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Journal of Electroanalytical Chemistry 457 (1998) 155–162

JOURNAL OF ELECTROANALYTICAL CHEMISTRY

Phospholipid monolayers at water | oil interfaces: theoretical modelling of surface pressure–molecular area isotherms

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Received 28 March 1998; received in revised form 29 June 1998

Abstract

The phospholipid adsorption and surface pressure–molecular area isotherms at interfaces are interpreted theoretically from two-dimensional (2D) lattice and real gas models that incorporate a minimum number of adjustable parameters. The first model is based on the lattice statistics of binary solutions and the molecular parameters introduced are the energy changes involved in the mixing process of the phospholipid and organic solvent molecules and the effective phospholipid head area. The surface pressure is interpreted in terms of the difference between the two liquid surface tensions. The second model makes use of (i) a non-localised adsorption model with a square-well potential energy term for the calculation of the surface concentration of the phospholipids at the interface as a function of the volume concentration of the phospholipids in the organic solvent phase, and (ii) a 2D hard disc gas model with a mean-field term accounting for the attractive interactions between the tails of the adsorbed phospholipids. The molecular parameters introduced in this model are the interfacial phospholipid adsorption energy, the effective hard disc diameter of the phospholipid head and the interaction energy between the phospholipid tails. The surface pressure is interpreted in terms of a 2D gas pressure in this model. The theoretical results obtained are compared with experimental data for the water | 1,2-dichloroethane and water | air interfaces. The two models predict correctly the typical order of magnitude for surface concentration and pressure values, as well as some qualitative features of the experimental isotherms, for low phospholipid surface concentrations.

Keywords: Phospholipid monolayers; Adsorption of phospholipids at interfaces; Surface pressure–molecular area isotherms; Theoretical modelling

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1. Introduction

Ion transfer across phospholipid monolayers formed at the interface between two immiscible electrolyte solutions (ITIES) is regarded as a promising model to elucidate the permeability properties of lipid membranes [1]. Basically, two experimental developments have been followed in the study of phospholipid films at water | air and water | oil interfaces [1,2]. Since phospholipids are, in general, highly soluble in some organic solvents (e.g. 1,2-dichloroethane (DCE) and nitrobenzene), the most common method for monolayer formation is adsorption from the solution to the interface [3]. The other approach utilises the fact that a phospholipid solution spreads at the water | air or water | oil interface to form thin films of molecular dimensions.

When modelling biomembranes, it is important to know the state of the phospholipid monolayer [4]. According to the literature, the state of adsorbed monolayers seems to be dependent on the organic phase; Wandlowski et al. [5,6] and Kakiuchi et al. [7–11] have noted a strong adsorption of different lipids with some lateral interaction at the water | nitrobenzene interface, while Thoma et al. [12,13] reported domains of lipids at water | hydrocarbon inter-

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PII S0022-0728(98)00296-4

faces. Furthermore, Grandell and Murtomäki [14] have recently shown, by applying the Langmuir technique to the water | DCE interface, that the lipids behaved like a two-dimensional (2D) gas at low surface concentration, though they appear to deviate from this behaviour for high surface concentrations.

Many theoretical models and computer simulations (see [15,16] and references therein) have been devoted to the modelling of monolayers at interfaces. As a preliminary contribution to the study of the ion transfer across phospholipid monolayers formed at the interface between two immiscible solutions, we have modelled here the state of the adsorbed monolayer using two simple molecular approaches for phospholipid adsorption and surface pressure–molecular area isotherms on the basis of previous experimental data [14,17] for the water | DCE and water | air interfaces.

The first model is based on the lattice theory of binary solutions and the molecular parameters introduced are the energy change involved in the mixing of phospholipid and solvent molecules, and the phospholipid head effective area. The second model makes use of: (i) a non-localised adsorption model with a square-well potential energy term for the calculation of the surface concentration of the phospholipids at the interface as a function of the volume concentration of the phospholipids in the organic solvent phase, and (ii) a 2D hard disc gas model, with a mean-field term accounting for the attractive interactions between the tails of the adsorbed phospholipids, for the calculation of the surface pressure of the gas as a function of the surface concentration. These theoretical approaches reproduce the qualitative features shown by the experimental isotherms with very few adjustable parameters.

