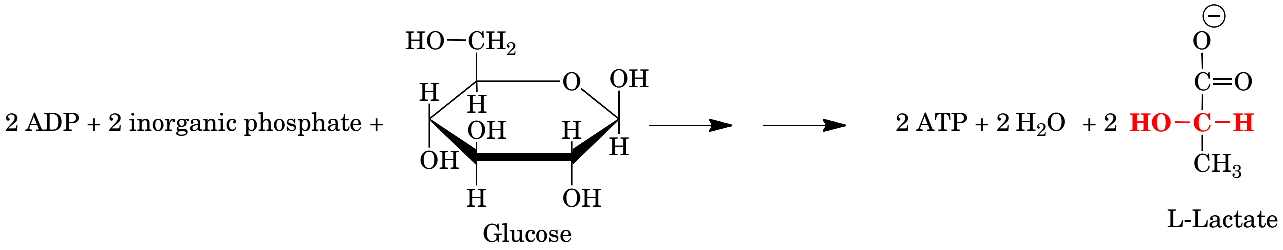
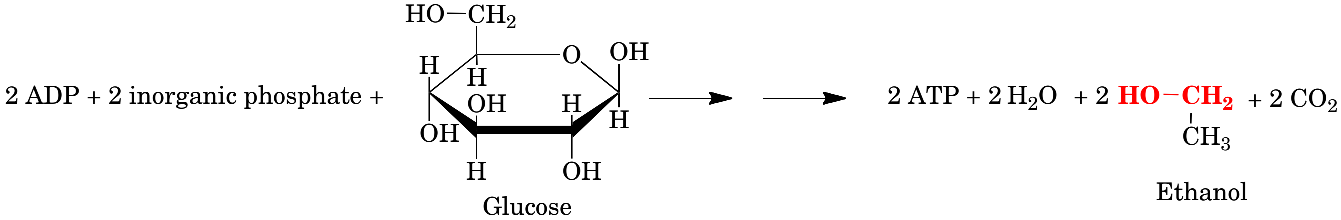
# Glycolysis and Fermentation





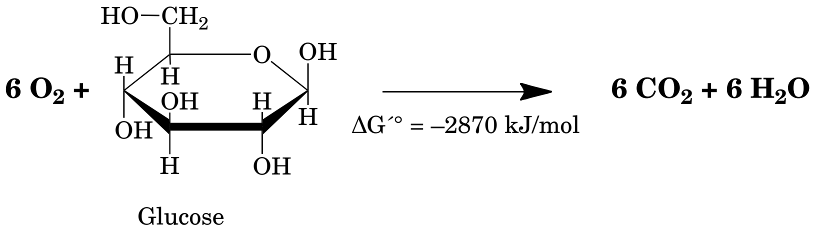
2 ADP + 2 inorganic phosphate $\longrightarrow$ 2 ATP + 2 $H_2O$   $\Delta G'^\circ = +61.0$ kJ/mol

Glucose $\longrightarrow$ 2 L-Lactic acid   $\Delta G'^\circ = -183.6$ kJ/mol

---

**Overall Process**

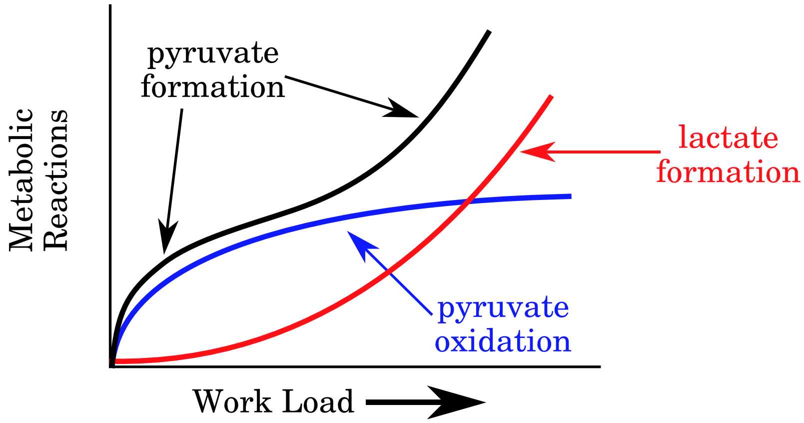
Glucose +
2 ADP + 2 inorganic phosphate $\longrightarrow$ 2 L-Lactic acid+
2 ATP + 2 $H_2O$   $\Delta G'^\circ = -122.6$ kJ/mol



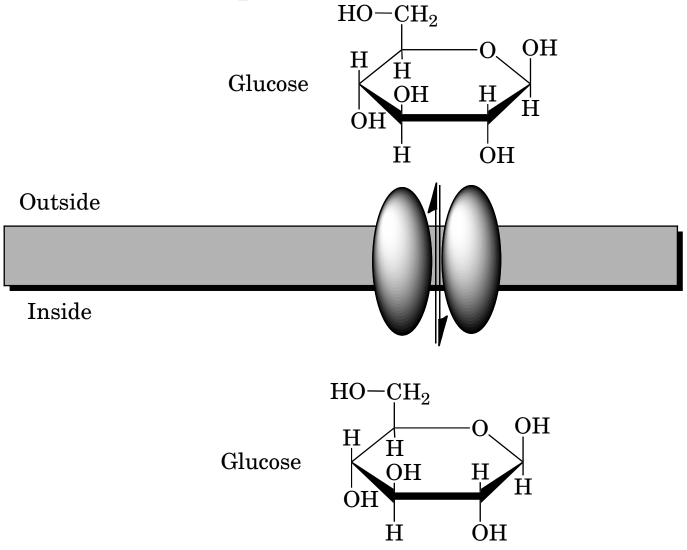
## Pyruvate and Lactate

Glucose + 2 ADP + 2 phosphate → 2 **Pyruvate** + 2 ATP + 2 $H_2O$
**+ 2 NAD** **+ 2 NADH**

Glucose + 2 ADP + 2 phosphate → 2 **L-Lactic acid** + 2 ATP + 2 $H_2O$



## Glucose Transport

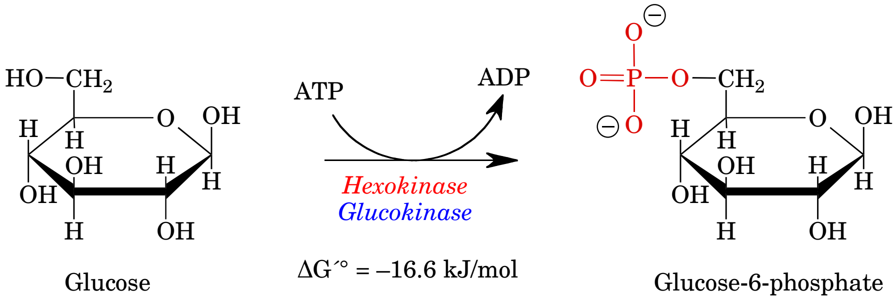


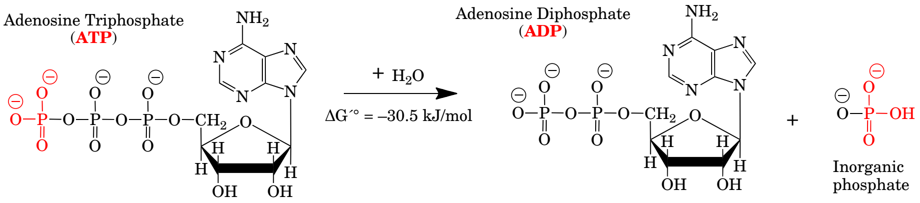
Most cells:

