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Bending of charged flexible membranes due to the presence of macroions

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Abstract. We investigate the bending of flexible charged membranes due to the presence of rigid rodlike macroions in the framework of the Debye-Hückel approximation. When the macroions are fixed in space at some distance from the bilayer the membrane bends towards them; we calculate the exact deformation profile. On the other hand a macroion which is adsorbed on the membrane causes a deflection of the bilayer. Finally, we consider swollen lamellar polyanion/charged-lipid complexes where the macroions are intercalated between charged lipid bilayers. We predict the occurrence of a double adsorption (pinching effect) of the macroion for sufficiently flexible membranes.

PACS. 68.10.-m Fluid surfaces and fluid-fluid interfaces – 64.70.Md Transitions in liquid crystals – 82.70.Kj Emulsions and suspensions

1 Introduction

Recent experimental studies have reported the self-assembly of biological polyanions (DNA, polypeptides...) and cationic lipids into lamellar complexes with the macroions intercalated between the charged lipid bilayers [1,2]. An understanding of the interaction between the macroions and the charged membranes is of much current interest since cationic lipids are used as non-virial vectors for DNA and protein delivery (a discussion of the different strategies for human gene transfer can be found in Ref. [3]).

The present theoretical studies focus on the case of condensed lamellar DNA/lipid complexes where the water gap between neighboring bilayers is of the same order as the diameter of the DNA molecule and where the DNA form a two-dimensional smectic array. Dan explains some experimental findings on these complexes by identifying two mechanisms which determine the DNA spacing, namely the electrostatic repulsion between the rods as well as the perturbation of the lipid bilayers near to the DNA [4]. Bruinsma and Mashl calculate more explicitly the repulsive electrostatic force between the DNA rods by assuming that the cationic lipids (which are mixed with neutral ones) act as a two-dimensional gas of "counter-lipids" [5].

Experiments on both DNA, and polypeptide/cationic-lipid complexes, have been performed where the relative amounts of neutral lipids were varied, thereby changing the charge density of the bilayer [1,2]. For the DNA complexes investigated by Rädler *et al.* [1] it was found that the distance d_R between the rods increases strongly with decreasing charge density of the bilayer whereas the membrane spacing d increases only slightly. On the other hand in a recent study on polypeptide/cationic-lipid complexes it was shown by Subramanian *et al.* [2] that d increases significantly upon dilution of the charged lipids. For high lipid dilution it was found that the water gap between the membranes is much larger than the diameter of the macroions. Compared to the densely packed system observed by Rädler *et al.* these swollen lamellar structures have more degrees of freedom due to the presence of much free space. A given macroion may be adsorbed on either membrane and may cause its bending near the adsorption side. Alternatively, a double adsorption may occur: the macroion may be pinched between both neighboring membranes which bend towards it. Although the persistence length of DNA is much larger than that of polypeptide chains, experiments indicate that the difference in the dilution behaviors of the systems investigated in references [1,2] is mainly due to the different flexibilities of the bilayers; the membranes in reference [2] are roughly two times as flexible.

There exist many studies on the problem of the bending of charged bilayers where the electrostatic contribution to the bending modulus is calculated for different regimes of the membrane surface charge density and aqueous electrolyte strength [6–13]. On the other hand, there is – to our best knowledge – no study on the membrane bending due to the presence of polyions. We restrict the current study to the case where salt is present so that the electrostatic interaction is screened (Debye-Hückel regime). We note that the salt-free case is much more involved due to the non-linearity of the problem (Poisson-Boltzmann

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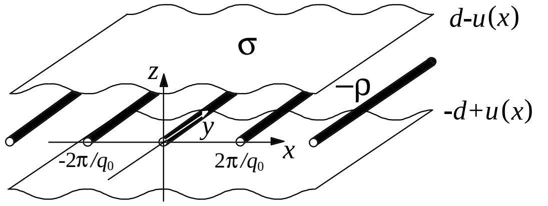

Fig. 1. A regular lattice of polyanions between two cationic membranes. Schematically depicted is the deformation of the membranes.

equation); a discussion of the electrical potential around a rod embedded in a *flat* membrane can be found in reference [14].

In the next section we discuss how the membrane is deformed due to the presence of macroions fixed in space at some distance from the membrane; in the strong-electrolyte limit this problem can be calculated rigorously. In Section 3 we discuss how an adsorbed macroion affects the membrane conformation. In Section 4 we consider lamellar polyion/cationic-lipid complex and discuss the possibility of a pinching effect. We close the paper in Section 5 with a summary of conclusions.

2 Polyions fixed in space near a membrane

In this section we calculate how charged, say cationic membranes are deformed due to the presence of rodlike polyanions which are *fixed* in space. We consider two charged membranes which are parallel to the XY-plane and have the mean positions $z = \pm d$ (see Fig. 1). These membranes may represent two neighboring layers in a stack of membranes in the lamellar state or they may belong to two vesicles in near contact. Each membrane consists of a bilayer of cationic surfactants and carries the uniform (fixed) charge density $\sigma/2$ on each side. We impose the boundary condition $\partial\Phi/\partial n|_{S_M} = 2\pi\sigma/\varepsilon$ on the electrical potential Φ in between the two membranes; n denotes the inward normal at S_M, the inner surface of the membrane. This boundary condition assumes implicitly the independence of the inner and outer potentials, *i.e.*, the membrane is taken to be opaque. This is a reasonable approximation as long as the energy stored in the electrical field within the membrane is negligible; one can show that this is the case as long as the thickness d_M of the membrane fulfills $d_M \gg \varepsilon_L/\varepsilon\kappa$ (ε: permittivity of water, ε_L: permittivity of the lipid within each membrane) [6,8,11]. Typically $\varepsilon/\varepsilon_L \approx 40$ and $d_M \approx 20$ Å so that this is here a reasonable assumption. In the following we assume the presence of polyanions between the membranes; they are modelled as rigid rods with radius r_0 and length L with $L \gg d \gg r_0$. The surface charge density of the cylindrical macroions is denoted by $-\sigma_R$ and their charge density per length by $-\rho = -2\pi r_0 \sigma_R$. We assume that the rods are located at the midplane of the two membranes, *i.e.* at $z = 0$ and that their axes point towards the Y-direction. Furthermore they form a regular lattice with the wavevector q_0 (*cf.* Fig. 1). As we will see, this simple geometry allows a rigorous calculation of the problem (for small deformations); furthermore it resembles in some cases the typical arrangement in polyanion/cationic-lipid complexes (see Sect. 4).

