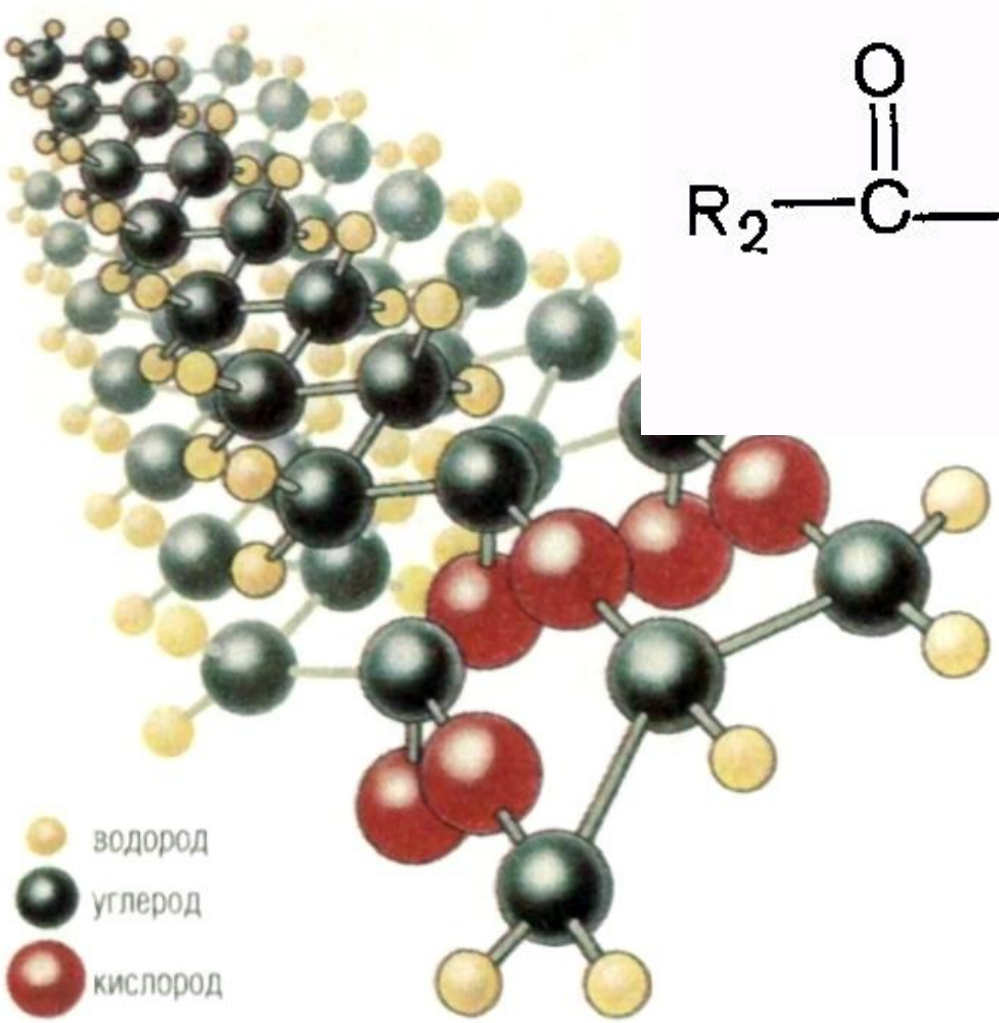
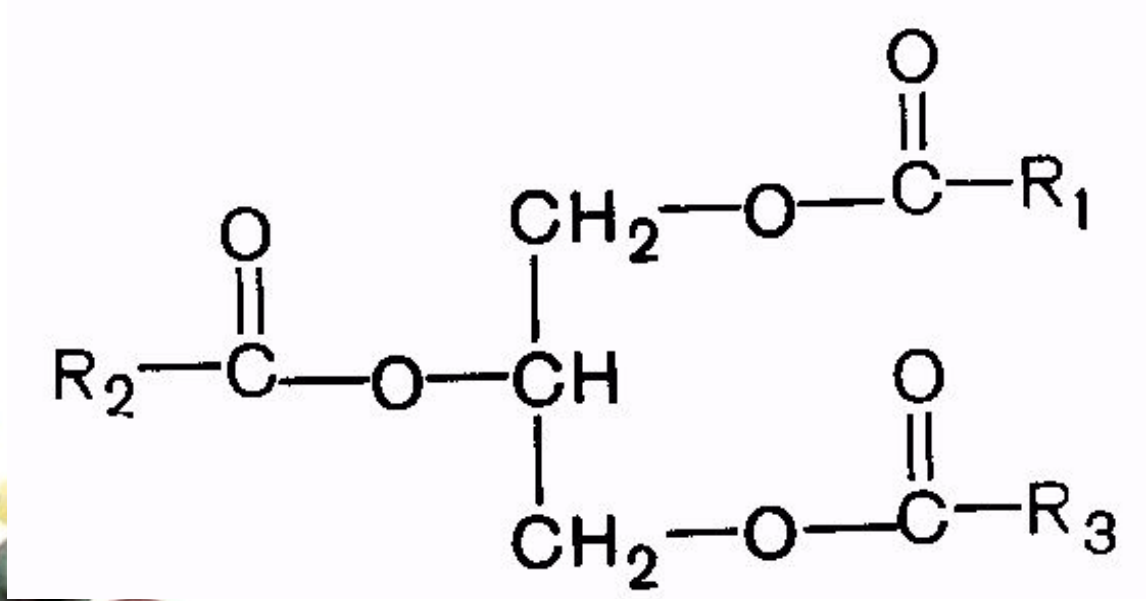
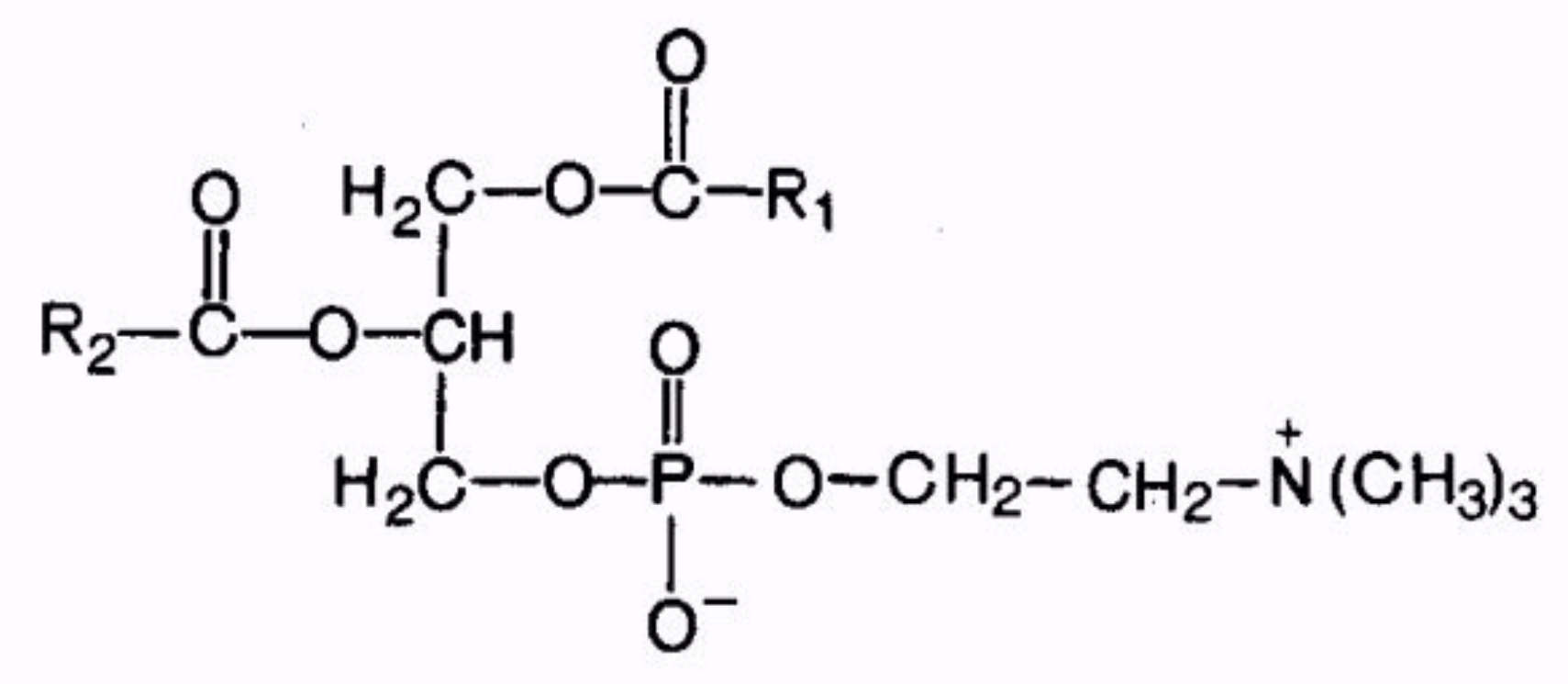
LIPID METABOLISM

Fats (Triacylglycerols)



