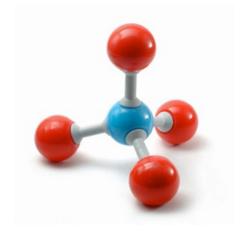


Making islands from molecules. How lipids create cell membranes.



version 1.0

© Nick DeMello, PhD. 2007-2015

Cell Membranes

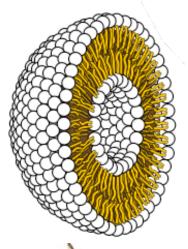


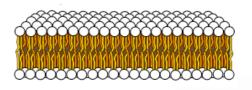
Ch15

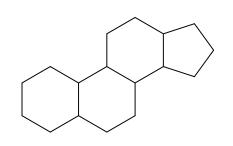
- Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin
- Steroids
 - Steroid Ring System
 - Cholesterol
 - Digestion
 - Lipoproteins
 - Hormones



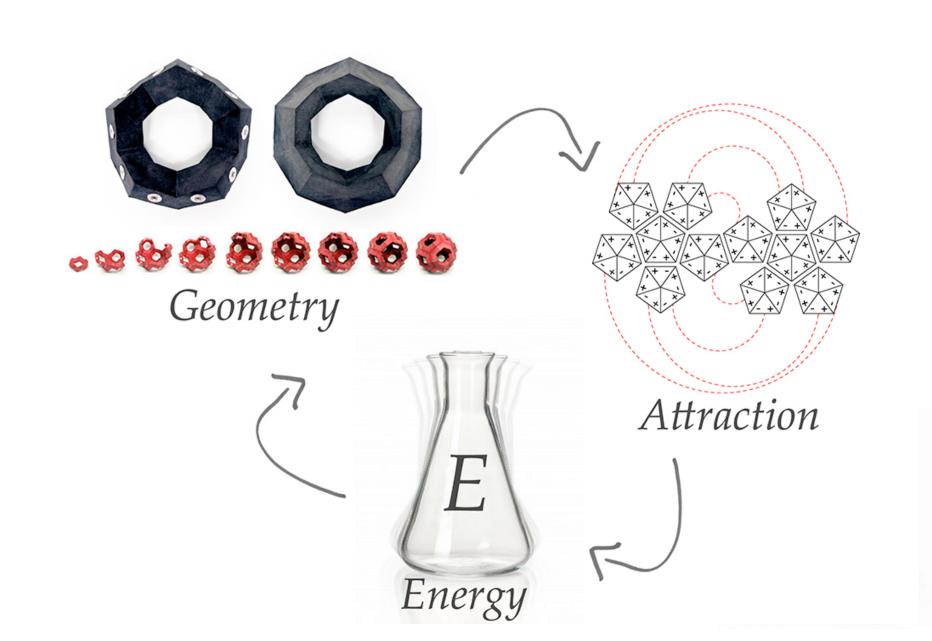
- Cell Membranes
 - Forming Membranes
 - Membrane Structure
 - Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport





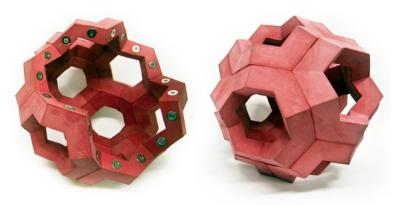


Self Assembly



Self Assembly Examples

- Self Assembling Geometry
 - http://chem.ws/selfassemble
- Aerial Assembly
 - http://chem.ws/aerial
- Self Assembling Chair
 - http://chem.ws/chair





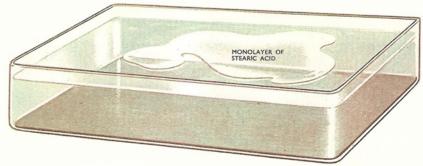
Amphiphile

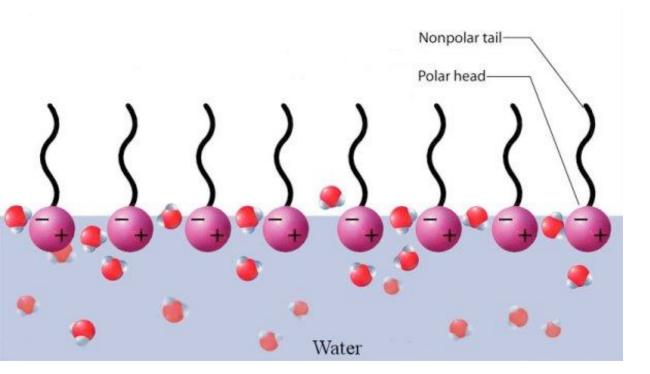
- Hydrophilicity is the property of a substance to mix with water or other polar substances.
- Lipophilicity is the property of a substance to mix with alkanes or other non-polar substances.
 - Triglycerides are lipophilic. They'll mix with non-polar substances but run away from polar ones.
 - Triglycerides are our containers for the carbon chains we need to build molecules in our bodies. Bodies that contain a lot of water.
 - Lipophilic substances tend to be hydrophobic, they run away from water.
- Biologies solution is to modify those triglycerides to give them the necessary property to live in both worlds.
- Amphiphilicity is a property of substances to have both hydrophilic (water-loving, polar) and lipophilic (fat-loving, non-polar) properties.
 - In the same molecule.
 - It's uncommon.
- Phospholipids are molecules that contain lipids (fatty acids) but have this dual nature.
- Amphilphilicity allows molecules to self assemble into complex and useful structures.

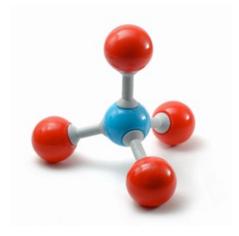


Amphiphile Behavior

- Amphiphiles form monolayers on the surface of water.
- With one end being attracted to water and the other repelled they form very ordered structures.

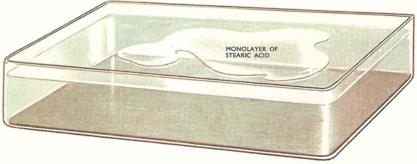






Amphiphile Behavior

- Amphiphiles form monolayers on the surface of water.
- With one end being attracted to water and the other repelled they form very ordered structures.
- It's possible to produce a layer of stearic acid on water surface that is one molecule thick.





Cell Membranes

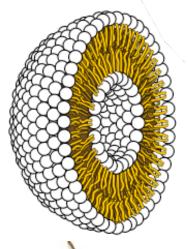
Self Assembly

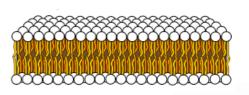
Ch15

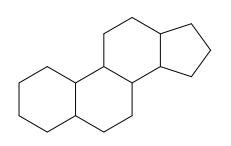
- Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin
- Steroids
 - Steroid Ring System
 - Cholesterol
 - Digestion
 - Lipoproteins
 - Hormones



- Cell Membranes
 - Forming Membranes
 - Membrane Structure
 - Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport

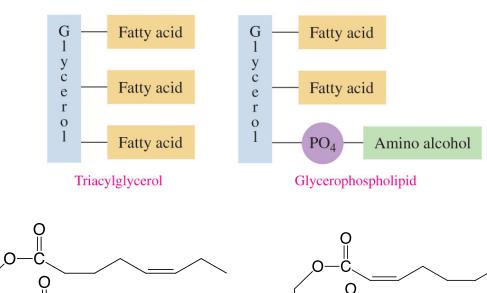






Phospholipids

- The phospholipids are a family of lipids similar in structure to triacylglycerols.
- They include glycerophospholipids and sphingomyelin.
- They incorporate an amino alcohol and a phosphate group.



