Lipids

Lipids are mainly insoluble in water, soluble in organic solvents

Uses in cell:

**Storage** (fatty acids, oils, triacylglycerols, waxes)

**Membrane/Structural** (Phospholipids, glycolipids, sterols)

**Signaling, Cofactor, Pigment** (phosphatidylinositols, eicosanoids, steroid hormones, vitamins, quinones, dolichols)
Fatty Acids
Hydrocarbon derivatives (highly reduced)
Oxidation of fatty acids (CO\textsubscript{2} and H\textsubscript{2}O) is highly exergonic
Carboxylic acids with hydrocarbon chains (C\textsubscript{4} to C\textsubscript{36})
Chain can be fully saturated (no double bonds) and unbranched
Chain can be unsaturated (double bonds) and branched
Naming  \#carbons : \#double bonds
Most common FA have an even number of carbon atoms
Most double bonds at C9, C12, C15

**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(^{1})</th>
<th>Common name (derivation)</th>
<th>Melting point ((^{\circ})C)</th>
<th>Solubility at 30(^{\circ})C (mg/g solvent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:0</td>
<td>(\text{CH}_3(\text{CH}<em>2)</em>{10}\text{COOH})</td>
<td>(n)-Dodecanoic acid</td>
<td>Lauric acid (Latin <em>laurus</em>, &quot;laurel plant&quot;)</td>
<td>44.2</td>
<td>2.603</td>
</tr>
<tr>
<td>14:0</td>
<td>(\text{CH}_3(\text{CH}<em>2)</em>{12}\text{COOH})</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>(\text{CH}_3(\text{CH}<em>2)</em>{14}\text{COOH})</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>(\text{CH}_3(\text{CH}<em>2)</em>{16}\text{COOH})</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>(\text{CH}_3(\text{CH}<em>2)</em>{18}\text{COOH})</td>
<td>(n)-Eicosanoic acid</td>
<td>Arachidic acid (Latin <em>Arachis</em>, legume genus)</td>
<td>76.5</td>
<td>26.5</td>
</tr>
<tr>
<td>24:0</td>
<td>(\text{CH}_3(\text{CH}<em>2)</em>{22}\text{COOH})</td>
<td>(n)-Tetracosanoic acid</td>
<td>Lignoceric acid (Latin <em>lignum</em>, &quot;wood&quot; + cere, &quot;wax&quot;)</td>
<td>86.0</td>
<td>26.5</td>
</tr>
<tr>
<td>16:1((\Delta^{9}))</td>
<td>(\text{CH}_3(\text{CH}<em>2)</em>{16}\text{CH}==\text{CH(CH}<em>2)</em>{7}\text{COOH})</td>
<td>cis-9-Hexadecenoic acid</td>
<td>Palmitoleic acid</td>
<td>1.0-5</td>
<td>1.34</td>
</tr>
<tr>
<td>18:1((\Delta^{9}))</td>
<td>(\text{CH}_3(\text{CH}<em>2)</em>{18}\text{CH}==\text{CH(CH}<em>2)</em>{6}\text{COOH})</td>
<td>cis-9-Octadecenoic acid</td>
<td>Oleic acid (Latin <em>oleum</em>, &quot;oil&quot;)</td>
<td>1.34</td>
<td>10.5</td>
</tr>
<tr>
<td>18:2((\Delta^{9,12}))</td>
<td>(\text{CH}<em>3(\text{CH}<em>2)</em>{17}\text{CH}==\text{CH(CHOH)}</em>{2}\text{COOH})</td>
<td>cis,cis-9,12-Octadecadienoic acid</td>
<td>Linoleic acid (Greek <em>linon</em>, &quot;flax&quot;)</td>
<td>1.5-5</td>
<td>1.1</td>
</tr>
<tr>
<td>18:3((\Delta^{9,12,15}))</td>
<td>(\text{CH}<em>3(\text{CH}<em>2)</em>{16}\text{CH}==\text{CH(CHOH)}</em>{2}\text{COOH})</td>
<td>cis,cis,cis-9,12,15-Octadecatrienoic acid</td>
<td>(\alpha)-Linolenic acid</td>
<td>1.1</td>
<td>11</td>
</tr>
<tr>
<td>20:4((\Delta^{5,8,11,14}))</td>
<td>(\text{CH}<em>3(\text{CH}<em>2)</em>{18}\text{CH}==\text{CH(CHOH)}</em>{2}\text{COOH})</td>
<td>cis,cis,cis-5,8,11,14-Octadecatetraenoic acid</td>
<td>Arachidonic acid</td>
<td>1.495</td>
<td>-11</td>
</tr>
</tbody>
</table>

\(^{1}\)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.

