Chapter Six
The Behavior of Proteins: Enzymes

Enzyme are effective biological catalysts

- **Enzyme:**

- With the exception of some RNA ribozymes that catalyze their own splicing, all other enzymes are globular proteins.

- In the absence of catalysts → most reaction in biological system *would take place far* ***too slowly*** to provide products .
  - enzymes can increase the rate of a reaction by a factor of up to 10^{20} over an uncatalyzed reaction

- Enzymes are highly specific and can distinguish stereoisomer of a giving compound

- Enzymes does not interfere with the equilibrium constant of the reaction they catalyze

Reaction thermodynamics

$$\Delta G^{\circ} = \Delta G_{products} - \Delta G_{reactants}$$

- ***△ G: -ve (spontaneous process, exergonic).***
  - ***Free Energy is an indicator of Spontaneity***
- ***△ G: +ve (not spontaneous process, endergonic).***
- ***△ G = 0 (process at equilibrium).***

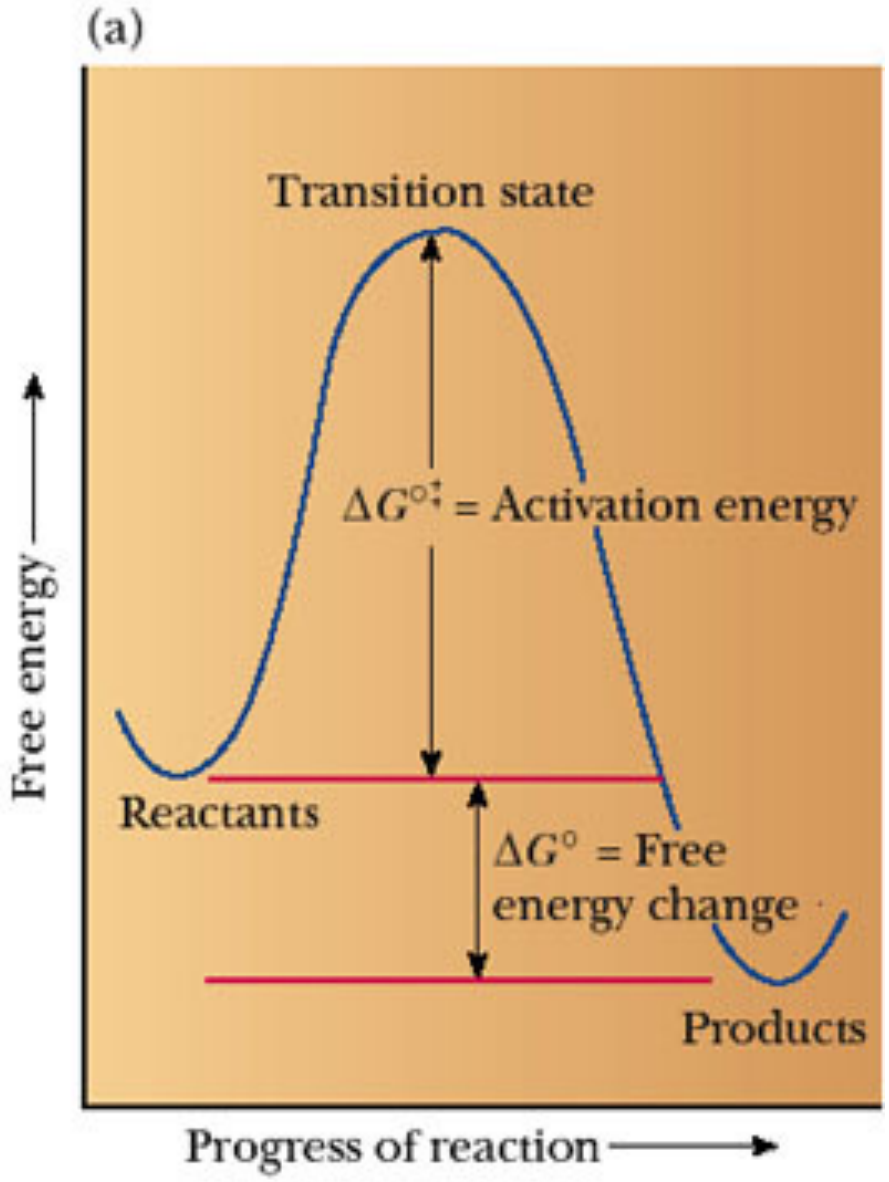
Enzymes lowers the activation energy Catalysis

The rate of a reaction depends on its **activation energy**,

$\Delta G^{\circ\ddagger}$ (Free energy of activation)
The energy input required to initiate the reaction

Or

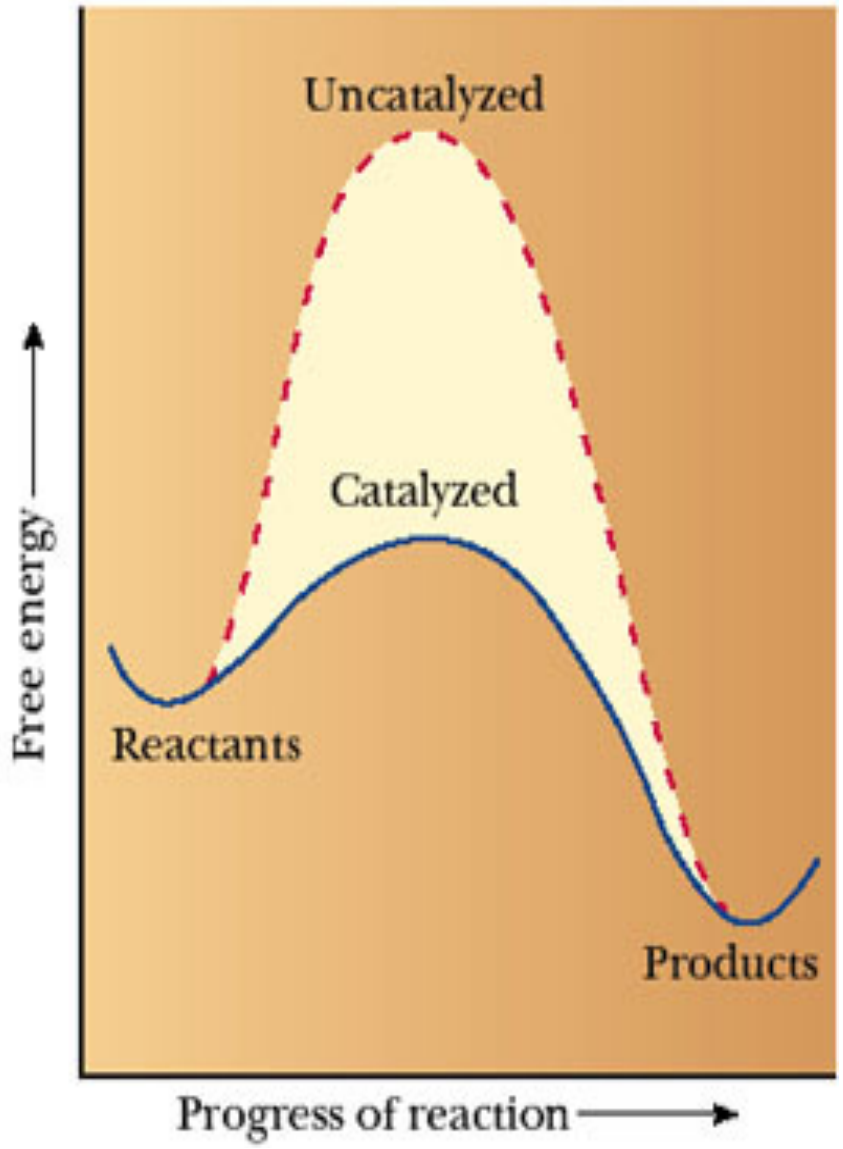
The amount of free energy required to bring the reaction to the transition state.



ΔG° free energy change = $\Delta G_{products} - \Delta G_{reactants}$

Enzymes lowers the activation energy Catalysis

- Enzyme speed up reactions but they can not alter equilibrium constant or ΔG° .
- $\Delta G^{\circ\ddagger}$ is higher in the un-catalyzed reaction.
- Un-catalyzed reaction requires more energy to get started ➔ *rate is slower than catalyzed reaction*



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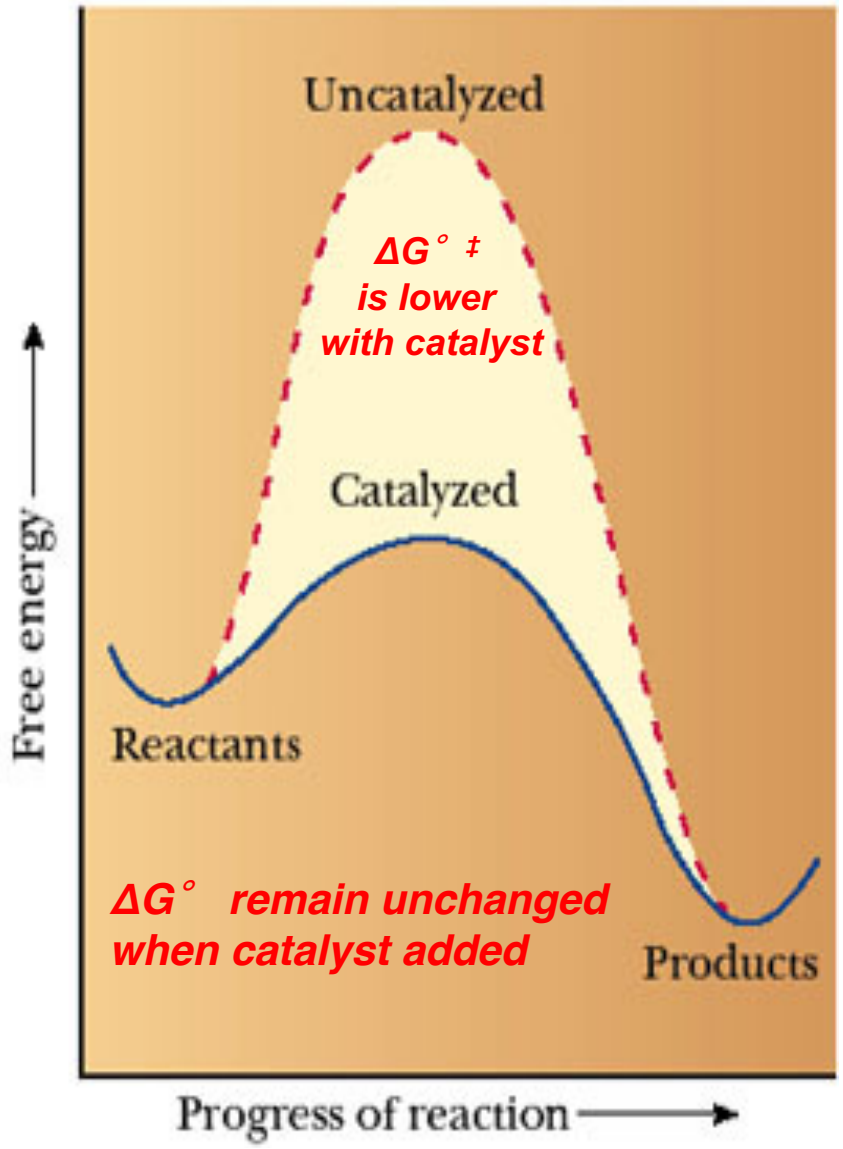


ΔG° free energy change $= \Delta G_{products} - \Delta G_{reactants}$

Enzymes VS Temperature

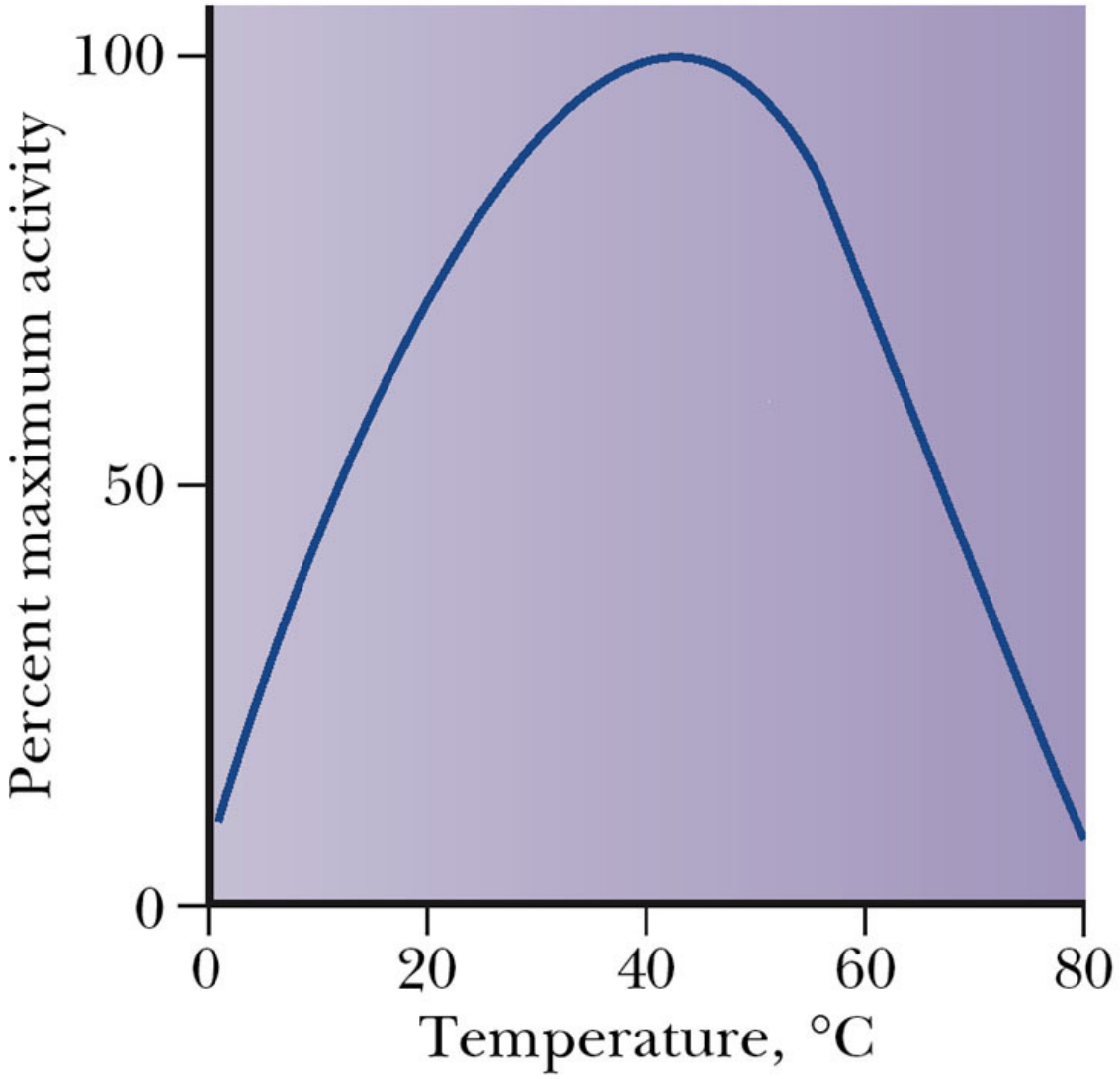
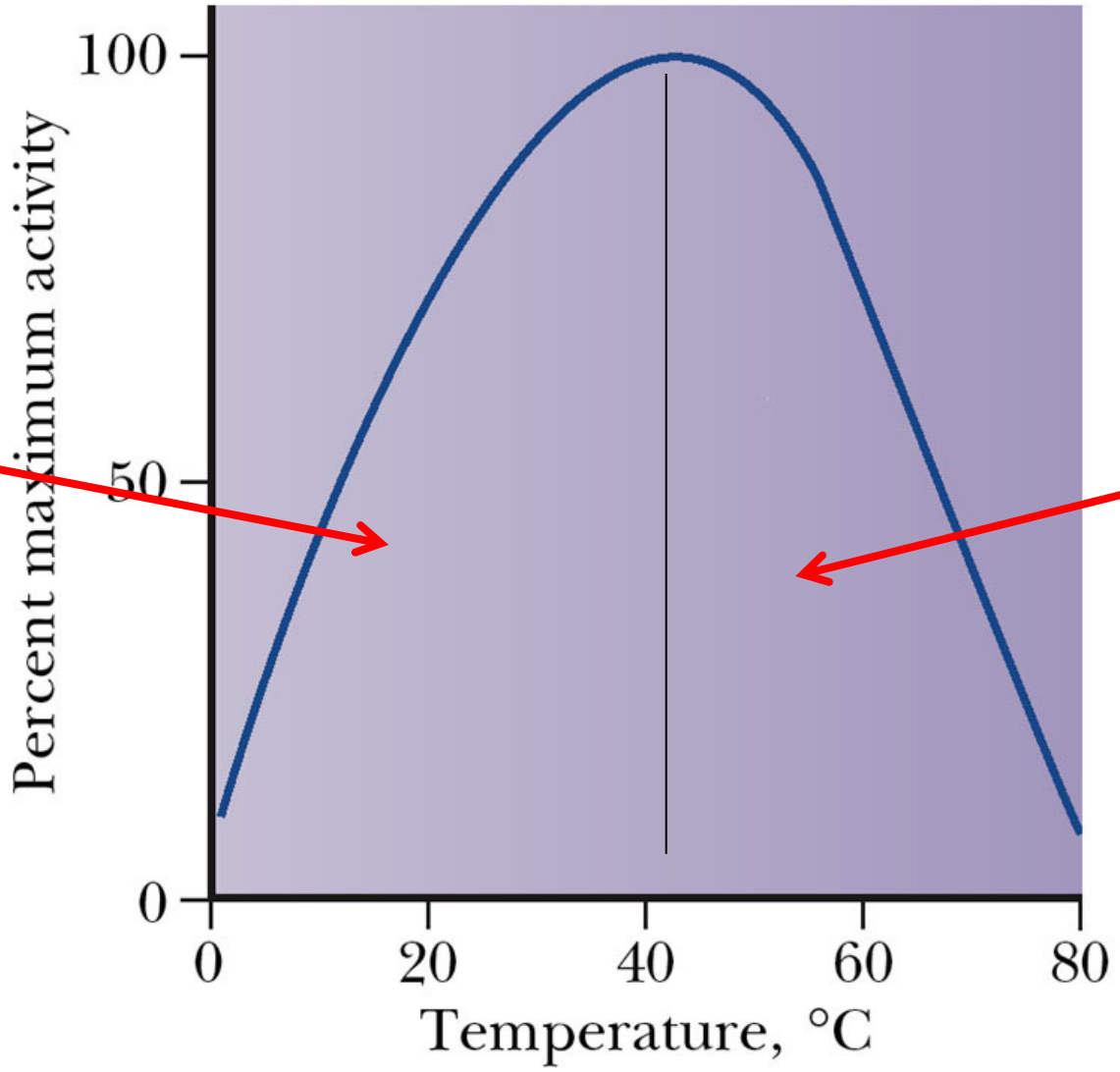


Fig. 6-2, p.134

Enzymes VS Temperature



Free energy of activation increases

Denaturation

Fig. 6-2, p.134

Enzymes VS Temperature

- In the body, reactions take place at constant temperature and pressure

Increase in temperature

Increases the energy available to the reactants to reach transition state.