Ο

Ο

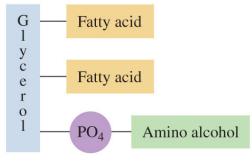
O



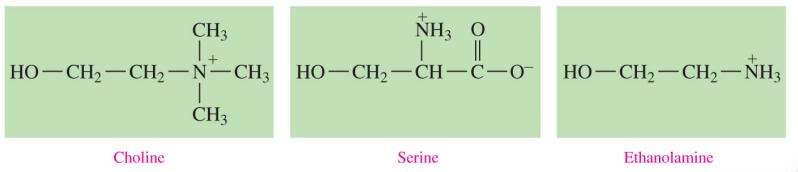
Ο

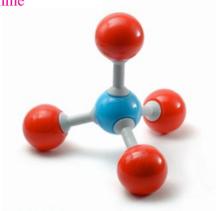
റ

- Amino alcohols found in glycerophospolipids
 - are choline, erine, and ethanolamine
 - are ionized at physiological pH of 7.4
- These amino alcohols are attached with a phosphate group.



Glycerophospholipid

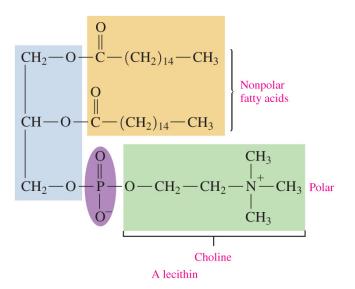


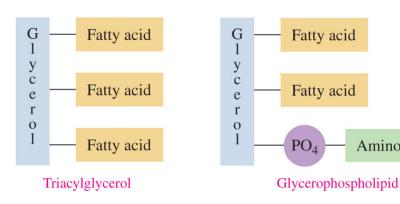


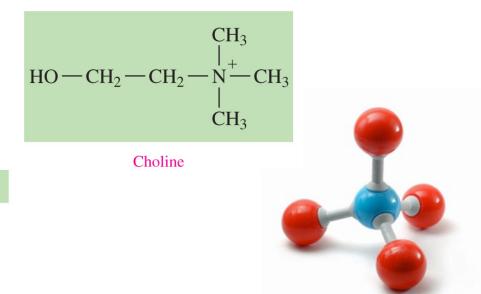
Lecithin

Amino alcohol

- Lecithin a type of glycerophospholipid
 - It's used in brain and nerve tissue.
 - It's like a triglycerol, but one of the ester bonds is replaced with phosphoester bond.
 - Phophate links an amino acohol (choline) in one of the ester "sockets"
 - The other two sockets are free to carry or utilize various fatty acids.

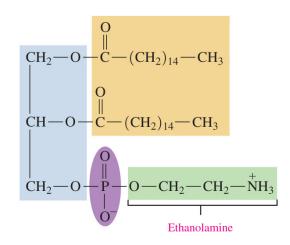




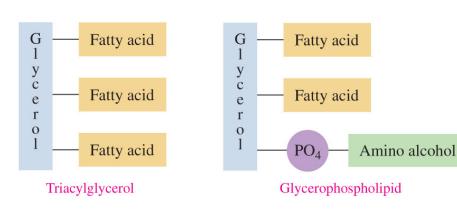


Cephalin

- Cephalin is another type of glycerophospholipid.
 - It's also used in brain and nerve tissue.
 - It's like a triglycerol, but one of the ester bonds is replaced with phosphoester bond.
 - Phophate links an amino acohol (ethanolamine) in one of the ester "sockets"
 - In brain tissue it sometimes uses serine instead.
 - The other two sockets are free to carry or utilize various fatty acids.

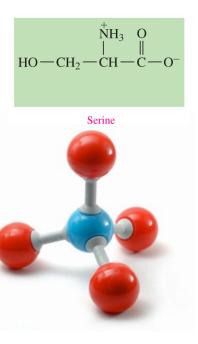


A cephalin

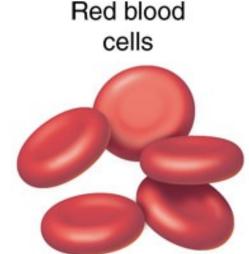


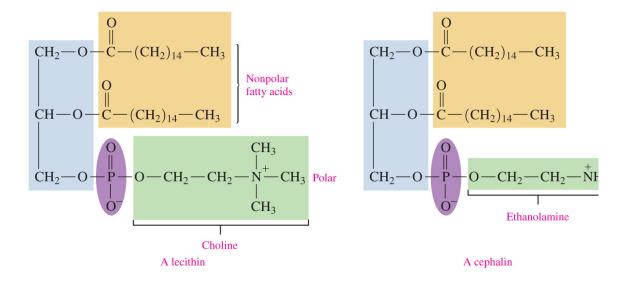
$$HO-CH_2-CH_2-NH_3$$

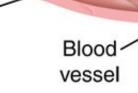
Ethanolamine



- Both lecithin and cephalin...
 - Are found in egg yolk, wheat germ, and yeast.
 - Are used to build structures, including the cell walls of red blood cel
 - Are used to build an insulating envelope that surrounds the core of a nerve fiber.
 - Called the medullary sheath of myelin sheath.
 - These glycerophospholipids facilitate the transmission of nerve impulses and long the fiber.

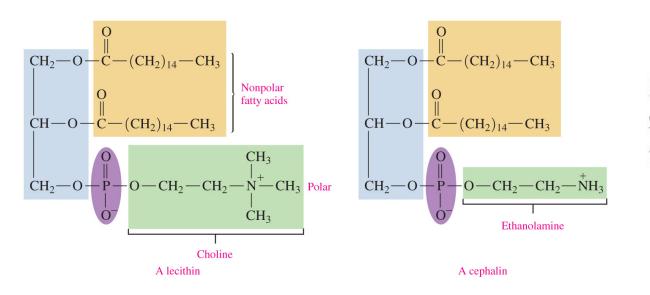


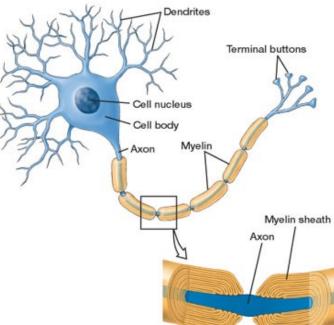




Plasma

- Both lecithin and cephalin...
 - Are found in egg yolk, wheat germ, and yeast.
 - Are used to build structures, including the cell walls of red blood cells.
 - Are used to build an insulating envelope that surrounds the core of a nerve fiber.
 - Called the medullary sheath of myelin sheath.
 - These glycerophospholipids facilitate the transmission of nerve impulses and long the fiber.



