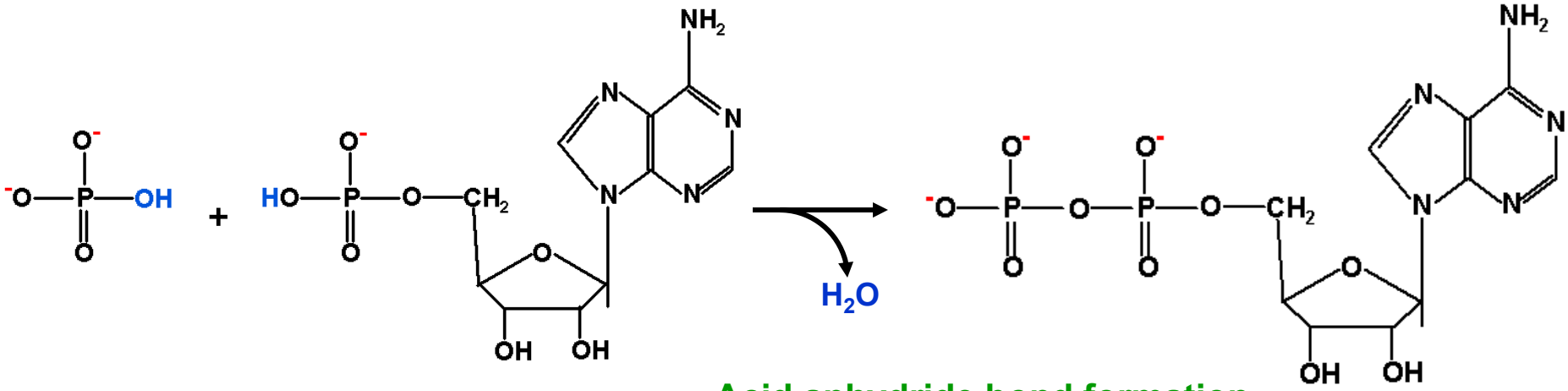
BIO 311C
Spring 2010

Lecture 22 – Wednesday 24 Mar.

Consider the formation of ADP



Acid anhydride bond formation

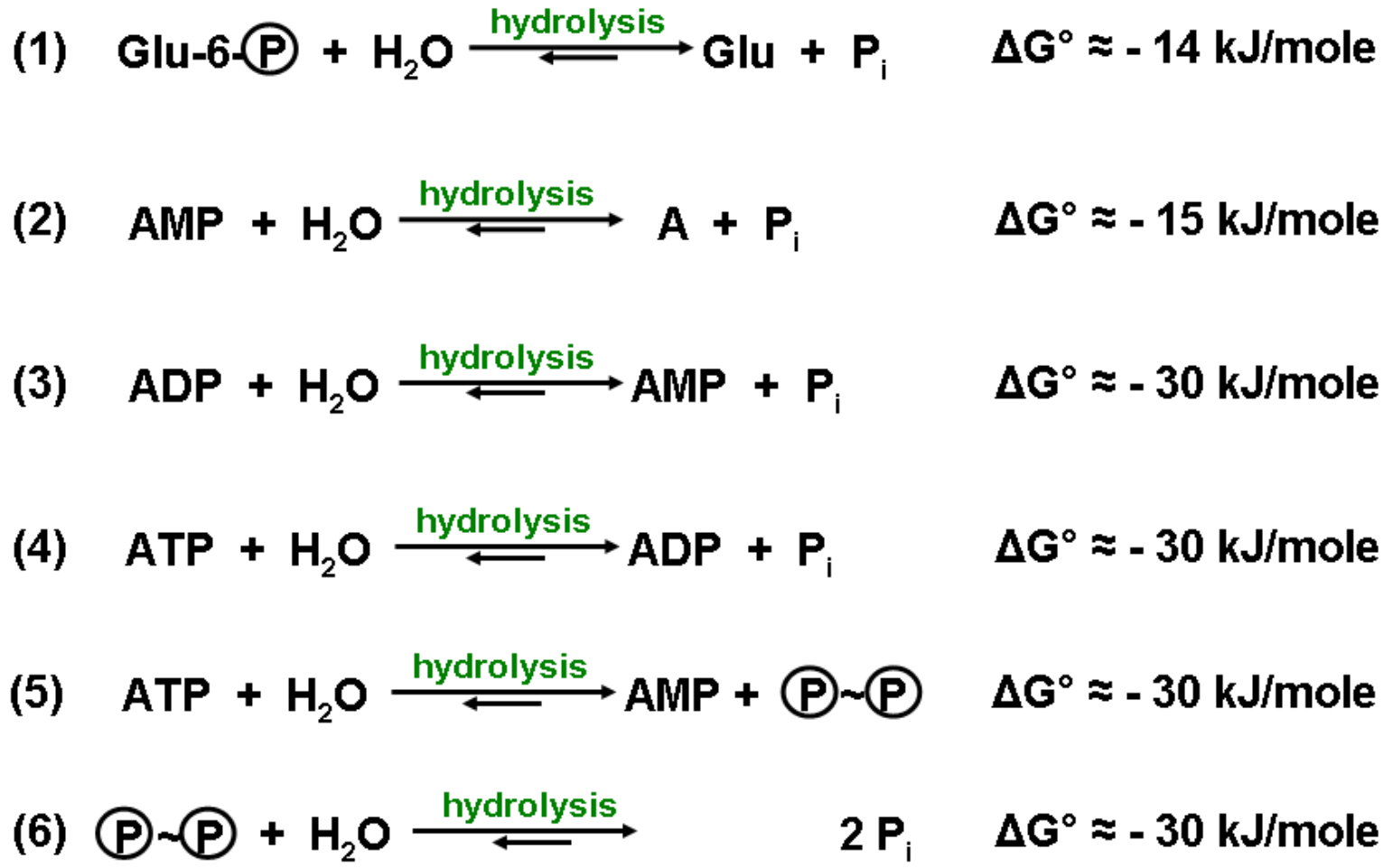
Dehydration rx.

