Gaussian random field description of fluctuating fluid vesicles

P. Pieruschka[1,2] and H. Wennerström[2]
[1]Groupe de Dynamique des Phases Condensées, URA 233 de CNRS, Université Montpellier II, 34095 Montpellier 5, France
[2]Physical Chemistry 1, Chemical Center, University of Lund, Lund 22100, Sweden
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Gaussian random processes on spheres are studied as models of fluctuating fluid vesicles. We derive expressions for the mean volume, surface area, curvature, and square curvature of vesicles with arbitrarily strong Gaussian fluctuations. A Feynman-Hellman approximation allows, by variational minimization, a consistent derivation of structure factor and free energy of vesicles. As an example, we investigate a fluctuating vesicle with fixed mean surface area and volume for a wide range of values of the bending modulus.

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I. INTRODUCTION

It is now well established that systems of fluid surfactant membranes (or monolayers) can be described by the curvature-elastic Hamiltonian of the surfactant film [1–3]

$$\mathcal{H}=\int_S dS[2\kappa(H-H_0)^2+\bar{\kappa}K], \tag{1}$$

where H and K denote mean and Gaussian curvatures, H_0 is the spontaneous curvature (which is zero for bilayer membranes), and κ, $\bar{\kappa}$ are the bending and saddle-splay moduli (in units of k_BT), respectively. However, a satisfactory representation of all the complex shapes which the membrane film can form remains a challenge in particular for systems characterized by strong thermal fluctuations. In the case of closed membranes (vesicles), there have so far been two major ways of dealing with the problem of representing the effective surface of the vesicle: (i) for stiff systems ($\kappa \gg 1$) one can model vesicles as objects that fluctuate slightly around given equilibrium shapes [4–7] or—neglecting the thermal fluctuations of the membrane entirely—as surfaces of revolution, e.g., [8—11]; (ii) for "soft" membranes with $\kappa = O(1)$, numerical simulations can be used [12,13] to study the equilibrium shapes of the vesicle. The aim of this paper is to explore the possibilities of an analytical description of—possibly strongly—fluctuating vesicles which is suitable in both the high and low κ regimes. The paper is organized as follows. We first introduce random fields on spheres as models of closed membranes and derive the curvature and other important physical quantities commonly used in the description of fluctuating vesicles. Then a variational theorem is applied to consistently derive the structure factor and the free energy (i.e., including the entropy term) of fluctuating vesicles. Application of this model to the simple case of one fluctuating vesicle with constant mean surface area and volume and zero spontaneous curvature reveals, among other things, the possibility of an "order"-"disorder" transition upon change of the bending modulus (formally similar to the one observed in microemulsions and sponge phases [14]) and entropically stabilized shapes with significant contributions from odd l modes.

II. ISOTROPIC RANDOM FIELDS ON SPHERES

We consider a random process ξ on a sphere $\mathcal{S}$ in n dimensions whose correlation function is isotropic, i.e., only depends on the spherical distance γ between two points $\mathbf{r}\in\mathcal{S}, \mathbf{r}'\in\mathcal{S}$ and which can be represented as [15]

$$\langle \xi(\mathbf{r})\xi(\mathbf{r}')\rangle = \Omega^{-1}\sum_{l=0}^{\infty} b_l h(l,m)\frac{C_l^{(n-2)/2}(\cos\gamma)}{C_l^{(n-2)/2}(1)}, \tag{2}$$

where the C denotes Gegenbauer polynomials and where

$$b_l \geq 0, \quad \sum b_l h(l,m) < \infty. \tag{3}$$

The respective random process can be represented as a sum [15]

$$\xi(\mathbf{r}) = \sum_{lm} \xi_{lm} S_{lm}(\mathbf{r}), \tag{4}$$

where the S_{lm} are spherical harmonics and the random variables ξ_{lm} observe

$$\langle \xi_{lm}\rangle = 0, \quad \langle \xi_{lm}\xi_{l'm'}\rangle = b_l\delta_{ll'}\delta_{mm'}.$$

In practice, $n=2$ [16,17] and $n=3$ are interesting. In particular, for $n=3$ one can represent the random process as a dimensionless sum [15,18,19] which we denote

$$g(\theta,\phi) = \sum_{lm} a_{lm} Y_{lm}(\theta,\phi) \tag{5}$$

with a two-point correlation function [18,21]

$$\langle g(\theta,\phi)g(\theta',\phi')\rangle = \frac{1}{4\pi}\sum_{lm} |a_{lm}|^2 P_l(\cos\gamma), \tag{6}$$

where the P_l are Legendre polynomials and $\cos\gamma = \cos\theta\cos\theta' + \sin\theta\sin\theta'\cos(\phi-\phi')$.

If we further specialize to amplitudes a_{lm} that have Gaussian distributions, the process Eq. (5) becomes also a Gaussian process in real space and is thus completely determined by its mean and variance. Without loss of

generality, we can consider processes with zero mean.

