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Solvent Driven Formation of Bolaamphiphilic Vesicles

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Abstract

We show that a spontaneous bending of single layer bolaamphiphiles results from the frustration due to the competition between core-core and tail-solvent interactions. We find that spherical vesicles are stable under rather general assumptions on these interactions described within the Flory-Huggins theory. We consider also the deformation of the vesicles in an external magnetic field that has been recently experimentally observed.

Molecular aggregates, like biological matter, possess the ability to organize into well defined mesoscopic structures, such as layers, fibers, vesicles[1, 2, 3, 4]. Addressing this issue for molecular aggregates is relevant not only for applications in pharmacology, catalysis, and other fields, but also to understand the behaviour of model systems simpler but related to biological matter. The self-organized structures result from the concomitant effect of non-covalent interactions, such as hydrogen bonding and $\pi - \pi$ stacking between molecules, as well as by entropic contributions. A theory capable of predicting the shape of the aggregate from the knowledge of the microscopic molecular structure is still missing. Among the forms of self-organization, the formation of empty vesicles in, possibly aqueous, solution is particularly important for the wealth of possible applications, from microreactors to drug delivery. Surprisingly, vesicle formation has been observed not only in the well known case of amphiphiles bilayers, like lipid membranes[1, 2, 5] but also in several bolaamphiphiles[6, 7, 8] formed by an hydrophobic core and two, usually symmetric, lateral hydrocarbon tails terminated by hydrophilic groups[9]. Notice that the term bolaamphiphiles has been first introduced to describe synthetic analogs of archaebacterial membranes[10, 11]. Here we provide a model predicting spontaneous bending due to frustration resulting from competing core-core and tail-solvent interactions.

We refer, in particular, to the case of sexithiophenes bolaamphiphiles (see Fig. 1) that have been found to form vesicles albeit in isopropanol[8]. The formation of stable vesicles seems to be favoured by increasing length of the tails[7]. Conversely, layer-like structures have been found in liquid crystal bolaamphiphiles with short or rigid lateral blocks[12, 13].

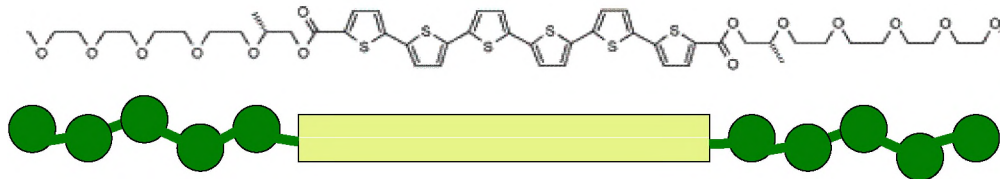


Figure 1: Structural formula of 2,5''''-(R-2-methyl- 3,6,9,12,15-pentaoxahehexadecyl ester) sexithiophene and its schematic representation.

We consider a simplified model of a bolaamphiphile layer with the cores on a two-dimensional surface and symmetric flexible tails, each formed by m monomers as sketched in Fig.2.

As illustrated in Fig.3, the cores define a surface S_0 with local coordinates (u_1, u_2) such that $\vec{r}_0 = \vec{r}(u_1, u_2)$ gives cartesian coordinates on the surface. If the tails, due to covalent bonding to the cores, tend to be perpendicular to the surface, the interactions with the solvent are supposed to take place on the two surfaces S_{\pm} with coordinates

$$\vec{r}_{\pm} = \vec{r}(u_1, u_2) \pm \vec{n}(u_1, u_2)D \quad (1)$$

where \vec{n} is the vector normal to S_0 and D is the effective length of the tails.

The elementary area vector on S_0 is

$$d\vec{S}_0 = (\vec{r}_1 \times \vec{r}_2) du_1 du_2 \quad (2)$$

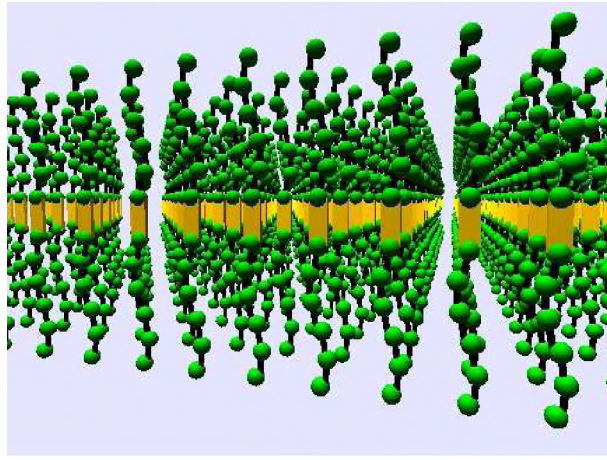


Figure 2: Sketch of a layer formed by self-assembled bolaamphiphiles. The spacing between hydrophilic tails (green) is fixed by the hydrophobic cores (yellow) to a value which might be not optimal for tail-solvent interactions.

