Lipid Structure and Metabolism

Lipids are non-polar (hydrophobic) compounds, soluble in organic solvents. Most membrane lipids are **amphipathic**, having a **non-polar** end and a **polar** end.

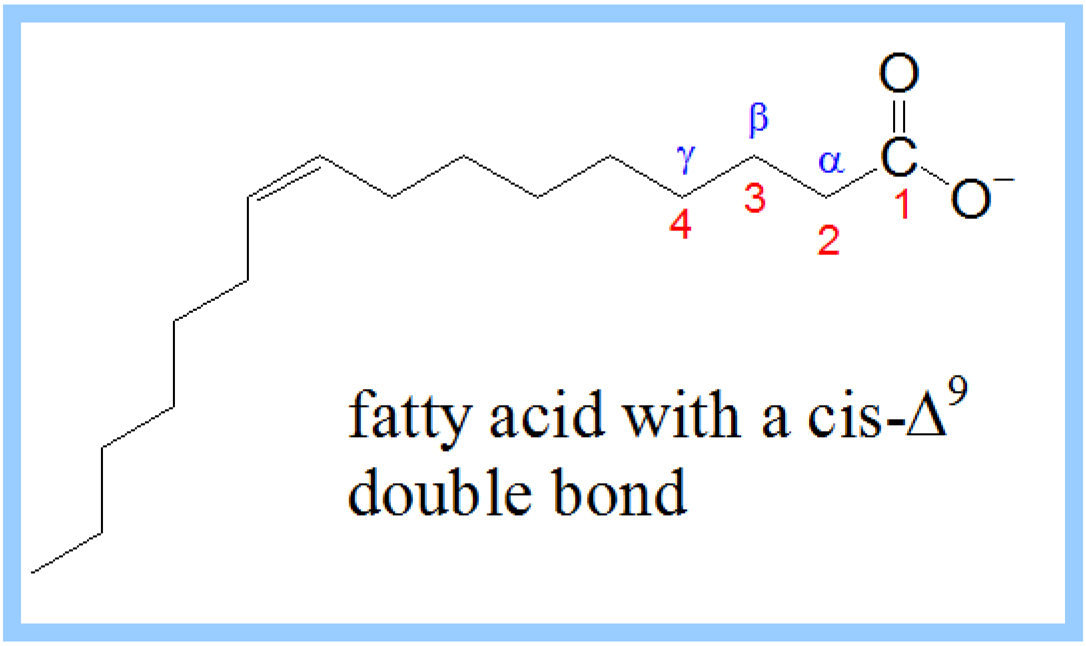
Fatty acids consist of a hydrocarbon chain with a carboxylic acid at one end.

A 16-C fatty acid: **CH_3 $(CH_2)_{14}$- COO^-**

Non-polar polar

A 16-C fatty acid with one cis double bond between C atoms 9-10 may be represented as **16:1 cis Δ^9**. Double bonds in fatty acids usually have the **cis** configuration.

Most naturally occurring fatty acids have an **even number** of carbon atoms



fatty acid with a cis-Δ^9 double bond

<u>Some fatty acids and their common names</u>:

14:0 myristic acid; 16:0 palmitic acid; 18:0 stearic acid;

18:Δ1 cisΔ^{9} oleic acid

18:2 cis$\Delta^{9,12}$ linoleic acid

18:3 cis$\Delta^{9,12,15}$ α -linonenic acid

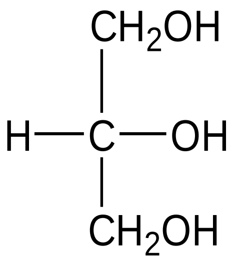
20:4 cis$\Delta^{5,8,11,14}$ arachidonic acid

20:5 cis$\Delta^{5,8,11,14,17}$ eicosapentaenoic acid (an omega-3)

There is free rotation about **C-C** bonds in the fatty acid hydrocarbon, except where there is a double bond. Each cis double bond causes a **kink** in the chain. Rotation about other **C-C** bonds would permit a more linear structure than shown, but there would be a kink

