CHAPTER 10
Lipids

Key topics:

– Biological roles of lipids
– Structure and properties of storage lipids
– Structure and properties of membrane lipids
– Structure and properties of signaling lipids
Lipids: Structurally Diverse Class

Organic molecules that are characterized by low solubility in water, that is, are relatively hydrophobic.
Biological Functions of Lipids

• Storage of energy
  – Reduced compounds: lots of available energy
  – Hydrophobic nature: good packing

• Insulation from environment
  – Low thermal conductivity
  – High heat capacity (can “absorb” heat)
  – Mechanical protection (can absorb shocks)

• Water repellant
  – Hydrophobic nature: keeps surface of the organism dry
    • Prevents excessive wetting (birds)
    • Prevents loss of water via evaporation

• Buoyancy control and acoustics in marine mammals
  – Increased density while diving deep helps sinking (just a hypothesis)
  – Spermaceti organ may focus sound energy: sound stun gun?
More Functions

- **Membrane structure**
  - Main structure of cell membranes

- **Cofactors for enzymes**
  - Vitamin K: blood clot formation
  - Coenzyme Q: ATP synthesis in mitochondria

- **Signaling molecules**
  - Paracrine hormones (act locally)
  - Steroid hormones (act body-wide)
  - Growth factors
  - Vitamins A and D (hormone precursors)

- **Pigments**
  - Color of tomatoes, carrots, pumpkins, some birds

- **Antioxidants**
  - Vitamin E
Lipids can provide pigment

Canthaxanthin (bright red)

Zeaxanthin (bright yellow)
Classification of Lipids

- Based on the structure and function
  - Lipids that do not contain fatty acids: cholesterol, terpenes, ...
  - Lipids that contain fatty acids (complex lipids)
    - can be further separated into:
      - storage lipids and membrane lipids
Fatty Acids

- Carboxylic acids with hydrocarbon chains containing between 4 to 36 carbons
- Almost all natural fatty acids have an **even** number of carbons
- Most natural fatty acids are **unbranched**
- **Saturated**: no double bonds between carbons in the chain
- **Monounsaturated**: one double bond between carbons in the alkyl chain
- **Polyunsaturated**: more than one double bond in the alkyl chain
Fatty Acid Nomenclature

- Omega-3 fatty acids are essential nutrients
  - Humans need them but cannot synthesize them
  - Including ALA, DHA, and EPA
    - Although DHA and EPA can be synthesized from ALA

(a) 18:1(Δ⁹) cis-9-Octadecenoic acid

(b) 20:5(Δ⁵,8,11,14,17) Eicosapentaenoic acid (EPA), an omega-3 fatty acid
# Fatty Acid Nomenclature

