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A Molecular Dynamics Simulation Study of Nanomechanical Properties of Asymmetric Lipid Bilayer

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Abstract A very important part of the living cells of biological systems is the lipid membrane. The mechanical properties of this membrane play an important role in biophysical studies. Investigation as to how the insertion of additional phospholipids in one leaflet of a bilayer affects the physical properties of the obtained asymmetric lipid membrane is of recent practical interest. In this work a coarse-grained molecular dynamics simulation was carried out in order to compute the pressure tensor, the lateral pressure, the surface tension and the first moment of lateral pressure in each leaflet of such a bilayer. Our simulations indicate that adding more phospholipids into one monolayer results in asymmetrical changes in the lateral pressure of the individual bilayer leaflets. Interestingly, it has been observed that a change in phospholipid density in one leaflet affects the physical properties of unperturbed leaflet as well. The asymmetric behavior of the physical properties of the two leaflets as a result of a change in the contribution of the various intermolecular forces in the presence of additional phospholipids may be expressed formally.

Keywords Molecular dynamics · Nanomechanical property · Lipid bilayer

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Introduction

In biophysics it is challenging and interesting to study the structure and dynamics of the supramolecular assembly of lipids in biological membranes and to modulate their properties. In traditional understanding of membrane deformations the membrane is modeled as a smooth, structureless sheet with energetic penalties due to bending and stretching (Helfrich 1973; Canham 1970). When a more detailed study is required, the molecular details of each monolayer come into play as well. At the macroscopic level, liquid crystal theory tells us that the orientation of the lipids must be taken into account (Frank 1958). On smaller length scales, the monolayer surfaces are no longer smooth and include molecular protrusions (Lipowsky and Grotehans 1994; Israelachvili 1985; Perozo and Rees 2003).

The hydrophobic and hydrophilic properties of the semi-flexible phospholipid molecule emerged from characteristics including the chemical nature of its headgroup and type as well as the length of its fatty acyl chains. The amphiphilic property of individual lipid molecules and chemical composition of nanobiomembranes are responsible for a wide range of physical and biological properties. As a result of the different types of possible interactions between headgroups and acyl chains, one may expect an inhomogeneity in the membrane, which gives rise to a nonuniform pressure profile.

Many theoretical and computational approaches have been used to investigate the pressure distribution in lipid

bilayers in the past two decades (Szleifer et al. 1990; Goetz and Lipowsky 1998; Xiang and Anderson 1994; Harries and Benshaul 1997; Venturoli and Smit 1999; Cantor 1998, 1999a, b; Lindahl and Edholm 2000; Shillcock and Lipowsky 2002; Gullingsrud and Schulten 2004; Mukhin and Baoukina 2005; Patra 2005; Carrillo-Tripp and Feller 2005; Frischknecht and Frink 2006). Theoretical models are usually based on a mean-field approximation and focus on descriptions of the hydrocarbon chain conformations in a lattice or continuum representation. The headgroups are not treated explicitly; their contribution enters as a function of the lipid surface density. Interactions between the hydrophobic and hydrophilic parts are usually localized at the interface by setting an effective surface tension. These models allow calculation of the pressure distribution in the hydrocarbon chain region for lipid bilayers.

While theoretical models can consider such properties as the magnitude of surface tension, headgroup repulsion, length, and unsaturation of the hydrocarbon chains, they are still unable to cover the molecular details of the system. Computer simulations can supply an atomic level of detail and include all intermolecular interactions. Molecular dynamics (MD) simulations have been used to study lateral pressure profiles in lipid bilayers of varying composition, containing sterol alcohols (Griepernau and Bockmann 2008; Terama et al. 2008) and polyunsaturated hydrocarbon chains (Ollila et al. 2007a, b).

It should be mentioned that MD simulations, both of coarse-grained (CG) and atomistic models, also have been used to study the lateral pressure profiles in lipid monolayers (Baoukina et al. 2010).

Although calculation of pressure profiles itself is an important subject in biological studies, from another point of view it is important in analysis of different functions of mechanosensitive channels, geometric models of protein conformational equilibrium, and so on (Cantor 1999a, b; Anglin and Conboy 2008). In an interesting study, a 3D pressure profile was calculated by Ollila et al. (2009), and a position-dependent pressure distribution across the interface was obtained in bilayers with coexisting gel and liquid crystalline phases.

Lateral pressure profiles in lipid bilayers are significant because they may affect the function of proteins in cell lipid bilayer membranes (de Kruijff 1997). If the protein activity involves nonuniform changes in its cross-sectional area, then variations in the bilayer lateral pressure profile can shift the protein conformational equilibrium (Cantor 1997; Baoukina et al. 2010). Also, perturbations of bilayer lateral pressure induced by small amphiphilic solutes have been proposed as a mechanism of general anesthesia (Cantor 1997; Gruner and Shyamsunder 1991; Seddon and Templer 1995).

In the literature the subject of asymmetric lipid bilayers usually refers to bilayers that are constructed from different phospholipid molecule types (Bretscher 1972; Gurtovenko 2005).

