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ION SORPTION AND THE POTENTIAL PROFILE NEAR A MODEL LECITHIN MEMBRANE

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SUMMARY

1. The Poisson–Boltzmann equation is numerically solved for conditions approximating the surface of a lecithin membrane. The Debye–Hückel approximation is not used.

2. It is shown that potentials due to fixed dipole membranes may be large, with maximum field intensity and range comparable to those for fixed charge membranes.

3. The variation of potential, electric field, range of potential and adsorbed charge with electrolyte concentration and type is presented and compared with some published data.

INTRODUCTION

Lipid membranes[1] have been studied intensively in the last 8 years as simplified model systems for the cell membrane. Many of the phospholipids, which are common components of biological[2] and artificial[1] membranes, terminate in a hydrophilic group which has a permanent dipole moment. The behaviour of membrane- (or electrode-) solution interfaces with fixed net charge is relatively well understood[3,4], but the case of fixed dipoles has not received the same attention.

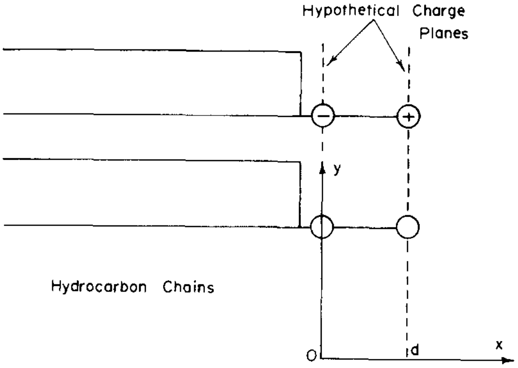
Considerations of stability suggest[5] that lipid membranes should have relatively low net surface charge densities; the behaviour of a membrane–solution interface with fixed dipoles is thus of some interest. Hanai *et al.*[6] have considered the potential profile for such an interface, and concluded that the maximum potential was relatively small (of order $2kT/e$, where the symbols have their usual meaning). However, their conclusion was based on a derivation which assumed $V < kT/e$; the present work avoids this approximation.

Calculations for dipole arrays which do not include the effects of counterions and of the dielectric constant of the aqueous medium[7,8,37,38] cannot supply information relevant to a membrane–solution system.

Some authors have proposed models based in part on potential profiles[9–11] which do not appear to derive from any calculation based on membrane structure. The present work proposes a method whereby potential profiles can be computed, even for systems of some complexity, and examines the degree to which membrane properties can be predicted by this method.

THEORY

The interface between an aqueous solution and a bilayer membrane of a polar phospholipid (such as phosphatidylethanolamine or phosphatidylcholine) may be approximated by a simplified model to facilitate mathematical treatment. In the present work we are concerned only with adsorption of ions to one interface, since interactions across the membrane will be small. The second interface will not be considered. Fig. 1 illustrates the essential features of the hypothetical interface: the fatty acid region $x < 0$ is ion-impermeable; the negative (phosphate) groups are located in and smeared uniformly over the plane $x = 0$, and the positive charge similarly in the plane $x = d$; the aqueous region $x > 0$ is completely permeable to ions. The membrane is taken to have infinite dimensions in the y and z planes, thereby eliminating variation of parameters in other than the x-direction.



X Axis Scaling (d = 5 Å)

Region (Å)	0		5		100		500		3500
Unit Interval (Å)		0.05		0.5		5		100	
Point Number	1		100		290		370		400

Fig. 1. Membrane model. The charge is assumed to be distributed in two planes. The region $x < 0$ is impenetrable to ions, and $x > 0$ is fully penetrable.

In the absence of ions there will be a potential due to the charge planes:

$$\begin{aligned} V_0(x) &= -\frac{4\pi}{\varepsilon A} fe(d-x) & 0 \leqslant x < d \\ V_0(x) &= 0 & x \geqslant d \end{aligned} \tag{1}$$

where ε is the permittivity of the medium, f is the fractional ionisation of the dipole charges (assumed equal, since we are considering the case of zero net charge), and A is the area per phospholipid molecule.

The ions in solution will tend to redistribute in response to this potential, the concentration of an ion i of valence $\delta_i n_i$ ($\delta_i = +1$ or -1) being given by the Boltzmann distribution function

$$\rho_i(x) = \delta_i n_i \rho_i(\infty) \exp(\delta_i n_i e V(x)/kT) \tag{2}$$

for any point x at potential V, when the concentration of ion i in the subsolution is $\rho_i(\infty)$.

The redistributed charge will lead to another component of the potential given by Gauss' law:

$$V_1(x) = -\frac{4\pi}{\varepsilon}\int_{\infty}^{x} dx \int_{\infty}^{x} \rho(x)dx \tag{3}$$

The usual procedure[6,12] is to solve the resulting equation (the Poisson–Boltzmann equation) analytically, for a uni–univalent electrolyte, using the assumption $eV < kT$. However, there is reason to expect the potential in this case to exceed the thermal scale potential kT/e (27 mV at room temperature). Indeed in any system for which $eV < kT$ the electric potential will not significantly influence membrane processes. Consequently the use of a numerical technique is required.

