Fed-Batch Bioreactor

File: `Ch02_Bioreactor_Fedbatch.m`

The following example is a Matlab implementation of a model for a fed-batch bioreactor described in section 2.4.9 of SEMD. Use the Matlab 'publish' command to view the results. There are no software dependencies.

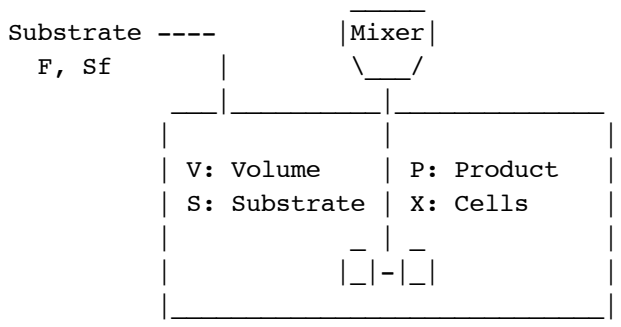
Contents

Version History

```
2012/02/02 JCK
2012/02/03 JCK Additional documentation, diagrams
2012/02/05 JCK Updated documentation, shortened display section
2012/04/06 JCK Added to the public directory.
```

Process Description

Operation of a fed-batch bioreactor begins with an initial batch of cells. A growth substrate is added to the reactor at a programmed rate F(t) over the period of operation. Substrate is consumed and a desired product produced during the course of normal cell growth and metabolism.



State Variables and Initial Conditions

Simulating systems of differential equations in Matlab requires all of the variables to be included in a single Matlab vector. The following table shows how the model variables are mapped to the Matlab vector `x` for simulation.

```
MATLAB  SYMBOL       DESCRIPTION     IC     UNITS
  x(1)       X        Cell Conc.   0.05   g/liter
```

```
  x(2)       S   Substrate Conc.   10.0   g/liter
  x(3)       P     Product Conc.    0.0   g/liter
  x(4)       V            Volume    1.0     liter
```

```
ic = [0.05; 10.0; 0.0; 1.0];
```

Parameter Values

Parameter values for the fed-batch bioreactor are from Table 2.3 of SEMD.

```
MATLAB   PARAMETER           DESCRIPTION   VALUE     UNITS
 mumax    mu_{max}   Maximum Growth Rate    0.20    1/hour
    Ks         K_s        Monod Constant    1.00   g/liter
   Yxs     Y_{X/S}            Cell yield     0.5       g/g
   Ypx     Y_{P/X}         Product yield     0.2       g/g
    Sf         S_f   Feed Substrate Conc    10.0   g/liter
```

```
mumax = 0.20;
Ks    = 1.00;
Yxs   = 0.5;
Ypx   = 0.2;
Sf    = 10.0;
```

Reaction Rate Expressions

Rate equations for cell growth are implemented using anonymous functions. The following lines implement the rate models given by equations (2-93) through (2-95) in SEMD.

```
mu = @(S) mumax*S./(Ks + S);     % Monod Equation (2-94)
rg = @(X,S) mu(S)*X;             % Rate of cell growth (2-93)
rp = @(X,S) Ypx*rg(X,S);         % Rate of product formation (2-95)
```

Inlet Flowrate

In this example the inlet flowrate is a constant function of time. In feedback control, the flowrate may also be a function of process state.

```
F = @(t) 0.05;
```

Reactor Model

The differential equations given in SEMD model the rate of change for total cell mass, product mass, substrate mass, and volume. These are implemented using anonymous functions.

```
dXV = @(t,x) x(4)*rg(x(1),x(2));
dPV = @(t,x) x(4)*rp(x(1),x(2));
dSV = @(t,x) F(t)*Sf - x(4)*rg(x(1),x(2))/Yxs;
dV  = @(t,x) F(t);
```

The model equations are for total the total mass of cells, product, and substrate. The state variables, however, are expressed in concentration, not total mass. Therefore we need to use the chain rule to reformulate the differential equations in terms of concentration. Applying the chain rule to total cell mass

$$\frac{dXV}{dt} = V\frac{dX}{dt} + X\frac{dV}{dt}$$

then solving for rate of change of cell concentration gives

$$\frac{dX}{dt} = \frac{1}{V}\left(\frac{dXV}{dt} - X\frac{dV}{dt}\right)$$

Applying the same process to all of the concentration variables and implementing in Matlab results in the following functions.

```
dX = @(t,x) (dXV(t,x) - x(1)*dV(t,x))/x(4);
dS = @(t,x) (dSV(t,x) - x(2)*dV(t,x))/x(4);
dP = @(t,x) (dPV(t,x) - x(3)*dV(t,x))/x(4);
```

The right hand sides of the differential equations are assembled into a corresponding function that produces a vector of function values.

```
f = @(t,x) [dX(t,x); dS(t,x); dP(t,x); dV(t,x)];
```

Integration

Use `ode45` for the integration.

```
tspan = [0 30];
[t,x] = ode45(f,tspan,ic);
```

Display Results

The simulation results are displayed in a format similar to Figure 2.14 of SEMD.

