

Plasma membrane: protection and nutrient acquisition

Architecture, asymmetry, protein anchoring and selective permeability

Robbins, Cotran & Kumar · Pathologic Basis of Disease

11th edition · Chapter 1

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Learning objectives

By the end of the lecture, you should be able to:

Explain the amphipathic bilayer and its permeability barrier

Map major lipids to their preferred membrane leaflets

Relate signaling lipids, membrane domains and protein anchors to function

Describe the glycocalyx, epithelial polarity and passive diffusion

The membrane is an organized biological interface

Three linked functions

One physical boundary integrates three cellular tasks.

Protection

A lipid core separates aqueous compartments

Selective exchange

Transport proteins and vesicular pathways regulate entry and exit

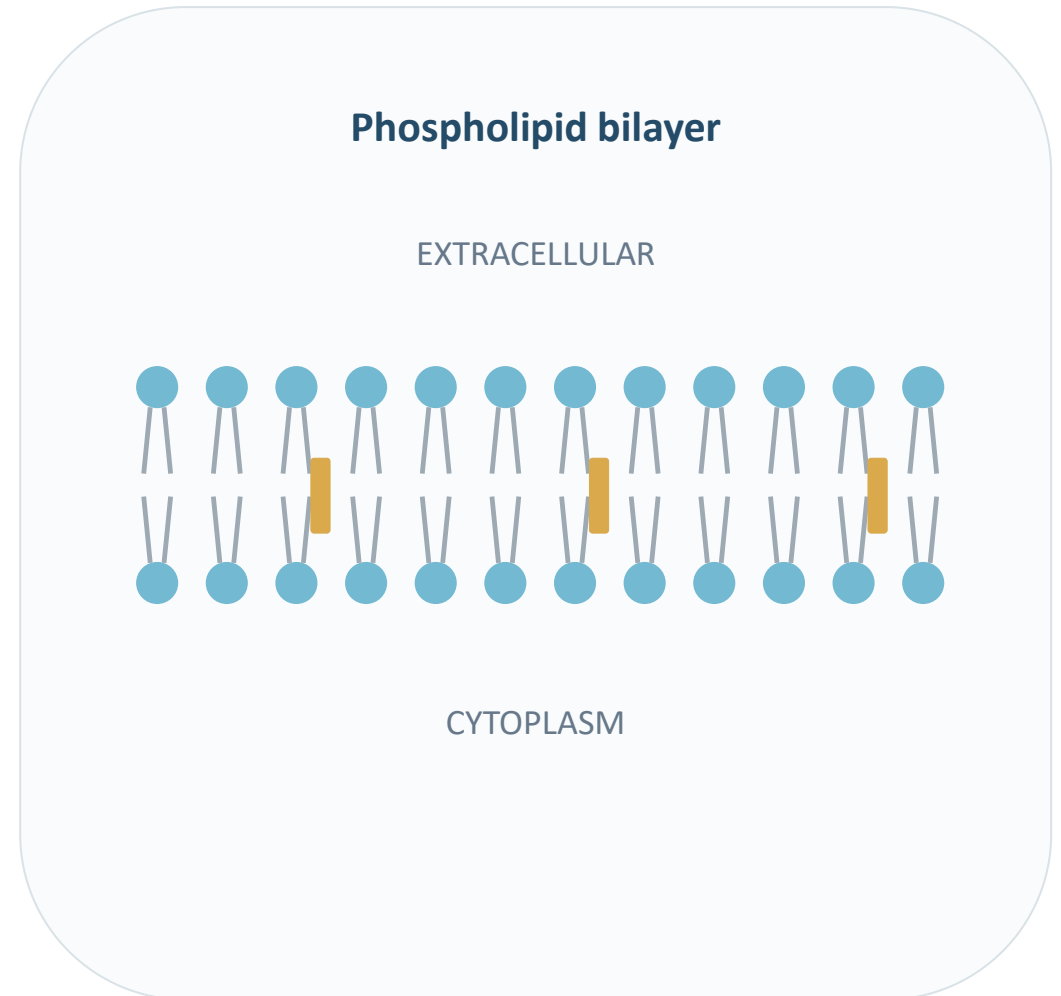
Communication

Membrane proteins and lipids organize signaling and adhesion

The bilayer is fluid rather than a static sheath

The foundational architecture

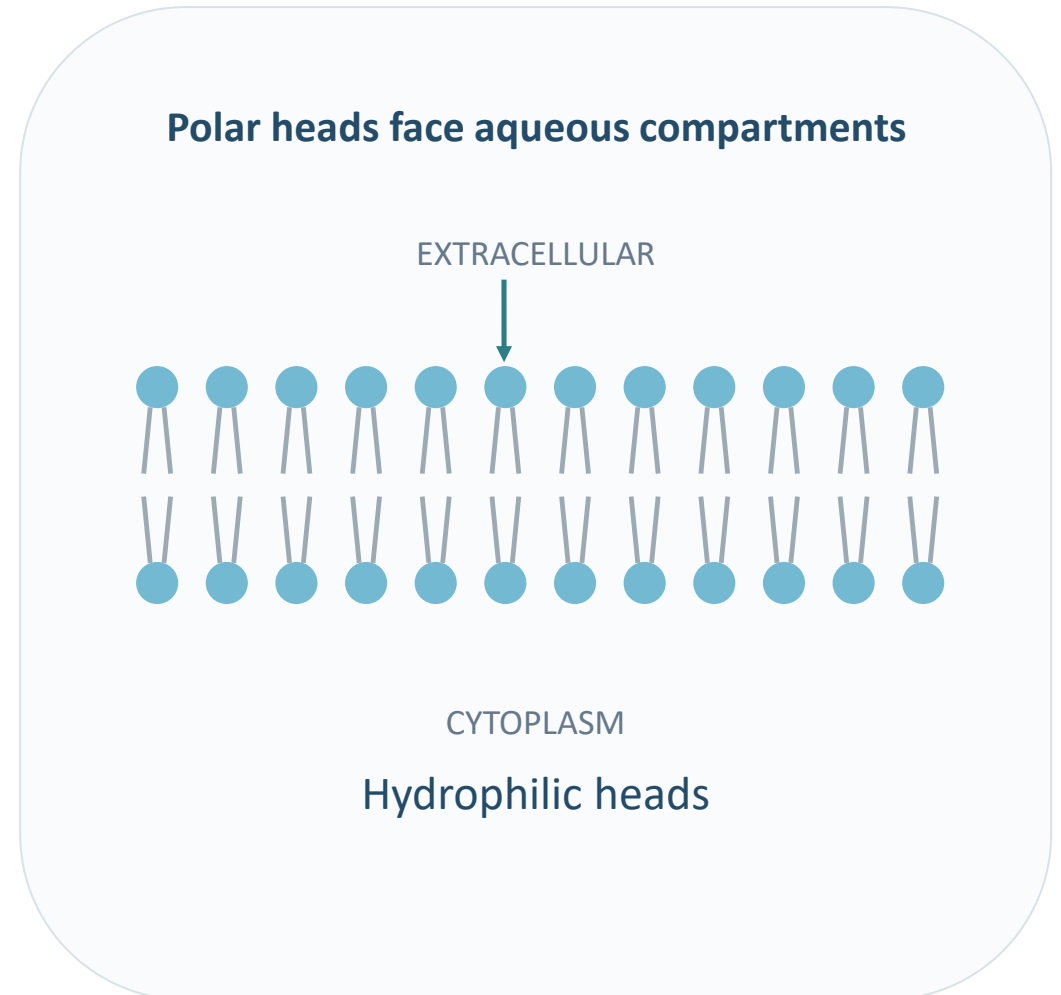
- Amphipathic phospholipids self-organize into a bilayer
- Hydrophilic groups face extracellular fluid or cytoplasm
- Hydrophobic acyl tails face one another



Amphipathic phospholipids explain membrane orientation

Two chemically different regions

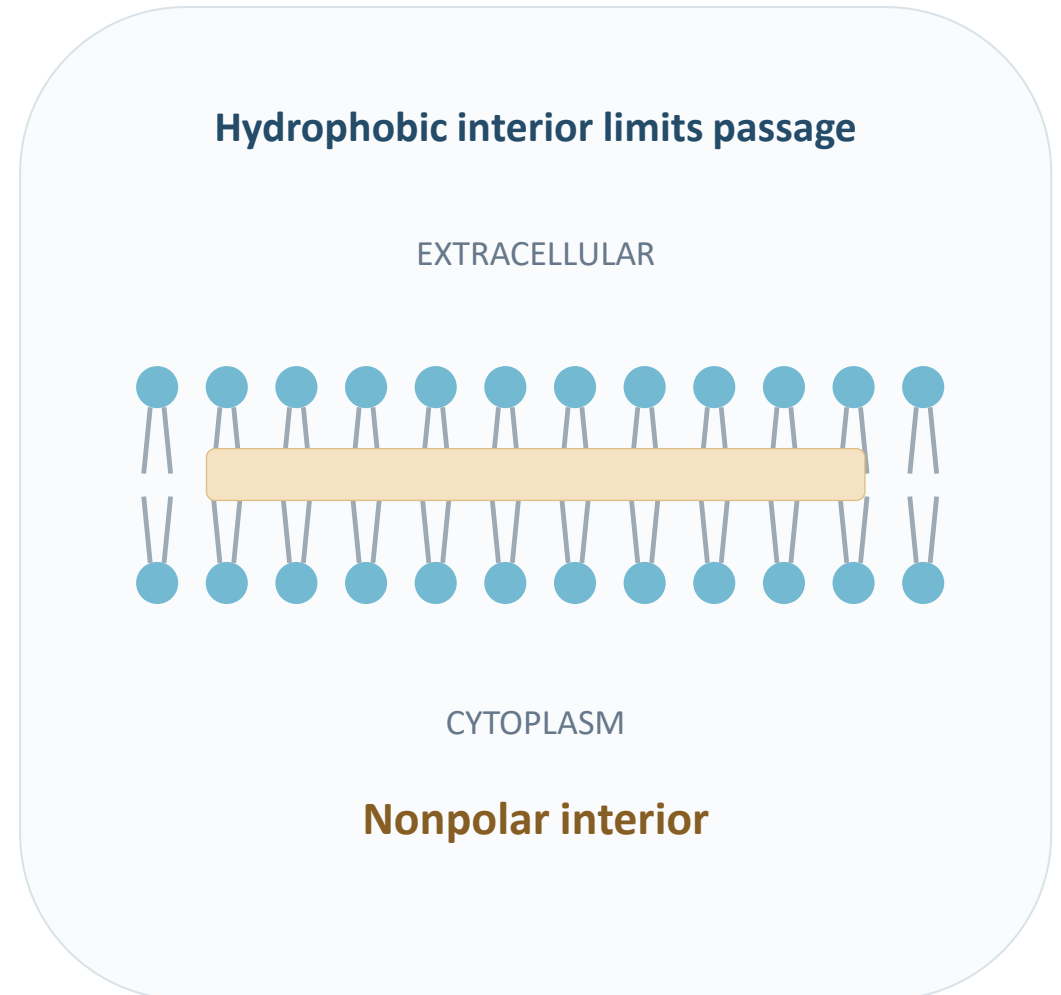
- Polar head groups interact with surrounding water
- Hydrophobic tails pack in the interior
- The molecular geometry generates a nonpolar core



The hydrophobic core creates a diffusion barrier

Why a membrane is selectively permeable

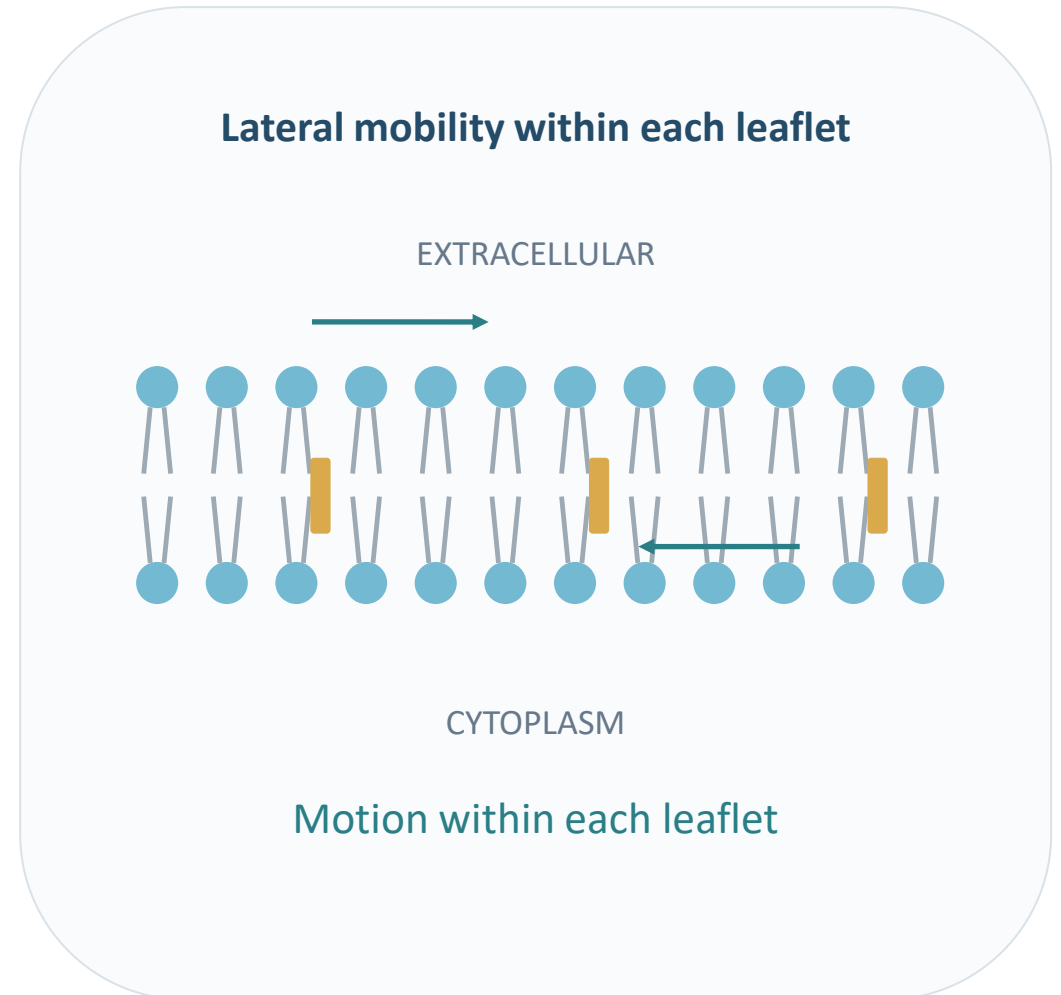
- Large or charged solutes cannot diffuse freely
- Lipid solubility helps determine direct passage
- Protein-dependent routes are needed for many solutes



Membrane constituents move laterally

Fluidity within the plane of the membrane

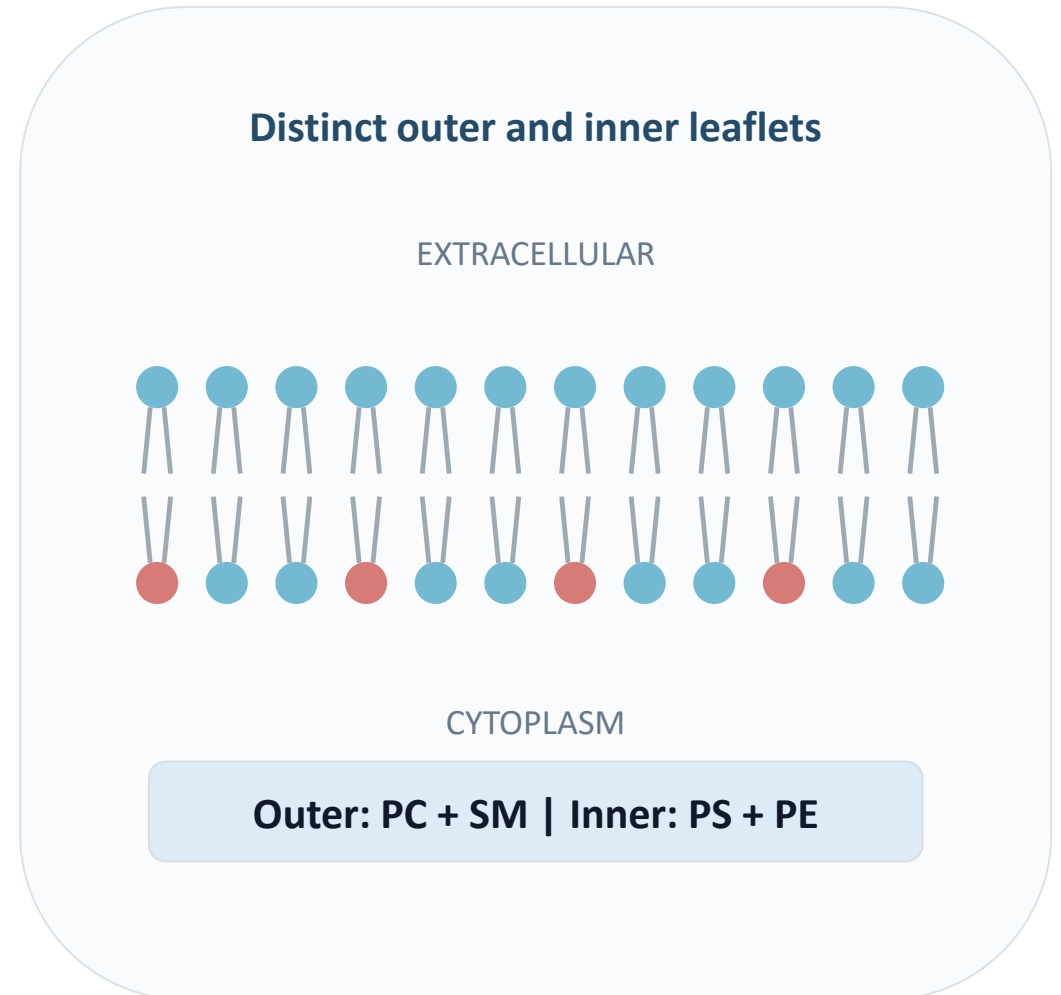
- Many molecules diffuse sideways in each leaflet
- Lateral movement permits local redistribution of components
- Specialized domains remain possible despite this mobility



