Observation of cholesterol structure in lipid rafts

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Rafts, or functional domains, are transient nano- or mesoscopic structures in the plasma membrane and are thought to be essential for many cellular processes such as signal transduction, cell adhesion, signalling, cell trafficking and lipid/protein sorting. Observations of these membrane heterogeneities have proven challenging, as they are thought to be both small and short-lived. With a combination of coarse grained molecular dynamics simulations and neutron diffraction using deuterium labeled cholesterol molecules, we observed small, ordered domains in a binary lipid/cholesterol membrane and determined, for the first time, the cholesterol structure within these rafts.

Experiments were conducted using the triple-axis spectrometer N5 at the Canadian Neutron Beam Centre. Three structures were observed in simulations and experiments: (1) A fluid-like structure with strongly bound pairs of cholesterol molecules as manifestation of the liquid-disordered (ld) phase. (2) A highly ordered lipid/cholesterol phase where the lipid/cholesterol complexes condense in a monoclinic structure, in accordance with the umbrella model, and (3) triclinic cholesterol plaques, i.e., cholesterol bilayers conciliating with the lamellar membranes. Raft-like domains were previously reported only from so-called “raft forming mixtures”, which form stable phase-separated structures, not likely related to domains in real cells. The small and fluctuating domains observed in binary systems may be more closely related to what rafts are thought to be, and potentially the nuclei that may lead to rafts in biological membranes.