THE MOLECULAR ELECTROSTATIC POTENTIAL OF PHOSPHOLIPID MONOLAYERS AND BILAYERS

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1. Introduction

In [1] we presented the results of computations on the molecular electrostatic potential for a single phospholipid molecule, 1,2-dilauroyl-phosphatidylethanolamine (PE) and for its model monolayer. The geometry of PE as well as the arrangement of the molecules in the monolayer were those observed in the PE crystal structure [2]. Here we extend our computations to the PE bilayer, with the particular view of investigating the difference, if any, between the potentials associated with the monolayer and the bilayer.

2. Methods

The procedure for calculating molecular electrostatic potentials has been presented in [1] and described in [3,4]. The representation of the potential adopted in this paper refers as in [1] to its distribution on the surface envelope of the system investigated. This envelope is formed from the intersection of spheres centered on each atom of the molecules, with radii proportional to their atomic Van der Waals' radii [1,5]. For technical reasons explained in [1] the proportionality factor used is 1.7. We shall center here our attention on the potential on the surface envelope covering the array of polar heads of the layers.

3. Results and discussion

In the crystal of PE [2], the molecules are arranged to form a bilayer, with their polar heads situated in the *bc* plane. The unit cell consists of 4 molecules, 2 belonging to each monolayer. The pair of molecules in each monolayer are mirror images of each other and oriented in such a way that their dipole moments are antiparallel.

Fig.1 illustrates this arrangement for the monolayer. The surface envelope was constructed covering this assembly of polar heads and the potential was calculated for an area of the size of the *bc* dimensions of the crystal unit cell, indicated by the square in the center of fig.1, for varying numbers of surrounding PE molecules.

Following the procedure in [1], the distribution of the potential on the 3-dimensional surface envelope is represented by its projection on a 2-dimensional graphic. Fig.2 contains such a presentation of the potential calculated for a monolayer built up of 49 cells (98 PE molecules) (48 cells surrounding symmetrically the central cell whose potential is presented; although the dimensions of fig.2 are larger than those of the central square of fig.1, there is no difficulty in correlating corresponding zones). The significance of the different degrees of shading is indicated in table 1.

The most striking feature of the distribution shown is the dominance of positive potential centered on the two $-NH_3^+$ end groups with a maximum (fig.2 (x)) of 57.8 kcal/mol, associated with the nitrogen atom. Small zones of weak negative potential are situated above the phosphate groups with a minimum (fig.2 (M)) of −2.9 kcal/mol, associated with one of the phosphate anionic oxygens. This situation contrasts with results for single PE molecule or a pair of them for which the magnitudes of the positive and negative potentials associated with the ammonium and phosphate groups of the polar head are comparable

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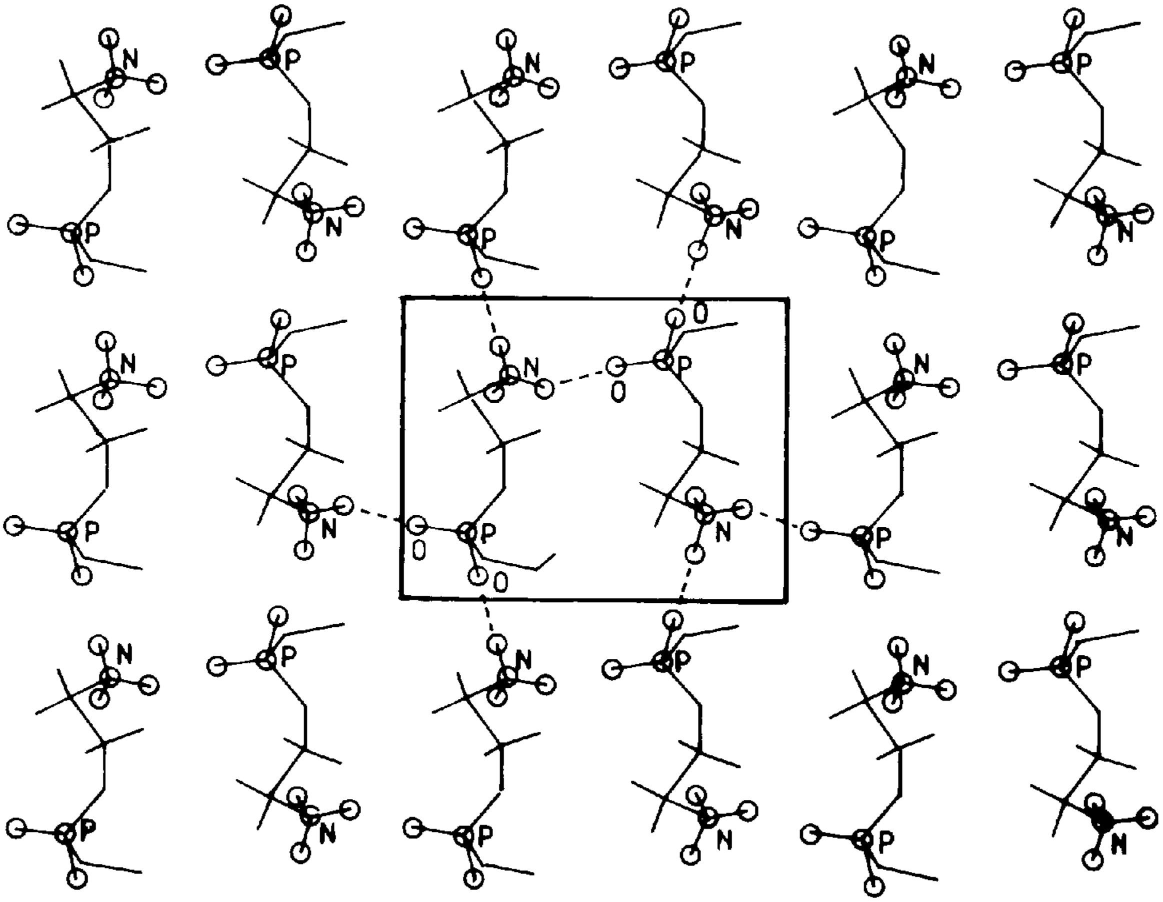

