Enzymes & coenzymes 1

Editing File

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- Main Text (black)
- Female Slides (Pink)
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- Important (Red)
- Dr's Notes (Green)
- Extra Info (Grey)

Objectives

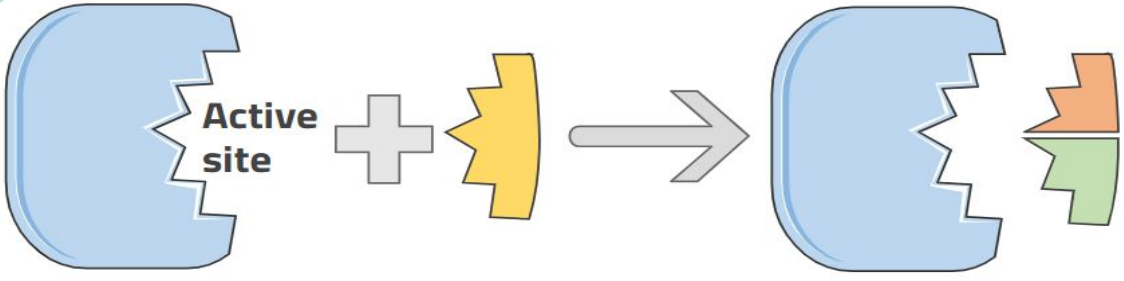
- Understand how enzymes are able to speed up the rate of biochemical reactions in the body.
- Identify classes of enzymes based on the type of reactions they catalyze.
- Comprehend basic terms of: coenzymes, isoenzymes, enzyme activity & specificity along with factors affecting their activity.
- Understand the enzyme kinetics.

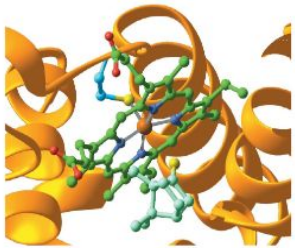
Enzymes

"**Biological catalysts** that speed up the rate of a reaction **without being consumed**/changed in the reaction"

Properties			Function	Structure
Regulation •	**Specificity** •	**Active site** •		
enzymes can be activated or inhibited so that the **rate of product formation** responds to the **need of the cell** • some enzymes also have **regulatory sites** that control the active site in different ways (next lecture's topic)	enzymes are **highly specific** • they interact with only **1 or few** substrates if they have very similar structures • they catalyze only **1 type** of reaction even if it's the same substrate (437)	all enzymes have ≥1 **active : sites** regions where "substrate binds" catalysis) occurs once (they bind	bind to specific **substrate** "substance upon which enzymes act" (like a reactant) to convert them to **(products)**	all enzymes are **protein** in nature, but NOT all proteins are enzymes (some may be structural or transporters, etc.) Exception: ribozymes are RNA (ribonucleic acid) molecules with enzymatic activity

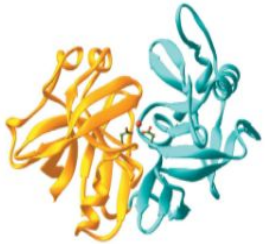
Enzymes





an **enzyme** with its active site

Trypsin (a digestive enzyme in small intestine)

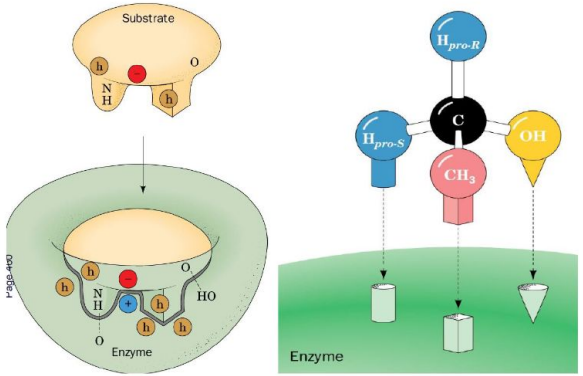


Pepsin (a digestive enzyme in stomach)

Models of enzyme-substrate binding

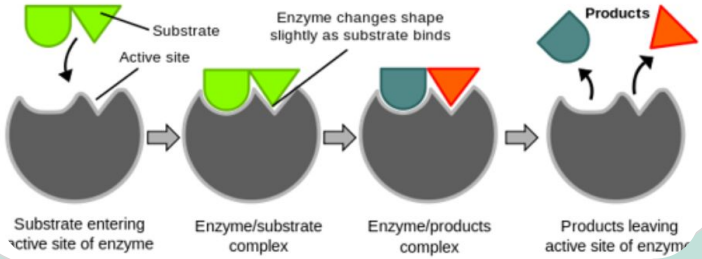
Lock & key binding

Active site fits the **exact dimensions** of substrate
[exactly complementary]
زي القفل ما يفتحه إلا مفتاح واحد نفس شكله بالضبط



