Lipids

Lipids possess several levels of complexity and are highly diverse:

- Simple lipids - a lipid that cannot be broken down to smaller constituents by hydrolysis.
  - Fatty acids, waxes and cholesterol
- Complex lipids - a lipid composed of different molecules held together mostly by ester linkages and susceptible to cleavage reactions.
  - Acylglycerols - mono, di and triacyl glycerols (fatty acids and glycerol)
  - Phospholipids (also known as glycerophospholipids) - lipids which are made of fatty acids, glycerol, a phosphoryl group and an alcohol. Many also contain nitrogen
  - Glycolipids (also known as glycosphingolipids): Lipids which have a spingosine and different backbone than the phospholipids
- Cholesterol and cholesterol esters and steroids
- Waxes and terpenes

Lipids as Diverse Molecules

Precursor and derived lipids - these include several of the initial long chain hydrocarbons and other molecules that make up lipids, such as ketone bodies.

Lipids are defined as those molecules soluble in organic solvents and not water

All biological lipids are amphipathic

Fatty acids, Triacylglycerol, Glycerophospholipids, Sphingolipids Waxes, Isoprene-based lipids (including steroids)

Polar Bears Prefer Nonpolar Food

Polar bears face an ironic dilemma. They are surrounded by water they cannot use. Ice and snow are too cold and seawater is too salty. They produce all the water they need from metabolism of fat: \((\text{CH}_2 + 1.5\text{O}_2 \rightarrow \text{CO}_2 + \text{H}_2\text{O})\)

Interestingly, adult polar bears consume only fat (from seals they catch). By not consuming protein (and merely recycling their own proteins into new ones), they have no need to urinate or defecate and go for months without doing so, thus saving precious body water.

Fats and cooking

Lipids and fats greatly influence our cooking

- Fat globules from milk create a creaminess and sweet flavor in ice cream and chocolate
- Provides smooth lubricated moist mouthfeel in meats
- Limit protein (gluten) cross-linking in pastries (that’s why fats is called shortening)
- Used to transfer heat – but chain length can burn (smoke point)

Properties of fatty acids

- Fatty acids are alkyl chains with carboxyl group
- Free fatty acids are found associated with carrier proteins such as albumin in blood
- Commonly esterified to glycerol, mono, di and tri-acylglycerols (good old fashioned fat)
- These are amphipathic molecules with various carbon chain lengths
- Can be up to 30 carbons long but generally less than 20

- Saturated fatty acids are saturated with hydrogen. No double bonds.
- Unsaturated fatty acids contain at least one double bond separated by a methyl group.
  - These are typically cis-in nature. Trans unsaturated fatty acids have been linked to cancer and heart disease.
- Polyunsaturated fatty acids - duh

Common FA – recognize names and general features!
**FA Nomenclature**

Common name most often used

The systematic name for saturated acids ends in -anoic. Unsaturated fatty acids end in -enoic.
- The number one carbon is the carboxyl carbon
- Carbon #1 = alpha carbon
- Carbon #2 = beta carbon
- Carbon #3 = gamma carbon
- Omega vs. delta fatty acids
- Double bonds counted from the first carbon are delta desaturations
- Double bonds counting from the methyl end are the omega desaturations

Melting points and membrane fluidity

Both length and level of unsaturation determine the stability of the hydrophobic interactions and thus shift the transition phase - melting point of membranes
- Double bonds - usually cis. This results in bends the chain.
- Reductions in hydrophobic effect reduce energy required to disrupt the crystalin structure of a membrane or oil. Think of animal fat with lower unsaturated fatty acids - butter and plant oils that are polyunsaturated, corn oil.
- The longer the fatty acids the higher the melting point.
- Again the more hydrophobic interactions effects the more the energy it takes to break the order. Decreases in the packing efficiency decreases the mp
- The van der Waals forces then come apart more easily at lower temperatures.
- Animal alter the length and unsaturated level of the fatty acids in lipids (cholesterol too) to deal with the cold temps

**Fatty Acid Derivatives**

Ecosanoids - derived from arachidonic acid. Important in many biochemical roles.

