Metabolism

Enzymes

Metabolism

- A cell's metabolism is all the organism's chemical reactions.
- Metabolism manages the material and energy resources of the cell.

- Energy is the capacity to do work.

Metabolism

- 2 types of Energy Pathways:
  - Catabolic Pathways
  - Anabolic Pathways

Metabolic Pathways - Catabolic

- **Catabolic Pathways**: metabolic pathways which **RELEASE** energy by breaking down complex molecules to simpler molecules
  - **"downhill"** metabolic pathway – energy is released from storage (glycogen to glucose)
  - **Ex**: Triglycerides are broken down into free fatty acids for energy usage

Metabolic Pathways - Anabolic

- **Anabolic Pathways:** metabolic pathways which **CONSUME/USE** energy to build complex molecules from simpler ones.
  - **"uphill"** metabolic pathway – energy used to drive uphill reactions.
  - **Ex**: synthesis of proteins from amino acids

Laws of Energy Transformations

- We live in open systems – energy is transferred from the organisms (the matter in a particular area) and their surroundings

- *First Law of Thermodynamics*
  - Energy can neither be created or destroyed
  - Energy can be transferred and transformed

Laws of Energy Transformations

- With every energy transfer or transformation some becomes unusable energy or unavailable to do work

- *Second Law of Thermodynamics*
  - Every energy transfer or transformation increases the entropy (randomness) of the universe
  - Organisms can increase their order, as long as the order of their surroundings decrease

Free Energy

- Organisms live at the expense of free energy and require a highly ordered system
  - Order is maintained by constant free energy input into the system
  - Loss of order or free energy flow results in death
  - Increased disorder and entropy are offset by biological processes that maintain or increase order

Free Energy

- Living systems do not violate the 2nd law of thermodynamics because
  - Order is maintained by coupling cellular processes that increase entropy (negative free energy change) with those that decrease entropy (positive free energy change)
  - Energy input must exceed free energy lost to entropy to maintain order and power cellular processes

Free Energy

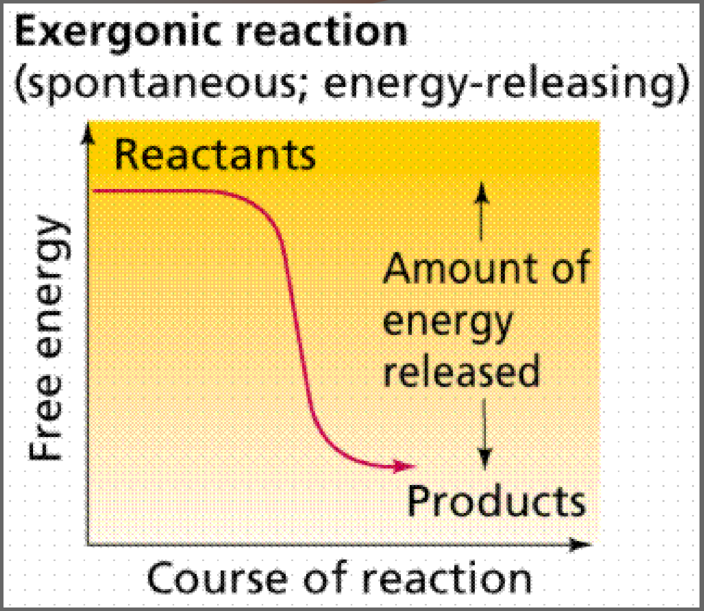
- Gibb’s Equation: $\Delta G = \Delta H - T\Delta S$
  - ΔG = change in free energy
  - ΔH = change in system’s enthalpy
  - T = temperature in Kelvin units
  - ΔS = change in system’s entropy
- Systems will move toward greater stability (low ΔG) and eventually reach a point of equilibrium

Metabolic Pathways

- Metabolic pathways are composed of MANY individual reactions.
- **Two types of chemical reactions**:
  1. Exergonic reactions
  2. Endergonic reactions