The polyions will induce a bending of the flexible membranes towards them; we denote the (mean) position of the upper and the lower bilayer by $d - u(x)$ and $-d + u(x)$, respectively. Assuming that the displacement $u(x)$ has the same periodicity as the underlying lattice of macroions, *i.e.* $u(x + 2\pi/q_0) = u(x)$, we can express $u(x)$ by the following Fourier series:

$$u(x) = \sum_{n=1}^{\infty} a_n \cos(nq_0 x). \tag{1}$$

Due to the strong screening the amplitudes of the different modes are very small so that they are (nearly) decoupled. Furthermore it can be shown that undulations with other wave vectors (for instance $q_0/2$) are energetically not favorable.

The free energy F per unit area has the form

$$F = F_{bend} + F_{el} \tag{2}$$

where F_{el} denotes the electrostatic contribution and F_{bend} is the cost in curvature energy $k_c\left(\nabla^2 u\right)^2$ of the *two* membranes with k_c being the bending rigidity. F_{bend} may be rewritten as [15]

$$F_{bend} = k_c \sum_n a_n^2 n^4 q_0^4. \tag{3}$$

(In Eq. (2) the surface tension is explicitly taken to be zero).

In the following we assume a high concentration of salt so that we can use the Debye-Hückel approximation in which the Poisson-Boltzmann equation for the electric potential Φ becomes linear: $\Delta\Phi = \kappa^2\Phi$. Here the Debye screening length κ^{-1} is given by $\kappa^{-1} = (8\pi n_\infty l_B)^{-1/2}$ where n_∞ is the bulk electrolyte concentration and $l_B = e^2/\varepsilon T$ denotes the Bjerrum length (T is the temperature in units of the Boltzmann constant k_B and e is the electronic unit charge); in an aqueous solution $\varepsilon \approx 80$ and thus $l_B \approx 7$ Å. Now F_{el} is the sum of the electrostatic contribution and of the translational entropy of the small salt ions. In the Debye-Hückel regime it is given by [16,17]

$$F_{el} = \frac{1}{2A}\int dS\sigma'\Phi \tag{4}$$

where the integration extends over the boundaries of the system having the charge density σ'; A is the corresponding area in the XY-plane. In our problem the boundaries are constituted by the two membranes and by the rods with the charge densities $\sigma' = \sigma/2$ and $\sigma' = -\sigma_R$, respectively. In the following we calculate the potential Φ_M of the two membranes (without the macroions in between); as we will see we can determine F_{el} from Φ_M alone.

In order to calculate Φ_M (up to first order in the amplitudes a_n) we have to solve the Debye-Hückel equation subject to the following two boundary conditions: (i) due to symmetry the Z-component of the field is zero at $z = 0$. (ii) At $\pm d \mp u(x)$ one has $\partial\Phi_M/\partial n = 2\pi\sigma/\varepsilon$. More explicitly, the boundary condition at $z = d - u(x)$ takes the form (neglecting terms of the order a_n^2)

$$-\frac{\partial\Phi_M}{\partial x}\sum_{n=1}^{\infty} a_n n q_0 \sin(nq_0x) + \frac{\partial\Phi_M}{\partial z} = \frac{2\pi\sigma}{\varepsilon}\cdot \qquad (5)$$

Expanding Φ_M in the amplitudes a_n up to first order leads to $\Phi_M = \varphi^{(0)} + \sum_n a_n\varphi^{(n)}$ where each $\varphi^{(n)}$ fulfills the Debye-Hückel equation separately. The $\varphi^{(n)}$ can be expanded in Fourier series $\varphi^{(n)} = \sum_m B_m^{(n)}(z)\cos(mnq_0x)$ and thus $B_m^{(n)}(z) = b_m^{(n)}\cosh(\kappa_{nm}z)$ with $\kappa_{nm} = \sqrt{\kappa^2 + (nmq_0)^2}$. The coefficients $b_m^{(n)}$ follow from the boundary condition and it turns out that only the diagonal terms $b_n^{(n)}$ are non-vanishing. From this procedure it follows that

$$\Phi_M = \frac{2\pi\sigma}{\varepsilon\kappa}\Big(\frac{\cosh(\kappa z)}{\sinh(\kappa d)} + \kappa^2\coth(\kappa d) \times \sum_{n=1}^{\infty} a_n\kappa_n^{-1}\frac{\cosh(\kappa_n z)}{\sinh(\kappa_n d)}\cos(nq_0x)\Big). \qquad (6)$$

Note that due to symmetry $\partial\Phi_M/\partial n|_{S_R} \equiv 0$ for a vanishing radius of the rods, *i.e.* for $r_0 \to 0$ (S_R denotes the surfaces of the rods).

