

# Geometrical aspects of the frustration in the cubic phases of lyotropic liquid crystals

(lipid bilayers/lipid-phase transitions/phospholipids/constant-curvature surfaces)

DAVID M. ANDERSON<sup>†‡</sup>, SOL M. GRUNER<sup>§¶</sup>, AND STANISLAS LEIBLER<sup>||††</sup>

<sup>†</sup>Departments of Mathematics and Polymer Sciences, University of Massachusetts, Amherst, MA 01003; <sup>§</sup>Department of Physics, Princeton University, Princeton, NJ 08544; and <sup>||</sup>Baker Laboratory, Cornell University, Ithaca, NY 14853

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**ABSTRACT** Bicontinuous cubic phases, composed of bilayers arranged in the geometries of periodic minimal surfaces, are found in a variety of different lipid/water systems. It has been suggested recently that these cubic structures arrive as the result of competition between two free-energy terms: the curvature energy of each monolayer and the stretching energy of the lipid chains. This scenario, closely analogous to the one that explains the origin of the hexagonal phases, is investigated here by means of simple geometrical calculations. It is first assumed that the lipid bilayer is of constant thickness and the distribution of the (local) mean curvature of the phospholipid–water interfaces is calculated. Then, assuming the mean curvature of these interfaces is constant, the distribution of the bilayer’s thickness is calculated. Both calculations quantify the fact that the two energy terms are frustrated and cannot be satisfied simultaneously. However, the amount of the frustration can be smaller for the cubic phase than for the lamellar and hexagonal structures. Therefore, this phase can appear in the phase diagram between the other two, as observed in many recent experiments.

## I. Introduction

Although cubic phases in amphiphilic systems have been known and studied for many years (1), their physical origins are rather poorly understood. This can be traced to the complexity of both the microscopic and mesoscopic structures encountered in these systems. At a microscopic level, the amphiphilic molecules exhibit complexity typical of other macromolecules, such as polymers or liquid crystals. They have many internal degrees of freedom, resulting in numerous allowed conformations of the hydrocarbon chains and amphiphilic headgroups. Because of complexity, an attempt to describe the collective behavior of assemblies of such molecules must be based on a simplified model that is mainly phenomenological in nature. It is well known that the Landau approach has been very successful in the description of the phase (e.g., the critical) behavior of other similar systems, and it is, therefore, tempting to adopt it here. Thus, instead of dealing with microscopic variables one introduces collective variables, such as the position and the curvature of interfaces, their mutual separation, etc., and constructs a phenomenological Hamiltonian, which is a function of these variables.

Although this standard approach has been quite successful in many other problems, in cubic phases an extra difficulty comes from complexity at the mesoscopic level. In many cases, the lipid–water interfaces are not of simple geometrical shapes or topology. For example, it is now believed that many lipid–water cubic phases are bicontinuous structures composed of bilayers arranged in complicated networks to-

pologically equivalent to periodic minimal surfaces (see, e.g., refs. 2 and 3). Therefore, before building a thermodynamical or statistical mechanical description of these phases one must first study their geometrical aspects. The main purpose of this paper is to explore these geometrical aspects as they relate to phenomenological terms in the free energy of the bilayers.

## II. Phenomenological Model: Origins of Frustration

To build a phenomenological model that accounts for cubic phases, let us first consider phases that have much simpler geometry—namely, the fluid lamellar ( $L_\alpha$ ) and the inverted hexagonal ( $H_{II}$ ) phases (4, 5). In phase diagrams in which bicontinuous cubics appear, the cubics are often sandwiched between lamellar and hexagonal phases. In a lamellar phase, the phospholipid bilayers alternate with water lamellae so that only the hydrophilic parts of the molecules are exposed to water. An  $H_{II}$  phase consists of a hexagonally packed array of parallel water-cored tubes (4, 5). Of course, the molecules in  $L_\alpha$  and  $H_{II}$  phases still have many allowed molecular conformations and possess translational and rotational degrees of freedom, making it difficult to build and solve a detailed statistical model of these phases based on the microscopic variables. However, instead of dealing with molecular degrees of freedom, one can view the lamellar and the hexagonal phases as ensembles of interacting water–phospholipid interfaces. One can then introduce an effective interface Hamiltonian for these collective variables and base the statistical description on this phenomenological Hamiltonian. This was, in fact, the spirit of the approach used by Kirk *et al.* (6). The interface Hamiltonian they used consisted of three terms  $\mathcal{F} = \mathcal{F}_{\text{curv}} + \mathcal{F}_{\text{chain}} + \mathcal{F}_{\text{inter}}$ , where (i)  $\mathcal{F}_{\text{curv}}$  is the curvature energy of the phospholipid monolayers, first studied in detail by Helfrich (7). It is given by

