Lecture Outline: Thermodynamics, Metabolism, and Enzymes

I. **Unit Introduction: Thermodynamics, Metabolism, and Enzymes**
  A. **Biochemical Pathways**
    1. Multiple reactions connected in series (daisy-chained).
    2. Product of one reaction serves as the reactant for the next.
    3. Involves a starting substance and a final product.
    4. Products made along the way are called **intermediates**.
    5. Examples include cellular respiration and photosynthesis.
  B. **Definition and Forms of Energy**
    1. Energy is difficult to define; it is not a substance or a structure.
    2. Often defined as the **capacity to do work**.
    3. Organisms continuously process energy to live.
    4. Energy exists in many forms (e.g., electrical energy, radiant energy/light).
    5. Two main categories:
      a. **Potential Energy**: Stored energy, energy that could be used but is not at the moment.
        (1) Chemical potential energy is found in food.
        (2) Can be converted from kinetic energy (e.g., climbing stairs converts kinetic energy into gravitational potential energy).
      d. **Kinetic Energy**: Energy of motion, energy that is being used.
        (1) Example: A person jumping off a diving platform converts potential energy into kinetic energy.
        (2) Easily interconvertible with potential energy.

II. **Thermodynamics**
  A. **Definition**: The study of energy transactions and the flow of heat.

B. **Thermodynamic Systems**: A defined part of the universe.

1. The **universe** consists of the system and its **surroundings**.
2. Categories of systems:
   a. **Open System**: Exchanges both matter and energy with its surroundings (e.g., all organisms).
   b. **Closed System**: Exchanges energy but not matter with its surroundings (e.g., a technically closed hydroelectric system).
   c. **Isolated System**: Exchanges neither matter nor energy (a theoretical concept, not truly real, though a thermos attempts to be one).

C. **Laws of Thermodynamics** (Focus on First and Second for biology)

1. **First Law of Thermodynamics** (Law of Conservation of Energy):
   a. Energy cannot be created or destroyed.
   b. The total amount of energy in the universe remains constant.
   c. Energy can be **transferred** (moved from one object to another) or **transformed** (changed from one form to another, e.g., radiant energy to heat energy).
2. **Second Law of Thermodynamics** (Law of Entropy):
   a. **Entropy** is defined as disorder or randomness.
   b. In any energy transaction, the **entropy of the universe increases**; the universe is becoming more disordered over time.
   c. In any energy transaction, **some energy is "lost" as heat**.
      (1) "Lost" means unusable for useful work, not destroyed (which would violate the First Law).
      (2) All energy transactions are at least somewhat **inefficient** (no 100% efficient transaction).
      (3) Example: An internal combustion engine wastes most of its fuel's energy as heat.

III. **Free Energy and Reaction Types**

A. **Free Energy (G)**: Also known as Gibbs free energy.

1. Represents the potential energy in a thermodynamic system.

        2. The maximum amount of energy available to perform work.
    B. **Change in Free Energy (Delta G, ΔG)**: G final - G initial.
        1. **Negative Delta G**: Indicates a loss of free energy.
            a. Corresponds to a **spontaneous process**, meaning it can happen on its own.
            b. Systems tend toward lower free energy, which is a more stable state (and generally higher entropy).
            c. Examples: A person falling, diffusion, or the breakdown of a complex molecule into simpler parts.
            d. Associated with **exergonic reactions** (energy is released, "energy out").
            e. Associated with **catabolic reactions** (breakdown of larger, complex molecules into smaller, less complex ones, increasing disorder).
        2. **Positive Delta G**: Indicates an increase in free energy.
            a. Corresponds to a **non-spontaneous process**, meaning it requires an input of energy to occur.
            b. Associated with **endergonic reactions** (energy is required/taken in, "energy in").
            c. Associated with **anabolic reactions** (building larger molecules from smaller ones, decreasing disorder).
    C. **Organisms as Multi-Step Open Systems**
        1. Organisms are open thermodynamic systems that constantly exchange matter and energy.
        2. Unlike a single-step energy release, organisms utilize energy from food through multi-step biochemical pathways.
        3. This allows for a gradual release of energy, similar to a multi-step open hydroelectric system.

IV. **ATP: The Energy Currency of the Cell**
    A. **Structure of ATP (Adenosine Triphosphate)**:
        1. An example of a **nucleotide triphosphate**.
        2. Consists of a **pentose sugar** (ribose), a **nitrogenous base** (adenine),

    and three **phosphate groups**.
  3. Variations include ADP (adenosine diphosphate, two phosphates) and AMP (adenosine monophosphate, one phosphate).
  4. More phosphates attached means more energy stored.

B. **Role as Energetic Middleman**:
  1. Organisms cannot directly use energy from fuel (food) for cellular processes.
  2. Energy released from fuel is used to build ATP molecules, which store this energy temporarily.
  3. ATP is then dismantled to release its stored energy, which directly powers cellular activities.