$$AMP + P_i \rightleftharpoons ADP + H_2O \qquad \Delta G^\circ \approx +30 \text{ kJ/mole}$$

The formation of a acid anhydride bond from two phosphoric acid functional groups in a dehydration reaction under standard conditions requires an input of approximately 30 kJ/mole of energy, twice the amount of energy that is required in the formation of an ester bond.

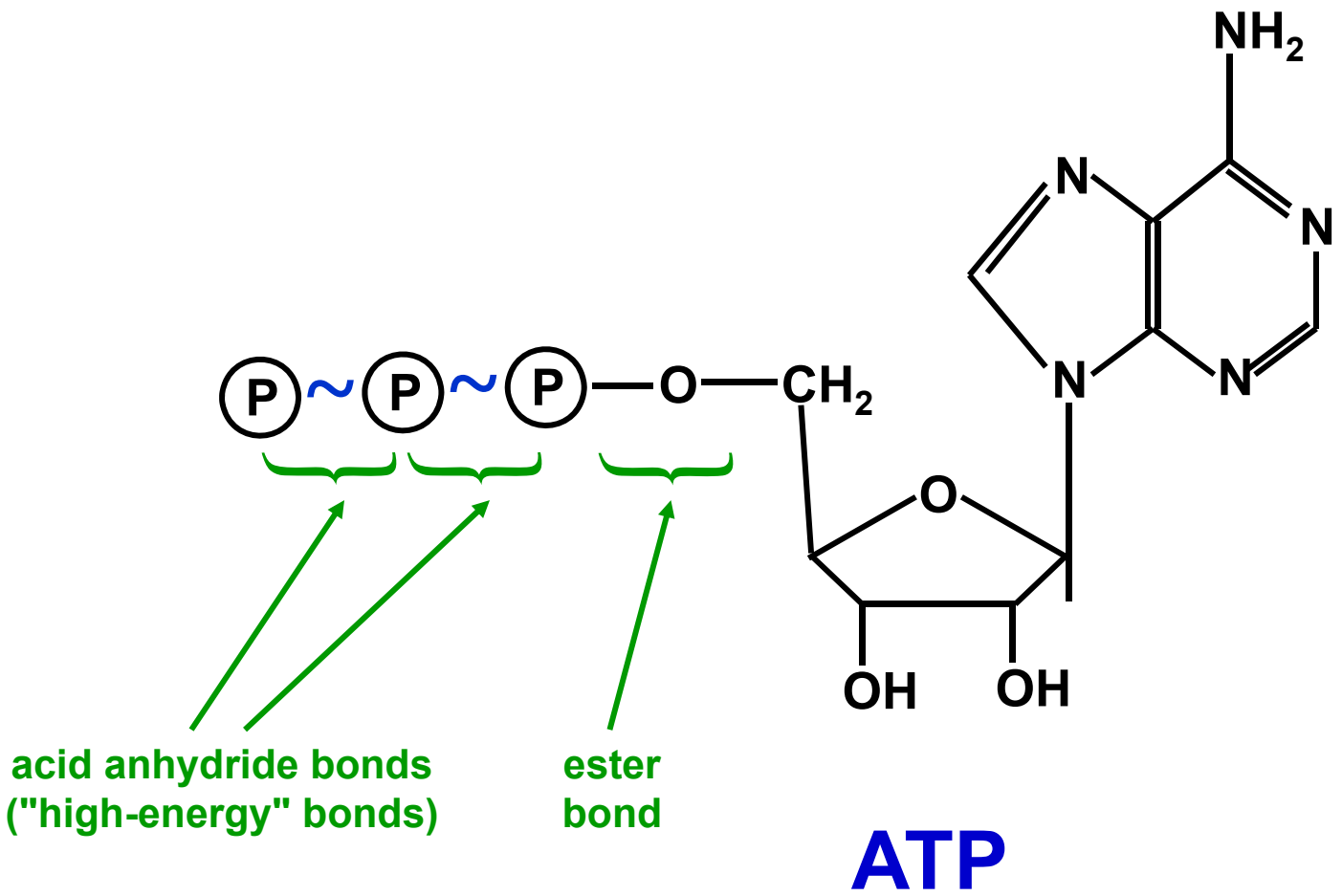
The formation of ATP from ADP + P_i also requires approx. 30 kJ/mole of energy under standard conditions. *

Now consider some hydrolysis reactions, the reverse of dehydration reactions.



Hydrolysis of an acid anhydride bond releases about twice as much energy as does the hydrolysis of an ester bond. *

Hydrolyses of each of the acid anhydride bonds of ATP releases about twice as much energy as does hydrolyses of the ester bond.



