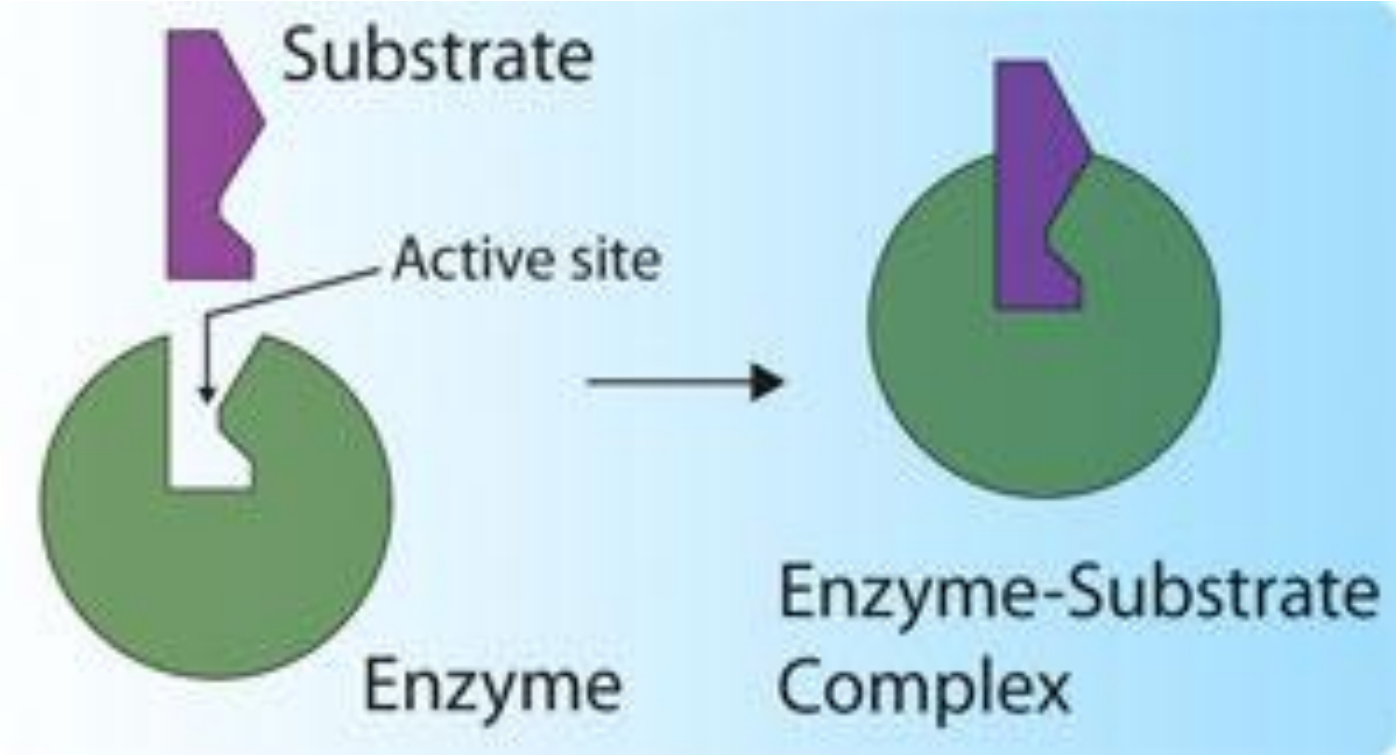
Enzymes



ENZYME

- Usually a **protein**, acting as **catalyst** in specific biochemical reaction
- An enzyme is a highly selective catalyst that greatly accelerates both the rate and specificity of metabolic reactions.
- Each cell in the human body contains 1,000s of different enzymes – **Every reaction in the cell requires its own specific enzyme**
- Enzymes undergo **all the reactions of proteins.**
- Enzymes **denaturation due to pH or temperature change**
- A person suffering high fever runs the risk of denaturing certain enzymes

