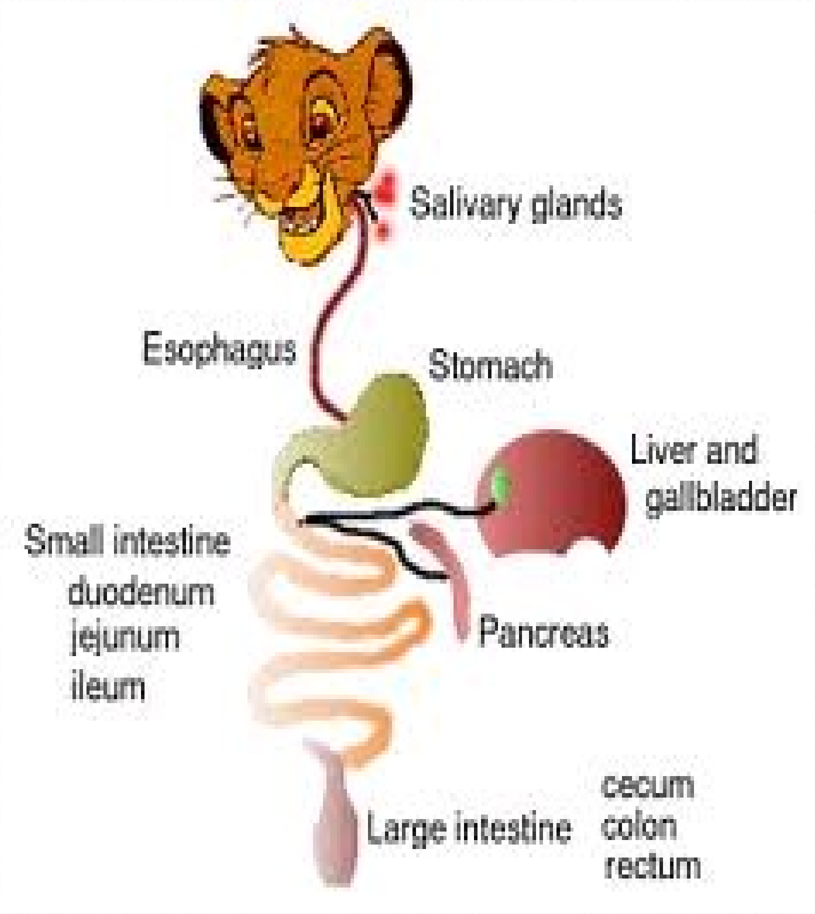
Digestion and Absorption of carbohydrates



Absorption and digestion of carbohydrates

- CHO taken in diet are:
  - polysaccharides,
  - disaccharides
  - monosaccharides
- These are supplied from external sources, hence called exogenous CHO
- These may be
  - digestible or
  - indigestible

- Digestion of CHO takes place in;
  - mouth
  - stomach
  - Intestine
- Absorption takes place form small the intestine

Digestion: Mouth

- At slightly acidic pH, salivary amyalse (ptyalin) acts on starch, which is converted into maltose and isomaltose
- The enzyme get inactivated in stomach

$$2(C_6H_{10}O_5)_n + nH_2O \longrightarrow nC_{12}H_{22}O_{11}$$

starch maltose and isomaltose

Stomach

- HCl can cause hydrolysis of starch into maltose and isomaltose and that of maltose to glucose but the reaction is of little significance inside stomach

Small intestine

In the small intestine pancreatic amylase converts 87% starch to maltose and isomaltose and 13 % glucose

$$(C_6H_{10}O_5)n + nH_2O \longrightarrow nC_6H_{12}O_6$$

- Disaccharides present in brush border of epithelial cells are lactose, sucrose, maltose and isomaltose
- Lactase, sucrase, maltase and isomaltase hydrolyze disaccharides into their components as:

  Sucrose into glucose and fructose

  Maltose into glucose

  Lactose into glucose and galactose

Absorption

- Glucose (80-85%) and few disaccharides are absorbed from small intestine through capillaries of intestinal mucosa
- The order of ease of absorption of monosaccharides is galactose > glucose > fructose > mannose > pentose

Mechanism of absorption

- Simple diffusion
- Active transport

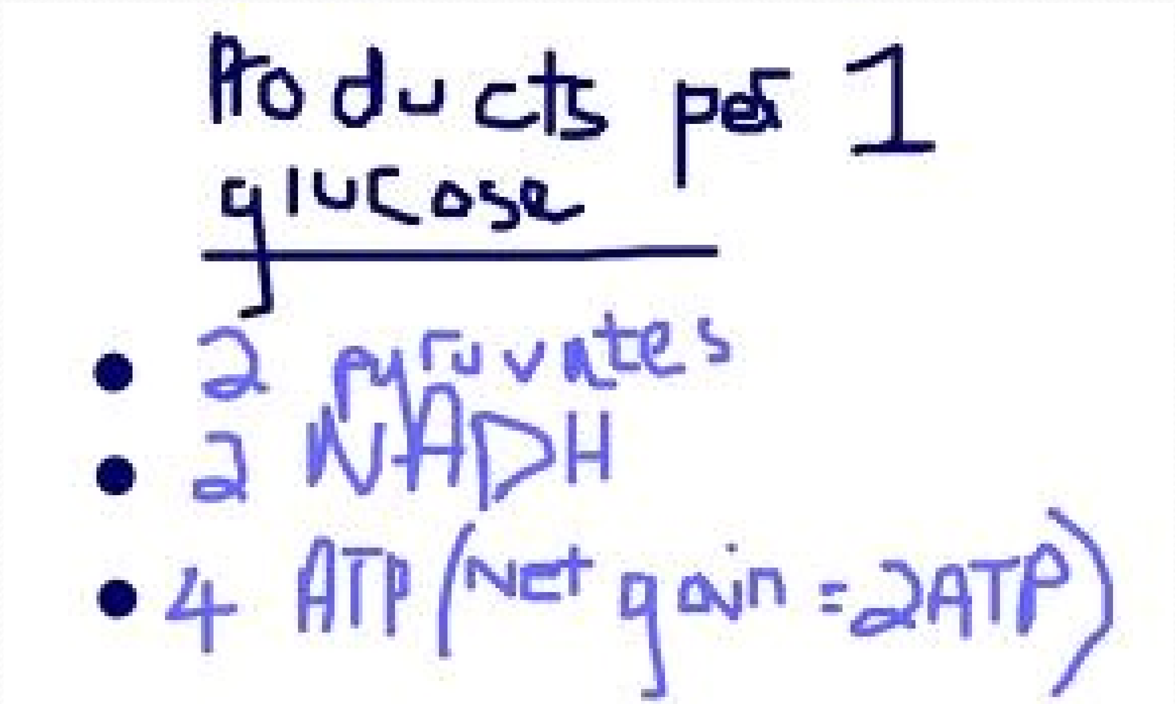
Factors upon which absorption of CHO depends are given as:

- Physical factors (how long food stays in intestine)
- Hormone
  - thyroid hormones increase the rate of absorption
  - hormones of adrenal cortex facilitate absorption

Facts about absorption of monosaccharides

- Chemical nature of the most actively transported monosaccharides has following features in the choice of the carrier:
  - Presence of 6 and more carbon atoms
  - D-pyarnose structure
  - Intact OH at carbon 2

Glycolysis



- Glucose and glycogen are broken down in the body by a complex chain of reactions catalyzed by many enzymes
- There are many metabolic pathways by which glucose can be utilized in the body; the most important one is the Embden-Meyerhof pathway followed by citric acid cycle
- Glycolysis is of two types:
  - anaerobic and
  - aerobic

Anaerobic glycolysis

- It takes place in cytosol (extra-mitochondrial)
- Glucose is broken into two molecules of pyruvic acid, which is then converted into lactic acid by utilizing NADH/H^+
- It can not continue indefinitely;
  - lactic acid lowers the pH to a level that is not suitable for cellular function
  - On the other hand NADH/H^+ becomes unavailable, if aerobic metabolism remains suspended for a long time

Aerobic glycolysis

- In the presence of oxygen the pyruvic acid is formed in the same way as anaerobic glycolysis but it does not give rise to lactic acid
- Pyruvic acid is converted into acetyle-CoA which then enters in citric acid cycle
- Reactions of citric acid cycle occur in mitochondria

Main Features

- The oldest of the Pathways
- Occurs in Soluble Phase of Cytoplasm (Cytosol)
- Anaerobic Phase Energy
- Generates ATP
- Produces Pyruvate/Lactate
- Produces Many Important Intermediates of other Pathways

