Fed-Batch Reactor with Product Formation (Monod model parameters from Shuler & Kargi Prob. 6.8)
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Operation conditions:

$s_f := 1$ ... Feed substrate concentration (g/L)

$F := 0.17$ ... Flow rate (L/h)

$V := 1$ ... Fermentor volume (L)

Constitutive relations:

$\mu(s) := \Phi(s)\cdot\frac{0.7\cdot s}{0.02+s}$ ... Monod specific growth rate

The following equation avoids overshoot:

$\mu(s) := \mathrm{if}\left(s \le 0, 0, \frac{\mu_m\cdot s}{K+s}\right)$

$Y(s) := 0.5$ ... substrate-cell yield coefficient

$Yp := 0.15$ ... substrate-product yield coefficient

$\alpha(s) := 0.1$ ... growth related product formation

$\beta(s) := \Phi(s)\cdot 0.02$ ... maintenance-related product formation

Dynamic Equations:

$$dxdt(x,s,p,v) := \left(\mu(s) - \frac{F}{v}\right)\cdot x$$

$$dsdt(x,s,p,v) := \frac{F}{v}\cdot\left(s_f - s\right) - \frac{1}{Y(s)}\cdot\mu(s)\cdot x - \frac{1}{Yp}\cdot(\alpha(s)\cdot\mu(s)\cdot x + \beta(s)\cdot x)$$

$$dpdt(x,s,p,v) := \alpha(s)\cdot\mu(s)\cdot x + \beta(s)\cdot x - \frac{F}{v}\cdot p$$

$$dvdt(x,s,p,v) := F$$

$$ydot(t,y) := \begin{bmatrix} dxdt\left(y_0,y_1,y_2,y_3\right) \\ dsdt\left(y_0,y_1,y_2,y_3\right) \\ dpdt\left(y_0,y_1,y_2,y_3\right) \\ dvdt\left(y_0,y_1,y_2,y_3\right) \end{bmatrix}$$

Initial conditions: $x_0 := 0.1$ $s_0 := s_f$ $p_0 := 0$ $v_0 := 0.1$

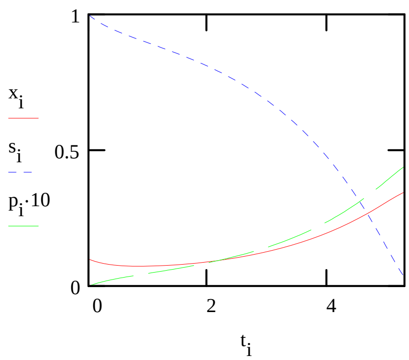
$$y_{initial} := \begin{bmatrix} x_0 \\ s_0 \\ p_0 \\ v_0 \end{bmatrix}$$
... biomass
... substrate
... product
... volume

Solve the coupled set of ODEs (integrate from $t_0 := 0$ to $t_f := \frac{V - v_0}{F}$ in $nstep := 100$

$yout := rkfixed\left(y_{initial}, t_0, t_f, nstep, ydot\right)$

$t := yout^{\langle 0\rangle}$ $x := yout^{\langle 1\rangle}$ $s := yout^{\langle 2\rangle}$ $p := yout^{\langle 3\rangle}$ $v := yout^{\langle 4\rangle}$

Plot of state variables $i := 0 .. last(t)$



Productivity

Cells ... $\dfrac{v_{nstep} \cdot x_{nstep} - v_0 \cdot x_0}{t_f} = 0.06355$

Product ... $\dfrac{v_{nstep} \cdot p_{nstep} - v_0 \cdot p_0}{t_f} = 0.00833$

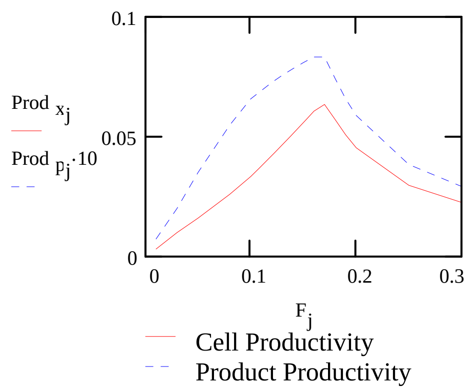
Harvest time $t_f = 5.294$

Change F at the beginning of this document and see how productivity of cells and products change. The following table was entered manually by following this what-if procedure.