The electrostatic free energy of the system is given by equation (4) and consists here of two parts: the contribution of the membrane-membrane interaction $F_{MM} = \frac{q_0\sigma/2}{4\pi}\int_{S_M} dx\Phi_M$ and the rod-membrane part $F_{MR} = -2\frac{q_0\sigma_R}{4\pi}\int_{S_R} dx\Phi_M$. The prefactor 2 in the expression for F_{MR} accounts for the integration of the potential Φ_R of the rods along the membranes which leads exactly to the same value than the integration of Φ_M along the rods[1].

The membrane-membrane part follows from $F_{MM} = \frac{q_0\sigma}{4\pi}\int_0^{2\pi/q_0} dx\Phi_M(x, d - u(x))$ which leads to

$$F_{MM} = \frac{\pi\sigma^2}{\varepsilon\kappa}\coth(\kappa d). \qquad (7)$$

In equation (7) we have neglected terms of the order a_n^2. As discussed by Pincus, Joanny and Andelman [10] these terms lead to a renormalization of the bending constant, $k_c' = k_c + \delta k|_{el}$ where $\delta k|_{el} = 3\pi\sigma^2/8\varepsilon\kappa^3 \approx T/\kappa^3 l_B\lambda^2$ ($\lambda = e/2\pi l_B\sigma$ is the Gouy-Chapman length). Note that due to $\kappa\lambda \gg 1$ and $\kappa l_B \ll 1$ one has $\delta k|_{el} \ll k_c$ for a wide range of parameters. In the following we use the bare bending rigidity k_c, keeping in mind that one has to replace it by k_c' when $\delta k|_{el}$ becomes comparable to k_c.

The rod-membrane interaction term is given by $F_{MR} = -2\frac{q_0\sigma_R}{4\pi}2\pi r_0\Phi_M(x = z = 0)$. From equation (6) we find

$$F_{MR} = -\frac{\sigma\rho q_0}{\varepsilon\kappa}\big(\sinh^{-1}(\kappa d) + \kappa^2\coth(\kappa d)\sum_n a_n\kappa_n^{-1}\sinh^{-1}(\kappa_n d)\big). \qquad (8)$$

Assuming $\kappa d \gg 1$ and $\kappa q_0^{-1} \gg 1$ equation (8) can be approximated by

$$F_{MR} = -\frac{2\sigma\rho q_0}{\varepsilon\kappa}\exp(-\kappa d)\left(1 + \kappa\sum_n a_n\right). \qquad (9)$$

In the summation over n in equation (9) we have neglected terms of the order $n^2q_0^2d/\kappa$. Assume, for instance, that $q_0d \approx 1$; then the summation in equation (9) breaks down at $n = n_0 \approx (\kappa d)^{1/2}$. The modes with $n \gg n_0$ are damped exponentially (*cf.* Eq. (8)). However, since – due to the bending rigidity – the amplitude a_n decreases rapidly with n (see below) one may use equation (9) also for larger n-values.

We can now determine the deformation profile $u(x)$ of the membranes, equation (1). The amplitudes a_n follow from the minimization of F, equation (2), which leads to

$$a_n = \frac{\sigma\rho\exp(-\kappa d)}{\varepsilon k_c q_0^3}\frac{1}{n^4}\cdot \qquad (10)$$

The n^{-4}-dependence of the amplitudes reflects the fact that undulations with shorter wavelengths are suppressed due to the curvature energy (*cf.* Eq. (3)); the exponential term follows from the screened interaction between the macroions and the charged surfactants. From equations (1, 10) we find for the displacement $u(x)$ of the bilayers

$$u(x) = \frac{\sigma\rho\exp(-\kappa d)}{\varepsilon k_c q_0^3}\sum_{n=1}^{\infty}\frac{\cos(nq_0x)}{n^4} = \frac{\sigma\rho\exp(-\kappa d)}{\varepsilon k_c q_0^3}\left(\frac{\pi^4}{90} - \frac{1}{48}(q_0x(2\pi - q_0x))^2\right). \qquad (11)$$

The expression on the right-hand side is valid for $0 \le q_0x \le 2\pi$[18], *i.e.*, for the part of the membrane between the two polyions fixed at $x = 0$ and $x = 2\pi/q_0$. The continuation to other parts of the bilayer is straightforward. The resulting undulation has a similar appearance as the single first mode with $n = 1$; due to the additional higher modes, however, it is slightly more pointed towards the polyions and slightly more flat in the other parts. We note that these considerations can be easily translated to the case when the membranes and macroions are

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[1] The potential Φ can be decomposed in two parts: Φ_M which is a part of Φ that obeys $\partial\Phi_M/\partial n|_{S_M} = 2\pi\sigma/\varepsilon$ and $\partial\Phi_M/\partial n|_{S_R} = 0$ and Φ_R that obeys $\partial\Phi_R/\partial n|_{S_M} = 0$ and $\partial\Phi_R/\partial n|_{S_R} = -4\pi\sigma_R/\varepsilon$. Now $\Phi = \Phi_M + \Phi_R$ and one finds from equation (4) two contributions to the rod-membrane interaction, namely $F_1 = -(\sigma_R/2A)\int_{S_R} dS\Phi_M$ and $F_2 = (\sigma/4A)\int_{S_M} dS\Phi_R$. It can be shown rigorously that $F_1 = F_2$. Hence $F_{MR} = 2F_1$.

equally charged. Then one has to replace σ by $-\sigma$, a_n by $-a_n$ and $u(x)$ by $-u(x)$. Furthermore, we note that another geometry, namely an infinite stack of membranes (at the mean positions $z = \pm d, \pm 3d, \pm 5d, ...$) can also be calculated. Assume the following positions of the rods: $x = 0, \pm 2\pi/q_0, \pm 4\pi/q_0, ...$ for $z = 0, \pm 4d, \pm 8d...$ and $x = \pm \pi/q_0, \pm 3\pi/q_0, ...$ for $z = \pm 2d, \pm 6d, \pm 10d...$ Due to symmetry the Fourier components a_n' are now given by $a_n' = 2a_n$ for n odd and $a_n' = 0$ for n even. The resulting deformation profile of each membrane shows then symmetric undulations that reflect the symmetry of the positions of the macroions.

