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The structure of cholesterol in lipid rafts

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Transient nano- or mesoscopic structures in the plasma membrane, termed rafts or functional domains, are thought to be essential for many cellular processes such as signal transduction, cell adhesion, signalling, cell trafficking and lipid/protein sorting. Experimental observations of these membrane heterogeneities have proven challenging, as they are thought to be both small and short-lived. First evidence of highly ordered lipid domains in the liquid-ordered (lo) phase of cholesterol-rich DPPC membranes has recently been reported from molecular dynamics simulations [1] and neutron diffraction [2]. With a combination of neutron scattering using deuterium labeled cholesterol molecules and molecular dynamic simulations we are able to determine the cholesterol structure within these rafts.

We studied the structure of the cholesterol molecules in the liquid ordered phase of DPPC membranes containing 32.5 mol% cholesterol using neutron diffraction. By changing the experimental setup in situ, the spatial resolution could be drastically increased, as compared to a typical setup. Bragg peaks corresponding to ordering of the cholesterol molecules were observed. The peaks can be indexed by two different structures: cholesterol ordered in agreement with the umbrella model in equilibrium with immiscible cholesterol patches. From coarse grained computer simulations these structures could be characterized as small ordered 'domains' of a highly dynamic nature. For the first time we determine the structure of cholesterol molecules in rafts in binary cholesterol lipid membranes. These small-scale domains can be speculated to be the nuclei that may lead to 'rafts'in biological membranes [3].

References

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