

## Brownian Motion

Q: Does anyone know what Brownian Motion is?  
Any examples?

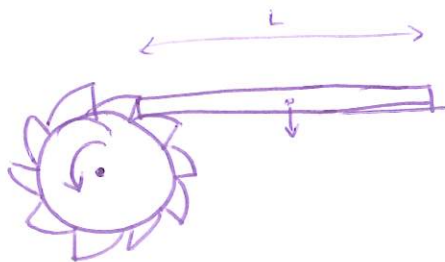
What scales do you think BM is important?

★ BM is the random motion of particles resulting from collisions by atoms or molecules in the surrounding media.

As you will see, the mathematical convenience of BM models has led it to be used in many different ways.

e.g. stock market, spread of disease, evolution, genetics, computer algorithms, ecology, and of course biology and physics.

But let's first think of a concrete example to illustrate scale of BM in a physical system,



$L = 1 \text{ m}$  : Only CCW movement

$L = 10 \text{ nm}$  : CCW and CW movement

At small size, fluctuations dominate and directed motion gets destroyed by collisions from fast molecules in surrounding environment.

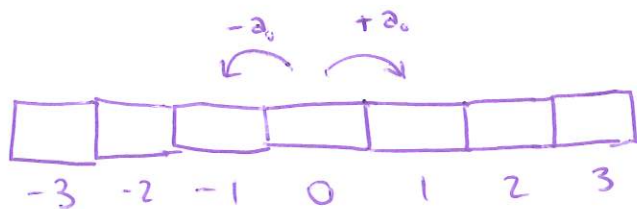


Problem: We have a model for the ideal gas law, but no apparent link b/w the microscopic and macroscopic world.

- Fortunately:
- Brown (1828) observed dancing Pollen grains. He initially believed it was living movement (Active molecules) but his experiments showed "life" was not necessary.
  - At this point atoms and molecules had been theorized but not precisely.
  - Einstein (1905) explained BM in precise detail forming the theory for the existence of atoms and molecules.
  - Perrin (1908) experimentally verified Einstein's predictions providing definitive proof of the existence of atoms and molecules.

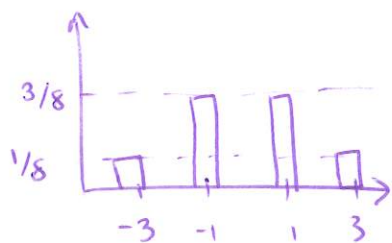
Lets begin with the simplest and possibly most powerful model of BM.

## Random Walk



For each step there are 2 possibilities;  $+a$  or  $-a$

After 3 steps there are  $2 \cdot 2 \cdot 2 = 8$  possibilities



What is the maximum distance after  $N$  steps? minimum?

What is the average distance after  $N$  steps?

Recall: Average:  $\langle a \rangle = \frac{1}{m} \sum_i^m a_i$   $m$  is # of realizations  
 $i$  is the  $i$ th realization  
 $= \sum p_i a_i$   $p_i$  is the probability to find  $a_i$

variance:  $\langle a^2 \rangle = \frac{1}{m} \sum_i^m (a_i - \langle a \rangle)^2$   
 $= \sum p_i (a_i - \langle a \rangle)^2$

Exercise: Calc mean and variance after 3 steps

$$\langle a \rangle = \sum_{a_i=-3}^3 p_i a_i = \frac{1}{8}(-3) + \frac{3}{8}(-1) + \frac{3}{8}(1) + \frac{1}{8}(3) = 0 \quad \rightarrow \text{remark about small number statistics}$$

$$\langle a^2 \rangle = \sum_{a_i=-3}^3 p_i (a_i - \langle a \rangle)^2 = \frac{1}{8}(-3)^2 + \frac{3}{8}(-1)^2 + \frac{3}{8}(1)^2 + \frac{1}{8}(3)^2 = 3$$

Group Exercise: Calc mean and variance after 4 steps.

Construct  $p(a_i)$ .

