BIOLOGICAL PHYSICS

CHAPTER 1 –BASIC CONCEPTS OF BIOLOGY FOR THE PHYSICAL SCIENTIST

Poopalasingam Sivakumar

What is Biophysics

- **Biophysics: A Specialized Approach**: Biophysics uses principles from physics to explain how biological systems function, from molecular interactions to cellular processes and physiological behavior.
  - Biophysics applies the laws of physics to understand living systems.
  - It connects biological questions with quantitative models and physical principles.
  - The field spans scales from molecules and cells to tissues and whole organisms.

  Examples: Explain protein folding, ions movement across cell membranes, energy conversion, mechanical forces.

What is Biophysics

- **An Interdisciplinary Science**: Biophysics combines physics, biology, chemistry, mathematics, engineering, and computer science to study the physical principles underlying life.
- Tools and Approaches: Statistical mechanics and thermodynamics, Molecular modeling and simulations, Imaging and spectroscopy, Data analysis and computational methods.
- Applications: Medicine and biomedical engineering, Drug discovery and diagnostics, Neuroscience and systems biology

The Interplay of Physics and Biology

- **Bridging Physics and Biology**: Establishing a strong connection between physics and biology is crucial for gaining a deeper understanding of life processes.
- "**Key Biological Questions**: This involves investigating fundamental biological questions:
  - ✓ How do biological molecules interact and function?
  - ✓ How do cells form and organize?
  - ✓ How do living systems operate and evolve over time and space?

The Interplay of Physics and Biology

- **The Challenge of Complexity:** The intricate nature of biomolecules and the dynamic complexity of living systems present significant challenges in their study.

- **The Power of Physics**: Physics provides a powerful framework for:
  - ✓ Quantifying biological processes with precision.
  - ✓ Developing sophisticated models to simulate biological systems.
  - ✓ Designing and implementing innovative experimental techniques.

The Power of Biophysics: Unraveling the Structure of DNA

- **A Landmark Discovery**: The discovery of the double-helical structure of DNA in **1953 by James Watson and Francis Crick** stands as a landmark achievement in the history of science.
- **A Multidisciplinary Effort**: This groundbreaking discovery was a product of a multidisciplinary collaboration, involving expertise in biology, physics, and chemistry.
- **Key Contributors**:
  - ✓James Watson, a biologist with expertise in genetics.
  - ✓Francis Crick, a physicist with a background in protein structure.
  - ✓Rosalind Franklin, a biophysicist and X-ray crystallographer who provided crucial X-ray diffraction data.

The Power of Biophysics: Unraveling the Structure of DNA

A Multifaceted Approach: The elucidation of DNA structure involved:

- ✓ Biochemical techniques: To purify and isolate DNA.
- ✓ Crystallography: To obtain high-quality X-ray diffraction patterns of DNA crystals.
- ✓ Physical science principles: To interpret the X-ray data and deduce the three-dimensional structure of the DNA molecule.

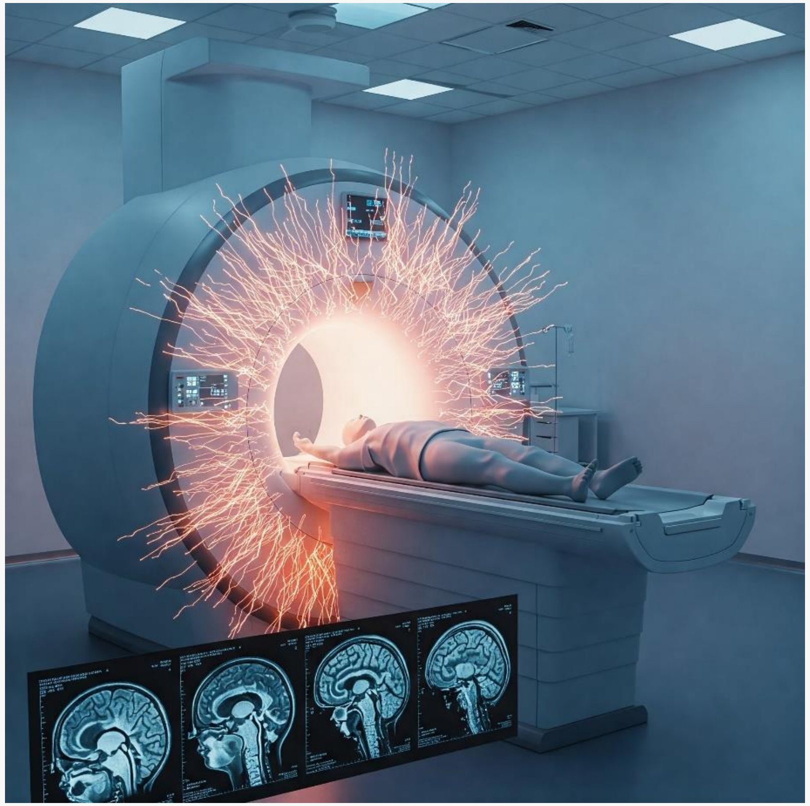
The Power of Biophysics: Small-Angle X-ray Scattering (SAXS)