2. Theory

2.1. Pressure–area isotherms from a lattice model

Since the phospholipids are amphiphiles, they tend to be found at interfaces such as water | oil, or water | air interfaces. The Gibbs equation then implies that the surface tension of the interface is lowered by the presence of the phospholipids, namely from γ_o to γ. The decrease in interfacial tension may be considered as a '2D gas pressure' exerted by the phospholipid monolayer due to the translational energy of the molecules [18]. Although this interpretation might seem rather strange (there is no 'gas' but a condensed system), it constitutes a useful analogy in many cases [18], and has also been invoked for the osmotic pressure of dilute liquid solutions [19].

The study of pressure as a function of the amount of phospholipids at the interface requires first a description of the interface. The classical Good-Fowkes model for calculating the interfacial tension of a liquid | liquid interface [18,20] considers implicitly a molecularly sharp interface. However, the sharpness of the liquid | liquid interface has been the subject of recent discussions in relation to electrochemical studies. While Girault and Schiffrin [21] proposed a model with a mixed solvent layer, the capacitance analysis by Wandlowski et al. [22] is more consistent with a molecularly sharp interface. Monte Carlo and molecular dynamic calculations of the density profile of liquid | liquid model interfaces show that the thickness of the transition region at the interface is of the order of 10 Å, with capillary wavelike distortions [23–25].

In addition to the difficulties in describing the structure of the water | oil interface, the behaviour of phospholipid monolayers is dictated also by the fact that the polar heads (and the first one or two hydrocarbon groups [26]) are immersed in the substrate water interacting strongly with the water molecules, while the nonpolar tails also interact attractively with each other and their cohesion is reduced by the organic solvent molecules. The theoretical modelling then requires identification of the main contributions that are responsible for the monolayer behaviour. In particular, the equation of state at low densities and the transition to liquid-like states can be described by considering the phospholipid monolayer as a 2D fluid of interacting phospholipids (p) in a medium of solvent molecules (o).

We adopt a 2D lattice model [19] in which each phospholipid molecule is localised on one of N_s available sites in a plane parallel to the interface and derive the equation of state from a statistical thermodynamics approach. In particular, we aim to evaluate the decrease of the interfacial tension $\pi \equiv \gamma_o - \gamma$ due to the presence of the phospholipids as a function of the molecular area $a \equiv A/N_p$, where A is the film area and N_p the number of phospholipid molecules. The film area A is $N_s a_s$, a_s being the area of every cell in the lattice. The solvent particles occupy the remaining sites, $N_o = N_s - N_p$, and we assume implicitly that the effective areas of the solvent and the phospholipid molecules are equal, so that they are interchangeable in the lattice. The coordination number of the lattice, i.e. the number of nearest neighbours to a given site, is denoted by n.

Assuming that only nearest-neighbour interactions are significant, the change in surface energy due to the presence of phospholipids can be estimated as

$$E_p = E - E_o = w_{oo}N_{oo} + w_{pp}N_{pp} + w_{op}N_{op} - w_{oo}N_i \quad (1)$$

where N_{ij} is the number of interactions between molecules i and j, and w_{ij} denotes the respective pair interaction energy. The term E_o in expression (1) represents the energy associated with molecular interactions at the interface in the absence of phospholipids, and therefore is evaluated as the interaction energy w_{oo} times the total number of pairwise interactions, $N_i =$

$nN_s/2$. Note that $N_{oo}+N_{pp}+N_{op}=nN_s/2$ is also satisfied. Eq. (1) can be transformed with the help of relations

$$N_{oo}+N_{op}/2=nN_o/2 \tag{2a}$$

$$N_{pp}+N_{op}/2=nN_p/2 \tag{2b}$$

to give

$$E_p=(w_{pp}-w_{oo})nN_p/2+\Delta wN_{op}/2 \tag{3}$$

where $\Delta w \equiv 2w_{op}-w_{oo}-w_{pp}$ is the energy change associated with the mixing of molecules [27]. Energetically the mixing is favoured when $\Delta w<0$ and prevented when $\Delta w>0$.

