Lecture 16:

Glycolysis
Control of glycolytic pathway
Synthesis of Glucose

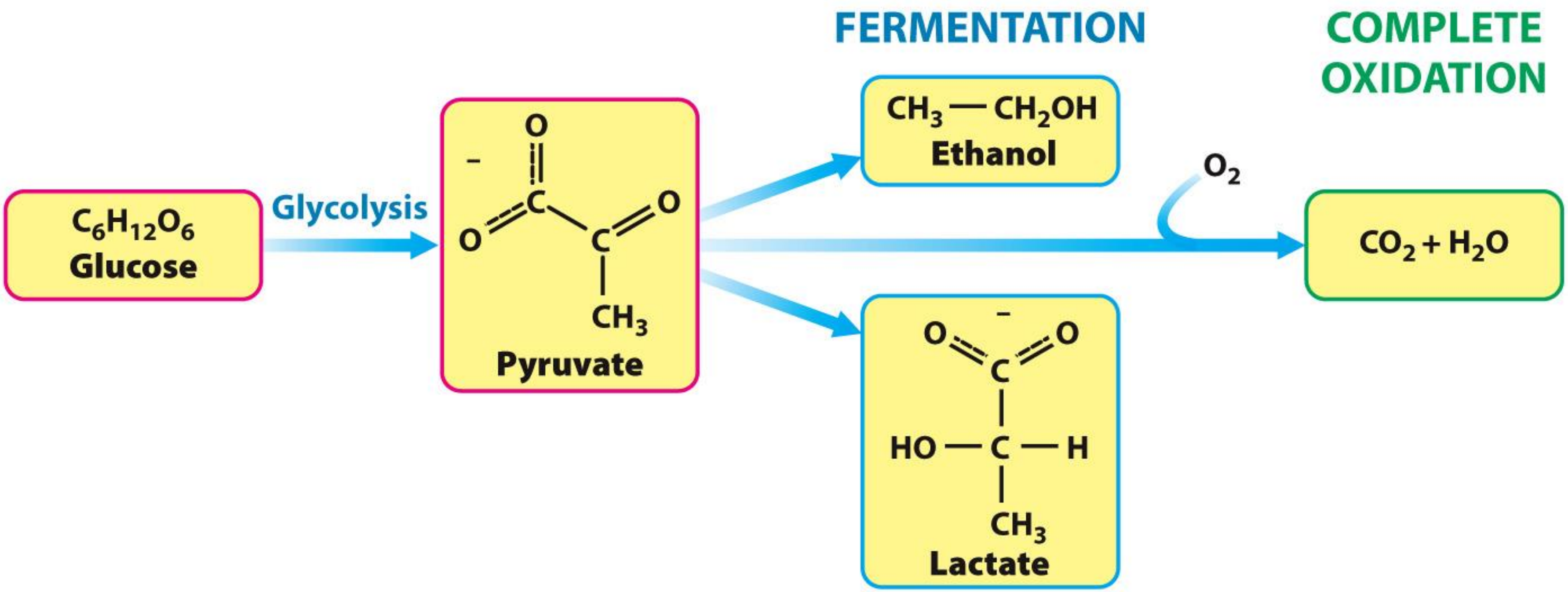

Figure 16.1
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Oligosaccharides digestion

Pancreatic and salivary **α-amylase** cleave the α-1, 4-bonds of starch and glycogen to yield maltose and maltotriose.

Maltase and **α-glucosidase** complete the digestion of the di- and trisaccharides into glucose.

The molecule remaining after amylase digestion is limit dextrin, which is rich in α-1, 6-bonds. **α-Dextrinase** degrades the limit dextran.

Sucrase hydrolyzes sucrose, whereas lactase cleaves lactose.

Why is glucose such a prominent fuel in all life forms?

1. Glucose may have been available for primitive biochemical systems because it can form under prebiotic conditions.

2. Glucose is the most stable hexose.

3. Glucose has a low tendency to nonenzymatically glycosylate proteins.

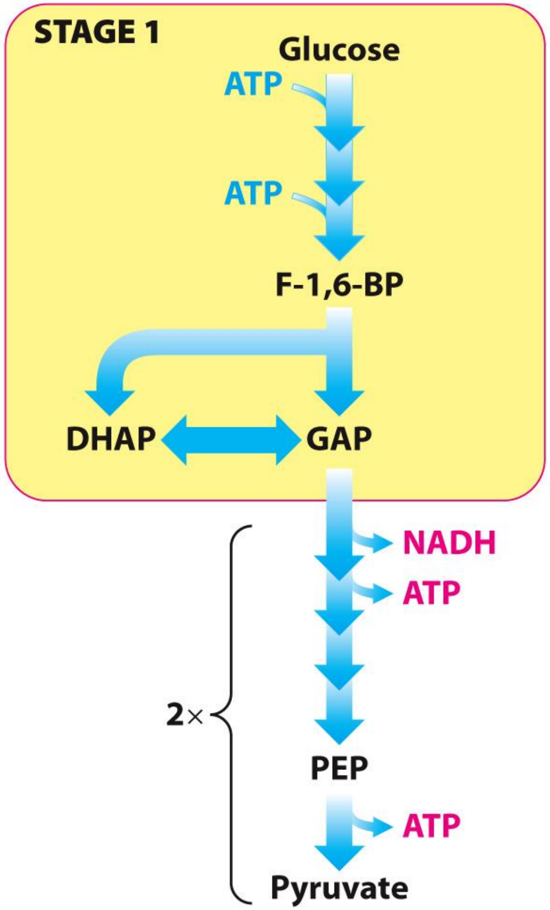
Glycolysis

Glycolysis converts one molecule of glucose into two molecules of pyruvate with the generation of two molecules of ATP.

Glycolysis can be thought of as occurring in two stages:

1. Stage 1 traps glucose in the cell and modifies it so that it can be cleaved into a pair of phosphorylated 3-carbon compounds.