Because the correlation function, Eq. (6), is infinitely often continuously differentiable, all its derivatives are also Gaussian random processes [19]. In particular, we will need the correlation functions involving the first and second derivatives that can be gained by appropriately differentiating Eq. (6); cf. the Appendix.

III. STATE REPRESENTATION AND STATISTICAL AVERAGES

The vesicle representations commonly used throughout the literature are (i) slightly fluctuating shapes [4–6] and (ii) surfaces of revolution, e.g., [8–11]. Both are suitable for describing very stiff systems with little or no fluctuations. The former have been used in numerous papers trying to gain the bending constant of a membrane from measuring the fluctuation spectrum of a vesicle, e.g., [7,20–22]. The latter were applied to calculate various red blood cell shapes. Recently, Heinrich, Svetina, and Žekš have tried to go beyond the restrictions of representations (i) and (ii) in [23] by expanding into a *nonrandom* series of spherical harmonics (in contrast to our representation, which is based on the correlation theory of *random* fields).

We start from representations formally similar to those used in (i). The interface is given by the nodal surface $u(r,\theta,\phi)=0$ through a scalar field $u(r,\theta,\phi)$,

$$u(r,\theta,\phi)=r-\rho\Gamma(g(\theta,\phi)), \tag{7}$$

so that the radial coordinate is single valued. We also demand that $\Gamma(g)$ be continuously differentiable. A form often used in the literature is [4]

$$\Gamma[g]=1+g(\theta,\phi). \tag{8}$$

It is neither unique nor particularly well behaved because it can lead to complications when the random process g reaches values that are large and negative. We will nevertheless use it because it is mathematically very simple, it will allow us later to compare with known results in certain limits, and, most importantly, because its entropy can be systematically approximated. To avoid pathological states arising from zero or negative values of the radial component, one could more conveniently employ state representations of the form

$$\Gamma[g]=1+g^2(\theta,\phi), \tag{9}$$

whose bending energy, surface area, etc. can also be rigorously evaluated [albeit more cumbersomely than for Eq. (8)] and which might therefore be useful as models of nonaxisymmetric shapes in theories based on pure energy minimizations. On the other hand, the evaluation of the entropy of transformed random fields of type Eq. (9) is, to our knowledge, currently not known so that we will not follow it up in the context of this work.

Next we have to establish the differential operators related to the bending Hamiltonian Eq. (1) and possibly to energies associated with changes in surface area or volume. The normal vector is $\mathbf{n}=\nabla u/|\nabla u|$ [for Eq. (8), $\nabla u=(1,-g_\theta/r,-g_\phi/(r\sin\theta))$ where subscripts denote derivatives] and determines the main physical operators for curvature $H=\frac{1}{2}\mathrm{div}\,\mathbf{n}$ and surface area $dS=r^2|\nabla u|\,d\Omega$.

There are two ways of proceeding from here. (i) Throughout the literature one usually performs a surface integration first and (implicitly, because of the ubiquitous use of the equipartition theorem) a Gaussian ensemble integration second. After the surface integration is performed, no statistical quantities are left and the Gaussian ensemble integral results in a trivial factor of unity. One assumes commonly g and its derivatives to be small and expands the relevant operators up to second order. Using the usual angular momentum Casimir operator L^2, one can perform the required surface integrals up to second [4–6] or higher (but finite) order in g [17,24]. (ii) One can reverse the order of integrations and exploit the fact that g is a random process to perform ensemble (or time) integrations first and the surface integration second. Explicitly, for any differential operator O on a surface given by Eq. (7) [25],

$$\begin{aligned}\left\langle\int\int\int\delta(u)|\nabla u|O\,dV\right\rangle_0&=\left\langle\int\int\int\delta(u)|\nabla u|Or^2\sin\theta\,d\theta d\phi dr\right\rangle_0\\&=\left\langle\int\int|\nabla u|\rho^2\Gamma^2O\sin\theta\,d\theta d\phi\right\rangle_0\\&=4\pi\rho^2\langle|\nabla u|\Gamma^2O\rangle_0\,,\end{aligned}$$

where $\langle\ \rangle_0$ denotes ensemble averaging and where we have assumed translational invariance of the problem in the last step. For the bending Hamiltonian (with $\bar{\kappa}=0$ because we cannot investigate topological changes) this means

$$\langle\mathcal{H}\rangle_0=4\pi\rho^2\langle|\nabla u|\Gamma^2[2\kappa(H-H_0)^2]\rangle_0\,. \tag{10}$$

Similarly, one can write the terms involving surface area and volume as

$$\left\langle\int_S dS\right\rangle_0=4\pi\rho^2\langle\Gamma^2|\nabla u|\rangle_0 \tag{11}$$

and

$$\left\langle\int_V dV\right\rangle_0=\frac{1}{3}\left\langle\int_S\mathbf{r}\cdot\mathbf{n}\,dS\right\rangle_0=\frac{4\pi}{3}\rho^3\langle\Gamma^3\rangle_0\,, \tag{12}$$

