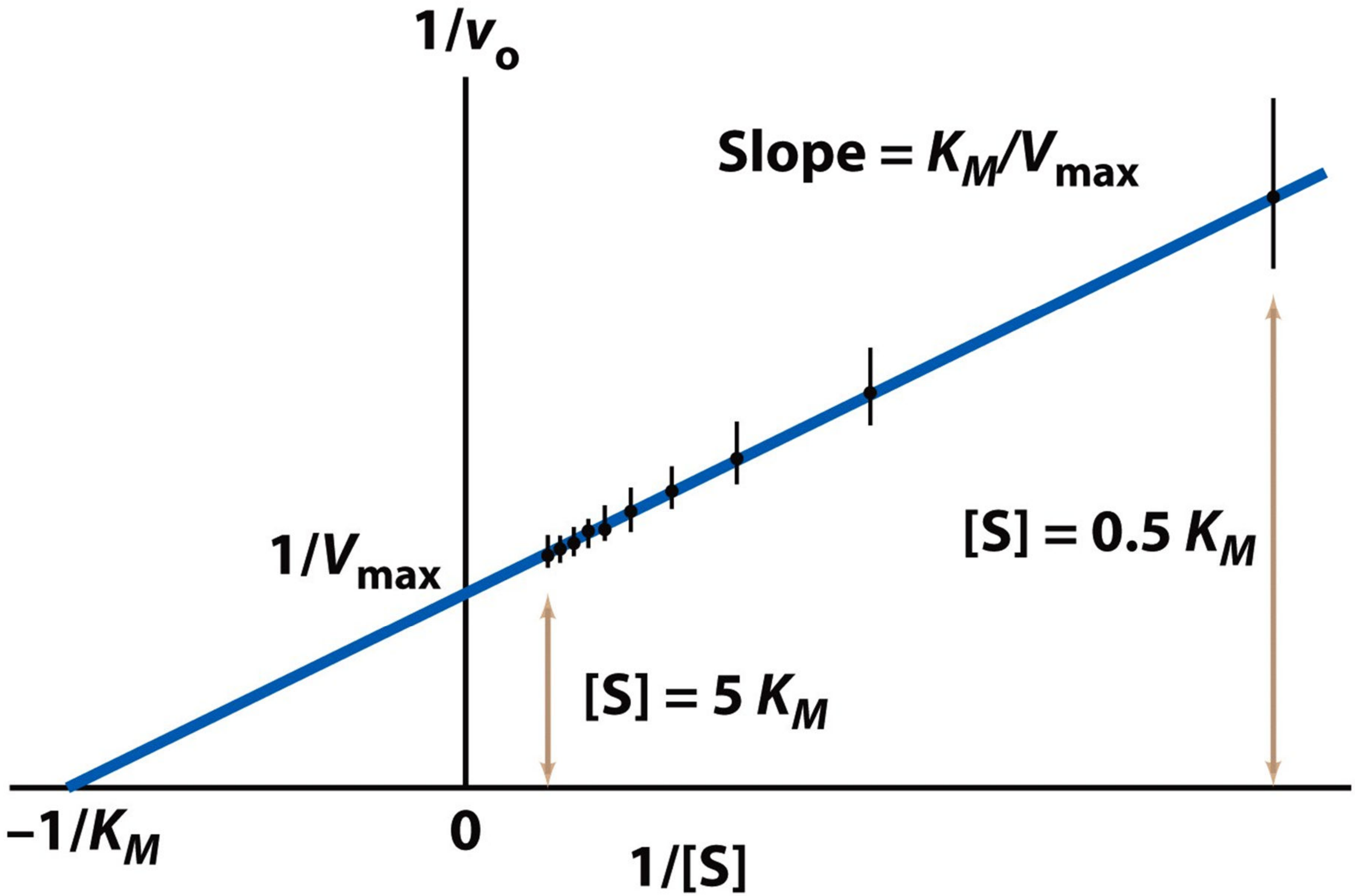
The double-reciprocal (Lineweaver-Burk) plot allows easy calculation of K_m and V_{max}



Many factors influence the activity of an enzyme

- pH
- Temperature
- Concentration of molecules that bind to enzyme
  - Substrate
  - Reversible inhibitors
  - Irreversible inhibitors (inactivators)
  - Allosteric effectors
- Covalent modification
- Enzyme concentration

