Chapter 6

Enzymes & Metabolism

Flow of energy through life

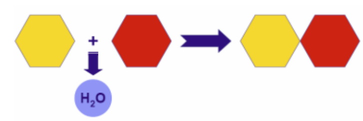
- Life is built on chemical reactions


Chemical reactions of life

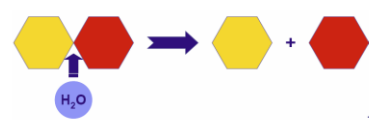
- Metabolism
  - Forming bonds between molecules
    - Dehydration synthesis
    - Anabolic reactions
  - Breaking bonds between molecules
    - Hydrolysis
    - Catabolic reactions

Examples

- Dehydration Synthesis

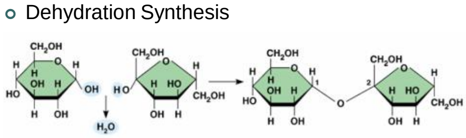


- Hydrolysis

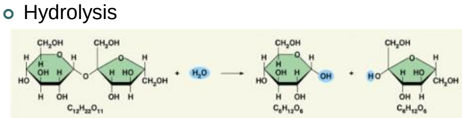


Examples

- Dehydration Synthesis



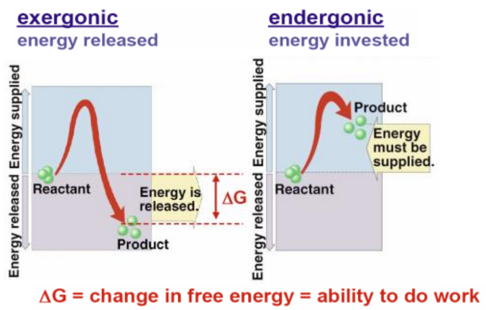
- Hydrolysis



Chemical reactions & energy

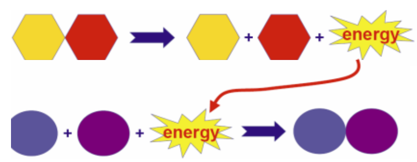
- Some chemical reactions release energy
  - Exergonic
  - Digesting polymers
  - Hydrolysis = catabolism
- Some chemical reactions require input of energy
  - Endergonic
  - Building polymers
  - Dehydration synthesis = anabolism

Endergonic vs. Exergonic



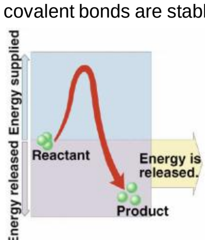
Energy & life

- Organisms require energy to live
  - Where does that energy come from?
    - Coupling **exergonic reactions** (releasing energy) with **endergonic reactions** (needing energy)



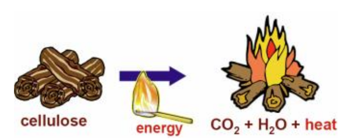
Spontaneous reactions

- If reactions are "downhill," why don't they just happen spontaneously?
  - Because covalent bonds are stable



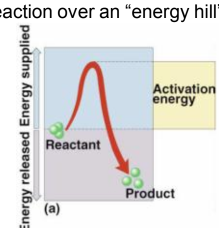
Activation Energy

- Breaking down large molecule requires an initial input of energy
  - **Activation energy**
  - Large biomolecules are stable
  - Must absorb energy to break bonds



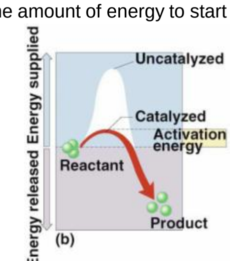
Activation energy

- The amount of energy needed to destabilize the bonds of a molecule
  - Moves the reaction over an "energy hill"



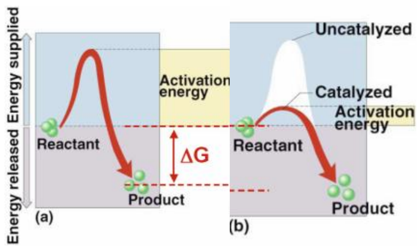
Reducing Activation energy

- Catalysts
  - Reducing the amount of energy to start a reaction

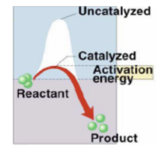


Catalysts

- So what's a cell to do to reduce activation energy?
  - Get help….chemical help…ENZYMES



