6.3 Biotechnology and batch cultures

Biotechnology in production, the growth curve and commercial applications of biotechnology

What is biotechnology?

The term **biotechnology** refers to technological processes which involve the use of living organisms. Biotechnology today is used in a very wide range of fields. It can be utilised to help produce foodstuffs, drugs and many more products. Biotechnology was first described some 100 years ago, but the process itself has been happening for thousands of years, for example producing cheese and yoghurt.

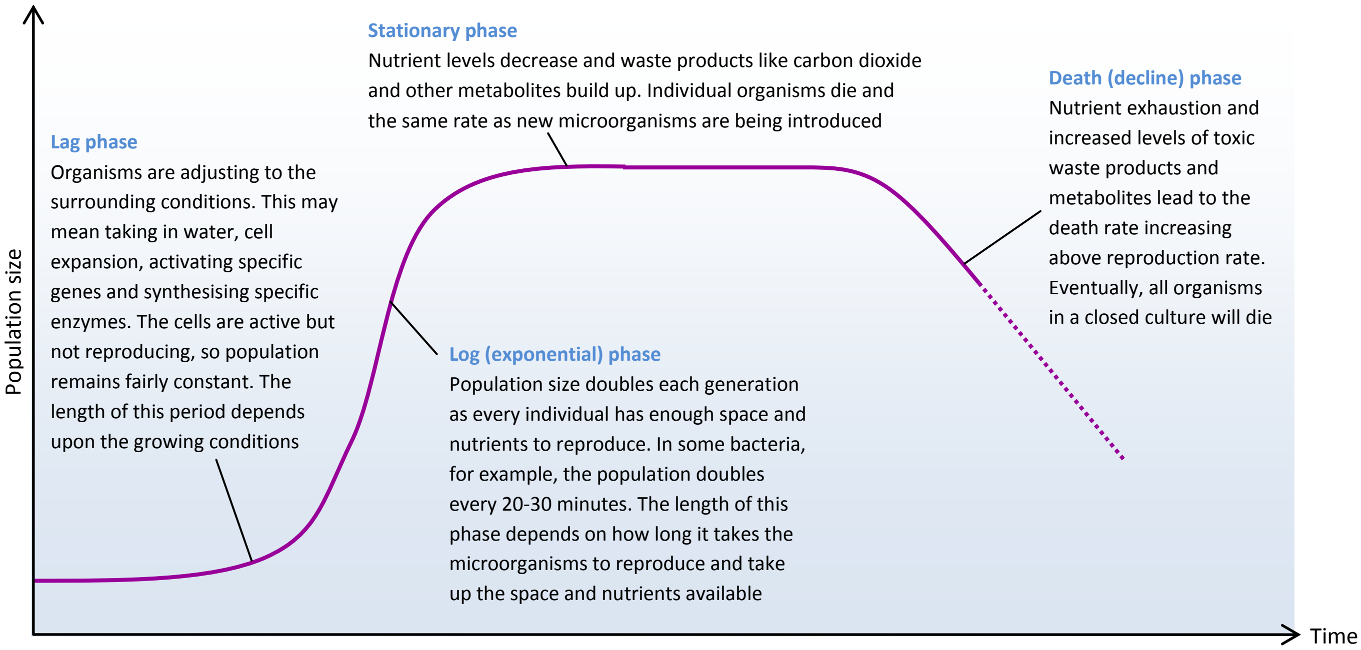
Purpose	Examples	Organisms involved
Food production	Cheese and yoghurt making	Bacterial growth in milk changes the flavour and texture to generate different foods, and the bacteria prevents the growth of other bacteria which would cause the food to spoil
	Mycoprotein	Growth of a specific fungus in a culture: the fungal mycelium produced is separated and processed as food
Drug production	Penicillin	*Penicillium* fungus is grown in culture to produce the antibiotic as a by-product of its metabolism
	Insulin	*E. coli* can be genetically modified to carry the human insulin gene so they manufacture and secrete the hormone
Production of other substances	Enzymes: pectinase	A fungus, *A. niger*, is grown in certain conductions to produce and secrete the enzyme pectinase, used in fruit juice extraction

