Diffusion in Biological Systems

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FLUCTUATION ⟷ DISSIPATION

Diffusion

Viscosity

STOKES-EINSTEIN RELATIONSHIP

$$\boxed{6\pi\eta a D = k_B T}$$

Fluctuation-Dissipation Theorem (simple definition):

At equilibrium, a process that *dissipates* heat (eg. viscosity) is directly related to another process (diffusion) associated with *thermal fluctuations ($k_B T$)*

FLUCTUATION ⟷ DISSIPATION

Diffusion

Viscosity

STOKES-EINSTEIN RELATIONSHIP → Does not have a molar analogy!

$$\boxed{6\pi\eta a D = k_B T}$$

Bulk property

Molecular property

Unlike . . .

$$k \propto e^{-\Delta G/k_BT}$$

$$\text{or } k \propto e^{-\Delta G/RT}$$

No direct molecular analogy!

$$6\pi\eta a D = \frac{(RT)}{N_A}$$

Diffusion Equations:

$$\langle \boldsymbol{r}_N{}^2 \rangle = (2d)\,(D)\,(T)$$

$$\zeta D = k_B T$$

$$6 \pi \eta a D = k_B T$$

Dimensions and Units of dynamic viscosity

$$[\eta] = [\text{pressure}]\,[\text{time}]$$

$$\equiv [M L^{-1} T^{-1}]$$

SI units: Pa-s $\equiv 1 \text{ kg m}^{-1} \text{s}^{-1}$

Commonly used Units: Poise or Centipoise (cP)

$$1 \text{ poise} = 1 \text{ g cm}^{-1} \text{s}^{-1}$$

$$= 0.1 \text{ Pa} \cdot \text{s}$$

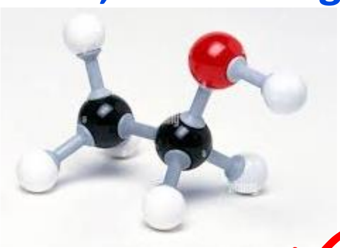
Do the interconversions

Diffusion Equations:

$$\boxed{\langle r_N^2 \rangle = (2d)\,(D)\,(T)}\;*$$

$$6\pi\eta\,a\,D = k_B T$$

radius, a = 4.4 Angs



η at 25°C:
1.074 centipoise (cP)

Eg 1. **self-diffusion of pure Ethanol**

- How will you approximately estimate the time to diffuse across a given length, say 5 cm?
- What does your answer indicate?

$$D = \frac{k_B T}{6\pi\eta a}$$

$$= \frac{(1.38\times10^{-23})\times(298)}{6\times(3.14)\times(1.074\times10^{-3})\times(4.4\times10^{-10})}$$

