FDE 328
INDUSTRIAL MICROBIOLOGY

Production Methods

Production Methods

- **Surface Culture Method**

- **Submerged Culture Method**

Microbial fermentations in liquid media can be carried out under different operating conditions;

- **Batch cultivation**
- **Fed-batch cultivation**
- **Continous cultivation**

Surface Culture Method

- In this method, microorganisms are grown on liquid semi-solid and solid substrates.
- Often a membrane is formed on the substrate, and a micelle cover is formed in molds.
- Although other microorganisms stay only in this surface part of the medium, mold micelles descend to the lower layers.
- In this method, the higher the ratio of substrate surface to depth, the faster the production.

Submerged Culture Method

- In this method, microorganisms are grown in the substrate.
-
- Necessary air is given into the substrate with the help of ventilation devices.
- The simplest application of this method is shaking and is often used in the laboratory for the preparation of starter culture (pre-culture).
- In larger volume fermenters, air is introduced into the substrate just below the mixer. Thus, the air given is distributed thoroughly in the substrate.
- In the submerged culture (deep culture) method, especially when working with aerobic microorganisms, it is necessary to provide sufficient amount of air continuously.

Batch cultivation

- **Batch processes** are closed systems where there are no additions following inoculation, apart from acid or alkali for pH control and input of air for aerobic fermentations.
- In **batch fermentations** there is a definite beginning and end to the process.
- A fermenter is loaded, sterilized and inoculated, and the organism is grown through a typical batch profile.
- The product is then harvested and the fermenter must be cleaned before restarting the cycle. This non-productive phase is referred to as ‘down-time’.
- Examples of this mode of operation include the production of alcoholic beverages, most amino acids, enzymes, organic acids, etc.

Batch cultivation

- The advantages of batch systems are that initial capital expenditure is lower and, if contamination occurs, it is relatively simple to terminate and restart a new fermentation cycle.
- Batch systems are successfully used in the production of many traditional fermentation products; and for producing secondary metabolites, such as antibiotics, where the cells are first grown beyond the rapid growth phase prior to the accumulation of these metabolites.
- However, batch fermentations are theoretically less effective for the production of biomass and primary (growth-associated) metabolic products.
- Only a small fraction of each batch fermentation cycle is productive, as there may be a considerable lag period and it is only in the later stages of the exponential phase that large quantities of the product are generated.
- Other disadvantages of batch systems are the batch-to-batch variability of the product; plus increased non-productive down-time, involving cleaning, sterilizing, refilling and poststerilization cooling.
- The increased frequency of sterilization may also cause greater stress on instruments and probes. In addition, the running costs are greater for preparing and maintaining stock cultures, and generally more personnel are required for operating batch processes.

Fed-batch cultivation

- For this mode of operation, extra nutrients are added as the fermentation progresses, which increases the fermentation volume.
- Additions may be made continuously, intermittently or as a single supplementation, often when a batch culture approaches the end of the rapid growth phase.
- Fed-batch operation can extend the product formation phase and may overcome problems associated with the use of repressive, rapidly metabolized, substrates.
- This method is also useful where a substrate causes viscosity problems or is toxic at high concentrations.
- Fed-batch with recycle of cells (biomass) can also be used for specific purposes, e.g. some ethanol fermentations and waste-water treatment processes.
- Fed-batch systems have been successfully used for producing baker's yeast and penicillin.

Continous cultivation

- Continuous culture is an open system where fresh medium is continuously added and culture is simultaneously removed at the same rate, resulting in a constant working volume.
- In continuous systems, cells grow exponentially for extended periods at a specified predetermined growth rate. Furthermore, the system has the property of reaching a steady state in which the concentration of limiting nutrient and the cell number do not vary with time.
- Consequently, in theory, such systems are more productive than batch systems.
- Continuous fermentations are particularly well suited for the production of biomass and growth-associated primary metabolites.
- Their reduced down-time and lower operating costs are also desirable attributes.
- However, they require higher initial capital expenditure and, to date, relatively few large-scale industrial examples have become established, other than for biomass, fuel/industrial ethanol and effluent treatment.

Continous cultivation

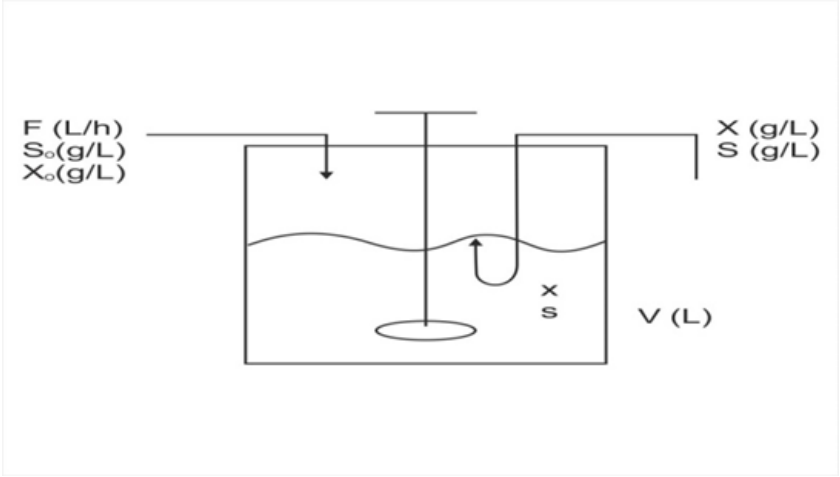
- Problems associated with continuous culture processes, other than waste-water treatment, include the fact that throughout their 20–50 days or longer operation, sterility must be maintained and a continuous supply of media of constant composition provided.
- However, these difficulties can be overcome by GMP and good microbiological practices.
- Nevertheless, the operating conditions place strong selection pressure on the organism.
- Any genetic instability may lead to the generation of low-yielding mutants that may outgrow the original high-yielding strain.

Continous cultivation

- Microorganism growth can be preserved for a long time in continuous culture.

- Also; culture conditions such as cell concentration, specific growth rate, substrate and product concentrations can be maintained in a "**steady state**" where they do not change with time.

Continous cultivation



Continous cultivation

- In continuous culture, if the substrate feed rate is adjusted according to the chemical composition of the culture medium (ie the chemical environment), this is called a "**chemostat**";

- If it is adjusted based on the cell concentration in the culture vessel by measuring the optical density of the culture medium, it is called a "**turbidiostat**".