CHAPTER 8 : Enzymes

Enzymes are the catalysts of biochemical reactions

Main characteristics : (1) catalytic power

(2) specificity

Most enzymes are proteins

active site / substrate

apoenzyme + cofactor } holoenzyme

cofactors < metals
org. compounds (coenzymes)

TABLE 8.1 Rate enhancement by selected enzymes

Enzyme	Nonenzymatic half-life	Uncatalyzed rate (k_{un} s^{-1})	Catalyzed rate (k_{cat} s^{-1})	Rate enhancement (k_{cat}/k_{un})
OMP decarboxylase	78,000,000 years	2.8×10^{-16}	39	1.4×10^{17}
Staphylococcal nuclease	130,000 years	1.7×10^{-13}	95	5.6×10^{14}
AMP nucleosidase	69,000 years	1.0×10^{-11}	60	6.0×10^{12}
Carboxypeptidase A	7.3 years	3.0×10^{-9}	578	1.9×10^{11}
Ketosteroid isomerase	7 weeks	1.7×10^{-7}	66,000	3.9×10^{11}
Triose phosphate isomerase	1.9 days	4.3×10^{-6}	4,300	1.0×10^{9}
Chorismate mutase	7.4 hours	2.6×10^{-5}	50	1.9×10^{6}
Carbonic anhydrase	5 seconds	1.3×10^{-1}	1×10^{6}	7.7×10^{6}

Abbreviations: OMP, orotidine monophosphate; AMP, adenosine monophosphate.
Source: After A. Radzicka and R. Wofenden. *Science* 267 (1995):90–93.

TABLE 8.2 Enzyme cofactors

Cofactor	Enzyme
Coenzyme	
Thiamine pyrophosphate	Pyruvate dehydrogenase
Flavin adenine nucleotide	Monoamine oxidase
Nicotinamide adenine dinucleotide	Lactate dehydrogenase
Pyridoxal phosphate	Glycogen phosphorylase
Coenzyme A (CoA)	Acetyl CoA carboxylase
Biotin	Pyruvate carboxylase
5′-Deoxyadenosyl cobalamin	Methylmalonyl mutase
Tetrahydrofolate	Thymidylate synthase
Metal	
Zn^{2+}	Carbonic anhydrase
Zn^{2+}	Carboxypeptidase
Mg^{2+}	*Eco*RV
Mg^{2+}	Hexokinase
Ni^{2+}	Urease
Mo	Nitrate reductase
Se	Glutathione peroxidase
Mn^{2+}	Superoxide dismutase
K^{+}	Propionyl CoA carboxylase

TABLE 8.3 Six major classes of enzymes

Class	Type of reaction	Example
1. Oxidoreductases	Oxidation-reduction	Lactate dehydrogenase
2. Transferases	Group transfer	Nucleoside monophosphate kinase (NMP kinase)
3. Hydrolases	Hydrolysis reactions (transfer of functional groups to water)	Chymotrypsin
4. Lyases	Addition or removal of groups to form double bonds	Fumarase
5. Isomerases	Isomerization (intramolecular group transfer)	Triose phosphate isomerase
6. Ligases	Ligation of two substrates at the expense of ATP hydrolysis	Aminoacyl-tRNA synthetase

International Classification of Enzymes*

No.	Class	Type of reaction catalyzed
1	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)
2	Transferases	Group-transfer reactions
3	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)
4	Lyases	Addition of groups to double bonds, or formation of double bonds by removal of groups
5	Isomerases	Transfer of groups within molecules to yield isomeric forms
6	Ligases	Formation of C—C, C—S, C—O, and C—N bonds by condensation reactions coupled to ATP cleavage

*Most enzymes catalyze the transfer of electrons, atoms, or functional groups. They are therefore classified, given code numbers, and assigned names according to the type of transfer reaction, the group donor, and the group acceptor.