Consider now the curvature u_{xx} of the membranes (again for the geometry depicted in Fig. 1). For $0 \leq q_0 x \leq 2\pi$ it is given by

$$u_{xx}(x) = \frac{\sigma\rho\exp(-\kappa d)}{4\varepsilon k_c q_0}\left(q_0 x(2\pi - q_0 x) - \frac{2\pi^2}{3}\right). \quad (12)$$

For other parts of the membrane one has to shift the argument accordingly. Note that at the x-positions of the rods, *i.e.* at $x = 0, \pm 2\pi/q_0, \pm 4\pi/q_0...$, the curvature has cusps, a fact which comes from the approximation which is made by going from equation (8) to (9). Indeed, all modes beyond $n > n_0 \approx (\kappa d)^{1/2}$ (assuming $q_0 d \approx 1$; see above) are suppressed exponentially, so that the cusps of the curvature will be smoothed out for length scales of the order $(n_0 q_0)^{-1}$.

In this section we assumed that the membranes are only slightly deformed and therefore calculated the free energy only up to the lowest order terms in a_n. From equation (11) follows that due the bending of the membranes their nearest distance to the polyions is lowered by $\Delta d = (\pi/720)\sigma\rho\exp(-\kappa d)\, d_0^3/\varepsilon k_c$ where $d_0 = 2\pi/q_0$ denotes the distance between neighboring rods. Due to the screening $\Delta d \propto \exp(-\kappa d)$ so that usually the displacement is small. Note, however, that one has $\Delta d \propto d_0^3/k_c$; thus for a large separation d_0 between the rods and/or very flexible membranes Δd may become of the order of d. In this regime our approximation breaks down; especially the electrostatic membrane-membrane repulsion plays then a crucial role whereas this effect was neglected above (see the discussion below Eq. (7)).

Ultimately, very flexible membranes may touch the macroion. In this case the polyion is pinched between the membranes: even if we release the condition that the macroion is fixed in space it cannot move anymore. We will discuss this pinching effect in more detail in Section 4 when we compare it with other possible rod-membrane interactions. In the next section we will discuss the case of a macroion adsorbed on a single membrane.

3 Adsorbed macroion

Consider a rigid polyanion adsorbed on a cationic membrane which carries the fixed constant charge density σ. Assume that the charge of the polyion is located along a thin rigid rod with charge density (per length) $-\rho$ and total length $L \gg \kappa^{-1}$. Due to the geometry of the polyion (uncharged side groups, hydration shell *etc.*) there is a typical minimal distance $r_0 \ll L$ between the charged rod and the membrane. The attraction between the rod and the membrane will lead to a bending of the bilayer as schematically depicted in Figure 2. In this section we estimate the deflection angle α due to the presence of the macroion using simplified models.

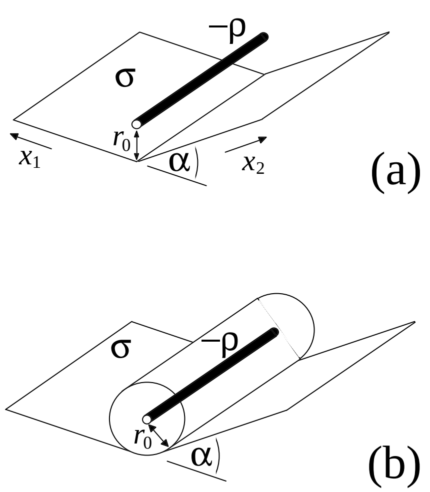

Fig. 2. Deflection of a flexible cationic bilayer due to the presence of an adsorbed polyanion. (a) and (b) depict two simplified models from which the deflection angle α can be estimated (see text for details).

It is clear that the strongest bending of the membrane is near the adsorption side since there the electrical field emanating from the rod is perpendicular to the surface of the bilayer. In the most simple approach we assume that the membrane is folded at the adsorption side and flat elsewhere (*cf.* Fig. 2a). This assumption is reasonable as long as the bending rigidity can be neglected compared to the electrostatic effects (see below). The deflection angle α is then determined by the interplay between two antagonistic effects: (i) with increasing α the free energy F_{MR} of the rod-membrane interaction decreases. (ii) On the other hand an increasing deflection leads to an increase of the interaction energy F_{MM} between the two flat parts of the membrane at the left and right of the adsorption side.

