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Chapter 8

Lipids

Slide 2

Functions of Lipids

- Energy Storage
- Thermal Insulation
- Structural Components of Membranes
- Protective Coatings of Plants and Insects
- Hormonal Regulation
- Chemical Signaling of Various Kinds
- Enzymatic Cofactors
- Electron Carriers

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Structural Nature of Lipids

- Most diverse class
- Based on solubility rather than a single structural feature
  - Soluble in organic solvents
  - Poorly soluble or insoluble in water
    - Forming aggregate structures in water
- Amphipathic structure—major part of molecule is non-polar

Proteins, polysaccharides, and nucleic acids are polymers classified according to their building blocks. Lipids as a classification is based upon solubility characteristics which can come from a variety of structural features.

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Non-Polar Residues of Lipids

- Fatty Acid Chains
- Sphingolipid Chains
- Isoprenoid Chains
- Sterols

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Fatty Acids

- Saturated fatty acids
  - Alkyl chain with carboxyl group in position 1
- Unsaturated fatty acids
  - One (monounsaturated) or more (polyunsaturated) double bonds in the chain
  - Double bonds usually have *cis* configuration
- See Figure 8.1 for some typical structures
  - Some 3-D structures are shown under "External links, Chapter 8"

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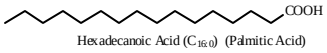
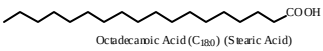
Fatty Acid Nomenclature

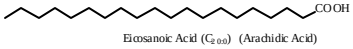
- Saturated Fatty Acids
  - (Systematic Name, Symbol, Common Name)



Hexadecanoic Acid ($C_{16:0}$) (Palmitic Acid)



Octadecanoic Acid ($C_{18:0}$) (Stearic Acid)



Eicosanoic Acid ($C_{20:0}$) (Arachidic Acid)

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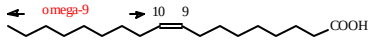
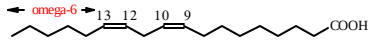
Fatty Acid Nomenclature, con't.

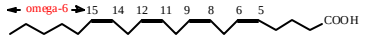
- Unsaturated Fatty Acids



9-Octadecenoic Acid (9-$C_{18:1}$) (Oleic Acid)



9,12–Octadecadienoic Acid (9,12-$C_{18:2}$) (Linoleic Acid)



5,8,11,14–Eicosatetraenoic Acid (5,8,11,14-$C_{20:4}$) (Arachidonic Acid)

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Fatty Acid Nomenclature, con't.

- Learn Names and Structures from Table 8.1
- Omega nomenclature is intended to show biosynthetic relationship between fatty acids.
  - Animals can only introduce double bonds toward carboxyl end.
  - Arachidonic acid is made from **dietary** linoleic acid

As we will see later when we study lipid metabolism, arachidonic acid is important as a precursor of highly active lipids called **eicosanoids**, which include prostaglandins and leukotrienes. We must obtain the precursor to arachidonic acid (primarily linoleic acid) from the diet, however, hence linoleic acid is an **essential fatty acid**.

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Fatty Acid Properties

- Solubility decreases with chain length
- Unsaturation prevents close packing of chains and lowers the melting point of the fatty acids, thereby making membrane regions more "fluid"
  - Some bacteria use branching to accomplish this (See Figure 8.2)
- Salts of long chain fatty acids aggregate as micelles

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Triacylglycerols, (triglycerides)

- Fatty acid ester of glycerol
  - (See Figure 8.3)
- Very non-polar and insoluble
- Mixture of fatty acids, so “fat” is a class of compounds, not a pure compound
- Also find **monoglycerides** and **diglycerides**

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Triacylglycerols, Function

- Major energy source—both dietary and storage
  - highly reduced
  - no solvation, so no water mass in storage
- Other advantages as well (especially whales and Arctic mammals)
  - body insulation
  - source of metabolic water (when the fatty acids are oxidized)

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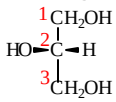
Other Glycerolipids

- Derivatives of 1,2 diacylglycerol
- Glycerol is **pro-chiral**, so once a group is attached to one of the primary alcohols, it becomes chiral
- **Stereospecific numbering** of glycerol is based on writing it in the **L** configuration



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Glycerophospholipids

- Derivatives of **sn** 1,2-diacyl-3-phosphoglycerol (phosphatidic acid)
  - See Figure 8.4
- Fatty acids in 1-position predominantly saturated, those in 2-position predominantly unsaturated
- Various alcohols esterified to phosphate
  - See Figure 8.6, and **learn these structures**

Phospholipids aggregate to form bilayered structures rather than spherical micelles, and this aggregation is the structural basis for the formation of membranes (See Chapter 9 for more detail). Lysophospholipids, on the other hand, tend to form spherical micelles. They are good detergents and will mix with membrane lipids and disrupt the bilayer structure.

