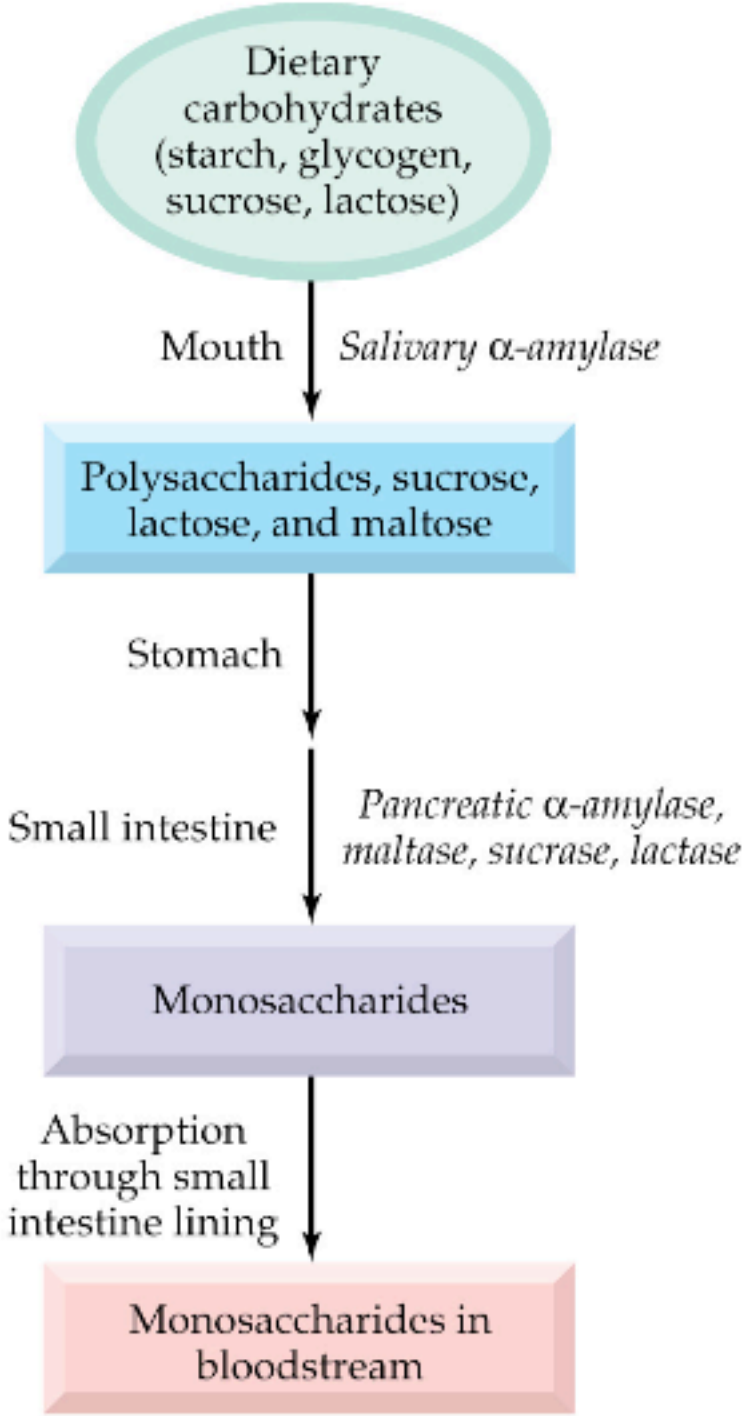
Review of Carbohydrate Digestion



Glycolysis

Glycolysis is a nine step biochemical pathway that oxidizes glucose into two molecules of pyruvic acid.

During this process, energy is released and some of it is captured in the form of ATP.

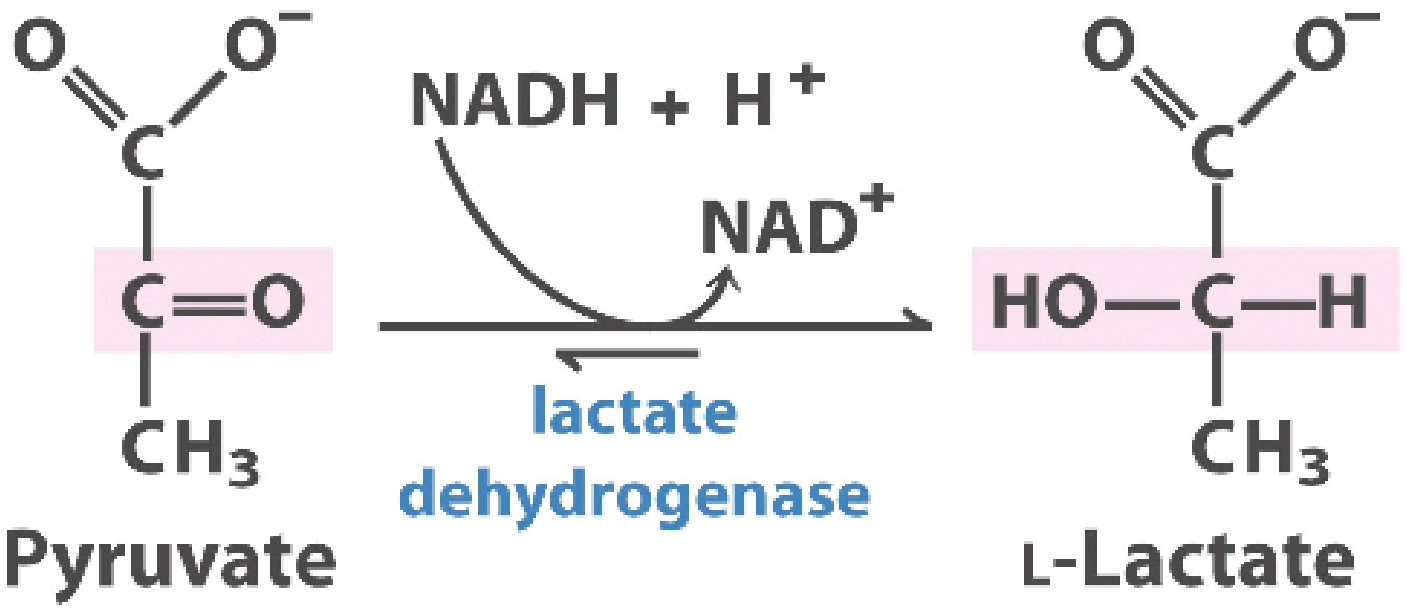
The electrons removed from glucose are captured in the form of NADH.

$$C_6H_{12}O_6 + 2\ NAD^+ + 2\ ADP + 2\ P_i \longrightarrow 2\ C_3H_4O_3 + 2\ ATP + 2\ NADH + 2\ H^+ + 2\ H_2O$$

The pyruvic acid formed may be

- ***oxidized to carbon dioxide and water in the citric acid cycle***
- ***or***
- ***may be reduced to L-lactic acid***