**Examples are prostaglandins, thromboxanes, and leukotrienes**

Eicosanoids
- These are a diverse group of hormonelike molecules produced in nearly II mammalian cells
- Stem from the greek word eikosi meaning twenty
- Because they act on the same organ they are produced in they are autocrines, vs a paracrine which act distal to the site of origin
- Most are derived from arachidonic acid 20:4 D5,8,11,14
- Source if from the hydrolytic actions of PLA2

-Leukotrienes are hydroxylated fatty acid derivatives of arachidonate
- Initially found in leukocytes - white blood cells
- Often conугuated
- Secreted by damaged cells during anaphylaxis
- Promotes bronchioconstriction and vasioconstriction
- Acts as a chemottractant to bring white blood cells to fight infection
- Aspirin inhibits the formation of cyclic ecosanoids
- Inhibition is by NSAIDs
- The Serine in the active site of the enzyme cyclooxygenase is acetlyated by aspirin
- Prostaglandins have a cyclopentane ring and is hydroxylated at various carbons. There are several versions each with a different effect. Different types and concentrations of prostaglandins are found in different tissues.
- Induce inflammation and cause fever and pain
- Ovulation and uterine contraction during conception and labor
- Antiplatelet aggregation
- Vasiiodialation
- Smooth muscle contraction
- Thromboxanes produced by platelets to cause aggregation at sites of cardiovascular injury. Leads to clot formation and foam cell formation (platelets differentiate into cells that cause plaques in arteries)
- Alterations in double bonds in arachidonate still leads to TxB formation but they are less able to aggregate platelets
- These fatty acids are found in some cold fish oils omega 3 fatty acids

- Prostacyclin produced by blood vessels and inhibit platelet aggregation
- These are antagonistic to thromboxanes
- The omega 3 fatty acids leads to a more potent antiaggregant activity

**Triacylglycerols**

- TAGs are the major form of fatty acid storage. Found in adipose tissue in specialized cells. These fat cells are filled with TAGs and can grow in size.
- Fatty acids released into the bloodstream are carried via albumin.
- The acylated acyl chains are typically different at each position of glycerol.
- Each of the three carbons on glycerol are different. The 1 and 3 carbons are steriochemically different and recognized as such by enzymes. The carbons are labeled sn1, sn2, sn3

**TAG and Energy Storage**

- TAGs possess a large amount of metabolic energy available in the storage of TAGs. *(NOT HIGH ENERGY BONDS!)*
- These are highly reduced molecules with low amounts of water associated. The result is a molecule that can undergo repeated oxidation steps transferring the energy to form ATP.
- The low water content increases the gram per gram energy available vs. carbohydrates

**Phospholipids**

- Phospholipids are the largest constituent of the membrane
- Phospholipids serve two important purposes (different than TAGs) structural and signaling. Although DAG is an important signaling molecule as well
- There are two general classes of phospholipids
  - Glycerophospholipids, phospholipids or phosphate esters (same thing)
  - Sphingolipids.

**glycerophospholipid**

- The 1 and 2 positions on glycerol are esterified. The 2 carbon is typically unsaturated. Differences of FA and saturation do occur between tissues and organism
Head group defines phospholipids
- Phosphatidic acid is the base glycerophospholipid but is not found in high concentrations.

