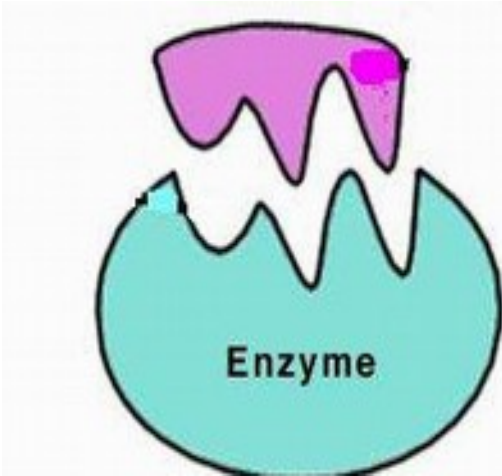
ENZYMES

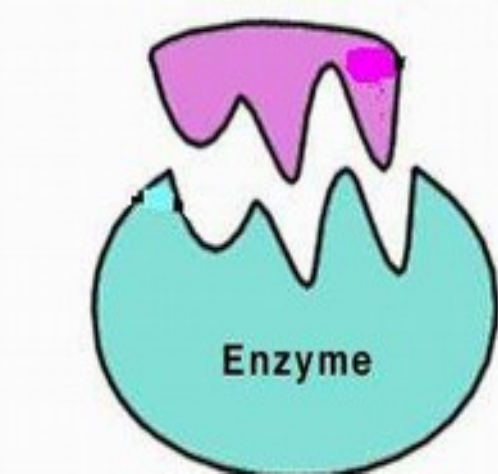
Dr Sairindhri Tripathy



Introduction

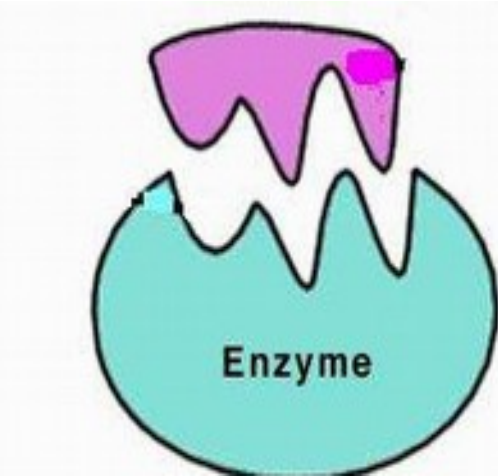
Enzymes are

- soluble
- colloidal organic catalyst formed by living cells
- specific in action
- protein in nature
- inactive at 0^0C
- Destroyed by moist heat at 100^0C



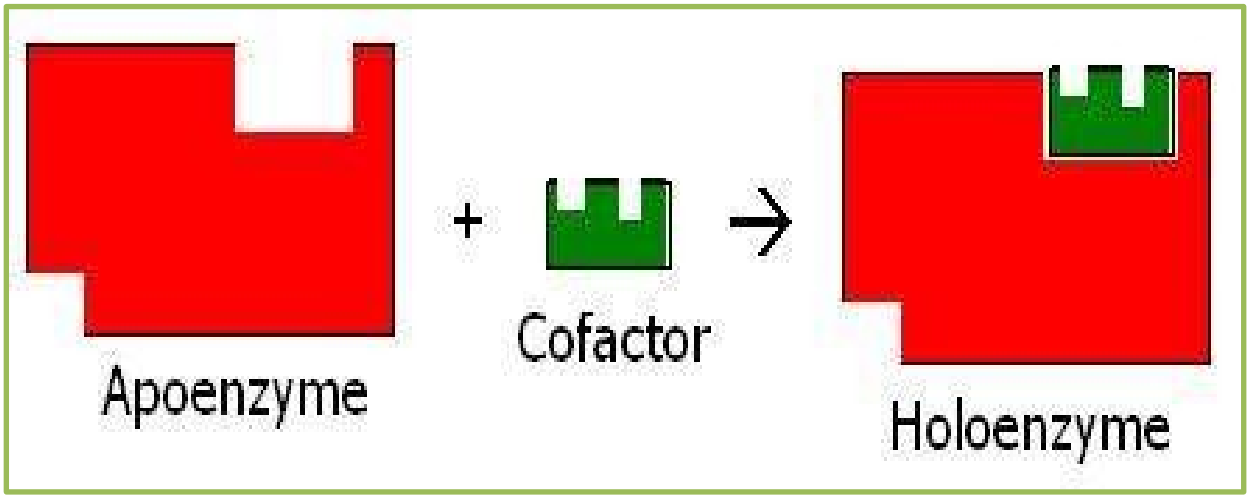
Enzymes as Proteins

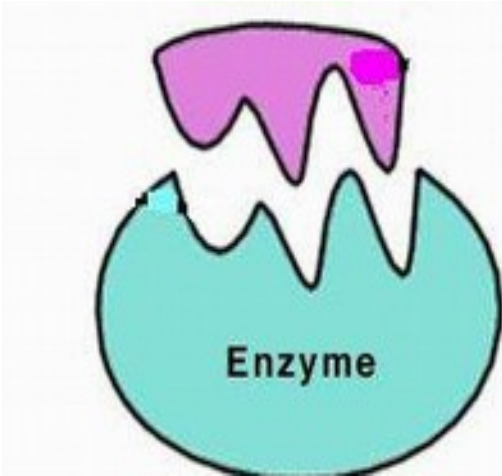
- Expect some catalytic RNA all enzymes are proteins
- Activity is lost when-
- Loss of integrity of native protein conformation
- Enzyme denaturation
- Dissociation into subunits/ Component aminoacids
- Molecular wt 12,000 to more than 1million



Many enzymes require the presence of other compounds - cofactors - before their catalytic activity can be exerted.

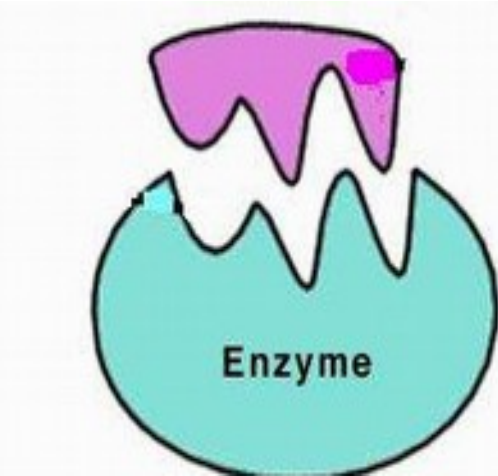
This entire active complex is referred to as the holoenzyme; i.e., apoenzyme (protein portion) plus the cofactor (coenzyme, prosthetic group or metal-ion-activator) is called the holoenzyme.





HOLOENZYME

1. **Coenzyme**- a non-protein organic substance which is dialyzable, thermostable and loosely attached to the protein part.
2. **Prosthetic group** - an organic substance which is dialyzable and thermostable which is firmly attached to the protein or apoenzyme portion.
3. **Metal-ion-activator** - these include K^{+}, Fe^{++}, Zn^{++}, Mg^{++}, Ca^{++}



ENZYMES CAN BE

Monomeric / Oligomeric Enzymes

- One or more aminoacids

Multienzyme Complexes

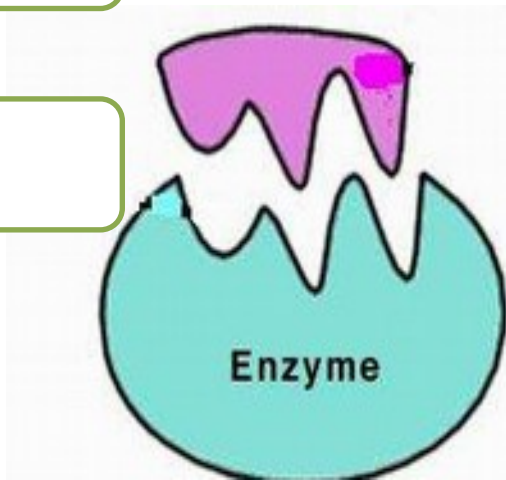
- Possess specific sites to catalyse diff reaction in sequence

Intracellular Enzymes

- Functional within the cell

Extracellular enzymes

- Active outside the cell



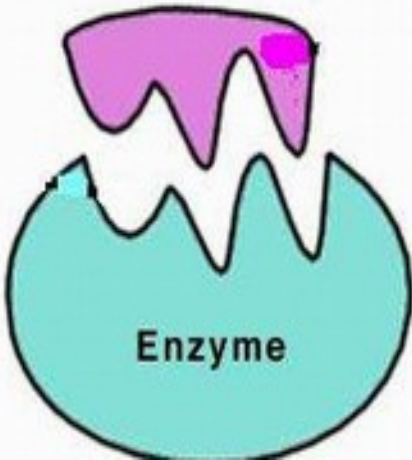
ENZYMES SECRETION

ZYMase Secretion

- Extracellular enzymes are secreted ready for action
- Eg: Amylase of saliva

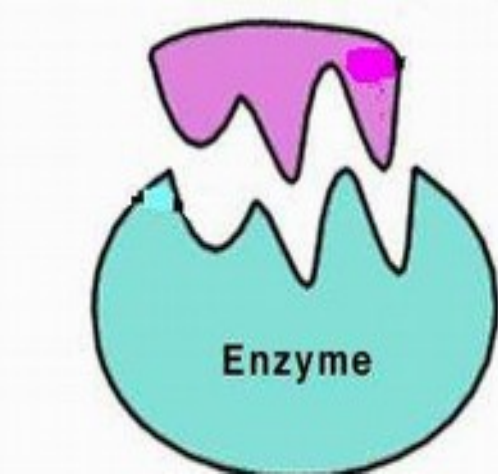
ZYMogen Secretion

- Enzyme secreted inactive form & ultimately activated by an agent secreated from other cells
- Eg: Prothrombin to thrombin



Trival name

- Gives no idea of source, function or reaction catalyzed by the enzyme.
- Example: trypsin, thrombin, pepsin.



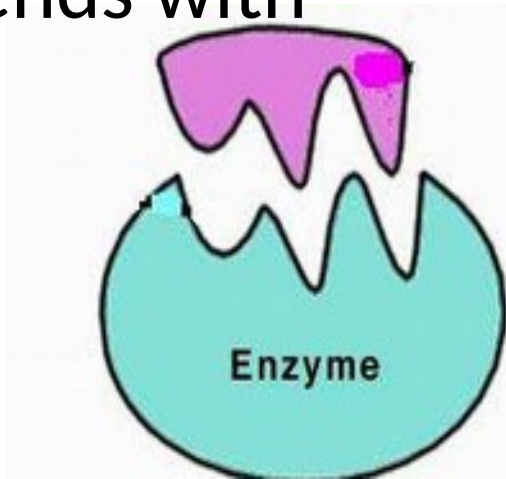
Systematic Name

- According to the International union Of Biochemistry an enzyme name has two parts:

  -First part is the name of the substrates for the enzyme.

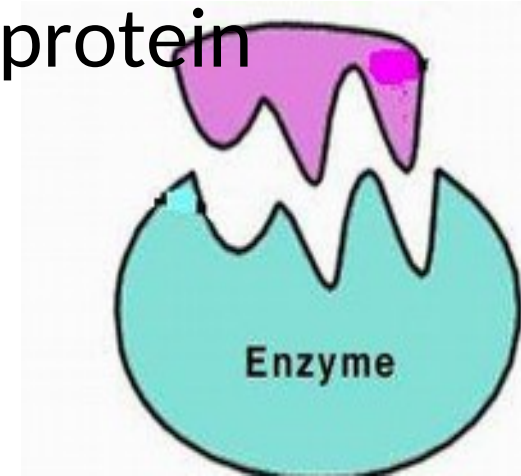
  -Second part is the type of reaction catalyzed by the enzyme.This part ends with the suffix “ase”.

Example: Lactate dehydrogenase



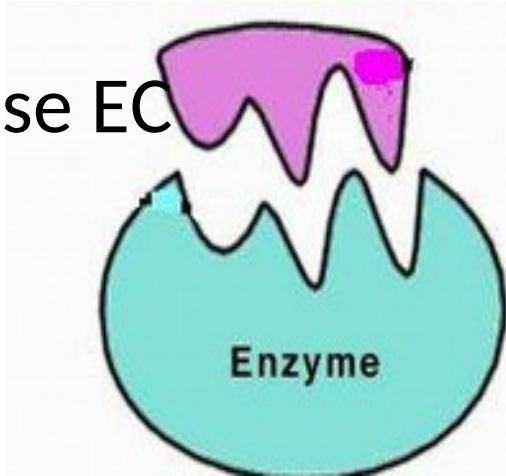
EC number

Enzymes are classified into six different groups according to the reaction being catalyzed. The nomenclature was determined by the Enzyme Commission in 1961 (with the latest update having occurred in 1992), hence all enzymes are assigned an **“EC” number**. The classification does not take into account amino acid sequence (ie, homology), protein structure, or chemical mechanism.



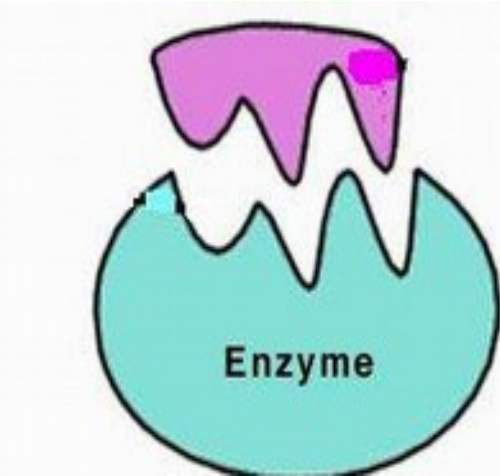
EC numbers

- EC numbers are four digits, for example a.b.c.d, where “a” is the class, “b” is the subclass, “c” is the sub-subclass, and “d” is the sub-sub-subclass. The “b” and “c” digits describe the reaction, while the “d” digit is used to distinguish between different enzymes of the same function based on the actual substrate in the reaction.
- Example: for Alcohol:NAD^+oxidoreductase EC number is 1.1.1.1



The Six Classes

- **EC 1. Oxidoreductases**
- **EC 2. Transferases**
- **EC 3. Hydrolases**
- **EC 4. Lyases**
- **EC 5. Isomerases**
- **EC 6. Ligases**



EC 1. Oxidoreductases

- **EC 1. Oxidoreductases :catalyze the transfer of hydrogen or oxygen atoms or electrons from one substrate to another,**
- **AH_2+B ⟶ A + BH_2**

Oxidases :tyrosinase, Uricase

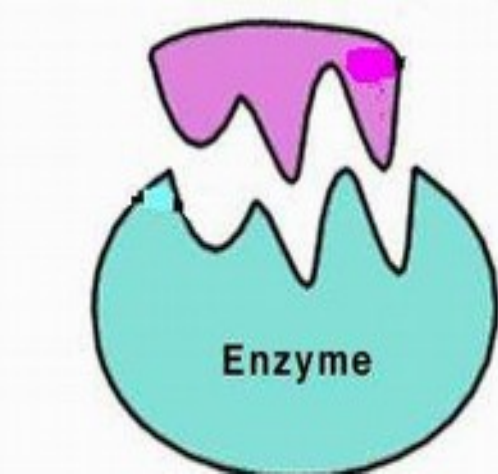
Anaerobic Dehydrogenases : Malate dehydrgenase, Lactate dehydrogenase

Hydroperoxidases :Peroxidase, Catalase

Aerobic Dehydrogenases : Xanthine oxidase

Oxygenases : Tryptophan oxygenase

Hydroxylase : Phenylalanine hydroxylase



EC 2. Transferases

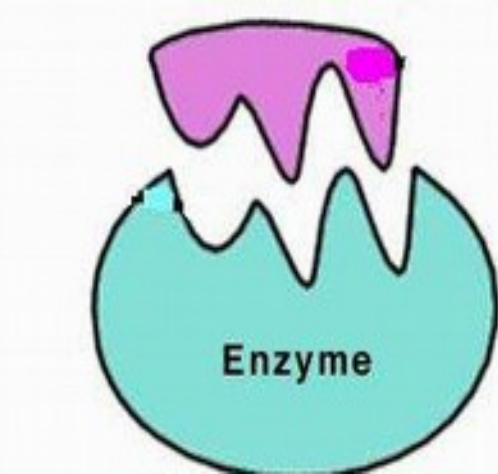
- **EC 2. Transferases – catalyze group transfer reactions, excluding oxidoreductases (which transfer hydrogen or oxygen and are EC 1). These are of the general form:**
- A-X + B ↔ BX + A

Transphosphorylase : Hexokinase

Trans glycosidase : phosphorylase

Transacylase : Choline acetyl transferase

Transaminase : Aspartate aminotransferase



EC 3. Hydrolases

- **EC 3. Hydrolases – catalyze hydrolytic reactions. Includes *lipases, esterases, peptidases/proteases. These are of the general form:***
- $A\text{-}X + H_2O \leftrightarrow X\text{-}OH + HA$

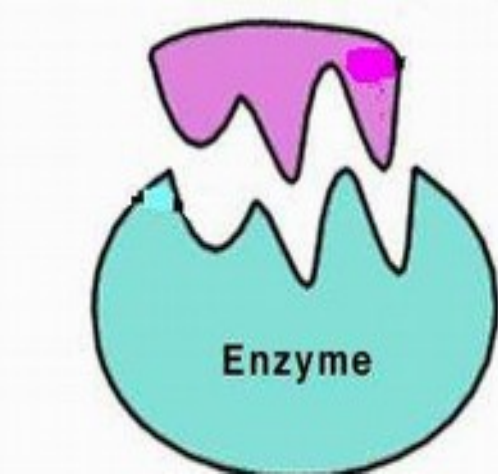
Enzyme acting on glycosyl compounds: beta galactosidase

Acting on peptide bond: Pepsin, Chymotrypsin

Esterases: Lipases, Phosphatases

Amidases: Urease, Arginase

Hydrolytic Deaminase



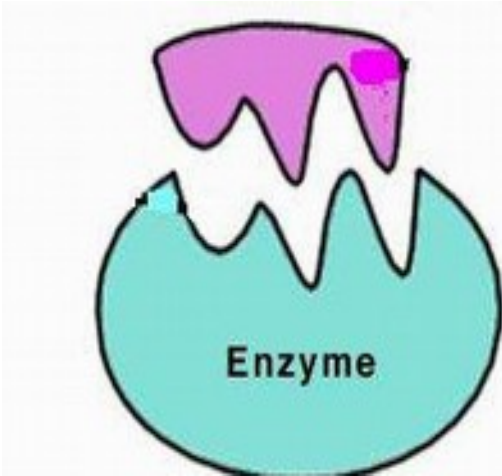
EC 4. Lyases

- **EC 4. Lyases – catalyze non-hydrolytic (covered in EC 3) removal of functional groups from substrates, often creating a double bond in the product; *or the reverse reaction, ie, addition of function groups across a double bond.***
- ***A-B + X- Y → AX + BY***

Decarboxylases

Aldolases in the removal direction

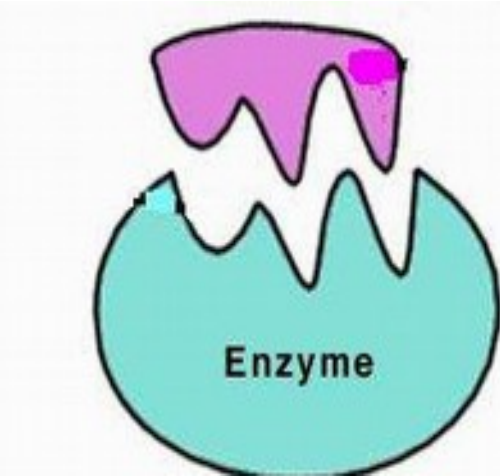
Synthases in the addition direction.



