Chapter 8

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November 13, 2020

- A living cell is like a miniature factory, where thousands of reactions occur, which converts energy in many ways
- All of these chemical reactions transform energy from one form to another
    1. Example: Plants convert solar energy to ATP and organic molecules
- A **metabolic pathway** begins with a specific molecule and ends with a product
- Each step is catalyzed by a specific enzyme
- Catabolic Reactions:
    1. **Breaking bonds** between molecules releases energy (hydrolysis)
    2. Example: cellular respiration breaks down glucose
- Anabolic Reactions:
    1. **Forming bonds** between molecules consumes energy (dehydration synthesis)
    2. Example: Protein synthesis
- Organisms are **endergonic** systems. What is energy used for?
    1. Synthesis (making biomolecules)
    2. Reproduction
    3. Movement
    4. Active Transport
    5. Temperature Regulation
- Energy is obtained from using **exergonic** (catabolic) reactions to fuel **endergonic** (anabolic) reactions

- Energy is obtained through:
    1. Eating high energy **organic molecules**
    2. Breaking those molecules down
    3. Capture released energy in a form the cell can use (ATP)
- An energy currency:
    1. A way to pass energy around
    2. A short-term way of storing energy (ATP)
- What is an ATP?
    1. A modified nucleotide = adenine + ribose $+P_i \rightarrow$ AMP (monophosphate)
    2. AMP + $P_i \rightarrow$ ADP (diphosphate)
    3. ADP + $P_i \rightarrow$ ATP (triphosphate)
    4. Adding phosphates is endergonic
    5. High energy bonds are located between phosphates
- Subsequent PO_4 molecules become more and more difficult to add
- Bonding of the negative P_i groups is unstable, and is "spring-loaded" in that it may be taken off to release energy easily
- ATP to ADP releases about $\Delta G = 7.3$ [ ]
- This fuels other reactions
- The molecules phosphorylate (therefore, it is a **kinase**)
- ATP can not be stored (this is why it is short-term)
- Carbohydrates and fats are long-term energy storage
- Breaking down large molecules requires an initial input of energy (**activation energy**). Large biomolecules are stable, and, therefore, require more energy.
- Activation Energy − Amount of energy needed to destabilize the bonds of a molecule, and move the reaction over an "energy hill"
- Catalysts − Proteins that reduce the amount of energy needed to start a reaction
- An enzyme is a type of catalyst, as they increase the rate of reaction without being consumed, as well as reduce the activation energy required, and they do not change free energy (ΔG) released or required.

- Catalysts are highly specific, as they are used on a specific substrate (also, catalysts are required to sustain life)
- **Substrate** − A reactant which binds to an enzyme, and form enzyme-substrate complexes, which are a temporary association.
- **Active Site** − An enzyme's catalytic site, where the substrate fits in.
- **Reaction Specific** − Each enzyme only works with a specific substrate (chemical fit between active site and substrate).
- Single enzyme molecules are not consumed during reactions
- Enzymes are affected by any condition that affects protein structure (temperature, pH, salinity)
- Example: **Sucrase** breaks down sucrose
- Substrate binding causes enzymes to change shape to become a tighter fit (known as **conformational change**), and bring chemical groups to a position to catalyze the reaction
- There are multiple ways catalysts lower activation energy:
    1. Synthesis − active site orients substrates in correct position for reaction (enzyme brings substrate closer together)
    2. Digestion − active site binds substrate and puts stress on bonds that must be broken, making it easier to separate molecules
- What factors affect enzyme function:
    1. Enzyme concentration
    2. Substrate concentration
    3. Temperature
    4. pH
    5. Salinity
- As enzyme concentration increases, the reaction rate increases
    1. Reaction rate may level off when the substrate becomes a limiting factor, meaning that not all enzyme molecules may find a substrate
- As substrate concentration increases, the reaction rate increases
    1. Reaction rate may level off when the enzyme is saturated (reaches maximum level of reaction rate)

- Enzymes have optimal temperature (temperature at which greatest collisions occur)
    1. **Optimum Temperature** − Around 35 to 40 degrees Celsius for humans
    2. Heat will increase movement of molecule to certain extent, which will cause the bonds in the enzyme and the bonds between enzyme and substrate to disrupt (known as **denaturation**, when a structure loses 3D shape)
    3. Cold makes molecules move slower and collide less often, causing less reactions
    4. Optimal Temperature depends on organism (for example, bacteria in geysers will need to be able to take heat)
- A certain level of pH is most optimal
    1. Adding or removing H^+ ions may disrupt bonds and cause denaturation
    2. Optimal pH for humans is around 6-7
    3. Pepsin (in stomach) functions best around 2-3
    4. Trypsin (in small intestines) functions best around 8
- Salt concentration also has an optimal level
    1. Changes in salinity can cause removal or addition of cations (+) and anions (-)
    2. Dead sea is dead for a reason
- **Activators** − Compounds which aid enzymes
    1. **Cofactors** − Non-protein, small, inorganic compounds and ions (Ex. Mg, K, Ca, Zn, Fe, and Cu)
    2. **Coenzymes** − Non-protein, small, organic molecules (bind to enzyme near active site, includes many vitamins)
- Inhibitors
    1. Molecules reduce enzyme activity
    2. Competitive Inhibitor
    3. Noncompetitive Inhibitor
    4. Irreversible Inhibition
    5. Feedback Inhibition
- Competitive Inhibitor:
    1. Compete for active site with substrate
    2. Example: penicillin blocks enzyme bacteria use to build cell walls

3. Example: Disulfiram (antabuse) treats chronic alcoholism by blocking enzyme that breaks down alcohol, and causes severe hangover and vomiting 5-10 minutes after drinking
4. Can be overcome by increasing substrate concentration

- Noncompetitive Inhibitor:

1. Binds to other sites than active site
2. Allosteric Inhibitor − binds to allosteric site, causing enzyme to change shape (conformational change), and active site becomes non-functional
3. Example: Cyanide inhibits production of ATP by stopping Cytochrome C, an enzyme involved in cellular respiration.

- Irreversible Inhibitor:

1. Competitors bind to active site permanently
2. Allosterics bind to allosteric site, permanently changing shape of enzyme
3. Allosteric regulation causes conformational changes by regulatory molecules (inhibitors will keep enzymes in inactive form, while activators keep enzyme in active form)

- Metabolic pathways are results of evolution and increase efficiency with intermediate branching points, and increase control and regulation
- A product is used in the next step of a pathway. A final product is usually an inhibitor of a previous step. This is called **feedback inhibition**, and it helps unnecessary accumulation of a product
- Example: Synthesis of amino acid isoleucine from amino acid threonine causes more isoleucines to form, which are allosteric inhibitors of the first step in teh pathway