Cell Membrane Structure & Function

Lecture 6

Objectives

- Describe the "fluid mosaic" model of cell membrane
- 3 major lipids of the animal cell membrane
- Phospholipid flipping and enzymes to undo flipping
- Glycolipids: structure + role
- Cholesterol: function in membrane
- Membrane proteins (integral and peripheral) and their functional types or classes
- Glycoproteins: basic structure
- Glycocalyx: components + roles
- Lipid rafts: general description
- Cell membrane functions / purposes

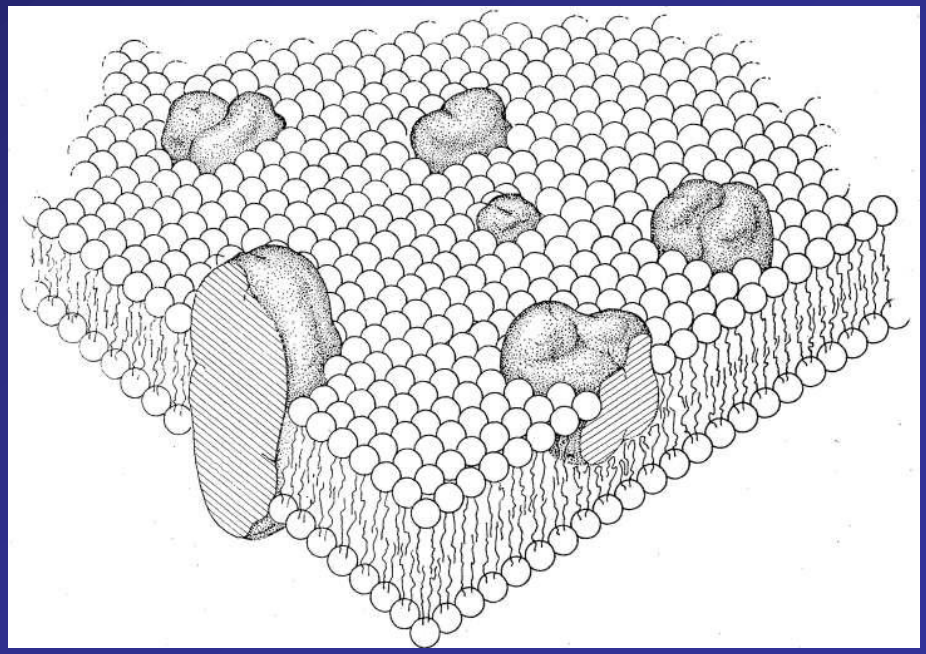
Cell Membranes

- "Plasma membranes"

  the other more usual (correct?) name
- Structure
  - role of polar lipids (phospholipids and variants)
  - role of proteins embedded in them or attached to them
- Function
  - container
  - barrier
  - gate/sentry

The Fluid-Mosaic Model

- Not until the early 1970s did biologists get an idea of the composition of the cell membrane
- Singer proposed that it was a lipid bilayer of phospholipids and that proteins bound to the membrane studded it much like a "mosaic"
- The model said that all molecules (proteins and Plipids) moved transversely throughout the cell membrane, as if it were a fluid and not gelled or fixed into position



