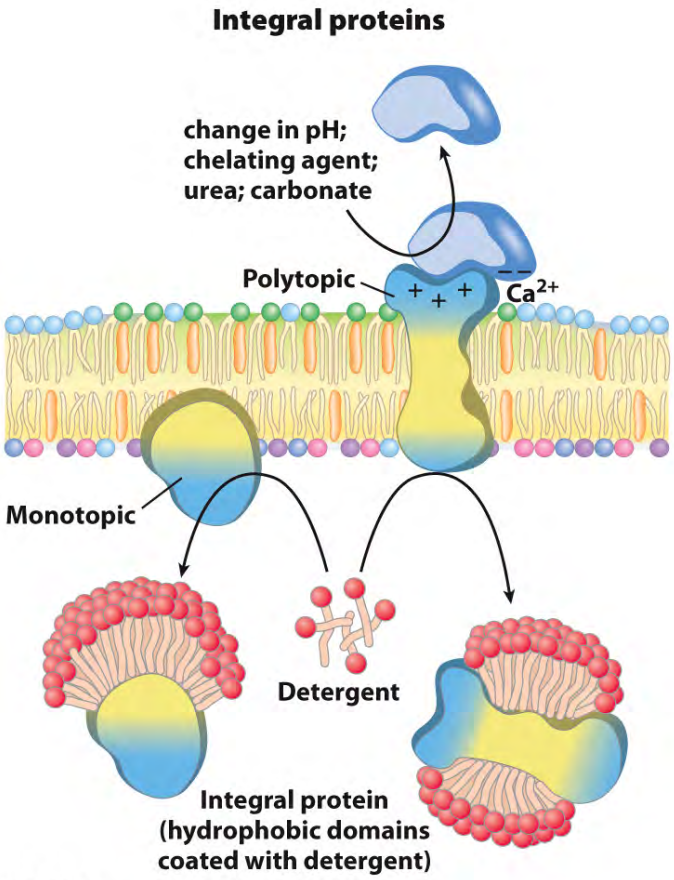
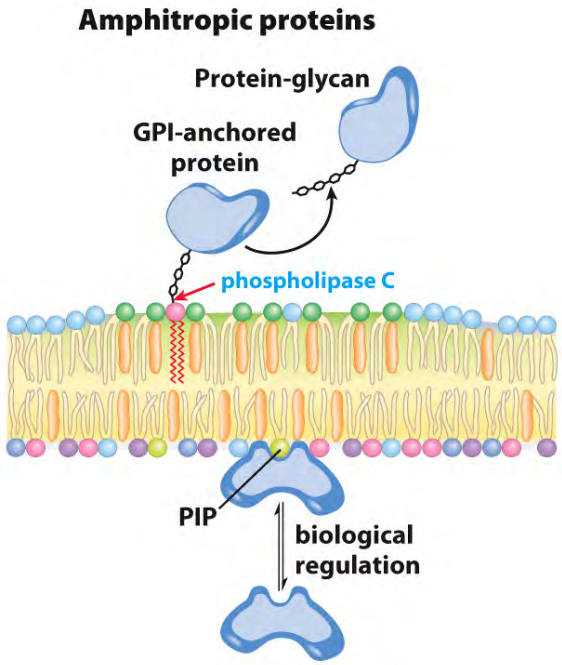
Biological Membrane Transport

Review of membrane structure
Membrane dynamics
Membrane transport
- Energetics
- Types

Three Types of Membrane Proteins





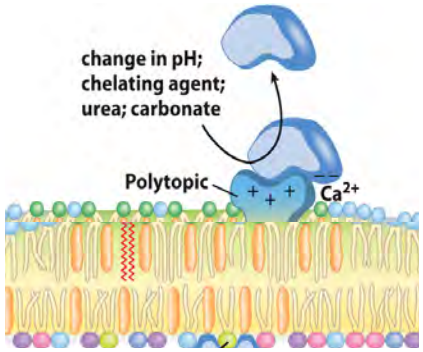
Peripheral (non-GPI linked) membrane proteins can be dissociated from the membrane fairly easily during changes in ionic strength like pH changes.

Amphitrophic and GPI-linked proteins are linked to the membrane during specific regulatory events and can be reversibly removed.

In the presence of strong detergents, integral membrane proteins can be removed from the membrane.

