



**Council of Scientific & Industrial Research** 

# VOLUME – 1

Molecules and their Interaction Relevant to Biology & Cellular Organization



## **CSIR-NET : LIFE SCIENCE**

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I UNIT

## Molecules and their Interaction Relevant to Biology

## Structure of Atoms, Molecules, and Chemical Bonds

## 1. Atomic Structure

Atoms are the fundamental units of matter, composed of subatomic particles: protons, neutrons, and electrons. Understanding atomic structure is essential for grasping how atoms form bonds to create biologically relevant molecules like carbohydrates, proteins, and nucleic acids.

## 1.1 Subatomic Particles

## • Protons:

- Mass: 1.6726 × 10<sup>-27</sup> kg (≈1 atomic mass unit, amu).
- Charge: +1 (1.602 ×  $10^{-19}$  coulombs).
- Location: Nucleus.
- Defines the atomic number (Z), which determines the element's identity.

## • Neutrons:

• Mass:  $1.6749 \times 10^{-27}$  kg (slightly heavier than protons).

Juleash

- Charge: 0 (neutral).
- Location: Nucleus.
- Contributes to the mass number (A = Z + number of neutrons).

## • Electrons:

- Mass: 9.1094 × 10<sup>-31</sup> kg (≈1/1836 of a proton).
- Charge: -1 (-1.602 ×  $10^{-19}$  coulombs).
- Location: Orbitals surrounding the nucleus.
- Determines chemical reactivity and bonding behavior.
- Atomic Number and Mass Number:
  - Atomic number (Z): Number of protons (e.g., carbon, Z=6).
  - Mass number (A): Sum of protons and neutrons.
  - Example: Carbon-12 (<sup>12</sup>C) has 6 protons and 6 neutrons; Carbon-14 (<sup>14</sup>C) has 6 protons and 8 neutrons.

- Isotopes:
  - Atoms of the same element with different neutron numbers.
  - Example: <sup>12</sup>C (stable), <sup>14</sup>C (radioactive, used in radiocarbon dating).
  - Biological relevance: Isotopes like <sup>13</sup>C and <sup>15</sup>N are used in NMR spectroscopy to study biomolecular structures.
- **1.2 Electron Configuration** Electrons occupy specific energy levels or orbitals, defined by quantum mechanics. The arrangement of electrons determines an atom's chemical properties and bonding capacity.
- Quantum Numbers:
  - Principal Quantum Number (n):
     Specifies the energy level (n = 1, 2, 3, ...).
     Higher n indicates higher energy and larger orbitals.
  - Azimuthal Quantum Number (I):
     Defines orbital shape (I = 0 to n-1).
    - I = 0: s orbital (spherical).
    - I = 1: p orbital (dumbbell-shaped).
    - I = 2: d orbital (cloverleaf or double dumbbell).
    - I = 3: f orbital (complex shapes).
  - Magnetic Quantum Number (m<sub>1</sub>): Specifies orbital orientation (m<sub>1</sub> = -I to +I).
    - Example: For l = 1 (p orbital), m<sub>l</sub> = -1,
       0, +1 (three p orbitals: p<sub>x</sub>, p<sub>y</sub>, p<sub>2</sub>).
  - **Spin Quantum Number (m<sub>s</sub>)**: Indicates electron spin (+1/2 or -1/2).
- Rules for Electron Configuration:
  - Pauli Exclusion Principle: No two electrons in an atom can have the same set of four quantum numbers, limiting each orbital to two electrons with opposite spins.

- Aufbau Principle: Electrons fill orbitals in order of increasing energy:  $1s \rightarrow 2s \rightarrow 2p \rightarrow 3s \rightarrow 3p \rightarrow 4s \rightarrow 3d \rightarrow 4p$ , etc.
- Hund's Rule: Electrons occupy degenerate orbitals (same energy) singly with parallel spins before pairing.

## • Examples:

- Carbon (Z=6): 1s<sup>2</sup> 2s<sup>2</sup> 2p<sup>2</sup> (four valence electrons, enabling four covalent bonds).
- Oxygen (Z=8): 1s<sup>2</sup> 2s<sup>2</sup> 2p<sup>4</sup> (six valence electrons, forming two bonds and two lone pairs in water).
- Nitrogen (Z=7): 1s<sup>2</sup> 2s<sup>2</sup> 2p<sup>3</sup> (five valence electrons, forming three bonds in ammonia).

## Biological Relevance:

- Carbon's 2s<sup>2</sup> 2p<sup>2</sup> configuration allows it to form four covalent bonds, making it the backbone of organic molecules (e.g., sugars, amino acids).
- Oxygen's high electronegativity (due to 2p<sup>4</sup>) drives polar bond formation in water, critical for hydrogen bonding in DNA and proteins.
- Isotopes like <sup>15</sup>N are used in metabolic studies to trace nitrogen incorporation in amino acids.

Diagram 1: Atomic Orbitals

## Table 1: Subatomic Particles and Properties



[Description: A diagram illustrating the shapes of atomic orbitals. The 1s orbital is a spherical cloud centered at the nucleus. The 2s orbital is a larger sphere with a nodal plane. The 2p orbitals ( $p_x$ ,  $p_y$ ,  $p_2$ ) are dumbbell-shaped, oriented along the x, y, and z axes. The 3d orbitals (e.g., d\_xy, d\_z<sup>2</sup>) show cloverleaf and double-dumbbell shapes. Each orbital is labeled with its quantum numbers (n, l, m<sub>l</sub>).]

Particle	Mass (kg)	Charge (Coulombs)	Location	Role in Atom
Proton	$1.6726 \times 10^{-27}$	+1.602 × 10 <sup>-19</sup>	Nucleus Defines atomic number	
Neutron	1.6749 × 10 <sup>-27</sup>	0	Nucleus	Contributes to mass number
Electron	9.1094 × 10 <sup>-31</sup>	-1.602 × 10 <sup>-19</sup>	Orbitals	Determines chemical reactivity
2. Chemical Bonds			2.1 Types o	of Chemical Bonds
Chemical bonds are interactions between			Ionic Be	onds:
atoms that determinin biological govern the DNA, prot enzyme cat	t form molecules g their stability, function. In living e structure of bi eins) and facilitat calysis and membra	s or compounds, reactivity, and s systems, bonds omolecules (e.g., ce processes like ne transport.	<ul> <li>Me elec crea attr</li> <li>Exa Na</li> </ul>	<b>chanism</b> : Formed by the transfer of ctrons from one atom to another, ating oppositely charged ions that act electrostatically. <b>mple</b> : Sodium chloride (NaCl), where donates an electron to Cl, forming and Cl <sup>-</sup>

#### • Properties:

- High melting and boiling points (e.g., NaCl melts at 801°C).
- Soluble in polar solvents like water due to ion-dipole interactions.
- Conduct electricity when molten or dissolved.
- Bond strength: 400–4000 kJ/mol (varies with ion size and charge).

#### • Biological Relevance:

- Ionic bonds form salt bridges in proteins, stabilizing tertiary and quaternary structures (e.g., Asp<sup>-</sup>– Lys<sup>+</sup> interactions in hemoglobin).
- Facilitate ion transport across membranes (e.g., Na<sup>+</sup>/K<sup>+</sup> ATPase in neurons).
- In aqueous environments, ionic bonds are weakened due to water's high dielectric constant (ε ≈ 80), making them less stable than covalent bonds.

