

Enzymes

Objectives

- ❑ After studying this chapter, you should be able to:
- ❑ Define enzymes
- ❑ Explain their way of classification
- ❑ Describe their properties
- ❑ Study mechanisms of action
- ❑ Differentiate factors that affect enzyme activity
- ❑ Explain how enzyme activity is inhibited
- ❑ Describe mechanisms for regulation of enzymes

- ❖ Enzymology: is the study of enzymes their properties, function, regulation and kinetics.
- ❖ Catalyst : a substance that increases the rate of a reaction without itself being consumed (changing)
- ❖ Virtually all reactions in the body are mediated by enzymes.
- ❖ are protein catalysts that **increase the rate of reactions without being changed** in the overall process.
- ❖ Among the many biologic reactions that are **energetically possible**, enzymes **selectively channel reactants** (substrates) into useful pathways.
- ❖ Enzymes thus **direct all metabolic** events.

Nomenclature

- ❖ Each enzyme is assigned two names.
- ✓ The first is **its short, recommended name**, convenient for everyday use.
- ✓ The second is **the more complete systematic name**, which is used when **an enzyme must be identified without ambiguity**.

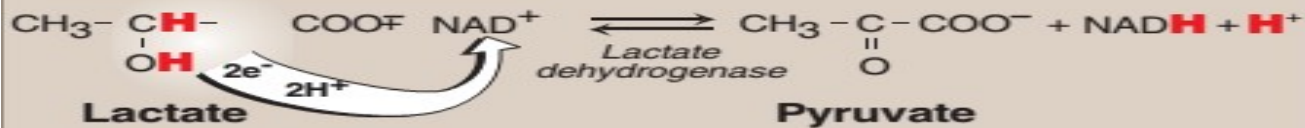
A. Recommended Name

- ✓ Most commonly used enzyme names have **the suffix “-ase”** attached to **the substrate of the reaction** (**glucosidase and urease**)
- ✓ to a description of **the action performed** (lactate dehydrogenase and adenylyl cyclase).
- ✓ Note: Some give no hint of the associated enzymic reaction, for example, **trypsin and pepsin**.

- In the systematic naming system, **enzymes are divided into six major classes**, each with numerous subgroups.
- For a given enzyme, **the suffix -ase** is attached to a fairly complete description of the chemical reaction catalyzed, including the **names of all the substrates**; for example, **lactate: NAD⁺ oxidoreductase**.
- ✓ Note: Each enzyme is also assigned a classification number.
- The systematic names are **unambiguous and informative**, but are frequently too cumbersome to be of general use.

1. Oxidoreductases

Catalyze oxidation-reduction reactions, such as:



2. Transferases

Catalyze transfer of C-, N-, or P-containing groups, such as:



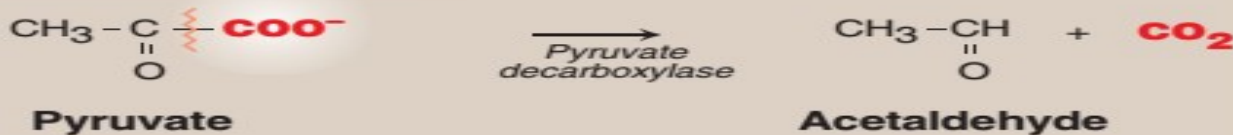
3. Hydrolases

Catalyze cleavage of bonds by addition of water, such as:



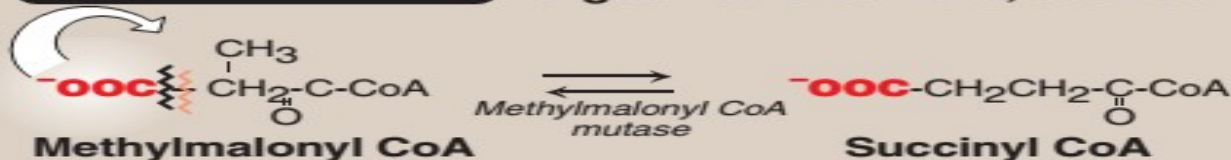
4. Lyases

Catalyze cleavage of C-C, C-S and certain C-N bonds, such as:



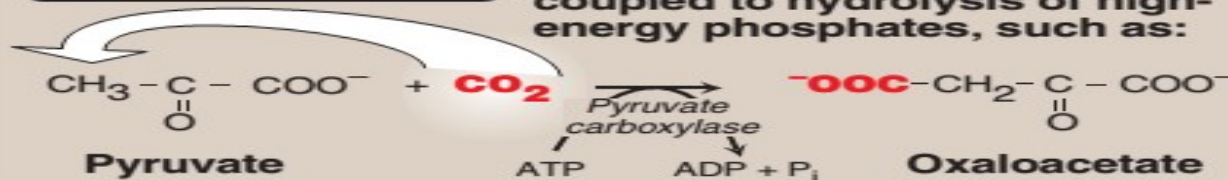
5. Isomerases

Catalyze racemization of optical or geometric isomers, such as:



6. Ligases

Catalyze formation of bonds between carbon and O, S, N coupled to hydrolysis of high-energy phosphates, such as:

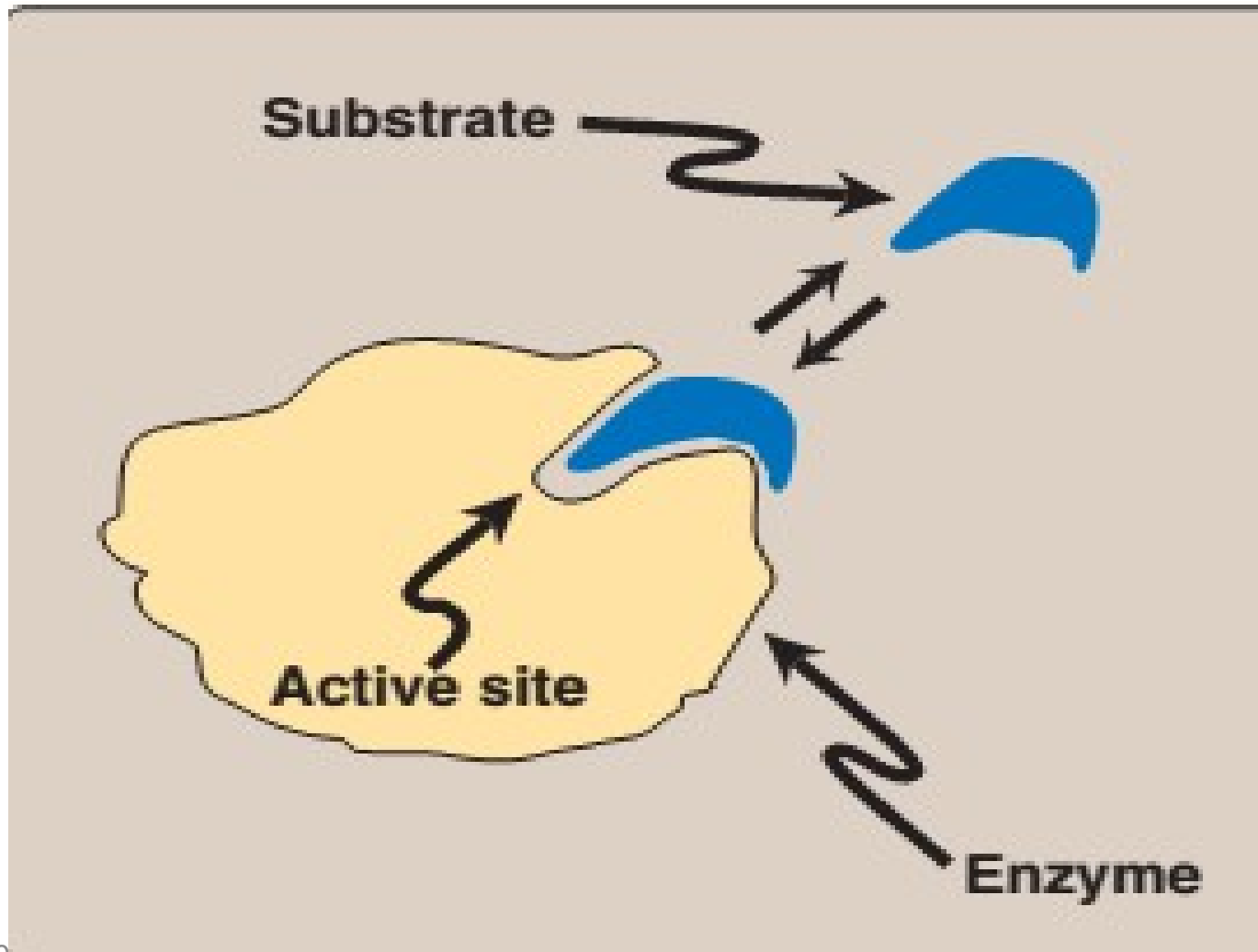


Properties of Enzymes

- ❖ **Enzymes** are protein catalysts that **increase the velocity of a chemical reaction**, and **are not consumed during the reaction**.
- ❖ Note: Some RNAs can act like enzymes, usually catalyzing the **cleavage and synthesis of phosphodiester bonds**.
- ❖ **RNAs with catalytic activity** are called **ribozymes**, and are much less commonly encountered than protein catalysts.

- Enzyme molecules contain a **special pocket** or **cleft** called the **active site**.
- The active site contains **amino acid side chains** that participate in **substrate binding** and **catalysis**.
- The substrate binds the enzyme, forming an **enzyme-substrate (ES) complex**.
- Binding is thought to **cause a conformational change** in the enzyme (**induced fit**) that **allows catalysis**.
- ES is converted to an **enzyme-product (EP) complex** that subsequently **dissociates** to **enzyme** and **product**.

An enzyme with one active site binding a substrate molecule



- ❖ Enzyme-catalyzed reactions are **highly efficient**, proceeding from **10^3 - 10^8 times** faster than **uncatalyzed reactions**.
- ❖ The number of molecules of **substrate converted to product** per **enzyme molecule** per second is called **the turnover number** or **k_{cat}** and typically is **10^2 - 10^4 s⁻¹**.