2. Stage 2 oxidizes the 3-carbon compounds to pyruvate while generating two molecules of ATP.



First stage of glycolysis. The first stage of glycolysis begins with the phosphorylation of glucose by hexokinase and ends with the isomerization of dihydroxyacetone phosphate to glyceraldehyde 3-phosphate.

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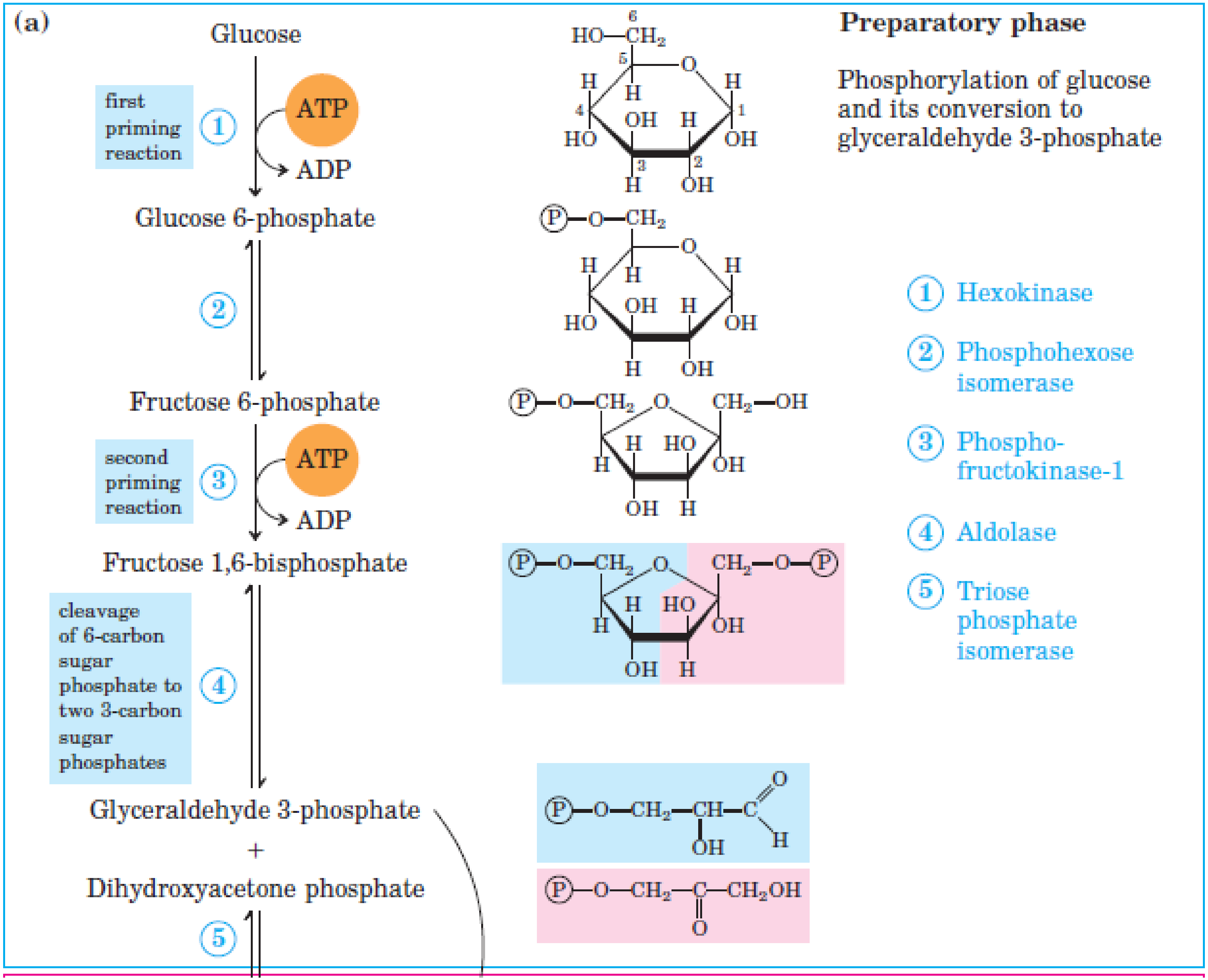
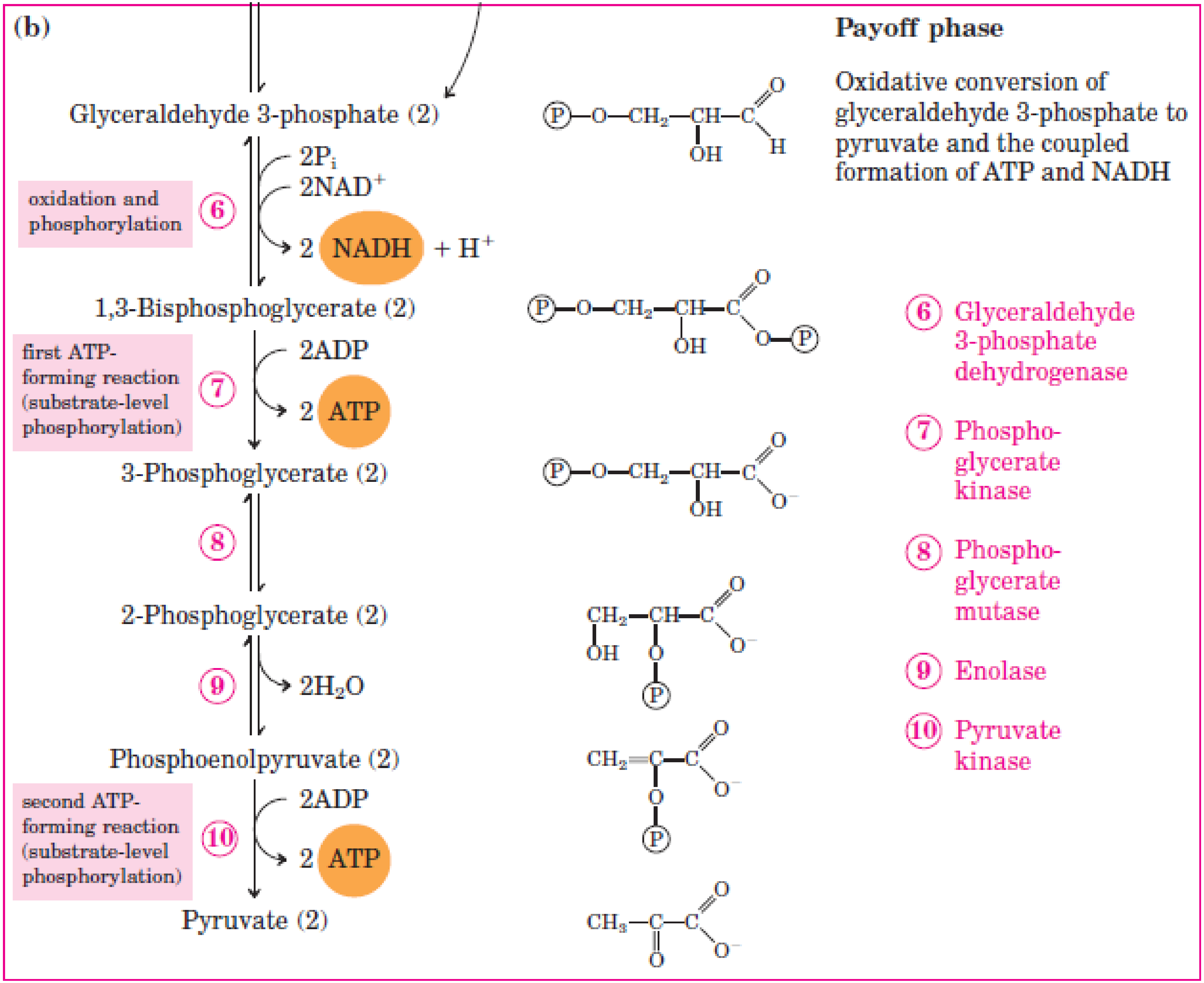
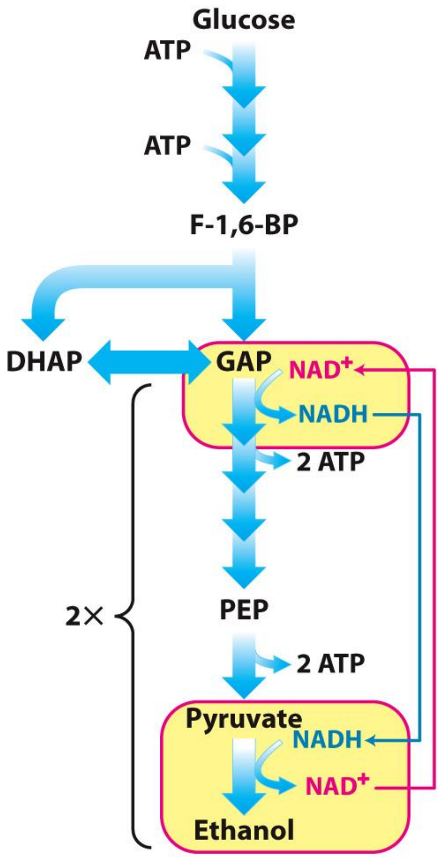

