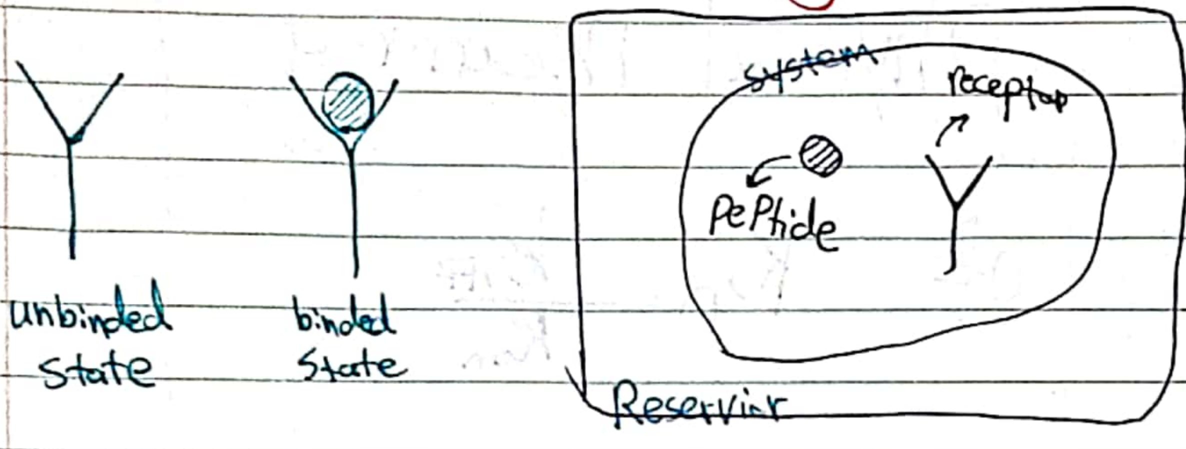
Physical Meaning of $K_D = \frac{k_{off}}{k_{on}}$

In this note, I will describe the ~~ca~~physical meaning of dissociation constant $K_D = \frac{k_{off}}{k_{on}}$.
To do that I ~~..~~ will use Boltzman statistics as well as simple rate differential equations.

1. Basic explanation using Canonical ens.



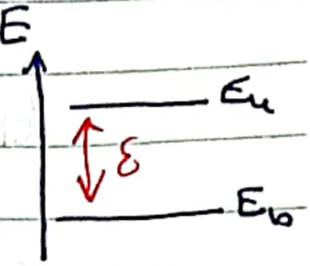
suppose that our system has two states. binded state and unbinded state. suppose that we are using Canonical ensemble (so our system consisting of 1 peptide and 1 receptor is in thermal contact with the reservior). so:

$$P(s) = \frac{e^{\frac{-ds}{k_B T}}}{Z} \quad ; \quad ds = \frac{1}{T}du + \underbrace{\frac{P}{T}dv}_{0} - \underbrace{\frac{\mu}{T}dN}_{0}$$

$$\Rightarrow \boxed{P(s) = \frac{e^{-E(s)/k_B T}}{Z}}$$

Now suppose that the binded state has the lowest energy and unbinded state has ε more energy. So:

$$E(b)=0 \quad ; \quad E(u)=\varepsilon$$



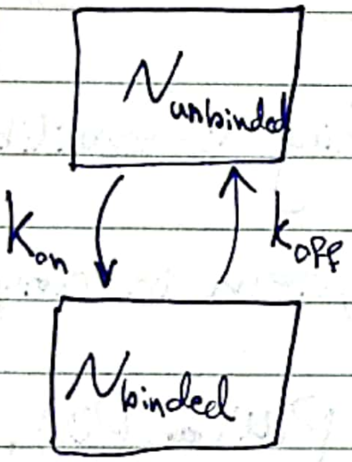
$$\rightarrow \boxed{P(b)=\frac{1}{1+e^{-\beta\varepsilon}} \quad ; \quad P(u)=\frac{e^{-\beta\varepsilon}}{1+e^{-\beta\varepsilon}}} \qquad \text{I}$$

it means that after reaching to equilibrium, the probability of finding system in any of those states is equal to $P(u)$, $P(b)$. this Calculation shows the results for $t\rightarrow\infty$.

In the Case that we have N_{tot} peptides, then $P(u)$ and $P(b)$ shows the fraction of population that is unbinded or binded respectively.

