Effect of a model scramblase peptide on viscoelastic properties of phspholipid bilayers

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Biological membranes consist mainly of phospholipids and proteins. During cellular processes, the morphology of lipid membranes changes dynamically, which is governed by interactions between lipids and proteins. Binding of cytosolic proteins to the membrane is often accompanied by the membrane deformation, such as invagination and tubulation. Many theoretical studies suggest that viscoelastic properties of the membrane play an important role in the membrane deformation. Some of the viscoelastic parameters can be determined by measuring the thermal fluctuations of the membrane, i.e., bending and thickness fluctuations, using neutron spin echo (NSE) spectroscopy.

Several studies suggested that lipid transbilayer movement (flip-flop) promoting peptides and proteins are involved in membrane deformation. We have previously developed a model "scramblase" peptide, TMP23Q, which has a glutamine residue in the center of the hydrophobic sequence and promotes phospholipid flip-flop. The specific aim of the present study is thus to evaluate how the presence of TMP23Q changes the thermal fluctuation and viscoelastic properties of the lipid membrane using NSE spectroscopy.

Thickness fluctuation measurement requires both tail-deuterated lipids, which are available only for saturated lipids. 1,2-Dimyristoyl-sn-glycero-3-phosphocholine (DMPC) has the most similar property in saturated lipids to that of biological membranes at 37 °C. Therefore, we use a lipid mixture of DMPC and 1,2-dimyristoyl-sn-glycero-3-phosphoglycerol (DMPG) at a 95:5 molar ratio for bending fluctuation measurements, and a lipid mixture of 1,2-dimyristoyl-d54-sn-glycero-3-phosphocholine, DMPC, and DMPG at a 90:5:5 molar ratio for thickness fluctuation measurements. Here, 5% DMPG is included to prevent the formation of multilamellar vesicles. We prepared DMPC/DMPG vesicles containing TMP23Q or a negative control peptide TMP23L in D2O.

Intermediate scattering function obtained by bending fluctuation measurement was fit to a single-membrane fluctuation model proposed by Zilman and Granek with including the effect of internal dissipation within the bilayer proposed by Watson and Brown. The intrinsic bending modulus values were changed by the presence of neither peptides. The relaxation rate obtained from thickness fluctuation measurement at q ˜ 1.0 nm − 1 showed discrepancy from Zilman-Granek theory (Fig. 1). Although we calculated the area compressibility modulus K_A, peptide inclusion in the membrane did not have any effect on K_A values. However, both peptides increased the relaxation time due to the thickness fluctuation τ_TF. Considering the relationship between the membrane viscosity and τ_TF, these results suggests that the presence of transmembrane peptides in the membrane increase the membrane viscosity.

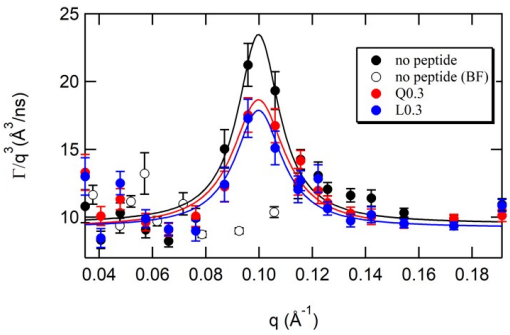

Fig. 1. Normalized relaxation rate Γ/q3 for tail-deuterated DMPC vesicles with/without peptides.