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Calculation of the optimal surface area for amphiphile molecules using the hard core method

D. Popescu [a] and G. Victor [b]

[a] *Membrane Biophysics Group, Institute of Biological Sciences, Spl. Independenţei, Nr. 296, Bucharest 77748 and* [b] *Faculty of Physics, University of Bucharest, Bucharest, Roumania*

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In this work, we have calculated the optimal surface area per amphiphile molecule using a two-dimensional gas of electric dipoles interacting with hard cores. The optimal surface area can be evaluated according to a formula (in the two-body approximation) or as a root of an equation (in the three-body approximation). If the equation has more than one positive root, which is greater than the hard core area, then a polydisperse dimensional distribution of supramolecular aggregates is possible.

1. Introduction

It is well known that amphiphile molecules which are dissolved in water organize themselves into supermolecular structures when the concentration is above a certain level. This problem of spontaneous self-assembly has been dealt with especially by Tanford [1] who used thermodynamic considerations in dealing with the stability of the aggregates and compatibility geometrical restrictions of the form of structures. The author introduced an important parameter, a_0, designated the optimal surface area per amphiphile molecule.

If every amphiphile molecule occupies a surface area equal to a_0 in an aggregate, then the aggregate will have minimum free energy and maximum stability. Via analysis of a large body of experimental data, Tanford found that the a_0 values fall within the range 60–70 $Å^2$ for both amphiphile molecules with one or two alkyl chains.

In ref. 2, an explicit formula for the standard chemical potential of amphiphiles was obtained (of optimal surface area a_0) based on the principle of opposing forces. In this paper, the repulsive surface energy, determined by the electrostatic interactions between electrical charges situated on and around the head group, was calculated using a capacitator model.

In this work, we present a new formula for the calculation of the optimal surface area, a_0, based on the dipolar interactions between the polar head groups of amphiphile molecules, using a two-dimensional gas of electric dipoles interacting with the hard core model.

2. The hard core model

In the model, each polar head group is considered as a disk of mass m and hard core radius r_0 [3]. An electric dipole of magnitude $\vec{p}$ is parallel to the plane of the disk and is situated upon it.

Correspondence address: D. Popescu, Membrane Biophysics Group, Institute of Biological Sciences, Spl. Independenţei, Nr. 296, Bucharest 77748, Roumania.

Experimental results are available which demonstrate that the dipole moment of lipid head groups is parallel to the surface of supramolecular structures [4]. If the dipole moments of the lipid molecules are not parallel to the aggregate's surface, then p represents the projection of the dipole moment onto the disk plane. We consider a reference fixed system and each random oriented disk is identified by its spatial coordinate $\vec{r}_j$, and dipole moment $\vec{p}_j$. The orientation of the disk 'j' is in fact its electric dipole moment orientation and is given by angle ϕ_j relative to one of the axes of the reference system.

The potential energy of interaction between both disks $D_i(\vec{r}_i, \vec{p}_i)$ and $D(\vec{r}_j, \vec{p}_j)$ has the usual form [5]:

$$V(\vec{r}_i, \vec{p}_i; \vec{r}_j, \vec{p}_j) = \begin{cases} \infty & \text{if } |\vec{r}_i - \vec{r}_j| \leqslant 2r_0 \\ \dfrac{1}{4\pi\epsilon r_{ij}^3}\left[\vec{p}_i \cdot \vec{p}_j - 3 \cdot \dfrac{(\vec{p}_i \cdot \vec{r}_{ij}) \cdot (\vec{p}_j \cdot \vec{r}_{ij})}{r_{ij}^3}\right] & \\ \quad \text{if } |\vec{r}_i - \vec{r}_j| > 2r_0 & \end{cases} \tag{1}$$

where $\vec{r}_{ij} = \vec{r}_i - \vec{r}_j$ and ϵ is the permittivity of the medium.