## TABLE 10-1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

<table>
<thead>
<tr>
<th>Carbon skeleton</th>
<th>Structure*</th>
<th>Systematic name*</th>
<th>Common name (derivation)</th>
<th>Melting point (°C)</th>
<th>Solubility at 30 °C (mg/g solvent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:0</td>
<td>CH(CH₂)₁₀COOH</td>
<td>n-Dodecanoic acid</td>
<td>Lauric acid (Latin <em>laurus</em>, &quot;laurel plant&quot;)</td>
<td>44.2</td>
<td>0.063</td>
</tr>
<tr>
<td>14:0</td>
<td>CH(CH₂)₁₂COOH</td>
<td>n-Tetradecanoic acid</td>
<td>Myristic acid (Latin <em>Myristica</em>, nutmeg genus)</td>
<td>53.9</td>
<td>0.024</td>
</tr>
<tr>
<td>16:0</td>
<td>CH(CH₂)₁₄COOH</td>
<td>n-Hexadecanoic acid</td>
<td>Palmitic acid (Latin <em>palma</em>, &quot;palm tree&quot;)</td>
<td>63.1</td>
<td>0.0083</td>
</tr>
<tr>
<td>18:0</td>
<td>CH(CH₂)₁₆COOH</td>
<td>n-Octadecanoic acid</td>
<td>Stearic acid (Greek <em>stear</em>, &quot;hard fat&quot;)</td>
<td>69.6</td>
<td>0.0034</td>
</tr>
<tr>
<td>20:0</td>
<td>CH(CH₂)₁₈COOH</td>
<td>n-Eicosenoic acid</td>
<td>Arachidic acid (Latin <em>Arachis</em>, legume genus)</td>
<td>76.5</td>
<td></td>
</tr>
<tr>
<td>24:0</td>
<td>CH(CH₂)₂₀COOH</td>
<td>n-Tetracosanoic acid</td>
<td>Lignoceric acid (Latin <em>lignum</em>, &quot;wood&quot; + <em>cera</em>, &quot;wax&quot;)</td>
<td>86.0</td>
<td></td>
</tr>
<tr>
<td>16:1(Δ⁹)</td>
<td>CH(CH₂)₁₀=CHCH(CH₂)₉COOH</td>
<td>cis-9-Hexadecenoic acid</td>
<td>Palmitoleic acid</td>
<td>1 to 0.5</td>
<td></td>
</tr>
<tr>
<td>18:1(Δ⁹)</td>
<td>CH(CH₂)₁₂=CHCH(CH₂)₁₁COOH</td>
<td>cis-9-Octadecenoic acid</td>
<td>Oleic acid (Latin <em>oleum</em>, &quot;oil&quot;)</td>
<td>13.4</td>
<td></td>
</tr>
<tr>
<td>18:2(Δ⁹,₁₂)</td>
<td>CH(CH₂)₁₂=CHCH(CH₂)₁₁=CHCH(CH₂)₁₀COOH</td>
<td>cis,cis-9,12-Octodecadienoic acid</td>
<td>Linoleic acid (Greek <em>linos</em>, &quot;flax&quot;)</td>
<td>1–5</td>
<td></td>
</tr>
<tr>
<td>18:3(Δ⁶,₁₂,₁₅)</td>
<td>CH(CH₂)₁₳CH=CH CH(CH₂)₁₁=CHCH(CH₂)₁₀=CHCH(CH₂)₉COOH</td>
<td>cis,cis,cis-9,12,1₅-Octodecatrienoic acid</td>
<td>α-Linolenic acid</td>
<td>-11</td>
<td></td>
</tr>
<tr>
<td>20:4(Δ⁶,₁₂,₁₅,₁₈)</td>
<td>CH(CH₂)₁₴=CHCH(CH₂)₁₳CH CH(CH₂)₁₁=CHCH(CH₂)₁₀=CHCH(CH₂)₉COOH</td>
<td>cis,cis,cis,cis-9,12,1₅,1₈-Octodecatetraenoic acid</td>
<td>Arachidonic acid</td>
<td>-49.5</td>
<td></td>
</tr>
</tbody>
</table>

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

*The prefix *n-* indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "n-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

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*Table 10-1*  
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Solubility and Melting Point of Fatty Acids

- **Solubility**
  - decreases as the chain length increases

- **Melting Point**
  - decreases as the chain length decreases
  - decreases as the number of double bonds increases
Conformation of Fatty Acids

- The saturated chain tends to adopt extended conformations.
- The double bonds in natural unsaturated fatty acids are commonly in *cis configuration*, which *kinks* the chain.
Melting Point and Double Bonds

- Saturated fatty acids pack in a fairly orderly way
  - extensive favorable interactions
- Unsaturated cis fatty acid pack less orderly due to the kink
  - less-extensive favorable interactions
- It takes less thermal energy to disrupt disordered packing of unsaturated fatty acids:
  - unsaturated cis fatty acids have a lower melting point
Trans Fatty Acids

- **Trans fatty acids form by partial dehydrogenation of unsaturated fatty acids**
  - Done to increase shelf life or stability at high temperature of oils used in cooking (especially deep frying)
- A *trans double bond* allows a given fatty acid to adopt an extended conformation
- **Trans fatty acids can pack more regularly and show higher melting points than cis forms**
- **Consuming trans fats increases risk of cardiovascular disease**
  - Avoid deep-frying partially hydrogenated vegetable oils
  - **Current trend:** reduce trans fats in foods (Wendy’s, KFC)
TABLE 10–2  Trans Fatty Acids in Some Typical Fast Foods and Snacks

<table>
<thead>
<tr>
<th></th>
<th>Trans fatty acid content</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In a typical serving (g)</td>
<td>As % of total fatty acids</td>
<td></td>
</tr>
<tr>
<td>French fries</td>
<td>4.7–6.1</td>
<td>28–36</td>
<td></td>
</tr>
<tr>
<td>Breaded fish burger</td>
<td>5.6</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Breaded chicken nuggets</td>
<td>5.0</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Pizza</td>
<td>1.1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Corn tortilla chips</td>
<td>1.6</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Doughnut</td>
<td>2.7</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Muffin</td>
<td>0.7</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Chocolate bar</td>
<td>0.2</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>


Note: All data for foods prepared with partially hydrogenated vegetable oil in the United States in 2002.
**Triacylglycerols (Nonpolar)**

