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Most Enzymes are Proteins

Cofactor

Coenzyme

Prosthetic group

Holoenzyme

Apoenzyme

Apoprotein

TABLE 6–1 Some Inorganic Ions That Serve as Cofactors for Enzymes

Ions	Enzymes
Cu^{2+}	Cytochrome oxidase
Fe^{2+} or Fe^{3+}	Cytochrome oxidase, catalase, peroxidase
K^{+}	Pyruvate kinase
Mg^{2+}	Hexokinase, glucose 6-phosphatase, pyruvate kinase
Mn^{2+}	Arginase, ribonucleotide reductase
Mo	Dinitrogenase
Ni^{2+}	Urease
Se	Glutathione peroxidase
Zn^{2+}	Carbonic anhydrase, alcohol dehydrogenase, carboxypeptidases A and B

Table 6-1
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TABLE 6–2 Some Coenzymes That Serve as Transient Carriers of Specific Atoms or Functional Groups

Coenzyme	Examples of chemical groups transferred	Dietary precursor in mammals
Biocytin	CO_2	Biotin
Coenzyme A	Acyl groups	Pantothenic acid and other compounds
5′-Deoxyadenosylcobalamin (coenzyme B_{12})	H atoms and alkyl groups	Vitamin B_{12}
Flavin adenine dinucleotide	Electrons	Riboflavin (vitamin B_2)
Lipoate	Electrons and acyl groups	Not required in diet
Nicotinamide adenine dinucleotide	Hydride ion ($:H^-$)	Nicotinic acid (niacin)
Pyridoxal phosphate	Amino groups	Pyridoxine (vitamin B_6)
Tetrahydrofolate	One-carbon groups	Folate
Thiamine pyrophosphate	Aldehydes	Thiamine (vitamin B_1)

Note: The structures and modes of action of these coenzymes are described in Part II.

Table 6-2
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Nomenclature

Remember the five basic reactions in biochemistry

TABLE 6–3 International Classification of Enzymes

Class no.	Class name	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 cleavage of ATP or similar cofactor

Table 6-3
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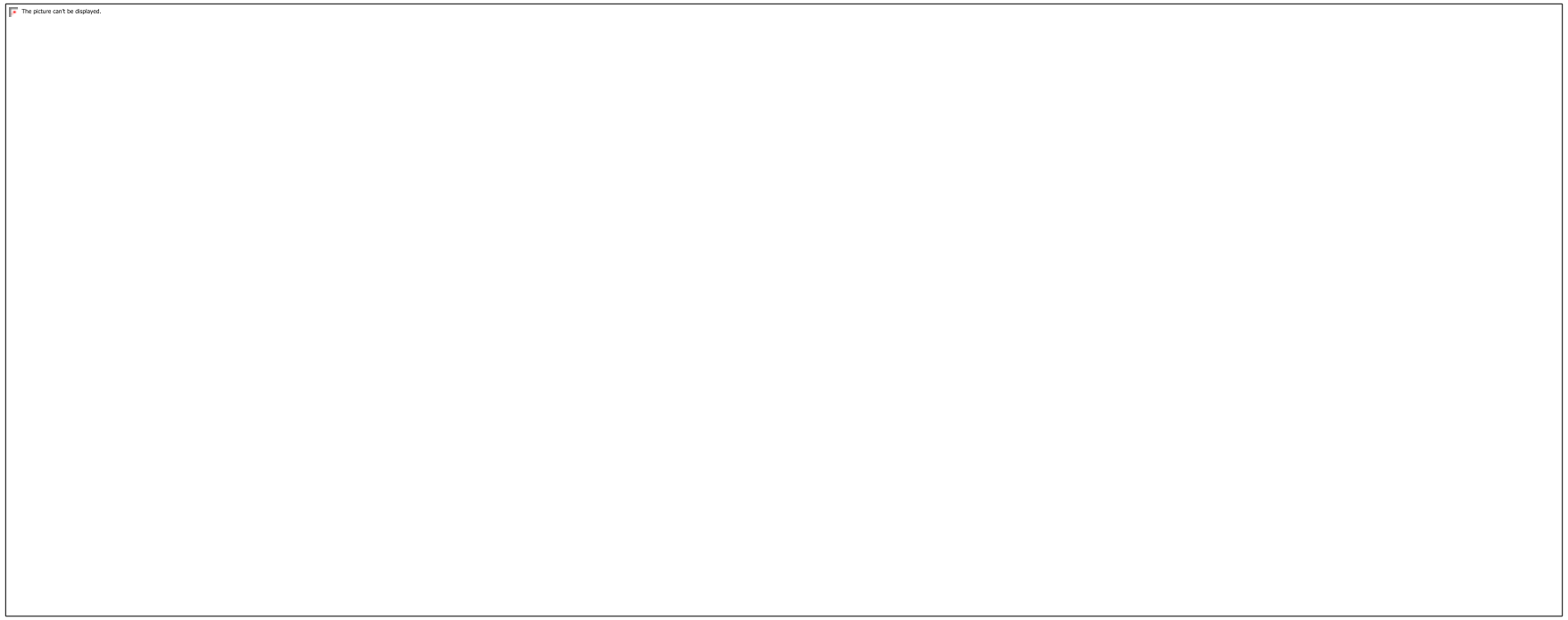
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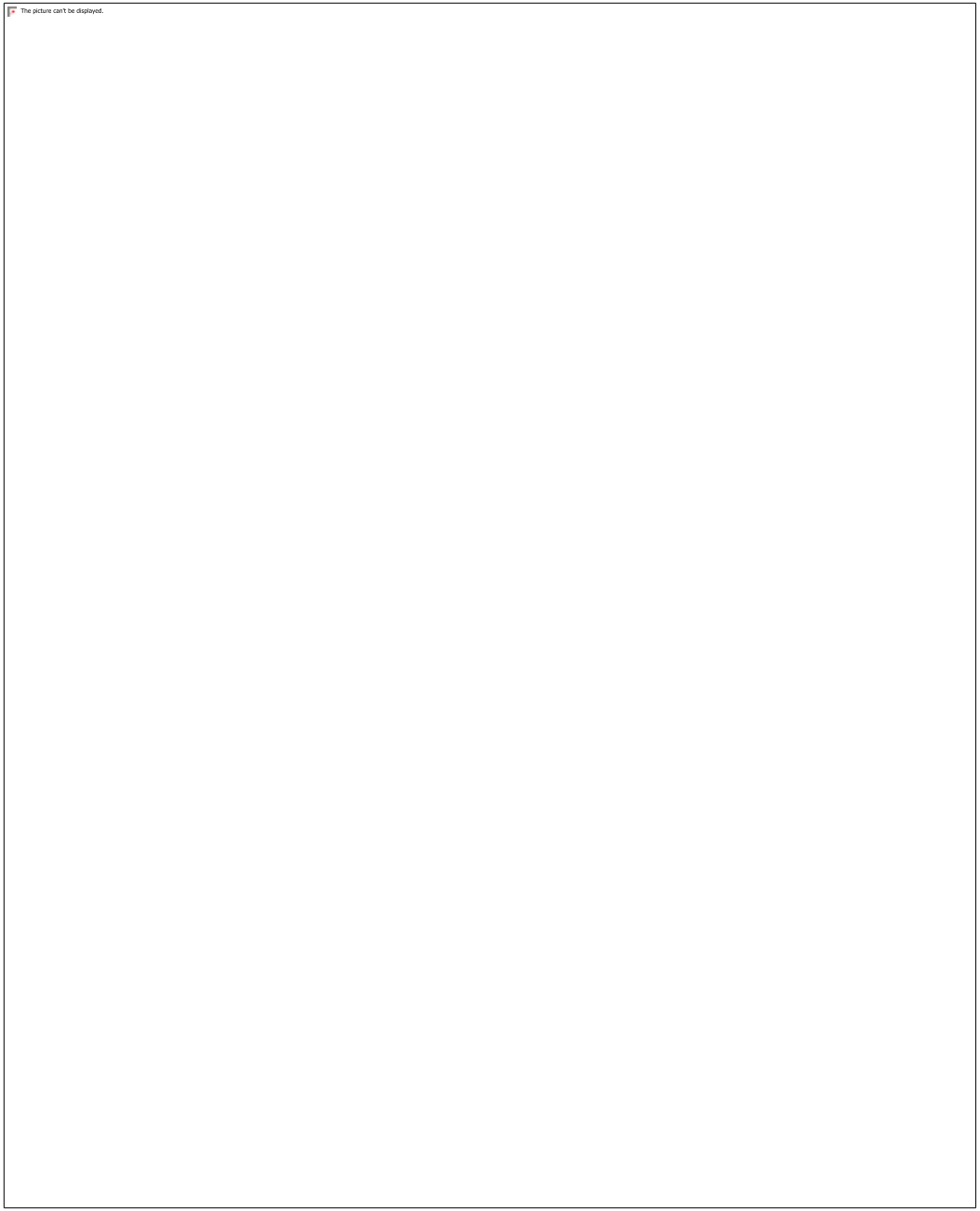
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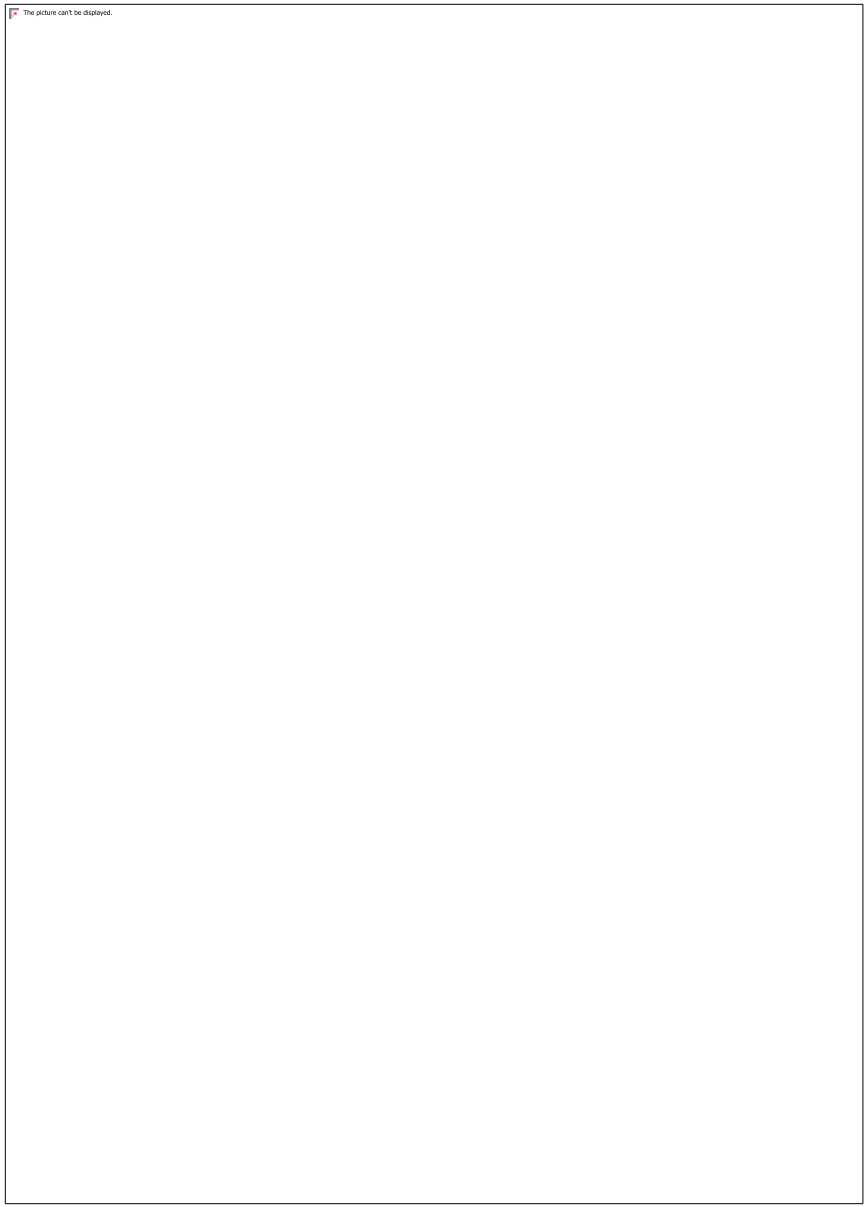
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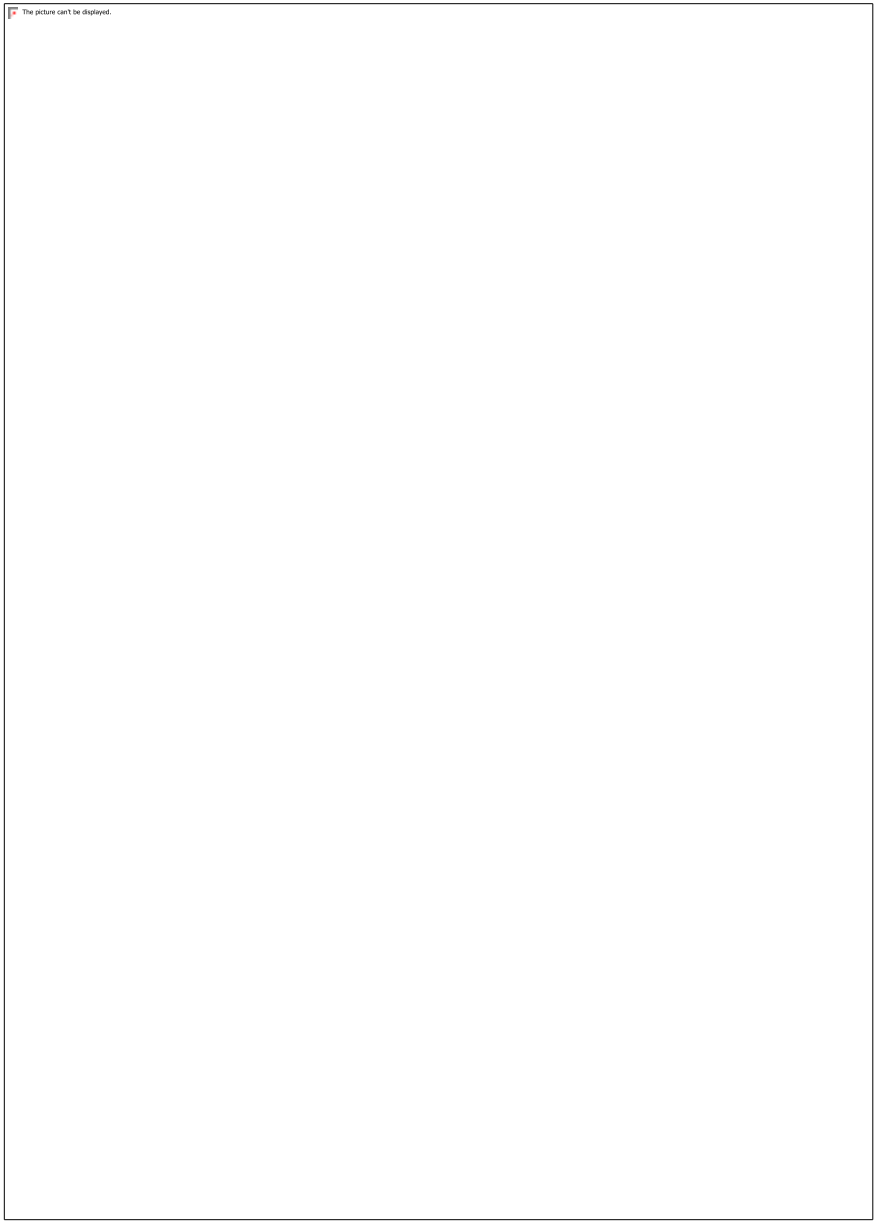
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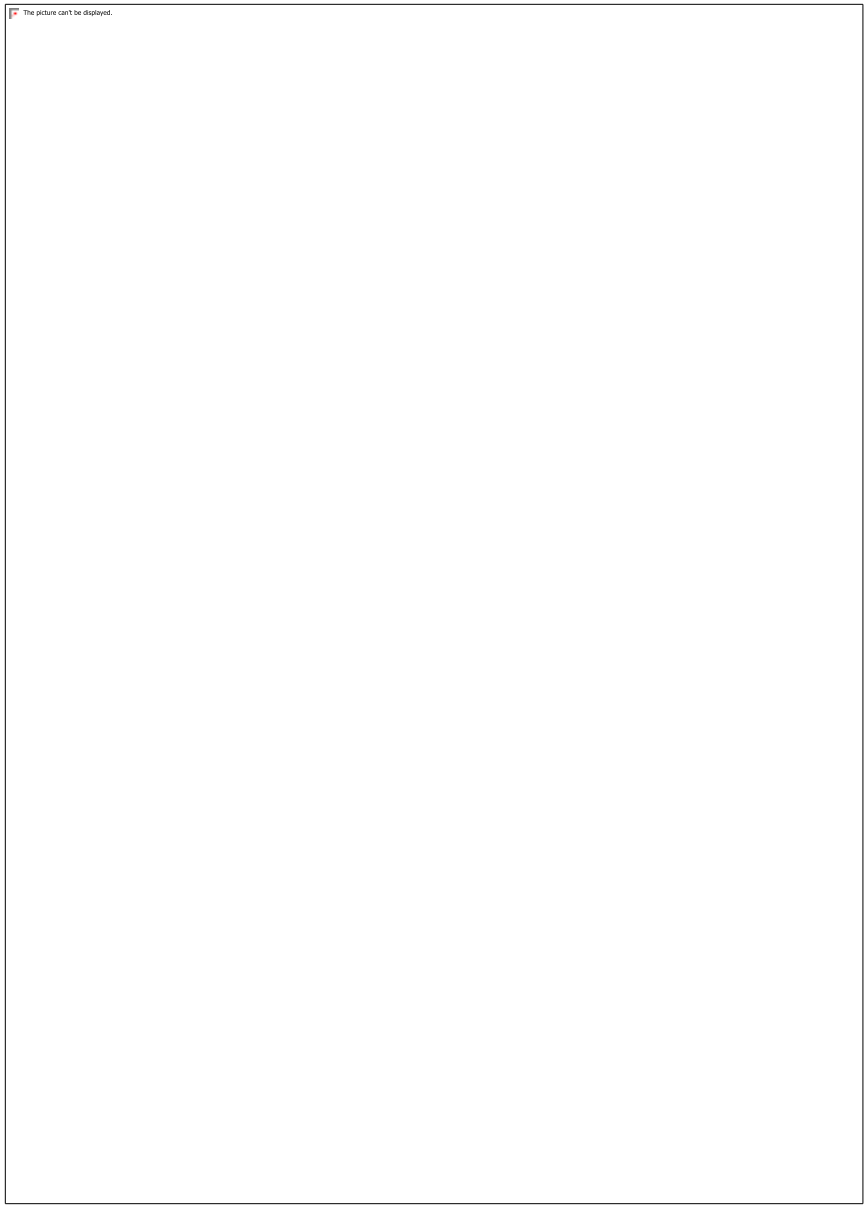
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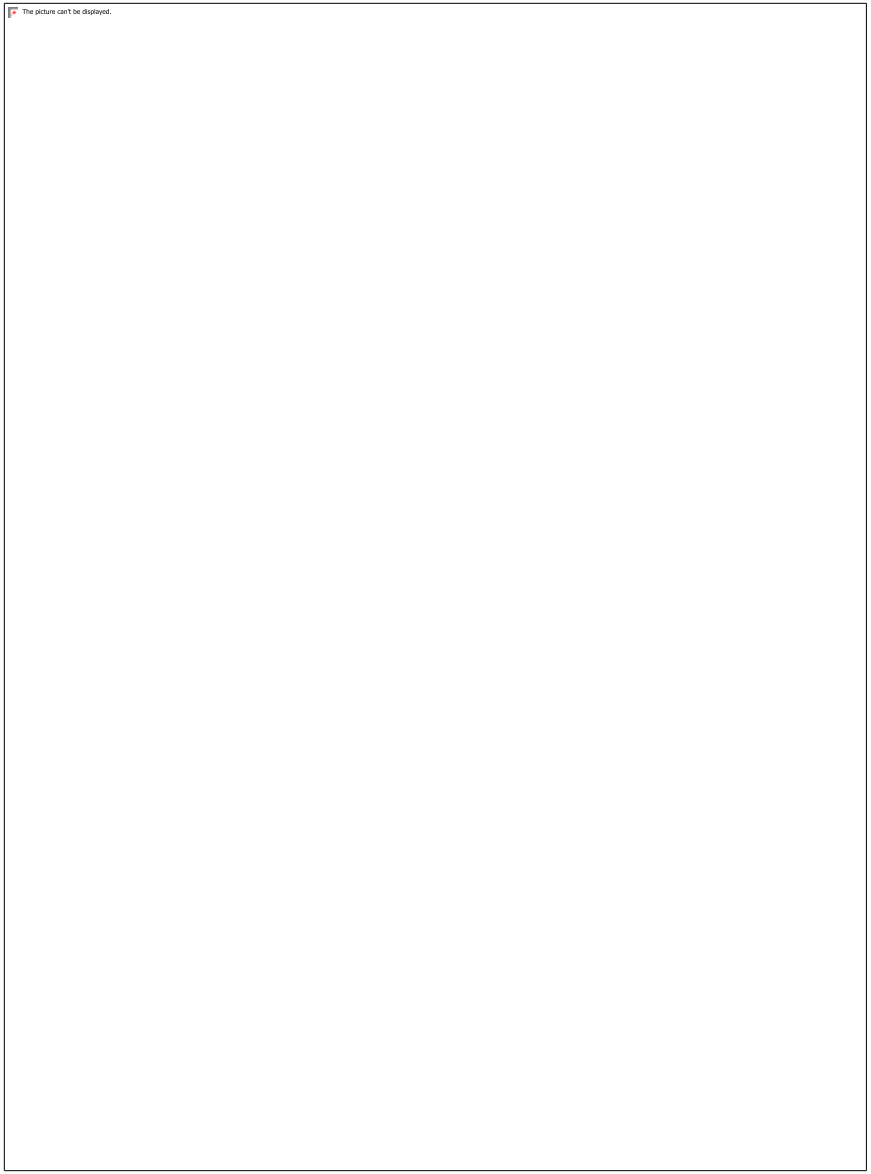
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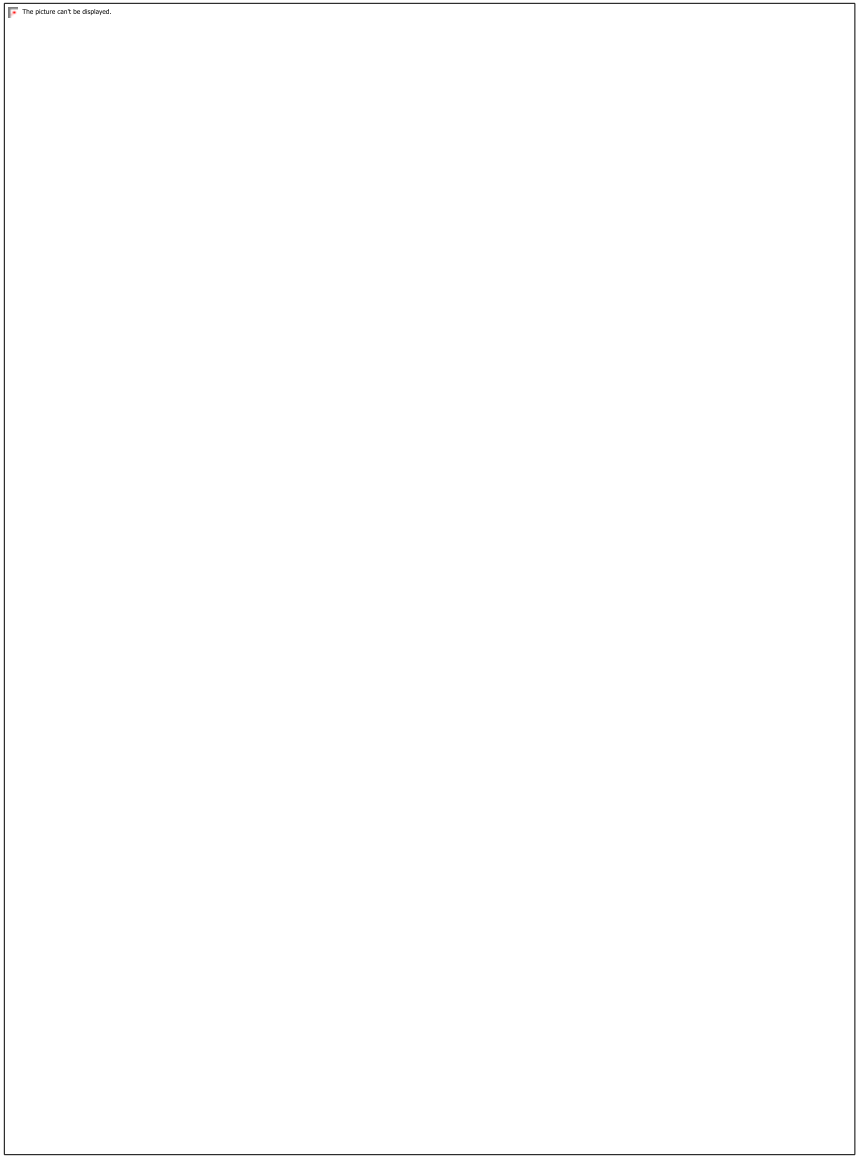
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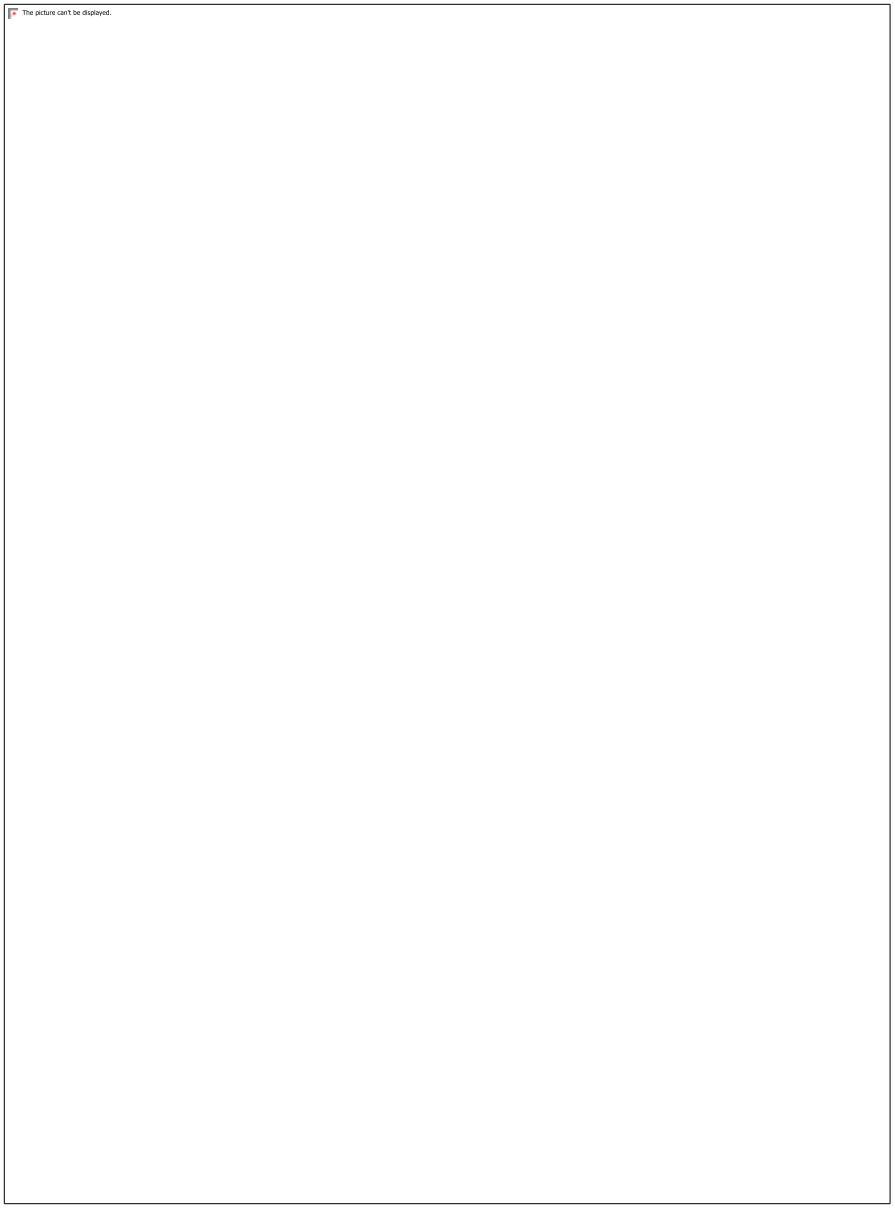
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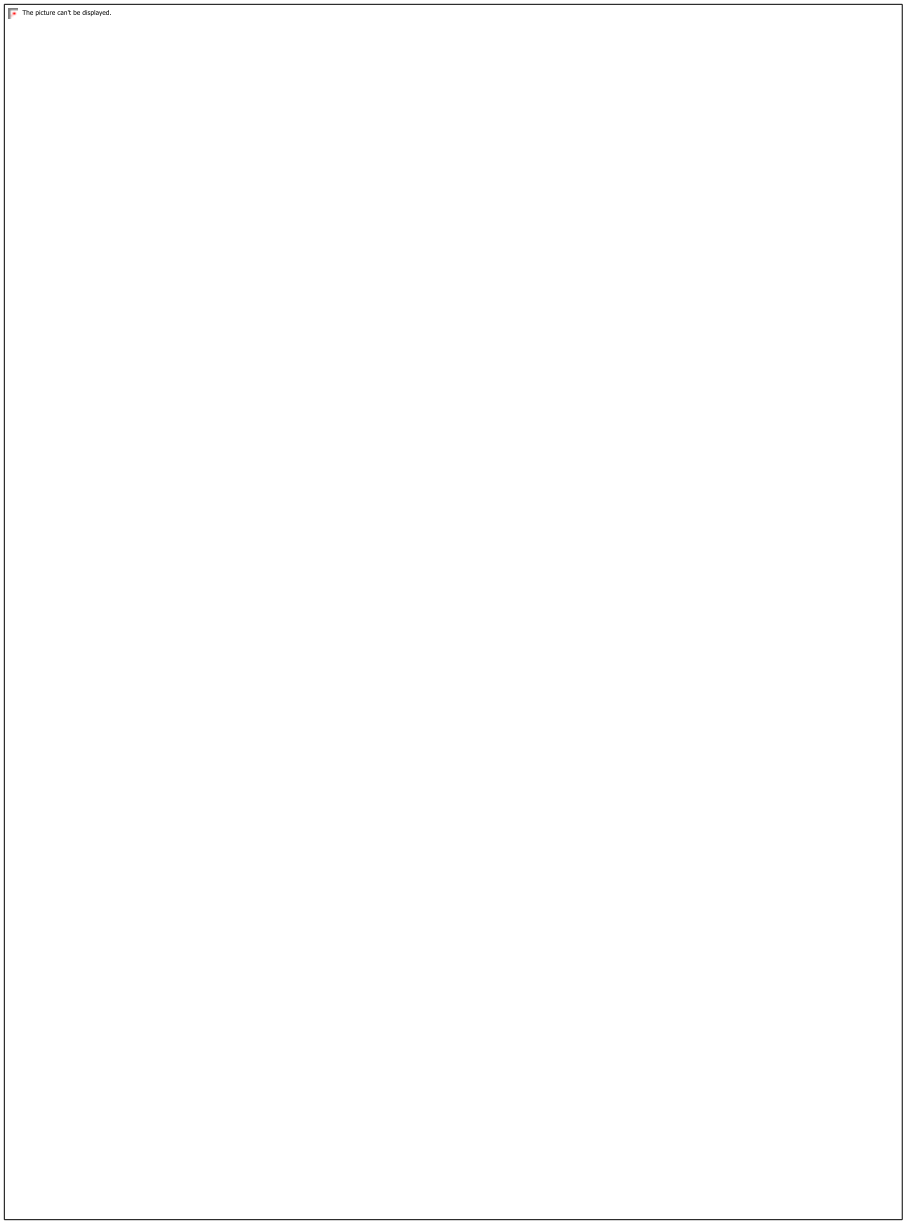
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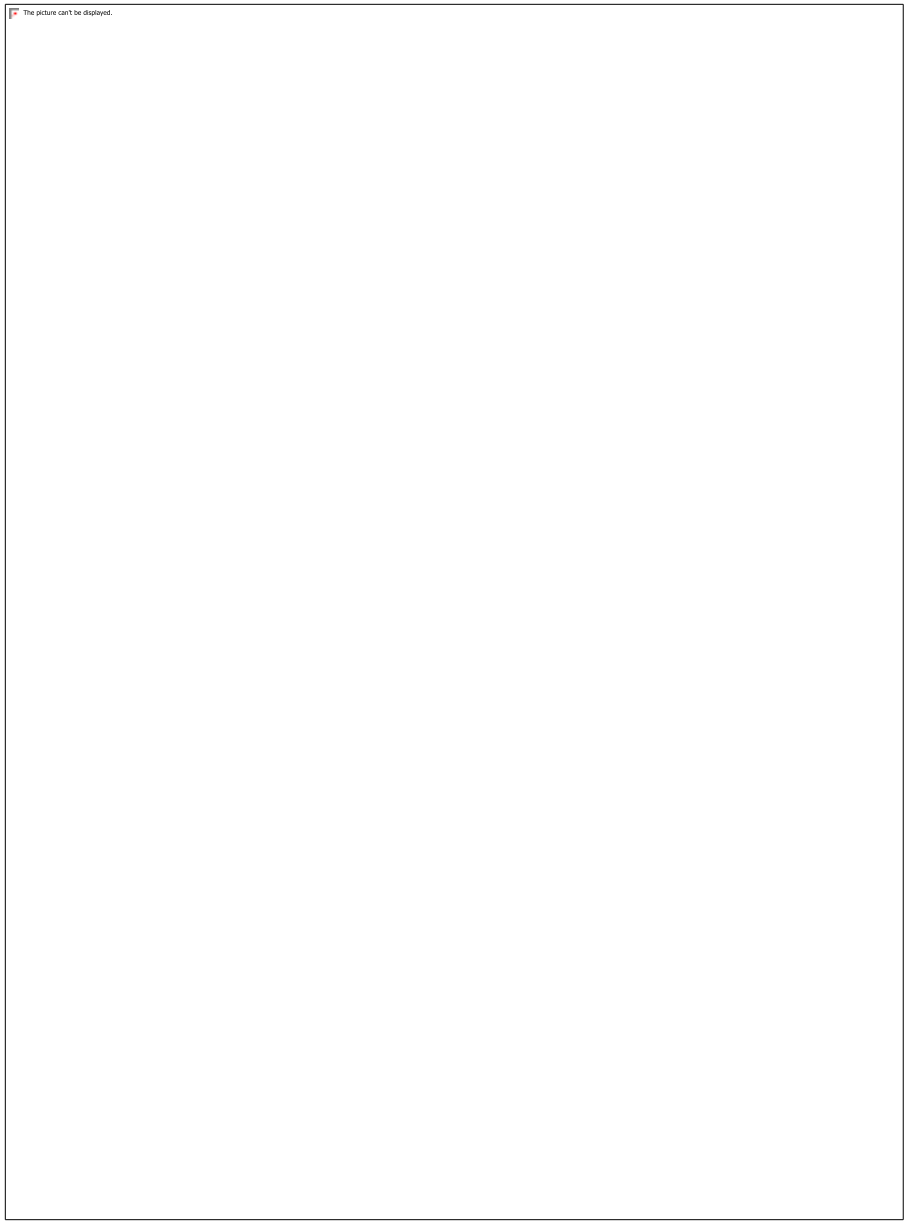
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EC 1.1.1.1