- Developed in the 1930s, SAXS was initially applied to non-biological materials.
- Over time, the technique has been successfully adapted to study biological macromolecules, such as proteins, nucleic acids, and protein complexes.
- It measures the scattering of X-rays at very small angles (typically 0.1° to 5°).
- A Powerful Tool for Nanometer-Scale Structural Analysis, provides information about structural features ranging from 1 to 150 nanometers in size.
- Provides low-resolution information on the shape, conformation, and assembly state of biological macromolecules. Can be used to study:
  - Protein structure and dynamics
  - Nucleic acid folding and interactions
  - Protein-protein and protein-nucleic acid interactions
  - Structure of protein complexes

The Power of Biophysics: Magnetic Resonance Imaging (MRI)

MRI is a non-invasive medical imaging technique that uses strong magnetic fields and radio waves to produce detailed images of the body's1 organs and tissues.

- MRI works by aligning the protons in the body's water molecules with a strong magnetic field.
- Radio waves are then used to disrupt this alignment, causing the protons to emit signals that are detected by the MRI scanner.
- MRI provides high-resolution images of soft tissues, which are difficult to see with other imaging techniques such as X-ray.
- It does not use ionizing radiation, making it a safe imaging technique for most people.



The Power of Biophysics: Vibrational Spectroscopy

Two prominent examples of vibrational spectroscopy techniques are Fourier Transform Infrared (FT-IR) Spectroscopy and Raman Spectroscopy. They often complement each other, as they are sensitive to different vibrational transitions

- FT-IR Spectroscopy
  - It measures the absorption or transmission of infrared radiation by a sample. Infrared radiation interacts with the vibrational modes of molecules, causing specific bonds to vibrate.
  - IR spectroscopy measures the change in dipole moment of a molecule during vibration.
- Raman spectroscopy
  - It utilizes the inelastic scattering of light by molecules. When light interacts with a molecule, it can be scattered with a slight change in frequency.
  - It detects the change in polarizability of a molecule during vibration. Polarizability refers to the ease with which the electron cloud of a molecule can be distorted by an electric field.

Essential Elements of Life

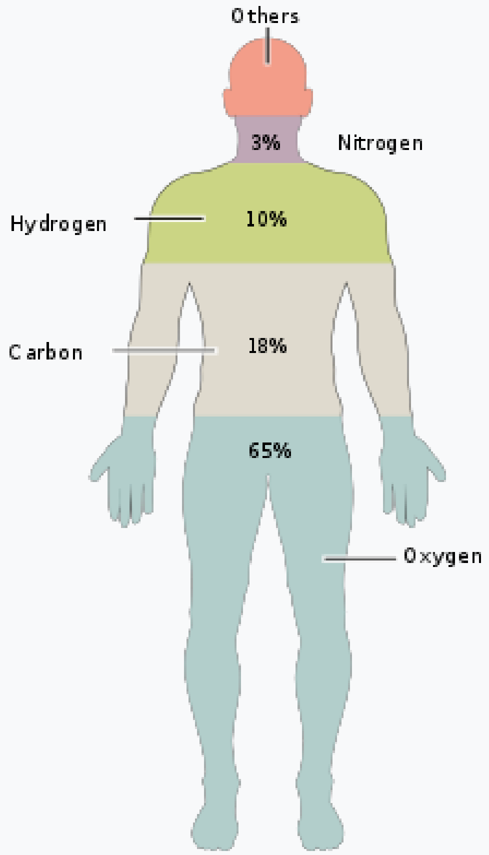
- Only a small subset of the known elements are essential for life

- **Most abundant elements (≈ 96%** of body mass): Carbon (C), Hydrogen (H), Oxygen (O), and Nitrogen (N) are the most abundant elements.

  - H and O are abundant due to water, making up to 60% of human body.

