

# Molecular Theory for Amphiphile Packing and Elastic Properties of Monolayers and Bilayers

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## 1. Introduction

In a number of recent papers we have presented and developed a statistical thermodynamic theory for amphiphile chain packing in micellar aggregates and membrane bilayers[1]. The central quantity in the theory is the (singlet) probability distribution function (pdf) of chain conformations, with the aid of which one can calculate conformational properties (e.g. bond order parameters and chain segment spatial distributions), as well as relevant thermodynamic functions such as the average internal (gauche/trans) energy, conformational entropy and free energy. The conformational pdf accounts explicitly for the packing constraints imposed on a given chain by (excluded volume interactions with) its neighbors. These constraints, and consequently the pdf depend on the geometrical characteristics of the microenvironment in which the chains are packed; namely, the curvature of the hydrocarbon-water interface of the micelle, membrane or monolayer and the surface density of polar heads.

Conformational and thermodynamic properties calculated by our mean-field type theory show very good agreement with corresponding results from large-scale molecular dynamics simulations[2] and available experimental data. Similarities and differences with respect to other theoretical approaches (e.g. [2-4]) have been discussed in detail elsewhere[1]. We have applied the theory to study a variety of issues pertaining to the conformational and thermodynamic properties of amphiphilic systems. These include, for example, the relative importance of (hydrocarbon) 'tail' vs. (hydrophilic) 'head' free energies in determining the preferred micellar geometry, energetic vs. entropic contributions to the packing free energy, the extent and importance of the hydrocarbon-water surface roughness and the conformational statistics and thermodynamics of mixed amphiphilic aggregates. Another important and natural extension of the theory is its application to calculating elastic properties of membrane bilayers and interfacial films (monolayers). In section 3 we briefly present a few preliminary results concerning this application. Before doing so, we briefly outline, in section 2, the formal and physical basis necessary for such calculations.

## 2. Packing Constraints and Conformational Statistics

Many and various experiments, as well as theory, reveal that the density of hydrocarbon chain segments (monomers) in the hydrophobic interior of amphiphilic bilayers is uniform throughout, and its value is similar to that in the bulk liquid hydrocarbon[5-7]. (We consider here only the liquid or so-called 'liquid-crystalline' state of the chains. Also, although the discussion below is general our calculations correspond to amphiphiles with simple alkyl chains). Uniform segment density does not imply random configurational chain statistics. In fact, apart from the boundary condition associated with the confinement of chains to one side of the water-hydrocarbon interface, the uniform density condition is the (only) relevant constraint on chain-packing statistics in our theory, as explained below. The uniform monomer density (i.e. no 'holes') is ensured by the attractive long-range (van der Waals) interactions responsible for the cohesiveness of the hydrocarbon core. In the case of surfactant monolayers at oil-water interfaces, uniform density does not require that the hydrocarbon chains form a 'compact' film of constant thickness. This is because the oil molecules (in the case of a good solvent) can fill up the 'bays' characterizing a rough chain-oil interface, Fig. 1. The extent of this roughness, which allows more conforma-

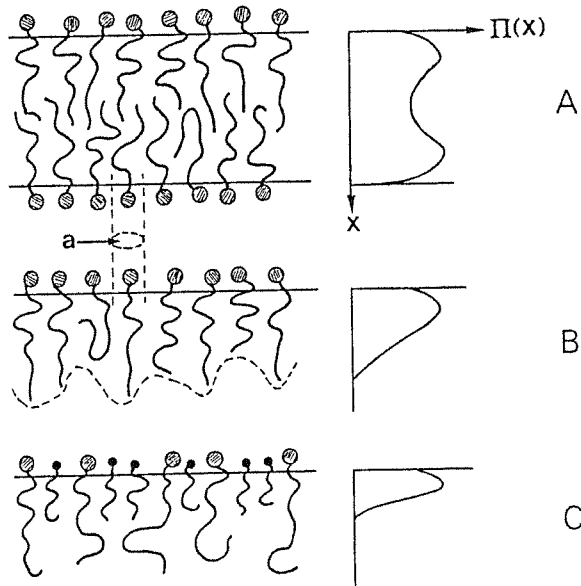


Fig.1 Schematic pictures of a bilayer (A), a monolayer (B), and a mixed monolayer (C)

tional freedom to the chains, decreases with chain length and surface density of head-groups. It should also be noted that bilayers, although often treated as such, are not a 'sandwich of two compact monolayers' either. Rather, the two monolayers interdigitate each other, often significantly, thereby gaining configurational free energy, Fig. 1. All these qualitative notions regarding chain packing can be expressed in simple mathematical terms, as shown below.