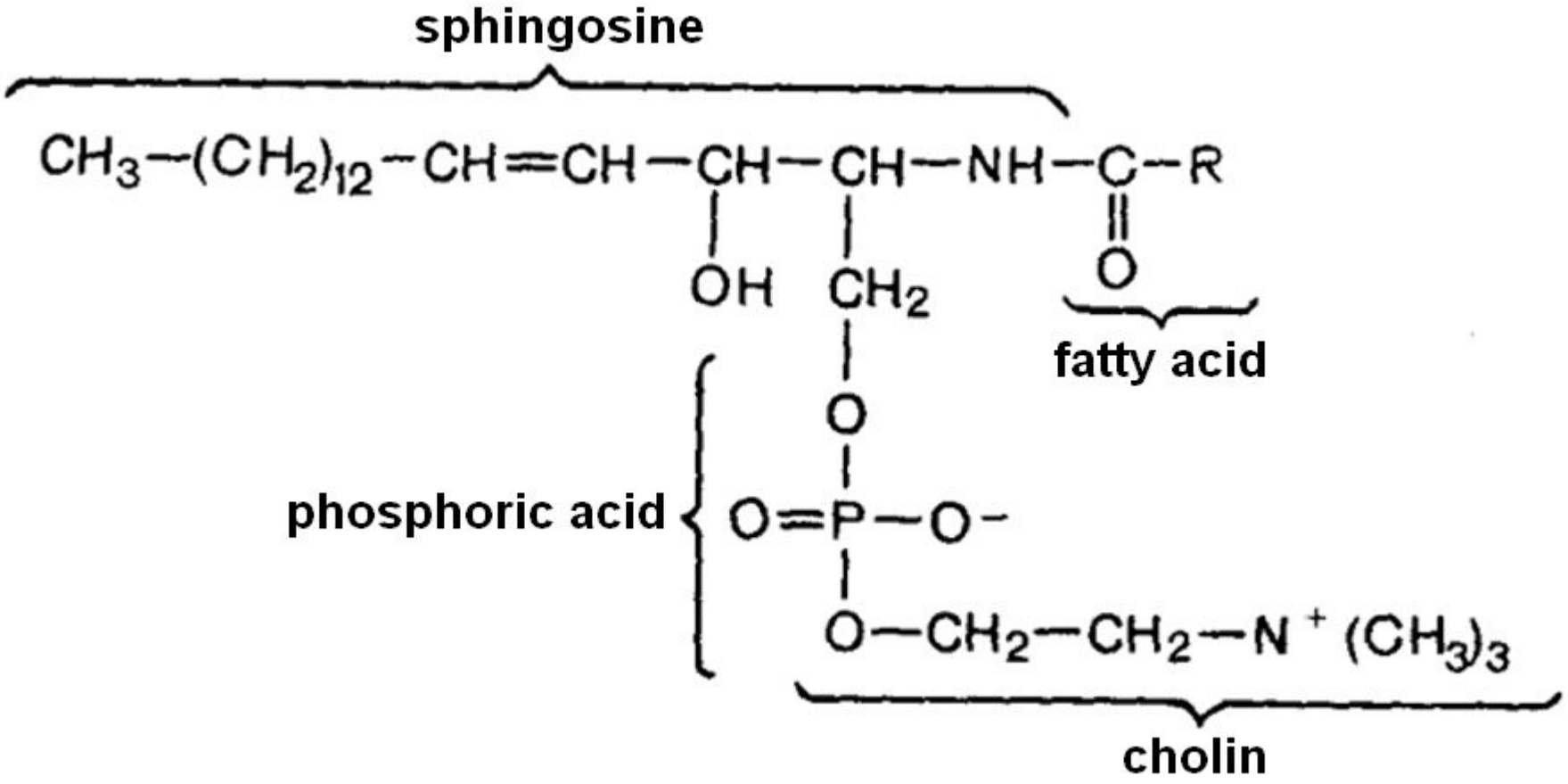


Phospholipids



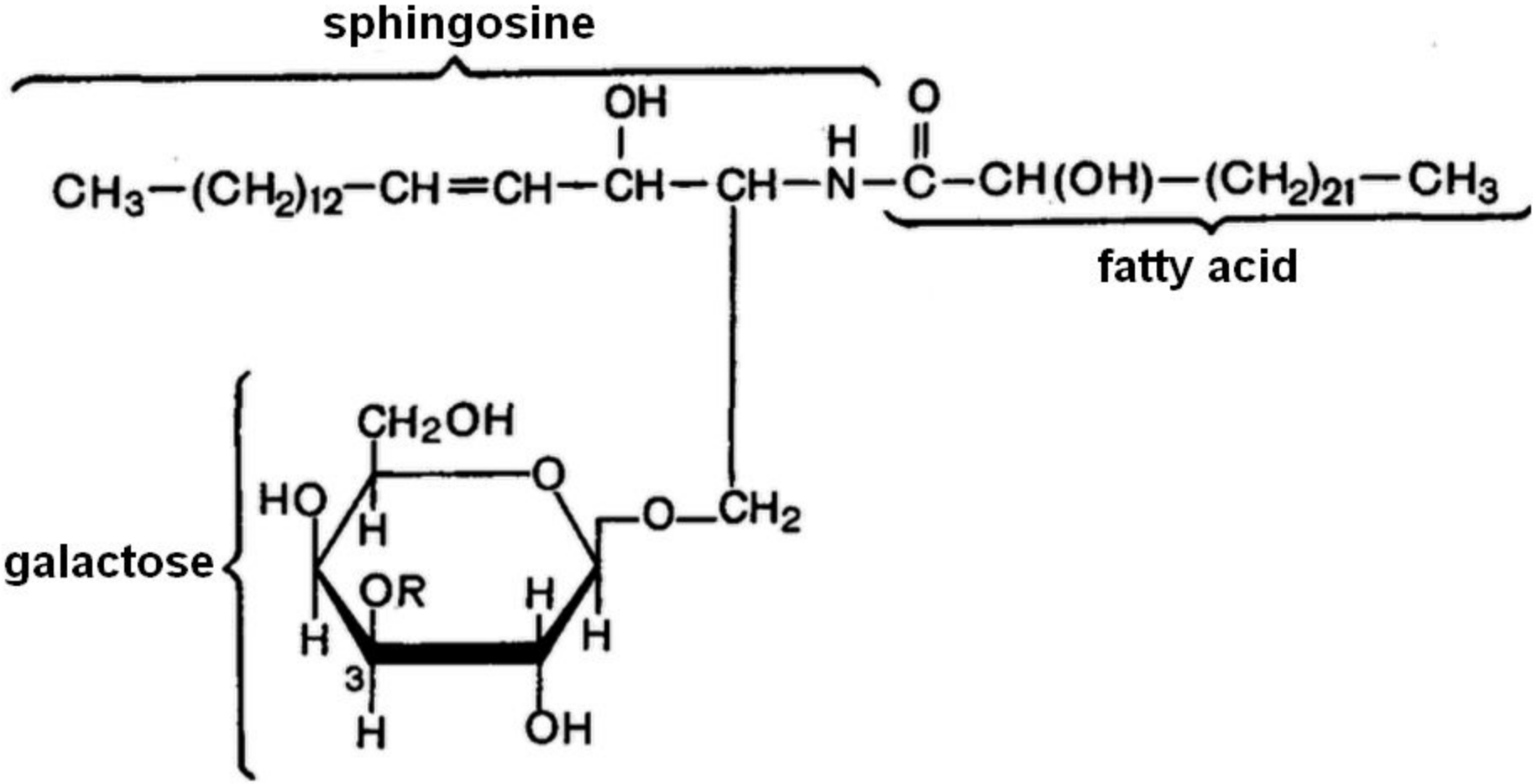
acetylcholine

Sphingophospholipids

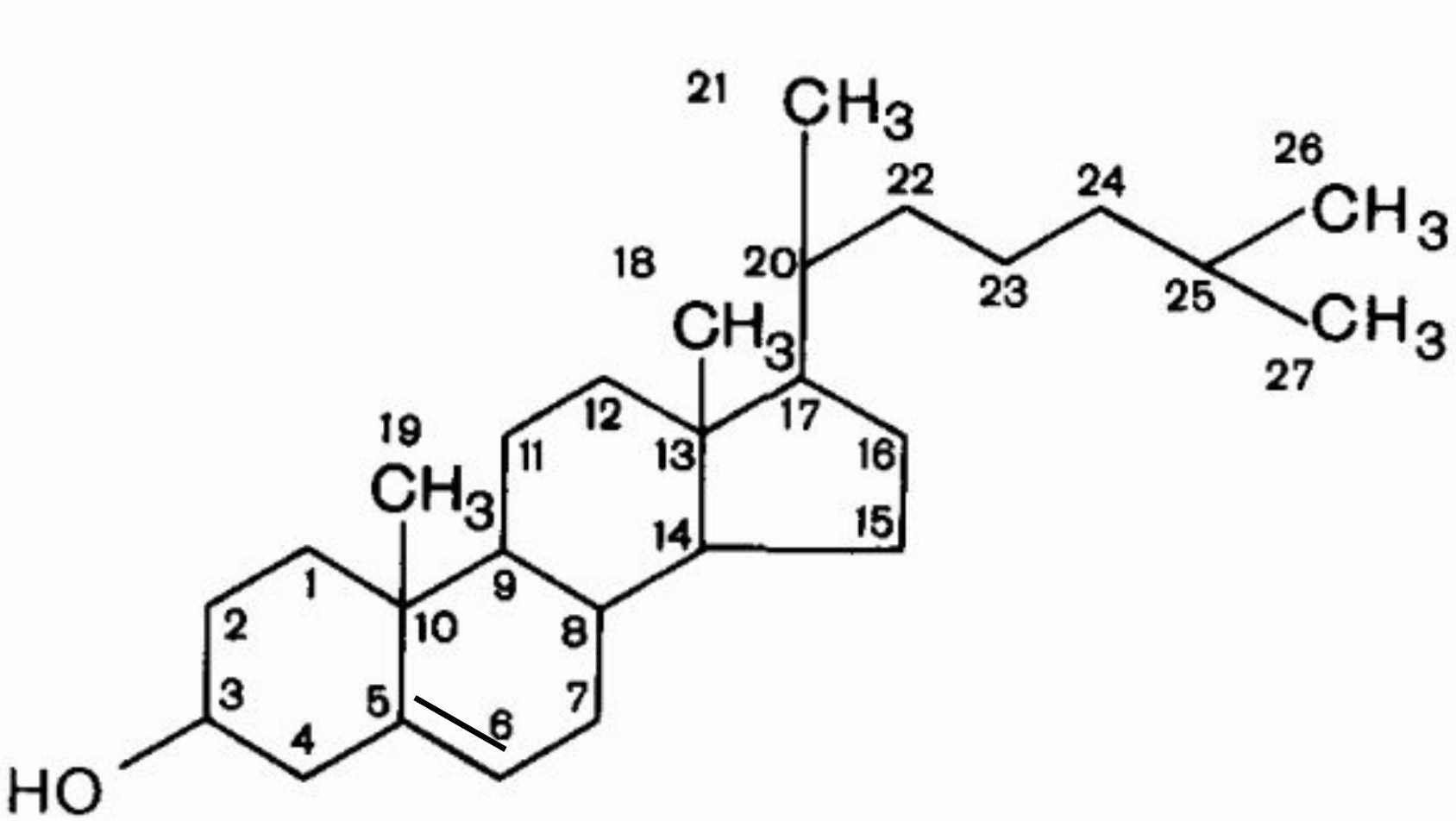


sphingomyelin

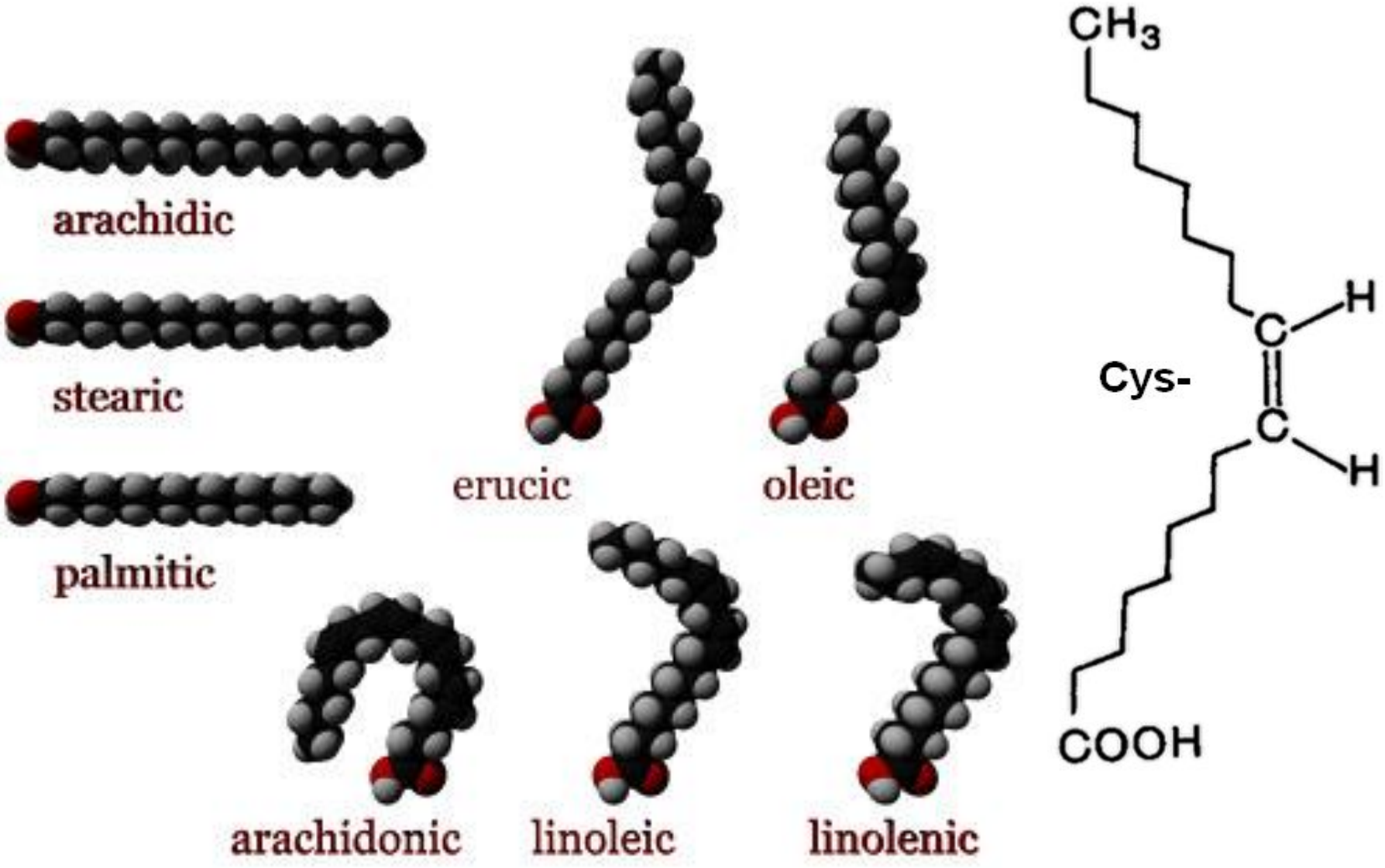
Glycolipids



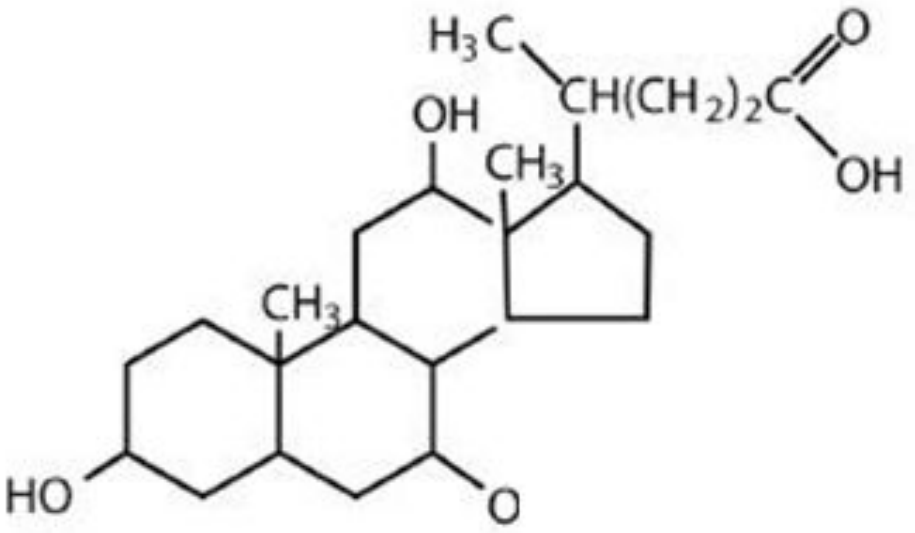
Cholesterol



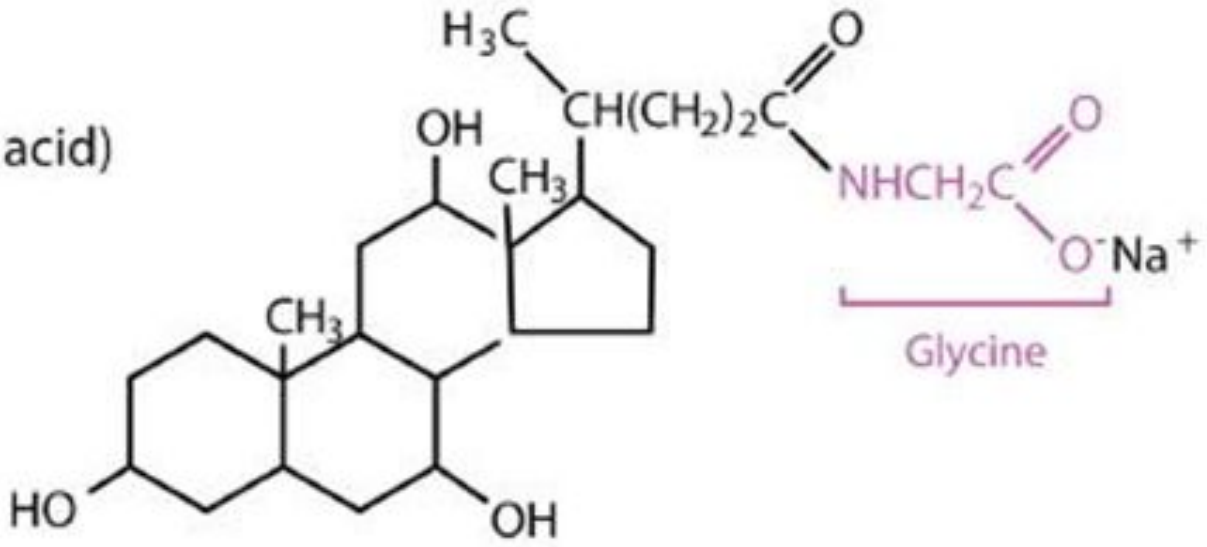
Fatty acids


arachidic
stearic
palmitic
erucic
oleic
arachidonic
linoleic
linolenic
CH3
Cys-
C
C
H
H
COOH

Bile acids



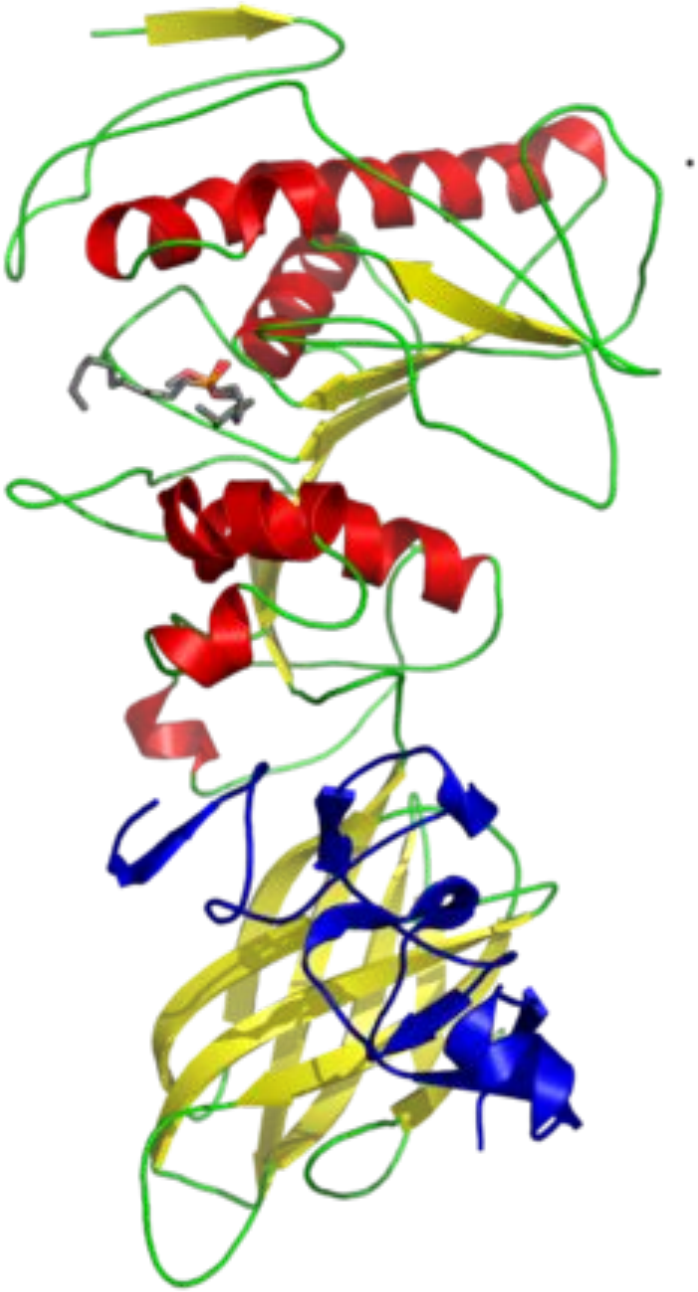
(a) Cholic acid (a bile acid)



(b) Sodium glycocholate (a bile salt)

Lipid functions

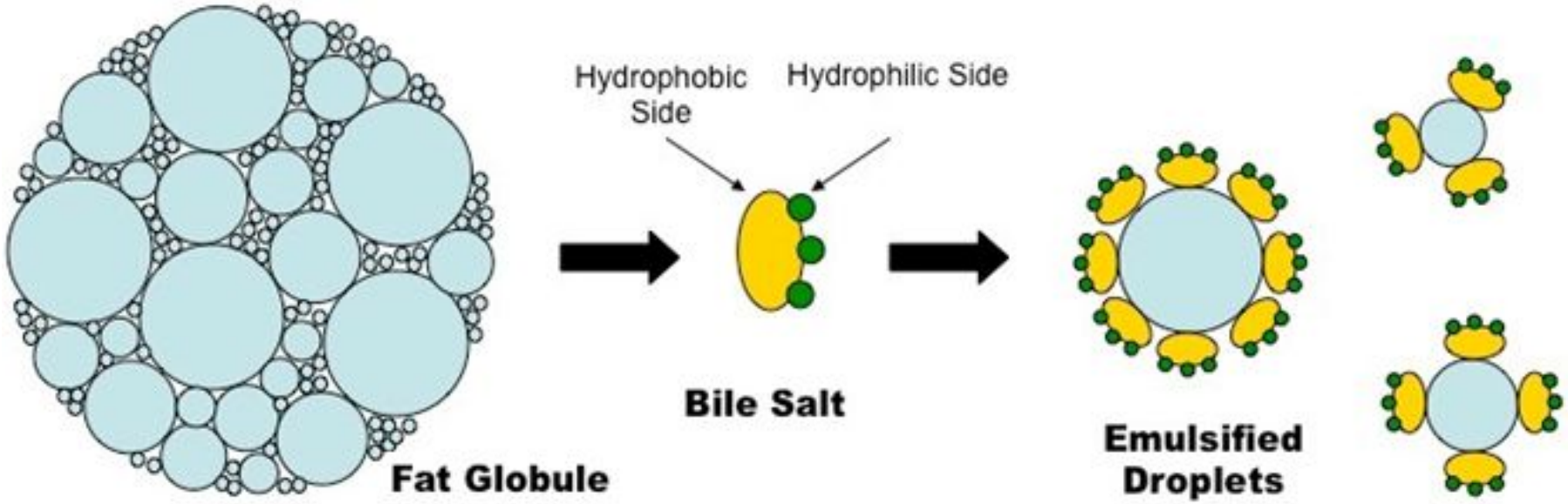
- Storage form of energy
- Supply essential fatty acids
- Structural components of cell membranes
- Electrical insulation
- Protect body from cold
- Mechanical protection of internal organs
- Metabolic regulators (hormones)
- Help transport fat soluble vitamins



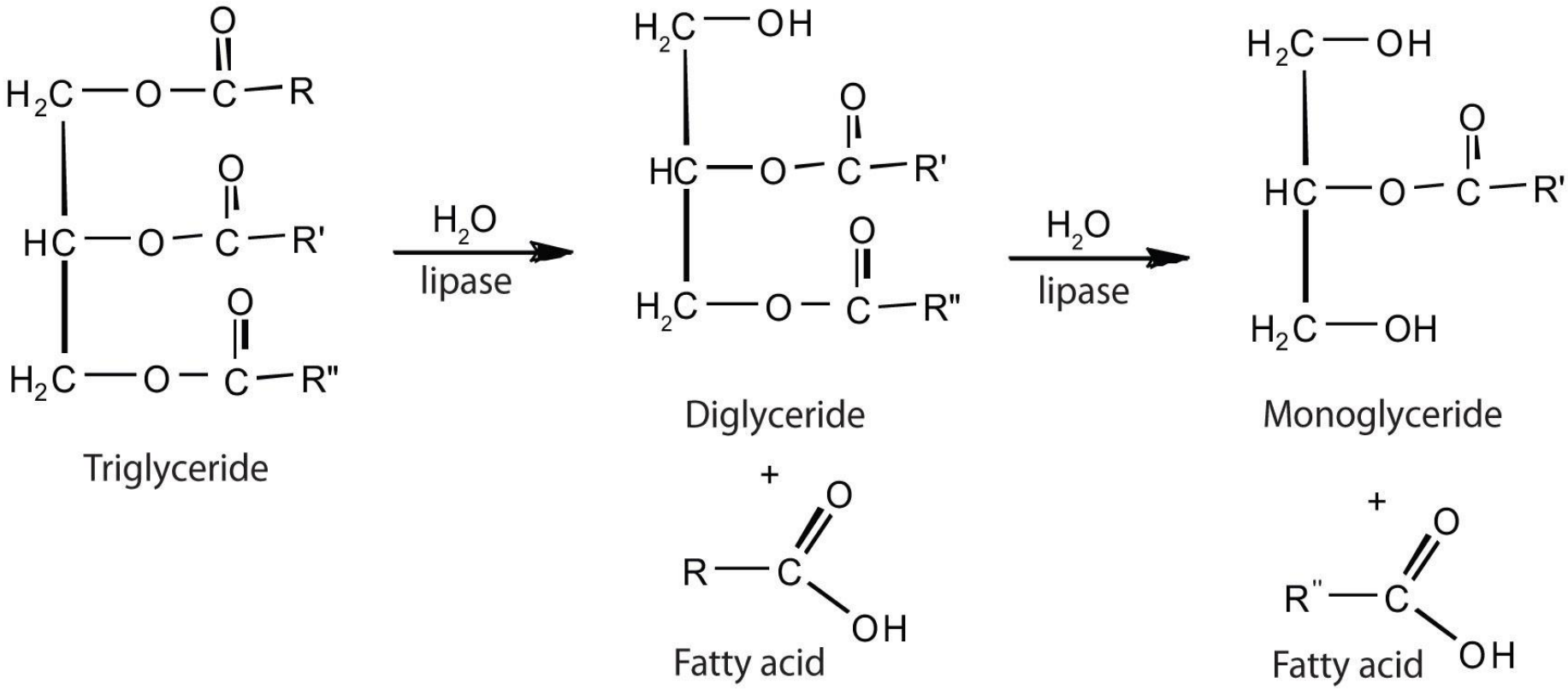
Human pancreatic lipase (activation by colipase)

