Lipids include any biological compounds that are insoluble in water and can dissolve in nonpolar organic solvents.

Lipids are highly diverse in both function & structure:

1. Triglycerides (energy storage)
2. Phospholipids & glycolipids (membrane structure)
3. Sterols (cholesterol & steroids)
4. Eicosanoids (inflammation & pain)

Lipids serve important functional roles at the tissue and organism levels:

- **Pigments**
  - Color of tomatoes, carrots, pumpkins, some birds
- **Waxes (from algae & insects)**
  - Waxes are lipids used to store energy ("bug fat")
- **Secreted oils (water repellents)**
  - Prevents excessive wetting of skin (wet climate)
  - Prevents excessive evaporation (dry climate)
- **Fat-soluble vitamins**
  - Antioxidants (Vitamin E)
  - Blood clotting (Vitamin K)
  - Electron transfer (Coenzyme Q)

Lipids are typically classified according to differences in their structure & biological function:

Two major **structural** classes of lipids:

1. Lipids that contain or are derived from fatty acids
   - Energy storage lipids (triglycerides)
   - Structural lipids (membrane lipids)
   - Signaling lipids (eicosanoids)

2. Lipids that are not associated with fatty acids:
   - Sterols (cholesterol & steroid hormones)
   - Vitamins
CHAPTER 13: Lipids: Structure and Function

OUTLINE

• 13.1 Energy Storage Lipids: Triglycerides
• 13.3 Fatty Acid Catabolism
• 13.2 Membrane Lipids: Phospholipids and Glycolipids
• 13.4 Cholesterol and Other Steroid Hormones

CHAPTER 13: Lipids: Structure and Function

FATTY ACID STRUCTURES

• Fatty acids are long-chain hydrocarbons that end with a carboxylic acid:
  ➢ Typically 12-20 carbons in length
  ➢ Naturally occurring fatty acids have an even number of carbons (due to their synthetic route)
• Fatty acids can be saturated or unsaturated:
  ➢ Saturated fatty acids are alkanes (all C-C bonds)
  ➢ Unsaturated fatty acids are alkenes (have 1 or more C=C double bonds)
  ➢ Polyunsaturated fatty acids have multiple C=C bonds

FATTY ACID CARBON NUMBERING

• Two nomenclature systems are used to identify the length & double bonds in fatty acids:
  1. The delta system (blue)
     ➢ The carbonyl carbon is designated as #1 carbon
     ➢ double bonds specified with a ∆ symbol followed by the superscripted number of the first carbon in the double bond
  2. The omega system (pink)
     ➢ begins numbering with the carbon at the end of the chain (ω-1)
     ➢ double bonds are specified relative to end carbon

Example: Linoleic acid
Delta system: 18:2 ∆9,12
Omega system: 18:2 ω-6
Fatty acids are primarily nonpolar molecules:
- Primarily interact by dispersion forces between the hydrocarbon chains
- The more contacts between these chains, the higher the melting point of fatty acids

Two things impact melting points:
1. Hydrocarbon chain length
   - More carbons = more interactions
2. C=C double bonds
   - "Cis" bond kinks decrease interactions so unsaturated fatty acids have lower MP

Naturally occurring fatty acids may be saturated or unsaturated:
- Animal fats contain more saturated fatty acids (ex: butter)
- Plant oils are unsaturated fatty acids (ex: cooking oils)

Naturally unsaturated fatty acids always contain cis C=C bonds:
- Trans fats are a by-product of industrially processed plant oils
- Have properties between those of natural fatty acids

The most important class of energy storage lipids are triacylglycerols (aka. triglycerides or "fat"):
The name describes structure:
- Tri = three
- Acyl = carbonyl-containing hydrocarbon
- Glycerol = 3-carbon tri-alcohol

Remember HOW fatty acids are connected to the glycerol "backbone"
FATTY ACID COMPOSITION IN TRIGLYCERIDES

- Triglycerides may contain a variety of fatty acids:
  - **Animal fats** are semi-solid, composed mostly of saturated fatty acids (e.g., palmitic)
  - **Plant oils** are liquid, and contain mostly unsaturated fatty acids (e.g., linolenic acid)

THE SATFAT GRAPH

- The graph below indicates the composition of fatty acids in a wide variety of common triglycerides

  - Which of these contain more energy per fatty acid...and why?
  - Which of these are "healthier" for you to use in cooking?

FATTY ACIDS AND INFLAMMATION

- **Arachidonic acid** is an important polyunsaturated fatty acid (20:4Δ5,8,11,14) for production of eicosanoids:
  - Eicosanoids are lipids involved in the regulation of inflammation, pain, blood clotting & muscle contraction
  - **Non-steroidal anti-inflammatory drugs (NSAIDs)** inhibit the enzymes that produce some eicosanoids:
    - Ibuprofen, aspirin, and naproxen are all in this class
    - Used to decrease aspects of inflammation such as fever, pain, itching, and swelling
1. Which vegetable oils are high in saturated fat and should, therefore, be included in limited amounts in the diet?

