Problem 9.2 of Shuler & Kargi. Two fermentors in series.

Instructor: Nam Sun Wang

Cell growth parameters:

$\mu_m := 0.3\,hr^{-1}$ $K_s := 0.1\,\frac{g}{liter}$ $\mu_1(s) := \frac{\mu_m \cdot s}{K_s + s}$

no growth in 2nd reactor

$\mu_2(s) := 0$ $Y_s := 0.4\,\frac{g\_cell}{g\_S}$

Product formation parameters:

$Y_p := 0.6\,\frac{g\_P}{g\_S}$ $q_p := 0.02\,\frac{g\_P}{g\_cell \cdot hr}$

Substrate feed rate:

$F := 100\,\frac{liter}{hr}$ $s_f := 5\,\frac{gm}{liter}$ $D_{washout} := \mu_1(s_f)$

Numerical Solution.

Dynamic equations for the first fermentor. $V_1 := 500\,liter$ $D_1 := \frac{F}{V_1}$ $D_1 = 0.2\ hr^{-1}$

$$dx1_{dt}(x_1, s_1) := \mu_1(s_1) \cdot x_1 - D_1 \cdot x_1$$

$$ds1_{dt}(x_1, s_1) := D_1 \cdot (s_f - s_1) - \frac{1}{Y_s} \cdot \mu_1(s_1) \cdot x_1$$

At steady-state, d/dt=0

$x_1 := 1$ $s_1 := 0$

Given $dx1_{dt}(x_1, s_1) = 0$

$ds1_{dt}(x_1, s_1) = 0$

$$\begin{pmatrix} x_1 \\ s_1 \end{pmatrix} := Find(x_1, s_1) \qquad \begin{pmatrix} x_1 \\ s_1 \end{pmatrix} = \begin{pmatrix} 1.92 \\ 0.2 \end{pmatrix}$$

Dynamic equations for the second fermentor. $V_2 := 300\,liter$ $D_2 := \frac{F}{V_2}$ $D_2 = 0.333\ hr^{-1}$

$$dx2_{dt}(x_1, x_2, s_2) := D_2 \cdot (x_1 - x_2) + \mu_2(s_2) \cdot x_2$$

$$ds2_{dt}(x_2, s_1, s_2) := D_2 \cdot (s_1 - s_2) - \frac{1}{Y_s} \cdot \mu_2(s_2) \cdot x_2 - \frac{1}{Y_p} \cdot q_p \cdot x_2$$

$$dp2_{dt}(x_2, p_2) := q_p \cdot x_2 - D_2 \cdot p_2$$

At steady-state, d/dt=0

$x_2 := 1$ $s_2 := 0$ $p_2 := 0$

Given $dx2_{dt}(x_1, x_2, s_2) = 0$

$ds2_{dt}(x_2, s_1, s_2) = 0$

$dp2_{dt}(x_2, p_2) = 0$

$$\begin{bmatrix} x_2 \\ s_2 \\ p_2 \end{bmatrix} := Find(x_2, s_2, p_2) \qquad \begin{bmatrix} x_2 \\ s_2 \\ p_2 \end{bmatrix} = \begin{pmatrix} 1.92 \\ 0.008 \\ 0.115 \end{pmatrix}$$

Analytical Solution.

Steady-state equations for the first fermentor.

$$\frac{dx_1}{dt} = 0 = \mu_1 \cdot x_1 - D_1 \cdot x_1 \longrightarrow \mu_1 = \frac{\mu_m \cdot s_1}{K_s + s_1} = D_1 \qquad s_1 := \frac{D_1 \cdot K_s}{\mu_m - D_1} \qquad s_1 = 0.2$$

$$\frac{ds_1}{dt} = 0 = D_1 \cdot (s_f - s_1) - \frac{1}{Y_s} \cdot \mu_1 \cdot x_1 \longrightarrow x_1 = Y_s \cdot (s_f - s_1) \qquad x_1 := Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1}\right) \qquad x_1 = 1.92$$

Steady-state equations for the second fermentor.