"I think that enzymes are molecules that are complementary in structure to the activated complexes of the reactions that they catalyze, that is, to the molecular configuration that is intermediate between the reacting substances and the products of reaction for these catalyzed processes. The attraction of the enzyme molecule for the activated complex would thus lead to a decrease in its energy and hence to a decrease in the energy of activation of the reaction and to an increase in the rate of reaction."

—Linus Pauling
Nature 161(1948):707

Common features of the active sites:

- The active site takes up a relatively small part of the total volume of an enzyme
- The active site is a 3D entity formed by groups that come from different parts of the linear aa sequence
- Substrates are bound to enzymes by multiple weak attractions
- Active sites are clefts or crevices
- The specificity of binding depends on the precisely defined arrangement of atoms in an active site

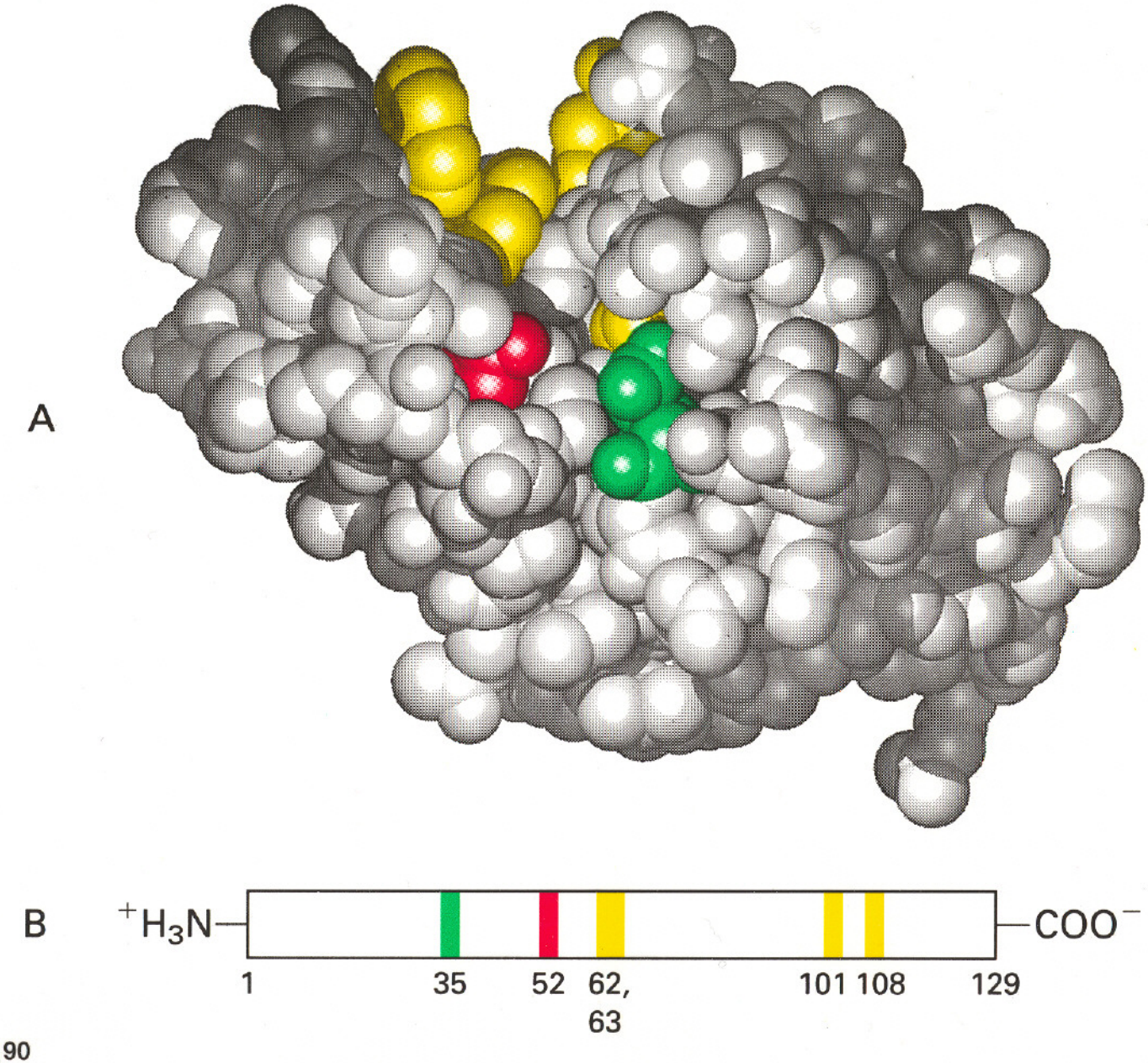


Figure 8-11, page 190

(A) space-filling model of lysozyme

The existence of ES complexes has been shown in a variety of ways:

- **By studying the velocity of an enzyme- catalyzed reaction**
- **ES complexes have been directly visualized by electron microscopy and X-ray crystallography**
- **The spectroscopic characteristics of many enzymes and substrates change upon formation of an ES complex**