(a)
Preparatory phase
Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate
Glucose
first priming reaction
1
ATP
ADP
Glucose 6-phosphate
2
Fructose 6-phosphate
second priming reaction
3
ATP
ADP
Fructose 1,6-bisphosphate
cleavage of 6-carbon sugar phosphate to two 3-carbon sugar phosphates
4
Glyceraldehyde 3-phosphate
+
Dihydroxyacetone phosphate
5
1 Hexokinase
2 Phosphohexose isomerase
3 Phospho-fructokinase-1
4 Aldolase
5 Triose phosphate isomerase


(b)
Payoff phase
Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH
Glyceraldehyde 3-phosphate (2)
oxidation and phosphorylation
6
2Pi
2NAD+
2 NADH + H+
1,3-Bisphosphoglycerate (2)
first ATP-forming reaction (substrate-level phosphorylation)
7
2ADP
2 ATP
3-Phosphoglycerate (2)
8
2-Phosphoglycerate (2)
9
2H2O
Phosphoenolpyruvate (2)
second ATP-forming reaction (substrate-level phosphorylation)
10
2ADP
2 ATP
Pyruvate (2)
6 Glyceraldehyde 3-phosphate dehydrogenase
7 Phosphoglycerate kinase
8 Phosphoglycerate mutase
9 Enolase
10 Pyruvate kinase

Metabolism of pyruvate leads to the formation of two molecules of ATP

The conversion of glucose into pyruvate generates ATP, but for ATP synthesis to continue, NADH must be reoxidized to NAD^+.

NAD^+ can be regenerated by further oxidation of pyruvate to CO_2, or by the formation of ethanol or lactate from pyruvate.