\(^{1}\)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.
Lipids
Storage

Fatty Acids Melting points
Lower for unsat’d because it takes less thermal energy to disorder

(a) Carboxyl group
(b) Hydrocarbon chain

(c) Saturated fatty acids
(d) Mixture of saturated and unsaturated fatty acids
Lipids
Storage

Triacylglycerols (triglycerides, fats)
Fatty acid esters of glycerol
Three fatty acids each in ester linkage to 1 glycerol
Insoluble in water

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

Triacylglycerols (triglycerides, fats)
In vertebrates, adipocytes (fat cells) store lots of triacylglycerols as fat droplets
In seeds, stored as oils for energy
Lipases catalyze hydrolysis of triacylglycerols (when need fuel)

How is stored fat better than stored polysaccharides (carbs)?
(1) Fatty acids more reduced and oxidation produces 2x energy gram for gram
(2) Fatty acids hydrophobic so no associated water to carry around

Fat stores could meet energy needs for long time
BUT human body can only store less than one day’s energy as polysaccharide
Lipids Storage

Triacylglycerols (triglycerides, fats)
Some animals use fat stores as insulation (seals, walruses, penguins)
Hibernating bears use fat stores as energy and insulation

Sperm whales use fat stores to match buoyancy of their bodies to surroundings deep under water

4 tons oil
(triacylglycerols & waxes)
Liquid at 37 °C, frozen at ~30 °C

During deep dives for food oils crystallize and become denser
Deep under water, water gets colder and denser
Buoyancy of whale changes to match buoyancy of seawater
Lipids
Storage

Waxes (storage and water repellent)
Esters of long-chain (C\textsubscript{14} to C\textsubscript{36}) sat’d and unsat’d fatty acids with long-chain alcohols (C\textsubscript{16} to C\textsubscript{30})

\[
\begin{align*}
\text{CH}_3(\text{CH}_2)_{14} & - \text{C} - \text{O} - \text{CH}_2 - (\text{CH}_2)_{28} - \text{CH}_3 \\
\text{Palmitic acid} & & \text{1-Triacontanol}
\end{align*}
\]

Plankton - storage of fuel
Skin glands - secrete wax to protect hair, skin
Birds - secrete wax on feathers to keep them water-repellent
Plants - wax to protect against parasites and to prevent evaporation
Bees - beehive made of beeswax is water-repellent
Lanolin - from lamb’s wool used as ointment
Membrane lipids are **amphipathic** (amphiphilic) - one end is hydrophobic and the other is hydrophilic
Directs packing into micelles, **bilayers** (membranes), liposomes

**Membrane lipids:**
**Phospholipids** - (glycerophospholipids & sphingolipids)
hydrophobic region attached to polar group by phosphate

**Glycolipids** - (sphingolipids & galactolipids)
hydrophobic region attached to polar group (sugar)

**Sterols** - rigid system of four fused hydrocarbon rings
I. Glycerophospholipids (phosphoglycerides)

Two fatty acids attached in ester linkage to C1 and C2 of glycerol
Highly polar or charged group attached through phosphodiester to C3

<table>
<thead>
<tr>
<th>Name of glycerophospholipid</th>
<th>Name of X</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>-1</td>
</tr>
<tr>
<td>Phosphatidylethanolamine</td>
<td>Ethanolamine</td>
<td>CH₂—CH₂—NH₃</td>
<td>0</td>
</tr>
<tr>
<td>Phosphatidylcholine</td>
<td>Choline</td>
<td>CH₂—CH₂—N(CH₃)₃</td>
<td>0</td>
</tr>
<tr>
<td>Phosphatidylserine</td>
<td>Serine</td>
<td>CH₂—CH—NH₃</td>
<td>-1</td>
</tr>
<tr>
<td>Phosphatidylglycerol</td>
<td>Glycerol</td>
<td>CH₂—CH—CH₂—OH</td>
<td>-1</td>
</tr>
<tr>
<td>Phosphatidylinositol 4,5-bisphosphate</td>
<td>myo-Inositol 4,5-bisphosphate</td>
<td></td>
<td>-4</td>
</tr>
<tr>
<td>Cardiolipin</td>
<td>Phosphatidylglycerol</td>
<td>CH₂—CH₂—O—CH₂</td>
<td>-2</td>
</tr>
</tbody>
</table>
Lipids
Structural in Membranes

Interesting Phospholipids with ether linkages
Found in animal tissues and some unicellular organisms

Vertebrate heart tissue

Plasmalogen

Leukocytes
Stimulates platelet aggregation
Stimulates serotonin release (vasoconstrictor)
Role in inflammation, allergic response
II. Sphingolipids
1 sphingosine, 1 long-chain FA, 1 polar head group

<table>
<thead>
<tr>
<th>Name of sphingolipid</th>
<th>Name of X</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{2-} \text{CH}_2\text{CH}_2\text{N(CH}_3\text{)}_3 )</td>
</tr>
<tr>
<td>Neutral glycolipids</td>
<td>Glucose</td>
<td></td>
</tr>
<tr>
<td>Glucosylceribioside</td>
<td></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>

Neu5Ac - \( N\)-acetylneuraminic acid (sialic acid)
Negative charge
GalNAc - \( N\)-acetyl-D-galactosamine
Lipids
Structural in Membranes