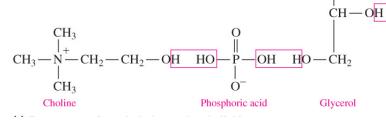


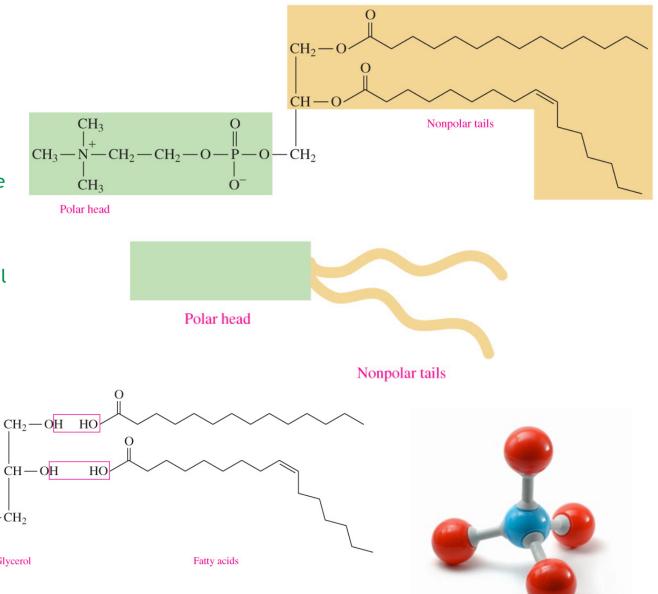
Myelin sheath

of healthy nerve

Axon

- Glycerophospholipids
 - have both polar and nonpolar regions that allow them to interact with polar and nonpolar substances
 - have a polar head containing the ionized amino alcohol and phosphate portion, which is strongly attracted to water
 - have a nonpolar hydrocarbon tail portion soluble only in nonpolar substances such as lipids
 - are the most abundant lipids in cell membranes and play an important role in cellular permeability





- Glycerophospholipids order themselves to form a bilayer.
- This bilayer forms into sheets, including the myelin sheath and cell walls.
- Ways the body segments off areas at the cellular level, provides insulation, protection or directs the flow of processes.

Nonpolar tails

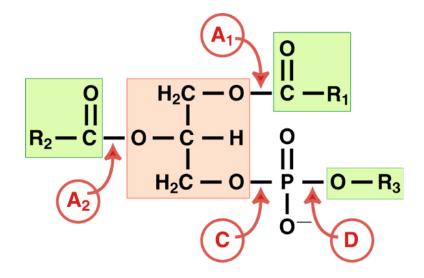


Polar head

Snake Venom

- Snake venom contains phospholipases.
- Phospholipases are enzymes that release fatty acids from the second carbon group of glycerol.
- The particular phospholipases in snake venom specifically recognizes the sn-2 acyl bond of phospholipids and catalytically hydrolyzes the bond releasing arachidonic acid and lysophospholipids.
- It breaks down glycerophospholipids and therefore all the structures built from them.
 - Including blood cells, brain matter, nerve insulation...







Snake Venom

- Snake venom contains phospholipases.
- Phospholipases are enzymes that release fatty acids from the second carbon group of glycerol.
- The particular phospholipases in snake venom specifically recognizes the sn-2 acyl bond of phospholipids and catalytically hydrolyzes the bond releasing arachidonic acid and lysophospholipids.
- It breaks down glycerophospholipids and therefore all the structures built from them.
 - Including blood cells, brain matter, nerve insulation...





Cell Membranes

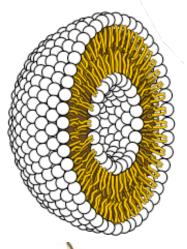
Self Assembly

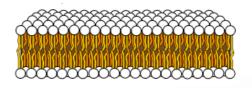
Ch15

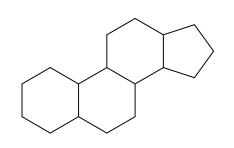
- Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin
- Steroids
 - Steroid Ring System
 - Cholesterol
 - Digestion
 - Lipoproteins
 - Hormones



- Cell Membranes
 - Forming Membranes
 - Membrane Structure
 - Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport

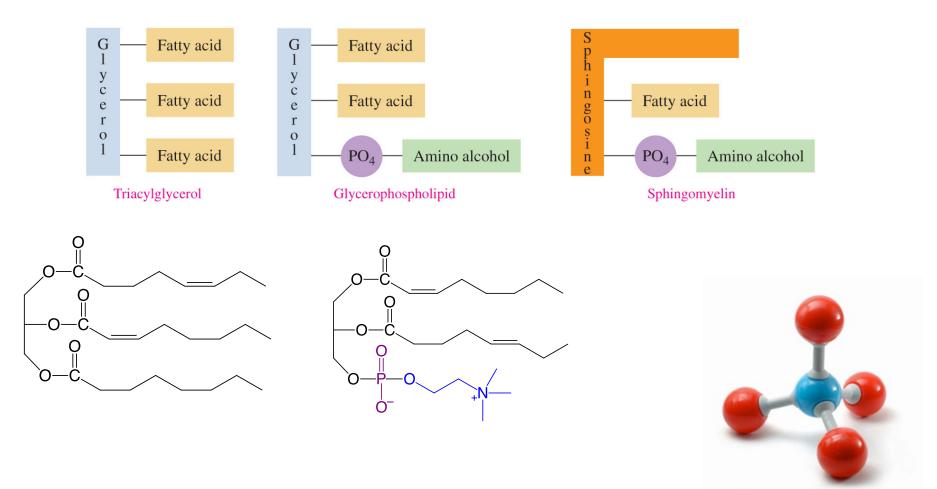






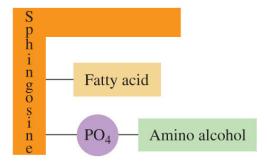
Phospholipids

- The phospholipids are a family of lipids similar in structure to triacylglycerols.
- They include glycerophospholipids and sphingomyelin.
- They incorporate an amino alcohol and a phosphate group.

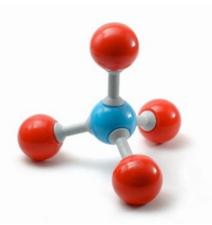


Sphingomyelin

- In a sphingomyelin,
 - the amine group of sphingosine forms an amide bond to a fatty acid
 - the hydroxyl group forms an ester bond with phosphate, which forms another phosphoester bond to choline or ethanolamine
- Sphingomyelins are abundant in the white matter of the myelin sheath.
- The make up about 20% of blood plasma membrane lipids.

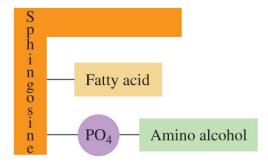


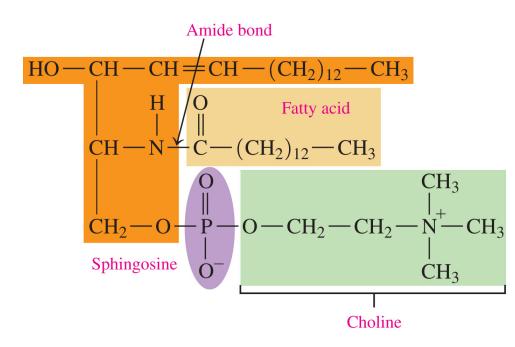
HO - CH - CH = CH -
$$(CH_2)_{12}$$
 - CH₃
 $|$
CH - NH₂
 $|$
CH₂ - OH
Sphingosine

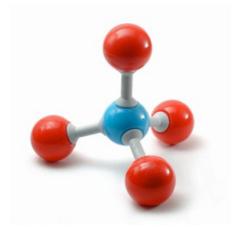


Sphingomyelin

- In a sphingomyelin,
 - the amine group of sphingosine forms an amide bond to a fatty acid
 - the hydroxyl group forms an ester bond with phosphate, which forms another phosphoester bond to choline or ethanolamine
- Sphingomyelins are abundant in the white matter of the myelin sheath.
- The make up about 20% of blood plasma membrane lipids.

