluation The Most Beautiful Flowers Introduction to systems biology Bannermans ghosts Mary Janes Food Fun Laughter Someone like you file Book of business law Dungeons and dragons basic game 2006 Joe tidd managing innovation Grizzly Bear Hunting American ideals: American ideals. Cyber cafe management system project umentation Pour Out My Heart An introduction to agent-based modeling modeling natural social and JPS Commentary on the Haggadah (JPS Commentary) Optimization practice problems and solutions Preparing an environment supportive of behavior change Pt. 3. Bearing kingdom fruit Introduction to applied linguistics Doubt, the Beginning of Philosophy The Jeff Corwin Experience Spanish Serpentacular! (The Jeff Corwin Experience Spanish) Shibori designs and techniques Pride and prejudice revision guide V.2 David and Bathshua. Donna Marina. Undine. Intraneural injections for rheumatoid arthritis and osteoarthritis ; And, a reprint for physicians and la Proposed form of constitution by-laws of the Western Canada Irrigation Association Victorian Dundee at worship Turn into recipe book onlin Big book alcoholics anonymous 3rd edition Incredible Journey Through Life with Christ (incredible testimonials of my life) Ms project 2013 tutorial portugues Aint going to study war no more high voice