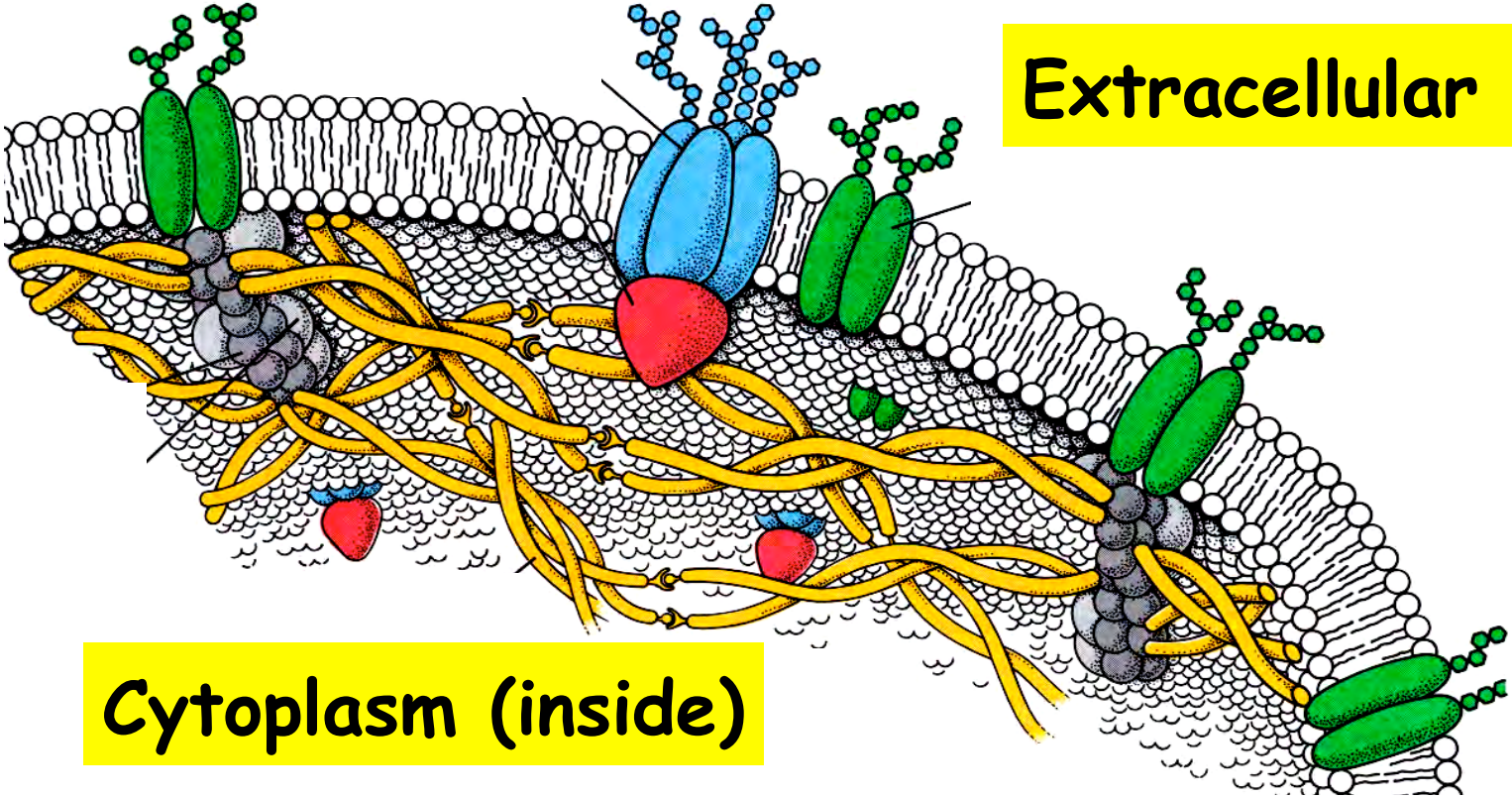
Simulating Membrane Channels

- Brief Introduction to Membrane and a few examples of Membrane Channels
- Aquaporin Water Channels
  - How to model membrane proteins in membrane
  - How much can we learn from simulations?
  - How to analyze the data? Where to look?
- Nanotubes and today's exercises
  - Nanotubes as simple models for water channels
  - Theory and MD simulation of water transport through channels

Why Do Living Cells Need Membrane Channels (Proteins)?

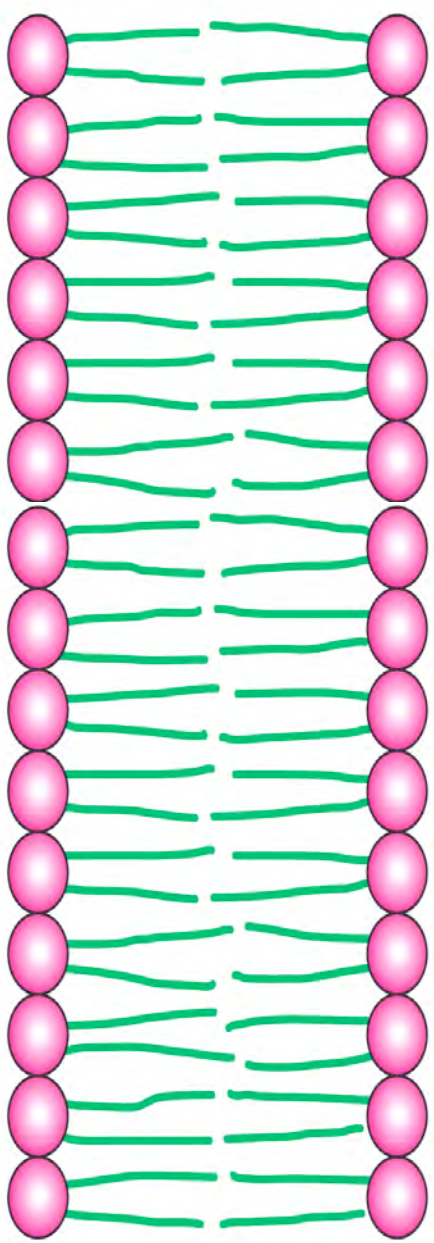
- Living cells also need to exchange materials and information with the outside world

