Science Education Collection

# Overview of Bioprocess Engineering

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## Abstract

Bioprocessing is a method that uses living organisms to produce a desired target product. Often, bioprocessing refers to the use of bioreactors to produce protein products from genetically engineered organisms. This field is responsible for the large-scale manufacture of biotherapeutics; drugs that have become essential to improving the quality of life for many with complex diseases like cancer, autoimmune diseases and HIV/AIDS.

This video will introduce the engineering approach to designing a targeted protein-production system. The prominent methods in the field, as well as some key challenges, and applications of the technology are also considered.

## Transcript

Bioprocess engineering is a field that uses many engineering disciplines to produce a specific product from living organisms. Typically, the organisms are genetically modified cells that are engineered to produce a specific product protein or chemical. The cells are then grown on the large scale in order to produce the product which is later purified using downstream processes, such as chromatography. This video will introduce an example bioprocess, review prominent methods in the field, as well as some key challenges and applications of the technology.

Let's take a look at an example bioprocess using cells to produce a product protein. First, the organism is selected, which can be bacterial, fungal, or mammalian, depending on its ability to produce the desired product. The cells are genetically modified to maximize their ability to produce the product and minimize unnecessary side processes. The modified cells are grown on the large scale called the upstream process. A common upstream technique is a suspension culture, which uses a vessel bioreactor to grow the cell culture. The culture is expanded and cell density increases by transitioning to larger and larger volumes. Once the culture has reached the desired volume, the product protein is harvested from the cells, either through secretion, where the cells spit out the protein, or by lysis, where the cell is broken to release it. The product is then purified in the downstream process to remove contaminants such as cell debris and other proteins. A typical downstream process uses many types of technology in series to purify and concentrate the product. Filtration is often used first to remove cell debris and large particulates. Chromatography is another technology used to isolate and concentrate the protein of interest. The purified final product is then lyophilized, or freeze-dried, to stabilize the protein for storage. Typical bioprocesses are first designed on the laboratory scale, then scaled up to pilot scale, before further scaling for manufacturing. Now that we've introduced a basic bioprocess, let's take a look at some prominent methods in the field.

Mammalian cell culture is most often used in the industrial production of recombinant protein therapeutics. Chinese hamster ovary cells, or CHO cells, are one of the most common cell types used. Unlike bacterial cells, mammalian cells are able to do complex post-translational modifications to proteins. These modifications are structural or chemical changes made to the protein after it is translated in the ribosome. This is essential to producing complex structures that are necessary for therapeutic proteins. Mammalian cell culture requires careful considerations during growth, as the cells are more sensitive than bacterial cells. Effective aeration is required. However, shear damage must be minimized. A well-controlled homogeneous environment is also necessary, with strict pH and temperature control and rapid removal of toxic products. Industrial processes are scaled-up to produce a high volume of the product. Scale-up isn't as easy as simply proportionally increasing the volume and therefore the size of the equipment. A scaling factor is used, which is the ratio of the mass flow of the full-scale unit to the pilot unit. Scaling factors are used to determine the size of geometrically similar tank reactors. For example, as volume scales, with the scaling factor S, the tank diameter scales with S to the 1/3. This is because of mass and heat transfer limitations with the larger tank volume.

The manufacture of biological products utilizes living organisms, which are susceptible to contamination. Contaminant organisms can be bacteria, fungi, or viruses, and can arise from personnel, materials, or equipment used in manufacturing. Microbial contamination introduces product variability and can cause degradation of the product protein. Many bioprocesses are used to produce drug products, which are heavily regulated by government agencies to ensure that they are safe and effective. The drug itself first goes through rigorous laboratory tests and clinical trials. Once the drug is approved, the manufacturing process must also undergo examination and approval. Regulation, though essential to ensuring a safe final product, results in added constraints on the engineering process. Strict limitations are placed on parameters, such as permissible reagents, contaminants, and concentrations.

Now that you've seen some of the common techniques and challenges in bioprocessing, let's take a look at some real world applications. Unlike small molecule drugs like aspirin and acetaminophen, many complex drugs are recombinant proteins and are made via bioprocessing. Recombinant protein therapeutics have rapidly increased in the last 25 years, with dozens of targeted therapies. AIDS, cancer, infectious diseases, wound healing, nutritional disorders, stroke, and septic shock are just a few of the areas where protein therapeutics are offered as therapy. Bioprocessing is also used to make biofuels, such as ethanol. Ethanol is produced from cellulosic material, such as sugar cane or corn. The process begins with the isolation of cellulose from feedstocks, followed by the enzymatic hydrolysis and fermentation with yeast. This bioprocess is performed on the manufacturing scale in order to produce large amounts of ethanol for alternative energy.

You've just watched JoVE's introduction to bioprocessing. You should now understand the basic bioprocess, some common methods and challenges, as well as applications of the technology. Thanks for watching.