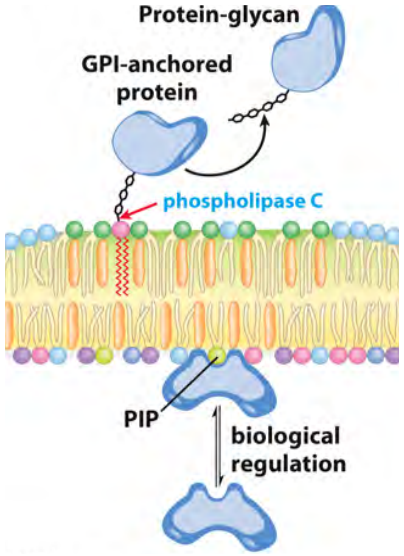
Three Types of Membrane Proteins

Peripheral



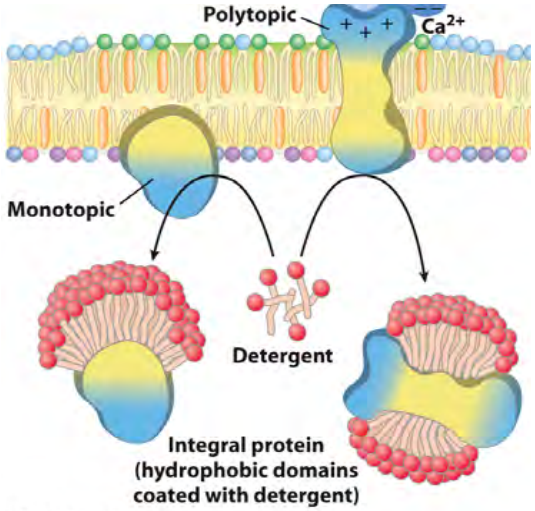
- Associate with the polar head groups of membranes
- Relatively loosely associated with membrane
  - through ionic interactions with the lipids or aqueous domains of integral membrane proteins
- Removed by disrupting ionic interactions either with high salt or change in pH
- Purified peripheral membrane proteins are no longer associated with any lipids.

Amphitrophic



- Amphitrophic proteins can be conditionally attached to the membrane by covalent interaction with lipids or carbohydrates attached to lipids.
- Biological regulation results in attachment to, or cleavage from, lipids.

Integral

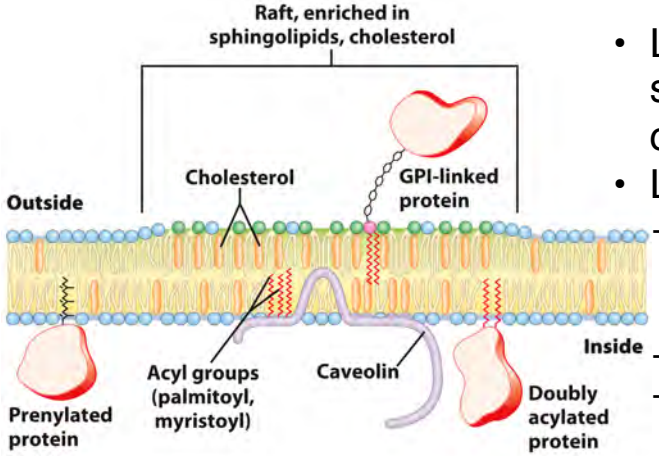


- Span the entire membrane
- Have asymmetry like the membrane
  - different domains in different compartments
- Tightly associated with membrane
  - Hydrophobic stretches in the protein interact with the hydrophobic regions of the membrane.
- Removed by detergents that disrupt the membrane
- Purified integral membrane proteins still have phospholipids associated with them.

