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THE STATISTICAL MECHANICS OF TWO-DIMENSIONAL VESICLES

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Abstract

Recent work on the statistical mechanics of model membranes and vesicles in two dimensions by Leibler, Singh and the author [1,2] is briefly summarized.

Bilipid membranes constitute an important class of physicochemical systems demanding a systematic theoretical treatment. When the membranes close on themselves one obtains a *vesicle*, which represents a primitive prototype of a biological cell. Indeed, red blood cells are closely related to artificial bilipid vesicles (or liposomes). As conditions of temperature, pH, etc. are changed, red blood cells display a surprising range of more-or-less well-defined *shapes*: discocytes, stomatocytes, echinocytes, ... At the same time, typical vesicles in aqueous solution are sufficiently small that they are subject to significant thermal fluctuations or "flickering": thus, a statistical mechanical theory is more appropriate than a purely mechanical or thermodynamical analysis.

From the more general perspective of the development of statistical mechanics, the importance of the spatial dimensionality d in strongly interacting systems has become increasingly evident, especially in the study of phases and phase transitions. However, the intrinsic dimensionality D of the primary fluctuating objects is also a crucial feature. Statistical mechanics for $D = 0$, that is, for *points* representing atoms or simple molecules, is by now very well developed in nearly all its aspects. The last two decades have also seen great progress in our understanding of the case $D = 1$, describing *lines* or *curves* and applicable to polymeric molecules, in dilute solution, near walls, in melts, etc. This case also represents vortices in superfluid liquid helium or flux lines in superconductors, etc. Only more recently, however, has statistical mechanics started to develop for $D = 2$, representing *surfaces*. In the everyday ($d = 3$)-dimensional world, important applications are to interfaces and membranes. In field theory, $D = 2$ corresponds to the theory of "strings" in $d = 3 + 1 = 4$ space–time dimensions. Note that one can also approach the classification in terms of the *codimension* of the basic fluctuating manifolds, namely, $\bar{D} = d - D$. Then surfaces in $d = 3$ spatial dimensions and curves in $d = 2$ dimensions, on which we will focus here, both correspond to $\bar{D} = 1$.

In modeling a membrane which, unlike a simple interface, has a distinct, well-developed chemicophysical structure, it is important to recognize specific properties beyond the overall shape. In particular, it is crucial to allow for rather strong *connectivity* and, also, for an intrinsic *rigidity* or resistance to bending. Furthermore, in contemplating closed membranes or vesicles ($\overline{D} = 1$), which separate an *interior* region from an *exterior* region, it is clear that the pressure difference,

$$\Delta p = p_{\text{int}} - p_{\text{ext}}, \tag{1}$$

must play an important role. Indeed, purely in mechanical terms one can see that the interplay of rigidity with pressure, which controls its conjugate variable, namely the enclosed volume (for $d = 3$) or the area (for $d = 2$), can lead to abrupt changes in the equilibrium shape of a vesicle.

In a first approach to these problems, in collaboration with Leibler and Singh [1–3], Monte Carlo simulations (using the Cornell Supercomputer) and scaling concepts have been applied. The treatment so far has been confined to $d = 2$ dimensions. Apart from the value of clarifying the simpler conceptual situation first, current computer limitations make the simulation (or other numerical approaches) very difficult for closed surfaces in $d = 3$ dimensions. (See, however, the Jerusalem Winter School Proceedings [4] for recent developments of the general theory and simulations for open membranes.)

The membrane is represented by the traditional "pearl necklace model" of polymer theory, i.e. by a closed string of N hard, nonoverlapping beads of diameter a connected by loose "tethers" of fixed maximum length l_0 (sufficiently short that a bead cannot squeeze between two adjacently connected beads). Bending rigidity, with modulus κ, is introduced via energy terms

$$E_i = (\kappa/a)(1 - \cos\theta_i), \tag{2}$$

which tend to reduce the angles θ_i between neighboring bead-to-bead vectors.

When one sets the bending modulus κ and the pressure differential Δp to zero, one obtains *flaccid* vesicles which correspond simply to closed self-avoiding random walks or polymer chains. As one increases N, the number of beads, characteristic nontrivial size-dependences and associated fractal shapes emerge. All properties scale with definite powers of N. In particular, the radius of gyration R_G and the mean area vary as

$$\langle R_G^2 \rangle \sim N^{2\nu}, \tag{3}$$

$$\langle A \rangle \sim N^{2\nu_A}. \tag{4}$$

The Monte Carlo data (for N up to about 100) yield [1] $\nu = 0.755 \pm 0.018$. (Owing to the difficulties of reaching equilibrium, larger values of N cannot be handled reliably.) The estimate for the exponent ν agrees well with the exact result for self-avoiding walks

in the plane now known to be $\nu = \frac{3}{4}$. The simulations also give $\nu_A/\nu = 1.007 \pm 0.013$: this confirms the natural theoretical expectation $\nu_A = \nu$, which means that, despite the overall fractal nature of the fluctuating closed chain, its mean area is proportional to the square of its mean linear dimension. This result also confirms an old estimate by Sykes and Hiley [5], who studied areas of N-step polygons on square and triangular lattices and concluded that $2\nu_A = 1.50 \pm 0.04$.