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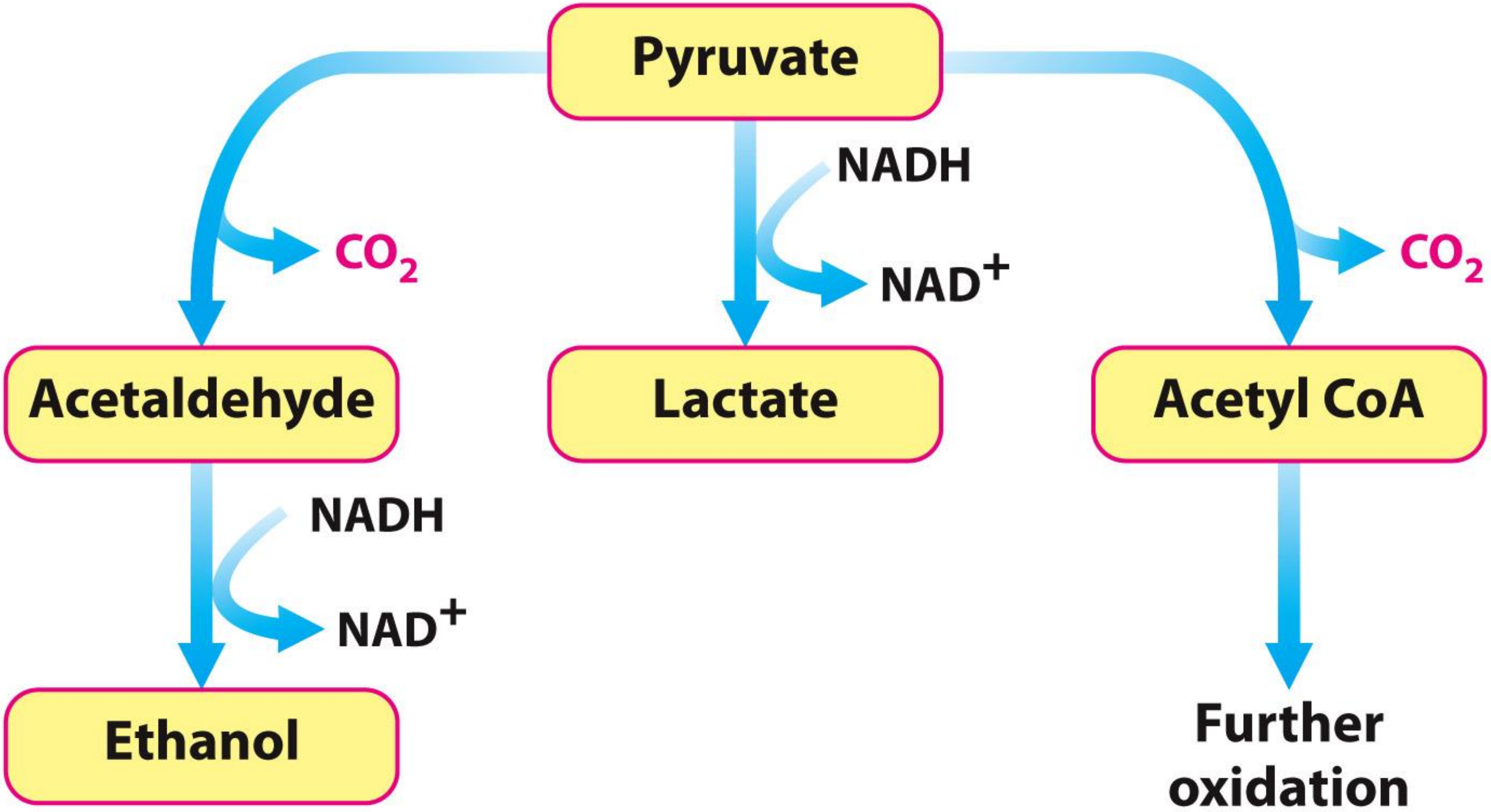
Regeneration of NAD^+.



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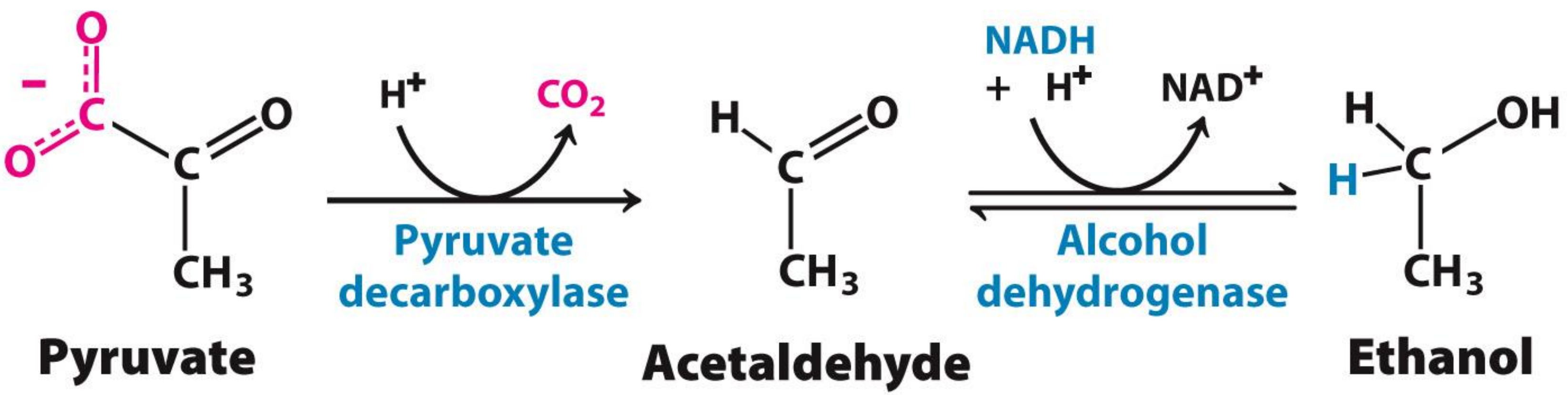
NAD$^+$ is regenerated from the metabolism of pyruvate

The regeneration of NAD$^+$ by processing pyruvate to ethanol is called alcoholic fermentation.