How many realizations are possible?  $2^4 = 16$

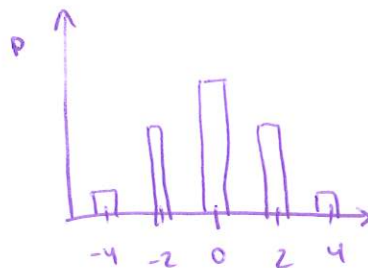
$$p(-4) = 1/16$$

$$p(-2) = 4/16$$

$$p(0) = 6/16$$

$$p(2) = 4/16$$

$$p(4) = 1/16$$



$$\langle a \rangle = \frac{1}{16}(-4) + \frac{4}{16}(-2) + \frac{6}{16}(0) + \frac{4}{16}(2) + \frac{1}{16}(4) = 0$$

$$\langle a^2 \rangle = \frac{1}{16}(-4)^2 + \frac{4}{16}(-2)^2 + \frac{6}{16}(0)^2 + \frac{4}{16}(2)^2 + \frac{1}{16}(4)^2 = 1 + 1 + 0 + 1 + 1 = 4$$

observe: 1 step:  $\langle a \rangle_1 = \frac{1}{2}(-1) + \frac{1}{2}(1) = 0$

$$\langle a^2 \rangle_1 = \frac{1}{2}(-1)^2 + \frac{1}{2}(1)^2 = 1$$

3 step:  $\langle a \rangle_3 = 0$

$$\langle a^2 \rangle_3 = 3$$

4 step:  $\langle a \rangle_4 = 0$

$$\langle a^2 \rangle_4 = 4$$



Guess a Law:

$$\langle a \rangle_N = 0 = N \cdot \langle a \rangle_1$$

$$\langle a^2 \rangle_N = N \cdot 1 = N \langle a^2 \rangle_1 \rightarrow N \cdot a_0^2$$

check w/ program!

Aside: The distribution for  $N_s$  is a binomial distribution.

e.g. suppose we take  $N_s = 10$  steps. To get to point  $2a$  we need a total of 6 steps in  $+a$  direction and 4 steps in  $-a$  direction.

### Connection b/w RW and Diffusion

Let's say for a time interval  $t_0$  you can take one step  $a_0$ .

$$\langle X_N^2 \rangle = N \cdot a_0^2$$

since  $t = N \cdot t_0$

$$\hookrightarrow N = t/t_0$$

we can rewrite,

$$\langle X(t)^2 \rangle = 2t \cdot \underbrace{\frac{a_0^2}{2t_0}}$$

the 2 is for convention...

$D$ : diffusion coefficient

MSD:

$$\boxed{\langle X(t)^2 \rangle = 2Dt} \rightarrow \text{First Law of Diffusion!}$$

rms:

$$\sqrt{\langle X(t)^2 \rangle} = \sqrt{2Dt}$$

## Practical Example

Diffusion <sup>time/</sup> Length for a small molecule.

↳ in a bacteria, cell, and axon.

$$D = 100 \mu\text{m}^2/\text{s}$$

To get time,  $t = \frac{\langle x^2 \rangle}{2D}$

$$l_{\text{bac}} = 1 \mu\text{m} \rightarrow t_{\text{bac}} = \frac{(1 \mu\text{m})^2}{2 \cdot 100 \mu\text{m}^2/\text{s}} = 5 \text{ ms}$$

$$l_{\text{cell}} = 20 \mu\text{m} \rightarrow t_{\text{cell}} = \frac{(20 \mu\text{m})^2}{2 \cdot 100} = 2 \text{ sec}$$

$$l_{\text{axon}} = 1 \text{ meter} \rightarrow t_{\text{axon}} = \frac{(10^6 \mu\text{m})^2}{2 \cdot 100} \approx 10^{10} \text{ sec} \approx 300 \text{ years}$$

Diffusion <sup>in cells</sup> is effective for small length scales!

For random transport, bacteria and cells may be able to rely on diffusion. Of course for organization in space this doesn't work.

Draw pictures of cell cytoskeleton.

What have we learned about <sup>1st law</sup> Diffusion?

- ① what distance a particle can travel by purely RANDOM motion.
- ② Diffusion is determined by one single parameter,  $D$ .
- ③  $D$  seems to connect the molecular world of single molecules (or derivation) with the macroscopic effect of diffusion.

## Diffusion

Does anyone remember what we talked about yesterday?

We ended the class discussing diffusion time...

Lets refresh our memories with an example.

Question: How long does it take for the T-RNA to find a ribosome?

For diffusion, how long on average before a T-RNA finds a ribosome?

In a bacteria,  $C_{T-RNA} = \frac{200,000 \text{ molecules}}{1 \text{ fl}}$

Average distance b/w,  $d = \sqrt[3]{\frac{1}{C}} = \left(\frac{1 \mu\text{m}^3}{200 \cdot 10^3}\right)^{1/3}$   
 $\approx 0.1 \mu\text{m} = 1/6$   
 $\approx 16 \text{ nm} = 0.016 \mu\text{m}$

Average time,  $t = \frac{\langle x^2 \rangle}{2D} = \frac{(0.01 \mu\text{m})^2}{100 \mu\text{m}^2/\text{s}} \approx \boxed{1 \mu\text{s}}$

The ribosome will find a T.RNA in only  $1 \mu\text{s}$ !