$$\frac{dx_2}{dt} = 0 = D_2 \cdot (x_1 - x_2) \longrightarrow x_2 := x_1 \qquad x_2 = 1.92$$

$$\frac{ds_2}{dt} = 0 = D_2 \cdot (s_1 - s_2) - \frac{1}{Y_p} \cdot q_p \cdot x_2 \longrightarrow s_2 := s_1 - \frac{1}{D_2} \cdot \frac{1}{Y_p} \cdot q_p \cdot x_2 \qquad s_2 = 0.008$$

$$s_2 = \frac{D_1 \cdot K_s}{\mu_m - D_1} - \frac{1}{D_2} \cdot \frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1}\right)$$

$$\frac{dp_2}{dt} = 0 = q_p \cdot x_2 - D_2 \cdot p_2 \longrightarrow p_2 := \frac{q_p \cdot x_2}{D_2} \qquad p_2 = 0.115 \qquad p_2 = \frac{q_p}{D_2} \cdot \left[Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1}\right)\right]$$

Non-negative s_1 constraint: $\quad 0 \le s_1 = \frac{D_1 \cdot K_s}{\mu_m - D_1} \le s_f \qquad 0 < D_1 \le D_{washout} < \mu_m$

(non-washout constraint)

Non-negative s_2 constraint: $\quad 0 \le s_2 = \frac{D_1 \cdot K_s}{\mu_m - D_1} - \frac{1}{D_2} \cdot \frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1}\right) \le s_1$

$$\longrightarrow \frac{\frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1}\right)}{\frac{D_1 \cdot K_s}{\mu_m - D_1}} \le D_2$$

product productivity (g product produced per total reactor volume per time)

$$prod = \frac{F \cdot p_2}{V_1 + V_2} = \frac{p_2}{\frac{V_1}{F} + \frac{V_2}{F}} = \frac{p_2}{\frac{1}{D_1} + \frac{1}{D_2}} \qquad prod(D_1, D_2, s_f) := \frac{q_p}{\frac{D_2}{D_1} + 1} \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1}\right)$$

Unconstrained optimization ⟶ no good -- leads to physically untenable results.

$$\frac{d(prod)}{d(D_2)} \qquad 0 = q_p \cdot D_1 \cdot Y_s \cdot \frac{s_f \cdot D_1 + D_1 \cdot K_s - s_f \cdot \mu_m}{(D_2 + D_1)^2 \cdot (\mu_m - D_1)} \longrightarrow D_1 := \frac{\mu_m \cdot s_f}{K_s + s_f} \qquad D_1 = 0.294$$ ... $D_{washout}$

$D_1 = \mu_1(s_f)$ This means $s_1 = s_f$; no cell growth, washout; not a valid answer.

$$\frac{d(prod)}{d(D_1)} \qquad 0 = q_p \cdot Y_s \cdot \frac{\left(D_2 \cdot s_f \cdot \mu_m^2 - 2 \cdot D_2 \cdot s_f \cdot \mu_m \cdot D_1 + D_2 \cdot s_f \cdot D_1^2 - 2 \cdot D_2 \cdot D_1 \cdot K_s \cdot \mu_m + D_2 \cdot D_1^2 \cdot K_s - D_1^2 \cdot K_s \cdot \mu_m\right)}{(D_2 + D_1)^2 \cdot (\mu_m - D_1)^2}$$

$$\longrightarrow \quad D_2 := \frac{D_1^2 \cdot K_s \cdot \mu_m}{s_f \cdot \mu_m^2 - 2 \cdot s_f \cdot \mu_m \cdot D_1 + s_f \cdot D_1^2 - 2 \cdot D_1 \cdot K_s \cdot \mu_m + D_1^2 \cdot K_s} \qquad D_2 = -0.294$$

... no good; negative.

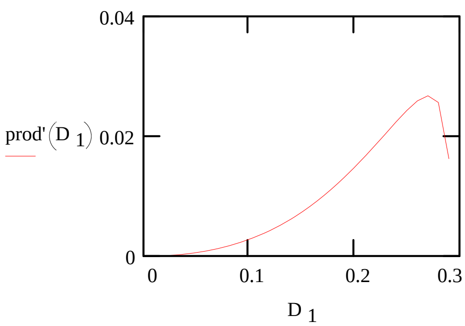
Constrained optimization ⟶ good.

