Enzyme Mechanism

Chapter 6: Pages 96 - 103

Topics

- Types
- Composition
- Specificity
- Catalytic Reaction
- Mechanisms for lowering EA
- Factor affecting enzymatic rate of reaction

Enzyme Function

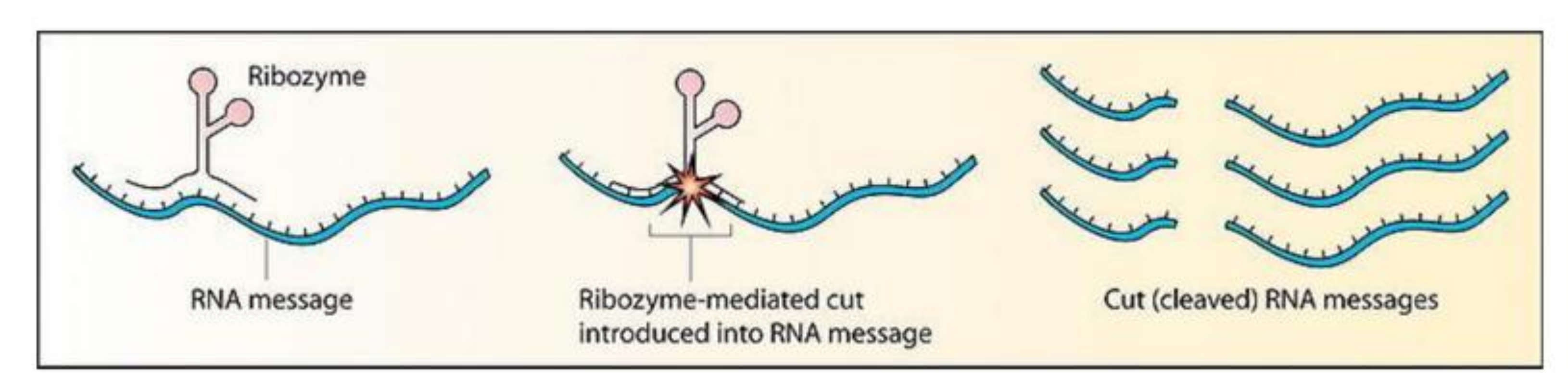
- **Enzyme:** biological catalyst that speed up rates of reaction that would otherwise be too slow to support life
- **Catalyst:** a chemical agent that changes the rate of a reaction without being consumed by the reaction
- Enzymes are unaffected by the reaction and are reusable

Enzyme Composition

Almost all enzymes are composed of proteins

Exception: Ribozyme

- RNA that catalyze reactions on other RNA
- Hydrolysis at phosphodiester bond



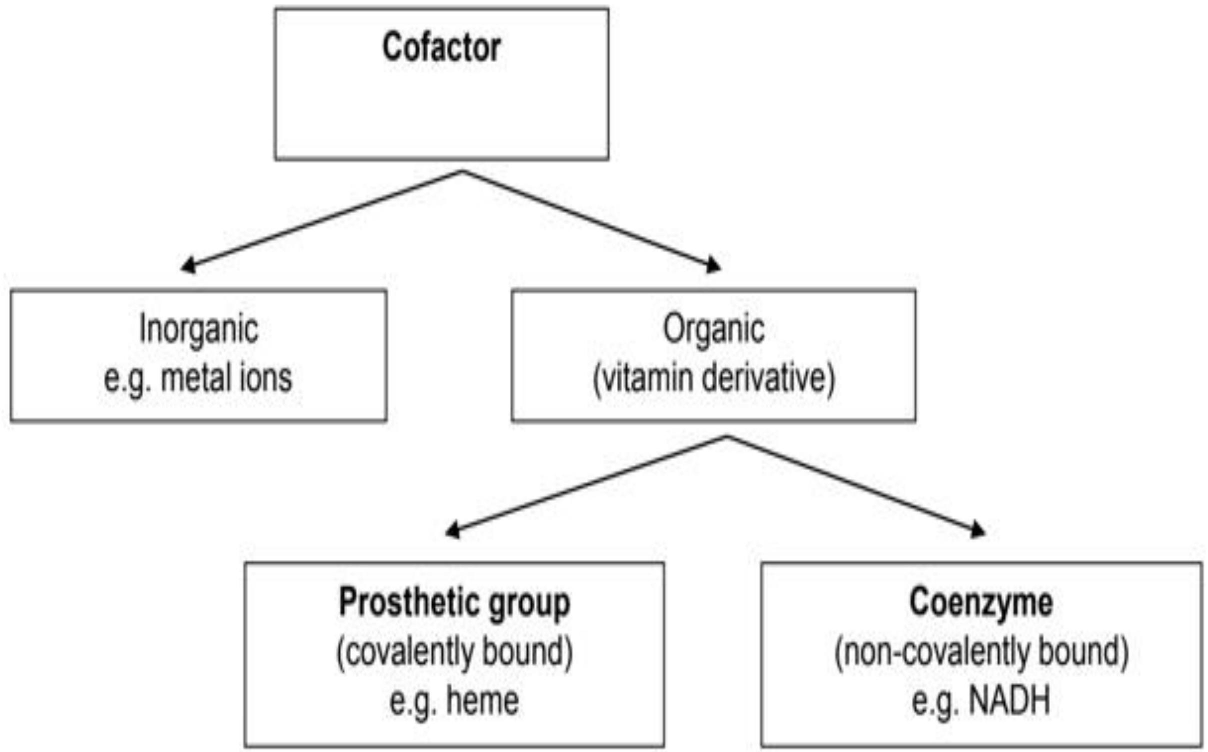
Enzyme Type

- Simple enzyme: composed only of protein component
- Complex enzyme: an enzyme that requires a cofactor to function in addition to its protein component
  - Apoenzyme: Inactive form of the enzyme because it is missing the cofactor
  - Holoenzyme: Active form of the enzyme; with cofactor

