Lipids (1)

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- **Lipids** are organic compounds that are insoluble in water but soluble in organic solvents such as benzene, ether and chloroform
- Lipids include fats, oils, waxes, phospholipids, cholesterol, bile salts, steroid hormones, sphingolipids, eicosanoids, fat-soluble vitamins (vitamins A, D, E, and K) and others.

- The lipids found in biological systems are either **hydrophobic** [containing only nonpolar groups example triacylglycerols] or **amphipathic** (amphiphilic)**,** which means they possess both polar and nonpolar groups example fatty acids.
- Lipids are not polymers because lipids are not composed of repeating units of the same molecules or atoms.

Biological Importance of Lipids:

1. Source of energy, In the absence or shortage of carbohydrate the liver converts fatty acids to ketone bodies that are oxidized by tissues such as heart, kidney, brain and muscle, but not the liver.
2. They are important constituents of the nervous system.
3. Tissue fat is an essential constituent of cell membrane
4. Stored lipids act as:
   - A store of energy.
   - A pad for the internal organs to protect them from outside shocks
   - A subcutaneous thermal insulator against loss of body heat.
5. Cholesterol is used for synthesis of steroid hormones,

   vitamin D, bile acids and bile salts.
6. Supply the body with essential fatty acids that cannot be synthesized and fat-soluble vitamins (A, D, E and K).

- Many vitamins are fat-soluble, meaning that they must be associated with fat molecules in order to be effectively absorbed by the body.

Lipids Classification

1. Simple lipids: are esters of fatty acids and alcohol example: Fats, Oils and Waxes.

2. Compound lipids: are esters of fatty acids and alcohol and other additional groups such as phosphate carbohydrates, nitrogen bases, proteins….. Examples :

a. **Phospholipids:** contain in addition to fatty acids and an alcohol, a phosphoric acid residue. They frequently have nitrogen containing bases and other substituents, eg, in **Phosphoglycerides** the alcohol is glycerol and in **sphingophospholipids** the alcohol is sphingosine.

b. **Glycolipids (glycosphingolipids):** contain a fatty acid, sphingosine (as alcohol) and carbohydrate.

c. **Lipoproteins** are lipids with protein (LDL, HDL…..) .

3. Derived lipids: they are derived from hydrolysis of both simple and compound lipids. Example ketone bodies, glycerol, steroids.

Fatty Acids

- A **fatty acid (FA)** is composed of

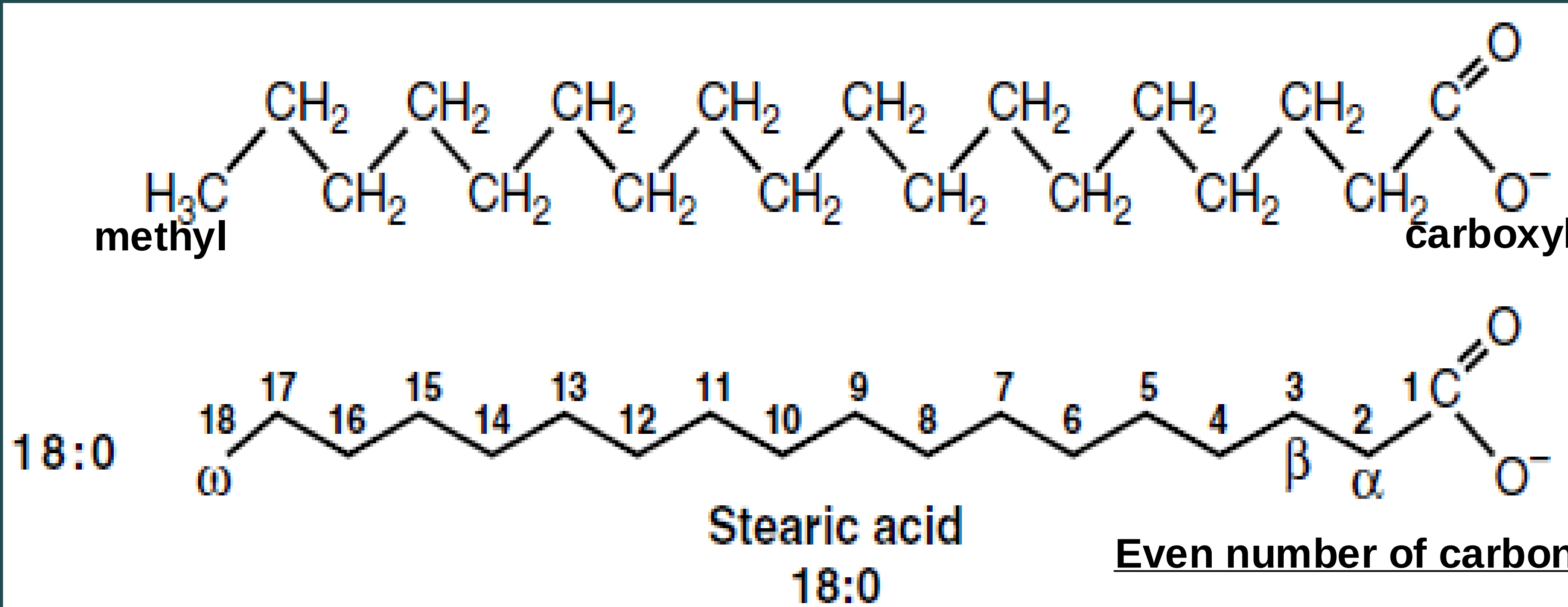
(a) Hydrocarbon chain: a long straight (unbranched) hydrophobic chain.