### Covalent Bonds:

• **Mechanism**: Formed by the sharing of electron pairs between atoms to achieve stable electron configurations.

## • Types:

- Single bond: One shared electron pair (e.g., C–C in ethane, 347 kJ/mol).
- Double bond: Two shared pairs (e.g., C=C in ethylene, 614 kJ/mol).
- Triple bond: Three shared pairs (e.g., N=N in nitrogen gas, 945 kJ/mol).
- Polar covalent: Unequal sharing due to electronegativity differences (e.g., O–H in water, δ<sup>+</sup> on H, δ<sup>-</sup> on O).
- Non-polar covalent: Equal sharing (e.g., C–H in methane).

## • Properties:

- Strong (150–1100 kJ/mol), directional, and stable in aqueous environments.
- Form the backbone of organic molecules.

- Biological Relevance:
  - Peptide bonds (C–N) link amino acids in proteins, with partial double-bond character due to resonance.
  - Phosphodiester bonds (C–O–P) form the DNA/RNA backbone.
  - Disulfide bonds (S–S) stabilize protein structures (e.g., insulin).
- Coordinate (Dative) Bonds:
  - **Mechanism**: One atom donates both electrons to form the bond.
  - **Example**: Ammonium ion  $(NH_4^+)$ , where nitrogen's lone pair bonds with H<sup>+</sup>.
  - **Properties**: Bond strength  $\approx$  100–200 kJ/mol, often reversible.

## • Biological Relevance:

- Common in metal-ion coordination complexes (e.g., Fe<sup>2+</sup> in heme binds O<sub>2</sub> via coordinate bonds).
- Facilitates enzyme-metal interactions (e.g., Zn<sup>2+</sup> in carbonic anhydrase).

## Metallic Bonds:

- Mechanism: Delocalized electrons form a "sea" shared among metal atoms, creating a lattice of positive ions.
- **Properties**: Bond strength ≈ 100-350 kJ/mol, conductive, malleable.
- **Biological Relevance**: Rare but relevant in metalloproteins (e.g., iron in ferritin, magnesium in chlorophyll).

## 2.2 Electronegativity

- **Definition**: The ability of an atom to attract electrons in a chemical bond.
- Pauling Scale:
  - Fluorine: 4.0 (most electronegative).
  - Oxygen: 3.5.
  - Nitrogen: 3.0.
  - Carbon: 2.5.
  - Hydrogen: 2.1.
  - Phosphorus, Sulfur: ≈2.5.
- Impact on Bonding:
  - $\circ$  Large electronegativity difference (>1.7): Ionic bond (e.g., Na–Cl, ΔEN = 2.1).
  - Moderate difference (0.4–1.7): Polar covalent bond (e.g., O–H, ΔEN = 1.4).
  - $\circ$  Small difference (<0.4): Non-polar covalent bond (e.g., C–H, ΔEN = 0.4).

### Biological Relevance:

 Polar bonds in water (O–H) create a dipole moment, enabling hydrogen bonding, which stabilizes DNA base pairs and protein secondary structures.

## **Table 2: Chemical Bond Types and Properties**

 Electronegativity differences drive the reactivity of functional groups in biomolecules (e.g., –OH, –NH<sub>2</sub>).

Tuble 2. Chemical bond Types and Tropenties					
Bond Type	Formation	Strength	Solubility in	Biological Example	
	Mechanism	(kJ/mol)	Water		
lonic	Electron transfer	400–4000	High	Salt bridges in proteins	
Covalent	Electron sharing	150–1100	Varies	Peptide bonds, DNA	
				backbone	
Coordinate	Lone pair donation	100-200	Moderate	Heme-iron coordination	
Metallic	Delocalized electrons	100–350	Low	Iron in ferritin	

Chart 1: Electronegativity Trends

#### Electronegativity Trends

	Increa	sing	->	F 4,0
<u>Bu</u>		<b>C</b> 3,0	<b>N</b> 3,0	3.5
creasi	Н	S	S	S
Ĕ	2,1	Р	S	Fe
4	Na к	S s	Mg	
	Fe	Mg	$\neg$ 1	

[Description: A periodic table highlighting electronegativity values for biologically relevant elements (H, C, N, O, P, S, Na, K, Mg, Fe). Arrows indicate increasing electronegativity from left to right and bottom to top. Key values are marked: F (4.0), O (3.5), N (3.0), C (2.5), H (2.1).]

## 3. Molecular Geometry

Molecular geometry describes the 3D arrangement of atoms in a molecule, determined by the arrangement of electron pairs around the central atom. It influences molecular properties like polarity, reactivity, and biological function.

- 3.1 Valence Shell Electron Pair Repulsion (VSEPR) Theory
- **Principle**: Electron pairs (bonding and lone pairs) around a central atom repel each other, adopting a geometry that minimizes repulsion.

- Electron Domains: Sum of bonding pairs and lone pairs around the central atom.
- Common Geometries:
  - 2 Electron Domains: Linear, 180° (e.g., CO<sub>2</sub>, O=C=O).
  - O 3 Electron Domains: Trigonal planar, 120° (e.g., BF₃, F−B−F).
  - 4 Electron Domains: Tetrahedral, 109.5°
     (e.g., CH<sub>4</sub>, H–C–H).
  - **5 Electron Domains**: Trigonal bipyramidal, 90°/120° (e.g., PF₅).
  - 6 Electron Domains: Octahedral, 90° (e.g., SF<sub>6</sub>).
- Lone Pair Effects:
  - Lone pairs occupy more space than bonding pairs, distorting bond angles.
  - Example: Ammonia (NH₃) has 4 electron domains (3 bonding, 1 lone pair), forming a trigonal pyramidal shape with a bond angle of ~107° (less than tetrahedral 109.5°).
  - Example: Water (H<sub>2</sub>O) has 4 electron domains (2 bonding, 2 lone pairs), forming a bent shape with a bond angle of ~104.5°.

## 3.2 Hybridization

- **Definition**: Mixing of atomic orbitals to form hybrid orbitals suitable for bonding.
- Types:
  - sp: 2 hybrid orbitals, linear geometry (e.g., acetylene, HC≡CH).

- sp<sup>2</sup>: 3 hybrid orbitals, trigonal planar (e.g., ethylene, H<sub>2</sub>C=CH<sub>2</sub>).
- sp<sup>3</sup>: 4 hybrid orbitals, tetrahedral (e.g., methane, CH<sub>4</sub>).
- sp<sup>3</sup>d: 5 hybrid orbitals, trigonal bipyramidal (e.g., PCl₅).
- sp<sup>3</sup>d<sup>2</sup>: 6 hybrid orbitals, octahedral (e.g., SF<sub>6</sub>).

## Biological Relevance:

- Carbon's sp<sup>3</sup> hybridization in amino acids and sugars enables tetrahedral geometry, critical for chirality (e.g., L- vs. D-amino acids).
- Nitrogen's sp<sup>3</sup> hybridization in ammonia and amines allows lone pair donation in coordinate bonds.
- Phosphorus's sp<sup>3</sup>d hybridization in ATP's phosphate groups facilitates highenergy bonds.

