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INFLUENCE OF ANISOTROPIC MEMBRANE PROPERTIES ON THE SHAPE OF THE MEMBRANE

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Abstract. Membranous structures that are composed of particles with in-plane C_2 group symmetry are studied. Starting from a single-constituent energy it is derived that the relevant invariants for description of such systems are the mean curvature and the curvature deviator; the energy of the system can be expressed in a simple and transparent form by these two invariants while their average values span the phase diagram of shapes that can be attained by the membrane enclosed structures.

A variational problem for axisymmetric shapes is stated where the shapes with extreme average mean curvature and extreme average curvature deviator at relevant constraints are sought for. It is shown that, at fixed membrane area and at fixed enclosed volume, the solutions of the variational problem correspond to spherical, cylindrical and toroidal shapes. These solutions form lines in the phase diagram of possible shapes that separate classes of shapes with different symmetry properties. Physically, these lines represent limits of trajectories formed by processes that cause change of the average mean curvature and/or average curvature deviator, such as intercalation of particles into the membrane. Correspondence with some experiments involving toroidal structures of erythrocyte membrane, induced by exogenously added amphiphilic molecules, is considered.

1. Introduction

The membrane is considered as a system with one of its extensions much smaller than the other two. Therefore the shape of the membranous structure resembles a two-dimensional surface embedded into a three-dimensional space $\mathbb{R}^3$.

The two-dimensional surface in $\mathbb{R}^3$ can be described in an elegant and easy-to-visualize way by a local 2×2 curvature tensor. However, within two dimensions the curvature cannot be directly perceived. In physical description, the membrane is composed of particles that act one upon another. The interaction between a chosen particle and its surrounding depends on the properties of the membrane constituents and their mutual configuration within the membrane. So, the particle directly perceives the local membrane curvature. In other words, the energy of the particle depends on the local membrane curvature. In describing the shape of the membranous structure as a shape of the two-dimensional surface in $\mathbb{R}^3$, we should have in mind that the membrane is really a three dimensional structure. In our description the "third dimension" is accounted for in the free energy of the system.

Knowing the curvature tensor in every point of the membrane and assuming that the system attains the shape of minimal free energy at given constraints, it is convenient to chose the invariants of the curvature tensor by which the free energy can be expressed in a simple and transparent way.

In this work, we determine the relevant invariants of the curvature tensor by the single-inclusion energy that forms an origin for the derivation of the free energy of the membrane. We study the shapes of the membranous structures within the frame of these invariants.

2. Single-Inclusion Energy

Any constituent of the membrane can be considered as an inclusion that is acted upon by a curvature field of the membrane. It is taken that the inclusions have a C_2 group symmetry with respect to the axis normal to the membrane surface and can therefore exhibit orientational effects.

Let us imagine that there exists a shape which would completely fit the inclusion. This shape is referred to as the membrane shape intrinsic to the inclusion. In general, the local membrane shape differs form the shape intrinsic to the inclusion.

The origin of the coordinate system is taken at the site of the inclusion. The

membrane shape at this site is described by the diagonalized curvature tensor $\mathbf{C}$,

$$\mathbf{C} = \begin{bmatrix} C_1 & 0 \\ 0 & C_2 \end{bmatrix}, \tag{1}$$

while the membrane shape intrinsic to the inclusion is described by the diagonalized curvature tensor $\mathbf{C}_{\mathrm{m}}$

$$\mathbf{C}_{\mathrm{m}} = \begin{bmatrix} C_{1\mathrm{m}} & 0 \\ 0 & C_{2\mathrm{m}} \end{bmatrix}. \tag{2}$$

The principal directions of the membrane are in general different from the principal directions intrinsic to the inclusion, the systems being mutually rotated for an angle ω.

