

GENERAL BIOCHEMISTRY - TOPICS

- **Biological macromolecules:**
 - ✓ **Carbohydrates**
 - ✓ **Lipids**
 - ✓ **Aminoacids and Peptides**
 - ✓ **Proteins**

- **Enzymes and enzymology**



BIOCHEMISTRY LABORATORY

- December 19th 2025, 9-11 AULA MAGNA DERMATOLOGIA -Sant'Orsola
Prof. Vadim Viviani «Bioluminescence: from biodiversity to biomedical analysis»
- January 9th 2025, 11-13 AULA MAGNA DERMATOLOGIA -Sant'Orsola
Clinical case presentations (4/5 people per group- G1 and G2)
- January 13th 2025, 9-11 AULA MAGNA DERMATOLOGIA - Sant'Orsola
Clinical case presentations (4/5 people per group- G3 and G4)
- January 15th 2025, 11-13 AULA MAGNA DERMATOLOGIA - Sant'Orsola
Prof. Antonio Pannuti «RNA in diagnostics and therapy»
- January 17th 2025, 9-11 AULA MAGNA DERMATOLOGIA - Sant'Orsola
«Mock exam – Chemistry and Biochemistry (with results discussion)»
- January 27th 2025, 9-11 AULA MAGNA DERMATOLOGIA - Sant'Orsola
Dr. Akram Ghantous «Epigenomics and Big Data: Linking the Environment with Health and Disease»

LIPIDS



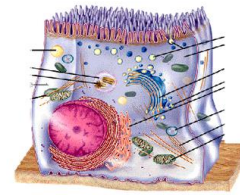
- The term lipids actually refers to a collection of organic molecules of different chemical composition.
- They are grouped together on the basis of their solubility in nonpolar solvent.

Functions

- ✓ **Energy source.** Like carbohydrates, lipids are an excellent source of energy for the body.
- ✓ **Energy storage.** Most of the energy stored in the body is in the form of lipids (triglycerides). Stored in fat cells called adipocytes, these fats are a particularly rich source of energy for the body.
- ✓ **Cell membrane structural components.** Phosphoglycerides, sphingolipids, and cholesterol make up the basic structure of all cell membranes.
- ✓ **Hormones.** The steroid hormones are critical chemical messengers that allow cells and tissues far apart to communicate.
- ✓ **Vitamins.** The lipid-soluble vitamins, A, D, E, and K, play a major role in the regulation of several critical biological processes, including blood clotting and vision.
- ✓ **Protection.** Fat serves as a shock absorber, or protective layer, for the vital organs.

Heat Production

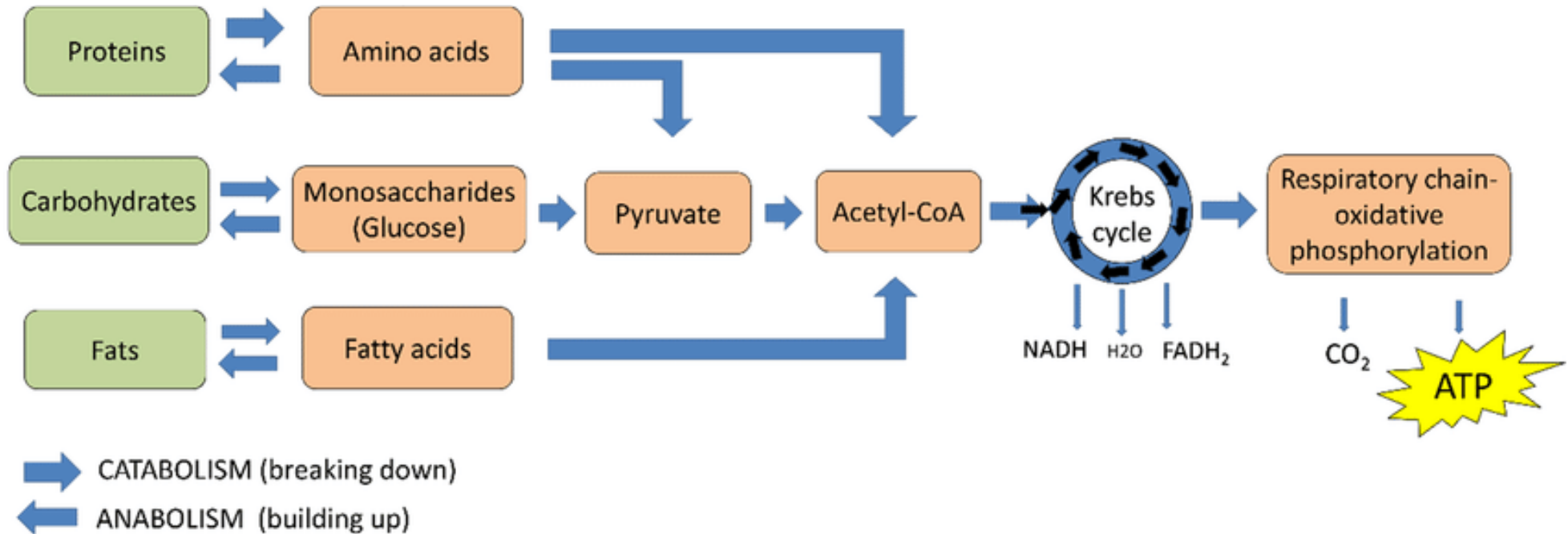
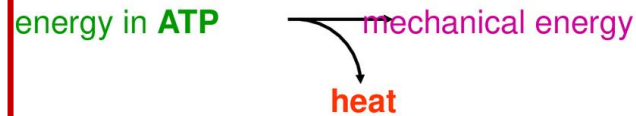
Body heat is generated from:



- 1) nutrient oxidation (ATP production)



- 2) ATP use



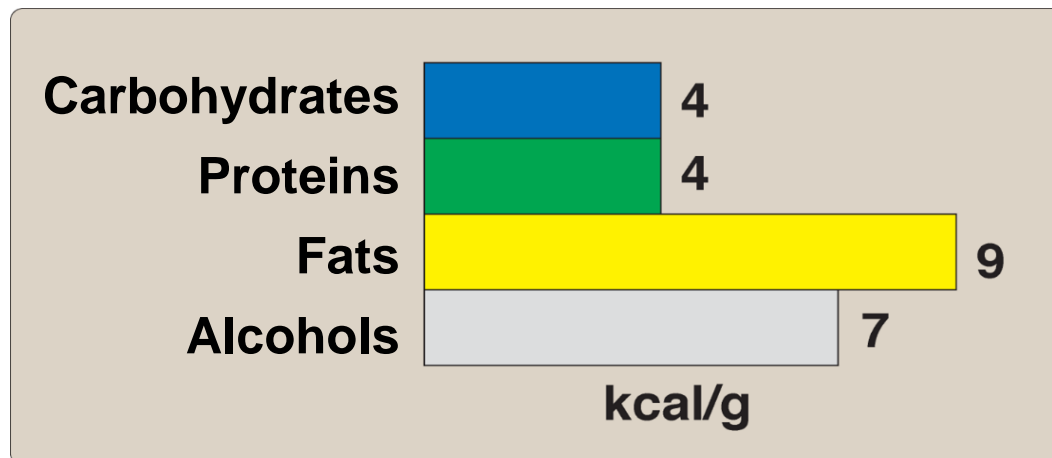
Glycogen

- Typically store a one day supply.
- Less energy per gram than for fat
 - about 70% by weight is water.

Fat

- Usually store a one month supply.
- May store **MUCH** more.
- More energy per gram - no water.
- Only released after the glycogen is gone.

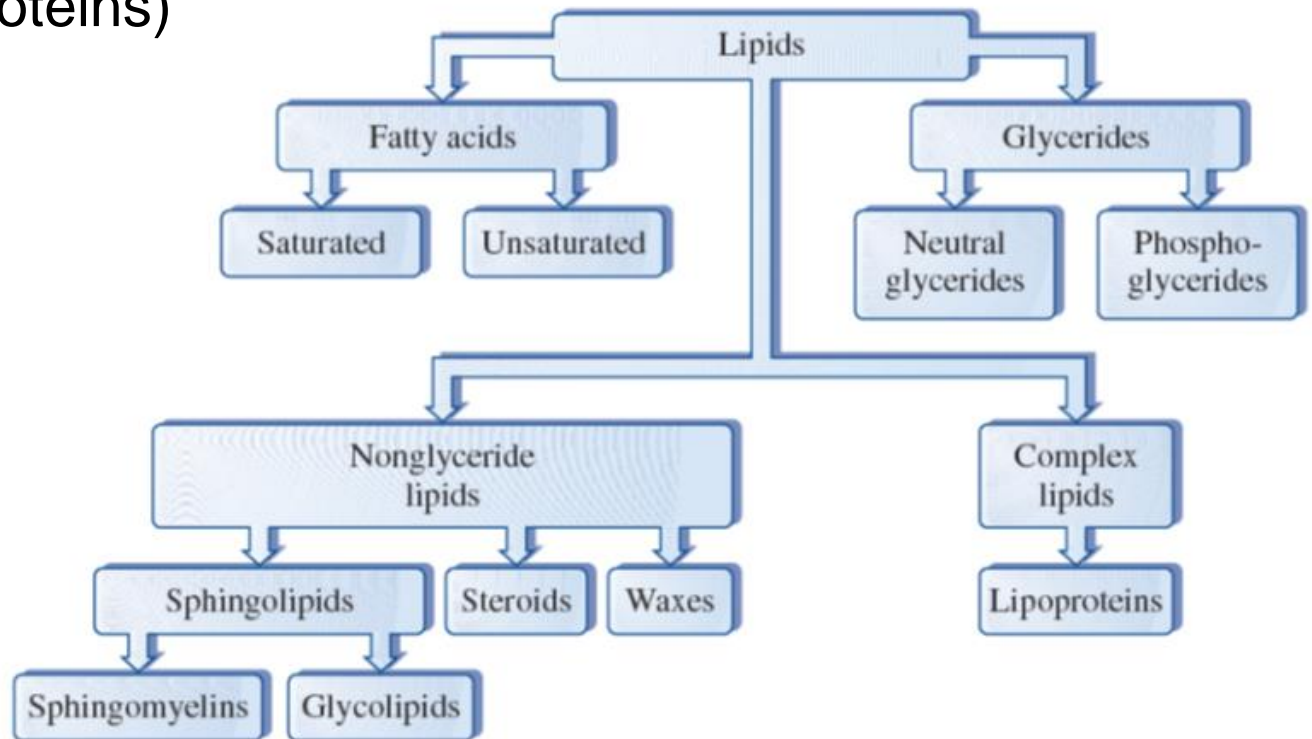
Energy value of nutrients



LIPIDS

Four main types:

- **Fatty acids** (saturated and unsaturated)
- **Glycerides** (glycerol-containing lipids)
- **Nonglyceride lipids** (sphingolipids, steroids, waxes)
- **Complex lipids** (lipoproteins)



Fatty acids

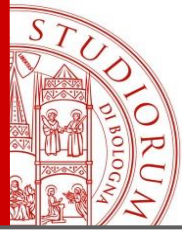


**Hydrophobic
hydrocarbon chain**



**Hydrophilic
carboxylic group
(ionized at pH 7)**

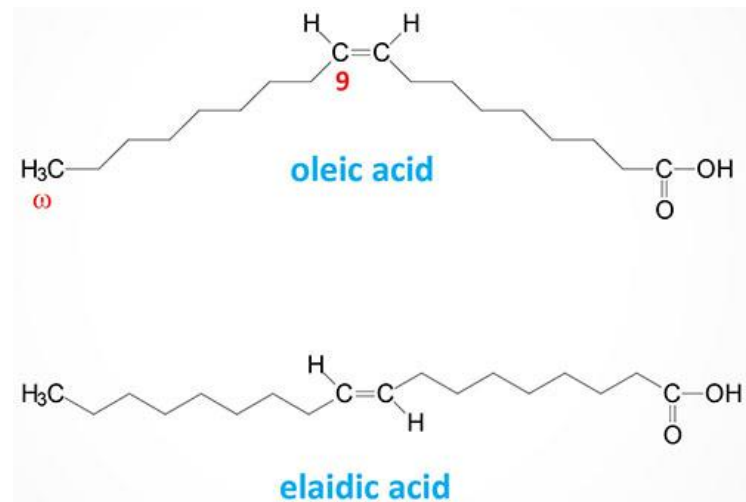
- Fatty acids are long-chain monocarboxylic acids, usually containing 12 – 24 not branched C atoms.
- In living organisms are found free only in small quantities, more often are present as constituents of lipids (covalently linked to other chemical groups).



FATTY ACIDS ARE CLASSIFIED ACCORDING TO THE STRUCTURE OF THE HYDROCARBON CHAIN

- **Length (n. of C atoms of the fatty acid):** short (1-5), medium (6-12), long (13-20) and very long (>20) C chain fatty acids
- **Presence of double bonds between C atoms:**
 - **saturated fatty acids** – no double bonds:
 - **monounsaturated fatty acids** - 1 double bond (C=C)
 - **polyunsaturated fatty acids** - at least 2 double bonds

The double bonds found in almost all naturally occurring unsaturated fatty acids are in the CIS CONFIGURATION.



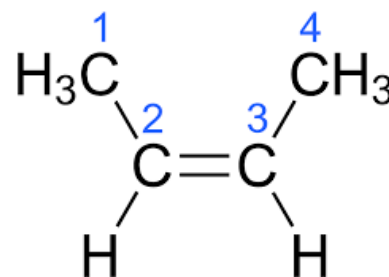


FATTY ACIDS ARE CLASSIFIED ACCORDING TO THE STRUCTURE OF THE HYDROCARBON CHAIN

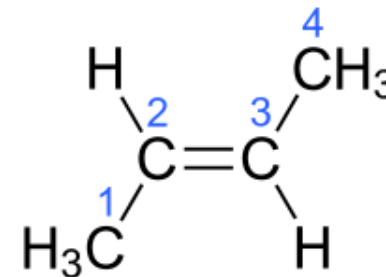
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CIS-TRANS ISOMERISM

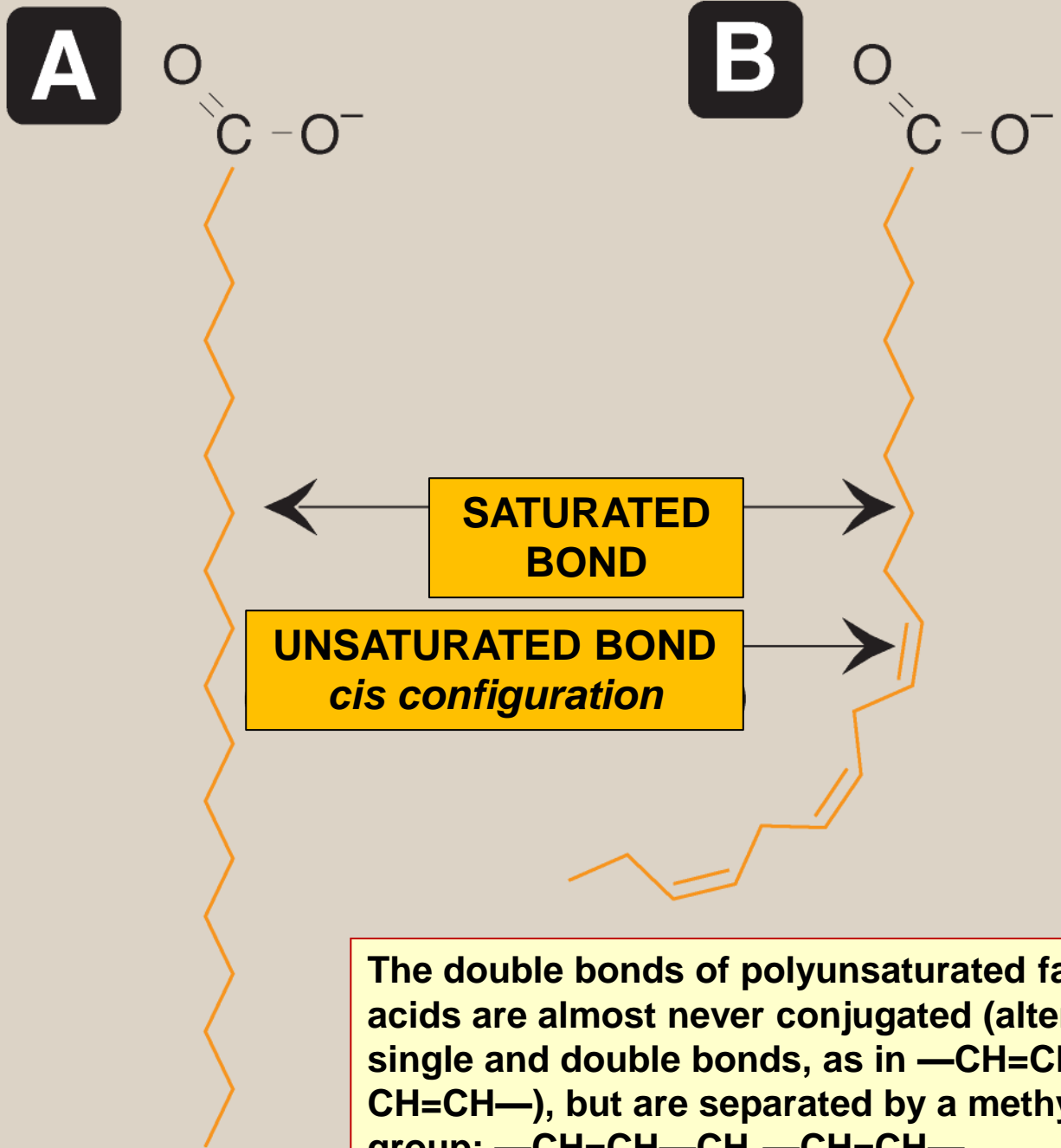
Cis bond, unlike the *trans* bond, generates a rigid angle in the hydrocarbon chain



cis 2-butene

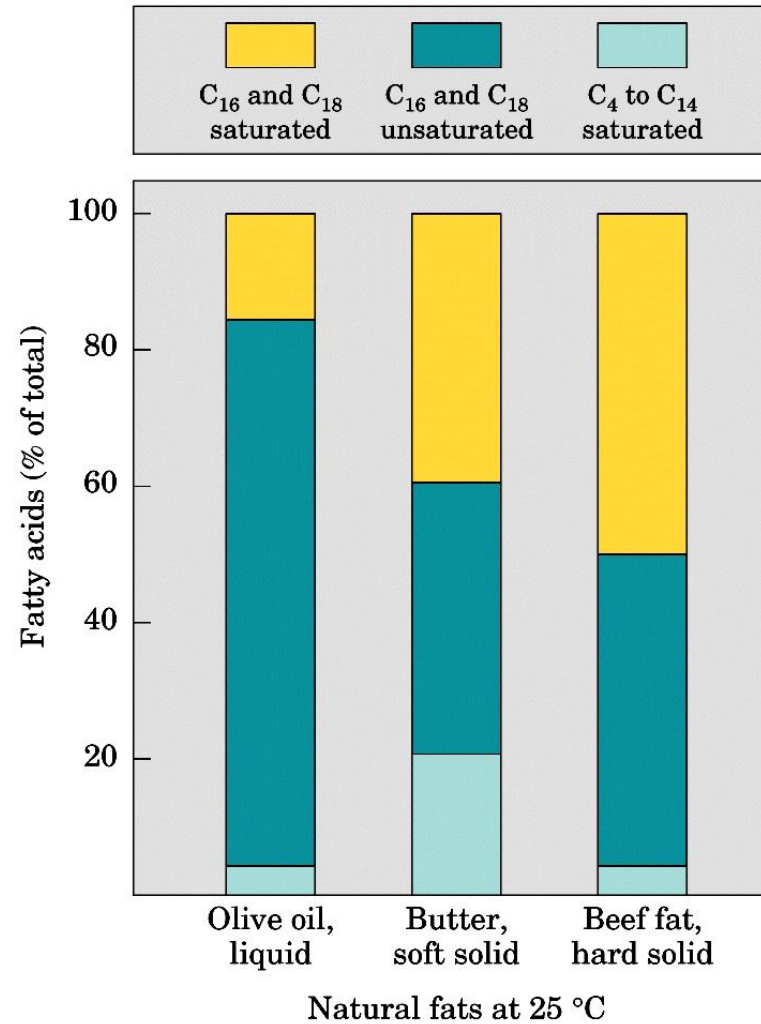


trans 2-butene



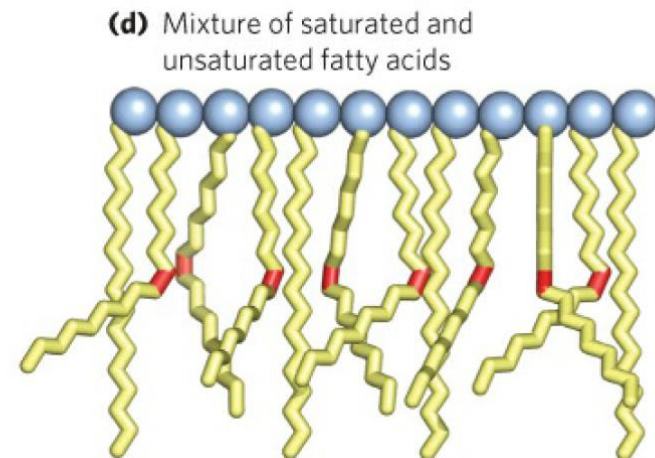
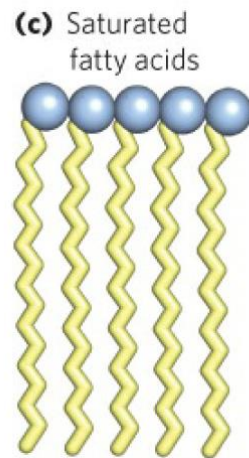
The double bonds of polyunsaturated fatty acids are almost never conjugated (alternating single and double bonds, as in $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$), but are separated by a methylene group: $-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}=\text{CH}-$.

PHYSICAL PROPERTIES



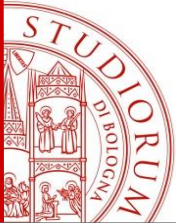
- **Saturated and long fatty acids** are generally **SOLID** at room temperature
- **Unsaturated or short fatty acids** are generally **LIQUIDS** at room temperature

- Melting points of both saturated and unsaturated fatty acids increase as the number of carbon atoms in the chain increases.
- The melting points of unsaturated fatty acids are lower than those of the corresponding saturated fatty acid with the same number of carbon atoms.
- As the number of double bonds in the chain increases, the corresponding melting point decreases.



Name	Structure	Mp (°C)
Stearic acid (0 C=C)		69
Oleic acid (1 C=C)		4
Linoleic acid (2 C=C)		-5
Linolenic acid (3 C=C)		-11

Increasing number of double bonds

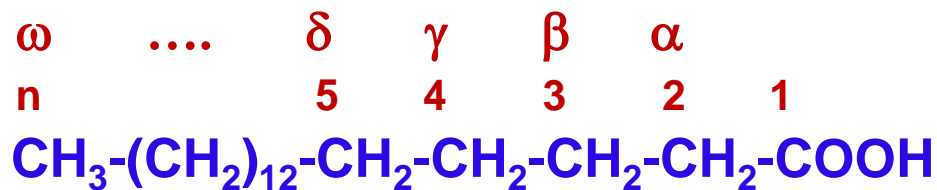


Numbering C atoms

-with numbers: beginning with carboxylic C (terminal $-\text{CH}_3$ is n)

-with the letters of the Greek alphabet:

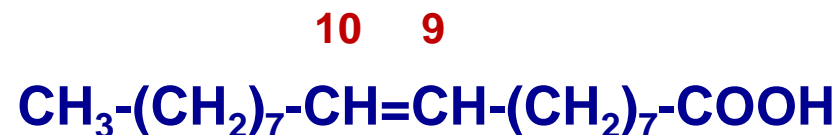
Starting from the C atom near the carboxyl group α (terminal $-\text{CH}_3$ is ω)



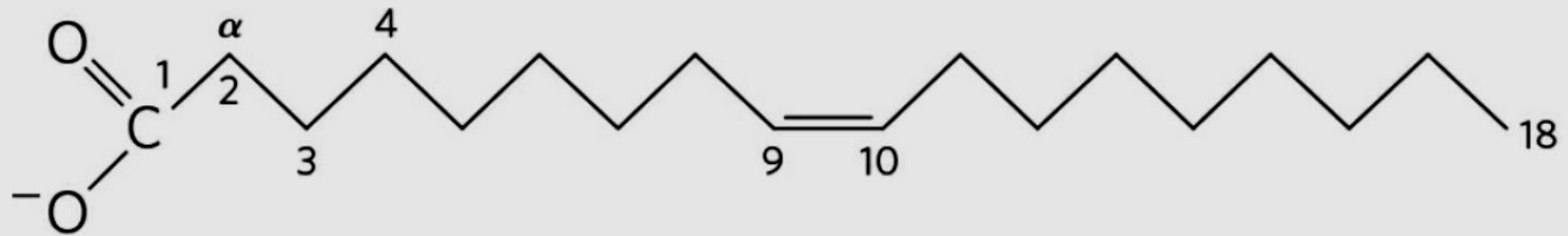
Stearic Acid C18:0

A fatty acid is identified by two numbers indicating the **number of carbon atoms in the chain and the number of double bonds**, separated by the two points.