The mixing process is affected also by entropic considerations so that the equilibrium number of o–p interactions, $N_{op,eq}$, is given by the minimisation of the Helmholtz energy

$$F=E-TS=E-kT\ \ln g(N_o, N_p, N_{op}) \tag{4}$$

where k is Boltzmann's constant, T is the temperature and $g(N_o, N_p, N_{op})$ denotes the number of possible arrangements of the molecules in the lattice with specified values of N_o, N_p and N_{op}. Using the quasi-chemical approximation [19] this number can be evaluated as

$$g(N_o, N_p, N_{op})=\left(\frac{N_o!N_p!}{N_s!}\right)^{n-1}\frac{N_i!}{N_{oo}!N_{pp}![(N_{op}/2)!]^2}. \tag{5}$$

The use of Stirling's formula and subsequent minimisation of Eq. (4) with respect to N_{op} leads to the result

$$K\equiv e^{-\Delta w/kT}=\frac{(N_{op,eq}/2)^2}{N_{oo,eq}N_{pp,eq}} \tag{6}$$

which gives the name to the approximation. Eqs. (2) and (6) then allow us to evaluate the equilibrium fraction $x_{op,eq}=N_{op,eq}/N_i$ of o–p interactions for a given fraction $x_p=N_p/N_s$ of surface coverage by phospholipids. This has been represented in Fig. 1 for different values of $\Delta w/kT$. The central curve in this plot corresponds to $\Delta w=0$, i.e. to a situation where o and p molecules like the opposite species as well as their own species from the energetic viewpoint. The distribution of molecules in the film is then random and the fraction of o–p interactions is $x_{op,random}=2x_ox_p$, which corresponds to the Bragg–Williams approximation [19,27].

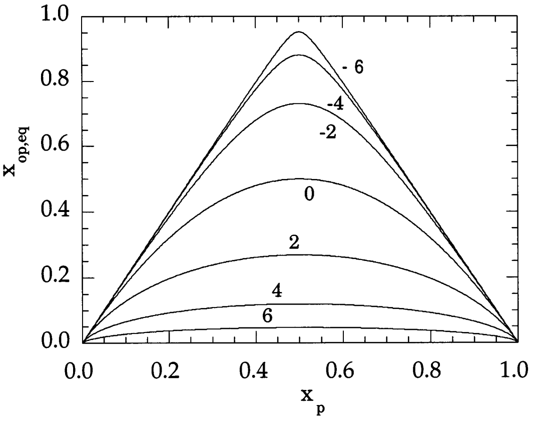

Fig. 1. Fraction of o–p interactions against the surface coverage $x_p=N_p/N_s$ by phospholipids for different values of the ratio $\Delta w/kT$. The phospholipid molecular area can be evaluated as $a=a_s/x_p$.

It is very difficult to solve exactly two or three-dimensional lattice statistical problems. Approximate methods are usually employed. In the Bragg–Williams approximation for a lattice gas with nearest-neighbour interactions, both the configurational degeneration and the average interaction energy are evaluated on the basis of a random distribution of molecules among sites. This only remains true at high temperatures. The quasi-chemical approximation is significantly better than the Bragg–Williams approximation but still not of unreasonable complexity. The main point of this approximation is that pairs of neighbouring sites are treated as independent of each other. The qualitative behaviour of the two approximations is, however, the same [19].

The film pressure π can now be evaluated as

$$\pi\equiv\gamma_o-\gamma=-\left(\frac{\partial F_{p,eq}}{\partial A}\right)_{N_p}=-\frac{1}{a_s}\left(\frac{\partial F_p}{\partial N_o}\right)_{N_p,N_{op,eq}} \tag{7}$$

where $F_{p,eq}$ is the value of $F_p=E_p-TS$ when the number of o–p interactions takes the equilibrium value $N_{op,eq}$. The minimum condition for $F_{p,eq}$, $(\partial F_p/\partial N_{op})_{N_o,N_p}=0$, has been used in the last step. Thus, the equation of state takes the form

$$\begin{aligned}\pi&=\frac{kT}{a_s}\left[(n-1)\ln x_o-\frac{n}{2}\ln x_{oo,eq}\right]\\&=\frac{kT}{a_s}\left\{(n-1)\ln x_o-\frac{n}{2}\ln\left[x_o-\frac{1-(1-4\beta x_ox_p)^{1/2}}{2\beta}\right]\right\}\end{aligned} \tag{8}$$

where $\beta\equiv 1-e^{\Delta w/kT}$ and the equilibrium fraction of o–o interactions $x_{oo,eq}$ is obtained from Eqs. (2a), (2b) and (6). To first order in $\Delta w/kT$, Eq. (8) simplifies to

$$\begin{aligned}\pi&\approx\frac{kT}{a_s}\left(-\ln x_o+\frac{n}{2}\beta x_p^2\right)\\&\approx-\frac{kT}{a_s}\left[\ln\left(1-\frac{a}{a_s}\right)+\frac{n\Delta w}{2kT}\frac{a_s^2}{a^2}\right]\end{aligned} \tag{9}$$

which constitutes the result given by the Bragg–William approximation [19]. Both Eqs. (8) and (9) yield the correct 'ideal gas' limiting case $\pi\approx N_pkT/A=kT/a$ for very dilute solutions ($x_p\ll 1$), and diverge logarithmically when $a\rightarrow a_s$ (i.e. $x_p\rightarrow 1$), as should be expected for a model where the phospholipids are constrained to remain at the interface.