Colipase is colored in blue

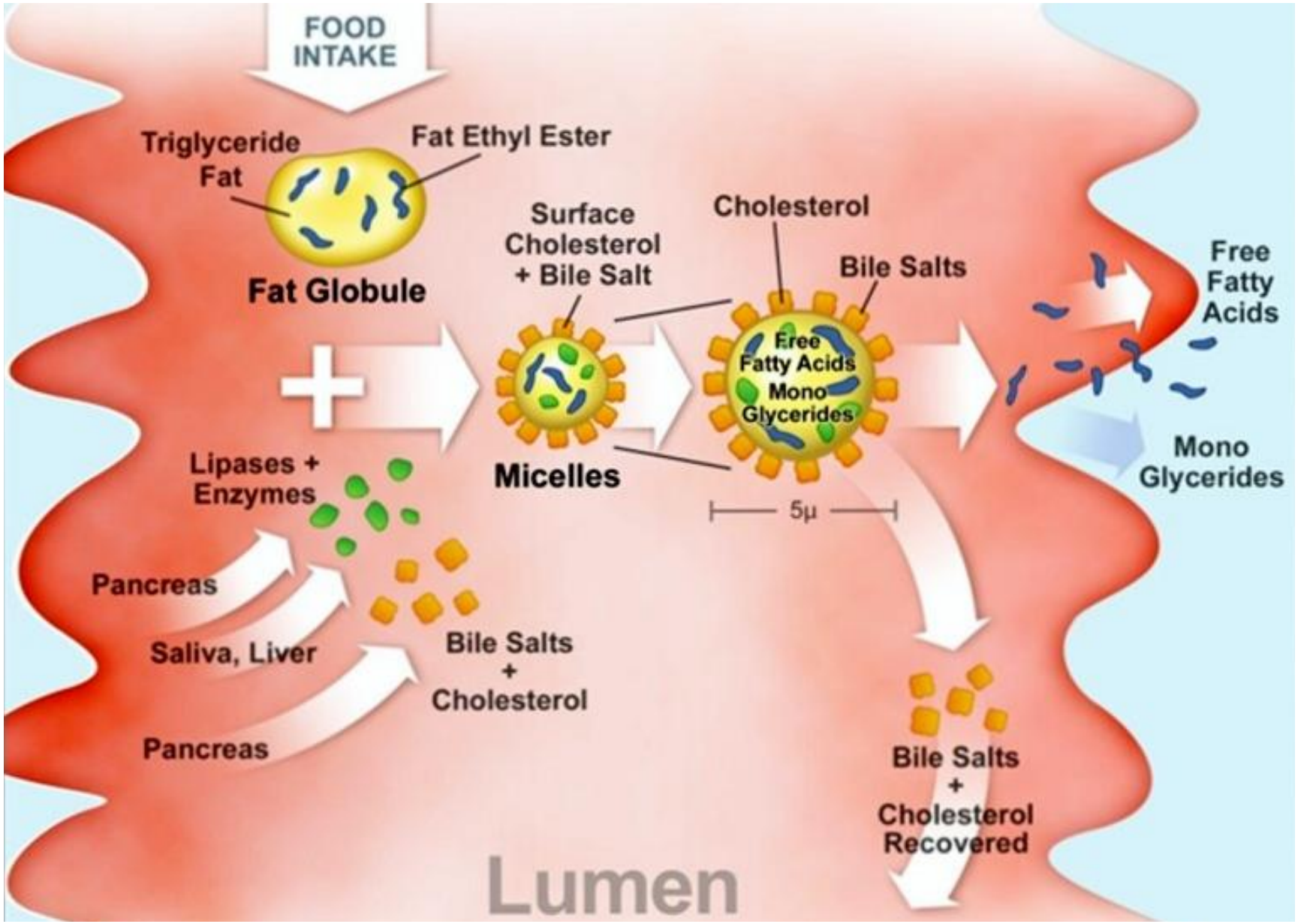
Emulsification

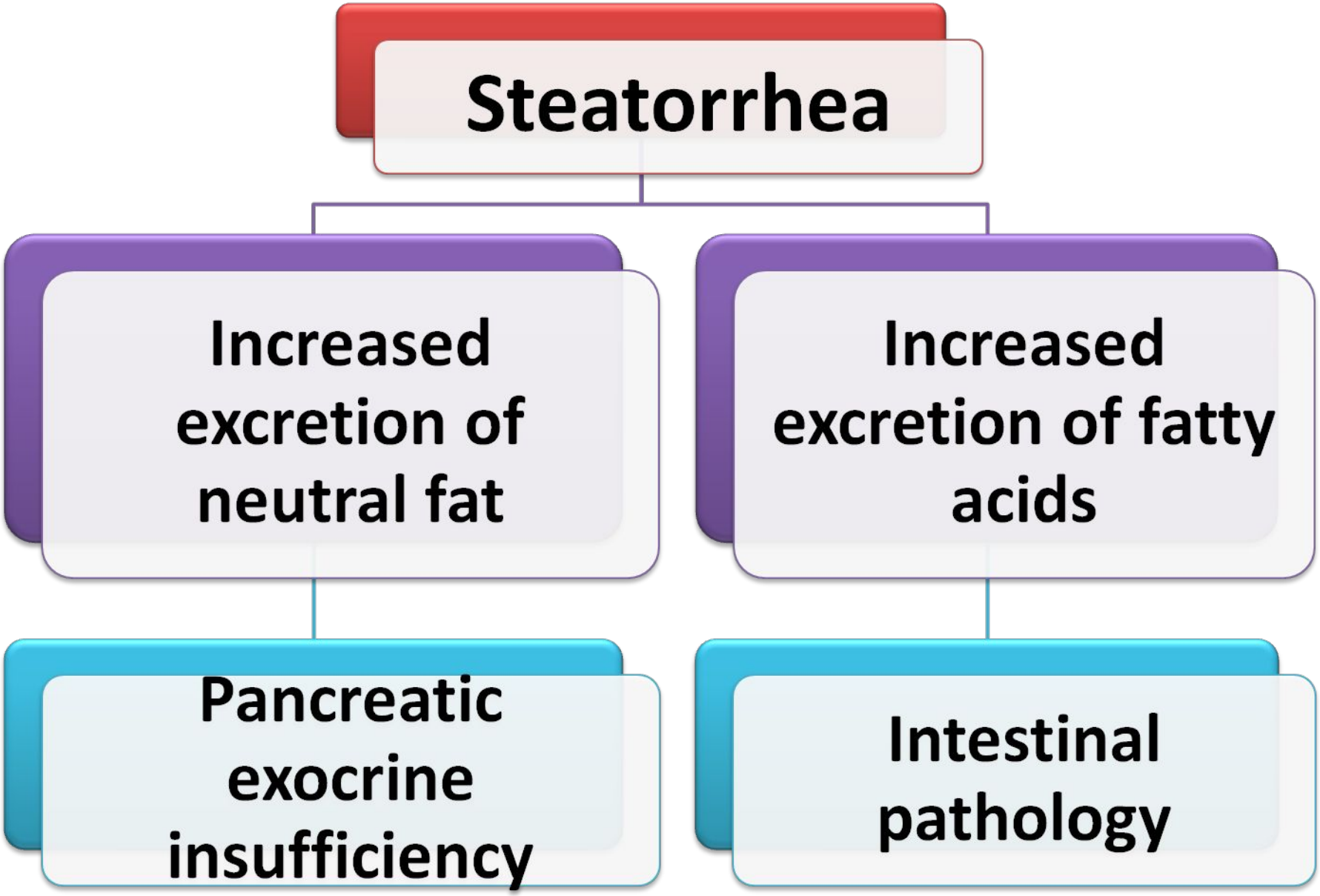


Breakdown of fats



Absorbtion


FOOD INTAKE
Triglyceride Fat
Fat Ethyl Ester
Fat Globule
Surface Cholesterol + Bile Salt
Cholesterol
Bile Salts
Micelles
Free Fatty Acids
Mono Glycerides
5μ
Free Fatty Acids
Mono Glycerides
Lipases + Enzymes
Pancreas
Saliva, Liver
Pancreas
Bile Salts + Cholesterol
Bile Salts + Cholesterol Recovered
Lumen


Steatorrhea
Increased excretion of neutral fat
Increased excretion of fatty acids
Pancreatic exocrine insufficiency
Intestinal pathology

Lipid resynthesis in cells of intestinal wall epithelium

β-monoglyceride pathway

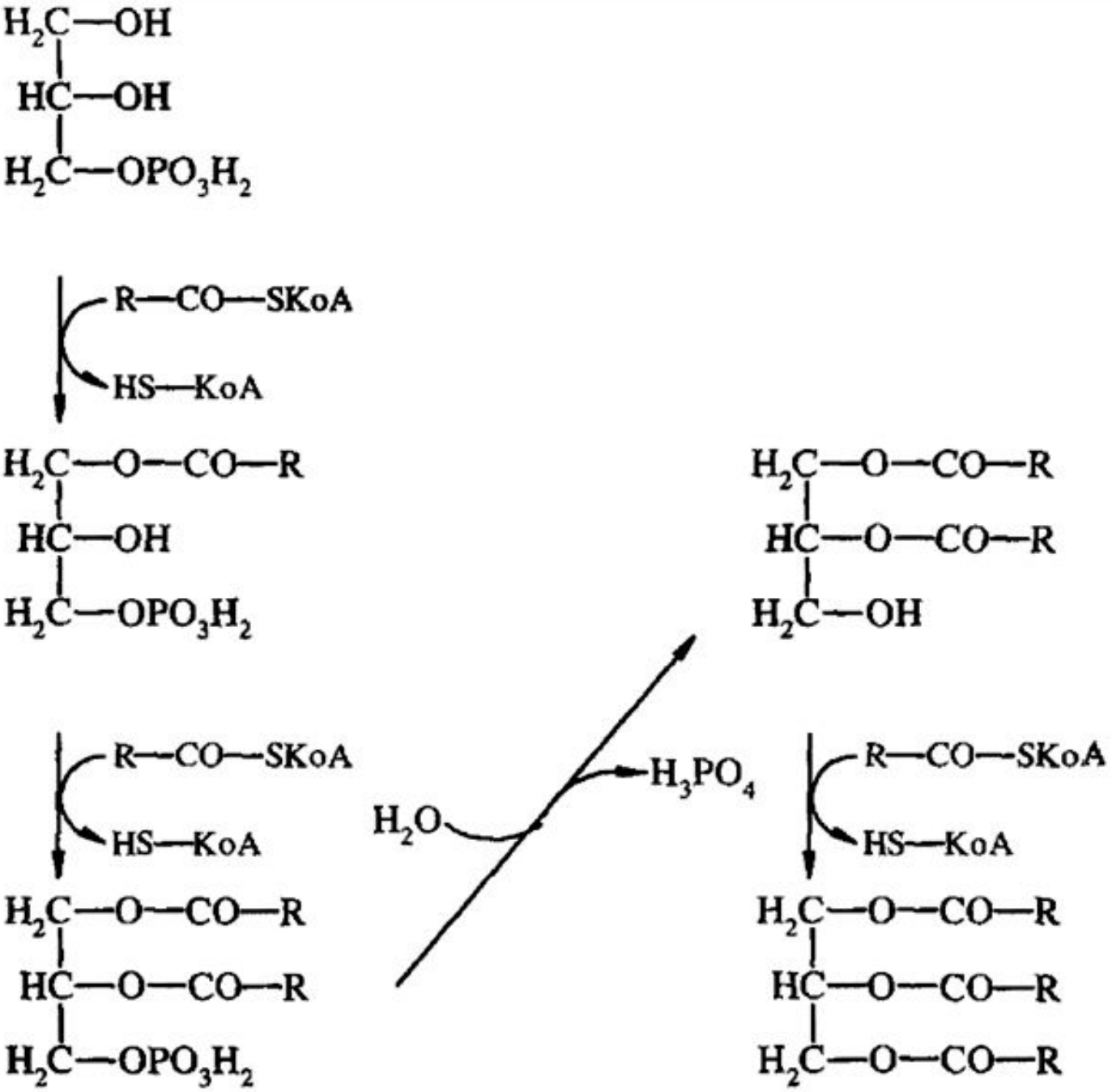
β-monoglyceride + R-CO-SCoA →

→ diglyceride + HS-CoA

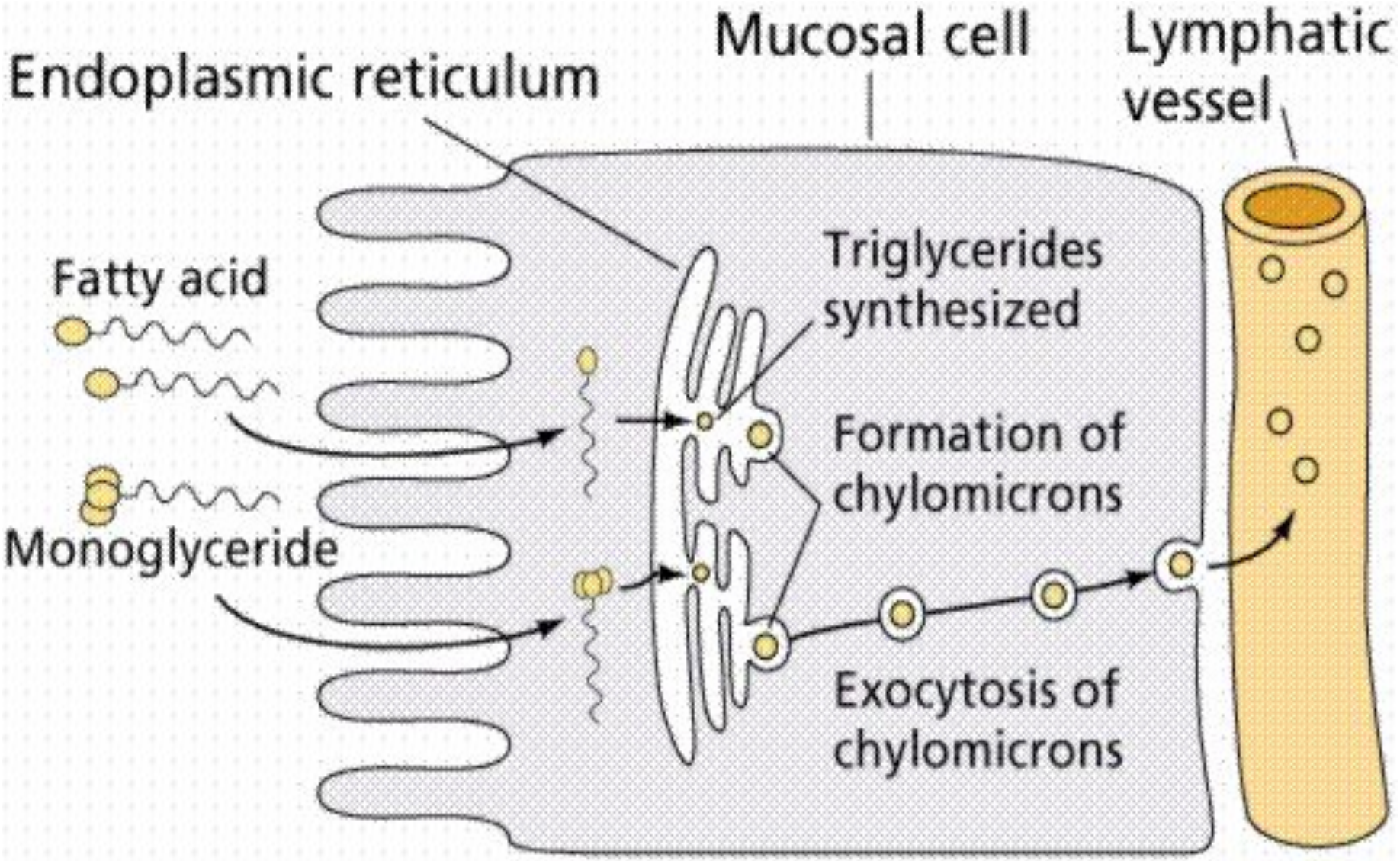
diglyceride + R-CO-SCoA →

→ triglyceride + HS-CoA

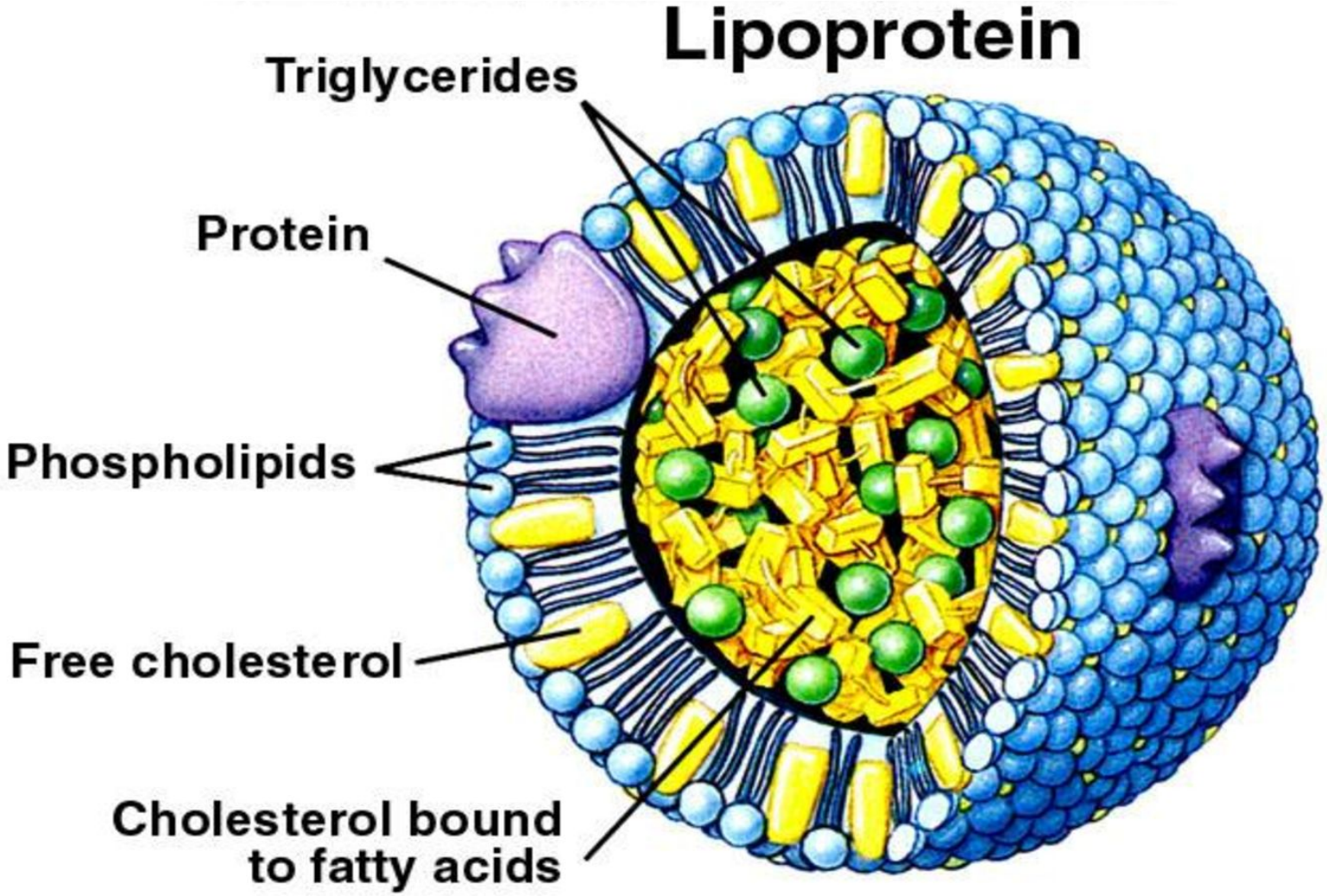
sphate


H2C—OH
HC—OH
H2C—OPO3H2
R—CO—SKoA
HS—KoA
H2C—O—CO—R
HC—OH
H2C—OPO3H2
H2C—O—CO—R
HC—O—CO—R
H2C—OH
R—CO—SKoA
HS—KoA
H2C—O—CO—R
HC—O—CO—R
H2C—OPO3H2
H2O
H3PO4
R—CO—SKoA
HS—KoA
H2C—O—CO—R
HC—O—CO—R
H2C—O—CO—R

