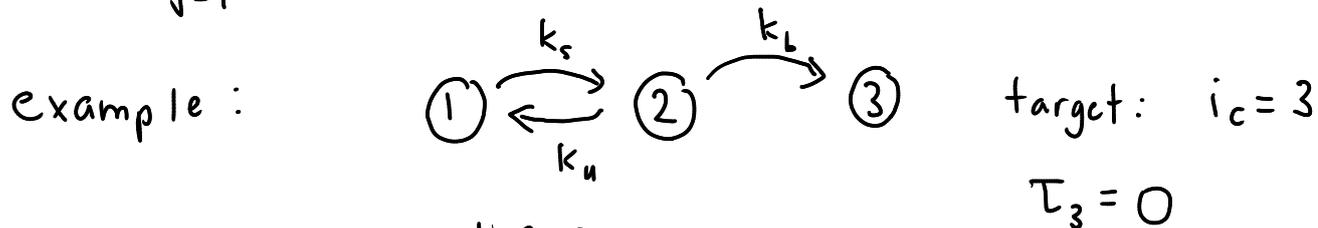


$\tau_i =$ mean time to go from i to i_c

$$i \neq i_c: \sum_{j=1}^N \tau_j \Omega_{ji} = -1 \quad \tau_{i_c} = 0$$



$$\Omega = \begin{matrix} & \begin{matrix} 1 & 2 & 3 \end{matrix} \\ \begin{matrix} 1 \\ 2 \\ 3 \end{matrix} & \begin{pmatrix} -k_s & k_u & 0 \\ k_s & -k_u - k_b & 0 \\ 0 & k_b & 0 \end{pmatrix} \end{matrix}$$

$$i=1: -k_s \tau_1 + k_u \tau_2 = -1$$

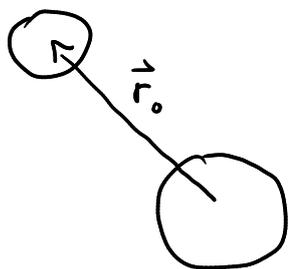
$$i=2: k_u \tau_1 - (k_u + k_b) \tau_2 + k_b \tau_3 = -1$$

$$\Rightarrow \text{solve for } \tau_1 = \frac{k_s + k_u + k_b}{k_s k_b}$$

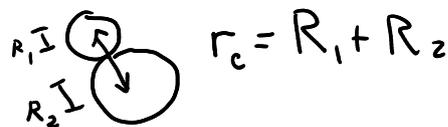
$$\frac{d p_i}{d t} = \sum_j \Omega_{ij} p_j \quad \sum_i p_i(t) = 1$$

$$\frac{d}{d t} \sum_i p_i(t) = 0$$

recall original motivation:



3D diffusion
of \vec{r} w/
diff. constant
 $D = D_1 + D_2$



first do this in 1D: do the continuous

space approximation: $p_j(t) \rightarrow p(x, t)$

$$\sum_j \Omega_{ij} p_j = \frac{d p_i}{d t} \rightarrow D \frac{\partial^2 p}{\partial x^2} = \frac{\partial p}{\partial t}$$

$$\text{b.c. } \left. \frac{\partial p}{\partial x} \right|_{x=0,L} = 0$$

do same approach for τ_i equations:

$$\tau_i \rightarrow \tau(x) = \text{avg. time to go from } x \text{ to } x_c$$

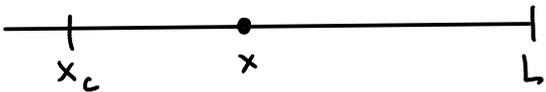
$$i_c \rightarrow x_c$$

$$i \neq i_c: \sum_j \tau_j \Omega_{ji} = -1$$

$$\rightarrow D \frac{\partial^2 \tau}{\partial x^2} = -1$$

$$\text{b.c. } \tau(x_c) = 0$$

$$\left. \frac{\partial \tau}{\partial x} \right|_L = 0$$



Solve:

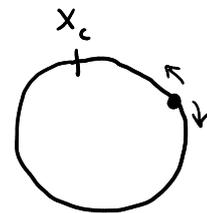
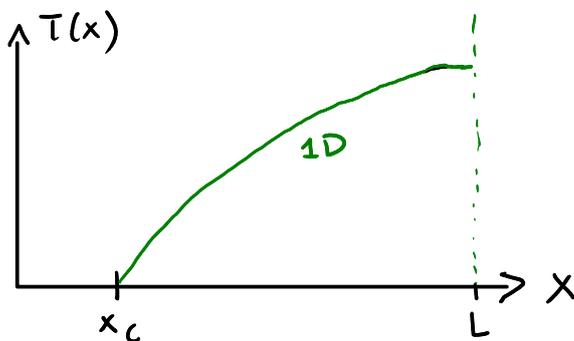
$$\frac{\partial \tau}{\partial x} = -\frac{x}{D} + c_1$$

$$\tau = -\frac{x^2}{2D} + c_1 x + c_2$$

$$\left. \frac{\partial \tau}{\partial x} \right|_L = 0 = -\frac{L}{D} + c_1 \Rightarrow c_1 = L/D$$

