Āris Kaksis, 2019. year, Riga Stradin`s University http://aris.gusc.lv/BioThermodynamics/LipidiEng.pdf

SAC Surface Active Compound-**Lipids** organize compartments separated diphilic double layer cell membranes as water and solutes impermeable wall

Theoretical concepts and terms. **Water** insoluble lipids are divided in two groups :

1. Lipids absolutely insoluble in **water** unlike proteins, carbohydrates, nucleic acids.

2. Lipids surface active compounds SAC with distinguish groups of atoms against **water**

organize diphilic double layer interface as cell membranes with:

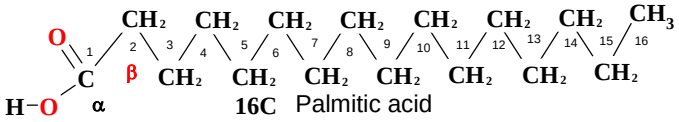
- Functional atomic groups-segments of molecule: hydrophilic and hydrophobic.

- Hydrophobic hydrocarbon string extended from methyl group $-CH_3$ on end of carbon chain string right side tail to hydrocarbon chain head along methylene $-CH_2-$ groups.

- In nature occurs Fatty acids carbon chains even numbers combinatorics 2 ,4 ,6 ,8 ,10 ,12 ,14 ,16 ,18 ,20 ,22:

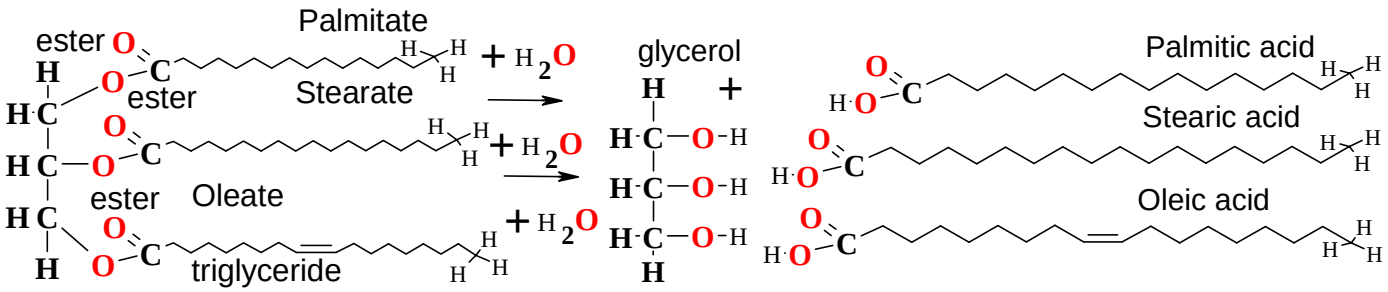
except 5C not even 2C, 4C, 5C, 6C, 8C, 10C, 12C, 14C, **16C**, 18C, 20C, 22C,.

Acyl-transferase enzymes elongate chain in cytosole and peroxisomes but shorten in peroxisomes and mitochondria with β-oxidation enzymes on second 2 beta β position.

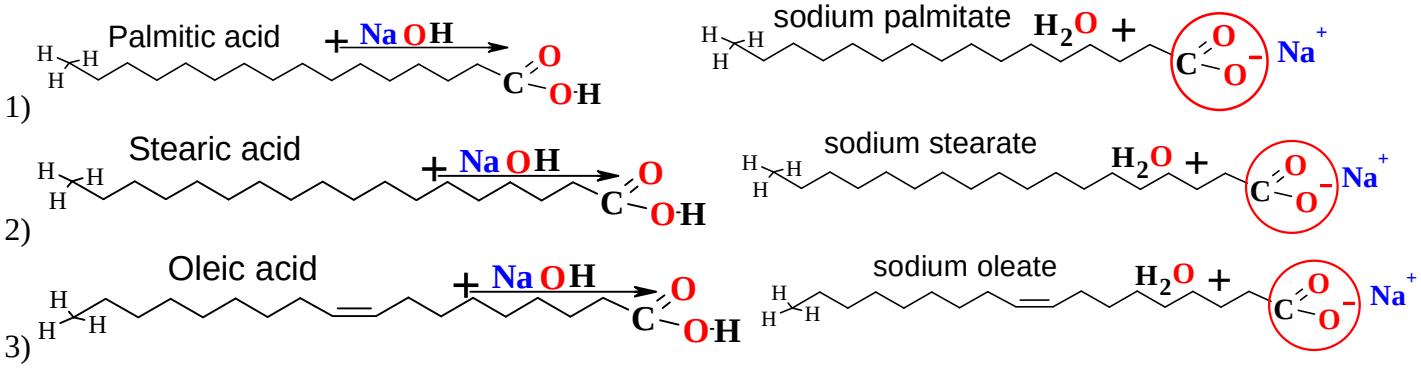


Ester bonds in triglycerides - fats and oils are Hydrolysed

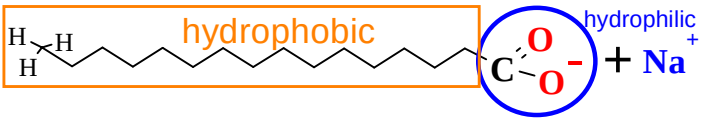
Triglyceride hydrolyse products are glycerol,, three fatty acids palmitic acid, stearic acid, oleic acid.



3 fatty acids neutralization reactions with **NaOH** products are salts and water.



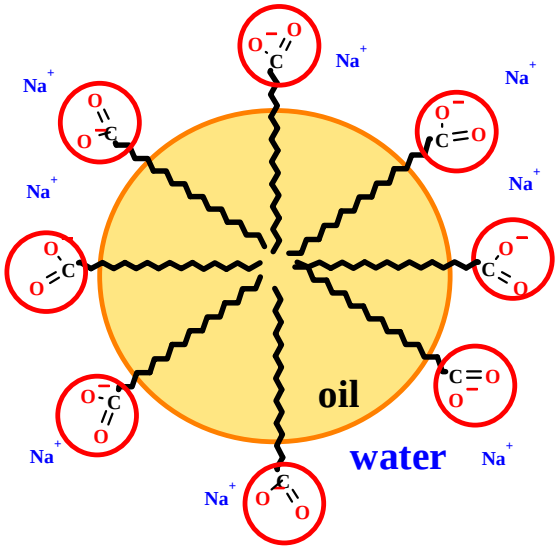
Water soluble SAC Surface active compounds have soluble hydrophilic in alkaline medium pH 11-12



part strong electrolyte dissociated salt $H_3C–(CH_2)_{14}–COO^-+Na^+$ and water insoluble non polar hydrophobic part.

In alkaline medium pH 11-12 Sodium palmitate is formed as **water** soluble surface active compound **SAC** salt – strong electrolyte.

$H_3C–(CH_2)_{14}–COO^-Na^+$ strong electrolyte dissociates in to positive cation Na^+ and negative carboxylic anion $H_3C–(CH_2)_{14}–COO^-$. If **16C** hydrocarbon chain $H_3C–(CH_2)_{14}–C\equiv$ deeps into **oil** droplet



Double layer is stabilized with carboxylic anion $–COO^-$ faced to **water** on interface **oil / water**. The sodium cations Na^+ are dissociated into **water** medium so supporting double layer stability for non polar **hydrophobic** droplet medium of **oil** against to polar dispersion medium of **water**. Negative charged droplets (-)⇔(-) repulse each other, prevent fuse together more, Oil droplets keep the distance from each other.

Oil/water emulsions are usual meet in Nature: milk, butter, in human blood: chylomicrons, VLDL very low density lipoprotein vesicles, LDL low density lipoproteins, HDL.

Water/oil emulsion type is very rare as like cream, unless common are

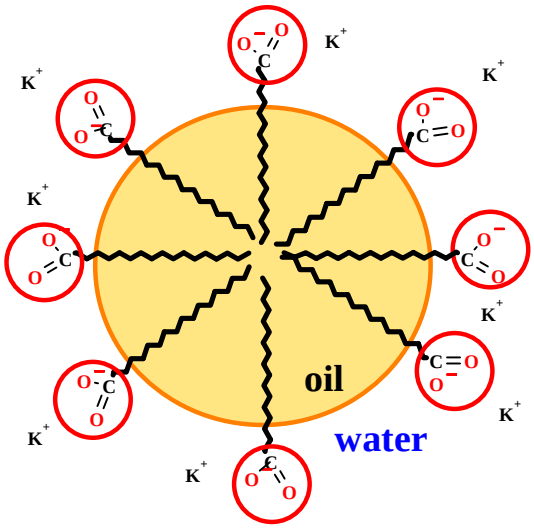
Like as from milk **oil/water** in air forms the cream **water/oil** as staining upper layer is cream, where soluble Na^+ and K^+ salts turned to insoluble fatty acids pH=6 and more acidic. Simulation experiment with 1% $CaCl_2$ forms insoluble fatty acid calcium salts like acidic medium in cream formation from milk.