Protein synthesis takes about 40 nucleotides/s

which is about 25 ms/nucleotide.

$\therefore$  This process is not limited by diffusion!



# Diffusion in a concentration field

1. What is a concentration?

$$c = \frac{\# \text{ of particles}}{\text{volume}}$$

2. If a concentration is not homogeneous, we have a position dependent concentration,  $c(\vec{r})$

↳ this is a field.  
see fig 13.9

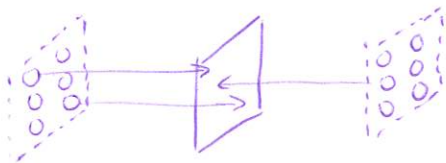
what do you expect to happen in an inhomogeneous field? → see fig 13.10.



what is flux?

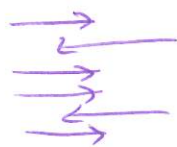
Flux is net number of particles that pass through an area  $A$  in a certain time → see fig. 13.11

Example.



$$j \propto 2(+1) + 1(-1) = 1$$

↑                      ↑  
direction                      direction



$$j \propto 2$$



$$j \propto -1$$



$$j \propto 0$$

Lets define Flux formally,

$$j = \frac{\# \text{ of particles}}{(\text{time step})(\text{Area of plane})} \quad \text{eg. } j = \frac{3}{1 \mu\text{s} \cdot 1 \mu\text{m}^2}$$

Example: Flux of water through bacteria membrane

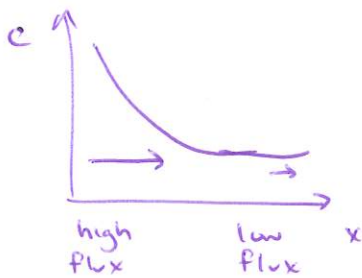
$$N_{\text{H}_2\text{O}} = 10^{10} \text{ molecules}$$

$$T_{\text{cycle}} = 3000 \text{ sec.}$$

$$A_{\text{bact}} = 6 \mu\text{m}^2$$

$$J = \frac{10^{10}}{(3000)(6)} = \frac{10^7}{18 \mu\text{m}^2/\text{s}} = 5 \cdot 10^5 \frac{1}{\mu\text{m}^2 \cdot \text{s}}$$

Now using the flux, lets try to guess how the flux depends on concentration,



$$j = -D \frac{\partial c}{\partial x} \quad \text{Fick's Law.}$$

check units:  $[j] = \frac{1}{\mu\text{m}^2 \cdot \text{s}}$

$$\left[ D \frac{\partial c}{\partial x} \right] = \left[ \frac{\text{m}^2}{\text{s}} \cdot \frac{1}{\text{m}^3} \cdot \frac{1}{\text{m}} \right] = \frac{1}{\text{m}^2 \cdot \text{s}} \quad \checkmark$$

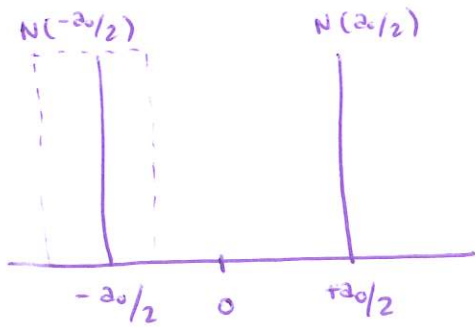
Discussion:

$$j = -D \frac{\partial c}{\partial x}$$

→ the stronger the local differences in concentration, the faster the flux!

→ the larger the diffusion constant,  $D$ , the faster the flux.

Can we derive Fick's Law from Statistics?



probability to jump  $\pm a_0$  in time  $t_0$   
is  $1/2$  in each direction.

