Introduction to USP – Fed-batch Operation

Your Objectives:

At the end of the lesson, you should be able to describe a fed-batch operation.

There are three strategies for cell culturing:

High cell-density culture

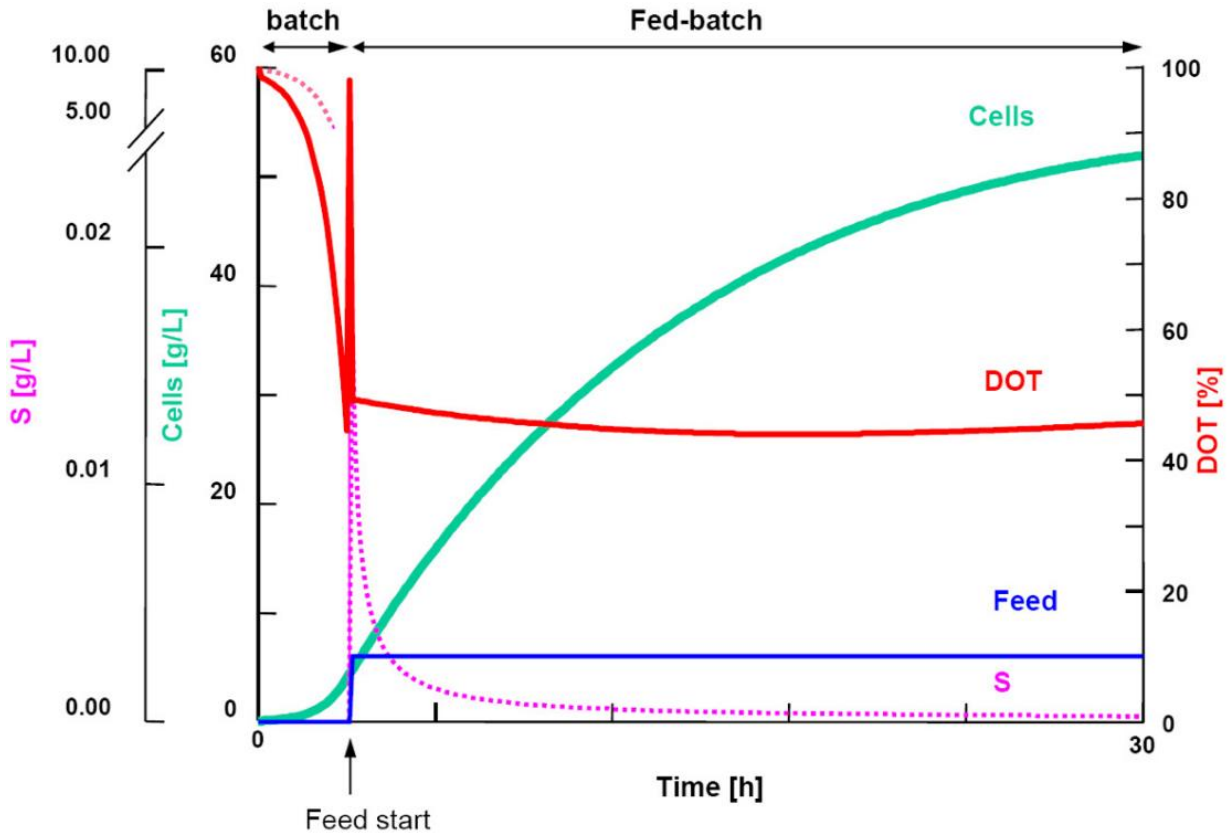
The fed-batch strategy is typically used in bio-industrial processes for reaching a high cell density in the bioreactor. Mostly, the feed solution is highly concentrated so as to avoid dilution in the bioreactor. Production of heterologous proteins by fed-batch cultures of recombinant microorganisms has been extensively studied.

Controlled addition of the a nutrient directly affects the growth rate of the culture and helps to avoid overflow metabolism (formation of side metabolites, such as acetate for Escherichia coli, lactic acid in mammalian cell cultures, and ethanol in Saccharomyces cerevisiae) as well as oxygen limitation (anærobiosis).

Constantly-fed-batch culture

The simplest fed-batch culture is one in which the feed rate of a growth-limiting substrate is constant. In other words, the feed rate is invariant during the culture, as is the case shown in the graph (where the culture volume is variable). This type of fed-batch culture, called constantly-fed-batch culture (CFBC), is well established, and both fixed-volume CFBC and variable-volume CFBC have been studied mathematically and experimentally.

The graph shows the principle of a substrate limited fed-batch cultivation with an initial batch phase. After consumption of the initial substrate (pink dotted lines), a continuous and constant feed of the substrate may begin.



Exponential-fed-batch culture

Under ideal conditions, cells grow exponentially. When the feed rate of the growth-limiting substrate is increased in proportion to the exponential growth rate of the cells, it is possible to maintain the cells' specific growth rate extendedly while keeping the substrate concentration in the culture liquid at a constant level. In order for this mode of fed-batch culture to qualify as an exponentially-fed-batch culture (EFBC), the required (volumetric or mass) feed rate must be increased exponentially with time.

Substrate limitation

Substrate limitation allows for the controlling of the reaction rates. Doing so avoids technological limitations connected with the cooling of the reactor and oxygen transfer. Substrate limitation also allows a metabolic control so as to avoid osmotic effects, catabolite repression and overflow metabolism of side products (impurities which appear during the reaction).

source: Wikipedia