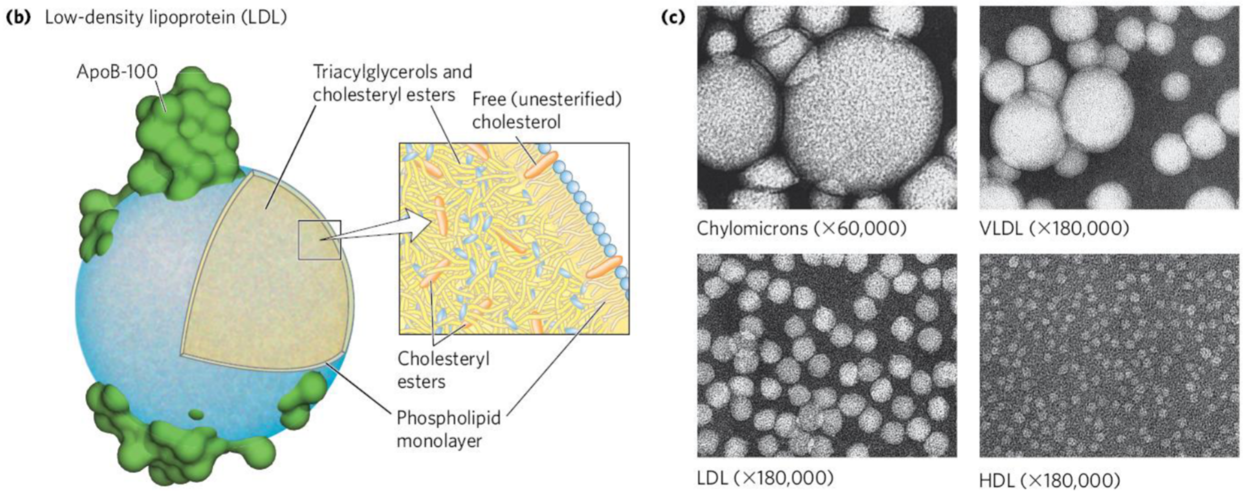
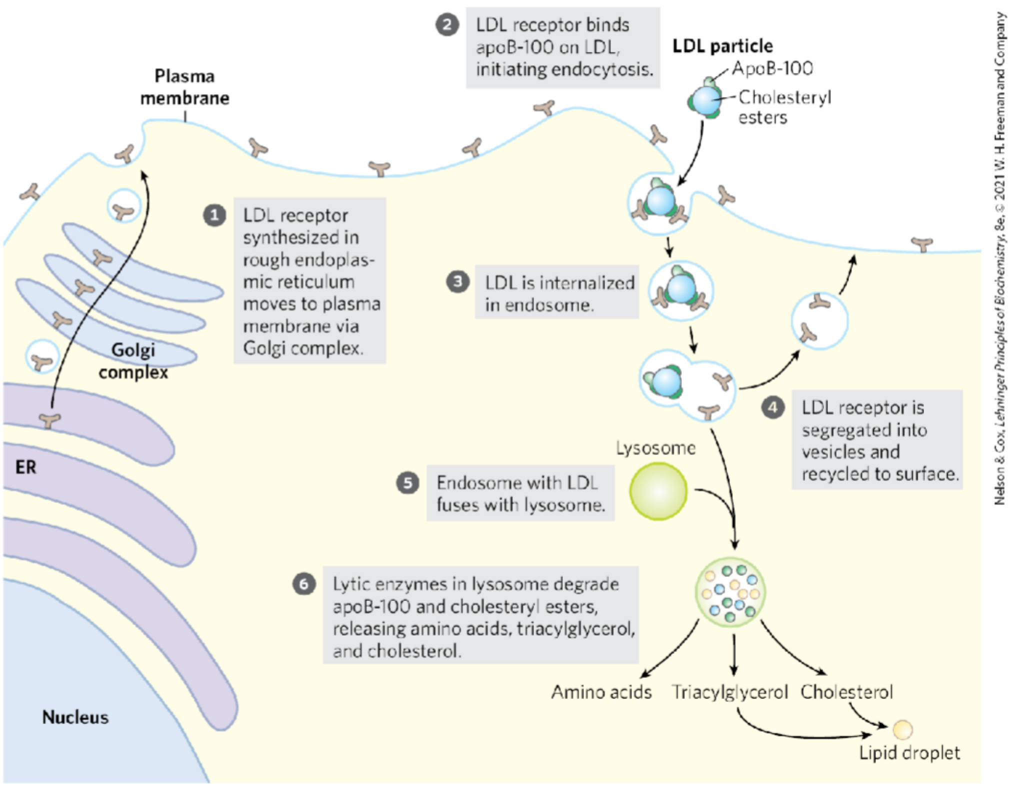
# Lipoproteins

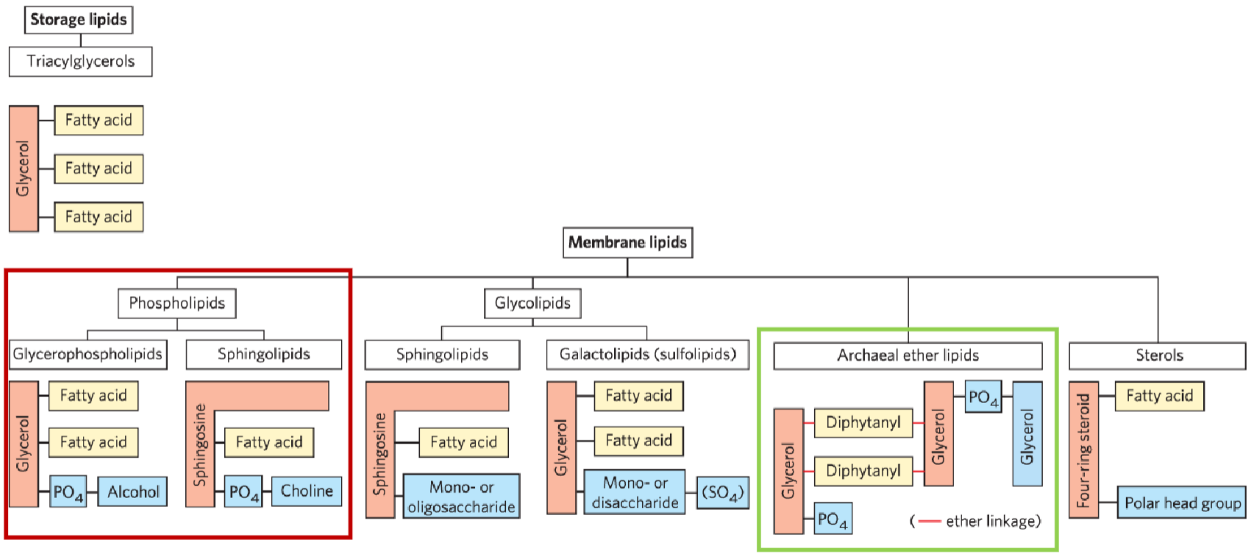



# Receptor-Mediated Endocytosis

apoB-100 of LDL is recognized by receptors in the plasma membrane.