Let  $P(\alpha)$  denote the probability of finding a chain in conformation  $\alpha$ . The conformation of a  $-(CH_2)_n-CH_3$  chain, in the rotational isomeric state (RIS) model, is fully specified by the sequence of trans/gauche bonds along the backbone and the three Euler angles describing the overall orientation of the chain relative to the interface. Let  $\phi(x;\alpha)dx$  denote the number of (centers of) chain segments which, for a chain in conformation  $\alpha$  are found in the interval  $x, x+dx$ , where  $x$  is the normal distance from the water-oil interface, Fig. 1. Equivalently,  $v\phi(x;\alpha)dx$  is the volume taken up by the chain in  $x, x+dx$  where  $v$  is the segment's volume ( $\approx 27\text{\AA}^3$  for  $CH_2$ ). Because of the nonzero volume (area) of the chains it is clear that the total area occupied by  $N$  equivalent chains originating from the interface can not exceed  $A(x)$ , the cross sectional area of a surface parallel to the interface at distance  $x$ . This implies that for all  $x$

$$\langle \phi(x) \rangle = \sum_{\alpha} P(\alpha) \phi(x;\alpha) \leq a(x), \quad (1)$$

where  $a(x) = A(x)/N$  is the average area available per chain at distance  $x$  from the interface. This inequality is the appropriate packing constraint on  $P(\alpha)$  for a monolayer. If there is some a priori reason to assume that the monolayer is compact and of width  $L$  then (1) should be used with the strict equality for all  $x \leq L$ . More generally, the equality applies when the chains are packed at uniform density. The extension of (1) to mixed monolayers and to bilayers (pure or mixed, symmetrical or asymmetrical) is straightforward[1]. Note that the packing constraints on  $P(\alpha)$  describe the average (mean-field) effect of excluded volume interactions of a given chain with its neighbors. The attractive interactions do not affect  $P(\alpha)$  because the density is uniform for all chain configurations.

The geometry of an amphiphile layer (or aggregate) enters the packing constraints via  $a(x)$ . Explicitly, for an interface with principal radii of curvature  $R_1$  and  $R_2$ ,

$$a(x) = a[1 - (c_1 + c_2)x + c_1 c_2 x^2] \quad (2)$$

where  $a = a(0)$  is the average area per head-group, at  $x=0$ , and  $c_i = 1/R_i$  are the principal curvatures.  $c_i$  is assumed positive when the center of curvature is on the hydrophobic side of the interface.

The conformational pdf of the system is the (unique)  $P(\alpha)$  which minimizes the (Helmholtz) free energy per chain,

$$f_c = \sum_{\alpha} P(\alpha) \epsilon(\alpha) + kT \sum_{\alpha} P(\alpha) \ln P(\alpha) \quad (3)$$

subject to the packing constraints (1). The two terms on the rhs of (3) are the average internal energy and the entropy, per chain, respectively.  $\epsilon(\alpha)$  is the energy of the trans/gauche bond sequence corresponding to  $\alpha$ . The minimization yields

$$P(\alpha) = \exp[-\beta \epsilon(\alpha) - \beta \int \pi(x) \phi(x; \alpha) dx] / z \quad (4)$$

where  $\beta = 1/kT$  and the partition function,  $z$ , ensures the normalization of  $P(\alpha)$ . The  $x$ -integration extends over the hydrophobic region. The important parameters in  $P(\alpha)$  are the lateral pressures (tensions)  $\pi(x)$  which are the Lagrange multipliers conjugate to the packing constraints. They are determined by substituting (4) into (1) and solving for the  $\pi(x)$ . In our calculations we simplify the solution by discretizing the problem, namely, we divide the hydrophobic region into, say  $L$ , imaginary layers parallel (concentric) to the interface. Then (1) and (4) yield a set of  $L$  coupled equations for the  $\pi_i$ 's ( $i=1, \dots, L$ ) which are easily solved by standard methods[1].

