**Lecture 26: Membranes & Membrane Proteins:**

**Key Terms:**

1. **Phospholipids**
2. **Liposomes/bilayer**
3. **Phase transition of bilayers**
4. **Biological Membranes**
5. **Membrane Protein Structure**

**Phospholipids** - G**lycerophospholipids:**

1. Head group + phosphate + glycerol + two fatty acids (**acyl chains**) of *various* types form a phospholipid.
2. Various **head groups** are attached to the phosphate, giving a diverse set of lipids.
3. The nomenclature indicates the type of fatty acid attached to the 1 and 2 positions of glycerol as well as the type of head group on the phosphate.

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| **Head group(-X)** | **Name of Phospholipid** | **Net Charge** |
| none | phosphatidic acid (PA) | -1 |
| Choline (-C-C-N+(CH3)3) | Phosphatidylcholine (PC), called lecithin | 0 (zwitterion) |
| Serine (linkage via sidechain)  | Phosphatidylserine (PS) | -1 |
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**Physical Properties of Pure Lipid Bilayers:**

1. Phospholipids self-assemble in water to form **bilayers** (two opposing layers of phospholipids). Bilayers are formed instead of micelles because the cross section of the head group is roughly equal to the cross section of the 2 fatty acid chains found in phospholipids.

2. The bilayers form closed, water filled, vesicles with a 40-50 Å thick wall. The non-polar acyl chain width is about 30 Å.

3. **Permeability properties:**

* Charged compounds do **not** cross the bilayer.
* Polar ones infrequently.
* Non-polar ones readily.

**Phase transition:**

1. Lipid bilayers undergo a *highly cooperative* (melts over a narrow temp range) phase transition with a defined Tm:
* Below Tm the lipids exist as a solid-like *gel*; the acyl chains are tightly packed.
1. Above Tm the lipids are in a liquid-like *liquid crystal phase*. The acyl chains are disordered. Thus the phase transition is called the gel to liquid-crystalline transition.
2. Above Tm rapid lateral diffusion of lipids and proteins occurs in the plane of the membranes.

The effect of chain length and cis-double bonds on TM is due to van der Waals packing.

DMPC (C14) = 23 C

DPPC (C16) = 41 C

DSPC (C18) = 58 C

DOPC (C18:1) = -22 C

**Cholesterol:**

1. Is a natural steroid, you produce about 1 g/day!
2. About the same length as C16 fatty acid; therefore it reaches across half of the bilayer.
3. *Essential* component of most mammalian membranes.
4. Destroys the phase transition of pure lipid membranes, thereby keeping the membranes fluid below the phase transition and more rigid above the phase transition. Often referred to as a membrane *plasticizer*.

**Peripheral Membrane Proteins:**

* Loosely attached to membranes via electrostatic interactions – released with high salt.
* Often involved in electron transport and, as specific binding proteins, e.g. sugar transport in bacteria.

**Structure of Integral Membrane Proteins:**

* Largely contained within in the membrane (solubilization requires disruption of the membrane by detergents).
* Stability energetics are similar to water soluble proteins, except that membrane proteins are "inside-out".

i. Non-polar groups interact with acyl chains in the membrane. The general rule here is: hydrophobic outside--hydrophilic or hydrophobic inside, depending on function.

ii. Virtually **all** hydrogen bonds for residues within the bilayer must be satisfied because there is no water available. Loss of these hydrogen bonds in the folded form costs +25kJ/mol, leading to instability of the folded form if they are not reformed when the protein inserts into the membrane. Acceptable secondary structures are:

β-barrel

α-helix

* Usually, the secondary structures are **amphipathic**, displaying a non-polar face to the lipids and a polar face to the interior of the protein. The polar groups in the interior are responsible for function.



**Energetics of Membrane Insertion:** Non-polar side chain must provide sufficient energy to overcome the unfavorable energy of +1 kcal/mol that is required to bury polar mainchain atoms in the non-polar environment.

The *overall* transfer energy for glycine is +1.0, alanine +0.5, and valine -0.6 kcal/mol-residue.

**Biological Membranes –** *Fluid mosaic model.*

**Peripheral Membrane Proteins:**

* Often involved in electron transport and, as specific binding proteins, e.g. sugar transport in bacteria.

**Integral Membrane Proteins:**

1. Transport (*e.g.* of protons, metabolites, electrons)

a. Passive transport (no energy required, molecules spontaneously go from high concentration to low)

b.Active transport (energy required, molecules are pushed from low to high concentration.)

2. Signal transduction.

3. Enzymes.



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| **Bacteriorhodopsin** | **K+ Channel:** |
| **br**Light activated proton-pump: converts light to energy! | **k-channel** |

**Osmotic Effects;**

* A concentration difference across a membrane represents a system that is not at equilibrium.
* ****Water will flow across the membrane to establish equal concentration on both sides of the membrane.
* Flow of water through the lipid bilayer is slow.
* Presence of **aquaporin** (water channel) increases the rate at which equilibrium is reached.
* Ions will not flow across the membrane, unless a channel is present.

**Hypertonic solution**: The concentration of salt is higher outside the cell than inside the cell.

**Isotonic solution:** The concentration of salt is the same inside and outside the cell.

**Hypotonic solution:** The concentration of salt is lower outside the cell than inside the cell.