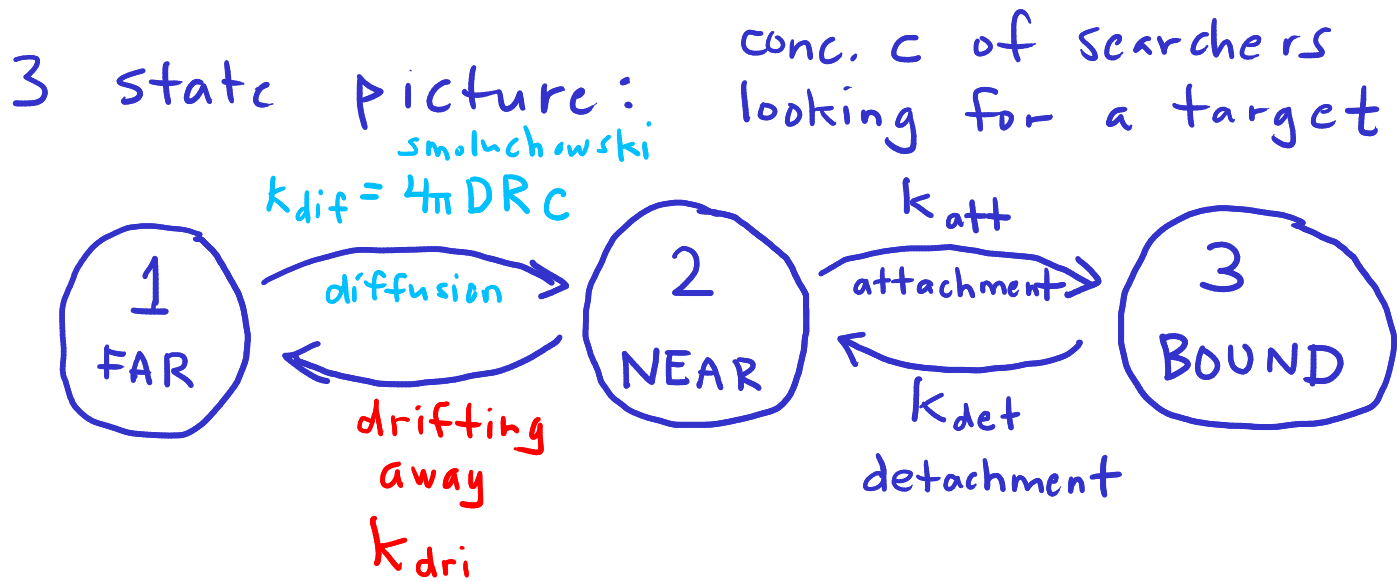


# PHYS 320/420 : Lecture 13



estimating scales:  $k_{dif} = k_s c$

but we know that

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

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

$$k_s = 4\pi DR \approx 10^8 \text{ M}^{-1} \text{ s}^{-1}$$

for typical proteins

$k_{dri}$ : to estimate this consider a molecule drifting a nm via

$$\text{diffusion} \sim \frac{R^2}{6D}$$

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

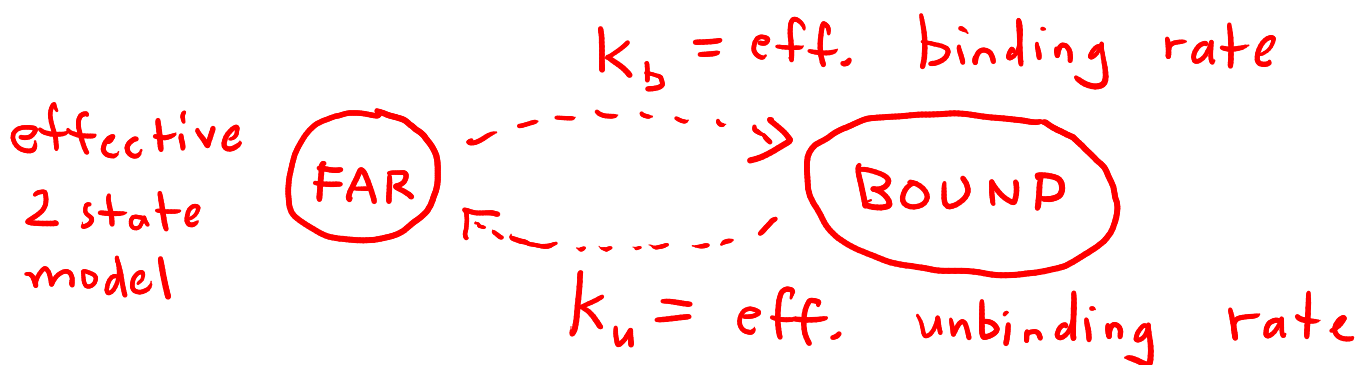
$$R = 1 \text{ nm}$$
$$D = 20 \text{ } \mu\text{m}^2/\text{s}$$