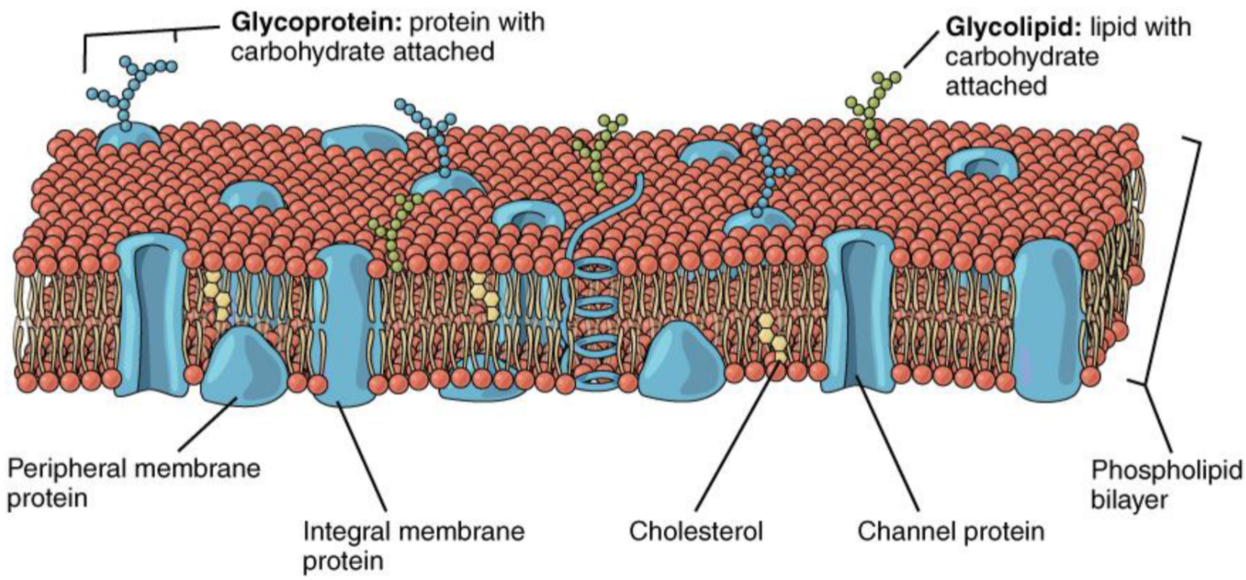


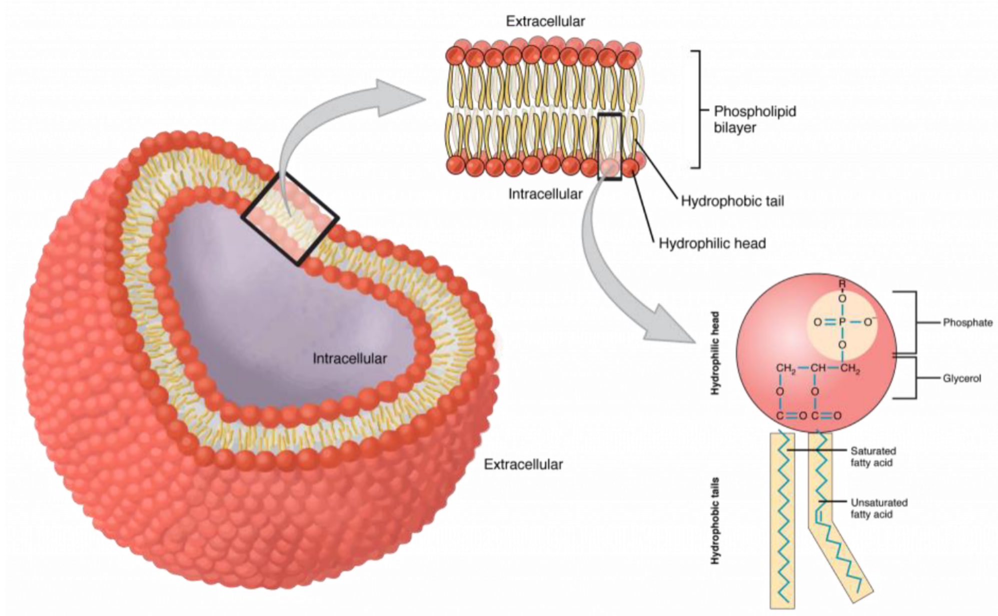
## Some Common Types of Storage and Membrane Lipids