For the actual evaluation of the Gaussian averages, the correlation matrices are required because the various random processes (the field g and its derivatives) are not

necessarily decoupled [26]. The matrix elements of the correlation matrix can be calculated straightforwardly; cf. the Appendix. With the definitions

$$\sigma_0=\frac{1}{4\pi}\sum_{lm}\nu_{lm}\ , \tag{13}$$

$$\sigma_1=\frac{1}{4\pi}\sum_{lm}\nu_{lm}\frac{1}{2}l(l+1)\ , \tag{14}$$

$$\sigma_2=\frac{1}{4\pi}\sum_{lm}\nu_{lm}\frac{1}{8}[l^2(l+1)^2-2l(l+1)]\ , \tag{15}$$

where $\nu_{lm}=|a_{lm}|^2$, the correlation matrix is (cf. the Appendix)

$$A=\begin{pmatrix} \sigma_0 & 0 & 0 & -\sigma_1 & 0 & -\sigma_1 \\ 0 & \sigma_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & \sigma_1 & 0 & 0 & 0 \\ -\sigma_1 & 0 & 0 & \sigma_1+3\sigma_2 & 0 & \sigma_1+\sigma_2 \\ 0 & 0 & 0 & 0 & \sigma_2 & 0 \\ -\sigma_1 & 0 & 0 & \sigma_1+\sigma_2 & 0 & \sigma_1+3\sigma_2 \end{pmatrix} \tag{16}$$

and the ensemble average $\langle Q\rangle_0$ over the quantity Q reads explicitly [26]

$$\langle Q\rangle_0=\frac{1}{\sqrt{(2\pi)^6|A|}}\int_{-\infty}^{\infty}\cdots\int_{-\infty}^{\infty}d\mathbf{x}\,Q \times\exp\left[-\frac{1}{2}\mathbf{x}A^{-1}\mathbf{x}^T\right]\ , \tag{17}$$

with $\mathbf{x}=(g,g_\phi,g_\theta,g_{\theta\theta},g_{\theta\phi},g_{\phi\phi})$. Before evaluating these integrals for specific representations, we see that owing to Eqs. (13)–(15) the result has to be a function of $l(l+1)$ which is essentially the eigenvalue of the only Casimir operator of the algebra so_3, as it should be. This has already been pointed out by Peterson [27]. Another important general property is that second derivatives of g do not appear in the complicated square root parts of the operators (implied by $|\nabla u|$). Gaussian integrations over the second derivatives can therefore be explicitly performed and one finds after some algebra that σ_2 appears only linearly in the final result. We will take advantage of this later. Finally, we see that the zeroth and second derivatives are coupled, signifying that the invariance of the energy under $l=0,1$ deformations [28] in the second order approximation will not hold in general.

We have thus derived the statistical averages over the relevant physical operators to all orders in g and its derivatives for single-valued representations of type Eq. (7) in terms of single to sixfold Gaussian integrals.

We can illustrate this for the example of representation equation (8), where we find for the mean square curvature

$$4\pi\left\langle\frac{1}{4}\frac{dS}{d\Omega}(\mathrm{div}\,\mathbf{n})^2\right\rangle_0=4\pi\frac{1}{\sqrt{2\pi\sigma_0}}\frac{1}{8\sigma_1}\int_{-\infty}^{\infty}\int_0^{\infty}dg\,dz\,e^{-g^2/(2\sigma_0)}e^{-z/(2\sigma_1)}r^{-2}\left[1+z\frac{\rho^2}{r^2}\right]^{-5/2} \times\left[\left[2r+3z\frac{\rho^2}{r}\right]^2+4\rho\frac{\sigma_1}{\sigma_0}g\left[2r+3z\frac{\rho^2}{r}\right]\left[1+\frac{1}{2}z\frac{\rho^2}{r^2}\right] +4\rho^2\left[\sigma_1-\frac{\sigma_1^2}{\sigma_0}+g^2\frac{\sigma_1^2}{\sigma_0^2}\right]\left[1+\frac{1}{2}z\frac{\rho^2}{r^2}\right]^2+8\rho^2\sigma_2\left[1+z\frac{\rho^2}{r^2}+\frac{3}{8}z^2\frac{\rho^4}{r^4}\right]\right] \tag{18}$$

the mean curvature,

$$4\pi\left\langle\frac{1}{2}\frac{dS}{d\Omega}\mathrm{div}\,\mathbf{n}\right\rangle_0=4\pi\frac{1}{\sqrt{2\pi\sigma_0}}\frac{1}{4\sigma_1}\int_{-\infty}^{\infty}\int_0^{\infty}dg\,dz\,e^{-g^2/(2\sigma_0)}e^{-z/(2\sigma_1)}\left[1+z\frac{\rho^2}{r^2}\right]^{-1} \times\left[2r+3z\frac{\rho^2}{r}+2g\rho\frac{\sigma_1}{\sigma_0}\left[1+\frac{1}{2}z\frac{\rho^2}{r^2}\right]\right] \tag{19}$$