(b) Methyl group (CH_3) at one end (known as omega ω end).

(c) Carboxyl group (COOH) (hydrophilic) at the other end.

The carboxyl group (COOH) pKa is 4.8 thus is normally ionized (COO^-) under physiological conditions which give the fatty acid its amphipathic nature. The COOH is what makes these molecules acids.

- Most of the fatty acids found in nature have an even number of carbon atoms (usually from 4 to 28) while in humans between 16-20. This is because they are biosynthesized from C2 building blocks found in acetyl-CoA.
- Fatty acids with odd numbers of carbon atoms are found in ruminant animals fat and milk and in some marine organisms.



Fatty acids structure

- The carbon atom adjacent to carboxyl carbon No. 2, 3, and 4 are also known as α, β, and γ respectively.

Fatty acids are classified according to chain length:

1- Very-long-chain fatty acids (VLCFA) (more than C20)

2- Long-chain fatty acids (LCFA) (C12–C20)

3- Medium-chain fatty acids (MCFA) (C6–C12)

- Medium-chain-length fatty acids are present principally in dairy fat (e.g., milk and butter), maternal milk, and vegetable oils.

4- Short-chain fatty acids (SCFA) less than C6 for example acetic acid (two carbon (CH_3COOH)), propionic acid (three carbon), and butyric acid (four carbon).

- In humans body the source of SCFA is colonic bacteria.
- The fatty acids oxidized as fuels are principally long-chain fatty acids.

Saturated and unsaturated Fatty acids

- Saturated fatty acids has no double bonds and all carbon–carbon bonds are single bonds

- Unsaturated fatty acids are of two types:

1- **Monounsaturated** if a fatty acid has a single double bond (Examples include olive oil known as oleic acid Omega-9).

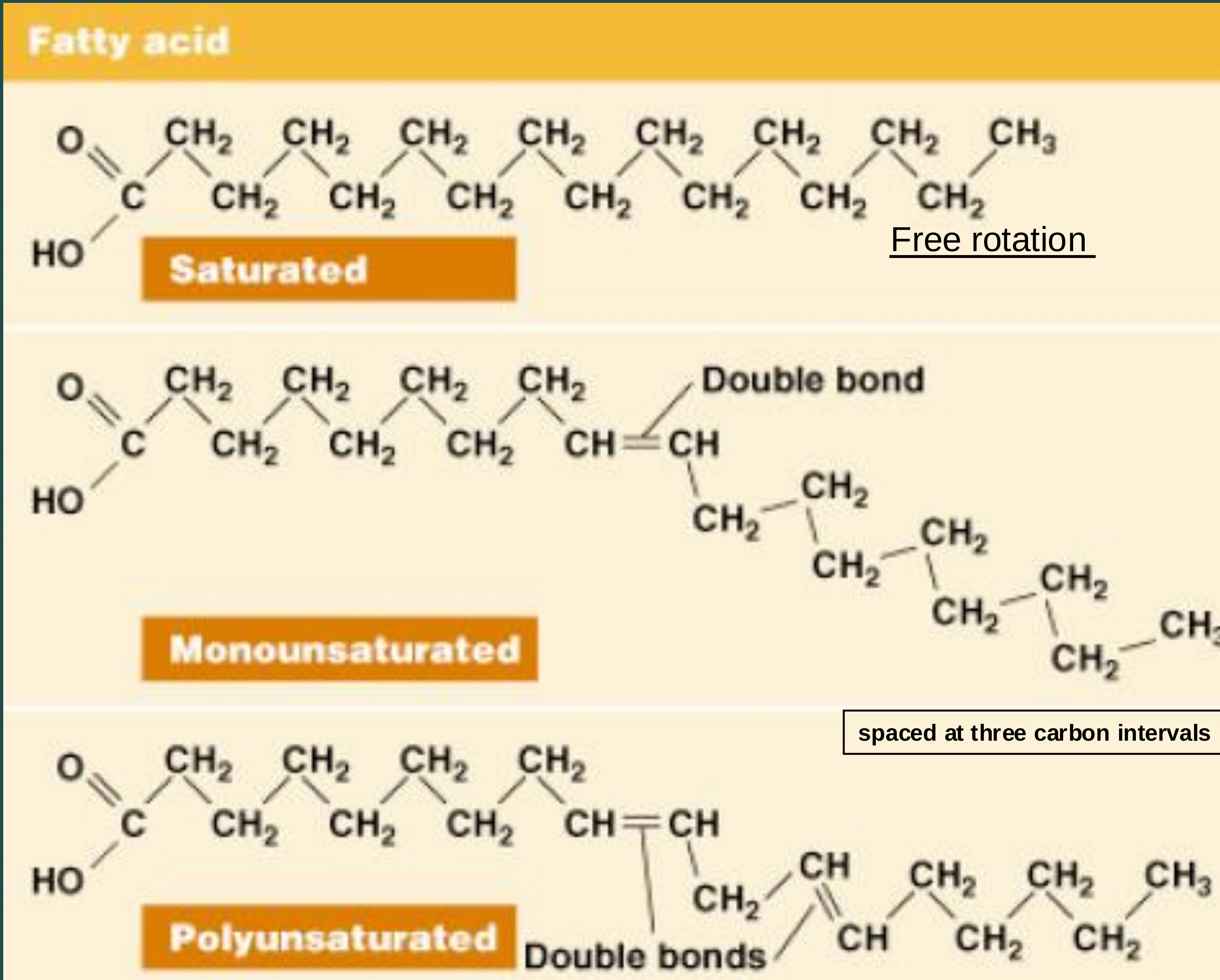
2- **Polyunsaturated** if it has more than one double bond (Examples include fish, sunflower, and corn oils). Omega-3 and Omega -6 fats are **polyunsaturated fats**.

