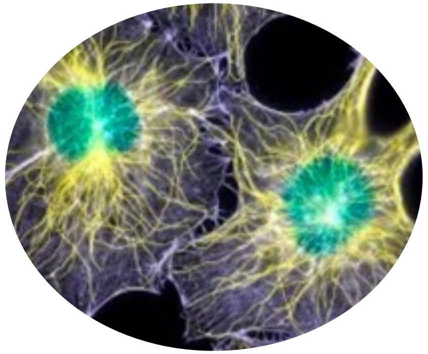
Fisiologia Celular e Molecular

Mestrado em Biologia Molecular e Genética

2º Semestre

6 ECTS



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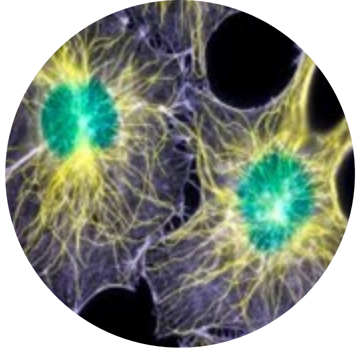
MEMBRANES

Membrane fluidity
Membrane fusion
Ion transport

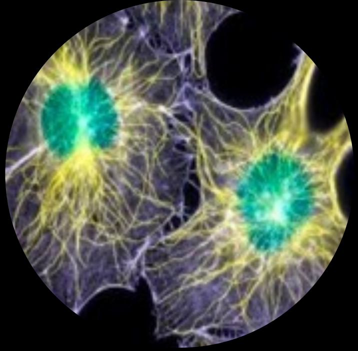


Fisiologia Celular e Molecular

MEMBRANE

The fluid mosic model

The Plasma Membrane and the Fluid Mosaic Model



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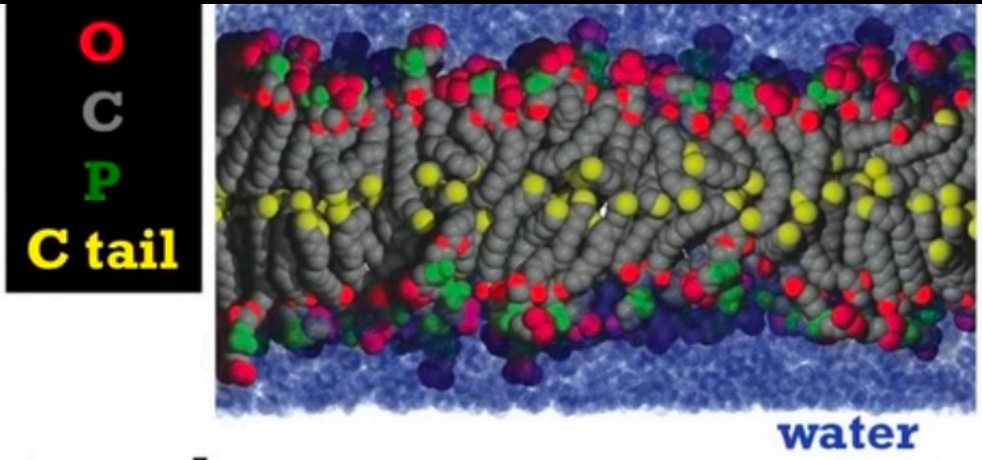
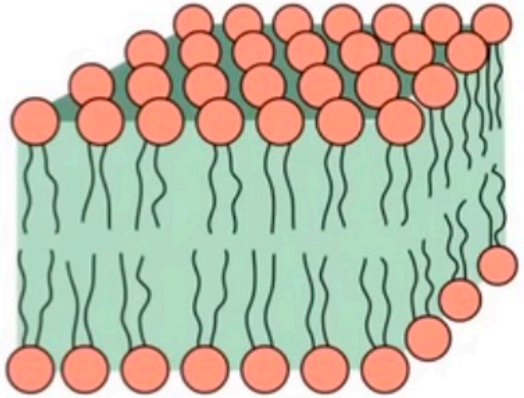
The fluid mosic model

Lipid Bilayer

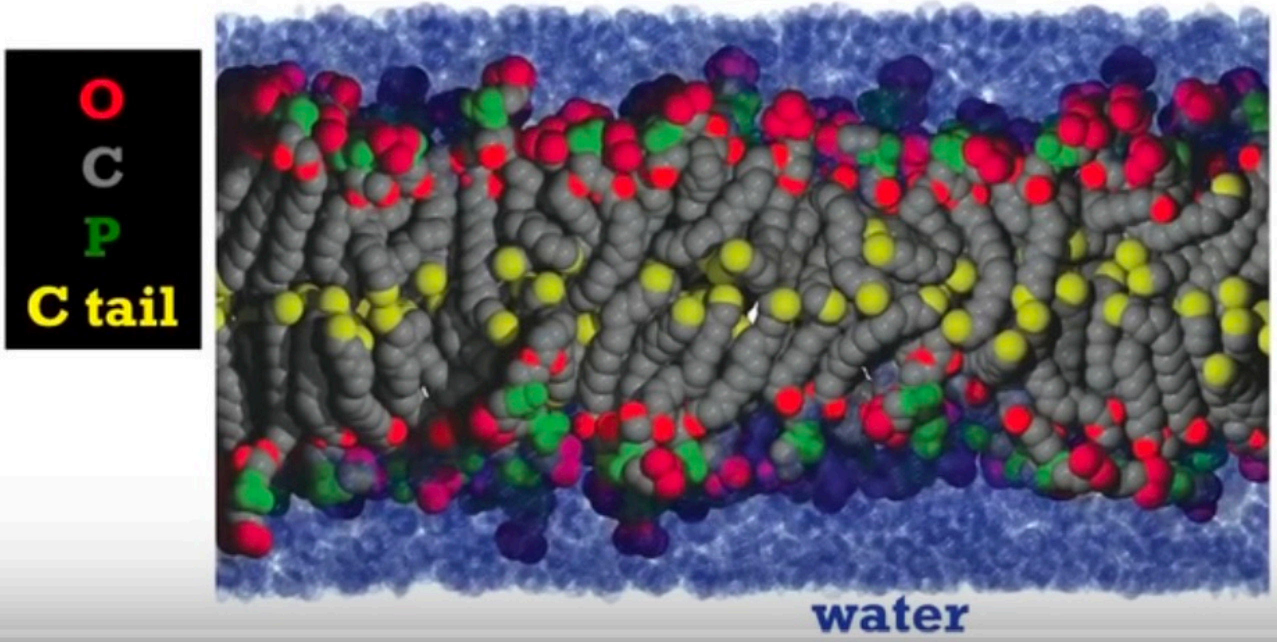


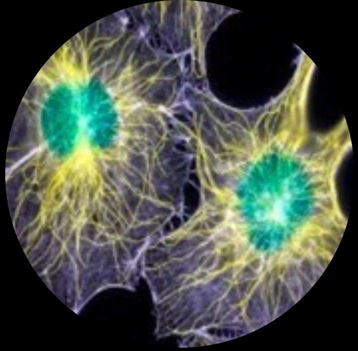
- Forms biological membranes
- 2D array of amphipathic molecules
  - Nonpolar tails associate away from aqueous interface
  - Head groups face outward to aqueous environment
- Forms spontaneously
  - Hydrophobic effect



Lipid Bilayer

- Bilayer is very fluid
  - No defined geometry
  - Dynamic assembly
- Self-sealing and very stable





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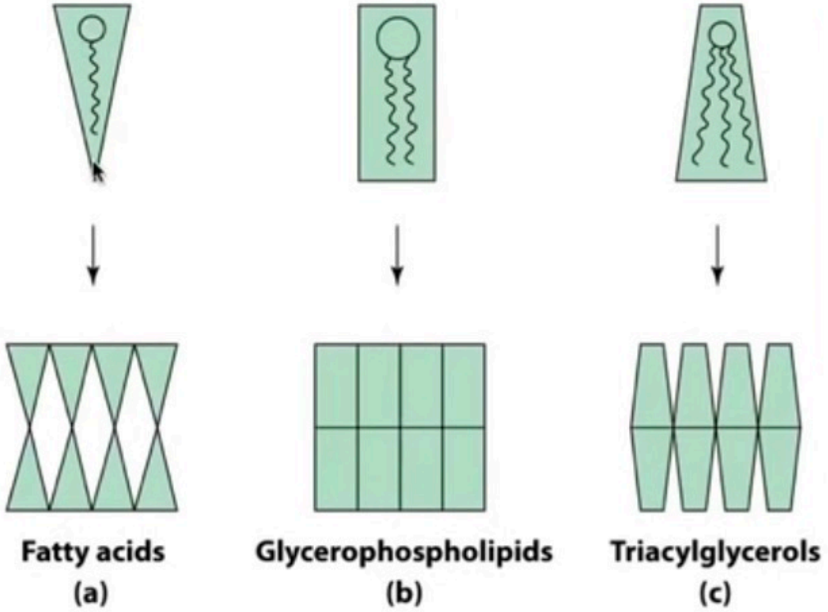
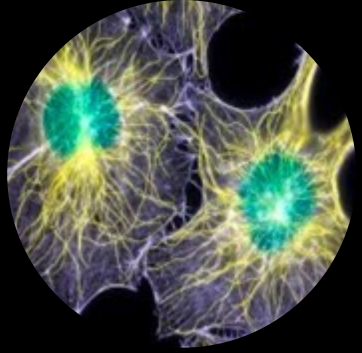
Lipid Bilayer

