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Programme: Biochemistry

Course Title: Intermediary Metabolism

COURSE CODE: BC201CR

Unit: 1

Introduction

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Major Classes of Biomolecules

- Biomolecules are the essential molecules of life, playing key roles in the structure, function, and regulation of cells and organisms. These molecules can be broadly classified into four major classes, each with distinct chemical properties and biological functions
- Carbohydrates are organic compounds made up of carbon (C), hydrogen (H), and oxygen (O).
- Proteins are made up of amino acids, which contain carbon, hydrogen, oxygen, nitrogen, and sometimes sulfur.
- Lipids are mainly composed of carbon, hydrogen, and oxygen, but they have a much lower proportion of oxygen than carbohydrates.
- Nucleic acids are made up of nucleotides, which contain a sugar, a phosphate group, and a nitrogenous base.

Forces Stabilizing Biomolecules:

- **covalent bonds** play a key role in stabilizing biomolecular structure. In proteins, for example, peptide bonds link amino acids together to form polypeptides, while phosphodiester bonds link nucleotides to form nucleic acids like DNA and RNA.
- **Hydrogen bonds** occur when a hydrogen atom, which is covalently bonded to an electronegative atom (like oxygen or nitrogen), forms an electrostatic attraction with another electronegative atom.
- **Van der Waals forces** are weak, short-range interactions that occur when transient dipoles (temporary differences in charge distribution) form between atoms or molecules.
- **Hydrophobic interactions** occur when nonpolar molecules or regions of a molecule aggregate to avoid contact with water, leading to the exclusion of water molecules.
- **Ionic bonds** form between positively and negatively charged ions. In biomolecules, these bonds typically occur between charged side chains in proteins or between nucleotides in nucleic acids.
- **Disulfide bonds** are covalent bonds formed between the sulfur atoms of two cysteine residues in a protein. These bonds are crucial for stabilizing the three-dimensional structure of some proteins.
- **Pi-pi stacking** involves interactions between aromatic rings, such as those found in the nitrogenous bases of nucleic acids.

METABOLISM

- Metabolic pathways are sequences of interconnected biochemical reactions that occur within a cell or organism to convert molecules into other molecules, ultimately supporting life processes such as energy production, growth, maintenance, and repair.
- These pathways are tightly regulated to ensure that cells respond appropriately to their environment and maintain homeostasis.
- Metabolic pathways are generally divided into two broad categories:

  Catabolic Pathways (breakdown of molecules, release energy)

  Anabolic Pathways (building of molecules, require energy input)

  Amphibolic pahways(both catabolism and anabolism takes place)

Thermodynamics

Thermodynamics deals with the transfer of energy from one place to another and from one form to another. The key concept is that heat is a form of energy corresponding to a definite amount of mechanical work.

- **The zeroth law of thermodynamics:** When two systems are each in thermal equilibrium with a third system, the first two systems are in thermal equilibrium with each other. This property makes it meaningful to use thermometers as the "third system" and to define a temperature scale.
- **The first law of thermodynamics**, or the law of conservation of energy. The change in a system's internal energy is equal to the difference between heat added to the system from its surroundings and work done by the system on its surroundings. In other words, energy can not be created or destroyed but merely converted from one form to another.
- **The second law of thermodynamics:** Heat does not flow spontaneously from a colder region to a hotter region, or, equivalently, heat at a given temperature cannot be converted entirely into work. Consequently, the entropy of a closed system, or heat energy per unit temperature, increases over time toward some maximum value. Thus, all closed systems tend toward an equilibrium state in which entropy is at a maximum and no energy is available to do useful work.
- **The third law of thermodynamics:** The entropy of a perfect crystal of an element in its most stable form tends to zero as the temperature approaches absolute zero. This allows an absolute scale for entropy to be established that, from a statistical point of view, determines the degree of randomness or disorder in a system.

Standard free energy

- The standard free energy is the change in the Gibbs free energy for a process when all reactants and products are in their standard states (usually at 1 bar pressure and 298 K temperature, though the specific conditions can vary).
- It is a key thermodynamic quantity that helps predict the spontaneity of chemical reactions.

$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

Where:

- ΔH° is the standard enthalpy change (the heat change at constant pressure).
- ΔS° is the standard entropy change (the change in disorder or randomness).
- T is the absolute temperature (in Kelvin).

Spontaneity and the Standard Free Energy:

- If $\Delta G^\circ < 0$, the reaction is spontaneous under standard conditions.
- If $\Delta G^\circ > 0$, the reaction is non-spontaneous under standard conditions.
- If $\Delta G^\circ = 0$, the system is at equilibrium.