Rate of chemical reactions increase

Enzyme Catalysis

$$H_2O_2 \rightarrow H_2O + O_2$$

Table 6.1

Lowering of the Activation Energy of Hydrogen Peroxide Decomposition by Catalysts

Reaction Conditions	Activation Free Energy		Relative Rate
	kJ mol^{-1}	kcal mol^{-1}	
No catalyst	75.2	18.0	1
Platinum surface	48.9	11.7	2.77×10^4
Catalase	23.0	5.5	6.51×10^8

Enzyme Kinetics

- **Kinetics** is the study of reaction rates (time-dependent phenomena)

- Rates of reactions are affected by
  - Enzymes/catalysts
  - Substrates
  - Effectors
  - Temperature
  - Concentrations

General Observations

- Enzymes are able to exert their influence at very low concentrations ~ [enzyme] = nM
- The initial rate (velocity) is linear with [enzyme].
- The initial velocity increases with [substrate] at low [substrate].
- The initial velocity approaches a maximum at high [substrate].

The initial velocity increases with [S] at low [S]

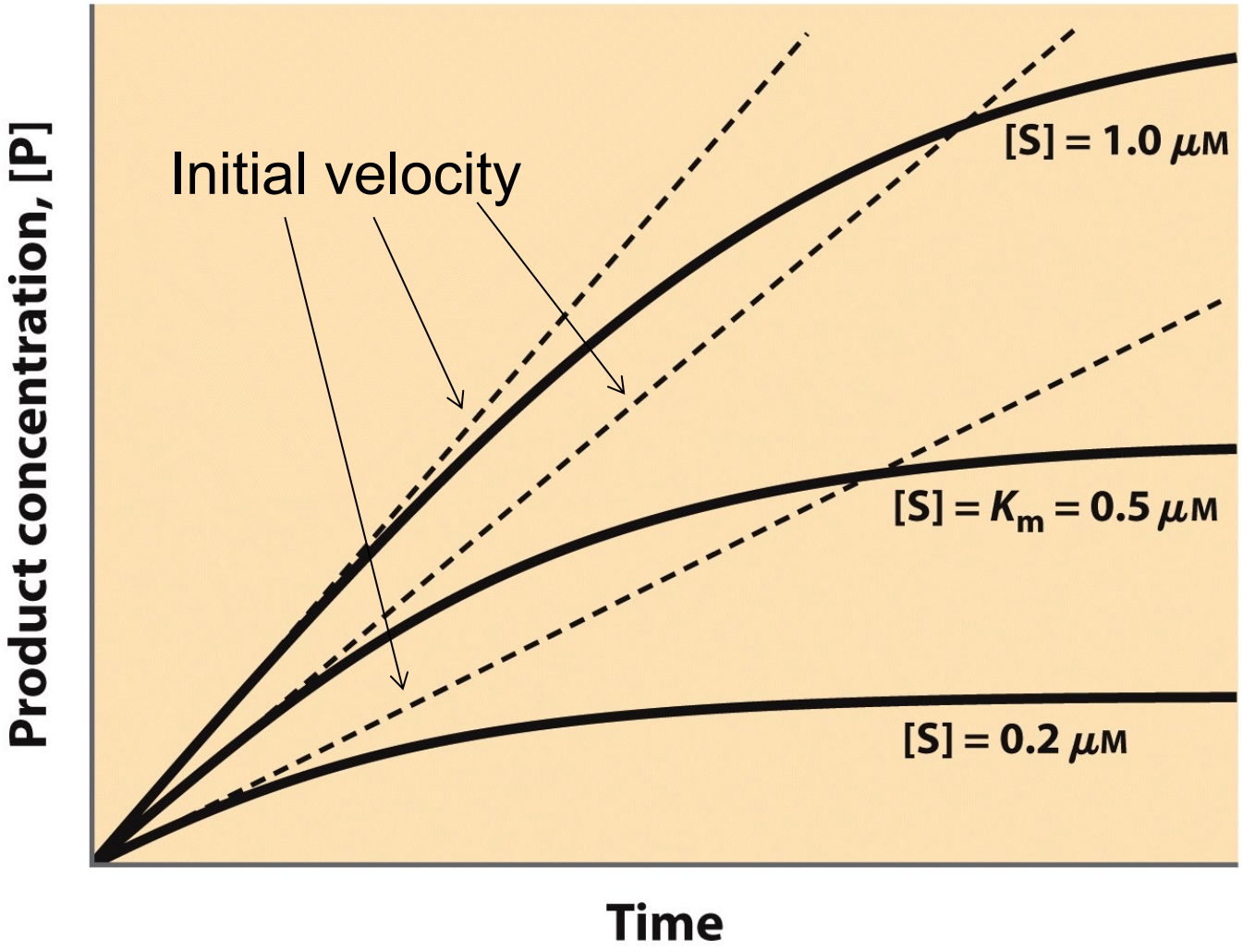
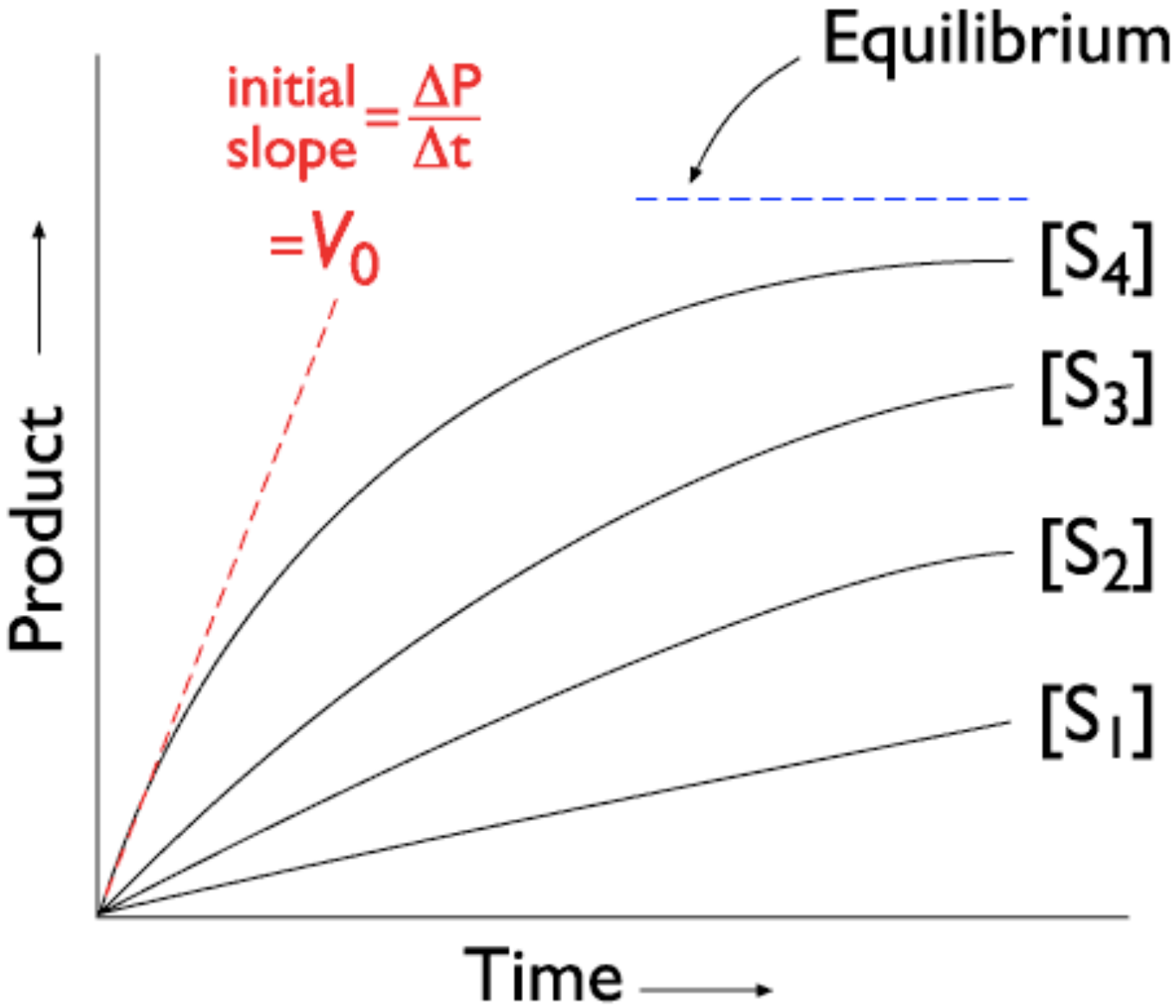


Figure 6-10
Lehninger Principles of Biochemistry, Fifth Edition

The initial velocity increases with [S] at low [S]



Enzyme Kinetic equation

The rate of reaction is expressed in term of a change in the concentration of a reactant or a product in a given time interval

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rate of disappearance of product

rate of appearance of product

$$\text{Rate} = -\frac{\Delta[A]}{\Delta t} = -\frac{\Delta[B]}{\Delta t} = \frac{\Delta[P]}{\Delta t}$$

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rate of disappearance of product

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$$\text{Rate} = -\frac{\Delta[A]}{\Delta t} = -\frac{\Delta[B]}{\Delta t} = \frac{\Delta[P]}{\Delta t}$$

$$\text{Rate} = k[A]^f[B]^g$$

Enzyme Kinetic equation

$$\text{Rate} = k[A]^f[B]^g$$

- k is a proportionality constant called the rate constant
- Exponents f and g:
  - Determined experimentally, may be 0,1,2.
  - Related to the number of molecules involved in detailed steps that constitute the mechanism
  - Overall Order of a reaction = f + g

The order of a reaction = the sum of exponents

- Generally, the order means how many molecules have to bump into each other at one time for a reaction to occur.

$$\mathbf{A \rightarrow B}$$

$$\mathbf{Rate = k\,[A]^1}$$

- Exponent for the concentration of A is 1 means that the reaction is first order with respect to A and first order overall.

The order of a reaction = the sum of exponents

$$^{32}P \longrightarrow \text{Decay product}$$

$$\text{Rate} = k\,[^{32}P]^{1}$$

- The rate of radioactive decay depends only on the concentration of ^{32}P (only one atom involve in the mechanism)

Second order

$$A + B \longrightarrow C + D$$

$$\text{Rate} = k[A]^1[B]^1$$

The reaction is said to be first order in A, first order in B, and second order overall

$$\text{Glycogen}_n + HPO_4^{2-} \longrightarrow \text{Glucose-1-phosphate} + \text{Glycogen}_{n-1}$$

$$\text{Rate} = k[\text{Glycogen}]^1[HPO_4^{2-}]^1 = k[\text{Glycogen}][HPO_4^{2-}]$$

Zero order

- Exponent in a rate equation my be = zero

$$A \rightarrow B$$

$$\text{Rate} = k[A]^0 = k$$

- Such a reaction is called ZERO order
- Rate is constant is independent of concentration of reactants but:
  - Depends on the presence of catalysts
  - Concentration of substrate is so high in which catalyst is completely saturated with reactants

Formation of Enzyme – substrate complex is the First step in Enzymatic Reaction

In an Enzyme-catalyzed reactions

E + S ⇔ E S → E + P

Enzyme + Substrate — transition state complex — Enzyme + Product

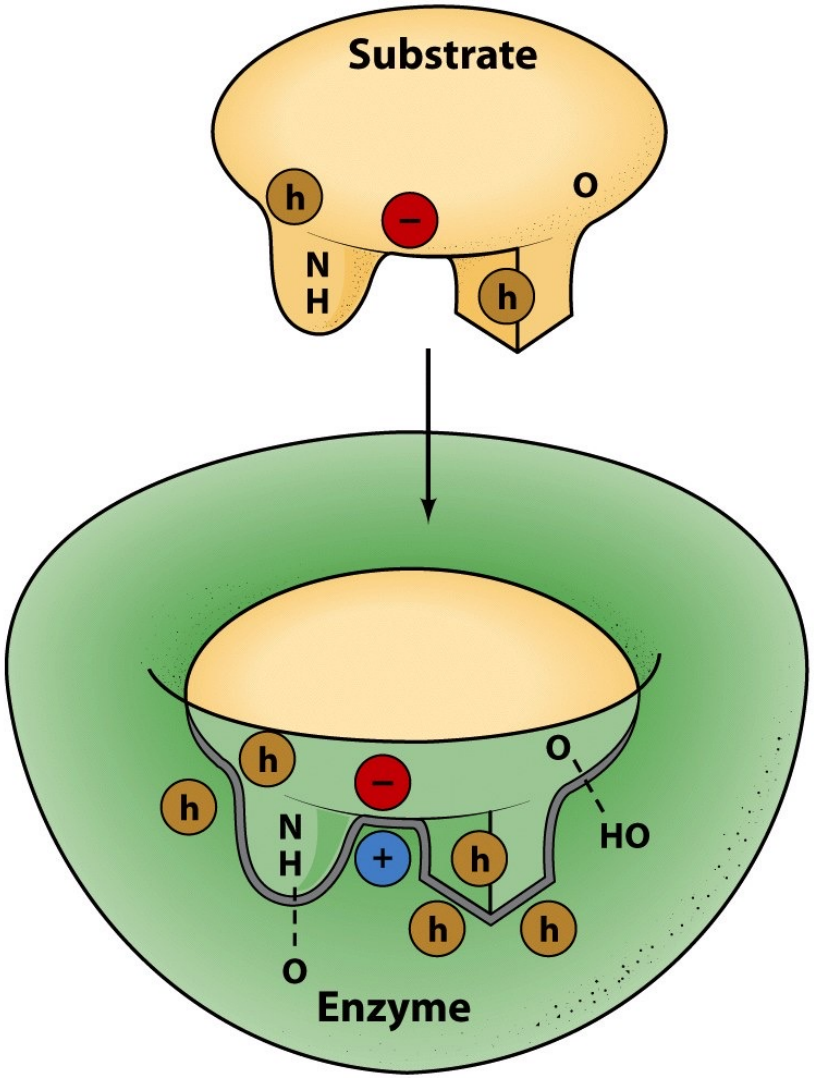
Formation of Enzyme – substrate complex is the First step in Enzymatic Reaction

- **Active site:** the small portion of the enzyme surface where the substrate(s) becomes bound by non-covalent forces:

1. hydrogen bonding
2. electrostatic attractions
3. van der Waals attractions

- consists of certain a.a's that are essential for enzyme activity

- highly specific interactions



Binding Models

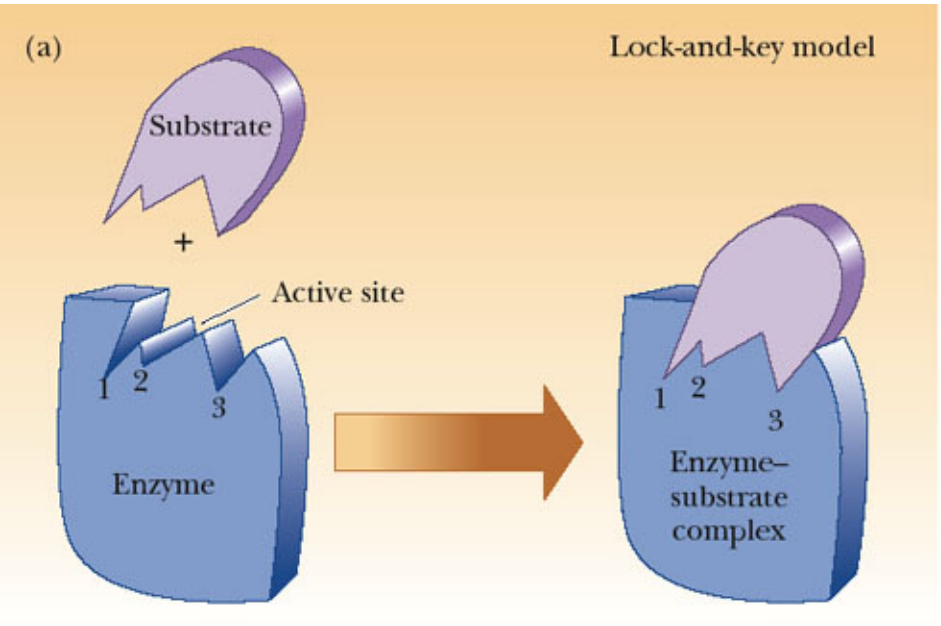
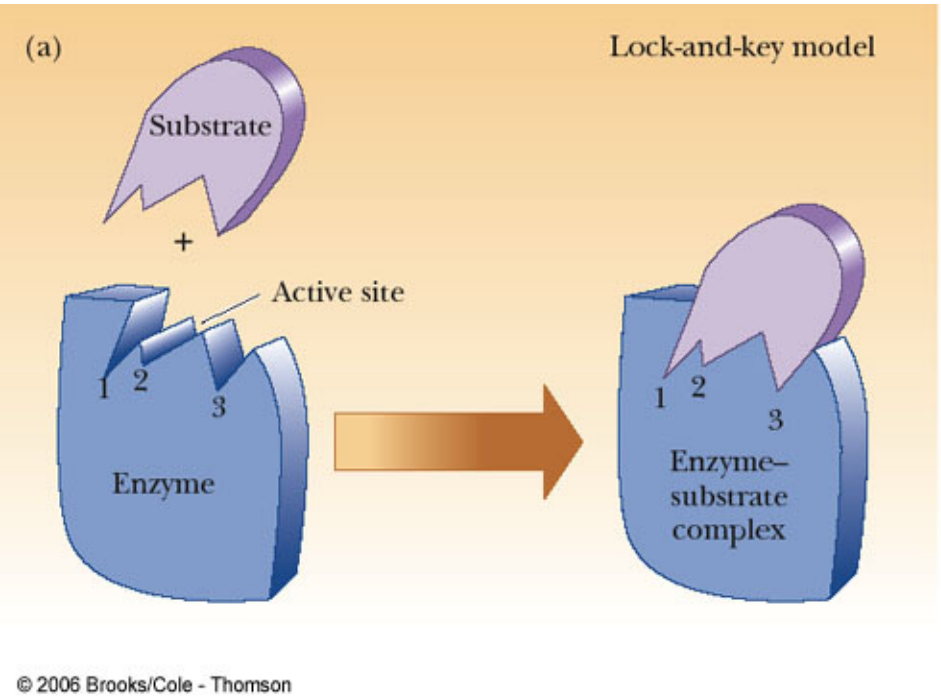
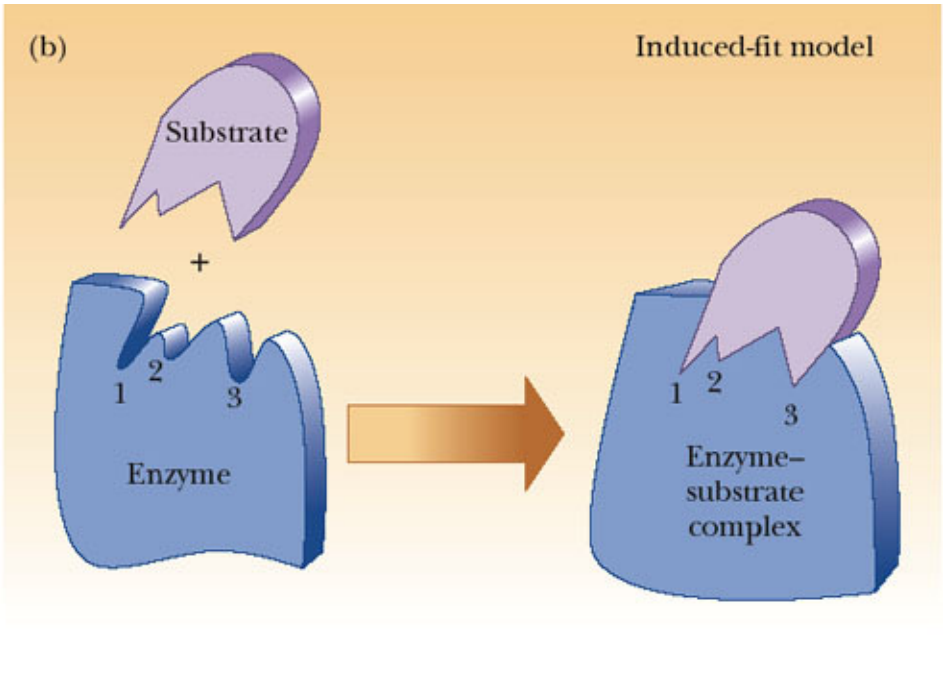


Fig. 6-3, p.136

Binding Models





The induced fit model is more accurate because it explain the nature of transition state and lowered activation energy

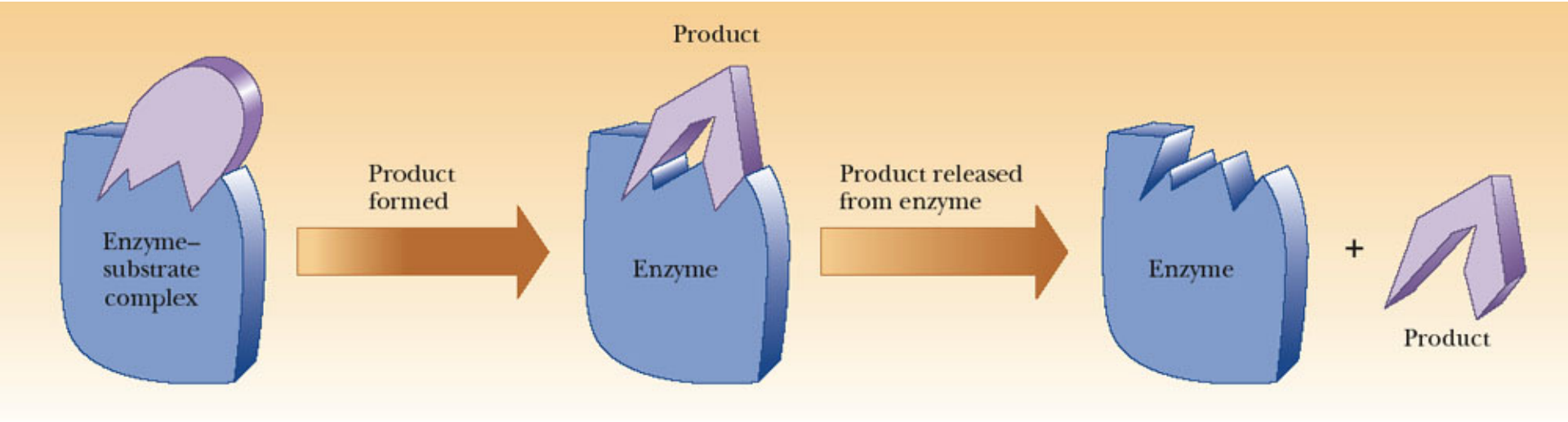
Fig. 6-3, p.136

Formation of Enzyme – substrate complex is the First step in Enzymatic Reaction

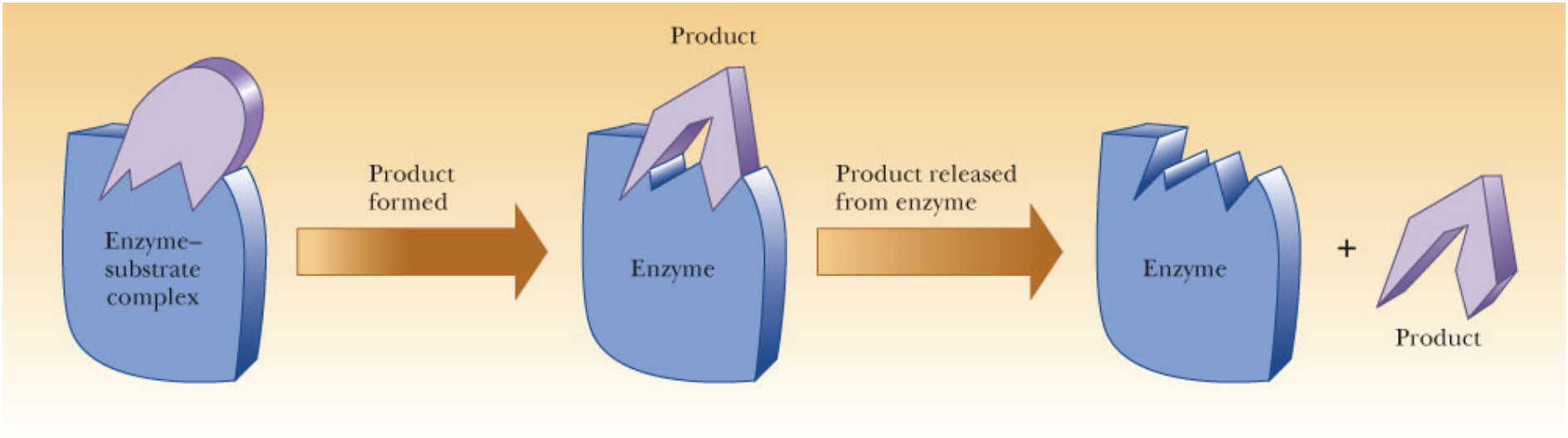
In an Enzyme-catalyzed reactions

E + S ⇔ E S → E + P

Enzyme + Substrate | transition state complex | Enzyme + Product



Formation of Product



The Substrate bound close to the atom with which it is to react

The substrate transformed to a product: Bonds are broken and new bonds are formed and

The product is released from the enzyme

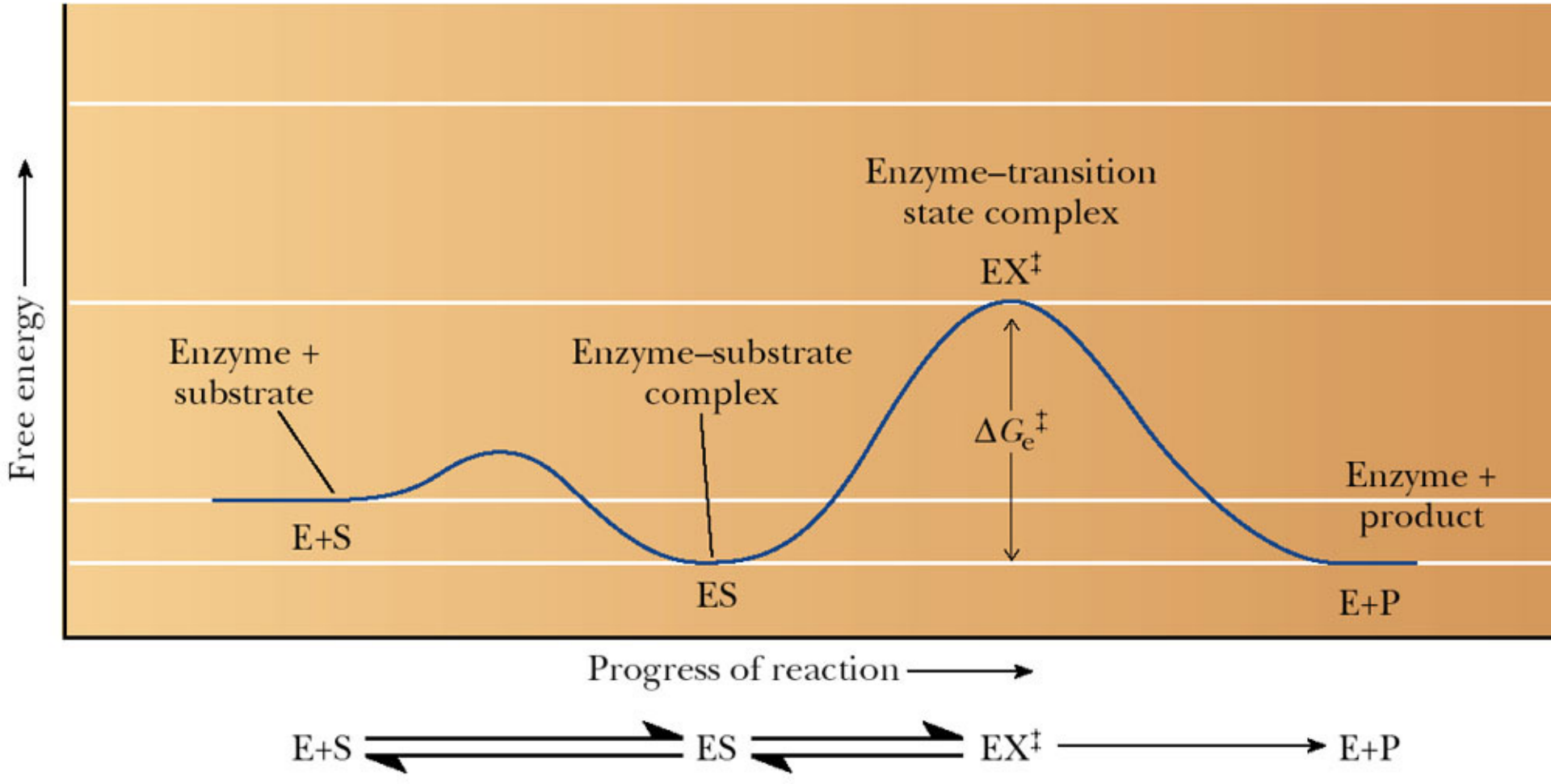
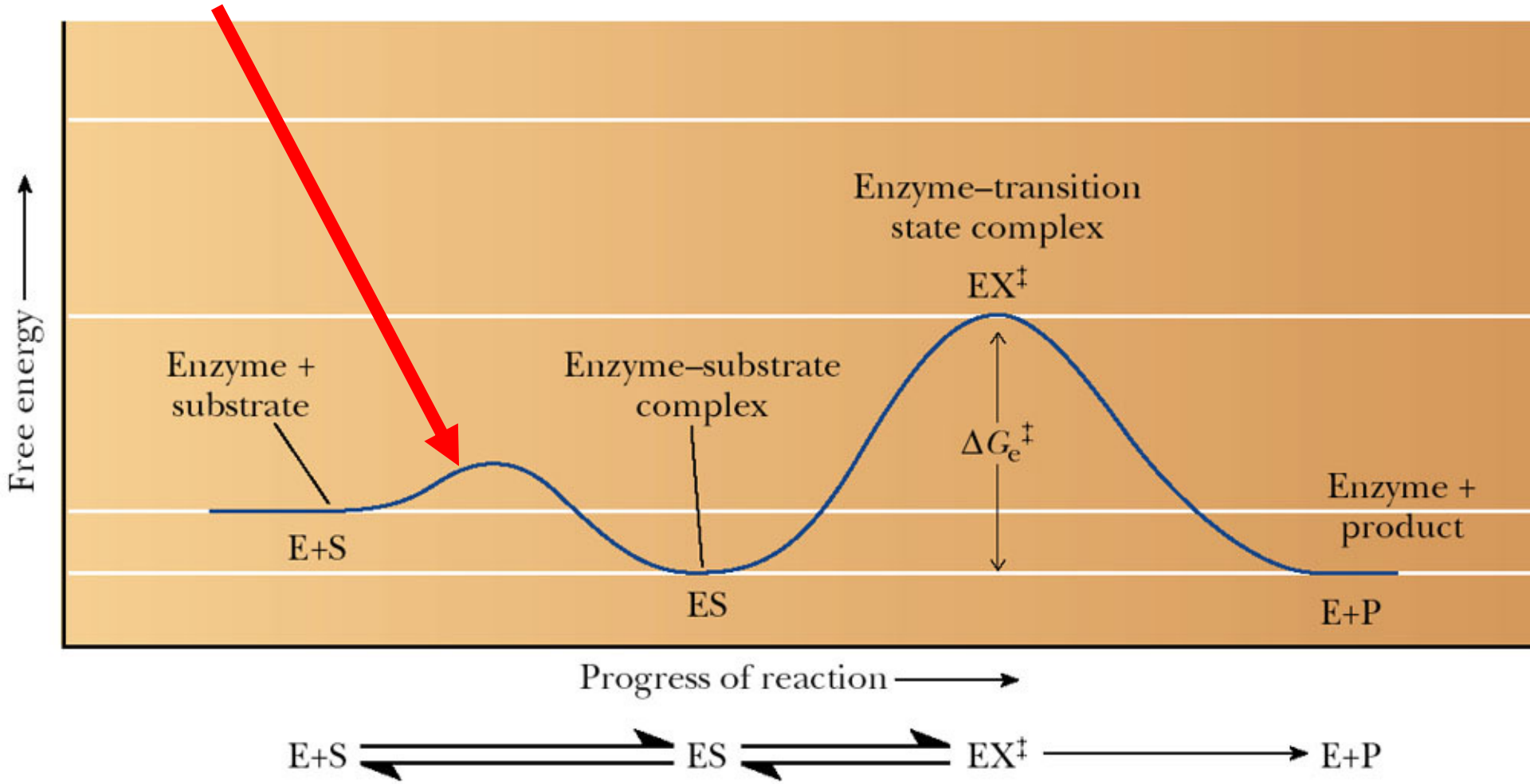


