Shape fluctuations of nearly spherical lipid vesicles and emulsion droplets

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It is known that the relaxation of the shape fluctuations of nearly spherical lipid vesicles is accompanied by a lateral displacement of the monolayers, comprising their bilayers. In this work a dissipation mechanism of the mechanical energy stored in the fluctuation is revealed that concerns the viscous friction of the flow in the liquid around the vesicle caused by this displacement. The time correlation functions of each of the vesicle's fluctuation modes are calculated as a function of the mechanical and rheological properties of the system which are the tension of the vesicle bilayer, its bending elasticities at free and blocked flip-flop, the viscosities of the liquids bathing the bilayer, the friction coefficient between the two monolayers, as well as the vesicle's dimensions: its bilayer thickness and radius. The correlations of the shape fluctuations of nearly spherical emulsion droplets are also calculated for different viscosities of the liquid inside and outside the droplet.

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I. INTRODUCTION

The living organisms, as they exist on earth, are made of cells. Each cell consists of a thin membrane (cell membrane, cell surface, and biomembrane), enveloping various biologically active molecules via which the life processes are realized. Nowadays, the model of Singer and Nicolson [1] is generally accepted, according to which the biological membrane consists of a lipid bilayer, similar to that of the lamellar liquid-crystalline phase, where integral proteins float as in a two-dimensional sea. The mechanical properties of the biomembranes, and especially their bending elasticities, are closely related to their basic functions: cellular interactions, cell fusion, adhesion, rheological properties of cell suspensions, etc. It is natural to suppose that the mechanical properties of the biomembranes are to a great extent determined by their lipid matrices. This is one of the main reasons for the interest in the mechanical properties of lipid bilayers.

The mechanical properties of the lipid bilayer are determined by its stretching elasticity, the bending elasticities at free and blocked exchanges of molecules between the monolayers, forming the bilayer, the saddle-splay bending elasticity, the spontaneous curvature, and the shear elasticity [2]. Later on we will refer to the free and blocked flip-flop exchanges of molecules between the monolayers as cases of free and blocked flip-flops. The shear elasticity modulus is different from zero in the gel state of the membrane, in which it can be modeled as a two-dimensional solid. Later on in this work, only lipid bilayers in a liquid-crystalline state that can be represented as a two-dimensional liquid will be considered. Spontaneous curvature can appear due to different factors. The most important of them are the difference in the chemical composition of the two monolayers and the difference in the liquid phases on the two sides of the bilayer. Attention deserves the case when the bilayer consists of identical molecules, the conditions on both sides of the membrane are similar, but the numbers of molecules in each of the monolayers are different. The elasticity of such a membrane has been investigated by the generalized bilayer-couple model, described in [3–6]. Their properties are described by using the bending elasticity in the case of blocked flip-flop.

From the theoretical point of view, the (micro)emulsion droplet differs from the lipid vesicle mainly by its membrane, which is a monolayer of amphiphilic molecules. The monolayer is characterized by only one bending elasticity and has its own spontaneous curvature. The other modules are similar to those of the bilayer of the vesicle.

One of the experimental methods for direct measurement of the lipid bilayer's bending elasticity is the analysis of thermally induced out-of-plane fluctuations of a flat membrane [7,8] or shape fluctuations of a nearly spherical lipid vesicle [9–16]. The theoretical studies of the fluctuations link the mechanical and the rheological properties of the bilayers with two experimentally measurable quantities. They are the mean-square amplitudes of the fluctuation modes of the vesicle or the flat membrane and the time autocorrelations of these amplitudes.

The mean-square amplitudes of the fluctuation modes have been calculated first by Brochard and Lennon for flat membranes [7] and by Milner and Safran for nearly spherical vesicles [17]. The membrane was considered as a liquid shell with only one bending elasticity. Later it was proved that in the case of a bilayer membrane, the bending elasticity, participating in the theoretical results is that of a free flip-flop [11,18]. This concerns the shape fluctuation of nearly spherical vesicles, but the same result can easily be obtained for the out-of-plane fluctuations of flat membranes, too. The above result was obtained by taking into account the lateral displacement of the monolayers.

The time autocorrelations of the amplitudes of the fluctuation modes have been first calculated by Brochard and Lennon for flat membranes [7] and by Schneider *etc.* [9] and Milner and Safran [17] for nearly spherical vesicles. These authors have used again the above-mentioned assumption that the membrane is a liquid shell with one bending elasticity. In their approach, the dissipation of stored energy is due to the viscous friction in the flow of liquid surrounding the membrane. The time autocorrelation of each mode is exponentially decaying with the correlation time.

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There is one more source of energy dissipation which is the viscous friction between the monolayers of the bilayer. It occurs because of the lateral displacements of the monolayers, when the bilayer fluctuates. A theory taking into account this source has been developed by Yeung and Evans [19] and by Bivas *et al.* [18] for the vesicle fluctuations. As a result of that, the amplitude autocorrelation function for each of the fluctuation modes was obtained as a sum of two exponentially decaying terms with different decay rates. Seifert and Langer considered the decay of a fluctuation in a flat bilayer [20]. They took into account two sources of dissipation: (1) the viscous flow, induced in the liquid phase by the normal membrane displacement and the lateral displacement of the monolayers, and (2) the intermonolayer friction.

Recently, Rodríguez-García *et al.* studied the spectrum of a fluctuating vesicle [15]. To explain their experimental results for the mean-square values of the fluctuation mode amplitudes, they proposed a heuristic generalization of the expressions of Brochard and Lennon [7]. In the experimental data from [15] the amplitude autocorrelation functions of the fluctuating modes were monoexponentially decaying with time with relaxation rates proportional to the square of the mode wave number. Such a behavior is predicted by the theory of Seifert and Langer for the case of curvature-dilation modes, accompanied by intermonolayer friction [20]. The conclusion made by Rodríguez-García *et al.* is that in the conditions of their experiments these modes become dominant.

In the present paper, the effects of the lateral monolayer displacement in a fluctuating nearly spherical vesicle are considered. The dissipation mechanisms of the energy stored in the fluctuations are identical to those used by Seifert and Langer who considered the case of planar geometry [20]. All the calculations are based on the well-known physical fundamentals, described elsewhere [2,15,18–20].

The mean-square values and the time autocorrelation functions of the of the fluctuation mode amplitudes are calculated. The autocorrelations of the shape fluctuations of nearly spherical emulsion droplets are also calculated for different viscosities of the liquid inside and outside the droplet. The results that could be used for the interpretation of experimental data from the studies of the shape fluctuations of nearly spherical lipid vesicles and (neutron) scattering of lyotropic lipid-water phases are discussed.

II. MECHANICAL ENERGY STORED IN THE SHAPE FLUCTUATIONS OF A NEARLY SPHERICAL LIPID VESICLE

Let us consider a nearly spherical lipid vesicle. The volume V of the vesicle is assumed to be independent of the fluctuations. Let R_0 be the radius of a sphere with a volume of V. Let the origin O of a laboratory reference frame be placed inside the vesicle. A point on the surface of the vesicle with polar coordinates (θ,φ) is chosen. Let $R(\theta,\varphi)$ be the modulus of the radius vector at this point. The dimensionless quantity $u(t)$ is defined as

$$R(\theta,\varphi,t) = R_0[1 + u(\theta,\varphi,t)], \tag{1}$$

where t is the time variable. The full orthonormal basis of spherical functions is denoted as $Y_{nm}(\theta,\varphi)$ [21]. For simplicity, we choose real spherical harmonics. The function $u(\theta,\varphi,t)$ can be decomposed into a series with respect to the spherical harmonics $Y_{nm}(\theta,\varphi)$,

$$u(\theta,\varphi,t) = \sum_{n=0}^{n_{max}} \sum_{m=-n}^{n} u_{nm}(t) Y_{nm}(\theta,\varphi). \tag{2}$$

A cutoff $n_{max} \sim R_0/\lambda$ is introduced in the sum, where λ is of the order of the intermolecular distance. As the harmonics with indices $n=1$ and $m=-1,0,1$ correspond to pure translation of the vesicle, the origin O is chosen in a way such that $u_{1m}=0$. Because of the requirement for volume V conservation, the amplitude $u_{00}(t)$ can be expressed as

$$u_{00}(t) = -\frac{1}{2\sqrt{\pi}} \sum_{n=2}^{n_{max}} \sum_{m=-n}^{n} [u_{nm}(t)]^2. \tag{3}$$

Bilayers, made up of identical molecules, whose lowest bending and stretching mechanical energy state is flat and tension free, with equal surface density of the molecules in the two monolayers, will be considered later on in this work.

