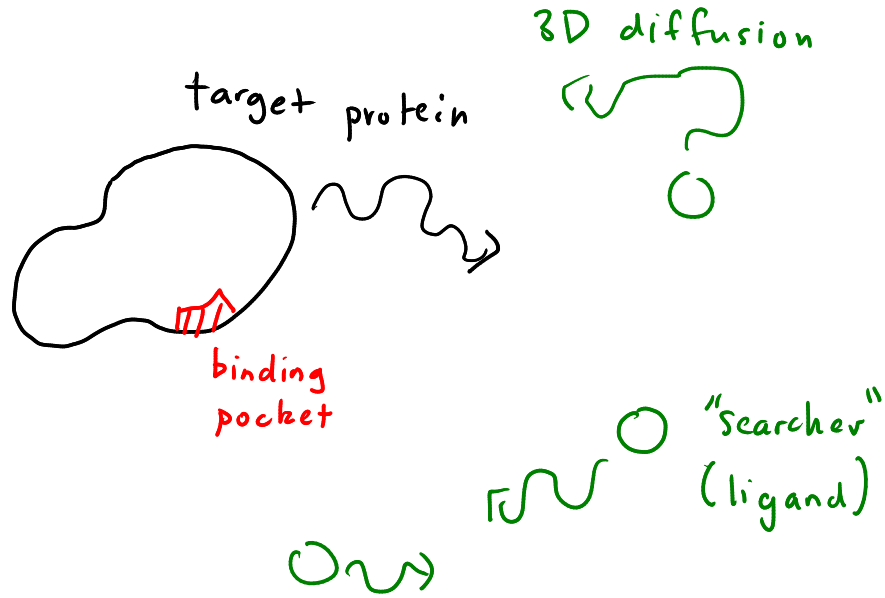
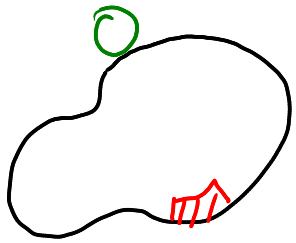
Next steps: what happens after diffusion?

3 state picture:

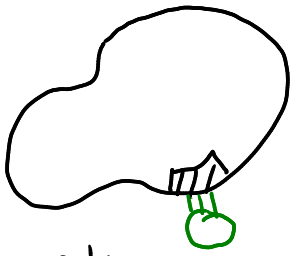


1) "FAR"

2) "NEAR"

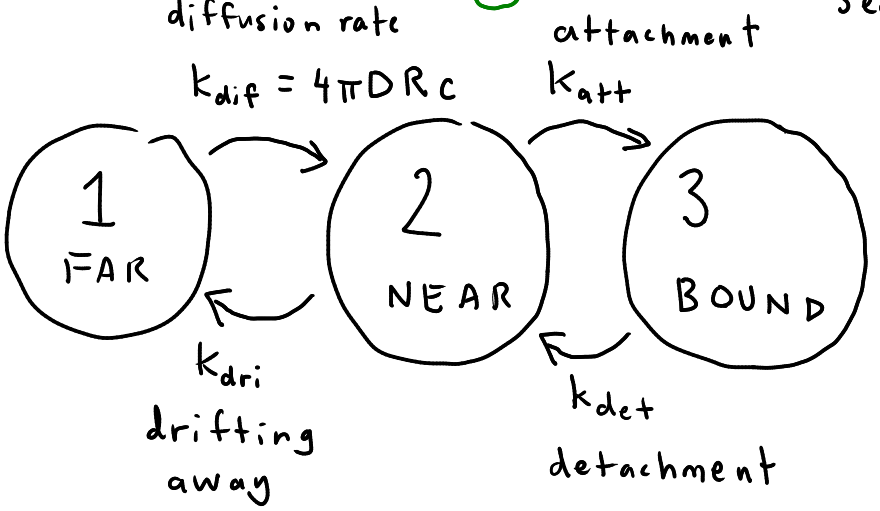


3) "BOUND"



C = conc. of searcher particle

model:



estimates: $K_{dif} = K_s C$

$C \sim 10\,nM - 0.1\,mM$

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

Smoluchowski coeff.