EC 5. Isomerases

- **EC 5. Isomerases – catalyzes isomerization reactions, including racemizations and cis-tran isomerizations.**

- **A ⟶ A’**



EC 6. Ligases

- **EC 6. Ligases -- catalyzes the synthesis of various (mostly C-X) bonds, coupled with the breakdown of energy-containing substrates, *usually ATP***
- *Formation of C-S Bond:*

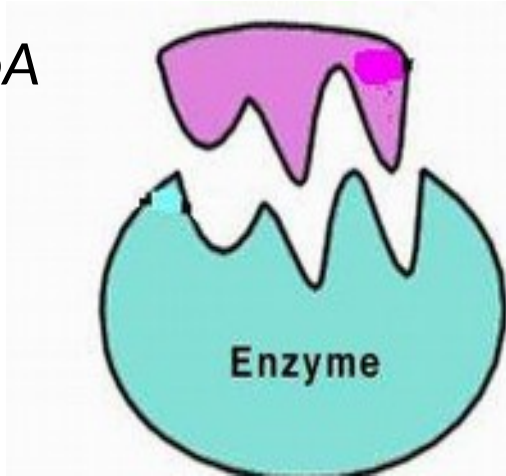
GTP + Succinate + CoA → *gdp + Pi + Succinyl CoA*

- *Formation of C-N Bond:*

ATP + L-Glutamate + NH_4 → *ADP + Orthophosphate + L- Glutamine*

- *Formation of C-C Bond:*

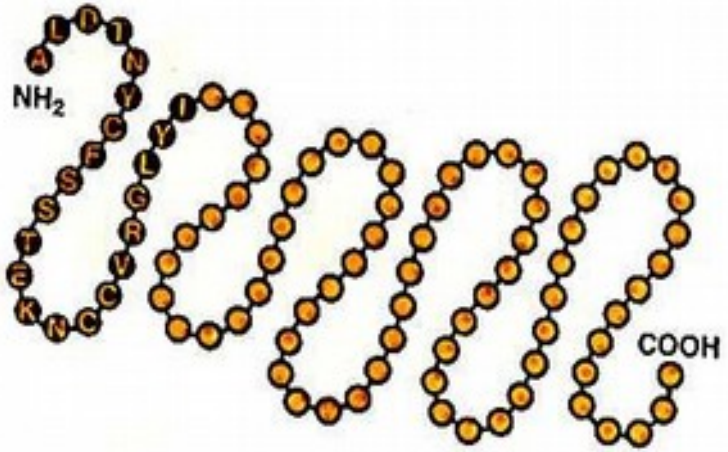
ATP + Acetyl Co A + CO_2 → *ADP +Pi + Malonyl CoA*

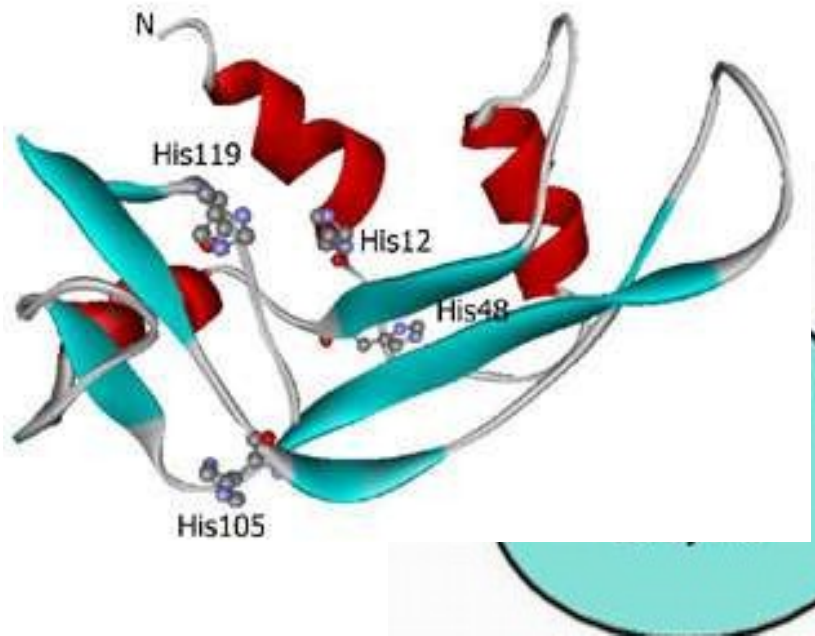


Active Site

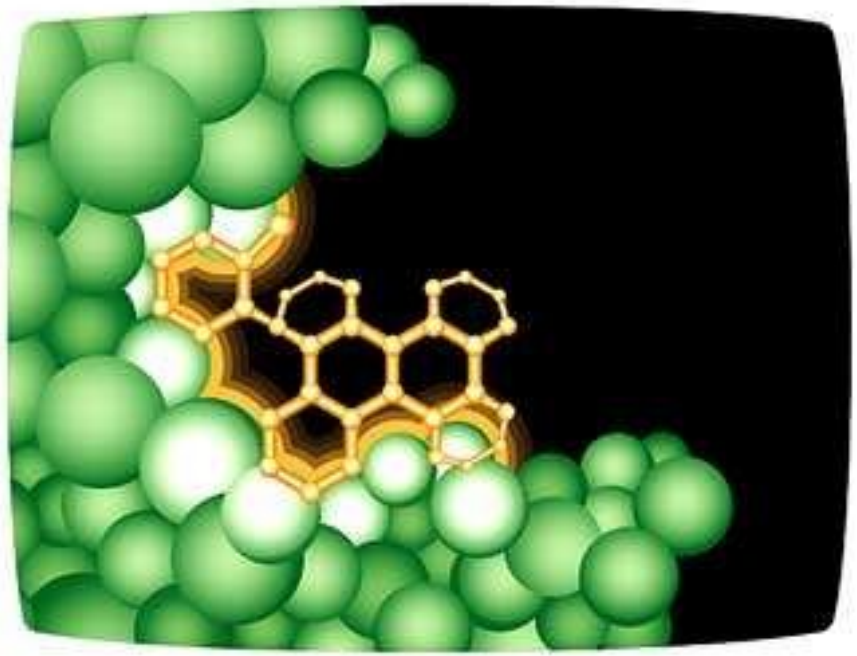
The enzyme binds to the substrates by its **active site**

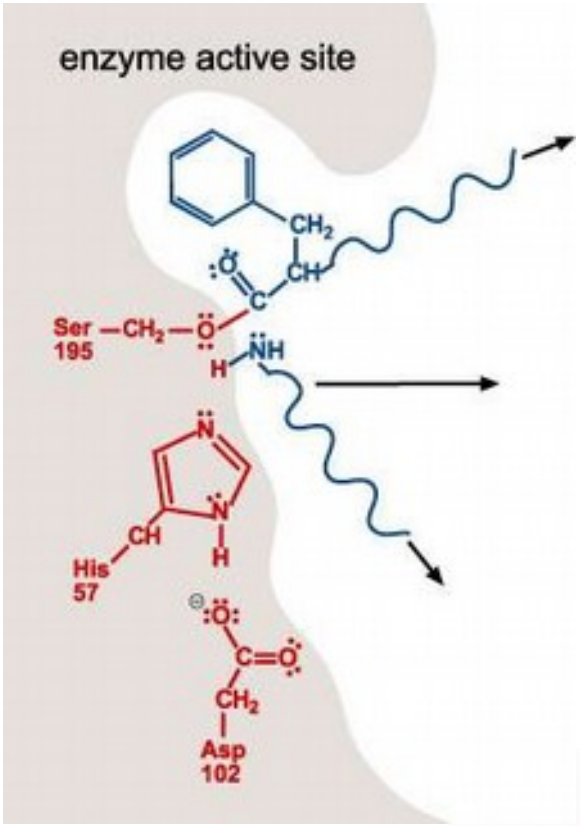
The active site is a pocket formed by the folding of the protein where the substrates bind.



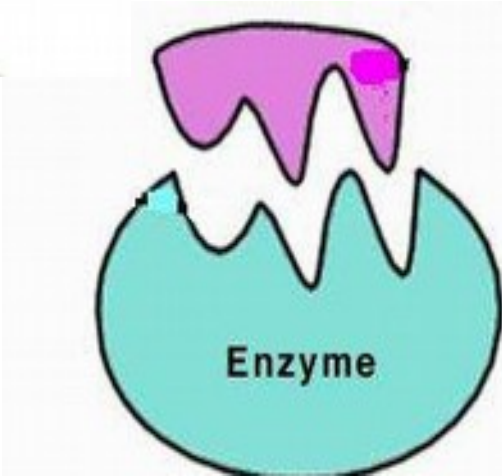


Active Site





The active site involves a small number of key residues that actually bind the substrates.
The rest of the protein structure is needed to maintain these residues in position.



Active Site

• Active sites usually contains –OH gp of serine, Phenolic gp of tyrosine, sulphydryl gp of cysteine or imidazolyl gp of histidine.

• Existence of active site is due to tertiary structure of protein resulting in 3 dimensional conformation.

• Active site is made up of amino acids which are far from each other in linear sequence. Lysoenzyme- 129AA's , AA at 35,52,62,63 & 101 – Active.

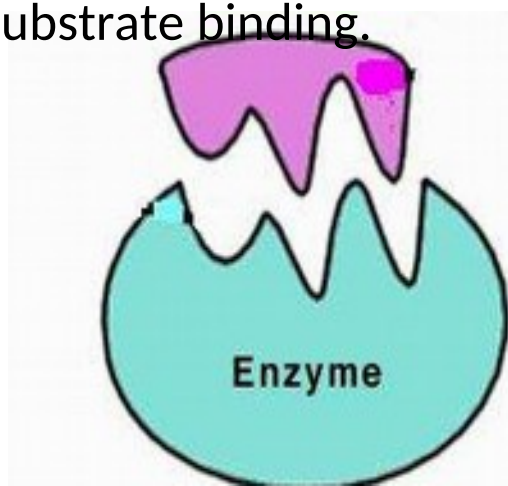
• They are in the form of clefts, crevices, pockets.

• Active site are not RIGID, it IS flexible to promote specific substrate binding.

• Active site can be Substrate binding site, Catalytic site

•Substrate binds with weak non covalent bonds

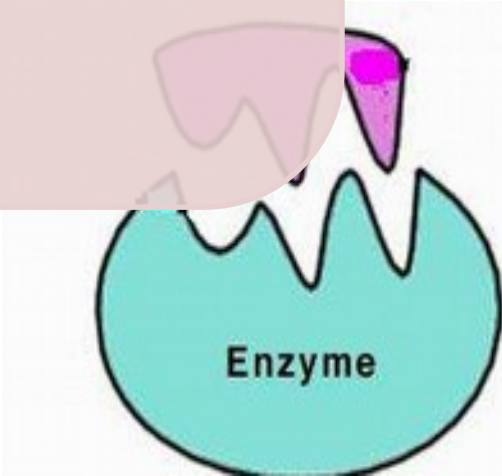
•Enzyme specificity due to active site.



ENZYME SPECIFICITY

STEREO SPECIFICITY

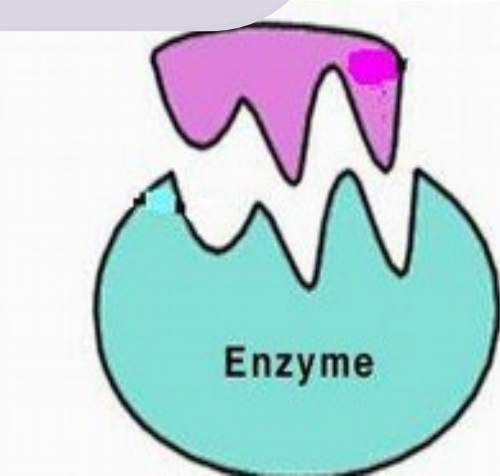
- Enzymes act on only one isomer
- Glucokinase acts on D-glucose only
- It is due to 3 distinct region of substrate molecule specifically binding with 3 complimentary region on the surface
- Isomerase donot exhibit stereo specificity.



ENZYME SPECIFICITY

REACTION SPECIFICITY

- Same substrate undergoes different types of reaction each catalyzed by different enzymes

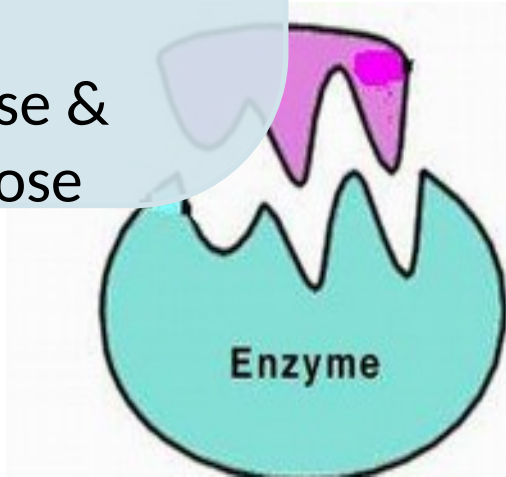


ENZYME SPECIFICITY

Substrate specificity

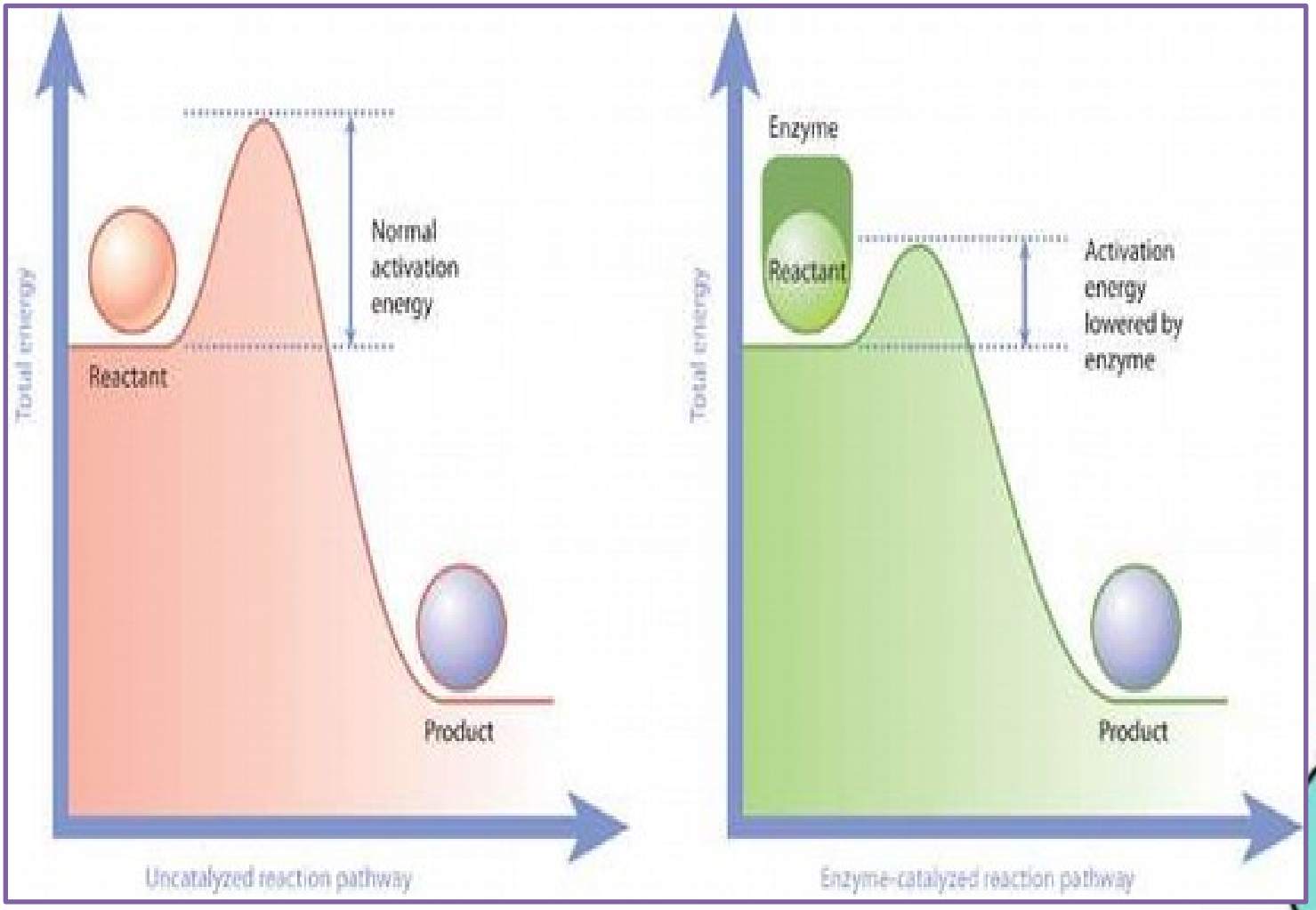
- Absolute: Enzymes act only on one sbstrate
- Relative: Some enzymes act on structurally related substances eg: trypsin
- Broad: Some enzymes act on closely related substances

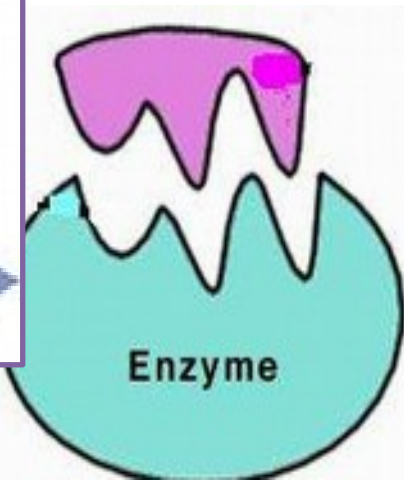
  Hexokinase acts on glucose & fructose but not on galactose



Mechanismm of enzyme action

1. Enzyme lower activation energy:





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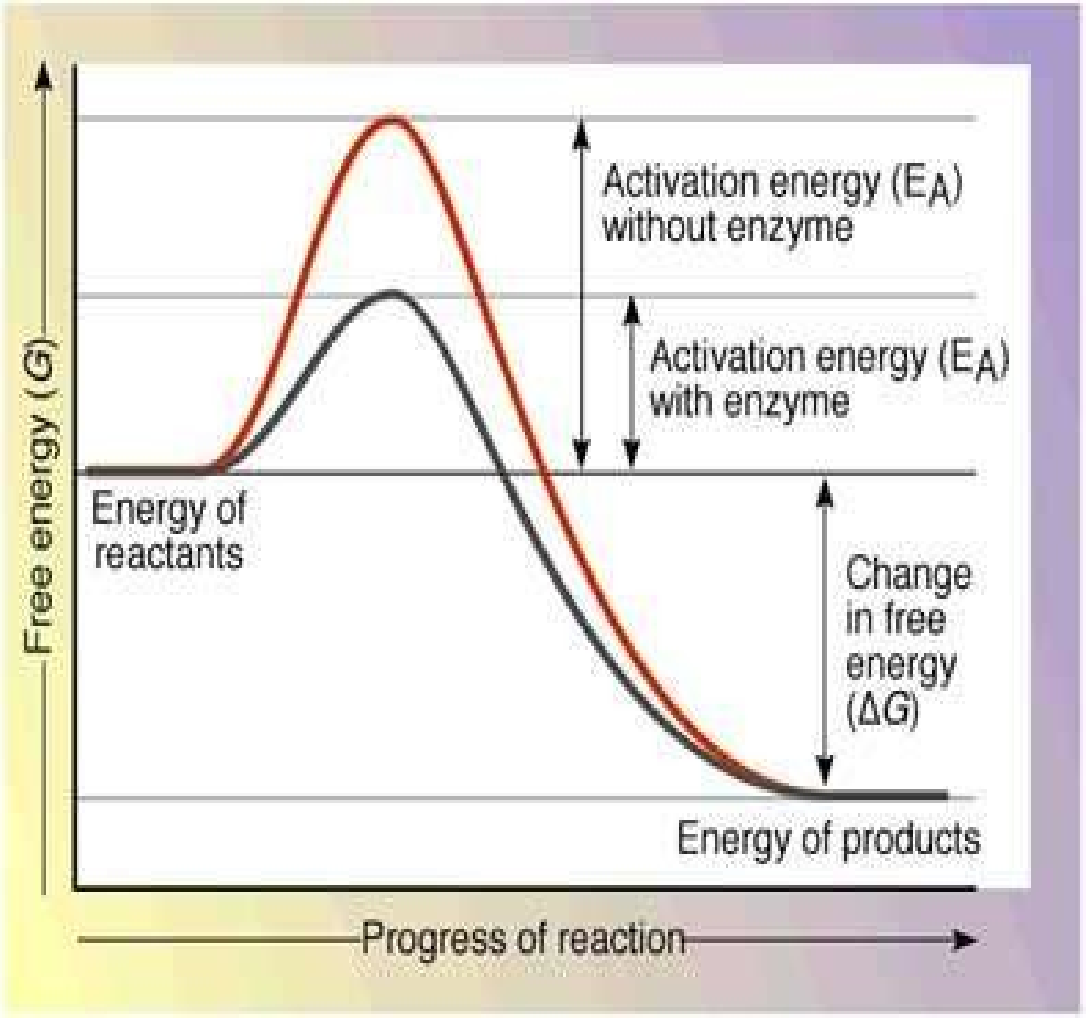
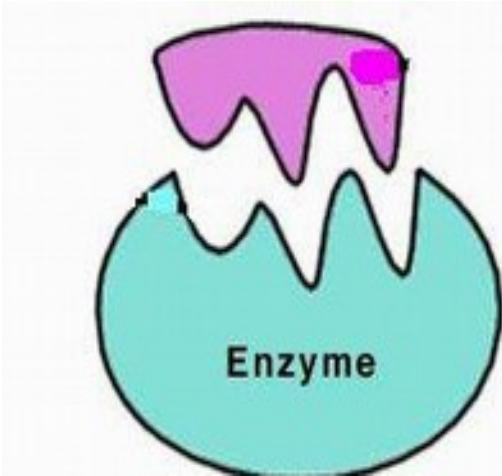


Enzymes donot alter the equilibrium constant, they only enhance velocity of reaction.



Mechanismm of enzyme action

2. Enzyme substrate complex formation:

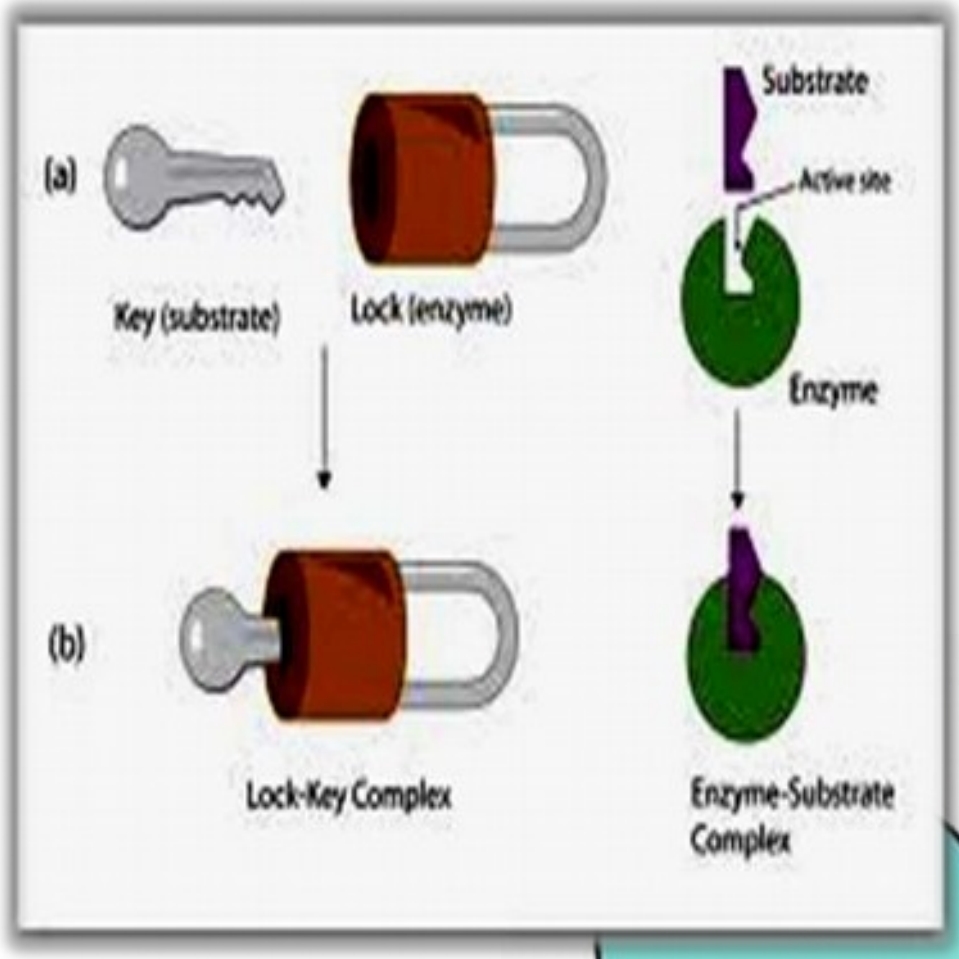
- **Lock & key model enzyme/ Fisher template theory**

•According to this theory the structure or conformations of enzymes are rigid

•Substrate fits to binding active site

•Assumes that active site is rigid or preshaped where only substrate can bind

•Fails to explain many facts of enzymatic reaction like allosteric modulation.