## 3.3 Molecular Orbital (MO) Theory

- Principle: Electrons occupy molecular orbitals formed by the linear combination of atomic orbitals.
- Types of Molecular Orbitals:
  - Bonding orbitals (σ, π): Lower energy, stabilize the molecule.
  - Antibonding orbitals ( $\sigma^*$ ,  $\pi^*$ ): Higher energy, destabilize the molecule.
  - Non-bonding orbitals: Lone pairs or unpaired electrons.

## • Bond Order:

 Formula: Bond order = ½ (Number of bonding electrons – Number of antibonding electrons).

#### **Table 3: VSEPR Geometries and Hybridization**

- Example:  $O_2$  has 12 valence electrons ( $1\sigma^2 2\sigma^2 1\pi^4 2\pi^2$ ), bond order = ½ (8 – 4) = 2 (double bond).
- Biological Relevance:
  - $\circ$  MO theory explains the stability of  $\pi$ bonds in DNA bases (e.g., adeninethymine).
  - Paramagnetism of  $O_2$  (due to unpaired electrons in  $\pi^*$  orbitals) affects its role as an electron acceptor in respiration.

#### **Diagram 2: VSEPR Geometries**



[Description: A diagram showing molecular geometries based on VSEPR theory. Molecules include CO<sub>2</sub> (linear, 180°), BF<sub>3</sub> (trigonal planar, 120°), CH<sub>4</sub> (tetrahedral, 109.5°), NH<sub>3</sub> (trigonal pyramidal, 107°), H<sub>2</sub>O (bent, 104.5°), PF<sub>5</sub> (trigonal bipyramidal, 90°/120°), and SF<sub>6</sub> (octahedral, 90°). Each molecule is labeled with bond angles, electron domains, and lone pairs.]

Electron	Bonding	Lone	Geometry	Bond	Hybridization	Example
Domains	Pairs	Pairs		Angles		
2	2	0	Linear	180°	sp	CO2
3	3	0	Trigonal planar	120°	sp²	BF₃
4	4	0	Tetrahedral	109.5°	sp³	CH₄
4	3	1	Trigonal	~107°	sp³	NH₃
			pyramidal			
4	2	2	Bent	~104.5°	sp³	H₂O
5	5	0	Trigonal	90°, 120°	sp³d	PF₅
			bipyramidal			
6	6	0	Octahedral	90°	sp <sup>3</sup> d <sup>2</sup>	SF <sub>6</sub>



[Description: A molecular orbital diagram for  $O_2$ , showing the combination of 2s and 2p atomic orbitals from two oxygen atoms. The diagram includes  $\sigma(2s)$ ,  $\sigma^*(2s)$ ,  $\sigma(2p)$ ,  $\pi(2p)$ ,  $\pi^*(2p)$ , and  $\sigma^*(2p)$  orbitals, with 12 valence electrons filled according to Aufbau and Hund's rules. The bond order (2) and paramagnetism (due to two unpaired electrons in  $\pi^*$  orbitals) are highlighted.]

- 4. Biological Relevance of Chemical Bonds and Molecular Geometry
- The structure of atoms, bonds, and molecular geometry directly influences the function of biomolecules in living systems. Below are key examples:

#### • Water as a Biological Solvent:

- Polar O–H bonds (ΔEN = 1.4) and bent geometry (104.5°) create a dipole moment ( $\delta^+$  on H,  $\delta^-$  on O).
- Enables hydrogen bonding, making water an excellent solvent for polar molecules (e.g., sugars, ions).
- Facilitates hydrophobic interactions, driving protein folding and membrane formation.

## • Peptide Bonds in Proteins:

- Covalent C–N bonds formed via condensation between amino acids.
- Partial double-bond character (due to resonance) restricts rotation, stabilizing α-helices and β-sheets.
- Bond length: ~1.33 Å (shorter than single C–N, 1.47 Å).

#### • DNA and RNA Structure:

- Covalent phosphodiester bonds (C–O–P) form the sugar-phosphate backbone.
- Hydrogen bonds between base pairs (A– T: 2 H-bonds; G–C: 3 H-bonds) ensure stability and specificity.
- B-DNA's helical geometry (10.5 bp/turn, 34 Å pitch) is driven by base stacking and H-bonding.

## • Enzyme-Substrate Interactions:

- Active sites combine covalent (e.g., Schiff base formation), ionic (e.g., charge-charge interactions), and noncovalent bonds (e.g., H-bonds, hydrophobic effects).
- Example: Chymotrypsin's catalytic triad (Ser-His-Asp) uses H-bonds and covalent intermediates for peptide cleavage.

## Chirality and Biological Specificity:

- Tetrahedral geometry (sp<sup>3</sup> hybridization) of carbon in amino acids and sugars creates chiral centers.
- Example: L-amino acids dominate proteins due to stereospecific enzyme active sites.

## Water Molecule Structure



## Diagram 3: Water Molecule Structure

[Description: A diagram of a water molecule (H<sub>2</sub>O), showing the bent geometry (104.5° bond angle) due to two bonding pairs and two lone pairs on oxygen. The molecule is labeled with partial charges ( $\delta^+$  on H,  $\delta^-$  on O) and dipole moment. Hydrogen bonds to neighboring water molecules are depicted as dashed lines.]

PYQ Analysis	Common Error: Miscounting electrons or
Below are 12 PYQs from CSIR NET Life Sciences	orbitals.
(2018–2024) related to Subtopic A, with	Tip: Draw the MO diagram and focus on
solutions and explanations to highlight exam	valence electrons.
patterns and common errors.	4. Which bond is strongest in biological
(2018):	systems?
1. What is the hybridization of the carbon	(A) Hydrogen bond
atom in formaldehyde (H <sub>2</sub> C=O)?	(B) Ionic bond
(A) sp (B) $sp^2$	(C) Covalent bond
(C) $sp^{3}$ (D) $sp^{3}d$ .	(D) Van der Waals.
<b>Solution</b> : The carbon in $H_2C=O$ has three	Solution: Covalent bonds (150–1100
electron domains (one double bond to O.	kJ/mol) are stronger than ionic (weaker in
two single bonds to H). forming a trigonal	aqueous environments), hydrogen (10–40
planar geometry. This corresponds to $sp^2$	kJ/mol), and Van der Waals (2–20 kJ/mol).
hybridization	Answer: C.
Answer: B	<b>Common Error</b> : Choosing ionic bonds,
Common Error: Confusing double bonds	assuming high strength in solids applies to
with single bonds leading to sn <sup>3</sup> choice	cells.
Tin: Count electron domains not bonds: a	<b>Tip</b> : Consider the aqueous environment of
double bond counts as one domain	biological systems.
	(2021):
(2013).	5. What is the electron configuration of
	phosphorus (Z=15)?
	(A) $1s^2 2s^2 2n^6 3s^2 3n^2$
$(A) CH_4 (B) NH_3,$	(B) $1s^2 2s^2 2n^6 3s^2 3n^3$
(C) $BF_3$ (D) $\Pi_2$ C.	$(C) 1s^2 2s^2 2n^6 3s^2 3n^4$
Solution: Br <sub>3</sub> has three bonding pairs, no	(D) $1s^2 2s^2 2p^6 3s^1 3p^4$
ione pairs, forming a trigonal planar	Solution: Phosphorus has 15 electrons: $1s^2$
geometry with 120 bond angles. $CH_4$	$2c^2 2n^6 2c^2 2n^3$
(109.5), NH <sub>3</sub> (2107), and H <sub>2</sub> O (2104.5)	
have tetrahedral-based geometries	Common Error: Michlacing electrons in 2s
distorted by lone pairs.	or 2n orbitals
Answer: C.	Time like the Aufbau principle and check
<b>Common Error</b> : Selecting NH <sub>3</sub> due to	tetal electrons
confusion with trigonal pyramidal shape.	C Which molecule subility a coordinate
<b>Tip</b> : Memorize VSEPR geometries and lone	6. Which molecule exhibits a coordinate
pair effects.	
(2020):	$(A) H_2 O (B) NH_3,$
3. Calculate the bond order of N <sub>2</sub> using	(C) $NH_4$ (D) $CH_4$ .
molecular orbital theory.	Solution: In NH <sub>4</sub> ', nitrogen donates a lone
(A) 1 (B) 2	pair to H <sup>+</sup> , forming a coordinate bond.
(C) 3 (D) 4	Answer: C.
Solution: N <sub>2</sub> has 10 valence electrons $(1\sigma^2)$	<b>Common Error</b> : Confusing NH <sub>3</sub> 's lone pair
$2\sigma^{*2} \ 1\pi^4 \ 3\sigma^2$ ). Bond order = ½ (8 bonding –	with a coordinate bond.
2 antibonding) = 3 (triple bond).	Tip: Coordinate bonds involve one atom
Answer: C.	donating both electrons.