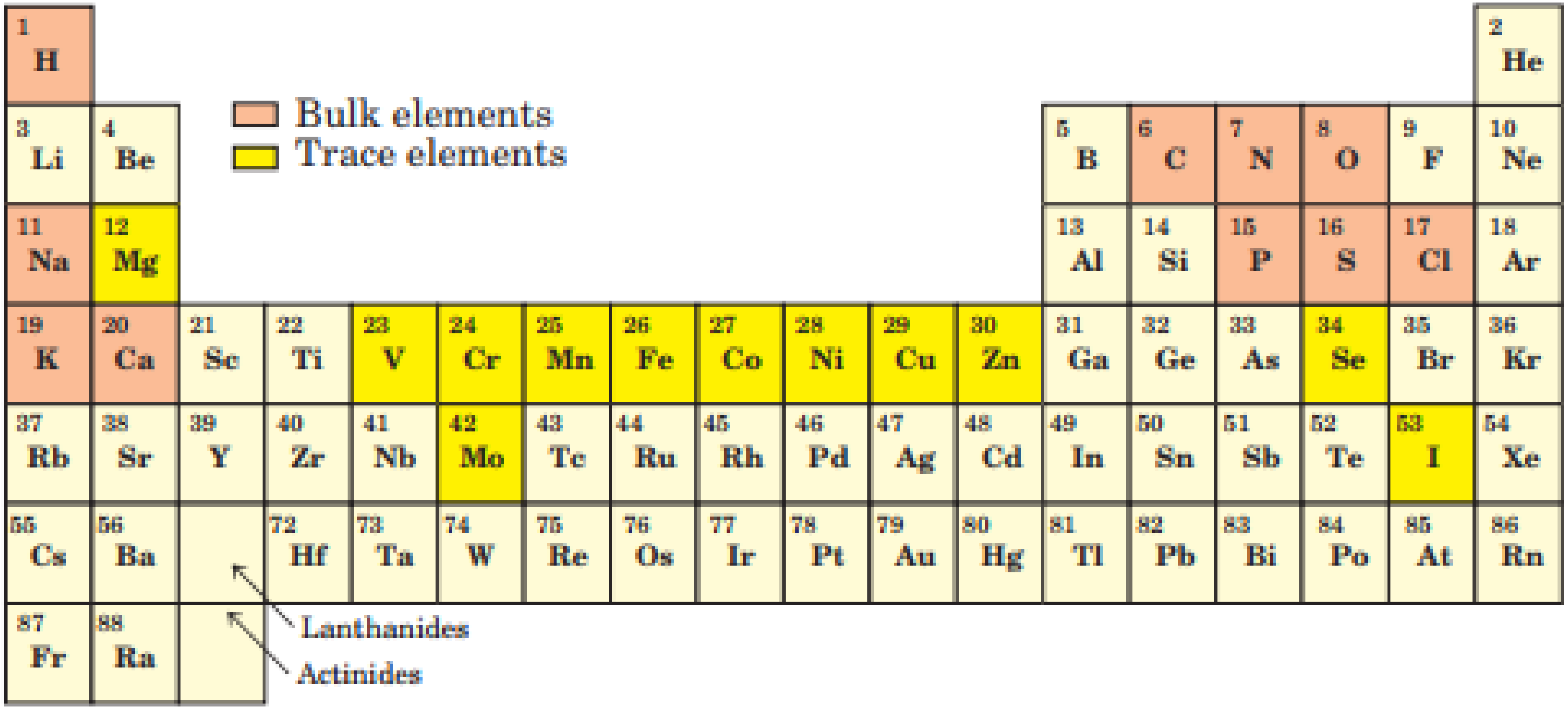
- **Macronutrients**: Calcium (Ca), Phosphorus (P), Potassium (K), Sulfur (S), Chlorine (Cl), Sodium (Na), and Magnesium (Mg). Essential for bone structure, nerve signaling, muscle function and metabolism.

- **Trace Elements** (required in very small amounts): iron (Fe), zinc (Zn), copper (Cu), and manganese (Mn). Play critical roles in enzyme activity, oxygen transport, cellular regulation, and more



Element	Symbol	% in body
Oxygen	O	65.0
Carbon	C	18.5
Hydrogen	H	9.5
Nitrogen	N	3.2
Calcium	Ca	1.5
Phosphorus	P	1.0
Potassium	K	0.4
Sulfur	S	0.3
Sodium	Na	0.2
Chlorine	Cl	0.2
Magnesium	Mg	0.2
Others		< 1.0

Essential Elements of Life:



C, N, O, and H, followed by Ca, P, K, S, Cl, Na, and Mg. Certain **trace elements** are also present in very small quantities.

