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

\[ D_{\text{lip}} = 10^{-8} \text{ cm}^2\cdot\text{s}^{-1} \]
\[ D_{\text{wat}} = 2.5 \times 10^{-5} \text{ cm}^2\cdot\text{s}^{-1} \]

Lateral diffusion

\[ D = 1 \mu\text{m}^2\cdot\text{s}^{-1} \]

50 Å in \( \sim 2.5 \times 10^{-5} \text{ s} \)

\(~9 \text{ orders of magnitude difference}~

Once in several hours!

\((10^4 \text{ s})\)
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

Also, increasing the time step by orders of magnitude.
Protein/Lipid ratio

- Pure lipid: insulation (neuronal cells)
- Other membranes: on average 50%
- Energy transduction membranes (75%)
  - Membranes of mitochondria 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 electrochemcial potential of membrane, gramicidin A acts as an antibiotic.
K binding sites in the selectivity filter