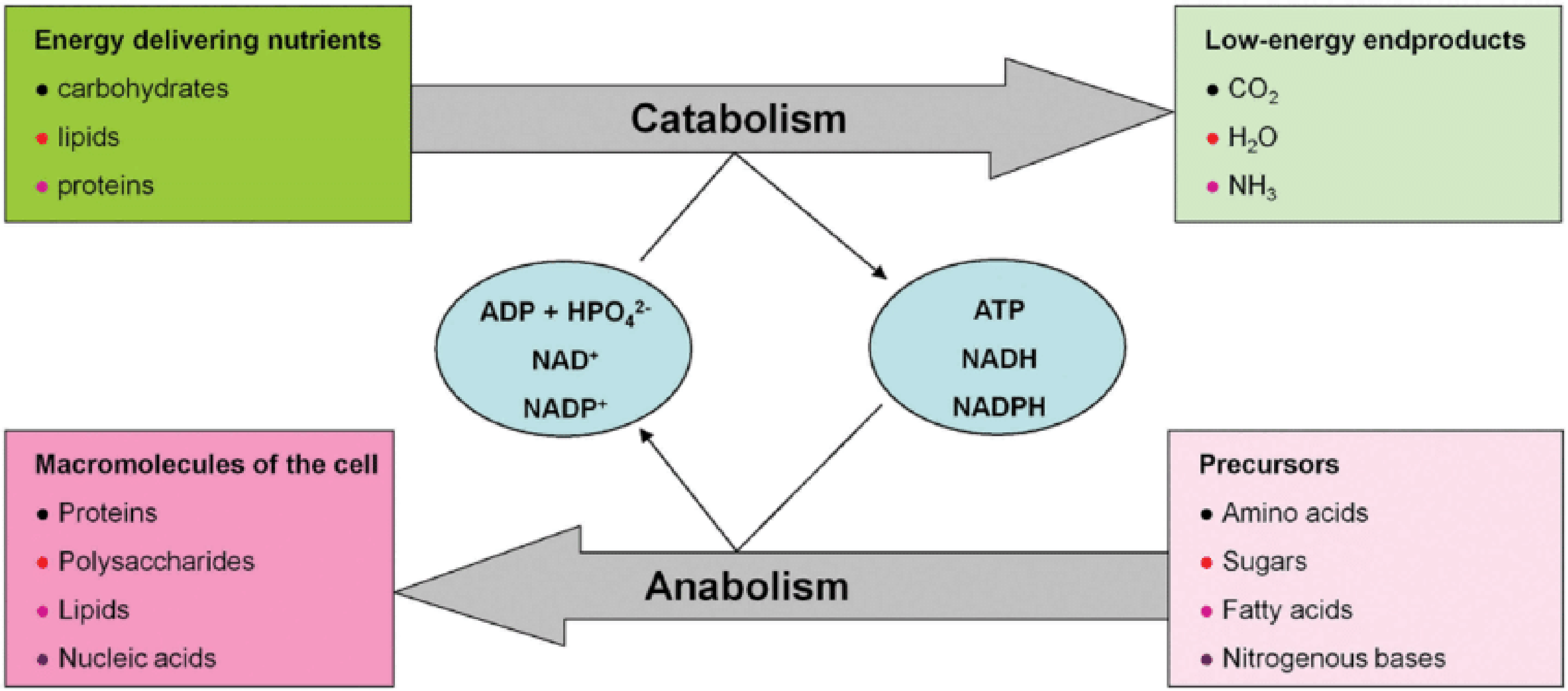
Lecture 1

Metabolism

A group of chain chemical reactions catalyzed by enzymes that occur inside the organism to produce energy or build tissues, and these processes include catabolism and building processes Anabolism.



Metabolism of carbohydrates

Digestion of carbohydrates:

- **In Buccal Cavity (30%)**

Starch —(salivary amylase (ptylin), pH 6.8)→ Maltose + Isomaltose + Limit Dextrins

- **In Stomach**

No any enzyme for carbohydrate digestion.

- **In small Intestine :-**

Starch —(pancreatic amylase)→ Maltose + Isomaltose + Limit Dextrins

Maltose —(maltase)→ Glucose + Glucose

Isomaltose —(isomaltase)→ Glucose + Glucose

Limit Dextrins —(dextrinase)→ Glucose

Sucrose —(sucrase)→ Glucose + Fructose

Lactose —(lactase)→ Glucose + Galactose

- **In ruminating animals :-**

Cellulose —(cellulase)→ acetic acid + propionic acid + butyric acid

The fate of glucose

Fate of glucose:

A. Uptake by different tissues (by facilitated diffusion)

B. Utilization by the tissues: in the form of:

1. Oxidation to produce energy:

- Major pathways (glycolysis & Krebs' cycle).
- Minor pathways (hexose monophosphate pathway & uronic acid pathway)

2. Conversion to other substances:

Carbohydrates: ribose (RNA,DNA), galactose (in milk), fructose (semen)

Lipids: Glycerol-3 P for formation of triacylglycerols.

Proteins: Non-essential amino acids which enter in formation of proteins.

C. Storage of excess glucose:

as glycogen in liver and muscles,

when these reserves are filled it is converted to TAG & deposited in adipose tissue.

D. Excretion in urine

If blood glucose exceeds renal threshold (180 mg/dL), it will be excreted in urine.

Carbohydrate metabolism pathways

Glycolysis

Krebs Cycle

Glyoxylate cycle

Phosphogluconate pathway

Electron transport and oxidative phosphorylation

Glycogenolysis

Glycogenesis

Gluconeogenesis

Glycolysis

Glycolysis metabolizes glucose and rapidly produces a small amount of ATP as well as acid, pyruvate, and NADH that can feed into the Krebs cycle. The overall reaction is:

Glucose + 2 ADP + 2 Pi + 2 NAD^+ → 2 pyruvate + 2 ATP + 2 NADH + 2 H^+ + 2 H_2O

Vital importance:

Energy production.

Production of two molecules of Pyruvate necessary for the Krebs cycle.

The formation of intermediate compounds used to build other important compounds for the cell (fats, amino acids).

Glycolysis reactions

The breakdown of glucose takes place in two stages:

- **The first stage: the preparatory phase:**

These are the first five reactions that start with glucose and end with glyceraldehyde-3-phosphate, in which energy (two ATP molecules) is consumed.

- **The second stage: Payoff Phase:**

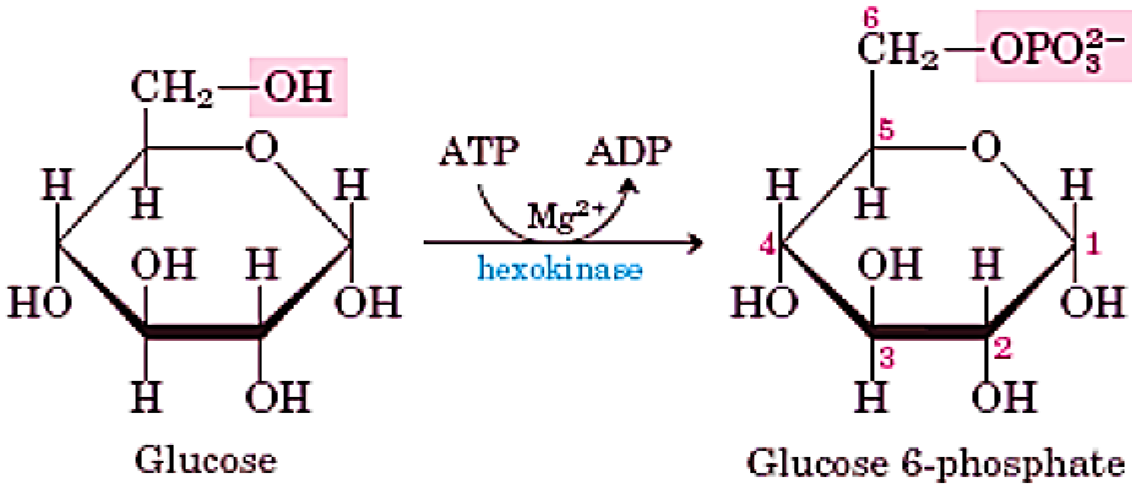
There are also five reactions (6-10), which start with glyceraldehyde - 3-phosphate and end with the formation of pyruvate, in which energy is produced (four molecules of ATP).