In order to calculate the change ΔF_{MR} of the rod-membrane interaction due to bending we have to calculate the potential Φ_R of the rodlike macroion. Due to symmetry (we do not account for the presence of the lipid bilayer, *i.e.*, we assume here the membrane to be transparent[2])

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[2] The presence of the lipid bilayer leads to an infinite set of images of the rod charges and the charges on the membrane. Consider a charge q at the distance $d \ll \kappa^{-1}$ from a bilayer of thickness d_M and permittivity ε_L. The contribution Φ_I of the image charges to the potential at the position of the charge can be calculated using the method presented in reference [19]. One finds $\Phi_I = \beta\int_0^\infty dk\left(e^{-2k(d+d_M)} - e^{-2kd}\right)/\left(1-\beta^2 e^{-2kd_M}\right)$ with $\beta = (\varepsilon_L - \varepsilon)/(\varepsilon_L + \varepsilon)$; this leads to the following limiting laws: $\Phi_I \simeq -(d_M/d)\left(\beta/\left(1-\beta^2\right)\right)(1/2d)$ for $d_M \ll d$

one has to solve the Debye-Hückel equation in cylindrical coordinates which leads to

$$\Phi_R\left(r\right)=-\frac{2\rho}{\varepsilon}K_0\left(\kappa r\right) \tag{13}$$

where K_0 is a modified Bessel function [21]. In the following we will often make use of the asymptotic behavior of K_0 for small and large arguments: $K_0\left(x\right)\simeq-\ln x$ for $x\ll1$ and $K_0\left(x\right)\simeq\left(\pi/2x\right)^{1/2}\exp\left(-x\right)$ for $x\gg1$. The rod-membrane interaction is now given by $F_{MR}=2\sigma L\int_0^\infty dx_1\Phi_R\left(r\left(x_1\right)\right)$ where $r\left(x_1\right)$ denotes the distance between the rod and the point x_1 on the membrane. For small α this distance is given by $r\left(x_1\right)=\left(x_1^2+r_0^2\right)^{1/2}-2^{-1}x_1r_0\left(x_1^2+r_0^2\right)^{-1/2}\alpha$. Hence

$$\begin{aligned}\Delta F_{MR}\simeq&-\frac{2\sigma\rho Lr_0\alpha}{\varepsilon}\int_0^\infty du\,uK_1\left(\left(u^2+\kappa^2r_0^2\right)^{1/2}\right)\\&\times\left(u^2+\kappa^2r_0^2\right)^{-1/2}\end{aligned} \tag{14}$$

where we used the relation $K_0'\left(z\right)=-K_1\left(z\right)$ [21]. In order to estimate the integral we use the fact that $K_1\left(x\right)=1/x$ for $x\ll1$ whereas for $x\gg1$ the integrand decays exponentially. Thus for $\kappa r_0\ll1$ ΔF_{MR} may be approximated as follows:

$$\begin{aligned}\Delta F_{MR}\approx&-\frac{2\sigma\rho Lr_0\alpha}{\varepsilon}\int_0^1du\frac{u}{u^2+\kappa^2r_0^2}\\\simeq&\frac{2\sigma\rho Lr_0\ln\left(\kappa r_0\right)}{\varepsilon}\alpha.\end{aligned} \tag{15}$$

Now we turn to the calculation of the interaction energy between the two flat parts of the membrane. The contribution of the electrical potential at x_2 which stems from a stripe of width dx_1 at x_1 is $d\Phi_M=2\sigma\varepsilon^{-1}K_0\left(\kappa l\left(x_1,x_2\right)\right)dx_1$ where $l\left(x_1,x_2\right)$ denotes the spacial distance between x_1 and x_2. For small α it is given by $l\left(x_1,x_2\right)\simeq x_1+x_2-\alpha^2x_1x_2/2\left(x_1+x_2\right)$. Now $F_{MM}=\sigma L\int_0^\infty dx_2\int_0^\infty d\Phi_M$ and thus

$$\begin{aligned}\Delta F_{MM}\simeq&\frac{\sigma^2L\alpha^2}{\varepsilon\kappa^2}\int_0^\infty du\int_0^\infty dvK_1\left(u+v\right)\frac{uv}{u+v}\\\simeq&\,0.251\frac{\sigma^2L\alpha^2}{\varepsilon\kappa^2}\cdot\end{aligned} \tag{16}$$

We find now α by minimizing $\Delta F=\Delta F_{MR}+\Delta F_{MM}$. From equations (15, 16) it follows that

$$\alpha\approx-\frac{4\kappa\rho}{\sigma}\kappa r_0\ln\left(\kappa r_0\right). \tag{17}$$

Note that equation (17) is valid for $\kappa r_0\ll1$; at $\kappa r_0=1$ we expect a crossover to an exponentially decreasing r_0-dependence of α due to screening. This shows together with $\alpha\rightarrow0$ for $r_0\rightarrow0$ (*cf.* Eq. (17)) that one has a non-monotonic dependence of α on r_0. It is indeed clear (in the framework of our approximation) that for $r_0=0$ the local bending of the otherwise flat membrane will not change the rod-membrane interaction F_{MR}. These considerations indicate that the deflection of the membrane will be maximal when κr_0 is of the order unity; we will show this more rigorously in the more refined model described below. Another interesting effect is the role of the charge densities: for $\kappa\rho\ll\sigma$ the membrane is only slightly disturbed by the adsorbed rod (see Eq. (17)). When the macroion is higher charged so that its charge is of the same order as the opposite charge of the neighboring part of the membrane, *i.e.* when $\kappa\rho\approx\sigma$, the rod-membrane attraction will overcome the repulsion between the two parts of the membrane and α is of the order unity (for $\kappa r_0\approx1$).

We note that this result also includes the case where both, the polyion and the bilayer carry charges of the same sign; one has then simply to replace in equation (17) ρ by $-\rho$. In this case α becomes negative, *i.e.*, the membrane bends away from the macroion. This situation is related to the seemingly remote problem of the structure of interpenetrating polyelectrolyte chains [22]. In a semidilute polyelectrolyte solution the conformation of a given chain shows deflections due to the presence of other chains so that its persistence length decreases. In the salt regime the angle θ of an individual deflection of a test chain due to the presence of a perpendicular rod at the distance r can be estimated to be $\theta\simeq\kappa r\exp\left(-\kappa r\right)$ [23]. Note that for $\rho=\kappa\sigma$ the angle α of deflection of the membrane, equation (17) scales similar to θ.