Common name: alcohol dehydrogenase

Reaction: an alcohol + NAD^+ = an aldehyde or ketone + NADH + H^+

Other name(s): aldehyde reductase; ADH; alcohol dehydrogenase (NAD); aliphatic alcohol dehydrogenase; ethanol dehydrogenase; NAD-dependent alcohol dehydrogenase; NAD-specific aromatic alcohol dehydrogenase; NADH-alcohol dehydrogenase; NADH-aldehyde dehydrogenase; primary alcohol dehydrogenase; yeast alcohol dehydrogenase

Systematic name: alcohol:NAD^+ oxidoreductase

Comments: A zinc protein. Acts on primary or secondary alcohols or hemi-acetals; the animal, but not the yeast, enzyme acts also on cyclic secondary alcohols.

CAS registry number: 9031-72-5

References:

1. Brändén, G.-I., Jörnvall, H., Eklund, H. and Furugren, B. Alcohol dehydrogenase. In: Boyer, P.D. (Ed.), *The Enzymes*, 3rd ed., vol. 11, Academic Press, New York, 1975, p. 103-190.

2. Jörnvall, H. Differences between alcohol dehydrogenases. Structural properties and evolutionary aspects. *Eur. J. Biochem.* 72 (1977) 443-452. [Medline UI: 77115786]

3. Negelein, E. and Wulff, H.-J. Diphosphopyridinproteid ackohol, acetaldehyd. *Biochem. Z*. 293 (1937) 351-389.

4. Sund, H. and Theorell, H. Alcohol dehydrogenase. In: Boyer, P.D., Lardy, H. and Myrbäck, K. (Eds.), *The Enzymes*, 2nd ed., vol. 7, Academic Press, New York, 1963, p. 25-83.

5. Theorell, H. Kinetics and equilibria in the liver alcohol dehydrogenase system. *Adv. Enzymol. Relat. Subj. Biochem.* 20 (1958) 31-49.

[EC 1.1.1.1 created 1961]

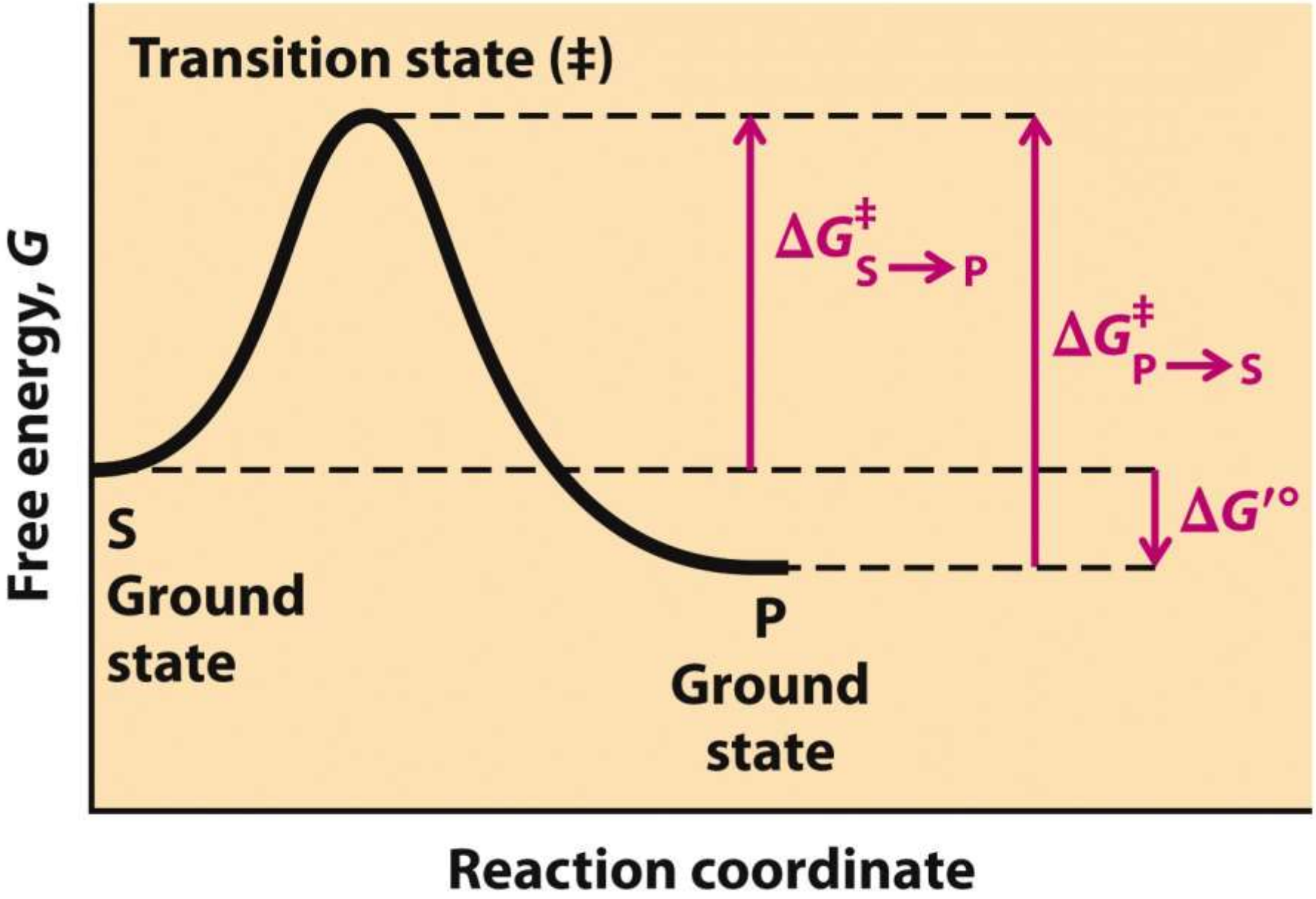

Figure 6-2
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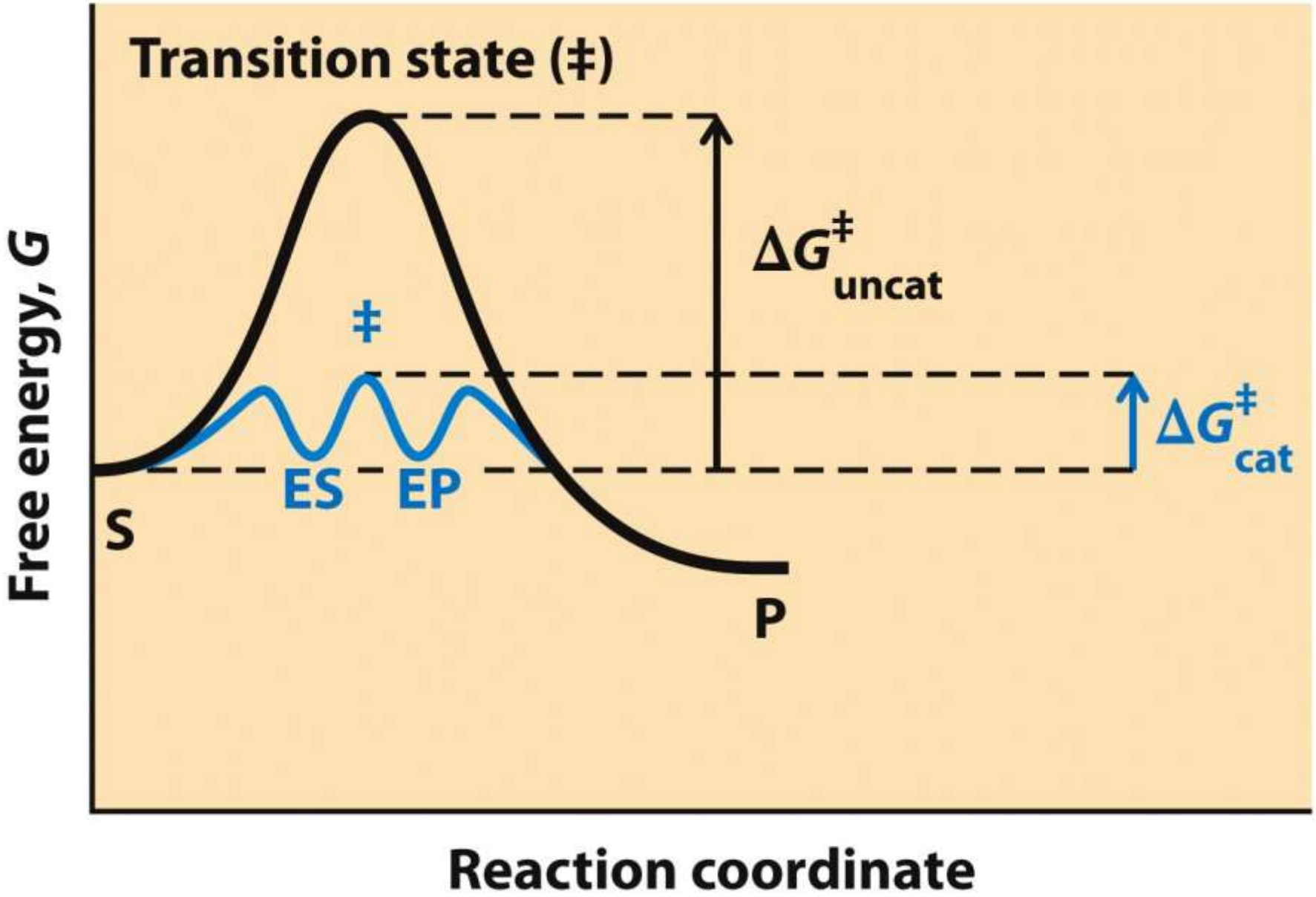