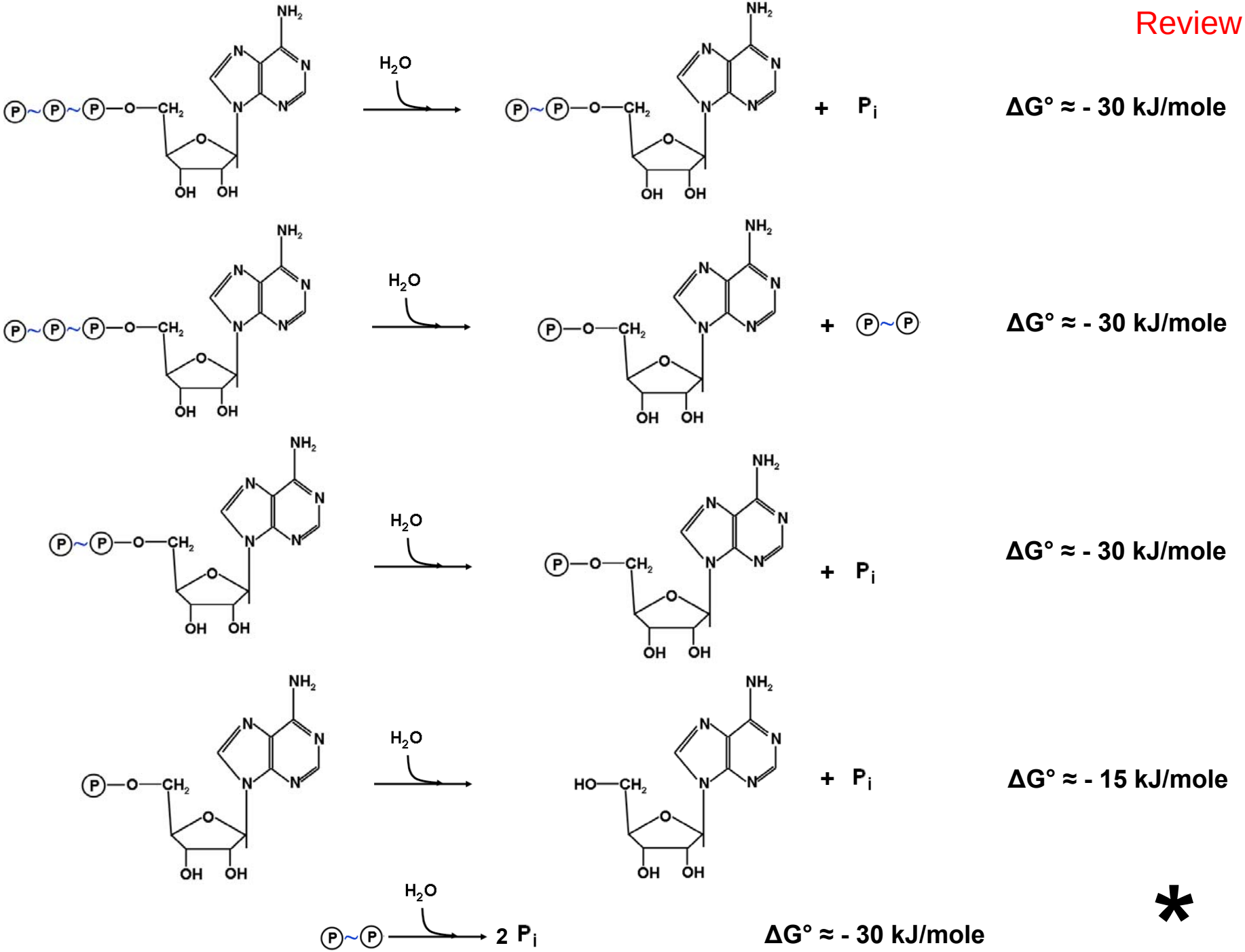
*

The Energy Currency of Cells

Reactions which release more than approximately 20 kJ/mole of energy produce a large enough amount of energy that some of the energy released during the reaction may be captured to perform useful work in a cell. The reverse of these reactions requires special mechanisms since they require the input of over 20 kJ/mole of energy.

ATP is sometimes called the "energy currency" of cells since its hydrolysis to ADP or AMP is used extensively to provide energy for cellular processes.

*


H_2O
+ P_i
ΔG° ≈ - 30 kJ/mole
H_2O
+ P_i
ΔG° ≈ - 30 kJ/mole
H_2O
+ P_i
ΔG° ≈ - 30 kJ/mole
H_2O
+ P_i
ΔG° ≈ - 15 kJ/mole
H_2O
2 P_i
ΔG° ≈ - 30 kJ/mole
*

Practice Problems

Suppose a large number of molecules X are placed into solution and a pathway exists to convert X into Y. The reaction is allowed to come to equilibrium under standard conditions, after which there are 1,000 times as many molecules Y as molecules X in the solutions. Then:

a. What is K_{eq} for the reaction X $\rightleftharpoons$ Y ?

b. What is K_{eq} for the reaction Y $\rightleftharpoons$ X ?

c. What is ΔG° for the reaction X $\rightleftharpoons$ Y ?

d. Is the reaction X $\rightleftharpoons$ Y endergonic or exergonic?

e. What is the ΔG for the reaction X $\rightleftharpoons$ Y when a steady-state equal concentration of X and Y are maintained as the reaction proceeds?

f. What is the ΔG for the reaction X $\rightleftharpoons$ Y if other reactions are coupled to the reaction to maintain 10,000 times higher concentration of Y than X as the reaction proceeds?