More on archeal lipids:
https://doi.org/10.1016/j.bbalip.2016.12.006

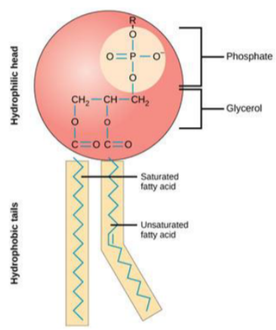
## Cell Membrane: Fluid Mosaic Model

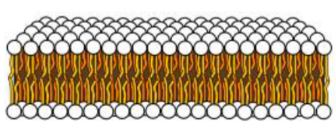


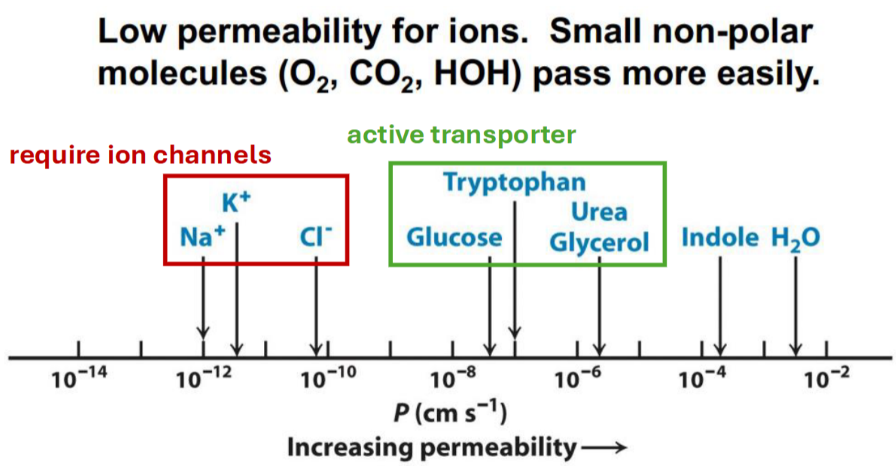



## Membrane Permeability

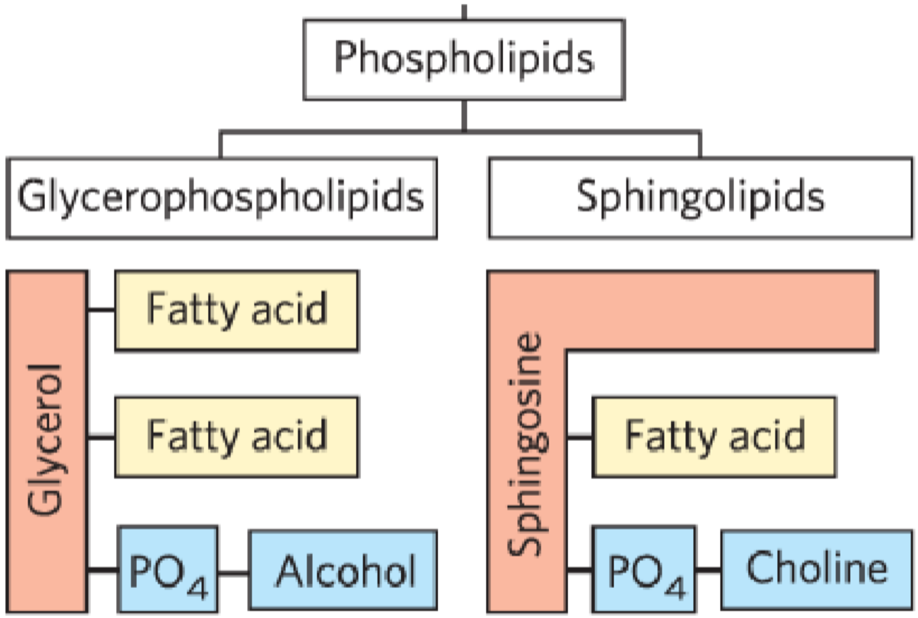
- Low permeability for ions.
- Small non-polar molecules ($O_2$, $CO_2$, $H_2O$) pass more easily.





### Types of Phospholipids



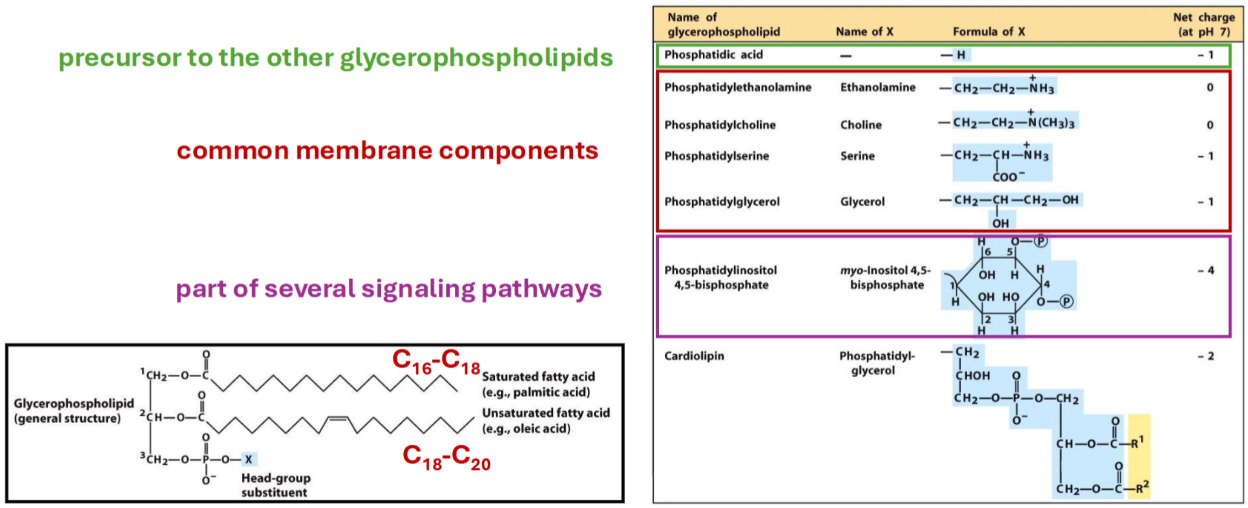

**Glycerophospholipids**

- Backbone: Glycerol
- Structure: Two fatty acids attached to the glycerol backbone, a phosphate group ($PO_4$) linked to an alcohol (e.g., choline or ethanolamine)
- Function: In cell membranes, it has a role in structural integrity and signaling

**Sphingolipids:**

- Backbone: Sphingosine
- Structure: One fatty acid attached to the sphingosine backbone, a phosphate group ($PO_4$) linked to choline or another alcohol group
- Function: In cell membranes, particularly in neural tissues, they contribute to signaling and cellular recognition