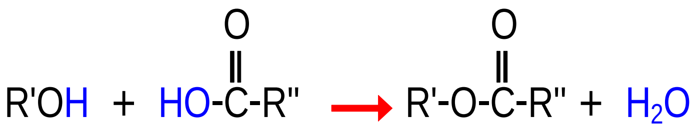
Glycerophospholipids (phosphoglycerides),

are common constituents of cellular membranes. They have a **glycerol** backbone. Hydroxyls at **C1** & **C2** are esterified to **fatty acids**. An **ester** forms when a hydroxyl reacts with a carboxylic acid, with loss of H_2O



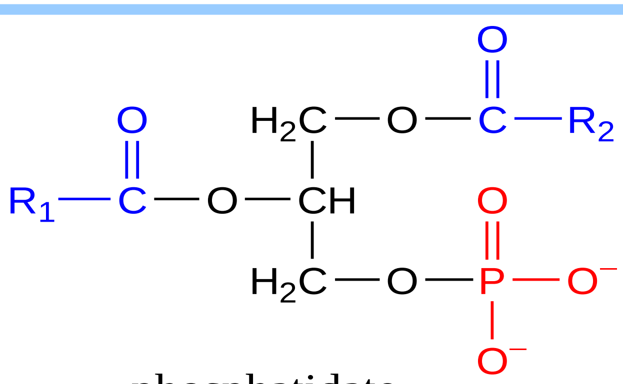
glycerol

Formation of an ester:



Phosphatidate

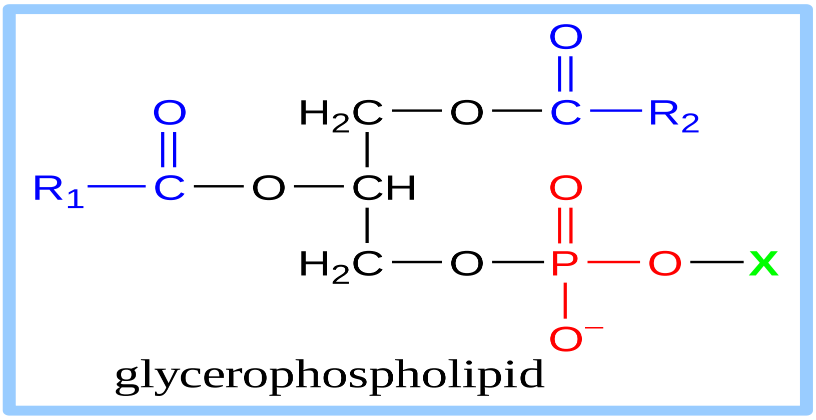
In **phosphatidate** the **fatty acids** are esterified to hydroxyls on **C1** & **C2** but the **C3** hydroxyl is esterified to **P$_i$**.

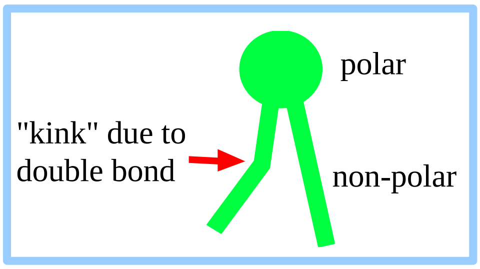


phosphatidate

In most **glycerophospholipids** (phosphoglycerides), **P_i** is in turn esterified to **OH** of a **polar head group** (**X**): e.g., **serine, choline, ethanolamine, glycerol, or inositol**.

The 2 fatty acids tend to be non-identical. They may differ in length and/or the presence/absence of double bonds.





Each glycerophospholipid includes

1. a **polar** region:
   glycerol, **carbonyl O** of fatty acids, **P_i**, & the polar head group (**X**)

2. **Non-polar** hydrocarbon tails of fatty acids (**R_1**, **R_2**).