Let us consider a small patch of the lipid bilayer with an area ΔS, tension σ, and area in its tension-free state ΔS^{tf}. Let n^{out} and n^{in} be the two-dimensional densities in the outer and inner monolayers of the patch measured on the dividing surface between the monolayers. The difference $n^{out}-n^{in}$ is denoted as δn. In the case of free flip-flop,

$$\delta n = \xi(c_1 + c_2), \tag{4}$$

where ξ is the flip-flop coefficient [2] and c_1 and c_2 are the main curvatures of the patch under consideration. From the definition of the neutral surface [22] it follows that the quantity ξ can be presented in the following way:

$$\xi = \frac{d_0}{s_0}, \tag{5}$$

where s_0 is the mean area per molecule in a monolayer of a flat tension-free bilayer and d_0 is the distance between the neutral surfaces of the two monolayers.

If the patch is tension free, then the bending energy density g_c^0 can be written in the following form [18–20]:

$$g_c^0(c_1,c_2,\delta n) = \tfrac{1}{2}K_c^{fr}(c_1 + c_2)^2 + \tfrac{1}{2}\Phi[\delta n - \xi(c_1 + c_2)]^2 + \bar{K}_c c_1 c_2, \tag{6}$$

where K_c^{fr} is the bending elasticity of the bilayer at free flip-flop, $\bar{K}_c$ is the saddle-splay bending elasticity, and Φ is a phenomenological constant, characterizing the bilayer. If $\delta n=0$, then the bilayer will have bending elasticity modulus at blocked flip-flop, denoted as K_c^{bl}. Therefore,

$$\Phi = \frac{K_c^{bl} - K_c^{fr}}{\xi^2}. \tag{7}$$

We define the quantity c_0, related to the difference between the two-dimensional molecule densities, in the following way:

$$c_0 = \left(1 - \frac{K_c^{fr}}{K_c^{bl}}\right)\frac{\delta n}{\xi}. \tag{8}$$

Another quantity that will be used in the calculations later on is the quantity K, defined as

$$K = \frac{d_0}{R_0}\frac{K_c^{bl}}{K_c^{bl} - K_c^{fr}}. \tag{9}$$

Then g_c^0 is written in the following form:

$$g_c^0(c_1, c_2, \delta n) = \frac{1}{2}K_c^{bl}\left[(c_1 + c_2)^2 - 2c_0(c_1 + c_2) + \frac{K_c^{bl}}{K_c^{bl} - K_c^{fr}}(c_0)^2\right] + \bar{K}_c c_1 c_2. \tag{10}$$

The bending energy ΔG_c of the whole patch is equal to the product

$$\Delta G_c = g_c^0(c_1, c_2, \delta n)\Delta S^{tf}. \tag{11}$$

In Eq. (11) ΔS^{tf} is used instead of ΔS, because otherwise the bending and stretching energies could not be separated [22].

If the patch is not tension free, then its stretching energy ΔG_s is expressed via its tension σ as

$$\Delta G_s = \frac{1}{2}\frac{\sigma^2}{K_s}\Delta S^{tf}, \tag{12}$$

where K_s is the stretching elasticity of the bilayer. Let ΔG be the total mechanical energy of the patch, which is

$$\Delta G = \Delta G_c + \Delta G_s. \tag{13}$$

The total deformation energy $G(t)$ of the vesicle will be obtained by integration of $\Delta G(t)$ on its surface $S(t)$,

$$G(t) = \oint_{S(t)} \Delta G(t). \tag{14}$$

At time t the surface of the vesicle is completely determined by the amplitudes $u_{nm}(t)$ from Eq. (2). The quantity c_0 from Eq. (8) also depends on t via $\delta n(t)$. Let us decompose it into a series with respect to the spherical harmonics $Y_{nm}(\theta, \varphi)$ as follows [18]:

$$c_0(\theta, \varphi, t) = \frac{1}{R_0}\left\{\frac{S_0}{S(t)}c_{00} + \frac{dS_0}{d[S(t)]}\sum_{n=1}^{n_{max}}\sum_{m=-n}^{n} c_{nm}(t)Y_{nm}(\theta, \varphi)\right\}. \tag{15}$$

Here, $S_0 = 4\pi(R_0)^2$ is the area of a sphere with radius R_0 and center O, and dS_0 is the area projection of the bilayer patch $d[S(t)]$ on this sphere. Let us denote with $\langle a(t)\rangle$ the time average of the time-dependent quantity $a(t)$. We will use the approximation that the fluctuations of the quantity $[\sigma(t) - \langle\sigma(t)\rangle]$ are not correlated with the fluctuations of $[u_{nm}(t)]^2$. In fact, this is a mean-field approximation, used by Milner and Safran [17]. We also assume that c_{00} does not depend on t. This is equivalent to the assumption that the number of molecules in each of the monolayers does not depend on t. Evidently, c_{00} is proportional to the difference in the numbers of molecules in the two monolayers.

As shown in [18], the mechanical energy $G(t)$ of the vesicle is expressed with second-order precision with respect to the variables $u_{nm}(t)$, $c_{nm}(t)$, and σ/K_s as follows:

$$G(t) = G_0(t) + \sum_{n=2}^{n_{max}}\sum_{m=-n}^{n} G_{nm}(t), \tag{16}$$

where $G_0(t)$ is independent of the vesicle shape and G_{nm}, where $n \geq 2$, is

$$G_{nm}(t) = \tfrac{1}{2}K_c^{bl}\{\alpha_n[u_{nm}(t)]^2 - 2\beta_n u_{nm}(t)c_{nm}(t) + \gamma[c_{nm}(t)]^2\}, \tag{17}$$

where

$$\alpha_n = (n-1)(n+2)\left[(n-1)(n+2) + \frac{K_c^{fr}}{K_c^{bl}}(\bar{\sigma} + 2)\right],$$

$$\beta_n = (n-1)(n+2),$$

$$\gamma = \frac{K_c^{bl}}{K_c^{bl} - K_c^{fr}},$$

$$\bar{\sigma} = \frac{\langle\sigma(t)\rangle(R_0)^2}{K_c^{fr}} + 2\frac{K_c^{bl} - K_c^{fr}}{K_c^{fr}} - \frac{\bar{K}_c}{K_c^{fr}} + 2\frac{K_c^{bl}}{K_c^{fr}}c_{00} - \frac{(K_c^{bl})^2}{K_c^{fr}(K_c^{bl} - K_c^{fr})}(c_{00})^2. \tag{18}$$

Using the equipartition theorem, the time mean squares $\langle[u_{nm}(t)]^2\rangle$ and $\langle[c_{nm}(t)]^2\rangle$ are calculated from Eq. (17) for $n \geq 2$ as [18]

$$\langle[u_{nm}(t)]^2\rangle = \frac{kT}{K_c^{fr}}\frac{1}{(n-1)(n+2)[n(n+1) + \bar{\sigma}]}, \tag{19}$$

$$\langle[c_{nm}(t)]^2\rangle = \frac{\alpha_n}{\gamma}\frac{kT}{K_c^{fr}}\frac{1}{(n-1)(n+2)[n(n+1) + \bar{\sigma}]}, \tag{20}$$

where kT is the Boltzmann factor.