Carbon: Backbone of Life

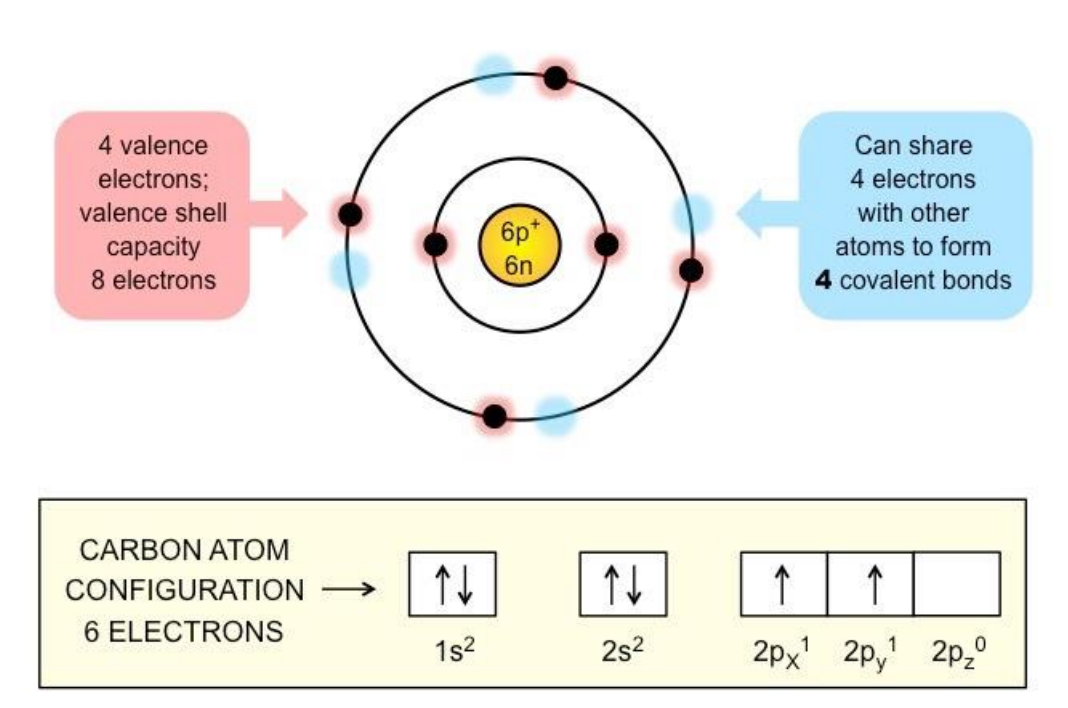
Carbon is the fundamental building block of biomolecules, forming the structural framework of proteins, lipids, carbohydrates, and nucleic acids.

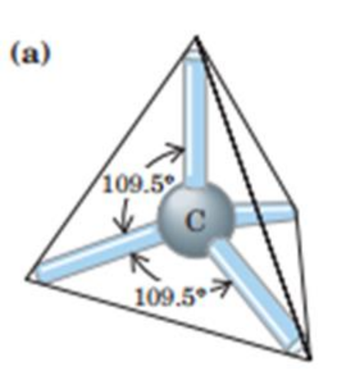
Formation four covalent bonds (Tetravalency):

- Carbon has four valence electrons, allowing it to form four stable covalent bonds.
- Bonds are typically arranged in a tetrahedral geometry

Structural Versatility:

- Forms single, double, and triple bonds
- Enables linear, branched, and ring structures
- Supports both rigid frameworks and flexible chains

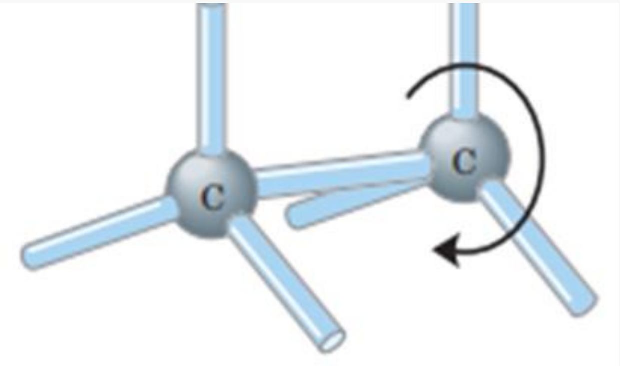


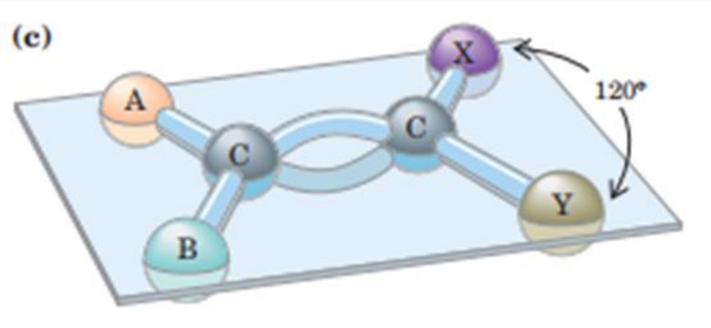


Carbon Bonding

Carbon's ability to bond with itself and H, O, N, and S creates the complex "backbones" of life

