The University of Burdwan
3-Year Degree/4-Year Honours in Zoology (NEP-CCFUP)
ZOOL3012 (Cell Biology)

Plasma Membrane

MEMBRANE LIPIDS AND PROTEINS

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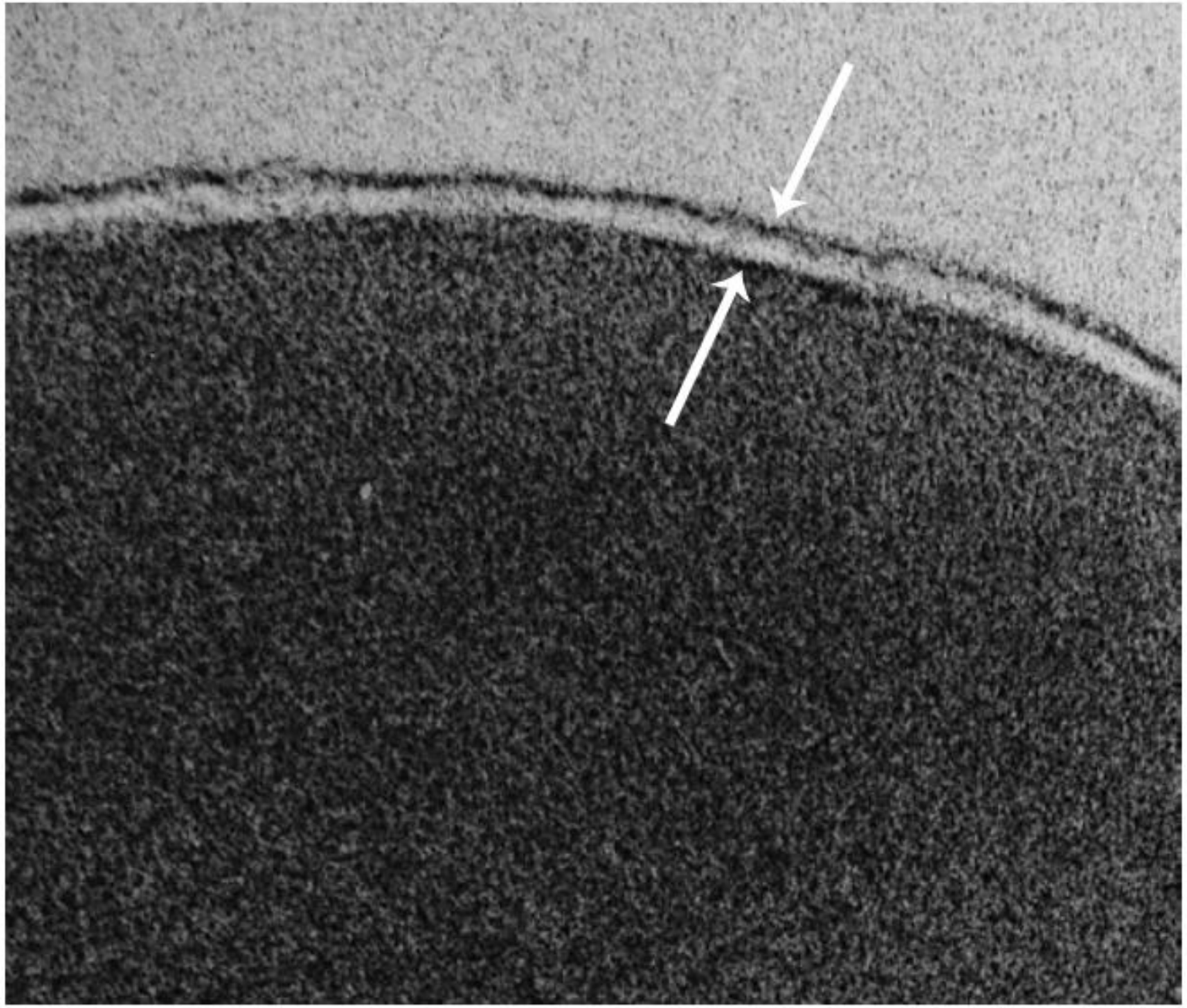
Learning Objectives

- **Identify and describe** the three major classes of membrane lipids (phosphoglycerides, sphingolipids, and cholesterol) and their structural components
- **Classify membrane proteins** into functional categories (integral, peripheral, and lipid-anchored) based on their organization and association with the lipid bilayer
- **Explain the core concepts** of the Fluid Mosaic Model of membrane structure as proposed by Singer and Nicolson (1972)
- **Compare and contrast** the original 1972 Fluid Mosaic Model with the updated 2014 model by Nicolson, highlighting new understanding of membrane organization
- **Relate membrane structure** to function, including the roles of asymmetry, fluidity, and dynamic properties in cellular processes

Introduction to Plasma Membrane

- **Physical Dimensions:**
  - **Thickness:** 5-10 nm (extremely thin—approximately 1/25,000 the width of a human hair)
  - Requires electron microscopy to visualize
  - Shows trilaminar (three-layered) appearance in electron micrographs
- **Functions:**
  - Encloses cell contents and defines cell boundaries
  - Maintains differences between cytosol and extracellular environment
  - Acts as selective permeability barrier
  - Central to cell signaling and communication
- **Composition:**
  - **Lipid-Protein assembly** held together by noncovalent bonds
  - **Approximate ratio:** 50% protein and 50% lipid by mass
  - However, there are roughly **50 lipid molecules for every 1 protein molecule** (by number)
- **Early Studies (1925 - Gorter & Grendel):**
  - First proposed lipid bilayer model based on lipid extraction studies from red blood cells
  - Calculated that extracted lipid could cover cell surface in two layers (bilayer)



Electron micrograph

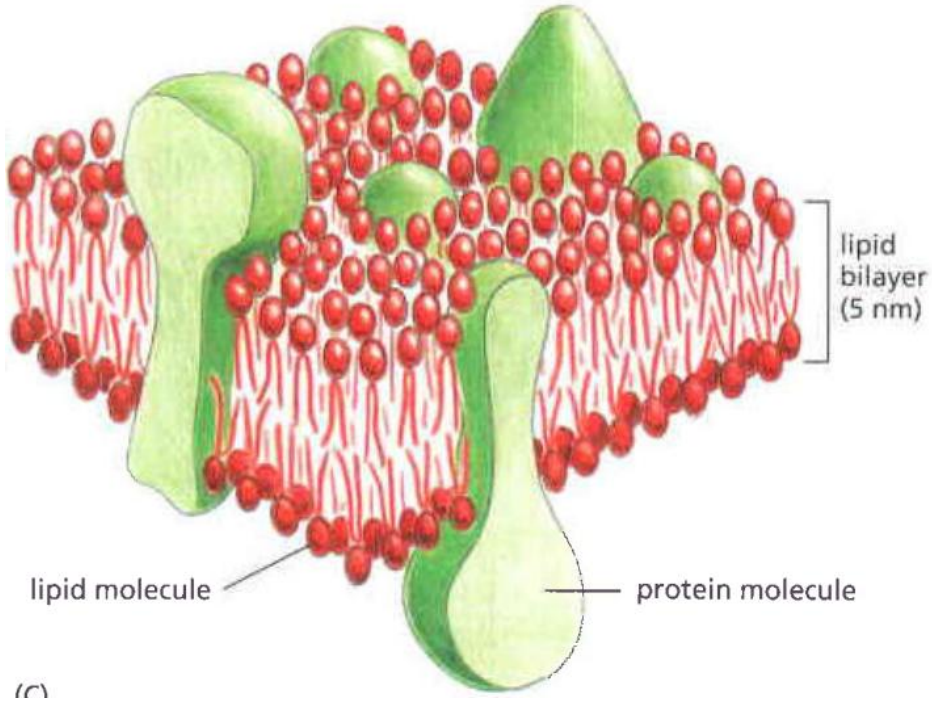
Electron micrograph showing the three-layered (trilaminar) structure of the plasma membrane of an erythrocyte after staining the tissue with the heavy metal osmium. Osmium binds preferentially to the polar head groups of the lipid bilayer, producing the trilaminar pattern. The arrows denote the inner and outer edges of the membrane.
[Source: Karp, G., 2013. Cell and Molecular Biology: Concepts and Experiments, 7th Edition]

Chemical composition

- The PM is mainly composed of protein, lipids, and a small amount of carbohydrates (5-10%).
- The chemical composition varies greatly between cell types.