C. Specificity

- ❖ Enzymes are **highly specific**, interacting with **one or a few substrates** and catalyzing **only one type of chemical reaction**.

- Some enzymes **require molecules** other than **proteins** for enzymatic activity.
- The term holoenzyme refers to **the active enzyme with its nonprotein component**, whereas the enzyme **without its nonprotein moiety** is termed an **apoenzyme (inactive)**.
- If the **nonprotein moiety** is a **metal ion** such as **Zn²⁺** or **Fe²⁺**, it is called a **cofactor**.
- If it is **a small organic molecule**, it is termed a **coenzyme**.
- ✓ Coenzymes that **only transiently associate** with

Cont...

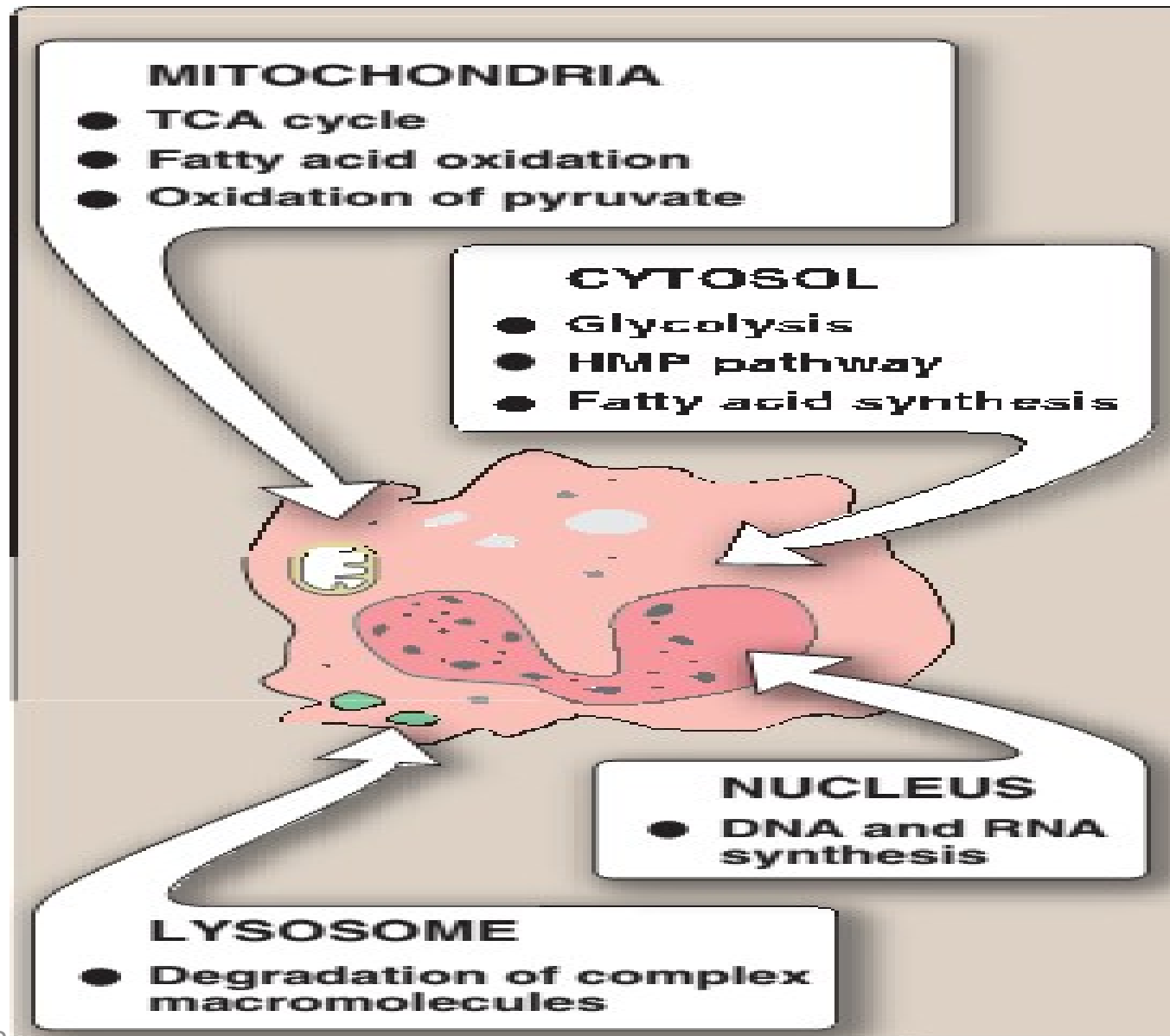
- **Cosubstrates** **dissociate** from the enzyme in an altered state (**NAD⁺** is an example).
- If the coenzyme is **permanently associated with the enzyme** and **returned to its original form**, it is called a **prosthetic group** (**FAD** is an example).
- Coenzymes frequently are **derived from vitamins**. For example, **NAD⁺** contains **niacin** and **FAD** contains **riboflavin**.

- ❖ Enzyme activity can be regulated (**increased or decreased**) so that the **rate of product formation** responds to **cellular need**.

F. Location within the cell

- are localized in **specific organelles** within the cell.
- Such compartmentalization **serves to isolate the reaction substrate or product** from other competing reactions.
- This provides **a favorable environment** for the reaction, and **organizes the thousands of**

The intracellular location of important biochemical pathways



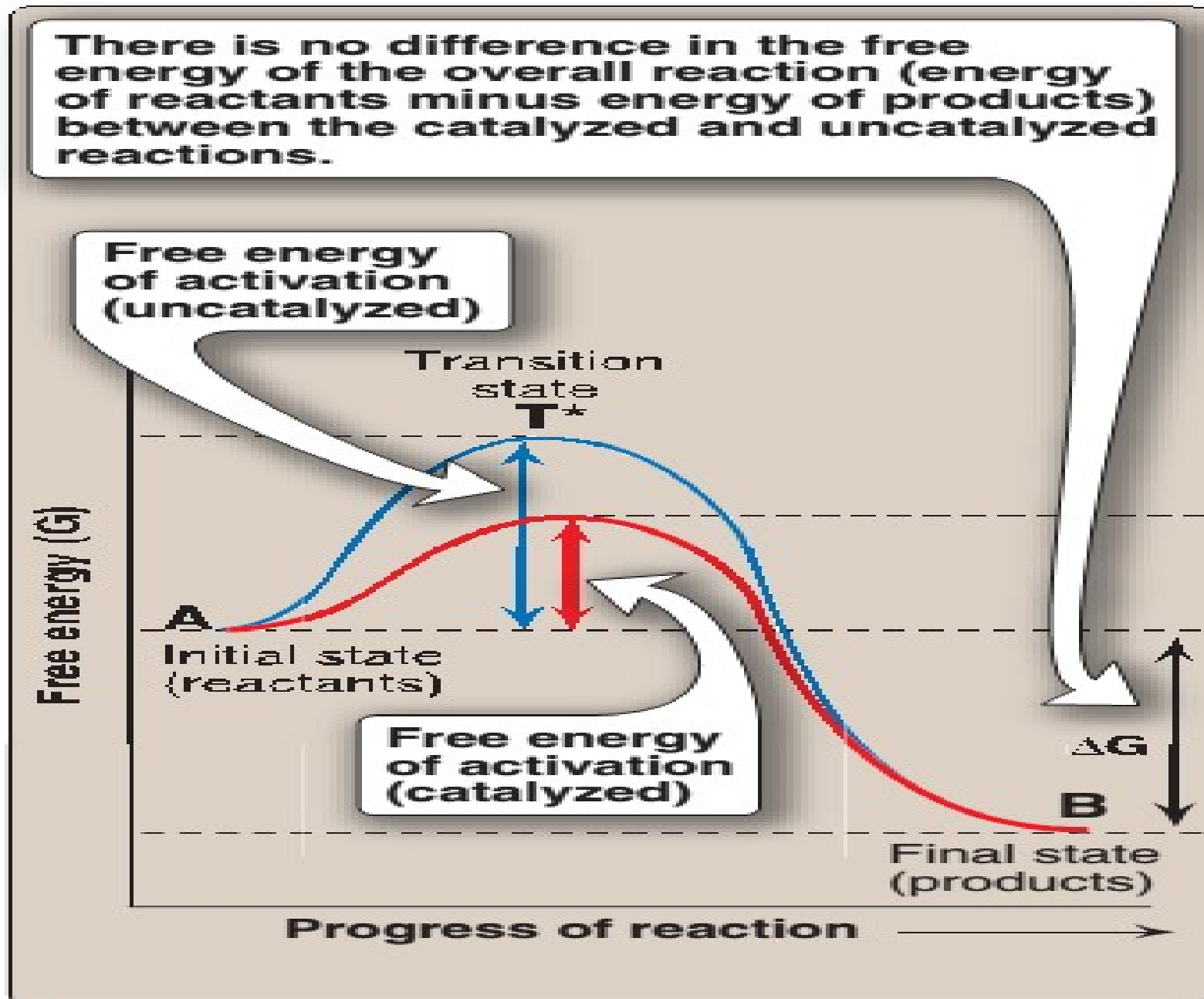
How Enzymes Work

❖ The mechanism of enzyme action can be viewed from **two different perspectives**.

1. Catalysis in terms of **energy changes** that **occur during the reaction**, that is, enzymes provide an **alternate, energetically favorable reaction pathway** different from the uncatalyzed reaction.
2. **How the active site chemically facilitates catalysis.**

- ❖ Virtually all chemical reactions have an **energy barrier** separating the **reactants** and **the products**. This barrier, called the **free energy of activation**.
- ❖ **Free energy of activation** is the energy difference between that of **the reactants** and **a high-energy intermediate** that occurs during the **formation of product**.
- ❖ For example, Figure shows the changes in energy during the conversion of a **molecule of reactant A** to **product B** as it proceeds through the **transition state (high-energy**
$$A \rightleftharpoons T^* \rightleftharpoons B$$

Effect of an enzyme on the activation energy of a reaction



1. Free Energy of Activation

- ✓ is the difference in free energy between the **reactant and T^*** ,
- ✓ Because of the **high free energy of activation**, the rates of **uncatalyzed chemical reactions** are **often slow**.

