

## Deviatoric spontaneous curvature of lipid membranes induced by Siamese macromolecular cosurfactants

C. M. MARQUES<sup>1</sup>(\*) and J. B. FOURNIER<sup>2</sup>(\*\*)

<sup>1</sup> *Department of Chemical Engineering, University of California  
Santa Barbara, California 93106, USA*

<sup>2</sup> *Materials Department, University of California  
Santa Barbara, California 93106, USA*

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**Abstract.** – We study the anisotropy of the spontaneous curvature induced by a membrane inclusion consisting of two geminated polymer-lipid molecules. The anisotropy is found to be of the order of the mean spontaneous curvature. Such a strong anisotropy yields a significant reduction of the membrane bending rigidity  $K$  as well as an increase of the saddle splay  $\bar{K}$ , which might lead to curvature instabilities.

Inclusions play an important role in lipid bilayers. In biological membranes, for instance, protein inclusions add functionality to the cell wall [1]: they provide specific receptor sites for host proteins, act as ionic pumps or hold the spectrin cytoskeleton. They also play a role in controlling membrane elasticity [2], an effect which has been extensively studied in surfactant bilayers. In these systems, small inclusions such as cosurfactants are commonly used to lower the bending rigidity of the bilayer [3]. Typically, the rigidity can be reduced from its bare value of order  $20 k_B T$  to a few  $k_B T$ . Another important effect of inclusions is that they can induce spontaneous curvature. However, a density difference is required across the membrane, otherwise there is a compensation resulting in a zero curvature. In biological membranes, a typical example is the crenation effect caused by the adsorption of small anaesthetic drugs on the exterior half of a red-blood-cell membrane [4]. It has recently been realized that *anisotropic inclusions* can induce a nonzero membrane curvature even when they have the same density on both sides of the bilayer [5]. Such inclusions promote different spontaneous curvatures in the directions parallel and perpendicular to their orientation in the plane of the membrane. Whereas the spontaneous curvatures of two isotropic inclusions do compensate when they face

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(\*) On leave from Institut Charles Sadron, 68083 Strasbourg Cedex, France.

(\*\*) On leave from Laboratoire de Physique des Solides, Université Paris-Sud, Bât. 510, F-91405 Orsay, France.

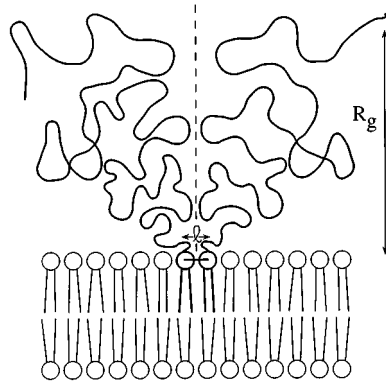


Fig. 1. – Schematic representation of a Siamese lipid-polymer molecule embedded in a lipid membrane.

each other across the bilayer, the corresponding effect for anisotropic inclusions adds up when they orient at right angles. In order to study this effect, it is important to tailor molecules with a strong deviatoric bending strength.

We propose a molecular architecture with this property, by combining two effects (fig. 1). First, the spontaneous curvature induced by polymer chains grafted on a surface. This feature has been studied both in the so-called brush regime [6], [7], where the grafted polymers interact strongly, and in the mushroom regime as a single-chain effect [8], [9]. Water-soluble polymers, such as poly(ethylene glycol), attached to lipid surfactants (PEG-lipids) are used to induce spontaneous curvature in fluid membranes and to promote arrays of defects resulting in gel phases [10]. The second effect relies on the asymmetry introduced by gemination of two molecules. In small surfactants, gemination has been studied [11] and is known to promote formation of thread-like micelles [12], [13]. Gemination of macromolecular surfactants can in principle lead to molecules with a strong and tunable spontaneous anisotropic curvature.

Macromolecular surfactants grafted to liquid membranes, as the PEG-lipid molecules mentioned above, are water-soluble polymers (typically PEO) chemically attached to a lipid molecule, the function of which is to anchor the polymer to the membrane. For the sake of simplicity we assume that the lipid anchor is identical to the membrane molecules, and therefore it has no effect on the properties of the inclusions. Each of the twin polymers in our Siamese macromolecule can then be regarded as a chain grafted to an impenetrable surface, the anchors being chemically connected by a rigid spacer of length  $\ell$  <sup>(1)</sup>.

The configuration of each arm is determined by the excluded-volume interactions within and between the chains, and the hard-wall repulsion from the membrane. A complete calculation that would include all these interactions in an arbitrarily curved geometry is a rather formidable task that is beyond the scope of this letter. In order to simplify the problem while retaining the main effects of the curvature and interarm repulsion, we model our Siamese molecules by two Gaussian chains grafted, at a distance  $\ell$  apart, to an impenetrable curved surface. The repulsion between the two arms is accounted for by prohibiting each arm to penetrate the space occupied by the other. Technically this is achieved by placing a hard-wall at the midplane of the two molecules (see fig. 1 and 2). This clearly overestimates the interarm repulsion but allows for calculating an upper bound to the spontaneous curvature anisotropy.