The positions of any double bonds, designated Δ (delta), are specified relative to C-1 by the number indicating the lower-numbered carbon in the double bond.



Oleic acid C18:1 Δ^9

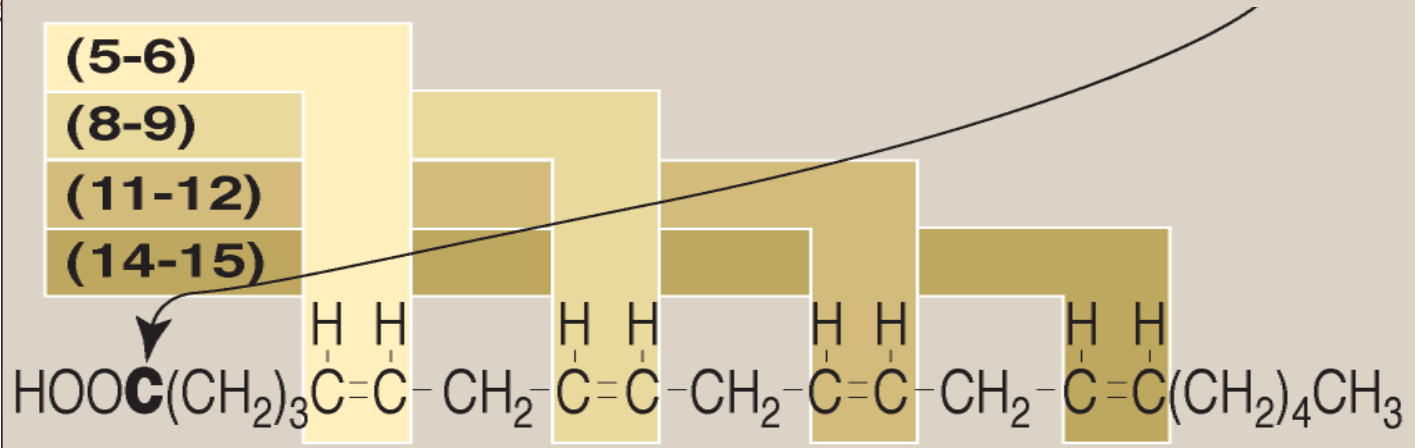


18:1(Δ^9) *cis*-9-Octadecenoic acid

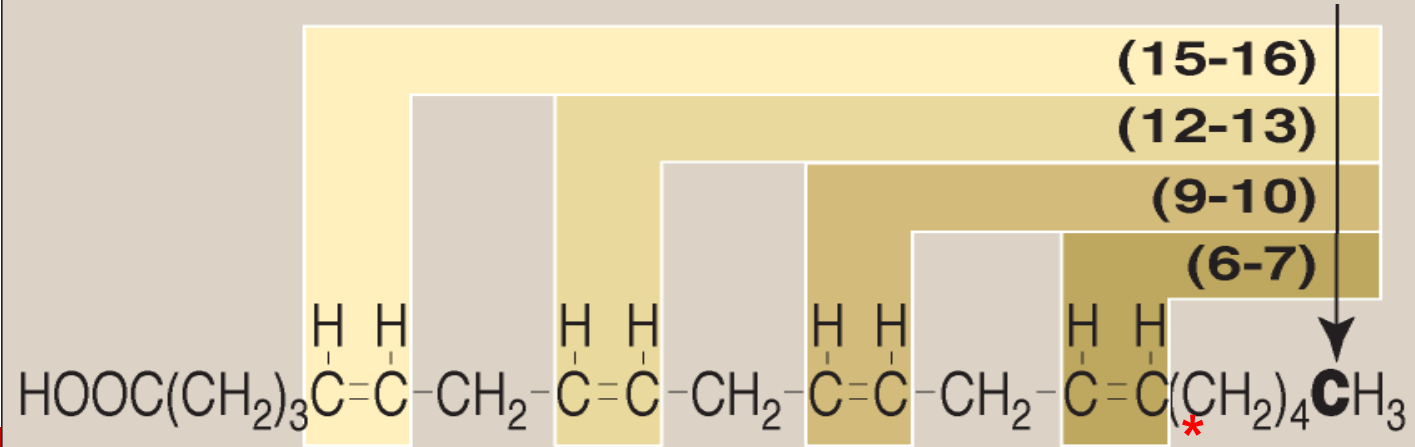


Arachidonic acid
C20:4 $\Delta^{5,8,11,14}$

A double bonds between carbon atoms numbered from carboxylic carbon



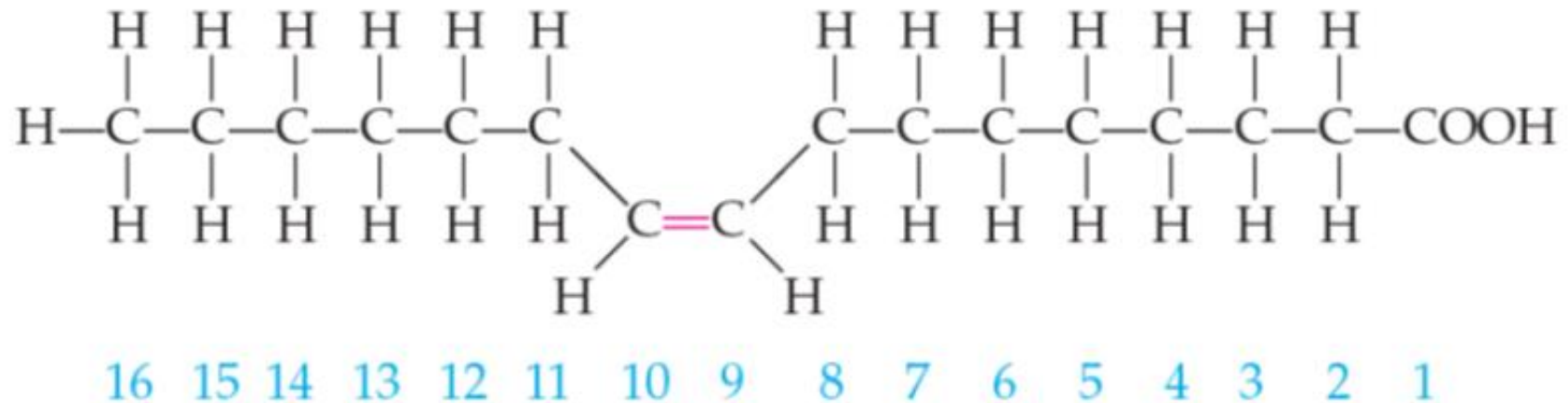
B the double bonds between the carbon atoms numbered starting from the end with the -CH₃ (ω)



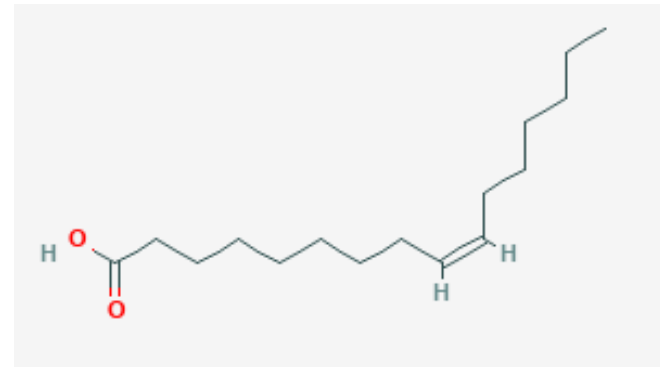
Arachidonic acid
C20:4 ω -6

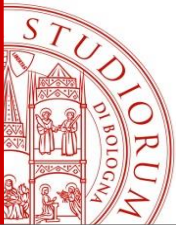
*starting from the terminal -CH₃ we find the first double bond in position ω -6

cis-9-hexadecenoic acid, commonly called palmitoleic acid



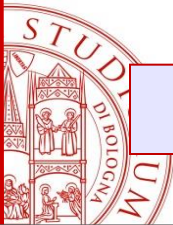
C16:1 Δ^9 or ω -6.





IUPAC numerical multiplier

Number	Multiplier	Number	Multiplier
1	mono-	32	dotriaconta-
2	di-	40	tetraconta-
3	tri-	50	pentaconta-
4	tetra-	60	hexaconta-
5	penta-	70	heptaconta-
6	hexa-	80	octaconta-
7	hepta-	90	nonaconta-
8	octa-	100	hecta-
9	nona-	200	dicta-
10	deca-	300	tricta-
11	undeca-	400	tetracta-
12	dodeca-	500	pentacta-
13	trideca-	600	hexacta-
14	tetradeca-	700	heptacta-
15	pentadeca-	800	octacta-
16	hexadeca-	900	nonacta-
17	heptadeca-	1000	killa-
18	octadeca-	2000	dilla-
19	nonadeca-	3000	trilla-
20	icosa-/elcosa-	4000	tetralla-
21	henicosa-/henelcosa-	5000	pentalia-
22	docosa-	6000	hexalia-
23	tricoso-	7000	heptalia-
30	triaconta-	8000	octalia-
31	hentriaconta-	9000	nonalia-



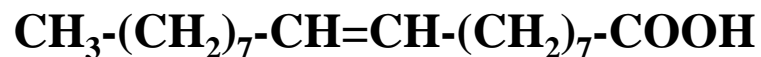
Common fatty acids with 18 C atoms

10 9



stearic acid (18:0)

10 9

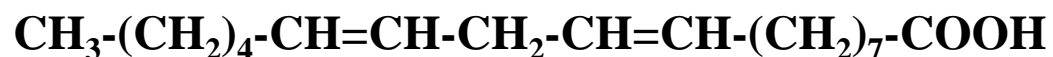


oleic acid (18:1 *cis*- Δ^9) n-9 (ω - 9)

n-6 (ω 6)

Essential fatty acid

13 12 10 9



linoleic acid (18:2 *cis*- $\Delta^{9,12}$)

n-6 (ω - 6)

n-3 (ω - 3)

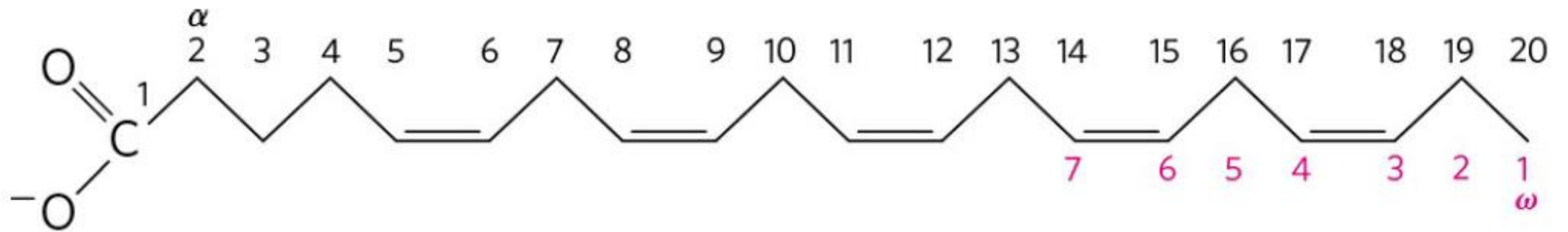
Essential fatty acid

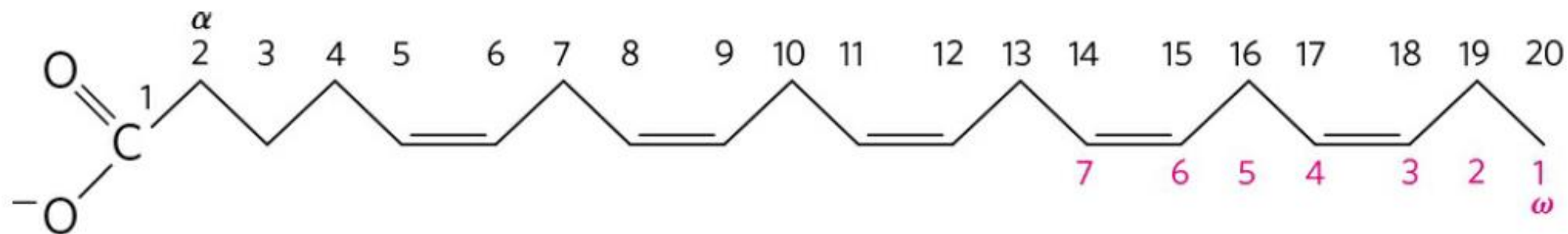
16 15 13 12 10 9



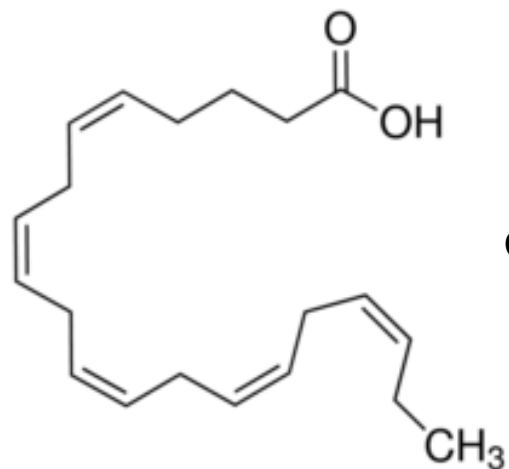
n-3 (ω - 3)

α -linolenic acid (18:3 *cis*- $\Delta^{9,12,15}$)





20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA)



cis-5,8,11,14,17-Eicosapentenoic acid



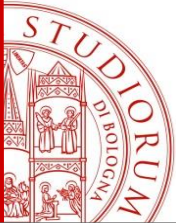
NOMENCLATURE

COMMON NAME

IUPAC NAME

C4:0	butirric acid	butanoic acid	CH₃(CH₂)₂COOH
C14:0	myristic acid	tetradecanoic acid	CH₃(CH₂)₁₂COOH
C16:0	palmitic acid	hexadecanoic acid	CH₃(CH₂)₁₄COOH
C18:0	stearic acid	octadecanoic acid	CH₃(CH₂)₁₆COOH
C20:0	arachidonic acid	eicosanoic acid	CH₃(CH₂)₁₈COOH
C24:0	lignoceric acid	tetracosanoic acid	CH₃(CH₂)₂₂COOH
C16:1 Δ⁹	palmitoleic acid	<i>cis</i> 9-hexadecenoic acid	
C18:1 Δ⁹	oleic acid	<i>cis</i> 9-octadecenoic acid	
C18:2 Δ^{9,12}	linoleic acid	<i>cis</i> 9,12-octadecadienoic acid	
C18:3 Δ^{9,12,15}	α-linolenic acid (ALA)	<i>cis</i> 9,12,15-octadecatrienoic acid	
C20:4 Δ^{5,8,11,14}	arachidonic acid	<i>cis</i> 5,8,11,14-eicosatetraenoic acid	
C20:5 Δ^{5,8,11,14,17}		<i>cis</i> 5,8,11,14,17-eicosapentaenoic acid (EPA)	
C22:6 Δ^{4,7,10,13,16,19}		<i>cis</i> 4,7,10,13,16,19-docosaesaenoic acid (DHA)	

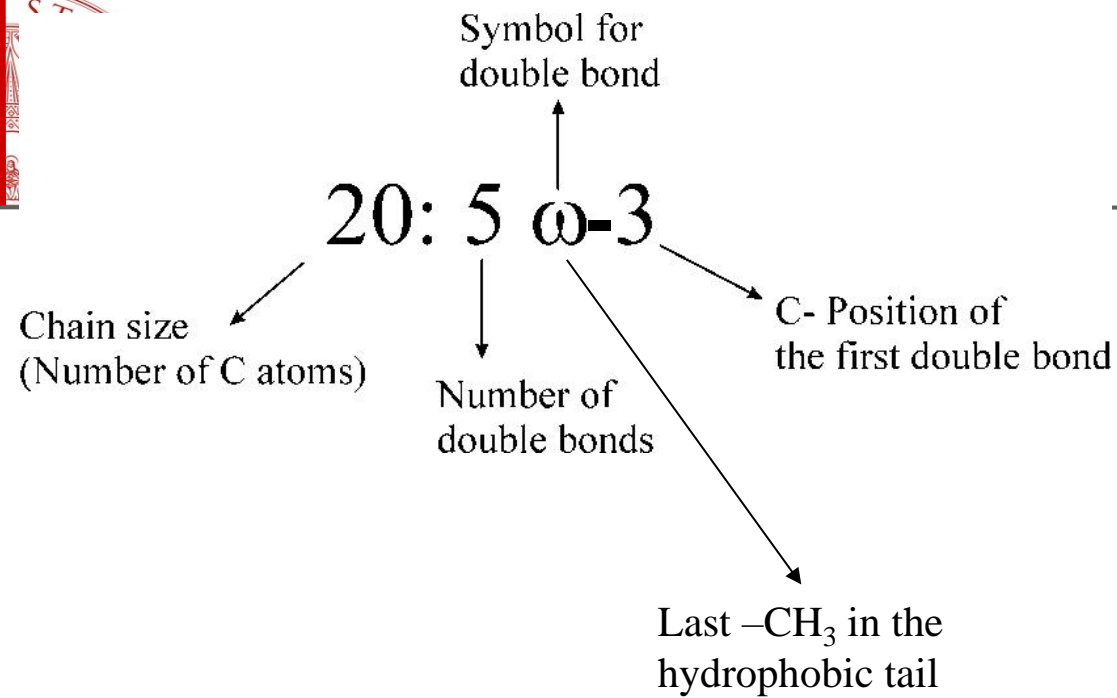
NOTE: being in ionic form at physiological pH, the more correct would be
palmitate instead of palmitic acid
stearate instead of stearic acid
oleate instead of oleic acid



IUPAC NOMENCLATURE FOR FATTY ACIDS

- 1) Naming of fatty acid is based on the number of C atoms present in the hydrocarbon chain
- 2) **Saturated fatty acids** end with suffix **-anoic**, e.g. octadecanoic acid (stearic acid)
- 3) **Unsaturated fatty acids** with double bonds end with suffix **-enoic**, e.g. octadecenoic acid
- 4) Carbon atoms are numbered **from the carboxyl carbon** (carbon n.1)
- 5) Add the number of C in which a double bond is present, e.g. *cis*-9-octadecenoic acid (oleic acid)

NOTE: *cis* configuration is the naturally present in all fatty acids while *trans* configuration is produced as by-product by partially hydrogenation that produces a mix of *trans* and saturated bonds (solid at room temperature).



A) SATURATED



B) MONOUNSATURATED



C) POLYUNSATURATED



Common Saturated Fatty Acids

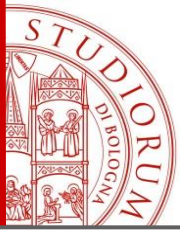
Common Name	IUPAC Name	Melting Point (°C)	Molar Mass	Condensed Formula
Capric	Decanoic	32	172.26	CH ₃ (CH ₂) ₈ COOH
Lauric	Dodecanoic	44	200.32	CH ₃ (CH ₂) ₁₀ COOH
Myristic	Tetradecanoic	54	228.37	CH ₃ (CH ₂) ₁₂ COOH
Palmitic	Hexadecanoic	63	256.42	CH ₃ (CH ₂) ₁₄ COOH
Stearic	Octadecanoic	70	284.48	CH ₃ (CH ₂) ₁₆ COOH
Arachidic	Eicosanoic	77	312.53	CH ₃ (CH ₂) ₁₈ COOH

Common Unsaturated Fatty Acids

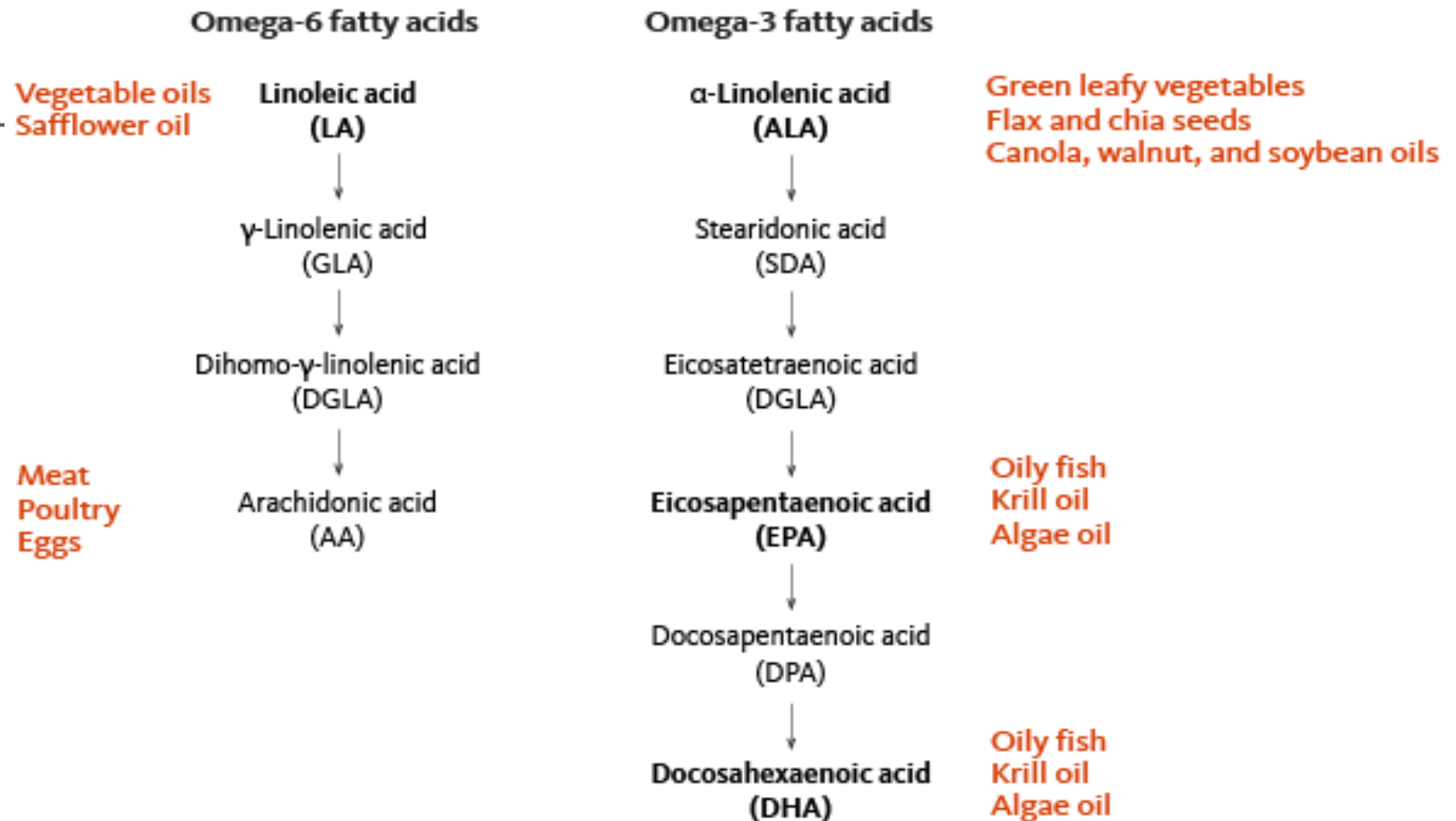
Common Name	IUPAC Name	Melting Point (°C)	Molar Mass	Number of Double Bonds	Position of Double Bond(s)
Palmitoleic	<i>cis</i> -9-Hexadecenoic	0	254.41	1	9
Oleic	<i>cis</i> -9-Octadecenoic	16	282.46	1	9
Linoleic	<i>cis,cis</i> -9,12-Octadecadienoic	5	280.45	2	9, 12
Linolenic	All <i>cis</i> -9,12,15-Octadecatrienoic	-11	278.43	3	9, 12, 15
Arachidonic	All <i>cis</i> -5,8,11,14-Eicosatetraenoic	-50	304.47	4	5, 8, 11, 14

Condensed Formula

Palmitoleic	CH ₃ (CH ₂) ₅ CH = CH(CH ₂) ₇ COOH
Oleic	CH ₃ (CH ₂) ₇ CH = CH(CH ₂) ₇ COOH
Linoleic	CH ₃ (CH ₂) ₄ CH = CH—CH ₂ —CH = CH(CH ₂) ₇ COOH
Linolenic	CH ₃ CH ₂ CH = CH—CH ₂ —CH = CH—CH ₂ —CH = CH(CH ₂) ₇ COOH
Arachidonic	CH ₃ (CH ₂) ₄ CH = CH—CH ₂ —CH = CH—CH ₂ —CH = CH—CH ₂ —CH = CH—(CH ₂) ₃ COOH



ESSENTIAL FATTY ACIDS



Omega-6 (n-6) and omega-3 (n-3) fatty acids comprise the two classes of essential fatty acids (EFA). The parent compounds of each class, linoleic acid (LA) and α -linolenic acid (ALA) (bold font), give rise to longer chain derivatives inside the body. Due to low efficiency of conversion of ALA to the long-chain omega-3 PUFA, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), it is recommended to obtain EPA and DHA from additional sources.