Our result from Eq. (19) has the same form as that derived by Milner and Safran [17]. Their K_c is replaced here with K_c^{fr}. Therefore, despite the conservation of the number of lipid molecules in each monolayer, data from the time mean-square amplitudes of the thermal shape fluctuation modes permit the experimental determination of the bending elasticity K_c^{fr} in the free flip-flop case [11,18,23].

III. HYDRODYNAMICS OF THE VESICLE: AUTOCORRELATIONS OF THE SHAPE FLUCTUATION MODES OF A NEARLY SPHERICAL LIPID VESICLE

Let, in a point with polar coordinates (θ, φ) at time t, $\boldsymbol{v}^{norm,out}(\theta, \varphi, t)$ and $\boldsymbol{v}^{norm,in}(\theta, \varphi, t)$ be the velocity components of the outer and inner monolayers normal to the membrane surface, and let $\boldsymbol{v}^{lat,out}(\theta, \varphi, t)$ and $\boldsymbol{v}^{lat,in}(\theta, \varphi, t)$ be the respective lateral components. Then

$$\boldsymbol{v}^{norm,out}(\theta,\varphi,t) = \boldsymbol{v}^{norm,in}(\theta,\varphi,t). \tag{21}$$

As far as the lateral velocity components $\boldsymbol{v}^{lat,out}(\theta,\varphi,t)$ and $\boldsymbol{v}^{lat,in}(\theta,\varphi,t)$ are concerned, we will consider a vesicle that does not rotate and whose membrane has no lateral density fluctuations of the molecules comprising it. Under these assumptions, the following relation is valid:

$$\boldsymbol{v}^{lat,out}(\theta,\varphi,t) + \boldsymbol{v}^{lat,in}(\theta,\varphi,t) = 0.$$

We denote

$$\delta\boldsymbol{v}^{lat}(\theta,\varphi,t) = \boldsymbol{v}^{lat,out}(\theta,\varphi,t) - \boldsymbol{v}^{lat,in}(\theta,\varphi,t). \tag{22}$$

Let $B(\theta,\varphi,t)$ be a scalar field with the property

$$\delta\boldsymbol{v}^{lat}(\theta,\varphi,t) = -\frac{1}{R_0}\nabla_0^s B(\theta,\varphi,t), \tag{23}$$

where ∇_0^s is the two-dimensional gradient, defined on the surface of the unit sphere. Equation (23) is written under the following assumption: when a fluctuation decays, the production of entropy is minimal, meaning that velocity curls do not appear.

We decompose the quantity $B(\theta,\varphi,t)$ into a series with respect to the spherical harmonics $Y_{nm}(\theta,\varphi)$ as follows:

$$B(\theta,\varphi,t) = \sum_{n=0}^{n_{max}} \sum_{m=-n}^{n} b_{nm}(t) Y_{nm}(\theta,\varphi). \tag{24}$$

From Eqs. (4), (8), (15), and (24) it follows that

$$\frac{d[\delta n(\theta,\varphi,t)]}{dt} = \frac{d_0}{s_0 R_0}\frac{K_c^{bl}}{K_c^{bl}-K_c^{fr}} \sum_{n=0}^{n_{max}} \sum_{m=-n}^{n} \frac{d[c_{nm}(t)]}{dt} Y_{nm}(\theta,\varphi). \tag{25}$$

The requirement for conservation of the molecule number in the membrane is expressed in the following way:

$$\frac{d[\delta n(\theta,\varphi,t)]}{dt} = \frac{1}{s_0 R_0}\nabla_0^s[\delta\boldsymbol{v}^{lat}(\theta,\varphi,t)]. \tag{26}$$

From Eqs. (23)–(26) and the properties of the spherical harmonics, for $n \geq 2$ we obtain

$$b_{nm}(t) = \frac{1}{n(n+1)}\frac{d_0 R_0 K_c^{bl}}{K_c^{bl}-K_c^{fr}}\frac{d[c_{nm}(t)]}{dt}. \tag{27}$$

Consequently, the derivatives $d[c_{nm}(t)]/dt$ permit the calculation of the velocity difference $\delta\boldsymbol{v}^{lat}(\theta,\varphi,t)$. From Eqs. (22)–(24) and (27) we obtain

$$\delta\boldsymbol{v}^{lat}(\theta,\varphi,t) = 2\boldsymbol{v}^{lat,out}(\theta,\varphi,t) = -2\boldsymbol{v}^{lat,in}(\theta,\varphi,t) = \sum_{n=0}^{n_{max}} \sum_{m=-n}^{n} \delta\boldsymbol{v}_{nm}^{lat}(\theta,\varphi,t), \tag{28}$$

where

$$\delta\boldsymbol{v}_{nm}^{lat}(\theta,\varphi,t) = -d_0\frac{K_c^{bl}}{K_c^{bl}-K_c^{fr}}\frac{1}{n(n+1)}\frac{d[c_{nm}(t)]}{dt}\nabla_0^s[Y_{nm}(\theta,\varphi)]. \tag{29}$$

The equal velocities $\boldsymbol{v}^{norm,in}(\theta,\varphi,t)$ and $\boldsymbol{v}^{norm,out}(\theta,\varphi,t)$ are expressed via the amplitudes $u_{nm}(t)$ as

$$\boldsymbol{v}^{norm}(\theta,\varphi,t) = \boldsymbol{v}^{norm,in}(\theta,\varphi,t) = \boldsymbol{v}^{norm,out}(\theta,\varphi,t) = \sum_{n=0}^{n_{max}} \sum_{m=-n}^{n} \boldsymbol{v}_{nm}^{norm}(\theta,\varphi,t), \tag{30}$$

with

$$\boldsymbol{v}_{nm}^{norm}(\theta,\varphi,t) = \left\{R_0\frac{d[u_{nm}(t)]}{dt}Y_{nm}(\theta,\varphi)\right\}\hat{\boldsymbol{n}}(\theta,\varphi). \tag{31}$$

Here, $\hat{\boldsymbol{n}}(\theta,\varphi)$ is a unit vector normal to the membrane in a point with polar coordinates (θ,φ) directed from the inside to the outside of the vesicle.

To calculate the dissipation of the stored in the fluctuations energy, we will use the solution of the Navier-Stokes equations for the case of creeping motion of an incompressible fluid at very low Reynolds numbers. Milner and Safran proved that this approximation can be used for vesicles with radius on the order of 10 μm and with liquid viscosities inside and outside the vesicle which are close to the water viscosity [17].

Without a loss of generality, we consider only one mode (n,m) with $n \geq 2$ and $-n \leq m \leq n$. Equations (29) and (31) give the boundary conditions for the solution. As it has been noted by Milner and Safran, if these boundary conditions are applied for each direction (θ,φ) to a sphere with radius R_0, the obtained velocity fields will represent the lowest-order term in a systematic sphere deviation expression [17]. The velocities are proportional to u_{nm} and c_{nm}. Therefore, with a higher-order precision concerning u_{nm} and c_{nm}, the vesicle shape can be assumed as spherical in the calculations to follow.

