Phase Behavior of Two-Component Lipid Vesicles

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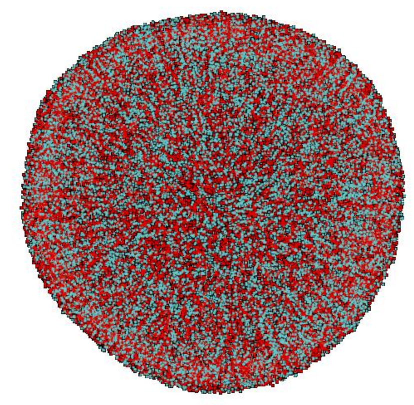


Introduction

•The main component of the plasma membrane is the phospholipid bilayer.

•Phospholipids are organic molecules that have a hydrophobic head group and usually two hydrophobic tail groups. Because of this structure, the spontaneously self-assemble into bilayers.

•Liposomes are artificially synthesized small vesicles composed of self-assembled lipids and and can be used for drug delivery. Liposomes are also synthesized by cells for the purpose of protein trafficking within the cell

•Self-assembled lipid bilayers exhibit two phases: A fluid phase at high temperatures and a gel phase at low temperatures. The melting point is the temperature at which the gel phase is transformed into a fluid phase.

•Here, we are interested in understanding the phase behavior of small (nanoscale) liposomes composed of two lipids with different melting transitions.

Model[2] and Method

•We use a coarse-grained lipid model recently developed by Laradji et al.[2]

•In this model, a lipid molecule is coarse-grained into three beads (one hydrophilic and two hydophobic beads). The beads are connected to each other by harmonic springs. The coarse-graining reduces the computational time. Furthermore, the solvent is implicit in this model, which allows for further reduction in the computational time of our simulations.

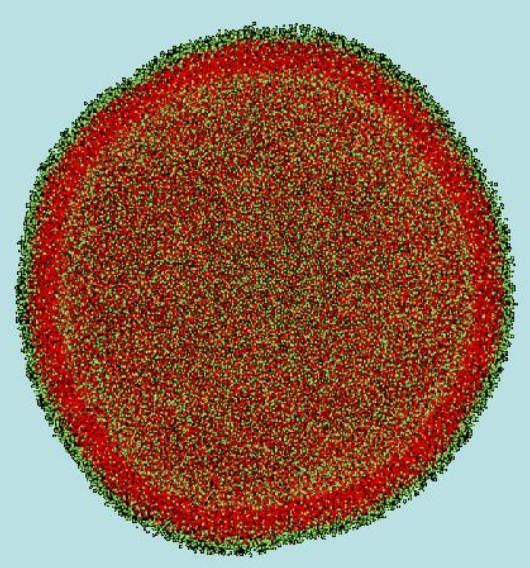
•Interactions between beads lead to their motion according to the second law of Newton.

• Lipid beads are moved using Langevin molecular dynamics.

•We consider a binary mixture of rigid and soft lipids.

•We vary the composition of the two lipid types, temperature and size of the liposome.

•Programs created by Laradji's group are run at various parameter sets, and the results, such as internal energy and heat capacity, are analyzed. Liposome configurations are visualized using VMD[1](Visual Molecular Dynamics).



Hydrophobic tails

Hydrophilic heads

A liposome composed of 40, 000 lipids in the fluid phase at temperature *T*=3.0. Notice the almost spherical shape of the liposome.