Chemical composition of some purified membranes (in % dry weight)

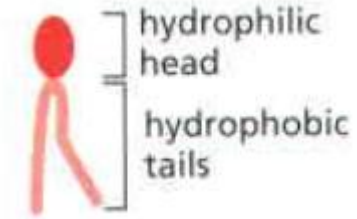
Membrane	Protein	Lipid	Carbohydrate
Human RBC	52	40	8
Amoeba	54	42	4
Mouse liver	44	52	4
Myelin sheath	18	79	3



Source: Bruce, A. *et al.* 2008. Molecular Biology of The Cell, 5th Edition

Membrane lipids

- All membrane lipids share a common characteristic: **AMPHIPATHIC structure**
  - **Hydrophilic (polar) head group** → faces aqueous environment
  - **Hydrophobic (nonpolar) tails** → buried in interior of bilayer
- The amphipathic nature is crucial—allows spontaneous self-assembly into bilayers in aqueous environments



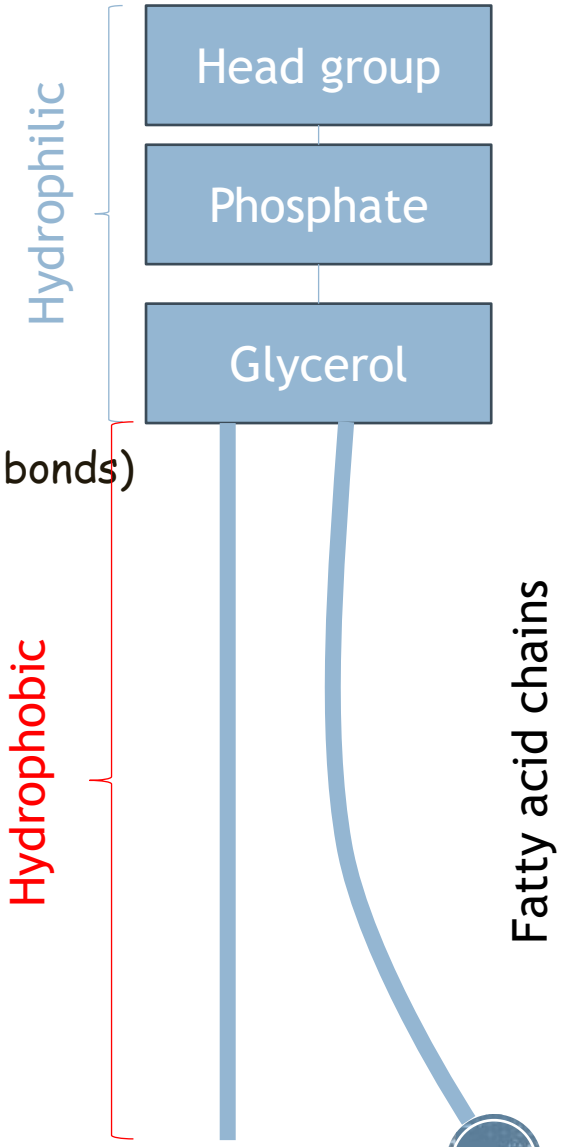
Lipid Class	Structure	Location in Membrane	Function
Phosphoglycerides	Glycerol backbone + 2 fatty acids + phosphate	Both leaflets (asymmetrically distributed)	Structural; signaling (especially PI)
Sphingolipids	Sphingosine backbone + fatty acid + head group	Outer leaflet & lipid rafts	Nervous system; cell recognition
Cholesterol	Steroid ring structure + hydroxyl group	Both leaflets; concentrated in rafts	Fluidity regulation; membrane stability

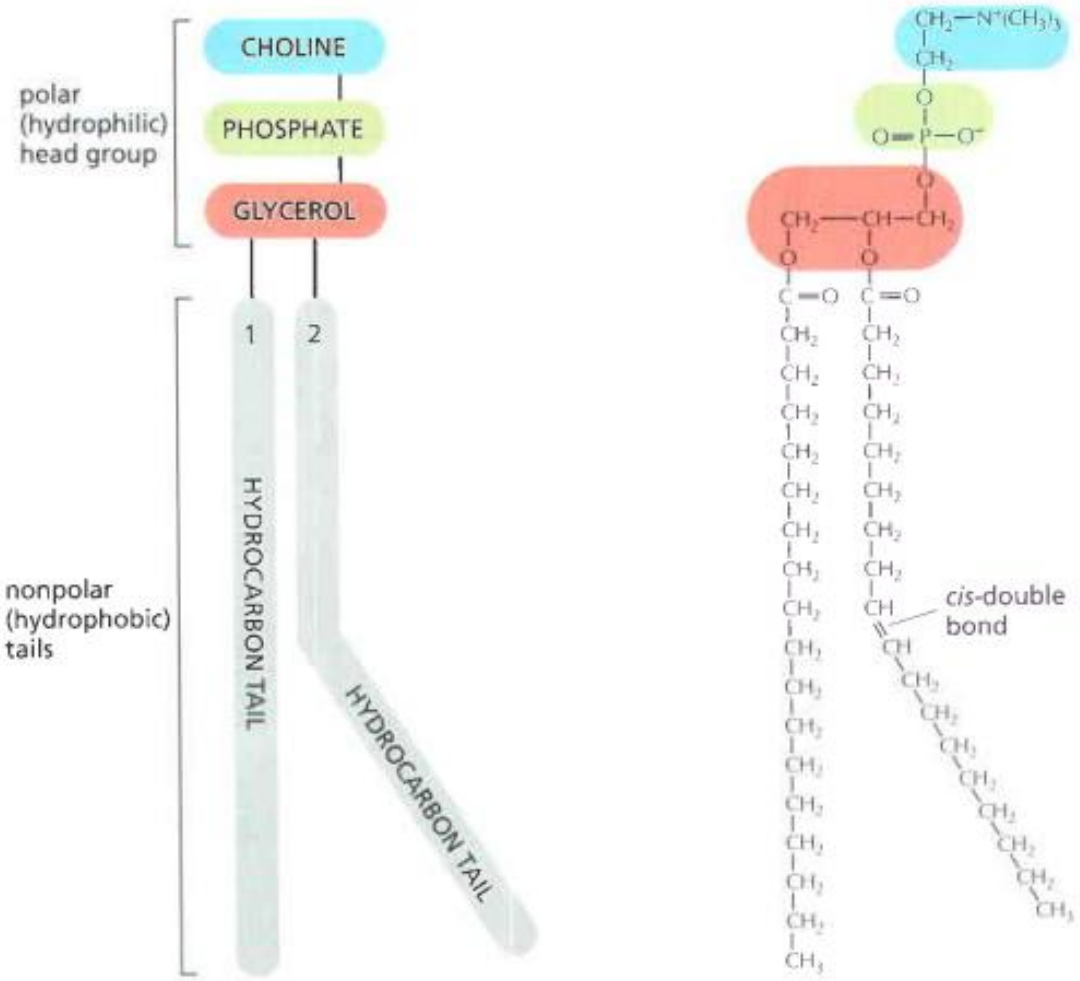
Alternative Classification Systems for Membrane Lipids

- Two complementary classification schemes exist:
  - System 1: Based on Backbone Structure (Used in this lecture)
    - Phosphoglycerides (glycerol backbone)
    - Sphingolipids (sphingosine backbone)
    - Cholesterol (steroid rings)
  - Based on Head Group Function (Some textbooks) - Phospholipids (contain phosphate groups)
    - Includes: PC, PE, PS, PI + Sphingomyelin
    - Glycolipids (contain carbohydrate groups)
    - Includes: Cerebrosides, Gangliosides
    - Sterols (cholesterol)
- **Key point:** Sphingomyelin is BOTH a sphingolipid (sphingosine backbone) AND a phospholipid (has phosphate group)—the only phospholipid NOT built on glycerol!