Fig. 6-4, p.137

Attraction level between E and S for binding



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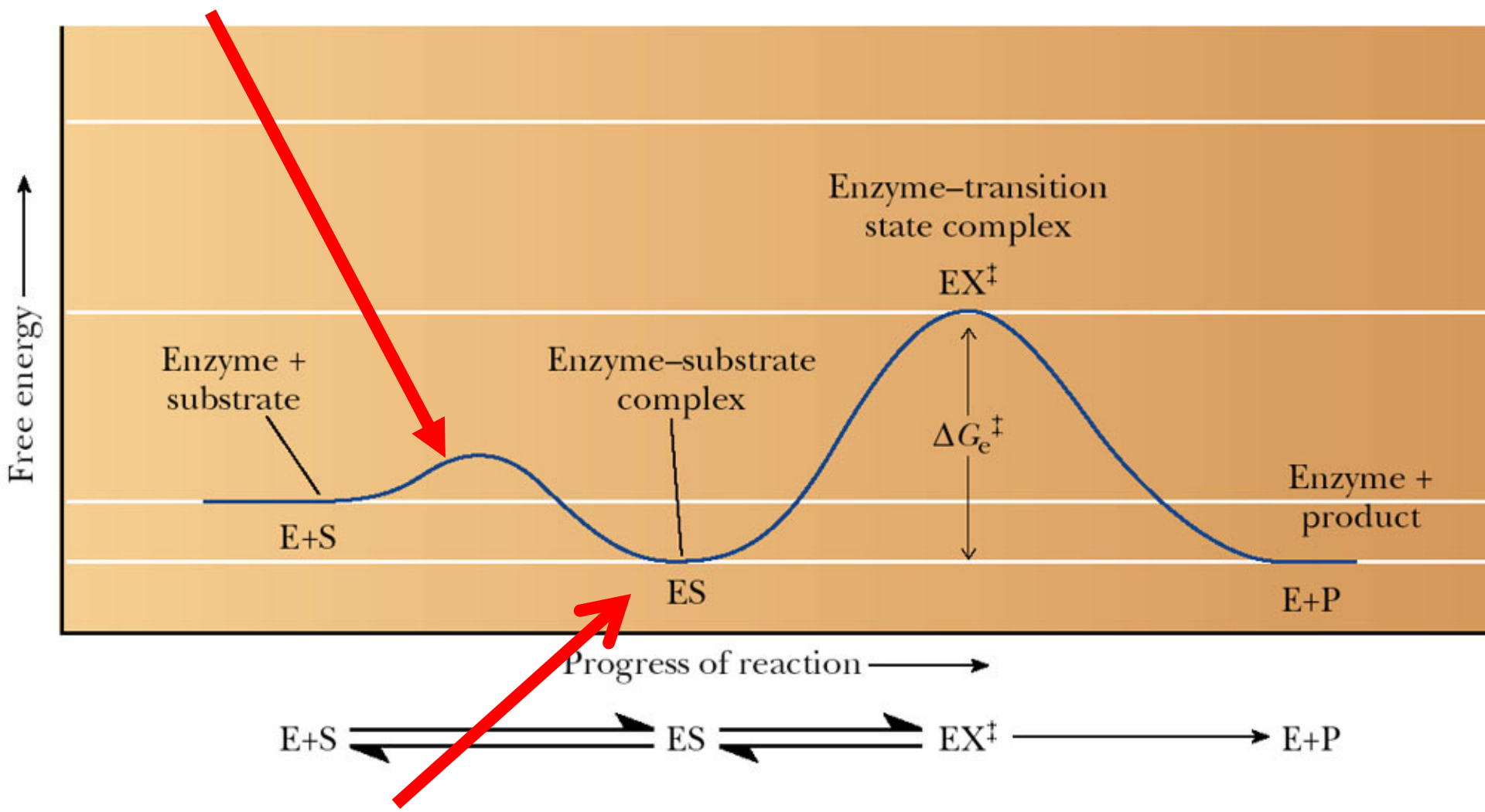
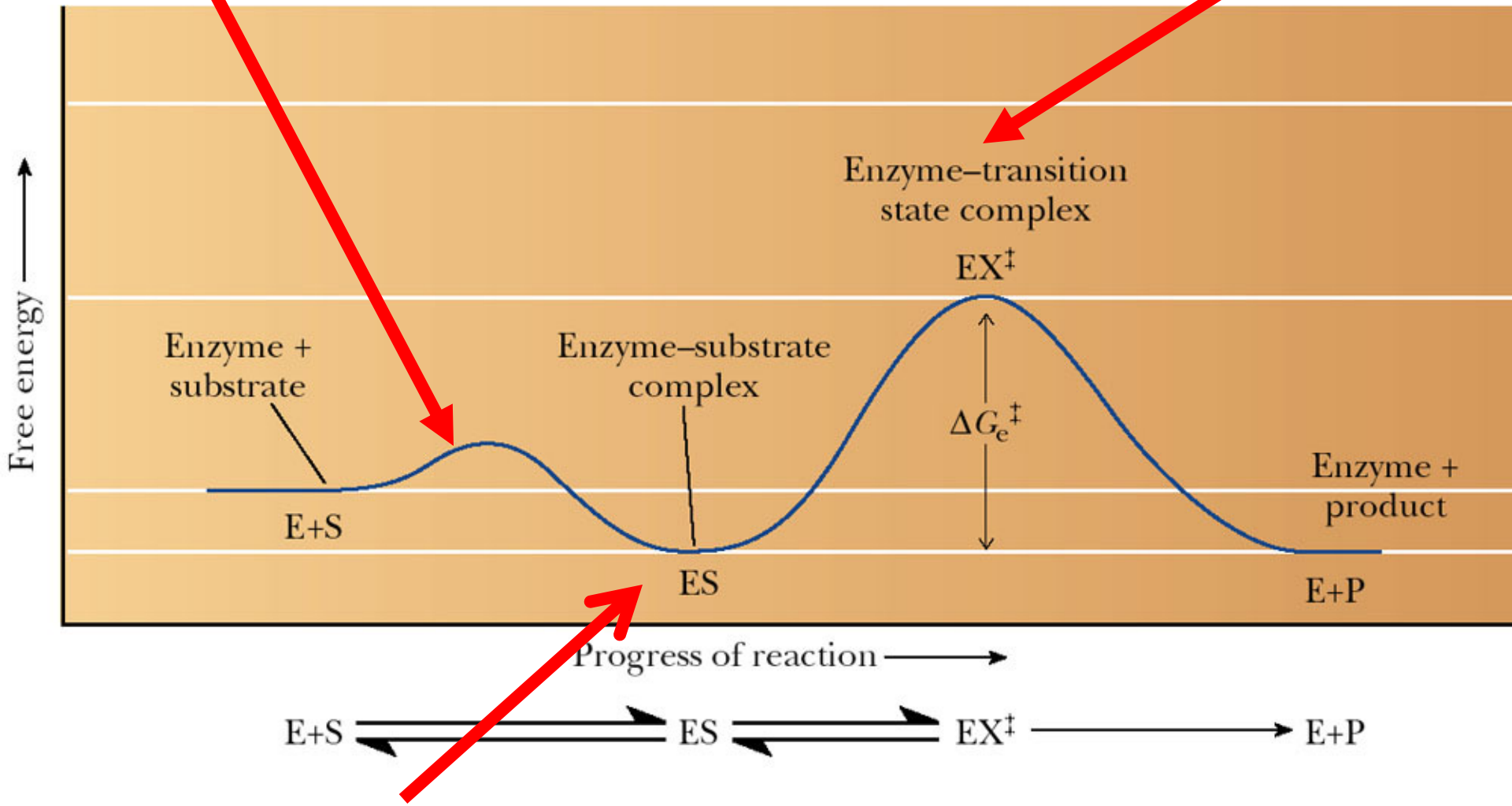


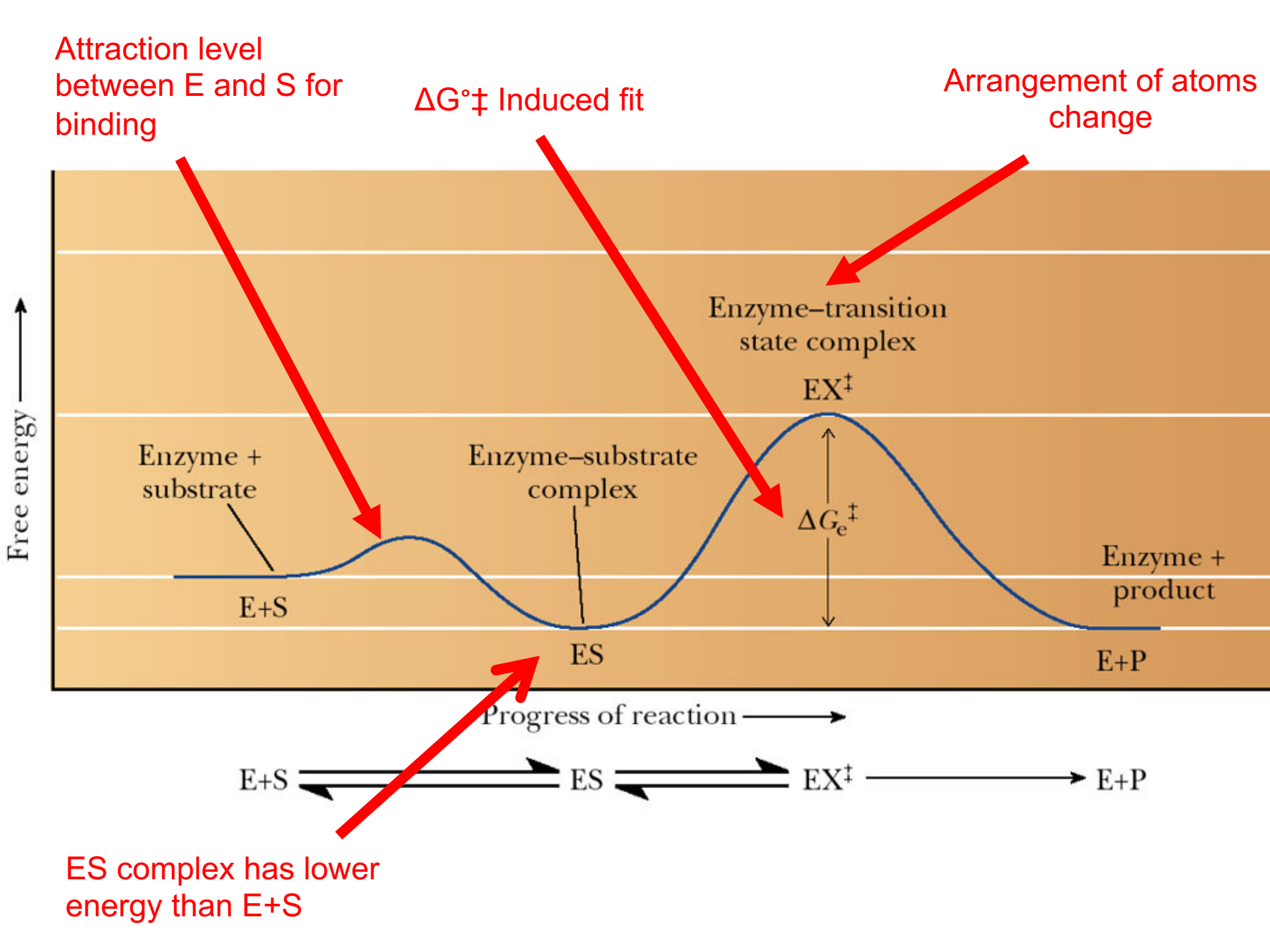
ES complex has lower energy than E+S

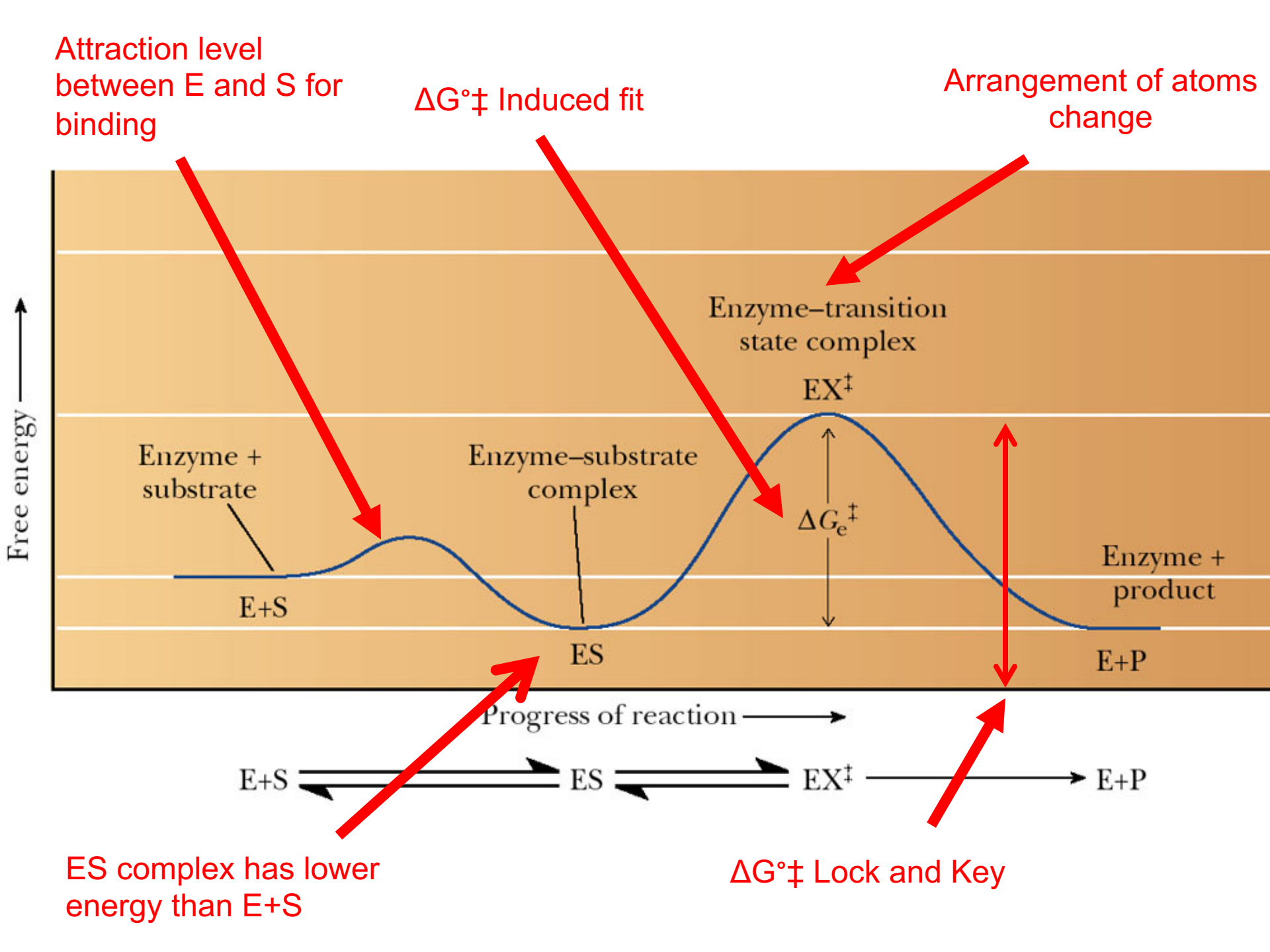
Attraction level between E and S for binding

Arrangement of atoms change



ES complex has lower energy than E+S


Attraction level between E and S for binding
ΔG°‡ Induced fit
Arrangement of atoms change
Enzyme–transition state complex
EX‡
Enzyme + substrate
Enzyme–substrate complex
$\Delta G_e^{\ddagger}$
Enzyme + product
E+S
ES
E+P
Free energy
Progress of reaction
E+S ⇌ ES ⇌ EX‡ → E+P
ES complex has lower energy than E+S


Attraction level between E and S for binding
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ΔGe‡
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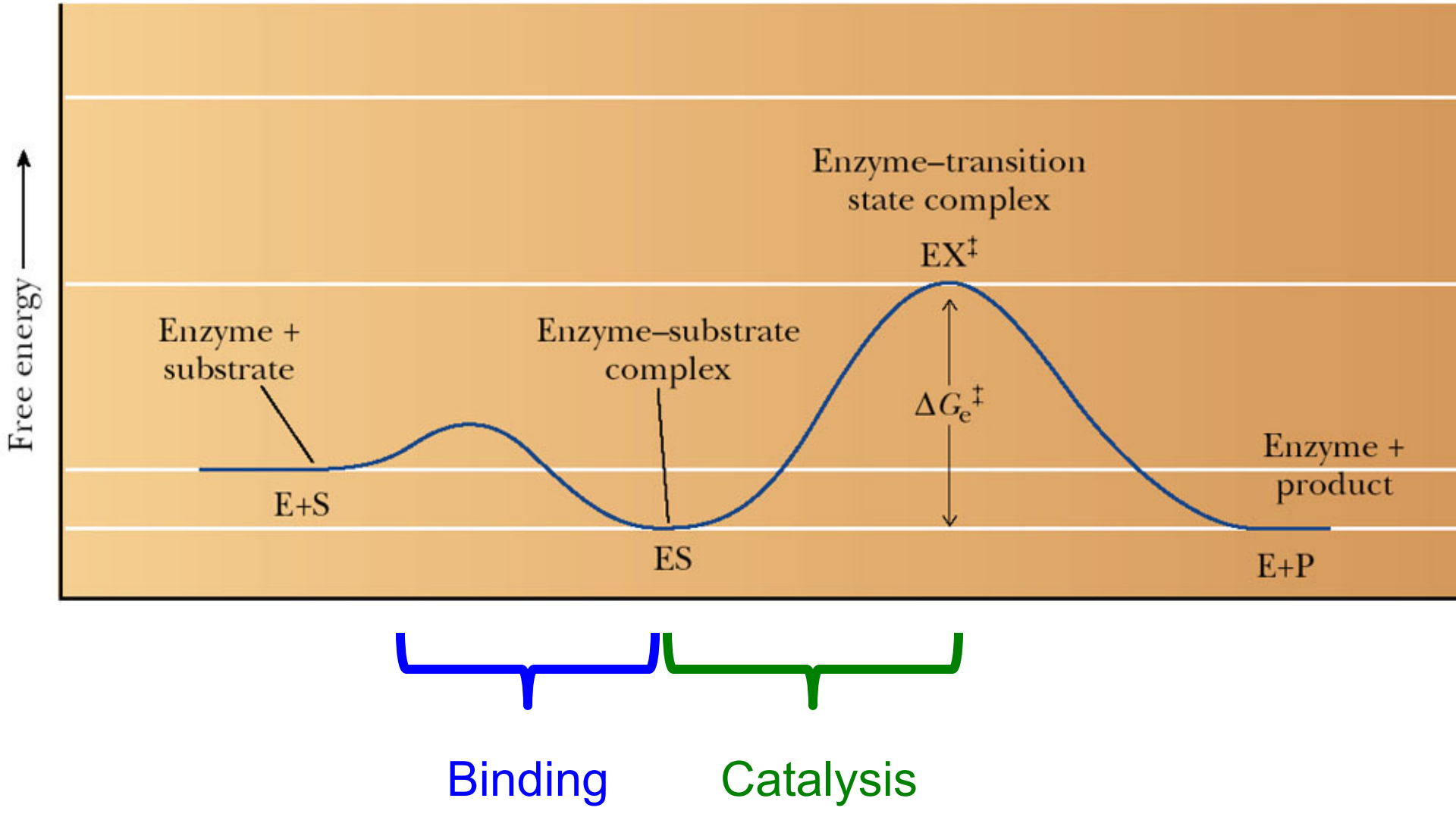
E+S
ES
E+P
Free energy
Progress of reaction
E+S ⇌ ES ⇌ EX‡ → E+P
ES complex has lower energy than E+S
ΔG°‡ Lock and Key


Free energy
Enzyme–transition state complex
EX‡
Enzyme + substrate
Enzyme–substrate complex
ΔG‡e
Enzyme + product
E+S
ES
E+P
Binding
Catalysis

Non-Allosteric Vs Allosteric Enzymes

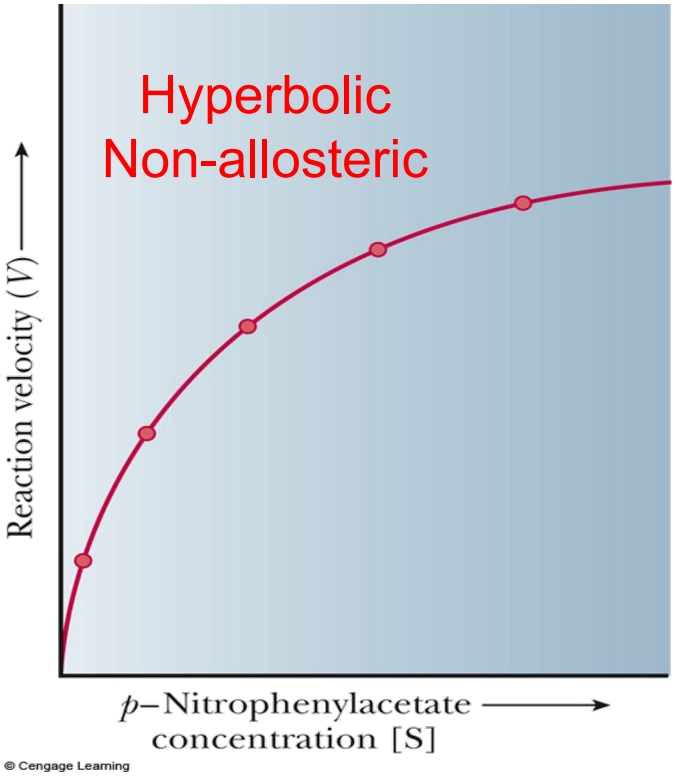
Reaction rate depends initially on [S] Concentration when [S] is low.