We will use the Lamb solutions of the creeping motion equations in spherical coordinates, as they are presented by Happel and Brenner [24]. Let $\boldsymbol{v}_{nm}^{in}(\theta,\varphi,t)$ and $\boldsymbol{v}_{nm}^{out}(\theta,\varphi,t)$ be the (n,m) modes of the velocities at the points of the inner and outer monolayers with polar coordinates (θ,φ) at time t. From Eqs. (28)–(31) they can be expressed as

$$\boldsymbol{v}_{nm}^{in}(\theta,\varphi,t) = R_0\left\{\left[\frac{du_{nm}(t)}{dt}Y_{nm}(\theta,\varphi)\right]\hat{\boldsymbol{r}}(\theta,\varphi) + \frac{1}{2}K\frac{dc_{nm}(t)}{dt}\nabla_0^s[Y_{nm}(\theta,\varphi)]\right\}, \tag{32}$$

$$\boldsymbol{v}_{nm}^{out}(\theta,\varphi,t) = R_0\left\{\left[\frac{du_{nm}(t)}{dt}Y_{nm}(\theta,\varphi)\right]\hat{\boldsymbol{r}}(\theta,\varphi) - \frac{1}{2}K\frac{dc_{nm}(t)}{dt}\nabla_0^s[Y_{nm}(\theta,\varphi)]\right\}, \tag{33}$$

where K is defined in Eq. (9) and $\hat{\boldsymbol{r}}(\theta,\varphi)$ is a unit vector parallel to the radius vector of a point with polar coordinates (θ,φ) on the membrane sphere with radius R_0. When the

membrane surface is replaced with a sphere, the vector $\hat{\boldsymbol{r}}(\theta,\varphi)$ coincides with the unit vector $\hat{\boldsymbol{n}}(\theta,\varphi)$ defined above.

Let μ^{in} and μ^{out} be the liquid viscosities inside and outside the vesicle. Let $\Pi^{in}_{nm}(\theta,\varphi,t)$ and $\Pi^{out}_{nm}(\theta,\varphi,t)$ be the stress tensors and $\boldsymbol{\Pi}^{in}_{nm}(\theta,\varphi,t)$ and $\boldsymbol{\Pi}^{out}_{nm}(\theta,\varphi,t)$ be the stress vectors acting on the points of the inner and outer monolayers with polar coordinates (θ,φ) at time t. Then

$$\boldsymbol{\Pi}^{in}_{nm}(\theta,\varphi,t) = \Pi^{in}_{nm}(\theta,\varphi,t) \bullet \hat{\boldsymbol{r}}(\theta,\varphi),$$

$$\boldsymbol{\Pi}^{out}_{nm}(\theta,\varphi,t) = -\Pi^{out}_{nm}(\theta,\varphi,t) \bullet \hat{\boldsymbol{r}}(\theta,\varphi),$$

where $\mathsf{A}\bullet\boldsymbol{B}$ is the vector product of a tensor A with a vector $\boldsymbol{B}$.

The Lamb solution of the Navier-Stokes equations for the boundary conditions on a sphere with radius R_0, given by Eqs. (32) and (33), has the stress vectors $\boldsymbol{\Pi}^{in}_{nm}(\theta,\varphi,t)$ and $\boldsymbol{\Pi}^{out}_{nm}(\theta,\varphi,t)$ calculated as

$$\boldsymbol{\Pi}^{in}_{nm}(\theta,\varphi,t) = \mu^{in}\left\{\left[-\frac{3}{2}K(n+1)\frac{dc_{nm}}{dt} + \frac{(2n^2+n+3)}{n}\frac{du_{nm}}{dt}\right]Y_{nm}(\theta,\varphi)\hat{\boldsymbol{r}}(\theta,\varphi) + \left[\frac{1}{2}(2n+1)K\frac{dc_{nm}}{dt} - \frac{3}{n}\frac{du_{nm}}{dt}\right]\boldsymbol{\nabla}^s_0[Y_{nm}(\theta,\varphi)]\right\}, \tag{34}$$

$$\boldsymbol{\Pi}^{out}_{nm}(\theta,\varphi,t) = \mu^{out}\left\{\left[-\frac{3}{2}Kn\frac{dc_{nm}}{dt} + \frac{(2n^2+3n+4)}{n+1}\frac{du_{nm}}{dt}\right]Y_{nm}(\theta,\varphi)\hat{\boldsymbol{r}}(\theta,\varphi) - \left[\frac{1}{2}(2n+1)K\frac{dc_{nm}}{dt} + \frac{3}{n+1}\frac{du_{nm}}{dt}\right]\boldsymbol{\nabla}^s_0[Y_{nm}(\theta,\varphi)]\right\}. \tag{35}$$

Let $d[E^{dis,liq}_{nm}(t)]/dt$ be the energy dissipation per unit time in the liquid phases inside and outside the vesicle. It is derived as

$$\frac{d[E^{dis,liq}_{nm}(t)]}{dt} = \oint_{S(t)}[\boldsymbol{\Pi}^{in}_{nm}(\theta,\varphi,t)\cdot\boldsymbol{v}^{in}_{nm}(\theta,\varphi,t)]ds + \oint_{S(t)}[\boldsymbol{\Pi}^{out}_{nm}(\theta,\varphi,t)\cdot\boldsymbol{v}^{out}_{nm}(\theta,\varphi,t)]ds,$$

where $\boldsymbol{C}\cdot\boldsymbol{D}$ is the scalar product of vectors $\boldsymbol{C}$ and $\boldsymbol{D}$. Then, from Eqs. (32)–(35) we obtain the following result:

$$\frac{d[E^{dis,liq}_{nm}(t)]}{dt} = \mu^{in}(R_0)^3\left\{\frac{(2n^2+n+3)}{n}\left[\frac{du_{nm}}{dt}\right]^2 - 3(n+1)K\frac{du_{nm}}{dt}\frac{dc_{nm}}{dt} + \frac{1}{4}(2n+1)n(n+1)K^2\left[\frac{dc_{nm}}{dt}\right]^2\right\} + \mu^{out}(R_0)^3\left\{\frac{(2n^2+3n+4)}{n+1}\left[\frac{du_{nm}}{dt}\right]^2 + 3nK\frac{du_{nm}}{dt}\frac{dc_{nm}}{dt} + \frac{1}{4}(2n+1)n(n+1)K^2\left[\frac{dc_{nm}}{dt}\right]^2\right\}. \tag{36}$$

Another origin of energy dissipation in the fluctuation decay is the friction between the monolayers [13–18,20–25]. Let f_s be the friction coefficient between them. If $\delta\boldsymbol{v}^{lat}$ from Eq. (22) is different from zero, the force per unit area $\boldsymbol{f}$, acting on the outer membrane, is

$$\boldsymbol{f} = -f_s\delta\boldsymbol{v}^{lat}. \tag{37}$$

The energy dissipation for the (n,m) mode per unit time due to the friction between the monolayers $dE^{dis,frict}_{nm}(t)/dt$ is presented as

$$\frac{dE^{dis,frict}_{nm}(t)}{dt} = \oint_{S(t)} f_s[\delta\boldsymbol{v}^{lat}_{nm}(\theta,\varphi,t)]^2 ds, \tag{38}$$

where $\delta\boldsymbol{v}^{lat}_{nm}(\theta,\varphi,t)$ is defined in Eqs. (28) and (29).

From Eqs. (29) and (38) it follows that

$$\frac{dE^{dis,frict}_{nm}(t)}{dt} = \frac{f_s}{n(n+1)}(R_0)^4K^2\left[\frac{dc_{nm}}{dt}\right]^2. \tag{39}$$

Let $dE^{dis}_{nm}(t)/dt$ be the total energy dissipation of the (n,m) mode per unit time. Then

$$\frac{dE^{dis}_{nm}(t)}{dt} = \frac{dE^{dis,liq}_{nm}(t)}{dt} + \frac{dE^{dis,frict}_{nm}(t)}{dt}, \tag{40}$$

where $dE^{dis,liq}_{nm}(t)/dt$ and $dE^{dis,frict}_{nm}(t)/dt$ are terms defined in Eqs. (36) and (39). Since energy dissipation is equal to the decrease in stored fluctuation energy, we obtain

$$\frac{dE^{dis}_{nm}(t)}{dt} = -\frac{dG_{nm}(t)}{dt}, \tag{41}$$

where $G_{nm}(t)$ is defined in Eq. (17). The derivative of this quantity is

$$\frac{dG_{nm}(t)}{dt} = K_c^{bl}\left\{\alpha_n u_{nm}(t)\frac{du_{nm}(t)}{dt} - \beta_n\left[u_{nm}(t)\frac{dc_{nm}(t)}{dt} + c_{nm}(t)\frac{du_{nm}(t)}{dt}\right] + \gamma c_{nm}(t)\frac{dc_{nm}(t)}{dt}\right\}. \quad (42)$$

