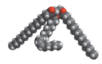
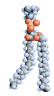
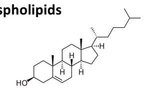
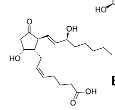
LIPIDS ARE A DIVERSE CLASS OF MOLECULES

- **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)


Triacylglycerides


Phospholipids

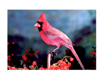

Sterols

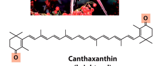

Eisosanoids

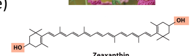
OTHER BIOLOGICALLY IMPORTANT LIPIDS

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)




Canthaxanthin (bright red)


Zeaxanthin (bright yellow)

CLASSIFICATION OF LIPIDS

- **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**
     - **Functional subclasses:**
       a) Energy storage lipids (triglycerides)
       b) Structural lipids (membrane lipids)
       c) Signaling lipids (eicosanoids)
  2. Lipids that are *not* associated with fatty acids:
     - **Functional subclasses:**
       a) Sterols (cholesterol & steroid hormones)
       b) Vitamins

CHAPTER 13: Lipids: Structure and Function

W. H. FREEMAN

OUTLINE

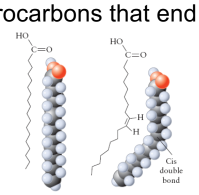
- 13.1 Energy Storage Lipids: Triglycerides
- 13.3 Fatty Acid Catabolism
- 13.2 Membrane Lipids: Phospholipids and Glycolipids
- 13.4 Cholesterol and Other Steroid Hormones

CHAPTER 13: Lipids: Structure and Function

W. H. FREEMAN

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

CHAPTER 13: Lipids: Structure and Function

W. H. FREEMAN

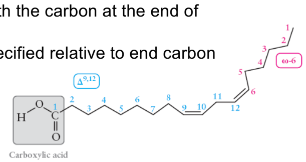
FATTY ACID CARBON NUMBERING

- 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 Δ 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 $\Delta^{9,12}$

Omega system: 18:2 ω-6

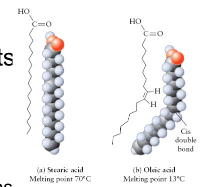


MELTING POINTS OF FATTY ACIDS

- 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**

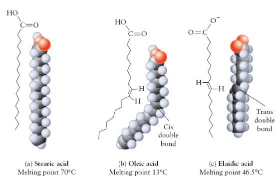
     More carbons = more interactions
  2. C=C **double bonds**

     "cis" bond kinks decrease interactions so unsaturated fatty acids have lower MP



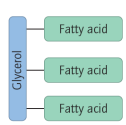
UNDERSTANDING UNSATURATION

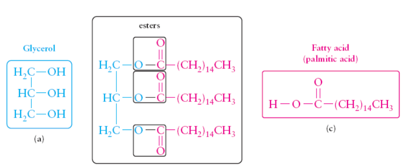
- Naturally occurring fatty acids may be saturated or unsaturated:
  - Animal fats contain more *saturated* fatty acids (ex: butter)
  - Plant oils are *unsaturated* fatty acids (ex: cooking oils)
- Naturally unsaturated fatty acids always contain *cis* C=C bonds:
  - ***Trans fats*** are a by-product of industrially processed plant oils
  - Have properties between those of natural fatty acids



TRIGLYCERIDES: ENERGY STORING LIPIDS

- 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



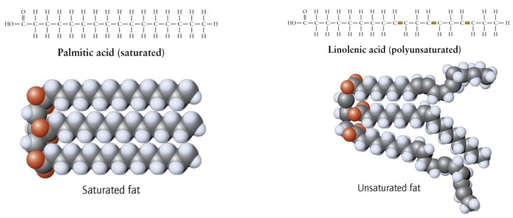


Remember HOW fatty acids are connected to the glycerol "backbone"

General, Organic, and Biochemistry Chapter 6

FATTY ACID COMPOSITION IN TRIGLYCERIDES

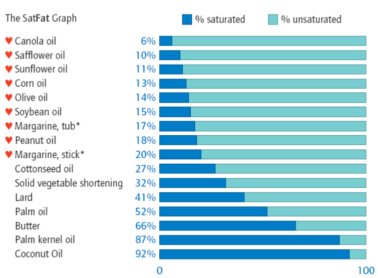
- Triglycerides may contain a variety of fatty acids:
  - **Animal fats** are semi-solid, composed mostly of *saturated* fatty acids (eg. **palmitic**)
  - **Plant oils** are liquid, and contain mostly *unsaturated* fatty acids (eg. **linolenic acid**)



CHAPTER 13: Lipids: Structure and Function

THE SAT**FAT** GRAPH

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

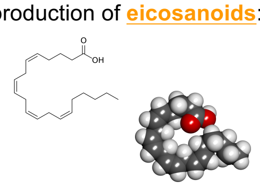


- Which of these contain more energy per fatty acid...and why?
- Which of these are "healthier" for you to use in cooking?