Lecture 2

Glycolysis reactions

Preparatory phase

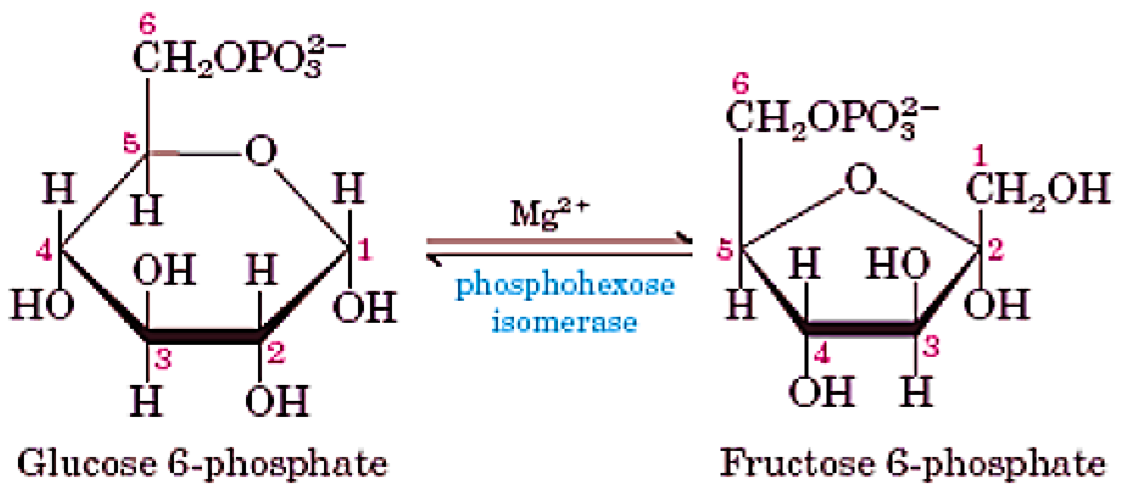
The first reaction: the phosphorylation of glucose into glucose-6-phosphate



Glycolysis reactions

Preparatory phase

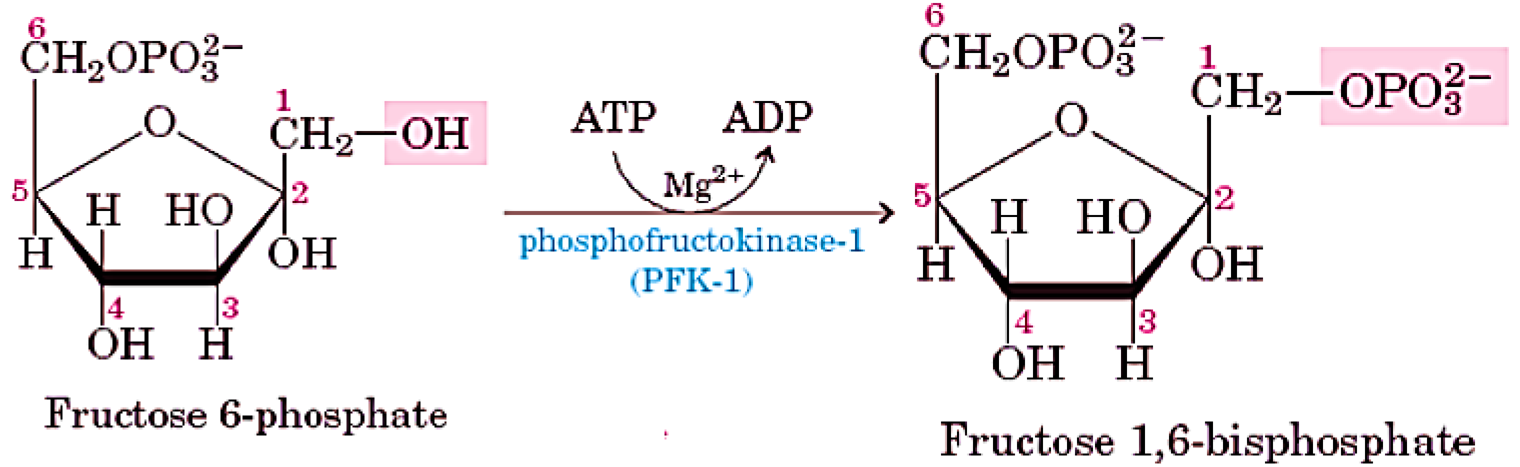
Second reaction: glucose-6-phosphate is converted to fructose-6-phosphate



Glycolysis reactions

Preparatory phase

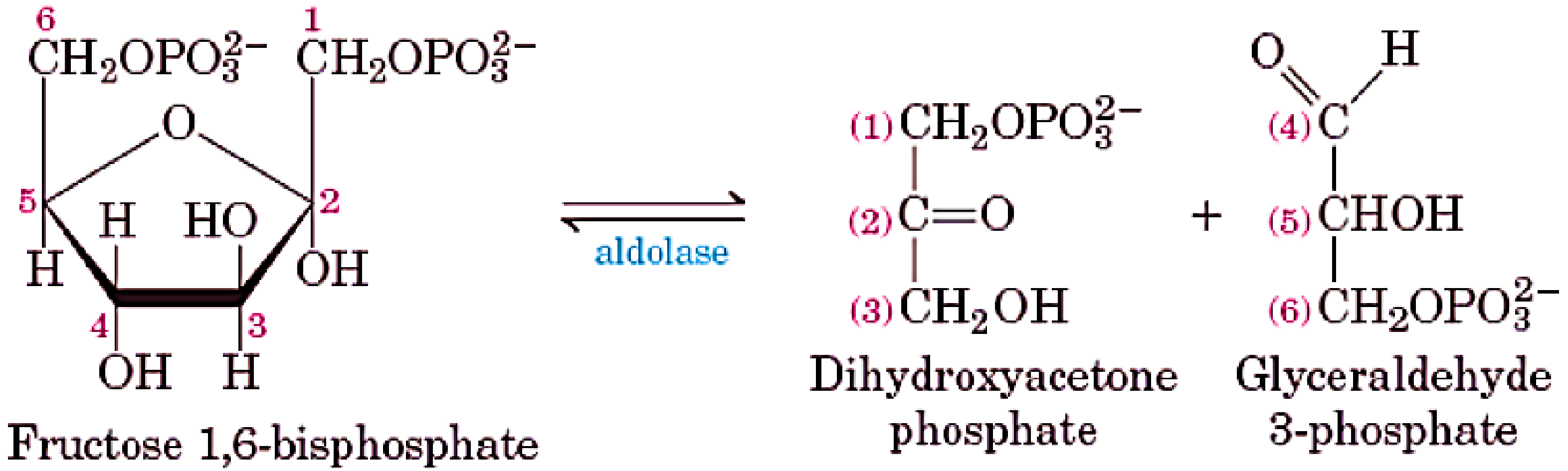
Third reaction: the conversion of fructose-6-phosphate to fructose-1,6-biphosphate



Glycolysis reactions

Preparatory phase

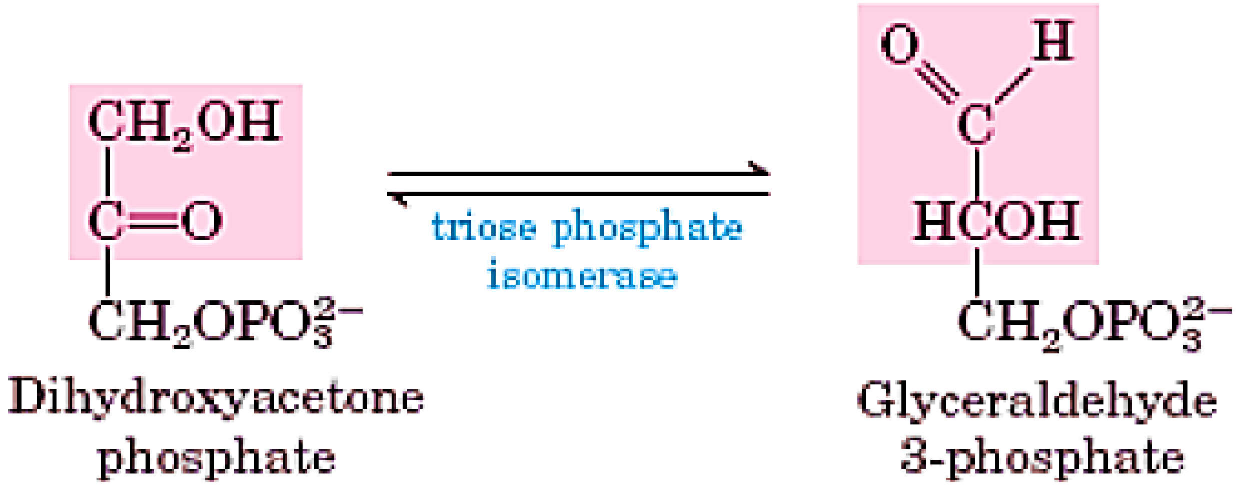
Fourth reaction: fission of fructose-1,6-biphosphate to dihydroxyacetone phosphate and glyceraldehyde-3-phosphate