Milk emulsion simulation with potassium oleate

To potassium oleate salt add vegetable oil and shaking obtains one milk like white opalescent liquid. Potassium oleate salt molecule with hydrophilic and hydrophobic part is SAC surface active compound.

$H_3C–(CH_2)$-**HC=CH**-$(CH_2)_7–COO^-$ K^+ strong electrolyte dissociated to positive cation K^+ and negative carboxylic anion $H_3C–(CH_2)$-HC=CH-$(CH_2)_7–COO^-$.

If **18C** hydrocarbon chain deeps into **oil** droplet



Double layer stabilizes with carboxylic anion $–COO^-$ faced to **water** on interface **oil/ water**. The potassium cations K^+ are dissociated into **water** medium so supporting double layer stability for non polar **hydrophobic** droplet medium of **oil** to polar **hydrophilic** dispersion medium of **water**.

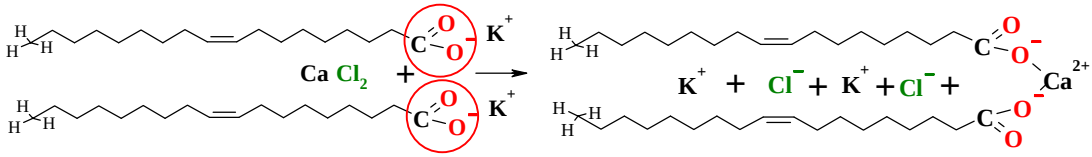
Negative charged droplets (-)⇔(-) repulse each other, prevent fuse together more, Oil droplets keep the distance from each other.

To add 1% **$CaCl_2$** solution, to shake, to observe staining upper layer or repeat unless staining upper layer.

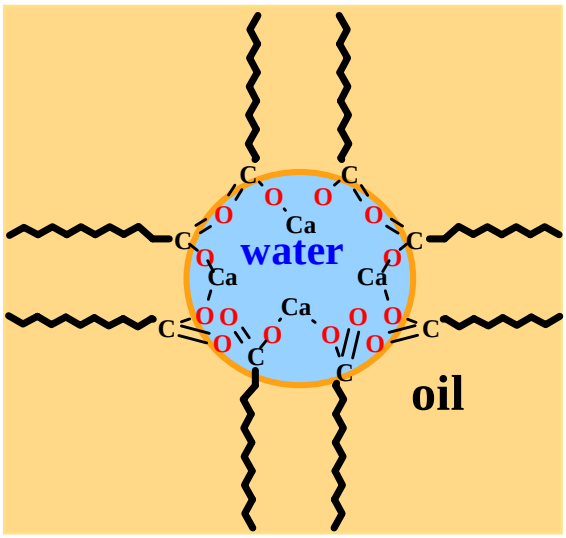
Cream staining upper layer with white cream-like opalescence.

Bottom layer becomes clear and transparent water solution.

Potassium oleate ion exchange with calcium ions to form water insoluble calcium oleate salt.



Potassium oleat electrolyte emulgator changes from **hydrophilic** to **hydrophobic**. So **hydrophobic** emulgator $H_3C–(CH_2)$-**HC=CH**-$(CH_2)_7$–**COO**$^-)_2Ca^{2+}$ calcium oleate is insoluble in **water**. It just touches to **water** droplet surface. **Hydrophobic** emulgator performs inversion replacing **hydrophilic** emulgator.



Fatty acid K^+ salts are strong electrolytes soluble in **water**.

Water insoluble non electrolytes as Ca^{2+} or Mg^{2+} salts.

That is inverse disperse system type **water/oil**.

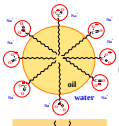
Due to disperse system phase type inversion

after **$CaCl_2$** addition, is in ion exchange reaction

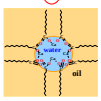
forming **water** insoluble

Ca^{2+} fatty acid salt calcium oleate.

Determination of disperse medium type:



droplets of **oil** into **water** **oil/water**



droplets of **water** into non polar **oil** **water/oil**.

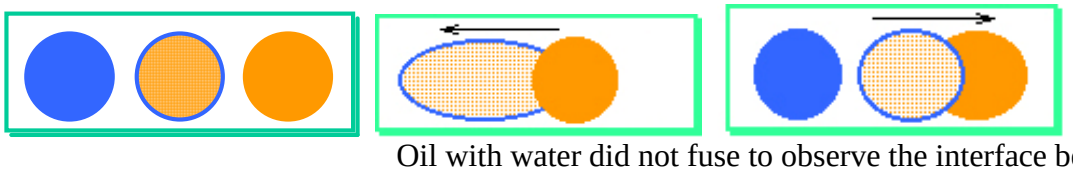
Knowing properties of dispersion medium can detect the type of disperse medium by distinguish:

a) Disperse medium which did not fuse are **hydrophilic** ● and **hydrophobic** **oil** ○;

b) of solubility into water **H_2O**; c) possible disperse medium colour by different panting;

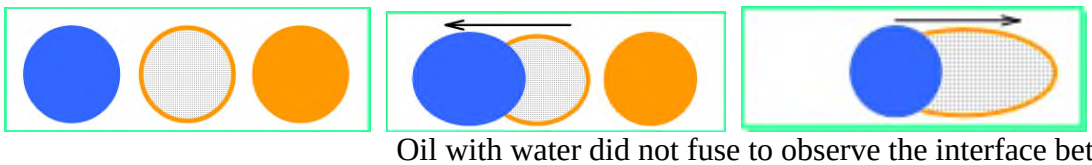
d) facilities disperse medium to conduct of electric current through.

To put on clean surface of slide close adjacent that touch the three drops **water** ●, emulsion ○, **oil** ○.



Oil with water did not fuse to observe the interface between

To put on clean surface of slide close adjacent that touch the three drops **water** ●, emulsion ○, **oil** ○.

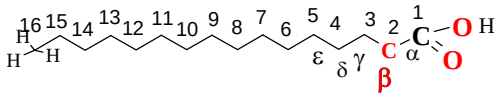


Oil with water did not fuse to observe the interface between

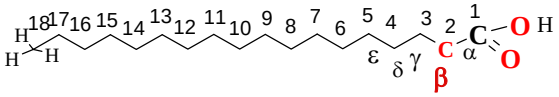
Fatty acids are saturated and unsaturated

Fatty acids are the linear shapes carbon atoms chains, in which carbon atoms count is changed per even every two carbon atoms 4C, 6C, 8C, 10C, 12C, 14C, 16C, 18C, 20C by acyl transferases enzymes at elongation and decomposition at β-oxidation in mitochondria and peroxisomes.

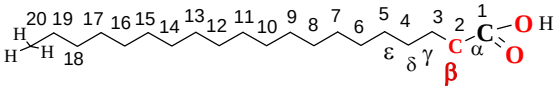
Saturated Fatty acids do not have double bonds on hydrocarbon chain:



IUPAC : hexadecanoic acid; medical: palmitic acid **C**16



IUPAC : octadecanoic acid ; medical: stearic acid **C**18



IUPAC : eicosanoic acid ; medical: arachidic acid **C**20

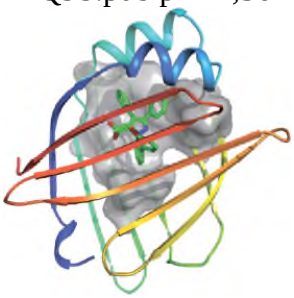
Unsaturated omega Fatty acids

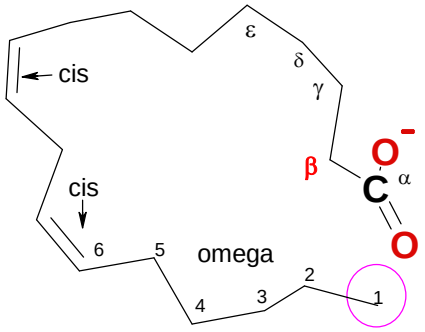
Maintenance of living functions for human organism are essential fatty acids (ω=6 or ω=3) unsaturated, which contains one double bond **C**_:1 or many (maximum four **C**_:4) double bonds.

