Physical Principles in Biology
Biology 3550
Fall 2017

Lecture 33

Permeability of Lipid Bilayers

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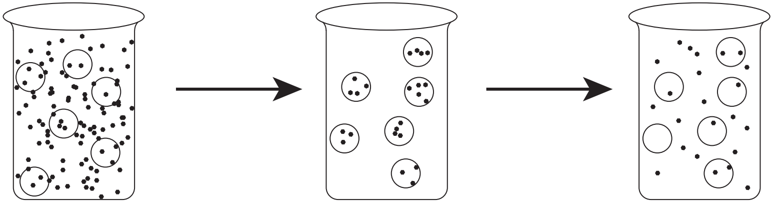
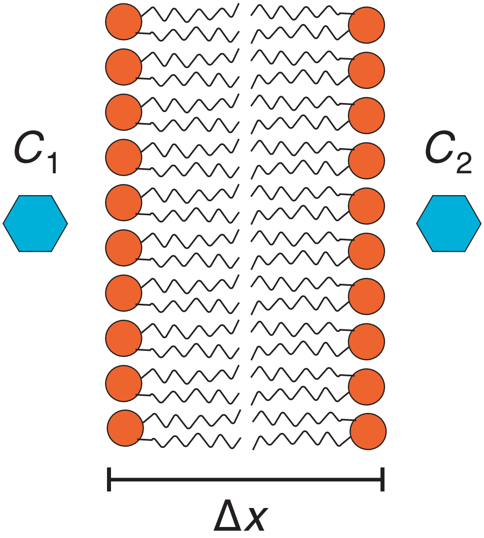
Using Vesicles to Measure Permeability of Bilayers



- Form vesicles in presence of molecules of interest.
- Separate vesicles from external molecules.
- Allow molecules to diffuse across bilayers.
- Separate vesicles from external molecules and measure concentrations.

Diffusion Across a Bilayer



- Fick's first law:

$$J = -D\frac{dC}{dx} \approx -D\frac{\Delta C}{\Delta x}$$

- The permeability coefficient, P

$$P = \frac{D}{\Delta x}$$

$$J = -P\Delta C$$

- Measure the flux and calculate P

$$P = -\frac{J}{\Delta C}$$

- P reflects properties of the membrane and the molecule.

Clicker Question #1 from Last Time

What kind of ions or molecules would you expect to have the **largest** permeability coefficients for phospholipid bilayers?

1. Sugars
2. Amino acids
3. Water
4. Nucleotides
5. Small ions like Na^+, K^+ or Cl^-

Results:

1	Sugars	11%
2	Amino acids	14%
3	Water	32%
4	Nucleotides	0%
5	Small ions	43%

Clicker Question #2 from Last Time

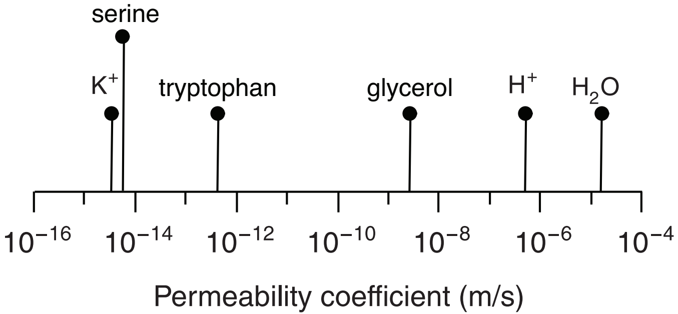
What kind of ions or molecules would you expect to have the **smallest** permeability coefficients for phospholipid bilayers?

1. Sugars
2. Amino acids
3. Water
4. Nucleotides
5. Small ions like Na^+, K^+ or Cl^-

Results:

1	Sugars	0%
2	Amino acids	4%
3	Water	4%
4	Nucleotides	71%
5	Small ions	21%

Measured Permeability Coefficients



- Range of permeabilities is extremely wide: 9 orders of magnitude.
- Charged ions have very low permeability.
- Polar small molecules have low to medium permeabilities.
- Permeabilities of water and H^+ are actually quite high!

Comparing Permeability Across Bilayers with Diffusion Coefficients in Water

- $P = D/\Delta x$
- Can calculate an "effective diffusion coefficient" by assuming a value for Δx.

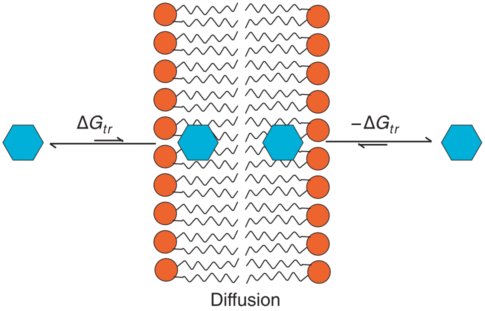
  $$D = P\Delta x$$

  Assume $\Delta x = 4\,\text{nm}$
- For ions:

  $$\begin{aligned} D = P\Delta x &= 10^{-14}\,\text{m/s} \times 4\times10^{-9}\,\text{m} \\ &= 4\times10^{-23}\,\text{m}^2/\text{s} \end{aligned}$$
- For small polar molecules:

  $$\begin{aligned} D = P\Delta x &= 10^{-10}\,\text{m/s} \times 4\times10^{-9}\,\text{m} \\ &= 4\times10^{-19}\,\text{m}^2/\text{s} \end{aligned}$$
- Compare to $D = 10^{-10}\,\text{m}^2/\text{s}$ for small molecules in water.

Solubility-Diffusion Model for Permeability



- Molecule equilibrates between aqueous and lipid phases.
- Molecule diffuses across lipid phase.
- Diffusion is rate limiting.

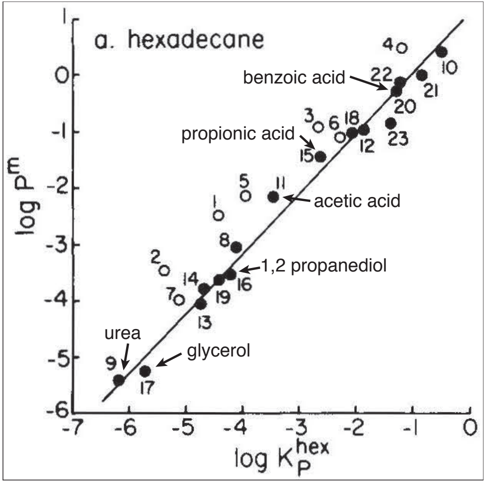
  $P = K_{tr} D_{hc} / \Delta x$

  K_{tr} is equilibrium constant between phases.

  D_{hc} is diffusion coefficient in hydrocarbon.

- Model predicts a correlation between measured ΔG_{tr} and P for molecules of similar size.

Correlation Between Permeability and Solubility in Non-polar Liquids



- Values are for small polar molecules.
- P^{m}: Bilayer permeability coefficient (cm/s).
- K_{p}^{hex}: Partition coefficient from water to hexadecane.
- Correlation supports “solubility diffusion” model.

Figure from: Walter, A. & Gutknecht, J. (1986). Permeability of small nonelectrolytes through lipid bilayer membranes. *J. Membrane Biol.*, 90, 207–217. http://dx.doi.org/10.1007/BF01870127