

Statistical mechanics of three-dimensional vesicles

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We consider a lattice model of three-dimensional vesicles in which the boundary of the vesicle is a self-avoiding plaquette surface, homeomorphic to a sphere. Surfaces with fixed area can enclose a variety of different volumes and we associate a fugacity with the enclosed volume to mimic the effect of a pressure difference across the surface. Pairs of plaquettes which share a common edge can be in the same plane or normal to each other and we associate a fugacity with adjacent pairs of plaquettes at right angles to represent a surface stiffness term. We discuss the behaviour of the surfaces in the infinite surface area limit, as a function of these two fugacities.

1. Introduction

Biological membranes and microemulsions share many interesting properties. Membranes are typically thin flexible sheets of amphiphilic molecules such as phospholipids and can be modelled as self-avoiding surfaces [1]. They can form closed structures which we refer to as vesicles, i.e. self-avoiding surfaces without boundary. Microemulsions are equilibrium systems consisting of oil, water and surfactant, with the surfactant preferentially adsorbed at the oil/water interface. These can also be modelled as self-avoiding surfaces and show a rich phase behaviour [2].

In an attempt to understand the behaviour of vesicles and, in particular, their sizes and shapes, Fisher and coworkers have carried out a series of studies of self-avoiding polygons in two dimensions [3–6]. These papers are particularly concerned with the way in which the dimensions (such as the radius of gyration) depend on the length of the perimeter and on the pressure difference across the boundary of the two-dimensional vesicle. Fisher et al. [7] have derived some rigorous results about the pressure dependence of the “free energy” in a lattice model of vesicles, and analysed the behaviour close to a tricritical point using scaling arguments and series analysis techniques. Maritan et al. [8] have studied a similar model by mapping it onto a gauge model. This work is mainly in two dimensions though some extensions to higher dimensions have appeared [7,9]. For an alternative approach to the shape changes in three dimensions see ref. [10].

In this paper we concentrate on a three-dimensional lattice model in which the

boundary is a plaquette surface homeomorphic to a sphere. (Note, however, that there is experimental evidence for the existence of toroidal vesicles [11].)

2. Some definitions and a statement of results

We shall be primarily concerned with the simple cubic lattice in three dimensions although many of our results also apply to the case of the d -dimensional hypercubic lattice. The vertices of the simple cubic lattice are the integer points in R^3 , and the edges join pairs of vertices separated by unit distance. A *plaquette* is the boundary and interior of a unit square with vertices in Z^3 . We say that two plaquettes are *joined* if they share a common edge, and *connected* if they are elements in a sequence of plaquettes such that neighbouring pairs in the sequence are joined. A surface is a collection of connected plaquettes and we shall be interested only in the case in which the surface is a manifold and in which every edge in the surface is incident on exactly two plaquettes. (This means that the surface has no boundary component and is *closed*.) Furthermore, we shall confine our attention to surfaces which are homeomorphic to a sphere and we shall call such embeddings in Z^3 *vesicles*.

We consider two embeddings to be distinct if they cannot be superimposed by translation. Let v_n be the number of vesicles with n plaquettes. Then [12] there exists a number $K < \infty$ such that

$$v_n^{1/n} \leq K \quad (2.1)$$

for all n . We write $v_n(k, m)$ for the number of vesicles with n plaquettes, in which k pairs of joined plaquettes are at right angles and which enclose volume m . We define the generating function

$$Z_n(\alpha, \beta) = \sum_{k, m} v_n(k, m) e^{\alpha k + \beta m}. \quad (2.2)$$

In section 3 we prove that the limit

$$A(\alpha, \beta) = \lim_{n \rightarrow \infty} n^{-1} \log Z_n(\alpha, \beta) \quad (2.3)$$

exists for all α and $\beta \leq 0$, and that $A(\alpha, \beta)$ is a convex function of α and β , again for $\beta \leq 0$. This implies continuity except possibly at $\beta = 0$, but left-continuity can be established there by a separate argument. From time to time we shall write χ for $A(0, 0)$.