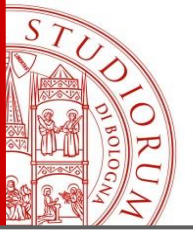
ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

- Polyunsaturated fatty acids(ω -3 e ω -6)
- Monounsaturated fatty acids (EVOO)

	Magnitude of the effect	Level of evidence	References
Lifestyle interventions to reduce TC and LDL-C levels			
Reduce dietary saturated fat	+++	A	63
Reduce dietary trans fat	+++	A	64
Increase dietary fibre	++	A	65
Reduce dietary cholesterol	++	B	66
Utilize functional foods enriched with phytosterols	+++	A	67
Reduce excessive body weight	+	B	68
Utilize soy protein products	+	B	69
Increase habitual physical activity	+	A	70
Utilize red yeast rice supplements	+	B	71, 72
Utilize policosanol supplements	-	B	73
Lifestyle interventions to reduce TG levels			
Reduce excessive body weight	+++	A	68
Reduce alcohol intake	+++	A	74
Reduce intake of mono- and disaccharides	+++	A	75, 76
Increase habitual physical activity	++	A	77
Reduce total amount of dietary carbohydrate	++	A	78
Utilize supplements of n-3 polyunsaturated fat	++	A	79
Replace saturated fat with mono- or polyunsaturated fat	+	B	63
Lifestyle interventions to increase HDL-C levels			
Reduce dietary trans fat	+++	A	64
Increase habitual physical activity	+++	A	77
Reduce excessive body weight	++	A	68
Reduce dietary carbohydrates and replace them with unsaturated fat	++	A	78
Use alcohol with moderation	++	B	80
Among carbohydrate-rich foods prefer those with low glycaemic index and high fibre content	+	C	-
Quit smoking	+	B	81
Reduce intake of mono- and disaccharides	+	C	-

+++ = general agreement on the effects on lipid levels.
 ++ = less pronounced effects on lipid levels; weight of evidence/opinion is in favour of efficacy.
 + = conflicting evidence; efficacy is less well established by evidence/opinion.
 - = not effective and/or uncertainties regarding safety.
 HDL-C = high-density lipoprotein-cholesterol; LDL-C = low-density lipoprotein-cholesterol; TG = triglyceride.



Relative Priority of Consumption

Essential: High Priority

Non-essential: Low Priority
(avoid)

Omega-3 PUFA

Some food sources are fatty fish and shellfish, flaxseed, walnuts, and canola oil.

- Eicosapentaenoic acid (EPA)-fish
- Docosahexaenoic acid (DHA)-fish
- α -Linolenic acid (ALA)-flax seed, walnuts
- Stearidonic acid (STD)-canola, fish
- Eicosatrienoic acid (ETE)-seafood
- Eicosatetraenoic acid (ETA)-seafood
- Docosapentaenoic acid (DPA)-seafood

Most Beneficial

- ▲ Cardioprotective
- ▲ Does not promote obesity

Omega-6 PUFA

Some food sources are nuts, seeds and vegetable oils such as sunflower, safflower, corn and soybean oils.

- Linoleic acid-seeds
- Dihomo-gamma-linolenic acid-metabolic product
- Arachidonic acid-metabolic product

Mono-unsaturated FA

Some food sources are canola oil and olive oil.

- Oleic acid-olive, canola oil
- Palmitoleic acid-vegetable oil

Saturated FA

Some sources are animal-based foods such as cream, butter, cheese, and fatty meats.

- Lauric acid-coconut, palm oil
- Myristic acid-dairy fat
- Palmitic acid-meat
- Stearic acid-meat

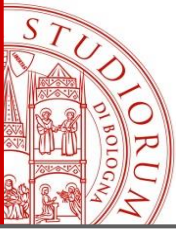
Trans-Saturated FA

Some food sources are margarine, fried foods, baked goods and processed foods.

- Elaidic acid-preservative
- Partially hydrogenated plant and vegetable oils

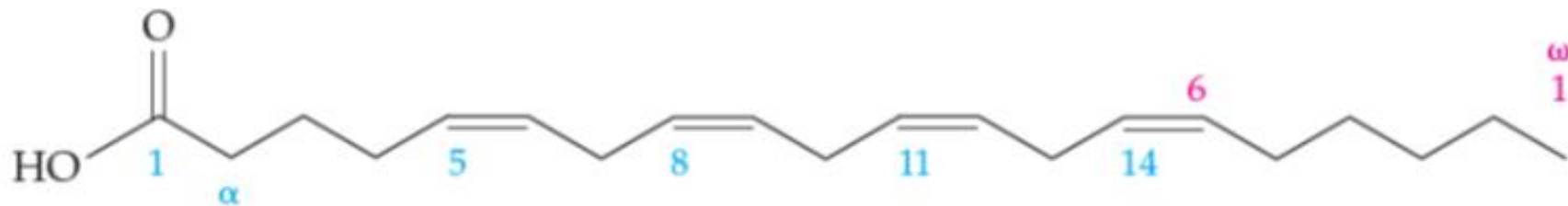
Most Harmful

- Promotes: ▼ Obesity
- ▼ Dyslipidemia
 - ▼ Atherosclerosis



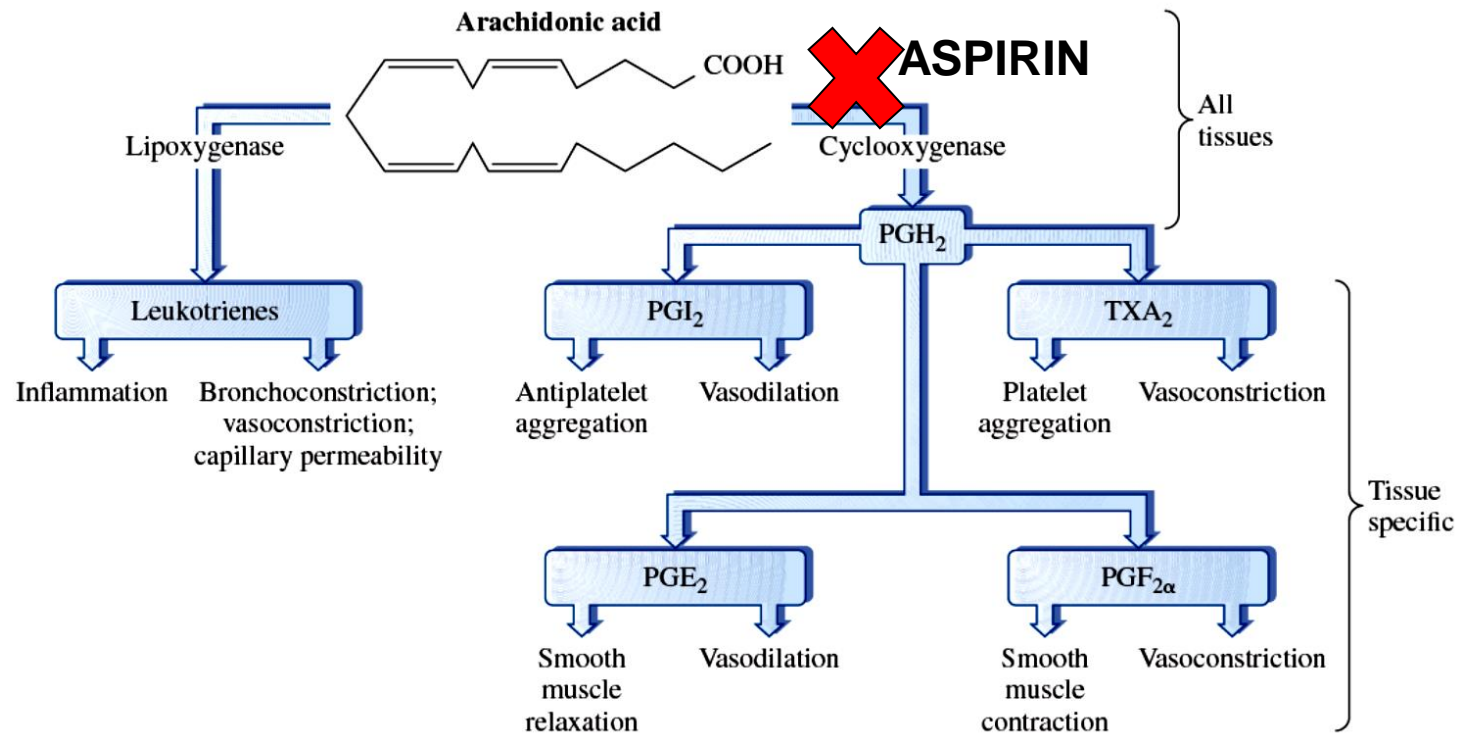
Eicosanoids: Prostaglandins, Leukotrienes, and Thromboxanes

- α -linolenic acid and linoleic acid, called the **essential fatty acids (EFA)**, are necessary for specific biochemical functions and must be supplied in the diet.
- Linoleic acid is required for the biosynthesis of **arachidonic acid**, the precursor of a class of hormone-like molecules known as **eicosanoids**.
- The eicosanoids include three groups of structurally related compounds: **prostaglandins, leukotrienes, and thromboxanes**.

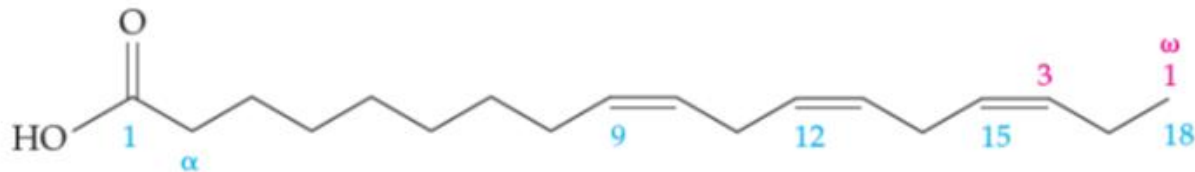


All *cis*-5,8,11,14-Eicosatetraenoic acid
(Arachidonic acid)

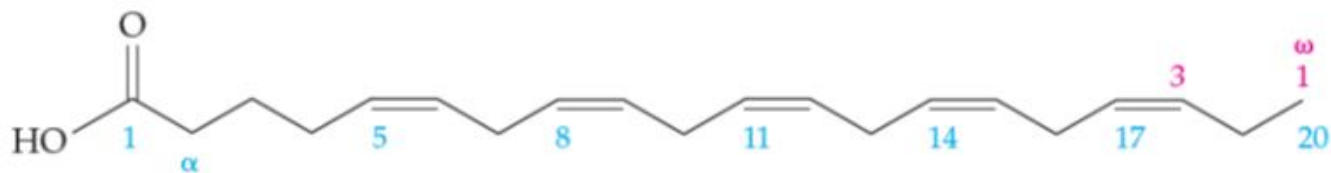
- **Eicosanoids** are extremely potent biological molecules with hormone-like activity, although they do not fit the formal definition of a hormone (a substance produced in a specialized tissue and transported by the circulatory system to target tissues elsewhere in the body), they are clearly strong biological regulators with far-reaching effects.



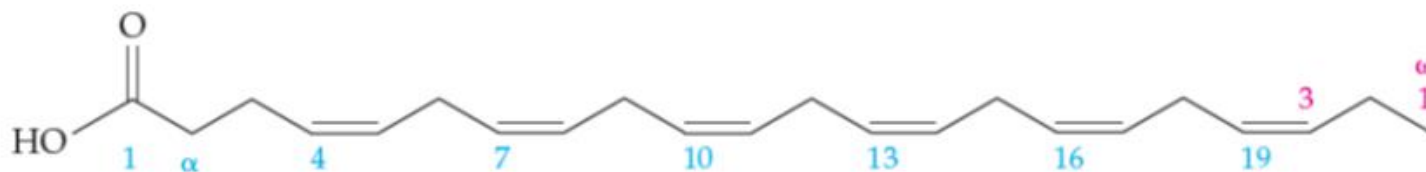
Omega-3 essential Fatty Acids



All *cis*-9,12,15-Octadecatrienoic acid
(α -Linolenic acid or ALA)



All *cis*-5,8,11,14,17-Eicosapentaenoic acid
(EPA)



All *cis*-4,7,10,13,16,19-Docosahexaenoic acid
(DHA)

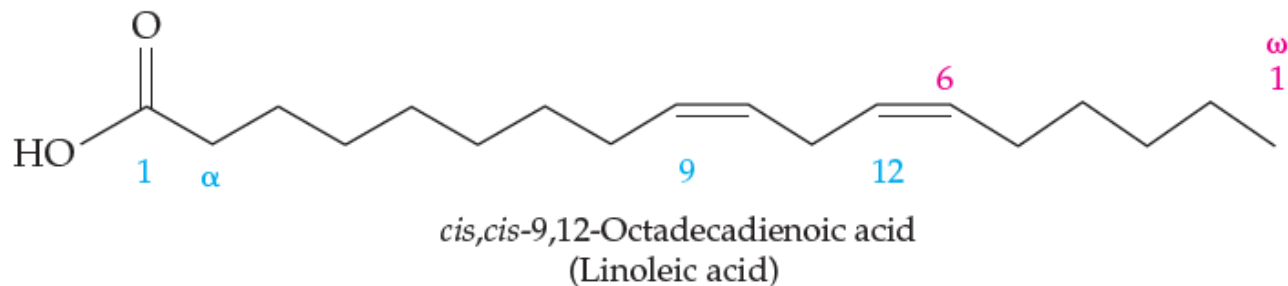


flax seed, soybeans, and canola, as well as in oil made from these plants



salmon, albacore tuna, sardines, lake trout, and mackerel

Omega-6 essential Fatty Acids



It is intriguing to note that the omega-3 fatty acids are precursors of prostaglandins that exhibit anti-inflammatory effects, and the omega-6 fatty acids are precursors of prostaglandins that have inflammatory effects.

This has led researchers to suggest that the amount of omega-6 fatty acids in our diets should not exceed 2–4 times the amount of omega-3.

Best Food Sources of LINOLEIC ACID



Black walnuts
1 cup chopped
42.2 g



Brazilnuts
1 cup whole
31.732 g



Almonds
1 cup whole kernels
17.864 g



Pistachio
1 cup
17.332 g



Kielbasa
1 link
17.320 g



Peanuts
1 cup
14.153 g



French fries
1 serving
11.862 g



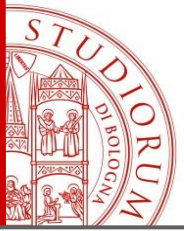
Mozzarella cheese sticks
1 serving
9.818 g



Turkey
3 oz
9.037 g

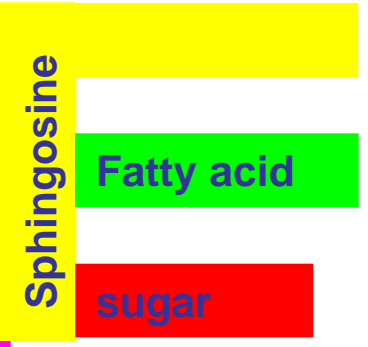
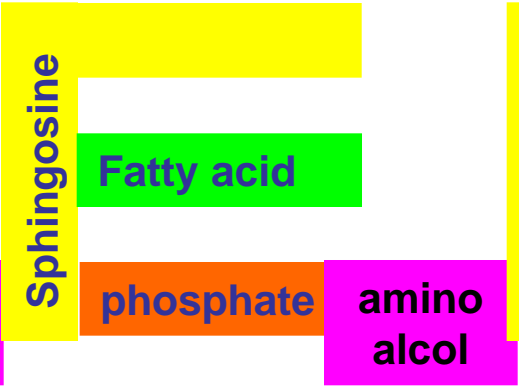
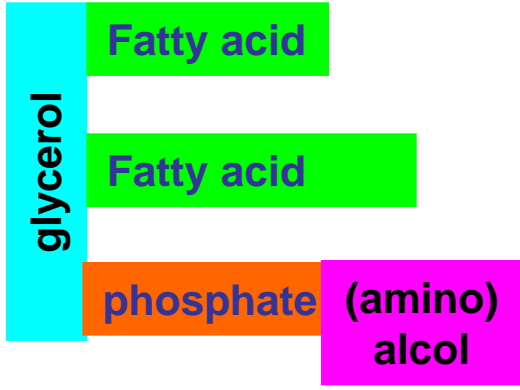
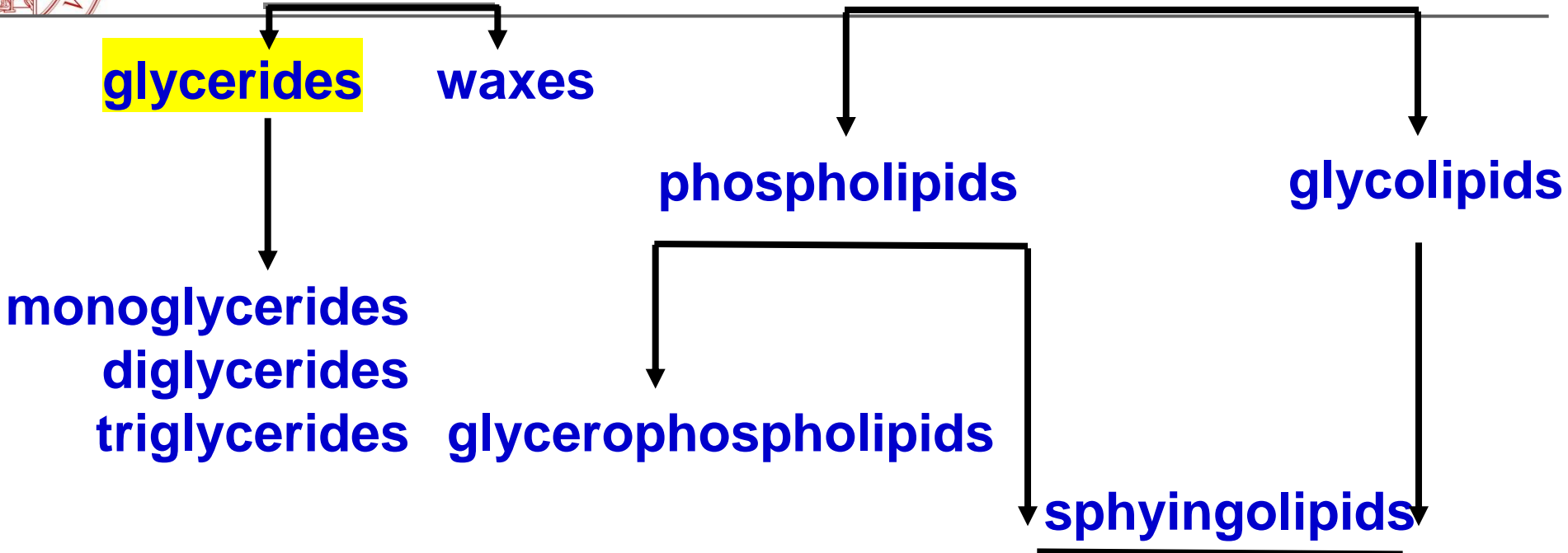


Hemp seed
3 tbsp
8.207 g



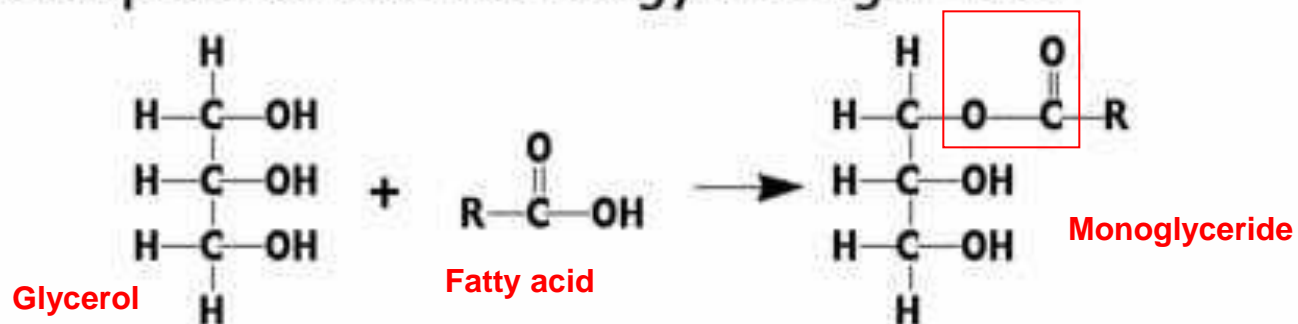
Neutral lipids

Polar lipids



Neutral glycerides or triglycerides

Ester of glycerol and a fatty acid.
Principal function is energy storage - fat.



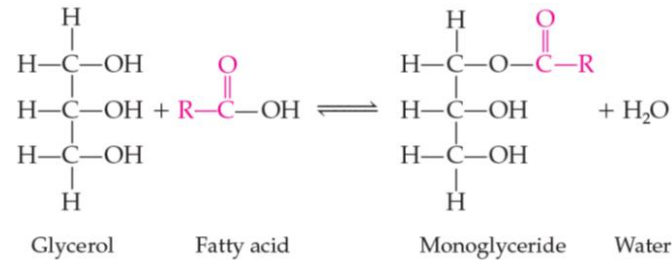
May have 1-3 fatty acids which can each be different.

- 1 - monoglyceride
- 2 - diglyceride
- 3 - triglyceride

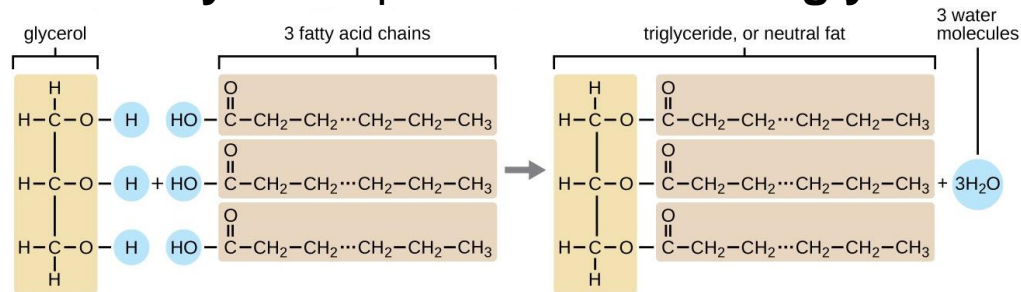
Glycerides

Glycerides are lipid esters that contain the glycerol molecule and fatty acids.

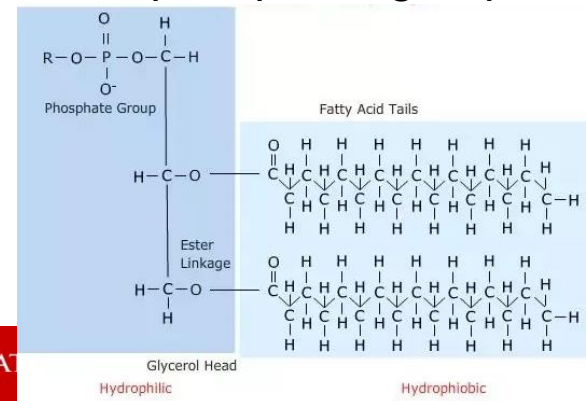
- Esterification may occur at one, two, or all three positions, producing **monoglycerides**, **diglycerides**, or **triglycerides**.



- The esterification of glycerol with **3 fatty acids** produces a **neutral glyceride** (nonionic and nonpolar).