Bilayer composition is heterogeneous

Not every membrane region has the same lipids

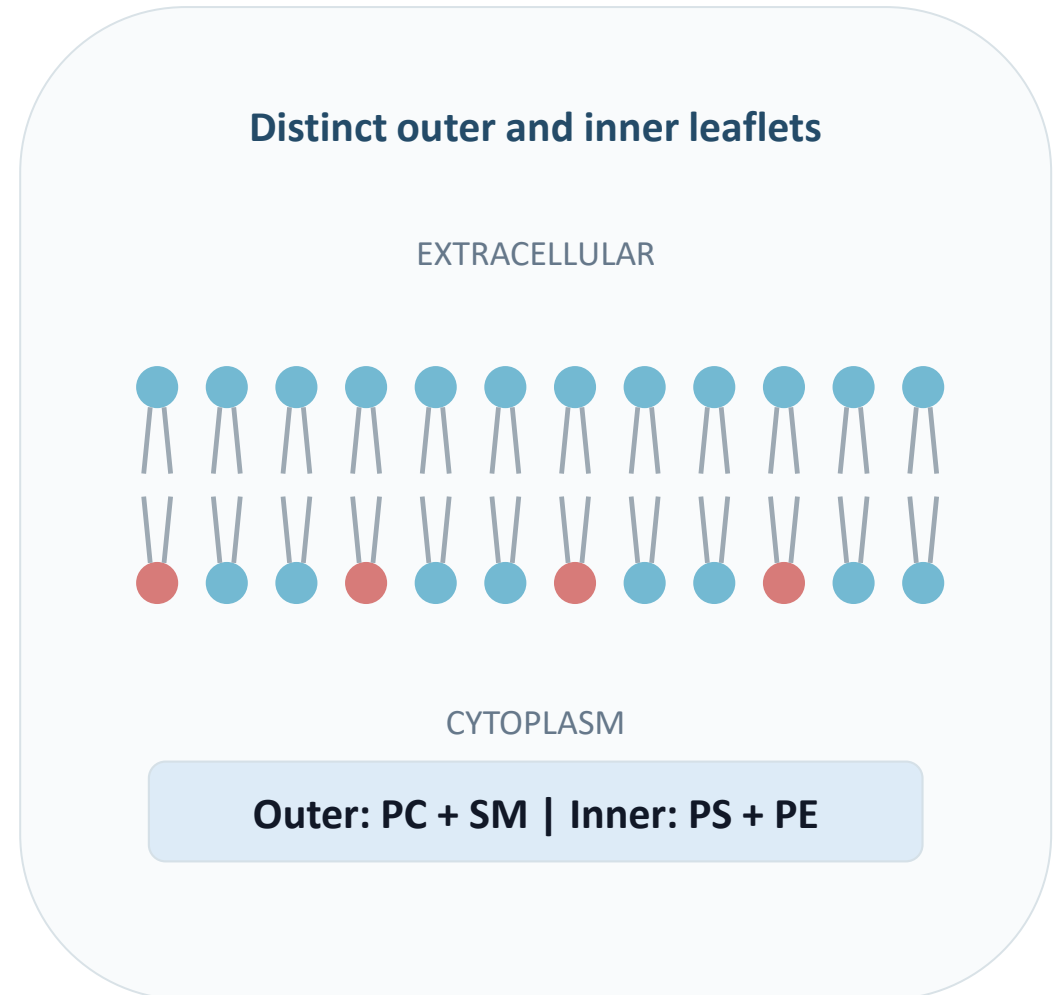
- Different phospholipids occupy different positions
- Local lipid composition influences membrane-protein behavior
- Some domains have distinctive lipid enrichment



The two membrane leaflets are not equivalent

Membrane asymmetry

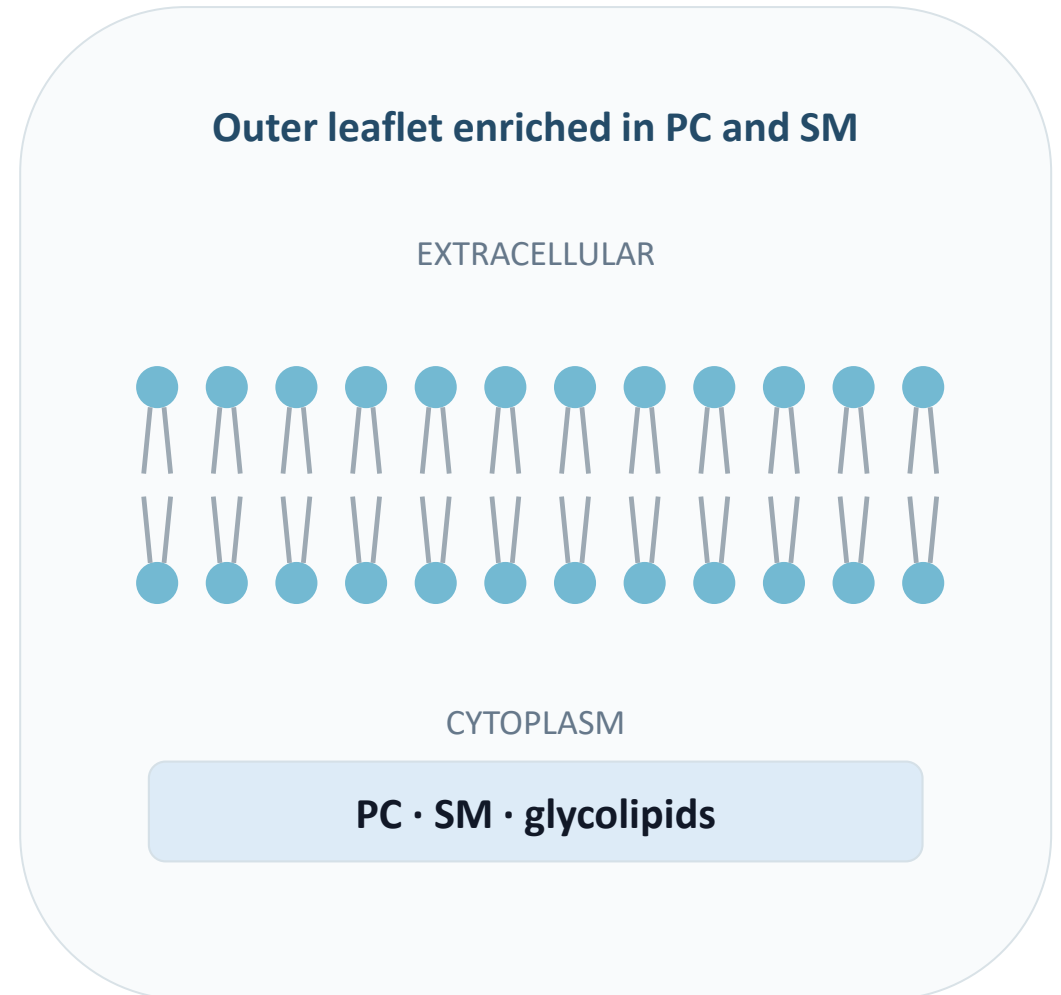
- Inner and outer faces have different lipid distributions
- This asymmetry is maintained by specific transport proteins
- Distribution contributes directly to membrane function



Outer-leaflet lipids have a characteristic pattern

Predominantly extracellular face

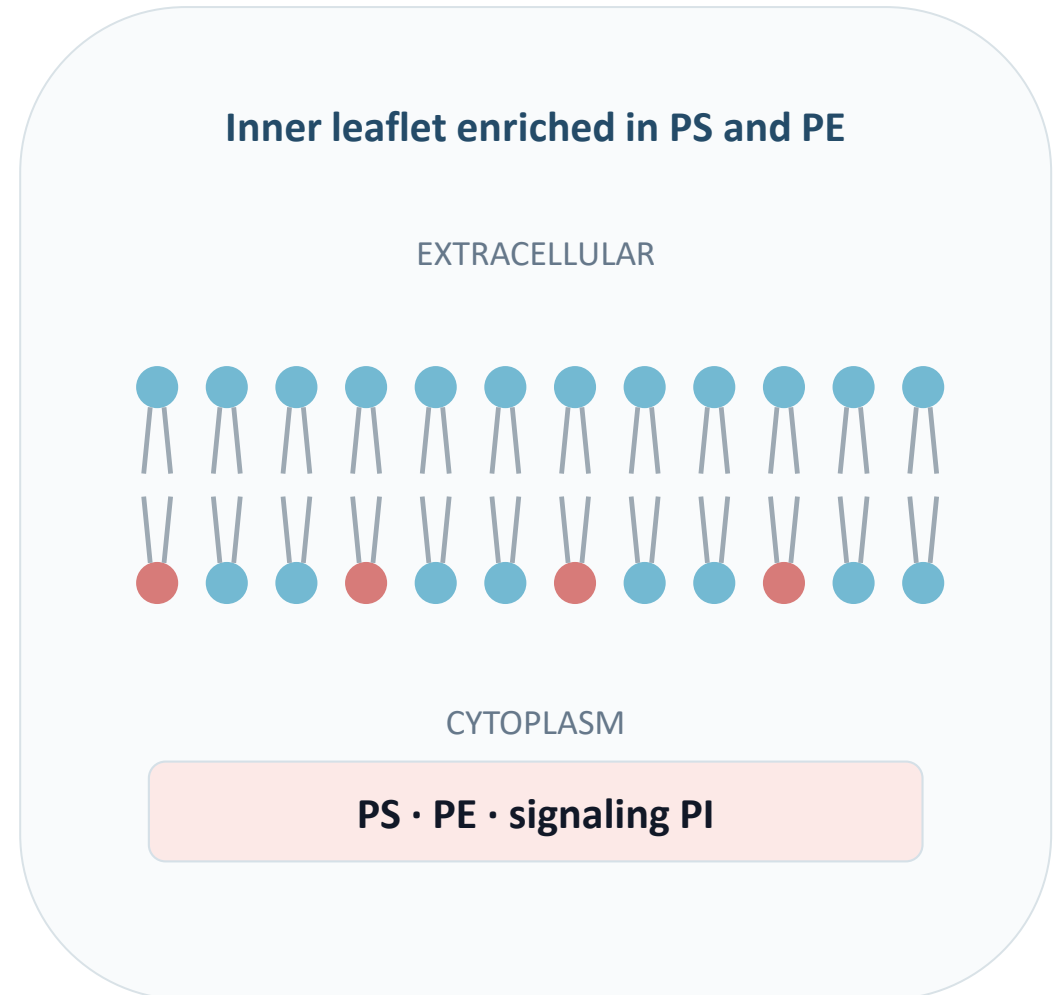
- Phosphatidylcholine is enriched on the outer face
- Sphingomyelin preferentially occupies this leaflet
- Glycolipids expose their carbohydrate groups outward



Inner-leaflet lipids support cytoplasmic functions

Predominantly cytoplasmic face

- Phosphatidylserine (PS) enriches the inner face
- Phosphatidylethanolamine (PE) is inner-leaflet predominant
- Signaling phosphatidylinositol pools interact with cytosolic proteins

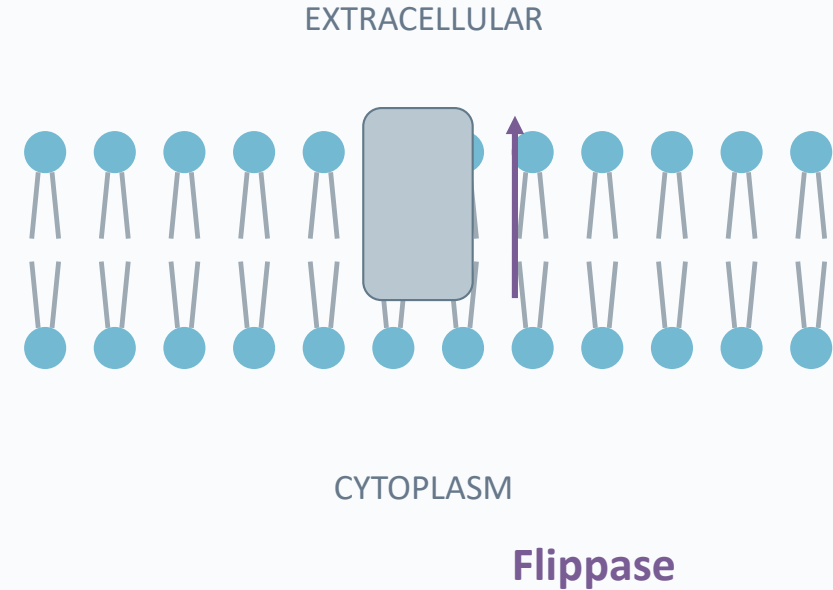


Flippases help maintain the transbilayer pattern

Asymmetry is actively organized

- Flippases transfer particular phospholipids between faces
- They contribute to the distribution shown Fig. 1.7
- Loss of normal distribution can alter biological signals

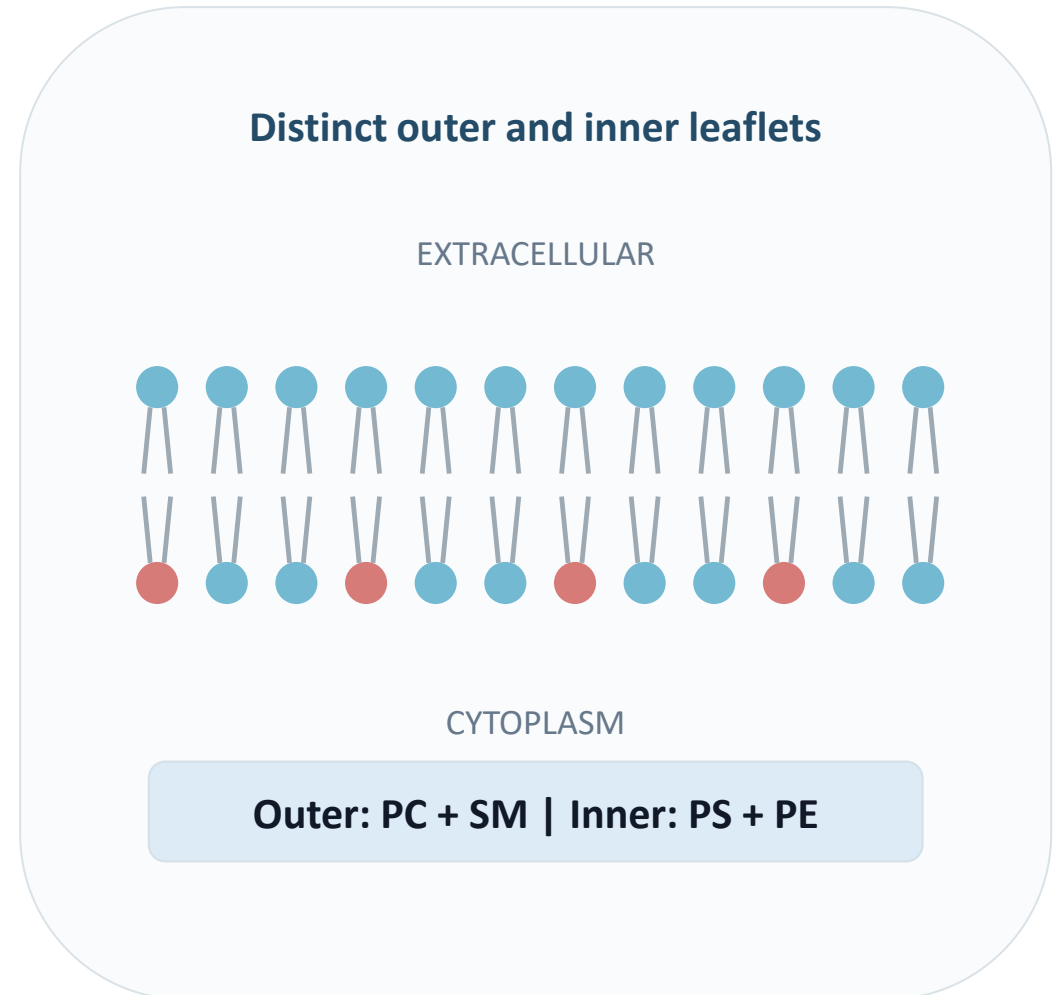
Flippases preserve asymmetric distribution



Lipid localization is functionally significant

Beyond a compositional difference

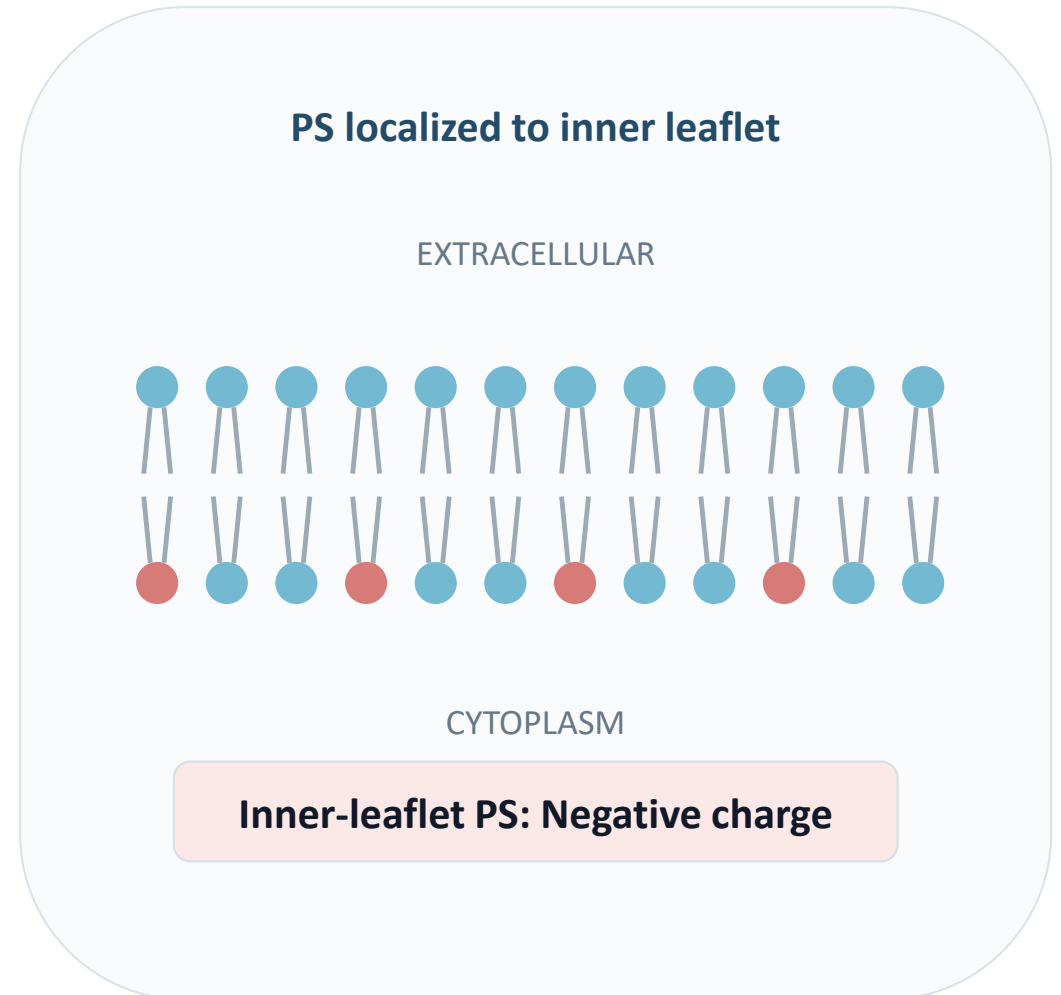
- Specific phospholipids interact with membrane proteins
- Leaflet position changes electrostatic interactions
- Redistribution can generate recognition signals