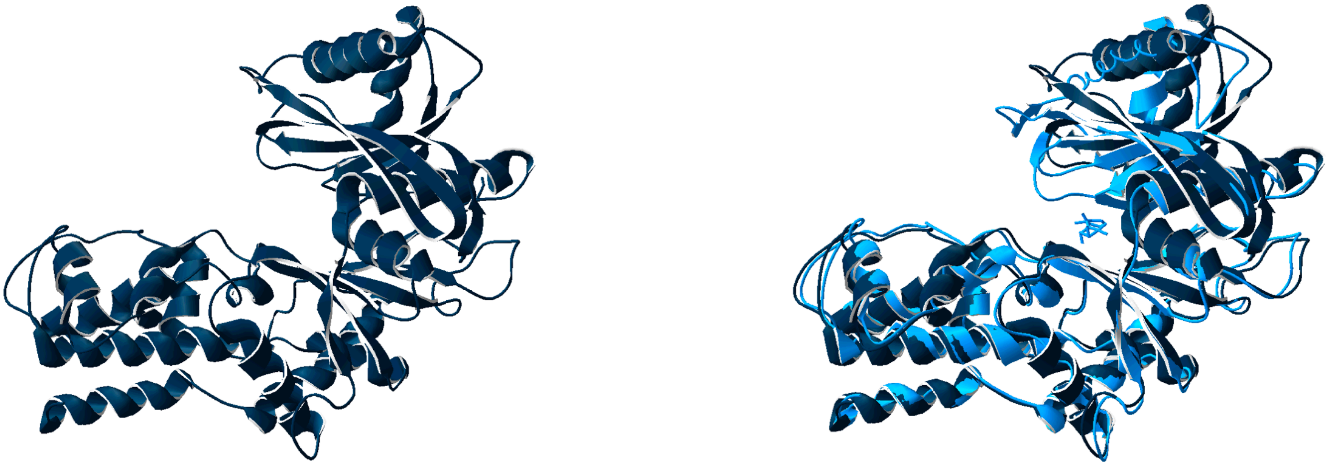
Skeletal Muscle & Adipose Tissue:

Liver:

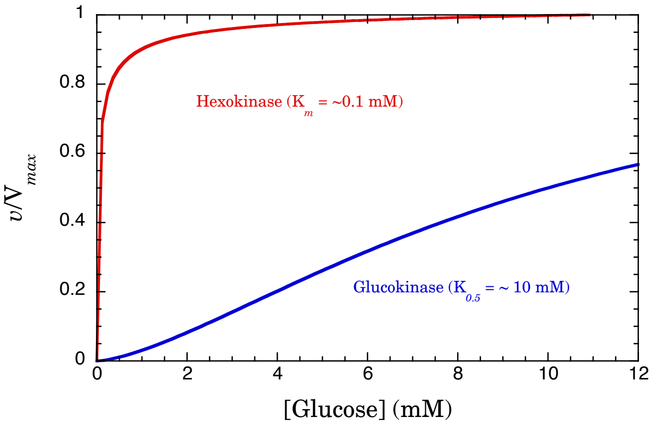
## Glucose Phosphorylation



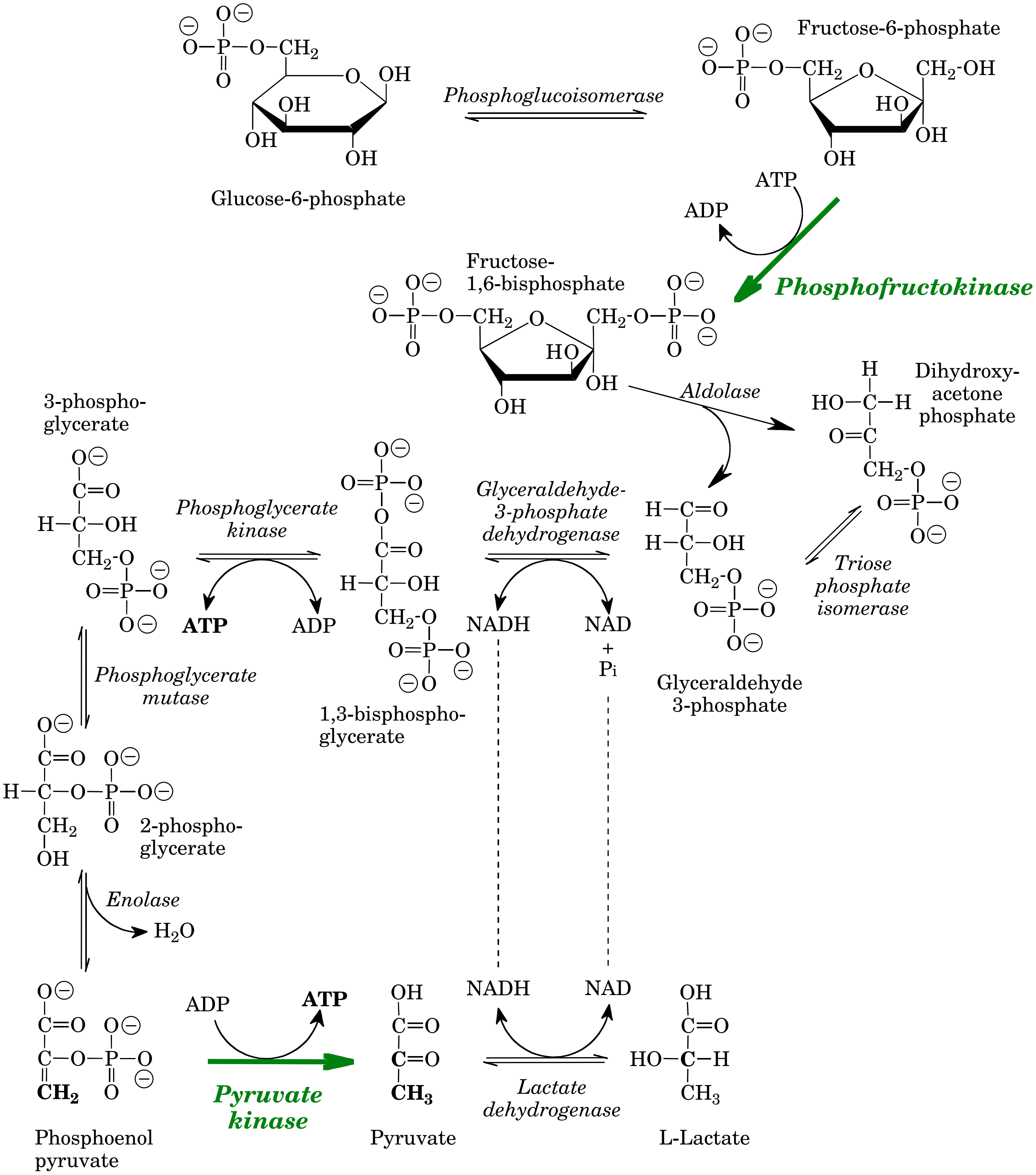


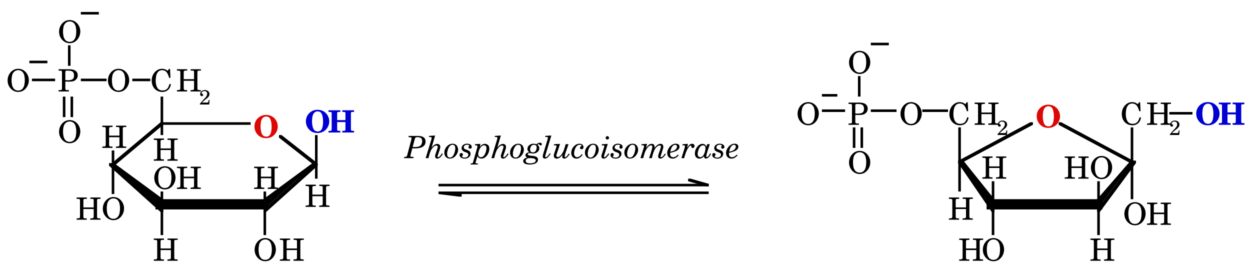


*Saccharomyces cerevisiae* hexokinase structures from pdb ID 2YHX (left) and 2YHX superimposed on 1HKG (right)