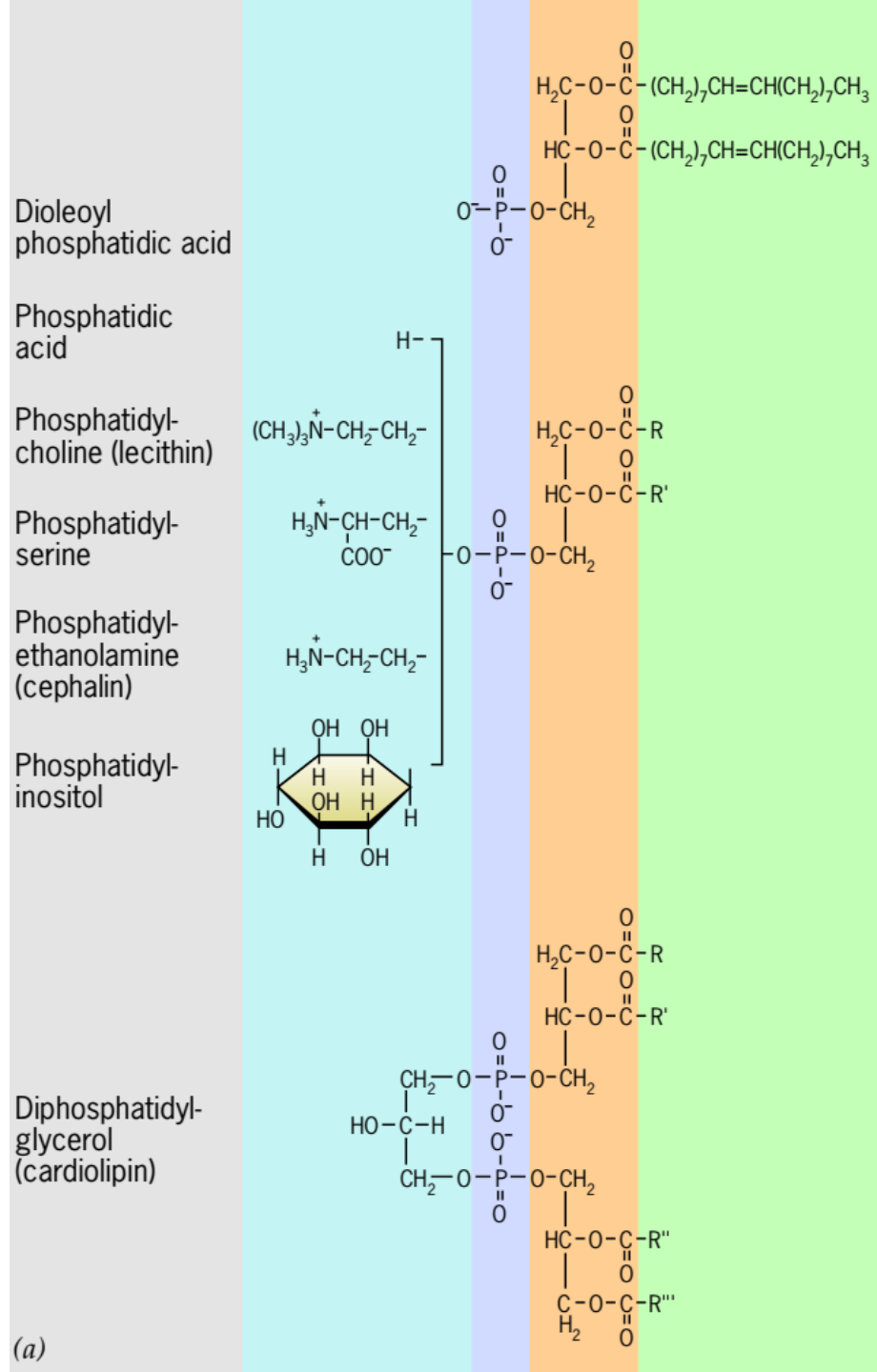
Phosphoglycerides - Structure and Chemistry

- **Basic Structure**
  - **Backbone:**
    - **3-carbon glycerol** molecule
    - Forms the "spine" of the phospholipid
  - **Fatty Acyl Chains:**
    - Two long-chain hydrocarbons (typically 16-22 carbons)
    - **One saturated chain** (no double bonds) + **one unsaturated chain** (one or more double bonds)
    - Straight, rigid saturated chains pack tightly
    - Kinked unsaturated chains reduce packing density
  - **Phosphate Group + Head Group:**
    - Third position on glycerol occupied by phosphate + hydrophilic head group
    - Creates a highly water-soluble domain at one end of the molecule
    - Determines charge and properties of phospholipid
- **Why This Structure?**
  - **Molecular stability** → prevents complete dissolution in water or lipid
  - **Flexibility** → allows rotation and lateral movement
  - **Specificity** → different head groups serve specific functions





Source: Bruce, A. *et al.* 2008. Molecular Biology of The Cell, 5th Edition



Source: Karp, G., 2013. Cell and Molecular Biology: Concepts and Experiments, 7th Edition

Four Major Phosphoglycerides in Plasma Membrane

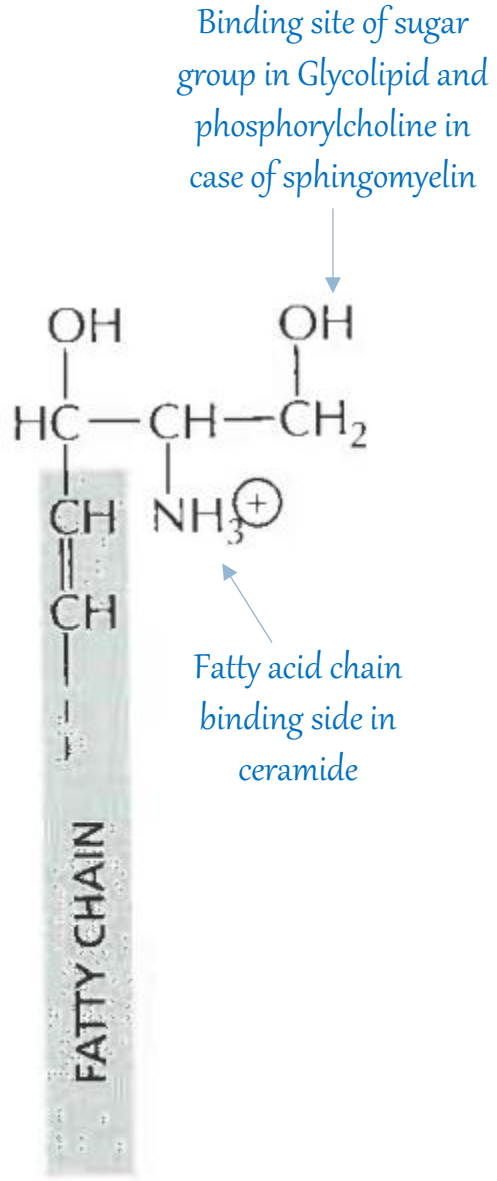
- **Phosphatidylcholine (PC) - "Lecithin"**
  - Head group: **Choline** (quaternary amine)
  - Charge: **Neutral** at physiological pH
  - Location: **Predominantly outer leaflet**
  - Percentage: ~50% of total phospholipids
  - Functions: Major structural component; precursor for signaling molecules
- **Phosphatidylethanolamine (PE) - "Cephalin"**
  - Head group: **Ethanolamine** (primary amine)
  - Charge: **Neutral** at physiological pH
  - Location: **Predominantly inner (cytoplasmic) leaflet**
  - Percentage: ~25-30% of total phospholipids
  - Functions: Structural component; involved in protein interactions
- **Phosphatidylserine (PS)**
  - Head group: **Serine** (amino acid)
  - Charge: **Negatively charged** at physiological pH
  - Location: **Exclusively inner (cytoplasmic) leaflet**
  - Percentage: ~5-10% of total phospholipids
  - Key Function: Critical for apoptosis signaling (exposed PS signals "eat me" to macrophages)
- **Phosphatidylinositol (PI)**
  - Head group: **Inositol** (6-carbon sugar with multiple hydroxyl groups)
  - Charge: **Negatively charged** at physiological pH
  - Location: **Inner (cytoplasmic) leaflet**
  - Percentage: ~2-5% of total phospholipids
  - Key Function: **Phosphorylated by PI kinases** to create docking sites for intracellular signalling proteins; extremely important for signal transduction
- **Clinical Significance**
  - These lipids are not merely structural—they participate actively in:
  - Cell signaling pathways
  - Apoptosis and cell death
  - Recognition and immune responses
  - Membrane protein function

Amine-containing phospholipids are mostly found on the cytoplasmic surface, e.g., phosphatidylethanolamine, phosphatidylserine

Choline-containing phospholipids (e.g., phosphatidylcholine) and sphingomyelin are enriched on the extracellular surface.