$$\mathcal{F}_{\text{curv}} = \int dS \frac{\kappa_m}{2} (H - H_0)^2. \quad [1]$$

Here  $H$  is the local mean curvature of the monolayers, and  $\kappa_m$  is its bending rigidity constant. The presence of the spontaneous curvature,  $H_0$ , in Eq. 1 expresses the fact that each interface wants to bend because of the mismatch between the head–head and tail–tail molecular interactions. We have neglected another elastic contribution, the so-called Gaussian curvature term:  $\int dS \bar{\kappa}_m K$ , where  $K$  is the local Gaussian curvature of the monolayers. There is no reason to think that in a generic situation the value of the Gaussian elastic constant  $\bar{\kappa}_m$  changes drastically with the temperature or the water content so as to induce changes in the topology of the

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<sup>‡</sup>Present address: Physical Chemistry 1, Chemical Center, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden.

<sup>¶</sup>To whom reprint requests should be addressed.

<sup>††</sup>Present address: Service de Physique Théorique, Centre d’Etudes Nucleaires-Saclay, 91191 Gif-sur-Yvette, France.

system; we thus assume, for simplicity, that its value is zero. However, more elaborate theories should of course take this term into account. Note also that this assumption says nothing about the effective Gaussian rigidity of the bilayers; in fact, the other terms in the Hamiltonian can effectively generate such a contribution (and, in particular, change its sign). (ii)  $\mathcal{F}_{\text{chain}}$  takes into account all chain degrees of freedom that are not included in  $i$ . It can be viewed as a packing energy for hydrocarbon chains. In particular, the stretched configurations of the molecules cost some entropic contribution included in  $\mathcal{F}_{\text{chain}}$ . From the point of view of collective interface coordinates, this term is an interaction between different interfaces. (iii)  $\mathcal{F}_{\text{inter}}$  includes all other interactions between the interfaces. Examples include the hydration energy, long-range van der Waals interactions, and electrostatic interactions if charged lipids are present (8).

For the sake of simplicity, the interaction term  $\mathcal{F}_{\text{inter}}$  will be neglected and we will assume a simple quadratic form:  $\mathcal{F}_{\text{chain}} = \lambda(l - l_0)^2$  where  $\lambda$  and  $l_0$  are constants and  $l$  is one-half the distance across a bilayer (i.e., the length of a lipid molecule). More elaborate forms of packing energies should not change the main conclusions as long as  $\mathcal{F}_{\text{chain}}$  increases monotonically with  $|l - l_0|$ . All these assumptions can of course prove to be quite drastic. In fact, recent theoretical studies of the phase transitions in lamellar phases of lipid/water systems (R. Goldstein and S.L., unpublished data) show that the interaction terms are crucial for understanding the phase behavior of these systems. Our aim in the present article is not to claim that our oversimplified description necessarily holds for real systems, but rather to explore the consequences of this simplest model.