Enzymes show maximum activity at their pH optimum

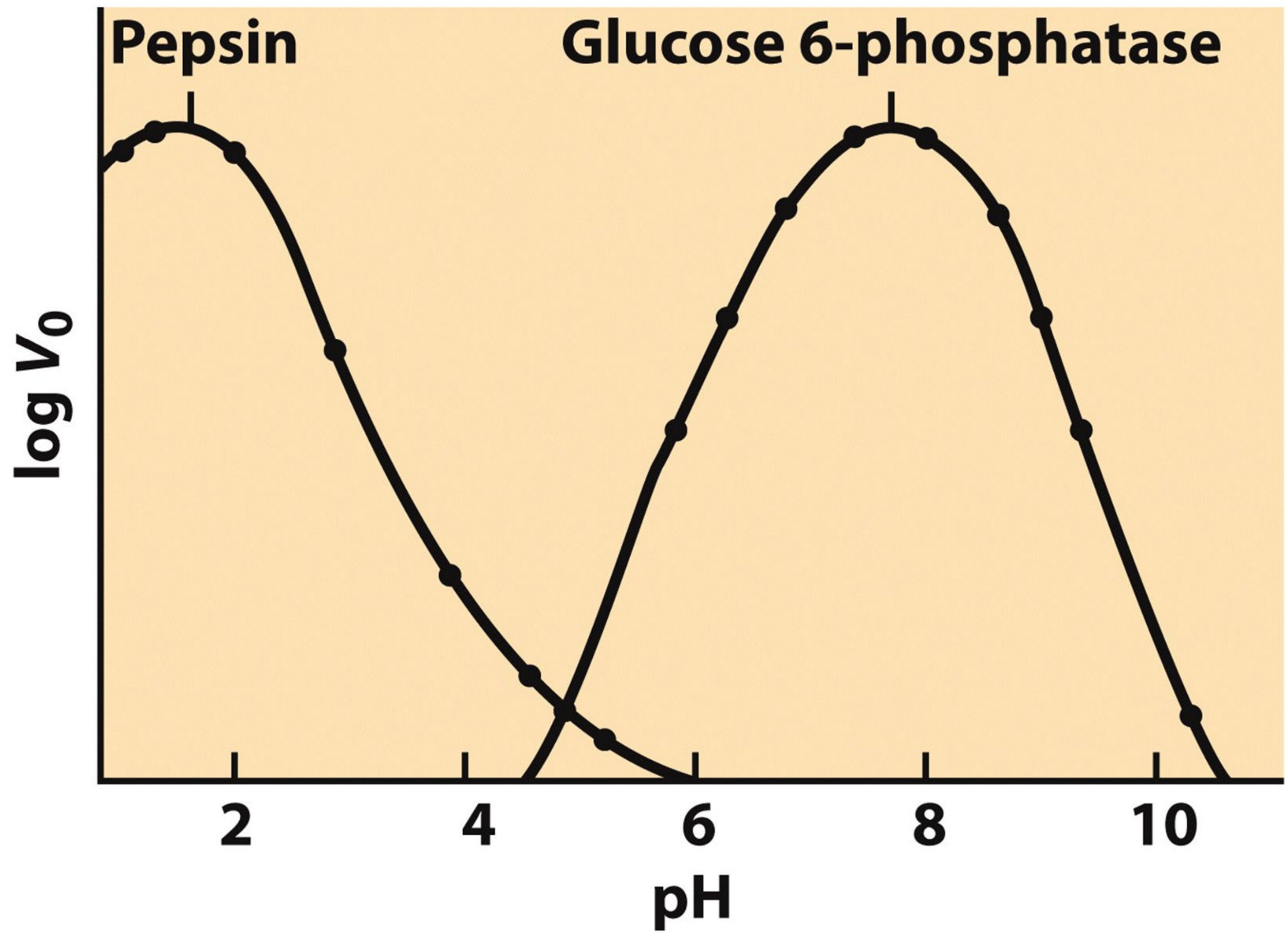


Figure 6-17
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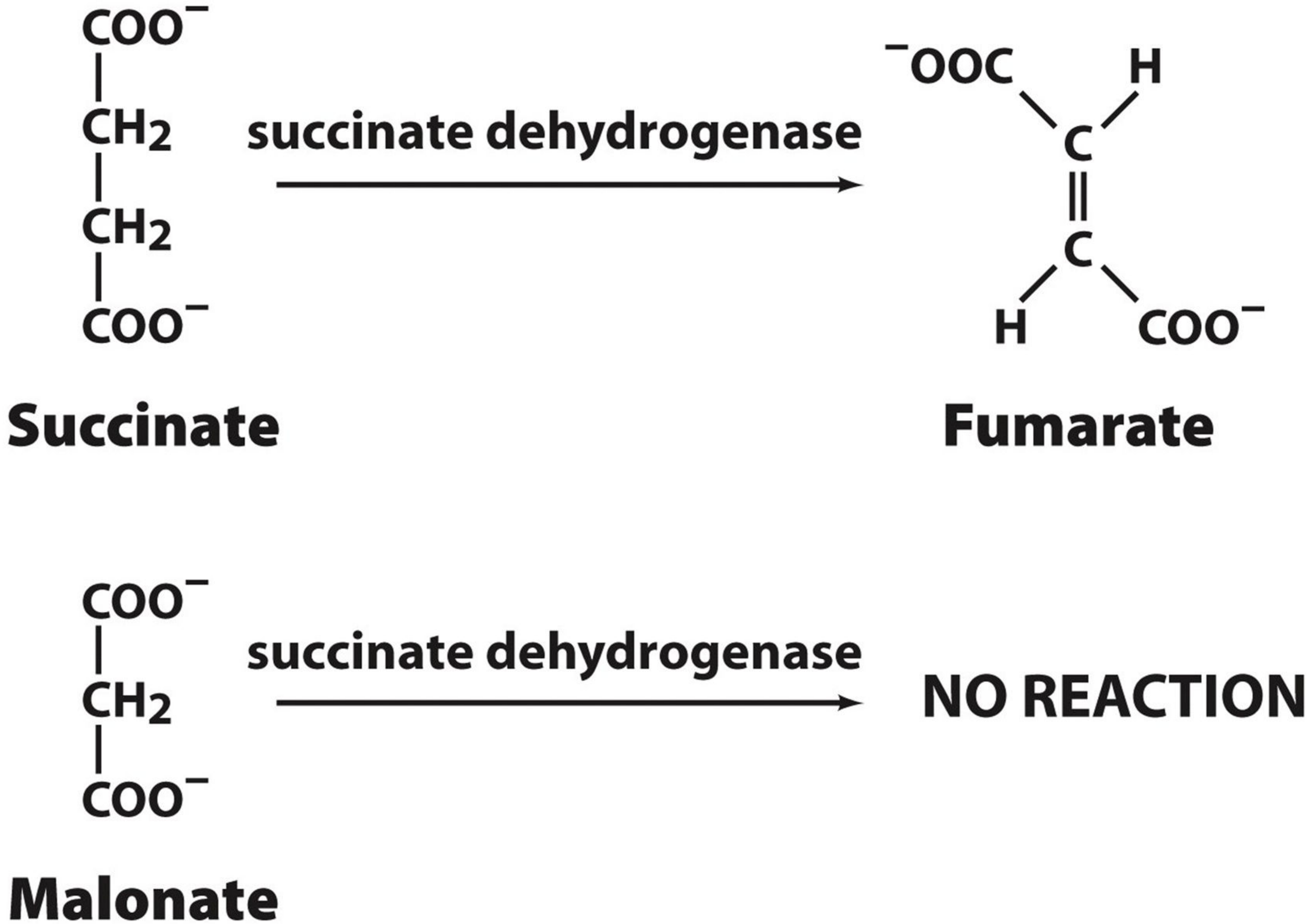
Enzymes can be inhibited by substrate analogs