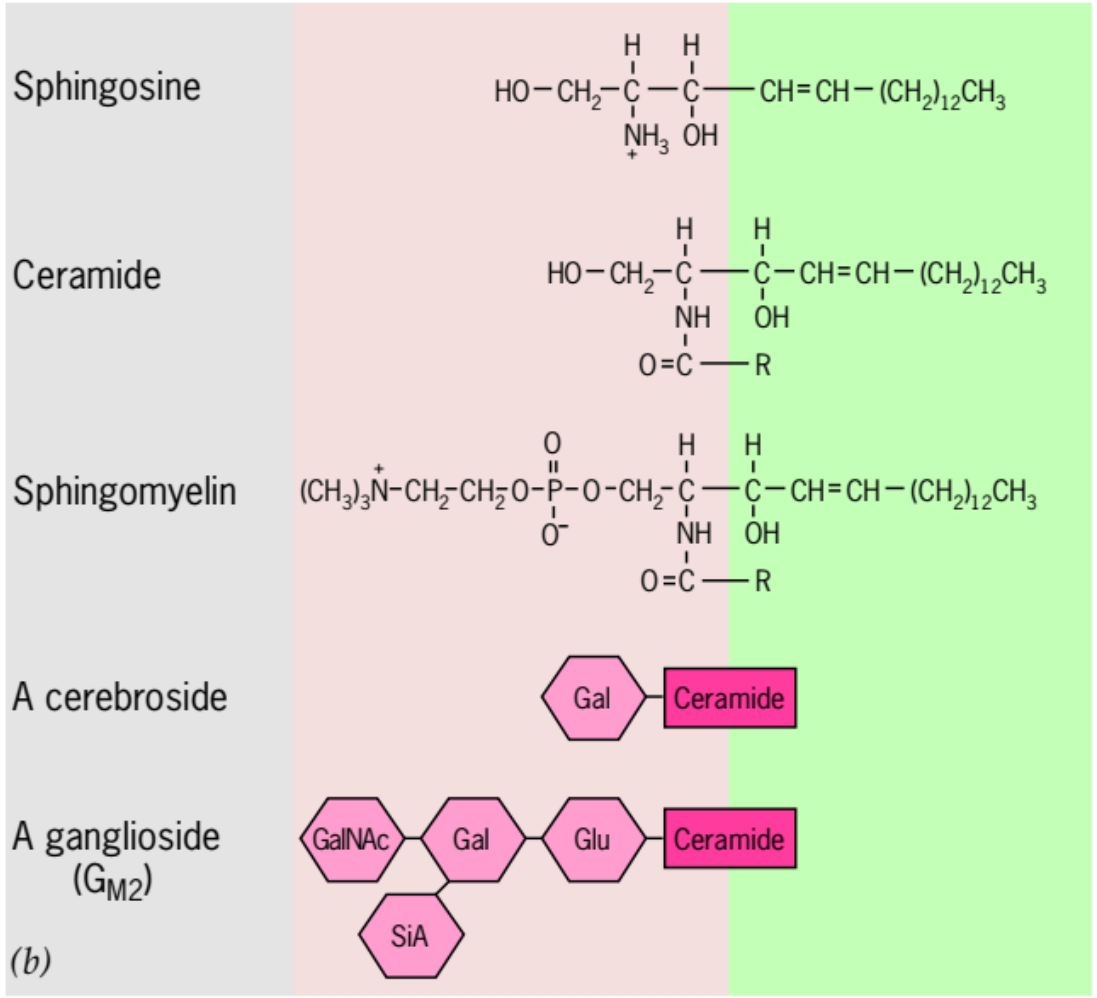
Sphingolipids - Structure and Types

- **Backbone:**
  - **Sphingosine** (not glycerol) - a long-chain amino alcohol
  - Contains amino group (unlike phosphoglycerides)
  - 18-carbon chain with one double bond (unsaturated)
- **Attachment:**
  - Fatty acid is linked to **amino group** of sphingosine via amide bond
  - Forms **ceramide** (sphingosine + fatty acid)
  - Ceramide is the "core" from which other sphingolipids are made
- **Key Differences from Phosphoglycerides**
  - **Longer, more saturated** fatty acid chains
  - **Enriched in nervous system** (especially brain and myelin)
  - **More ordered structure** → participate in lipid raft formation
  - **Neurological dysfunction** when deficient or absent



Three Classes of Sphingolipids

- **Sphingomyelin**
  - Additional group: **Phosphorylcholine**
  - **Only phospholipid NOT built on a glycerol backbone**
  - Highly abundant in myelin (nerve cell insulation)
  - More saturated fatty acids than phosphoglycerides
  - Enriched in lipid rafts
  - Sphingomyelin is the most common sphingophospholipid
- **Cerebrosides (Neutral Glycolipids)**
  - Additional group: **Single carbohydrate** (usually galactose)
  - Most common: **Galactocerebroside**
  - Very abundant in the brain and myelin
  - Deficiency leads to neurological disorders (e.g., Krabbe disease)
- **Gangliosides (Complex Glycolipids)**
  - Additional group: **Oligosaccharide chain including sialic acid** (negatively charged)
  - Hundreds of different gangliosides identified
  - Concentration: 5-10% of total lipid mass in nerve cell membranes
  - Functions: Cell recognition, immune signalling, toxin entry points (cholera toxin, influenza virus)

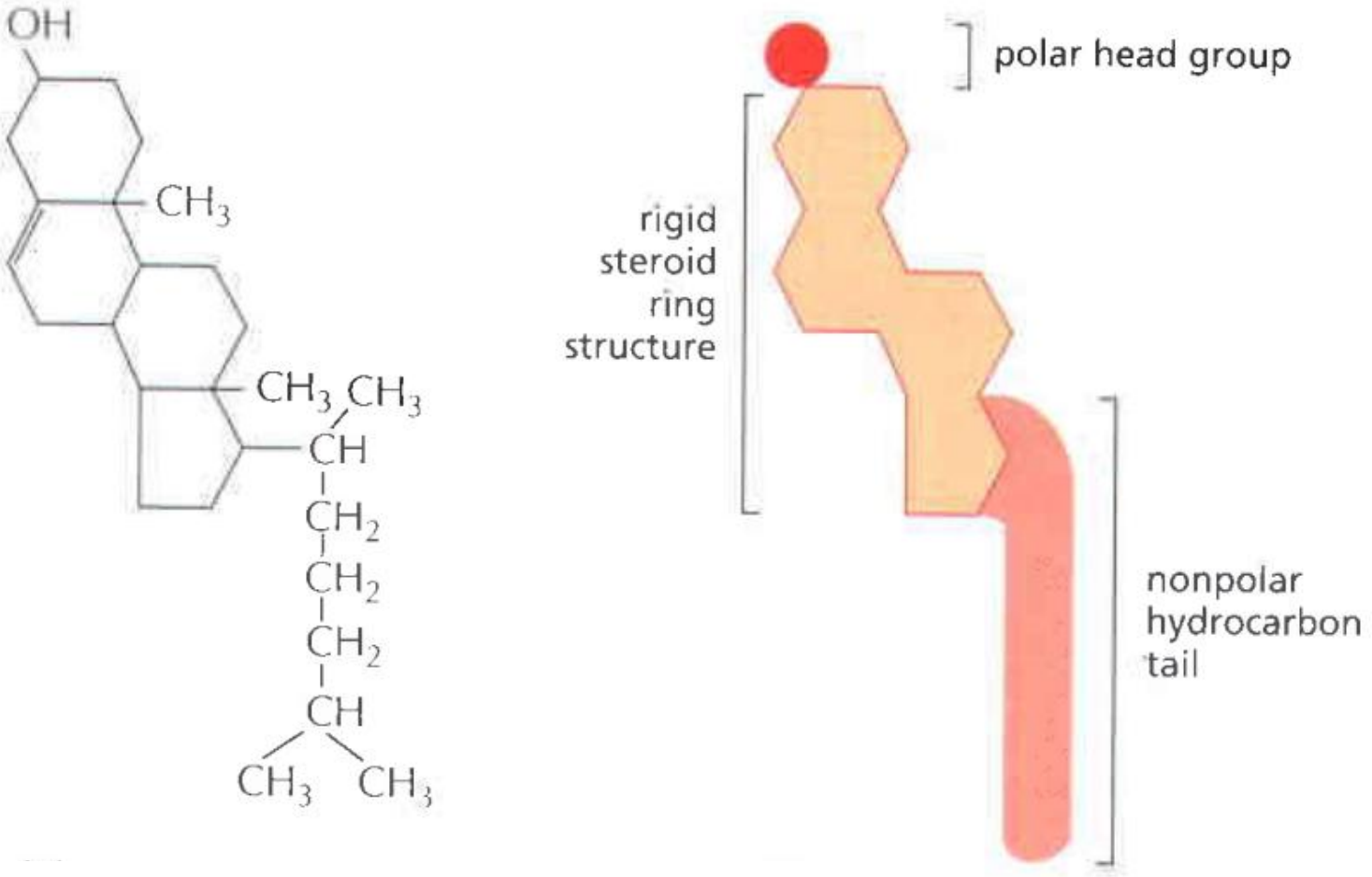


Source: Karp, G., 2013. Cell and Molecular Biology: Concepts and Experiments, 7th Edition