Glycolysis reactions

Preparatory phase

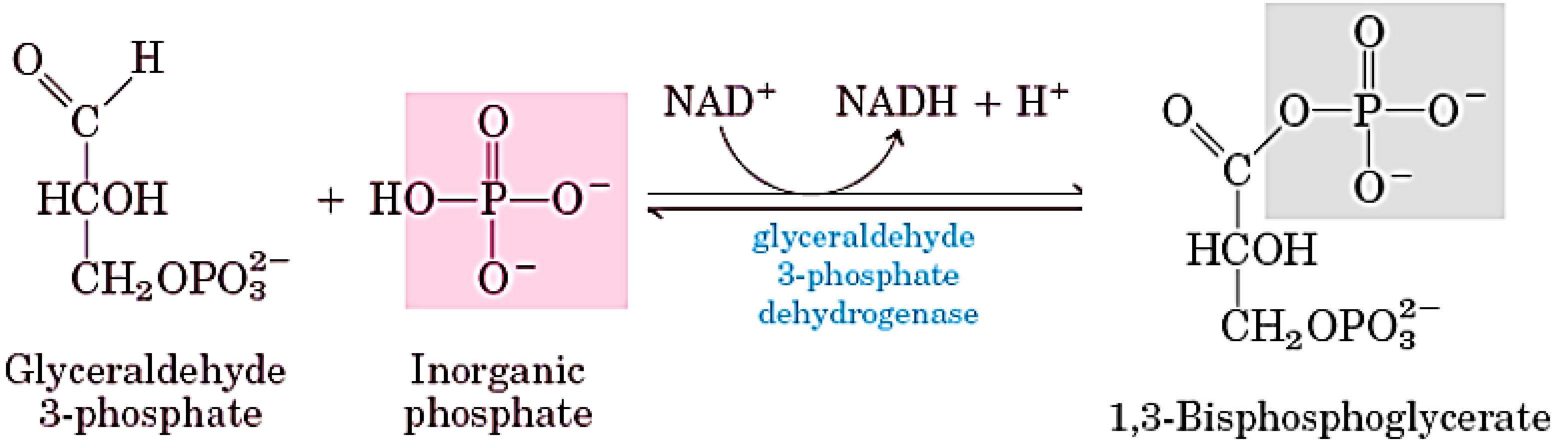
Fifth reaction: Dihydroxyacetone phosphate is converted to glyceraldehyde-3-phosphate



Glycolysis reactions

Preparatory phase

Sixth reaction: two molecules of glyceraldehyde-3-phosphate are converted to two molecules of 1,3-diphosphoglycerate. (Since one molecule of glucose forms two glyceraldehyde-3-phosphate in the first stage, both glyceraldehyde-3-phosphate molecules will follow the same path)

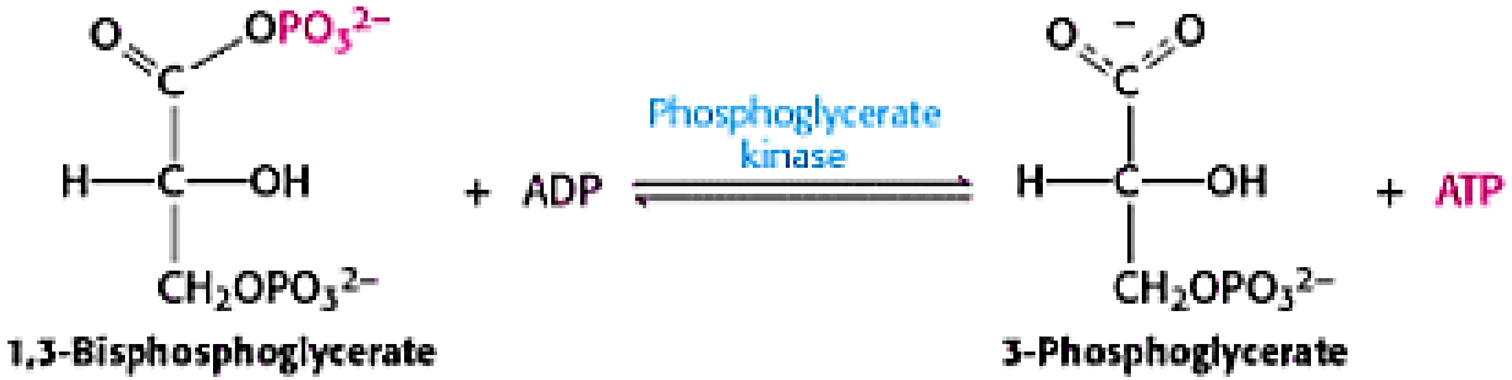


Lecture 3

Glycolysis reactions

Preparatory phase

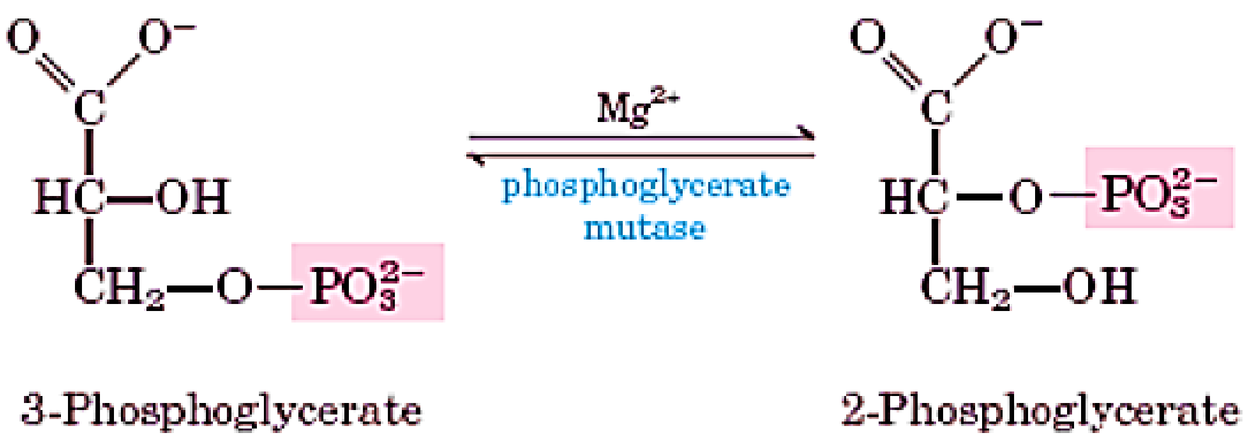
Seventh reaction: Two molecules of 1,3-diphosphoglycerate are converted into two molecules of 3-phosphoglycerate.



Glycolysis reactions

Preparatory phase

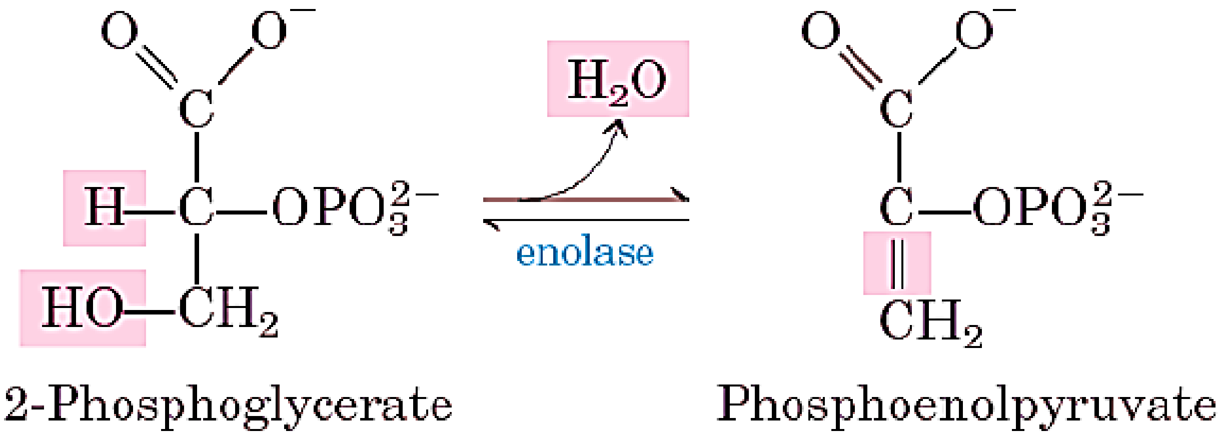
The eighth reaction: two molecules of 3-phosphoglycerate convert to two molecules of 2-phosphoglycerate.



