Chemistry of Glycolysis

C483 Spring 2013

1. During glycolysis, isomerization occurs during which of the following reactions?
A) Fructose 1,6-bisphosphate → dihydroxyacetone phosphate and glyceraldehyde 3-phosphate.
B) Fructose 6-phosphate → fructose 1,6-bisphosphate.
C) Glucose 6- phosphate → fructose 6- phosphate.
D) Glucose → glucose 6- phosphate.

2. Glyceraldehyde 3-phosphate dehydrogenase causes
A) the reduction and phosphorylation of glyceraldehyde 3-phosphate to produce 1,3-bisphosphoglycerate.
B) the oxidation of a molecule of NAD+ to NADH.
C) The reduction of phosphate
D) The oxidation of glyceraldehyde and formation of a high energy bond

3. Although the standard Gibbs free energy change for the reaction of glyceraldehyde -3-P DH is positive (+6.7 kJ/mole), the reaction proceeds to the right because
A) triose phosphate isomerase supplies so much starting material.
B) The product of the reaction is consumed as soon as it is made.
C) there are too few molecules of starting material available.
D) The Gibbs free energy is negative under cellular conditions
E) More than one of the above is an acceptable answer

4. Transfer of the phosphoryl group from PEP to ADP is an example of
A) a mutase reaction.
B) isomerization.
C) dehydrogenation.
D) substrate-level phosphorylation.
E) oxidation

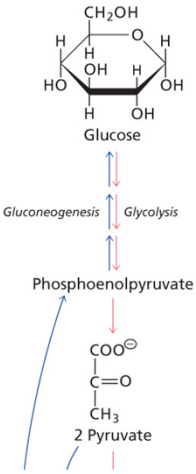
5. Histidine plays a role in the phosphoglycerate mutase reaction in glycolysis for muscle and yeast In what way?
A) Acts as a covalently bound phosphate intermediate
B) Acts as a covalently bound acyl intermediate.
C) Acts as an acid
D) Acts as a base

Expectations

- Memorize/learn Table 11.1
- Know overall reaction and stages
- Explain chemical logic of each step
- Enzyme mechanisms of aldolase and phosphoglycerate mutase

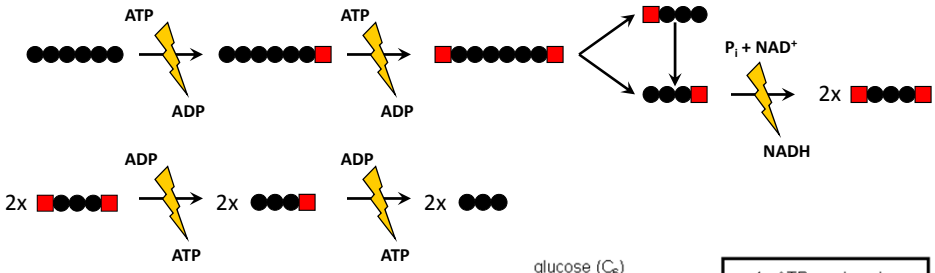
Glycolysis

- Ten enzymes that take glucose to pyruvate
- Cytosol
- ATP and NADH

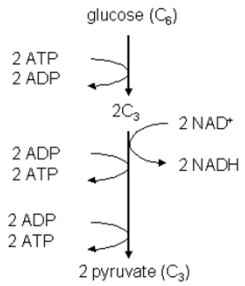


$$\text{Glucose} + 2\ \text{ADP} + 2\ \text{NAD}^{\oplus} + 2\ \text{P}_i \rightarrow 2\ \text{Pyruvate} + 2\ \text{ATP} + 2\ \text{NADH} + 2\ \text{H}^{\oplus} + 2\ \text{H}_2\text{O}$$

Reactions and Enzymes of Glycolysis



- Hexose stage and triose stage
- Overall energy harvest



4 ATP produced
- 2 ATP consumed
2 ATP net

2 NADH are also produced

Know this Table!