$j := 0 .. 100$

$F_j :=$	$Prod_{x_j} :=$	$Prod_{p_j} :=$
0.01	0.00323	0.00074
0.03	0.01007	0.00201
0.05	0.01616	0.00352
0.08	0.02604	0.00549
0.10	0.03348	0.00659
0.12	0.04226	0.00727
0.13	0.04676	0.00757
0.14	0.05135	0.00785
0.15	0.05601	0.00810
0.16	0.06076	0.00833
0.17	0.06355	0.00833
0.18	0.05725	0.00744
0.19	0.05084	0.00659
0.20	0.04550	0.00589
0.25	0.02981	0.00385
0.30	0.02267	0.00293

$j := 0 .. last(F)$



From the table and the plot, maximum productivity of cells and product occurs at F=0.17. This number depends on the operating conditions and the initial conditions. One can further manipulate the initial conditions such that they match the final conditions. Note that at maximum productivity, the substrate is just about depleted when the run is terminated.

Repeat the last step, but let the computer crank out data instead of manually doing the "what-if" for each flow rate (although it may take many minutes of computation). Let flow rate F be an argument of the various functions. To introduce F as an argument to the solution coming out of the ODE solver, we need to augment the set of ODEs with an extra dummy variable whose dynamics is described by d/dt=0.

Dynamic Equations:

$$dxdt(x,s,p,v,F) := \left(\mu(s) - \frac{F}{v}\right)\cdot x$$

$$dsdt(x,s,p,v,F) := \frac{F}{v}\cdot\left(s_f - s\right) - \frac{1}{Y(s)}\cdot\mu(s)\cdot x - \frac{1}{Yp}\cdot(\alpha(s)\cdot\mu(s)\cdot x + \beta(s)\cdot x)$$

$$dpdt(x,s,p,v,F) := \alpha(s)\cdot\mu(s)\cdot x + \beta(s)\cdot x - \frac{F}{v}\cdot p$$

$$dvdt(x,s,p,v,F) := F$$

$$ydot_F(t,y) := \begin{bmatrix} dxdt\left(y_0,y_1,y_2,y_3,y_4\right) \\ dsdt\left(y_0,y_1,y_2,y_3,y_4\right) \\ dpdt\left(y_0,y_1,y_2,y_3,y_4\right) \\ dvdt\left(y_0,y_1,y_2,y_3,y_4\right) \\ 0 \end{bmatrix}$$

⟵ dF/dt=0 so that F=constant during integration.

Solve the coupled set of ODEs (integrate from $t_0 := 0$ to $t_f(F) := \frac{V - v_0}{F}$ in $N := 100$ $\quad i := 0..N$

$$yout(F) := rkfixed\left(\left(x_0 \;\; s_0 \;\; p_0 \;\; v_0 \;\; F\right)^T, t_0, t_f(F), N, ydot_F\right)$$

Trajectory during the run:

$$tt(F) := yout(F)^{\langle 0\rangle}$$

$$xx(F) := yout(F)^{\langle 1\rangle} \qquad ss(F) := yout(F)^{\langle 2\rangle} \qquad pp(F) := yout(F)^{\langle 3\rangle} \qquad vv(F) := yout(F)^{\langle 4\rangle}$$

Reactor status at the end of the run:

$$x_N(F) := yout(F)_{N,1} \qquad s_N(F) := yout(F)_{N,2} \qquad p_N(F) := yout(F)_{N,3} \qquad v_N(F) := yout(F)_{N,4}$$

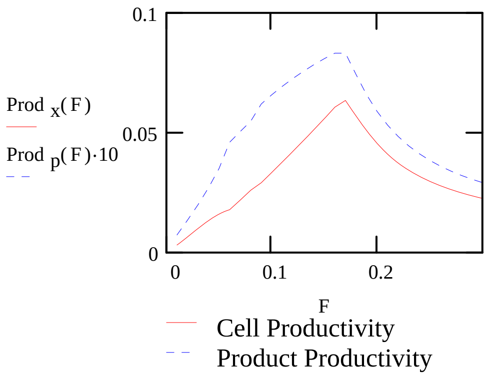
Productivity

Cells ... $Prod_x(F) := \frac{v_N(F)\cdot x_N(F) - v_0\cdot x_0}{t_f(F)}$ An Example: $Prod_x(0.17) = 0.0635$

Product ... $Prod_p(F) := \frac{v_N(F)\cdot p_N(F) - v_0\cdot p_0}{t_f(F)}$ An Example: $Prod_p(0.17) = 0.00833$

Now, with cell and product productivities defined explicitly as functions of the flow rate T, we can simply find productivities for a range the flow rates. By visual inspection of the productivity versus F plot, we can find the optimum flow rate.