Figure 6-3
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Ground state

Standard free-energy change

Biochemical standard free-energy change

Transition state

Activation energy

Reaction intermediate

Rate-limiting step

Rate-determining step

Equilibrium constant

Rate constant

Rate equation

Binding energy

TABLE 6–4 Relationship between K'_{eq} and $\Delta G'^{\circ}$

K'_{eq}	$\Delta G'^{\circ}$ (kJ/mol)
10^{-6}	34.2
10^{-5}	28.5
10^{-4}	22.8
10^{-3}	17.1
10^{-2}	11.4
10^{-1}	5.7
1	0.0
10^{1}	−5.7
10^{2}	−11.4
10^{3}	−17.1

Note: The relationship is calculated from $\Delta G'^{\circ} = -RT \ln K'_{eq}$ (Eqn 6–3).

Table 6-4
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TABLE 6–5 Some Rate Enhancements Produced by Enzymes

Cyclophilin	10^5
Carbonic anhydrase	10^7
Triose phosphate isomerase	10^9
Carboxypeptidase A	10^{11}
Phosphoglucomutase	10^{12}
Succinyl-CoA transferase	10^{13}
Urease	10^{14}
Orotidine monophosphate decarboxylase	10^{17}

Table 6-5
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Weak interactions optimized in the

transition state

No enzyme

Substrate (metal stick) → **Transition state (bent stick)** → **Products (broken stick)**

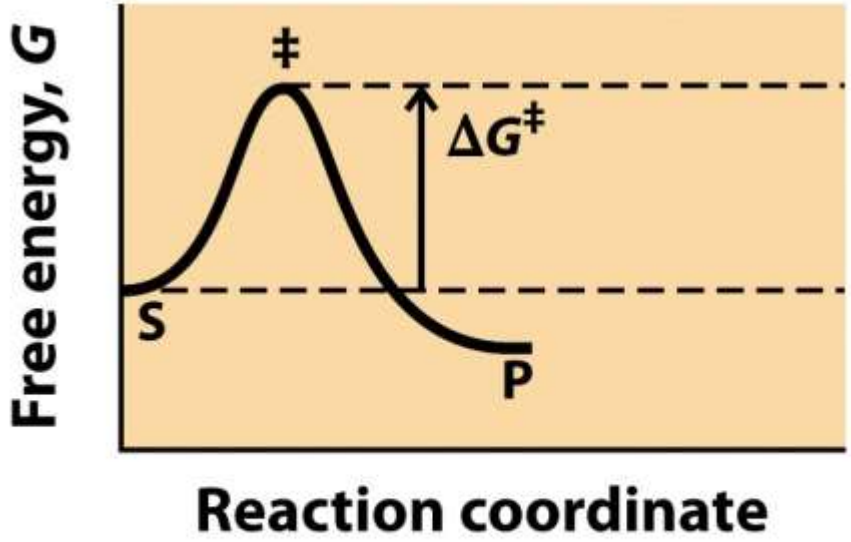

Figure 6-5a
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Enzyme complementary to substrate

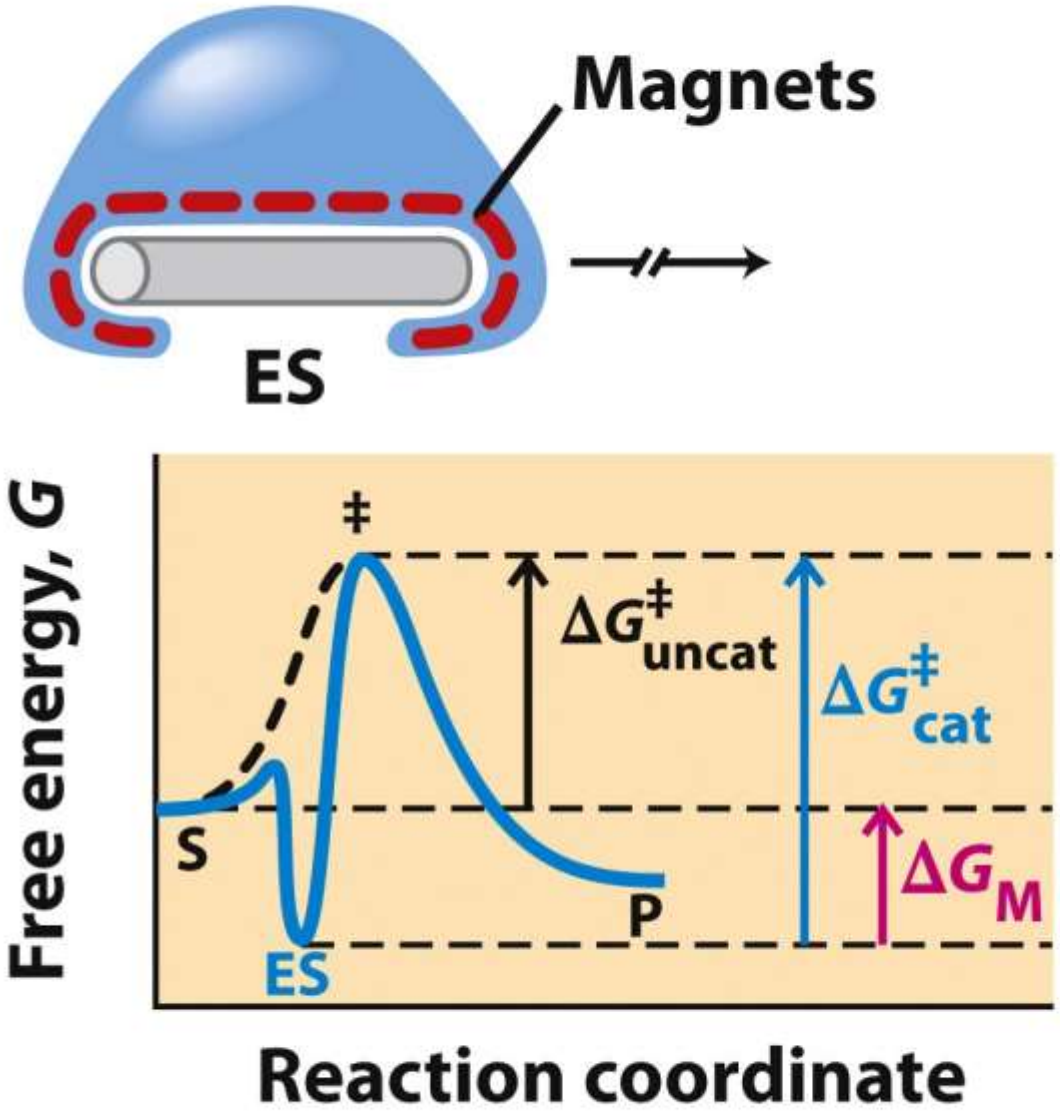

Figure 6-5b
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Enzyme complementary to transition state

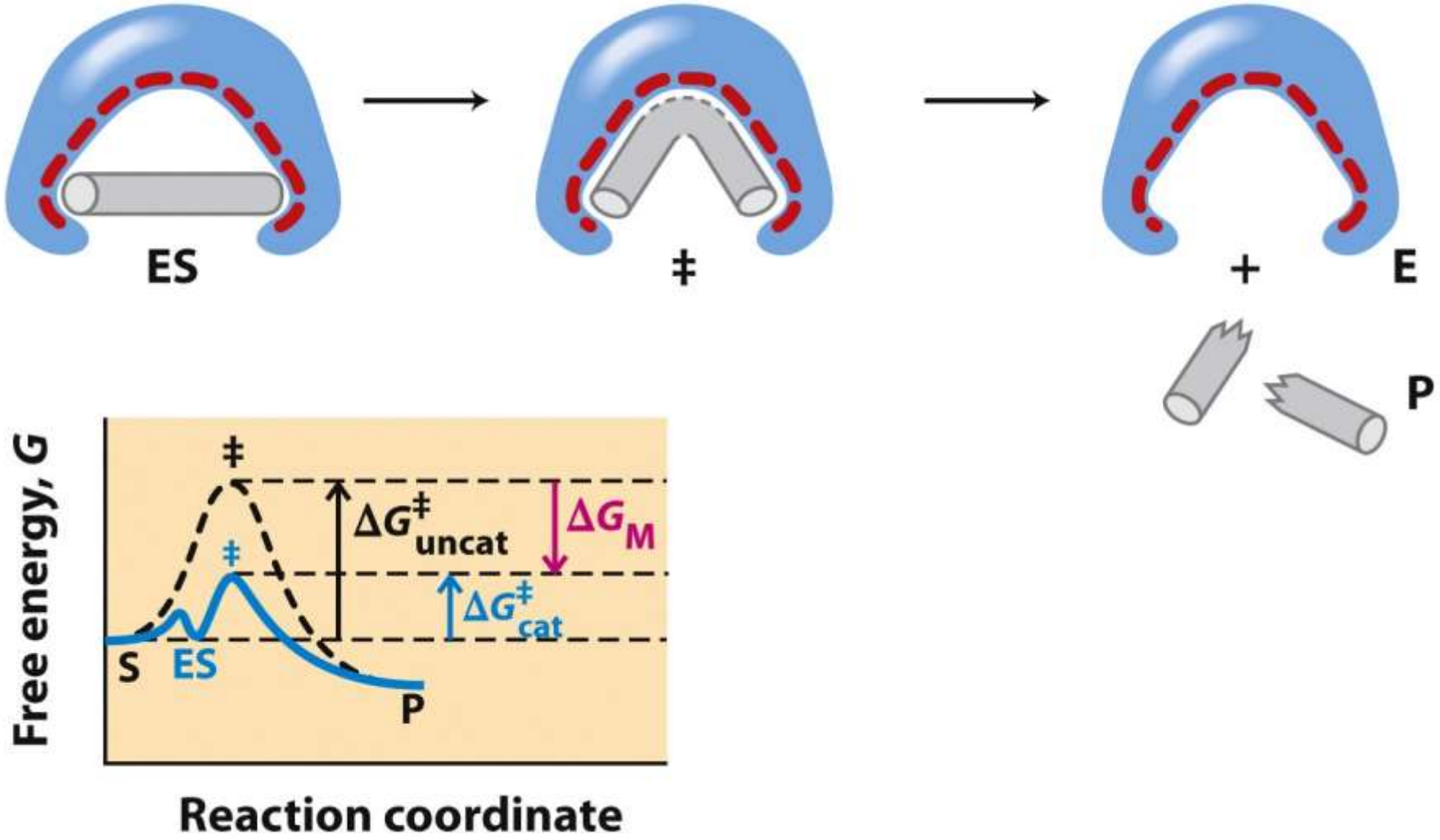

Figure 6-5c
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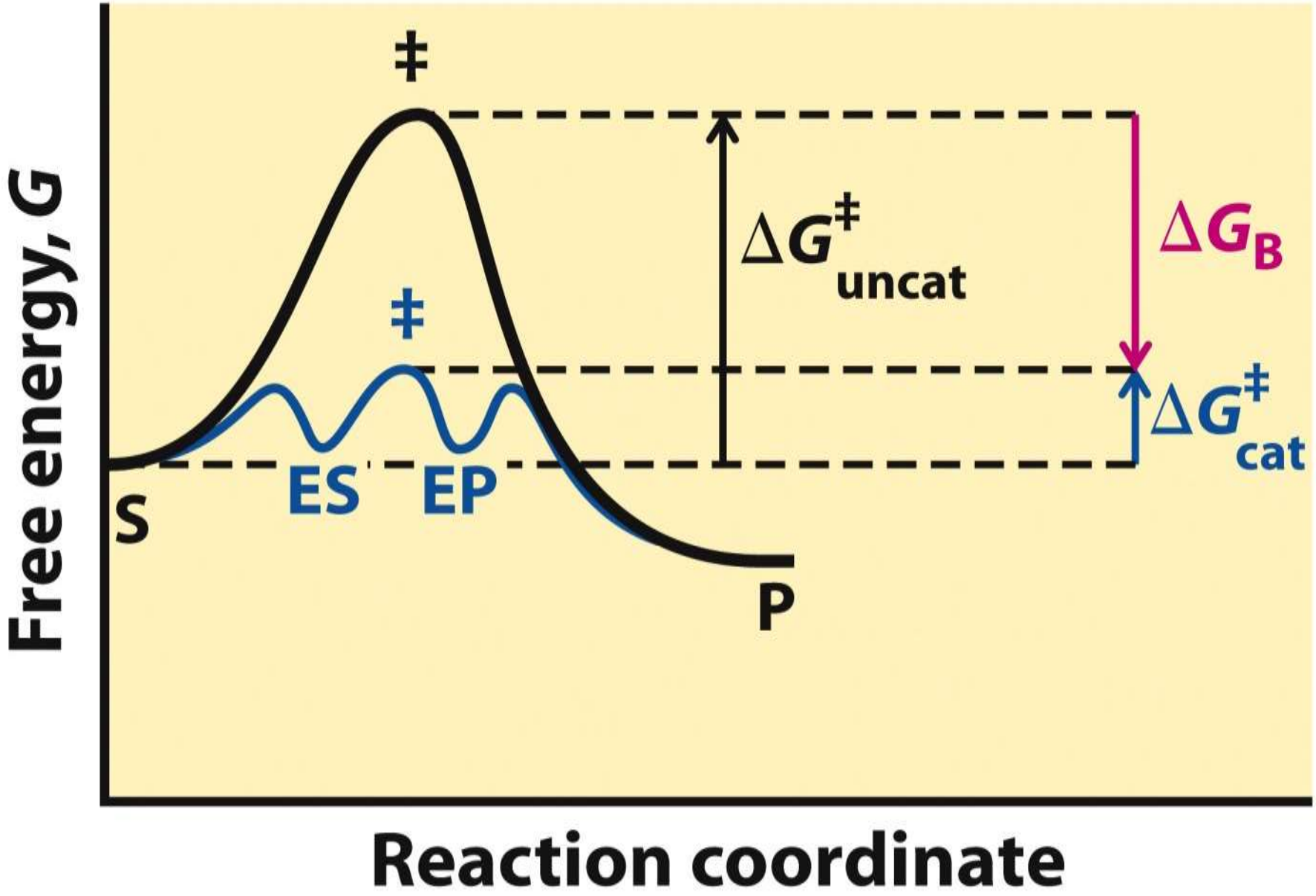

Figure 6-6
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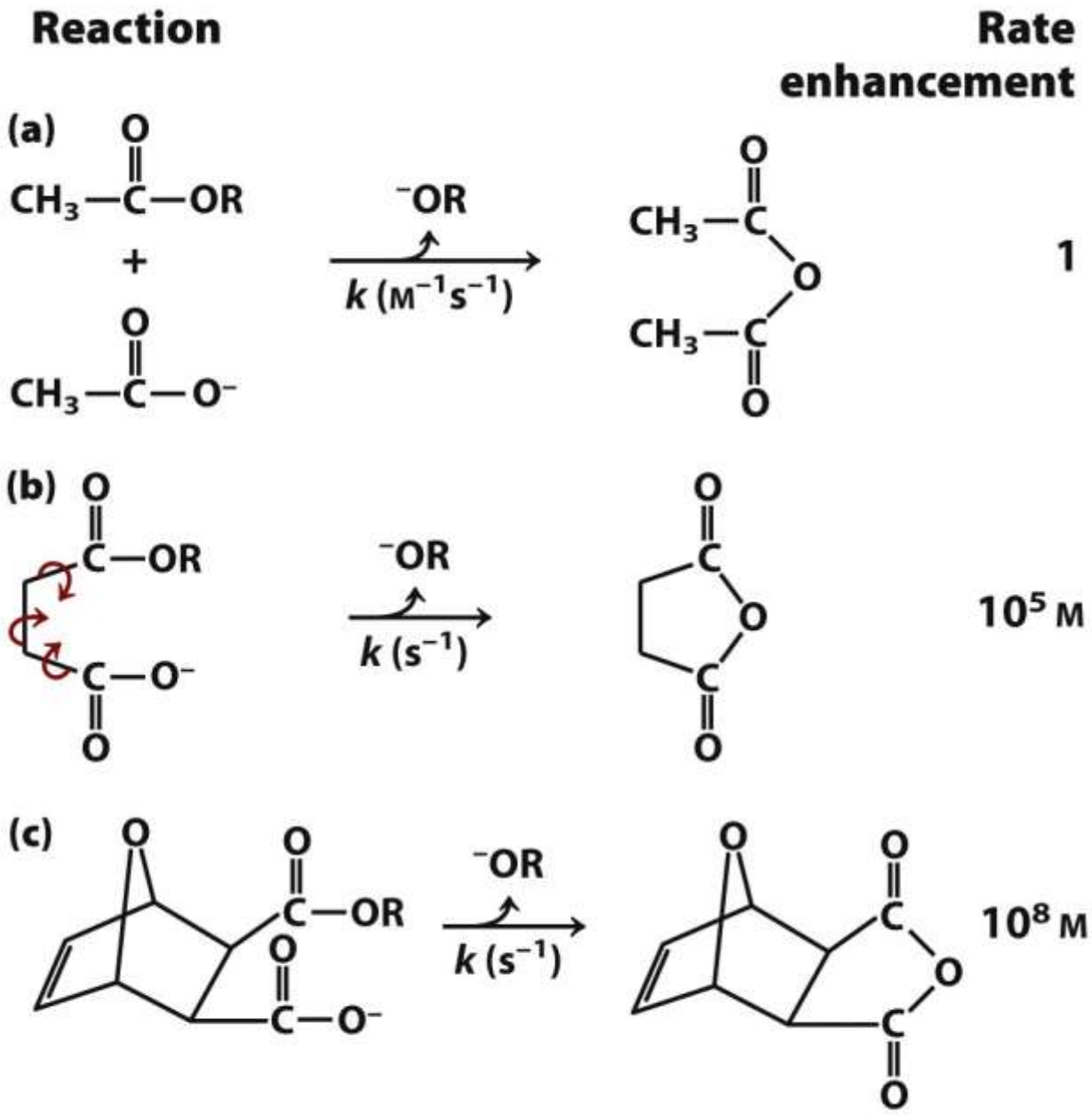