If both N and A are very large, but the superficial density, N/A, is assumed to be constant, then the concept of statistical thermodynamics is applicable. In this case, the Helmholtz free energy can be calculated from the canonical partition function, and depends on N, A, and T. Using the method of factor-cluster expansion [6] and retaining from the canonical partition function only that part responsible for the dipolar and hard core interactions, we find that the Helmholtz free energy is

$$F^0(N, A, T) = kT\left[\frac{N(N-1)\cdot a_{ex}}{2A}\cdot f(\lambda) + \frac{N(N-1)(N-2)}{6}\cdot\left(1 - \frac{3\sqrt{3}}{4\pi}\right)\cdot\frac{a_{ex}^2}{A^2}\right] \tag{2}$$

where $a_{ex} = 4\pi r_0^2$ is the surface area excluded to the other disks by any one hard disk, and

$$f(\lambda) = 1 - \tfrac{2}{3}\int_0^1 \frac{dx}{x^{5/3}}\left[I_0\left(\frac{\lambda x}{16}\right)\cdot I_0\left(\frac{3\lambda x}{16}\right) - 1\right] \tag{3}$$

accounts for the dipole-dipole interaction between two disks. In eq. 3, I_0 is the zeroth hyperbolic Bessel function and

$$\lambda = p^2/(4\pi\epsilon kTr_0^3) \tag{4}$$

Because the number of disks is very large, we can make the following approximation: $N = N - 1 = N - 2$.

At constant volume (here, area) and temperature, the contribution of the superficial repulsion energy, $\mu_{s.r}^0$, per amphiphile molecule in the aggregate is

$$\mu_{s.r}^0 = \left(\frac{dF^0}{dN}\right)_{A,T} = \frac{a_{ex}}{2\beta a}\cdot f(\lambda) + \left(1 - \frac{3\sqrt{3}}{4\pi}\right)\cdot\frac{a_{ex}^2}{6\beta a^2} \tag{5}$$

where $\beta = 1/kT$ and $a = A/N$ is the surface area occupied by an amphiphile molecule in the aggregate.

The first term in eq. 5 includes the dipole-didipole and hard core two-body interactions. The last term in eq. 5 includes only the contribution arising from hard core three-body interactions. Now, the standard chemical potential for an amphiphile molecule in an aggregate of N molecules is approximated by

$$\mu_N^0 = \gamma a + \frac{a_{ex}}{2\beta a}\cdot f(\lambda) + \left(1 - \frac{3\sqrt{3}}{4\pi}\right)\cdot\frac{a_{ex}^2}{6\beta a^2} + \mu_v(l, T) \tag{6}$$

where $\mu_v(l, T)$ is the bulk free energy per amphiphile molecule. It is a function only of the temperature and the length of the hydrocarbon chain. γ is the interfacial free energy per unit area.

If we consider only the two-body interaction, the optimal surface area per amphiphile has the following form:

$$a_0 = \sqrt{\frac{a_{ex} \cdot f(\lambda)}{2\beta\gamma}} \tag{5}$$

If we also include the contribution of the hard core interaction from simultaneous three-body collisions, then the optimal surface area per amphiphile molecule expressed by one of the three solutions of the equation:

$$a^3 - P \cdot a - Q = 0 \tag{6}$$

where

$$P = \frac{a_{ex} \cdot f(\lambda)}{2\beta\gamma} \text{ and } Q = \left(1 - \frac{3\sqrt{3}}{4\pi}\right) \cdot \frac{a_{ex}^2}{3\beta\gamma} \tag{7}$$

It is clearly observed that eq. 7 always has only a single positive real solution. This solution must be greater than the value for the hard core. This is evident proof that eq. 6 corresponds to the aim for which it was obtained.

3. Discussion

The value of the optimal area obtained from eq. 5 or 6 is valid for planar lipid monolayers and bilayers. It can be used for micelles of different geometrical shapes, modifying it with a curvature correction, often referred to as the geometrical form factor.

The effects of the surroundings on the polar head group interactions are considered using an estimate of ϵ. The advantage of this approach for calculating the optimal surface area per amphiphile molecule, a_0, consists in the establishment of a link between aggregation phenomena and phase transitions of lipids. This connection is realised by the common parameter r_0, owing to the fact that the hard core method is often used in order to study phase diagrams and phase transitions [8–10]. The hard core properties (especially the excluded area) for which this method gives a correct description of the phase diagram or phase transitions (in particular, the order-disorder polar head group transition) therefore agree well with the experiment, and can be used for calculation of the optimal surface area per amphiphile molecule. This becomes more evident if we take into account the same form of the Helmholtz free energy as a function of A, N, and T used to obtain the state equation of a hard core gas and the optimal surface area per amphiphile.

Also, the influence of temperature on the stability of supermolecular structures is taken into account. In this way the experimental results from phase diagram and phase transition phenomena can be used to study the aggregation of lipids. For example, one can calculate the excluded area from van der Waals interactions, or from the values of the pressure and temperature at the critical point [11].