## Glycerophospholipids



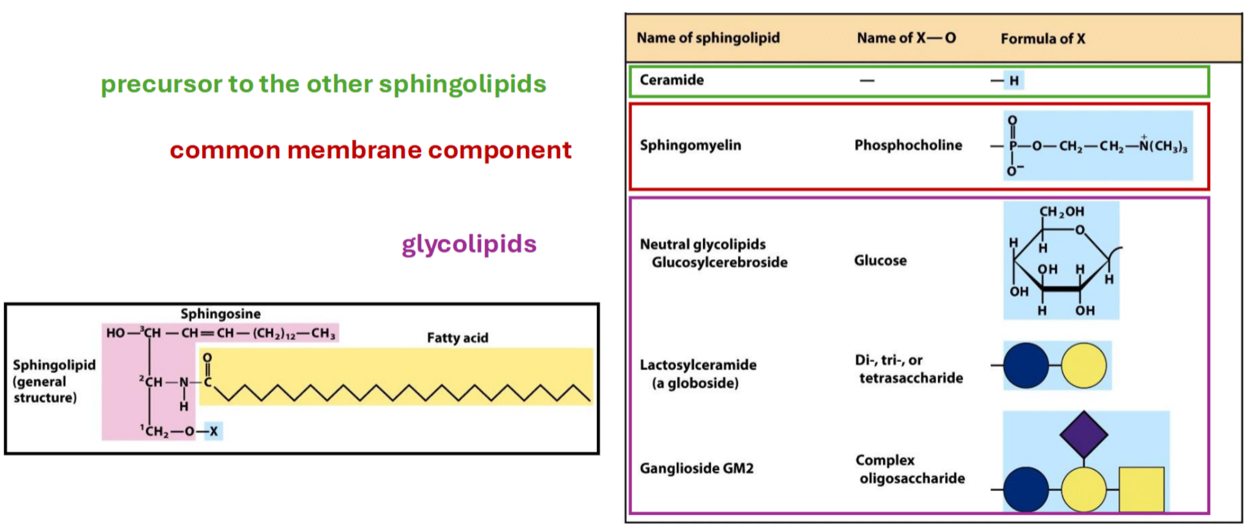

**Structure:** Glycerophospholipids are based on a glycerol backbone, with two fatty acids and a phosphate group attached. The phosphate group is further linked to a polar "head group" (e.g., ethanolamine, choline, serine, glycerol).

**Roles:**

1. **Precursor function:** Phosphatidic acid serves as the precursor to other glycerophospholipids
2. **Membrane components:** Glycerophospholipids like phosphatidylethanolamine, phosphatidylcholine, and phosphatidylserine are crucial for membrane structure and function
3. **Signaling pathways:** Specialized glycerophospholipids (e.g., phosphatidylinositol 4, 5-bisphosphate) participate in intracellular signaling, regulating processes like calcium release and enzyme activation

- **Cardiolipin:** Vital for mitochondrial membrane integrity and function

## Sphingolipids

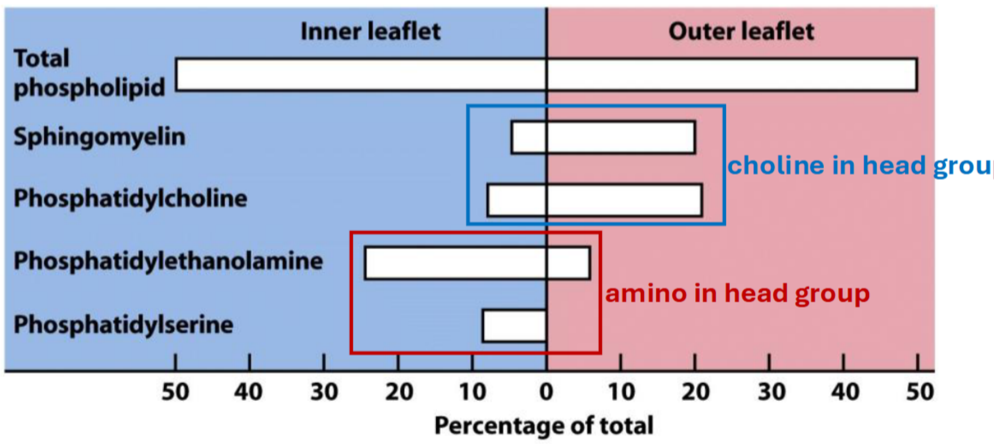



**Structure:** Sphingolipids are built on a sphingosine backbone (rather than glycerol), with a single fatty acid and a polar head group. The head groups can vary, producing different sphingolipid types **Roles:**

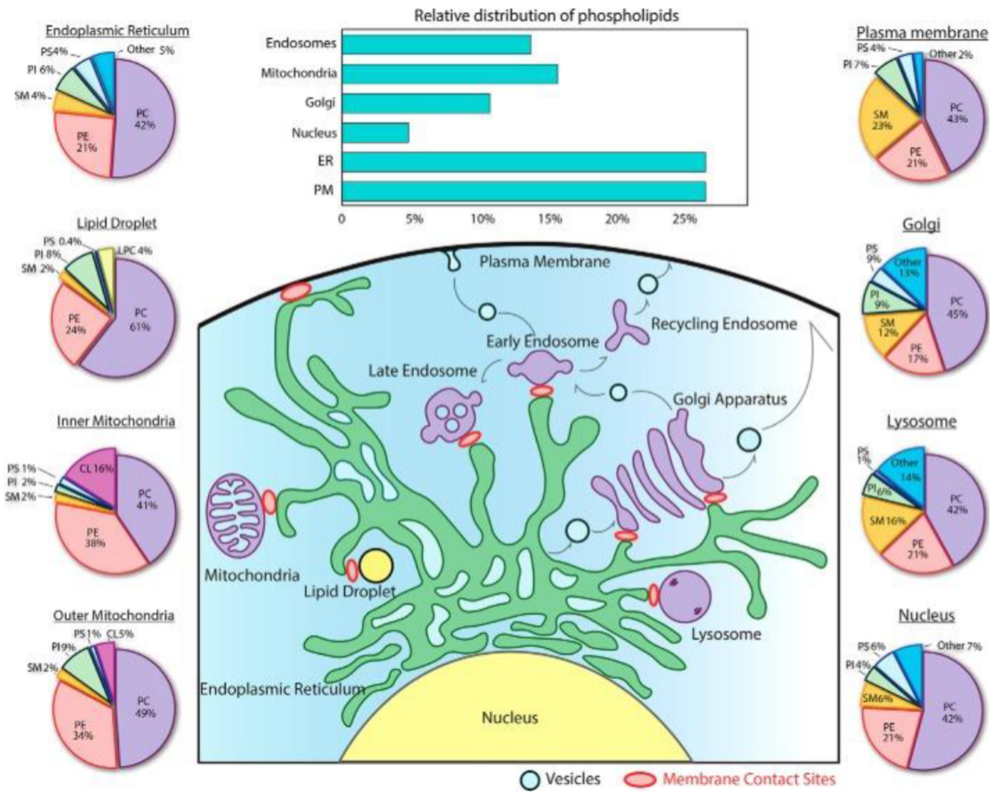
1. **Precursor function:** Ceramide acts as a precursor for more complex sphingolipids
2. **Membrane components:** Sphingomyelin is a major component of myelin sheaths in nerve cells
3. **Glycolipids:** These include neutral glycosphingolipids (e.g., glucosylceramide) and more complex gangliosides. These glycolipids play roles in cell recognition, signaling, and interactions.