*

Consider the reaction:

$$\text{glu-6-P} + H_2O \underset{\longleftarrow}{\xrightarrow{\text{hydrolysis}}} \text{glu} + P_i \qquad \Delta G^\circ \approx -14 \text{ kJ/mole}$$

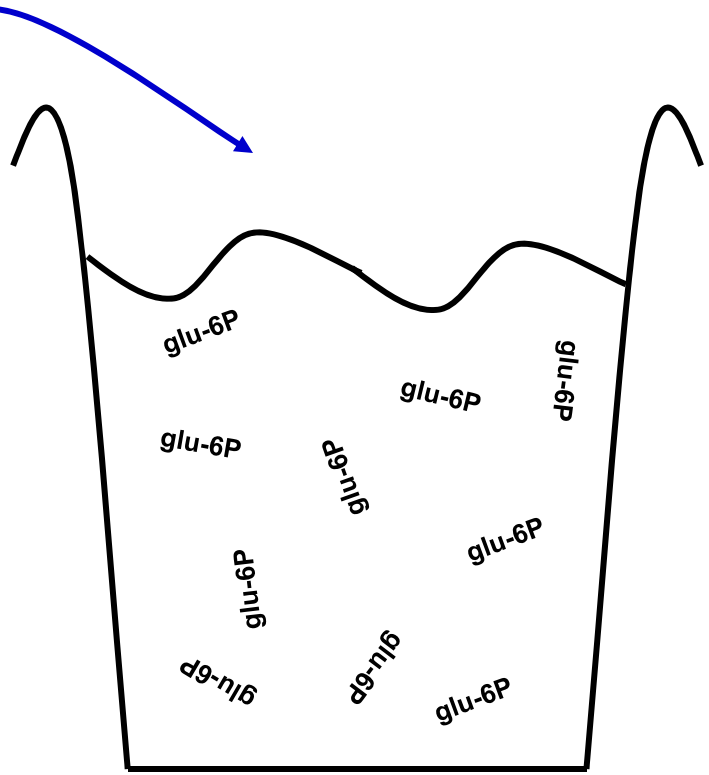
Do the following experiment: Place 1 mole of glu-6-P into a glass of water and stir it to fully dissolve. Then leave the solution set under a standard set of conditions and wait for the reaction to proceed.

According to the value of ΔG°, the equilibrium constant for this reaction is 428, so when the reaction comes to equilibrium there should be over 400 times as much glucose and inorganic phosphate present as there is glucose-6-P.

To determine K_{eq}, recall that: $\Delta G^\circ = -(5.7 \text{ kJ/mole})(\log_{10} K_{eq})$

*

dissolve glu-6-P into water

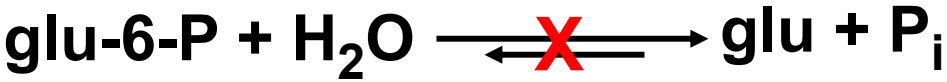


wait for equilibrium amounts of glu and P_i to be produced.

Even after several weeks, the glucose-6-phosphate concentration remains virtually unchanged and almost no glucose or inorganic phosphate appear in the container of water. Why?

Answer: Because the reaction has no pathway that allows it to proceed and it still has not reached equilibrium!

*



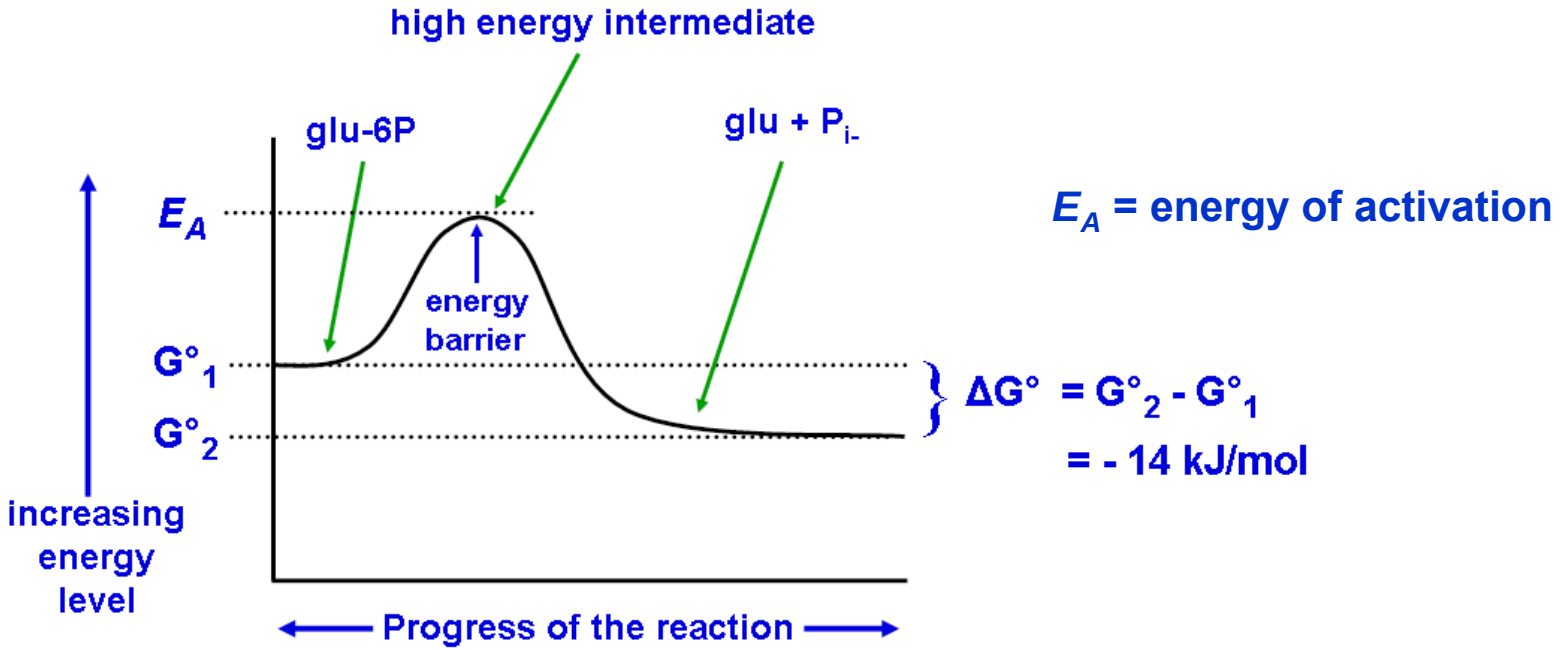
$\Delta G^\circ \approx -14$ kJ/mole

This reaction cannot proceed in either direction because no pathway (i.e. no mechanism) exists.

