**Legend:**

**Comments that were added**

**Changes proposed to the code**

% Penicillin G production simulator ODE set

% This file is called by pensim2.m wrapper file

%

% I/O structure : dy = pengsimv1\_6m(t,y,FLAG,inp1);

%

% Inputs:

% t: time span of integration

% y: initial conditions for that time span

% FLAG=[]; Matlab notation

% inp1: (1-by-14) vector of input parameters

%

% Output:

% dy: matrix of time stamps and ODE solutions

%

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%

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%

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function dy=pengsimv1\_6m(t,y,FLAG,inp1)

a=inp1(1); %a is Dissolved Oxygen Concentrarion in g/l. In the article, this variable is cL and it is explict in equations (2), (3), (10) and (12).

F=inp1(2); %F is Feed Flow Rate of Substrate in L/h. In the article, this variable is also named F and it is explicit in equations (5), (11), (14) and (17)

fgg=inp1(3); %fgg is Flow Rate of Oxygen. In the article, this variable is named fg and it is explicit in equation (13).

pww=inp1(4); %pww is Power Input. In the article, this variable is named Pw and it is explicit in equation (13).

Tf=inp1(5); % Tf is Feed Temperature of Substrate in K. In the article, this variable is named Tf and it is explicit in equation (17).

Fc=inp1(6); %Fc is Cooling Water Flow Rate in L/h. In the article, this variable is also named Fc and it is explicit in equation (17).

b=inp1(7); %b => flag for heating/cooling switching (b=0 : Cooling, b=1 : Heating). It is explicit in equation (17).

Fb=inp1(8); %Fa is Acid Flow Rate in L/h. In the article, this variable is also named Fa and it is explicit in equations (6) and (14).

Fa=inp1(9); %Fb is Base Flow Rate in L/h. In the article, this variable is also named Fb and it is explicit in equations (6) and (14).

cab=inp1(10); % cab is acid concentration in mol/L. In the article, this variable is not shown explicit but it is implicit in the terms Ca/b in equation (6) and Fa/b in equation (14) that is Fa\*cab/cb + Fb\*cab/cb.

cb=inp1(11); % cb is base concentration in mol/L. In the article, this variable is not shown explicit but it is implicit in the terms Ca/b in equation (6) and Fa/b in equation (14) that is Fa\*cab/cb + Fb\*cab/cb.

step1=inp1(12); %ODE solver step size as described in pensim2 line 142. However, in the article, this is the variable deltat in equations (5) and (6).

d1=inp1(13); %Constant used in ODE (pengsimv1\_6.m) acid/base equilibrium for equation (6) that describes B. If d1=1 PID routine works but it's designed to be used mainly for on-off controller

sf=600;% Feed Substrate Solution Concentration in g/L that is fed to the fermenter. In the article, this variable is also named Sf and it is explicit in equations (11) and (17).

a1=(1/0.45);% 1/(Yx/s). It is the inverse of the yield constant Yx/s. This term 1/(Yx/s) is in equation (11).

a2=(1/0.9);% 1/(Yp/s). It is the inverse of the yield constant Yp/s. This term 1/(Yp/s) is in equation (11).

a3=(1/0.04);% 1/(Yx/o). It is the inverse of the yield constant Yx/o. This term 1/(Yx/o) is in equation (12).

a4=(1/0.2);% 1/(Yp/o). It is the inverse of the yield constant Yp/o. This term 1/(Yp/o) is in equation (12).

a5=(1/7);% Constant relating CO2 to growth in mmol CO2/ g biomass. In the article, this variable is named alpha1 and it is explicit in equation (18).

mx=0.014;% Maintenance Coefficient on Substrate per h. In the article, this variable is also named mx and it is explicit in equation (11).

mo=0.467;% Maintenance Coefficient on Oxygen per h. In the article, this variable is also named mo and it is explicit in equation (12).

mux=0.092;% Maximum specific growth rate per h. In the article, this variable is named ux and it it explicit in equations (2), (3), and (4).

kx=0.15;% Contois Saturation Constant in g/L. In the article, this variable is also named Kx and it is explicit in equations (2) and (3).

mup=0.005;% Specific Rate of Penicillin Production per h. In the article, this variable is named up and it is explicit in equation (10).

kp=0.0002;% Monod saturation constant. In table 2, it is named as Inhibition Constant, Kp. It is explicit in equation (10).

ki=0.1;% Substrate inhibition const. for product formation in g/L. In the article, it is also named Ki and is explicit in equation (10).

mc=4e-7;% Constant relating CO2 to maintenance energy in mmol CO2 / (g biomass.h). In the article, this variable is named alpha2 and is explicit shown in equation (18).

k4=1e-4;% Constant relating CO2 to penicillin production in mmol CO2/(L.h). In the article, this variable is named alpha3 and is explicit in equation (18).

p=3;% It is a constant that is in the exponent in equation (10).

k=0.04;% 1st order decay rate const. for product. Penicilin Hydrolysis rate constant per h. In the article, it is also named K and it is explicit in equation (9).