In medicine designated as omega (ω=6 and ω=3) fatty acids, what shows the double bond position from the tail **H_3C–** of fatty acid chains. So ω=6 and ω=3 are essential:

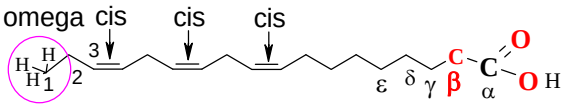
linoleiate **C**18:2 ω-6

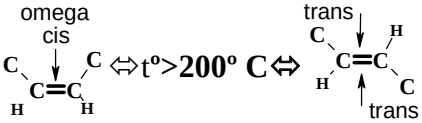
FAB4 protein pocket structure 2Q9S.pdb pH=7,36





α-linolenic acid **C**18:3 ω-3



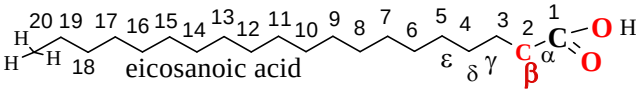
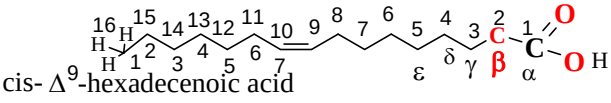
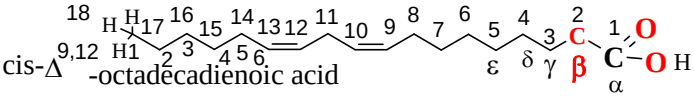
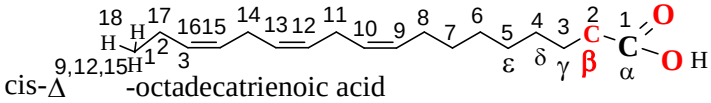


Harmful trans in Latvian food limited less 1%

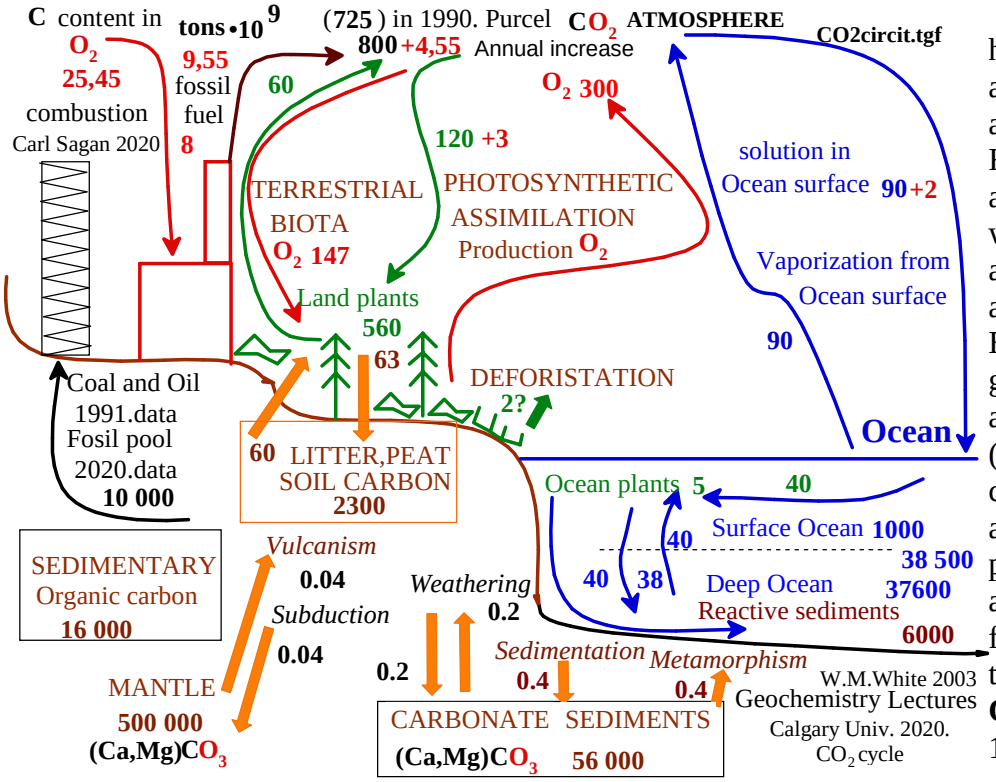
Omega unsaturated fatty acids count start from tail methyl **H_3C–** group. **Essential** are ω-6 and ω-3

Descriptive Name	Abbreviation system				
	Numeric	Δ □	n	**C:=**	ω
Palmitate	16:0				
Palmitoleate	9—16:1	16:01 Δ 9	16:1n-7	16:01	ω-7
Linoleate	9,12—18:2	18:02 Δ 9,12	18:2n-6	18:02	ω-6
α-Linolenate	9,12,15—18:3	18:03 Δ 9,12,15	18:3n-3	18:03	ω-3

Harmful trans double bonds are formed at heating over t ° **>200 ° C** and in microwave oven over 50% .

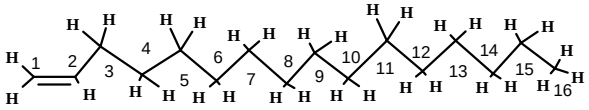
Table.	**Carbon**	**Structural Formulas.**	**IUPAC Systematic name**	**Common Name**	**mp(°C)**
A Some natural fatty acids.		*Fatty Acids break down in mitochondria through beta carbon oxidation reaction producing* **CO_2**, **H_2O** *and life energy*		Notional name	
		Saturated fatty acids	no double bonds between **C**&**C** atoms		
palm oil	16**C**	$CH_3(CH_2)_{14}$ CO_2H	hexadecanoic acid	palmitic acid	63
Greek *stear* fat	18**C**	$CH_3(CH_2)_{16}$ CO_2H	octadecanoic acid	stearic acid	70
Arachis Peanut	20**C**		eicosanoic acid	arachidic acid	77
		Unsaturated fatty acids			
Palm oil	$C_{16:1}$ ω-7		cis- Δ^9-hexadecenoic acid	palmitoleic acid ω-7	-1
Latin *oleum* oil	$C_{18:2}$ ω-6 linseed oil		cis-$\Delta^{9,12}$-octadecadienoic acid	linoleic acid **essential** ω-6	-5
Latin *linum* flax, and *oleum* }oil	$C_{18:3}$ ω-3		cis-$\Delta^{9,12,15}$-octadecatrienoic acid	α-linolenic acid **essential** ω-3	-11

Carbon atoms compound palmitate C16 plus 16 H_2O molecules fuel-life



Fuel is mixture of hydrocarbons, where carbon atoms are bound between **C-C-C-C-C-C** and completed by hydrogen atoms. Fuel engines use for heat, electric and mechanics energy. Civilization with combustion pollutions add to atmosphere $\mathbf{CO_2}\uparrow_{gas}$ content 100% about plus 1,2%. Ocean and in all Earth waters dissolute 47 times greater $\mathbf{CO_{2aqua}}$ amount as in atmosphere 100%, but carbonate (Ca,Mg)$\mathbf{CO_{3ciets}}$ sediments in Earth crust contains 70 times more $\mathbf{CO_2}$ as in atmosphere 100%. Green plant photosynthesis each year assimilates $\mathbf{CO_2}$ amount 15,4% from atmosphere 100% and water total 53*100%, producing glucose $\mathbf{C_6H_{12}O_6}$ 307,5 with carbon mass 120+3 Gt. Photosynthesis evolved oxygen amount in atmosphere 300-147=153 stabilises global $\mathbf{O_2}$ concentration in atmosphere 20,95%. Six carbon atoms **C-C-C-C-C-C** fuel combusts with six oxygen molecules produces six $\mathbf{CO_2}$ molecules. From glucose $\mathbf{C_6H_{12}O_6}$ in cellular synthesis creates long chain fatty acids 4C,6C,8C,10C,12C,14C,**16C**,18C.

Sixteen carbon atoms $\mathbf{C_{16}H_{32}}$ fuel 1-hexadecen combusts producing $\mathbf{CO_2}$ and $\mathbf{H_2O}$.

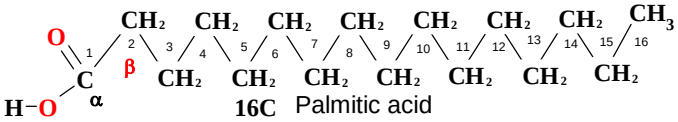


$$+24\mathbf{O_2}\uparrow_{gas} \xrightarrow{\text{combustion}} 16\mathbf{CO_2}\uparrow_{gas} +16\mathbf{H_2O} +\Delta G +\mathbf{Q}$$

Reaction is $\Delta\mathbf{G}_{Hess}$= -10251,9 $^{kJ}/_{mol}$ exoergic**;**
$\Delta\mathbf{H}_{Hess}$= -10541 $^{kJ}/_{mol}$ exothermic as heat **Q** evolved.

1. Engine fuel is water insoluble, therefore not soluble intracellular and in extracellular space.
2. Gases oxygen and carbon dioxide are deadly for cellular organisms (medical symptom emboly), broken and stuck the transport across membranes.

Fatty acids as palmitate C16 with 16 $\mathbf{H_2O}$ in mitochondria and peroxisomes beta oxidation are bio fuel.



$$+16\mathbf{H_2O}+23\mathbf{O_{2aqua}} \xrightarrow{\text{beta oxidation}} 16\mathbf{HCO_3^-}+16\mathbf{H_3O^+}+\Delta G +\mathbf{Q}$$

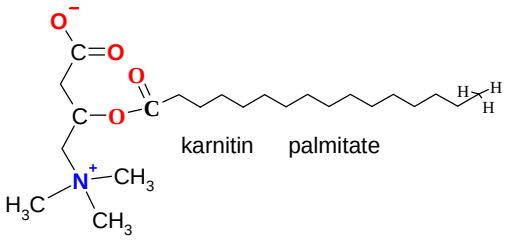
Reaction is $\Delta\mathbf{G}_{Hess}$= - 9075,6 $^{kJ}/_{mol}$ exoergic**;**
$\Delta\mathbf{H}_{Hess}$= - 9853,87 $^{kJ}/_{mol}$ exothermic as heat **Q** evolved.