Mechanismm of enzyme action

2. Enzyme substrate complex formation:

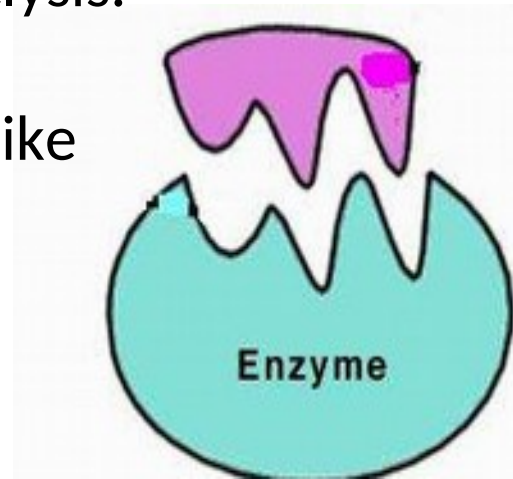
- **Induced fit theory / koshland's model**

•According to this theory the active site is not rigid or preshaped

• Intearction of substrate with enzyme induces a fit or a conformational change in enzyme resulting in formation of a strong substrate binding site.

•Due to induced fit the appropriate AA of enzyme is repositioned to form active site & bring about catclysis.

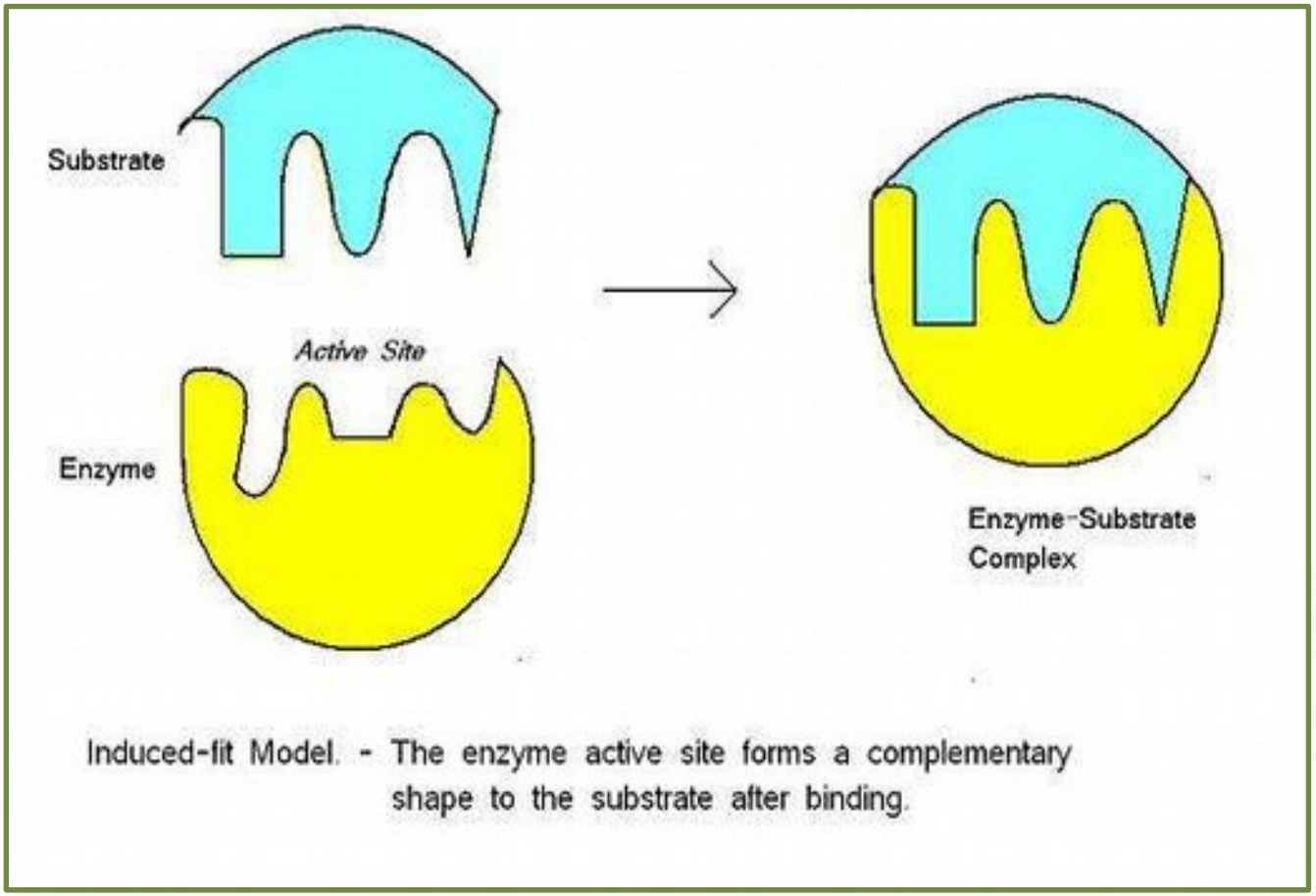
•Fails to explain many facts of enzymatic reaction like allosteric modulation.



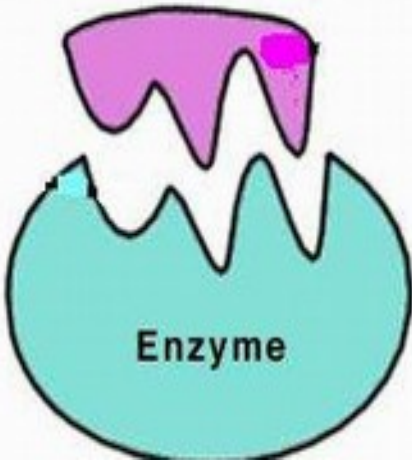
Mechanismm of enzyme action

2. Enzyme substrate complex formation:

- **Induced fit theory / koshland's model**



Induced-fit Model. - The enzyme active site forms a complementary shape to the substrate after binding.



Mechanism of enzyme action

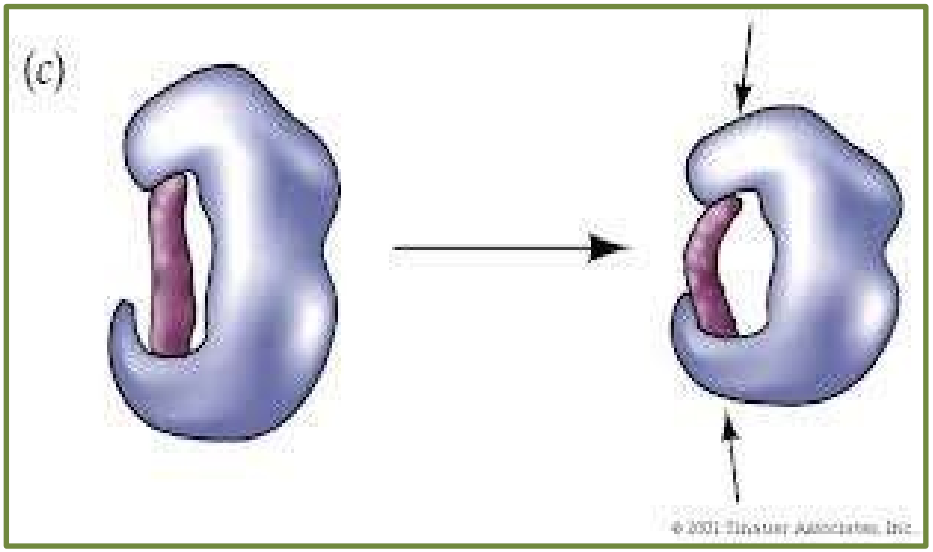
2. Enzyme substrate complex formation:

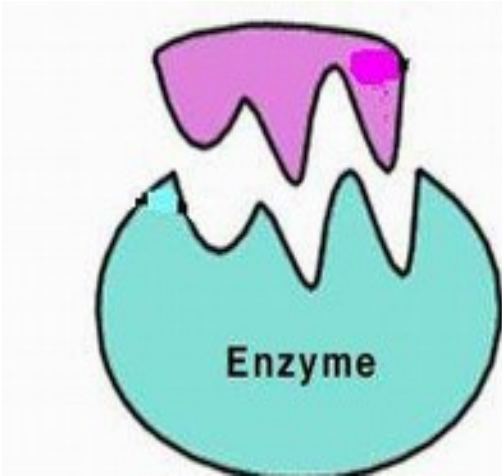
- **Substrate strain theory**

•According to this theory the substrate is strained due to the induced conformation change in the enzymes

• When substrate binds to the preformed active site the enzyme induces a strain to the substrate .

•The strained substrate leads to formartion of product.

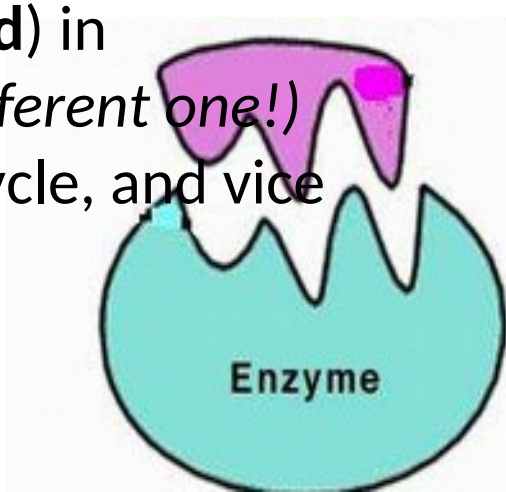




Mechanism of enzyme Catalysis

Acid-base catalysis

- Very often-used mechanism in enzyme reactions, e.g., hydrolysis of ester/ peptide bonds, phosphate group reactions, addition to carbonyl groups, etc.
- In active site of an enzyme a no.of AA side chain can similarly act as proton donor or acceptor -
  - **donating a proton** (act as a ***general acid***), or
  - **accepting a proton** (abstract a proton, act as a ***general base***)
- If a group *donates* a proton (acts as a **general acid**) in chemical mechanism, it has to *get a proton (a different one!) back* (act as a **general base**) by end of catalytic cycle, and vice versa

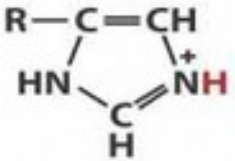
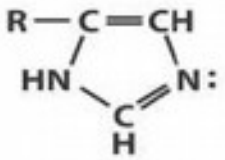


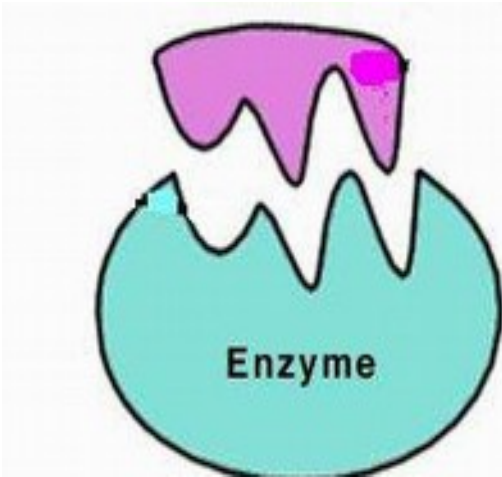
Mechanism of enzyme Catalysis

• These groups are precisely positioned in an enzyme active site to allow proton transfers providing rate enhancements

• Protein functional groups that can function as general acid/base catalysts:

e.g. His imidazole, α-amino group, α-carboxyl group, thiol of Cys, R group carboxyls of Glu, Asp, aromatic OH of Tyr, etc

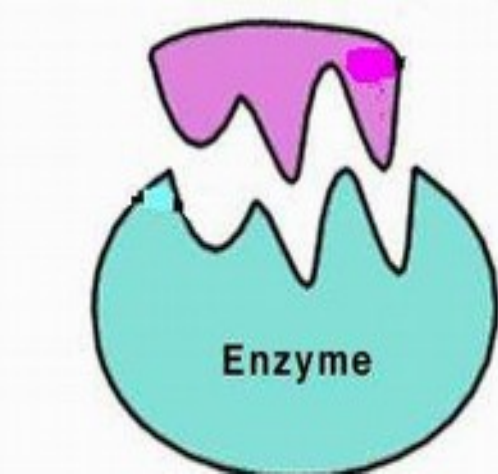
Amino acid residues	General acid form (proton donor)	General base form (proton acceptor)
Glu, Asp	R—COOH	R—COO⁻
Lys, Arg	R—$\overset{+}{\underset{H}{\overset{H}{N}}}$H	R—$\ddot{N}H_2$
Cys	R—SH	R—S⁻
His		
Ser	R—OH	R—O⁻
Tyr		

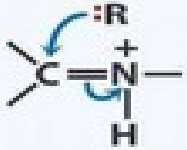


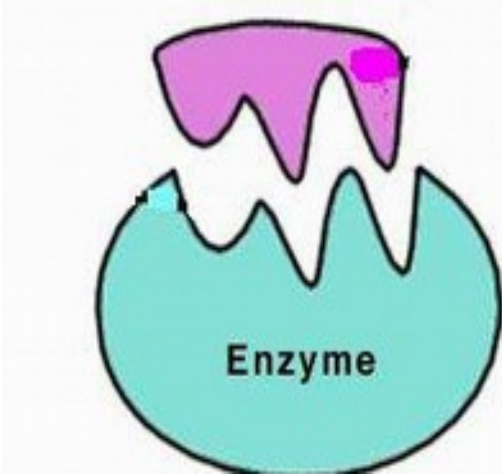
Mechanism of enzyme Catalysis

Covalent catalysis

- Rate enhancement by the **transient formation of a catalyst-substrate covalent bond**
- The modified enzyme becomes a reactant
- Covalent catalysis introduces a new reaction pathway whose activation energy is lower & is faster
- Chemical modification of enzyme is transient on completion of the reaction the enzyme returns to its original unmodified state
- It is common with-
  - Serine proteases: acyl-serine intermediate
  - Cysteine proteases: acyl-cystein intermediate



Nucleophiles	Electrophiles
 Negatively charged oxygen (as in an unprotonated hydroxyl group or an ionized carboxylic acid)	 Carbon atom of a carbonyl group (the more electronegative oxygen of the carbonyl group pulls electrons away from the carbon)
 Negatively charged sulfhydryl	 Pronated imine group (activated for nucleophilic attack at the carbon by protonation of the imine)
 Carbanion	 Phosphorus of a phosphate group
 Uncharged amine group	 Proton
 Imidazole	
 Hydroxide ion	



Mechanism of enzyme Catalysis

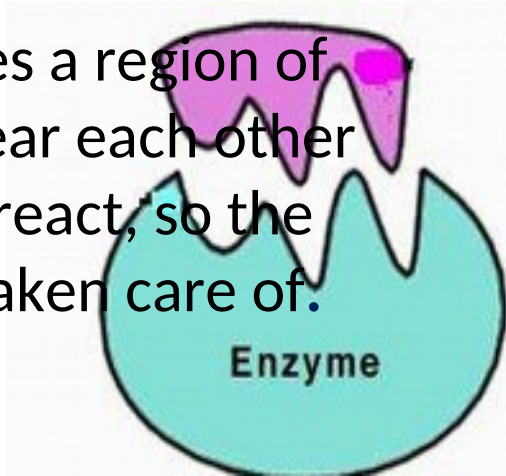
Proximity Effect

- **For molecules to react they must come within the bond forming distance of one another**
- **High concentration – more frequently encounter, more is rate of reaction**

Proximity: Reaction between bound molecules doesn't require an improbable collision of 2 molecules -- they're already in "contact" (increases the local concentration of reactants)

Orientation:

When enzyme binds to substrate molecule it creates a region of high local substrate conc**.** Reactants are not only near each other on enzyme, they're oriented in optimal position to react, so the improbability of colliding in **correct orientation** is taken care of.

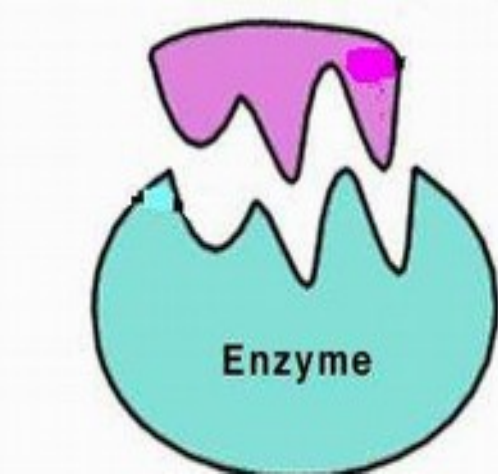


Mechanism of enzyme Catalysis

Proximity Effect

- **Example**

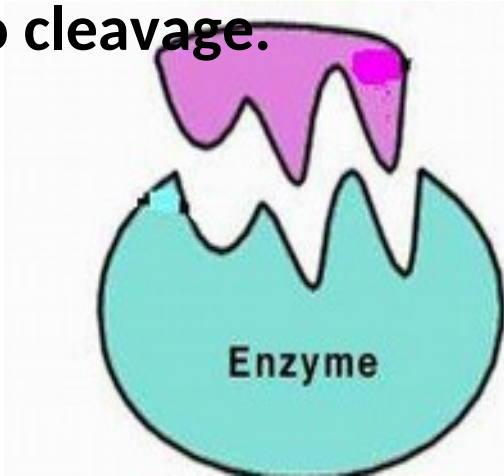
- **If a phosphate group is to be transferred from ATP to glucose**
- **The probability of collision is low in free solution.**
- **Chances of ATP & sugar colliding with other molecules is possible**
- **If ATP & glucose bind separately & tightly to the third component i.e the enzyme's active site, the two components can react with each other more efficiently.**



Mechanism of enzyme Catalysis

Substrate Strain:

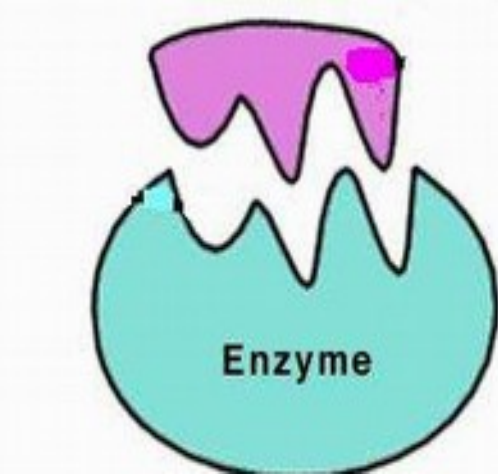
- Strain in substrate induce conformational change in enzyme.
- During the course of strain induction the energy level of substrate is raised leading to a transition state
- Enzymes that catalyze the lytic reactions, involve breaking a covalent bond typically bind their substrate in a conformation slightly unfavorable for the bond that will undergo cleavage
- This resulting strain stretches or distorts the targeted bond, weakening it and making it more vulnerable to cleavage.



Mechanism of enzyme Catalysis

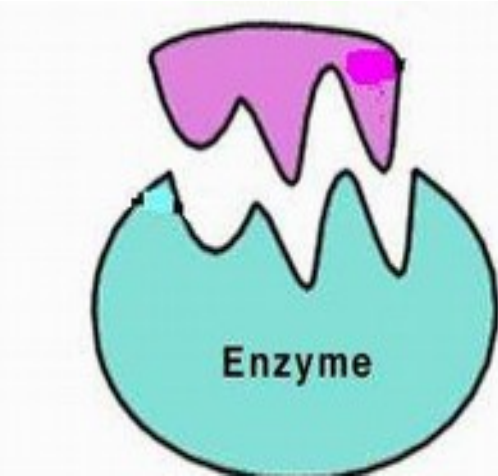
Entropy Effect:

- **Entropy: extent of disorder in a system**
- **Enzymes bring about a decrease in the entropy of reactants to come closer to enzyme & thus increase the rate of reaction.**



Factors affecting enzyme activity

- Temperature
- pH
- Product Concentration
- Effect of activators
- Effect of light & radiation
- Concentration of Enzyme
- Concentration of Substrate



Effect of temperature

• The temperature of a system is to some extent a measure of the kinetic energy of the molecules in the system. Thus the lower the kinetic energy, the lower the temperature of the system and , likewise, the higher the kinetic energy, the greater the temperature of the system.

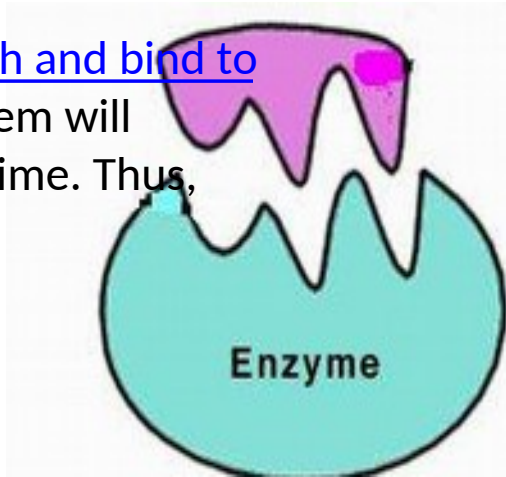
Increases in the temperature of a system results from increases in the kinetic energy of the system. This has several effects on the rates of reactions.