**Ether Phospholipids**

*Ether glycerophospholipids possess an ether linkage instead of an acyl group at the C-1 position of glycerol.*

![Diagram of ether linkages](image)

**Ether Phospholipids**  
**Plasmalogens** - One type of ether lipid containing an ether linked FA at the sn1 position
- Plasmalogens are ether glycerophospholipids in which the alkyl chain is unsaturated
- These are typically involved in platelet aggregation and vasodilation

**Sphingolipids**

Sphingolipids represent another class of lipids found frequently in biological membranes
- Sphingolipids are very different in location and concentration than glycerolipids
- **Sphingosine**, an 18-carbon alcohol, forms the backbone of these lipids rather

- **Glycosphingolipids** are ceramides with one or more sugars in beta-glycosidic linkage at the 1-hydroxyl group
- Glycosphingolipids with one sugar are cerebrosides
- Ceramides with 3 or more sugars, one of which is a sialic acid, are gangliosides

Gangliosides are important components of muscle and nerve membranes.

Gangliosides are ceramides with three or more sugars esterified, one of which is a sialic acid.
**Waxes are esters of long-chain alcohols with long-chain fatty acids**
- Waxes are insoluble in water, due to their mostly hydrocarbon composition
- Animal skin and fur are wax-coated and are water-repellent
- Leaves of many plants and bird feathers are similarly water-repellent
- Carnauba wax, from a palm tree in Brazil, is a hard wax used for high-gloss finishes for automobiles, boats, floors, and shoes
- Lanolin is a wool wax used in cosmetics; Oil of Olay is named for its lanolin content

**Terpenes**

*Terpenes are a class of lipids formed from combinations of isoprene units*

“Isoprene” is 2-methyl-1,3-butadiene

**Monoterpenes** consist of two isoprene units

**Sesquiterpenes** consist of three isoprenes

A **diterpene** consists of four isoprene units

- All **steroids** (including cholesterol and the steroid hormones) are terpene-based molecules

Many monoterpenes are readily recognized by their characteristic flavors or odors (limonene in lemons; citronellal in roses and perfumes; menthol used in cough drops).

The diterpenes include retinal (the visual pigment in rhodopsin), and phytol (found in chlorophyll). Gibberellic acid is a plant hormone.

The triterpene lanosterol is a constituent of wool fat and is also a precursor to cholesterol and the other steroids. Lycopene is a carotenoid found in ripe fruit, especially tomatoes.

**Steroids and their Cellular Functions?**

Steroids are polyisoprenyl (isoprene-based) molecules built on a core structure of three 6-membered rings and one 5-membered ring, all fused together

**Cholesterol** is the most common steroid in animals and precursor for all other steroids in animals

**Steroid Cellular Functions**

- **Cortisol** provides control of carbohydrate, protein, and lipid metabolism
- **Testosterone** is the primary male sex steroid hormone
- **Estradiol** is the primary female sex steroid hormone
- **Progesterone** is a precursor of testosterone and estradiol

**Bile salts – digestion**

The bile acids, including cholic acid and deoxycholic acid, are detergent molecules secreted in bile from the gallbladder that assist in the absorption of dietary lipids in the intestine.

**Bioactive Lipids**

Glycerophospholipids and sphingolipids play important roles as chemical signals in and on cells

Lipid signals act locally, either within the cell where they are made or on nearby cells

These signals typically initiate a cascade of reactions with multiple effects

The lifetimes of these signals are usually very short

The creation and breakdown of lipid signals is carefully regulated and timed

**Phospholipases**
- Phospholipase A1, A2, C and D all hydrolyze (know the reaction) at specific sites on phospholipids
Select lipases

- PLA2 often responsible for release of arachadonic acid. The free fatty acid is then metabolized to various ecosanoids. Lysophosphatidic acid (LPA) is also produced.
- LPA is a potent mitogen (causes cell growth) and at high concentrations can act as a detergent - lysing the cells
  • Active component of snake and scorpion venom

Select lipases

**Phospholipase C**
- PLC - releases inositol and diacylglycerol. Inositol increases intracellular release of calcium. DAG activates protein kinase C.

Select lipases

**Phospholipase D**
- PLD - Increases the production of phosphatidic acid. PA can be a potent mitogen and PA can be further metabolized to DAG

Cell effects
- PA kinase
- Recruits protein to memb
- Promote cell curvature