… however, in a highly selective manner.

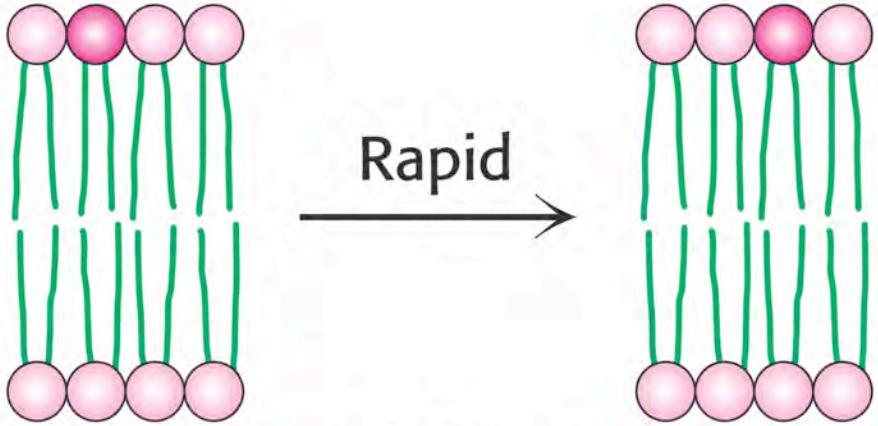


Lipid Bilayers Are Excellent For Cell Membranes

- **Hydrophobic interaction is the driving force**
- **Self-assembly in water**
- **Tendency to close on themselves**
- **Self-sealing (a hole is unfavorable)**
- **Extensive: up to millimeters**