2. Rate of Reaction

- ✓ For molecules to react, they must **contain sufficient energy** to overcome the **energy barrier** of the transition state.
- ✓ In the **absence of an enzyme**, **only a small proportion of a population of molecules** may possess **enough energy to achieve the transition state**.
- ✓ **The rate of reaction is determined** by **the number of such energized molecules**.
- ✓ In general, **the lower the free energy of activation**, the more molecules **have sufficient energy to pass through the transition state**, and, thus, **the faster the rate of the reaction**.

3. Alternate Reaction Pathway

- ❖ An enzyme allows a reaction **to proceed rapidly** under conditions prevailing in the cell by **providing an alternate reaction pathway** with a **lower free energy of activation**.
- ❖ The enzyme does not change **the free energies of the reactants or products** and, therefore, **does not change the equilibrium of the reaction**.
- ❖ It does, however, **accelerate the rate** with which **equilibrium is reached**.

B. Chemistry of the Active Site

- ❖ is a complex molecular machine **employing a diversity of chemical mechanisms** to facilitate the conversion of **substrate to product**.
- ❖ A number of factors are responsible for **the catalytic efficiency of enzymes**, including the following:

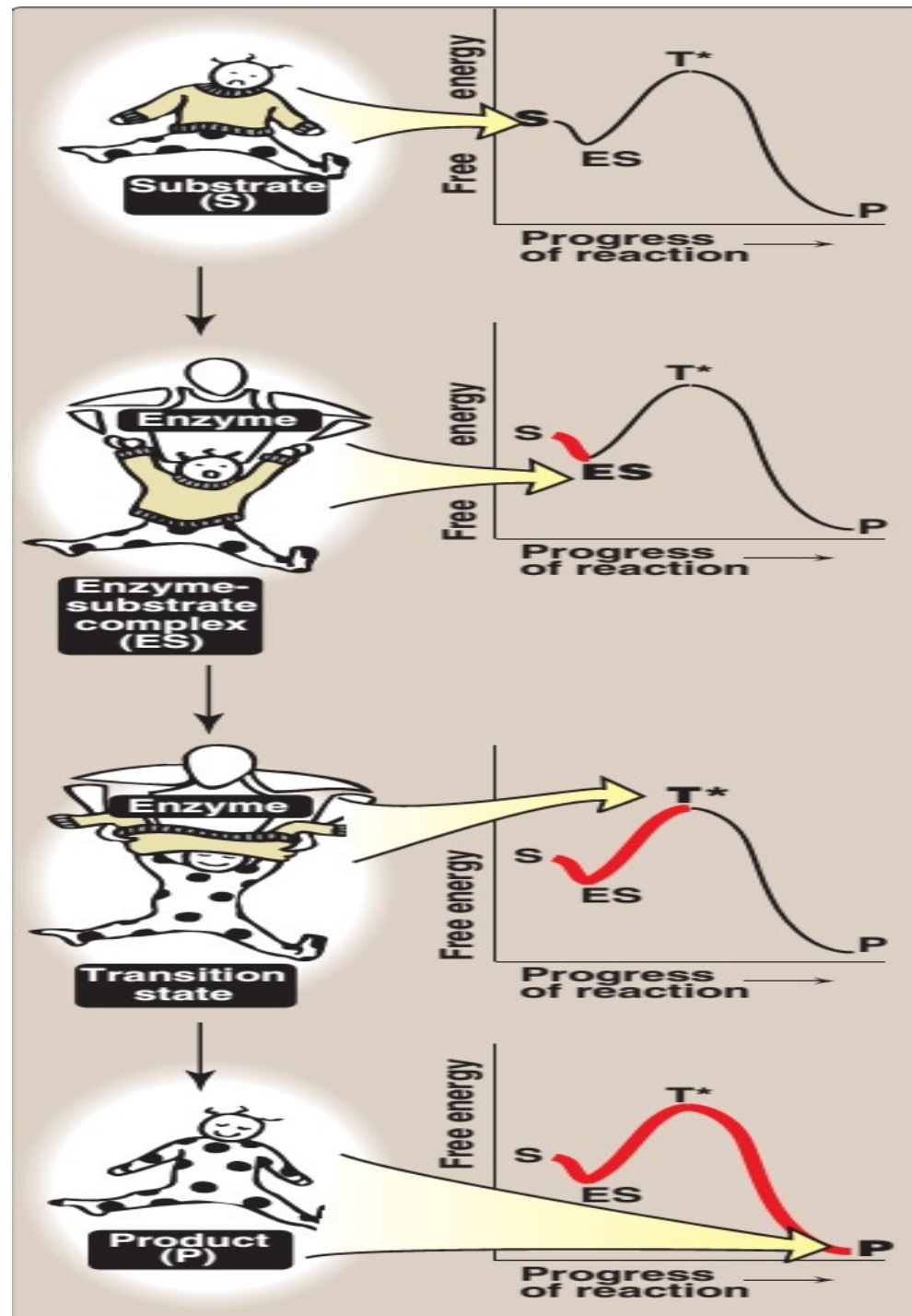
1. Transition-state stabilization

- ✓ The active site often acts as a **flexible molecular template** that binds the **substrate and initiates its conversion to the transition state**, a structure in which the **bonds are not like** those in the substrate or the product.
- ✓ By **stabilizing the transition state**, the enzyme greatly **increases the concentration of the reactive intermediate** that can be converted to **product** and, thus, **accelerates the reaction**.

2. Other Mechanisms

- The active site can **provide catalytic groups** that enhance the probability that the **transition state is formed**.
- In some enzymes, these groups can **participate in general acid base catalysis** in which amino acid residues **provide or accept protons**.
- In other enzymes, catalysis may involve **the transient formation of a covalent ES complex**.

- ✓ Note: The substrate bound to the enzyme (ES) is at a slightly lower energy than unbound substrate (S) and explains the small “dip” in the curve at ES.
- ✓ However, we can envision a parent acting as an enzyme, first coming in contact with the baby (forming ES), then guiding the baby’s arms into an extended, vertical position, analogous to the ES transition state.
- ✓ This posture (conformation) of the baby facilitates the removal of the sweater, forming the disrobed baby, which here represents product.



Factors Affecting Reaction Velocity

A. Substrate concentration

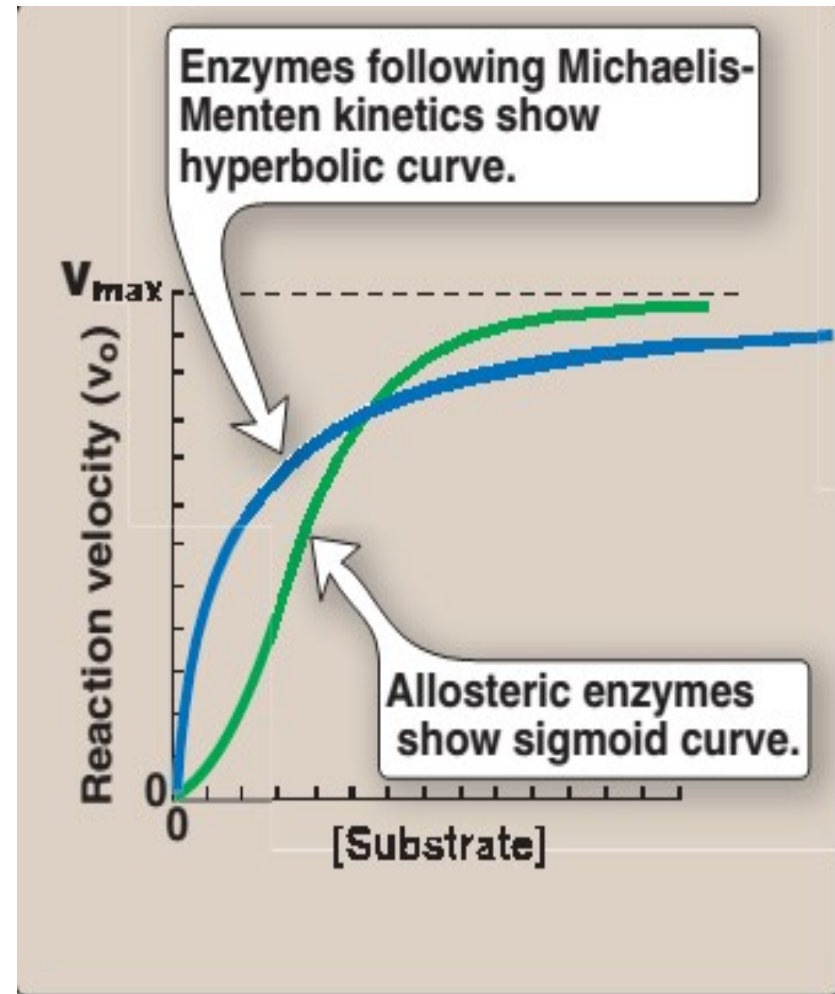
1. Maximal velocity

- ✓ The rate or velocity of a reaction (v) is **the number of substrate molecules converted to product per unit time**; expressed as $\mu\text{mol of product formed per minute}$.
- ✓ The **rate of an enzyme-catalyzed reaction increases with substrate concentration until a maximal velocity (V_{max}) is reached.**
- ✓ The **leveling off the reaction rate at high substrate concentrations** reflects **the saturation** (substrate occupy all available binding sites on the enzyme molecules present).

2. Hyperbolic Shape of the Enzyme Kinetics Curve

❖ Most enzymes show **Michaelis-Menten kinetics**, in which the plot of **initial reaction velocity (v_o)** against **substrate concentration ($[S]$)**, is **hyperbolic**.