Types of Cofactors

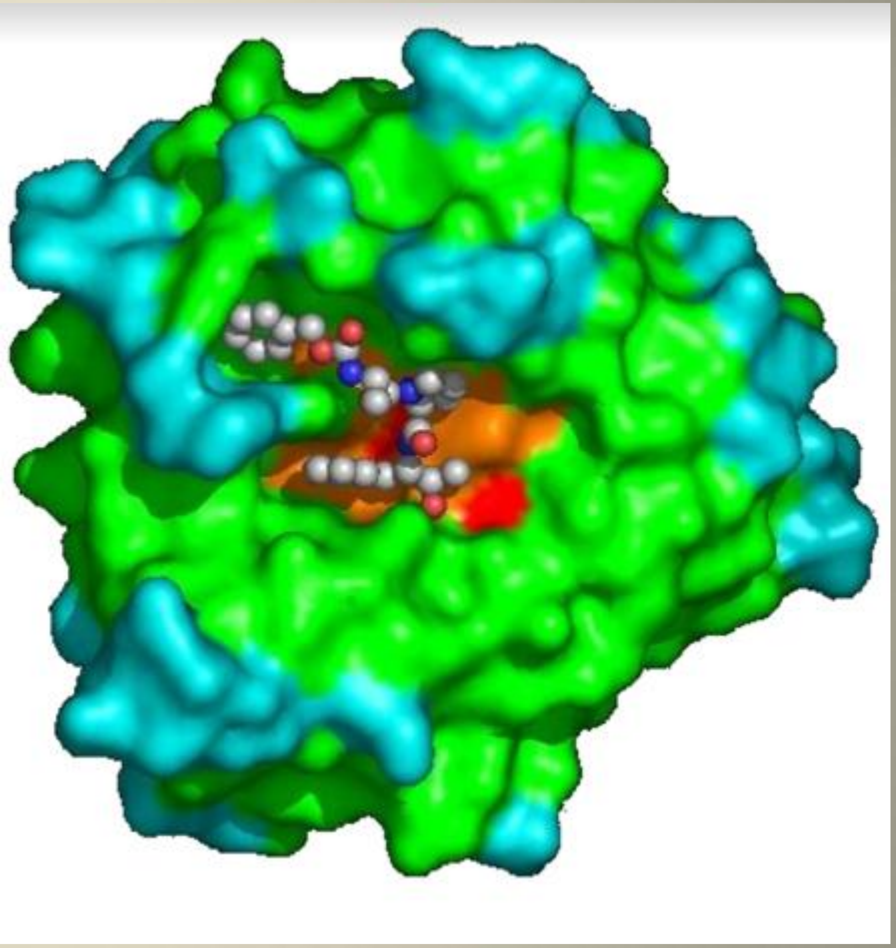
- Inorganic: metal ions
  - Most common: Zn, Fe, Cu
- Organic: usually from vitamins or their derivatives
  - Prosthetic group: covalently/permanently bonded to apoenzyme (e.g. heme)
  - Coenzyme: non-covalently/reversibly bound to apoenzyme (e.g. NADH)

Types of Cofactors



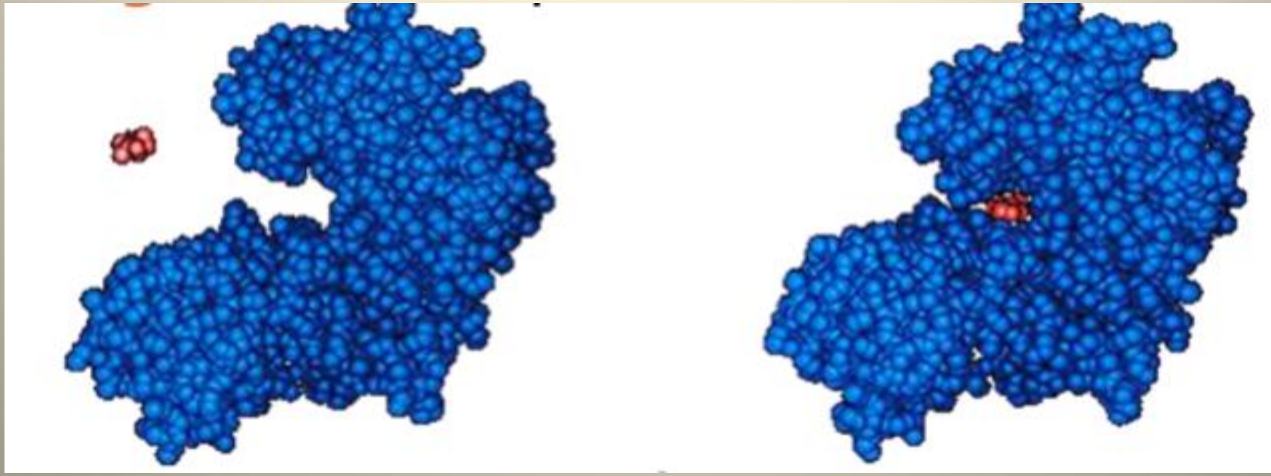
Enzyme Components

- Enzymes act on substrates at their active site
- **Substrate**: reactant that enzyme acts on
- **Active site**: a pocket where the substrate binds; catalytic center where substrate is converted to product