Lipid Diffusion in Membrane



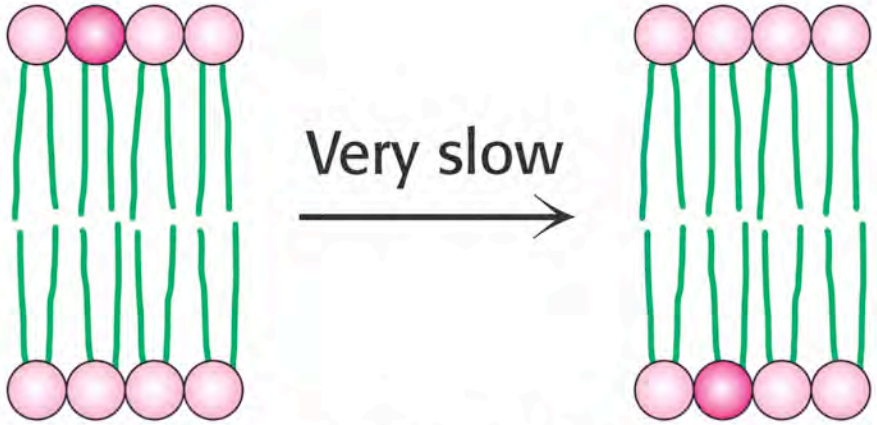
Lateral diffusion

$D = 1\ \mu m^2.s^{-1}$

50 Å in ~ 2.5×10^{-5} s

$D_{lip} = 10^{-8}\ cm^2.s^{-1}$

$D_{wat} = 2.5 \times 10^{-5}\ cm^2.s^{-1}$



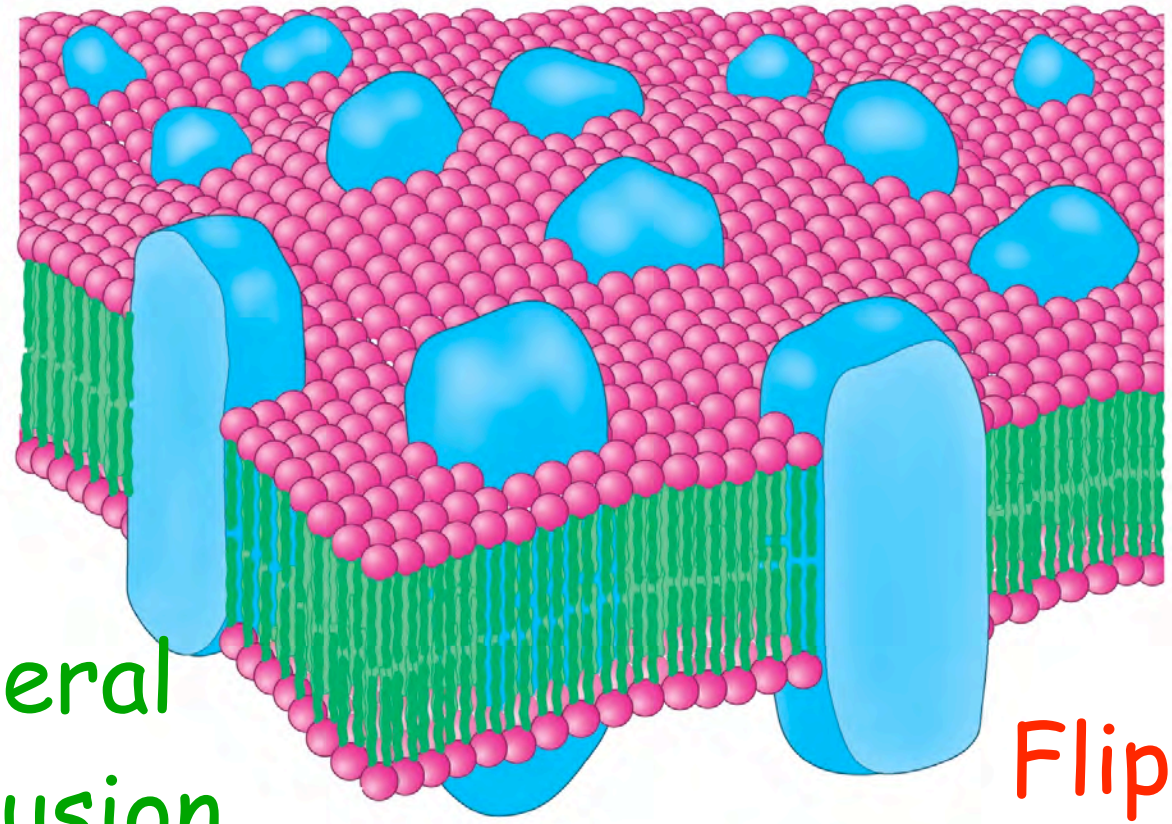
Tranverse diffusion
(flip-flop)

~9 orders of magnitude difference

Once in several hours!

(10^4 s)