We introduce the **mismatch tensor** $\mathbf{M}$,

$$\mathbf{M} = \mathbf{R}\mathbf{C}_{\mathrm{m}}\mathbf{R}^{-1} - \mathbf{C} \tag{3}$$

where $\mathbf{R}$ is the rotation matrix,

$$\mathbf{R} = \begin{bmatrix} \cos\omega & -\sin\omega \\ \sin\omega & \cos\omega \end{bmatrix}. \tag{4}$$

The single-inclusion energy is defined as the energy that is spent by adjusting the inclusion into the membrane. Since energy is a scalar quantity, it is determined by the terms composed of invariants of the mismatch tensor $\mathbf{M}$, i. e. the trace and the determinant of the tensor. The energy is approximated by the expansion of these invariants up to the second order in the elements of $\mathbf{M}$,

$$E = \frac{K}{2}(\mathrm{Tr}\,\mathbf{M})^2 + \bar{K}\det\mathbf{M}, \tag{5}$$

where K and $\bar{K}$ are constants. Using the expressions (1–5) yields the expression for the single-inclusion energy

$$E = \frac{\xi}{2}(H - H_{\mathrm{m}}) + \frac{\xi + \xi^{\star}}{4}(\hat{C}^2 - 2\hat{C}\hat{C}_{\mathrm{m}}\cos 2\omega + \hat{C}_{\mathrm{m}}^2) \tag{6}$$

where

$$H = \frac{1}{2}(C_1 + C_2), \qquad H_{\mathrm{m}} = \frac{1}{2}(C_{1\mathrm{m}} + C_{2\mathrm{m}}) \tag{7}$$

are the respective mean curvatures, while

$$\hat{C} = \frac{1}{2}(C_1 - C_2), \qquad \hat{C}_{\mathrm{m}} = \frac{1}{2}(C_{1\mathrm{m}} - C_{2\mathrm{m}}). \tag{8}$$

The constants used in Eq. (6) are $\xi = 2\bar{K} + 4K$ and $\xi^{\star} = -6\bar{K} - 4K$.

3. Free Energy of the Inclusions

The partition function q of a single inclusion is [5]

$$q = \frac{1}{\omega_0} \int_0^{2\pi} \exp\left(-\frac{E(\omega)}{kT}\right) \mathrm{d}\omega\,, \tag{9}$$

with ω_0 an arbitrary angle quantum and k the Boltzmann constant. In the partition function of the inclusion the contribution of the orientational states q_{orient} is distinguished from the contribution of the other states q_{c}, $q = q_{\mathrm{c}} q_{\mathrm{orient}}$,

$$q_{\mathrm{c}} = \exp\left[-\frac{\xi}{2kT}(H - H_{\mathrm{m}})^2 - \frac{\xi + \xi^\star}{4kT}(\hat{C}^2 + \hat{C}_{\mathrm{m}}^2)\right], \tag{10}$$

$$q_{\mathrm{orient}} = \frac{1}{\omega_0} \int_0^{2\pi} \exp\left[\frac{(\xi + \xi^\star)\hat{C}\hat{C}_{\mathrm{m}} \cos 2\omega}{2kT}\right] \mathrm{d}\omega\,. \tag{11}$$

The integration over ω yields

$$q_{\mathrm{orient}} = \frac{1}{\omega_0} \mathrm{I}_0\left(\frac{\xi + \xi^\star}{2kT}\hat{C}\hat{C}_{\mathrm{m}}\right) \tag{12}$$

where I_0 is the modified Bessel function. The values of $\hat{C}$ and $\hat{C}_{\mathrm{m}}$ in the expressions (10) and (12) can be replaced by its absolute values $D = |\hat{C}|$ and $D_{\mathrm{m}} = |\hat{C}_{\mathrm{m}}|$, where D and D_{m} are the respective curvature deviators. The curvature deviator is also an invariant of the curvature tensor as it can be expressed by the trace $\mathrm{Tr}\,\mathbf{C} = 2H$ and the determinant $\det \mathbf{C} = C_1 C_2$,

$$D = \sqrt{(\mathrm{Tr}\,\mathbf{C}/2)^2 - \det \mathbf{C}} = \sqrt{H^2 - C_1 C_2}\,. \tag{13}$$

The free energy of the inclusion is then obtained by the expression $F_{\mathrm{i}} = -kT \ln q$,

$$F_{\mathrm{i}} = \frac{\xi}{2}(H - H_{\mathrm{m}})^2 + \frac{\xi + \xi^\star}{4}(D^2 + D_{\mathrm{m}}^2) - kT \ln\left[\mathrm{I}_0\left(\frac{\xi + \xi^\star}{2kT} D D_{\mathrm{m}}\right)\right]. \tag{14}$$

Therefore we can say that the free energy of the inclusion is in a simple and transparent way expressed by the two invariants of the membrane curvature tensor: the **membrane mean curvature** H and the **curvature deviator** D.