the mean surface area,

$$4\pi\left\langle\frac{dS}{d\Omega}\right\rangle_0=4\pi\frac{1}{\sqrt{2\pi\sigma_0}}\frac{1}{2\sigma_1}\int_{-\infty}^{\infty}\int_0^{\infty}dg\,dz\,e^{-g^2/(2\sigma_0)}e^{-z/(2\sigma_1)}r^2\left[1+z\frac{\rho^2}{r^2}\right]^{1/2} \tag{20}$$

and the mean volume of the vesicle

$$\frac{4\pi}{3}\left\langle\frac{dV}{d\Omega}\right\rangle_0=\frac{4\pi}{3}\frac{1}{\sqrt{2\pi\sigma_0}}\int_{-\infty}^{\infty}dg\,e^{-g^2/(2\sigma_0)}r^3 \tag{21}$$

where $dS/d\Omega = r^2|\nabla u|$ and $r=\rho(1+g)$. Equation (18) appears to have a divergence for $r\to 0$. We can avoid this divergence by restricting the region of integration to the "well-behaved" part of the vesicle by introducing a finite-size, molecular cutoff r_c (later we set $r_c=1$) for the radial component r. This can be done by multiplying all operators with a Heaviside step function, which is equivalent to changing the integration range of g from $\int_{-\infty}^{\infty}$ to $\int_{-1+r_c/\rho}^{\infty}$; the omitted regions can be imagined to be filled by "patches" of surface that lie on a sphere of radius r_c. They should not have any crucial effect as long as the vesicle is large compared to a micelle. We will therefore neglect these problematic regions in the numerical example calculations below.

While Eqs. (18)–(21) give us the possibility of studying vesicle shapes that can deviate drastically from the spherical shape, our representation is still single valued. Hence excitations of elliptical, discocyte, dumbell, pear-shape, budding type, and moderate cup shape are covered but extreme stomatocytes are not. This restriction, however, should be more than offset by the capacity of the model to treat fluctuations more accurately, thus including soft vesicles with low values of the bending constant. Such "floppy" vesicles have been studied experimentally [29] and appear to have technological potential as drug delivery systems [30]; they have—according to [13]—so far only been investigated numerically.

IV. FREE ENERGY

To determine the free energy of vesicles, we use a variational method. An upper limit to the free energy $\mathcal{F}$ of a system characterized by a Hamiltonian $\mathcal{H}$ can be given by [31,25]

$$\underline{F} < F = \langle \mathcal{H}-\mathcal{H}_0\rangle_0 + \underline{F}_0 . \tag{22}$$

Here $\underline{F}$ is the free energy associated with the bending Hamiltonian $\mathcal{H}$ and $\underline{F}_0$ is the free energy of a Gaussian [25,32]

$$\underline{F}_0 = -\frac{1}{2}\sum_{lm} \ln \nu_{lm} . \tag{23}$$

$\langle \mathcal{H}_0\rangle_0$ is, according to the equipartition theorem, a constant and $\langle \mathcal{H}\rangle_0$ is given by Eqs. (18),(19). Equation (22) is markedly different from free energies based on the equipartition theorem (e.g., [6]) which assume a "quasi-rigid" regime $\kappa \gg 1$ [33]. We also note that our theory includes, in principle, all length scales so that application of renormalized rather than bare bending moduli is not necessary.

Surface tension and pressure can be included by adding terms of the sort $\sim\lambda\langle dS/d\Omega\rangle_0$ and $\sim\Delta p\langle dV/d\Omega\rangle_0$ to $\mathcal{H}$, where λ and Δp are, depending on the model, physical parameters or Lagrange multipliers. Similarly, the mean curvature term can either enter with constant spontaneous curvature H_0 (spontaneous curvature model, [8]) or be coupled by a Lagrange multiplier [bilayer coupling hypothesis (BCH), [34,9,22], which is not pursued here].

Minimization of the right-hand side of Eq. (22) with respect to the mode distribution ν_{lm} determines the best Gaussian ensemble that approximates the real ensemble characterized by the bending Hamiltonian [25,35]. This minimization depends on the specific physical situation and can be technically very complicated. In the following section we consider a simple example.

V. VESICLES WITH CONSTANT MEAN SURFACE AREA AND VOLUME

We can use our theory to investigate systems similar to the ones of Deuling and Helfrich [8], i.e., single vesicles with given mean surface area S_0 and mean volume V. The correspondence is, however, not exact because fluctuations around the mean are possible by definition (as we are dealing with random systems). Conservation of volume and area become rigorous only if we follow Helfrich and consider ensembles, (with fixed number N) of vesicles [6]; in ensembles area fluctuations can be interpreted as local fluctuations in the surfactant concentration which do not require further consideration. For a single vesicle area fluctuations can only be related to stretching and compression of the membrane. We should therefore restrict ourselves to (i) a vesicle made up of a large number of constituent molecules (number of degrees of freedom) and (ii) state of the vesicle whose volume and area fluctuate only slightly, in case such states are found to be stable. The second condition can always be enforced if we introduce an energy penalty for fluctuations of surface area and volume around their respective mean values. These are coupled to the energy by two moduli κ_s and κ_v, where κ_s is a stretch modulus [3].