# Glycolysis

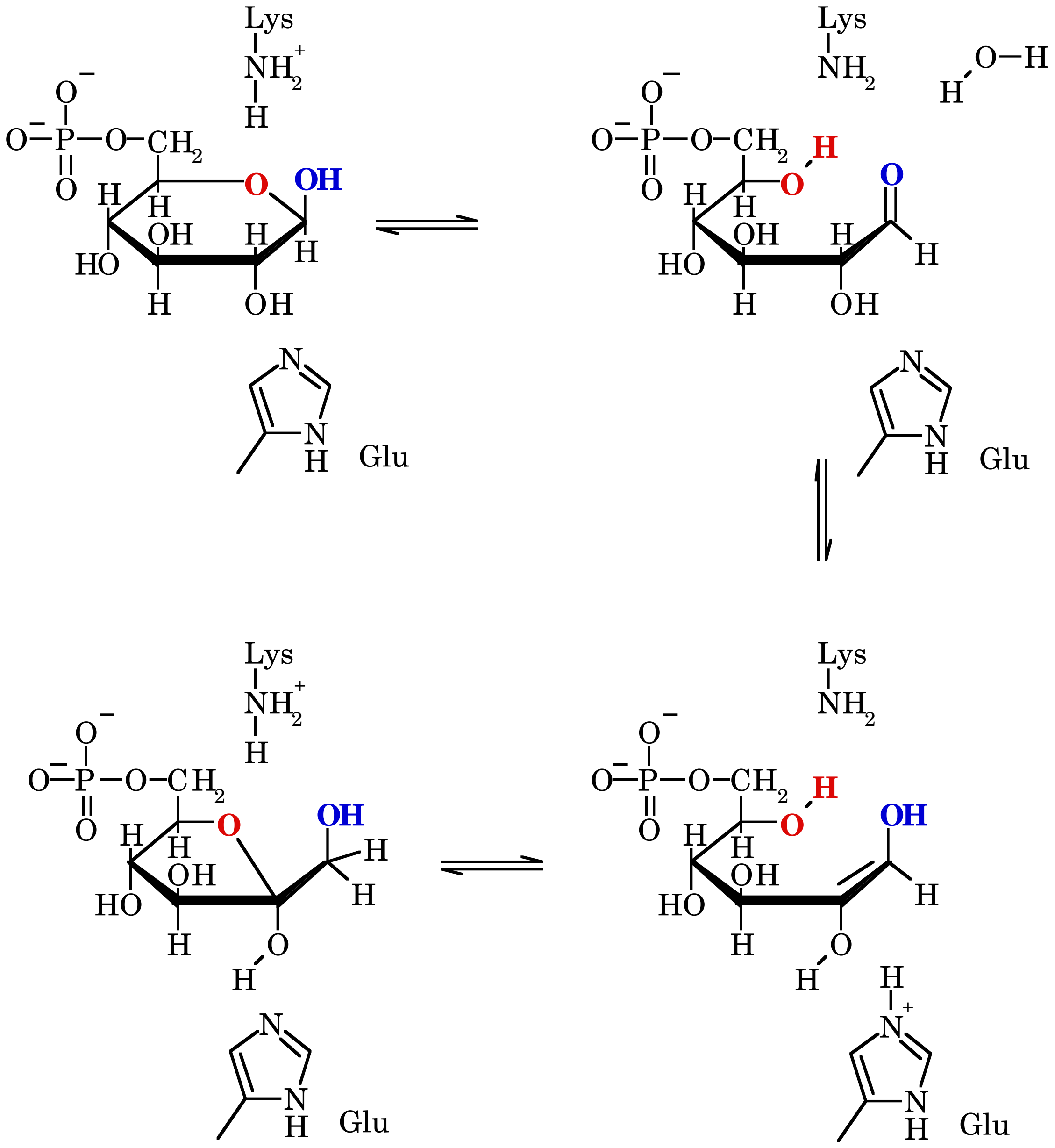

Glucose-6-phosphate
Phosphoglucoisomerase
Fructose-6-phosphate
ATP
ADP
Phosphofructokinase
Fructose-1,6-bisphosphate
Aldolase
Dihydroxyacetone phosphate
Triose phosphate isomerase
Glyceraldehyde 3-phosphate
Glyceraldehyde-3-phosphate dehydrogenase
NADH
NAD + Pi
1,3-bisphosphoglycerate
Phosphoglycerate kinase
ATP
ADP
3-phosphoglycerate
Phosphoglycerate mutase
2-phosphoglycerate
Enolase
H2O
Phosphoenol pyruvate
ADP
ATP
Pyruvate kinase
Pyruvate
NADH
NAD
Lactate dehydrogenase
L-Lactate

