Self-Assembly of Stratum Corneum Lipid Bilayers Via Coarse-Grained Simulations

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Overview
- Skin barrier function localized to stratum corneum (SC)
- Cholesterol, free fatty acids, and ceramides make up lipid matrix
- Connection between lipid composition, structure, and barrier function remains unclear

Coarse-grained (CG) Models
- CG models are computationally cheaper than atomistic models and allow for self-assembly to be simulated
- Self-assembly is used to study lipid assemblies without relying on the assumed initial configuration
- Interaction parameters derived from previous work in the group
- A 3:1 mapping was used for carbon tails
- Ceramide (eCER2): 4-bead headgroup with OH group beads and equal carbon tail lengths
- Free Fatty Acid (FFA16): Single bead headgroup with 16 carbon tail lengths
- Cholesterol (CHOL): OH group mapped to headgroup with 5-bead mesh rings

Results of CG Simulations

Self-Assembly Process

Start from gas and compress to target density
Massage the system to work out defects
Simulate longer to collect data

Simulation
- eCER2:FFA16:CHOL (2:1:1) 35.90 ± 0.013
- eCER2:FFA16:CHOL (2:2:1) 32.63 ± 0.013
- eCER2:FFA16 (1:1) 31.27 ± 0.007
- eCER2:FFA16 (2:1) 34.34 ± 0.007
- Pure eCER2 41.73 ± 0.008

As the percent of eCER2 increases, the area per lipid (APL) increases. Different morphologies and packing densities results that may have different properties such as permeability.

Simulation
- Tilt Angle
- eCER2:FFA16:CHOL (2:1:1) 8.48° ± 5.00
- eCER2:FFA16:CHOL (2:2:1) 9.63° ± 9.79
- eCER2:FFA16 (1:1) 5.00° ± 4.07
- eCER2:FFA16 (2:1) 5.25° ± 2.99
- Pure eCER2 5.40° ± 3.47

The addition of CHOL causes more tilt as the bulky ring structure affects the balance between the head and tail packing. This bulky ring spacing may be the cause of unstable bilayers in binary mixtures involving CHOL.

References

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Conclusion
- Systems containing FFA tend to have smaller APLs due to the single alkyl chain whereas eCER2 and CHOL have similar APLs due to similar cross-sectional areas
- Lamellar organization is mostly independent of lipid composition for the systems studied
- Systems with high concentrations of CHOL have difficulty forming lamellar structures like the other mixtures

Future Work
- Investigate the stability of bilayer systems with high concentrations of CHOL
- Examine mixtures over a wide composition range to uncover composition/structure relationships