The Role of Bilayer Tilt Difference in Equilibrium Membrane Shapes

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Abstract

Lipid bilayer membranes below their main transition have two tilt order parameters, corresponding to the two monolayers. These two tilts may be strongly coupled to membrane shape but only weakly coupled to each other. We discuss some implications of this observation for rippled and saddle phases, bilayer tubules, and bicontinuous phases. Tilt difference introduces a length scale into the elastic theory of tilted fluid membranes. It can drive an instability of the flat phase; it also provides a simple mechanism for the spontaneous breaking of inversion symmetry seen in some recent experiments.

The curvature model of fluid bilayer membranes has proved quite successful in explaining the shapes of membranes above their main transition [1]. In this model locality, coordinate invariance, and bilayer symmetry restrict the form of the energy functional for shapes to just two terms, involving the mean and Gauss curvature. In fixed topology the total Gauss curvature is constant, and so the minimum-energy conformation is a surface of vanishing mean curvature, for example a flat plane.

Below the main transition, additional degrees of freedom enter the elasticity of membranes as their hydrocarbon chains begin to order. In analogy to smectic liquid crystals, one expects a soft *tilt* degree of freedom to appear, reflecting the spontaneous breaking of rotational invariance in the plane. Helfrich and Prost began the systematic study of the mutual influence of tilt order and membrane shape [2]. A number of nonflat ground state phenomena found in membranes below their main transition have since been attributed to tilt, including rippled phases and tubule phases (see for example [3–6]). Tilt order also proves to be crucial for the intrinsic *chirality* of individual amphiphiles (if any) to influence the conformations of membranes [7].

Despite much progress, however, a number of mysteries remain in the study of one-component, symmetric bilayer membrane conformations. For example, experiments with racemic mixtures of lipids have found asymmetric ripple ground states, which are chiral [8]. Similarly, achiral amphiphiles can form tubules [9], which again appears to require chirality [4]. Even chiral lipids easily form helical ribbons of *either* handedness; sometimes a single ribbon appears to switch handedness in the middle of its growth [10]. Finally, cubic phases of bilayer membrane are predicted to be scale-invariant in the pure curvature model [11]. One might therefore expect them to collapse to a microscopic cell size, but in fact they can be stabilized at well-defined, mesoscopic scales [12]. Theoretically, selection of a length-scale of several nanometers has been attributed to higher order curvature terms both for cubic phases [11] and for a presumed hats and saddle super-structure of fluid bilayers [13].

In this letter we explore a new model for the conformation of membranes: we augment the curvature model with *two* tilt director fields corresponding to the two monolayers. Thus our work fits into the general program of taking more seriously the bilayer aspect of membranes, both in their equilibria and dynamics (e.g. [14–16]). When the directors are aligned we reproduce existing models; when they are not we get new physics. Imagining that the tilt in a monolayer induces spontaneous curvature orthogonal to its direction, in the corresponding bilayer the flat state with anti-parallel tilt then is frustrated and thus more costly than a saddle conformation in which the tilts are oriented orthogonal to each other. Without interaction between the two layers the flat state is always unstable locally against this kind of saddle conformation. Real membranes will always have at least some tendency to align the tilts. The instability will then occur only if the anisotropic spontaneous curvature is larger than a threshold value determined below.

There seems to be no direct experimental evidence for or against non-aligned tilt in bilayer phases. We will motivate the model, show how it gives a new mechanism for the transition from flat to rippled membranes, and comment on how it addresses the questions above.

Our work was first motivated by a desire to understand the origin of a nonanalytic curvature energy proposed by Fischer [17]. Our model is mathematically similar to one independently proposed by Fournier [18], but the physical motivation is quite different: while he considered an anisotropic *impurity* adsorbed onto a membrane, our tilt is an *intrinsic* property of a *pure* bilayer, and hence quite generic. Other differences will be noted below.

Model: We will restrict attention to systems of nonchiral amphiphiles. In the covariant notation developed in [7,19,22], this means we consider only elastic energy terms constructed without the in-plane antisymmetric tensor $\epsilon_{\alpha\beta}$. To focus attention on the new elements we will also impose an additional "nematic" symmetry (see below). This assumption is strictly for mathematical simplicity; we leave the full model to future work.