We define the flux through plane 0 by,

$$j = \frac{\text{particles } (\rightarrow) - \text{particles } (\leftarrow)}{t_0 \cdot A}$$

where,

$$\begin{aligned} \text{particles } (\rightarrow) &= N(-a_0/2) \cdot p(+a) \\ &= c(-a_0/2) \cdot V \cdot 1/2 \\ &= c(-a_0/2) \cdot A \cdot a_0 \cdot 1/2 \end{aligned}$$

$$\begin{aligned} \text{particles } (\leftarrow) &= N(a_0/2) \cdot p(-a) \\ &= 1/2 c(a_0/2) \cdot A a_0 \end{aligned}$$

Then,

$$j = \frac{1/2 c(-a_0/2) \cdot A a_0 - 1/2 c(a_0/2) A a_0}{t_0 \cdot A} \cdot \frac{a_0}{a_0}$$

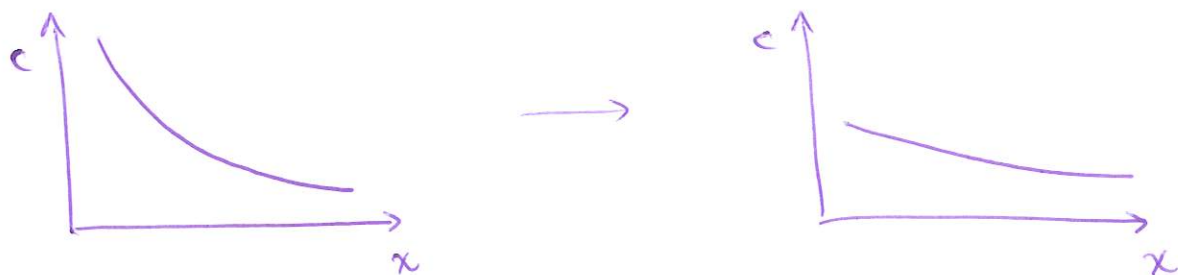
introduce

$$= \underbrace{\frac{a_0^2}{2t_0}}_D \cdot \underbrace{\frac{c(-a_0/2) - c(a_0/2)}{a_0}}_{\lim_{a_0 \rightarrow 0} = -\frac{\partial c}{\partial x}}$$

$$j = -D \frac{\partial c}{\partial x}$$

derived from statistics

But if there is flux, that means there is net particle motion, which means the concentration profile changes over time!



We need another law to account for this.

The Law of Mass Conservation!

Particles move, but they do not appear or disappear!

$$\left( \begin{array}{l} \text{particles} \\ \text{in box} \end{array} \right) = \left( \begin{array}{l} \text{particles} \\ \text{before} \end{array} \right) + \left( \begin{array}{l} \text{particles} \\ \text{that enter} \end{array} \right) - \left( \begin{array}{l} \text{particles} \\ \text{that leave} \end{array} \right)$$

$$N_{\text{box}} = c \cdot V$$

$$\frac{dN}{dt} = \frac{dc}{dt} \cdot V = \frac{dc}{dt} \Delta x \Delta y \Delta z$$

$$\rightarrow \frac{dc}{dt} \Delta x \Delta y \Delta z = \underbrace{j(x, y, z) \cdot \Delta y \cdot \Delta z}_{\text{particles enter}} - \underbrace{j(x + \Delta x, y, z) \Delta y \Delta z}_{\text{particles leave}}$$

$$= j(x, y, z) \cdot \Delta y \cdot \Delta z - \left( j(x, y, z) + \frac{\partial j}{\partial x} \Delta x \right) \Delta y \Delta z$$

$$\frac{dc}{dt} \Delta x \Delta y \Delta z = j(x, y, z) \Delta y \Delta z - j(x, y, z) \Delta y \Delta z - \frac{\partial j}{\partial x} \Delta x \Delta y \Delta z$$

$$\boxed{\frac{dc}{dt} = -\frac{dj}{dx}}$$

Law of mass conservation

Now use,  $j = -D \frac{dc}{dx} \rightarrow \frac{dc}{dt} = -\frac{d}{dx} \left( -D \frac{dc}{dx} \right)$

$$\boxed{\frac{dc}{dt} = D \frac{d^2c}{dx^2}}$$

classical Law of Diffusion!

applies when:

- ① if D does not depend on position
- ② no particles created/absorbed (no chem. reaction)

## Solutions of the diffusion eqn

Depends on initial condition!

Drop of ink in water:

$$\text{solution: } c(x, t) = \frac{N}{\sqrt{4\pi Dt}} \cdot \exp\left(\frac{-x^2}{4Dt}\right)$$

Show this is a solution! → exercise

↳ plug in to diffusion eqn and verify.

see Fig 13.15

Two main effects with time...

$$c(x, t) = \frac{N}{\sqrt{4\pi Dt}} \cdot \exp\left(\frac{-x^2}{4Dt}\right)$$

- prefactor decreases w/ t
- peak goes down

- variance increases w/ t
- curve gets wider

Fig. 13.16 → FRAP example?

Fig. 13.17 → result of calculation.

What have we learned?

