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THE ELECTROSTATIC POTENTIAL OF A MODEL PHOSPHATIDYLCHOLINE MONO- AND BILAYER

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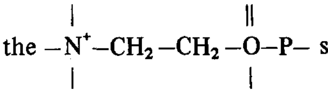
1. Introduction

We have undertaken a series of studies on the electrostatic potential of model phospholipid monolayers and bilayers. In [1,2] we have presented results obtained for 1,2-dilauroyl-phosphatidylethanolamine (PE). We now extend our study to a phosphatidylcholine (PC).

The interest in comparing these 2 important classes of phospholipids lies in the fact that although they are both amphophilic and generally assume a similar conformation of their polar heads [3–6] they differ significantly in two aspects likely to be of consequence for our investigation:

(1) There is no possibility in the case of phosphatidylcholines of the formation of hydrogen bonds between the phosphate and ammonium groups of neighbouring molecules while such a possibility exists with phosphatidylethanolamines;

(2) The positive charge of the PC head is distributed over the much bigger trimethylammonium group than is the case for the smaller ammonium group of PE.

As a representative of choline phospholipids we have taken 3-lauroyl-propandiol-1-phosphorylcholine (LPPC), a lysolecithin analogue which lacks the free hydroxyl group in the 2 position of the glycerol moiety. The LPPC molecule and the axis system used in the calculations are shown in fig.1. The reason for the choice of this compound is that the crystal structure of LPPC-monohydrate was solved in [4,7]. In this crystal, molecules are arranged in bilayers, with the polar heads lying parallel to the layer plane. The hydrocarbon chains form an angle of 41° with the layer normal and are interdigitated. The conformation of the LPPC polar head is very similar to that of phosphatidylethanolamine and glycerolphosphorylcholine [3], *trans–gauche*, in agreement with the quantum-mechanical demonstration of the intrinsic preference of the  $-\overset{|}{\underset{|}{N^+}}-CH_2-CH_2-O-\overset{\|}{\underset{|}{P}}-$ system involved for this conformation [8–10]. Furthermore, it is found, by the NMR technique, that there is a good agreement between the averaged conformation in solution and the crystal structure of LPPC [6]. Judging from the thickness of the layer and the molecular area the authors estimate that the LPPC crystal is a good model for the lamellar gel structure of lysophosphorylcholine and diacylphosphorylcholine.

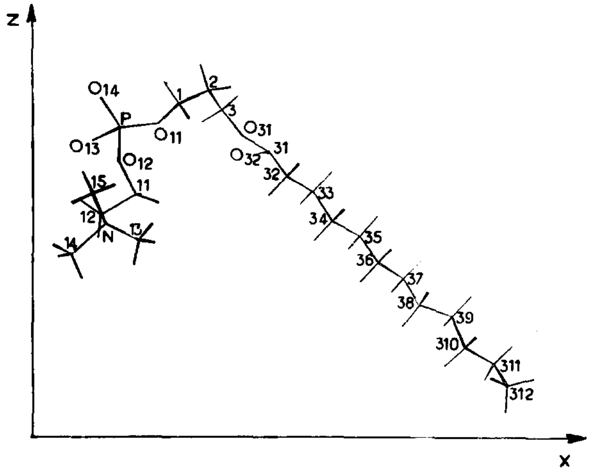


Fig.1. The molecular structure of 3-lauroyl-propandiol-1-phosphorylcholine (LPPC) and the axis system used in the calculations.

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2. The method

The technique of calculating the molecular electrostatic potential has been described in earlier publications from this laboratory (e.g., [11,12]).

The systems studied here are a model monolayer and a model bilayer. The arrangement of molecules in layers and their geometry are taken from the LPPC crystal structure [3].

The calculations have been performed for layers built up from 9 cells (18 LPPC molecules) and 25 cells (50 molecules) in each layer. As the results for both cases are qualitatively similar only the latter are presented.

The electrostatic potential was calculated for a fragment of the surface envelope constructed on the monolayer (vide infra), following the procedure used in [1,13]. The surface envelope was constructed from the intersection of spheres centered on each atom of the system with sphere radii proportional to the atomic van der Waals' radii. For technical reasons [1] the proportionality factor of 1.7 was employed.