1. Fatty acids binding proteins FABPs transfer lipids intracellular and in extracellular space.
2. Oxygen and water osmosis through aquaporins entrance cells, mitochondria and peroxisomes. Beta oxidation products generate concentration gradients $\mathbf{16HCO_3^-}$+$\mathbf{16H_3O^+}$ in direction from cells out through proton and bicarbonate channels. Oxygen and water osmosis through aquaporins going against osmolar concentration gradient ΔC_{osm} http://aris.gusc.lv/BioThermodynamics/ColigativeProperties.pdf intracellular direction of fatty acids beta_oxidation. Transport proteins FABPs, lipocalins, albumin maintained transports for fatty acids established homeostasis in organism. Sportsmens designated it as second breath at physical active load.

Note: beta oxidation occurs in mitochondria, peroxisomes:

Fatty acids yield similar energy in comparison with engine fuel calculated values~10000 $^{kJ}/_{mol}$..

Myoglobin molecule Mb oxygen adsorbtion bind long chain fatty acids 6C,8C,10C,12C,14C,**16C**,18C,20C acylkarnitin with **energy** from -15,8 to -30,7 *kJ/mol*. Oxygen desorption $\mathbf{O_2} \Leftrightarrow \mathbf{H^+}, \mathbf{HCO_3^-}$ of shuttle molecules Mb instantly release acylkarnitin but bind beta oxidation products $\mathbf{H^+}, \mathbf{HCO_3^-}$. So maintain concentration [$\mathbf{O_{2aqua}}$] , pH=7,36 stable. Mb shuttle serves as fuel suppliers to muscle and cardio myocite cells physiologic sustain [$\mathbf{O_{2aqua}}$] , pH=7,36 in homeostasis. 2016 J.Biol.Chem. 291:25133-25143.



Lipids cell **membrane** diphilic components

Lipids-SAC **S**urface **A**ctive **C**ompounds as molecules organize diphilic double layer interface which form **water** and **solutes** impermeable cell wall **membranes** in life organisms

Surface Active Compounds SAC are made of two specially separated functional groups-segments of molecule: **hydrophilic** and **hydrophobic** atomic groups.

hydrophilic (polar(-),(+)) group and **hydrophobic** (non polar) hydrocarbon chains.

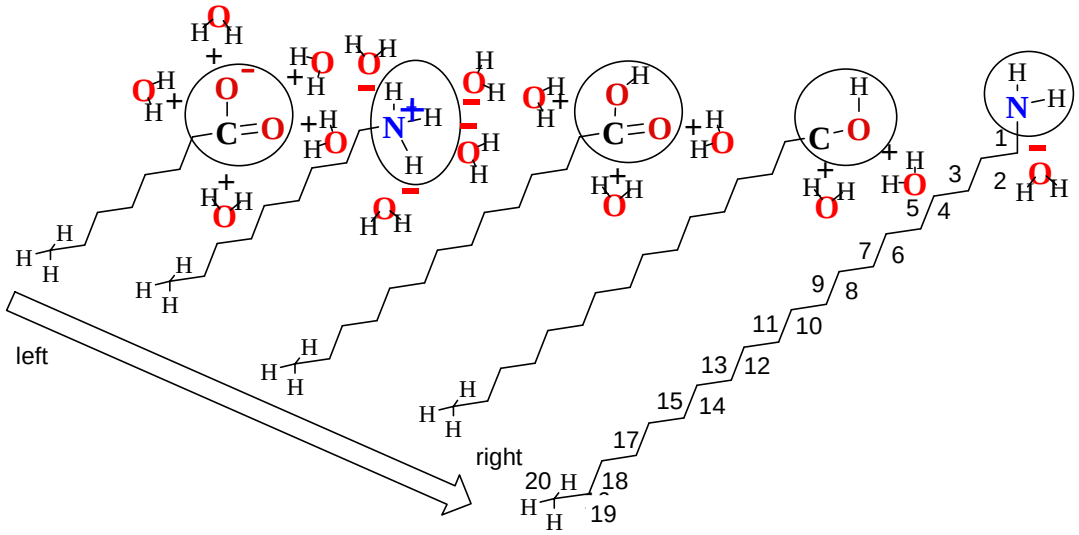
SAC **hydrophilic properties** decreases from left to right said →

SAC **hydrophobic properties** increases from left to right said →

Polar functional group interaction strength with **water** decreases to right said →

Hydrophobic hydrocarbon chain length l=n $(-CH_2-)_n$ increases from left to right said →

Polar or charged **(-)**,(+) group hydratation (+) H_2O **(-)** degree decreases from left to right said →



Hydrophobic hydrocarbon string $-CH_2-$ size forms carbon chain from first **hydrophilic** carbon part **1C** and last methyl group $-CH_3$ carbon on tail of string, for example, at amine–NH_2 with **1C** carbon begins dodeca amine chain and finish at **20C** in methyl group $-CH_3$ on tail of string.

SAC are **water** soluble and

water insoluble if **SAC** better in oil soluble unless **water**.

SAC forms double layer between **water** (polar **(-)**,(+)) and **oil** (non polar medium).

*That double layer becomes stabile, so **SAC** should be soluble in disperse medium unless disperse phase.*

Since this reason:

hydrophilic **SAC** stabilize double layer type **oil/ water** - **oil** droplets / in to **water** medium and **hydrophobic** **SAC** stabilize double layer type **water/oil** as **water** droplets /in **oil**, **fat**, **lipids** medium

Disperse systems.

Table *Colloid and Rough Disperse Systems division according aggregate state.*

Aggregate state for disperse phase	**Aggregate state for disperse medium**	**Disperse system name**	**Phase1/ Phase2 Symbols** g/l/s	**Samples and circumstances**
Gas	Gases	Aerosols	g/g	High pressure formed aerosols
Liquid	"	"	l/g	Fog, clouds, rein
Solid	"	"	s/g	Smokes, dusts
Gas	Liquids	Liosols	g/l	Foam
Liquid	"	"	l/l	Emulsions, Milk, Creams, Butters
Solid	"	"	s/l	Suspensions, Dirties, Turbid, Blood
Gas	Solid	Solid sols	g/s	Foam plastic, Bred, Porolone, Cheese
Liquid	"	"	l/s	Solid Emulsions, Pearls, Tissues in organisms
Solid	"	"	s/s	Solid Soles, Alloys

Disperse system has dispersed one phase particles into medium another phase.
Disperse phase: ? evaluates particle size and aggregate state.
Disperse medium:? define just……. aggregate state.

Compound which particles are dispersed in to other compound medium call as *disperse phase*,
At the same time compound in which medium locates disperse phase call as *disperse medium*.
According disperse phase particle size disperse systems classified in three groups:

1) **Real** solutions – with size <**1** nm (**10** Å = 10^{-9} m) are in medium separate single molecules, ions;
2) **Colloid** solutions – with size from **1**nm - to100 nm articles comprises molecules from thousand 10^3 to 10^6;
3) **Rough** disperse system – with size over >**100** nm (>**1000** Å).

Aerosols, emulsions and suspensions.

Organic body's members are cells, bacteria, viruses, milk, cream, butter, jelly.
Inorganic members are smokes, fogs, clouds, rein,

Soles liophilic and liophobic

According different affinity to **water** Liosols divide in two classes *liophilic* and *liophobic*.
Liophilic disperse system has strong solvatation (**water** medium hydratation). Therefore are spontaneous (**ΔG<0**) form, in contact with solvent. Typical is protein and lipid High Molecular Compound (**HMC**) solutions.
Liophobic disperse system has week solvatation. Therefore do not spontaneous (**ΔG > 0**) form.
Is necessary applying special methods, which achieve liophobic sole formation?
Typical liophobic soles are insoluble salt, or tin disperse metals and nonmetal colloid **water** solutions.
Four occurrence analysis shows distinguish ***liophilic*** and ***liophobic***!

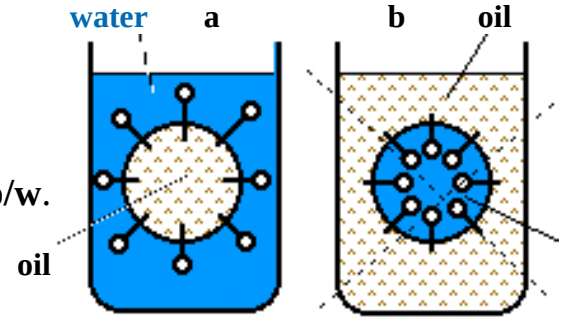
Hydrophilic SAC stabilize **o/w** double layer types

o/w double layer type forms if **oil** droplets dispersed in **water** medium.
Hydrophilic polar head of **SAC** faced to **water** line on drop surface. **Hydrophilic SAC** deeper in **water** medium than **oil** drop (look ***a***) and formed **oil** drops protecting barrier of coalescence (flow) for colliding drops.