Above the main transition we imagine the membrane to be two identical 2-dimensional fluid sheets of elastic monomers, independent except for the constraint that they lie a fixed distance above and below a common surface. We will label the layers arbitrarily as "+" and "−", but since the layers are identical we will insist that nothing changes if we reverse the labeling. To define the curvature tensor $K_{\alpha\beta}$ we will choose the normal vector $\mathbf{N}$ pointing from the "−" to the "+" side. Each sheet has its own bending stiffness, stretching modulus, and spontaneous curvature. When we combine the sheets, the bending stiffnesses and stretching moduli add, while the spontaneous curvatures cancel (for details see e.g. [16]). We will neglect the stretchiness of the membranes, leaving only the curvature stiffness.

Below the main transition each monolayer develops a local average tilt. We will not be interested in the main transition itself, so we will take the director of the amphiphiles to be at a fixed angle to the layer normal, and the degree of ordering to be constant. In other words, we will describe the tilt by a pair of unit vector fields $\mathbf{m}_\pm$ tangent to the surface: these are the normalized projections of the average molecular directors. The elastic energy is then a local functional of $\mathbf{m}_+$, $\mathbf{m}_-$, and the membrane shape, described by its curvature tensor $K_{\alpha\beta}$. As mentioned above, we will rather artificially assume invariance when either $\mathbf{m}_+$ or $\mathbf{m}_-$ changes sign.

Traditionally one takes $\mathbf{m}_+ = -\mathbf{m}_-$ (e.g. see [19]), or in other words assumes that the average directors in each layer are collinear. The reasoning is that while an overall rotation of both $\mathbf{m}_\pm$ is related to a broken symmetry, still the *relative* angle is not, and so is expected to lock to a preferred value. We propose to explore what happens when this assumption is relaxed. Our motivation is the observation that the degree of interdigitation of the lipid chains between the layers is in fact quite small, as deduced for example from measurements of the interlayer friction coefficient [14]. We will allow for some weak aligning potential $g((\mathbf{m}_+ \cdot \mathbf{m}_-)^2)$, but as we will show other energetic contributions can readily overcome it. For simplicity we will continue to assume that g is minimized at $\mathbf{m}_+ = -\mathbf{m}_-$, but later on we will reconsider this assumption too. In ref. [18], g was taken to be zero, an extreme limit of our model.

While the direct interaction of the tilts may be small, there will certainly be an important *indirect* interaction mediated by the coupling of tilt to the common *shape*. To lowest order in the curvature tensor the effect of tilt on a monolayer is to create an anisotropic spontaneous curvature, by adding the terms

$$f^\pm = \beta\, K_{\alpha\beta} m_\pm^\alpha m_\pm^\beta \equiv \beta\, \mathbf{m}_\pm \cdot \mathsf{K} \cdot \mathbf{m}_\pm \tag{1}$$

to the elastic free energy. β is a new parameter depending on the degree of ordering [20]. The combination $f^+ - f^-$ is then invariant under renaming the two leaves of the bilayer. It vanishes if $\mathbf{m}_+ = -\mathbf{m}_-$, but more generally we need to keep these terms. At higher order in curvature we have the more familiar terms $\kappa_3(K_{\alpha\beta}m_\pm^\alpha m_\pm^\beta)^2+\kappa_4 K_{\alpha\beta}K_{\beta\gamma}m_\pm^\alpha m_\pm^\gamma$ (see [22]). Since (1) will already drive our instability we will neglect the higher-curvature $\kappa_3,\ \kappa_4$ terms. All told, then, our simplified model is defined by the elastic energy density functional

$$\begin{aligned} f &= \tfrac{\kappa_1}{2}(K_\alpha{}^\alpha)^2+\tfrac{\kappa_2}{2}K_{\alpha\beta}K^{\alpha\beta}+g((\mathbf{m}_+\cdot\mathbf{m}_-)^2) \\ &+\sum_{\mathbf{m}=\mathbf{m}_\pm}\left[\pm\beta K_{\alpha\beta}m^\alpha m^\beta+\tfrac{k_1}{4}\nabla_\alpha m^\beta\nabla^\alpha m_\beta+\tfrac{k_2}{4}(\nabla_\alpha m^\alpha)^2\right]. \end{aligned} \tag{2}$$

The constants $\kappa_1,\ \kappa_2$ are related to the usual mean and Gaussian rigidities, while $k_1,\ k_2$ are related to the usual rigidities of the XY model.

