

## CHAPTER V: ANABOLISM and PRODUCTION of BIOMASS and METABOLITES

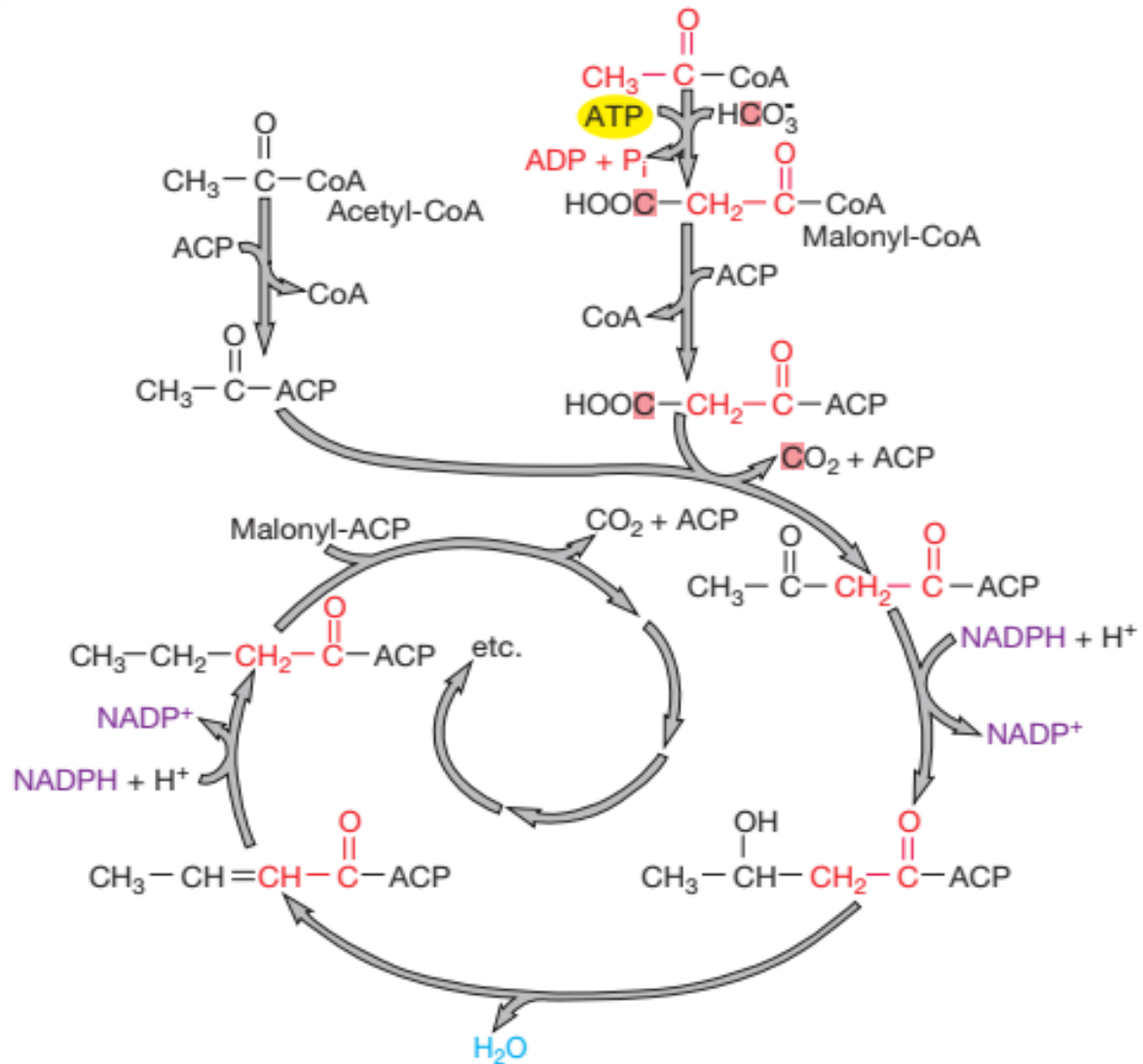
### 4. LIPID SYNTHESIS

#### 1. Introduction

A variety of lipids are found in microorganisms, particularly in cell membranes. Most contain **fatty acids** or their derivatives. Fatty acids are monocarboxylic acids with long alkyl chains that usually have an even number of carbons (the average length is 18 carbons). Some may be unsaturated that is, have one or more double bonds. Most microbial fatty acids are straight chained, but some are branched. Gram-negative bacteria often have cyclopropane fatty acids (fatty acids with one or more cyclopropane rings in their chains).