1) More energetic collisions

When molecules collide, the kinetic energy of the molecules can be converted into chemical potential energy of the molecules.As the temperature of a system is increased it is possible that more molecules per unit time will reach the activation energy. Thus the rate of the reaction may increase.

2) The number of collisions per unit time will increase.

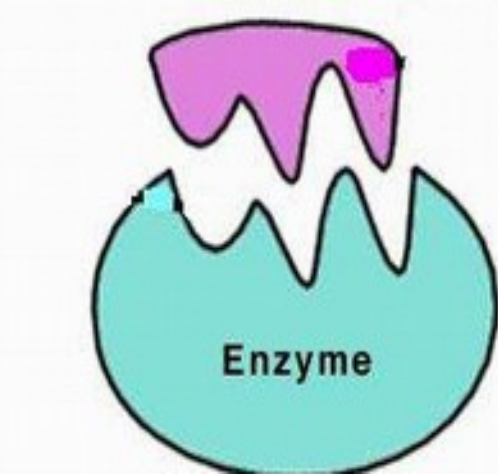
In order to convert substrate into product, enzymes must collide with and bind to the substrate at the active site. Increasing the temperature of a system will increase the number of collisions of enzyme and substrate per unit time. Thus, within limits, the rate of the reaction will increase.



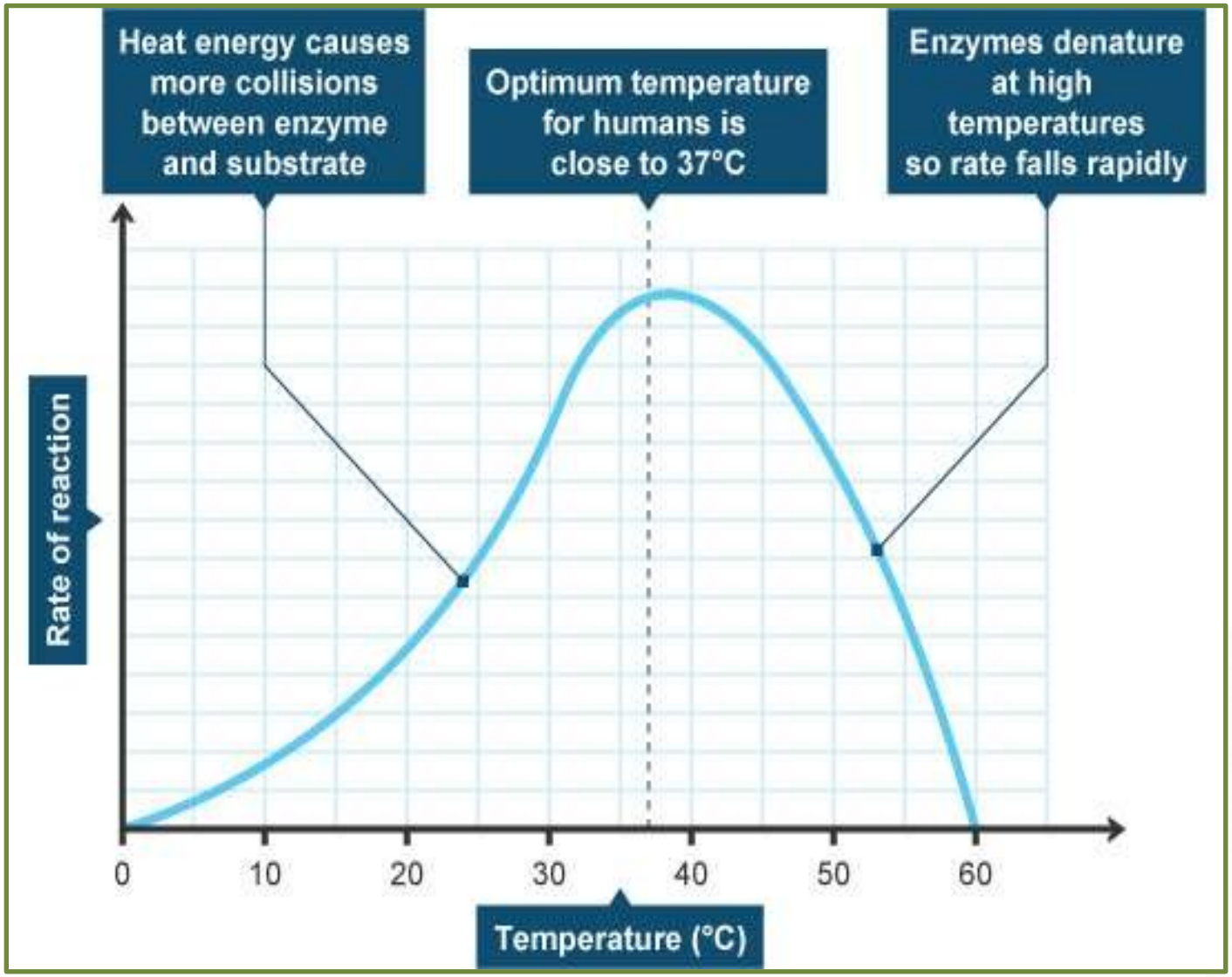
Effect of temperature

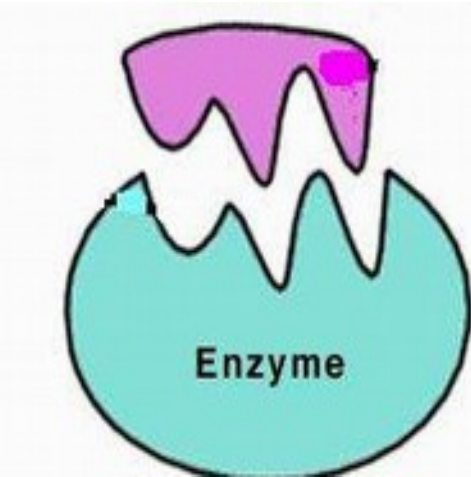
3) The heat of the molecules in the system will increase.
As the temperature of the system is increased, the internal energy of the molecules in the system will increase. Some of this heat may be converted into chemical potential energy. If this chemical potential energy increase is great enough some of the weak bonds that determine the three dimensional shape of the active proteins many be broken. This could lead to a **thermal denaturation** of the protein and thus inactivate the protein. Thus too much heat can cause the rate of an enzyme catalyzed reaction to decrease because the enzyme or substrate becomes denatured and inactive

Temperature Co-efficient: Q_{10} Increase in enzyme velocity when temperature is increased by 10^0C. For majority of enzyme Q_{10} is between 0- 40^0C.



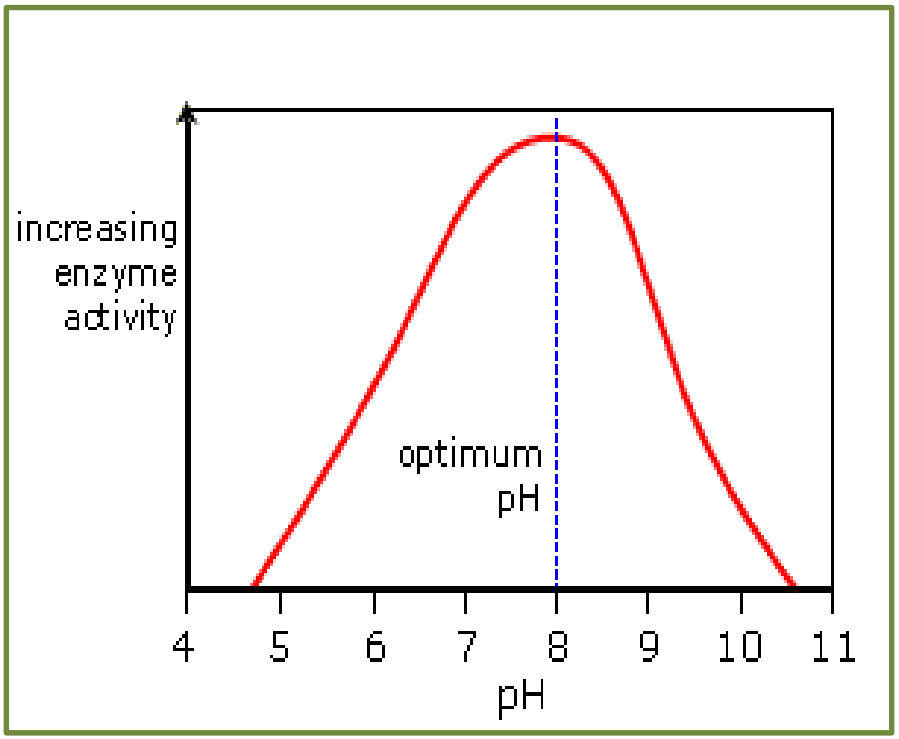
Effect of temperature

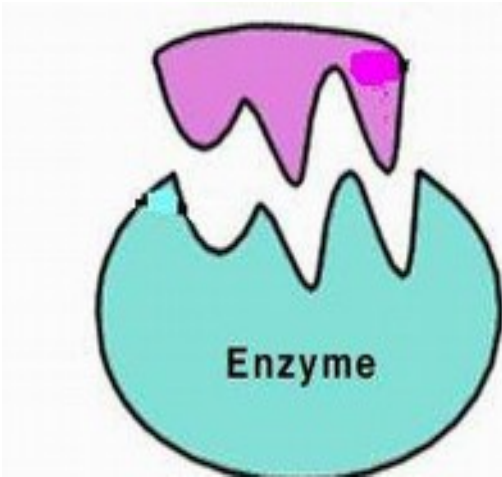




Effect of pH

- Each enzyme has an optimum pH at which the velocity is maximum.
- Increase in H^+ concentration influences the activity
- Below the optimum pH enzyme activity is lower & above the optimum pH enzyme is inactive
- Most enzyme have an optimum pH of 6-8



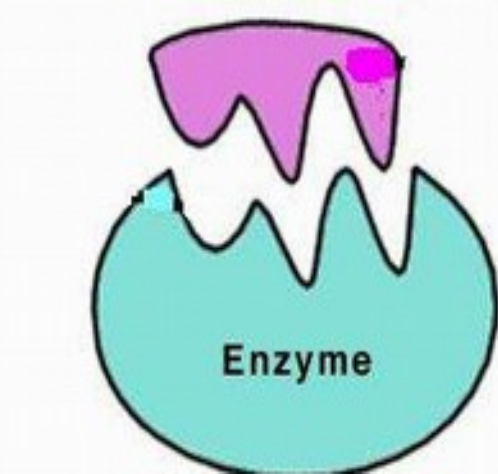


Effect of Product Concentration

- Accumulation of product decreases the velocity
- Product combines with active site & forms loose complex thereby increase the velocity

Effect of Light & Radiation

- Exposure to UV, beta, gamma, X-rays inactivates certain enzymes due to formation of peroxides



Effect of activators

Some enzymes requires inorganic metal cations Mg+2, Mn+2, Zn+2, Ca+2, Cu+2, Na+, K+ for their activity

Mechanism of activators:

-Combining with substrate

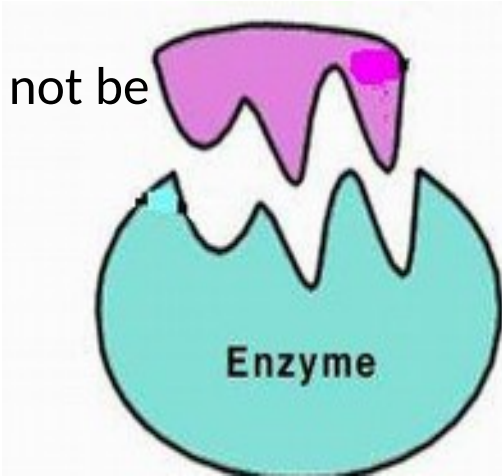
- Formation of ES-Metal Complex

- Direct Participation in reaction & bringing a conformational change in the enzyme

Two categories of enzyme:

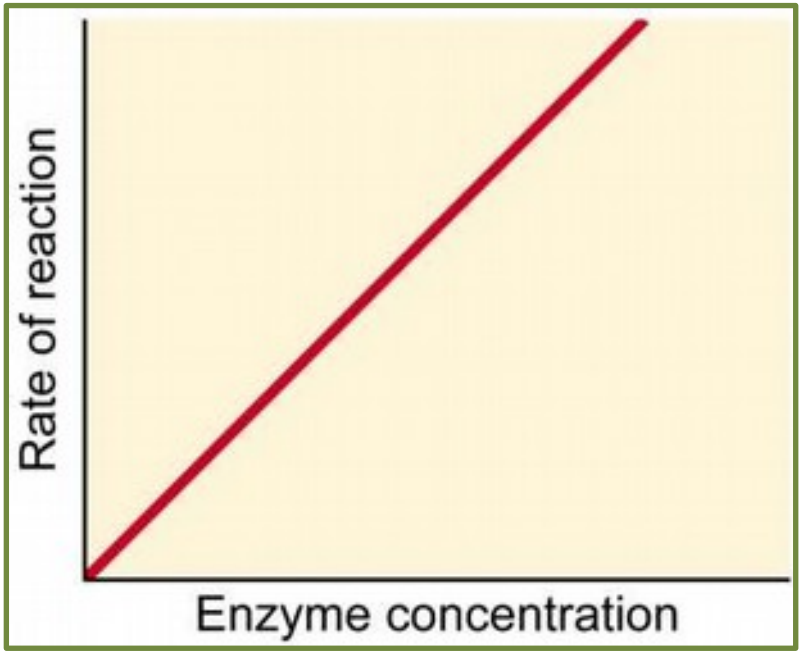
1. Metal activated enzyme: Metal not tightly held by the enzyme & can be exchanged easily

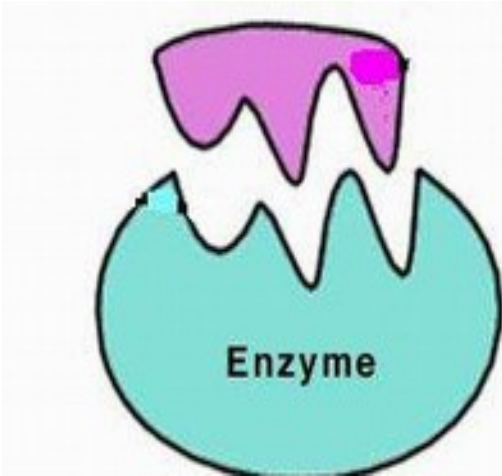
2. Metalloenzyme: Metal tightly held by the enzyme & can not be exchanged easily



Effect of Concentration of enzyme

- As the concentration of enzyme is more the velocity of reaction proportionally increases
- Increase in active site
- This property is used in determining the serum enzymes for diagnosis of disease
- Using known volume of serum keeping other factors constant enzymes can be assayed



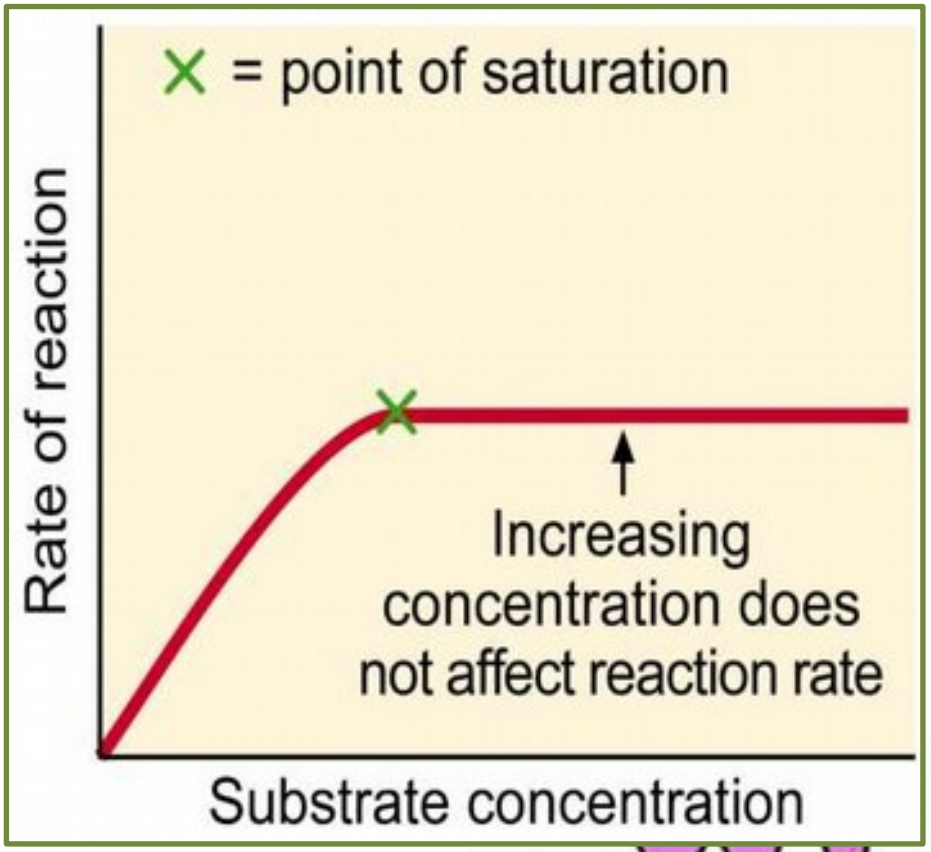


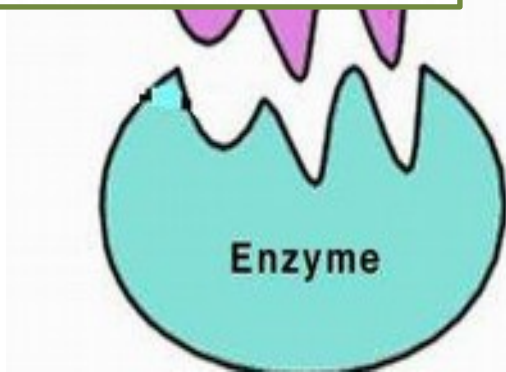
Effect of Concentration of substrate

• Increase in substrate concentration increases the velocity of reaction within the limited range of substrate level

• As the substrate concentration increases more & more active sites of the enzymes will be used for formation of ES complex

• The reaction rate will be more





Significance of K_M

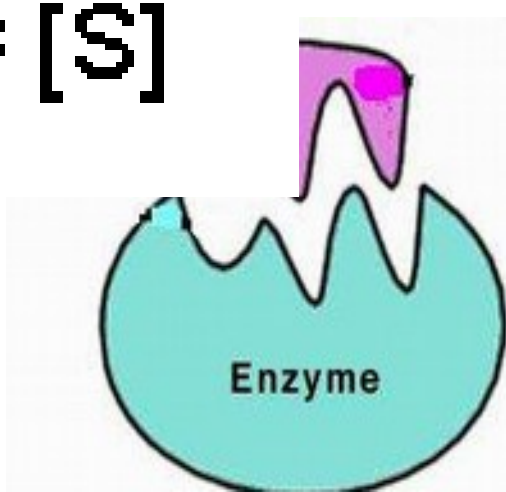
When V= ½ Vmax, what is [S]?

