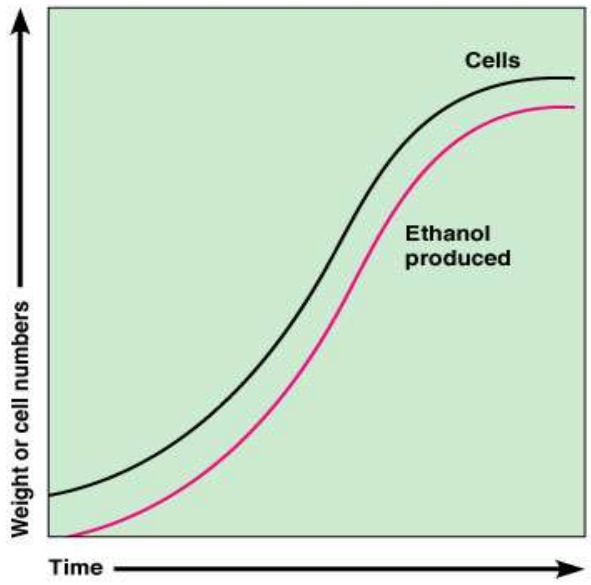
Microbial products of industrial use:

1-Primary metabolites:

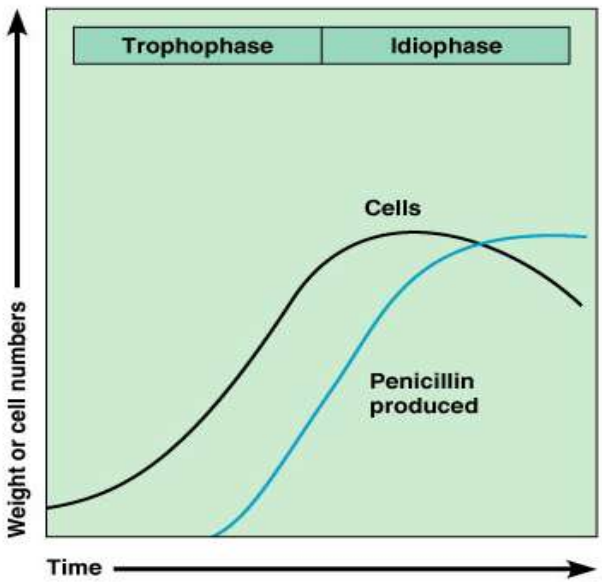
After inoculation when microbial growth is in exponential or trophophase many intermediate metabolic products are produced. These are further needed either in growth *(e.g.* amino acids, nucleotides, proteins, carbohydrates, lipids, vitamins, etc), or energy yielding catabolism *(e.g.* acetone, ethanol, butanol, organic acids, etc). Therefore, the metabolites produced during trophophase are known as 'primary metabolites'. The concentration of some of the metabolites exceeds many times more than required by the producers.

2-Secondary metabolites:

When the trophophase of growing culture is over, and then starts the idiophase. Microbial products other than primary metabolites produced during idiophase by slow growing or non-growing cells of microorganisms are known as secondary metabolites such as alkaloids & antibiotics, which are not essential for growth, produced only by few organisms **e.g:** spore-forming microorganisms(Fungi, *Streptomyces* & *Bacillus*).



Primary metabolites



Secondary metabolite

3- Microbial biomass: This refers to the biomass formed by the microorganisms on the suitable substrate. Numerous species of algae, bacteria, yeasts and fungi are used to produce biomass from the various carbon substrates available. Microbial biomass is produced commercially as single cell protein (SCP) for human food or animal feed, and as viable yeast cells (*Saccharomyces cerevisae*)to be used in the baking industry ,a bacterium (*Lactobacillus bulgaricus*) for Yogurt & an algae (*Spirulina*), the economics of the production of SCP as protein supplemented food, health food, in the therapeutic and natural medicine, in cosmetics. Microbial biomass is broadly used for three purposes:

1. Viable microbial cells are prepared as fermentation starter cultures and inoculum for food and beverage fermentations, waste treatment processes, silage production, agricultural inoculants, mineral leaching and as bio-pesticides

2. As a source of protein for human food, because it is often odorless and tasteless, and can therefore be formulated into a wide range of food items; and

3. Animal fodder.

4-Recombinant products: Genetic information in organisms is stored in their DNA. This molecule holds instructions for how the organism looks and functions.The techniques of DNA technology are sometimes used to modify the genome of a living cell or organism. The process of altering the genetic material of cells or organisms to allow them to make new substances is called genetic engineering. Recombinant DNA results when DNA from two different organisms is joined.

