Nanoscale Architecture of Biomembranes

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Biological membranes generate specific functions through compartmentalized regions, such as cholesterol-enriched nanodomains that host selected proteins [1].
Despite the biological significance of membrane nanodomains, details on their molecular structure remain uncertain [1]. They are elusive for most of the microscopic experimental techniques due to their small size, yet there is also a lack of atomistic simulation models able to describe spontaneous nanodomain formation in sufficiently simple but relevant complex membranes.

Here, we present a combined coarse-grained/atomistic (CG/AA) simulation approach in the study of ternary and quaternary lipid mixtures comprising cholesterol and/or sphingomyelin. Our approach allows to overcome the limitations on accessible time-scales and system-sizes of the AA models, and the insufficient accuracy of the CG force-fields [2].

The chosen lipid compositions form stable coexisting liquid-ordered/liquid-disordered (L_o/L_d) phases on a 10-μs time–scale at AA resolution, allowing to study the lateral organization of the lipids, and cholesterol. The L_o domains are characterized by substructures of hexagonally packed saturated hydrocarbon chains nanoclusters, separated by interstitial regions enriched in cholesterol. In the L_d domains, cholesterol shows spontaneous trans-bilayer motion, depending on the lateral heterogeneity of the membranes.

[1] Sezgin et al. Nat.Rev.Mol.Cell.Biol. 18, 361 (2017).

[2] W.F.D. Bennett et al, Biophysical J. 114,2595 (2018).