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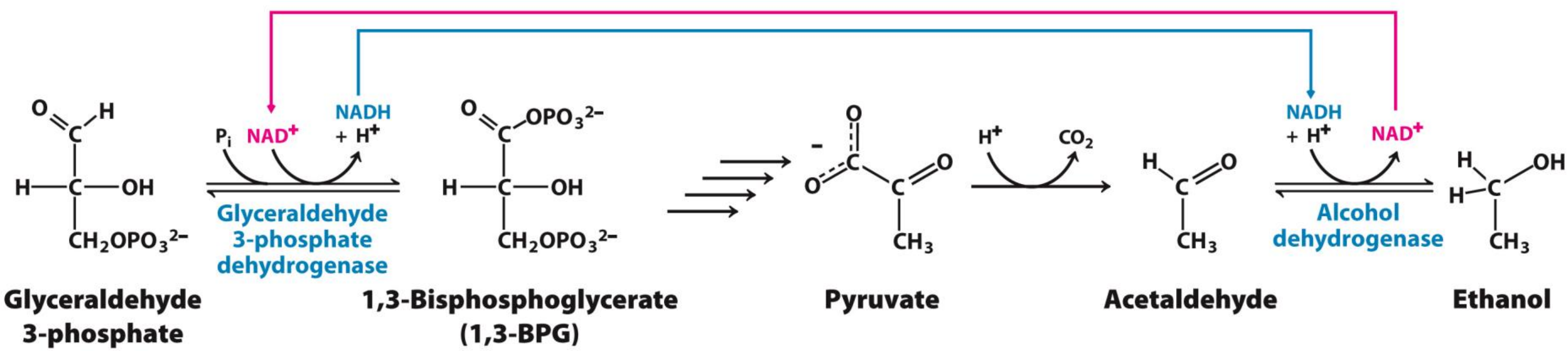
$$\text{Glucose} + 2\,P_i + 2\,\text{ADP} + 2\,H^+ \rightarrow 2\,\text{ethanol} + 2\,CO_2 + 2\,\text{ATP} + 2\,H_2O$$



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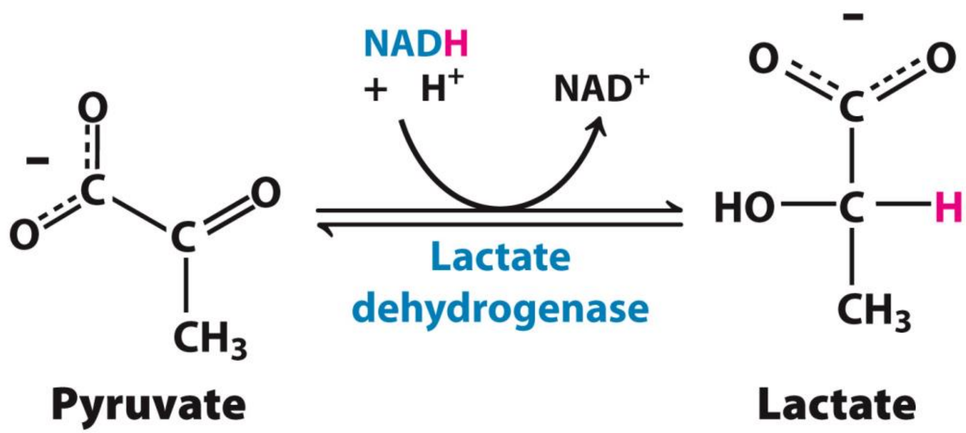
In lactic acid fermentation, pyruvate is reduced to lactate to regenerate NAD^+.



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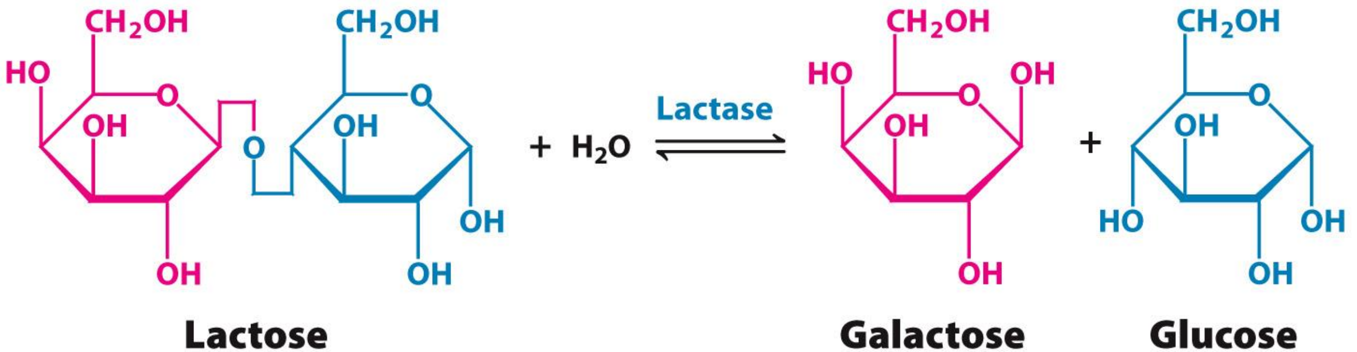
$$\text{Glucose} + 2\,P_i + 2\,\text{ADP} \rightarrow 2\,\text{lactate} + 2\,\text{ATP} + 2\,H_2O$$

Obligate anaerobes cannot survive in the presence of O2.

There are many more fermentations than just alcoholic and lactic acid fermentation.

Many adults are intolerant of milk because they are deficient in lactase

Lactose intolerance or hypolactasia occurs because most adults lack lactase, the enzyme that degrades lactose.



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Northern Europeans have a mutation that prevents the decline of lactase activity after weaning.

In lactase-deficient individuals, gut bacteria metabolize lactose, generating CH_4 and H_2, and disrupt water balance in the intestine.

