Fed-Batch Reactor with Product Formation (Repeated Cyclic Fill-Harvest Operation)
Satisfy the constraint of "initial condition = final condition" with the "sbval" function.
Caution: the "sbval" calculation takes a long time (5-10 minutes on a Pentium) to converge!
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Operation conditions:

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

$F := 0.2$ ... Flow rate (L/h) ⟵ **Change this number to optimize productivity**

$V := 1$ ... 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:

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

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

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

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

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

$$ydot\_dummy(t,y) := \begin{bmatrix} dxdt(y_0,y_1,y_2,y_3) \\ dsdt(y_0,y_1,y_2,y_3) \\ dpdt(y_0,y_1,y_2,y_3) \\ dvdt(y_0,y_1,y_2,y_3) \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

Call the "sbval" function to match the initial conditions of x, s, and p with the final conditions. (The last three dummy variables help carry the initial guesses contained in $y_{initial}$ to the final point for comparison in y_{final}, which is otherwise constrained by MathCad to be a function of only y at the final point but not a function of y at the initial point.)

$v_0 := 0.05 \cdot V$ ... Initial volume with a 5% inoculum

$guess := \begin{pmatrix} 1 \\ 0 \\ 0 \end{pmatrix}$ ... biomass, ... substrate, ... product

$$y_{initial}(t, guess) := \begin{bmatrix} guess_0 \\ guess_1 \\ guess_2 \\ 0.05 \cdot V \\ guess_0 \\ guess_1 \\ guess_2 \end{bmatrix} \begin{matrix} \text{... biomass} \\ \text{... substrate} \\ \text{... product} \\ \text{... volume} \\ \text{... dummy biomass} \\ \text{... dummy substrate} \\ \text{... dummy product} \end{matrix}$$

Match: initial=final

$$y_{final}(t, y) := \begin{bmatrix} y_0 - y_4 \\ y_1 - y_5 \\ y_2 - y_6 \end{bmatrix}$$

Integrate the ODEs (supplemented by dummy ones) from $t_0 := 0$ to $t_f := \dfrac{V - v_0}{F}$

$y0 := sbval(guess, t_0, t_f, ydot\_dummy, y_{initial}, y_{final})$

$y0 = \begin{pmatrix} 0.342 \\ 0.007 \\ 0.046 \end{pmatrix}$ $x_0 := y0_0$ $s_0 := y0_1$ $p_0 := y0_2$

Use the initial conditions found above to integrate the ODEs one more time.

$$y_{initial} := \begin{bmatrix} x_0 \\ s_0 \\ p_0 \\ v_0 \end{bmatrix}$$

Integrate ODEs from t_0 to t_f in $N := 100$ steps

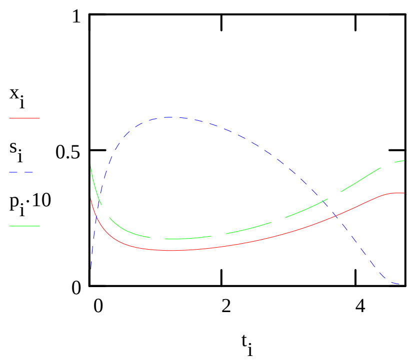
$yout := rkfixed(y_{initial}, t_0, t_f, N, ydot)$

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

Check: $x_N = 0.342$ $s_N = 0.00662$ $p_N = 0.0463$ $v_N = 1$

Plots of state variables

$i := 0 .. \mathrm{last}(t)$



Productivity

Cells ... $\dfrac{v_N \cdot x_N - v_0 \cdot x_0}{t_f} = 0.06846$

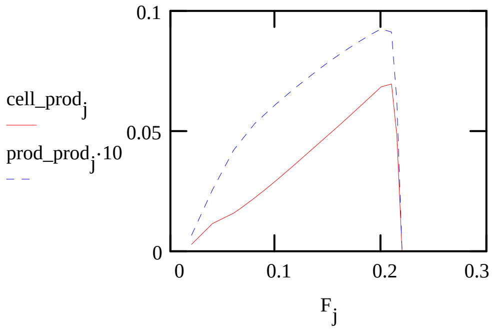
Product ... $\dfrac{v_N \cdot p_N - v_0 \cdot p_0}{t_f} = 0.00926$

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

$j := 0 .. 100$

$F_j :=$	$xN_j :=$	$sN_j :=$	$pN_j :=$	$cell\_prod_j :=$	$prod\_prod_j :=$	
0.02	0.290	0.0000	0.0665	0.00295	0.00067	
0.04	0.290	0.0000	0.0643	0.01161	0.00257	
0.06	0.265	0.00176	0.0701	0.01593	0.00421	
0.08	0.277	0.00182	0.0665	0.02218	0.00532	
0.10	0.295	0.00249	0.0612	0.02946	0.00612	
0.12	0.308	0.00320	0.0572	0.03693	0.00686	
0.14	0.318	0.00394	0.0539	0.04456	0.00755	
0.15	0.323	0.00433	0.0525	0.04844	0.00787	
0.16	0.327	0.00472	0.0511	0.05236	0.00818	
0.17	0.331	0.00513	0.0498	0.05632	0.00847	
0.18	0.335	0.00554	0.0486	0.06033	0.00875	
0.19	0.339	0.00597	0.0475	0.06438	0.00902	
0.20	0.342	0.00663	0.0463	0.06847	0.00926	⟵ optimum flow rate
0.21	0.332	0.04637	0.0435	0.06969	0.00913	
0.215	0.225	0.35485	0.0292	0.04843	0.00628	
0.22	0.	1	0	0	0	⟵ washout above F=0.215
0.25	0.	1	0	0	0	

$j := 0 .. \mathrm{last}(F)$



From the table and the plot, maximum productivity of cells and product occur at F=0.21 and F=0.20, respectively. These numbers depend on the operating conditions. The general shape of the productivity-versus-flow rate curve is similar to that of noncylic operation. In particular, there is a very sharp decrease in the productivity/profit when flow rate increases past the optimum value. It is safer to operate at a flow rate slightly below the optimum value to avoid washout. Note that at maximum productivity, the substrate is just about depleted when the run is terminated.