We use the notation introduced by Deuling and Helfrich: the equivalent radius R_0 of the vesicle is given by $S_0=4\pi R_0^2$ and the reduced volume by $v=V/V_0$. We have to minimize F (for $\bar{\kappa}=0$) under the constant mean area and volume constraints

$$F \to 4\pi\left[2\kappa\left\langle\frac{dS}{d\Omega}H^2\right\rangle_0 - 4\kappa H_0\left\langle\frac{dS}{d\Omega}H\right\rangle_0 + 2\kappa H_0^2\left\langle\frac{dS}{d\Omega}\right\rangle_0 + \lambda\left\langle\frac{dS}{d\Omega}\right\rangle_0 + \Delta p\left\langle\frac{dV}{d\Omega}\right\rangle_0\right] + \underline{F}_0 = \bar{F} + \underline{F}_0 . \tag{24}$$

This expression differs from previously considered free energies, which only contained the bending energy and the constraints in ensembles of nonrandom configurations.

The extremal structure factor can be derived by taking the derivative of F with respect to the ν_{lm}, $\partial F/\partial\nu_{lm}=0$; the second derivative shows that the extremal structure factor is minimal:

$$\nu_{lm} = \frac{1}{2}\left\{\frac{1}{4\pi}\left[\frac{1}{8}\frac{\partial\bar{F}}{\partial\sigma_2}l^2(l+1)^2 + \left[\frac{1}{2}\frac{\partial\bar{F}}{\partial\sigma_1} - \frac{1}{4}\frac{\partial\bar{F}}{\partial\sigma_2}\right]l(l+1) + \frac{\partial\bar{F}}{\partial\sigma_0}\right]\right\}^{-1} . \tag{25}$$

In general,

$$\nu_{lm}=[al^2(l+1)^2+bl(l+1)+c]^{-1} . \tag{26}$$

We note now that $\partial\bar{F}/\partial\sigma_2=\partial\bar{F}/\partial\sigma_2(\sigma_0,\sigma_1)$ because, as we saw, σ_2 enters Eq. (18) only linearly. On the other hand, the two constraints fix σ_0 and σ_1,

$$\left\langle\frac{dV}{d\Omega}\right\rangle_0=\left\langle\frac{dV}{d\Omega}\right\rangle_0(\sigma_0)=\text{const}=V, \tag{27}$$
$$\left\langle\frac{dS}{d\Omega}\right\rangle_0=\left\langle\frac{dS}{d\Omega}\right\rangle_0(\sigma_0,\sigma_1)=\text{const}=S_0 ,$$

so that the coefficient a is readily given as

$$a=\frac{\kappa}{2}\frac{\partial\langle dS/d\Omega H^2\rangle_0}{\partial\sigma_2} \tag{28}$$

and the remaining coefficients b,c are uniquely (cf. the Appendix) determined by the two equations

$$\sigma_0=\frac{1}{4\pi}\sum_{lm}\nu_{lm} ,$$
$$\sigma_1=\frac{1}{4\pi}\sum_{lm}\frac{1}{2}l(l+1)\nu_{lm} , \tag{29}$$

where ν_{lm} has the form Eq. (26) with a given by Eq. (28). A natural restriction on this equation system is given by Eq. (3), implying that a,b,c have to yield structure factors with $\nu_{lm}(a,b,c)\geq 0$.

Thus the problem is formally solved at fixed κ,H_0,S_0,V, and ρ for state representations of form Eq. (8). We have checked our formalism numerically and verified for various examples that indeed a minimum of the free energy had been found. To determine eventually the most physical Gaussian state for a vesicle given by Eq. (8) and at fixed $\kappa,\langle dS/d\Omega\rangle_0,\langle dV/d\Omega\rangle_0$, we have to minimize the free energies with respect to the (auxiliary) parameter ρ (note that the value of the stretch modulus κ_s enters only in the final minimization with respect to ρ but not in the variational minimization because σ_0,σ_1 are for given ρ fixed in the system discussed here).

To illustrate our theory, we have chosen a system characterized by a number of realistic parameters: with a membrane thickness $r_c=1$, the equivalent radius is $R_0=50$ so that $S_0=4\pi R_0^2, V_0=4/3\pi R_0^3$. In order to determine the upper summation cutoff in $\sum_{lm}$ we follow Helfrich and identify M, the number of degrees of freedom, with $(l_c+1)^2=2M$, where we prefer here unit patches of twice the molecular scale to stay closer to the regime where the linear elasticity Hamiltonian is valid [36]; hence, in our example $l_c\approx 88$.