- Majority of fatty acids in biological systems are found in the form of **triacylglycerols**
- Solid ones are called **fats**
- Liquid ones are called **oils**
- The primary storage form of lipids (**body fat**)
- Less soluble in water than fatty acids due to the lack of charged carboxylate group
- Less dense than water: **fats and oils float**
Triacylglycerols

Glycerol

1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol, a mixed triacylglycerol

Figure 10-3
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Fats Provide Efficient Fuel Storage

• The advantage of fats over polysaccharides:
  – Fatty acids carry more energy per carbon because they are more reduced
  – Fatty acids carry less water per gram because they are nonpolar

• Glucose and glycogen are for short-term energy needs, quick delivery
• Fats are for long-term (months) energy needs, good storage, slow delivery
Fats Provide Efficient Fuel Storage
Waxes

- Waxes are **esters of** long-chain saturated and unsaturated **fatty acids with long-chain alcohols**
- Insoluble and have high melting points
- Variety of functions:
  - Storage of metabolic fuel in plankton
  - Protection and pliability for hair and skin in vertebrates
  - Waterproofing of feathers in birds
  - Protection from evaporation in tropical plants and ivy
  - Used by people in lotions, ointments, and polishes

![Chemical Structure](image.png)
Wax: The Material of the Honeycomb

Beeswax is a mixture of a large number of lipids, including esters of triacontanol, and a long-chain alkane hentiacontane.
Structural Lipids in Membranes (Polar)

- Contain polar head groups and nonpolar tails (usually attached fatty acids)
- Diversification can come from:
  - modifying a different backbone
  - changing the fatty acids
  - modifying the head groups
- The properties of head groups determine the surface properties of membranes
- Different organisms have different membrane lipid head group compositions
- Different tissues have different membrane lipid head group compositions
Glycerophospholipids

- Primary constituents of cell membranes
- Two fatty acids form ester linkages with the first and second hydroxyl groups of L-glycerol-3-phosphate
- Head group is charged at physiological pH
General Structure of Glycerophospholipids

- Unsaturated fatty acids are commonly found connected to C2.
- The highly polar phosphate group may be further esterified by an alcohol; such substituent groups are called the head groups.

![Diagram of Glycerophospholipid Structure](Image)
### Examples of Glycerophospholipids

<table>
<thead>
<tr>
<th>Name of glycerophospholipid</th>
<th>Name of X —O</th>
<th>Formula of X</th>
<th>Net charge (at pH 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphatidic acid</td>
<td>—</td>
<td>H</td>
<td>—2</td>
</tr>
<tr>
<td>Phosphatidylethanolamine</td>
<td>Ethanolamine</td>
<td><img src="image" alt="Ethanolamine Structure" /></td>
<td>0</td>
</tr>
<tr>
<td>Phosphatidylcholine</td>
<td>Choline</td>
<td><img src="image" alt="Choline Structure" /></td>
<td>0</td>
</tr>
<tr>
<td>Phosphatidylserine</td>
<td>Serine</td>
<td><img src="image" alt="Serine Structure" /></td>
<td>—1</td>
</tr>
<tr>
<td>Phosphatidylglycerol</td>
<td>Glycerol</td>
<td><img src="image" alt="Glycerol Structure" /></td>
<td>—1</td>
</tr>
<tr>
<td>Phosphatidylinositol 4,5-bisphosphate</td>
<td><em>myo</em>-inositol 4,5-bisphosphate</td>
<td><img src="image" alt="myo-Inositol 4,5-bisphosphate Structure" /></td>
<td>—4*</td>
</tr>
<tr>
<td>Cardiolipin</td>
<td>Phosphatidylylglycerol</td>
<td><img src="image" alt="Cardiolipin Structure" /></td>
<td>0</td>
</tr>
</tbody>
</table>

*Figure 10-9*

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Phosphatidylcholine

- Phosphatidylcholine is the major component of most eukaryotic cell membranes.
- Many prokaryotes, including *E. coli*, cannot synthesize this lipid; their membranes do not contain phosphatidylcholine.
Ether Lipids: Plasmalogen

• Vinyl ether analog of phosphatidylethanolamine
• Common in vertebrate heart tissue
• Also found in some protozoa and anaerobic bacteria
• Function is not well understood
  – Resistant to cleavage by common lipases but cleaved by few specific lipases
  – Increase membrane rigidity?
  – Sources of signaling lipids?
  – May be antioxidants?
Ether Lipids: Plasmalogen

Figure 10-10
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Ether Lipids: Platelets-Activating Factor

- Aliphatic ether analog of phosphatidylcholine
- Acetic acid has esterified position C2
- First signaling lipid to be identified
- Stimulates aggregation of blood platelets
- Plays role in mediation of inflammation
Sphingolipids