At higher [S] concentration rate changes very little with addition of more substrate.

V_{max} is reached

V_{max}: Point at which the rate of reaction does not change with [S] enzyme is saturated, maximum rate of reaction is reached

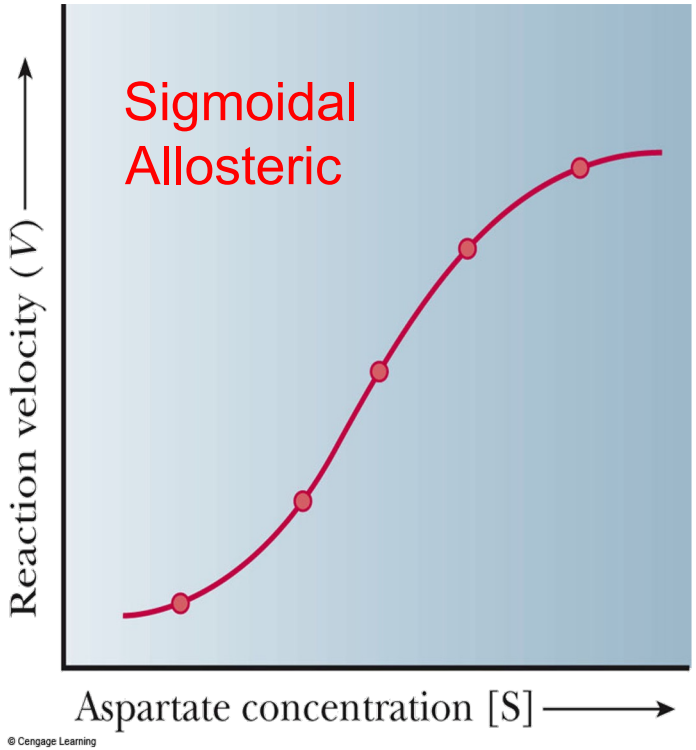
chymotrypsin



Hydrolysis of p-nitrophenyl acetate by chymotrypsin

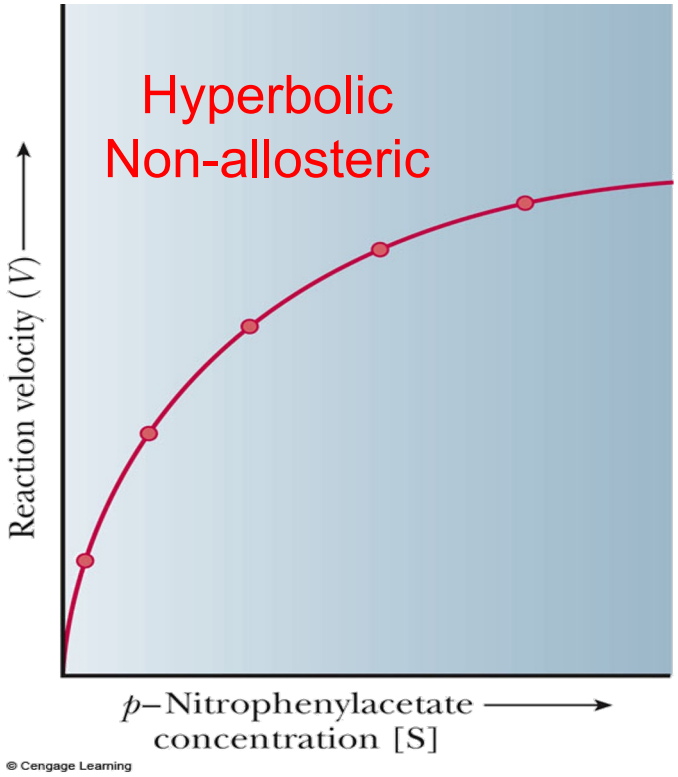
Non-Allosteric Vs Allosteric Enzymes

Aspartate transcabamoylase (ATCase)



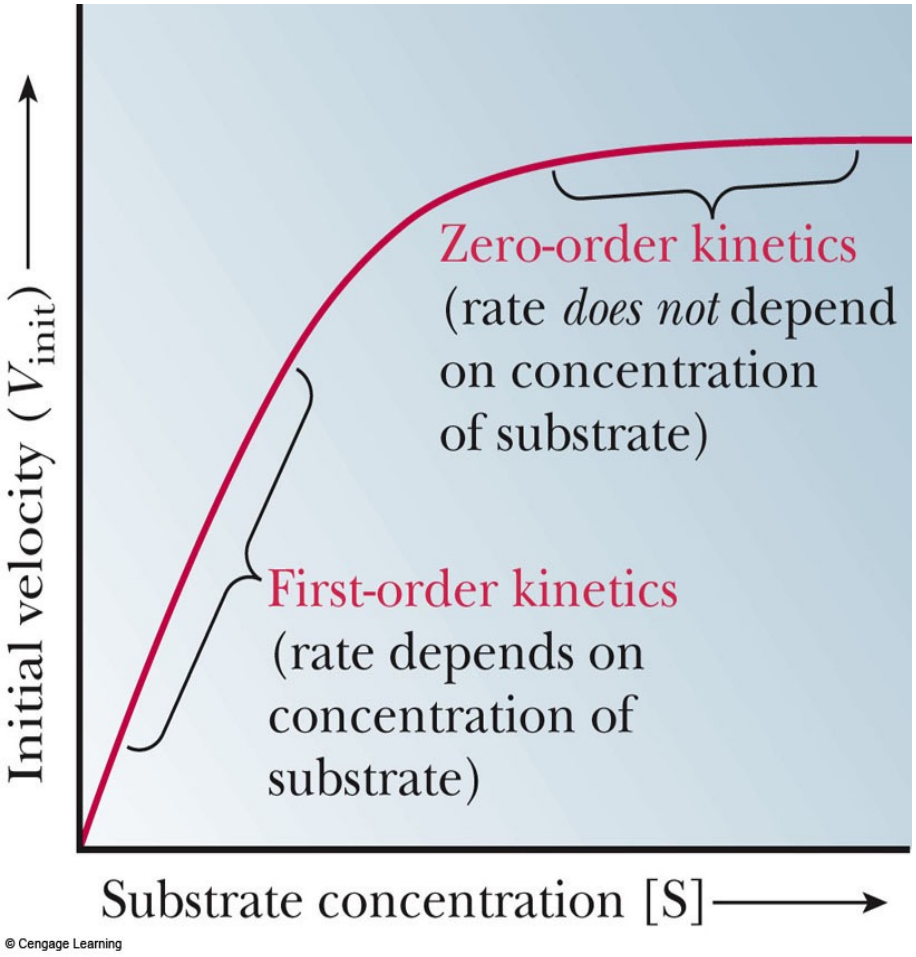
Carbamoyl phosphate + aspartate → carbamoyl aspartate + HPO_4^{-2}

chymotrypsin



Hydrolysis of p-nitrophenyl acetate by chymotrypsin

Michaelis-Menten Kinetics (Non-allosteric enzymes)



$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

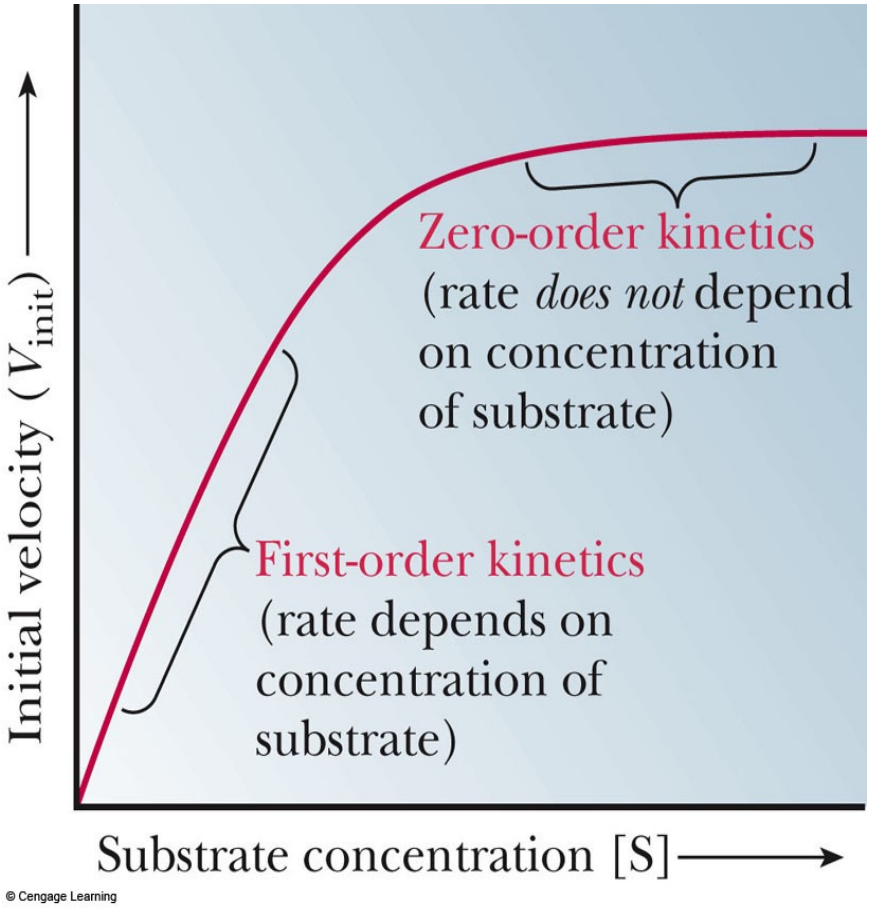
K_1 is the rate constant for ES formation from E+S
K_{-1} is the rate constant for dissociation of ES to E and S
K_2 is the rate constant for conversion of ES to P

Michaelis-Menten Kinetics (Non-allosteric enzymes)

- V_{init} or V_0 initial rate of reaction which depends on [s]
- *V_{max} = the maximum velocity at infinite [S] concentration*
- *Assumptions:*

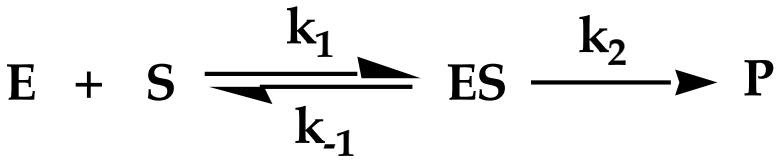
  P is not converted to S

  catalysts are regenerated



$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

Michaelis-Menten Model

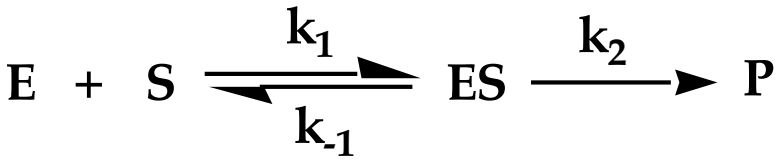


The rates of formation and breakdown of ES are given by these equations

$$\text{rate of formation of ES} = k_1[E][S]$$

$$\text{rate of breakdown of ES} = k_{-1}[ES] + k_2[ES]$$

Michaelis-Menten Model



The rates of formation and breakdown of ES are given by these equations

$$\text{rate of formation of ES} = k_1[E][S]$$

$$\text{rate of breakdown of ES} = k_{-1}[ES] + k_2[ES]$$

At steady state: the rate of ES formation = the rate its breakdown

$$k_1[E][S] = k_{-1}[ES] + k_2[ES]$$

Michaelis-Menten Model (Cont'd)

- When equilibrium is reached, the concentration of free enzyme is the total minus that bound in ES

$$[E] = [E]_T - [ES]$$

Michaelis-Menten Model (Cont'd)

- When equilibrium is reached, the concentration of free enzyme is the total minus that bound in ES

$$[E] = [E]_T - [ES]$$

- Substituting for the concentration of free enzyme [E]

$$k_1([E]T - [ES])\,[S] = k_{-1}\,[ES] + k_2\,[ES]$$

Michaelis-Menten Model (Cont'd)

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$$[E] = [E]_T - [ES]$$

- Substituting for the concentration of free enzyme [E]

$$k_1([E]T - [ES])\,[S] = k_{-1}\,[ES] + k_2\,[ES]$$

- collecting all rate constants in one term gives

$$\frac{([E]_T - [ES])\,[S]}{[ES]} = \frac{k_{-1} + k_2}{k_1} = K_M$$

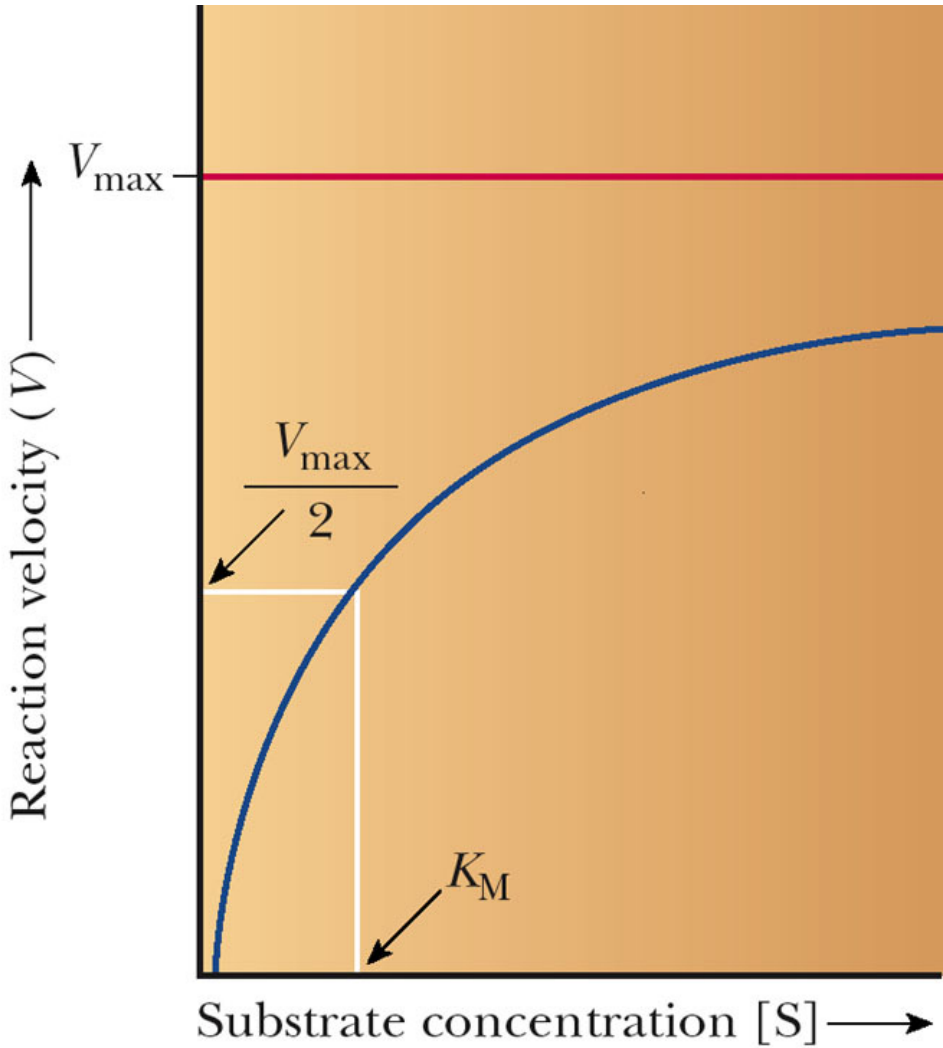
Michaelis-Menten Model (Cont'd)

K_M is called the Michaelis constant

Substrate concentration at which the reaction proceeds at one half is maximum velocity

Considered as an inverse measure of the affinity of the enzyme for the substrate

The lower the K_M , the higher the affinity



Michaelis-Menten Model (Cont'd)

- It is now possible to solve for the concentration of the enzyme-substrate complex, [ES]

$$\frac{([E]_T - [ES])\,[S]}{[ES]} = \frac{k_{-1} + k_2}{k_1} = K_M$$

$$\frac{[E]_T\,[S] - [ES][S]}{[ES]} = K_M$$

$$[E]_T\,[S] - [ES][S] = K_M[ES]$$

Michaelis-Menten Model (Cont'd)