If $\beta > 0$ we show that $n^{-1} \log Z_n(\alpha, \beta)$ diverges as $n \rightarrow \infty$, so that there is a jump discontinuity at $\beta = 0+$, for all (finite) values of α . In fact we show that, for positive β , the limit $\lim_{n \rightarrow \infty} n^{-3/2} \log Z_n(\alpha, \beta)$ exists and is finite, and that its value is independent of α . This means that the vesicle is expanded (in the sense that the

square of its volume scales with the cube of its area), independent of the value of α . A transition occurs at $\beta = 0$ from a “ramified” phase to an expanded phase, and the location of this transition is not affected by the local rigidity of the vesicle.

3. Convexity and continuity of the free energy

We first consider the case $\beta \geq 0$. We can find a lower bound on $Z_n(\alpha, \beta)$ by considering a vesicle with maximum volume. If $n = 6l^2$, where l is a positive integer, this is clearly a cube of side $\sqrt{n/6}$, enclosing volume $m_0 = (n/6)^{3/2}$. The number of pairs of joined plaquettes which are at right angles is $k_0 = 12\sqrt{n/6}$. This implies that

$$Z_n(\alpha, \beta) \geq e^{\alpha k_0 + \beta m_0} \quad (3.1)$$

and so

$$\liminf_{n \rightarrow \infty} n^{-3/2} \log Z_n(\alpha, \beta) \geq \beta/6^{3/2}. \quad (3.2)$$

Clearly

$$12\sqrt{n/6} \leq k \leq 2n, \quad (3.3)$$

so

$$\limsup_{n \rightarrow \infty} n^{-3/2} \log Z_n(\alpha, \beta) \leq \lim_{n \rightarrow \infty} n^{-3/2} \log v_n + \beta/6^{3/2}. \quad (3.4)$$

Then (3.2) and (3.4) together with (2.1) imply that

$$\lim_{n \rightarrow \infty} n^{-3/2} \log Z_n(\alpha, \beta) = \beta/6^{3/2} \quad (3.5)$$

for all $\beta \geq 0$, independent of α . This means that, in the expanded regime, when the internal pressure is larger than the external pressure, there is no dependence on the rigidity term in the $n \rightarrow \infty$ limit.

When we consider $\beta \leq 0$ the situation is more complex. To prove the existence of the limit in (2.3) we need a concatenation argument. Each vesicle has a right-most face ($x = x_R$), which is a plane containing plaquettes of the vesicle, such that no vertices of the vesicle have x -coordinate larger than x_R . Similarly, each vesicle has a left-most face $x = x_L$. Each plaquette in each of these two faces can be identified by the y and z coordinates of its midpoint. Using lexicographic ordering we can define the top-most plaquette in the right face and the bottom-most plaquette in the left face. We call these plaquettes the *top* and *bottom* plaquettes respectively.

For convenience, we first consider a subset of these vesicles, namely those in which there is a single plaquette in the left-most face and a single plaquette in the

right-most face. We call such vesicles *special vesicles*, and write s_n for the number (up to translation) of special vesicles with n plaquettes. Consider special vesicles with n plaquettes, having k pairs of adjacent plaquettes at right angles and enclosing volume m . For brevity we call this a (k, m, n) -special vesicle. Let the number (up to translation) of (k, m, n) -special vesicles be $s_n(k, m)$. We can concatenate a (k_1, m_1, n_1) -special vesicle and a (k_2, m_2, n_2) -special vesicle by translating so that the top plaquette of one special vesicle is coincident with the bottom plaquette of the other special vesicle, and removing these two coincident plaquettes to form a new vesicle. The vesicle obtained in this way is clearly a special vesicle and has $n_1 + n_2 - 2$ plaquettes, encloses volume $m_1 + m_2$ and has $k_1 + k_2 - 8$ pairs of plaquettes at right angles. Since each pair of vesicles gives rise to a distinct vesicle by this concatenation we have the inequality

$$\sum_{k_1} \sum_{m_1} s_{n_1}(k_1, m_1) s_{n-n_1+2}(k - k_1 + 8, m - m_1) \leq s_n(k, m). \tag{3.6}$$

Since $s_n \leq v_n, s_n^{1/n} \leq v_n^{1/n} \leq K < \infty$, and therefore $S_n(\alpha, \beta)^{1/n}$ is bounded above, for finite α and $\beta \leq 0$, where

$$S_n(\alpha, \beta) = \sum_{k,m} s_n(k, m) e^{\alpha k + \beta m}. \tag{3.7}$$

This, together with (3.6), establishes the existence of the limit

$$\lim_{n \rightarrow \infty} n^{-1} \log S_n(\alpha, \beta) \equiv \mathcal{S}(\alpha, \beta). \tag{3.8}$$