It is imagined that the membrane is divided into patches that are so small that the curvature is constant over the patch, however, they are large enough to contain a sufficiently large number of inclusions, so that they can be treated by statistical methods. A chosen patch can then be treated as a system with well defined field $\mathbf{C}$, given area A^{p}, given number of inclusions M and temperature

T and can therefore be subject to a local thermodynamic equilibrium. To describe the local thermodynamic equilibrium we chose canonical statistics [7].

We consider two simple cases. In the first case the inclusions are described as an "ideal gas" in the membrane continuum; the area density of the inclusions depends on the local membrane curvature. In the second case each membrane constituent is considered as an inclusion. The area density of the inclusions is taken to be uniform. Both cases can be described within a lattice model. In a chosen small patch of the membrane there is a fixed number of equal lattice sites. In the ideal gas model, only few of these sites are occupied by the inclusions while in the model describing the membrane composed of a single species of the molecules, all sites are occupied.

3.1. Lattice Gas Model for Inclusions Embedded in the Membrane Continuum

When the inclusions are treated as an ideal gas embedded in the membrane continuum, the canonical partition function of the inclusions in the small patch of the membrane is $Q = q^M/M!$ where q is the partition function of the inclusion and M is the number of the inclusions in the patch. Knowing the canonical partition function of the patch Q, we obtain the Helmholtz free energy of the patch, $F^{\mathrm{p}} = -kT \ln Q$. The Stirling approximation is used and the area density of the number of molecules $m = M/A^{\mathrm{p}}$ is introduced. This gives for the area density of the free energy

$$\frac{F^{\mathrm{p}}}{A^{\mathrm{p}}} = -kTm \ln \left[q_{\mathrm{c}} \mathrm{I}_0 \left(\frac{\xi + \xi^\star}{2kT} DD_{\mathrm{m}} \right) \right] + kT(m \ln m - m) . \qquad (15)$$

To obtain the free energy of the inclusions of the whole layer F_0 the contributions of all the patches are summed, i. e. the integration over the layer area A is performed $F_0 = \int \frac{F^{\mathrm{p}}}{A^{\mathrm{p}}} \, \mathrm{d}A$, where $\mathrm{d}A$ is the area element.

The explicit dependence of the area density m on the position can be determined by the condition for the free energy of all the membrane inclusions to be at its minimum in the thermodynamic equilibrium $\delta F_0 = 0$. It is taken into account that the total number of the inclusions M_{T} in the layer is fixed,

$$\int_A m \, \mathrm{d}A = M_{\mathrm{T}} \qquad (16)$$

and that the area of the membrane A is fixed. The above isoparametric problem is reduced to the ordinary variational problem by constructing a functional

$F_0 + \lambda_m \int_A m \, \mathrm{d}A = \int_A L(m) \, \mathrm{d}A$, where

$$L(m) = -kTm \ln \left[q_\mathrm{c} \mathrm{I}_0 \left(\frac{\xi + \xi^\star}{2kT} DD_\mathrm{m} \right) \right] + kT(m \ln m - m) + \lambda_m m \quad (17)$$

and λ_m is the Lagrange multiplier. The variation is performed by solving the Euler equation $\dfrac{\partial L}{\partial m} = 0$. Differentiating (17) with respect to m and taking into account (16) gives the Boltzmann distribution function modulated by the modified Bessel function I_0

$$\frac{m}{m_\mathrm{u}} = \frac{q_\mathrm{c} \mathrm{I}_0 \left(\dfrac{\xi + \xi^\star}{2kT} DD_\mathrm{m} \right)}{\frac{1}{A} \displaystyle\int q_\mathrm{c} \mathrm{I}_0 \left(\frac{\xi + \xi^\star}{2kT} DD_\mathrm{m} \right) \mathrm{d}A}, \quad (18)$$

where q_c is given by (11) and m_u is defined by $m_\mathrm{u} A = M_\mathrm{T}$.

To obtain the equilibrium free energy of the layer the equilibrium area density (18) is inserted into the expression (15) and integrated over the area A.