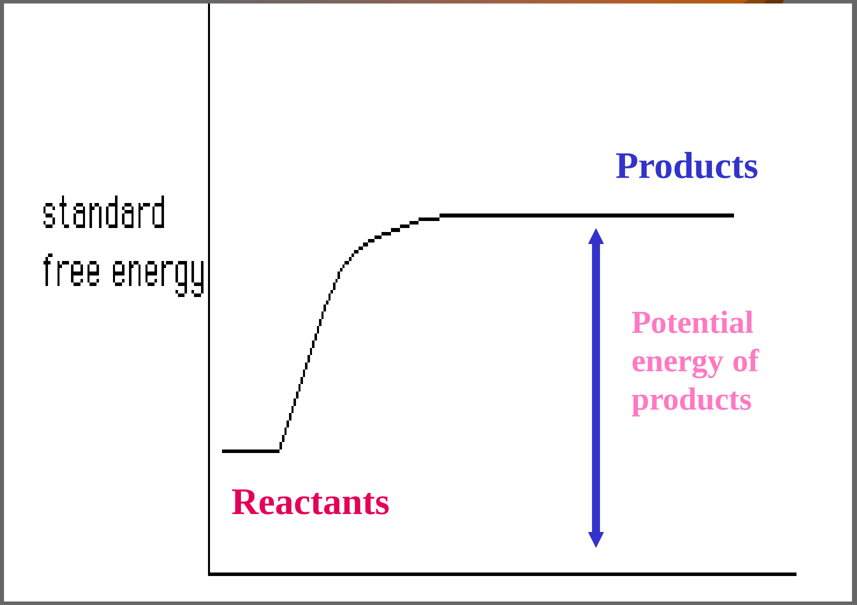
Exergonic Reactions

- **<u>Definition</u>**: Spontaneous chemical reaction in which there is a NET RELEASE of free energy ($\Delta G < 0$).
  - Total free energy of the products is less than the total free energy in the reactants **<u>(ENERGY IS GIVEN OFF DURING REACTION)</u>**
  - Occurs spontaneously and releases energy
  - REQUIRES activation energy
  - Example: food broken down and releases energy from chemical bonds



Endergonic Reactions

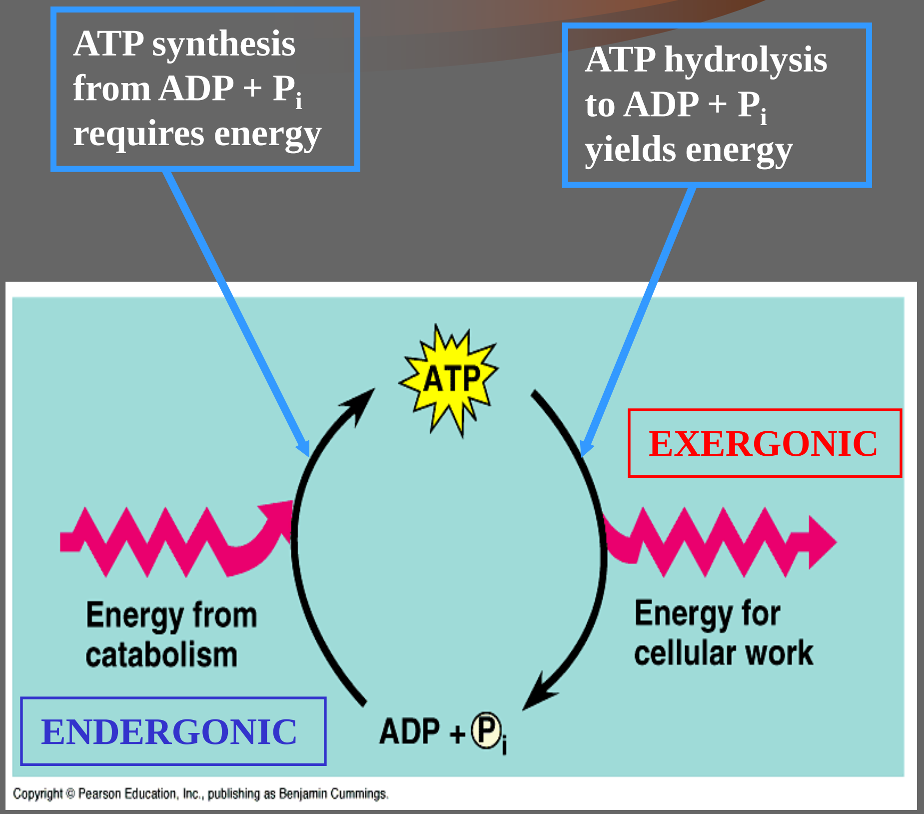
- **<u>Definition</u>** – Reactions that require the INPUT of energy ($\Delta G > 0$).
  - PRODUCTS have MORE energy than REACTANTS.
  - Absorb energy and are **<u>NOT SPONTANEOUS</u>**
  - Requires **LARGE AMOUNTS of ACTIVATION ENERGY**
  - **<u>Ex</u>**: plants use carbon dioxide and water to form sugars