Active site of an enzyme: The region that binds the substrate

Catalytic group: The residues of the active site

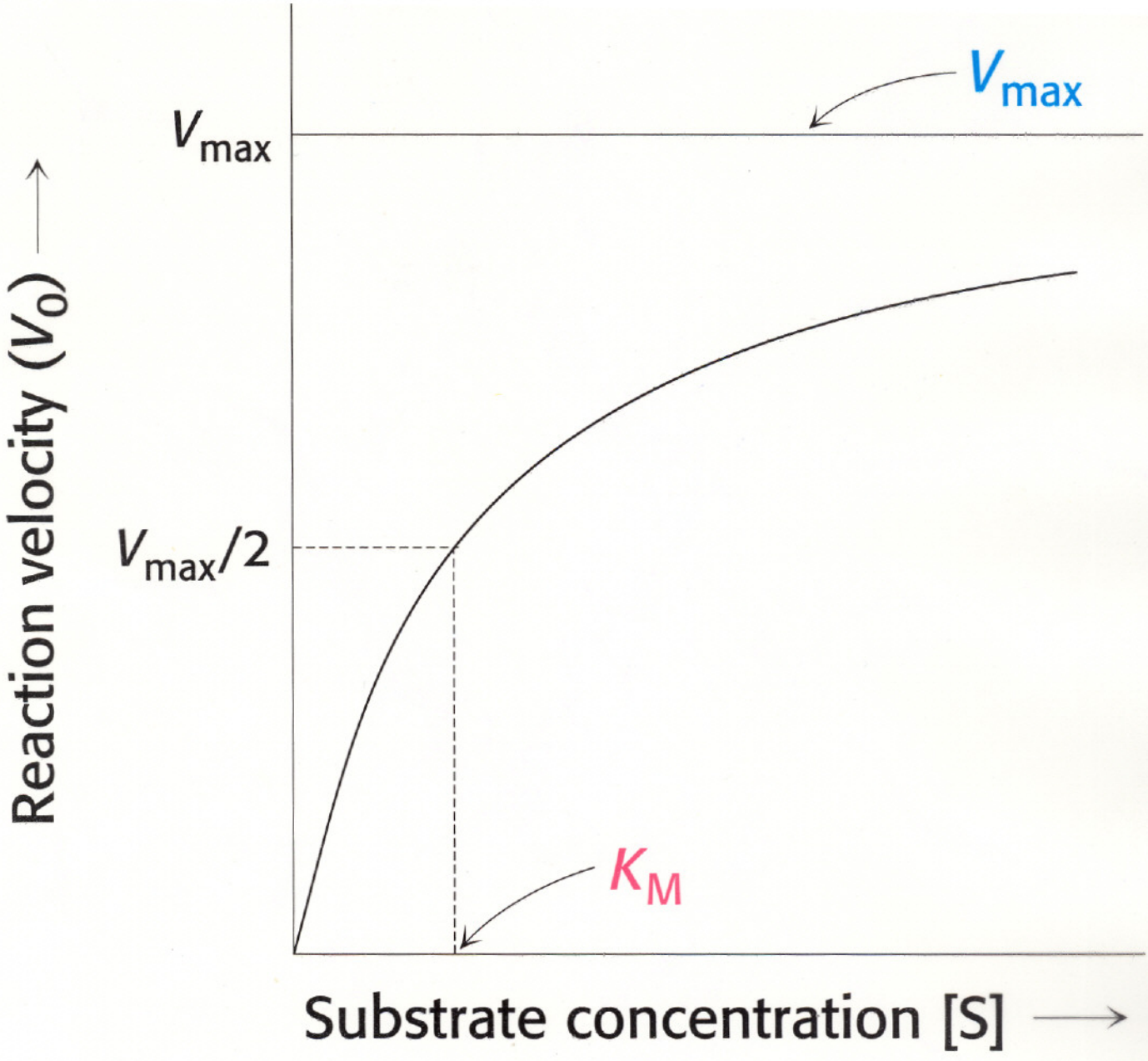