Rearranging the terms yields [10]

$$F_0 = -kTM_\mathrm{T} \ln \left[\frac{1}{A} \int q_\mathrm{c} \mathrm{I}_0 \left(\frac{\xi + \xi^\star}{2kT} DD_\mathrm{m} \right) \mathrm{d}A \right]. \quad (19)$$

3.2. Lattice Model for Membrane Composed of Single Species of Molecules

In this case we are describing a membrane that is composed of a single species of molecules. Each molecule is considered as an inclusion. The energy of the interaction between the inclusions and the membrane continuum F_m is obtained by multiplying the free energy of a single inclusion (Eq. (14)) by the area density of the inclusions $m_\mathrm{u} = M_\mathrm{T}/A$ and integrating over the membrane area:

$$F_\mathrm{m} = \int m_\mathrm{u} F_\mathrm{i} \, \mathrm{d}A \,, \quad (20)$$

$$\begin{aligned} F_\mathrm{m} = {} & \frac{\xi m_\mathrm{u}}{2} \int (H - H_\mathrm{m})^2 \, \mathrm{d}A + \frac{\xi + \xi^\star}{4} (D^2 + D_\mathrm{m}^2) \\ & - kTm_\mathrm{u} \int \ln \left[\mathrm{I}_0 \left(\frac{\xi + \xi^\star}{2kT} DD_\mathrm{m} \right) \right] \mathrm{d}A \,. \end{aligned} \quad (21)$$

Expressing the second term in the above expression by Eq. (13) and omitting the constant terms yields

$$F_{\mathrm{m}} = \frac{3\xi + \xi^{\star}}{4} m_{\mathrm{u}} \int (H - H_{\mathrm{m}})^2 \, \mathrm{d}A - \frac{\xi + \xi^{\star}}{4} m_{\mathrm{u}} \int C_1 C_2 \, \mathrm{d}A \\ - kT m_{\mathrm{u}} \int \ln \left[\mathrm{I}_0 \left(\frac{\xi + xi^{\star}}{2kT} D D_{\mathrm{m}} \right) \right] \mathrm{d}A \,. \tag{22}$$

The first two terms recover the energy of isotropic bending [6],

$$W_{\mathrm{b}} = \frac{k_{\mathrm{c}}}{2} \int (2H - \mathbb{h})^2 \, \mathrm{d}A + \kappa_{\mathrm{G}} \int C_1 C_2 \, \mathrm{d}A \tag{23}$$

where $\mathbb{h}$ is the spontaneous membrane curvature while k_{c} and κ_{G} are respectively, the **membrane splay modulus** and the **membrane saddle splay modulus**, $k_{\mathrm{c}} = (3\xi + \xi^{\star}) m_{\mathrm{u}}/8$ and $\kappa_{\mathrm{G}} = -(\xi + \xi^{\star}) m_{\mathrm{u}}/4$.

The above procedure, leading to Eq. (22), links the statistical mechanical derivation description to the continuum elastomechanics. It follows from Eq. (22) that the saddle splay modulus is negative for the one-component membrane. Also, we get an additional term (third term in Eq. (22)) that originates in orientational ordering of the membrane constituents. Therefore, we can say that C_2 symmetry of the membrane constituents yields the membrane bending energy but gives also a new term that is called the deviatoric splay.

It can be seen from Eq. (21) that the free energy of the membrane is in a simple and transparent way expressed by the two invariants of the local curvature tensor: by the mean curvature and the curvature deviator. We therefore chose these invariants as fundamental invariants for description of the membrane with in-plane orientational order, rather than the mean and the Gaussian curvatures that are considered as the fundamental invariants for description of isotropic continuum.

3.3. Determination of the Equilibrium Shape

The above expressions for the free energy of the inclusions are subject to local thermodynamic equilibrium and global thermodynamic equilibrium with respect to the distribution functions. However, the equilibrium shape, i. e. the principal membrane curvatures at each point of the membrane, are at this point not known. In order to determine the equilibrium shape the membrane free energy should be minimized also with respect to the shape at the relevant constraints.

To find the minimum of the membrane free energy F at the given area of the membrane A, and at the given volume enclosed by the bilayer membrane V,

we construct a functional G

$$G = F - \lambda_A \cdot \left(\int \mathrm{d}A - A \right) - \lambda_V \cdot \left(\int \mathrm{d}V - V \right) \tag{24}$$

where λ_A and Λ_V are the Lagrange multipliers, and $\mathrm{d}V$ is the volume element. The equilibrium shape is then obtained by solving the variational problem $\delta G = 0$. It would be preferred if this variational problem were rigorously solved. The rigorous solution would in general be given in a numerical form. However, to grasp the main characteristics of the behavior of the system, approximative solutions may be used. The limiting cases are studied, the analysis is restricted to certain classes of shapes and the probe functions with adjustable parameters are used.