Attempted iterative solution of the equations led to failure to obtain convergence. However, a modified technique was devised, which arrives at a solution by a pseudo-simulation of diffusion of ions into the membrane vicinity. Essentially

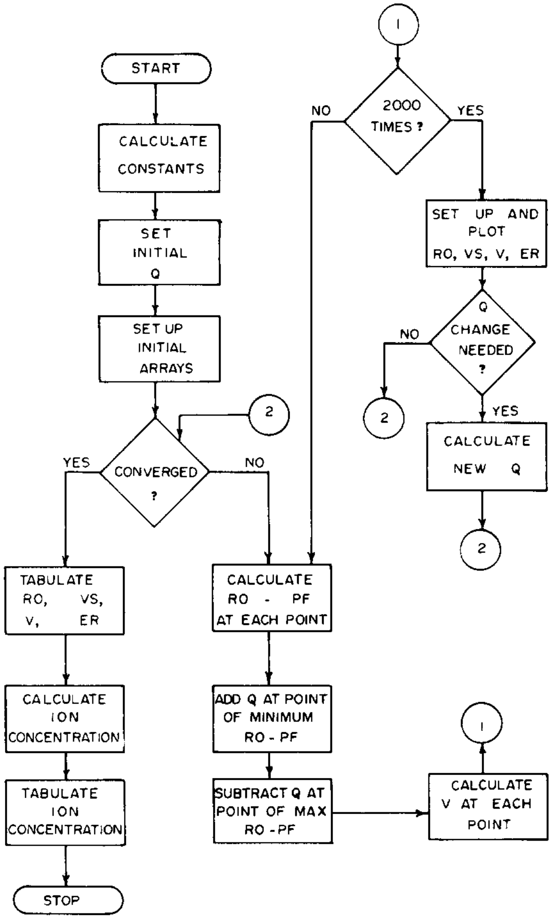


Fig. 2. Flow sheet of the computer program. The parameters are *RO*, total charge sorbed; *VS*, screening potential due to charge; *V*, total potential at each point; *PF*, 'expected' charge calculated from partition function, *ER* = *RO* – *PF*; *Q*, current unit of charge for addition.

this involves starting with the dipoles only, and adding charge pairs (which conveniently satisfies the macroscopic electroneutrality condition). For each charge addition the partition function for each ion (Eqn. 2) and the potential are calculated for a large number of points, and the positive and negative charges are added at the points which respectively have the largest positive and negative discrepancy between 'expected' charge and charge already added (*i.e.* maximum and minimum values of $PF-RO$, see Fig. 2). This technique has the further merit that it can be used for the case of mixed electrolytes.

The calculation was performed on an IBM 360/65 computer; the program is illustrated in Fig. 2. After each block of 2000 charge pairs has been added the charge density, potential and residual error functions are plotted. This was found to be necessary for diagnostic purposes, since it proved quite complex to obtain convergence within a reasonable time. Convergence time and accuracy were greatly improved by starting with a suitable large value for the added charge units, and reducing this one or more times as the solution is approached. The methods of selection of the charge unit value, and of determining the optimum stage at which to reduce this value, are not indicated as they are complex and empirical. In general the values used affected accuracy and execution time, but not the final result.

During the initial stages of each calculation more charge may be added at some points than is warranted in the final solution. This is automatically accounted for, since charge of opposite sign is subsequently added at such points; only the net charge is considered during this computation.

To achieve sufficient accuracy, the region $0 < x < d$ was divided into 100 parts, represented as points at which the parameters are calculated. An expanded scale was used for $x > d$ (where the potential and charge density vary more slowly). The calculation does not converge correctly if charge is added at the most extreme point, so three stages of scale expansion were necessary (see Fig. 1), to give a maximum range of 3500 Å with a total of only 400 points. In no case considered is the charge density significant (within residual error) at this range. The residual error is typically less than $2 \cdot 10^{-4}$ of the maximum charge density.

From the final solution the concentration of each ion was calculated for each point.

Assumptions

The assumptions on which this calculation is based require detailed consideration to clarify the interpretation of the results.

There is substantial evidence[13–15] to support a value of approximately 50 Å^2 for the limiting area of a lecithin molecule with saturated hydrocarbon chains. Similarly, the spacing between the charge centres of an extended polar group may be taken as $d = 5$ Å (refs. 16, 17).

The degree of ionization of the charged groups will depend substantially on the pH and ionic composition of the solution[5]. Thus the ionization is best described by assigning a pK_a value to each group[18]; but this approach does not permit solution by the present technique, as the charges (both fixed and counterionic) can no longer be assumed equal. Fortunately there is some evidence[5,19] that both positive and negative groups will be fairly strongly ionized, particularly in the case of phosphatidylcholine. The value assumed (80 % unless otherwise stated) should be conservative in this case.