Induced Fit Model

- As the substrate binds, the enzyme changes shape leading to a tighter fit, bringing chemical groups in position to catalyze the reaction.
- Binding of a substrate induces a favourable change in the shape of the active site



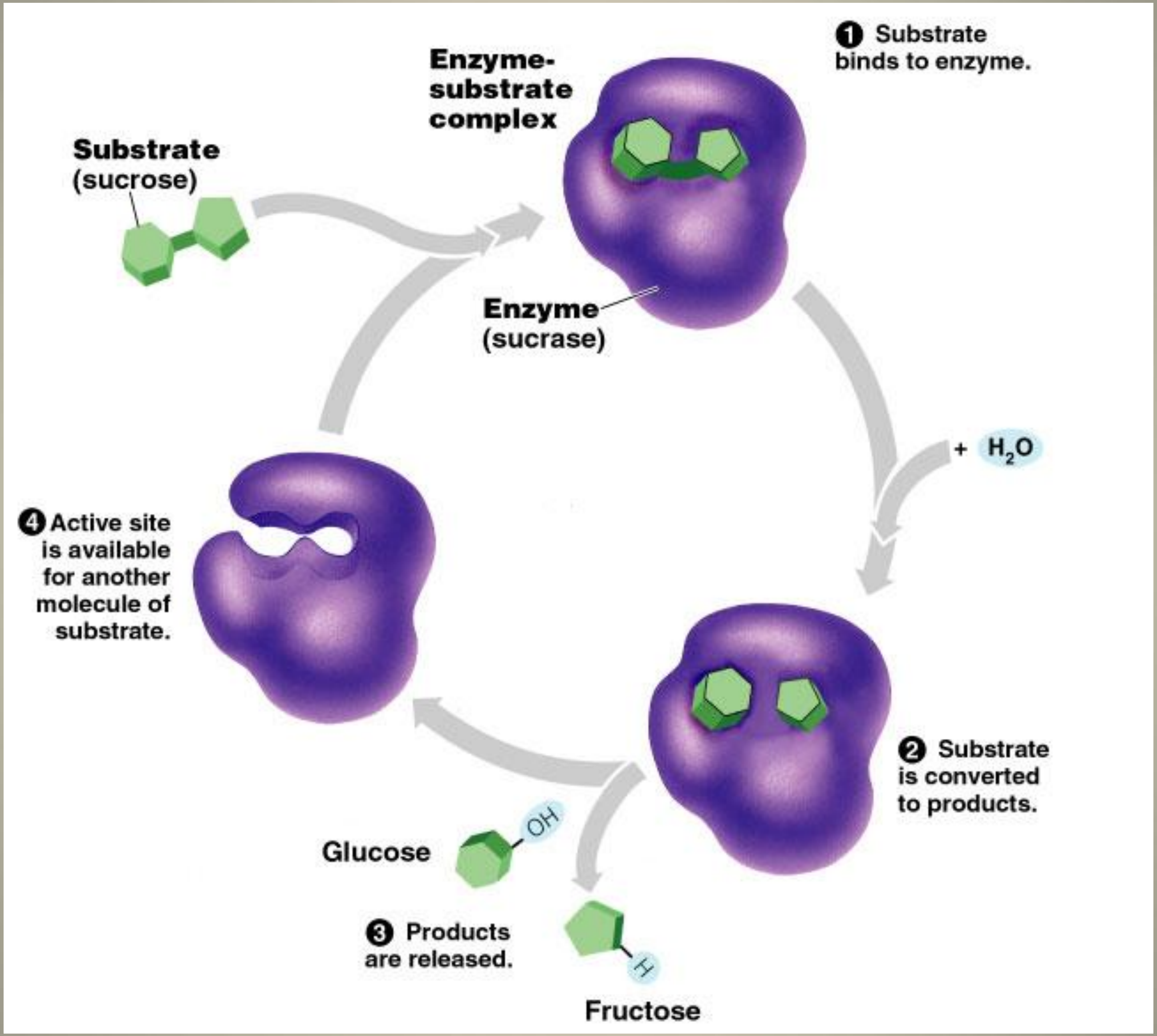
Enzyme Specificity: Reaction

- Reaction specific: Enzyme catalysis is specific for one chemical reaction

  - Example: Sucrase is an enzyme that only catalyzes the hydrolysis of sucrose

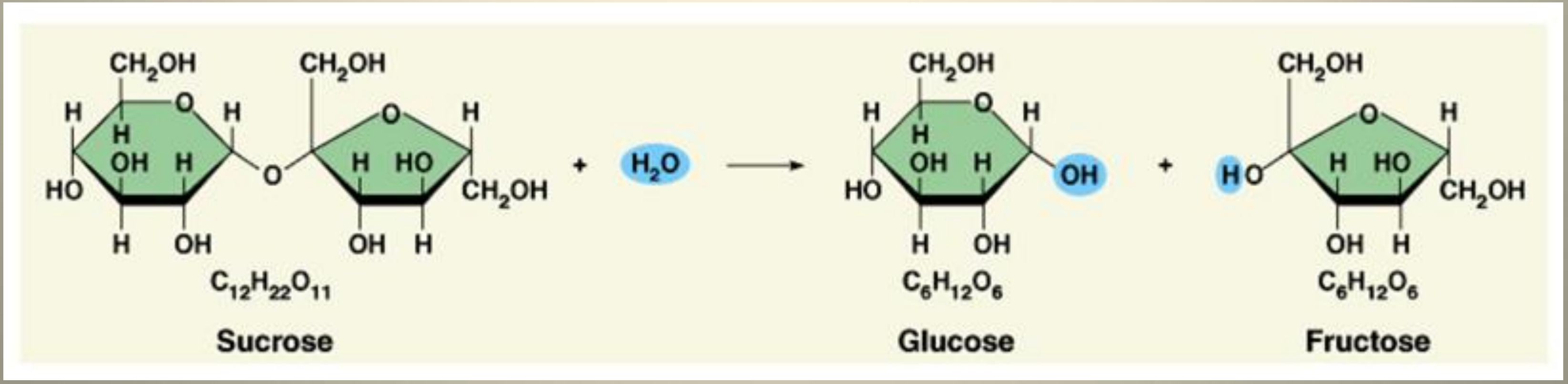
$$\text{Sucrose} + H_2O \xrightarrow{\text{Sucrase}} \text{Glucose} + \text{Fructose}$$