- **Single Bonds (C-C):** Allow free rotation about the bond axis, yielding 3D flexibility (protein folding)
- **Double Bonds (C=C)**: Shorter and stronger than single bonds. Restricted rotation due to π-bonding. Introduce rigidity and defined geometry (e.g., cis/trans) isomerism)
- **Triple Bonds (C≡C):** Very strong and linear bonds. Rare in biomolecules, but present in specialized natural products and synthetic probes





Atoms	e^- pairing	Covalent bond	Bond energy (kJ/mol)
H· + H· ⟶	H:H	H—H	436
·C· + H· ⟶	·C:H	—C—H	414
·C· + ·C· ⟶	·C:C·	—C—C—	343
·C· + ·N: ⟶	·C:N:	—C—N	292
·C· + ·O: ⟶	·C:O:	—C—O—	351
·C· + ·C· ⟶	C::C	C=C	615
·C· + ·N: ⟶	C::N:	C=N—	615
·C· + ·O: ⟶	C::O:	C=O	686
·O: + ·O: ⟶	·O:O·	—O—O—	142
·O: + ·O: ⟶	:O::O:	O=O	402
·N: + ·N: ⟶	:N:::N:	N≡N	946
·N: + H· ⟶	:N:H	N—H	393
·O: + H· ⟶	·O:H	—O—H	460

The Role of Carbon

- **Compatibility with Water (Aqueous Chemistry)**:
  - Many carbon-based molecules contain polar functional groups (–OH, $–COO^-$, $–NH_2$)→ Enable hydrogen bonding and solubility in water
  - Amphipathic carbon compounds (e.g., lipids)→ Self-assemble into membranes via the hydrophobic effect
  - Aqueous compatibility allows diffusion, molecular recognition, and biochemical reactions
- **Energy Storage in Carbon Compounds**
  - Carbohydrates: Rapidly accessible energy. Optimized for short-term storage and transport.
  - Lipids: Highly reduced carbon chains. Store ~2× more energy per gram than carbohydrates.
- Energy is released through oxidation of C–C and C–H bonds, driving cellular work

Why Carbon, Not Silicon?

Both carbon and silicon are in Group 4 of the periodic table, with four valence electrons

Key Differences:

i. **Atomic Size and Mass**: Silicon atoms are significantly larger and heavier than carbon atoms.

ii. **Bond Strength**: Silicon-silicon bonds are generally weaker than carbon-carbon bonds.

iii. **Bond Polarity**: Silicon-oxygen bonds are more polar than carbon-oxygen bonds.

iv. **Reactivity**: Silicon compounds tend to be more reactive and less stable over carbon counterparts.

v. **Solubility**: Silicon compounds are generally less soluble in water than carbon compounds.

Important of Liquid Medium

Key Liquid environments are crucial for:

i. **Facilitating biochemical reactions**: Liquid media allow molecules to collide and interact efficiently, enabling the chemical reactions necessary for life.

ii. **Transport of molecules**: Liquids enable the rapid and efficient transport of nutrients, waste products, and signaling molecules within and between cells.

Water possesses unique properties that make it an ideal solvent for carbon-based life:

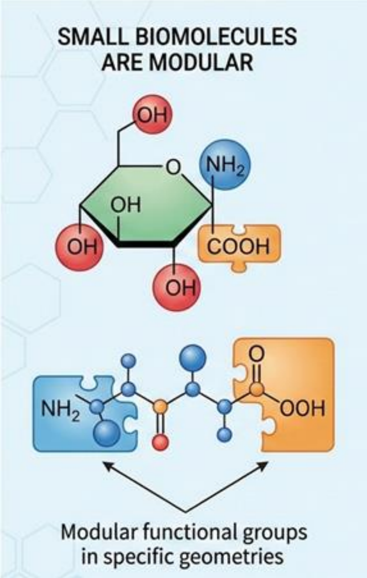
High polarity: Allows water to dissolve a wide range of polar and charged molecules.

High specific heat capacity: Helps to maintain a stable internal temperature for living organisms.

Biological Complexity

- **Even "simple" biomolecules are modular**: Small biomolecules are composed of multiple functional groups arranged in specific geometries, giving rise to distinct chemical and physical properties.

- Characteristic functional groups that determine the reaction of biomolecule.