Glycolysis reactions

Preparatory phase

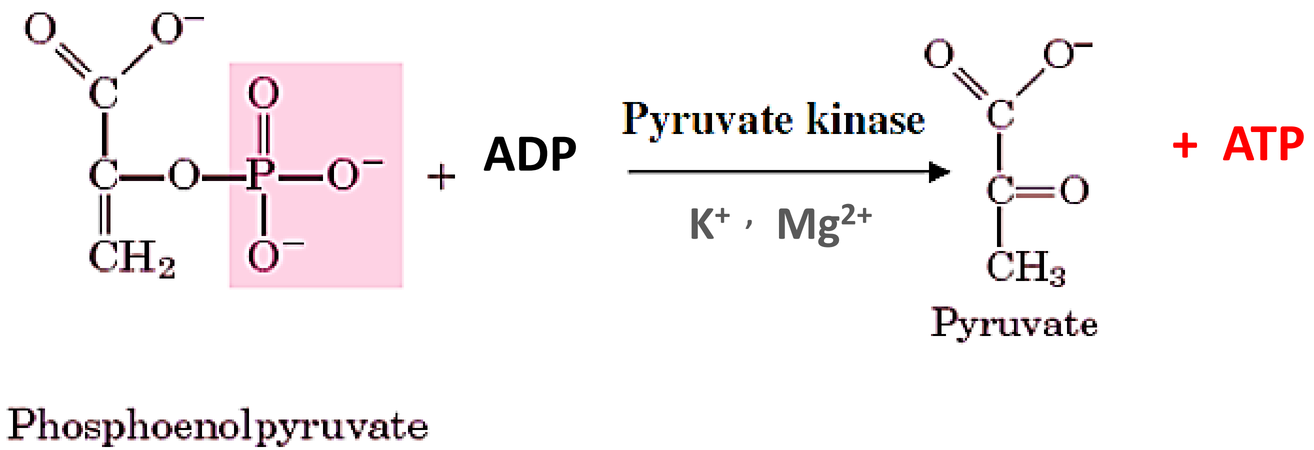
The ninth reaction: the formation of two phosphoenolpyruvate molecules from two molecules of 2-phosphoglycerate.



Glycolysis reactions

Preparatory phase

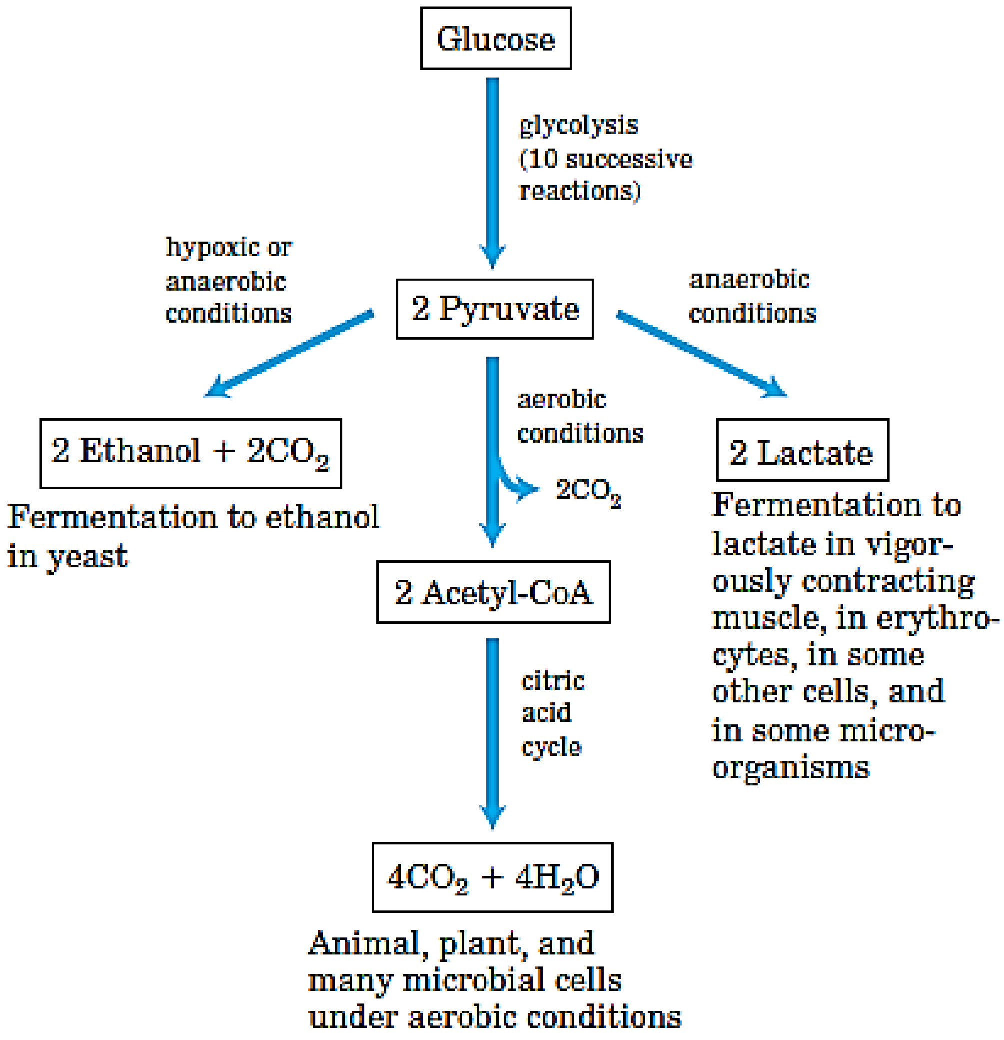
The tenth reaction: the formation of two pyruvate molecules from two phosphoenolpyruvate molecules



Regulation of Glycolysis

- Reaction 1 Hexokinase is inhibited by high levels of glucose-6-phosphate, which prevents the phosphorylation of glucose.
- Reaction 3 Phosphofructokinase, an allosteric enzyme, is inhibited by high levels of ATP and activated by high levels of ADP and AMP.
- Reaction 10 Pyruvate kinase, another allosteric enzyme is inhibited by high levels of ATP or acetyl CoA.

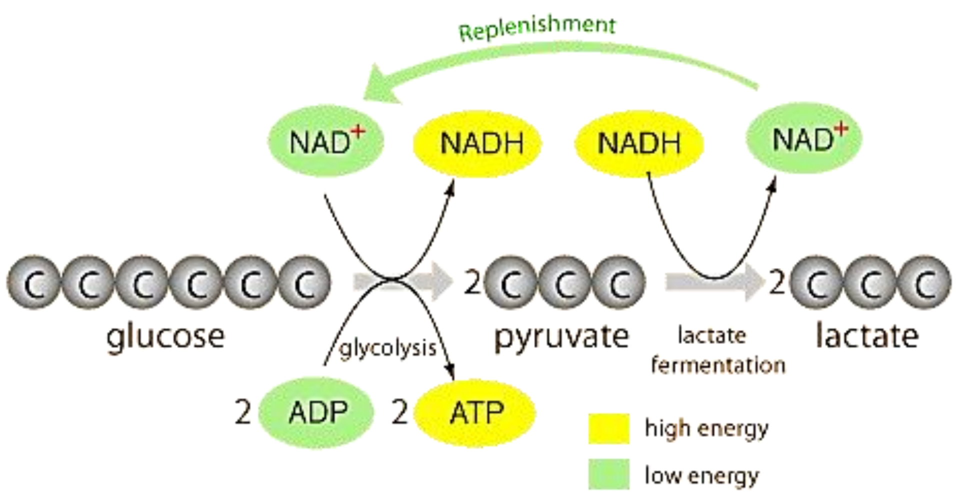
Fate of pyruvate produced from glycolysis



Lecture 4

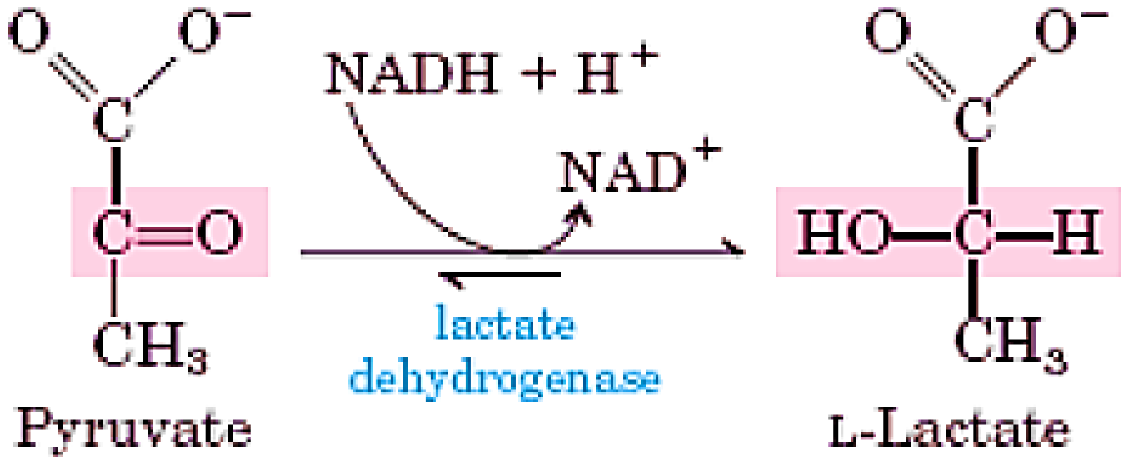
The fate of pyruvate from glycolysis

1- **Lactic acid fermentation:** Under anaerobic conditions, pyruvate has a different fate. Instead of entering mitochondria, the cytosolic enzyme *lactate dehydrogenase* converts pyruvate to lactate. Although lactate itself is not utilized by the cell as a direct energy source, this reaction also allows for the regeneration of NAD+ from NADH. NAD+ is an oxidizing cofactor necessary to maintain the flow of glucose through glycolysis. This process of breaking down glucose in the absence of oxygen is aptly named *anaerobic glycolysis*.