Unsaturated fat has less energy than saturated fat.

- If the fatty acid has two or more double bonds they are always spaced at three carbon intervals.
- Free rotation around each of the carbon–carbon bonds makes saturated fatty acids extremely flexible molecules.
- Unsaturated fatty acids are slightly more abundant in nature than saturated fatty acids, especially in higher plants. Rotation around a double bond is restricted.

- The most common saturated fatty acids present in the cell are palmitic acid (C16) and stearic acid (C18). The most common unsaturated fatty acid is **oleic acid** 18:1(9).

- Animal fat contains principally saturated and monounsaturated long-chain fatty acids, whereas vegetable oils contain polyunsaturated fatty acids and monounsaturated fatty acids.



Fatty acid
Saturated
Free rotation
Double bond
Monounsaturated
spaced at three carbon intervals
Polyunsaturated
Double bonds

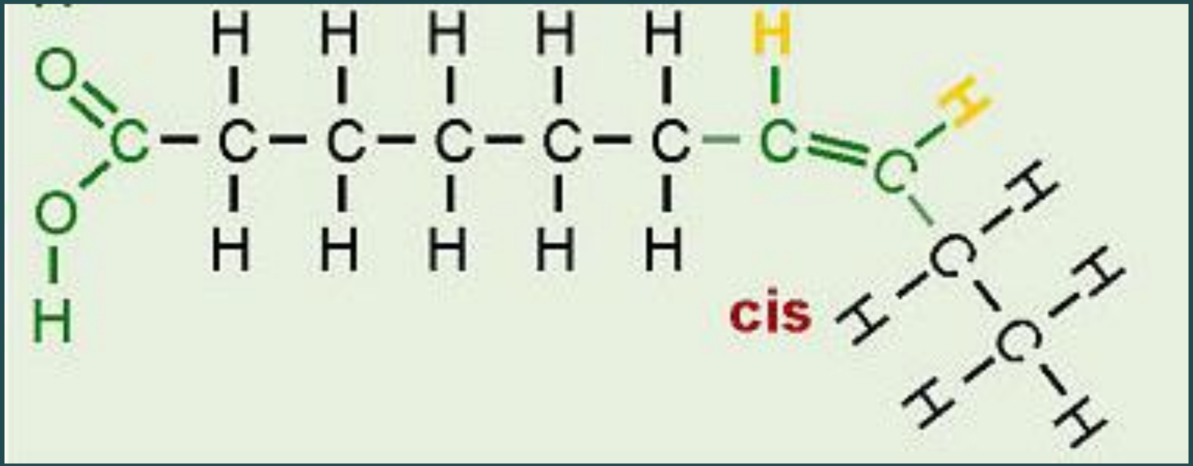
Common Biological Fatty Acids

Number of Carbons	Common Name	Systematic Name	Symbol	Structure
Saturated fatty acids				
12	Lauric acid	Dodecanoic acid	12:0	$CH_3(CH_2)_{10}COOH$
14	Myristic acid	Tetradecanoic acid	14:0	$CH_3(CH_2)_{12}COOH$
16	Palmitic acid	Hexadecanoic acid	16:0	$CH_3(CH_2)_{14}COOH$
18	Stearic acid	Octadecanoic acid	18:0	$CH_3(CH_2)_{16}COOH$
20	Arachidic acid	Eicosanoic acid	20:0	$CH_3(CH_2)_{18}COOH$
22	Behenic acid	Docosanoic acid	22:0	$CH_3(CH_2)_{20}COOH$
24	Lignoceric acid	Tetracosanoic acid	24:0	$CH_3(CH_2)_{22}COOH$
Unsaturated fatty acids (all double bonds are *cis*)				
16	Palmitoleic acid	9-Hexadecenoic acid	16:1	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$
18	Oleic acid	9-Octadecenoic acid	18:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
18	Linoleic acid	9,12-Octadecadienoic acid	18:2	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$
18	α-Linolenic acid	9,12,15-Octadecatrienoic acid	18:3	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$
18	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	18:3	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$
20	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	20:4	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$
24	Nervonic acid	15-Tetracosenoic acid	24:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$

