جامعة الملك سعود
King Saud University

بِسْمِ اللهِ الرَّحْمَنِ الرَّحِيمِ

MED437 KING SAUD UNIVERSITY

BIO TEAM

Enzymes and coenzymes 1

Biochemistry Team 437

Color index:
Doctors slides
Notes and explanations
Extra information
Highlights

Objectives:

- Understand how enzymes are able to speed up the rate of biochemical reactions in the body
- Identify classes of enzymes based on the type of reactions they catalyze
- Comprehend the basic terms of coenzymes, isoenzymes, enzyme activity and specificity along with factors affecting their activity
- Understand the enzyme kinetics, types of inhibition and regulation of enzyme activity
- Discuss the clinical role enzymes in the diagnosis of diseases

Titles:

1. What are enzymes?
2. Enzyme properties and specificity
3. Enzyme-substrate binding
   - Lock and key binding
   - Induced fit binding
4. Classification of Enzymes
5. Enzyme nomenclature (Naming)
6. Holoenzymes
7. Cofactors and Coenzymes
8. Ribozymes, Isoenzymes and zymogens
9. Enzymes decrease activation energy of a reaction
10. Enzyme Activity or Velocity
11. Factors that affect enzyme activity
12. Enzyme kinetics

Everything that ends with “ase” is mostly an enzyme

What are Enzymes?

biological catalysts that **speed up** the rate of a reaction **without being changed** in the reaction

All enzymes are **protein** in nature
All proteins **are not enzymes**

Substance upon which the enzymes act are called **substrates**
Enzyme converts substrates into **product(s)**

Catalysts: anything that speed up a reaction and not being changed in the process

Properties of Enzymes

Active site

The region of enzyme that binds with the substrate and **where catalysis occurs**
All enzymes have one or more active sites

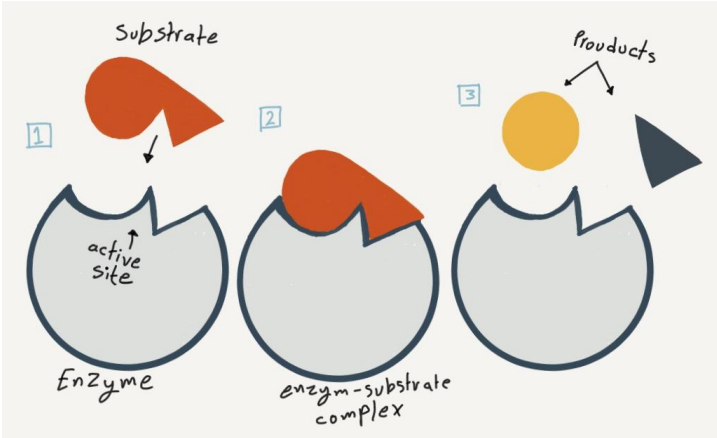
Enzymes must at least have one active site

Specificity

Enzymes bind to their **specific substrates in the active site** to convert them to product(s)
“not every substrate can bind to any enzyme”

Regulation

Enzymes can be **activated** or **inhibited** so that the rate of product formation responds to **the need of the cell**
“e.g. if we didn’t eat food, we don’t need digestive enzymes, therefore they are inhibited”



Enzyme specificity

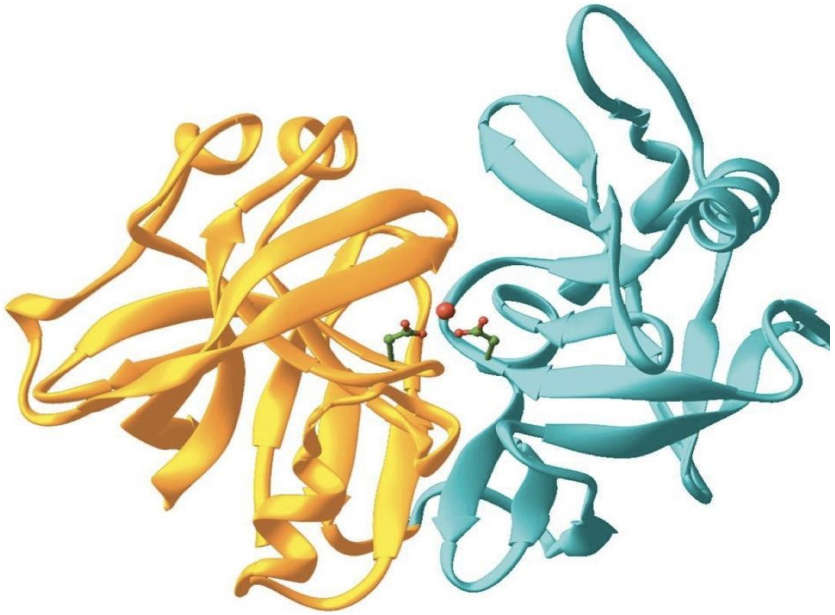
-Enzymes are **highly specific**

-Interact with **only one or a few of the substrates** **Depending on the number of active sites**

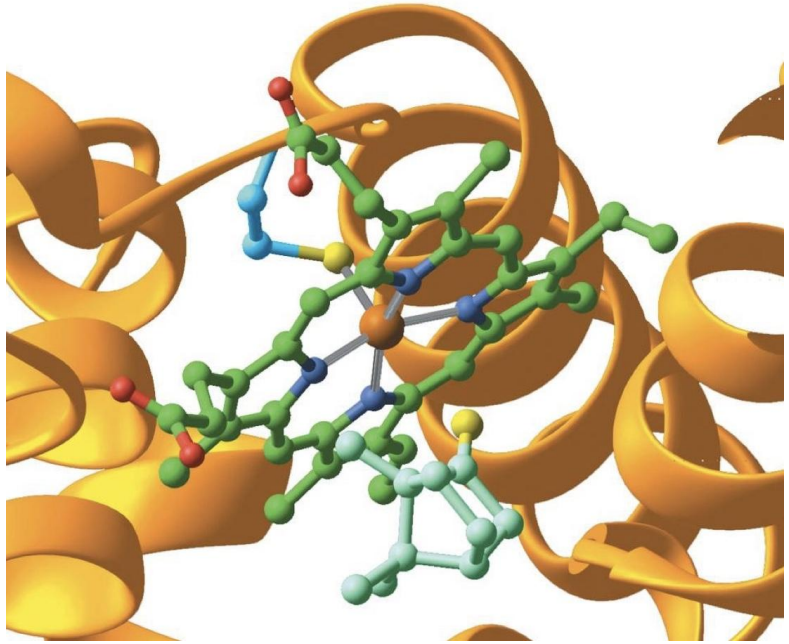
-**Catalyze only one type of reaction**
“If we need to do another reaction to the same substrate, we use a different enzyme”

