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

\[ \mu_m^1 := 0.3 \text{ h}^{-1} \quad \mu_m^2 := 0 \quad K_s := 0.1 \text{ g/liter} \quad Y_x := 0.4 \text{ g cell/g substrate} \]

\[ \mu_x(s,t,t_f^1) := \begin{cases} \mu_m^1 s \quad & (0 < t_f^1) \quad (0 < s) \text{ and } t_f^1 \leq t \\ \frac{\mu_m^1 s}{K_s + s} & (0 < s) \end{cases} \quad \mu_x(s) := (0 < s) \frac{\mu_m^1 s}{K_s + s} \]

Product formation parameters:

\[ Y_p := 0.6 \text{ g product/g substrate} \quad q_p(s,t,t_f^1) := (t_f^1 \leq t) \quad (0 < s) \cdot 0.02 \text{ g product/(g cell-h)} \]

Initial condition

\[ x_0 := 0.1 \quad s_0 := 5 \quad y_0 := 0 \quad p_0 := 0 \]

Dynamic equations for the first phase of batch fermentor.

Given

\[ x'(t) = \mu_x(s(t),t,t_f^1) x(t) \quad x(0) = x_0 \]

\[ s'(t) = \frac{1}{Y_x} \mu_x(s(t),t,t_f^1) x(t) - \frac{1}{Y_p} q_p(s(t),t,t_f^1) x(t) \quad s(0) = s_0 \]

\[ p'(t) = q_p(s(t),t,t_f^1) x(t) \quad p(0) = p_0 \]

\[ xsp(t_f^1,t_f^2) := \text{Odesolve} \left[ \begin{array}{c} x \\ s \\ p \end{array} \right] \quad t_f^1, t_f^2 \]

Maximize product productivity

\[ t_f^1 := 0, 1, 25 \]

Product Productivity

Provide initial guess

\[ t_f^1 := 10 \quad t_f^2 := 50 \quad \text{prod}(t_f^1,t_f^2) = 8.121 \times 10^{-3} \]

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

\begin{align*}
x'(t) &= (1 - P) \cdot \mu_x(s(t), t, t_{f1}) \cdot x(t) \quad 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) \quad 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) \quad s(0) = s_0 \\
p'(t) &= q_p(s(t), t, t_{f1}) \cdot x(t) \quad p(0) = p_0
\end{align*}

\[\text{Maximize product productivity} \]

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

\[\text{Provide initial guess} \]

\[t_{f1} := 5 \quad t_{f2} := 20 \quad \text{prod}(t_{f1}, t_{f2}) = 6.505 \times 10^{-3}\]

\[\begin{pmatrix} t_{f1} \\ t_{f2} \end{pmatrix} := \text{Maximize}(\text{prod}, t_{f1}, t_{f2}) = \begin{pmatrix} 9.1 \\ 27.817 \end{pmatrix} \quad \text{prod}(t_{f1}, t_{f2}) = 0.018\]
Optimal profile

\[
\begin{pmatrix}
  x \\
  y \\
  s \\
  p
\end{pmatrix} := \text{xy}sp(t_{f1}, t_{f2})
\]

Optimum Profile

Sub optimal profile \( t_{f1} := 5 \quad t_{f2} := 35 \)

Induction at 5h

Product concentration at end of the run
\[ p_F := p(t_{f2}) = 0.497 \quad \text{g/L} \]

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 \( t_{f1} := 10 \quad t_{f2} := 21 \)

Induction at 10h

Product concentration at end of the run
\[ p_F := p(t_{f2}) = 0.353 \quad \text{g/L} \]

Fraction of plasmid-free cells at end of the run
\[
\frac{y(t_{f2})}{x(t_{f2}) + y(t_{f2})} = 0.022
\]

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.