Let us turn to a more refined model that also accounts for the bare bending rigidity k_c of the membrane. It allows to estimate the first-order correction term to α for sufficiently small k_c. The polyanion is modelled as a cylinder of radius r_0 and length L, its charges are located in the middle axis of the cylinder, see Figure 2b. For simplicity we assume that the membrane can bend only directly at the rod with a curvature r_0^{-1} and is flat elsewhere. For a given angle of deflection α one finds for the cost in curvature energy

$$\Delta F_{bend}=\frac{k_cL}{2r_0}\alpha. \tag{18}$$

(thin membrane) and $\Phi_I\simeq-\beta/2d$ for $d_M\gg d$ (thick membrane) (*cf.* also the case of a charge next to a dielectric sphere [20]). The experimental situation in reference [2] ($d\approx10$ Å, $d_M\approx24$ Å) corresponds to the crossover region between these two limiting cases. We show now that even if we assume the membrane to be much thicker than the actual experimental value the effect of the image charges is usually smaller than the direct electrostatic interaction. Consider a rod at a distance d away from an semiinfinite dielectric $\varepsilon_L\approx2$. The potential of the rod image at the position of the rod is then $\Phi_1\simeq-2\rho\varepsilon^{-1}\ln\left(2\kappa d\right)\simeq0.018e$ Å^{-1} (for $\rho=0.67e$ Å^{-1}, $\varepsilon=80$, $\kappa^{-1}=60$ Å, $d=10$ Å). On the other hand, the interaction with the charges at the phase boundary (and their image charges) is given by $\Phi_2\simeq2\pi\left(2\sigma/2\right)\varepsilon^{-1}\kappa^{-1}\exp\left(-\kappa d\right)\simeq0.04e$ Å^{-1} (for $\sigma=0.01e$ Å^{-2}). The presence of image charges leads a repulsive contribution to the interaction between rod and membrane; however, in our calculations in Sections 3 and 4 we will only include the stronger direct electrostatic interaction.

The change of the interaction energy ΔF_{MR} between the rod and the membrane can be simply calculated by noting that due to symmetry the interaction between the charged rod and the flat parts of the membrane is *exactly* the same as the interaction energy between the rod and the completely flat membrane ($\alpha = 0$). Thus the interaction between the curved part of the membrane and the rod alone determine ΔF_{MR}:

$$\Delta F_{MR} = -\frac{2\sigma\rho L r_0 K_0\left(\kappa r_0\right)}{\varepsilon}\,\alpha. \tag{19}$$

For $\kappa r_0 \ll 1$ the change ΔF_{MM} in the electrostatic self energy of the membrane is again given by equation (16). Minimizing $\Delta F = \Delta F_{bend} + \Delta F_{MR} + \Delta F_{MM}$ with respect to α we find for $\kappa r_0 \ll 1$:

$$\alpha \simeq \frac{4\kappa\rho}{\sigma}\,\kappa r_0 K_0\left(\kappa r_0\right) - \frac{k_c \varepsilon \kappa^2}{\sigma^2 r_0}\cdot \tag{20}$$

The first term in equation (20) stems from the electrostatic interaction and shows indeed the same scaling as equation (17). The second term represents a reduction of α due to the bending rigidity. Equation (20) is only useful as long as the correction term is much smaller than the purely electrostatic contribution to α. This leads to the condition $k_c \ll -4\rho\sigma\varepsilon^{-1} r_0^2 \ln\left(\kappa r_0\right)$. For stiffer membranes the assumed geometry does not describe the situation properly since the cost in curvature energy for a local curvature r_0^{-1} is too high. For such membranes one has a smaller curvature $r^{-1} < r_0^{-1}$ near the polyion so that one may have a quite small deflection. Experimentally both situations may occur: the condition on k_c for the electrostatics-dominated case can be rewritten as $k_c < -4 l_B T r_0^2 \ln\left(\kappa r_0\right)/b A_\sigma$ where b denotes the average distance between charges on the rod and A_σ is the area per charge on the membrane. Typical values for polypeptide cationic lipid complexes are $r_0 \approx 10$ Å, $b \approx 1.5$ Å (assuming no Manning condensation) and $A_\sigma \approx 68{-}680$ Å^2 depending on the amount of neutral lipid [2]. This together with $k_c \approx 5T{-}20T$ shows that depending on the relative amount of neutral lipid and depending on κ both situations may occur.

Equation (20) describes the case $\kappa r_0 \ll 1$. For the case $\kappa r_0 \gg 1$ we have to reconsider ΔF_{MM}, equation (16), which describes the repulsion between the two flat parts of the membrane. Now $\kappa r_0 \gg 1$ and thus for $\alpha \gg \left(\kappa r_0\right)^{-1}$ the minimal distance between the flat parts is much larger than κ^{-1} and the interaction between them can be neglected. The leading contribution to ΔF_{MM} comes then from its curved part which can be easily calculated by using the electrostatic contribution to the curvature energy which is given by $\Delta F_{MM} = 2^{-1}\,\delta k|_{el}\, L r_0^{-1}\,\alpha$ with $\delta k|_{el} = 3\pi\sigma^2/8\varepsilon\kappa^3$ (see the discussion in the previous section). Thus we find that for $\kappa r_0 \gg 1$ the leading term of ΔF_{MM} grows linearly in α (instead of the α^2-dependence in Eq. (16)). Assume now that $k_c = 0$. Comparing ΔF_{MR} and ΔF_{MM} we find that $\alpha \to 0$ as long as $\sigma > (32/3)\left(2\pi\right)^{-1/2} \kappa\rho\left(\kappa r_0\right)^{3/2}\exp\left(-\kappa r_0\right)$. Since this is usually the case we find that α is extremely small for $\kappa r_0 \gg 1$. Thus one may have $\alpha \ll \left(\kappa r_0\right)^{-1}$; then ΔF_{MM} is again given by equation (16) and α by equation (20).