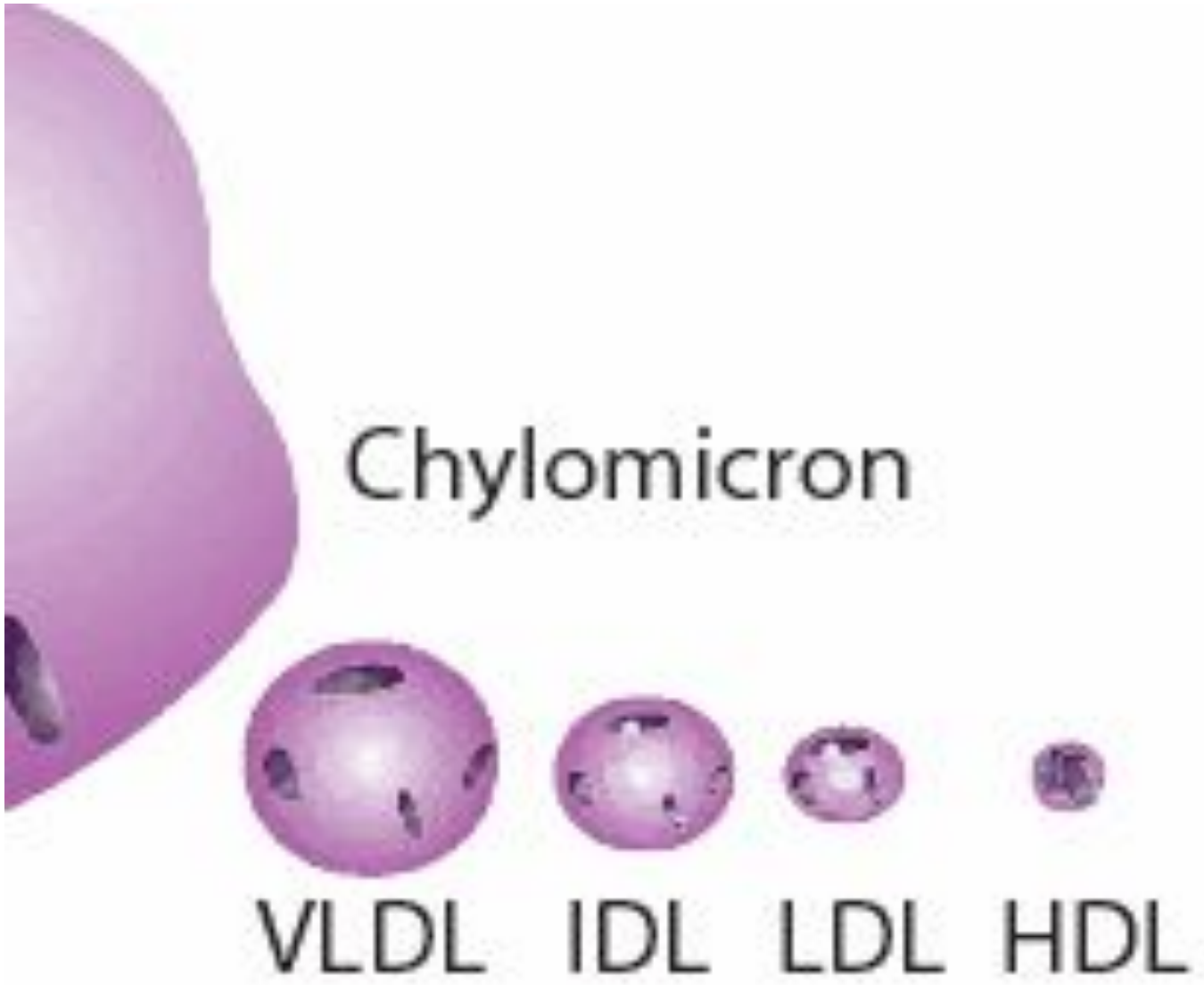
Formation of chylomicrons



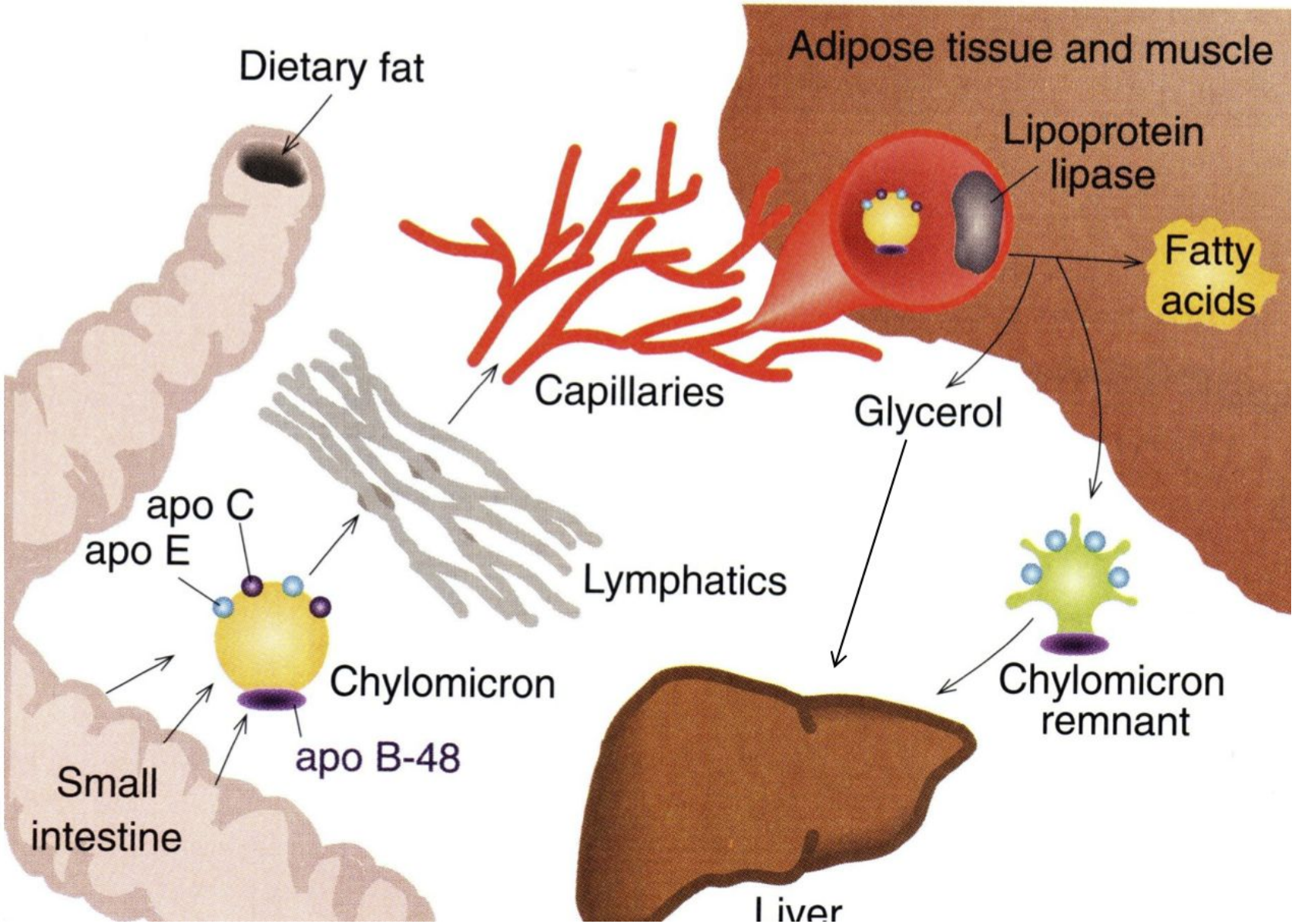
Lipoprotein structure



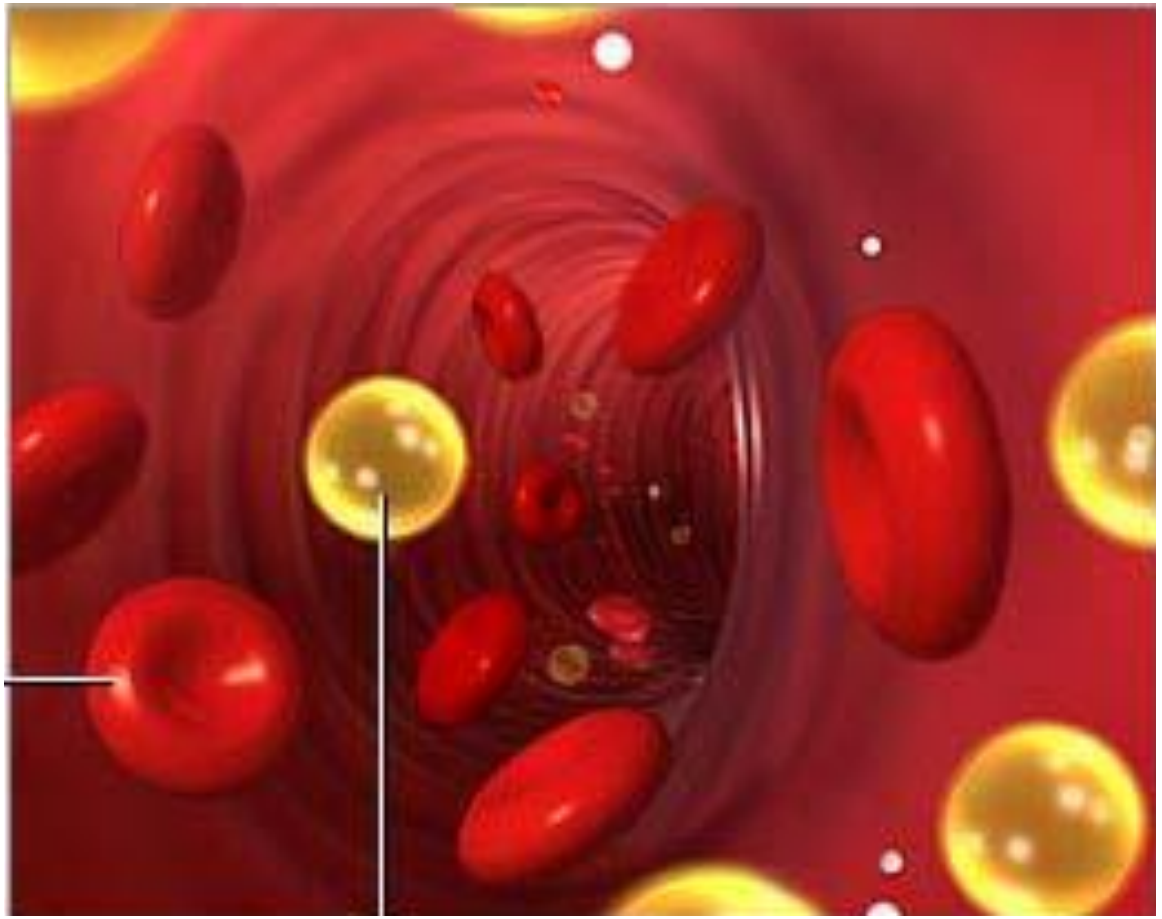
Transport lipoproteins

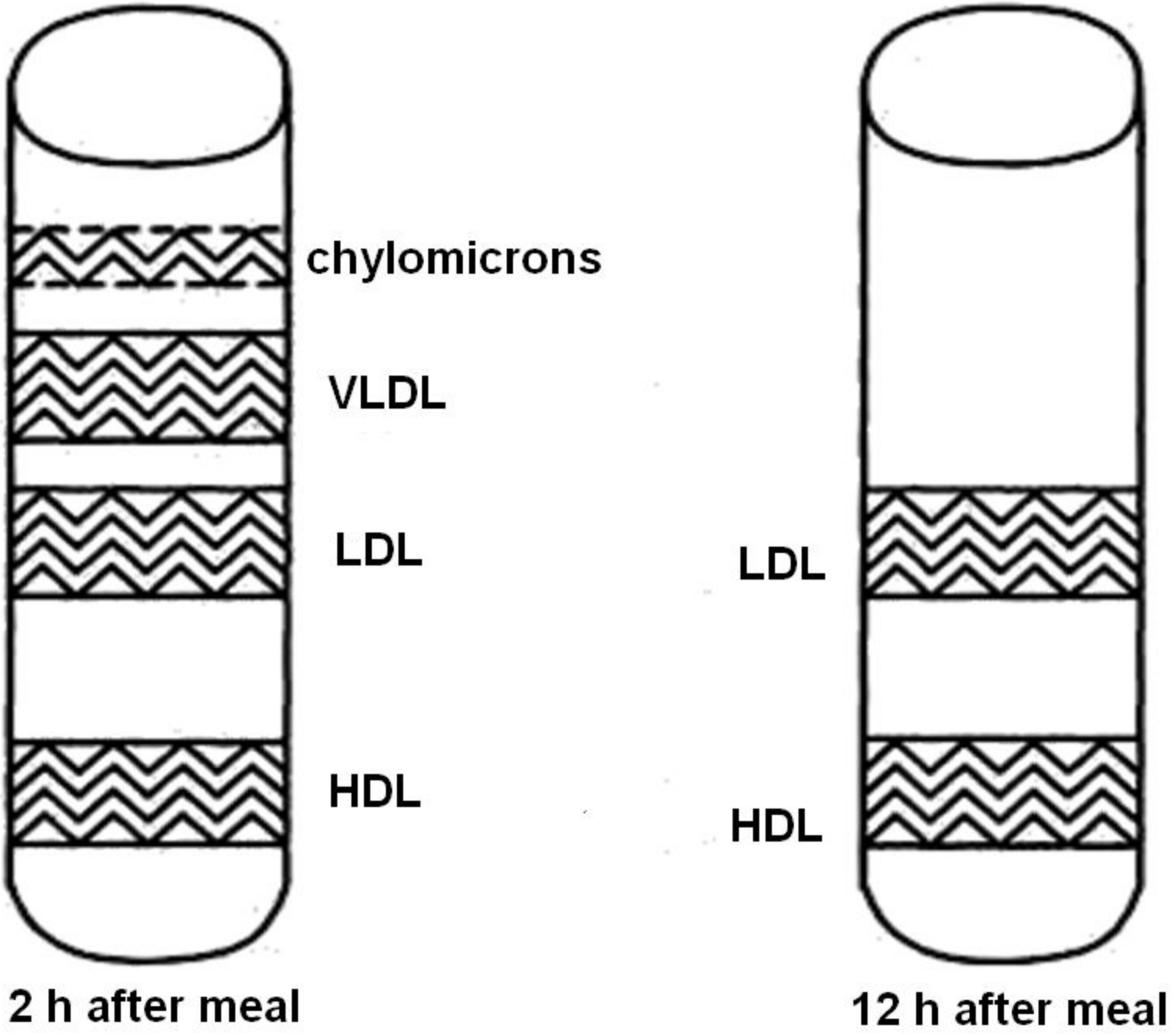


Fat transport



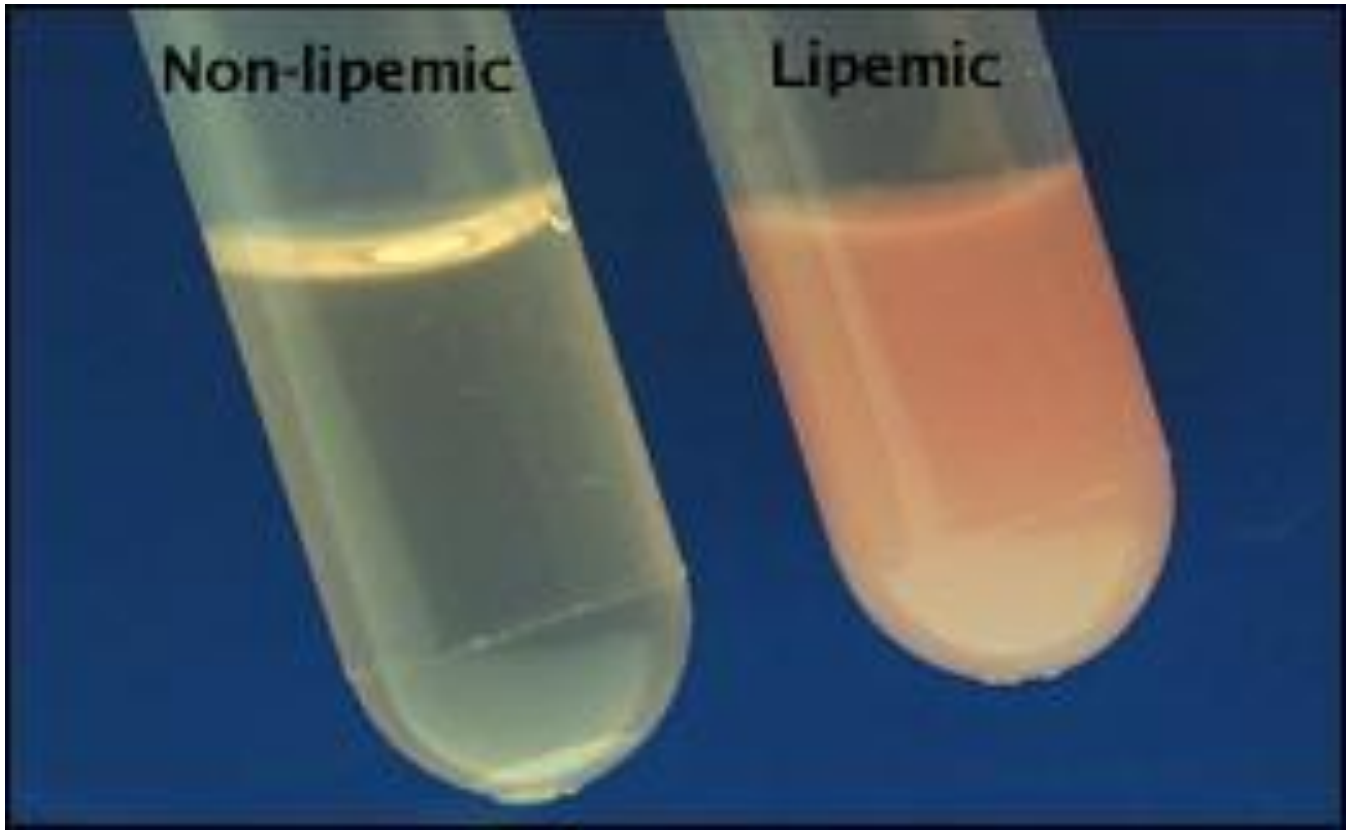
Artery section

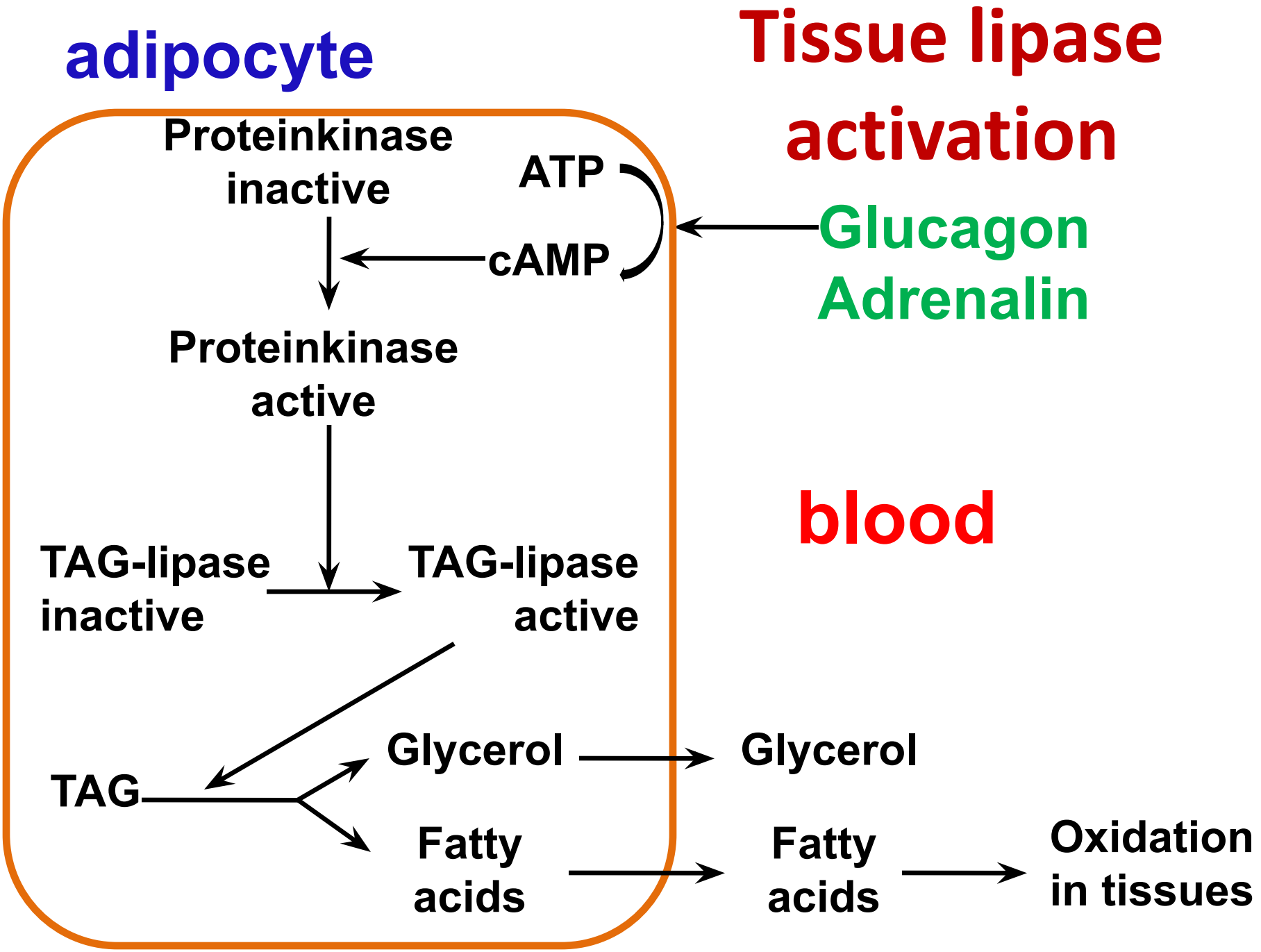



chylomicrons
VLDL
LDL
HDL
LDL
HDL
2 h after meal
12 h after meal

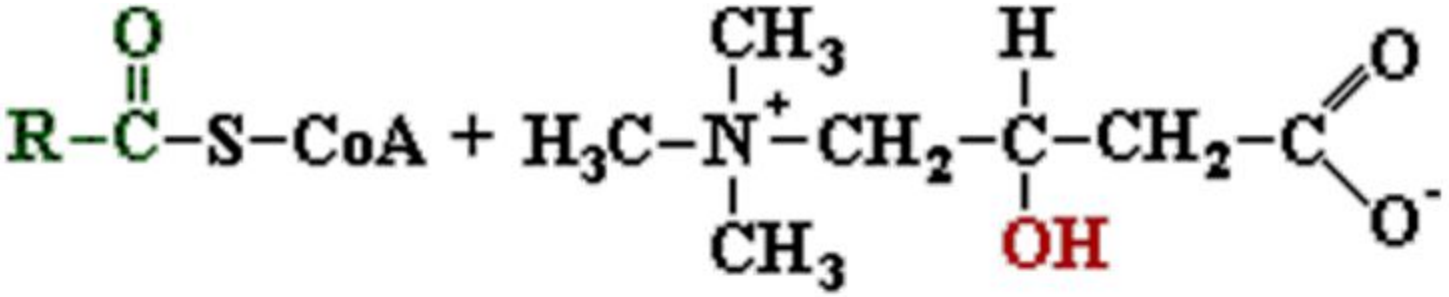
Dislipoproteinemia (hyperlipoproteinemia) Type I