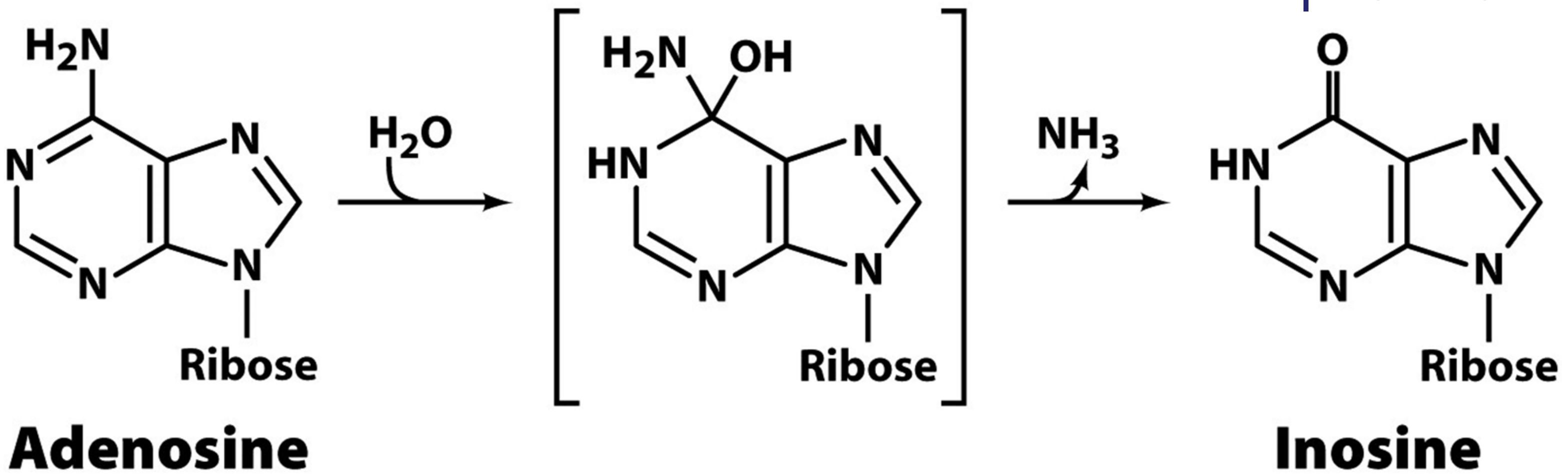


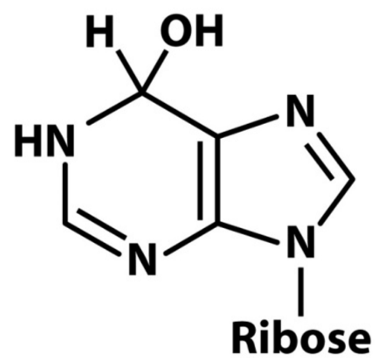
Enzymes are greatly inhibited by transition-state analogs

Adenosine deaminase

$K_m = 3 \times 10^{-5}$

Product inhibition:
$K_I = 3 \times 10^{-4}$





1,6-Dihydroinosine

TS analog:
$K_I = 1.5 \times 10^{-13}$

Competitive inhibition

$$\begin{array}{l} E + S \rightleftharpoons ES \longrightarrow E + P \\ + \\ I \\ \Big\updownarrow K_I \\ EI \end{array}$$

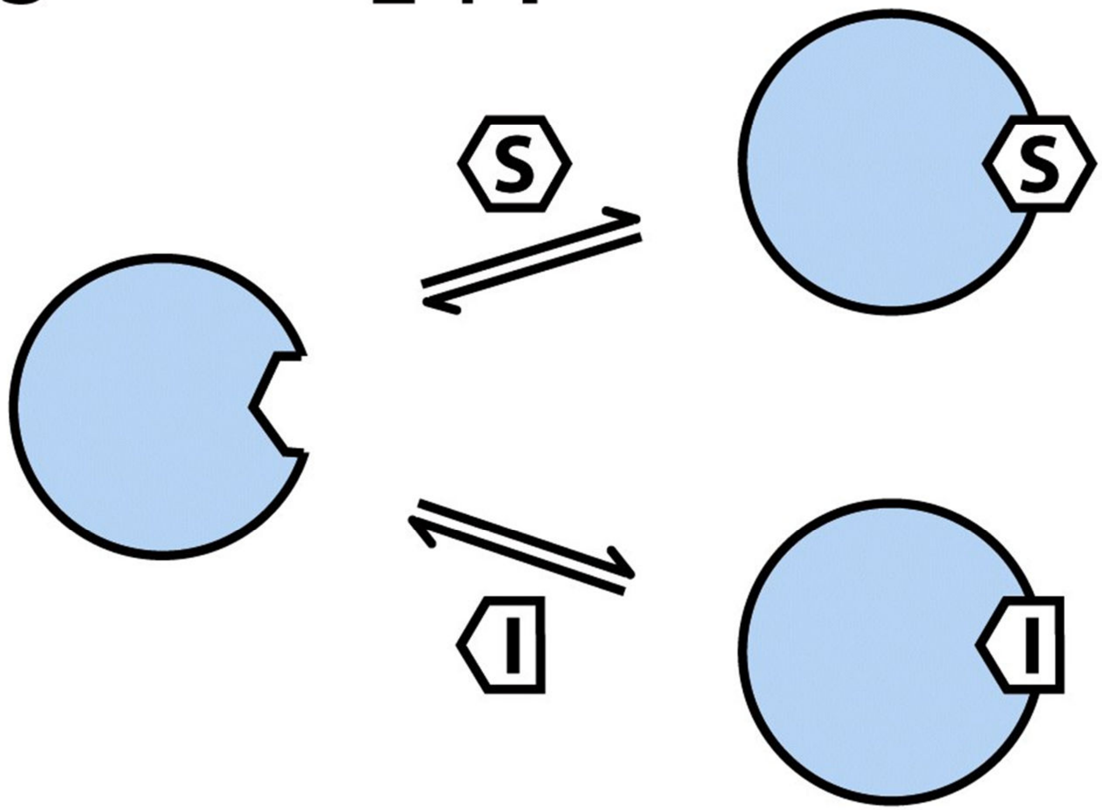


Figure 6-15a
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Uncompetitive inhibition

