0905423
Biochemical Engineering

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First Semester 2016/2017

INTRODUCTION

Biochemical Engineering

Biochemical engineering is concerned with conducting biological processes on an industrial scale. This area links biological sciences with chemical engineering.

The role of biochemical engineers has become more important in recent years due to the dramatic developments of biotechnology.

Biotechnology

Broad Definition

- Commercial techniques that use living organisms, or substances from those organisms, to make or modify a product, including techniques used for the improvement of the characteristics of economically important plants and animals and for the development of microorganisms to act on the environment.

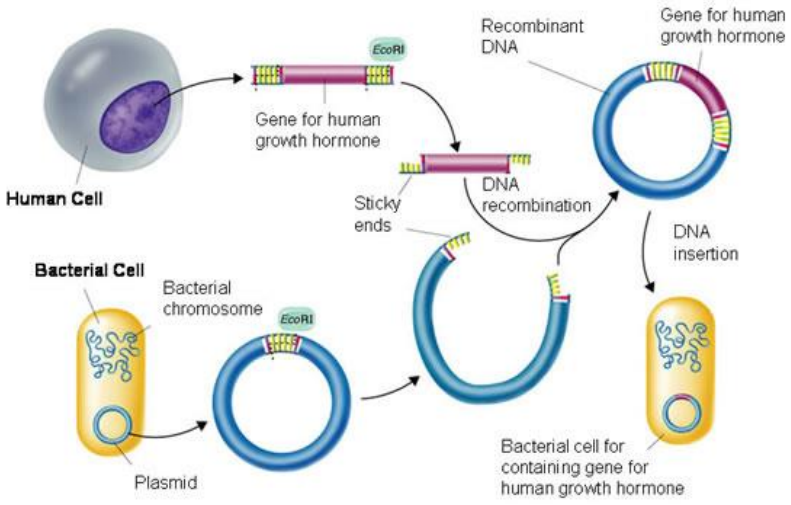
Historical Examples of Biotechnology

- Since ancient days, people knew …
  - how to utilize microorganisms to ferment beverage and food, *though they did not know what was responsible for those biological changes*.
  - how to crossbreed plants and animals for better yields.
- In recent years, the term *biotechnology* is being used to refer to novel techniques such as ***recombinant DNA*** and ***cell fusion***.

Biotechnology in Recent Years

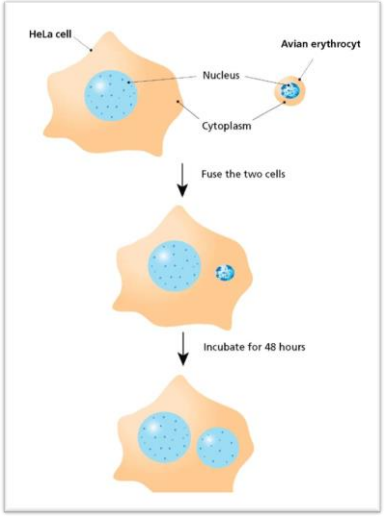
- **Recombinant DNA** allows the direct manipulation of genetic material of individual cells, which may be used to develop microorganisms that produce new products as well as useful organisms.
- The laboratory technology for the genetic manipulation within living cells is also known as *genetic engineering.*
- A major objective of this technique is to splice a foreign gene for a desired product into circular forms of DNA (plasmids), and then to insert them into an organism, so that the foreign gene can be expressed to produce the product from the organism.

Recombinant DNA



Biotechnology in Recent Years

- **Cell fusion** is a process to form a single hybrid cell with nuclei and cytoplasm from two different types of cells in order to combine the desirable characteristics of the two.



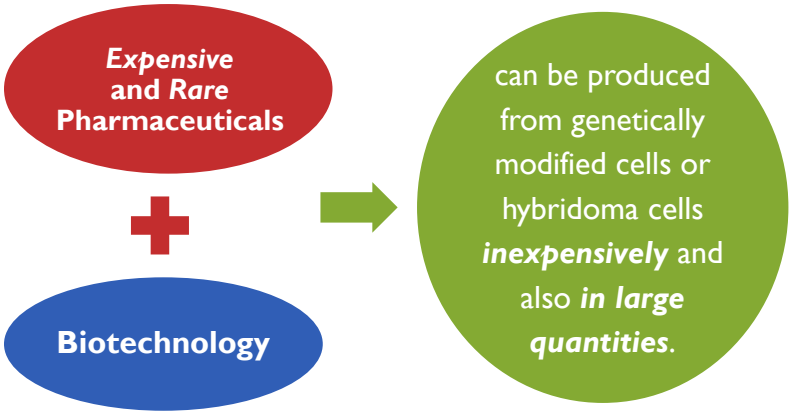
Cell Fusion Example

- *Specialized cells* of the immune system can **produce useful antibodies**. However, it is difficult to cultivate those cells because **their growth rate is very slow**.
- On the other hand, certain *tumor cells* have the traits for **immortality and rapid proliferation**.
- By **combining** the two cells by fusion, a hybridoma can be created that has **both traits**.
- The monoclonal antibodies (MAbs) produced from the hybridoma cells **can be used for** diagnosis, disease treatment, and protein purification.