Enzyme structure

- **SIMPLE ENZYMES**

Composed only of protein

- **CONJUGATED ENZYMES**

Composed of: Apoenzyme and Coenzyme or Cofactor

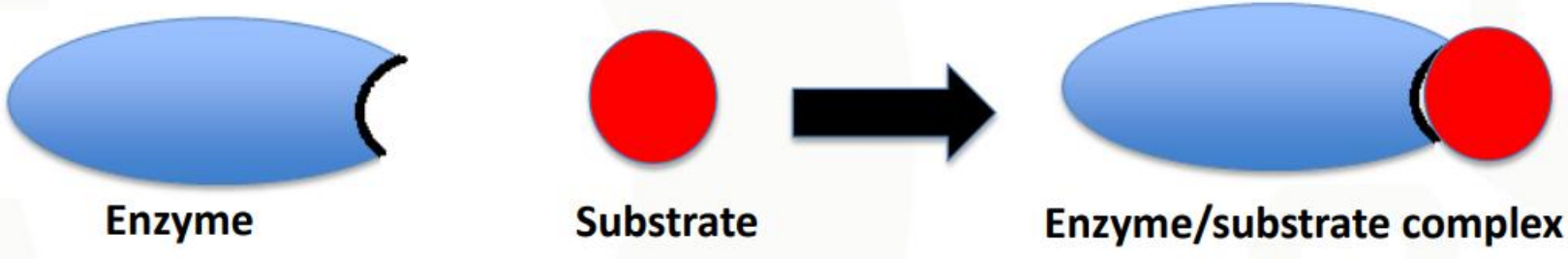
Enzyme definitions

Term	Definition
Enzyme (simple)	Protein only enzyme that facilitates a chemical reaction
Coenzyme	Compound derived from a vitamin (e.g. NAD^+) that assists an enzyme in facilitating a chemical reaction
Cofactor	Metal ion (e.g. Mg^{2+}) that that assists an enzyme in facilitating a chemical reaction
Apoenzyme	Protein only part of an enzyme (e.g. isocitrate dehydrogenase) that requires an additional coenzyme to facilitate a chemical reaction (not functional alone)
Holoenzyme	Combination of the apoenzyme and coenzyme which together facilitating a chemical reaction (functional)

Enzyme Nomenclature

- Enzymes are named according to the
  type of reaction they catalyze and/or their substrate
- **Substrate** = the reactant upon which the specific enzyme acts
  - Enzyme physically binds to the substrate

- **Suffix of an enzyme –ase**
  - *Lactase*, *amylase*, *lipase* or *protease*
    - Denotes an enzyme
- Some digestive enzymes have the suffix **–in**
  - *Pepsin*, *trypsin* & *chymotrypsin*
    - These enzymes were the first ones to be studied
- **Prefix** denotes the type of reaction the enzyme catalyzes
  - *Oxidase: redox reaction*
  - *Hydrolase: Addition of water to break one component into two parts*
- **Substrate identity** is often used together with the reaction type
  - *Pyruvate carboxylase*, *lactate dehydrogenase*