ENTHALPY

- Enthalpy (denoted as H) is a thermodynamic property that represents the total heat content of a system. It is useful for describing energy changes that occur at constant pressure, which is often the case in chemical reactions and processes.
- Enthalpy is defined as the sum of the internal energy (U)of a system and the product of its pressure (P) and volume (V):

$$H = U + \mathrm{P}V$$

Where:

H is the enthalpy of the system.

U is the internal energy of the system.

P is the pressure of the system.

V is the volume of the system.

ENTROPY

- Entropy (denoted as *S*) is a fundamental concept in thermodynamics that measures the disorder or randomness of a system.
- It can also be interpreted as a measure of the energy dispersal in a system.
- In simple terms, entropy quantifies the number of possible ways a system can be arranged at the microscopic level.
- The Second Law of Thermodynamics states that the total entropy of an isolated system tends to increase over time.
- Entropy is linked to heat transfer and phase changes (e.g., melting, boiling).
- The Third Law states that entropy approaches zero at absolute zero temperature for a perfect crystal.
- The Gibbs Free Energy equation helps predict the spontaneity of reactions by considering both entropy and enthalpy changes.

EXERGONIC REACTION

- An exergonic reaction is a chemical reaction that releases free energy. This occurs when the products of the reaction have lower free energy than the reactants.
- Spontaneity: Exergonic reactions are spontaneous under the given conditions (usually at constant temperature and pressure).
- Gibbs Free Energy: For an exergonic reaction, the change in Gibbs free energy (ΔG) is negative: $\Delta G<0$
- Energy Flow: Since energy is released, exergonic reactions often result in the release of heat or the formation of useful work (e.g., ATP hydrolysis).

ENDERGONIC REACTION

- An endergonic reaction is a chemical reaction that requires the input of free energy to proceed. In this type of reaction, the products have higher free energy than the reactants.
- Spontaneity: Endergonic reactions are non-spontaneous on their own. They require external energy (often in the form of heat, light, or electrical energy) to drive the reaction forward.
- Gibbs Free Energy: For an endergonic reaction, the change in Gibbs free energy (ΔG) is positive: $\Delta G>0$
- Energy Flow: Energy is absorbed from the surroundings, and the system stores this energy in the products.

OPEN SYSTEM

An open system can exchange both matter and energy with its surroundings.

- Matter: The system can exchange particles with the surroundings (e.g., gases, liquids).
- Energy: The system can exchange energy in the form of heat or work with its surroundings.
- Example:A boiling pot of water with an open lid is an open system. Heat can flow from the burner to the pot, and water vapor can escape into the air, transferring both energy and matter.

CLOSED SYSTEM

A closed system can exchange energy (in the form of heat and work) but not matter with its surroundings.

- Matter: The system cannot exchange matter with the surroundings (i.e., the mass inside remains constant).
- Energy: The system can still exchange energy (heat and work) with the surroundings.
- Example:A sealed container of gas: The gas inside can do work (e.g., expand or contract) and can exchange energy with the surroundings (e.g., via heat), but the gas itself cannot escape or enter the container.

ISOLATED SYSTEM

An isolated system cannot exchange matter or energy with its surroundings. It is completely isolated from the environment.

- Matter: The system does not exchange matter with its surroundings.
- Energy: The system does not exchange energy in the form of heat, work, or radiation with the surroundings.
- Example:A perfectly insulated thermos (in an ideal case) is an isolated system. It cannot exchange heat (energy) or matter (liquid or gas) with the outside environment.

OXIDATIVE PHOSPHORYLATION

- Oxidative phosphorylation denotes the phosphorylation of ADP into ATP, utilizing the energy from successive electron transports (hence the “oxidative”).
- The basic concept is that oxidation of NADH, being highly exergonic, can generate the energy needed to phosphorylate ADP.
- Since oxidation of NADH by oxygen can potentially release 52 kCal/mol (218 kJ/mol), and the energy needed to phosphorylate ATP is approximately 7.5 kCal/mol (30.5 kJ/mol)

Key components of Oxidative Phosphorylation:

- Electron Tranasport chain
- Chemiosmosis
- Oxygen as the final electron acceptor

ELECTRON TRANSPORT CHAIN

- The ETC is a series of protein complexes and other molecules embedded in the inner mitochondrial membrane.
- The primary function of the ETC is to transfer electrons from electron carriers (such as NADH and $FADH_2$) to molecular oxygen (O_2), which is the final electron acceptor.
- As electrons move through the ETC, they release energy that is used to pump protons (H^+ ions) from the mitochondrial matrix into the intermembrane space, creating an electrochemical gradient (also called a proton gradient or proton motive force).