Amphitropic Membrane Proteins

Lipid-linked Membrane Proteins & Lipid Anchors

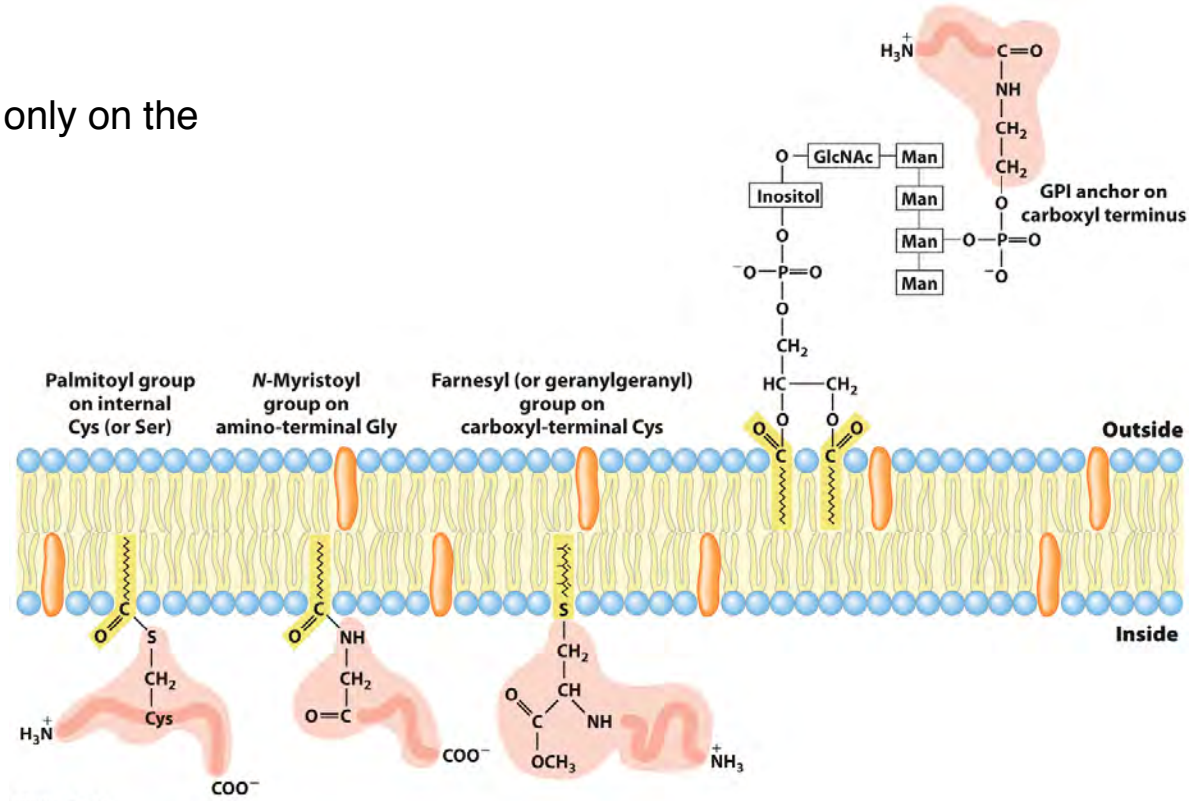
- Some membrane proteins are lipoproteins.
- They contain a covalently linked lipid.
  - long-chain fatty acids
  - isoprenoids
  - sterols
  - glycosylated phosphatidylinositol (PGI)
- The lipid part can become part of the membrane.
- The protein is now anchored to the membrane.
  - reversible process
  - allows targeting of proteins
  - Some, such as GPI anchors are found only on the outer face of plasma membrane.



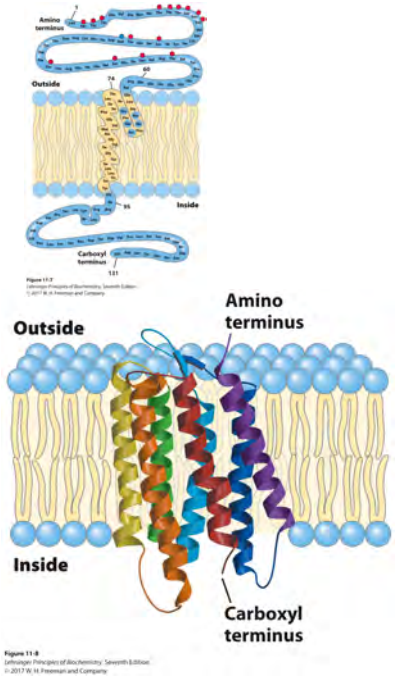
- Lipid distribution in a single leaflet is not random or uniform.
- Lipid rafts:
  - contain clusters of glycosphingolipids with longer-than-usual tails
  - are more ordered
  - contain specific doubly or triply acylated proteins
  - allow segregation of proteins in the membrane