❖ In contrast, **allosteric enzymes** do not follow **Michaelis-Menton kinetics** and show a **sigmoidal curve**.



1. Increase of velocity with temperature

- ✓ The reaction velocity **increases with temperature until a peak velocity is reached.**
- ✓ This increase is the result of **the increased number of molecules** having **sufficient energy** to pass over the **energy barrier.**

2. Decrease of velocity with higher temperature

- ❖ Further elevation of the temperature results in a decrease in reaction velocity as a result of **temperature-induced denaturation of the enzyme.**
- The optimum temperature for **most human enzymes** is between **35 and 40°C.**
- ✓ but **thermophilic bacteria** found in the hot springs have optimum temperatures of **70°C.**

1. Effect of pH on the ionization of the active site

- ❖ The concentration of H^+ affects reaction velocity in several ways.
- ❖ For example, catalytic activity may require that an amino group of the enzyme be in the protonated form ($-NH_3^+$).
- ❖ At alkaline pH, this group is deprotonated, and the rate of the reaction, therefore, declines.

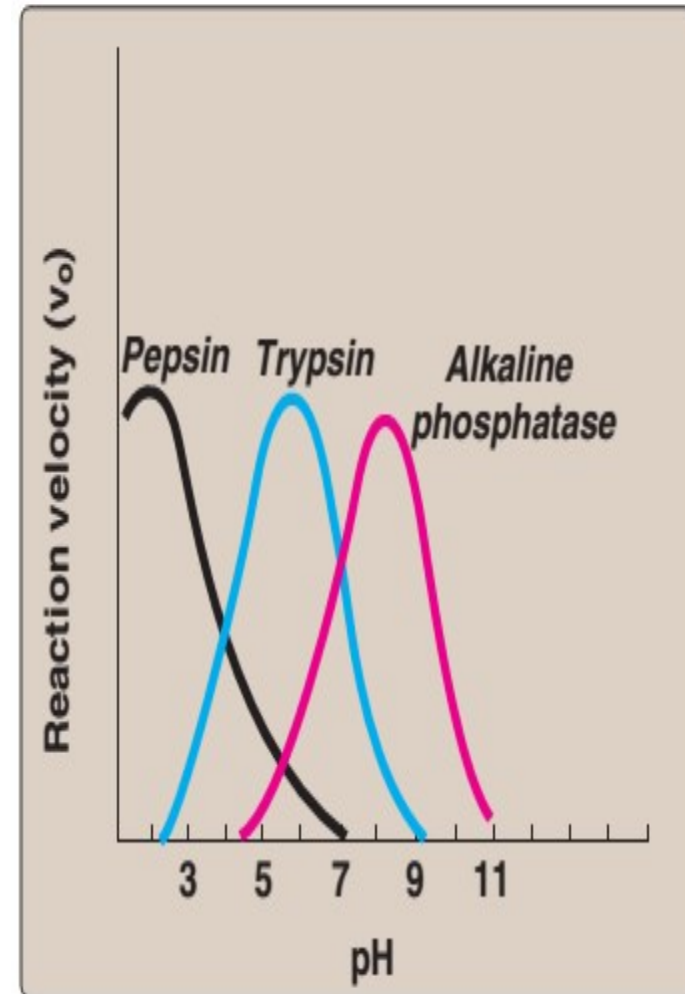
2. Effect of pH on enzyme denaturation

- ✓ Extremes of pH can also lead to denaturation of the enzyme, because the structure of the catalytically active protein molecule depends on the ionic character of the amino acid side chains.

3. The pH optimum varies for different enzymes

❖ The pH at which maximal enzyme activity is achieved is different for different enzymes, and often reflects the $[H^+]$ at which the enzyme functions in the body.

❖ **Pepsin**, a digestive enzyme in the stomach, is maximally active at **pH 2**, whereas other enzymes, designed to work at **neutral pH**, are denatured by such an acidic environment.



Michaelis-Menten Equation

A. Reaction Model

- Michaelis and Menten proposed a simple model that accounts for **most** of the features of **enzyme-catalyzed reactions**.
- In this model, the **enzyme reversibly combines** with its **substrate** to form an **ES complex** that subsequently yields **product**, regenerating the free enzyme.
- The model, involving one substrate molecule, is represented below:



where

S is the substrate

E is the enzyme

ES is the enzyme–substrate complex

P is the product

k_1 , k_{-1} , and k_2 are rate constants

- The Michaelis-Menten equation describes **how reaction velocity** varies with **substrate concentration**:

$$v_o = \frac{V_{\max} [S]}{K_m + [S]}$$

where

v_o = initial reaction velocity

$V_{\max}$ = maximal velocity

K_m = Michaelis constant = $(k_{-1} + k_2)/k_1$

$[S]$ = substrate concentration

Assumptions During Michaelis-Menten Rate Equation

1. Relative concentrations of **Enzyme** and **Substrate**

- ✓ The concentration of **substrate** ($[S]$) is **much greater than** the concentration of **enzyme** ($[E]$), so that the percentage of **total substrate** bound by **the enzyme** at any one time is **small**.

2. Steady-State Assumption

- ❖ $[ES]$ **does not change with time**, that is, **the rate of formation of ES is equal to that of the breakdown of ES** (to $E + S$ and to $E + P$).
- ❖ An intermediate in a **series of reactions** is said to be in **steady state** when its **rate of synthesis** is equal to its **rate of degradation**.

3. Initial velocity

- Initial reaction velocities (v_0) are used in the **analysis of enzyme reactions**.
- This means that **the rate of the reaction** is measured as soon as **enzyme** and **substrate** are **mixed**.
- At that time, **the concentration of product** is very small and, therefore, the rate of the **back reaction** from **P to S** can be **ignored**.

Conclusions about Michaelis-Menten kinetics

1. Characteristics of K_m

- ✓ is the **substrate concentration** at which the **reaction velocity** is equal to $1/2V_{max}$.
- ✓ Reflects the **affinity of the enzyme** for that substrate.
- ✓ K_m **does not vary** with the **concentration of enzyme**.

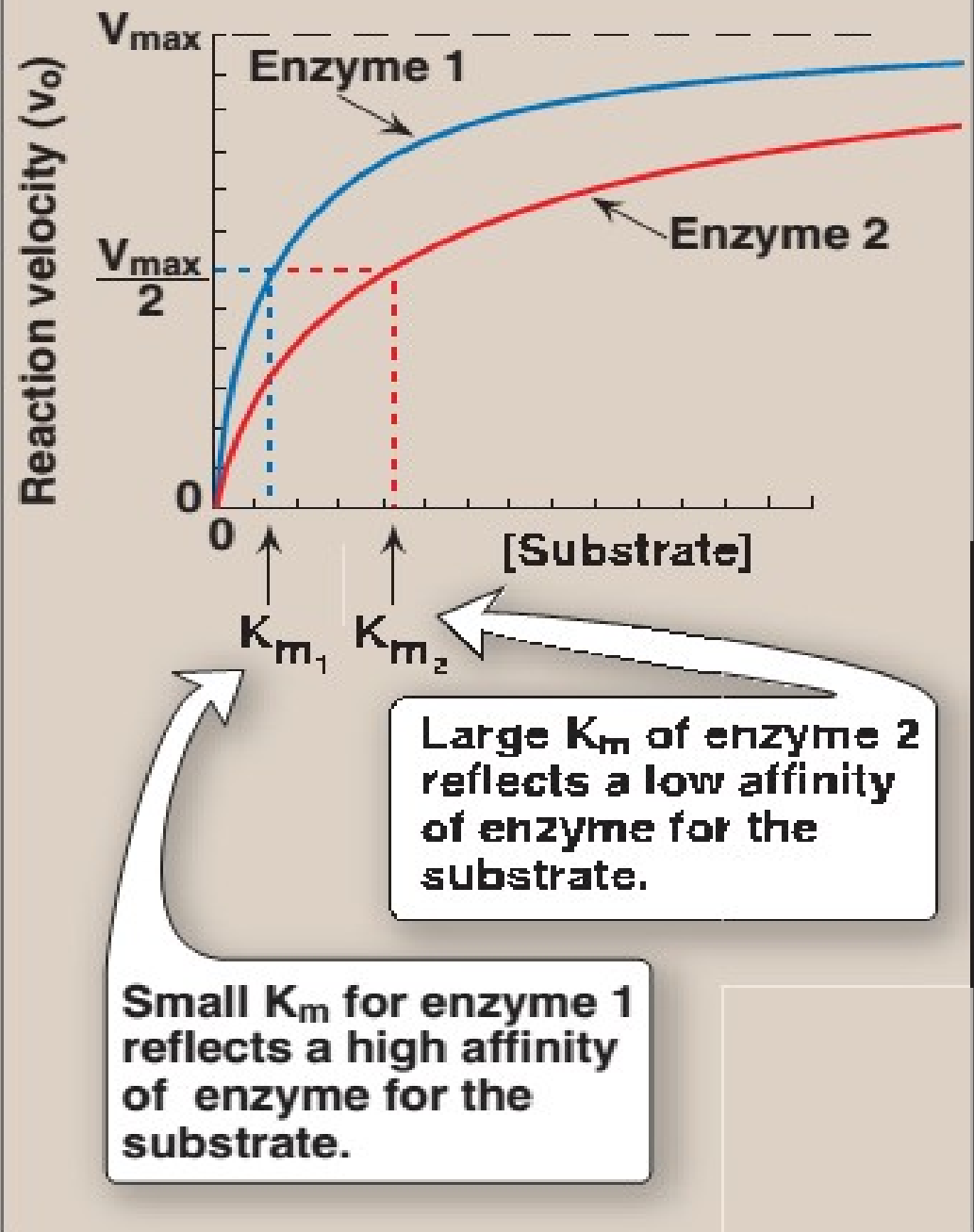
a. Small K_m

- ❖ Reflects a **high affinity** of the enzyme for substrate, because **a low concentration of substrate** is needed to **half-saturate the enzyme**.

b. Large K_m

- Reflects **a low affinity** of enzyme for substrate

- Effect of **substrate concentration** on reaction velocities for two enzymes
- ✓ enzyme 1 with a small K_m , and
- ✓ enzyme 2 with a large K_m .