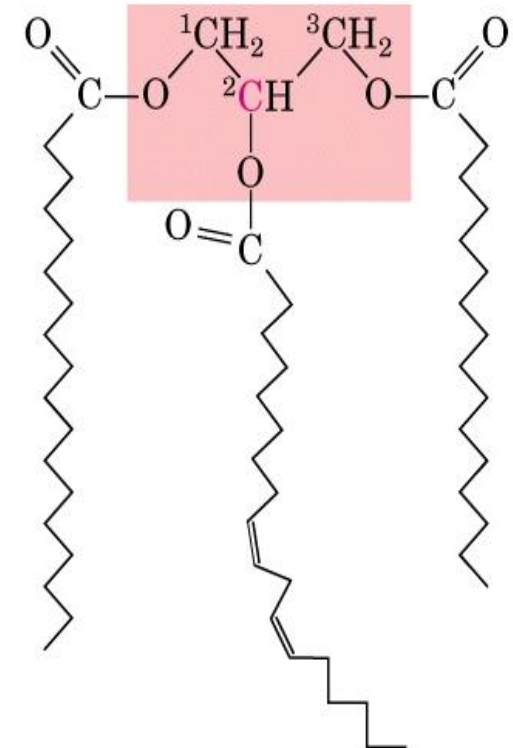
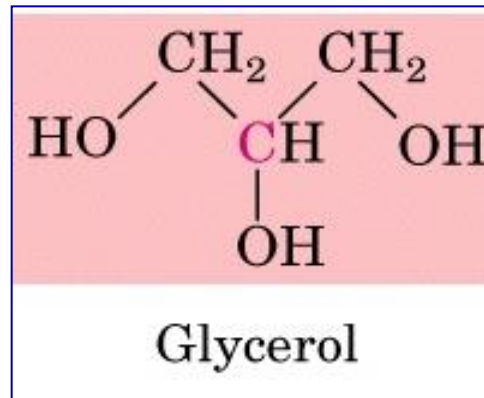
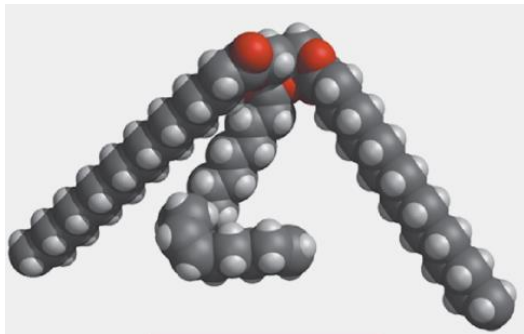
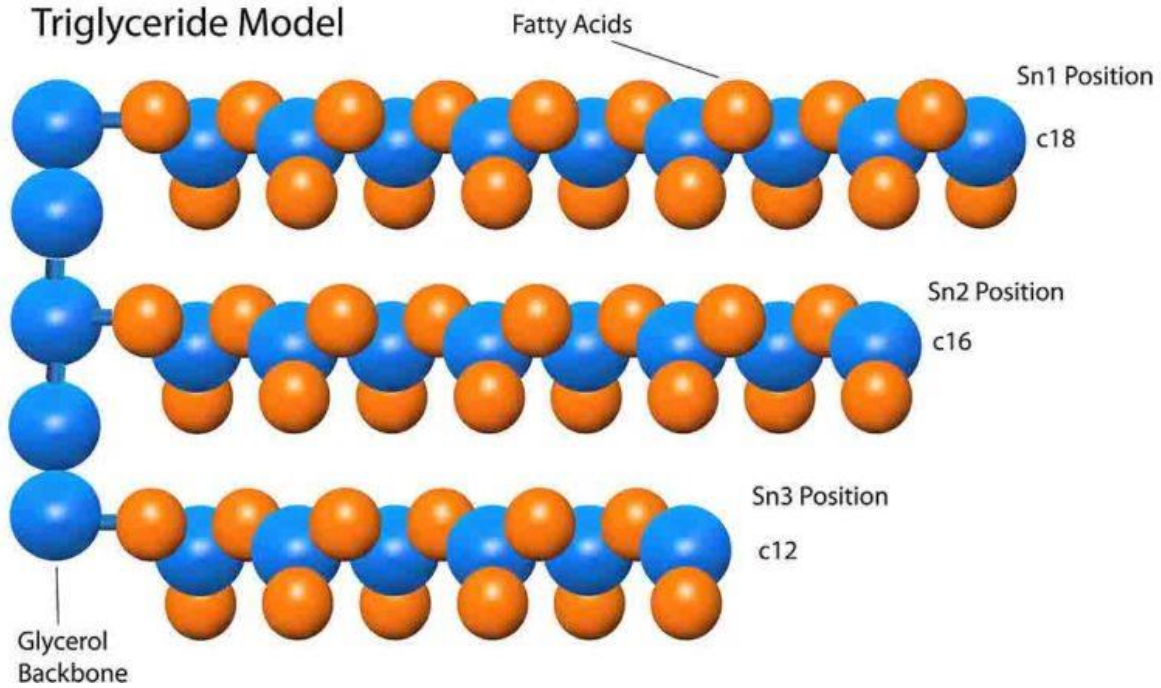


- Otherwise, **phosphoglycerides** have a polar region, the phosphate group, in addition to the nonpolar fatty acid tails.



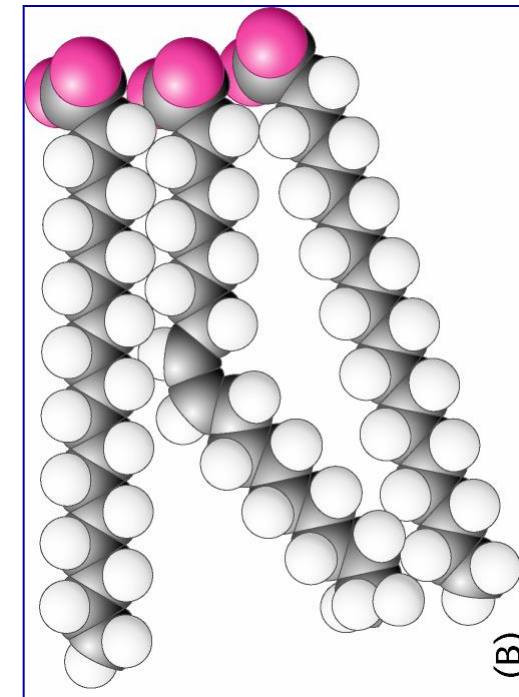
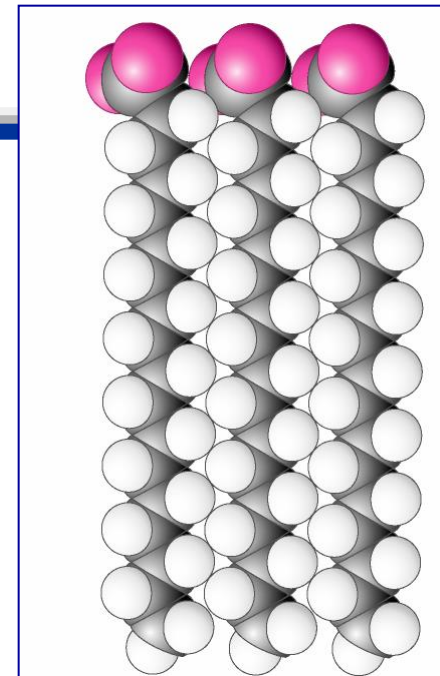
TRIGLYCERIDES

Triglyceride Model



TRIGLYCERIDE STRUCTURE

- Completely nonpolar molecules, whose density is lower than that of water
- Triglyceride can be constituted by 3 saturated fatty acids, equal to or different from each other, *e.g.* 3 molecules of palmitic acid
 - In this case the tails of the three fatty acids "pack" tightly
- Triglycerides can consist of 2 saturated fatty acids, and 1 monounsaturated, *e.g.* oleic acid
 - In this case the tails of the three fatty acids are NOT strictly packed because of the double bond in configuration "cis".
 - The fatty acid composition of a triglyceride strongly influences its physical state at physiological temperature





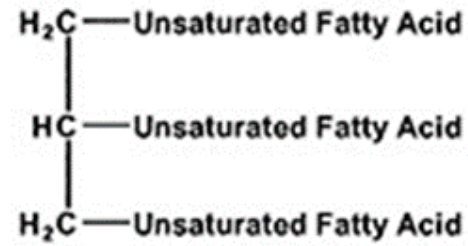
Monosaturated
(Di-unsaturated)



Disaturated
(Mono-unsaturated)



Trisaturated

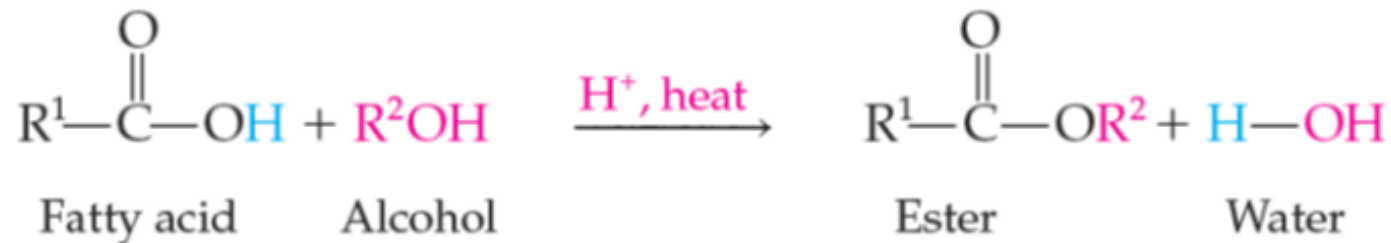


Triunsaturated

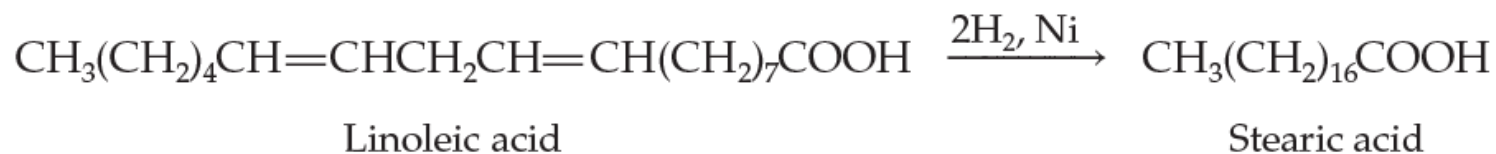
Chemical Reactions of Fatty Acids



Esterification: fatty acids react with alcohols to form esters and water according to the following general equation:



Addition at the double bond (hydrogenation): this generally involves the addition of hydrogen (H₂) to the double bond of an unsaturated fatty acid.

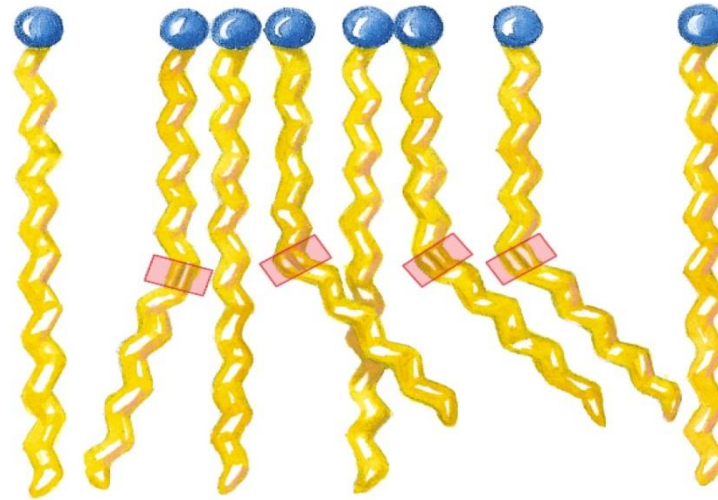


Hydrogenation is used in the food industry to convert polyunsaturated vegetable oils into saturated solid fats (ex. margarine produced from by partial hydrogenation of linoleic acid present in corn oil or soybean oil).



Saturated
fatty acids

(c)



Mixture of saturated and
unsaturated fatty acids

(d)

(c) Saturated fatty acids in their fully extended form are packaged in a compact form, that is stabilized by many interactions between the hydrocarbon chains.

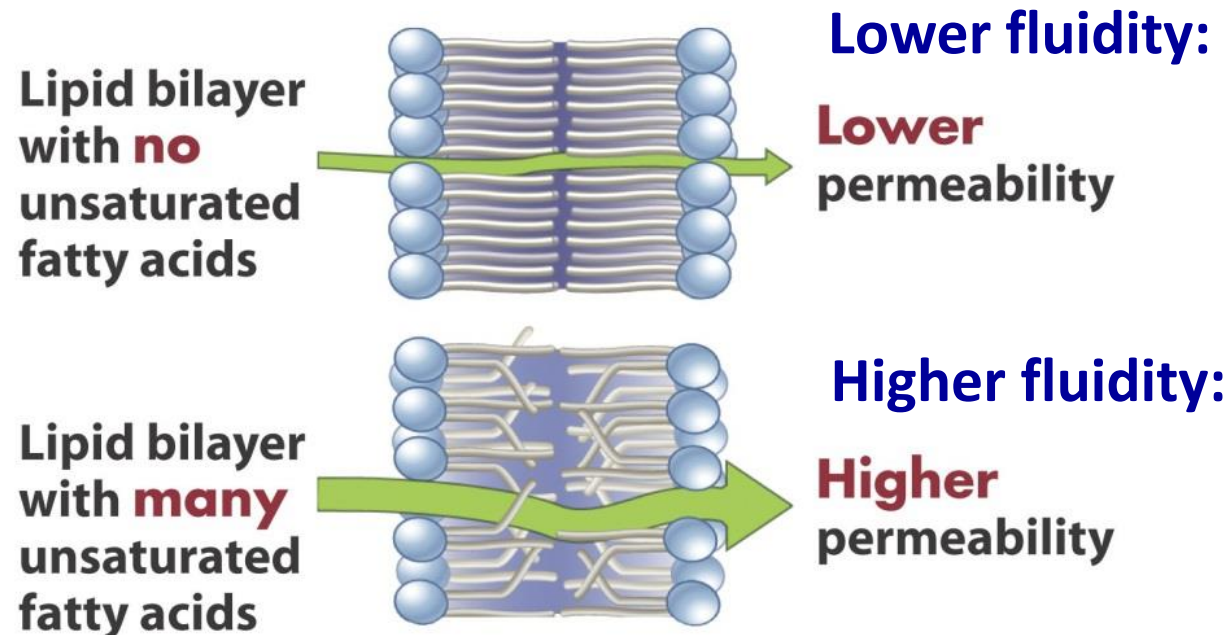
(d) The presence of one or more double cis bonds interferes with this arrangement and produces less stable aggregates.

➤ The presence of double bonds (and the degree of unsaturation) reduces the melting point, while the length of the chain increases it.

BIOLOGICAL CONSEQUENCE: MEMBRANE FLUIDITY DEPENDS ON THE STRUCTURE AND THE DEGREE OF UNSATURATION OF THE FATTY ACIDS IN PHOSPHOLIPIDS.

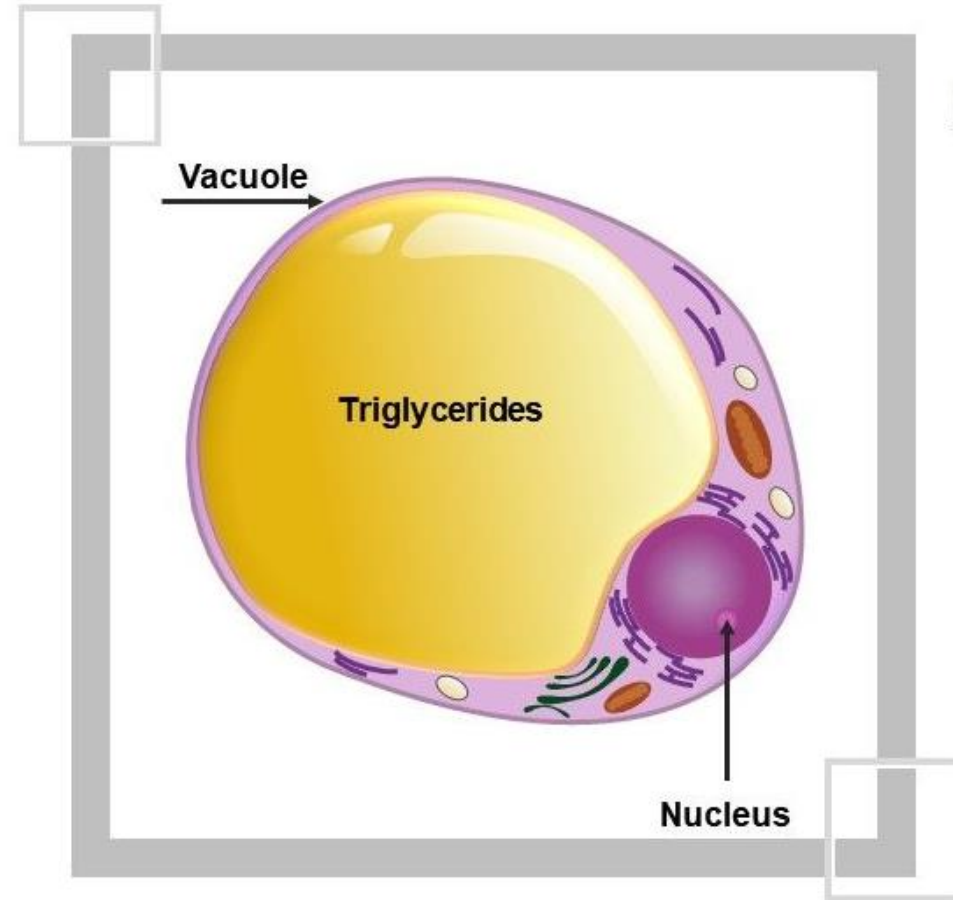
Doble bonds in cis configuration increase the fluidity.

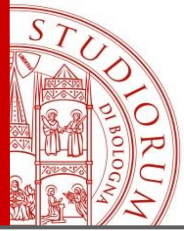
- **Membrane fluidity is influenced by presence/absence of unsaturated FA chains**
- **Fluidity of membranes is important for proper function**



TRIGLYCERIDES FUNCTIONS

- In mammals most triglycerides are contained in adipose tissue, composed of specialized cells called adipocytes.
- In adipocytes, triglycerides form oily droplets within the cytoplasm (in vacuoles).
- In mammals, the adipose tissue is located immediately below the skin and in the abdominal cavity, where it serves as an energy storage and for thermal insulation.
- When fatty acids of triglycerides have to be used for energy purposes, they are hydrolyzed (i.e. detached from the glycerol and made free) by specific enzymes called lipases.
- To reach the liver (the organ responsible for their catabolism) through the blood, the fatty acids need a carrier (proteins) because of their high hydrophobicity.

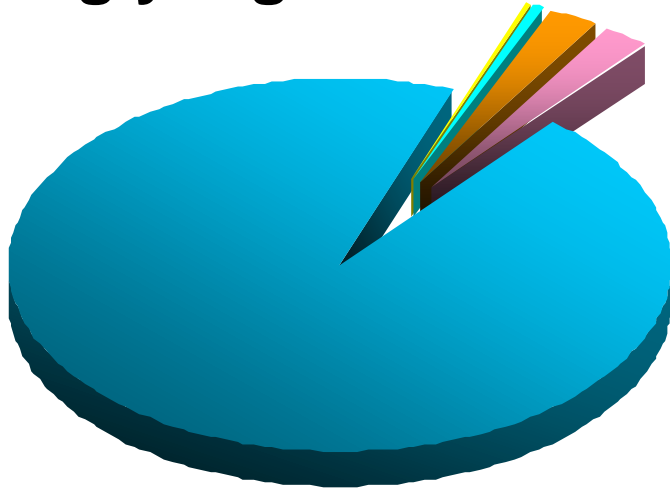




Fat mass, adipose tissue and energy stores

Liver triglycerides = 450 kcal

Liver glycogen = 400 kcal



**Muscle triglycerides =
3000 kcal**

**Muscle glycogen =
2500 kcal**

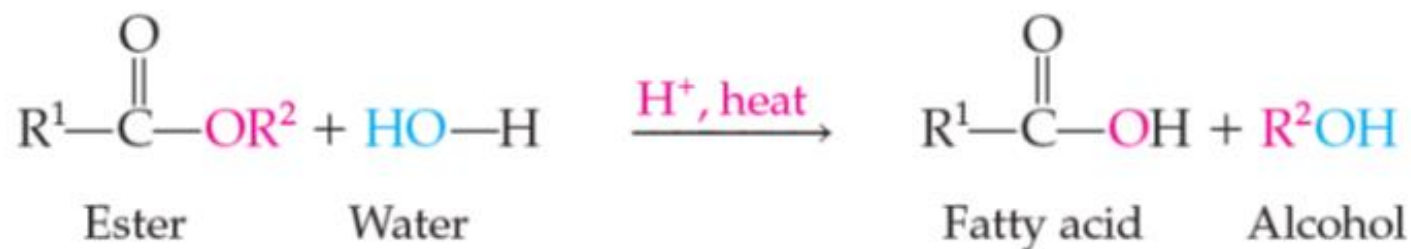
**Adipose tissue triglycerides =
120.000 kcal**

Data for a 70 kg lean subject. Subject with morbid obesity: x 8 TG



Chemical Reactions of Glycerides (esters)

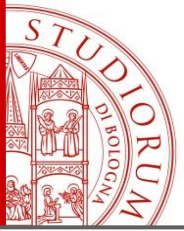
Acid hydrolysis: Breaking the ester bond of a glyceride by the addition of a water molecule in the presence of a strong acid. In acid hydrolysis of an ester, the products are a carboxylic acid (fatty acid, in this case) and an alcohol:



Saponification: Breaking the ester bond of a glyceride by the addition of a water molecule in the presence of a strong base. In saponification, the products are a carboxylic acid salt (fatty acid salt, in this case) and an alcohol:



The long-chain carboxylic acid salt or fatty acid salt that is the product of this reaction is a soap, a surfactant.



Neutral lipids

Polar lipids

glycerides

waxes

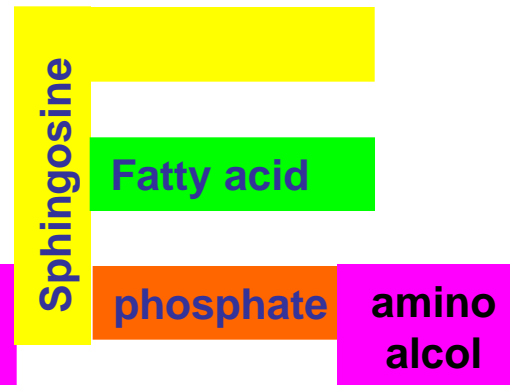
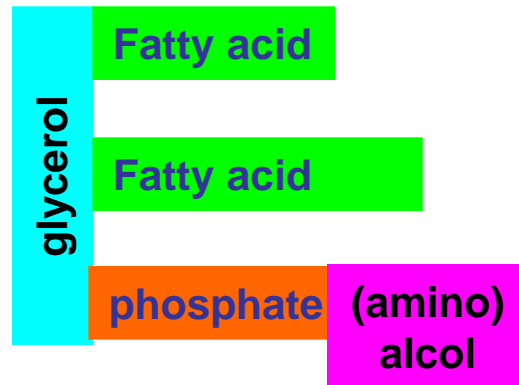
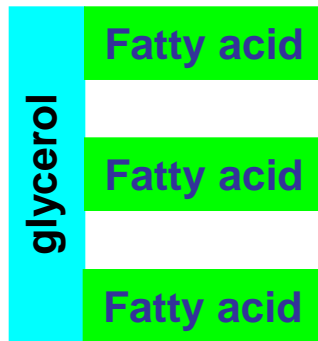
phospholipids

glycolipids

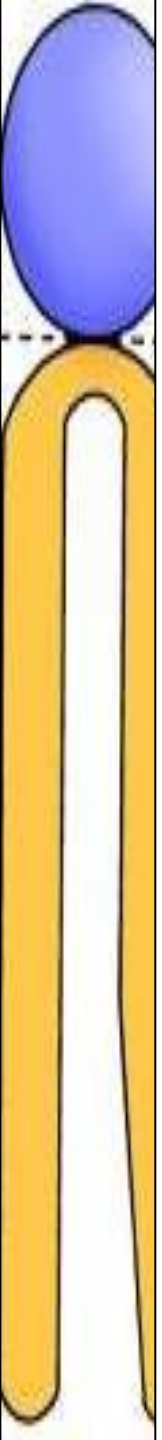
monoglycerides
diglycerides
triglycerides

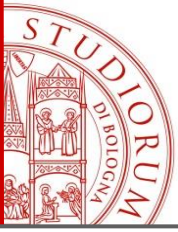
glycerophospholipids

sphingolipids



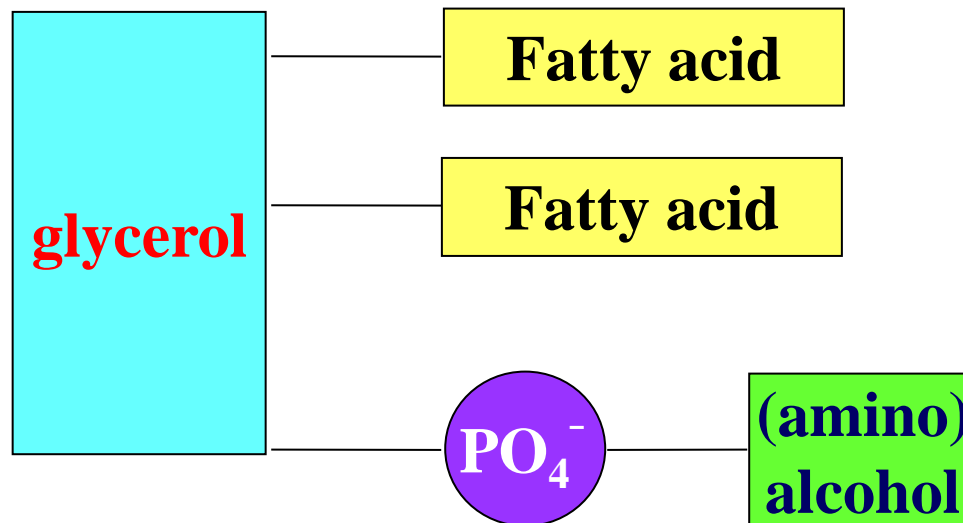
PHOSPHOLIPIDS

- 
- Phospholipids are characterized by having a **phosphate group** in the polar head of their molecule.
 - Made up of fatty acids + a molecule that acts as a skeleton (glycerol or sphingosine).
 - The skeleton can be of two types:
 - ✓ glycerol (glycerophospholipids)
 - ✓ sphingosine (sphingophospholipids)
 - These are the constituents of biological membranes, in which they play both structural and functional roles.
 - Some of them are involved in the signal transduction of some intracellular pathways (*e.g.* PI3K/Akt).