Phosphatidylserine confers negative surface charge

The normal inner-leaflet state

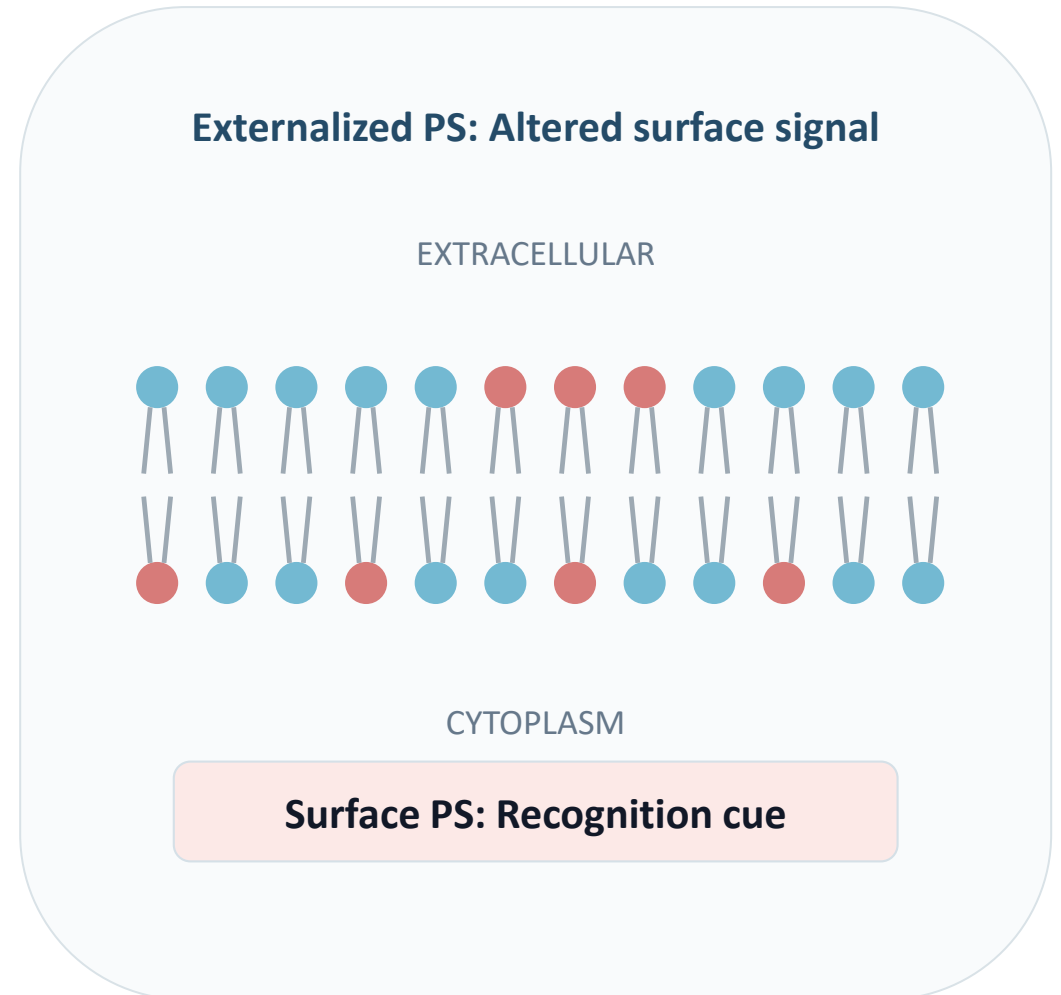
- PS is normally restricted predominantly to the inner face
- Its anionic character promotes electrostatic protein interactions
- Its outward translocation changes what other cells detect



Externalized phosphatidylserine signals apoptosis

An “eat me” surface cue

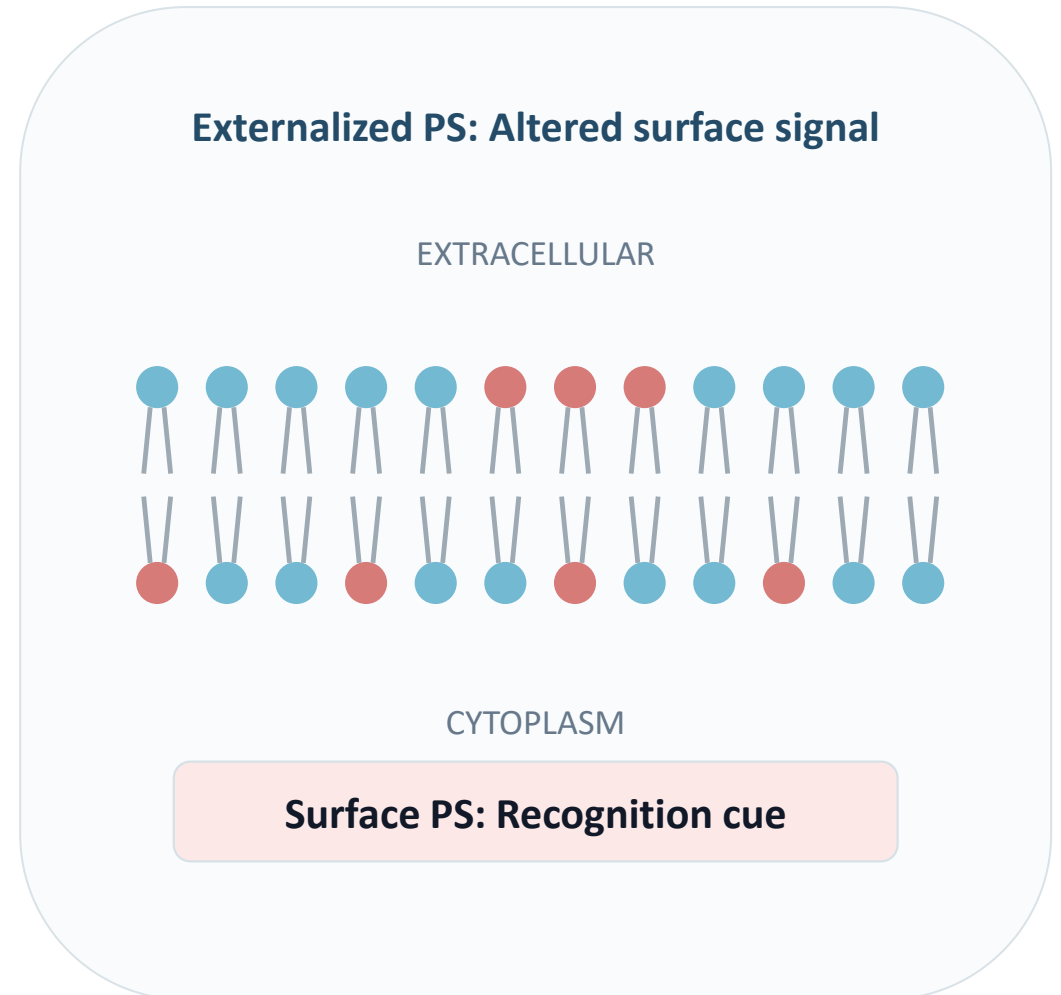
- Programmed cell death is accompanied by PS exposure
- External PS promotes recognition of dying cells
- The same lipid has different consequences depending on leaflet



Platelet phosphatidylserine supports coagulation

A second context for PS exposure

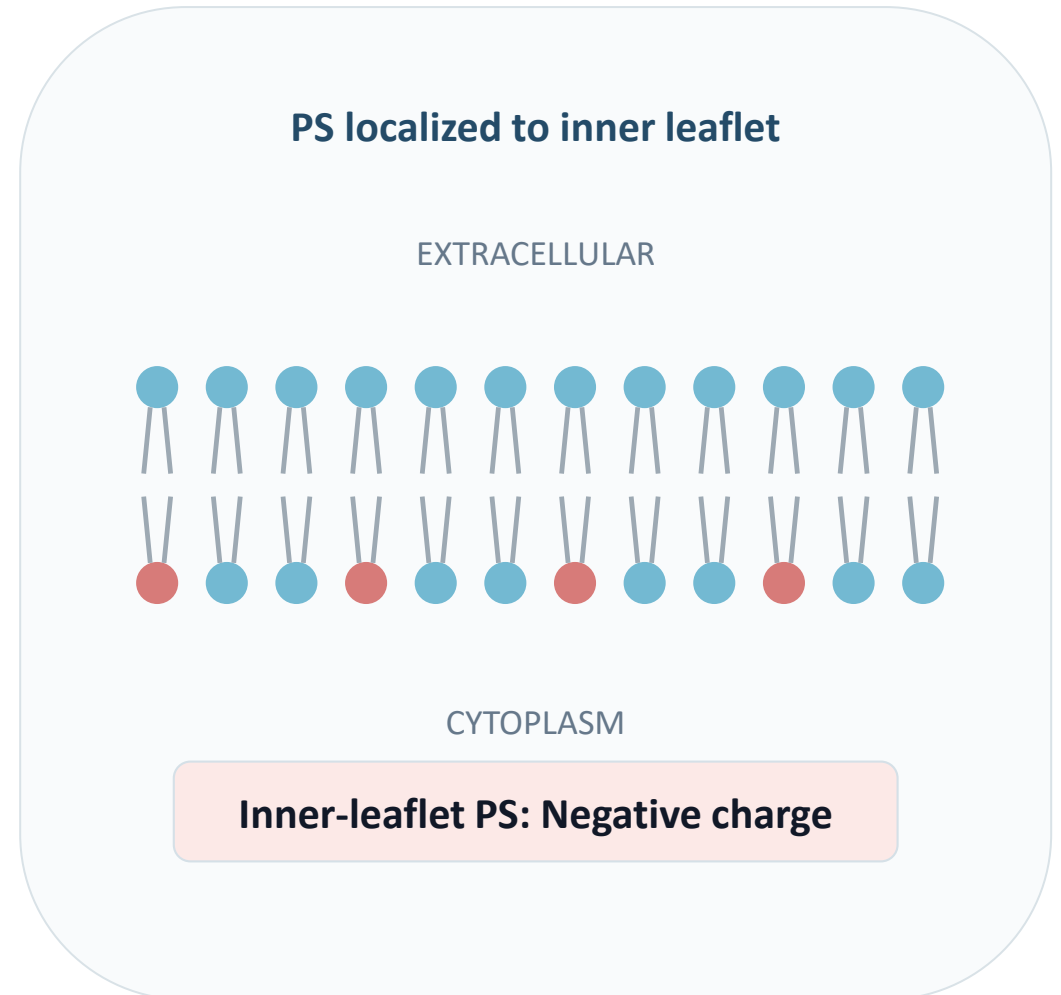
- Exposed PS acts as a cofactor in blood clotting
- Its biologic role depends on cell state and surface accessibility
- Apoptotic recognition and hemostasis are distinct outcomes



Anionic lipids recruit cytoplasmic proteins

Electrostatic membrane organization

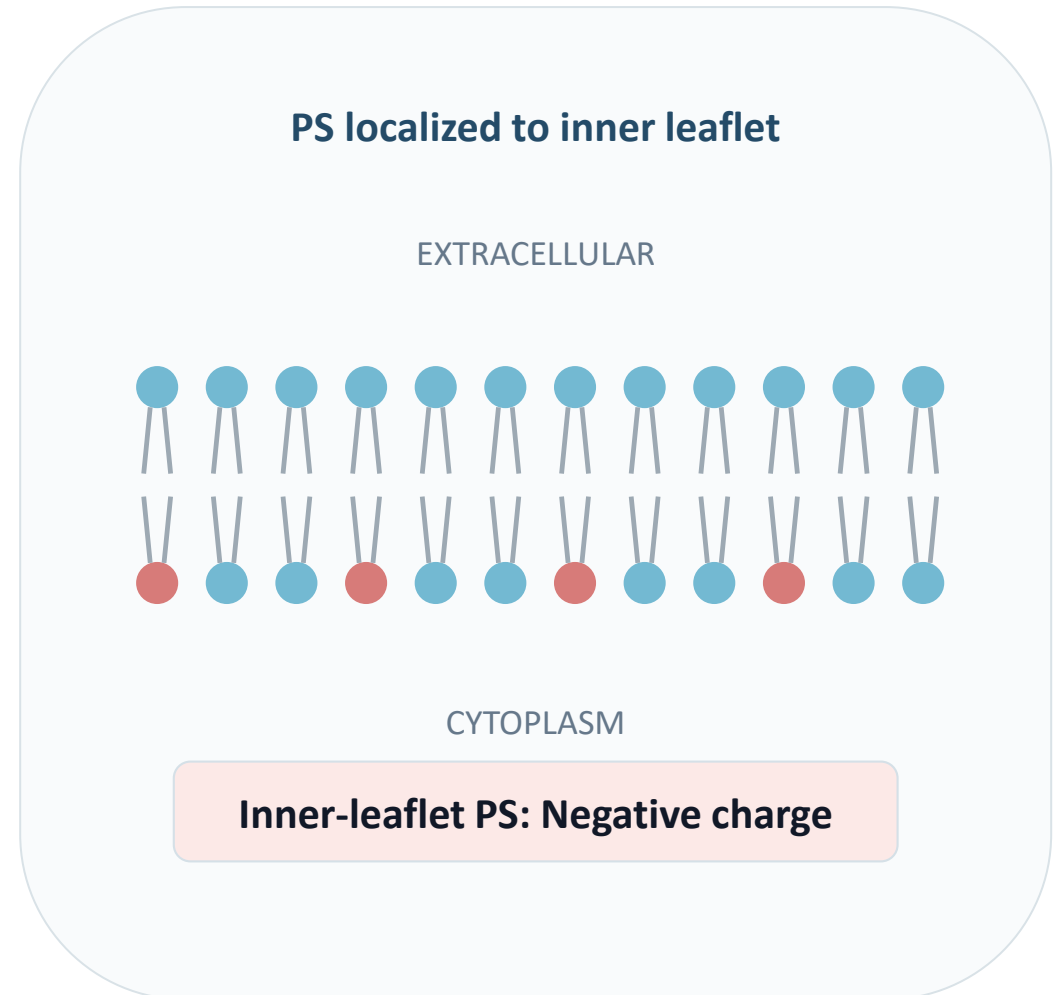
- Negative inner-leaflet charge helps position proteins
- Protein–lipid interactions can change protein distribution
- Localization influences signaling and membrane function



Phosphatidylinositol is a signaling platform

Functions of the cytosol-facing PI pool

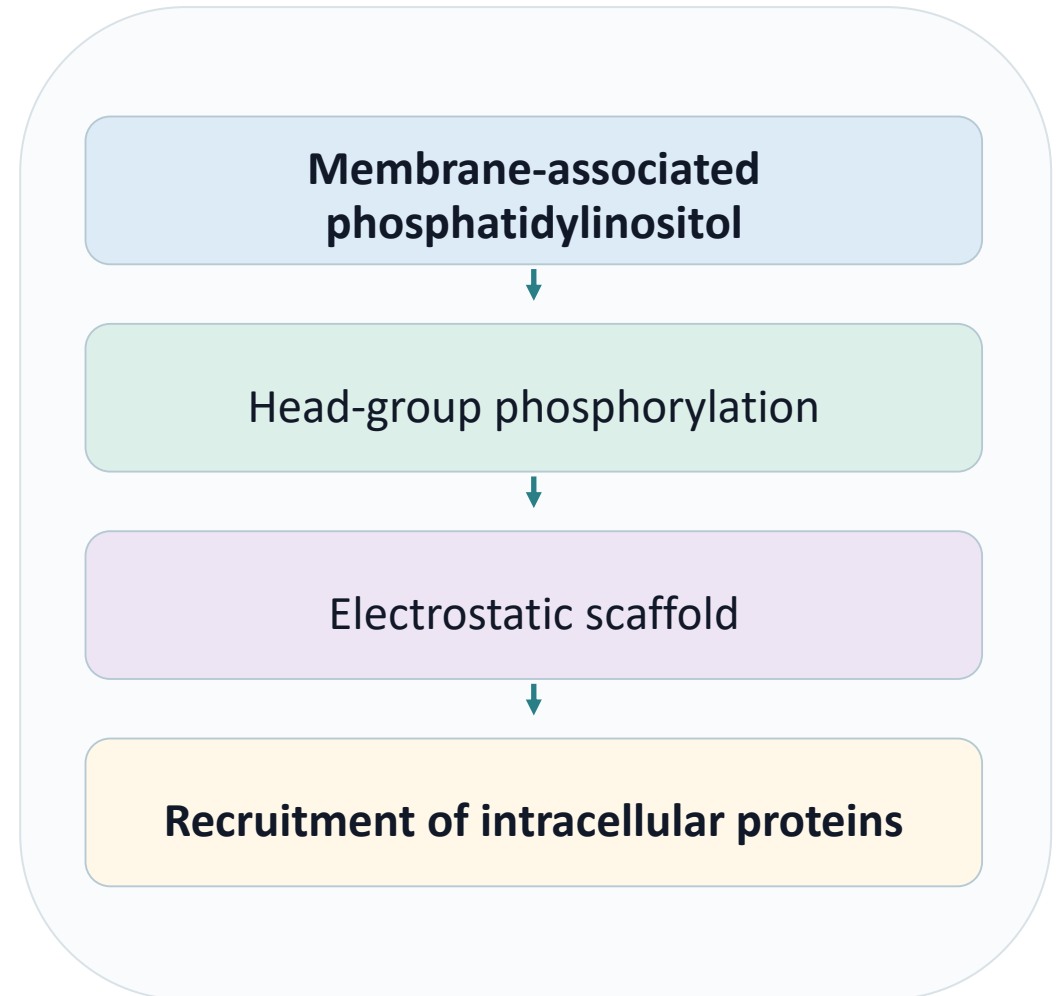
- Phosphatidylinositol (PI) can be phosphorylated
- Phosphorylated PI species provide electrostatic docking sites
- Their modified head groups can recruit intracellular proteins



Phosphorylation changes phosphoinositide function

From membrane lipid to binding site

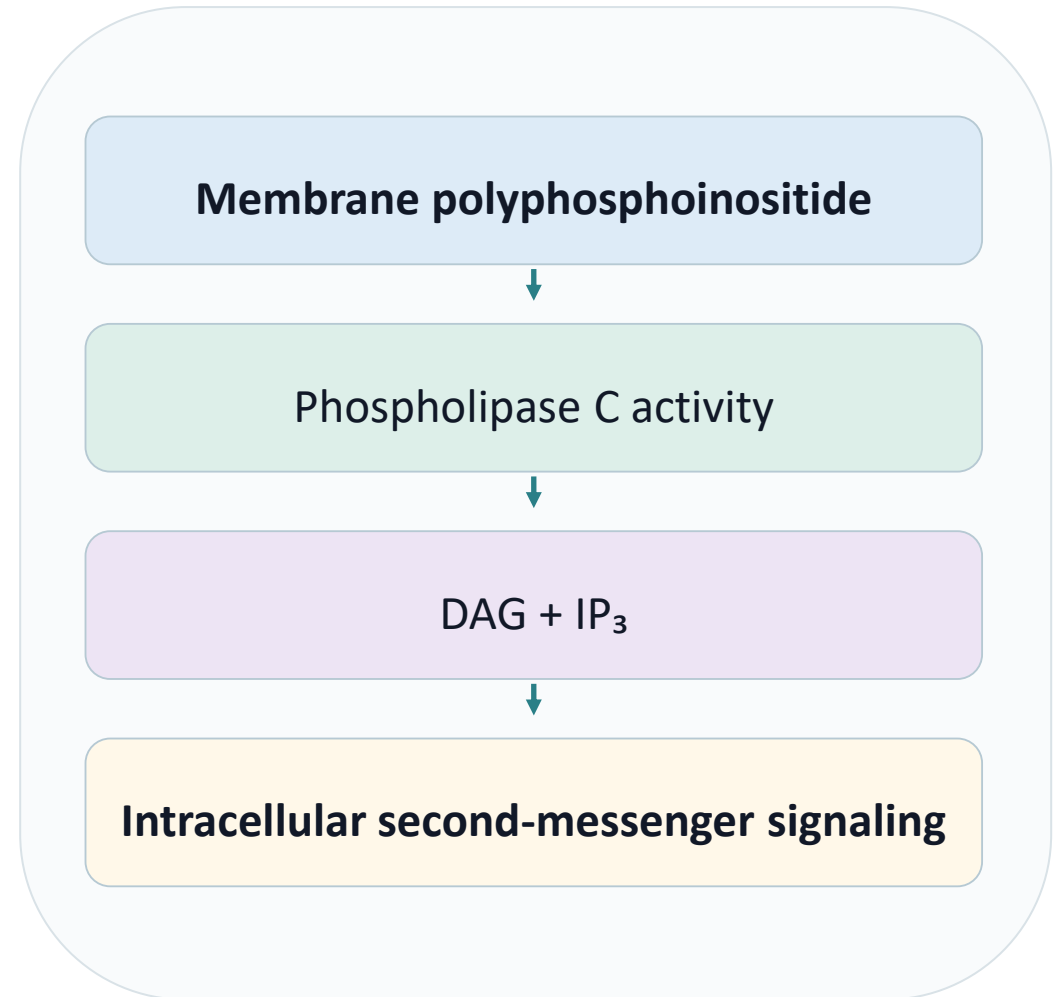
Head-group phosphorylation turns a lipid into a protein-binding platform.