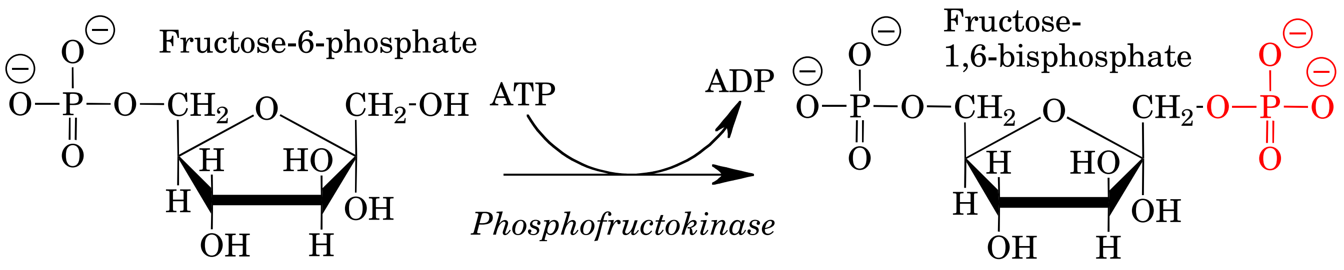


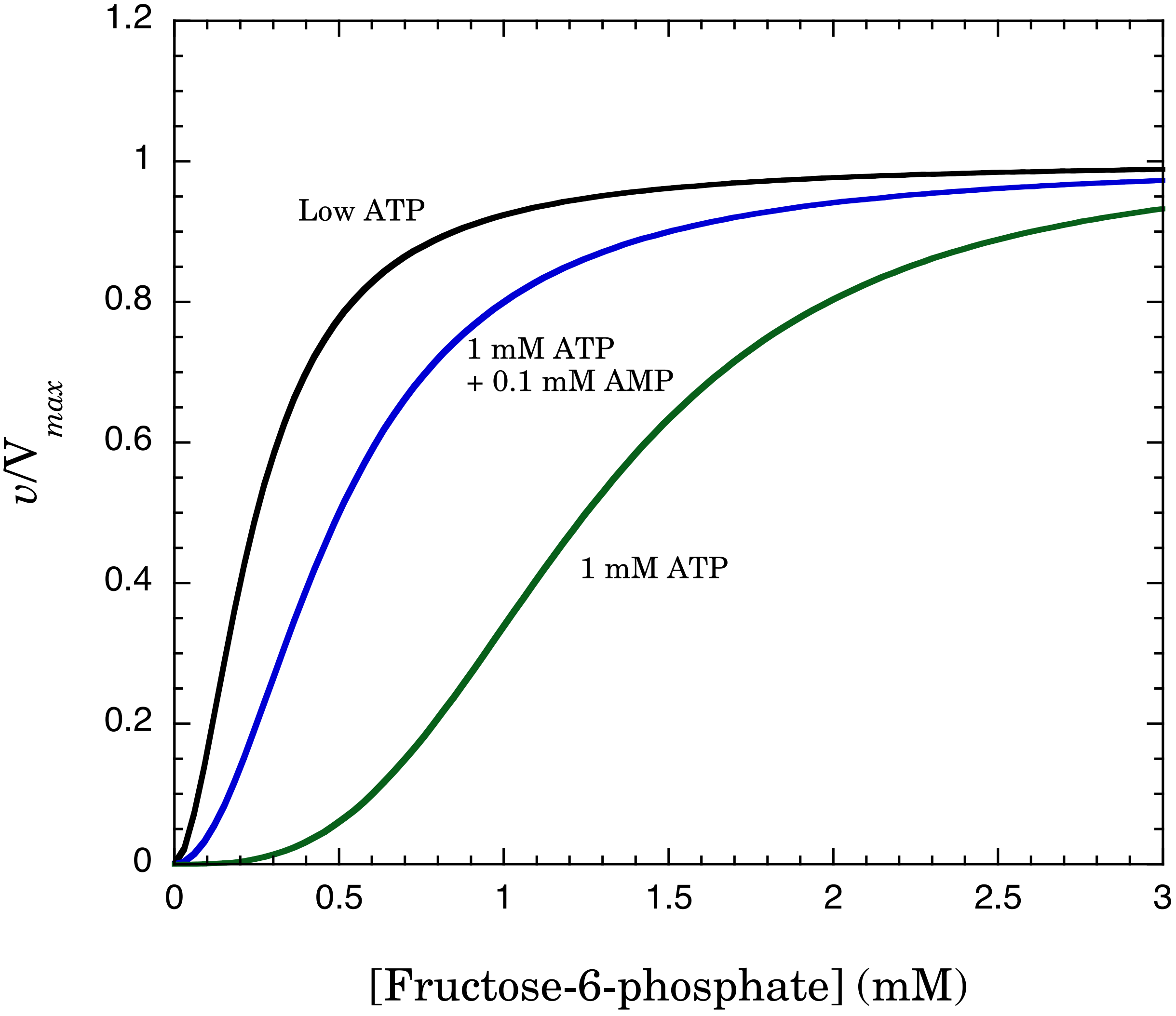
Glucose-6-phosphate

Fructose-6-phosphate

---





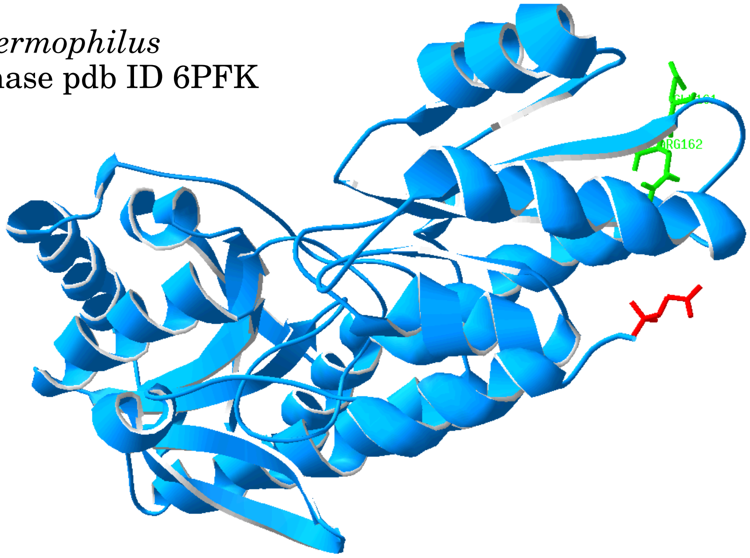


**Substrates**: ATP, Fructose-6-phosphate

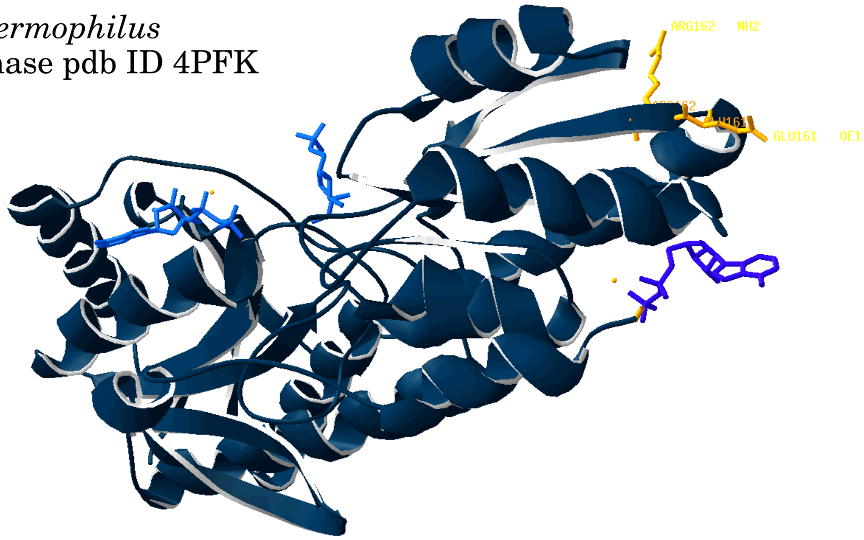
**Inhibitors**: ATP, citrate, phosphoenolpyruvate

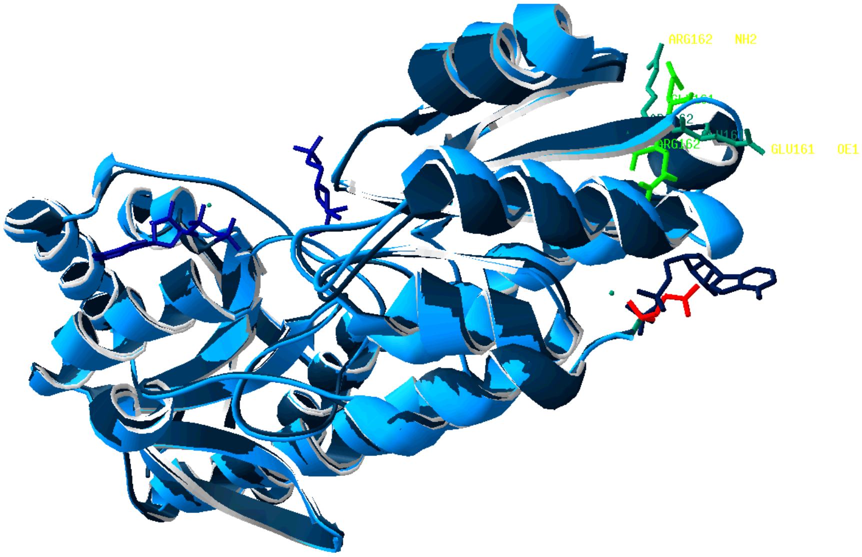
**Activators**: AMP, ADP, Fructose-1,6-bisphosphate, Fructose-2,6-bisphosphate, $NH_4^+$

