For BioResire students

Life sciences Material

Elite Batch

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Biomolecules

***IMPORTANT NOTE- Topics like Vitamins, Glycolysis, Kreb's Cycle, Oxidative Phosphorylation and fermentation are already been discussed in Nutrition and Metabolism unit**

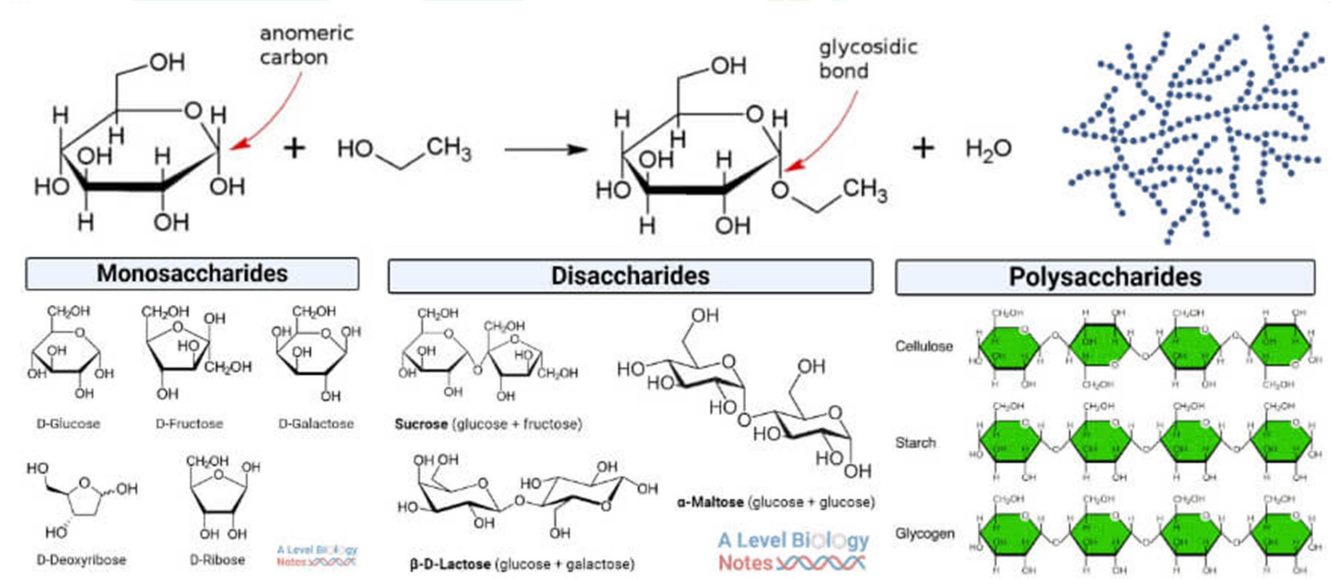
Biomolecules are organic compounds produced by living organisms. They are the building blocks and machinery of life.

Structure and Function

1. CARBOHYDRATES

Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield these upon hydrolysis. Their empirical formula is typically $(CH_2O)_n$.

A. Classification



1. **Monosaccharides (Simple Sugars):**
    - **Definition:** The simplest carbohydrates that cannot be hydrolyzed further.
    - **Classification by Carbon Atoms:**

- Trioses (C3): Glyceraldehyde, Dihydroxyacetone
- Tetroses (C4): Erythrose
- Pentoses (C5): **Ribose** (RNA), **Deoxyribose** (DNA), **Ribulose** (Calvin cycle)
- Hexoses (C6): **Glucose** (blood sugar), **Fructose** (fruit sugar), **Galactose** (milk sugar)

- **Isomerism:**
  - **Aldoses** (e.g., Glucose) vs. **Ketoses** (e.g., Fructose)
  - **D- and L- Isomers:** Based on the configuration of the asymmetric carbon farthest from the carbonyl group. Biological systems primarily use D-sugars.
  - **Anomers:** Isomers that differ only in the configuration around the anomeric carbon (α and β). This is crucial for ring structure (e.g., α-D-Glucose vs. β-D-Glucose).

2. **Disaccharides:**
   - **Definition:** Two monosaccharide units joined by a **glycosidic bond**.
   - **Examples:**
     - **Maltose:** Glucose + Glucose (α-1,4 linkage). Product of starch hydrolysis.
     - **Lactose:** Galactose + Glucose (β-1,4 linkage). Milk sugar.
     - **Sucrose:** Glucose + Fructose (α-1,2 linkage). Table sugar. It is a **non-reducing sugar**.
3. **Oligosaccharides:**
   - **Definition:** 3-10 monosaccharide units. Often found attached to proteins (glycoproteins) or lipids (glycolipids) on the cell surface, serving as recognition signals.

4. **Polysaccharides (Glycans):**
    - **Definition:** Polymers of monosaccharides (can be homo- or heteropolymers).
    - **Storage Polysaccharides:**
        - **Starch:** Plant storage. A mixture of **Amylose** (unbranched, α-1,4 linkages) and **Amylopectin** (branched, α-1,4 and α-1,6 linkages).
        - **Glycogen:** Animal storage (in liver and muscle). Highly branched (more than amylopectin) for rapid mobilization.
    - **Structural Polysaccharides:**
        - **Cellulose:** The major component of plant cell walls. A linear polymer of D-glucose with **β-1,4 linkages**. This configuration allows for extensive hydrogen bonding, making it strong and indigestible by humans.
        - **Chitin:** Found in the exoskeletons of arthropods and fungal cell walls. A polymer of N-Acetylglucosamine with β-1,4 linkages.

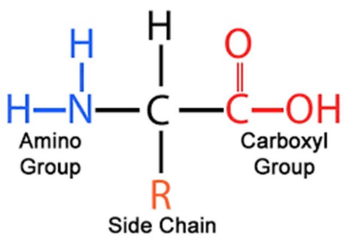
B. Biological Functions

- **Energy Source:** Glucose is the primary fuel for cells.
- **Energy Storage:** Starch and glycogen.
- **Structural:** Cellulose, chitin.
- **Cellular Recognition:** Oligosaccharides on cell surfaces.