Relationship to Other Pathways

- TCA Cycle
- Gluconeogenesis (in Liver and Kidney)
- Hexose Monophosphate Shunt (HMP)
- Metabolism of other Sugars, e.g., Fructose and Galactose
- Metabolism of certain amino acids
- Lipid metabolism
- Glycoprotein Synthesis

Transport of glucose into the cell

- Transportation of glucose is mediated by two types of systems that are given as follows:

1- Insulin-independent transport system

Hepatocytes, erythrocytes and brain cells do not need insulin for the entry of glucose. Transport occurs by a protein, which is an oligomer (MW 200,000) containing 4 sub-units of equal size

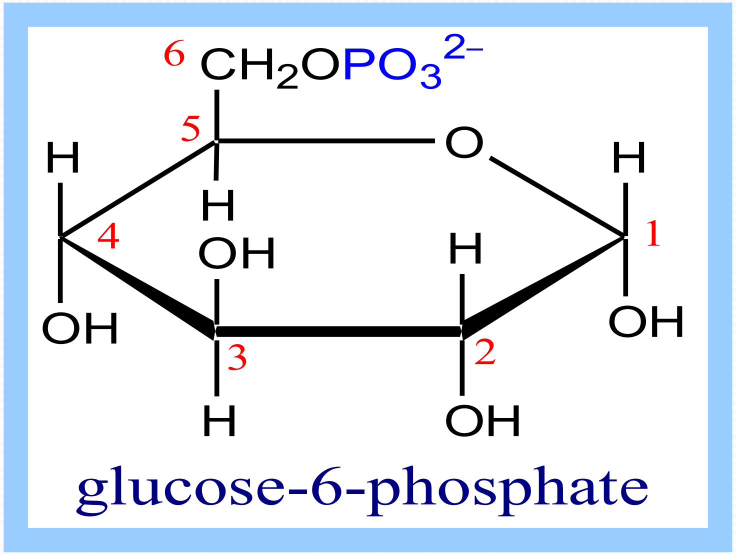
Transport of glucose into the cell

2- Insulin-dependent transport system

It occurs in muscles and adipose tissue cells. The binding of insulin to the receptors enhances the transport of glucose into cell by causing

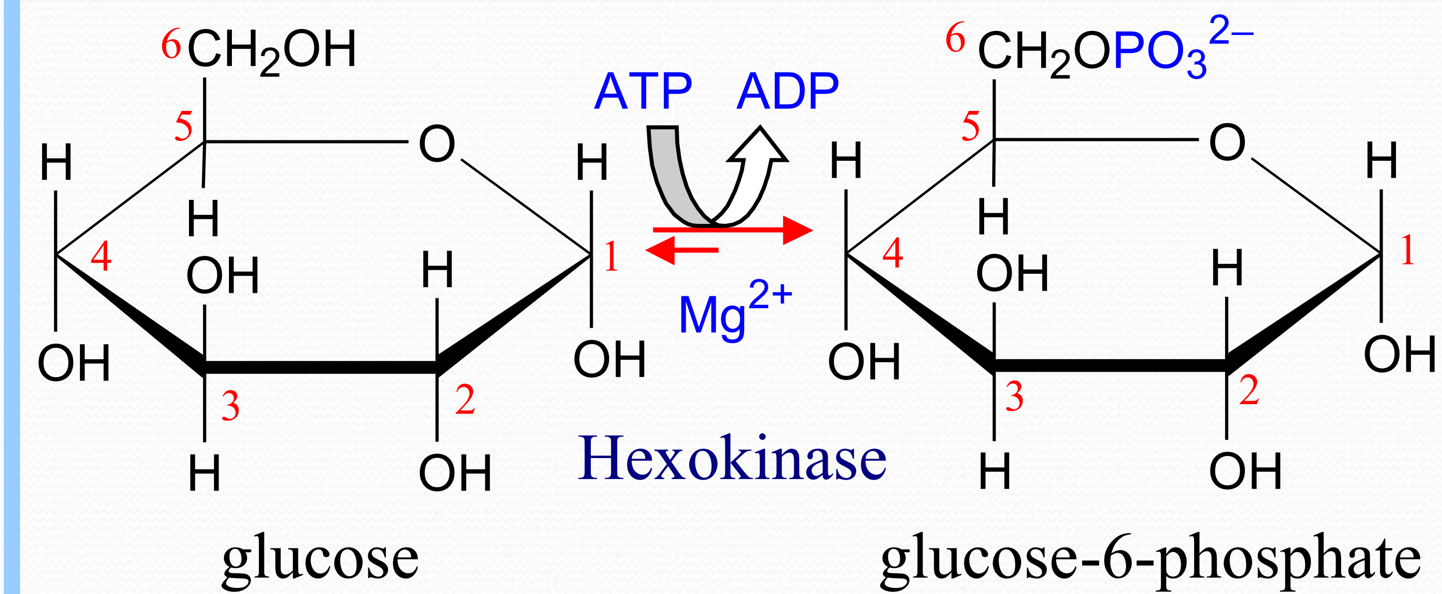
- migration of glucose transport protein from microsomes to plasma membrane
- and by increasing transport capacity of the transport proteins

Glycolysis (Embden-Meyerhof pathway)



Glycolysis takes place in the cytosol of the cells

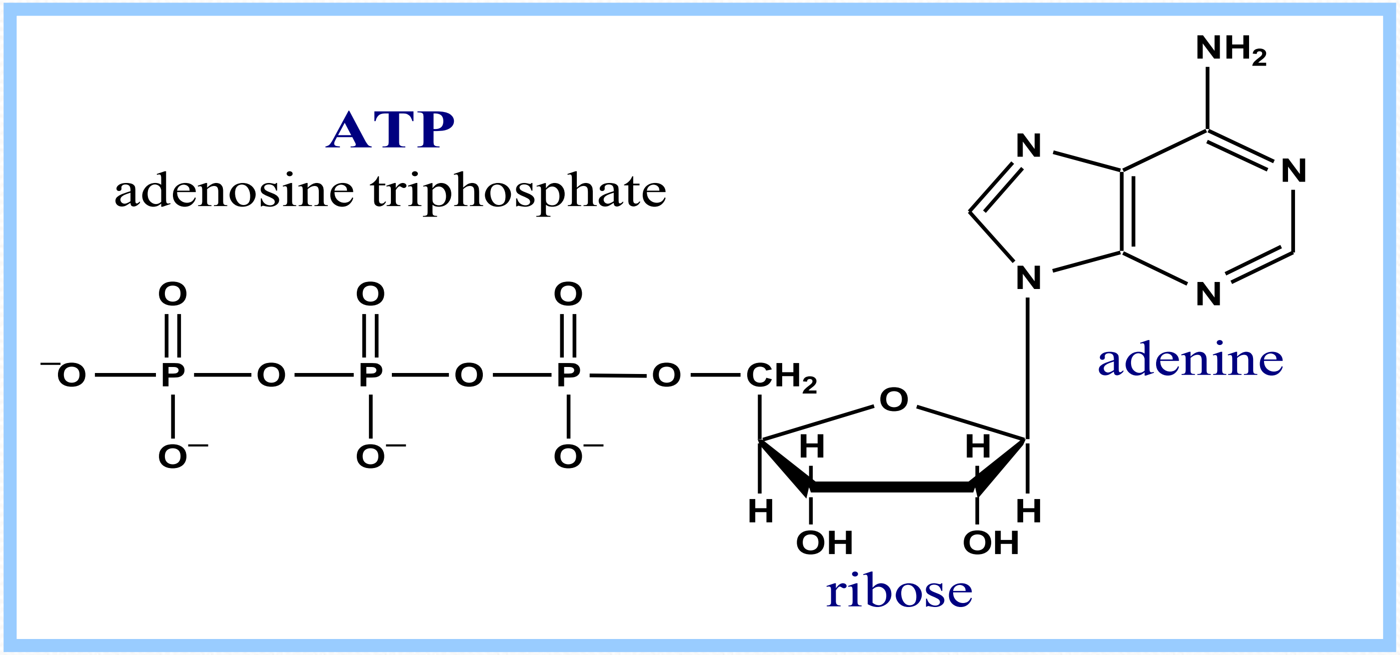
Glucose enters the glycolysis pathway by conversion to glucose-6-phosphate, which is initially an energy consuming step; energy input corresponding to one ATP



