# Membrane Structure

## Adrika Chaudhuri

The plasma membrane encloses the cell, defines its boundaries, and maintains the essential differences between the cytosol and the extraellular environment. The same goes for all other biological membranes inside the cell, which keep the environment inside the organelles separate from the outside. All these bio membranes have a very specific structure:

- a thin film of protein and lipid molecules held together by non-covalent bonds

### The lipid bilayer

- visible through **electron microscopy**
- 50% lipids, 50% proteins
- self-assembles into bilayers
- fluid

**Components of Bilayer lipids**:

- $10^9$ lipid molecules in cell membrane
- amphiphilic - hydrophilic head and hydrophobic tail
- most abundant - phospholipids (polar head group and two hydrophobic tails)

Talking about **phospholipids**, we have the following information:

- most abundant membrane lipids
- one saturated tail, and one unsaturated
- phosphoglycerides are the main ones - with a glycerol backbone. Two long chain fatty acids linked to adjacent carbon atoms through ester bonds, while third carbon is linked through phosphate group, that is linked to different polar head groups(phosphatidylethanolamine, phosphatidylserine, phosphatidylcholine)
- sphingomyeline is another main one - built from sphingosine(long acyl chain with amino and 2 hydroxyl groups). Fatty acid tail is added to amino group, and phosphocholine to OH - leaving one OH free. This OH can from hydrogen bonds with the head group of a neighbouring membrane lipid, water molecule, or membrane protein.

Here is a picture of a phosphoglyceride for reference.

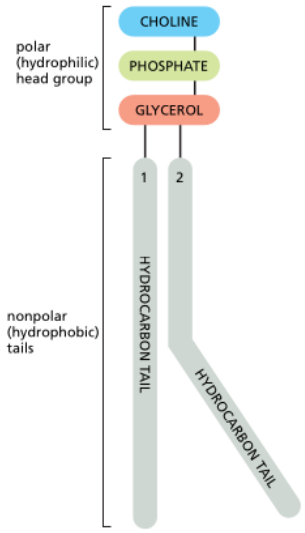


Figure 1: The parts of a phosphoglyceride molecule

And this is a sphingomyeline molecule.

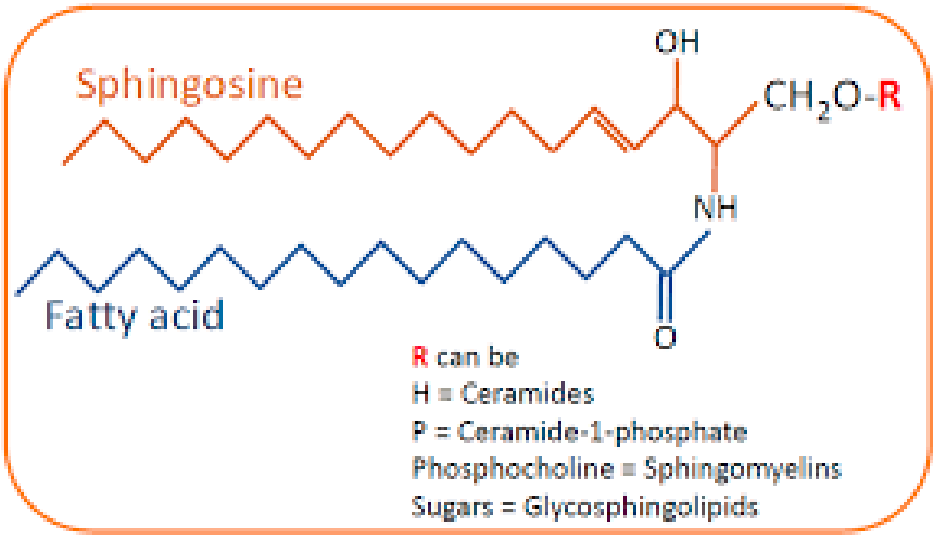


Figure 2: The parts of a sphingomyeline molecule

- also contains cholesterol and glycolipids, especially in eukaryotic plasma membrane. cholesterol has an OH group, which it orients close to the polar head groups of adjacent phospholipids.

**Spontaneous Bilayer formation**

- Depending on shape, it can be bilayer or micelle. Bilayer if lipid is cylindrical(like phospholipid) or micelle if cone-shaped.
- Why the clustering?

To minimise free energy cost. If dispersed in water, the hydrophobic parts of these molecules cannot bond favourably with water because of the non-polarity. They force the water o reorganise into ice-like cages which increases order and free energy. To reduce the no. of water molecules impacted, they cluster together into bilayers or micelles.