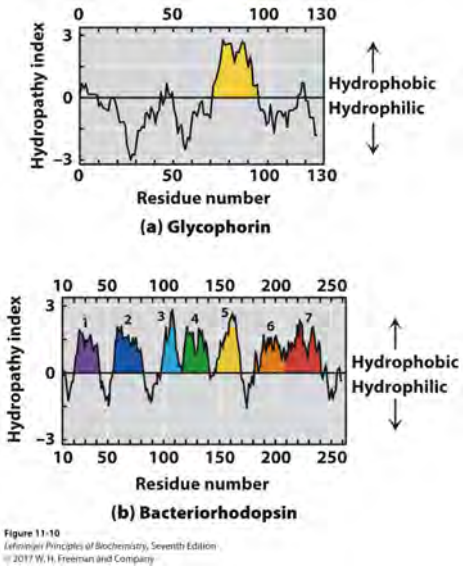
Example:

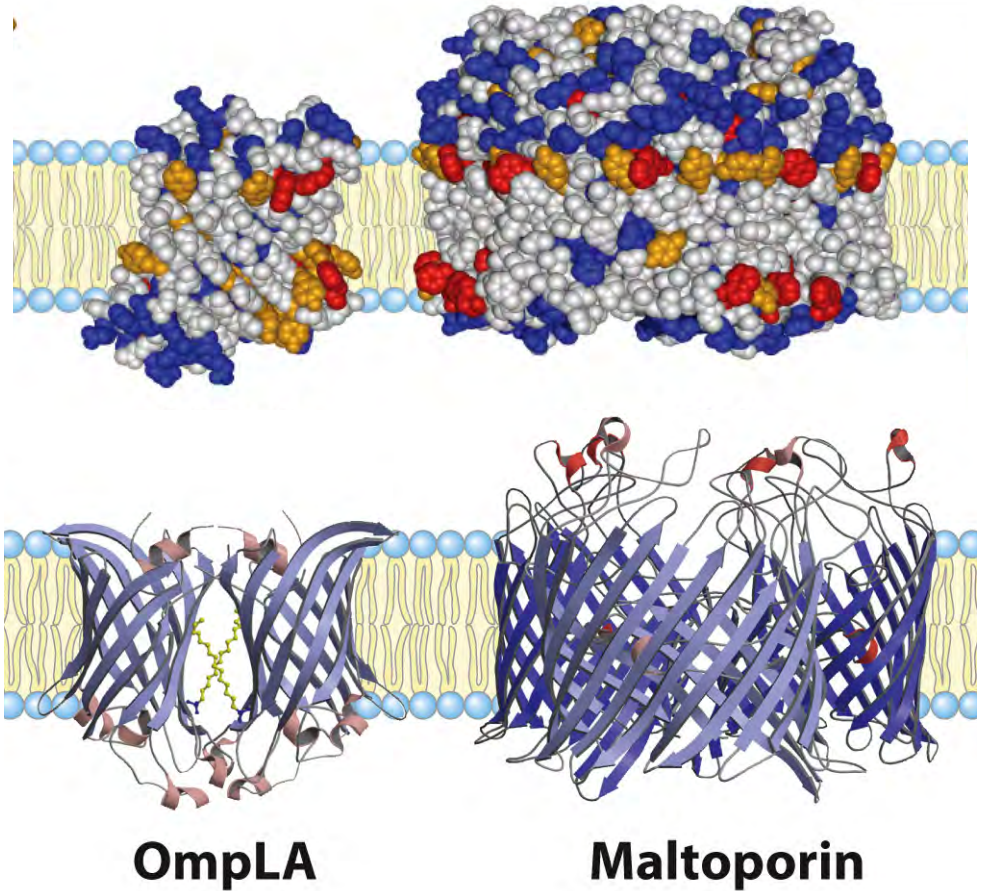
- Proteins can be targeted to the inner leaflet of the plasma membrane by farnesylation.
- Farnesylation can be an intermediate in the lipidation of proteins.
- Primary sequence of the protein contains a signature for farnesylation: CaaX.
  - C is a conserved Cys.
  - "a" is usually an aliphatic amino acid.
  - "X" is Met, Ser, Glu, or Ala.
- This reaction is catalyzed by farnesyl transferase.
- Nonfarnesylated proteins do not go to the membrane and are inactive.
  - promising cancer therapy (onco-Ras)