$$E + S \rightleftharpoons ES \longrightarrow E + P$$

$$ES + I \overset{K_I'}{\rightleftharpoons} ESI$$

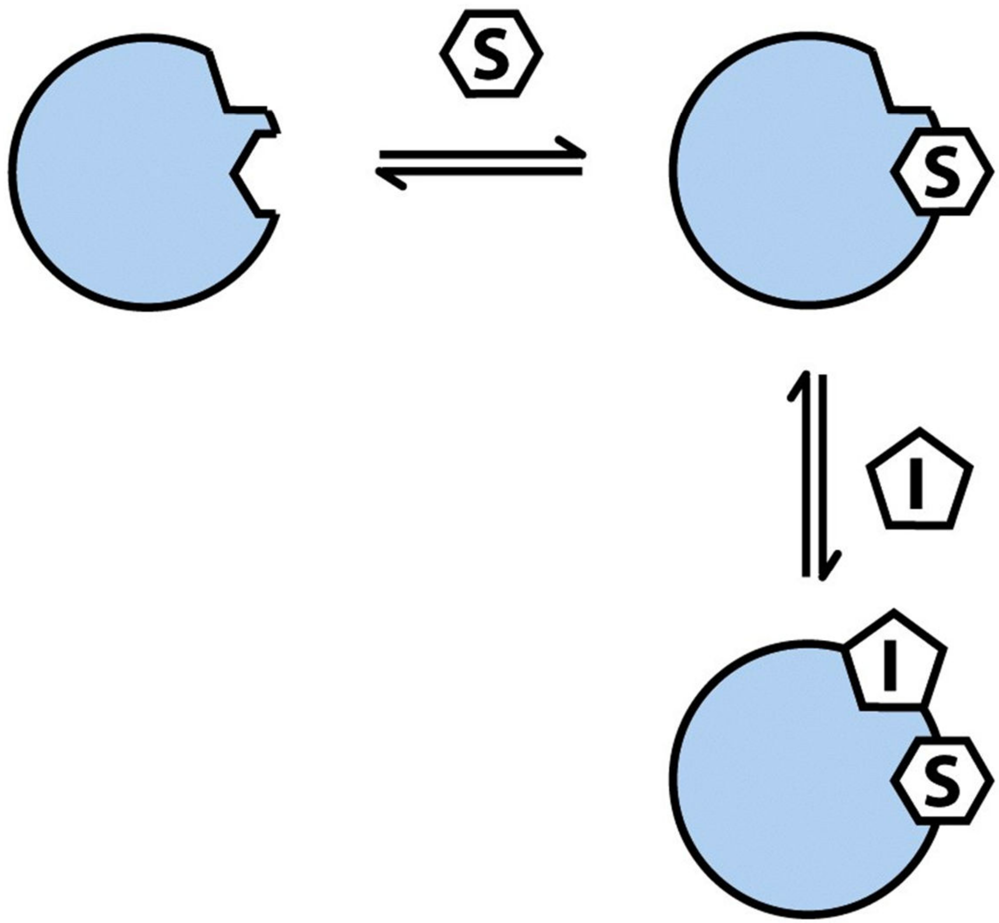

Figure 6-15b
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Mixed inhibition

$$\mathrm{E + S \rightleftharpoons ES \longrightarrow E + P}$$

$$\begin{array}{ccc} + & & + \\ \mathrm{I} & & \mathrm{I} \\ \Big\updownarrow K_\mathrm{I} & & \Big\updownarrow K_\mathrm{I}' \\ \mathrm{EI + S} & \rightleftharpoons & \mathrm{ESI} \end{array}$$

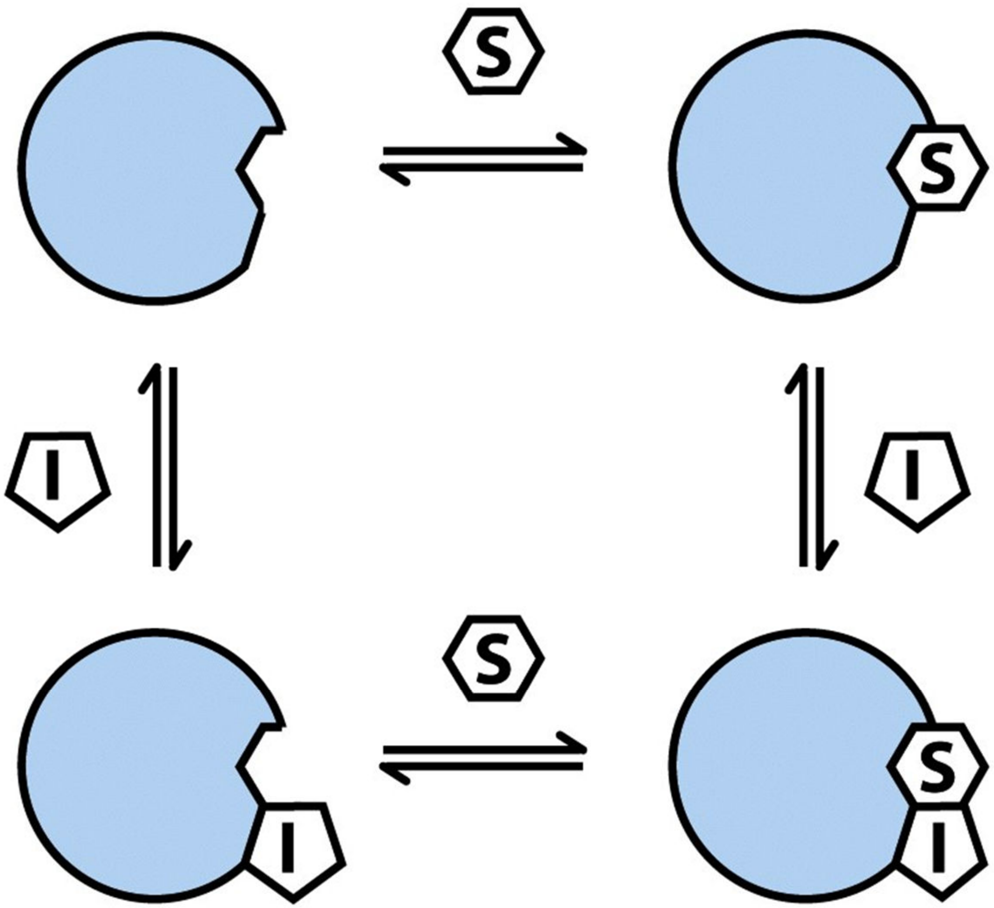

Figure 6-15c
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Competitive inhibition