Example: Sucrase enzyme only interact with sucrose and only do one reaction which is “hydrolysis” thus breaking the bond and releasing “fructose and glucose” as products. If we needed to do another reaction, we use another enzyme

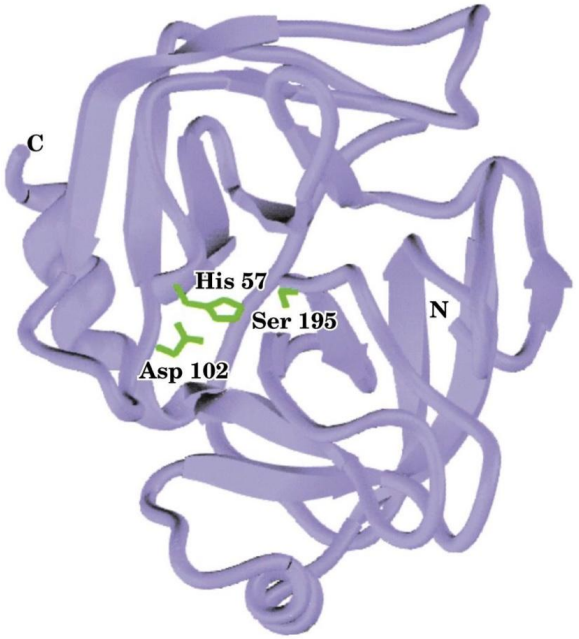
Structure of **pepsin** enzyme



An enzyme with its **active site**



Structure of **trypsin** enzyme



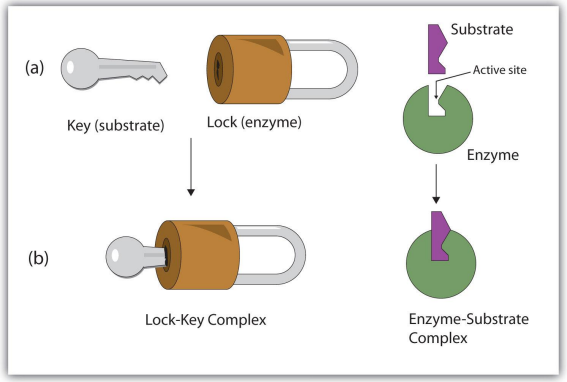
Structures are not for memorization

Enzyme-substrate binding

Lock and key binding

The enzyme has an active site that **fits the exact dimensions** of the substrate

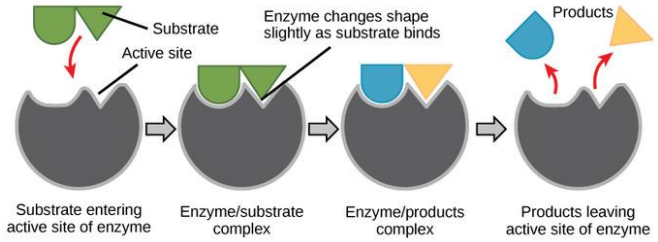
زي القفل ما يفتحه الا مفتاح واحد بنفس الشكل له



Induced fit binding

The enzyme has a **similar** shape to the substrate, After the binding of substrate, **the enzyme changes its shape** to fit more perfectly with substrate

هذا ما يعني انه يقدر يغير شكله لاي سبستراىت لكن هو فقط يسوي تعديلات بسيطه لشكله عشان يناسب السبستراىت المحدد له بشكل احسن



Classification of Enzymes

Classified into six types according to the reaction catalyzed

Oxidoreductases	**Oxidation-reduction reaction**
Transferases	**Transfer of functional groups**
Hydrolases	**Hydrolysis reaction**
Lyases	**Group elimination to form double bonds**
Isomerases	**Isomerization**
Ligases	**Bond formation coupled with ATP hydrolysis**

تحفظ بالترتيب**

Overseas travelers heard lyrics in london

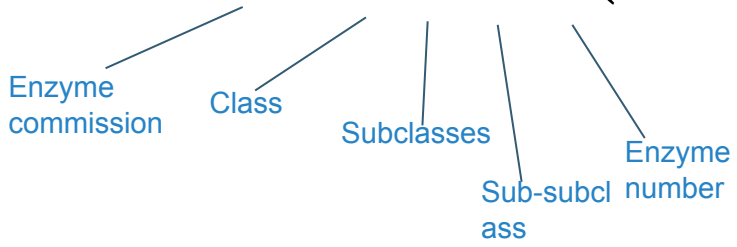
Enzymes Nomenclature (Naming)

Enzymes nomenclature is based on the rules given by IUBMB (International Union of Biochemistry and Molecular Biology).

Nomenclature order is:

Class.Subclass.Subsubclass.Enzyme number.

