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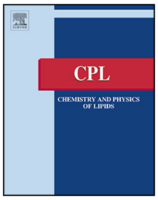

Fluctuation dynamics of bilayer vesicles with intermonolayer sliding: Experiment and theory

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ABSTRACT

The presence of coupled modes of membrane motion in closed shells is extensively predicted by theory. The bilayer structure inherent to lipid vesicles is suitable to support hybrid modes of curvature motion coupling membrane bending with the local reorganization of the bilayer material through relaxation of the dilatational stresses. Previous experiments evidenced the existence of such hybrid modes facilitating membrane bending at high curvatures in lipid vesicles [Rodríguez-García, R., Arriaga, L.R., Mell, M., Moleiro, L.H., López-Montero, I., Monroy, F., 2009. Phys. Rev. Lett. 102, 128201.]. For lipid bilayers that are able to undergo intermonolayer sliding, the experimental fluctuation spectra are found compatible with a bimodal schema. The usual tension/bending fluctuations couple with the hybrid modes in a mechanical interplay, which becomes progressively efficient with increasing vesicle radius, to saturate at infinity radius into the behavior expected for a flat membrane. Grounded on the theory of closed shells, we propose an approximated expression of the bimodal spectrum, which predicts the observed dependencies on the vesicle radius. The dynamical features obtained from the autocorrelation functions of the vesicle fluctuations are found in quantitative agreement with the proposed theory.

1. Introduction

Biological membranes are dynamic closed shell assemblies structurally based on the lyotropic self-organization as fluid lipid bilayers (Singer and Nicolson, 1972; Sheetz and Singer, 1974). The fluid lipid bilayer is composed of two monomolecular sheets, which are intrinsically characterized by a strong lateral cohesion and held together by weak van der Waals forces. Transverse and lateral forces in the bilayer are significant, since they not only determine cell shapes (Sackmann et al., 1986; Safran, 1994; Seifert et al., 2001) but also membrane dynamics (Kramer, 1971; Schneider et al., 1984; Milner and Safran, 1987). Deformation modes in lipid membranes are governed by the mechanical properties of the bilayer, their dynamics being relevant at the time scales determined by the different dissipation mechanisms present in the system (Levine and MacKintosh, 2002; Camley and Brown, 2011; Granek, 2011; Betz, 2012). In general, the mechanical response of a fluid lipid bilayer should occur through curvature deflections and stretching deformations. Curvature deflections are transverse motions, which define shape changes through two relevant rigidities: the surface tension (σ) and the bending modulus (κ) (Helfrich, 1973). The surface tension dominates the energy of the flexural deformations put into play through the excess area of the membrane, whereas the bending rigidity determines the strength of the net change in curvature with respect to the equilibrium conformation. Pure longitudinal motions are governed by the compression modulus of the constituting monolayers (K) (Boal, 2012). Exposed to lateral strain, lipid membranes are quite rigid as compared to flexural deformations, which is an inherent characteristic of the bilayer packing leading to its high mechanical stability. Consequently, net area changes are considered to be suppressed in lipid membranes,

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due to the large energy penalty associated to. Hence, the membrane area is usually assumed a system invariant in lipid bilayers. Ideally, lipid bilayers are considered as 2D-sheets characterized by a low tension, small bending resistance and global lateral incompressibility, a set of mechanical characteristics making them to behave as floppy membranes susceptible to undergo shape changes with very limited longitudinal deformation. The standard Helfrich's treatment of the fluctuating single-sheet membrane leads to a monomodal spectrum of the thermal curvature fluctuations exclusively governed by surface tension and bending forces (Helfrich, 1973). In the real thing, which is actually a bilayer with a finite thickness, however, a local deflection might cause a longitudinal reorganization of the lipid material in each monolayer. Particularly, one expects a dilation in the outer monolayer followed by an equivalent compression in the inner one as consequence of a change of curvature of the membrane. The extended theory of the composite bilayer membrane was seminally formulated by Helfrich (1977), and later put forward by Evans and co-workers (Evans et al., 1992; Yeung and Evans, 1995). This theory predicts the existence of coupled dilational–curvature modes supported by the bilayer structure, in addition to the pure flexural modes, a fact that has been recognized as crucial to understand membrane energetics (Lipowsky, 1991). Those coupled dilational–curvature stresses could become eventually relaxed by possible interbilayer transport and the energy dissipated by intra-/inter-monolayer friction, thus appearing a degree of freedom additional to the pure flexural mode, which is usually referred to as hybrid mode. In the limit of free slippage, except for the intrinsic viscous resistance of the lipid monolayers, they are free to slide relative to one another giving rise to a hybrid mode dynamically coupled within the density modes of the bilayer structure. The Helfrich's description formally corresponds to a planar sheet with free edges, thus no lateral compression deformations are drawn upon small bending. However, flexible membranes in a closed shell topology, e.g., bilayer lipid vesicles, represent a different elastic problem where curvature deformations necessarily imply a dilation of the membrane.