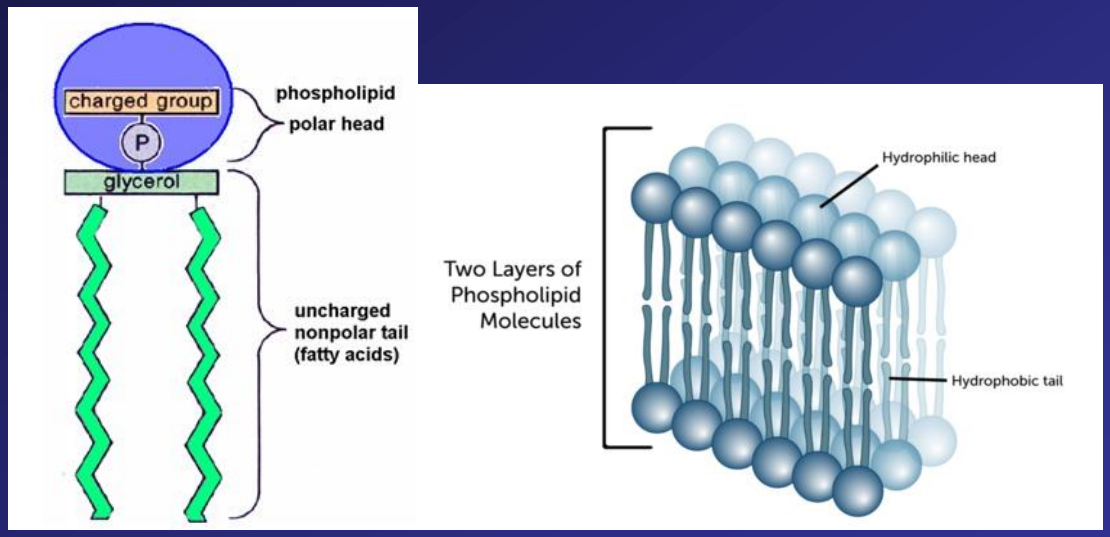
Original diagram of Singer-Nicholson model for the "fluid mosaic"

Membrane Lipids

- Phospholipids
- Glycolipids
- Cholesterol
- Many other types of lipids not addressed here
  e.g. sphingolipids and their glycosylated forms
  terpenes:

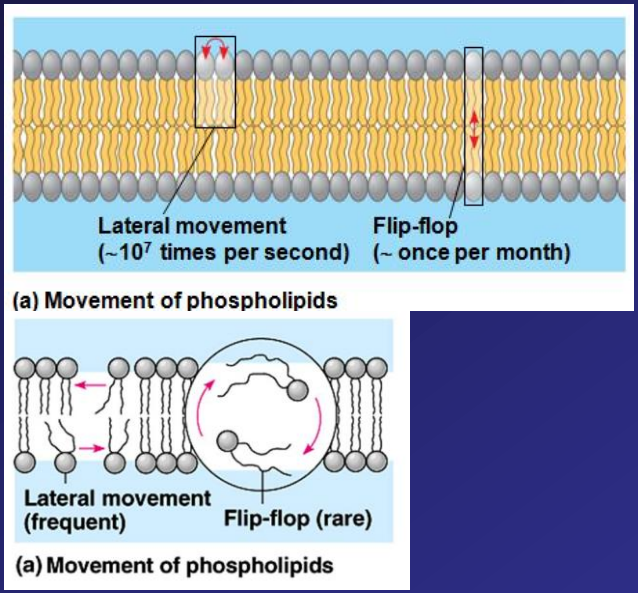
Phospholipids

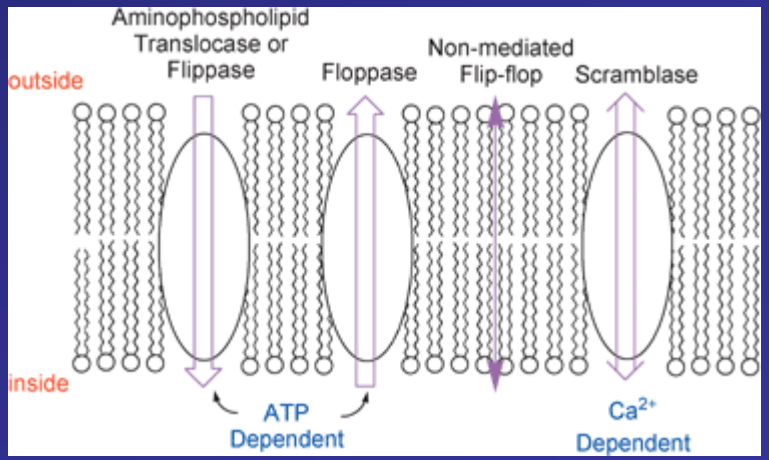
- The biochemistry was covered previously
- Phospholipids are natural membrane formers given their polar head and hydrophobic tails