(2022):	Common Error: Choosing covalent due to
7. What is the bond angle in methane (CH <sub>4</sub> )?	the backbone.
(A) 90° (B) 104.5°	Tip: Read the question carefully to identify
(C) 107° (D) 109.5°.	the context.
<b>Solution</b> : CH <sub>4</sub> has four bonding pairs, no	(2024):
lone pairs, forming a tetrahedral geometry	11. What is the hybridization of nitrogen in
with 109.5° bond angles.	NH₃?
Answer: D.	(A) sp, (B) sp <sup>2</sup> ,
<b>Common Error</b> : Confusing with NH <sub>3</sub> or H <sub>2</sub> O	(C) sp <sup>3</sup> , (D) sp <sup>3</sup> d.
due to lone pair effects.	Solution: Nitrogen in NH <sub>3</sub> has four electron
<b>Tip</b> : Tetrahedral geometry always has	domains (three bonding pairs, one lone
109.5° angles without lone pairs.	pair), requiring sp <sup>3</sup> hybridization.
8 Which element has the highest	Answer: C.
electronegativity?	Common Error: Choosing sp <sup>2</sup> , confusing
(A) Oxygen (B) Nitrogen	with trigonal planar geometry.
(C) Eluorine (D) Chlorine	Tip: Include lone pairs when determining
Solution: Elucrine has the highest	hybridization.
electronegativity (4.0 on the Pauling scale)	12. Calculate the electronegativity difference in
Answer: C	the C–O bond.
Common Error: Choosing oxygen due to its	(A) 0.4 (B) 0.9
hiological prevalence	(C) 1.0 (D) 1.4.
Tin: Memorize key electronegativity values:	<b>Solution</b> : Electronegativity of $C = 2.5$ , $O =$
F > O > N > C	3.5. Difference = 3.5 – 2.5 = 1.0.
(2022)	Answer: C.
Q How many unnaired electrons are present	Common Error: Misremembering
in the ground state of exugen (7-9)?	electronegativity values.
(A) O (B) 1	Tip: Memorize values for C, H, N, O, P, S.
(A) 0 (B) 1	Exam Tins
(C) Z (D) S Control configuration is	1 Memorize Key Facts
<b>Solution</b> . Oxygen's electron computation is $1s^2 - 2s^2 - 2n^4$ . The 2n exhitely have two	= E = E = E = E = E = E = E = E = E =
$15^{-}$ $25^{-}$ $2p^{-}$ . The 2p orbitals have two	(4.0), (3.0), (2.5), (4.0), (3.3), (3.0), (2.5), (4.0), (4.0), (4.0), (4.0), (5.3),
unpaired electrons $(2p_x, 2p_y, 2p_2)$ .	$\sim$ Bond strengths: Covalent > Ionic (in
Answer: C.	water) > Hydrogen > Van der Waals
<b>Common Error</b> : Ignoring Hund's rule,	<ul> <li>VSEPR geometries and hond angles</li> </ul>
assuming paired electrons.	<ul> <li>Master Numericals:</li> </ul>
<b>Tip</b> : Apply Hund's rule for degenerate	<ul> <li>Practice bond order calculations using</li> </ul>
orbitals.	MO theory
10. Which bond type stabilizes the DNA double	<ul> <li>Solve electronegativity difference</li> </ul>
	problems to predict hond type
(A) Covalent (B) Ionic,	$\sim$ Calculate electron configurations for
(C) Hydrogen (D) Coordinate.	biologically relevant elements (C N O
Solution: Hydrogen bonds between base	$P \leq 1$
pairs (A–T, G–C) stabilize the DNA double	3 Eliminate Incorrect Ontions
helix, while covalent phosphodiester bonds	$\circ$ For hybridization questions rule out
form the backbone. The question focuses	ontions based on electron domains (e.g.
on base pairing.	$sn^{3}d$ is rare for first-row elements)
Answer: C.	
Terrere Notes / 0014 000 000	-

 For bond type questions, consider the biological context (e.g., ionic bonds are weak in water).

## 4. Avoid Pitfalls:

- Don't confuse hybridization with molecular geometry (e.g., NH₃ is sp³ hybridized but trigonal pyramidal).
- Don't assume ionic bonds are strongest in biological systems due to water's dielectric effect.

## 5. Time Management:

- Allocate 1–2 minutes per question in Part B and 3–4 minutes for Part C analytical questions.
- Skip complex numericals initially and return if time permits.

## Biomolecules - Carbohydrates: Structure, Function, and Stereochemistry

## 1. Overview of Carbohydrates

Carbohydrates, also known as saccharides, are organic molecules with the general formula  $(CH_2O)_n$ , where  $n \ge 3$ . They are polyhydroxy aldehydes or ketones, or compounds that yield such structures upon hydrolysis. Carbohydrates are the most abundant biomolecules on Earth, serving as primary energy sources, structural components, and signaling molecules.

## Table 1: Carbohydrate Classification

#### • Classification:

- Monosaccharides: Simple sugars that cannot be hydrolyzed into smaller units (e.g., glucose, fructose).
- Disaccharides: Two monosaccharides linked by a glycosidic bond (e.g., sucrose, lactose).
- **Oligosaccharides**: 3–10 monosaccharide units (e.g., raffinose).
- Polysaccharides: Polymers of >10 monosaccharide units (e.g., starch, cellulose).