$$E + S \rightleftharpoons ES \longrightarrow E + P$$

$$+$$

$$I$$

$$\Big\updownarrow K_I$$

$$EI$$

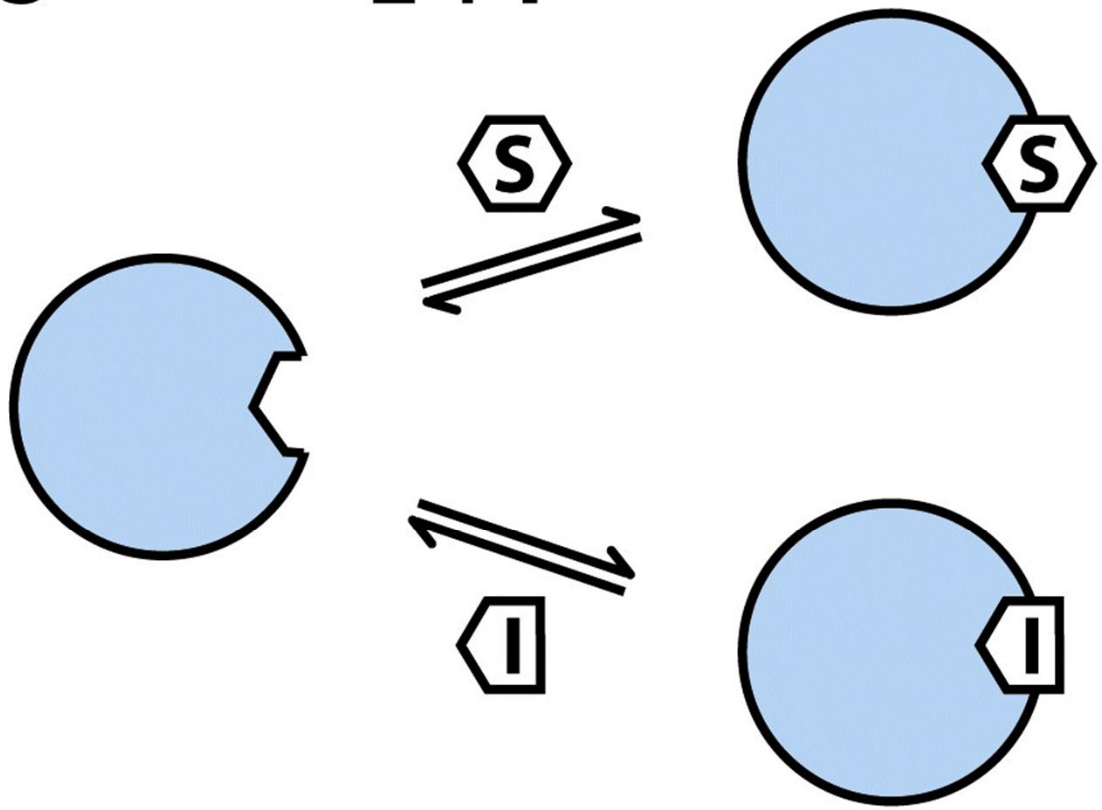