- The backbone of sphingolipids is NOT glycerol
- The backbone of sphingolipids is a long-chain amino alcohol sphingosine
- A fatty acid is joined to sphingosine via an amide linkage rather than an ester linkage as usually seen in lipids
- A polar head group is connected to sphingosine by a glycosidic or phosphodiester linkage
- The sugar-containing glycosphingolipids are found largely in the outer face of plasma membranes
Sphingolipids

<table>
<thead>
<tr>
<th>Name of sphingolipid</th>
<th>Name of X—O</th>
<th>Formula of X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceramide</td>
<td>—</td>
<td>—H</td>
</tr>
<tr>
<td>Sphingomyelin</td>
<td>Phosphocholine</td>
<td>( \text{PO}_4 - \text{CH}_2 - \text{CH}_2 - \text{N(CH}_3)_3 )</td>
</tr>
<tr>
<td>Neutral glycolipids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucosylcerebroside</td>
<td>Glucose</td>
<td></td>
</tr>
<tr>
<td>Lactosylceramide (a globoside)</td>
<td>Di-, tri-, or tetrasaccharide</td>
<td></td>
</tr>
<tr>
<td>Ganglioside GM2</td>
<td>Complex oligosaccharide</td>
<td></td>
</tr>
</tbody>
</table>

Figure 10-13

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Sphingomyelin

- Ceramide (sphingosine + amide-linked fatty acid) + phosphocholine attached to the alcohol
- Sphingomyelin is abundant in myelin sheath that surrounds some nerve cells in animals
Sphingomyelin is structurally similar to phosphatidylcholine.
Glycosphingolipids and Blood Groups

- The blood groups are determined in part by the type of sugars located on the head groups in glycosphingolipids.
- The structure of sugar is determined by an expression of specific glycosyltransferases
  - Individuals with no active glycosyltransferase will have the O antigen
  - Individuals with a glycosyltransferase that transfers an N-acetylgalactosamine group have A blood group
  - Individuals with a glycosyltransferase that transfers a galactose group have B blood group
Glycosphingolipids determine blood groups

Figure 10-15
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Defects in the turnover of membrane lipids lead to a number of diseases.
Sterols and Cholesterol

- Sterol
  - Steroid nucleus: four fused rings
  - Hydroxyl group (polar head) in the A-ring
  - Various nonpolar side chains
- The steroid nucleus is almost planar
Physiological Role of Sterols

- **Cholesterol** and related sterols are present in the membranes of most eukaryotic cells
  - Modulate fluidity and permeability
  - Thicken the plasma membrane
  - Most bacteria lack sterols

- Mammals obtain cholesterol from **food** or **synthesize** it *de novo* in the liver

- Cholesterol, bound to proteins, is transported to tissues via blood vessels
  - Cholesterol in **low-density lipoproteins** tends to deposit and clog arteries

- Many **hormones** are derivatives of sterols
Steroid Hormones

- Steroids are *oxidized derivatives of sterols*
- Steroids have the sterol nucleus, but lack the alkyl chain found in cholesterol
- **More polar** than cholesterol
- Steroid hormones are synthesized from cholesterol in gonads and adrenal glands
- They are carried through the body in the bloodstream, usually attached to carrier proteins
- Many of the steroid hormones are *male and female sex hormones*
Biologically Active Lipids

- Are present in much smaller amounts than storage or structural lipids
- Play vital roles as signaling molecules between nearby cells
- Lipid soluble vitamins (A, D, E, and K)
Arachidonic Acid Derivatives as Signaling Lipids

- Enzymatic oxidation of arachidonic acid yields
  - Prostaglandins (inflammation and fever)
  - Thromboxanes (formation of blood clots)
  - Leukotrienes (smooth muscle contraction in lungs)

![Diagram of arachidonic acid derivatives]

Figure 10-18
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Vitamin D regulates calcium uptake

Figure 10-20a
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Vitamin A (Retinol)

- Involved in visual pigment
- Precursor for other hormones involved in signaling
Vitamin E, K, and other lipid quinones are antioxidants.
Polyketides are biologically active lipids with medicinal uses.
Chapter 10: Summary

In this chapter, we learned:

• lipids are a structurally and functionally diverse class of molecules that are poorly soluble in water
• triacylglycerols are the main storage lipids
• phospholipids are the main constituents of membranes
• sphingolipids play roles in cell recognition
• cholesterol is both a membrane lipid and the precursor for steroid hormones
• some lipids carry signals from cell to cell and from tissue to tissue