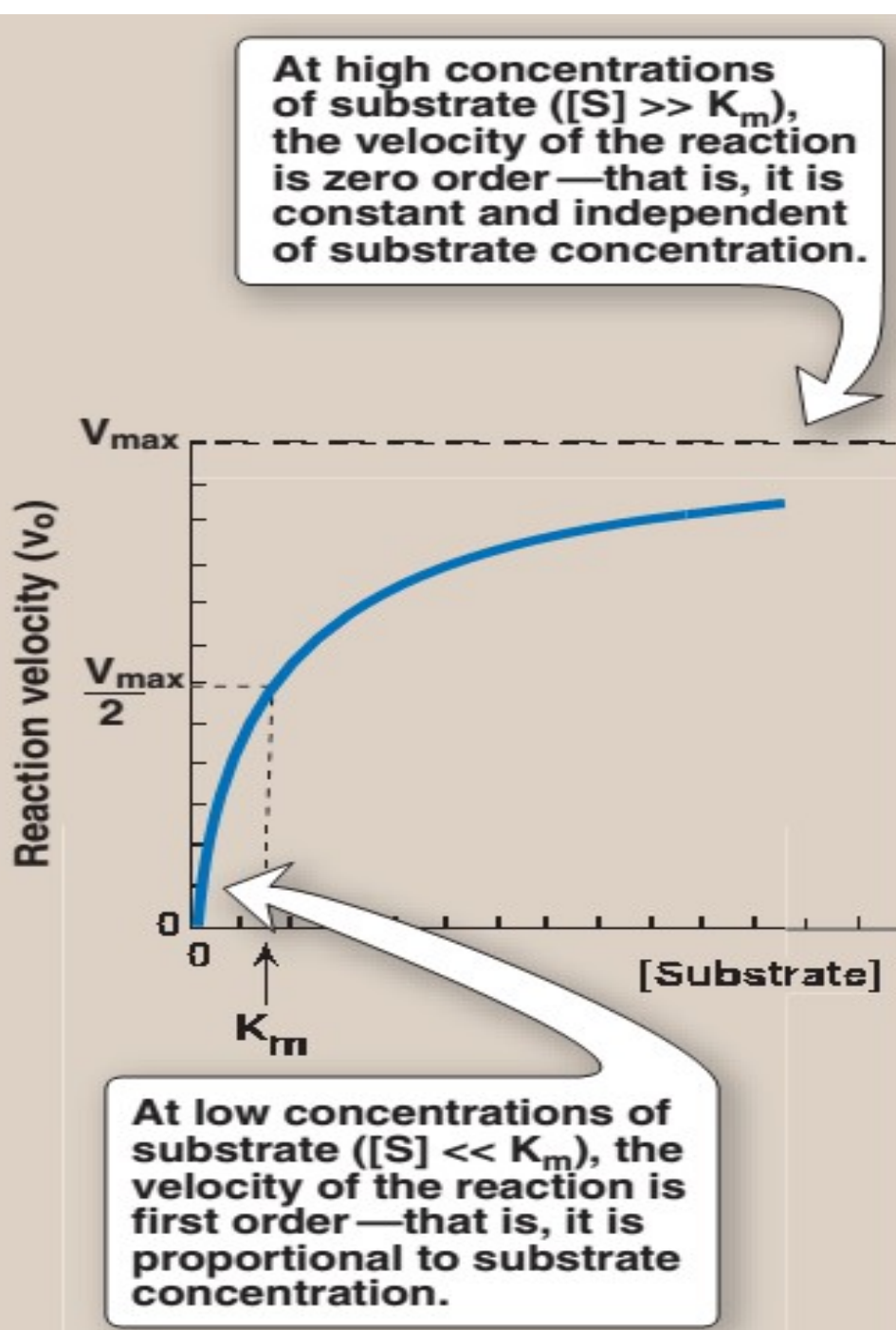
2. Relationship of velocity to enzyme concentration

- ❖ The **rate of the reaction** is directly proportional to the **enzyme concentration** at all **substrate concentrations**.
- ✓ For example, if the enzyme concentration is **halved**, the **initial rate of the reaction (v_0)**, as well as that of **V_{max}** , are **reduced to half** that of the original.

3. Order of Reaction

- ✓ When **$[S]$ is much less than K_m** , the **velocity of the reaction** is approximately **proportional to the substrate concentration**.

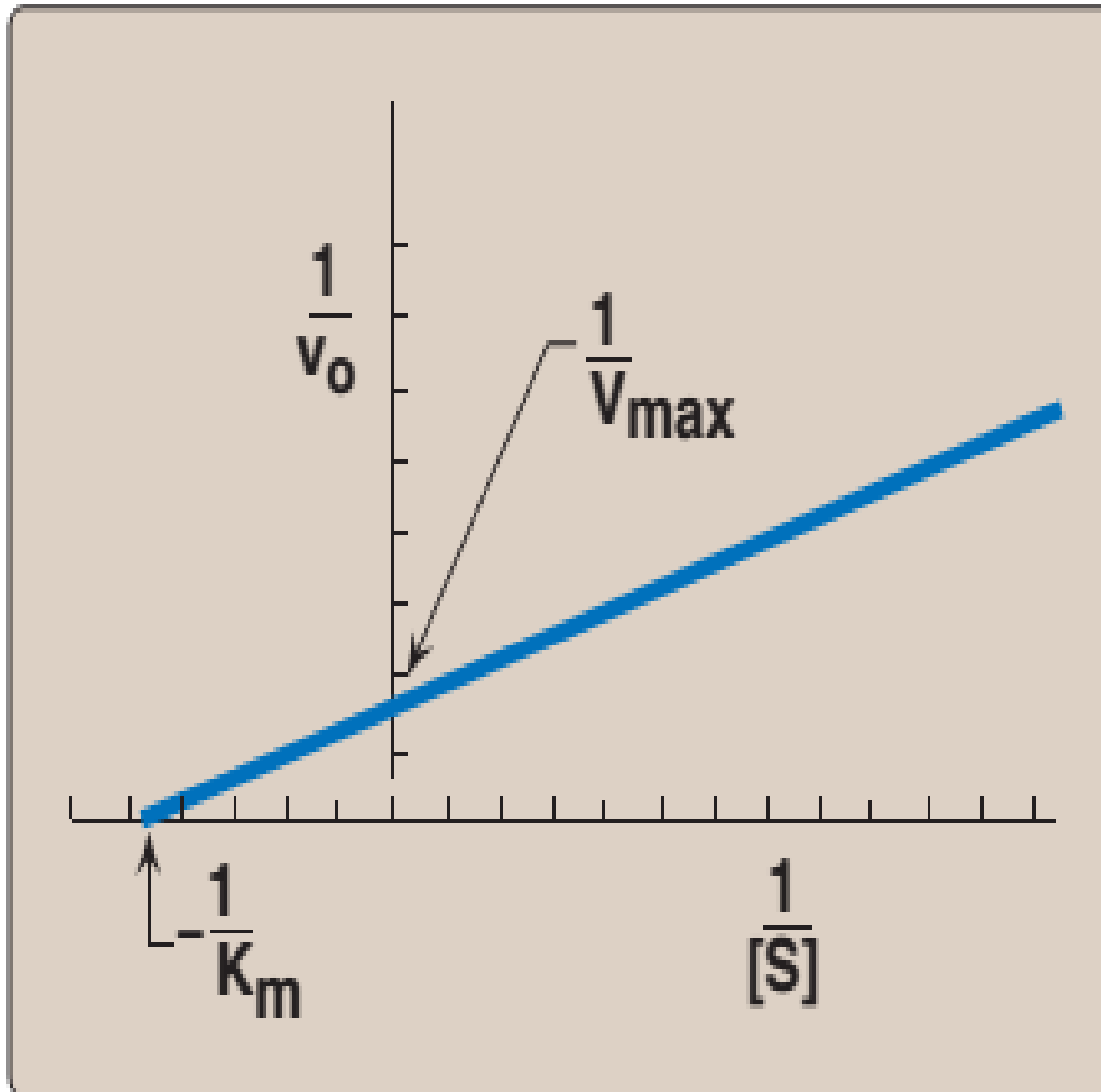
- ✓ When $[S]$ is much greater than K_m , the velocity is constant and equal to V_{max} .
- ✓ The rate of reaction is then independent of substrate concentration, and is said to be zero order with respect to substrate concentration.



- ✓ When v_o is plotted against $[S]$, it is not always possible to determine when **V_{max}** has been achieved, because of the **gradual upward slope of the hyperbolic curve at high substrate concentrations**.
- ✓ However, if **$1/v_o$** is plotted versus **$1/[S]$** , a **straight line** is obtained.
- ✓ This plot, the Lineweaver-Burk plot (a double-reciprocal plot) can be used to calculate **K_m** and **V_{max}** , as well as **to determine the mechanism of action of enzyme inhibitors**.
- ❖ The equation for the Lineweaver-Burk plot is:

$$\frac{1}{v_o} = \frac{K_m}{V_{max} [S]} + \frac{1}{V_{max}}$$
- ✓ where the intercept on the **x-axis** is equal to **$-1/K_m$** , and the intercept on the **y-axis** is equal to **$1/V_{max}$**

Lineweaver-Burk plot



Inhibition of Enzyme Activity

- ❖ Any substance that **can diminish the velocity** of an enzyme-catalyzed reaction is called **an inhibitor**.
- ❖ In general, **irreversible inhibitors** bind to enzymes through **covalent bonds**.
- ❖ **Reversible inhibitors** typically bind to enzymes through **noncovalent bonds**, thus **dilution of the enzyme-inhibitor complex** results in **dissociation** of the **reversibly bound inhibitor**, and recovery of enzyme activity.
- ❖ The **two** most commonly encountered types of **reversible inhibition** are **competitive** and **noncompetitive**.