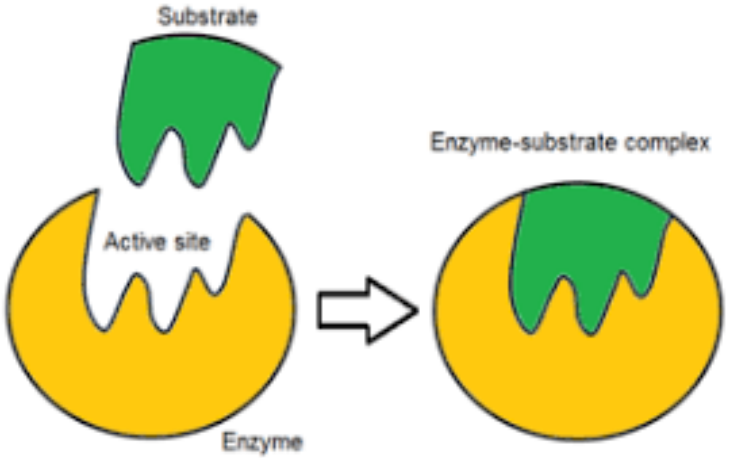
6 major classes of enzymes

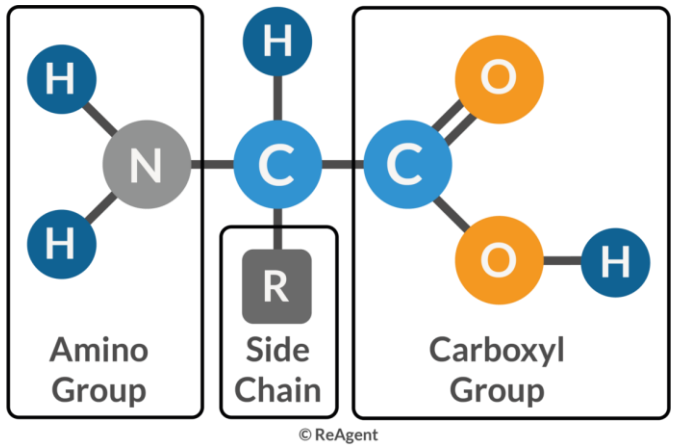
Enzyme Class	Reaction Catalyzed	Examples in Metabolism
Oxidoreductase	Redox reaction (reduction & oxidation)	Examples are **dehydrogenases** catalyse reactions in which a substrate is oxidised or reduced
Transferase	Transfer of a functional group from 1 molecule to another	**Transaminases** which catalyze the transfer of amino group or kinases which catalyze the transfer of phosphate groups.
Hydrolase	Hydrolysis reaction	**Lipases** catalyze the hydrolysis of lipids, and proteases catalyze the hydrolysis of proteins
Lyase	Addition / removal of atoms to / from double bond	**Decarboxylases** catalyze the removal of carboxyl groups
Isomerase	Isomerization reaction	**Isomerases** may catalyze the conversion of an aldose to a ketose, and mutases transfer functional group from one atom to another within a substrate.
Ligase	Synthesis reaction (Joining of 2 molecules into one, forming a new chemical bond, coupled with ATP hydrolysis)	**Synthetases** link two smaller molecules are form a larger one.

The table explains the functions of enzymes and how they are classified and named.

Enzyme Active Site

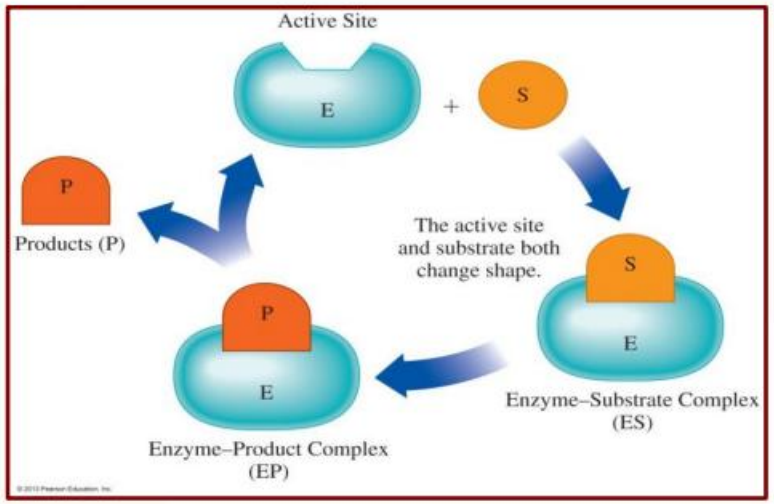
- Active site – The specific portion of an enzyme (location) where the substrate binds while it undergoes a chemical reaction
- The active site is a 3-D ‘crevice-like’ cavity formed by secondary & tertiary structures of the protein part of the enzyme – Crevice formed from the folding of the protein
- An enzyme can have more than only one active site.
- The amino acids R-groups (side chain) in the active site are important for determining the specificity of the substrate