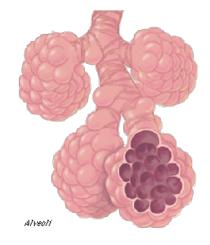






Respiratory Distress (RDS)

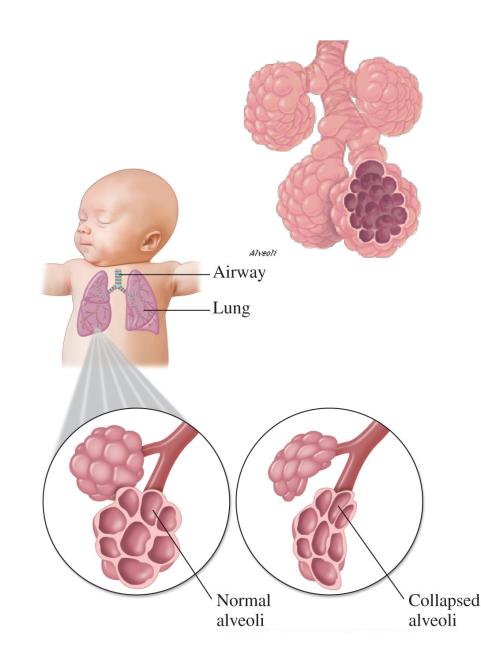
- Respiratory distress syndrome (RDS) is a breathing disorder that affects newborns. RDS rarely occurs in full-term infants.
- Lungs have air sacks, alveoli, where O₂ is taken into the body and CO₂ is released.
- These organic structures need to pull away from each other to allow air in.
- Your body promotes this by releasing a mixture phospholipids rich in sphingomyelin into the alveoli.
- The sphingomyelin coats the inside of the alveoli, the lipidophlic part binds to the inside of the lung reducing surface tension and causing the sacks to separate.
- Without enough sphingomyelin, aveoli collapse and the infant has to work harder to breath.





Respiratory Distress (RDS)

- Respiratory distress syndrome (RDS) is a breathing disorder that affects newborns. RDS rarely occurs in full-term infants.
- Lungs have air sacks, alveoli, where O₂ is taken into the body and CO₂ is released.
- These organic structures need to pull away from each other to allow air in.
- Your body promotes this by releasing a mixture phospholipids rich in sphingomyelin into the alveoli.
- The sphingomyelin coats the inside of the alveoli, the lipidophlic part binds to the inside of the lung reducing surface tension and causing the sacks to separate.
- Without enough sphingomyelin, aveoli collapse and the infant has to work harder to breath.



Cell Membranes

Self Assembly

Ch15

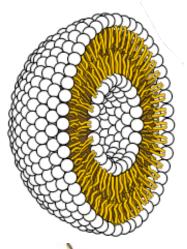
- Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin

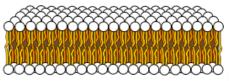
Steroids

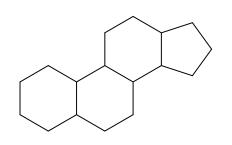
- Steroid Ring System
- Cholesterol
 - Digestion
 - Lipoproteins
 - Hormones

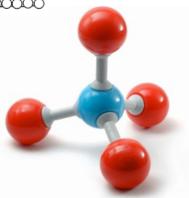


- Cell Membranes
 - Forming Membranes
 - Membrane Structure
 - Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport



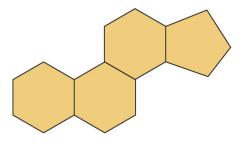


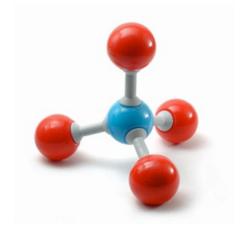




Steroids

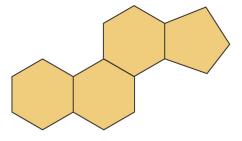
- Steroids are a family of compounds distinguished by a unique ring system.
- All steroids have a ring system of...
 - three cyclohexane rings
 - one cylopentane ring, fused together
- These rings are called the steroid nucleus.

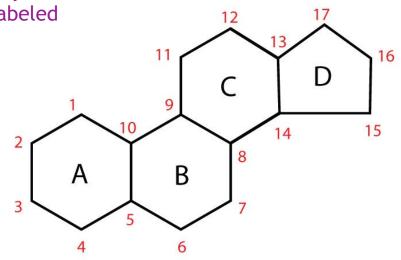


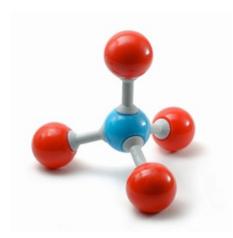


Steroids

- Steroids are a family of compounds distinguished by a unique ring system.
- All steroids have a ring system of...
 - three cyclohexane rings
 - one cylopentane ring, fused together
- These rings are called the steroid nucleus.
- Steroid
 - rings are designated as A, B, C, and D
 - carbon atoms are numbered beginning in ring A
 - two methyl groups that may be attached to carbon-10 and 13 are labeled carbons 18 and 19

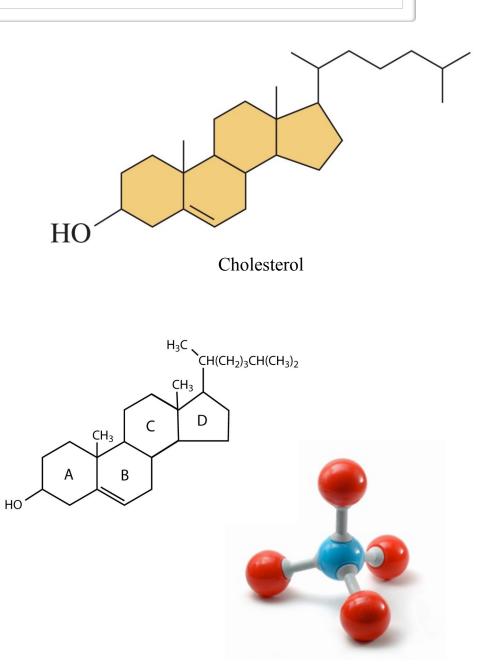






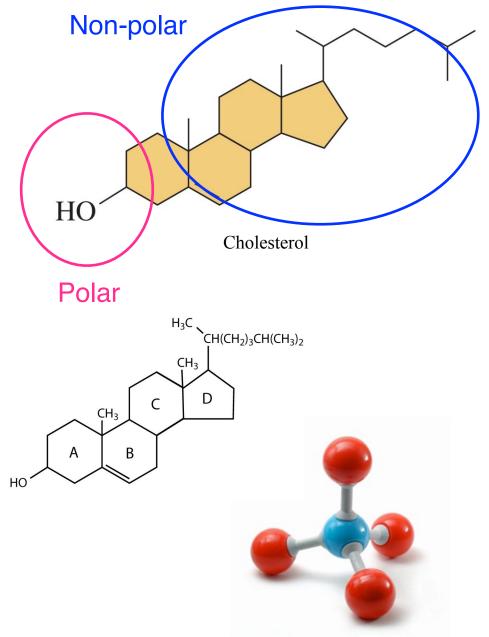
Cholesterol

- Cholesterol, from the Ancient Greek chole-(bile) and stereos (solid) followed by the chemical suffix -ol for an alcohol.
- Cholesterol
 - is the most important and abundant steroid in the body
 - ▶ has an hydroxyl group (- OH) on (carbon 3)
 - has a double bond between carbons 5 and 6
 - has methyl groups at carbons 10 and 13
 - has an alkyl chain at carbon 17
- Cholesterol is a sterol (an alcohol made from a modified steroid).
- It is made by all animal cells and is an essential structural component of all animal (not plant or bacterial) cell membranes
- It provide both membrane structural integrity and fluidity.