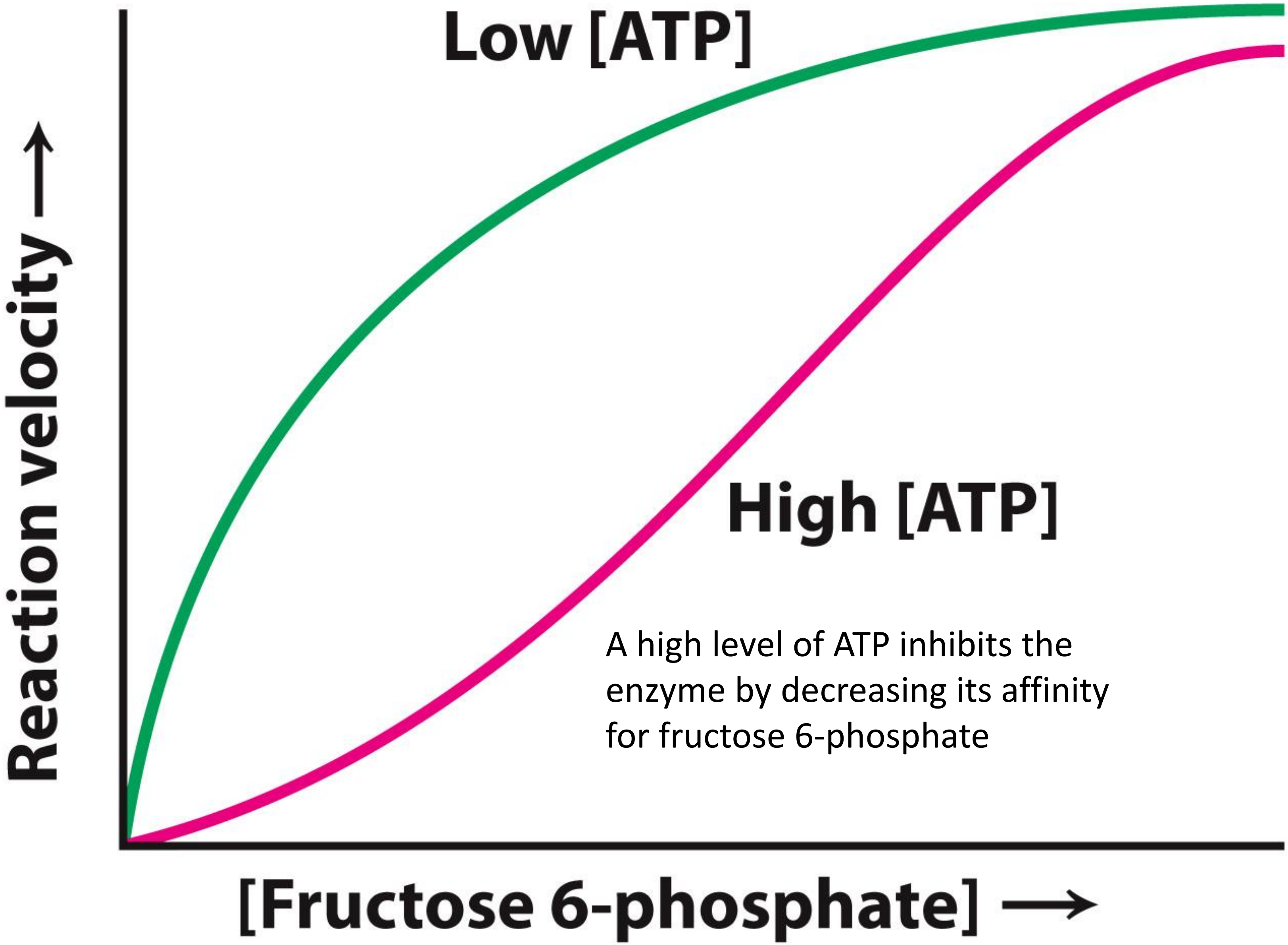
Glycolysis in muscle is regulated to meet the need for ATP

Phosphofructokinase is the key regulator of glycolysis in mammals. The enzyme is allosterically inhibited by ATP and allosterically stimulated by AMP.

When ATP needs are great, adenylate kinase generates ATP from 2 ADP.

AMP then becomes the signal for the low-energy state.

$$\text{ADP} + \text{ADP} \rightleftharpoons \text{ATP} + \text{AMP}$$



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Decarboxylation of pyruvate and Citric acid cycle takes place in mitochondria

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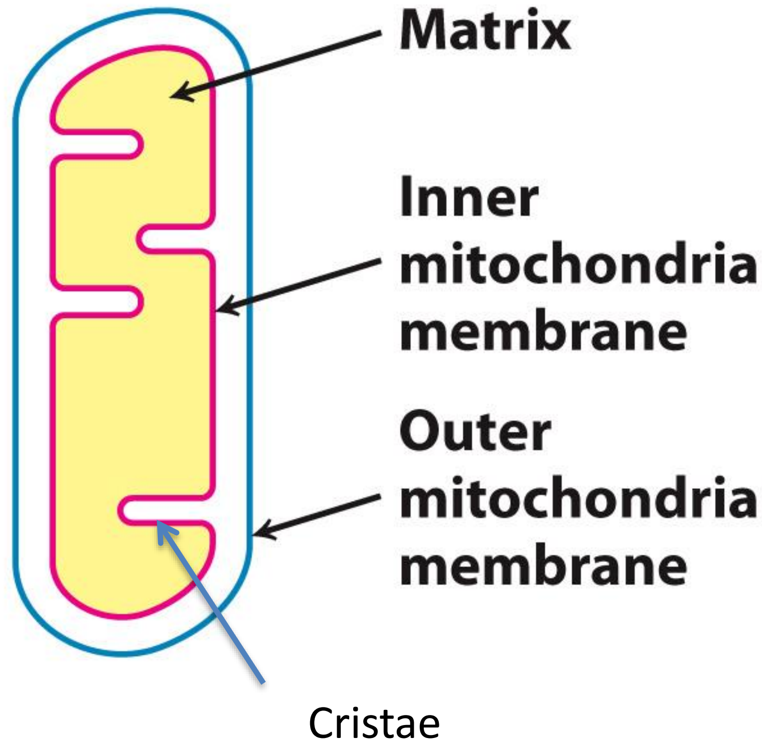

