Problem 9.2 of Shuler & Kargi. Batch fermentor operated in two stages. Given..Odesolve
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Cell growth parameters:

$\mu_{m1} := 0.3$ h-1 $\mu_{m2} := 0$ $K_s := 0.1$ g/liter $Y_x := 0.4$ g cell/g substrate

$$\mu_x(s,t,t_{f1}) := (t < t_{f1})\cdot(0 < s)\cdot\frac{\mu_{m1}\cdot s}{K_s + s} + (t_{f1} \le t)\cdot(0 < s)\cdot\frac{\mu_{m2}\cdot s}{K_s + s} \qquad \mu_y(s) := (0 < s)\cdot\frac{\mu_{m1}\cdot s}{K_s + s}$$

Product formation parameters:

$Y_p := 0.6$ g product/g substrate $q_p(s,t,t_{f1}) := (t_{f1} \le t)\cdot(0 < s)\cdot 0.02$ g product/(g cell·h)

Initial condition $x_0 := 0.1$ $s_0 := 5$ $y_0 := 0$ $p_0 := 0$

Dynamic equations for the first phase of batch fermentor.

Given

$$x'(t) = \mu_x(s(t),t,t_{f1})\cdot x(t) \qquad x(0) = x_0$$

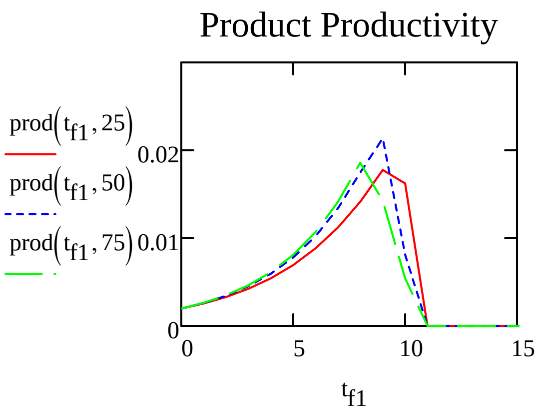
$$s'(t) = -\frac{1}{Y_x}\cdot\mu_x(s(t),t,t_{f1})\cdot x(t) - \frac{1}{Y_p}\cdot q_p(s(t),t,t_{f1})\cdot x(t) \qquad s(0) = s_0$$

$$p'(t) = q_p(s(t),t,t_{f1})\cdot x(t) \qquad p(0) = p_0$$

$$xsp(t_{f1},t_{f2}) := \text{Odesolve}\left[\begin{pmatrix} x \\ s \\ p \end{pmatrix},t,t_{f2}\right] \qquad p_f(t_{f1},t_{f2}) := \left| \begin{array}{l} \begin{pmatrix} x \\ s \\ p \end{pmatrix} \leftarrow xsp(t_{f1},t_{f2}) \\ p(t_{f2}) \end{array} \right. \qquad prod(t_{f1},t_{f2}) := \frac{p_f(t_{f1},t_{f2})}{t_{f2}}$$

Maximize product productivity

$t_{f1} := 0,1..25$

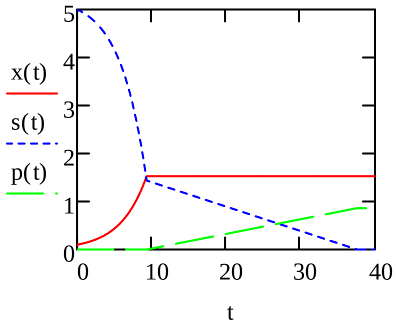


Provide initial guess $t_{f1} := 10$ $t_{f2} := 50$ $prod(t_{f1},t_{f2}) = 8.121 \times 10^{-3}$

$$\begin{pmatrix} t_{f1} \\ t_{f2} \end{pmatrix} := \text{Maximize}(prod,t_{f1},t_{f2}) = \begin{pmatrix} 9.336 \\ 40 \end{pmatrix} \qquad prod(t_{f1},t_{f2}) = 0.022$$

The productivity in 2 CSTRs in series was 0.027 g/(L·h)

profile $\begin{pmatrix} x \\ s \\ p \end{pmatrix} := xsp(t_{f1},t_{f2})$



The product is encoded in a plasmid. Upon cell division, there is a small probability P=0.001 of a plasmid-bearing cell x producing a plasmid-free offspring y.

$P := 0.001$

Given

$$x'(t) = (1 - P)\cdot\mu_x(s(t), t, t_{f1})\cdot x(t) \qquad x(0) = x_0$$

$$y'(t) = \mu_y(s(t))\cdot y(t) + P\cdot\mu_x(s(t), t, t_{f1})\cdot x(t) \qquad y(0) = y_0$$