Course of Reaction

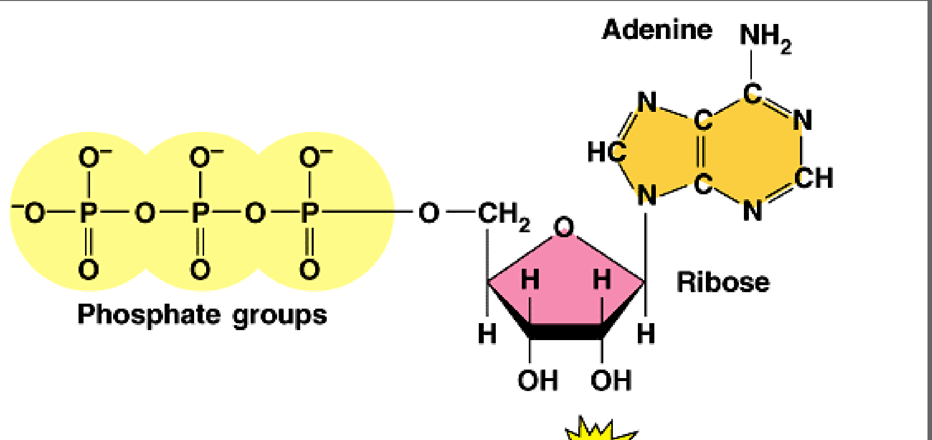
Energy Coupling

- Heat alone is an inefficient energy source
- **<u>Energy Coupling</u>**: the use of an exergonic reaction to drive an endergonic one.
  - Ex: the breakdown and formation of ATP
- ATP is responsible for MOST energy coupling in cells – ATP hydrolysis is coupled with endergonic reactions



Adenosine Triphosphate (ATP)

- ATP has 3 main components:
  - Nitrogen base – Adenine
  - Sugar molecule – Ribose
  - 3 Phosphate groups



(a) Structure of adenosine triphosphate

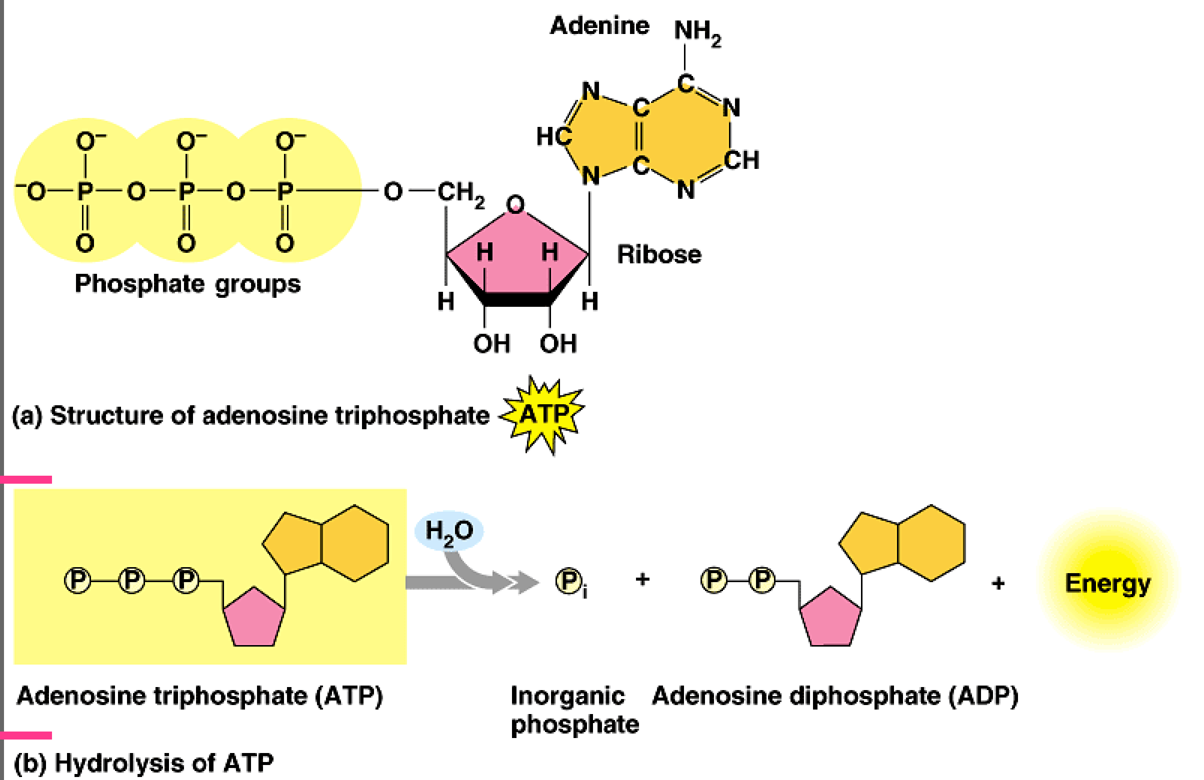
Adenosine Triphosphate (ATP)

- Bonds linking the phosphate groups may be broken by hydrolysis.

- At any given time there is a very high ratio of ATP to ADP
- ATP cannot be stockpiled for extended periods of time.
- Each second, ~ 10 million molecules of ATP are created and recycled.