Figure 6-7
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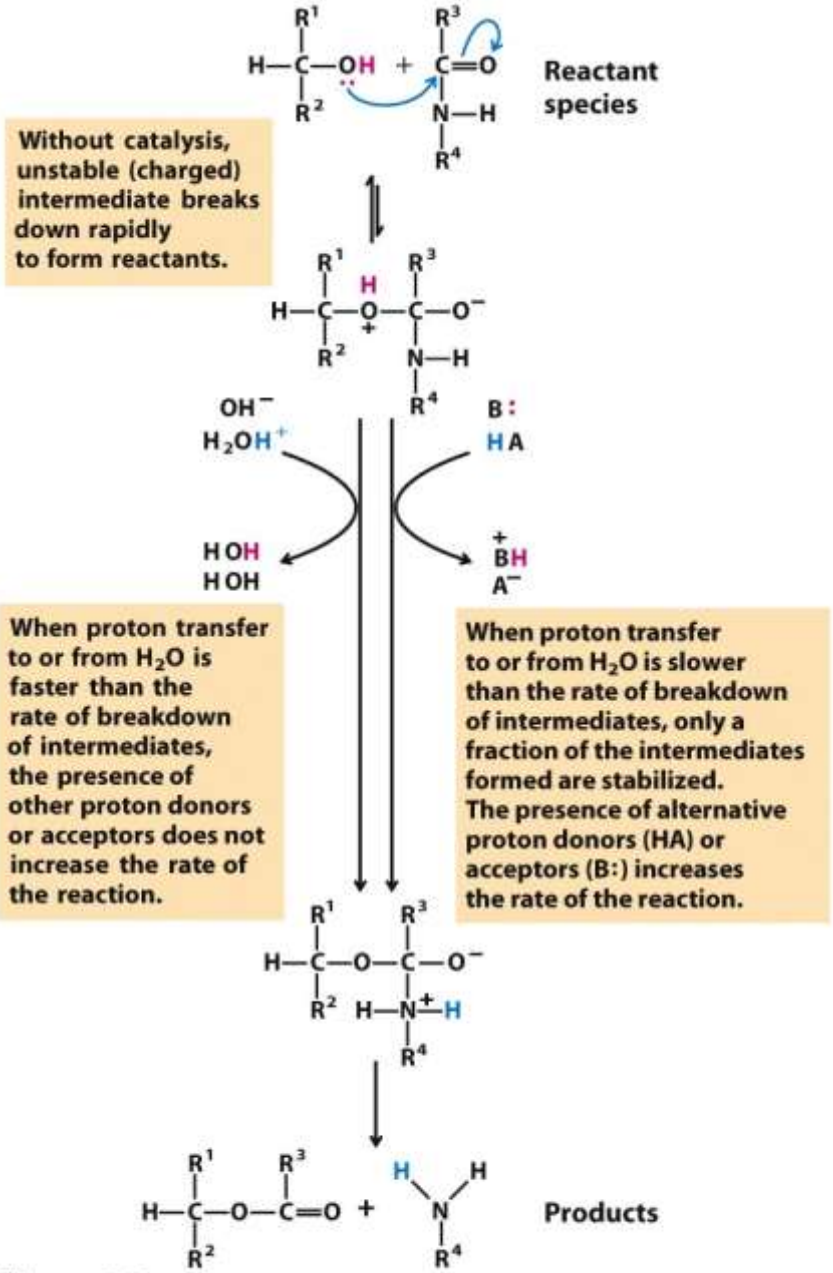

Figure 6-8

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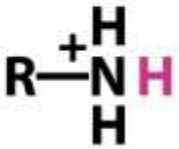
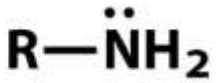
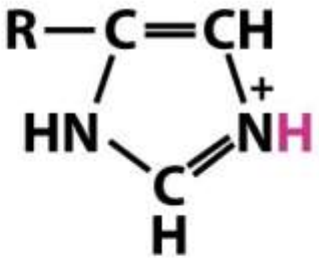
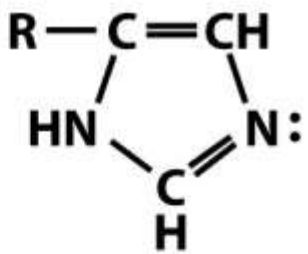
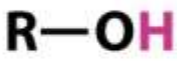
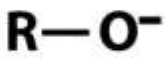
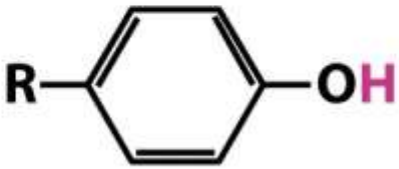
Amino acid residues	General acid form (proton donor)	General base form (proton acceptor)
Glu, Asp		
Lys, Arg		
Cys		
His		
Ser		
Tyr		

Figure 6-9

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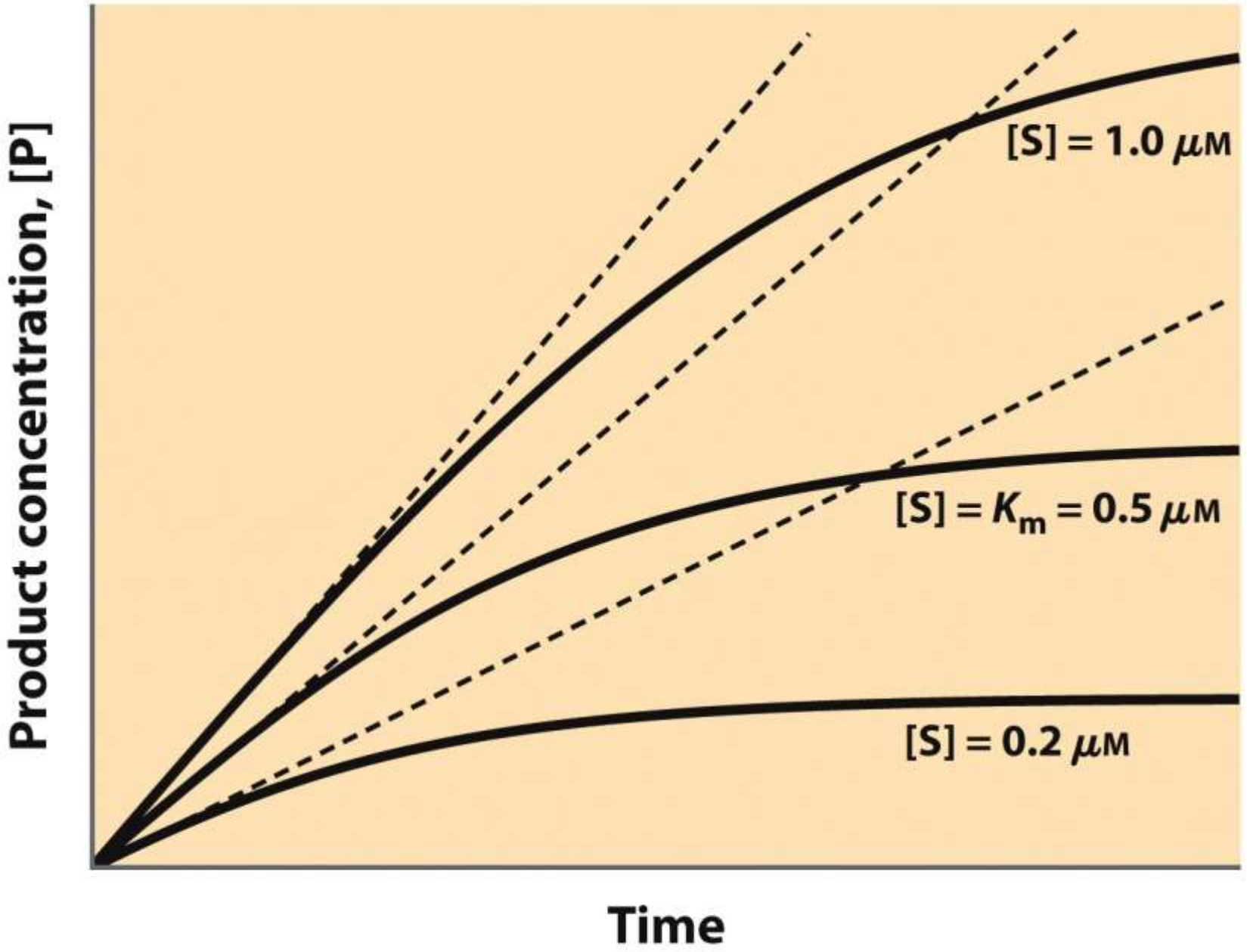

Figure 6-10
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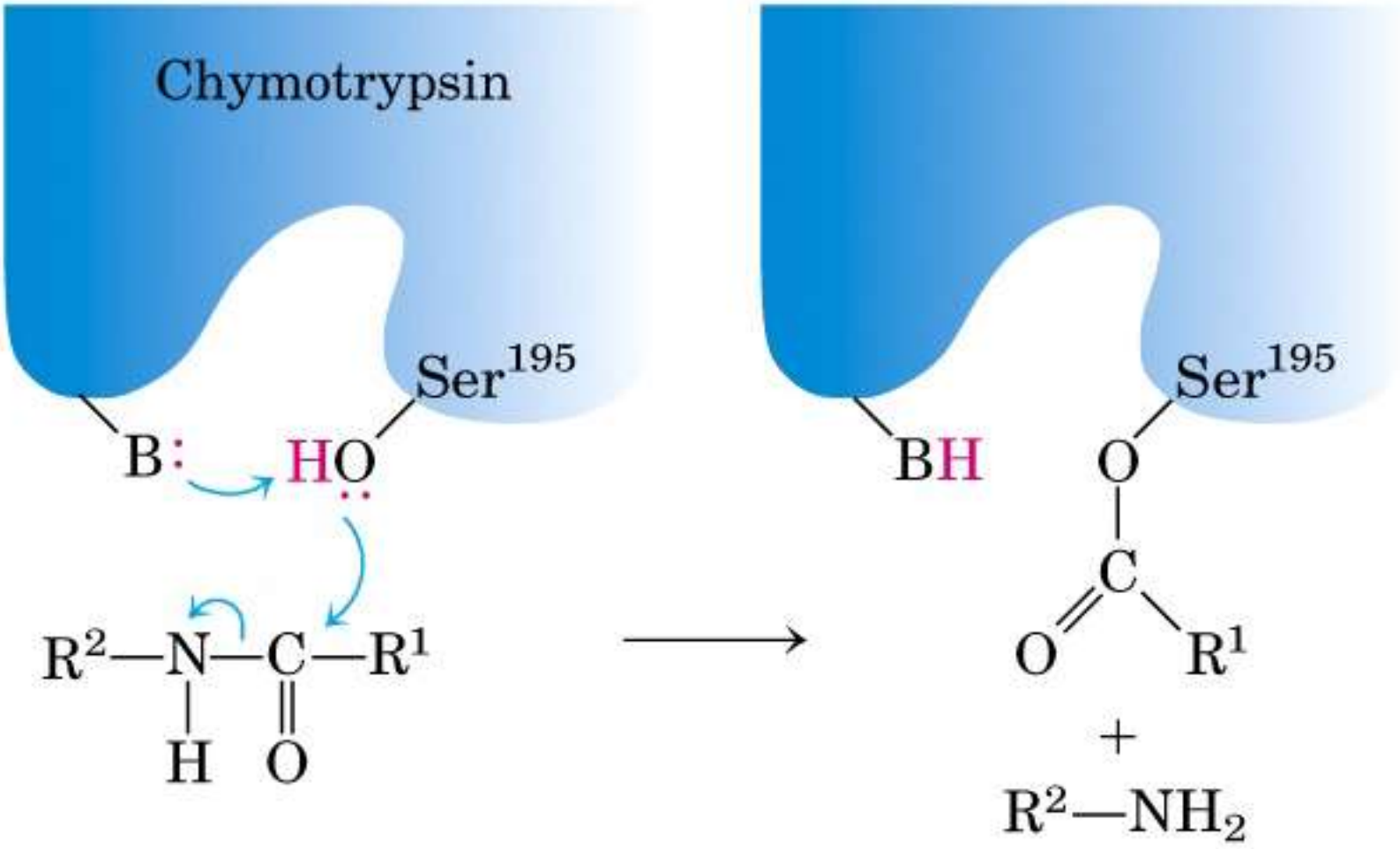
Chymotrypsin
Ser195
B:
HO
R2—N—C—R1
H O
BH
O
C
O
R1
+
R2—NH2

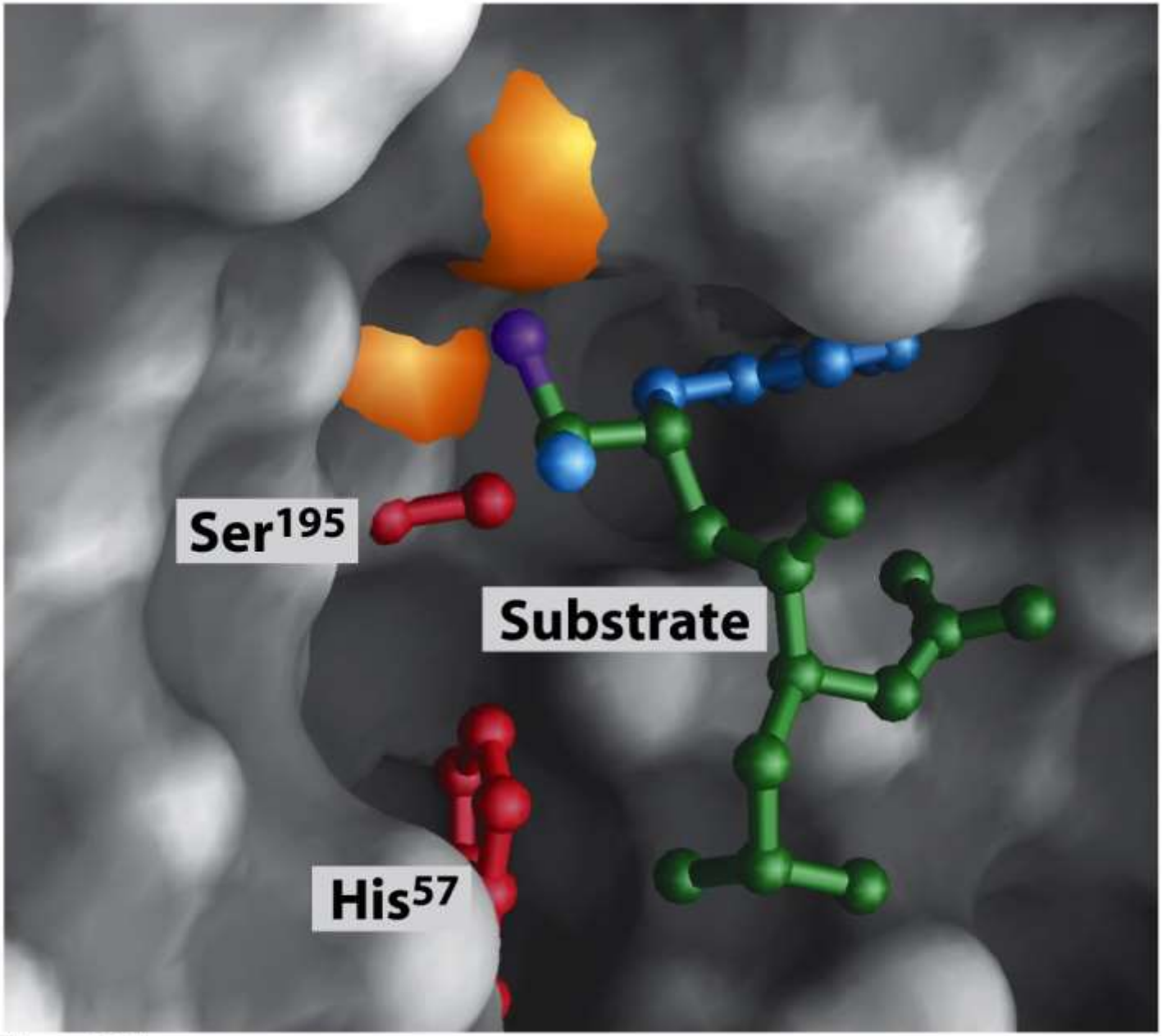

Figure 6-18d
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Enzyme Kinetics

Enzyme kinetics

Initial rate (or initial velocity)

Maximum velocity

Pre-steady state

Steady state

Steady-state kinetics

Steady-state assumption

Michaelis constant

Michaelis-Menten equation

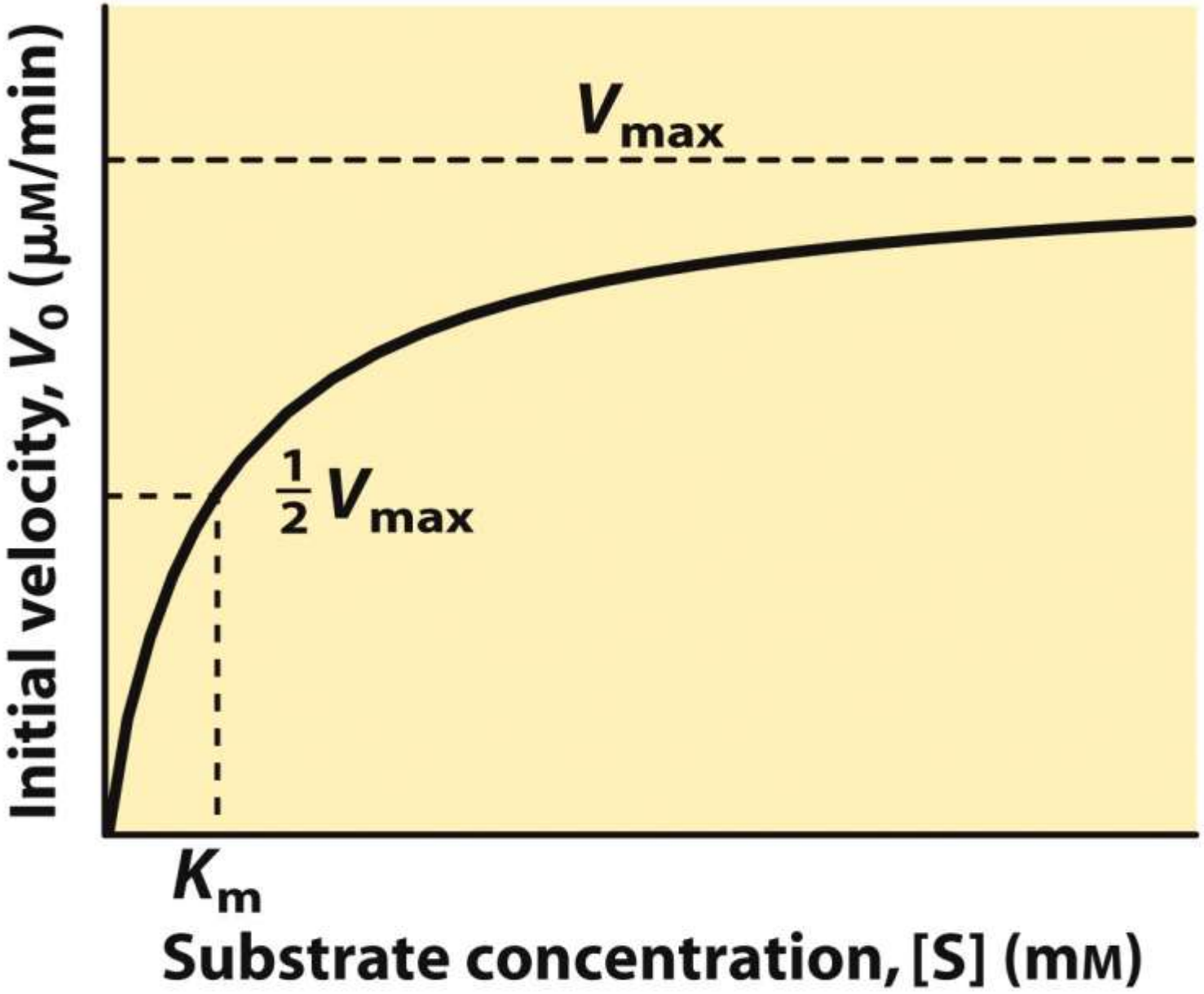

Figure 6-11
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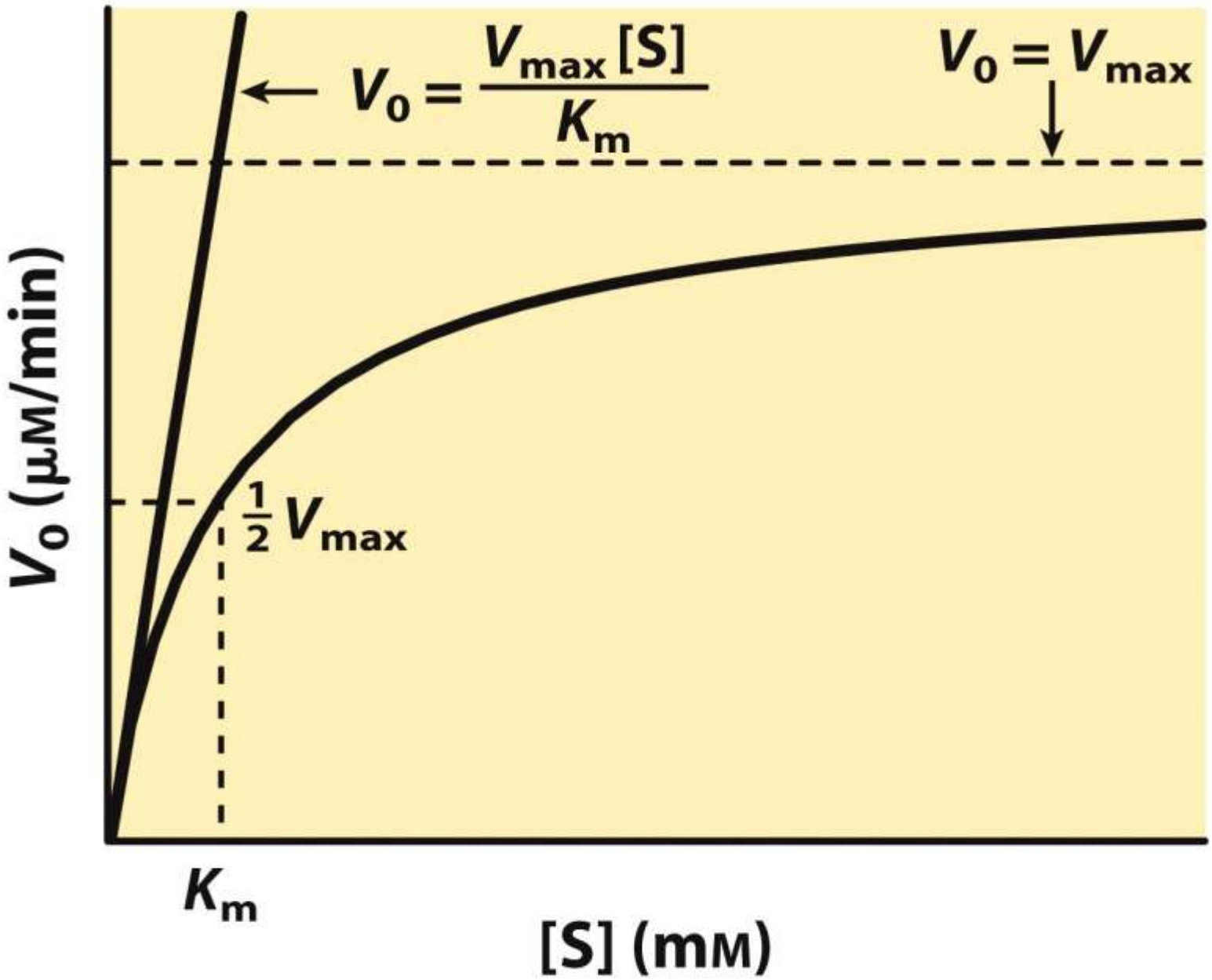