2. AMINO ACIDS AND PROTEINS

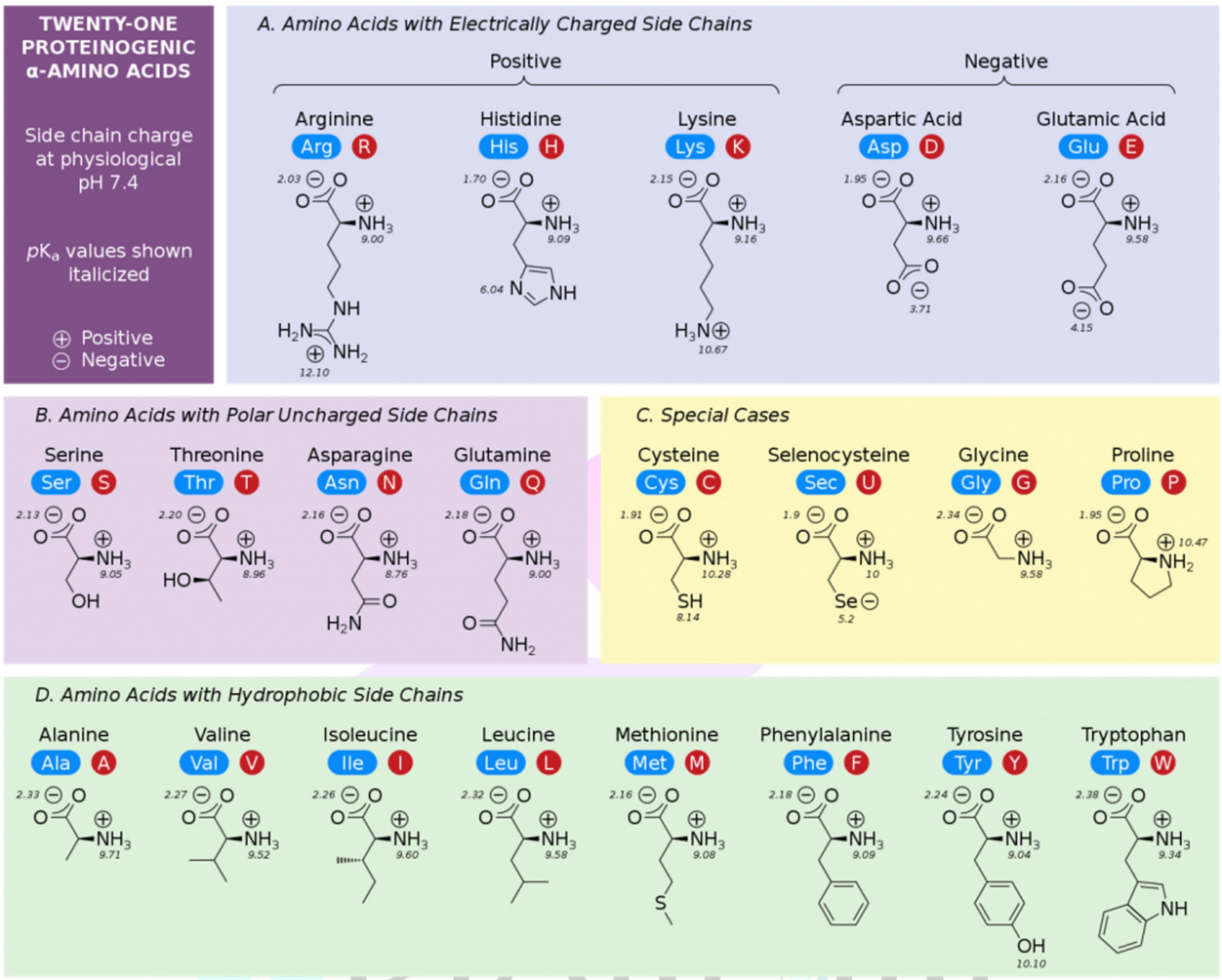
A. Amino Acids: The Building Blocks

- **General Structure:** An amino acid consists of a central **α-carbon** bonded to:
    1. An **amino group** ($-NH_2$)
    2. A **carboxyl group** (-COOH)



3. A **hydrogen atom** (-H)
4. A distinctive side chain

- **Classification based on R-group:**
  - **Non-polar, Aliphatic:** Glycine, Alanine, Valine, Leucine, Isoleucine, Proline. **Hydrophobic.**
  - **Aromatic:** Phenylalanine, Tyrosine, Tryptophan.
  - **Polar, Uncharged:** Serine, Threonine, Cysteine, Asparagine, Glutamine. Can form hydrogen bonds.
  - **Positively Charged (Basic):** Lysine, Arginine, Histidine.
  - **Negatively Charged (Acidic):** Aspartate, Glutamate.



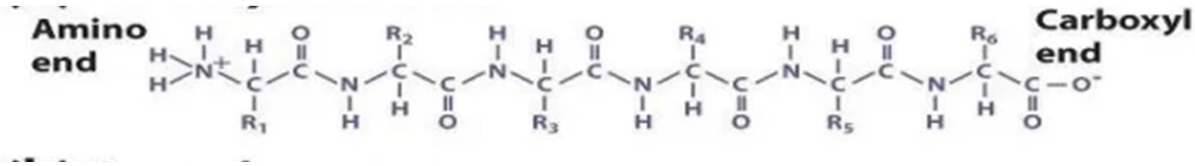
- **Key Properties:**
  - **Amphoteric:** Can act as both an acid and a base.
  - **Isoelectric Point (pI):** The pH at which the amino acid has no net charge.
  - **Chirality:** All amino acids (except Glycine) are chiral and in the **L-configuration** in proteins.