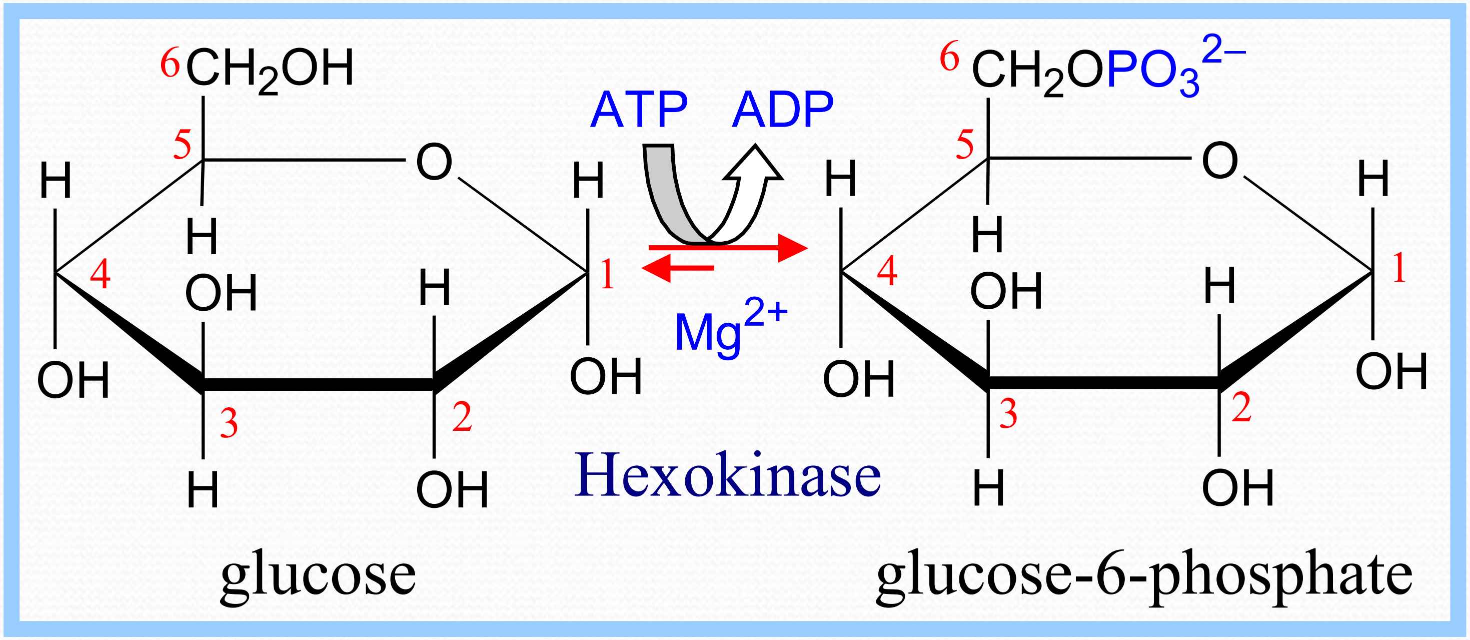
1. **Hexokinase** catalyzes:

Glucose + ATP → glucose-6-P + ADP

The reaction involves nucleophilic attack of C-6 hydroxyl of glucose by P of the terminal phosphate of ATP. ATP binds to the enzyme as a complex with **Mg**$^{++}$



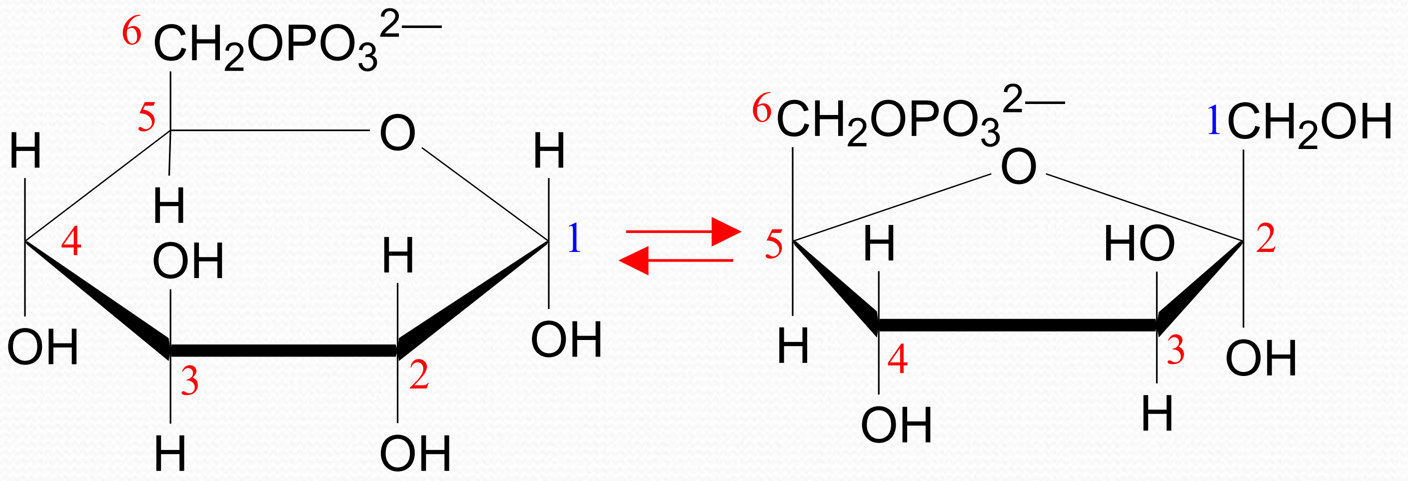
Mg++ interacts with negatively charged phosphate oxygen atoms, providing charge compensation & promoting a favorable conformation of ATP at the active site of the Hexokinase enzyme