Acknowledgements

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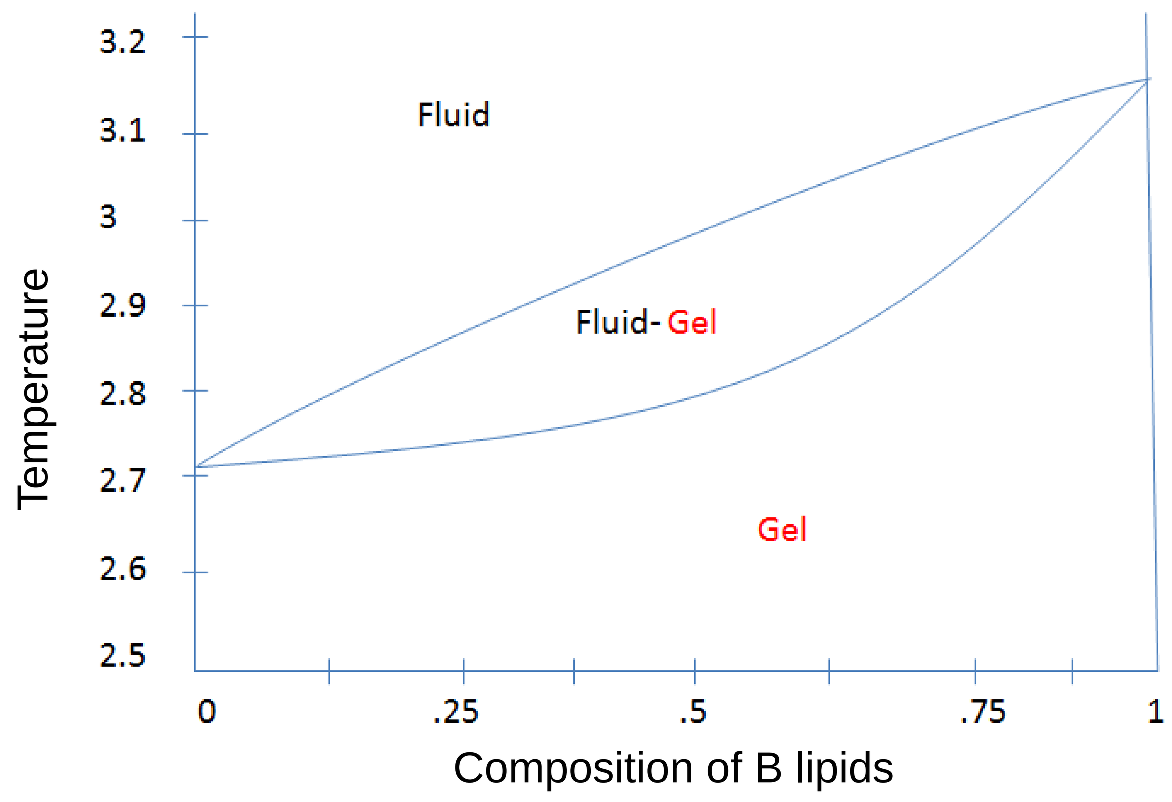
Objective

The objective of this research is to investigate the phase behavior of a mixture of two lipids with different rigidities.



Typical phase diagram[3] of a two-component lipid vesicle, as obtained from experiments. Our goal is to see if we can reproduce this phase diagram through simulations.

Conclusions

•Our results show that as the composition of the rigid lipid is increased, the melting temperature of the vesicle is increased.

•The vesicle is either in a gel phase at low temperatures or a fluid phase at high temperatures.

•However, there is no visible and distinct coexisting (large) fluid and gel domains around the melting transition.

•Therefore, the conventional lense in the phase diagram is not reproduced by the simulations.

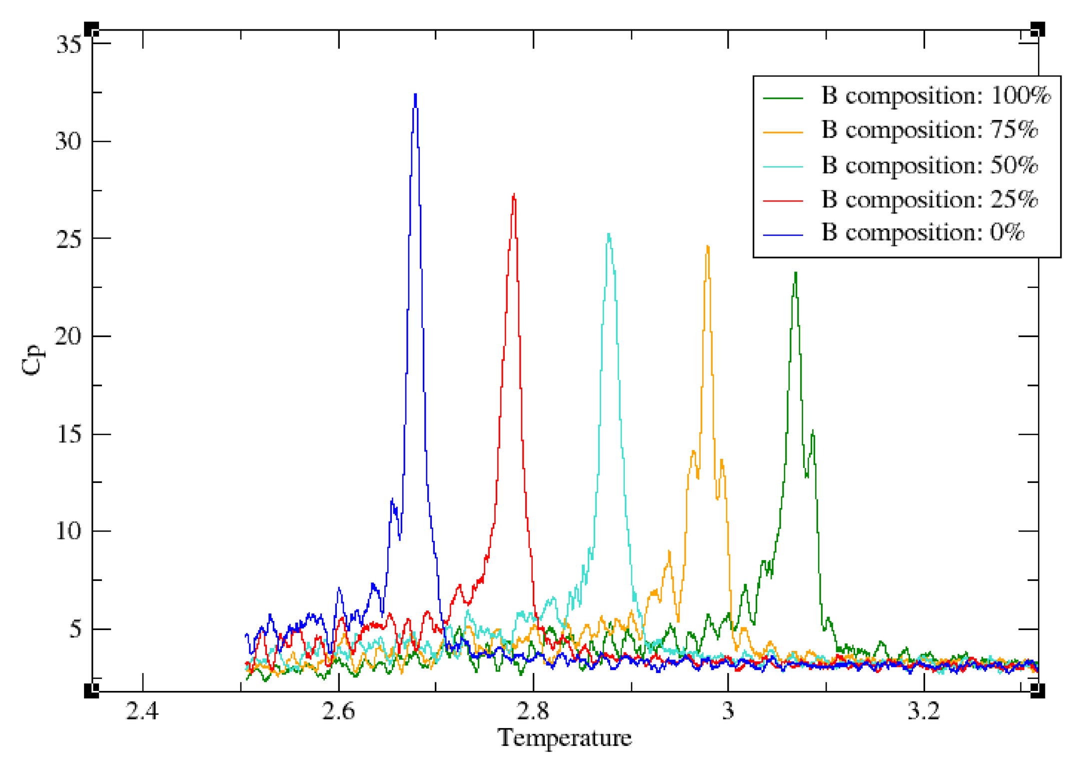
•This implies that either the experimental phase diagram is incorrect or our model needs modification or improvements.