EC 3.4.17.1 (carboxypeptidase A)



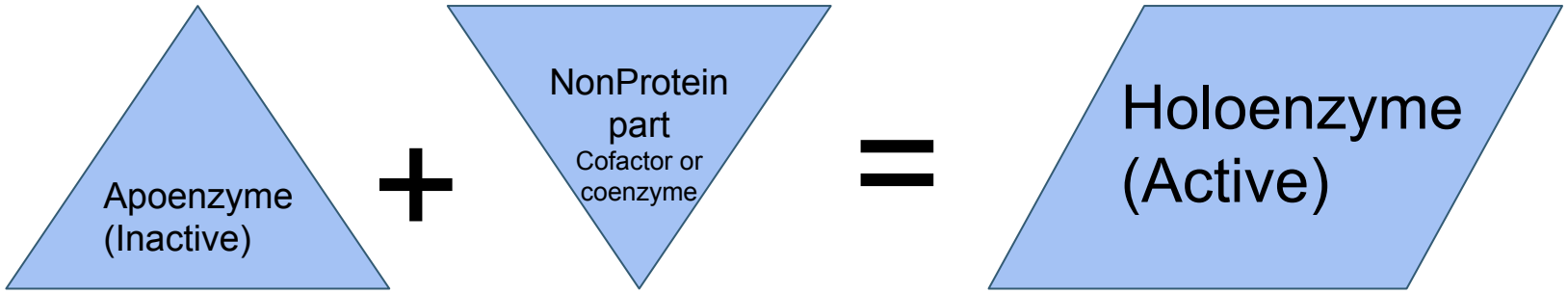
You don't have to memorize this name just know what each number means.

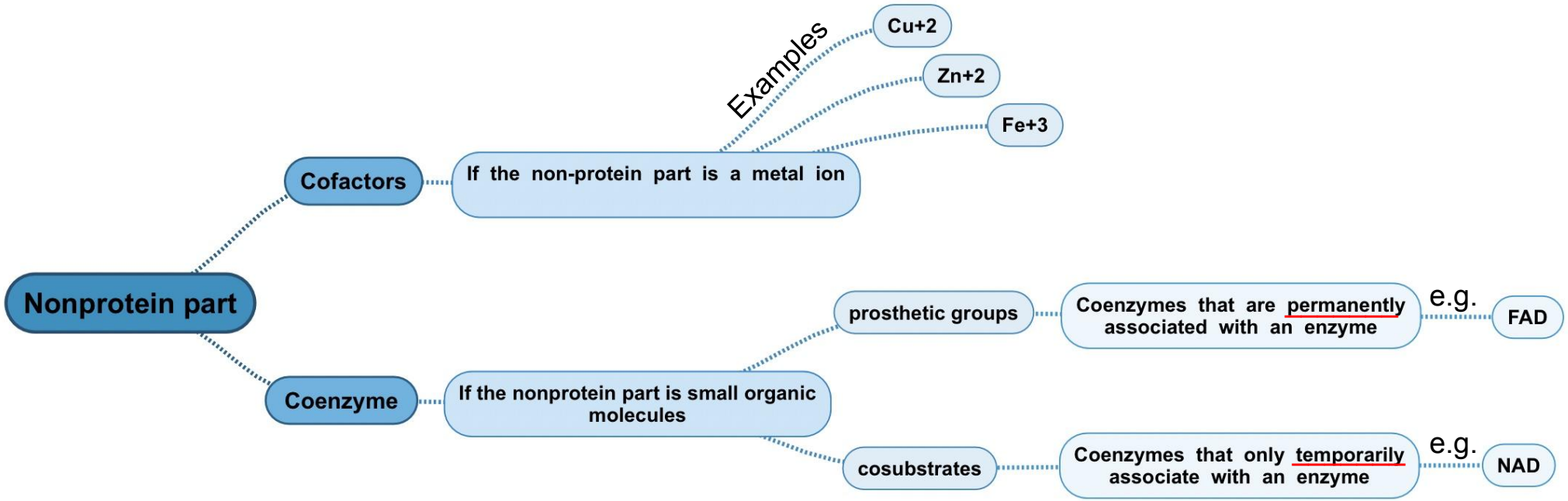
Holoenzymes

Inactive enzyme that binds to a nonprotein part to become active

Some enzymes require non-protein groups to become active

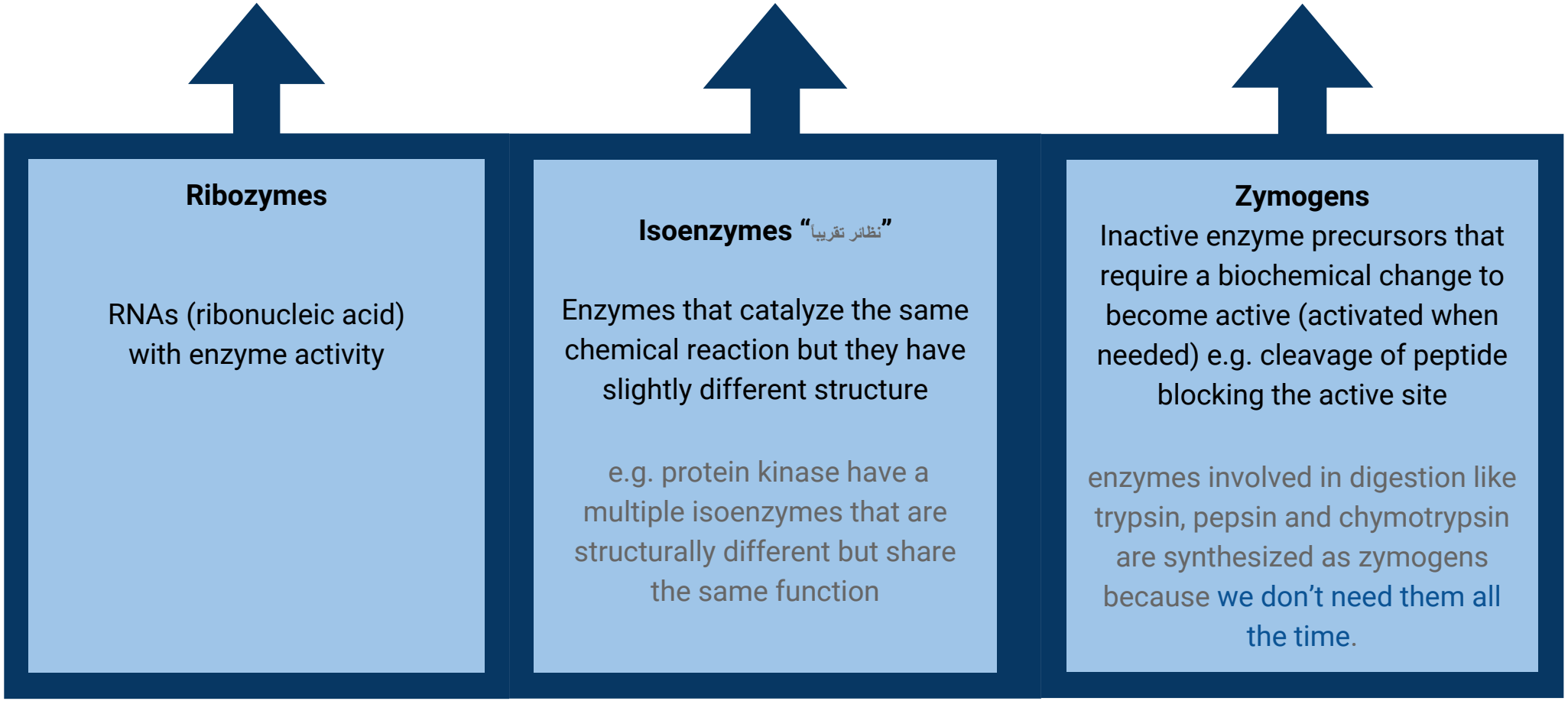
The inactive form of enzyme without its non-protein part is called an apoenzyme