Table (2): Recombinant products of industrial importance

Gene	Original source	Gene expressed in	Usage
Insulin	Human pancreas	*E.coli, Pichia pastoris*	Control of diabetes
Human growth hormone	Human pituitary gland	*E.coli*	Increase in height
Clotting factor VIII	Blood cells	*Saccharomyces cerevisiae , Pichia pastoris*	To stop bleeding
Tissue plasminogen activator	Blood cells	*Saccharomyces cerevisiae, Pichia pastoris*	Dissolution of blood clots

Important microbial products:

Industrial microbiology has provided products that have impacted our lives in many ways. They include industrial and agricultural products, food additives, medical products for human and animal health, and biofuels (Table:3)

Table 3: Major Microbial Products and Processes of Interest in Industrial Microbiology and Biotechnology

Substances	Microorganisms
Industrial Products	
Ethanol (from glucose)	*Saccharomyces cerevisiae*
Ethanol (from lactose)	*Kluyveromyces fragilis*
Acetone and butanol	*Clostridium acetobutylicum*
2,3-butanediol	*Enterobacter, Serratia*
Enzymes	*Aspergillus, Bacillus, Mucor, Trichoderma*
Agricultural Products	
Gibberellins	*Gibberella fujikuroi*
Food Additives	
Amino acids (e.g., lysine)	*Corynebacterium glutamicum*
Organic acids (citric acid)	*Aspergillus niger*
Nucleotides	*Corynebacterium glutamicum*
Vitamins	*Ashbya, Eremothecium, Blakeslea*
Polysaccharides	*Xanthomonas*
Medical Products	
Antibiotics	*Penicillium, Streptomyces, Bacillus*
Alkaloids	*Claviceps purpurea*
Steroid transformations	*Rhizopus, Arthrobacter*
Insulin, human growth hormone, somatostatin, interferons	*Escherichia coli, Saccharomyces cerevisiae,* and others (recombinant DNA technology)
Biofuels	
Hydrogen	Photosynthetic microorganisms
Methane	*Methanobacterium*
Ethanol	*Zymomonas, Thermoanaerobacter*

Antibiotics: Many antibiotics are produced by microorganisms, predominantly by *Actinomycetes* in the genus *Streptomyces* (*Streptomyces griseus*) and by filamentous fungi (*Penicillium chrysogenum*)

Amino Acids : Such as lysine and glutamic acid are used in the food industry as nutritional supplements in bread products and as flavor enhancing compounds such as monosodium glutamate . Production of glutamic acid and several other amino acids in large quantities is now carried out using mutants *Corynebacterium glutamicum* .

Polysaccharides: The bacterium *Xanthomonas campestris*, produces a polysaccharide called xanthan, which is used to stabilize and thicken foods and as a base for cosmetics. The bacterium *Leuconostoc mesenteroides* produces dextran is used to extend blood plasma.

Organic Acids: Citric, acetic (*Acetobacter*), lactic *(Lactobacillus delbrueckii*) ,fumaric (*Rhizopus nigricans*), and gluconic acids(*Aspergillus niger*) are major products. The essence of citric acid fermentation involves limiting the amounts of trace metals such as manganese and iron to stop *Aspergillus niger* growth at a specific point in the fermentation.

Enzymes: Produced during fermentation are mostly extracellular but a few are intracellular. Intracellular enzymes may be produced in industries, but with many difficulties. The important extracellular enzymes are amylases, cellulases, invertase, 6-galactosidase (lactase), esterase, lipases, proteases

Types of fermentation process:

1- Batch fermentation:

Substrate added to system all at once and taken through a limited run until product is harvested. It is a discontinuous process (closed system) and the fermentor has to be cleaned after each process and a fresh batch started. It includes the following five steps: Medium added, Fermentor sterilized, Inoculum added, Fermentation, followed to completion Culture harvested.

Characteristics of a batch fermentation system:

- Simplest fermentor operation.
- Sterilization can be performed in the reactor.
- All nutrients are added before inoculation.
- Maximum levels of C and N are limited by inhibition of cell growth.
- Biomass production limited by C/N load and production of toxic waste products

Advantages: - Used where end product required in more quantities at a given period of time.

- Useful where the shelf life of the end product is short.

- Useful specifically for the product produced only at the stationary phase.

2- Fed batch fermentation:

This fermentation is intermediate of both batch and continuous fermentation. Sterile nutrients are added periodically.

Characters of fed batch fermentation:

- Initial medium concentration is relatively low.
- Medium constituents are added continuously or in increment
- Controlled feed results in higher biomass and product yields.
- Fermentation is still limited by accumulation of toxic end products.
- Finally the products are harvested in one stroke.