- How and why do they self-heal?

A small tear in the bilayer creates free edge with water, which is energetically unfavourable. **Must be eliminated**. The only way to do this for a bilayer is to close in on itself and form a sealed compartment. For larger tears, repair is done by fusion of intracellular vesicles.

**Fluidity**

**Individual lipid molecules can diffuse freely within bilayers.**

- learnt from study of synthetic membranes - either spherical vesicles called liposomes, or planar bilayers called black membranes
- How do we track indicidual lipid molecules?
  1. Tagging with fluorescent dye or gold particle attached to polar head group
  2. spin label on head group , which carries unpaired electron detectable through Electron Spin Resonance
- Flip-flop motion: Rare migration of a molecule from one leaflet to another, occuring less than a month for a phospholipid molecule, but very frequently for something like cholesterol.
- Rapid lateral diffusion within a leaflet
- Very rapid rotation about long axis

**Why are flip-flop movements rare?**
Flip-flop movement of membrane lipids does not occur spontaneously; in the case of phospholipids, the polar portion of the molecule does not penetrate easily through the hydrophobic zone of the double layer. For this reason, the change from one leaflet to the other must be catalyzed by enzymes.

| |
|---|
| Phospholipid molecules are only synthesised in the cytosolic membrane of the ER membrane. If none of these newly made molecules could migrate reasonably promptly to the noncytosolic monolayer, new lipid bilayer could not be made. The problem is solved by a special class of transmembrane enzymes called phos- pholipid translocators, which catalyze the rapid flip-flop of phospholipids from one monolayer to the other. |

• Flippases move phospholipids from the outer leaflet to the inner leaflet. In order to maintain the charge gradient across the membrane, flippases predominantly transport phosphatidylserine and to a lesser extent phosphatidylethanolamine. (ATP-dependent process) • Scramblases: exchange phospholipids between the two leaflets in a calcium activated, via an ATP-independent process

- The functional capability of lipid bilayer depends on its fluidity. Fluidity depends on composition and temperature.
- Phase transition - A synthetic bilayer made from a single type of phospholipid changes from liquid state to a gel state at a characteristic freezing point.
- How does fluidity depend on tail structure?

The temperature at which phase transition occurs is lower if the hydrocarbon chains are shorter or have double bonds.A shorter chain length reduces the tendency of the hydrocarbon tails to interact with one another, in both the same and opposite monolayer, and cis-double bonds produce kinks in the hydrocarbon chains that make them more difficult to pack together, so that the membrane remains fluid at lower temperatures. As the temperature falls, for instance, the cells of cold-blooded organisms synthesize fatty acids with more cis-double bonds, and they avoid the decrease in bilayer fluidity that would otherwise result from the temperature drop.

- Cholesterol modulates fluidity of membranes. When mixed with phospholipids, it enhances the permeability-barrier properties of the lipid bilayer. It inserts into the bilayer with its hydroxyl group close to the polar head groups of the phospholipids, so that its rigid, platelike steroid rings interact with—and partly immobilize—those regions of the hydrocarbon chains closest

to the polar head groups. By decreasing the mobility of the first few CH2 groups of the hydrocarbon chains of the phospholipid molecules, cholesterol makes the lipid bilayer less deformable in this region and thereby decreases the permeability of the bilayer to small water-soluble molecules. Although cholesterol tightens the packing of the lipids in a bilayer, it does not make membranes any less fluid. At the high concentrations found in most eucaryotic plasma membranes, cholesterol also prevents the hydrocarbon chains from coming together and crystallizing.

Here is a reference.