2. Are most unsaturated fats obtained from vegetable or animal sources?

3. Which product is healthier: coconut oil or canola oil? Explain.

4. Why does arachidonic acid have a lower melting point than linolenic acid, even though it has two more carbon atoms in its chemical formula?

**PRACTICE PROBLEMS**

**WHY STORE ENERGY IN FAT?**

- For some tissues (liver and heart), fatty acids provide most of the energy needs for cells.
- Saturated fats provide more energy density than carbohydrates:
  1. Fatty acids carry more energy per carbon because they are more reduced.
  2. Fatty acids carry less water per gram because they are nonpolar (higher density).

  *Fats are more efficient energy storage molecules.*

**STAGES IN LIPID CATABOLISM**

1. **Stage 1:** Triglycerides are hydrolyzed into glycerol and fatty acids.

2. **Stage 2:** Fatty acids are oxidized to acetyl CoA.

3. **Stage 3:** Acetyl CoA is converted into ATP energy and CO₂ via citric acid cycle and oxidative phosphorylation.
STAGE 1: TRIGLYCERIDE HYDROLYSIS

- Dietary triglycerides are initially present as fat globules which must be partially digested prior to absorption in the small intestine:
  - Bile salts (from liver) act as natural detergents that produce fine droplets of solubilized fat.
  - Fatty acids are released from the glycerol backbone by enzymes called lipases.

LIPID TRANSPORT

- Because lipids are insoluble in water, they must be packaged in forms to allow transport in the blood
- Lipoproteins are lipid transport particles:
  - Spherical particles with a lipid core of fatty acids & cholesterol
  - Covered with a single membrane layer
  - Decorated with proteins that target the particles to specific cell types for uptake & catabolism

LIPOPROTEIN CATEGORIES

- The categories of lipoproteins are based on density:
  - Proteins have much greater density than lipids
  - Density is a reflection of lipid/protein ratios

<table>
<thead>
<tr>
<th>Lipoprotein Category</th>
<th>Density (g/mL)</th>
<th>Triglycerides (%)</th>
<th>Cholesterol (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLDL (very low density)</td>
<td>0.95</td>
<td>45</td>
<td>4</td>
</tr>
<tr>
<td>LDL (low density)</td>
<td>1.05</td>
<td>35</td>
<td>7</td>
</tr>
<tr>
<td>HDL (high density)</td>
<td>1.20</td>
<td>15</td>
<td>20</td>
</tr>
</tbody>
</table>

“Bad” cholesterol: HDL (low density)
“Good” cholesterol: HDL (high density)
• Fatty acid oxidation takes place in the mitochondrial matrix:
  - Same location as the citric acid cycle
  - Products feed into the citric acid cycle & electron transport chain
• In several steps, the oxidation of fatty acids produces acetyl CoA, NADH, and FADH$_2$.
  - Steps occur in cycles removing 2 carbon units per cycle

CHAPTER 13: Lipids: Structure and Function

STAGE 2: FATTY ACID OXIDATION

- Import of fatty acids into the mitochondria prior to catabolism requires that they first be "activated"
- Activation involves the formation of an acyl CoA, a thioester similar to acetyl CoA:
  - Enzymatic condensation reaction (acyl CoA synthase)
  - Requires energy from ATP to make thioester

Note the cost: -2 ATP equivalents are "invested"

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FATTY ACID ACTIVATION

- Oxidation steps occur at the third carbon (the β-carbon)
- Each cycle produces 2 carbon units as acetyl-CoA at each cycle

β-OXIDATION

- β-oxidation is a cycle of four reactions that are repeated many times to break down the fatty acid down by two carbons at a time:
  - The oxidation steps occur at the third carbon (the β-carbon)
  - Each cycle produces 2 carbon units as acetyl-CoA at each cycle
SUMMARY OF β-OXIDATION

1. The alkane acyl chain is oxidized to an alkene intermediate using FAD
2. The C=C double bond is hydrated to a secondary alcohol
3. The secondary alcohol is oxidized to a ketone using NAD+
4. Acyl chain transfer to a new CoA-SH, while acetyl-CoA is removed

ENERGY YIELD IN β-OXIDATION

The products of β-oxidation are energy-rich!!!

- A saturated, 16-carbon fatty acid (palmitate) produces the following in 7 cycles:
  1. 8 two-carbon acetyl CoA units to citric acid cycle
  2. 7 FADH₂ molecules to electron transport chain
  3. 7 NADH molecules

The number of β-oxidation cycles is half the total number of carbon atoms minus one, because the last step produces two acetyl CoA molecules (a four-carbon chain split into two).

ENERGY ACCOUNTING IN β-OXIDATION

The ATP yield from one palmitic acid (C-16:0) is:

1. Initial activation of palmitic acid = -2 ATP
2. 8 acetyl CoA molecules x 10 ATP = 80 ATP
3. 7 FADH₂ molecules x 1.5 ATP = 10.5 ATP
4. 7 NADH molecules x 2.5 ATP = 17.5 ATP

Total = 106 ATP

Note: this number differs from textbook due to estimated yields from FADH₂ & NADH
1. What are the two kinds of oxidation that occur in each cycle of β-oxidation?