From Eqs. (36) and (39)–(42) we obtain the following relation:

$$p_n\left[\frac{du_{nm}(t)}{dt}\right]^2 - q_n\frac{du_{nm}(t)}{dt}\frac{dc_{nm}(t)}{dt} + r_n\left[\frac{dc_{nm}(t)}{dt}\right]^2 + K_c^{bl}\left\{\alpha_n u_{nm}(t)\frac{du_{nm}(t)}{dt} - \beta_n\left[u_{nm}(t)\frac{dc_{nm}(t)}{dt} + c_{nm}(t)\frac{du_{nm}(t)}{dt}\right] + \gamma c_{nm}(t)\frac{dc_{nm}(t)}{dt}\right\} = 0, \quad (43)$$

where

$$p_n = (R_0)^3\left[\frac{(2n^2+n+3)}{n}\mu^{in} + \frac{(2n^2+3n+4)}{n+1}\mu^{out}\right],$$

$$q_n = (R_0)^3[3(n+1)\mu^{in} - 3n\mu^{out}]K,$$

$$r_n = (R_0)^3\left[\frac{1}{4}(2n+1)n(n+1)(\mu^{in}+\mu^{out}) + \frac{1}{n(n+1)}f_s R_0\right]K^2. \quad (44)$$

In the case when the fluctuation energy is much larger than the thermal energy kT, Eq. (43) allows the calculation of the relaxation rates, determining the relaxation decay of the fluctuation over time. For that purpose, we exchange the variables (u_{nm}, c_{nm}) with (x_{nm}, y_{nm}) using the transformation

$$u_{nm} = \cos(\varepsilon_n)x_{nm} - \sin(\varepsilon_n)y_{nm},$$

$$c_{nm} = \sin(\varepsilon_n)x_{nm} + \cos(\varepsilon_n)y_{nm}, \quad (45)$$

where ε_n is determined by the equation

$$\varepsilon_n = -\frac{1}{2}\arctan\left(\frac{q_n}{p_n - r_n}\right). \quad (46)$$

After variables (u_{nm} and c_{nm}) are exchanged in Eq. (43), an equation is obtained that does not contain a term of the kind $(dx_{nm}/dt)(dy_{nm}/dt)$. This equation is

$$\frac{dx_{nm}}{dt}\left\{p_n'\frac{dx_{nm}}{dt} + K_c^{bl}\{\cos(\varepsilon_n)\alpha_n u_{nm} - \beta_n[\sin(\varepsilon_n)u_{nm} + \cos(\varepsilon_n)c_{nm}] + \sin(\varepsilon_n)\gamma c_{nm}\}\right\} + \frac{dy_{nm}}{dt}\left\{r_n'\frac{dy_{nm}}{dt} + K_c^{bl}\{-\sin(\varepsilon_n)\alpha_n u_{nm} - \beta_n[\cos(\varepsilon_n)u_{nm} - \sin(\varepsilon_n)c_{nm}] + \cos(\varepsilon_n)\gamma c_{nm}\}\right\} = 0, \quad (47)$$

where the quantities p_n' and r_n' are defined as follows:

$$p_n' = p_n\cos^2(\varepsilon_n) - q_n\sin(\varepsilon_n)\cos(\varepsilon_n) + r_n\sin^2(\varepsilon_n),$$

$$r_n' = p_n\sin^2(\varepsilon_n) + q_n\sin(\varepsilon_n)\cos(\varepsilon_n) + r_n\cos^2(\varepsilon_n). \quad (48)$$

The solution of Eq. (47), describing the physical relaxation of the fluctuation, assures that the two expressions in the large outer braces on the left-hand side of this equation are equal to zero. In fact, this is a system of two equations, containing the variables dx_{nm}/dt, dy_{nm}/dt, u_{nm}, and c_{nm}. From Eqs. (45), the derivatives dx_{nm}/dt and dy_{nm}/dt are expressed by du_{nm}/dt and dc_{nm}/dt as follows:

$$\frac{dx_{nm}}{dt} = \cos(\varepsilon_n)\frac{du_{nm}}{dt} + \sin(\varepsilon_n)\frac{dc_{nm}}{dt},$$

$$\frac{dy_{nm}}{dt} = -\sin(\varepsilon_n)\frac{du_{nm}}{dt} + \cos(\varepsilon_n)\frac{dc_{nm}}{dt}. \quad (49)$$

In the system of the two equations describing the physical relaxation, we replace the derivatives dx_{nm}/dt and dy_{nm}/dt with Eqs. (49). Transforming this system in a way assuring that each of the two equations contains only one of the derivatives du_{nm}/dt and dc_{nm}/dt, we obtain

$$\frac{du_{nm}(t)}{dt} + \omega_{nm}^{uu}u_{nm}(t) + \omega_{nm}^{uc}c_{nm}(t) = 0,$$

$$\frac{dc_{nm}(t)}{dt} + \omega_{nm}^{cu}u_{nm}(t) + \omega_{nm}^{cc}c_{nm}(t) = 0, \quad (50)$$

where the relaxation rates ω_{nm}^{uu}, ω_{nm}^{uc}, ω_{nm}^{cu}, and ω_{nm}^{cc} are defined as follows:

$$\omega_{nm}^{uu} = \frac{K_c^{bl}}{p_n'}[\alpha_n\cos^2(\varepsilon_n) - \beta_n\sin(\varepsilon_n)\cos(\varepsilon_n)] + \frac{K_c^{bl}}{r_n'}[\alpha_n\sin^2(\varepsilon_n) + \beta_n\sin(\varepsilon_n)\cos(\varepsilon_n)],$$

$$\omega_{nm}^{uc} = \frac{K_c^{bl}}{p_n'}[-\beta_n\cos^2(\varepsilon_n) + \gamma\sin(\varepsilon_n)\cos(\varepsilon_n)] + \frac{K_c^{bl}}{r_n'}[-\beta_n\sin^2(\varepsilon_n) - \gamma\sin(\varepsilon_n)\cos(\varepsilon_n)],$$

$$\omega_{nm}^{cu} = \frac{K_c^{bl}}{p_n'}[\alpha_n\sin(\varepsilon_n)\cos(\varepsilon_n) - \beta_n\sin^2(\varepsilon_n)] + \frac{K_c^{bl}}{r_n'}[-\alpha_n\sin(\varepsilon_n)\cos(\varepsilon_n) - \beta_n\cos^2(\varepsilon_n)],$$

$$\omega_{nm}^{cc} = \frac{K_c^{bl}}{p_n'}[-\beta_n\sin(\varepsilon_n)\cos(\varepsilon_n) + \gamma\sin^2(\varepsilon_n)] + \frac{K_c^{bl}}{r_n'}[\beta_n\sin(\varepsilon_n)\cos(\varepsilon_n) + \gamma\cos^2(\varepsilon_n)]. \quad (51)$$

The terms α_n, β_n, and γ in the above equations are defined in Eq. (18). The results in Eqs. (50) and (51) rigorously describe the shape fluctuation relaxation of the vesicle.