Applications of Biotechnology

- See distributed Table 1.1
- **Assignment # 1**
  - Choose a partner, then together choose from the table one application of biotechnology, write 2 pages paper (400 words) about this application.
  - Due: Thursday 22/9/2016

Applications of Biotechnology



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- The recombinant DNA or cell fusion technologies have been initiated and developed by **pure scientists**, whose ***end results*** can be the development of a new breed of cells in minute quantities that can produce a product.
- Successful **commercialization** of this process requires the *development of a large-scale process* that is ***technologically viable*** and ***economically efficient***.
- To scale up a laboratory-scale operation into a large industrial process, **we cannot just make the vessel bigger**.

Biochemical Engineering

- For example, in a laboratory scale of 100 mL, a small Erlenmeyer flask on a shaker can be an excellent way to cultivate cells, but for a large-scale operation of 2,000 L, we cannot make the vessel bigger and shake it.
- ***We need to design an effective bioreactor to cultivate the cells in the most optimum conditions.***
- Therefore, ***biochemical engineering*** is one of the major areas in biotechnology important to its commercialization.

Biochemical Engineering

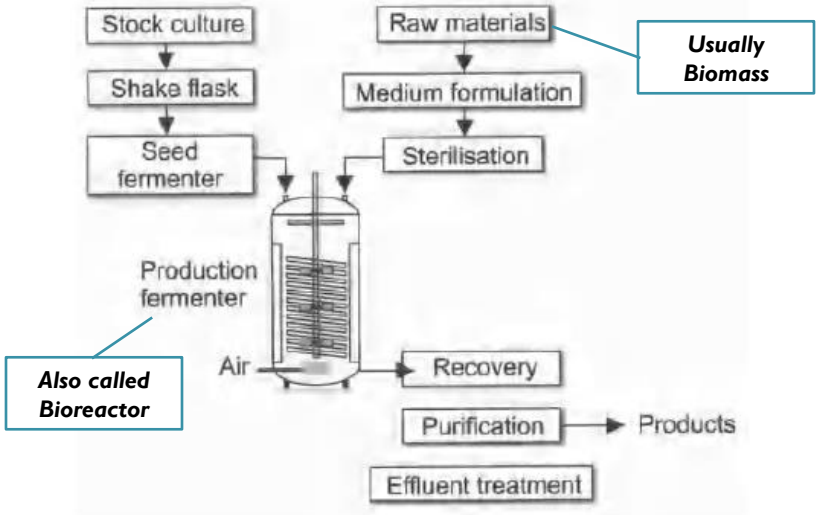
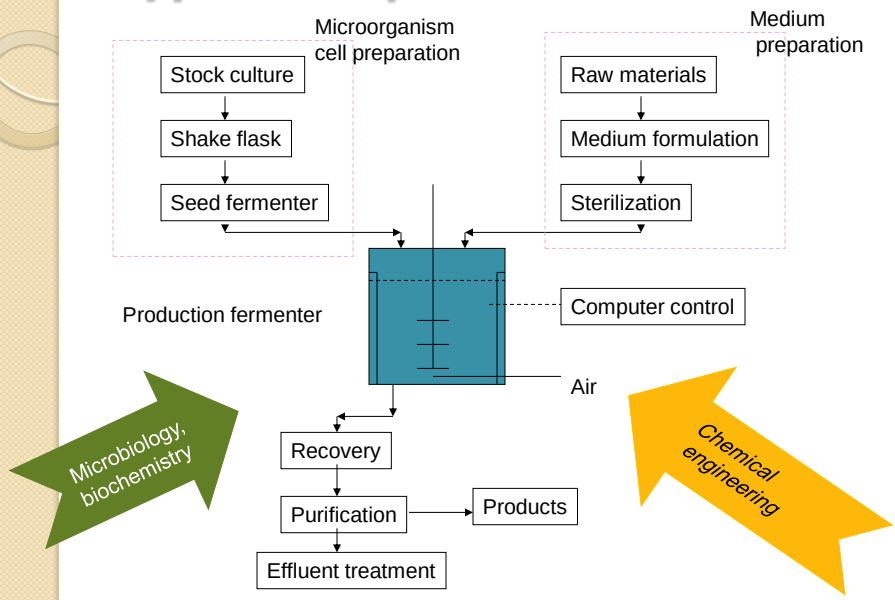


Fig. 1.1 Typical biological process

Typical Bioprocess



Batch Fermenter

Biochemical Engineering

- To carry out a bioprocess on a large scale, biochemical engineers need to work together with biological scientists:
  1. to obtain the **best biological catalyst** (microorganism, animal cell, plant cell, or enzyme) for a desired process
  2. to create the **best possible environment** for the catalyst to perform by designing the bioreactor and operating it in the **most efficient way**
  3. to separate the desired products from the reaction mixture in the **most economical way**

Process Development and Design Questions

1. *What change can be expected to occur?*
2. *How fast will the process take place?*
3. *How can the system be operated and controlled for the maximum yield?*
4. *How can the products be separated with maximum purity and minimum costs?*

1. What change can be expected to occur?

- To answer this question, one must have an understanding of the basic sciences for the process involved.
- These are microbiology, biochemistry, molecular biology, genetics, and so on.
- Biochemical engineers need to study these areas to a certain extent.
- It is also true that the contribution of biochemical engineers in selecting and developing the best biological catalyst is quite limited unless the engineer receives specialized training.
- However, it is important for biochemical engineers to get involved in this stage, so that the biological catalyst may be selected or genetically modified with a consideration of the large-scale operation.