**T state**
*Bacillus stearothermophilus*
phosphofructokinase pdb ID 6PFK

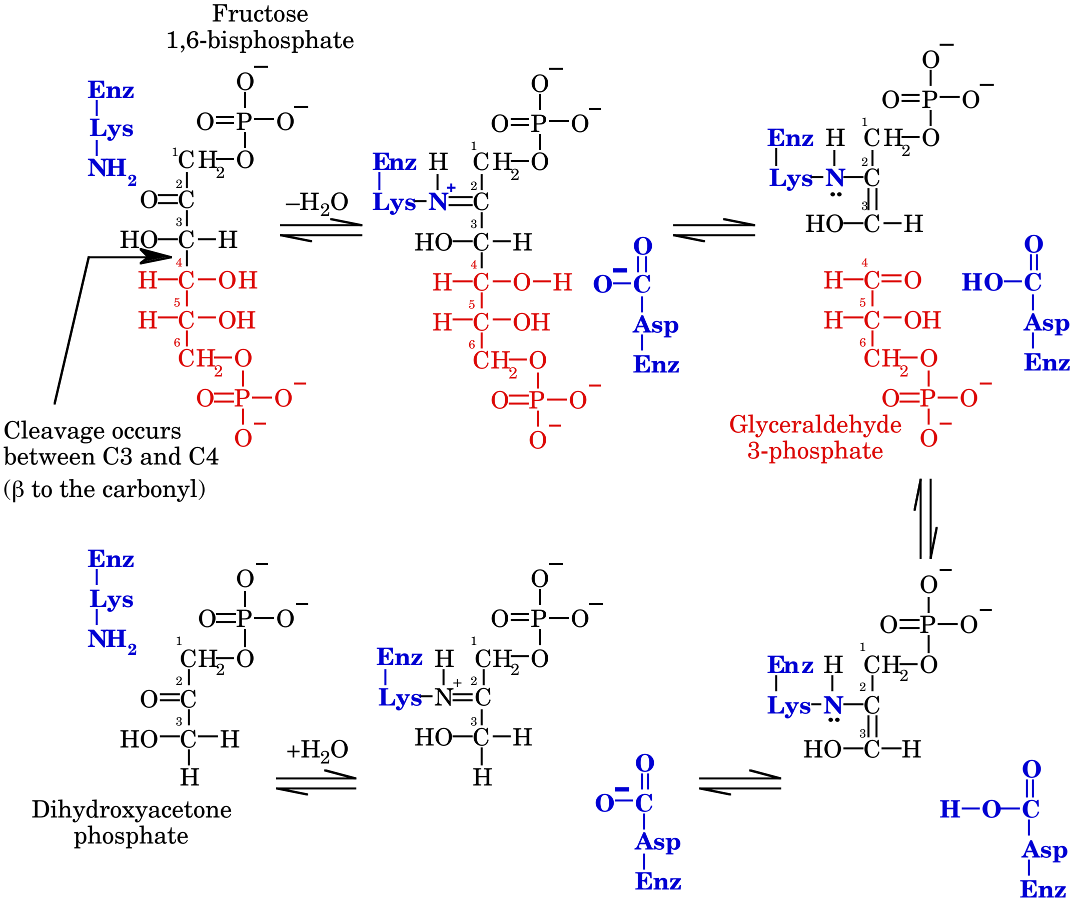


**R state**
*Bacillus stearothermophilus*
phosphofructokinase pdb ID 4PFK

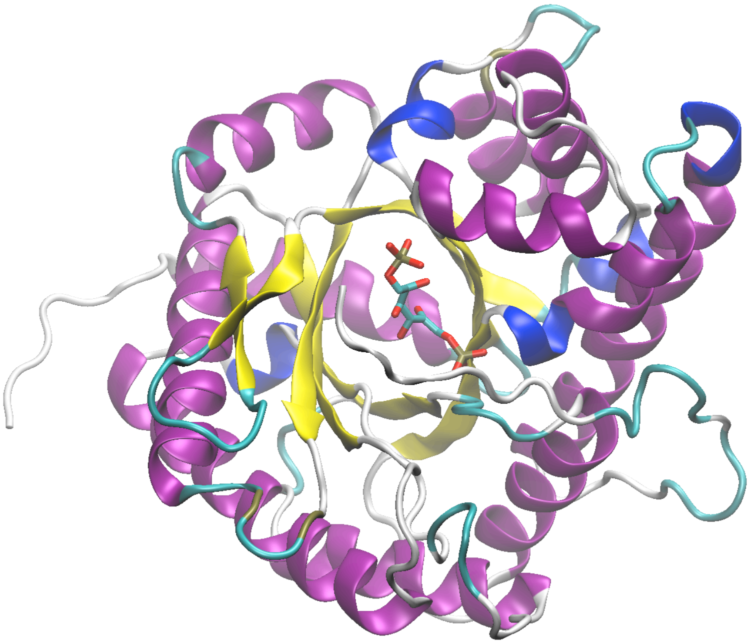




# Aldolase

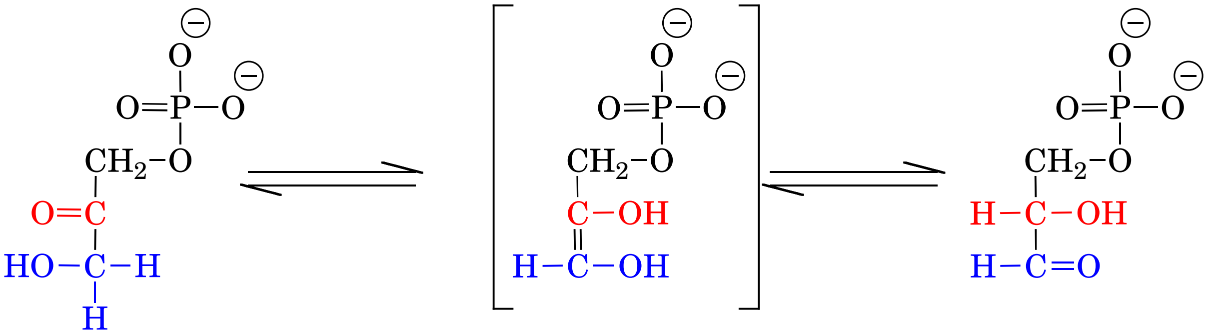


Cleavage occurs between C3 and C4 (β to the carbonyl)



*Homo sapiens* aldolase bound to fructose-1,6-bisphosphate (pdb ID 4ALD)