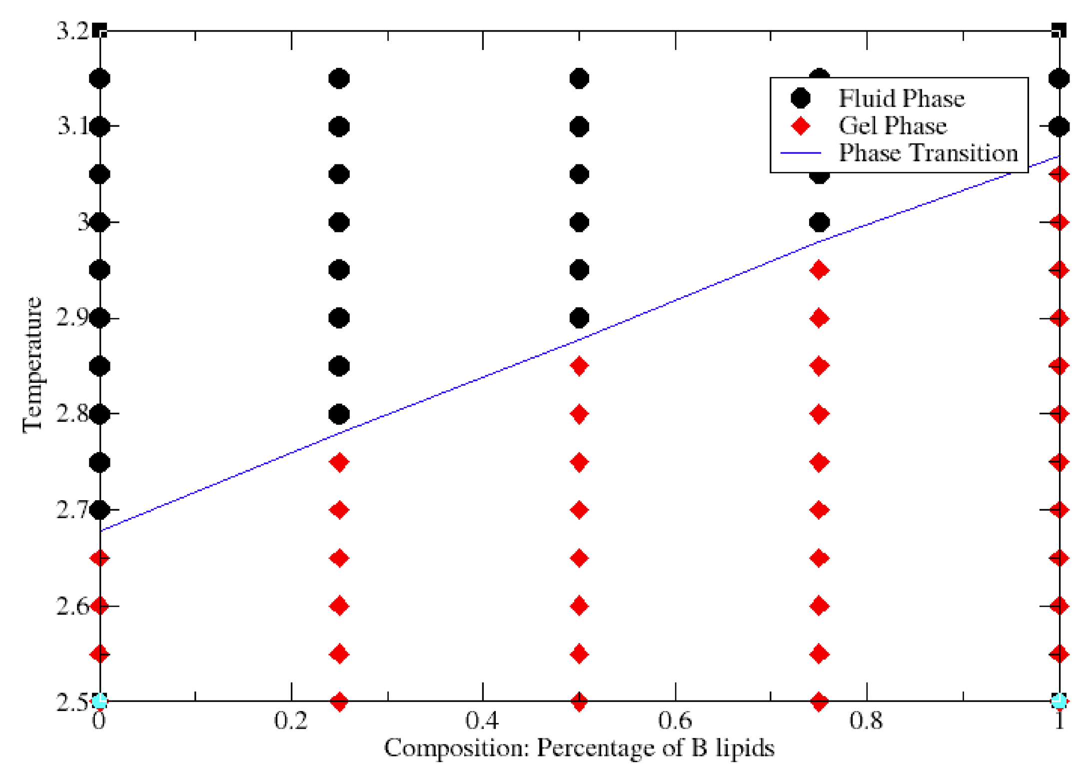
References

1. Humphrey, W., Dalke, A. and Schulten, K., "VMD - Visual Molecular Dynamics", J. Molec. Graphics, 1996, vol. 14, pp. 33-38.
2. Spangler, E. J., Kumar, P. B. S., Laradji, M., Anomalous freezing behavior of nanoscale liposomes, *Soft Matter*, 2012, **8**, 10896.
3. Mouritsen, O. G., *Life – As a Matter of Fat – The Emerging Science of Lipidomics*, Springer – Verlag, Berlin Heidelberg, 276 p.