Cholesterol in membrane - Structure

- **Chemical Structure:**
  - **Steroid** (not a phospholipid)
  - **Rigid, fused ring system** (4 fused hydrocarbon rings)
  - **Small polar hydroxyl group (-OH)** on one end
  - Remainder of molecule is **nonpolar/hydrophobic**
- **Orientation in Bilayer:**
  - **Hydroxyl group** faces aqueous environment (outer surface)
  - **Ring structure and hydrocarbon tail** embedded in hydrophobic core
  - Lies roughly **parallel to fatty acid chains** of adjacent phospholipids
  - **Not symmetrically distributed** - higher concentration in outer leaflet
- **Concentration**
  - Comprises up to 50% of lipid molecules (by number, not weight) in plasma membranes of animal cells—approximately 20-25% by mass
  - Highest in: plasma membrane, myelin, adrenal cortex
  - **Lower in:** mitochondrial membranes, bacterial membranes
  - **Absent in:** plants and most bacteria (though plants have plant sterols: stigmasterol and sitosterol)

Cholesterol in membrane - Structure



Source: Bruce, A. *et al.* 2008. Molecular Biology of The Cell, 5th Edition

Cholesterol in membrane - Functions

- **Modulates Fluidity:**
  - At high temperatures: Restricts phospholipid movement → decreases fluidity
  - At low temperatures: Prevents tight packing → increases fluidity
  - Creates **intermediate fluidity** state optimal for biological function
- **Reduces Permeability:**
  - Fills gaps between phospholipid chains
  - Reduces passage of small polar molecules
  - Increases mechanical strength
- **Stabilizes Membrane:**
  - Reduces phase transitions
  - Prevents excessive rigidity or fluidity
  - Maintains optimal membrane integrity

Lipid composition of some biological membranes

Lipid	Human erythrocyte	Human myelin	Beef heart mitochondria	*E. coli*
Phosphatidic acid	1.5	0.5	0	0
Phosphatidylcholine	19	10	39	0
Phosphatidyl-ethanolamine	18	20	27	65
Phosphatidylgycerol	0	0	0	18
Phosphatidylserine	8.5	8.5	0.5	0
Cardiolipin	0	0	22.5	12
Sphingomyelin	17.5	8.5	0	0
Glycolipids	10	26	0	0
Cholesterol	25	26	3	0

*The values given are weight percent of total lipid.
Source: C. Tanford, *The Hydrophobic Effect*, p. 109, copyright 1980, John Wiley & Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc.

Source: Karp, G., 2013. Cell and Molecular Biology: Concepts and Experiments, 7th Edition

Lipid Bilayer Formation - Spontaneous Self-Assembly

The Hydrophobic Effect - Driving Force

When amphipathic lipids are placed in water:

- **Step 1: Initial Challenge**
  - Lipid molecules have hydrophobic tails that cannot form favourable interactions with water
  - Exposing hydrophobic tails to water costs ~2-3 kcal/mol per CH_2 group
  - This **unfavourable entropy** drives lipid molecules to minimise water contact
- **Step 2: Spontaneous Assembly**
  - Lipid molecules self-organise to **minimise free energy**
  - Hydrophobic tails cluster together → minimize water contact
  - Hydrophilic heads remain exposed to water
- **Step 3: Bilayer Formation**
  - Most stable configuration: **Two-layer arrangement (bilayer)**
  - Hydrophilic heads form outer surfaces (face water both outside and inside)
  - Hydrophobic tails form a continuous interior (away from water)
  - Creates a **sealed compartment** with no free edges
- **Why Bilayer and Not Micelle?**
  - Bilayer provides maximum surface area for head groups
  - Interior has maximum hydrophobic interactions
  - **No energetically unfavourable free edges**
  - More stable than unimolecular layers or micelles for large-scale structures
- **Biological Significance**
  - **Self-assembly requires no proteins or energy**
  - Can spontaneously repair small tears
  - Explains why all biological membranes are lipid bilayers
  - Demonstrates fundamental thermodynamic principle

Lipid Bilayer Formation - Spontaneous Self-Assembly

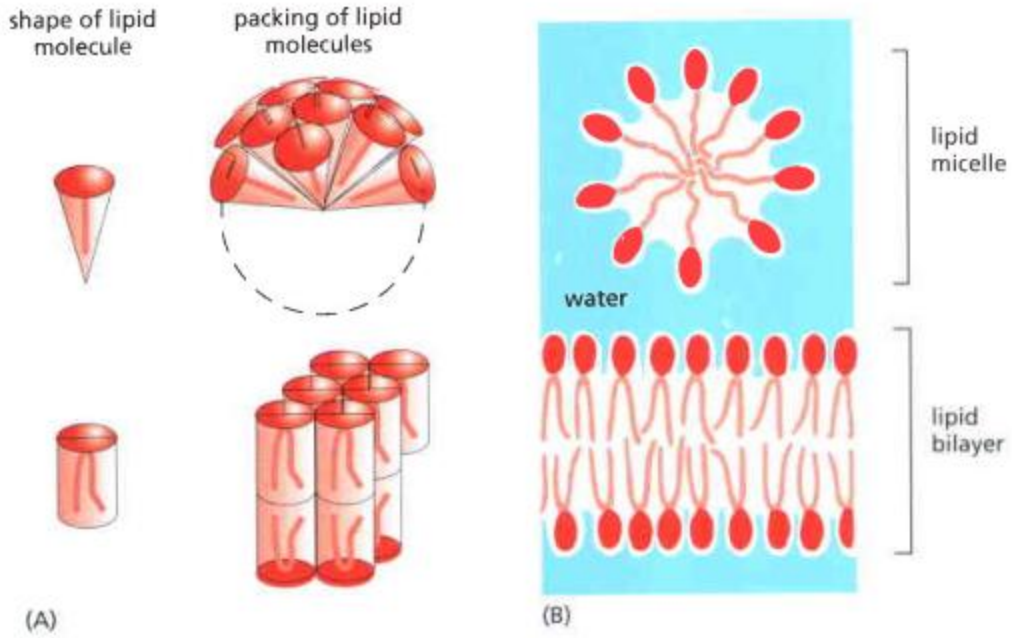


Figure 10–7 Packing arrangements of lipid molecules in an aqueous environment. (A) Cone-shaped lipid molecules *(above)* form micelles, whereas cylinder-shaped phospholipid molecules *(below)* form bilayers. (B) A lipid micelle and a lipid bilayer seen in cross section. Lipid molecules spontaneously form one or the other structure in water, depending on their shape.

Source: Bruce, A. *et al.* 2008. Molecular Biology of The Cell, 5th Edition

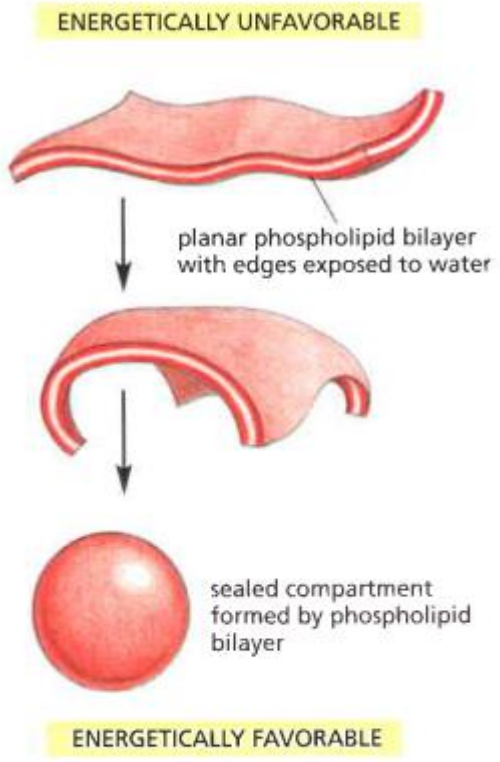


Figure 10–8 **The spontaneous closure of a phospholipid bilayer to form a sealed compartment.** The closed structure is stable because it avoids the exposure of the hydrophobic hydrocarbon tails to water, which would be energetically unfavorable.

