9.3.3. Fed-Batch Operation

What is a Fed-Batch Operation?

A Variable-Volume Semi-Batch Operation with Feed but Withdrawal only at the End

A Semi-Batch Operation in Which the Feed Containing Sources of Carbon, Nitrogen, and Others are Fed either Intermittently or Continuously During the Course of Otherwise a Batch Operation

Why a Fed-Batch Operation?

- To Overcome Substrate Inhibition
- To Overcome Glucose Effect
- To Overcome Catabolite Repression
- To Utilize Auxotrophs
- To Achieve High Cell and Metabolite Density
- To Extent Operational Period
- To Alleviate High Broth Viscosity
- To Make Up for Water Loss by Evaporation

To Increase Reaction Rates and/or Yields

and Overcome Physical Difficulties

Products Using Fed-Batch Operation

- Antibiotics
- Baker`s Yeast
- Enzymes
- Microbial Cells
- Natural Lipids
- Nucleotides
- Organic Acids
- r-DNA Products
- Solvents
- Vitamins
- Yeasts

Specific Growth Rate

$$\mu = \frac{1}{XV}\frac{d(XV)}{dt}$$

- Batch $$\mu = \frac{1}{X}\frac{dX}{dt}$$

- Fed-Batch $$\mu = \frac{1}{X}\frac{dX}{dt} + \frac{1}{V}\frac{dV}{dt}$$

Growth Yield

$$Y = \frac{\Delta X}{\Delta S}$$

$$= -\frac{dX}{dS}$$

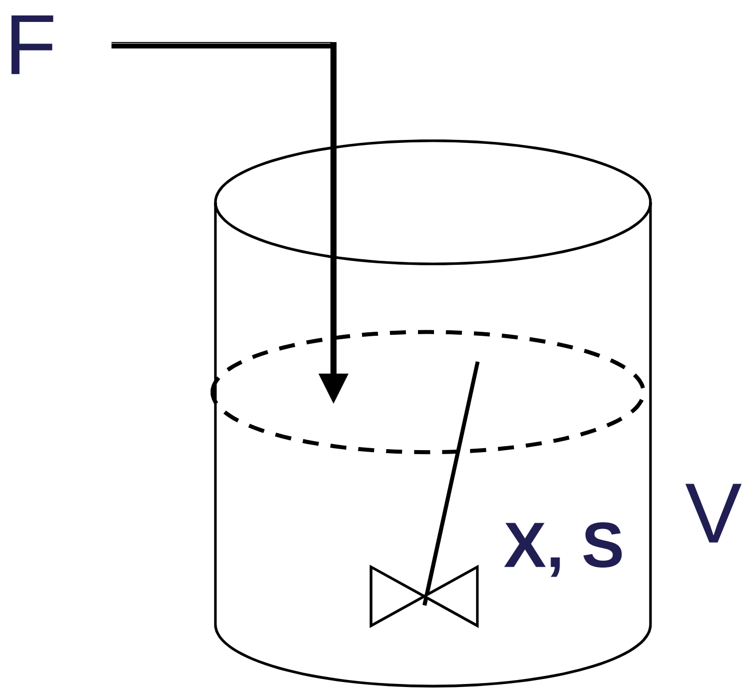
Mass Balance

Acc = In – Out + Gen – Con

Accumulation rate = Input rate – Output rate + Generation rate – Consumption rate

$$\frac{d(\quad)}{dt} =$$

Fed-Batch Operation



F (L/h) : Flow Rate
V (L) : Working Volume
X (g/L) : Cell Concentration
S (g/L) : Substrate Concentration

Mass Balances

- cell

$$\frac{d(XV)}{dt} = \mu XV \quad ----(1)$$

- substrate

$$\frac{d(SV)}{dt} = S_F F - \frac{1}{Y}\mu XV \quad ---(2)$$

- Total

$$\frac{dV}{dt} = F \quad ------(3)$$

Determination of Feed Rate

(using mass balance equations)

- cell

$$\frac{d(XV)}{dt} = \mu XV \rightarrow \frac{dX}{dt} = (\mu - \frac{F}{V})X - - - - (1)$$

- substrate

$$\frac{d(SV)}{dt} = S_F F - \frac{1}{Y}\mu XV \rightarrow \frac{dS}{dt} = (S_F - S)\frac{F}{V} - \frac{\mu X}{Y} - - - (2)$$

- Total $\frac{dV}{dt} = F - - - - - - (3)$

With $\frac{dS}{dt} = 0$

(2) → $F = \frac{\mu X}{Y}\frac{V}{S_F - S}$ .... (4)

Determination of Feed Rate

(using mass balance equations)

- cell

$$\frac{d(XV)}{dt} = \mu XV$$

$$XV = X_0 V_0 e^{\mu t} \text{.......(5)}$$

(4) →

$$F = \frac{\mu X}{Y}\frac{V}{S_F - S} = \frac{\mu X_0 V_0}{Y(S_F - S)} e^{\mu t}$$

↑ (5)