A remarkable feature of (2) is that the parameter β has dimensions of inverse length. This is a key qualitative difference from the case of parallel tilt directors: achiral symmetric bilayers with one tilt admit only *dimensionless* couplings [23,19]. One might expect that the value of such a parameter would be very large, on the order of the microscopic wavenumber, and would create correspondingly small structures. From its geometric origin, however, it is easy to see how β could be smaller than naïve dimensional analysis would suggest. For example, the average tilt could be rather small, leading to a small net spontaneous curvature. In this way our term could set a mesoscopic scale.

Stability of flat surfaces: To understand the physics of the model (2), we first note that if the director in the "+" layer is pointing in the x direction, and the one in the "−" layer in the y direction, the β term becomes $\beta[K_{xx}-K_{yy}]$, which favors saddles (or other non-spherical shapes).

For a quantitative stability analysis of the flat state in which both nematic fields are parallel, we need an explicit form of the interaction g. A simple form that favors parallel alignment is $g=\gamma(1-(\mathbf{m}_+\cdot\mathbf{m}_-)^2)/2$. We parametrize small deviations from this parallel state for the director fields as $\mathbf{m}_\pm=\binom{\cos\phi}{\pm\sin\phi}\approx\binom{1-\phi^2/2}{\pm\phi}$. In this representation, the coupling term between the two layers becomes $g=2\gamma\phi^2$.

Adding up all energies to quadratic order in a Fourier representation for $\phi(x,y)$ and the height $h(x,y)$ leads to

$$f = \tfrac{\kappa}{2}(\mathbf{q}^2)^2 h_{\mathbf{q}}^2 + 4\beta q_x q_y h_{\mathbf{q}}\phi_{\mathbf{q}} + 2\gamma\phi_{\mathbf{q}}^2$$
$$+ \quad \left(\tfrac{k_1}{2}(q_x^2+q_y^2) + \tfrac{k_2}{2}q_y^2\right)\phi_{\mathbf{q}}^2 \qquad (3)$$

with $\kappa \equiv \kappa_1 + \kappa_2$. Minimizing with respect to $h_{\mathbf{q}}$ yields $h_{\mathbf{q}} = -4\beta\frac{q_x q_y}{\kappa(\mathbf{q}^2)^2}\phi_{\mathbf{q}}$. Inserting this result into (2) leads to the effective energy for the ϕ field as

$$f = \left[\frac{-8\beta^2 q_x^2 q_y^2}{\kappa(\mathbf{q}^2)^2} + 2\gamma + \frac{k_1}{2}(q_x^2+q_y^2) + \frac{k_2}{2}q_y^2\right]\phi_{\mathbf{q}}^2 \ . \qquad (4)$$

The stability criterion for the flat phase is now obvious. For weak enough interlayer coupling,

$$\gamma < \beta^2/\kappa, \qquad (5)$$

the flat phase becomes unstable to a long-wavelength modulation. This is our main result. The preferred directions for the q vectors are $q_x = \pm q_y = \pm\sqrt{\mathbf{q}^2}/2$. Adding just two modes with $\mathbf{q}_1 = -\mathbf{q}_2$ yields a ripple shape whereas adding four modes with $\pm q_x = \pm q_y$ leads to a egg-carton-like square modulated phase.

Lubensky and MacKintosh also obtained symmetric ripples in a nonchiral model. Then balanced an effectively negative $(\nabla\mathbf{m})^2$ term against a stabilizing $(\nabla^2\mathbf{m})^2$ term [3]. Far from the main transition such a balance is likely to select a microscopic length scale. In contrast, we have seen how our model can select long lengths. Other models assumed hexatic order [3,5], while we have not.

