

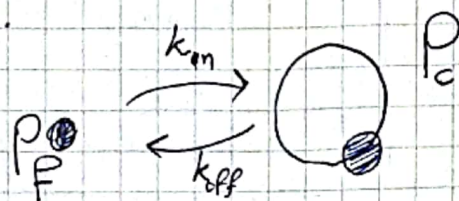
# Quasi Steady State Analysis :

## Example 1:

Suppose that we have protein  $P_F$  (F stands for Free) which diffuses in the environment with  $D_F$  and decays with rate  $k$  :

$$\frac{\partial P_F}{\partial t} = D_F \frac{\partial^2 P_F}{\partial x^2} - k P_F$$

We can change the rate of diffusion and decay by introducing a larger molecule to the environment that  $P_F$  can bind and unbind to.



Since  $P_C$  (C stands for Complex) is large, then its diffusion coefficient will be smaller. Also note that the  $P_C$  complex will not decay anymore (do not fit the enzyme). Also we assume that there is unlimited amount of larger molecule.

$$\begin{cases} \frac{\partial P_C}{\partial t} = D_C \frac{\partial^2 P_C}{\partial x^2} - k_{off} P_C + k_{on} P_F \\ \frac{\partial P_F}{\partial t} = D_F \frac{\partial^2 P_F}{\partial x^2} - k P_F + k_{off} P_C - k_{on} P_F \end{cases}$$

By assuming that the binding and unbinding kinetics is very fast, we can assume that the free and bound species equilibrate very quickly.

$$\Rightarrow k_{on} P_F - k_{off} P_C = 0 \Rightarrow \boxed{\frac{P_F}{P_C} = \frac{k_{off}}{k_{on}}} \quad (I)$$



Equation I means that since  $P_f$  and  $P_c$  equilibrate very quickly their ratio can be assumed to be constant at any time.

Now define the total amount of protein (binded or unbinded)

$$P = P_c + P_f \quad \text{II}$$

Using I, II we can write

$$P_f = \frac{k_{off}}{k_{on}} P_c ; P = P_c + P_f$$

$$\Rightarrow P = \left( \frac{k_{on} + k_{off}}{k_{on}} \right) P_c \Rightarrow \begin{cases} P_c = \frac{k_{on}}{k_{on} + k_{off}} P \\ P_f = \frac{k_{off}}{k_{on} + k_{off}} P \end{cases} \quad \text{III}$$

Now by summing the two sides of ODE system and using II, III we will have:

$$\frac{\partial P}{\partial t} = \left( D_c \frac{k_{on}}{k_{on} + k_{off}} + D_f \frac{k_{off}}{k_{on} + k_{off}} \right) \frac{\partial^2 P}{\partial x^2} - \frac{k k_{off}}{k_{on} + k_{off}} P$$

$$\Rightarrow \frac{\partial P}{\partial t} = D \frac{\partial^2 P}{\partial x^2} - K P$$

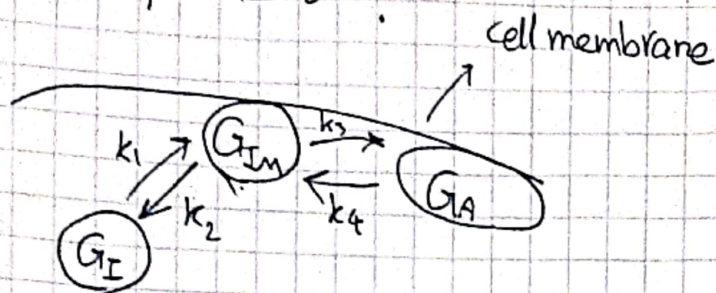
$$D = D_c \frac{k_{on}}{k_{on} + k_{off}} + D_f \frac{k_{off}}{k_{on} + k_{off}}$$

$$K = k \frac{k_{off}}{k_{on} + k_{off}}$$

As you can see by playing with  $k_{on}$  and  $k_{off}$  parameters we can have different behavioural diffusion rate and decay rate



## Example II 8



Suppose that we have a protein that have two states: Active and Inactive. The inactive form diffuses in the environment with  $D_I$  and binds and unbinds to membrane with  $k_1, k_2$ .  $G_{Im}$  (inactive form binded to membrane) then diffuses and turns into  $G_A$  with  $k_3, k_4$ :

$$(1) \quad \frac{\partial G_I}{\partial t} = D_I \frac{\partial^2 G_I}{\partial x^2} - k_1 G_I + k_2 G_{Im}$$

$$(2) \quad \frac{\partial G_{Im}}{\partial t} = D_{Im} \frac{\partial^2 G_{Im}}{\partial x^2} + k_1 G_I - k_2 G_{Im} - k_3 G_{Im} + k_4 G_A$$

$$(3) \quad \frac{\partial G_A}{\partial t} = D_A \frac{\partial^2 G_A}{\partial x^2} + k_3 G_{Im} - k_4 G_A$$

Using the assumption that kinetic between  $G_I$  and  $G_{Im}$  is very fast and equalibrate very quickly we can write:

$$k_1 G_I - k_2 G_{Im} = 0 \Rightarrow \boxed{\frac{G_I}{G_{Im}} = \frac{k_2}{k_1}} \quad (I)$$

let  $G_i$  be:

$$\boxed{G_i = G_I + G_{Im}} \quad (II)$$

Considering I and II we can write:

$$G_{Im} = \frac{k_1}{k_1 + k_2} G_i$$

$$G_I = \frac{k_2}{k_1 + k_2} G_i$$

And by summing 1 and 2:

$$\checkmark \quad \begin{cases} \frac{\partial G_i}{\partial t} = \left( D_I \frac{k_2}{k_1 + k_2} + D_{Im} \frac{k_1}{k_1 + k_2} \right) \frac{\partial^2 G_i}{\partial x^2} - \frac{k_1 k_3}{k_1 + k_2} G_i + k_4 G_A \\ \frac{\partial G_A}{\partial t} = D_A \frac{\partial^2 G_A}{\partial x^2} + \frac{k_1 k_3}{k_1 + k_2} G_i - k_4 G_A \end{cases}$$