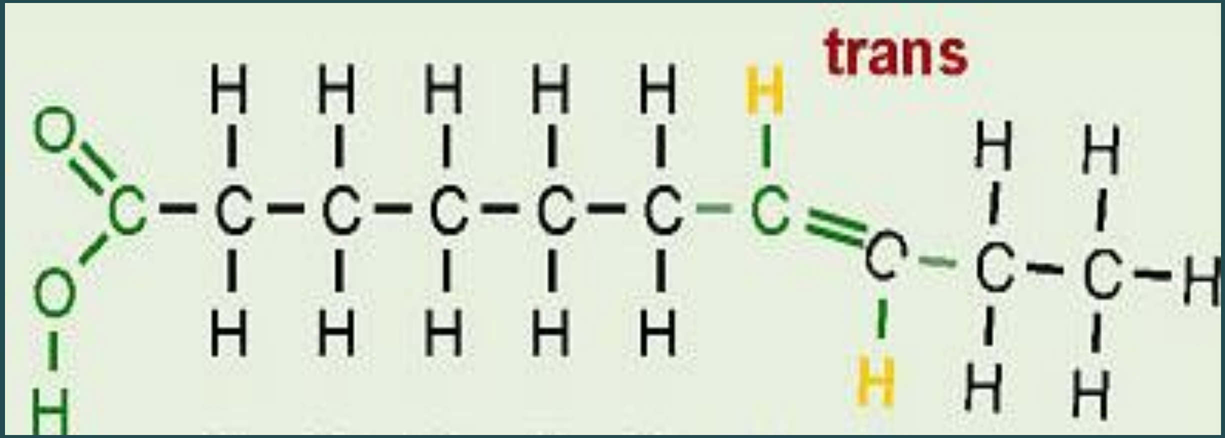
Cis & trans unsaturated fatty acids

- **Cis fatty acids:** cis double bond causes the fatty acid to bend or "kink" at that position which prevents the fatty acids from packing tightly, keeping them liquid at room temperature.
- The double bonds in most naturally occurring fatty acids are in the cis configuration.
- **Trans-fatty acids:** most trans-fatty acids are not natural and are manufactured by a process known as hydrogenation by adding atoms of hydrogen to cis unsaturated fat, eliminating the double bonds between carbon atoms and making them saturated. **Trans fats may be monounsaturated or polyunsaturated**.
- Trans fat raise LDL (bad cholesterol) levels and are linked to heart disease. Trans configuration involves the arrangement of hydrogen atoms in a more linear way, which changes the properties of the fat including the melting point, shelf life, flavor and stability. These properties are favorable for the commercial food industry such as margarine.
- Naturally-occurring trans fats are produced in the gut of some animals and foods made from these animals (e.g., milk and meat products) may contain small quantities of these fats.