Utilization of fatty acids as a fuel:

Performed by three stages

1- Mobilization of fatty acid (FA) from triglyceride (TG) into tissues
2- Activation and transportation of FA into mitochondria
3- Degradation of FA by oxidation into acetyl-CoA

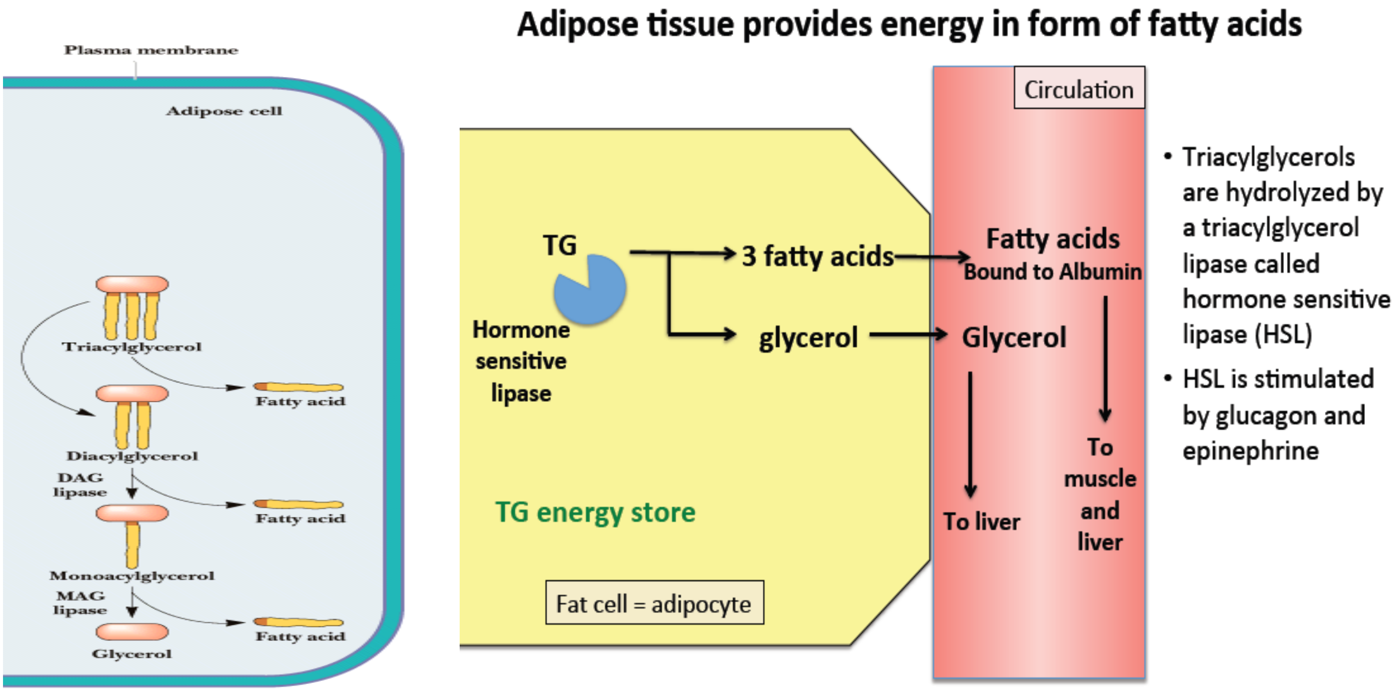


Figure shows Mobilization of FA from TG into tissues

Fate of Glycerol

In liver glycerol convert to Dihydroxyaceton Phosphate which in turn either convert to pyruvate in glycolysis or convert to glucose by gluconeogenesis

Oxidation of FATTY ACIDS

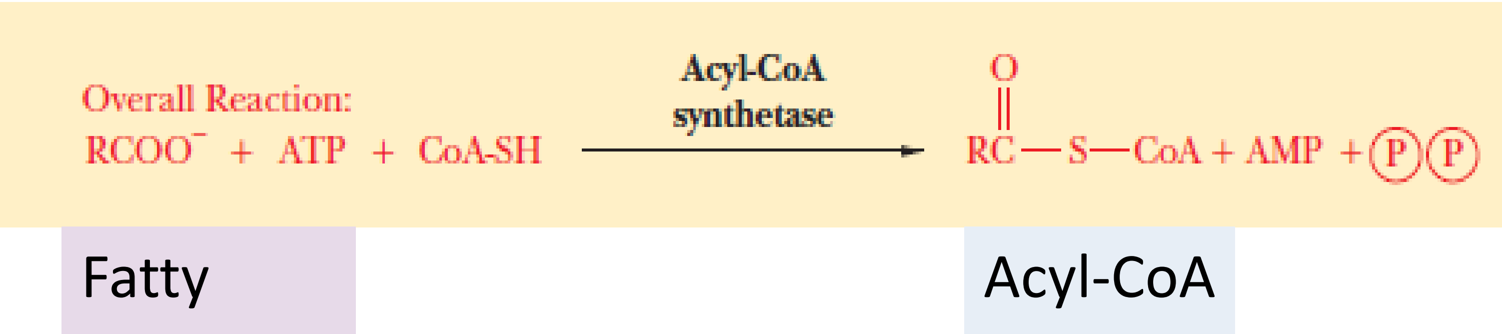
β Oxidation of fatty acid is oxidation of fatty acid at the β carbon atom with successive removal of two carbon atoms as acetyl CoA and occurs in the mitochondria matrix of all tissue except brain and RBCs.The process begins with oxidation of the carbon that is "beta" to the carboxyl carbon, so the process is called "beta-oxidation"