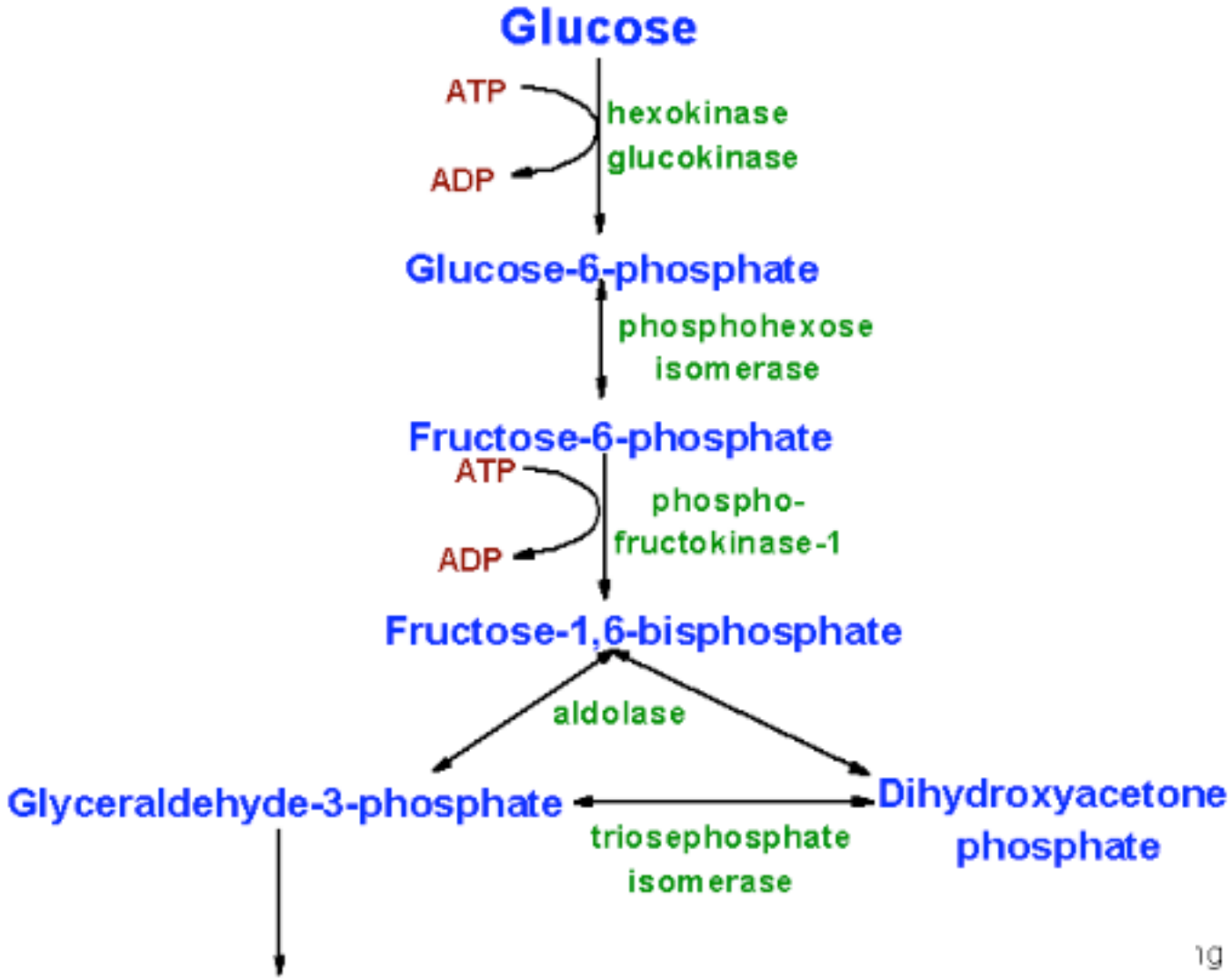
Lactate Dehydrogenase Reaction



$\Delta G'^{\circ} = -25.1$ kJ/mol

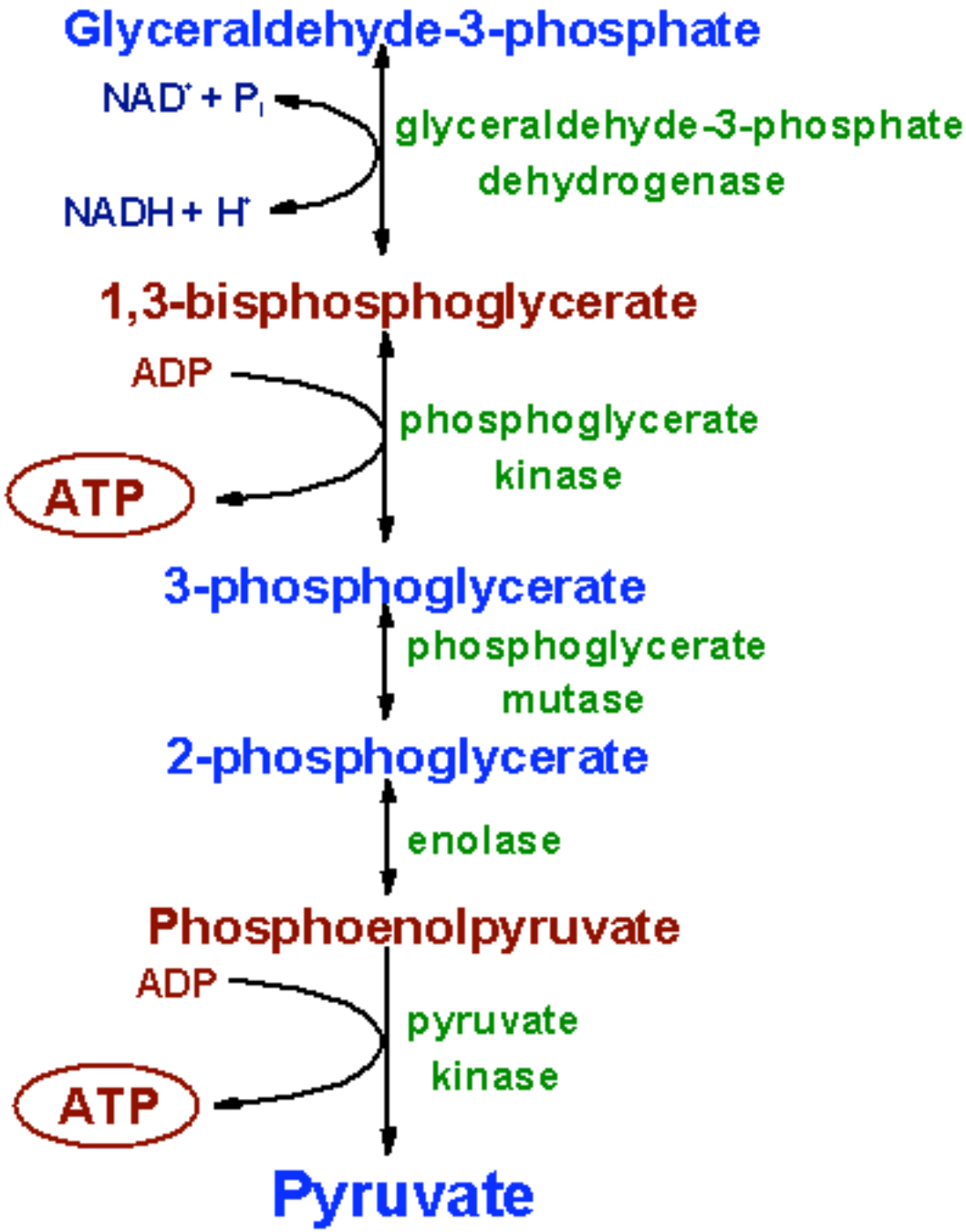
Two Stages of Glycolysis:

Stage 1: *Glucose and other hexoses are converted into glyceraldehyde-3-phosphate.*



Two Stages of Glycolysis:

Stage 2: *Glyceraldehyde-3-phosphate is oxidized and converted into two molecules of pyruvate.*

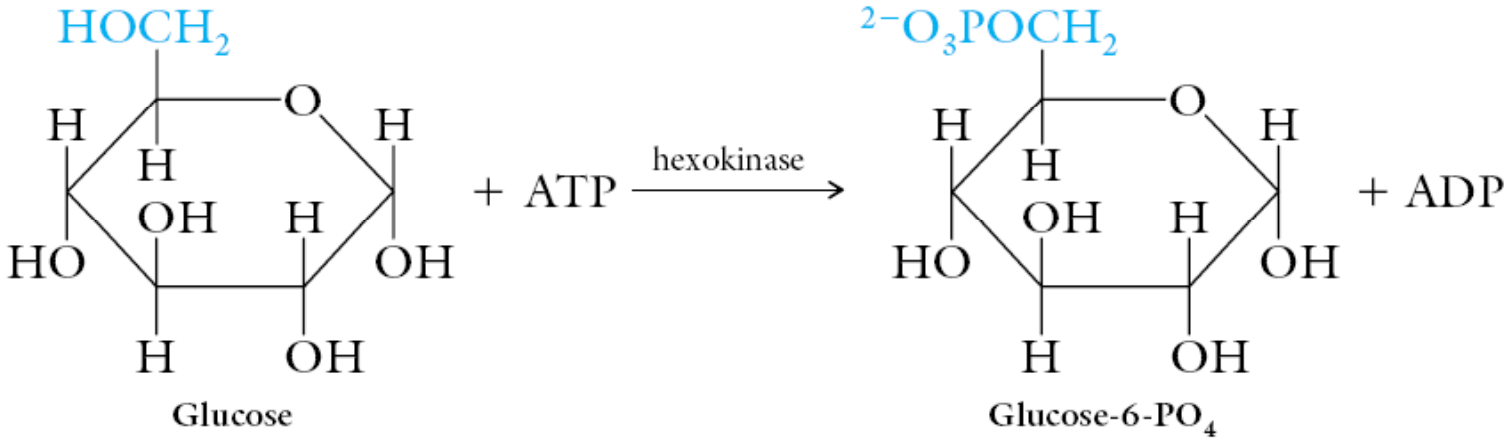


If the pyruvate produced by glycolysis is converted into lactate, the NADH generated during stage 2 is used to reduce the pyruvate molecules.