where $\vec{r}'_i = \partial \vec{r} / \partial u_i$. The derivative of the normal \vec{n} with respect to u_i is given by the so-called Weingarten equations[15], whence

$$d\vec{S}_\pm = d\vec{S}_0 (1 \mp 2HD + KD^2) \quad (3)$$

where $H = (\kappa_1 + \kappa_2)/2$ and $K = \kappa_1\kappa_2$ are, respectively, the mean and gaussian curvature defined in terms of the principal curvatures κ_1 and κ_2 . The tail density in contact with the solvent is determined by the tail density n_0 imposed by the core so that $n_\pm d\vec{S}_\pm = n_0 d\vec{S}_0$ leading to an exact expression for the tail density on S_\pm in terms of the curvature

$$n_\pm = \frac{n_0}{1 \mp 2HD + KD^2}. \quad (4)$$

If the tails were not rigidly connected to the cores, they would form a solution with free energy per unit volume

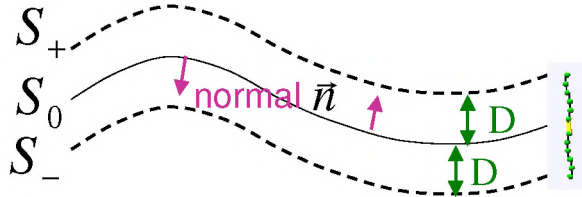


Figure 3: Schematic geometry of our model. The surface S_0 is the locus of the center of mass of the hydrophobic cores and S_\pm are the surfaces formed by the tail ends. The unit vector \vec{n} is normal to all three surfaces and D is the effective tail length.

$\phi(n)$. Therefore, we write the bending free energy as

$$\delta F = D \int dS [\phi(n_+) + \phi(n_-)] + A \int dS H^2 + B \int dS K. \quad (5)$$

The first term is the free energy of the tail/solvent subsystem whereas the terms proportional to A and B represent the bending elasticity of the core layers[1, 2, 5]. To account phenomenologically for bent surfaces for lipid bilayers, the term AH^2 is usually replaced by the so-called Canham-Helfrich (CH) bending energy $A(H - H_0)^2$ with $A > 0$ so that negative linear terms in H are responsible for bending[1]. However, the CH expression is not appropriate for symmetric bolaamphiphiles where odd terms vanish by symmetry. Moreover, the spontaneous curvature H_0 is introduced phenomenologically and is not justified by any microscopic model. We also note that the term $B \int dS K$ is usually neglected because due to the Gauss-Bonnet theorem[15] it is constant within a given topology of the surface and it actually depends on the number of handles. We consider

mesoscopic vesicles with curvature much larger than the molecular size, namely $|\kappa_i|D \ll 1$. Within this approximation we can expand $\phi(n_{\pm})$ up to second order in D as

$$\begin{aligned} \phi(n_{\pm}) &= \phi(n_0) \pm n_0 \phi'(n_0) 2HD + \\ &+ n_0 \phi'(n_0) [4H^2 D^2 - KD^2] + \frac{1}{2} n_0^2 \phi''(n_0) 4H^2 D^2 \end{aligned} \quad (6)$$

where $\phi'(n_0) = d\phi/dn|_{n=n_0}$ and $\phi''(n_0) = d^2\phi/dn^2|_{n=n_0}$. Notice that the sum of the terms linear in H in the integrand of Eq.5 vanishes whereas other terms contribute to the term proportional to H^2 so that

$$A \rightarrow \tilde{A} = A + \delta A = A + 4D^3 [n_0^2 \phi'' + 2n_0 \phi'] \quad (7)$$

We will show that \tilde{A} can become negative and lead to spontaneous bending as a result of the microscopic tail/solvent interactions. The reason for a negative δA is that the available volume per tail on the two sides of a bent surface may be different and a specific curvature can minimize the resulting free energy.

We can further specify the driving term δA by calculating it, within the Flory-Huggins theory for polymers solvent mixtures[14, 1]

$$\begin{aligned} \frac{\phi(n)}{T} &= \chi \frac{m n n_1}{n_1 + m n} + \\ &+ n_1 \ln \left(\frac{n_1}{n_1 + m n} \right) + n_2 \ln \left(\frac{m n}{n_1 + m n} \right) \end{aligned} \quad (8)$$

where n_1 is the solvent density, m is the number of monomers per tail, $\chi \sim (2W_{ts} - W_{ss} - W_{tt})/T$ with W_{ts} , W_{ss} and W_{tt} the tail-solvent, solvent-solvent and tail-tail interaction energies respectively and T is the temperature. Substitution of Eq.8 into Eq.7 gives

$$\begin{aligned} \frac{\delta A}{T} &= \frac{2\chi m n_1^3 n_0}{(n_1 + m n_0)^2} - \frac{n_1}{(n_1 + m n_0)^2} \cdot \\ &\cdot [m(m-2)n_0 + (2m-3)n_1] \end{aligned} \quad (9)$$

For hydrophilic tails, $\chi < 0$ leading to a free energy gain for bent surfaces. This constitutes a possible microscopic mechanism for vesicle formation, albeit within the Flory-Huggins theory which is more qualitative than quantitative[16]. Furthermore, the last term that accurately represents entropy is always negative unless $m = 1$ and increases as m^2 for $m \gg 1$. The observation of planar structures in liquid crystals bolaamphiphiles with rigid tails could be explained by this entropic reason. This completes our microscopic analysis. Our model leads naturally to a negative contribution to the free energy of the term quadratic in the curvature that does not need to be imposed phenomenologically as done for amphiphile bilayers.

