Modeling the CO system

The system

CO binds to CooA (An activator), It activates it, and so the activated activator ((CooA)2CO) binds to promoter and initiates transcription.

The Reactions that take place

1. [CO]+[CooA] ↔[(CooA)2CO]

The **dissociation constant** of this reaction is given by:

$$KI = \frac{[\mathrm{CO}] \cdot [\mathrm{CooA}]}{[\ (\mathrm{CooA})2\mathrm{CO}]}$$

Where $[\mathrm{CO}]$, $[\mathrm{CooA}]$, $[\ (\mathrm{CooA})2\mathrm{CO}]$ are the corresponding concentrations at equilibrium.

The second reaction that takes place is the binding of the [(CooA)2CO] to the promoter'S binding site and is described as follows.

2. [CooA)2CO] ↔[(CooA)2CO·Pr]

Where [(CooA)2CO·Pr] stands for the [(CooA)2CO] bound to the promoter.

The **dissociation constant** of this reaction is given by:

$$KP = \frac{[(\mathrm{CooA})2\mathrm{CO}]}{[\ (\mathrm{CooA})2\mathrm{CO} \cdot \mathrm{Pr}]}$$

What we want to model?

We want to model how the concentration of the chromoprotein changes with time. Since the concentration of the chromoprotein depends on the concentration of mRNA, we will develop first an equation that describes how the concentration of mRNA changes with time.

Developing an equation that describes how mRNA concentration changes with time:

The change in [mRNA] with time ($\frac{d[mRNA]}{dt}$) is equal to the formation rate of mRNA minus its degradation rate.

$$\frac{d(mRNA)}{dt} = k_{on1} \cdot P_{\exp} - \gamma_1 \cdot [mRNA]$$

Change in concentration of the chromprotein in time = formation rate - degradation rate

Where kon1 represents the formation constant of mRNA, γ_1 is the degradation constant of mRNA and Pexp is the probability that the promoter will be activated.

The initial condition for this equation is assumed to be:

[mRNA (t=0)]=0 molar

This means that at time t=0 sec, there isn't any mRNA molecules, encoding for the chromoprotein, present in the cell.

But what does Pexp means?

Pexp is the probability that the promoter will be activated and is calculated as follows:

$$Pexp = \frac{number\ of\ situations\ in\ which\ the\ promoter\ will\ be\ activated}{total\ number\ of\ situations} = \frac{w}{z}$$

Since we assume that: Only one molecule of the complex [(CooA)2CO] can be bound to the promoter at any moment, and that reaction 1 reaches equilibrium before transcription begins , the number of situations in which the promoter will be activated is equal to [(CooA)2CO · Pr].

That is to say,

$$w = [\ (\mathrm{CooA})2\mathrm{CO} \cdot \mathrm{Pr}] = \frac{[(\mathrm{CooA})2\mathrm{CO}]}{\mathrm{Kp}}$$

The number of situations in which the promoter will not be activated is equal to 1. That is because the only situation in which transcription will not take place is when there are no molecules bound to the promoter at all.

$$Z = w + 1 = \frac{[(\mathrm{CooA})2\mathrm{CO}]}{\mathrm{Kp}} + 1$$

Total number of situations

Number of situations in which the promoter will be activated

Number of situations in which the promoter will not be activated

$$Pexp = \frac{w}{z} = \frac{\frac{[(\mathrm{CooA})2\mathrm{CO}]}{\mathrm{Kp}}}{\frac{[(\mathrm{CooA})2\mathrm{CO}]}{\mathrm{Kp}} + 1}$$

As we want Pexp to be expressed in terms of [CO] and [CooA] instead of [(CooA)2CO] ,we repeat these calculations by taking into consideration reaction number 1 and its KI.

$$\text{Pexp}=\frac{\dfrac{[CooA]\cdot\dfrac{\dfrac{[CO]}{K_I}}{1+\dfrac{[CO]}{K_I}}}{K_p}}{1+\dfrac{[CooA]\cdot\dfrac{\dfrac{[CO]}{K_I}}{1+\dfrac{[CO]}{K_I}}}{K_p}}$$

**REMEMBER THIS EQUATION BECAUSE IT IS GOING TO SHOW UP IN THE MATLAB CODE ☺

As can be deduced from the above calculation, Pexp depends only on the concentration of [CO] and [CooA].

Recall the equation mentioned before that describes how the concentration of mRNA changes with time:

$$\frac{d(mRNA)}{dt}=k_{on1}\cdot P_{\exp}-\gamma_1\cdot[mRNA]$$

The initial condition was [mRNA (t=0)] =0 molar

The analytical solution for this differential equation is equal to:

$$[mRNA]=\frac{k_{on1}\cdot P_{\exp}}{\gamma_1}(1-e^{-\gamma_1 t})$$

Developing an equation that describes how chromoprotein concentration changes with time:

The equation that describes how the concentration of the chromoprotein ("[CP]") changes with time is defined as follows

$$\frac{d(CP)}{dt} = k_{on2} \cdot [mRNA] - \gamma_2 [CP]$$

Change in concentration of the chromprotein in time = formation rate- degradation rate

Where kon2 is the formation rate constant of the cp and γ_2 stands for the degradation rate constant of the cp

And the initial condition for this equation is assumed to be:

[CP(t=0)]=0 molar

The Analytical Solution for this equation is:

$$[CP] = k_{on2} \cdot \frac{k_{on1} \cdot P_{\exp}}{\gamma_1 \cdot \gamma_2}(1 - e^{-\gamma_2 t}) + k_{on2} \cdot \frac{k_{on1} \cdot P_{\exp}}{\gamma_1 \cdot (\gamma_2 - \gamma_1)}(e^{-\gamma_2 t} - e^{-\gamma_1 t})$$

Assumptions:

1. Reaction number 1 and 2 reach equilibrium before the transcription begin.
2. Only one molecule of the complex [CooA)2CO] can be bound to the promoter at one time.
3. [mRNA(t=0)]=0 molar
4. [CO] and [CooA] concentrations inside the cell are constant.

Finding a numerical solution

After finding the analytical solution this is actually a piece of cake. First we need to write a function called ODEfun and save it.

This is how we write the function ODEfun

```
function dx= ODEfun(t,x)

dx=zeros(1,2);
%x is a vector (x(1),x(2))
%x(1)=[mRNA]
%x(2)=[chromoprotein]
KI=0.6; %KI - dissociation constant of the binding of co to CooA
KP=0.8; %KP-dissociation constant of the binding of (CO2CooA) to the
promoter.
Kon1=0.8; %Kon1 - formation rate constant of mRNA
Kon2=0.7;  %Kon2-formation rate constant of the cp
gama1=0.04; %Degradation rate constant of mRNA
gama2=0.02; % Degradation rate constant of the cp
co=5; %co- concentration of co
cooa=6;%cooa-concentration of CooA
w=(cooa*co/(KI*(1+co/KI)))/KP;
z=(cooa*co/(KI*(1+co/KI)))/KP+1;
P_exp=w/z;
dx1=(Kon1*P_exp)-(gama1*x(1)); %rate equation of mRNA
dx2=(Kon2*x(1))-(gama2*x(2)); %rate equation of cp
dx=[dx1;dx2];
end
```

then we have to call the function by using the following code:

```
time_range=10000;

[T,X]=ode45(@ODEfun,[0 time_range],[0 0]);

figure(1);

plot(T,X(:,2),'r');

hold on

plot(T,X(:,1));

plot(T,X(:,2),'g');

hold off
```