Computational Simulation of the Interaction between a Cholate molecule and a DMPC bilayer

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Abstract

Molecular dynamics was used to investigate the interaction between a cholate molecule and a dimyristoylphosphatidylcholine (DMPC) bilayer. Visual molecular dynamics was used to visualize the system. The GROningen MAchine for Chemical Simulations (GROMACS) was used to run the simulation. The simulation was run at constant temperature and pressure. The benefits of this study is to enhance drug delivery methods. Many drugs being used are not water soluble. Micelles formed from compounds like cholate will be used to transport drugs into the cell. The simulation showed that cholate forms a weak bond with the bilayer. The cholate does not stay attached for very long. The cholate molecule did not enter into the bilayer. By using the principal axes, the orientation of the cholate with respect to the bilayer was determined.

Methodology

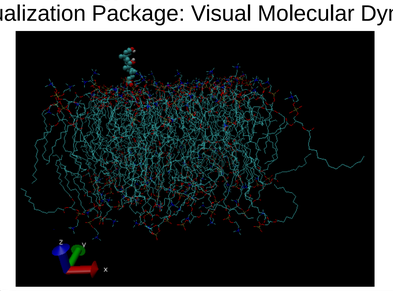
System set-up:
- Temperature: 310 K
- Pressure: 1 atm, semi-isotropic

Total atom count: 18035

Molecule Count: 4168
- Water: 4038
- Cholate: 1
- DMPC: 128
- Na ion: 1

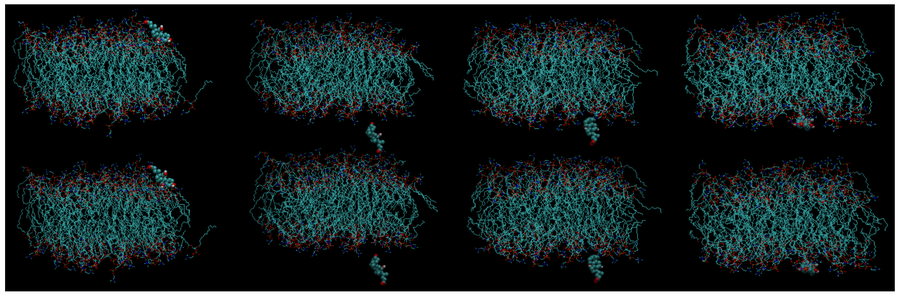
Supercomputer: Queenbee (LSU)
- # of nodes: 3
- Processors per node: 8

Simulation Package: GROningen MAchine for Chemical Simulations[1]
Potential Energy Parameters: GROMOS 54a7[2]
Visualization Package: Visual Molecular Dynamics (VMD)[3]

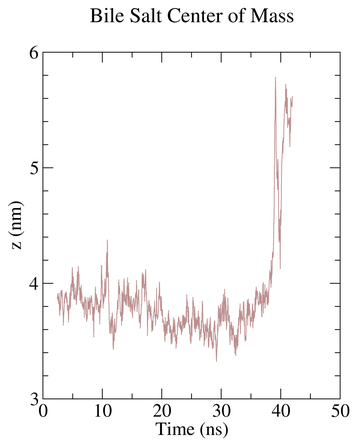


This image shows the original position of the system without the water.

Results



These snapshots are depicting the simulation after the first 35 nanoseconds. The cholate of interest is the one between the central bilayer and its periodic image. The cholate moves from the "top" of the central bilayer to the "bottom" of its periodic image. This suggests that the cholate only has a weak bond with the DMPC bilayer.

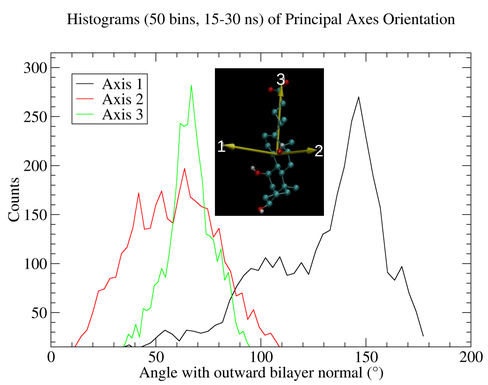


This graph is a representation of what is occurring in the snapshots above.

The graph plots the center of the cholate and along the z direction versus time.

The cholate remains close to the central bilayer for approximately the first 35 nanoseconds.

Then the cholate moves from the central bilayer and attaches to the periodic image of the central bilayer.



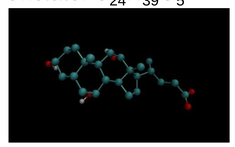
This graph tells the frequency the angle taken on by each principal axis[4] with respect to the outward bilayer normal.

Axis 1 points towards the hydrophilic face, and most often points diagonally towards the bilayer at approximately a 145° angle.

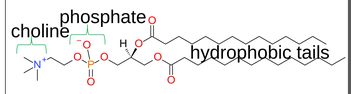
Axis 2 usually points away from the bilayer with an angle from 10-110°.

Axis 3 is the long axis pointing towards the ionic carboxylate group, and generally points slightly diagonally away from the bilayer at a 70° angle.

Cholate: $C_{24}H_{39}O_5$



DMPC: $C_{36}H_{72}NO_8P$



Summary

- The cholate molecule never enters the bilayer.
- The cholate molecule sits on top of the bilayer.
- The cholate is loosely bound to the DMPC bilayer.
- The hydroxyl groups face the bilayer with the hydrophobic side facing the water.
- The 4 rings of the cholate molecule lie mostly flat, parallel to the bilayer.
- The cholate is loosely bound to the DMPC bilayer.

Future work

- Investigate the interaction between a cholate micelle and a DMPC bilayer
- Investigate the transportation of cholesterol via micelles
- Enhance drug delivery methods

References

1. B. Hess *et al.*, J. Chem. Theory Comput. **4**, 435 (2008).
2. N. Schmid *et al.*, Eur. Biophys. J. Biophys. Lett. **40**, 843 (2011).
3. W. Humphrey, A. Dalke, and K. Schulten, J. Mol. Graphics **14**, 33 (1996).
4. Principal axes calculated using a VMD plugin written by Paul Grayson: http://www.ks.uiuc.edu/Research/vmd/script_library/scripts/orient/.

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