As noted above, for 'compact' films or aggregates in which the hydrophobic region is uniformly packed only by segments of the chains, the constraints in (1) are strict equalities. For non-compact films (1) is a real constraint only for some regions of  $x$ , while for others the inequality is trivially satisfied. More explicitly, for a given  $x$ , (1) is a relevant constraint only if  $\langle \phi(x) \rangle_f > a(x)$ , the lateral extension of a free chain (i.e. a single chain with no neighbors around) exceeds  $a(x)$ , so that the packed chain must be squeezed in order to fit (on the average) into the area available to it. Consistent with this notion  $\pi(x) = 0$  for all  $x$  where (1) is an 'irrelevant' constraint. On the other hand  $\pi(x) > 0$  for all  $x$  where (1) is a real constraint ensuring  $\langle \phi(x) \rangle = a(x)$ . In general, large values of  $\pi(x)$  indicate strong chain confinement at the corresponding  $x$ . Typical lateral pressure profiles are shown schematically in Fig. 1. It is seen for example that for a monolayer  $\pi(x)$  decreases from finite values at small  $x$  (where chains push each other), to zero towards the rough region where both chain and oil segments are present. It is interesting to note that the lateral pressure profile in a bilayer is very nearly a superposition of the  $\pi(x)$  for two, non-compact, monolayers. Consistent with this observation we find that many other bilayer properties (e.g. chain free energies) are, to a good approximation, a superposition of the corresponding monolayer properties.

After evaluating the  $\pi(x)$  we can use  $P(\alpha)$  to calculate any desired chain conformational or thermodynamic property, e.g. the conformational free energy (3). Formally, substituting (4) into (3), and noting that  $\langle \phi(x) \rangle = a(x)$  for all  $\pi(x) \neq 0$ , we find  $f_c = -kT \ln z - \int dx \pi(x) a(x)$ . Noting also that  $\langle \phi(x) \rangle = -kT \partial \ln z / \partial \pi(x)$  it follows that the free energy changes associated with changing the geometry of the system, i.e. changing  $a(x)$ , are given by

$$\delta f_c = - \int dx \pi(x) \delta a(x) + \delta^{(2)} f_c + \dots \quad (5)$$

with  $\pi(x) = -\partial f_c / \partial a(x)$ . [For compact, 'volume-preserving' systems such as bilayers the rhs includes in addition the term  $(\partial f_c / \partial L) \delta L$ , accounting for changes in the thickness of the chains' layer].

The first order terms in (5) determine the equilibrium (minimal  $f_c$ ) state of the chains.  $\delta^{(2)} f_c$  stands for second order variations involving second order derivatives of  $f_c$  (first derivatives of  $\pi$ ). When evaluated at the equilibrium state these derivatives give the chain contribution to the elastic constants[8-10]. Based on our theory we can calculate  $f_c$  for any desired geometry, and thus evaluate its derivatives with respect to geometrical parameters such as the area per head

group,  $a$ , and the curvatures  $c_i$ , cf (2). However,  $f_c$  is not the only geometry dependent term in the free energy of the amphiphilic layer,  $f$ . In particular  $f$  includes an important contribution from the head-group region,  $f_h$ . This quantity is usually modeled in terms of the opposing forces[6,7]: namely, the effective attraction between molecules resulting from the tendency to minimize oil-water contact on the one hand, and the (electrostatic or excluded volume) repulsion between head-groups on the other. The attraction is usually described by a phenomenological surface tension term  $\gamma a$ , with  $\gamma \sim 0.1 kT/\text{\AA}^2 \sim 50 \text{ dyn/cm}$ . The repulsion is often expressed as  $K/a'$  where  $a'$  is the area per head-group at the surface of repulsion[7,11]. If this surface is located at a distance  $d$  from the oil-water interface then  $a' = a[1+d(c_1+c_2)+d^2c_1c_2]$ . Thus, for a monolayer  $f_h = \gamma a + K/a'$  becomes (up to quadratic terms in  $dc_i$ ),

$$f_h = \gamma a + (\gamma a_h^2/a)[1-d(c_1+c_2)+d^2(c_1^2+c_2^2+c_1c_2)] \quad (6)$$

where  $a_h = (K/\gamma)^{1/2}$  is the value of  $a$  which minimizes  $f_h$  for a planar layer,  $c_1=c_2=0$ . It should be noted that although  $a_h$  is often referred to as the 'optimal area per head group'[7], this statement ignores the  $a$ -dependence of  $f_c$ . Namely, the real optimum,  $a_0$ , is the value of  $a$  which minimizes the sum  $f = f_c + f_h$ . This minimization yields  $a_0$  which is intermediate between  $a_h$  and  $a_c$  where  $a_c$  is the optimal area for chain packing. In some cases identification of  $a_0$  with the experimental equilibrium area, and using the calculated  $a_c$  yields  $a_h$  which is much smaller than  $a_0$ , sometimes even smaller than  $a_t \sim 21 \text{\AA}^2$  which is the minimal (all-trans) area allowed for chain packing. This implies that the dominant repulsion balancing the interfacial attraction  $\gamma a$  is due to the chains and not to the heads. Consequently, the form of the head-group repulsive term, as well as the exact value of the parameter  $a_h$ , are of secondary importance.

