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

Saponification

Strong aqueous base catalyzes fat hydrolysis

\[
\begin{align*}
\text{A fat or oil} & \quad \text{NaOH} \quad \text{H}_2\text{O} \\
\overset{\text{OH}}{\overset{\text{H}_2\text{O}}{\text{C}}} & \overset{\text{C}}{\text{O}} \overset{\text{R}}{\text{CH}_2} \\
\overset{\text{O}}{\overset{\text{C}}{\text{O}}} & \overset{\text{C}}{\text{R}}' \\
\overset{\text{O}}{\overset{\text{R}}{\text{CH}_2}} & \overset{\text{C}}{\text{O}} \overset{\text{Na}^+}{\overset{\text{C}}{\text{O}^-}} \\
\text{Glycerol} & \quad \text{Fatty acid salts (soap)}
\end{align*}
\]
Amphipathic Lipids

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, which allows their assembly into **cell membranes**.
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>$-\text{H}$</td>
<td>Phosphatidate</td>
<td>Basic structure of glycerophospholipids</td>
</tr>
<tr>
<td>Choline</td>
<td>$-\text{CH}_2\text{CH}_2\text{N}((\text{CH}_3)_3$</td>
<td>Phosphatidylcholine</td>
<td>Basic structure of lecithins; most abundant membrane phospholipids</td>
</tr>
<tr>
<td>Ethanolamine</td>
<td>$-\text{CH}_2\text{CH}_2\text{NH}_3$</td>
<td>Phosphatidylethanolamine</td>
<td>Membrane lipids</td>
</tr>
<tr>
<td>Serine</td>
<td>$-\text{CH}_2-\text{CH}$</td>
<td>Phosphatidylserine</td>
<td>Present in most tissues; abundant in brain</td>
</tr>
<tr>
<td><em>myo</em>-Inositol</td>
<td><img src="image" alt="Diagram" /></td>
<td>Phosphatidylinositol</td>
<td>Relays chemical signals across cell membranes</td>
</tr>
</tbody>
</table>
Sphingolipids are amphipathic hydrolyzable lipids based on the amino alcohol sphingosine, instead of glycerol:
Sphingolipids contain an amide linkage at C2 rather than an ester linkage as in the glycerophospholipids. There are two types of sphingolipids:

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

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

\[
\text{Saccharide group} \quad \text{HOCH}_2\quad \text{H} \quad \text{H} \quad \text{O} \quad \text{O} \quad \text{O} \quad \text{O} \quad \text{H} \quad \text{H} \quad \text{OH} \quad \text{OH} \quad \text{OH}
\]

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

A sphingomyelin (a sphingolipid)
Sphingolipids

A sphingomyelin
Amphipathic Lipids in Solution

Glycerophospholipids, sphingolipids, and cholesterol all have:

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

Structure of the membrane glycolipid G_{M1}
Biological Membranes
Amphipathic Lipids in Solution

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

- 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 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 Membrane Components

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:

**Myelin sheath membranes** (insulate nerve cell axons)
are rich in sphingosphospholipids.
~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 Components

**Lipid Bilayer**

HYDROPHILIC

- phosphate
- glycerol

HYDROPHOBIC

- fatty acid

**Lipid Bilayer**
Cell Membrane Lipids

(A)

Phosphoglyceride

Sphingomyelin

Archaeal lipid

(B)

Shorthand depiction
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.
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

- Simple diffusion
- Facilitated diffusion
- Passive transport
- Active transport

Active transport requires energy to occur.

Passive transport does not need energy to occur.
Transport Through Membranes

- Uniport
- Symport
- Antiport

transported molecule

co-transported ion

coop-transport
Classification of Lipids

Hydrolyzable Lipids
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- Glycerophospholipids
- Sphingolipids
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  - Sphingoglycolipids

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

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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.
Nonhydrolyzable Lipids - Steroids

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
**Action of Cholic Acid**

**Lipases** only function at the surface of fat globules in the intestines.

**Bile salts** function as soaps to break up larger fat globules into smaller ones in order to increase the total surface area and thus increase the rate of digestion.

Bile salts also help to solubilize cholesterol in the bile which aids in the elimination of excess cholesterol through the intestinal tract.

Bile salts are also involved in the absorption of the fat soluble vitamins from the intestines (A, D, E, and K).
Nonhydrolyzable Lipids - Eicosanoids

Membrane Lipid

Phospholipase

Arachidonic Acid
Nonhydrolyzable Lipids - Eicosanoids

Eicosanoids are nonhydrolyzable lipids derived from arachidonic acid.

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH} \equiv \text{CHCH}_2\text{CH} \equiv \text{CHCH}_2\text{CH} \equiv \text{CHCH}_2\text{CH} \equiv \text{CHCH}_2\text{CH}_2\text{CH}_2\text{COOH}
\]

Arachidonic acid

\[
\text{COOH}
\]

Arachidonic acid (bent)

Leukotriene D\textsubscript{4}

\[
\text{O} \quad \text{COOH}
\]

Prostaglandin E\textsubscript{1}

\[
\text{OH} \quad \text{COOH}
\]

Thromboxane B\textsubscript{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
Nonhydrolyzable Lipids - Eicosanoids

*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 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

**Fat-Soluble Vitamins**

- **Vitamin A (retinol)**
  - Plays a key role in vision by its conversion into \( 11-cis \)-retinal and subsequently into rhodopsin (see Box 12.2). Aids proper functioning of mucous membranes and epithelial tissues.
  - Deficiency: dry eyes and skin, sterility in males, night blindness

- **1,25-dihydroxyvitamin D\(_3\)** (active form of Vitamin D)
  - Regulates calcium and phosphate use and deposition in bone and cartilage.
  - Deficiency: rickets in children (bowlegs, spinal curvature, knock-knees, pelvic and thoracic deformities); osteomalacia in adults (weakened bones susceptible to fracture)

- **Vitamin E (\( \alpha \)-tocopherol)**
  - Acts as antioxidant to protect unsaturated fatty acid components of cell-membrane lipids against oxidation by air and free radicals (see Section 10.5).
  - Deficiency: scaly skin, muscular weakness and atrophy, sterility

- **Vitamin K\(_2\)**
  - Regulates formation of prothrombin, needed for blood clotting.
  - Deficiency: increased time for blood clotting, a serious problem when a person is bruised, wounded, or undergoing surgery