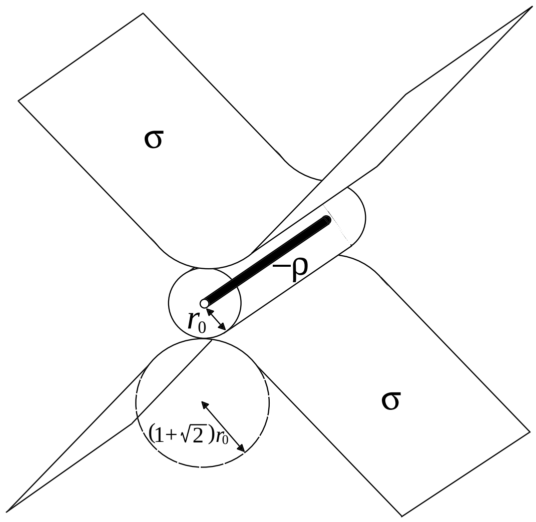

Fig. 3. Polyanion adsorbed between two neighboring membranes (pinching effect).

4 Double adsorption versus single adsorption in swollen lamellar structures

Here we discuss the possible ways in which the polyanions are localized within a lamellar structure of cationic lipids. When we are above the adsorption threshold[3] there are in general two possibilities: (i) the polyions may be adsorbed on one of the two neighboring membranes (single adsorption), *cf.* Figure 2. (ii) On the other hand the macroions may be pinched between both neighboring membranes (double adsorption) as depicted in Figure 3. In this section we will compare the free energy for single and double adsorption and show under which circumstances pinching is favored. In Section 2 we discussed already the case when the distance between the macroions and the neighboring membranes is large and – due to screening – the deformation Δd of the membrane is small; we showed that $\Delta d \approx \sigma\rho\exp\left(-\kappa d\right) d_0^3/\varepsilon k_c$. This result indicates that

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[3] The adsorption threshold may be estimated by the following simple argument. Consider an adsorbed cylindrical macroion (length L, radius r_0, charged middle axis with density $-\rho$) at a charged membrane. Assuming the membrane to be flat the adsorption energy E_{ad} can be easily calculated by using the fact that the potential Φ of the membrane at a point with distance z from the bilayer is given by $\Phi(z) = 2\pi\sigma\varepsilon^{-1}\kappa^{-1}\exp\left(-\kappa z\right)$. Hence $E_{ad} = -\left(2\pi\sigma\rho L/\varepsilon\kappa\right)\exp\left(-\kappa r_0\right)$. For $|E_{ad}| < T$ the polyion will not be adsorbed whereas for $|E_{ad}| > T$ it will stick to the membrane. This means, for instance, that by increasing the salt content beyond a given value so that $\kappa^{-1} < \kappa_c^{-1}$ the initially adsorbed macroion will be desorbed; here κ_c^{-1} is given by $\kappa_c^{-1} \simeq \varepsilon T/2\pi\sigma\rho L$ for $\kappa r_0 \ll 1$ and by $\kappa_c^{-1} \approx r_0/\ln\left(2\pi\sigma\rho L r_0/\varepsilon T\right)$ for $\kappa r_0 \gg 1$.

for sufficiently high charged systems (large σ and ρ) and sufficiently flexible membranes (small k_c) one may have pinching. Note that Δd is predicted to increase also with decreasing density of macroions, *i.e.* with increasing d_0. These considerations are, however, only valid for small deflections. We will show in this section that the condition for pinching indeed depends on σ, ρ and k_c but it is independent of d_0; furthermore a microscopic parameter, namely the radius of the rod enters into the corresponding expressions.

Using similar methods as in Section 3 we calculate now the adsorption energy in the case of double adsorption and compare it to the energy gain due to single adsorption. For $\kappa r_0 \ll 1$ the two membranes have to approach very closely which leads to a strong repulsion between them. When this electrostatic repulsion is much larger than the bending energy one has large deflection angles $\alpha \approx \pi/2$ as depicted in Figure 3. The electrostatic contribution to the free energy can be estimated easily by replacing the conformation depicted in Figure 3 by two flat membranes which cross each other perpendicular at the position of the macroion; the error can be shown to be of the order κr_0. One finds $\Delta F_{MM} \simeq 4\pi\sigma^2 L/\varepsilon\kappa^2$ and $\Delta F_{MR} \simeq -(8\sigma\rho L/\varepsilon\kappa)\int_0^\infty du K_0(u) = -4\pi\sigma\rho L/\varepsilon\kappa$. Furthermore the bending rigidity can be estimated to be $\Delta F_{bend} \simeq (\pi/4) k_c L/\left(2\left(1+\sqrt{2}\right)r_0\right) \simeq 0.16 k_c L/r_0$ (*cf.* Fig. 3). The adsorption energy for the pinched state is then $E_P = \Delta F_{bend} + \Delta F_{MM} + \Delta F_{MR}$. We compare now E_P with the energy gain E_S for the adsorption at a single membrane. For $\kappa r_0 \ll 1$ the bending due to the macroion is small (*cf.* Eq. (20)) and therefore its contribution to the adsorption energy is negligible. Then E_S is given by $E_S = -(4\sigma\rho L/\varepsilon\kappa)\int_0^\infty du K_0(u) = -2\pi\sigma\rho L/\varepsilon\kappa$ and is thus the half of the rod-membrane interaction ΔF_{MR} in the pinching case. Comparing E_P and E_S one finds that for