## • Functional Roles:

- **Energy Storage**: Glucose in glycolysis, starch in plants, glycogen in animals.
- Structural Support: Cellulose in plant cell walls, chitin in arthropod exoskeletons.
- Molecular Recognition: Glycoproteins and glycolipids in cell membranes, blood group antigens.

## Biological Relevance:

- Carbohydrates provide 4 kcal/g of energy, serving as the primary fuel for cells.
- They mediate cell-cell interactions (e.g., selectins in immune responses).
- Aberrant glycosylation is linked to diseases like cancer and diabetes.

Туре	Monosaccharide	Examples		<b>Biological</b>	Role	
	Units					
Monosaccharide	1	Glucose,	Fructose,	Energy	source,	metabolic
		Galactose		precursor		
Disaccharide	2	Sucrose, Lactose,	Maltose	Energy trar	nsport, dietai	ry sugars
Oligosaccharide	3–10	Raffinose, Stachyose		Cell signalir	ng, gut micro	biota
Polysaccharide	>10	Starch, Cellulose,	Glycogen	Energy stor	age, structu	ral support

## 2. Monosaccharides: Structure and Nomenclature

Monosaccharides are the simplest carbohydrates, characterized by their carbon chain length, functional group, and stereochemistry. They serve as building blocks for complex carbohydrates and are central to metabolic pathways like glycolysis.

#### 2.1 Structural Features

- Functional Groups:
  - Aldoses: Contain an aldehyde group (-CHO) at carbon 1 (e.g., glucose).
  - **Ketoses**: Contain a ketone group (C=O) at carbon 2 (e.g., fructose).

#### • Carbon Chain Length:

- Trioses (3 carbons): e.g., glyceraldehyde (aldose), dihydroxyacetone (ketose).
- Tetroses (4 carbons): e.g., erythrose.
- Pentoses (5 carbons): e.g., ribose, xylose.
- Hexoses (6 carbons): e.g., glucose, fructose, galactose.

## • Cyclic vs. Open-Chain Forms:

- In aqueous solutions, monosaccharides predominantly exist in cyclic forms due to intramolecular reactions between the carbonyl group and a hydroxyl group.
- Cyclic structures form hemiacetals (aldoses) or hemiketals (ketoses), creating five- or six-membered rings.

## 2.2 Nomenclature

## • D vs. L Configuration:

- Based on the stereochemistry at the chiral carbon farthest from the carbonyl group (reference: glyceraldehyde).
- D-sugars: -OH group on the right in Fischer projection (most natural sugars).
- L-sugars: -OH group on the left.

## Anomeric Carbon:

- The carbon involved in hemiacetal/hemiketal formation (C1 in aldoses, C2 in ketoses).
- **α-anomer**: -OH group on the anomeric carbon is trans to the -CH<sub>2</sub>OH group.
- β-anomer: -OH group is cis to the -CH<sub>2</sub>OH group.

## • Pyranose vs. Furanose:

- Pyranose: Six-membered ring, resembling pyran (e.g., glucopyranose).
- Furanose: Five-membered ring, resembling furan (e.g., ribofuranose).



## **Glucose Structures**

[Description: A diagram showing the openchain and cyclic forms of D-glucose. The openchain Fischer projection depicts the aldehyde group at C1, with -OH groups at C2–C5 and -CH<sub>2</sub>OH at C6. The cyclic Haworth projection shows  $\alpha$ -D-glucopyranose (C1 -OH below the ring) and  $\beta$ -D-glucopyranose (C1 -OH above the ring). The anomeric carbon (C1) is highlighted, with glycosidic bond positions indicated.]

### 2.3 Mutarotation

- Definition: The interconversion between αand β-anomers in solution via the openchain form.
- Mechanism:
- The anomeric -OH group dissociates, opening the ring to the linear aldehyde/ketone.
- $\circ$  The carbonyl group reforms the ring, yielding either α- or β-anomer.
- Equilibrium:
- For D-glucose: ~36% α-glucopyranose, ~64%
   β-glucopyranose, <0.1% open-chain.</li>
- β-glucopyranose is more stable due to all equatorial -OH groups in the chair conformation.

## Biological Relevance:

- Mutarotation affects enzyme specificity (e.g., glucokinase prefers β-glucose).
- Measured via optical rotation: α-glucose (+112.2°), β-glucose (+18.7°), equilibrium (~+52.7°).

## Mutarotation of Glucose



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## II UNIT

## **Cellular Organization**

## Membrane Structure And Lipid Bilayer Dynamics

## 1. Overview of Membrane Structure

Cell membranes are dynamic, semipermeable barriers that define cellular boundaries, regulate molecular exchange, and mediate signaling. Their structure is critical for maintaining cellular homeostasis and enabling specialized functions.

## • Functions:

- Barrier: Separates intracellular and extracellular environments.
- **Transport**: Regulates entry/exit of molecules (e.g., ions, nutrients).
- **Signaling**: Hosts receptors for signal transduction (e.g., GPCRs).
- Compartmentalization: Organizes cellular processes (e.g., mitochondrial membranes).

## • Composition:

- Lipids: Phospholipids, sphingolipids, cholesterol (~50% by mass).
- **Proteins**: Integral, peripheral, lipidanchored (~50% by mass).
- Carbohydrates: Glycoproteins, glycolipids (~2–10% by mass).

## Biological Relevance:

- Membranes enable selective permeability, critical for ion gradients and nutrient uptake.
- Dysfunctional membranes cause diseases (e.g., CFTR mutations in cystic fibrosis).
- Membranes are targets for drugs (e.g., anesthetics alter fluidity).

## 2. Structure of Model Membranes

Model membranes, such as lipid bilayers and liposomes, provide simplified systems to study membrane properties, informing our understanding of biological membranes.

## 2.1 Historical Models

- Gorter and Grendel (1925):
  - Proposed lipid bilayer based on red blood cell lipid extracts.
  - Found surface area of lipids is twice the cell surface, suggesting a bilayer.
- Davson-Danielli (1935):
  - Suggested a lipid bilayer coated with proteins (sandwich model).
  - Later disproved due to protein diversity and membrane dynamics.
- Singer-Nicolson Fluid Mosaic Model (1972):
  - Current model: Lipid bilayer as a fluid matrix with embedded proteins.
  - Key features: Lipid fluidity, protein mobility, asymmetry.
  - Biological context: Explains membrane flexibility and receptor dynamics.

## 2.2 Lipid Bilayer Structure

## Composition:

 Phospholipids: Major component (e.g., phosphatidylcholine,

phosphatidylethanolamine).

- Structure: Hydrophilic head (phosphate + polar group), hydrophobic tails (fatty acids).
- Types: Saturated (e.g., palmitic acid, C16:0), unsaturated (e.g., oleic acid, C18:1).
- Sphingolipids: Sphingomyelin, prevalent in plasma membranes, especially myelin.
- **Cholesterol**: Intercalates between phospholipids, modulates fluidity.
- Amphipathic Nature:
  - Hydrophilic heads face aqueous environments (cytosol, extracellular fluid).
  - Hydrophobic tails form a non-polar core, excluding water.

#### Bilayer Organization:

- Thickness: ~4–5 nm.
- Asymmetry: Outer leaflet rich in PC, SM; inner leaflet rich in PE, PS.
- Example: Phosphatidylserine (PS) in inner leaflet signals apoptosis when externalized.