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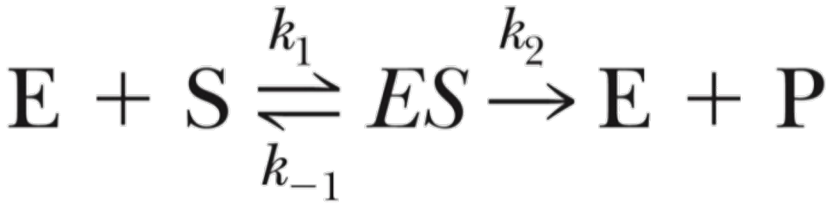
$$\frac{[E]_T\,[S] - [ES][S]}{[ES]} = K_M$$

$$[E]_T\,[S] - [ES][S] = K_M[ES]$$

Rearrange $[E]_T\,[S] = K_M\,[ES] + [ES][S]$

$$[E]_T\,[S] = [ES](K_M + [S])$$

$$[ES] = \frac{[E]_T\,[S]}{K_M + [S]}$$



- In the initial stages (**little P is present**) thus the initial rate of reaction (**V_o**) depends on the rate of **ES** breakdown into **P + E**

$$\mathbf{V = k_2 [ES]}$$

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

- In the initial stages (**little P is present**) thus the initial rate of reaction (**V_o**) depends on the rate of **ES** breakdown into **P + E**

$$\mathbf{V = k_2\,[ES]} \longleftarrow \boxed{[\mathrm{ES}] = \frac{[\mathrm{E}]_\mathrm{T}\,[\mathrm{S}]}{\mathrm{K_M} + [\mathrm{S}]}}$$

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

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$$\mathbf{V = k_2\,[ES]} \longleftarrow \boxed{[\mathrm{ES}] = \frac{[\mathrm{E}]_T\,[\mathrm{S}]}{K_M + [\mathrm{S}]}}$$

$$\mathbf{V = \frac{k_2[E]_T\,[S]}{K_M + [S]}}$$

- If substrate concentration is so high that is the E is completely saturated with substrate **Then $[ES] = [E]_T$ ---- the reaction proceeds to its maximum speed (V_{max})**

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

- substituting $[E]_T$ for [ES]

$$\mathbf{V_{init} = V_{max} = k_2[E]_T}$$ *As in zero order reaction*

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- Substituting $k_2[E]_T = V_{max}$ into

$$V = \frac{k_2[E]_T\,[S]}{K_M + [S]}$$

$$V_{init} = \frac{V_{max}\,[S]}{K_M + [S]}$$ **Michaelis-Menten equation**

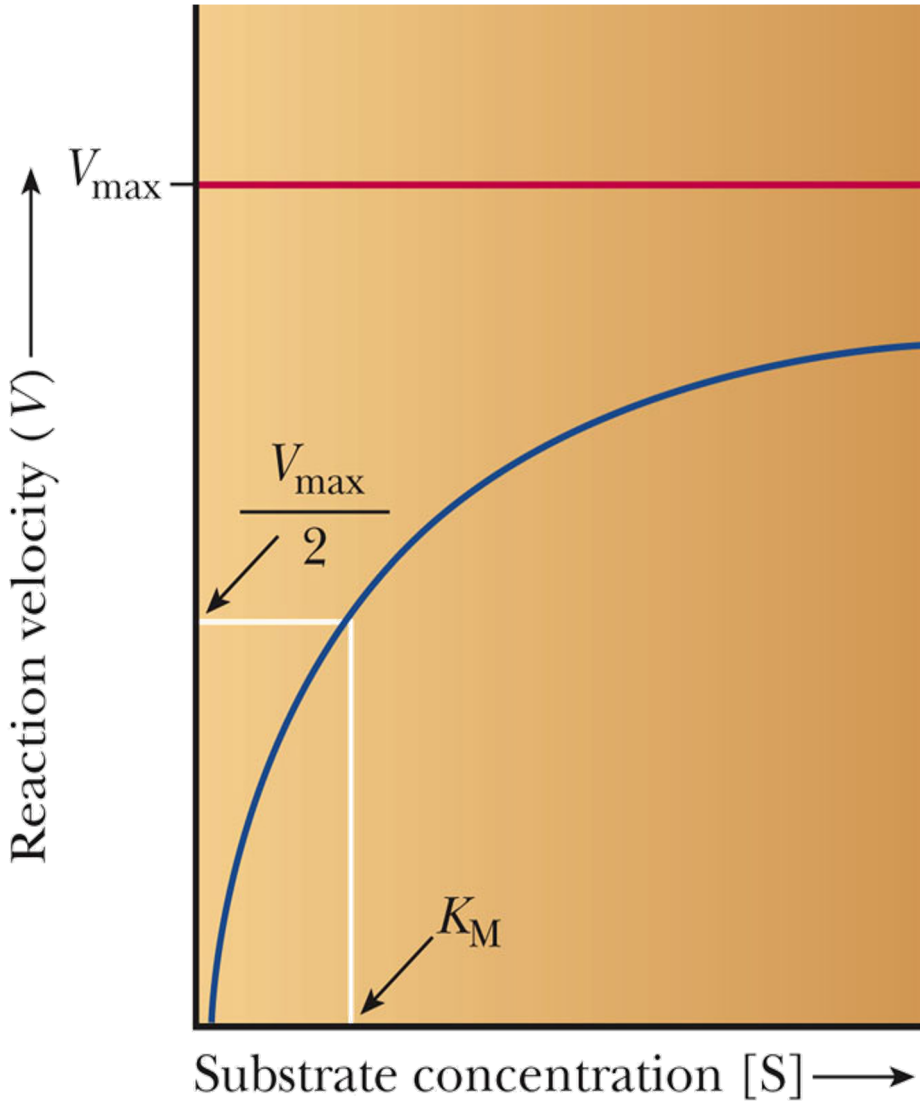
Michaelis-Menten Model (Cont'd)

- When experimental conditions are adjusted so that

$$[S] = K_M$$

$$V = \frac{V_{max}[S]}{K_M + [S]} = \frac{V_{max}[S]}{[S] + [S]} = \frac{V_{max}}{2}$$

- When the [S] = Km the rate of the reaction is half its maximum value

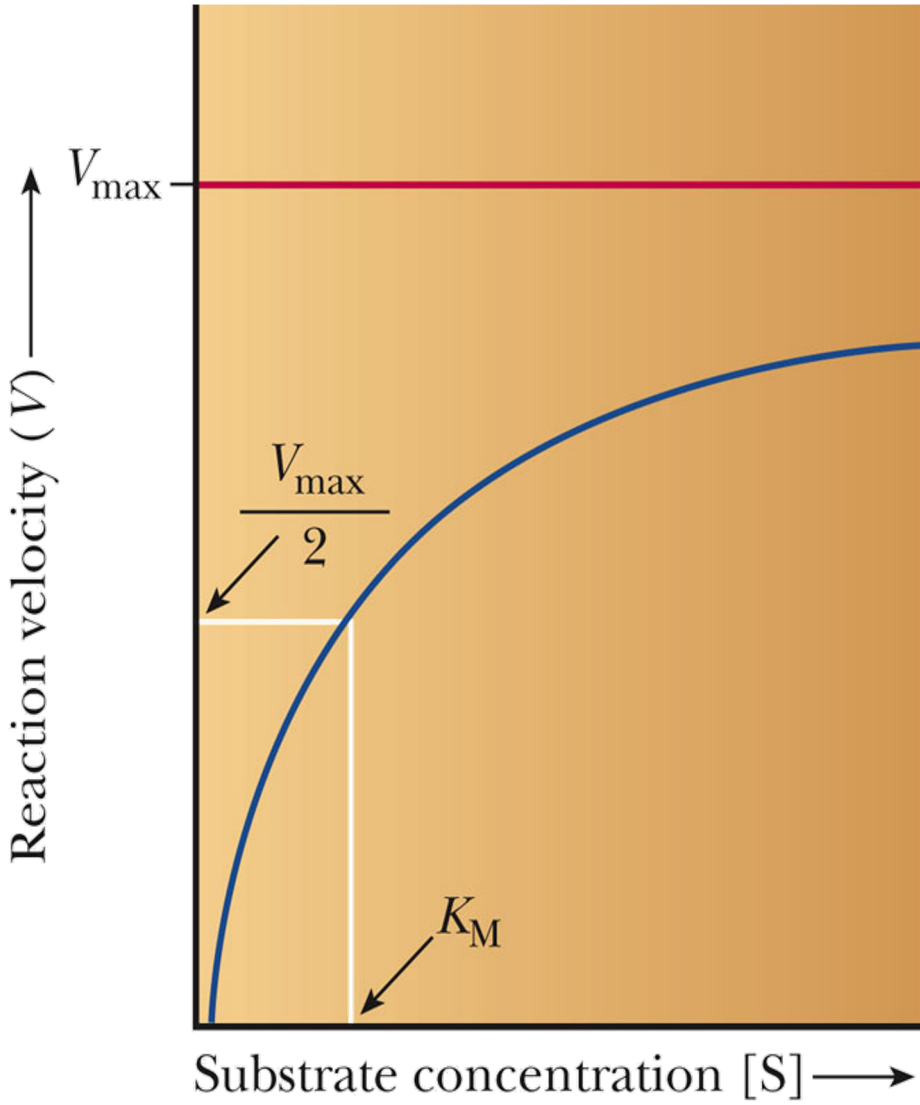


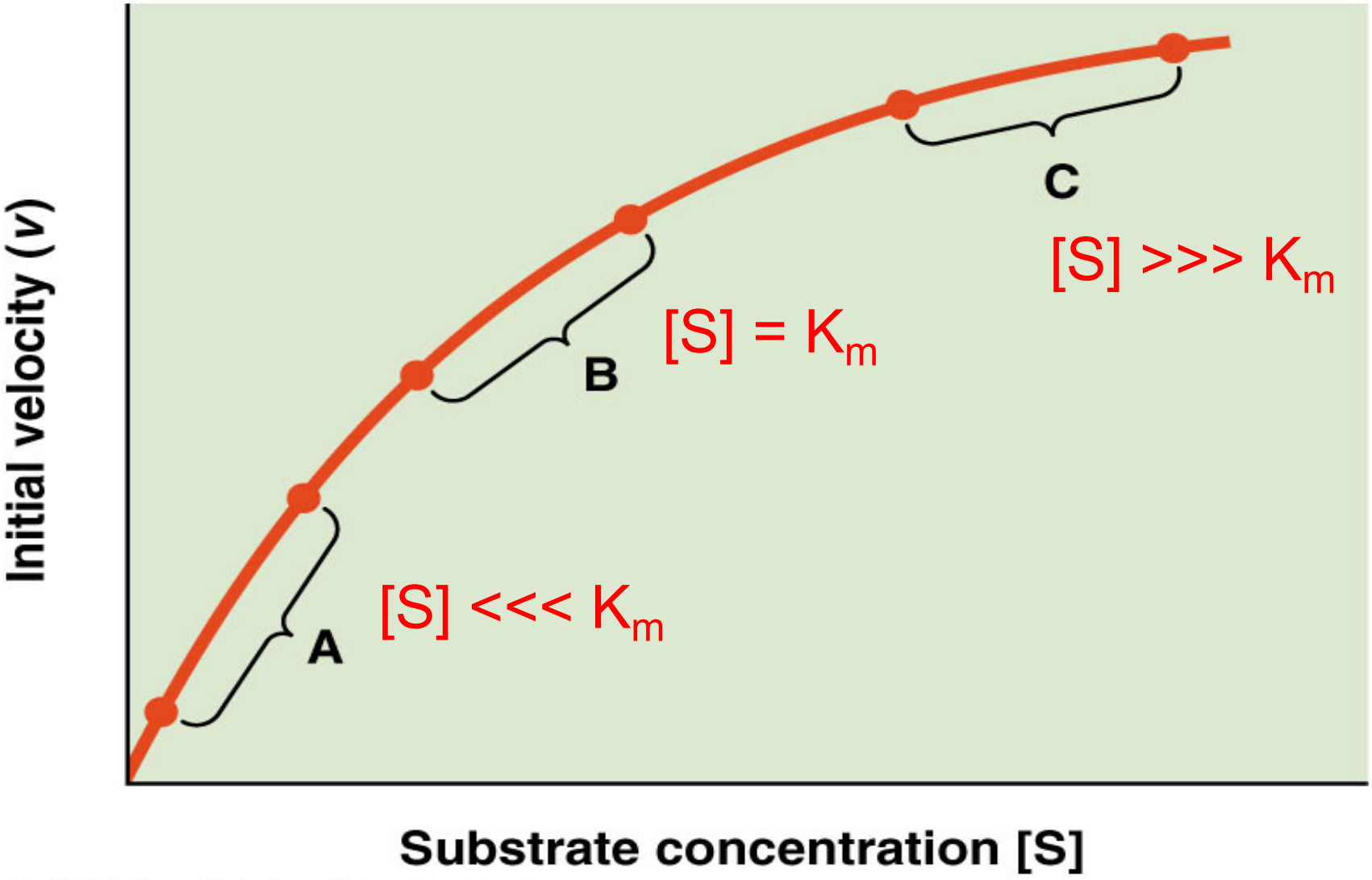
Michaelis-Menten Model (Cont'd)

$$V = \frac{V_{max}[S]}{K_M + [S]} = \frac{V_{max}[S]}{[S] + [S]} = \frac{V_{max}}{2}$$

- For enzyme with multiple substrates the same equation my be used but only one substrate can be studied at time.

- Km is appropriate only for enzymes exhibits a hyperpolic (non Allosteric) curve of velocity versus substrate concentration





Meaning of K_m and V_{max}

- **[S]<<K_m** (very low [S])
  - v = [S]; first order region, velocity increases linearly with [S]; v ~ proportional to [S]

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- **V_{max} is maximum velocity**, as [S] reaches infinity, v is the upper limit of the reaction = enzyme saturation
  - dependent on time required for catalytic event and release of product and the [E] present
  - ↓ K_M means lower [S] needed

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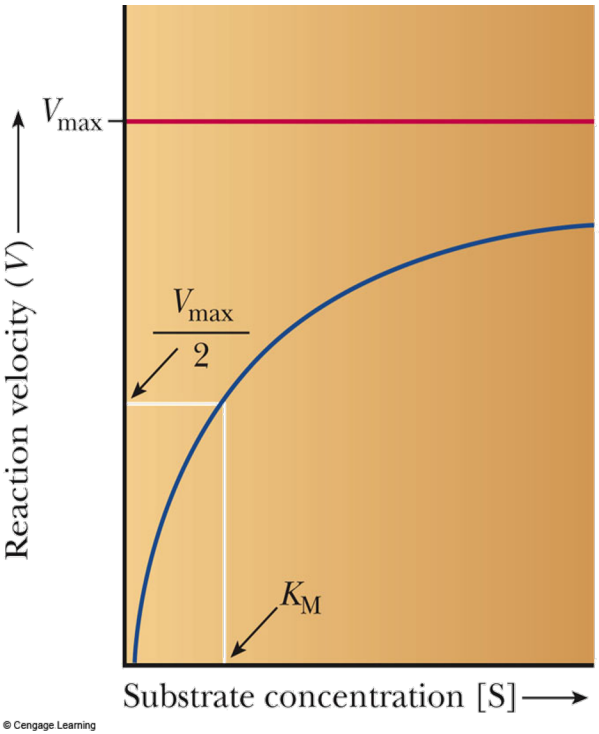
- **[S] = K_M**
  - Specific [S] at which the reaction occurs at ½ V_{max}
  - K_m is fixed for a given enzyme - Michaelis constant, how 'good' your enzyme behaves

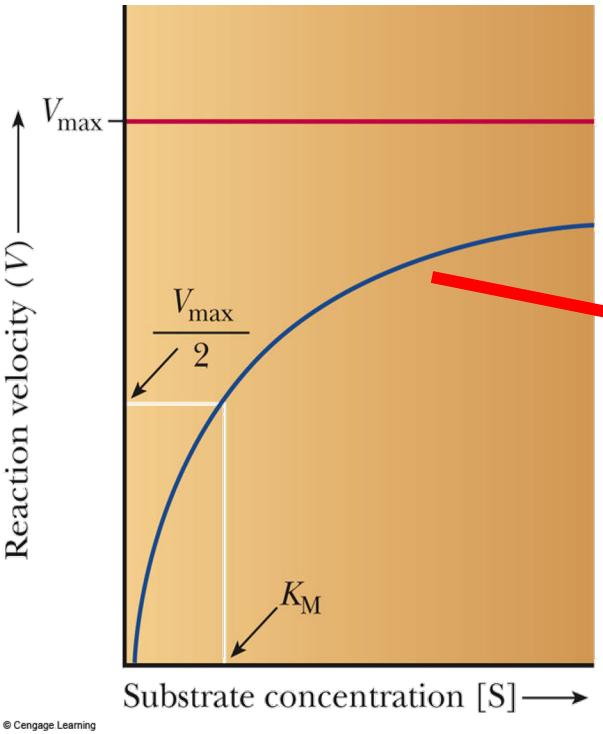
Linearizing The Michaelis-Menten Equation

