Lipids II

Amphipathic Lipids, Membranes, and Non-Hydrolyzable Lipids
Classification of Lipids

Hydrolyzable Lipids

Triacylglycerols
- Fats
- Oils

Waxes

Glycerophospholipids

Sphingolipids
- Sphingophospholipids
- Sphingoglycolipids

Neutral Lipids

Amphipathic Lipids
Amphipathic Lipids - Soaps

Strong aqueous base catalyzes fat hydrolysis

**Saponification**

\[
\begin{align*}
\text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} \\
\text{CH}_2\text{OH} & \quad \text{R}^\prime \quad \text{R}''^\prime \quad \text{R}''
\end{align*}
\]

A fat or oil

Glycerol

Fatty acid salts (soap)
Most *cell-membrane lipids* are one of two main classes of *amphipathic hydrolyzable lipids*.

**Glycerophospholipids** (phosphoglycerides): based on glycerol.

**Sphingolipids**: based on sphingosine.

Unlike the triacylglycerols, the glycerophospholipids and sphingolipids have *one highly hydrophilic group*. The hydrophilic group is responsible for the amphipathic nature of these lipids.
Glycerophospholipids are similar to triacylglycerols except that one of the fatty acid esters is replaced by a phosphodiester group.

The combination of glycerol, two fatty acids, and one phosphate group is called **phosphatidic acid**. Further esterification of the phosphate group with a second alcohol leads to the formation of a phosphodiester group:
## Glycerophospholipids

<table>
<thead>
<tr>
<th>Precursor of X</th>
<th>X</th>
<th>Name</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>—H</td>
<td>Phosphatidate</td>
<td>Basic structure of glycerophospholipids</td>
</tr>
<tr>
<td>Choline</td>
<td>—CH₂CH₂N(CH₃)₃</td>
<td>Phosphatidylcholine</td>
<td>Basic structure of lecithins; most abundant membrane phospholipids</td>
</tr>
<tr>
<td>Ethanolamine</td>
<td>—CH₂CH₂NH₃</td>
<td>Phosphatidylethanolamine</td>
<td>Membrane lipids</td>
</tr>
<tr>
<td>Serine</td>
<td>—CH₂—CH—CH₃</td>
<td>Phosphatidylinerine</td>
<td>Present in most tissues; abundant in brain</td>
</tr>
<tr>
<td><em>myo</em>-Inositol</td>
<td><img src="instructure.png" alt="Bond site" /></td>
<td>Phosphatidylinositol</td>
<td>Relays chemical signals across cell membranes</td>
</tr>
</tbody>
</table>
Glycerophospholipids

Non polar portion

Polar portion
Sphingolipids are amphipathic hydrolyzable lipids based on the amino alcohol *sphingosine*, instead of glycerol:

\[
\text{Sphingosine}
\]

\[
\text{HO}^3\text{CH}^2\text{CH=CH}^3\text{CH}^1\text{(CH}_2\text{)}^2\text{CH}_3
\]

\[
\text{CH}^2\text{NH}_2
\]

\[
\text{CH}_2\text{OH}
\]
Sphingolipids contain an amide linkage at C2 rather than an ester linkage as in the glycerophospholipids. There are two types of sphingolipids:

**Sphingophospholipid**

\[
\text{HO—CH—CH═CH(CH}_2\text{)}_{12}\text{CH}_3
\]

\[
\text{O—P—OR}^1
\]

**Sphingoglycolipid**

\[
\text{HO—CH—CH═CH(CH}_2\text{)}_{12}\text{CH}_3
\]

\[
\text{CH—N—C—R}
\]

\[
\text{Saccharide group}
\]

\[
\text{R}^1 \text{ represents the same set of alcohols found in the glycerophospholipids.}
\]

Sphingoglycolipids, or glycolipids, contain an acetal linkage to a monosaccharide or oligosaccharide unit.
Sphingolipids

Fatty acid acyl group

Amide link

\[ \text{CH}_3(\text{CH}_2)_{14}-\text{C}-\text{NH}-\text{CH} \]

\[ \text{CH}_2-\text{O}-\text{P}-\text{O}^- \]

\[ -X \]