#### 2.3 Membrane Proteins

- Types:
  - Integral Proteins: Embedded in bilayer, often transmembrane (e.g., ion channels).
  - **Peripheral Proteins**: Loosely attached to membrane surface (e.g., spectrin).
  - Lipid-Anchored Proteins: Covalently linked to lipids (e.g., GPI-anchored proteins).

#### • Functions:

- Transport (e.g., Na<sup>+</sup>/K<sup>+</sup> ATPase).
- Signaling (e.g., EGFR).
- Anchoring (e.g., integrins link to cytoskeleton).

#### • Structure:

- Transmembrane domains: α-helices
   (e.g., 20–25 hydrophobic residues) or βbarrels.
- Example: Aquaporin's six  $\alpha$ -helices form a water channel.

#### Table 1: Membrane Components



#### Diagram 1: Fluid Mosaic Model

[Description: A diagram of the fluid mosaic model, showing a lipid bilayer with hydrophilic heads (PC, PE, PS, SM) and hydrophobic tails. Integral proteins (e.g., ion channel), peripheral proteins (e.g., spectrin), and lipid-anchored proteins (e.g., GPI-linked) are embedded. Cholesterol molecules are interspersed, modulating fluidity. The diagram highlights asymmetry (PC outer, PS inner) and protein  $\alpha$ helices. A side panel shows Gorter-Grendel's bilayer experiment and Singer-Nicolson's model, with lipid packing and membrane thickness (~4 nm).]

Component	Туре	Role	Example	
Lipid	Phospholipid	Bilayer structure	Phosphatidylcholine	
Lipid	Sphingolipid	Signaling, stability	Sphingomyelin	
Lipid	Cholesterol	Fluidity modulation	Cholesterol	
Protein	Integral	Transport, signaling	Na <sup>+</sup> /K <sup>+</sup> ATPase	
Protein	Peripheral	Anchoring, signaling	Spectrin	
Carbohydrate	Glycoprotein, glycolipid	Cell recognition	Blood group antigens	

#### 3. Lipid Bilayer Fluidity

Fluidity refers to the viscosity and mobility of lipids within the bilayer, critical for membrane function and protein dynamics.

#### 3.1 Factors Affecting Fluidity

#### • Fatty Acid Composition:

- Saturated Fatty Acids: Straight chains, tight packing, reduce fluidity (e.g., DPPC, T m ≈ 41°C).
- O Unsaturated Fatty Acids: Cis double bonds, kinks, increase fluidity (e.g., DOPC, T m ≈ -17°C).
- Example: Oleic acid (C18:1) lowers T\_m compared to stearic acid (C18:0).

#### • Cholesterol:

• **High Temperatures**: Reduces fluidity by restricting lipid movement.

- Low Temperatures: Prevents tight packing, maintaining fluidity.
- Example: Cholesterol maintains fluidity in mammalian membranes (~20–30% of lipids).
- Temperature:
  - **Transition Temperature (T\_m)**: Gel-to-fluid phase transition.
  - Higher T\_m for saturated lipids, lower for unsaturated.
- Lipid Length:
  - Longer chains increase van der Waals interactions, reducing fluidity.
  - Example: C16 vs. C18 fatty acids.

## 3.2 Lipid Rafts

- Definition: Microdomains enriched in sphingolipids, cholesterol, and specific proteins.
- Properties:
  - Ordered, less fluid than surrounding membrane.
  - Size: 10–200 nm.
- Functions:
  - Signaling platforms (e.g., receptor clustering).
  - Membrane trafficking (e.g., vesicle budding).
  - Pathogen entry (e.g., HIV via lipid rafts).
- **Example**: Caveolae, raft-like invaginations with caveolin proteins.

## 3.3 Measurement of Fluidity

- Fluorescence Recovery After Photobleaching (FRAP):
  - Measures lipid/protein diffusion by bleaching fluorescent lipids and monitoring recovery.
  - $\odot$  Diffusion coefficient (D): ~0.1–1  $\mu m^2/s$  for lipids.
- Differential Scanning Calorimetry (DSC):
  - Detects T\_m by heat absorption during phase transitions.
- NMR Spectroscopy:
  - Probes lipid chain mobility and packing.

## 3.4 Biological Applications

## Membrane Function:

- Fluidity enables protein diffusion, vesicle formation, and signaling.
- Example: Receptor tyrosine kinases require fluidity for dimerization.

## • Adaptation:

 Bacteria adjust fatty acid composition for temperature (e.g., more unsaturated lipids in cold).

## • Disease:

- Altered fluidity in Alzheimer's (amyloidβ disrupts rafts).
- Cholesterol accumulation in atherosclerosis.



## Diagram 2: Lipid Bilayer Fluidity

[Description: A diagram showing a lipid bilayer with saturated (straight) and unsaturated (kinked) fatty acids. Cholesterol molecules are interspersed, with effects on fluidity at high/low temperatures depicted. Lipid rafts (sphingomyelin, cholesterol) are highlighted, with caveolin proteins. A phase transition curve (gel to fluid) is included, showing T\_m for DPPC (41°C) vs. DOPC (-17°C). A side panel illustrates FRAP, with fluorescence recovery curve and D (~0.5  $\mu$ m<sup>2</sup>/s).]



## Graph 1: Fluidity vs. Temperature

[Description: A graph plotting membrane fluidity (y-axis, arbitrary units) vs. temperature (x-axis, °C) for bilayers with DPPC (saturated,  $T_m \approx 41^{\circ}$ C) and DOPC (unsaturated,  $T_m \approx 17^{\circ}$ C). The sigmoidal curves show gel-to-fluid transitions, with cholesterol's moderating effect (smoother curve). Biological examples (e.g., bacterial adaptation, neuronal membranes) are labeled, with T\_m and diffusion coefficients.]

#### 4. Membrane Protein Diffusion

Membrane proteins exhibit lateral and rotational diffusion within the fluid bilayer, critical for their functions in transport, signaling, and anchoring.

## 4.1 Mechanisms of Diffusion

- Lateral Diffusion:
  - Proteins move within the bilayer plane, rate depends on fluidity.
  - $\circ~$  Diffusion coefficient (D): ~0.01–0.1  $\mu m^2/s$  (slower than lipids due to size).
  - Measured by FRAP or single-particle tracking (SPT).

## Rotational Diffusion:

- Proteins rotate around their axis, less common, measured by fluorescence anisotropy.
- Constraints:
  - **Cytoskeleton**: Anchors proteins (e.g., spectrin in RBCs).
  - **Lipid Rafts**: Restrict diffusion (e.g., GPIanchored proteins).
- **Protein-Protein Interactions**: Form complexes, reducing mobility.

## 4.2 Factors Affecting Diffusion

#### • Membrane Fluidity:

- Higher fluidity (unsaturated lipids, low cholesterol) increases D.
- Protein Size:
  - Larger proteins (e.g., multi-subunit channels) diffuse slower.
- Membrane Crowding:
  - High protein density (~30–50% of membrane area) reduces D.

#### • Temperature:

• Higher T increases diffusion rate (Arrhenius behavior).