$$\tau(x_c) = 0 \Rightarrow c_2 = \frac{x_c^2}{2D} - \frac{Lx_c}{D}$$

$$\Rightarrow \tau(x) = \frac{(x-x_c)(2L-x-x_c)}{2D}$$



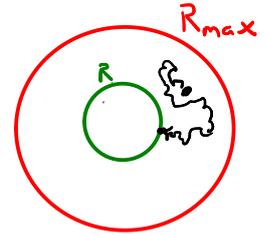
3D: $\tau(\vec{r}) = \text{mean time to go from initial separation } \vec{r} \text{ to separation } R = R_1 + R_2$
 $= \tau(r)$ by symmetry where $r = |\vec{r}|$

$$3D: \quad D \left[\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \right] \tau(\vec{r}) = -1$$

"
 (x,y,z)

$$\tau(\vec{r} \in \text{sphere of radius } R) = 0$$

$$\nabla \tau(\vec{r}) \Big|_{\vec{r} \in \text{outer boundary}} = 0$$

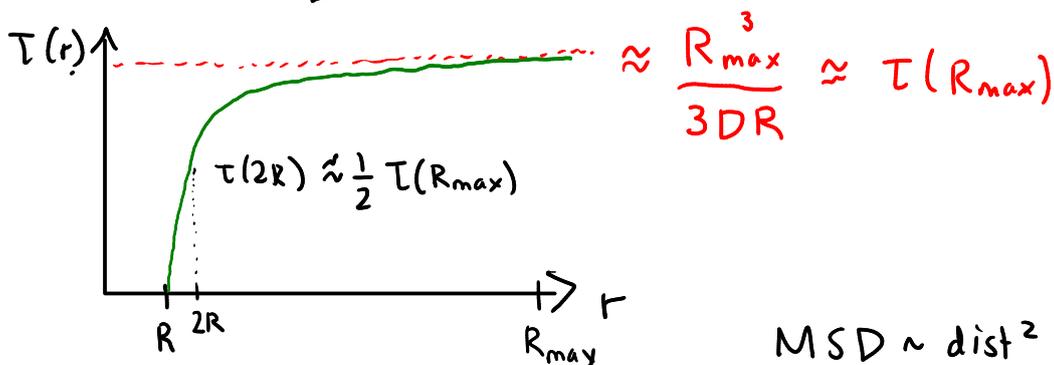


$$\vec{r} = (r, \theta, \phi) \quad \tau(\vec{r}) = \tau(r)$$

$$D \left[\frac{\partial^2}{\partial r^2} + \frac{2}{r} \frac{\partial}{\partial r} \right] \tau(r) = -1$$

$$\tau(R) = 0 \quad \frac{\partial \tau}{\partial r} \Big|_{R_{\max}} = 0$$

$$\Rightarrow \tau(r) = \frac{R_{\max}^3}{3DR} - \frac{R_{\max}^3}{3Dr} - \frac{r^2}{6D} + \frac{R^2}{6D}$$



$$\text{MSD} \sim \text{dist}^2 \approx 6Dt$$

time for two molecules to meet in 3D

(in a volume of radius $\sim R_{\max}$):

$$\tau \approx \frac{R_{\max}^3}{3DR} \quad (\text{good approx. when initial sep.} > \text{a few nm})$$

$$D = D_1 + D_2$$

$$R = R_1 + R_2$$

$$= \underbrace{\left(\frac{R_{\max}^2}{6D} \right)}_{\text{avg. time to cover dist. } R_{\max} \text{ (time to visit whole cell)}} \left(\frac{2R_{\max}}{R} \right) \rightarrow \text{additional factor req. for a collision to occur}$$

typical protein:

$$R_1 = R_2 \sim 1 \text{ nm}$$

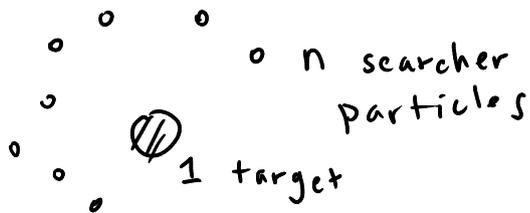
$$R_{\text{max}} = 1 \mu\text{m}$$

for bacteria

$$D_1 = D_2 = 10 \mu\text{m}^2/\text{s}$$

$$\Rightarrow \tau = (8.3 \times 10^{-3} \text{ s})(1000) = 8.3 \text{ s}$$

Speed up \Rightarrow have more particles



$$\tau = \left(\frac{R_{\text{max}}^2}{6D} \right) \left(\frac{2R_{\text{max}}}{Rn} \right)$$

timescale to explore cell

↑
chance of collision increases by a factor of n

$$V = \frac{4}{3} \pi R_{\text{max}}^3 \quad (\text{spherical volume})$$

$$\Rightarrow \tau = \frac{V}{4\pi DRn} = \frac{1}{4\pi DRc}$$

$$c = \frac{n}{V}$$

concentr. of searcher particles

rate of searchers hitting target:

$$k = \frac{1}{\tau} = 4\pi DRc$$

Smoluchowski rate

"speed limit" for any chem. reaction that requires 3D diffusion