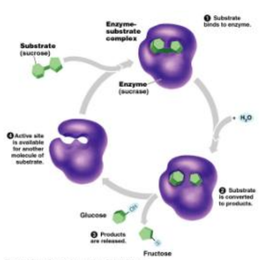
Enzymes



- Biological catalysts
  - Proteins
  - Facilitate chemical reactions
    - Increase rate of reaction without being consumed
    - Reduce activation energy
    - Don't change free energy (ΔG)
  - Required for most biological reactions
  - Highly specific
    - Thousands of different enzymes in cells
  - Control reactions

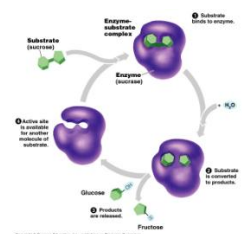
Enzymes & substrates

- Substrate
  - Reactant which binds to enzyme
  - Enzyme-substrate complex: temporary association
- Product
  - End result of reaction



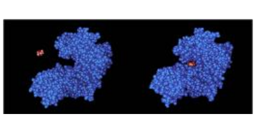
Enzyme & substrates

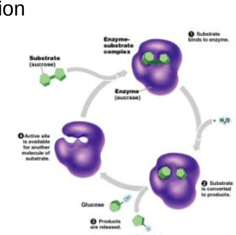
- Enzyme + substrates → products
  - Sucrase:
    - Enzyme breaks down sucrose
    - Binds to sucrose & breaks disaccharide into fructose & glucose
  - DNA polymerase
    - Enzyme builds DNA
    - Adds nucleotide to growing DNA strand



Lock & Key model

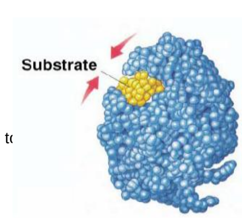
- Simplistic model of enzyme action
  - 3-D structure of enzyme fits substrate
- Active site
  - Enzyme's catalytic center
  - Pocket or groove on surface of globular protein
  - Substrate fits into active site





Induced fit model

- More accurate model of enzyme action
  - 3-D structure of enzyme fits substrate
  - As substrate binds, enzyme changes shape leading to a tighter fit
    - "conformational change"
    - Bring chemical groups into position t catalyze the reaction



How does it work?

- Variety of mechanisms to lower activation energy & speed up reaction
  - Active site orients substrates in correct position for reaction
    - Enzyme brings substrate closer together
  - Active site bonds substrate & puts stress on bonds that must be broken, making it easier to separate molecules

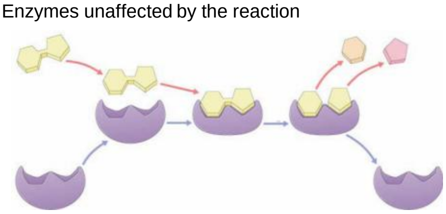
Properties of Enzymes

Specificity of enzymes

- Reaction specific
  - Each enzyme is substrate specific
    - Due to fit between active site & substrate
      - Substrate held in active site by weak interactions
        - H bonds
        - Ionic bonds
    - Enzymes names for reaction they catalyze
      - Sucrase breaks down sucrose
      - Protease break down proteins
      - Lipase breaks down lipids
      - DNA polymerase builds DNA
      - Pepsin breaks down proteins (polypeptides)

Reusable

- Not consumed in reaction
  - Single enzyme molecule can catalyze thousands or more reactions per second
  - Enzymes unaffected by the reaction

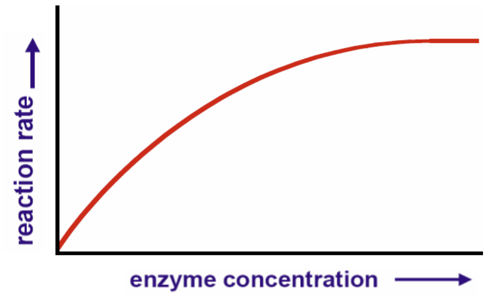


Factors that affect enzymes

Factors Affecting enzymes

- Enzyme concentration
- Substrate concentration
- Temperature
- pH
- Salinity
- Activators
- Inhibitors