At $v=V/V_0=1$, a value of $\kappa=0.5$ and 2.5 and zero stretch modulus, the free energy decreases steadily for decreasing values of ρ. Closer investigation shows that entropy drives the vesicle towards increasingly fluctuating ensembles. The structure factors of the vesicle are, for all ρ, monotonically decreasing (i.e., peaked at $l=0$) and represent thus a disordered state with no dominant mode that could give the vesicle a well-defined shape. High values of the stretch modulus, on the other hand, stabilize the vesicle and for $\kappa_s\to\infty$ (when all fluctuations are suppressed) the shape of a perfect sphere is retrieved. For $\kappa=2.5$ the situation is more complex. There we find (for $\kappa_s=0$) two free energy minima at large $\rho\approx 48$ and at very small ρ. The large ρ minimum is characterized by weak fluctuations and can be reasonably identified as a (metastable) spherical vesicle state. Its structure factor shows again no dominant nonzero mode. The global minimum appears as in the case $\kappa=0.5$ to be at very low $\rho\ll R_0$. For higher κ the local minimum deepens but does not become global (up to a value of $\kappa=10$ considered here).

For $v=0.75$ and $\kappa=0.5$ there is a local free energy minimum close to the saturation value of ρ. In contrast to $v=1$ the free energy is now not dominated by the entropic contribution, and competition with the bending energy leads to the formation of a shallow free energy minimum. The structure factor resembles qualitatively that of $\kappa=0.5$, $v=1$, i.e., the coefficient b in Eq. (26) is positive and hence the vesicle shape is disordered. For $\kappa=2.5$ the local minimum has deepened and the structure factor Eq. (26) now has a peak at nonzero l, i.e., $b<0$ in Eq. (26) meaning that between $\kappa=0.5$ and $\kappa=2.5$ an order-disorder line has been crossed that is conceptually similar to the disorder line observed in microemulsions and sponge phases [14]. The structure of the vesicle is dominated by the $l=2$ mode as often seen in theories based on the minimization of the bending energy only. Indeed, the mechanism that accounts for the stability of the vesicle differs qualitatively from the case $\kappa=0.5$ in that the bending energy itself shows now a minimum at high ρ. For higher bending moduli, $\kappa=5$ and $\kappa=10$, the large ρ minima become deeper, as expected; for $\kappa=5$ both the $l=2$ and $l=3$ modes are dominant while for $\kappa\gtrsim 10$ excitations of type $l=3$ prevail. We note that the strong $l=3$ mode is indicative of a shape with broken "up-

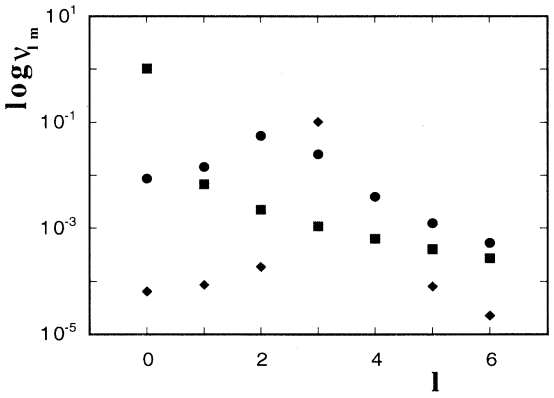

FIG. 1. Approximate structure factors ν_{lm} of a vesicle at reduced volume $v=0.75$ for values of $\kappa=0.5$ (■), 2.5 (●), and 100 (◆); the area of the vesicle is specified in the text. The appearance of ν_{lm} changes from monotonic to peaked at $0.5<\kappa<2.5$. The full domain of $0\leq l\leq l_c=88$ has, for the sake of clarity, not been plotted. The free energy minima were evaluated at a finite step size of $\Delta\rho=0.5$, so that small deviations of the minimal structure factors from the ones plotted here are possible.

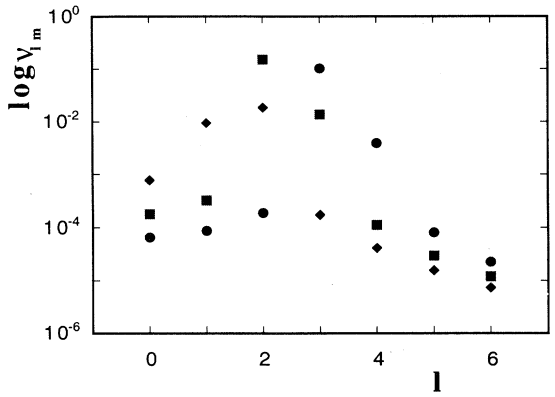

FIG. 2. Approximate structure factors v_{lm} of a vesicle at bending modulus $\kappa=100$ for values of $v=0.75$ (●), 0.85 (■), and 0.975 (◆).

down" symmetry such as stomatocytes (or pears) [11], while strong $l=2$ modes are, for example, characteristic of prolate and oblate ellipsoids, dumbbell, and discocyte shapes. It would be interesting to actually plot detailed real-space images of the corresponding real-space structures for comparison with the (nonrandom) shapes typically found in the $\kappa\rightarrow\infty$ theories, e.g., [8,9,11]; the computational effort to do so with good statistical accuracy goes, however, beyond the scope of this paper and will be pursued elsewhere.