$$\Rightarrow k_{dri} \sim 10^8 \text{ s}^{-1} \text{ very fast!}$$

one solution: weak (non-specific)

interactions like electrostatics that make  $k_{dri}$  rate smaller

Use mean first passage time analysis to calc. how long on avg. it takes to go from 1  $\rightarrow$  3.



$$k_b = \frac{1}{\tau_{1 \rightarrow 3}} \leftarrow \text{MFPT from 1 to 3}$$

$$k_u = \frac{1}{\tau_{3 \rightarrow 1}}$$

$\tau_{1 \rightarrow 3}$  calculation:

$$\Omega = \begin{matrix} & \begin{matrix} 1 & 2 & 3 \end{matrix} \\ \begin{matrix} 1 \\ 2 \\ 3 \end{matrix} & \left( \begin{array}{ccc|ccc} -k_{dif} & k_{dri} & 0 & & & \\ k_{dif} & -k_{att} & k_{det} & & & \\ 0 & k_{att} & -k_{det} & & & \end{array} \right) \end{matrix}$$

target  $i_c = 3$

$$\sum_{j \neq i_c} \tau_j \Omega_{ji} = -1 \quad \text{for } i = 1, 2$$

$$\tau_{i_c} = 0$$

⇒ solution:

$$\tau_{1 \rightarrow 3} = \frac{k_{dif} + k_{dri} + k_{att}}{k_{dif} k_{att}}$$

binding  $k_b = k_{dif} \left[ \frac{k_{att}}{k_{dif} + k_{dri} + k_{att}} \right]$

all rates

$$k_{mn} \geq 0$$

$$\equiv \alpha_b$$

$$0 \leq \alpha_b \leq 1$$

$k_b \leq k_{dif}$  (Smoluchowski dif. rate is indeed a "speed limit")

typically,  $k_{dif} \ll k_{dri}$  and  $k_{att}$

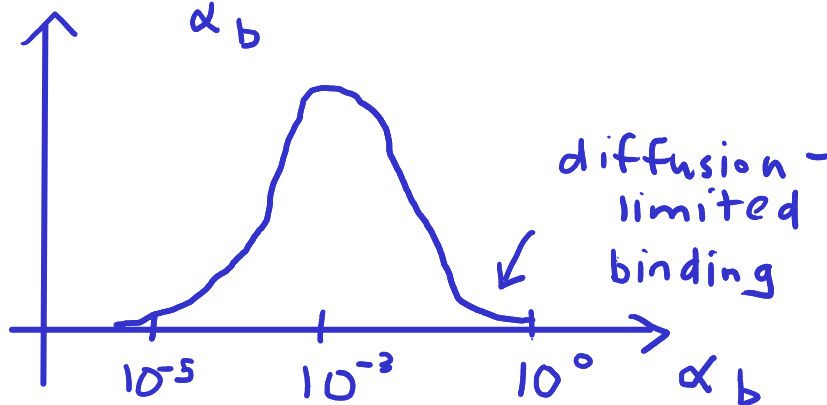
$$\alpha_b \approx \frac{k_{att}}{k_{dri} + k_{att}}$$