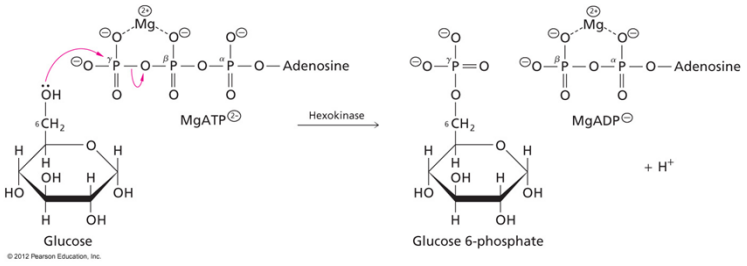
- Know substrates, co-substrates, products, enzyme names
- Fill in the blank problems

Table 11.1 The reactions and enzymes of glycolysis

1. Glucose + ATP ⟶ Glucose 6-phosphate + ADP + $H^{\oplus}$	Hexokinase, glucokinase
2. Glucose 6-phosphate ⇌ Fructose 6-phosphate	Glucose-6-phosphate isomerase
3. Fructose 6-phosphate + ATP ⟶ Fructose 1,6-*bis*phosphate + ADP + $H^{\oplus}$	Phosphofructokinase-1
4. Fructose 1,6-*bis*phosphate ⇌ Dihydroxyacetone phosphate + Glyceraldehyde 3-phosphate	Aldolase
5. Dihydroxyacetone phosphate ⇌ Glyceraldehyde 3-phosphate	Triose phosphate isomerase
6. Glyceraldehyde 3-phosphate + $NAD^{\oplus}$ + P_i ⇌ 1,3-*Bis*phosphoglycerate + NADH + $H^{\oplus}$	Glyceraldehyde 3-phosphate dehydrogenase
7. 1,3-*Bis*phosphoglycerate + ADP ⇌ 3-Phosphoglycerate + ATP	Phosphoglycerate kinase
8. 3-Phosphoglycerate ⇌ 2-Phosphoglycerate	Phosphoglycerate mutase
9. 2-Phosphoglycerate ⇌ Phosphoenolpyruvate + H_2O	Enolase
10. Phosphoenolpyruvate + ADP + $H^{\oplus}$ ⟶ Pyruvate + ATP	Pyruvate kinase

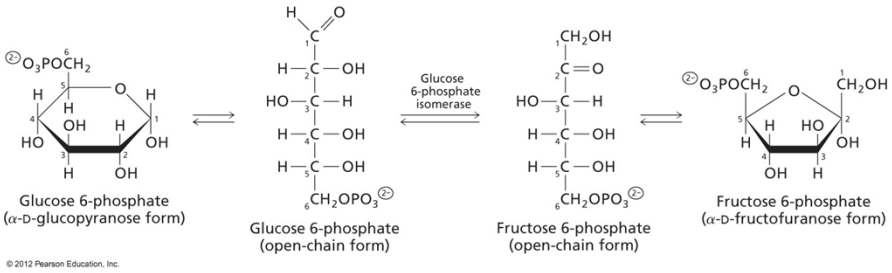
1. Hexokinase

- Previous concepts: Induced fit, kinase
- Energy use/production?
- Chemical logic?
- Isozyme: glucokinase



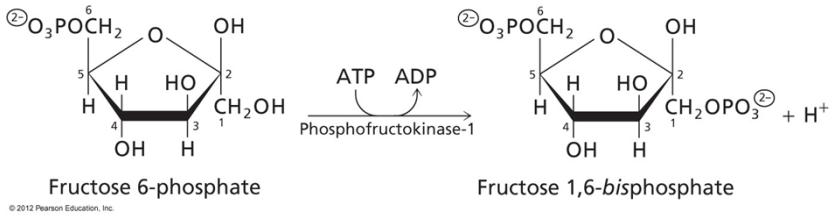
2. G-6-P Isomerase

- Previous concepts: Isomerization
- Energy use/production? CONCEPT: NET FLUX
- Chemical logic?
- Stereochemistry—reverse does not produce mannose!



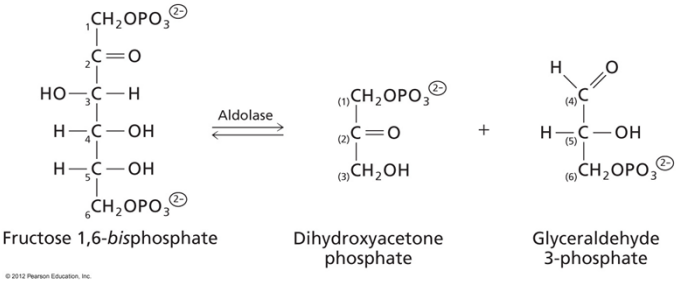
3. PFK-1

- Previous concepts: Allosteric inhibition
- Energy use/production?
- Chemical logic?
- First committed step of glycolysis