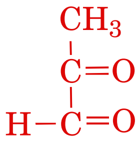
## Triose Phosphate Isomerase



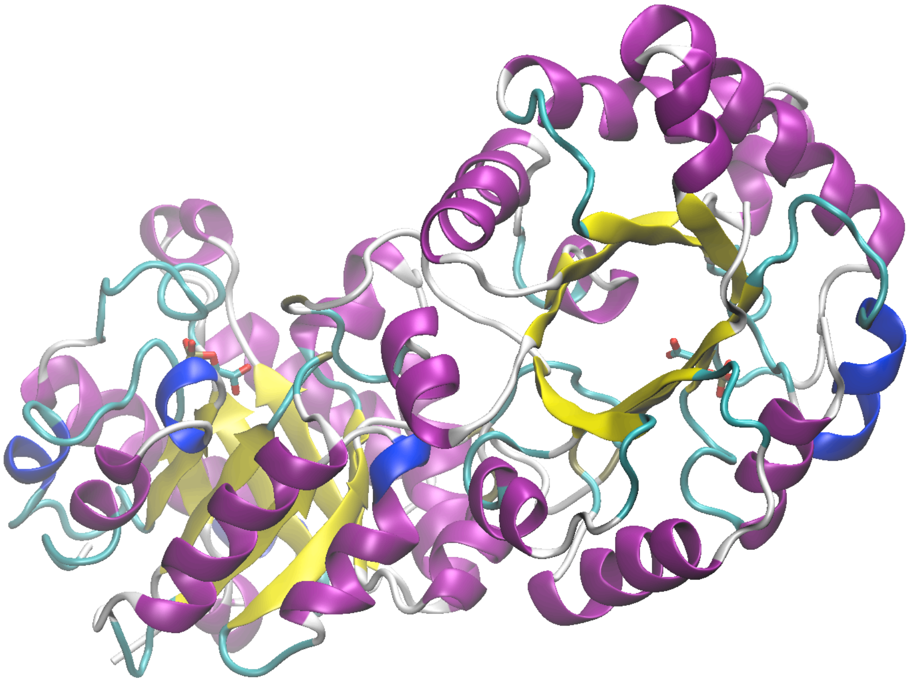
Dihydroxyacetone phosphate

Enediol intermediate

Glyceraldehyde 3-phosphate

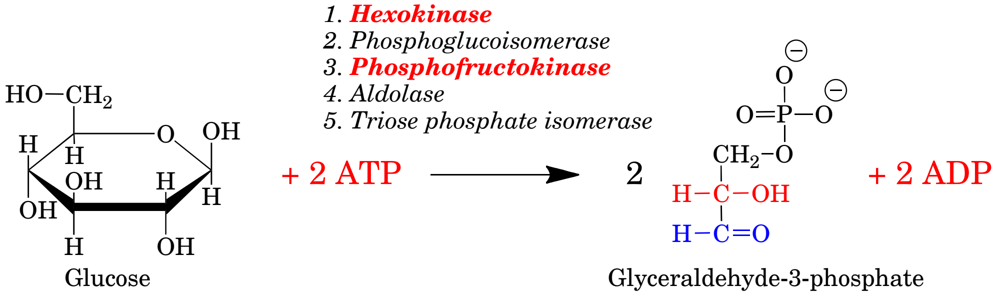


Methyl glyoxal

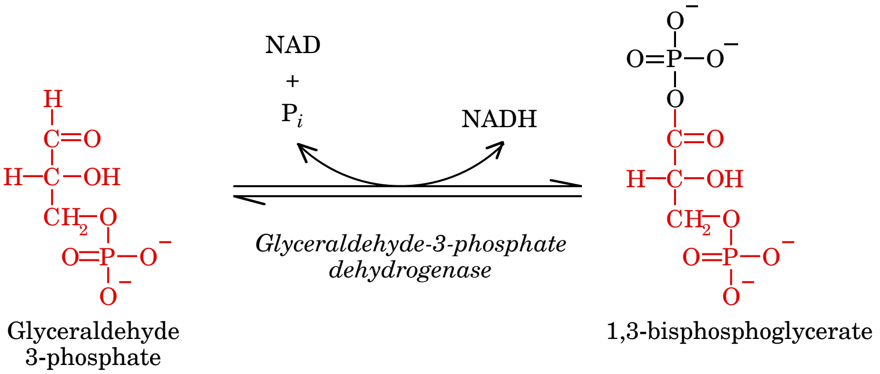


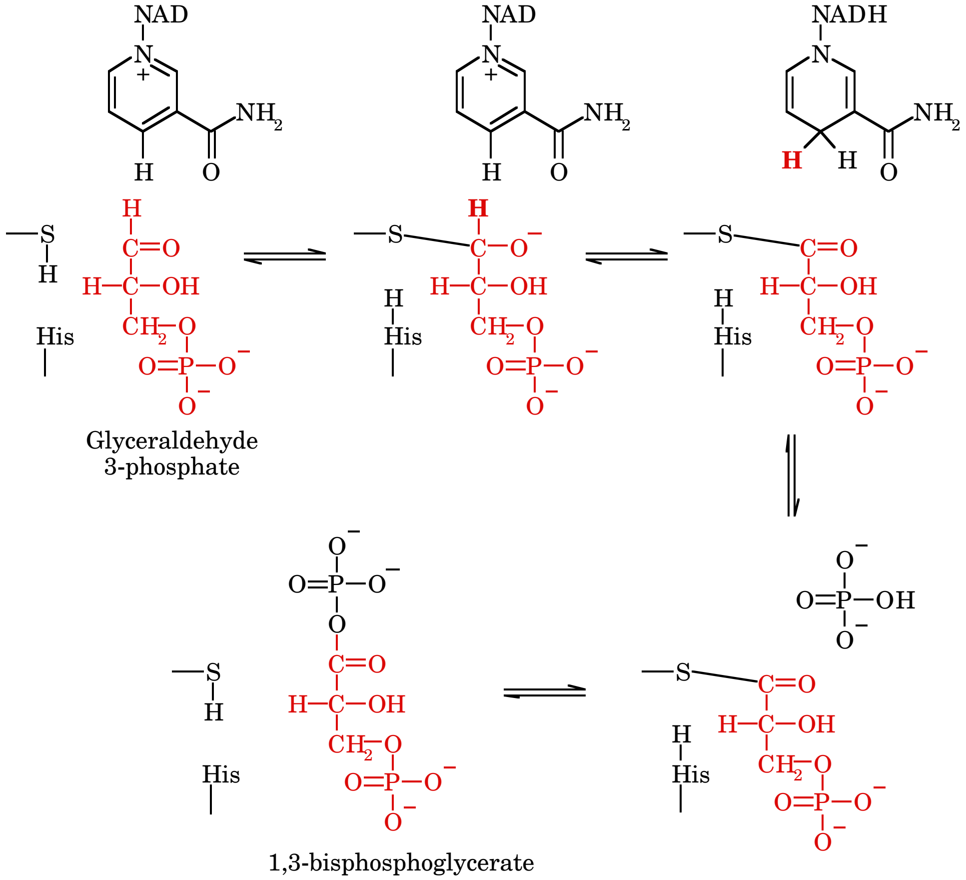
*Saccharomyces cerevisiae* triose phosphate isomerase bound to 2-phosphoglycolate (pdb ID 2YPI)