Then, it is easy to observe that the remaining two terms of the phenomenological free energy, the curvature term,  $\mathcal{F}_{\text{curv}}$ , and the packing term,  $\mathcal{F}_{\text{chain}}$ , cannot be minimized simultaneously. Indeed, if  $H_0 \neq 0$ , then: (i) in a lamellar phase in which packing energy can be easily minimized—e.g., by requiring a constant half-thickness,  $l_0$ , of the lamellae—the curvature energy contribution is nonzero; and (ii) if, on the contrary, the interfaces curve themselves in such a way as to minimize the curvature term—e.g., by forming cylinders of radius  $1/H_0$ , then the variation of half-distances,  $l$ , between them cost a nonzero packing energy. In particular, the chains of the phospholipid molecules must stretch to cover the regions in the middle of the neighboring water cylinders (6, 9). One often refers to such a situation as “the frustration” (10). In fact, it has been shown that one can decrease this frustration by adding a small amount of flexible hydrophobic molecules (9, 11, 12). In an inverted hexagonal phase these molecules are believed to preferentially partition into the regions in the middle between the water cylinders, where the chains of the phospholipid molecules are stretched and thus decrease the stretching of the chains. The addition, for instance, of 1.5 mol% of dolichol into a suitable lipid mixture reduced the temperature at which the  $H_{II}$  phase first appeared by 50 K (9)! In the language of our phenomenological model, the inverted hexagonal phase is now very stable since both the curvature and chain packing terms of the energy are reduced.

### III. Cubic Phases as a Relief to the Frustration

The idea that the frustration between the curvature energy of monolayers and the packing energy of the hydrocarbon chains results in the appearance of the cubic phases has recently been explored by Sadoc and Charvolin (13). In this purely geometrical approach, the frustration is relieved by embedding the amphiphilic system into the space of constant positive curvature ( $S^3$ ). Then, one returns back to  $R^3$  Euclidean space by introducing curvature defects—i.e., disclina-

tions; this leads (13) to the family of cubic structures observed in experiments. Similarly, it has recently been shown (H. Karcher, personal communication) that triply periodic surfaces of constant mean curvature can be obtained by projecting minimal surfaces in  $S^3$  down to  $R^3$ ; conversely, overlying every surface of constant mean curvature in  $R^3$  is a minimal surface in  $S^3$  (14).

The approach used in this paper is also geometrical but conceptually simpler. An estimate of the frustration in a cubic phase is obtained by performing a “geometrical measurement,” similar to the one described for the  $L_\alpha$  and  $H_{II}$  phases. The idea is to determine whether a cubic phase can be a solution to the frustration problem—namely, whether the curvature of the monolayers in a bicontinuous cubic phase can be kept constant (at its preferred value of  $H_0$ ), while simultaneously satisfying the packing energy of the chains (which, in this simplified model, means that the thickness of the bilayers remains constant at some preferred value).

To do this, it is first assumed that the bilayers have a constant half-thickness,  $l$ , everywhere, and then the variations of the monolayers’ local mean curvature,  $H$ , are computed. Next, the opposite case of constant mean curvature monolayers is considered, in which the variation of the bilayer thickness is calculated. Both calculations are performed for an example of Pn3m cubic structure (15) (see Fig. 1), which has been observed in various lipid–water systems such as in monoglycerides, tetraether lipids, and others (1). The results for the first calculation also hold for the cubic phase structures based on the Schwarz primitive minimal surface [which are of space group Im3m, consistent with diffraction observed in experiments (16)], and on the “gyroid” (17) [corresponding to space group Ia3d, also observed in experiments (18)], because these minimal surfaces have the same distribution of Gaussian curvature as the Schwarz diamond minimal surface.

### IV. Geometrical Measurements of the Frustration

**Constant-Thickness Case.** We begin by considering the triply periodic minimal surface that corresponds to a Pn3m cubic structure (Fig. 1), the so-called Schwarz diamond or D-type minimal surface (19, 20). It has a vanishing mean curvature  $H = 0$  at every point, this being the definition of a minimal surface. This surface divides space into two congruent, periodic, interwoven, but unconnected volumes. Any patch on a minimal surface represents the area-minimizing surface patch spanning the boundary curve.<sup>‡‡</sup> This surface can be thought of as being the midsurface traced out by the terminal methyl groups of lipid chains. Now assume that the monolayers on both sides of the midsurface are of constant half-thickness,  $l$ , so that the interfaces pertinent to a curvature energy calculation are parallel to this surface. The two lipid–water interfaces are likely to be near these parallel surfaces (22).

