Three Modes in the Operation of the Semi-batch Bioreactor

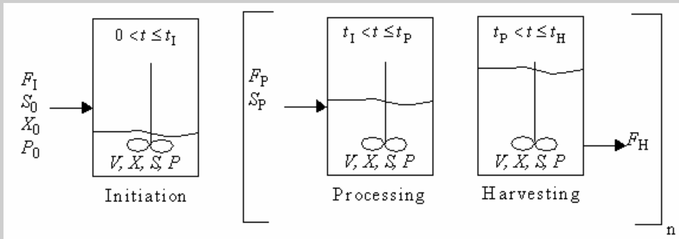


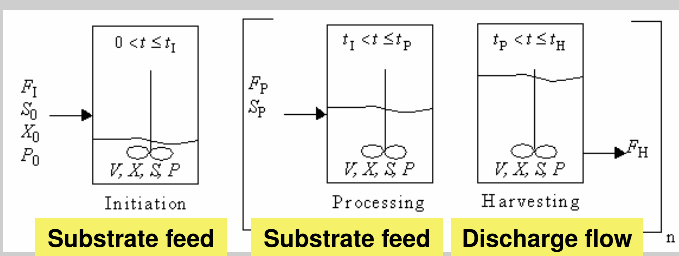
Table 14–7 Differential Equations for Fed Batch and Cyclic Fed Batch Bioreactors

Differential Equations	Initiation	Processing	Harvesting
$\frac{dN_X}{dt} =$	$F_I X_0 + \mu_{net} XV$	$\mu_{net} XV$	$-F_H X + \mu_{net} XV$
$\frac{dN_S}{dt} =$	$F_I S_0 - \frac{\mu_{net} XV}{Y_{X/S}}$	$F_P S_P - \frac{\mu_{net} XV}{Y_{X/S}}$	$-F_H S - \frac{\mu_{net} XV}{Y_{X/S}}$
$\frac{dN_P}{dt} =$	$\frac{\mu_{net} XV}{Y_{X/P}}$	$\frac{\mu_{net} XV}{Y_{X/P}}$	$-F_H P + \frac{\mu_{net} XV}{Y_{X/P}}$
$\frac{dV}{dt} =$	F_I	F_P	$-F_H$

$$\mu_{net} = \mu_g = \frac{\mu_m S}{K_S + S + S^2/K_I}$$

S (substrate, reactant) + X (cell) = P (product) + nX

Three Modes in the Operation of the Semi-batch Bioreactor



Substrate feed rate F_I

Final volume V_I

Substrate feed rate F_P

Final Volume V_H

Discharge flow rate F_H

Final Volume V_I

***n* – cycle number**

***n* = 1 fed-batch operation**

S (substrate, reactant) + X (cell) = P (product) + nX

The biochemical reaction is inhibited by the substrate

Optimal substrate feed concentration is required with fixed set of operating conditions

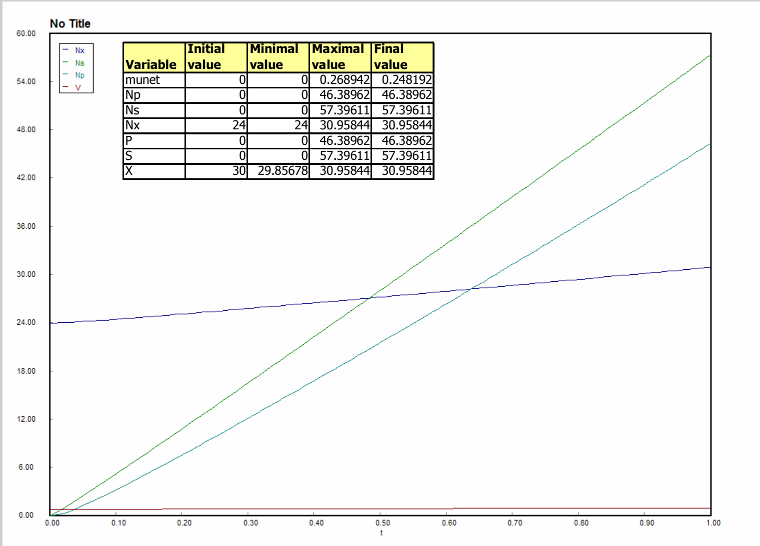
POLYMATH Model for the Initiation Mode of the Semi-batch Bioreactor