*

Energetic changes during progress of the reaction:

$$\text{glu-6-P} + H_2O \rightleftharpoons \text{glu} + P_i$$



E_A = energy of activation

Most reactions involving making and breaking covalent bonds do not occur at normal temperatures without the aid of an appropriate catalyst because the substrates cannot obtain enough energy to overcome the energy barrier (energy of activation) of the reaction.

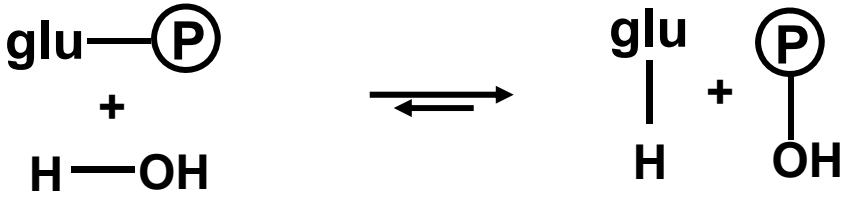
*

Most metabolic reactions involve breaking two covalent bonds and forming two new covalent bonds:

Generic example: $A + B \rightleftharpoons C + D$

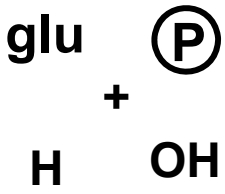
Specific example: glu—Ⓟ + H—OH ⇌ glu—H + HO—P_i

Another way of writing this specific example:



stable molecules (relatively low energy)

stable molecules (relatively low energy)

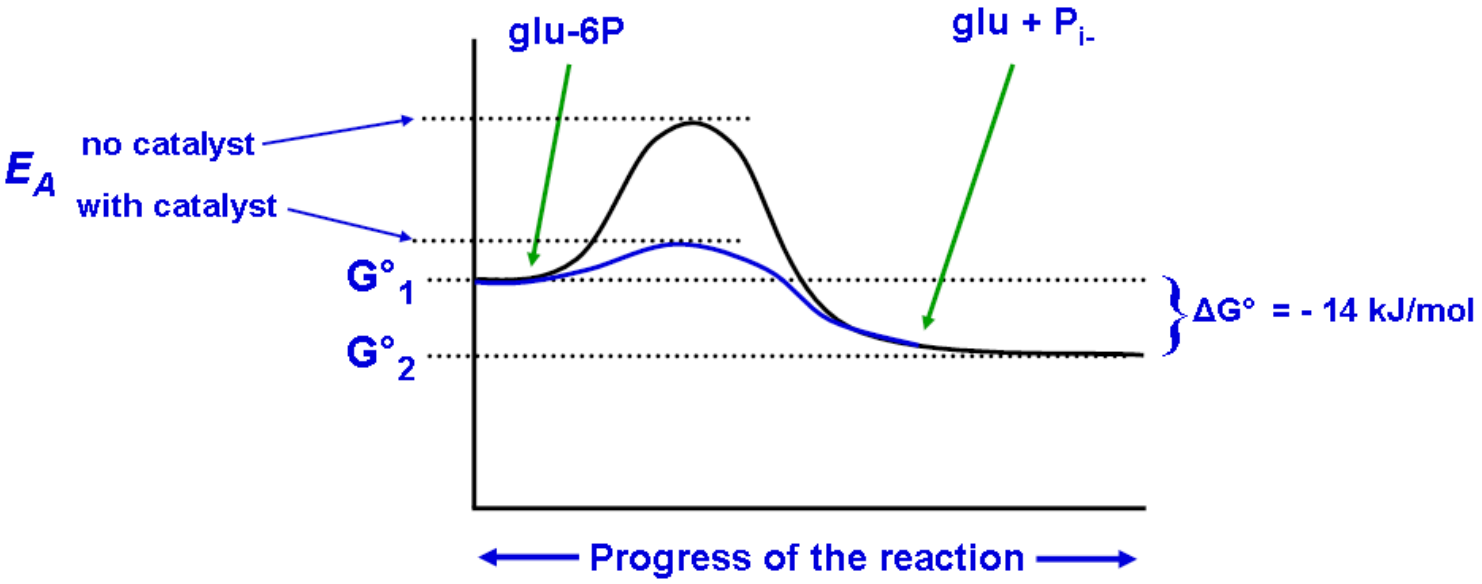


Hypothetical intermediate unstable molecules (high energy)

*

The addition of a catalyst to a chemical reaction changes the energy of activation, but not the ΔG of the reaction. i.e. Catalysts change the kinetics, but not the overall energetics of the reaction. Enzymes are catalysts.