Let us consider a special case of a one-component membrane where H_m and/or D_m are much larger than any H or D in the membrane. Also, let $(\xi + \xi^\star) D D_\mathrm{m} / 2kT \geq 1$ so that we can expand the modified Bessel function for large arguments ($\ln[\mathrm{I}_0(x)] \simeq x$).

Considering the above assumptions, it follows from Eq. (21) that the membrane free energy is up to a constant equal to

$$F_\mathrm{m} = -\xi H_\mathrm{m} \langle H \rangle - \frac{1}{2} (\xi + \xi^\star) D_\mathrm{m} \langle D \rangle \tag{25}$$

where

$$\langle H \rangle = \frac{1}{A} \int H \, \mathrm{d}A, \qquad \langle D \rangle = \frac{1}{A} \int D \, \mathrm{d}A \,, \tag{26}$$

$\langle H \rangle$ is the average mean curvature and $\langle D \rangle$ is the average curvature deviator. We can see from Eq. (25) that the shape of the minimal free energy would in this special case have an extreme average mean curvature (the nature of this extreme depending on the sign of H_m) and/or a maximal average curvature deviator (since deviator is always positive). The shapes of the extreme average invariants of the curvature tensor are therefore distinguished shapes in the set of possible shapes.

4. Shapes of Extreme Averages of Curvature Tensor Invariants

In order to obtain the shapes of the membrane of an extreme average mean curvature $\langle H \rangle$ and the shapes of an extreme average curvature deviator $\langle D \rangle$ at a given area of the membrane surface A and a given volume enclosed by the membrane V, the variational problems are stated by constructing the respective functionals

$$G_H = \langle H \rangle - \lambda_A \cdot \left(\int \mathrm{d}A - A \right) + \lambda_V \cdot \left(\int \mathrm{d}V - V \right) , \tag{27}$$

$$G_D = \langle D \rangle + \lambda_A \cdot \left(\int \mathrm{d}A - A \right) - \lambda_V \cdot \left(\int \mathrm{d}V - V \right) \tag{28}$$

where λ_A and λ_V are the Lagrange multipliers while $\langle H \rangle$ and $\langle D \rangle$ are given by Eq. (26). The analysis is restricted to axisymmetric shapes. It is chosen that the symmetry axis of the body coincides with the x axis. The shape is given by the rotation of the function $y(x)$ around the x axis. In this case the principal curvatures are expressed by $y(x)$ and its derivatives with respect to x: $y' = \partial y/\partial x$ and $y'' = \partial^2 y/\partial x^2$ as $C_1 = \pm y^{-1}(1 + y'^2)^{-1/2}$ and $C_2 = \mp y''(1 + y'^2)^{-3/2}$. The area element is $\mathrm{d}A = 2\pi(1 + y'^2)^{1/2} y \, \mathrm{d}x$ and the volume element is $\mathrm{d}V = \pm\pi y^2 \, \mathrm{d}x$. By $\pm$ it is taken into account that the function $y(x)$ may be multiple valued. The sign may change in the points where $y' \to \infty$. Inserting the above expressions for C_1, C_2, $\mathrm{d}A$ and $\mathrm{d}V$ into Eqs (27) and (28) and rearranging, the functionals become

$$G_H = \int g_H(x, y, y', y'') \, \mathrm{d}x \,, \qquad G_D = \int g_D(x, y, y', y'') \, \mathrm{d}x \,, \tag{29}$$

with

$$g_H(x, y, y', y'') = \pm 1 \mp \frac{y y''}{1 + y'^2} - \lambda_A y \sqrt{1 + y'^2} \mp \frac{1}{2} \lambda_V y^2 \,, \tag{30}$$

$$g_D(x, y, y', y'') = \mp 1 \mp \frac{y y''}{1 + y'^2} - \lambda_A y \sqrt{1 + y'^2} \mp \frac{1}{2} \lambda_V y^2 \,. \tag{31}$$

The variations $\delta G_H = 0$ and $\delta G_H = 0$ are performed by solving the corresponding Euler–Poisson equations

$$\frac{\partial g_i}{\partial y} - \frac{\mathrm{d}}{\mathrm{d}x} \left(\frac{\partial g_i}{\partial y'} \right) + \frac{\mathrm{d}^2}{\mathrm{d}x^2} \left(\frac{\partial g_i}{\partial y'} \right) = 0 \,, \qquad i = H, D \,. \tag{32}$$