<sup>(1)</sup>This spacer itself provides a contribution to the bending rigidity of the order of  $kT\ell_p\ell$  per molecule, where  $\ell_p$  is the spacer persistence length. However, it does not contribute to the spontaneous curvature.

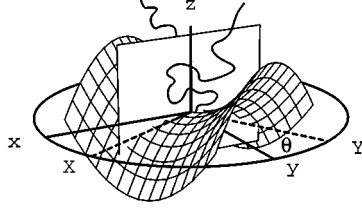


Fig. 2. – Geometry of the membrane surface where the Siamese molecule is grafted. The middle plane separating the two polymer coils is rotated by an angle  $\theta$  with respect to the saddle's principal axes.

The free energy for our calculation is that of two Gaussian chains tethered to a surface with equation  $z = \xi(x, y)$ . The grafting points are  $(\pm l/2, 0, \xi(x, y) + a)$  with  $a$  the typical monomer length. The impenetrable midplane is the  $x = 0$  plane (fig. 2). The partition function of each chain is  $Z(\frac{l}{2}, 0, \xi(x, y) + a; N)$ , with

$$Z(\mathbf{r}; N) = \int d\mathbf{r}' G_N(\mathbf{r}, \mathbf{r}'), \quad (1)$$

where  $G_N(\mathbf{r}, \mathbf{r}')$ , the Green function of the Gaussian polymer, obeys the Edwards equation [14]

$$\frac{a^2}{6} \Delta_{\mathbf{r}} G_N(\mathbf{r}, \mathbf{r}') = \frac{\partial G_N}{\partial N}(\mathbf{r}, \mathbf{r}'), \quad (2)$$

with the following boundary conditions:  $G_N(\mathbf{r}, \mathbf{r}') = 0$  at the walls  $x = 0$  and  $z = \xi(x, y)$ , and  $G_{N \rightarrow 0}(\mathbf{r}, \mathbf{r}') = \delta(\mathbf{r} - \mathbf{r}')$ .

In the reference, flat case ( $\xi(x, y) = 0$ ), the Green function  $G_N^{(0)}(\mathbf{r}, \mathbf{r}')$  can be factorized as  $G_N^{(0)}(\mathbf{r}, \mathbf{r}') = G_N^{(0)}(x, x') \times G_N^{(0)}(y, y') \times G_N^{(0)}(z, z')$ , leading to

$$G_N^{(0)}(\mathbf{r}, \mathbf{r}') = \left[ \frac{3}{2\pi a^2 N} \right]^{3/2} \left( \exp \left[ -\frac{3}{2} \frac{(x-x')^2}{Na^2} \right] - \exp \left[ -\frac{3}{2} \frac{(x+x')^2}{Na^2} \right] \right) \times \\ \times \exp \left[ -\frac{3}{2} \frac{(y-y')^2}{Na^2} \right] \times \left( \exp \left[ -\frac{3}{2} \frac{(z-z')^2}{Na^2} \right] - \exp \left[ -\frac{3}{2} \frac{(z+z')^2}{Na^2} \right] \right). \quad (3)$$

From eq. (1), the partition function is

$$Z^{(0)}(\mathbf{r}; N) = \text{erf} \left[ \frac{x}{2R_g} \right] \times 1 \times \text{erf} \left[ \frac{z}{2R_g} \right], \quad (4)$$

where  $R_g = \sqrt{Na^2/6}$  is the gyration radius of the chain, and erf is the error function [15].

In order to calculate the deviation from the flat case, we consider a weakly curved membrane of equation  $z = -\frac{1}{2}X^2/R_1 - \frac{1}{2}Y^2/R_2$  in the frame of its axes of principal curvature. In general, these axes are at an angle  $\theta$  with respect to the reference frame  $xyz$  of the Siamese molecule, and the membrane equation reads

$$\xi(x, y) = -\frac{1}{2} \left( \frac{1}{R_1} \cos^2 \theta + \frac{1}{R_2} \sin^2 \theta \right) x^2 - \left( \frac{1}{R_1} - \frac{1}{R_2} \right) \cdot \\ \cdot \sin \theta \cos \theta x y - \frac{1}{2} \left( \frac{1}{R_1} \sin^2 \theta + \frac{1}{R_2} \cos^2 \theta \right) y^2. \quad (5)$$