The orientation of the polar groups is a matter of controversy. Alignments both perpendicular[20,21] and parallel[22,23] to the membrane have been supported. A distribution of orientations[16,24] appears a more realistic proposal. In this case the mean spacing between charge planes could be a function of the quantity of charge adsorbed[21,23]. However, for simplicity full extension in the perpendicular direction has been assumed; this is probably a reasonable approximation after addition of ions, which reduce the electrostatic free energy of this configuration substantially. One of the best indications of the actual orientation is perhaps the degree to which membranes approximate the behaviour predicted on this basis.

It is usual in double-layer calculations for charged surfaces to apply a correction (the STERN[25] correction) representing the inability of ions to approach the surface to within an arbitrarily small distance, due to their finite size. In the present case the surface is not very well defined, but will presumably correspond substantially to the interface between the glycerol backbone and the aqueous medium, which is approximately 1 Å to the left (Fig. 1) of the plane of the phosphate groups. This is of the same order as the radii* of Na^+, K^+ and Ca^{2+}, suggesting that the problem can be conveniently simplified by taking the plane of closest approach at $x = 0$ as shown.

Due to avoidance of the Debye-Hückel approximation, the calculated charge density at points of high potential ($|V| > kT/e$) may be very large. To eliminate physically ridiculous values of the charge density a maximum was established, arbitrarily taken as 25 M for univalent ion. This is of the order of half the concentration of atoms in solid Na. It is clearly a dubious procedure to use the term 'concentration' when discussing dimensions < 1 Å, especially when it is very difficult to define a boundary for containment of the charge. This question will be discussed later; it will be established that for most purposes the maximum value assumed is not critical over a wide range.

The value assumed for the dielectric constant of the aqueous medium was 40. This is approximately half the value for water near room temperature, but due to saturation may be as much as double the value applicable in the high field region between the charge planes[26,27]. The compromise value was selected to avoid the added complication of using a dielectric constant which was a function of position (or of potential gradient). The major effect of this compromise is to substantially underestimate the initial potential due to the charge planes. This error is increased somewhat due to the partial (up to 25 %) filling of the region $0 < x < d$ by the methylene groups (*cf.* the calculation by SALEM[27] for lipid–protein interaction), which at fixed orientation will have a low dielectric constant. The error due to the underestimate of dielectric constant for $x > d$ is discussed later.

The consequences of finite size of a dipole array have been examined[28,8]. However, if the dielectric constant of the medium and the screening effect of the ions in solution are properly taken into account, finite array size does not have a significant effect over the dimensions of interest. Thus the calculation for a membrane infinitely

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* Although these ions will presumably retain most or all of their first hydration shells, the energy associated with the position of an ion in the electric field is much greater than the energy of rearrangement of the water molecules about the ion. Thus the water should not impede close association of the ion with the phosphate groups and the glycerol backbone, and the ion will pack as though not hydrated.

extended in the y-z plane should be applicable to any system which can be approximated as planar over dimensions $> 10^{-6}$ cm.

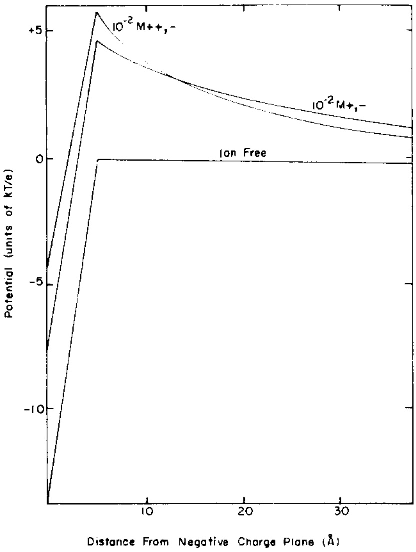
The assumption that the charges are smeared over two planes is necessary to reduce the problem to a sufficient degree of simplicity to permit computation. However, since the interdipole spacing is of the same order as the zwitterion separation within a dipole, this is evidently a poor approximation. The electric field components E_y and E_z will in fact be substantial in the vicinity of the dipoles. Furthermore, even to consider the fixed charges as points would be clearly erroneous, as the zwitterion radii sum to approx. 5 Å (ref. 27). Infinite divisibility of the ions, and distribution without regard to ion dimensions or stereochemistry of the polar groups are also substantial approximations.

However, the major factor determining the potential near the membrane is the distribution of negative charge for $x > d$. At a distance from the dipoles the above approximations are quite good. Divisibility of the ions can be approximated by spatial redistribution of ions of opposite sign, in contrast to the dipole region where effectively only ions of one sign will be present at a given value of x.

As a consequence of the above approximations the results are at best related to the probability of finding an ion as a function of distance from the membrane. This should be sufficient to achieve the stated purpose.