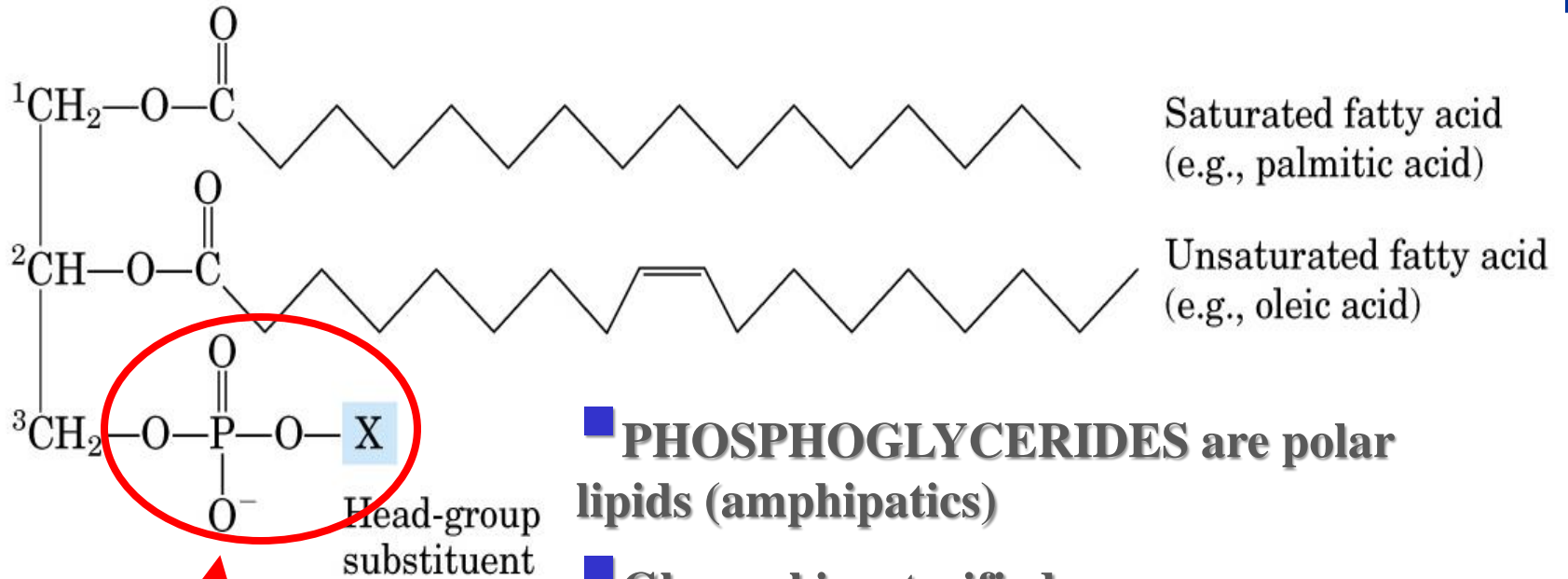


Glycerophospholipids

- The most abundant in cell biological membranes
- Composed by *glycerol*, 2 fatty acids, phosphate group and an (amino) alcohol.



PHOSPHOGLYCERIDE STRUCTURE



Polar head

■ **PHOSPHOGLYCERIDES** are polar lipids (amphipatics)

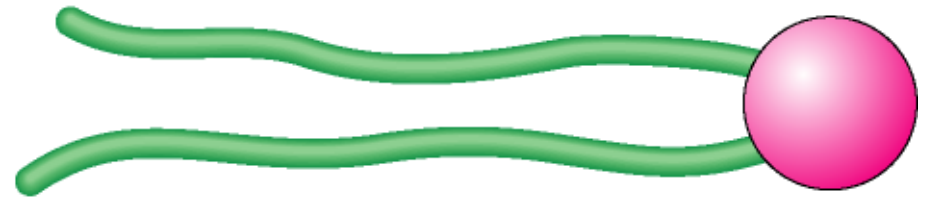
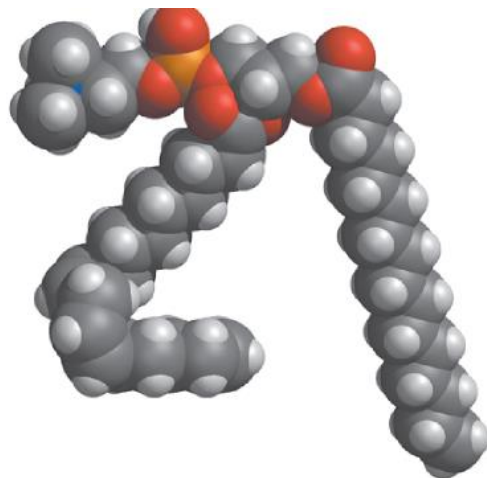
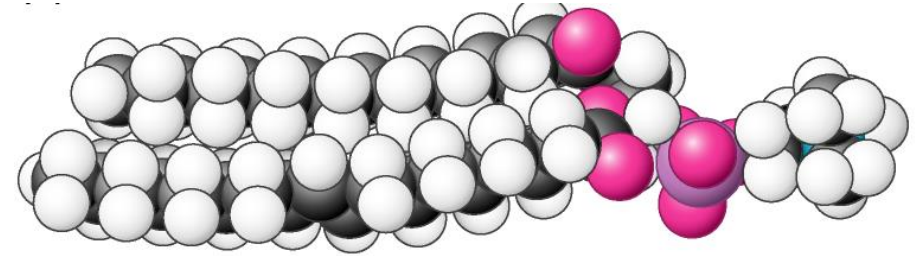
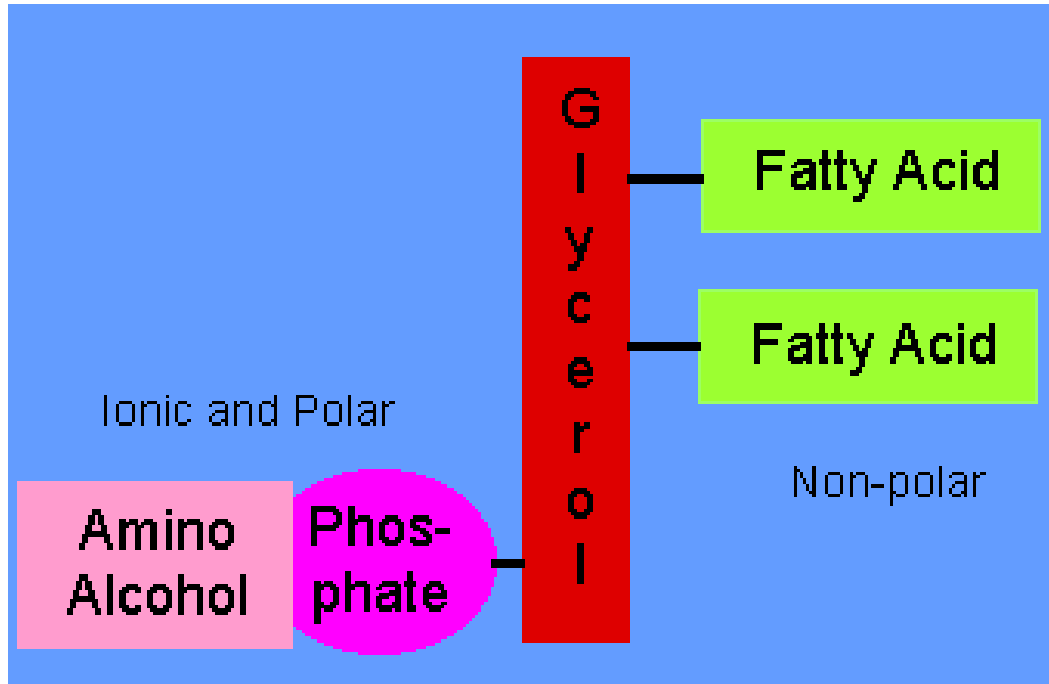
■ **Glycerol is esterified:**

- With 2 fatty acids (nonpolar tails)

- With a phosphate group (polar head)

■ The phosphate group in turn is esterified with another alcohol here indicated with **X** (included in the polar head)

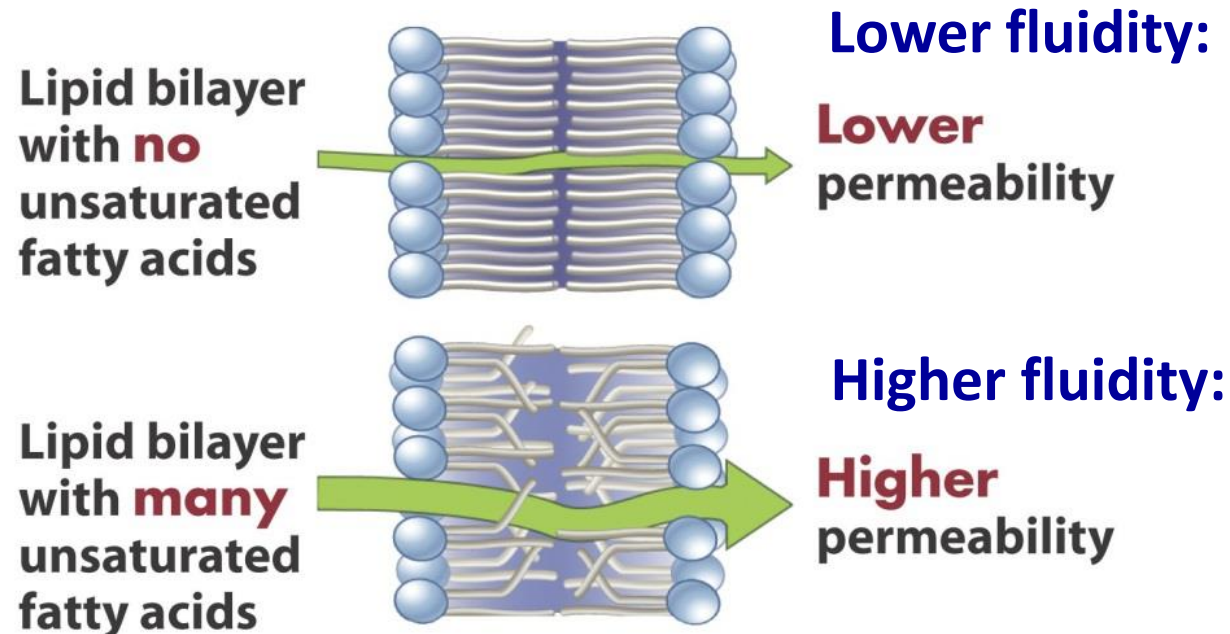
PHOSPHOGLYCERIDES OR PHOSPHOACYLGLYCEROLS

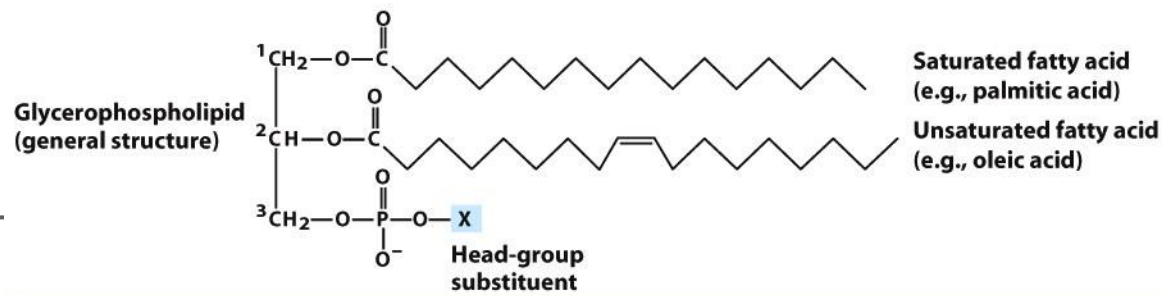




The number of double bonds in FA determines the fluidity of cell plasma membranes

- Membrane fluidity is influenced by presence/absence of unsaturated FA chains
- Fluidity of membranes is important for proper function



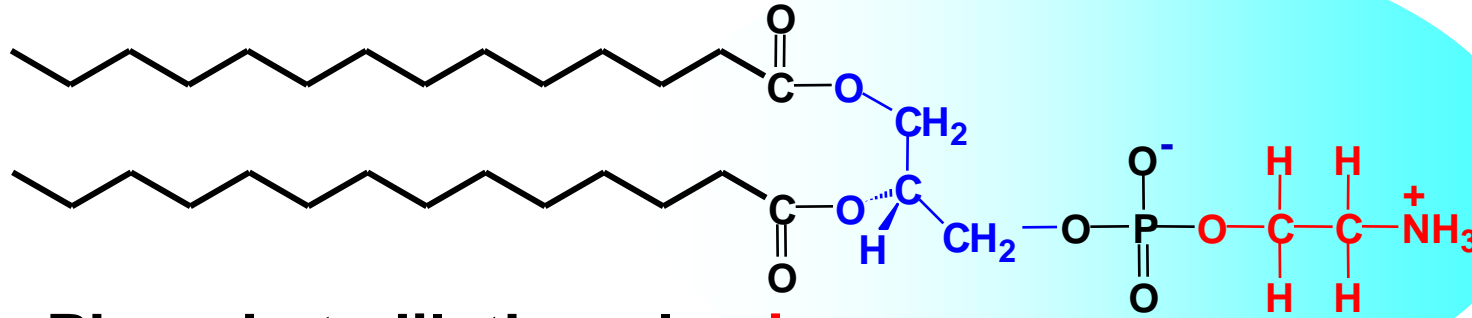


Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	— H	- 1
Phosphatidylethanolamine	Ethanolamine	— CH ₂ —CH ₂ —NH ₃ ⁺	0
Phosphatidylcholine	Choline	— CH ₂ —CH ₂ —N(CH ₃) ₃ ⁺	0
Phosphatidylserine	Serine	— CH ₂ —CH(NH ₃ ⁺)—COO ⁻	- 1
Phosphatidylglycerol	Glycerol	— CH ₂ —CH(OH)—CH ₂ —OH	- 1
Phosphatidylinositol 4,5-bisphosphate	<i>myo</i> -Inositol 4,5-bisphosphate		- 4
Cardiolipin	Phosphatidyl-glycerol	$ \begin{array}{l} \text{— CH}_2 \\ \\ \text{CHOH} \\ \\ \text{CH}_2\text{-O-P(=O)(O^-)-O-CH}_2 \\ \\ \text{CH-O-C(=O)-R}^1 \\ \\ \text{CH}_2\text{-O-C(=O)-R}^2 \end{array} $	- 2

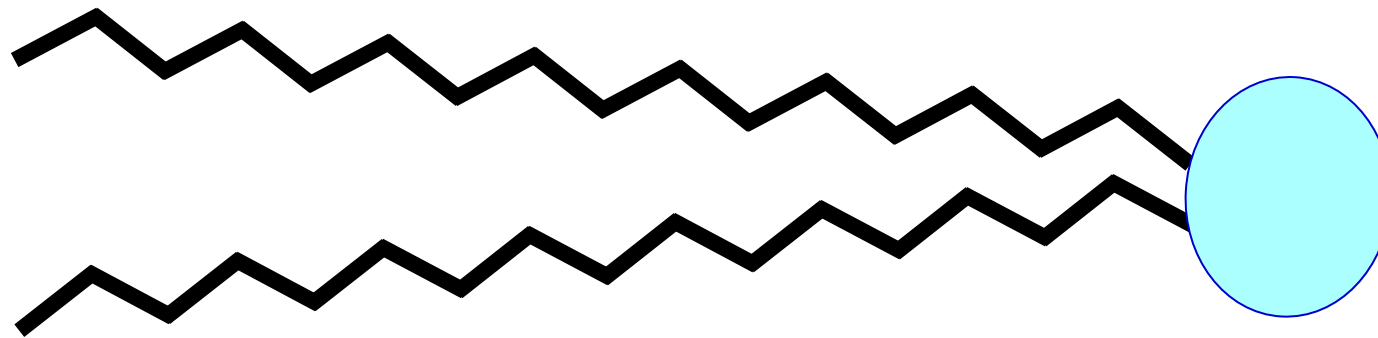
Other glycerides, which do not contain a phosphate group, but sugars, are galactolipids and sulphatides, present in membranes of plant cells

Figure 10-9
Lehninger Principles of Biochemistry, Fifth Edition
 © 2008 W. H. Freeman and Company

Glycerophospholipids are amphipatic molecules that make up the membranes



Phosphatidylethanolamine

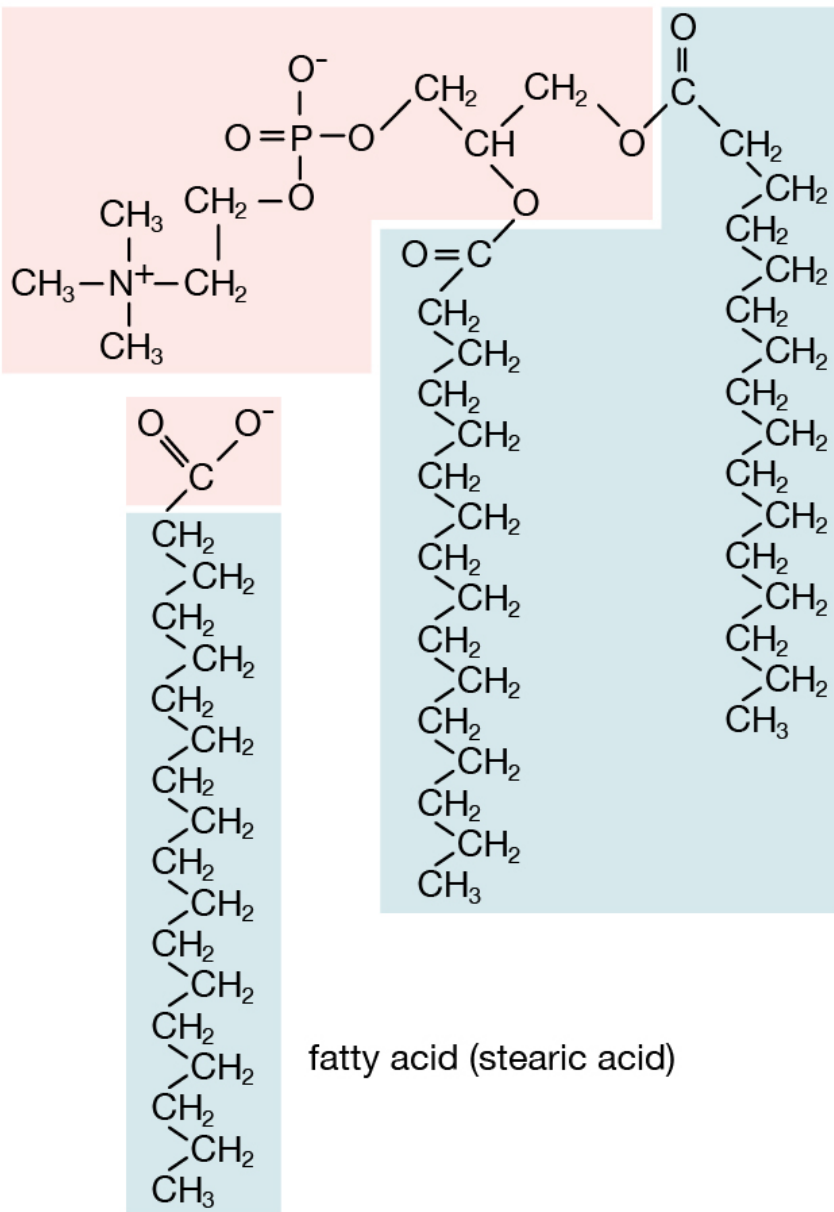


Nonpolar tail

polar head

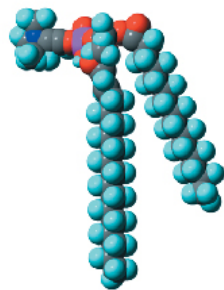
structural formula

phospholipid (phosphatidylcholine)



space-filling model

phospholipid molecule

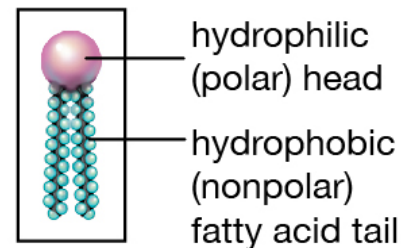


fatty acid molecule

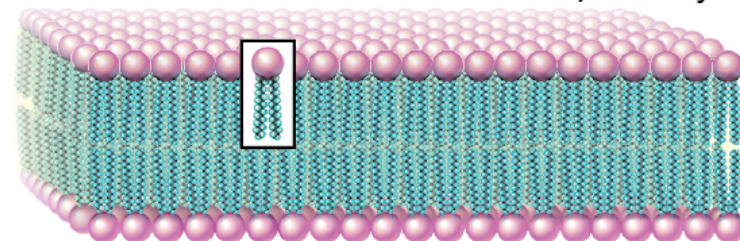


generic simplified depiction

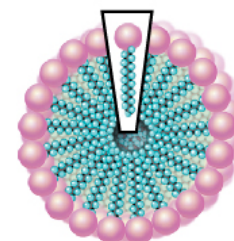
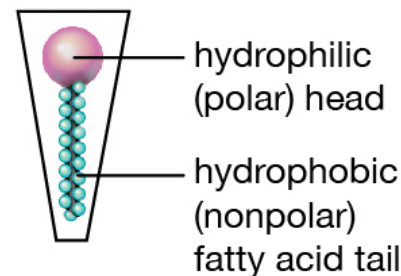
phospholipid molecule



lipid bilayer



fatty acid molecule



micelle

Hydrophilic
polar head

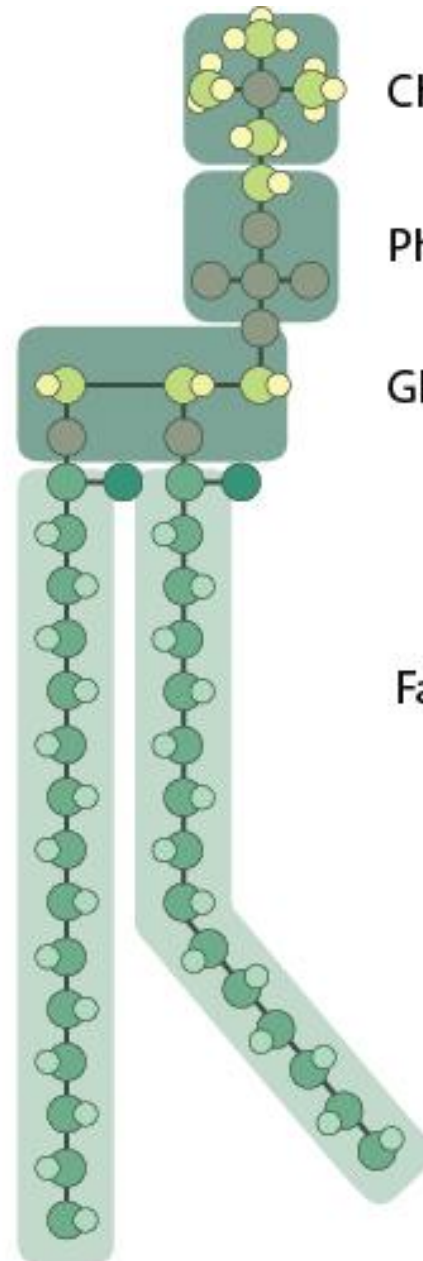
Choline

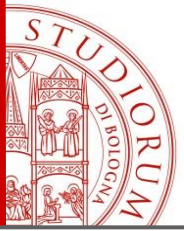
Phosphate

Glycerol

Hydrophobic
non-polar tail

Fatty acids





Neutral lipids

Polar lipids

glycerides

waxes

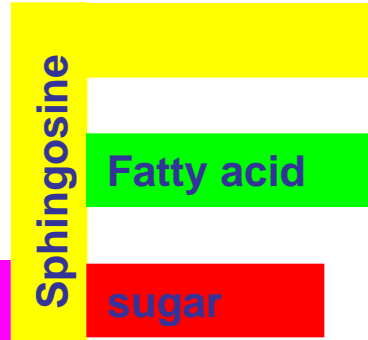
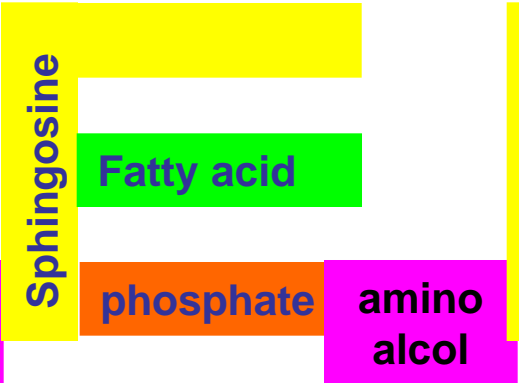
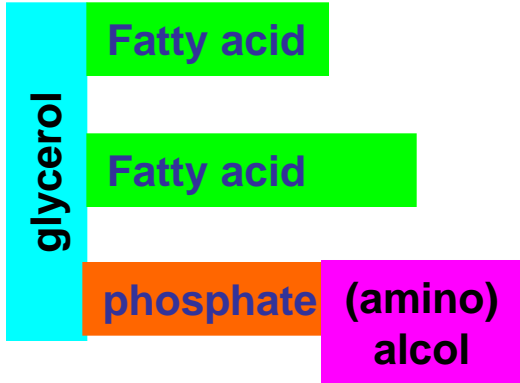
phospholipids

glycolipids

monoglycerides
diglycerides
triglycerides

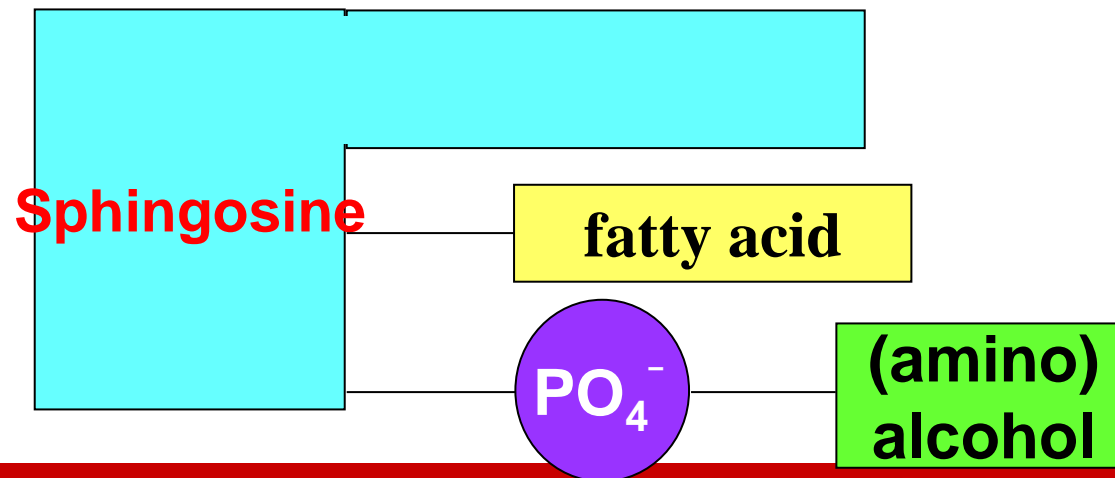
glycerophospholipids

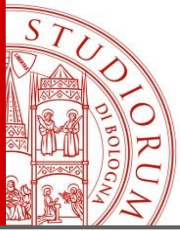
sphingolipids



Sphingolipids

- They are similar to phosphoglycerides but not derived from glycerol.
- They are derived from sphingosine, a long-chain, nitrogen-containing (amino) alcohol + fatty acid + a phosphate group linked with an amino alcohol.
- Like phospholipids, sphingolipids are amphipathic, having a polar head group and two nonpolar hydrocarbon tails, one of which is derived from a fatty acid.
- The sphingolipids include **sphingomyelins, glycosphingolipids and gangliosides.**

