BE.342/442 Tuesday, November 1, 2005
Topic: Lipids as Building Materials

We've discussed amino acids as building blocks of protein-based materials and nucleic acids as building blocks of DNA-based materials. Today we'll discuss lipids as building blocks of membranes. Next, we'll discuss sugars as building blocks of cellulose, starch, and other materials.

Cell Membranes

Membranes are ubiquitous in living systems and absolutely crucial to establish an isolated environment and entity. Individual lipid molecules are ~2 nm in size and cannot form covalently linked polymers, but they are able to form very stable and ordered assemblies. In solution, lipids self-assemble into micelles, vesicles, nano- and micro-tubules, liposomes, organized tubular clusters, and reverse micelles. These self-assembled structures can then be functionalized, metalized, and modified for a number of applications.

Membranes are present both around the cell and around organelles such as the nucleus, endosomes, mitochondria, the Golgi apparatus, the endoplasmic reticulum, and others. Biological membranes contain bilayers of lipids, with the polar heads facing the solution on the inner and outer side of the membrane, and the hydrophobic tails aggregated on the inside. Six cells contain a mole (Avogadro's number) of lipids! Proteins can be fully or partially embedded in the membrane. The outside surface of cell membranes is typically rich in glycoproteins, which present sugar groups on the surface of the cell to identify its phenotype (for example, blood types). The inside surface is typically rich in lipoproteins, or proteins are linked to hydrophobic tails, which anchor them to the cell membrane. Other important membrane proteins include the elements of cellular respiration, which pump protons across the membrane and use the concentration gradient to synthesize ATP, flagellum motors that rotate flagella for mobility, and a variety of proteins for signal transduction.

(Review of figures from our textbook illustrating signal transduction mechanisms, energy photosystems, and membranes for neurons, cell bodies, axons, and dendtrites.)

Multilayered membranes called "myelin sheaths" around Schwann cells protect neurons such as those in the spinal cord, insulating them for bioelectrical activity. Breaking this protective layer can result in crippling injury to the nervous system. Myelin is now being explored for applications in liquid crystal materials.

Aquaporin, a water-transport membrane protein, can transport 400 million water molecules per second across a lipid bilayer! IBM now dedicates entire computational projects to modeling of lipids, so complex is their dynamics.

Compositions of some purified membranes:

Membrane	% Protein	% Lipid	% Carbohydrate
Myelin	18	79	3
Plasma membrane: human erythrocyte (blood cell)	49	43	8
Plasma membrane: Mouse liver	44	52	4
Plasma membrane: Amoeba	54	42	4
Chloroplast spinach lamellae	70	30	0
Halobacterium purple membrane	75	25	0
Mitochondrial inner membrane	76	24	0
Source: G. Guidotti, 1972, *Ann. Rev. Biochem.* 41:731.			

Lipids include a polar head group and some number of long carbohydrate chains. Fluidity of lipids depends on saturation. The more double bonds are present in a lipid, the lower its melting point. In a membrane, saturated lipids have a gel-like consistency, whereas unsaturated lipids have a fluid-like consistency. Additionally, lipids are very temperature-sensitive. An increase in temperature can give lipids a more liquid-like consistency in the membrane, and a decrease in temperature can cause a solidification of the lipid bilayer. This makes the range of temperatures that we can tolerate quite restrictive: it's not just an issue of protein denaturation. Some lipids are zwitterions: they include both a positive and a negative charge.

In the text, observe the molecular models of:

Phosphatidylcholine
Triacylglycerol
Cholesterol
Palmitate
Oleate (ionized form of oleic acid)
plasma membrane (Figure 14-7)

Membrane proteins can be purified and coated with micelles to keep them in their native conformations by providing an environment of the appropriate hydrophobic and hydrophilic patterns. One-third of the human genome -- ten thousand genes! -- codes for membrane proteins, but only one structure has been determined because of the incredible challenge of crystallization of membrane proteins. Imagine how much money the pharmaceuticals could save if we could truly understand membrane proteins, rather than chasing "guesses" of drugs that could enter through membrane proteins. Likewise, solar energy harvesting through biology might replace petroleum if we knew how it worked.

Nature cover article (441:924-927) 21 June 2001, by Pascale Aussilous & David Quéré (available on the course website):
Water droplets dropped onto a hydrophobic powder become surrounded with powder and are no longer wettable. The structure is like the opposite of a lipid: hydrophobic "heads" of powder coat the droplet, allowing it to act like a "liquid marble" on the micron to millimeter scale. This "non-stick water" no longer sticks to surfaces, and rolls like a solid ball. Both water and water/glycerol balls were used. Powder materials include lycopodium grains and silica. Water forced through the powder formed doughnut shapes or peanut shapes.

Washington's Naval Research Lab studies lipid microtubules that can be coated with metals. These materials can be used as antifouling paints to prevent barnacles from sticking on the surfaces of ships. Tubules can also form vesicles for drug delivery, twisted chiral structures, and templates for metallization.

Source for chiral lipid tubules:
J.M. Schnur, B. R. Ratna, et al. "Diacetylenic Lipid Tubules: Experimental Evidence for a Chiral Molecular Architecture" Science **264** (3 May 1994) 946.

Sources for metal-coated tubules:
J.M. Schnur, *Science* **262** 1669 (1993)
J.M. Schnur, R. Price, and A. S. Rudolph, *J. Controlled Release* **28** 3 (1994)
Y.M. Lvov et al., *Langmuir* **16** 5932 (2000)

More examples of biomolecular self-assembling materials:

Bacterial membrane with a hexagonal lattice of bacteriorhodopsin tripers

Alkane thiols conjugated to lipid tails as monolayers or bilayers anchor proteins

Source: S. Heyse et al. *Biochimica et Biophysica Acta* 85507 (1998) 319-338

These molecules can bind and release proteins and orient proteins to give them the correct directional function.

Lipids can also be designed to support concentration gradients.

Finally, consider the proteins, a simpler material that may have acted in the place of lipids in the origins of life. Is it possible to design peptide-based surfactants and detergents? Find out next time!