B. Proteins: Structure and Function

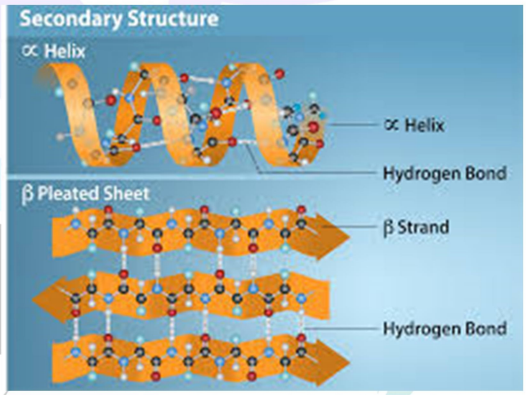
Proteins are polypeptides (linear chains of amino acids linked by **peptide bonds**) that fold into specific 3D structures.

- **Levels of Protein Structure:**

1. **Primary Structure:** The linear sequence of amino acids. Determined by covalent peptide bonds.



2. **Secondary Structure:** Local folding patterns stabilized by hydrogen bonds between backbone atoms.
    - **α-Helix:** A right-handed coiled rod. Stabilized by H-bonds between every 4th amino acid.
    - **β-Sheet:** Formed by adjacent β-strands connected by H-bonds. Can be parallel or antiparallel.



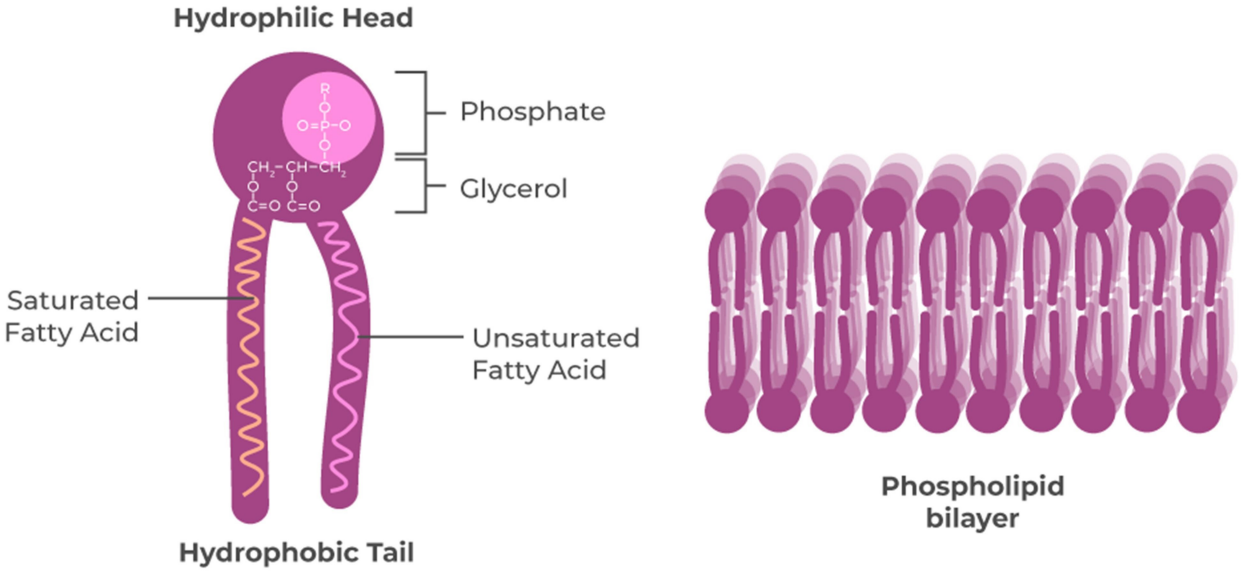
3. **Tertiary Structure:** The overall 3D shape of a single polypeptide chain. Stabilized by interactions between R-groups: hydrophobic interactions, hydrogen bonds, ionic bonds, van der Waals forces, and **disulfide bridges**.
4. **Quaternary Structure:** The arrangement of multiple polypeptide chains (subunits) into a functional protein (e.g., Hemoglobin has 4 subunits).

- **Protein Denaturation:** The loss of 3D structure (and thus function) due to disruption of non-covalent interactions by heat, pH change, or chemicals. The primary structure remains intact.
- **Functions of Proteins:**

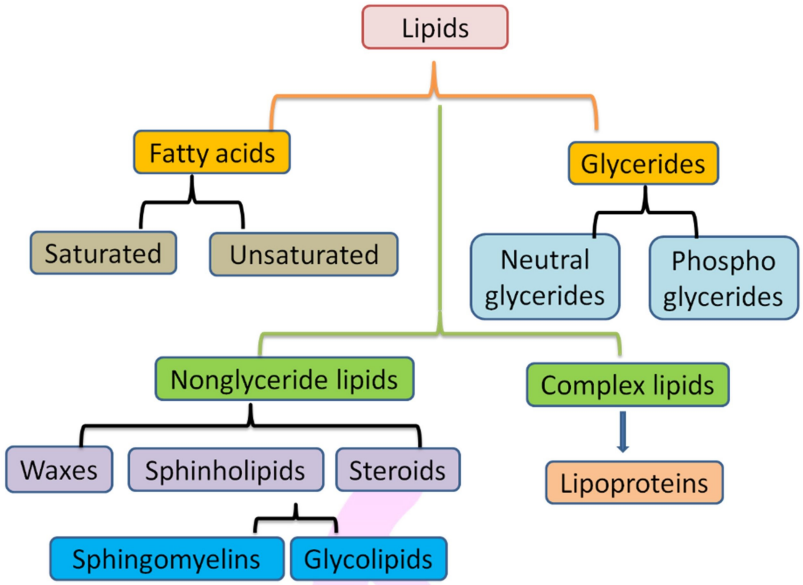
- Enzymes (catalysis)
- Structural support (Collagen, Keratin)
- Transport (Hemoglobin, Serum Albumin)
- Motion (Actin, Myosin)
- Defense (Antibodies)
- Regulation (Hormones, Receptors)

LIPIDS

Lipids are a heterogeneous group of biomolecules that are **insoluble in water** but soluble in non-polar solvents. They are defined by a property, not a structure.