### 3. Elastic Constants

Writing

$$\delta f = \delta^{(1)}f_c + \delta^{(1)}f_h + \delta^{(2)}f_c + \delta^{(2)}f_h + \dots \quad (7)$$

we can determine the equilibrium geometry of a layer from the first order variations and its elastic moduli from the second order terms. As a first example let us consider the stretching elasticity of a planar bilayer. Fig. 2 shows  $f_c$ , calculated by our theory, for a bilayer of  $-(CH_2)_{11}-CH_3$  chains as a function of  $a$ , revealing a minimum for  $f_c$  at  $a_c \approx 45 \text{\AA}^2$ . Also shown

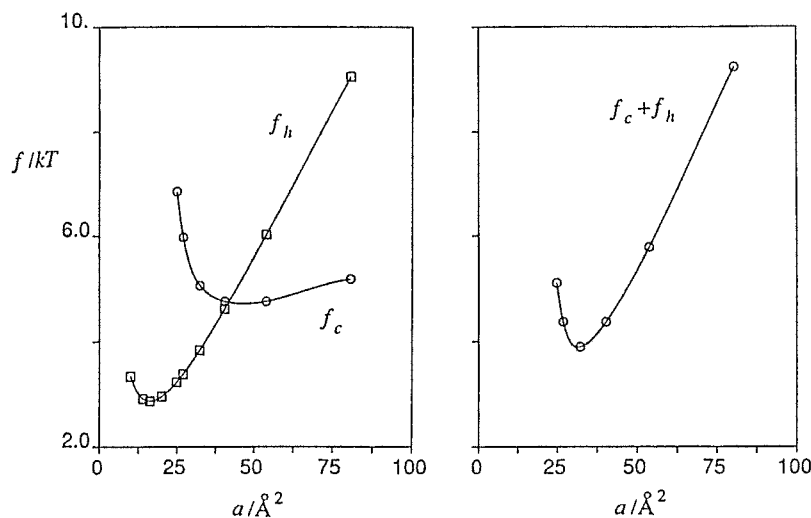


Fig.2 Free energies of a planar bilayer of 12-carbon chains as a function of the area per molecule. The separate contributions of heads and chains are shown on the left and their sum on the right

is  $f_h$ , with the parameters  $\gamma=0.12kT/\text{\AA}^2$  and  $a_h \approx 16\text{\AA}^2$ , chosen such that the minimum in  $f=f_c+f_h$  occurs at an experimentally typical value,  $a_0 \approx 33\text{\AA}^2$ . The figure reveals quite clearly that the optimal area is due primarily to the balance between the attractive surface term  $\gamma a$  in  $f_h$  and the strong chain repulsion operative at  $a < a_0$ . Formally, the equilibrium condition is  $\delta^{(1)}f = \delta^{(1)}f_c + \delta^{(1)}f_h = 0$  with  $\delta a(x) = \delta a = \text{const}$  and  $c_1 = c_2 = 0$  in (2). Using (5) and (6) this yields  $\int \pi(x) dx = \gamma [1 - (a_h/a_0)^2]$ .

From the behavior of  $f$  around  $a=a_0$  one can derive a stretching elastic constant  $k_s$ , defined via[8]

$$\delta f / a_0 = (1/2) k_s (\delta a / a_0)^2 \quad (8)$$

For the example in Fig. 2 we obtain  $k_s \approx 0.70kT/\text{\AA}^2 \approx 300 \text{erg/cm}^2$ .  $\delta f$  and correspondingly  $k_s$  is a sum of chain and surface (head) terms. From (6) one finds that the surface contribution to  $k_s$  is  $2\gamma(a_h/a_0)^2$  which for the chosen parameters gives  $\sim 0.05kT/\text{\AA}^2$ , i.e. considerably smaller than the chain term.