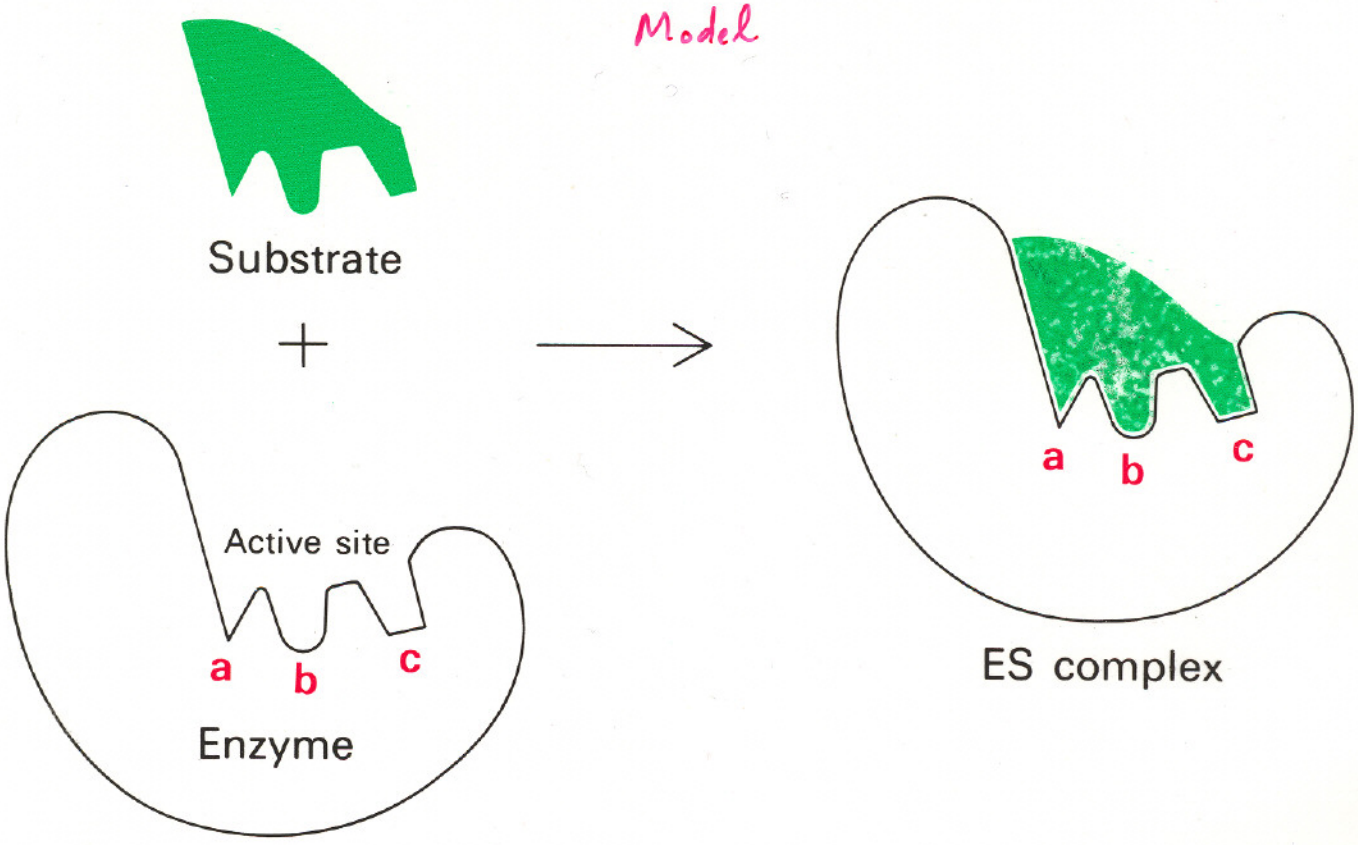
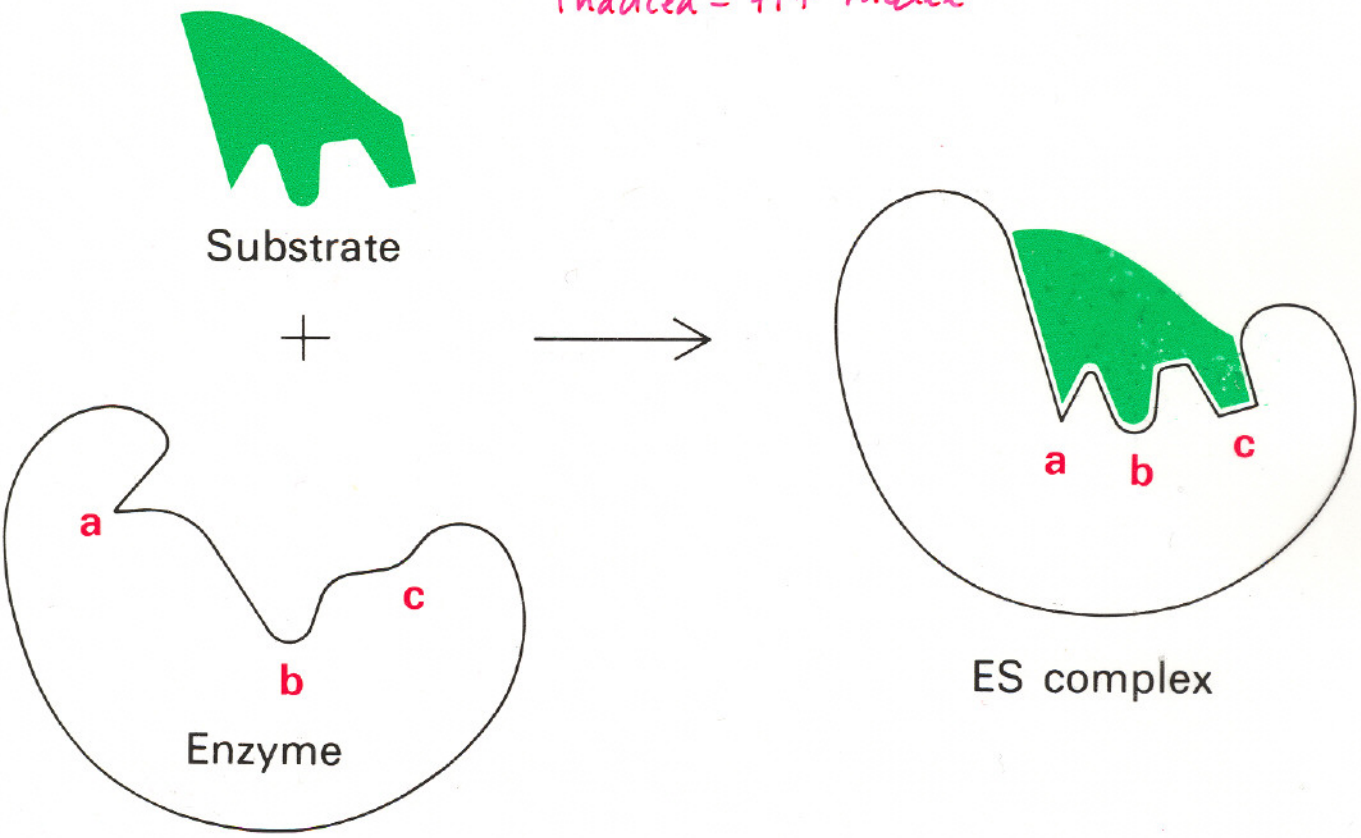


