i. Concept of atoms and molecules

i. Concept of atoms and molecules, molecular interactions, stereochemistry and their importance in biological systems

Concept of Atoms and Molecules

Atomic Structure and Biological Relevance

1. **Subatomic Particles**
   - **Protons** (positively charged, define atomic number), **Neutrons** (neutral, contribute to isotopes), **Electrons** (negatively charged, define chemical behavior).
   - Atoms of the same element can vary in neutron number (isotopes), some of which (e.g., radioisotopes) have biological and diagnostic applications (e.g., 14C^{14}\mathrm{C}14C in radiolabeling).
2. **Electron Configuration and Valency**
   - The arrangement of electrons in orbitals (s, p, d, f) determines bonding patterns.
   - **Valence electrons** govern reactivity and the type of chemical bonds formed (ionic, covalent).
   - Biological molecules predominantly rely on **covalent** bonding (carbon-based frameworks).
3. **Elements in Biology**
   - **Major Elements**: C, H, O, N (comprise bulk of biomolecules—proteins, nucleic acids, carbohydrates, lipids).
   - **Minor/Trace Elements**: P, S, Fe, Mg, Ca, etc., essential for specific biochemical functions (e.g., enzyme cofactors, signal transduction).

Molecules and Chemical Bonds

1. **Covalent Bonds**
   - **Definition**: Shared electron pairs between atoms, creating stable structural backbones (e.g., C–C, C–H, C–O bonds in organic molecules).
   - **Bond Strength**: Generally strong (50–110 kcal/mol). Can be single, double, triple, influencing molecule rigidity/flexibility.
2. **Ionic Bonds**
   - **Definition**: Electrostatic attraction between oppositely charged ions (e.g., Na^+ and Cl^-).
   - Common in physiological contexts (e.g., salt bridges within proteins, membrane potentials) but weaker in aqueous environments due to solvation.
3. **Polar vs. Nonpolar Bonds**
   - **Polar Bonds** (e.g., O–H, N–H) arise from electronegativity differences, leading to partial charges (δ^+/δ^-).
   - **Nonpolar Bonds** (e.g., C–H) have relatively even electron distribution, crucial for hydrophobic interactions in lipids.
4. **Functional Groups**
   - **Hydroxyl** (–OH), **carbonyl** (–C=O), **carboxyl** (–COOH), **amino** ($-NH_2$), **phosphate** ($-PO_4^{3-}$), **sulfhydryl** (–SH), etc.
   - Confer specific chemical reactivities and properties (e.g., acidity, basicity, hydrogen bonding capacity) to biomolecules.

Molecular Interactions

Noncovalent Interactions

1. **Hydrogen Bonds (H-bonds)**
   - Form between a hydrogen attached to an electronegative atom (e.g., O, N) and another electronegative atom.
   - Important in stabilizing protein secondary structures (α-helices, β-sheets), DNA double helix base pairing, and water's unique properties.
2. **Van der Waals Forces**
   - **London Dispersion** (induced dipole–induced dipole), **Debye** (dipole–induced dipole), **Keesom**

(dipole–dipole).
   - Weak individually, but collectively significant in stabilizing macromolecular conformations and protein-ligand interactions.
3. **Electrostatic (Ionic) Interactions**
   - Charged groups (e.g., side chains of Asp, Glu vs. Lys, Arg) form salt bridges.
   - Influenced by dielectric constant of the medium; in proteins, help maintain tertiary/quaternary structures.
4. **Hydrophobic Interactions**
   - Nonpolar molecules cluster to minimize contact with polar solvents (especially water).
   - Critical in protein folding (burying nonpolar residues) and membrane formation (phospholipid bilayers).

Biological Context of Molecular Interactions

1. **Protein Folding and Stability**
   - Balanced interplay of H-bonds, hydrophobic effects, ionic bonds, van der Waals attractions ensures stable native conformations.
   - Chaperones can assist in correct folding, preventing aggregation.
2. **Enzyme-Substrate Binding**
   - Often involves a “lock-and-key” or induced-fit model where specific noncovalent interactions orient substrates optimally for catalysis.
   - Strength and specificity governed by cumulative weak forces and complementary stereochemistry.
3. **Nucleic Acid Structure**
   - **Base Pairing**: Hydrogen bonds (A–T, G–C) in DNA, plus base stacking (van der Waals) stabilize the double helix.
   - **Backbone**: Phosphodiester linkages, with ionic interactions influencing shape and stability in ionic media.
4. **Membrane Assemblies**
   - **Lipid Bilayers** form spontaneously due to hydrophobic interactions of fatty acid tails; polar head groups interact with aqueous environment.
   - Embedded/associated proteins rely on specific interactions (hydrophobic domains, ionic/polar residues at surface).