Figure 6-12
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Double-reciprocal plot

Dissociation constant

Turnover number

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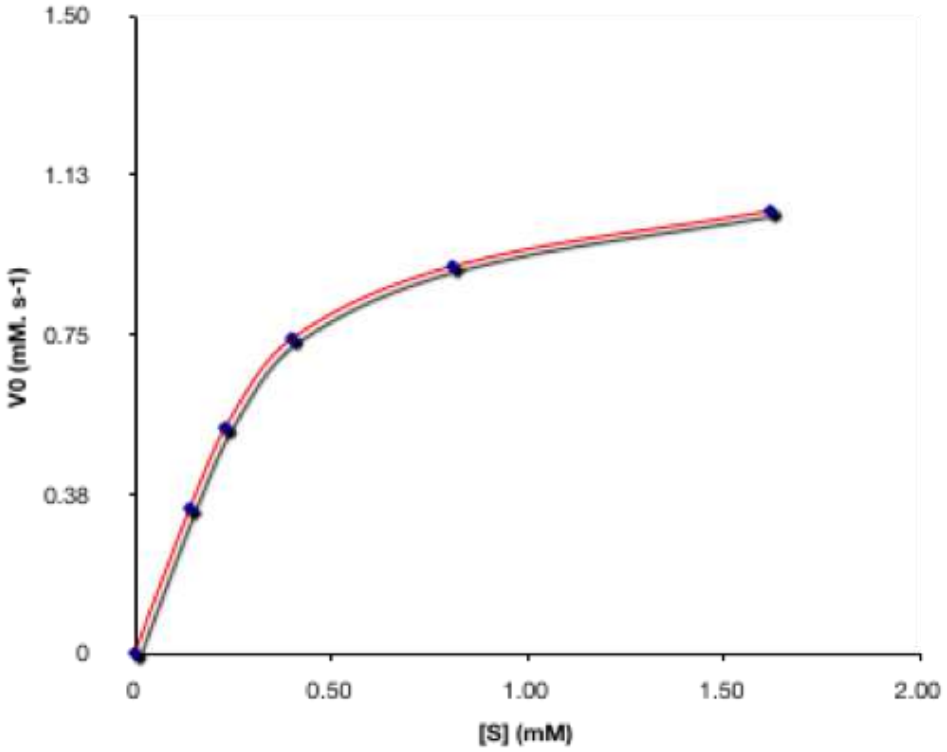
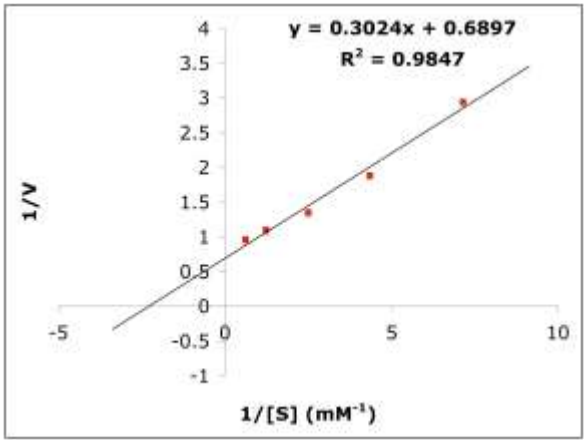


Lineweaver-Burk Plot



$V_{max} = 1/0.6897 = 1.45$

$K_m = -1/(-2.28) = 0.44$ ⌈M)

Eadie-Hofstee Plot

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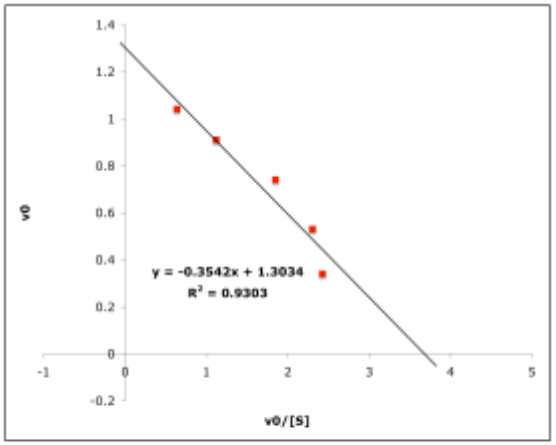

$V_{max} = 1.30$

$K_m = 0.354$

Haynes-Woolf Plot

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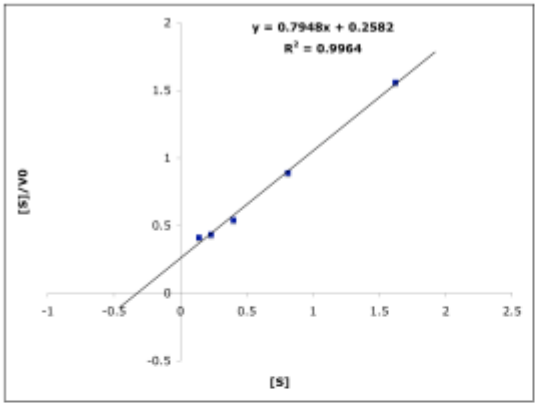

$K_m = 0.32$

$V_{max} = 0.80$

Eisenthal-Cornish-Bowden Direct Plot

Direct Linear Plot

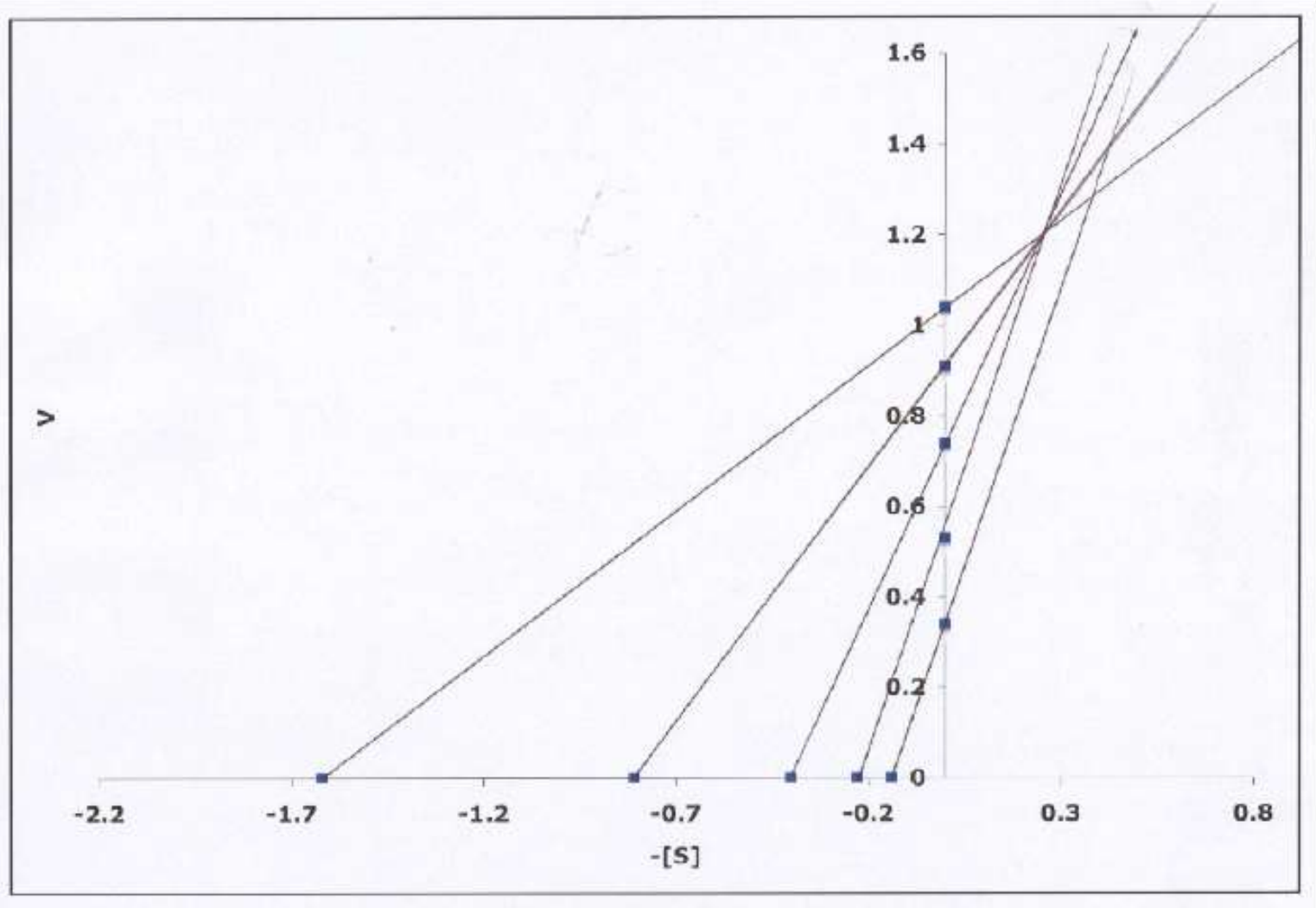

TABLE 6–6 K_m for Some Enzymes and Substrates

Enzyme	Substrate	K_m (mM)
Hexokinase (brain)	ATP	0.4
	D-Glucose	0.05
	D-Fructose	1.5
Carbonic anhydrase	HCO_3^-	26
Chymotrypsin	Glycyltyrosinylglycine	108
	N-Benzoyltyrosinamide	2.5
β-Galactosidase	D-Lactose	4.0
Threonine dehydratase	L-Threonine	5.0

Table 6-6
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TABLE 6–7 Turnover Numbers, k_{cat}, of Some Enzymes

Enzyme	Substrate	k_{cat} (s^{-1})
Catalase	H_2O_2	40,000,000
Carbonic anhydrase	HCO_3^-	400,000
Acetylcholinesterase	Acetylcholine	14,000
β-Lactamase	Benzylpenicillin	2,000
Fumarase	Fumarate	800
RecA protein (an ATPase)	ATP	0.5

Table 6-7
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TABLE 6–8 Enzymes for Which k_{cat}/K_m Is Close to the Diffusion-Controlled Limit (10^8 to 10^9 $M^{-1}s^{-1}$)

Enzyme	Substrate	k_{cat} (s^{-1})	K_m (M)	k_{cat}/K_m ($M^{-1}s^{-1}$)
Acetylcholinesterase	Acetylcholine	1.4×10^4	9×10^{-5}	1.6×10^8
Carbonic anhydrase	CO_2	1×10^6	1.2×10^{-2}	8.3×10^7
	HCO_3^-	4×10^5	2.6×10^{-2}	1.5×10^7
Catalase	H_2O_2	4×10^7	1.1×10^0	4×10^7
Crotonase	Crotonyl-CoA	5.7×10^3	2×10^{-5}	2.8×10^8
Fumarase	Fumarate	8×10^2	5×10^{-6}	1.6×10^8
	Malate	9×10^2	2.5×10^{-5}	3.6×10^7
β-Lactamase	Benzylpenicillin	2.0×10^3	2×10^{-5}	1×10^8

Source: Fersht, A. (1999) *Structure and Mechanism in Protein Science*, p. 166, W. H. Freeman and Company, New York.

Table 6-8
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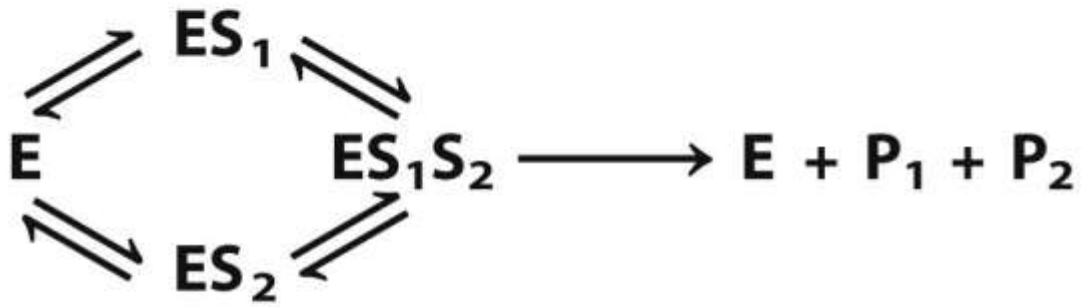
More complex systems

(a) Enzyme reaction involving a ternary complex

Random order



Ordered

(b) Enzyme reaction in which no ternary complex is formed

Figure 6-13
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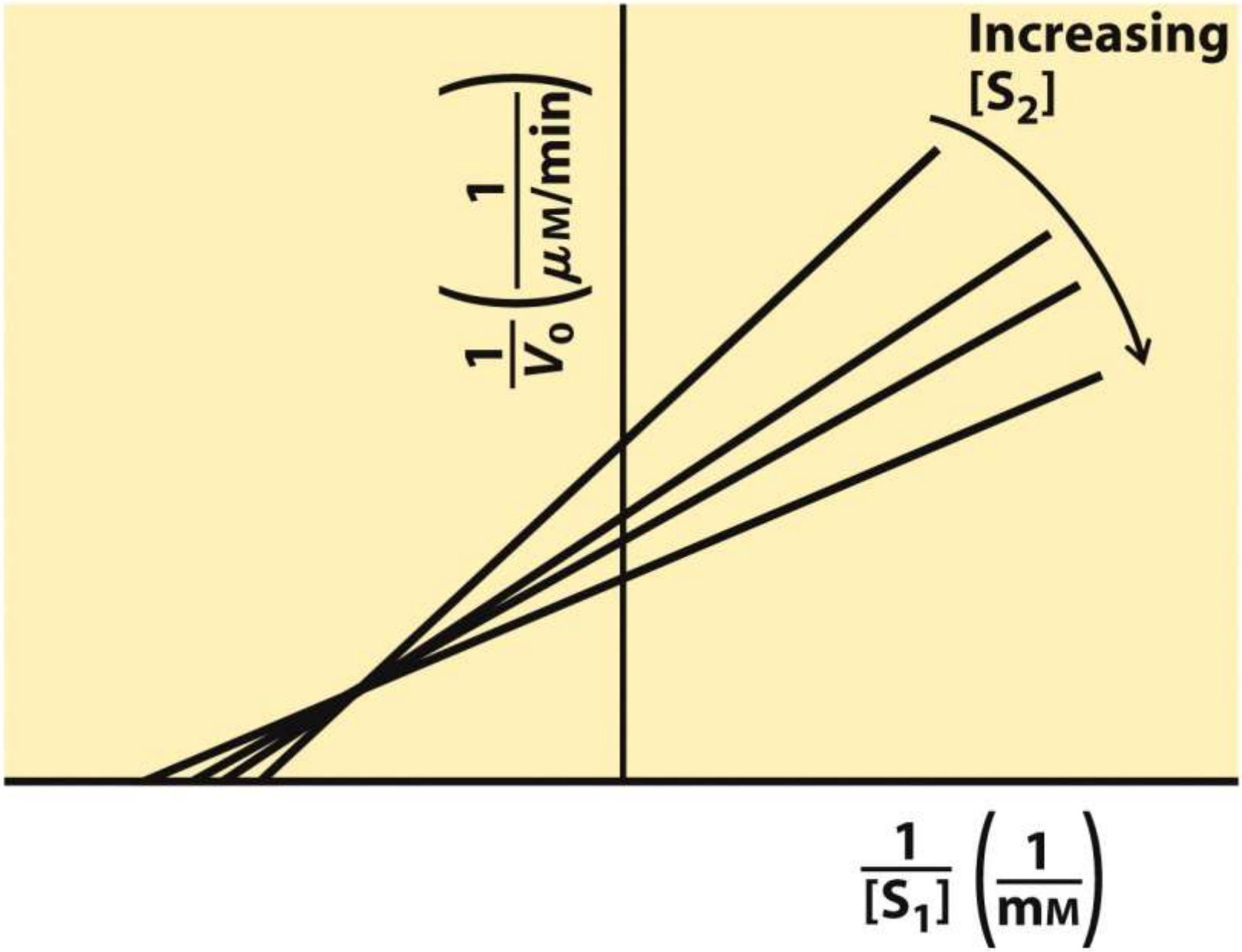

Figure 6-14a
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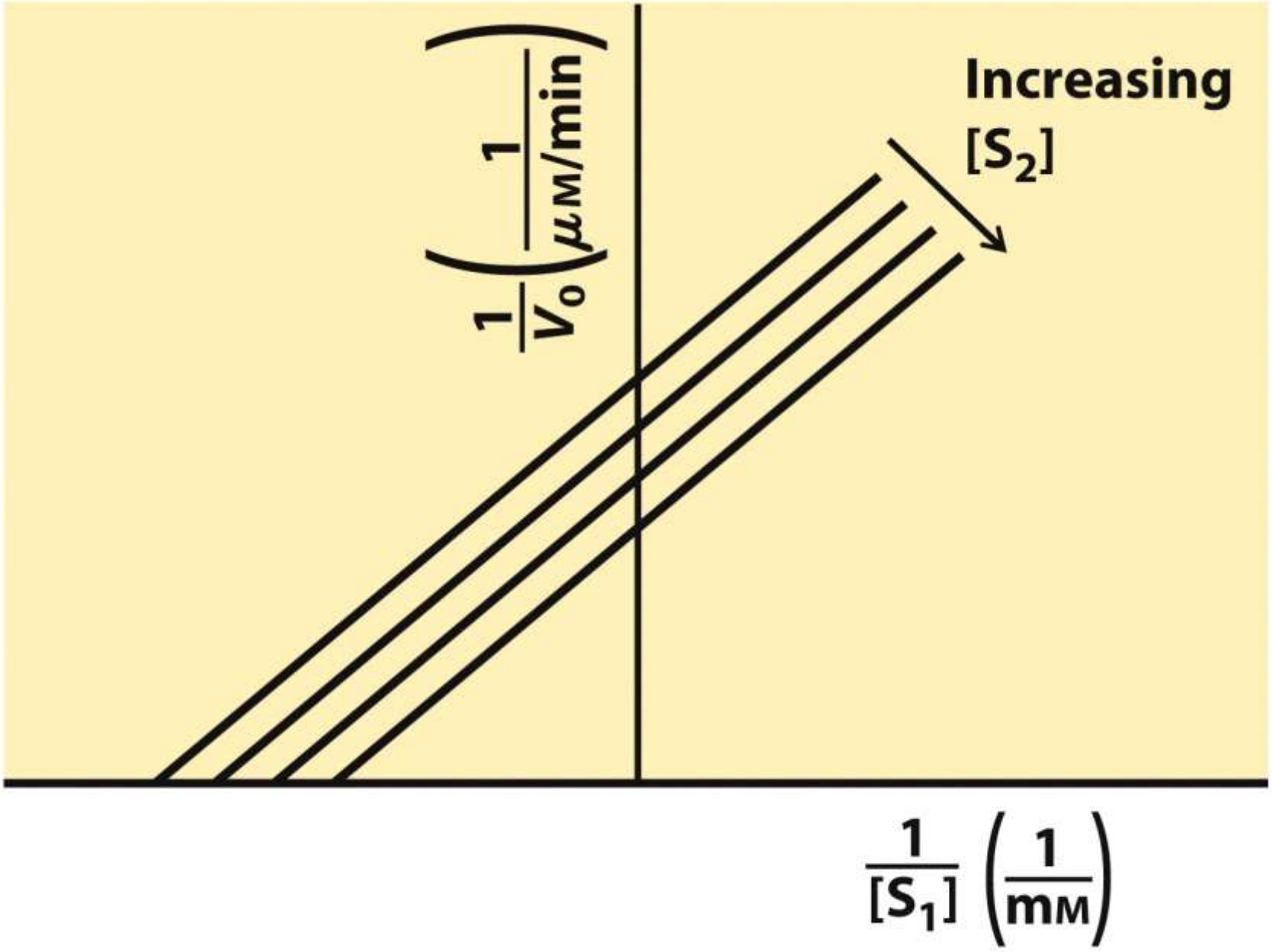