More elaborate lattice models have been put forward previously (see [3,15,16,18] and references therein). In particular, Bell et al. [28] presented a lattice model to account for second-order phase transitions in phospholipid monolayers, as opposed to the first-order transitions described by the above theoretical modelling. The nature of the transition, however, is still under discussion [29].

2.2. Pressure–area isotherms from a 2D real gas model

The gas model considers the monomolecular film as a system of N_p phospholipid molecules that are restricted to move in a plane of area A with a 2D translational kinetic energy that produces the surface pressure π [18]. This spatial restriction is incorporated in the model by assuming that the phospholipids are within a square well of the potential energy$-u_{ads}$. The model should not be applied to phospholipid molecular areas a close to that corresponding to the monolayer collapse [14], since in this case translation is greatly impeded. The short-range interaction between the phospholipids is described in the mean-field approximation by using an effective potential energy u_{ef} that accounts for the attractive van der Waals interactions between the phospholipid tails. The partition function of the 2D system is then given by [31,32]

$$Z = z^{N_p}/N_p! \tag{10}$$

where

$$z = (1/\Lambda^2)(A - A_{ex}) \exp(-u_{ef}/kT) \exp(u_{ads}/kT) \tag{11}$$

is the partition function of one phospholipid and $\Lambda \equiv h/(2\pi mkT)^{1/2}$ is the thermal de Broglie wavelength; m denotes the phospholipid mass. Note that Eq. (11) omits the contributions to Z from degrees of freedom other than the translational.

In Eq. (11), A_{ex} is the surface area excluded by the phospholipid heads (assumed to behave as uncharged hard discs). At low surface concentrations (dilute gas limit), A_{ex} can be estimated by considering that the presence of a central molecule of radius r makes a circular area of radius $\sigma = 2r$ inaccessible to a second molecule centre. Thus, we can write [20,30]

$$A_{ex} = N_p \pi \sigma^2/2 \equiv N_p a_{ex} \tag{12}$$

where the factor 1/2 comes from the fact that the excluded area $\pi\sigma^2$ corresponds to a pair of molecules. Although Eq. (12) is not correct for high surface concentrations, it can be used as a first approximation [20].

Following similar arguments, the mean-field energy u_{ef} seen by a molecule can be calculated as

$$u_{ef} = N_p \bar{u}/2, \quad \bar{u} \equiv \frac{1}{A}\int_\sigma^\infty u(r) 2\pi r \, dr \tag{13}$$

In particular, for the short-range, weakly-attracting hard disc potential [30]

$$u(r) = \begin{cases} \infty, & r < \sigma \\ -u_0(\sigma/r)^s, & r > \sigma \quad (s > 2) \end{cases}, \tag{14}$$

Eq. (13) yields

$$u_{ef} = -2u_0 a_{ex}/a(s-2) \tag{15}$$

where $a = A/N_p$ is the molecular area, and parameter s can be set equal to six [32]. Eq. (11) is obtained by focusing our attention on a single molecule that moves in the effective potential of Eqs. (13)–(15) produced by the other molecules. This physical procedure is crude but it does not assume specifically that the gas is of low density. Therefore, the equations derived could be qualitatively valid to describe condensed systems provided that the translational kinetic energy of the molecules is still important.

From Eqs. (10)–(15) and $s = 6$, the surface pressure of the phospholipid gas can be calculated as [30]

$$\pi = kT\left(\frac{\partial \ln Z}{\partial A}\right)_{T,N_p} = -\frac{kT}{a_{ex}}\left(\frac{1}{1 - a/a_{ex}} + \frac{u_0}{2kT}\frac{a_{ex}^2}{a^2}\right) \tag{16}$$

The molecular area per phospholipid, a, can be varied by the compression of the monolayer. It is assumed that when compression proceeds, some solvent molecules are squeezed out of the monolayer [14], and then both the total surface area A and the molecular area a decrease.