When nonzero pressure differences are introduced, dramatic changes in shape and size eventually develop. It is found that the scaling variable

$$x = \frac{\Delta p a^2}{k_B T} N^{\varphi\nu} \tag{5}$$

controls the behavior for large N. For x of order unity, and positive or negative, eqs. (3) and (4) go over to the scaling forms [1]

$$\langle R_G^2 \rangle \approx N^{2\nu} X(x), \tag{6}$$

$$\langle A \rangle \approx N^{2\nu} Y(x), \tag{7}$$

where we have accepted $\nu = \nu_A$. Theoretical analysis indicates that the crossover exponent φ should take the value 2, since the pressure couples to the area. Fits to the simulations give $\varphi = 2.13 \pm 0.17$.

When x becomes large and positive, the vesicles become inflated into increasingly circular shapes, as is to be anticipated: ultimately, $\langle R_G^2 \rangle$ and $\langle A \rangle$ must increase as N^2. On the other hand, if Δp is made *negative*, the behavior of $X(x)$ and $Y(x)$ for large x describes how the vesicles "wrinkle up" and shrink. Eventually, for $x \gtrsim 10$, a new scaling regime is reached, in which one finds

$$X(x) \sim 1/|x|^{\sigma} \quad \text{and} \quad Y(x) \sim 1/|x|^{\tau}, \tag{8}$$

with exponents $\sigma = 0.13 \pm 0.05$ and $\tau = 0.25 \pm 0.04$. In this *collapsed regime*, the vesicles typically look skinny and branched like seaweed! Indeed, the exponents σ and τ are consistent with the expectation $\langle A \rangle \sim N$, which must hold under minimal area conditions, *and* with an overall size dependence on N corresponding to that expected for branched polymers or "lattice animals" (which are believed to belong to the same universality class [6]). Specifically, we find the size exponent $\nu_- = \nu(1 - \sigma\varphi) = 0.65 \pm 0.04$ compared with $\nu_- = 0.6408$ expected for branched polymers [7].

Introduction of nonzero rigidity κ leads to new phenomena. Small values of κ in the flaccid regime, where Δp vanishes or x is small, have only the effect of renormalizing the interbead distance or effective diameter; i.e. the Kuhn length is smoothly increased but exponents and shapes do not alter. However, in the deflated

regime with Δp negative and $|x| \gg 1$, the rigidity produces more startling effects. Indeed, one discovers that the model vesicles assume a series of well-defined characteristic shapes which have been termed *cytotypes*. A variety of shapes, illustrated graphically in refs. [1,2], are seen. Some are ellipsocytes, i.e. elliptical of variable eccentricity, tuned by the interplay of Δp, κ, and N. Others are bi-lobocytes, reminiscent of the cross-sections of real discocytes, i.e. resembling dumbbells with two rounded lobes separated by a narrower straight section. In some cases, planar stomatocytes or cup-shaped forms are obtained. Near borderline values of the parameters, the observed shapes in the Monte Carlo simulation appear to fluctuate between two or three quite distinct forms, as seen in a finite-size simulation of a particle or magnetic system near a bulk first-order phase transition [1].

To analyze the appearance of cytotypes, it is helpful to express the parameters in terms of characteristic lengths. Thus, one has the *contour* or *chemical length*

$$L = Na, \tag{9}$$

the *pressure* or *baric length*

$$l_p = |k_B T/\Delta p|^{1/2}, \tag{10}$$

and the *rigidity length*

$$l_\kappa \equiv \kappa/k_B T. \tag{11}$$

One can then argue [1] that the cytotype regime sets in when $l_\kappa > L \gtrsim 1$ and $\rho^*/L \lesssim 1$, where ρ^* is a characteristic smallest radius of curvature of a lobe or other feature in a cytotype. By minimization of the pressure and bending energy, this can be estimated as

$$\rho^* = (l_\kappa l_p)^{1/3} \sim (\kappa/\Delta p)^{1/3}. \tag{12}$$

Using the criterion $\rho^* = O(L)$, one can expect to realize the same cytotype for different values of N. In current work [8], this surmise is being tested and the various cytotype domains are being mapped out. The small equilibrium flickering of the cytotypes will be studied, as well as the nonlinear flickering observed [1] near the transitions from one cytotype to another. The sense in which the transitions might become true phase transitions in an appropriate large-N limit remains to be clarified. Note, however, that increasing N at *fixed* Δp and *fixed* κ leads only to inflated balloon-like vesicles (for $\Delta p > 0$), to flaccid self-avoiding rings (for $\Delta p = 0$), or to collapsed branched-polymer forms (for $\Delta p < 0$). Evidently, appropriate new scaling regimes must be elucidated.

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