Figure 6-14b
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Reversible Inhibition

Competitive inhibition

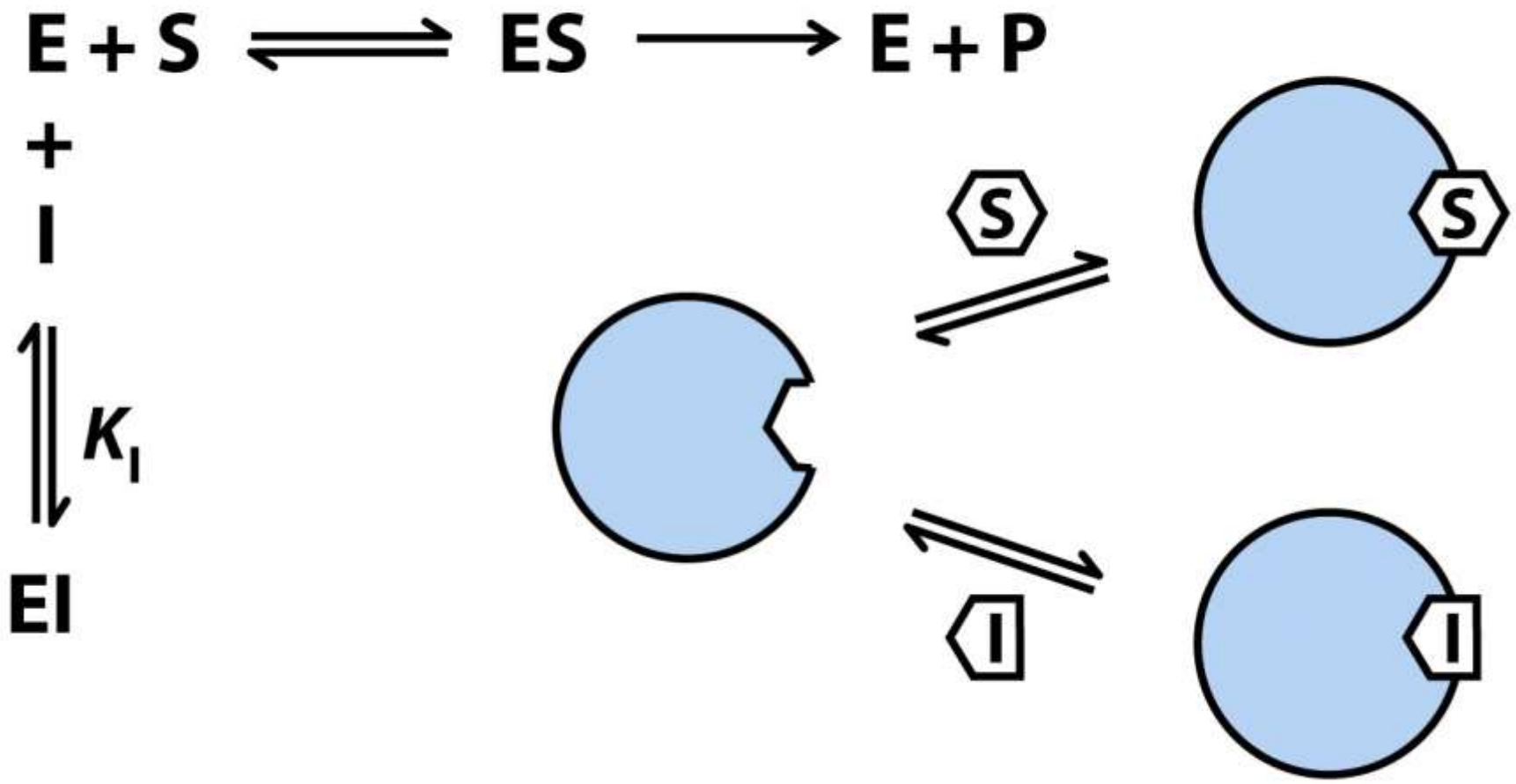

Figure 6-15a
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Uncompetitive inhibition

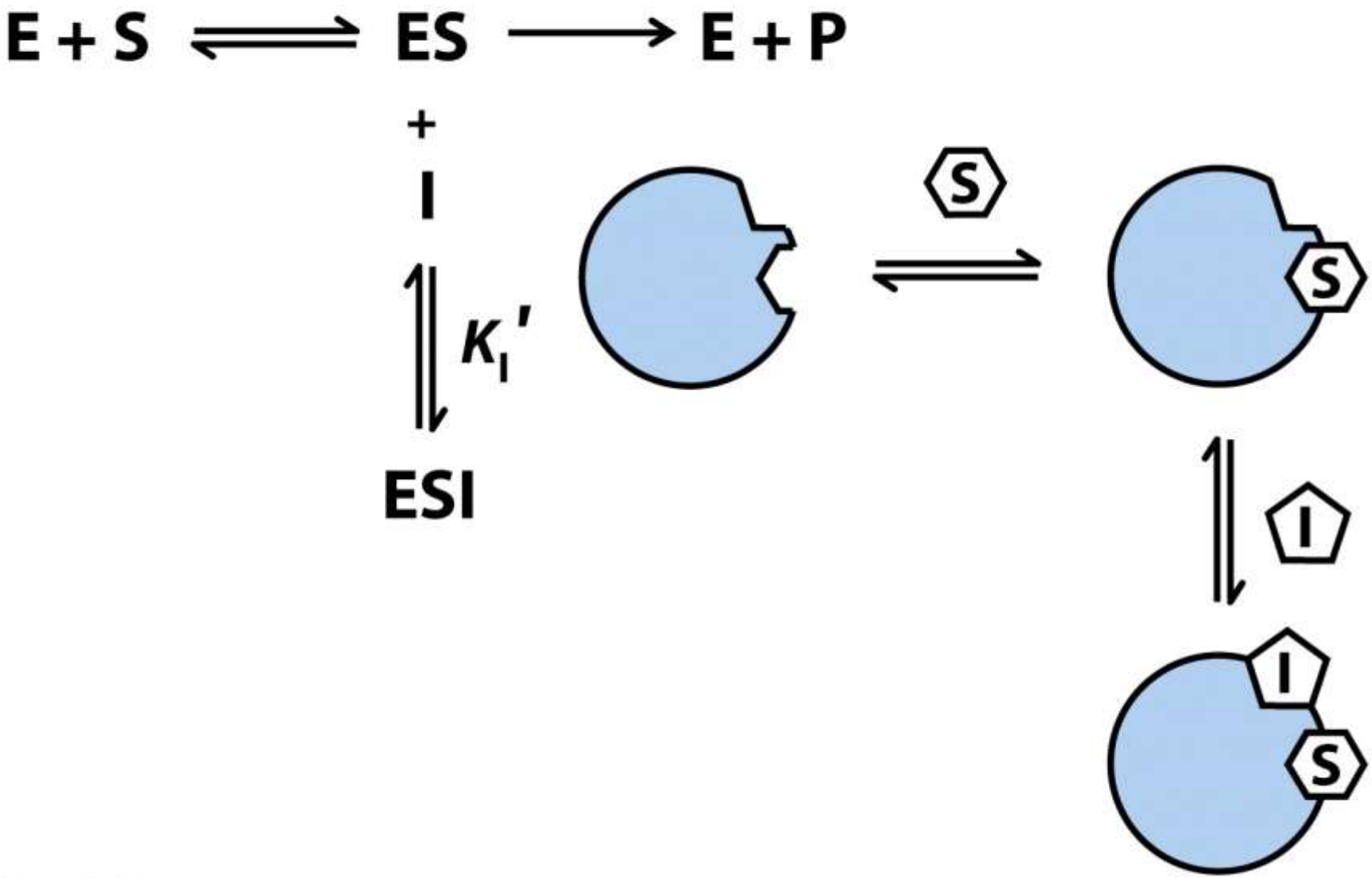

Figure 6-15b
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Mixed inhibition

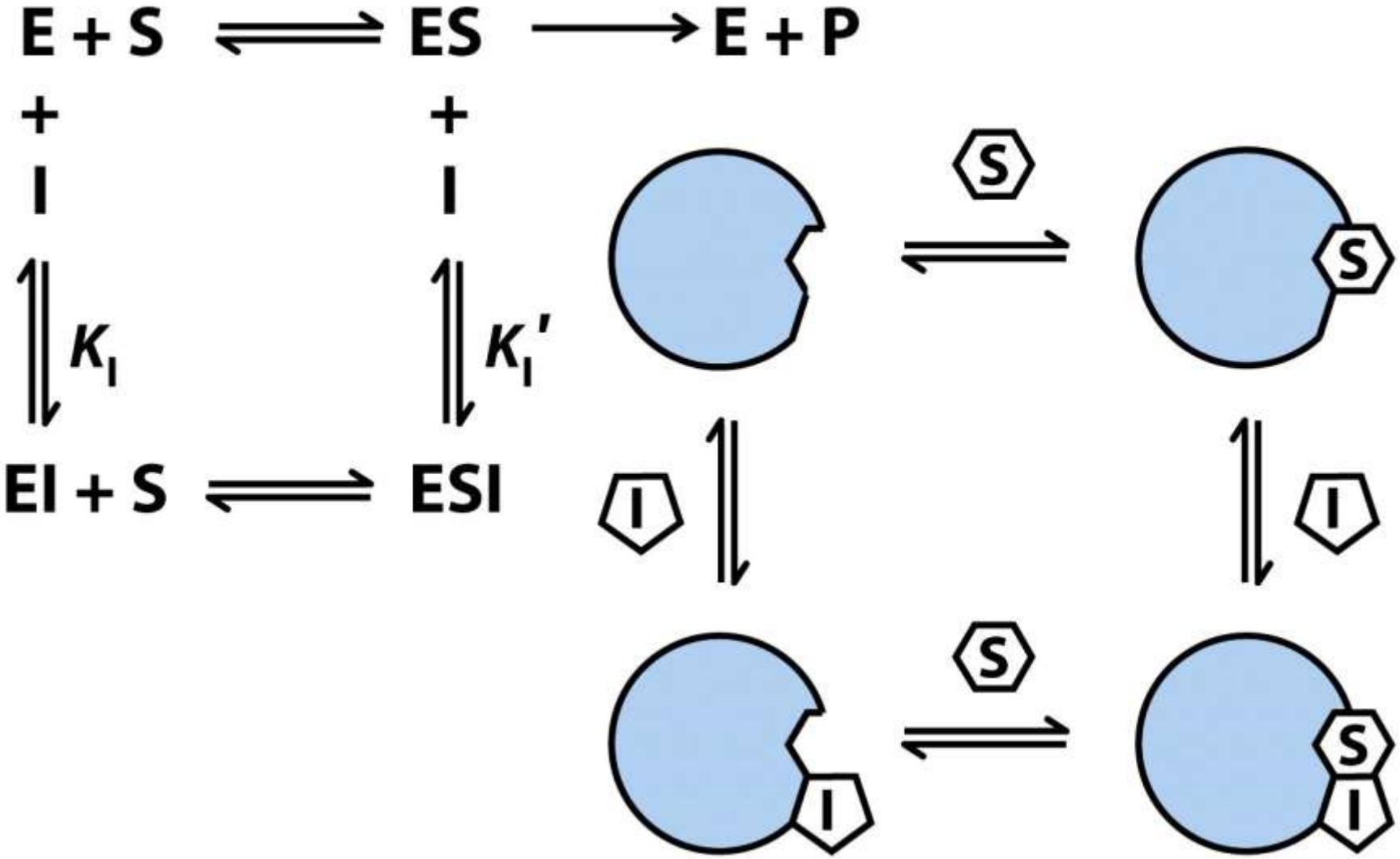

Figure 6-15c
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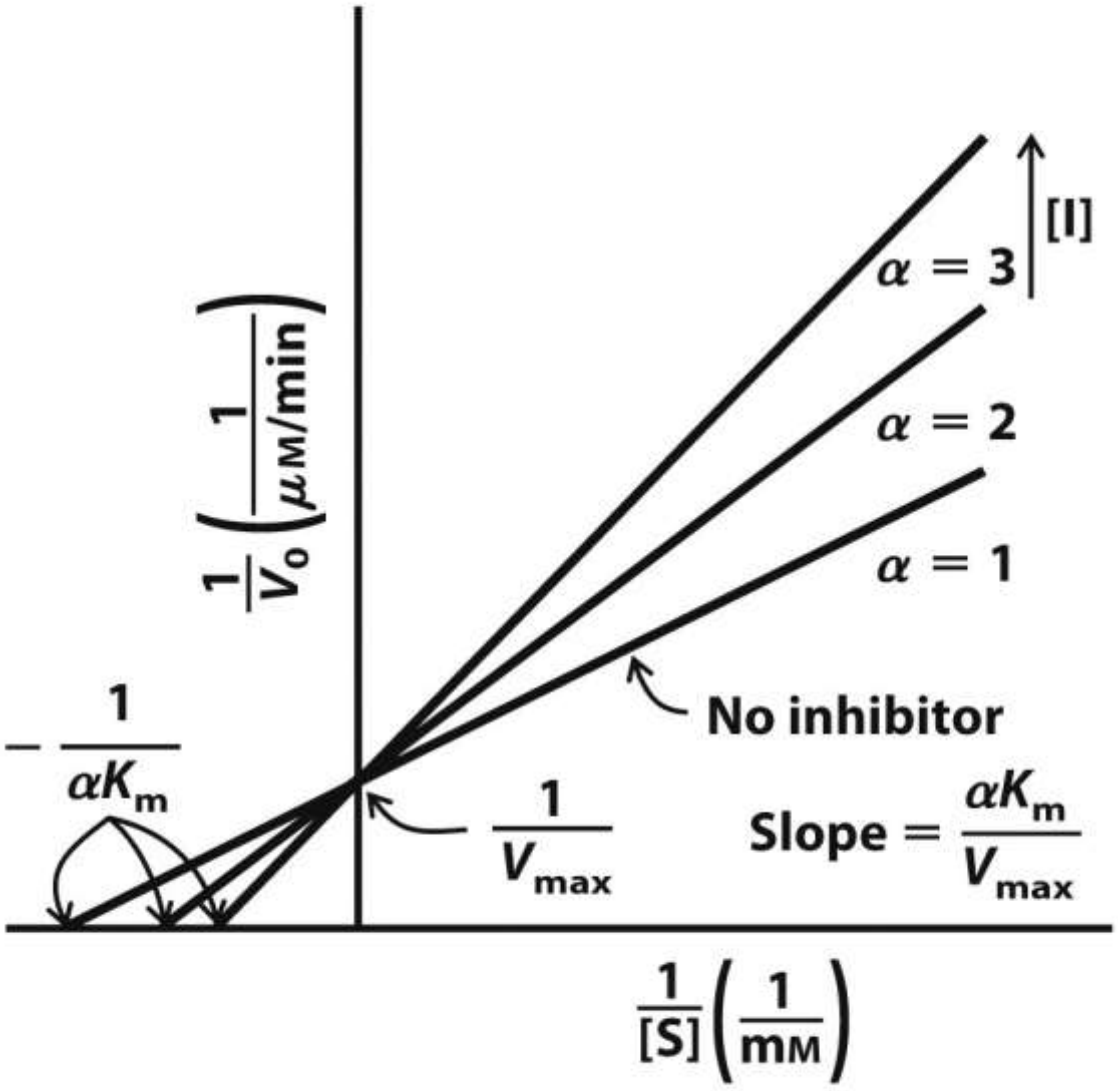
$$\frac{1}{V_0} = \left(\frac{\alpha K_m}{V_{max}}\right)\frac{1}{[S]} + \frac{1}{V_{max}}$$



Box 6-2 figure 1
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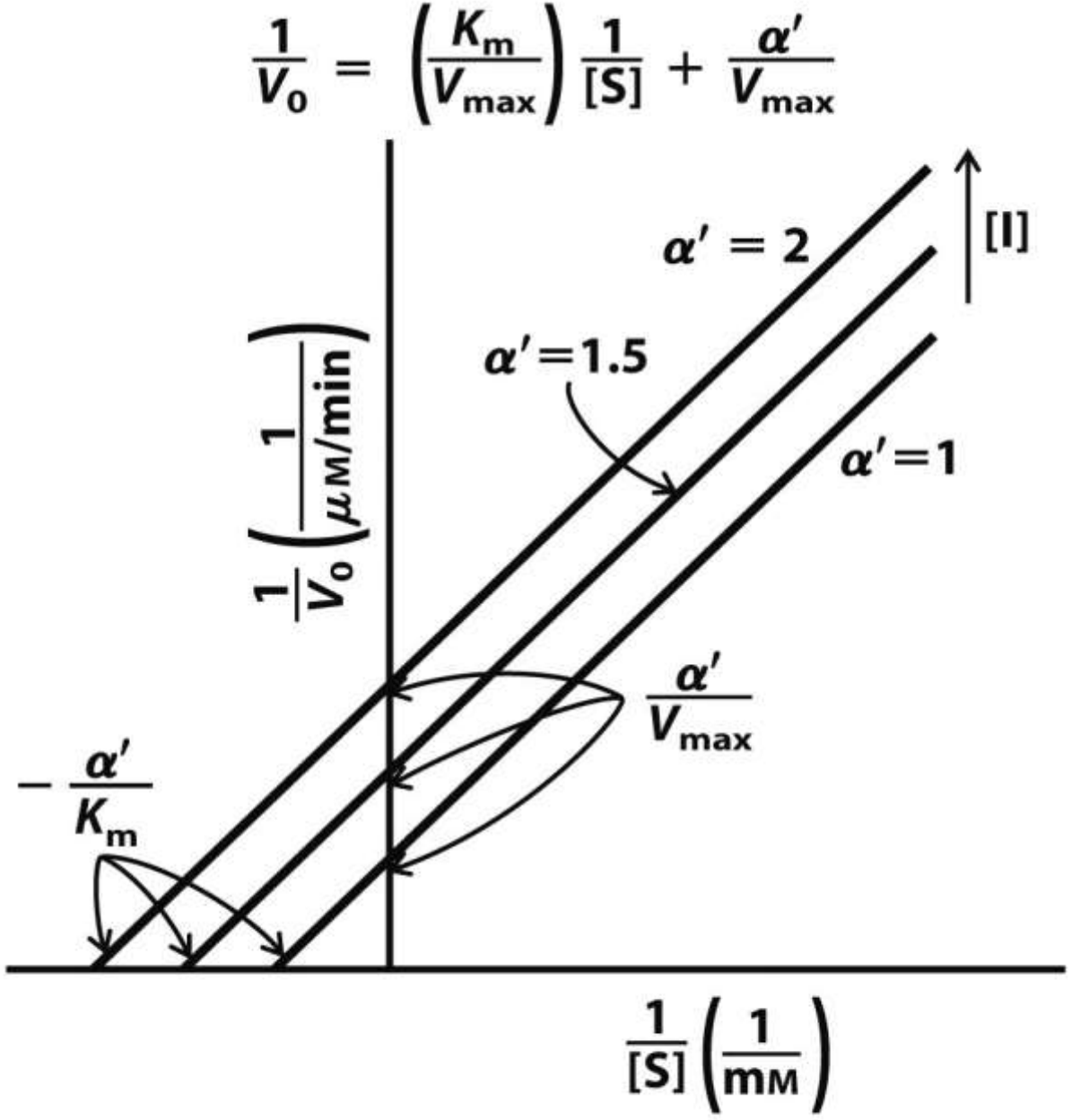
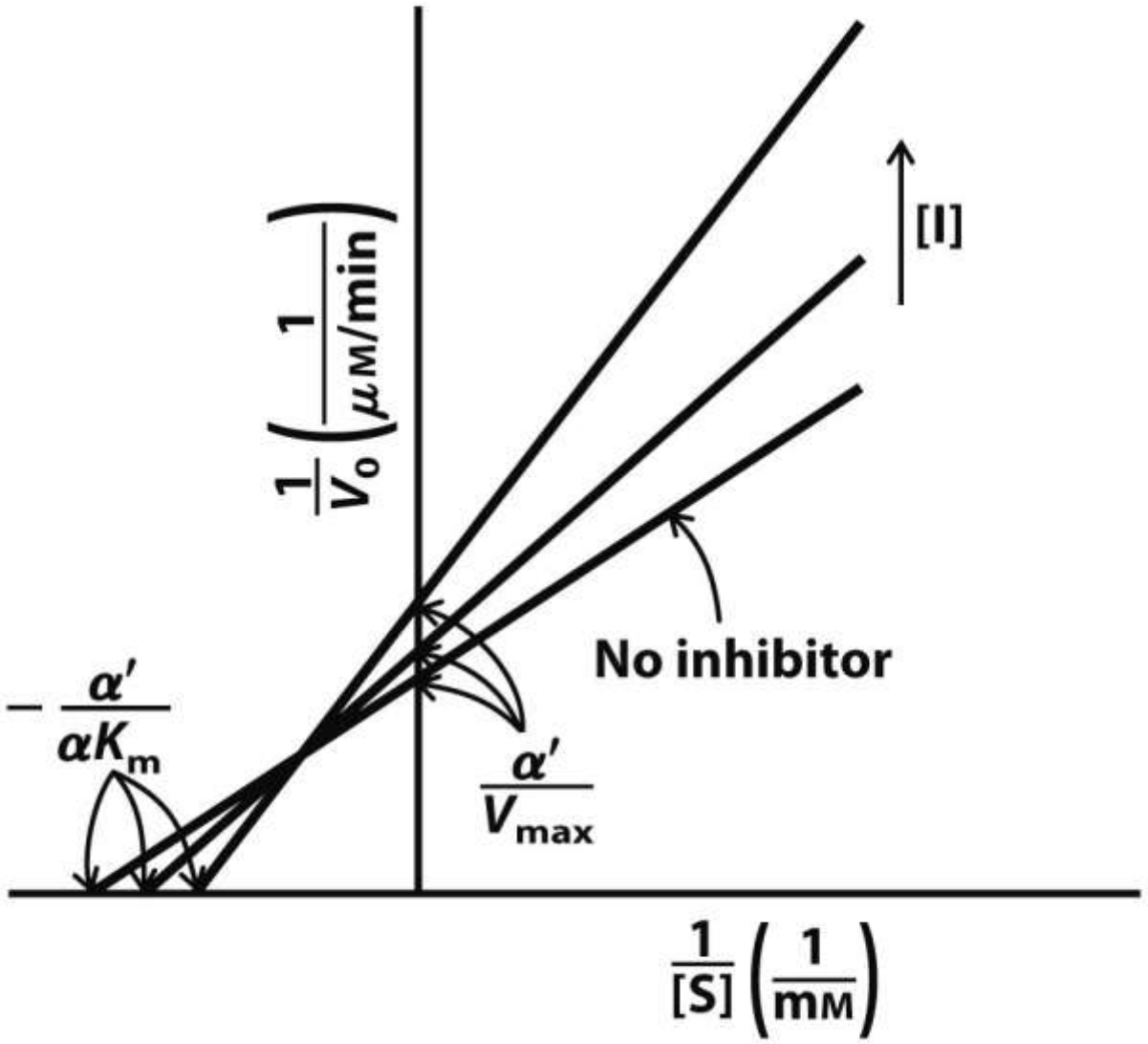