## Mid-point of Glycolysis

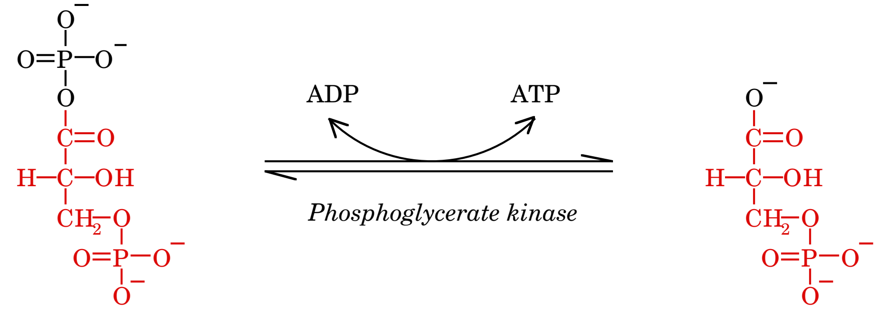


## Glyceraldehyde-3-phosphate dehydrogenase



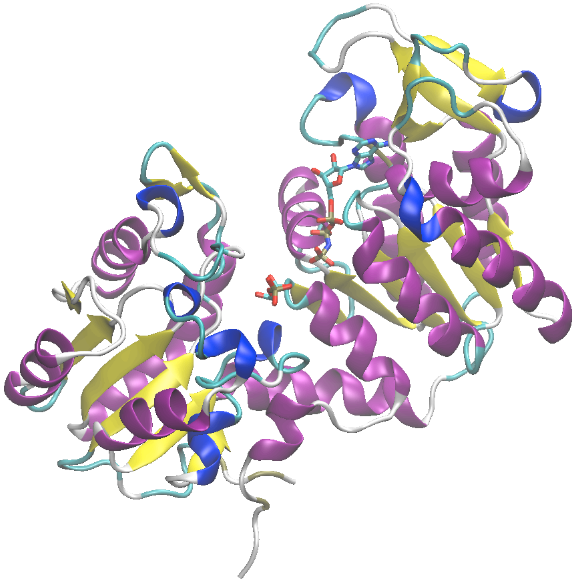


## Phosphoglycerate kinase



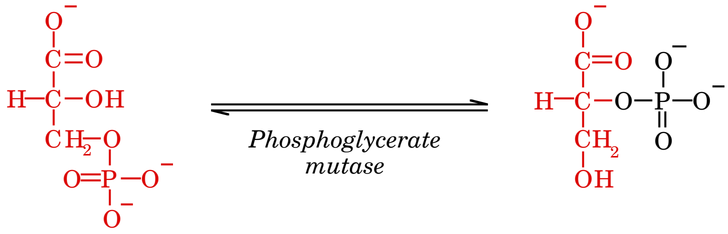
1,3-bisphosphoglycerate

3-phosphoglycerate

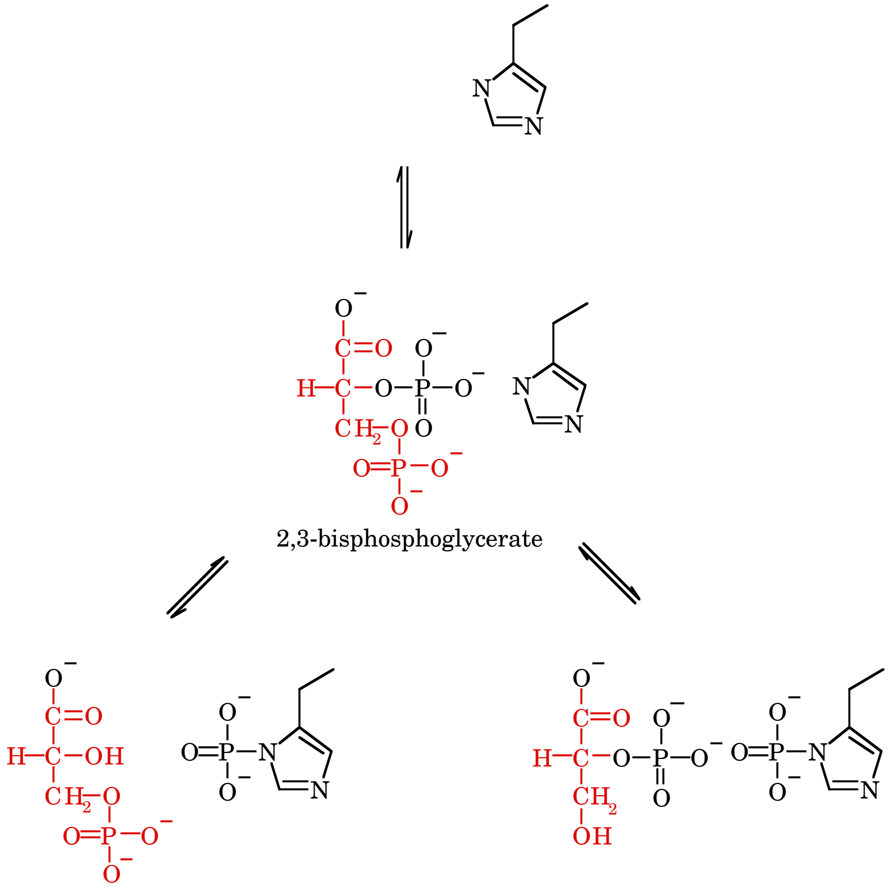


*Thermotoga maritima* phosphoglycerate kinase (pdb ID 1VPE)