Let  $H_l = H_l(u, v)$  denote the (local) mean curvature of one of the interfaces, where  $u$  and  $v$  are the conformal coordinates in the Weierstrass representation of the minimal surface (19). Then the curvature energy of each monolayer is

$$E_{\text{curve}} = \frac{\kappa_m}{2} (\langle H_l^2 \rangle_l - 2H_0 \langle H_l \rangle_l + H_0^2 A_l), \quad [2]$$

<sup>‡‡</sup>The boundary curve represents Plateau boundary conditions (21). However, Schwarz (19) proved that under orthogonality boundary conditions expressing Pn3m symmetry and topological equivalence to the D-type minimal surface, the  $H = 0$  surface is not area minimizing. Recently, a family of  $H = \text{constant}$  surfaces with Pn3m symmetry and fixed topological type have been computed in which the D-type minimal surface actually represents a local maximum in area (15).

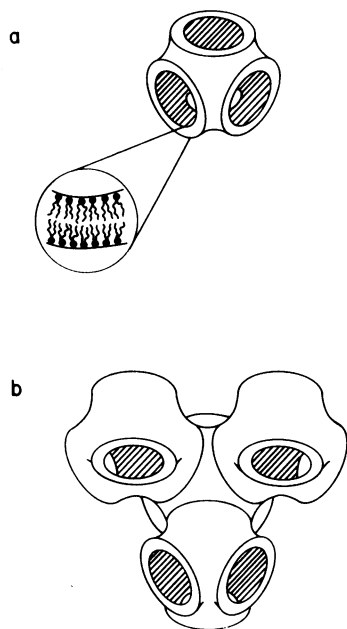


FIG. 1. (a) Artist's representation of the repeating unit out of which cubic phases with Pn3m symmetry are constructed. The centers of the four circular openings of the unit may be imagined as forming the vertices of an inscribed tetrahedron. The walls consist of a bilayer (Inset) with water on either side of the wall. The units stack together as shown in b. The minimal surface is midway between the lipid head groups—i.e., it is the surface traced out by the terminal methyl groups of the lipid chains. The head group surfaces are nearly congruent to the two types of surfaces considered in this paper: surfaces of constant mean curvature,  $H$ , and surfaces that are a constant distance,  $l$ , off the minimal surface; the near congruence of these two surface types is fundamentally why this cubic structure can be a good compromise to the curvature vs. chain stretch competition. Note that in the interests of visual clarity the bilayer wall has been drawn as being thin. In real lipid cubic phases, the lipid/water volume may exceed unity. An artist's rendition of this figure was used instead of the more exact numerical data used in the calculations in the text because the computer-generated color figures are difficult to reproduce by xerography.

where  $\langle \dots \rangle = (\int \dots dA_l)/A_l$  and  $A_l = \int dA_l$  denote the averages obtained by integrating over a unit cell of the parallel surface. In this calculation, and in the constant-curvature case, we perform the area integrations over the surface representing the lipid-water interface, rather than over the minimal midsurface, reflecting the fact that the area per head group is quite constant so that this integration is essentially a summation over lipid molecules. Moreover, an experimental study of the energy required to alter the curvature of the lipid cylinders in  $H_{II}$  phases demonstrated that Eq. 1 held if  $H$  and  $H_0$  were measured with respect to the lipid-water interface (22).  $E_{\text{curve}}$  is calculated by taking advantage of a simple connection existing between the curvature  $H_l$  and the area element  $dA_l$  of the parallel surface and the Gaussian curvature  $K$  and the area element  $dA$  of the minimal ( $H = 0$ ) surface,  $H_l = (-lK)/(1 + Kl^2)$ ,  $dA_l = (1 + Kl^2) dA_0$ . The distribution of the Gaussian curvature,  $K$ , over the unit cell of the periodic minimal D-type surface is shown in figure 3.4a' of Anderson (15) in the form of  $K = \text{constant}$  contour lines. Then, the area,  $A_l$ , and the averages  $\langle H_l \rangle_l$  and  $\langle H_l^2 \rangle_l$  can be expressed as  $A_l = A_0(1 + l^2 \langle K \rangle_0) = A_0 + l^2(2\pi\chi)$ ,  $A_l \langle H_l \rangle_l = -lA_0 \langle K \rangle_0 = -2\pi\chi l$ ,  $A_l \langle H_l^2 \rangle_l = A_0 l^2 \langle (K^2) \rangle_0 / (1 + Kl^2)_0$ , where  $\langle \dots \rangle_0$  denotes the averages over the minimal surface,  $A_0$  is the area of the unit cell of this surface ( $A_0 = 1.9188903 \dots$  when the Pn3m lattice parameter is equal to unity), and  $\chi = -2$  for the D-type minimal surface.