RESULTS

The potential as a function of distance from the negative charge plane is shown in Fig. 3 for two different electrolytes, and for the ion-free case. The latter is shown only to indicate the initial condition for the calculation, since even the best distilled



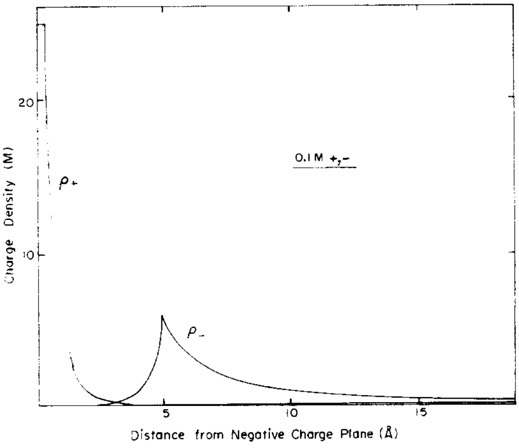


Fig. 3. Potential profile for two electrolytes compared with the initial potential. The electrolytes are 10 mM bi-univalent and uni-univalent, illustrating the greater screening by the former.

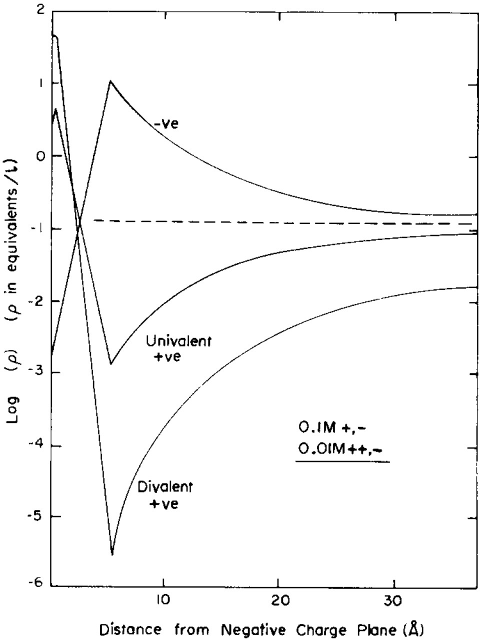
Fig. 4. A typical calculated charge density profile, showing separately the sorbed positive and negative charges.

water will contain sufficient ions (including H^+ and OH^-) to substantially modify the potential. The greater screening effect of the divalent cation is clearly demonstrated; in this case the magnitude of the maximum positive potential has become greater than that of the negative potential.

A calculated ion density for a 0.1 M uni-univalent electrolyte is shown in Fig. 4. Points of interest are the maximum charge density cutting off the very steep rise near $x = 0$, the lower charge density at $x = d$, and the virtual exclusion of anion from the vicinity of the negative charge plane and conversely for the cation. The ratio of positive to negative charge is shown more clearly in Fig. 5, which illustrates a typical result for a mixed electrolyte, with charge density plotted on a logarithmic scale. The reduced density of positive univalent ions near $x = 0$ is a consequence of competition from the divalent ion. Despite a 10-fold lower concentration in the solution, the divalent cation is predominant in regions of potential lower than -62 mV ($-2.3\ kT/e$).

Calculations were made for a variety of electrolytes over the range of interest for various aspects of membrane studies. The results are summarized in Figs. 6–10. The mixed electrolytes are composed of the indicated ion at various concentrations in a 0.1 M uni-univalent salt solution (represented as "A"). In these cases the curves tend at low additive concentration to an asymptote shown as a dashed line.

The maximum potential is defined as the potential at $x = d$; similarly the



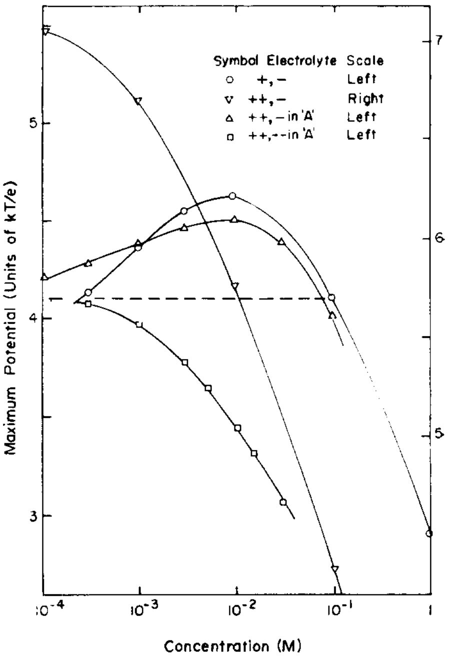
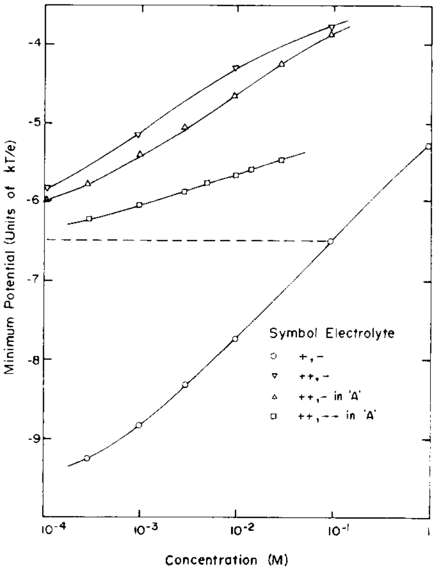


Fig. 5. Charge density profile for a mixed electrolyte. The charge density scale is logarithmic to indicate more clearly the large charge concentration ratios between anions and cations at points of large potential.