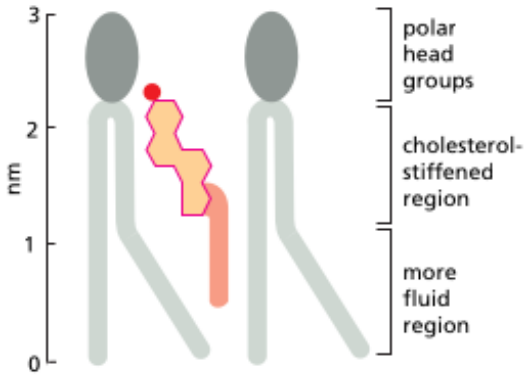


Figure 3: Cholesterol modulating membrane fluidity

**Lipid Rafts**

- Van der Waals forces between neighbouring hydrocarbon tails are not selective enough to hold groups of phospholipids together.
- However, with certain lipid mixtures, like **phosphatidylcholine, sphingomyeline, cholesterol**, the van der Waals forces between the long and saturated hydrocarbon chains of the sphingomyeline molecules can be strong enough to hold the adjacent molecules together, transiently.
- These transient domains are called lipid rafts, and are stabilised by specialised proteins that accumulate there.
- hydrocarbon chains of sphingolipids are longer and straighter, hence lipid rafts are **thicker** than the surrounding membrane domains - better accommodating certain membrane proteins.
- Mutually stabilising, lipid rafts help organise membrane proteins, concentrating them for transport in membrane vesicles or working together in protein assemblies.

**Lipid Droplets**

- Excess of lipids are stored in lipid Droplets
- Lipid droplets store neutral lipids like triacylglycerides, and cholesterol - made in the ER membrane
- Stored as droplets instead of bilayers- because they are predominantly hydrophobic
- Similarly, they do not need bilayer membranes, simple monolayer of phospholipids suffice
- the shape of LDs is almost always spherical, which minimizes the interface between the hydrophobic lipid esters and the aqueous cytosol
- a repository for the building blocks for biological membranes, such as phospholipids and sterols. When needed, these lipids can be generated from catabolism and mobilization of lipids in LD
- By compartmentalizing lipids, LDs buffer cells from the toxic effects of excessive amounts of lipid
- form from the endoplasmic reticulum membrane where many enzymes of lipid metabolism are localized.

Here is a reference.

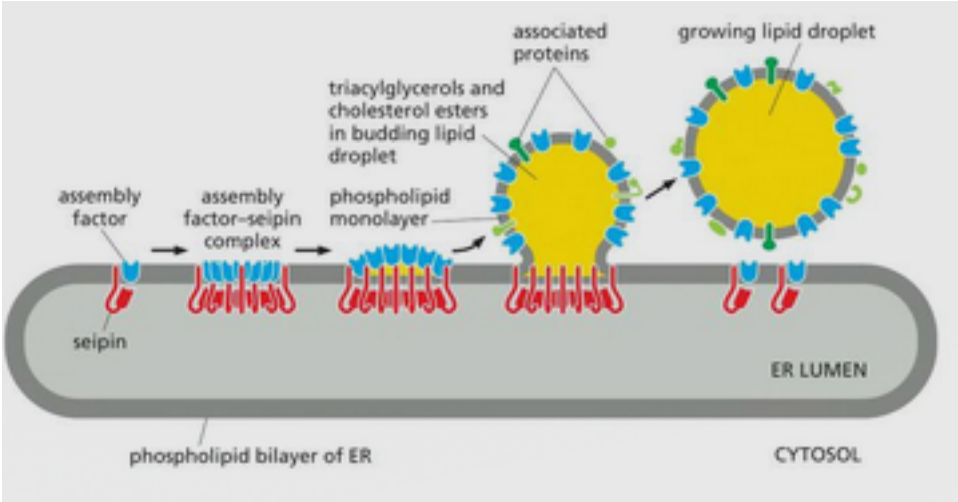


Figure 4: Budding of Lipid Droplets

**Asymmetry of Lipid Bilayer**

- lipid composition of two leaflets significantly different
- all choline containing phospholipids in outer layer, all with tertiary primary amino group in inner layer
- asymmetry important for converting extracellular signals into intracellular ones
- specific head groups might be modified to create protein-binding sites at a particular time and space, e.g., phosphatidylinositol
- phosphatidylserine, which is normally confined to the cytosolic (or inner) monolayer of the plasma membrane lipid bilayer, rapidly translocates to the extracellular (or outer) monolayer when cells are dead - signals to macrophages to phagocytose dead cells

**Glycolipids**

- mostly found on outer leaflet
- self-associate into lipid rafts
- asymmetric distribution of glycolipids in the bilayer results from the addition of sugar groups to the lipid molecules in the lumen of the Golgi apparatus.
- the gangliosides, contain oligosaccharides with one or more sialic acid moieties, which give gangliosides a net negative charge
- glycolipids are confined to the exposed apical surface, where they may help to protect the membrane against the harsh conditions frequently found there (such as low pH and high concentrations of degradative enzymes)
- Charged glycolipids, such as gangliosides, may be important because of their electrical effects: their presence alters the electrical field across the membrane and the concentrations of ions—especially $Ca^{2+}$ —at the membrane surface