Let $\Theta^u_{nm}(\tau)$ and $\Theta^c_{nm}(\tau)$ be time autocorrelation functions, defined as

$$\Theta^u_{nm}(\tau) = \langle u_{nm}(t)u_{nm}(t+\tau)\rangle = \lim_{T\to\infty}\frac{1}{T}\int_{-T/2}^{T/2} u_{nm}(t)u_{nm}(t+\tau)dt, \tag{52}$$

$$\Theta^c_{nm}(\tau) = \langle c_{nm}(t)c_{nm}(t+\tau)\rangle = \lim_{T\to\infty}\frac{1}{T}\int_{-T/2}^{T/2} c_{nm}(t)c_{nm}(t+\tau)dt. \tag{53}$$

To calculate $\Theta^u_{nm}(\tau)$, we have to take into account the thermal excitations of the shape fluctuations. We do this by introducing the random forces $z^u_{nm}(t)$ and $z^c_{nm}(t)$ exciting $u_{nm}(t)$ and $c_{nm}(t)$ and having white noise properties. Using these forces, we can describe the time evolution of $u_{nm}(t)$ and $c_{nm}(t)$ as follows:

$$\frac{du_{nm}(t)}{dt} + \omega^{uu}_{nm}u_{nm}(t) + \omega^{uc}_{nm}c_{nm}(t) = z^u_{nm}(t),$$

$$\frac{dc_{nm}(t)}{dt} + \omega^{cu}_{nm}u_{nm}(t) + \omega^{cc}_{nm}c_{nm}(t) = z^c_{nm}(t). \tag{54}$$

To obtain explicit expressions for the autocorrelation functions $\Theta^u_{nm}(\tau)$ and $\Theta^c_{nm}(\tau)$, a spectral decomposition of the quantities $u_{nm}(t)$, $u_{nm}(t)$, $z^u_{nm}(t)$, and $z^c_{nm}(t)$ has to be done. The approach used by Landau and Lifshitz [26] is used for that.

Let $a(t)$ be a real time-dependent function, defined in the interval $[-\infty,\infty]$. Let its mean square $\langle|a(t)|^2\rangle$ exist and be defined as

$$\langle|a(t)|^2\rangle = \lim_{T\to\infty}\frac{1}{T}\int_{-T/2}^{T/2}|a(t)|^2dt. \tag{55}$$

Let $\tilde{a}(t,T)$ be a function, equal to $a(t)$, if t belongs to the interval $[-\frac{T}{2},\frac{T}{2}]$ and $\tilde{a}(t,T)$ is equal to zero outside this interval. This function is decomposed in a Fourier integral as follows:

$$\tilde{a}(t,T) = \int_{-\infty}^{\infty}\tilde{A}(\omega,T)\exp(i\omega t)d\omega, \tag{56}$$

where i is the imaginary unit. The mean-square value of $\tilde{a}(t,T)$ in the interval $[-\frac{T}{2},\frac{T}{2}]$, denoted with $\tilde{a}^{ms}(T)$, is

$$\tilde{a}^{ms}(T) = \frac{1}{T}\int_{-T/2}^{T/2}\tilde{a}(t,T)[\tilde{a}(t,T)]^*dt. \tag{57}$$

From Eqs. (56) and (57) it follows that

$$\tilde{a}^{ms}(T) = \int_{-\infty}^{\infty}d\omega\int_{-\infty}^{\infty}d\omega'\tilde{A}(\omega,T)[\tilde{A}(\omega',T)]^* \times\frac{1}{T}\int_{-T/2}^{T/2}\exp[i(\omega-\omega')t]dt. \tag{58}$$

From Eq. (55) and the definition of $\tilde{a}^{ms}(t,T)$ it follows that $\langle|a(t)|^2\rangle = \lim_{T\to\infty}\tilde{a}^{ms}(T)$.

We denote with $A(\omega)$ the following limit:

$$A(\omega) = \lim_{T\to\infty}\frac{\tilde{A}(\omega,T)}{\sqrt{(T)}}. \tag{59}$$

Taking into account that

$$\lim_{T\to\infty}\int_{-T/2}^{T/2}\exp[i(\omega-\omega')t]dt = 2\pi\delta(\omega-\omega'), \tag{60}$$

where $\delta(\omega)$ is the Dirac function, we obtain

$$\langle|a(t)|^2\rangle = 2\pi\int_{-\infty}^{\infty}|A(\omega)|^2d\omega. \tag{61}$$

The limit in Eq. (59) exists because we assumed that the value of $\langle|a(t)|^2\rangle$ is finite.

As evident from Eq. (59), for high enough T, Eq. (56) can be presented in the following form:

$$\tilde{a}(t,T) \approx \sqrt{T}\int_{-\infty}^{\infty}A(\omega)\exp(i\omega t)d\omega. \tag{62}$$

From the above definition of $\tilde{a}(t,T)$, for each t the following relation is valid:

$$a(t) = \lim_{T\to\infty}\tilde{a}(t,T). \tag{63}$$

In the same way as we defined $\tilde{a}(t,T)$ and $\tilde{A}(\omega,T)$, we define the functions $\tilde{u}_{nm}(t,T)$, $\tilde{c}_{nm}(t,T)$, $\tilde{z}^u_{nm}(t,T)$, and $\tilde{z}^c_{nm}(t,T)$ and the spectra $U_{nm}(\omega)$, $C_{nm}(\omega)$, $Z^u_{nm}(\omega)$, and $Z^c_{nm}(\omega)$, corresponding to the functions $u_{nm}(t)$, $c_{nm}(t)$, $z^u_{nm}(t)$, and $z^c_{nm}(t)$.

We decompose the functions $\tilde{u}_{nm}(t,T)$, $\tilde{c}_{nm}(t,T)$, $\tilde{z}^u_{nm}(t,T)$, and $\tilde{z}^c_{nm}(t,T)$ in integrals of Fourier as follows:

$$\tilde{u}_{nm}(t,T) \approx \sqrt{T}\int_{-\infty}^{\infty}U_{nm}(\omega)\exp(i\omega t)d\omega,$$

$$\tilde{c}_{nm}(t,T) \approx \sqrt{T}\int_{-\infty}^{\infty}C_{nm}(\omega)\exp(i\omega t)d\omega,$$

$$\tilde{z}^u_{nm}(t,T) \approx \sqrt{T}\int_{-\infty}^{\infty}Z^u_{nm}(\omega)\exp(i\omega t)d\omega,$$

$$\tilde{z}^c_{nm}(t,T) \approx \sqrt{T}\int_{-\infty}^{\infty}Z^c_{nm}(\omega)\exp(i\omega t)d\omega. \tag{64}$$

We replace Eqs. (64) in Eqs. (54) and let the limit $T\to\infty$ for which Eqs. (54) are valid. Then using for each of the quantities $\tilde{u}_{nm}(t,T)$, $\tilde{c}_{nm}(t,T)$, $\tilde{z}^u_{nm}(t,T)$, and $\tilde{z}^c_{nm}(t,T)$ Eq. (63), we obtain the following system of equations:

$$(i\omega+\omega^{uu}_{nm})U_{nm}(\omega) + \omega^{uc}_{nm}C_{nm}(\omega) = Z^u_{nm}(\omega),$$

$$\omega^{cu}_{nm}U_{nm}(\omega) + (i\omega+\omega^{cc}_{nm})C_{nm}(\omega) = Z^c_{nm}(\omega). \tag{65}$$

It has to be noted that $U_{nm}(\omega)$ and $C_{nm}(\omega)$ have the dimension $(\text{time})^{1/2}$ and that $Z^u_{nm}(\omega)$ and $Z^c_{nm}(\omega)$ have the dimension $(\text{time})^{-1/2}$.