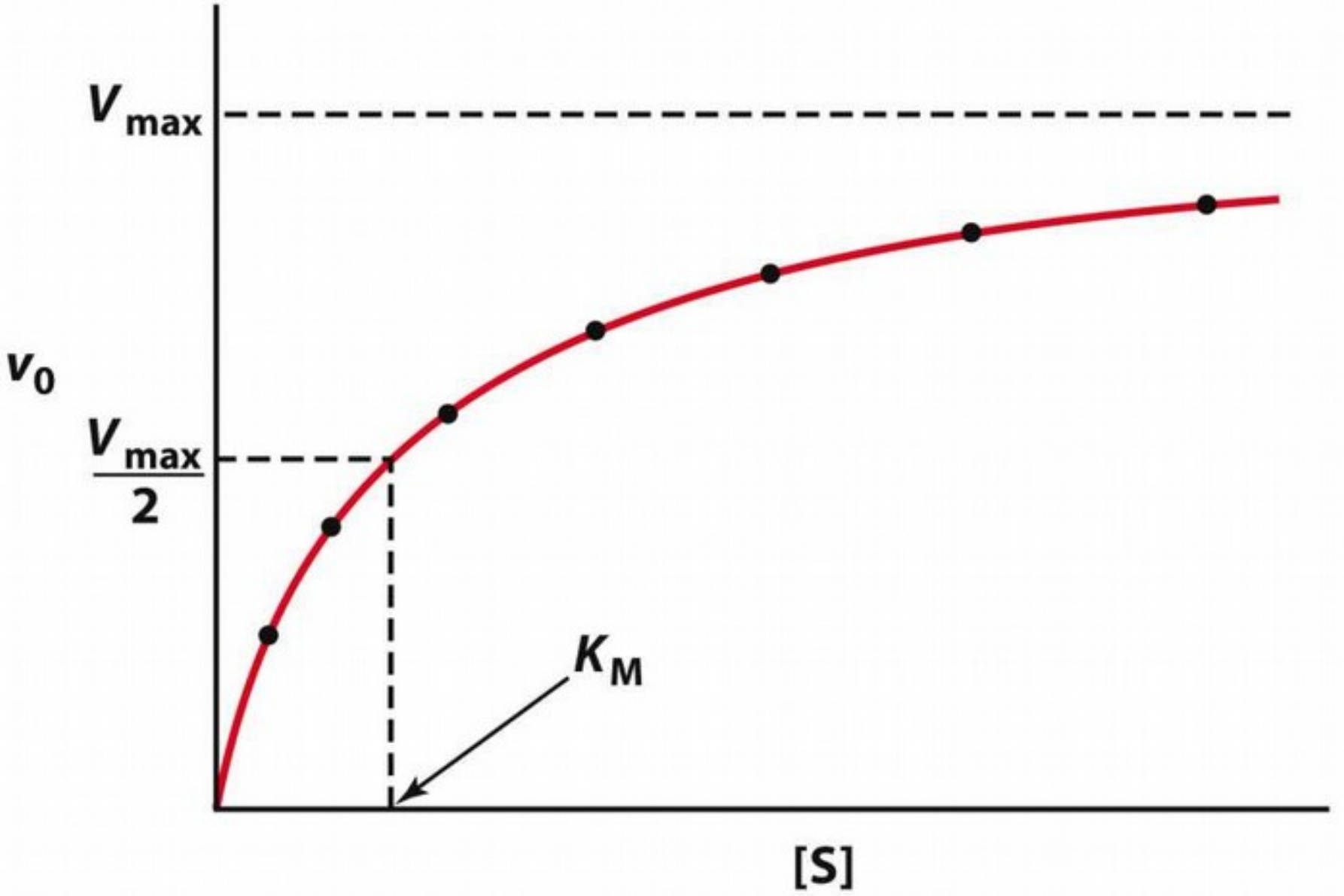
$$\frac{V_{max}}{2} = \frac{V_{max}[S]}{K_M + [S]}$$

$$K_M + [S] = 2[S]$$

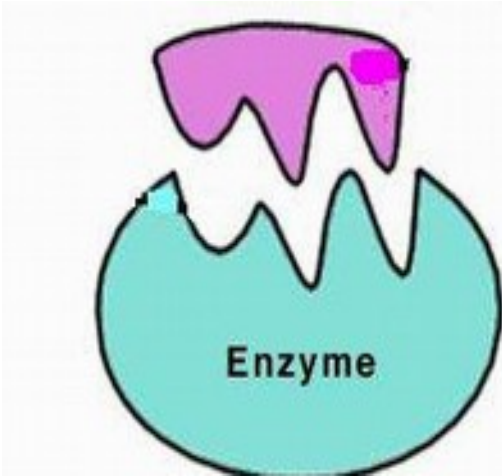
$$\frac{1}{2} = \frac{[S]}{K_M + [S]}$$

$$K_M = [S]$$

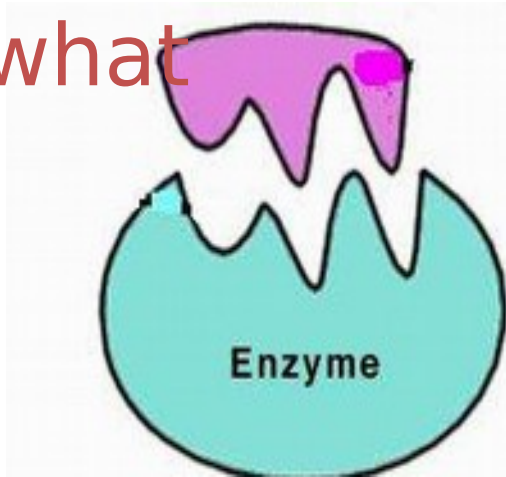




The K_M of an enzyme is the substrate concentration at which the reaction occurs at half of the maximum rate.



There are limitations in the quantitative (i.e. numerical) interpretation of this type of graph, known as a Michaelis plot. The V_{max} is never really reached and therefore V_{max} and hence K_M values calculated from this graph are somewhat approximate



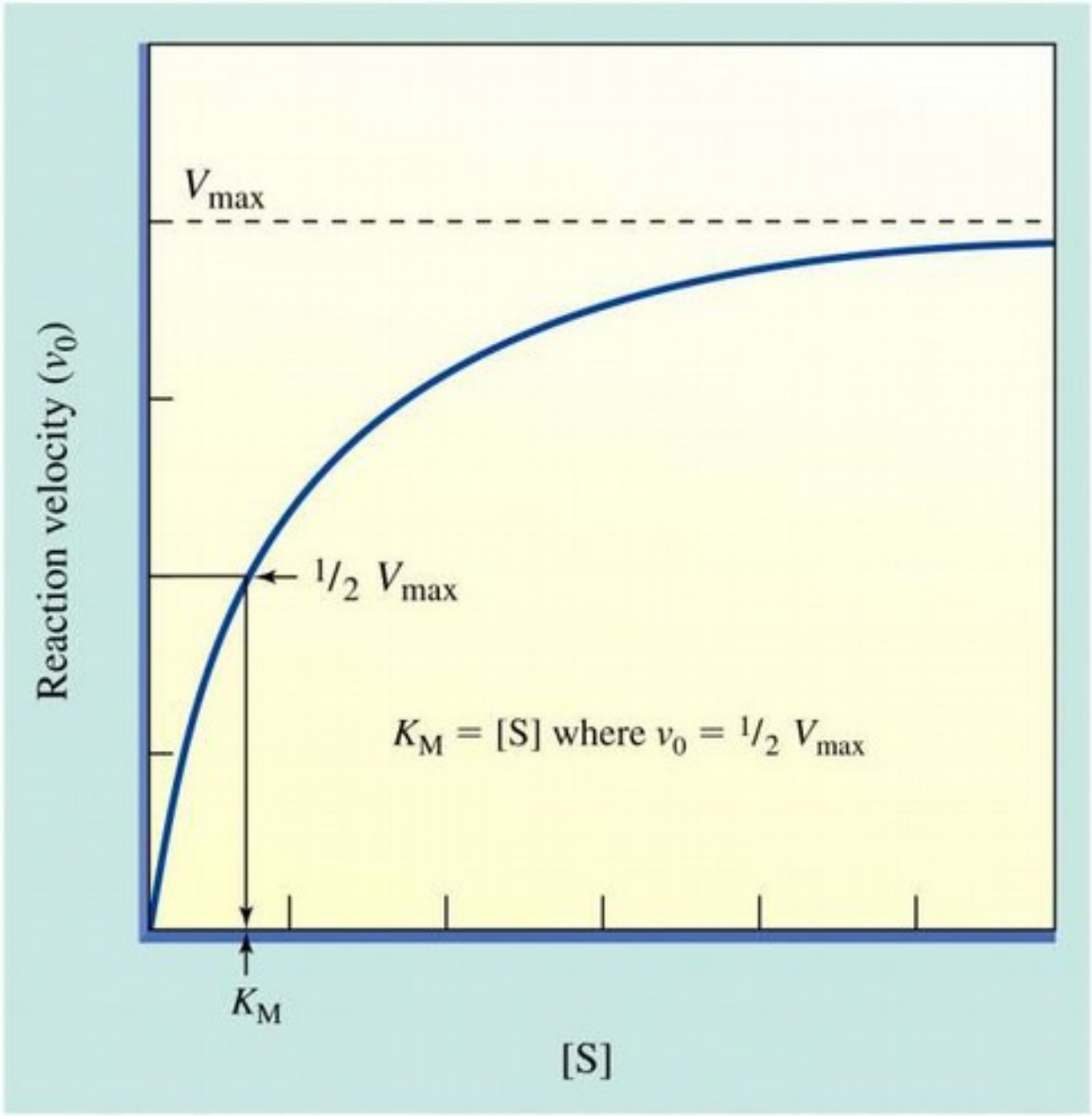
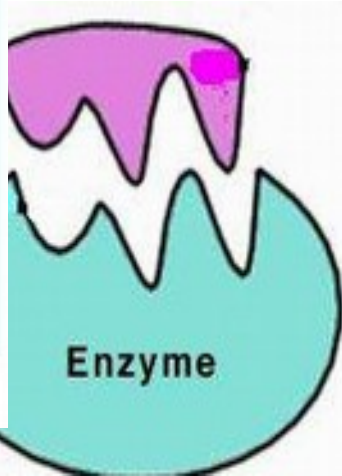
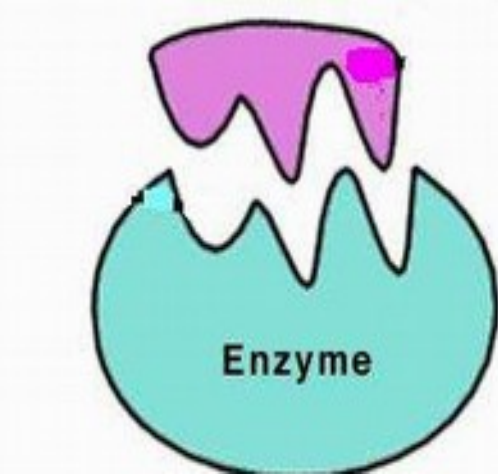


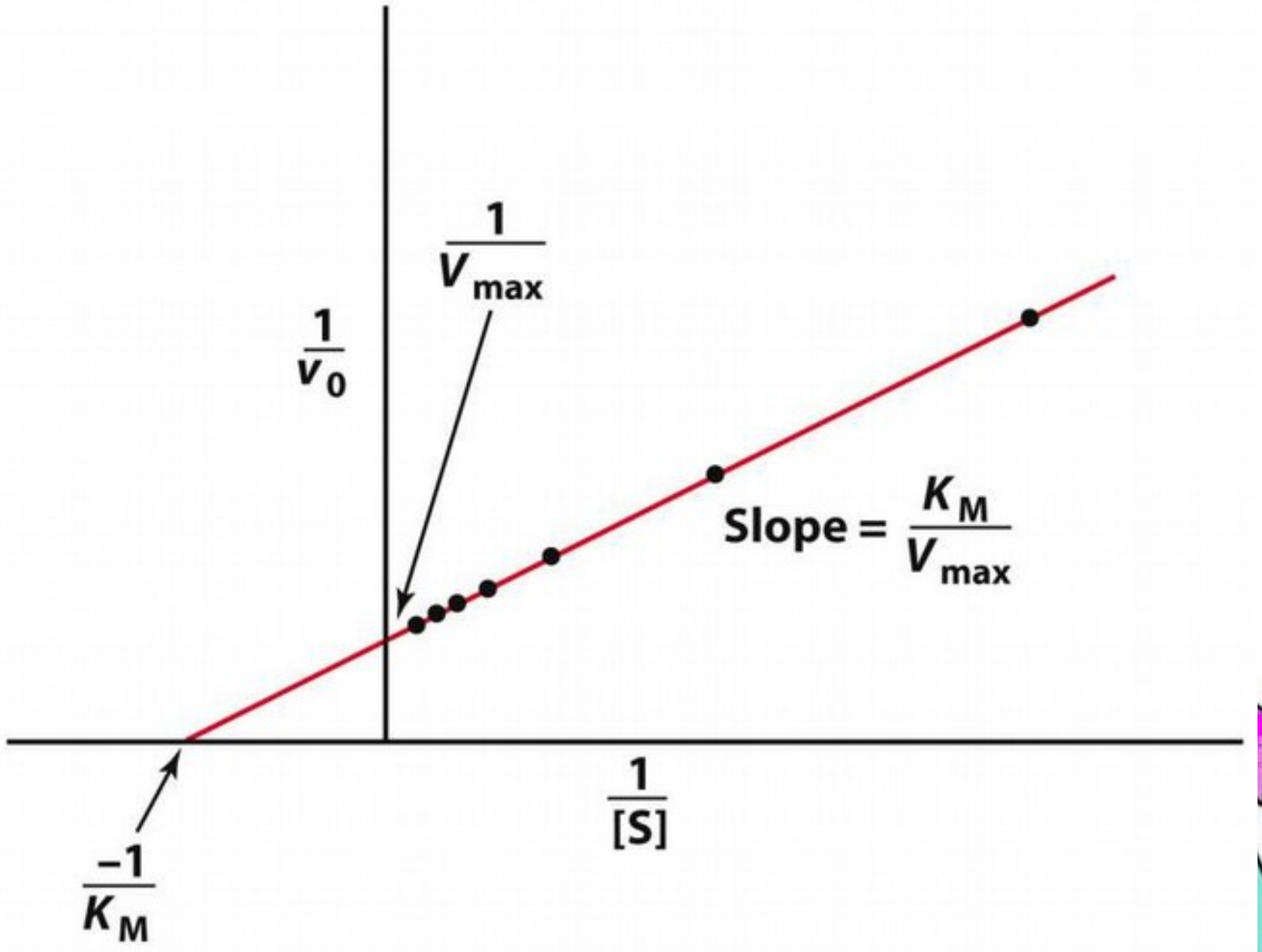
Figure 5-4 Concepts in Biochemistry, 3/e



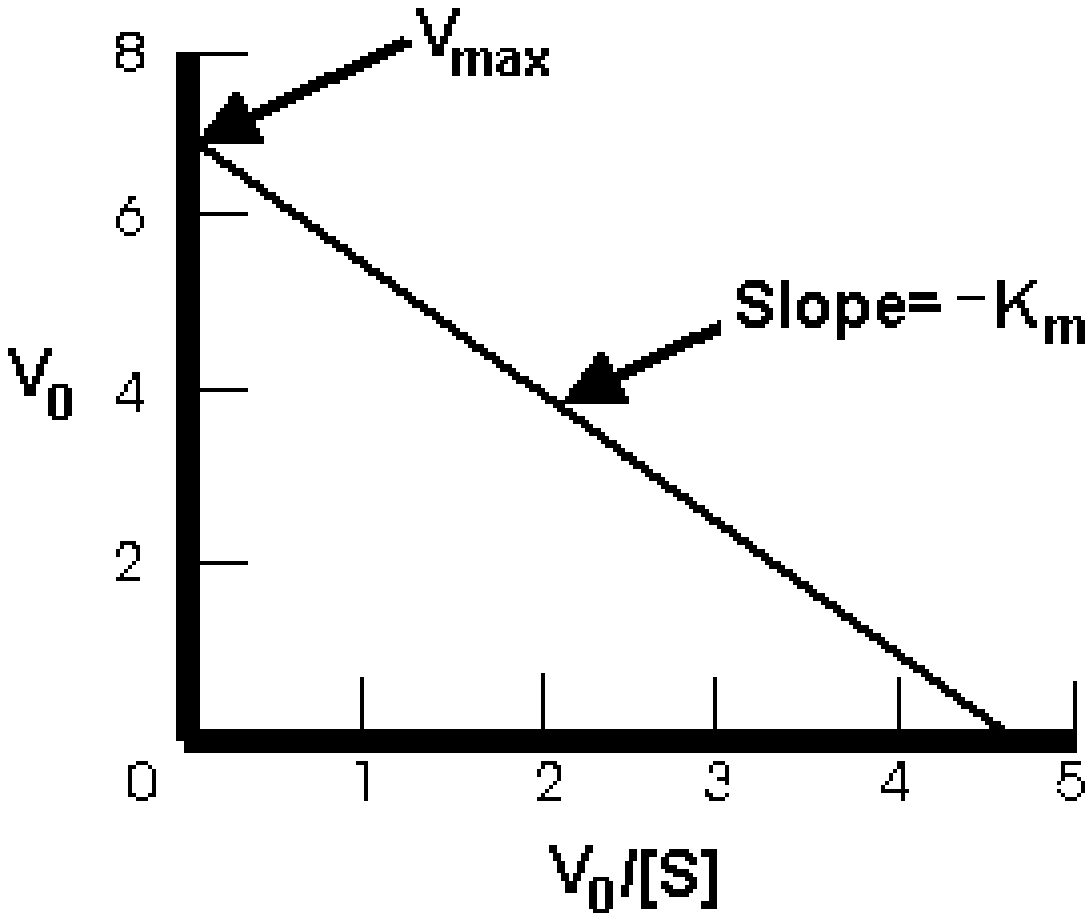
Lineweaver- Burk plot

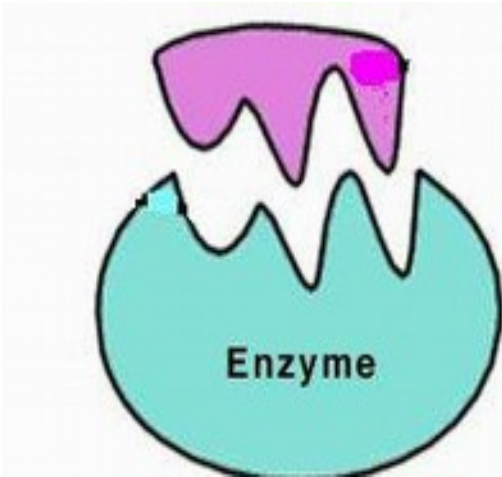
$$\frac{1}{V} = \frac{[S] + K_M}{V_{max}[S]} = \frac{[S]}{V_{max}[S]} + \frac{K_M}{V_{max}[S]} = \frac{1}{V_{max}} + \frac{K_M}{V_{max}} \cdot \frac{1}{[S]}$$





Eadie-Hofstee plot



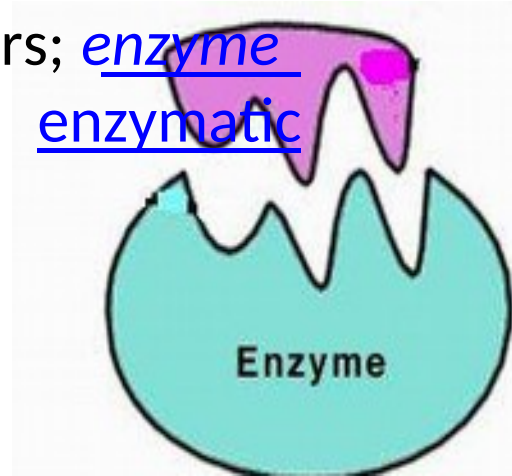


Enzyme Inhibition

Inhibition – means the *prevention or reduction of function*

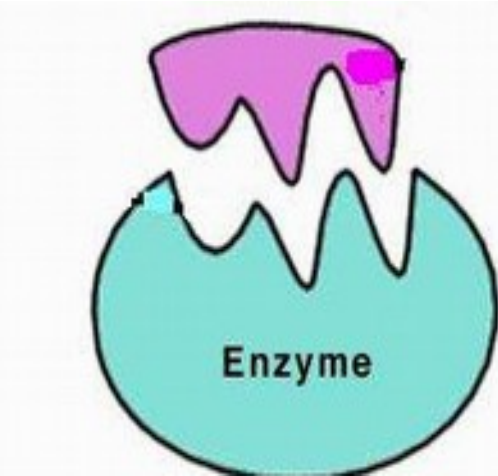
Enzyme inhibitors are molecules that interact in some way with the enzyme to prevent it from working in the normal manner.

Since blocking an enzyme's activity can kill a pathogen or correct a metabolic imbalance, many drugs are enzyme inhibitors.
They are also used as herbicides and pesticides.
Not all molecules that bind to enzymes are inhibitors; *enzyme activators* bind to enzymes and increase their enzymatic activity.



Enzyme Inhibitors

- **Irreversible**
- **Reversible**
  1. Competitive
  2. Uncompetitive
  3. Non-Competitive



Classification of Reversible Inhibitors

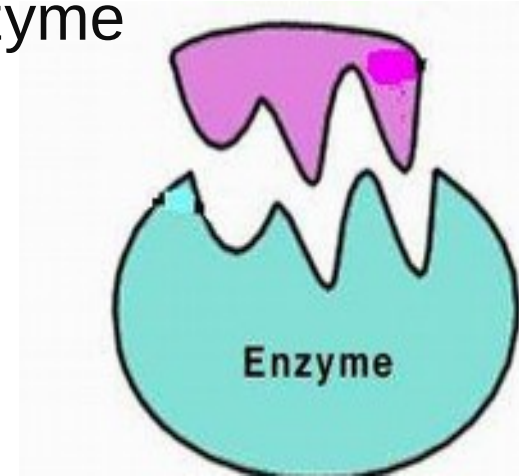
Can bind either to free enzyme or enzyme-substrate complex (usually non-covalently)

- **Competitive** – bind only to free enzyme

- **Uncompetitive** – bind only to enzyme-substrate Complex

- **Noncompetitive** – bind equally well to free enzyme and enzyme-substrate complex

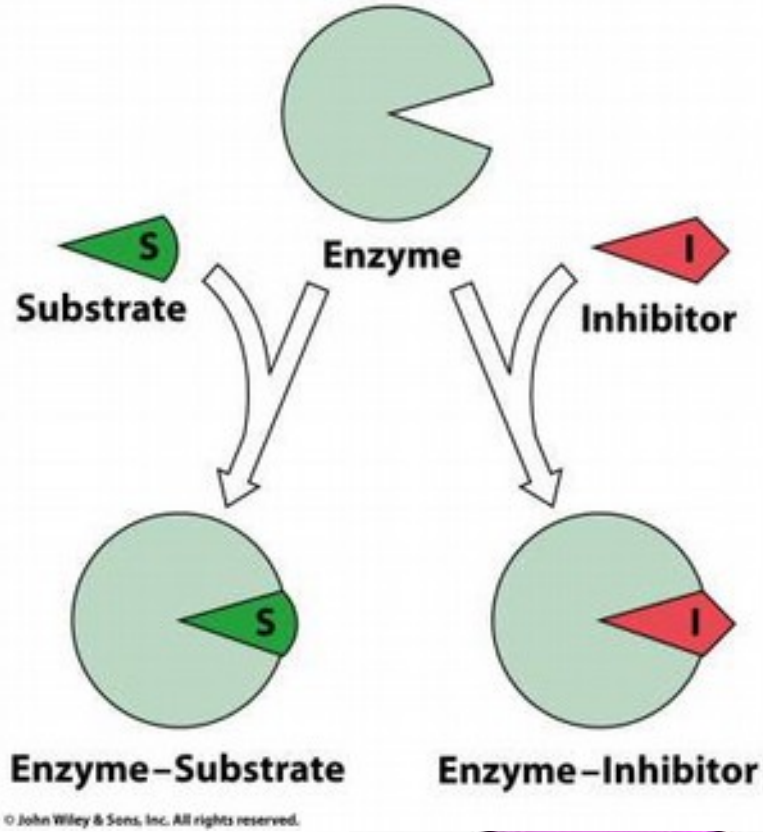
- **Mixed** – binds to both free enzyme and enzyme substrate complex, but with different affinities