Phospholipase C cleaves polyphosphoinositides

An alternative outcome for signaling PI lipids

One membrane lipid can yield two intracellular second messengers.



DAG and IP₃ are lipid-derived second messengers

Two products of phosphoinositide hydrolysis

Phosphoinositide cleavage produces two distinct signals.

Diacylglycerol (DAG)

Lipid-derived signal

Associated with the membrane

Inositol trisphosphate (IP₃)

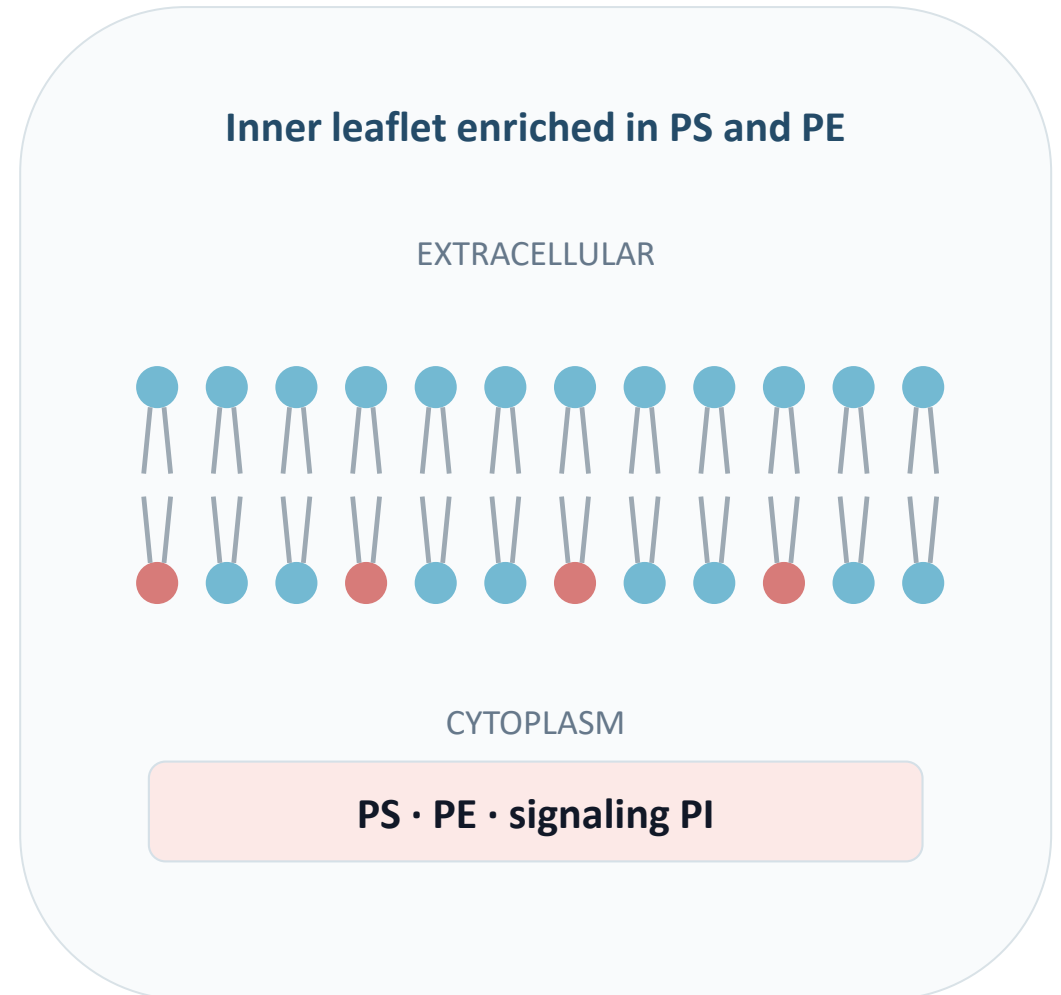
Inositol phosphate signal

Acts inside the cell

Phosphatidylethanolamine favors the inner leaflet

A major feature of leaflet asymmetry

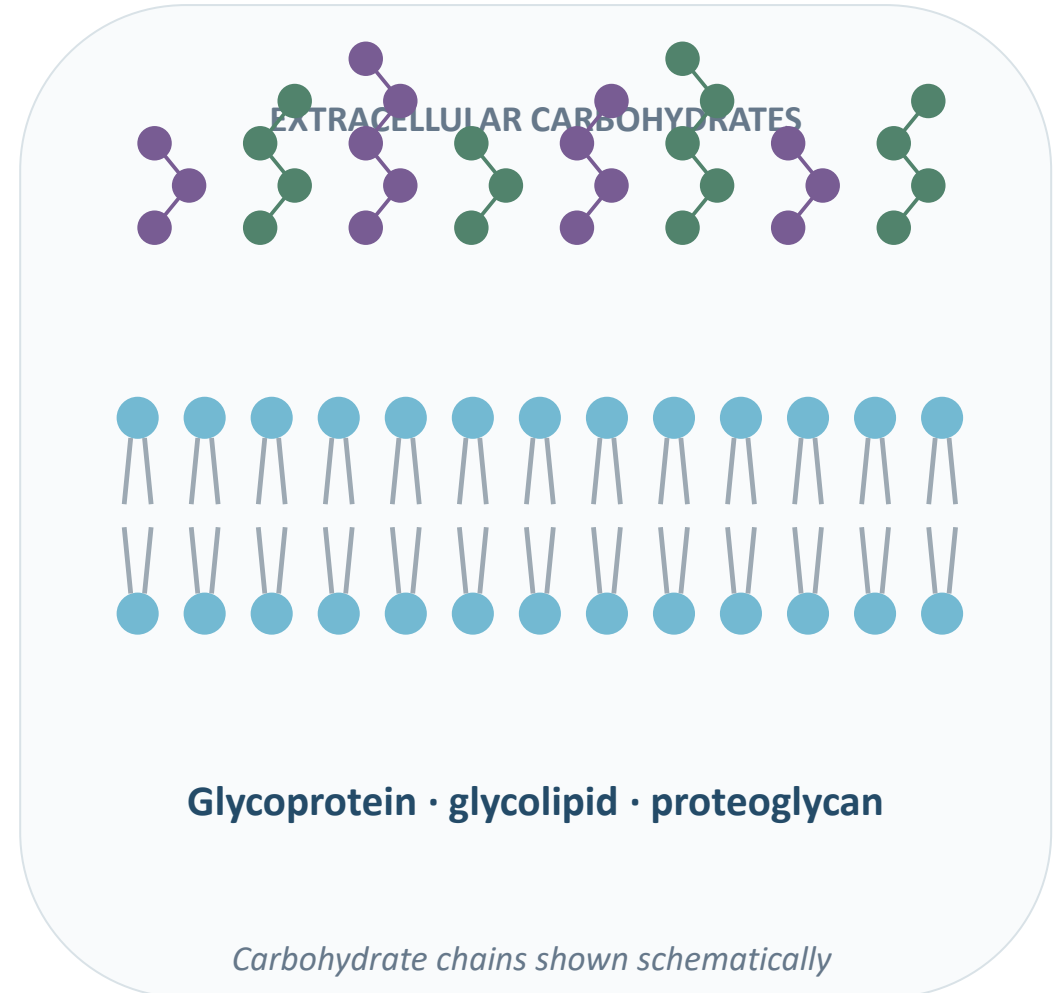
- PE is predominantly cytoplasmic in the illustrated membrane
- PE differs in localization from sphingomyelin
- The collective lipid pattern defines membrane organization



Glycolipids project carbohydrates externally

Extracellular surface chemistry

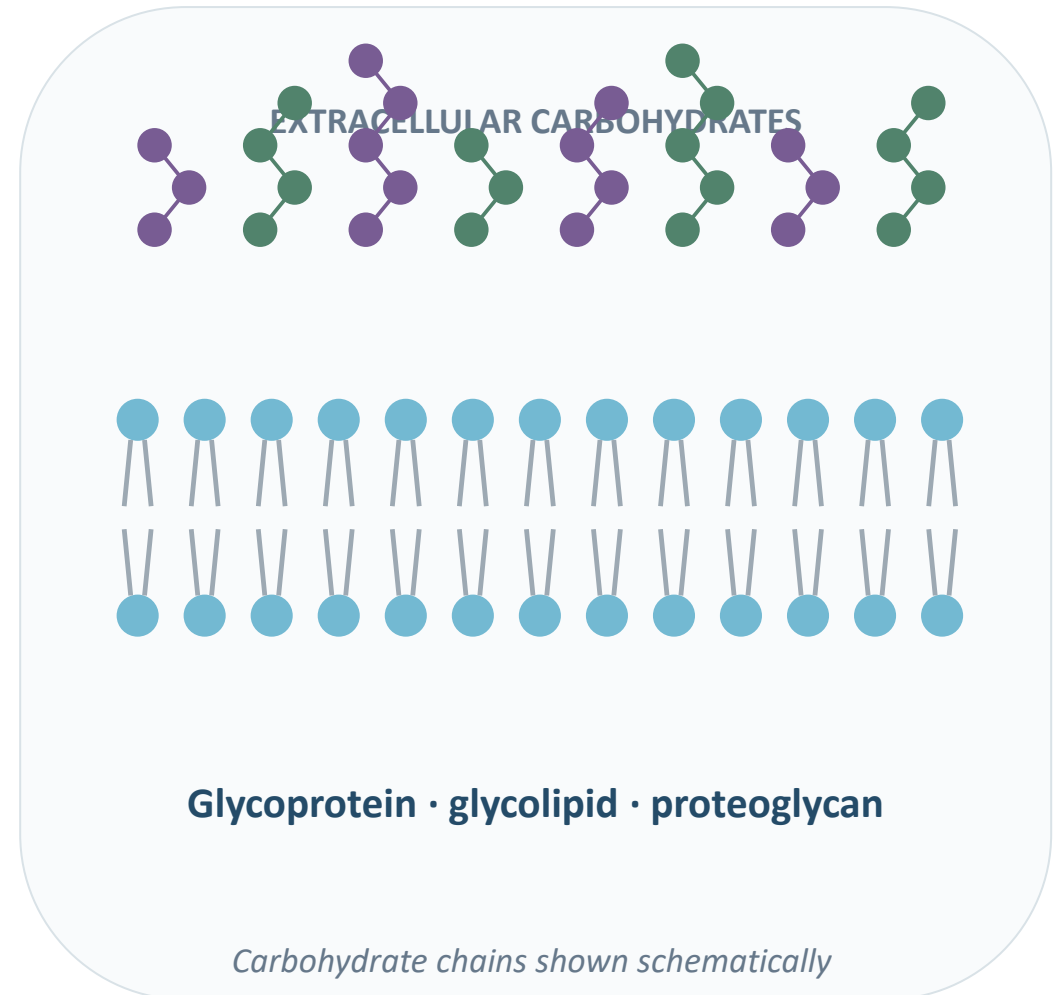
- Glycolipids occur on the outward-facing surface
- Their carbohydrate moieties add chemical complexity
- Together with glycoproteins, they contribute to the glycocalyx



Gangliosides bear complex sugar and sialic acid groups

Surface carbohydrate specialization

- Gangliosides are glycolipids with complex sugar chains
- Terminal sialic acids contribute negative charge
- This surface chemistry supports charge-dependent interactions



Glycolipids contribute to intercellular interactions

Two examples given

Surface carbohydrate chemistry participates in cell recognition.

Inflammatory cell recruitment

Extracellular carbohydrate and charge-based interactions

Sperm–egg fusion

Surface glycolipid interactions contribute to recognition

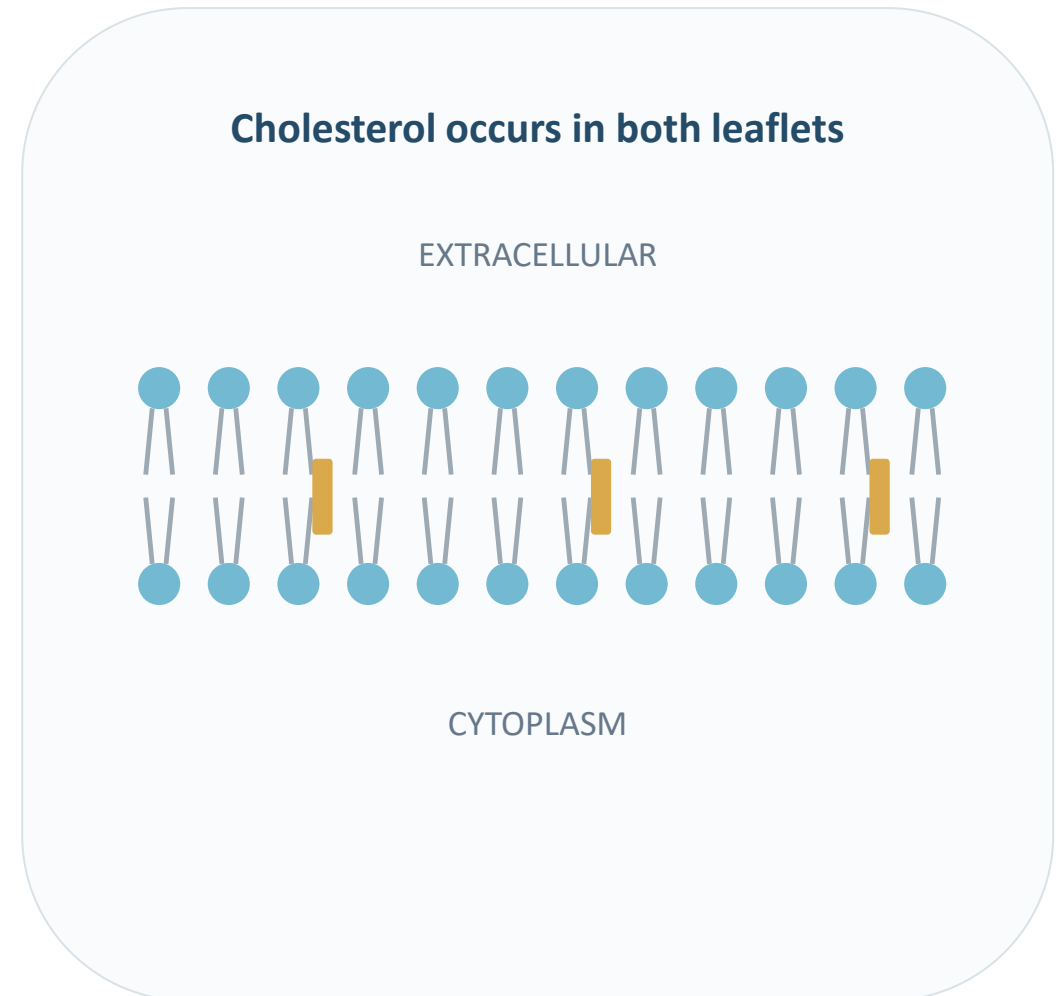
Membrane organization

Glycolipids can enrich specific lipid domains

Cholesterol is present in both leaflets

A key component of membrane domains

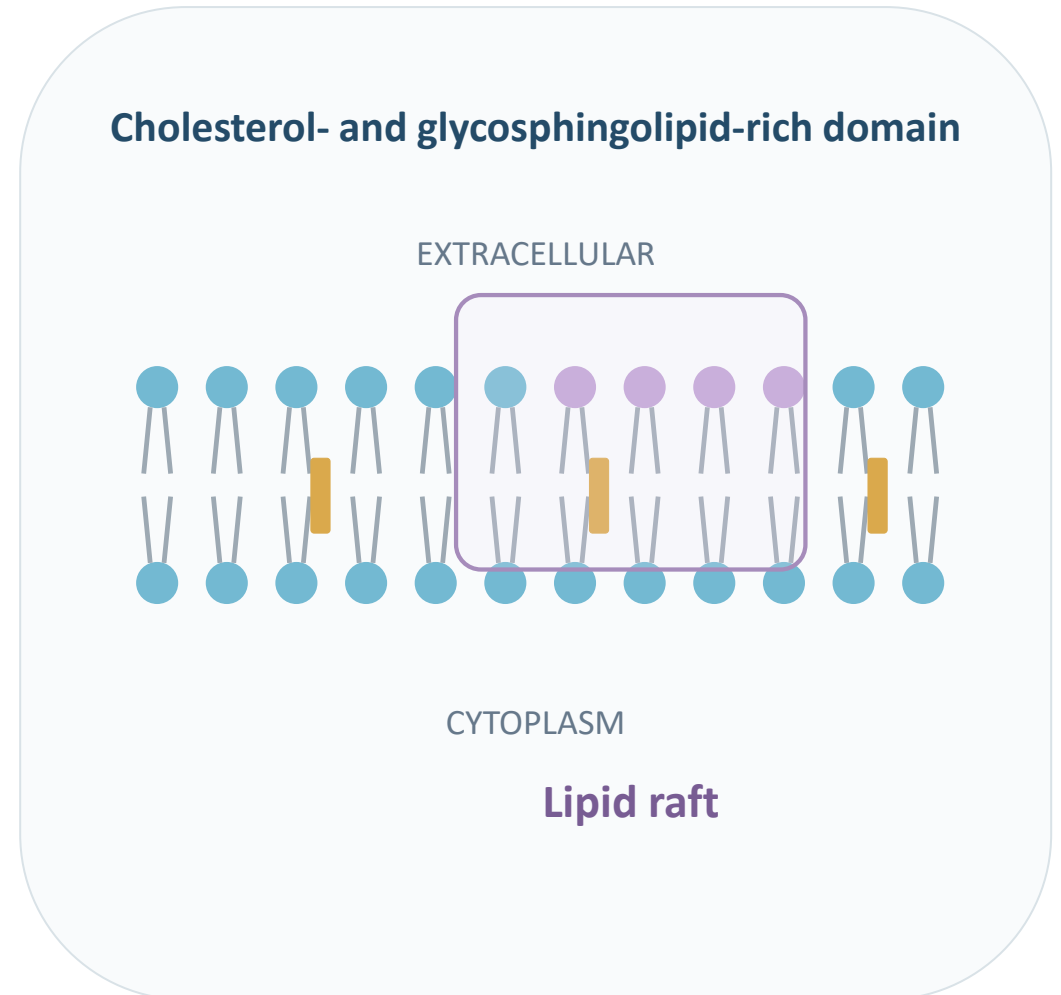
- Cholesterol is distributed across the bilayer
- It enriches particular lateral membrane regions
- It occurs with glycosphingolipids in lipid rafts