here  $\alpha_b$  becomes indep. of  $c$

⇒ some constant

histogram of  $\alpha_b$

all enzymes



$$k_b \approx k_{dif}$$
$$\alpha_b \approx 1$$

$$k_b \approx \alpha_b k_{dif} = \alpha_b k_s c \quad \text{with} \\ \alpha_b \ll 1 \text{ usually}$$

similar argument:  $T_3 \rightarrow 1$

$$k_u = \frac{k_{det} k_{dri}}{k_{det} + k_{dri} + k_{att}}$$

= const. indep. of  $c$

Build up a more comprehensive theory for biochemistry:

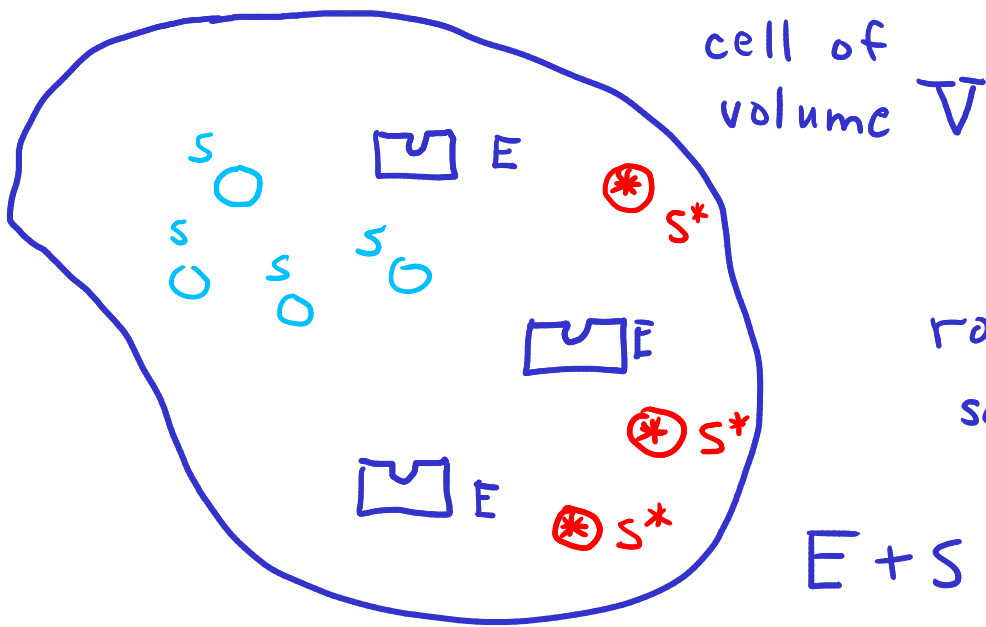
focus on enzyme chemistry

since proteins are typically enzymes catalyzing biochemical reactions,

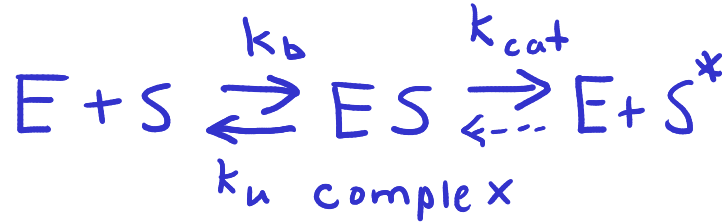
Imagine an enzyme  $E$  (one protein)

+ substrate  $S$  (another protein or small molecule)

+ the reaction  $S \rightarrow S^*$  chemically modified substrate



rough scheme:



$\leftarrow$  is typically small  
(enzyme bound to substrate)

+ can be ignored (most of the time)

$k_{cat}$  = rate at which the enzyme catalyzes reaction

Chemical "state" is actually quite complex + can be described by a vector:

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

where  $n_\alpha$  = # of molecules of type  $\alpha$

$$\Omega_{mn} \longrightarrow \Omega_{\vec{m}\vec{n}} \quad \text{trans. between state } \vec{n} \rightarrow \vec{m}$$