Let $\pm i\tilde{\omega}_{nm}$ and $\pm i\tilde{\Omega}_{nm}$, where $\tilde{\Omega}_{nm} \geq \tilde{\omega}_{nm} > 0$, be the four solutions of the biquadratic equation

$$\omega^4 + \omega^2[2(\omega_{nm}^{uc}\omega_{nm}^{cu} - \omega_{nm}^{uu}\omega_{nm}^{cc}) + (\omega_{nm}^{uu} + \omega_{nm}^{cc})^2] + (\omega_{nm}^{uc}\omega_{nm}^{cu} - \omega_{nm}^{uu}\omega_{nm}^{cc})^2 = 0. \tag{66}$$

The amplitudes $|Z_{nm}^u|$ and $|Z_{nm}^c|$ do not depend on ω because $z_{nm}^u(t)$ and $z_{nm}^c(t)$ are white noise. Then, the amplitude squares $|U_{nm}|^2$ and $|C_{nm}|^2$, calculated from Eqs. (65), are

$$|U_{nm}(\omega)|^2 = \frac{1}{(\tilde{\Omega}_{nm})^2 - (\tilde{\omega}_{nm})^2}\left\{\frac{[(\omega_{nm}^{cc})^2 - (\tilde{\omega}_{nm})^2]|Z_{nm}^u|^2 + (\omega_{nm}^{uc})^2|Z_{nm}^c|^2}{(\omega)^2 + (\tilde{\omega}_{nm})^2} + \frac{[(\tilde{\Omega}_{nm})^2 - (\omega_{nm}^{cc})^2]|Z_{nm}^u|^2 - (\omega_{nm}^{uc})^2|Z_{nm}^c|^2}{(\omega)^2 + (\tilde{\Omega}_{nm})^2}\right\}, \tag{67}$$

$$|C_{nm}(\omega)|^2 = \frac{1}{(\tilde{\Omega}_{nm})^2 - (\tilde{\omega}_{nm})^2}\left\{\frac{(\omega_{nm}^{cu})^2|Z_{nm}^u|^2 + [(\omega_{nm}^{uu})^2 - (\tilde{\omega}_{nm})^2]|Z_{nm}^c|^2}{(\omega)^2 + (\tilde{\omega}_{nm})^2} - \frac{(\omega_{nm}^{cu})^2|Z_{nm}^u|^2 + [(\omega_{nm}^{uu})^2 - (\tilde{\Omega}_{nm})^2]|Z_{nm}^c|^2}{(\omega)^2 + (\tilde{\Omega}_{nm})^2}\right\}. \tag{68}$$

Replacing the terms $\tilde{u}_{nm}(t,T)$, $\tilde{c}_{nm}(t,T)$, $\tilde{z}_{nm}^u(t,T)$, and $\tilde{z}_{nm}^c(t,T)$ of Eqs. (64) in Eqs. (52) and (53), and letting again the limit $T \to \infty$, we obtain

$$\Theta_{nm}^u(\tau) = 2\pi\int_{-\infty}^{\infty} |U_{nm}(\omega)|^2 \exp(i\omega\tau)d\omega, \tag{69}$$

$$\Theta_{nm}^c(\tau) = 2\pi\int_{-\infty}^{\infty} |C_{nm}(\omega)|^2 \exp(i\omega\tau)d\omega. \tag{70}$$

From Eqs. (67)–(70) and from the well-known relation

$$\int_{-\infty}^{\infty} \frac{\exp(i\omega\tau)}{\omega^2 + a^2}d\omega = \frac{\pi}{a}\exp(-a\tau),$$

the following results are calculated:

$$\Theta_{nm}^u(\tau) = a_{nm}^{u\tilde{\omega}} \exp(-\tilde{\omega}\tau) + a_{nm}^{u\tilde{\Omega}} \exp(-\tilde{\Omega}\tau), \tag{71}$$

$$\Theta_{nm}^c(\tau) = a_{nm}^{c\tilde{\omega}} \exp(-\tilde{\omega}\tau) + a_{nm}^{c\tilde{\Omega}} \exp(-\tilde{\Omega}\tau), \tag{72}$$

where

$$a_{nm}^{u\tilde{\omega}} = \frac{2\pi^2}{(\tilde{\Omega}_{nm})^2 - (\tilde{\omega}_{nm})^2}\left\{\frac{[(\omega_{nm}^{cc})^2 - (\tilde{\omega}_{nm})^2]|Z_{nm}^u|^2 + (\omega_{nm}^{uc})^2|Z_{nm}^c|^2}{\tilde{\omega}}\right\},$$

$$a_{nm}^{u\tilde{\Omega}} = \frac{2\pi^2}{(\tilde{\Omega}_{nm})^2 - (\tilde{\omega}_{nm})^2}\left\{\frac{[(\tilde{\Omega}_{nm})^2 - (\omega_{nm}^{cc})^2]|Z_{nm}^u|^2 - (\omega_{nm}^{uc})^2|Z_{nm}^c|^2}{\tilde{\Omega}}\right\},$$

$$a_{nm}^{c\tilde{\omega}} = \frac{2\pi^2}{(\tilde{\Omega}_{nm})^2 - (\tilde{\omega}_{nm})^2}\left\{\frac{(\omega_{nm}^{cu})^2|Z_{nm}^u|^2 + [(\omega_{nm}^{uu})^2 - (\tilde{\omega}_{nm})^2]|Z_{nm}^c|^2}{\tilde{\omega}}\right\},$$

$$a_{nm}^{c\tilde{\Omega}} = \frac{2\pi^2}{(\tilde{\Omega}_{nm})^2 - (\tilde{\omega}_{nm})^2}\left\{-\frac{(\omega_{nm}^{cu})^2|Z_{nm}^u|^2 + [(\omega_{nm}^{uu})^2 - (\tilde{\Omega}_{nm})^2]|Z_{nm}^c|^2}{\tilde{\Omega}}\right\}. \tag{73}$$

To determine the quantities $|Z_{nm}^u|^2$ and $|Z_{nm}^c|^2$ we use the relations, obtained from Eqs. (52) and (53) for the case $\tau = 0$, as follows:

$$\Theta_{nm}^u(0) = \langle[u_{nm}(t)]^2\rangle,$$

$$\Theta_{nm}^c(0) = \langle[c_{nm}(t)]^2\rangle, \tag{74}$$

where the time mean squares $\langle[u_{nm}(t)]^2\rangle$ and $\langle[c_{nm}(t)]^2\rangle$ are determined by Eqs. (19) and (20). Consequently, $|Z_{nm}^u|^2$ and $|Z_{nm}^c|^2$ are the solutions of the two-equation system defined by Eqs. (74). Finally, the result for $\Theta_{nm}^u(\tau)$ is expressed as

$$\Theta_{nm}^u(\tau) = \langle[u_{nm}(t)]^2\rangle \times\left[\frac{1}{1+T_{nm}}\exp(-\tilde{\omega}\tau) + \frac{T_{nm}}{1+T_{nm}}\exp(-\tilde{\Omega}\tau)\right]. \tag{75}$$

In Eq. (75) T_{nm} is the ratio between the pre-exponential factor of the exponent with relaxation rate $\tilde{\Omega}_{nm}$ and the exponent with relaxation rate $\tilde{\omega}_{nm}$. The result calculated for this ratio is

$$T_{nm} = \frac{\tilde{\omega}_{nm}}{\tilde{\Omega}_{nm}} \frac{[(\tilde{\Omega}_{nm})^2 - (\omega_{nm}^{cc})^2]L_{nm} - (\omega_{nm}^{uc})^2 M_{mn}}{[(\omega_{nm}^{cc})^2 - (\tilde{\omega}_{nm})^2]L_{nm} + (\omega_{nm}^{uc})^2 M_{mn}}, \quad (76)$$

where

$$L_{nm} = (\omega_{nm}^{uu})^2 + \tilde{\omega}_{nm}\tilde{\Omega}_{nm} - \frac{\alpha_n}{\gamma}(\omega_{nm}^{uc})^2,$$

$$M_{nm} = \frac{\alpha_n}{\gamma}(\omega_{nm}^{cc})^2 + \frac{\alpha_n}{\gamma}\tilde{\omega}_{nm}\tilde{\Omega}_{nm} - (\omega_{nm}^{cu})^2. \quad (77)$$

The variables T_{nm}, $\tilde{\Omega}_{nm}$, and $\tilde{\omega}_{nm}$ are functions of the mechanical and rheological properties of the vesicle and its dimensions. In the practical implementation of the above results, the quantities ω_{nm}^{uu}, ω_{nm}^{uc}, ω_{nm}^{cu}, and ω_{nm}^{cc} are calculated from Eqs. (51), where ε is expressed in Eq. (46); p_n' and r_n' are defined by Eqs. (48); p_n, q_n, and r_n are defined in Eqs. (44); α_n, β_n, and γ are those from Eqs. (18); and $\tilde{\omega}_{nm}$ and $\tilde{\Omega}_{nm}$ are obtained through the solution of Eq. (66).