Fluid Mosaic Model of Membrane



Lateral Diffusion Allowed

Flip-flop Forbidden

Ensuring the conservation of membrane asymmetric structure

Technical difficulties in Simulations of Biological Membranes

- Time scale
- Heterogeneity of biological membranes ☹

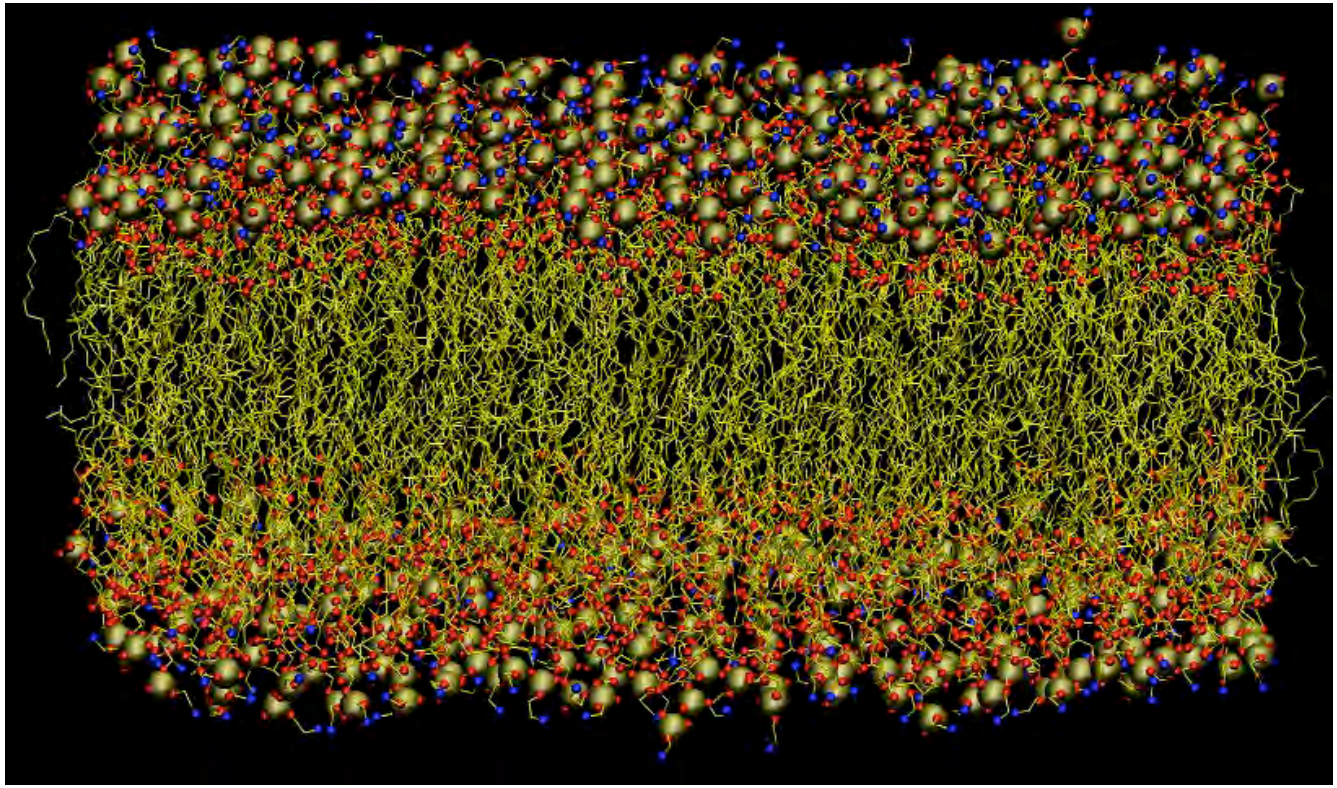
60 x 60 Å

Pure POPE

5 ns

~100,000

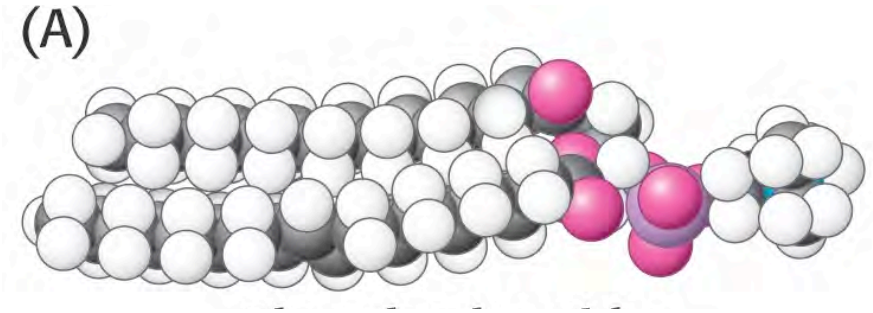
atoms

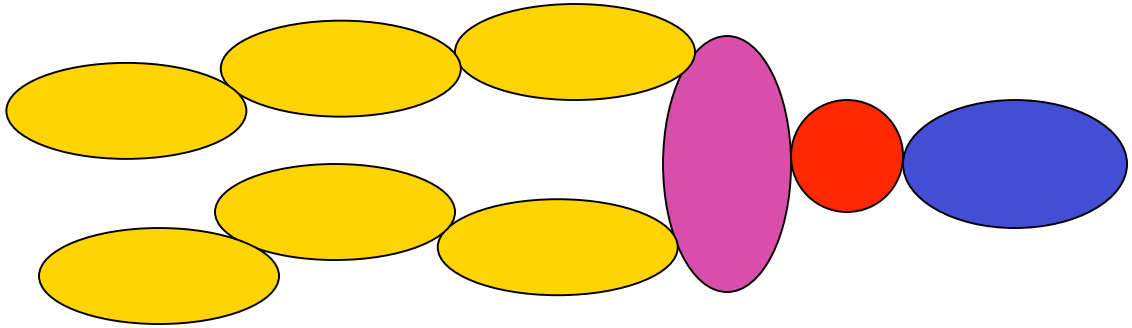