Lipid rafts are compositionally specialized domains

Nonrandom lateral organization

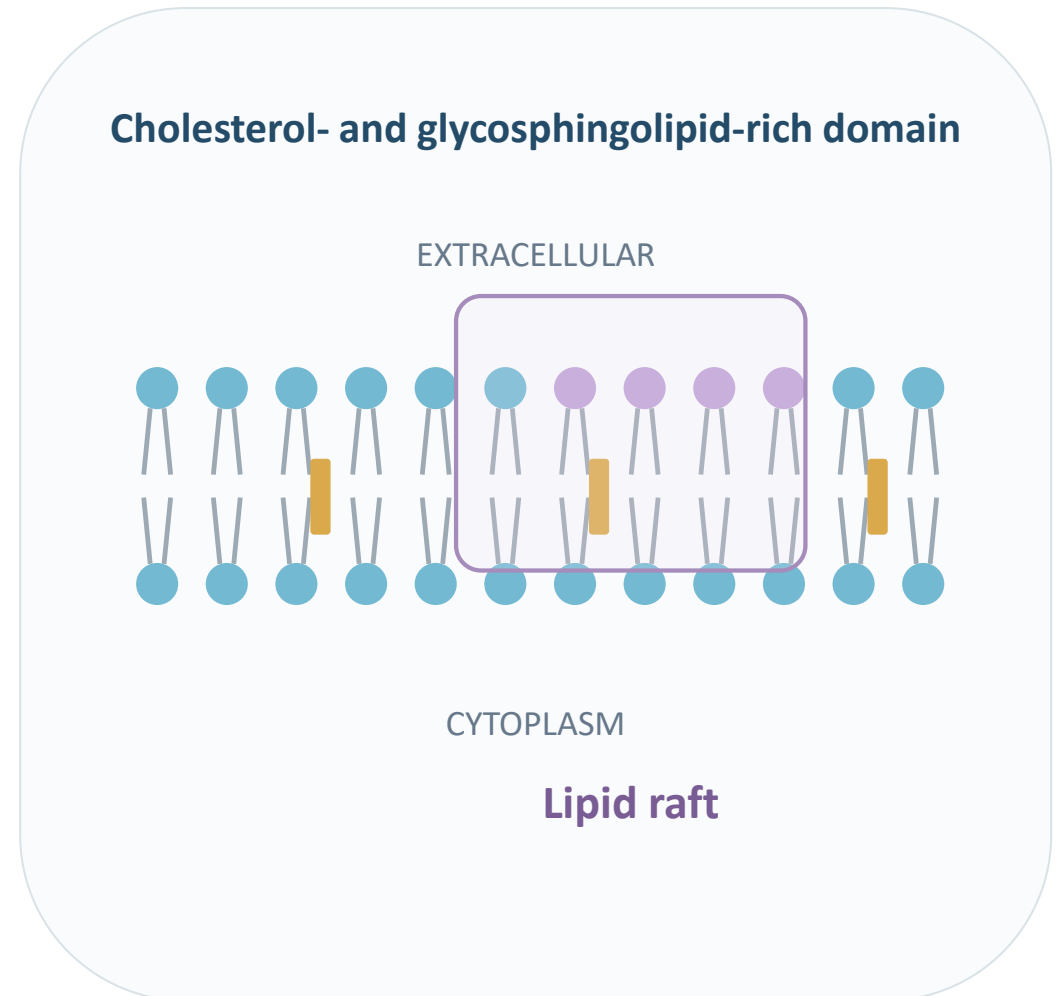
- Some membrane regions are cholesterol-rich
- Glycosphingolipids are also enriched in these areas
- Rafts coexist with overall lateral membrane fluidity



Protein partitioning depends on local lipid composition

Not every protein enters every domain

- Proteins differ in solubility across lipid environments
- That difference generates nonrandom protein distributions
- Lipid composition therefore helps spatially organize function



Membrane domains coordinate cellular operations

Consequences of geographic organization

Spatial localization organizes signaling, adhesion and membrane traffic.

Signaling

Local concentration of receptors and other effectors

Adhesion

Cell–cell and cell–matrix interaction sites

Membrane traffic

Specialized sites for vesicle budding or fusion

Membrane proteins mediate essential cellular functions

Three major functional classes

Membrane proteins determine which tasks a cell surface can perform.

Transport

Ions, metabolites and other solutes

Macromolecule uptake

Fluid-phase and receptor-mediated entry

Interfaces

Cell–ligand, cell–matrix and cell–cell interactions

Protein attachment often predicts functional role

A useful structural rule of thumb

The way a protein contacts the bilayer helps predict its function.

Multi-pass proteins

Often pores

Often molecular
transporters

Superficial attachments

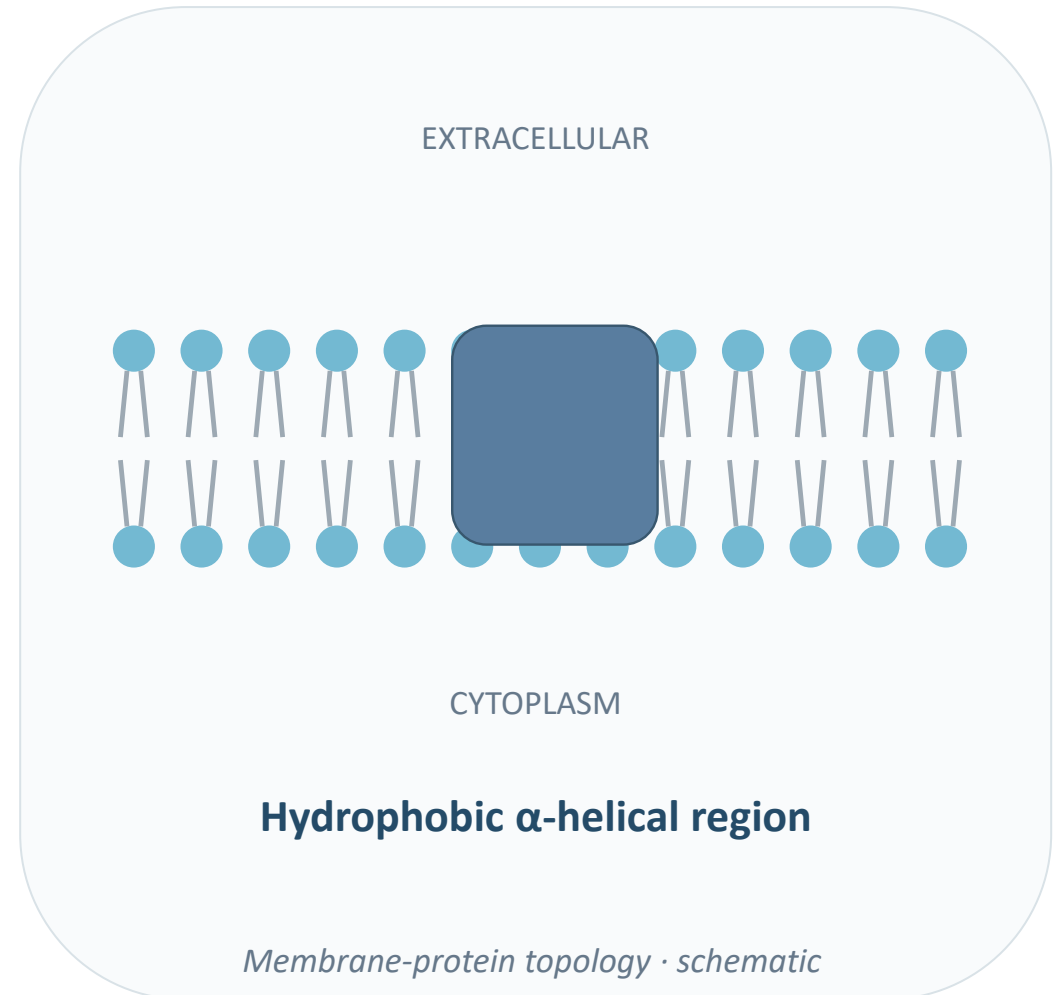
More often
participate in
signaling

May be stabilized by
lipid linkages

Integral proteins traverse the lipid bilayer

One of four attachment mechanisms

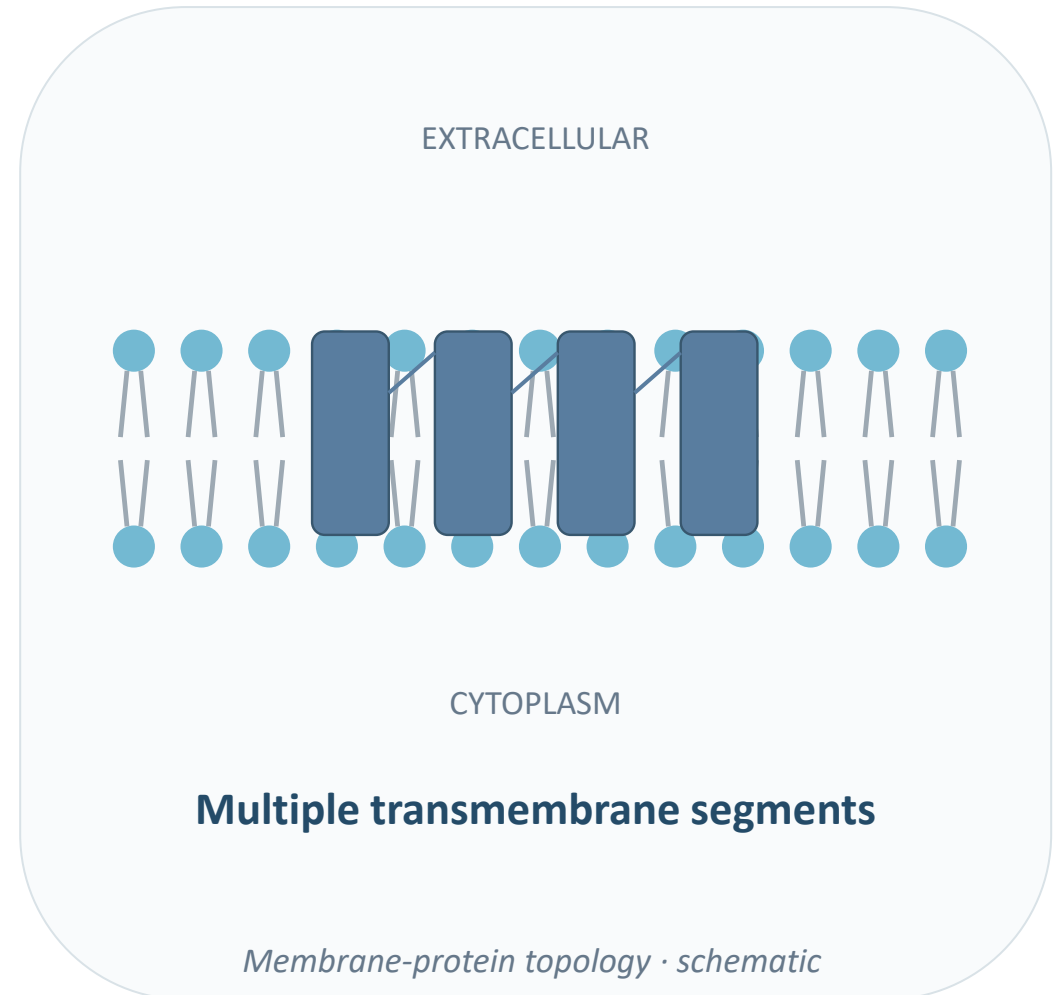
- One or more hydrophobic α -helical segments cross the membrane
- The segments provide a stable lipid-facing interface
- Transmembrane proteins transmit signals across the bilayer



Multiple membrane-spanning regions support transport

A topology commonly associated with pores

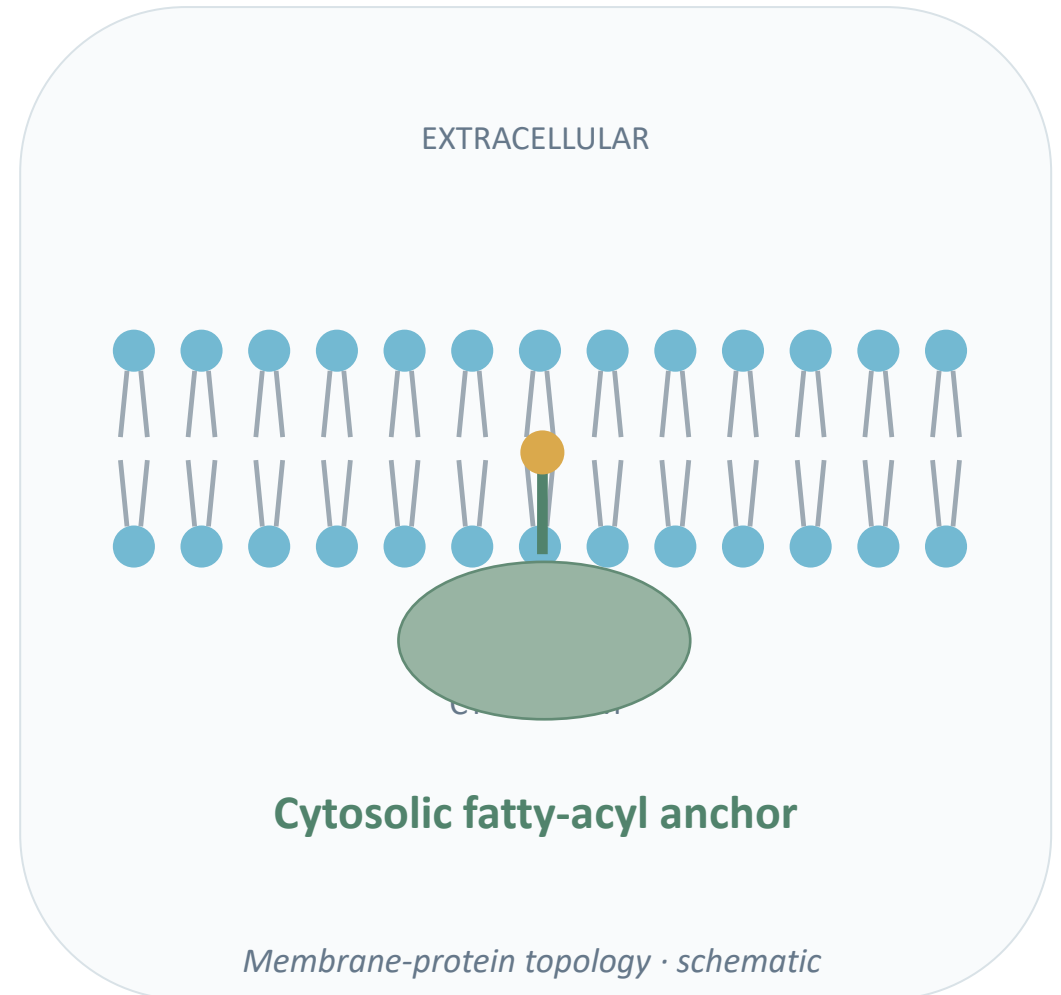
- Some transmembrane proteins cross the bilayer repeatedly
- Multi-pass architecture often marks channels or carriers
- Specific transport mechanisms are covered in the next topic



Membrane proteins may be tethered by fatty acids

Posttranslational lipid anchors

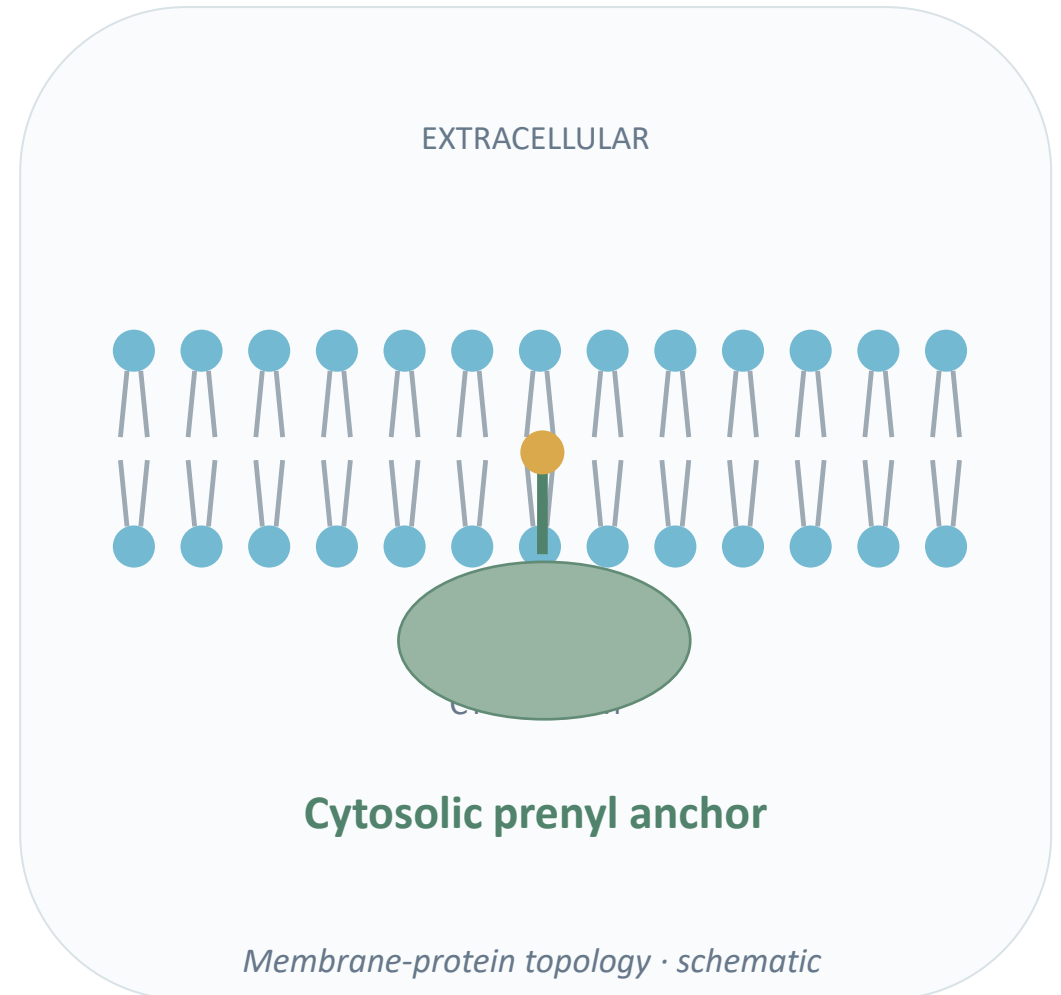
- Fatty acids are added after protein synthesis
- Examples include palmitic and myristic acids
- These groups insert into the cytoplasmic face