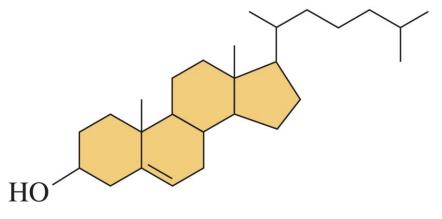
Cholesterol

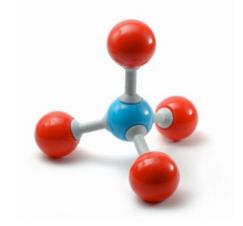
- Cholesterol, from the Greek chole- (bile) and stereos (solid) followed by the chemical suffix -ol for an alcohol.
- Cholesterol is amphiphilic.
 - ▶ It has a polar hydrophilic end.
 - ▶ It has a non-polar lipophilic end.



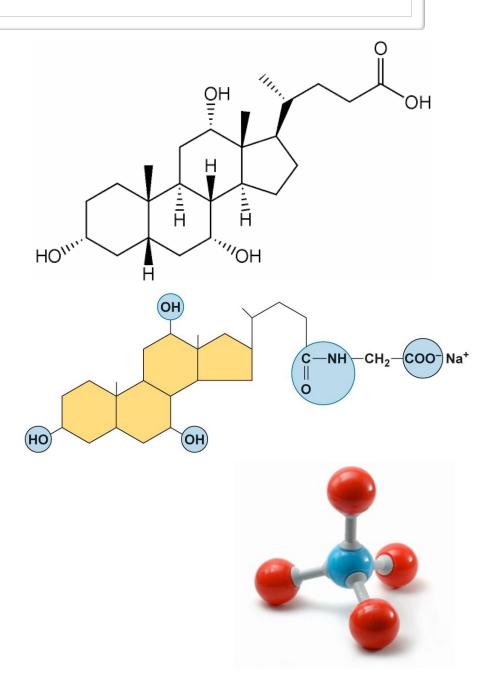
Cholesterol

- How we use cholesterol.
 - Digestion
 - Bile Salts & Micelles
 - Fatty Acid Esters
 - Lipoproteins
 - ► LDL
 - ► HDL
 - Steroid Hormones

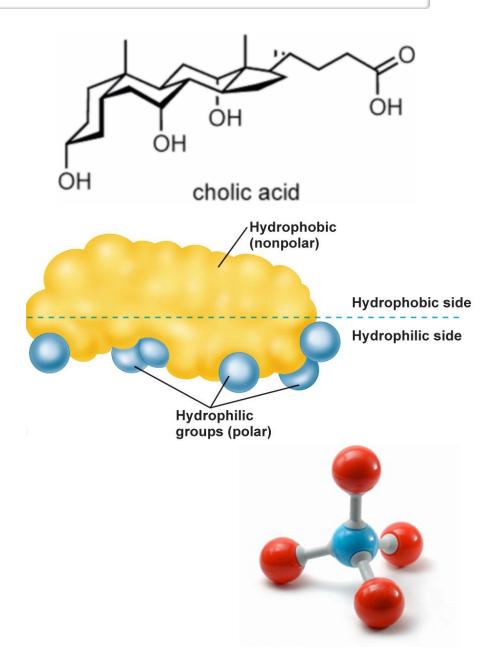




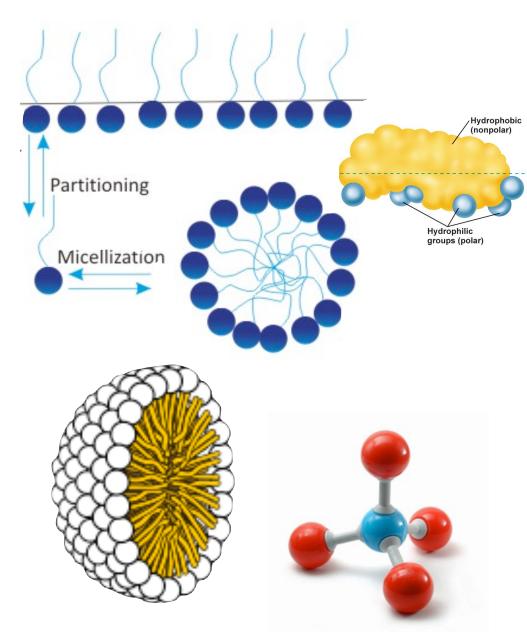
- One of the principle uses of cholesterol in the body is the production of bile acids.
- Cholic acid is the primary bile acid produced.
- Synthesis of bile acids is a major route of cholesterol metabolism in most species other than humans.
- The body produces about 800 mg of cholesterol per day and about half of that is used for bile acid synthesis producing 400-600 mg daily.
- Human adults secrete between 12-18 g of bile acids into the intestine each day, mostly after meals.
- Cholic acid is amphiphilic, it has polar and non-polar regions.



- One of the principle uses of cholesterol in the body is the production of bile acids.
- Cholic acid is the primary bile acid produced.
- Synthesis of bile acids is a major route of cholesterol metabolism in most species other than humans.
- The body produces about 800 mg of cholesterol per day and about half of that is used for bile acid synthesis producing 400-600 mg daily.
- Human adults secrete between 12-18 g of bile acids into the intestine each day, mostly after meals.
- Cholic acid is amphiphilic, it has polar and non-polar regions.

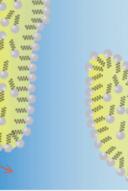


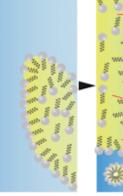
- Cholic acid assembles into a monolayer on the lipid water interface.
- As the concentration builds up, cholic acid cholesterol molecules break off and form micelles.
 - Micelles are usually made of less than 10 molecules.
 - But can form with up to 100 molecules, depending on cholic acid and fat concentrations.
 - Micellization pulls other lipids from the lipid layer into micelle as it forms.
 - This process of breaking apart and solubilizing fats is emulsification.
 - Emulsification aids digestion.
 - The emulsion droplets (micelles) are where digestion occurs.
 - Emulsification greatly increases the surface area and accessibility of the fats to the digestive process.

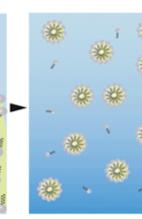


- Cholesterol assembles into a monolayer on the lipid water interface.
- As the concentration builds up, cholesterol cholesterol molecules break off and form micelles.
 - Micelles are usually made of less than 10 cholesterol molecules.
 - But can form with up to 100 molecules, depending on cholesterol and fat concentrations.
 - Micellization pulls other lipids from the lipid layer into micelle as it forms.
 - This process of breaking apart and solubilizing fats is emulsification.
 - Emulsification aids digestion.
 - The emulsion droplets (micelles) are where digestion occurs.
 - Emulsification greatly increases the surface area and accessibility of the fats to the digestive process.