Curvature elasticity is usually modeled in terms of Helfrich formula for the free energy per unit area[8-10]

$$f/a = (1/2)k(c_1 + c_2 - c_0)^2 + \bar{k}c_1c_2 \quad (9a)$$

$$= (2k + \bar{k})c^2 - 2kc_0c + (1/2)kc_0^2 \quad (c_1 = c_2) \quad (9b)$$

where  $k$  and  $\bar{k}$  are the bending constants corresponding to splay and saddle splay deformations, respectively. The second equality corresponds to spherical deformations ( $c_1 = c_2$ ), and  $c_0$  is the spontaneous curvature related to the equilibrium curvature  $c_{eq} = (k/2K)c_0$ . In analogy to  $k_s$  the phenomenological parameters in (9) can be determined by calculating  $\delta f = \delta f_c + \delta f_h$  for different values of  $c_1$  and  $c_2$  (i.e. different deformations) and evaluating the appropriate coefficients. (Combinations of the parameters can be related to moments of the lateral tensions[8-10]). Again, the bending constants are sums of chain and surface terms. In Fig. 3 we

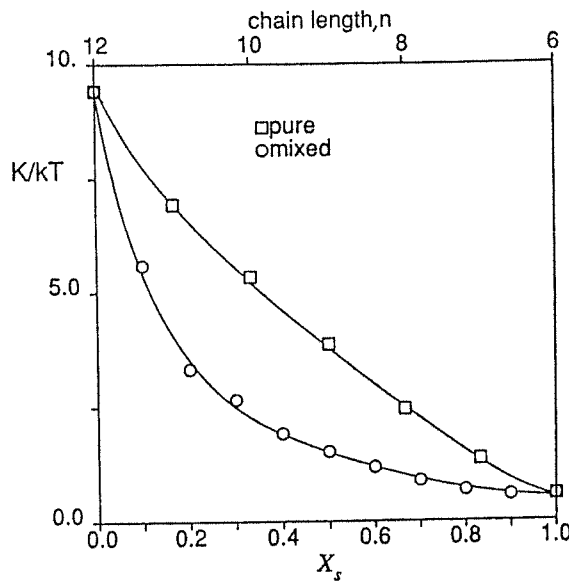


Fig.3 Bending constants,  $K \equiv k + \bar{k}/2$ , of a mixed,  $C_{12}/C_6$ , monolayer as a function of short chain fraction, (lower scale, circles), and of a pure monolayer as a function of chain length, (upper scale, squares)

show  $K_c$ , the chain contribution to  $K \approx k + \bar{k}/2$  for a mixed monolayer of 12 and 6 carbon chains  $[-(CH_2)_{n-1}-CH_3]$  with  $n=12$  and 6] as a function of the short chain fraction,  $X_s$ . Also shown is  $K_c$  of a pure monolayer as a function of chain length  $n$ . It should be stressed that the results in Fig. 3 correspond to the same area per chain for all cases,  $a = a_0 = 32 \text{ \AA}^2$  regardless of  $n$  or  $X_s$ . This would be the case if  $a_0$  is dictated solely by the balance between the opposing surface forces, and if the head groups are the same for all chains. Otherwise one must take into account the variation of  $a_0$  with chain length and composition. Another assumption employed in the calculation of  $K_c$  is that the  $a = a_0$  is kept constant upon bending, i.e. the neutral surface is assumed to coincide with the water-oil interface. The values of  $K_c$  obtained in this way are approximate (upper bounds) since the location of the neutral surface generally depends on chain length as well as on the specific parameters of head group interactions. In the same approximation the head group contribution to  $K$  can be estimated from the quadratic terms in (6), namely,  $K_h \sim 6\gamma(a_h/a_0)^2 d^2 \sim \gamma d^2$ . Using  $\gamma \sim 0.1 kT/\text{Å}^2$  and, e.g.  $d \sim 3 \text{ \AA}$  this yields  $K_h \sim kT \sim 5 \times 10^{-14} \text{ erg}$  which is considerably smaller than  $K_c$  for the long chain film. For mixed monolayers, particularly surfactant-alcohol films,  $K_c$  is expected to decrease significantly. But  $K_h$  will also decrease (approximately linearly) due to the screening of electrostatic repulsion resulting from the addition of alcohol[12].

The most significant qualitative trend apparent from the results in Fig. 3 is the very efficient lowering of the bending constant of a ('long chain') surfactant film by dilution with short chain molecules. A similar behavior has been observed experimentally[13]. Qualitatively, this follows from the fact that addition, even of a small amount, of short chains relieves much of the conformational strain associated with confining the longer chains to small cross sectional areas, as schematically shown in Fig. 1. In terms of the packing constraints: a small amount of short chains suffices to make (1) an irrelevant packing constraint for  $x > l_s$  where  $l_s$  is the average length of a short chain in the film. The fast decrease of  $K_c$  with  $X_s$  should be contrasted with its nearly linear variation with chain length. [A faster decrease of  $K_c$  with  $n$  is expected when the  $n$  dependence of  $a_0$  is taken into account. This behavior can be explained by simple scaling arguments]. Extensive and more accurate calculations of elastic constants for pure and mixed bilayers and monolayers are now in progress[14].

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