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Some Variations on Glycerophospholipid Structure

- Lysophospholipids—fatty acid removed from position 2 by **phospholipase A_2**
- Ether glycerophospholipids
  - ether linkage in position 1 (Fig. 8.8)
  - platelet activating factor (Fig. 8.9)
- Plasmalogens
  - vinyl ether linkage in position 1 (Fig. 8.10)
  - acid hydrolysis produces an **aldehyde**

The name is derived from the fact that they will **lyse** blood cells. The poisonous venom of snakes contains phospholipase A_2, which cleaves the fatty acid from the two position, leading to rupture of blood cells (see box on page 246).
Ether phospholipids are found in some types of bacteria, but the platelet activating factor is an example of a potent signaling molecule in mammals (See box page 247)

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Sphingolipids

- Derivatives of sphingosine, an 18 carbon amino alcohol (Fig. 8.11)
  - Named by Thudichum after the Sphynx
- Fatty acid amide of sphingosine is called **ceramide**
- All sphingolipids are derivatives of ceramide with different groups in ester linkage to the primary alcohol

Plasmalogens are named by changing the **yl** of the phosphoglyceride name to **al** (standing for "aldehyde"). For example, phosphatid**al** choline, phosphatid**al** ethanolamine, phosphatid**al** glycerol, etc.

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Sphingolipids, con't.

- Phosphosphingolipids
  - Sphingomyelin (Fig. 8.12)
    - Structurally very similar to phosphatidyl choline
    - Compare the 3-dimensional structures
      (through Chapter 8 external links)
- Glycosphingolipids
  - Cerebrosides (glucose or galactose)
  - (Fig. 8.13)
  - Gangliosides (contain sialic acid) (Fig. 8.14)

These are just a few representative sphingolipids. Sphingomyelin is found along with phosphatidylcholine in membranes. Glycosphingolipids are also found in membranes, usually the plasma membrane where the oligosaccharide structure may play some role in cellular recognition.

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Waxes

- Esters of long chain alcohol and long chain fatty acid (Fig. 8.15)
- Very insoluble
- Forms coatings on plant leaves, helping to prevent dehydration
- Also coating of animal skin, fur, and bird feathers

The receptor for the cholera toxin uptake is a ganglioside. Gangliosides, and their name implies, are particularly rich in brain. A number of metabolic diseases known as **sphingolipid storage diseases** result from defects in enzymes responsible for degradation of sphingolipids, and intermediates in the degradation pathway accumulate.

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Terpenes

- Derived from 5-carbon unit called **isoprene** (2-methyl-1,3-butadiene) (See Fig. 8.16)
  - Monoterpene (C_{10}) (two units)
  - Sesquiterpene (C_{15}) (three units)
  - Diterpene (C_{20}) (four units)
  - Triterpene (C_{30}) (six units)
- Large variety of structures, especially in plants (See Fig. 8.17)

The ganglioside in Figure 8.14 is a particularly noteworthy example which accumulates in brains of infants in a disease called **Tay Sachs** disease. Accumulation usually leads to death by age 3.

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Polyisoprenoids

- Polyisoprenoids with terminal alcohol are called **polyprenols**
  - dolichol phosphate (animals)
    - intermediate carrier in synthesis of glycoprotein oligosaccharides
  - bactoprenol (bacteria)
    - intermediate carrier in synthesis of bacterial cell walls
- Polysioprenoids also side chains of other important lipids (Vitamin E, Vitamin K, Coenzyme Q)
- See Figure 8.18

Cholesterol and cholesterol ester is the culprit in formation in blood vessels of lipid deposits known as atherosclerotic plaques. We will discuss this problem later when we talk about plasma lipoproteins. Many factors contribute to elevated cholesterol levels in the blood which lead to these plaques

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Steroids

- Cholesterol (See Fig. 8.19)
  - Membrane constituent
  - Precursor of other steroids
- Steroid Hormones
  - Androgens, Estrogens, Mineralcorticoids, Glucocorticoids
- Bile Acids
  - Detergents for solubilizing dietary lipids
- See Fig. 8.20

. For some still unkown reason, consumption of diets high in saturated fat tend to raise the cholesterol levels in blood, while diets rich in polyunsaturated acids tend to lower them. One possible approach to inhibiting cholesterol uptake from dietary sources which could cut down on total body cholesterol is the consumption of plant sterols. Plant sterols differ slightly in structure from cholesterol. See the box on page 256.

Several metabolic diseases are known which result from defects in the various pathways by which hormones are formed from cholesterol. One, described in the book on page 257, is a defect in the enzyme which catalyzes the last step in the formation of testosterone. Lack of this enzyme causes males to be delayed in the development of male sexual characteristics.