Eq. (16) constitutes the surface pressure–molecular area isotherm of the 2D real gas model and plays a role analogous to Eq. (9) in the lattice model. However, the interpretation of π is now different. The physical origin of the surface pressure in Eq. (16) is not the difference between the surface tensions (see Eq. (7)) but the translational kinetic energy of the adsorbed phospholipids. The first term of Eq. (16) gives the ideal gas pressure corrected for the hard disc's excluded area. The second term decreases π with respect to the case of the absence of interaction ($u_0 = 0$) because the attractive interaction between the tails of the adsorbed phospholipids makes the molecular translation more difficult. From a phenomenological viewpoint, Eq. (16) can be regarded as a van der Waals (vdW) fluid equation [18,19] where the two usual empirical constants have now been expressed in terms of the molecular parameters σ and u_0.

2.3. Adsorption isotherms from the 2D real gas model

The isothermal adsorption process that leads the phospholipids from the organic solution to the interfacial region under a thermodynamic equilibrium is ruled by the equality of the chemical potentials of the phospholipids in these two regions. This equilibrium condition allows one to determine the phospholipid molecular area in the monolayer $a = N_p/A$ as a function of the phospholipid molar concentration c in the organic subphase. The gas model is suitable for the description of this adsorption process. In particular, since the adsorbed phospholipids have been considered free to move within a square well of the potential energy$-u_{ads}$, this results in a non-localised adsorption molecular model [31].

The chemical potential of the phospholipid real 'gas' at the interface can be obtained from Eqs. (10)–(15) as

$$\mu_{2D} = -kT\left(\frac{\partial \ln Z}{\partial N_p}\right)_{T,A} \approx -kT\ln\frac{z}{N_p} + u_{ef} + kT\frac{A_{ex}}{A-A_{ex}}. \qquad (17)$$

In the organic solution, given the relatively low values of the phospholipid molar concentration usually employed ($c \sim 10$ μmol l^{-1} [6,17]), the phospholipids can be treated as a 3D ideal gas and their chemical potential then becomes [30]

$$\mu = \mu^0 + kT\ln c = kT\ln(N_A\Lambda^3) + kT\ln c \qquad (18)$$

where N_A is Avogadro's constant. Note that Eq. (18) does not take into account the solvent explicitly, i.e. the solvent is assumed to be an incompressible fluid that provides a suspension medium for the phospholipids.

The equality of the right hand side terms of Eqs. (17) and (18) yields the adsorption isotherm

$$\frac{\Theta}{1-\Theta}\exp\left(-\frac{u_0}{kT}\Theta + \frac{\Theta}{1-\Theta}\right) = Bc \qquad (19)$$

where $B \equiv N_A a_{ex}\Lambda\exp(u_{ads}/kT)$ and $\Theta \equiv a_{ex}/a$ denotes the surface coverage. Note that Θ has the same meaning as x_p in the lattice model. Since the Frumkin isotherm is often used in experimental studies of phospholipid monolayers at water | oil interfaces [3,6,29,33], we should explain the differences between Eq. (19) and the Frumkin isotherm. The isothermal adsorption described by the Frumkin equation corresponds to localised adsorption with interacting adsorbates. This interaction is treated in the Frumkin isotherm using a mean-field, Bragg–Williams approximation, e.g. local fluctuations are neglected in the calculation of the averages over all available sites and an energetically uniform site distribution is assumed.

The Frumkin equation can then be derived from a lattice model for the phospholipid monolayer [3]. On the contrary, the gas model employed in the derivation of the adsorption isotherm allows for translation of the adsorbates and, therefore, corresponds to non-localised adsorption with interacting adsorbates. Furthermore, the empirical constants in the Frumkin isotherm have been evaluated in terms of molecular parameters. The difference between localised and non-localised adsorption is given by the factor $\exp(\Theta/1-\Theta)$ that appears in the left hand side of Eq. (19) but not in the Frumkin isotherm. This factor was previously found by Lyklema in his studies of adsorption of small ions at solid | liquid interfaces [34].