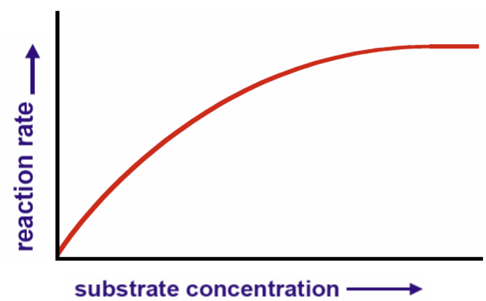
Enzyme concentration



Enzyme concentration

- Effect on rates of enzyme activity
  - As ↑enzyme = ↑reaction rate
    - More enzymes = more frequently collide with substrate
  - Reaction rate levels off
    - Substrate becomes limiting factor
    - Not all enzyme molecules can find substrate

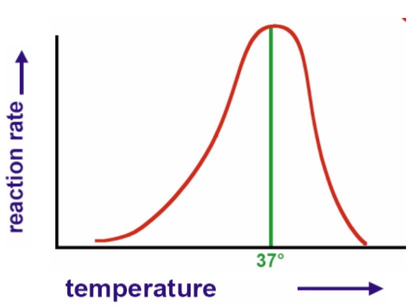
Substrate concentration



Substrate concentration

- Effect on rates of enzyme activity
  - As ↑substrate = ↑reaction rate
    - More substrate = more frequently collide with enzymes
  - Reaction rate levels off
    - All enzymes have active site engaged
    - Enzyme is <u>saturated</u>
    - Maximum rate of reaction

Temperature

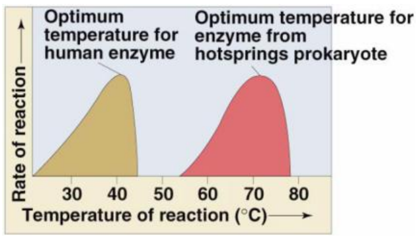


Temperature

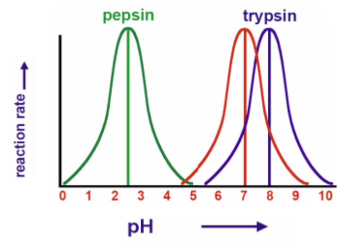
- Effects on rates of enzyme activity
  - Optimum Temp
    - Greatest number of molecular collisions
    - Human enzymes = 35°-40°C (body temp = 37°C)
  - Increase beyond optimum temp
    - Increased agitation of molecules disrupts bonds
    - <u>Denaturation</u> = lose 3D shape (3° structure)
  - Decrease temp
    - Molecules move slower
    - Decrease collisions

Enzymes & temperature

- Different enzymes functional in different organisms



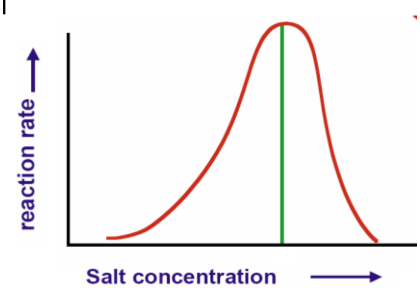
pH



pH

- Effect on rate of enzyme activity
  - Protein shape (conformation)
    - Attraction of charged amino acids
  - pH changes
    - Changes charges (add or remove)
    - Disrupts bonds, disrupt 3D shape
      - Affect 3º structure
    - Most human enzymes = pH 6-8
      - Depends on localized conditions
      - Pepsin (stomach) = pH 3
      - Trypsin (small intestine) = pH 8

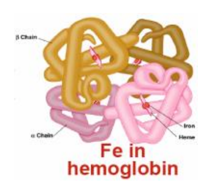
Salinity



Salt concentration

- Effect on rates of enzyme activity
  - Protein shape (conformation)
    - Depends on attraction of charged amino acids
  - Salinity changes
    - Change [inorganic ions]
    - Chnages charges (add + or -)
    - Disrupt bonds, disrupts 3D shape
      - Affect 3º structure
  - Enzymes intolerant of extreme salinity
    - Dead Sea is called dead for a reason!