- Most metabolic enzymes can catalyze a reaction in both the **forward** and **reverse** direction


1 Substrate binds to enzyme.
Enzyme-substrate complex
Substrate (sucrose)
Enzyme (sucrase)
+ H_2O
4 Active site is available for another molecule of substrate.
2 Substrate is converted to products.
Glucose
OH
3 Products are released.
H
Fructose

Catalytic Reactions

- Chemical reactions between molecules involve both bond breaking and forming.
- Example: sucrose hydrolysis
  - bond between glucose and fructose is broken
  - new bonds formed with H+ and OH-



Enzyme Specificity: Substrate

- Substrate specific: recognize one specific set of substrates related to the reaction it catalyzes

- Example: sucrase can bind all 4 molecules and only these 4
  1. Sucrose
  2. Water
  3. Glucose
  4. Fructose

$$\text{Sucrose} + H_2O \xrightarrow{\text{Sucrase}} \text{Glucose} + \text{Fructose}$$

Enzyme Specificity: Substrate

- Specificity can even distinguish between particular configurations (e.g. enantiomers)

  - exception: racemase (an isomerase) which recognize both enantiomers and will interconvert between the two forms
- Substrate specificity due to the fit between the active site and substrate

Enzyme Specificity: Substrate

- the reverse is not true: a given substrate may be acted on by a number of different enzymes

- Examples with substrate glucose:
  - Glucose + glucose → maltose
  - Glucose + galactose → lactose
  - Glucose + fructose → sucrose

Each reaction is catalyzed by a different enzyme and glucose is a substrate for each one

Video: Enzyme Specificity

Tutorial Animation

- http://www.wiley.com//legacy/college/boyer/0470003790/animations/enzyme_binding/enzyme_binding.htm

Enzyme Names

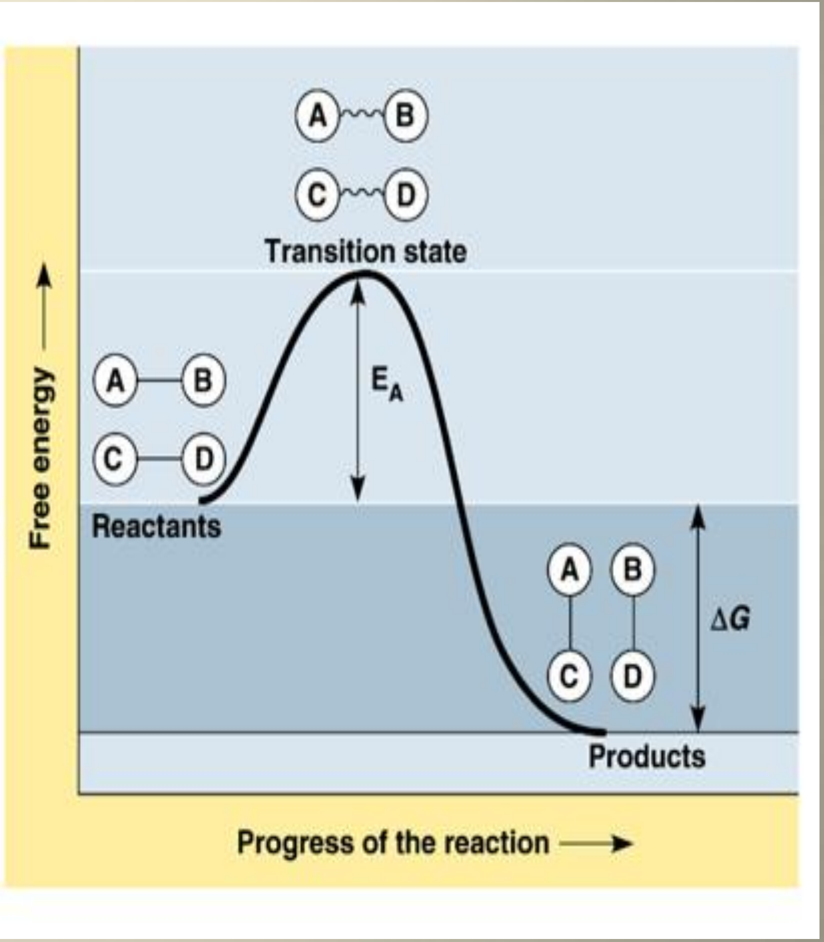
- Most enzymes have an –ase ending
- The root name suggests the catalytic reaction, either:

  - what molecule it acts upon or

  - what molecule is generated as the product
- Example: ATPase

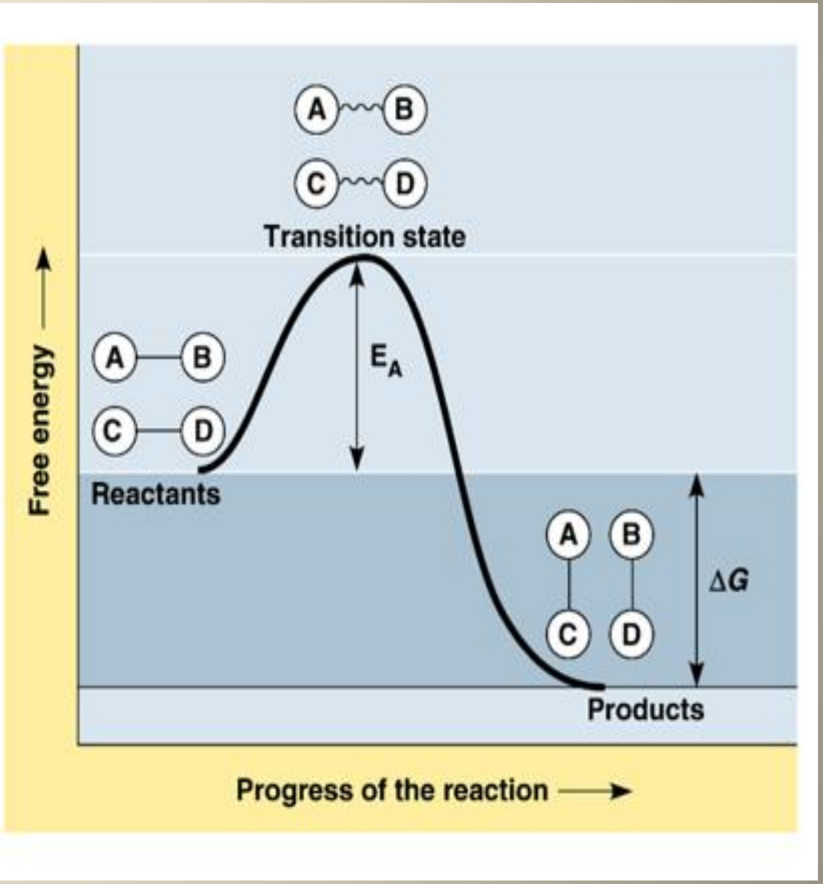
Exergonic reaction

- A reaction that releases Energy
- But reaction still needs an initial investment of energy to break bonds in the reactant
- Energy usually supplied in the form of heat (thermal energy)



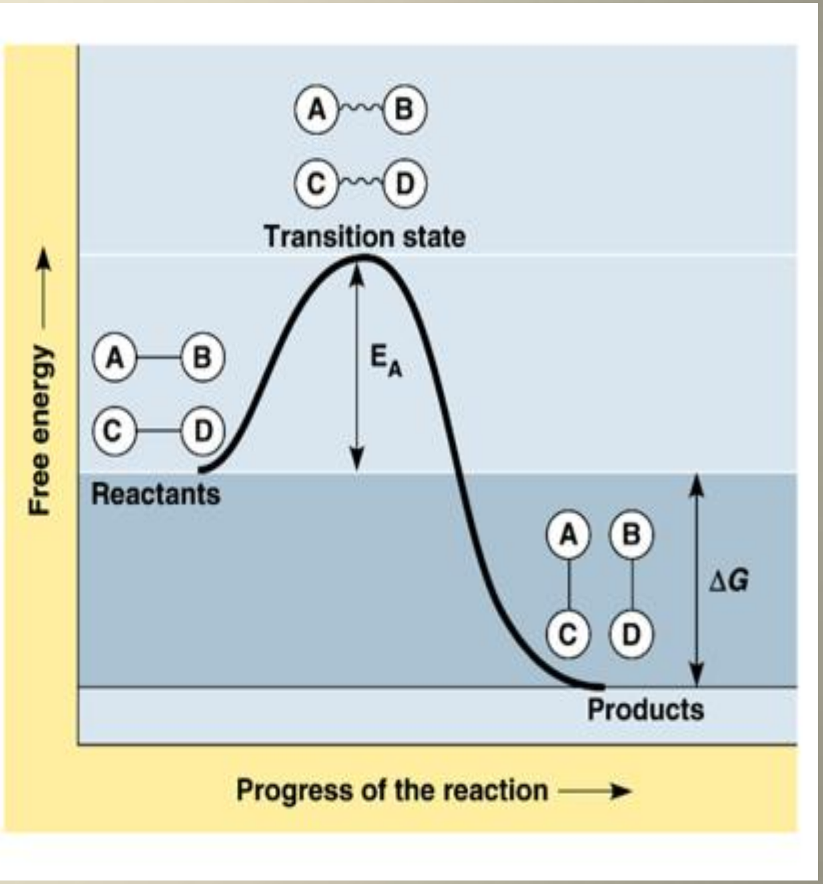
Activation Energy (EA)

- Amount of energy needed to push the reactants over an energy barrier.
- Reactants absorb energy becoming unstable
  - Thermal agitation increase speed of molecules and number & strength of collisions
  - Peak of instability = transition state
- Eventually bond breaks