#### 2. Fatty acid synthesis

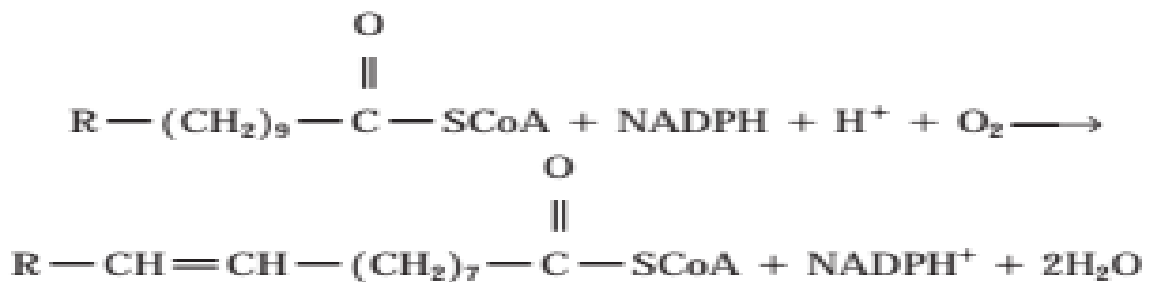
Fatty acid synthesis is catalyzed by the *fatty acid synthase complex* with acetyl-CoA and malonyl-CoA as the substrates and NADPH as the electron donor. Malonyl-CoA arises from the ATP driven carboxylation of acetyl-CoA (**Fig. 01**). Synthesis takes place after acetate and malonate have been transferred from coenzyme A to the sulfhydryl group of the **Acyl Carrier Protein (ACP)**, a small protein that carries the growing fatty acid chain during synthesis. The synthase adds two carbons at a time to the carboxyl end of the growing fatty acid chain in a two-stage process (**Fig. 01**). First, malonyl-ACP reacts with the fatty acyl-ACP to yield CO<sub>2</sub> and a fatty acyl-ACP two carbons longer. The loss of CO<sub>2</sub> drives this reaction to completion. Notice that ATP is used to add CO<sub>2</sub> to acetyl-CoA, forming malonyl-CoA. The same CO<sub>2</sub> is lost when malonyl-ACP donates carbons to the chain. Thus, carbon dioxide is essential to fatty acid synthesis but it is not permanently incorporated. Indeed, some microorganisms require CO<sub>2</sub> for good growth, but they can do without it in the presence of a fatty acid like oleic acid (an 18-carbon unsaturated fatty acid). In the second stage of synthesis, the β-keto group arising from the initial condensation reaction is removed in a three-step process involving two reductions and a dehydration. The fatty acid is then ready for the addition of two more carbon atoms.



**Figure 01:** Fatty acid synthesis.

[The cycle is repeated until the proper chain length has been reached. Carbon dioxide carbon and the remainder of malonyl-CoA are shown in red. ACP stands for acyl carrier protein].