Beyond instability: In order to distinguish the two alternatives, ripple or saddle, we have to go beyond the instability. We will do so in the following using exact analysis, a simple variational shape and numerical minimization. To keep our formulas tractable, in this section we will neglect the tilt stiffness terms, i.e. we set $k_1 = k_2 = 0$. Thus the tilt fields track the curvature exactly, and in particular can change discontinuously by $\pi/2$ when the mean curvature changes sign. A more realistic model would broaden these discontinuities into domain walls, with an energy cost per unit length.

First, we discuss the ripple phase. For a one-dimensionally modulated conformation, the free energy density takes the form

$$
\begin{aligned}
f = \quad & (\kappa/2)(h_{xx})^2 + \beta h_{xx}(\cos^2\phi^+ - \cos^2\phi^-) \\
& + \tfrac{\gamma}{2}(1 - (\cos\phi^+\cos\phi^- + \sin\phi^+\sin\phi^-)^2).
\end{aligned} \tag{6}
$$

One could try as a trial variational function a sinusoidal ripple with wavenumber q and height h_q and nematic fields always arranged perpendicular to each other which leads to an energy density of $f/\kappa = -\frac{1}{2}(\beta^2\frac{8}{\pi^2} - \gamma)$. However one can easily see that the sinusoidal shape is far from optimal. If the tilts are orthogonal, thus rendering the β term $-|\beta h_{xx}|$, ripples that consist of circular arcs of radius κ/β are lower in energy than sinusoidal ripples. A straightforward calculation shows that allowing the fields to assume a non-orthogonal configuration does not lead to a lower energy for $\gamma < \beta^2/\kappa$ which is the region of interest. Thus, in summary, as long as only one-dimensionally modulated phases are considered, a ripple phase consisting of circular arcs with the nematic fields orthogonal in the two layers is the most favorable configuration. Due to the absence of gradient terms for the director fields, these fields jump whenever the curvature changes sign. Including the gradient terms would thicken the jump region to a domain wall; the energy of this wall would then favor long wavelength (fewer walls per unit length), breaking the degeneracy we have found so far.

When modulation of the membrane in two dimensions is allowed, the free energy density takes the form

$$
\begin{aligned}
& f = (\kappa/2)(h_{xx} + h_{yy})^2 + (\gamma/2)(1 - \cos^2(\phi^+ - \phi^-)) \\
& + \beta[h_{xx}(\cos^2\phi^+ - \cos^2\phi^-) + h_{yy}(\sin^2\phi^+ - \sin^2\phi^-) \\
& \qquad + h_{xy}(\sin 2\phi^+ - \sin 2\phi^-)].
\end{aligned} \tag{7}
$$

Again a variational trial function sinusoidal in two directions is not the best choice. It leads to an energy density of $f/\kappa = -\frac{1}{2}(\beta^2\frac{64}{\pi^4} - \gamma)$. Using the fact that the lowest energy ripple conformation had constant curvature, we construct a saddle phase in which the curvature is piecewise constant. This leads to a saddle conformation in which the corrugations are parabolic arcs. In regions where the principal curvatures have the same sign, we allow the nematic fields to be parallel (thus gaining from the γ term), and where they have opposite signs the fields remain orthogonal. The free energy density of this state is $f/\kappa = -\frac{1}{4}(\beta^2 - \gamma)$. This energy is never lower than either the flat phase or the circular arc ripples even though it improves the value of the sinusoidal saddle for a large range of γ values.

Having exhausted the range of analytic saddle conformations, we turned to a numerical minimization of the full free energy (7). While we could improve on the parabolic saddles, still we found no saddle phase with lower energy than either the circular ripples or the flat phase.

Discussion: We have not obtained a unique wave-length for the instability. What we found was rather that the tilt-difference coefficient β sets a preferred *curvature* for cylindrical segments. For small amplitudes this means that the combination $h_q q^2$, but not q itself, is fixed. This happened because we neglected the gradient terms in the tilt fields: the energy of a configuration is then invariant under a rescaling of $h(x,y) \to \lambda h(\lambda x, \lambda y)$ if at the same time $\gamma \to \gamma/\lambda^2$ and $\beta \to \beta/\lambda$. Gradient terms in $\mathbf{m}$, of course, would favor large wave-length, up to a maximum of $\sim \kappa/\beta$, where the membrane rolls up into cylinders. One way to stabilize finite-wavelength ripples would be to stretch the membrane with a lateral tension.