Flip-Flopping

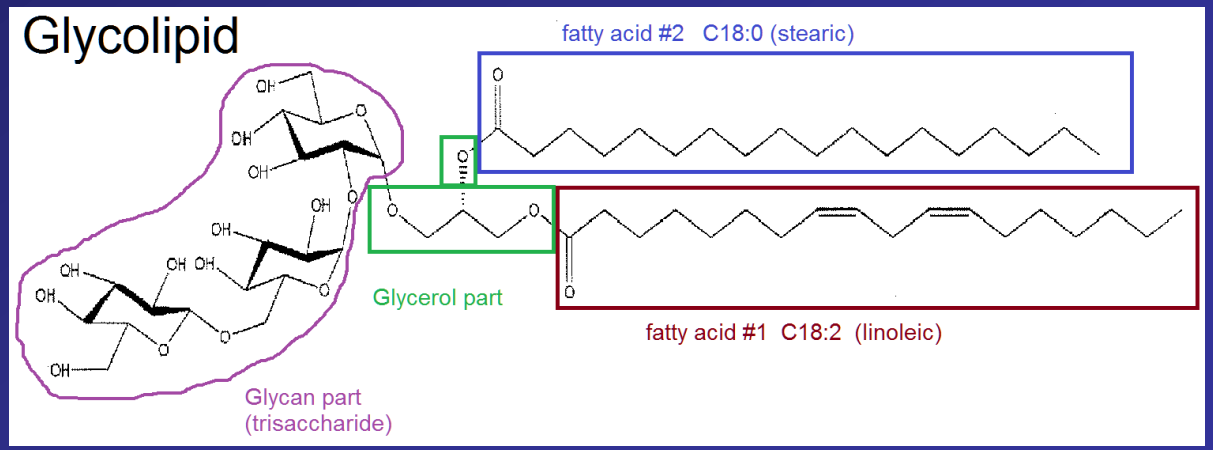
- Do phospholipids on one side traverse (flip) to the other side?
- It is believed that there is one such event every 24 h (other estimates vary)
- There are enzymes that typically use cell's energy to flip (=from out to in) or flop (=from in to out) the phospholipids so that they are in the correct side. These are flippases and floppases, respectively





Glycolipids

- 5% of the membrane lipids
- Oligosaccharides attach as a glycosidic bond to one of the glycerol carbons
- Glycolipids are positioned on the layer *opposite* from the cytoplasmic layer of the membrane
- Recall they are involved in cell-cell recognition (they mark the identity of the cells) and they can be used by the cell for energy



Cholesterol

- 20% of the lipid of membranes
- Its single –OH group gives it slight polarity
- Molecular structure is that of a flat, plate-like wall in appearance

- "hardens" the membrane (reduces fluidity)
- likely stabilizes cell membrane structure if there are temperature changes

Membrane Proteins

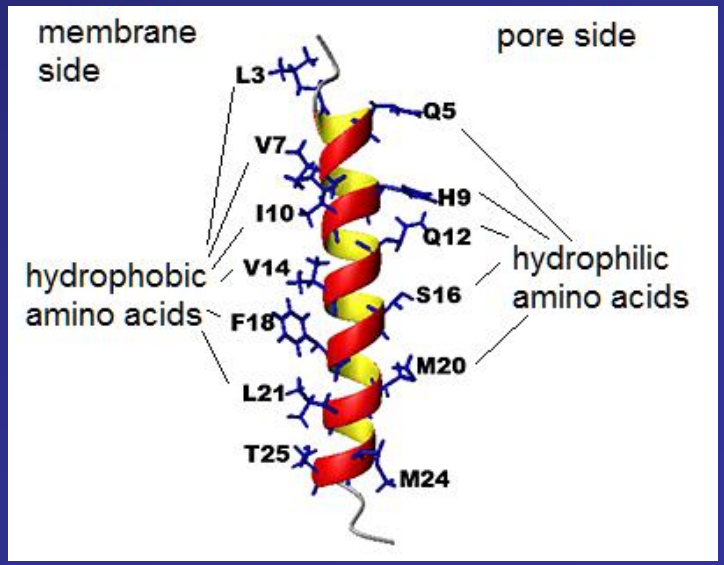
- ~50% of mass of membrane
- Proteins diffuse in the plane of the membrane freely, except for proteins that make attachments to interior proteins making up cytoskeleton ("tethering")
- Membrane proteins are either
  - integral
  - peripheral

