BIOREACTOR ENGINEERING
Chapter 5
Culture Kinetic Study of Modifying Batch Fermentation

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Chapter Description

- Topic Outcome
  - Perform culture kinetic calculation on modifying batch bioreactor operation

- References

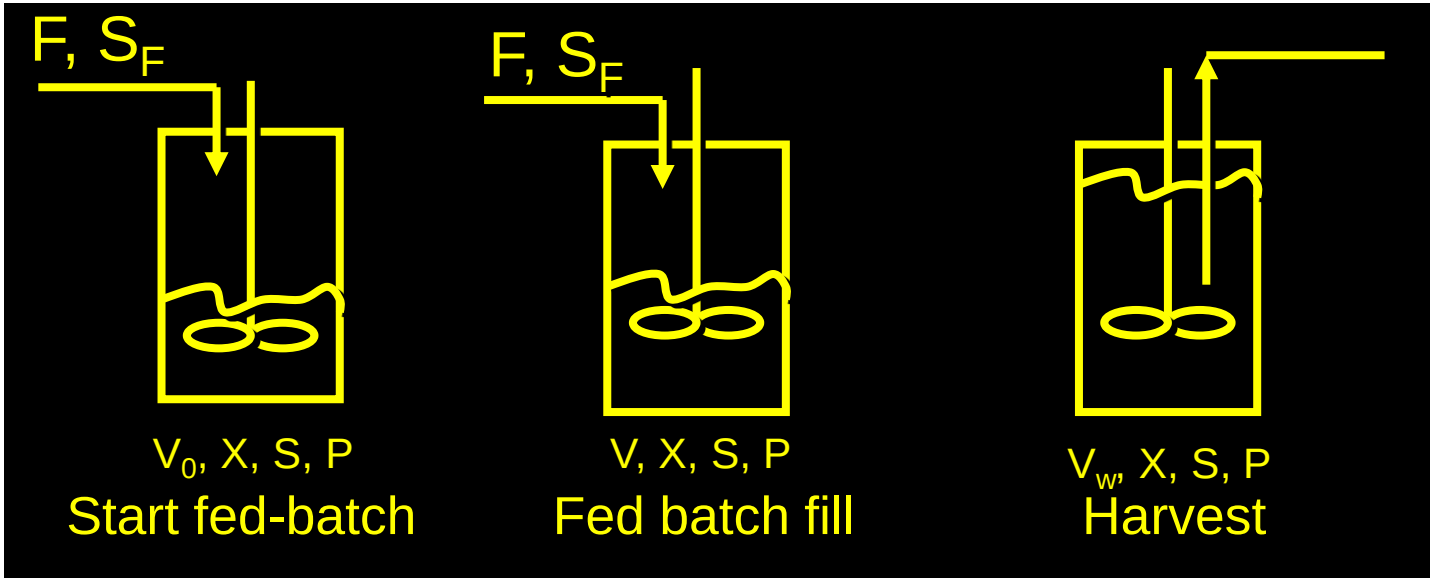
  - Doran, P.M. (2013) Bioprocess Engineering Principles. Elsevier.
  - Liu, S. (2013) Bioprocess Engineering: Kinetics, Biosystem, Sustainability and Reactor Design. Elsevier.
  - Rao, D.G. (2010) Introduction to Biochemical Engineering. McGraw Hill.

Topic Outline

- Fed-batch Operation

Fed-batch Operation

- In fed-batch cultures, substrate is fed gradually into the culture until the maximum liquid fermenter volume is reached
- No removal of the culture until the end of the process
- The concentration of substrate fed into the culture can be controlled by changing the feed rate.



Fed-batch Operation

ADVANTAGES:

- Fed-batch reactor can maintain LOW limiting substrate concentration. They are thus suited for producing product/cells when:
  - The substrate is inhibitory.
  - The oxygen uptake rate must be restricted/controlled.
  - The product/cell yields are highest at low substrate concentrations.
  - Product/cell formation is dependent on a specific nutrient composition.

Fed-batch Operation

ADVANTAGES:

- Fed-batch reactor can maintain LOW limiting substrate concentration. They are thus suited:
  - The extension of stationary phase.
  - Prolong microbe growth.
  - Feed does not need to contain all the nutrients needed to sustain growth.
  - No additional special piece of equipment required compared with the continuous fermentation mode of operation.
  - Can be operated in a various ways.
  - Allow the replacement of water loss (by evaporation) and decrease of the viscosity of the medium.

Fed-batch Operation

DISADVANTAGES:

- Higher operation cost.
- It requires previous analysis of the microorganisms.

