LIPIDS II:

1. TRIACYLGlyCEROLS:
   - How are they broken down?
     - Hydrolyzed into 3 fatty acids and 1 glycerol
     - Physiologically in body:
       - Enzyme called a **LIPASE** present in adipocytes and intestines

   ![Chemical Reaction Diagram](image)

   - **Saponification**
     - Treat with base (NaOH) and heat to produce soaps (salts of FAs) and glycerol
     - Used to (and still do!) boil animal fat with lye (NaOH) to make soap!

   ![Chemical Reaction Diagram](image)
2. PHOSPHOACYLGLYCEROLS (Phospholipids; Phosphoglycerides)

- Very similar in structure to triacylglycerols except one of the alcohols of glycerol is esterified by phosphoric acid instead of a fatty acid = phosphatidic acid (PA)

- The phosphoric acid group is then esterified by a second alcohol to form the phosphoacylglycerol

16-18 FAs most common
Position 1 favors SATURATED FAs

Position 2 favors UNSATURATED FAs

These alcohols give very different properties to the phospholipids due to different structures

<table>
<thead>
<tr>
<th>Name of X</th>
<th>Structure of X</th>
<th>Name of Glycerophospholipids</th>
<th>Glycerophospholipid (general structure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Hydrogen</td>
<td>$-H$</td>
<td>Phosphatidic acid</td>
<td><img src="image1" alt="Phosphatidic acid structure" /></td>
</tr>
<tr>
<td>(b) Ethanolamine</td>
<td>$-CH_2-CH_2-NH_3^+$</td>
<td>Phosphatidylethanolamine</td>
<td><img src="image2" alt="Phosphatidylethanolamine structure" /></td>
</tr>
<tr>
<td>(c) Choline</td>
<td>$-CH_2-CH_2-N(CH_3)_3$</td>
<td>Phosphatidylcholine</td>
<td><img src="image3" alt="Phosphatidylcholine structure" /></td>
</tr>
<tr>
<td>(d) Serine</td>
<td><img src="image4" alt="Serine structure" /></td>
<td>Phosphatidylserine</td>
<td><img src="image5" alt="Phosphatidylserine structure" /></td>
</tr>
<tr>
<td>(e) Inositol</td>
<td><img src="image6" alt="Inositol structure" /></td>
<td>Phosphatidylinositol</td>
<td><img src="image7" alt="Phosphatidylinositol structure" /></td>
</tr>
</tbody>
</table>

16-18 FAs most common
Position 1 favors SATURATED FAs
Position 2 favors UNSATURATED FAs
- Phospholipids are MUCH MORE amphiphilic than triacylglycerols due to CHARGED groups at neutral pH
  - Has both hydrophilic and hydrophobic regions
- Therefore we can say that phospholipids have:
  - One POLAR HEAD
  - TWO NON-POLAR TAILS
An amphiphilic lipid

Lipid bilayer

GLYCEROLIPIDS WITH OTHER HEAD GROUPS:

Phosphatidylcholine

Phosphatidylyethanolamine

Phosphatidylserine

Phosphatidylglycerol

Diphosphatidylglycerol (Cardiolipin)

Phosphatidylinositol

Figure 8-9 Concepts in Biochemistry, 3/e
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- Phospholipids can be degraded to their component parts by a family of enzymes called **PHOSPHOLIPASES**

  - **EXAMPLE: SNAKE VENOM**

  - Venoms of poisonous snakes contain (among other things) phospholipases which cause the breakdown of the phospholipids
    - Western Diamondback Rattlesnake and Indian Cobra contain **Phospholipase A2**
    - **Phospholipase A2** catalyzes the hydrolysis of fatty acids at the C2 Position

- Remaining compound called **lysolethicin**
  - “one-legged” phospholipids
  - Acts as a detergent
  - Dissolved membranes in red blood cells causing them to rupture

**Phospholipase A2 cleaves at C2**

**LYSOLECITHIN:**

Acts like a detergent that disrupts and dissolves membranes in red blood cells
3. SPHINGOLIPIDS
- Membrane lipids based on the core structure of SPHINGOSINE, a long chain amino alcohol
- Glycerol is replaced by sphingosine

**General Form:**

1. Fatty acid linked to sphingosine at an **AMINO** group at position 2
2. 2\textsuperscript{nd} esterification takes place at the **HYDROXYL** (-OH) on sphingosine

If $X = H \rightarrow$ Ceramide
- Sugar $\rightarrow$ cerebroside
- Phosphocholine $\rightarrow$ sphingomyelin
- Complex oligosaccharide $\rightarrow$ ganglioside
Sphingolipids:
- Much more amphiphilic than triacylglycerols
- **Sphingomyelin**
  - Insulates nerve axons
  - Major lipid of myelin sheaths
- **Cerebrosides and Gangliosides**
  (glycolipids)
  - Abundant in brain and nervous system membranes
  - Improper degradation results in many metabolic diseases
  - **Tay-Sachs Disease**
    - Gangliosides accumulate in nerve cells, brain, and spleen → Death!
  - **Gaucher Disease**
    - Accumulation of glucocerebrosides
      - Enlarged liver and spleen
      - Bone pain
      - Anemia
    - Deficiency in the enzyme glucocerebrosidase
4. **NON-SAPONIFIABLE LIPIDS/STEROIDS**
   - Based on a fused ring system – **RIGID** structure
   - No ester linkages
   - Includes **HORMONES** (testosterone, progesterone, estrogen)

![Chemical structures of isoprene, estradiol, testosterone, cortisol, cholate, and glycocholate.](image)

- **Cholesterol**
  - Common membrane lipid
  - Almost exclusive to animal cells
  - Very hydrophobic but amphiphilic
    - Hydrophilic group is the –OH on ring A
  - Serves as the starting point for synthesis of steroid hormones
LIPID VITAMINS

Cholesterol

Vitamin D<sub>2</sub>

Vitamin D<sub>3</sub>

Phyloquinone (vitamin K)

α-Tocopherol (vitamin E)
BIOLOGICAL MEMBRANES
- Membranes surround all cells and organelles
- Membranes are based on LIPID BILAYERS (double layer of lipid)
  - Made up of phospholipids, glycosphingolipids, sphingolipids and cholesterol (if animal)
  - Non-polar components minimize exposure to water by forming a bilayer
  - Polar head groups face outward and H-bond with water
  - Lipid fatty acid chains face inward and interact via hydrophobic interactions

LIPID BILAYERS

Membranes are:
- Fluid not static
  - Consistency of vegetable oil
  - Nature of the lipids (length, degree of saturation) dictates fluidity and melting temperature
    - Saturated versus non-saturated – saturated higher melting temperature
    - Length of fatty acids – longer generally higher melting temperature
    - Saturated less fluid than unsaturated
- Lipids are constantly moving LATERALLY (side to side)
- Rarely flip from one leaflet to the other
- When does, requires a lot of energy
- Use proteins called **FLIPPASES**

**Transverse diffusion (flip-flop)**

1. Lipid molecule diffuses to flippase protein
2. Flippase flips lipid to opposite side of bilayer
3. Lipid diffuses away from flippase

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Because of this, lipid bilayers are **asymmetric**
- Some lipids on inner leaflet only
- Some lipids on outer leaflet only
- Distribution is NOT random

**LIPID BILAYER**

- **C** = gray & yellow; **O** esters = red; **Phosphate** = green
- **Choline head groups** = magenta; **Water** = blue spheres

**LIPID MOVEMENT ANIMATIONS:**

http://www.d.umn.edu/~sdowning/Membranes/animationindx.html