HYDROLYSIS of ATP

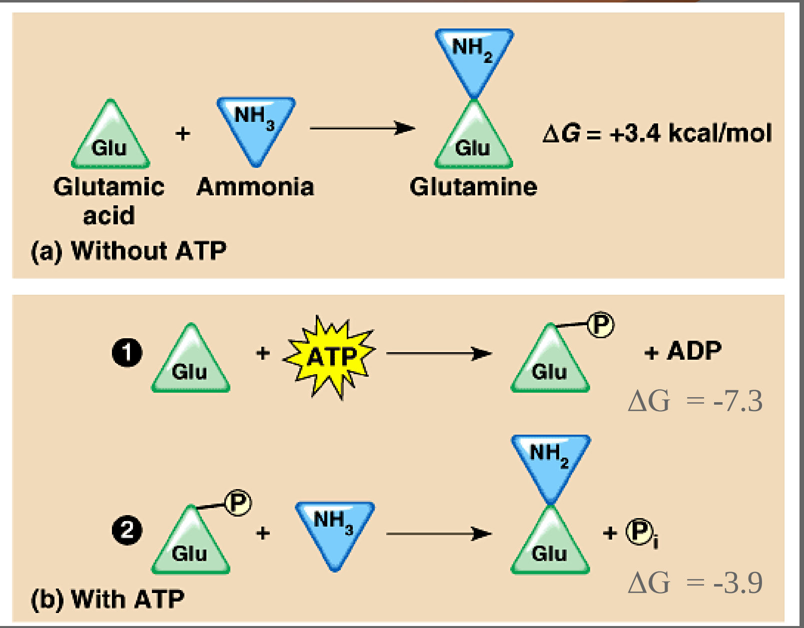
Energy released from this process is free to do work.



Exothermic reaction: releasing energy

Breakdown (HYDROLYSIS) of ATP

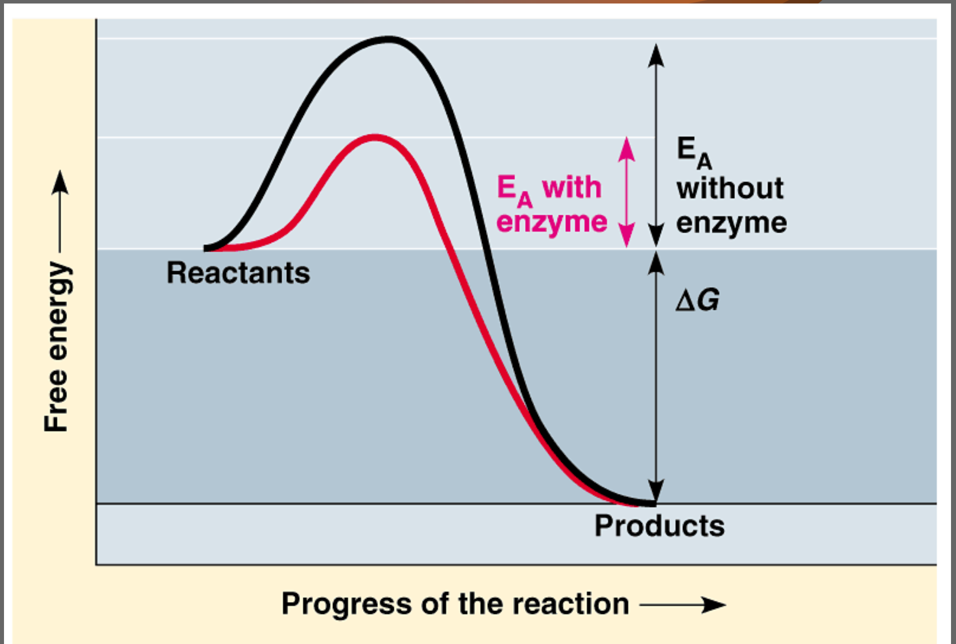
- Hydrolysis of ATP releases heat to surrounding environment.
- Heat alone is **INEFFICIENT** as an energy source
- Energy from ATP hydrolysis is coupled to endergonic reactions by transferring P_i from ATP to another molecule = **PHOSPHORYLATION**



Phosphorylated molecule is more reactive, therefore able to perform work.

ENZYMES

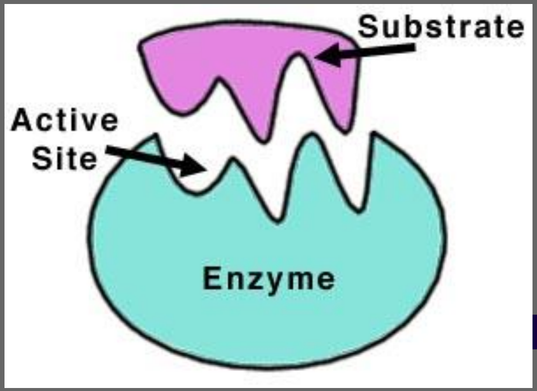
- **<u>CATALYSTS</u>** speed up the rate of chemical reactions without being used up in the process
- **<u>ENZYMES</u>** are proteins that act as biological catalysts
- Enzymes lower the activation energy of a reaction
- **<u>ACTIVATION ENERGY</u>** is the amount of energy needed to start a reaction