Integral Membrane Proteins

- These proteins embed or anchor themselves into the cell membrane such that they make contact with the lipid part of the membrane
- Those integral proteins that span the membrane to the other side are called transmembrane proteins
  - The polypeptide sequences that cross through and make contact with the hydrocarbon/lipid part of the phospholipids are called transmembrane segments

The Transmembrane Segment

- As a transmembrane segment, an α-helix often passes through the cell membrane as part of the wall of an integral protein that may form a pore in the membrane
- As the helix turns, the side chains of the amino acids making up the segment that face the pore (hydrophilic) side are polar or electrically charged
- But side chains of the amino acids that face the membrane side & make contact with the lipophilic/hydrophobic tails of phospholipids are themselves lipophilic/hydrophobic
- In the figure, notice that as the helix turns, the hydrophilic amino acids face the pore side, while those facing the membrane side have lipophilic side chains



Peripheral Membrane Proteins

- These proteins do not have segments passing to the other side of the membrane
- They may be "anchored" to the membrane by
  - a bond, usually covalent, to any part of a phospholipid molecule
  - attachment or "assembly" to a separate protein that itself is an integral protein

    this attachment should not make it a part of the protein when it is first synthesized

Membrane Protein Functions

- Integral Membrane Proteins
  - Receptors (transmembrane)

    these bind to a hormone/ligand on outside of cell and change structure internally to start an intracellular process

    Example: insulin-like growth factor I receptor
  - Channels (transmembrane)

    pore-forming proteins that allow substances to cross in or out

    Example: aquaporin
  - Transporters/Carriers/Pumps/Exchangers (transmembrane)

    pore-forming proteins that use cell's energy or the energy of a concentration gradient to move substances against their concentration gradient

    Example: Na^+/K^+-ATPase exchanger

Membrane Protein Functions

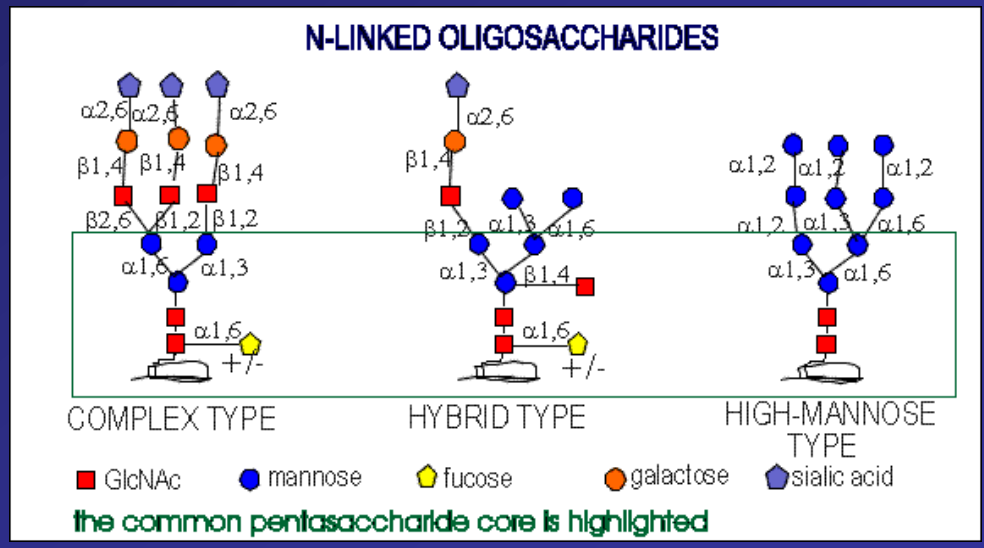
- Peripheral Membrane Proteins
  - Cytoskeletal proteins