Prenylation is another cytosolic membrane anchor

Lipid modification of protein

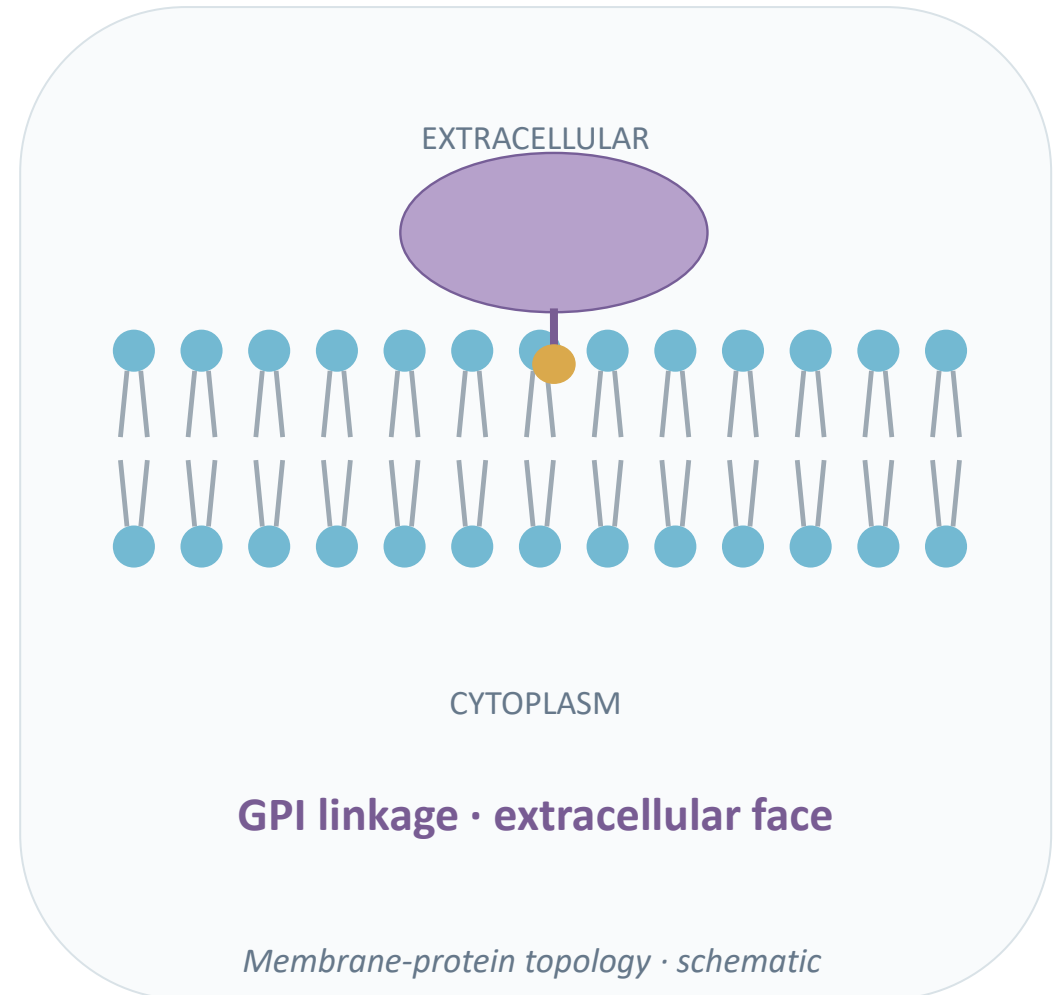
- Prenyl groups provide hydrophobic membrane attachment
- Farnesyl groups are an example
- These modified proteins associate with the inner face



GPI anchors attach proteins externally

A different membrane-facing orientation

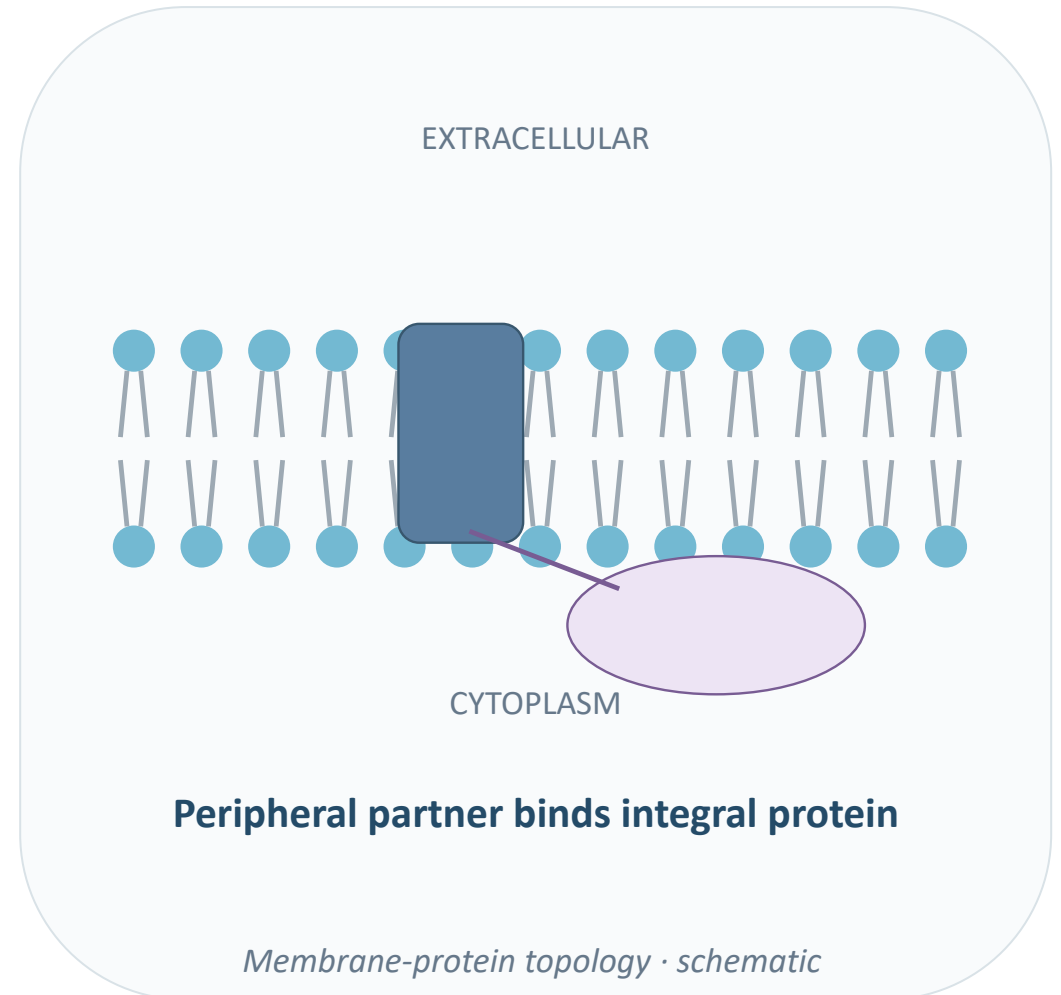
- Glycosylphosphatidylinositol (GPI) tails are added after synthesis
- The linkage holds proteins at the extracellular face
- GPI linkage is distinct from cytoplasmic lipid modifications



Peripheral proteins can bind indirectly

Noncovalent membrane association

- Some proteins contact integral membrane proteins
- Noncovalent interactions maintain their attachment
- They need not themselves penetrate the lipid core



Membrane association: Four major mechanisms

Topology and linkage determine location

Four structural solutions for linking protein to membrane

Crosses or anchors the bilayer

Integral transmembrane

Cytosolic lipid modification

Association without spanning

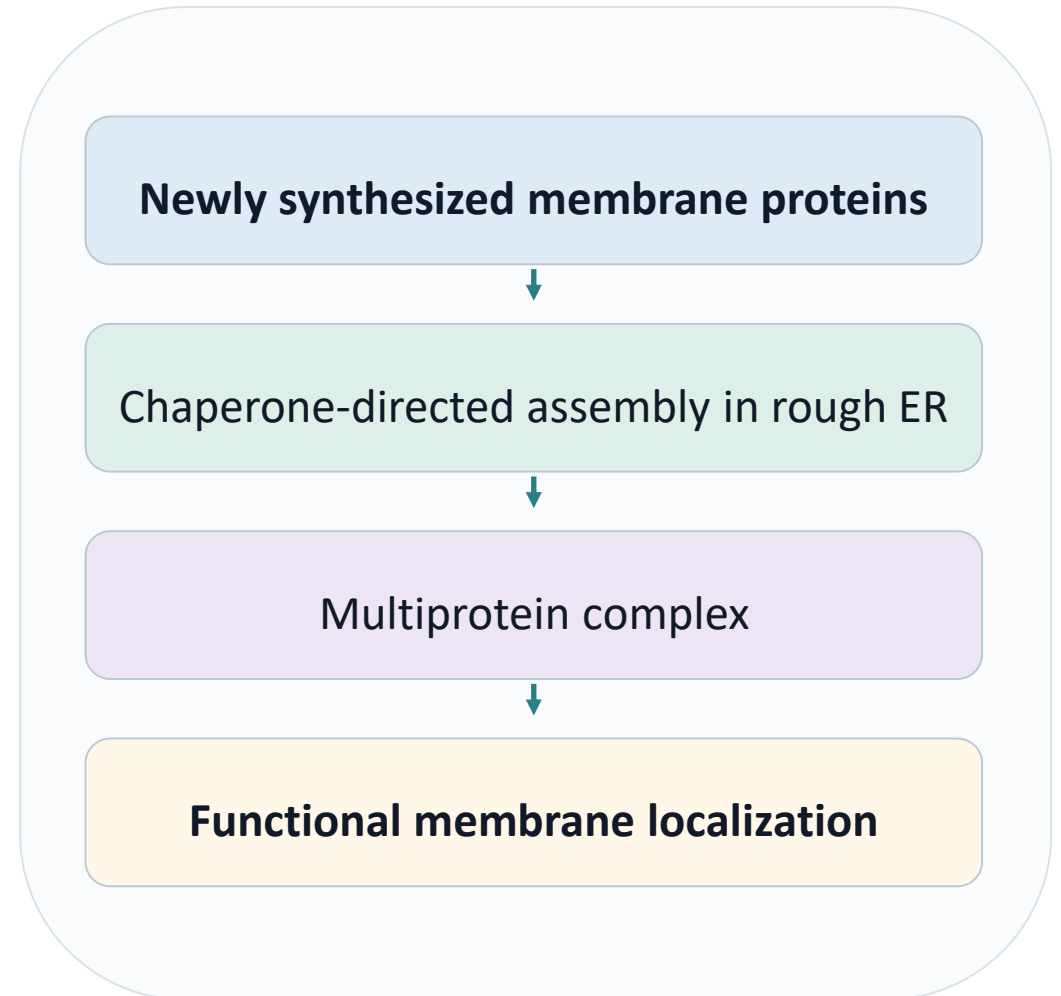
External GPI linkage

Noncovalent association

Protein complexes can assemble in the rough ER

The assembly site need not be the cell surface

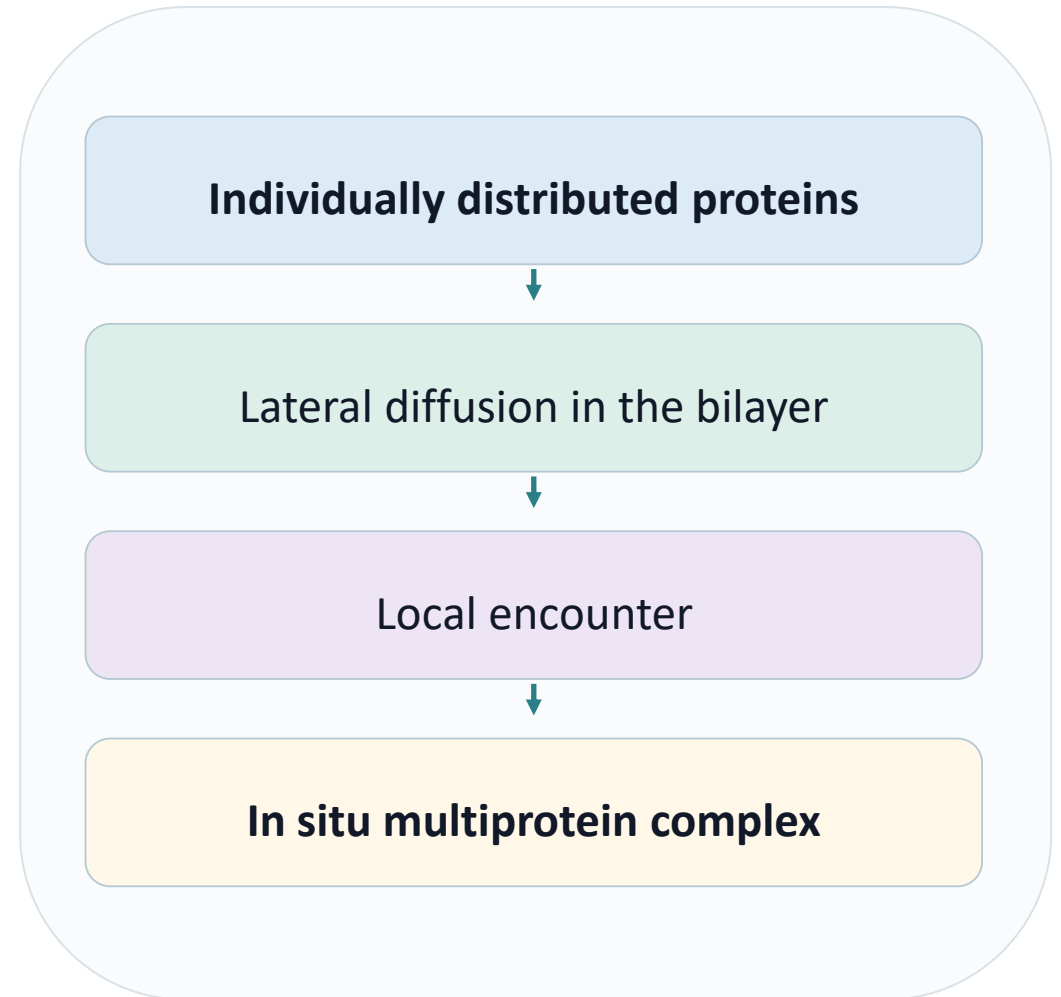
Some membrane complexes assemble before reaching the cell surface.



Membrane proteins can assemble after lateral diffusion

Complex formation at the plasma membrane

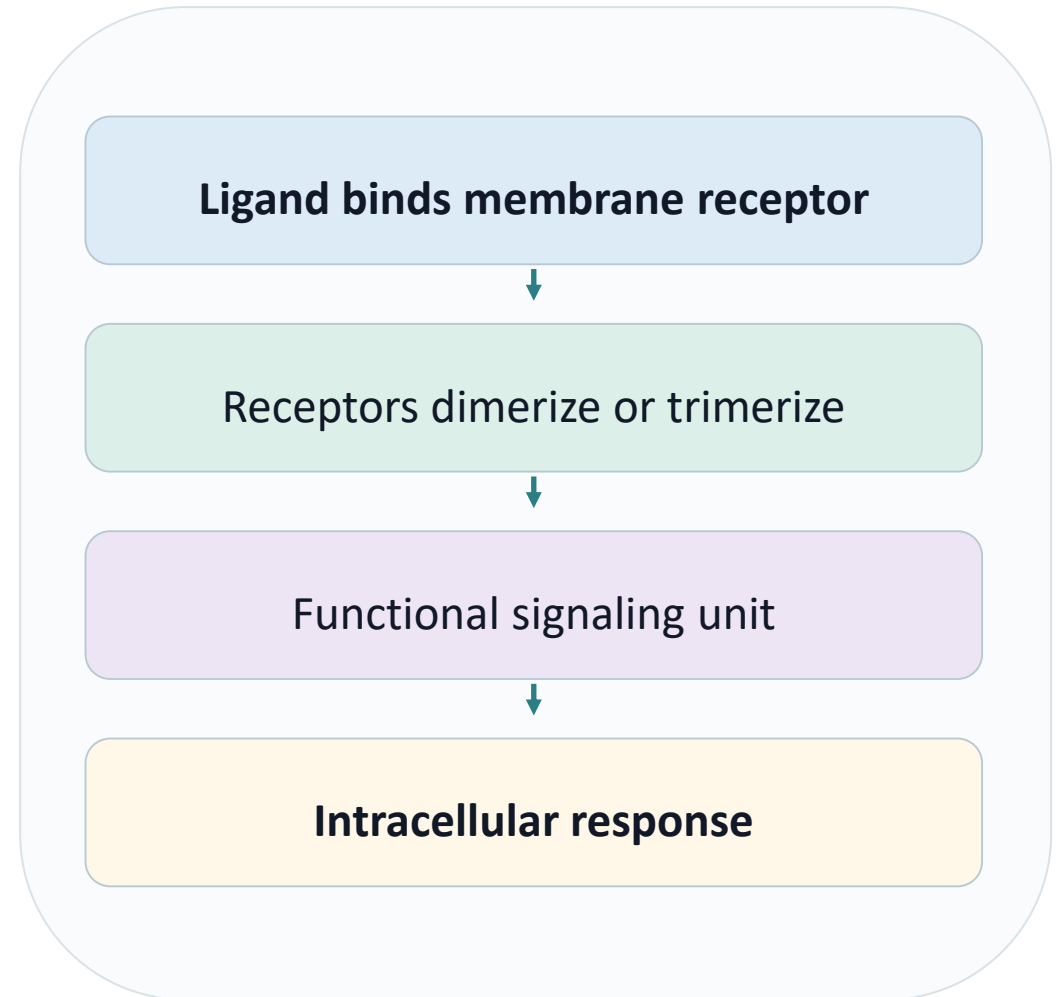
Other protein complexes form directly on the plasma membrane.



Ligand binding can promote receptor oligomerization

Functional signaling assemblies

Ligand binding promotes an active multi-subunit receptor unit.



Fluid membranes still establish physical boundaries

Two localization strategies

Mobility coexists with spatial boundaries.