Fed-batch Operation

Material balance across the reactor:

Culture volume in – Culture volume out = Culture volume accumulation

$$F\rho_o - 0 = \frac{d(\rho V)}{dt}$$

V_i= initial culture volume

F= constant flow rate of addition stream during fed-batch

ρ=density of the reactor contents

ρ_o= density of the feed stream

- Assume $\rho = \rho_o$ is constant.
- Rate of increase in culture volume is: $\frac{dV}{dt} = F$
- Integrate: $V = V_i + Ft$

Fed-batch Operation

Material balance on the cells:

- Cell maintenance and death are assumed to be small

Cell in – Cell out + Cell growth = Cell accumulation

$$FX_o - 0 + \mu XV = \frac{dVX}{dt}$$

- X_o= cell concentration in the feed = 0 & $\frac{dV}{dt} = F$
- Please derive the formula to get → $\frac{dX}{dt} = \mu X - DX$

Fed-batch Operation

Material balance on the substrate:

Substrate in – Substrate out – Substrate consumed = Substrate accumulation

$$FS_o - 0 - \left(\frac{\mu X}{Y_{X/S}} + \frac{q_p X}{Y_{P/S}} + mX\right)V = \frac{dVS}{dt}$$

- S_o= substrate concentration in the feed = 0 & $\frac{dV}{dt} = F$
- Assume:
  - $mX \ll \frac{\mu X}{Y_{X/S}}$ can be neglected.
  - If no product is formed

Please derive the formula to get →

$$\frac{dS}{dt} = D(S_o - S) - \frac{\mu X}{Y_{X/S}}$$

Fed-batch Operation

- Fed-batch culture is an unsteady-state process. The values of D, V, X, S, and P inside the vessel may be changing with time.
- We assume fed-batch operation starts after the fermenter is operating as a batch process (cell concentration is high, substrate is exhausted).
- As substrate is fed, it is totally consumed, cell concentration remains high. So, $\frac{dX}{dt} = 0$

Fed-batch Operation

- The process reaches quasi-steady state (when nutrient consumption rate is nearly equal to nutrient feed rate).
- So, $\frac{dX}{dt} = 0$ and Monod equation: $\mu = \mu_{max} \frac{S}{K_s + S}$
- From mass balance on cells, $S \cong \frac{K_S D}{\mu_{max} - D}$

Fed-batch Operation

- The process reaches quasi-steady state (when nutrient consumption rate is nearly equal to nutrient feed rate).
- So, $\frac{dS}{dt} = 0$
- From mass balance on substrate, $X \approx Y_{X/S} S_o$

Fed-batch Operation

- The cell concentration in the vessel at any time t is: $X = \frac{X^t}{V}$
- The rate of change in cell concentration is:

$$\frac{dX}{dt} = \frac{d\left(\frac{X^t}{V}\right)}{dt} = \frac{V\left(\frac{dX^t}{dt}\right) - X^t\left(\frac{dV}{dt}\right)}{V^2}$$

- At quasi-steady state, $\frac{dX}{dt} = 0$
- Rearrange: $\frac{dX^t}{dt} = \frac{X^t}{V}\frac{dV}{dt} = XF = Y_{X/S}S_oF$

Fed-batch Operation

- Integrate: $X^t = X_i^t + Y_{X/S} S_o F t$ OR $X^t = V_i X_i + XFt$

where

X^t = mass of cells in the fermenter after t

X^t_i = mass of cells in the fermenter at the initial of fed-batch feeding

X_i = concentration of cells in the fermenter at the initial of fed-batch feeding

t = fed-batch time after feeding commencement

Fed-batch Operation

Material balance on the product:

Product in – Product out + Product synthesis = Product accumulation

$$0 \quad -0 \quad +q_p XV = \frac{dVP}{dt}$$

At quasi-steady state, $\frac{dP}{dt} = 0$

Please derive the formula to get → $q_p X = DP$

Fed-batch Operation

- The product concentration in the vessel at any time t is:

$$P = \frac{P^t}{V}$$

- The rate of change in product concentration is:

$$\frac{dP}{dt} = \frac{d\left(\frac{P^t}{V}\right)}{dt} = \frac{V\left(\frac{dP^t}{dt}\right) - P^t\left(\frac{dV}{dt}\right)}{V^2}$$

- At quasi-steady state, $\frac{dP}{dt} = 0$

- Rearrange: $\frac{dP^t}{dt} = \frac{P^t}{V}\frac{dV}{dt} = PF$

Fed-batch Operation

- Combine $q_p X = DP$ $\frac{dP^t}{dt} = PF$
- We obtain: $\frac{dP^t}{dt} = q_p X^t$
- From previous, $X^t = V_i X_i + XFt$
- Thus, $\frac{dP^t}{dt} = q_p \left(V_i X_i + XFt \right)$

Fed-batch Operation

- Integrate:

$$P^t = P_i^t + q_p t\left(V_i X_i + \frac{XFt}{2}\right)$$

$$P = P_i \frac{V_i}{V} + q_p t\left(\frac{V_i X_i}{V} + \frac{XDt}{2}\right)$$

where

P^t = amount of product in the fermenter at t

P^t_i = amount of product in the fermenter at the initial of fed-batch feeding

P_i = concentration of product in the fermenter at the initial of fed-batch feeding

t = fed-batch time after feeding commencement

Fed-batch Operation

- Exercise 1
- Exercise 2

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