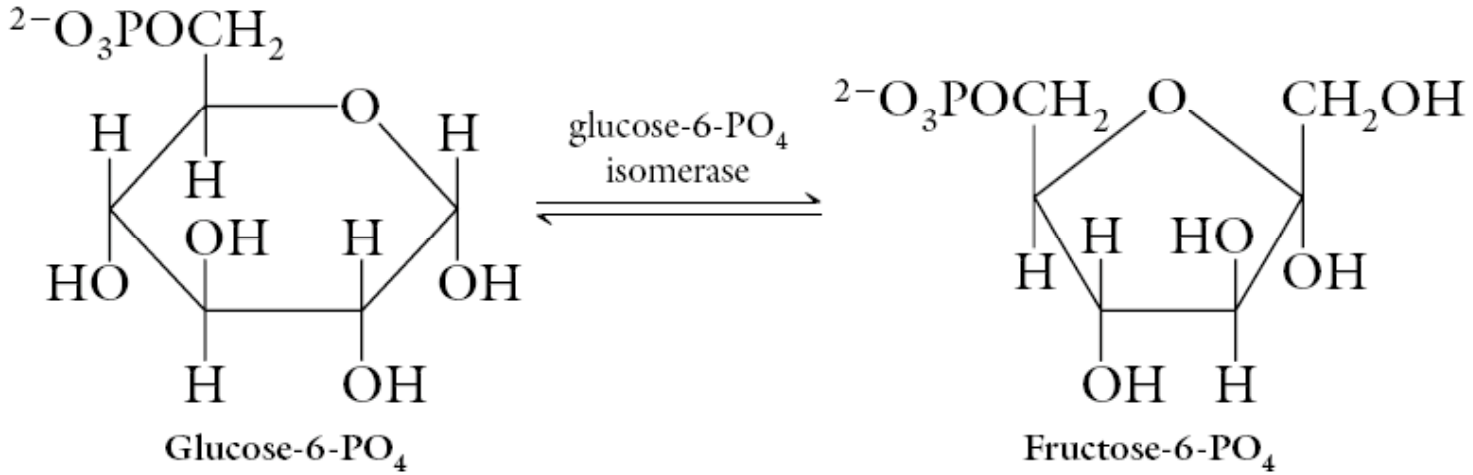
Chemical Transformations of Glycolysis

The First Stage of Glycolysis

Step 1

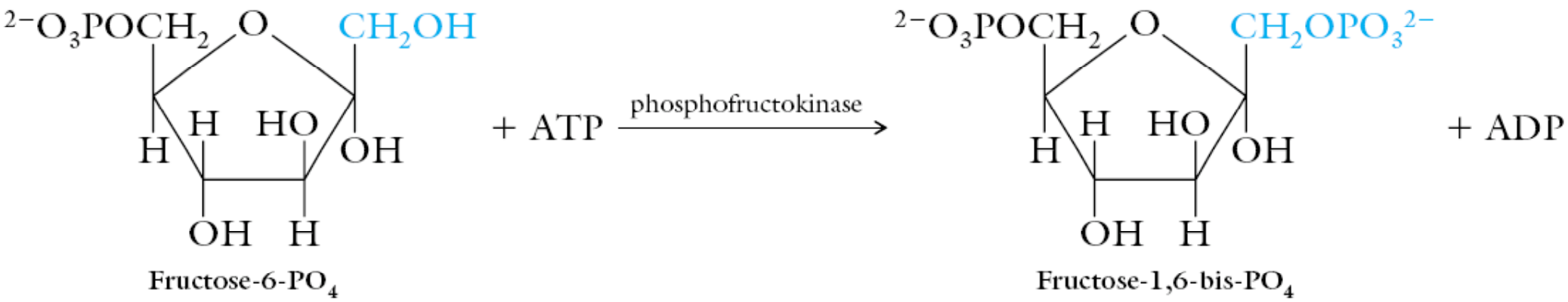


Step 2



Chemical Transformations of Glycolysis

Step 3



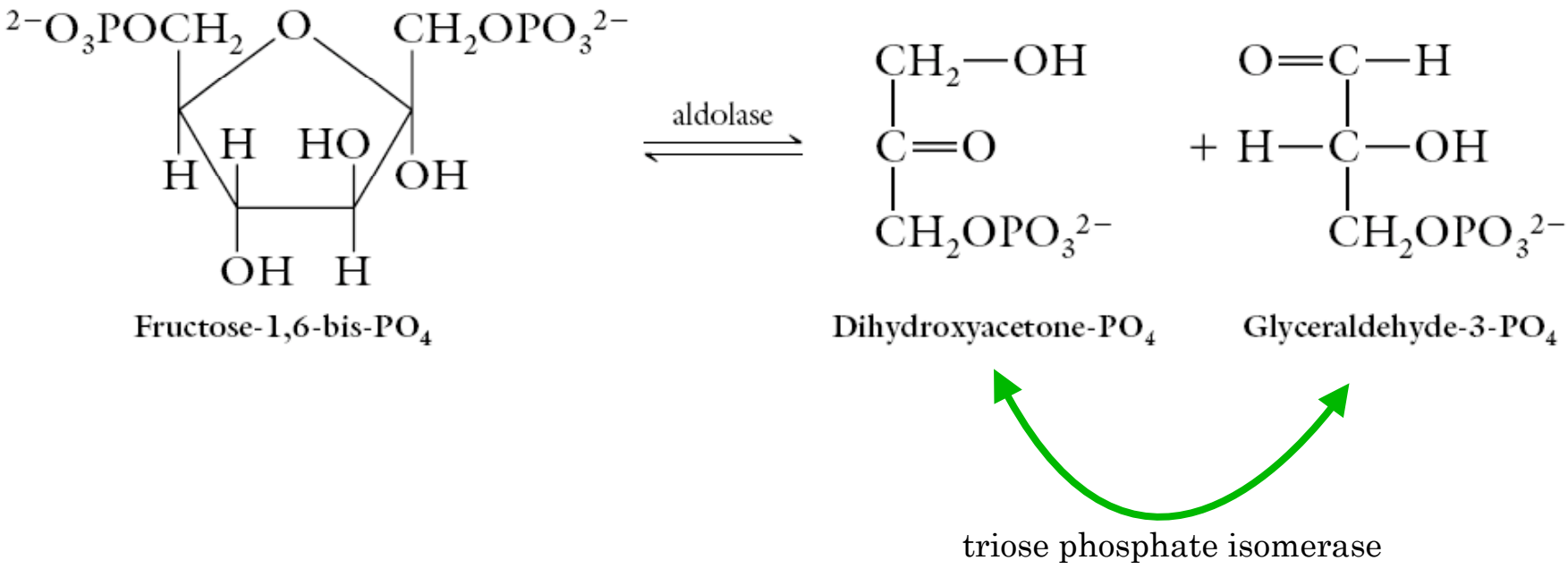
Fructose-6-PO_4

Fructose-1,6-bis-PO_4

Phosphofructokinase is the key control point in glycolysis. It is inhibited by high ATP concentrations, when there is no need to put glucose through this pathway. Under these conditions, glucose is instead stored as glycogen.

Chemical Transformations of Glycolysis

Step 4



Fructose-1,6-bis-PO_4 | Dihydroxyacetone-PO_4 | Glyceraldehyde-3-PO_4

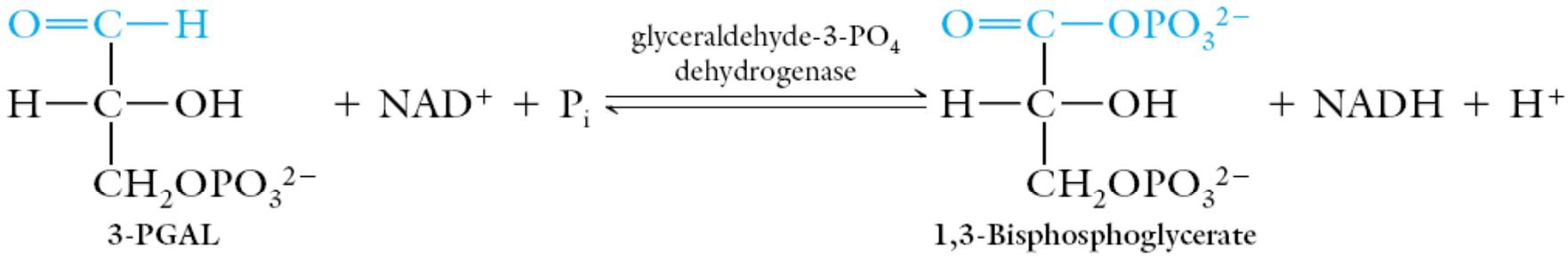
The dihydroxyacetone phosphate formed in this reaction is rapidly converted to glyceraldehyde-3-phosphate by the enzyme triose phosphate isomerase.

In effect, a molecule of fructose-1,6-bisphosphate is converted into two molecules of glyceraldehyde-3-phosphate.(3-PGAL)