Fig.1. The organisation of PE polar heads in the crystal monolayer. The central square denotes the area of potential on the surface envelope to which the computations refer. The phosphorous and nitrogen atoms of the PE polar head are denoted P and N, respectively and small circles indicate the phosphate anionic oxygens and ammonium hydrogens.

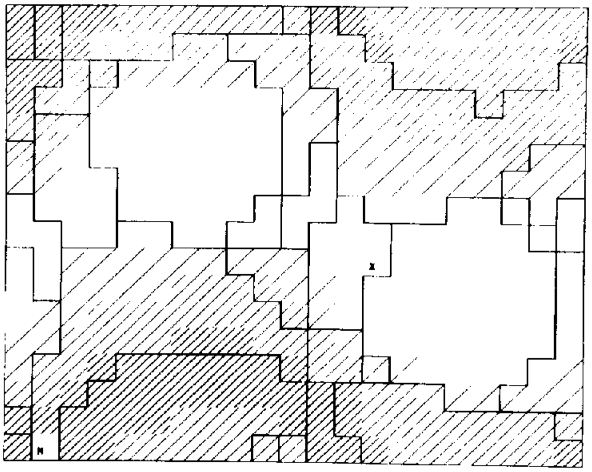

Fig.2. The electrostatic potential on the monolayer surface envelope calculated for 49 cells. For details of shading see table 1.

(≃ 70 kcal/mol for a single PE, ≃ 60 kcal/mol for a pair) [1]. It was shown [1] that the dominance of the positive potential on the monolayer surface may be attributed to the cancelation of the phosphate negative potentials due to the formation of the hydrogen bonds in the monolayer. This cancelation is more pronounced for the negative potentials of the phosphate than for the positive potentials of the ammonium groups, since in the former both ionic oxygens are involved in hydrogen bonds, while in the latter only 2 out of 3 protons take part in such bonds.

The distribution of the electrostatic potential in a model bilayer was calculated for the same surface area as for the monolayer. The second layer of PE molecules was placed following the arrangement observed in the crystal. Fig.3 shows this arrangement

Table 1
Shading used in electrostatic potential graphics

SHADING	POTENTIAL (kcal/mol)
□	58.0 → 41.0
⧄	41.0 → 24.0
▨	24.0 → 8.0
▨	8.0 → - 8.0
⊠	- 8.0 → -25.0
⊠	-25.0 → -42.0

in a cut through the bilayer corresponding to the *ab* face of the PE crystal.

The electrostatic surface potential calculated for the model bilayer built up from 49 cells (98 PE molecules) on each layer is shown in fig.4. The general aspect of the distribution of the potential is similar to that for the monolayer, with the positions of the maximum and the minimum unchanged. The overall potential, however, has become much more negative, the value of the maximum being reduced from 57.8 kcal/mol to 19.9 kcal/mol and the value of the minimum being decreased from –2.9 kcal/mol to –41.7 kcal/mol. In fact the major part of fig.4 is associated with negative values of the potential.

The second layer is thus shown to contribute a negative and nearly constant (within 2 kcal/mol) component to the potential over the whole surface studied. This effect is apparently related to the conformation of the polar head of the PE molecule. As can be seen in fig.3, for the conformation present in the crystal, the positively-charged ammonium group of the PE head is situated somewhat further to the outside of the bilayer than is the negatively-charged phosphate group. This results in a weak negative contribution of ~–0.5 kcal/mol to the potential of the monolayer surface from a single molecule placed in the opposing layer. For 100 molecules, these small