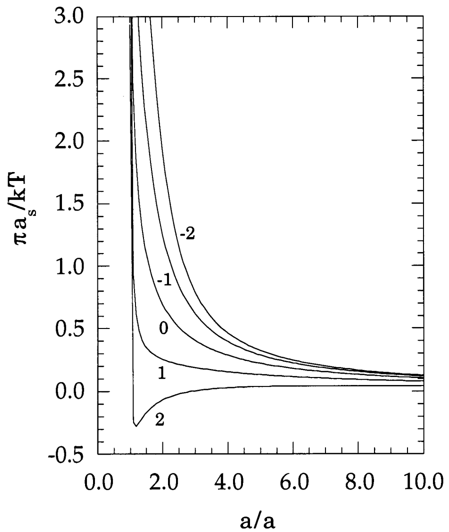

Fig. 2. Theoretical isotherms calculated from the 2D lattice model (see Eq. (8)) for $n = 4$ and the values of $\Delta w/kT$ shown on the curves. The critical behaviour is observed when $\Delta w/kT = 1.385$.

3. Results and discussion

Fig. 2 shows the pressure–area isotherms given by Eq. (8) for different values of $\Delta w/kT$. Note that the mixing process is energetically unfavourable when $\Delta w > 0$, and then there is a tendency for phase separation. In particular, the critical behaviour is obtained in the quasi-chemical approximation when $\Delta w/kT = 1.385$. The S-shaped region of the theoretical isotherm with $\Delta w/kT < 1.385$ corresponds to a phase transition [19] of the monolayer. This behaviour could be interpreted as a transition from a disordered fluid phase to another more ordered phase [15,18], although it is well known that monolayer isotherms can show many different phases [16,20]. The S-shaped region is a theoretical artefact of the quasi-chemical approximation that becomes a plateau region when exact calculations are carried out [19,35]. Also, the exact critical value for the ratio $\Delta w/kT$ obtained for a square lattice without using the quasi-chemical approximation differs from that in Fig. 2 [19]. In spite of these facts, the results shown in Fig. 2 are qualitatively valid [15,16,18,20].

Fig. 2 also exhibits reasonable results in quantitative terms. From an effective radius in the range $r = 2.5$–4 Å for the phospholipid heads and organic solvent molecules, the site area a_s can be estimated to be between 20 and 50 Å^2 [14,18,36]. Taking into account the energetics of the organic solvent and phospholipid molecular interactions, we could assume that $\Delta w > 0$ with $n\Delta w$ of the order of a few kT units [18,32]. Thus, the calculated surface pressure values at 25°C are of the same order of magnitude as the experimental values ($\pi \sim 10$ mN m^{-1} = 10 dyn cm^{-1} [14–16,18,20,32,37]).

Fig. 3 gives the theoretical surface pressure–molecular area isotherms obtained with the 2D real gas model (see Eq. (16)) for different values of u_0/kT. The π values calculated from this model agree also with those observed experimentally [16,20]. Again, the phase transition is not shown as a horizontal (plateau) region but in the form of an S-shaped region. The hard disc exclusion area a_{ex} that appears in Fig. 3 can be estimated to be of the order of 57 Å^2 if we take $r = 3$ Å ($\sigma = 6$ Å) for the phospholipid effective head radius. However, this excluded area could be significantly lower for high phospholipid surface concentrations because of the hard disc overlapping effect ignored in Eq. (12). Finally, the energy u_0 can be estimated to be of the order of a few kT units [32] since the presence of the organic solvent reduces the interactions between phospholipid tails considerably when compared with those characteristic of the water | air interface [14,18].

Eq. (16) can also be used to calculate the surface pressure–molecular area isotherms of different 2D gas models. Fig. 4 shows such calculations and compares the theoretical results with measured values. As expected, all gas models give the ideal gas behaviour in the limit of low surface concentration [14,16,20]. The S-shaped region (see inset) of the isotherm could be interpreted in this model as a phase transition of the phospholipid monolayer from a 'gas' state to a more condensed 'liquid' state, and is a theoretical artefact of the mean-field approximation introduced in Eqs. (10)–(15) [19,35]. As in the case of the lattice model, this S-shaped region becomes a plateau region when exact calculations are carried out, though the results of Fig. 4 are sufficient for qualitative purposes [19,35]. The experimental nature of phase transitions in monolayers is still under discussion [38,39]. First and second-order transitions have been reported. The quasi-chemical approximation for a lattice gas and the van der Waals model used here lead to first-order phase transitions.

