Molecular Dynamics Simulation of Melittin in a Dimyristoylphosphatidylcholine (DMPC) Bilayer Membrane

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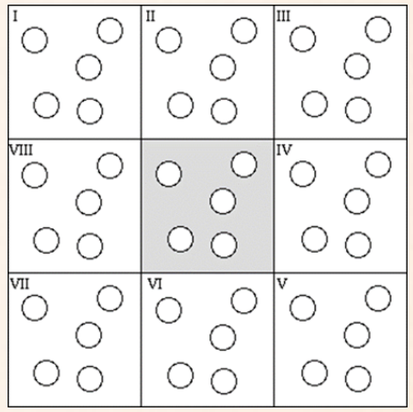
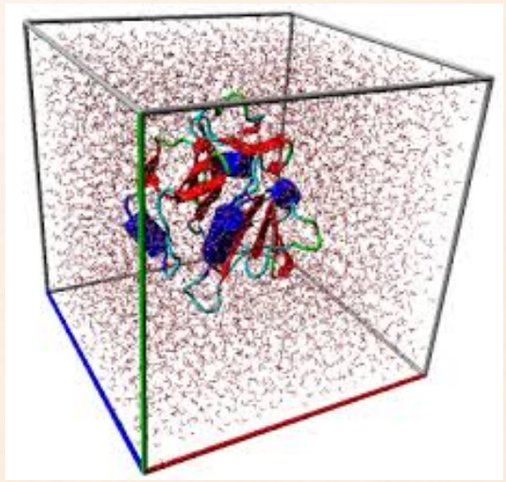
MOLECULAR DYNAMICS (MD) SIMULATION -A DIGITAL LABORATORY

"In the real world, this could eventually mean that most chemical experiments are conducted inside the silicon of chips instead of the glassware of laboratories."



- Classical Newtonian mechanics
  This is a simplification of what is actually going on
- Molecules in Solution
  proteins, RNA, and DNA are immersed in a sea of water molecules
- Periodic Boundary Conditions
  Simulate a segment of molecules in a larger solution by having repeatable regions
- Cutoff Methods
  Ignore atoms at large distances from each other



MELITTIN-DMPC MODEL

- Specific lipid-protein interactions involved in the anchoring and stabilization of membrane-bound proteins are of central importance in a large number of fundamental processes occurring at the surface of the cell.

- Other powerful techniques: x-ray crystallography, electron microscopy and nuclear magnetic resonance (NMR)

- Dimyristoylphosphatidylcholine (DMPC) bilayer membrane

- Melittin: Major protein component of the bee venom that has a pronounced effect on the lysis of membranes

PROPOSED MECHANISMS FOR THE LYTIC ACTIVITY OF MELITTIN

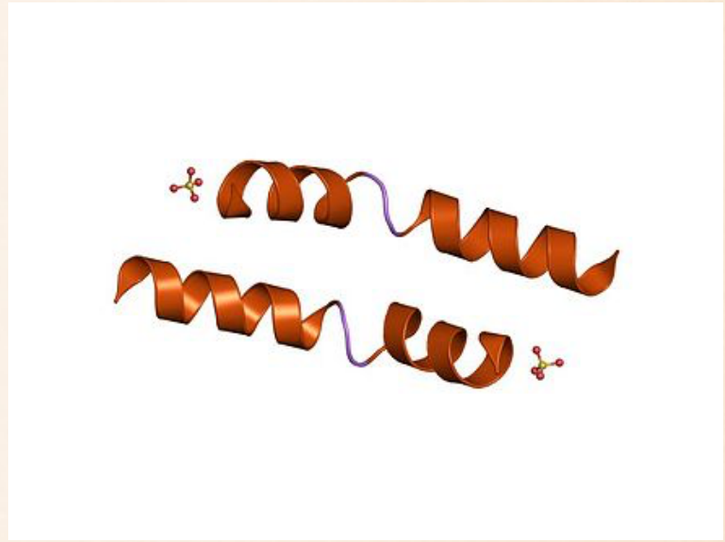
- Melittin increases membrane permeability by partial penetration of the bilayer
- A canal structure by the aggregation of four transbilayer melittin molecules
- Aggregated melittin is involved in the solubilization of large lipid disks (leaving large holes in membrane)
- Binding of melittin to other membrane proteins is involved

SIMULATION

Object

To investigate the effect of melittin (a pore forming peptide) on the dynamics of lipid bilayer by MD simulations and neutron experiments.

The quasielastic neutron scattering (QENS)experiments will be performed at ORNL by Veerendra Sharma and Eugene Mamontov. We are going to examine the effects of cholesterol and phase state(temperature) of the bilayer on the lipid-melittin interaction.



melittin

Experiment systems

- DMPC + Melittin
  Melittin : DMPC = 1:500
- DMPC + CHL + Melittin
  CHL : DMPC = 1:4, Melittin : DMPC = 1:500

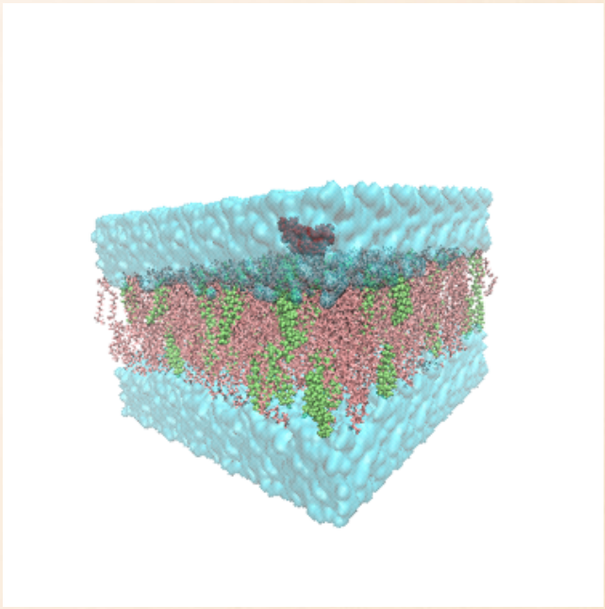
DMPC melting temperature is 297 K. The experiments are done for two temperatures 280 K for Gel phase and 310 K for liquid phase.

Simulation systems

- 500 DMPC: 275K, 280K, … , 315K
- 500 DMPC + 1 Melittin: 275K, 280K, … , 315K
- 400 DMPC + 100 CHL: only 280K and 310K
- 400 DMPC + 100 CHL + 1 Melittin: only 280K and 310K

- Temperature scan for DMPC only system and DMPC+Melittin system for phase transition comparison.

- Observe the effects melittin and Cholesterol have on the dynamics of DMPC at both liquid and gel phases



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Questions?