As the first terms on the right side of Eqs (30) and (31), that originate from C_1, are constant, this curvature does not influence the solution of the variational problem. Further, by the particular choice of the sign before the Lagrange multipliers in Eqs (27) and (28) we can express both variational problems with a single Euler–Poisson equation. Obtaining the necessary differentiations, this Euler–Poisson equation is

$$\delta_i \frac{2y''}{(1 + y'^2)^2} + \lambda_A \left(\frac{1}{\sqrt{1 + y'^2}} - \frac{y y''}{(\sqrt{1 + y'^2})^3} \right) - y \lambda_V = 0 \,, \quad i = H, D \tag{33}$$

where $\delta_H = \pm 1$ while the choice of the sign of δ_D depends also on the sign of $(C_1 - C_2)$. It follows from the above that the solutions for the extremes of the average invariants of the curvature tensor are equal. The nature of the obtained extreme may however be different. So it is possible that some solution

corresponds to the maximal average mean curvature and the maximal average curvature deviator. Some other solution may correspond to the minimum of the average mean curvature and the maximum of the average curvature deviator, etc.

We will consider some simple analytic solutions of Eq. (33). The ansatz $y = \lambda_A/\lambda_V$ fulfills Eq. (33) [8, 11]. This solution represents a cylinder of the radius $r_{\text{cyl}} = \lambda_A/\lambda_V$. Another analytical solution of Eq. (33) is given by a circle of the radius r_{cir}, $y = y_0 \pm \sqrt{r_{\text{cir}}^2 - x^2}$ where $(0, y_0)$ is the center of the circle. If $y_0 = 0$ the ansatz fulfills Eq. (33) for two different radii [8], $(r_{\text{cir}})_{1,2} = \frac{2}{\left(\lambda_A \pm \sqrt{\lambda_A^2 - 2\lambda_V}\right)}$, representing spheres with two different radii. If $y_0 \neq 0$, the circle is the solution of Eq. (33) only when the Lagrange multipliers are interdependent, $\lambda_A^2 = 2|\lambda_V|$. For $r_{\text{cir}} < y_0$, the solution represents a torus of the thickness $2r_{\text{cir}}$ and radius y_0, and a torocyte [9].

As a sum of the solutions of the differential equation within each of the above categories is also a solution of the same equation at the chosen constraints, different combinations of shapes within the corresponding category are possible, provided that the combined shape fulfills the constraints [2]. If the area A and the volume V are fixed, two independent parameters can be determined from the respective constraints. The cylinder, the two spheres, the torus, the cylinder ended by the hemispheres of the cylinder radius, and the sequence of a fixed number of beads are some of the possible shapes that are characterized by exactly two parameters each. The two constraints determine the shape completely so that these shapes are the shapes of the extreme $\langle H \rangle$ and of the extreme $\langle D \rangle$.

The equilibrium shape can be characterized by a volume to area ratio defined as the isoperimetric quotient $IQ = 36\pi V^2/A^3$ and both average invariants of the curvature tensor, and can be presented in a $(\langle H \rangle, \langle D \rangle, IQ)$ phase diagram. The shapes of the extreme average invariants of the curvature tensor form curves in this phase diagram (Fig. 1). These lines in turn form limits of the trajectories that correspond to the processes with changing average curvature invariants.

5. Some Examples Outlining the Deviatoric Splay

Intercalation of specific amphiphilic molecules into the red blood cell membrane can induce membrane invaginations or evaginations which can finally close, forming an endovesicle or exovesicle, respectively. Spherical, cylindrical and torocyte shaped vesicles were observed [1, 11]. In this work we will briefly describe endovesicles with a toroid-like periphery and a large flat and thin