## Phospholipid Asymmetry

- Cell membranes maintain asymmetry in phospholipid content
- Why? Likely helps maintain different electric environments and contribute to structure - also relevant for biological regulation
- If phosphatidiylserine (PS) is seen on the outer membrane, it's targeted for phagocytosis
  - In platelets, this triggers aggregation



## Lipids in Organelles



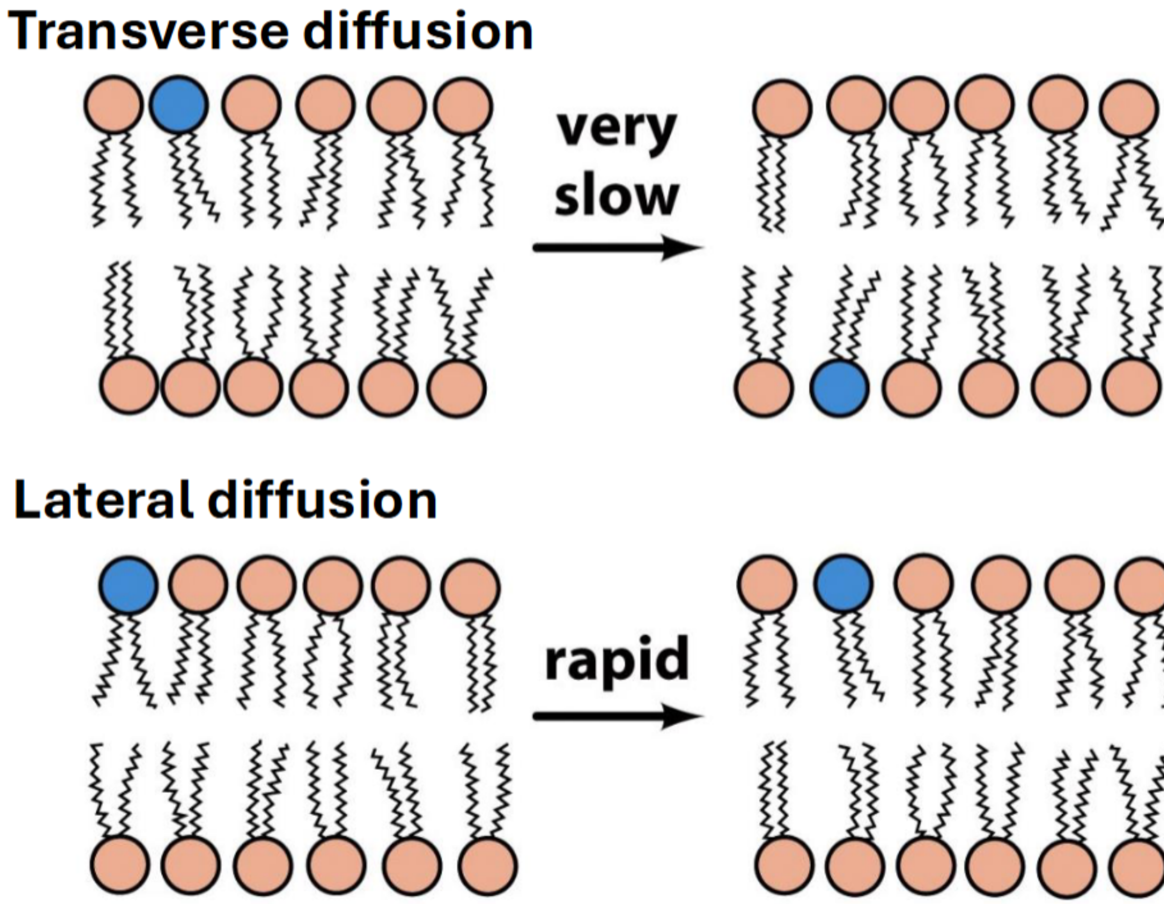

doi:10.1074/jbc.R117.000582

Abbreviations for the pie charts:

- Phosphatidylcholine (PC)
- Phosphatidylethanolamine (PE)
- Phosphatidylserine (PS)
- Phosphatidylglycerol (PG)
- Cardiolipin (CL)
- Sphingomyelin (SM)
- Other - Includes Phosphatidic Acid (PA)
- Diacylglycerol (DAG) and Lysolipids

- Lipids show distinct distributions and functions acroos different organelles, with specific abundances in organelles/compartments such as the **endoplasmic reticulum (ER), mitochondria, lysosomes, nucleus, Golgi apparatus, plasma membrane (PM), endosomes,** and **lipid droplets.**