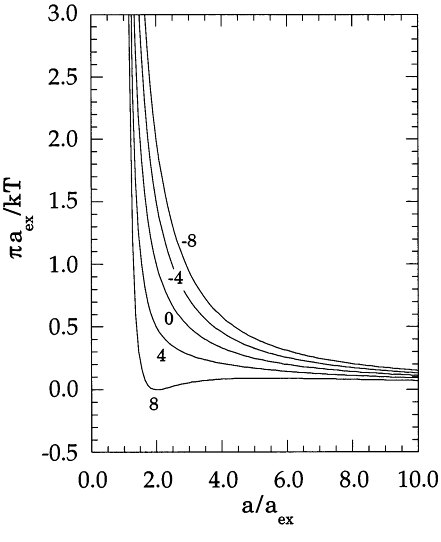

Fig. 3. Theoretical isotherms calculated from the 2D real gas model (see Eq. (16)) for the values of u_0/kT shown on the curves.

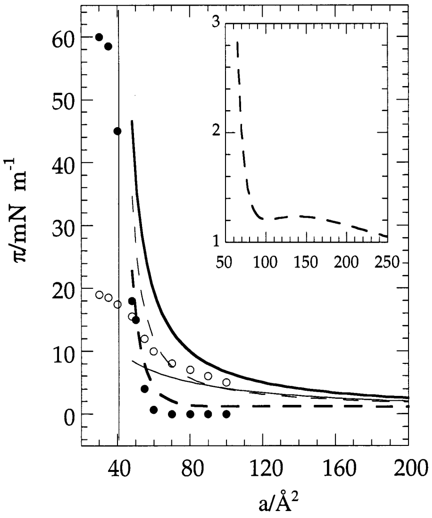

Fig. 4. Some isotherms predicted by Eq. (16): (thin solid line) ideal gas ($\sigma = 0$, $u_0 = 0$), (thick solid line) hard disc gas ($\sigma = 5$ Å, $u_0 = 0$), (thin dashed line) vdW gas with $\sigma = 5$ Å and $u_0/kT = 3$, and (thick dashed line) vdW gas with $\sigma = 5$ Å and $u_0/kT = 7$. The symbols represent the experimental data in Grandell and Murtomäki [14] for the water | DCE (○) and water | air (●) interfaces. The vertical line corresponds to the hard disc exclusion area, and denotes the onset of the monolayer collapse [14]. The inset zooms the theoretical isotherm for the vdW gas with $\sigma = 5$ Å and $u_0/kT = 7$.

The symbols in Fig. 4 represent experimental data obtained by Grandell and Murtomäki [14] for the water | DCE and water | air interfaces. The phospholipid employed in these measurements is distearoyl phosphatidylcholine (DSPC). We have assumed the hard disc exclusion area $a_{ex} \approx 40$ Å^2 in the theoretical calculations. The vertical line in Fig. 4 corresponds to this exclusion area, and gives the onset of the monolayer collapse in the isotherm [14]. The experimental results shown are those of DSPC with phosphate buffer (pH 7.6) [14]. For this pH value, both the acid group (whose pK_a is ca. 2 [14]) and the basic group (whose pK_a is ca. 11–12 [40,41]) are charged, so that the phospholipid head has no net electrical charge. We have thus considered only the phospholipid tail interactions in the model and ignored the head group interactions. Note also that because these groups are embedded in the water volume phase, the latter interactions should be partly screened.

The experimental results of Fig. 4 show a marked plateau region in the water | air isotherm that is absent in the case of the water | DCE isotherm. This plateau region could be due to the significant van der Waals hydrophobic interactions between the hydrocarbon chains at the water | air interface. The interactions should be partly screened by the organic solvent molecules, since these molecules can penetrate the phospholipid monolayer structure in the case of the water | DCE interface [14,18,20], which gives a less defined isotherm. Apparently, we could simulate the above effects in the vdW gas model by assuming different values for the interaction energy u_0 in Eq. (14) (see Fig. 4).

The calculations of Fig. 4 show also that the vdW gas model can explain some qualitative aspects of the experimental isotherms for relatively low molecular areas ($a = 50-100$ Å^2), which is not the case of the ideal [14] and hard discs models. Modified vdW gas models have usually proved useful to analyse monolayers at air | water interfaces [18,20,37]. However, all the gas models considered here fail badly when $a \lesssim a_{ex}$, where the collapse of the phospholipid monolayer begins. This is also the case of the lattice model (see Figs. 2 and 4), since in this model multilayer occupation [14] is also not allowed.