Ed=50000;% Activation energy for cell death in cal/mol. In the article, it is also named Ed and it is explicit in equation (3) and (7).

kdd=1e33;% Arrhenius constant for cell death. In the article, it is named Kd and explicit in equation (3) and (7).

Eg=5100;% Activation energy for growth in cal/mol. In the article, it is also named Eg and it is explicit in equation (3) and (7).

kdg=7e3;%Arrhenius constant for growth. In the article, it is named Kg and explicit in equation (3) and (7).

ck=(1e-5);% Proportionality constant, present in table 2, in mol H+/g biomass. In the article, it has the symbol gama and is explicit in equation (5).

k1=1e-10;% Constants for [H+] in mol/L. Constant K1 named in the article. It is explicit in equations (3) and (4).

k2=7e-5;% Constants for [H+] in mol/L. Constant K2 named in the article. It is explicit in equations (3) and (4).

rcp=(1/1500);% 1/(ro\*cp) in 1/(cal/L.C) for the bulk in fermenter. In the article, it is named pCp and is explicit in equation (17).

rq1=60;% heat generated by fermentation in cal/g biomass. Yield of heat generation. In the article, it is named rq1 and is explicit in equation (16).

rq2=1.6783e-4;% heat generated by fermentation in cal/g biomass.h. Constant in heat generation. In the article, it is named rq2 and explicit shown in equation (16).

a10=0.6; % Constant b. In the article, it is also named b and explicit shown in equation (17).

Tc=290;% Cold water inlet temp. This equation is not shown explicit but it is in energy balance (written in the program). The energy balance is equation (17).

Th=323;% Hot water inlet temp. This equation is not shown explicit but it is in energy balance (written in the program). The energy balance is equation (17).

% if b=1 the system is being heated. Otherwise, it is being cooled.

if b==1

a9=8e5; % This variable is Heat Transfer coeff. of cooling/heating liquid in cal/(h.C). In the article, it is named a and explicit shown in equation (17).

else

a9=1e3;% This variable is Heat Transfer coeff. of cooling/heating liquid in cal/(h.C). In the article, it is named a and explicit shown in equation (17).

end

clstar=a; %Clstar is the Dissolved Oxygen Concentration at saturation of oxygen ib g/L. In table 2 shows the value for cstar=1.16. It is in equation to calculate Kox and Kop (below).

% Oxygen Limitation Decision

kox=2e-2\*clstar\*(1+tanh(50\*(0.58-y(2))))/2; %Kox and Kop are Oxygen Limitation Constants, present in table 2. They are in equations (2), (3).

kop=5e-4\*(1+tanh(50\*(0.58-y(2))))/2;% Kox and Kop are Oxygen Limitation Constants, present in table 2. They are in equation (10).

%y1=>S; %y2=>CL; %y3=>X; %y4=P %y5=V %y6=CO2 %y7=H %y8=T %y9=Qrxn

c1=y(1)/(kx\*y(3)+y(1)); %This corresponds to the first term of the equation (2).

c2=y(2)/(kox\*y(3)+y(2)); %This corresponds to the second term of the equation (2).

c3=y(1)/(kp+y(1)\*(1+y(1)/ki)); %This corresponds to the first term of the equation (10).

c4=(y(2)^p)/(kop\*y(3)+(y(2)^p)); %This corresponds to the second term of the equation (10).

c6=kdd\*(exp(-Ed/(1.987\*y(8)))); %This is the fifth term of the equation (3) and the second of the equation (7).

c7=kdg\*(exp(-Eg/(1.987\*y(8)))); %This is the fourth term of the equation (4) and first of the equation (7).

c8=(1/(1+k1/y(7)+y(7)/k2)); %This corresponds to the first term of the equations (3) and (4).

c9=y(3)\*(mux\*c1\*c2\*c8\*c7-F/y(5)-c6); %This is the first term of the equation (5), uX -FX/V.

c5=rq1\*c9\*y(5)+rq2\*y(3)\*y(5);%Heat generated by fermentation in calories. This is the equation (16).

c10=F+d1\*Fb\*cab/cb+d1\*Fa\*cab/cb-1e-4\*y(5)\*[exp(0.05\*(y(8)-273))-1];$$Wrong$$ % Volume correction. This is the equation (14). The last term of this equation is Floss, which is equation (15).