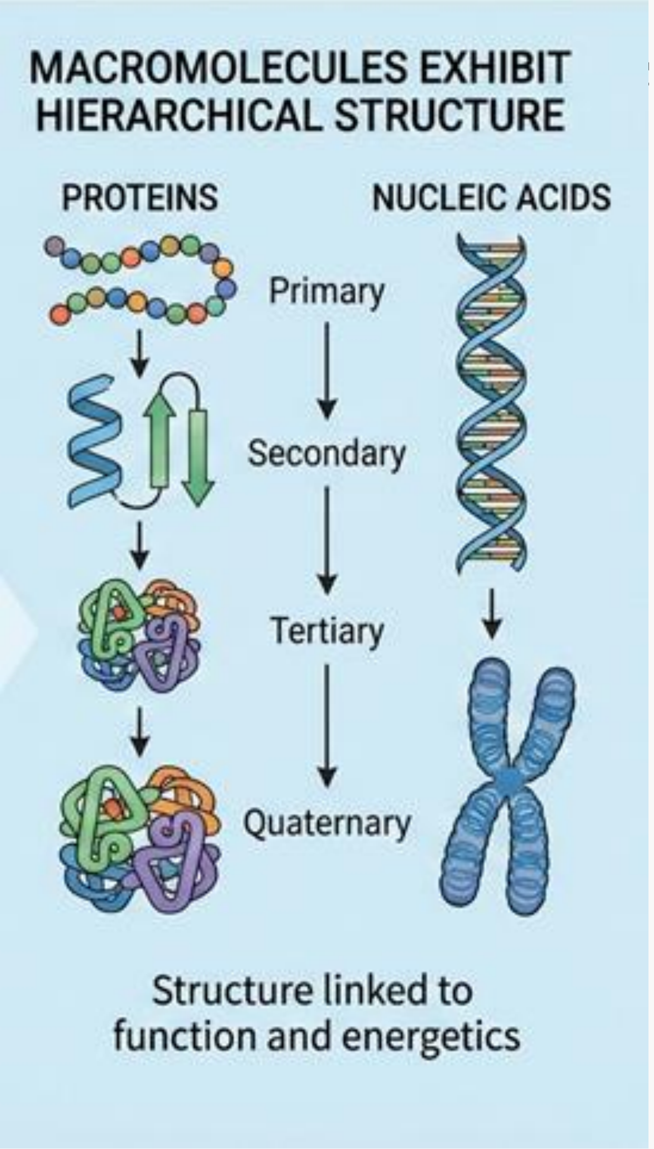
Functional Groups of Biochemical Importance

Class of Compound	General Structure	Characteristic Functional Group	Name of Functional Group	Example
Alkenes	$RCH{=}CH_2$ $RCH{=}CHR$ $R_2C{=}CHR$ $R_2C{=}CR_2$	$C{=}C$	Double bond	$CH_2{=}CH_2$
Alcohols	ROH	$—OH$	Hydroxyl group	CH_3CH_2OH
Ethers	ROR	$—O—$	Ether group	CH_3OCH_3
Amines	RNH_2 R_2NH R_3N	$—N<$	Amino group	CH_3NH_2
Thiols	RSH	$—SH$	Sulfhydryl group	CH_3SH
Aldehydes	$R—C(=O)—H$	$—C(=O)—$	Carbonyl group	$CH_3C(=O)H$
Ketones	$R—C(=O)—R$	$—C(=O)—$	Carbonyl group	$CH_3C(=O)CH_3$
Carboxylic acids	$R—C(=O)—OH$	$—C(=O)—OH$	Carboxyl group	$CH_3C(=O)OH$
Esters	$R—C(=O)—OR$	$—C(=O)—OR$	Ester group	$CH_3C(=O)OCH_3$
Amides	$R—C(=O)—NR_2$ $R—C(=O)—NHR$ $R—C(=O)—NH_2$	$—C(=O)—N<$	Amide group	$CH_3C(=O)N(CH_3)_2$
Phosphoric acid esters	$R—O—P(=O)(OH)—OH$	$—O—P(=O)(OH)—OH$	Phosphoric ester group	$CH_3—O—P(=O)(OH)—OH$
Phosphoric acid anhydrides	$R—O—P(=O)(OH)—O—P(=O)(OH)—OH$	$—P(=O)(OH)—O—P(=O)(OH)—$	Phosphoric anhydride group	$HO—P(=O)(OH)—O—P(=O)(OH)—OH$