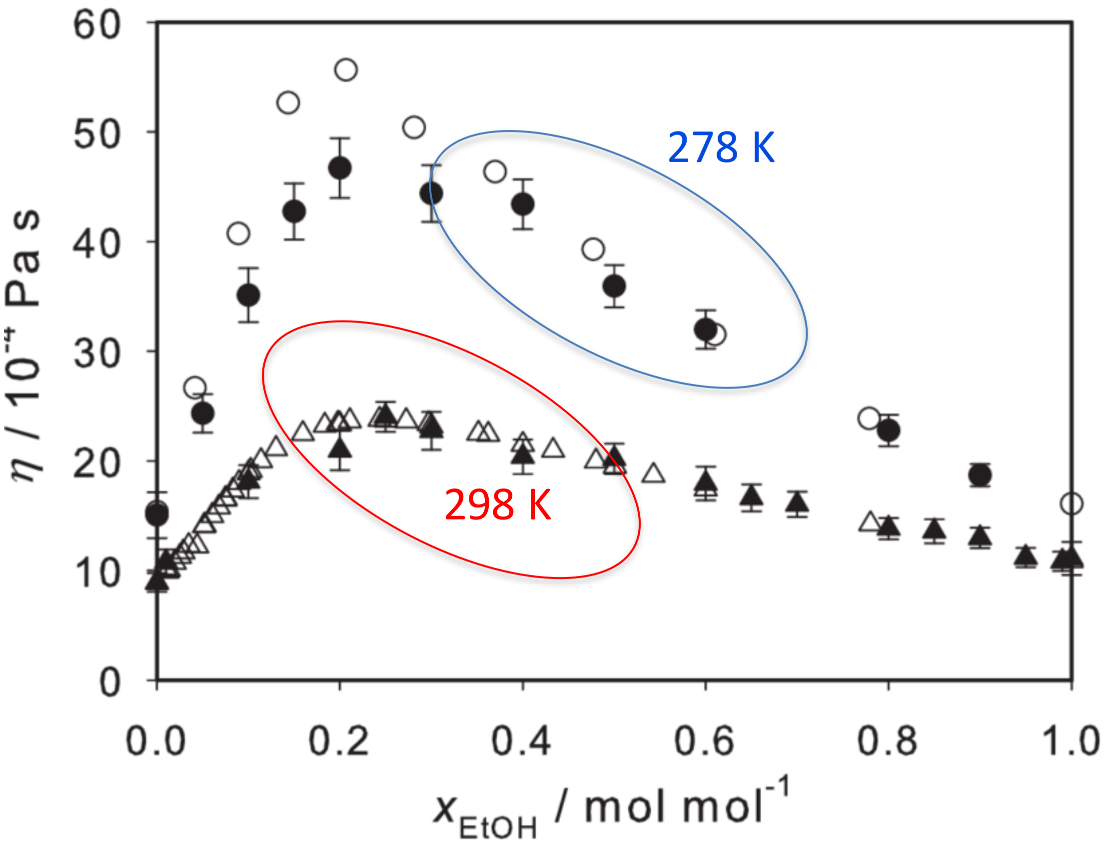
$$= (4.62)\times10^{-10}\ m^2 s^{-1}$$

$$\langle r^2 \rangle = 25\times10^{-4}\ m^2 = 6\times(4.62\times10^{-10})(\text{time})$$