Coarse grain modeling of lipids

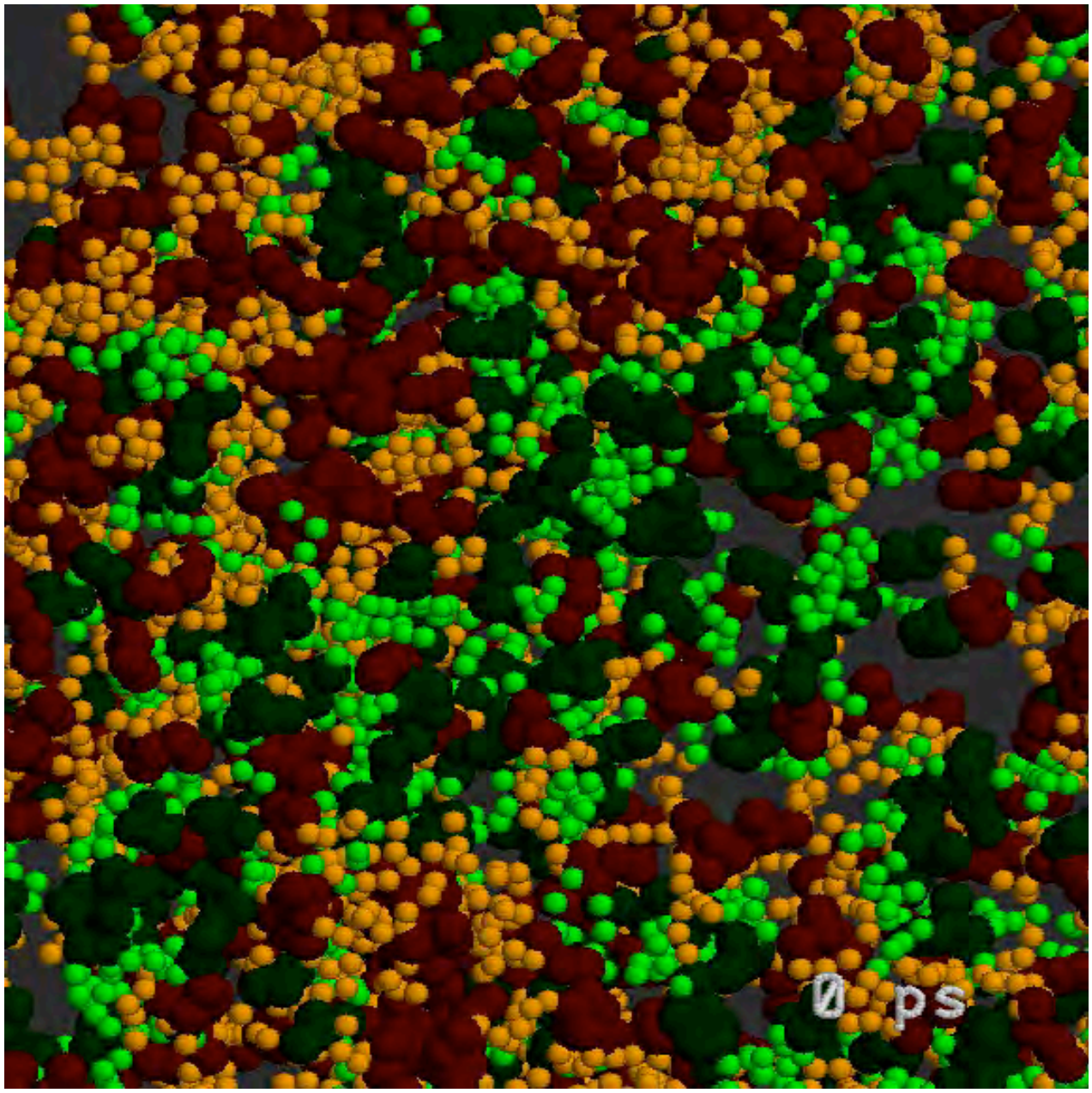
150 particles

9 particles!





Also, increasing the time step by orders of magnitude.



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Protein/Lipid ratio

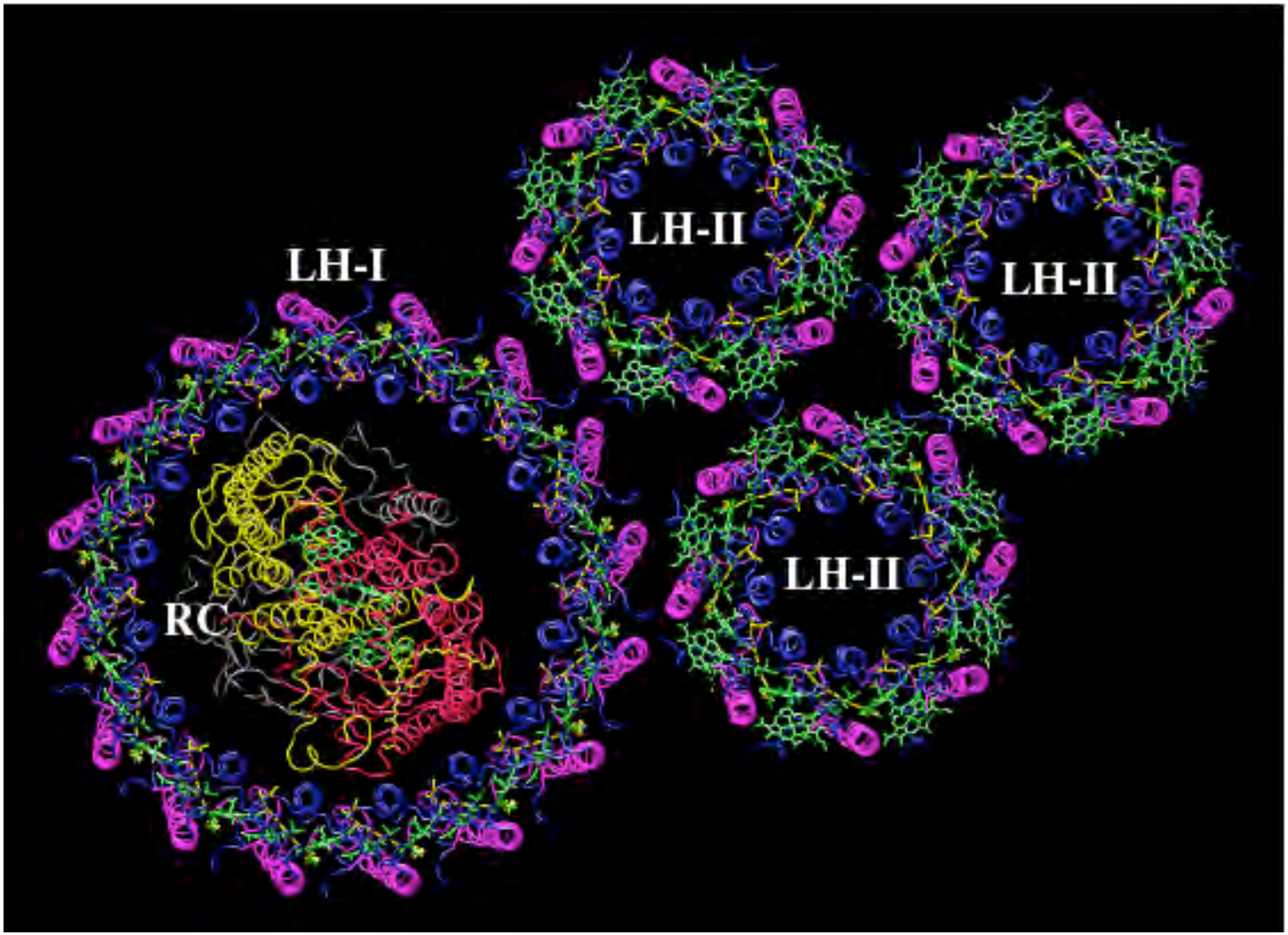
- Pure lipid: insulation (neuronal cells)
- Other membranes: on average 50%
- Energy transduction membranes (75%)