## Phosphoglycerate mutase



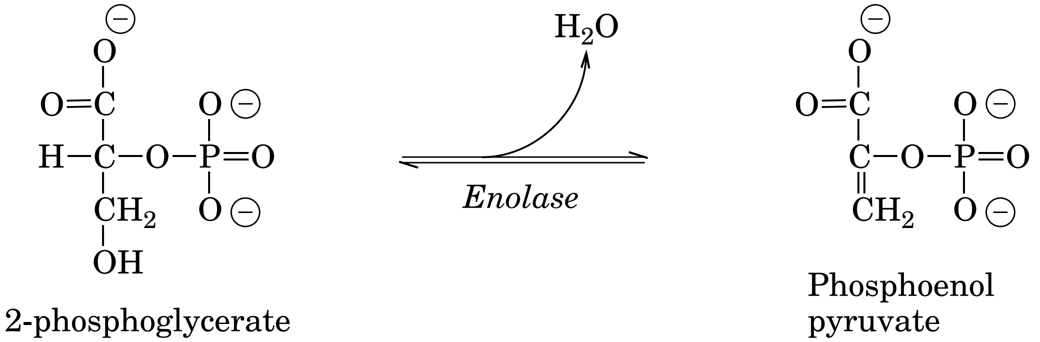
3-phosphoglycerate 2-phosphoglycerate



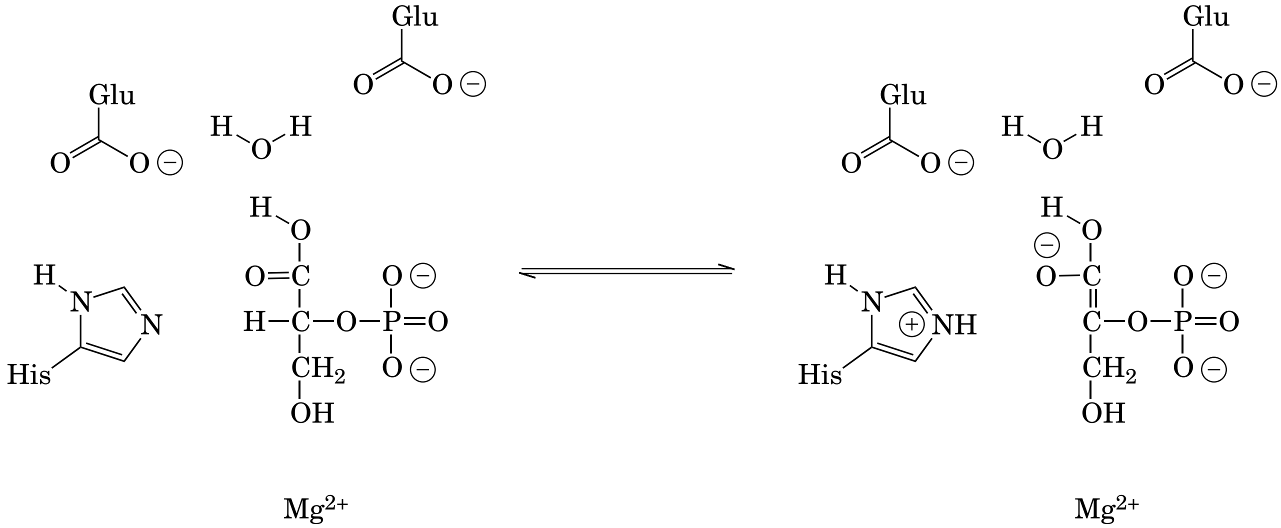
2,3-bisphosphoglycerate

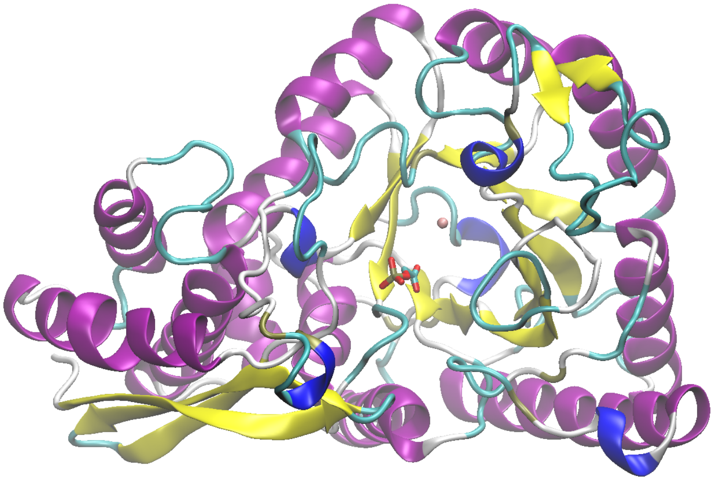
3-phosphoglycerate 2-phosphoglycerate

## Enolase

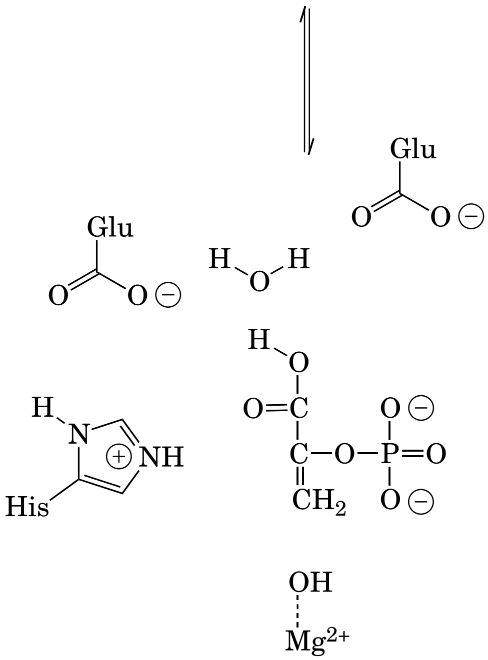


---

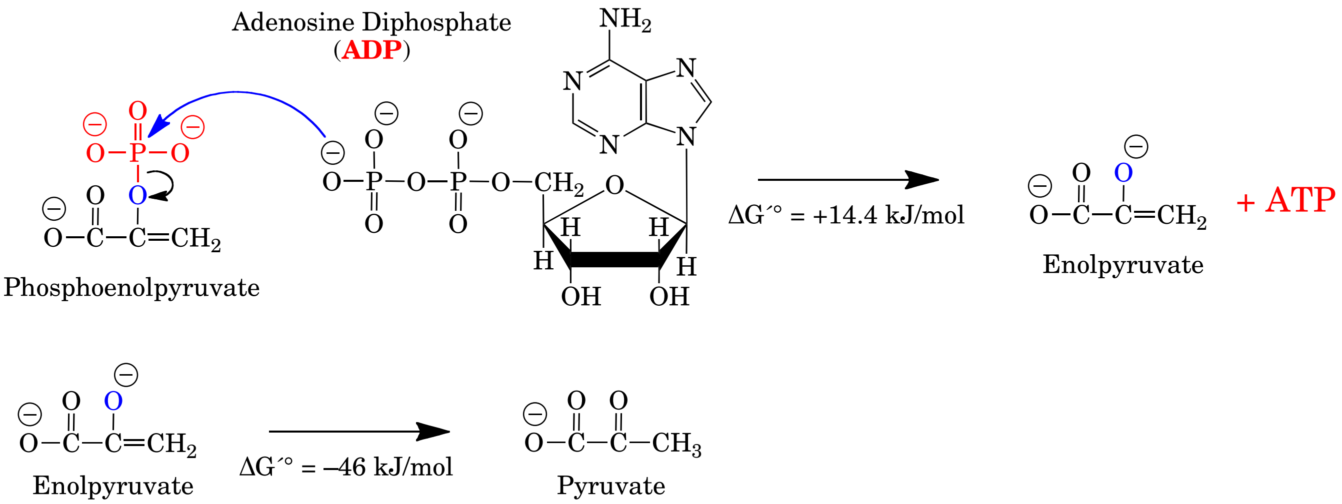




*Homarus gammarus* (lobster) enolase bound to 2-phosphoglycolate and manganese (pdb ID 1PDZ)

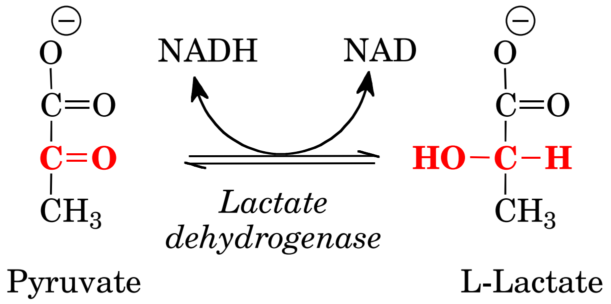


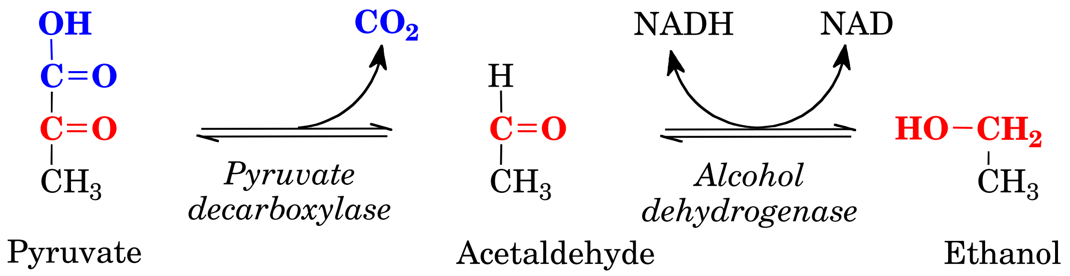
## Pyruvate kinase



| Reaction | ΔG´° (kJ/mol) | Approximate ΔG under erythrocyte cellular conditions (kJ/mol) |
|---|---|---|
| ***Hexokinase*** | -16.7 | -33.9 |
| Phosphoglucoisomerase | +1.67 | -2.92 |
| ***Phosphofructokinase*** | -14.2 | -18.8 |
| Aldolase | +23.9 | -0.23 |
| Triose phosphate isomerase | +7.56 | +2.41 |
| GAP dehydrogenase | +6.30 | -1.29 |
| Phosphoglycerate kinase | -18.9 | +0.1 |
| Phosphoglycerate mutase | +4.4 | +0.83 |
| Enolase | +1.8 | +1.1 |
| ***Pyruvate kinase*** | -31.7 | -23.0 |
| ***Lactate dehydrogenase*** | -25.2 | -14.8 |

## Pyruvate Reduction





## Fructose Metabolism