Here, we address the question of how curvature deformations in a lipid bilayer vesicle could efficiently couple with longitudinal dilations occurring in the constituting monolayers. Such a coupling should provide an enhanced local deformability (Helfrich, 1977), mainly at highly curved regions where bending deformations could somewhat become governed by lateral intrabilayer stresses. On the one hand, an enhanced coupling is expected in closed membranes of curved vesicles, resulting in a certain influence of the hybrid dilatation–curvature modes on the global shape fluctuations (Rodríguez-García et al., 2009). The effect is so important that even for slightly curved vesicles ($R/h \gg 1$), thermal fluctuations are expected with an increased amplitude at low wavevectors ($qR \approx 1$) (Rodríguez-García et al., 2009). On the other hand, no strong influence of the hybrid modes should occur in large vesicles ($R \to \infty$), where large-scale lateral motions are expected to release longitudinal stresses in a very efficient way, similarly to flat-bilayers with free edges.

1.1. Intermonolayer friction affects dilation–curvature coupling in bilayer systems

Previous experiments with bilayer vesicles have demonstrated the effect of interlayer coupling in membrane mechanics through the influence of intermonolayer friction on their relaxation dynamics (Méléard et al., 1990; Pott and Méléard, 2002; Arriaga et al., 2009a, 2010). Additional evidence of intermonolayer coupling was demonstrated in tether pulling experiments (Raphael and Waugh, 1996) and from its retarding effect on the lateral diffusion of fluorescent probes (Merkel et al., 1989). With regard to dissipation dynamics, theoretical analyses by Seifert and cols. (Seifert and Langer, 1993; Kraus and Seifert, 1994) have shown that the two dissipative mechanisms, namely conventional bulk friction and intermonolayer drag, are important on different length scales. Whereas the single-sheet Helfrich's theory of membrane fluctuations is monomodal (flexural mode only), the extended theory demonstrates the existence of different fluctuation modes undergoing different dissipative pathways (Camley and Brown, 2011; Seifert and Langer, 1993; Kraus and Seifert, 1994): (1) pure flexural mode, which is restored by membrane tension (σ) and bending curvature (κ) and dissipates through bulk friction. (2) Pure dilational mode, governed by lateral compression elasticity (K) and monolayer viscosities. (3) Hybrid dilation–curvature, which couples flexural deformations with lateral dilations. For this hybrid mode, the restoring force is accounted for by the compression modulus (K), and the viscous dissipation by the intermonolayer friction (b). Transverse motions are caused by both, the pure flexural mode (1) and the hybrid dilation–curvature mode (3), which appear merged as two normal modes in a bimodal distribution of flexural modes (Kraus and Seifert, 1994). Separately, the pure dilational mode (2), which is the third normal mode of the composite membrane problem, appears completely decoupled from the others. In addition, this pure dilational mode is "hidden" to usual experimental methods based on the tracking of the shape fluctuations, which exclusively "see" membrane deflections. Because every fluctuation mode is dominated by different energetics and different dissipative hydrodynamics, they might appear dynamically separated with different relative amplitudes depending on the scale probed. For long wavelength fluctuations, for which membrane tension dominates, viscous relaxation is barely governed by bulk viscosity (Arriaga et al., 2009a), as predicted by the conventional MS theory of the membrane fluctuations (Milner and Safran, 1987). From the extended theory (Seifert and Langer, 1993; Kraus and Seifert, 1994; Watson and Brown, 2010), it is concluded that viscous resistance to curvature changes should be dominated by interlayer dissipation in the mesoscopic regime. In this regime, coupling between the ordinary bending mode and the hybrid dilation–curvature mode stands, producing a dynamic exchange of energy between the modes that cause the enhancement of the flexural deformations of the membrane (Seifert and Langer, 1993; Kraus and Seifert, 1994). In the limit of total adhesion between the monolayers, the membrane behaves as a uniform plate with a bending rigidity that obeys the relationship $\kappa_{\mathrm{mon}} = (h^2/12)K$ (Landau and Lifshitz, 1986), which drops to the bilayer value $\kappa_{\mathrm{bil}} = (h^2/48)K\,(=\kappa_{\mathrm{mon}}/4)$ if the plate is sliced into two leaflets free to slide past each other (Boal, 2012). Mutual monolayer interdigitation leading to intermediate intermonolayer friction is accounted for by the "polymer brush" model (Rawicz et al., 2000), which predicts the intermediate result $\kappa_{\mathrm{brush}} = (h^2/24)K$. These models of intermonolayer coupling lead, depending on the degree of intermonolayer friction, to a generalized bending rigidity $\kappa = h^2K/\alpha$, where the numerical constant α spans from: $\alpha = 12$ for total monolayer sticking, up to $\alpha = 48$, for ideal sliding. From a structural standpoint, chain interdigitation at the bilayer midplane causes mechanical coupling between the two monolayers. Such a structural coupling might determine the compositional dependence of the coupling constant α. Therefore, the degree of intermonolayer coupling not only determines the velocity differences between the two monolayers, leading to subsequent viscous friction, but also modifies the actual value of the bending rigidity. In qualitative terms: the weaker the coupling between the monolayers, the softer the membrane when stressed upon bending and the lower the intermonolayer friction. Therefore, if the sliding between the monolayers increases, then, the lateral redistribution of the lipid material is favored and the