Nano-droplets formed



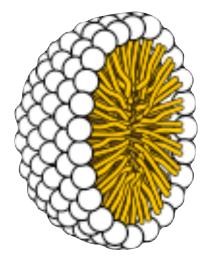


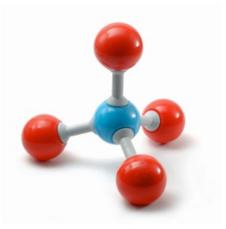


Initial System

Surfactant moves to water phase

O/W Nanoemulsion





Cell Membranes

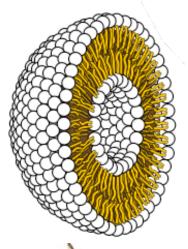
Self Assembly

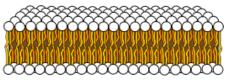
Ch15

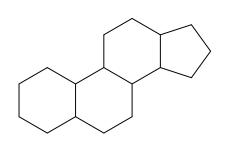
- Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin
- Steroids
 - Steroid Ring System
 - Cholesterol
 - Digestion
 - Lipoproteins
 - Hormones

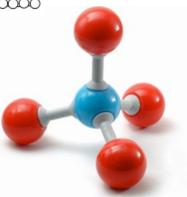


- Cell Membranes
 - Forming Membranes
 - Membrane Structure
 - Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport



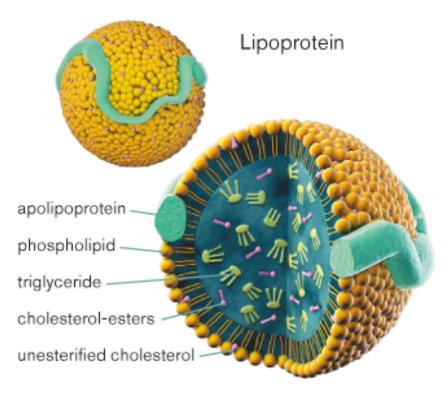


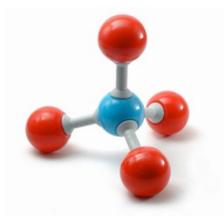




Lipoproteins

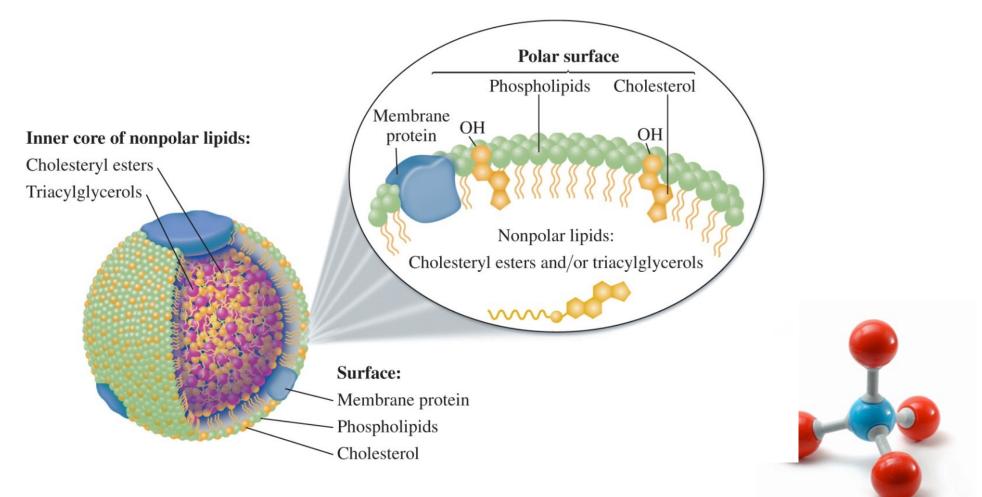
- Cholesterol and other amphiphilic lipids can form larger assemblies.
- Lipoproteins are assemblies used to transport fats in the body.
- They're made of of protein and thousands of cholesterol, triglycerides, and phospholipids.
- Lipoproteins have a single layer of phospholipid molecules on their outside, surrounding a central core.
- There are difference sizes of lipoproteins, but even the smallest can hold thousands of molecules.





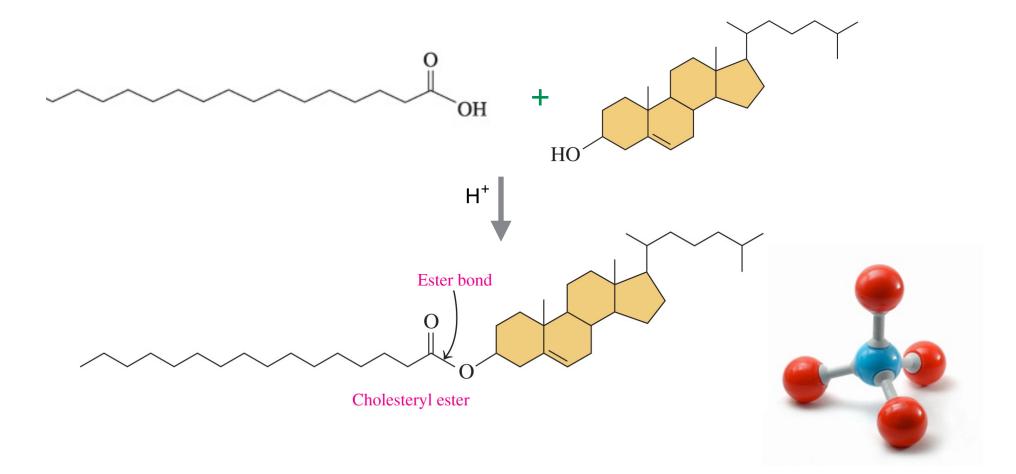
Lipoproteins

- Cholesterol in the surface of lipoproteins gives it a greater structure and rigidity.
- Cholesterol is also transported inside the lipoprotein, in the form of cholesterol esters.



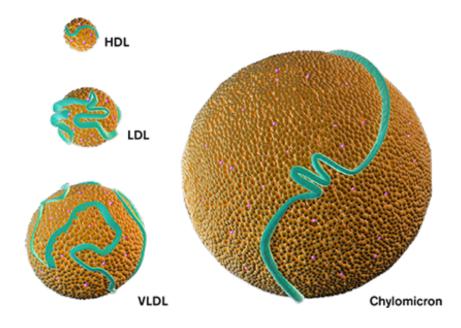
Fatty Acid-Cholesterol Esters

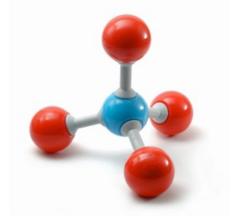
- Cholesterol can form esters with fatty acids.
- This allows both to be transported inside the non-polar centers of lipoproteins.



