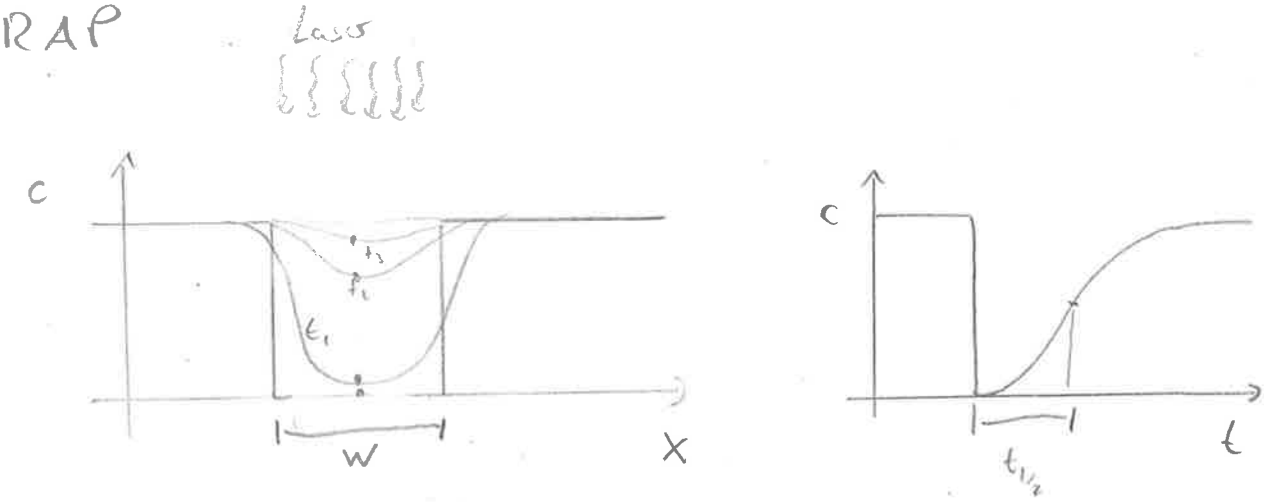
Diffusion constants

FRAP



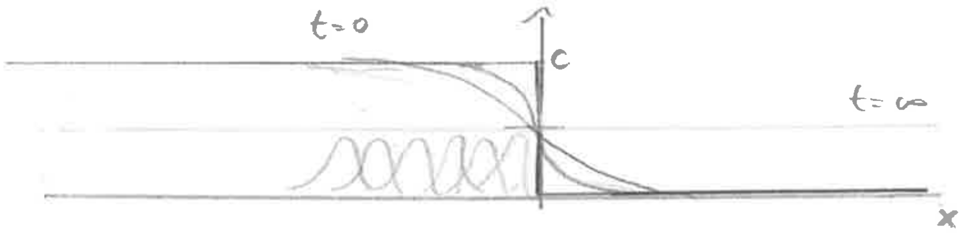
how is $t_{1/2}$ related to D & w?

- D: $\left[\frac{\text{length}^2}{s}\right]$

$\rightarrow \quad D \sim \frac{w^2}{t_{1/2}}$ the only way we can combine w & $t_{1/2}$ to obtain the correct units!

$\rightarrow \quad \Delta x \sim \sqrt{2Dt} \sim w \rightarrow D \sim \frac{w^2}{2t}$

Calculation



discrete approx: $$P(x,t) = c \sum_i \frac{dx}{\sqrt{4\pi Dt}} e^{-\frac{(x+i\,dx)^2}{4Dt}}$$

$dx \to \infty$

$$= c \int_{-\infty}^{0} dx_0 \frac{1}{\sqrt{4\pi Dt}} e^{-\frac{(x-x_0)^2}{4Dt}}$$

$$= \frac{c}{2}\left[1 - \operatorname{erf}\left(\frac{x}{\sqrt{4Dt}}\right)\right]$$

- obviously our prev crit of $P(d,t) = \frac{c}{2}$ doesn't work
- let's look at the time to $P(d,t) = \frac{c}{4}$
- $\operatorname{erf}\left(\frac{d}{\sqrt{4Dt}}\right) = \frac{1}{2} \Rightarrow D = 1.1\,\frac{d^2}{t}$

Diffusion constants

- GFP: $25\ \frac{\mu m^2}{s}$ or $10\ \mu m^2/s$
  Euk. prok
- mRNA: $.2\ \frac{\mu m^2}{s}$
- water molecule: $2000\ \frac{\mu m^2}{s}$
- H^+: $7000\ \frac{\mu m^2}{s}$

Diffusion times

- one bacterial cell diameter: $\Delta x = 1\mu m \rightarrow t = \frac{\Delta x^2}{20} = \frac{1}{20}\,s$
- eukaryotic cell: $\Delta x = 10\mu m \rightarrow t = 5s$
- $\Delta x = 1mm \rightarrow t = 5000s \approx 83m$
- $1m \rightarrow 160y$

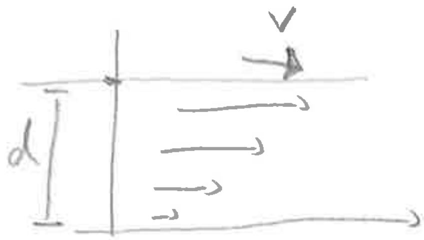
$\Rightarrow$ short distance $\rightarrow$ diffusion

long distances $\rightarrow$ something else

Stokes - Einstein relation

Is there a general law?