    proteins that hook themselves to two locations: one, the membrane, and two, to a "fiber-like" linear structure inside the cell for the purpose of being part of a scaffold to arrange the internal order of the cytoplasm or to help in locomotion of the cell
  - Receptor-regulating proteins

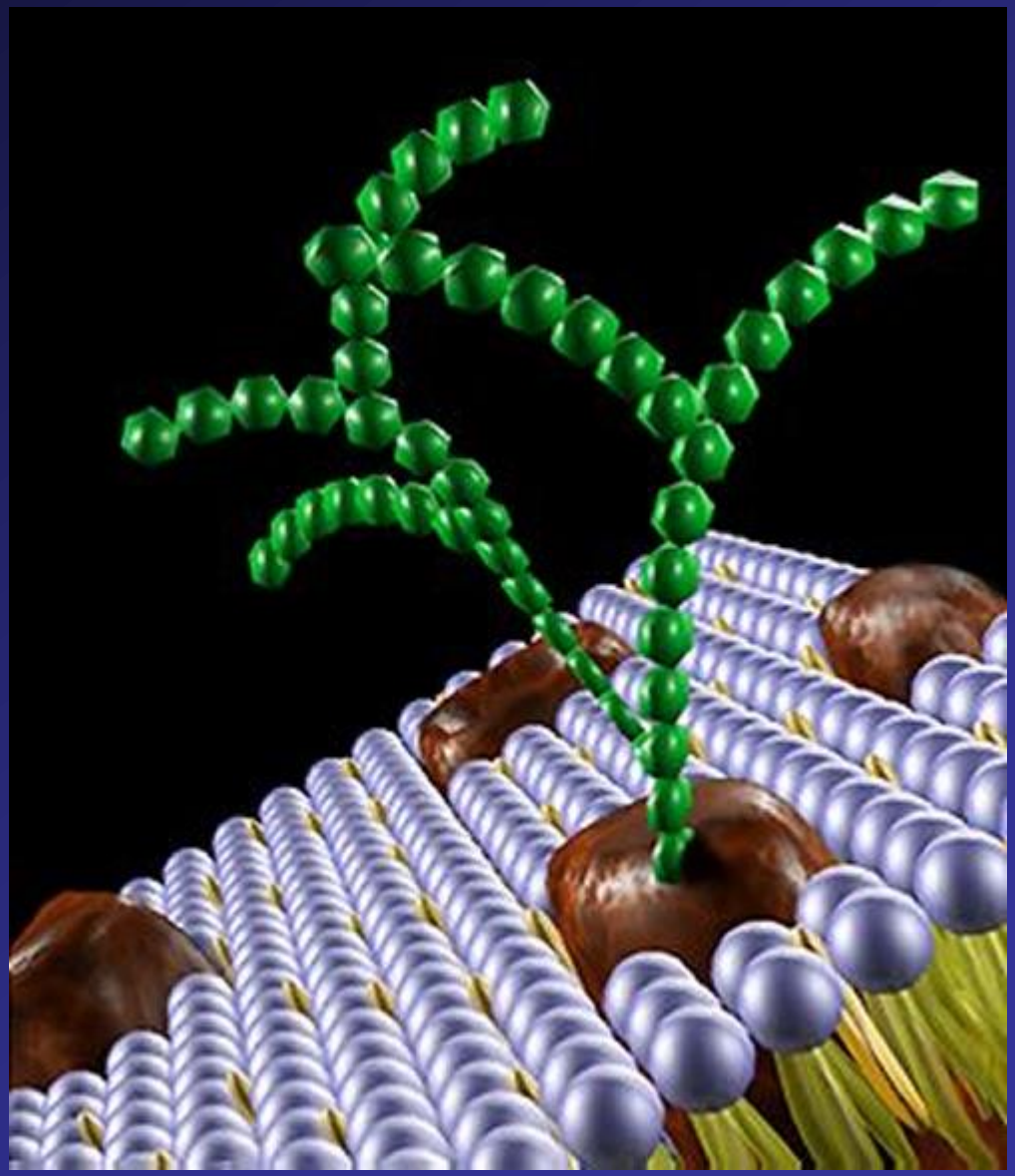
    proteins that attach to receptors (usually in the cell interior) to modulate (up or down) the function of the receptor