A. Classification and Types



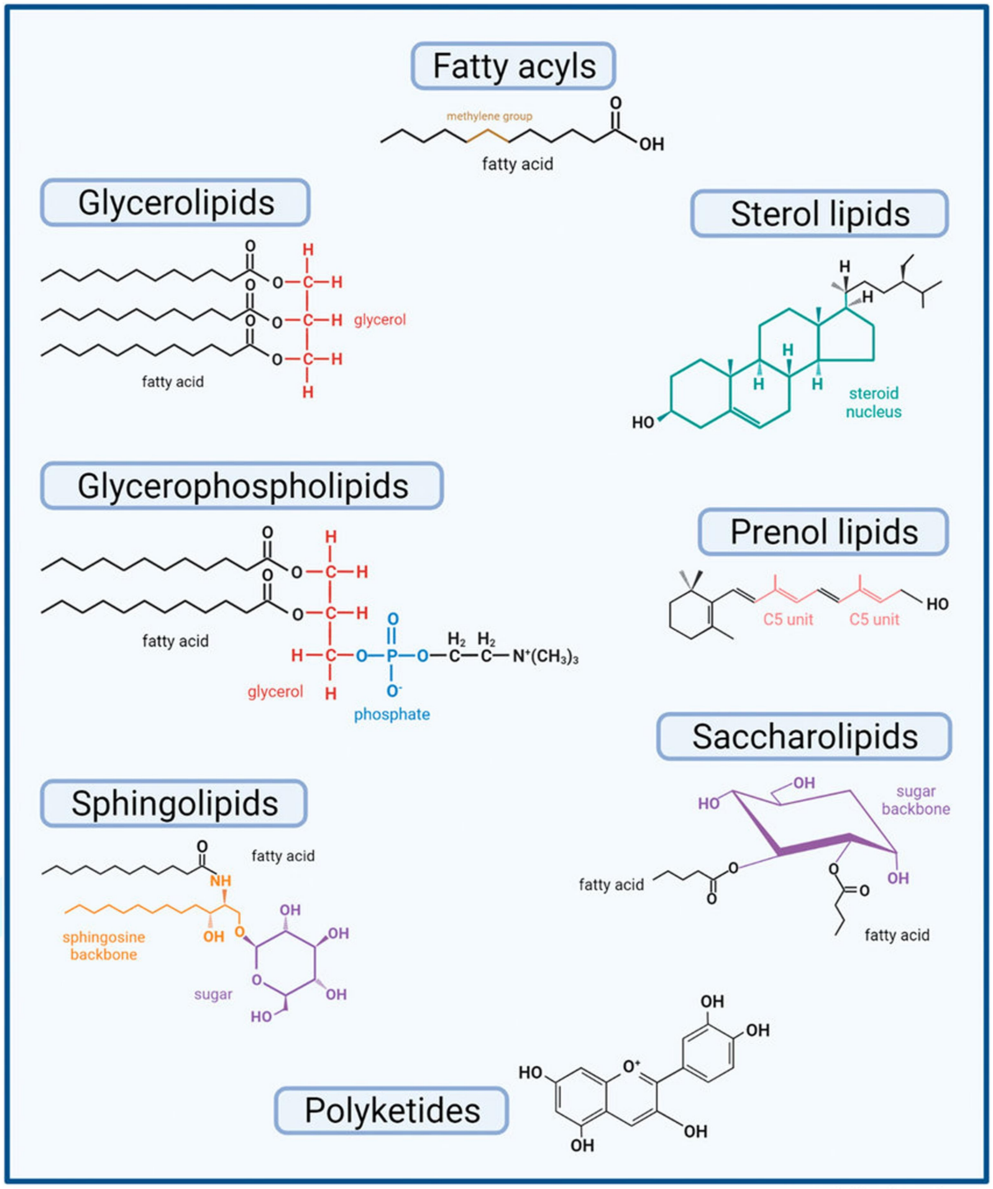
1. **Fatty Acids:**
    - Long hydrocarbon chains with a terminal carboxyl group.
    - **Saturated:** No double bonds (e.g., Palmitic acid). Solid at room temp.
    - **Unsaturated:** One (monounsaturated) or more (polyunsaturated) double bonds (e.g., Oleic acid, Linoleic acid). Liquid at room temp (oils).
2. **Triacylglycerols (Triglycerides):**
    - **Structure:** Three fatty acids esterified to a glycerol backbone.
    - **Function: Primary energy storage** molecules in adipose tissue.
3. **Phospholipids:**
    - **Structure:** Glycerol + two fatty acids + a phosphate group + a polar head group (e.g., choline, serine).
    - **Function:** The main structural component of all biological membranes. They are **amphipathic** (have both hydrophilic and hydrophobic regions), forming bilayers.
4. **Steroids:**

- **Structure:** Four fused hydrocarbon rings (three 6-membered and one 5-membered).
- **Examples:**
  - **Cholesterol:** A crucial component of animal cell membranes, modulates fluidity. Precursor to all other steroids.
  - **Steroid Hormones:** Cortisol, Testosterone, Estradiol.

5. **Other Lipids:**
   - **Waxes:** Esters of long-chain fatty acids with long-chain alcohols. Highly water-repellent.
   - **Eicosanoids:** Signaling molecules derived from arachidonic acid (e.g., Prostaglandins, Leukotrienes).