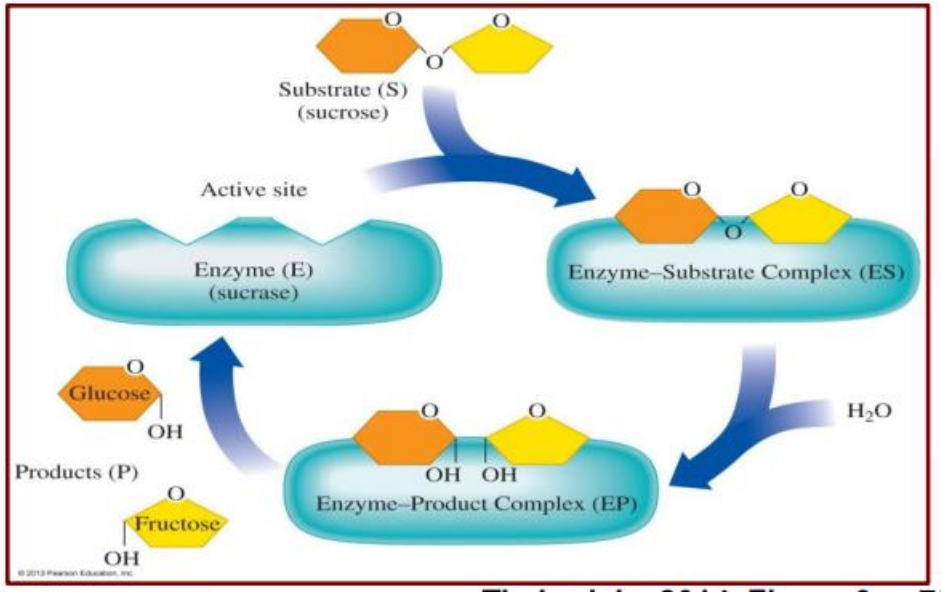




Enzyme – Substrate Complex

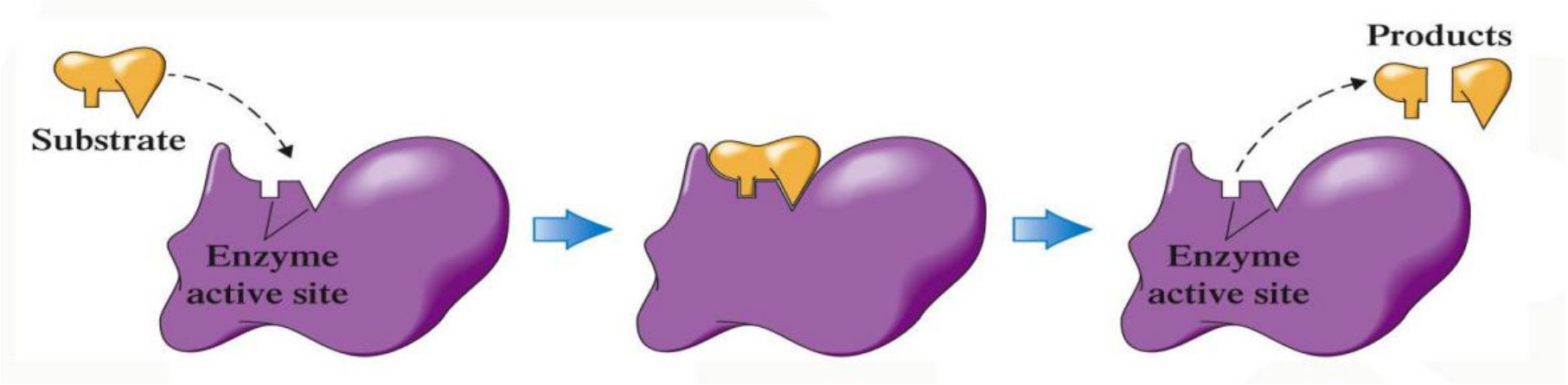
- When the substrate binds to the enzyme active site an Enzyme-Substrate Complex is formed temporarily – Allows the substrate to undergo its chemical reaction much faster.





Lock & Key Model of Enzyme Action

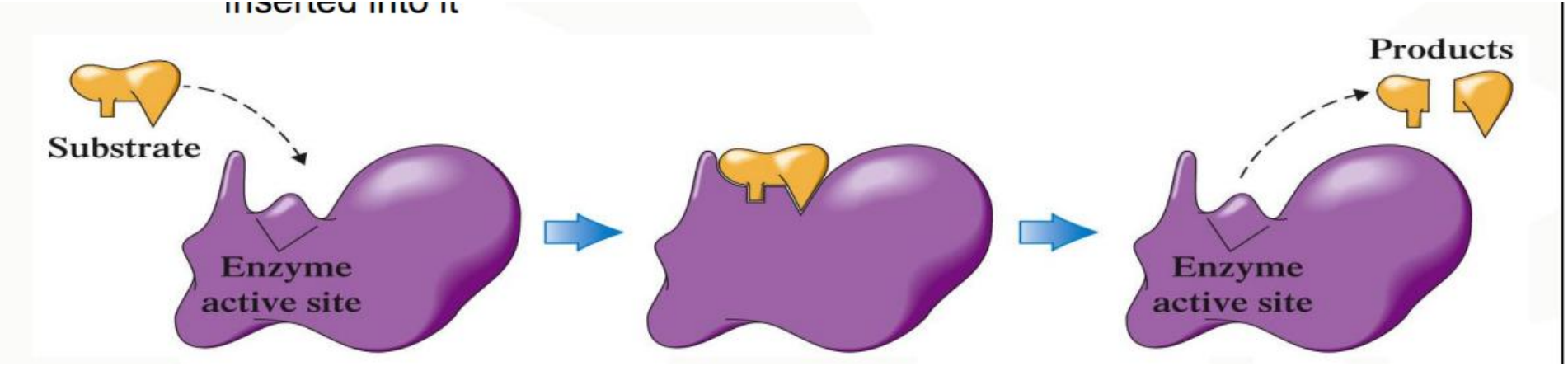
- The active site is fixed, with a rigid shape (LOCK)
- The substrate (KEY) must fit exactly into the rigid enzyme (LOCK)
- Complementary shape & geometry between enzyme and substrate – Key (substrate) fits into the lock (enzyme)
- Upon completion of the chemical reaction, the products are released from the active site, so the next substrate molecule can bind



