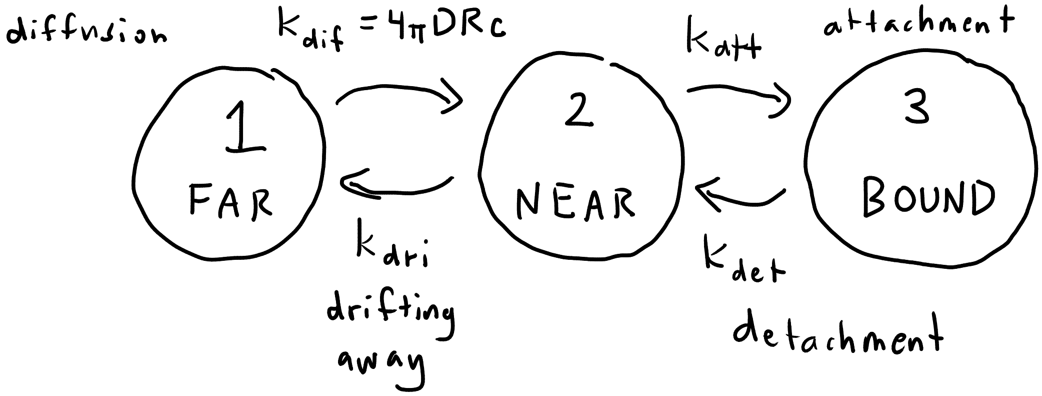


C = conc. of searcher particle

estimates: $k_{dif} = K_s c$ $\qquad K_s = 4\pi D R \approx 10^8\, M^{-1} s^{-1}$

Smoluchowski coeff.

$c \sim 10\text{ nM} - 0.1\text{ mM}$

$\Rightarrow k_{dif} \sim 1\, s^{-1} - 10^4\, s^{-1}$

$k_{dri} \Rightarrow$ a molecule diffusing 1 nm away from target

$$\text{time} \sim \frac{R^2}{6D} \qquad R = 1\text{ nm}, \quad D = 20\ \mu m^2/s$$

$$\sim 8\text{ ns}$$

$$k_{dri} \sim \frac{1}{8\text{ ns}} = 10^8\, s^{-1}$$

To find $\tau_{1\to3}$ (avg. time from FAR to BOUND)

use example from earlier lecture: $\sum \Omega_{ij} \tau_i = -1$

$$\tau_{1\to3} = \frac{k_{dif} + k_{dri} + k_{att}}{k_{att}\, k_{dif}}$$

effective rate from $1\to3$

$$k_b \equiv \frac{1}{\tau_{1\to3}} = k_{dif} \underbrace{\left[\frac{k_{att}}{k_{dif} + k_{dri} + k_{att}}\right]}_{\equiv\, \alpha_b \text{ coefficient}}$$

↑ binding rate

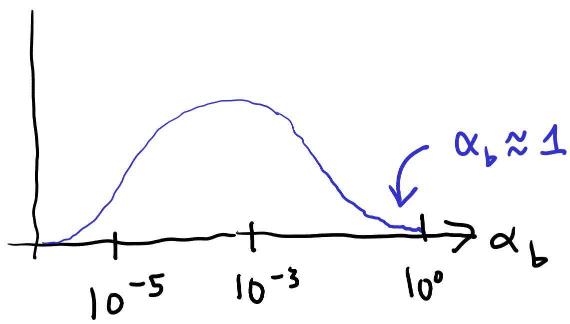
$$0 \le \alpha_b \le 1$$

$$\Rightarrow \quad k_b = \alpha_b k_{dif} = \alpha_b k_s c \le k_{dif}$$

"speed limit"

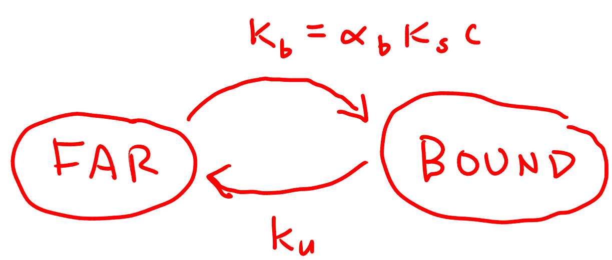
since $k_{dif} \ll k_{dri} \Rightarrow \alpha_b \approx \dfrac{k_{att}}{k_{dri} + k_{att}}$ approx. indep. of c

histogram of α_b over all biochemical reactions



theoretical limit: "diffusion-limited" reactions

effective 2 state approx.