Box 6-2 figure 2

Lehninger Principles of Biochemistry, Fifth Edition

$$\frac{1}{V_0} = \left(\frac{\alpha K_m}{V_{max}}\right)\frac{1}{[S]} + \frac{\alpha'}{V_{max}}$$



Box 6-2 figure 3
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TABLE 6–9 Effects of Reversible Inhibitors on Apparent V_{max} and Apparent K_m

Inhibitor type	Apparent V_{max}	Apparent K_m
None	V_{max}	K_m
Competitive	V_{max}	αK_m
Uncompetitive	V_{max}/α'	K_m/α'
Mixed	V_{max}/α'	$\alpha K_m/\alpha'$

Table 6-9
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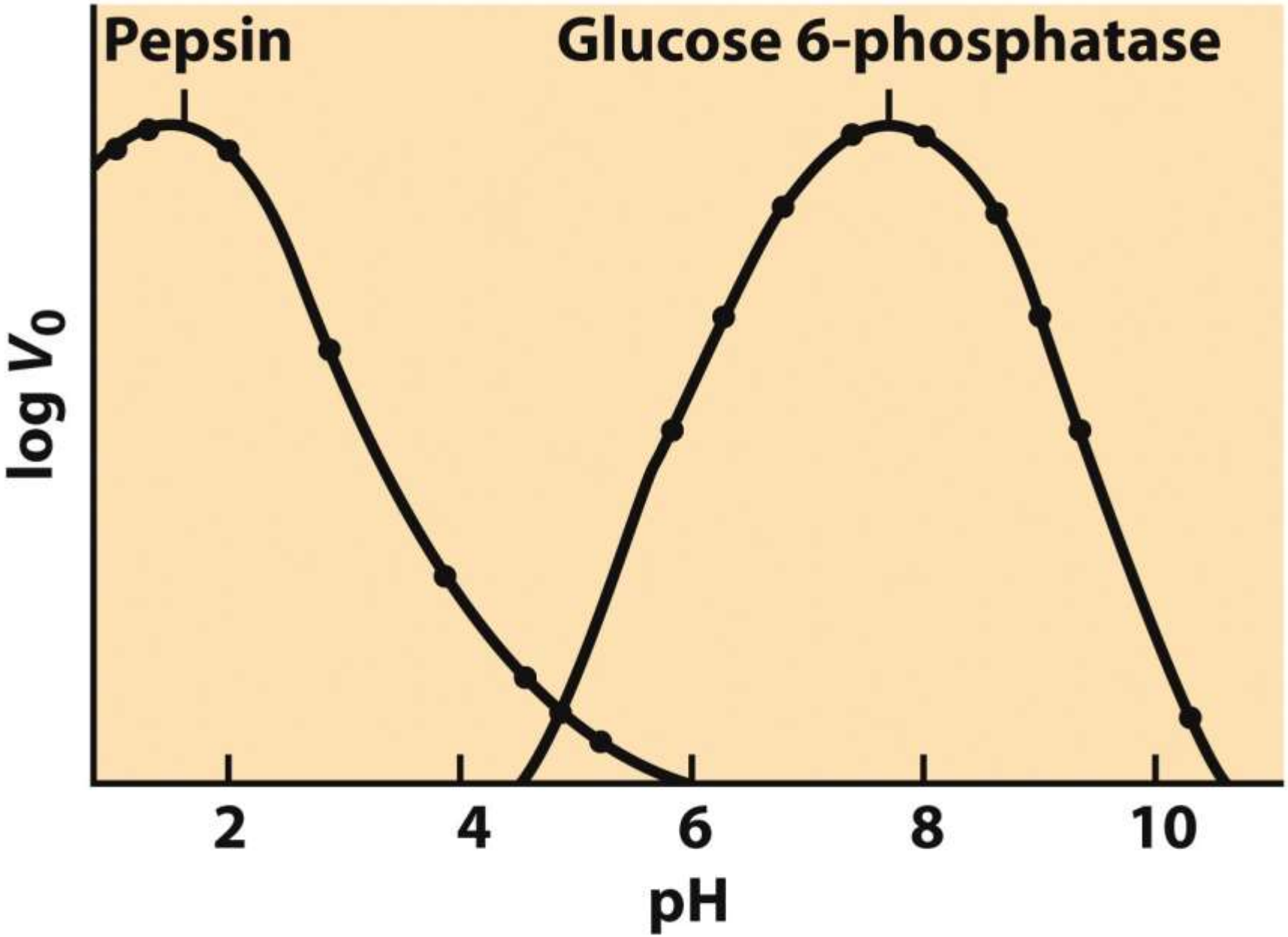

Figure 6-17
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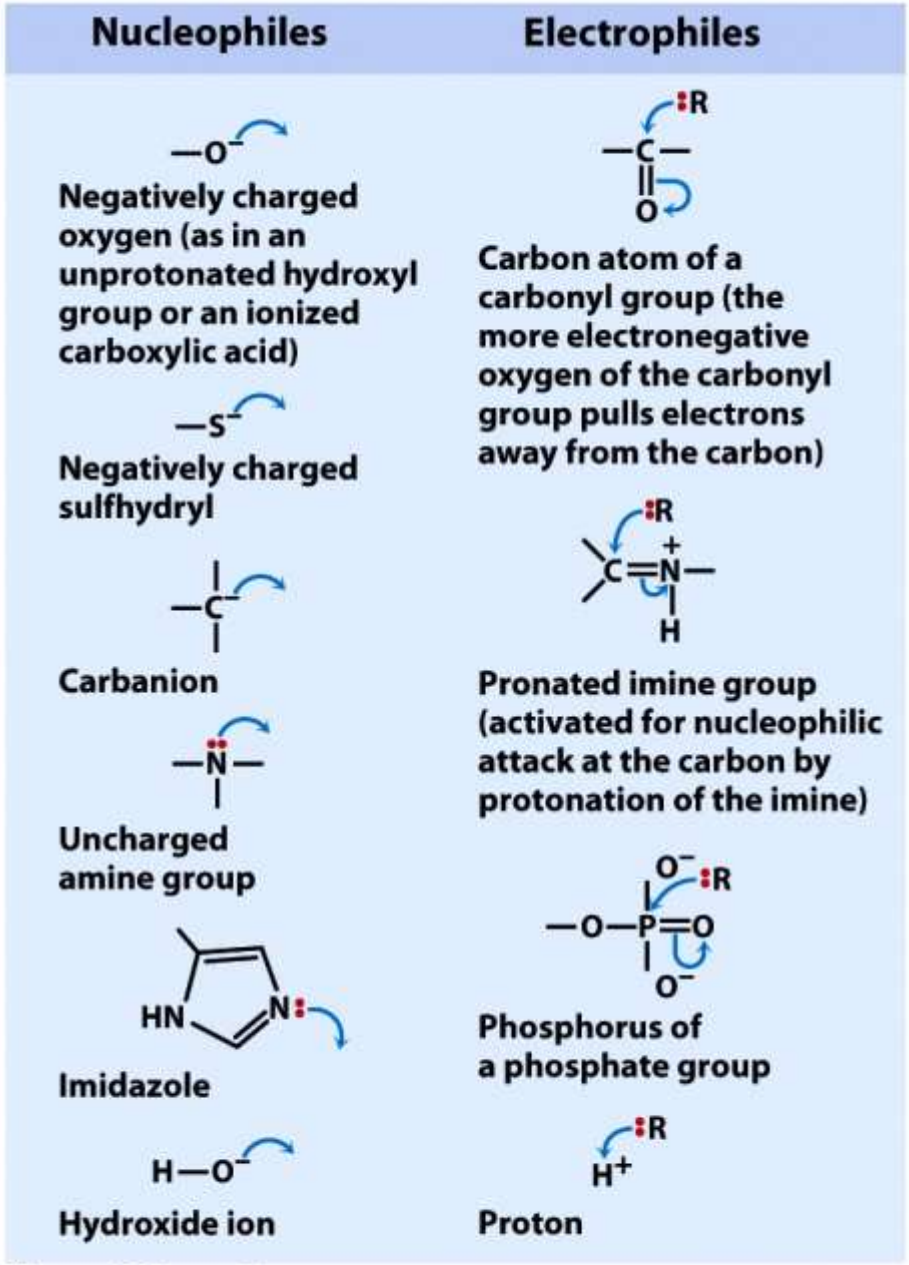

Figure 6-21 part 1

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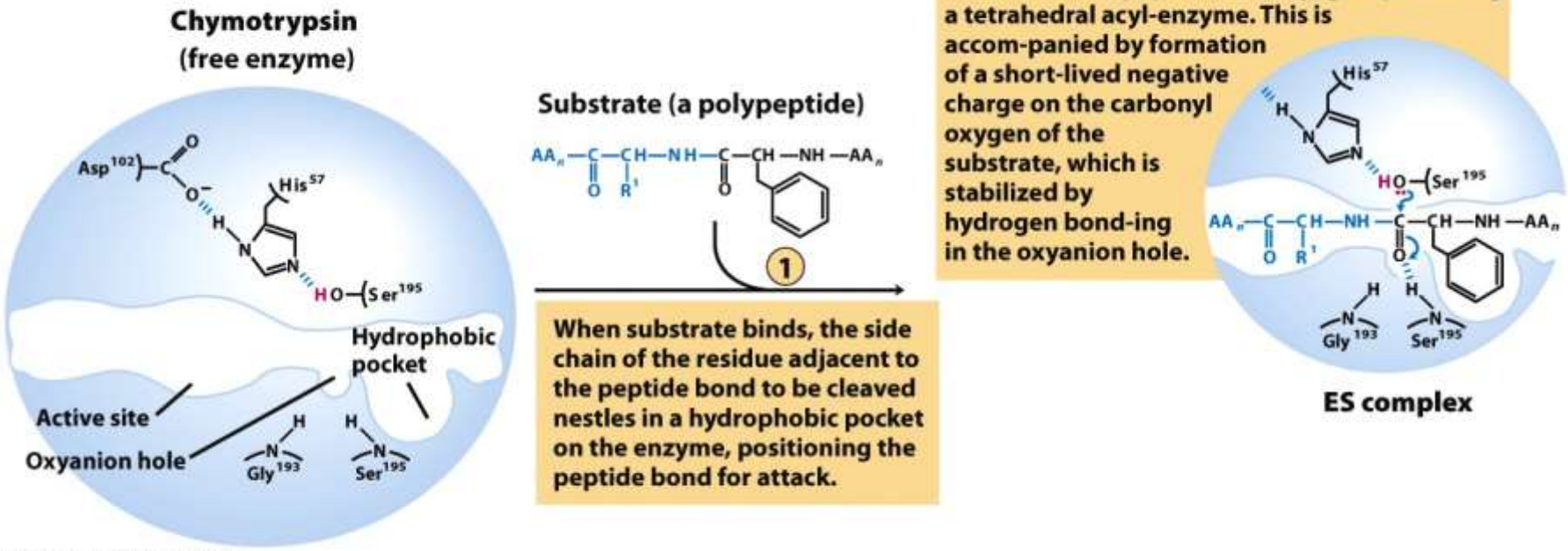

Figure 6-21 part 2a

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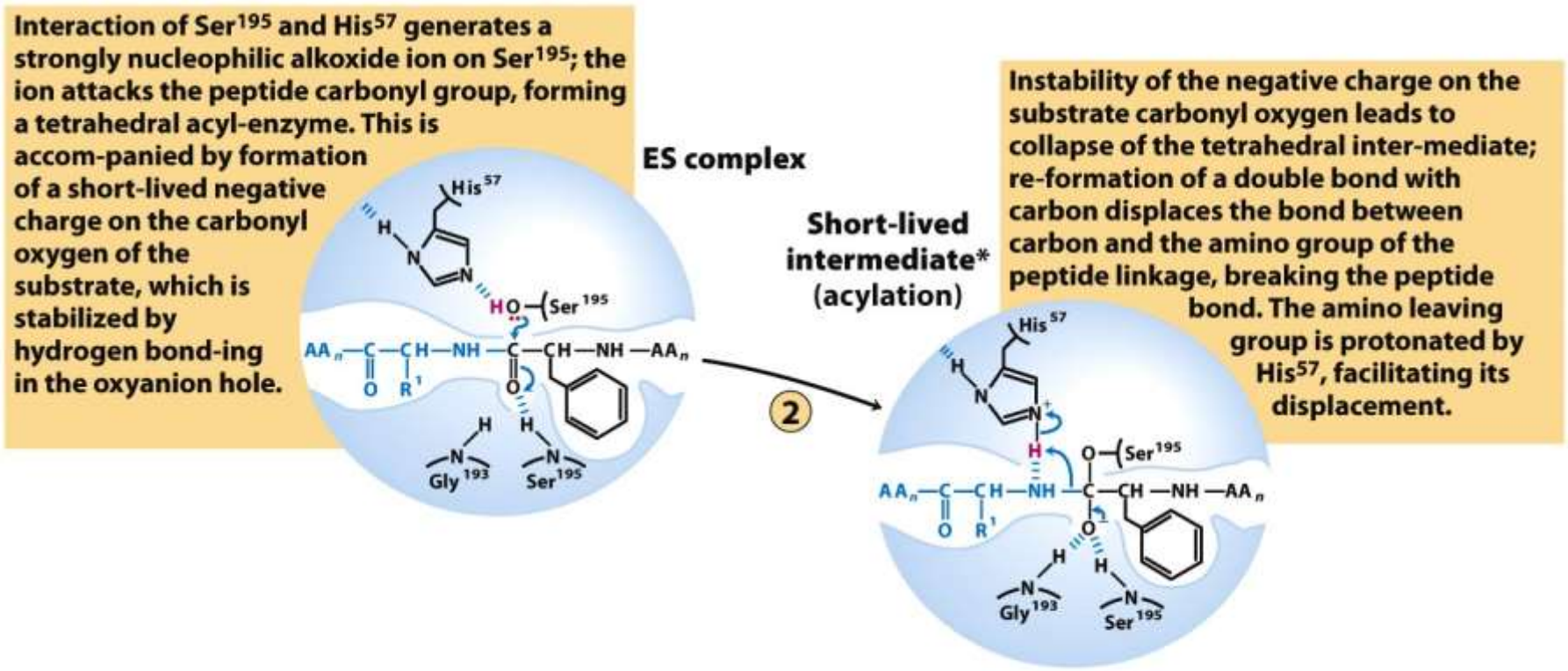

Figure 6-21 part 2b

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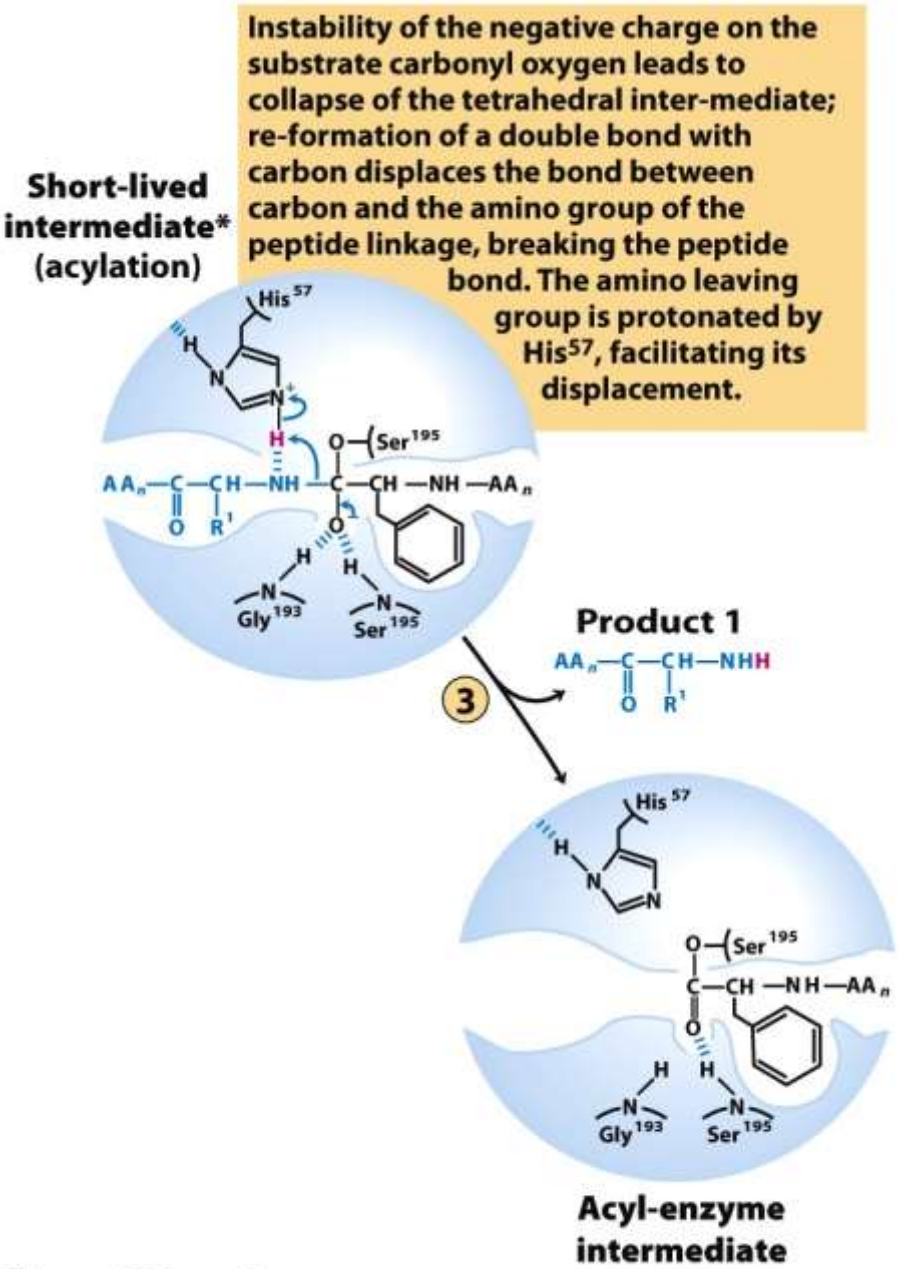