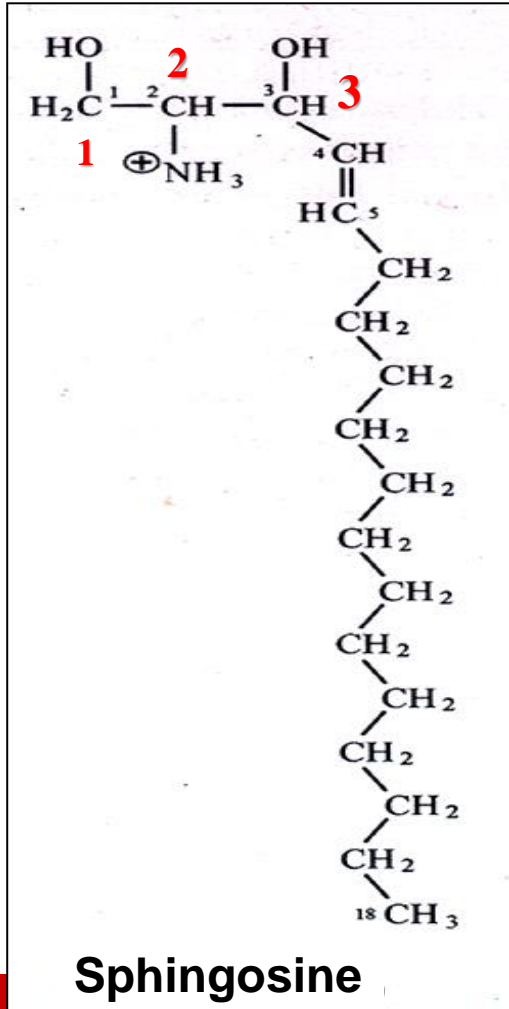




SPHINGOLIPID STRUCTURE

Derived from sphingosine, an unsaturated 18-C amino alcohol: C-1, 2, 3 structure "resembles" glycerol

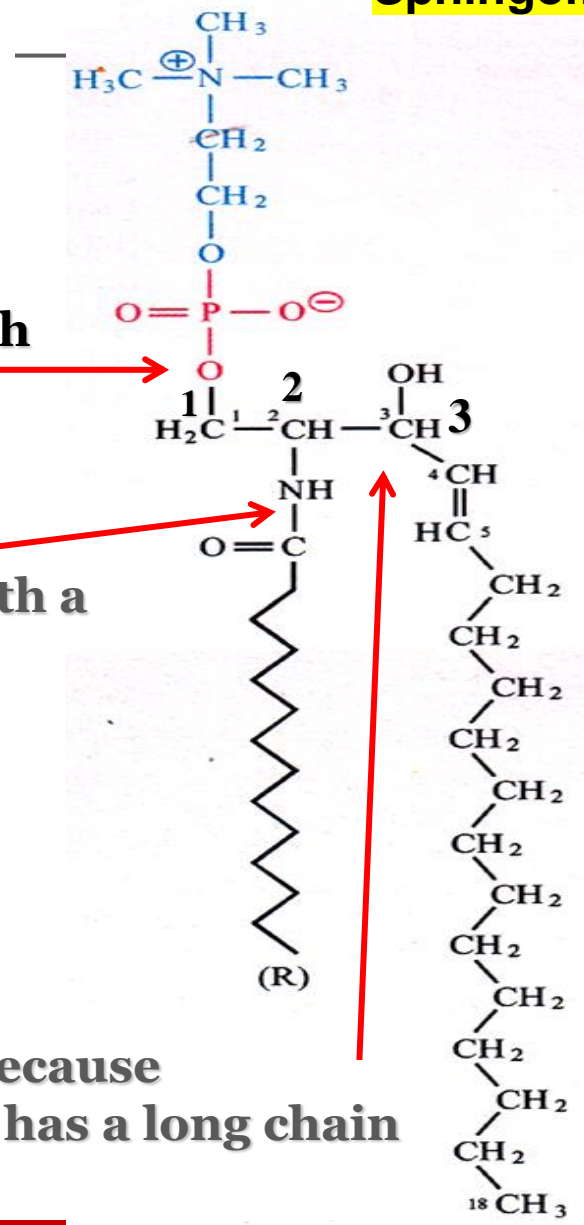
Spingomyelin



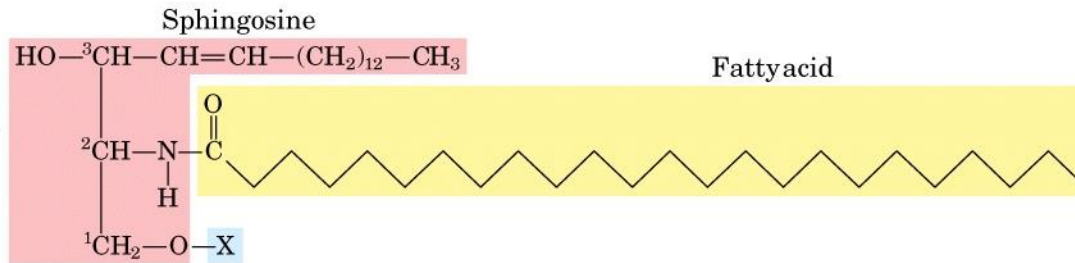
C1: OH esterified with phosphocholine

C2: amide bond with a fatty acid (usually saturated)

C3: no addition, because sphingosine itself has a long chain in this position.



Sphingolipid
(general
structure)



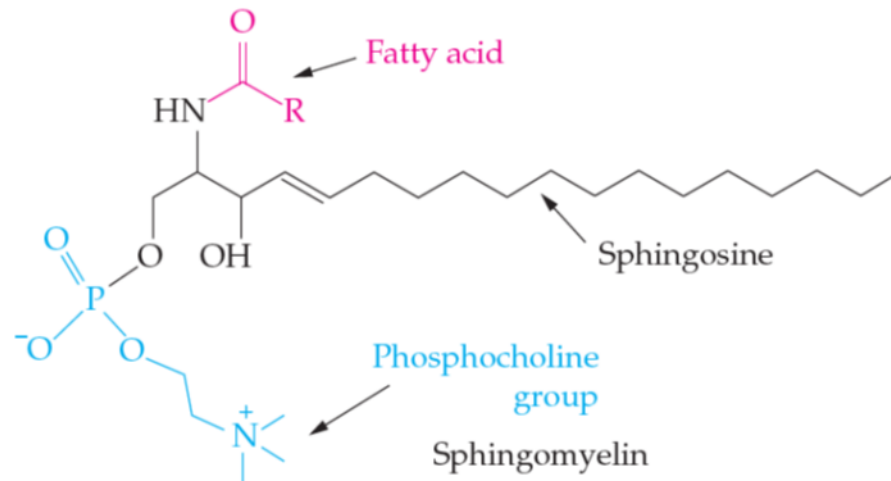
**Other sphingolipids
do not contain
phosphate, but
carbohydrates (they
are glycolipids, not
phospholipids)**

Name of sphingolipid	Name of X	Formula of X
Ceramide	—	— H
Sphingomyelin	Phosphocholine	$-\text{P}(=\text{O})(\text{O}^-)-\text{O}-\text{CH}_2-\text{CH}_2-\text{N}^+(\text{CH}_3)_3$
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Sphingomyelins

The sphingomyelins are the only class of sphingolipids that are also phospholipids.

In sphingomyelin, the acyl group of the fatty acid is bonded to sphingosine through an amide bond while the phosphate group can be esterified with choline or ethanolamine.



- They are found in abundance in the myelin sheath that surrounds and insulates axons in the central nervous system

GLYCERO- and SPHINGO-PHOSPHOLIPIDS are the constituents of CELL MEMBRANES

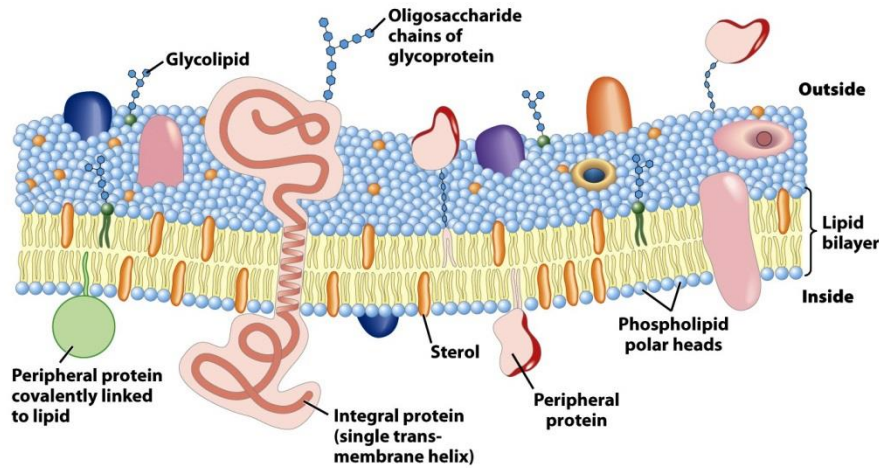
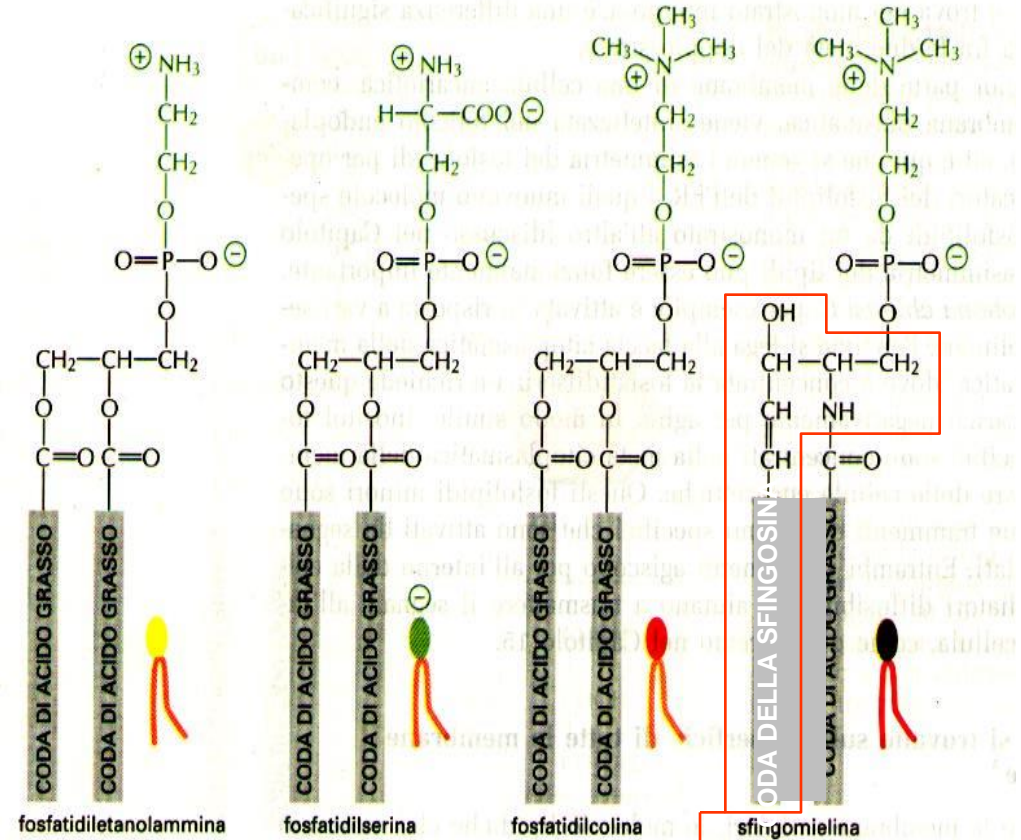


Figure 11-3
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W.H. Freeman and Company

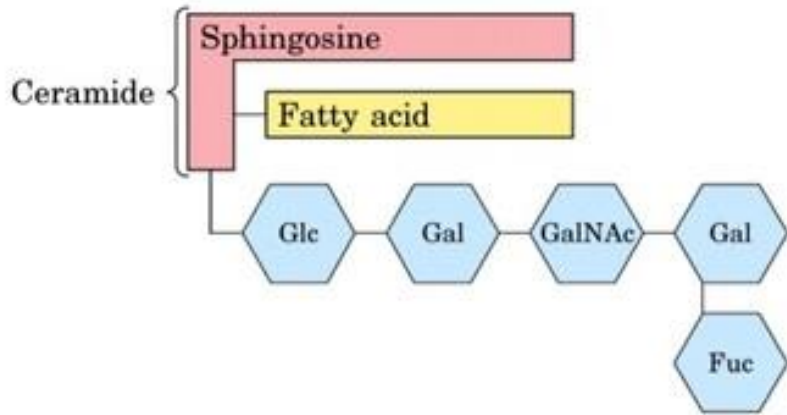
Phospholipids form a two-dimensional solvent for membrane proteins and polar heads can interact with them specifically



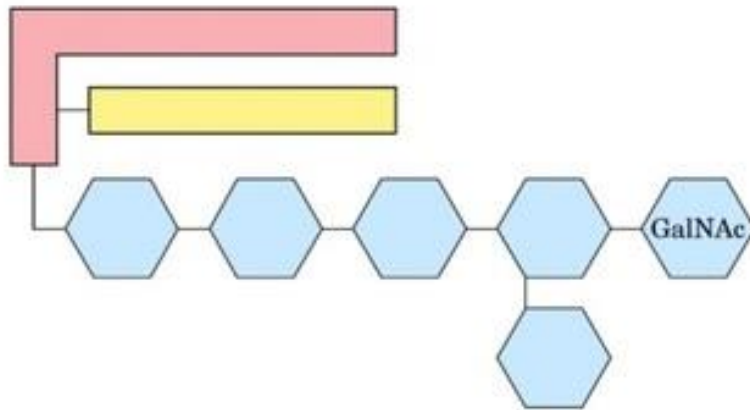
sfingosine

Glycero- and sphingo-phospholipids have not significant differences in their structure and function; usually, sphingo-phospholipids are more saturated than glycerophospholipids and are more abundant in nervous system cells.

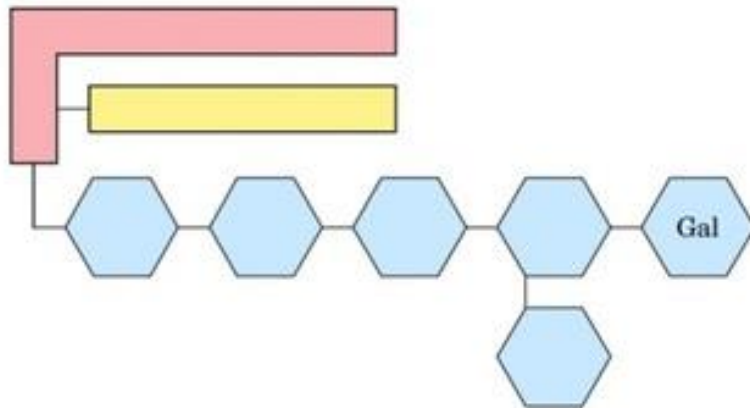
A, B, AB and 0 blood types



O Antigen

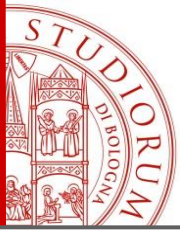


A Antigen



B Antigen

- Sphingolipids can act as cell surface antigens, defining various blood types.
- The human blood group is determined by the sugars present in the sphingolipids of the PM of erythrocytes.
- If we have in our DNA the gene that encodes for the protein that transfers a N-acetylgalactosamine group to the sphingolipid, we have the antigen A.

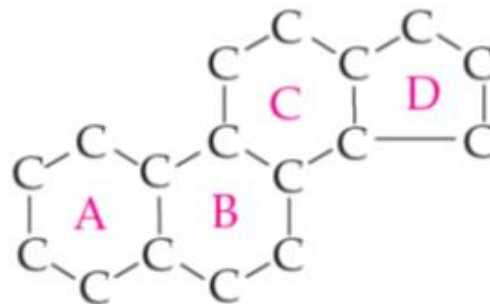
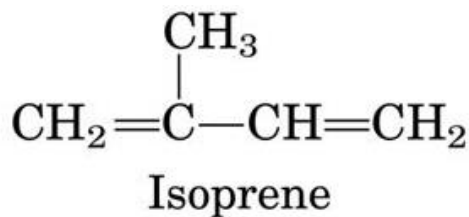


Steroids

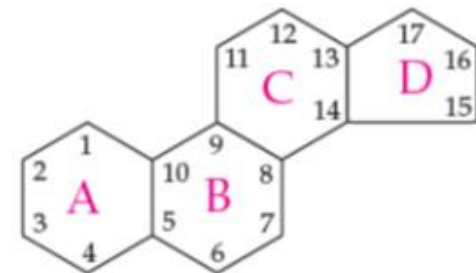
The steroids are members of a large, diverse collection of lipids called the “isoprenoids”. All of these compounds are built from one or more 5-carbon units called **isoprene**.

Terpene is the general term for lipids that are synthesized from isoprene units. Examples of terpenes include steroid hormones (e.g. estrogens), lipid-soluble vitamins (A,D,E and K), chlorophyll, and pigments.

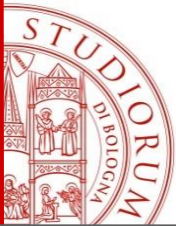
All steroids contain the steroid nucleus (steroid carbon skeleton).



Carbon skeleton of the steroid nucleus



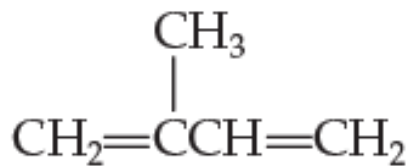
Steroid nucleus



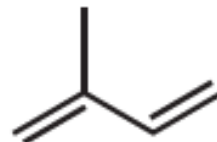
Alkenes in nature

TERPENES

Terpenes (or polyenes) are alkenes with several double bonds, and there are a surprising number of these molecules found in nature. Although they have wildly different properties and functions, they are built from one or more five-carbon units called **isoprene (IUPAC 2-methyl -1,3 – butene)**.



Isoprene



The molecules produced from isoprene are called *isoprenoids*, or *terpenes*. Terpenes include **chlorophyll** and **carotenoid** pigments that function in photosynthesis; and the **lipid-soluble vitamins A, D, E, and K**.

Retinol, is a form of vitamin A; it is able to penetrate the outer layers of skin and stimulate the formation of collagen and elastin.

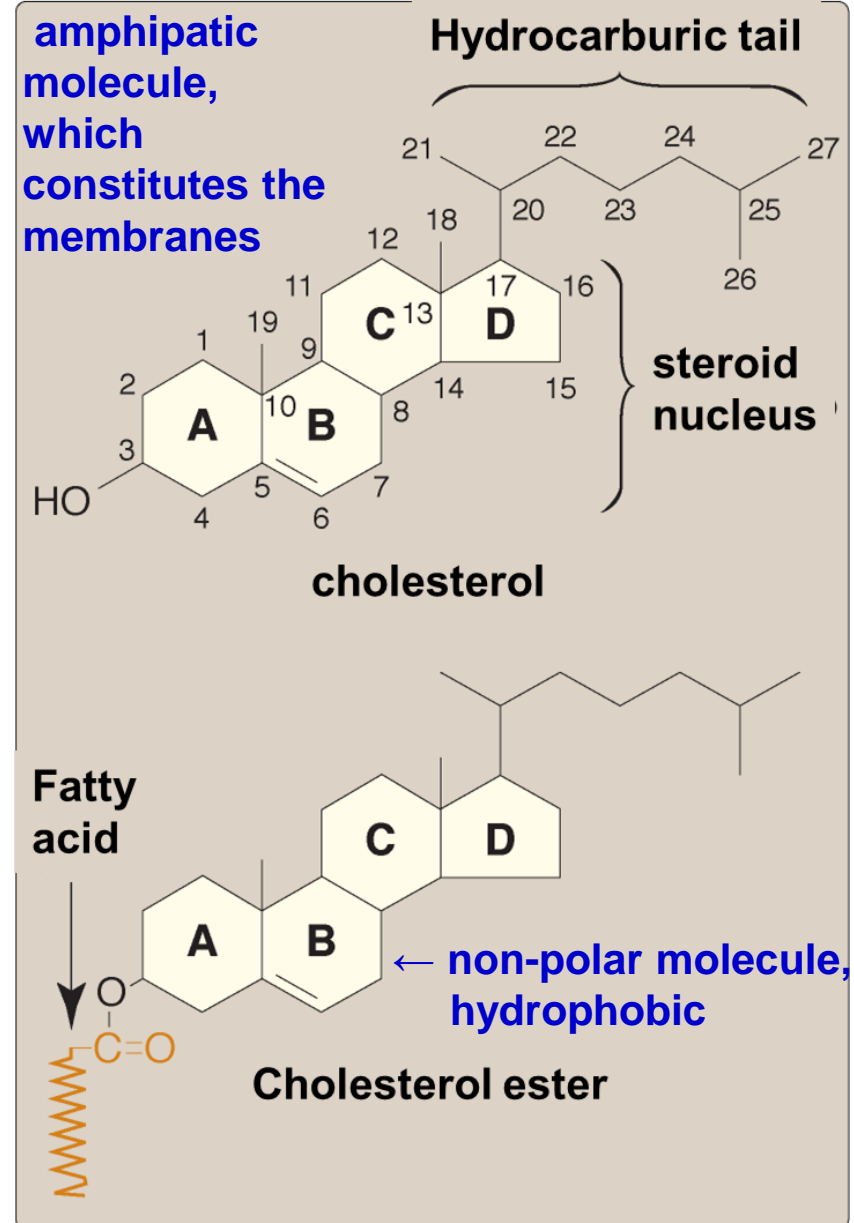
11-cis-retinal, a derivative of Retinol, is involved in the eye's ability to see under low light conditions.

CHOLESTEROL STRUCTURE

■ It is an amphipathic molecule and is readily soluble in the hydrophobic region of membranes.