ENZYMES

- Have no effect on the overall free energy (G) of the reaction, they just force the reaction to occur faster.
- Reactants can only breakdown when they have absorbed enough energy to reach the **transition state**

- The specificity of an enzyme is due to its 3D shape and the levels of organization in the protein

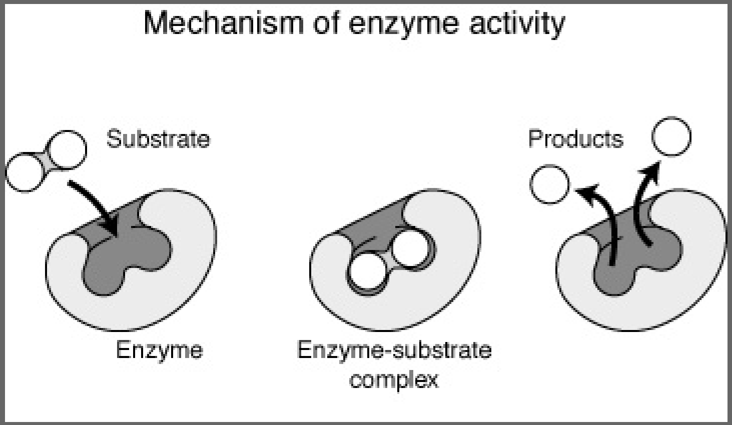


ENZYMES

- The reactant the enzyme acts on is referred to as the enzyme's **SUBSTRATE**
- Only a restricted region of the enzyme molecule actually binds to the substrate
  - This area is called the enzyme's **ACTIVE SITE**

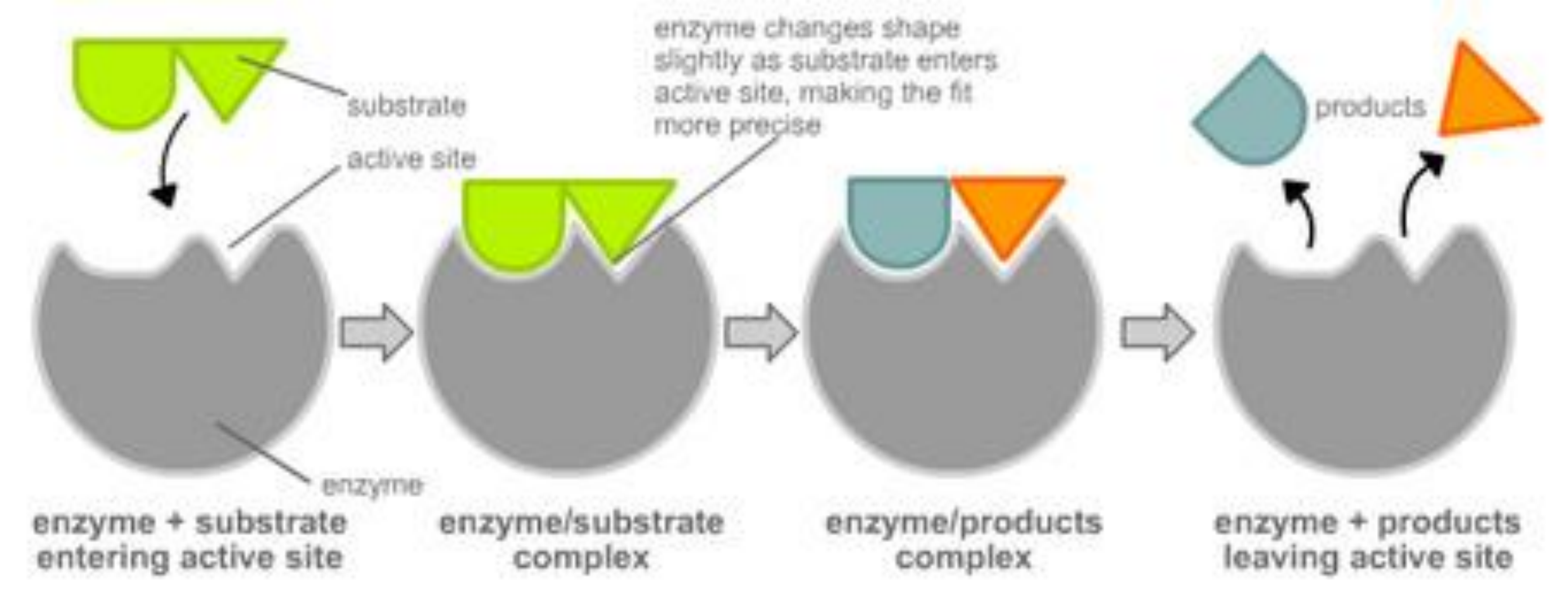
Enzymes

- The active site is usually a pocket or groove on the surface of the enzyme
- When the enzyme binds to the substrate, a temporary enzyme-substrate complex is created.