- the bigger, the slower → r [length]
- thermal → kT [energy]
- viscosity of the medium : η $\left[\frac{\text{Force} \cdot \text{time}}{\text{length}^2}\right]$



$$F = A \cdot \frac{v}{d} \cdot \eta$$

area, velocity gradient, viscosity

Is there a way to combine these to give $\frac{\text{length}^2}{s}$?

$\frac{kT}{\eta}$ has units of $\frac{\text{energy} \cdot \text{length}^2}{\text{Force} \cdot \text{time}} = \frac{\text{length}^3}{\text{time}}$

$\Rightarrow$ maybe $D \sim \frac{kT}{\eta r}$

Einstein developed a simple argument to derive a relationship between diffusion & viscosity.

Flux: $j(x,t) = \mu F P(x,t) - D \frac{\partial P(x,t)}{\partial x}$

$= -\mu \frac{\partial \varphi}{\partial x} P(x,t) - D \frac{\partial P(x,t)}{\partial x}$

potential $F = -\frac{\partial \varphi}{\partial x}$

- lets make it simple: $\varphi = \frac{x^2}{2}$ → harmonic

⇒ at eq: $\frac{\partial P(x)}{\partial x} = -\frac{\mu x}{D} P \rightarrow P \sim e^{-\frac{\mu x^2}{2D}}$

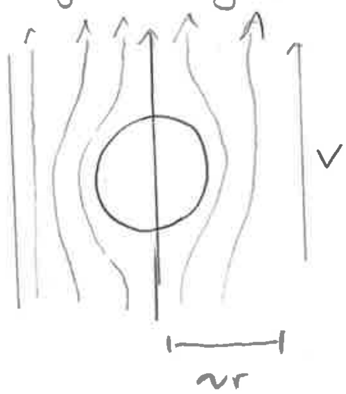
- but in thermal equilibrium: $P(x) \sim e^{-\frac{\varphi(x)}{kT}}$

⇒ $D = \mu k T$

- the mobility μ connects force & velocity.

$v = \mu F$

- for a spherical particle of radius r, μ is given by Stokes' law: $\mu = \frac{1}{6\pi\eta r}$



while the 6π factor requires a calculation, the scaling can be obtained by dimensional analysis

- velocity gradient $\sim \frac{v}{r}$
- area: $2\pi r \cdot r$ (a cylinder of length r)

⇒ $\mu \sim \frac{1}{2\pi\eta r}$

⇒ $\boxed{D = \frac{kT}{6\pi\eta r}}$ Stokes - Einstein relation

How does S-E-relation compare to measurements?

- viscosity of water: $\eta_0 = 10^{-3} \frac{Ns}{m^2} = 10^{-5} \frac{Ns}{\mu m^2} \simeq 10^{-3} \frac{pNs}{\mu m^2}$

- cytosol: $\eta \simeq 3\eta_0$

cytosolic diffusion constants: $D = \frac{kT}{6\pi\eta r} \approx \frac{4 pN nm (\mu m)^2}{20 \cdot 3 \cdot 10^{-3} pNs} \frac{1}{r}$

$$= \frac{1}{r} \frac{\mu m^3}{15 s}$$

- The typical protein has a radius of 2nm

$\Rightarrow D \simeq 30 \frac{\mu m^2}{s}$

- water molecule $r = 0.1 nm$

$\Rightarrow 660 \frac{\mu m^2}{s}$

Different dimensions

- most of our arguments were done in 1D
- how does this generalize to multiple dims?

→ 1d : diffusion on DNA

→ 2d : diffusion on membranes

- since random kicks in different dimensions are independent

  → solutions are factorize

$$P(x,y,z,t) = P(x,t)\,P(y,t)\,P(z,t)$$

$$\rightarrow \frac{1}{(4\pi Dt)^{3/2}} e^{-\frac{x^2+y^2+z^2}{4Dt}} = \frac{1}{(4\pi Dt)^{3/2}} e^{-\frac{r^2}{4Dt}}$$

$\Delta x = \sqrt{2dDt}$ → variances in different dimensions add

Mean free path & speed

- kinetic energy: $\frac{mv^2}{2} = \frac{kT}{2} \Rightarrow v = \sqrt{\frac{kT}{m}} = \sqrt{\frac{4pNnm}{m}}$

$$= \sqrt{\frac{4\times10^{21}\,Nm}{m}} = \sqrt{\frac{4\times10^{21}\,kg}{m}}\,\frac{m}{s}$$

- 30 kDa protein $= 5\times10^{-23}\,kg$

$$\rightarrow v = 10\,\frac{m}{s}$$

- how often does it change direction? $\delta x = v\,\delta t$
- # steps in time $t \Rightarrow n = \frac{t}{\delta t}$

$$\Delta x = \sqrt{2Dt} \approx \sqrt{\delta x^2 n} = \sqrt{v^2 \delta t\, t} \Rightarrow D = v^2 \delta t$$

$$\Rightarrow \delta t = \frac{20\,\mu m^2}{100\,\frac{m^2}{s^2}} \approx 0.2\times10^{-12}\,s$$

$$\delta x = 0.2\times10^{-11}\,m = 0.02\,\text{Å}$$