Bilayer Arrangements of Phospholipids: A Structural Analysis of 1,2-Dilauroyl-(±)-phosphatidylethanolamine: Acetic Acid and its Implications for Membrane Models

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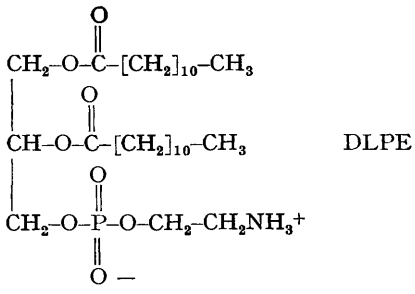
Summary A structural analysis of 1,2-dilauroyl-(±)-phosphatidylethanolamine is summarised; intermolecular packing is in the form of a bilayer.

THE interpretations of *X*-ray diffraction data from synthetic and natural membranes[1-3] rely heavily on structural models of phospholipids for which detailed bond lengths and conformations have not been available experimentally, largely because of the difficulty of obtaining suitable single crystals for a diffraction analysis. We have succeeded in preparing thin plates of 1,2-dilauroyl-(±)-phosphatidylethanolamine (DLPE) which, by ordinary crystallographic standards, were of mediocre quality but were ordered well enough to provide data of sufficient precision to allow an *X*-ray analysis.

The crystals of DLPE (containing an acetic acid molecule of crystallisation) are monoclinic with $a = 46{\cdot}2$, $b = 7{\cdot}72$, $c = 9{\cdot}95$ Å, $\beta = 92{\cdot}0°$; space group $P2_1/c$; $Z = 4$. The structural analysis was achieved, after much difficulty, by



DLPE

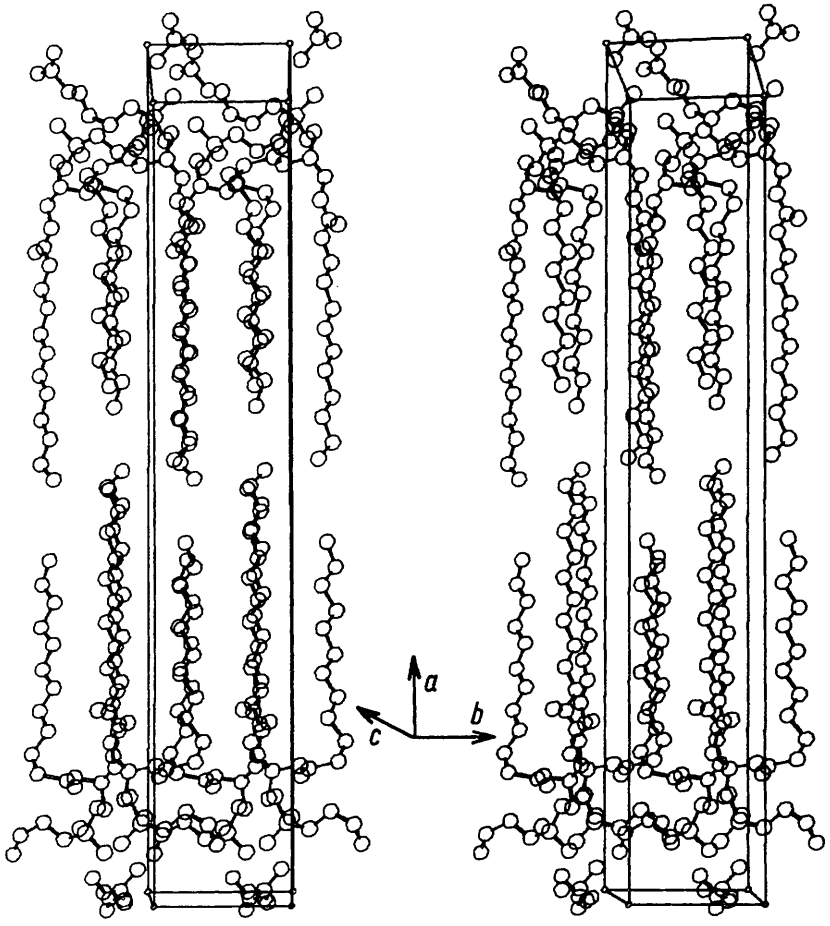


FIGURE 1. 1,2-Dilauroyl-(±)-phosphatidylethanolamine–acetic acid. A stereoscopic view of the inter-molecular arrangement.

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a direct solution of the phase problem and least-squares refinement of atomic co-ordinates and isotropic thermal parameters has converged to an unweighted discrepancy index, $R_1 = 0{\cdot}28$.

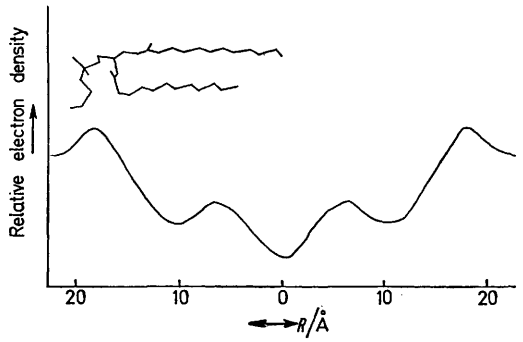

FIGURE 2. DLPE: The calculated electron density across the bilayer.

We shall describe details of the intra-molecular bond lengths and conformation elsewhere[4] but so far as the molecular conformation is concerned, it can be noted that it differs from those predicted theoretically.[5] The lipid hydrocarbon chains in the molecule are essentially parallel to one another and the dihedral angle between the planes containing the two chains is only 8°. The phosphodiester moiety has a double *gauche* conformation and the phosphorylethanolamine group lies approximately parallel to the plane of the bilayer (see below). Inter-molecular P–O · · · H–N hydrogen bonding modifies the conformation of the polar head group from that anticipated for an isolated phosphatidylethanolamine residue.

Our main emphasis here is on the inter-molecular packing which is shown in Figure 1. The phospholipid molecules pack in the form of a classical lipid bilayer,[6] the bilayers being separated by acetic acid molecules of crystallisation. The polar group separation across a bilayer is 39 Å, compared with separations in dry and wet dipalmitoyl lecithin of 44 Å and 50 Å respectively.[1] Each lipid chain is close-packed by six others, the chain-chain separation being 4·6 Å, a value again close to that suggested for the synthetic membranes. A low-resolution electron-density synthesis, computed from 100, 200, 300, and 400 reflexion structure factors with phases (0, 0, 0, π), is shown in Figure 2 and has a striking similarity to those derived for dipalmitoyl and egg lecithin–water model membranes and to those for rabbit and frog myelin.[3] Although the phase assignments for the phospholipid crystal reflexions are different from those of the lecithin and myelin membranes, a similar electron-density profile results.

The hydrocarbon chains have few close inter- or intra-molecular contacts as they project into the centre of the bilayer. This is reflected by Debye-Waller factors for the carbon atoms which increase progressively along the chain, with the result that towards the centre of the bilayer substantial disorder exists. This is in agreement with conclusions derived from e.s.r.-spin labelling and n.m.r. studies on model and natural membranes,[7] again suggesting that chain disorder increases from the carboxyl group to the terminal methyl group.

The crystal structure analysis of DLPE allows us to examine the structure of a phospholipid, analogous to that present in cell membranes, at atomic resolution. It may also be used to predict the conformation and structure of other biologically-important phospholipids.

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