We seek for a perturbative solution to the partition function of the form

$$Z = Z^{(0)} + \frac{1}{R_1} Z_1^{(1)} + \frac{1}{R_2} Z_2^{(1)} + \dots, \quad (6)$$

where  $Z^{(0)}$  is defined in eq. (4). Each perturbative term obeys an Edwards equation

$$\frac{a^2}{6} \Delta_{\mathbf{r}} Z_i^{(1)} = \frac{\partial Z_i^{(1)}}{\partial N} \quad (i = 1, 2), \quad (7)$$

with boundary conditions  $Z_1^{(1)}(x, y, 0) = (\frac{1}{2}x^2 \cos^2 \theta + xy \sin \theta \cos \theta + \frac{1}{2}y^2 \sin^2 \theta) \times \partial Z^{(0)} / \partial z|_{z=0} \equiv f_1(x, y)$ ;  $Z_1^{(1)}(0, y, z) = 0$  and a similar set of BCs for  $Z_2^{(1)}$ . The magic-rule solution [16] to the diffusion equations (7) allows then to write

$$Z_1^{(1)}(\mathbf{r}; N) = \frac{a^2}{6} \int_0^N dN' \int_0^\infty dx' \int_{-\infty}^\infty dy' f_1(x', y'; N') \times \\ \times \frac{\partial G_{N-N'}^{(0)}}{\partial z'}(x, y, z, x', y', z')|_{z'=0}. \quad (8)$$

The  $xy$  contribution from  $f_1$  to the magic rule vanishes because the average  $\langle y \rangle$  is zero for a Gaussian integral in the free space. The  $x^2$  and  $y^2$  contributions correspond to the particular cylindrical surfaces with axis parallel and perpendicular to the Siamese midplane  $x = 0$ , respectively. In the limit of interest where the mushrooms interact strongly,  $|\mathbf{r}| \ll R_g$ , we get

$$Z(\mathbf{r}) = \frac{xz}{\pi R_g^2} \left[ 1 + \frac{7\sqrt{\pi} R_g}{8} \left( \frac{1}{R_1} + \frac{1}{R_2} \right) + \frac{3\sqrt{\pi} R_g}{8} \left( \frac{1}{R_1} - \frac{1}{R_2} \right) \cos 2\theta \right]. \quad (9)$$

The free energy of the two-arm Siamese molecule  $F = -2k_B T \ln Z(\frac{\ell}{2}, 0, \xi(x, y) + a; N)$  can be written as

$$F = F_0 + \alpha \left( \frac{1}{R_1} + \frac{1}{R_2} \right) + \omega \left( \frac{1}{R_1} - \frac{1}{R_2} \right) \cos 2\theta, \quad (10)$$

with the coefficients  $\alpha$  and  $\omega$  given by

$$\alpha = -\frac{7\sqrt{\pi}}{4} k_B T R_g, \quad \omega = \frac{3\sqrt{\pi}}{4} k_B T R_g, \quad (11)$$

to leading order in  $a/R_g$ . The anisotropy of the spontaneous curvature  $\omega/\alpha$  is therefore, for this Siamese molecule, of order unity. Note that the curvature contribution in (10) has the same structure as the coupling between an anisotropic inclusion described by an in-plane orientation vector and the curvature tensor [5]. At first order in curvature, the three-dimensional structure of the polymers is thus effectively reduced to a nematic-like order parameter.

It has been shown [5] that anisotropic inclusions with spontaneous curvature of the form (10) renormalize the elastic constants of the membrane  $K$  and  $\bar{K}$  according to

$$\Delta K = -\frac{1}{2} \Delta \bar{K} = -\frac{\sigma \omega^2}{2k_B T}, \quad (12)$$

where  $\sigma$  is the surface density of the inclusions. From eqs. (11) we obtain

$$\Delta K = -\frac{1}{2} \Delta \bar{K} = -\frac{9\pi}{32} k_B T \sigma R_g^2. \quad (13)$$

This anisotropically induced renormalization of the bending constants is of opposite sign to the usual contribution from isotropic polymer inclusions which tend to increase  $K$  and reduce  $\bar{K}$ . For instance, from eq. (8), in the limit  $|\mathbf{r}| \gg R_g$ , we obtain for a single-arm grafted polymer  $\Delta K = (\pi + 2)/2 k_B T \sigma R_g^2$  and  $\Delta \bar{K} = -2k_B T \sigma R_g^2$ . Although the explicit calculation of the bare contribution of the Siamese molecule to the bending constants is beyond the scope of this

paper, we expect that contribution to be of the same order of magnitude of the renormalization induced by the anisotropy of the spontaneous curvature (13). This leads to several interesting possibilities when Siamese molecules are grafted to lipid bilayers. For instance, dense coating of membranes with grafted polymers could be achieved without significantly increasing the rigidity by using such Siamese molecules. Also, these molecules might drive instabilities by lowering the rigidity constant  $K$  leading to the formation of cylindrical vesicles [5] or gel phases induced by a high defect density in lamellar systems [10].

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