2. Calculate the number of ATP molecules produced from complete catabolism of stearic acid (18:0).

3. What would happen to ATP yield if a single C=C double bond were added to stearic acid to make oleic acid (18:1Δ9)?

CHAPTER 13: Lipids: Structure and Function

PRACTICE PROBLEMS

The cell membrane is a semi-permeable structure that defines the boundaries of all cell types:

Fluid mosaic model
- It is composed of lipids, proteins & carbohydrates
- Semi-fluid composition allows lateral diffusion

The cell membrane has many roles:
1. Controlling flow of ions into and out of cells
2. Uptake of nutrients and disposal of waste
3. Cell recognition and communication

CHAPTER 13: Lipids: Structure and Function

CELL MEMBRANE FUNCTION

- The central structural component of membranes is its different lipids, which include:
  1. Phospholipids
     - Major membrane component
     - Fatty acids with a phosphodiester attached along with some other polar "head group"
  2. Glycolipids
     - Fatty acids covalently attached to a carbohydrate
  3. Cholesterol
     - Non-fatty acid lipid component of membrane
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**TYPES OF MEMBRANE LIPIDS**

- **Glycerophospholipids**
- **Sphingomyelins**
- **Sphingolipids**
- Fatty-acid containing lipids
- Sterols (no fatty acids)

Membrane lipids can be linked to fatty acids by two different types of "backbones":

- **Glycerol** = simple 3-carbon, tri-alcohol
- **Sphingosine** = more complex hydrocarbon:
  - Two alcohols
  - Amine
  - Long-chain alkene

**TWO BACKBONES FOR MEMBRANE LIPIDS**

- Membrane lipids can be linked to fatty acids by two different types of **backbones**:
  - **Glycerol** = simple 3-carbon, tri-alcohol
  - **Sphingosine** = more complex hydrocarbon:
    - Two alcohols
    - Amine
    - Long-chain alkene

**GLYCEROPHOSPHOLIPID STRUCTURES**

- Cartoon Structure
- **Components:**
  1. Glycerol backbone (like triglycerides)
  2. Two fatty acid chains
  3. Phosphoryl group (phosphodiester)
  4. Amino alcohol head group

Fatty acids are attached by **ester** bonds.
CHAPTER 13: Lipids: Structure and Function

SPHINGOLIPID STRUCTURES

Components:
1. Sphingosine backbone
2. One fatty acid chain
3. Phosphoryl group (phosphodiester)
4. Amino alcohol head group

- The amino alcohol "head group" associated with phospholipids varies in structure & charge:
  - ethanolamine
  - choline
  - serine
- The head groups vary in terms of their charge at physiological pH

CHAPTER 13: Lipids: Structure and Function

AMINO ALCOHOL HEAD GROUPS

- The amino alcohol "head group" associated with phospholipids varies in structure & charge:
  - ethanolamine
  - choline
  - serine
- The head groups vary in terms of their charge at physiological pH

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GLYCOLIPID STRUCTURES

Components:
1. Sphingosine backbone
2. One fatty acid chain
3. Carbohydrate head group

- Fatty acid are attached by an amide bond
MEMBRANE LIPIDS ARE AMPHIPATHIC

- **Amphipathic** compounds contain both polar regions and nonpolar regions:
  - The polar regions of membrane lipids contain charged phosphate & head group
  - The nonpolar region is the hydrocarbon chains of the fatty acid “tails”

CELLE MEMBRANE STRUCTURE

- Cell membranes consist of two layers of amphipathic lipid, termed a **lipid bilayer**:
  - Layers are aligned so that the polar heads are in contact with water inside & outside the cell
  - Nonpolar tails form an internal hydrophobic environment not in contact with water

STEROLS

- **Sterols** are compounds derived from cholesterol that contain a basic 4-ring system:
  - **Cholesterol** is found in animal cell membranes:
    - Acts as a “buffer” for membrane fluidity
    - Used as a precursor for other key sterols
**Bile Acids**

- Bile acids are **amphipathic** molecules that are used in the digestion of dietary lipids:
  - Made in the liver and stored in the gall bladder
  - Released into the intestine after a meal rich in fats

**Vitamin D<sub>3</sub>**

- Vitamin D<sub>3</sub> is formed by the action of sunlight on cholesterol derivatives in the skin:
  - The ultraviolet (UV) wavelengths cause ring opening
  - Vitamin D<sub>3</sub> is a hormone that is required for the uptake of dietary calcium ions

**Steroid Hormone Function**

- Cholesterol is the starting point for the biosynthesis of the 5 **steroid hormone** classes:
  - **Adrenal steroids**:
    - Include the glucocorticoids and mineralocorticoids
    - Regulate metabolism, immune system activity & ion balance
  - **Sex steroids** (gonadal hormones):
    - Include the progestins, estrogens, and androgens
    - Regulate reproductive processes