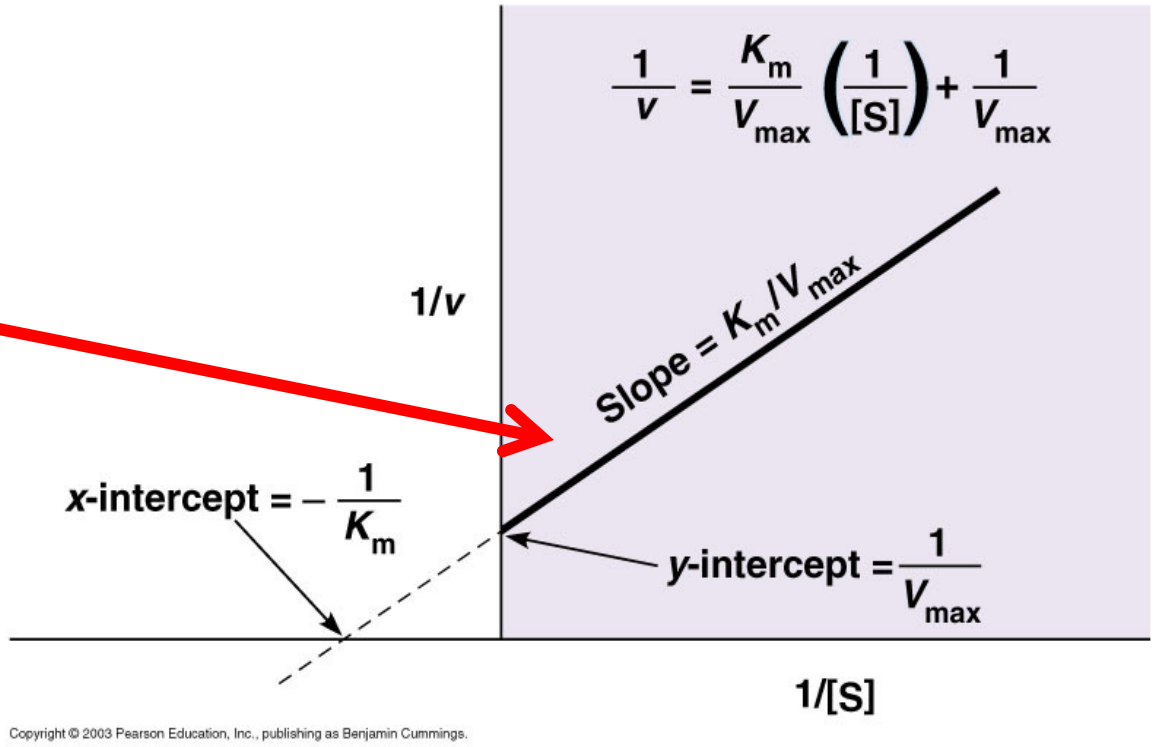


$$V = \frac{V_{max}[S]}{K_M + [S]}$$

(an equation for a hyperbola)

Linearizing The Michaelis-Menten Equation





$$V = \frac{V_{max}[S]}{K_M + [S]}$$

(an equation for a hyperbola)

$$\frac{1}{V} = \frac{K_M}{V_{max}[S]} + \frac{1}{V_{max}}$$

Linearizing The Michaelis-Menten Equation

- V_{max} is difficult to be estimated form hyperpolic curve
  - (need high quantity of a substrate –costly and solubility limits)

$$V = \frac{V_{max}[S]}{K_M + [S]}$$ **(an equation for a hyperbola)**

Linearizing The Michaelis-Menten Equation

- V_{max} is difficult to be estimated form hyperpolic curve
  - (need high quantity of a substrate –costly and solubility limits)

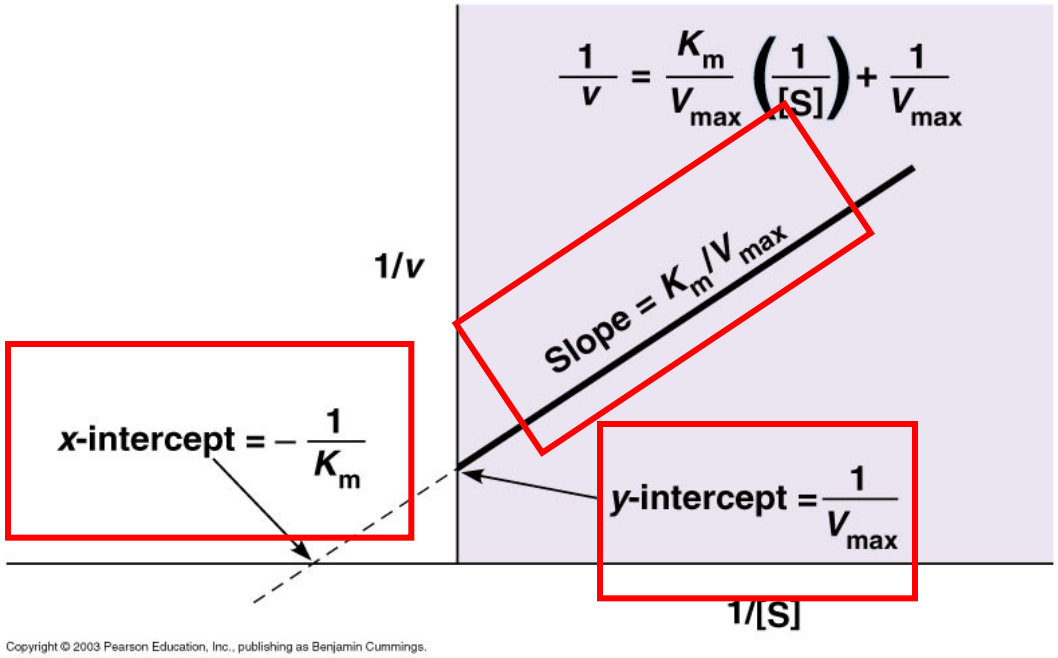
$$V = \frac{V_{max}[S]}{K_M + [S]} \quad \textbf{(an equation for a hyperbola)}$$

- Can be transformed into the equation for a straight line by taking reciprocals of both sides

$$\frac{1}{V} = \frac{K_M + [S]}{V_{max}[S]} = \frac{K_M}{V_{max}[S]} + \frac{[S]}{V_{max}[S]}$$

$$\frac{1}{V} = \frac{K_M}{V_{max}[S]} + \frac{1}{V_{max}}$$

Lineweaver-Burk Reciprocal Plot



- The linear plot has the form : y = mx + b, and is the formula for a straight line

$$\frac{1}{V} = \frac{K_M}{V_{max}} \cdot \frac{1}{[S]} + \frac{1}{V_{max}}$$

$$y = m \cdot x + b$$

- a plot of 1/V versus 1/[S] will give a straight line with slope of K_m/V_{max} and y intercept of $1/_{Vmax}$

K_M is the concentration of substrate at which 50% of the enzyme active site is occupied by substrate

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} P$$

$$\frac{k_{-1} + k_2}{k_1} = K_M$$

If E + S → ES take place more frequently that ES → P then the rate dissociation constant k_{-1} is greater that the rate constant for product formation K_2 (K_{-1} >>> K_2)

then K_M is approximately = K_{-1}/K_1

K_M is the concentration of substrate at which 50% of the enzyme active site is occupied by substrate

The equilibrium constant for ES dissociation

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES$$

$$K_{eq} = \frac{[E]\,[S]}{[ES]} = \frac{k_{-1}}{k_1}$$

$k_{-1}/k_1 = K_{eq}$ = dissociation constant of ES and it measure the affinity of enzyme to substrate

The greater the value of K_M, the less tightly S is bound to E

Turnover number

- V_{max} is related to the turnover number of the enzyme which is equal to K_2

- At high [S], the enzyme is saturated, so $[E]_T = ES$

$$\mathbf{V_{max} = k_2[E]_T}$$

Turnover number

- V_{max} is related to the turnover number of the enzyme which is equal to K_2
- At high [S], the enzyme is saturated, so $[E]_T = ES$

$$\mathbf{V_{max} = k_2[E]_T}$$

- So,

$$\mathbf{V / [E]_T = \text{turnover number} = k_{cat}}$$

Turnover number

- Turnover number of enzyme : K_{cat} or K_p catalytic constant. Which describe the breakdown of ES to P and E
- V_{max} is related to the efficacy of enzyme
- Is the number of moles of substrate converted to product per mole of enzyme per unit time (second).
    - Assuming full saturation of E and rate of reaction to P is maximum

Turnover number

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    - Assuming full saturation of E and rate of rxn to P is maximum

Table 6.2

Turnover Numbers and K_M for Some Typical Enzymes

Enzyme	Function	k_{cat} = Turnover Number*	K_M**
Catalase	Conversion of H_2O_2 to H_2O and O_2	4×10^7	25
Carbonic Anhydrase	Hydration of CO_2	1×10^6	12
Acetylcholinesterase	Regenerates acetylcholine, an important substance in transmission of nerve impulses, from acetate and choline	1.4×10^4	9.5×10^{-2}
Chymotrypsin	Proteolytic enzyme	1.9×10^2	6.6×10^{-1}
Lysozyme	Degrades bacterial cell-wall polysaccharides	0.5	6×10^{-3}

- Means: Transform 40 million moles of substrate to product every second

Enzyme Inhibition

- **Enzyme inhibitor**: a substance that interferes with enzyme action and slow down the rate of a reaction

- Reversible inhibitor: binds to the enzyme and subsequently be released leaving enzyme in its original condition

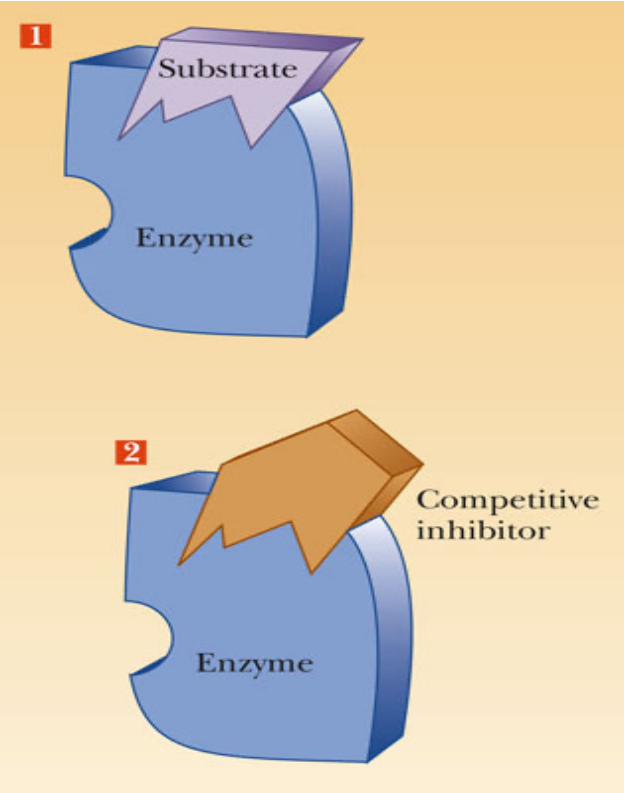
- Irreversible inhibitor: reacts with enzyme to produce protein that is enzymatically not active and from which the original enzyme cannot be regenerated
  - usually involves formation or breaking of covalent bonds to or on the enzyme

Reversible inhibitor

Two major classes distinguished based on the site on the enzyme to which they bind:

1. **<u>Competitive inhibition</u>:**

- Inhibitor competes with substrate on active site
- Very similar structure to the substrate
- Inhibitor can bind to the active site and block the substrate access to it
- Can be overcome by increasing [S]

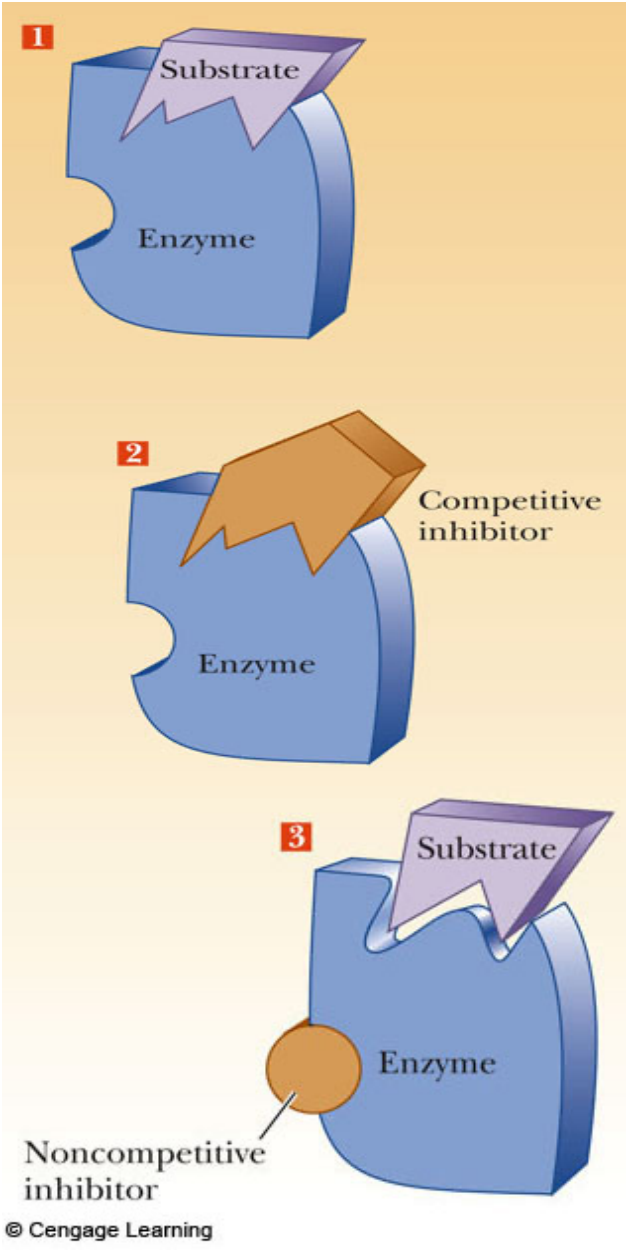


Reversible inhibitor

Two major classes distinguished based on the site on the enzyme to which they bind:

2. Noncompetitive

- Bind to the enzyme at a site other than active site
- Cause change in the structure of the enzyme especially the (active site)
- Substrate can bind to enzyme but can not catalyze reaction



Competitive Inhibition

- Substrate competes with inhibitor for the active site; more substrate is required to reach a given reaction velocity

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- The dissociation constant (K_I) for enzyme inhibitor complex (EI)

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- The dissociation constant (K_I) for enzyme inhibitor complex (EI)

- The value of Km increased by $1 + [I]/K_I$

Competitive Inhibition

No inhibition

$$\frac{1}{V} = \frac{K_M}{V_{max}} \cdot \frac{1}{S} + \frac{1}{V_{max}}$$

$$y = m \cdot x + b$$

Competitive Inhibition

No inhibition

$$\frac{1}{V} = \frac{K_M}{V_{max}} \cdot \frac{1}{S} + \frac{1}{V_{max}}$$

$$y = m \cdot x + b$$

In the presence of a competitive inhibitor

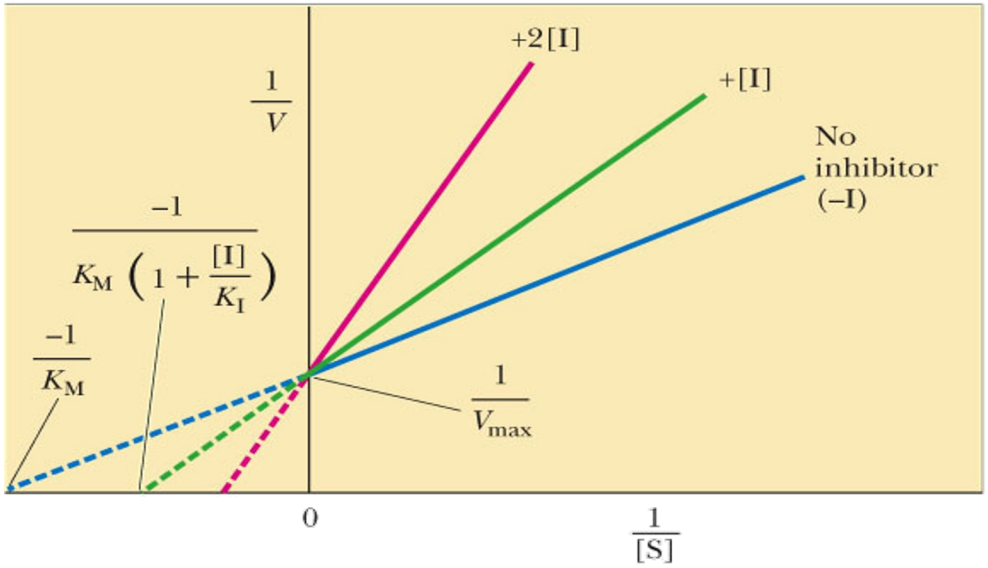
$$\frac{1}{V} = \underbrace{\frac{K_M}{V_{max}}\left(1 + \frac{[I]}{K_I}\right)}_{m} \frac{1}{S} + \frac{1}{V_{max}}$$

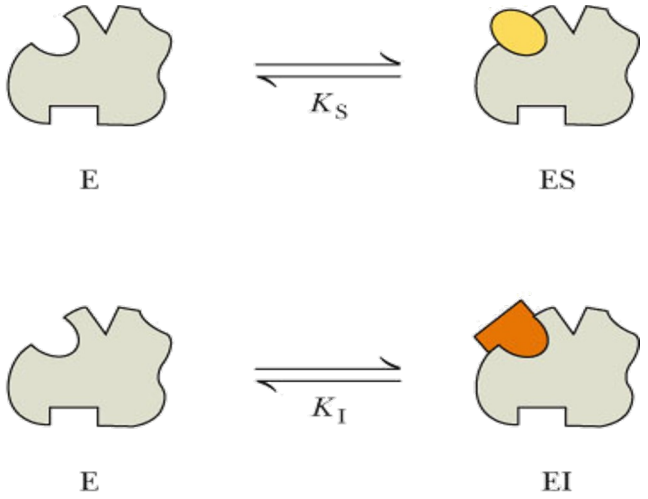
$$y = m \cdot x + b$$

In a Lineweaver-Burk plot of 1/V vs 1/[S], the slop (and the x intercept) changes but the V_{max} does not change

A Lineweaver-Burke Plot, Competitive Inhibition

- slope plot is changed
- x intercept is changed
- K_M ➔ increases
- y intercept is unchanged
- V_{MAX} is unchanged
- Competitive inhibitor can over come by a sufficiently high substrate conc.