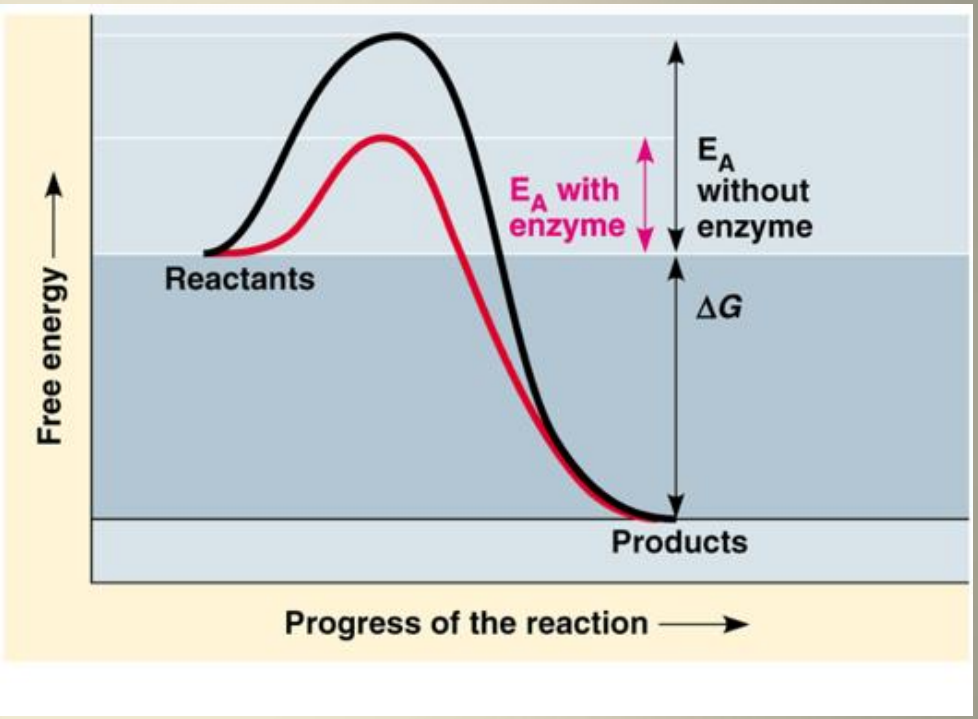
Change in Free Energy (ΔG)

- New bonds release more energy than the initial investment to break bonds.
- Difference in free energy between products and reactants is the ΔG.
- ΔG is negative in an exergonic reaction.



Enzymes lower EA

- Allows transition state to occur at a lower temperature which speeds up the reaction.
- ΔG is unchanged



Mechanism for Lowering EA

1. Proximity & Orientation
2. Bond strain
3. Microenvironment
4. Covalent Catalysis

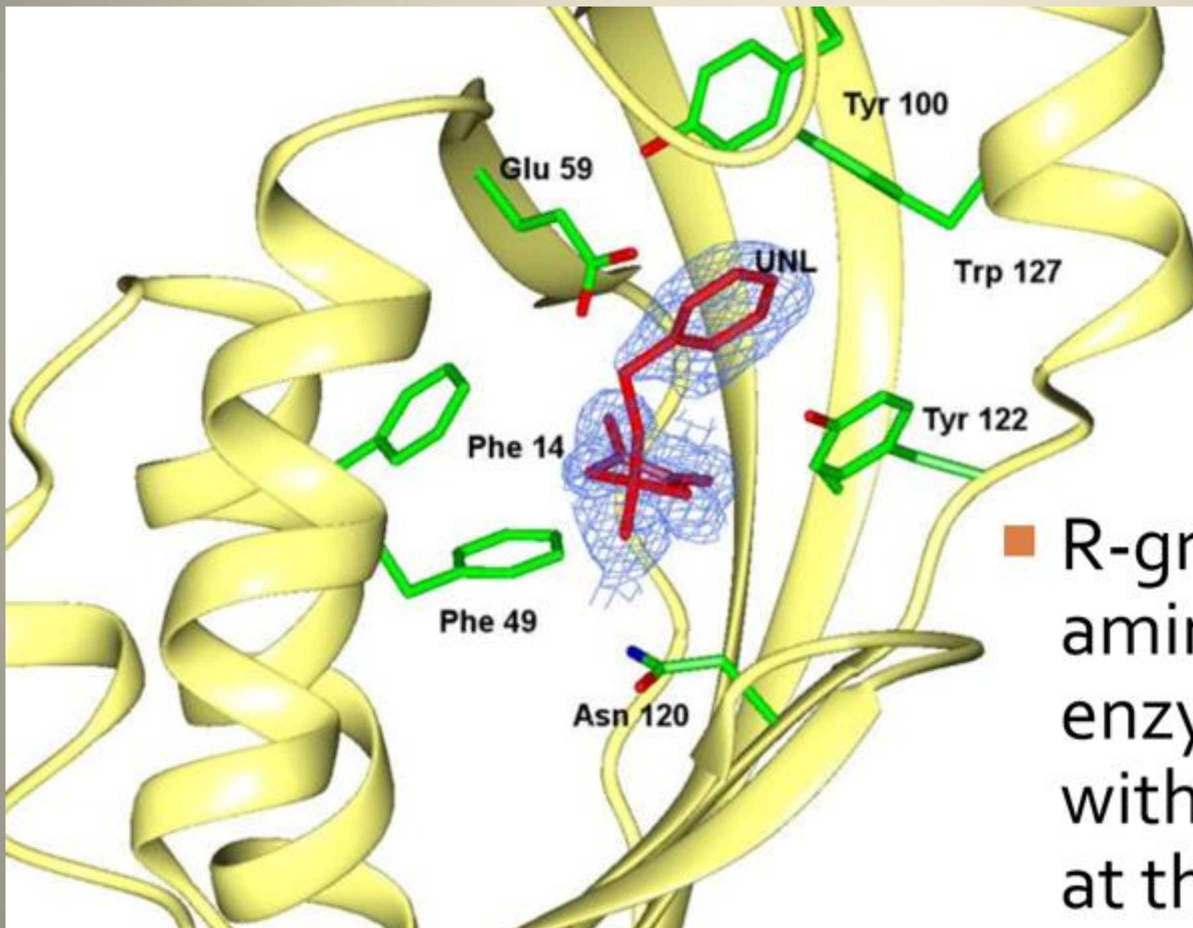
1. Proximity and Orientation

- active site brings reactants closer together and in the correct orientation

2. Bond strain

- active site bends bonds in substrate making it easier to break

3. Microenvironment



- R-groups on amino acids of the enzyme interact with the substrate at the active site