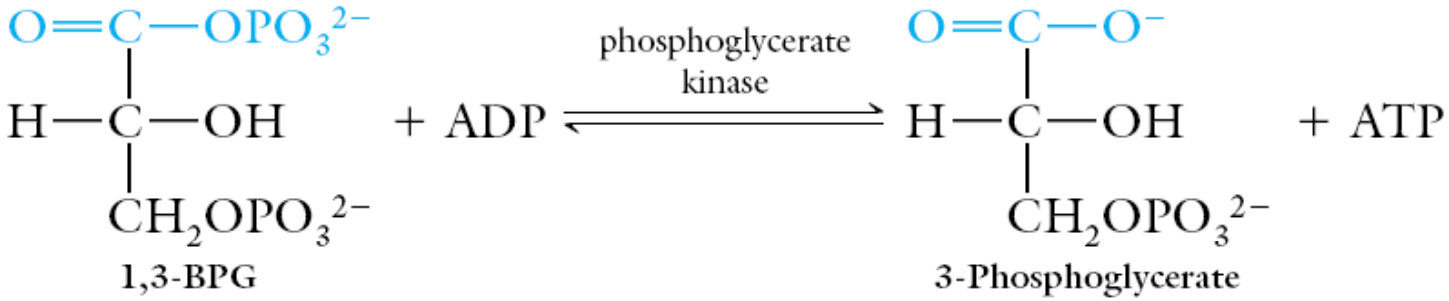
Chemical Transformations of Glycolysis

The Second Stage of Glycolysis

Step 5



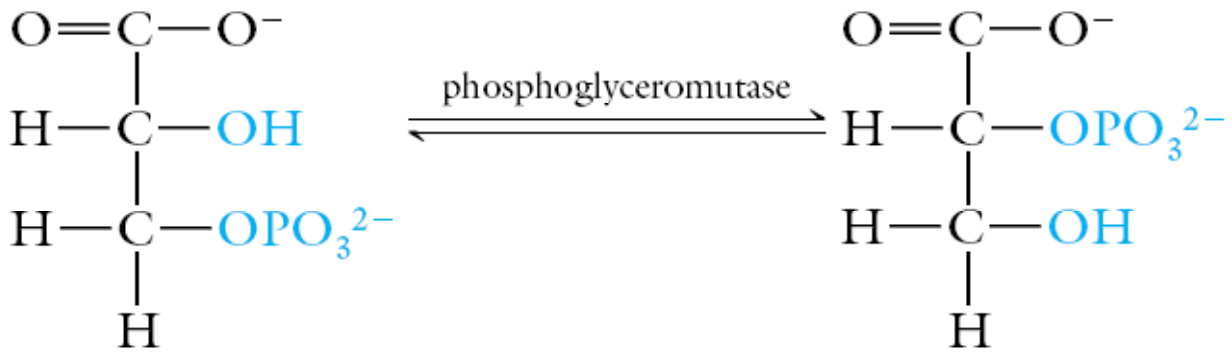
Step 6



The formation of ATP in this step is called a substrate level phosphorylation.

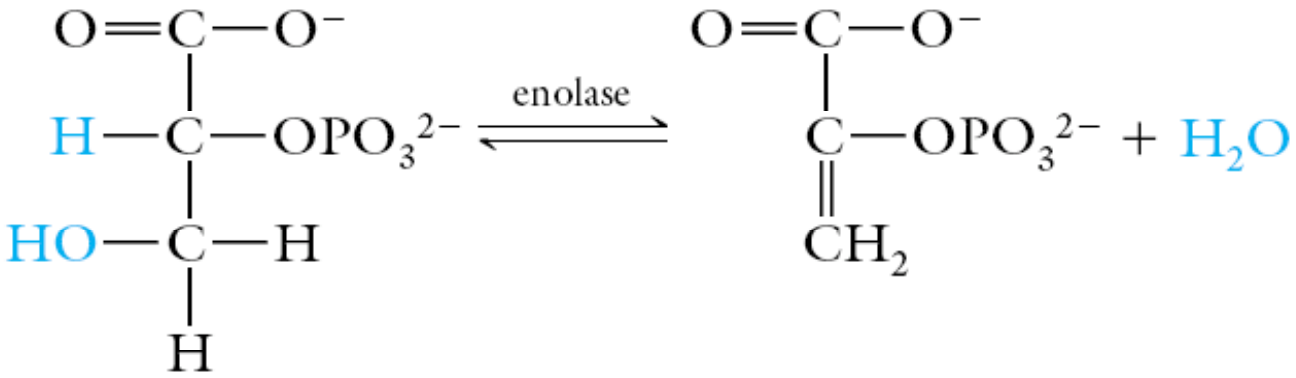
Chemical Transformations of Glycolysis

Step 7



3-Phosphoglycerate 2-Phosphoglycerate

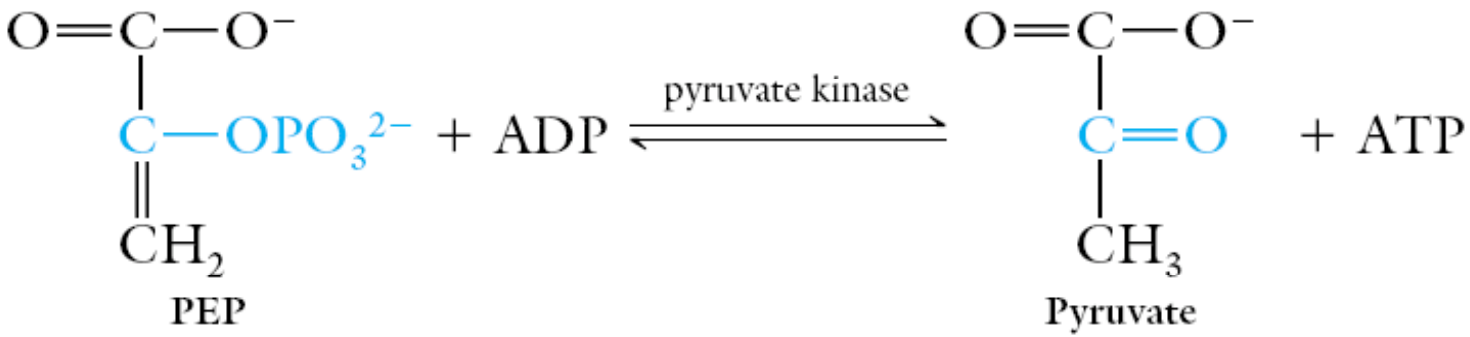
Step 8



2-Phosphoglycerate Phosphoenolpyruvate

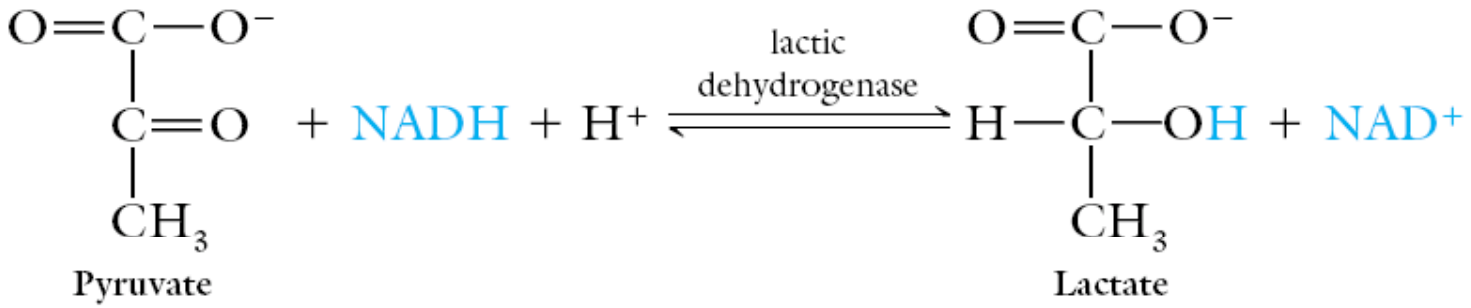
Chemical Transformations of Glycolysis

Step 9



In extremely active skeletal muscle, the pyruvate formed in step 9 is reduced to lactate by the NADH produced in step 5.