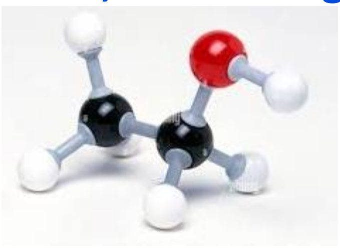
$*$

$$(\text{time}) \equiv 0.9\times10^{6}\ \text{sec}$$

Eg 2. **diffusion of Ethanol in binary mixture:**



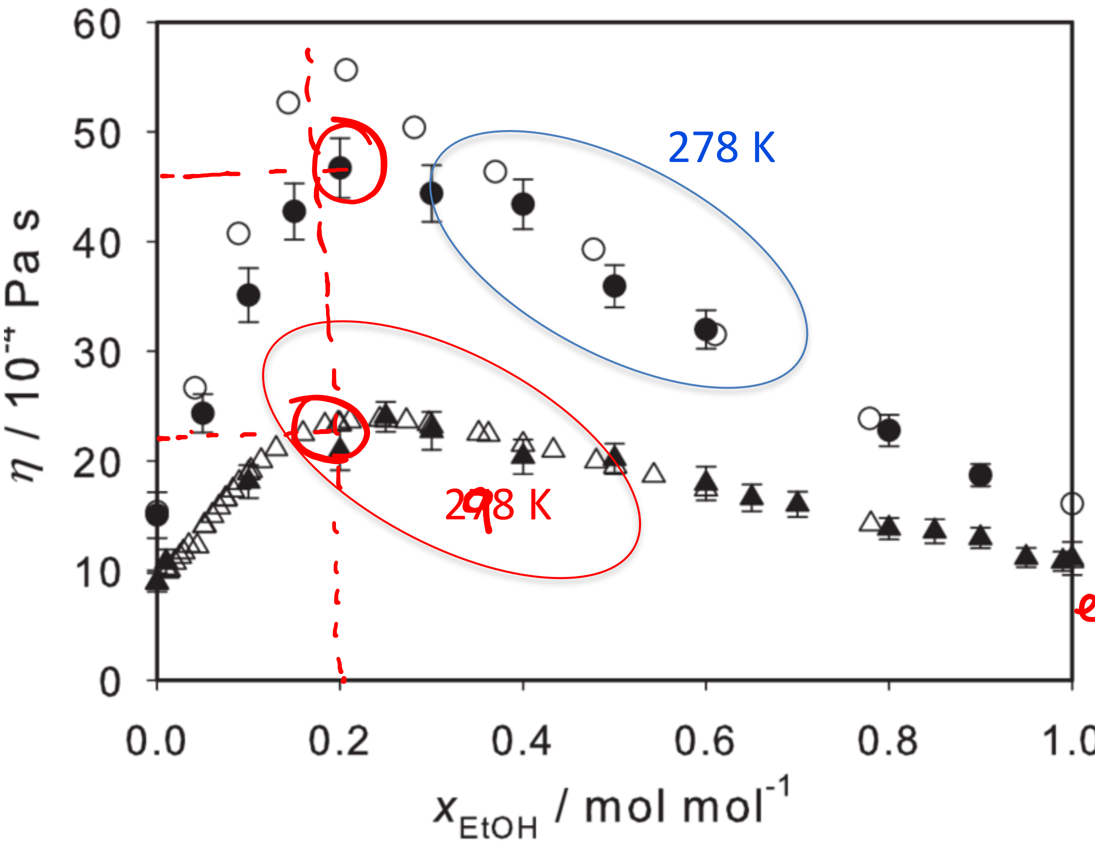
radius, a = 4.4 Angs



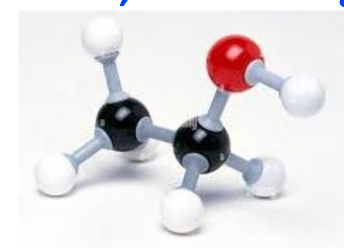
- Here, one must consider viscosity of the medium
- The two different molecules will have different diffusion coefficients

Viscosity of the mixture (water + ethanol).
Computational results (full symbols) Vs.
Experimental data (empty symbols)

Eg 2. **diffusion of Ethanol in binary mixture:**



radius, a = 4.4 Angs



- Here, one must consider effective viscosity of the medium
- The two different molecules will have different diffusion coefficients

Viscosity of the mixture (water + ethanol).
Computational results (full symbols) Vs.
Experimental data (empty symbols)

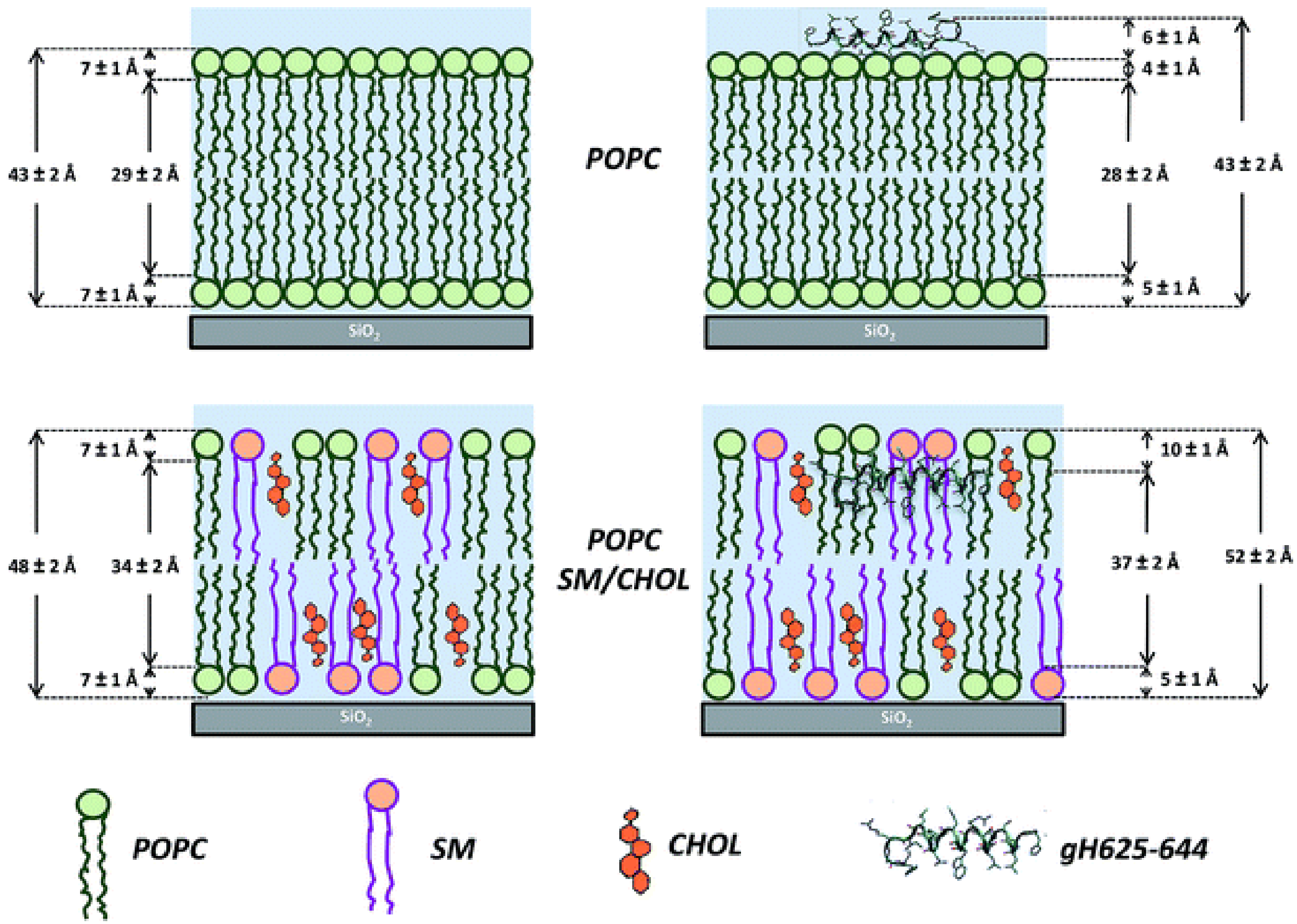
Typical “room temperature” Diffusion Coefficients:

Molecule	Molecular Weight (g/mol)	Diffusion Coefficient (cm^2/s)
H^+	1.008	9.31×10^{-5}
Na^+	22.99	1.33×10^{-5}
K^+	39.098	1.96×10^{-5}
Ca^{2+}	40.078	0.79×10^{-5}
Cl^-	35.453	2.03×10^{-5}
Ammonia (NH_3)	17.031	1.51×10^{-5}
Oxygen (O_2)	31.999	2.10×10^{-5}
Carbon dioxide (CO_2)	44.01	1.97×10^{-5}
Urea	60.055	1.38×10^{-5}
Glucose	180.156	5×10^{-6}
Sucrose	342.296	5.23×10^{-6}
Hemoglobin	68,000	6.9×10^{-7}
DNA	6,000,000	1.3×10^{-8}

a

'a'

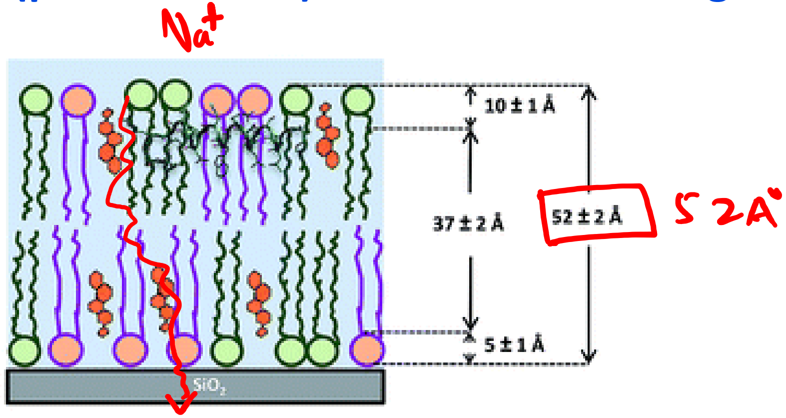
Eg. 3. Consider a typical membrane bilayer to be permeable to each of the molecules (previous slide). Estimate the average time taken to diffuse across the bilayer.



Spatial dimension to consider?

Soft Matter, 2015, **11**, 3003-3016

Eg. 3. Consider a typical membrane bilayer to be permeable to each of the molecules (previous slide). Estimate the average time taken to diffuse across the bilayer.



Using d=3, how long does it take these ions to cross the bilayer?

Molecule	Molecular Weight (g/mol)	Diffusion Coefficient (cm^2/s)
H^+	1.008	9.31×10^{-5}
Na^+	22.99	1.33×10^{-5}
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$$6\pi\eta a D = k_B T$$

Stokes-Einstein Equation:

$$6 \pi \eta a D = k_B T$$

$$a^3 \propto (\text{mol. wt.})$$

$$\frac{a_1^3}{a_2^3} = \frac{(mw)_1}{(mw)_2} = \frac{17}{64.5}$$

$$\frac{a_1}{a_2} = \left(\frac{17}{64.5}\right)^{1/3}$$

$$= 0.641$$

Consider 'size' to be directly proportional to the molecular weight (mw) of a class of proteins. Myoglobin (1) and Hemoglobin (2) have mw of 17 kDa and 64.5 kDa, respectively.

What are the approx. ratio of their times taken to cover a distance of 1 micrometre, in media of similar viscosities, if T(1) and T(2) are 300 K and 320 K, respectively?