  Membranes of mitocondria and chloroplast

  Purple membrane of halobacteria

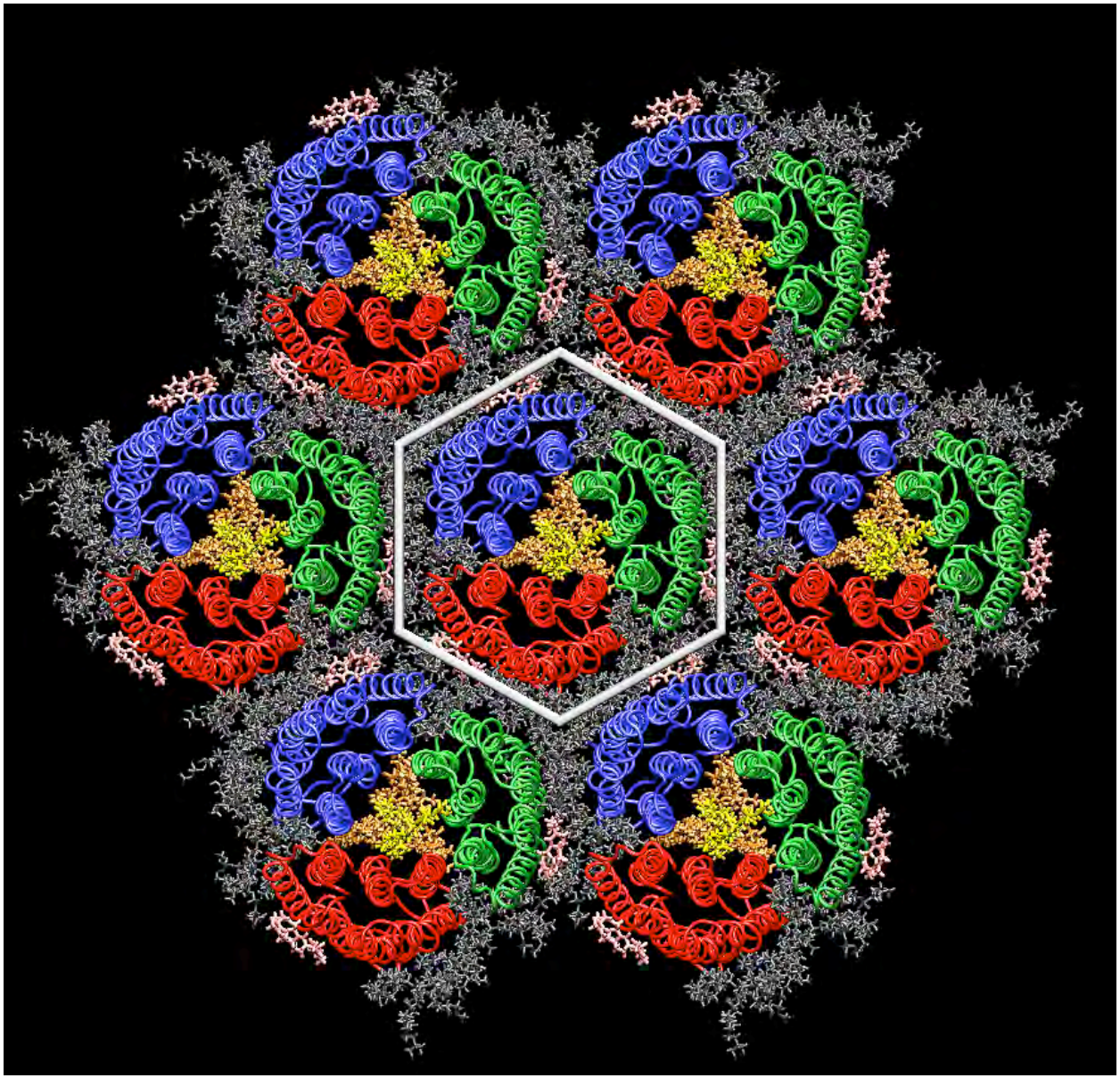
- Different functions = different protein composition