- Reduced activity of lipoprotein lipase (LPL)
- Deficiency of apoCII (LPL activator)




adipocyte
Tissue lipase activation
Proteinkinase inactive
ATP
cAMP
Glucagon
Adrenalin
Proteinkinase active
blood
TAG-lipase inactive
TAG-lipase active
TAG
Glycerol
Glycerol
Fatty acids
Fatty acids
Oxidation in tissues

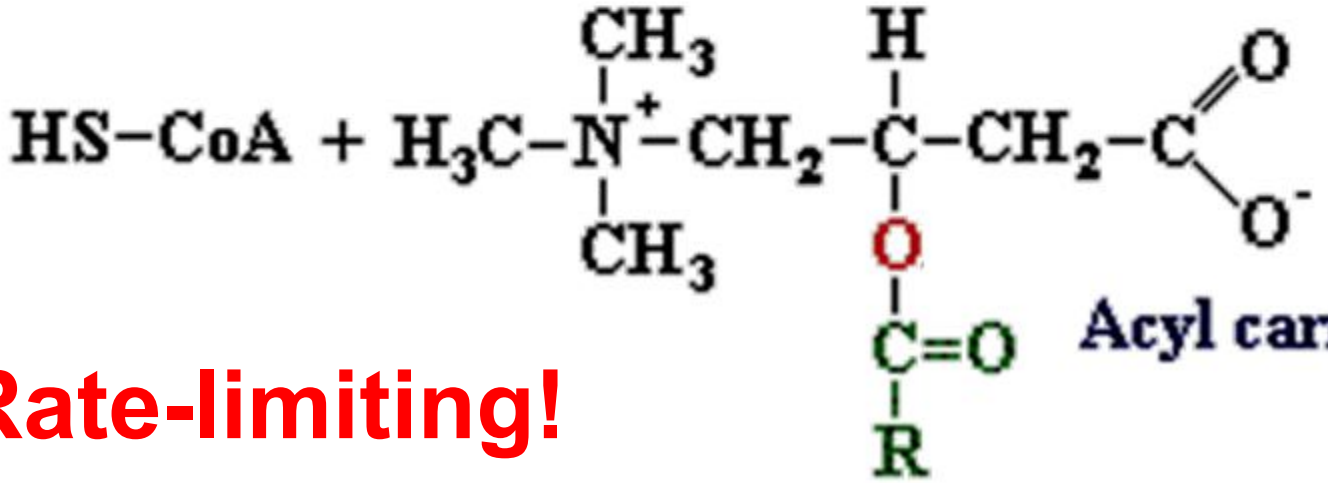
β-Oxidation of fatty acids



Acyl Coa

Carnitine

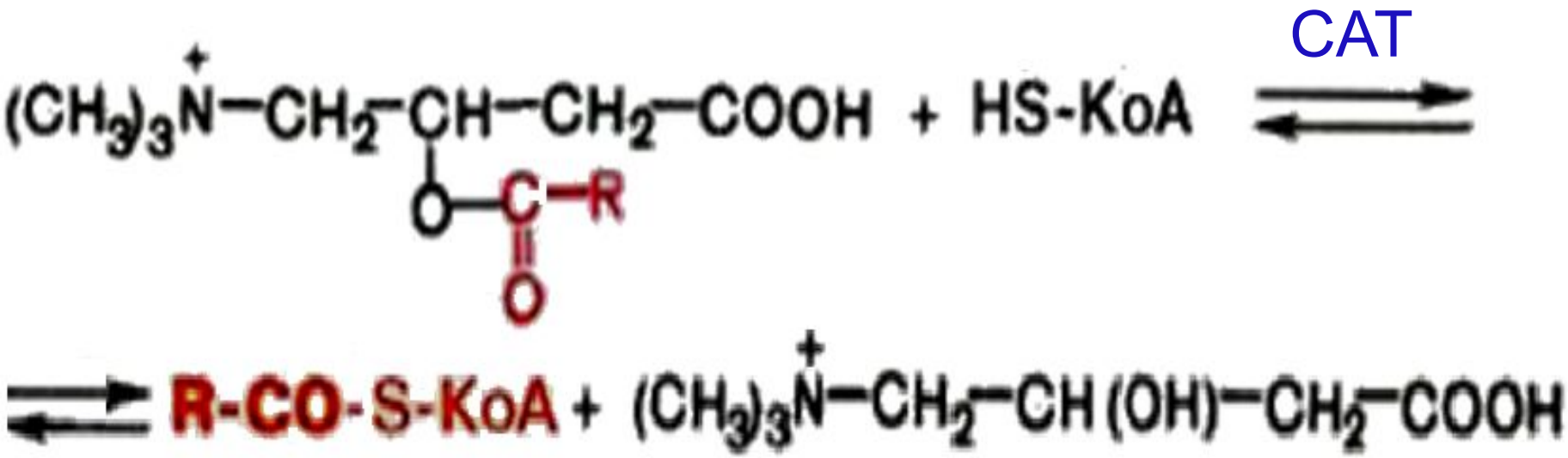
carnitine acyl transferase



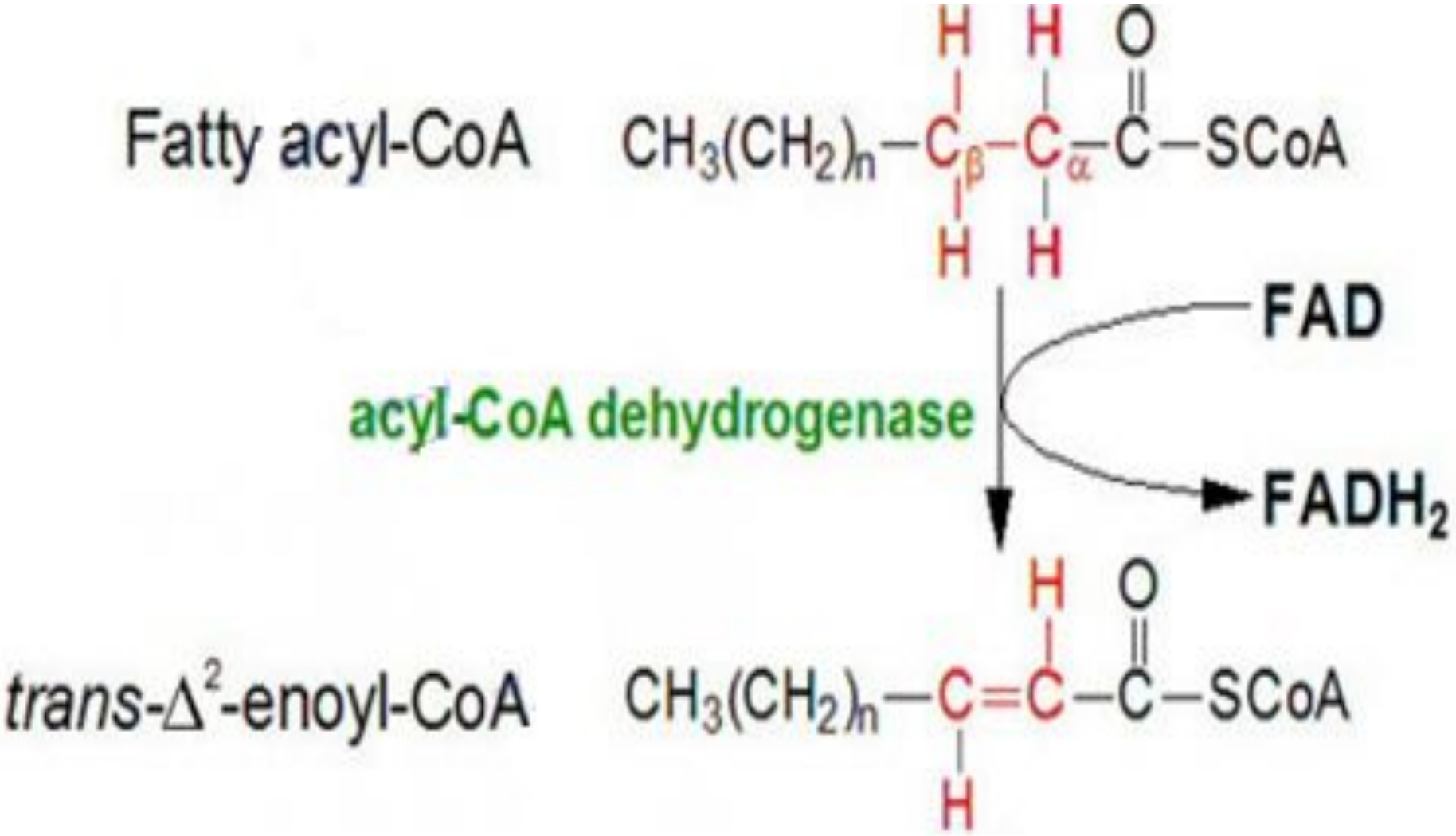
Acyl carnitine

Rate-limiting!

