

Cholesterol's Location in Bilayers of Omega-3 PUFA Chains

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Polyunsaturated fatty acids (PUFAs) are essential for normal growth and development. There are two classes of PUFA: omega-3 and omega-6. The lateral sequestration of lipids with polyunsaturated fatty acid (PUFA) chains into membrane domains depleted of cholesterol has been hypothesized to have an important role in neurological function and in alleviating a number of health-related problems. There seems to be a strong aversion of the disordered polyunsaturated chains to the rigid planar surface of cholesterol. Recently, neutron studies of deuterated cholesterol incorporated into bilayers composed of PC lipids with two omega-6 polyunsaturated chains (di-20:4 PC, DAPC) found cholesterol sequestered at the bilayer midplane, in contrast to its usual upright orientation with the hydroxyl group located near the lipid/water interface [1,2]. It was later discovered that the incorporation of monounsaturated 1-palmitoyl-2-oleoylphosphatidylcholine (16:0-18:1 PC, POPC) into DAPC causes an abrupt flipping of cholesterol to its upright position at 50 mol% replacement, whereas disaturated 1,2-dimyristoylphosphatidylcholine (di-14:0 PC, DMPC) has the same effect at only 5 mol% replacement [3,4].

The aforementioned studies were conducted with an omega-6 PUFA (di-20:4 PC) however no one has examined cholesterol's behaviour in an omega-3 PUFA bilayer. It is unclear if cholesterol's aversion to PUFAs is a universal property of PUFAs or behaviour unique to omega-6 PUFAs. In this study we examined cholesterol- d_{40} in di-14:0 PC bilayers (saturated), di-20:4 PC bilayers (omega-6) and the omega-3 PUFA 1,2-didocosahexaenoylphosphatidylcholine (di-22:6 PC, DDPC).

Neutron diffraction demonstrates the distribution of cholesterol- d_{40} is centred in the bilayer centre for both PUFA bilayers examined. This result for di-20:4 PC is consistent with previous work reporting the distribution of cholesterol- d_6 [1] and is the first observation of cholesterol located in the centre of di-22:6 PC. Interestingly, d_{40} labeled cholesterol in di-22:6 PC demonstrates cholesterol very deep in the hydrocarbon core. In fact, cholesterol- d_{40} distribution is centred at the centre of the di-22:6 PC bilayer with very similar distribution shapes as observed in the label distribution in di-20:4 PC. The distributions of di-22:6 PC and di-20:4 PC are very different from the distribution of cholesterol- d_{40} in di-14:0 PC, see Figure 1. This data suggests that, in fact, cholesterol's unique behaviour in PUFA containing membrane is the same in both omega-6 PUFA and omega-3 PUFA bilayers.

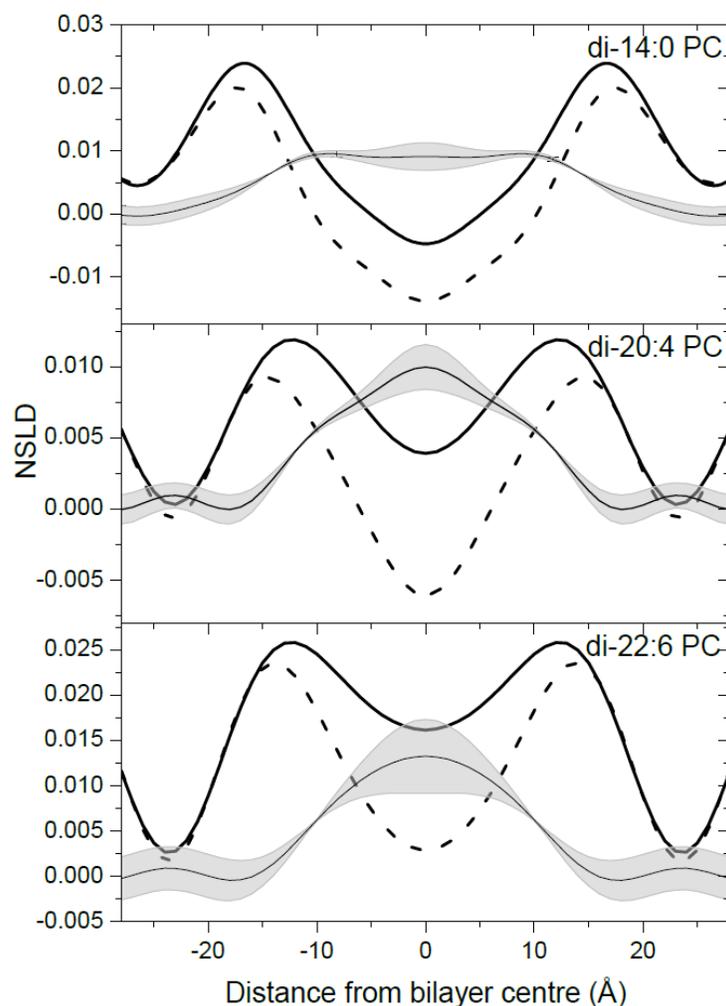


Figure 1 The NSLD profiles and distribution of cholesterol of d_{40} -cholesterol in di-20:4 PC (top) and d_{40} -cholesterol in di-22:6 PC (bottom). The solid lines are the NSLD profile for bilayers containing d_{40} -cholesterol, and the dashed are bilayers.

References

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