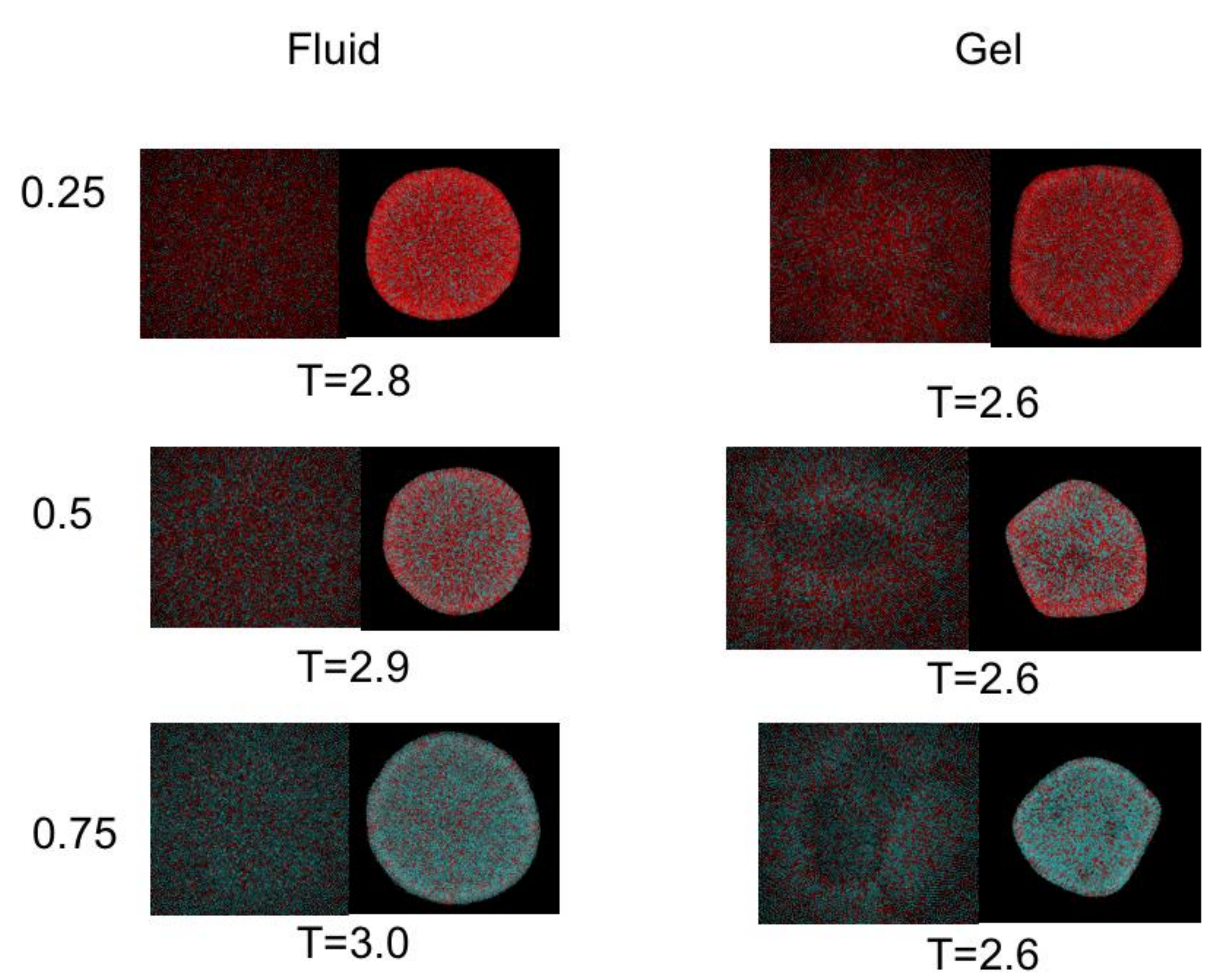
Heat Capacity

•The position of the peak indicates the phase transition from gel to fluid.
•The location of the phase transition depends on the composition of the two lipids.
•The phase transition point at 0% B lipids is lower than that of the 100% B lipids.





Phase Diagram of Mixture: The transition line is obtained from the locations of the peaks of the heat capacities.



Liposomes composed of 40, 000 lipids. Notice the spherical shape of the vesicle in the fluid phase. Notice the faceted regions in the gel phase. Only the tail particles of the vesicles are depicted.

We do not see large blue and red domains, which implies that we are not able to observe coexistence between gel and fluid phases.