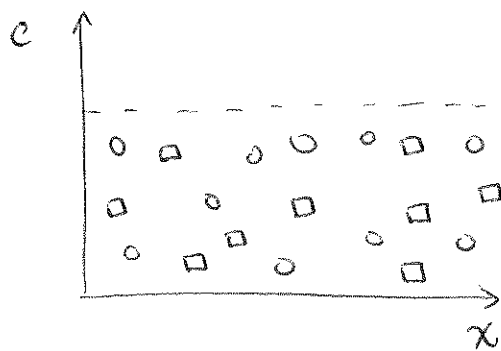
- ① Diffusion can be described by a molecular random walk!
- ② Diffusion distance depends on square root of time!  
 $\langle x^2 \rangle = 2Dt$
- ③ Diffusion creates flux, → flow from high to low concentration  
 $j = -D \frac{dc}{dx}$
- ④ If molecules are conserved,  $c(t)$  depends on spatial change of flux,  
 $\frac{dc}{dt} = -\frac{dj}{dx}$
- ⑤ The local change of  $c(t)$  depends on curvature of  $c(x)$ ,  
 $\frac{dc}{dt} = D \frac{d^2c}{dx^2}$



# Applications of Diffusion

Reminder: what have we learned? (notes from yesterday)

Now let's suppose we have a box w/ particles of uniform concentration.



$$c = \text{const}$$

$$\frac{dc}{dx} = 0$$

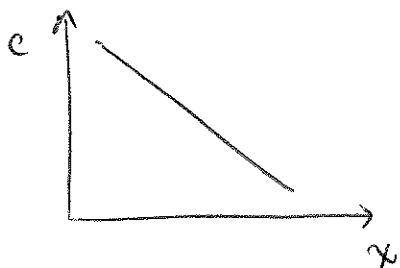
$$\frac{d^2c}{dx^2} = 0$$

$$\Rightarrow \left[ \frac{dc}{dt} = 0 \right]$$

Static Equilibrium! No change in ~~concentration~~ <sup>concentration</sup> and no net flux!

But BM still exists! Thought experiment... if you label the particles separately (Left vs. Right), will they stay separated? No!

Now consider a linear concentration profile,



$$c = -kx$$

$$\frac{dc}{dx} = -k$$

$$\frac{d^2c}{dx^2} = 0$$

→ constant flux from L to R

→ no change in concentration profile (assuming large reservoirs)

Notice there is a constant flux ( $\frac{dc}{dx} = -k$ ) but there is no change in the concentration profile ( $\frac{d^2c}{dx^2} = 0$ )!

This is a non-equilibrium steady state. E.g. channel b/w 2 reservoirs.



Generally,

- Flux is highest, where the concentration changes a lot. ( $\frac{dc}{dx}$ )
- Concentration changes, where the "curvature" of concentration is strongest. ( $\frac{d^2c}{dx^2}$ )

## Example: Diffusion through a Membrane

Membranes are permeable to many molecules.

These molecules diffuse through the membrane, which has a "permeability",  $P_m$  for the molecule,  $m$ .

For the flux of the molecule through the membrane it can be shown,

$$j_m = -P_m \cdot \Delta C \quad \xrightarrow{C_R - C_L}$$

Ex. A spherical cell ( $R = 10 \mu\text{m}$ ) will be put in a solution containing alcohol with concentration,  $C_0$ .

$$P_A = 20 \mu\text{m/s}$$

Q. How does the concentration change over time?

Recall concentration is,

$$c_i(t) = \frac{N_i(t)}{V}$$

and flux is,

$$j = -P \cdot \Delta C \quad \text{where} \quad \Delta C = C_0 - c_i(t)$$

How does concentration inside change?

$$\rightarrow \frac{dc_i}{dt} = \frac{dN_i}{dt} \cdot \frac{1}{V}$$

but recall the definition of flux as,  $\frac{dN_i}{dt} = -j \cdot A$   
combined w/ permeability to get,

$$\frac{dN_i}{dt} = P \cdot \Delta C \cdot A$$

which we can combine to get,

$$\frac{dc_i}{dt} = \frac{P \cdot \Delta C \cdot A}{V}$$

Given,

$$\frac{dc_i(t)}{dt} = \frac{P \cdot \Delta C \cdot A}{V}$$

notice  $C_0 = \text{const}$

$$\begin{aligned} \text{and } \frac{d(\Delta C)}{dt} &= \frac{d}{dt} \cdot (C_0 - C_i) \\ &= \underbrace{\frac{dC_0}{dt}}_0 - \frac{dC_i}{dt} \rightarrow \frac{d(\Delta C)}{dt} = -\frac{dC_i}{dt} \end{aligned}$$

Thus we can rewrite,

$$\boxed{\frac{d\Delta C}{dt} = -\frac{P \cdot \Delta C \cdot A}{V}} \quad *$$

Now this is an eqn we can solve. For a 1<sup>st</sup> order Diff Eqn we always guess an exponential form...