Activators



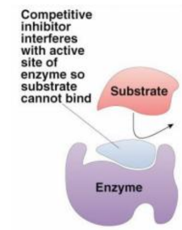
- Compounds which help enzymes
- Cofactors
  - Non-protein, small inorganic compounds & ions
    - Mg, K, ca, Ze, Fe, Cu
    - Bounds in enzyme molecule
- Coenzymes
  - Non-protein, organic molecules
    - Bond temporarily or permanently to enzyme near active site
  - Many vitamins
    - NAD (niacin; B3)
    - FAD (riboflavin; B2)
    - Coenzyme A

Inhibitors

- Regulation of enzyme activity
  - Other molecules that affect enzyme activity
- Selective inhibition & activation
  - Competitive inhibition
  - Noncompetitive inhibition
  - Irreversible inhibition
  - Feedback inhibition

Competitive inhibitor

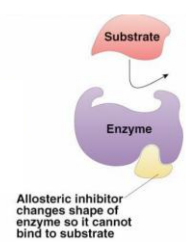
- Effect
  - Inhibitor & substrate “compete” for active site
    - Ex: Penicillin blocks enzyme that bacteria use to build cell wall
  - Overcome by increasing substrate concentration
    - Saturate solution with substrate so it out-competes inhibitor for active site on enzymes



(a) Competitive inhibition

Non-competitive inhibitor

- Effect
  - Inhibitor binds to site other than active site
    - Allosteric site
    - Called allosteric inhibitor
      - Ex: some anti-cancer drugs inhibit enzymes involved in synthesis of nucleotides & therefore in building DNA = stop DNA production, stop division of more cancer cells
    - Causes enzyme to change shape
      - Conformational change
    - Renders active site unreceptive



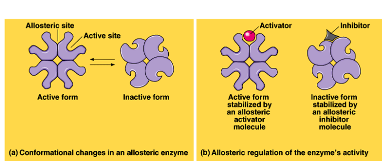
(b) Noncompetitive inhibition

Irreversible inhibition

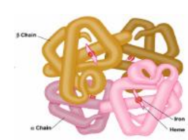
- Inhibitor permanently binds to enzyme
  - Competitor
    - Permanently binds to active site
  - Allosteric
    - Permanently changes shape of enzyme

Action of Allosteric control

- Inhibitors & activators
  - Regulatory molecules attach to allosteric site causing conformational (shape) change
  - Inhibitor keeps enzyme in active form
  - Activator keeps enzymes in active form

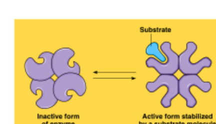


Cooperativity

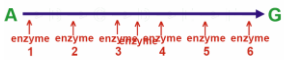


- Substrate acts as an activator
  - Substrate causes conformational change in enzyme
    - Induced fit
  - Favors binding of substrate at 2nd site
  - Makes enzyme more active & effective
    - Ex: hemoglobin

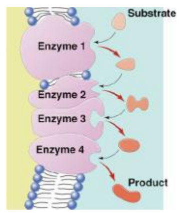
4 polypeptide chains:
- **bind 4 O_2;**
- **1st O_2 binds**
- **makes it easier for other 3 O_2 to bind**



Metabolic pathways

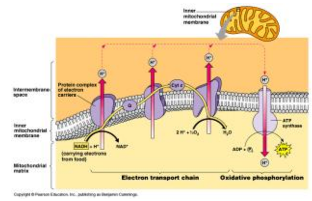


- Chemical reactions of life are organized in pathways
  - Divide chemical reactions into may small steps
    - Efficiency
    - Control = regulation



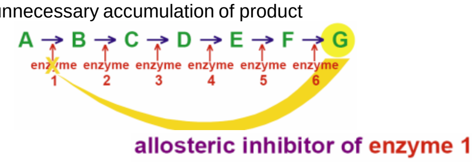
Efficiency

- Groups of enzymes organized
  - If enzyme are embedded in membrane they are arranged sequentially
- Link endergonic & exergonic reactions



Feedback inhibition

- Regulation & coordination of production
  - Product is used y next step in pathway
  - Final product is inhibitor of earlier step
    - Allosteric inhibitor of earlier enzyme
    - Feedback inhibition
  - No unnecessary accumulation of product



Feedback inhibition

- Example
  - Synthesis of amino acid, isoleucine from amino acid threonine