The magnitude of a_0 is directly determined by the excluded area and the interfacial free energy per unit area, γ. The dipole moment of the polar head groups and the temperature influence the magnitude of the optimal surface area through both the parameter, λ and the excluded area. We can also take into account the coupling between the sizes of the polar head group area and the cross-section of the hydrocarbon chains.

In conclusion, calculation of the optimal surface area using the hard core method has two advantages: (a) all physical parameters which influence the aggregation of the lipid molecules into supermolecular structures (ϵ, r_0, γ, T) appear in the calculation of the optimal area; (b) a link between aggregation phenomena and phase diagrams can be made.

In the calculation performed for the determination of the optimal surface area, a value of 21 Å^2 [1] was taken for πr_0^2 for single-chain molecules and 38 Å^2 [3] for molecules with two chains.

In the two-body approximation, the following results were obtained: $a_0 = 29.54$ Å^2 for molecules with a single chain ($p = 1.7$ Debye) [12] and $a_0 = 39.73$ Å^2 for amphiphile molecules with two chains ($p = 35$ Debye) [4].

Taking into account the hard core contribution to the third virial coefficient, we obtained the following results: $a_0 = 39.9$ Å^2 for amphiphile molecules with a single chain and $a_0 = 52.25$ Å^2 for amphiphile molecules with two chains. In both cases $\epsilon = 80\epsilon_0$ and $\gamma = 0.02$ J/m^2 [12].

The calculation of the canonical partition function by the cluster expansion method is used for low liquid densities [13]. In this case, the convergence of the expansion is evidently rapid. The virial expansion becomes more inadequate with increasing density of liquid. In other words, the convergence of the expansion becomes slower with increasing number of interacting molecules. In our case, the supermolecular aggregates of phospholipid molecules do not represent the result of very strong forces among their molecules, or of cooperative effects involving a very large number of molecules. In our opinion, the hydrophobic effect is the dominant factor in the organization of aggregation of lipid molecules into supermolecular structures and is an external 'force'. The dipole and dispersion interactions make the aggregate more stable, however, the action of either one alone cannot maintain the amphiphiles in supermolecular structures. Neither dipole interactions nor dispersion forces appear to be simultaneous interactions among such large numbers of molecules so that cluster expansion is inapplicable.

The above argumentation and our intuitive understanding lead us to believe that simultaneous interaction among more than three bodies is a rare event. In order to calculate the optimal area in a more tractable manner, the dipole interactions in the three-body interactions were not taken into account, considering that the hard core interactions are dominant. Therefore, the contribution of higher order corrections in the expansion must be relatively less important. If we take into account the effect of hydrocarbon chains on the hard core radius and the dipole interaction in the third virial coefficient, then the convergence of the expansion will be more rapid, without excessively changing the value of the optimal surface area obtained by the three-body approximation.

References

1 C. Tanford, The hydrophobic effect: Formation of micelles and biological membranes, 2nd edn (Wiley, New York, 1980).
2 J.N. Israelachvili, D.J. Mitchell and B.W. Ninham, J. Chem. Soc. Faraday Trans. II, 72 (1976) 1525.
3 H.L. Scott, Biochim. Biophys. Acta 648 (1981) 129.
4 J. Seeling, Biochim. Biophys. Acta 515 (1978) 105.
5 L. Landau and E. Lifchitz, Theorie des champs (Mir, Moscow, 1970) p. 138.
6 P.A. Westhaus and J.W. Clark, J. Math. Phys. 9 (1967) 131.
7 G.N. van Kampen, Physica 27 (1961) 783.
8 H.L. Scott and W.H. Cheng, Biophys. J. 28 (1979) 117.
9 H.L. Scott, J. Chem. Phys. 62 (1975) 1347.
10 H.L. Scott, Biochim. Biophys. Acta 643 (1981) 161.
11 P.A. Westhaus, J. Theor. Biol. 100 (1983) 181.
12 A. Raudino and D. Mauzeral, Biophys. J. 50 (1986) 441.
13 I.G. Abidor, V.B. Arakelyan, L.V. Chernomordik, Yu.A. Chizmadzhev, V.F. Pastushenko and M.R. Tarasevich, Bioelectrochem. Bioenerg. 6 (1979) 37.
14 C.A. Croxton, Introduction to liquid state physics (Wiley, London, 1974) p. 26.