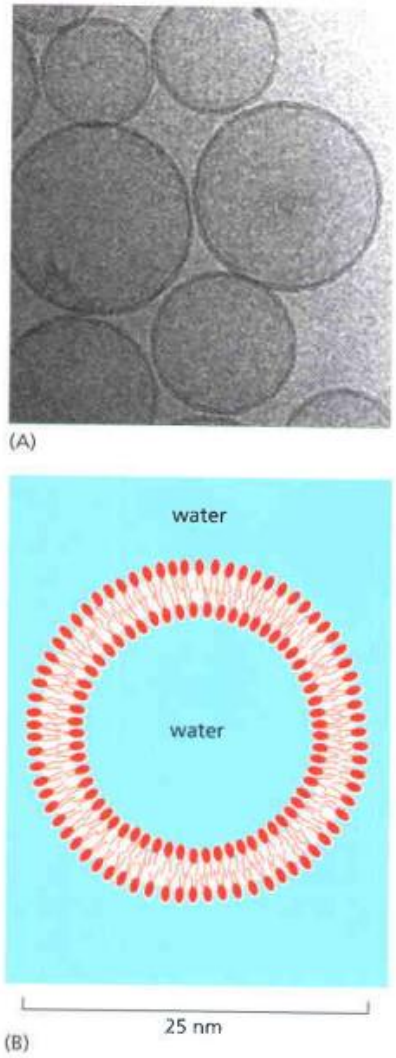


Figure 10–9 **Liposomes.** (A) An electron micrograph of unfixed, unstained phospholipid vesicles—liposomes—in water rapidly frozen to liquid nitrogen temperature. (B) A drawing of a small spherical liposome seen in cross section. Liposomes are commonly used as model membranes in experimental studies. (A, from P. Fröderk-2005. Hubert, *Meth. Enzymol.* 391:431, 2005. With permission from Elsevier.)

Membrane Asymmetry - Different Lipid Distributions in Two Leaflets

Outer Leaflet (Extracellular-Facing)

- **Lipid Composition:**
  - **Phosphatidylcholine (PC)** - ~55% of outer leaflet phospholipids
  - **Sphingomyelin** - ~20-25% (especially enriched)
  - **Glycolipids (cerebrosides, gangliosides)** - ~5-10%
  - **Cholesterol** - higher concentration
  - **NO phosphatidylserine** - always absent
  - **NO phosphatidylinositol** - always absent
- **Characteristics:**
  - More **ordered, rigid structure**
  - Enriched in **carbohydrate groups** (glycolipids and glycoproteins)
  - Higher **lipid raft concentration**
  - Contains all glycosylated components

Inner Leaflet (Cytoplasmic-Facing)

- **Lipid Composition:**
  - **Phosphatidylethanolamine (PE)** - ~40-50% of inner leaflet phospholipids
  - **Phosphatidylserine (PS)** - ~5-10% (exclusively located here)
  - **Phosphatidylinositol (PI)** - ~2-10% (exclusively/predominantly here)
  - **Cholesterol** - lower concentration
  - **NO glycolipids** - none
  - **NO complex carbohydrates** - reducing environment
- **Characteristics:**
  - More **fluid, disordered structure**
  - **NO carbohydrate groups**
  - Rich in **signaling lipids** (especially PI derivatives)
  - Reducing environment (free sulfhydryl groups, no disulfide bonds)

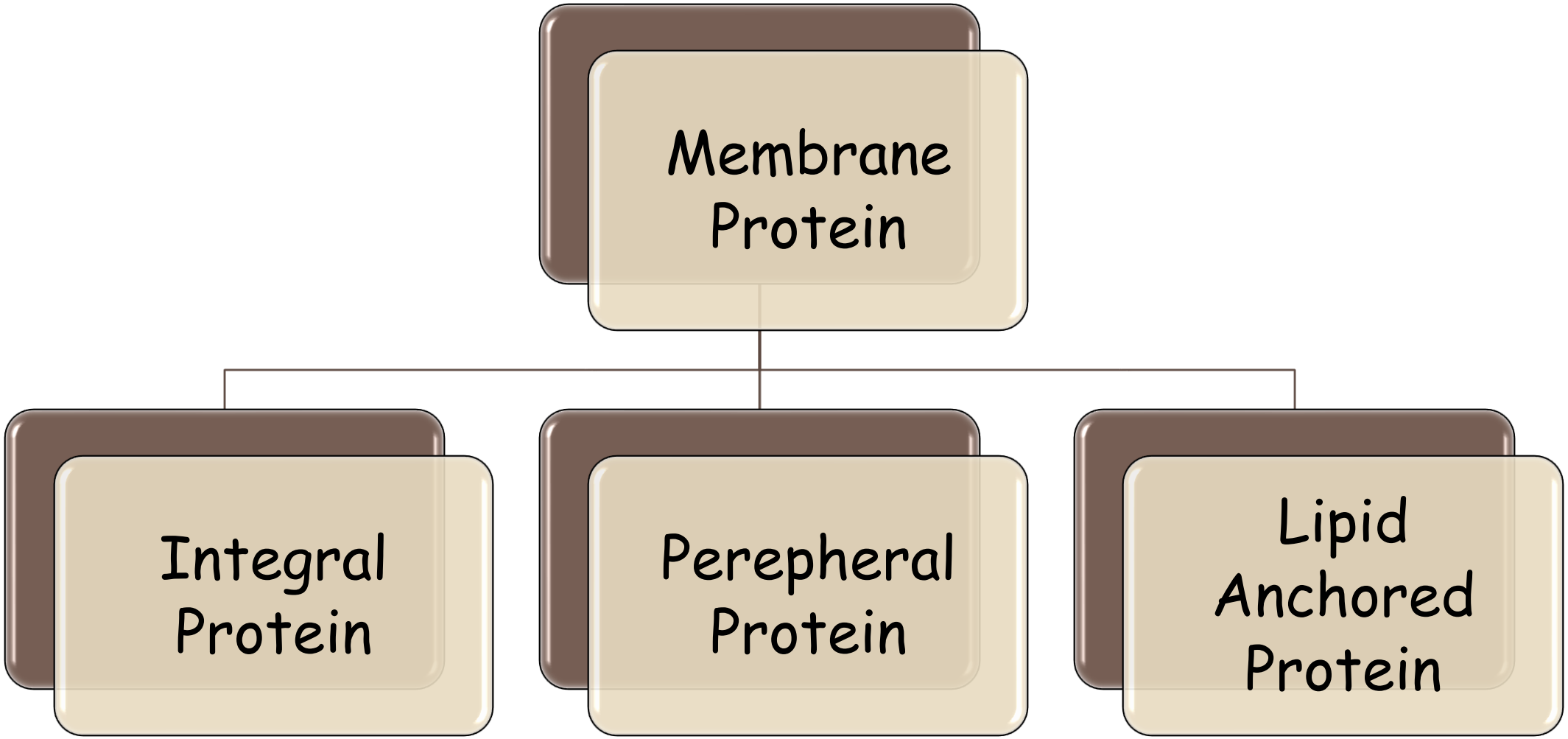
Mechanisms Maintaining Asymmetry

- **Vectorial Synthesis:**
  - Lipids synthesised by enzymes in specific membrane compartments
  - ER synthesis places lipids in the outer leaflet initially
  - Transport vesicles deliver lipids to specific locations
- **Phospholipid Translocators (Flippases/Floppases):**
  - ATP-dependent enzymes that selectively move lipids between leaflets
  - **Flippases** (ATP-dependent): pump PS, PE inward
  - **Floppases** (ATP-dependent): pump lipids outward
  - **Scramblases**: activated during apoptosis, disrupt asymmetry
- **Barriers to Spontaneous Flip-Flop:**
  - Hydrophilic head groups cannot easily cross the hydrophobic interior
  - Spontaneous flip-flop occurs very slowly (~hours to days)
  - Requires active enzyme catalysis for rapid translocation