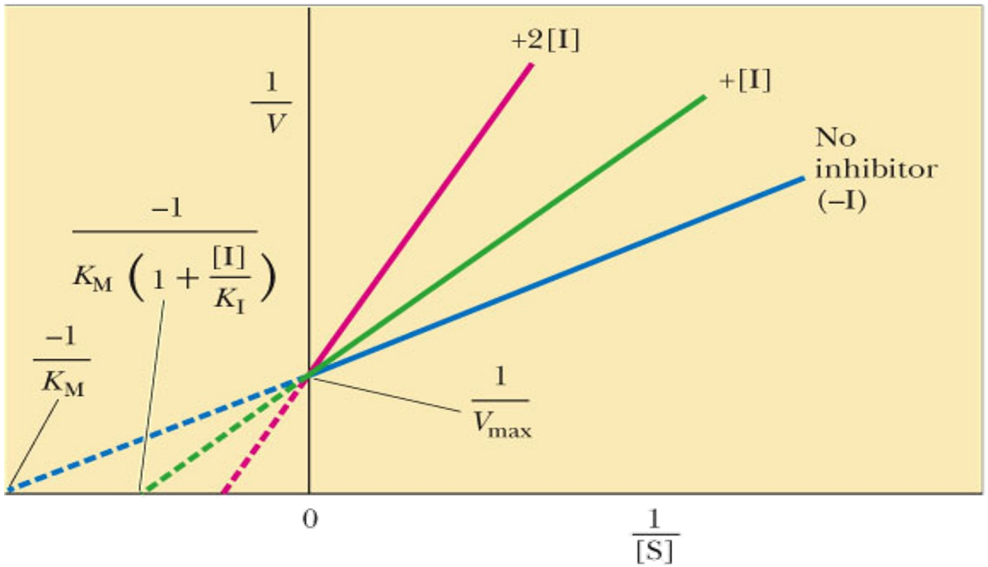


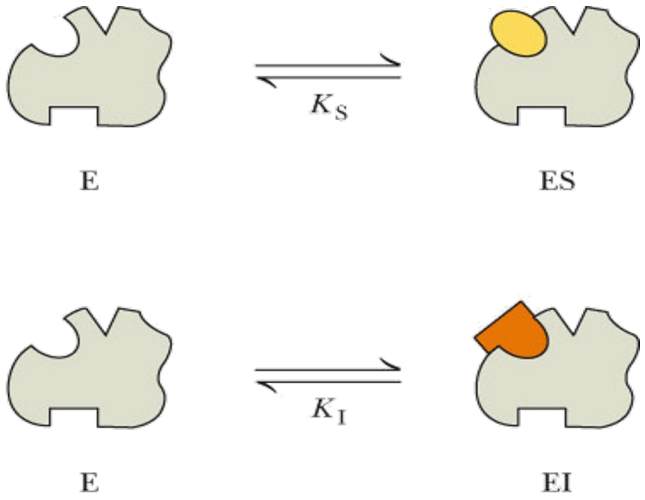


$$EI \rightleftharpoons I + E + S \rightleftharpoons ES \longrightarrow P$$

$$\frac{k_{-1} + k_2}{k_1} = K_M$$

A Lineweaver-Burke Plot, Competitive Inhibition





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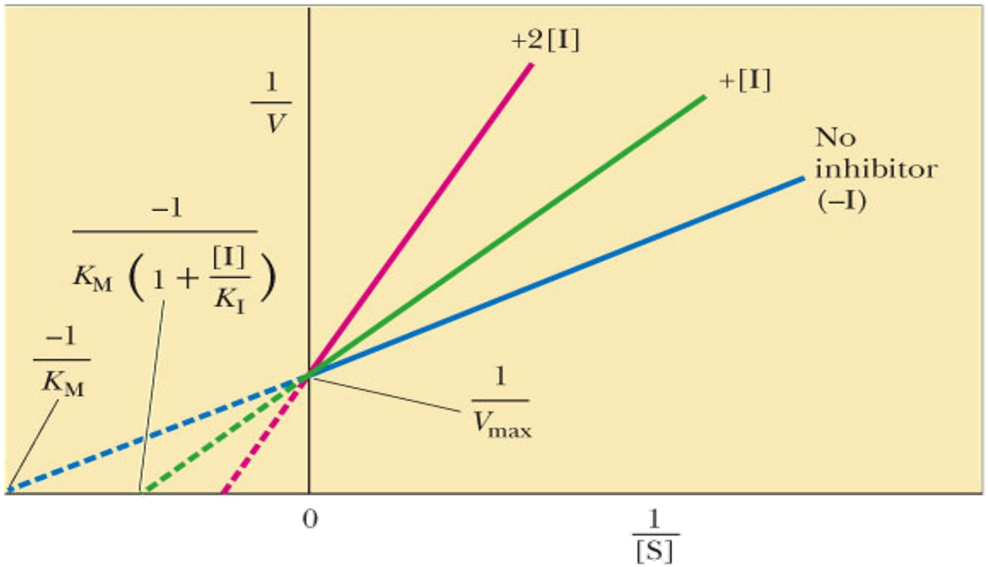
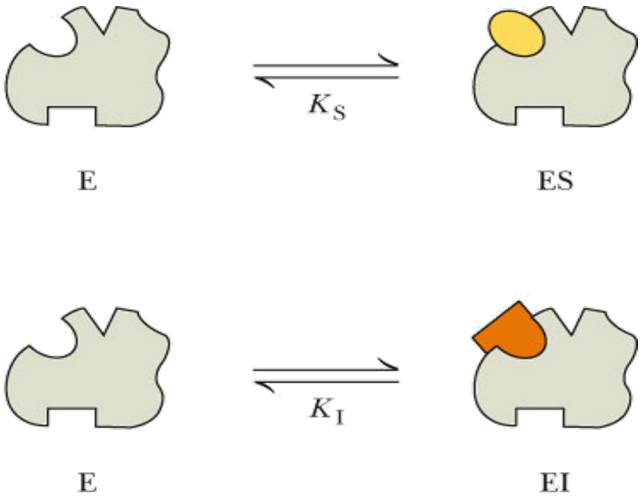
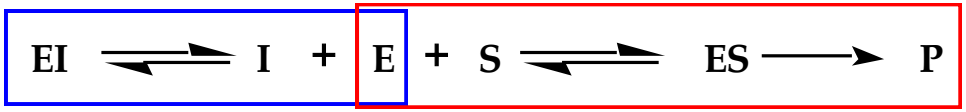


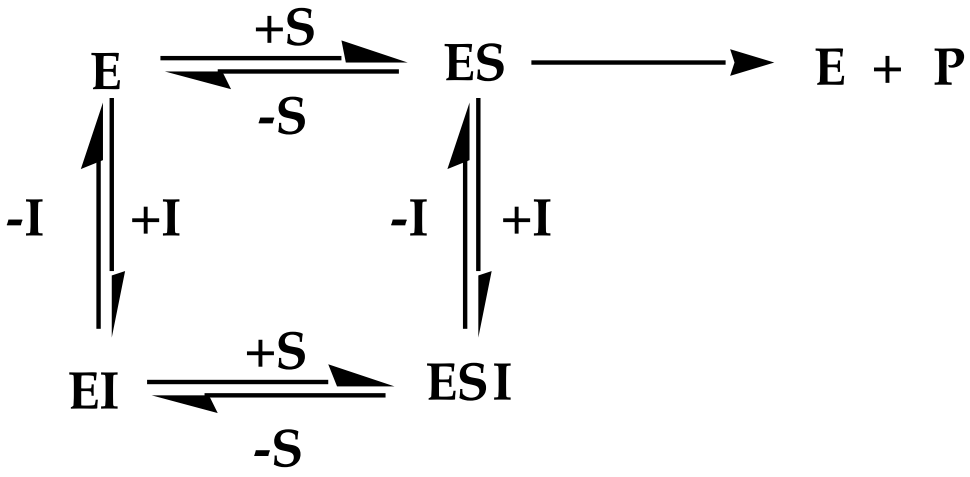




- slope plot is changed
- x intercept is changed
- KM ➔ increases
- y intercept is unchanged
- V_{MAX} is unchanged
- Competitive inhibitor can over come by a sufficiently high substrate conc.

Noncompetitive Inhibition

- Several equilibria are involved



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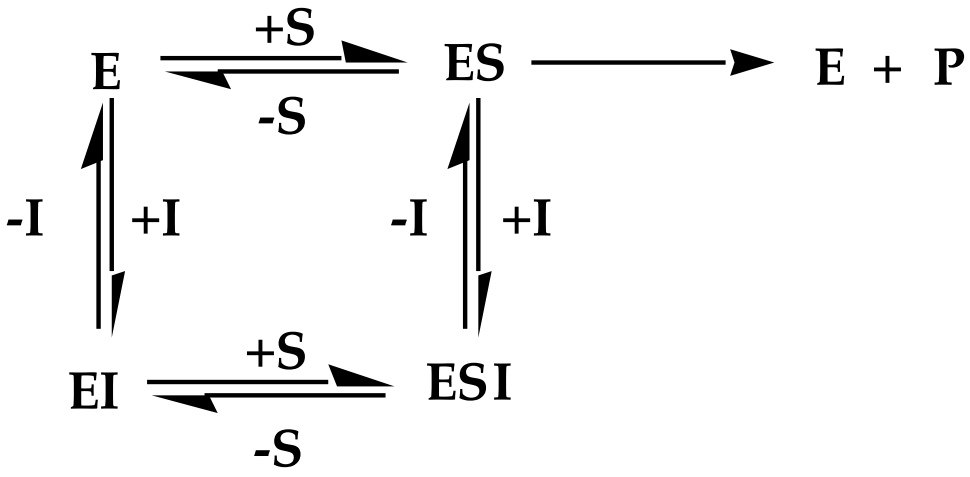

- The maximum velocity V_{max} has the form

$$V^{I}_{max} = \frac{V_{max}}{1 + [I]/K_I}$$

Lineweaver-Burke Plot, Noncompetitive Inhibition

- Because the inhibitor does not interfere with substrate binding to the active site, K_M is unchanged
- Increasing substrate concentration does not overcome noncompetitive inhibition

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No inhibition

$$\frac{1}{V} = \frac{K_M}{V_{max}} \cdot \frac{1}{S} + \frac{1}{V_{max}}$$

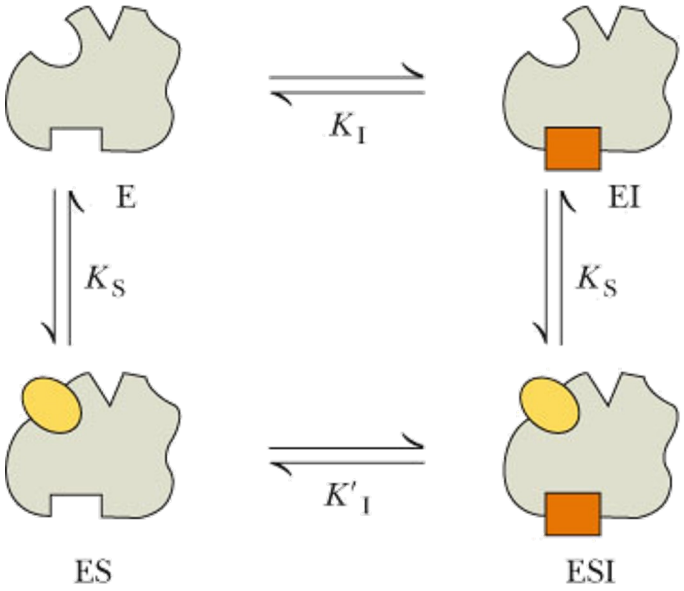
$$y = m \cdot x + b$$

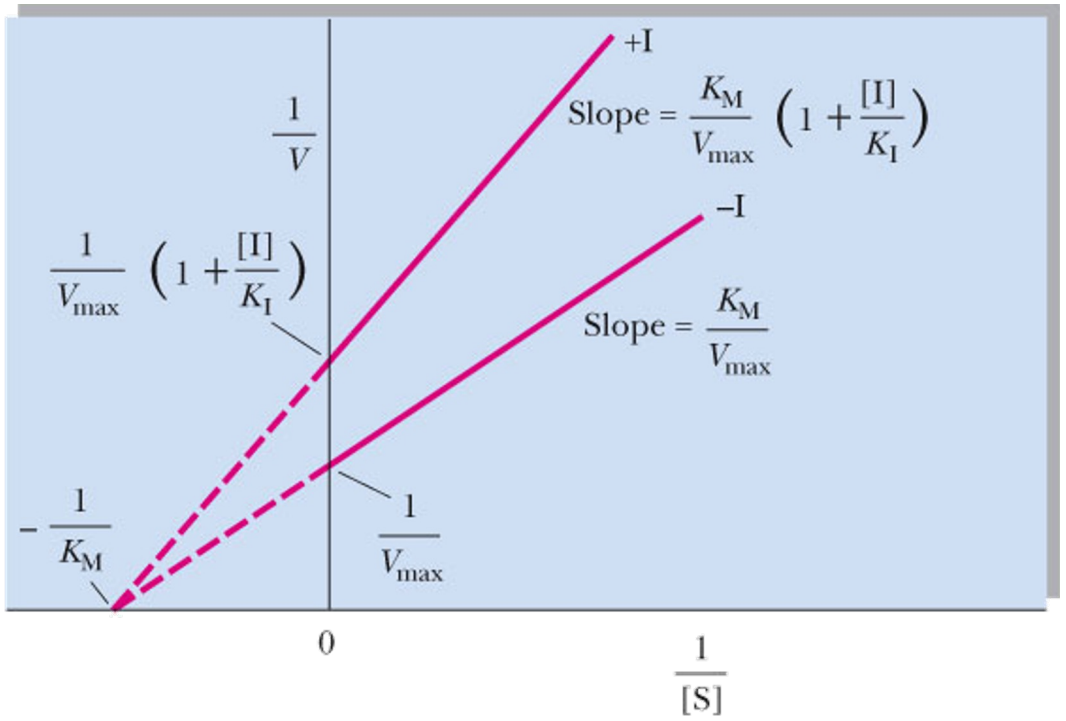
In the presence of a noncompetitive inhibitor

$$\frac{1}{V} = \underbrace{\frac{K_M}{V_{max}}\left(1 + \frac{[I]}{K_I}\right)}_{m} \frac{1}{S} + \underbrace{\frac{1}{V_{max}}\left(1 + \frac{[I]}{K_I}\right)}_{b}$$

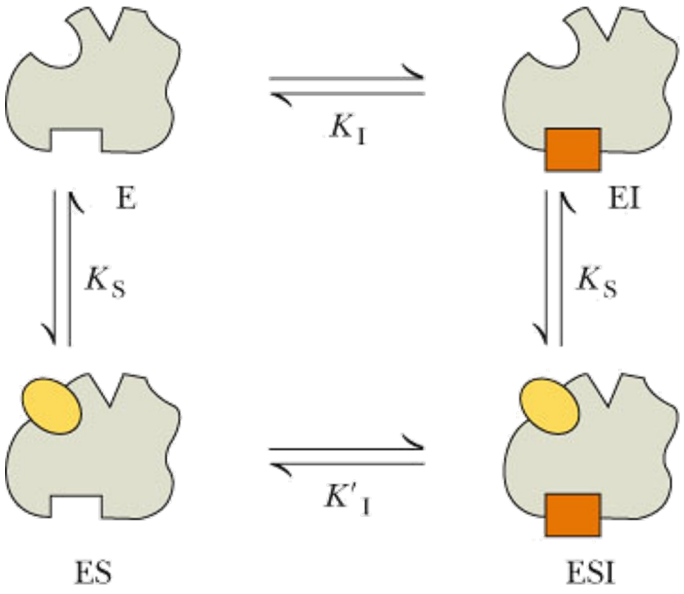
$$y = m \cdot x + b$$

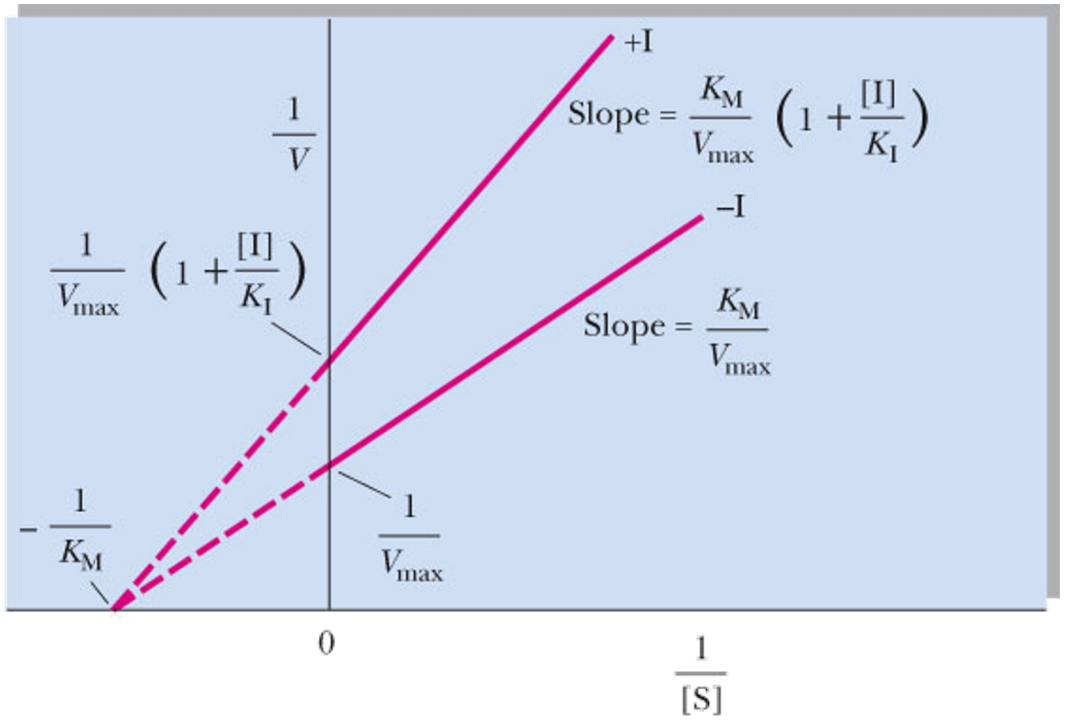
Lineweaver-Burke Plot, Noncompetitive Inhibition





Lineweaver-Burke Plot, Noncompetitive Inhibition





- Both slop and y intercept changed
- X intercept no change
- V_{max} decreases
- K_m remain the same

Other Types of Inhibition

- **Uncompetitive inhibition** - inhibitor can bind to the ES complex but not to free enzyme
  - V_{max} decreases and K_M decreases.

- **Mixed inhibition** - Similar to noncompetitive, but binding of I affects binding of S and vice versa.
  - K_M increases and V_{max} decreases