The final results to be presented refer to the adsorption isotherm given by Eq. (19). Apart from parameters u_0 and a_{ex} that have already been discussed, this expression incorporates the microscopic parameters u_{ads} and m (the phospholipid molecular mass that determines the thermal de Broglie wavelength). For the latter, $mN_A \approx 800$ g mol^{-1} can be considered as a typical value [14,17]. The adsorption energy can be roughly estimated from the Born solvation equation [42]

$$u_{ads} = \frac{e^2}{4\pi\varepsilon_0 r}\left(\frac{1}{\varepsilon_{r,o}} - \frac{1}{\varepsilon_{r,w}}\right) \tag{20}$$

since we have considered that the adsorbed phospholipid head is directed to the aqueous phase. In Eq. (20), e is the electron charge, ε_0 is the vacuum electrical permittivity, and $\varepsilon_{r,o} = 10.2$ and $\varepsilon_{r,w} = 79$ are the dielectric constants of the organic solvent (DCE in this estimation) and water, respectively. If we assume $r = 3$ Å ($\sigma = 6$ Å) for the phospholipid effective head radius, then $u_{ads} \approx 16kT \approx 40$ kJ mol^{-1} and $a_{ex} \approx 57$ Å^2. Although this value for u_{ads} might seem reasonable, it must be emphasised that Eq. (20) constitutes an oversimplification, and more elaborate models for u_{ads} should be used for quantitative purposes.

Fig. 5 gives the calculated phospholipid surface coverage Θ as a function of the phospholipid volume concentration c in the organic solution (see Eq. (19)) for different values of the ratios u_0/kT and u_{ads}/kT. This figure shows that the attractive intermolecular interaction ($u_0 = 2kT$) increases the surface coverage with respect to the case of absence of interaction ($u_0 = 0$). To differentiate between Eq. (19) and the Frumkin isotherm, a dotted curve has also been included in Fig. 5. This curve corresponds to the adsorption isotherm of Eq. (19) without the $\exp(\Theta/1-\Theta)$ factor. The asymptotic approach to saturation is slower in the case of Eq. (19) than in the case of the Frumkin isotherm. The adsorption isotherms shown in Fig. 5 are in qualitative agreement with experimental observations [6] and lead to phospholipid surface concentrations of the same order of magnitude ($\Theta/N_A a_{ex} \sim 1$ μmol m^{-2}) as those reported in the literature [17].

4. Summary

As a preliminary contribution to the study of the ion transfer across phospholipid monolayers formed at the interface between two immiscible solutions, we have modelled the state of the adsorbed monolayer using two simple molecular approaches for the phospholipid adsorption and surface pressure–molecular area isotherms. These theoretical approaches are modellistic in the sense that they invoke extrathermodynamic concepts such as a 'lattice of sites' for which surface tension decreases because of a 'mixing process' and a '2D molecular gas' of phospholipids with 'translational kinetic energies' to explain the observed surface pressure [18]. The molecular parameters introduced in the models have been assigned reasonable values and the theoretical results have been compared qualitatively with experimental data. Despite their simplicity and different physical nature, both models appear to predict correctly the typical order of magnitude values observed for the surface concentration and pressure of phospholipid monolayers. Also, they reproduce some of the qualitative features shown by the experimental isotherms for not too high phospholipid surface concentrations. Given the considerable uncertainties in both the monolayer physical structure and the molecular parameters used, a quantitative comparison between

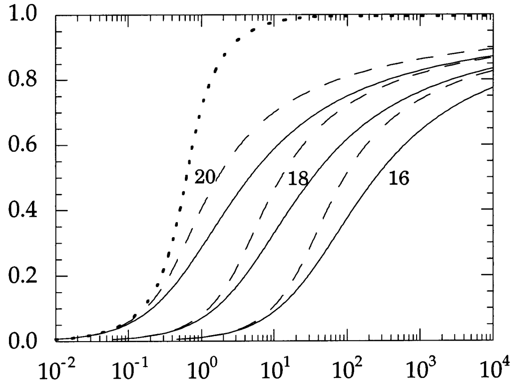

Fig. 5. Adsorption isotherms calculated from Eq. (19) with $u_0/kT = 0$ (solid line) and $u_0/kT = 2$ (dashed line), and the values of the ratio u_{ads}/kT shown in the figure. The dotted line is intended to represent a Frumkin-like isotherm and has been computed from Eq. (19) with $u_0/kT = 2$, $u_{ads}/kT = 20$ and omitting the factor $\exp(\Theta/1-\Theta)$ in the left hand side of this equation.

the results of the two models and experiments is not warranted at this preliminary stage.

Acknowledgements

Financial support from the European Union (Training and Mobility of Researchers programme, Project No. CHRX-CT96-0078) and the DGICYT (Project No. PB95-0018) are gratefully acknowledged.

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