Competitive Inhibition

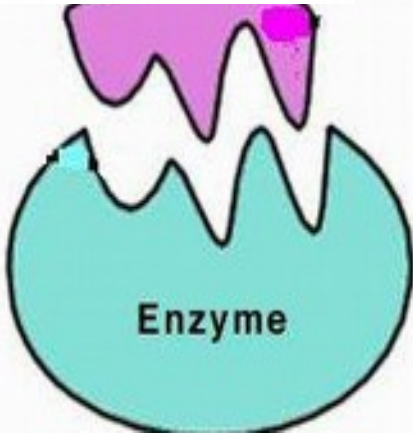
- Inhibitor binds only to free enzyme

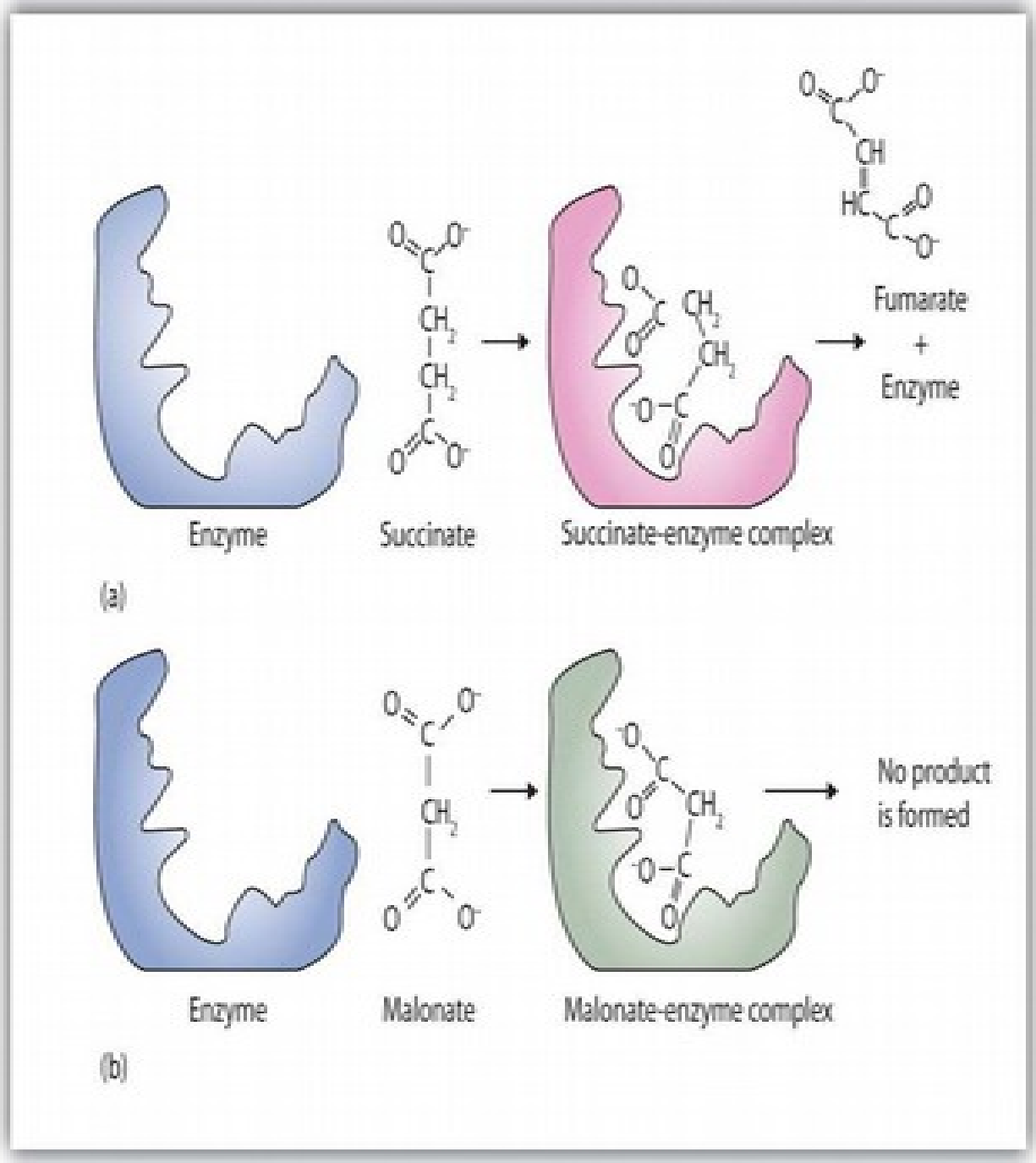
$$E + S \rightleftharpoons E{\cdot}S \rightarrow E + P$$
$$+$$
$$I$$
$$\rightleftharpoons$$
$$E{\cdot}I$$

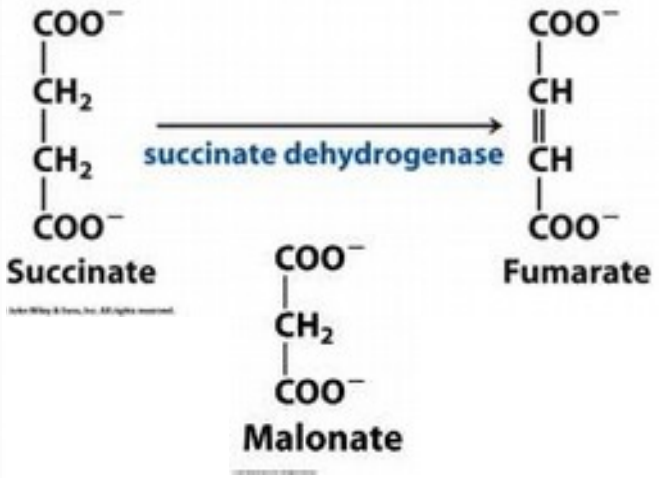


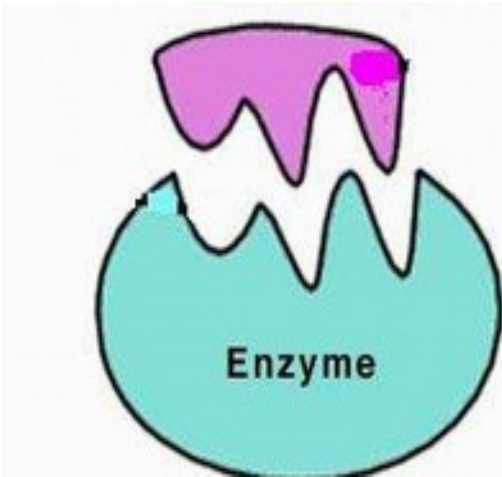
- Competitive inhibitors often mimic the substrate.

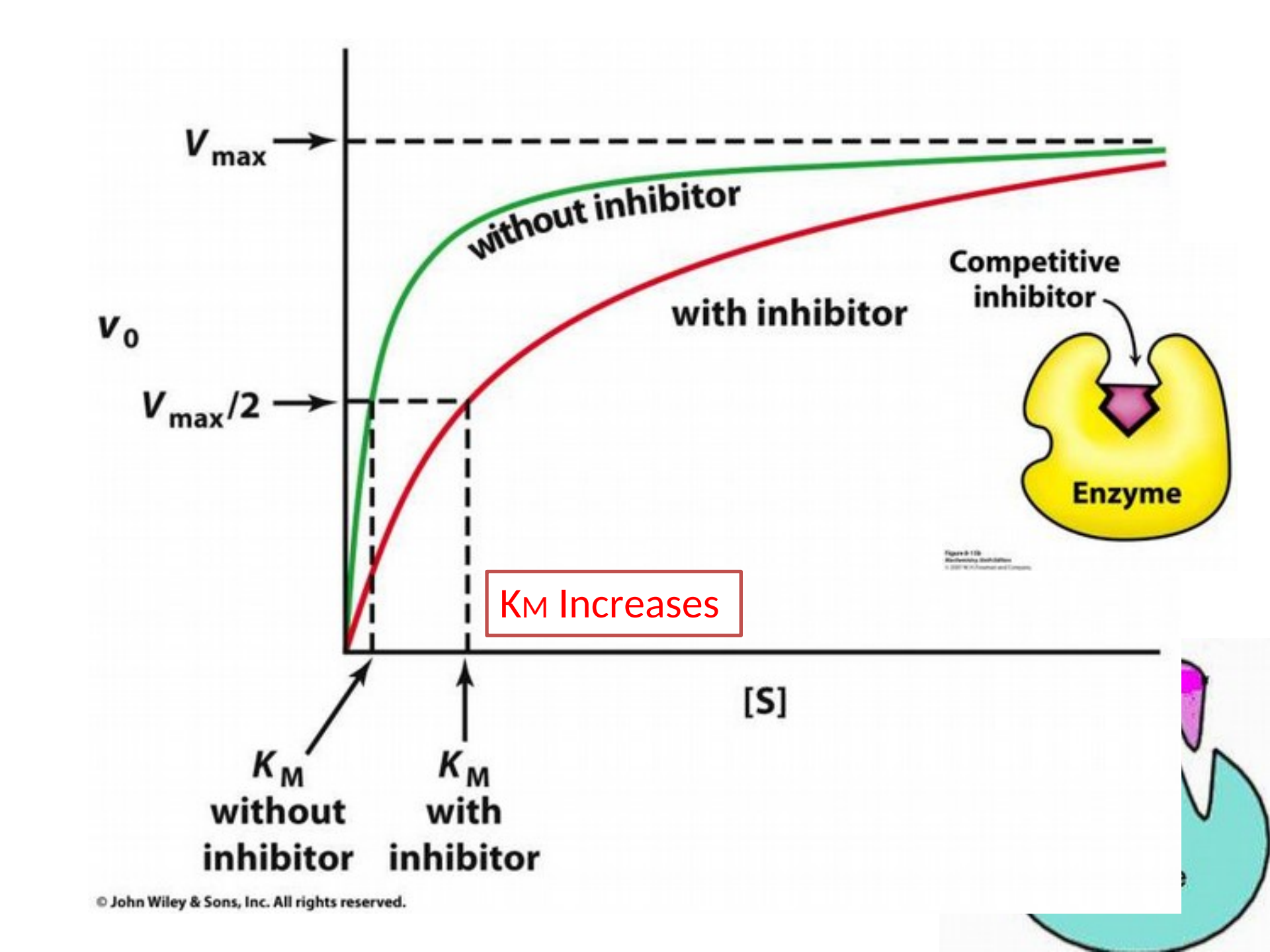
- Inhibitor disfavors formation of the E·S complex, but does not affect catalytic step.



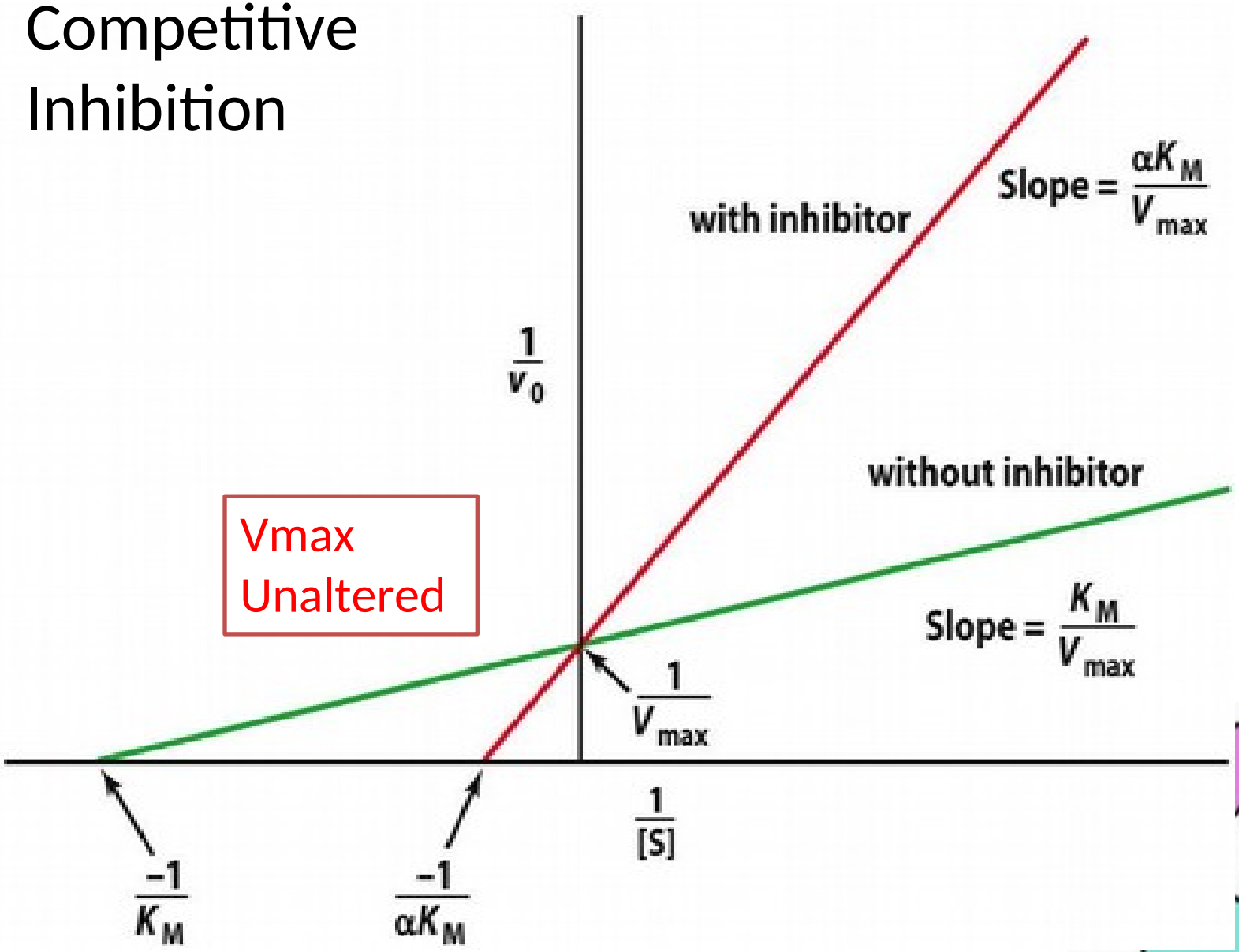

Fumarate
+
Enzyme
Enzyme
Succinate
Succinate-enzyme complex
(a)
No product
is formed
Enzyme
Malonate
Malonate-enzyme complex
(b)


succinate dehydrogenase
Succinate
Fumarate
Malonate

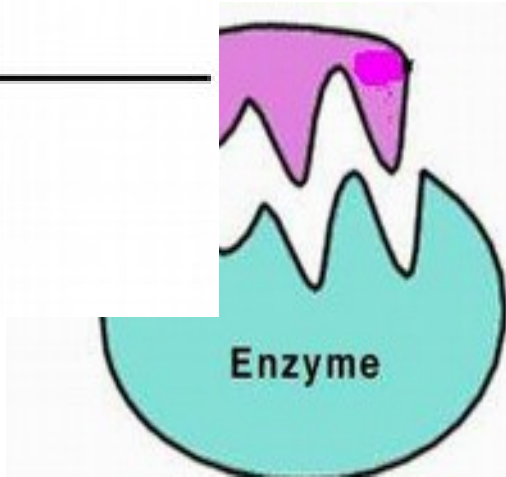

Enzyme



Competitive Inhibition

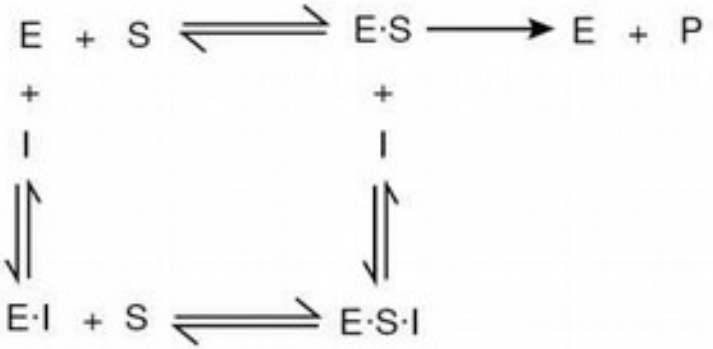


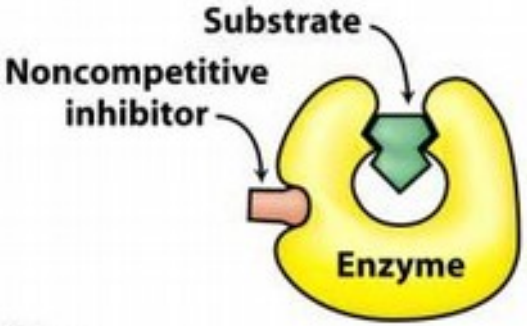
Vmax Unaltered



Noncompetitive Inhibition

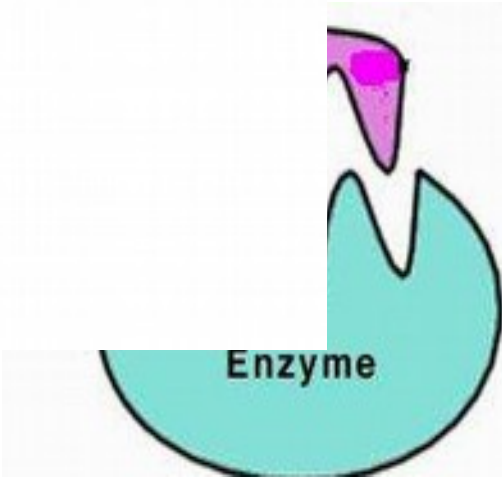
- Inhibitor binds to both free enzyme and enzyme-substrate complex



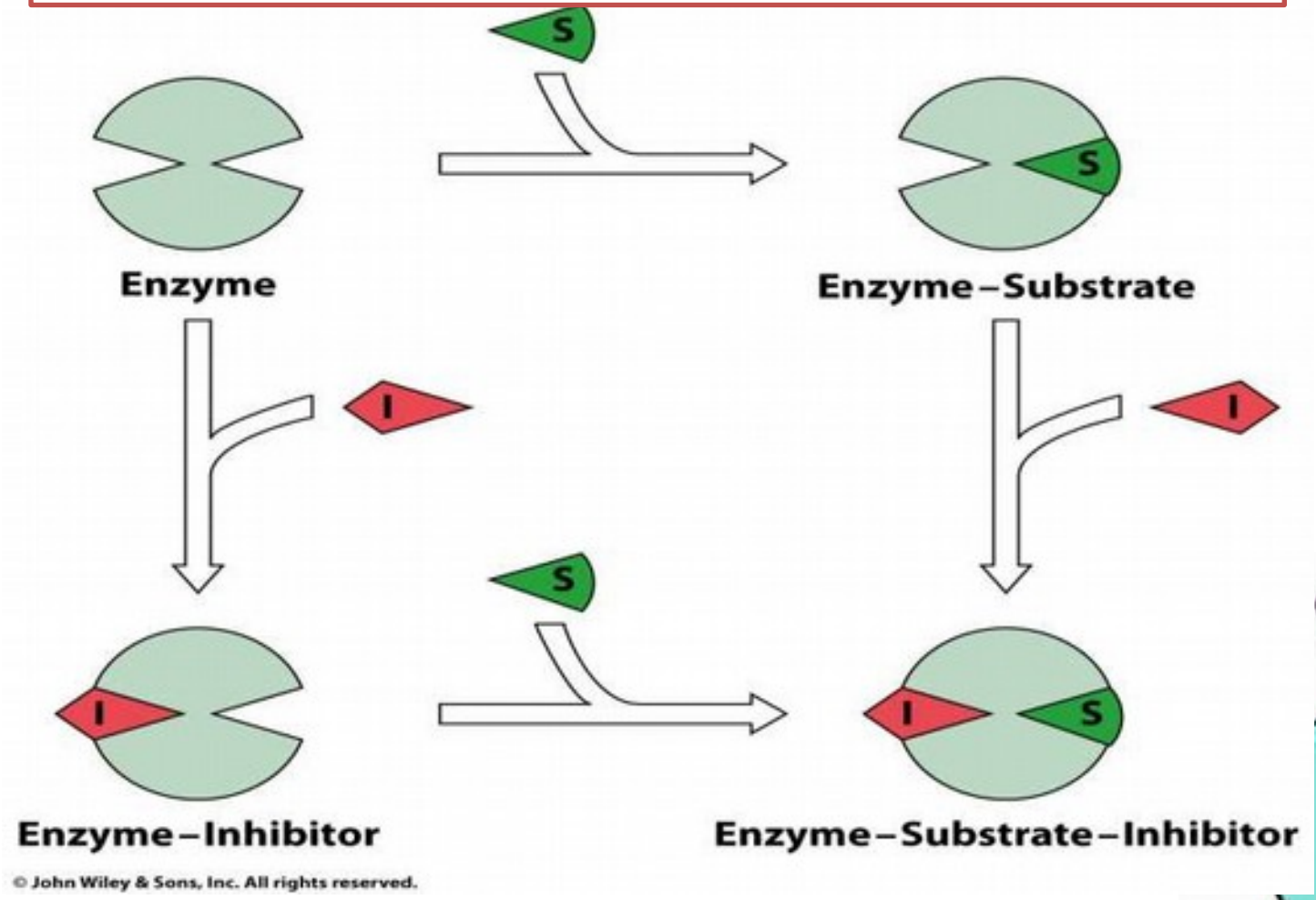


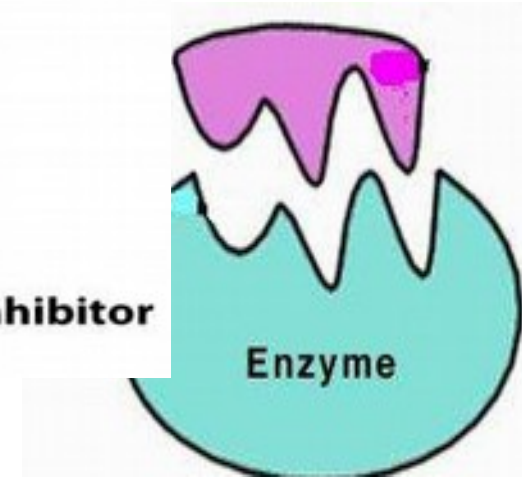
- Noncompetitive inhibitors bind independently of the substrate.