Fig. 6. Potential at $x = d$ *vs.* electrolyte composition. 'A' is 0.1 M uni-univalent electrolyte. ○, is +, − (left hand scale); ▽, is 2 +, − (right hand scale); △, is 2 +, − in 'A' (left hand scale); □, is 2 +, 2 − in 'A' (left hand scale).

minimum potential is at $x = 0$. The range is arbitrarily taken as the distance from $x = d$ at which the potential is half maximum. Since the potential does not follow any simple function, the range as defined does not accurately indicate the behaviour at any other point, but is merely a useful basis for comparison of the influence of



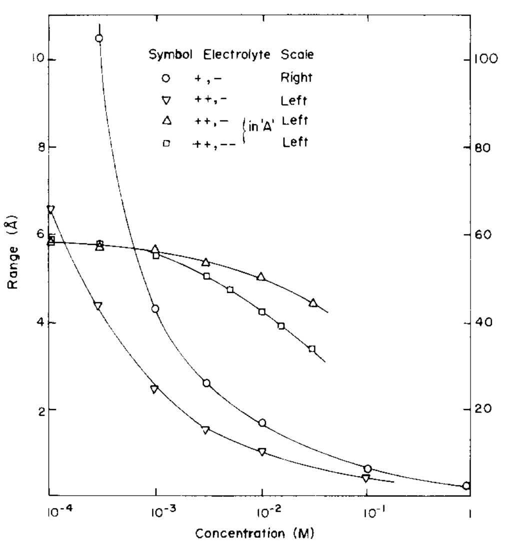


Fig. 7. Potential at $x = 0$ *vs.* electrolyte composition. 'A' is 0.1 M uni-univalent electrolyte. ○, +, −; ▽, 2 +, −; △, 2 +, − in 'A'; □, 2 +, 2 − in 'A'.

Fig. 8. Dependence of the range of the potential on electrolyte composition. Range is defined as the distance in Å from $x = d$ for the potential to reduce by 50%.

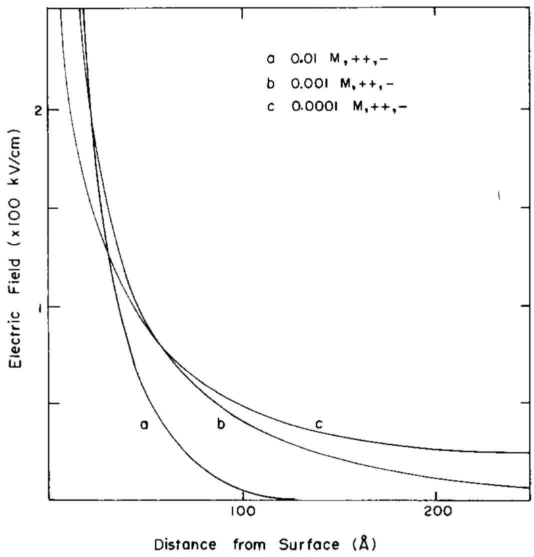
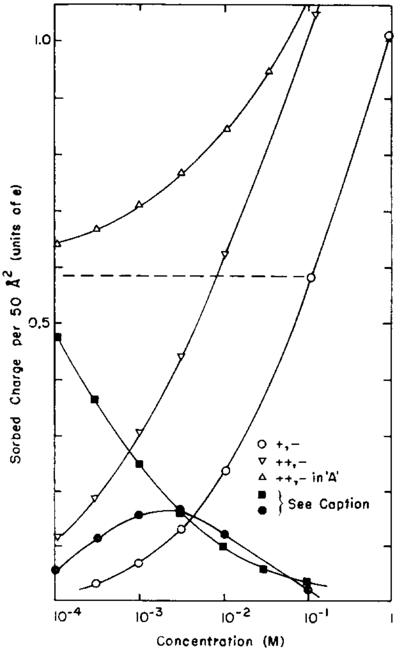


Fig. 9. Variation of electric field intensity with distance from the positive charges ($x = d$) for three bi-univalent electrolytes.

various electrolytes. The long-range behaviour is better represented in Fig. 9, which shows the electric field as a function of distance from the positive charge plane, for three concentrations of bi-univalent salt. It is evident that low concentrations may produce substantial fields up to several hundred Å from the membrane.

The sorbed charge (Fig. 10) is defined as the total positive charge in the region of negative potential, less the quantity in an equal volume of bulk solution. Also shown in this figure are the sorbed charge attributable to the univalent cation in a mixed electrolyte, and the extra bivalent cation sorbed due to the presence of the uni-univalent salt.