B. Biological Functions of Lipids

- Energy storage (Triacylglycerols)
- Membrane structure (Phospholipids, Cholesterol)
- Signaling (Steroid hormones, Eicosanoids)
- Insulation and protection



PORPHYRINS

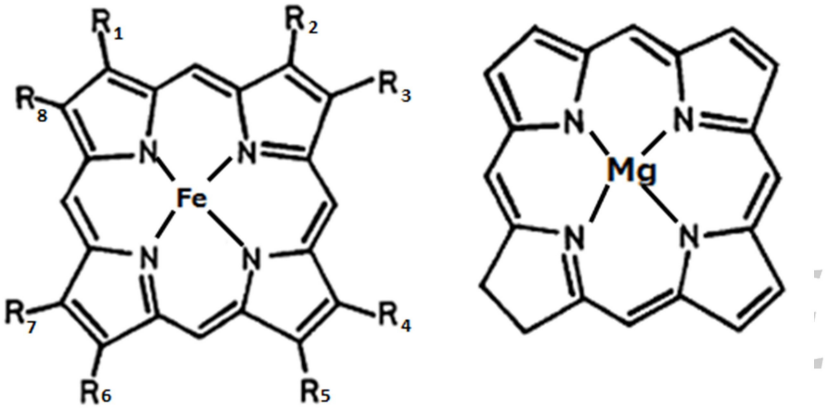
Porphyrins are complex, cyclic organic molecules that form the core structure of many vital biomolecules.

A. Structure

- A **porphyrin ring** is a large, planar, heterocyclic structure formed from four **pyrrole** subunits linked by methine bridges.
- A key property is their ability to chelate metal ions at the center.

B. Biological Significance

- **Heme:** The most important porphyrin. It consists of a **protoporphyrin IX** ring chelating an **iron (Fe^{2+}) ion**.
    - **Function:**
        - **Oxygen binding** in **hemoglobin** and **myoglobin**.
        - **Electron carrier** in **cytochromes** of the electron transport chain.
- **Chlorophyll:** The photosynthetic pigment in plants. It is a porphyrin ring chelating a **magnesium (Mg^{2+}) ion**, with a long phytol tail.
- **Vitamin B_{12}:** Contains a **corrin ring**, which is a modified porphyrin, chelating a **cobalt (Co) ion**.



C. Porphyrias

These are a group of rare genetic disorders caused by defects in the heme biosynthesis pathway, leading to the accumulation of porphyrin precursors. Symptoms can include photosensitivity and neurological issues.

Enzymes: Biological Catalysts

Enzymes are highly specific biological catalysts that increase the rate of biochemical reactions without being consumed. Most enzymes are proteins (except for catalytic RNA molecules called ribozymes).

1. **Classification and Mode of Action**

A. Classification (IUBMB System)

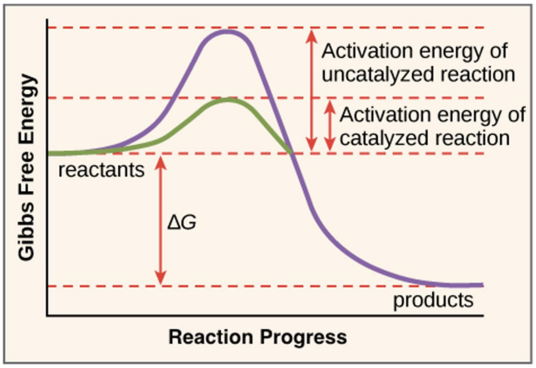
Enzymes are classified into six major classes based on the type of reaction they catalyze.

No.	Class	Type of reaction catalysed	Examples
1.	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)	Dehydrogenases, oxidases
2.	Transferases	Group transfer reactions	Transaminase, kinases
3.	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)	Estrases, digestive enzymes
4.	Lyases	Addition of groups to double bonds or formation of double bonds by removal of groups	Phospho hexo isomerase, fumarase
5.	Isomerases	Transfer of groups within molecules to yield isomeric forms	Decarboxylases, aldolases
6.	Ligases	Formation of C–C, C–S, C–O, and C–N bonds by condensation reactions coupled to ATP cleavage	Citric acid synthetase

Nomenclature: Each enzyme has a systematic name (e.g., ATP:glucose phosphotransferase) and a common name (e.g., Hexokinase). The EC number (Enzyme Commission number) is a four-digit code (e.g., EC 2.7.1.1 for Hexokinase).

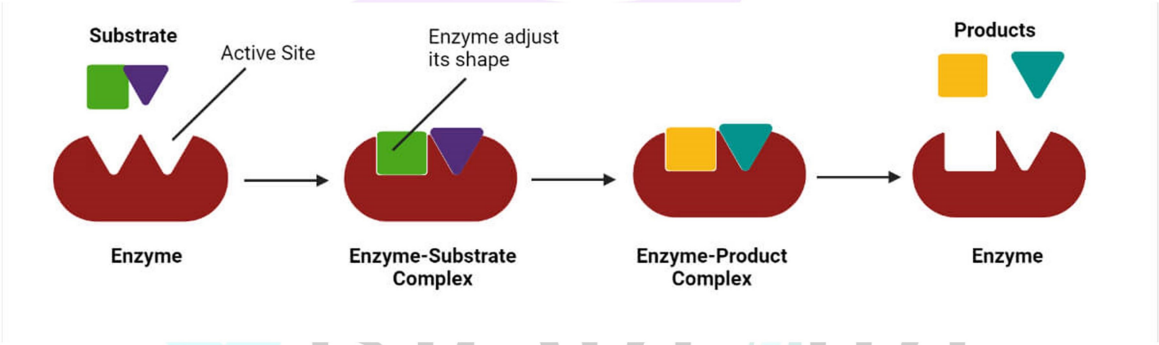
B. Mode of Action

- **Lowering Activation Energy:** Enzymes stabilize the **transition state** of a reaction, thereby lowering the activation energy (E_a) required for the reaction to proceed.



- **Formation of Enzyme-Substrate Complex:** The reaction occurs in a specific region of the enzyme called the **active site**.

    1. **Induced Fit Model:** The active site is not a rigid structure; it changes shape upon substrate binding to optimally fit the substrate and catalyze the reaction.