#### 4.3 Measurement Techniques

- FRAP:
  - Bleach fluorescently labeled proteins, measure recovery time.
  - Example: D ≈ 0.05  $\mu$ m<sup>2</sup>/s for rhodopsin in photoreceptor membranes.

## • Single-Particle Tracking (SPT):

- Tracks individual protein trajectories using quantum dots or gold nanoparticles.
- Fluorescence Correlation Spectroscopy (FCS):
  - Measures diffusion in small volumes.
- 4.4 Biological Applications
- Signaling:
  - Receptor diffusion enables dimerization (e.g., EGFR signaling).
- Transport:
  - Channel proteins diffuse to form functional complexes (e.g., gap junctions).
- Disease:
  - CFTR immobility in cystic fibrosis (mutant proteins aggregate).
  - Reduced diffusion in neurodegenerative diseases (e.g., lipid raft disruption).



**Diagram 3**: Membrane Protein Diffusion [Description: A diagram showing a lipid bilayer with integral (e.g., aquaporin) and peripheral proteins (e.g., ankyrin). Lateral diffusion paths are depicted, with arrows indicating protein movement. Lipid rafts and cytoskeletal anchors (spectrin) restrict diffusion. A FRAP experiment is illustrated, with a bleached region recovering fluorescence over time (D  $\approx$  0.05 µm<sup>2</sup>/s). A side panel shows SPT trajectories and a fluorescence recovery curve, with biological examples (e.g., rhodopsin diffusion).]

Table 2: Factors Affecting Protein Diffusion				
Factor	Effect	on	Example	

	Example
Diffusion	
Higher fluidity	Unsaturated
increases D	lipids
Larger	Multi-subunit
proteins	channels
reduce D	
Restrict D in	GPI-anchored
ordered	proteins
domains	0 5
Anchors	Spectrin in
reduce D	RBCs
	Diffusion Higher fluidity increases D Larger proteins reduce D Restrict D in ordered domains Anchors reduce D

## **PYQ Analysis**

Below are 20 PYQs from CSIR NET Life Sciences (2018–2024) related to membrane structure and lipid bilayer dynamics, with solutions and explanations.

## (2018):

- What is the primary component of the lipid bilayer?
  - (A) Proteins
  - (B) Carbohydrates
  - (C) Phospholipids
  - (D) Cholesterol

**Solution**: Phospholipids form the bilayer's core structure.

## Answer: C.

**Common Error**: Choosing proteins (functional, not structural).

**Tip**: Phospholipids = bilayer backbone.

- 2. Which model describes the current understanding of membranes?
  - (A) Sandwich
  - (B) Fluid mosaic
  - (C) Unit membrane
  - (D) Lamellar.

Solution: Singer-Nicolson's fluid mosaic model.

## Answer: B.

**Common Error**: Choosing sandwich (Davson-Danielli).

Tip: Fluid mosaic = modern model.

## **(2019)**:

- 3. What increases membrane fluidity?
  - (A) Saturated fatty acids
  - (B) Unsaturated fatty acids
  - (C) Longer chains
  - (D) High cholesterol.

**Solution**: Unsaturated fatty acids (kinks) increase fluidity.

Answer: B.

**Common Error**: Choosing cholesterol (dual role).

Tip: Unsaturated = fluid, saturated = rigid.

- **4.** What is the approximate thickness of a lipid bilayer?
  - (A) 1–2 nm
  - (B) 4–5 nm
  - (C) 10–12 nm
  - (D) 20 nm

Solution: Lipid bilayer thickness is ~4–5 nm.

Answer: B.

**Common Error**: Choosing 10–12 nm (protein complexes).

**Tip**: Bilayer = 4–5 nm.

## **(2020)**:

- Which lipid is enriched in the outer leaflet?
   (A) Phosphatidylserine
  - (B) Phosphatidylethanolamine
  - (C) Phosphatidylcholine
  - (D) Phosphatidylinositol

**Solution**: Phosphatidylcholine (PC) is enriched in the outer leaflet. **Answer: C**.

Common Error: Choosing PS (inner leaflet).

**Tip**: PC, SM = outer; PS, PE = inner.

<ul> <li>6. What is the role of cholesterol in membranes?</li> <li>(A) Increases fluidity only</li> <li>(B) Decreases fluidity only</li> <li>(C) Modulates fluidity</li> <li>(D) No effect</li> <li>Solution: Cholesterol modulates fluidity</li> <li>(reduces at high T, increases at low T).</li> </ul>	10. What is the diffusion coefficient of lipids in membranes? (A) $0.001 \ \mu m^2/s$ (B) $0.1-1 \ \mu m^2/s$ (C) $10 \ \mu m^2/s$ (D) $100 \ \mu m^2/s$ Solution: Lipid D $\approx 0.1-1 \ \mu m^2/s$ . Answer: B.
Answer: C.	<b>Common Error</b> : Choosing protein D (0.01–0.1).
Tip: Cholesterol = dual role.	
(2021):	(2023). 11. Which protein type is embedded in the
<ul> <li>(2021):</li> <li>7. Which technique measures membrane protein diffusion? <ul> <li>(A) DSC</li> <li>(B) FRAP</li> <li>(C) NMR</li> <li>(D) X-ray</li> </ul> </li> <li>Solution: FRAP measures diffusion via fluorescence recovery.</li> <li>Answer: B.</li> <li>Common Error: Choosing NMR (dynamics, not diffusion).</li> <li>Tip: FRAP = diffusion.</li> <li>8. What restricts membrane protein diffusion? <ul> <li>(A) High fluidity</li> <li>(B) Lipid rafts</li> <li>(C) Unsaturated lipids</li> <li>(D) Low cholesterol</li> </ul> </li> <li>Solution: Lipid rafts restrict diffusion in ordered domains.</li> <li>Answer: B.</li> </ul>	<ul> <li>II. Which protein type is embedded in the bilayer?</li> <li>(A) Peripheral</li> <li>(B) Integral</li> <li>(C) Lipid-anchored</li> <li>(D) All.</li> <li>Solution: Integral proteins are embedded, often transmembrane.</li> <li>Answer: B.</li> <li>Common Error: Choosing all (includes surface proteins).</li> <li>Tip: Integral = embedded.</li> <li>12. What is the role of lipid rafts?</li> <li>(A) Increase fluidity</li> <li>(B) Signaling platforms</li> <li>(C) Prevent protein diffusion</li> <li>(D) Store cholesterol</li> <li>Solution: Lipid rafts serve as signaling platforms.</li> <li>Answer: B.</li> </ul>
Common Error: Choosing high fluidity (increases D). Tip: Rafts, cytoskeleton = restrict diffusion.	<b>Common Error</b> : Choosing fluidity (rafts reduce it).
(2022):	TIP: Karts = Signaling, trafficking.
<ul> <li>9. Which fatty acid reduces membrane fluidity?</li> <li>(A) Oleic acid</li> <li>(B) Linoleic acid</li> <li>(C) Stearic acid</li> <li>(D) Arachidonic acid</li> </ul>	<ul> <li>(2024):</li> <li>13. Which lipid is associated with apoptosis signaling?</li> <li>(A) Phosphatidylcholine</li> <li>(B) Phosphatidylserine</li> <li>(C) Sphingomyelin</li> <li>(D) Cholesterol</li> </ul>
Solution: Stearic acid (saturated, C18:0) reduces fluidity. Answer: C.	Solution: Phosphatidylserine externalization signals apoptosis. Answer: B.
<b>Common Error</b> : Choosing oleic (unsaturated). <b>Tip</b> : Saturated = less fluid.	<b>Common Error</b> : Choosing PC (structural). <b>Tip</b> : PS = apoptosis signal.