Examples of Integral Membrane Proteins







OmpLA **Maltoporin**

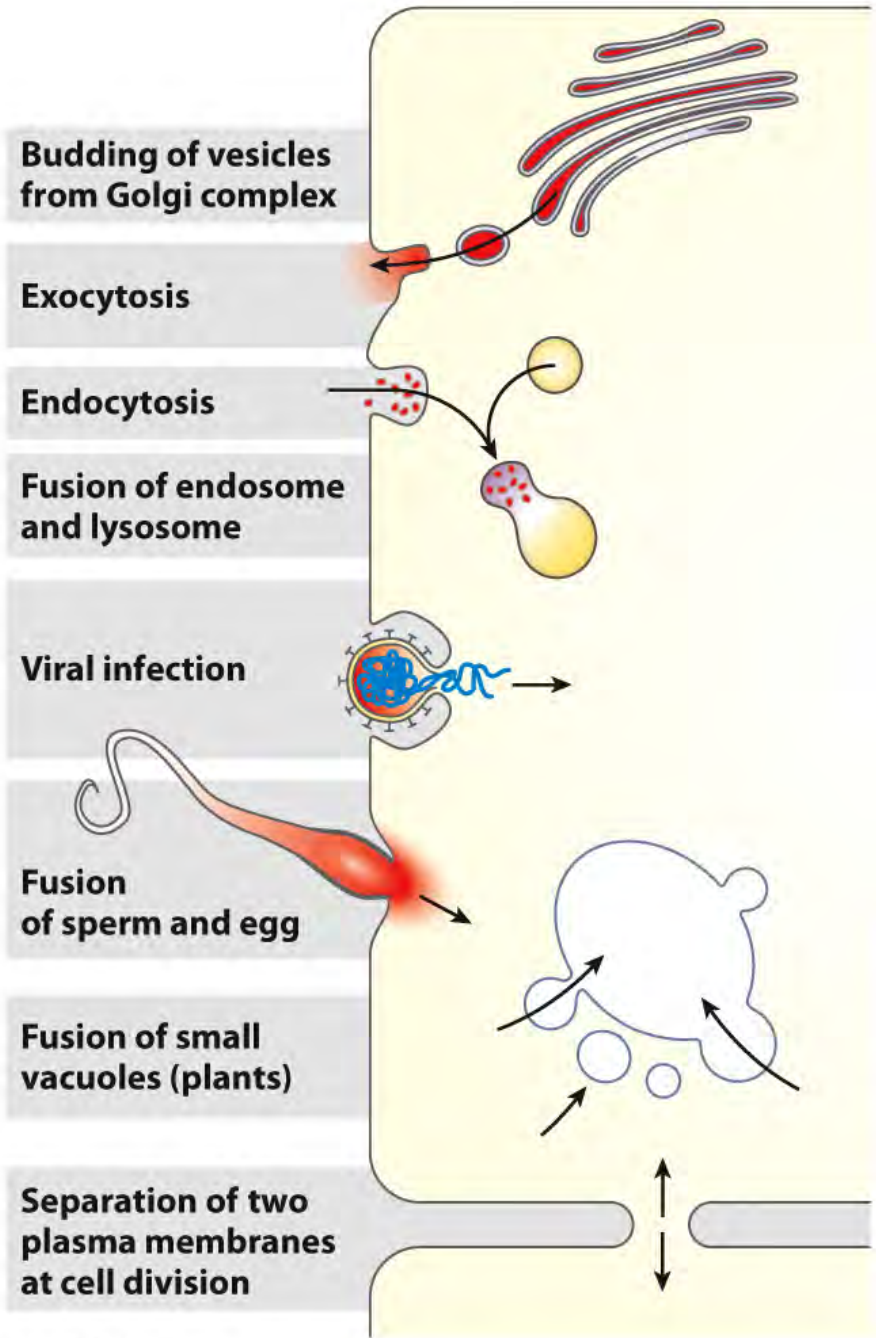
- Transmembrane segments are predominantly hydrophobic.
- Tyr and Trp cluster at nonpolar/polar interface.
- Charged amino acids are only found in aqueous domains.

Physical Properties of Membranes

- Not permeable to large polar solutes and ions
- Permeable to nonpolar compounds and some small polar compounds (e.g., water)
- Permeability can be artificially increased by chemical treatment.
  - when we want to get DNA into the cell
- Very stable yet dynamic and flexible structures
- Can exist in various phases and undergo phase transitions
- Can fuse

Examples of Membrane Fusion

- Membranes can fuse with each other without exposure of lipids to aqueous solvent.
- Fusion can be spontaneous or protein mediated.
- These fusion events require membrane curvature



Examples of Membrane Fusion

Caveolin Forces Membrane Curvature

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small invaginations in the plasma membrane