Biological Complexity

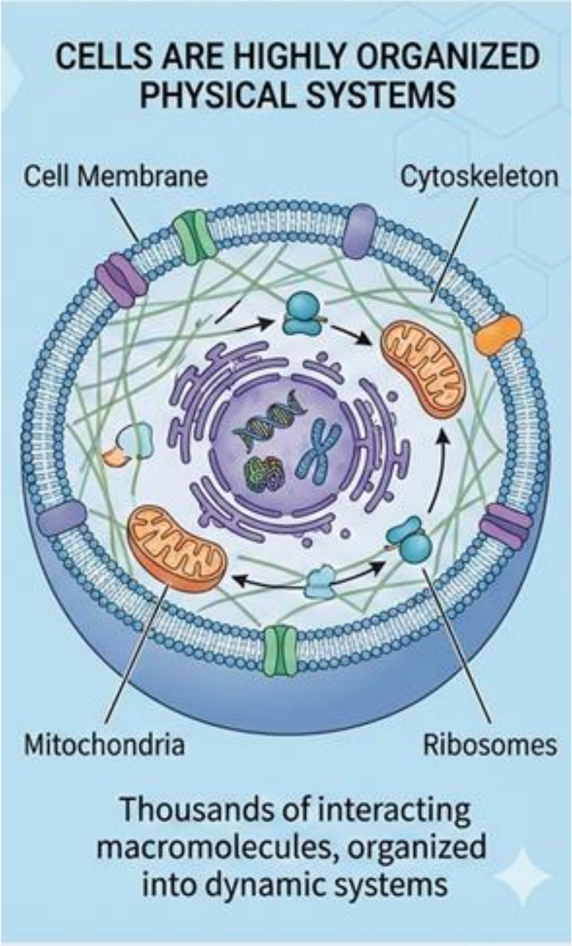
- **Macromolecules exhibit hierarchical structure**:
  - Proteins: Primary → secondary → tertiary → quaternary structure
  - Nucleic acids: Base sequence → secondary folding → higher-order organization.

Structure is tightly linked to function and energetics.