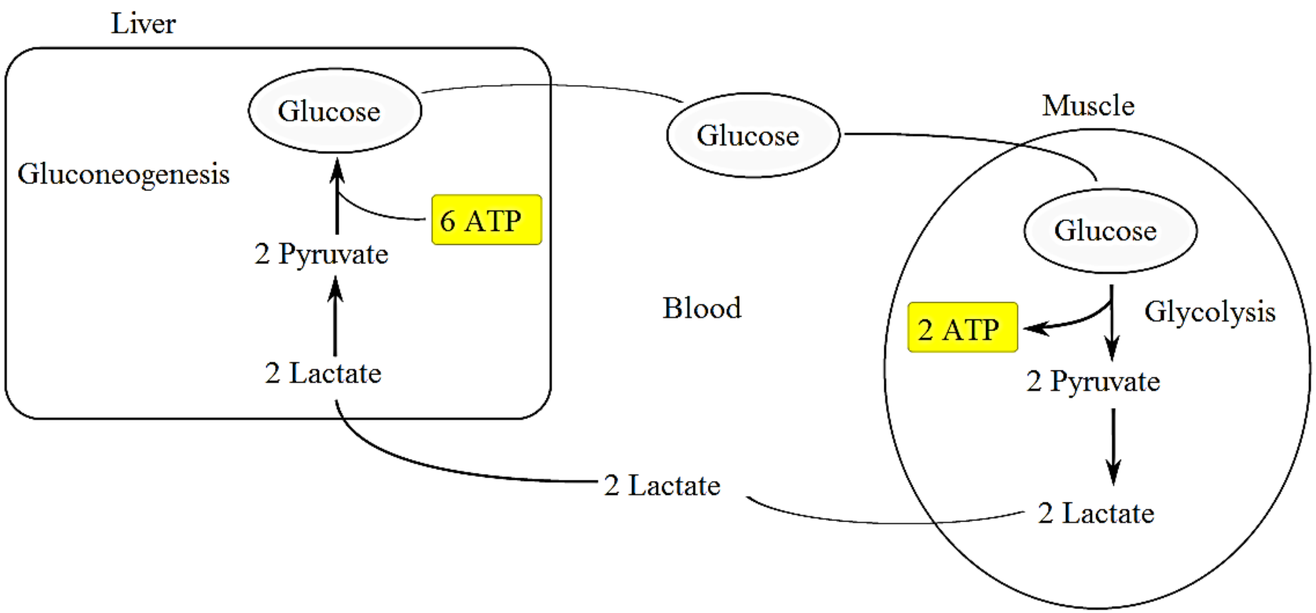
Lactate fermentation

The fate of pyruvate from glycolysis



$$\text{Glucose} + 2\text{ADP} + 2\text{Pi} \longrightarrow 2\text{Lactate} + 2\text{ATP}$$

How does the Cori cycle help muscles continue to work during high-intensity exercise?

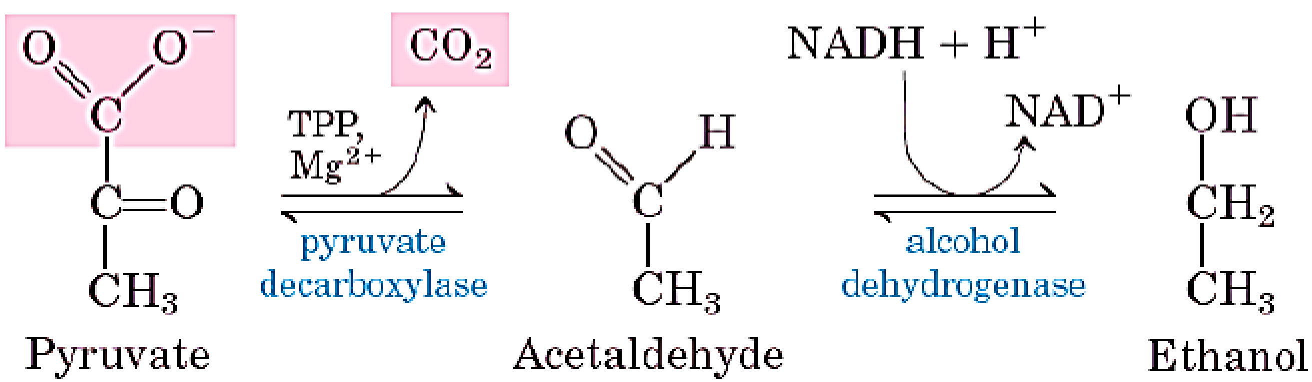


Cori cycle

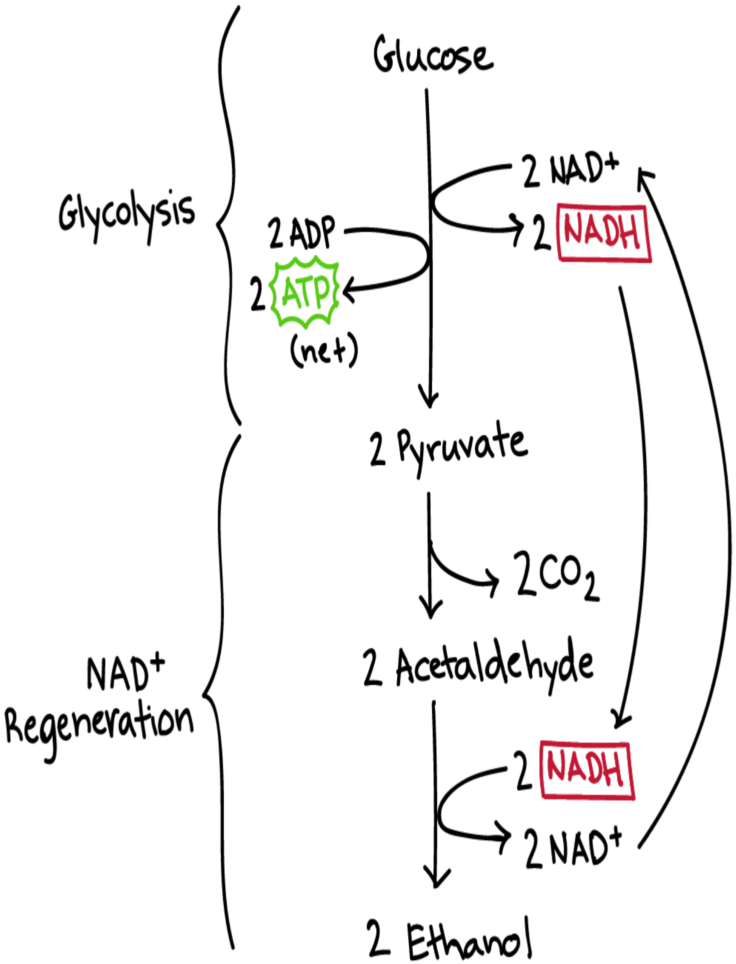
The fate of pyruvate from glycolysis

2- Alcoholic fermentation

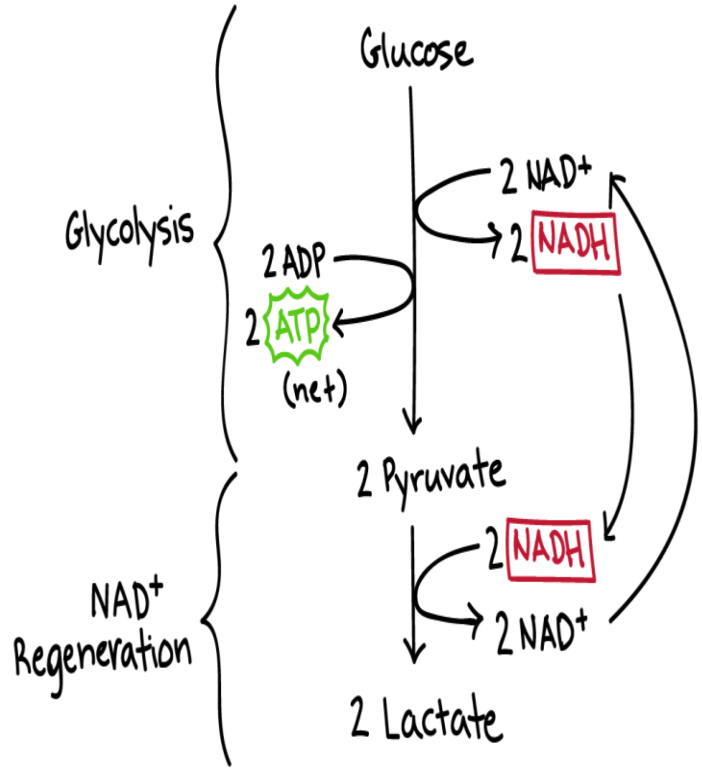
In alcoholic fermentation, pyruvic acid is broken down into ethanol and carbon dioxide.