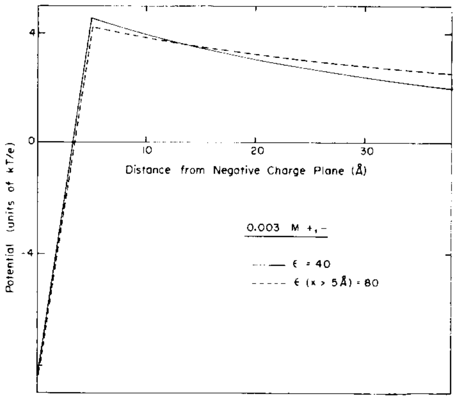


Fig. 10. Total sorbed positive charge *vs.* electrolyte composition. 'A' is 0.1 M uni-univalent electrolyte. Filled squares, sorbed univalent cation from 'A' *plus* indicated concentration of bi-univalent electrolyte; filled circles, extra bivalent cation sorbed due to the addition of 0.1 M uni-univalent electrolyte to the indicated concentration of bi-univalent electrolyte.

Fig. 11. Influence of the dielectric constant, ε, of the subsolution ($x > 5$ Å) on the potential profile.

DISCUSSION

The results in Figs. 3–10 demonstrate that ion–dipole interactions can be expected to control in a quite complex manner the local potential profile and the sorption of ions (particularly cations) for subsolution concentrations in the physiological range. Since lecithin membranes are studied under a wide variety of conditions it is unlikely that these particular calculations will be directly relevant to many cases of interest. Their usefulness lies in indicating the type of behaviour that can be predicted from this model, and establishing the limitations of the model.

Some of the limitations due to mathematical idealisations have been discussed in an earlier section. It is possible to determine the sensitivity of the results to some of these assumptions by performing calculations for different conditions.

A more realistic distribution of dielectric constant with distance from the membrane is $\varepsilon = 40$ (see earlier) for $0 < x < 5$ Å and $\varepsilon = 80$ (the value for bulk water[29]) for $5 \text{ Å} < x < \infty$. A typical potential profile for this regime is shown in Fig. 11 compared with the corresponding simpler case ($\varepsilon = 40$, $0 < x < \infty$) in the charge plane region. The maximum and minimum potentials are little affected, but the range is almost doubled. This suggests that the calculated range (Fig. 8) is conservatively small, but that other parameters are insensitive to variation of the assumed dielectric constant in the region $x > 5$ Å. This lack of sensitivity reflects the negative feedback nature of the sorption phenomenon, together with the large "gain" provided by the exponential factor (Eqn. 2).

Similarly the potentials, the sorbed charge and the range are not greatly influenced by variation in the assumed maximum charge density (Fig. 12). The case illustrated is the most critical in the range computed; the sensitivity will be much greater for the reduced area model discussed later, but in this case a less arbitrary value of the maximum charge density is available.

In real membranes a number of further factors must be considered. Phospholipid bilayer membranes frequently contain cholesterol and hydrocarbon in addition to one or more phospholipid components. The position of the cholesterol and hydrocarbon is probably simply interstitial, promoting closer packing of the hydrocarbon interior, but with increased area per phospholipid head group[15]. Many of the common head groups are not dipoles, and few studies are restricted to those with only dipole components.

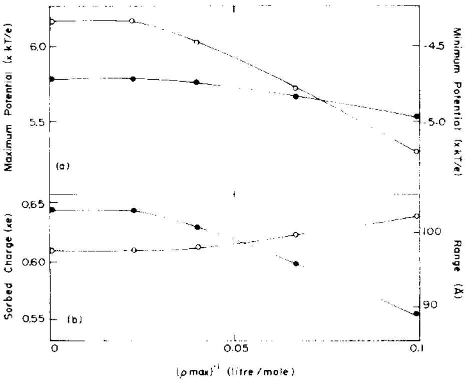


Fig. 12. Sensitivity of the potential, sorbed charge and range to the assumed maximum charge density. Solid symbols refer to the left hand scales, and open symbols to the right. The value used for all calculations (unless otherwise stated) is $1/\rho_{\max} = 0.04$.

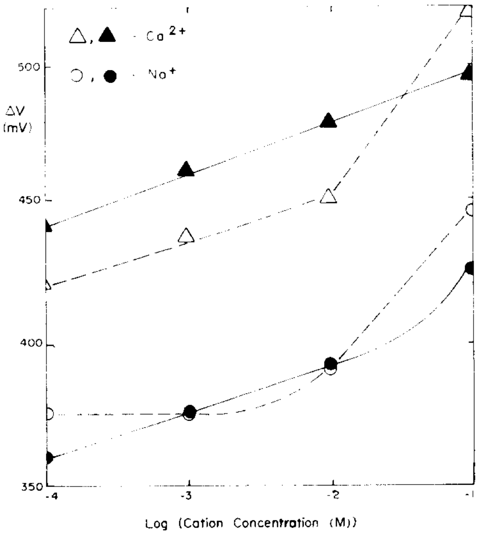


Fig. 13. Comparison of published data for the surface potential of dipalmitoyl lecithin monolayers (from ref. 21, open symbols) with the equivalent calculated values (solid symbols), assuming an internal dipole potential $V_0 = 600$ mV.