Protein / Lipid Composition



Light harvesting complex of purple bacteria

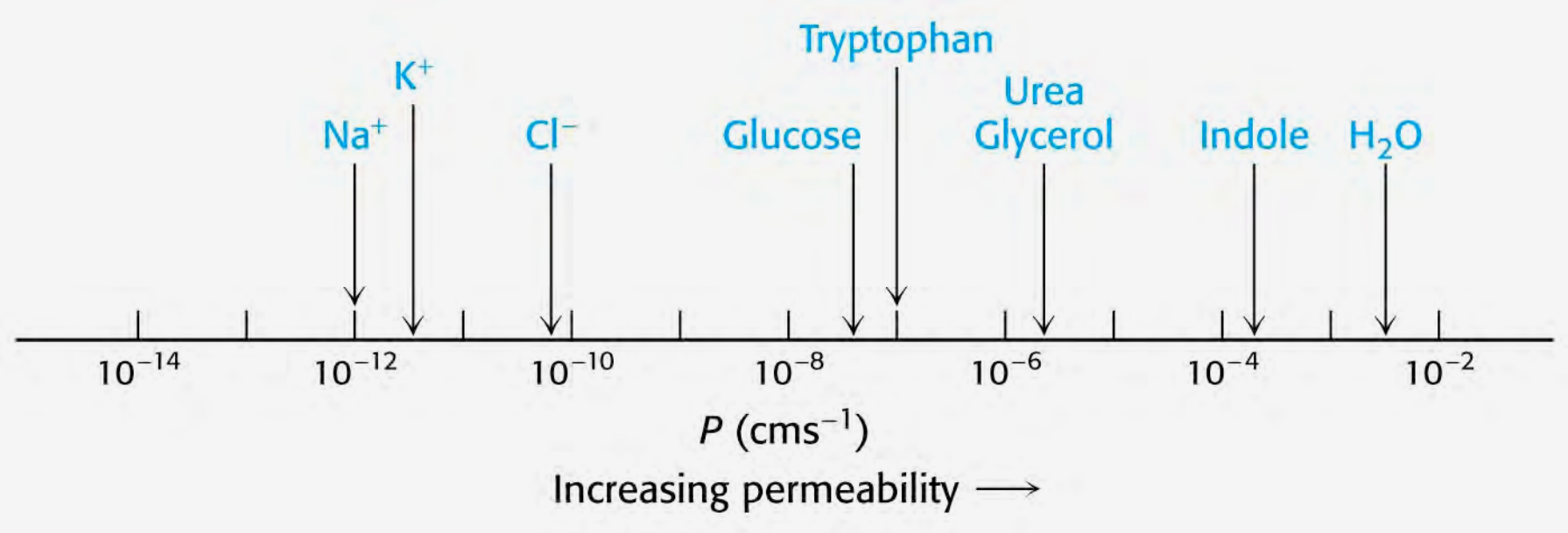
Protein / Lipid Composition



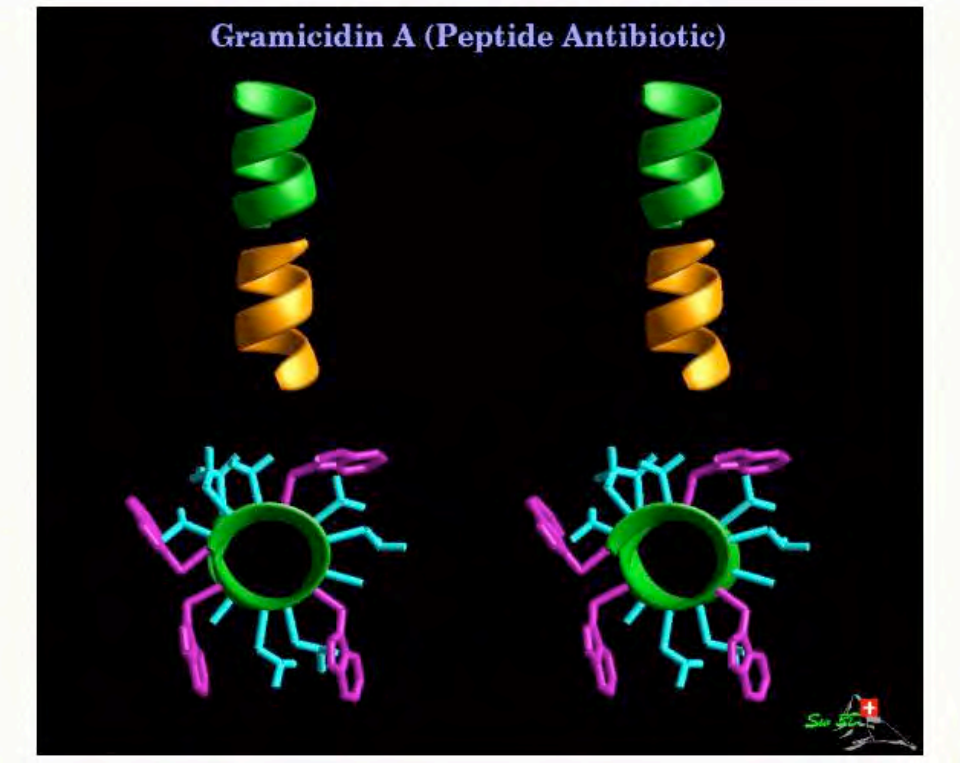
The purple membrane of halobacteria

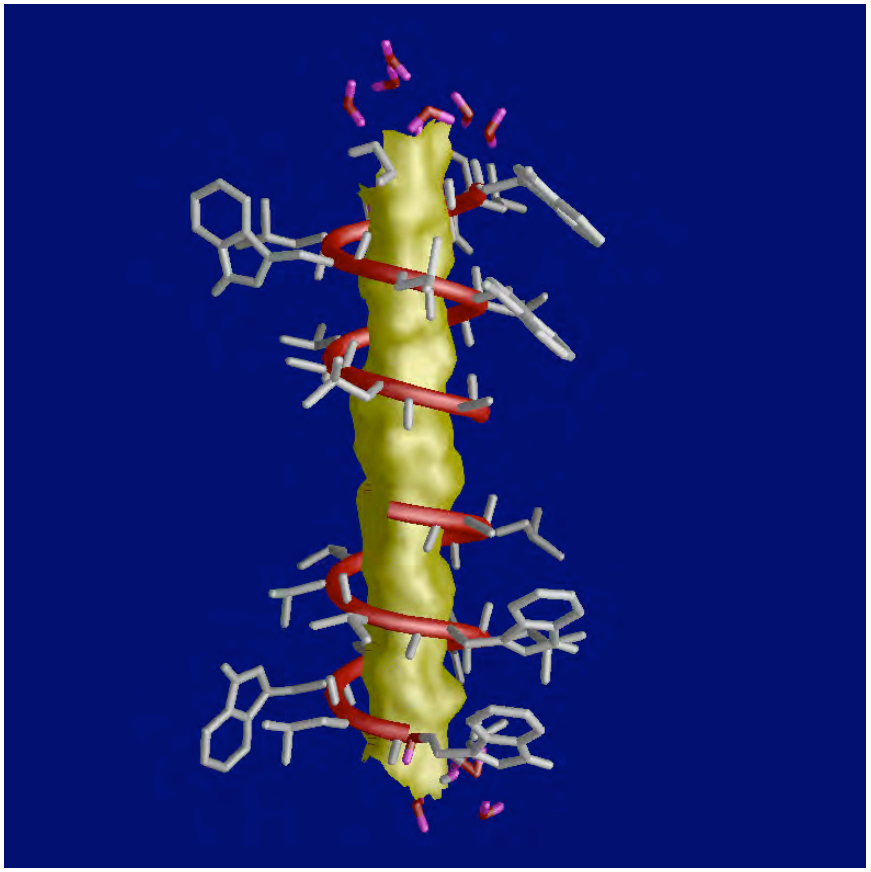
Bilayer Permeability

- Low permeability to charged and polar substances