The reaction catalyzed by Hexokinase is highly spontaneous

A phosphoanhydride bond of ATP (**~P**) is cleaved

The phosphate ester formed - glucose-6-phosphate - has a lower ΔG of hydrolysis

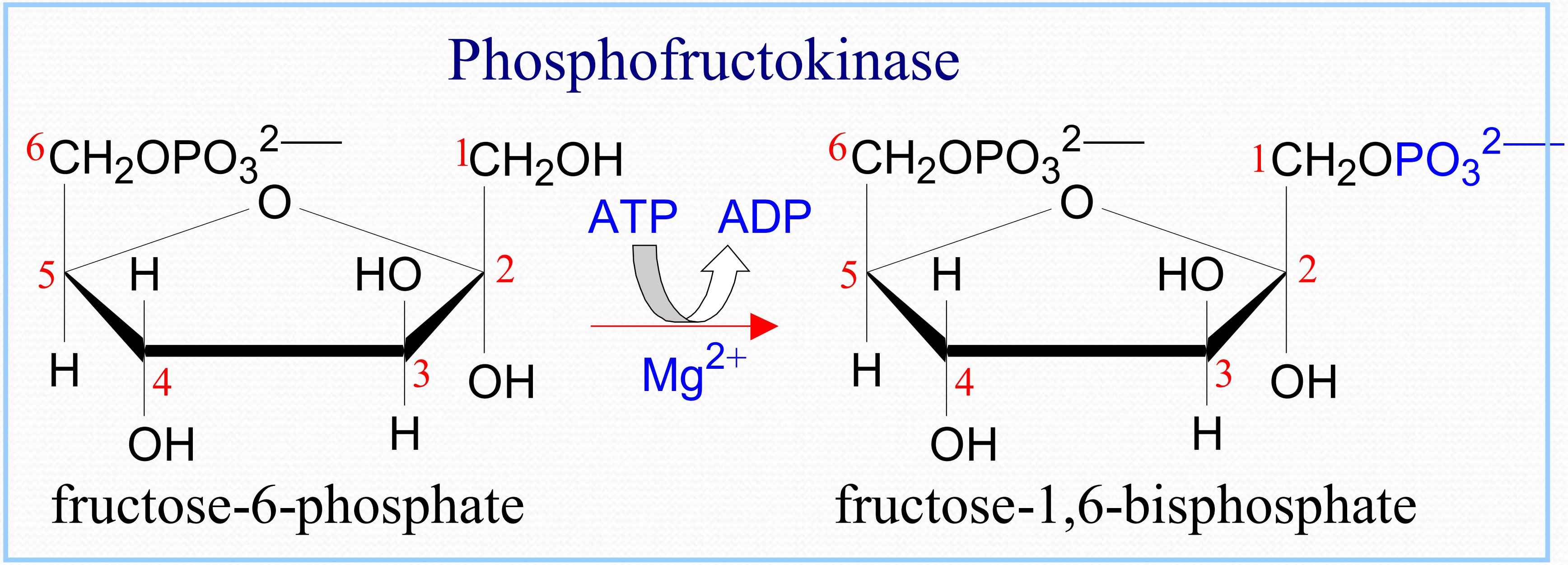


Phosphoglucose Isomerase

glucose-6-phosphate fructose-6-phosphate

2. Phosphoglucose Isomerase catalyzes:

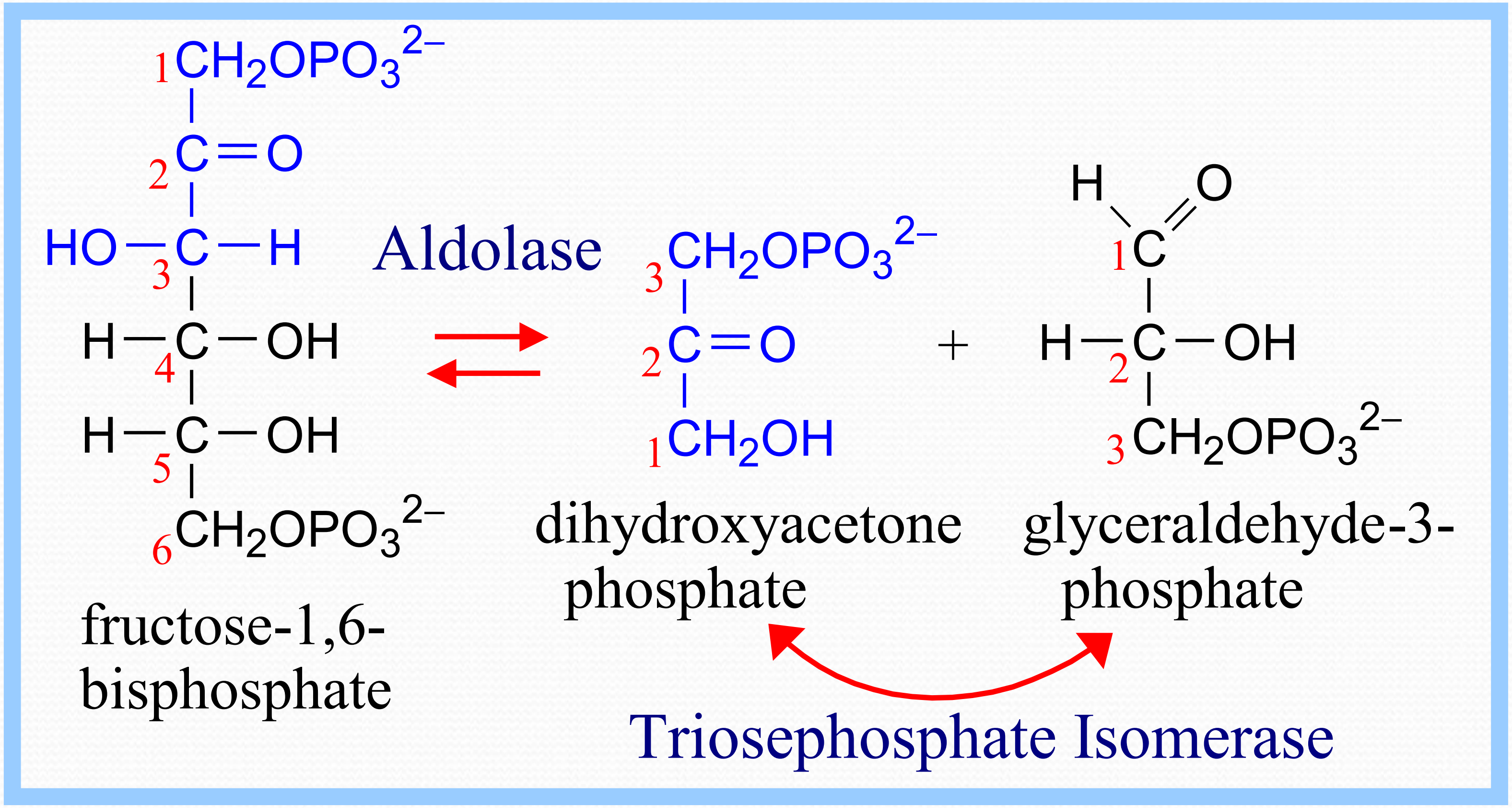
glucose-6-P (aldose) ←→ **fructose-6-P** (ketose)



3. Phosphofructokinase catalyzes:

fructose-6-P + ATP → fructose-1,6-bisP + ADP

The Phosphofructokinase reaction is the rate-limiting step of Glycolysis.