Substitute the constraint that relates D_2 to D_1 (derived from the constraint $0 \le s_2$).

$$\frac{\frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1} \right)}{\frac{D_1 \cdot K_s}{\mu_m - D_1}} \le D_2$$

$$prod'(D_1) := \frac{q_p}{\dfrac{\dfrac{\frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1} \right)}{\frac{D_1 \cdot K_s}{\mu_m - D_1}}}{D_1} + 1} \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1} \right)$$

$$D_1 := 0.01, 0.02 .. D_{washout}$$



Maximum profit is around $D_1 = 0.27$

To find the point of maximum profit numerically, take derivative of prod wrt D1, by |Symbolic|Differentiate on Variable|, then simplify. Set $d(prod(D_1))/dD_1 = 0$

$$0 = -\frac{q_p}{\left[\frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \frac{s_f - D_1 \cdot \frac{K_s}{\mu_m - D_1}}{D_1^2 \cdot K_s} \cdot (\mu_m - D_1) + 1 \right]^2} \cdot Y_s \cdot \left(s_f - D_1 \cdot \frac{K_s}{\mu_m - D_1} \right) \cdot \left[\frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \frac{-\frac{K_s}{\mu_m - D_1} - D_1 \cdot \frac{K_s}{(\mu_m - D_1)^2}}{D_1^2 \cdot K_s} \right.$$

$D_1 := 0.25$ ... initial guess Given

$$0 = -\left(4 \cdot q_p \cdot Y_s \cdot s_f \cdot \mu_m^2 \cdot K_s \cdot D_1 - 2 \cdot q_p \cdot Y_s \cdot s_f^2 \cdot \mu_m^3 + 5 \cdot q_p \cdot Y_s \cdot s_f^2 \cdot \mu_m^2 \cdot D_1 - 4 \cdot q_p \cdot Y_s \cdot s_f^2 \cdot \mu_m \cdot D_1^2 - 6 \cdot q_p \cdot Y_s \cdot s_f \cdot \mu_m \cdot D_1^2 \cdot \right.$$

$$D_1 := Find(D_1) \qquad D_1 = 0.271$$

$$D_2 := \frac{\frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1} \right)}{\frac{D_1 \cdot K_s}{\mu_m - D_1}} \qquad D_2 = 0.057$$

Note that the following constrained optimization is not valid. When maximum occurs at the constraint boundary, derivative taken along the constraint boundary is 0, but the derivative taken along D_1 is *not* 0; neither is the derivative taken along D_2.

$D_1 := 0.1 \quad D_2 := 0.1$ ... initial guess

Given

$\frac{d(prod)}{d(D_1)}$ $\quad 0 = D_2 \cdot s_f \cdot \mu_m^2 - 2 \cdot D_2 \cdot s_f \cdot \mu_m \cdot D_1 + D_2 \cdot s_f \cdot D_1^2 - 2 \cdot D_2 \cdot D_1 \cdot K_s \cdot \mu_m + D_2 \cdot D_1^2 \cdot K_s - D_1^2 \cdot K_s \cdot \mu_m$

non-negative s_2 $\quad 0 = \frac{D_1 \cdot K_s}{\mu_m - D_1} - \frac{1}{D_2} \cdot \frac{1}{Y_p} \cdot q_p \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1} \right)$

$\begin{pmatrix} D_1 \\ D_2 \end{pmatrix} := \text{Find}(D_1, D_2) \qquad \begin{pmatrix} D_1 \\ D_2 \end{pmatrix} = \begin{pmatrix} 0.238 \\ 0.16 \end{pmatrix} \qquad prod(D_1, D_2, s_f) = 0.02207$ ... These are wrong answers.

In practice, we can also maximize wrt s_f. The model gives a monotonically increasing product productivity or profit (which takes into consideration the cost of substrate) with increasing s_f. This linear relationship between profit and s_f is unrealistic, because substrate inhibition eventually becomes important in practice.

$prod(D_1, D_2, 10^{10}) = 4.78 \cdot 10^7$ Huge unrealistic productivity unless we apply a constraint on the value of s_f.

$price\_ratio := 0.01$ feed rate of sf $\quad \frac{F \cdot s_f}{V_1 + V_2} = \frac{s_f}{\frac{1}{D_1} + \frac{1}{D_2}}$

$$profit(D_1, D_2, s_f) := prod(D_1, D_2, s_f) - price\_ratio \cdot \frac{s_f}{\frac{1}{D_1} + \frac{1}{D_2}}$$

$$profit(D_1, D_2, s_f) = \frac{q_p}{\frac{D_2}{D_1} + 1} \cdot Y_s \cdot \left(s_f - \frac{D_1 \cdot K_s}{\mu_m - D_1} \right) - price\_ratio \cdot \frac{s_f}{\frac{1}{D_1} + \frac{1}{D_2}}$$

$s_f := 0, 1 .. 10$ Profit is a linear function of s_f ——→ exhibit no maximum