Step 10



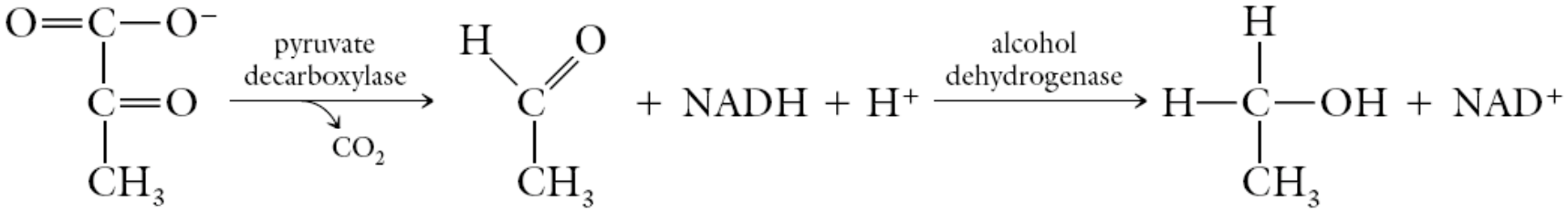
Chemical Transformations of Glycolysis

The overall reaction of steps 1-10 is:

$$\text{Glucose} + 2\ \text{ADP} + 2\ \text{P}_\text{i} \longrightarrow 2\ \text{lactate} + 2\ \text{ATP}$$

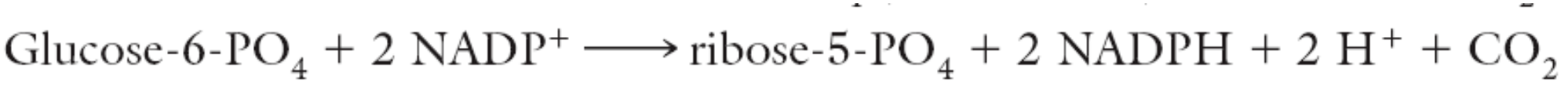
In cells where a high rate of ATP production is not needed, the pyruvate formed by glycolysis is not reduced to lactate, but instead is oxidized to carbon dioxide and water in the mitochondria.

This allows the cell to capture a greater amount of energy from the original glucose molecule.



Note:In some microorganisms, such as yeast, pyruvate is first decarboxylated and the resulting acetaldehyde is reduced to ethanol, regenerating NAD^+.

The Pentose Phosphate Pathway



The pentose phosphate pathway utilizes glucose to produce pentoses (for DNA, RNA) and NADPH (for reductive biosynthesis).

This pathway includes additional enzymes that allow the interconversion of pentoses and hexoses.

This allows the cell four alternatives:

Produce both pentoses and NADPH.

Produce only NADPH when pentoses are not required.

Produce only pentoses when NADPH is not required.

Produce ATP (glycolysis) and NADPH when both are required.

Metabolic Pathways of Glucose

Name	Derivation of Name	Function
Glycolysis (Section 23.3)	*glyco*–, glucose (from Greek, meaning "sweet"	Conversion of glucose to pyruvate
Gluconeogenesis (Section 23.11)	*gluco*–, glucose –*neo*–, glucose	Synthesis of glucose from amino acids, pyruvate, and other noncarbohydrates
Glycgenesis (Section 23.10)	*glyco(gen)*–, glycogen –*genesis*, creation	Sythesis of glycogen from glucose
Glycogenolysis (Section 23.10)	*glycogen*–, glycogen –*lysis*, decomposition	Breakdown of glycogen to glucose
Pentose phosphate pathway (Section 23.12)	*pentose*–, a five–carbon sugar *phosphate*	Conversion of glucose to five–carbon sugar phosphates

Gluconeogenesis

Gluconeogenesis is the biosynthesis of glucose from lactate and certain other small molecules.

Gluconeogenesis occurs in the liver.

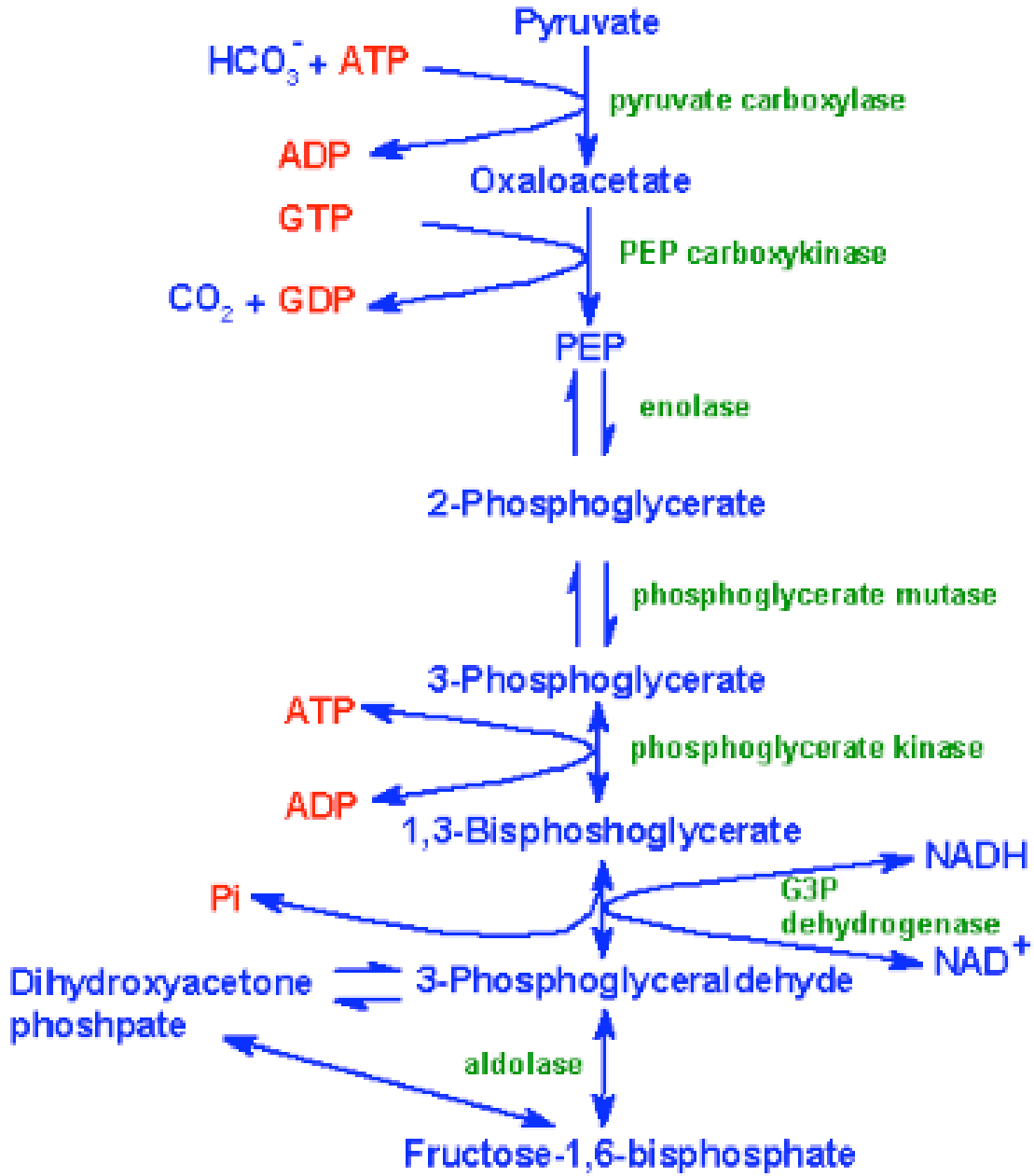
To accomplish glucose biosynthesis, a liver cell reverses many of the reactions in glycolysis, however, three irreversible reactions must be bypassed using different reactions and enzymes.