- ❑ Occurs when the **inhibitor binds reversibly** to the **same site** that the substrate would normally occupy and, therefore, **competes** with the substrate for that site.

1. Effect on V_{max}

- ❖ Effect of competitive inhibitor is **reversed** by **increasing [S]**.
- ✓ At **high substrate concentration**, the **reaction velocity reaches the V_{max}** observed in the absence of inhibitor.
- ✓ So, **no change on V_{max}** .

2. Effect on K_m

- ✓ A competitive inhibitor **increases** the apparent **K_m** for a given substrate.

3. Effect on the Lineweaver-Burk plot

- ❖ **Competitive inhibition** shows a characteristic Lineweaver-Burk plot in which the plots of the inhibited and uninhibited reactions intersect on the y-axis at $1/V_{\max}$ ($V_{\max}$ is unchanged).
- ❖ The **inhibited** and **uninhibited** reactions show different x-axis intercepts, indicating that the apparent K_m is increased in the presence of the competitive inhibitor because $-1/K_m$ moves closer to zero from a negative value.

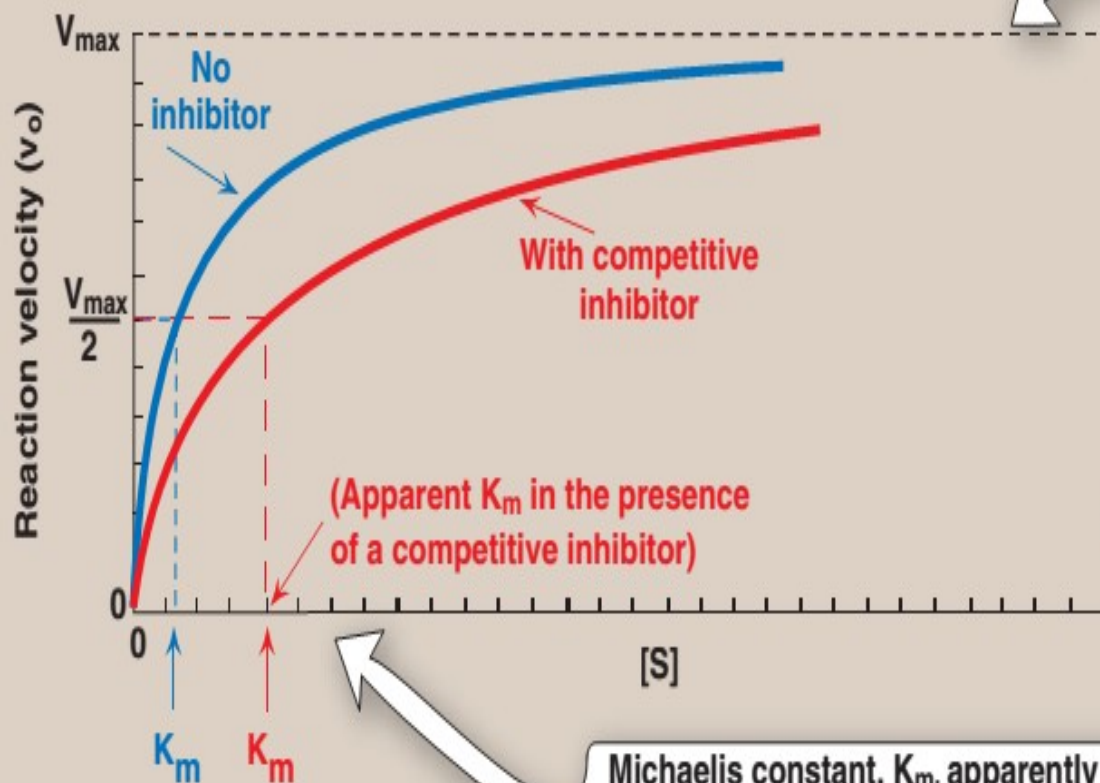
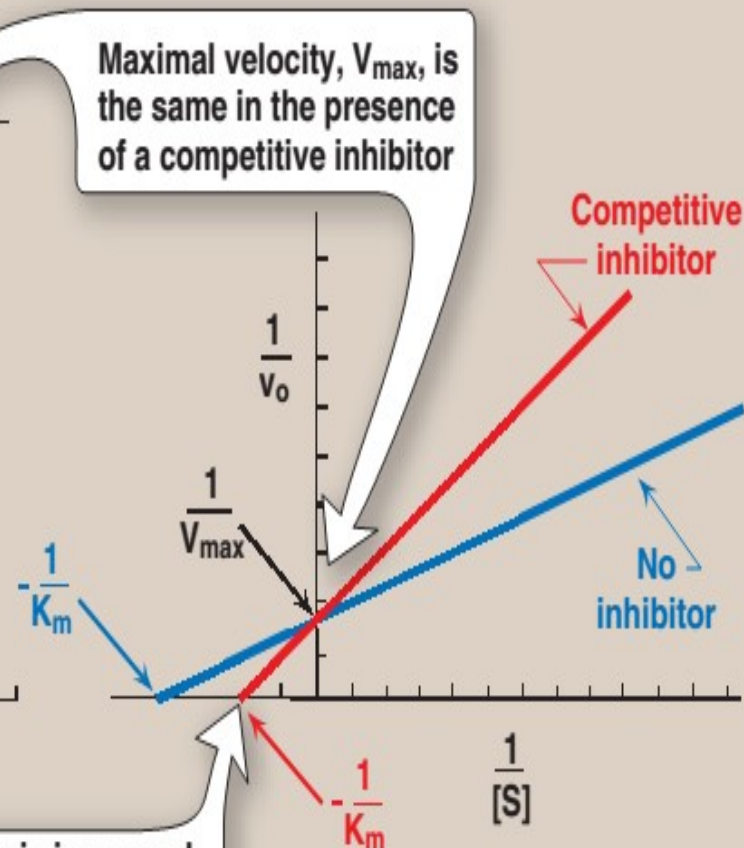
A**B**

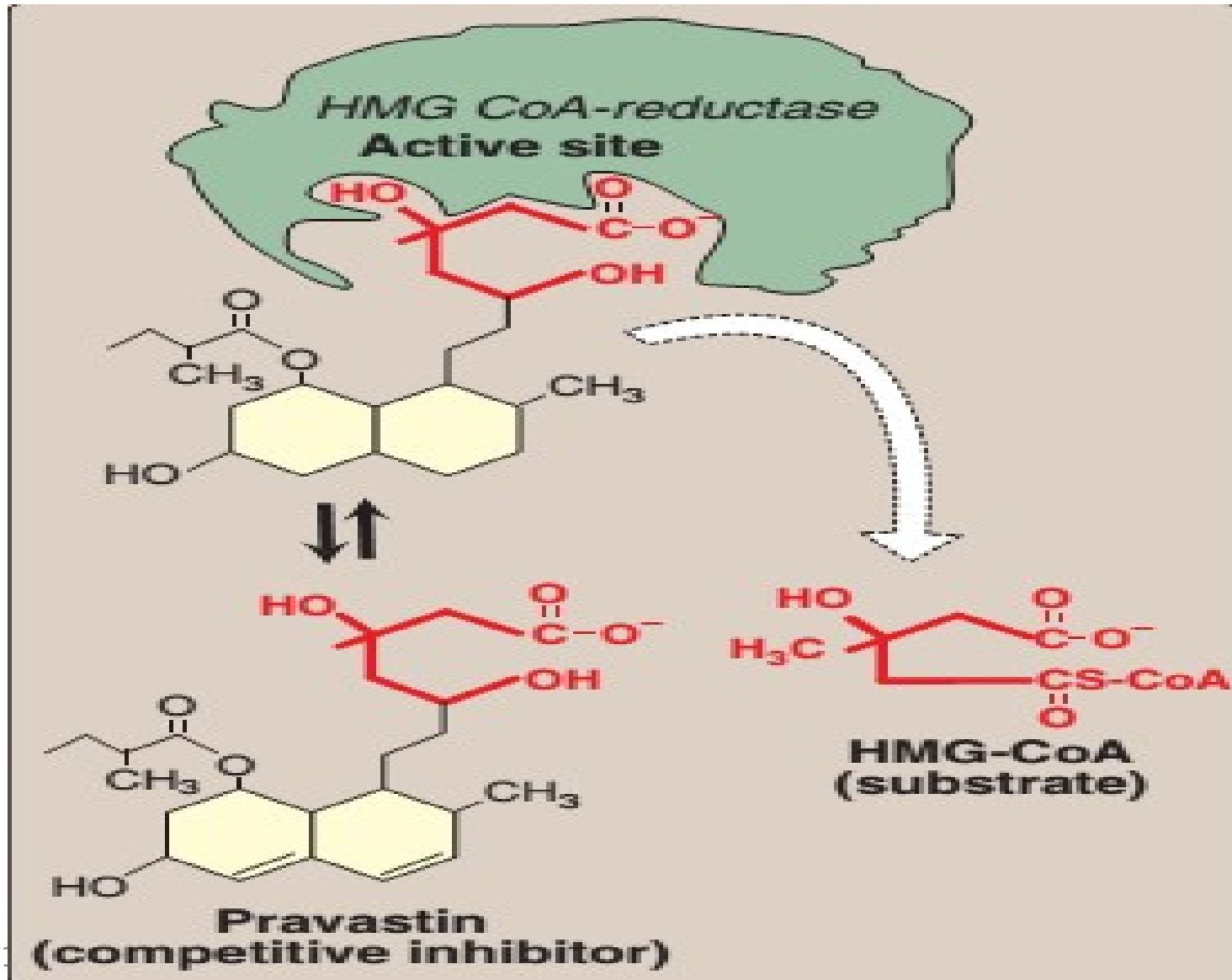
Figure 5.12

A. Effect of a competitive inhibitor on the reaction velocity (v_o) versus substrate ($[S]$) plot. B. Lineweaver-Burk plot of competitive inhibition of an enzyme.