Lipid-domain sorting

Distinct lipid compositions

Preferential protein partitioning

Intercellular junctions

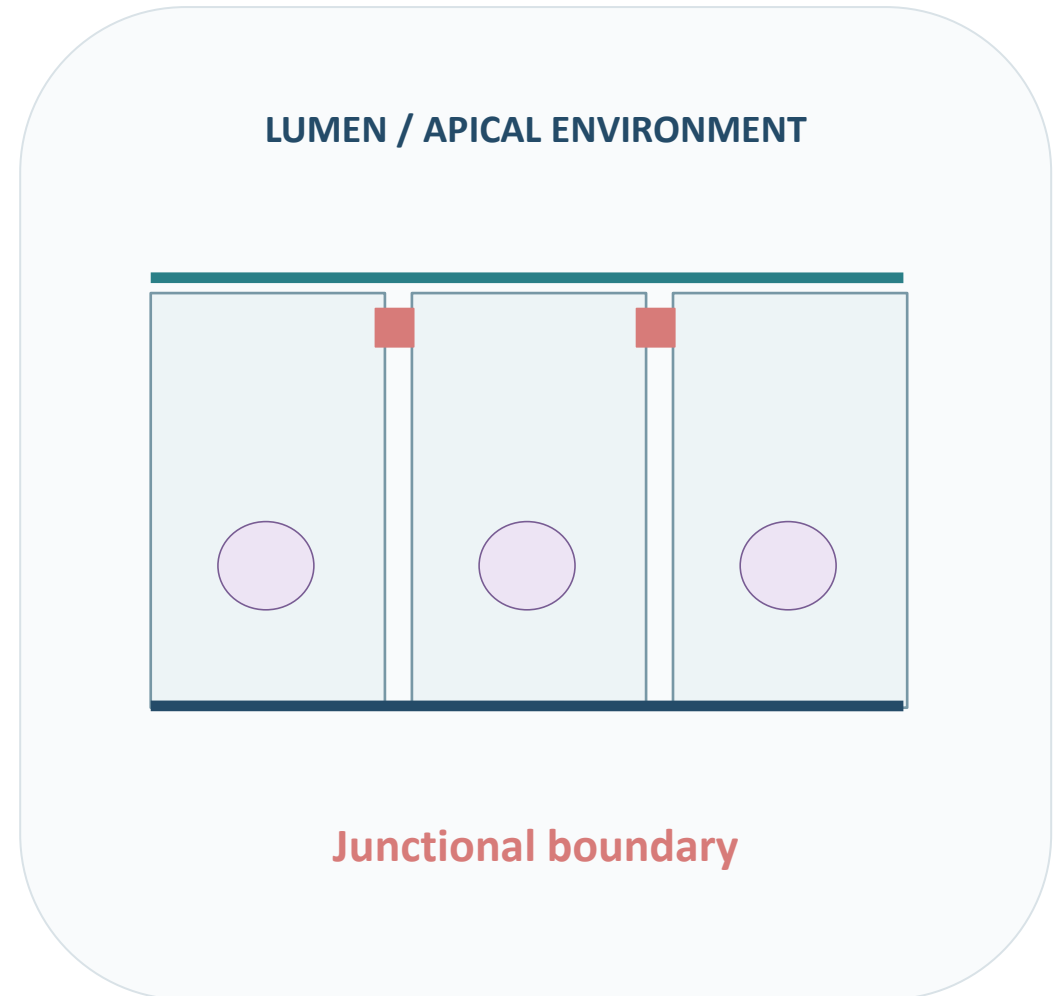
Protein–protein junctional contact

Boundaries between membrane regions

Tight junctions can delimit membrane compartments

Membrane domains remain distinct

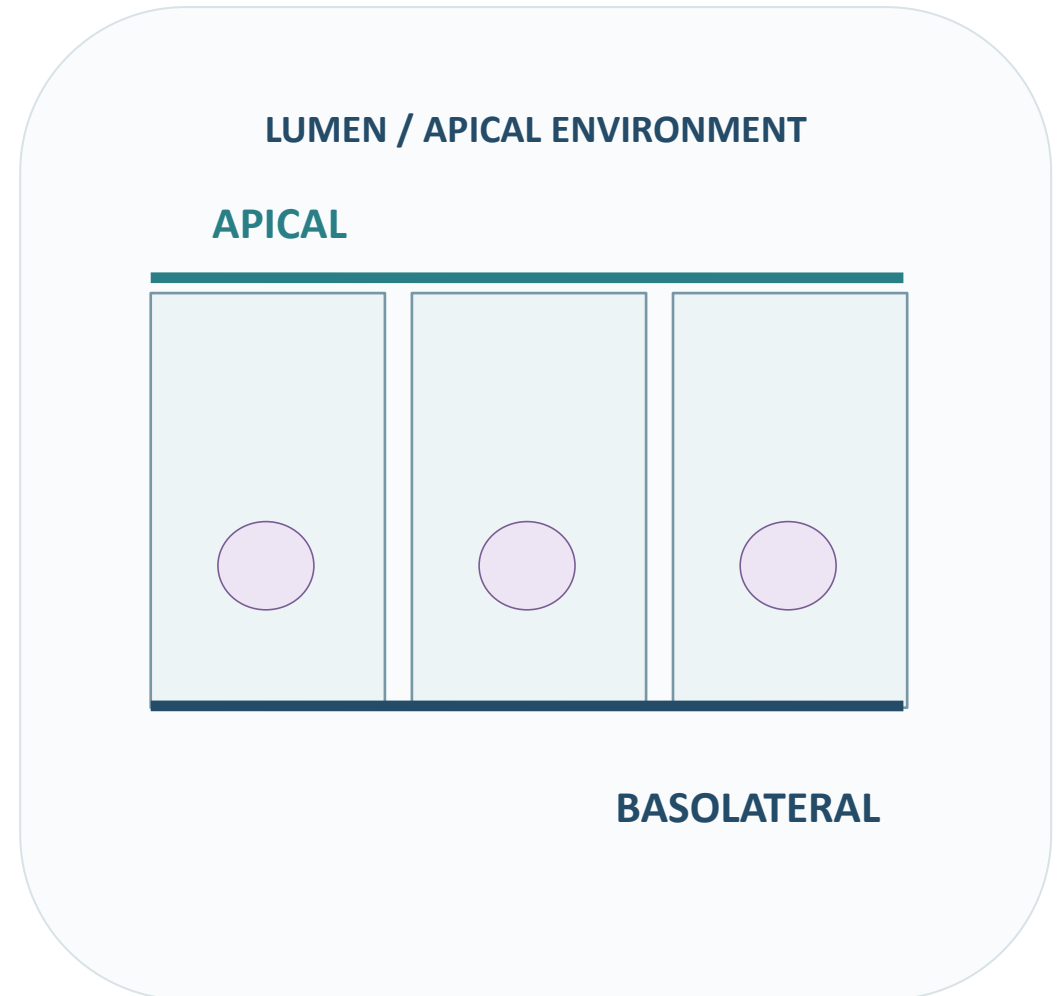
- Intercellular protein interactions establish boundaries
- Distinct domains maintain differing compositions
- This strategy is important in epithelial polarity



Epithelial cells maintain apical–basolateral polarity

Different membrane domains, different roles

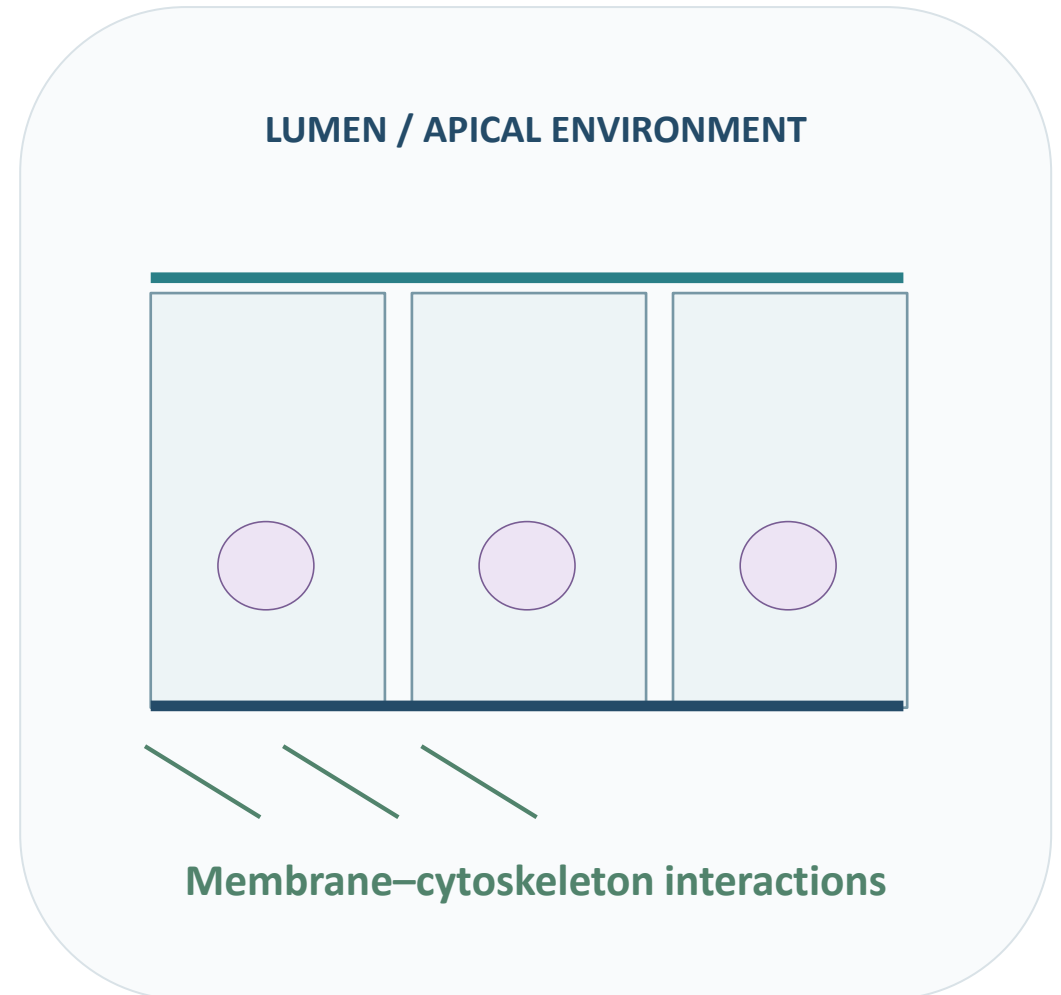
- Apical membrane faces the luminal environment
- Basolateral membrane faces a different environment
- Compartmentalization supports specialized cell functions



Polarity depends on more than lipid rafts

Multiple interacting organizing systems

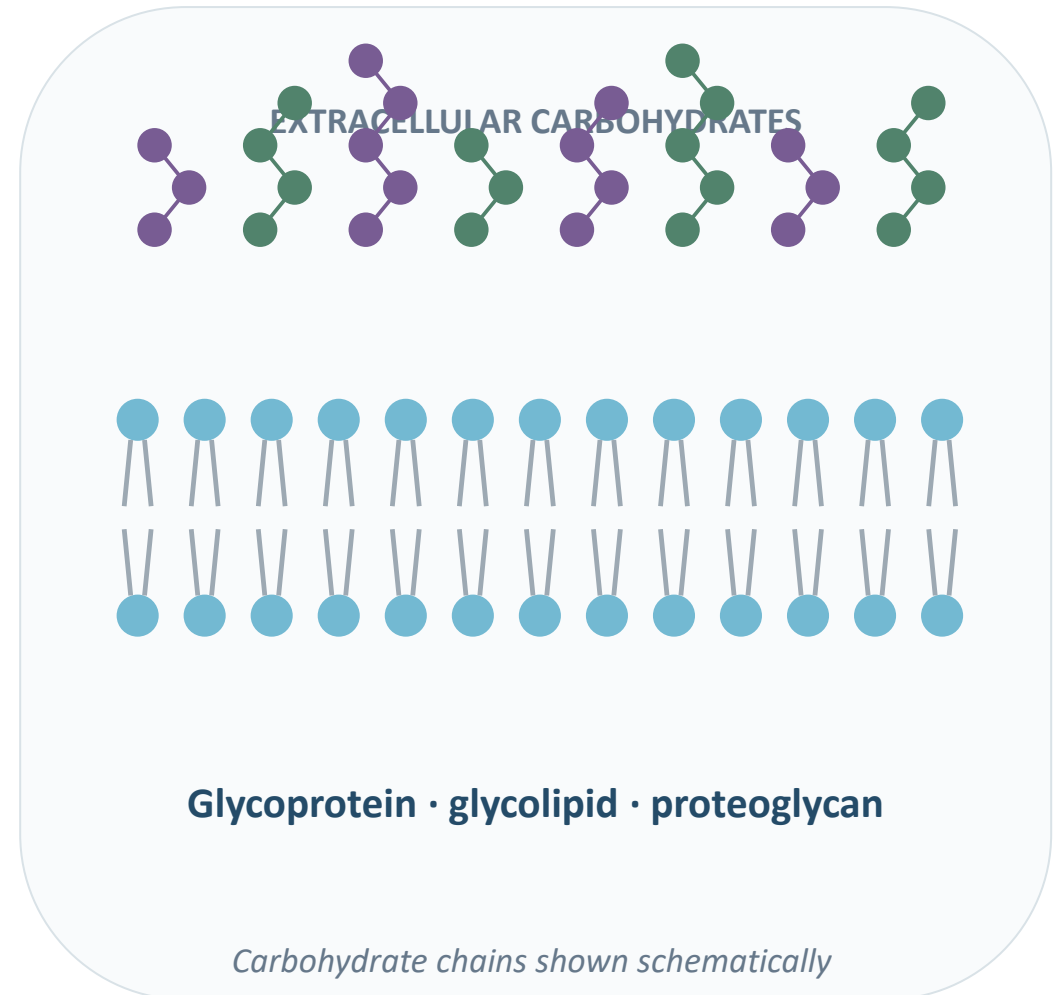
- Cell–cell interactions help define boundaries
- Membrane proteins interact with one another
- Cytoskeletal attachment helps maintain membrane organization



Surface carbohydrates form the glycocalyx

A diffuse extracellular carbohydrate coat

- Oligosaccharides decorate glycoproteins and glycolipids
- Polysaccharide chains attach to membrane proteoglycans
- These components collectively build the glycocalyx



The glycocalyx provides two types of protection

An extracellular protective layer

Extracellular carbohydrate chains build a protective surface.

Chemical barrier

Carbohydrate-rich surface chemistry

Mechanical barrier

Surface coating contributes a physical interface

Surface organization

Glycoproteins, glycolipids and proteoglycans coexist

Barrier properties govern modes of exchange

How material crosses a plasma membrane

Solute chemistry determines the required route across membranes.

Bilayer diffusion

For sufficiently small or lipid-soluble molecules

Transport proteins

For many ions, metabolites and water

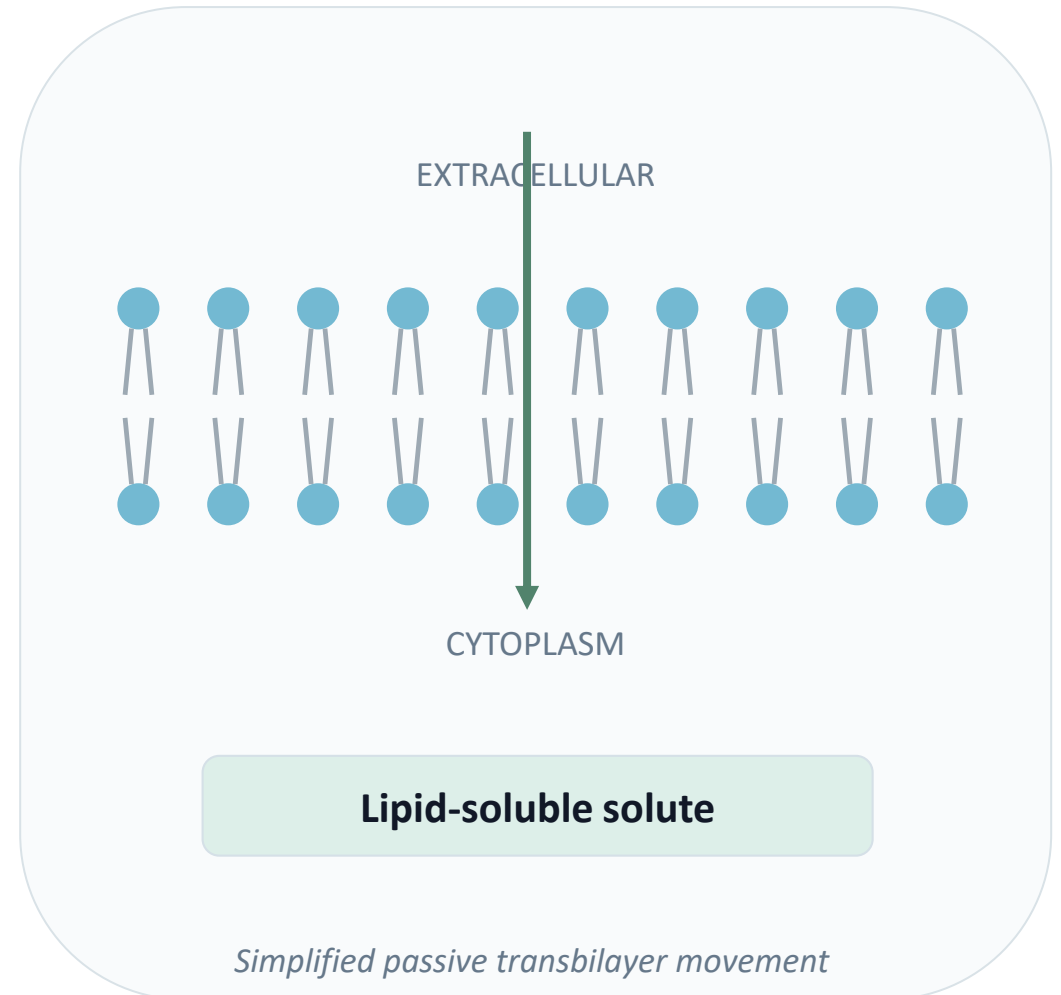
Vesicular pathways

For uptake and movement of macromolecules

Small nonpolar gases readily diffuse

Direct movement through lipid

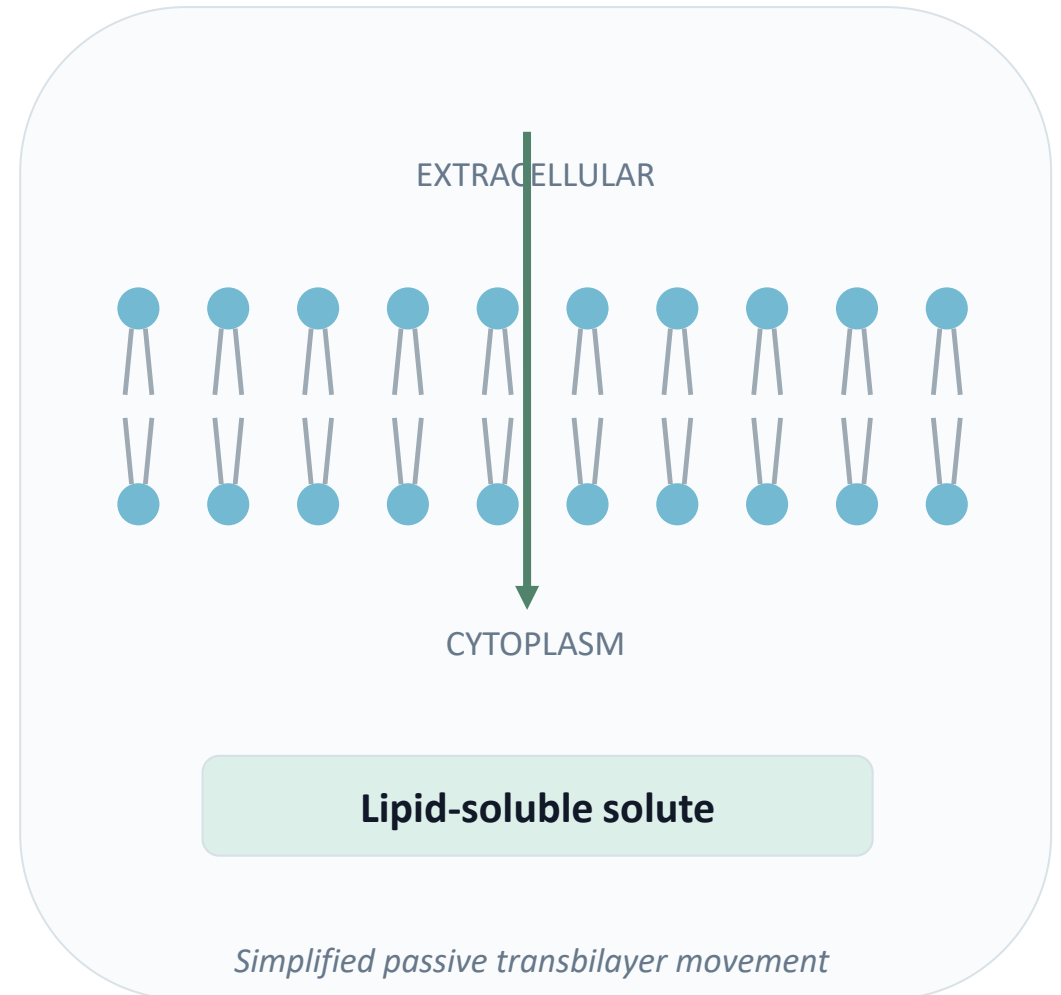
- Oxygen (O_2) dissolves in the bilayer
- Carbon dioxide (CO_2) also crosses readily
- A dedicated channel is not required for this form of passage



