2D Lattice Model of a Lipid Bilayer: Quantifying the degeneracy and complexity in biomembrane lateral organization

Sahithya S. Iyer and Anand Srivastava*

Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012, India

Rich structural complexity of biomembranes arises from the chemical diversity of its constituents. This high complexity inevitably gives rise to degeneracy of great biological relevance. Degeneracy refers to structurally different species that perform same or different function according to the constraints imposed [1]. Here we focus on degeneracy in lateral organization of the membrane which plays a key role in processes such as signal transduction, pathogen intake and assembly of protein complexes.

Variety of lateral organization on the membrane surface occur due to preferential segregation and clustering of certain types of lipids and proteins owing to their differential inter and intra-molecular interactions. In this work, we explore the molecular-origin and degeneracy in the variety of organization using tools from simple statistical mechanics theories. We develop a physics-based Hamiltonian for membrane organization using long atomistic trajectories on systems that exhibit liquid-ordered and liquid-disordered (Lo/Ld) coexistence. Recently, Lyman's group at Delaware carried out multiple long microseconds timescales all-atom (AA) simulations with carefully chosen lipid compositions to reproduce a variety of phases [2, 3]. The three systems with their fractional compositions are (i) DPPC/DOPC/Chol (0.37/0.36/0.27) (ii) PSM/DOPC/Chol (0.43/0.38/0.19) (iii) PSM/POPC/Chol (0.47/0.32/0.21). These systems have very different molecular-level substructures and unique Lo/Ld interface boundaries.

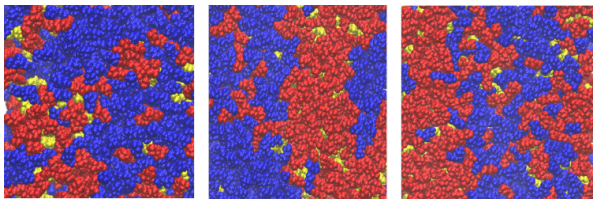

FIG. 1. AA L_o/L_d phase separated systems (Left) DPPC/DOPC/CHOL, (Middle) PSM/DOPC/CHOL and (Right) PSM/POPC/CHOL with different molecular level substructures [Red - unsaturated lipids, Blue - saturated lipids, Yellow - Cholesterol].

We evolve the Hamiltonian using Monte Carlo (MC) algorithm to recapitulate the lateral organization in the above-mentioned AA systems. The interaction potential is written as a function of the degree of non-affinity in topological rearrangement of the lipids (χ^2). The configuration of lattice sites is evolved while keeping the probability distribution of χ^2 (unique to the three systems) in the corresponding AA system conserved. The final configurations of the evolved states are mapped to AA equilibrium configurations [4, 5] and their energy values are reported. On evolving a given system with the Hamiltonian of another system, our preliminary calculations indicate that the lateral organization from the given Hamiltonian is captured with reduced probability for the new system and with a higher energy penalty. This provides us with an early indication of degeneracy in membrane organization between different composition.

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* Corresponding author: anand@iisc.ac.in

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