eff. unbinding rate $= \dfrac{1}{\tau_{3\to 1}} = \dfrac{k_{det} k_{dri}}{k_{det} + k_{dri} + k_{att}}$

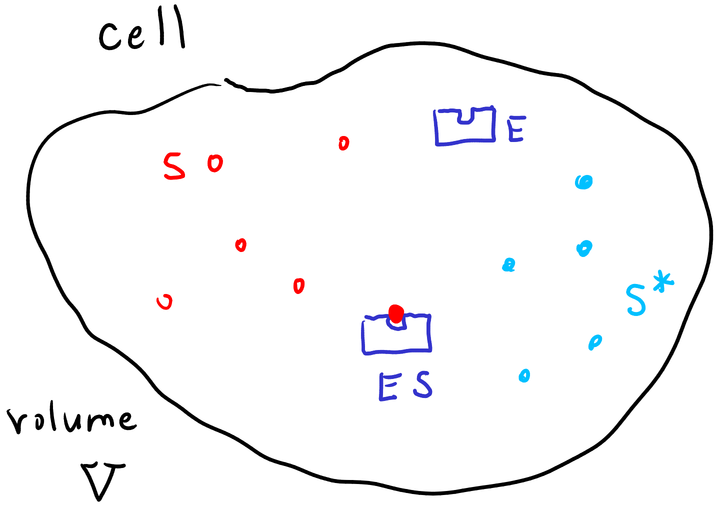
const. indep. of c

focus on a full chemical reaction:

enzyme E (one type of protein)

substrate S (another protein or small molecule)

reaction $S \to S^*$ (modified version of substrate)



reaction scheme:

catalysis rate

$$E + S \underset{\text{unbinding } k_u}{\overset{\text{binding } k_b}{\rightleftarrows}} ES \xrightarrow{k_{cat}} E + S^*$$

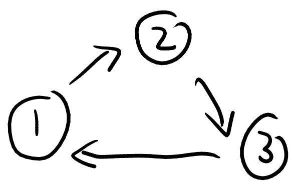
"complex" of E + S together

usually quite small & can be ignored

chemical state:

$$\vec{n} = (n_S, n_E, n_{ES}, n_{S^*})$$

$$n_\alpha = \# \text{ of type } \alpha \text{ in cell}$$



Ω_{nm} $m \to n$ $\rightsquigarrow$ generalize $\Omega_{\vec{n}\vec{m}} \equiv$ trans. rate from state $\vec{m}$ to $\vec{n}$ (for $\vec{m} \neq \vec{n}$)

probability $p_{\vec{n}}(t) =$ prob. to be in state $\vec{n}$ at time t

$$\underbrace{\sum_{\vec{n}}}_{\sum_{n_S=0}^{\infty} \sum_{n_E=0}^{\infty} \cdots} p_{\vec{n}}(t) = 1$$

columns of $\Omega_{\vec{n}\vec{m}}$ sum to zero

$$\sum_{\vec{n}} \Omega_{\vec{n}\vec{m}} = 0$$

$$\frac{d}{dt} p_{\vec{n}}(t) = \sum_{\vec{m}} \Omega_{\vec{n}\vec{m}} p_{\vec{n}}(t)$$

chemical master equ. (accurate, but hard way of doing chemistry)

Conservation laws (stoichiometry)

$$n_S + n_{ES} + n_{S^*} = \text{const.} \equiv M_S$$

$$n_E + n_{ES} = \text{const.} \equiv M_E$$

example: $M_S = 2, \quad M_E = 2$

allowed states

$$\vec{n} = \begin{array}{cccc} n_S & n_E & n_{ES} & n_{S^*} \\ \hline \end{array}$$

$$\vec{n} = \begin{pmatrix} 2 & 2 & 0 & 0 \end{pmatrix}$$

binding

$$\begin{pmatrix} 1 & 1 & 1 & 0 \end{pmatrix}$$

catalysis

$$\begin{pmatrix} 1 & 2 & 0 & 1 \end{pmatrix}$$

binding

$$\cdots$$

$$\begin{pmatrix} 0 & 0 & 2 & 0 \end{pmatrix}$$

catalysis

$$\begin{pmatrix} 0 & 1 & 1 & 1 \end{pmatrix}$$