Lipoprotein Types

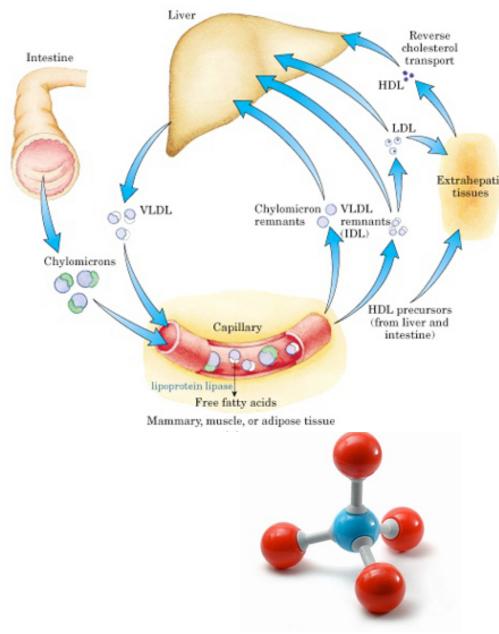
- Different types of lipoproteins have different functions.
 - Chylomicrons carry triglycerides (fat) from the intestines to the liver, muscles, and adipose tissue. (how we move stuff you eat)
 - Very-low-density lipoproteins (VLDL) carry (newly synthesised) triglycerides from the liver to adipose tissue. (how we move stuff you make)
- These lipoproteins are converted to LDL and HDL
 - Low-density lipoproteins (LDL) carry 3,000 to 6,000 fat molecules (phospholipids, cholesterol, triglycerides) to cells all over the body.
 - LDL particles are sometimes referred to as "bad" lipoprotein because they can leave behind plaque (deposited cholesterol) in your arteries.
 - High-density lipoproteins (HDL) collect fat molecules (phospholipids, cholesterol, triglycerides, etc.) from the body's cells/tissues, and take it back to the liver.
 - HDLs are sometimes referred to as "good" cholesterol because they scavenge plaque from your arteries.



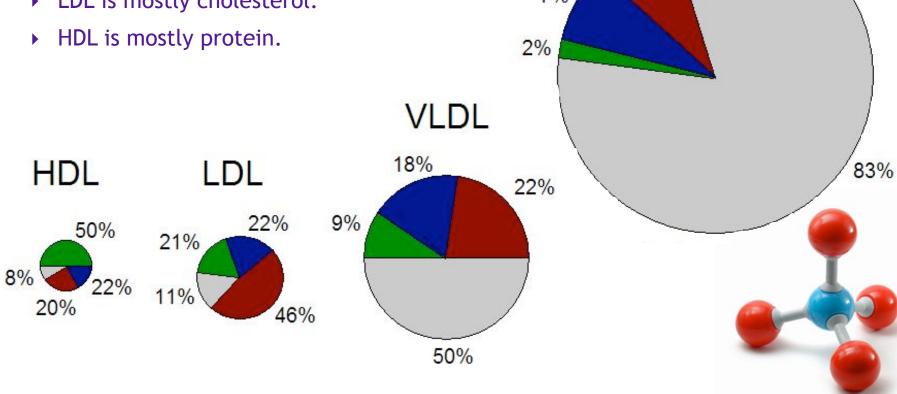


Lipoprotein Function

- Different types of lipoproteins have different functions.
 - Chylomicrons carry triglycerides (fat) from the intestines to the liver, muscles, and adipose tissue. (how we move stuff you eat)
 - Very-low-density lipoproteins (VLDL) carry (newly synthesised) triglycerides from the liver to adipose tissue. (how we move stuff you make)
- These lipoproteins are converted to LDL and HDL
 - Low-density lipoproteins (LDL) carry 3,000 to 6,000 fat molecules (phospholipids, cholesterol, triglycerides) to cells all over the body.
 - LDL particles are sometimes referred to as "bad" lipoprotein because they can leave behind plaque (deposited cholesterol) in your arteries.
 - High-density lipoproteins (HDL) collect fat molecules (phospholipids, cholesterol, triglycerides, etc.) from the body's cells/tissues, and take it back to the liver.
 - HDLs are sometimes referred to as "good" cholesterol because they scavenge plaque from your arteries.



Lipoprotein Composition Cholesterol Protein Phospholipids Triglycerides Chylomicron Lipoprotein types have different composition. 8% Chylomicron and VLDL are mostly triglycerides. 7% • LDL is mostly cholesterol.



Cell Membranes

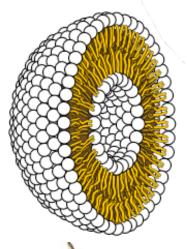
Self Assembly

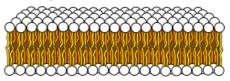
Ch15

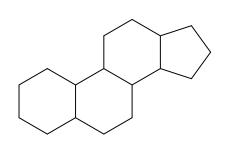
- Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin
- Steroids
 - Steroid Ring System
 - Cholesterol
 - Digestion
 - LipoproteinsHormones

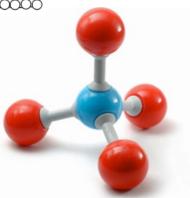


- Cell Membranes
 - Forming Membranes
 - Membrane Structure
 - Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport



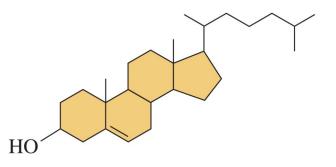


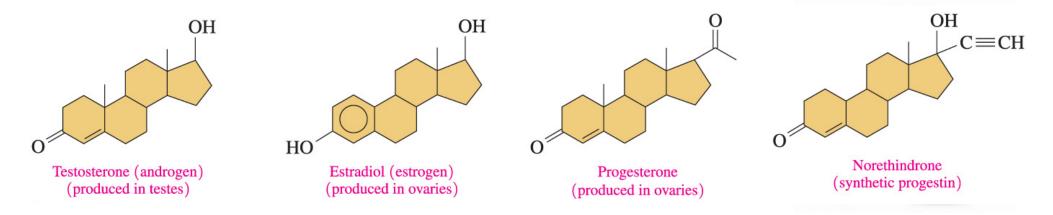




Steroidal Hormones

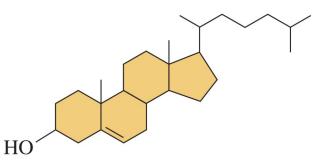
- Cholesterol is also used to build steroidal hormones.
- Steroid hormones are
 - chemical messengers that serve as a communication system for the body
 - produced from cholesterol
 - male sex hormones, testosterone and androsterone
 - female sex hormones, estrogens and progesterone
 - adrenal corticosteroids from adrenal glands
 - mineralocorticoids (electrolyte balance)
 - glucocorticoids (regulate glucose level)

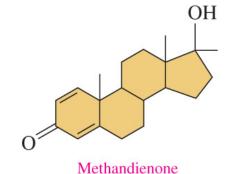


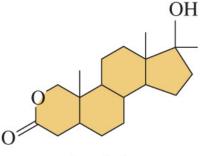


Steroidal Hormones

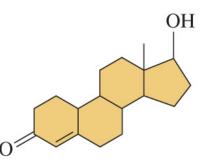
- Anabolic steroids
 - are derivatives of testosterone (a naturally occurring steroid)
 - are used illegally to increase muscle mass
 - have side effects including fluid retention, hair growth, sleep disturbance, and liver damage

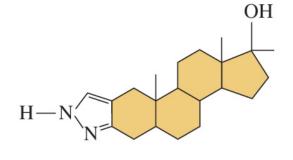






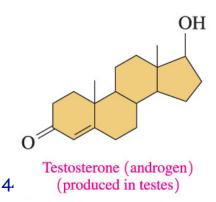
Oxandrolone





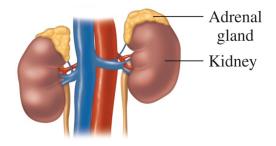
Nandrolone

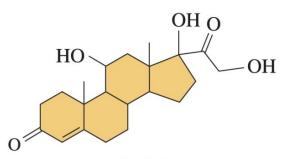
Stanozolol



Steroidal Hormones

- Adrenal cortical steroids or corticosteroids are hormones synthesized by the adrenal cortex.
- There are two types of corticosteroids:
 - glucocorticoids and mineralocorticoids.
- Glucocorticoids e.g. cortisol and cortisone, are essential for the utilization of carbohydrate, fat and protein by the body and for normal response to stress.
- Naturally occurring and synthetic glucocorticoids have very powerful anti-inflammatory effects and are used to treat conditions that involve inflammation.