Ansatz:  $\Delta C(t) = \Delta C(0) \cdot \exp(-t/\tau)$

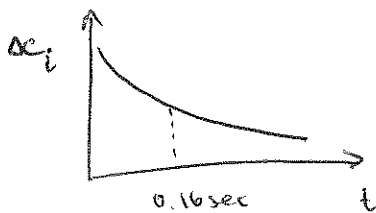
$$\frac{d\Delta C(t)}{dt} = -\frac{\Delta C(0)}{\tau} \exp(-t/\tau)$$

Plugging this into \*

$$-\frac{\Delta C(0)}{\tau} \exp(-t/\tau) = -\frac{PA}{V} \cdot \Delta C(0) \exp(-t/\tau)$$

$$\tau = \frac{V}{PA}$$

$$\tau = \frac{\frac{4}{3}\pi r^3}{\rho \cdot 4\pi r^2} = \frac{r}{3\rho} = \frac{10 \mu\text{m}}{3 \cdot 20 \mu\text{m/s}} = \boxed{0.16 \text{ sec}}$$



recall  $\Delta C = C_0 - C_i$

so then  $C_i = C_0 - \Delta C$

## Drunk on a hill

Now lets imagine a very drunk person who is stumbling around randomly. Now lets put them on a steep hill, just for fun!

This can be modeled as a biased RW process which is useful for many physical processes.

For example, • particles landing on a slanted microscope slide.  
• molecules moving during electrophoresis.

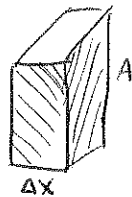
So, lets say we have a force  $F$  acting on molecules in solution.

In this case, we have a velocity,  $v$ , that depends on the friction  $\gamma$  w/ the solution.

$$F = v \cdot \gamma \quad \text{or} \quad v = F / \gamma \rightarrow \text{friction coeff.}$$

The molecule travels a distance  $\Delta x$  in a time  $\Delta t$ ,

$$\Delta x = v \Delta t$$



$$N = c \cdot V \\ = c \cdot A \Delta x$$

Recall flux,  $\vec{j} = \frac{\# \text{ of particles}}{\text{Area} \cdot \Delta t}$

so the flux due to this force is,

$$j_{\text{Force}} = \frac{N}{A \cdot \Delta t} = \frac{c \cdot A \Delta x}{A \cdot \Delta t} = c \cdot v$$

$$j_{\text{Force}} = c \cdot \frac{F}{\gamma} \rightarrow \text{Flux due to force!}$$

Now the total flux must include diffusion as well,

$$j_{\text{tot}} = j_{\text{diff}} + j_{\text{force}}$$

$$j_{\text{Tot}} = -D \frac{dc}{dx} + \frac{F}{\gamma} c$$

Now lets look at a simple scenario:

Equilibrium  $\rightarrow$  no net flux  $\rightarrow j_{TOT} = 0$

$$\rightarrow D \frac{dc}{dx} = \frac{F}{\gamma} c$$

Now if we express the force as change in potential energy,

$$F = -\frac{dU}{dx}$$

we have,

$$D \frac{dc}{dx} = -\frac{c}{\gamma} \frac{dU}{dx} \quad \text{solve by sep. of var.}$$

$$\gamma D \frac{1}{c} dc = -dU$$

$$\int_{c(x)}^{c(x)} \gamma D \frac{1}{c} dc = - \int_{U(x)}^{U(x)} dU$$

$$\gamma D (\log c(x) - \log c(x)) = -U(x) - (-U(x))$$

$$\log \frac{c(x)}{c(x)} = \frac{-(U(x) - U(x))}{\gamma D}$$

$$\frac{c(x)}{c(x)} = \exp\left(\frac{-U(x)}{\gamma D} - \frac{-U(x)}{\gamma D}\right) = \exp\left(\frac{-U(x)}{\gamma D}\right) / \exp\left(\frac{-U(x)}{\gamma D}\right)$$

Recall Boltzmann:  $\frac{c(x)}{c(x)} = \frac{\exp\left(\frac{-U(x)}{kT}\right)}{\exp\left(\frac{-U(x)}{kT}\right)}$

Now identify:

$$\gamma D = k_B T \quad \Rightarrow \quad \boxed{D = \frac{k_B T}{\gamma}}$$

Einstein Relation

Another connection can be made w/ mass conservation,  $\frac{dc}{dt} = -\frac{dj}{dx}$

$$\text{with } j = -D \frac{dc}{dx} + \frac{F}{\gamma} c$$

$$\rightarrow \boxed{\frac{dc}{dt} = D \frac{d^2c}{dx^2} - \frac{F}{\gamma} \frac{dc}{dx}}$$

Smoluchowski Eqn

$\rightarrow$  This tells you how diffusion occurs in the presence of a force.