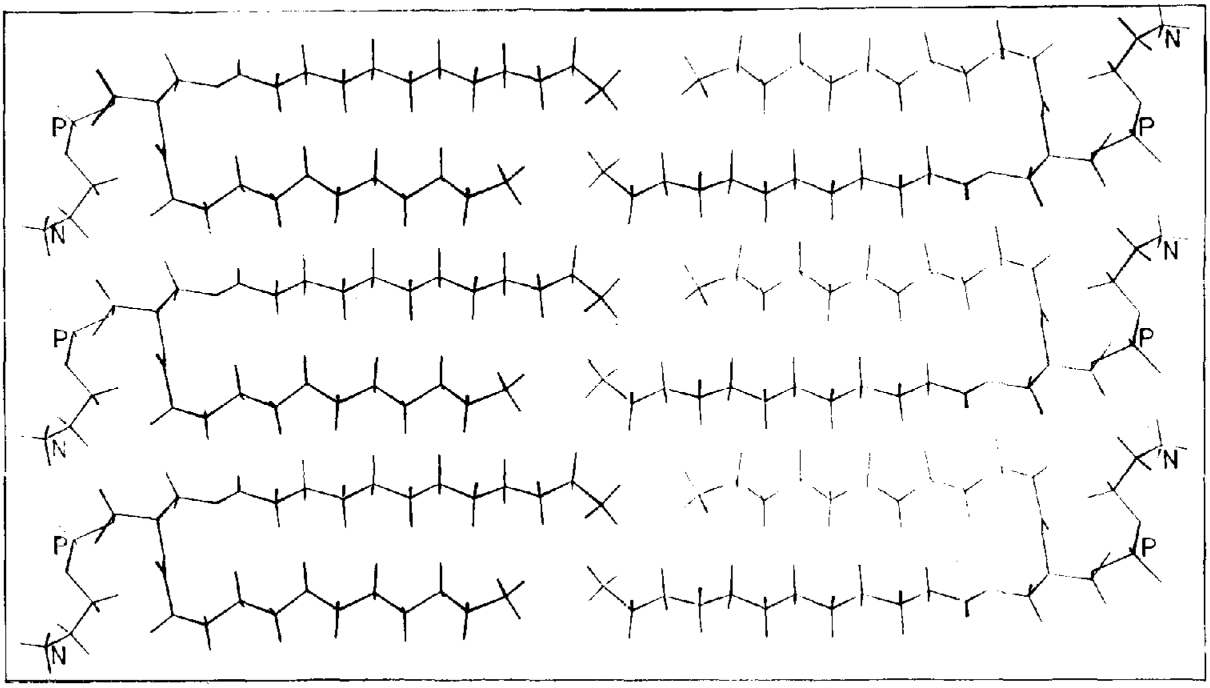

Fig.3. The organisation of PE molecules in the crystal bilayer.

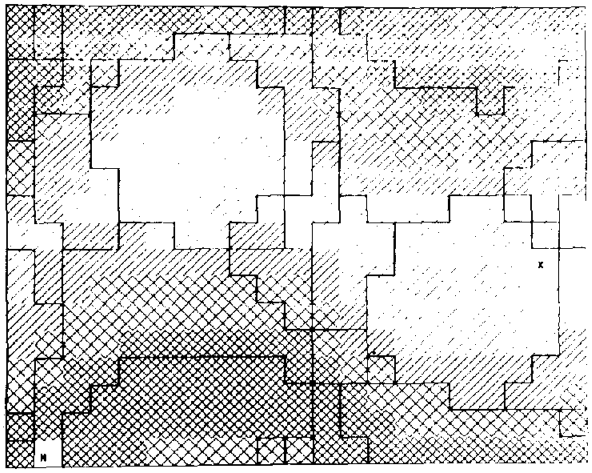

Fig.4. The electrostatic potential on the bilayer envelope calculated for 49 cells (on each layer). For details of shading see table 1.

contributions add up to ~—40 kcal/mol.

In table 2 the values of the potential maxima and minima for the PE mono- and bilayers of various dimensions are reproduced. It can be seen that for the monolayer the values do not change significantly with the increasing size of the layer. In the case of the bilayer, on the contrary, the values for the potential maximum and minimum become less positive and more negative, respectively, with the increase in the number of molecules of the system. It can be seen from table 2 that the limiting values have not been reached. A rough estimation shows that convergence should be expected only for several hundred cells in the second layer.

4. Conclusions

These results allow two main conclusions as to the essential features of the distribution of the electrostatic molecular potential in phospholipid layers:

Table 2
The values of potential (kcal/mol) maximum and minimum for the PE mono- and bilayers of different dimensions

No. cells on each layer	Monolayer		Bilayer	
	Max	Min	Max	Min
9	58.5	−9.2	49.2	−18.9
25	58.3	−4.1	35.9	−27.5
49	57.8	−2.9	19.9	−41.7

(1) The electrostatic potential created by phospholipid layers depends strongly on the conformation of the constituent molecules, particularly their polar heads, as well as on the organization of the molecules in the layers.

(2) The electrostatic properties of bilayers can be substantially different from those of monolayers.

Caution should therefore be exercised when using experimental results on monolayers for the interpretation of behaviour of bilayer systems.

Acknowledgement

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