Free-Energy Changes of Glycolytic Reactions in Erythrocytes

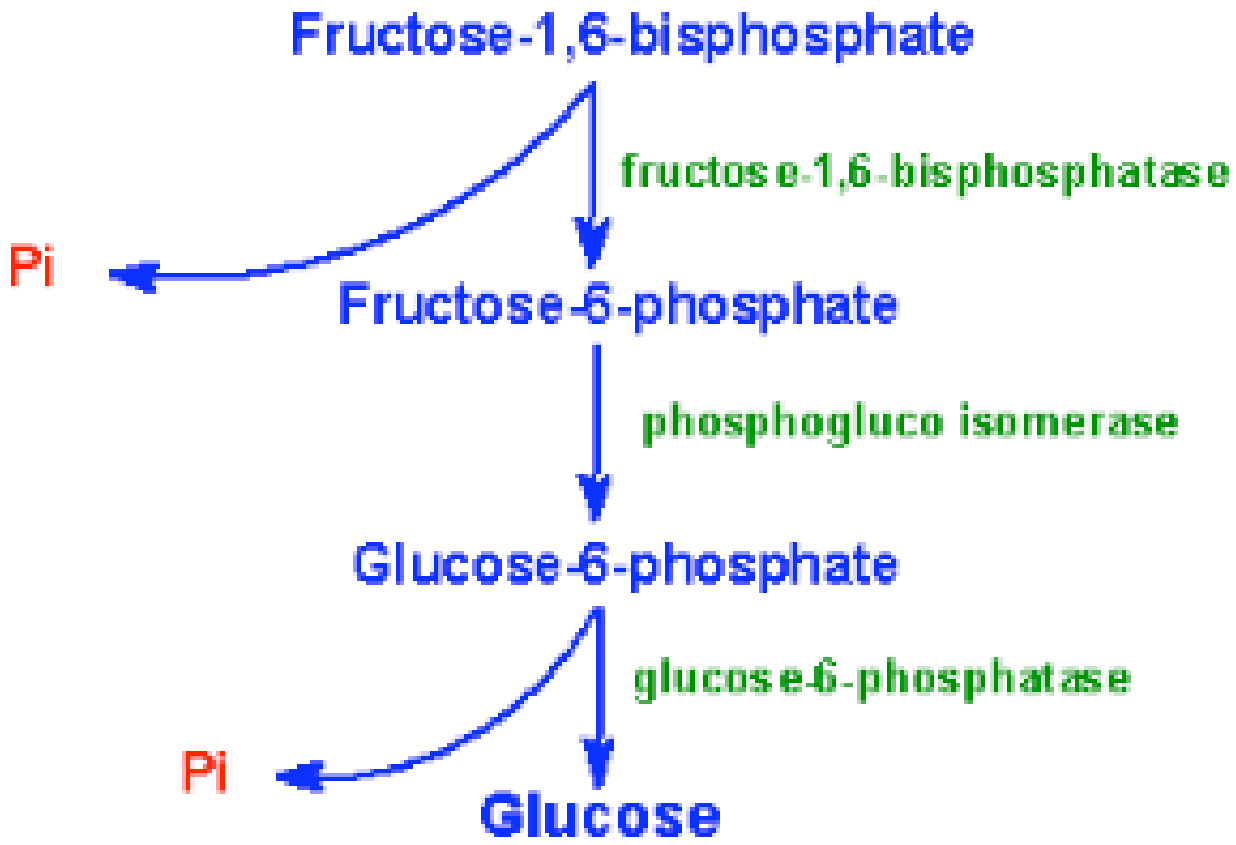
Glycolytic reaction step	$\Delta G'^{\circ}$ *(kJ/mol)*	ΔG *(kJ/mol)*
(1) Glucose + ATP ⟶ glucose 6-phosphate + ADP	−16.7	−33.4
(2) Glucose 6-phosphate ⇌ fructose 6-phosphate	1.7	0 to 25
(3) Fructose 6-phosphate + ATP ⟶ fructose 1,6-bisphosphate + ADP	−14.2	−22.2
(4) Fructose 1,6-bisphosphate ⇌ dihydroxyacetone phosphate + glyceraldehyde 3-phosphate	23.8	0 to −6
(5) Dihydroxyacetone phosphate ⇌ glyceraldehyde 3-phosphate	7.5	0 to 4
(6) Glyceraldehyde 3-phosphate + P_i + NAD^+ ⇌ 1,3-bisphosphoglycerate + NADH + H^+	6.3	−2 to 2
(7) 1,3-Bisphosphoglycerate + ADP ⇌ 3-phosphoglycerate + ATP	−18.8	0 to 2
(8) 3-Phosphoglycerate ⇌ 2-phosphoglycerate	4.4	0 to 0.8
(9) 2-Phosphoglycerate ⇌ phosphoenolpyruvate + H_2O	7.5	0 to 3.3
(10) Phosphoenolpyruvate + ADP ⟶ pyruvate + ATP	−31.4	−16.7

Note: $\Delta G'^{\circ}$ is the standard free-energy change, as defined in Chapter 13 (p. 491). ΔG is the free-energy change calculated from the actual concentrations of glycolytic intermediates present under physiological conditions in erythrocytes, at pH 7. The glycolytic reactions bypassed in gluconeogenesis are shown in red. Biochemical equations are not necessarily balanced for H or charge (p. 506).