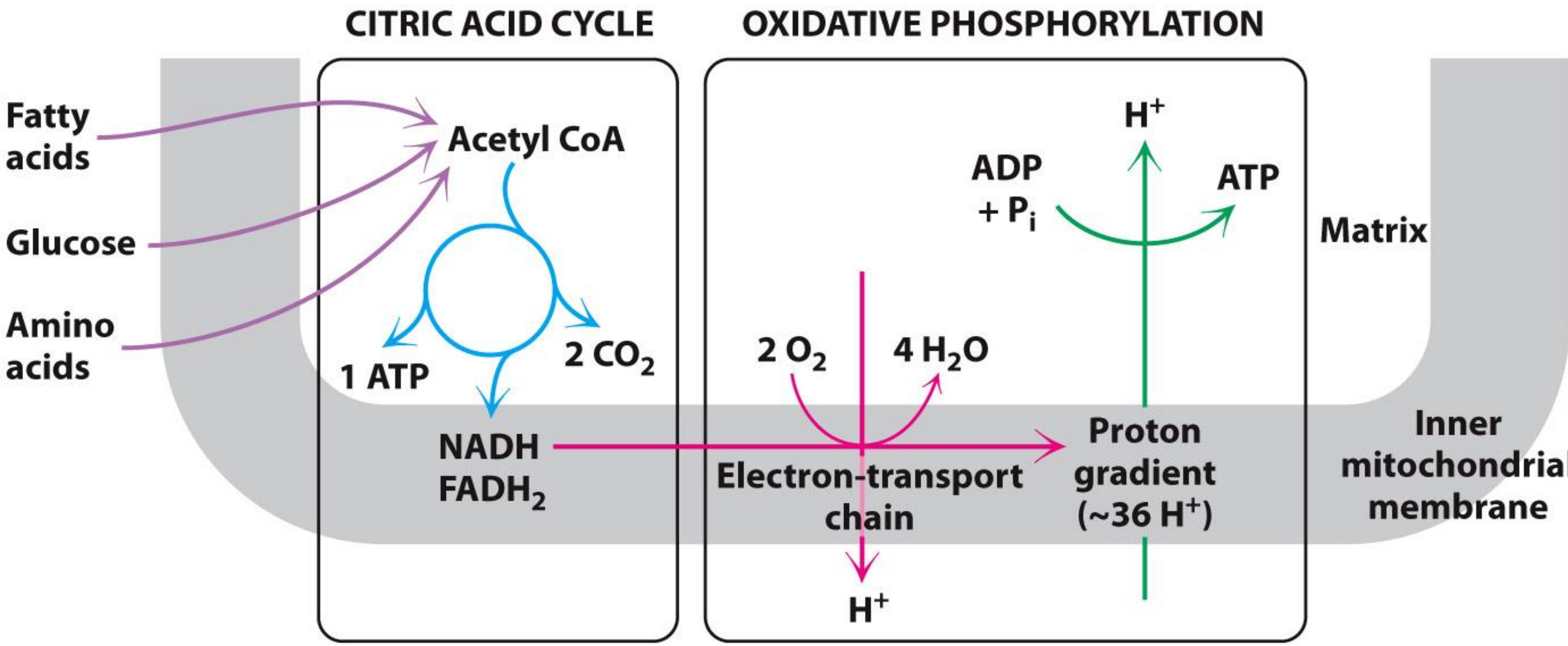

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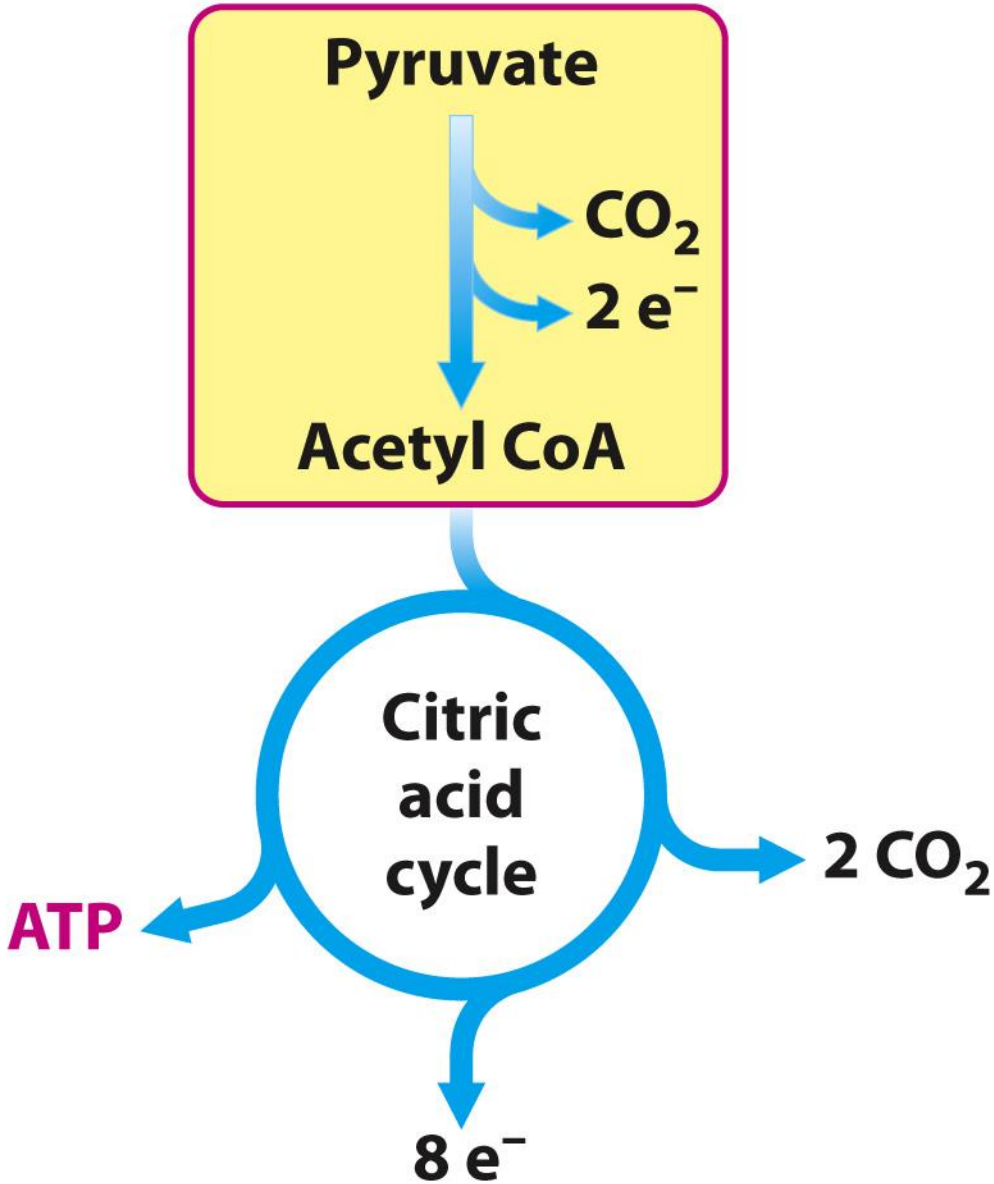
PYRUVATE DEHYDROGENASE

