Lecture #9

Lipid Bilayer Membranes

One of the critical features of cells is that they are separated from the surrounding environment by a barrier that allows them to preserve their identity, take up food and give off waste. For eukaryotic cells the barrier is typically a plasma membrane that has glycoproteins and a lipid bilayer that is 5 nm thick. The lipid bilayer forms the permeability barrier and glycoproteins are responsible for regulating the traffic of material to and from the cytoplasmic space. We will talk about the important physical features of the plasma membrane.

Hydrophobic Effect and the Bilayer Phase

The physical basis of the lipid bilayer membrane is the hydrophobic effect, i.e. the inability of hydrocarbons to hydrogen bond with water. At the interface between hydrocarbon and water, there is a higher energy state for the water because hydrogen bonds are lost. It is energetically favorable for the hydrocarbon to associate with hydrocarbon and to minimize the surface area of contact with water. Amphiphilic compounds such as fatty acids have hydrocarbon regions and hydrophilic regions. Fatty acids can stabilize hydrocarbon in water by covering the hydrocarbon surface with their hydrophilic regions while their hydrocarbon regions associate with hydrocarbons, i.e. like associates with like. When fatty acids (soaps) are suspended in water, they form micelles, spherical complexes of tens to hundreds of fatty acid molecules with hydrocarbon on the inside and carboxylic acid groups on the outside. The size of the micelle and its shape are determined in part by the relative surface area occupied by the hydrocarbon and hydrophilic portions of the molecules. When the hydrophobic portion is much smaller in area than the hydrophilic, micelles tend to be small with a high curvature. When the two portions are approximately equal, micelles are much larger and have reduced curvature. In terms of free energy, the mixing of hydrocarbon and water causes a decrease in entropy (another way of saying this is that the entropy of water is decreased at the interface between hydrocarbon and water). A practical consequence is that hydrophobic interactions are stronger at high temperatures than low (we will talk about this again when we discuss microtubule assembly).

To create a hydrophobic barrier around cells, nature has developed phospholipids, which have nearly equal areas of their hydrophobic and hydrophilic portions. Phospholipids typically have two fatty acid chains esterified to a glycerol backbone and on the third glycerol hydroxyl there is a phosphate group which is derivatized with a hydrophilic moiety such as ethanolamine, choline, inositol or serine. Bilayers are two dimensional complexes of lipids with their phosphate groups at the water-bilayer interface and fatty acids internal.

As a rule of thumb, molecules with a fatty acid chain of 4 carbons or less can have reasonable solubility in water. Above 8 carbons, molecules bind strongly to a membrane or proteins with hydrophobic pockets (transport proteins that carry either phospholipids or fatty acids through cytoplasm have been identified). Energy of binding increases (~1.2 kcal/mol for each carbon) and the force needed to pull a phospholipid from the membrane is only about 10 pN.

Physical Properties of Biological Membranes

Thickness	5 nm
Area per Lipid molecule	0.5 nm^2
Lipid Fluidity	Fluid but high viscosity (100 X water, about 1 Poise)
Diffusion coefficient	10^{-8} lipid to 10^{-14} cm^2/sec for some proteins
Stretch (elastic modulus)	very little (4% at lysis, tension of 10 mN/m)
Asymmetry in vivo	Plasma membrane asymmetric (Outside PC and Sphingomyelin; Inside PE, PS and PI, PIP, PIP2)
Bending Stiffness	2×10^{-19} Nm
Shear modulus	very low
Membrane Dynamics	Endocytosis of an area = plasma membrane/hr.

Bending Stiffness of Membranes

A major factor in the shaping of membranes is the bending stiffness of the bilayer. Erythrocytes assume a biconcave disc shape because it is the lowest bending energy shape for the surface area to volume ratio of the erythrocyte. If we have a flat membrane and we form a tether by pulling vertically on the membrane, then the change in energy of the membrane (dE) is

$$dE = (B/2)(1/R_t)^2 dA \qquad (14)$$

where B is membrane bending stiffness (measured values range from 1.6 to 2.7 x 10^{-19} Nm and we will assume a value of 2 x 10^{-19} Nm), R_t is the radius of the curved membrane, and dA is the area of the membrane that is moved from the flat region to the curved region.

Fluid Shear Resistance

The lipid bilayer components of biological membranes are fluid; therefore, there is no shear elasticity of the bilayer, only viscous resistance to shear. Membrane proteins associated with the bilayer often form an extensive network that has elastic deformation properties on the time scale of seconds. However, when deformations are held for minutes, the cytoskeleton dynamics results in an accommodation to the new shape. In the deformation of cells the lipid is normally a passive component, which flows around moving proteins.

Membrane Diffusion

The combination of the relatively slow diffusion rates of membrane proteins and rapid exchange of membranes, means that regional differences in protein concentration can be easily created in membranes.

Problems:

1. If the bilayer has an elastic modulus of 10 mN/m for dA/A = 0.04 and we assume that half of the bilayer has half of that elastic modulus, then the addition of an amphiphilic compound that expands one half of the bilayer by 0.5% will cause an expansive tension in the other half of the bilayer of ___?

2. In the video, we observed that a tube of membrane could go to several beads on a string. If we consider only bending stiffness of the membrane (2 x 10^{-19} Nm), then which is the lower energy configuration, a tube of constant diameter (0.2 microns) or a combination of a sphere and a tube of smaller diameter (overall length is 10 microns, i.e. 6.28 microns squared of membrane). (a partial proof is fine using the formula (14) above to calculate the energy needed to form a couple different spheres and tubes from a flat bilayer)

3. A membrane protein has a diffusion coefficient of 10^{-10} cm^2/sec and yet it travels 1.5 microns in 25 sec toward the leading edge. What is the probability that the protein would move in this way from a simple consideration of one-dimensional diffusion (remember the Gaussian (Normal) distribution curve)?