Sphingosine

A sphingomyelin (a sphingolipid)
Sphingolipids
Amphipathic Membrane Lipids

- **Polar head group**
  - Amino alcohol or other group
  - Phosphate

- **Alcohol**
  - Glycerol

- **Fatty acid chains**

- **Glycerophospholipid**

- **Sphingomyelin**

- **Glycolipid**

**Phospholipids**

**Sphingolipids**

- Amino alcohol
  - Phosphate

- Sugar
Amphipathic Membrane Lipids

1) a long hydrophobic tail, and
2) a short hydrophilic head

Glycerophospholipids, sphingolipids, and cholesterol, all have:

- A glycerophospholipid (a phosphatidylcholine)
- A sphingomyelin
- A glycolipid
- Cholesterol

Polar head and Non-polar tails
Biological Membranes
Amphipathic Lipids in Solution

- Polar head (hydrophilic)
- Nonpolar tail (hydrophobic)

Membrane lipid

Lipid bilayer

Liposome
Every cell, whether prokaryotic or eukaryotic, is separated from its extracellular environment by a cell membrane.

Eukaryotic cells contain internal organelles. These organelles are the sites for specific metabolic functions, and each is also surrounded by a membrane:

- **Nucleus**: Storage of genetic information, Synthesis of nucleic acids
- **Lysosomes**: Digestion of macromolecules
- **Mitochondria**: Metabolism of carbohydrates and lipids
- **EPR**: Synthesis of proteins and lipids
- **Golgi apparatus**: Synthesis of oligosaccharides, glycolipids, and glycoproteins

Membranes are highly selective permeability barriers that regulate the molecular and ionic composition within cells and organelles.

Membranes may also have metabolic functions themselves.
Cell membranes contain proteins and mixtures of different glycerophospholipids, sphingolipids, and cholesterol.

The actual lipid composition of a cell membrane varies depending upon the specific function of the membrane:

**Mylein sheath membranes** (insulate nerve cell axons) are rich in sphingophospholipids. 
~80% lipid, ~20% protein

**Cell surface membranes** (cell recognition functions) are rich in sphingoglycolipids 
~50 % lipid, ~50% protein

**Organelle membranes** (metabolic functions) are rich in sphingoglycolipids 
~20 % lipid, ~80% protein
Cell Membrane Lipids

(A) Phosphoglyceride

(B) Sphingomyelin

Archaecal lipid

Shorthand depiction
Cell Membranes

EXTRACELLULAR FLUID

Glycolipids of glycopaixy
Phospholipid bilayer
Integral protein with channel
Integral glycoproteins
Hydrophobic tails
Hydrophilic heads
Cytoskeleton (Microfilaments)

Gated channel
Peripheral protein
Cell membrane
Cholesterol

CYTOPLASM

= 2 nm
The lipid tails are oriented toward the membrane interior and the heads towards the inner and outer membrane surfaces.

Protein components are attracted to lipid components through secondary interactions.
Integral proteins have hydrophobic and hydrophilic regions which enable them to interact with both the hydrophobic interior of the membrane, and its hydrophilic surface and surrounding water.

Peripheral proteins interact with the membrane surface through secondary attractive forces with one side of the membrane or with an integral protein.

Carbohydrates are sometimes attached to membrane lipids and proteins and serve as receptor sites in cell-recognition and cell-communication processes.
The inner and outer surfaces of membranes have different lipid and different protein compositions.

Each surface itself is also asymmetrical with different compositions and functions at different locations.

Individual lipid molecules and proteins can diffuse laterally along a membrane’s surface, but cannot move from one side of the membrane to the other. Membranes are said to be fluid.
The fluidity of membranes varies with membrane composition and temperature:
Shorter and unsaturated fatty acids ----------> increase fluidity

Lower temperature -------------------> decreased fluidity

Cholesterol - modulates fluidity

low cholesterol --------------------> strengthens membrane

high cholesterol ------------------> membranes which are too rigid
Transport Through Membranes

**Passive Processes**

**Simple diffusion**

Movement through a membrane along a concentration gradient from the high concentration side to the low concentration side.