$$\text{Glucose} + 2\text{ADP} + 2\text{Pi} \longrightarrow 2\text{Ethanol} + 2\text{ATP} + 2\text{CO}_2$$



Alcoholic fermentation

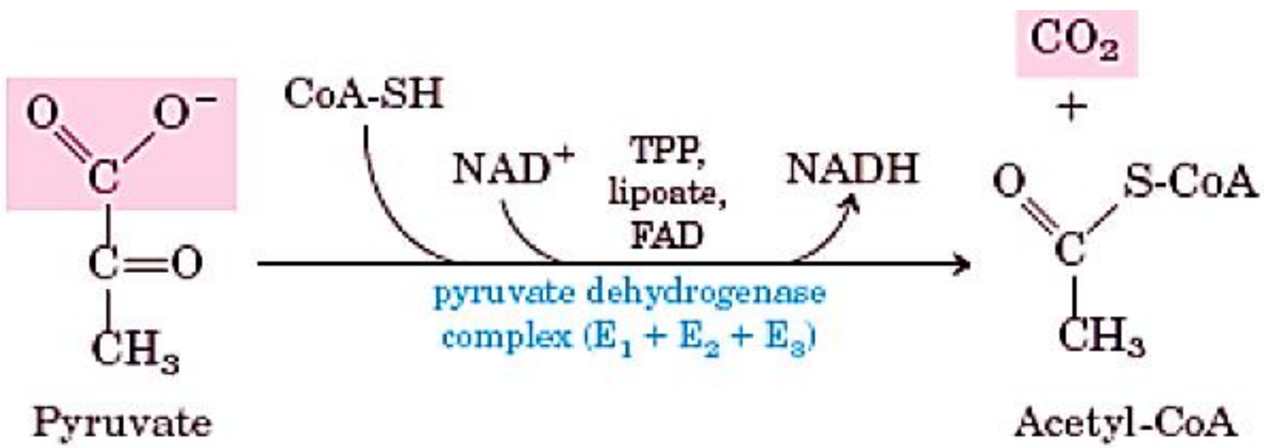


Lactic acid fermentation (Homolactic fermentation)

Lecture 5

The fate of pyruvate from glycolysis

3- The conversion of pyruvate to Acetyl-CoA: The pyruvate is transported to the mitochondria where the enzyme Pyruvate dehydrogenase complex deletes the carboxyl group of pyruvate (irreverse reaction) and produces NADH (in the presence of aerobic oxygen conditions). This transformation is significant through the entry of Acetyl-CoA into the Krebs cycle, which includes a series of oxidation reactions that end with its conversion to CO2 + H2O and energy.



$$\text{Glucose} + 3NAD^{+} + 2ADP + 2Pi + 2CoA\text{-}SH \longrightarrow 2\text{Acetyl CoA} + 3NADH + 3H^{+} + 2ATP + 2CO_2$$

Connecting Other Sugars to Glucose Metabolism

Glycolysis is the main way to break down most types of simple and Polysaccharides after converting them to glucose or one of the intermediate compounds in glycolysis.

Entry of simple sugars (other than glucose): Polysaccharides and disaccharides decompose into monosaccharides after the end of the digestion of sugars in the intestine.

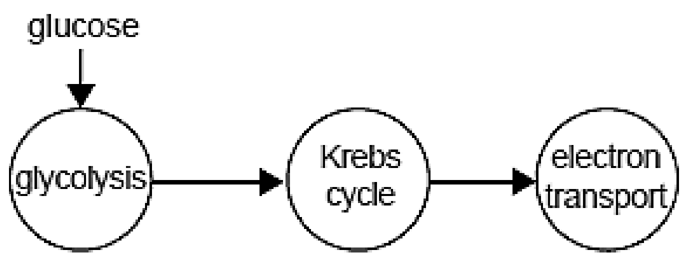
Fructose: is phosphorylated to Fructose-6-P by the enzyme Hexokinase and enters the pathway.

Mannose: After phosphorylation by Hexokinase, it is converted to Mannose-6-P, which is converted to Fructose-6-P by the enzyme PhosphoMannose Isomerase.

Galactose: It is first converted to Galactose-1-P by the enzyme Galactokinase and then converted to Glucose-1-P by two different enzymes: Galactose-1-phosphate uridylyltransferase and Uridine diphosphate galactose 4′-epimerase. Finally, Glucose-1-P is converted to Glucose-6-P by the action of the enzyme phosphoglucomutase.

Krebs Cycle

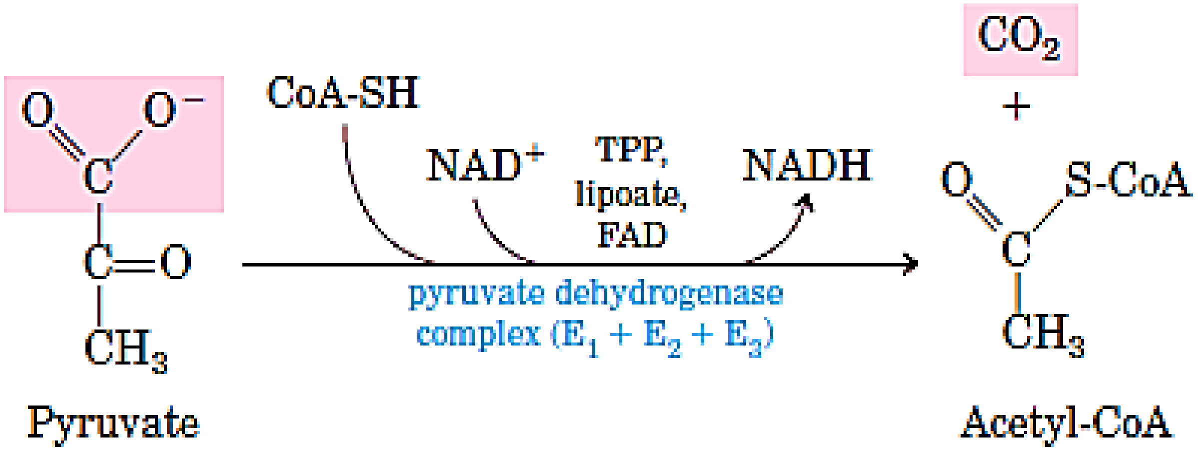
The **Krebs Cycle** has a total of **8** metabolic **reactions** involved in the full oxidation of our food molecules into carbon dioxide