Lipid-soluble steroid molecules can cross readily

Hydrophobicity favors passive passage

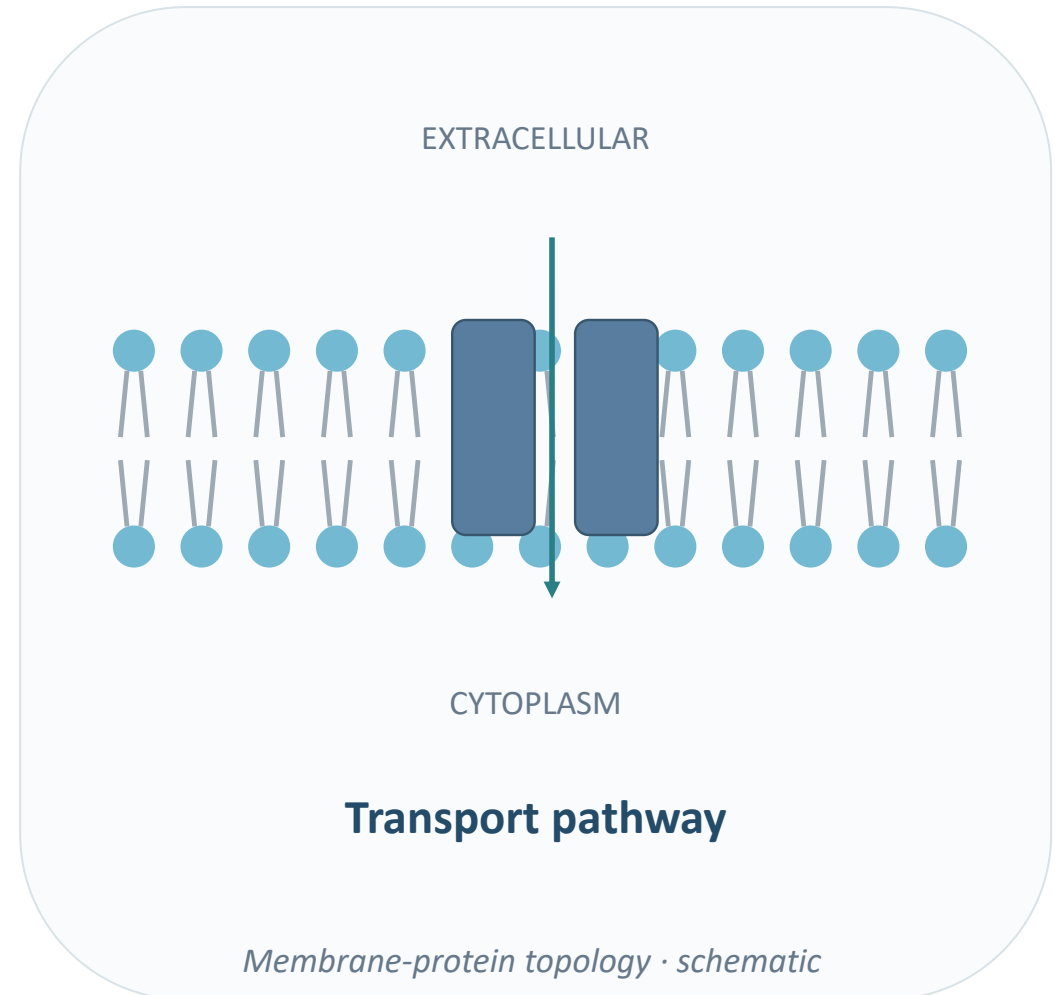
- Estradiol is a steroid-based example
- Vitamin D is another lipid-soluble example
- Larger hydrophobic molecules may still penetrate bilayers



Water shows both diffusion and channel-mediated movement

A special case among small polar solutes

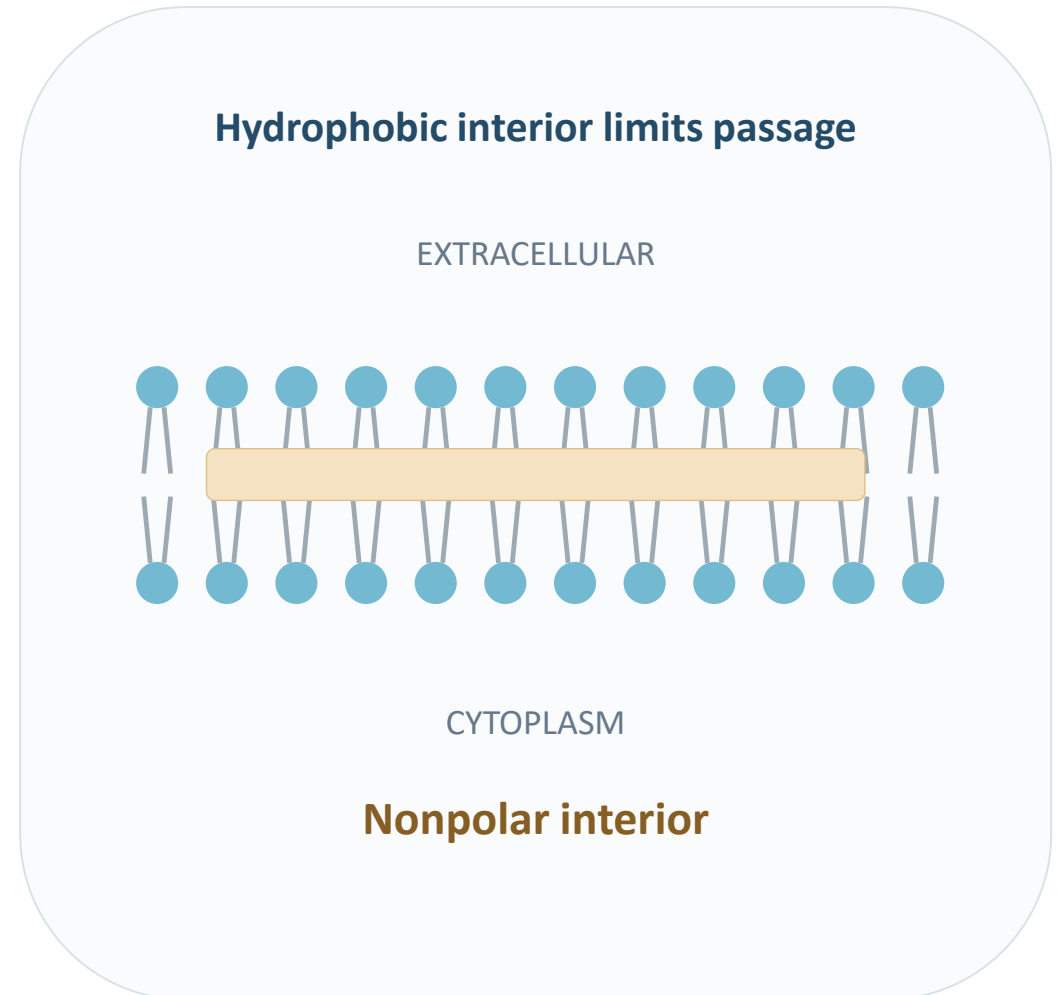
- Water is small (18 Da) and can cross slowly
- Aquaporins provide transmembrane water channels
- Renal tubular epithelium is a tissue where water control matters



Glucose and ions are excluded by the lipid core

Size, polarity and charge all matter

- Glucose (180 Da) is effectively excluded from direct passage
- The source describes strong exclusion of larger polar molecules
- Ions cannot pass freely because of charge and hydration



Permeability differs strongly across solute classes

Conceptual comparison

- Nonpolar gases: Readily permeable
- Water: Limited bilayer diffusion, channels important
- Glucose and ions: Require non-bilayer transport routes

O₂ / CO₂

Diffusion through bilayer



**Estradiol /
vitamin D**

Lipophilic passage



Water

Slow diffusion; Aquaporins



Glucose

Bilayer excludes



Hydrated ions

Bilayer impermeable



Application: A dying cell exposes an inner-leaflet lipid

Apply membrane organization to a short problem

Select one answer and explain why the alternatives are less appropriate.

Which component provides the “eat me” recognition cue?

A. Phosphatidylserine

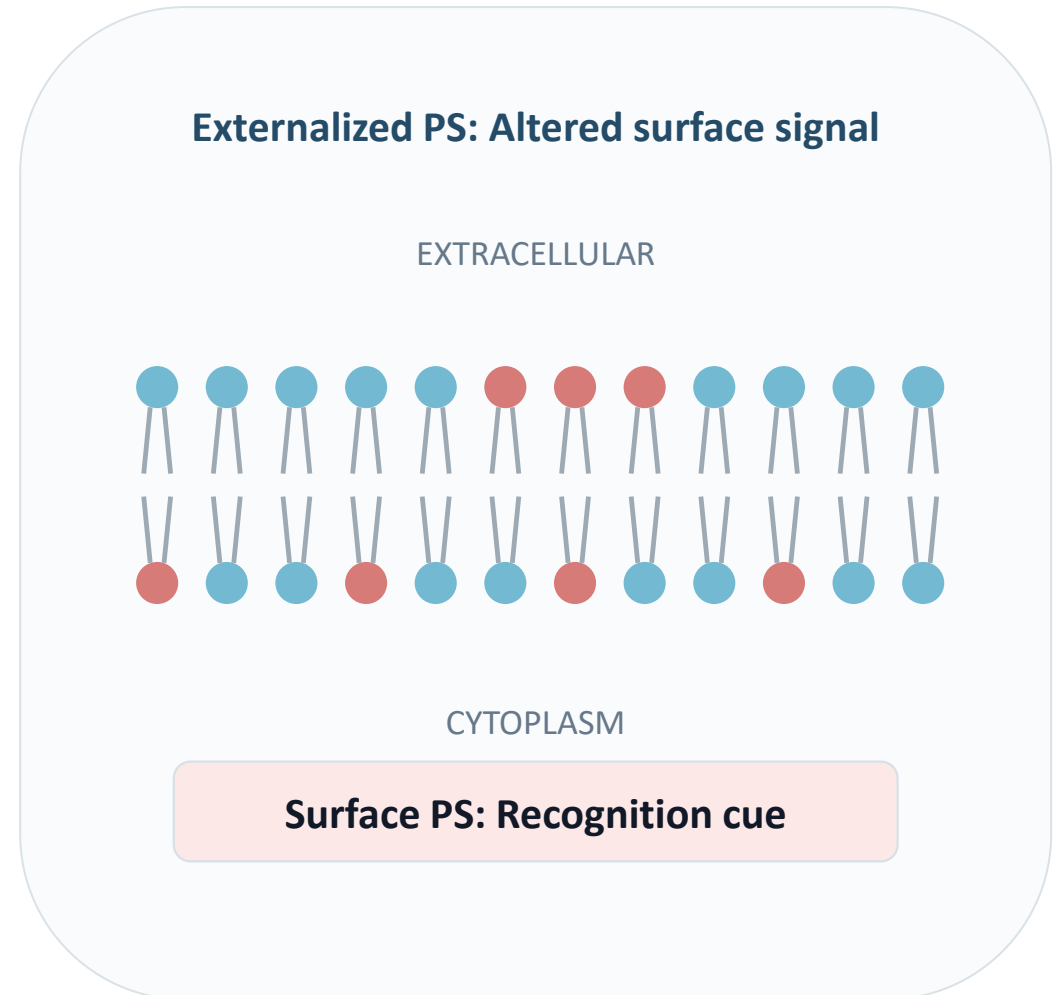
B. Sphingomyelin

C. Glycosylphosphatidylinositol

Application: Exposed phosphatidylserine marks dying cells

Correct answer: Phosphatidylserine

- PS is normally located predominantly on the cytosolic face
- External exposure creates a recognition signal during apoptosis
- The biological interpretation depends on the context of exposure



Application: An epithelium loses membrane polarity

Apply membrane organization to a short problem

Select one answer and explain why the alternatives are less appropriate.

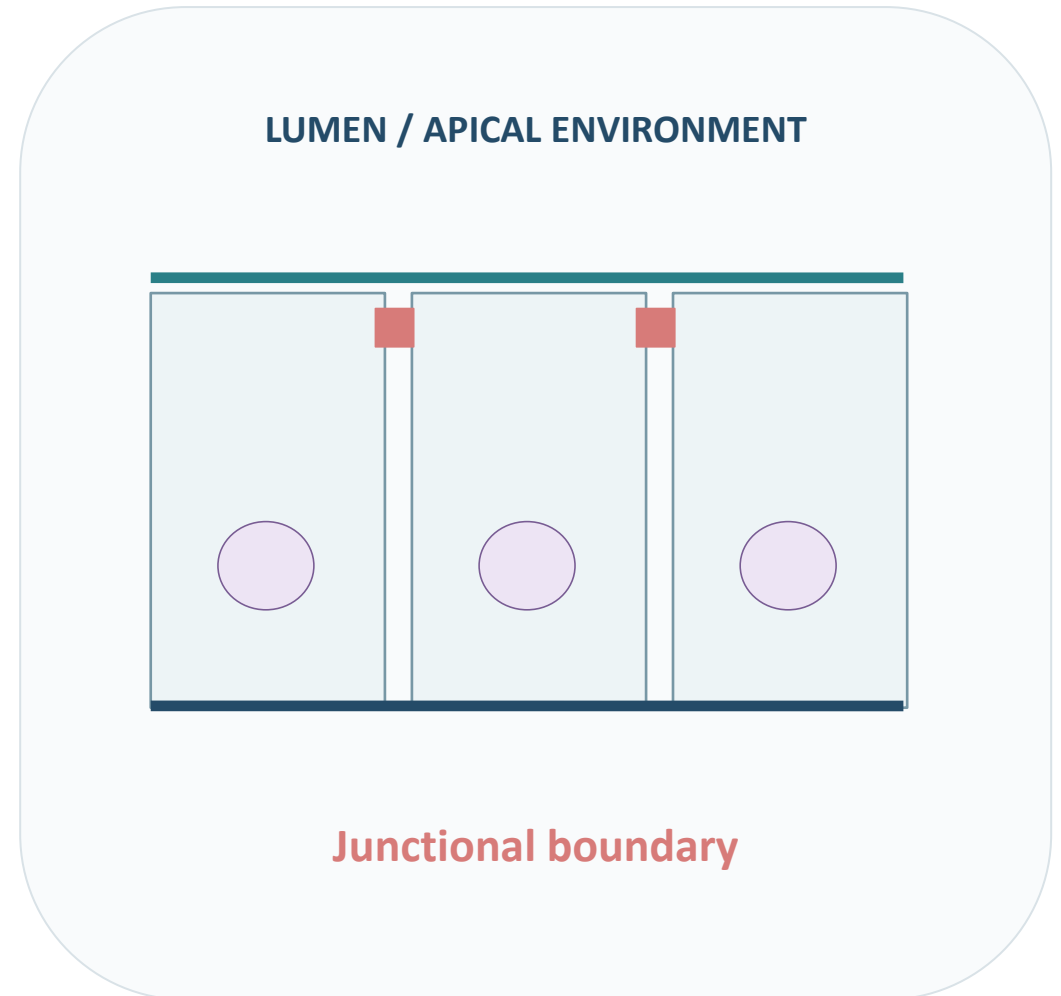
Which structure helps establish apical versus basolateral domains?

- A. Tight-junction boundary
- B. Unrestricted lateral mixing
- C. Uniform lipid composition

Application: Tight junctions maintain membrane domains

Correct answer: Tight-junction boundary

- Cell–cell protein interactions delimit membrane regions
- These boundaries contribute to epithelial polarity
- Membrane proteins and cytoskeleton also support organization



Application: A protein faces the extracellular space

Apply membrane organization to a short problem

Select one answer and explain why the alternatives are less appropriate.

Which anchor is specifically described for an extracellular-face protein?

A. GPI linkage

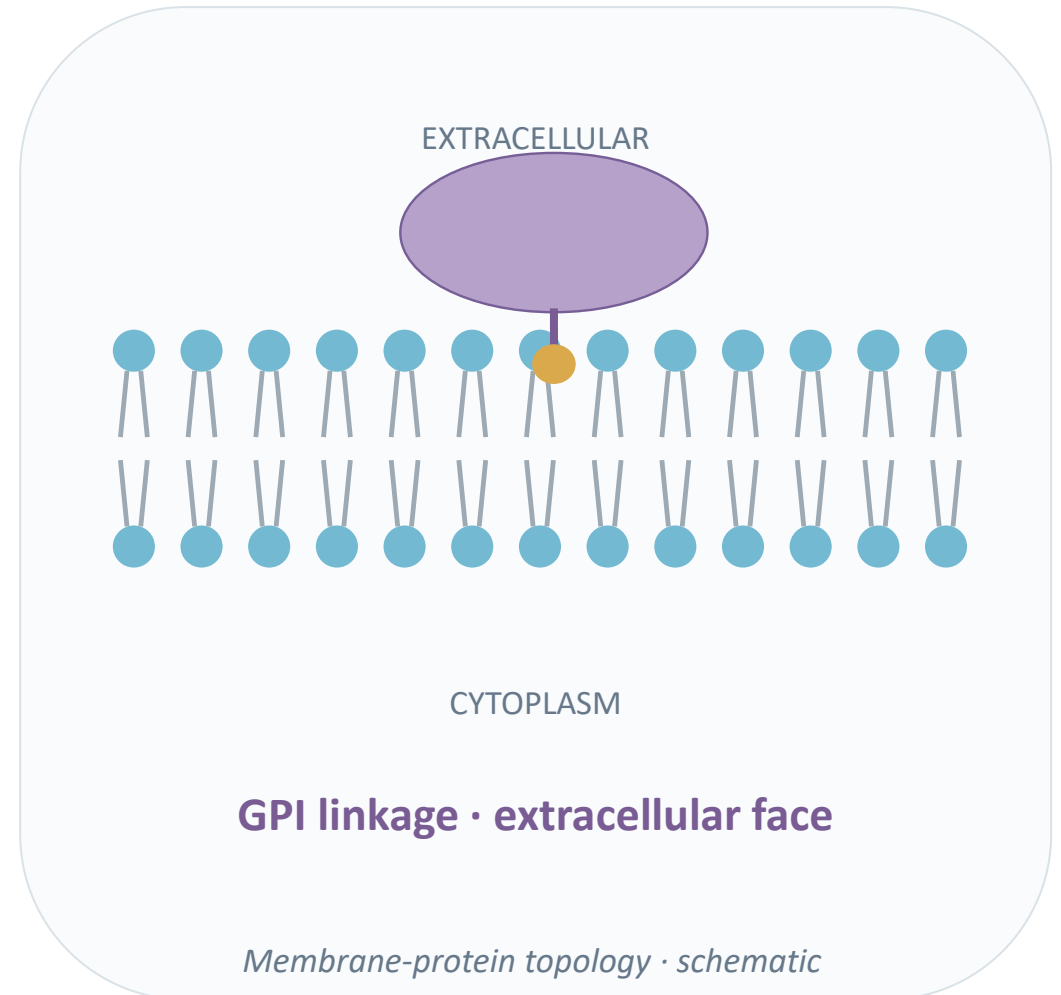
B. Cytosolic farnesyl anchor

C. Cytosolic myristoyl anchor

Application: GPI linkage fixes extracellular orientation

Correct answer: Glycosylphosphatidylinositol

- GPI tails are added posttranslationally
- They link proteins to the extracellular face
- Prenyl and fatty-acyl attachments localize to the cytosolic face



Integrated model: Structure determines function

The membrane as an organized interface

**Architecture governs permeability,
recognition and communication.**

Amphipathic bilayer → diffusion barrier



**Asymmetric lipids → signaling and
recognition**



**Domains + anchored proteins → spatial
specialization**



**Glycocalyx + polarity → tailored external
interfaces**

Core principles to retain

Five organizing principles

The bilayer is fluid, asymmetric and selectively permeable.

PS exposure, phosphoinositide cleavage and surface glycolipids have distinct functions.

Membrane proteins use four major association mechanisms.

Rafts, junctions and cytoskeleton organize spatially specialized membranes.

The glycocalyx provides a carbohydrate-rich protective surface.

Primary source and figure provenance

Textbook source

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026).
- Chapter 1, The Cell as a Unit of Health and Disease, pp. 7–9.
- Sections: Plasma Membrane; Membrane Transport; Passive Diffusion.
- Membrane diagrams: original editable schematics based on concepts in Fig. 1.7.

Schematic provenance

All diagrams were constructed with editable PowerPoint text, lines and shapes. Robbins Fig. 1.7 is used as an information source, not reproduced.

No authentic microscopy or patient-derived images appear in this foundational cell-biology lecture.