Find the steady-state values for a continuous bioreactor with **cell recycle**.
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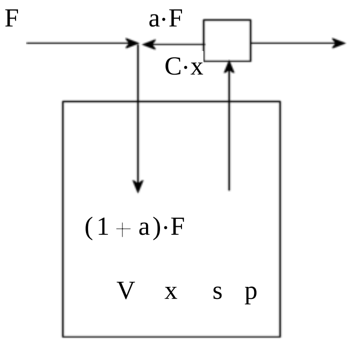


F ... flow rate

a ... recycle ratio (Note that textbook uses the symbol α, which denotes growth related product formation here.)

C ... biomass concentration factor

V ... bioreactor volume

x, s, p ... biomass, substrate, & product concentration

The kinetics of formation of the desired product is mixed (i.e., partially cell growth related and partially non-growth related). A cell-free feed stream continuously enters the fermentor of volume V at a flow rate of F, and the fermentor content is also continuously withdrawn. A cell separator concentrates the biomass by a factor of C, and the recycle loop has a flow rate of f=a*F. Substrate and product are not concentrated. Assume that the limiting substrate is utilized only for cell growth but not for product formation. The following Contois equation of growth describes high-density cell fermentation where cell growth is suppressed when the fermentor becomes too crowded.

$$\mu(x,s) = \frac{\mu_m \cdot s}{K\cdot x + s}$$ ... Contois equation of cell growth

Analytical Solution

Steady-state conditions:

dx/dt= $0 = (\mu - (1 + a - a\cdot C)\cdot D)\cdot x$ ... Biomass

ds/dt= $0 = D\cdot\left(s_f - s\right) - \frac{1}{Y}\cdot\mu\cdot x$ ... Substrate

Given

dp/dt= $0 = \alpha\cdot\mu\cdot x + \beta\cdot x - D\cdot p$ ... Product

The non-washout solution of the above equations satisfies:

$$\mu = \frac{\mu_m\cdot s}{K\cdot x + s} \qquad \mu = (1 + a - a\cdot C)\cdot D \qquad x = \frac{Y\cdot\left(s_f - s\right)}{1 + a - a\cdot C}$$

$$\text{Find}(x,s,p,\mu) \rightarrow \begin{bmatrix} -Y\cdot s_f\cdot\dfrac{\left(D\cdot a\cdot C - D\cdot a + \mu_m - D\right)}{\left(-K\cdot D\cdot Y - K\cdot D\cdot a\cdot Y + K\cdot D\cdot a\cdot C\cdot Y + D + 2\cdot D\cdot a - 2\cdot D\cdot a\cdot C + D\cdot a^2 - 2\cdot D\cdot a^2\cdot C + D\cdot a^2\cdot C^2 - \mu \cdots\right.} \\ D\cdot K\cdot s_f\cdot\dfrac{Y}{\left(D\cdot a\cdot C - D\cdot a + K\cdot D\cdot Y + \mu_m - D\right)} \\ Y\cdot s_f\cdot\dfrac{\left(D\cdot a\cdot C - D\cdot a + \mu_m - D\right)}{\left(-K\cdot D\cdot Y - K\cdot D\cdot a\cdot Y + K\cdot D\cdot a\cdot C\cdot Y + D + 2\cdot D\cdot a - 2\cdot D\cdot a\cdot C + D\cdot a^2 - 2\cdot D\cdot a^2\cdot C + D\cdot a^2\cdot C^2 - \mu_m - \mu_m\cdot a + \mu \cdots\right.} \\ D + D\cdot a - D\cdot a\cdot C \end{bmatrix}$$

Numerical Solution

Express the biomass/substrate/product concentrations at steady-state as functions of D and s_f (by copying the formula from above). Washout at $\mu=(1+a-a\cdot C)\cdot D=\mu_m\cdot s_f/(K\cdot 0+s_f)=\mu_m$