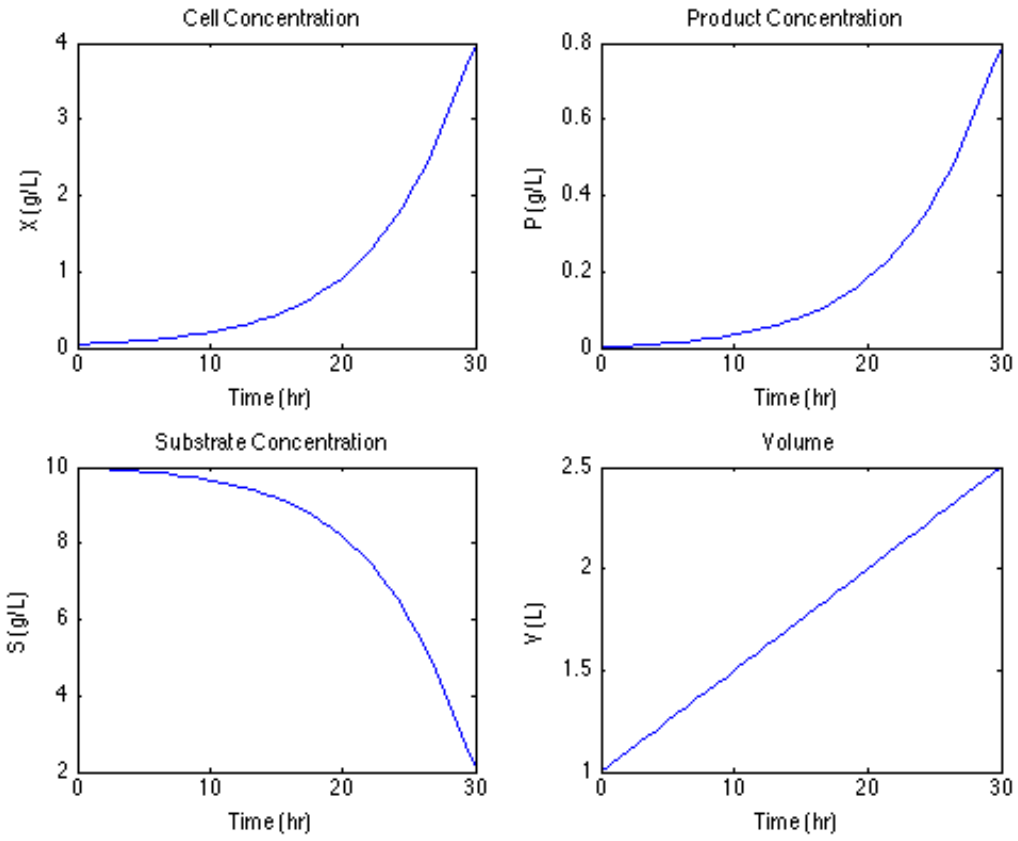
```
subplot(2,2,1);
plot(t,x(:,1));
xlabel('Time (hr)');
ylabel('X (g/L)');
title('Cell Concentration');

subplot(2,2,2);
plot(t,x(:,3));
xlabel('Time (hr)');
ylabel('P (g/L)');
title('Product Concentration');

subplot(2,2,3);
plot(t,x(:,2));
xlabel('Time (hr)');
ylabel('S (g/L)');
```

```
title('Substrate Concentration');

subplot(2,2,4);
plot(t,x(:,4));
xlabel('Time (hr)');
ylabel('V (L)');
title('Volume');
```



Suggested Exercises

1. Repeat the above calcuations to confirm the results in Section 2.4.9 SEMD for F(t) = 0.02.
2. Problem 2.15 SEMD. Modify the model and simulation for the case of a continuous bioreactor. Use the Matlab command `fsolve` for the necessary equation solving for the steady state analysis in parts (b), (c), and (d). Use |ode45) to integrate the model differential equations to steady state to confirm the your calculations for part (d).
3. Problem 2.17 SEMD. You can solve this problem by trial and error. Alternatively, you can create an anonymous function which, given a final time, performs the necessary simulation to compute fraction of substrate converted. Then use `fsolve` to find the time necessary to convert 90% of the the substrate. necessary simulation

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