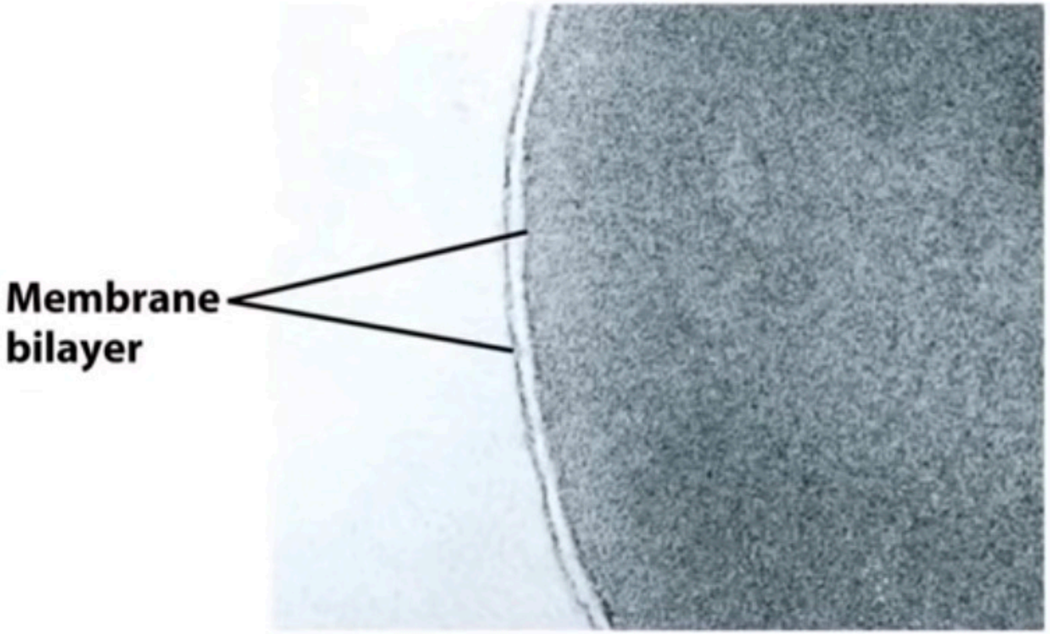


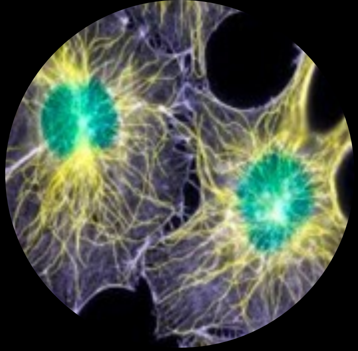
- Formed from glycerophospholipids and sphingolipids
  - Has to do with geometry of molecules
  - Cholesterol can partition in membrane, but cannot form bilayer of itself
- Fatty acids and triglycerides cannot form bilayers
  - Geometry wrong



Lipid Bilayer

- 25-30 Å thick
  - Thickness varies depending on length of acyl chains and how they interact
  - Also depends on size of head groups





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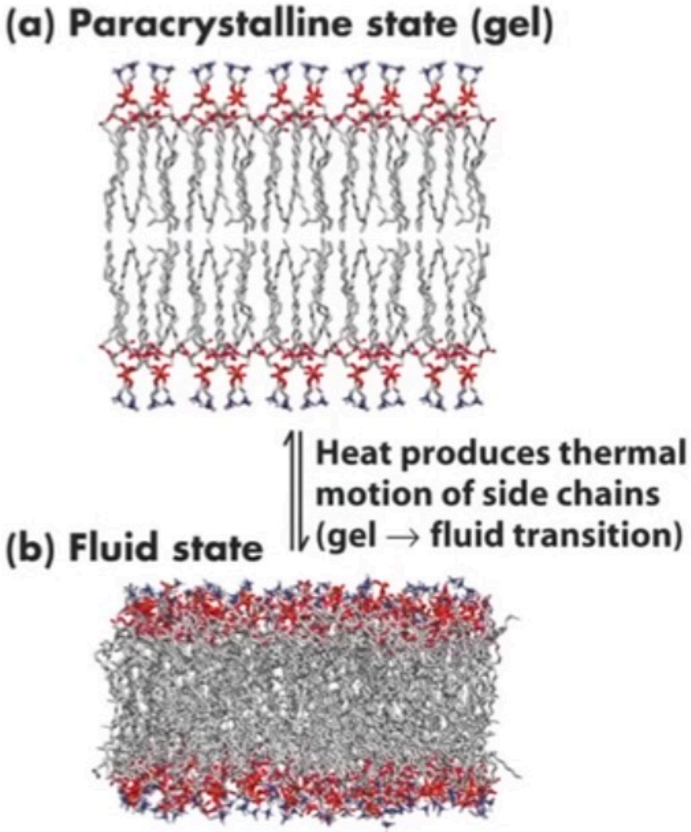
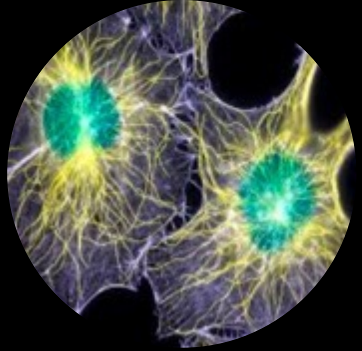
The fluid mosic model

Membrane Fluidity

- Lipid melting point (T_m)
  - T of transition from ordered crystalline state to fluid state
  - Acyl chains pack together in crystalline form
    - van der Waals





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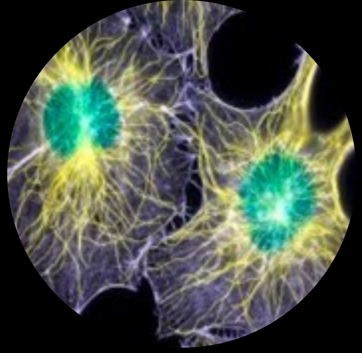
The fluid mosic model

Membrane Fluidity

- Lipid melting point
  - Given the melting points of some fatty acids, what factors influence the melting point?
    - 12:0 means a 12-C chain with no double bonds
    - Which FAs melt more readily and why?
      - Polyunsaturated chains

Fatty acid	Melting point (°C)
Laurate (12:0)	44.2
Linoleate (18:2)	-9
Linolenate (18:3)	-17
Myristate (14:0)	52
Oleate (18:1)	13.2
Palmitate (16:0)	63.1
Stearate (18:0)	69.1



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Membrane Fluidity

- **Lipid melting point**
  - Given the melting points of some fatty acids, what factors influence the melting point?
    - Which FAs have the highest T_m and why?

  - Longest chains
  - Degree of saturation more important than length of chain

Fatty acid	Melting point (°C)
Laurate (12:0)	44.2
Linoleate (18:2)	-9
Linolenate (18:3)	-17
Myristate (14:0)	52
Oleate (18:1)	13.2
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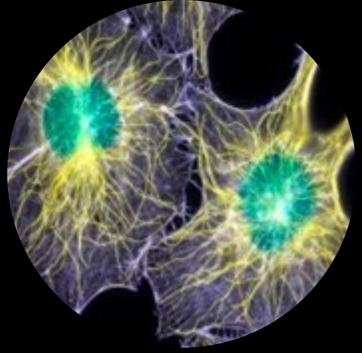
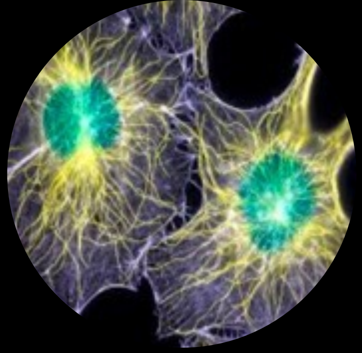


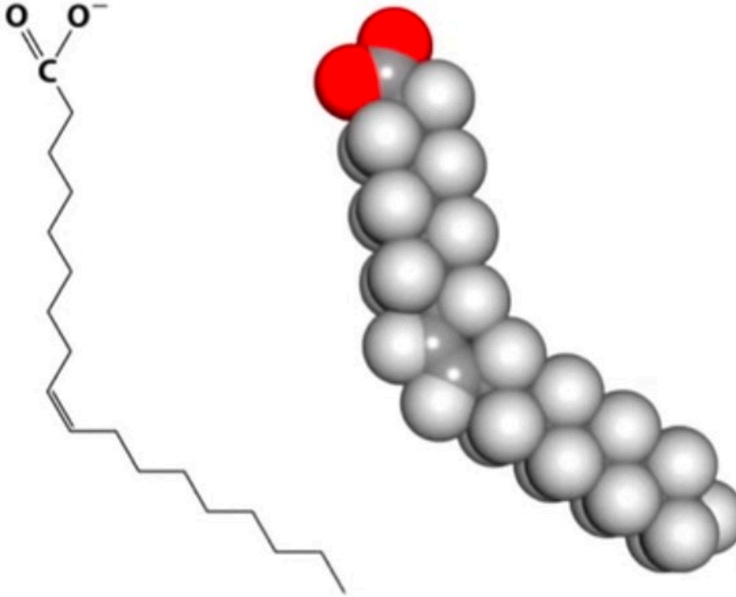
Membrane Fluidity

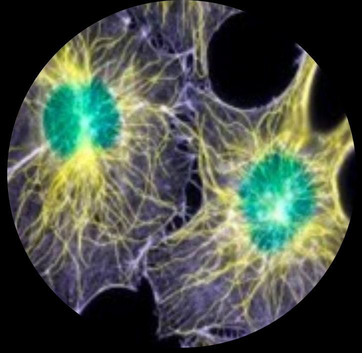
- Lipid melting point
  - Depends on length of chain and degree of saturation
    - For saturated chain, T_m ↑ as chain length ↑
    - Takes more energy to disrupt extensive vdW interactions



+ Membrane Fluidity

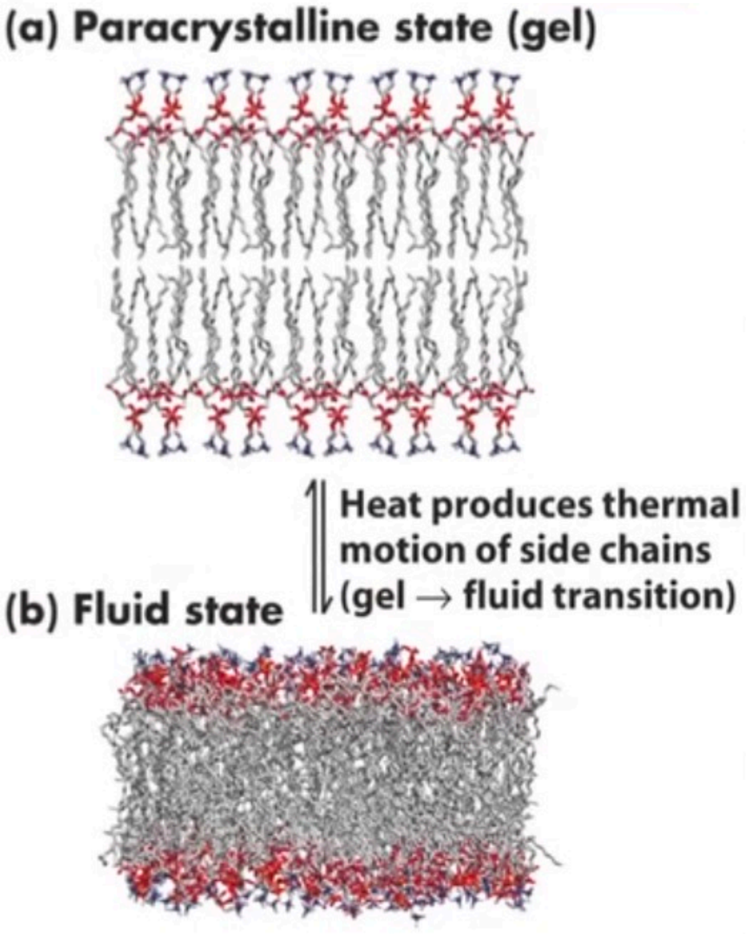
- Lipid melting point
  - Depends on length of chain and degree of saturation
    - Double bond introduces “kink” – less efficient packing
      - Lower T_m
  - Longer chains less mobile than shorter
  - Saturated less mobile than unsaturated