Biotechnology makes use of microorganisms – the use of fungi and bacteria is common because microorganisms:

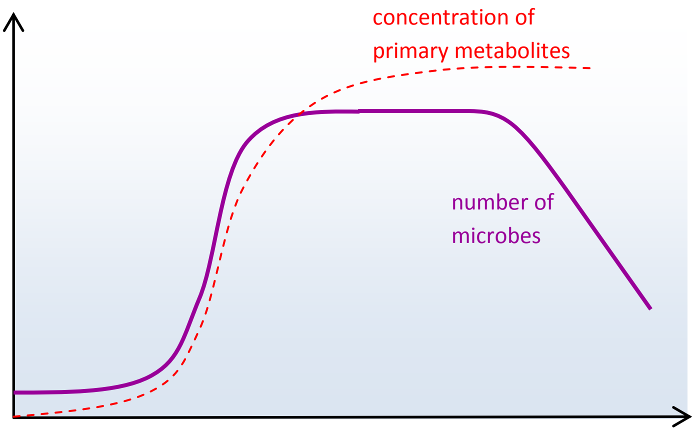
- ✓ grow rapidly in favourable conditions, being able to grow sometimes at a **generation rate** (time taken to double in numbers of microorganisms in the batch) of just 30 minutes
- ✓ often produce proteins or chemicals that are given out to the surroundings, which we can harvest
- ✓ can be genetically engineered to produce specific desired products

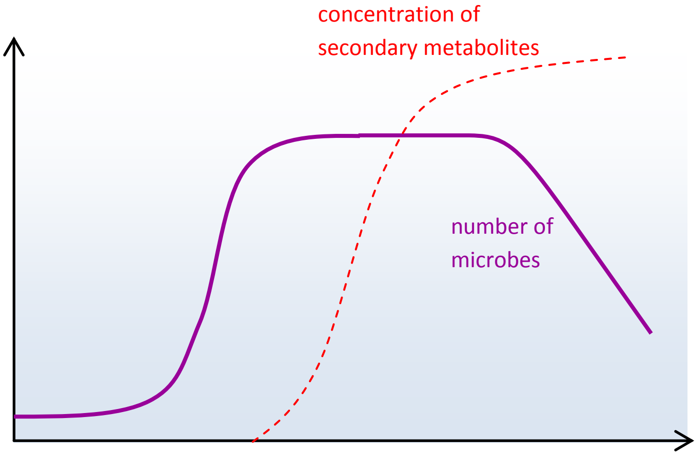
Cultures and the standard growth curve

A **culture** is a population of one type of microorganism that has been grown under controlled conditions. A **closed culture** is when growth takes place in a vessel that's isolated from the external environment – extra nutrients aren't added and waste products aren't removed from the vessel during growth. In such a closed culture, a population of microorganisms follows a standard **growth curve**.



When growing conditions are favourable (mostly during the exponential phase), microorganisms produce **primary metabolites** – small molecules which are essential for the normal growth of microorganisms. When those conditions are less favourable (mainly during the stationary phase) they produce **secondary metabolites**: products which are not essential for growth but are useful in other ways. An example of a secondary metabolite is the penicillin antibiotic, produced by the fungus *Penicillium*, which helps it to survive by killing bacteria which inhibit its growth. This is also an example of a secondary metabolite we harvest during **fermentation**. Penicillin is desirable to biotechnological industries, and so it is *cultured* on an industrial scale. Remember that *metabolism* is a process which the microorganisms undergo during the culturing, and *metabolites* are the products – not the raw materials.