This pathway involved three steps

Step 1- Activation of fatty acids in the cytosol:

in which Acyl-CoA synthetase condenses **fatty acids** with CoA

Step 1



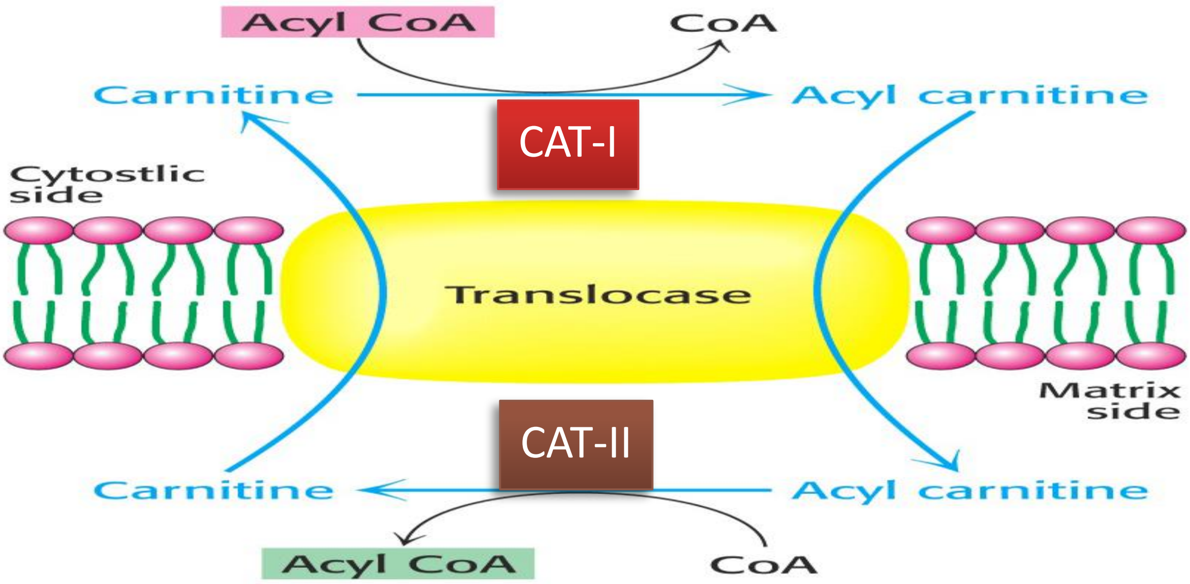
This figure shows step 1 Activation of fatty acids in the cytosol Occurs in outer mitochondrial membrane for long chain fatty acids

Step 2- *Transport of activated fatty acids in to mitochondria*:

β-oxidation occurs in the mitochondria, requires import of long chain acyl- CoAs . Acyl-CoAs are converted to acyl-carnitines by carnitine acyltransferase I (CAT I).