3. Results and discussion

3.1. *Single molecule*

Fig.2 presents the molecular graphic of an LPPC molecule viewed from the negative *x* direction (for the axis system seen fig.1). The corresponding electrostatic potential calculated on the surface envelope is presented in fig.3. The explanations of the shadings used are given in table 1. There is a distinctive zone of negative potential connected with the phosphate group, with a minimum value of −68.8 kcal/mol, (denoted by M in fig.2), situated on the surface of the phosphorous atom between the two anionic oxygens. There is also a large region of positive potential around the trimethylammonium group. The maximum value of the potential denoted by X in fig.3, is 42.4 kcal/mol, and is located on one of the hydrogen atomic spheres of the ammonium group.

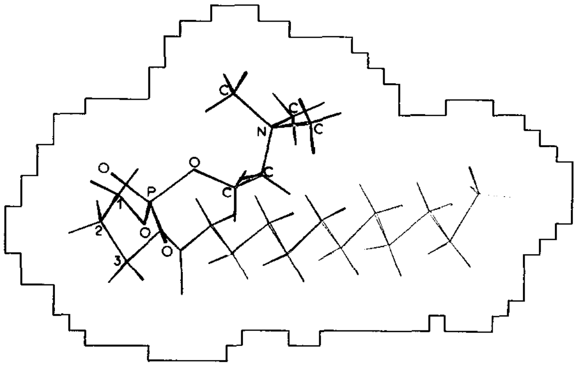

Fig.2. Molecular graphic of LPPC viewed in the direction normal to the layer plane. Only heavy atoms of the polar head are lettered and 3 carbon atoms of the glycerol moiety are numbered.

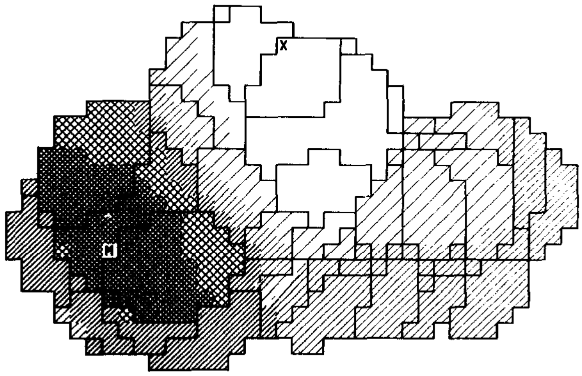

Fig.3. Electrostatic potential calculated on the surface envelope of a single LPPC molecule. For details of shading see table 1.

Table 1
Shadings used in the electrostatic potential graphics

Shading	Potential (kcal/mol)	
	Graphic 2 single molecule	Graphics 4 and 6 mono- and bilayer
□	42. ↓ 23.	28. ↓ 9.
⧄	23. ↓ 5.	9. ↓ −9.
▨	5. ↓ −13.	−9. ↓ −28.
▨	−13. ↓ −31.	−28. ↓ −47.
⊠	−31. ↓ −50.	−47. ↓ −66.
▩	−50. ↓ −69.	−66. ↓ −86.

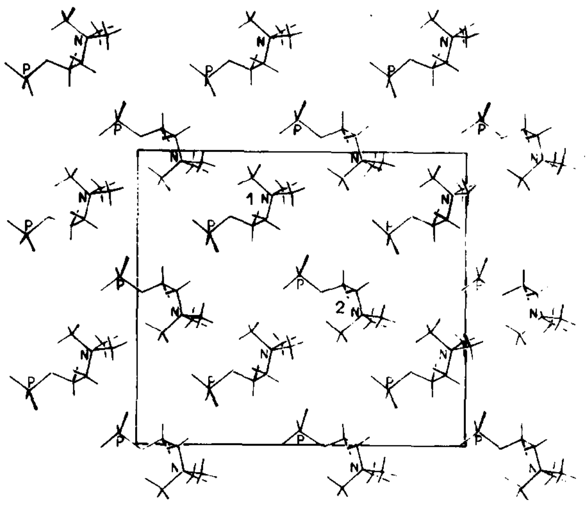

Fig.4. Organisation of LPPC in the crystal monolayer. The central rectangle denotes the area of potential studied on the surface envelope. Phosphorus and nitrogen atoms are denoted P and N, respectively.