Enzymes

- The enzymatic cycle happens so fast that a single enzyme molecule typically converts about 1000 substrate molecules per second over to product.
- Enzymes emerge from the reaction in their original form.
- However, the Induced Fit Model refers to a slight change in shape to produce a tight fit around the substrate


substrate
active site
enzyme
enzyme changes shape slightly as substrate enters active site, making the fit more precise
products
enzyme + substrate entering active site
enzyme/substrate complex
enzyme/products complex
enzyme + products leaving active site

Enzymes and Activation Energy

- How can enzymes lower the activation energy?
  - Allows reactants to get into the proper orientation to react
  - Stretches the substrate to cause bonds to break easier (helps reach the transition state faster)
  - Creates a microenvironment more conducive for the reaction to occur
  - Direct participation of the active site in the reaction – may bind to the substrate temporarily

Factors Affecting Enzymatic Activity

1. Temperature
2. pH
3. Salt concentrations (Salinity)
4. Cofactors
5. Enzyme inhibitors

Temperature & Enzymatic Activity

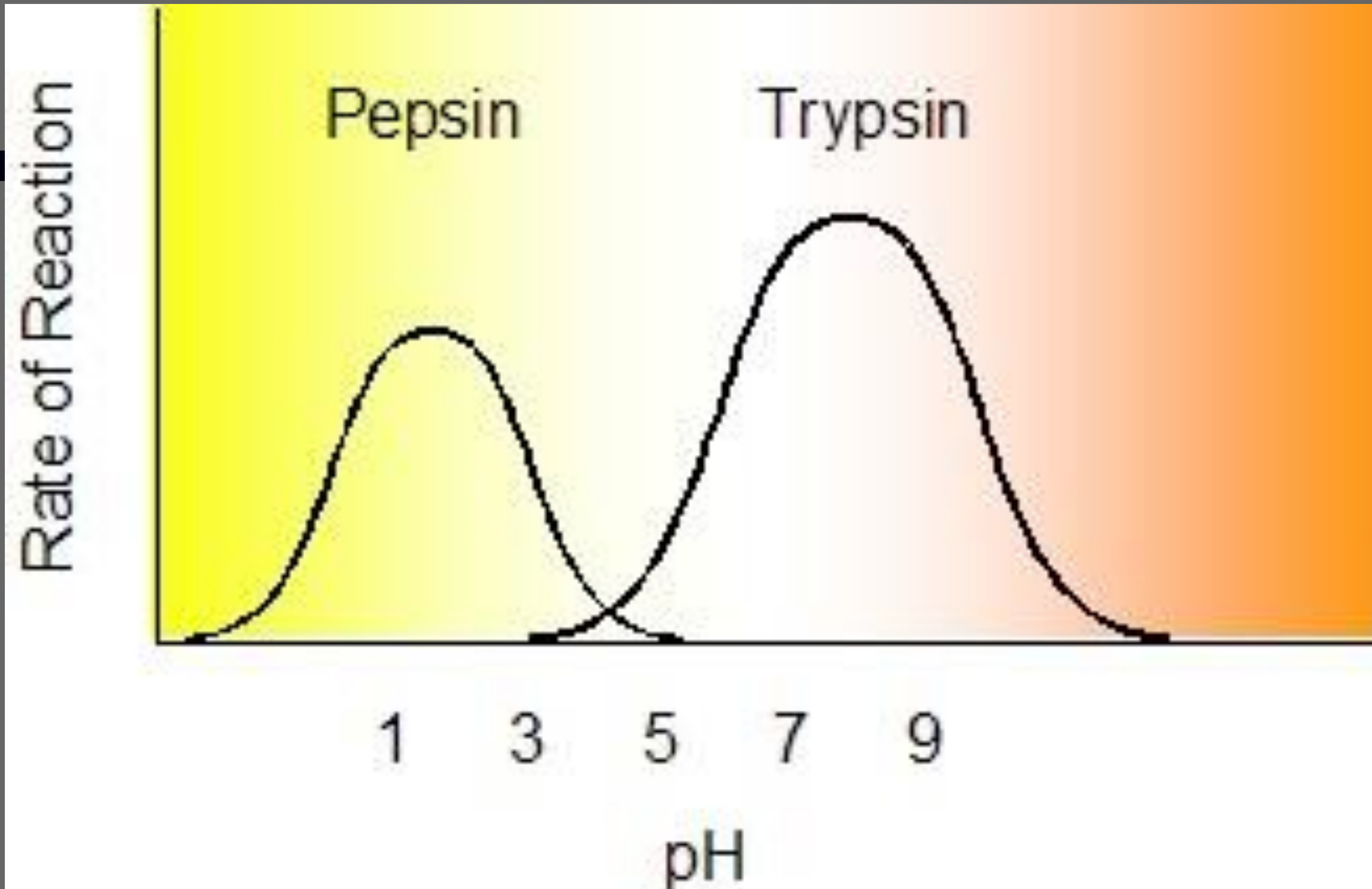
- Up to a certain point, the velocity of an enzymatic reaction **INCREASES** with increasing temperatures
- INCREASED TEMPERATURE = increase in molecular movement resulting in greater collisions between enzymes and molecules
- Temperatures that get TOO high result in thermal agitation of the enzyme molecule
  - This enzyme becomes **DENATURED**