- Water is an exception: small size, lack of charge, and its high concentration
- Desolvation of ions is very costly.

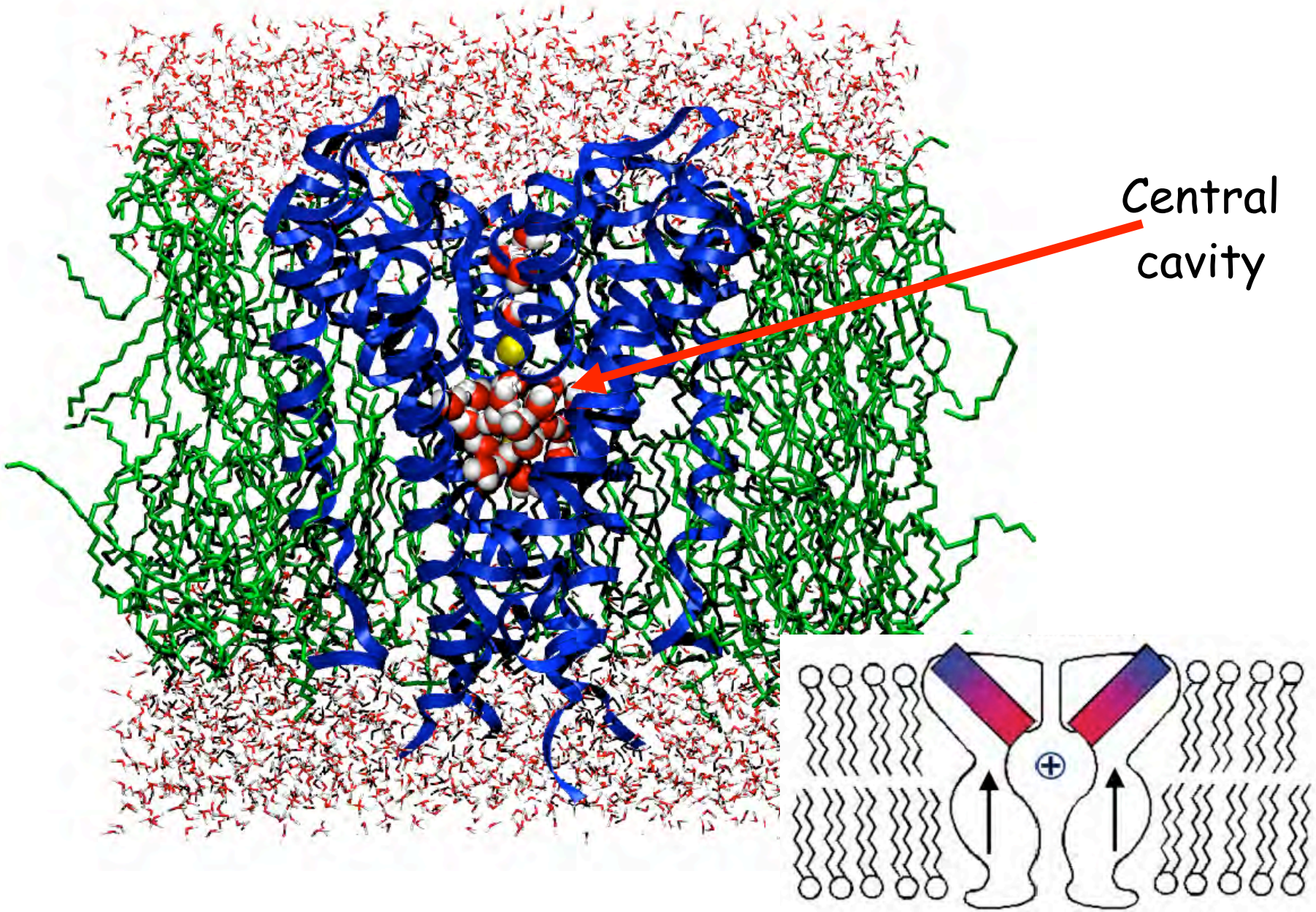


Gramicidin A
an ion leak inside the membrane





Through dissipating the electrochecmical potential of membrane, gramicidin A acts as an antibiotic.


Central
cavity

K binding sites in the selectivity filter