Cis & Trans Fatty acids

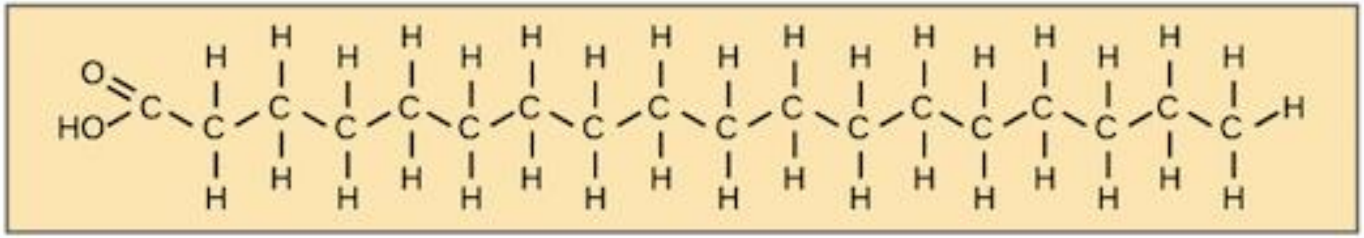


Cis double bond: hydrogen atoms are positioned on same side of double bond

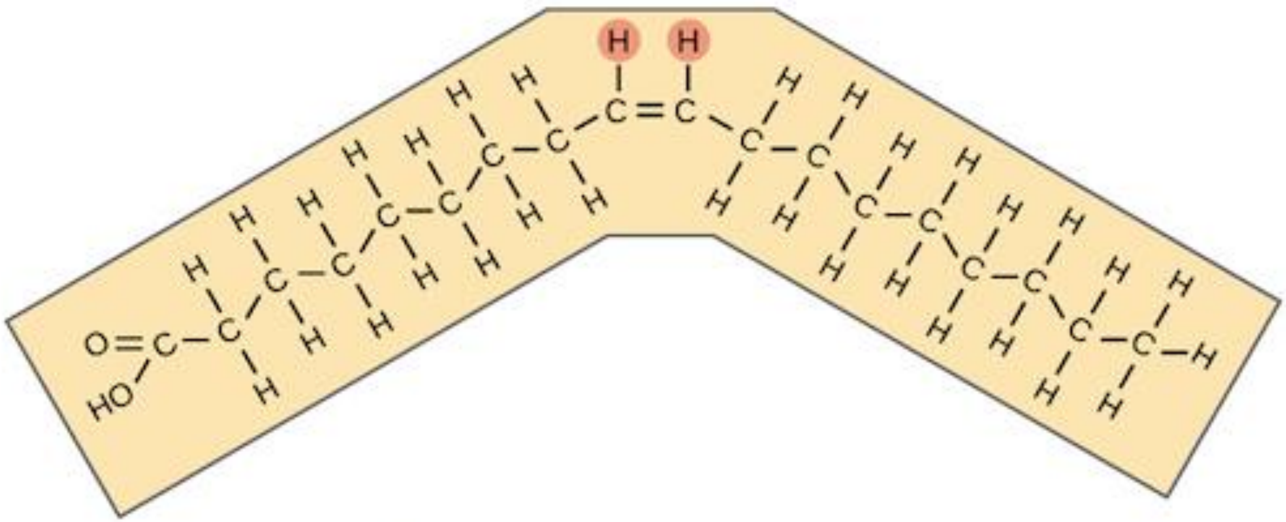


Trans double bond: hydrogen atoms are positioned on opposite side of double bond

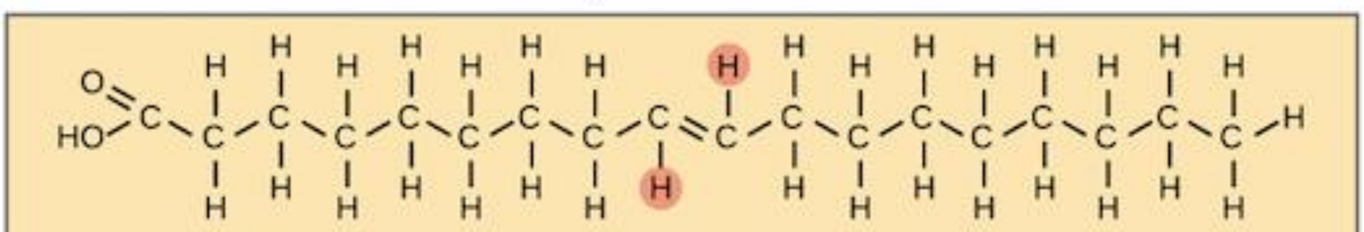
Saturated fatty acid



Cis-Unsaturated fatty acids



Trans-Unsaturated fatty acids



Numbering carbon atoms in fatty acids

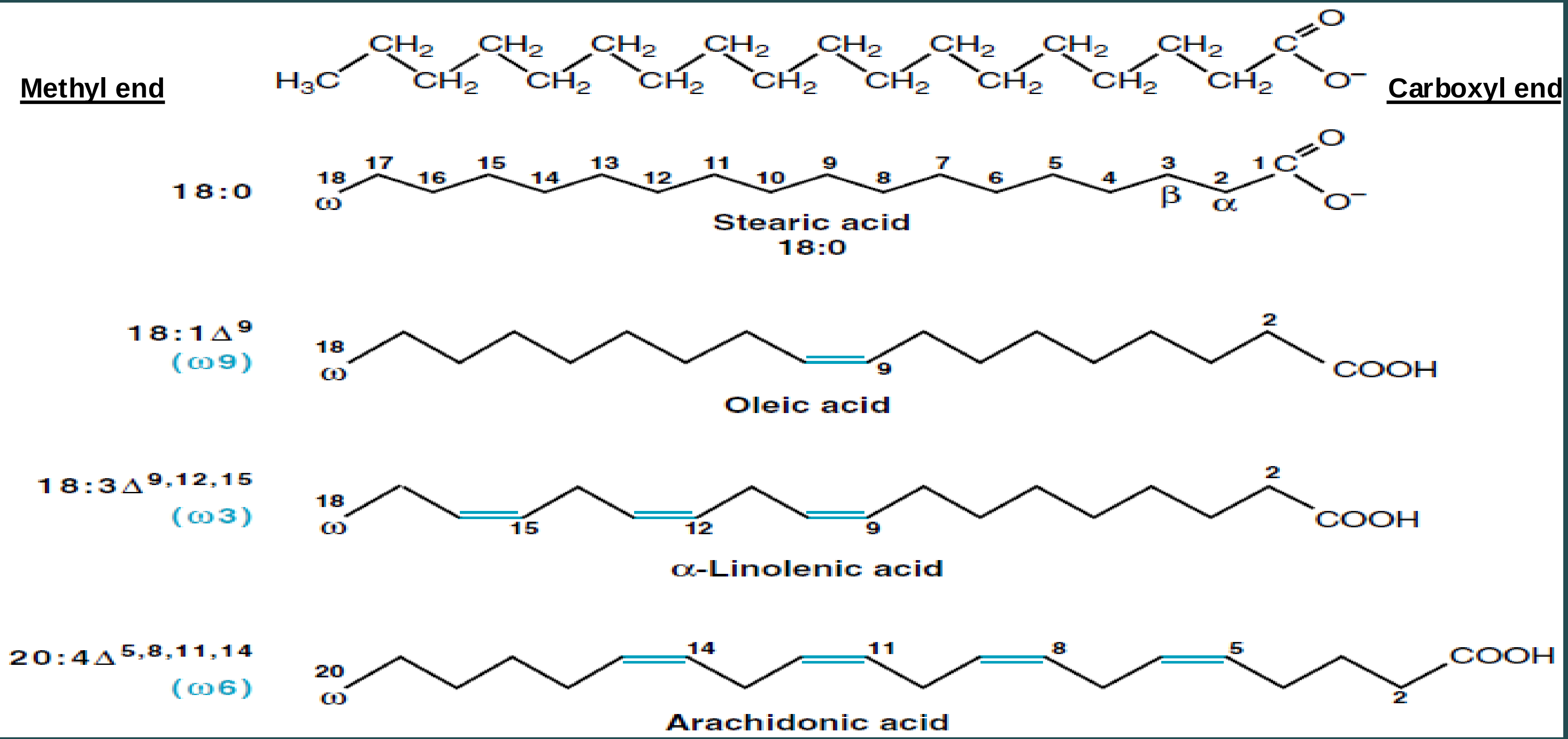
There are two system for numbering carbon atoms in fatty acids:

1- **Delta Δ numbering system:** Start numbering carbon atoms beginning with the carboxyl carbon as carbon number one.

- For example: arachidonic acid 20:4 $\Delta^{5, 8, 11, 14}$ this means that arachidonic acid has 20 carbon atoms and has 4 double bonds between carbons 5-6, 8-9, 11-12 and 14-15.

2- **Omega ω system:** The carbons in a fatty acid can also be counted beginning at the methyl-terminal end of the chain. Arachidonic acid is referred to as an ω 6 (also called an n-6) **fatty acid** because the closest double bond to the ω end begins six carbons from that end. Another ω-6 fatty acid is the essential **linoleic acid**. In contrast, **linolenic acid** is an ω-3 **fatty acid.**

Numbering carbon atoms in fatty acids



The carbons are either numbered starting with the carboxyl group or given Greek letters starting with the carbon next to the **carboxyl** group.
The **methyl** (or ω) carbon at the end of the chain is always called the ω-carbon regardless of the chain length. 18:0 refers to the number of carbon atoms which is (18) and the number of double bonds which is (0).

- **Essential fatty acids**
- Our body cant synthesize essential fatty acids
- Thus we get essential fatty acids from our diet.

- **The essential fatty acids to humans include:**

1- **linoleic acid:** is the precursor of arachidonic acid.

- Arachidonic acid is a polyunsaturated fatty acid present in the phospholipids of cell membrane and is the substrate for prostaglandin synthesis. Prostaglandin is important mediator in pain and inflammatory responses
- Prostaglandins mediate inflammation, produce pain, and induce sleep as well as being involved in the regulation of blood coagulation and reproduction.
- Nonsteroidal anti-inflammatory drugs such as aspirin act by inhibiting prostaglandin synthesis.

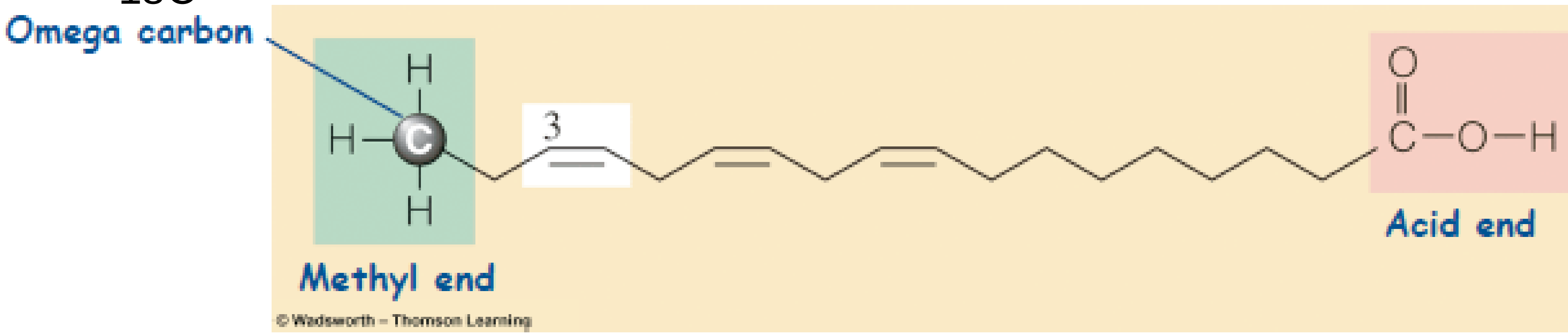
2- **α-linolenic acids** the precursor of some ω-3 fatty acids important for growth and development.