Transiently= temporary

Ribozymes, isoenzymes and zymogens

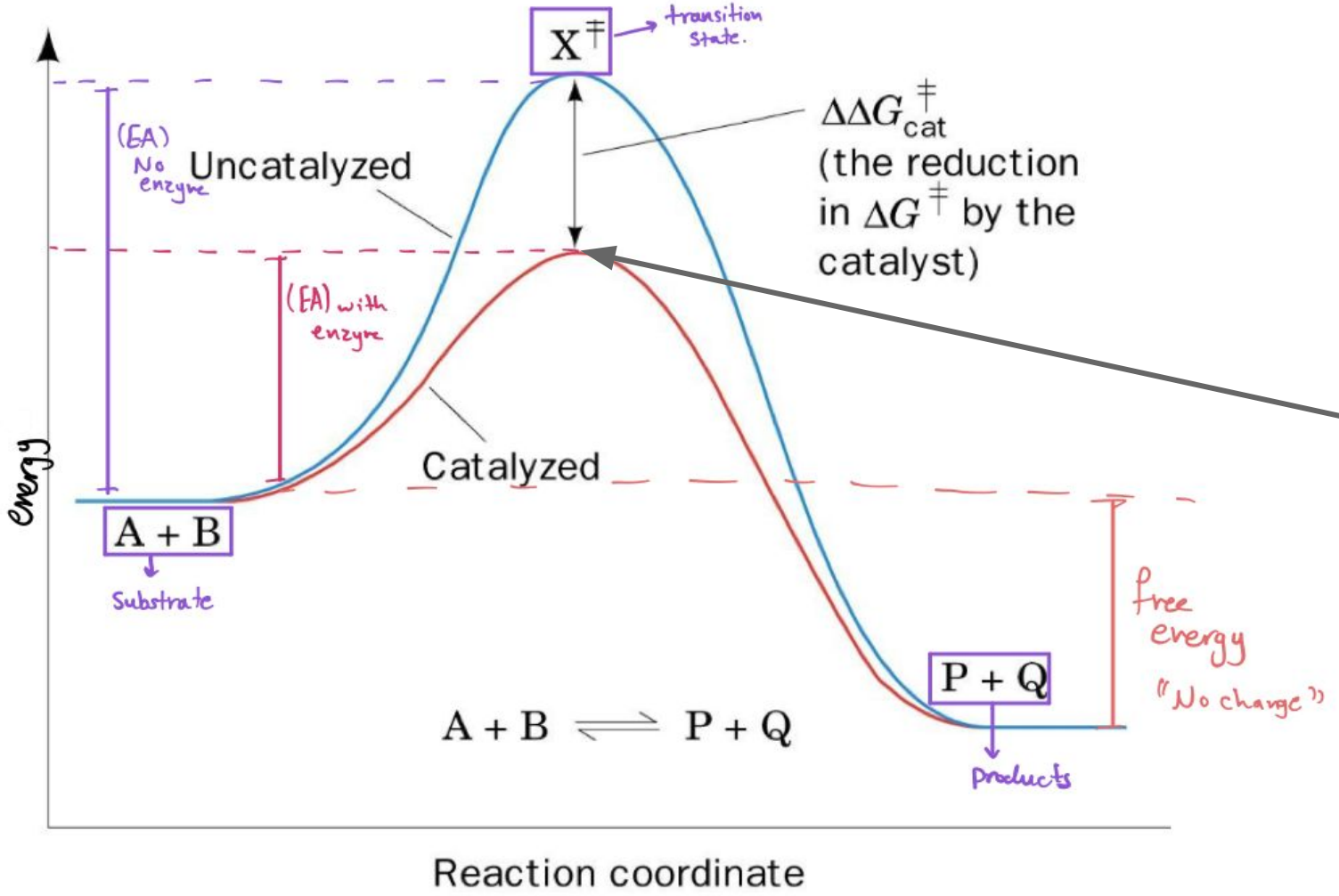


Zygomens are a group of proteins that display no catalytic activity but are transformed within an organism into enzymes

Enzymes decrease activation energy of a reaction

- In every chemical reaction, the reactants pass through a transition state that has greater energy than that of the reactants or products alone
- The difference in energy between the reactants and the transition state is called the activation energy (Ea)
- If the activation energy is available then the reaction can proceed forming products
- An enzyme reduces the activation energy required for a reaction
- It provides an alternative transition state of lower energy called the enzyme-substrate complex and thus speeds up the reaction
- Enzymes decrease the activation energy but they do not alter the change in the free energy (ΔG)

The effect of catalyst on the transition state diagram of a reaction



catalysts lowers the energy required to reach the transition state which make the formation of a product faster but it <u>doesn't change the free energy</u>

Free energy change of the reaction is the difference of reactants and products.