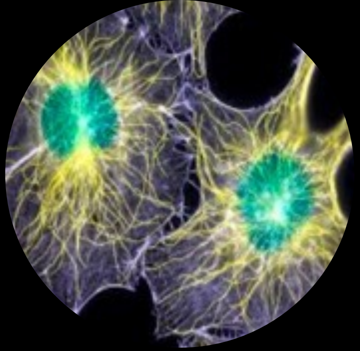




Membrane Fluidity

- Biological membranes composed of many types of lipids
  - Fluidity maintained over range of T
  - Can alter types of fatty acid chains to improve/limit fluidity
    - E.g. bacterium can incorporate more unsaturated FA at low T





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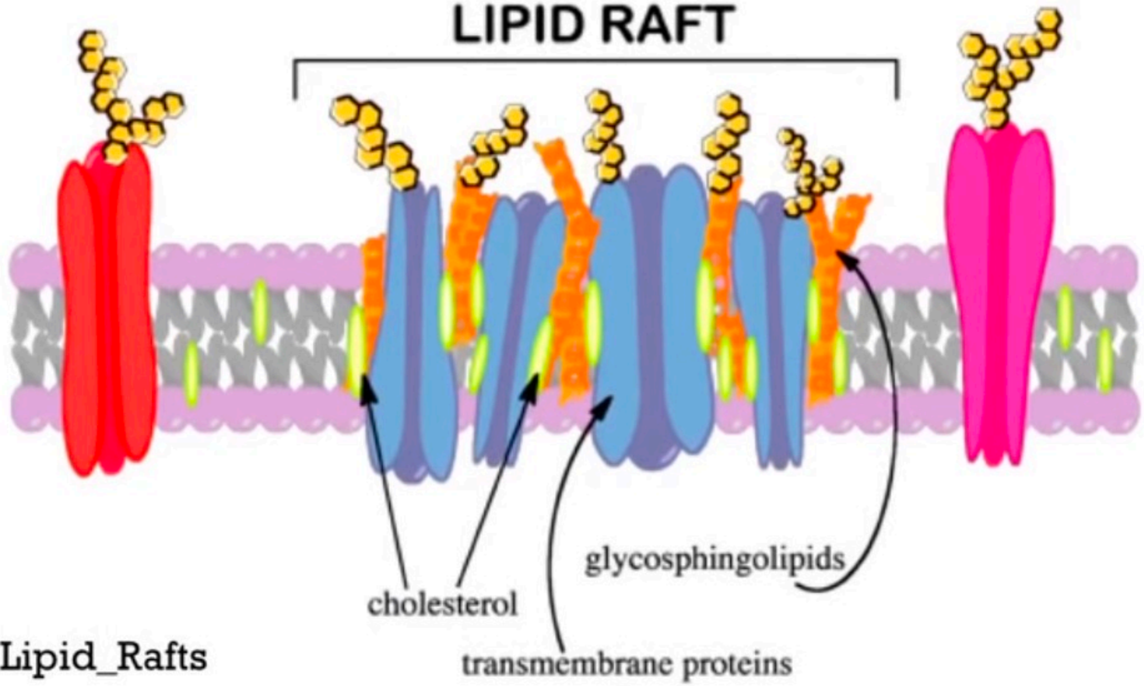
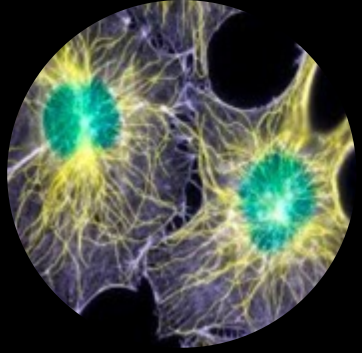
Membrane Fluidity

- May be local regions of membrane that are nearly crystalline
  - Lipid rafts
  - Contain cholesterol and sphingolipids



http://en.wikibooks.org/wiki/Structural_Biochemistry/Lipids/Lipid_Rafts



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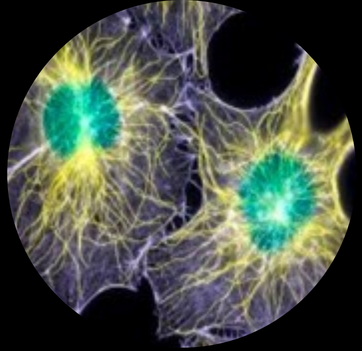
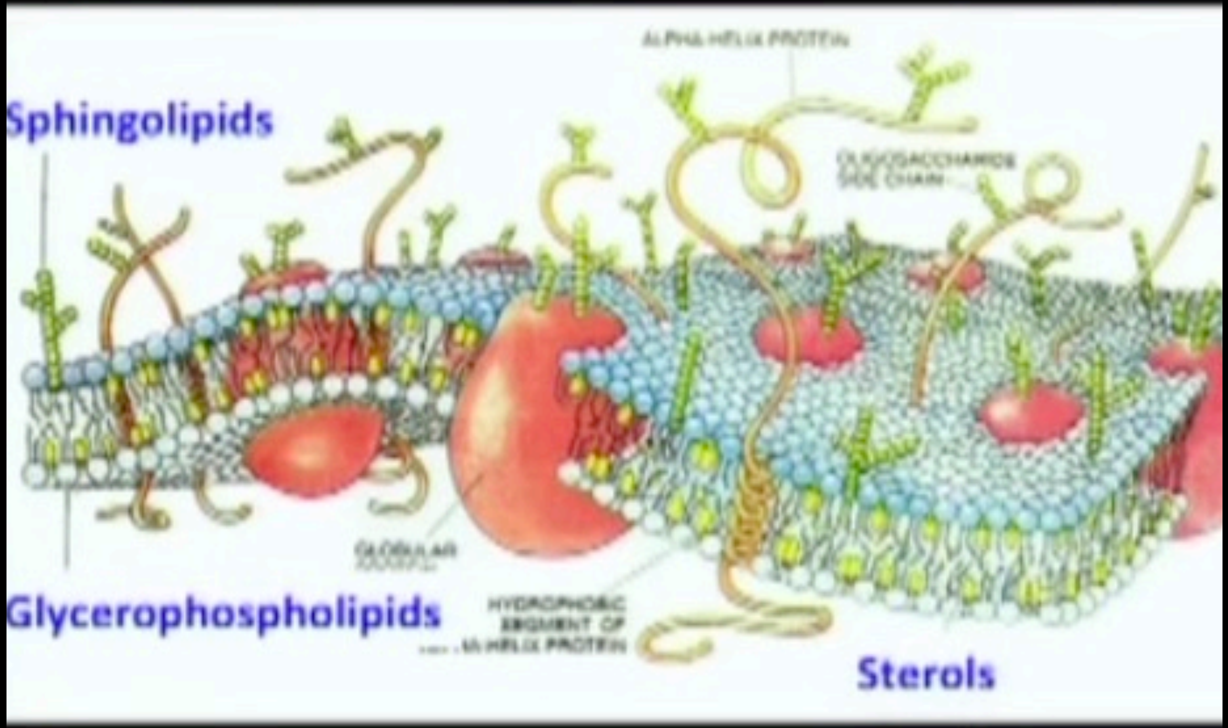
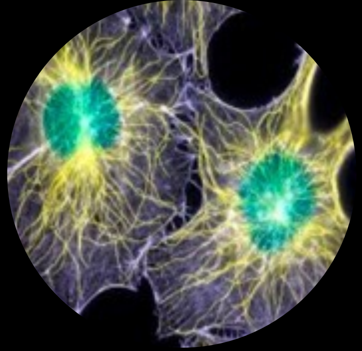


Cell membranes are two-dimensional solutions of oriented proteins and lipids



Scientific American, Bretscher, 1985



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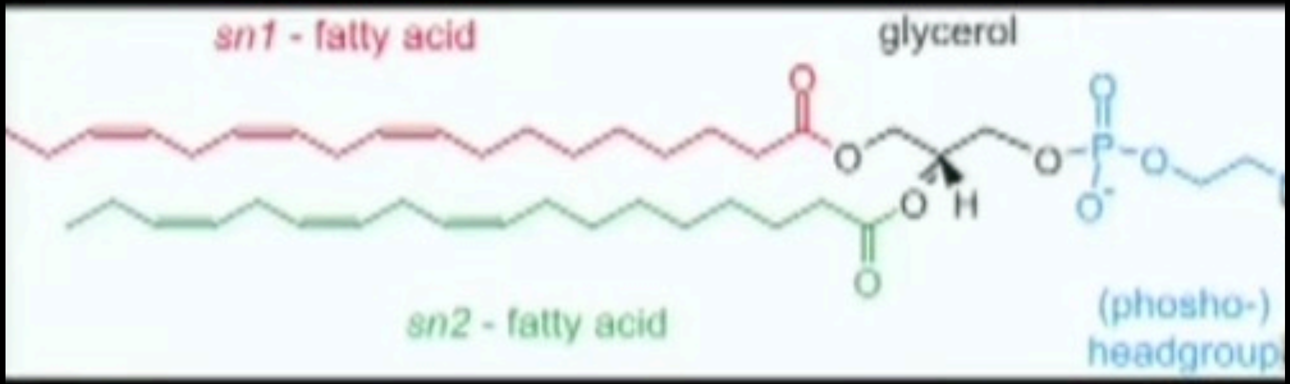
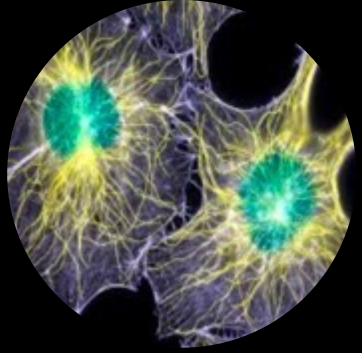
The fluid mosic model