CHEMIOSMOSIS

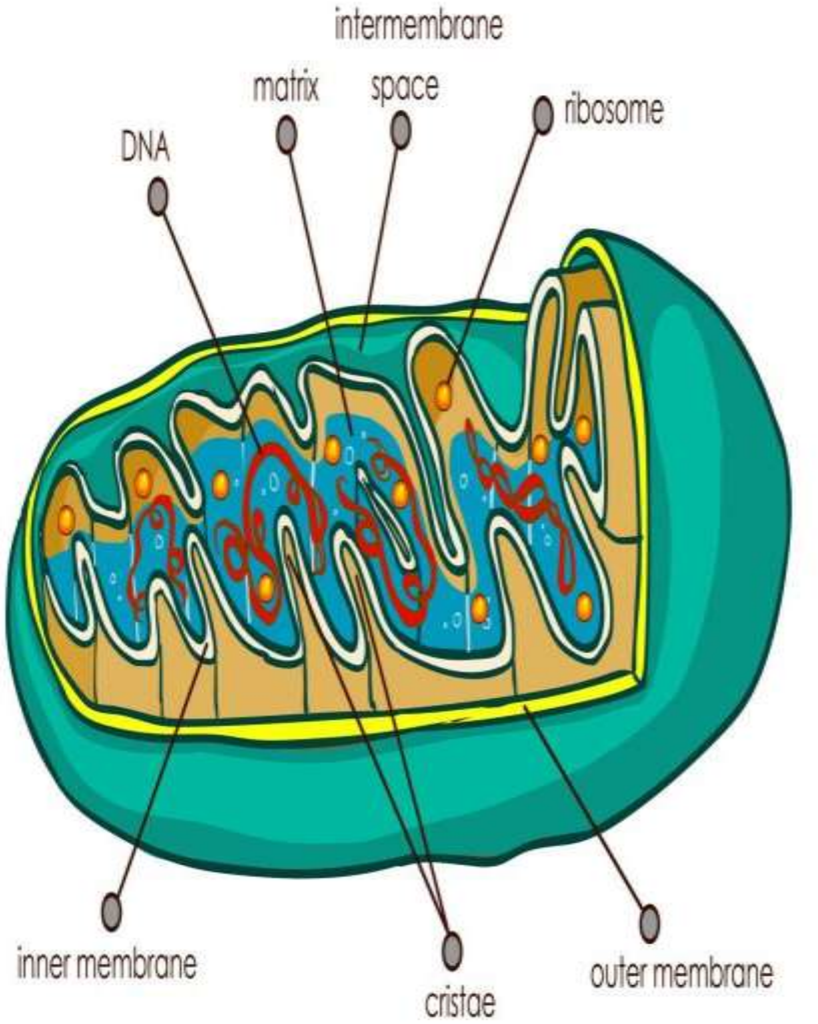
- Chemiosmosis is the process by which ATP is synthesized using the energy stored in the proton gradient created by the ETC.
- Protons (H^+) flow back into the mitochondrial matrix through a membrane-bound enzyme called ATP synthase, which uses the energy from the proton gradient to drive the conversion of ADP (adenosine diphosphate) and inorganic phosphate (Pi) into ATP.
- This process is often referred to as phosphorylation because it results in the addition of a phosphate group to ADP to form ATP.

OXYGEN AS THE FINAL ELECTRON

- The last step in the electron transport chain involves the transfer of electrons to oxygen (O_2), which combines with protons to form water (H_2O).
- Without oxygen, the ETC cannot function, and ATP production via oxidative phosphorylation ceases, which is why oxygen is crucial for aerobic respiration.

Electron Transport Chain:

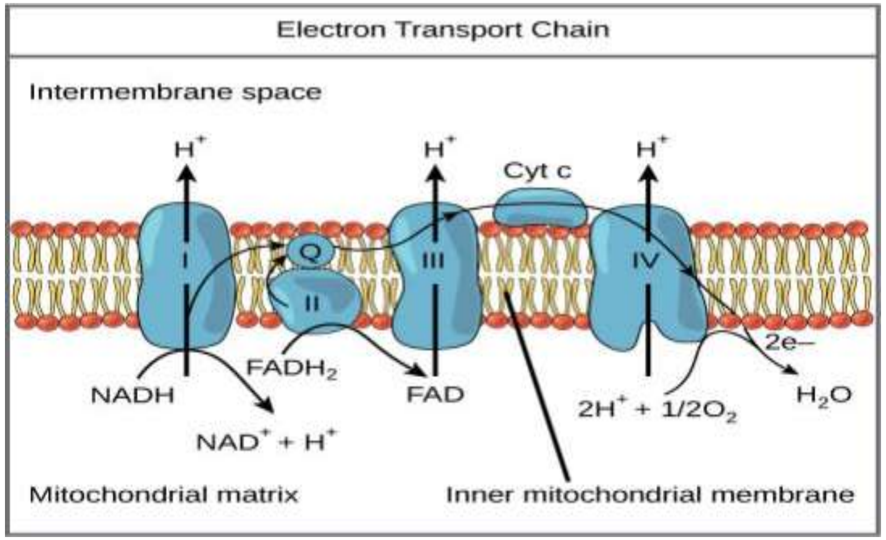
- The ETC is a collection of proteins bound to the inner mitochondrial membrane and organic molecules, which electrons pass through in a series of redox reactions, and release energy.
- The metabolic Pathway through which the electron passes from one carrier to another is called ELECTRON TRANSPORT CHAIN.
- It's embedded in the inner mitochondrial membrane and is part of the process of producing adenosine triphosphate (ATP).
- This chain is located in the inner mitochondria membrane of cell.
- Protons are transported from the matrix of the mitochondria across the inner mitochondrial membrane to the intermembrane space located between the inner and outer mitochondrial membrane.
- The process takes place in units arranged on the cristae membrane of mitochondria.



Source: https://images.app.goo.gl/osqaNqYtjSewgi3D8

Components of ETC:

- The various components of the respiratory chain occur within the mitochondria.
- Complex are formed by Proteins.
- Each of the 4 complexes contain up to 40 individual polypeptide chains.
- There are 4 complex used in electron transport chain.
- Complex I (NADH dehydrogenase): Accepts electrons from NADH, pumps protons across the membrane, and passes electrons to ubiquinone (CoQ).
- Complex II (succinate dehydrogenase): Accepts electrons from FADH2, transfers them to CoQ, but does not pump protons.
- Complex III (cytochrome bc, complex): Accepts electrons from CoQ and transfers them to cytochrome c, pumping protons across the membrane.
- Complex IV (cytochrome c oxidase): Accepts electrons from cytochrome c, transfers them to oxygen (O2), and combines with protons to form water (H_2O).



Source:https://courses.lumenlearning.com/wm-biology1/chapter/reading-electron-transport-chain/

Redox Potential:

- Also known as oxidation reduction potential
- Redox potential of any substance is a measure of its affinity for electrons.
- The redox potential of a biological system is usually compared with the potential of H electrode expressed at pH 7.0
- The oxidation-reduction potential may be defined as a quantitative expression of the tendency that a compound has to give or receive electrons.
- The redox potential of a system may be calculated from the following equation.
- 0.0592 71 E = E+ log Conc. Of Reducing agent Conc. Of Oxidising agent
- In Bioenergetics Redox Potential is the ratio of NAD to NADH + H*.
- Describes the availability of NAD for metabolism.

Standard Free Energy Change Of Chemical Reaction:

- The standard free energy change ($\Delta G°$) of a chemical reaction is the change in free energy that occurs when one or more substances are converted to other substances, all in their standard states.
- The standard state is defined as 1 bar pressure and 298 K.
- The standard free energy change indicates how thermodynamically favorable a chemical or physical process.
- The value of $\Delta G°$ can be calculated using the following equations:
- From standard enthalpy and entropy changes: $\Delta G° = \Delta H° - T\Delta S°$
- From the equilibrium constant: $\Delta G° = -RT\ln K$, where R is the universal gas constant, T is the temperature in Kelvin, and ln is the natural logarithm.
- The value of $\Delta G°$ means for a reaction:
- Negative: The process is thermodynamically favored and spontaneous
- Positive: The process is non-spontaneous
- Zero: The reaction is in equilibrium

ATP and High Energy Phosphate:

- Adenosine triphosphate (ATP) is often referred to as the “energy currency” of the cell.
- Adenosine triphosphate (ATP) is a high-energy phosphate (HEP) that is the primary energy source for all cellular processes in the body.
- ATP is a molecule with three phosphate groups that are linked by phosphodiester bonds.
- The phosphate groups are high energy because of the repelling force between their electronegative charges.

Role of ATP in Energy Transfer:

- ATP stores energy in the phosphate bonds, especially the bond between the second and third phosphate groups (terminal phosphate).
- Hydrolysis of ATP releases energy for cellular processes:
- ATP → ADP + Pi (inorganic phosphate) + Energy
- This energy is utilized in various cellular functions, such as:
- Muscle contraction
- Active transport of ions and molecules
- Biosynthetic reactions
- Signal transduction
- Substrate-Level Phosphorylation: Direct transfer of a phosphate group to ADP (e.g., in glycolysis).
- Oxidative Phosphorylation: Occurs in mitochondria, driven by the electron transport chain.