Enzyme Activity or Velocity

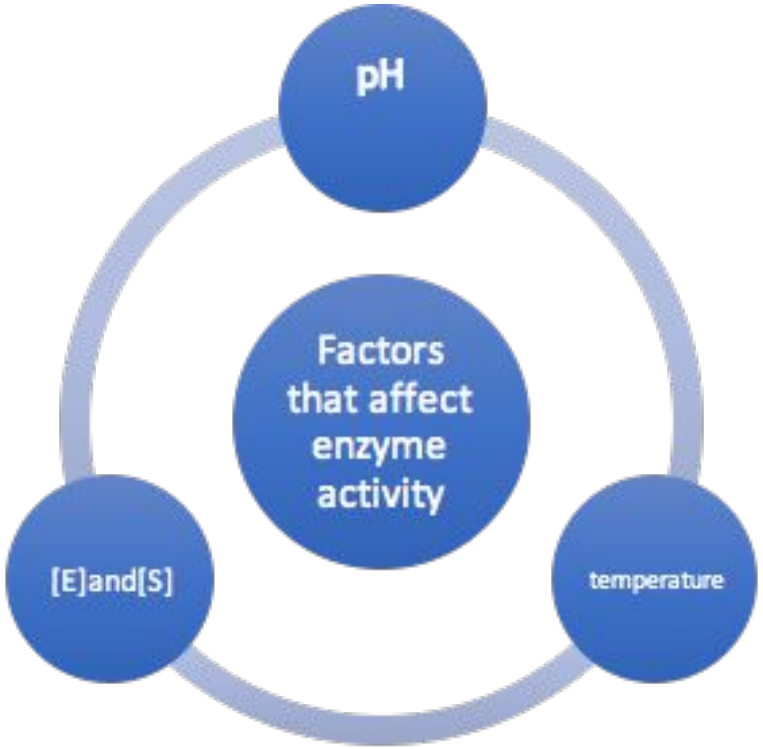
-Velocity is the rate of a reaction catalyzed by an enzyme ."How many substrates were converted into products for a unit time"

- Enzyme activity is expressed as

***m*moles** of product formed**/min/mg** enzyme

Millimoles / min / milligram
Or
Micromoles / min / microgram

"Always use the same unit"



1) Effect of temperature:

– Every enzyme has an **optimal temp**. for catalyzing a reaction (In humans most enzyme have an optimal temp. of **37C**)

– The rate of an enzyme reaction initially **increases** with rise in temperature.

–At high temp. enzymes are **denatured** and become inactive.

– In humans, most enzymes have an optimal temp of 37 c

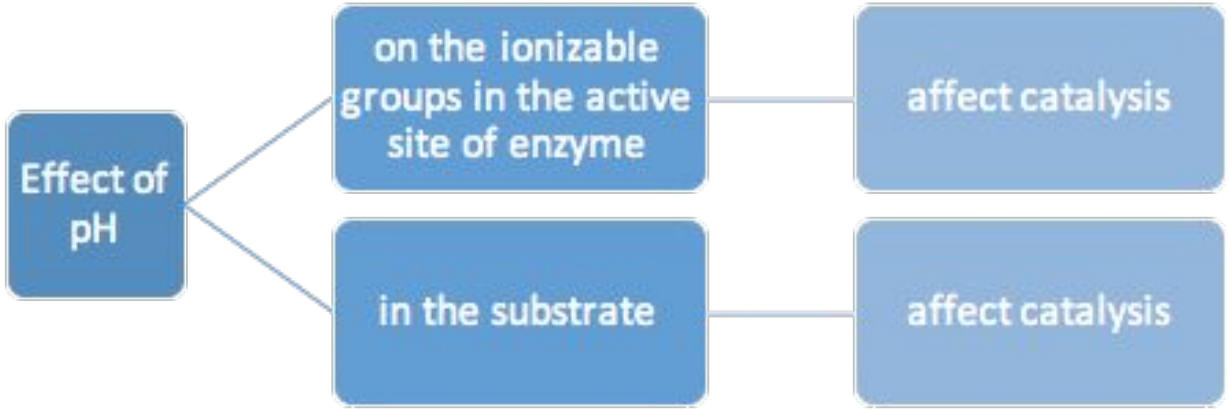
كل انزيم له درجه حراره محدده يعمل فيها وكل مازادت درجه الحراره يزداد rate of reaction ولكن اذا وصلت درجه حراره عاليه مره راح يتأثر الانزيم وبالتالي ما راح يشتغل (الشيء اذا زاد عن حده انقلب ضده)

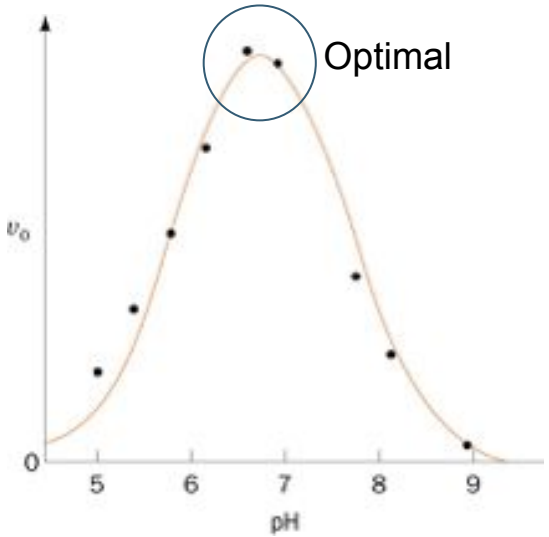
2) Effect of pH:

(the bell-shaped curve) Effect of pH on the initial rate of the reaction catalyzed by most enzymes

Every enzyme has an optimal pH for catalyzing a reaction

- Most enzymes have highest activity between **pH 6 and pH 8**
- Pepsin (digestive enzyme in the stomach) has highest activity at **pH 2**