- Presence of inhibitor blocks catalytic step.

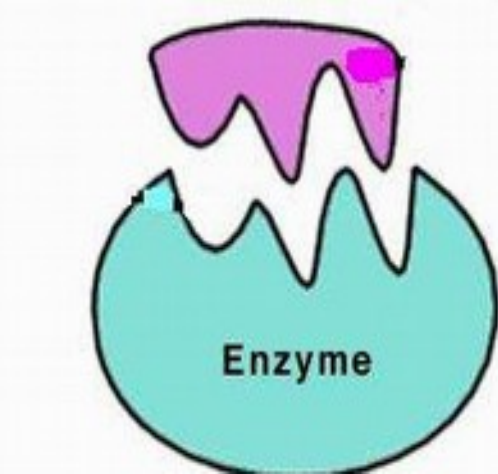


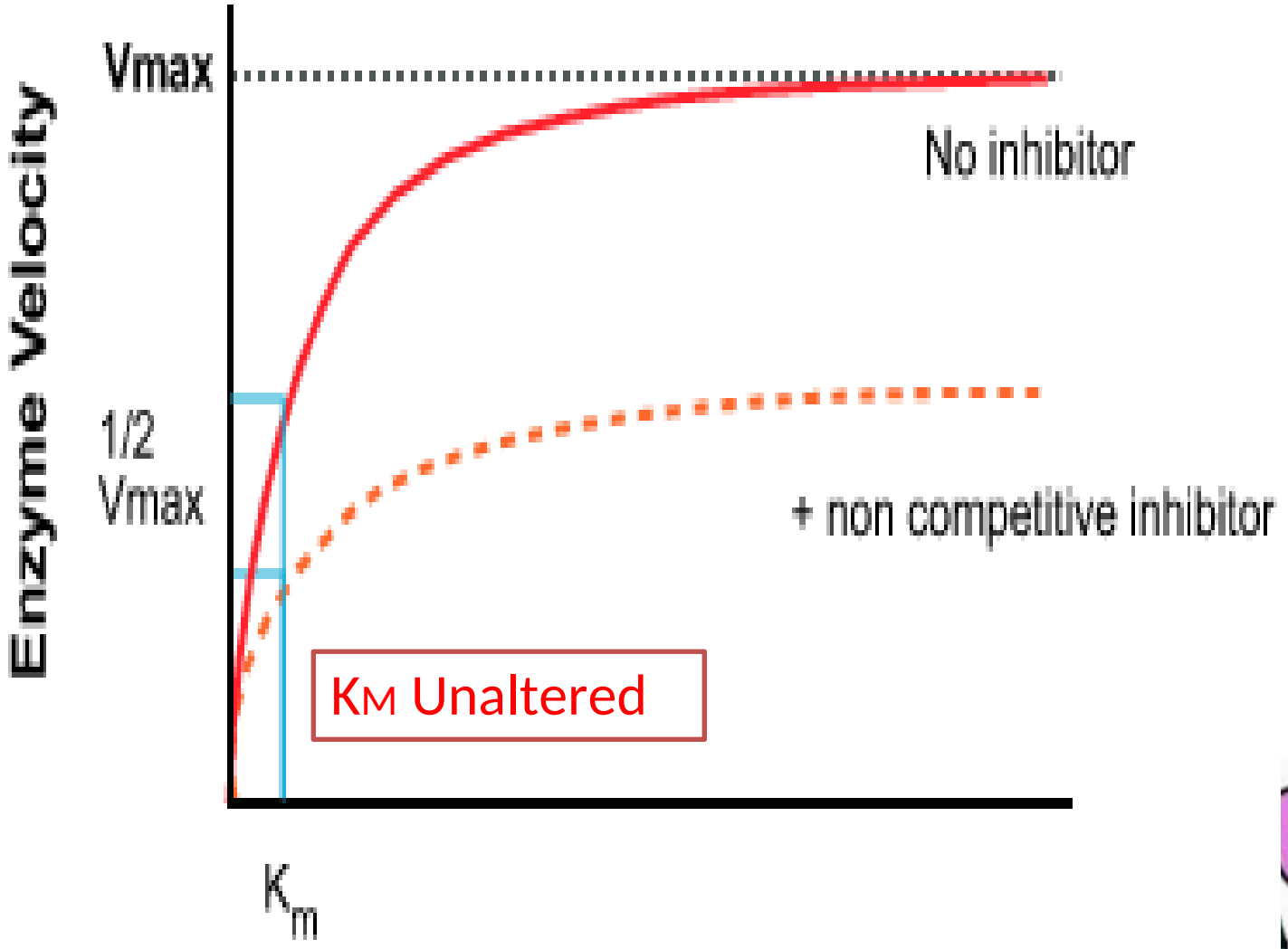
•No competition
• No structural resemblance
• Binds to allostearic site
Eg: Various heavy metals inhibit the activity of variety of enzymes

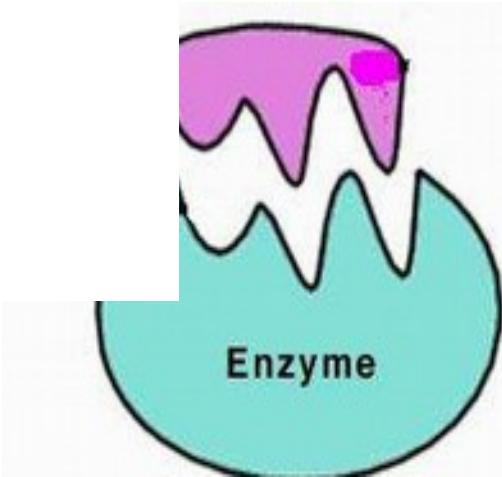




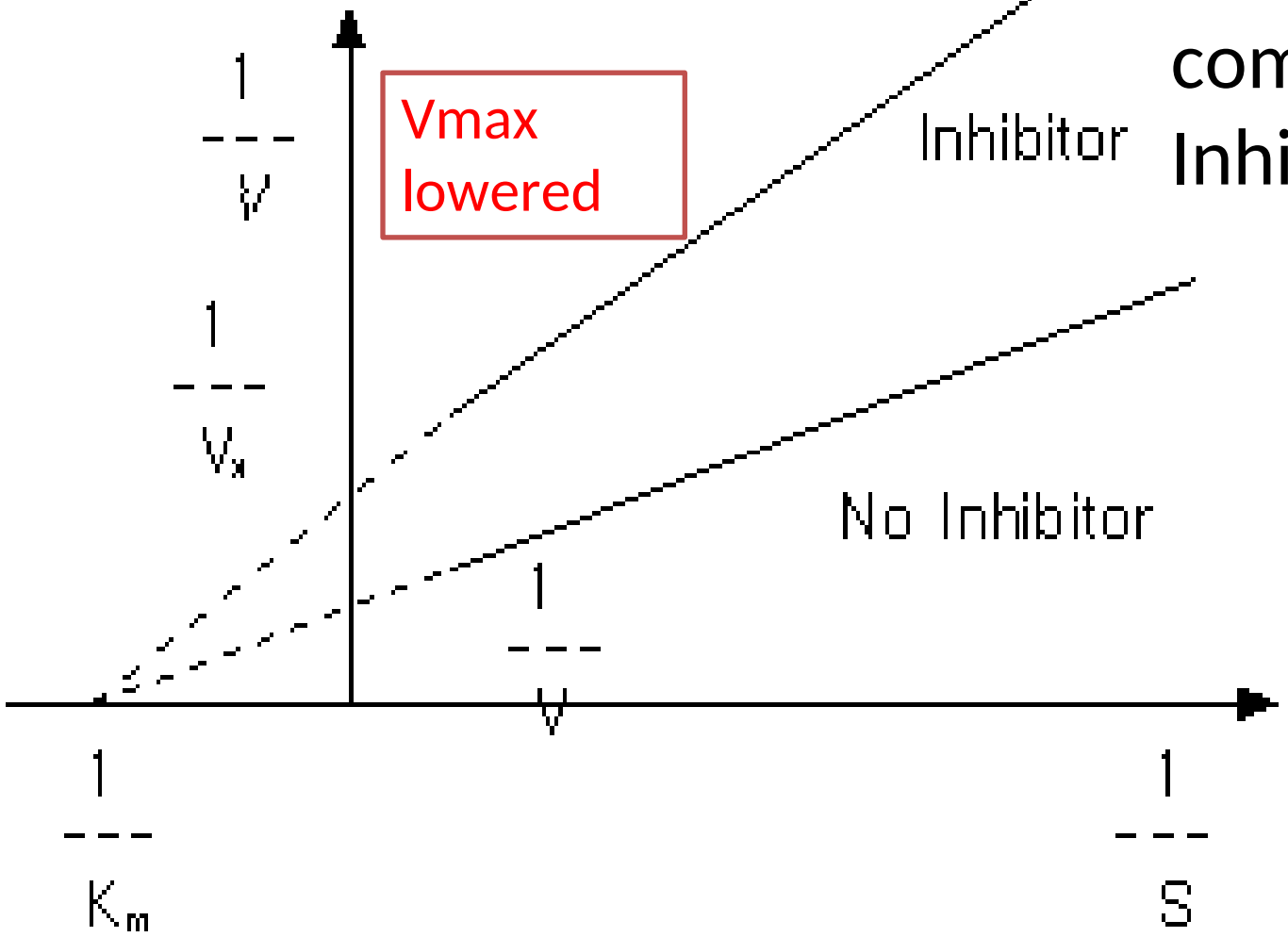
Lead forms covalent bonds with the sulphydryl side chains of cysteine in proteins. The binding of the heavy metal shows non-competitive inhibition because the substrate still has access. For example, lead inhibits the enzyme **Ferrochelatase** which catalyses the insertion of Fe^{2+} into protoporphyrin.

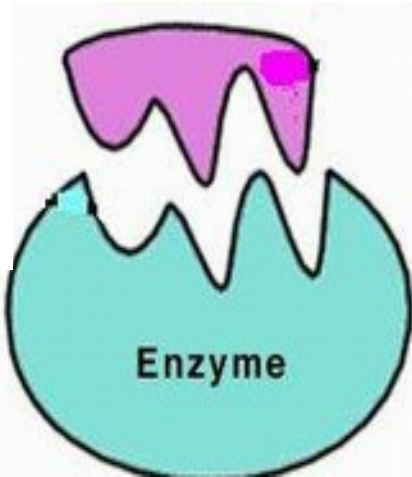



Vmax
Enzyme Velocity
No inhibitor
1/2
Vmax
+ non competitive inhibitor
KM Unaltered
Km
[Substrate]


Enzyme

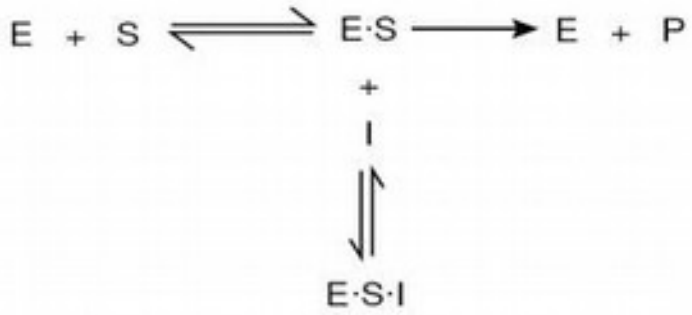
Non competitive Inhibition

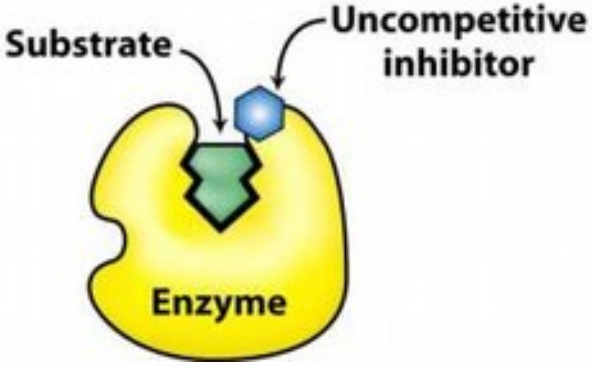




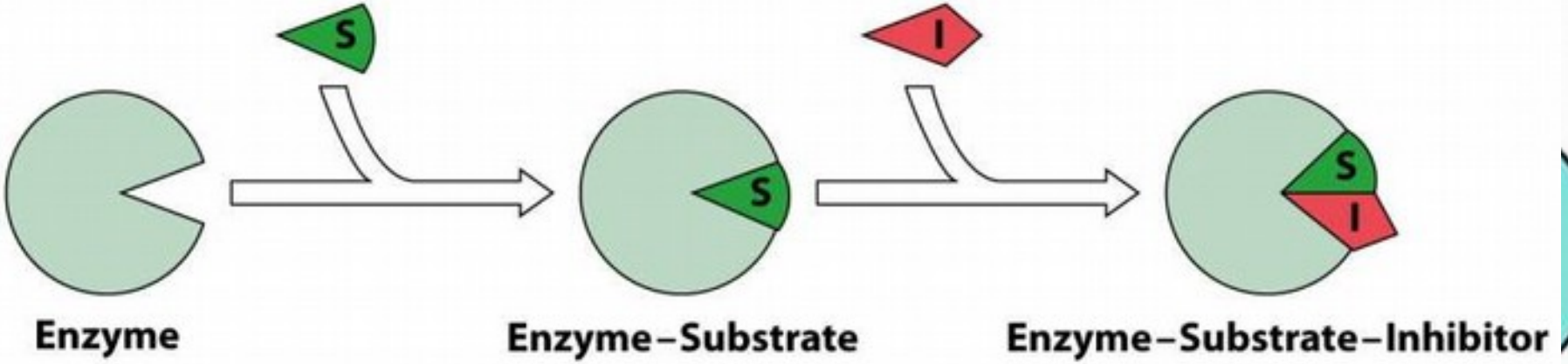
Uncompetitive Inhibition

- Inhibitor binds only to the enzyme-substrate complex

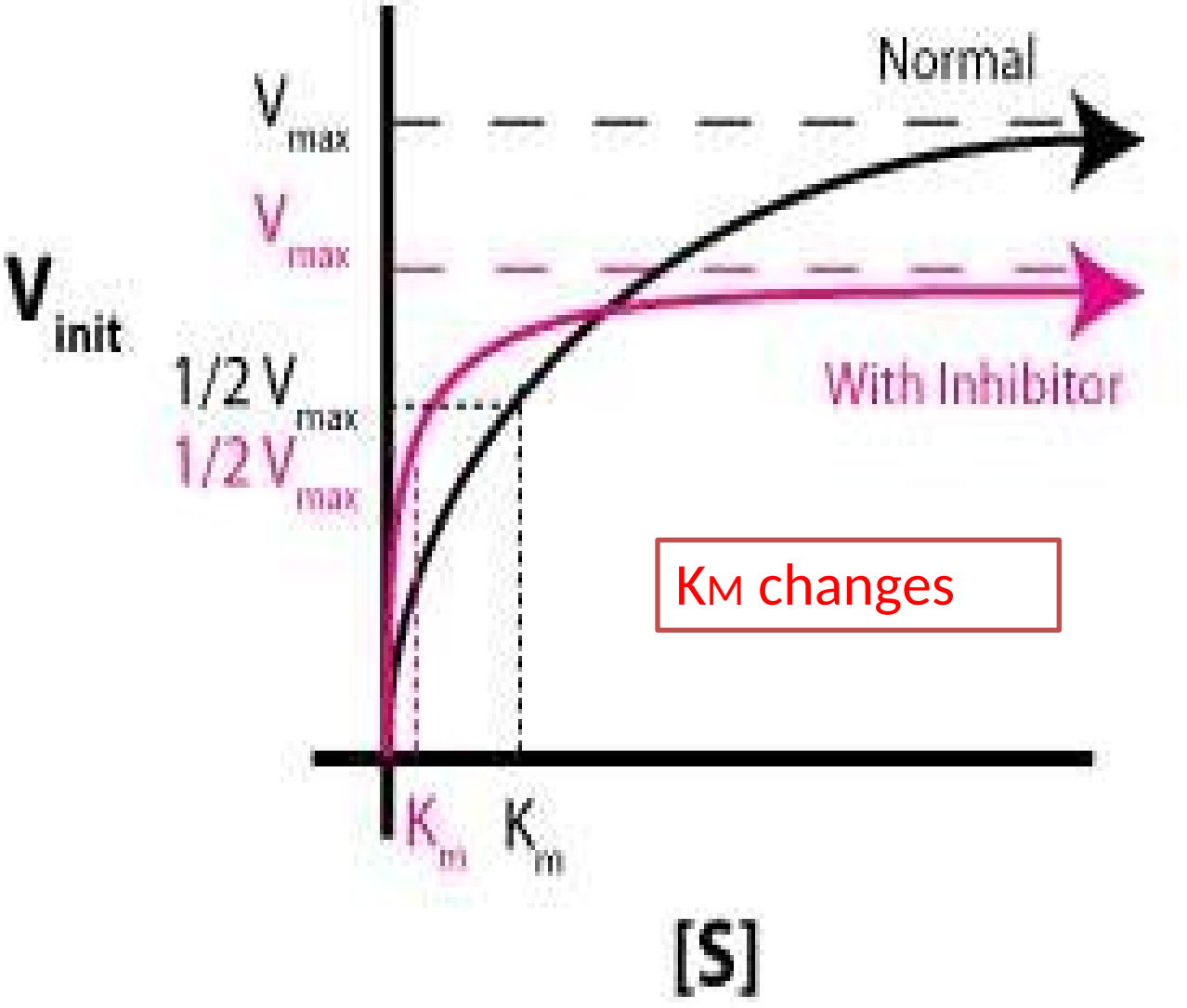




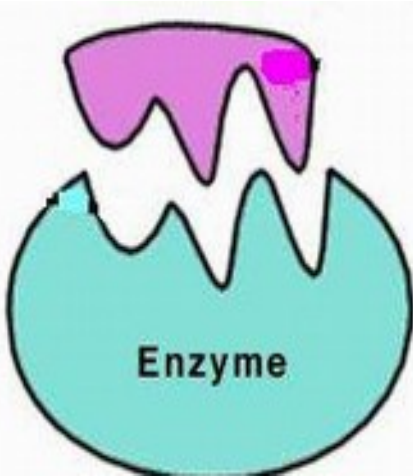
- Inhibitor actually favors substrate binding, but ternary complex is inactive.

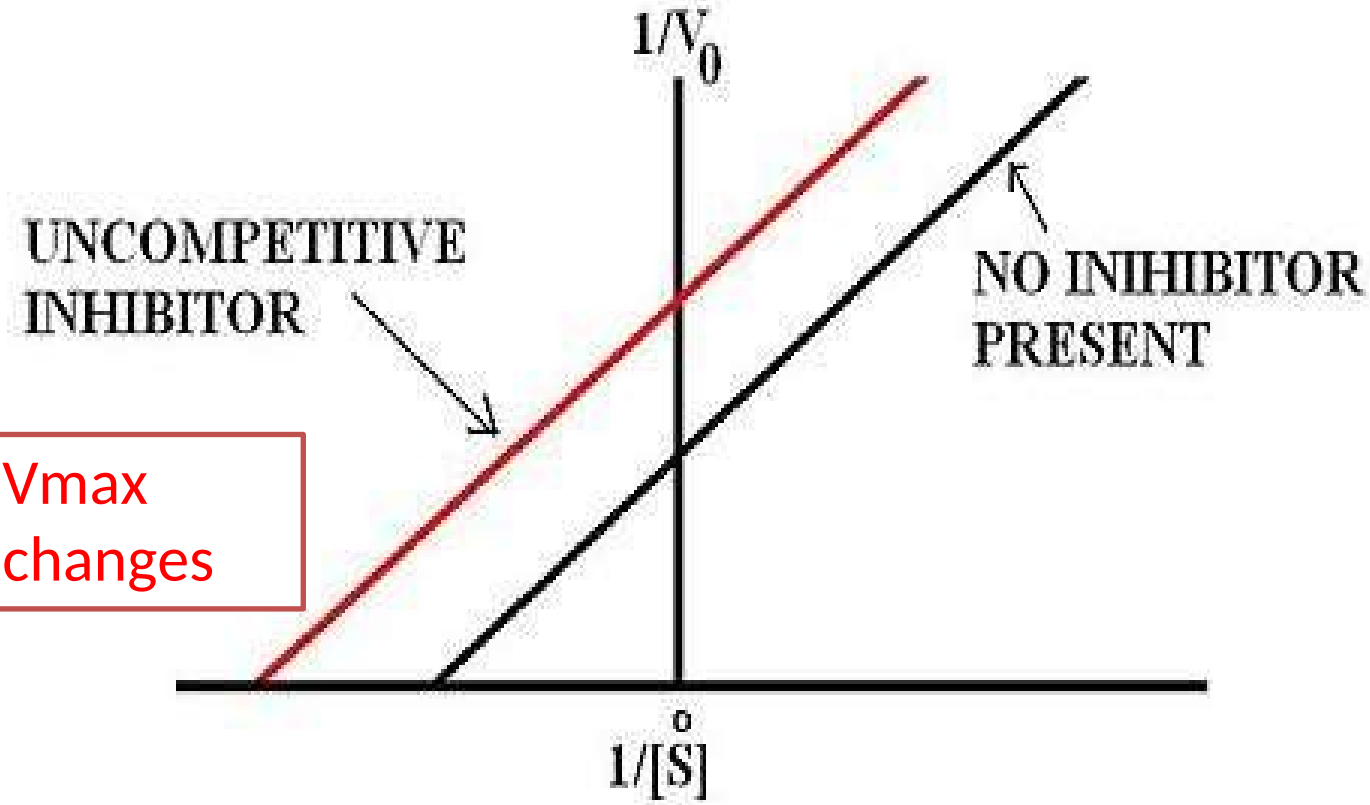


Uncompetitive Inhibitors

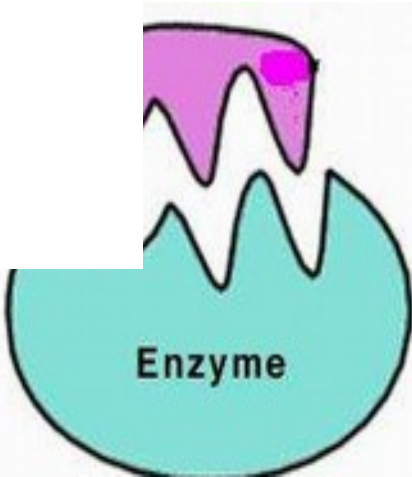


K_M changes

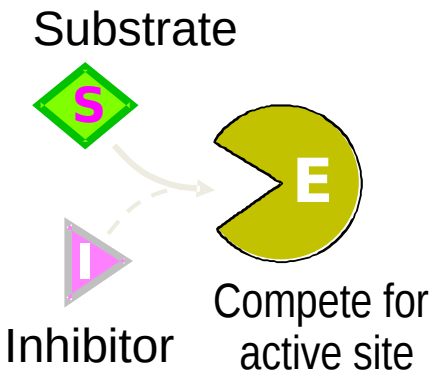
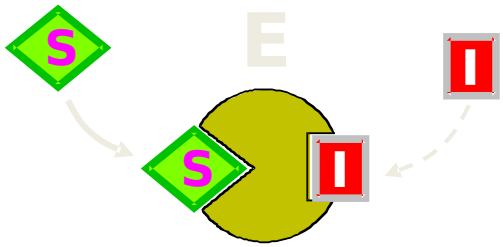
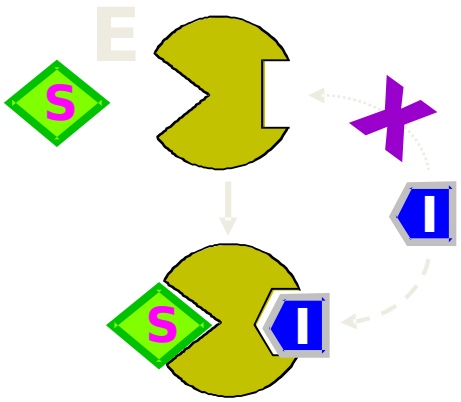