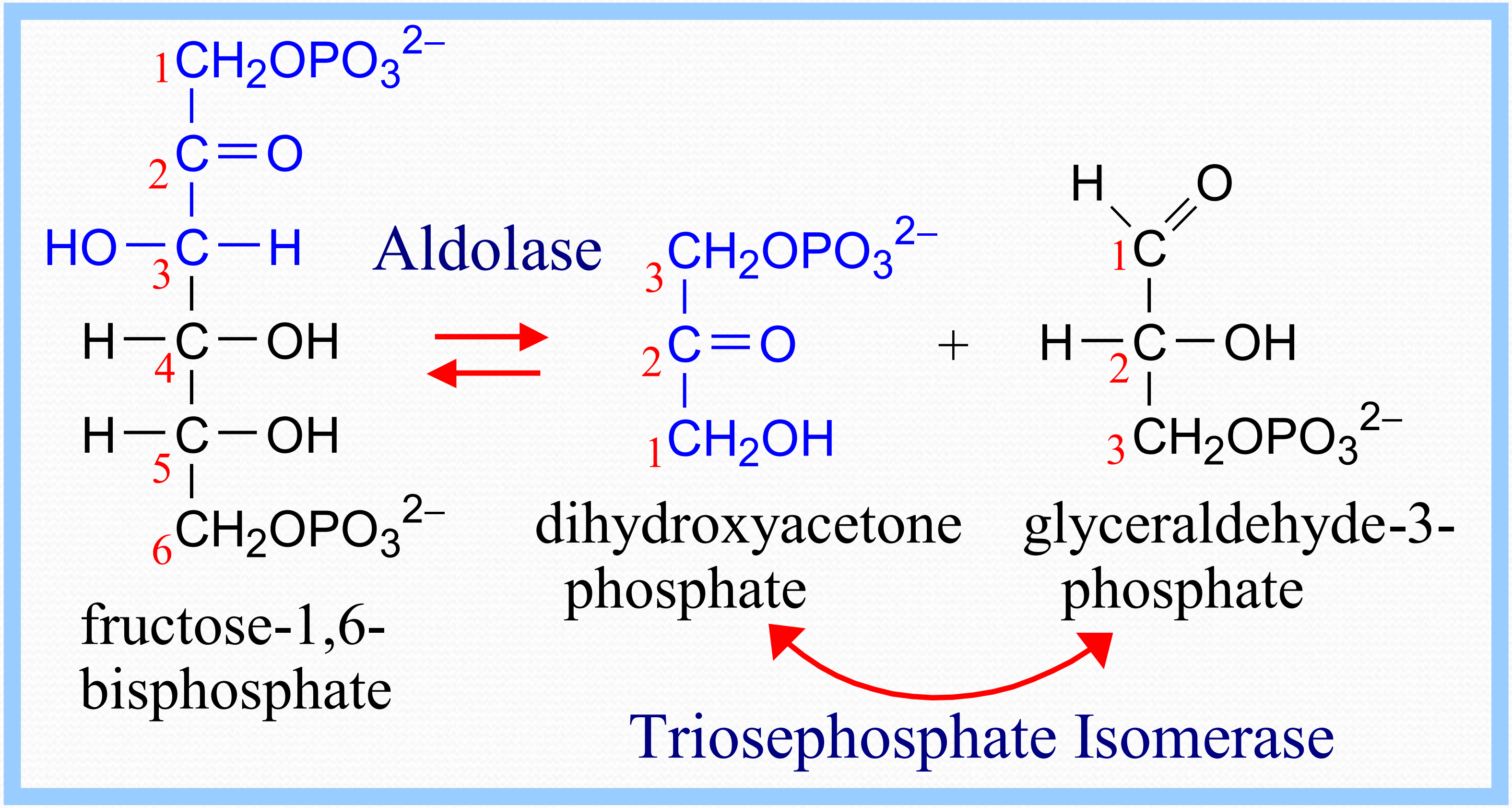


4. Aldolase catalyzes:

fructose-1,6-bisphosphate ←→

dihydroxyacetone-P + glyceraldehyde-3-P

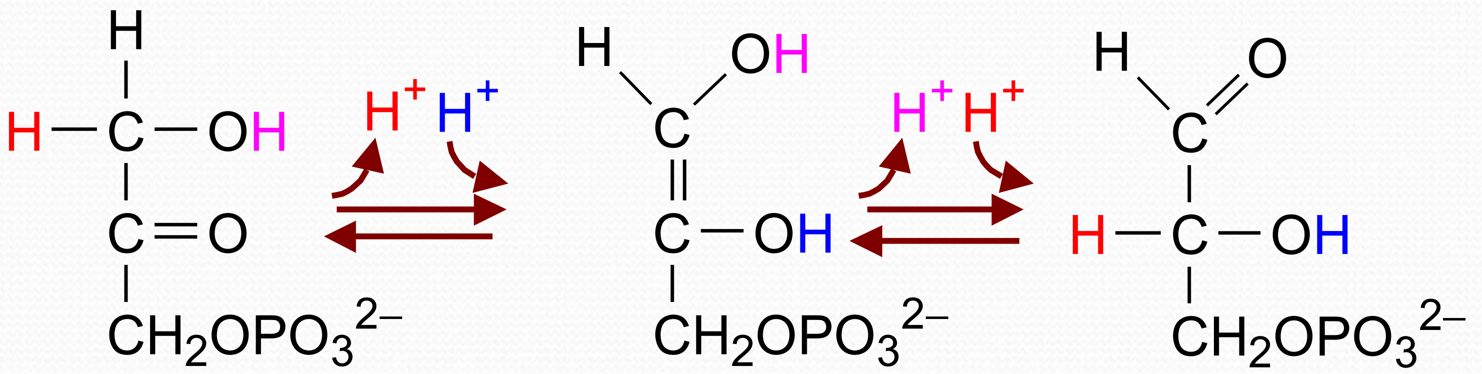
The reaction is an **aldol cleavage**, the reverse of an aldol condensation.



5. Triose Phosphate Isomerase catalyzes:

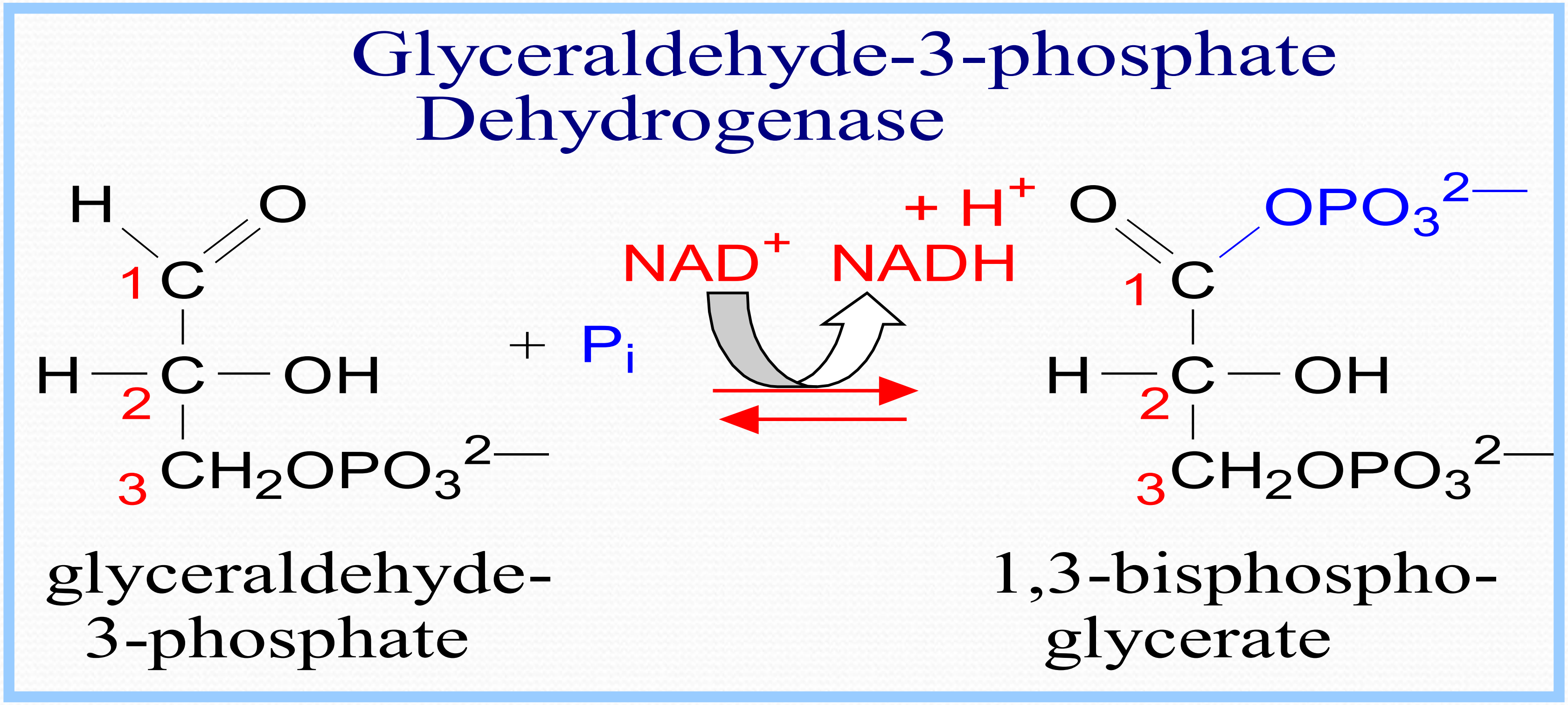
dihydroxyacetone-P ←→ glyceraldehyde-3-P

Triosephosphate Isomerase



dihydroxyacetone phosphate — enediol intermediate — glyceraldehyde-3-phosphate

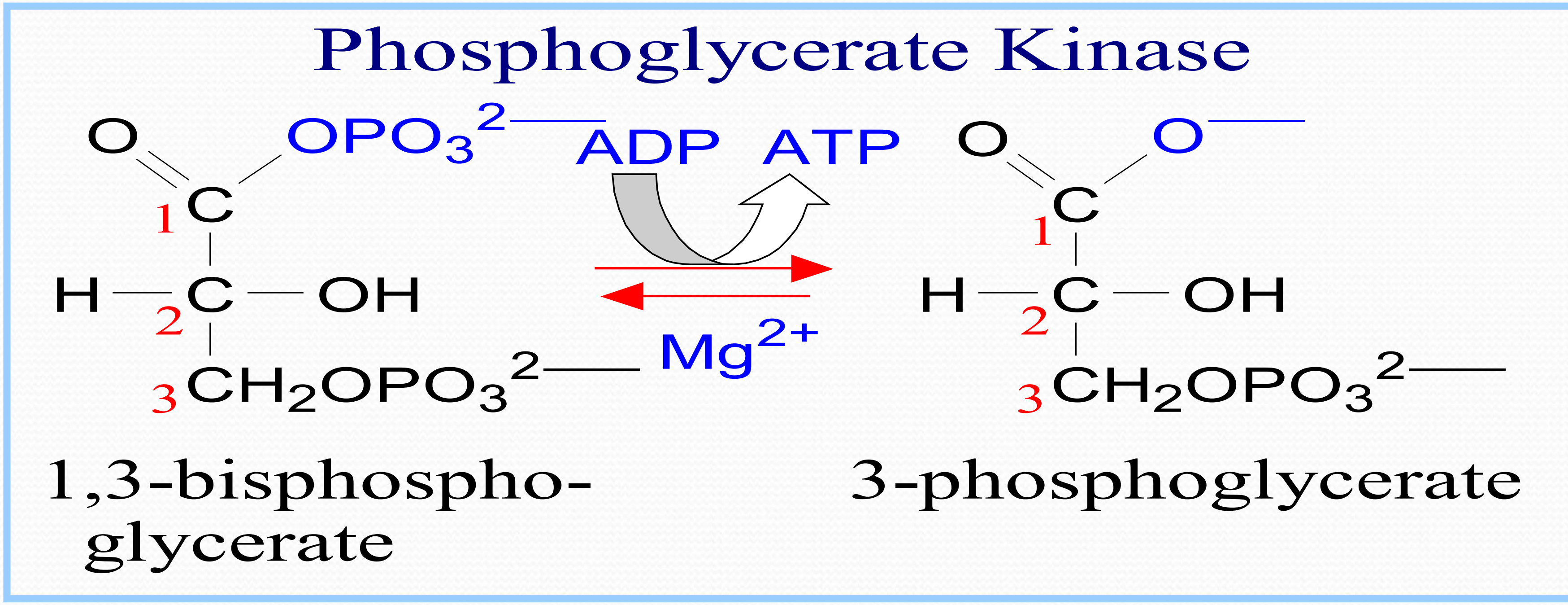
The ketose/aldose conversion involves acid/base catalysis, and is thought to proceed via an enediol intermediate, as with Phosphoglucose Isomerase.