Gluconeogenesis



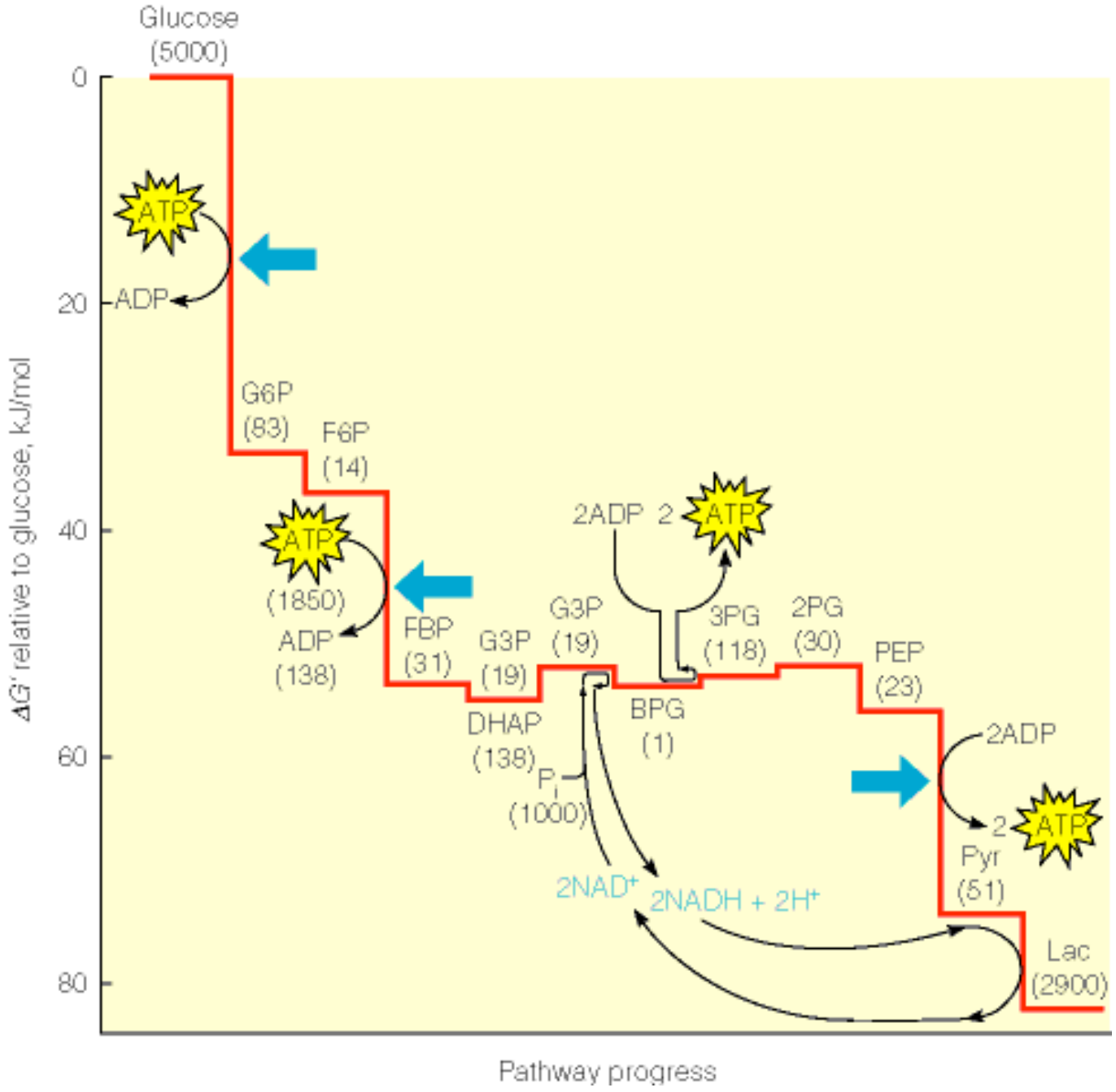
Gluconeogenesis



2

3

Glycolysis Free Energy Changes



Gluconeogenesis

The **first enzymatic bypass** involves several reactions, both in the mitochondria and the cytosol:

Pyruvate + CO_2 + ATP → oxaloacetate + ADP mitochondria

Oxaloacetate + NADH + H+ → L-malate + NAD+ mitochondria

L-malate (mitochondria) → L-malate (cytosol)

L-malate + NAD+ → Oxaloacetate + NADH + H+ cytosol

Oxaloacetate + GTP → **Phosphoenolpyruvate** + CO_2 + GDP cytosol

The final reaction only occurs when the ATP levels are high in the cell:

ATP + GDP → ADP + GTP

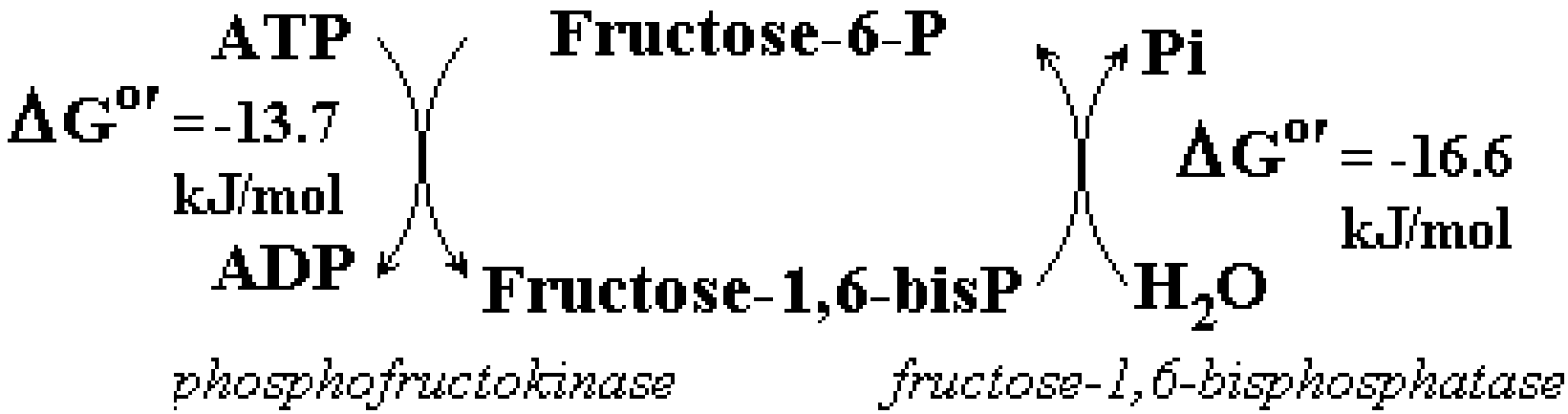
(The carboxylation of pyruvate depends upon the presence of the cofactor biotin.)

Gluconeogenesis

The **second enzymatic bypass** forms fructose-6-phosphate from fructose-1-6-bisphosphate:

Fructose-1,6-bisphosphate + H_2O → Fructose-6-phosphate + Pi

(fructose-1,6-bisphosphatase)



Gluconeogenesis

The **third enzymatic bypass** forms glucose from glucose-6-phosphate:

Glucose-6-phosphate + H_2O → Glucose + Pi.

(Glucose-6-phosphatase)

Only the liver contains glucose-6-phosphatase and can release free glucose into the bloodstream.