A translocase then imports Acyl carnitine into the matrix while simultaneously exporting free carnitine to the cytosol . Acyl-carnitine is then converted back to acyl-CoA in the matrix by carnitine acyltransferase Π (CAT Π)

Step 2

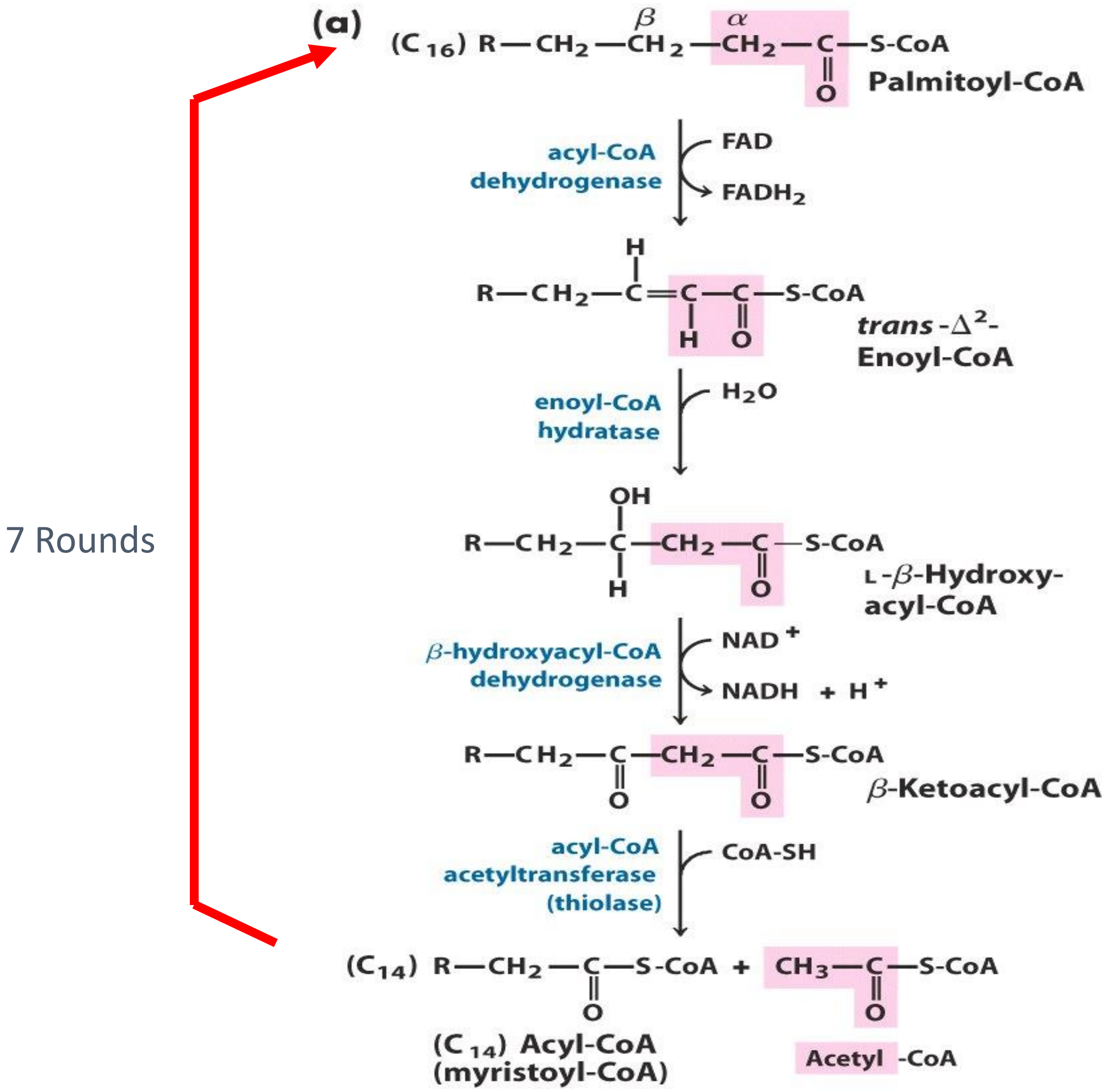


Step 3 *<u>β-Oxidation proper in the mitochondria</u>*

The strategy of this step of beta oxidation is create a carbonyl group on the β-C by First 3 reactions. The fourth reaction cleaves the "β-ketoester". The Products of each β-Oxidation are an acetyl-CoA and a fatty acid two carbons shorter