So far we have been talking about equilibrium. are there any chances to linke these variables to the values that appear when we evaluate the kinetic of the model (like k_{on}, k_{off}, ...)

let's write a model to describe the kinetics of the binding.



$$\frac{dN_u}{dt} = k_{off} N_b - k_{on} N_u$$

$$\frac{dN_b}{dt} = k_{on} N_u - k_{off} N_b$$

let's solve this differential equations analytically

$$\begin{pmatrix} \dot{N}_b \\ \dot{N}_u \end{pmatrix} = \dot{N} = \underbrace{\begin{pmatrix} -k_{off} & k_{on} \\ k_{off} & -k_{on} \end{pmatrix}}_{A} \begin{pmatrix} N_b \\ N_u \end{pmatrix}$$

$$\Rightarrow \dot{N} = A N$$

one possible solution $\Rightarrow$ $N = c_1|\lambda_1\rangle e^{\lambda_1 t} + c_2|\lambda_2\rangle e^{\lambda_2 t}$

in which $|\lambda_1\rangle, |\lambda_2\rangle$ are eigen vectors and λ_1, λ_2

are corresponding eigen values.

So let's find eigenvectors and eigenvalues of A

$$\det\begin{pmatrix} -k_{off}-\lambda & k_{on} \\ k_{off} & -k_{on}-\lambda \end{pmatrix} = (k_{off}+\lambda)(k_{on}+\lambda) - k_{off}k_{on} = 0$$

$$\Rightarrow \lambda^2 + (k_{on}+k_{off})\lambda = 0 \Rightarrow \begin{cases} \lambda_1 = 0 \\ \lambda_2 = -(k_{on}+k_{off}) \end{cases}$$

after a little bit of calculation

$$|\lambda_1\rangle = \begin{pmatrix} \frac{k_{on}}{k_{off}} = \frac{1}{k_D} \\ 1 \end{pmatrix}$$

$$|\lambda_2\rangle = \begin{pmatrix} -1 \\ 1 \end{pmatrix}$$

So we can write:

$$\begin{pmatrix} N_b \\ N_u \end{pmatrix} = C_1 \begin{pmatrix} \frac{1}{k_D} \\ 1 \end{pmatrix} + C_2 \begin{pmatrix} -1 \\ 1 \end{pmatrix} e^{-(k_{on}+k_{off})t}$$

by applying the boundary condition

$$N_b(0) = N_b^0$$
$$N_u(0) = N_u^0 \quad ; \quad N_{tot} = N_b^0 + N_u^0$$

we can write $C_1 = \frac{k_D}{k_D+1} N_{tot}$. So in $t \to \infty$ limit:

$t \to \infty$

$$\boxed{\begin{pmatrix} N_b \\ N_u \end{pmatrix} = N_{tot} \begin{pmatrix} \frac{1}{k_D+1} \\ \frac{k_D}{k_D+1} \end{pmatrix}}$$

This is a very important equation. by deviding two sides by N_{tot} we have:

$$\boxed{\begin{pmatrix} P(b) \\ P(a) \end{pmatrix} = \begin{pmatrix} \frac{1}{k_D+1} \\ \frac{k_D}{k_D+1} \end{pmatrix}} \quad \text{II}$$

Comparing that with equ. I, we can conclude

$$\boxed{k_D = e^{-\beta \varepsilon}} \quad \text{III} \quad \varepsilon = -k_B T \ln(k_D)$$

So k_D both depends on environment $\left(\beta = \frac{1}{k_B T}\right)$ and on the nature of reaction.

in fact if we write the process as following chemical reaction: $\text{labeled} \underset{k_{on}}{\overset{k_{off}}{\rightleftharpoons}} \text{unlabeled}$

then we can look at k_D as equilibirum constant which ~~~~ is $\boxed{k_D = \frac{\text{Forward rate}}{\text{Backward rate}} = \frac{k_{off}}{k_{on}}}$

In chemistry we call the $\frac{\text{Forward rate}}{\text{backward rate}}$ as the equilibrium constant of the reaction.

By doing a little bit of research (for example in the wikipedia page of Equilibrium Constant we can find the following amazing relation ship that really excites me!

$$\boxed{\Delta G = -k_B T \ln(k_D)} \quad IV$$

This equation is the same as equation III that we just derived! the only difference is that since I am using Canonican ensemble to derive equation III, instead of ΔG as the left hand side I got $\Delta U = \varepsilon$. we should possibly derive equation "IV" by using grandCanonical ens.