# ASIDE

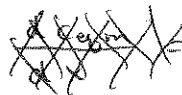
Another way to get Einstein's Relation,

In equilibrium w/ no net flux recall,

$$j_{\text{TOT}} = 0 \rightarrow D \frac{dc}{dx} = \frac{F}{\gamma} c \quad *$$

Now we know in equilibrium from Boltzmann that

$$c(x) = c_{\text{eqm}} \propto \exp\left(\frac{-U(x)}{k_B T}\right)$$



Substitute into \*

$$D \frac{d}{dx} c_{\text{eqm}} = \frac{F}{\gamma} c_{\text{eqm}}$$

This step is algebraically confusing...

$$\frac{D}{k_B T} \frac{d}{dx} (-U(x)) = \frac{F}{\gamma} - \frac{1}{\gamma} \frac{d}{dx} (U(x))$$

$$D = \frac{k_B T}{\gamma}$$

## Diffusion to Reactions

Fig. 13.20 and 13.21

Does anyone remember anything about diffusion?

### Modeling the Cell Signaling

See Fig. 13.22

How do we model the concentration profile and the uptake of a cell?

Recall diffusion,  $\frac{dc}{dt} = -D \frac{d^2c}{dx^2}$  in 1D

In 3D,

$$\frac{dc}{dt} = -D \nabla^2 c$$

cartesian:  $\nabla^2 c = \frac{d^2c}{dx^2} + \frac{d^2c}{dy^2} + \frac{d^2c}{dz^2}$

spherical:  $\nabla^2 c = \frac{1}{r^2} \frac{d}{dr} \left( r^2 \frac{dc}{dr} \right)$

For the steady state situation  $\frac{dc}{dt} = 0$

$$\rightarrow \frac{dc}{dt} = -D \nabla^2 c = 0$$

$$D \frac{1}{r^2} \frac{d}{dr} \left( r^2 \frac{dc}{dr} \right) = 0$$

is 0 if  $r^2 \frac{dc}{dr} = \text{const}$

$$\rightarrow r^2 \frac{dc}{dr} = A \quad \text{solve by sep of var.}$$

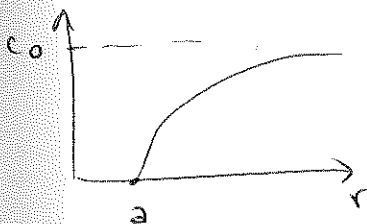
$$\int dc = \int \frac{A}{r^2} dr$$

$$c = -\frac{A}{r} + B$$

$$c = -\frac{A}{r} + B$$

where  $c(a) = 0$   
 $c(\infty) = c_0$

$$\rightarrow \boxed{c = c_0 \left( 1 - \frac{a}{r} \right)}$$



Now, what is the uptake of the sphere?

Look at the flux,

$$j(r) = -D \frac{dc}{dr}$$
$$= -D \frac{\partial c_0}{r^2}$$

Now at  $r = a$ ,

$$j(a) = -\frac{Dc_0}{a}$$

Recall definition of flux,

$$j = \frac{*}{A \cdot \Delta t} \rightarrow \frac{dn}{dt} = -j \cdot A$$
$$= \frac{Dc_0}{a} \cdot A \quad \rightarrow A = 4\pi a^2$$

$$\boxed{\frac{dn}{dt} = 4\pi D a c_0} \quad \rightarrow \text{uptake of sphere!}$$

This can be used for many systems,

- receptor-ligand signaling
- filament growth

This can also be used to differentiate b/w Diffusion & Reaction limited processes

## Distribution of Receptors

Before: Perfect absorber  $\rightarrow$  every molecule that hits is absorbed

Now: Only a certain number of receptors are present and therefore the uptake is not perfect.

How do we model this?