CHAPTER 13: Lipids: Structure and Function

FATTY ACIDS AND INFLAMMATION

- **Arachidonic acid** is an important polyunsaturated fatty acid (20:4$\Delta^{5,8,11,14}$) 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

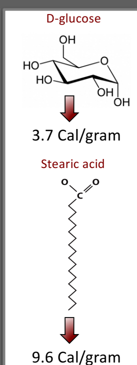
PRACTICE PROBLEMS

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?

WHY STORE ENERGY IN FAT?

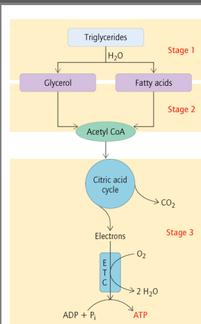
- For some tissues (liver and heart), fatty acids provide most of the energy needs for cells
- Saturated fats provide more ***energy density*** than carbohydrates:
  1. Fatty acids carry more energy per carbon because they are more reduced
  2. Fatty acids carry less water per gram because they are nonpolar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

Fats are more efficient energy storage molecules



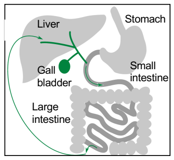
STAGES IN LIPID CATABOLISM

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 CO_2 via citric acid cycle and oxidative phosphorylation.

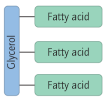


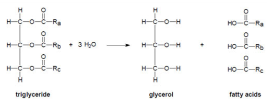
STAGE 1: TRIGLYCERIDE HYDROLYSIS

- 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.



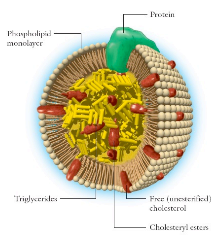
- Fatty acids are released from the glycerol backbone by enzymes called **lipases**:





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**

Higher density is better!

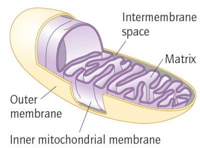
"Bad" cholesterol

"Good" cholesterol

Lipoprotein	Size (drawn to scale)		Density (g/mL)	Lipid/Protein Ratio	Triglyceride/Cholesterol Ester Ratio
Chylomicrons	(10× larger than VLDL)	1 μm (1000 nm) = 1 micron	0.95	66	29
VLDL (very-low-density)		70 nm	0.98	11	3.9
IDL (intermediate-density)		40 nm	1.01	8	0.82
LDL (low-density)		20 nm	1.04	3.8	0.18
HDL (high-density)		10 nm	1.13	1.2	0.16

STAGE 2: FATTY ACID OXIDATION

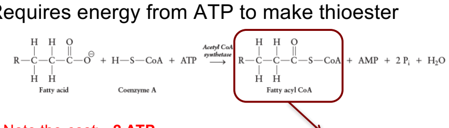
- Fatty acid oxidation takes place in the **mitochondrial matrix**:
  - Same location as the citric acid cycle
  - Products feed into the citric acid cycle & electron transport chain



- 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

FATTY ACID ACTIVATION

- 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

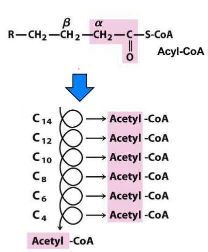


Note the _cost_: **-2 ATP** equivalents are "invested"

To mitochondrial matrix

β-OXIDATION

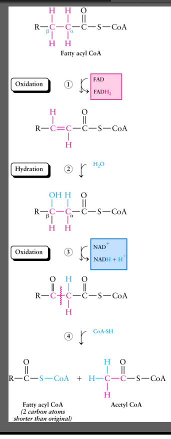
- **β-oxidation** is a cycle of **four reactions** that are repeated many times to break down the fatty acid down by two carbons at a time:
  - The oxidation steps occur at the _third carbon_ (the β-carbon)
  - Each cycle produces 2 carbon units as acetyl-CoA at each cycle