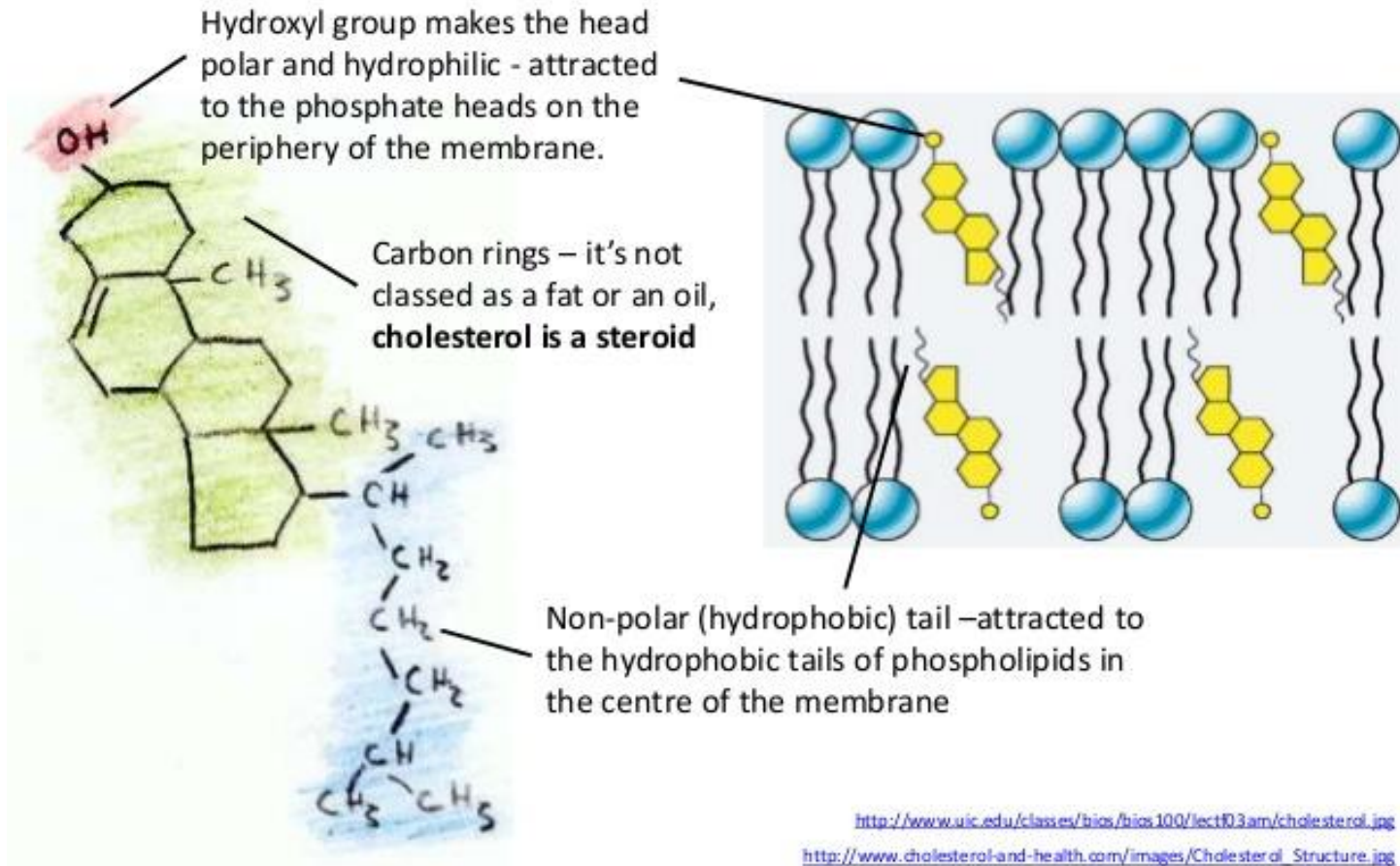
■ In its “free” form, it is involved in the regulation of the fluidity of the membrane as a result of the nonpolar fused ring. However, the hydroxyl group is polar and functions like the polar heads of sphingolipids and phospholipids.

■ It may also be esterified with a fatty acid, becoming hydrophobic due to the loss of the group –OH.



1.3.U3 Cholesterol is a component of animal cell membranes.

Cholesterol



CHOLESTEROL FUNCTIONS

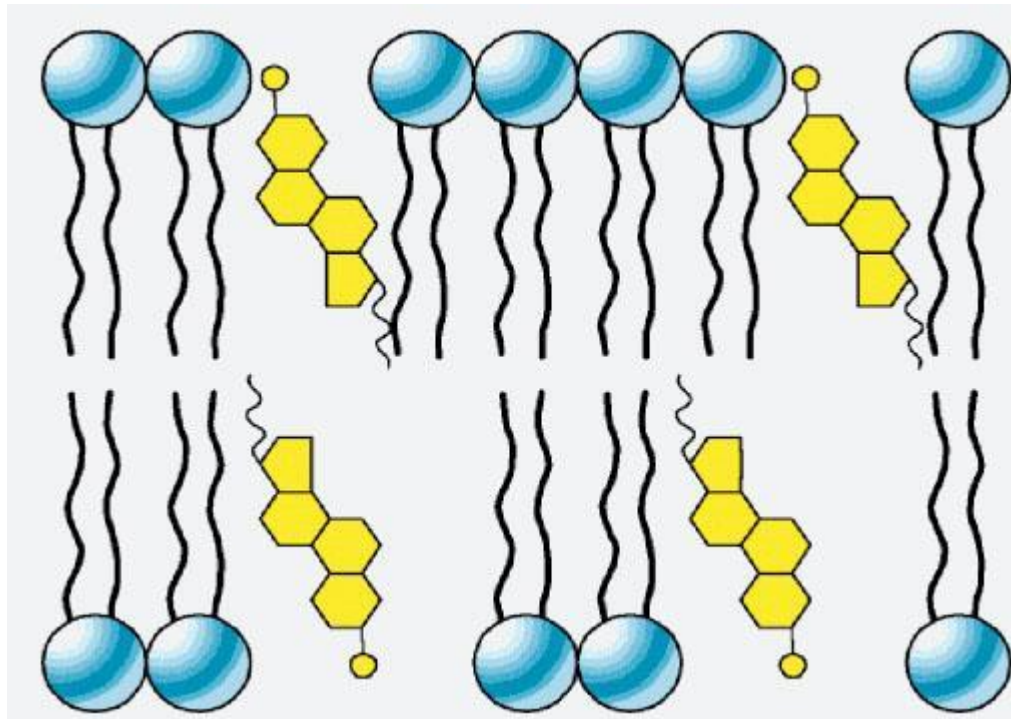
- **Essential component of plasma membranes**, it regulates membrane fluidity
- **Precursor of bile acids**, (cholate and chenodeoxycholate). Synthesized in the liver, stored in the gallbladder (main constituents of bile) and released in the small intestine, where these emulsifying agents have the task of solubilizing lipids from the diet.
- **Precursor of sexual steroid hormones**: **progesterone** (hormone associated with pregnancy), **testosterone** (male sex hormone found in the testes), **estrogens** (female sex hormone).
- **Precursor of corticosteroid hormones**: **aldosterone** (participates in blood sodium ion levels regulation), **cortisone** (promotes glycogen synthesis, gluconeogenesis and inhibits inflammatory responses)
- **Vit D precursor**: **7-dehydrocholesterol**, present in the epidermis, when irradiated by sunlight it converts to **cholecalciferol, vit D₃**

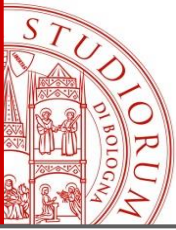


CHOLESTEROL AND PLASMA MEMBRANES

Cholesterol modulates the fluidity of the membranes:

- reducing it at high or medium temperatures, and increasing it at low temperatures;
- limits the movement of unsaturated fatty acid chains, but makes long saturated fatty acid chains more fluid.





SOURCES OF CHOLESTEROL

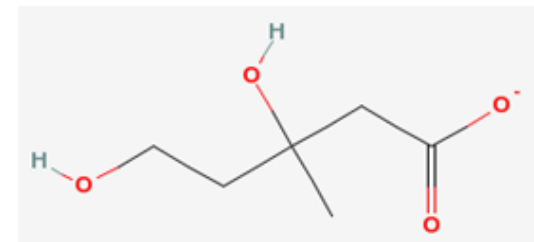
Cholesterol is derived from

- **diet**
- **de novo synthesis and**
- **from the hydrolysis of cholesteryl esters.**
- A little more than half the cholesterol of the body arises by synthesis (about 700 mg/d), and the remainder is provided by the average diet.
- The majority of cholesterol is **synthesized in the liver**, which produces ~50% of the total daily cholesterol requirement (~1 gr)
- Virtually all tissues containing nucleated cells are capable of cholesterol synthesis, which occurs in the **endoplasmic reticulum and the cytosol.**

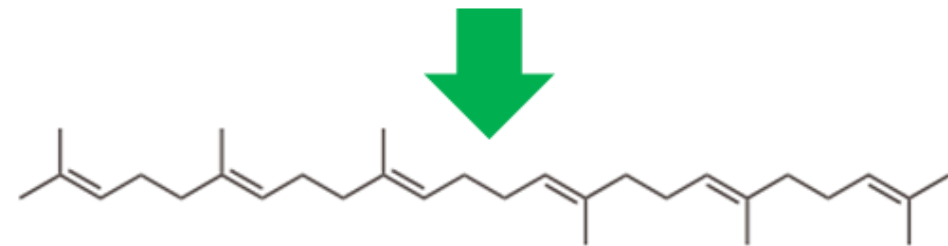
Almost equal amount of cholesterol is derived from diet (eggs, dairy, meat) and synthesis in the body

Acetyl CoA → Acetoacetyl CoA → 3-hydroxy-3-methylglutaryl CoA (HMG CoA)

HMG CoA Reductase  Statins

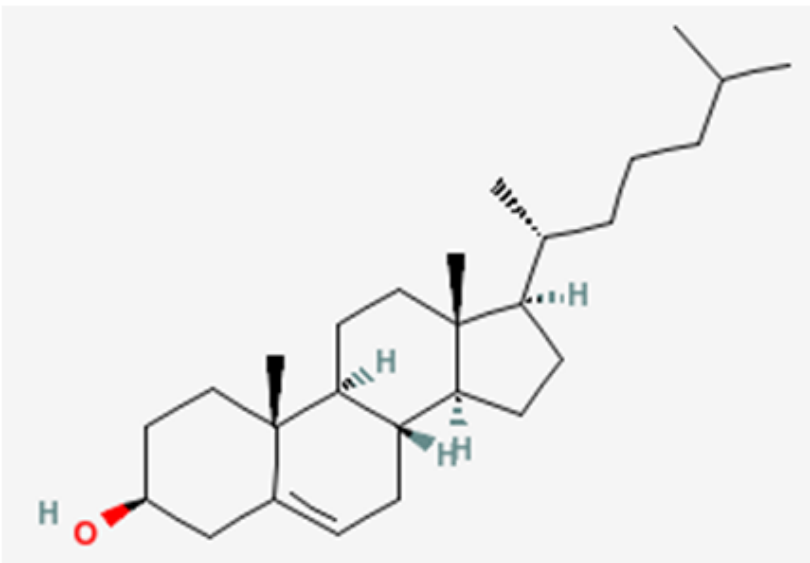


Mevalonate



Squalene

Cyclized 



Cholesterol

Almost equal amount of cholesterol is derived from diet (eggs, dairy, meat) and synthesis in the body.

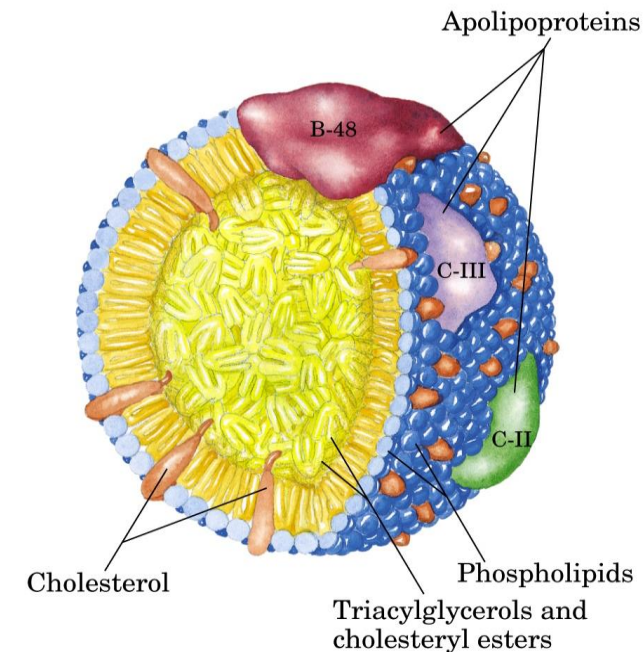
PLASMA LIPOPROTEINS

Lipids are only sparingly soluble in water, and the movement of lipids from one organ to another through the bloodstream requires a transport system that uses **plasma lipoproteins**.

Lipoprotein particles are spheres that consist of a core of hydrophobic lipids surrounded by an outer layer or shell of amphipathic proteins, phospholipids, and cholesterol.

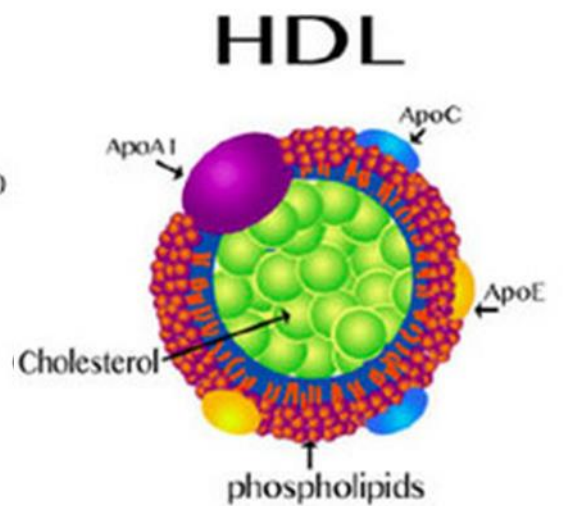
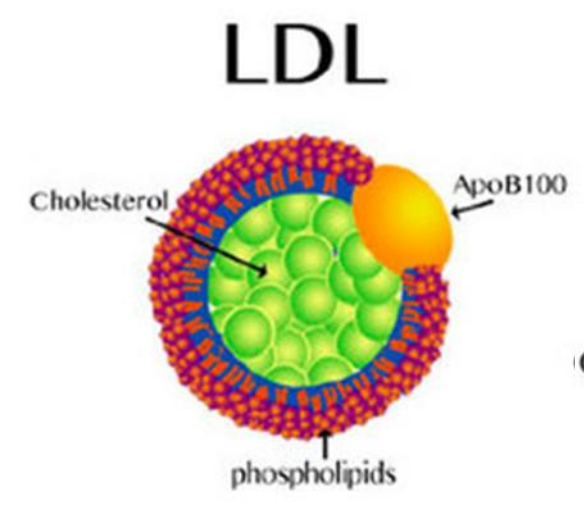
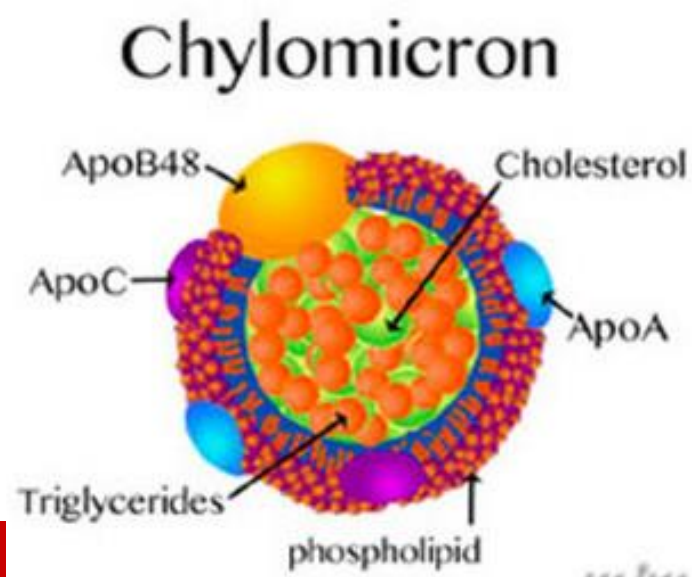
There are four major classes of human plasma lipoproteins:

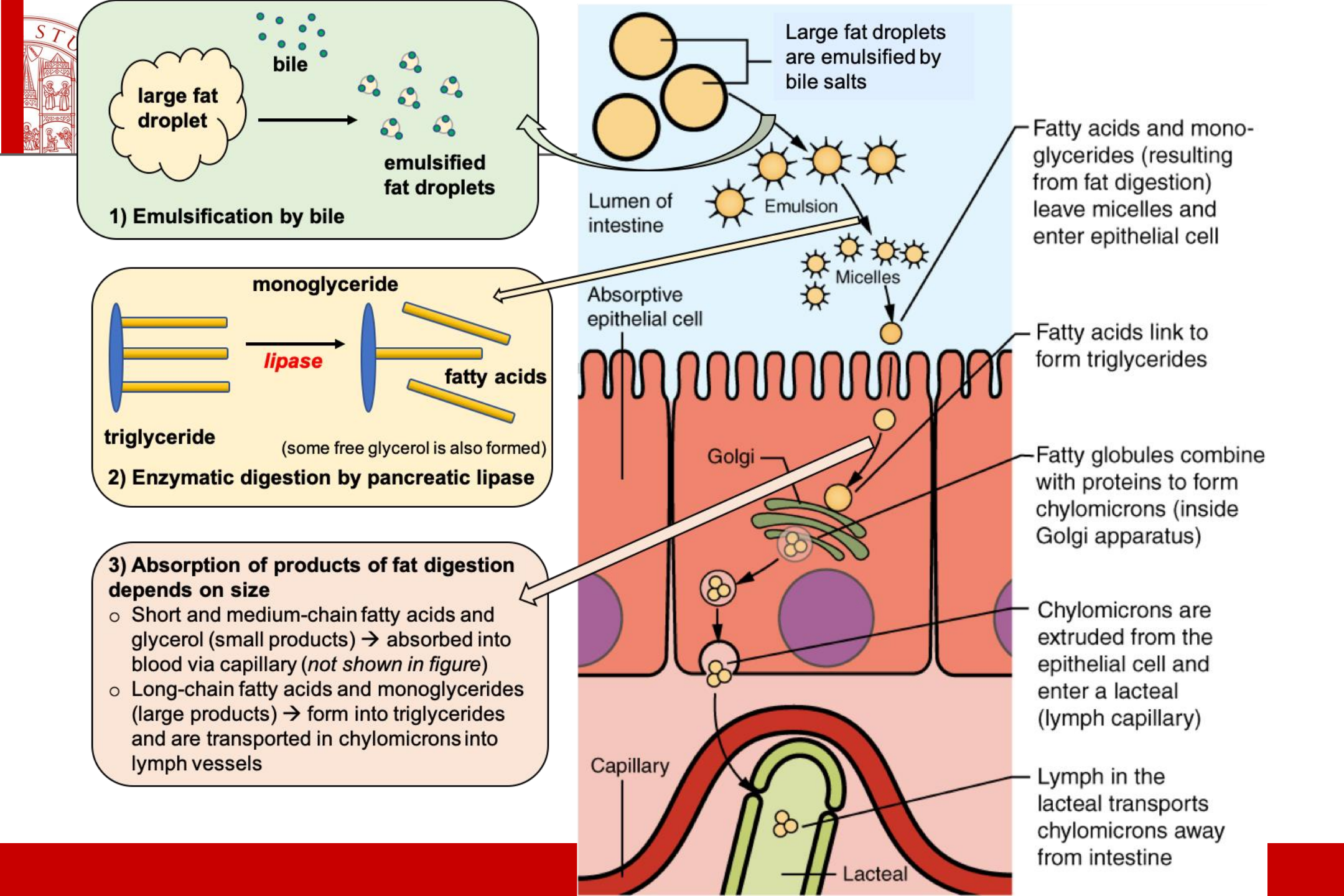
- **Chylomicrons**, that carry dietary triglycerides and cholesterol from the intestine to liver and other tissues.
- **Very low density lipoproteins (VLDL)** that bind triglycerides synthesized in the liver and carry them to adipose and other tissues for storage.
- **Low-density lipoproteins (LDL)** that carry cholesterol and TG from the liver to peripheral tissues and regulates cholesterol levels in those tissues. These are richest in cholesterol.
- **High-density lipoproteins (HDL)** that transport cholesterol from peripheral tissues to the liver.

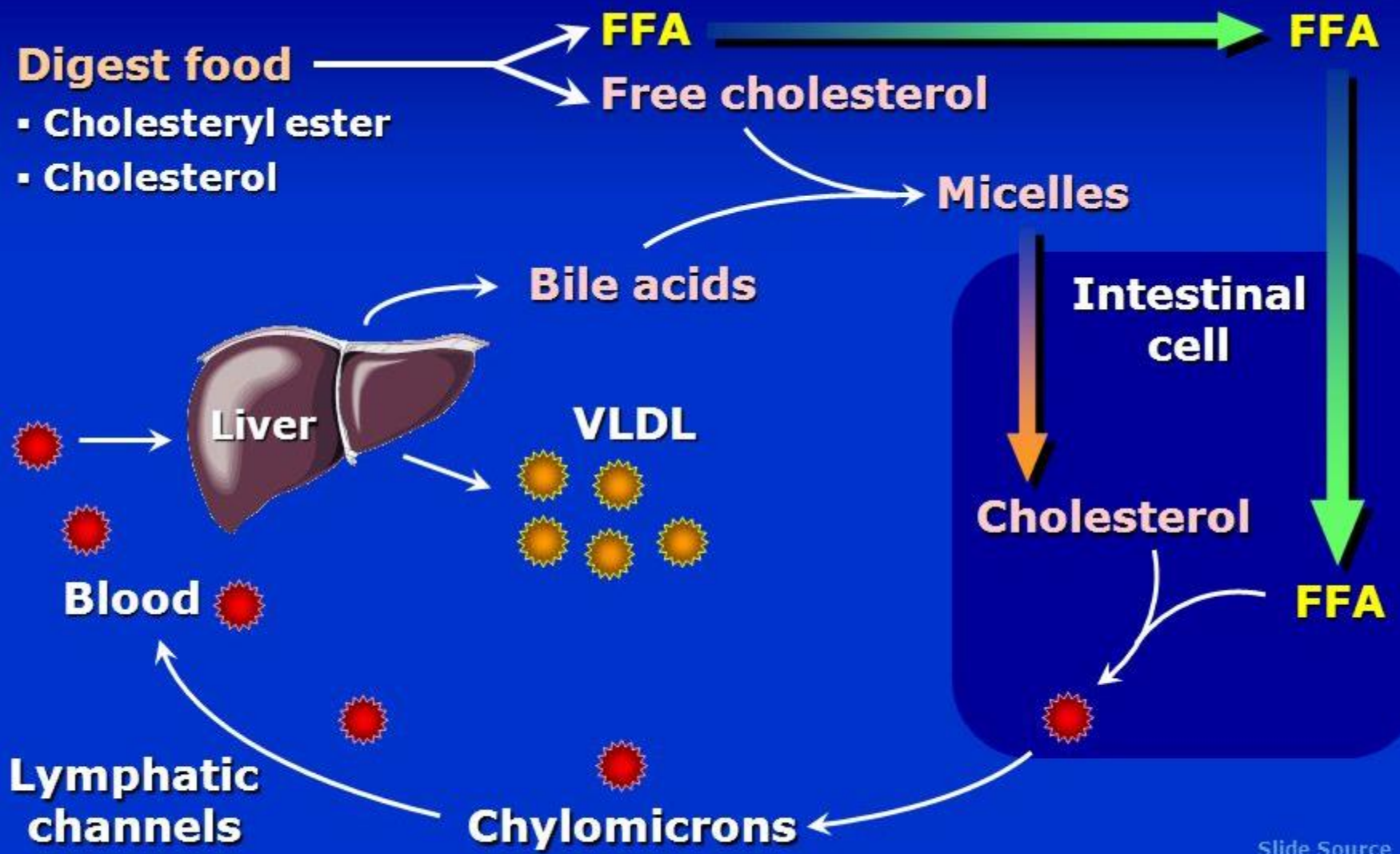




	Chylomicron	LDL	HDL
Diagram			
● Triacylglycerol			
● Cholesterol			
○ Phospholipid			
■ Apoprotein			



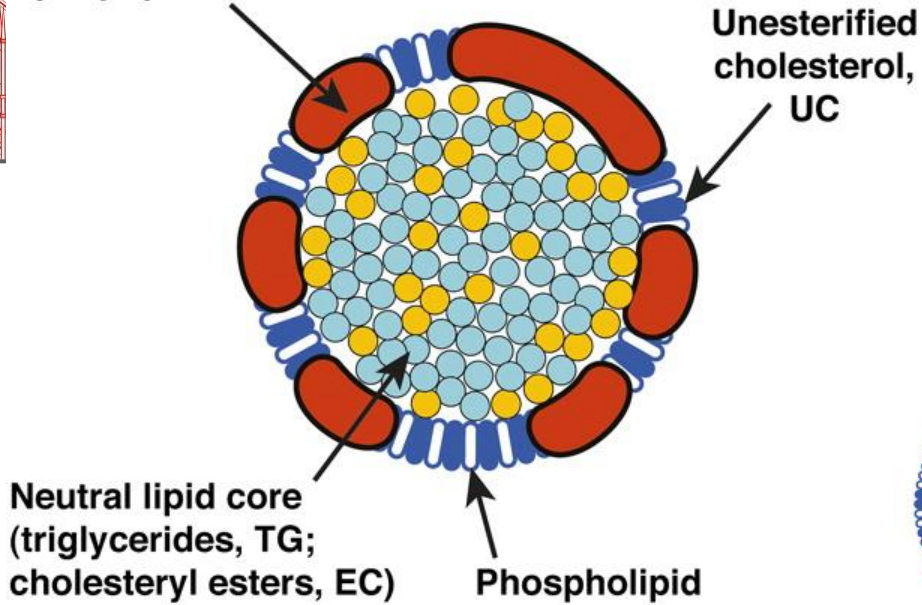




Slide Source
LipidsOnline
www.lipidsonline.org



Apolipoproteins

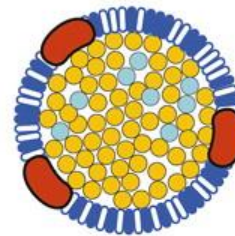


600 nm

60 nm

25 nm

12-7 nm



Ultracentrifugation

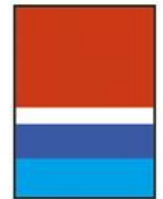
Chylomicrons (CM)