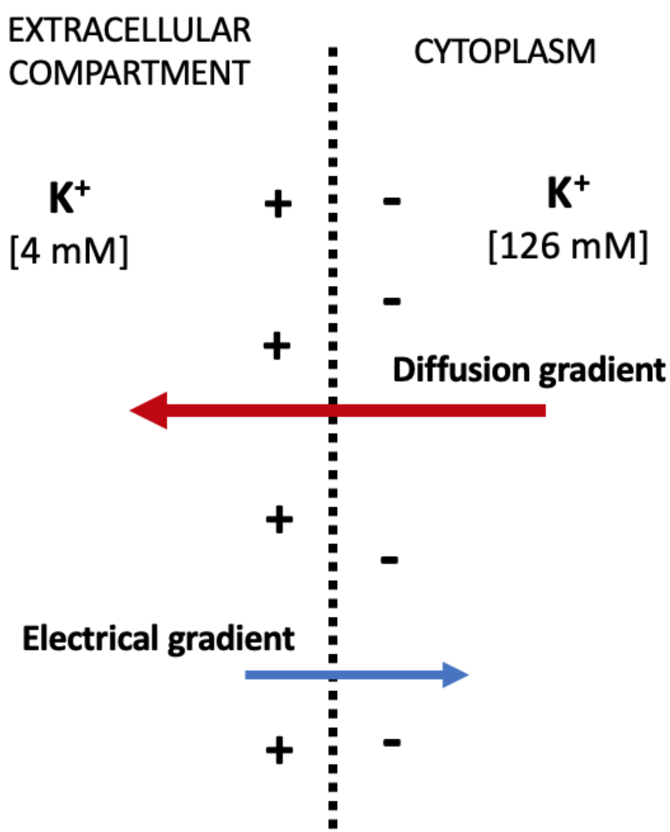
$$\frac{a_1 D_1}{a_2 D_2} = \frac{T_1}{T_2}$$

$$0.641\left(\frac{D_1}{D_2}\right) = \frac{300}{320}$$

$$D_1 = (\quad) D_2$$

Offsetting diffusion: Nernst Eqn. sets the scale for membrane potentials

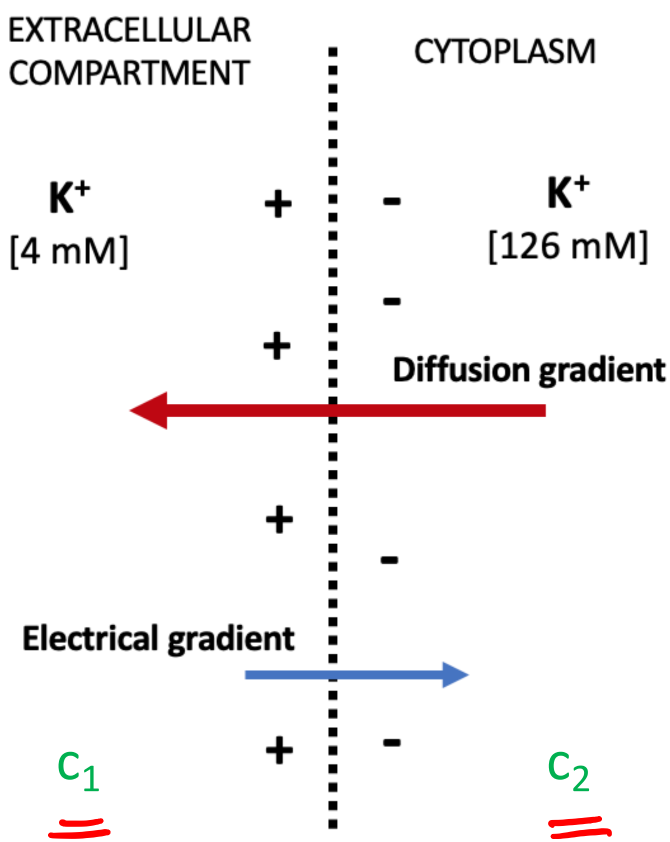
$$\Delta(\ln c) = -\frac{q\,\Delta V}{k_B T}$$