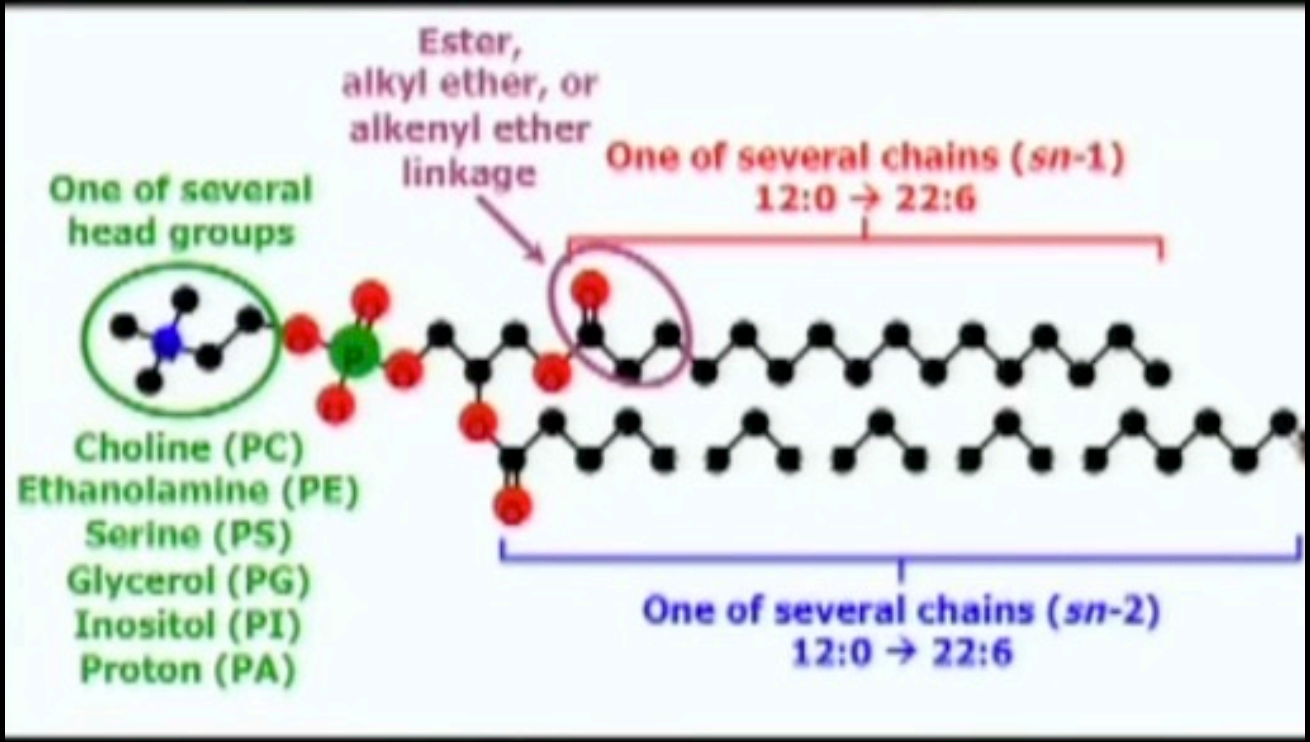
Structural complexity of glycerophospholipids

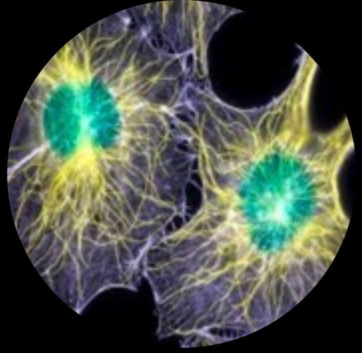


Over 1000 individual lipid species



Structural complexity of glycerophospholipids





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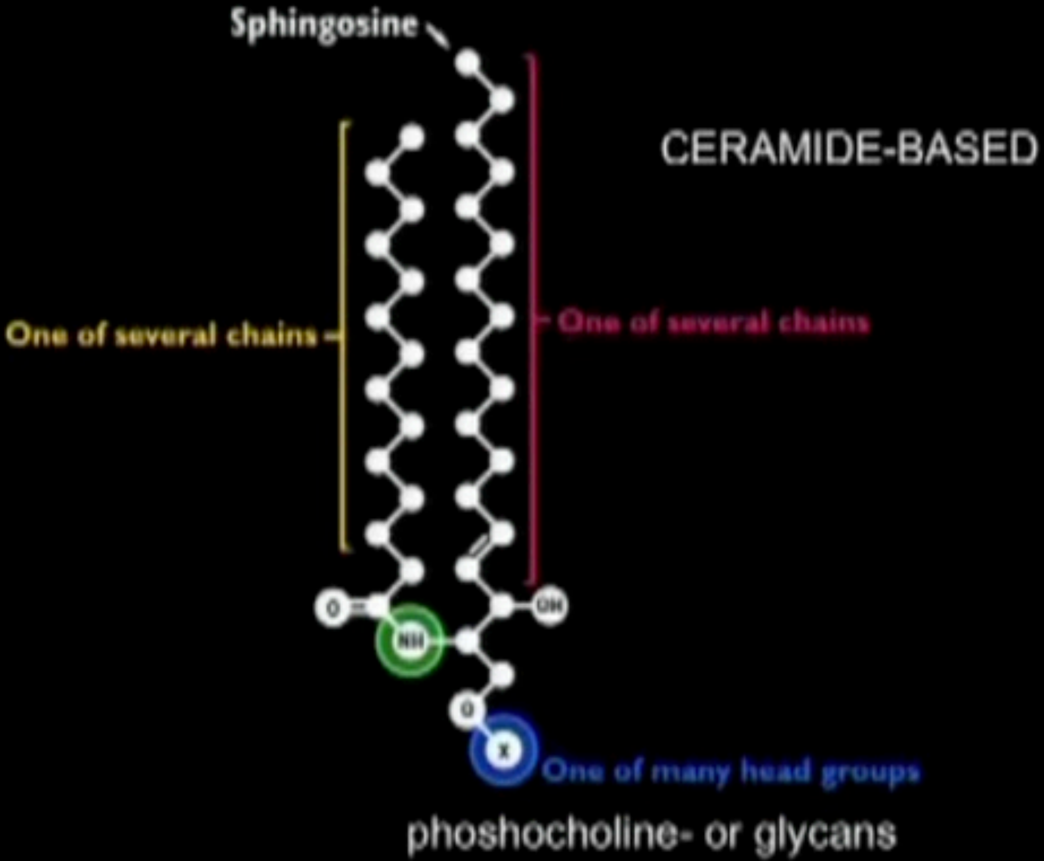
Structural complexity of sphingolipids



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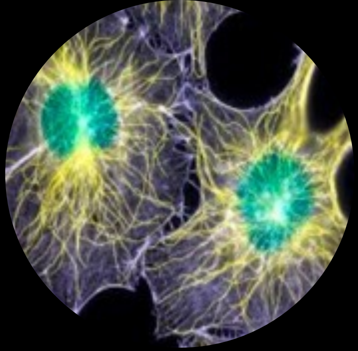
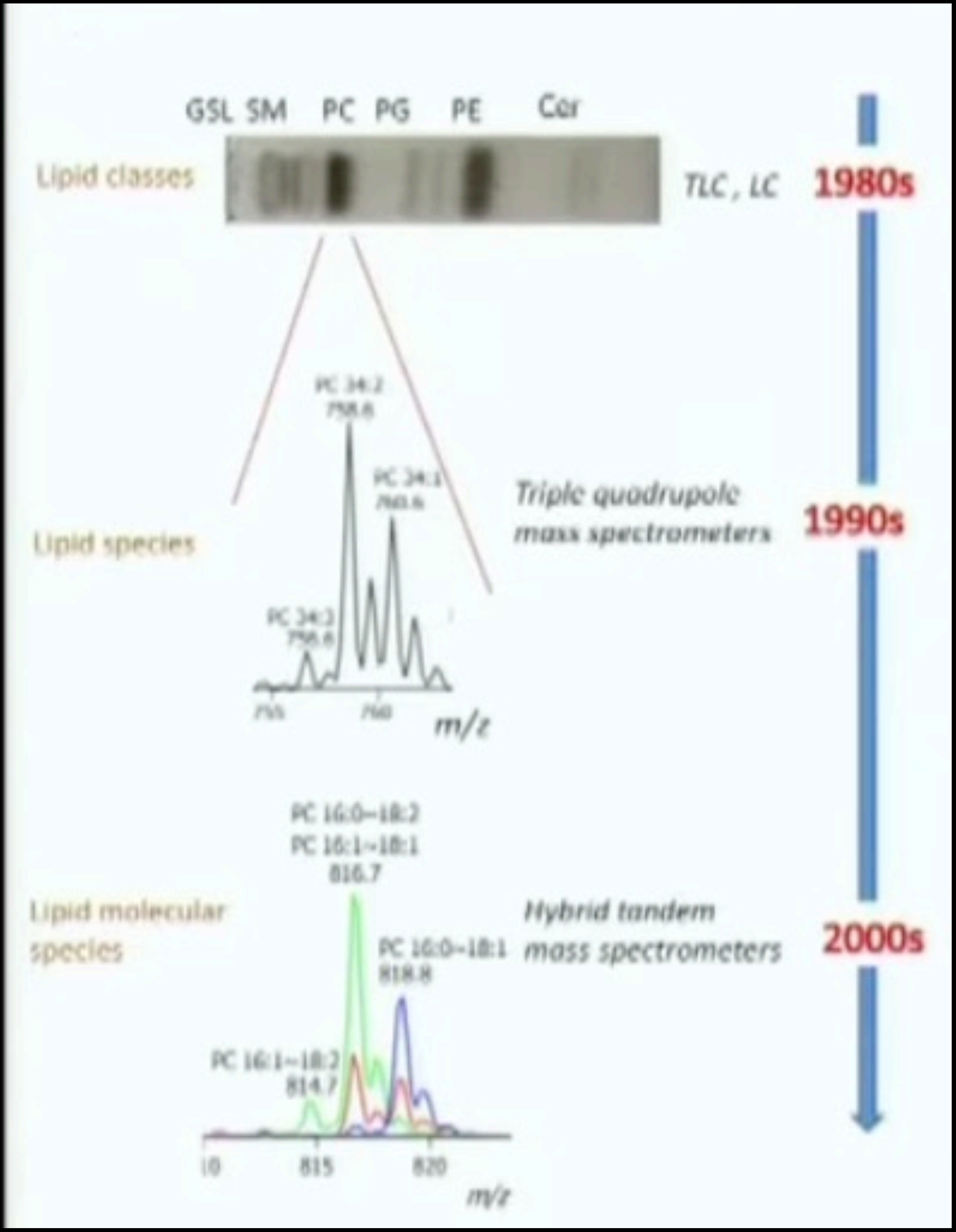
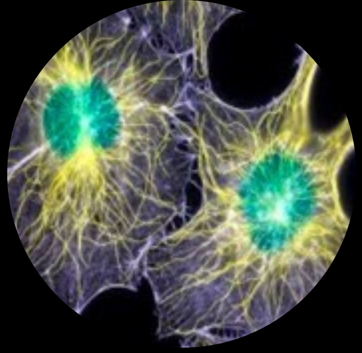
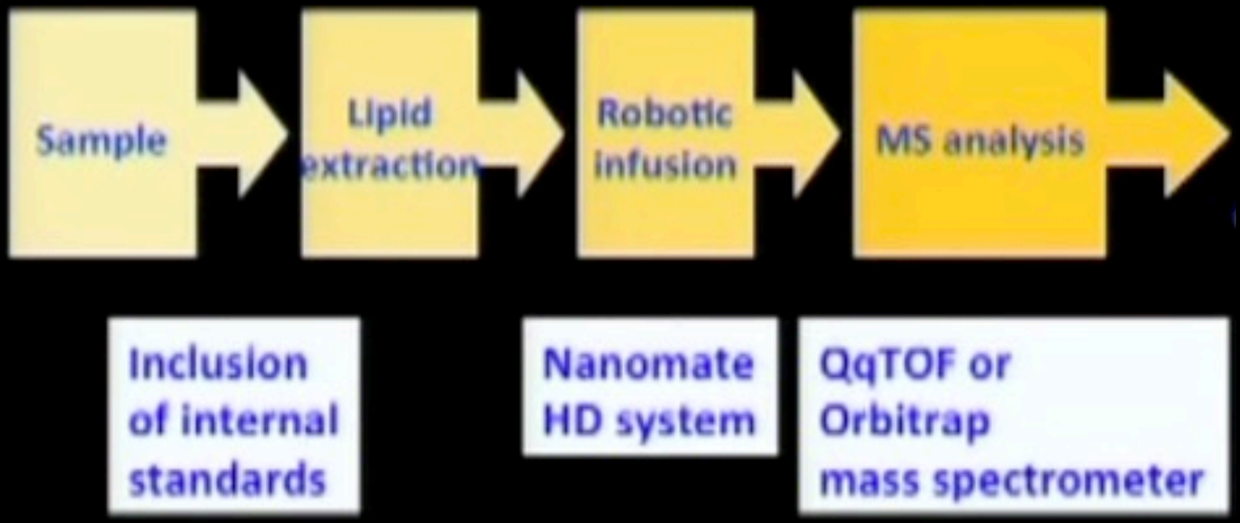