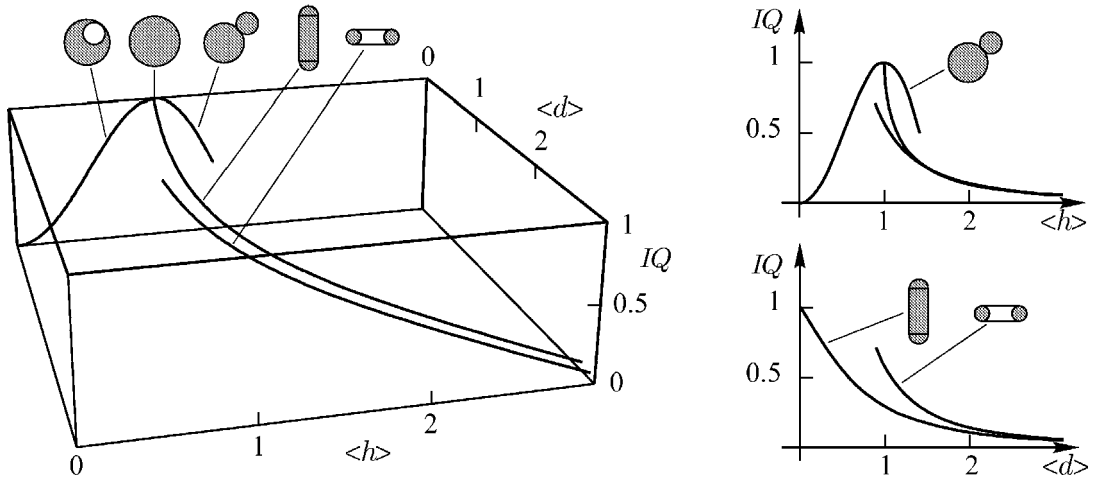

Figure 1. The $(\langle h\rangle, \langle d\rangle, IQ)$ phase diagram, where dimensionless quantities are: $\langle h\rangle = \sqrt{A/4\pi}\langle H\rangle$, $\langle d\rangle = \sqrt{A/4\pi}\langle D\rangle$ and $IQ = 36\pi V^2/A^3$. The lines pertaining to three sets of limit shapes are depicted: the set of shapes composed of two spheres, the set of tori and the set of shapes composed of a cylinder ended by two hemispheres. The corresponding projections to the $\langle d\rangle = 0$ and to the $\langle h\rangle = 0$ planes are also shown

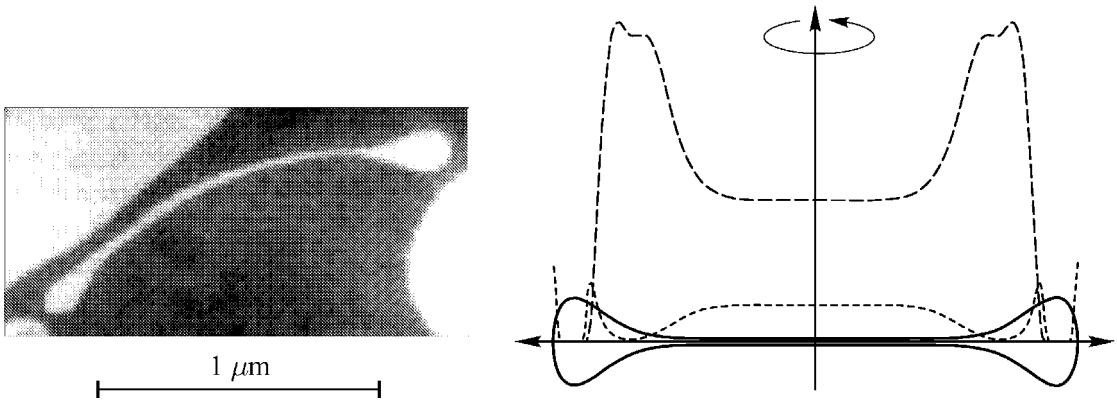

Figure 2. The image on the left is a transmission electron micrograph of the torocyte vesicle of the human erythrocyte membrane [1, 9]. The vesiculation was induced by incubating the erythrocyte suspension with C12E8 [1, 9]. The figure on the right shows the cross-section of the calculated equilibrium vesicle shape obtained by minimization of the membrane free energy where contribution of the C12E8 induced inclusions was taken into account [4]. The distribution of the inclusions over the outer membrane layer (dashed line) and over the inner layer (dotted line) is also depicted. It was taken that 80 % of the inclusions are in the outer layer and 20 % in the inner layer. It was also taken that $\xi = \xi^*$, $M_T kT/8\pi k_c = 100$ and $\xi/kTR_0^2 = 1$, $C_{1m} = -2.6R_0$, $C_{2m} = 0$ and $R_0 = \sqrt{A/4\pi}$ [4]

central region, called torocytes (see Fig. 2). These vesicles were observed after incubation of erythrocyte suspension with nonionic surfactant octaethyleneglycol dodecilether (C12E8). Let us consider the membrane of a torocyte as a continuum with anisotropic C12E8 inclusions (see section 3.1). The inclusions consist of a single C12E8 molecule and of the surrounding membrane constituents that are significantly distorted due to the presence of the embedded C12E8 molecule. It was shown [4] that the equilibrium shapes that resemble the observed torocytes can be obtained by considering that the C12E8 inclusions are anisotropic (Fig. 2).