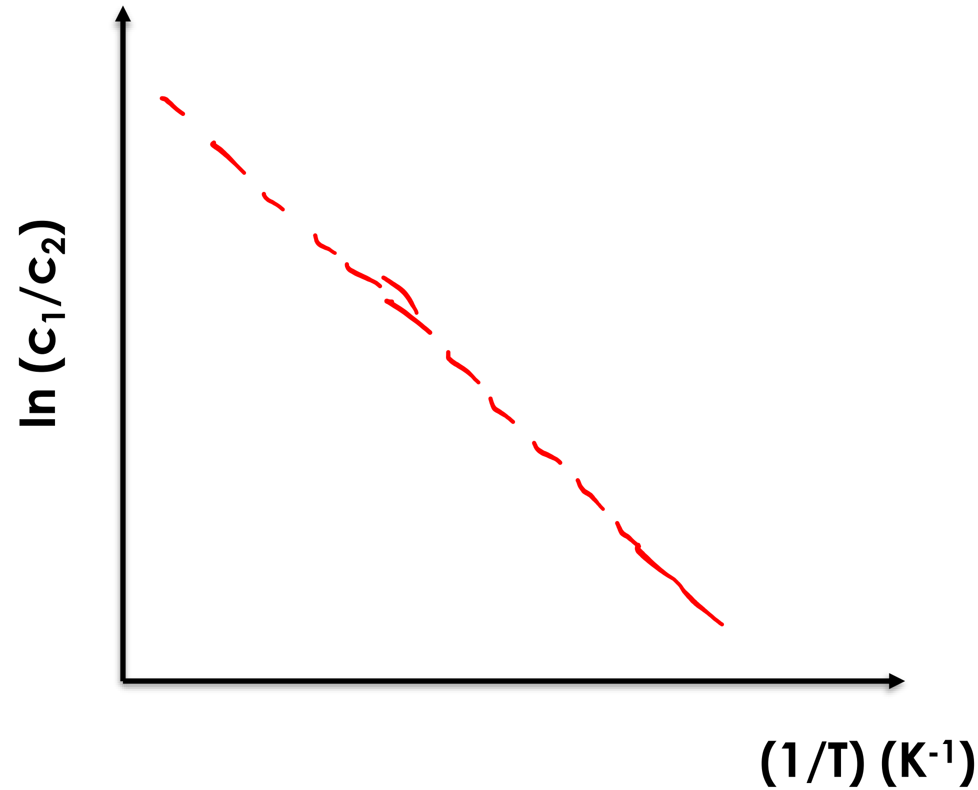
Offsetting diffusion: Nernst Eqn. sets the scale for membrane potentials

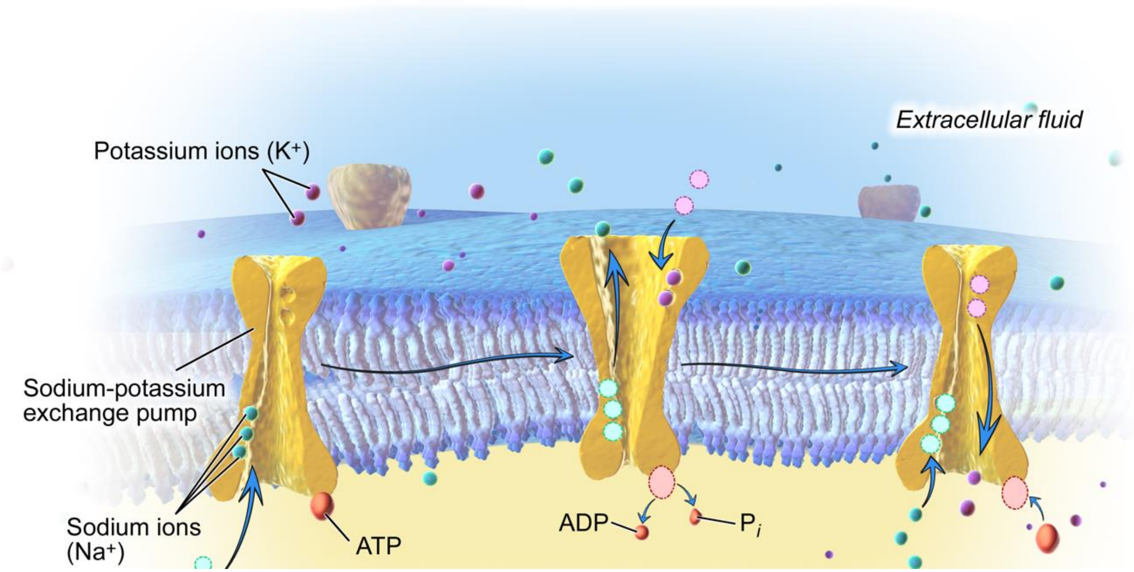
$$\ln\left(\frac{c_1}{c_2}\right) = -q(\Delta V)/k_B T$$

$$\Delta(\ln c) = -\frac{q\Delta V}{k_B T}$$



How will the plot appear?