$\kappa\rightarrow\infty$ theory predicts for zero spontaneous curvature a sequence stomatocyte-oblate-prolate upon increase of v, with a critical $v\approx 0.59$ for the oblate-stomatocyte transition. We observe similar qualitative behavior when investigating systems with $0.75\leq v\leq 1$, $H_0=0$, and large $\kappa=100$: for values of v up to $0.8\leq v\leq 0.85$ we find dominant $l=3$ modes, while the spectra peak at $l=2$ for v up to ≈ 0.975. Above $v\approx 0.975$ the entropic contribution to the free energy begins to stabilize appreciably strong $l=1$ components (the energy term by itself would significantly weaken $l=1$ in favor of $l=2$ modes). This appears to be consistent with the prediction by Peterson [27], who found that $\kappa\rightarrow\infty$ systems (where no entropic effects are taken into account) favor $l=2$ deformations in the limit $v\rightarrow 1$.

In Figs. 1 and 2 we show structure factors evaluated for the above sample systems $v=0.75$ ($\kappa=0.5$, 2.5, 100), and $\kappa=100$ ($v=0.75$, 0.85, 0.975), respectively. Structure factors predicted by the random field model could, in principle, serve as the theoretical input in measurements of the bending moduli of membranes [7,20–22] and should improve the accuracy of these measurements, in particular for membranes in the low κ regime [29], or for membranes whose equilibrium state is nonspherical [22]. The (technical) disadvantage of a genuine low κ treatment would be that numerical evaluation of the structure factors replaces the simple analytical formulas available in high κ theory.

VI. CONCLUSION

We have presented in this paper a random field approach to the problem of the parametrization of fluctuating vesicles. A general formalism based on Gaussian random field theory was developed and physical quantities related to the internal energy of a closed membrane (including, e.g., mean surface area and mean curvatures) were calculated to all orders in the fluctuations of the membrane (for the class of single-valued representations). The energy terms together with the entropy of a Gaussian process constitute a systematic, variational upper bound to the free energy of a vesicle (or ensembles of vesicles). Minimization of the free energy bound made it possible to consistently derive the approximate structure factor and free energy of the vesicle.

The model goes beyond previous investigations of vesicles by permitting the description of strongly fluctuating nonspherical shapes unlike, e.g., [4–6], by minimizing the free energy of these shapes (and not merely the bending energy) in contrast with, e.g., [8–11] and by providing a relatively simple theoretical framework with no necessity for extensive numerical simulations [13].

As a first—and simplest—example, we studied the behavior of a vesicle at given mean surface area and volume as a function of the bending modulus κ and the reduced volume v. Our main observations include (i) the distinction of states of the fluctuating vesicle—similar to microemulsions and sponge phases—as disordered and ordered, depending on whether the structure factor shows a peak at nonzero wave vector, and (ii) that even in the minimalistic example studied here, a rich variety of strongly fluctuating (random and nonaxisymmetric) shapes emerges, including entropically stabilized excitations of odd l type.

The main shortcomings of our formulation are the single-valuedness of the representation (a restriction not encountered in theories based on surfaces of revolution or in simulations) that also prevents us from studying the important possibility of topological transitions (disintegration of one closed membrane into several vesicles should be expected at very small bending stiffness) and, on a more formal level, the assumption of mode independence of the model ensemble that might not be a good approximation under all circumstances [37].

Nevertheless, our results encourage application of the random field description to more complicated physical systems (such as ensembles of fluctuating vesicles [38]), which will be investigated in future work.

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APPENDIX

1. Correlation function

$$\langle g(\theta,\phi)g(\theta',\phi')\rangle_0=\sum_{ll'mm'}\langle a_{lm}a_{l'm'}\rangle_0 Y_{lm}(\theta,\phi)Y_{l'm'}(\theta',\phi').$$

The averages over the random amplitudes can be explicit-

ly derived because the Gaussian probability densities are known to be

$$\sim\exp\left[\left[\frac{\mathrm{Re}(a_{lm})^2+\mathrm{Im}(a_{lm})^2}{2\nu_{lm}}\right]\right]$$

and $\langle a_{lm}a_{l'm'}\rangle_0\sim\delta_{l-l',0}\delta_{m-m',0}$ [cf., e.g., [32]). With the Condon-Shortley phase convention [i.e., $a_{l,-m}=(-1)^m a^*_{lm}$ and $Y_{l,-m}=(-1)^m Y^*_{lm}$] and the addition theorem of spherical harmonics we find, finally, Eq. (6).