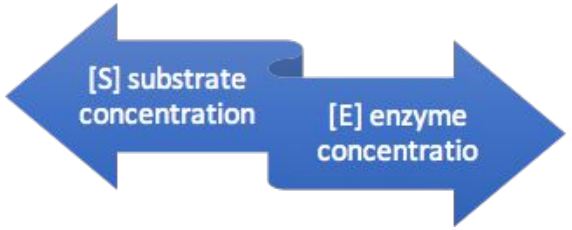




Effect of temperature and pH

حمضية أو قاعدية الوسط المناسب لعمل الإنزيم تعتمد على مكان عمله؛ اذا كان يعمل في بيئة حامضية مثل المعدة، يكون الوسط المناسب له حامضي؛ أو قاعدية مثل الأمعاء يكون الوسط المناسب له قاعدي

3) Effect of [E]and[S]:



- The reaction velocity increases initially with increasing [S]
Until excess substrate causes the reaction velocity to be constant *Further addition of substrate has no effect on enzyme velocity (v)* (because enzyme is saturated).

- If [S] > enzyme => the rate of enzyme reaction will be directly proportional to the concentration of enzyme.

اذا كان [S] اكثر من [E] في هذه الحاله سرعه التفاعل راح تعتمد بشكل طردي على [E] فكل مازادت تركيز الانزيمات يكون التفاعل اسرع

- At low [S], the reaction rate is proportional to [S]

Increase of the substrate concentration will increase the rate of the enzyme; until the enzymes reaches saturation and then further increase of the [S] will have no effect. “Is no longer a limiting factor”

Increase of the enzyme concentration will increase the rate of the enzyme; until all substrate are used up and bound to their enzymes; then further increase of enzyme concentration will have no effect “ no longer a limiting factor”

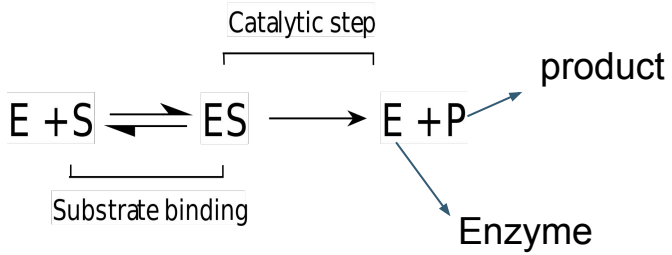
Effect of [E]and[S]

Enzyme kinetics

The model of enzyme kinetics was first proposed by Michaelis and Menten in 1913 and later modified by Briggs and Haldane.

The Michaelis Menten equation describes the relationship of initial rate of an enzyme reaction to the [S]

Initial rate= when nothing is limiting "plenty of substrates and enough enzymes"



Initial rate of enzyme reaction

1. Pre-steady state: The time they take to get arranged

*Enzyme + high concentration of substrate= an initial short period of time (a few hundred microseconds) during which intermediates of products gradually build up..**NO PRODUCT DURING THIS PHASE**.*

Enzyme-substrate complex formation only

2. steady state:

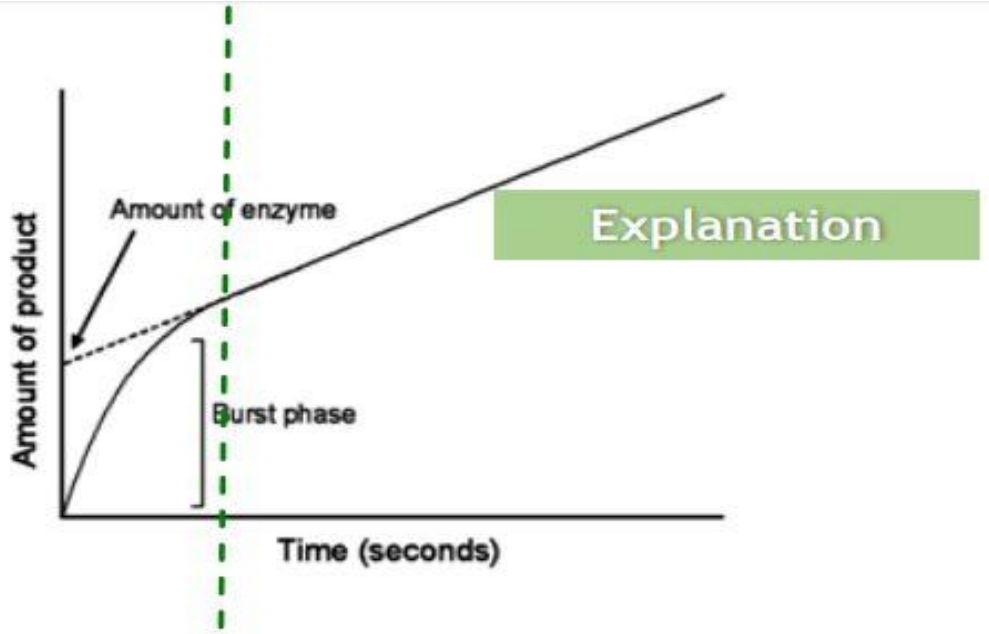
occurs after initial state, when the reaction rate and the concentration of intermediates change slowly with time

*An intermediate changes into steady state when the rate of its synthesis becomes **equal** to its rate of degradation.*

very useful video :)

an additional slide

TEAM 436



Explanation

Pre-steady state kinetics

- مرحلة إرتباط الإنزايم بالسبستريت عشان يتكوّن لي ال ES
وهو ليس بروودكت إنما "انزايم مرتبط مع سبستريت"
(Enzyme-substrate complex)
- هذه الخطوة تعتبر قصيرة جداً لأن كمية السبستريتس اكبر بكثير من كمية الانزايم فبالتالي تصبح نسبة ارتباط هذه السبستريتز بالانزايم قليلة.