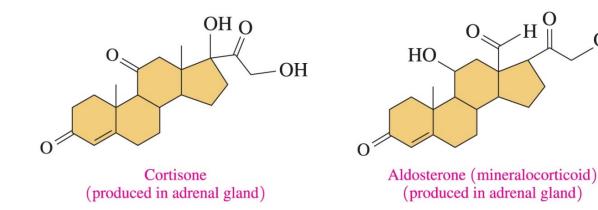






OH





Ch15

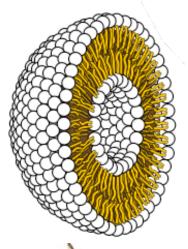
Cell Membranes

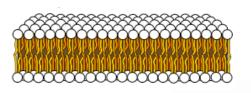
- Self Assembly
 - Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin
- Steroids
 - Steroid Ring System
 - Cholesterol
 - Digestion
 - Lipoproteins
 - Hormones

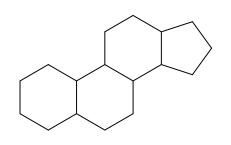


Cell Membranes

- Forming Membranes
- Membrane Structure
- Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport

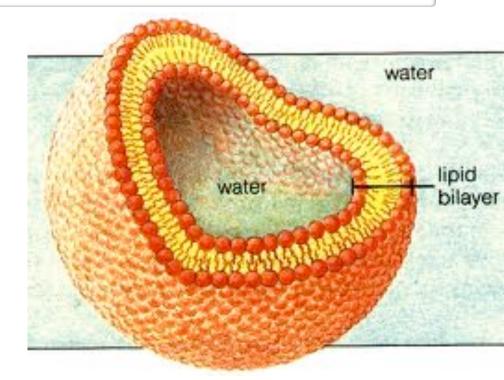


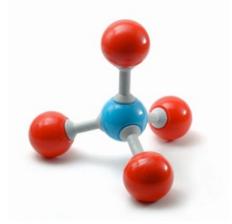




Cell Membranes

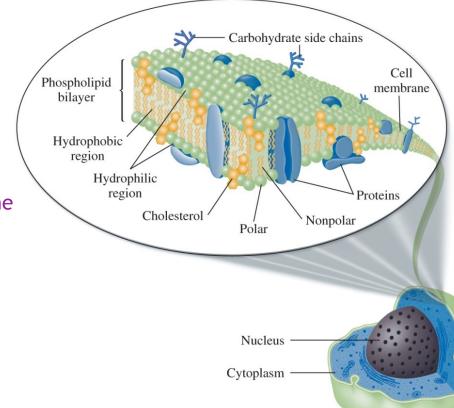
- Phospholipids and cholesterol also form into still larger assemblies.
- Cell membranes are a barrier that separates the inside of a cell from the outside.
- They're formed from a lipid bilayer that completely encloses the inside of the cell.
- These membranes are selectively permeable, some substances can cross the barrier, others are contained or kept out.
- The basic function of the cell membrane is to protect the cell from its surroundings.
- It also serves as a base of attachment for the cytoskeleton in some organisms and the cell wall in others.
- Animal cells, plant cells, prokaryotic cells, and fungal cells have cell membranes.





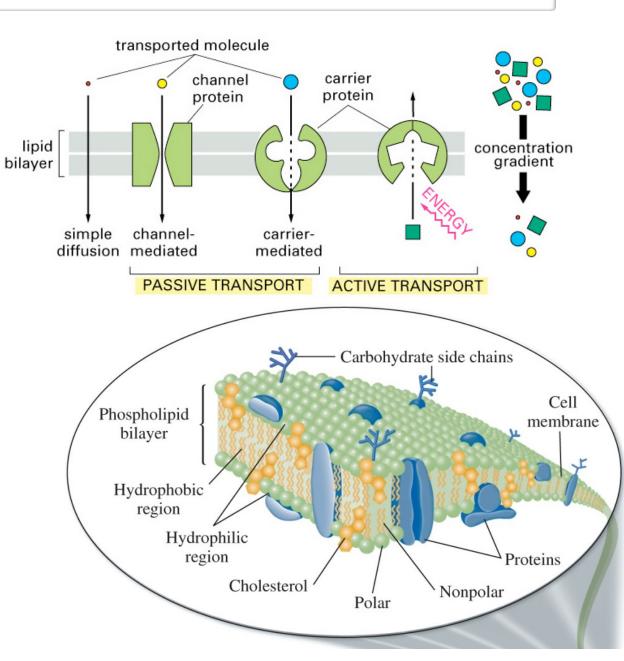
Structure of Cell Membranes

- The cell membrane is primarily composed of a mix of proteins and lipids.
- Depending on the membrane's location and role in the body, lipids can make up anywhere from 20 to 80 percent of the membrane, with the remainder being proteins.
- Cell membranes
 - have unsaturated fatty acids that make cell membranes fluid-like rather than rigid
 - have proteins and carbohydrates on the surface that communicate with hormones and neurotransmitters
 - provide intelligence and identification of the cell
 - is semipermeable meaning it
 - substances can be transported across a cell membrane by
 - diffusion (passive) transport
 - facilitated transport
 - active transport



Transport Through Membranes

- The transport of substances through cell membranes involves
 - diffusion, which moves particles from a higher to a lower concentration
 - facilitated transport, which uses protein channels to increase the rate of diffusion
 - active transport, which moves ions against a concentration gradient
 - Active transport is work, and takes energy to accomplish.



Cell Membranes

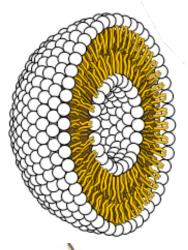
Self Assembly

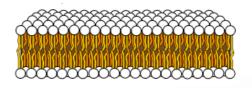
Ch15

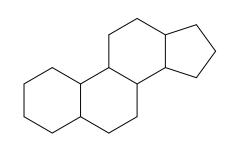
- Amphiphilicity
 - Living in two worlds
- Phospholipids
 - Glycerophospholipids
 - Lecithin
 - Cephalin
 - Forming Bilayers
 - Sphingomyelin
- Steroids
 - Steroid Ring System
 - Cholesterol
 - Digestion
 - Lipoproteins
 - Hormones



- Cell Membranes
 - Forming Membranes
 - Membrane Structure
 - Transport Across Membranes
 - Diffusion
 - Facilitated & Active Transport







Questions?

