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0001 // A biomolecular proportional integral controller based on feedback regulations of protein level and
      activity
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0004 // SI: Scilab code for simulations of the biochemical pathway (Figure 2)
0005
0006 xdel(winsid())
0007 clear
0008 global kcat vout Ks Ky kd ka ki vf n thetaf thetai
0009
0010 //// Model parameters
0011 kcat=10; vout=10; Ks=0.5; Ky=0.5; kd=0.05; ka=120;
0012 ki=90; vf=0.1; n=3; thetaf=0.3; thetai=0.3;
0013
0014 //// Computation of steady-states
0015 s_ref=1;
0016 y_ref=thetai*(vf/kd-1)^(1/n);
0017 xstar_ref=vout/kcat * y_ref/(Ky+y_ref) * (Ks+s_ref)/s_ref;
0018
0019 x_ref_I= ki/ka*xstar_ref;
0020 X_ref_I= xstar_ref + x_ref_I;
0021
0022 x_ref_PI= ki* y_ref^n / (thetai^n+y_ref^n) /ka *xstar_ref;
0023 X_ref_PI= xstar_ref + x_ref_PI;
0024
0025 //// Parameters of the linear I and PI controllers (given by Eq. (2.4))
0026
0027 KP= ki*n*y_ref^(n-1)*thetai^n / (thetai^n+y_ref^n)^2 * ka * X_ref_PI / (ka+ki*y_ref^n/(thetai^n+y_ref^n))^2;
0028 KI_PI= ka* vf*thetaf^n *n* y_ref^(n-1) / (thetaf^n+y_ref^n)^2 / (ka+ki*y_ref^n/(thetai^n+y_ref^n));
0029 KI_I= ka* vf*thetaf^n *n* y_ref^(n-1) / (thetaf^n+y_ref^n)^2 / (ka+ki);
0030
0031 //// Model equations
0032
0033 function dx=sysI(t, x) // system with biomolecular I control
0034 global kcat vout Ks Ky kd ka ki vf n thetaf thetai
0035 s=1;
0036 if t>0 then // s upshift
0037     s=5;
0038 end
0039
0040 dx(1)=kcat*x(3)* s/(Ks+s) - vout*x(1)/(Ky+x(1)); // y
0041 dx(2)= vf* thetaf^n / (thetaf^n + x(1)^n) - kd; // X
0042 dx(3)=ka * (x(2)-x(3))- ki *x(3); // x*
0043 endfunction
0044
0045 function dx=sysPI(t, x) // system with biomolecular PI control
0046 global kcat vout Ks Ky kd ka ki vf n thetaf thetai
0047 s=1;
0048 if t>0 then // s upshift
0049     s=5;
0050 end
0051
0052 dx(1)=kcat*x(3)* s/(Ks+s) - vout*x(1)/(Ky+x(1)); // y
0053 dx(2)= vf* thetaf^n / (thetaf^n + x(1)^n) - kd; // X
0054 dx(3)= ka * (x(2)-x(3)) - ki*x(1)^n / (thetai^n + x(1)^n) *x(3); // x*
0055 endfunction
0056
0057 function dx=sysI_linear(t, x) // system with linear I control
0058 global kcat vout Ks Ky kd ka ki vf n thetaf thetai
0059 s=1;
0060 if t>0 then // s upshift
0061     s=5;
0062 end
0063
0064 er=x(1)-y_ref; // error
0065 xstar= xstar_ref - KI_I * x(2) ;
0066
0067 dx(1)=kcat*xstar* s/(Ks+s) - vout*x(1)/(Ky+x(1)); // y
0068 dx(2)=er; // error integral
0069 endfunction
0070
0071 function dx=sysPI_linear(t, x) // system with linear PI control
0072 global kcat vout Ks Ky kd ka ki vf n thetaf thetai

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0002     s=1;
0003     if t>0 then // s upshift
0004         s=5;
0005     end
0006
0007     er=x(1)-y_ref; // error
0008     xstar= xstar_ref - KP * er - KI_PI * x(2) ;
0009
0010     dx(1)=kcat*xstar* s/(Ks+s) - vout*x(1)/(Ky+x(1)); // y
0011     dx(2)=er; // error integral
0012 endfunction
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0084 ///// Simulations
0085 tf=25;
0086 t=-5:0.002:tf;
0087 x0=[0.3;.9; 0.45];
0088 x0_I=[y_ref;X_ref_I;xstar_ref];
0089 x0_PI=[y_ref;X_ref_PI;xstar_ref];
0090 xI=ode(x0_I,t(1),t,sysI);
0091 xPI=ode(x0_PI,t(1),t,sysPI);
0092 xI_linear=ode([y_ref;0],t(1),t,sysI_linear);
0093 xPI_linear=ode([y_ref;0],t(1),t,sysPI_linear);
0094
0095 ///// Plot
0096 scf(3)
0097 subplot(6,1,2)
0098 plot([-5 0 0 tf],[1 1 5 5],"k",'linewidth',1);
0099 aa=gca()
0100 aa.data_bounds=[-5 0;tf 6]
0101 aa.y_label.text="\texttrm{Substrate concentration}\; s \$";
0102 aa.y_label.font_size=3;
0103
0104 subplot(3,1,2)
0105 plot(t,xI(1,:), 'g', 'linewidth',3)
0106 plot(t,xI_linear(1,:), 'g', 'linewidth',1)
0107 plot(t,xPI(1,:), 'm', 'linewidth',3)
0108 plot(t,xPI_linear(1,:), 'm', 'linewidth',1)
0109 plot([-5 tf],[y_ref y_ref],'k--','linewidth',1)
0110 legend("Biomolecular I feedback", "Classical I controller", "Biomolecular LA-PI feedback", "Classical
PI controller", "Set-point y_ref",1);
0111 aa=gca()
0112 aa.data_bounds=[-5 0.28;tf 0.53]
0113 aa.y_label.text="\texttrm{Output concentration}\; y \$";
0114 aa.y_label.font_size=3;
0115
0116 subplot(3,1,3)
0117 plot(t,xI(2,:)-xI(3,:), 'g', 'linewidth',3, 'linestyle', '-.')
0118 plot(t,xI(3,:), 'g', 'linewidth',3)
0119 plot(t,xPI(2,:)-xPI(3,:), 'm', 'linewidth',3, 'linestyle', '-.')
0120 plot(t,xPI(3,:), 'm', 'linewidth',3)
0121 legend("x (Biomolecular I feedback)", "x* (Biomolecular I feedback)", "x (Biomolecular LA-PI
feedback)", "x* (Biomolecular LA-PI feedback)",1);
0122 aa=gca()
0123 aa.data_bounds=[-5 0.1;tf 0.7]
0124 aa.y_label.text="\texttrm{Enzyme concentrations}\; x \; \texttrm{and}\; x^* \$";
0125 aa.y_label.font_size=3;
0126 aa.x_label.text="\texttrm{time}\ t\$";
0127 aa.x_label.font_size=3;

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