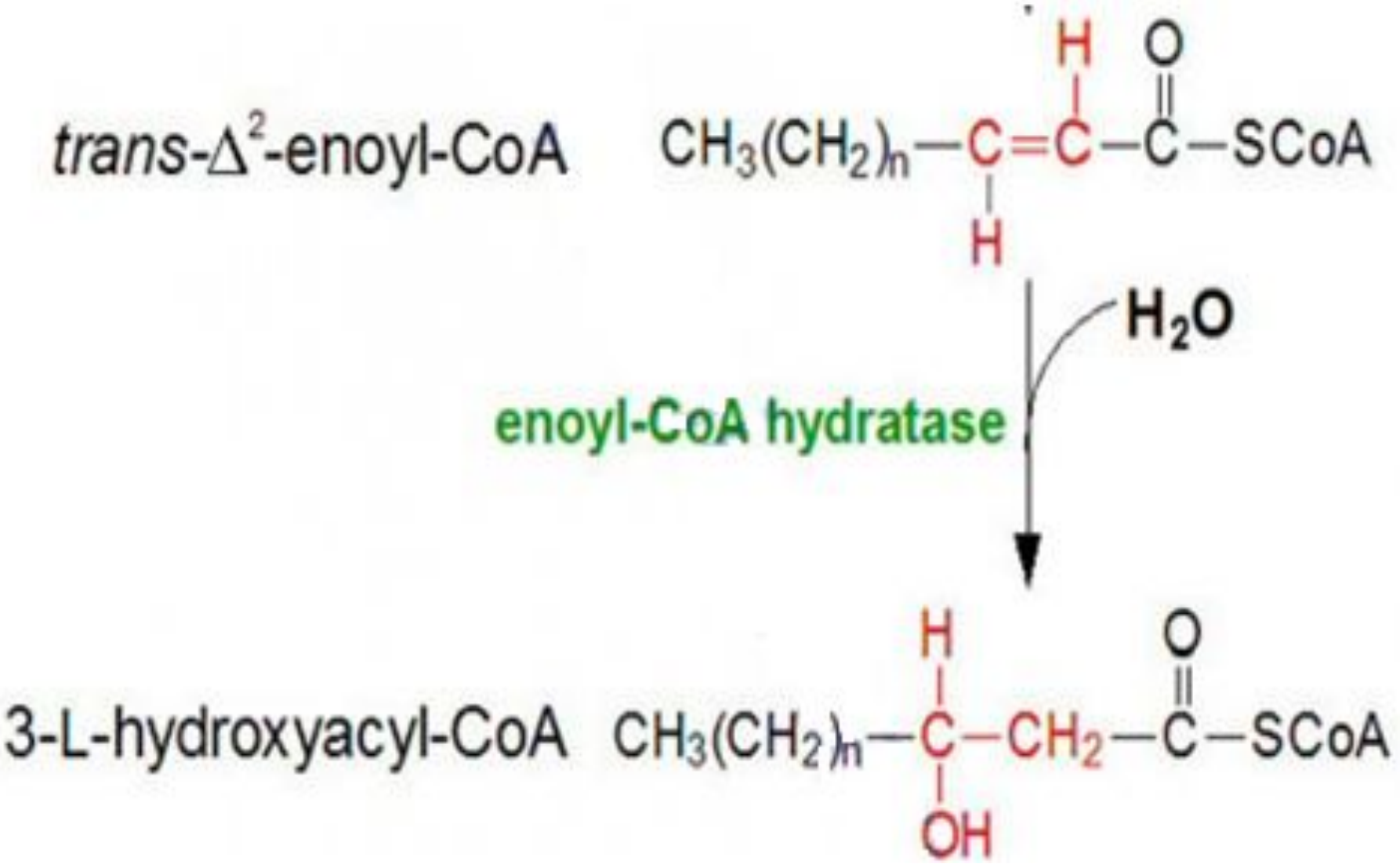
Breakdown of acyl carnitin in mitochondria



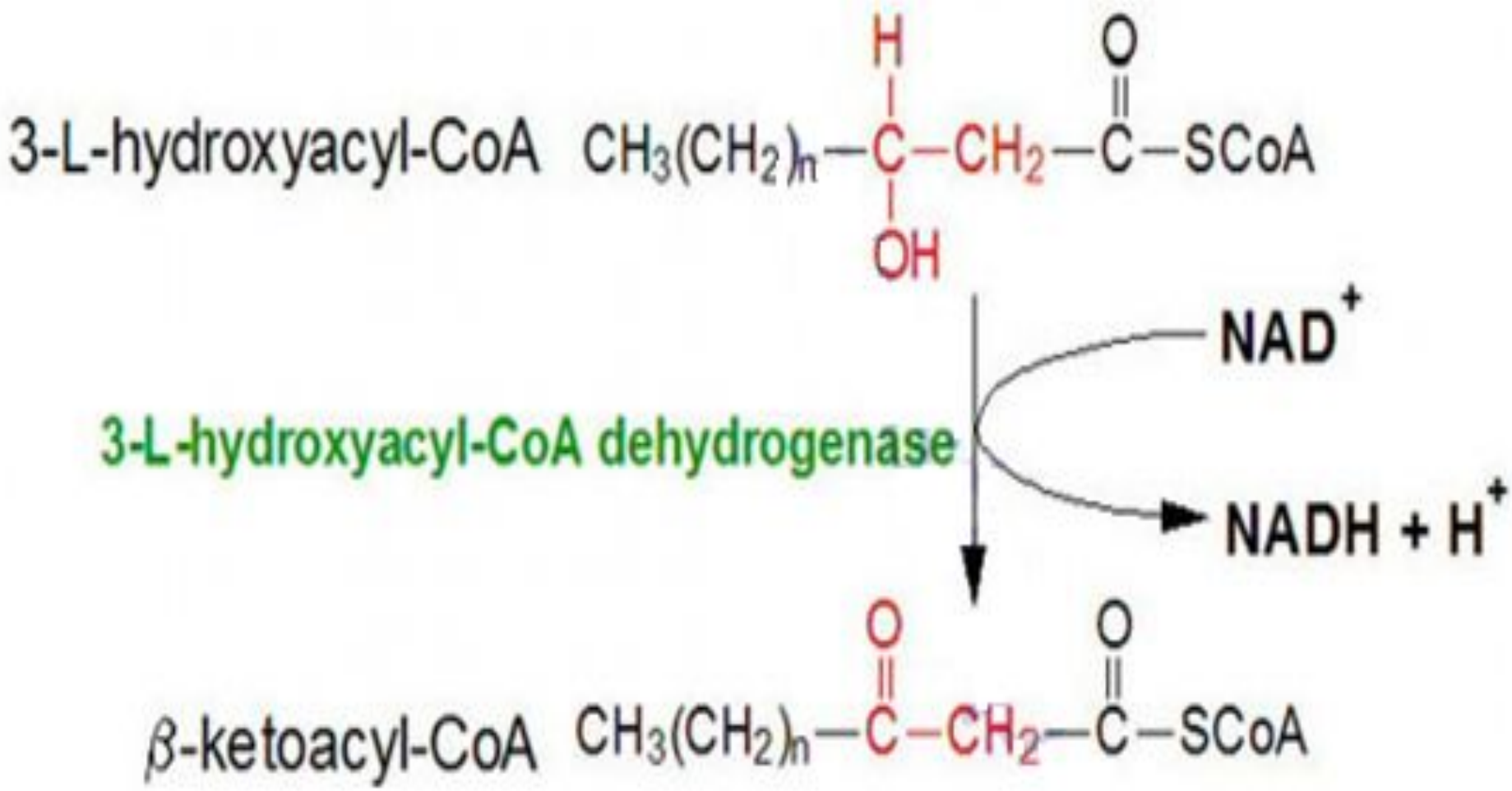
Dehydrogenation



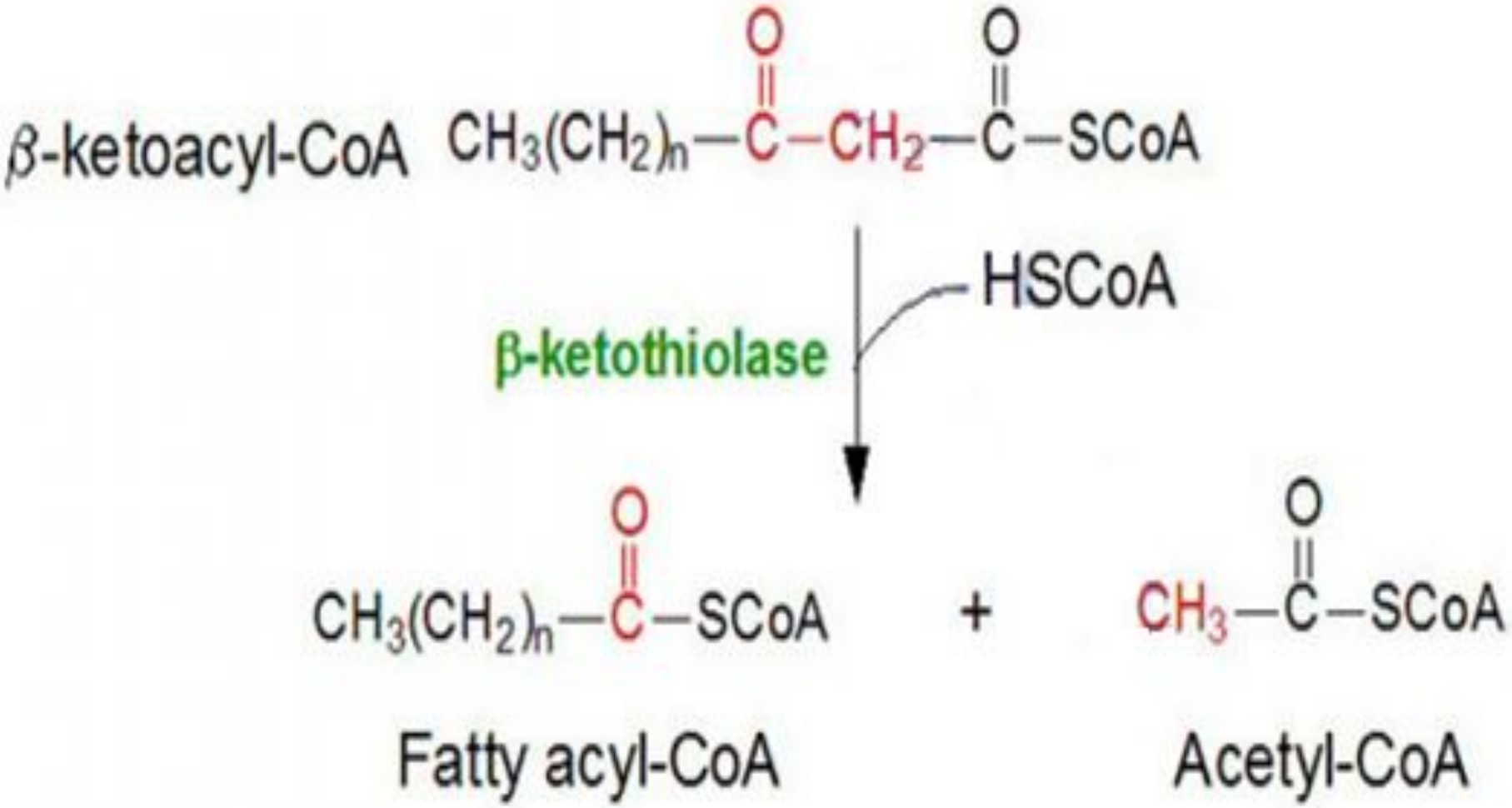
Hydration


trans-Δ²-enoyl-CoA
CH3(CH2)n—C=C—C—SCoA
H
H
O
H2O
enoyl-CoA hydratase
3-L-hydroxyacyl-CoA
CH3(CH2)n—C—CH2—C—SCoA
H
OH
O

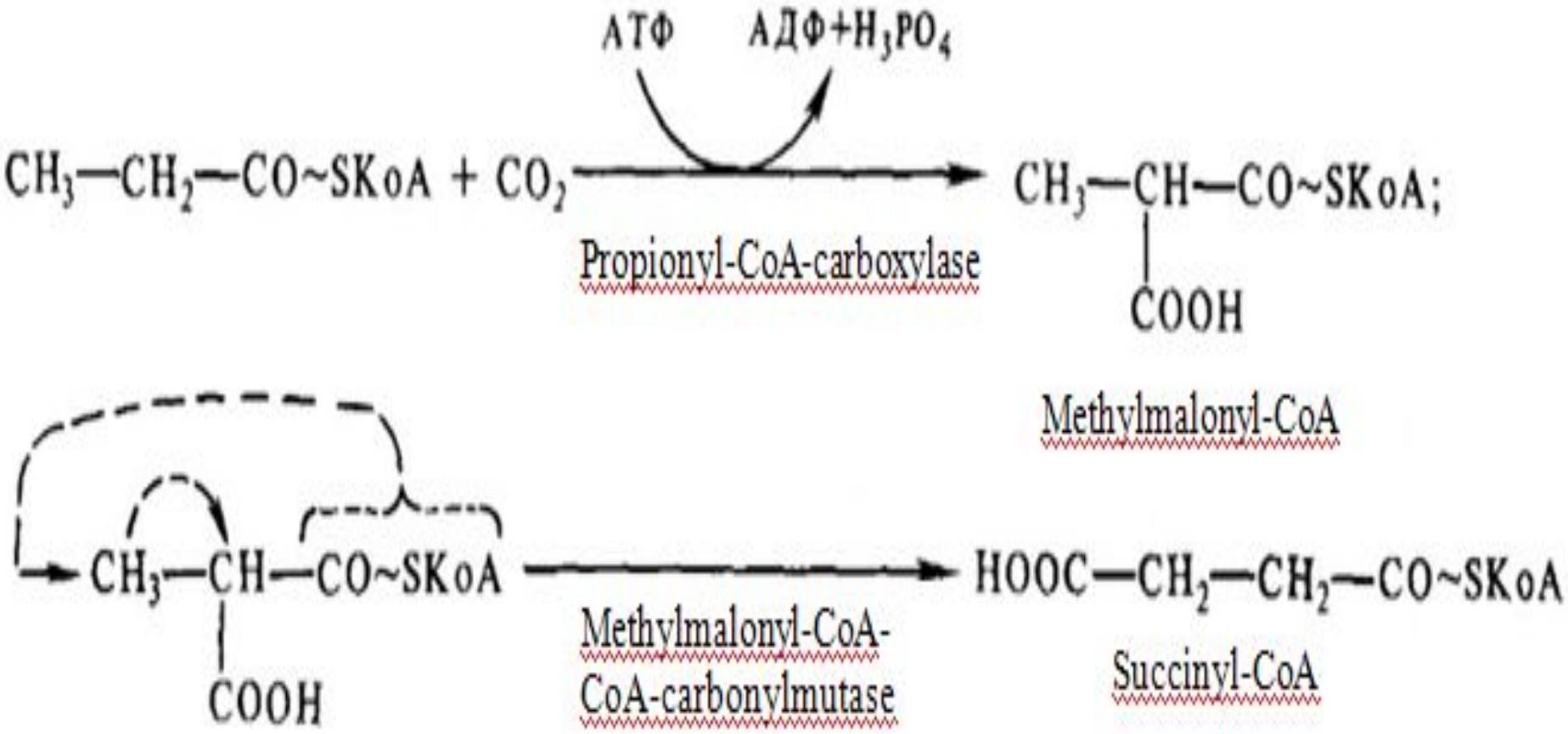
Dehydrogenation

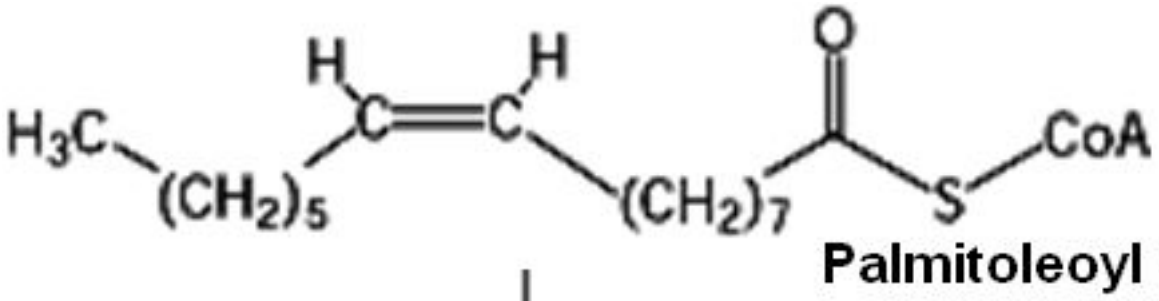


Thiolase reaction

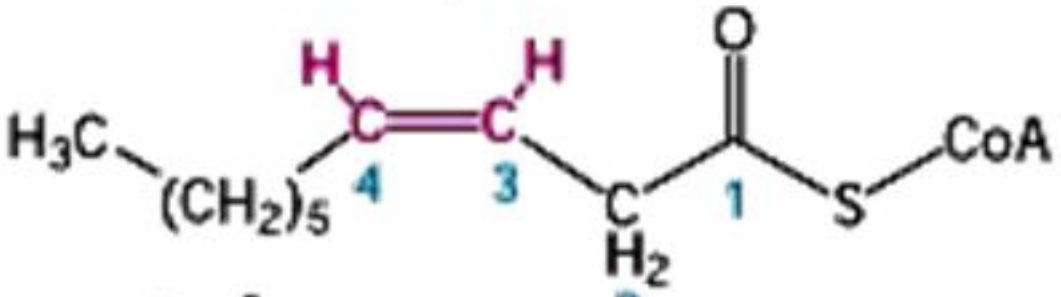


Propionyl-CoA metabolism

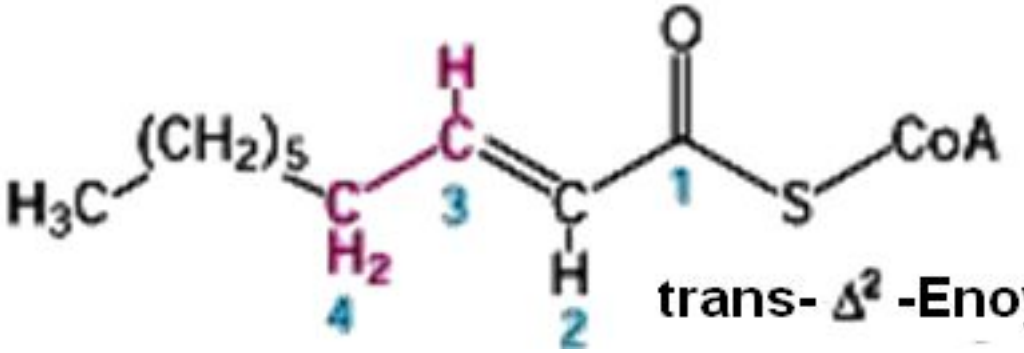




Palmitoleoyl CoA



cis-Δ^3-Enoyl CoA



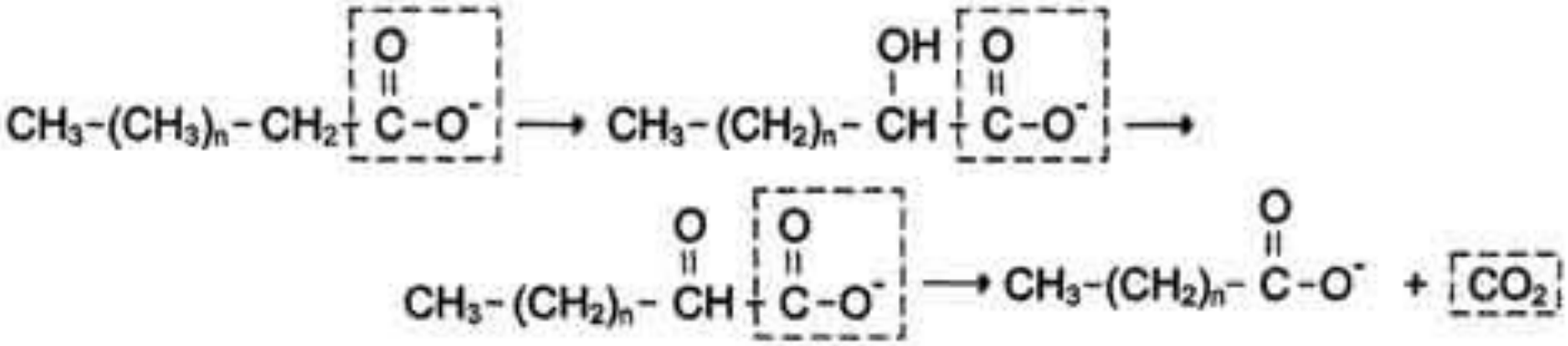
trans- Δ^2 -Enoyl CoA

ıidadion of

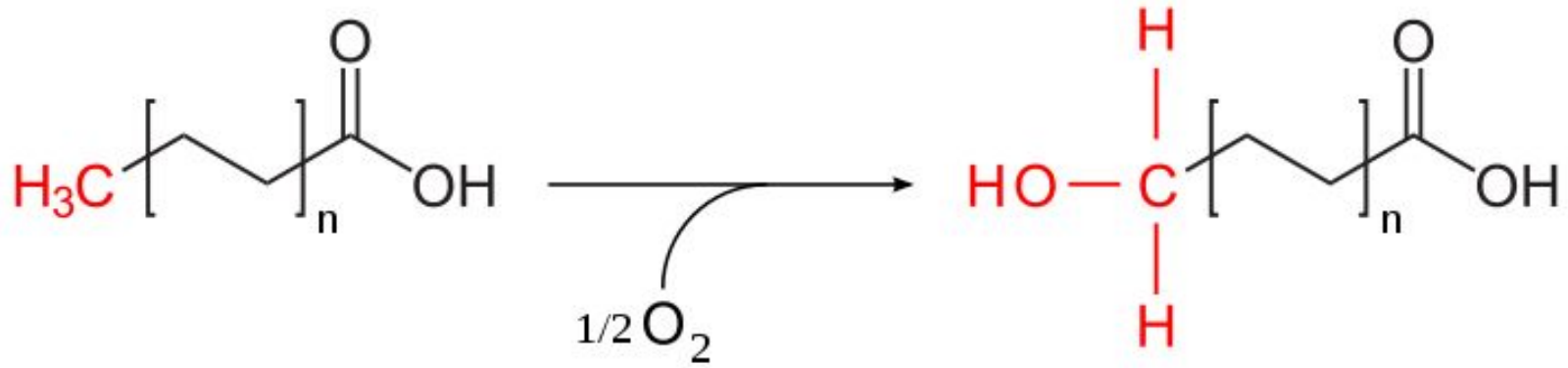
ısaturated

atty acids

α-Oxidation (nervous tissue, > 20 C)