Monolayer studies indicate that the surface pressure of the film can influence the surface potential[21] and ion sorption[19]. Furthermore, the surface pressure or area per molecule may be modified in turn by the presence of ions, particularly polyvalent cations[19,30,31]. While this may not cause very large changes in the area per molecule it is possible that small changes could have a profound influence if for any reason head group spacing is critical. For example, the layer of water near the membranes will certainly be highly ordered (ice-like), and the lattice dimensions of ice are comparable to the head group spacing, as are the dimensions of hydrated ions. Steric factors have been neglected throughout, but could conceivably be of paramount importance in some cases (*e.g.* see discussion of the role of cholesterol by Vandenheuvel[15] and suggestions by Shah and Schulman[21,14] for membrane–Ca^{2+} interaction). One aspect of this problem is considered in more detail below.

Two properties of lipid monolayers which have received considerable attention, and which should be reasonably comparable to the corresponding bilayer properties, are ion sorption (detected via enhanced β-emission from $^{45}Ca^{2+}$ in the subsolution[17,13,19,28,32])* and surface potential (usually measured with a radioactive electrode[14,21] or a vibrating plate electrometer[30]).

Comparison with this data is of course subject to the limitation that a monolayer cannot be equated with half a bilayer[19]; in fact the molecular organization may be quite different. In particular, the surface energy of the internal fatty acid–fatty acid interface(s) is the basis of the stability of the bilayer structure[33]. A further factor for consideration, in interpreting the surface potential measurements, is the possible contribution from polar and polarizable bonds in the glycerol backbone and fatty acid chains[14]; this contribution may be quite large, so that the absolute magnitude of measured potentials will not relate directly to the ion sorption component. However, changes in surface potential with variation of electrolyte concentration should be largely attributable to sorption of ions and so can be expected to compare with potential changes calculated in this work.

The surface potential of lipid monolayers has been the subject of a number of experimental studies. In most cases, the data are such that comparison with the present work is not possible. However, Shah and Schulman[21] have measured the surface potential of synthetic phosphatidyl(dipalmitoyl)choline at 50 Å² per molecule, pH 5.6 and 25°, as a function of the concentration of NaCl and $CaCl_2$ in the subsolution.

Their data are compared in Fig. 13 with the calculated values of

$$\Delta V = V(0) - V(\infty) + V_0 \qquad (4)$$

where V_0 (arbitrarily taken as + 600 mV for comparison) represents the contribution from internal dipoles mentioned above. The value of V_0 required to superimpose the curves has the correct sign and order of magnitude. Apparently the general trends and the difference between $CaCl_2$ and NaCl are adequately represented by the model, although the experimental lines show more curvature.

Ion sorption can be profoundly influenced by pH (ref. 28), lipid composition[13],

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* It has been suggested[21] that the depletion of cations over the region of positive potential may lead to a substantial underestimate of sorbed Ca^{2+} in measurements by this method. This is not supported by the present calculation; in all cases the depletion was less than 10% of the sorption.

degree of saturation of the fatty acid chains[34,14], and the surface area per lipid molecule[19]. In most studies, one or more of these variables is unknown, or outside the range of the present work.

KIMIZUKA AND KOKETSU[32] have studied adsorption of $^{45}Ca^{2+}$ onto dipalmitoyl lecithin monolayers at 60 Å^2 per molecule. This work should be comparable with the present calculations, although the higher area per molecule would give rise to a lower initial potential gradient due to the dipoles. However, their measurements indicate sorption of one Ca^{2+} per two lipid molecules for concentrations in the subsolution greater than 1 mM. This contrasts with a calculated value of 0.3 Ca^{2+} per two lipid molecules at this concentration (Fig. 10).

This discrepancy illustrates a substantial limitation of the method of calculation; it is a poor approximation to regard the membrane as a fixed structure when considering sorption of polyvalent ions. The point is further emphasized by the prediction that addition of 100 mM NaCl should enhance sorption of Ca^{2+} over the concentration range 0.1–100 mM (Fig. 10), contrasted with the well-documented phenomenon of Ca^{2+} displacement by NaCl[13, 19, 28]. SHAH AND SCHULMAN[34] have proposed that, provided the monolayer is in a liquid state, the lipid molecules rearrange in order to share a Ca^{2+} between two adjacent phosphate groups. The initial potential derived using the charge plane model is inappropriate for a membrane with such dipole pair ordering, or indeed for any non-uniform distribution of dipoles.

It is possible to adapt the calculation to some degree to include this concept. The local field of two polar groups, brought into close proximity by a Ca^{2+}, can be represented simply by the field for some reduced value of the area per lipid molecule in terms of the original model. This should in fact be a better approximation for the region between the adjacent polar groups, due to the greater ratio of "charge plane" separation to dipole spacing (Fig. 14).