Example: $\text{glu-6-P} + H_2O \rightleftharpoons \text{glu} + P_i$



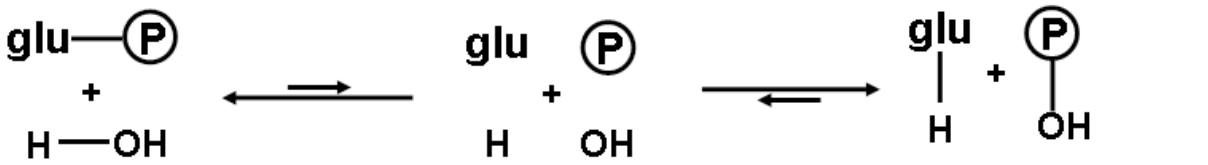
*

Comparison of the Mechanism of the Same Reaction When Catalyzed by an Enzyme or Not Catalyzed

Example: glu—Ⓟ + H—OH ⇌ glu—H + HO—P_i

---

not catalyzed

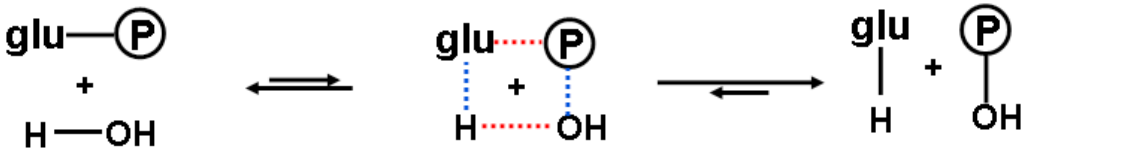


stable (relatively low energy)

very unstable (high energy)

stable (relatively low energy)

Catalyzed by the enzyme called glucose-6-phosphatase



stable (relatively low energy)

somewhat unstable (only slightly higher energy)

stable (relatively low energy)

····· old bonds partially broken

····· new bonds partially formed

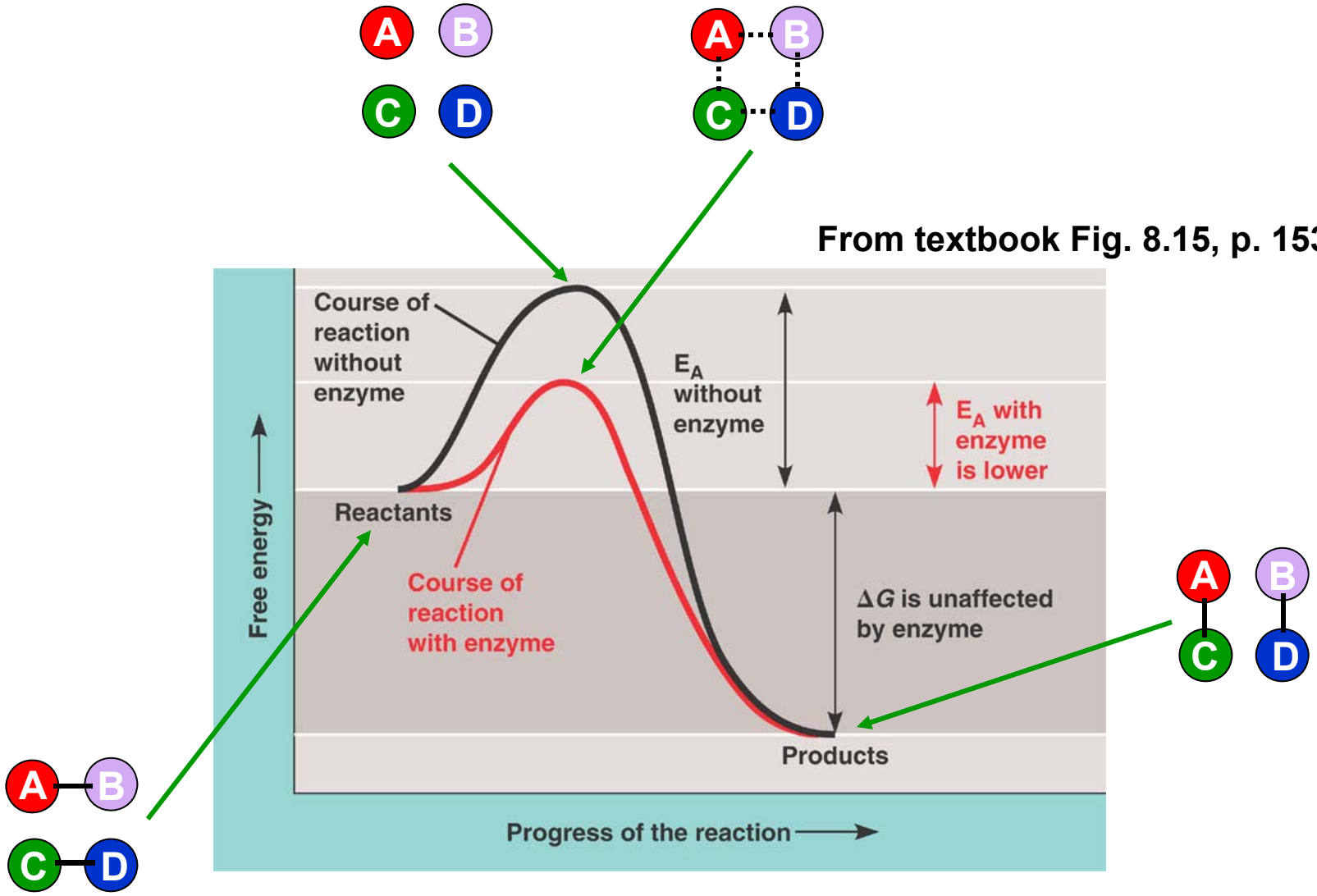
transition state

*

Differences in transition-state intermediates, depending on whether or not a reaction is catalyzed by an enzyme.