The second example also involves C12E8 molecules intercalated into the lipid bilayer. Large molecules can pass through the cell membrane trough transient pores. Artificially, the formation of pores in the membrane can be achieved by applying an electric field across the membrane. This phenomenon is known as electroporation [12]. Some recent experiments [13] indicate that C12E8 molecules in lipid bilayers make transient pores, that are created by electroporation, more stable. It was shown theoretically [3] that anisotropic inclusions may stabilize circular pore in a flat membrane segment, where the edge of the pore was described as a part of a torus (see Fig. 3).

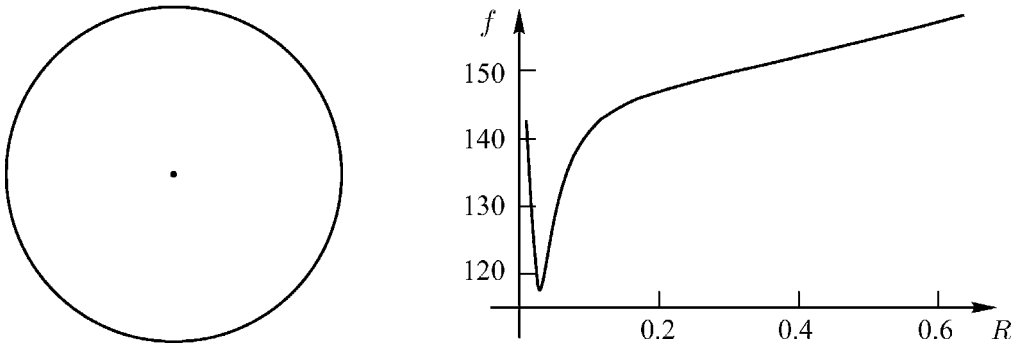

Figure 3. The diagram on the right shows the relative membrane free energy $f = F/8\pi k_c$ as a function of the relative radius of the pore R (see below). A flat circular segment of the double-layered membrane is considered [3]. The circular pore is in the center of the segment and the edge of the pore forms the inner half of a torus with larger relative radius R and smaller relative radius r. The unit of length is the radius of the circular membrane segment without a pore $l_0 = \sqrt{A/2\pi}$. The membrane free energy reaches minimum at $R_{\min} = 0.029$ (for lipid bilayer of the thickness $2r \approx 5$ nm this gives $R_{\min} \approx 10$ nm). The drawing on the left represents the top view of the corresponding membrane segment with a pore of the radius $R_{\min}$. The values of the parameters are $C_{1\mathrm{m}} = -50l_0$, $C_{2\mathrm{m}} = 100l_0$, $\xi = \xi^*$, $M_{\mathrm{T}}kT/8\pi k_c = 10$, $\xi/kTl_0^2 = 0.01$ and $r = 0.01$

6. Conclusions

In this work a single-particle energy was expressed by the invariants of the curvature tensor of two-dimensional surface. Therefrom the membrane free energy was derived. Usually, it is considered that the fundamental invariants for the description of two-dimensional surface are the mean curvature and the Gaussian curvature. Our results indicate that for determination of the equilibrium shape this is not always appropriate. It is suggested that when the membrane is composed of particles that have an in-plane C_2 group symmetry, the relevant invariants are the mean curvature and the curvature deviator.

If we assume that the reference state of the membrane is isotropic, which would be true for the membrane composed solely of particles that are axisymmetric with respect to the axis normal to the membrane, the use of either set of invariants is equivalent, i. e. the equilibrium shapes would not depend on the choice of the set of the invariants. However, for the membrane containing particles that may be orientationally ordered, the choice of the set of the invariants is important.

The presented results could probably be generalized by considering three-, four- or even n-dimensional differentiable manifold. A possibility should be considered, that the reference state of the system is not isotropic.

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