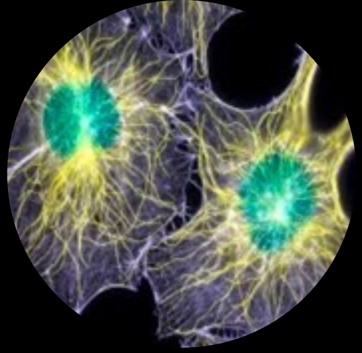




Shotgun lipidomics platform



(Schwudke et al., Anal Chem, 2006)
(Ejsing et al., *Anal Chem*, 2006)



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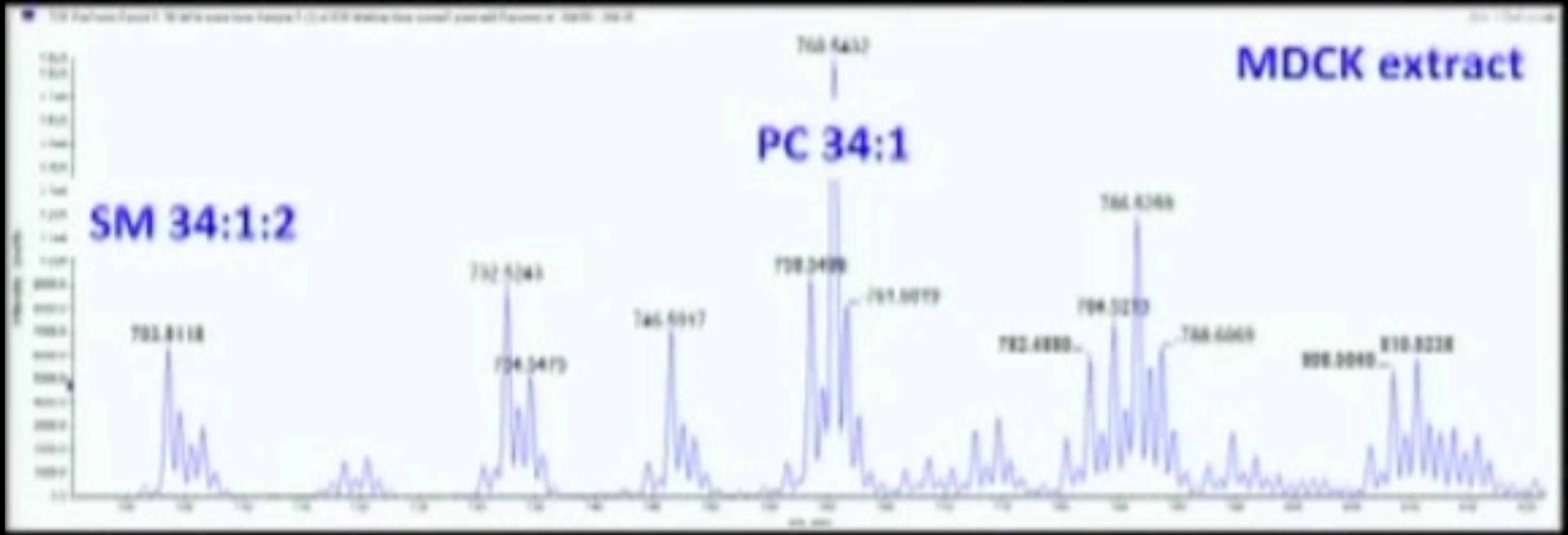
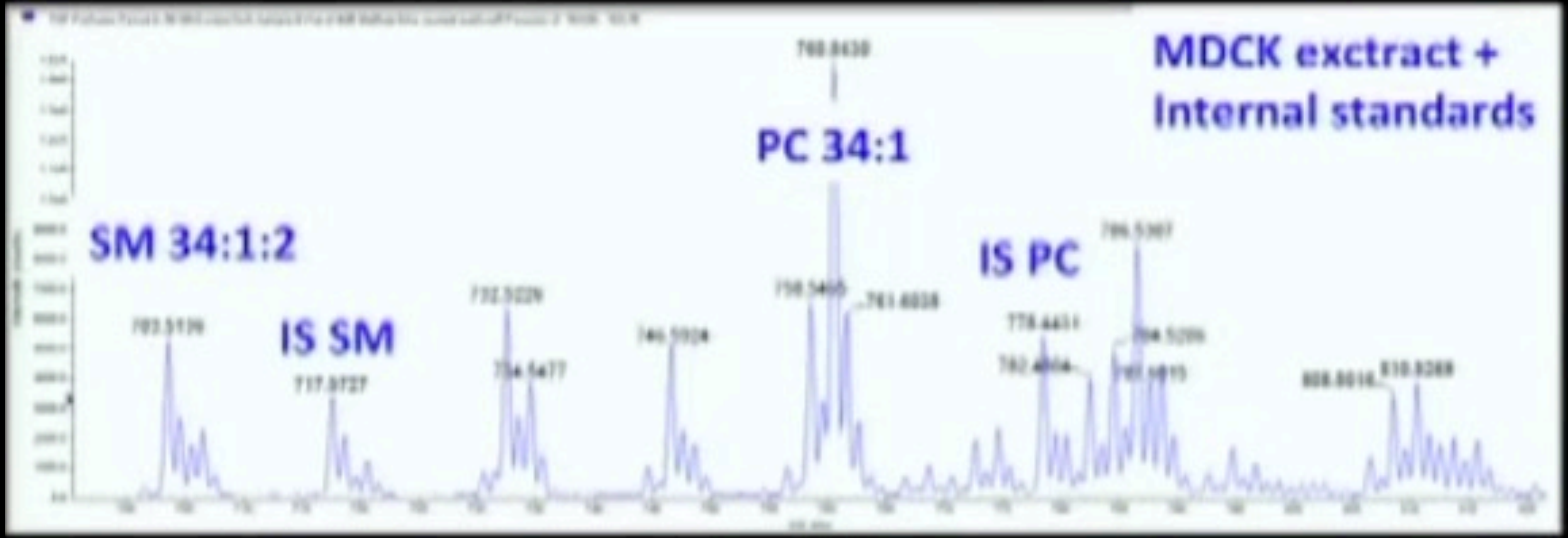
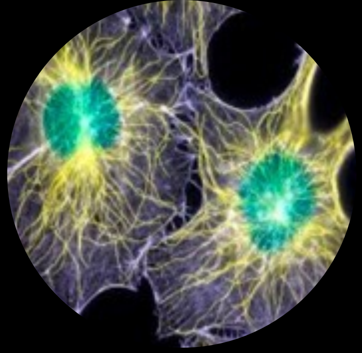
Lipid quantification