Figure 6-15a
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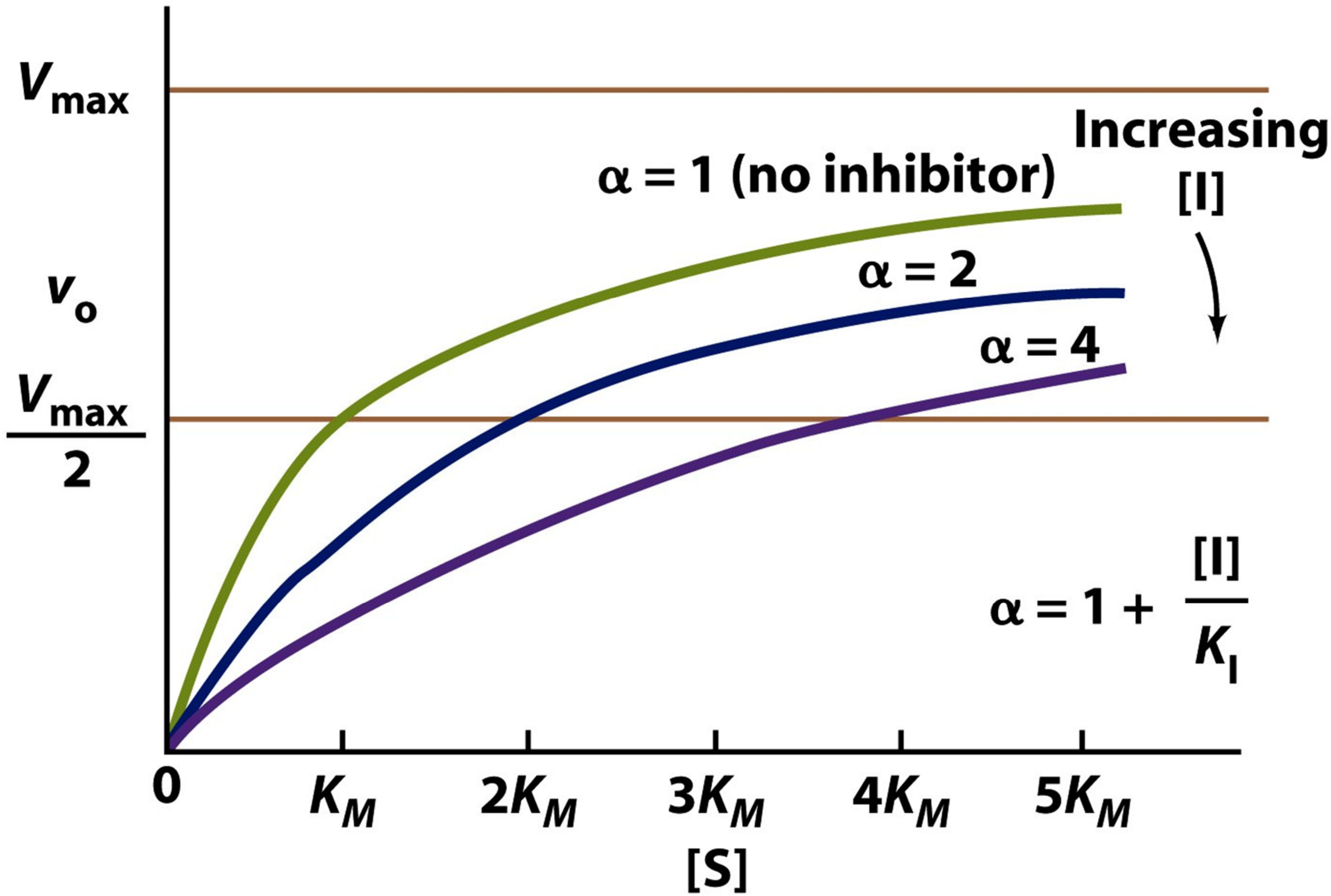
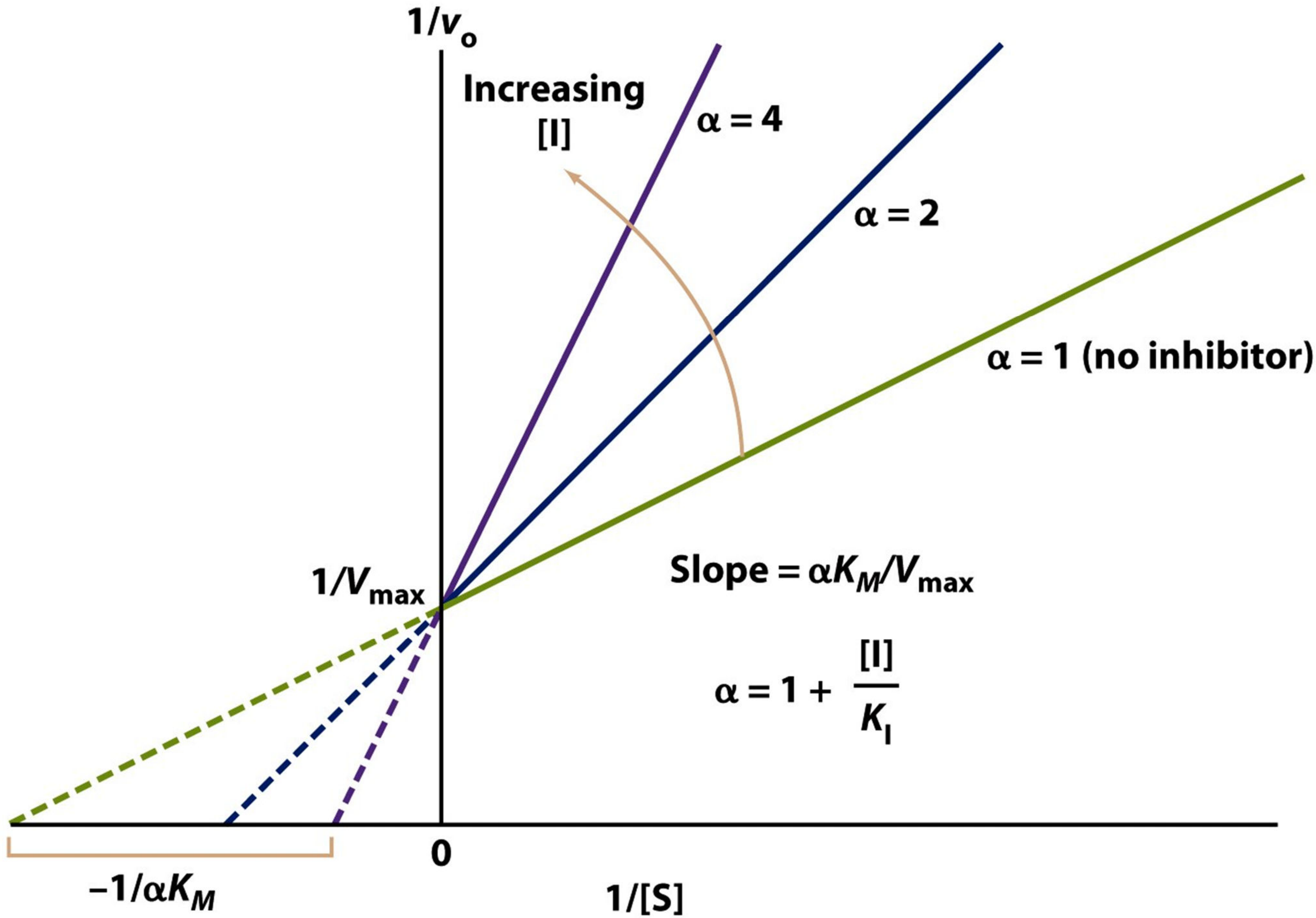