Draw a graph to show this trend

pH & Enzymatic Activity

- The optimal range for most enzymes is **pH 6-8**
- One EXCEPTION: **Pepsin**: digestive enzyme in the stomach – works best at pH 2
- An environment that is TOO ACIDIC or TOO ALKALINE can denature an enzyme

Draw a graph to show this trend

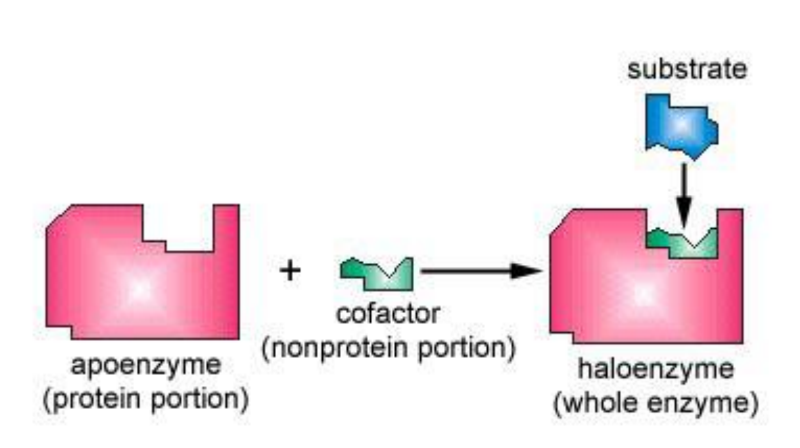

Pepsin
Trypsin
Rate of Reaction
1
3
5
7
9
pH

Salinity & Enzymatic Activity

- Most enzymes can’t tolerate environmental conditions that are too SALINE (salty)
- This will also cause the enzyme to denature

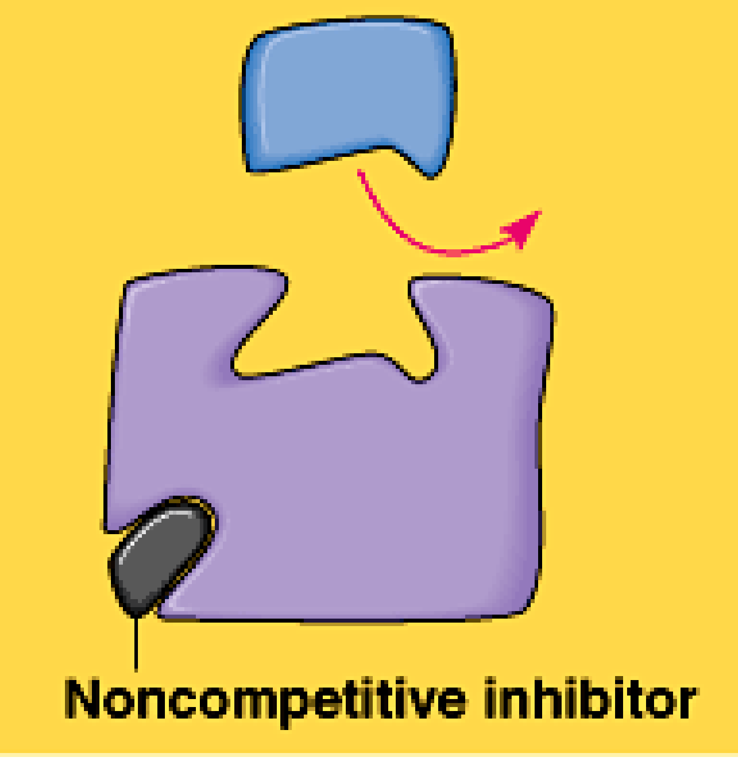
Cofactors & Enzymatic Activity

- Many enzymes require non-protein helpers for catalytic activity = **COFACTORS**
  - Inorganic cofactors include: Mg, Ca, Fe, Cu, Zn, & Mn.
- Organic cofactors are called **COENZYMES**
  - ATP, Vitamins, and Coenzyme A (CoA) are also coenzymes
- Cofactors can bind tightly to the active site of the enzyme permanently or they may bind loosely and release along with the substrate.