Induced Fit Model of Enzyme Action

- Many enzymes are flexible & constantly change their shape – The shape of the active site changes to accept & accommodate the substrate

• Conformation change in the enzyme's active site to allow the substrate to bind • Analogy: a glove (enzyme) changes shape when a hand (substrate) is inserted into glove.

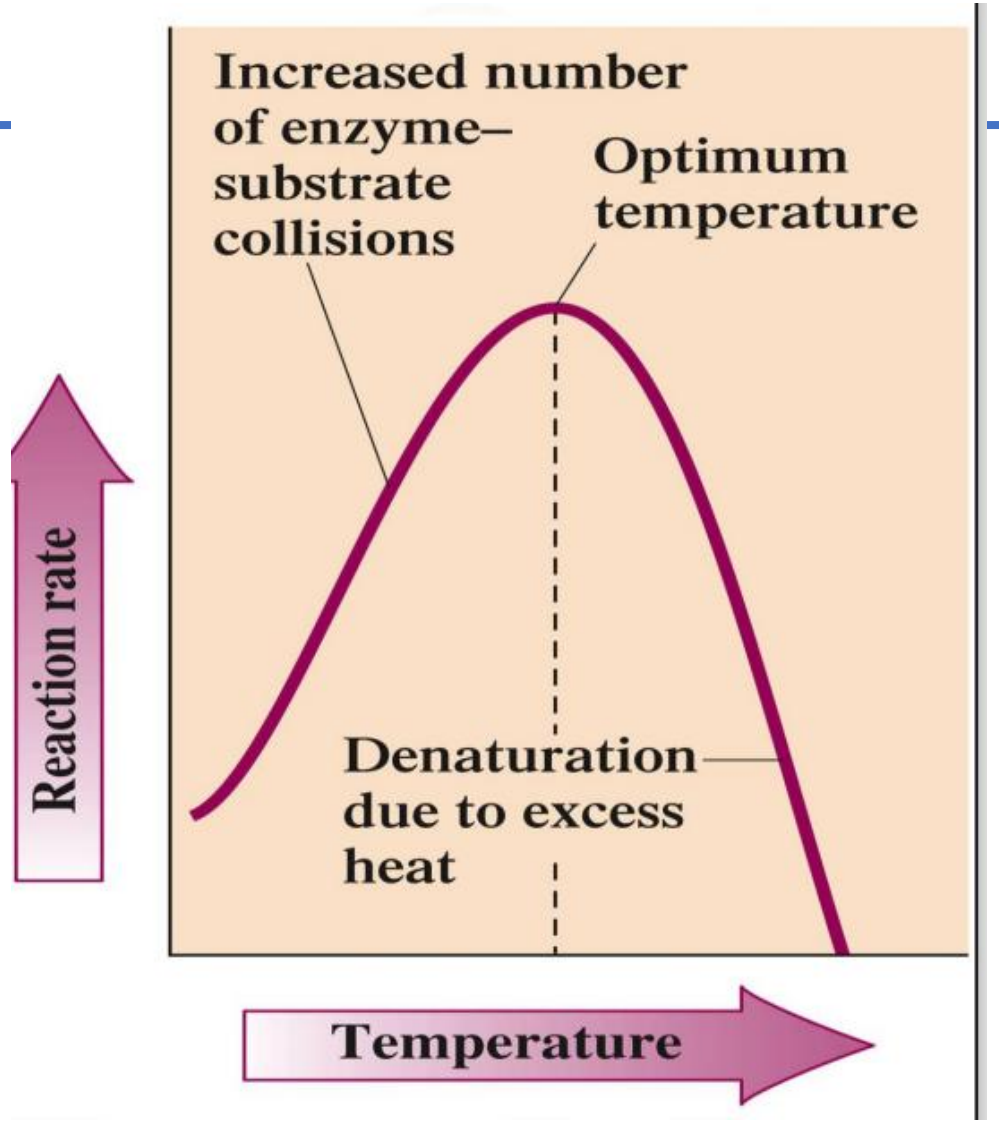


Factors affecting enzyme activity

- Enzyme activity can be affected by a variety of factors,.
  - Temperature,
  - pH, and
  - Enzyme concentration
  - Substrate concentration