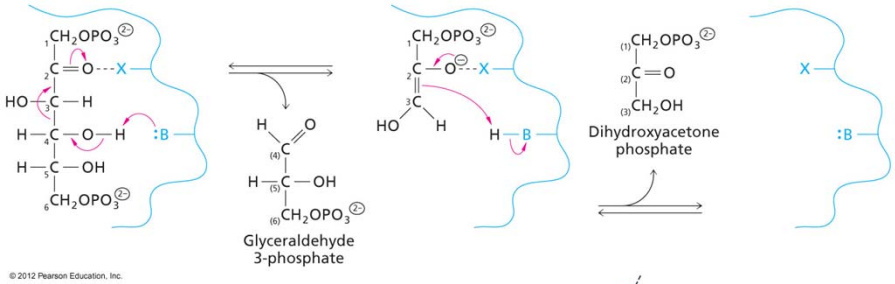


4. Aldolase

- Previous concepts: Standard free energy is +28kJ, but it is a near equilibrium reaction
- Energy use/production?
- Chemical logic?
- Beginning of triose stage

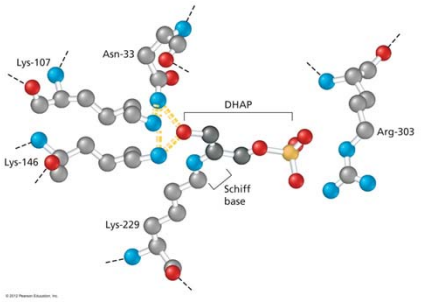


Aldolase Mechanism



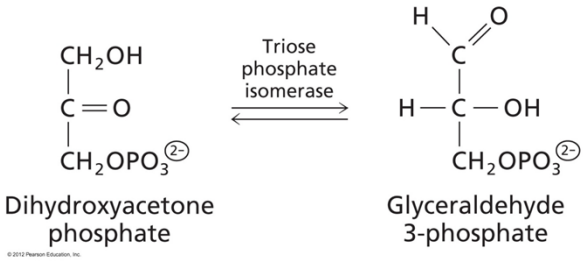
Class 1: Schiff base

Class 2: zinc ion

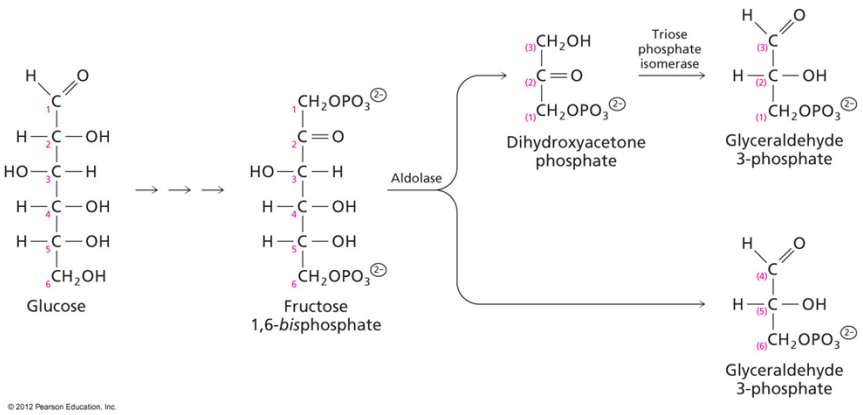


5. Triose Phosphate Isomerase

- Previous concepts: Catalytic perfection
- Energy use/production?
- Chemical logic?
- Most similar to which previous reaction?

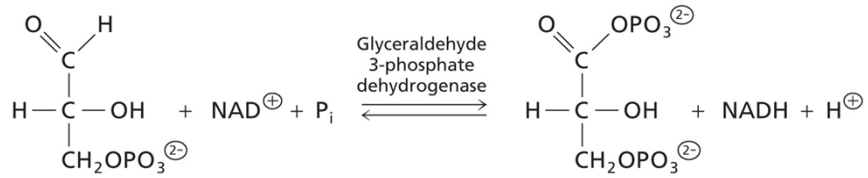


Radiolabelling studies



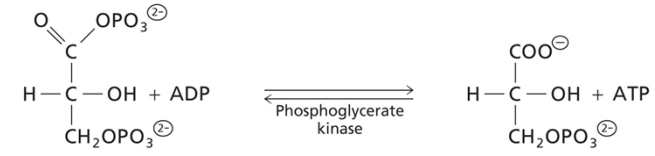
6. Glyceraldehyde-3-P DH

- Previous concepts: Redox and dehydrogenase
- Energy use/production?
- Chemical logic?
- Effective [1,3bPG] = zero