IV. EMULSION AND MICROEMULSION DROPLETS

The approach used in the present work can be applied to the description of the shape fluctuations of nearly spherical emulsion and microemulsion droplets, too. We will present a short survey of the results for this case.

The surface of the emulsion droplet is covered by a monolayer of amphiphilic molecules and, because of this, there are no effects related to lateral movements of the membrane. We denote with K_c^{mono} and C_0^{mono} the bending elasticity and the spontaneous curvature of the monolayer. This is exactly the case, considered by Milner and Safran in [17]. The amplitudes $u_{nm}^{mono}(t)$ of the (n,m) mode are introduced in the same way as in the case of a vesicle [see Eq. (2)]. Their mean-square amplitudes $\langle|u_{nm}^{mono}(t)|^2\rangle$ are given by their well-known expression [17],

$$\langle|u_{nm}^{mono}(t)|^2\rangle = \frac{kT}{K_c^{mono}} \frac{1}{(n-1)(n+2)[n(n+1)+\bar{\sigma}^{mono}]}. \quad (78)$$

In this equation, $\bar{\sigma}^{mono}$ depends on the tension and the spontaneous curvature of the membrane [17].

The autocorrelation function $\langle u_{nm}^{mono}(t)u_{nm}^{mono}(t+\tau)\rangle$ consists of one exponent [17],

$$\langle u_{nm}^{mono}(t)u_{nm}^{mono}(t+\tau)\rangle = \langle|u_{nm}^{mono}(t)|^2\rangle \exp(-\omega_{nm}^{mono}\tau). \quad (79)$$

Applying the calculation procedure, used for the bilayer vesicle membrane, to the monolayer of an emulsion droplet, for the relaxation rate ω_{nm}^{mono} we obtain

$$\omega_{nm}^{mono} = \frac{K_c^{mono}(n-1)(n+2)[n(n+1)+\bar{\sigma}^{mono}]}{(R_0)^3\left(\frac{2n^2+n+3}{n}\mu^{in} + \frac{2n^2+3n+4}{n+1}\mu^{out}\right)}. \quad (80)$$

The result from Eq. (80) allows us to take into account the difference between the viscosities of the fluids inside and outside the emulsion droplet.

In the particular case when $\mu^{in}=\mu^{out}=\mu$, the result for ω_{nm}^{mono} is presented in the following form:

$$\omega_{nm}^{mono} = \frac{K_c^{mono}}{\mu(R_0)^3} \frac{n(n+1)+\bar{\sigma}^{mono}}{Z(n)}, \quad (81)$$

where

$$Z(n) = \frac{(2n+1)(2n^2+2n+3)}{(n-1)n(n+1)(n+2)}. \quad (82)$$

Our results from Eqs. (81) and (82) are very similar to those of Milner and Safran [17]. The difference is that our term $(2n^2+2n+3)$ in the numerator of the fraction on the right-hand side of Eq. (82) is equal to $(2n^2+2n-1)$ according to Milner and Safran.

V. DISCUSSION

The shape fluctuations of a nearly spherical lipid vesicle are accompanied by monolayer lateral displacements. The present work takes into account the displacement effects on the relaxation rates and time autocorrelations of the fluctuation modes. These autocorrelations depend on the mechanical and rheological properties of the vesicle and on the vesicle's dimension.

Concerning the emulsion droplets, the viscosities of the liquid inside and outside the droplet are usually different. Our results show how the time autocorrelations of the droplet shape fluctuations depend on these two viscosities.

Two limiting cases can be considered, namely, when the friction coefficient between the monolayers f_s tends to zero and to infinity, respectively. In the first case, the autocorrelation $\Theta_{nm}^u(\tau)$ will remain as a sum of two exponents. This is due to the flow in the liquid phase, created by the lateral displacements of the monolayers and the normal movements of the membrane. In the second case $\tilde{\omega}$ will tend to zero, T_{nm} will tend to infinity, and $\Theta_{nm}^u(\tau)$ will tend to one exponent as in Eq. (79).

Our aim with this theory is to provide a model for the interpretation of experimental data, obtained from shape fluctuations of nearly spherical lipid vesicles. One of the experimental methods for such an investigation is the observation of the fluctuating vesicle under an optical microscope. With this optical method not the entire vesicle is observed, but only its contour [9,10], which is its equatorial cross section. Despite this restriction, methods have been developed for the experimental determination of the mean-square values of the fluctuation mode amplitudes [10,12], as well as the time autocorrelations of these amplitudes [12,27]. The mean squares depend on the temperature T, the number n of the

mode u_{nm}, the bending elasticity K_c^{fr} for the case of free flip-flop, and the reduced tension $\bar{\sigma}$ [see Eq. (19)]. The tension $\bar{\sigma}$ changes from vesicle to vesicle, while the other quantities must be the same for all the vesicles observed. The temperature can be kept constant in the experiment. Consequently, the experimental data fit for the mean-square values would permit the determination of K_c^{fr} and $\bar{\sigma}$. The amplitude autocorrelations are sums of two exponents [see Eq. (75)], whose decay rates and pre-exponential factors depend on T, n, K_c^{fr}, and $\bar{\sigma}$ and on the following additional characteristics of the vesicle: the bending elasticity K_c^{bl} for the case of blocked flip-flop, the distance between the neutral surfaces of the monolayers, included in K [see Eq. (9)], the vesicle's radius R_0, the viscosities of the liquid phases on both sides of the bilayer η^{in} and η^{out}, and the friction coefficient f_s between the monolayers. R_0 is determined by averaging the contours of each vesicle. The quantities K_c^{bl}, K, η^{in}, η^{out}, and f_s, can be determined by fitting experimentally obtained autocorrelation functions. If we manage to determine some of these material constants (e.g., η^{in} and η^{out}) by additional experiments, the remaining ones (K_c^{bl}, K, and f_s in this example) can be obtained by fitting the experimental fluctuation data. Similar experimental and fitting approach has been applied by Méléard and Pott [13] and by Arriaga *et al.* [28] to simpler mathematical models. These authors proved experimentally that the autocorrelation functions of the fluctuating amplitudes are two-exponential functions.

In another method, measuring the neutron scattering of lamellar and sponge lipid-water phases, the scattering data are explained by the out-of-plane membrane fluctuations. In this method, the experimentally obtained quantity is the structure factor $S(q,\tau)$, which depends on the wave number q and the time τ. According to the theory of Zilman and Granek [29,30], this factor is presented as a stretched exponent, $S(q,\tau) \sim \exp(-\Gamma_q \tau)^{2/3}$, with a decay rate $\Gamma_q \sim (kT/K_c)^{1/2} kTq^3/\eta$, where kT is the Boltzmann factor, K_c is the bending elasticity of the bilayer, and η is the viscosity of the liquid phase around the membrane. It is important to note that the decay rate Γ_q is similar to ω_{nm}^{mono} from Eq. (81) but is not identical with it. To obtain the above term for Γ_q, these authors made assumptions, similar to those applied in the deduction of Eqs. (79) and (80). In their calculations the decay rate of the q-mode amplitude is a monoexponential function of the kind included in Eq. (79). Our results could be used for a more precise calculation of Γ_q since they take into account also the energy dissipation of the liquid phase flow, induced by the lateral movement of the monolayers. It is the author's belief that the suggested theory could be very useful for setting limits of the validity for assumptions regarding mean-square values and autocorrelation functions of the amplitudes of the fluctuation modes, as reported, e.g., in [15].

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