***a* - SAC** forms stabile double layer type **o/w.**

Hydrophilic SAC forms barrier, which stabilize double layer type **o/w.**

b Unstable double layer type **w/o** at **hydrophilic SAC** presence do not forms.



stabile double layer unstable double layer

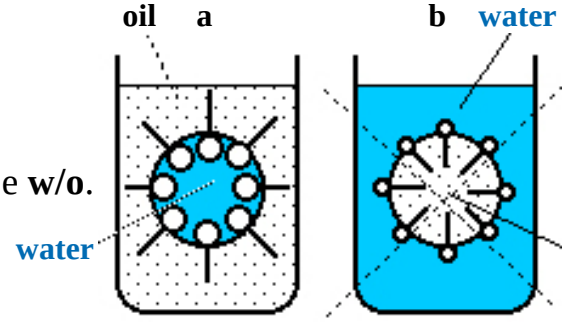
Hydrophobic SAC stabilize double layer type **w/o**

w/o double layer type forms if **water** droplets dispersed in **oil** medium.
Hydrophobic polar head of **SAC** faced to **water** line on drop surface. **Hydrophobic SAC** deeper located in **oil** medium than **water** drop (look ***a***) and formed double layer barrier of water drops protect of coalescence (flow) for colliding drops.

***a* – SAC** forms stabile double layer type **w/o.**

Hydrophobic SAC forms barrier, which stabilize double layer type **w/o.**

b Unstable double layer type **o/w** **hydrophobic SAC** presence do not forms.



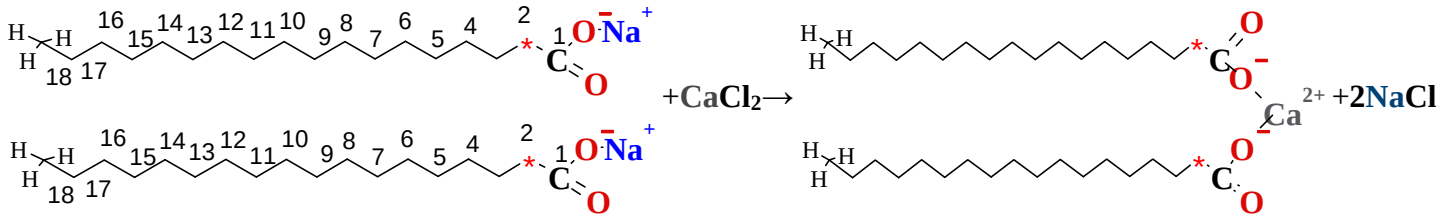
stabile double layer unstable double layer

Double Layer type inversion change SAC **hydrophility** or **hydrophobity**

How to inverse disperse system phases? Usual are **oil**/water, but rear opposite.

1. Adding high amounts opposite **SAC types** hydrophobic.
2. Fatty acids are soluble in **water** as Na^+ or K^+ salts and insoluble in **water** as Ca^{2+} or Mg^{2+} salts.

That inverse disperse system type. If we take one fatty acid Na^+ salt stearate or palmitate. Due to disperse system phase type inversion is added $CaCl_2$, which results in ion exchange reaction forming **water** insoluble Ca^{2+} fatty acid salt calcium stearate: sodium stearate calcium stearate is better Ca^{2+} is better



soluble in **oil** as in **water** insoluble. This way disperse system inverse from **oil**/**water** in to **water**/**oil**.

Solubilisation vesicles chylomicrons, VLDL, LDL, HDL, micelle - boll.

*Solubilisation is process, which with **SAC** double layer forms **water** insoluble compound into **water** soluble in shape of vesicles 1000 nm to 8 nm (chylomicrons, VLDL, LDL, HDL, micelle).*

Solubilisation occurs at presence of high concentration **SAC**. If **SAC** **hydrophobic** radical build from **10C** to **20C** carbon atoms is possible forming micelles **water** solutions (*c* figure). Micelle formation begins at **SAC** concentration $\mathbf{C_{VAV}}$, which overflow critical concentration and higher.

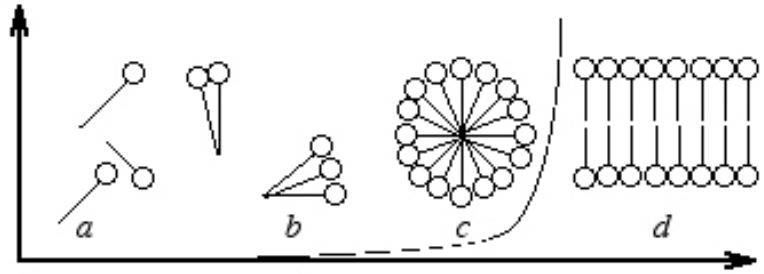
a At low concentrations $\mathbf{C_{VAV}}$ exist individual **SAC** molecules,

b At higher concentrations $\mathbf{C_{VAV}}$ **SAC** molecules associates as two and three ,

c At *critical micelle formation concentrations* (KMC) $\mathbf{C_{kritSAC}}$ start formation spherical boll like structures , which call one as colloidal micelles,

d At very high concentrations forming planar plate like structures (lipid membranes analogs).

n, number of molecules in micelle micelle boll formation



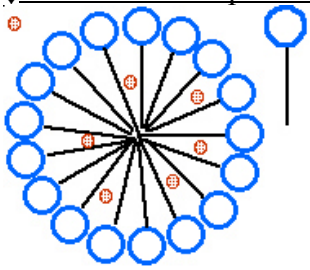
If **SAC** concentration overflow **KMC** , than **SAC** solution is only in form of micelle. **SAC** formed micelles have double layer building features – interior layer has **hydrophobic** orientation (**hydrophobic** medium formation) and outer interface has hydrated, polar – **hydrophilic** **SAC** molecule parts.

$\mathbf{C_{kritVAV}}$ $\mathbf{C_{VAV}}$ **SAC** concentration in solution

Such double layer structure is energetically favorable (**ΔG<0**), where **water** medium is bound with **SAC** double layer from **hydrophobic** medium preventing direct contact between reciprocally insoluble phases.

In such ball formation can "hide" **water** insoluble compound molecules (**hydrophobic** or non polar compounds), lipoprotein vesicles contains up to $\mathbf{n}=10^6$ molecule of **water** insoluble lipids (fats, cholesterine, oils).

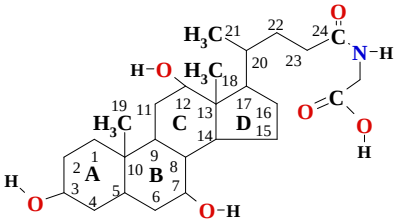
↓Solubilized compound molecules- lipids **water** insoluble because is **hydrophobic**



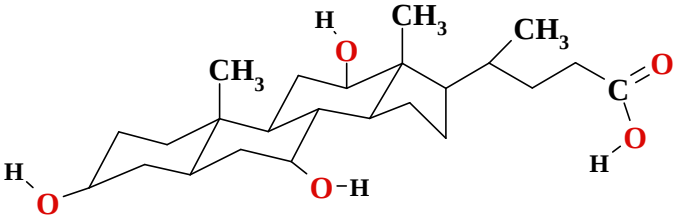
←**SAC** molecules

Water insoluble fats Solubilisation intestinal system digestive apparatus favored with **SAC** bile acids (cholesterolic acids) high concentration $\mathbf{C_{SAC}}$ over KMC . Therefore can form micelles.

It explains, that due to insufficient bile arise disturbance for fats assimilation – dissolution as well than cannot use in nutrition fatty food.



Glyco cholesterolic acid (primary bile acid)



Litocholesterolic acid (secondary bile acid)

Cholesterol

Lipid Cholesterol 27 carbon steroid (inflexible steric frame) hydrocarbon molecule.