For mixtures of ions:

$$\Delta V_{effective} = \sum_{i=1}^{N_{types}} \Delta V_i$$

Intracellular and extracellular concentrations and Nernst equilibrium potential values for a few ions of physiological importance

Ionic Species	Intracellular Concentration c_1	Extracellular Concentration c_2	Equilibrium Potential Verify!
Sodium (Na^+)	15 mM	145 mM	V_{Na} = +60.60 mV
Potassium (K^+)	150 mM	4 mM	V_K = −96.81 mV
Calcium (Ca^{2+})	70 nM	2 mM	V_{Ca} = +137.04 mV
Hydrogen ion (proton, H^+)	63 nM (pH 7.2)	40 nM (pH 7.4)	V_H = −12.13 mV
Magnesium (Mg^{2+})	0.5 mM	1 mM	V_{Mg} = +9.26 mV
Chloride (Cl^-)	10 mM	110 mM	V_{Cl} = −64.05 mV
Bicarbonate (HCO_3^-)	15 mM	24 mM	V_{HCO3-} = −12.55 mV

(T = 310 K, ie. physiological temperature)

The Nernst potential is typically between 50 and 100 milliVolts (50 – 100 mV)

Offsetting Diffusive Effects:

$$\ln\left(\frac{c_2}{c_1}\right) \equiv \frac{[\text{force}][\text{length}]}{(k_B T)}$$

Centrifugal force:

At a distance *r*,

$$\ln\left(\frac{c_r}{c_0}\right) \equiv \frac{[m\,\omega^2 r][r]}{(k_B T)}$$

$$\equiv \left(\frac{m}{k_B T}\right) \times \frac{4\pi^2 (r.p.m)^2}{3600} \times r^2$$

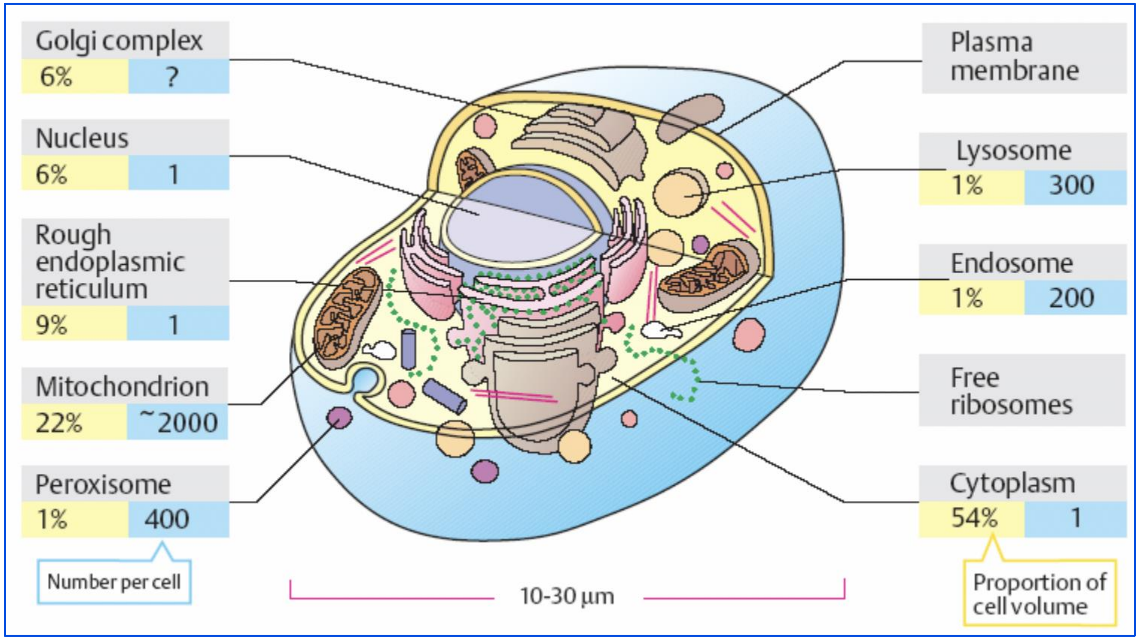
Biocompare.com

Prob. Consider a solution of proteins that are of mass 50 kiloDa (Note: 1 Da ~ 1 g/mol). The solution is spun in a low-powered centrifuge that achieves the highest rotation per minute (**rpm**) of 100.

a) Find the *concentration ratio* in the centrifuge tube at (r = 0 cm) with that at (r = 5 cm).
b) What is the **rpm** required for a *concentration ratio of 1000*?

~ 3500 r.p.m ??