4. Statin Drugs as Competitive Inhibitors

- ❖ This group of antihyperlipidemic agents competitively inhibits the first committed step in cholesterol synthesis.
- ❖ This reaction is catalyzed by hydroxymethylglutaryl-CoA reductase (HMG-CoA reductase).
- ❖ Statin drugs (atorvastatin (Lipitor) and pravastatin (Pravachol)), are structural analogs of the natural substrate for this enzyme, and compete effectively to inhibit HMG-CoA reductase.
- ✓ By doing so, they inhibit de novo cholesterol synthesis, thereby lowering plasma cholesterol levels.

Pravastatin competes with **HMG CoA** for the active site of **HMG CoA reductase**



B. Noncompetitive inhibition

- ❑ Occurs when the inhibitor and substrate bind at different sites on the enzyme.
- ❑ This type of inhibition is recognized by its characteristic effect on **V_{max}** .

1. Effect on V_{max} :

- ❖ Can not be overcome by increasing the concentration of substrate.
- ❖ Thus, noncompetitive inhibitors decrease the apparent V_{max} of the reaction.

2. Effect on K_m :

- Do not interfere with the binding of substrate to enzyme.
- Thus, the enzyme shows **the same K_m** in the presence or absence of the noncompetitive inhibitor.

3. Effect on Lineweaver-Burk plot

- ❑ The apparent $V_{\max}$ decreases
- ❑ K_m is unchanged

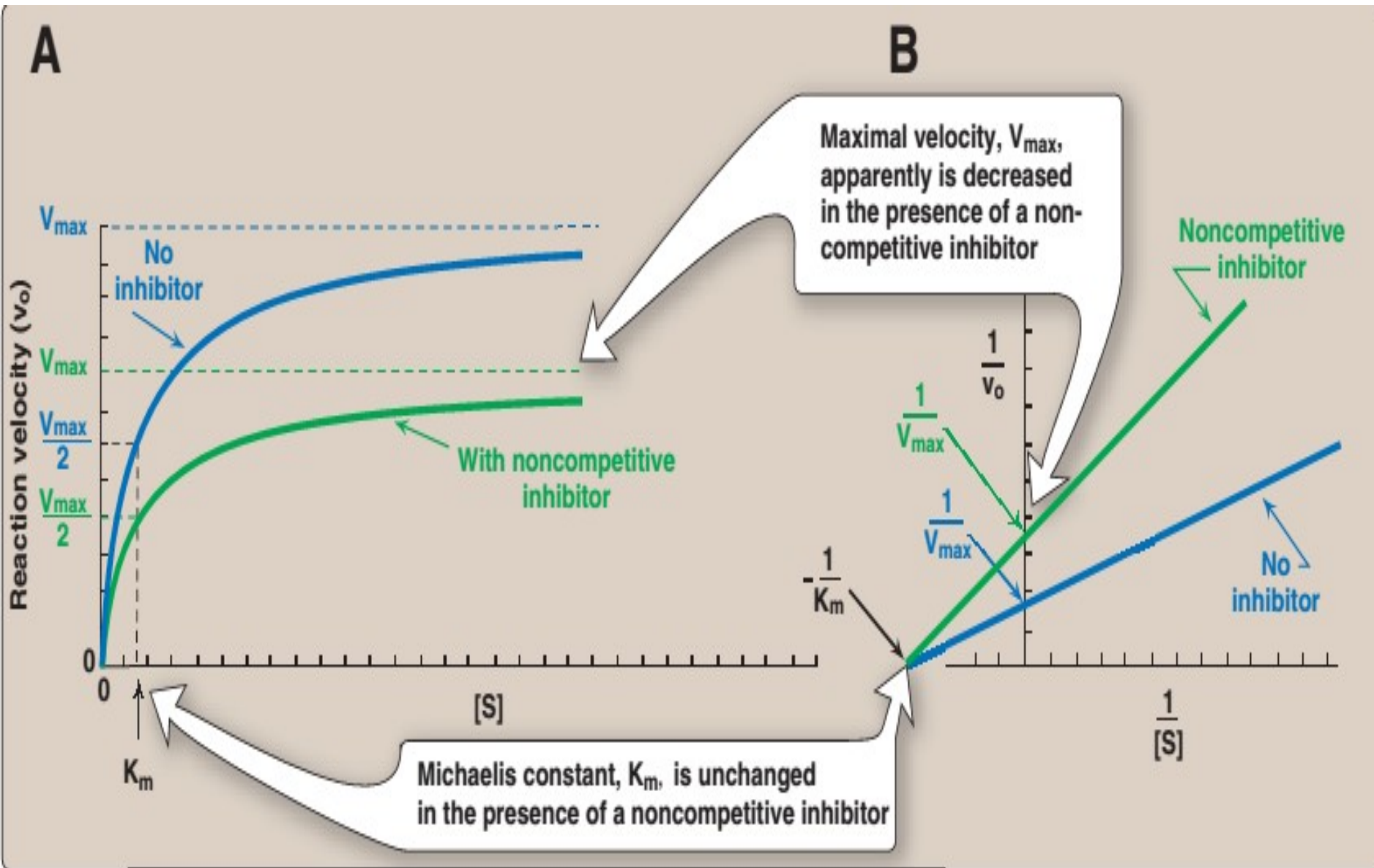
4. Examples of noncompetitive inhibitors:

- Some inhibitors act by forming covalent bonds with specific groups of enzymes.
- ✓ For example, **lead** forms covalent bonds with the **sulfhydryl side chains** of cysteine in proteins.
- ✓ The binding of the heavy metal shows

Cont....

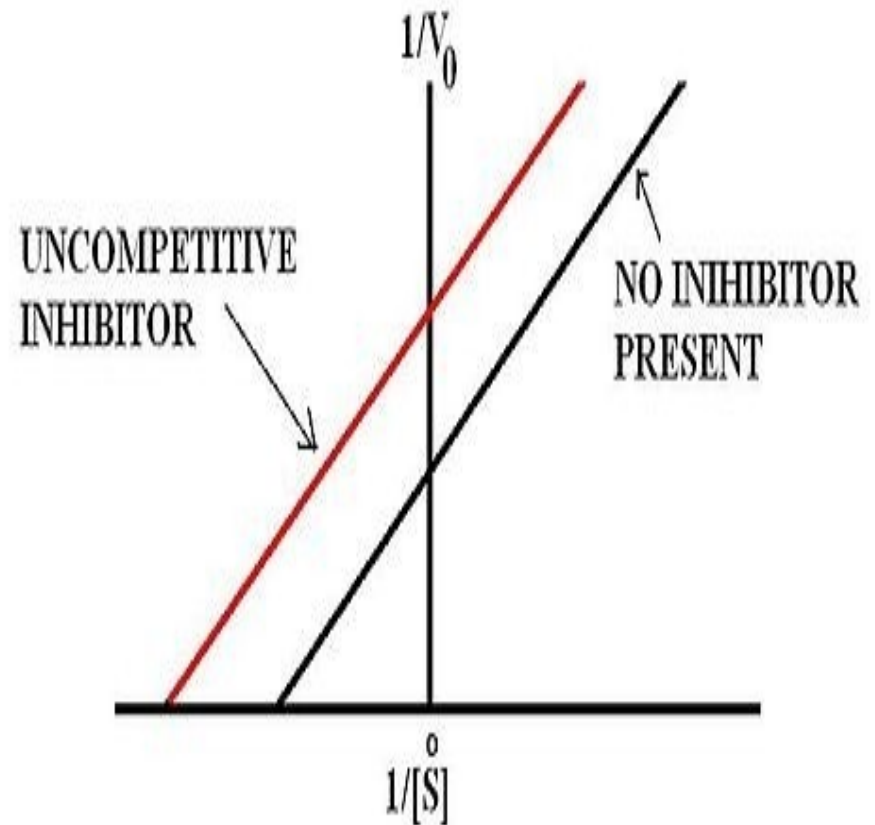
- **Ferrochelatase**, an enzyme that catalyzes the **insertion of Fe^{2+}** into **protoporphyrin**, is an example of an enzyme sensitive to **inhibition by lead**.
- Other examples of noncompetitive inhibition are certain **insecticides**, whose **neurotoxic effects** are a result of their **covalent binding** at the catalytic site of the enzyme **acetylcholinesterase**.
- ✓ Note: Even though covalent bonds are formed, **if active enzyme can be recovered**, the inhibition is reversible.

Effect of a noncompetitive inhibitor on the reaction velocity (v_o) versus substrate ($[S]$) plot.



Uncompetitive Enzyme Inhibition

- ▶ Inhibitor binds to **enzyme- substrate complex**.
- ▶ Both **V_{max}** and **K_m** are **decreased**.
- ✓ e.g; Inhibition of **placental alkaline phosphatase** (Regan isoenzyme) by **phenylalanine**.



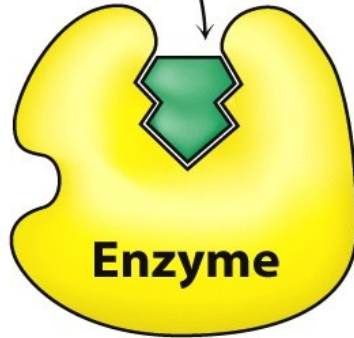
Why K_m & V_{max} Decreased???

- ▶ Since uncompetitive inhibitors **only block processes beyond ES formation**, one might expect only V_{max} to be suppressed with no effect on K_m , but as the **inhibitor binds to and stabilizes the ES complex**, it makes it **more difficult for S to dissociate or be converted to product**, **increasing enzyme affinity for S** and **so reducing substrate K_m** .
- ▶ This mode of action is attractive for drug design as the inhibitors bind to the enzyme target only when the **target is active and substrate present**.