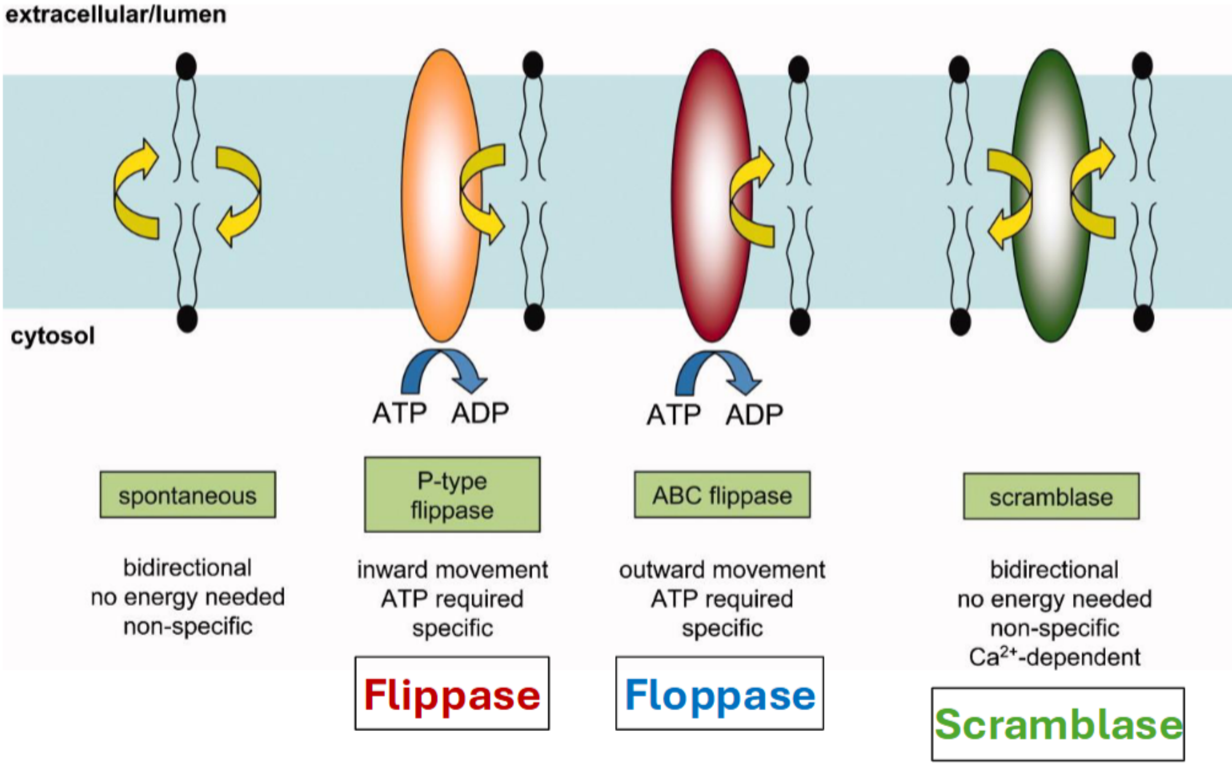
### Phospholipid Diffusion

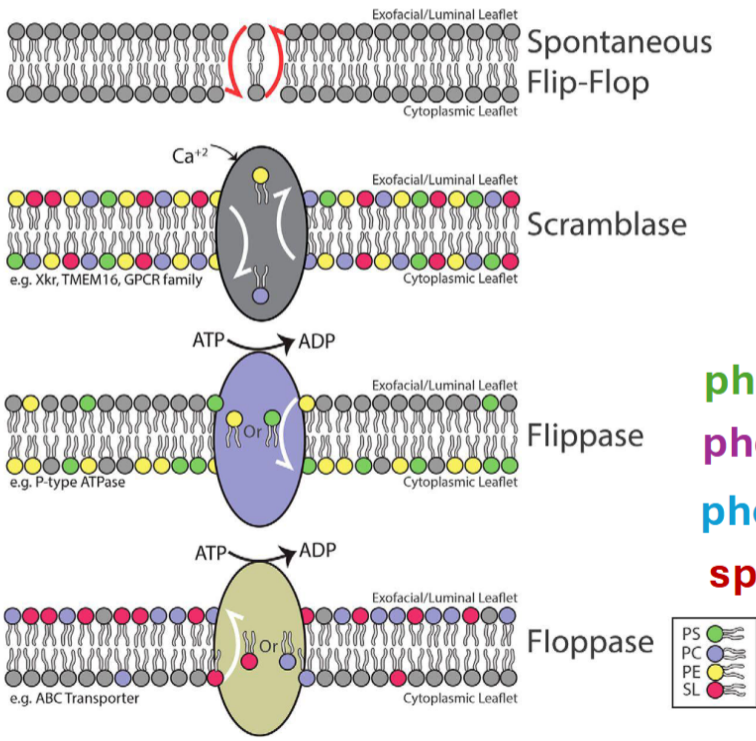



Changes in lipid organization can affect various cellular functions, such as membrane trafficking or signal transduction. These membrane-related effects can cause disease in living organisms due to genetic alterations, environmental factors (e.g., high dietary intake of saturated fats), or both

## Flippase, Floppase, and Scramblase

- **Flippase and Floppase** maintain asymmetry by putting phospholipids where they're "supposed" to be
- **Scramblase** indiscriminately flips phospholipids both directions - what would happen if scramblase dominated?
  - Phospholipid content would **even out** (50:50 equilibrium)
  - This would include PS
- **Scramblase** is activated by levels of $Ca^{2+}$ signaling that trigger in case of damage - beginnings of apoptosis (conversely flippase and floppase are inhibited)