The correlation functions involving derivatives can be calculated by

$$\left\langle\frac{\partial^{p+q}}{\partial\theta^p\partial\phi^q}g(\theta,\phi)\frac{\partial^{p'+q'}}{\partial\theta'^{p'}\partial\phi'^{q'}}g(\theta',\phi')\right\rangle_0 = \frac{\partial^{p+q+p'+q'}}{\partial\theta^p\partial\phi^q\partial\theta'^{p'}\partial\phi'^{q'}}\langle g(\theta,\phi)g(\theta',\phi')\rangle_0$$

and the corresponding moments that enter the correlation matrix follow by setting $\theta=\theta'$, $\phi=\phi'$ in the final formulas. The moments are usually θ dependent and the general form of the correlation matrix contains many nonzero matrix elements posing technical difficulties. However, because both the field and the operators in the Hamiltonian are so_3 invariants, the final result cannot depend on θ. We can, therefore, choose any convenient angle. For $\theta=\pi/2$ the matrix simplifies into Eq. (16). As a cross check of our calculations, it is apt to perform the integrations over the physical operators for arbitrary θ at least for the quite simple operators for surface area, volume, and mean curvature. With the transformation

$$g_\phi\to g_\phi\sin\theta,\quad g_{\theta\phi}\to g_{\theta\phi}\sin\theta,\quad g_{\phi\phi}\to g_{\phi\phi}\sin\theta$$

it is possible to arrive at the same results as those given in the text for the conveniently chosen value of $\theta=\pi/2$. Similarly, we have successfully checked our results by rederiving the well-known second order results of Safran [4] and Helfrich [6] using the general form of the correlation matrix.

Finally, for the first example in Sec. V ($v=1$) we compared numerically the values of the exact integrals for surface, curvature, etc. with the approximate expressions given by Helfrich [6] and found increasingly good agreement for $\rho\to R_0$, as it should be.

2. Uniqueness of the solution

To investigate the uniqueness of the solution of Eq. (29), it is convenient to change to the approximate integral representation [6]. The equation system reads then approximately

$$\int_0^{l_c}(2l+1)\nu_{lm}\,dl=4\pi\sigma_0\ ,$$
$$\int_0^{l_c}(2l+1)l(l+1)\nu_{lm}\,dl=8\pi\sigma_1\ ,$$

with $\nu_{lm}^{-1}=al^2(l+1)^2+bl(l+1)+c$. Consider two distinct solutions b_1,c_1 and b_2,c_2 and abbreviate $2l+1=\lambda_p$, $l(l+1)=\lambda^2$, $(al^2(l+1)^2+b_1l(l+1)+c_1)(al^2(l+1)^2+b_2l(l+1)+c_2)=D$. Then

$$\int_0^{l_c}\lambda_pD^{-1}[(b_2-b_1)\lambda^2+(c_2-c_1)]dl=0\ ,$$
$$\int_0^{l_c}\lambda_pD^{-1}\lambda^2[(b_2-b_1)\lambda^2+(c_2-c_1)]dl=0\ ,$$

with $D>0$ for all l. Therefore, a change in the sign of the integrands can only be effected by the factor $(b_2-b_1)\lambda^2+(c_2-c_1)$. This term is parabolic and can—because we are only interested in positive l—become zero at most one point $\lambda_0\leftrightarrow l_0$, $0<l_0<l_c$. The integrals can be split into two integrals by $\int_0^{l_c}\cdots\to\int_0^{l_0}\cdots+\int_{l_0}^{l_c}\cdots$, each of which has an integrand that is either ≥0 or ≤0 over its respective integration range. Then

$$\int_0^{l_0}\lambda_pD^{-1}[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl = -\int_{l_0}^{l_c}\lambda_pD^{-1}[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl\ ,$$
$$\int_0^{l_0}\lambda_pD^{-1}\lambda^2[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl = -\int_{l_0}^{l_c}\lambda_pD^{-1}\lambda^2[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl\ .$$

These equations can be divided (because $b_1\neq b_2, c_1\neq c_2$ are assumed) and the ratio of the integrals can be called Λ^2, so that

$$\int_0^{l_0}\lambda_pD^{-1}\lambda^2[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl = \Lambda_1^2\int_0^{l_0}\lambda_pD^{-1}[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl\ , \quad \text{(A1)}$$
$$\int_{l_0}^{l_c}\lambda_pD^{-1}\lambda^2[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl = \Lambda_2^2\int_{l_0}^{l_c}\lambda_pD^{-1}[(b_2-b_1)\lambda^2+(c_2-c_1)]\,dl\ , \quad \text{(A2)}$$

with

$$\Lambda_1^2=\Lambda_2^2=\Lambda^2\ . \quad \text{(A3)}$$

On the other hand, the generalized mean value theorem of integral calculus states that for two continuous functions $F(x)$, $G(x)$ with either $G(x)\geq0$ or $G(x)\leq0$ for all x, $\int_{\xi_1}^{\xi_2}F(x)G(x)dx=F(\xi)\int_{\xi_1}^{\xi_2}G(x)dx$ with $\xi_1\leq\xi\leq\xi_2$. Applied to our case [$F(x)\to\lambda^2$], this leads to equations formally identical to Eqs. (32), (33) but with

$$0\leq\Lambda_1^2\leq l_0^2,\quad l_0^2\leq\Lambda_2^2\leq l_c^2\ . \quad \text{(A4)}$$

The equality signs in the above inequalities can be excluded because λ^2 is strictly monotonic; hence, a contradiction with Eq. (A3) has been found.

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