2. How fast will the process take place?

- If a certain process can produce a product, it is important to know how fast the process can take place.
- Kinetics deals with rate of a reaction and how it is affected by various chemical and physical conditions.
- This is where the expertise of chemical engineers familiar with chemical kinetics and reactor design plays a major role.
- Similar techniques can be employed to deal with enzyme or cell kinetics.
- To design an effective bioreactor for the biological catalyst to perform, it is also important to know how the rate of the reaction is influenced by various operating conditions.
- This involves the study of thermodynamics, transport phenomena, biological interactions, clonal stability, and so on.

3. How can the system be operated and controlled for the maximum yield?

- For the optimum operation and control, reliable on-line sensing devices need to be developed.
- On-line optimization algorithms need to be developed and used to enhance the operability of bioprocess and to ensure that these processes are operated at the most economical points.

4. How can the products be separated with maximum purity & minimum costs?

- For this step, the downstream processing (or bioseparation), a biochemical engineer can utilize various separation techniques developed in chemical processes such as ….

  distillation, absorption, extraction, adsorption, drying, filtration, precipitation, and leaching.
- In addition to these standard separation techniques, the biochemical engineer needs to develop novel techniques which are suitable to separate the biological materials.
- Many techniques have been developed to separate or to analyze biological materials on a small laboratory scale, such as chromatography, electrophoresis, and dialysis.
- These techniques need to be further developed so that they may be operated on a large industrial scale.

Biological Process

- Industrial applications of biological processes are to use living cells or their components to effect desired physical or chemical changes.
- Major advantages of Biological over traditional chemical processes:
  1. *Mild reaction condition*
  2. *Specificity*
  3. *Effectiveness*
  4. *Renewable resources*
  5. *Recombinant DNA technology*

Biological Process Advantages

1. *Mild reaction condition*
   - at room temperature, atmospheric pressure, and fairly neutral medium pH

   ➔ the operation is less hazardous, and the manufacturing facilities are less complex compared to typical chemical processes.
2. *Specificity*
   - An enzyme catalyst is highly specific and catalyzes only one or a small number of chemical reactions.
   - A great variety of enzymes exist that can catalyze a very wide range of reactions.

Biological Process Advantages

3. *Effectiveness*
   - Rate of an enzyme-catalyzed reaction is usually much faster than that of the same reaction when directed by nonbiological catalysts.
   - Small amount of enzyme is required to produce the desired effect.
4. *Renewable resources*
   - The major raw material is biomass which provides both the carbon skeletons and the energy required for synthesis for organic chemical manufacture.
5. *Recombinant DNA technology*
   - The development of this technology promises enormous possibilities to improve biological processes.

Biological Process Disadvantages

1. *Complex product mixtures*
2. *Dilute aqueous environments*
3. *Contamination*
4. *Variability*

Biological Process Disadvantages

1. ***Complex product mixtures***
   - In cases of cell cultivation (microbial, animal, or plant), multiple enzyme reactions are occurring in sequence or in parallel, the final product mixture contains cell mass, many metabolic by-products, and a remnant of the original nutrients.
   - The cell mass also contains various cell components.

Biological Process Disadvantages

2. ***Dilute aqueous environments***
   - Components of commercial interests are only produced in small amounts in an aqueous medium
     →separation is very expensive.
   - Products of bioprocesses are frequently heat sensitive, traditional separation techniques cannot be employed. → novel separation techniques that have been developed for analytical purposes, need to be scaled up.

Biological Process Disadvantages

3. ***Contamination***
   - Fermenter system can be easily contaminated, since many environmental bacteria and molds grow well in most media.
   - The problem becomes more difficult with the cultivation of plant or animal cells because their growth rates are much slower than those of environmental bacteria or molds.
4. ***Variability***
   - Cells tend to mutate due to the changing environment and may lose some characteristics vital for the success of process.
   - Enzymes are comparatively sensitive or unstable molecules and require care in their use.

Fermentation

- Traditional Definition:
  - the process for the production of alcohol or lactic acid from glucose ($C_6H_{12}0_6$)

$$C_6H_{12}O_6 \xrightarrow{yeast} 2C_2H_5OH + 2CO_2$$

$$C_6H_{12}O_6 \xrightarrow{enzymes} 2CH_3CHOHCOOH$$

- Broader Definition:
  - an enzymatically controlled transformation of an organic compound