Induced-fit binding

After the binding of substrate, the **enzyme changes its shape** or conformation to fit more perfectly with substrate
[not fully complementary, after the reaction is done, it goes back to its original shape to be able to function again**]**
زي القفاز يأخذ شكل اليد بعد ما ينلبس



Classification of enzymes

Classified into 6 types according to the type of reaction

Type of reaction (439)	class
Oxidation-reduction reaction	**1. Oxidoreductases**
Transfer of functional groups	**2. Transferases**
Hydrolysis (breaking bonds by adding water)	**3. Hydrolases**
Group elimination to form double/triple bonds	**4. Lyases**
Isomerization (form isomers) b they change the position of the group with in the same molecule	**5. Isomerases**
Bond formation coupled with ATP hydrolysis	**6. Ligases**

(436): Omar Tried Hard Learning International Languages

Nomenclature (naming)

Systematic name	Common name	
based on the rules given by **IUBMB** (International Union of Biochemistry & Molecular Biology): **EC Class . Subclass . Subsubclass . Enzyme number** (**EC** = Enzyme Commission)	Suffix **"-ase"**	**Rule**
Example: **EC 3.4.17.1** (carboxypeptidase A) Hydrolase, breaks a bond Which bond? peptide (439) Which enzyme exactly? hypothetically #1 Which peptide bond? alanine & serine for ex. *This is just an example, don't memorize it	(E.g. amylase) Exceptions: pepsin, trypsin	**Example**

Basic terms

Some enzymes require **non-protein** groups to catalyze a reaction : (become active)

Apoenzyme	+	Non-protein part	=	Holoenzyme
inactive form of enzyme **without its non-protein part**		required by some enzymes to become active; help to catalyze a reaction		**active** complex

- The majority of enzyme require these molecules
- They are present in the active site as an additional molecule

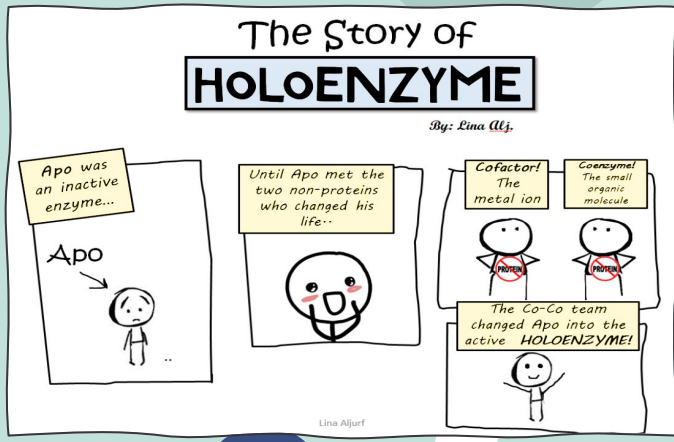
coenzyme	cofactor
small **organic** molecules (E.g. NAD^+, FAD, vitamins)	**metal** ion (E.g. Cu^{2+}, Fe^{3+}, Zn^{2+})

Prosthetic Group

permanently associated with enzyme (E.g. **FAD**)
always attached

Cosubstrate

temporarily associate with enzyme (E.g. **NAD**)
only attached during the reaction



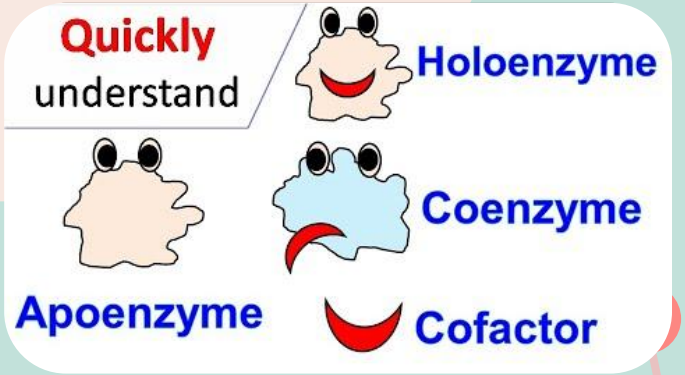
(434): notice that zymogens & apoenzymes need different things to become active:
Apoenzymes require a coenzyme/cofactor
Zymogens require a biochemical change