Uptake Rate: 
$$\frac{dn}{dt} = M \cdot K_{on} \cdot C(a)$$

$\nwarrow$  \* of receptors       $\downarrow$  uptake constant for each receptor       $\searrow$  concentration at surf of sphere

Recall that  $\frac{dn}{dt} = -j \cdot A$  and thus in our spherical case,

$$\frac{dn}{dt} = D \frac{\partial c}{\partial r} 4\pi r^2$$

So combining,

$$D \frac{\partial c}{\partial r} 4\pi r^2 = M K_{on} C(a)$$

$$\int_{c(a)}^{c(r)} dc = \int_a^r \frac{M K_{on} C(a)}{4\pi D r^2} dr$$

$$c(r) - c(a) = \frac{M K_{on} C(a)}{4\pi D} \left( \frac{1}{a} - \frac{1}{r} \right)$$

we know that  $c(\infty) = C_0$

$$\rightarrow \boxed{C_a = \frac{C_0}{1 + \frac{M K_{on}}{4\pi D a}}}$$

The concentration on the cell as a function of,  $K_{on}$  and  $M$ !

Investigate the limits,

$$\frac{M K_{on}}{4\pi D a} \gg 1 \rightarrow C(a) = \frac{C_0}{\text{big } \#} \approx 0$$

this is the limit of the perfect absorber.

$$\frac{M K_{on}}{4\pi D a} \ll 1 \rightarrow C(a) = \frac{C_0}{1 + \text{small}} \approx C_0$$

uptake is way slower than diffusion

We can now answer a biological question!

Q: How many receptors should I have to be a good absorber?

The absorption rate is,

$$\frac{dn}{dt} = M k_{on} (a)$$

$$\boxed{\frac{dn}{dt} = \frac{M k_{on} C_0}{1 + \frac{M k_{on}}{4\pi D a}}}$$

Lets say that a good absorber can absorb half the molecules delivered by diffusion

Recall from diffusion,

$$\boxed{\frac{dn}{dt} = 4\pi D a C_0}$$

So if we say the cell absorbs half of these then we can combine these equations to get

$$\frac{4\pi D a C_0}{2} = \frac{M k_{on} C_0}{1 + \frac{M k_{on}}{4\pi D a}} \quad \text{multiply by } 4\pi D a$$

$$\frac{4\pi D a C_0}{2} = \frac{M k_{on} \cdot 4\pi D a C_0}{1 + \frac{M k_{on}}{4\pi D a}}$$

$$\frac{1}{2} = \frac{\beta}{1 + \beta} \quad \text{where } \beta = \frac{M k_{on}}{4\pi D a}$$

And  $\beta = 1$  !

Thus we can calculate the number of receptors a cell must have to be a good absorber!

$$\boxed{M = \frac{4\pi D a}{k_{on}}}$$



Now lets look at a typical cell,

$$a = 10 \mu\text{m}, \quad D_{\text{prot}} = 100 \mu\text{m}^2/\text{s}$$

$$k_{\text{on}} = 10 \frac{1}{\mu\text{M}\cdot\text{s}} \quad \leftarrow \text{on rate of actin.}$$

Lets change the units of  $k_{\text{on}}$ ,

$$1 \mu\text{M} = 6 \cdot 10^{23} \text{ molecules} \cdot 10^{-6} \frac{1}{10^{15} \mu\text{m}^3} = 600 \frac{\text{molecules}}{\mu\text{m}^3}$$

$$k_{\text{on}} = \frac{10}{600 \frac{\text{mol}}{\mu\text{m}^3} \cdot \text{s}}$$

$$\rightarrow M = \frac{4\pi \cdot 100 \frac{\mu\text{m}^2}{\text{s}} \cdot 10 \mu\text{m}}{1/60 \frac{\mu\text{m}^3}{\text{mol} \cdot \text{s}}} \approx 12 \cdot 6 \cdot 10^4 \approx 10^5 \text{ receptors}$$

Estimate the distance b/w receptors,

$$d^2 = \frac{4\pi a^2}{10^5} = \frac{12 \cdot 100 \mu\text{m}^2}{10^5} \approx 10^{-2} \mu\text{m}^2$$

$$\approx 100 \text{ nm} \times 100 \text{ nm}$$

$\therefore$  The avg distance b/w receptors is 100 nm

What membrane fraction is covered?

If the area of one receptor is  $10 \text{ nm}^2$  this is  $10^{-5} \mu\text{m}^2$ .

Thus the fraction of the total area is,

$$\frac{(10^5 \text{ receptors})(10^{-5} \mu\text{m}^2)}{4\pi a^2} = \frac{1 \mu\text{m}^2}{12 \cdot 100 \mu\text{m}^2} = \left| \frac{1}{1200} \right|$$

Only  $1/1200$  of the cell must have receptors to absorb 50% of all delivered particles!