Steady state kinetics

بعد ما تكوّن عندي ES (Enzyme-substrate complex)
سيصبح تركيزه يزداد بشكل ثابت مع الوقت (نلاحظ إن الميل في الصورة يزداد بثبات)

Michaelis Menten Equation

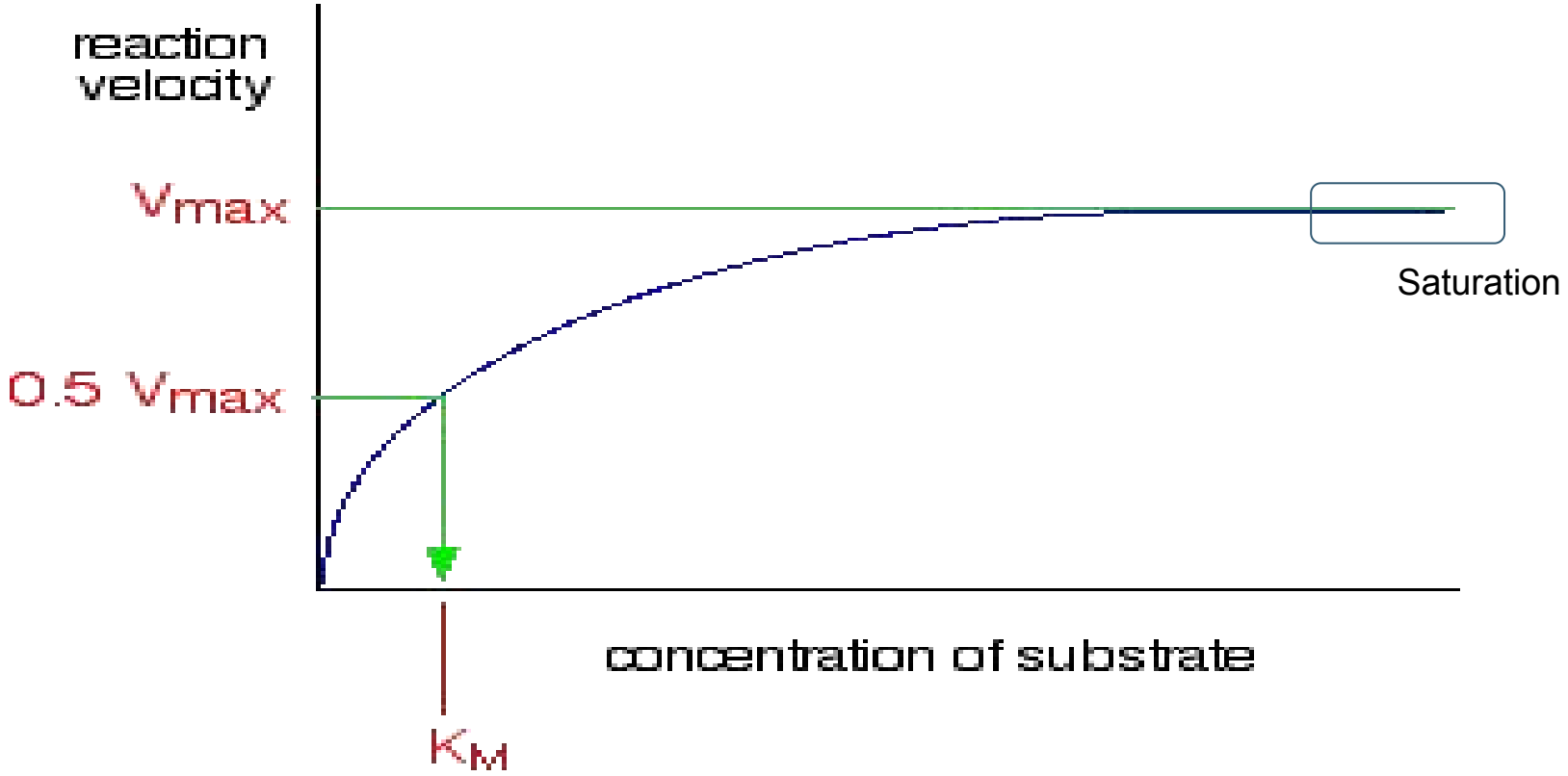
- It measures the initial velocity (vo) of an reaction enzyme

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

- *[S] = substrate concentration*
- *Vmax = maximum velocity*
- *Km = Michaelis constant*

You might be asked to either find (Vo, or Vmax, or Km or [S]) using this equation

Initial velocity Vo of a simple Michaelis Menten reaction- *versus* the substrate concentration



K_m (Michaelis Constant)

You must know the definitions.

K_m is the substrate concentration at which the initial rate is one-half of the maximum rate (½ V_{max})

It is the [S] (substrate concentration) required to saturate half of all of the active sites of an enzyme

- **The K_m value of a substrate depends on its affinity with the enzyme**
- **High K_m means low affinity with enzyme (more substrate needed to saturate the enzyme)**
- **Low K_m means high affinity with enzyme (less substrate needed to saturate the enzyme)**

