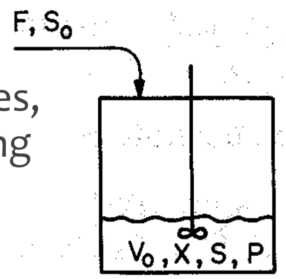
Fed-Batch Operation

- Nutrients are continuously or semi-continuously fed, while effluent is removed discontinuously.
- Usually used
  - to overcome substrate inhibition or catabolite repression by intermittent feeding of substrate by maintaining low substrate concentration.
  - for production of secondary metabolites, e.g. antibiotics, lactic acid, E. Coli making proteins from recombinant DNA technology.

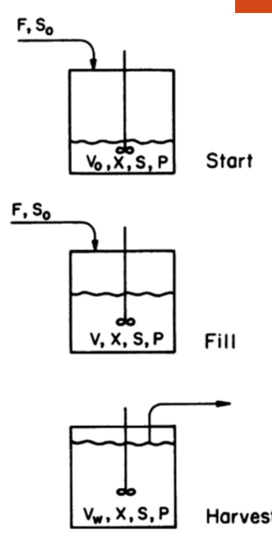


Fed-Batch Operation

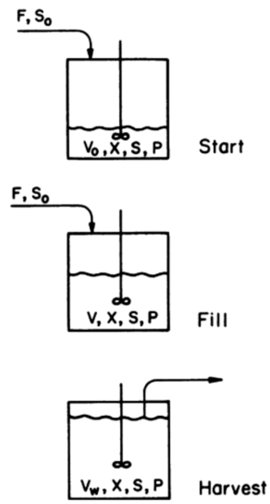
- Analysis of fed-batch with substrate continuously fed and no output: at t=0, $V=V_o$, $X_o=0$, F is constant.
- Volume: $\frac{dV}{dt} = F \Rightarrow \boxed{V = V_o + Ft}$
- At quasi steady state, S added=S consumed, X, S, P concentrations are constant.
- Cell mass balance: $FX_O + V\mu_{net}X = \frac{d(XV)}{dt}$

since $\frac{d(XV)}{dt} = V\frac{dX}{dt} + X\frac{dV}{dt}$, then $\cancel{FX_O} + V\mu_{net}X = V\cancel{\frac{dX}{dt}} + X\frac{dV}{dt}$

$$V\mu_{net}X = X\frac{dV}{dt} \Rightarrow \mu_{net} = \frac{1}{V}\frac{dV}{dt} = \frac{F}{V} = D$$



Fed-Batch Operation



$$V\mu_{net}X = X\frac{dV}{dt} \Rightarrow \mu_{net} = \frac{1}{V}\frac{dV}{dt} = \frac{F}{V} = D$$

$$\mu_{net} = \frac{F}{V} = \frac{F}{V_0 + Ft} = \frac{D_o}{1 + D_0 t}$$

$$\mu_{net} = D = \frac{\mu_m S}{K_s + S} \text{ if } k_d \approx 0$$

Then $\boxed{S \cong \frac{K_s D}{\mu_m - D}}$

(Monod growth model applied)

Fed-Batch Operation

Total Biomass: X_t (g cells) vs time $\boxed{X = \frac{X_t}{V}}$

$$\frac{dX}{dt} = 0 \quad \text{or} \quad \frac{d\left(\frac{X_t}{V}\right)}{dt} = \frac{V\left(\frac{dX_t}{dt}\right) - X_t\left(\frac{dV}{dt}\right)}{V^2} = 0$$

rearranging $\frac{dX_t}{dt} = \frac{X_t}{V}\frac{dV}{dt} = X_m F = Y^M_{X/S} S_o F$ **where S≈0**

$\boxed{X_t = X_m V}$

integrating $\boxed{X_t = X_{to} + Y^M_{X/S} S_o F t} = (V_o + Ft)X_m$

where $X_t = X_{t0}$ at $t = 0$

Fed-Batch Operation

Product Formation: total product, $P_t = PV$ (g)

For many secondary products, the specific rate of product formation is a constant $= q_P$ (g product/g cells-min)

$$\frac{dP_t}{dt} = q_P X_t = q_P (V_o + Ft) X_m \qquad \text{at } t=0,\ P_t = P_{t0}$$

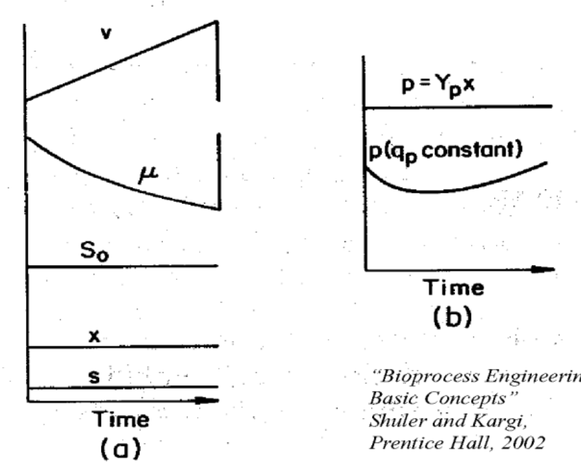
integrating, $P_t = P_{to} + q_P X_m (V_o + \frac{Ft}{2})t$

or $P = \frac{P_o V_o}{V} + q_P X_m (\frac{V_o}{V} + \frac{Dt}{2})t$

or $P = \frac{P_o V_o}{(V_o + Ft)} + q_P X_m (\frac{V_o}{(V_o + Ft)} + \frac{Ft}{2(V_o + Ft)})t$

Fed-Batch Operation

Behavior of X, S, P, V, and μ over time at quasi steady state



"Bioprocess Engineering: Basic Concepts" Shuler and Kargi, Prentice Hall, 2002

Example: Fed- Batch Operation

In a fed-batch culture operating with intermittent addition of glucose, the value of V is given at time t = 2hr, when the system is at quasi-steady state.

$$F = \frac{dV}{dt} = 200\ \text{ml/h},\ V = 1000\ \text{ml},\ S_0 = 100\ \text{g glucose/L}$$

$$Y_{X/S}^{M} = 0.5\ \text{g cells/g glucose};\ \mu_m = 0.3\ \text{h}^{-1},$$

$$K_S = 0.1\ \text{g/L},\ X_{t0} = 30\ \text{g cells}$$

- Determine V_0.
- At t = 2 h, find S, X and X_t and P at quasi-steady state if q_p= 0.2 g product/g cells-h, P_0=0.