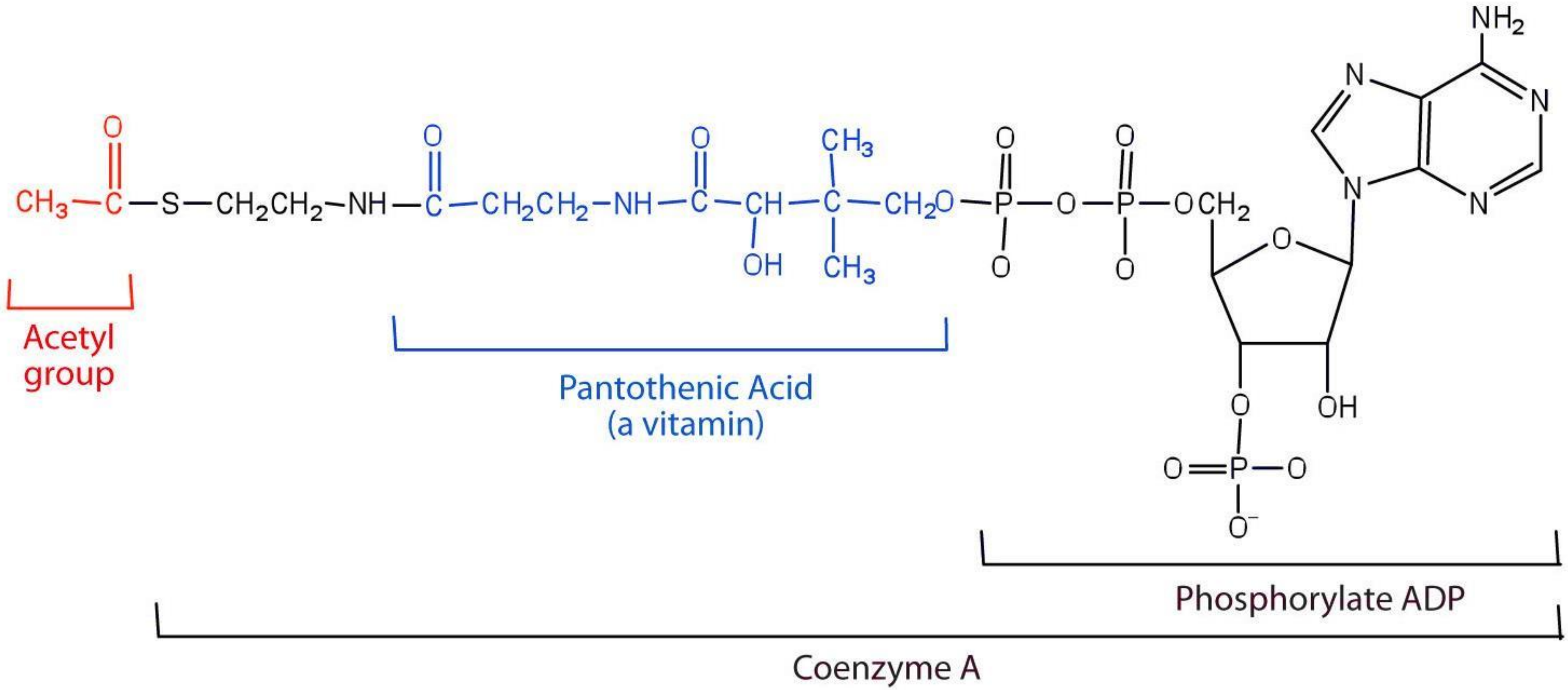


$$\text{Acetyl CoA} + 3NAD^{+} + FAD + GDP + Pi + 2H_2O \longrightarrow \text{CoA-SH} + 3NADH + 3H^{+} + FADH_2 + GTP + 2CO_2$$

Vital importance:
Energy production and preparation of intermediate compounds used to form other important compounds for the cell, such as amino acids, fatty acids and other important compounds.

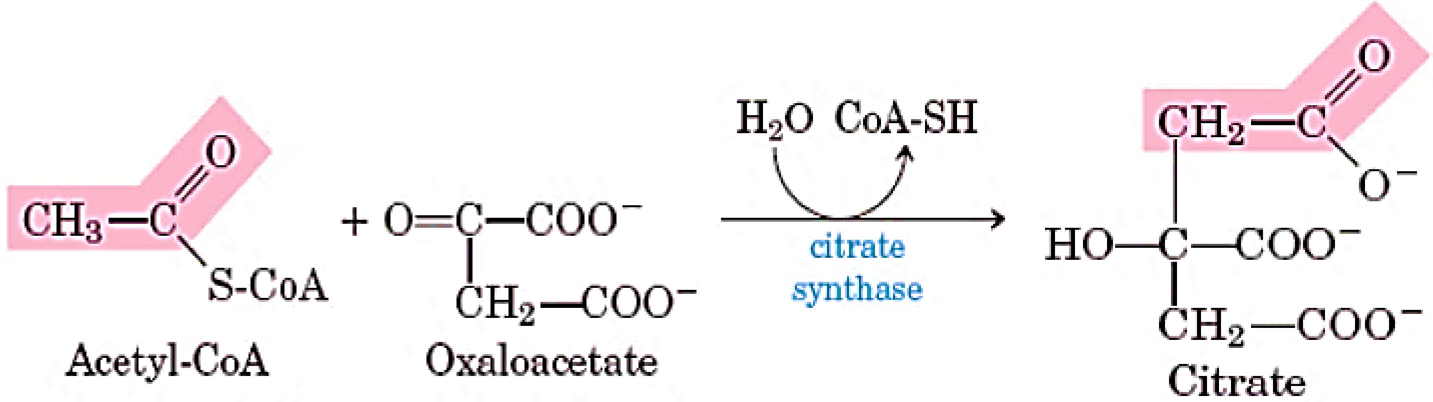
The pyruvate formed in the glycolysis pathway enters the mitochondria (in the presence of oxygen). To be oxidized and carbon dioxide removed from it through several reactions catalyzed by the enzyme complex Pyruvate dehydrogenase complex (which consists of three enzymes combined).5 enzymatic compounds also participate in these interactions. This reaction is an oxidative decarboxylation, which means an oxidation reaction in which a carboxyl group is removed




CH3
C
O
S
CH2CH2
NH
CH2CH2
CH
OH
CH2O
P
OCH2
NH2
N
Acetyl group
Pantothenic Acid (a vitamin)
Phosphorylate ADP
Coenzyme A

Krebs cycle reactions

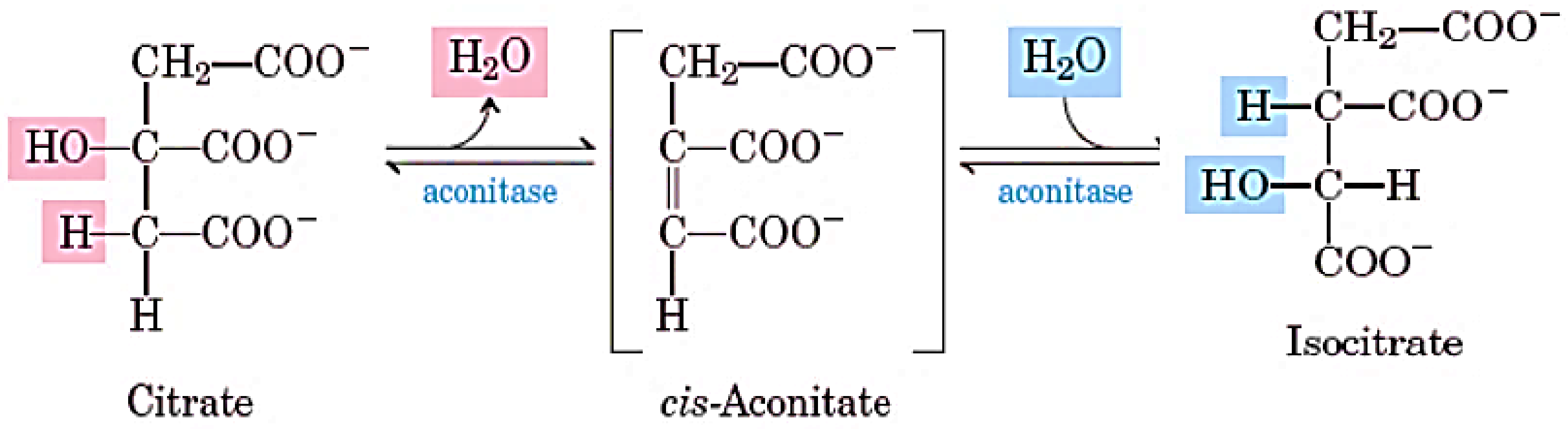
1- Citrate formation from Acetyl CoA condensation reaction with Oxaloacetate by catalyzing the enzyme citrate synthase



Lecture 6

Krebs cycle reactions

2- Citrate is converted to isoctrate by the enzyme Aconitase



Krebs cycle reactions

3- Oxidation of Isocitrate to α-Ketoglutarate by the action of Isocitrate dehydrogenase enzyme