CHAPTER 13: Lipids: Structure and Function

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



CHAPTER 13: Lipids: Structure and Function

ENERGY YIELD IN β-OXIDATION

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

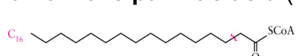
- A saturated, 16-carbon fatty acid (**palmitate**) produces the following in 7 cycles:
  1. 8 two-carbon acetyl CoA units → **to citric acid cycle**
  2. 7 $FADH_2$ molecules } **to electron transport chain**
  3. 7 NADH molecules }

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).*

CHAPTER 13: Lipids: Structure and Function

ENERGY ACCOUNTING IN β-OXIDATION

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



Activated palmitoyl-CoA

1. Initial activation of palmitic acid			=	-2 ATP
2. 8 acetyl CoA molecules	x	10 ATP	=	80 ATP
3. 7 $FADH_2$ 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 $FADH_2$ & NADH

PRACTICE PROBLEMS

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** (18:1Δ^9)?

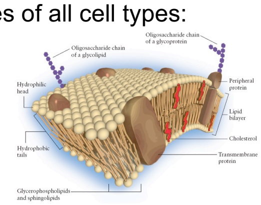
CHAPTER 13: Lipids: Structure and Function

CELL MEMBRANE FUNCTION

- 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***



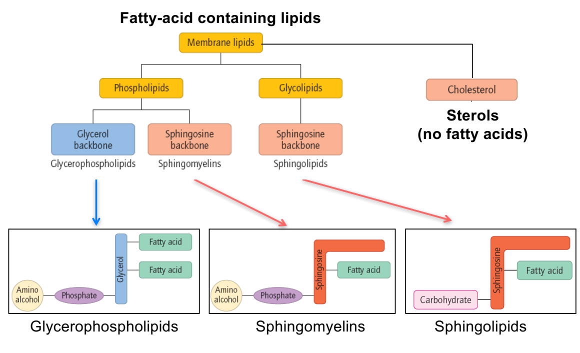
- The cell membrane has many roles:
  1. Controlling flow of ions into and out of cells
  2. Uptake of nutrients and disposal of waste
  3. Cell recognition and communication

CHAPTER 13: Lipids: Structure and Function

CELL MEMBRANE COMPOSITION

- The central structural component of membranes is its different lipids, which include:
  1. **Phospholipids**
     - Major membrane component
     - Fatty acids with a *phospodiester* 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

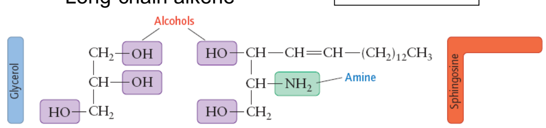
TYPES OF MEMBRANE LIPIDS



TWO BACKBONES FOR MEMBRANE LIPIDS

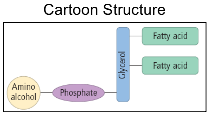
- Membrane lipids can be linked to fatty acids by two different types of "**backbones**":
  - **Glycerol** = simple 3-carbon, tri-alcohol
  - **Sphingosine** = more complex hydrocarbon:
    - Two alcohols
    - Amine
    - Long-chain alkene

Note the cartoon designations for each backbone



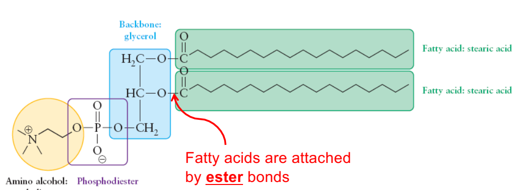
GLYCEROPHOSPHOLIPID STRUCTURES

Cartoon Structure



Components:

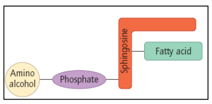
1. Glycerol backbone (like triglycerides)
2. Two fatty acid chains
3. Phosphoryl group (phosphodiester)
4. Amino alcohol head group



Fatty acids are attached by **ester** bonds

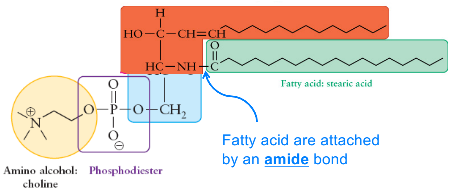
SPHINGOLIPID STRUCTURES

Cartoon Structure



Components:

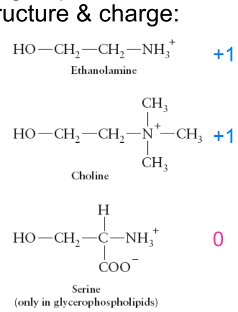
1. Sphingosine backbone
2. One fatty acid chain
3. Phosphoryl group (phosphodiester)
4. Amino alcohol head group



Fatty acid are attached by an **amide** bond

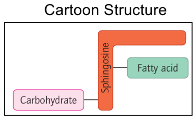
AMINO ALCOHOL HEAD GROUPS

- 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



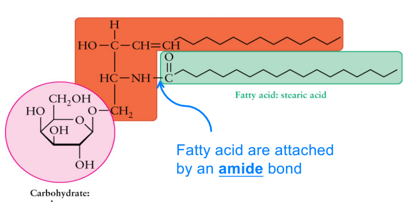
GLYCOLIPID STRUCTURES

Cartoon Structure



Components:

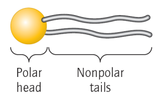
1. Sphingosine backbone
2. One fatty acid chain
3. Carbohydrate head group

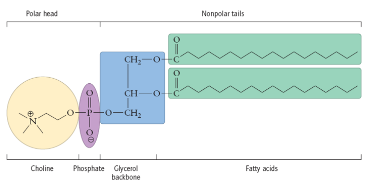


Fatty acid are attached by an **amide** bond

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"



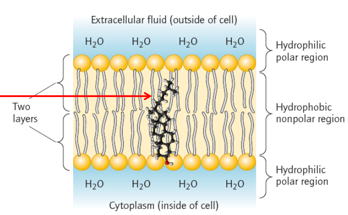


Amphipathic membrane lipids contain one polar "head" and two nonpolar "tails."

CELL MEMRANE STRUCTURE

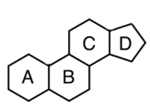
- Cell membranes consist of two layers of amphipathic lipid, termed a **lipid bilayer**:
  - Layers are aligned so that the polar heads are in contact with water inside & outside the cell
  - Nonpolar tails form an internal hydrophobic environment not in contact with water

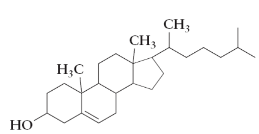
Other nonpolar molecules—such as **cholesterol**—are embedded within the lipid part of the bilayer



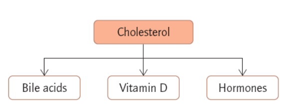
STEROLS

- **Sterols** are compounds derived from **cholesterol** that contain a basic 4-ring system:



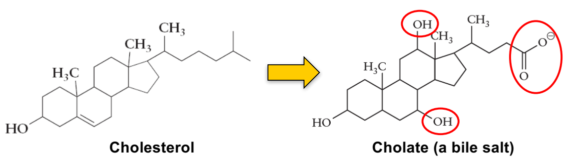


- **Cholesterol** is found in animal cell membranes:
  - Acts as a "buffer" for membrane fluidity
  - Used as a precursor for other key sterols



BILE ACIDS

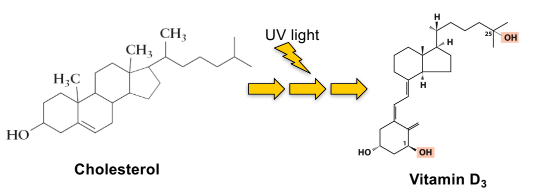
- **Bile acids** are *amphipathic* molecules that are used in the digestion of dietary lipids:
  - Made in the liver and stored in the gall bladder
  - Released into the intestine after a meal rich in fats



What are the key chemical differences between these molecules?

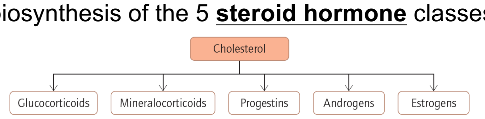
VITAMIN D_3

- **Vitamin D_3** is formed by the action of sunlight on cholesterol derivatives in the skin:
  - The ultraviolet (UV) wavelengths cause ring opening
  - Vitamin D_3 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