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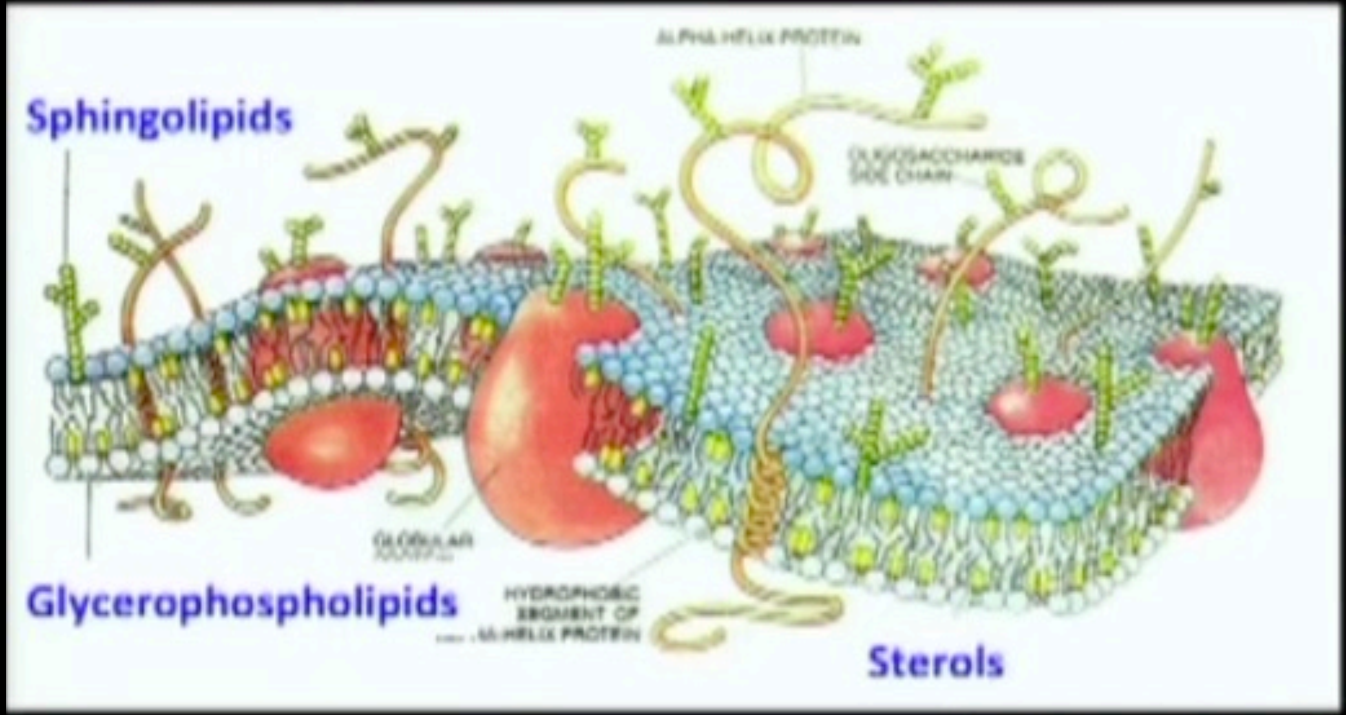
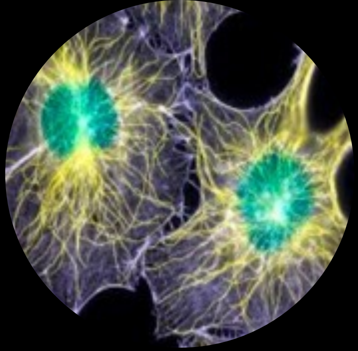
Biological membranes

Cellular lipidomes may contain up to 7000 distinct



Scientific American, Bretscher, 1985



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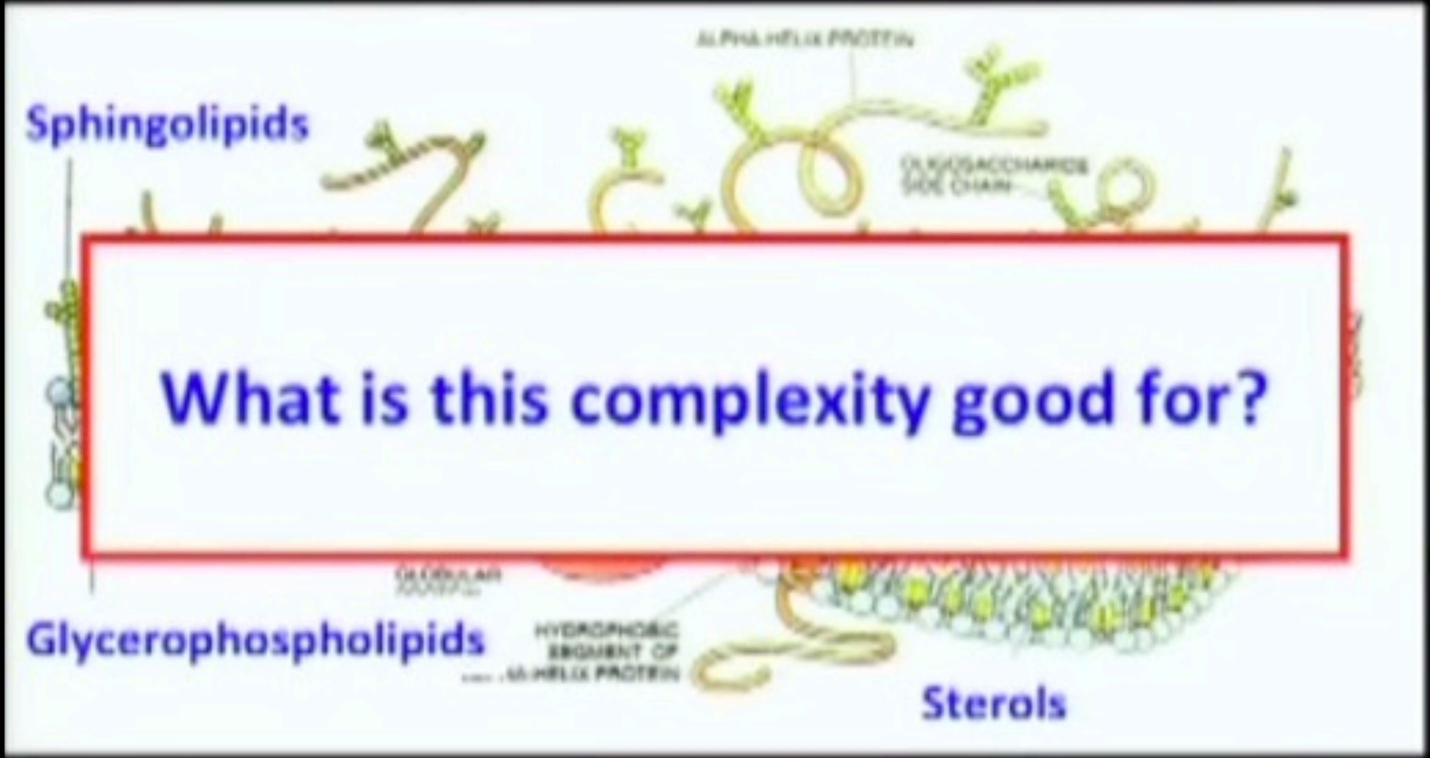

Scientific American, Bretscher, 1985

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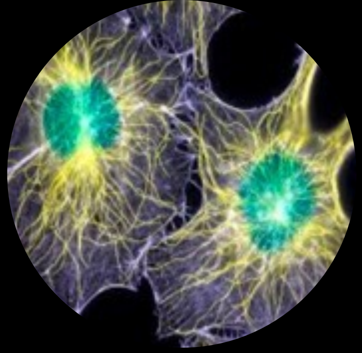
Topics

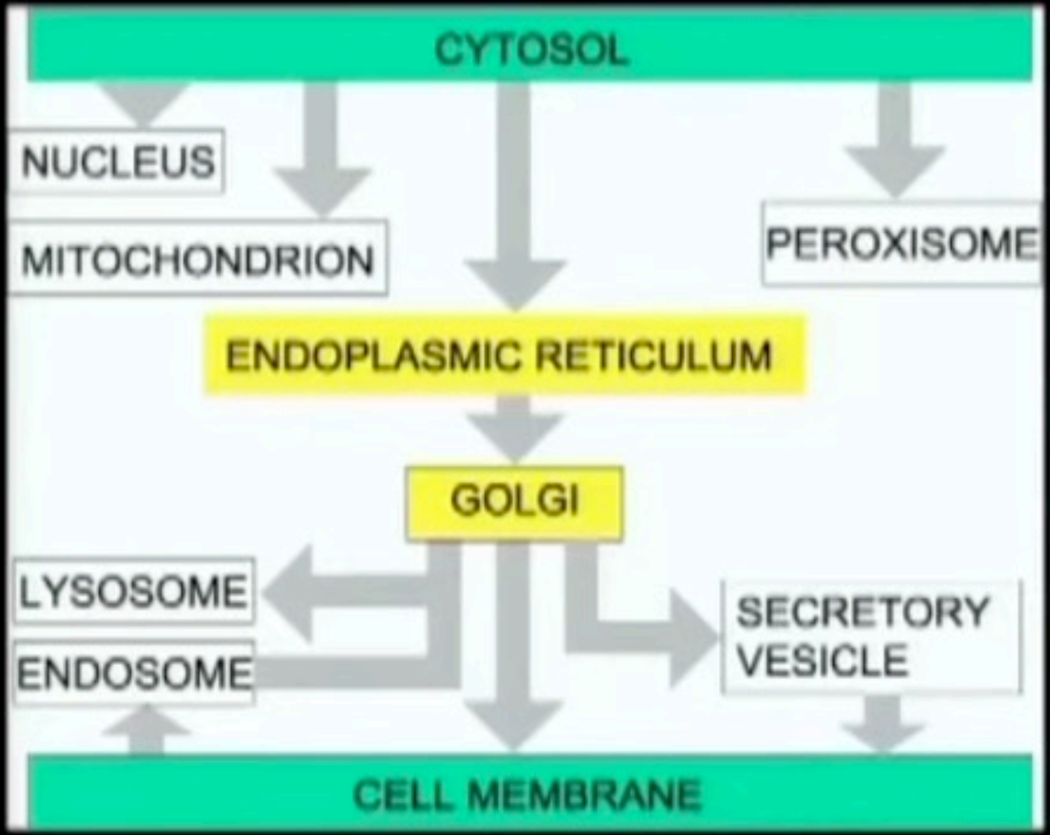
I Role of lipids in organizing the biosynthetic pathway from the endoplasmic reticulum to the cell surface

II Lipid rafts as a membrane organizing principle

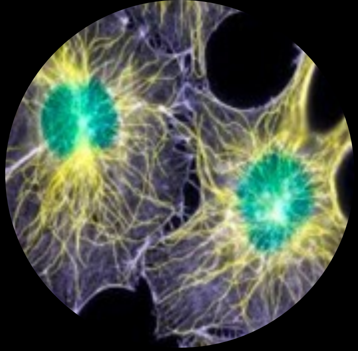
III Biogenesis of the glycolipid-rich apical cell surface membrane in epithelial cells