VLDL

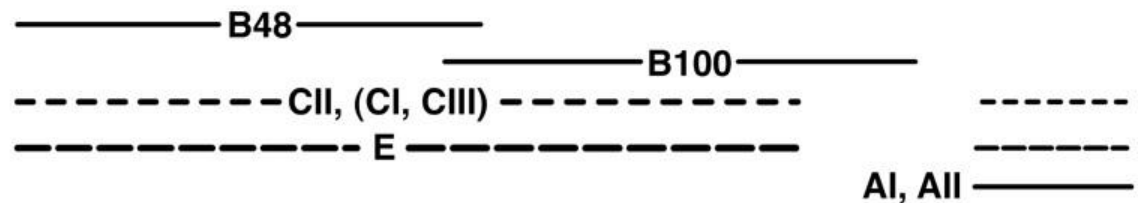
LDL

HDL

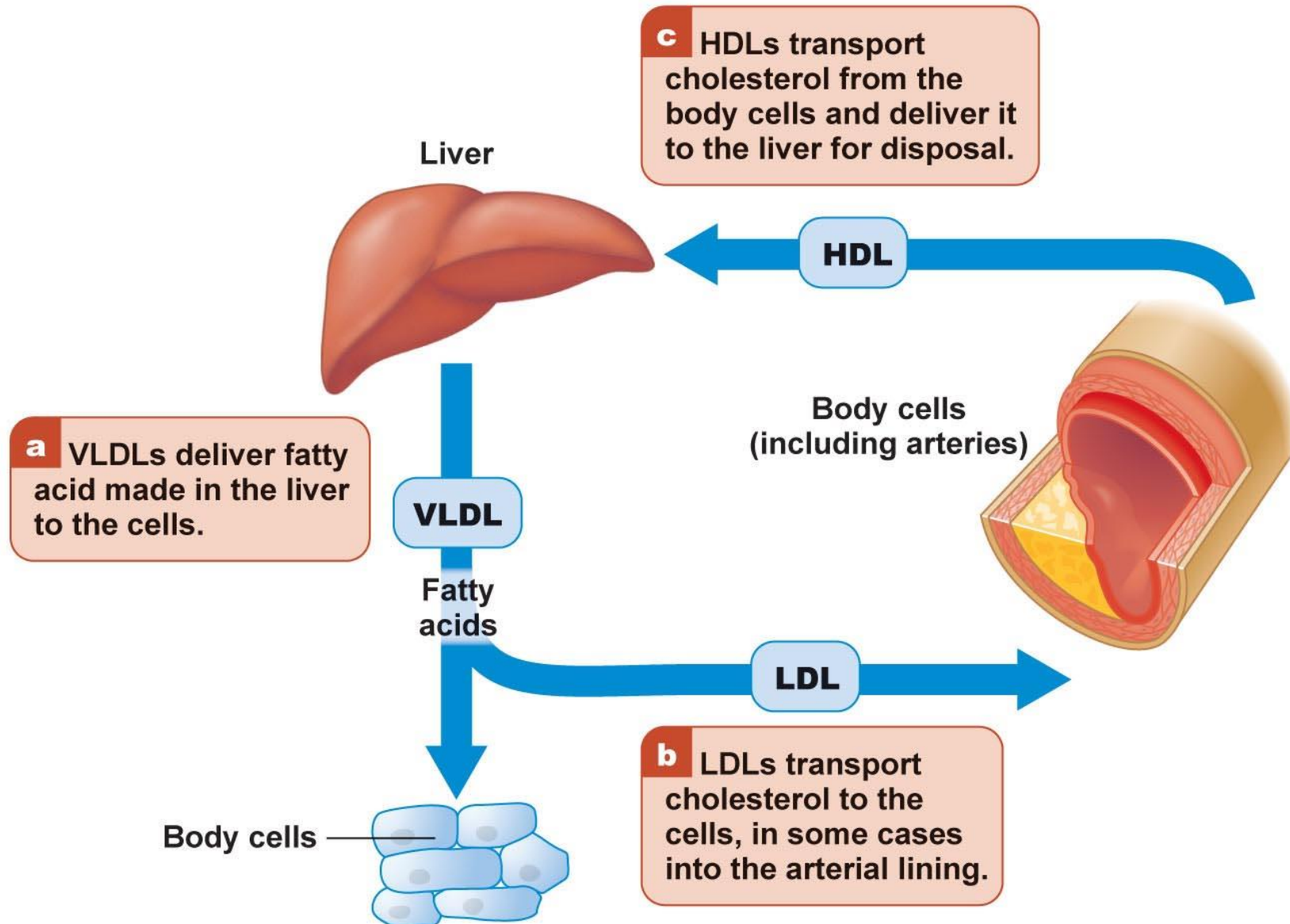
Composition

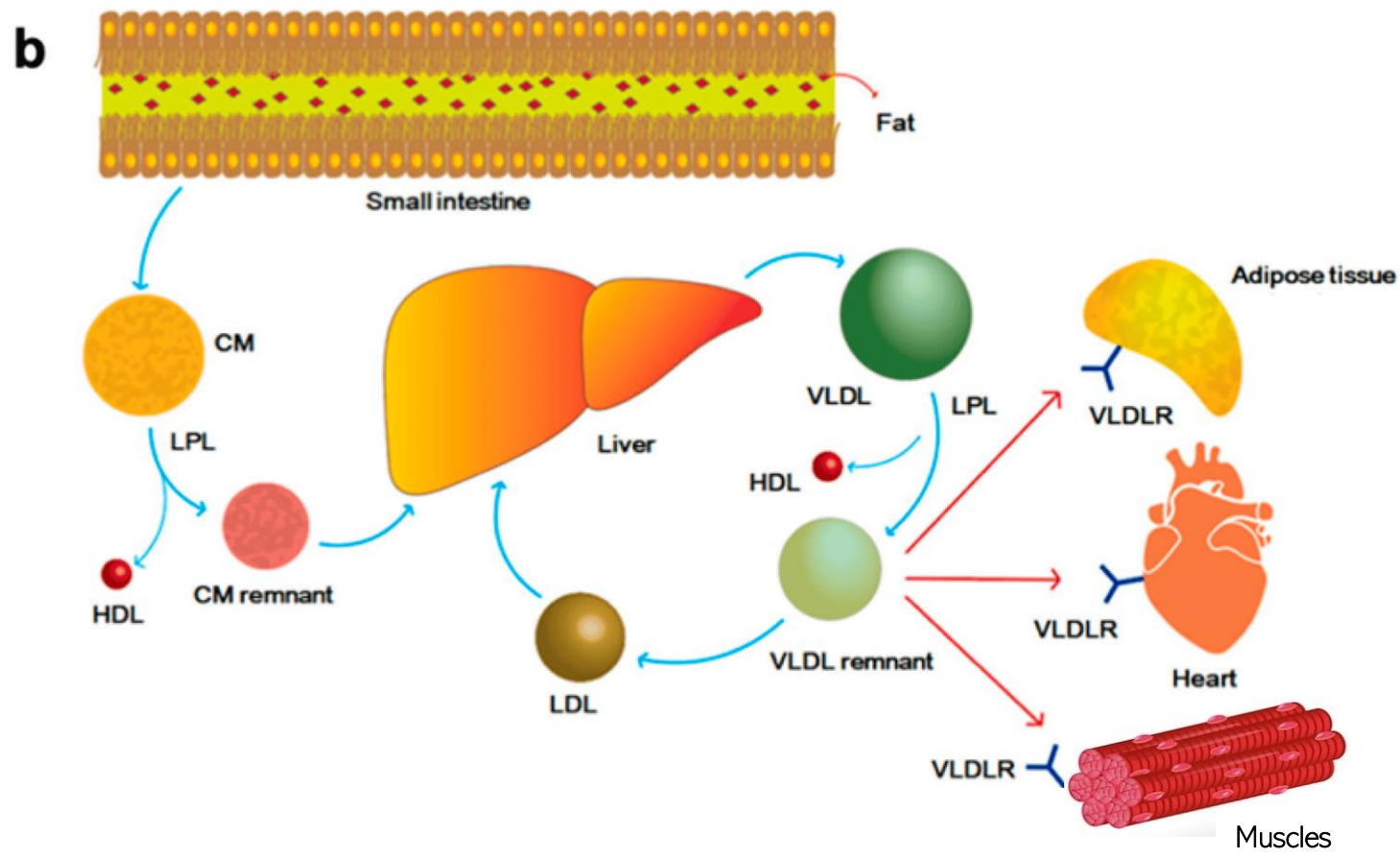
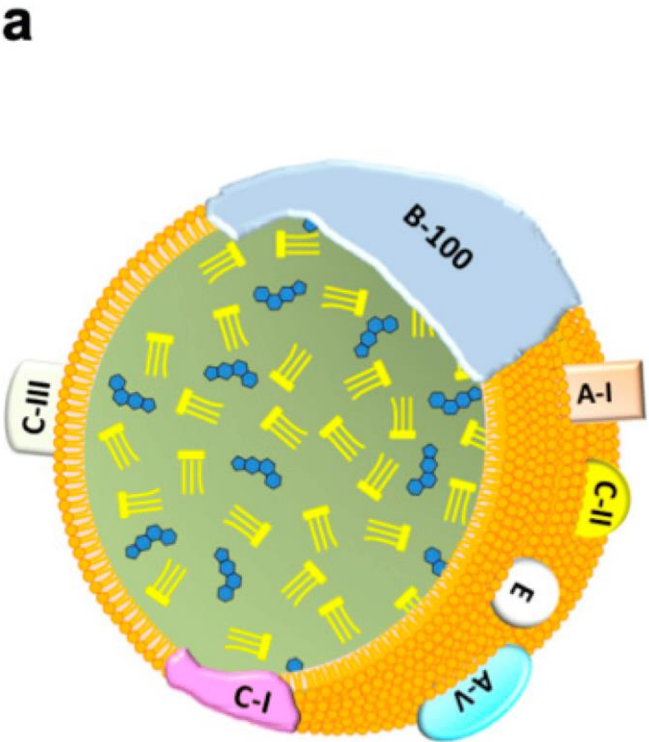


Apolipoproteins



The Roles of VLDL, LDL, and HDL Lipoproteins

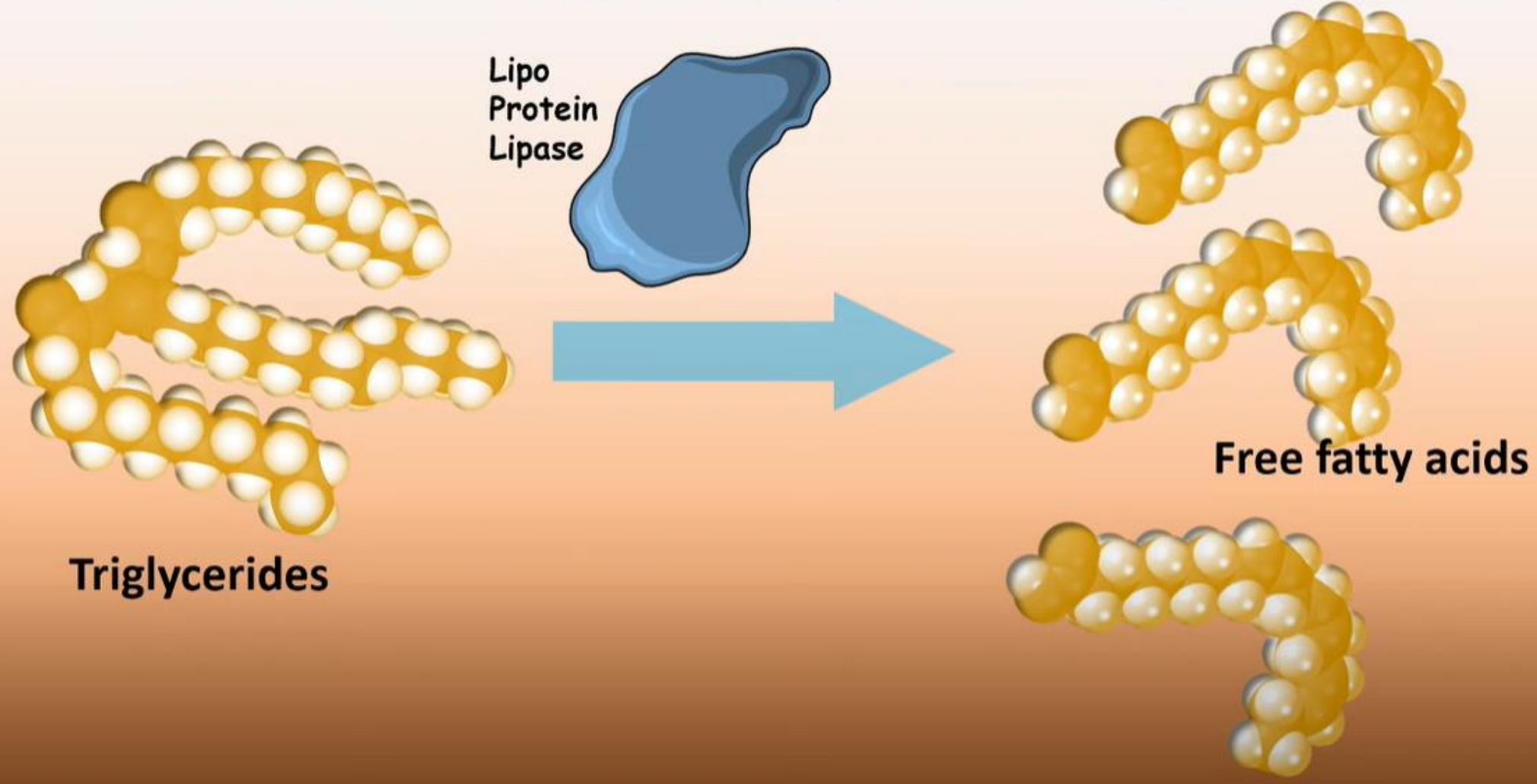




Int. J. Mol. Sci. 2022, 23(8), 4300; <https://doi.org/10.3390/ijms23084300>

https://www.google.com/search?q=VLDL+LDL+function&source=lmns&tbn=vid&bih=911&biw=1920&rlz=1C1GCEU_itIT1060IT1060&hl=it&sa=X&ved=2ahUKEwjvZKM1oeEaxWLnf0HHZLbCIEQ0pQJKAJ6BAgBEAY#fpstate=ive&vld=cid:266b0813,vid:9dghtf7Z7fw,st:0

The fatty acids are stored (by the adipose) or used for energy (by the muscle).



Bad vs. Good Cholesterol



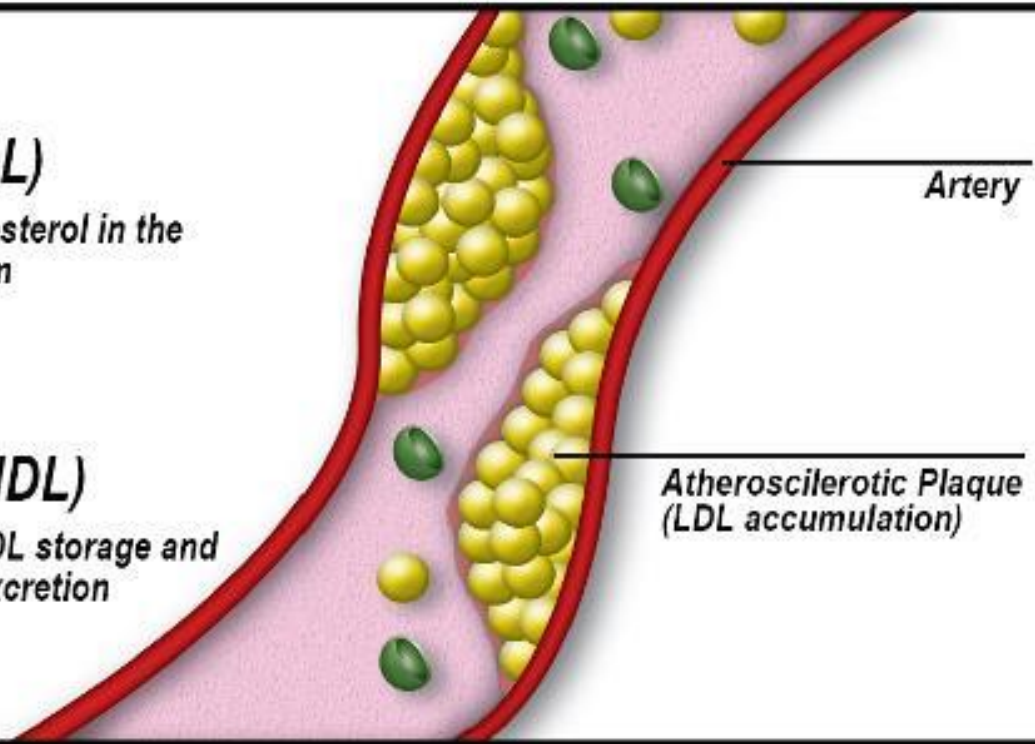
Bad (LDL)

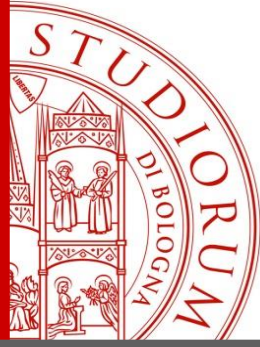
stores cholesterol in the blood stream



Good (HDL)

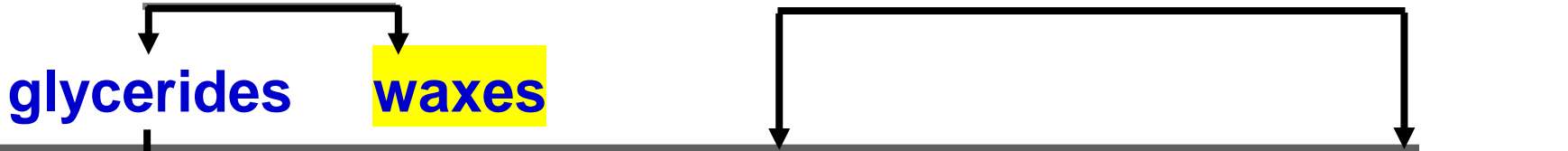
regulates LDL storage and promotes excretion





Neutral lipids

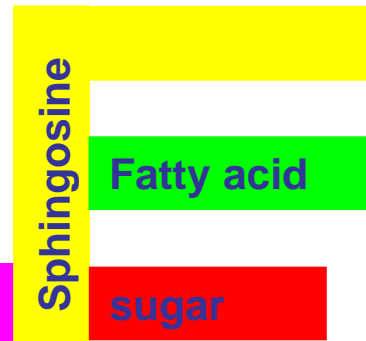
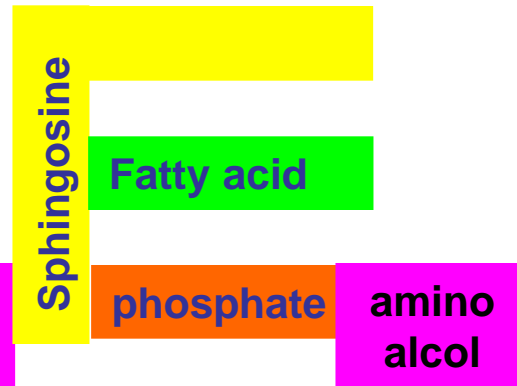
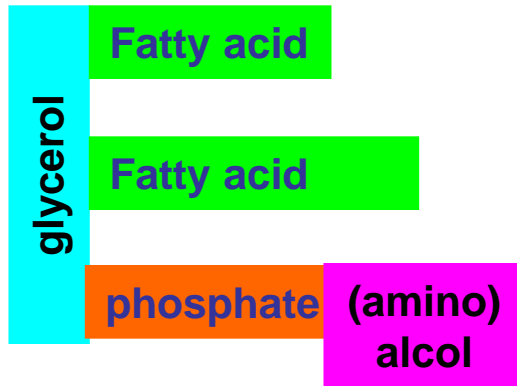
Polar lipids



monoglycerides
diglycerides
triglycerides

glycerophospholipids

sphingolipids

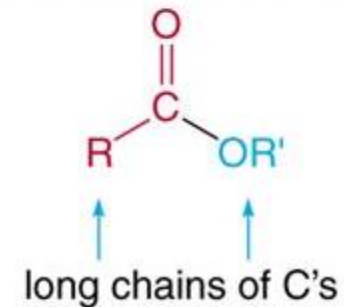


WAXES

- **Waxes** are esters (RCOOR') formed from a **fatty acid** and a high molecular weight **alcohol**.

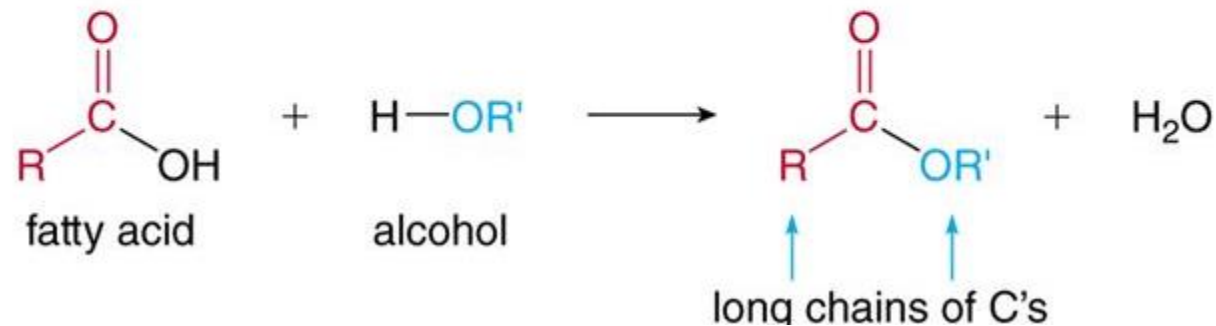
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- **General structure of waxes:**

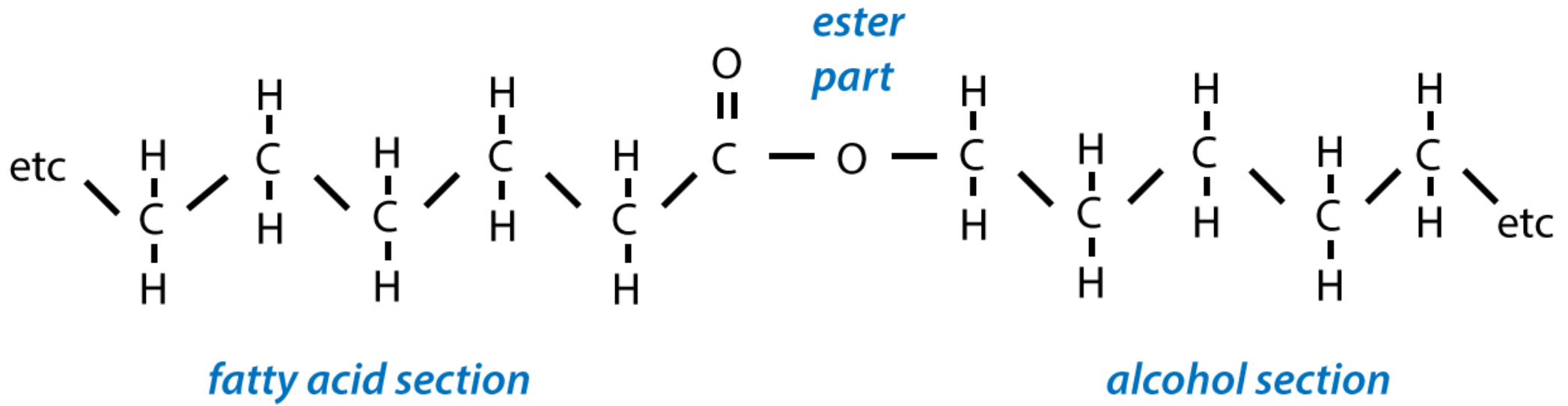


- **General formation of waxes:**

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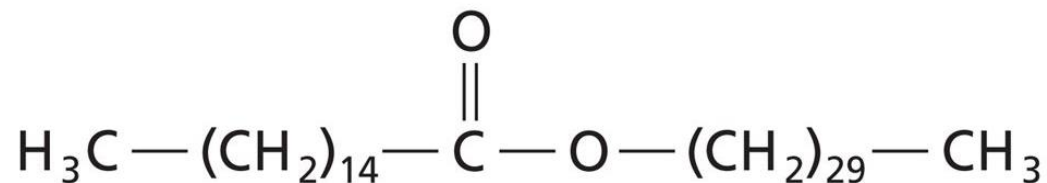


WAXES



WAXES

■ These are long-chain saturated and unsaturated fatty acid esters (C₁₄ to C₃₆) with long-chain alcohols (C₁₆ to C₃₀), with high melting points (60-100°C). These are solid at room temperature, due to their high molar masses.



Palmitic acid, a major component of beeswax to build honeycomb cells



- Because the long hydrocarbon tails are extremely hydrophobic, waxes are completely insoluble in water.
- In plants, waxes cover the external parts, like epidermis of leaves and fruits, to prevent the loss of water.
- Lanolin, which serves as a protective coating for hair and skin, is used in skin creams and surfactants. Carnauba wax is used in car polish.

Kahoot!