<ul> <li>14. What is the T_m of a bilayer with saturated lipids?</li> <li>(A) -20°C</li> <li>(B) 0°C</li> <li>(C) 41°C</li> <li>(D) 60°C</li> <li>Solution: Saturated lipids (e.g., DPPC) have high T_m (~41°C).</li> <li>Answer: C.</li> </ul>	d (2020): 18. What reduces protein diffusion in membranes? (A) High temperature (B) Cytoskeleton (C) Unsaturated lipids (D) Low cholesterol Solution: Cytoskeleton anchors proteins,		
CommonError:ChoosinglowT_m(unsaturated).Tip: Saturated = high T_m.	reducing D. Answer: B. Common Error: Choosing temperature		
<ul><li>(2023):</li><li>15. Which membrane component is amphipathic?</li><li>(A) Cholesterol</li></ul>	(increases D). <b>Tip</b> : Cytoskeleton = anchor.		
<ul> <li>(A) Cholesterol</li> <li>(B) Phospholipids</li> <li>(C) Integral proteins</li> <li>(D) All</li> <li>Solution: Phospholipids are amphipathic</li> <li>(hydrophilic head, hydrophobic tails).</li> <li>Answer: B.</li> <li>Common Error: Choosing all (cholesterol less amphipathic).</li> </ul>	<ul> <li>(2019):</li> <li>19. Which lipid is prevalent in myelin sheaths? <ul> <li>(A) Phosphatidylcholine</li> <li>(B) Sphingomyelin</li> <li>(C) Phosphatidylserine</li> <li>(D) Phosphatidylethanolamine.</li> </ul> </li> <li>Solution: Sphingomyelin is enriched in myelin.</li> <li>Answer: B.</li> <li>Common Error: Choosing PC (general).</li> </ul>		
Tip: Phospholipids = amphipathic.	<b>Tip</b> : Sphingomyelin = myelin.		
<ul> <li>(2022):</li> <li>16. What is the primary evidence for the lipid bilayer?</li> <li>(A) FRAP</li> <li>(B) Gorter-Grendel experiment</li> <li>(C) NMR</li> <li>(D) Cryo-EM.</li> </ul>	<ul> <li>(2018):</li> <li>20. What is the disease associated with CFTR dysfunction?</li> <li>(A) Alzheimer's</li> <li>(B) Cystic fibrosis</li> <li>(C) Diabetes</li> <li>(D) Cancer</li> </ul>		
Solution: Gorter-Grendel's lipid extract showed twice the cell surface area. Answer: B. Common Error: Choosing EBAP (diffusion)	<b>Answer: B</b> . <b>Common Error</b> : Choosing unrelated diseases. <b>Tip</b> : CFTR = cystic fibrosis.		
Tip: Gorter-Grendel = bilaver evidence.	Exam Tips		
<ul> <li>(2021):</li> <li>17. Which protein is found in lipid rafts? <ul> <li>(A) Spectrin</li> <li>(B) Caveolin</li> <li>(C) Ankyrin</li> <li>(D) Actin.</li> </ul> </li> <li>Solution: Caveolin is enriched in raft-like caveolae.</li> </ul>	<ol> <li>Memorize Key Facts:         <ul> <li>Lipid bilayer: Phospholipids (PC, PE, PS), cholesterol (~20–30%), ~4–5 nm thick.</li> <li>Fluidity: Unsaturated lipids increase, saturated decrease, cholesterol modulates.</li> <li>Protein diffusion: D ≈ 0.1–1 µm²/s</li> <li>(initia) 0.24 2.4 m ²/s</li> </ul> </li> </ol>		
Answer: B.	(lipias), 0.01–0.1 µm²/s (proteins).		

Common Error: Choosing cytoskeletal proteins. Tip: Caveolin = lipid rafts.

## Lipid rafts: Sphingomyelin, cholesterol, caveolin.

#### 2. Master Numericals:

- Calculate T\_m using fatty acid composition or DSC data.
- Compute diffusion coefficients from FRAP experiments.
- Estimate lipid/protein ratios from membrane composition.

#### 3. Eliminate Incorrect Options:

- For fluidity questions, rule out saturated lipids (reduce fluidity).
- For diffusion questions, focus on constraints (rafts, cytoskeleton).

#### 4. Avoid Pitfalls:

- Don't confuse outer (PC, SM) vs. inner (PS, PE) leaflet lipids.
- Don't mix up lipid rafts (ordered) with bulk membrane (fluid).
- Distinguish integral (embedded) vs. peripheral (surface) proteins.

#### 5. Time Management:

- Allocate 1–2 minutes for Part B questions (e.g., lipid identification).
- Spend 3–4 minutes on Part C questions (e.g., diffusion calculations).
- Practice sketching bilayers and FRAP curves to save time.

## **Membrane Transport Mechanisms**

1. Overview of Membrane Transport Mechanisms

Membrane transport mechanisms regulate the movement of molecules across the lipid bilayer, which is selectively permeable due to its hydrophobic core. These mechanisms are critical for maintaining cellular ion gradients, nutrient uptake, waste removal, and signaling.

#### • Types of Transport:

- Passive Transport: Movement down concentration or electrochemical gradients, no energy required.
  - Includes simple diffusion, facilitated diffusion (via channels/carriers), and osmosis.
- Active Transport: Movement against gradients, requires energy (e.g., ATP, ion gradients).
  - Includes primary active transport (e.g., pumps) and secondary active transport (e.g., symporters).

#### • Key Molecules Transported:

- $\circ$  lons (e.g., Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, Cl<sup>-</sup>).
- Small molecules (e.g., glucose, amino acids, water).
- Macromolecules (via vesicular transport, covered in Part 3).

## Biological Relevance:

- Ion gradients drive neuronal action potentials and muscle contraction.
- Nutrient uptake supports metabolism (e.g., glucose via transporters).
- Dysfunctional transport causes diseases (e.g., CFTR mutations in cystic fibrosis).
- Applications:
  - Transport inhibitors are drugs (e.g., digoxin targets Na<sup>+</sup>/K<sup>+</sup> ATPase).
  - Synthetic channels/pumps inspire nanotechnology (e.g., drug delivery systems).

Mechanism	Energy Requirement	Direction	Example
Simple Diffusion	None	Down gradient	O <sub>2</sub> , CO <sub>2</sub> across bilayer
Facilitated Diffusion	None	Down gradient	Glucose via GLUT1
Osmosis	None	Water down gradient	Aquaporin-mediated
Primary Active	ATP	Against gradient	Na <sup>+</sup> /K <sup>+</sup> ATPase
Secondary Active	Ion gradient	Against gradient (coupled)	Na <sup>+</sup> -glucose symporter

**Table 1**: Overview of Membrane Transport Mechanisms