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

upper bound on k_{dri} : a molec. diffusing 1 nm away from target

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

$$\sim 8\ ns$$

$$k_{dri} \leq 10^8\ s^{-1}$$

Let's find $\tau_{1\to 3} = \tau_1$ (FAR → BOUND) avg. time time to get from $i = 1$ to $i_c = 3$

Use example from earlier lecture:

$$i \neq i_c: \quad \sum_i \Omega_{ij} \tau_i = -1 \qquad \tau_{i_c} = 0$$

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

effective rate from $1 \to 3$

$$k_b \equiv \frac{1}{\tau_{1\to 3}} = k_{dif} \underbrace{\left[\frac{k_{att}}{k_{dif} + k_{dri} + k_{att}} \right]}_{\equiv \alpha_b \text{ binding coeff.}}$$

k_b ↑ binding rate

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

$$k_b = \alpha_b k_{dif} = \alpha_b K_s C \leq k_{dif}$$

"speed limit"

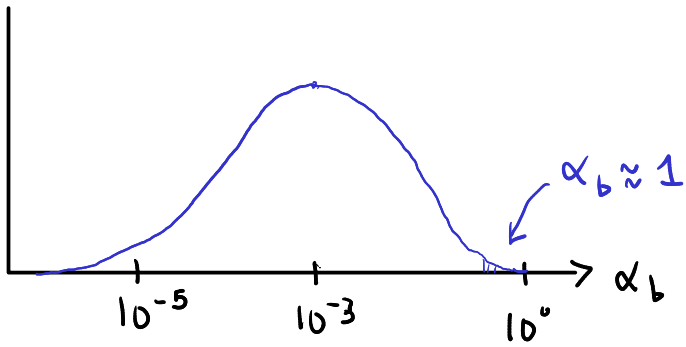
if $k_{att} \to \infty$ $\alpha_b \to 1$

$\to 0$ $\alpha_b \to 0$

in general $k_{dif} \ll k_{dri} \Rightarrow \alpha_b \approx \dfrac{k_{att}}{k_{dri} + k_{att}}$

roughly indep. of c

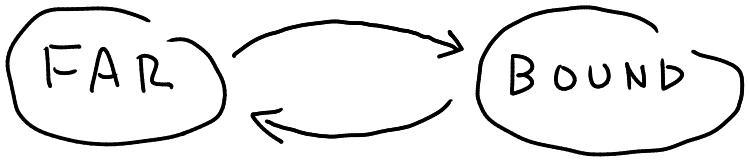
histogram of α_b over all biochemical reactions (enzymes)



near theor. limit: "diffusion-limited reactions

next step: effective 2 state approx:

$k_b = \alpha_b K_s C$



k_u

unbinding rate

$$= \frac{1}{\tau_{3\to 1}} = \frac{k_{det}\, k_{dri}}{k_{det} + k_{dri} + k_{att}}$$

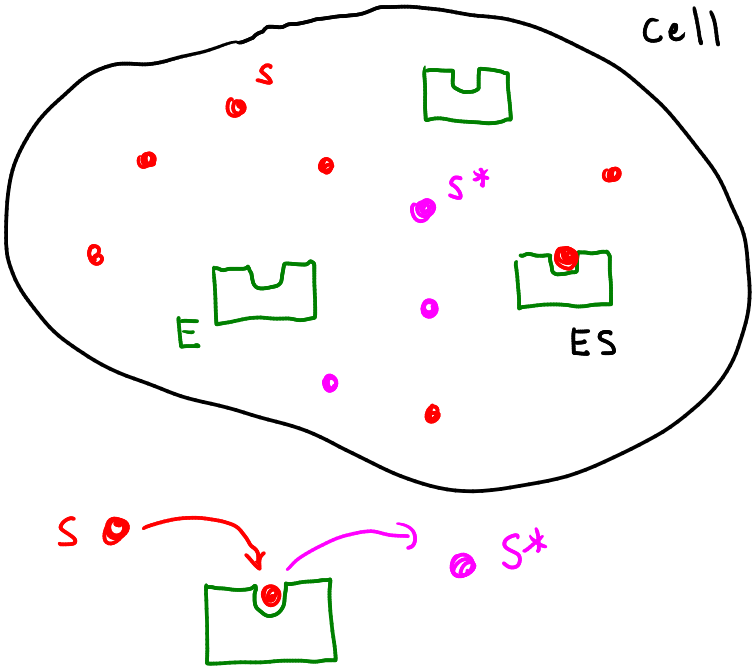
const. indep. of c

Focus on a full reaction (enzyme catalyzing transf. of a substrate):

enzyme E (type of protein)

substrate S (another protein or small molecule)

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



reaction scheme:

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

binding / unbinding

k_{cat}: catalysis rate

usually quite small & can be ignored