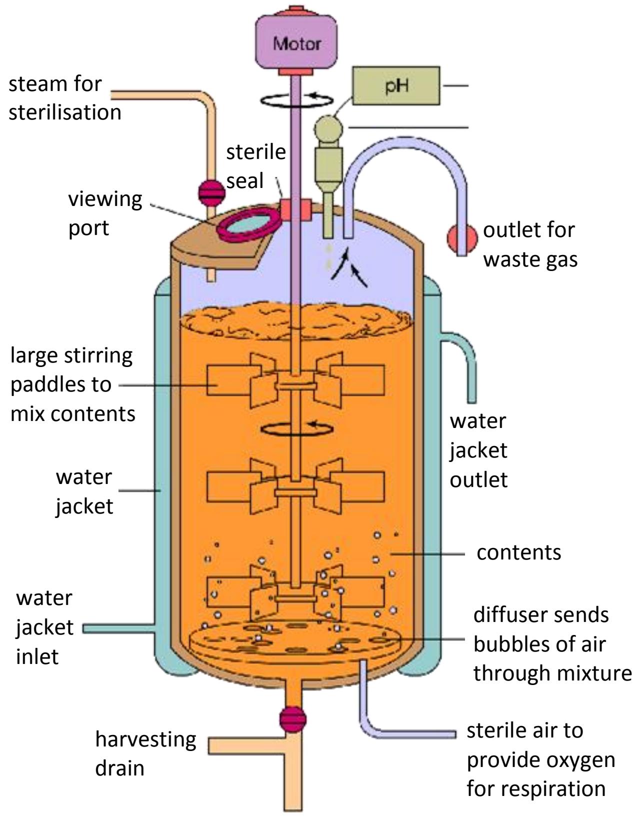


Industrial fermenters

The term fermentation refers to the culturing of microorganisms in **fermenters** (or fermentation tanks). The substances generated by the growth of microorganism cultures are separated and treated to produce the final useful product.

Cultures of microbes are grown in these large vessels, where the conditions inside are maintained to **optimum** levels for growth to maximise the yield of the desirable products, such as penicillin.

- The **pH** is monitored using a pH probe so it can be kept at optimal levels to increase enzyme efficiency, keeping the rate of reaction as high as possible to increase output
- The **temperature** is kept at optimum level using an outer **water jacket**, which controls enzyme action also
- Microbes are kept in contact with fresh medium by paddles that circulate the medium around the vessel, increasing yield as microbes have constant access to nutrients
- The volume of oxygen is kept at just the right level needed for aerobic respiration, by pumping sterile air when needed: raising yield due to increased respiration, which means microbes have more energy for growth
- Vessels are **sterilised** between uses with **superheated steam** to kill any unwanted organisms (increasing yield as it means the microbes do not have to compete with other organisms)



These industrial fermenters can be used to produce two types of culture: **batch cultures** produce metabolites in batches, so the *starter culture* is added with a set amount of growth medium, and the culture is left to grow, until it is harvested and the microbes are removed – the vessel is emptied and ready to be used again.

A **continuous culture** on the other hand has new nutrients added and waste products removed from the vessel at regular intervals, continuously. This is more useful for harvesting human hormones from bacteria, such as insulin from *E. coli*.

Batch culture	Continuous culture
A fixed volume of growth medium is added to the fermentation vessel at the start of the culture and no more is added – it is a *closed culture*	Growth medium flows through the vessel at a steady rate so there is a constant supply of fresh nutrients (an open system)
Each culture goes through the lag, exponential, stationary and death phases	The culture begins with the lag phase but is then maintained at the exponential growth phase
Product is harvested once, during the stationary phase	Product continuously harvested at a steady rate
Used when you want to produce secondary metabolites	Used when you want to harvest the primary metabolites or the actual microbes themselves

Asepsis

This is the practice of preventing **contamination** of cultures from unwanted biological microbes. **Asepsis** is very important when culturing microorganisms because contamination will affect their growth. Also, in laboratory experiments, an infected test culture can provide inaccurate results, giving invalid conclusions.

Contamination on an industrial scale can prove to be very expensive, because an entire culture needs to be disposed of, which is a large amount of wastage. There are a few aseptic techniques that can be used when working with microbes:

- washing, disinfecting and steam-cleaning the fermenter regularly and its associated pipes also
- fermenter surfaces are made of a polished stainless steel which is impenetrable and easy to clean
- sterilising the nutrient medium before adding it to the fermenter
- fine filters on all inlets and outlets on the fermenter to prevent entry for unwanted microbes