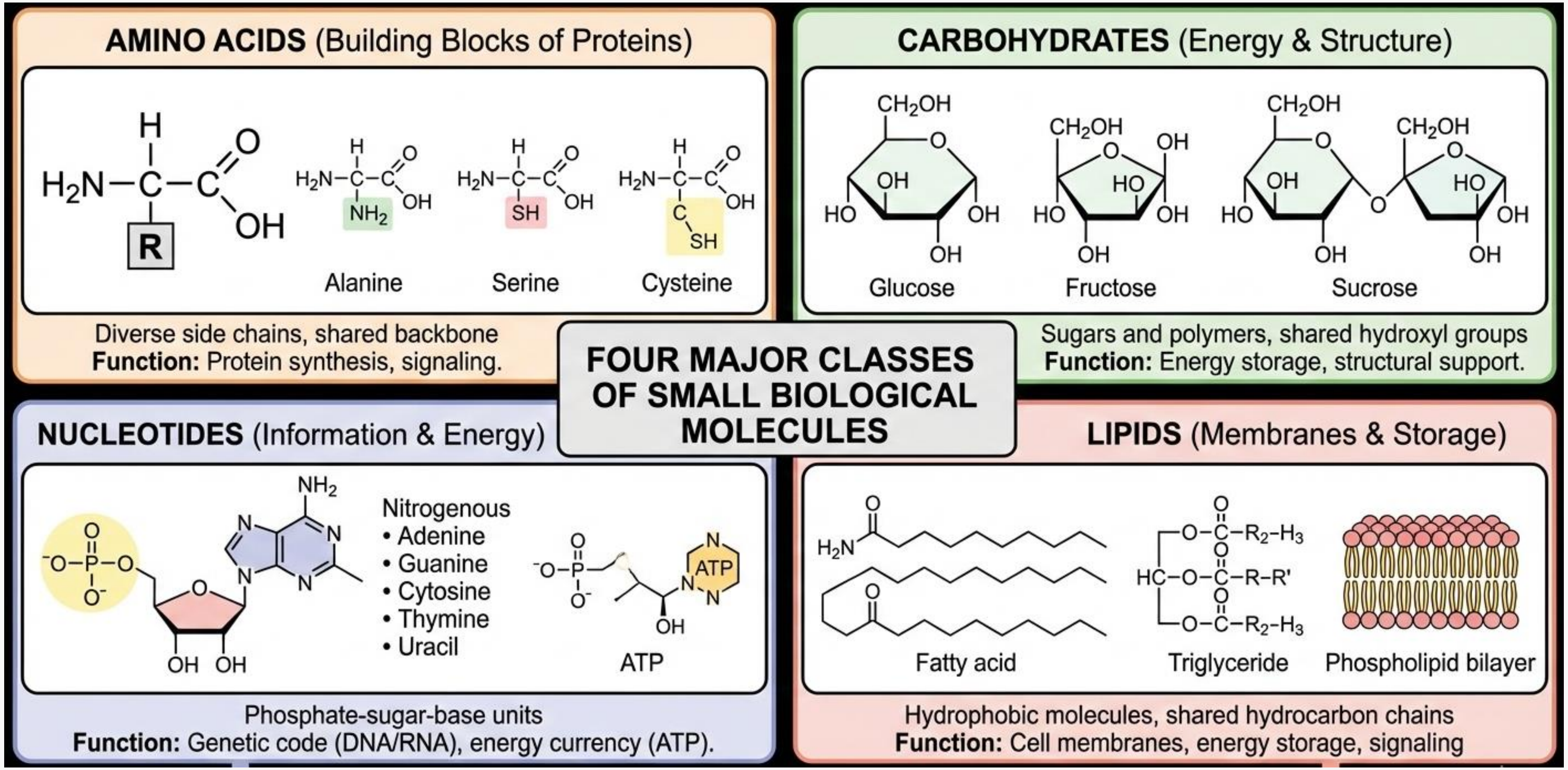
Biological Complexity

- **Cells are highly organized physical systems**: Living cells contain thousands of interacting macromolecules, organized into membranes, cytoskeleton, and dynamic molecular machines.



Major Classes of Biomolecules

Most of the cell’s small molecules fall into four major classes. Although each class contains many chemically diverse members, they are unified by shared structural features and biological functions.



Basic Units used in Life Sciences

Atomic Mass Unit (amu or u)

- 1 atomic mass unit (amu) is defined as 1/12 the mass of a single atom of carbon-12 (^{12}C).
- By definition: **^{12}C = exactly 12 amu**
- The average atomic mass of natural carbon is 12.011 amu due to isotopic abundance

Basic Units used in Life Sciences

Dalton (Da)

The Dalton (Da) is numerically equivalent to the amu:

- **1 Da = 1 amu**

Commonly used to express molecular masses of biomolecules.

Frequently used with prefixes:

- **kDa (kilodalton) = 10^3 Da**

Examples:

- Typical protein: 10–100 kDa
- DNA base pair: ≈660 Da

Basic Units used in Life Sciences

Concentration Units: Concentration is typically expressed as moles per liter:mol·L^{-1}, also written as M (molar). Typical biological concentrations range from mM to nM.

Prefix	Symbol	Power of 10
Mega	M	10^6
Kilo	k	10^3
Milli	m	10^{-3}
Micro	µ	10^{-6}
Nano	n	10^{-9}
Pico	p	10^{-12}
Femto	f	10^{-15}

Basic Units used in Life Sciences

Length (Distance) Scales

- Ångström (Å):1 Å = 10^{-10} m
- Nanometer (nm):1 nm = 10 Å

Examples:

- C–C bond length: ≈ 1.5 Å
- DNA double helix diameter: ≈ 2 nm (20 Å)
- Typical protein size: a few nm

Basic Units used in Life Sciences

Time Scales in Life Sciences: Biological processes span **many orders of magnitude in time**, from atomic motion to cell division.

Time Scale	Typical Unit	Examples
Femtoseconds (10^{-15} s)	fs	Bond vibrations, electronic transitions
Picoseconds (10^{-12} s)	ps	Hydrogen bond dynamics, solvent relaxation
Nanoseconds (10^{-9} s)	ns	Protein side-chain motion, fluorescence lifetimes
Microseconds (10^{-6} s)	µs	Protein folding intermediates
Milliseconds (10^{-3} s)	ms	Enzyme turnover, ion channel gating
Seconds–Hours	s–h	Metabolism, gene expression

Basic Units used in Life Sciences

Energy Units in Biophysics: Energy scales determine stability, binding, and reaction rates.

Energy Unit	Typical Use
kBT	Thermal energy scale (≈ 4.1 pN·nm ≈ 0.6 kcal/mol at 300 K)
kcal/mol	Biochemical reactions and binding energies
kJ/mol	SI unit commonly used in thermodynamics
eV (electron-volt)	Electronic transitions, spectroscopy

Key comparisons:

- Hydrogen bond: ~1–5 kcal/mol
- Covalent bond: ~50–100 kcal/mol
- ATP hydrolysis: ~7 kcal/mol (physiological conditions)

Biophysical Insight: Thermal energy (kBT) sets the scale for molecular fluctuations and stability.

Basic Units used in Life Sciences

Units linked to Experimental Techniques.

Technique	**Key Units**	**What It Probes**
X-ray crystallography	Å, nm	Atomic-level structure
NMR spectroscopy	MHz, ms–s	Structure & molecular dynamics
Fluorescence microscopy	ns, µm	Dynamics & cellular localization
AFM / Optical tweezers	pN, nm	Mechanical forces & elasticity
Calorimetry (ITC)	kcal/mol	Binding energetics
Electrophysiology	mV, ms	Ion channels & membrane potentials

Thank you very much for your attention