Glycoproteins

- After a protein is made in the ER, it can be glycosylated with an oligosaccharide
- The glycoprotein then travels through the Golgi complex where the initial oligosaccharide is trimmed of some monosaccharides, or has more added, or is modified in some way, often to put electrical charges on the monosaccharides at the end of the tails
- The figure at right shows oligosaccharide structure for 3 types of N-glycoproteins
- Each polymer that branches off is called an "antenna" The first one at left is called a triantennary oligosaccharide



A visual look at a glycoprotein sitting in the cell membrane



Glycocalyx

- All the oligosaccharide (sugar) parts of glycoproteins & glycolipids are oriented to stick OUT of the cell (positioned on extracellular side)
- This sugary goo on the outside is called the glycocalyx
- This layer (looking like hairs sticking out on an electron microscope) helps cells recognize each other, among other functions

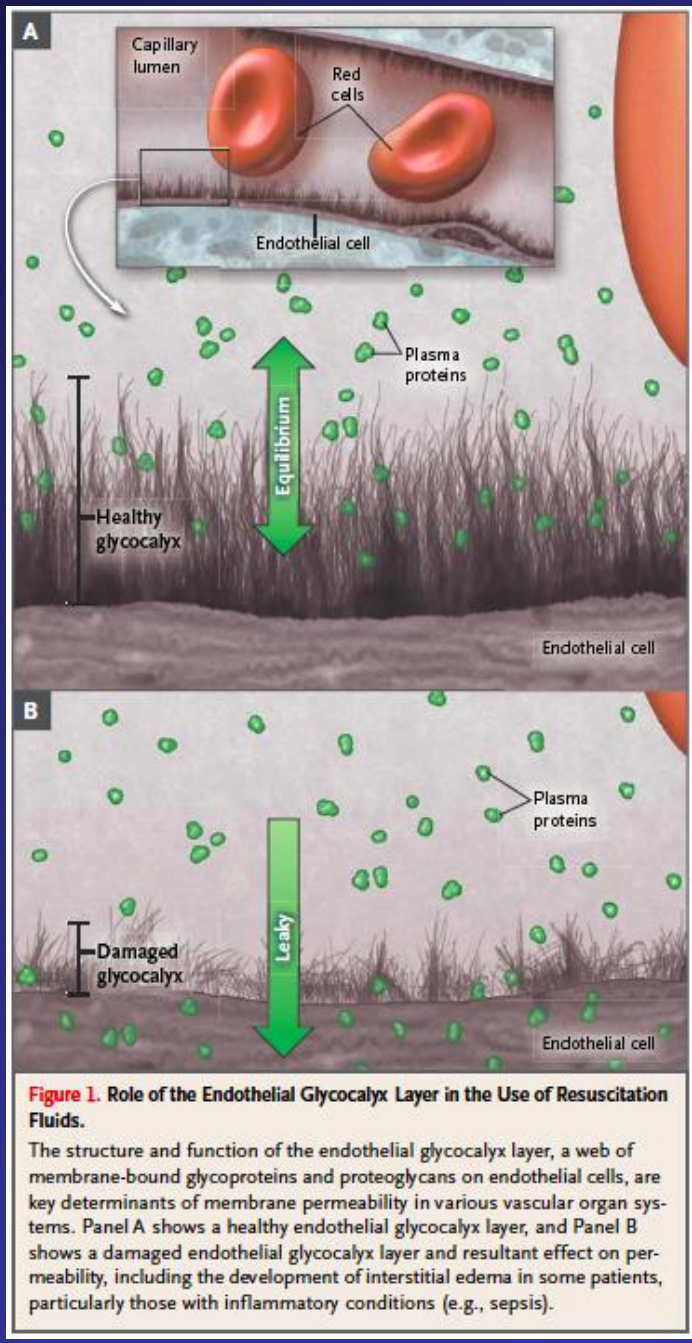
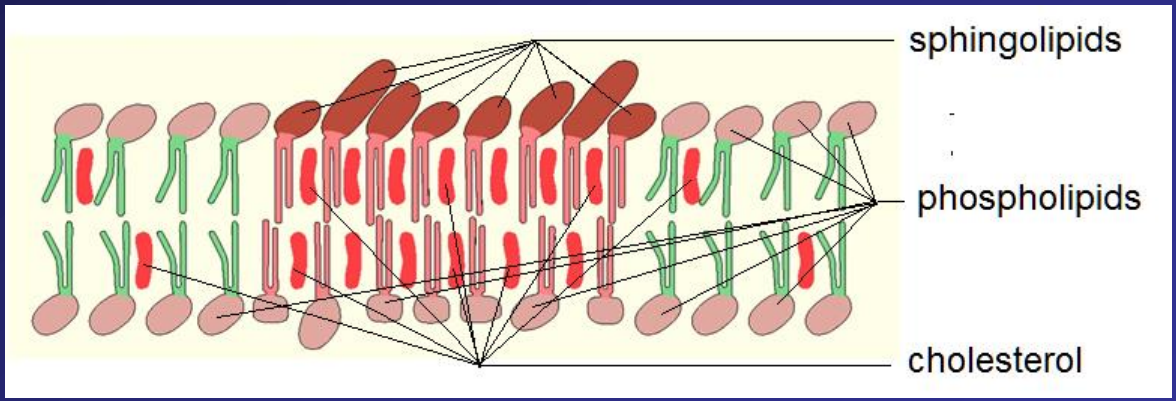