α is the factor by which [S] must be increased to overcome the presence of inhibitor



1/v_o
Increasing [I]
α = 4
α = 2
α = 1 (no inhibitor)
1/V_{max}
Slope = $\alpha K_M/V_{max}$
$\alpha = 1 + \frac{[I]}{K_I}$
$-1/\alpha K_M$
0
1/[S]

Uncompetitive inhibition

$$E + S \rightleftharpoons ES \longrightarrow E + P$$

$$\begin{array}{c} ES \\ + \\ I \\ \Big\updownarrow K_I' \\ ESI \end{array}$$

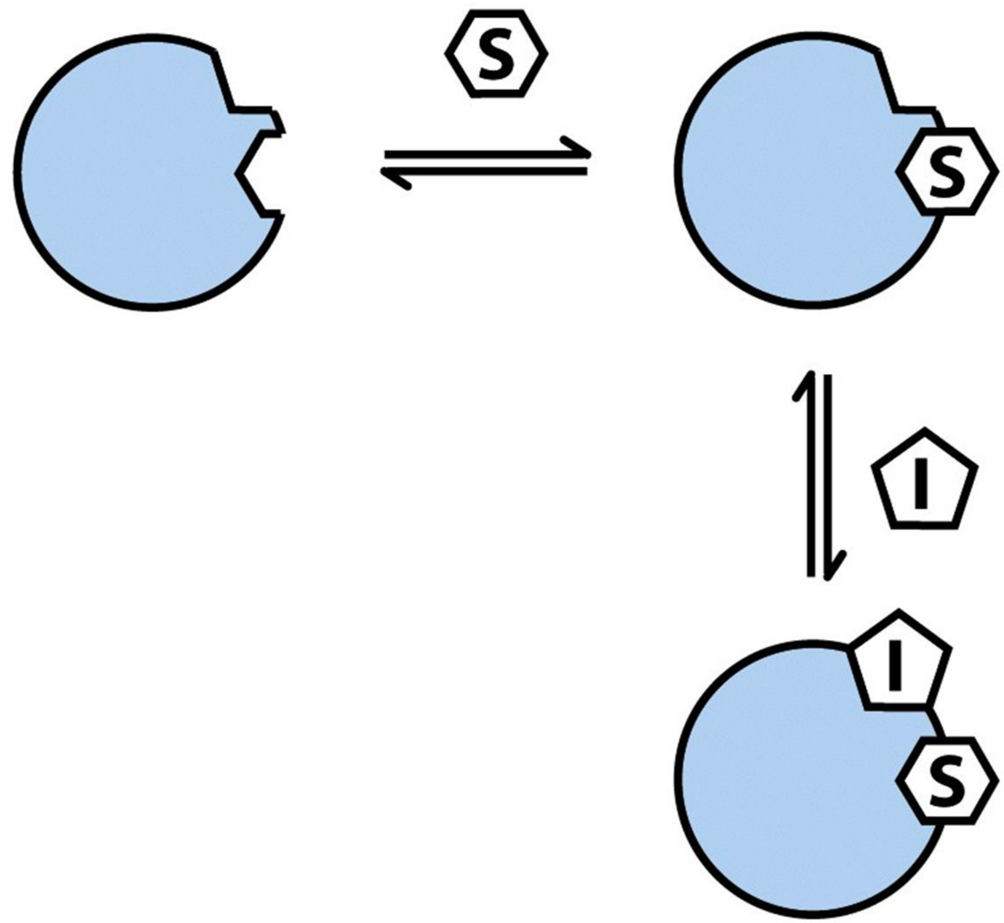


Figure 6-15b
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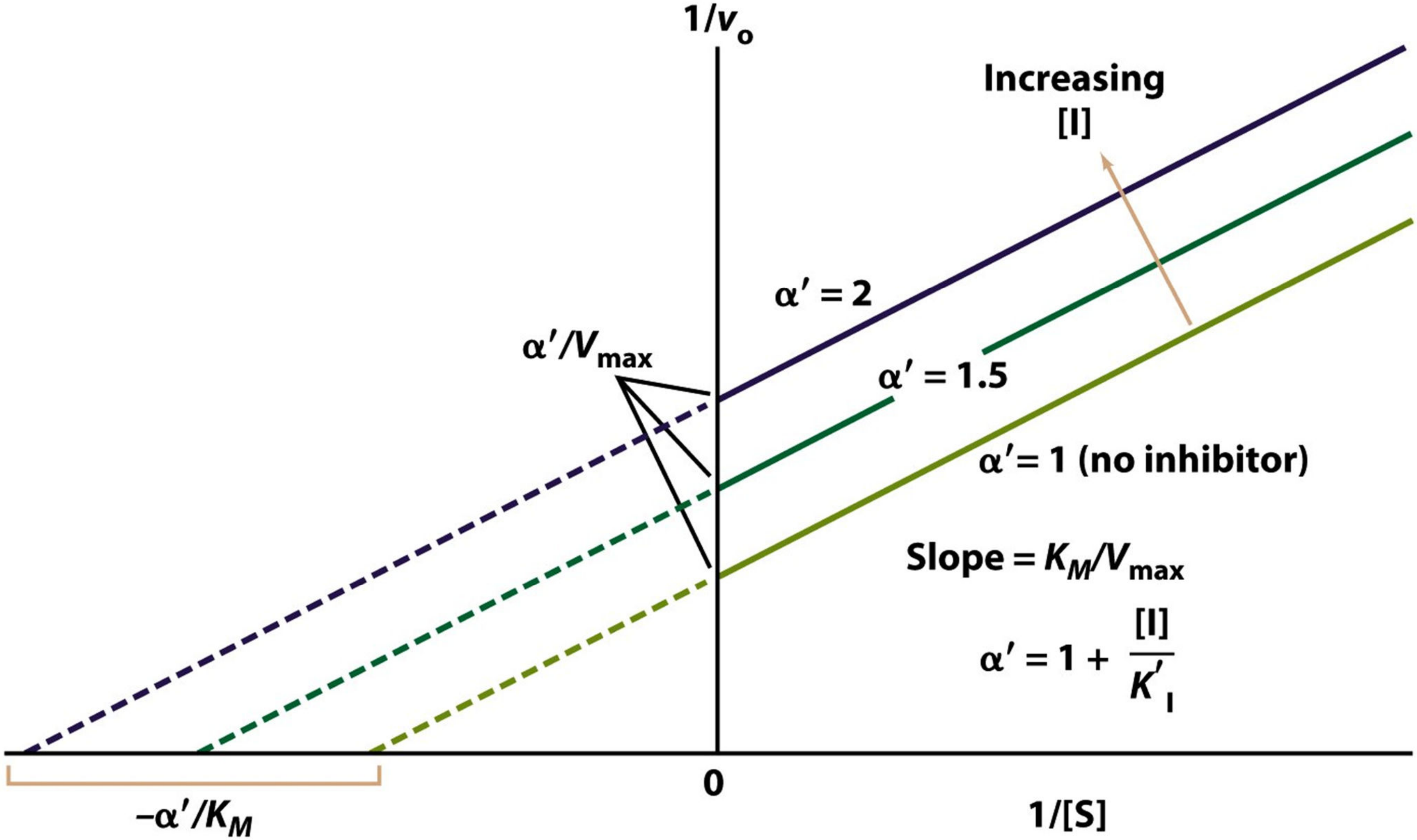

$1/v_o$
Increasing
[I]
$\alpha' = 2$
α'/V_{max}
$\alpha' = 1.5$
$\alpha' = 1$ (no inhibitor)
Slope = K_M/V_{max}
$\alpha' = 1 + \frac{[I]}{K'_I}$
0
$-\alpha'/K_M$
1/[S]

