Packing Parameter Matching of Cholesterol with Oxidized Phospholipid Species in Lipid Bilayers

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Abstract:

We claim that (1) cholesterol protects bilayers from disruption caused by lipid oxidation by sequestering conical shaped oxidized lipid species such as 1-palmitoyl-2-azelaoyl-sn-glycero-3-phosphocholine (PZPC) away from phospholipid, because cholesterol and the oxidized lipid have complementary shapes and not because cholesterol orders lipid bilayers and (2) mixtures of cholesterol and oxidized lipids can self-assemble into bilayers much like lysolipid– cholesterol mixtures. The evidence for bilayer protection comes from molecular dynamics (MD) simulations and dynamic light scattering (DLS) measurements. In simulations, bilayers containing high amounts of PZPC become porous, unless cholesterol is also present. The evidence for the pairing of cholesterol and PZPC comes mainly from correlated 2-D density and thickness plots from simulations, which show that these two molecules co-localize in bilayers. Further evidence that the two molecules can cohabitate comes from self-assembly simulations, where we show that cholesterol-oxidized lipid mixtures can form lamellar phases at specific concentrations, reminiscent of lysolipid–cholesterol mixtures. The additivity of the packing parameters of cholesterol and PZPC explains their cohabitation in a planar bilayer. Our hypothesis has important consequences for cellular cholesterol trafficking; diseases related to oxidized lipids, and to biophysical studies of phase behaviour of cholesterol-containing phospholipid mixtures.