Sphingomyelin

Plasma membrane of animals
Prominent in myelin (sheath that surrounds and insulates axons of neurons)
Lipids
Structural in Membranes

Glyco/Sphingolipids
Carbohydrate part of certain sphingolipids define human blood group

Type O (46%) - universal donor, accept blood from O
Type A (42%) - give blood to A or AB, accept blood from A or O
Type B (9%) - give blood to B or AB, accept blood from B or O
Type AB (3%) - give blood to AB, universal acceptor
**Lipids**

**Structural in Membranes**

**Phospholipid and Sphingolipid degradation**

Cells degrade and replace membrane lipids

- Infant mental retardation, death
- Problems in development
- Paralysis
- Blindness
- Death by 3/4 years old
III. Sterols
Present in most eukaryotic cell membranes, bacteria cannot synthesize sterols

**Cholesterol**
 amphipathic

Sterols are also precursors to **Steroid hormones**
potent biological signals that regulate gene expression
Lipids
Signals, Cofactors, Pigments

Potent **signalers** - Hormones

**Enzyme cofactors** - involved in electron-transfer in chloroplasts and mitochondria

**Pigment molecules** - conjugated double bonds, absorb visible light, light-capturing in vision and photosynthesis
Produce natural coloration of pumpkin, carrots, canary feathers
Phosphatidylinositols
Intracellular signals

Phosphatidylinositol
  phosphorylation in plasma membrane
  2ATP
  2ADP

Phosphatidylinositol 4,5-bisphosphate
  hormone-sensitive phospholipase C in plasma membrane
  H₂O

Inositol 1,4,5-trisphosphate
  Release of intracellular Ca²⁺
  Regulation of other enzymes (by Ca²⁺)

Diacylglycerol
  Activation of protein kinase C
  Regulation of other enzymes (by protein phosphorylation)
Lipids
Signals, Cofactors, Pigments

Eicosanoids
Paracrine hormones - Carry messages to nearby cells
Involved in reproduction, inflam, fever, pain, blood clotting, etc.
Derived from arachidonic acid, 20:4 ($\Delta^5, 8, 11, 14$)
Three types: prostaglandins, thromboxanes, leukotrienes

Eicosanoids

Prostaglandins (PG)
First found in prostate gland, stimulate contraction of smooth muscle of uterus during labor and menstruation, affect blood flow, cause fever, inflammation and pain

Thromboxanes (TBX)
Produced in thrombocytes (platelets), act in blood clotting

Leukotrienes (LT)
Found in leukocytes, induce contraction of muscle lining lung airways, overproduce LTs - asthmatic attacks

NSAIDS (non-steroidal antiinflammatory drugs) - aspirin, ibuprofen, acetominophen - inhibit synthesis of PGs and TBXs

Anti-asthmatics - prednisone

Anti-astmatics (prednisone)
Lipids
Signals, Cofactors, Pigments

Steroid Hormones
Oxidized derivatives of sterol
After synthesis move through blood on protein carriers to target
Enter cell, bind to receptor, trigger effect
Hormones have high affinity for receptors, so very low concentration needed to produce effect

![Chemical structures of Testosterone, Estradiol, Cortisol, Aldosterone, Prednisolone, Prednisone]
Lipids
Signals, Cofactors, Pigments

Vitamins (Hormone precursors)
Needed for health, cannot be synthesized in body, need to get in diet
Fat-soluble (A, D, E, K)

Vitamin D
Found in milk, butter
Vitamin D deficiency - defective bone formation, rickets (need sunlight)
Vitamin D$_3$ - formed in skin from 7-dehydrocholesterol & UV light
regulates metabolism of calcium uptake in kidney, intestine, bone

Vitamin A (retinol)
Hormone and visual pigment of vertebrate eye
Found in fish oils, liver, eggs, whole milk, butter
β-carotene (pigment in carrots) can be converted to vitamin A
Deficiency - dry skin & eyes, retarded development, night blindness

Retin-A
Severe acne
Wrinkled skin

Helps rod and cone cells in retina
respond to light
Lipids
Signals, Cofactors, Pigments

Vitamins E and K and Lipid quinones

(a) Vitamin E: an antioxidant

Vitamin E
Associate with cell membranes
Destroy oxygen radicals
Found in eggs, oils, wheat germ
Deficiency - scaly skin, muscle weakness

(b) Vitamin K₁: a blood-clotting cofactor (phyllloquinone)

Vitamin K
Undergoes redox during formation of prothrombin
Vitamin K deficiency slows blood clotting
Newborns given a 1 mg injection of vitamin K₁
K₁ found in green plant leaves

(c) Warfarin: a blood anticoagulant

Warfarin (cumadin)
Rat poison - causes internal bleeding
Anticoagulant drug to treat those at risk of blood clotting

(d) Ubiquinone: a mitochondrial electron carrier (coenzyme Q)

Ubiquinone
Electron carriers in the redox reactions that drive ATP synthesis in mitochondria and chloroplasts