C. **ATP Hydrolysis (Energy Release)**:
  1. The process of breaking down ATP into ADP and an inorganic phosphate (P_i).
  2. This is a **spontaneous, exergonic, and catabolic** process.
  3. Requires water (**hydrolysis reaction**).
  4. Releases energy that powers endergonic processes in the cell.
  5. Example: Powering active transport like sodium-potassium pumps.
  6. Also known as **dephosphorylation**.

D. **ATP Synthesis (Energy Storage)**:
  1. The process of adding a phosphate to ADP to form ATP.
  2. This is a **non-spontaneous, endergonic, and anabolic** process.
  3. Requires energy input, typically from the catabolism of fuels (food).
  4. Removes water (**dehydration reaction**).
  5. Also known as **phosphorylation**.

E. **Coupling of Reactions**:
  1. Cells perform endergonic processes by **coupling** them with exergonic processes.
  2. The energy released from exergonic reactions (like ATP hydrolysis) is used to drive endergonic reactions (like building glutamine).

3. The overall coupled reaction must have a negative delta G to be spontaneous.

F. **ATP Cycle**:

1. Cells continuously cycle between higher-energy ATP and lower-energy ADP + P_i.
2. ADP is phosphorylated using energy from fuel to make ATP.
3. ATP is then hydrolyzed to release energy for cellular work, returning to ADP.
4. This cycle continuously matches the cell's energy demand.

G. **Categories of Work Performed by ATP**:

1. **Transport work**: Movement of substances across membranes (e.g., active transport pumps).
2. **Mechanical work**: Movement of things within the cell along the cytoskeleton (e.g., motor proteins on microtubules).

V. **Enzymes: Biological Catalysts**

A. **Nature of Enzymes**:

1. Chemically, enzymes are **proteins**.
2. Functionally, they are **biological catalysts**.
3. They speed up chemical reactions, often by at least a million times.
4. Enzymes are not consumed or changed during a reaction; they are **reusable**.
5. While not strictly necessary for a reaction, they make spontaneous reactions happen fast enough to support life.

B. **Enzyme-Substrate Interaction**:

1. The reactants in an enzyme-catalyzed reaction are called **substrates.**
2. Substrates bind to a specific region on the enzyme called the **active site**.
3. Enzymes are highly **specific**, typically catalyzing only one type of reaction due to their unique shape.
4. The binding of a substrate to an enzyme induces a slight change in the enzyme's shape, known as **induced fit**, which enhances the fit and

facilitates the reaction.

5. This forms a temporary **enzyme-substrate complex**.

C. **Mechanism of Action: Reducing Activation Energy (E_A)**:

1. For a chemical reaction to occur, it must overcome an "energy hill" called the **activation energy**.
2. The transition state, where bonds are breaking and forming, has the highest free energy (G value) and is the most unstable.
3. Enzymes function by **reducing the activation energy**, making it easier for the reaction to proceed with available environmental energy (e.g., heat).
4. Enzymes **do not change the delta G** value of a reaction, as delta G is determined solely by the difference in free energy between reactants and products.
5. Ways enzymes reduce E_A:
   a. For catabolic enzymes, they may stress or distort the substrate's bonds.
   b. For anabolic enzymes, they may perfectly position multiple substrates for bond formation.

D. **Factors Affecting Enzyme Activity**:

1. Enzymes have an **optimum temperature** and **optimum pH** at which they function best.
2. Deviations from the optimum can cause the enzyme's protein shape to change (**denaturation**), drastically reducing or eliminating its activity.
3. Optimal conditions vary depending on the specific enzyme and the organism it comes from (e.g., human enzymes vs. thermophilic bacterial enzymes).

E. **Enzyme Regulation**:

1. Control over reactions is exercised by controlling enzyme activity.
2. More efficient to regulate enzyme activity (on/off switch) than to destroy and rebuild enzymes.
3. Types of inhibition:

a. **Competitive Inhibition**:

    (1) An inhibitor molecule competes with the substrate for binding to the **active site**.

    (2) If the inhibitor binds, it blocks the active site, preventing the substrate from binding and the reaction from occurring.

    (3) Many drugs work as competitive inhibitors.

e. **Non-competitive Inhibition** (also called **Allosteric Regulation**):

    (1) An inhibitor (or activator) binds to a site on the enzyme **other than the active site**.

    (2) This binding causes a **conformational change** (shape change) in the enzyme.

    (3) In non-competitive inhibition, the shape change alters the active site, making it unsuitable for substrate binding.

    (4) Allosteric regulation can also be **allosteric activation**, where binding stabilizes the enzyme in an active shape.

j. **Feedback Inhibition**:

    (1) A common type of non-competitive inhibition (allosteric inhibition) in biochemical pathways.

    (2) The **end product** of a pathway acts as an allosteric inhibitor of an enzyme earlier in the pathway (often the first enzyme).

    (3) This prevents the unnecessary production of the end product and intermediates, conserving energy and materials.