Figure 8-11
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

Lock-and-key Model



Induced-fit model



Figures 8-13 and 8-14, page 191

LAWS OF THERMODYNAMICS

- A <u>system</u> is defined as the matter within a defined region of space
- The matter in the rest of the universe is called the <u>surroundings</u>

The First Law of Thermodynamics states that the total energy of a system and its surroundings is constant.

different forms of energy: chemical energy
kinetic energy
potential energy
heat

The Second Law of Thermodynamics states that the total entropy of a system and its surroundings always increases for a spontaneous process.

- Entropy is a measure of the level of randomness or disorder in a system (S).

Free energy (G): a thermodynamic function that combine the first and the second laws of thermodynamics, introduced by Gibbs in 1878.

$$\Delta G = \Delta H - T \Delta S$$

ΔG : the change in free energy of a system undergoing a transformation at constant pressure (P) and temperature (T)

ΔH : the change ~~of~~ in enthalpy (heat content) of this system

ΔS : the change in entropy of this system

- A reaction can occur spontaneously only if ΔG is negative
- A system is at equalibrium and no net change can take place if ΔG is zero
- A reaction cannot occur spontaneously if ΔG is positive
- The ΔG of a reaction is independent of the path (or molecular mechanism) of the transformation
- The ΔG provides no information about the rate of a reaction

→ Enzymes accelerate the attainment of equilibria but do not shift their position

→ Enzymes accelerate reactions by stabilizing transition states

$$S \rightleftharpoons S^{\ddagger} \longrightarrow P$$

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_3} E + P$$

$$A + B \rightleftharpoons C + D$$

$$\Delta G = \Delta G^{\circ} + RT \log_e \frac{[C][D]}{[A][B]}$$

At equilibrium, $\Delta G = 0$

$$0 = \Delta G^{\circ'} + RT \log_e \frac{[C][D]}{[A][B]} \Rightarrow$$

$$\Delta G^{\circ'} = -RT \log_e \frac{[C][D]}{[A][B]}$$

Equilibrium constant under standard conditions $K'_{eq} = \frac{[C][D]}{[A][B]}$

$$\Delta G^{\circ'} = -RT \log_e K'_{eq}$$

$$\Delta G^{\circ'} = -2.303\, RT \log_{10} K'_{eq}$$

Dihydroxyacetone phosphate

Glyceraldehyde 3-phosphate

At equilibrium, $\frac{[\text{Glyceraldehyde 3-phosphate}]}{[\text{Dihydroxyacetone phosphate}]} = 0.0475$

(pH = 7, T = 25°C = 298 K)

$$\Delta G^{\circ\prime} = -2.303\, RT \log_{10} K'_{eq}$$

$$= -2.303 \times 1.987 \times 10^{-3} \times 298 \times \log_{10}(0.0475)$$

$$= +1.8 \text{ kcal/mol}$$

$$\Delta G = \Delta G^{\circ\prime} + RT \log_e \frac{3 \times 10^{-6} M}{2 \times 10^{-4} M}$$

$$= 1.8 \text{ kcal/mol} - 2.5 \text{ kcal/mol}$$

$$= -0.7 \text{ kcal/mol}$$