Centrifugation

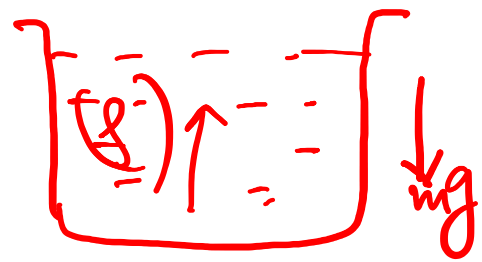


Material	Density (g/cm³)
Microbial cells	1.05 - 1.15
Mammalian cells	1.04 - 1.10
Organelles	1.10 - 1.60
Proteins	1.30
DNA	1.70
RNA	2.00

Sedimentation *time scale*,

$$t = \frac{m_{net}}{\zeta}$$

viscous friction coeff



$m_{net} = (m - \rho v)g$

where $\rho \rightarrow$ density

$v \rightarrow$ drift velocity.

Sedimentation coefficient is defined as:

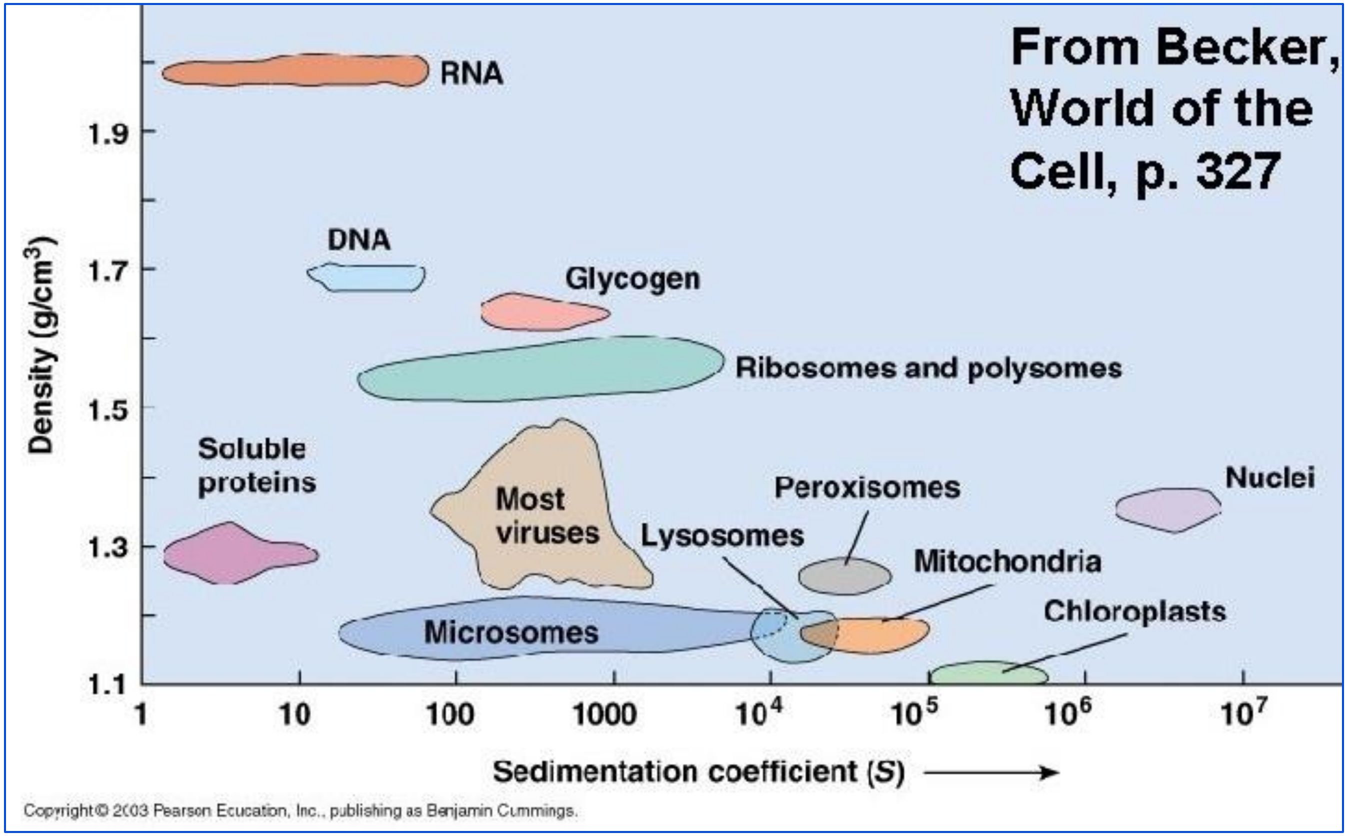
1 Svedberg (s),

$s = 10^{-13}$ s

Sedimentation coefficients are not additive

Sedimentation *time scale*,

$$t = \frac{m_{net}}{\zeta}$$



1 Svedberg,

s = 10^{-13} *s*