Inhibitors & Enzymatic Activity

- **Irreversible inhibition**:
  - If the inhibitor attaches to the enzyme by covalent bonds, inhibition is USUALLY IRREVERSIBLE
  - **Example**: penicillin blocks the active site of an enzyme that many bacteria use to make their cell walls
  - Example: sarin (nerve gas) and DDT (pesticide) can impact the nervous system by binding to acetylcholinesterase

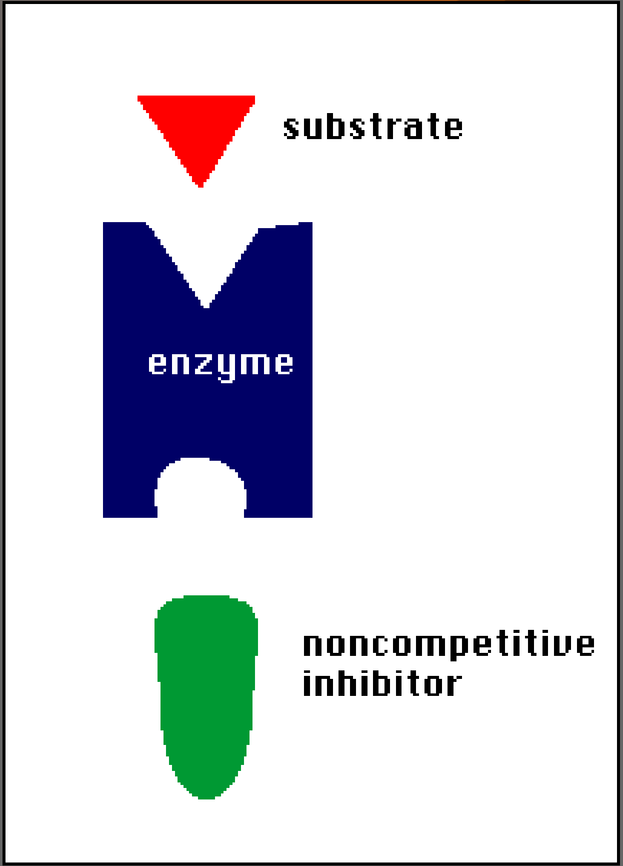


Inhibitors & Enzymatic Reactions

- **Reversible Inhibition**:
  - Inhibitor attaches to the enzyme using weak interactions
  - Reversible inhibition can be competitive or non-competitive

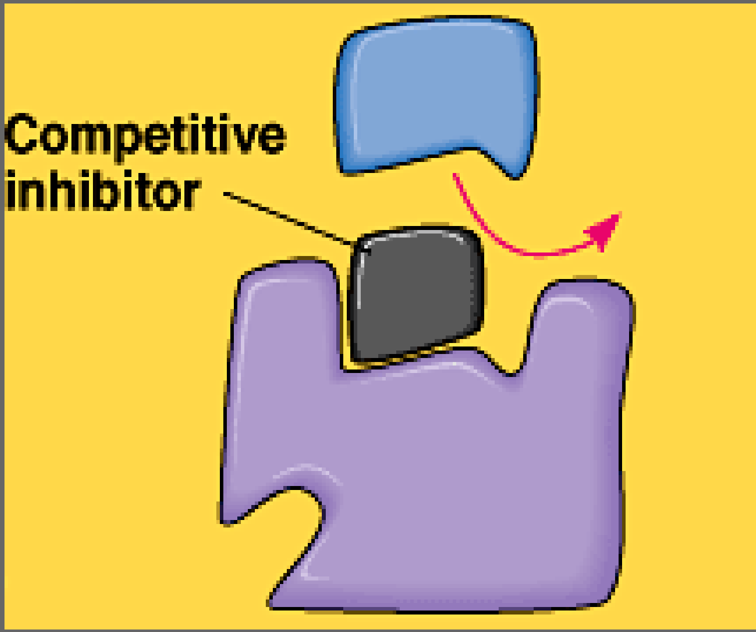
Inhibitors & Enzymatic Reactions

- **<u>Non-Competitive Inhibitors</u>**:
  - Impede the enzymatic reactions by binding to a part of the enzyme away from the active site
  - This causes the enzyme to change its shape rendering the active site unreceptive



Inhibitors & Enzymatic Reactions

- **<u>Reversible – Competitive Inhibitors</u>**:
  - Resemble the normal substrate molecule and compete for admission into the active site
  - They reduce the productivity of enzymes
  - Increasing the number of substrate molecules reduces the effectiveness of competitive inhibitors



Regulation of Enzyme Activity

- Allosteric regulation involves the binding of a molecule to an enzyme other than at its active site
- This causes the enzyme to be stimulated or inhibited depending on the molecule
- ATP can inhibit activity while ADP can stimulate activity on the same enzyme

Regulation of Enzyme Activity

- Cooperativity is an amplification of enzyme activity when one substrate binds to one active site and stimulates the other subunits

Regulation of Enzyme Activity

- Feedback inhibition is when a metabolic pathway is switched off by the inhibitory binding of the end product to an enzyme
- This stops the pathway from continuing
- Example: synthesis of amino acids

Location of Enzymes in Cell

- Some are grouped into complexes, some incorporated into membranes and others are contained inside organelles (lysosomes)
- Bacteria (prokaryotic cells) have enzymes located in the cytosol

Enzymes

- Animations