- **Catalytic Mechanisms:**

    1. **Acid-Base Catalysis:** Amino acid side chains (e.g., Asp, Glu, His, Lys, Cys) donate or accept protons.
    2. **Covalent Catalysis:** A transient covalent bond is formed between the enzyme and the substrate (e.g., in serine proteases).
    3. **Metal Ion Catalysis:** Metal ions (e.g., Zn^{2+}, Mg^{2+}, Fe^{2+}) can stabilize negative charges, participate in oxidation-reduction, or orient the substrate correctly.
    4. **Proximity and Orientation:** Binding the substrate(s) in the correct orientation and close proximity within the active site increases the probability of a successful reaction.

2. Enzyme Assay and Enzyme Units

A. Enzyme Assay

An enzyme assay is a procedure to measure the **rate** (velocity, V) of an enzyme-catalyzed reaction. The goal is to measure the **initial velocity (V_0)**, which is the rate measured before 10% of the substrate is consumed, to avoid complications from product inhibition or the reverse reaction.

- **Methods:**
    - **Continuous Assay:** The progress of the reaction is monitored in real-time (e.g., by measuring a change in absorbance using a spectrophotometer).
    - **Discontinuous Assay:** Samples are taken from the reaction mixture at specific time intervals, and the reaction is stopped (quenched) to measure the amount of product formed.

B. Enzyme Units

- **International Unit (U):** The amount of enzyme that catalyzes the conversion of **1 micromole of substrate per minute** under standard conditions (specific pH and temperature).
- **Katal (kat):** The SI unit for enzyme activity. It is the amount of enzyme that converts **1 mole of substrate per second**.
    - **Conversion:** 1 U = 1 µmol/min = (1/60) µmol/s ≈ 16.67 nkat
- **Specific Activity:** The number of enzyme units per milligram of total protein (U/mg). It is a measure of enzyme purity.
- **Turnover Number (k_cat):** The maximum number of substrate molecules converted to product per enzyme molecule per unit time (per second) when the enzyme is fully saturated. It is a measure of the **catalytic efficiency**.

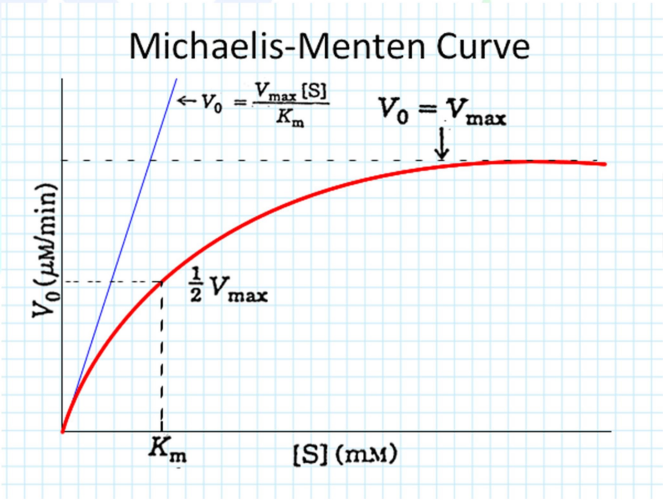
3. Enzyme Kinetics

Enzyme kinetics is the study of the rates of enzyme-catalyzed reactions.

A. Michaelis-Menten Kinetics

This model describes the relationship between substrate concentration [S] and reaction velocity (V).

- **Key Parameters:**
  - **V_max:** The maximum reaction velocity when the enzyme is fully saturated with substrate.
  - **K_m (Michaelis Constant):** The substrate concentration at which the reaction velocity is half of V_max. It is a measure of the **enzyme's affinity for the substrate**. A **low K_m** indicates **high affinity**.
- **Michaelis-Menten Equation:**
  $V_0 = (V_{max} * [S]) / (K_m + [S])$
- **Graph:** The plot of V_0 vs. [S] is a rectangular hyperbola.



B. Lineweaver-Burk Plot (Double-Reciprocal Plot)

This is a linear transformation of the Michaelis-Menten equation.

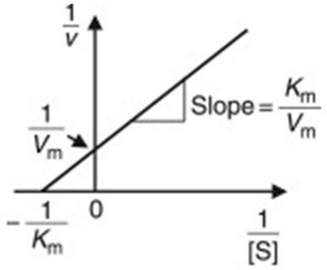
- **Equation:** $1/V_0 = (K_m / V_{max}) * (1/[S]) + 1/V_{max}$
- **Graph:** A plot of $1/V_0$ vs. $1/[S]$ gives a straight line.
  - **Y-intercept** = $1/V_{max}$

- **Slope** = K_m / V_max
- **X-intercept** = -1/K_m

- **Use:** Primarily used to determine K_m and V_max accurately from experimental data and to diagnose the type of enzyme inhibition.