Only a few molecules move by this mechanism: O2, N2, H2O, urea, and ethanol.

Ions and larger polar molecules are excluded by the oily interior of the membrane.

**Facilitated diffusion**

Similar to simple transport except specific integral proteins called transporters or permeases facilitate and speed up the transfer.

Movement is still from the high concentration to the low concentration side of the membrane. The protein transporters act as selective gates or channels for binding and transport of specific solutes.

**Active transport:**

Transport against the concentration gradient across a membrane.

A source of energy must be coupled to this process. The transporters act as pumps to drive the solute in the energetically unfavorable direction against the concentration gradient.
Transport Through Membranes

Lipid bilayer

Simple diffusion
Facilitated diffusion

Channel protein
Transported molecule
Carrier protein

Passive transport
Active transport

Passive transport does not need energy to occur
Transport Through Membranes

- Uniport
- Symport
- Antiport

co-transport

transported molecule

co-transported ion
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  - Oils
- Waxes
- Glycerophospholipids
- Sphingolipids
  - Sphingophospholipids
  - Sphingoglycolipids

Nonhydrolyzable Lipids

- Steroids
- Eicosanoids
- Fat-soluble vitamins
Steroids are high molecular weight, nonhydrolyzable lipids that contain the **steroid ring structure**:

![Steroid Ring Structure](image)

Steroids include **cholesterol, adrenocortical and sex hormones, and bile salts**. The biological effects vary considerably and depend on functional groups attached to the rings and shape.
From a structural standpoint, it is important to consider the characteristics of a fused ring system.

**trans-decalin**

**cis-decalin**
Cholesterol is the major steroid in animals. It contains 8 tetrahedral stereocenters, but exists as a single stereoisomer.

1) Cardiovascular disease
2) Membrane component
3) Precursor to other steroids.
Cortisol:

1) Adrenocortical hormone
2) Metabolic regulator
3) Immune regulator
Testosterone:

1) Sex hormone

2) Reproductive cycle

3) Growth and development
Cholic acid:

1) Secreted by gall bladder

2) Active in digestion of fats

3) A/B ring cis fused
Bile salts function as soaps to break up larger fat globules into smaller ones and increase the rate of digestion.

Bile salts also help to solubilize cholesterol in the bile, and are also involved in the absorption of the fat soluble vitamins from the intestines.
**Bile salts** function as soaps to break up larger fat globules into smaller ones and increase the rate of digestion.

**Pancreatic Lipase** functions at the surface of fat globules in the intestines.
Nonhydrolyzable Lipids - Eicosanoids

Membrane Lipid

\[
\text{Phospholipase} \quad \xrightarrow{\text{Membrane Lipid}} \quad \text{Arachidonic Acid}
\]
Nonhydrolyzable Lipids - Eicosanoids

Eicosanoids are nonhydrolyzable lipids derived from arachidonic acid.

Arachidonic Acid

Leukotriene $D_4$  Prostaglandin $E_1$  Thromboxane $B_2$
Eicosanoids act as local hormones. They are not transported through the bloodstream.

Eicosanoids are produced in most tissues and play roles in:

1) inflammatory response in joints, skin, muscle, eyes*
2) production of pain and fever in disease and injury
3) regulation of blood pressure
4) blood clotting
5) induction of labor
6) regulation of the sleep cycle
7) allergic and asthmatic reactions
*Pain and swelling (arthritis and related illnesses) result from the production of prostaglandins.

The anti-inflammatory drugs aspirin, ibuprofen, acetaminophen, naproxen sodium, and indomethacin sodium prevent the synthesis of these prostaglandins through inhibition of cyclooxygenase enzymes.
Vitamins

Vitamins are organic compounds needed in trace amounts for normal metabolism but not synthesized by the organism that requires them.

Vitamins can be subclassified:

Water soluble: B and C complex

Fat soluble: A, D, E, K

**Vision, proper function of mucous membranes and epithelial cells**

**Bone and cartilage, calcium and phosphate metabolism**

**Cell membrane integrity, antioxidant action**

**Blood clotting, prothrombin formation**