Figure 1. Role of the Endothelial Glycocalyx Layer in the Use of Resuscitation Fluids.

The structure and function of the endothelial glycocalyx layer, a web of membrane-bound glycoproteins and proteoglycans on endothelial cells, are key determinants of membrane permeability in various vascular organ systems. Panel A shows a healthy endothelial glycocalyx layer, and Panel B shows a damaged endothelial glycocalyx layer and resultant effect on permeability, including the development of interstitial edema in some patients, particularly those with inflammatory conditions (e.g., sepsis).

Lipid Rafts

- These are membrane microdomains* composed of with concentration of sphingolipids and glycolipids on the extracellular leaf of the membrane bilayer with cholesterol molecules between them, and also surrounded by a phospholipid-rich bilayer.
- The lipid hydrophobic tails in these rafts are saturated (red two-legged shapes), while the surrounding phospholipids have shorter unsaturated tails (green)
- A microdomain in a membrane is one where the composition of lipids making up the local region cause the membrane to have different packing properties, such as being more ordered or tightly packed



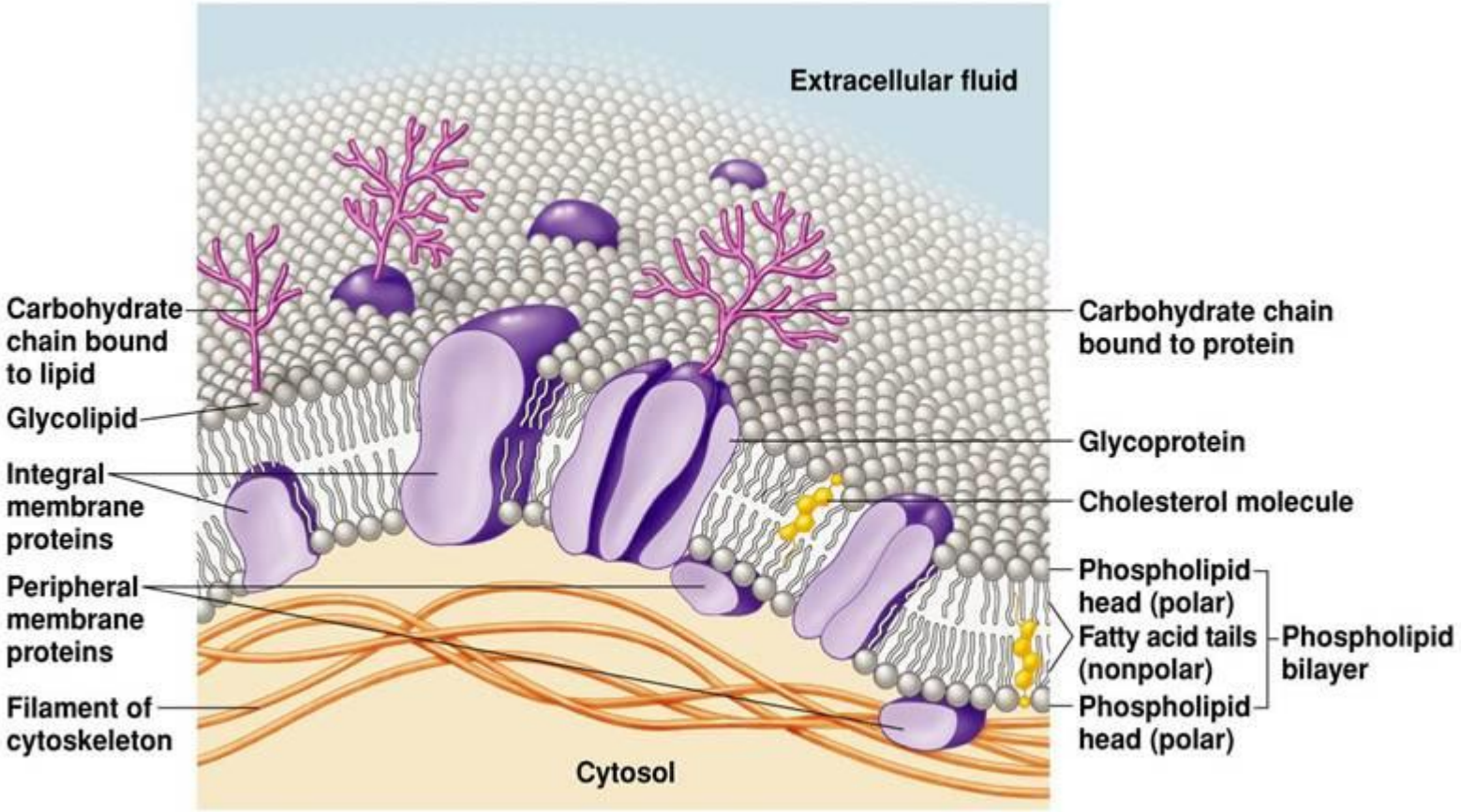
Purposes of the Cell Membrane

- Physiological Container

  contain all structures and biochemicals in a way that permits metabolism ("life")
- Gate/Sentry

  regulates the nutrients and other biomolecules that can pass
- Protection
  - barrier to harsh chemical/physical environments
  - barrier infectious agents
- Identity
  - protein markers on surface identify cell to others
- Cytoskeleton
  - For cells capable of locomotion, works with internal cytoskeletal features to produce it
  - Can act as anchor to help cytoskeleton to position internal contents

Taking it all in



Reading (Sources)

- Becker's WotC: Chapter 7
- Raven: Chap 5.1, 5.2
- Marieb: Chapter 3: pp 65-66