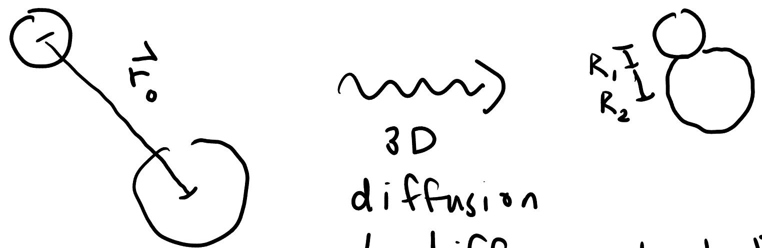
$\tau_i =$ mean time from $i \to i_c$

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

recall original motivation: target: "capture" radius

$r_c = R_1 + R_2$



w/ diff. constant $D = D_1 + D_2$

Start w/ 1D version: continuous space approx.

$$p_j(t) \to p(x,t)$$

$$\frac{dp_i}{dt} = \sum_j \Omega_{ij} p_j \to \frac{\partial p}{\partial t} = D \frac{\partial^2 p}{\partial x^2}$$

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

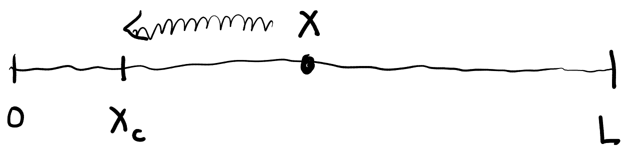
Same approach: $\tau_i \to \tau(x) =$ avg. time to go from $x \to x_c$

$$i_c \to x_c$$

$$i \neq i_c: \quad \sum_j \tau_j \Omega_{ji} = -1 \to D \frac{\partial^2 \tau}{\partial x^2} = -1$$

$$\tau_{i_c} = 0 \qquad \tau(x_c) = 0$$

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



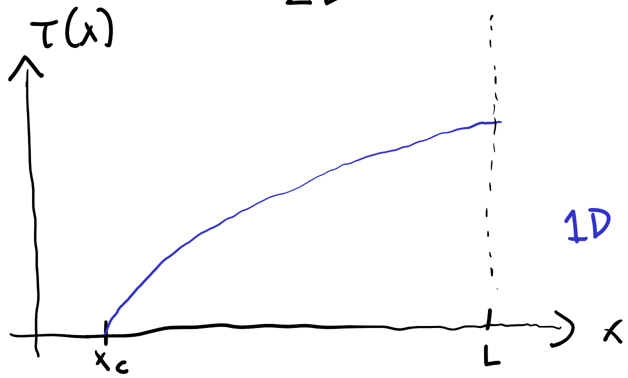
solve: $$\frac{\partial \tau}{\partial x} = -\frac{1}{D}x + C_1$$

$$\tau = -\frac{x^2}{2D} + C_1 x + C_2$$

$$\left.\frac{\partial \tau}{\partial x}\right|_L = 0 = -\frac{L}{D} + C_1 \Rightarrow C_1 = \frac{L}{D}$$

$$\tau(x_c) = 0 \Rightarrow C_2 = \frac{x_c^2}{2D} - \frac{Lx_c}{D}$$

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



1D diffusion to capture

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

$= \tau(r)$ by symmetry (where $r = |\vec{r}|$)

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

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

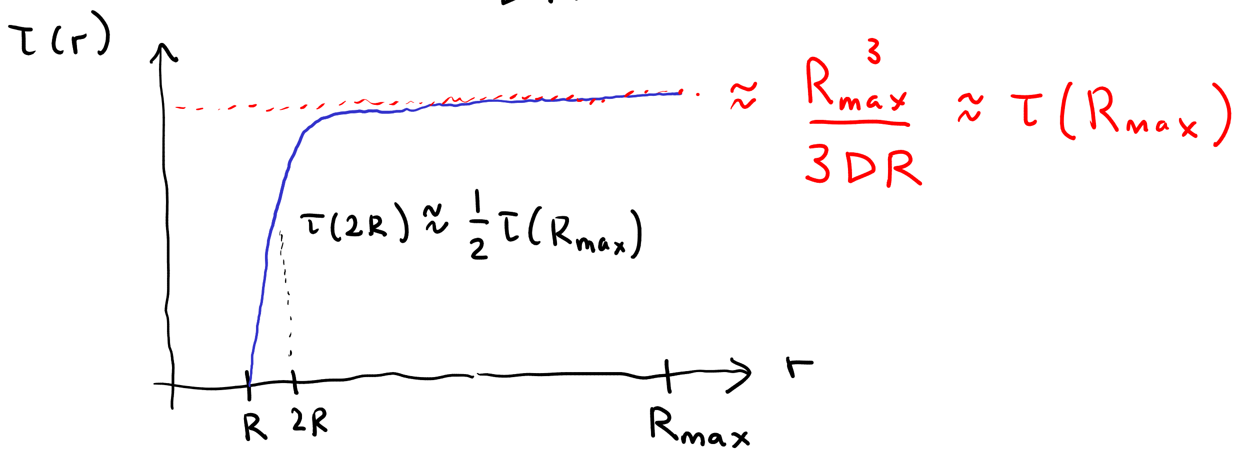
$$\left.\nabla \tau(\vec{r})\right|_{\vec{r} \in \text{outer boundary}} = 0$$

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

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

$$\tau(R) = 0 \qquad \left.\frac{\partial \tau}{\partial r}\right|_{R_{max}} = 0$$

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



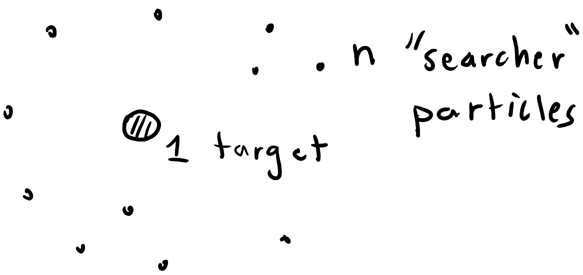
to a good approx: time for two molecules to meet in 3D (in a vol. of size $\sim R_{max}$)

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

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

typical protein:
$R_1 = R_2 \sim 1$ nm $D \sim 10\ \mu m^2/s$ $\Rightarrow \tau = (8.3\times10^{-3} s)(1000)$
$R_{max} = 1\ \mu m$ for bacteria $= 8.3$ s

Speed up $\Rightarrow$ have more particles



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

time scale to explore cell

chance of collision increases by a factor n (dec. time)

$V = \frac{4}{3}\pi R_{max}^3$ (spher. volume)

$$\Rightarrow \tau = \frac{V}{4\pi D R n} = \frac{1}{4\pi D R c}$$

$c = \frac{n}{V}$ concent. of searcher particles

rate of searchers hitting target:

$$k_{smol} \equiv \boxed{k = \frac{1}{\tau} = 4\pi D R c}$$

Smoluchowski rate

"speed limit" for any chemical reaction that requires 3D diffusion

any reaction rate $k \leq k_{smol} = 4\pi D R c$

how can biology optimize speed?

$\Rightarrow$ increasing c

$\Rightarrow$ cell more crowded

$\Rightarrow$ smaller diffusion constant D

ϕ = volume fraction of stuff in cell (proteins, DNA/RNA, etc.)