The pyruvate dehydrogenase complex, a component of the mitochondrial matrix, is composed of three distinct enzymes that oxidatively decarboxylate pyruvate to form acetyl CoA.

This reaction is an irreversible link between glycolysis and the citric acid cycle.

$$\text{Pyruvate} + \text{CoA} + \text{NAD}^+ \longrightarrow \text{acetyl CoA} + \text{CO}_2 + \text{NADH} + \text{H}^+$$



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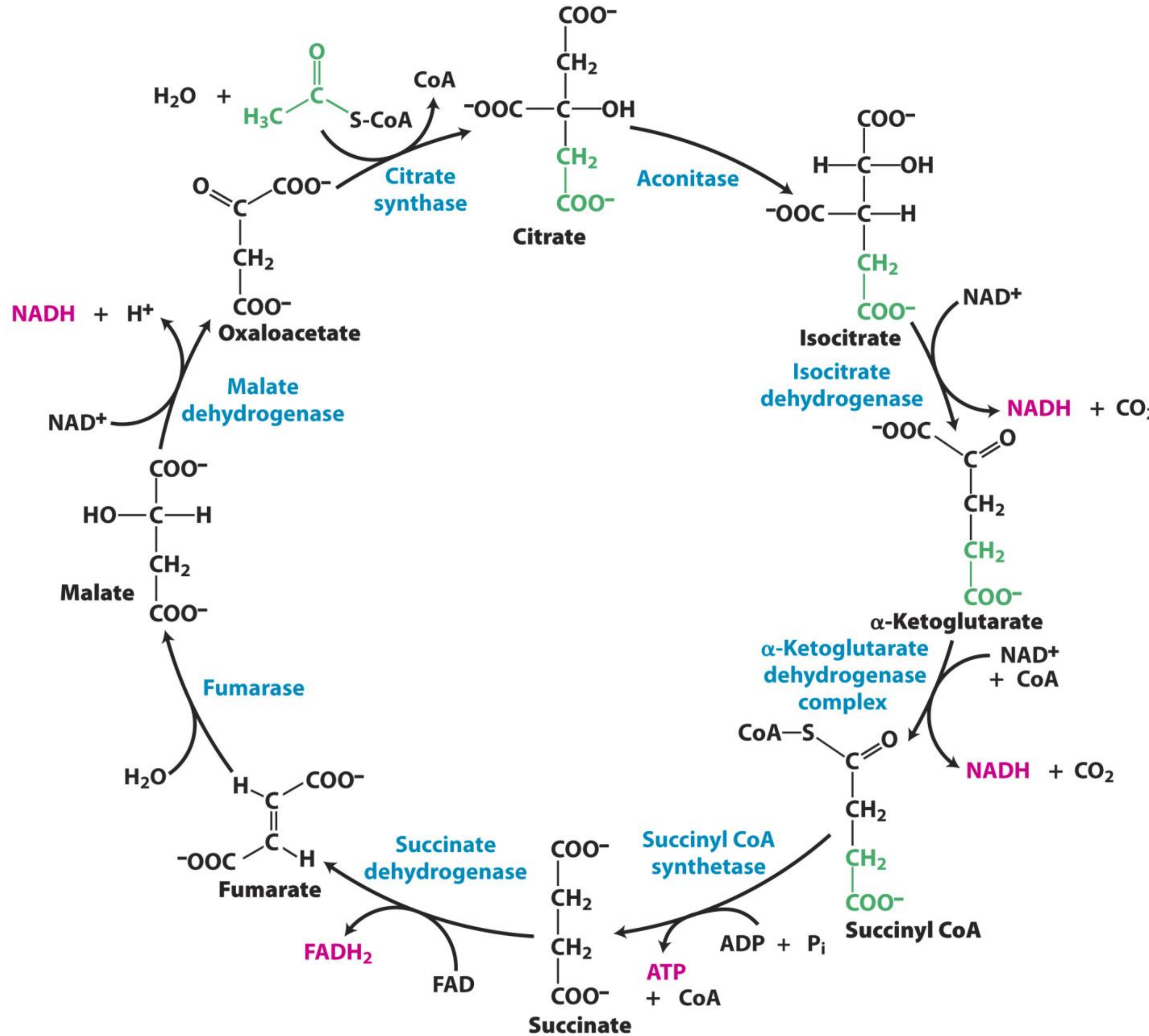

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Oxidative phosphorylation