$$k_c < k_0 \simeq \left(1+\sqrt{2}\right) 16 \left(\frac{\sigma\rho r_0}{\varepsilon\kappa} - \frac{2\sigma^2 r_0}{\varepsilon\kappa^2}\right) \tag{21}$$

pinching is energetically more favorable than adsorption on a single membrane. Note that for $\kappa\rho < \sigma$ equation (379) predicts a negative value of k_0, *i.e.*, here the membrane is so highly charged that one has no double adsorption due to the strong membrane-membrane repulsion.

Until now we have assumed that $\alpha \approx \pi/2$; let us release now this constraint. If both membranes have a given deflection angle α one finds for the membrane-membrane repulsion $\Delta F_{MM} \simeq 4\pi\sigma^2 L/\left(\varepsilon\kappa^2 \sin\alpha\right)$ whereas one still has $\Delta F_{MR} \simeq -4\pi\sigma\rho L/\varepsilon\kappa$. The bending energy scales now similar to equation (18), *i.e.* $\Delta F_{bend} \approx k_c L\,\alpha/r_0$. The deflection angle α follows from the minimization of $E_P = \Delta F_{bend} + \Delta F_{MM} + \Delta F_{MR}$ which leads to

$$\frac{\cot\alpha}{\sin\alpha} \approx \frac{\varepsilon\kappa^2 k_c}{4\pi\sigma^2 r_0}\,. \tag{22}$$

Assume now that $\alpha = (\pi/2) - \Delta\alpha$ with $\Delta\alpha \ll 1$. Then one finds from equation (22) that $\Delta\alpha \approx \varepsilon\kappa^2 k_c/\pi\sigma^2 r_0$. As expected $\Delta\alpha$ increases with k_c. Note that equation (21) was derived under the assumption that $\Delta\alpha \ll 1$ for $k_c \approx k_0$. This is only valid for sufficiently small values of k_0, namely $k_0 \ll \sigma^2 r_0/\varepsilon\kappa^2$. The α-dependence in the opposite case $\alpha \ll 1$ follows also from equation (22); one finds $\alpha \approx \left(8\pi\sigma^2 r_0/\varepsilon\kappa^2 k_c\right)^{1/2}$. Comparing the adsorption energy E_P with the value E_S for the single adsorption one finds for the critical bending rigidity (for $\alpha \ll 1$)

$$k_0 \approx 0.4\frac{\rho^2 r_0}{\varepsilon}\,. \tag{23}$$

Note that in this regime k_0 is independent of σ but quadratic in ρ.

Let us summarize the results of this section. (1) For highly charged membranes or a weakly charged macroion so that $\kappa\rho < \sigma$ single adsorption is always more favorable. (2) For $\kappa\rho > \sigma$ double adsorption is favored when the membranes have a sufficiently low bare bending rigidity k_c:

(2a) for very flexible membranes (with $k_c \ll \sigma^2 r_0/\varepsilon\kappa^2$) one has double adsorption (with $\alpha \approx \pi/2$) as long as $k_c < k_0$ where k_c is given by equation (21);
(2b) for stiffer membranes (with $k_c \gg \sigma^2 r_0/\varepsilon\kappa^2$) double adsorption is favored as long as $k_c < k_0$ with k_0 given by equation (23); the bending angle is then very small, $\alpha \ll 1$.

All cases are derived under the assumption $\kappa r_0 \ll 1$. We note that in the opposite case $\kappa r_0 \gg 1$ pinching is usually favorable as long as $|E_{ad}| > T$. The reason is that pinching leads to the double value of the adsorption energy whereas due to geometry and screening the cost in bending energy as well as the membrane-membrane repulsion is negligible.

At the present stage no direct comparisons of our predictions with experiments are available. The polypeptide/cationic-lipid complexes studied by Subramanian [2] correspond to the non-salt case. Our results may, however, also shed some light on this case: let us assume $\kappa^{-1} = 50$ Å (*i.e.* a screening length that is of the order of the spacing of the lamellar structure [2]) and $r_0 = 10$ Å. Even for a moderately diluted charged membrane with $\sigma = e/200$ Å^2 one has a ratio $\sigma^2 r_0/\varepsilon\kappa^2$ that is of the order of $4T$, a value that is smaller than the bending rigidity $k_c \approx 5T$–$20T$. Using equation (23) we find for the critical value $k_0 \approx 12T$ (assuming $\rho = e/1.5$ Å). This indicates that pinching may occur in these complexes.

5 Conclusion

In conclusion, we have studied the bending of charged flexible membranes due to the presence of macroions. Rodlike polyions which are hold in some distance from the bilayer induce a bending of the membrane towards them. We demonstrated this for the case of a regular lattice of macroions where the deformation profile of the membrane can be calculated rigorously in the framework of the Debye-Hückel theory. Furthermore, we investigated the case of adsorbed polyions. We estimated the deflection angle of the membrane and showed how this angle depends on properties of the membrane (charge density, bending rigidity) as well as of the macroion (diameter, line density). Finally, we considered the case where polyanions are localized within a lamellar structure of cationic lipids. Especially, we demonstrated the possibility of a double adsorption of the macroion between its two neighboring membranes (pinching effect). We showed that for sufficiently flexible membranes double adsorption is more favorable than single adsorption.

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