How enzymes work

Isoenzymes catalyze the same chemical reaction but they have slightly different structures

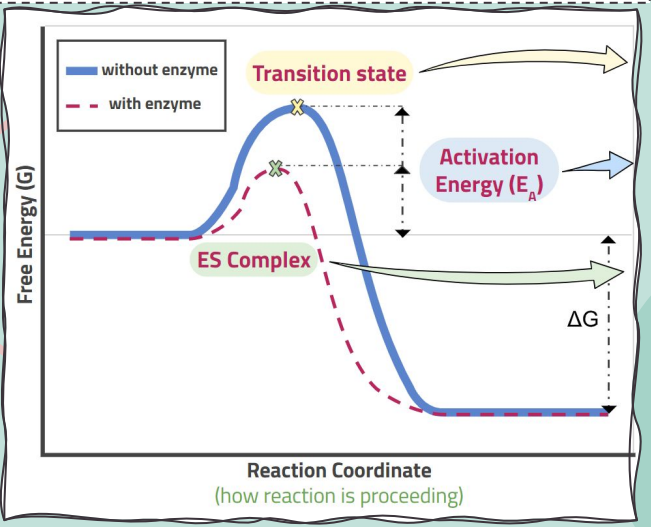
Apoenzyme (inactive) + Cofactor = Holoenzyme (active)
Apoenzyme (inactive) + Coenzyme = Holoenzyme (active)

Ribozymes are RNA (ribonucleic acid) with enzymatic activity
Zymogens are inactive forms of enzymes (Inactive enzyme precursors that require biochemical change to become active e.g. cleavage of a peptide blocking the active site)
They are activated when needed



How enzymes work

(434): notice that zymogens apoenzymes need different things to become active:
Apoenzymes: require coenzyme/cofactor
Zymogens: Require a biochemical change



Transition State: It is a **high-energy** intermediate that reactants pass through in every chemical reaction; it has **greater energy** than that of reactants or products alone

Activation Energy: It is the **difference in energy** between **reactants & transition state**
- If activation energy is available, the reaction can proceed forming products
- Uncatalyzed reactions are often slow due to high E_A

In order for enzymes to speed up reactions, they must:
1) **decrease the activation energy** required for a reaction, providing an **alternative transition state** of **lower energy** called **enzyme-substrate complex** and thus speed up the reaction.
2) **NOT alter the change in the free energy (ΔG)** "energy that can do work"
Why? because we don't want them to change the equilibrium of the reaction; rather, we need them to accelerate the rate by which equilibrium is reached, speeding up both forward & reverse rates

Isoenzymes catalyze the same chemical reaction but they have slightly different structures

Summary of how enzymes work:
1) Activation energy is reduced
2) Free energy remains the same

(436)
Enzyme induction = increasing activity
Enzyme inhibition = decreasing activity

ΔG of products must be less than ΔG of reactants

Factors that affect enzyme activity:

Enzyme activity or Velocity
Velocity: is the rate of a reaction catalyzed by an enzyme
Enzyme activity: is expressed as u moles of a product formed min/mg

Factors that affect enzyme activity

Enzyme velocity can be measured by either:
- How much product is increases/formed (more common)
- How much substrate conc. is decreased

Temperature

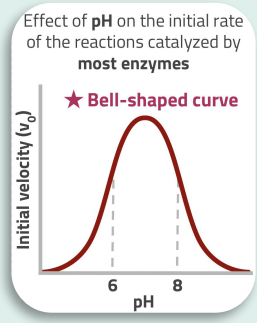
1

Every enzyme has an optimal temp for catalyzing a reaction in humans most enzymes have an optimal temp is 37 C
- The rate of an enzyme reaction initially increases with rise in temp. (Increase in velocity until it reaches peak velocity (very active)
- But at high temp. [E.g. above 40 C] enzymes are denatured become inactive

pH

2

Every enzyme has an optimal pH for catalyzing a reaction, which is the peak of a bell shaped curve. Most have highest activity between pH 6-8 [Exception: pepsin has highest activity at pH 2 in the stomach]
- pH affects catalysts through either the substrate or ionizable groups in the active site of enzyme



[S] & [E] concentration

[ ] Square brackets depict concentration

[S] and [E] means substrate conc. And Enzyme conc.