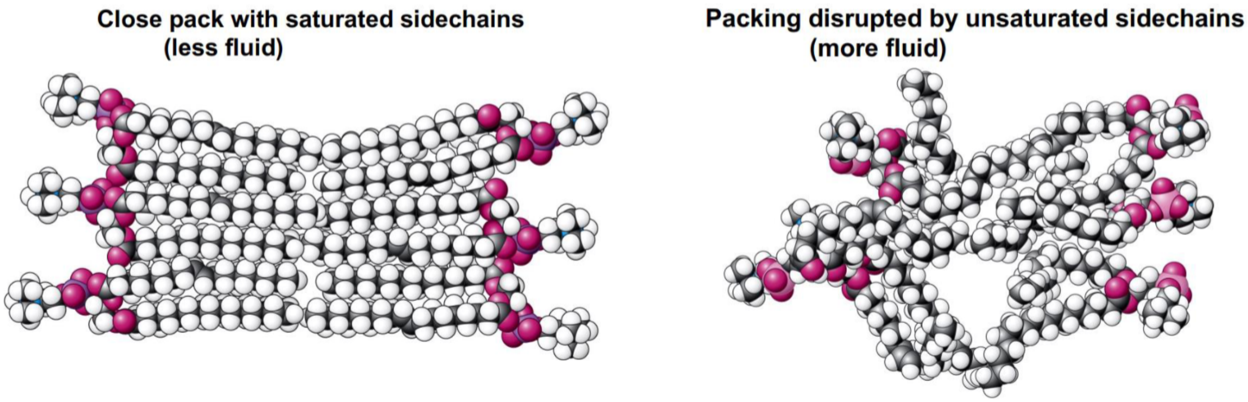

phosphatidylserine

phosphatidylcholine

phosphatidylethanolamine

sphingomyelin

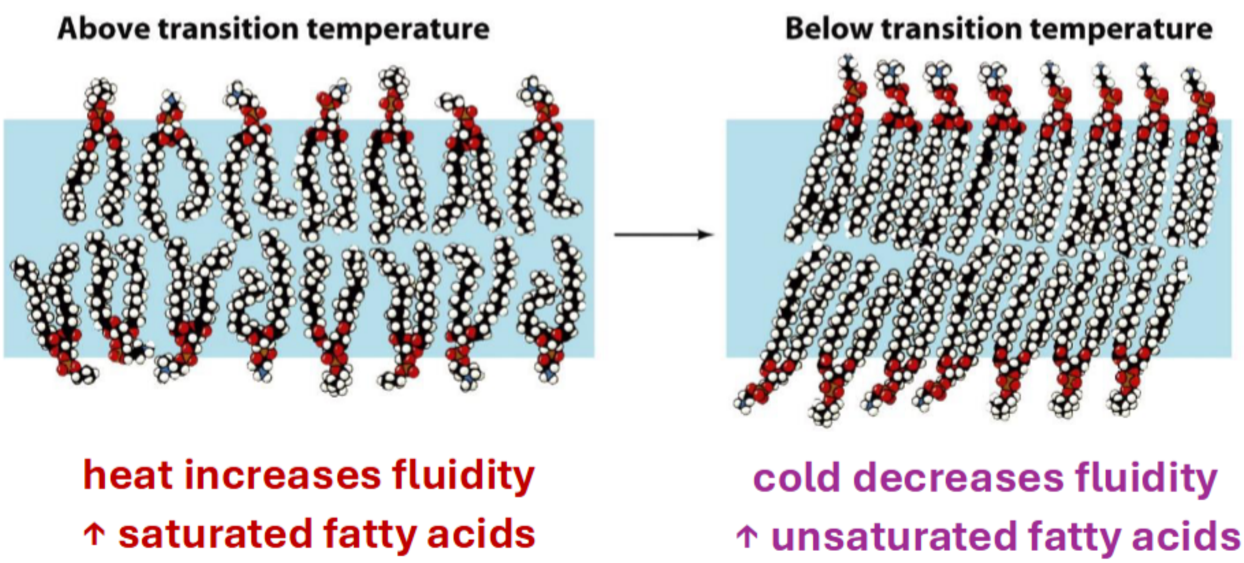
### Saturated and Unsaturated Phospholipid Structure




- Saturated phospholipids generate more rigid structures (Left).
- Unsaturated phospholipids generate more fluid structures (Right).

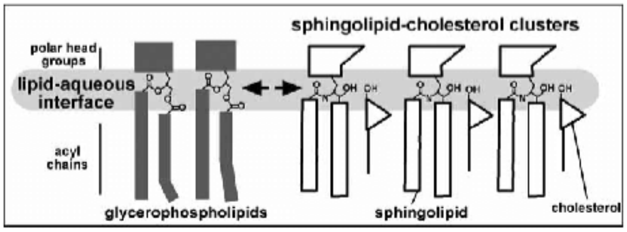
### Phospholipids - Cell Regulation

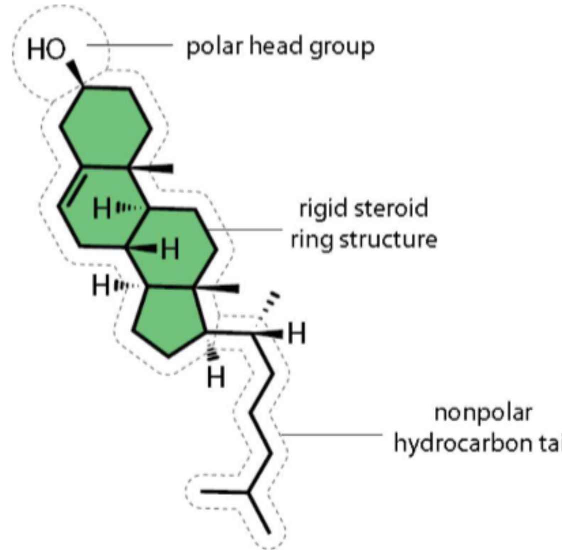
Cells can regulate their own lipid composition to maintain membrane fluidity (called **homeoviscous adaptation**)



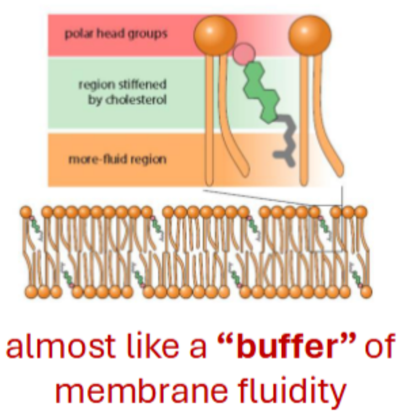

### Moderation of membrane fluidity by Cholesterol

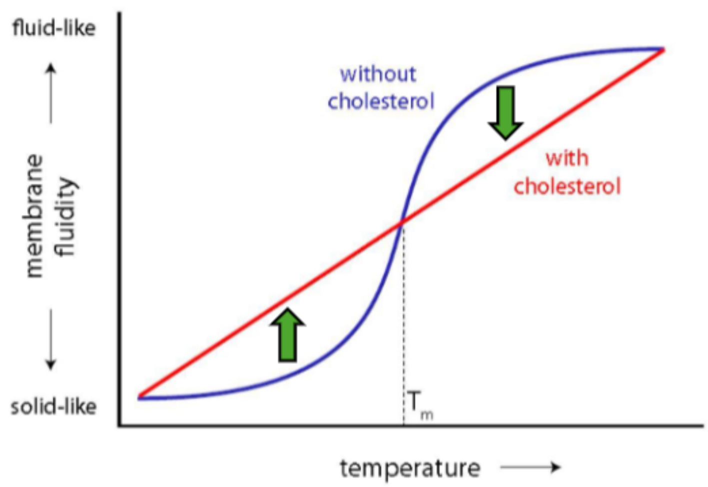
- As we've already discussed, cholesterol serves as a biosynthetic precursor to sterol hormones
- Also serves as an important membrane structural component
- Polar head group (-OH) creates hydrogen bonding with sphingolipids, creating **lipid rafts**