1) Four rings of the steroid are labeled A, B, C and D;

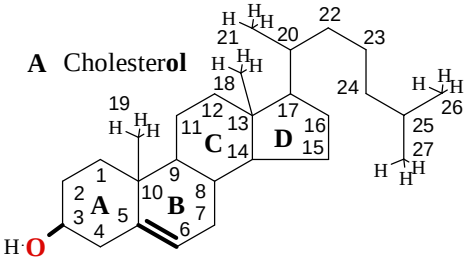
2) Angular methyl $-CH_3$ groups labeled 18 and 19;

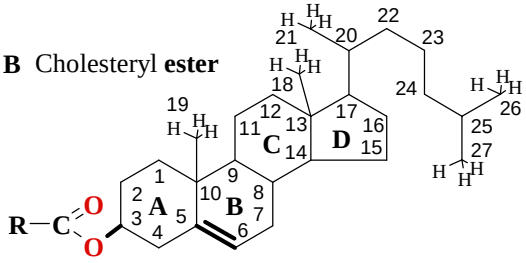
3) Three methyl $-CH_3$ groups labeled 21, 26 and 25 tail fork, rod, hook shape as splinter are good clutch fixing close hydrocarbon chains in membrane;

4) Double bond between carbon atoms >C=C< 5 and 6 to frame solid, inflexible four rings;

5) Alcohol **HO** - at carbon 3 ;

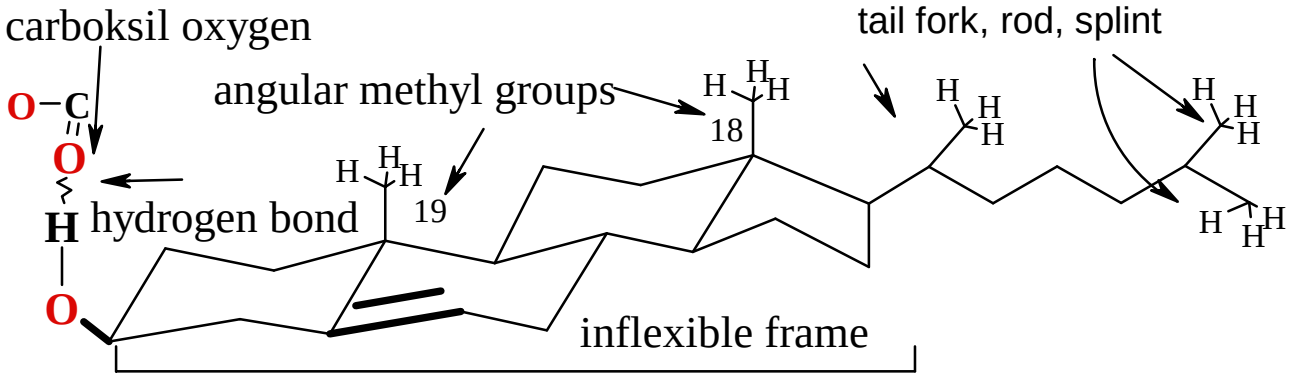
Hydroxyl group **HO**- forms hydrogen bond -**OH**...**O**=**C**< with carboxyl oxygen of fatty acids : Oleate or one another fatty acid carboxyl oxygen >**C**=**O**...**HO**-;





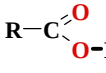
Cholesteril **ester-cholesterin** saved and collected in liver and extra hepatic (leukocytes, macrophages) cells as small lipid droplets.

Steroid **alcohol** = cholester**ol** cholesteryl **ester – cholesterin**



Steroid hormones are made from cholesterol, primarily derived from lipoproteins or lipocalins that enter cells via receptor-mediated endocytosis. In endo-lysosomes, cholesterol is released from cholesterol esters by lysosomal acid lipase (LAL; disordered in Wolman disease) and exported via Niemann-Pick type C (NPC) proteins (disordered in NPC disease).These diseases are characterized by accumulated cholesterol and cholesterol esters in most cell types. Mechanisms is known for trans-cytoplasmic cholesterol transport, membrane insertion, and retrieval from membranes with **lipocalin** proteins. Cholesterol esters and “free” cholesterol are enzymatic interconvert in lipid droplets.

Cholesterol transport with **StAR** to the cholesterol-poor outer mitochondrial membrane (OMM) appears to involve **cholesterol transport** proteins **StAR**. Then on the inner mitochondrial membrane (IMM) Cytochrom P450scc (CYP11A1) initiates steroid genesis by converting cholesterol to pregnenolone. Acute steroidogenic responses are regulated by **cholesterol delivery** from OMM to IMM, triggered by the steroidogenic acute regulatory **StAR** protein. Chronic steroidogenic capacity is determined by CYP11A1 gene transcription. **StAR** mutations cause congenital lipoid adrenal hyperplasia, with absent steroid genesis, potentially lethal salt loss, and 46,XY sex reversal. **StAR** mutations initially destroy most, but not all steroid genesis; low levels of **StAR**-independent steroid genesis are lost later due to cellular damage, explaining the clinical findings. Rare P450scc mutations cause a similar syndrome. This review addresses these early steps in steroid biosynthesis.

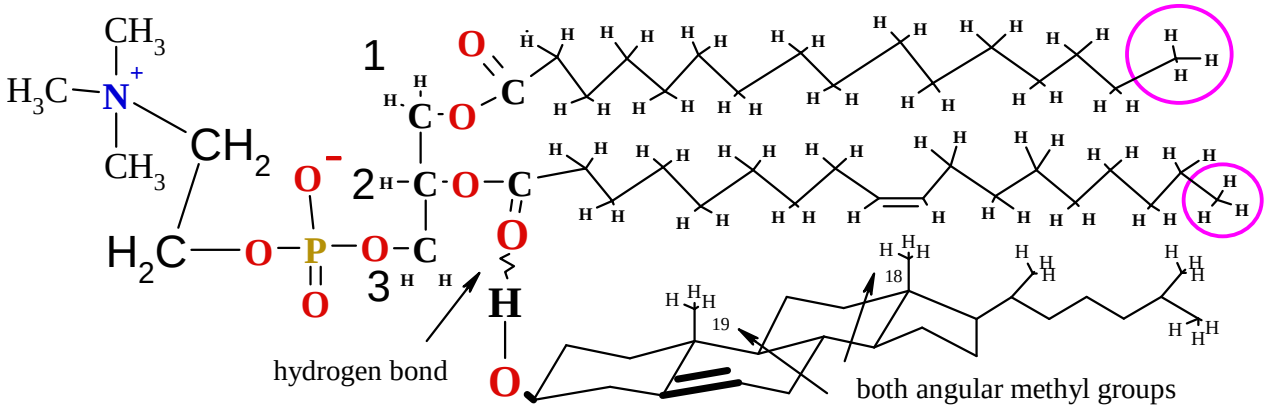
Cholesterol having hydroxyl group **HO**- constitute 1/3 mass fraction of membranes. Cholesteryl esters as cholesterol alcohol group attached to an acyl 

are resulting in apolar **cholesteryl ester-cholesterin**.

Cholesterol and Phospho Lipid complex C/PL=1/1 in cell membranes

Phospho Lipids mass fraction of Membranes to make 33.3% mass fraction (1/3) of total 100%.
Second third part (1/3) of Membranes mass constitutes 27 carbon steroid (inflexible steric frame) hydrocarbon **Lipid-Cholesterol** molecules.

Cholesterol molecules. Four rings **A**, **B**, **C** and **D.** Methyl **–CH_3** groups angular as well tail fork, rod, splinter are good clutch fixing close hydrocarbon chains. Double bond between carbon atoms **>C=C<** 5 and 6 to frame inflexible four rings. Hydroxyl group **HO-** at carbon 3 forms hydrogen bond **-OH...O=C<** with carboxyl oxygen **O=C<** of fatty acid.



Cholesterol as **Steroid** makes membranes mechanically stable and so prevent leaking of water molecules and of water solution components: salts and bioorganic molecules.

$\frac{\text{Cholesterol}}{\text{Phospho\_Lipid}}$ mole ratio $\frac{C}{PL}$ of human red blood cell membranes ranges from a normal value of 0.9 to 1.0 (Journal of Cellular Biochemistry 2004 V8, 4, p 413-430) first publication in 1978.

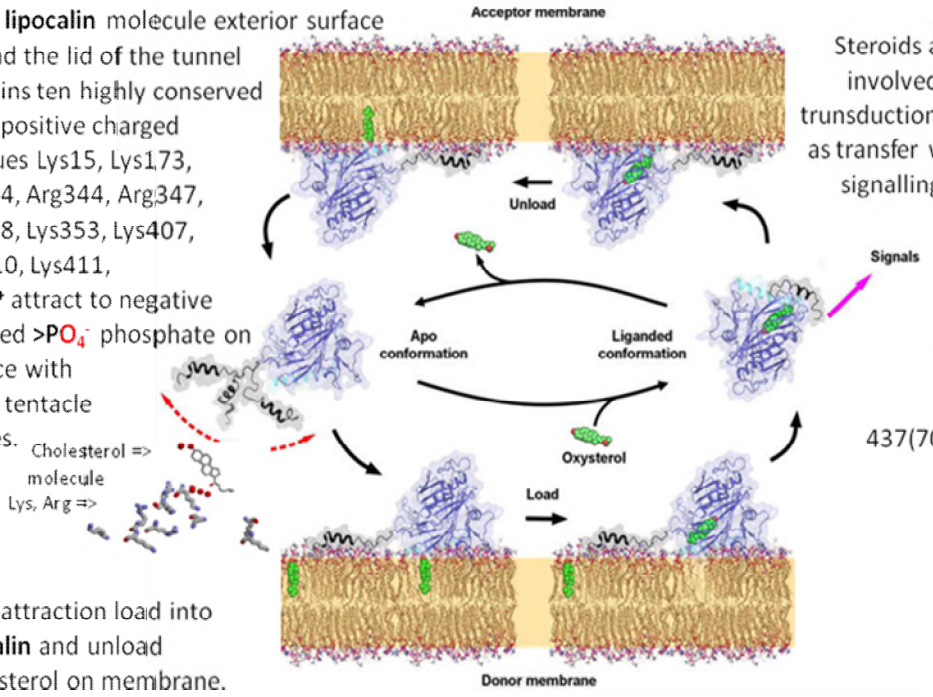
If Cholesterol amount decreases up to 0,5 = C / PL, then membranes leak cell content out, but
if Cholesterol amount increases up to 1,5 = C / PL, then membrane becomes solid, inflexible and squeeze channels, aquaporins, receptors does not work.