The reason for the observed[32] maximum Ca^{2+} to lipid molecule ratio of 1:2 is then quite clear. The electric field (and thus the potential) in the more open areas between pairs will be greatly reduced, so that sorption of ions in these areas will be relatively insignificant. Thus a ratio greater than 1:2 requires more than one Ca^{2+} between some of the dipole pairs. In the available volume, two ions would be very close or in contact, leading to prohibitively large repulsion forces. Consideration of

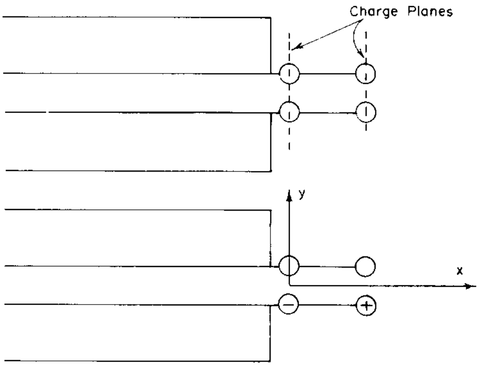

Fig. 14. Modified model using local 'charge planes' of reduced area to approximate the electric field due to dipoles paired by sorption of Ca^{2+}.

the local potential profile for a region with two Ca^{2+} leads also to a small negative potential at the sorption site, which is energetically unfavourable.

Calculations using a reduced area per dipole to determine the initial potential indicate that one Ca^{2+} is sorbed per two lipid molecules at 1 mM subsolution concentration for a local area per dipole of 30 Å². Of course the above mechanism limiting the sorption to this value is in no way implicit in the mathematical treatment, which may add fractions of an ion. Consequently the predicted concentration increases for higher subsolution concentrations (Fig. 15).

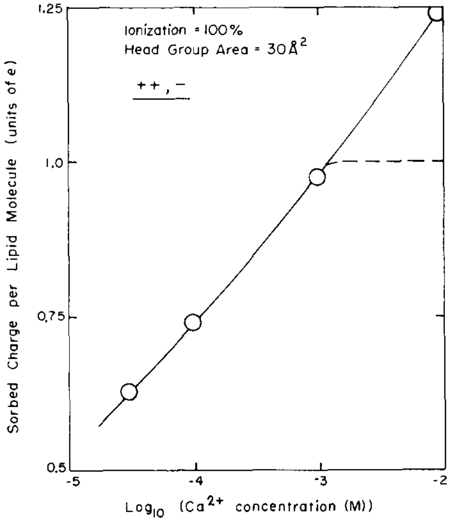

Fig. 15. Predicted sorbed Ca^{2+} *vs.* concentration using the reduced head group area model. The sorbed charge has the correct magnitude at 1 mM for a reasonable value of the effective area, but does not limit at this value in contrast with experimental results.

Distribution of one Ca^{2+} over a volume defined by the high field area (30 Å²), within the favourable potential region, leads to a maximum concentration of 12.5 M (the value used in the above computation), which lies near one extreme of the range evaluated in Fig. 12. The arbitrary nature of the boundaries has of course become even more evident in this case. However, it is of some significance to express the degree of sorption as a local concentration, since both the above value, and the value assumed for the earlier calculations (25 M) greatly exceed the usual water solubilities of salts of Ca and Na (solubility of NaCl at 0° is 6.1 M (ref. 35)).

The solubility of a salt is dependent on the solubilities of the individual ions. In normal circumstances solution of a salt requires that the anions and cations be distributed in the same volume; *i.e.* a uni-univalent salt will have anions and cations present in equimolar concentrations. We have for NaCl the solubility product

$$[Na^+]\,[Cl^-] = 6.1^2 \tag{5a}$$

$$\text{where } [Na^+] = [Cl^-] \tag{5b}$$

Fig. 4 clearly illustrates that this situation does not obtain at a membrane interface, where the solution of a quantity of Na^+ in a small volume at the surface entails the solution of an equal quantity of Cl^- distributed in a much larger volume. Eqn. 5a still applies, if it is assumed that the concentration of each ion is constant over a defined volume (for a rigorous treatment a much more complex calculation involving the energy of the whole ion distribution is required). For example, if the Cl^- is assumed to be confined to a region where its concentration is only 3 M, the Na^+ solubility will be $[Na^+] = 6.1^2/3.0 = 12.4$ M.

The approximation also neglects the energies of interaction both between ions and with the dipole potential, which will be considerable. However, the example serves to show that the maximum concentration of an ion near a membrane is not limited to the solubility of the salt used. This property has also been derived from measurements of lag time for diffusion of Na^+ through membranes[36].

The calculation for reduced polar group area involves use of $A = 30$ Å² for $x < 5$ Å whereas evidently $A = 50$ Å² is required for large x, where the field must be uniform. The arrangement used was to distribute the field (and charge) uniformly in 30 Å² for $x < 5$ Å and in 50 Å² for $x > 5$ Å. The results are quite insensitive to this approximation and discontinuity; indeed, the $A = 30$ Å² region may be extended to $x = \infty$ without substantial effects. This result suggests that models exhibiting inhomogeneity in the y–z plane may be calculable using an analogous technique, with different regions coupled to a common subsolution *via* such discontinuities. This method is currently under investigation.

In conclusion, the model appears to present a more valid and useful approach to ion–membrane interactions than does the 'ion binding' concept, although the latter can qualitatively include steric factors which are difficult to incorporate in the distributed-charge model. The calculation indicates that the results of ion–membrane interaction can be quite complex, even with a very simple model, and that intuitive conceptions of the potential profile and ion sorption may be in error. Some features of the model suggest that modification to more adequately account for dipole pairing and ion competition effects should be possible.

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