$Y := 0.5 \quad \mu_m := 0.5 \quad K := 1 \quad \alpha := 0.5 \quad \beta := 0.1 \quad s_f := 1$

$$s(D, s_f, a, C) := \text{if}\left[D \ge \frac{\mu_m}{1+a-a\cdot C}, s_f, \frac{K\cdot D\cdot s_f\cdot Y}{D\cdot K\cdot Y-(1+a-a\cdot C)\cdot D+\mu_m}\right]$$

$$x(D, s_f, a, C) := \text{if}\left[D \ge \frac{\mu_m}{1+a-a\cdot C}, 0, \frac{Y\cdot\left(s_f - s(D, s_f, a, C)\right)}{1+a-a\cdot C}\right]$$

$$p(D, s_f, a, C) := \text{if}\left[D \ge \frac{\mu_m}{1+a-a\cdot C}, 0, \left[\alpha\cdot(1+a-a\cdot C)+\frac{\beta}{D}\right]\cdot x(D, s_f, a, C)\right]$$

fraction of recycle flow

$a := 0.5$

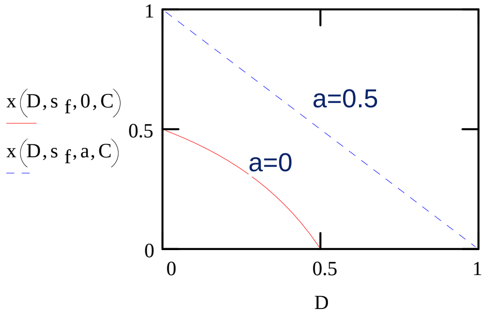
cell concentration factor

$C := 2$

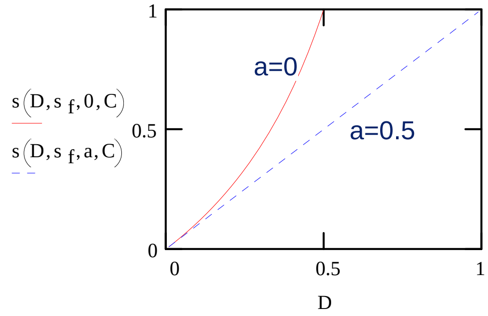
Comparison of steady-state variables /w and /wo cell recycle

$D := 0.01, 0.02 .. 0.99$

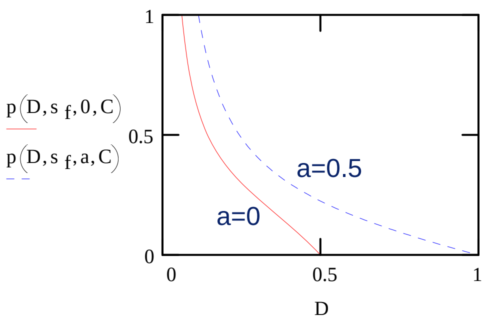
Biomass Concentration



Substrate Concentration

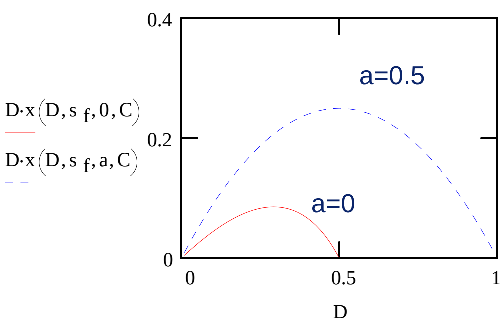


Product Concentration

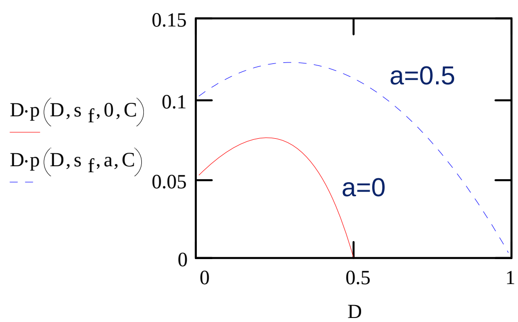


Comparison of steady-state cell/product productivities /w and /wo cell recycle

Cell productivity



Product Productivity



It is clear from the graph that both cell and product concentrations are higher with cell recycle. Intuitively, cell recycle always increase the level of cells in a bioreactor. In turn, more cells yield more product. The same can be said of cell and product productivities.

$$\cdots_m - \mu_m \cdot a + \mu_m \cdot a \cdot C)$$

$$\cdots_m \cdot a \cdot C) \cdot \frac{(-D \cdot \alpha - \alpha \cdot D \cdot a + \alpha \cdot D \cdot a \cdot C - \beta)}{D}$$