Affinity= tendency to bind to a substrate

Lineweaver-Burk plot

Definition

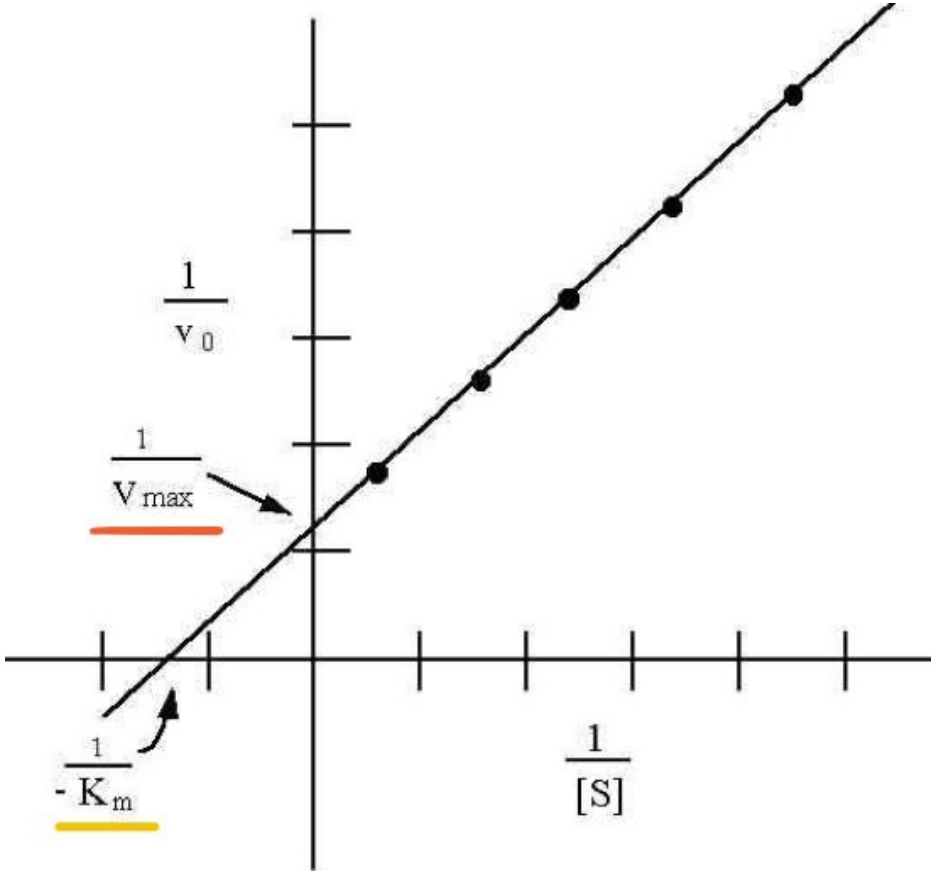
- **Also called the double-reciprocal plot, obtained by taking reciprocals of the Michaelis Menten equation**

Usage:

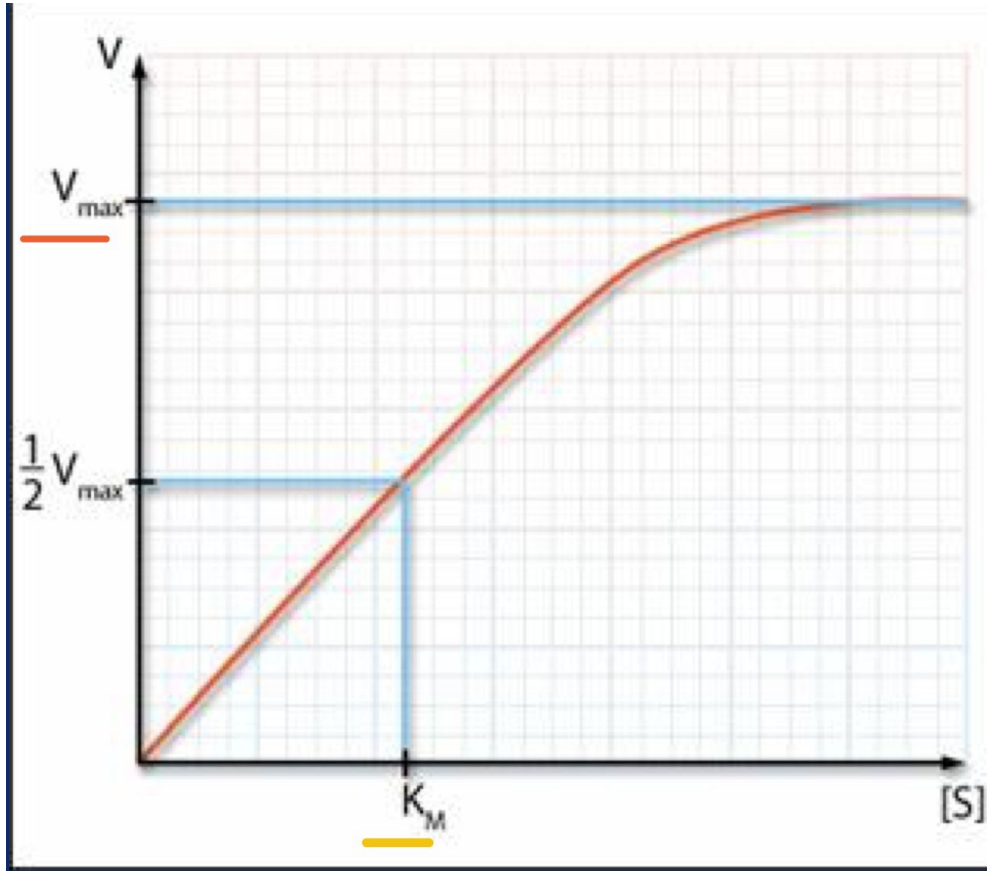
- **It is plotted to [1] calculate the Km and Vmax values and to [2] determine the mechanism of action of enzyme inhibitors**

The graphs are for further understanding, but you should be able to recognize each graph.

Lineweaver-Burk plot



Initial velocity Vo of a simple Michaelis Menten reaction- *versus* the substrate concentration



Mcq:

Which of the following statements about enzymes or their function is true?

A. Enzymes do not alter the overall change in free energy for a reaction
B. Enzymes are proteins whose three-dimensional form is key to their function
C. Enzymes speed up reactions by lowering activation energy
D. All of the above

Answer: D

The term apoenzyme is applicable to

a) Simple enzyme
b) Protein part of conjugate enzyme
c) Organic cofactor of a conjugate enzyme
d) Inorganic cofactor of a conjugate enzyme

Answer: b

Enzymes having slightly different molecular structures but performing identical activity are:

a) holoenzymes
b)apoenzymes
c) isoenzymes
d) coenzymes

Answer:c

Which factor is responsible for inhibition enzymatic process during feed back?

a) Enzymes
b) End product
c) Temperature
d) Substrate

Answer: b

An enzyme is

a-lipid
b-cabrohydrates
c-protein
d-nucleic acid

Answer: c

The Michaelis constant depends on?

a) The affinity of an enzyme to a receptor.
b)The concentration of substrates.
c)The affinity of a substrate to an enzyme.
d)The dissociation rate of a substrate to an enzyme.

`Answer :c

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