Mixed inhibition

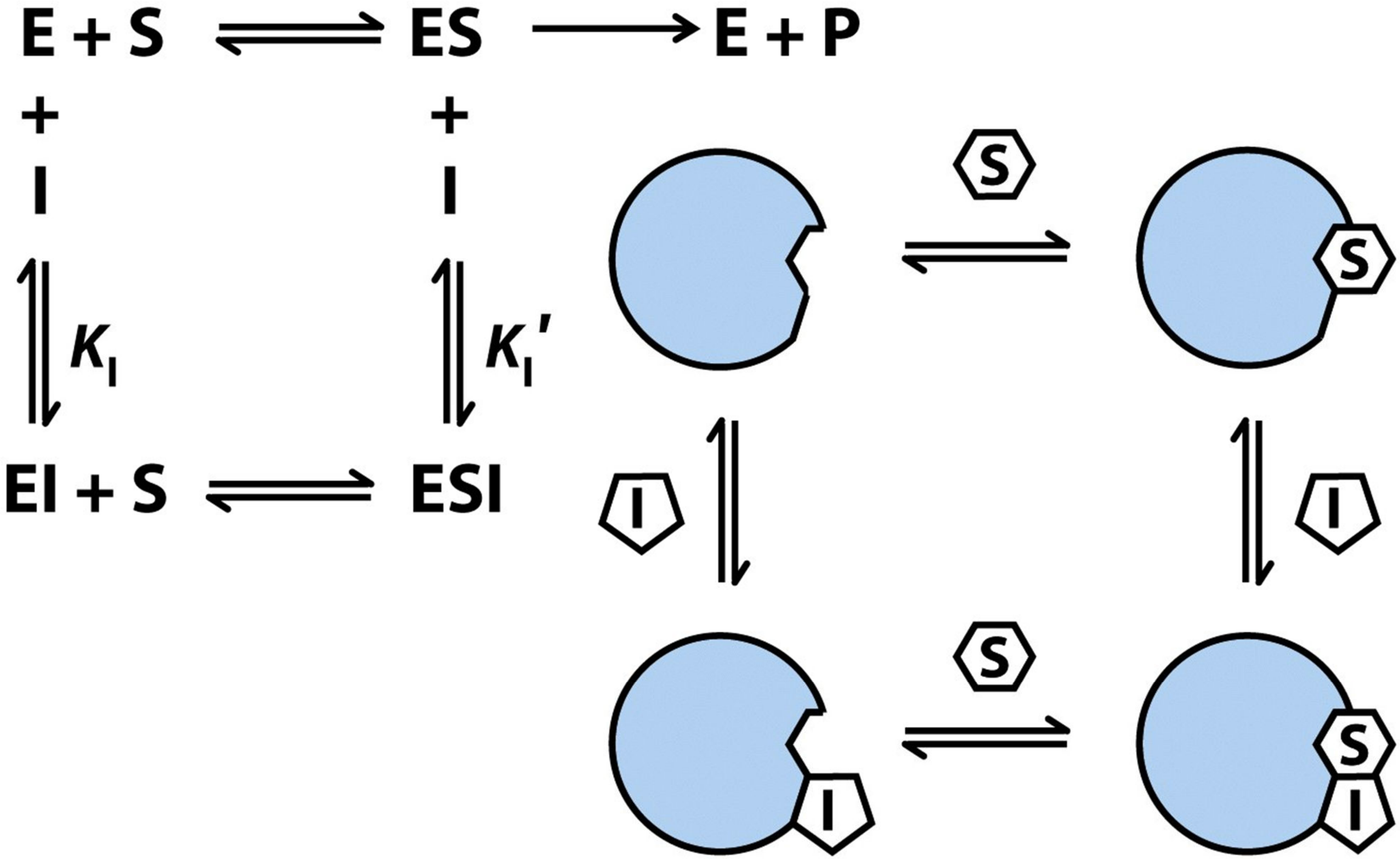

Figure 6-15c
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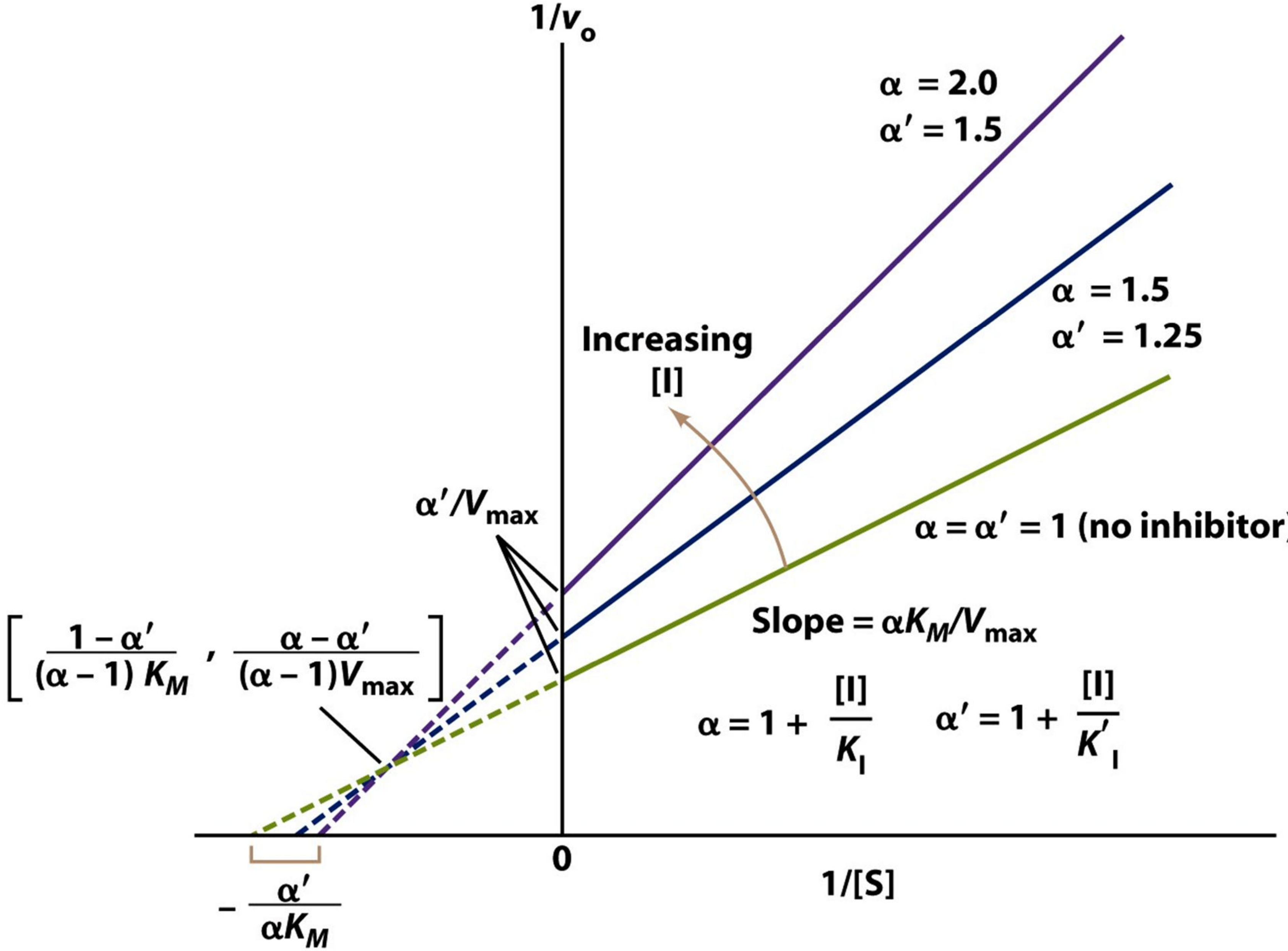
1/v_o
$\alpha = 2.0$
$\alpha' = 1.5$
$\alpha = 1.5$
$\alpha' = 1.25$
Increasing [I]
α'/V_{max}
$\alpha = \alpha' = 1$ (no inhibitor)
Slope = $\alpha K_M/V_{max}$
$\left[\frac{1-\alpha'}{(\alpha-1)K_M}, \frac{\alpha-\alpha'}{(\alpha-1)V_{max}} \right]$
$\alpha = 1 + \frac{[I]}{K_I}$
$\alpha' = 1 + \frac{[I]}{K'_I}$
0
1/[S]
$-\frac{\alpha'}{\alpha K_M}$

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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Table 12-2 Effects of Inhibitors on Michaelis–Menten Reactions[a]

Type of Inhibition	Michaelis–Menten Equation	Lineweaver–Burk Equation	Effect of Inhibitor
None	$v_o = \frac{V_{max}[S]}{K_M + [S]}$	$\frac{1}{v_o} = \frac{K_M}{V_{max}}\frac{1}{[S]} + \frac{1}{V_{max}}$	None
Competitive	$v_o = \frac{V_{max}[S]}{\alpha K_M + [S]}$	$\frac{1}{v_o} = \frac{\alpha K_M}{V_{max}}\frac{1}{[S]} + \frac{1}{V_{max}}$	Increases K_M^{app}
Uncompetitive	$v_o = \frac{V_{max}[S]}{K_M + \alpha'[S]} = \frac{(V_{max}/\alpha')[S]}{K_M/\alpha' + [S]}$	$\frac{1}{v_o} = \frac{K_M}{V_{max}}\frac{1}{[S]} + \frac{\alpha'}{V_{max}}$	Decreases K_M^{app} and V_{max}^{app}
Mixed (noncompetitive)	$v_o = \frac{V_{max}[S]}{\alpha K_M + \alpha'[S]} = \frac{(V_{max}/\alpha')[S]}{(\alpha/\alpha')K_M + [S]}$	$\frac{1}{v_o} = \frac{\alpha K_M}{V_{max}}\frac{1}{[S]} + \frac{\alpha'}{V_{max}}$	Decreases V_{max}^{app}; may increase or decrease K_M^{app}

[a] $\alpha = 1 + \frac{[I]}{K_I}$ and $\alpha' = 1 + \frac{[I]}{K_I'}$