3

At low [S]
- The reaction velocity/rate (v) is proportional [S] (increases initially with increasing [S])

At high [S]
- Further addition of substrate has no effect on enzyme velocity because enzyme is saturated & all active sites are engaged
- The rate of an enzyme reaction is directly proportional to [E] if [S] is higher than [E]

Enzyme Kinetics

In this reaction model, ES complex has 2 fates:

1) Continue to form product [right]
2) Go backwards [left]

S = substrate
E = enzyme
ES = enzyme-substrate complex
P = product
K1, k-1, k2 = rate constants

Extra:
Why is k–2 missing? Although step 2 is reversible, we do not consider its reverse reaction because our study of kinetics is during the early phase, where there is a very low concentration of product, so k–2 is negligible

Initial Rate of an Enzyme Reaction

Pre steady state Kinetics

- When an enzyme is mixed with high [S], there is an initial period of time (a few 100 microseconds) , during which intermediates leading to the formation of the product .
- (ES) gradually build up (no product has formed yet)

Steady state Kinetics

- After initial state the reaction rate and concentration of the intermediates changes slowly with time.
- The intermediate is said to be in steady state because its rate of synthesis is equal to its rate of degradation

Summary		
	Pre-steady state	▪ ES builds up ▪ No product yet
	Steady state	▪ ES is constant ▪ Product forms

Michaelis-Menten

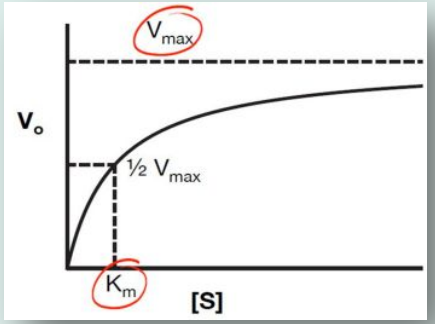
- The model of enzyme kinetics was first proposed by Michaelis-Menten in 1913 and later modified by Briggs & Haldane
- The Michaelis-Menten equation describes the relationship of initial rate of an enzyme reaction to the [s]
- It measures the initial velocity (Vo) of an enzyme reaction

Equation:

$$V_0 = \frac{V_{MAX} \times [S]}{K_M + [S]}$$

V_{max} : max velocity
[s]: Substrate Concentration
K_M: Michaelis Constant

Graph:



K_M: Michaelis-Constant

Quantitatively (Numerically):

- It is the substrate concentration at which the initial rate is one-half of the maximum rate (½ V_{max})
- It is the substrate concentration required to saturate half of all the active sites of an enzyme

Qualitatively (how it benefits us or what it indicates)

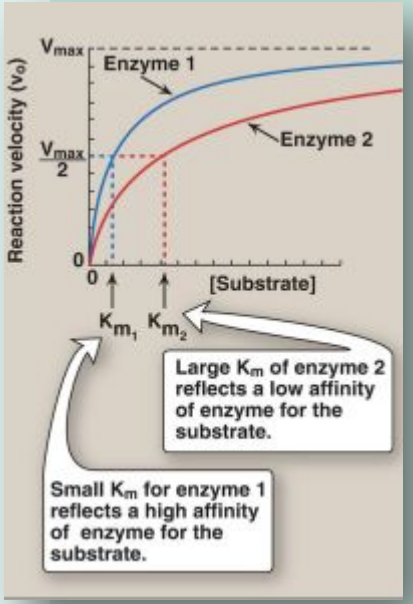
The K_m value of a substrate depends on its affinity with an enzyme

High K_m

Means low affinity with enzyme (more substrate is needed to saturate the enzyme)

Low K_m

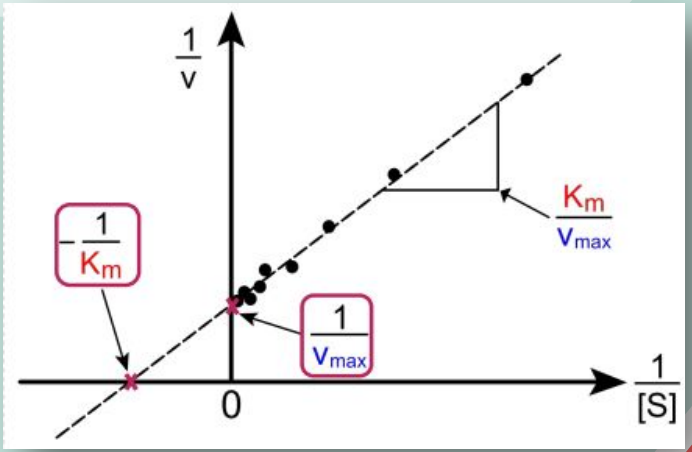
Means high affinity with enzyme (less substrate is needed to saturate the enzyme)