6. Glyceraldehyde-3-phosphate Dehydrogenase catalyzes:

glyceraldehyde-3-P + NAD^+ + P_i ←→

1,3-bisphosphoglycerate + NADH + H^+

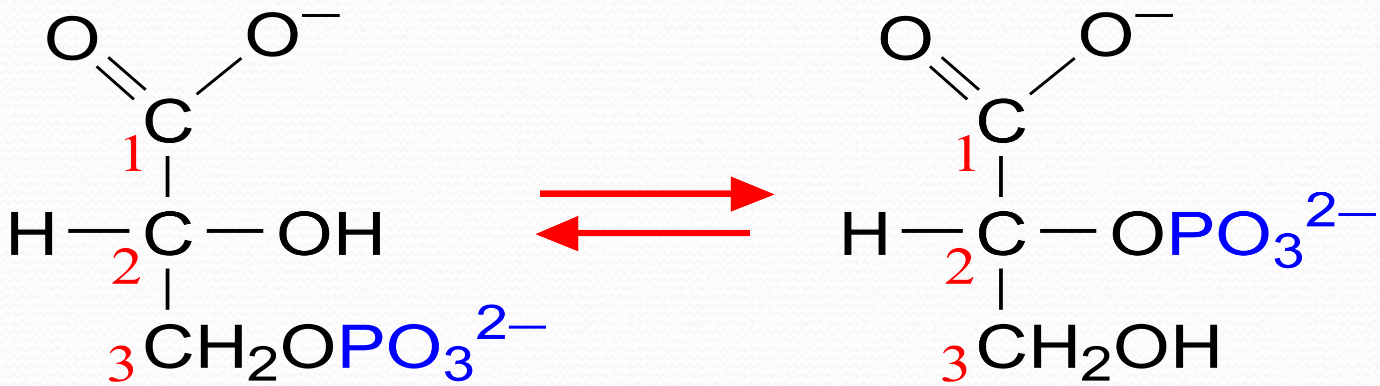


7. Phosphoglycerate Kinase catalyzes:

1,3-bisphosphoglycerate + ADP ←→

3-phosphoglycerate + ATP

Phosphoglycerate Mutase

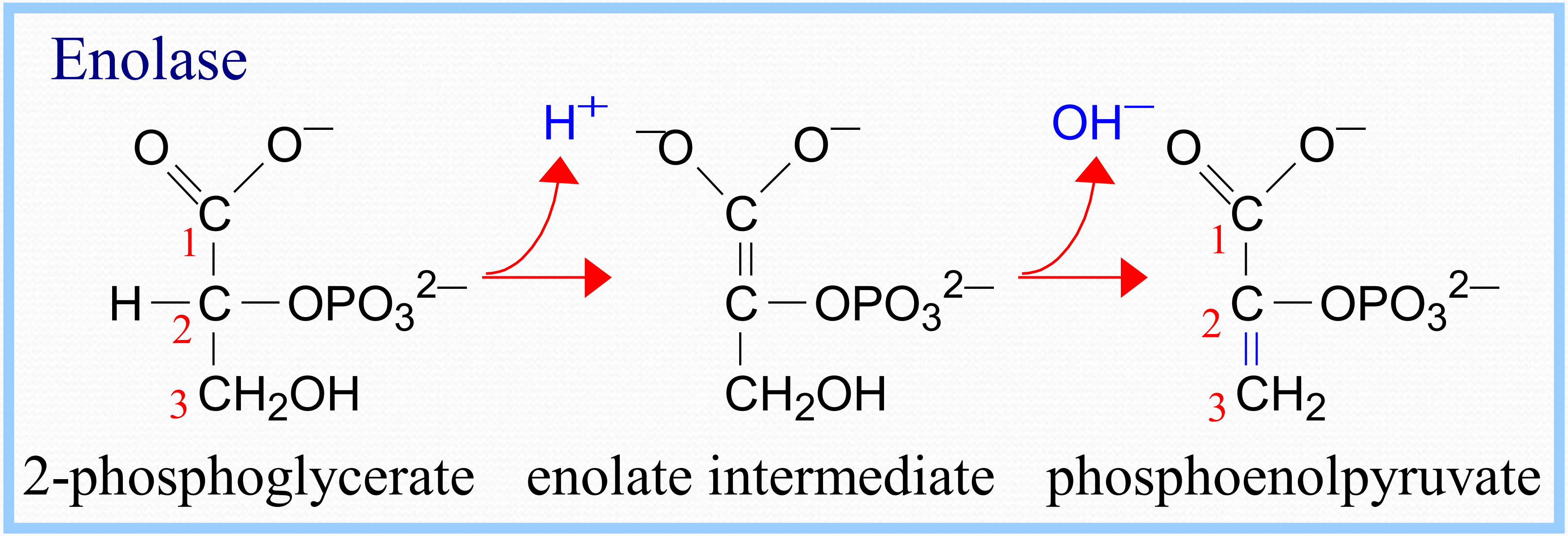


3-phosphoglycerate 2-phosphoglycerate

8. Phosphoglycerate Mutase catalyzes:

3-phosphoglycerate ←→ 2-phosphoglycerate

Phosphate is shifted from the OH on C3 to the OH on C2.

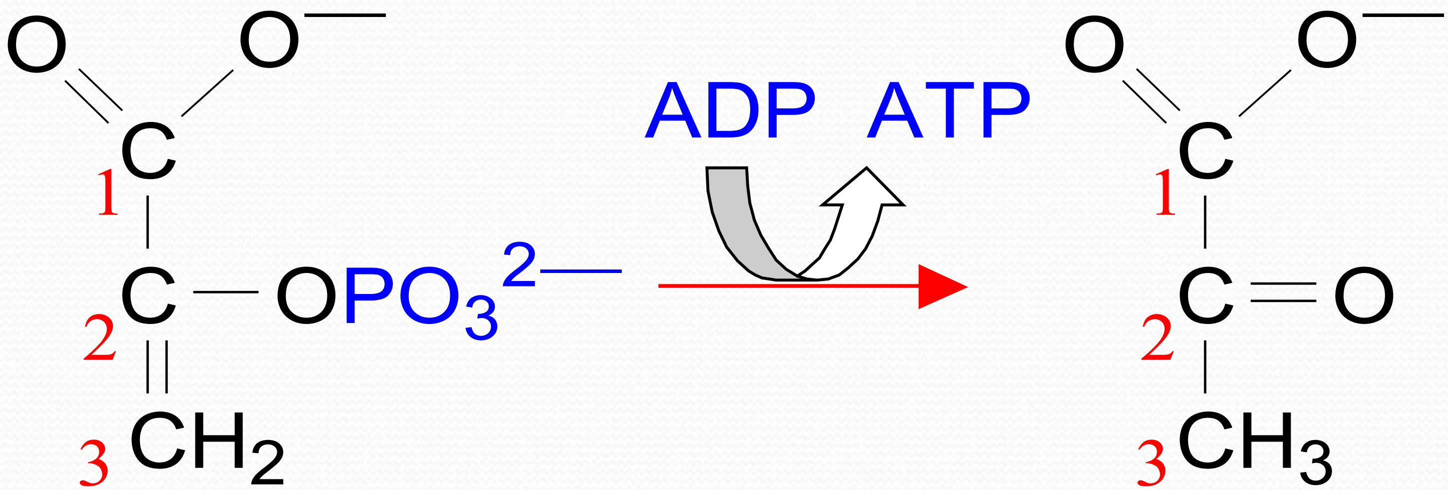


9. Enolase catalyzes:

2-phosphoglycerate ←→ phosphoenolpyruvate + H_2O

This dehydration reaction is **Mg^{++}- dependent**.