Lipocalins water transport of Cholesterol, Steroid hormones, vitamins K,E,D,A

9th page : http://aris.gusc.lv/06Daugavpils/Research/LipidBiLayerMembran.doc

OSBP (oxy-sterol binding protein) oxy-sterol transport protein involved in cholesterol metabolic transport across membranes surface load from and unload to membranes, that keep homeostasis 33.3% mass fraction 1/3 of 100% membrane mass. **Lipocalins** like as **OSBP** mechanism is retinol **ORPs** and other **Lipocalins** for A,K,E,D vitamin transport proteins. Human has12 **OSBP** isoforms. Human isoform **OSBP4** cholesterol exchange between membranes shown here:

OSB4 lipocalin molecule exterior surface around the lid of the tunnel contains ten highly conserved basic positive charged residues Lys15, Lys173, Lys334, Arg344, Arg347, Lys348, Lys353, Lys407, Arg410, Lys411, **–NH_3^+** attract to negative charged **>PO_4^-** phosphate on surface with three tentacle helixes.



Steroids and vitamins involved into signal trunsduction with **lipocalins** as transfer water insoluble signalling molecules.

Nature. 2005 September 1; 437(7055): 154–158

After attraction load into **lipocalin** and unload cholesterol on membrane.

Phospho Lipids distinguish as extracellular and intracellular space

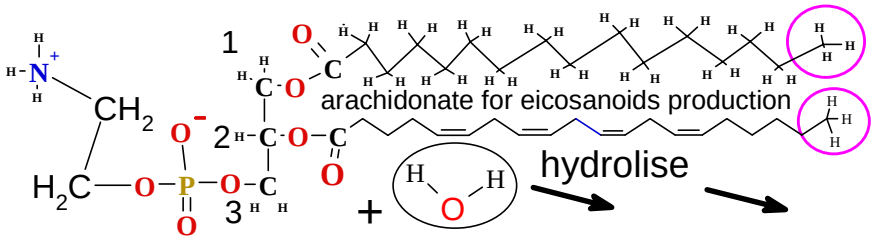
Membrane inner location vital source:

1) of Arachidonic acid for Eicosanoids and Anandamide production;

after hydrolyze 2) of inositol triphosphate signaling molecule;

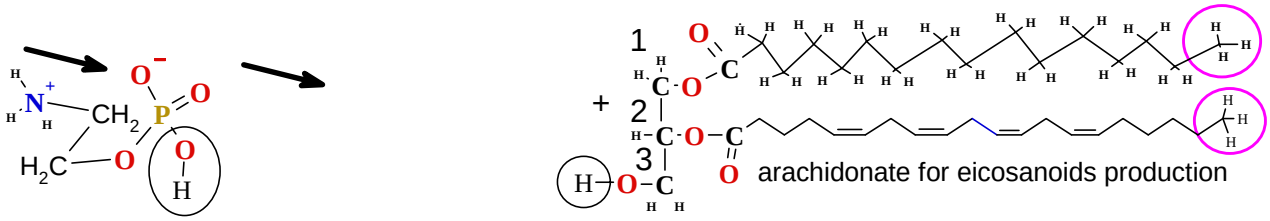
of Inositol phosphate, Ethanolamine 3) left diacylglyceride DAG signaling communication molecule;

Cephalin phosphatidyl ethanolamine at pH=7,36 protonated $\mathbf{H^+}$ with positive charge —$\mathbf{N^+H_3}$

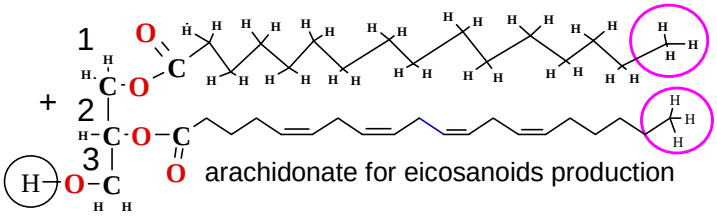


Ethanol amine phosphate ester

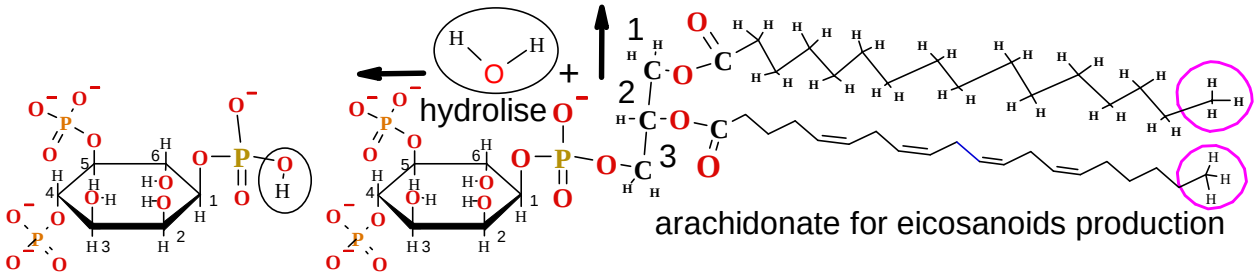
Left cleaved diacylglyceride DAG signaling communication molecule



Inositol triphosphate IP3 and diacylglyceride DAG source intracellular signaling communication molecule:

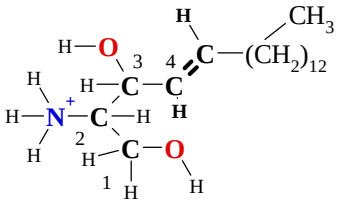


inositol triphosphate IP3 signaling molecule



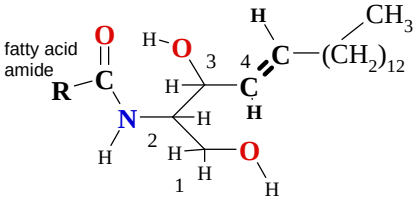
Sphingolipids are derivatives of **sphingosine**, an amino alcohol

Sphingosine is a C18 compound with hydroxyl groups -**OH** on C1 and C3, an amino group —$\mathbf{NH_3^+}$ on C2 and a trans double bond = at C4

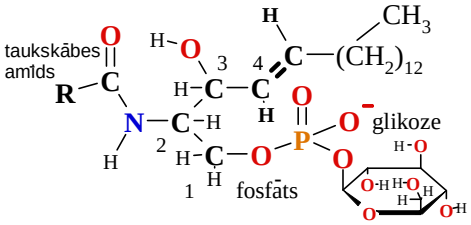


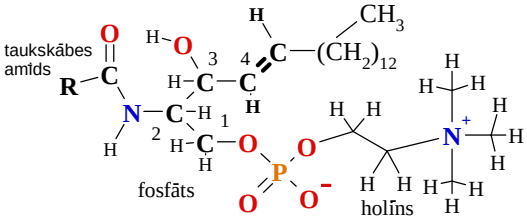
Glucosyl ceramide (cerebroside)

Ceramide fatty acid amide

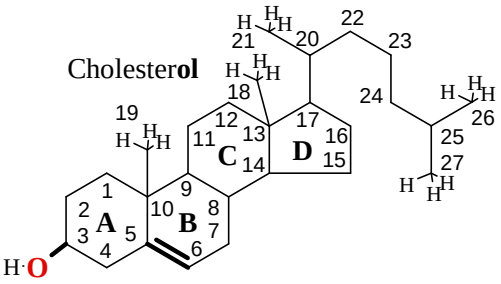


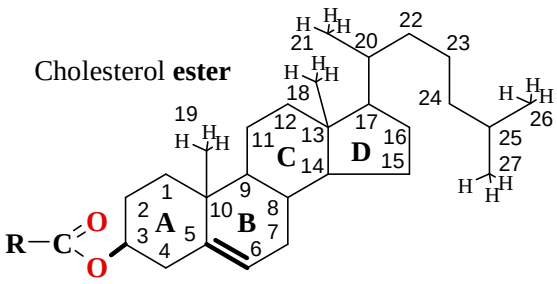
Sphingomyelin





oligosaccharide ceramide (ganglioside)