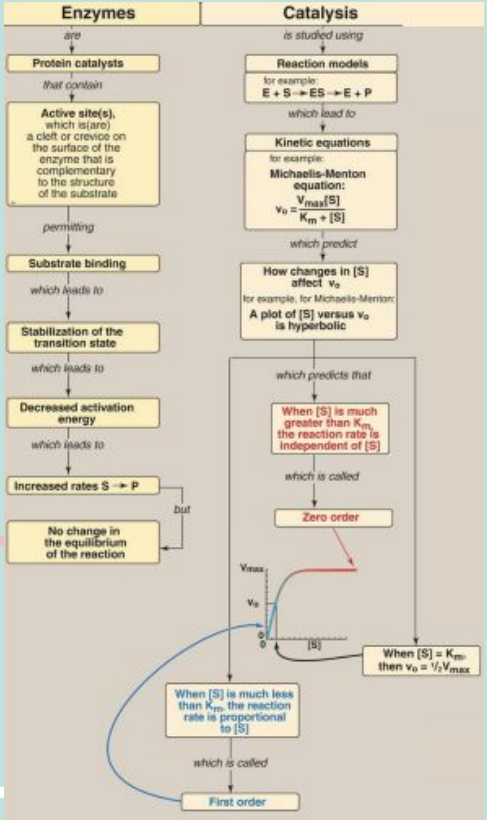
Lineweaver-Burk

- **Also called** double-reciprocal
- **It's obtained from** taking reciprocals of the Michaelis Menten Equation.
- **It's plotted to**
  1) Calculate the K_m and V_{max} values more accurately.
  2) Determine the mechanism of action of enzyme inhibitors.

How is it different than the Michaelis-Menten plot? The Michaelis-Menten plot is hyperbolic (curved), which makes it inaccurate as it gives multiple values for Vmax. Thus, Lineweaver & Burk suggested to linearize it (graph the same data as a straight line) to improve accuracy

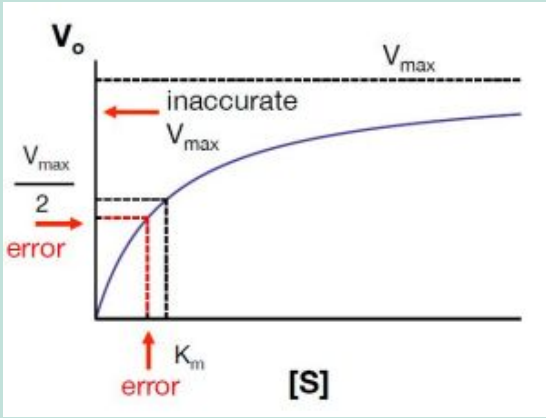


Summary

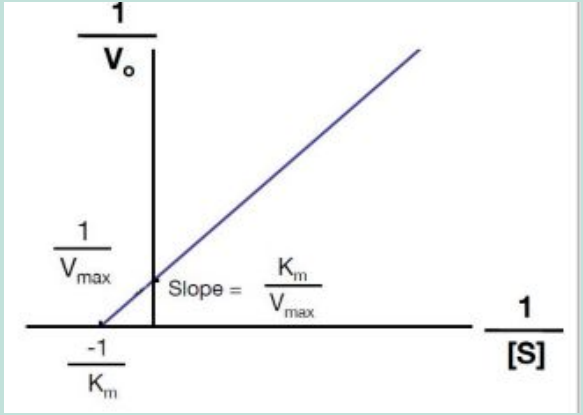


Side by side Comparison

Michaelis-Menten



Lineweaver-Burk



Question 1

High Km value indicates

A. Low affinity with enzymes

B. High affinity with enzymes

C. Initial velocity equals zero

D. Steady state reaction

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Question 2

Which is true about isoenzymes?

A They catalyse the same reaction

C They react with the same substrate

B They have the same structure

D A & C

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Question 3

Which phase contains the highest energy

A Reactants

C Transition

B Products

D A & B

Question 3

Which phase contains the highest energy

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B Products

D A & B

Question 4

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

A Holoenzymes

C Coenzymes

B Apoenzymes

D Ligases

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Question 5

When classifying enzymes, which class functions to eliminate groups?

A Oxidoreductases

B Transferases

C Lyases

D Ligases

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