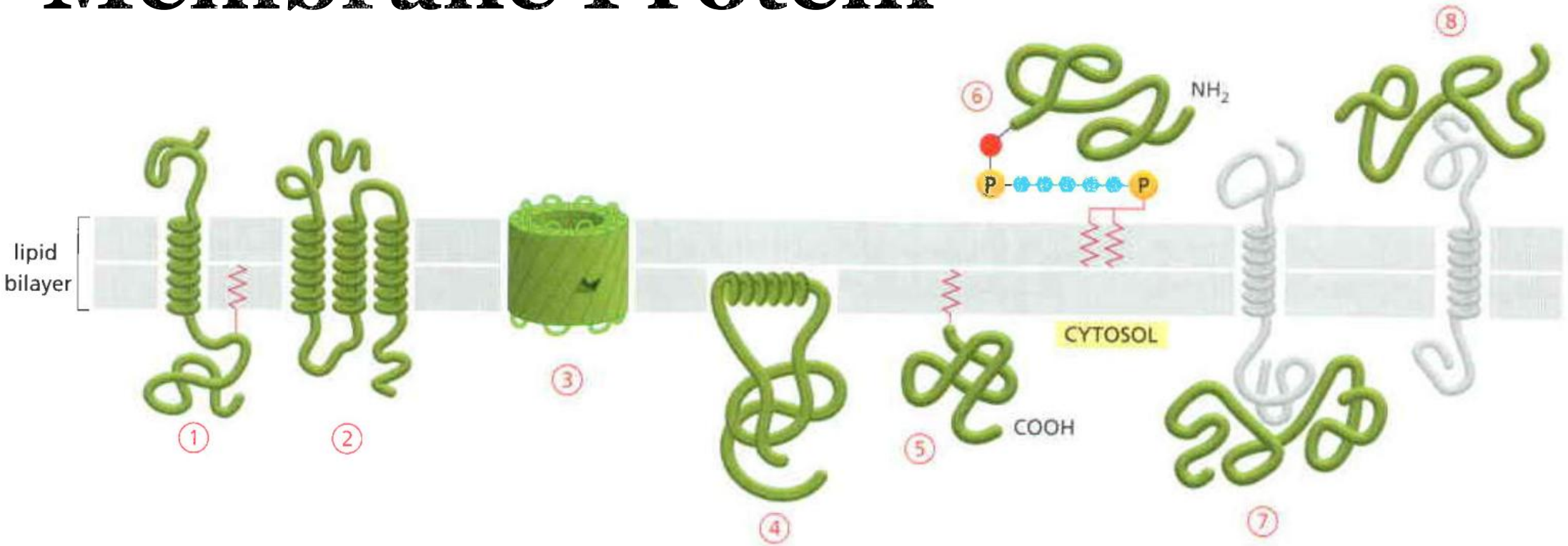
Functional Consequences of Asymmetry

- **Signal Transduction:**
  - PI and PI derivatives present ONLY on the inner leaflet
  - Allows specific localisation of signalling complexes
- **Apoptosis Recognition:**
  - PS is normally hidden in the inner leaflet
  - During apoptosis: PS flipped to the outer leaflet
  - Serves as an "eat me" signal for phagocytes
- **Protein Orientation:**
  - Determines which proteins face the extracellular space
  - Controls insertion and trafficking of membrane proteins
- **Membrane Protein Function:**
  - Many proteins specifically recognise lipid head groups
  - Asymmetry determines which proteins can interact
- **Selective Permeability:**
  - Different composition creates directional transport properties
  - Affects ion channel selectivity

Membrane Proteins



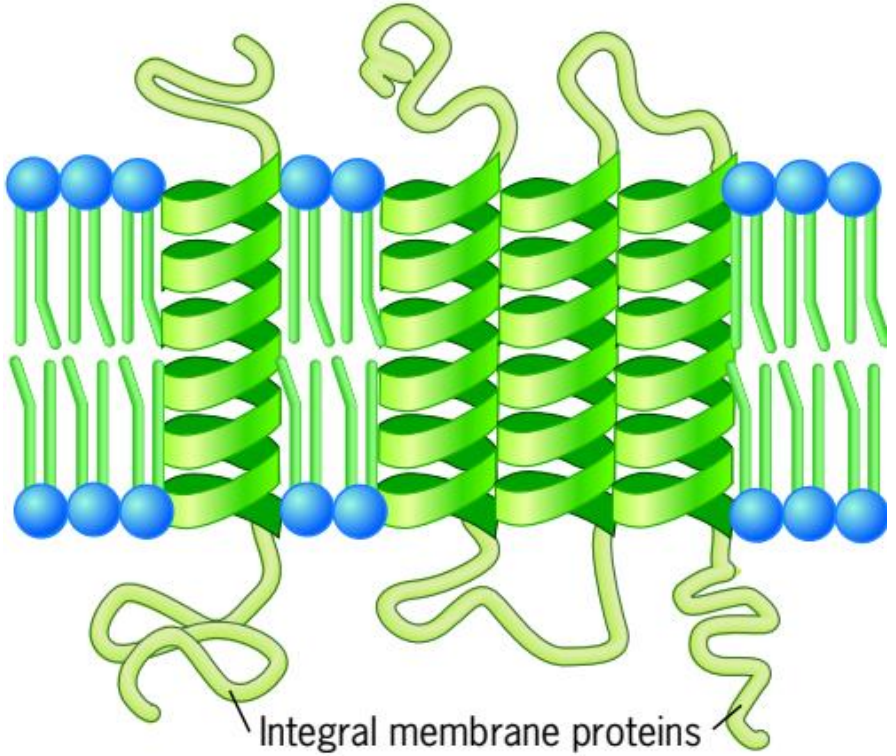
Membrane Protein



Various ways in which membrane proteins associate with the lipid bilayer. Most transmembrane proteins are thought to extend across the bilayer as (1) a single α helix, (2) as multiple α helices, or (3) as a rolled-up β sheet (a β barrel). Some of these "single-pass" and "multipass" proteins have a covalently attached fatty acid chain inserted in the cytosolic lipid monolayer (1). Other membrane proteins are exposed at only one side of the membrane. (4) Some of these are anchored to the cytosolic surface by an amphiphilic α helix that partitions into the cytosolic monolayer of the lipid bilayer through the hydrophobic face of the helix. (5) Others are attached to the bilayer solely by a covalently attached lipid chain—either a fatty acid chain or a prenyl—in the cytosolic monolayer or (6) via an oligosaccharide linker, to phosphatidylinositol in the noncytosolic monolayer—called a GPI anchor. (7, 8) Finally, many proteins are attached to the membrane only by noncovalent interactions with other membrane proteins. Source: Bruce, A. et al. 2008. Molecular Biology of The Cell, 5th Edition

Integral (transmembrane) Protein

- **Definition:**
  - Proteins that span the entire thickness of the lipid bilayer
  - Cannot be removed by mild extraction procedures
  - They are embedded in the lipid by layer and contain one (monotopic) or more (polytopic) transmembrane regions.
  - Amphipathic proteins have both polar amino acid residues (outer surface) and non-polar amino acid residues (inner surface).
  - Genome-sequencing studies suggest that integral proteins constitute 25–30 per cent of all encoded proteins and roughly 60 per cent of all current drug targets.
  - Glycophorin is the major monotopic integral protein of RBC, containing 131 amino acid residues, the first membrane protein for which the complete amino acid sequence was determined.



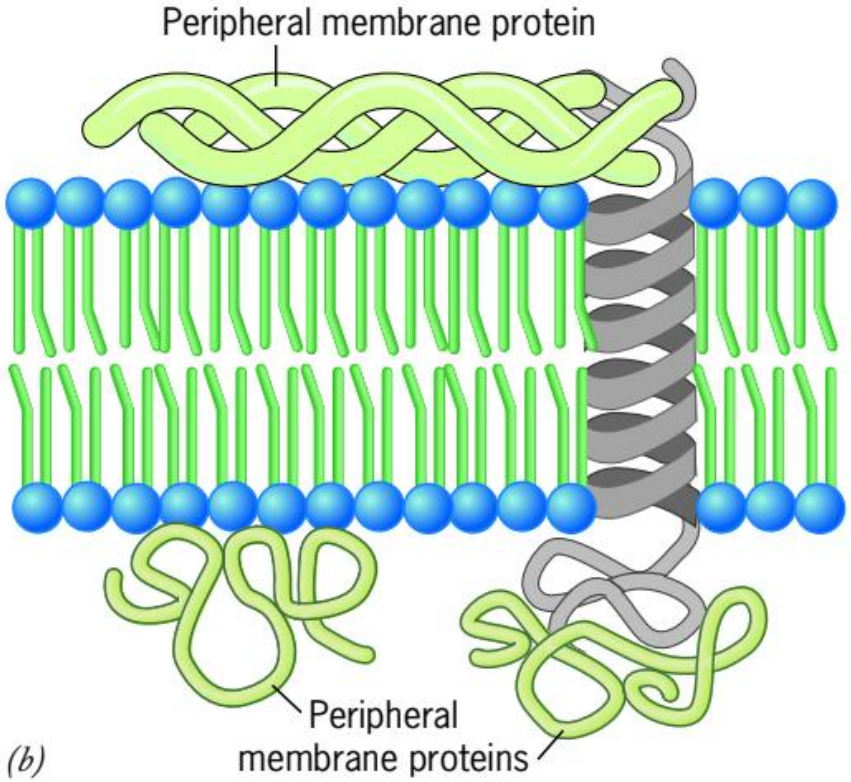
Type	Structure	Examples	Functions
Single-Pass	One α-helix spans bilayer	Glycophorin A, transferrin receptor	Receptors; markers
Multi-Pass	Multiple α-helices or β-barrel	G-protein coupled receptors, bacteriorhodopsin, ion channels	Transport; signaling; energy transduction