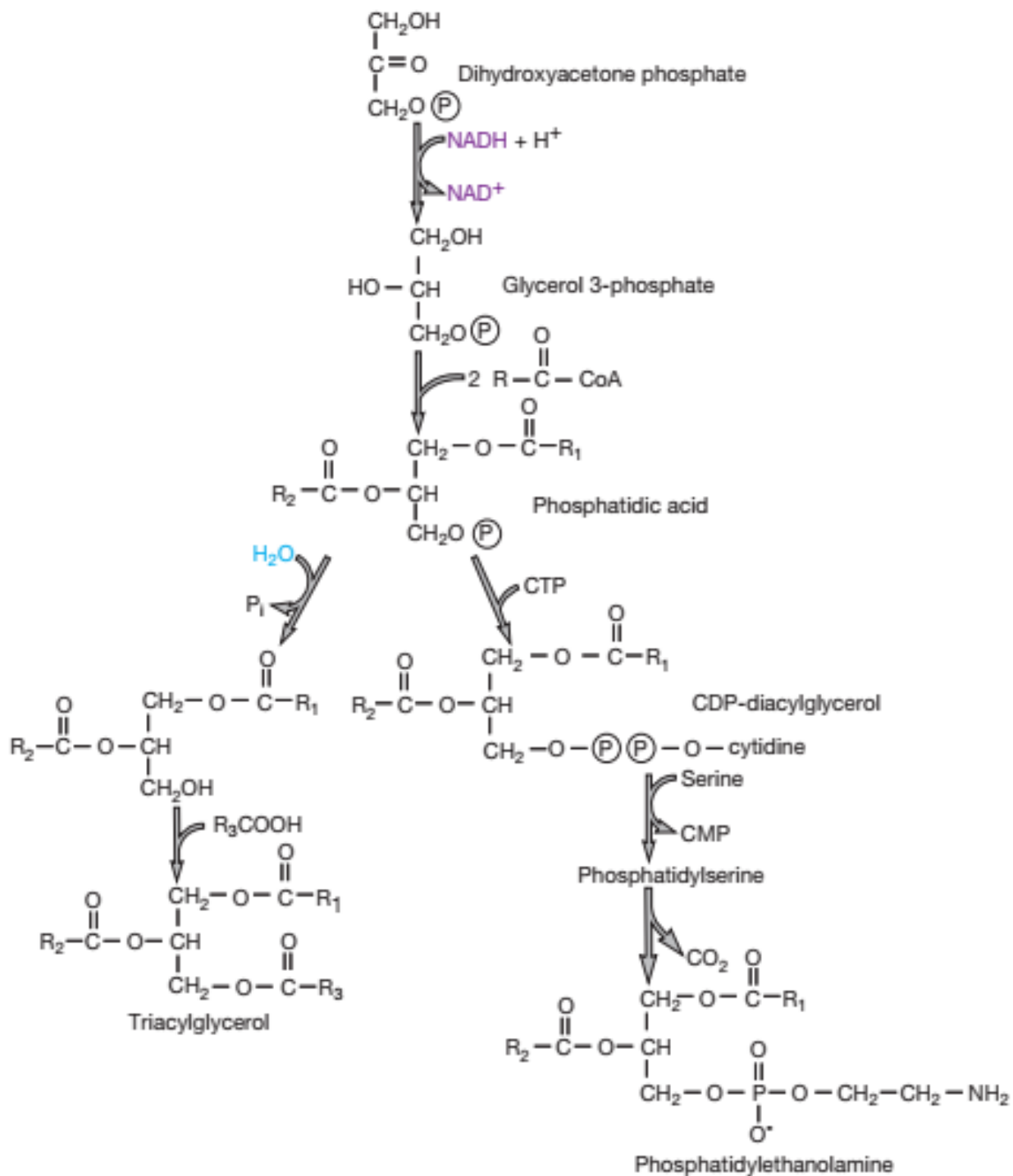
Unsaturated fatty acids are synthesized in two ways. Eucaryotes and aerobic bacteria like *B. megaterium* employ an aerobic pathway using both NADPH and O<sub>2</sub>.



A double bond is formed between carbons nine and ten, and O<sub>2</sub> is reduced to water with electrons supplied by both the fatty acid and NADPH. Anaerobic bacteria and some aerobes create double bonds during fatty acid synthesis by dehydrating hydroxy fatty acids. Oxygen is not required for double bond synthesis by this pathway. The anaerobic pathway is present in a number of common Gram-negative bacteria (e.g., *E. coli* and *Salmonella* spp.), Gram-positive bacteria (e.g., *Lactobacillus plantarum* and *Clostridium pasteurianum*), and *Cyanobacteria*.

Eucaryotic microorganisms frequently store carbon and energy as **triacylglycerol**, glycerol esterified to three fatty acids. Glycerol arises from the reduction of the precursor metabolites dihydroxyacetone phosphate to glycerol 3-phosphate, which is then esterified with two fatty acids to give **phosphatidic acid** (Fig. 02). Phosphate is hydrolyzed from phosphatidic acid giving a diacylglycerol, and the third fatty acid is attached to yield a **triacylglycerol**.

**Phospholipids** are major components of eucaryotic and bacterial cell membranes. Their synthesis also usually proceeds by way of phosphatidic acid. A special Cytidine DiPhosphate (**CDP**) carrier plays a role similar to that of uridine and adenosine diphosphate carriers in carbohydrate biosynthesis. For example, bacteria synthesize **phosphatidylethanolamine**, a major cell membrane component, through the initial formation of CDP-diacylglycerol (Fig. 02). This CDP derivative then reacts with serine to form the phospholipid phosphatidylserine, and decarboxylation yields phosphatidylethanolamine. In this way a complex membrane lipid is constructed from the products of glycolysis, fatty acid biosynthesis, and amino acid biosynthesis.



**Figure 02:** Triacylglycerol and Phospholipid synthesis.