Competitive V/S Non competitive V/S Uncompetitive Enzyme Inhibition

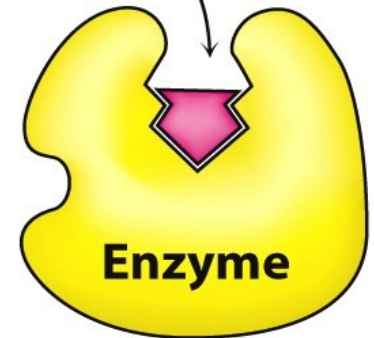
(A)

Substrate



(B)

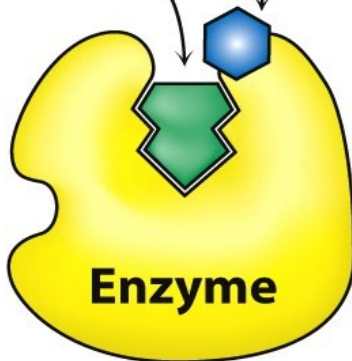
Competitive inhibitor



(C)

Substrate

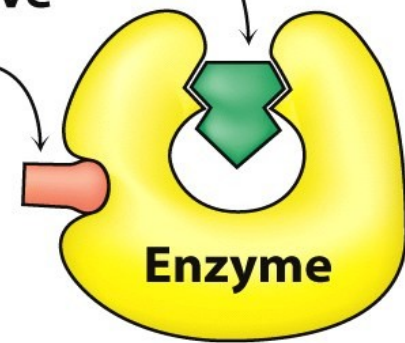
Uncompetitive inhibitor



(D)

Noncompetitive inhibitor

Substrate



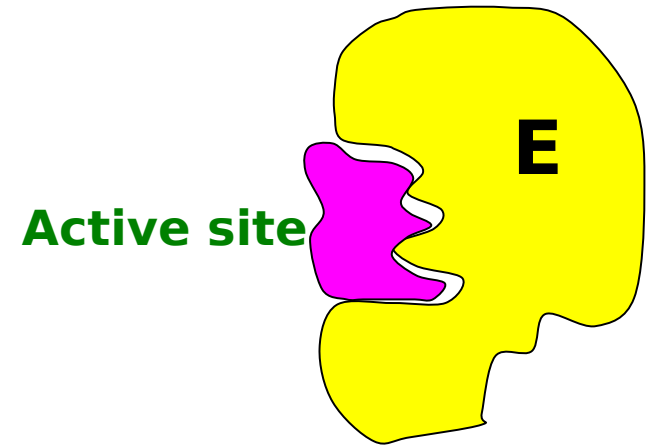
Suicide Inhibition

- ▶ Is irreversible inhibition.
- ▶ **Structural analog of the substrate** is converted to **more effective inhibitor** with the **help of enzyme** to be inhibited.
- ▶ The **new product irreversibly binds** to the enzyme & **inhibits further reaction**.
- ▶ **Aspirin** action is based on suicide inhibition.
 - **Acetylates a serine residue** in the active center of **cyclo oxygenase** . Thus **Prostaglandine synthesis is inhibited** so **inflammation subsides**.
- ▶ **Disulfiram**- used in treatment of **alcoholism**.
 - Drug **irreversibly inhibits the enzyme aldehyde dehydrogenase** preventing further **oxidation of acetaldehyde** which produces **sickening effects** leading to **aversion to alcohol**.

Allosteric Inhibition

▶ Allosteric means “**other site**”

❖ These enzymes have **one catalytic site (Active site)** where the **substrate binds** and **another separate allosteric site** where the **modifier binds**.



❖ The allosteric sites **may or may not be physically adjacent**.

❖ The binding of the **modifier** may **enhance (Positive modifier)** or **inhibit**

Allosteric Inhibition- Salient features

- ▶ Inhibitor is **not a substrate analogue**.
- ▶ **Partially reversible**, when **excess substrate is added**.
- ▶ K_m is usually increased.
- ▶ V_{max} is reduced.
- ▶ When the **inhibitor binds the allosteric site**, the **configuration of the active site is changed** so that the **substrate can not bind properly**.
- ▶ Most **allosteric enzymes** possess **quaternary structure**.

Regulation of Enzyme Activity

- is essential if an organism is **to coordinate its numerous metabolic processes**.
- The rates of most enzymes are **responsive to changes in substrate concentration**, because the **intracellular level of many substrates** is in the **range of the K_m** .
- ✓ Thus, an **increase in substrate concentration** prompts an **increase in reaction rate**, which tends to return the concentration of substrate toward normal.
- Some enzymes **with specialized regulatory functions** respond to allosteric effectors or **covalent modification**, or they show **altered rates of enzyme synthesis** (or degradation) when **physiologic conditions are changed**.

- ❖ Allosteric enzymes are regulated by molecules called **effectors** (modifiers) that bind **noncovalently** at a site other than the active site.
- ❖ are usually composed of **multiple subunits**, and the regulatory (allosteric) site that binds the effector may be located on a subunit that is not itself catalytic.
- ❖ The presence of an allosteric effector can **alter the affinity of the enzyme for its substrate**, or **modify the maximal catalytic activity of the enzyme**, or **both**.
- ❖ Effectors that **inhibit enzyme activity** are termed **negative effectors**, whereas those that

- ❑ Many enzymes may be regulated, most frequently by the **addition or removal of phosphate groups** from specific **serine, threonine, or tyrosine residues** of the enzyme.
- ❑ **Protein phosphorylation** is recognized as one of the **primary ways** in which **cellular processes are regulated**.

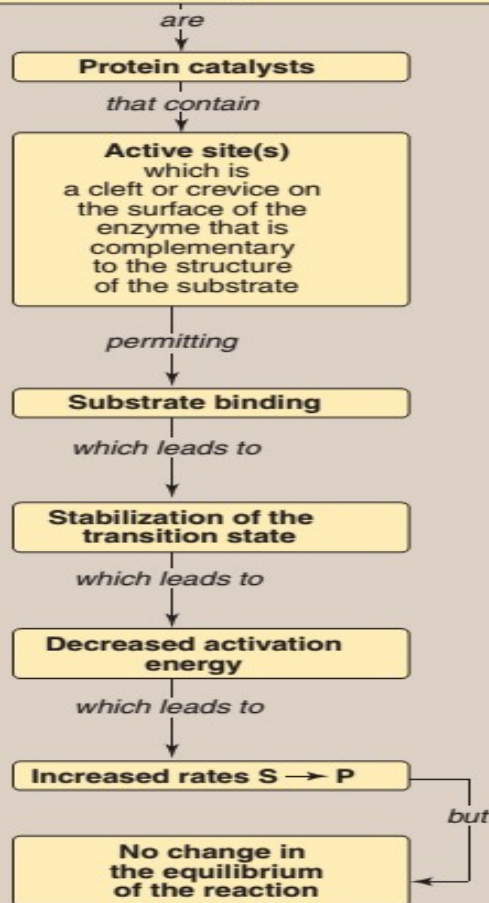
1. Phosphorylation and dephosphorylation

- ✓ Phosphorylation reactions are catalyzed by a family of enzymes called **protein kinases** that use **adenosine triphosphate (ATP)** as a **phosphate donor**.
- ✓ Phosphate groups are **cleaved** from phosphorylated enzymes by the action of **phosphoprotein phosphatases**.

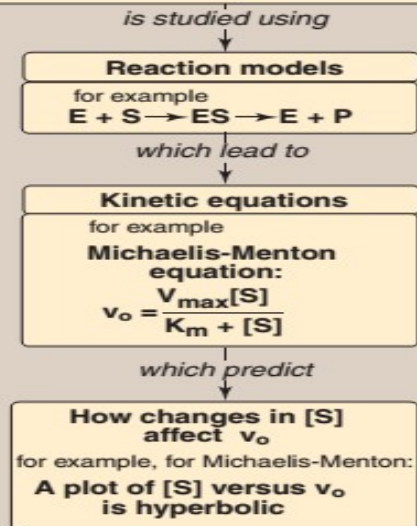
C. Induction and Repression of enzyme synthesis

- ❖ The regulatory mechanisms described above **modify the activity** of **existing** enzyme molecules.
- ❖ However, cells can also **regulate the amount of enzyme present** by **altering the rate of enzyme degradation** or, more typically, **the rate of enzyme synthesis**.
- ❖ The **increase (induction)** or **decrease (repression)** of enzyme synthesis leads to an **alteration** in the **total population of active sites**.
- ❖ Enzymes subject to regulation of synthesis are often those that are **needed at only one stage of development** or under **selected physiologic conditions**.
- ✓ For example, elevated levels of **insulin** as a result of **high blood glucose levels** cause an increase in the synthesis of key enzymes involved in **glucose metabolism**.

Enzymes



Catalysis

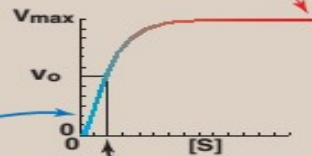


which predicts that

When $[S]$ is much greater than K_m , the reaction rate is independent of $[S]$

which is called

Zero order



When $[S] = K_m$ then $v_o = 1/2 V_{max}$

When $[S]$ is much less than K_m , the reaction rate is proportional to $[S]$

which is called

First order

Rate of enzymic reactions

is often influenced by

- Enzyme concentration
- Temperature
- Coenzymes, cofactors
- pH
- Substrate concentration
- Covalent modification
- Inhibitors

classified as

Competitive

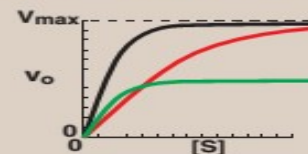
when

**Apparent K_m is increased
 V_{max} is unchanged**

Noncompetitive

when

**K_m is unchanged
Apparent V_{max} is decreased**



Allosteric enzymes

often

- Are composed of multiple subunits
- Catalyze the committed step
- Bind substrate cooperatively
- Show a sigmoid curve when v_o is plotted against $[S]$
- Bind allosteric effectors

which leads to

Activation

Inhibition

leading to

Changes in V_{max} , affinity for substrate ($K_{0.5}$), or both