- A deficiency of linolenic acid results decreased vision and altered learning behaviours.

Essential fatty acids

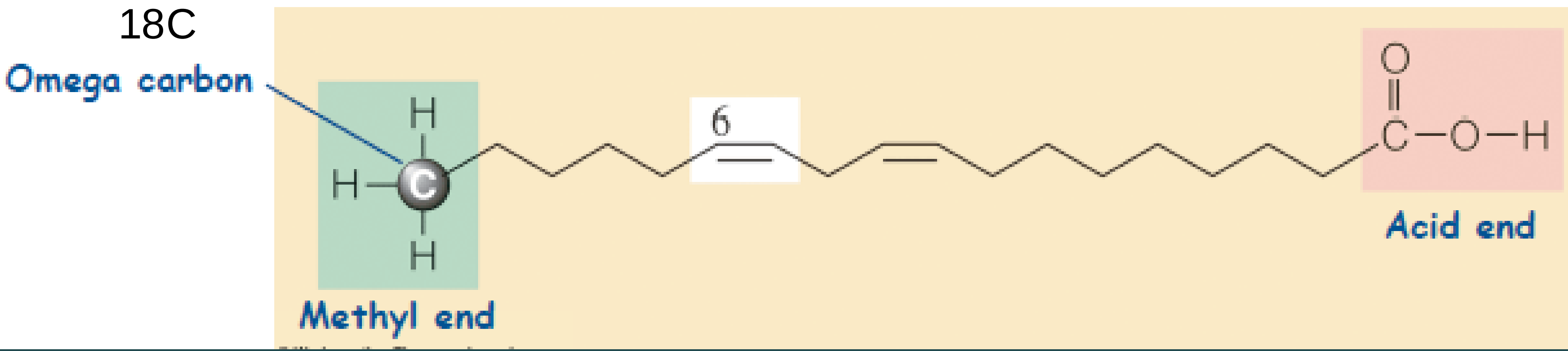
α-Linolenic acid, an omega-3 fatty acid

18C



Linoleic acid, an omega-6 fatty acid

18C



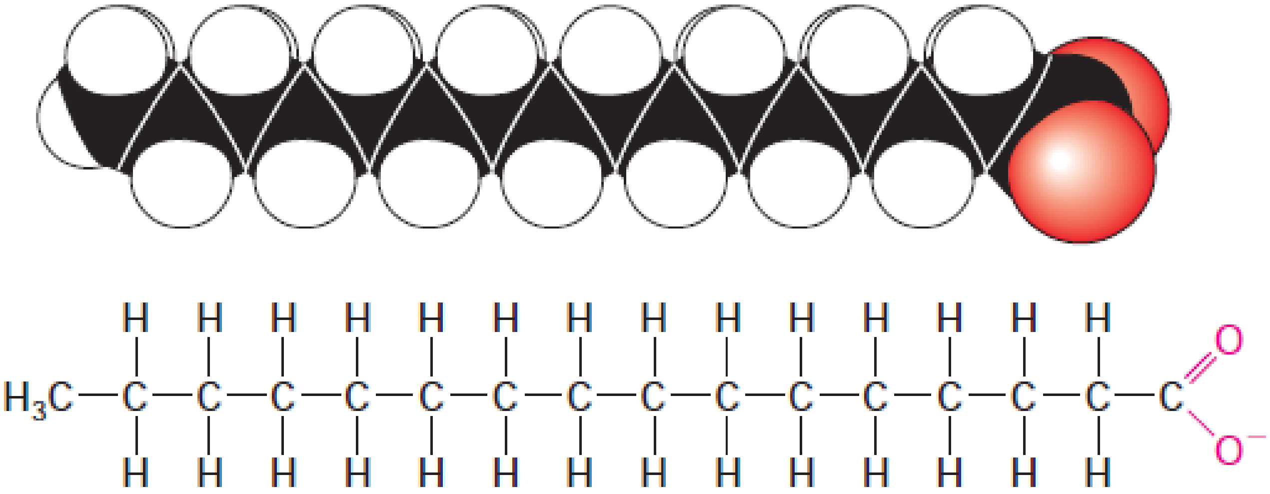
Melting Points of Saturated vs. Unsaturated Fatty Acids:

The unsaturated fatty acids have lower melting points than the saturated fatty acids.

The saturated fatty acids are relatively linear which allows fatty acid molecules to be closely packed together. As a result, close intermolecular interactions result in relatively high melting points.