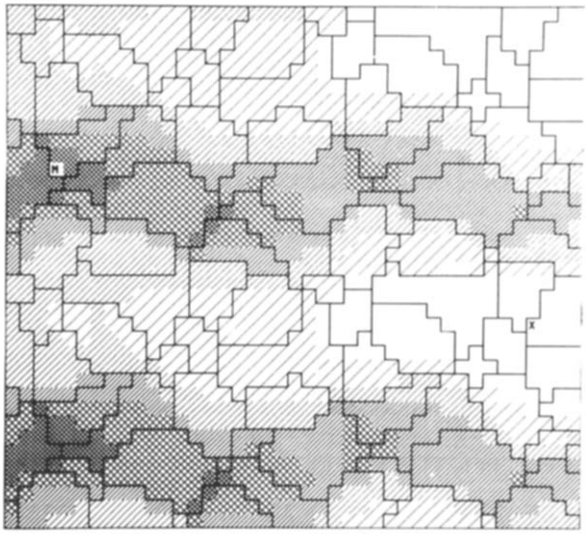

Fig.5. Electrostatic potential on the monolayer envelope calculated with 50 LPPC molecules. For details of shading see table 1.

3.2. *Model monolayer*

The arrangement of LPPC polar heads in the model monolayer is illustrated in fig.4. This arrangement is strikingly different from that of the layers of PE molecules [14] in that it has a much 'looser' structure, the surface occupied by a polar head being 52 Å as compared to 36 Å^2 for PE. The molecules are arranged with their dipole moments following a zig-zag path unlike the antiparallel arrangement of the dipole moments of the PE molecules. It can be seen in fig.4 that the phosphate groups and the trimethylammonium groups are arranged in characteristic alternating horizontal bands. The molecules denoted 1 and 2 in fig.4 are the two molecules belonging to the central unit cell. The rectangle denotes the fragment of the surface envelope for which the electrostatic potential was calculated.

The electrostatic potential is given in fig.5 (for details of shading see table 1). Quite clearly horizontal bands of potential can be distinguished in correspondance with the arrangement of the phosphate and ammonium groups of the polar heads. The minimum value –85.7 kcal/mol, denoted by M in fig.4, is located on the surface of an anionic oxygen of molecule 1, but an almost identical value (–85.5 kcal/mol) is found in the second deep band at the bottom of the figure. The maximum value calculated for the region studied, 28.2 kcal/mol denoted as X in fig.5, is located on a hydrogen atom of a trimethylammonium group. The corresponding local maximum in the light upper band is 27.8 kcal/mol.

3.3. *Model bilayer*

The configuration of the molecules in the bilayer is shown in fig.6. This view corresponds to the *xz* plane of the crystal structure. It indicates the main features of this crystal, namely the interdigitation of the hydrocarbon chains and the tilt of the chains with respect to the layer normal of 41°. As a result, the thickness of the bilayer is rather small, being ~25 Å (against 46 Å for the PE layer).

The electrostatic potential calculated on the same fragment of the surface envelope as in fig.4 for the bilayer containing 50 molecules in each layer is shown in fig.7 (for the details of shading see table 1). The arrangement of the potentials in horizontal bands which was observed for the monolayer is maintained. The global minimum for the surface is in the lower band of negative potential and values –75.6 kcal/mol. The corresponding value for the upper band is –75.3 kcal/mol. Both these minima are situated on the surface of the anionic oxygens of the phosphate groups. The potential maximum, situated in the lower positive band, denoted as X, is 22.8 kcal/mol (with a nearly identical value of 22.6 kcal/mol in the corresponding upper band), both situated on the surface of a hydrogen atom of the methylammonium group.