%Proposed c10: c10=F+d1\*Fb\*cab/cb+d1\*Fa\*cab/cb-2.5e-4\*y(5)\*[exp(0.05\*(y(8)-273))-1];

kla=70\*sqrt(fgg)\*((pww/y(5))^0.4);% fgg=inflow air rate, pww=agitator power. This is the equation (13).

B=[(1e-14/y(7)-y(7))\*y(5)-d1\*cab\*Fa\*step1+d1\*cab\*Fb\*step1]/(y(5)+d1\*Fb\*step1+d1\*Fa\*step1);$$Wrong$$ %This is the term B in the equation (5). This entire equation corresponds to equation (6).

%Proposed B: B=((1e-14/y(7)-y(7))\*y(5)-d1\*cab\*Fa\*step1-d1\*cab\*Fb\*step1)/(y(5)+d1\*Fb\*step1+d1\*Fa\*step1);

%---------ODEs-----

dy(1)=-y(3)\*(mux\*a1\*c1\*c2\*c8\*c7+mup\*a2\*c3\*c4+mx-a1\*c6)+F\*sf/y(5)-y(1)\*c10/y(5); %This is the ODE dS/dt, equation (11).

dy(2)=-y(3)\*(mux\*a3\*c1\*c2\*c8\*c7+mup\*a4\*c3\*c4+mo-a3\*c6)+kla\*(clstar-y(2))-y(2)\*F/y(5); $$Wrong$$ %This is the ODE dCL/dt, equation (12).

%Proposed dy(2): dy(2)=-y(3)\*(mux\*a3\*c1\*c2\*c8\*c7+mup\*a4\*c3\*c4+mo-a3\*c6)+kla\*(clstar-y(2))-y(2)\*c10/y(5);

dy(3)=c9; $$Wrong$$ %This is de ODE dX/dt, equation (1).

%Proposed dy(3): dy(3)= y(3)\*(mux\*c1\*c2\*c8\*c7-c6)-y(3)\*c10/y(5);

dy(4)=mup\*c3\*c4\*y(3)-k\*y(4)-y(4)\*F/y(5); $$Wrong$$ %This is the ODE dP/dt, equation (9).

%Proposed dy(4): dy(4)= mup\*c3\*c4\*y(3)-k\*y(4)-y(4)\*c10/y(5);

dy(5)=c10; %This is the ODE dV/dt, equation (14).

dy(6)=a5\*y(3)\*(mux\*c1\*c2\*c8\*c7-F/y(5)-c6+mc)+k4; $$Wrong$$ %This is the ODE dCO2/dt, equation (18).

%Proposed dy(6): dy(6)= a5\*dy(3)+ mc\*y(3)+ k4;

dy(7)=[ck\*c9+[(-B+sqrt(B^2+4e-14))/2-y(7)]/step1]; $$Wrong$$ %This is the ODE dH+/dt, equation (5).

%Proposed dy(7): dy(7)= ck\*c9 + ((-B+sqrt((B^2)+4e-14))/2 - y(7))/step1;

dy(8)=rcp\*y(9)/y(5)+F\*(Tf-y(8))/y(5)-tfl\*[((rcp/y(5))\*a9\*(Fc^(a10+1))\*(y(8)-b\*Th-(1-b)\*Tc))/(Fc+(a9\*(Fc^a10))/2000)]; $$Wrong$$ %This is the ODE dT/dt, equation (17).

%Proposed dy(8): dy(8)= rcp\*y(9)/y(5)+F\*(Tf-y(8))/sf-tfl\*(((rcp/y(5))\*a9\*(Fc^(a10+1))\*(y(8)-b\*Th-(1-b)\*Tc))/(Fc+(a9\*(Fc^a10))/2000));

dy(9)=c5; $$Wrong$$ %This is the equation dQrxn/dt, equation (16).

%Proposed dy(9): dy(9)= rq1\*dy(3)\*y(5) + rq2\*y(3)\*y(5);

dy=[dy(1);dy(2);dy(3);dy(4);dy(5);dy(6);dy(7);dy(8);dy(9)]; % This put the ODE's in a column vector.