Sequence of Reactions of β-oxidation

- Oxidation by FAD
- Hydration
- Oxidation by NAD
- Thiolys



ENERGETICS OF COMPLETE OXIDATION OF PALMITIC ACID

B-oxidation of palmitate (C16:0) yields 106 molecules of ATP

• C 16:0-CoA + 7 FAD + 7 NAD+ + 7 H20 + 7 CoA → 8 acetyl-CoA + 7 FADH2 + 7 NADH + 7 H+

2.5 ATPs per NADH = 17.5

1.5 ATPs per FADH2 = 10.5

10 ATPs per acetyl-CoA = 80

Total = 108 ATPs

• 2 ATP equivalents (ATP → AMP + PPi, PPi = 2 Pi) consumed during activation of palmitate to acyl-CoA

• Net yield = 106 ATPs

REGULATION OF β-OXIDATION

β-OXIDATION regulated by availability of fatty acid which controlled by glucagon , epinephrine and insulin while Inhibition of carnitine acyl transferase I by malonyl CoA lead to fatty acid synthesis

β-oxidation of odd chain fatty acids

Odd chain fatty acids are less common. This process formed by some bacteria that occur in the stomachs of ruminants and the human colon.

β-oxidation of odd chain similar that in even chain fatty acids until the final thiolase cleavage which results in a 3 carbon acyl-CoA (propionyl CoA)

Special set of 3 enzymes are required to further oxidize propionyl-CoA to resulted the final Product(succinyl-CoA) that enters TCA cycle

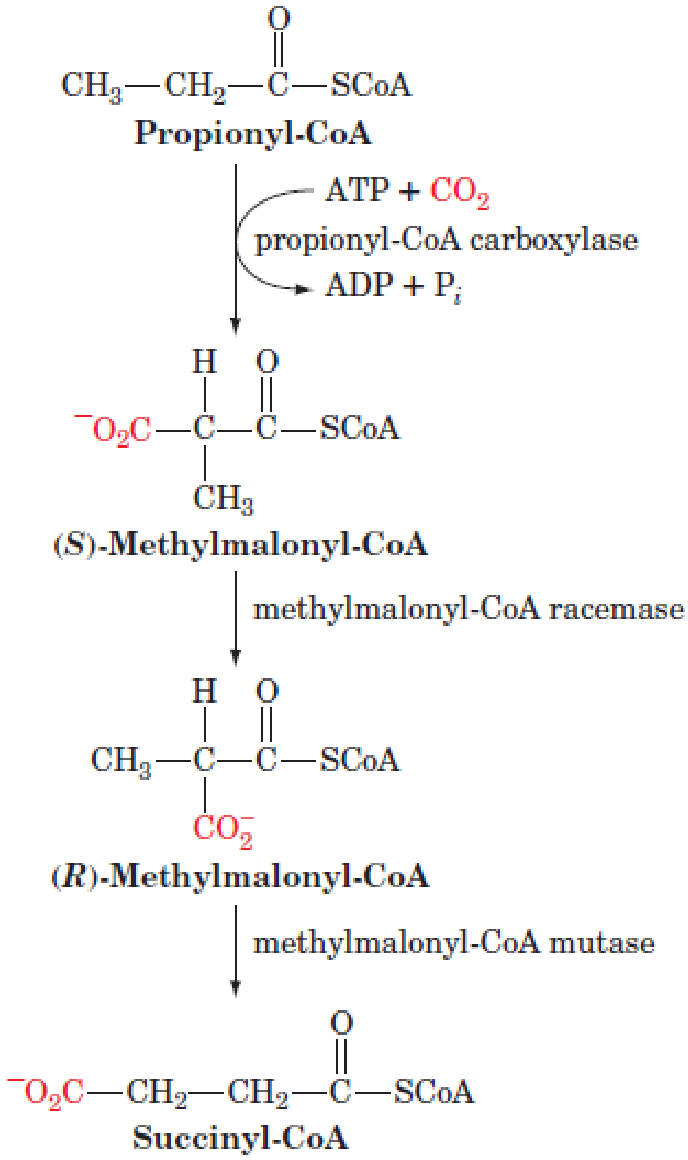


Figure shows β-OXIDATION OF ODD CHAIN FATTY ACIDS

β-oxidation of unsaturated fatty acids

Requires additional enzymes such as Isomerase and reductase