LECTURES 30-36: Receptor-Ligand Binding

Problem 1

Obtain the half-time for the following ligand given the binding to the receptor and the following conditions.

k_{-1}=0.04 min^{-1} k_D = 25 μM

C_{L0} = 2, 20, 100 μM

Solution: The Half-time period for the receptor –ligand binding is given by

$$t_{1/2} = \frac{\ln 2}{k_{-1}\left(1+\frac{C_{L0}}{k_D}\right)} \tag{8.1}$$

For C_{L0} = 2 μM, $t_{1/2} = 16.04\ \text{min}$

For $C_{L0} = 20\ \mu M$, $t_{1/2} = 9.627$ min

For $C_{L0} = 200\ \mu M$, $t_{1/2} = 1.9254$ min

Problem 2

Use the following data to determine the specific binding of a ligand A to a receptor B as well as the values of k_d and the number of receptors per cell.

C_{L0}, M	Amount bound without unlabeled ligand	Amount bound with 100 excess unlabeled ligand
1.5×10^{-10}	16, 000	6, 000
6×10^{-10}	60, 000	24, 000
2.1×10^{-9}	120, 000	60, 000
7.5×10^{-9}	350, 000	260, 000
1.5×10^{-8}	600, 000	510, 000

Solution: The specific binding of ligand to receptor is given below.

C_{L0}, µM	Specific binding of a ligand A to receptor B (N_c)
1.5×10^{-4}	10, 000
6×10^{-4}	36, 000
2.1×10^{-3}	60, 000
7.5×10^{-3}	90, 000
1.5×10^{-2}	90, 000

Calculating N_c/C_{L0} and after plotting N_c/C_{L0} Vs. N_c we get

$$k_d = 6.67\times10^{-10}\text{ M}$$

$$N_{RT}/k_d = 7.2\times10^{7}\text{ receptors/cell/µM}$$

Therefore $$N_{RT} = 4.8\times10^{4}$$

Problem 3: The model equation for ligand depletion is given by

$$\frac{du}{d\tau} = (1-u)(1-\eta u)\alpha - u \qquad (1)$$

with $u = u_0 = \dfrac{N_{C0}}{N_{RT}}$ at $\tau = 0$.

Solve the model equation to establish a relationship between u and τ.

Solution: From equation (1), we can write

$$\frac{du}{\left[(1-u)(1-\eta u)\alpha - u\right]} = d\tau \qquad (11.1)$$

After algebraic manipulations, we get

$$\frac{du}{\left[\eta\alpha u^2 - (\eta\alpha + \alpha + 1)u + \alpha\right]} = d\tau \qquad (11.2)$$

Taking out $\eta\alpha$ common from the denominator, we get

$$\frac{du}{\eta\alpha\left[u^2-\frac{(\eta\alpha+\alpha+1)}{\eta\alpha}u+\frac{1}{\eta\alpha}\right]}=d\tau \qquad (11.3)$$

Adjusting the terms in denominator to form quadratic equation in terms of *u*,

$$\frac{du}{\eta\alpha\left[\left(u-\frac{(\eta\alpha+\alpha+1)}{2\eta\alpha}\right)^2+\left(\frac{1}{\eta}-\frac{(\eta\alpha+\alpha+1)^2}{4\eta^2\alpha^2}\right)\right]}=d\tau \qquad (11.4)$$

Integrating equation (11.4) on both sides

$$\frac{1}{\eta\alpha}\int \frac{du}{\left[\left(u-\frac{(\eta\alpha+\alpha+1)}{2\eta\alpha}\right)^2+\left(\frac{1}{\eta}-\frac{(\eta\alpha+\alpha+1)}{4\eta^2\alpha^2}\right)\right]}=\int d\tau \qquad (11.5)$$

Let

$$\left(\frac{1}{\eta}-\frac{(\eta\alpha+\alpha+1)}{4\eta^2\alpha^2}\right)=\pm K^2$$

Equation (11.5) becomes,

$$\frac{1}{\eta\alpha}\int \frac{du}{\left[\left(u-\frac{(\eta\alpha+\alpha+1)}{2\eta\alpha}\right)^2\pm K^2\right]}=\int d\tau \qquad (11.6)$$

Equation (11.6) is of the form $\int \frac{dx}{\left(x^2 \pm a^2\right)}$ having solution $\frac{1}{a}\tan\left(x/a\right)+C$

Therefore the solution of equation (11.6) is

$$\tau = \frac{1}{\eta\alpha K}\tan\frac{\left[\left(2\eta u+\eta+1\right)+1\right]}{2K\eta}+C \qquad (11.7)$$

Put initial condition in equation (11.7), then we obtain

$$\tau = \frac{1}{\eta\alpha K}\left(\tan\frac{\left[\left(2\eta u+\eta+1\right)+1\right]}{2K\eta}-\tan\frac{\left[\left(2\eta u_0+\eta+1\right)+1\right]}{2K\eta}\right)$$

(11.8)