Figure 6-21 part 2c

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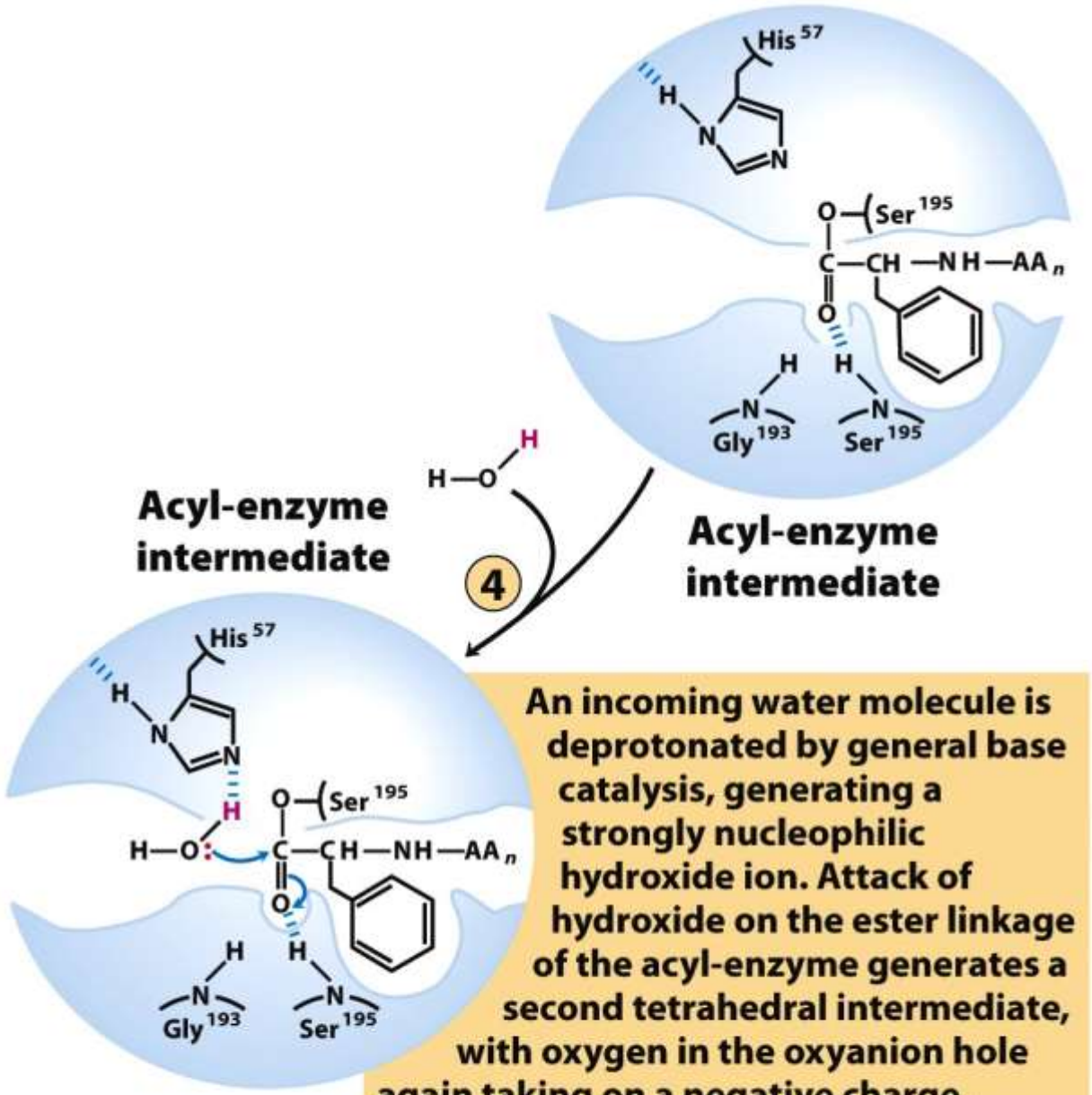

Figure 6-21 part 2d

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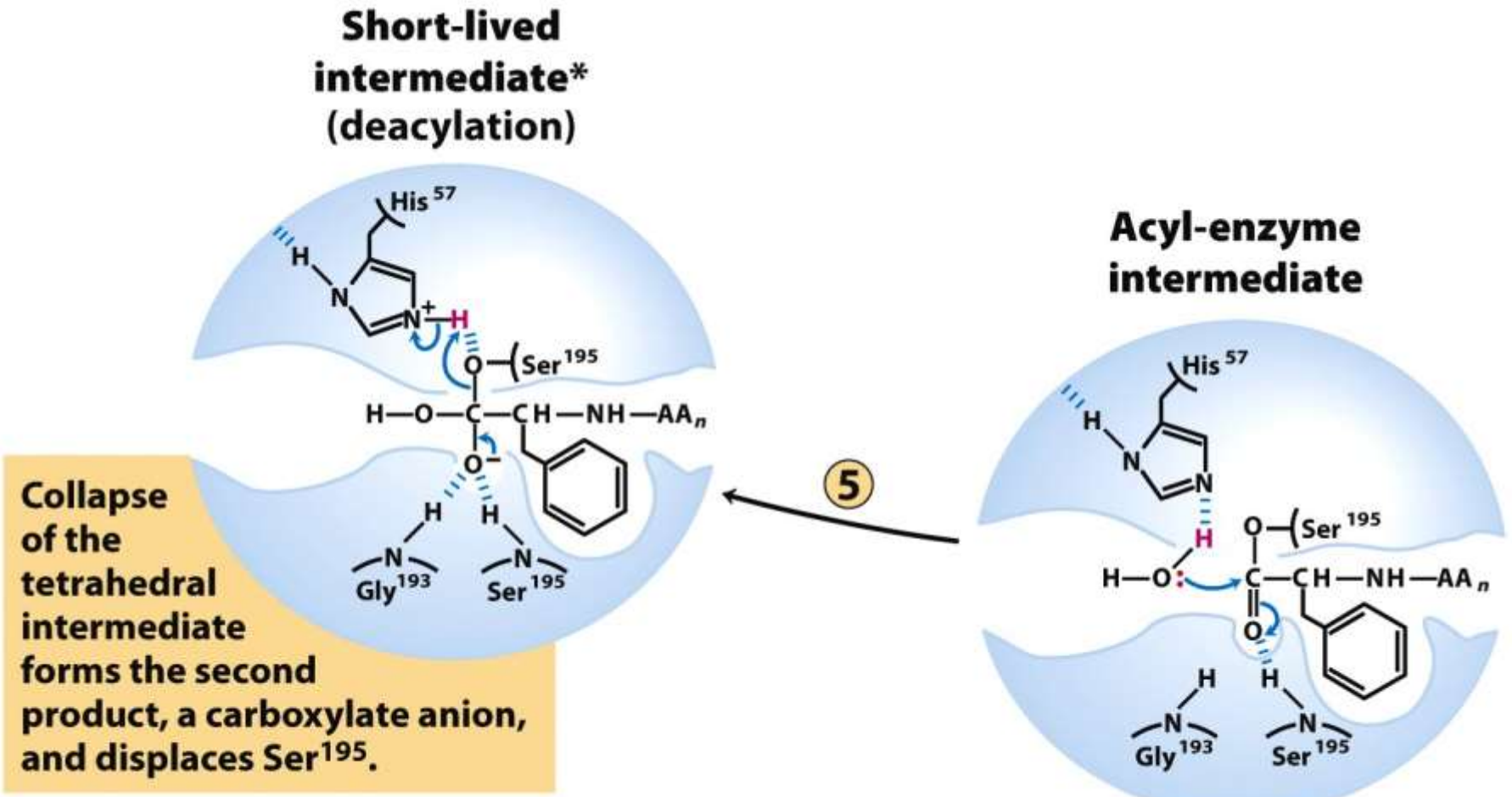

Figure 6-21 part 2e
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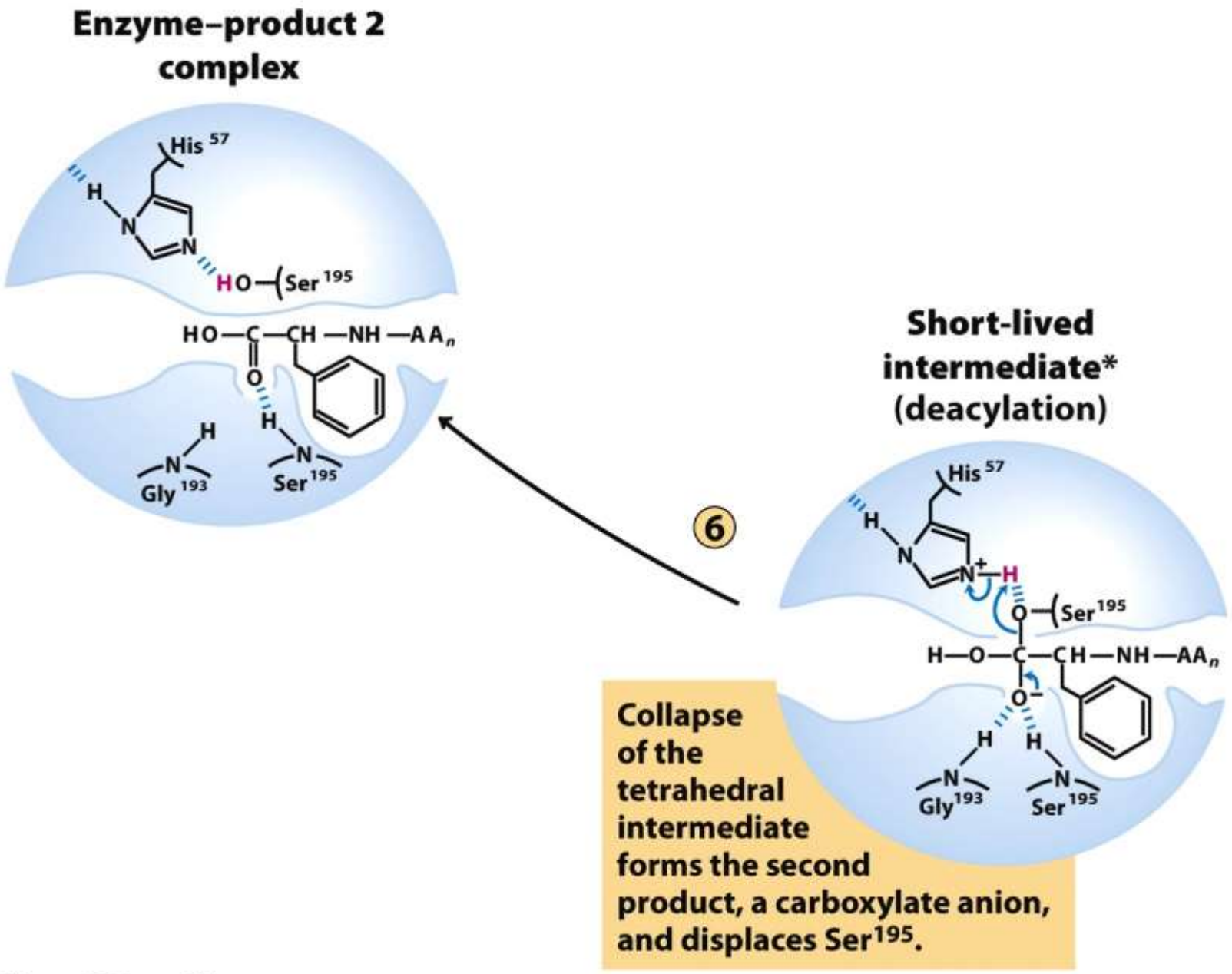

Figure 6-21 part 2f
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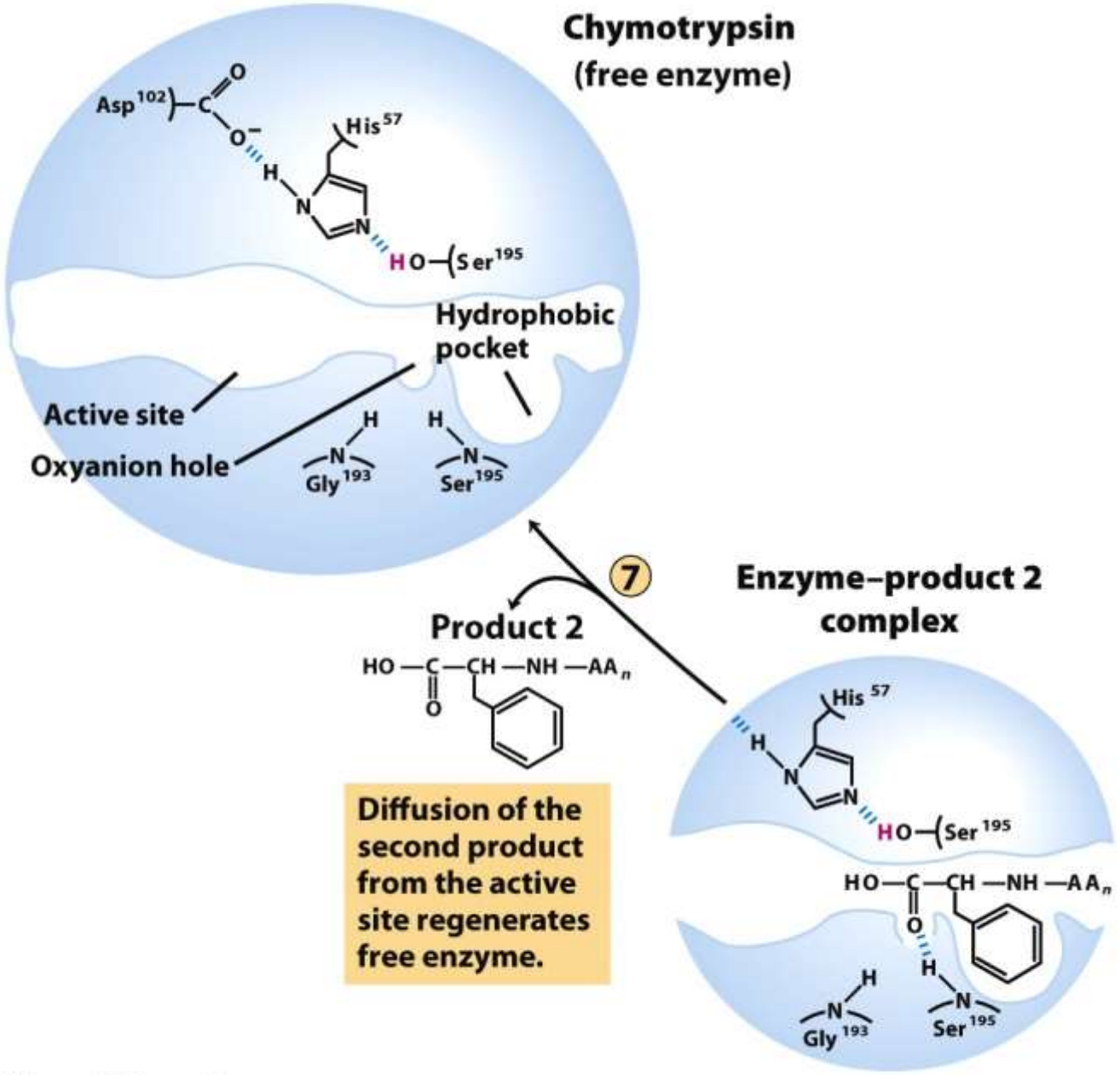

Figure 6-21 part 2g

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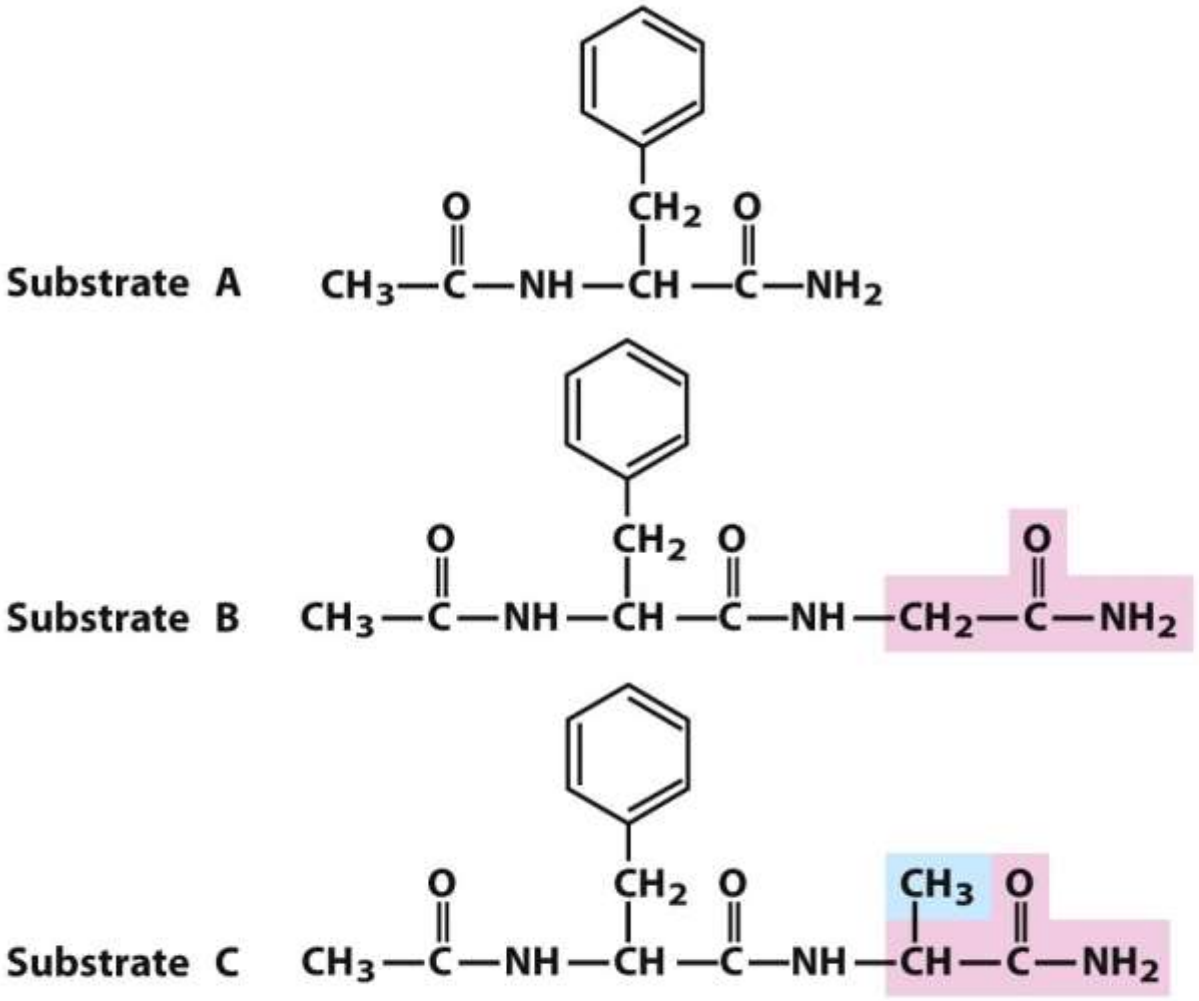

k_{cat} (s^{-1})	K_m (mM)	k_{cat}/K_m ($M^{-1}\,s^{-1}$)
0.06	31	2
0.14	15	10
2.8	25	114

Box 6-3 figure 1
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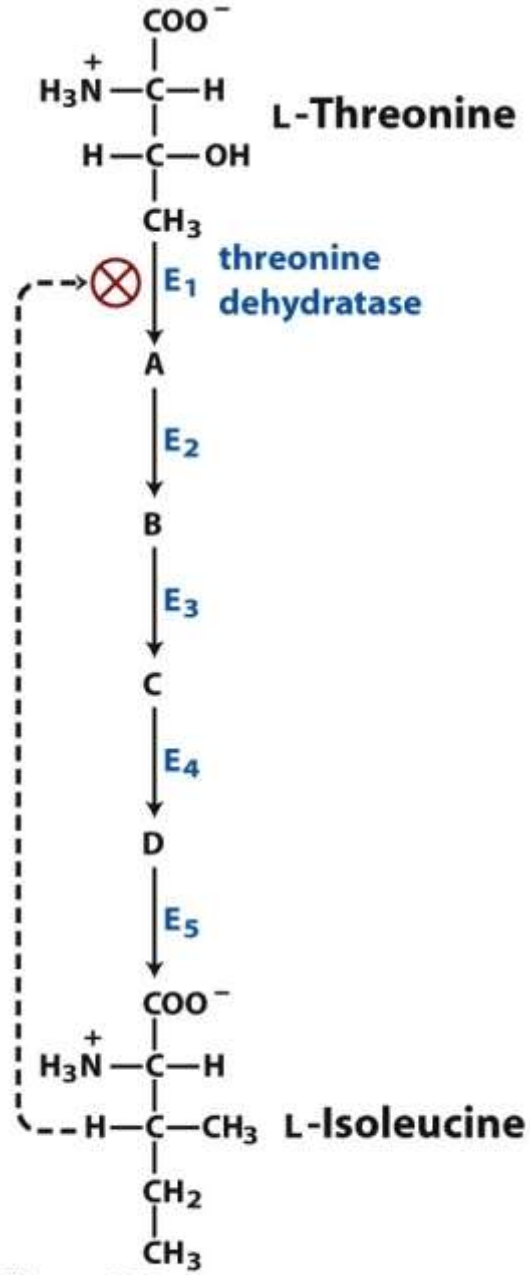

Figure 6-33

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