$$AB + CD \rightleftharpoons AC + BD$$

From textbook Fig. 8.15, p. 153



*

Components of an Enzyme Catalyzed Reaction

~~Enzyme~~ + ~~Cofactor(s)~~ + Reactant(s) $\rightleftharpoons$ Product(s) + ~~Enzyme~~ + ~~Cofactor~~

Can be written as:

$$\text{Reactant(s)} \xrightleftharpoons[\text{Cofactor(s)}]{\text{Enzyme}} \text{Product(s)}$$

A cofactor is a portion of the enzyme other than polypeptide chain(s). The polypeptide chain(s) portion of an enzyme is called an apoenzyme. Some cofactors are tightly bound to an apoenzyme as a prosthetic group; other cofactors, are loosely bound and easily removed from an enzyme and are called coenzymes.

Many, but not all, enzyme-catalyzed reactions require a cofactor.

The enzyme and cofactor(s) are the same at the end of the reaction as they were at the beginning of the reaction, although they are transiently altered while they bind to substrates during the reaction.

*

Some Unique Aspects of Enzymes as Catalysts

1. They are proteins.
   - All are globular.
   - Many are conjugated.
   - Some are monomeric, others are oligomeric.

2. Each one is very specific:
   - for the substrates it recognizes and acts on.
   - for the functional groups it modifies or moves.
   - for the kind of reaction it catalyzes.

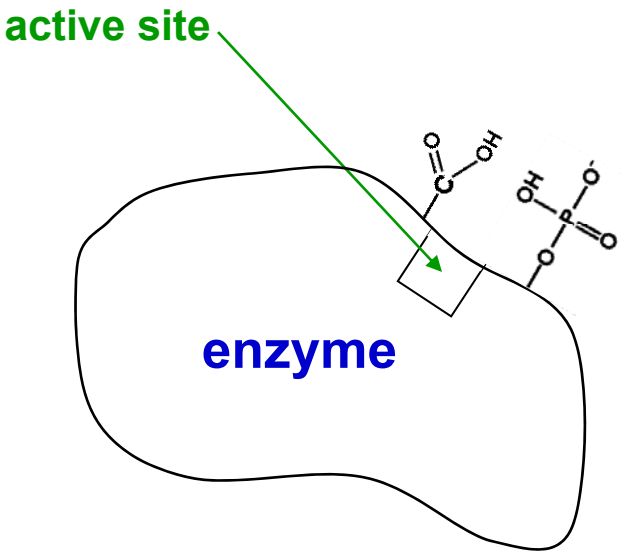
3. They function in a rather narrow environmental range:
   - at a narrow temperature range.
   - at a narrow pH range.

4. Some are regulatory and are subject to sensitive control of their rate of catalysis.

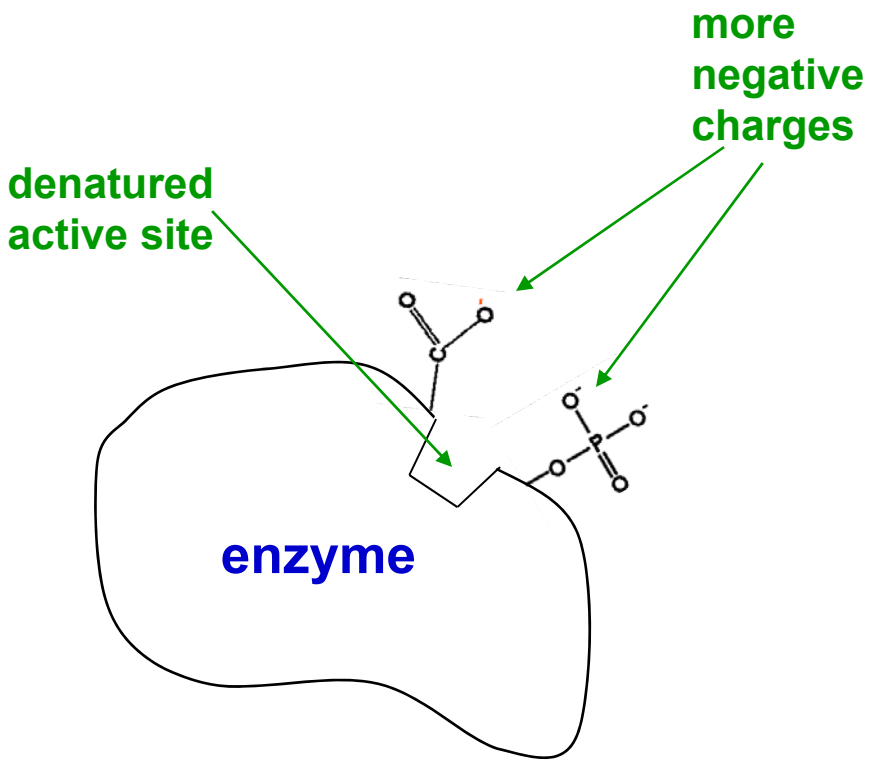
5. Some are able to couple two reactions together.