- Enzymes work best within specific temperature and pH ranges, and sub-optimal conditions can cause an enzyme to lose its ability to bind to a substrate.

Temperature

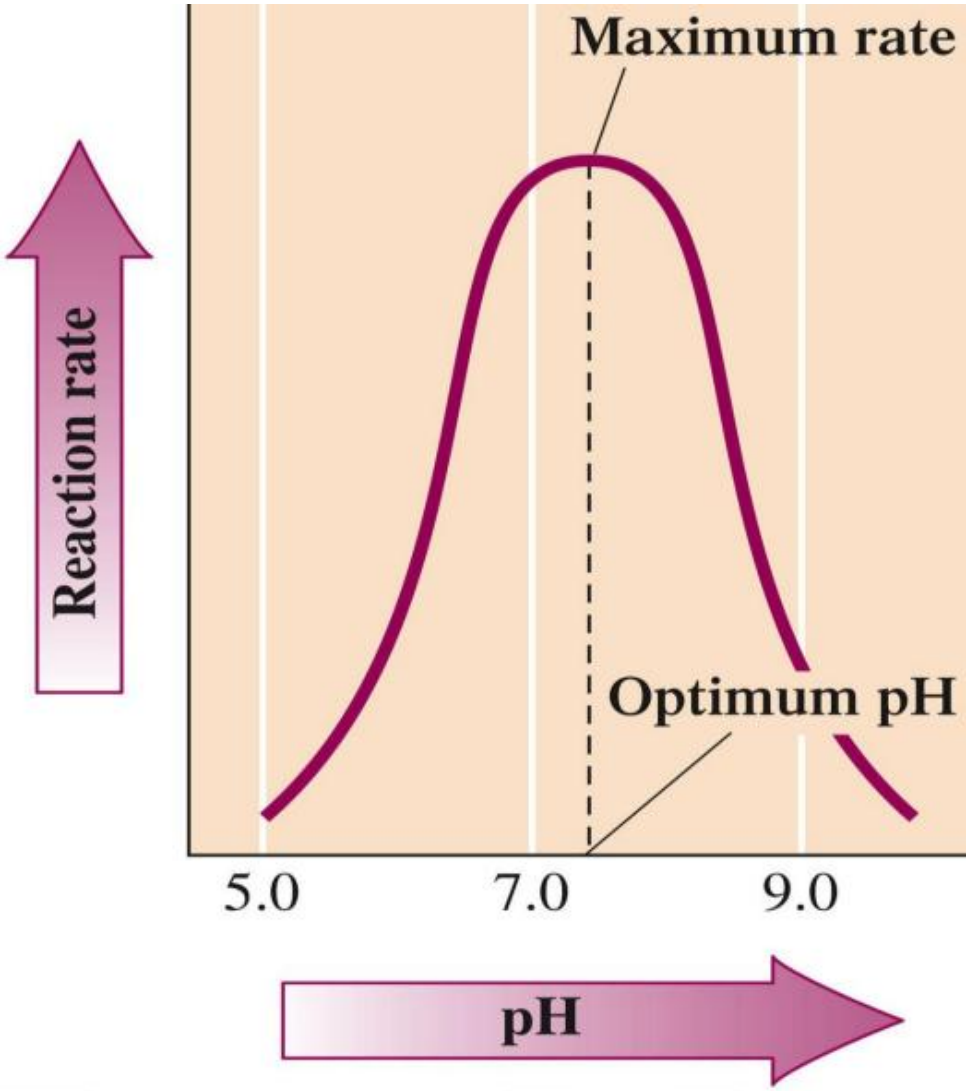
- With increased **t** the E_{KIN} increases
  - More collisions
  - Increased reaction rate
- ***Optimum temperature*** ***(t_{OPT})*** is the **t,** at which the enzyme exhibits maximum activity
  - The t_{OPT} for human enzymes = 37^0C
- When the **t** increases beyond t_{OPT}
  - Changes in the enzyme's tertiary structure occur, inactivating & denaturing it (e.g. fever)
- Little activity is observed at low **t**