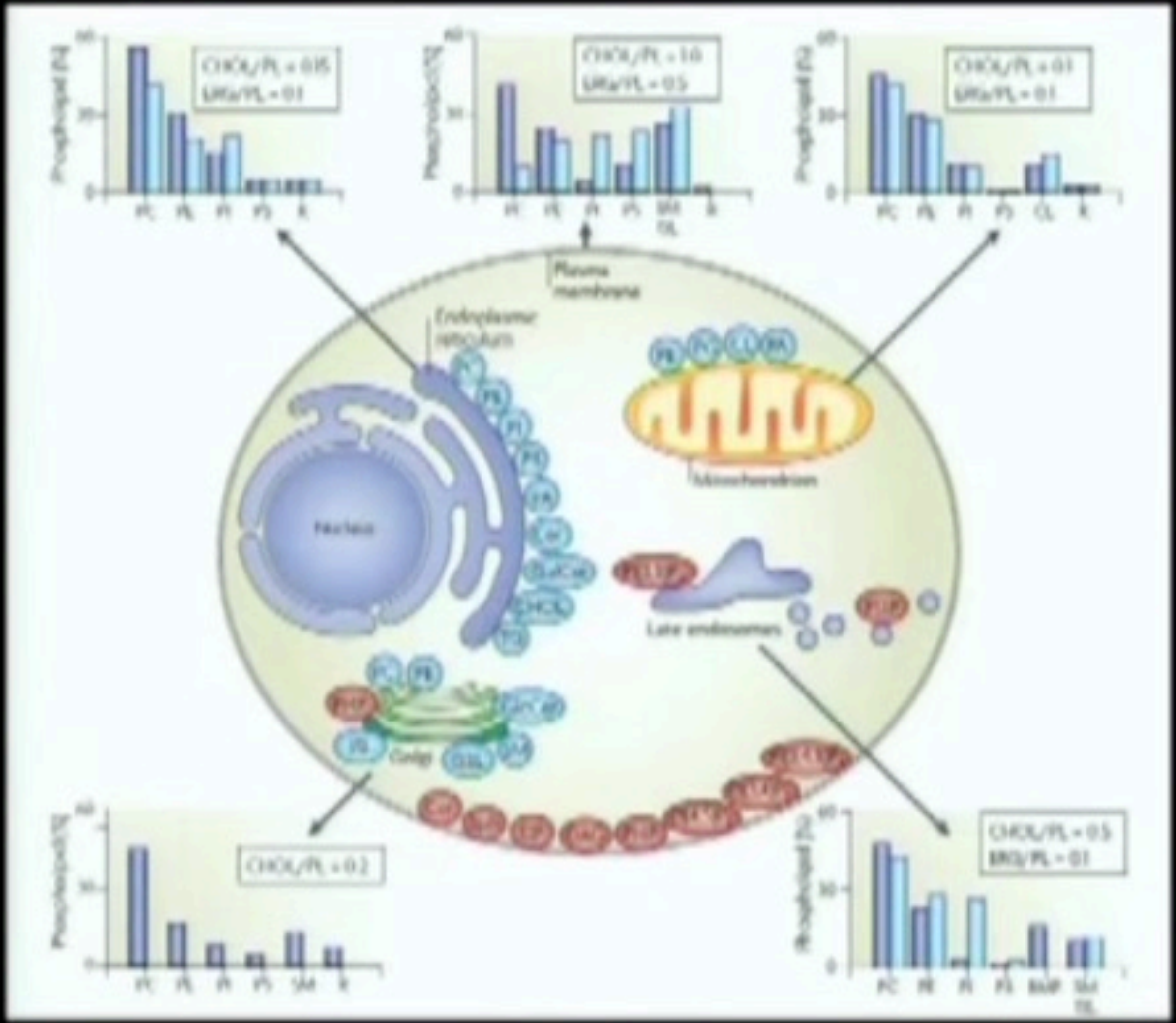
Protein synthesis in the cytosol and subsequent distribution to different sites



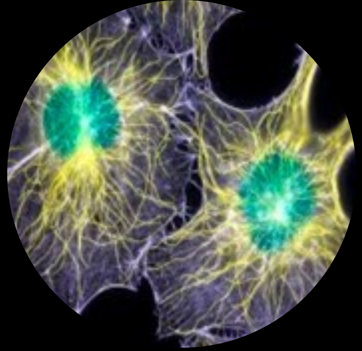
Molecular Biology of the Cell, Alberts et. al.



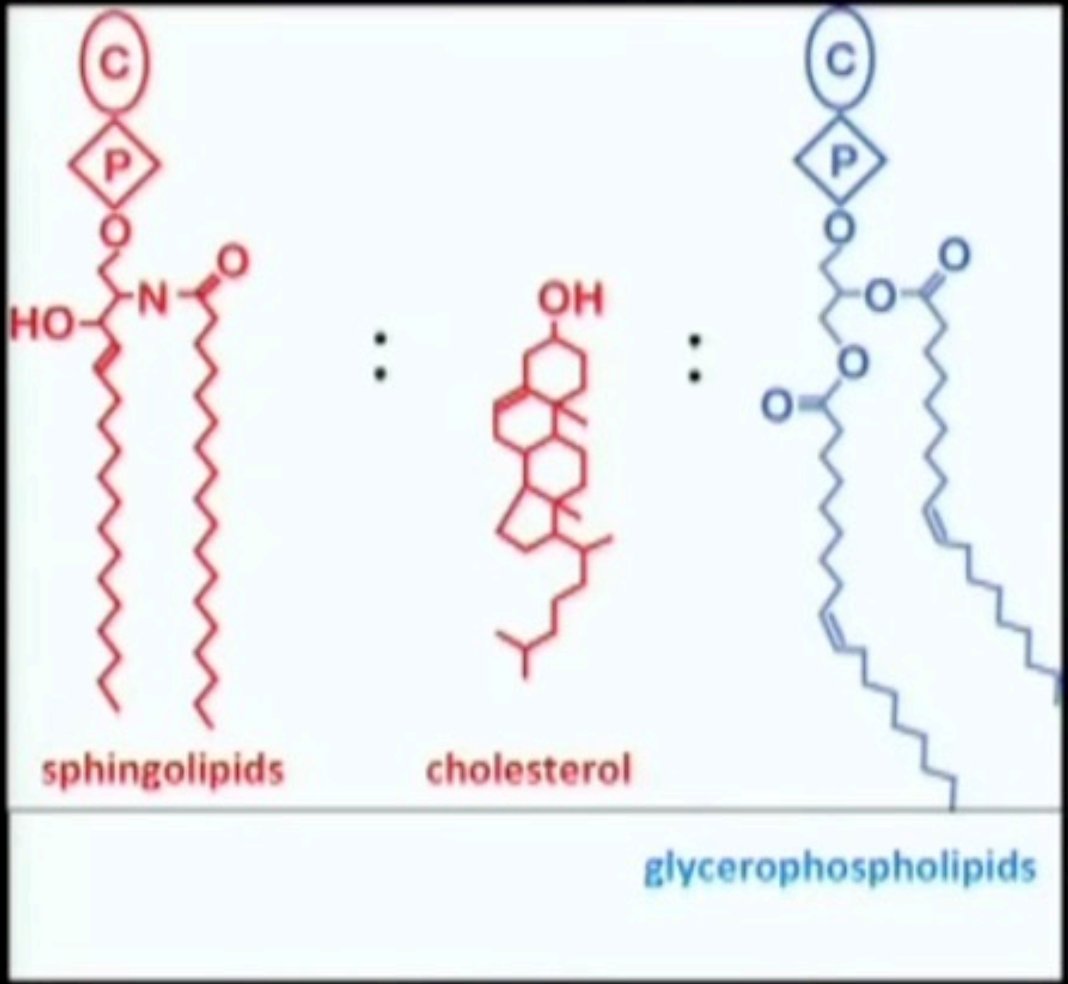
Lipid distribution in eukaryotic cells



Van Meer G. et al. Nat Rev Mol Cell Biol. 2008



Membrane lipids in eukaryotic cells



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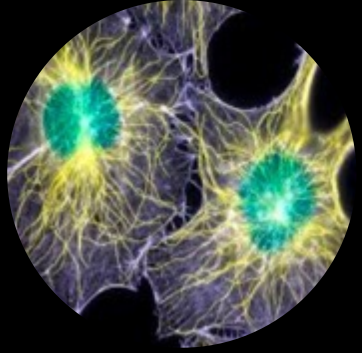
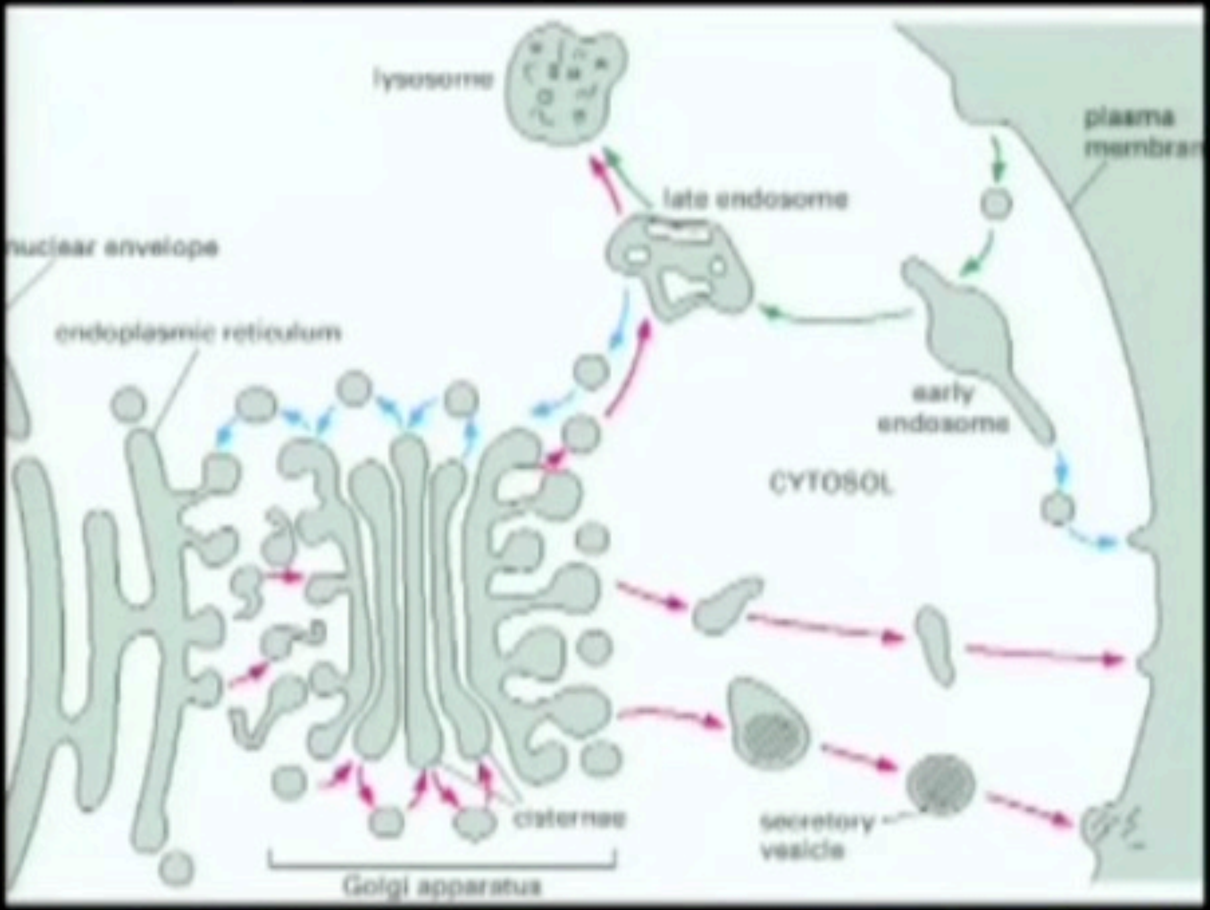


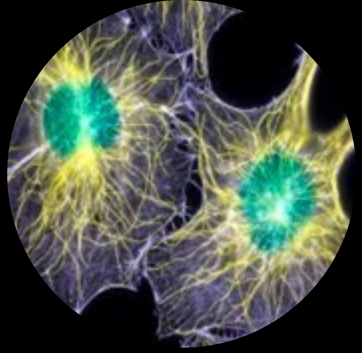
Cholesterol is synthesized in the ER



Molecular Biology of the Cell, Alberts et. al.