- R-groups at the active site provides a favourable environment for the reaction

4. Covalent Catalysis

- Enzymes may bind covalently to substrates in an intermediate step before returning to normal
- Increases reaction rate by:

  - Properly orienting the substrate

  - Changing the chemistry at the active site

Factors Affecting Reaction Rate

- A single enzyme molecule can catalyze thousands or more reactions a second
- Limitations to enzyme activity and thus reaction rate:

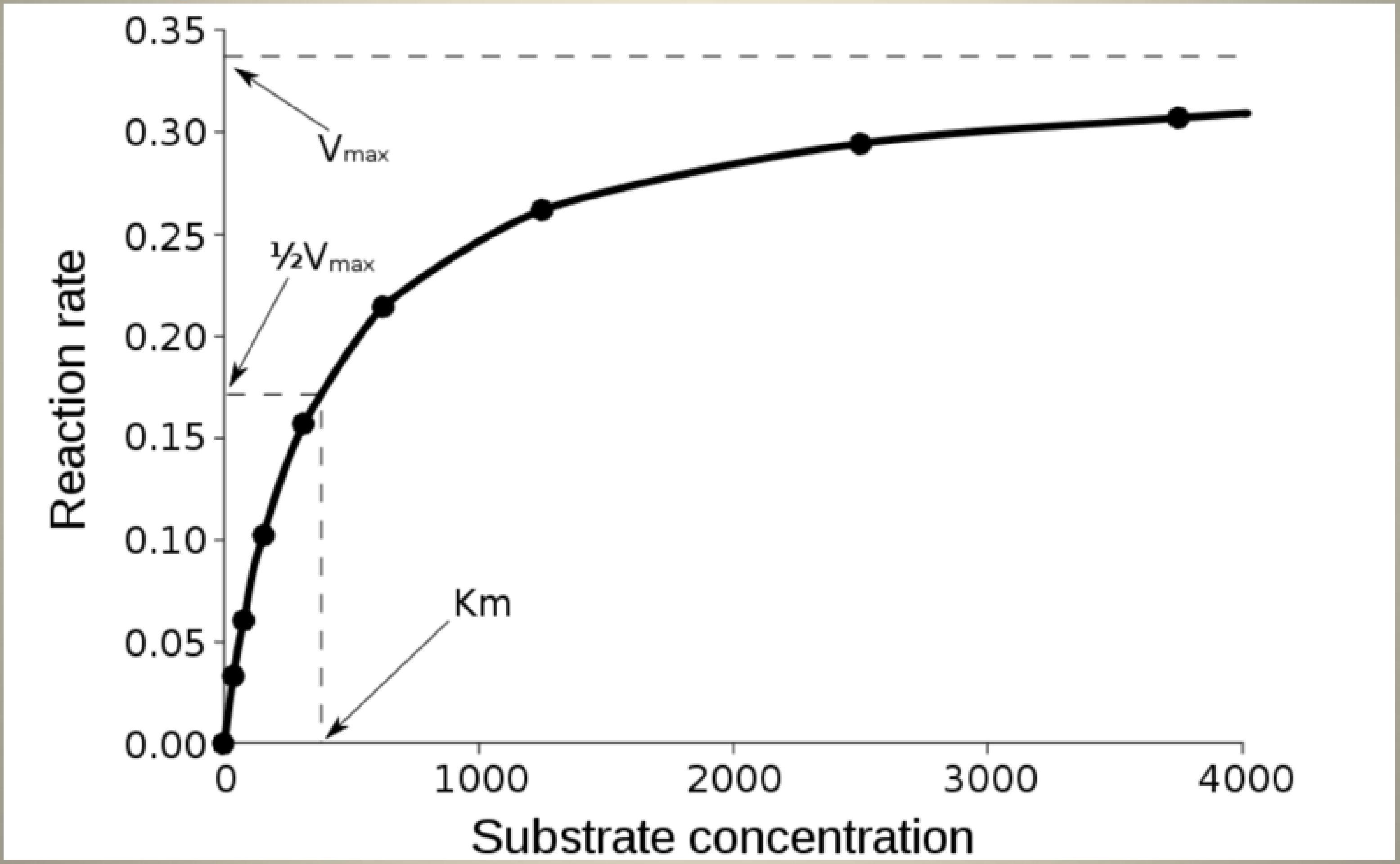
  - Substrate concentration

  - Temperature

  - pH

  - Availability of cofactors

Saturation Curve



Substrate concentration on Rate of Reaction

- Low substrate concentrations:

  - Direct correlation between [S] and rate

  - ↑[S], ↑speed of binding to active sites, ↑reaction rate

- High substrate concentrations:

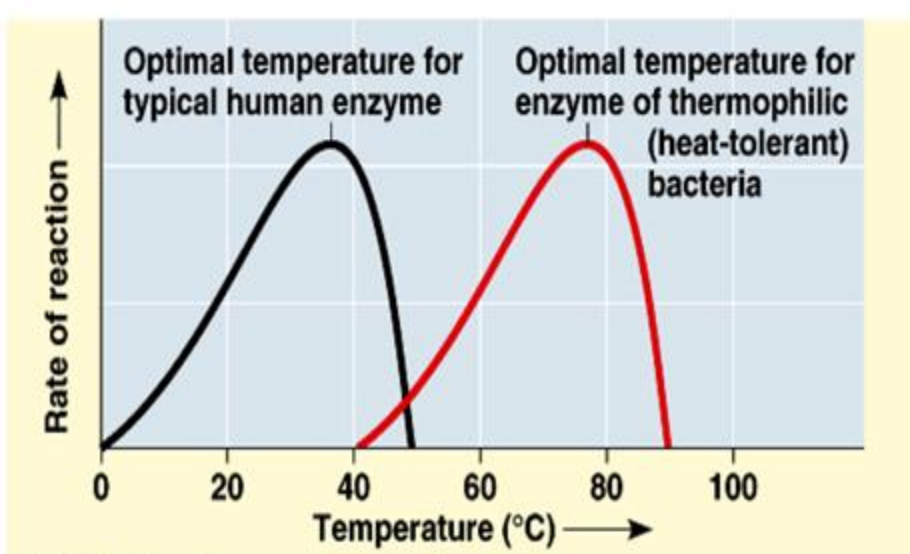
  - Enzyme saturation: active sites on all enzymes are engaged

  - The only way to increase productivity at this point is to add more enzyme molecules.

Temperature Effects on enzyme activity

- ↑ temperature, ↑ speed of molecules, ↑ collisions between substrate & active site
- Each enzyme has an optimal temperature

    - If temperature is too high, bonds are disrupted and the protein denatures



(a) Optimal temperature for two enzymes

pH Effects on enzyme activity

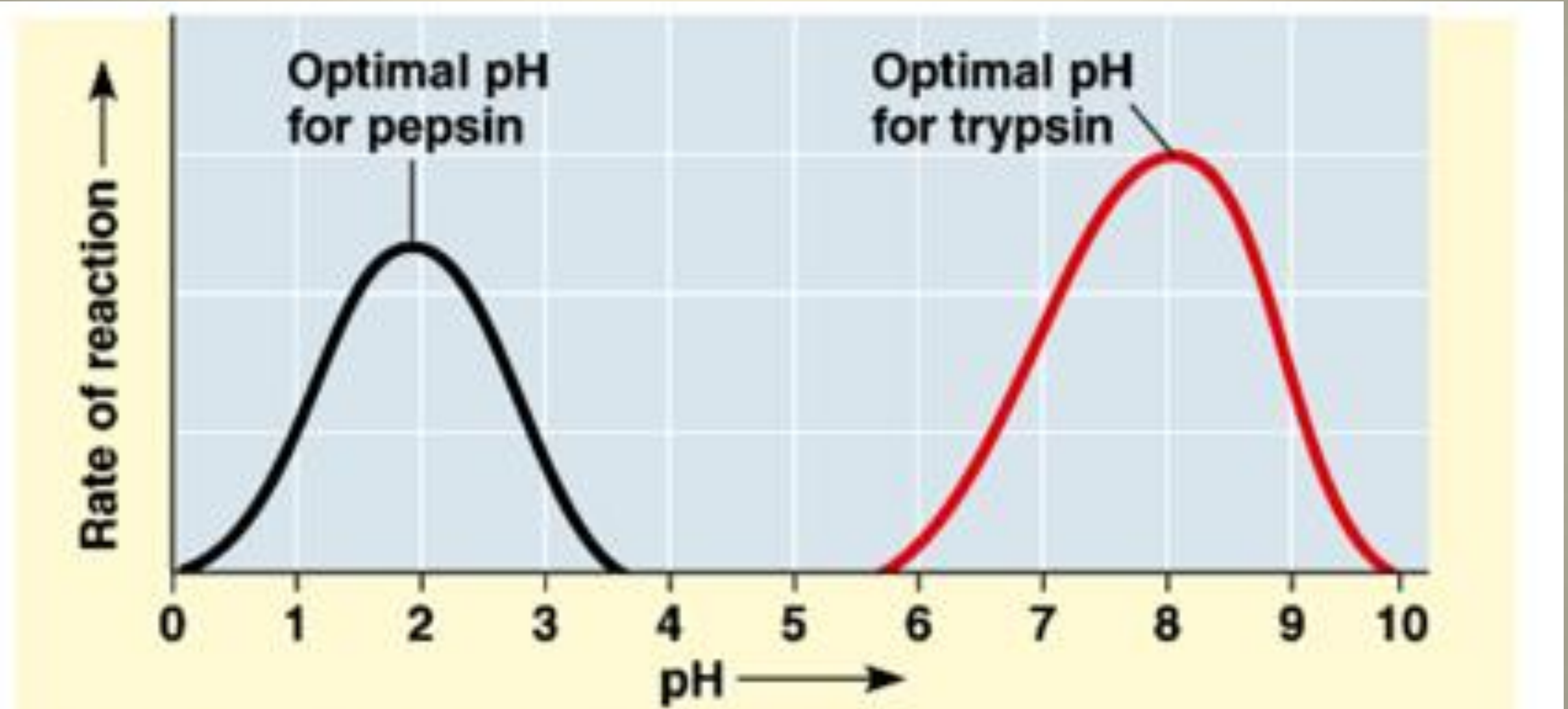
- Each enzyme has an optimal pH
- Most between pH 6-8
- Exception: digestive enzymes

  - those in the stomach work best at pH 2

  - those in the intestine are optimal at pH 8

  - both are suitable for their working environments.

pH Effects on enzyme activity



(b) Optimal pH for two enzymes