RKF45 ☐ Table ☐ Graph ☑ Report

Differential Equations: 5 | Auxiliary Equations: 12 | Ready for solution

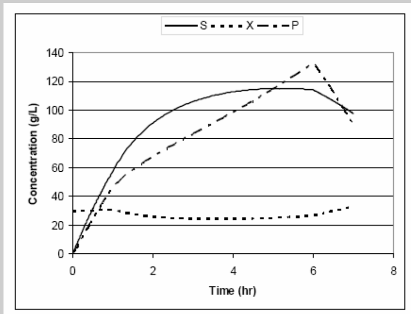
```
d(Nx) / d(t) = (Fl*X0+munet*V*X) # Quantity of cells (g)
d(Ns)/d(t)= (Fl*S0+munet*V*X/Yxs) # Quantity of glucose (g)
d(Np)/d(t)=(munet*V*X/Yxp) # Quantity of fermentation products (g)
d(V)/d(t)=Fl # Culture volume (L)
d(PR)/d(t)=0 # Production rate (g/hr)
mum=0.3 # Maximal specific growth rate (1/hr)
Ks=1 # Monod constant (g glucose/L)
Kl=300 # Monod constant (g glucose/L)^2
Yxs=0.4 # Yield Coefficient (g cells/g glucose)
Yxp=0.15 # Yield Coefficient (g cells/g product)
S0=200 # Feed sustrate concentration, initialization stage (g glucose/L)
Fl=0.2 # Feed flow rate, initialization stage (L/hr)
munet=mum*S/(Ks+S+S^2/Kl) # Specific growth rate (g product/L-hr)
X=Nx/V # Cell concentration (g/L)
S=Ns/V # Substrate concentration (g/L)
P=Np/V # Product concentration (g/L)
X0=0 # Feed cell concentration (g/L)
Nx(0) = 24 # Initial quantity of cells (g)
Ns(0)=0 # Initial quantity of substrate (g)
Np(0)=0 # Initial quantity of products (g)
V(0)=.8 # Initial culture volume (L)
PR(0)=0 # Initial production rate (g)
t(0) = 0
t(f) = 1
```

POLYMATH Model for the Initiation Mode of the Semi-batch Bioreactor



Variable	Initial value	Minimal value	Maximal value	Final value
munet	0	0	0.268942	0.248192
Np	0	0	46.38962	46.38962
Ns	0	0	57.39611	57.39611
Nx	24	24	30.95844	30.95844
P	0	0	46.38962	46.38962
S	0	0	57.39611	57.39611
X	30	29.85678	30.95844	30.95844

Fed-batch Bioreactor Operation – Initialization and one Cycle of Processing and Harvesting



Separate POLYMATH models are prepared for the processing and harvesting modes of operation and the results are combined manually

For modeling the cyclic operation and carrying out optimization programming is essential

Variable		Initiation	Processing	Harvesting
Time (hr)	0	1	6	7
Nx (g)	24	30.96	93.90	33.43
Ns (g)	0	57.40	400.05	97.80
Np (g)	0	46.39	465.97	89.14
V (L)	0.8	1.00	3.50	1.00
X (g/L)	30	30.96	26.83	33.43
S (g/L)	0	57.40	114.30	97.80
P (g/L)	0	46.39	133.14	89.14
PR (g)	0	0.00	0.00	280.21

POLYMATH generated MATLAB Function for the Initiation Mode Operation of the Bioreactor

No.	Command % Comment
1	function dYfuncvecdt = ODEfun(t,Yfuncvec);
2	Nx = Yfuncvec(1);
3	Ns = Yfuncvec(2);
4	Np = Yfuncvec(3);
5	V = Yfuncvec(4);
6	PR = Yfuncvec(5);
7	mum = .3; % Maximal specific growth rate (1/hr)
8	Ks = 1; % Monod constant (g glucose/L)
9	KI = 300; % Monod constant (g glucose/L)^2
10	Yxs = .4; % Yield coefficient(g cells/g glucose)
11	Yxp = .15; %Yield coefficient (g cells/g product)
12	S0 = 200; % Feed sustrate concentration, initialization stage (g glucose/L)
13	FI = .2; % Feed flow rate, initialization stage (L/hr)
14	S = Ns / V; % Substrate concentration (g/L)
15	X = Nx / V; % Cell concentration (g/L)
16	munet = mum * S / (Ks + S + S ^ 2 / KI); % Specific growth rate (g product/L-hr)
17	P = Np / V; % Product concentration (g/L)
18	X0 = 0; % Feed cell concentration (g/L)
19	dNxdt = FI * X0 + munet * V * X; % Quantity of cells (g)
20	dNsdt = FI * S0 + munet * V * X / Yxs; % Quantity of glucose (g)
21	dNpdt = munet * V * X / Yxp; % Quantity of fermentation products (g)
22	dVdt = FI; % Culture volume (L)
23	dPRdt = 0; % Production rate (g/hr)
24	dYfuncvecdt = [dNxdt; dNsdt; dNpdt; dVdt; dPRdt];