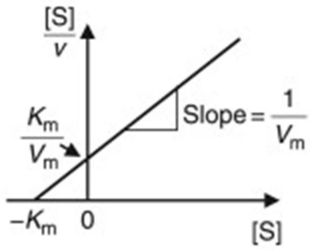
Lineweaver–Burk (L–B) plot

$$\frac{1}{v} = \frac{1}{V_m} + \frac{K_m}{V_m}\frac{1}{[S]}$$



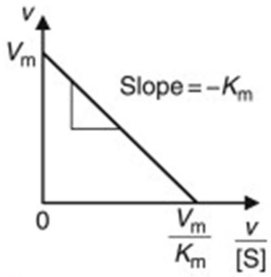
Hanes–Woolf plot

$$\frac{[S]}{v} = \frac{K_m}{V_m} + \frac{1}{V_m}[S]$$



Eadie–Hofstee plot

$$v = V_m - K_m\frac{v}{[S]}$$



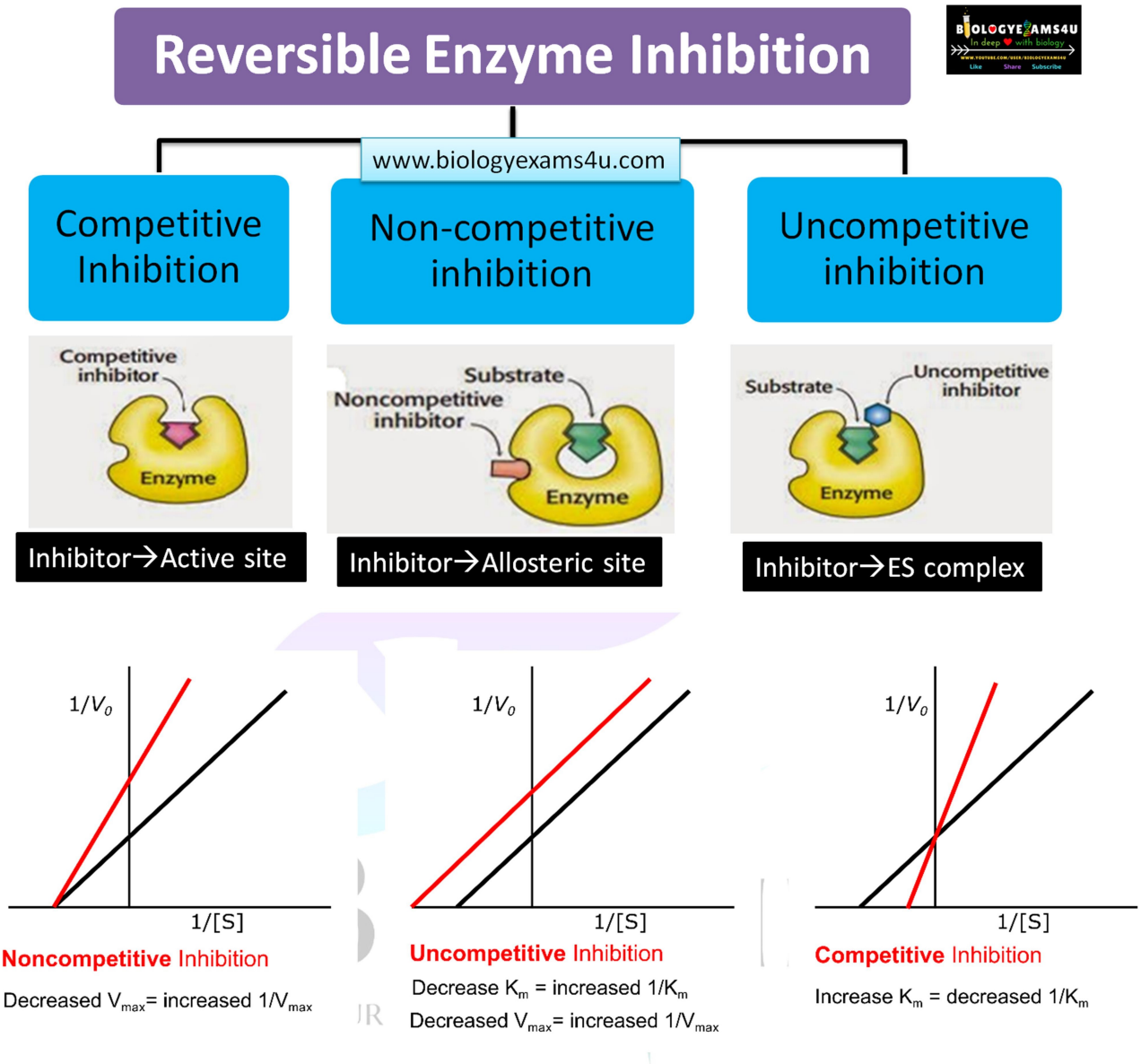
Enzyme Inhibition

Enzyme inhibitors are molecules that decrease enzyme activity. They can be reversible or irreversible.

A. Reversible Inhibition

The inhibitor (I) binds non-covalently to the enzyme and can dissociate.

- **Example of Competitive Inhibition:** Statin drugs (e.g., Lovastatin) competitively inhibit HMG-CoA reductase, a key enzyme in cholesterol synthesis.
- **Example of Non-Competitive Inhibition:** Heavy metal ions (e.g., Pb^{2+}, Hg^{2+}).



Irreversible Inhibition

The inhibitor binds covalently to the enzyme, permanently inactivating it.

- **Example:** Penicillin irreversibly inhibits the transpeptidase enzyme involved in bacterial cell wall synthesis. Diisopropylphosphofluoridate (DIPF) irreversibly inhibits acetylcholinesterase by modifying a critical serine residue.