We now relate $Z_n(\alpha, \beta)$ to $S_n(\alpha, \beta)$. Each (k, m, n) -vesicle can be converted into a special vesicle by attaching a unit cube to the top plaquette and a second unit cube to the bottom plaquette, and deleting the two pairs of coincident plaquettes. The surface area increases by 8 and the volume by 2. k increases to $k + k_0$, where k_0 can be any even integer from 8 to 16. Similarly, any special vesicle has two unit cubes which can be removed to reverse this transformation. Hence

$$s_n(k, m) = \sum_{p=4,8} v_{n-8}(k - 2p, m - 2) \tag{3.9}$$

from which it follows that the limit

$$\lim_{n \rightarrow \infty} n^{-1} \log Z_n(\alpha, \beta) \equiv A(\alpha, \beta) \tag{3.10}$$

exists, and is equal to $\mathcal{S}(\alpha, \beta)$.

We now turn to the question of convexity. Using Cauchy's inequality we obtain

$$\begin{aligned}
Z_n(\alpha_1, \beta_1) Z_n(\alpha_2, \beta_2) &= \left(\sum_{k,m} v_n(k, m) e^{\alpha_1 k + \beta_1 m} \right) \left(\sum_{k,m} v_n(k, m) e^{\alpha_2 k + \beta_2 m} \right) \\
&\geq \left(\sum_{k,m} v_n(k, m) e^{[(\alpha_1 + \alpha_2)/2]k + [(\beta_1 + \beta_2)/2]m} \right)^2 \\
&= \left[Z_n \left(\frac{\alpha_1 + \alpha_2}{2}, \frac{\beta_1 + \beta_2}{2} \right) \right]^2, \tag{3.11}
\end{aligned}$$

so that $n^{-1} \log Z_n(\alpha, \beta)$ is a convex function of α and β . Since the limit, when it exists, of a sequence of convex functions is itself convex [13], it follows from (2.3) that $A(\alpha, \beta)$ is a convex function of α and β , for all α and for $\beta \leq 0$. Since $A(\alpha, \beta)$ is bounded above for $\alpha < \infty$ and for $\beta \leq 0$, convexity implies continuity for all finite α and for $\beta < 0$ [13]. Left-continuity at $\beta = 0$ can be proved by an extension of an argument given in ref. [7].

4. Bounds on $A(\alpha, \beta)$

We first establish upper bounds on $Z_n(\alpha, \beta)$ for $\beta \leq 0$ and, from these, upper bounds on $A(\alpha, \beta)$. We consider separately the cases $\alpha \leq 0$ and $\alpha \geq 0$. For $\alpha \leq 0$ we have

$$Z_n(\alpha, \beta) \leq v_n \max_{k,m} e^{\alpha k + \beta m} = v_n e^{\alpha k_{\min} + \beta m_{\min}}. \tag{4.1}$$

Now

$$k_{\min}(n) \geq 12\sqrt{n/6}, \tag{4.2}$$

where the bound is realised when the plaquettes can form a cube. Similarly, $m_{\min} \geq (n-2)/4$ so that

$$A(\alpha, \beta) \leq \lim_{n \rightarrow \infty} n^{-1} \log v_n + \beta/4 = \chi + \beta/4. \tag{4.3}$$

For $\alpha \geq 0$ we have

$$Z_n(\alpha, \beta) \leq v_n \max_{k,m} e^{\alpha k + \beta m} = v_n e^{\alpha k_{\max} + \beta m_{\min}}, \tag{4.4}$$

and $k_{\max}(n) \leq 2n$, so that

$$A(\alpha, \beta) \leq \chi + 2\alpha + \beta/4. \tag{4.5}$$

If we set $\beta = 0$ (so that there is no pressure difference across the vesicle), then the behaviour is determined by the local rigidity. This is a particularly interesting regime in that it corresponds, at least loosely, to the problem of the rod-coil transition in walks [14]. From (4.3) and (4.5) we see that $A(\alpha, 0) \leq \chi$ for $\alpha \leq 0$ and

$A(\alpha, 0) \leq \chi + 2\alpha$ for $\alpha \geq 0$. We now look at lower bounds for $A(\alpha, 0)$. For $\alpha \leq 0$ we bound $Z_n(\alpha, 0)$ by the terms in the series corresponding to k_{\min} , giving

$$Z_n(\alpha, 0) = \sum_{k,m} v_n(k, m) e^{\alpha k} \geq \sum_m v_n(k_{\min}, m) e^{\alpha k_{\min}} \quad (4.6)$$

and using (4.2) we have $A(\alpha, 0) \geq 0$. Similar arguments, together with monotonicity, establish that, for $\alpha \geq 0$, $A(\alpha, 0) \geq \max[\chi, 2\alpha]$. Although we expect a transition associated with changing the rigidity, these techniques are not sufficiently sharp to establish the existence of such a transition.