The last integral over the minimal surface can be written in the form of an expansion:

$$A_0 l^2 \left\langle \frac{K^2}{1 + Kl^2} \right\rangle_0 = \sum_{N=0}^{\infty} (-1)^N l^{2N+2} \langle K^{N+2} \rangle_0 \\ \equiv \sum_{N=0}^{\infty} (-1)^N l^{2N+2} S_{N+2},$$

and then calculated numerically by the method described in the Appendix. By truncating this expansion at the sixth term one makes an error smaller than 1%. Actual values of the coefficients  $S_i$  are given in the Appendix.

Putting together the equations of the last two paragraphs, one can calculate the curvature energy Eq. 2. Instead of this, we calculate the normalized variance

$$R_H = \frac{\langle (H_l - H_0)^2 \rangle_l}{H_0^2}. \quad [3]$$

$R_H$  measures deviation from a constant value,  $H_0$ , of the mean curvature over the surface, which is at a fixed distance  $l$  off the minimal surface. If this quantity were zero it would mean that one could build a bilayer of cubic symmetry with a constant thickness, for which the water-lipid interfaces would have a constant (imposed) mean curvature. Thus, the frustration would be released in the cubic phases as suggested by Sadoc and Charvolin (13).

Fig. 2A shows the plots of  $R_H$  as the function of the volume fraction of the water  $\Phi_w = 1 - \Phi_l$ , where  $\Phi_l$  = volume fraction of lipid. The water fraction is varied simply by varying the ratio  $l/a$  of the half-thickness to the lattice parameter. There exists a simple analytical formula for the volume fraction as a function of  $\mu = l/a$ —namely,  $\Phi_l = 2A_0\mu - 8\pi\mu^3/3$ . Different plots correspond to different values of  $\langle H_l \rangle_l / H_0$ . If the constraint of constant thickness of the bilayers is imposed, the variations of  $H$  are quite dramatic, implying a finite cost of the curvature energy Eq. 2. Therefore, it is concluded from these plots that in these cubic phases one cannot simultaneously satisfy both the conditions of the constant thickness and of the constant curvature of the monolayers.

Note that one should not be surprised that the values of  $R_H$  are so large. The curvatures  $H$  are the second derivatives of the positions of the interfaces, so that even if the surfaces are perturbed rather slightly the curvatures can vary greatly.

**Constant Curvature Case.** Now consider the case of constant curvature interfaces. The ideal hexagonal structure is an example of such a case, as is the lamellar; the question that thus arises is whether the cubic phase in which one imposes the constant curvature interfaces will have smaller packing energy than the  $H_{II}$  phase. To answer this question, at least from a purely geometrical point of view, start again with the midsurface of a bilayer and assume that it is a minimal surface. The first problem encountered is to determine what happens to this surface if one tries to impose on it a nonzero constant mean curvature  $H_0$ . Can the surface still remain periodic with the given symmetry and, more importantly, can it remain non-self-intersecting? Although the problem of periodic minimal ( $H_0 = 0$ ) surfaces has been studied for many years (17, 19, 21), it is only recently that the case of constant  $H$  surfaces of given three-dimensional symmetry has attracted attention. In particular, Anderson (15) has explicitly computed such surfaces by numerical techniques, whereas H. Karcher (personal communication) has demonstrated their existence in a rigorous sense. The answer for the above question is therefore "yes," at least in the case that  $H^* = H_0 a$  (where  $a$  is the size of the unit cell) is smaller than a maximum value  $H_m^* \approx 2.8$ , which represents the limit for the branch of solutions examined by Anderson (15).