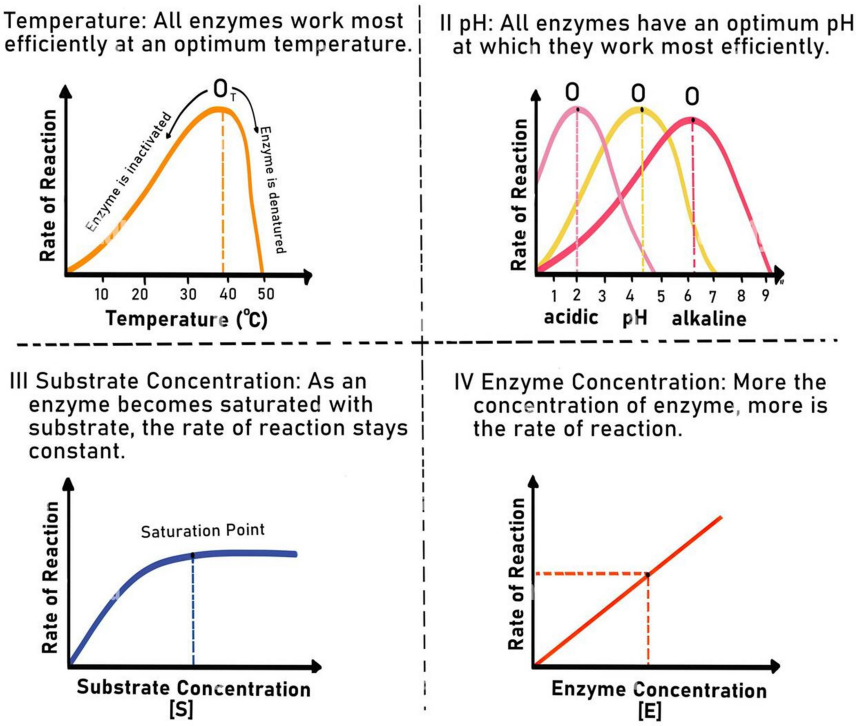
Reversible inhibitors	Irreversible inhibitors
Enzymes do follow Michaelis-Menten rate equation and Lineweaver-Burk plot.	Enzymes do not follow Michaelis-Menten rate equation and Lineweaver-Burk plot.
Plot [V] versus [S] curve is Rectangular hyperbolic shape curve.	Plot [V] versus [S] curve is Sigmoidal curve.
Dissociate very rapidly from targeted enzyme because of loosely bound.	Dissociate very slowly from targeted enzyme because of tightly bound.
Classified into three categories. Competitive, non-competitive and mixed inhibitors	Classified into three categories. Group specific reagents, substrate analogs and suicide inhibitors.
Competitive inhibitors can be reversed by increasing substrate concentration.	Substrate analogs imitate enzyme substrate and irreversibly modify the active site of the enzyme.
Reversible inhibitors bind to enzyme by hydrogen bonding, hydrophobic interactions and ionic bonds.	Irreversible inhibitors bind to enzyme through covalent interactions which modify amino acid residues by reactive functional groups.

Factors Regulating Enzyme Action

Several factors control the rate of enzyme-catalyzed reactions.

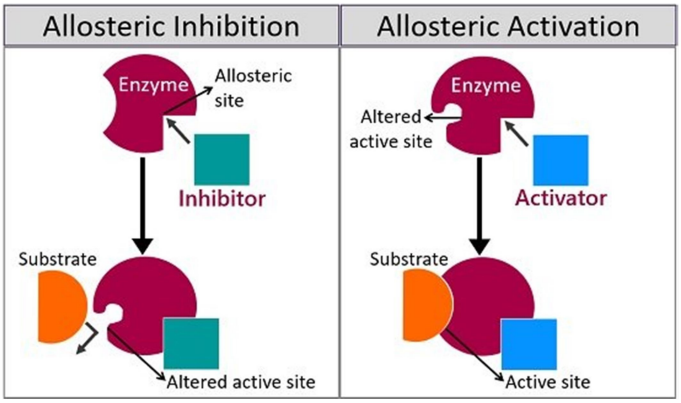
1. **Enzyme Concentration:**
    - At a saturating [S], the reaction velocity (V_0) is directly proportional to the enzyme concentration [E]. This is the basis for using enzyme activity to determine enzyme concentration.
2. **Substrate Concentration:**
    - As described by Michaelis-Menten kinetics, V_0 increases with [S] until it reaches V_max.
3. **Temperature:**
    - **Effect:** Reaction rate increases with temperature (Q_{10} effect) up to an optimum point.
    - **Optimum Temperature:** The temperature at which the enzyme has maximum activity. For human enzymes, it's typically ~37°C.
    - **Denaturation:** At high temperatures, the enzyme denatures, and activity drops sharply.
4. **pH:**
    - **Effect:** Enzymes have an **optimum pH** at which they are most active. Changes in pH can alter the ionization state of the active site residues or the substrate, reducing activity.

- **Examples:** Pepsin (stomach, pH ~2), Trypsin (intestine, pH ~8).

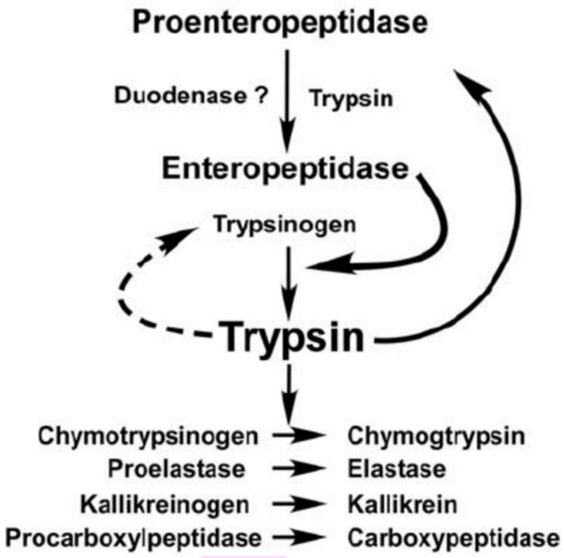


5. **Allosteric Regulation:**

   - Allosteric enzymes have a site distinct from the active site where an **effector** molecule binds.
   - **Allosteric Activator:** Increases enzyme activity (shifts kinetics from sigmoidal to hyperbolic, decreases $K_{0.5}$).
   - **Allosteric Inhibitor:** Decreases enzyme activity (makes the sigmoidal curve more pronounced, increases $K_{0.5}$).
   - **Example:** ATP is an allosteric inhibitor of Phosphofructokinase-1 (PFK-1) in glycolysis.



6. **Covalent Modification:**
    - Reversible covalent modification (e.g., phosphorylation/dephosphorylation, acetylation, ubiquitination) can rapidly activate or inactivate an enzyme.
    - **Example:** Glycogen phosphorylase is activated by phosphorylation; glycogen synthase is inactivated by phosphorylation.
7. **Zymogen Activation:**
    - Some enzymes are synthesized as inactive precursors (**zymogens** or proenzymes) and are activated by proteolytic cleavage.
    - **Example:** Trypsinogen (inactive) is cleaved in the small intestine to form active Trypsin. This prevents the enzyme from digesting the tissues where it is synthesized.



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"The future belongs to those who explore the unseen — where biology meets innovation and discovery begins."