7. Phosphoglycerate Kinase

- Previous concepts: High energy bond
- Energy use/production?
- Chemical logic?
- Substrate level phosphorylation



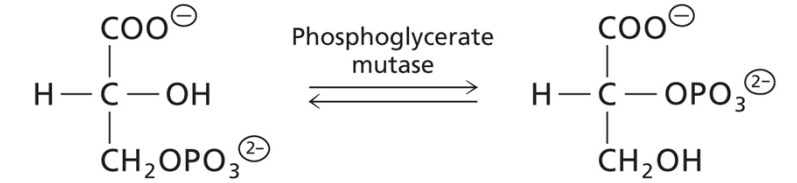
Glyceraldehyde 3-phosphate + $NAD^{\oplus}$ ⟶ 1,3-*Bis*phosphoglycerate + NADH + $H^{\oplus}$

1,3-*Bis*phosphoglycerate + ADP ⟶ 3-Phosphoglycerate + ATP

Glyceraldehyde 3-phosphate + $NAD^{\oplus}$ + P_i + ADP ⟶ 3-Phosphoglycerate + NADH + $H^{\oplus}$ + ATP

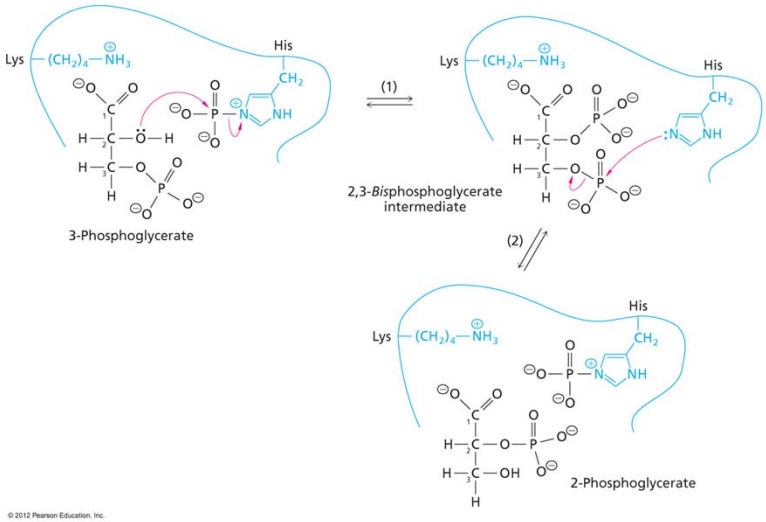
8. Phosphoglycerate Mutase

- Previous concepts: Covalent catalysis
- Energy use/production?
- Chemical logic?
- Mutase—isomerzation with P transfer



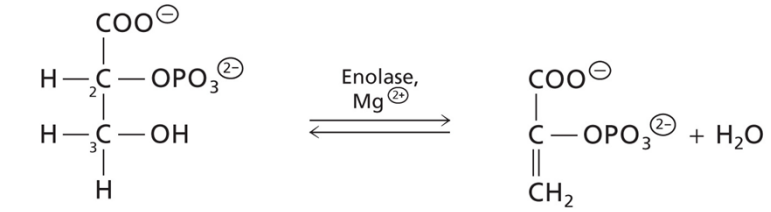
3-Phosphoglycerate 2-Phosphoglycerate

Mechanism



9. Enolase

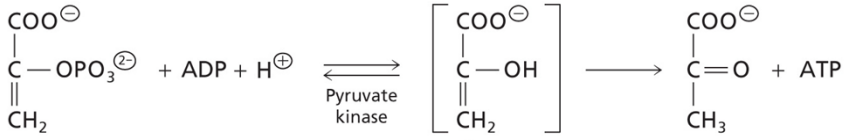
- Previous concepts: Phosphoryl group transfer potential
- Energy use/production?
- Chemical logic?



2-Phosphoglycerate Phosphoenolpyruvate

10. Pyruvate Kinase

- Energy use/production?
- Chemical logic?
- Payback phase



Phosphoenolpyruvate Enolpyruvate Pyruvate

Answers

1. C
2. D
3. E
4. D
5. A