

Lipids degeneracy in the (sub-100nm) membrane organization: Thermodynamics costs behind maintaining complex lipid diversity

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The rich structural complexity of biological membranes arises from the chemical diversity of its constituents. Differential inter and intra-molecular interactions result in preferential segregation and clustering of certain types of lipids and proteins, giving rise to a variety of lateral organization on the membrane surface. Recently, Edward Lyman's group at Delaware carried out multiple long timescales all-atom molecular dynamics simulations (tens of microseconds long) with carefully chosen lipid compositions to reproduce a variety of phases [1, 2]. We focus on the systems that exhibit liquid-ordered and liquid-disordered (Lo/Ld) co-existence. The three systems with their fractional compositions are (i) PSM/POPC/Chol (0.47/0.32/0.21) (ii) PSM/DOPC/Chol (0.43/0.38/0.19) (iii) DPPC/DOPC/Chol (0.37/0.36/0.27).

We analyze these trajectories and numerically calculate the degree of non-affineness of individual lipids in their local neighborhood and their topological rearrangements [3]. We use these data to distinguish between the Lo and Ld regions in the membrane system at molecular length scales [4].

The three chosen systems exhibit different molecular-level sub-structures and unique Lo/Ld interface boundaries. We also explore the molecular-origin of this variety in organization using tools from simple statistical mechanics theories. And try to quantify the thermodynamics cost of arriving at a given mem-

brane sub-structure using a different lipid types and compositions.

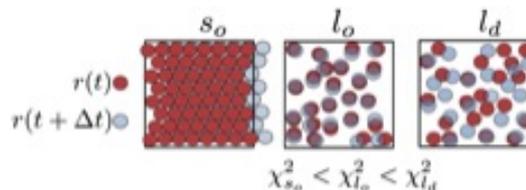


FIG. 1. The non-affine deformation (χ^2) is used as a marker for lipid order/disorder

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- [1] A. J. Sodt, R. W. Pastor, and E. Lyman, *Biophys. J.*, 109, 948-955 (2015)
- [2] A. J. Sodt, M. L. Sandar, K. Gawrisch, R. W. Pastor, and E. Lyman, *JACS*, 136, 725-732 (2014)
- [3] M. Falk and J. Langer, *PRE*, 57, 7192-7203 (1998).
- [4] S. S. Iyer*, M. Tripathy*, and A. Srivastava, *Biophys. J.*, 115, 117-128 (2018) *Contributed Equally