Lipids and Membrane structure

I. Membrane structure
Membranes are composed primarily of proteins and lipids. There are several types of lipids: phospholipids, cholesterol and glycolipids. As shown in V&V p. 280, Fig. 11-3, most phospholipids are composed of a glycerol backbone on which carbons 1 and 2 are esterified with fatty acids. Fatty acids have the general structure:

\[ \text{CH}_3(\text{CH}_2)_n\text{COOH} \]

in which \( n \) is always an even number due to the fact that the chains are formed by the sequential addition of acetate, which has 2 C’s. The total number of C’s in the chain, that is, \( n + 2 \), is usually 14 to 24.

A. Types of phospholipid head groups
Phosphatidic acid itself is rare in membranes; in most cases the phosphate group is also esterified by a second group (in addition to the glycerol backbone). These head groups are listed below (see V&V p. 281 Fig. 11-2 for structures of the complete phospholipids for each group, as well as for inositol).

- **choline**: a quaternary ammonium; phosphatidylcholine or PC is a zwitterion (has a negative and a positive charge and is neutral overall)

- **ethanolamine**: -----> phosphatidylethanolamine or PE, also neutral

- **serine**: -----> phosphatidylserine or PS, net negative charge

- **glycerol**: (a second molecule of glycerol attached to the P) phosphatidylglycerol, net negative

- **inositol**: a sugar ring of 6 carbons, with OH groups which can also be phosphorylated - phosphatidylinositol or PI, net negative

In addition, one type of phospholipid has a backbone of sphingosine rather than glycerol. The full compound discussed is called sphingomyelin or SM, has a choline group attached, and is a neutral zwitterion (see V&V p. 282, Fig. 11-6).

B. Chain length and melting point
The length of fatty acid chains ranges from 14-24 carbons. Comparing the melting temperature of fatty acids of different lengths reveals that as the chains get longer, the melting temperature gets higher. (V&V p. 278 Table 11-1). This can be understood by remembering that the more van der Waals interactions there are between molecules, the more strongly they’re held together; since two long chains have more surface area with which to interact, the interchain bonds are stronger for two long chains and thus a higher temperature is required to pull them apart, that is, to melt them.
C. Saturation  In addition to length, the degree of saturation on the hydrocarbon chain of a fatty acid also affects its melting point. While R1, the fatty acid chain on C1, is almost always saturated (that is, has no double bonds), R2 chains are often unsaturated (have one or more double bonds, usually cis). Unsaturation lowers the melting point of a fatty acid. As can be seen in V&V p. 281 Fig. 11-4, a double bond causes a kink in the chain, and, as a result, the chains can’t pack together as well and are thus easier to pull apart at a lower temperature.

II. Fatty Acid Behaviour
Fatty acid behavior in an aqueous environment arises from the fact that fatty acids have a long nonpolar hydrocarbon tail and a negatively charged head.

D. Phospholipid monolayer  If phospholipids were injected very close to the surface of a tray of water, an interesting phenomenon is observed. It forms a monolayer at the surface so that its polar side is in water and the nonpolar side sticks up into the nonpolar air (illustrated in V&V p. 285 Fig. 11-10). This behaviour allows us to measure the surface area occupied by a monolayer, and therefore confirm the packing differences between phospholipids with saturated and unsaturated chains.

In the experimental set-up shown below, a spring balance which measures surface pressure to its right and its left is positioned in a tray of water. A defined amount of phospholipids (PL) are added to the right of it and the surface area over which the PL spread is controlled by moving the bar on the right. The surface tension of the water goes down in the presence of PL.

When the surface pressure is plotted against the surface area occupied by the lipids, the graph contains a long linear region. This region corresponds to the formation of a lipid monolayer. If this line is extrapolated to the x-axis, the intersection represents the surface area occupied by the monolayer. Since you know how many lipid molecules you put into the tray, the surface area per lipid molecule can be calculated. For a phospholipid with saturated chains (18.0, 18.0, meaning two 18-carbon chains with no unsaturated bonds), this value is approximately 48 Å²/molecule. For a lipid with 18.0, 18.1, which has one saturated chain and one chain with one unsaturated bond, the surface area is 75Å²/molecule.
Thus, as suggested by the melting point data, saturated phospholipids pack more tightly than unsaturated ones.

**E. Micelles** When fatty acids are placed in water at a high enough concentration, they often form micelles with the negative heads facing outwards and the hydrocarbon tails clustered inside away from the water (V&V p. 285 Fig. 11-11). This is especially true for single-tailed lipids, since they have a roughly triangular shape (wide heads and thin tails) which allows them to fit together in a circle like pieces of pie. On the other hand, phospholipids with two fatty acid chains, often including one unsaturated chain, are closer to rectangles in geometry and can only line up side by side.

**F. Phospholipid bilayer** Another, more physiologically relevant, way to hide the nonpolar side of a monolayer from water is to match it up with the nonpolar side of another monolayer, thus forming a bilayer (see V&V p. 286 Fig. 11-13). Although bilayers are nearly flat, they have enough curvature to form the surface of a cell or vesicle, and indeed the plasma membrane is formed from such a bilayer.

**G. Dimensions** The diameter of a lipid bilayer (the distance between the tips of corresponding heads on opposite layers) is about 5 nm, of which the central hydrocarbon tails constitute 3 nm.

**H. Fluidity** The internal hydrocarbon region of a bilayer is viscous, similar to oil, and the more unsaturated the fatty acid tails are the more fluid the region becomes; that is, as the tails pack less efficiently, they allow easier diffusion. Fluidity can also be measured by tagging a phospholipid molecule and measuring its lateral translation along the monolayer. This experiment shows that the diffusion coefficient (D) is about $10^{-6}$ cm²/s. This is calculated by $D = \frac{x^2}{4t}$, where $x$ is the distance travelled, and $t$ is time. The velocity of lateral diffusion (in one dimension), $v$, is about 2µm/s.

**G. Bilayer assymmetry** We’ve seen that phospholipid molecules move around within a monolayer, but do they ever flip from one monolayer to the other? Studies in
artificial bilayers suggest that they do not (or only extremely rarely). This makes sense when you consider the unfavorability of passing the polar head groups through hydrophobic interior of the membrane. Studies of red blood cell (RBC) membranes have shown that during their 128 days of existence they never lose their asymmetric arrangement. PS (which has a net negative charge) and PE stay on the inner leaflet of the RBC bilayer (the monolayer on the cytoplasmic side of the bilayer), while PC and SM remain on the outer leaflet. This observation, in conjunction with the lack of observable flipping in artificial membranes, suggests that RBC membranes are synthesized asymmetrically. How asymmetry arises is a complicated issue that must involve proteins which can flip phospholipids directionally from one leaflet to another. This is a good problem to puzzle over!