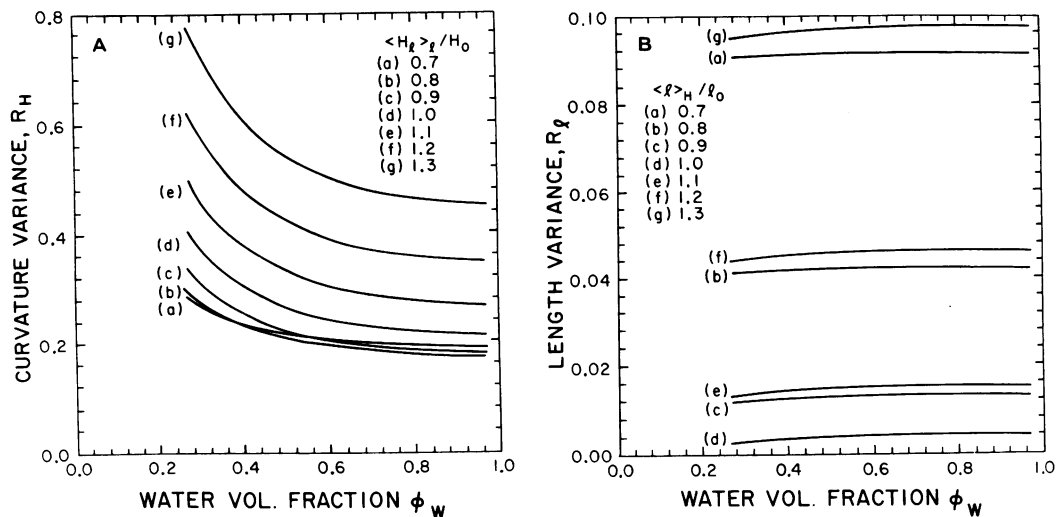


FIG. 2. (A) The normalized variance  $R_H$  is a measure of the deviation from a constant value,  $H_0$ , of the mean curvature over the surface, which is at a fixed distance,  $l$ , off the minimal surface.  $R_H$  is shown vs. the lipid volume fraction  $\phi_l$  for different values of the ratio of  $\langle H \rangle_l / H_0$ , where  $\langle H \rangle_l$  is the average curvature of the surface, which is a constant distance off the minimal ( $H = 0$ ) surface. If  $R_H$  were zero, then this parallel surface would have a mean curvature equal to  $H_0$  at every point. (B)  $R_l$  measures the deviation from a constant value  $l_0$  of the distance between the minimal surface and the surface of constant mean curvature  $H$ . It is shown vs. the lipid volume fraction for different values of  $\langle l \rangle_H / l_0$ , where  $\langle l \rangle_H$  is the average distance of the constant  $H$  surfaces from the minimal surface. The fact that  $R_l$  is so small means that if the lipid head groups conform to the proper constant curvature surfaces, then the thickness of the bilayer is nearly constant.

One can now superimpose two such surfaces, each of them corresponding to one lipid-water interface. The space that is formed between the two surfaces corresponds to the interior of the bilayer and its exterior corresponds to the water region (Fig. 1). We want to measure the distribution of the half-thickness,  $l$ , of the lipid interior region. In particular, the variance of this distribution

$$R = \frac{\langle l^2 \rangle_H - \langle l \rangle_H^2}{\langle l \rangle_H^2}, \quad [4]$$

where  $\langle \dots \rangle_H = \int \dots dS / \int dS$  (the integration is performed over the lipid-water interface surface, as in the previous case), should give us a measure of the frustration in the system, since the energy of the chains is

$$E_{\text{chain}} = \lambda \langle l^2 \rangle_H - 2\lambda \langle l \rangle_H + \lambda l_0^2 \approx \lambda l_0^2 R \quad (\text{if } l_0 \approx \langle l \rangle_H). \quad [5]$$