*

Effect pH on an Enzyme



acidic pH

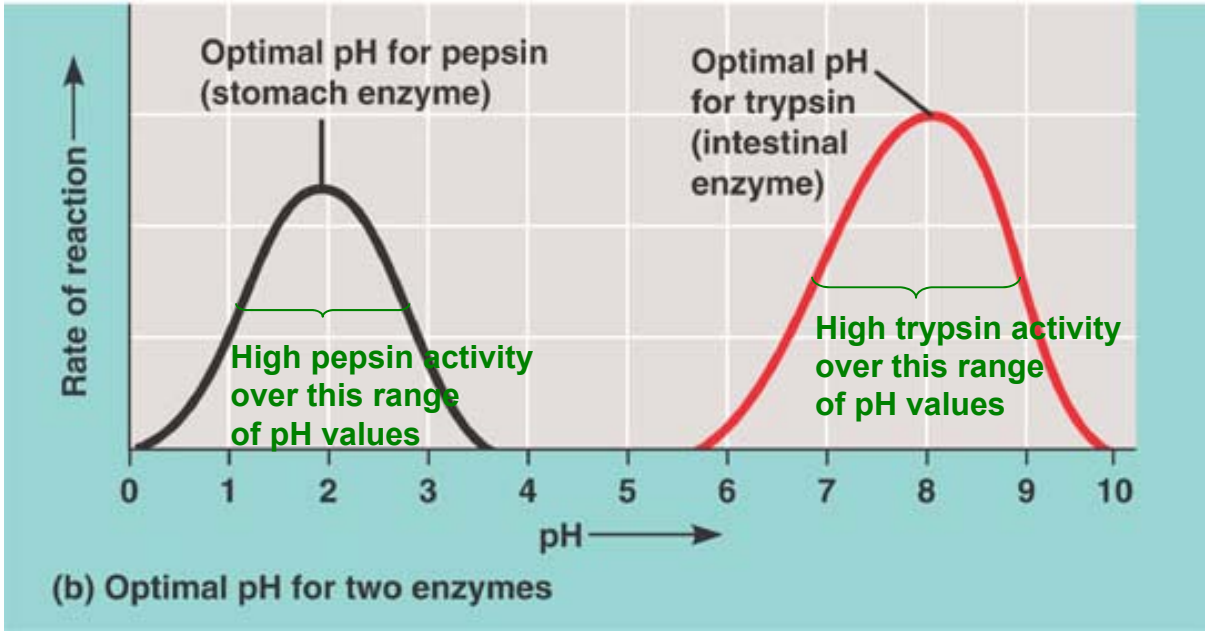


neutral or basic pH

Shape of enzyme is altered by electrical repulsion between adjacent negatively-charged functional groups

*

Each enzyme is designed such that it functions optimally at the pH value of its normal environment.



From textbook Fig. 8.18, p. 155.

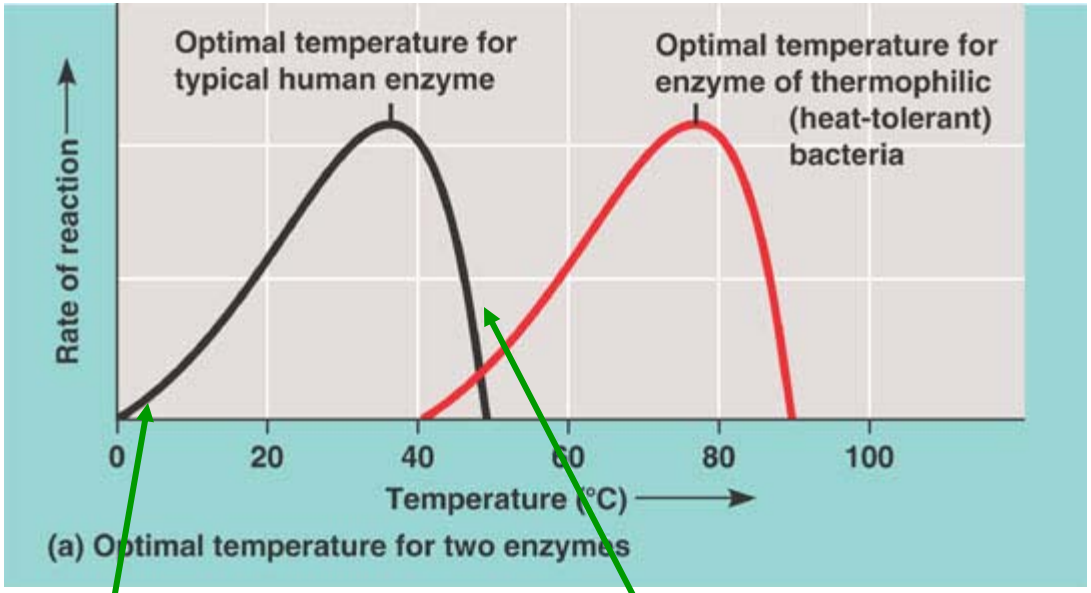
An enzyme whose 3-dimensional shape has been altered such that it is not catalytically active is said to be denatured. An enzyme that is in its correct 3-dimensional shape, so it functions properly, is said to be in its native conformation.

The enzyme trypsin is mostly in its native conformation at pH values of approximately 6.5 – 9, but becomes mostly denatured at pH values lower than ~ 6.5 or pH values higher than ~ 9. In contrast, the enzyme pepsin is mostly in its native conformation at pH values of approximately 1 – 3, but becomes denatured a pH values lower than ~ 1 or higher than ~ 3.

*

Enzymes function optimally over a rather narrow range of temperatures. Each enzyme operates optimally at a temperature of its normal environment.

From textbook Fig. 8.18, p. 155.



diminished activity due to lower kinetic energy of substrates and enzyme at low temperature.

Diminished activity due to denaturation of the enzyme at high temperature.

*