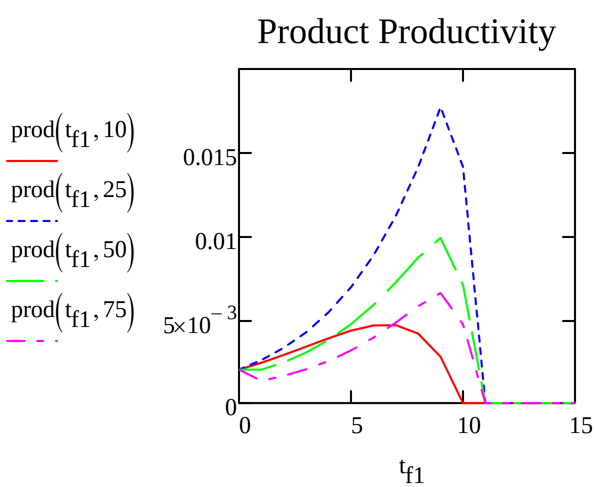
$$s'(t) = -\frac{1}{Y_x}\cdot\mu_x(s(t), t, t_{f1})\cdot x(t) - \frac{1}{Y_x}\cdot\mu_y(s(t))\cdot y(t) - \frac{1}{Y_p}\cdot q_p(s(t), t, t_{f1})\cdot x(t) \qquad s(0) = s_0$$

$$p'(t) = q_p(s(t), t, t_{f1})\cdot x(t) \qquad p(0) = p_0$$

$$xysp(t_{f1}, t_{f2}) := \text{Odesolve}\left[\begin{pmatrix} x \\ y \\ s \\ p \end{pmatrix}, t, t_{f2}\right] \qquad p_f(t_{f1}, t_{f2}) := \left| \begin{array}{l} \begin{pmatrix} x \\ y \\ s \\ p \end{pmatrix} \leftarrow xysp(t_{f1}, t_{f2}) \\ p(t_{f2}) \end{array} \right. \qquad prod(t_{f1}, t_{f2}) := \frac{p_f(t_{f1}, t_{f2})}{t_{f2}}$$

Maximize product productivity

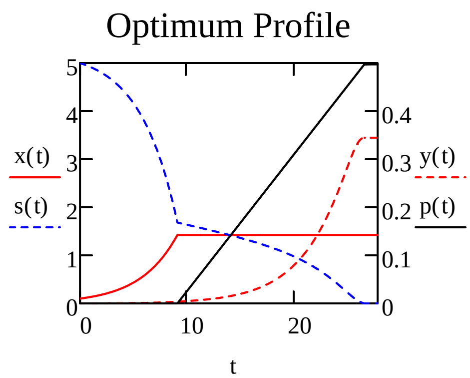
$t_{f1} := 0, 1 .. 15$



Provide initial guess $\quad t_{f1} := 5 \quad t_{f2} := 20 \quad prod(t_{f1}, t_{f2}) = 6.505 \times 10^{-3}$

$$\begin{pmatrix} t_{f1} \\ t_{f2} \end{pmatrix} := \text{Maximize}(prod, t_{f1}, t_{f2}) = \begin{pmatrix} 9.1 \\ 27.817 \end{pmatrix} \qquad prod(t_{f1}, t_{f2}) = 0.018$$

Optimal profile $\begin{pmatrix} x \\ y \\ s \\ p \end{pmatrix} := xysp(t_{f1}, t_{f2})$



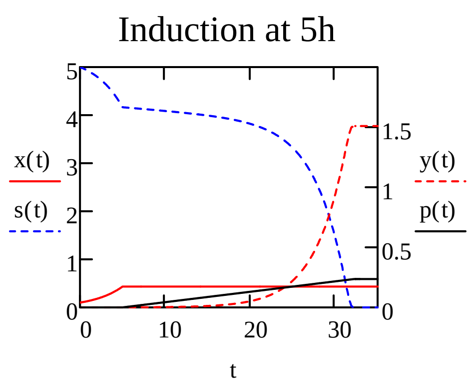
product concentration at end of the run

$p_f := p(t_{f2}) = 0.497$ g/L

Fraction of plasmid-free cells at end of the run

$$\frac{y(t_{f2})}{x(t_{f2}) + y(t_{f2})} = 0.195$$

Sub optimal profile $t_{f1} := 5$ $t_{f2} := 35$ $\begin{pmatrix} x \\ y \\ s \\ p \end{pmatrix} := xysp(t_{f1}, t_{f2})$



product concentration at end of the run

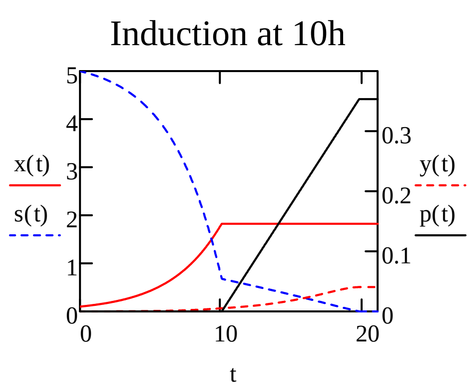
$p_f := p(t_{f2}) = 0.236$ g/L

Fraction of plasmid-free cells at end of the run

$$\frac{y(t_{f2})}{x(t_{f2}) + y(t_{f2})} = 0.777$$

Fermentation time for 5-h induction was longer than that for 10-h induction (~32h versus ~20h). Product concentration for 5-h induction was lower than that for 10-h induction (0.236 g/L versus 0.353 g/L). 5-h induction led to a fermentor full of nonproductive plasmid-free cells, the fraction of nonproductive plasmid-free cells being 0.777 for 5-h induction versus 0.022 for 10-h induction.

Sub optimal profile $t_{f1} := 10$ $t_{f2} := 21$ $\begin{pmatrix} x \\ y \\ s \\ p \end{pmatrix} := xysp(t_{f1}, t_{f2})$



product concentration at end of the run

$p_f := p(t_{f2}) = 0.353$ g/L

Fraction of plasmid-free cells at end of the run

$$\frac{y(t_{f2})}{x(t_{f2}) + y(t_{f2})} = 0.022$$