ω-Oxidation (in pathology)

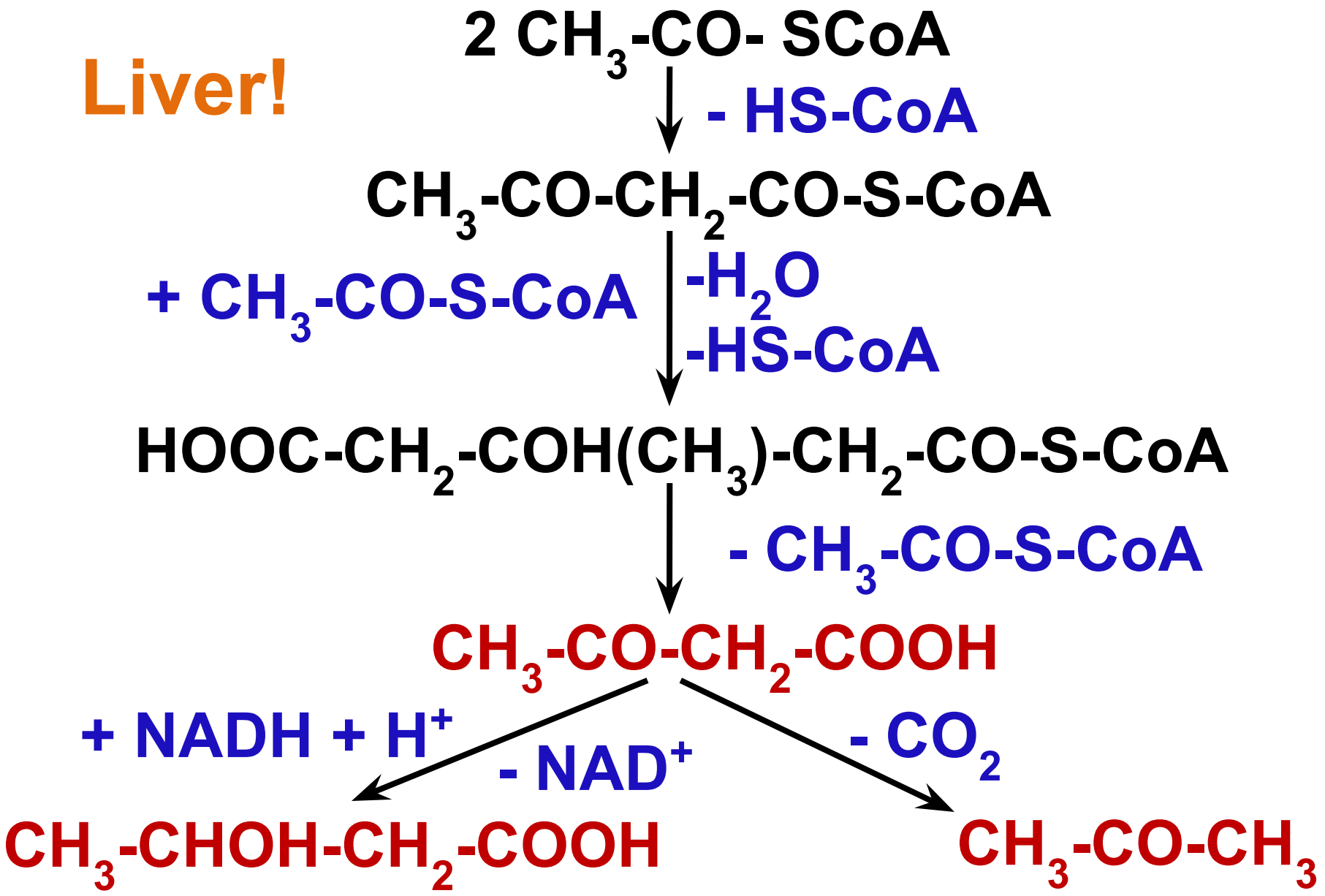


Violations of fatty acid oxidation

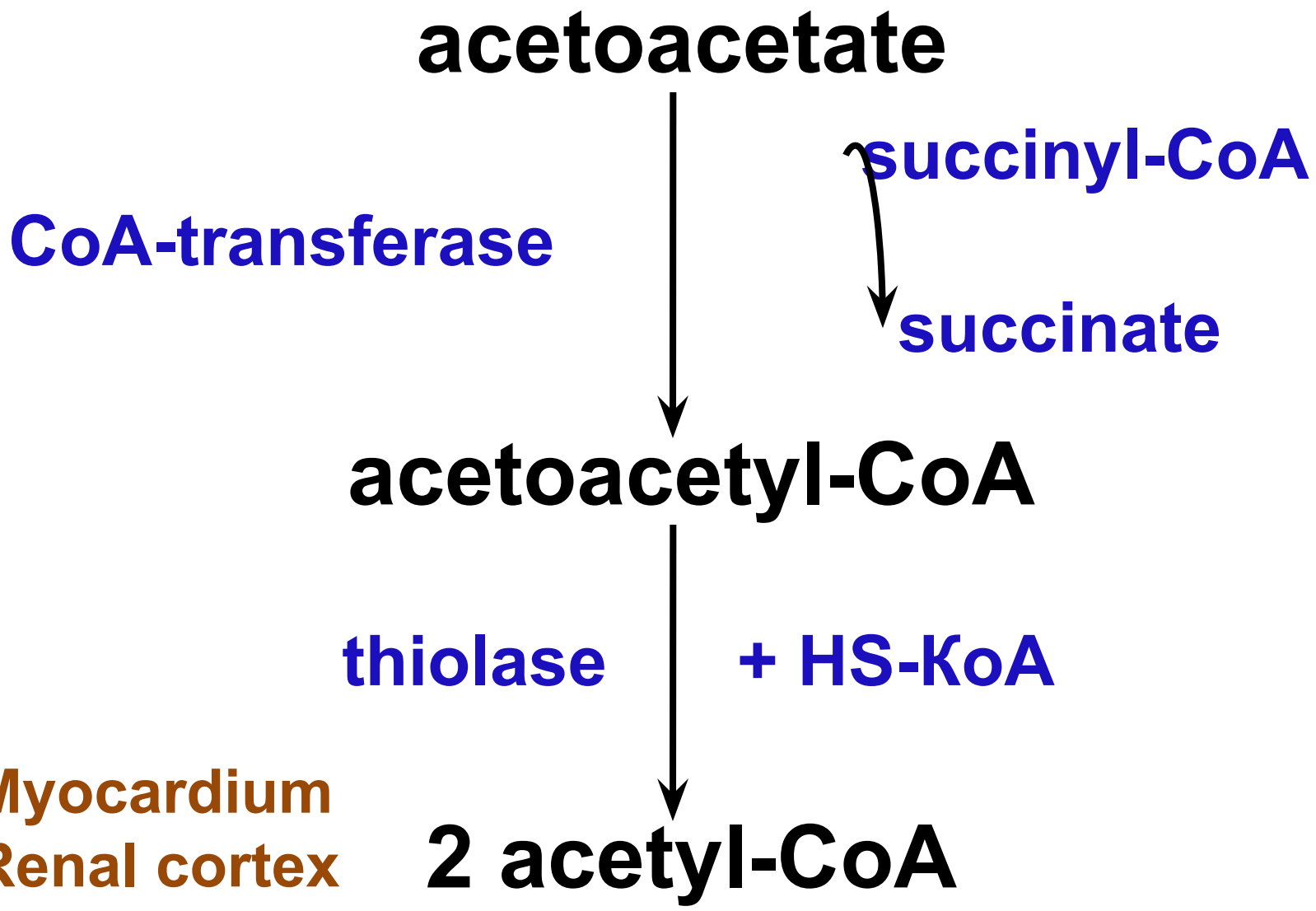
- **Hereditary defects of carnitine acyl transferase I or enzymes of carnitine synthesis**
- **Genetic defect of dehydrogenase of fatty acids with medium chain**

Synthesis of ketone bodies

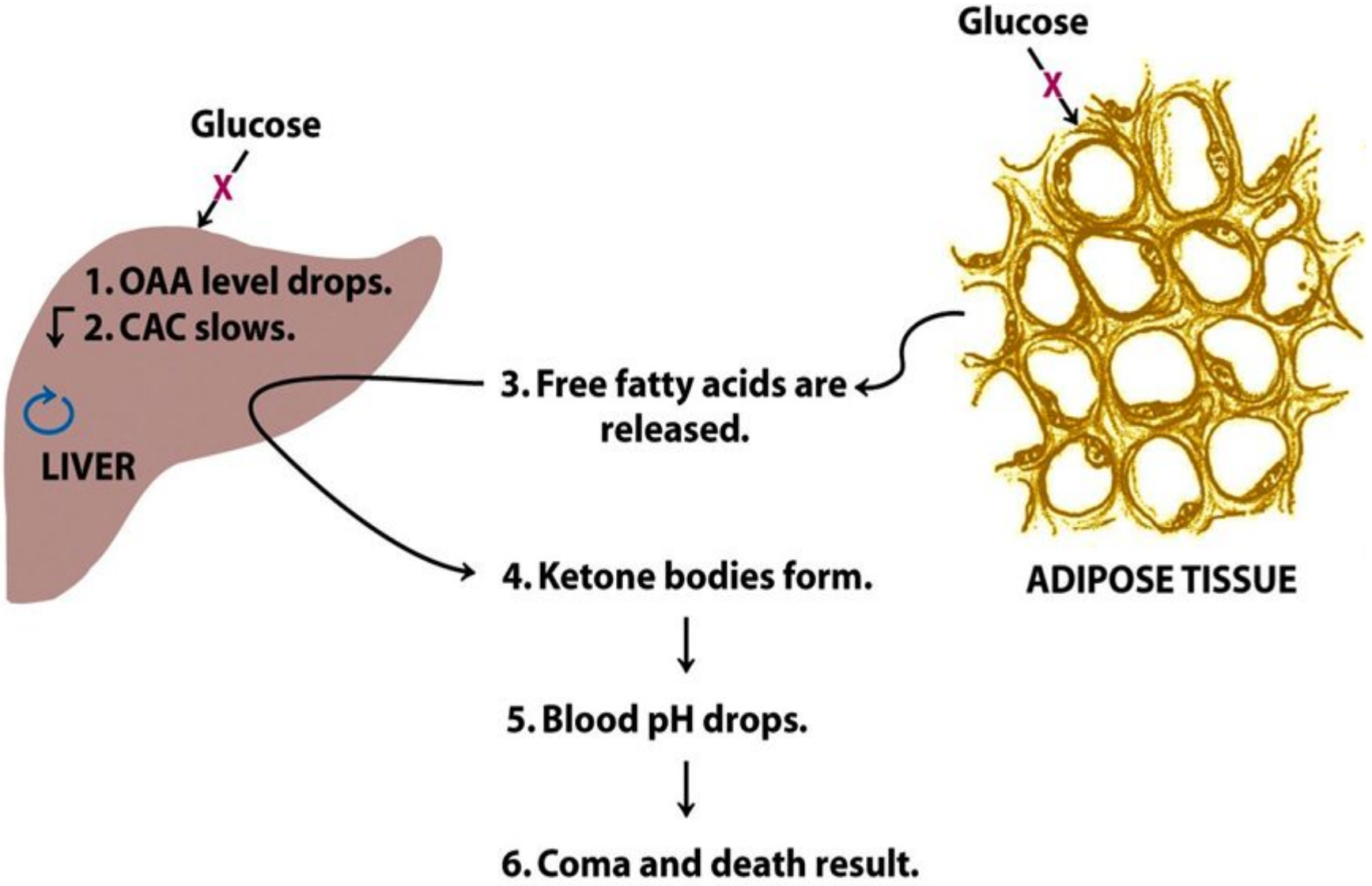
Liver!