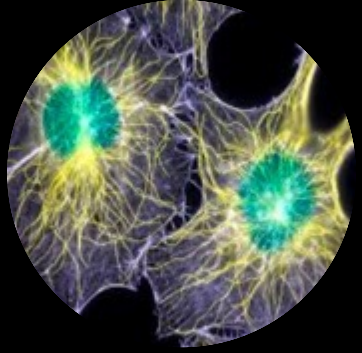
Endoplasmic reticulum:
max. 5 mol%

Plasma membrane:
about 40 mol%

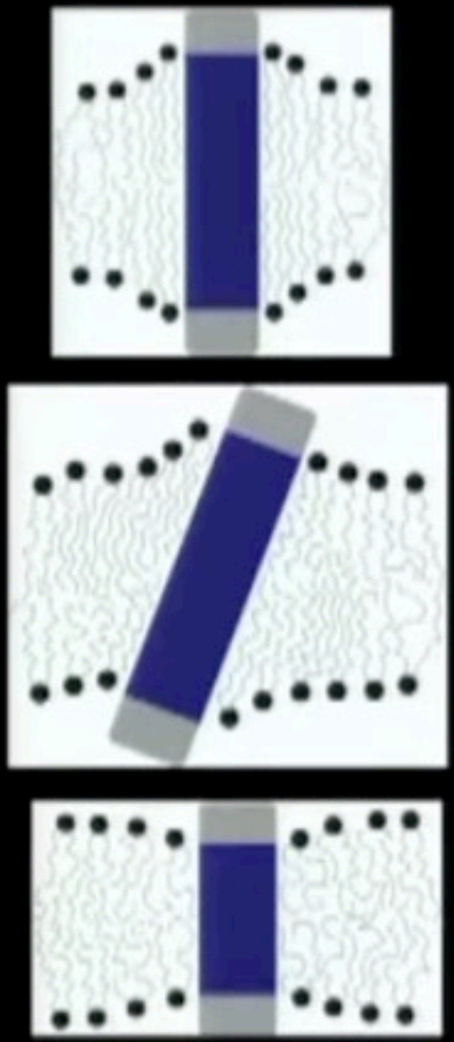


Functions of cholesterol

- Makes the bilayer more impermeable
- Thickens the bilayer

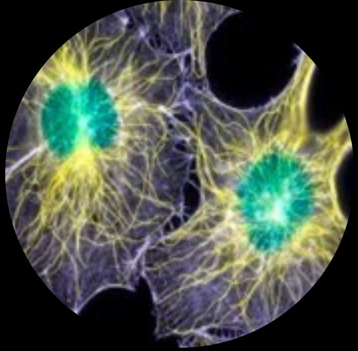


Matching bilayer thickness to the length of the hydrophobic transmembrane domains in proteins



Lipid extension
&
ordering

Lipid compression
&
disordering



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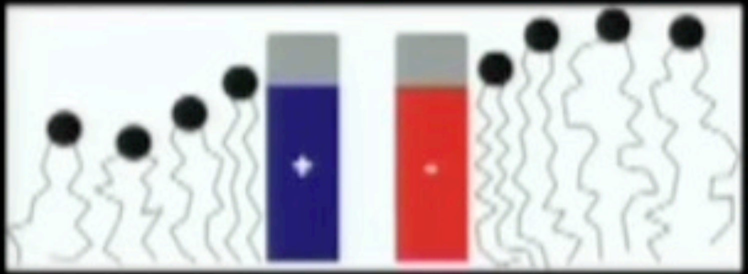
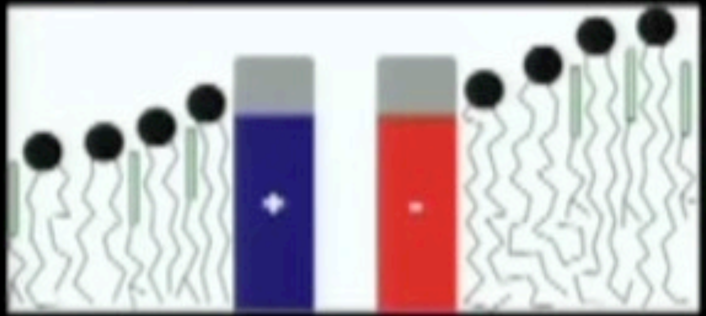
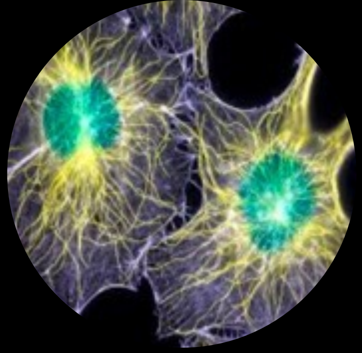
Hydrophobic matching



Cholesterol-depleted membranes
- are deformable environments
- do not discriminate mismatching proteins



Cholesterol-rich membranes
- mismatch and lipid packing are correlated
- can accommodate short proteins if short lipids are available



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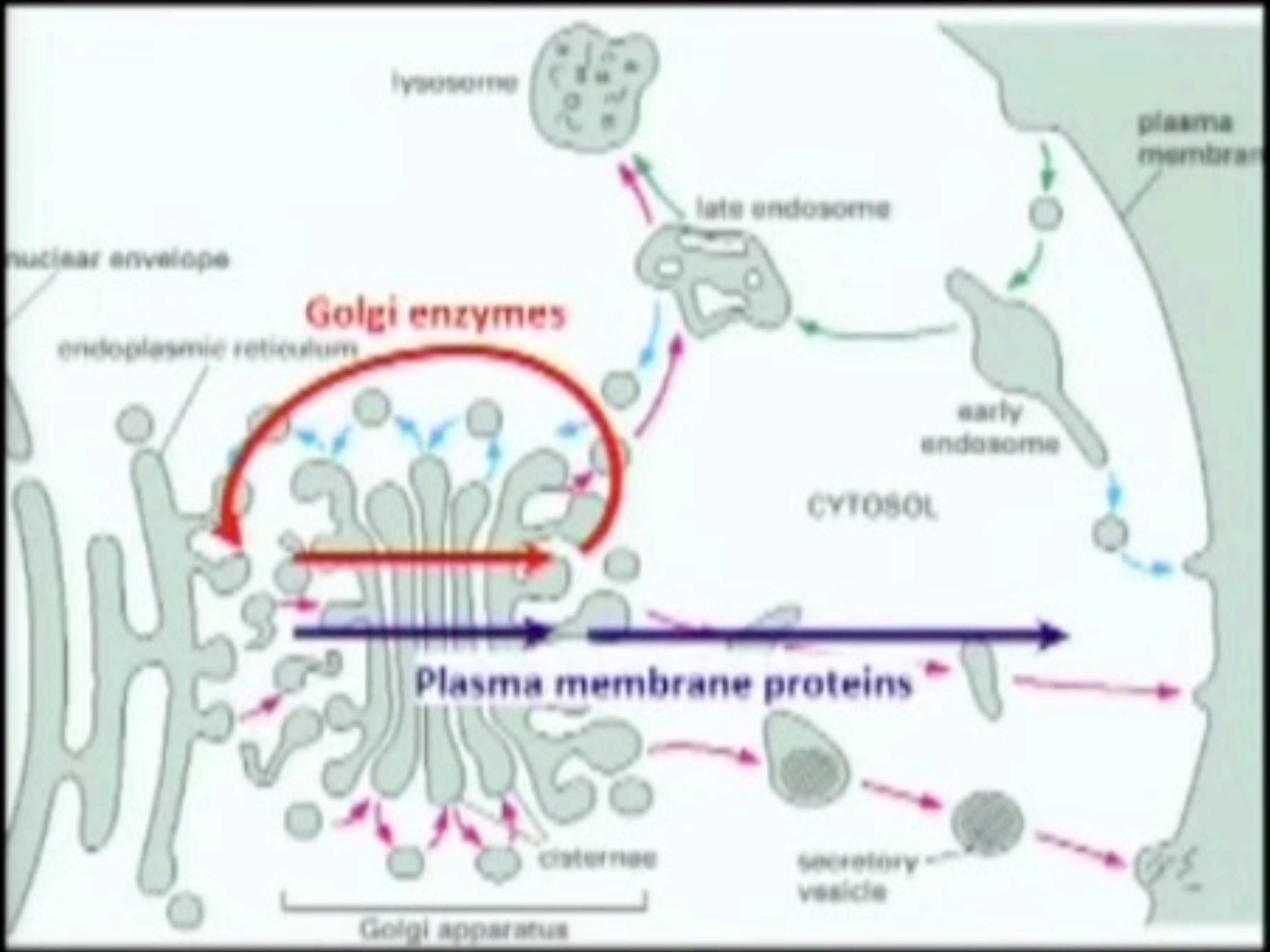
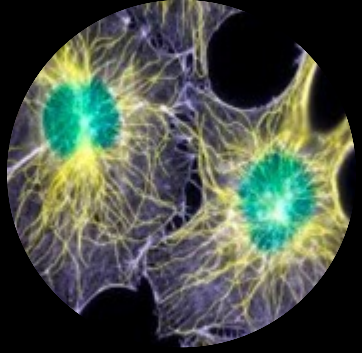
Proteins and lipids get sorted



Molecular Biology of the Cell, Alberts et. al.



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The fluid mosic model

Fim da aula FCM T4