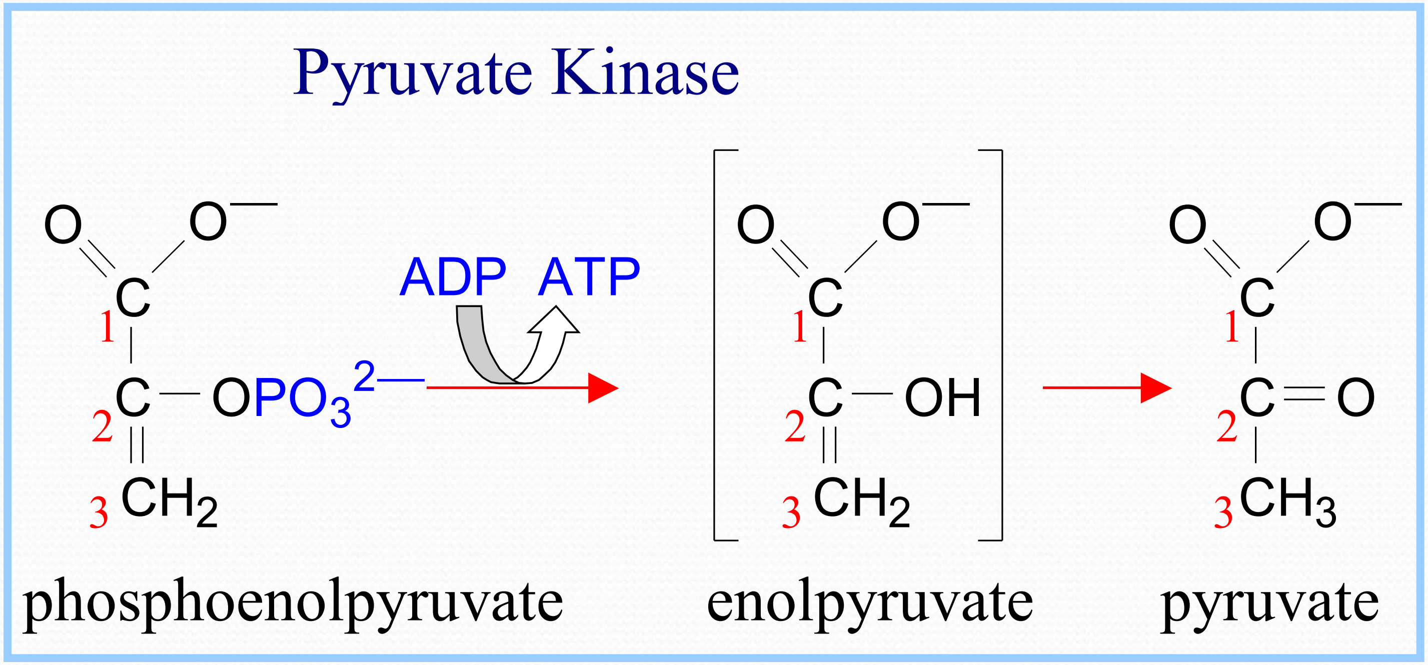
Pyruvate Kinase



phosphoenolpyruvate pyruvate

10. Pyruvate Kinase catalyzes:

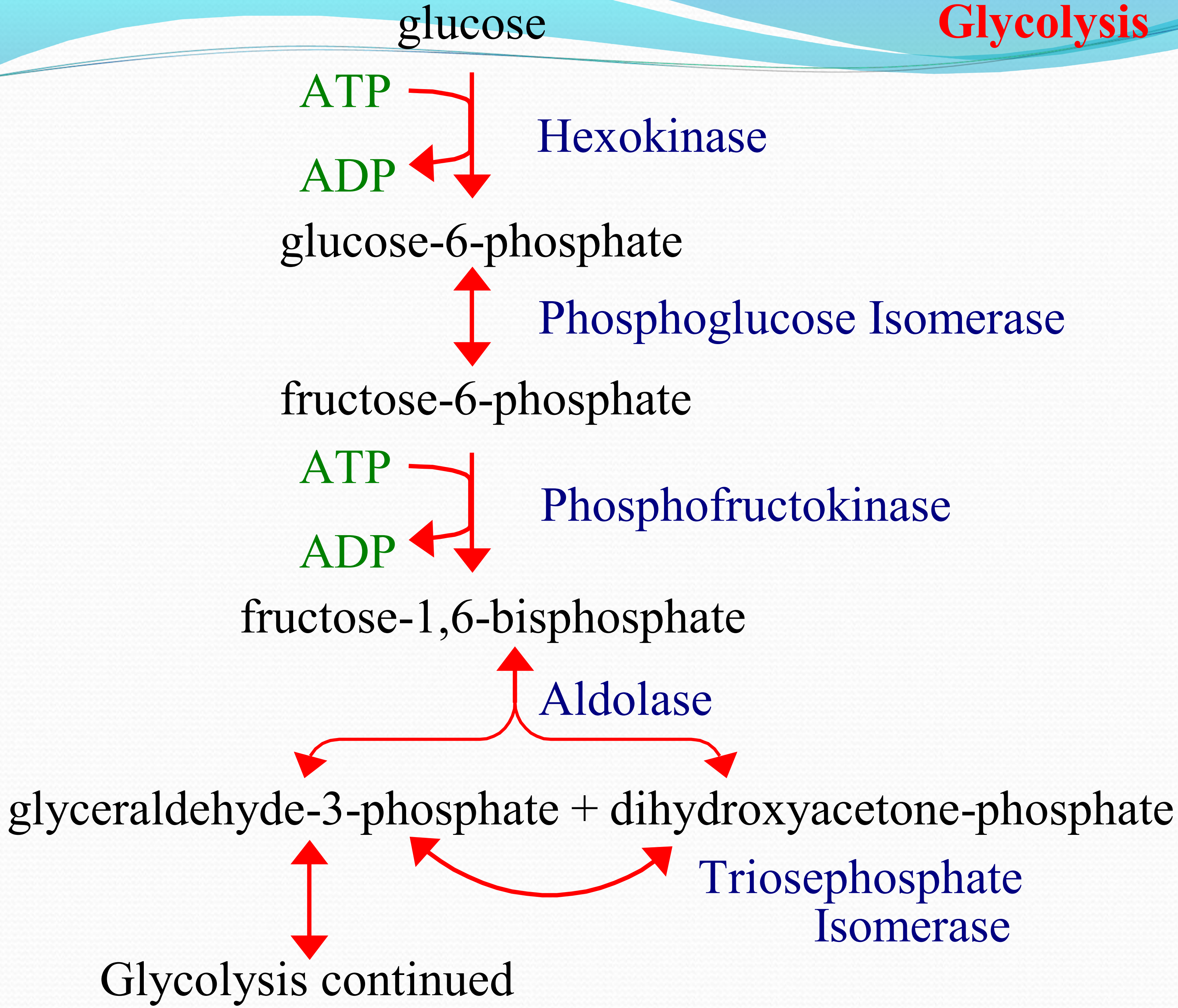
phosphoenolpyruvate + ADP → pyruvate + ATP