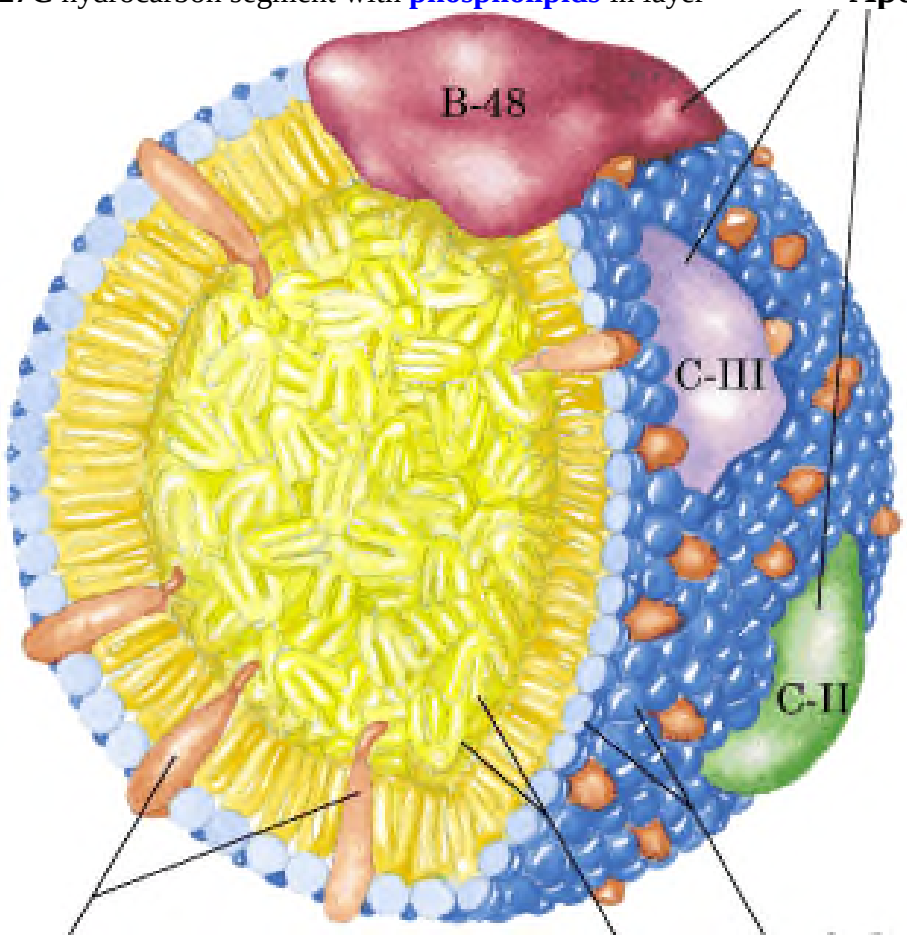




Cholesterol is **membrane** layer component as **hydrophilic HO-** hydroxyl and **hydrophobic 27C** hydrocarbon segment with **phospholipids** in layer

Cholesterine non polar cholesterol and fatty acid ester **hydrophobic**

Apo lipoproteins B-48, C-III, C-II



Chylomicron molecular structure. Surface layer form **phospholipids**, with **phosphate head group** faced to **water** phase. **Triacylgliceride** locates inside **interior** (**yellow**) forms **chylomicron** mass over fraction **80%** of total mass forms **hydrophobic interior** together with two fatty acid and glycerol esters in **phospholipids** molecules.

Some **apolipoproteins**, which squeezes outside on surface (**B-48**, **C-lll**, **C-ll**) work as signaling molecules receptor enzymes **chylomicron** content metabolisation use for surrounded tissue cells and **B-48** connect to cell receptors (liver) to engulf in to cell. **Chylomicron** diameters rank from **80 nm** to **1000 nm**.

Five lipids transport forms in blood plasma

Lipoprotein vesicles with cross size from 8 nm up to 1000 nm

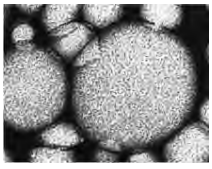
Cholesterol

Triacylglycerol and **Phospholipids**

cholesterin - cholesterol ester

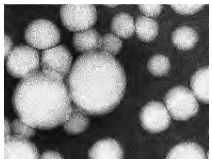
Albumin transport form for fatty acid and **water** insoluble medicine

chylomicron



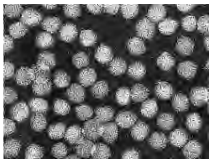
80…200 nm

VLDL very low density **lipoprotein**



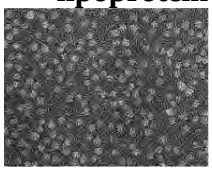
28…70 nm

LDL low density **lipoprotein**



20…25 nm

HDL high density **lipoprotein**



8…12 nm.....

Solubilisation micelle and lipoprotein vesicle building difference

Lipoprotein and Solubilisation balls formation processes seem like, because two reciprocally insoluble liquids form disperse phase with support of **SAC**. Common feature for both processes are double layer formation if one liquid forms droplets in to other liquid and tin **SAC** layer (emulgators, **phospholipids**) defense drops from coalescence (flow), however high amount **SAC** form micelles and small amount disperse phase can hide micelle inside, still lipoproteins formed **phospholipids** vesicles system is much comprehensive (comprise up to 10^6 molecules) and maintains very stable transport form for lipids (**hydrophobic**) in blood plasma (in **water** medium).

Obesity and cholesterol esters plaque on Blood Vessels as Hart strike and Brain insult cause

Fat soluble compounds in human organism call about **lipids**. For example, fats, vegetable oils, vitamins, cholesterol, cholesterol esters (cholesterines), hormones as well as fat soluble medicines and drugs.

Already at eighties on 20. century scientists reveal, that lipids circulation in human blood in globular form of spherical lipoproteins is important transport way of water insoluble compounds in organism, that transfer up to any organism cell necessary compounds: fats, cholesterol, cholesterol esters, hormones, vitamins K, E, D, A and introduced in body fat soluble curative medicines and drugs.

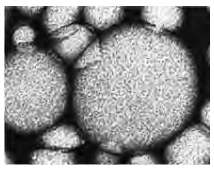
Compounds exchange for life happy human organism in healthy and in harmony with nature take a part on life friendly environmental medium, which is formed cosy(mājīgs) and human life friendly, provided sustainable healthy development of human society as a whole.

Obesity, cholesterol ester precipitation in blood vessels as plaque and blood vessels blocking frustrate the healthy harmony with nature. That raises blood circulation disturbances, what we recognize under disease terms: hart strikes -infarcts and blood effusions in brain – insults.

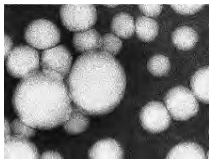
To caching cold or mechanical trauma occasions or infection influence blood vessels cell walls inflame and that involve protection cells leucocytes exited gathering activity against inflammation focus and who, attacking infection agents, bombard agents with peroxide $\mathbf{H_2O_2}$ molecules chemically changed foreign bodies and binds with them clean organism of foreign bodies. Unfortunately near these events are also low density lipoprotein vesicles, whose Protein compound too oxidizes with peroxide, and after oxidation firm stick to blood vessel wall. In years process accumulates forming cholesterol plaque, which insoluble in blood, because are insoluble in water. Blood vessel inflammation provoke also increased radiation, for example, in Chernobyl crash liquidator organism usually has observed blood vessel cholesterol blocking, which rises due to blood vessel inflammation with getting in organism radioactive atom isotopes and its high energy radiation of α, β, γ particles.

Excessive abuse fats and oils on nutrition provoke as well as in organism unconsumed fats accumulate in adipose cells increasing fatty cells size and take place body obesity.

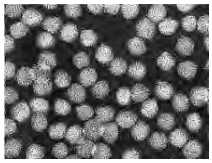
Fats in human organism “burn down” in result of high physical load and that happens in sportsman organism match time. That fats “burn down” process would not take place traumatic for muscle cells (over load provoke muscle also hart cells inflammation and destruction), than organism has to be well trained, because fat burn down necessary mach oxygen, what supply well developed blood circulation system, what can improve correct training of organism in longer time period.



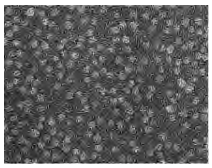
80…200 nm
Chylomicrons
Hylē *Greeks* is substance, material
lipoprotein’s initial form after eating.
Translation from *Greeks* <u>*micron material*</u>



28…70 nm
VLDL
very low density lipoproteins



20…25 nm
LDL
low density lipoproteins



8…12 nm
HDL
high density Lipoproteins

7. att. On electron microscope in blood can observe small size fat vesicles, which size decreases in such sequence chylomicrons, very low density lipoproteins, low density lipoproteins and high density lipoproteins. Lipids are fats, cholesterols and vitamins K,E,D,A, which are water insoluble and insoluble in blood. Bile, intestinal and liver cells convert in small vesicles with food ingested lipids, which free swim in blood water medium. Lipids binding protein molecule covers vesicle surface and prevent it from adhesion and precipitation on blood vessel wall. Therefore these fat vesicles are called lipoproteins. Lipoproteins are just shape for human organism how delivers to any organism cell water insoluble lipids: fats, cholesterol, cholesterol esters, hormones, vitamins K, E, D, A and curative compounds of medicines.