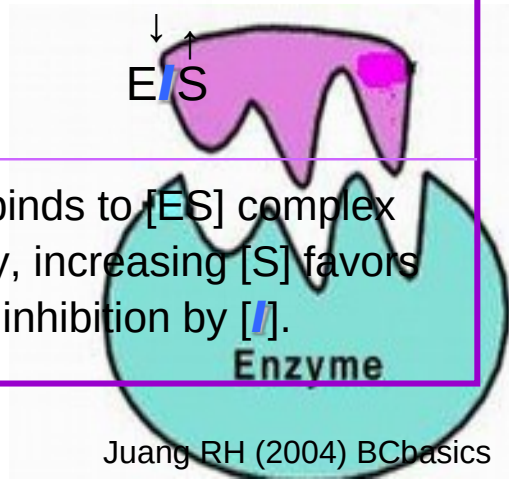


Vmax changes



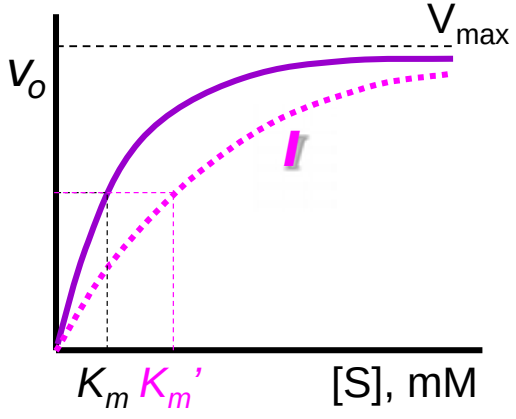
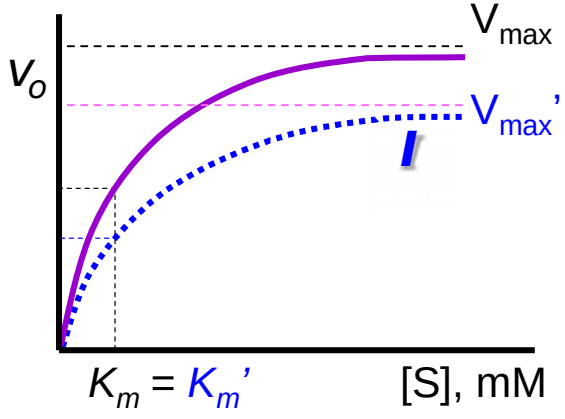
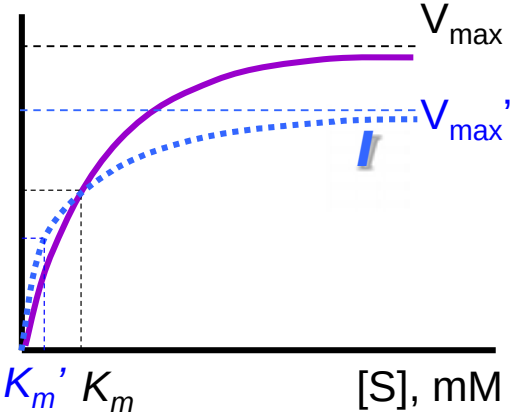
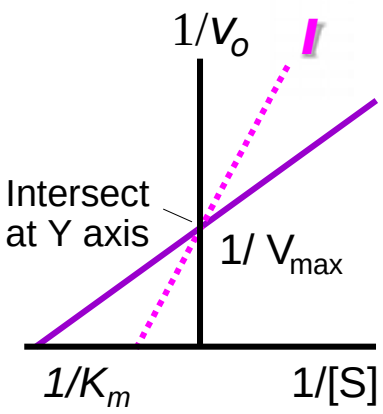
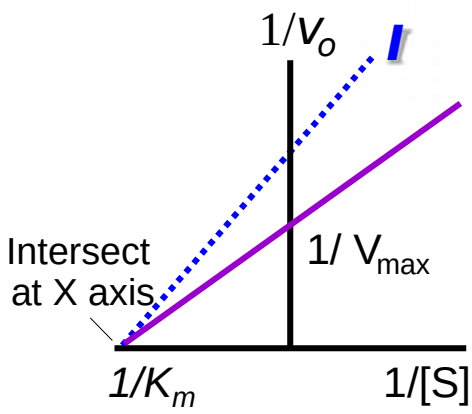
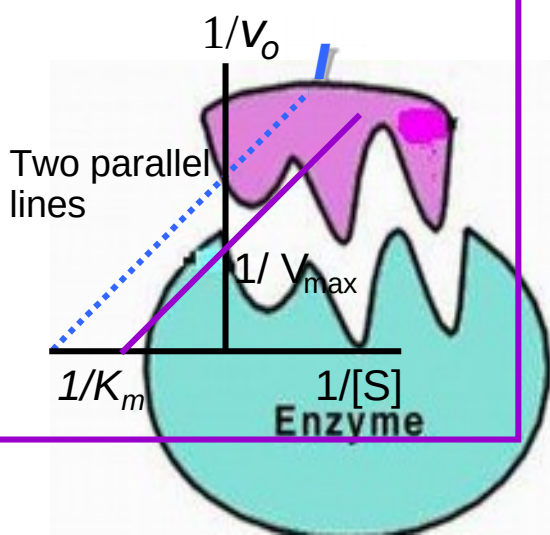
Enzyme Inhibition (Mechanism)

	Competitive	Non-competitive	Uncompetitive
Cartoon Guide			
Equation and Description	$E + S \rightleftarrows ES \rightarrow E + P$ $+$ I $\downarrow\uparrow$ EI	$E + S \rightleftarrows ES \rightarrow E + P$ $+ \quad +$ $I \quad I$ $\downarrow\uparrow \quad \downarrow \uparrow$ $EI + S \rightarrow EIS$	$E + S \rightleftarrows ES \rightarrow E + P$ $+$ I $\downarrow\uparrow$ EIS
	[I] binds to free [E] only, and competes with [S]; increasing [S] overcomes Inhibition by [I].	[I] binds to free [E] or [ES] complex; Increasing [S] can not overcome [I] inhibition.	[I] binds to [ES] complex only, increasing [S] favors the inhibition by [I].



Juang RH (2004) BCbasics

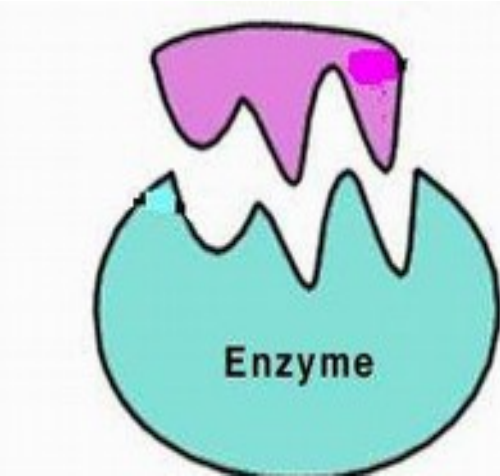
Enzyme Inhibition (Plots)

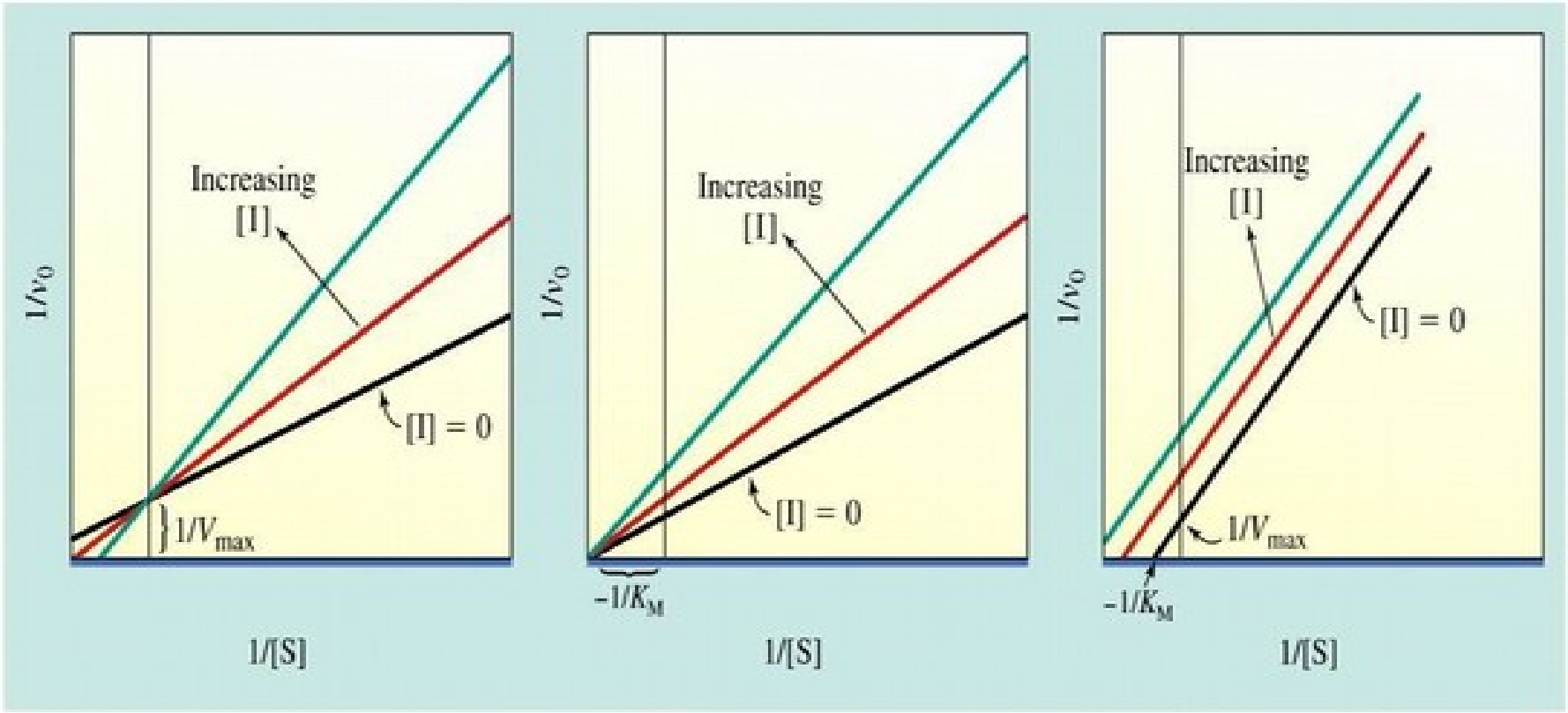
	Competitive	Non-competitive	Uncompetitive
Direct Plots			
	V_{max} unchanged K_m increased	V_{max} decreased K_m unchanged	Both V_{max} & K_m decreased
Double Reciprocal			

Kinetic characteristics of reversible inhibition

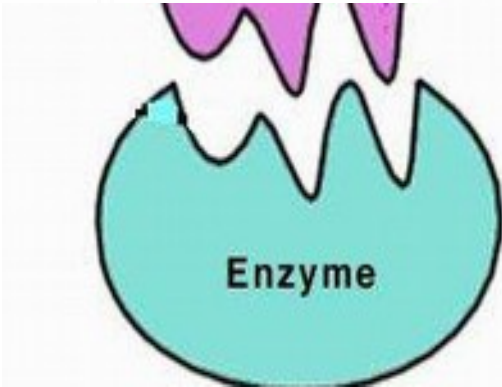
	Effect of Inhibition[a]		
Type of Inhibition	K_M	V_{max}	K_M/V_{max} (slope)
Competitive	Higher	Same	Increase
Uncompetitive	Lower	Lower	Same
Noncompetitive			
Pure	Same	Lower	Increase
Mixed	Higher	Lower	Increase

[a] Compared to uninhibited reaction.



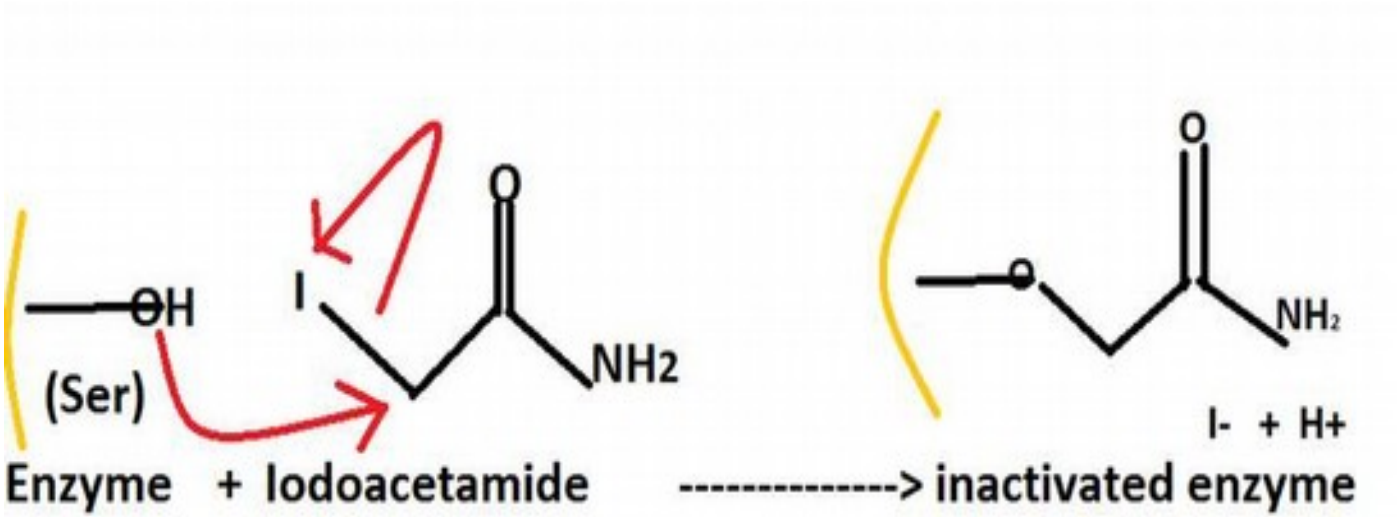


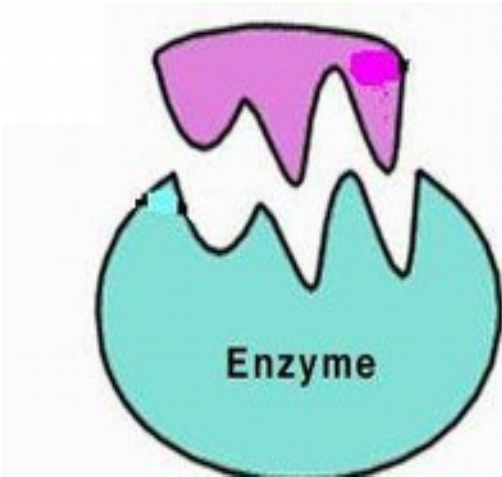
(a) Competitive inhibition (b) Noncompetitive inhibition (c) Uncompetitive inhibition



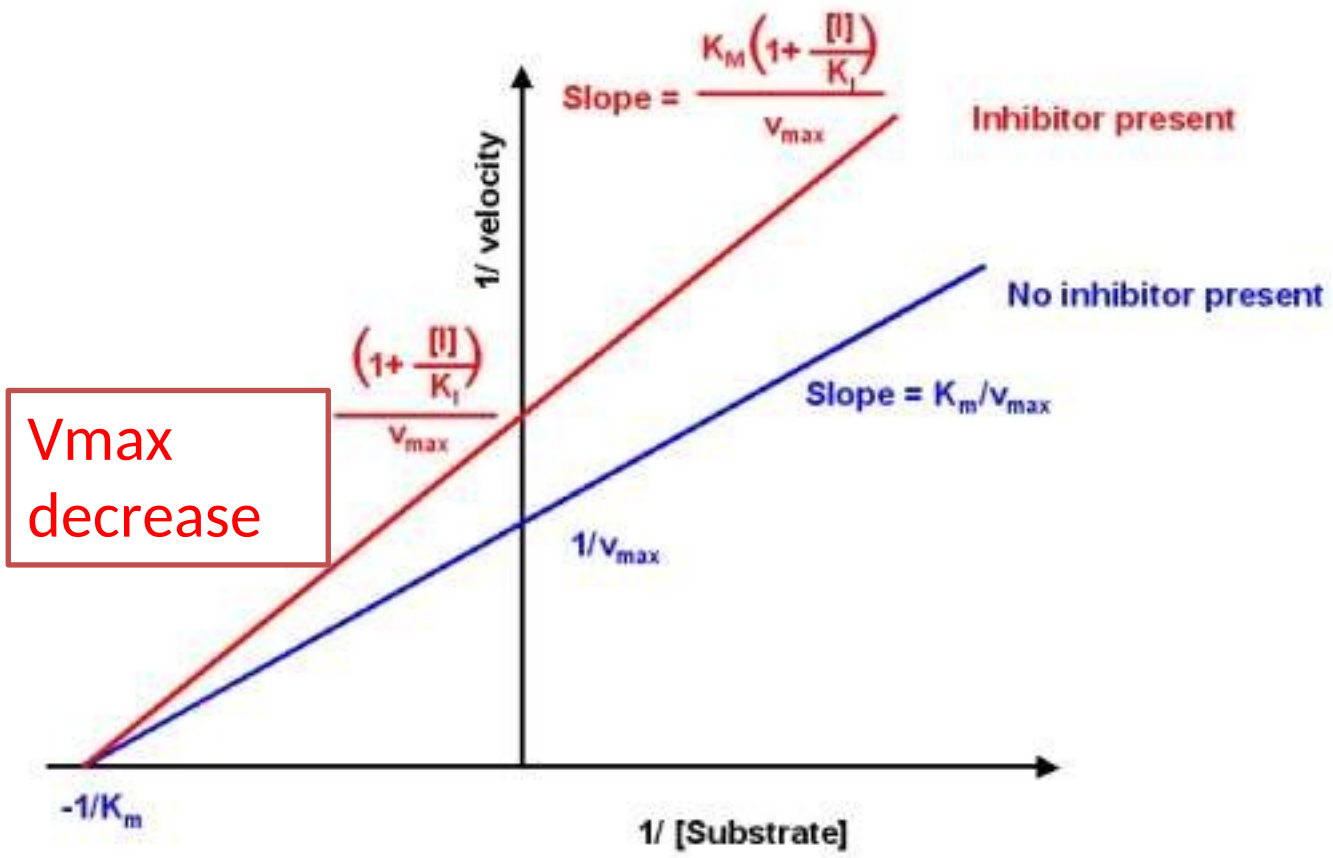
Irreversible Inhibitiors

- Bind covalently or Non covalently with enzyme and inactivate them
- Destroy the functional group of enzyme required for the activity

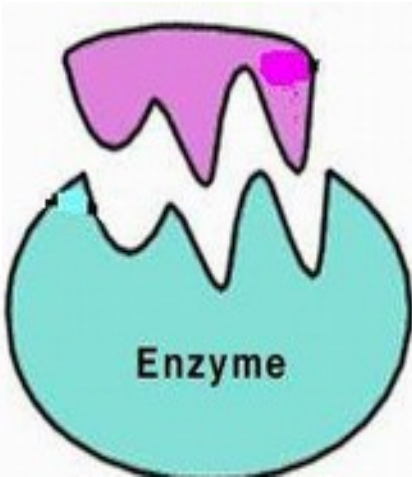




Irreversible Inhibitiors



Vmax decrease



Suicide Inhibition

- Original inhibitor gets converted into more potent form
- Eg: Allopurinol an inhibitor of xanthine oxidase gets converted into alloxanthine a more effective inhibitor of enzyme