pH

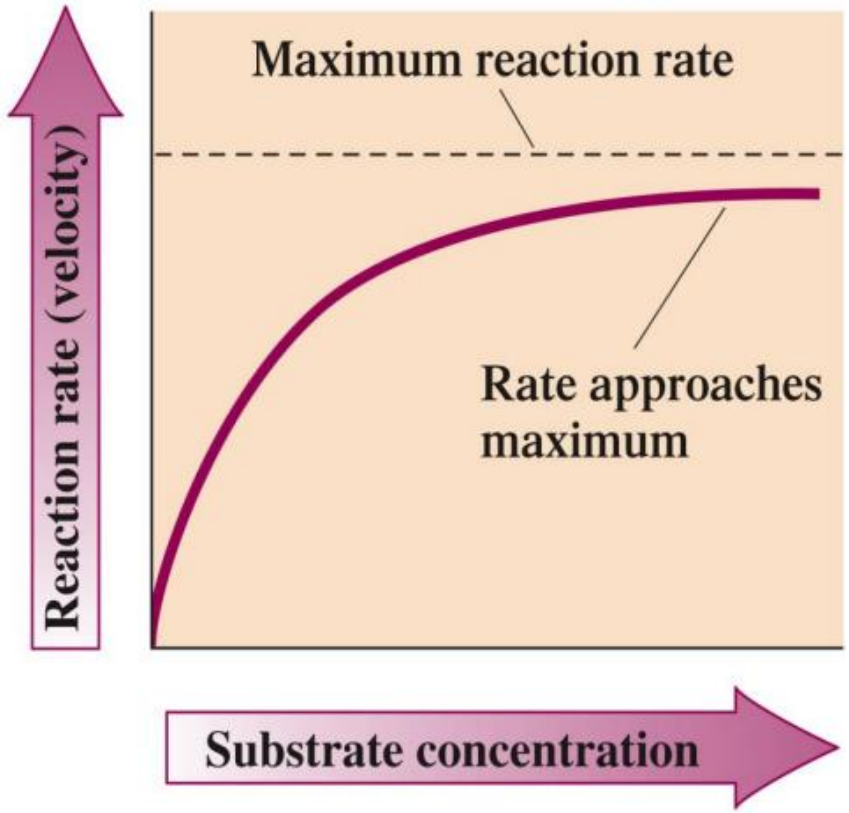
- ***Optimum pH (pH_{OPT})*** is the **pH**, at which the enzyme exhibits maximum activity
- Most enzymes are active over a **very narrow pH range**
  - Protein & amino acids are properly maintained
  - Small changes in pH (low or high) can result in enzyme denaturation & loss of function
- Each enzyme has its characteristic ***pH_{OPT}***, which usually falls within physiological pH range 7.0 - 7.5
- ***Digestive enzymes are exceptions:***
  - ***Pepsin*** (in stomach) – ***pH_{OPT}*** = 2.0
  - ***Trypsin*** (in SI) – ***pH_{OPT}*** = 8.0

Small intestine



Substrate concentration

- If [enzyme] is kept constant & the [substrate] is increased
  - The reaction rate increases until a ***saturation point*** is met
    - At saturation the reaction rate stays the same even if the [substrate] is increased
  - **At saturation point** substrate molecules are bound to all available active sites of the enzyme molecules
- Reaction takes place at the active site
  - If they are all active sites are occupied the reaction is going at its maximum rate
    - Each enzyme molecule is working at its maximum capacity
  - The incoming substrate molecules must "wait their turn"



Enzyme concentration

- If the [substrate] is kept constant & the [enzyme] is increased
  - The reaction rate increases
  - The greater the [enzyme], the greater the reaction rate
- **RULE:**
  - The rate of an enzyme-catalyzed reaction is always directly proportional to the amount of the enzyme present
- ***In a living cell:***
  - The [substrate] is much higher than the [enzyme]
    - Enzymes are not consumed in the reaction
    - Enzymes can be reused many times