$F := 0.01, 0.02 .. 0.3$



Alternatively, we can numerically find the maximum value, instead of by visual inspection. Because there is little curvature at the maximum, we expect difficulties in finding the point at which the derivative of cell or product productivity wrt the flow rate F is zero. This "Find" approach is shown below, but commented out because of the expected difficulties.

Initial Guess: $F := 0.15$ Given $\frac{d}{dF}Prod_x(F) = 0$ $F_{opt} := Find(F)$

Initial Guess: $F := 0.15$ Given $\frac{d}{dF}Prod_p(F) = 0$ $F_{opt} := Find(F)$

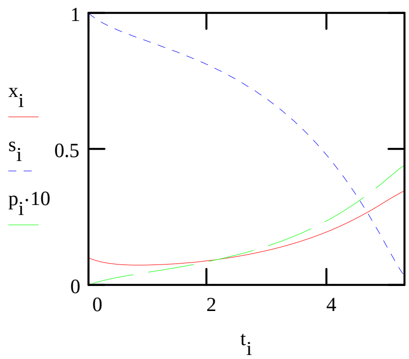
Instead, we will maximize with the "Minerr" function rather than the "Find" function.

Initial Guess: $F := 0.15$ Given $Prod_x(F) = 0.1$ $F_{opt} := Minerr(F)$ $F_{opt} = 0.168$

Initial Guess: $F := 0.15$ Given $Prod_p(F) = 0.01$ $F_{opt} := Minerr(F)$ $F_{opt} = 0.167$

Plot of state variables at optimum F $F := 0.17$

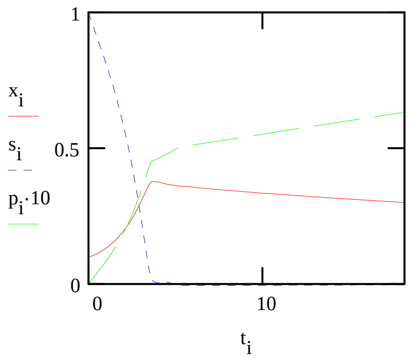
$Yout := yout(F)$ $t := Yout^{\langle 0 \rangle}$ $x := Yout^{\langle 1 \rangle}$ $s := Yout^{\langle 2 \rangle}$ $p := Yout^{\langle 3 \rangle}$ $v := Yout^{\langle 4 \rangle}$



← Substrate is just depleted at t_f. Just right!

Plot of state variables at sub-optimum $F<F_{opt}$ $F := 0.05$

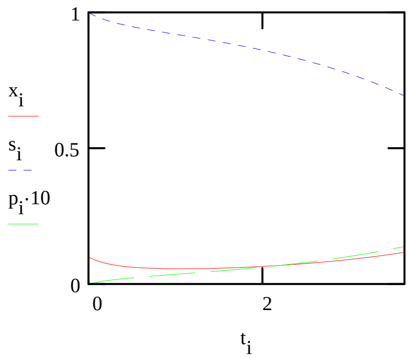
$Yout := yout(F)$ $t := Yout^{\langle 0 \rangle}$ $x := Yout^{\langle 1 \rangle}$ $s := Yout^{\langle 2 \rangle}$ $p := Yout^{\langle 3 \rangle}$ $v := Yout^{\langle 4 \rangle}$



← Substrate is depleted before t_f. Need to reduce t_f.

Plot of state variables at sub-optimum $F>F_{opt}$ $F := 0.25$

$Yout := yout(F)$ $t := Yout^{\langle 0 \rangle}$ $x := Yout^{\langle 1 \rangle}$ $s := Yout^{\langle 2 \rangle}$ $p := Yout^{\langle 3 \rangle}$ $v := Yout^{\langle 4 \rangle}$



← Substrate remains at t_f. Need to increase t_f.

Thus, we find that the optimum flow rate is one such that the substrate is just depleted at the harvest time t_f.