$R$  is estimated numerically via a method developed by Anderson (15) (see Appendix). One may calculate the local thickness of the region included between two  $H$  constant surfaces by extending the normals to these surfaces at one point of each of the triangular elements (see Appendix) and then determining the points where these normals intersect with the minimal ( $H = 0$ ) midsurface. Triangulation of the surface with 19,200 triangles per unit cell of the D-surface was used, so the measurement is quite accurate. Calling  $\Phi(H^*)$  the volume fraction of the unit cell corresponding to the lipids, and  $A(H^*)$  the area per unit cell of the surfaces (the area of lipid-water interfaces), we obtain the following expansion for these quantities:

$$\Phi_l = c_1 H^* - c_3 H^{*3} + c_6 H^{*6} + \dots, \quad [6a]$$

$$A/a^2 = c_0 - \frac{c_1}{2} H^{*2} + \frac{3c_3}{4} H^{*4} - \frac{6c_6}{7} H^{*7} + \dots, \quad [6b]$$

where  $c_0 \approx 1.91889$ ,  $c_1 \approx 0.55928$ ,  $c_3 \approx 0.07748$ ,  $c_6 \approx 0.00348$ .

Thus, one can express the variance of the thickness distribution in the form of an expansion in  $\Phi_l$ :

$$\langle l^2 \rangle_H - \langle l \rangle_H^2 = c \Phi_l^2 + \dots, \quad [7]$$

where  $c \approx 3.5 \times 10^{-4}$ . The expansion (Eq. 7) agrees with the numerical results over the whole range of  $\Phi_l$  values. Finally, Fig. 2B shows the dependence of a more general quantity

$$R_l = \frac{\langle (l - l_0)^2 \rangle_H}{l_0^2}, \quad [8]$$

on the volume fraction  $\Phi_l$ .  $R_l$  measures the deviation from a constant value,  $l_0$ , of the distance between the minimal surface and the surface of constant mean curvature  $H$ . As we can see, the behavior of  $R_l$  is remarkably constant and its values are small over the entire range of the lipid concentrations considered. (Notice that  $\Phi_l$  is bounded by  $\Phi_l^m \approx 0.739$ , which corresponds to the maximum value attainable in this family.) Thus, if  $\langle l \rangle_H = l_0$ , for example, then the value of  $R_l$  does not exceed 1%.

The cubic-phase  $R_l$  values are smaller than may be expected for hexagonal phases in which the central water cylinder radius is large compared to the mean lipid thickness. Consider, for example, the lipid 1,2-dioleoyl-*sn*-glycero-3-phospho-*N*-methylethanolamine, which has been shown to form Pn3m/Pn3 cubic phases at 25°C, but which will form  $H_{II}$  phases if the chain frustration is artificially relieved by the addition of several percent of a light oil, such as dodecane (23). Tate (24) derives an expression for  $\langle (l - l_0)^2 \rangle_H$  for an  $H_{II}$  geometry with cylindrical cores from which one may obtain  $R_l$ . Although  $l_0$  is not known for 1,2-dioleoyl-*sn*-glycero-3-phospho-*N*-methylethanolamine, it is reasonable to assume that  $l_0$  is roughly equal to the thickness of the  $H_{II}$  monolayers—i.e.,  $d = 2(R_w + l_0)$ . Using 15–20 Å as a liberal range of  $l_0$  values (23, 24), we get  $R_l = 3.8\%$ .

The fact that the value of  $R_l$  can be so small in the cubic phase shows that the frustration in the cubic phase can be small compared to the hexagonal phase. Therefore, under a change of control parameters of the system (such as the temperature or the hydration), which favors a moderate curving of monolayers, one may expect to transform the lamellar

phase into a cubic phase and not into the inverted hexagonal, at least for certain values of  $\kappa_m$ ,  $\lambda$ , and  $l_0$ . In fact, experimentally, inverted cubic phases are found between the lamellar and hexagonal phases (3, 23, 25).