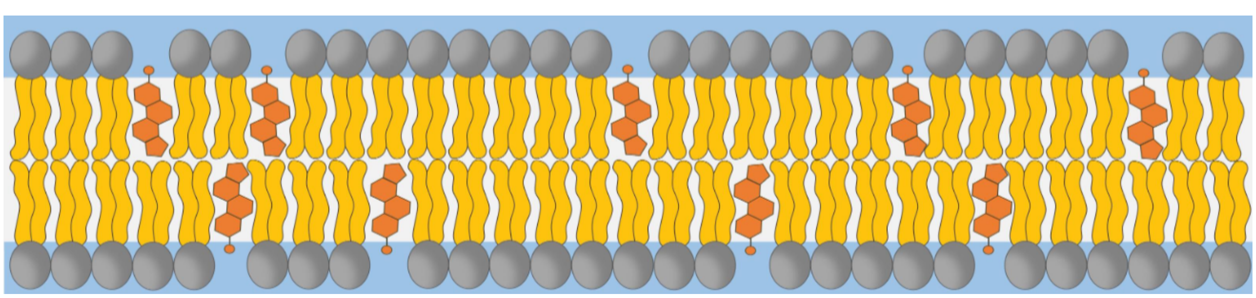




- At low temperatures, phospholipids pack tightly, but cholesterol's rigid four ring structure reduces extent of packing
- At high temperatures, phospholipids pack loosely, but the intermolecular interactions with cholesterol keeps phospholipids somewhat closer together
- All in all, this means that cholesterol moderates membrane fluidity.




- The mammals have evolved sophisticated and complex mechanisms to maintain plasma cholesterol levels, as well as cell membrane cholesterol levels, within a narrow physiological range.

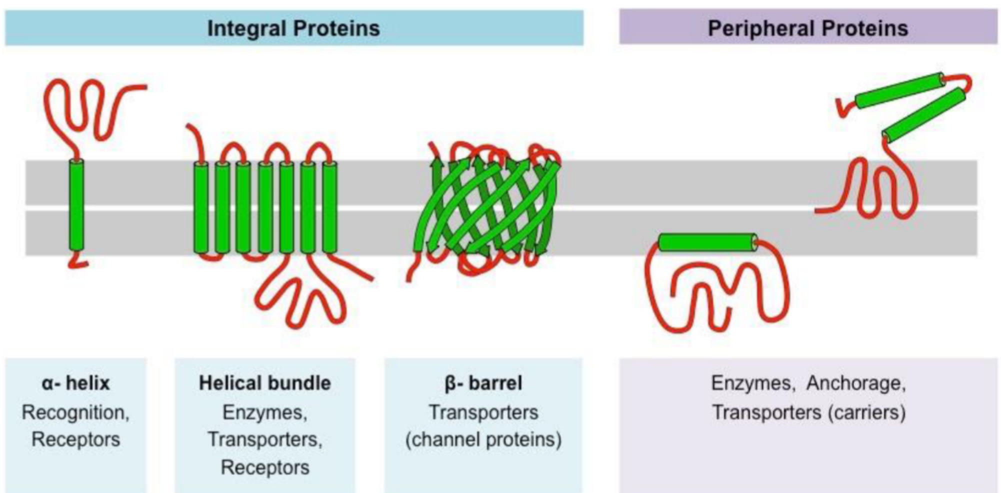


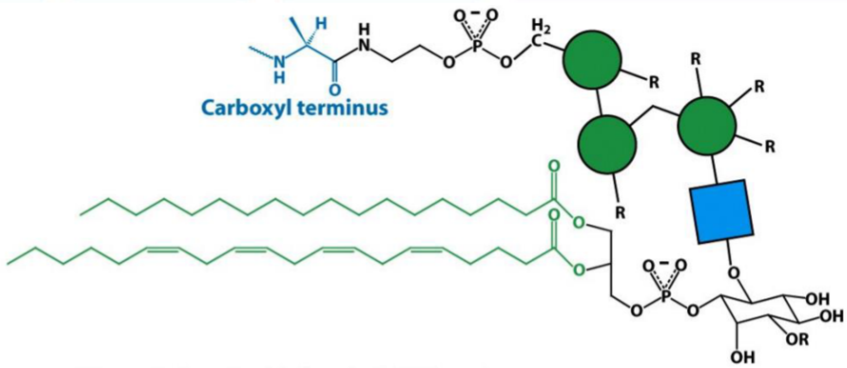
## Cholesterol Homeostasis

- Animal cells maintain cholesterol homeostasis by transporting cholesterol from one membrane to another. Cholesterol derived from low-density lipoprotein (LDL) is taken into cells through endocytosis mediated by LDL receptors (LDLRs)
- The LDL-derived cholesterol is released in lysosomes and then transported to the plasma membrane (PM), where it plays a structural role, and to the endoplasmic reticulum (ER) membrane.

## Membrane Proteins Redux

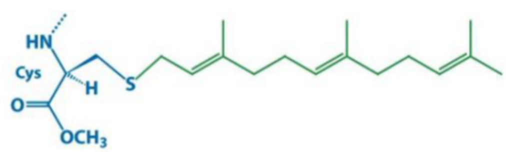
- We've dealt with how proteins use their primary/secondary structures to associate with membranes, but not with any lipid-based solutions.
- Enter **lipid-anchored proteins**, proteins located on the surface of the cell membrane that are covalently attached to lipids embedded within the cell membrane




**Glycosyl phosphatidylinositol (GPI) anchor**


***S*-Palmitoylcysteine**




**C-terminal *S*-farnesylcysteine methyl ester**