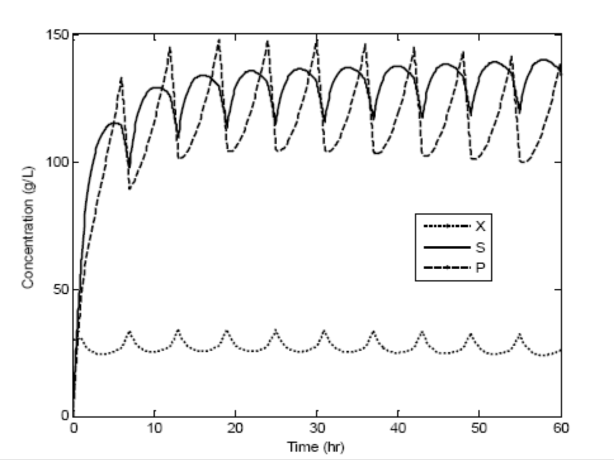
Conversion of vector contents to variable names

Collection of the variables into a column vector

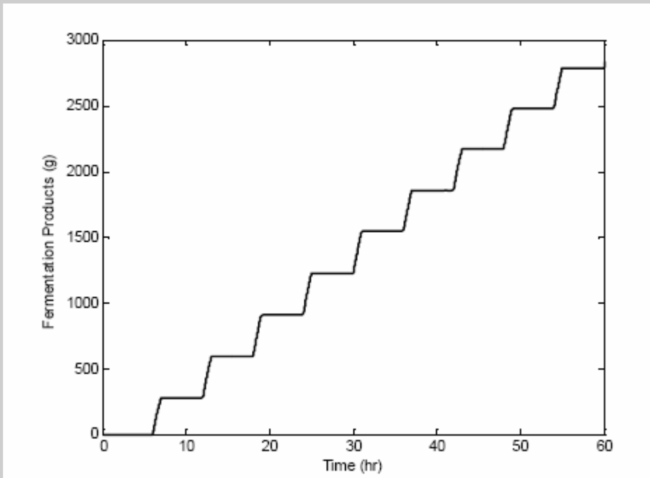
Part of the MATLAB "Main Program" for Simulation of Ten Process Cycles

No.	Command % Comment
1	tspan = [0 1.]; % Range for the independent variable
2	y0 = [24.; 0; 0; 0.8; 0]; % Initial values for the dependent variables
3	tg=[]; Nx=[]; Ns=[];Np=[]; V=[]; PR=[];
4	[t,y]=ode45(@ODEfunIni,tspan,y0); ← **Initialization**
5	tg=[tg; t]; Nx=[Nx; y(:,1)]; Ns=[Ns; y(:,2)]; Np=[Np; y(:,3)];V= [V; y(:,4)]; PR=[PR; y(:,5)];
6	tspan=[t(end) t(end)+5];
7	y0=y(end,:);
8	ncycle=10;
9	for j=1:ncycle
10	[t,y]=ode45(@ODEfunProc,tspan,y0); ← **Processing**
11	tg=[tg; t]; Nx=[Nx; y(:,1)]; Ns=[Ns; y(:,2)]; Np=[Np; y(:,3)];V= [V; y(:,4)]; PR=[PR; y(:,5)];
12	tspan=[t(end) t(end)+1];
13	y0=y(end,:);
14	[t,y]=ode45(@ODEfunHarv,tspan,y0); ← **Harvesting**
15	tg=[tg; t]; Nx=[Nx; y(:,1)]; Ns=[Ns; y(:,2)]; Np=[Np; y(:,3)];V= [V; y(:,4)]; PR=[PR; y(:,5)];
16	tspan=[t(end) t(end)+5];
17	y0=y(end,:);
18	end

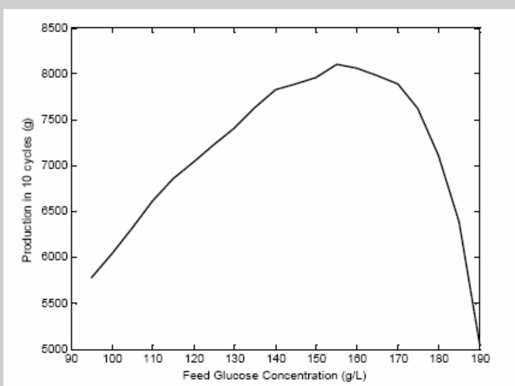
Results of Ten Cycles of Processing and Harvesting



Amount of Harvested Fermentation Products in Cyclic Operation of the Bioreactor



Maximizing the Harvested Fermentation Products (P_R) as Function of Feed Glucose Concentration (S_P)



The maximum found using the MATLAB *fminbnd* library function is P_R=8.144 kg when S_P = 156.7 g/L