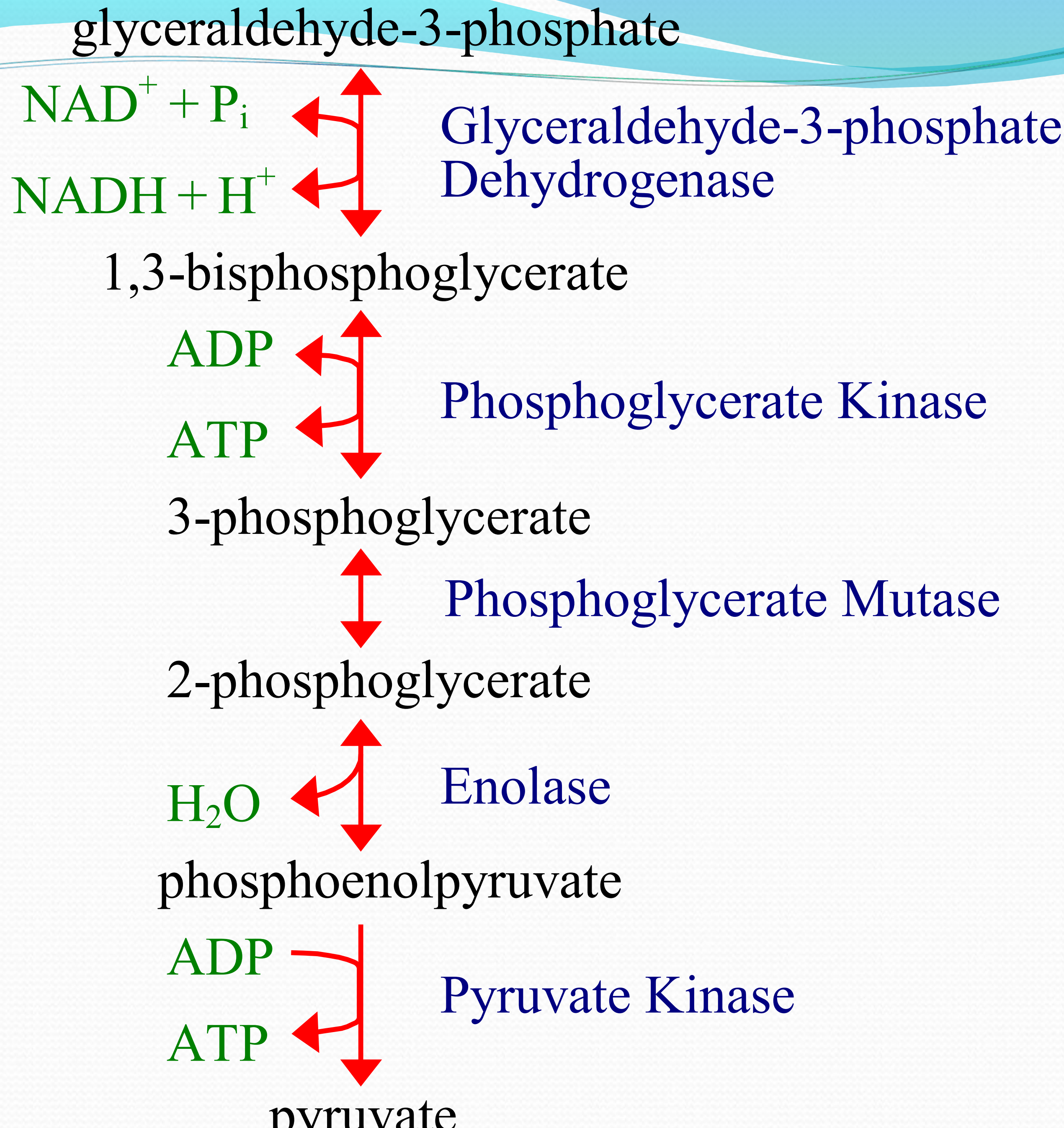


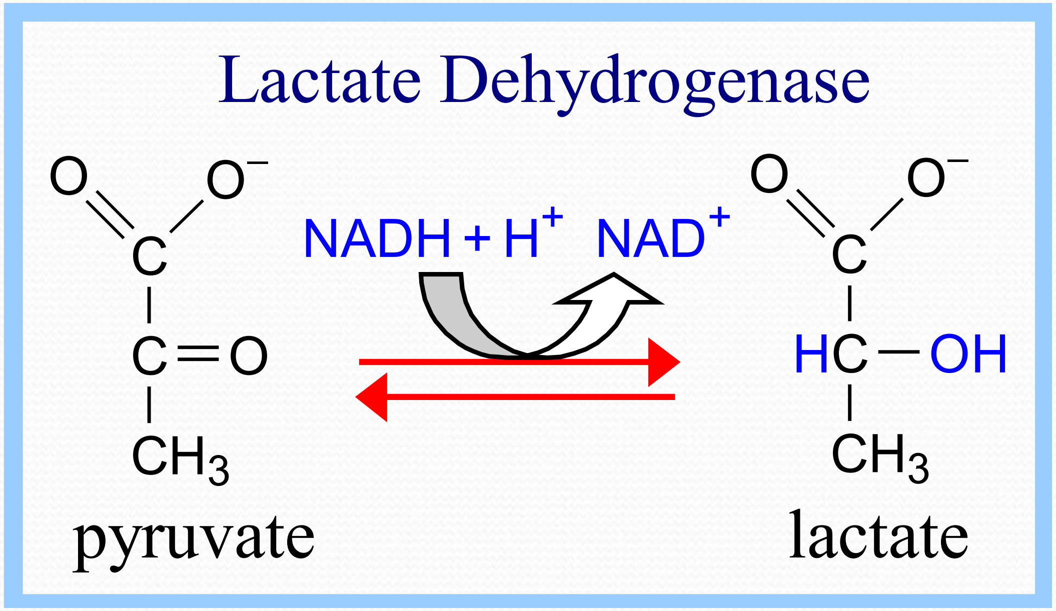
This phosphate transfer from PEP to ADP is **spontaneous**

- PEP has a larger ΔG of phosphate hydrolysis than ATP
- Removal of P_i from PEP yields an unstable enol, which spontaneously converts to the keto form of pyruvate

Glycolysis


glucose
ATP
ADP
Hexokinase
glucose-6-phosphate
Phosphoglucose Isomerase
fructose-6-phosphate
ATP
ADP
Phosphofructokinase
fructose-1,6-bisphosphate
Aldolase
glyceraldehyde-3-phosphate + dihydroxyacetone-phosphate
Triosephosphate Isomerase
Glycolysis continued

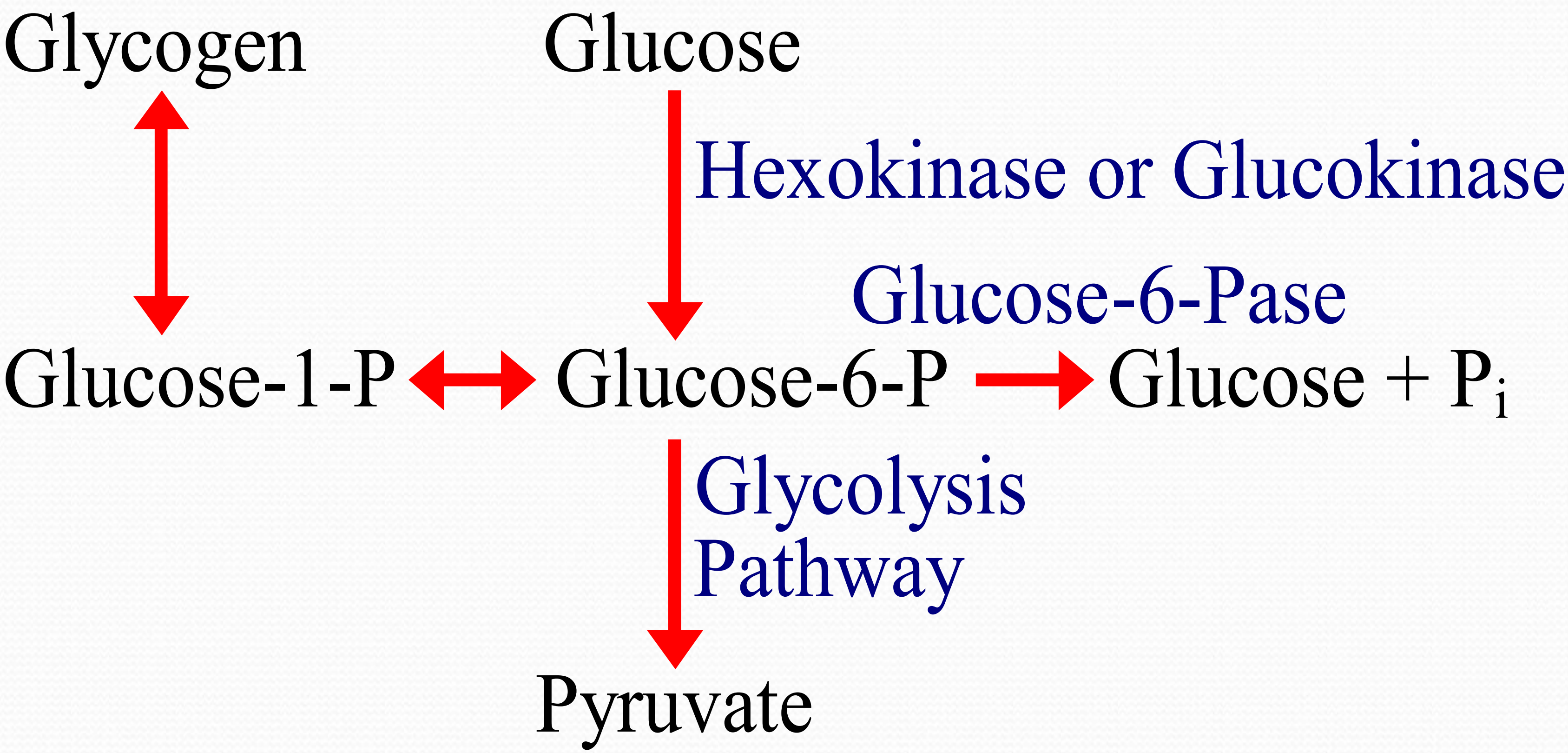

glyceraldehyde-3-phosphate
$NAD^+ + P_i$
$NADH + H^+$
Glyceraldehyde-3-phosphate Dehydrogenase
1,3-bisphosphoglycerate
ADP
ATP
Phosphoglycerate Kinase
3-phosphoglycerate
Phosphoglycerate Mutase
2-phosphoglycerate
H_2O
Enolase
phosphoenolpyruvate
ADP
ATP
Pyruvate Kinase
pyruvate



E.g., **Lactate Dehydrogenase** catalyzes **reduction** of the keto in **pyruvate** to a hydroxyl, yielding **lactate**, as NADH is oxidized to NAD^+.

Lactate, in addition to being an end-product of fermentation, serves as a **mobile** form of **nutrient energy**, & possibly as a **signal** molecule in mammalian organisms.

Cell membranes contain **carrier** proteins that facilitate transport of lactate.



Glucose metabolism in liver.

Energy from glycolysis

ATP consumed	2 moles
ATP produced direct	4 moles
ATP indirect (NADH/H)	6 moles
Net ATPs =	10-2= 8 moles
If anaerobic glycolysis	2 moles