Our results can be cast in the form of an effective Landau Hamiltonian, i.e. we can write the free energy F as a Taylor expansion in terms of the curvatures H and K . These quantities, or more precisely κ_1 and κ_2 , take the apparent role of order parameters assuming their smallness in comparison to a typical inverse molecular size. However, κ_1 and κ_2 are not independent at different points of the surface, implying that F is not a true Landau Hamiltonian and that a local analysis is insufficient. In fact, the local free energy density has not a minimum but a saddle point for a sphere ($\kappa_1 = \kappa_2$) if $c_2 + 2c_3 < 0$, in contradiction with the numerical data presented below. Since the term proportional to H^2 resulting from our microscopic model is negative, higher order terms are needed to stabilize the mean curvature to a finite value. Up to fourth order terms in κ_1 and κ_2 we can write

$$F = \int dS [-|A|H^2 + bHK + b'H^3 + c_1H^4 + c_2H^2K + c_3K^2] \quad (10)$$

The odd terms in b and b' that can lead to first order phase transitions have to vanish for the symmetric bolaamphiphiles considered here so that we take $b = 0$ and $b' = 0$. Moreover, $c_1 + c_2 + c_3 > 0$. Since, in general, the bending energy is much smaller than the surface tension, we go to the limit of infinite surface tension that allows to perform minimization of F on a surface of constant area. We have minimized Eq.10 numerically for surfaces topologically equivalent to spheres with radius $R = \sqrt{2(c_1 + c_2 + c_3)/|A|}$ and found that spheres are always the solution.

Our model can be extended to consider the recently observed effect of external magnetic fields B on the equilibrium shape of bolaamphiphilic vesicles[8]. To this purpose we add to Eq.10 the diamagnetic energy term

$$E_{mag} = - \sum_i \frac{D_i B^2}{2\mu_0} \int dS \left(\chi_{\perp}^i \sin^2 \theta + \chi_{\parallel}^i \cos^2 \theta \right) \quad (11)$$

where D_i is the effective thickness of the core layer ($i = 1$) or of the tails ($i = 2$), χ_{\perp}^i , χ_{\parallel}^i are the components of the corresponding magnetic susceptibility and θ is the polar angle of the direction of the magnetic field B . Due to the tendency of the aromatic rings in the core segment to align parallel to the magnetic field, the spherical vesicles will be transformed into ellipsoids, as predicted by Helfrich[17] for amphiphilic bilayers. This deformation in high magnetic fields has been recently observed experimentally for sexithiophene[8], that is an example of symmetric bolaamphiphiles[8] where the CH model of free energy is not correct. In Fig.4 we present the deformation calculated by minimizing the sum of Eqs. 10 and 11 for constant surface as a function of magnetic field, compared to the one resulting from the CH model. In both cases, the deformation is proportional to B^2 for low fields and flattens out as the field increases. However, for the same initial slope, our model predicts smaller deformations at high fields, the details of the curve being determined by the parameters c_1, c_2, c_3 .

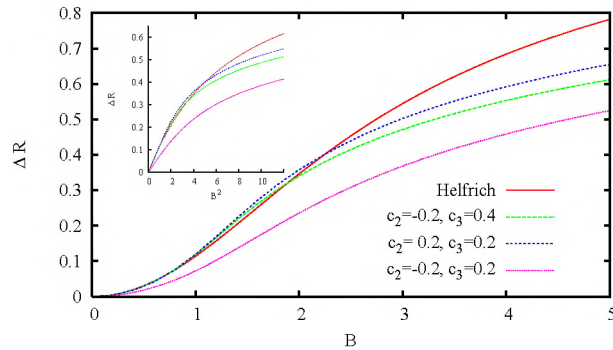


Figure 4: Difference ΔR between short and long axis of the ellipsoid resulting from minimization of the free energy in a magnetic field B for three choices of c_2 and c_3 ($c_1 + c_2 + c_3 = 1$ and $|A| = 1$), compared with the Helfrich model ($H_0 = 1$). The inset shows that initial B^2 dependence of the distortion depends mostly on $c_2 + 2c_3$.

In summary, we have demonstrated that the frustration resulting from competing core-core and tail-solvent interactions can lead to spontaneous bending of single bolaamphiphilic layers. By describing the tail solvent interactions within the Flory-Huggins theory, we have constructed a Landau-like free energy appropriate to describe symmetric bolaamphiphiles that gives a rationale for the formation of spherical vesicles. Measurement of their deformation in high magnetic fields can provide information about the parameters of the theory, opening the possibility to validate microscopic models of interactions in these systems.

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