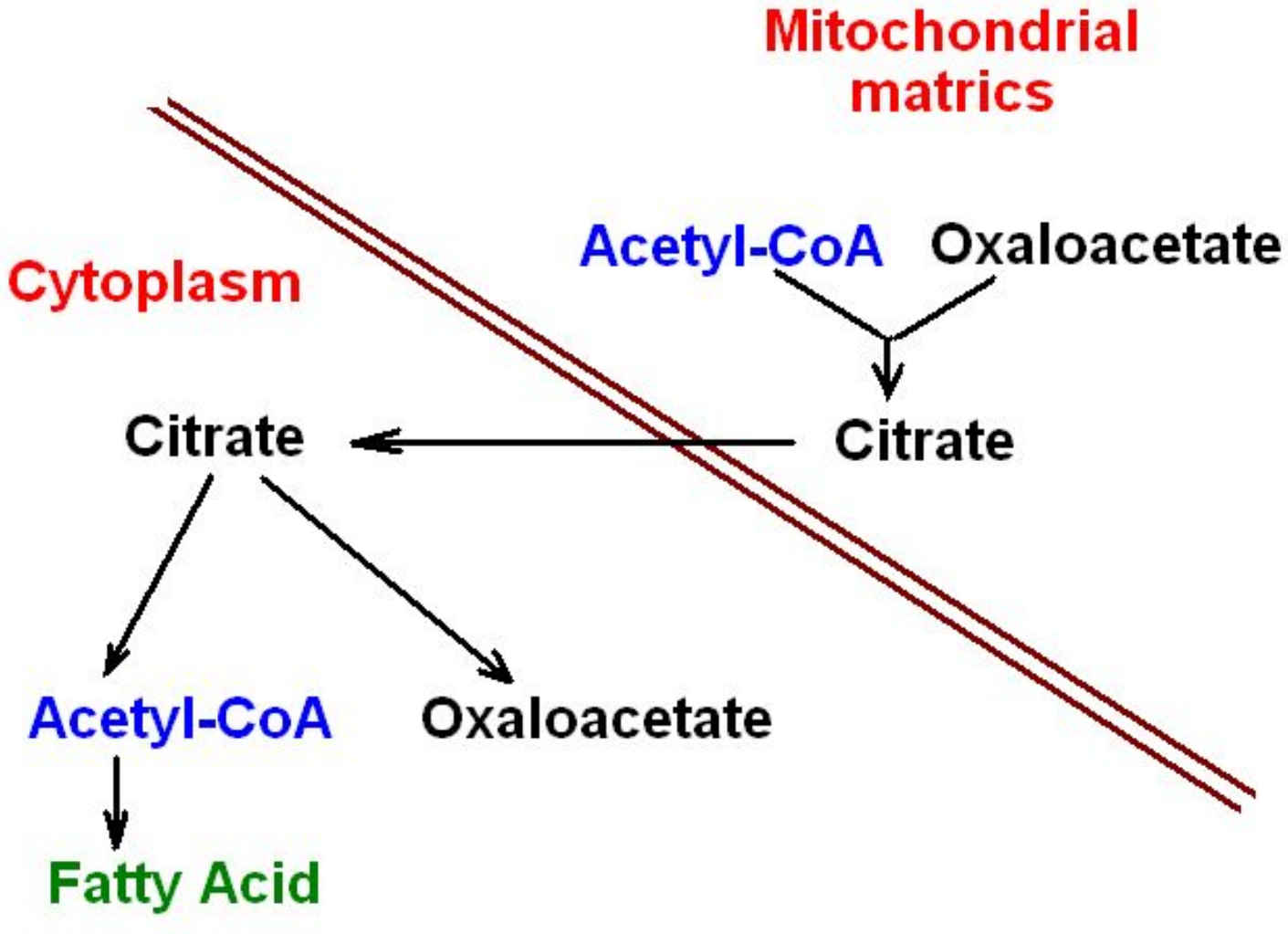
Oxidation of ketone bodies



Mechanism of ketosis



Lipogenesis
Acetyl-CoA transport



Lipogenesis

CO_2 + ATP + biotin-enzyme →

→ carboxybiotin-enzyme + ADP + P_i

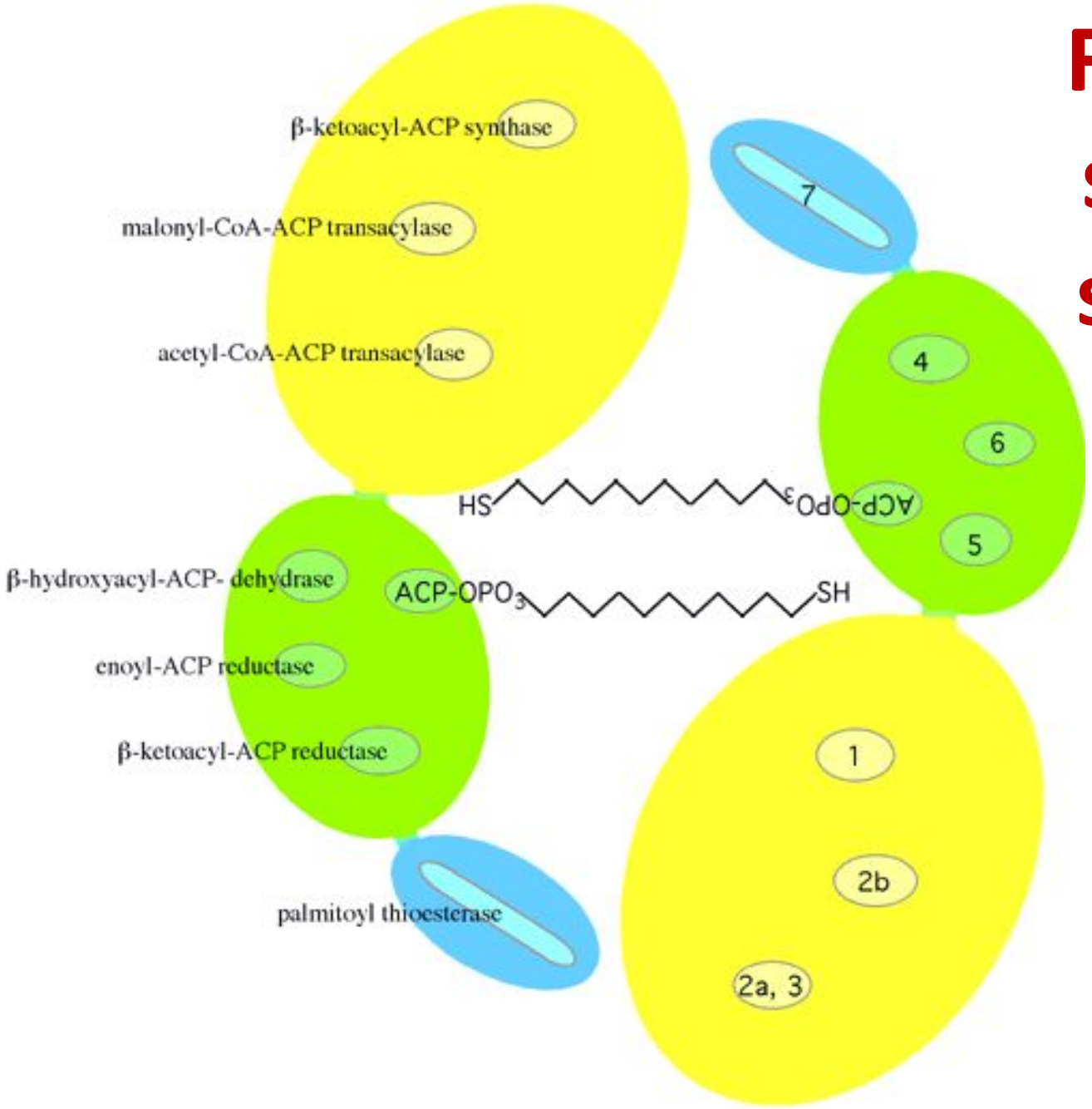
carboxybiotin-enzyme + CH_3-CO-SKoA →

→ HOOC-CH_2-CO-S-KoA + biotin-enzyme

malonyl-CoA

Rate-limiting!

Fatty acid synthase structure



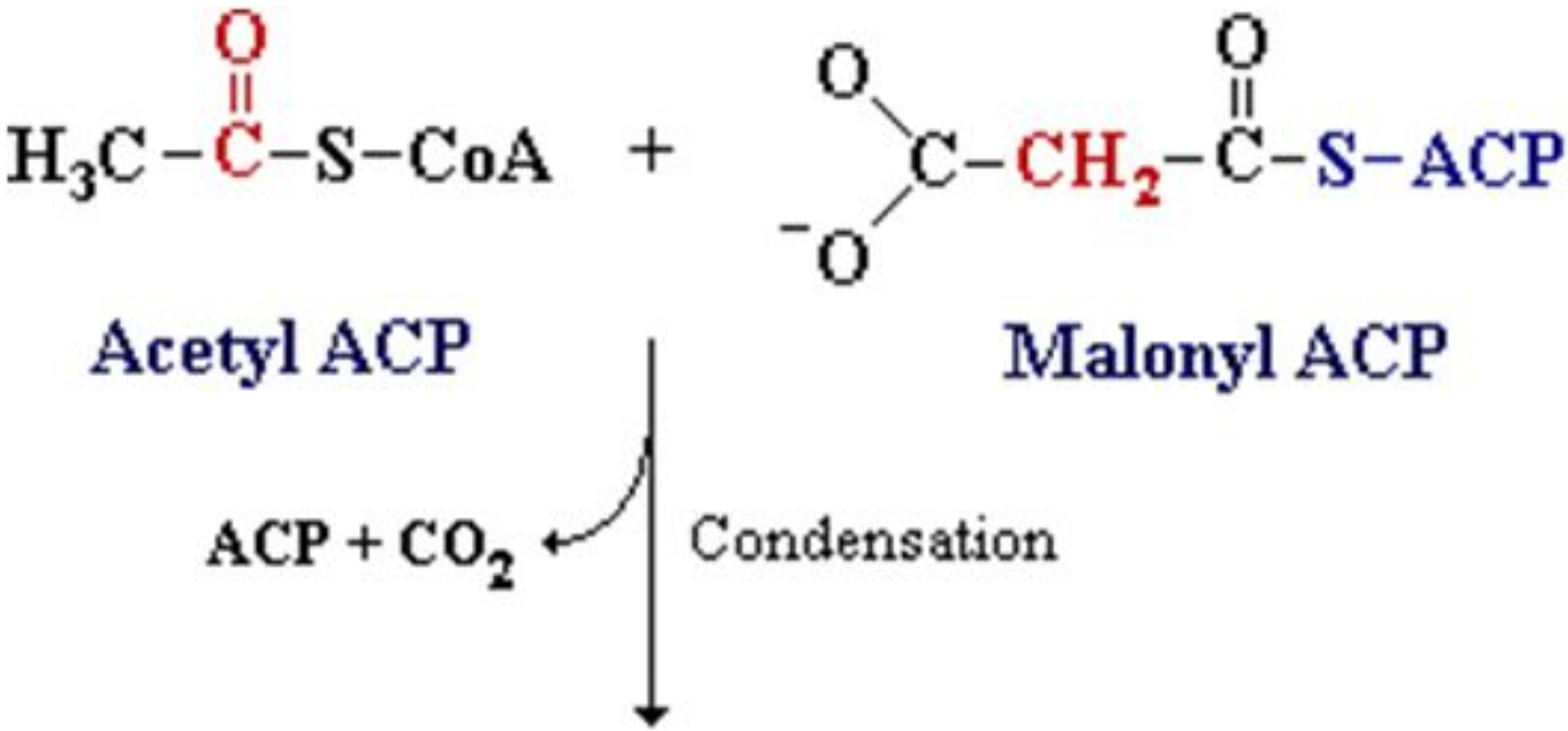
acetyl transacylase

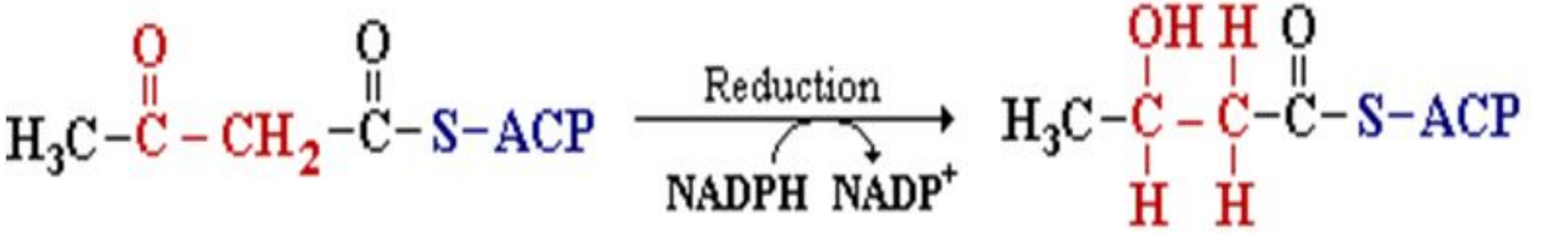
Acetyl CoA + ACP ⟶ Acetyl-ACP + HSCoA

malonyl transacylase

Malonyl CoA + ACP ⟶ Malonyl-ACP + HSCoA

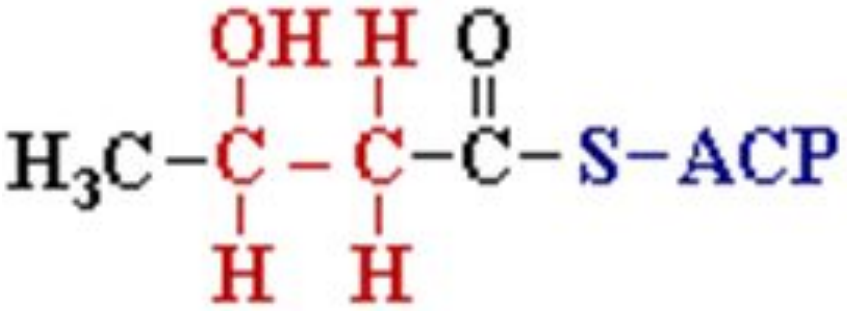
(ACP = acyl carrier protein)


H3C–C–S–CoA
+
C–CH2–C–S–ACP
Acetyl ACP
Malonyl ACP
ACP + CO2
Condensation
H3C–C – CH2–C– S–ACP
Acetoacetyl-ACP

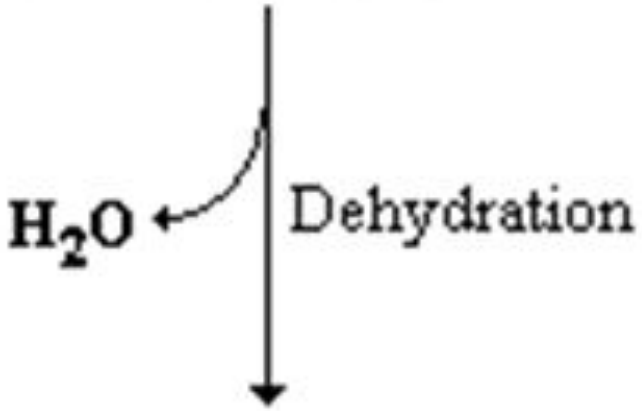


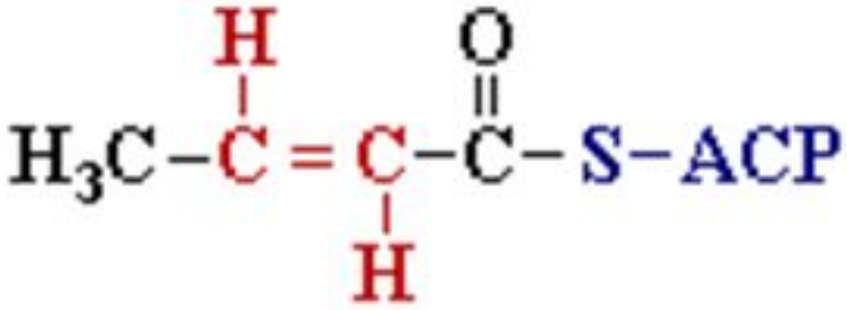
Acetoacetyl-ACP

D-3-Hydroxybutyryl-ACP

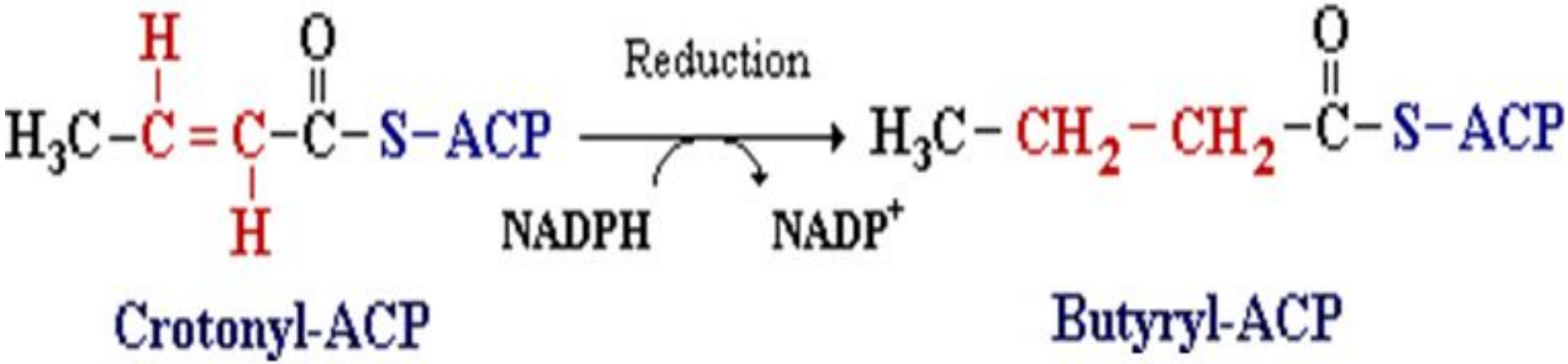


D-3-Hydroxybutyryl-ACP



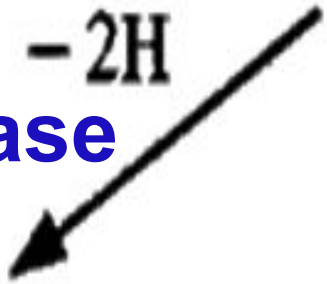


Crotonyl-ACP


Reduction
NADPH
NADP+
Crotonyl-ACP
Butyryl-ACP

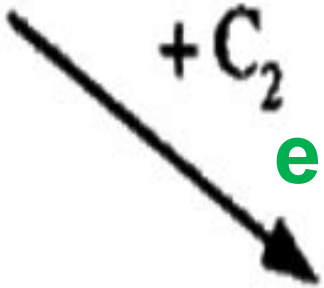
Formation of other fatty acids

Palmitic acid 16:0



desaturase

Palmitoleic Acid 16:1 (9)

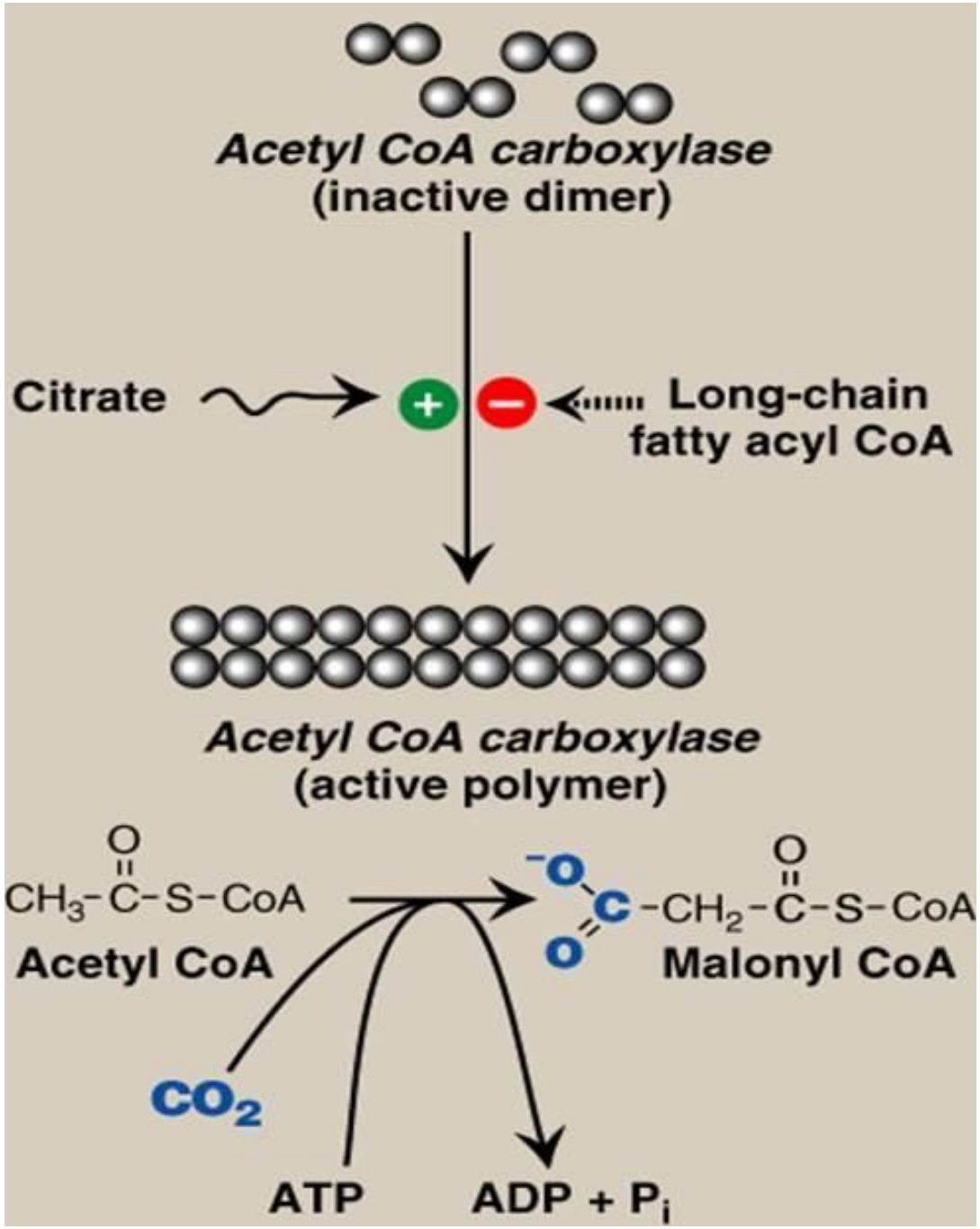


elongase

Stearic acid 18:0

desaturase

Oleic acid 18:1(9)



Regulation of acetyl-CoA carboxylase activity

Regulation of acetyl-CoA carboxylase activity