## V. Conclusions

The simple geometrical calculation presented in this paper should be thought of as a first step of the phenomenological model of Section II. Many improvements are necessary before the results of such a model could be applied to the description of real systems. From the geometrical point of view, it could be useful to extend the space of possible structures beyond constant  $l$  or constant  $H$  surfaces. More importantly, the interactions between the interfaces must be introduced into the calculation. Recent results from a similar phenomenological model (R. Goldstein and S.L., unpublished data) for lamellar phases show that the "interacting-interfaces" picture can give a good description of the thermodynamic behavior of amphiphilic systems, provided that the molecular interactions such as hydration or van der Waals forces are taken into account. A good description of the chain packing entropy that enters the phenomenological Hamiltonian is also needed.

It seems to us that, despite the various simplifications, the geometrical calculation described above shows that the appearance of the cubic phases in the lipid-water mixtures (and similarly in other macromolecular systems) can, in some cases, be due to the frustration between the curvature and the chain packing energies.

## Appendix

We first describe the calculation of the coefficients  $S_N$  defined by  $S_N = \int \int K^N dA$ , where  $K$  and  $dA$  are defined on the minimal surface. Begin by splitting  $K^N dA$  into  $K^{N-1}$  and  $K dA$ , because the latter can be very easily written in terms of the surface coordinates  $(u, v)$  in the Weierstrass representation of the minimal surface:  $K dA = -4/(1 + u^2 + v^2)^2 dudv$ . The expression for  $K$  involves the complex norm of an 8-order polynomial:

$$K = -(8/\kappa^2)|1 - 14(u + iv)^4 + (u + iv)^8| / (1 + u^2 + v^2)^4, \quad [9]$$

where  $\kappa = 0.8389222985$ . . . The integral that must be performed is thus:

$$S_N = -96 \int \int_D [-(8/\kappa^2)|1 - 14(u + iv)^4 + (u + iv)^8|]^{N-1} / (1 + u^2 + v^2)^{4N-2} dudv. \quad [10]$$

The patch  $D$  of the Riemann surface over which this integral must be performed is a portion of the "Kreisbogenverecht" described by Schwarz:  $D: \{(u + iv) | 0 \leq u, v; (u + \sqrt{2}/2)^2 + (v + \sqrt{2}/2)^2 \leq 2\}$ . This was done by Gaussian quadrature over a  $10,000 \times 10,000$  square mesh.

The values for the first eight  $N$  are  $S_1 = -4\pi$ ;  $S_2 = 100.294$ ;  $S_3 = -865.936$ ;  $S_4 = 7.82252 \times 10^3$ ;  $S_5 = -7.28926 \times 10^4$ ;  $S_6 = 6.95520 \times 10^5$ ;  $S_7 = -6.76358 \times 10^6$ ;  $S_8 = 6.68197 \times 10^7$ . By evaluating an upper bound for the remainder in the series expansion, one can show that for  $l/a \leq 0.21$  the error is  $<1\%$ ; this value of  $l$  corresponds to  $\phi_l = 0.73$ .

The calculation of the  $\langle l^2 \rangle_l$  and  $\langle l \rangle_l$  for a set of constant mean curvature surfaces begins with the calculation of the equation, in Cartesian coordinates, of each triangular patch

$T_j, j = 1, 800$  in the finite element representation of a fundamental portion of the minimal surface. Then for each Gauss point  $p_i$  on the corresponding fundamental portion of the constant  $H$  surface, the surface normal and differential area element are calculated. The intersection  $r_{ij}$  of this normal with each  $T_j$  is calculated, converted to the  $(u, v, w)$  coordinates in the finite element representation of the surface. If the  $(u, v)$  coordinates in the computational domain (which is a square) lie in the mesh triangle underlying  $T_j$ , then  $r_{ij}$  is the intersection of the normal with the minimal surface. The distance  $l = |p_i - r_{ij}|$  and  $l^2$  are calculated and multiplied by the differential area element and summed over the Gauss points.

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