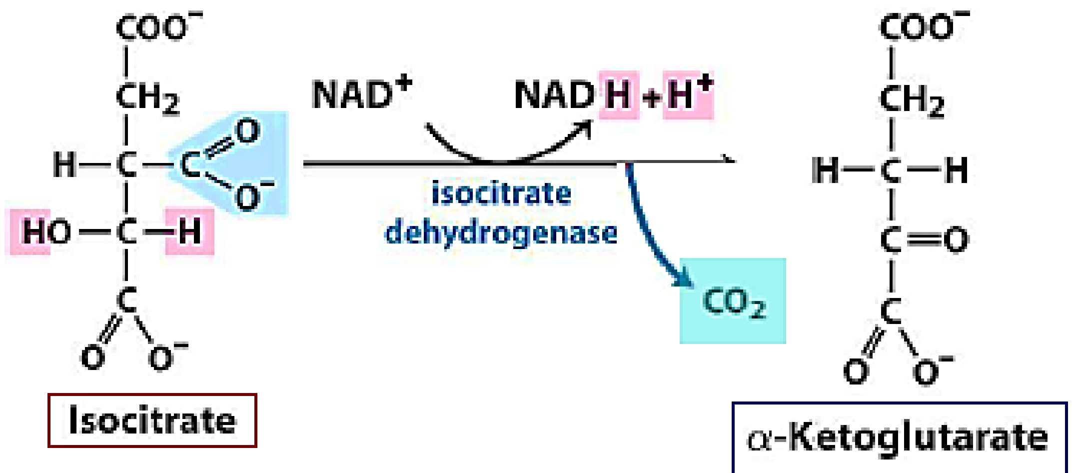
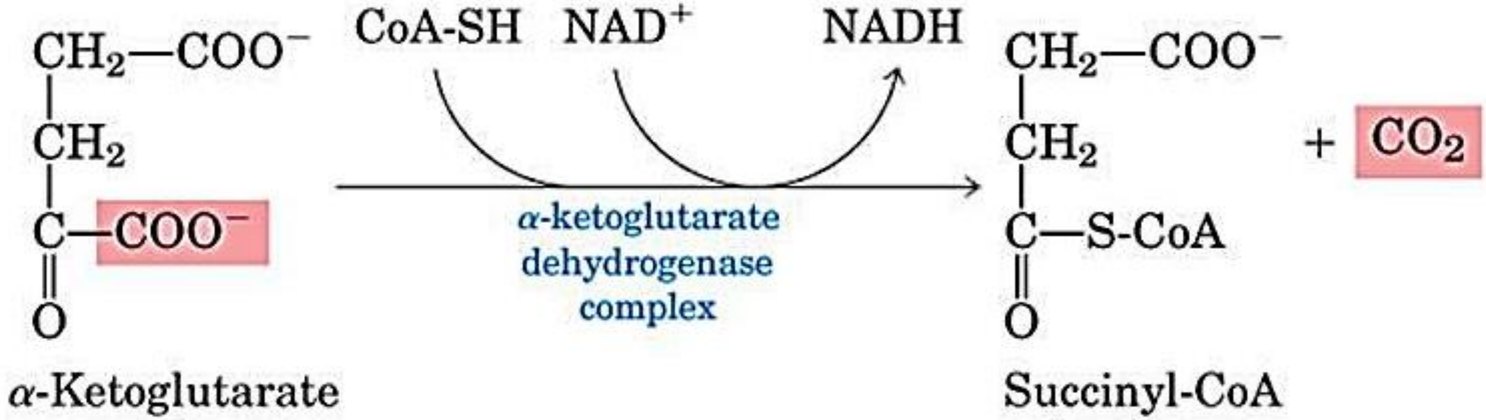


Figure 4

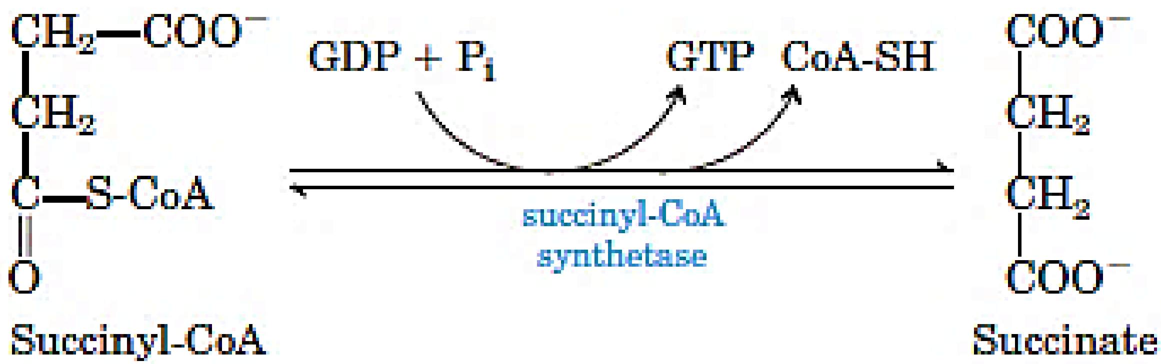
Krebs cycle reactions

4- Oxidation of α-ketoglutarate to Succinyl-CoA by enzyme action α-ketoglutarate dehydrogenase complex



Krebs cycle reactions

5- The conversion of Succinyl-CoA to Succinate by the action of the enzyme Succinyl-CoA synthetase.

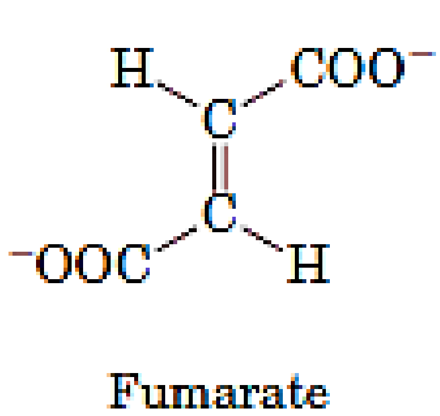


nucleoside-diphosphate kinase

$$GTP + ADP \rightleftharpoons ATP + GDP$$

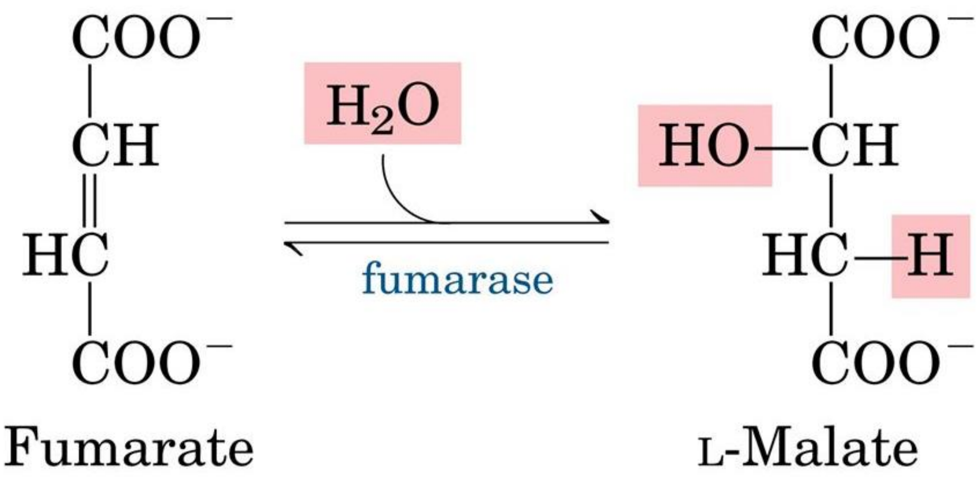
Krebs cycle reactions

6- Oxidation of succinate to fumarate by succinate dehydrogenase enzyme



Krebs cycle reactions

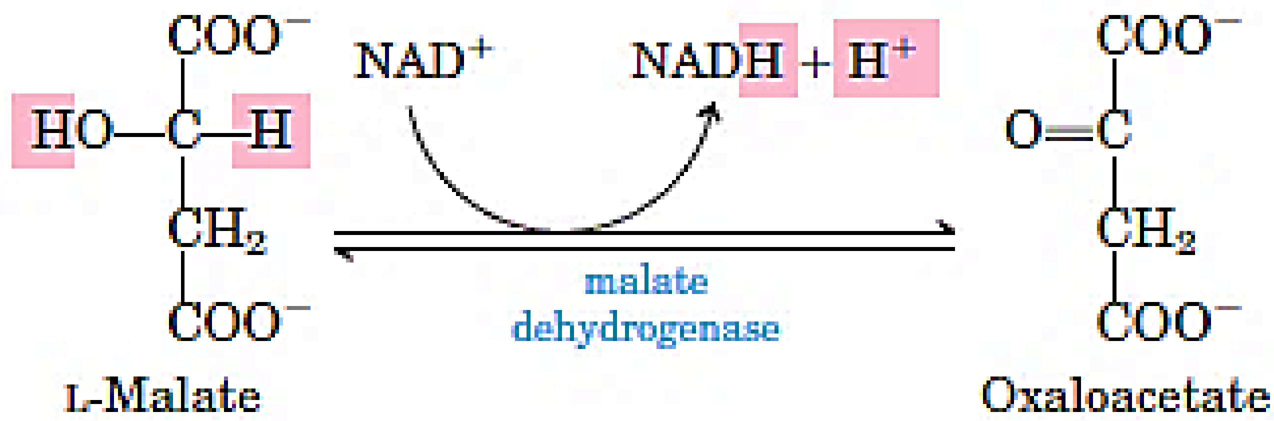
7- Reaction of adding water to Fumarate to form malate by Fumarase enzyme



Lecture 7

Krebs cycle reactions

8- Oxidation of malate to oxaloacetate by the enzyme malate dehydrogenase



Krebs Cycle Regulation

Regulation of TCA cycle exerted on the 3 committed steps regulated by the 3 key regulatory enzymes:

a- Citrate synthase

b- Isocitrate dehydrogenase

c- α ketoglutarate dehydrogenase complex

Product of one turn of TCA cycle

3 NADH
1 $FADH_2$
1 GTP or ATP
2 CO_2

Rajesh Chaudhary

Total ATP production from one Glucose molecule

Process	Energy Molecules Produced	ATP yield
Glycolysis	2 ATP 2 NADH	2 ATP 5 ATP
Oxidative decarboxylation	2 NADH	5 ATP
Krebs Cycle	6 NADH 2 $FADH_2$ 2 ATP	15 ATP 3 ATP 2 ATP
Total		32