3-Continuous fermentation:

It is a continuous process where the nutrient is continuously added to the fermentor at a fixed rate. The organisms are continuously maintained at logarithmic stage, the products are recovered continuously. The fermentor in this type are called "flow through'' fermentation.

Disadvantages: - Complete sterilization is difficult.

- More prone to contamination.

4- Solid state fermentation:

Is a microbial process in which a solid material is used as the substrate or the inert support of microorganisms growing on it. The moisture content of solid substrate ranges between 12-80%. SSF's are usually used for the fermentation of agricultural products or foods, such as rice, wheat, barley, corn and soybeans. Some food fermentations involving SSF: Wheat by *Aspergillus* , Soybean by *Rhizopus* ,Soybean by *Aspergillus*.

Characteristics of solid state fermentation:

1-The microbial distribution occurs on the solid surface, and microbial growth and product formation also occur mainly on the surface. The substrate is not uniform and not easily agitated. The culture environment is therefore heterogeneous.

2. The moisture content of a solid structure substrate is normally low, depending on the physical or chemical characteristics of the substrate.

3. Heat derived from the metabolism and growth of the microorganism raises the temperature of the solid substrate bed and causes the loss of moisture.

4. SSF substrates are usually natural materials, e.g., cereals, soybeans, agricultural biomass, and solid waste.

5. The microorganisms generally used in SSF are molds that can produce amylases to degrade starch and penetrate into the solid substrate.

6. Since agitation of the substrate bed is very difficult and some activities are sensitive to shear stress, cultivation is normally stationary, except for the rotating drum and fluidized-bed fermentors.

Advantages: - A lower chance of contamination due to low moisture levels.

- High volumetric productivity,
- Relatively higher concentration of the products,
- Less effluent generation,
- Requirement for simple fermentation equipments.

Disadvantages: - Agitation of the substrate bed is difficult.

- Temperature control of the heat is very difficult because the solid substrate bed has a low thermal conductivity

- Rapid determination of microbial growth and other

fermentative parameters is very difficult

- Molds or other filamentous fungi are suitable, but bacterial growth is rare except for xerophiles (is an extremophilic organism that can grow and reproduce in conditions with a low availability of water).

Control of chemical and physical conditions:

1- Agitation of suspended cell fermentation:

Is performed to mix the three phases within a fermentor. The liquid phase (contains dissolved nutrients and metabolites) the gaseous phase (is predominantly oxygen and carbon dioxide), and the solid phase (is made up of the cells and any solid substrates) that may be present.

The agitation is most important in case of aerobic fermentation due to:

- Microorganisms can take up oxygen only from the liquid phase.
- It enhances rate of transfer of gases into liquid.
- It prolongs retention of air bubbles in suspension
- It reduces bubble size to increase the surface area for oxygen transfer,
- Prevents bubble coalescence
- And decreases the film thickness at the gas-liquid interface.

2- Heat transfer:

In fermentor design, efficient heat transfer is important in controlling the temperature during sterilization of the fermentor & maintaining constant incubation temperature in the fermentation media. Heat generated in the fermentation is primarily due to metabolic activity of microorganisms and mechanical agitation processes. If this heat is not controlled ,the fermentation will shut down because of rise of temperature. No direct contact exists between the cooling/ heating system and the fermentation medium. The heat is conducted through the vessel wall, coils and baffles. These systems are also used to sterilize the vessel and contents before inoculation, by the injection of pressurized steam. Automatic temperature control during the fermentation is accomplished by injecting either cold or hot water into the outer jacket and/or internal coils.

3- Mass transfer:

The growth of microorganisms is dependent on the amount of soluble nutrients present in the media& microorganisms are unable to take up insoluble nutrients. The transfer of nutrients from aqueous phase into microbial cells is straightforward as the nutrients are normally provided in excess.The majority of fermentation processes are aerobic **.**Oxygen is the most important gaseous substrate for microbial metabolism, and carbon dioxide is the most important gaseous metabolic product **.**The oxygen transfer in aerobic fermentations is rather more complex. It is usually provided in the form of air. Sterilized air is added to fermentor in the form of small air bubbles in order to provide large surface area compared to its volume.

Table 30.1 **Fermentor sizes for various industrial processes**

Size of fermentor (liters)	Product
1–20,000	Diagnostic enzymes, substances for molecular biology
40–80,000	Some enzymes, antibiotics
100–150,000	Penicillin, aminoglycoside antibiotics, proteases, amylases, steroid transformations, amino acids, wine, beer
200,000–500,000	Amino acids (glutamic acid), wine, beer