5. Adsorption of vesicles

In this section we take a brief look at the adsorption of vesicles at a plane surface [15]. We shall be interested in vesicles which have at least one plaquette in a prescribed plane surface and which are confined to lie in or on one side of this surface. An appropriate question to ask is what fraction of the plaquettes are in the surface, as a function of some variable which plays the role of temperature? Let $v_n(m)$ be the number of vesicles with n plaquettes confined to a half-space and having m plaquettes in the plane $z = 0$. Then the partition function is given by

$$Q_n(\gamma) = \sum_{m \geq 1} v_n(m) e^{\gamma m}, \quad (5.1)$$

where γ is an energy divided by kT . The corresponding reduced limiting free energy is given by

$$A(\gamma) = \lim_{n \rightarrow \infty} n^{-1} \log Q_n(\gamma). \quad (5.2)$$

It can be shown by a concatenation argument that the limit in eq. (5.2) exists for $\gamma < \infty$. Similarly it is easy to show that the free energy is convex and continuous.

We note that, by adding a unit cube and translating the vesicles, we have the inequality

$$v_{n-4} = v_n(1), \quad (5.3)$$

which leads, for $\gamma \leq 0$, to the lower bound

$$v_{n-4} e^{\gamma} = v_n(1) e^{\gamma} \leq Q_n(\gamma), \quad (5.4)$$

which, together with monotonicity, gives

$$A(\gamma) = \chi \quad (5.5)$$

for all $\gamma \leq 0$. Since for $\gamma > 0$,

$$e^{\gamma m_{\max}} \leq Q_n(\gamma) \leq v_n e^{\gamma m_{\max}}, \quad (5.6)$$

where $m_{\max} = n/2 + o(n)$, then

$$\gamma/2 \leq \mathcal{A}(\gamma) \leq \chi + \gamma/2. \quad (5.7)$$

This establishes the existence of a phase transition since $\mathcal{A}(\gamma)$ is a non-analytic function of γ for some non-negative γ .

If we consider a membrane with free boundaries and homeomorphic to a disc and write $d_n(m)$ for the number of embeddings of a disc with n plaquettes confined to a half-space and having m plaquettes in $z = 0$, then a similar argument shows that

$$\liminf_{n \rightarrow \infty} n^{-1} \log \sum_m d_n(m) e^{\gamma m} \geq \gamma. \quad (5.8)$$

This implies that the adsorption thermodynamics must be different from that of a vesicle at sufficiently large γ .

6. Discussion

This paper has been concerned with the response of a vesicle in three dimensions to a change in the pressure difference across the surface of the vesicle. Perhaps the most interesting prediction is that, in the large surface area limit, the vesicle changes from a crenated or ramified object to an expanded object, as soon as the pressure outside becomes less than the pressure inside. Moreover, this transition is independent of the local rigidity of the vesicle.

Apart from their interest in statistical physics, these results may have some relevance to biological situations. For instance, there has been a continuing interest [16–18] in predicting the shape of the red blood cell. The primary biological purpose of the erythrocyte is to deliver oxygen and, to do this, it must traverse small capillaries and be able to deform without fragmentation. The membrane consists of a lipid bilayer and a membrane skeleton, consisting largely of protein, and associated with the lipid bilayer through protein–lipid interactions. The rigidity (or, equivalently, the deformability) of the membrane seems to be largely associated with the protein skeleton [18]. The typical biconcave shape of the cell is thought to be associated with the minimum bending energy [17]. In hypotonic solutions the cells swell and become much more spherical in shape [17]. On the other hand, in hypertonic solutions the cells are crenated [16]. Entropic effects seem to have been largely ignored in treatments of the erythrocyte shape and it may be worthwhile to incorporate these terms into future treatments.

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