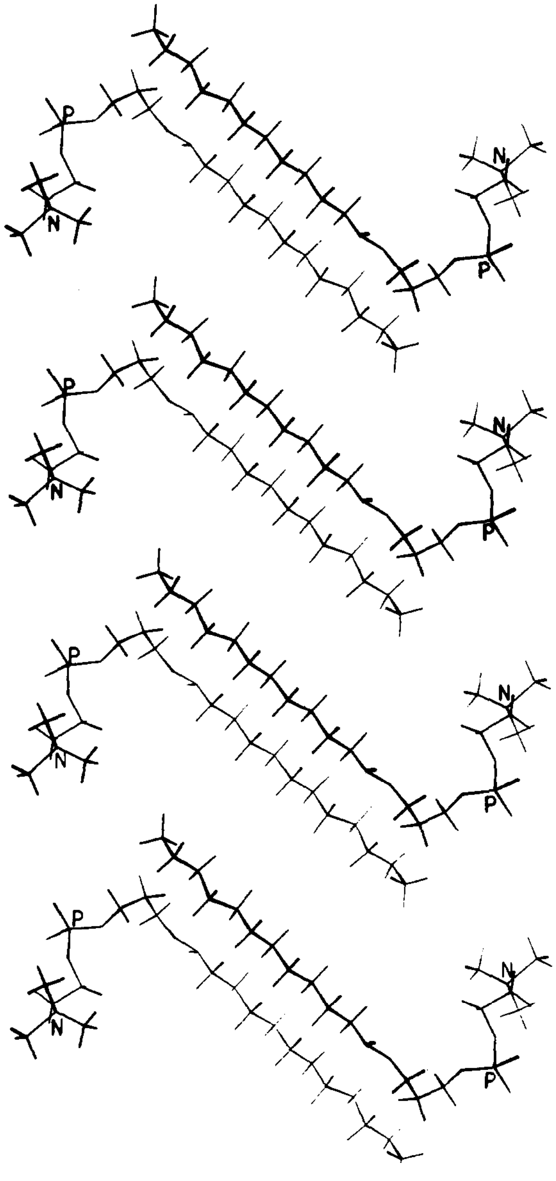

Fig.6. Organisation of LPPC molecules in the crystal bilayer viewed in the direction normal to the ac crystal face. Only the first slice of molecules is shown. Phosphorus and nitrogen atoms are denoted by P and N, respectively.

The numerical values of the minima and maxima of the electrostatic potential can thus be seen to be rather similar in a single molecule, a monolayer and a bilayer. The potential minimum becomes somewhat more negative for the monolayer (–85.7 kcal/mol) than for a free molecule (–68.8 kcal/mol) but is reduced for the bilayer to –75.6 kcal/mol. The potential maximum decreases in the order: free molecule, monolayer, bilayer, the corresponding values being 42.4, 28.2 and 22.8 kcal/mol, respectively.

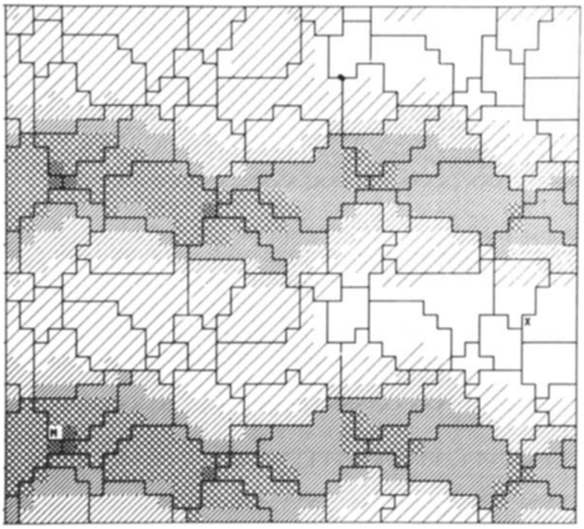

Fig.7. Electrostatic potential in the central rectangle of the monolayer envelope of fig.4 calculated for a bilayer containing 50 molecules in each layer. For details of shading see table 1.

4. Conclusions

The results of calculations of the electrostatic potential for a model of a phosphaditylcholine mono- and bilayer and their comparison with those for a model of a phosphatidylethanolamine show the dependence of the potentials on the structure and the configuration of the molecules in the layers. In contrast to the results for PE [1,2], the values of the potential for the monolayer and bilayer of PC are quite similar and not very different from that for a single molecule. This result appears to be due to the much weaker intermolecular interactions in the latter case.

Provided, that the conformation and configuration of the molecules observed in the LPPC crystal resemble that of a lamellar gel structure of natural lyso-PC [3], the results obtained can give some indications on the electrostatic potential created by these phospholipids. It should be remembered, however, that the electrostatic potential may be quite sensitive to the conformation of the polar heads. Computations on the influence of this factor are under way.

Acknowledgement

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