Alternatively we can take our results as indicating an instability to a phase of cylinders or other curved objects, especially saddles. Particularly intriguing is the possibility that the tilt-difference term could set a scale for bicontinuous phases without resorting to microscopic (higher-curvature) terms as in [11].

We now consider briefly the possibility of breaking spatial inversion symmetry. Other authors have obtained rippled or striped phases in tilted bilayers by explicitly breaking parity invariance (e.g. [3,4]). In particular, explicit parity-violating terms in the free energy have so far been necessary to obtain *asymmetric*, or sawtooth, rippled phases. But the presence of chiral amphiphiles does not guarantee a parity-breaking Landau energy [24]. Moreover as mentioned earlier, several arguments point to the possibility of *spontaneous breaking* of parity invariance: the Landau energy has parity invariance, but its *minima* do not.

In an elegant paper, Selinger *et al.* have proposed possible mechanisms for spontaneous parity breaking in monolayers [25]. Two of these could also apply to pure bilayers: (a) if the membrane has both tilt and hexatic order, the corresponding directors may lock to a fixed, nonzero *relative* angle; (b) conceivably two distinct local packings of molecules could be preferred, each of which is the other's mirror image. We would like to point out a very simple, concrete option with some elements of each of these: (c) a tilted membrane may prefer on packing grounds to order its two tilt directors at a fixed relative angle $\alpha = \pm\alpha_0$, i.e. $\mathbf{m}_+ \cdot \mathbf{m}_- = \cos\alpha_0$. This option may prove more generic than the ones above.

To see how our proposal leads to parity breaking, note that $\psi \equiv (\mathbf{m}_+ \times \mathbf{m}_-) \cdot \mathbf{N}$ is a well-defined pseudoscalar order parameter. ψ vanishes as $\alpha \to 0$, as required.

We can write $\mathbf{m}_\pm = \begin{bmatrix} \cos\alpha/2 & \pm\sin\alpha/2 \\ \mp\sin\alpha/2 & \cos\alpha/2 \end{bmatrix} \mathbf{m}$, where $\mathbf{m}$ is a common tilt variable. Writing $\mathbf{1}$ for the unit matrix and $\varepsilon = \begin{bmatrix} 0 & 1 \\ -1 & 0 \end{bmatrix}$, the terms (1) now read

$$\begin{aligned} f^+ - f^- = \beta\mathbf{m} \cdot [&(\cos\tfrac{\alpha}{2}\mathbf{1} - \sin\tfrac{\alpha}{2}\varepsilon)\mathsf{K}(\cos\tfrac{\alpha}{2}\mathbf{1} + \sin\tfrac{\alpha}{2}\varepsilon) \\ &- (\cos\tfrac{\alpha}{2}\mathbf{1} + \sin\tfrac{\alpha}{2}\varepsilon)\mathsf{K}(\cos\tfrac{\alpha}{2}\mathbf{1} - \sin\tfrac{\alpha}{2}\varepsilon)] \cdot \mathbf{m}\ . \end{aligned} \tag{8}$$

Rewriting this as $(2\beta\sin\frac{\alpha}{2})\mathbf{m}\cdot[\varepsilon\mathsf{K}]\cdot\mathbf{m}$, we recognize the chiral tilt-shape coupling introduced by Helfrich and Prost [2], in the coordinate-invariant form given in [19]. This is precisely the term responsible for the formation of asymmetric ripples in the work of Lubensky and MacKintosh [3]. A similar analysis, dropping the requirement of nematic symmetry, could also yield the chiral term which gives rise to tubules and helices [4].

In conclusion, we have shown that tilt difference may be expected quite generally to affect the conformations of symmetric bilayer membranes, introducing a new intermediate length scale and favoring cylindrical and saddle curvature over flat or spherical shapes. Tilt difference could also provide an attractively general mechanism for the spontaneous breaking of parity invariance.

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