Examples of Transmembrane Proteins

- **Glycophorin A (Single-Pass)**
  - Major protein of red blood cell membrane
  - One transmembrane α-helix (amino acids 73-92)
  - Of 20 residues: 17 are hydrophobic
  - Extracellular domain: heavily glycosylated (16 oligosaccharides)
  - Forms homodimers through interactions of transmembrane helices
  - Functions as a blood group antigen; cell recognition
- **Bacteriorhodopsin (Seven-Pass)**
  - Archaeal light-driven proton pump
  - Seven transmembrane α-helices
  - Retinal chromophore covalently linked to lysine
  - Light-driven conformational changes pump H^+ across the membrane
  - Prototype for G-protein coupled receptors (GPCRs)
  - Same structure despite different function and sequence from GPCRs

Peripheral Proteins

- **Definition:**
  - Associated with the membrane surface only
  - Do NOT cross lipid bilayer
  - Interact with the membrane mainly through **noncovalent bonds** (electrostatic, hydrogen bonds)
  - Can be solubilised by high salt concentration or extreme pH
  - **Attachment Modes:**
- Associate with **polar head groups** of lipids
  - Bind to **exposed domains** of integral proteins
  - Form **loose associations** with the membrane
- **Locations:**
  - **Inner (cytoplasmic) surface:** Membrane skeleton proteins (e.g., spectrin in red blood cells)
  - **Outer surface:** Some receptors, complement proteins, enzymes
- **Functions:**
  - Mechanical support and structural integrity
  - Enzyme activity
  - Signal transduction intermediates
  - Anchors for cytoskeletal filaments
- **Dynamic Nature:**
  - Recruited to the membrane in response to signals
  - Released from the membrane when signals terminate
  - Allow for rapid regulation of membrane function

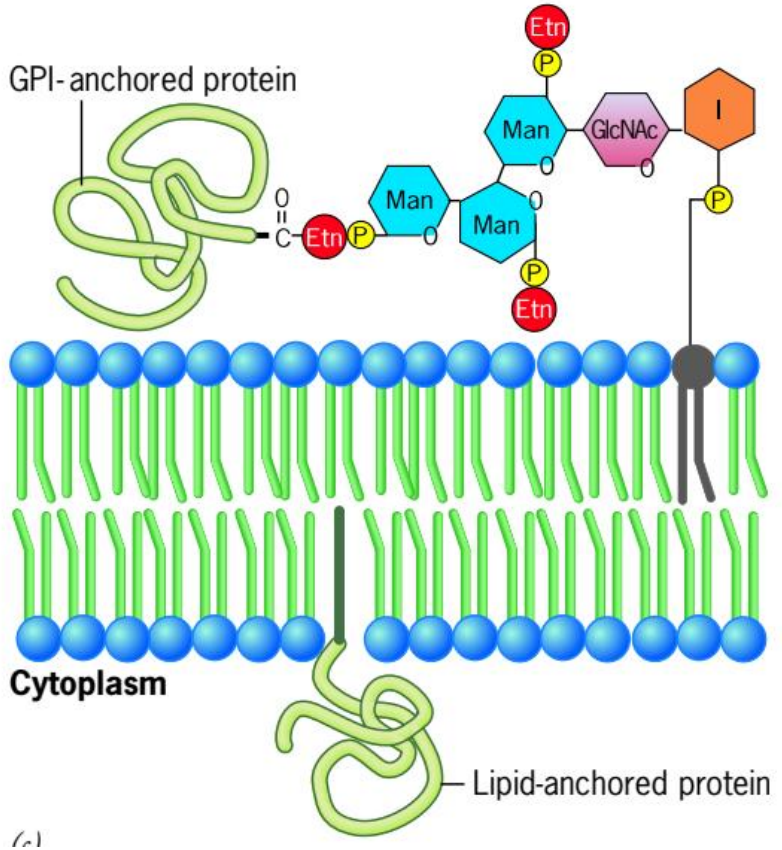


Lipid-anchored Protein

- **Definition:**
  - Attached to the membrane through a covalent linkage to lipid molecules
  - Soluble proteins modified after synthesis with lipid moieties
  - Associated with one or both leaflets, depending on lipid type
- **Properties:**
  - **Single lipid anchor** provides weak attachment
  - Many proteins use **dual anchors** (e.g., myristoyl + palmitoyl) for stronger attachment
  - Lipid anchor can be **added/removed** in response to signals
  - Allows dynamic recruitment to/from the membrane
- **GPI-Anchored Proteins:**
  - Anchored via glycosylphosphatidylinositol (GPI)
  - Attached to **phosphatidylinositol in the outer leaflet**
  - Precursor is synthesised as a transmembrane protein
  - Signal sequence removed; GPI anchor added in ER
  - Released from the membrane by PI-specific phospholipase C

Lipid-anchored Protein

Anchor Type	Linkage	Location	Examples
Fatty Acyl	Thioester (Cys) or amide (N-terminal Gly)	Inner leaflet	Src kinase, other tyrosine kinases
Prenyl Groups	Thioether (Cys)	Inner leaflet	Ras proteins
GPI Anchor	Oligosaccharide to PI	Outer leaflet	CD55, CD59, prion proteins



Protein Orientation is Determined and Asymmetric

- **Glycosylation:**
  - Oligosaccharides **ONLY on extracellular (noncytosolic) surface**
  - Sugars added in ER/Golgi lumen (outside-equivalent compartment)
  - Never present in cytoplasm
- **Disulfide Bonds:**
  - Form **ONLY on extracellular/noncytosolic surface**
  - Oxidising environment outside the cell permits formation
  - Reducing the environment of the cytosol prevents disulfide bonds
  - Cysteine residues in cytoplasm remain as free -SH (sulfhydryl)
- **Charged Amino Acids:**
  - Positive charges often line the cytoplasmic end of transmembrane helices
  - Interact with negatively charged phospholipid head groups
  - Help anchor proteins in a specific orientation
- **Functional Domains:**
  - Domains on extracellular surface: ligand binding sites, receptors
  - Domains on cytoplasmic surface: signalling, enzyme activity, protein interactions

Membrane Protein Functions and Asymmetry Consequences

- **Signal Transduction**
  - **Extracellular Domain:**
    - Binds extracellular signals (hormones, growth factors, neurotransmitters)
    - Contains ligand-binding sites
    - Often glycosylated (affects specificity and stability)
  - **Cytoplasmic Domain:**
    - Generates intracellular signals
    - Binds signaling proteins
    - Often phosphorylated to create docking sites
    - Recruits effector proteins (kinases, phosphatases)
- **Transport Proteins**
  - **Channel/Transporter Asymmetry:**
    - Different selectivity or regulation from two sides
    - Ion channels more permeable from certain direction
    - Transporters have distinct entry/exit gates
  - **Functional Consequence:**
    - Allows directional transport
    - Permits energy-dependent accumulation
    - Controls solute entry/exit independently
- **Recognition and Adhesion**
  - **Extracellular Domains:**
    - Contain recognition sequences
    - Carbohydrate "codes" for cell-cell identification
    - Adhesion molecules present on surface
  - **Intracellular Domains:**
    - Link to cytoskeleton
    - Connect to signaling machinery
    - Transmit mechanical forces
- **Why Asymmetry is Non-Negotiable**
  - Function requires specific orientation
  - Protein folding occurs in specific compartments
  - Glycosylation, disulfide bonds specify orientation
  - Once established, orientation determines biological activity

Summary

- Three Major Lipid Classes
  - Phosphoglycerides (PC, PE, PS, PI) - structural and signalling
  - Sphingolipids (sphingomyelin, cerebrosides, gangliosides) - nervous system
  - Cholesterol - fluidity regulation
- Membrane Organisation
  - Lipid bilayer forms spontaneously (hydrophobic effect)
  - Asymmetric distribution between leaflets (functional significance)
  - Maintained by flippases, floppases, scramblases
- Three Categories of Membrane Proteins
  - Integral proteins - span bilayer (receptors, channels, transporters)
  - Peripheral proteins - surface association (structural support, enzymes)
  - Lipid-anchored proteins - covalent lipid attachment (dynamic recruitment)
- Key Principles
  - Amphipathic nature drives self-assembly
  - Asymmetry is functionally essential
  - Protein orientation determined during synthesis
  - Structure enables diverse cellular functions

Next Lecture: Fluid Mosaic Model (Singer & Nicolson 1972; Nicolson 2014)