Stereochemistry and Its Importance in Biology

Chirality and Isomerism

1. **Chirality**
   - A **chiral center** (most often a tetrahedral carbon with four different substituents) creates non-superimposable mirror images, called **enantiomers**.
   - Biological macromolecules often exhibit chirality (e.g., L-amino acids in proteins, D-sugars in carbohydrates).
2. **Types of Stereoisomers**
   - **Enantiomers**: Mirror-image isomers differing in optical activity (rotate plane-polarized light in opposite directions, labeled (+)/(-) or D/L).
   - **Diastereomers**: Stereoisomers not related as mirror images (e.g., many sugar configurations, cis/trans or E/Z in alkenes).
   - **R/S Nomenclature**: Assigns priorities to substituents around a chiral center for unambiguous configuration naming.
3. **Conformation vs. Configuration**
   - **Conformation**: Spatial arrangement achievable through rotation about single bonds (e.g., staggered/eclipsed in alkanes, different conformers of proteins).
   - **Configuration**: Requires bond breaking to interconvert (e.g., enantiomers, cis/trans isomers).

Biological Significance of Stereochemistry

1. **Enzyme Specificity**
   - Enzymes often discriminate sharply between enantiomers; only one enantiomer fits the active site orientation for catalysis.

  - **Example**: D-sugars are metabolized by glycolytic enzymes, while L-forms typically are not recognized.
2. **Drug-Target Interactions**
   - Many drugs are chiral, and only one enantiomer may be pharmaceutically active (e.g., L-DOPA for Parkinson's).
   - The other enantiomer can be inactive or even harmful (e.g., thalidomide's enantiomeric toxicity).
3. **Structural Features**
   - Chirality in amino acids results in **chiral polymers** (proteins) with specific secondary/tertiary structures.
   - **Carbohydrates**: D-glucose and related epimers differ in reactivity, shape, and biological function.
4. **Energy Utilization**
   - Metabolic pathways evolved to utilize stereospecific substrates (ensuring substrate-enzyme match and preventing interference from incorrect isomers).

Integrating Chemical Principles in Biological Systems

1. **Macromolecular Assembly**
   - Polypeptides, nucleic acids, polysaccharides, and complex lipids rely on covalent bonds for polymer backbone, plus noncovalent interactions for higher-order structures.
2. **Self-Organization**
   - **Emergent Behavior**: Phospholipid self-assembly into bilayers, protein folding guided by hydrophobic effect, S–S bonds, etc.
   - Facilitated by water's properties (polarity, hydrogen bonding) and the unique stereochemical constraints of biomolecules.
3. **Regulation of Biochemical Pathways**
   - Allosteric enzymes exhibit conformational changes (altering active site affinity) in response to ligand binding, reliant on subtle intramolecular interactions.
   - Signal transduction often depends on transient protein–protein or protein–lipid binding events with stereochemical matching.
4. **Evolutionary Implications**
   - Early biochemical pathways likely selected for stable, replicable chiral molecules.
   - Consistent use of one stereoisomer (e.g., L-amino acids) across life suggests an ancient evolutionary choice reinforced by functional optimization.

Concluding Remarks

In **biochemistry**, the understanding of **atoms and molecules**, their **bonding and interactions**, and the crucial concept of **stereochemistry** underpins every aspect of **biological function**, from how enzymes recognize substrates to how membranes form and how proteins fold. These chemical foundations explain why life is exquisitely selective—favoring certain isomers, leveraging weak interactions for dynamic regulation, and ensuring robust yet adaptable molecular architectures.

Grasping these principles is essential for fields ranging from **drug design** (chiral synthesis, enantiopure compounds) to **structural biology** (crystallography, NMR, cryo-EM) and **systems biology** (emergent properties of complex networks). Ultimately, the interplay of **atomic and molecular properties** with **biological context** exemplifies how seemingly small changes—like a single chiral center or the arrangement of hydrogen bonds—can produce profound differences in **organismal physiology and survival**.