On the other hand, the introduction of one or more double bonds in the hydrocarbon chain in unsaturated fatty acids results in one or more "bends" or “kink” in the molecule thus preventing these molecules to pack very closely. Thus the intermolecular interactions are much weaker than saturated molecules as a result, the melting points are much lower for unsaturated fatty acids

The addition of double bonds decreases the melting temperature (Tm) of a fatty acid (thus saturated FA are more solid at room temperature than unsaturated FA), whereas increasing the chain length increases the Tm.

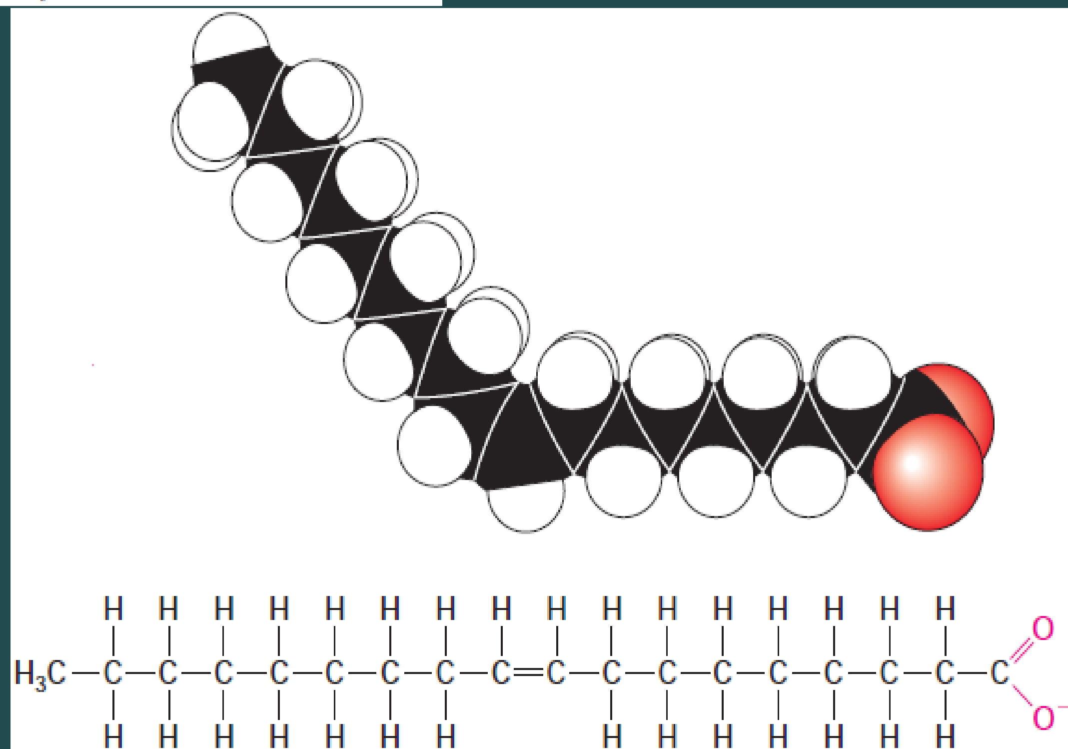


Palmitate
(ionized form of palmitic acid)

chemical structures of the ionized form of palmitic acid, a saturated fatty acid with 16 C atoms, and oleic acid, an unsaturated one with 18 C atoms.

In saturated fatty acids, the hydrocarbon chain is often linear;

The cis double bond in oleate creates a rigid kink in the hydrocarbon chain



Oleate
(ionized form of oleic acid)

Oxidation

- 1g carbohydrates produces about 4 kcal/g,
- 1g proteins produces 4 kcal/g
- 1g fats produces 9 kcal/g.
- Energy is also expressed in joules. One kilocalorie equals 4.18 kilojoules (kJ).
- **Why do lipids store more energy than carbohydrates and proteins?**
- Because of the oxidation states of the carbon atoms in each molecule. Lipids are largely hydrocarbon in nature and they represent highly reduced forms of carbon.
- All carbon atoms in glucose have oxidation states of -1, 0 or +1, **while** nearly all carbon atom in palmitic acid (a fatty acid) for example have oxidation states of -2 or -3. This means that the carbon atoms in fatty acids have more electrons around them.
- In the electron transport chain when electrons passes from one molecule to another energy is released which is then stored in the form of ATP.
- Therefore, the greater the number of electrons the more energy.

Fat vs carbohydrates in our body

1. Fat storage occupy less space than carbohydrate

- The body stores glucose as glycogen which is highly branched and glucose unites are covalently linked to each others thus occupy more space.
- Fats, on the other hand are stored as triglycerides in adipocytes (fat cells). These adipocytes can grow to large sizes. As each triglyceride molecule is not covalently linked to the other in a vacuole, they can be packed close together.

2. Fats are hydrophobic, thus fat is stored with no water associated with it.

- While in glycogen every 1 glycogen molecule is linked to about 2 grams of water.

3. Fat breakdown is less rapid than that of glucose while brain uses only glucose as a source of energy.

Glycogen