In only a few studies are cases in which a difference between the number of phospholipids (i.e., density of phospholipids) in the two leaflets of the bilayer described as asymmetry in the membrane (e.g., Perozo and Rees 2003).

In this study we focus on the asymmetry resulting from different densities of phospholipids in each leaflet. The presence of additional phospholipids in one of the membrane's leaflets, which leads to having an asymmetric bilayer as a consequence, affects the pressure profile and the accompanying lateral pressure. Such physical effects may have profound biological consequences. In some interesting cases like liposome formation and gating of mechanosensitive membrane channels, it is very important to know the effect of asymmetric distribution of phospholipids on the mechanical properties of the lipid bilayer (Perozo and Rees 2003; Melzak et al. 2008; Liang et al. 2004). It should be explained that the structure of some biological systems like liposomes is based on the difference between the density of phospholipids in two leaflets. Thus, it is essential to investigate the effect of asymmetry of phospholipid density on the physical properties of the system. Moreover, it is important to know what will happen if some additional phospholipids insert in a monolayer that includes a membrane protein or binds with another type of proteins or peptides.

We propose that adding some phospholipids into one leaflet of the bilayer changes the pressure profile in the membrane and modulates the surface tension of each monolayer in an asymmetric way. One of the interesting observations of this study is that the change in phospholipid density in one leaflet affects the unperturbed leaflet as well. Our computational method for calculation of a pressure tensor is based on a computational procedure implemented on GROMACS as a modified version for computing a 3D pressure field (Ollila et al. 2009).

Materials and Methods

Various steps of the present work from system preparation to final properties calculations are illustrated below.

Step 1: Fine-Grained System Preparation

The GROMACS package was used for MD simulations (Berendsen et al. 1995). The equilibrated united-atom representation of POPC molecules in a planar bilayer arrangement was adopted as a membrane model in our fine-grained (FG) simulations (Kukol 2009). The solvated and neutralized system was composed of a bilayer normal to

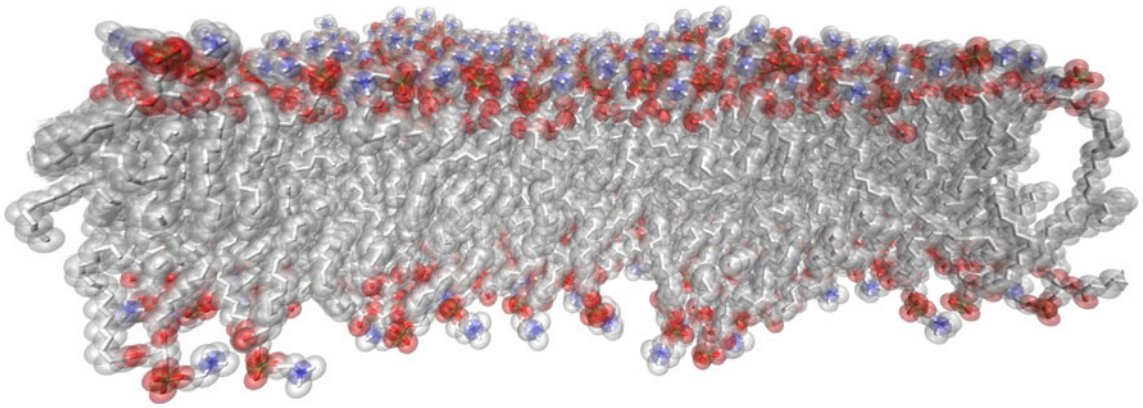

Fig. 1 POPC lipid membrane simulated with coarse-grained MARTINI force field

the z direction with 256 POPC molecules at the box center. At constant volume and temperature [number, volume, temperature (NVT), 300 K], a successive procedure of minimization and short-length MD simulation was employed in order to remove bad contacts and set up equilibrium atomic velocities, respectively. A final 30 ns of MD simulation was carried out under constant pressure and temperature [number, pressure, temperature (NPT), 1 bar and 300 K] to stabilize the predefined pressure and corresponding box volume. Water was modeled as a three-point molecule, while ffG53a6 force field parameters were used to model other constituents of the system. All simulations were performed on a dual quad core Xeon system with a clock speed of 2.4 GHz.

Step 2: Coarse-Grained MD Simulation

In order to characterize a near-realistic pressure field, it was necessary to convert the system to the CG configuration (Ollila et al. 2009). For the simulation, a CG MARTINI force field was used, along with a previously proposed CG simulation procedure (Marrink et al. 2004, 2007; Monticelli et al. 2008) (Fig. 1). Following energy minimization and short-length NVT simulation, the system was subjected to a 500 ns NPT equilibration (1 bar, 300 K). A 1 μs NPT simulation was performed in order to produce the required input data for the pressure distribution calculations. In all simulations, the CG time step was set to 20 fs. To evaluate the effect of the presence of some additional phospholipids on the membrane pressure field, five different system sizes were prepared using 256, 257, 258, 260 and 264 POPC molecules. The respective symmetric system with 256 functioned as the reference system. The size of the simulation box in the CG model with 256 phospholipids was 9.53 × 9.54 × 12.21 nm.

Step 3: Calculation of the 3D Pressure Field

A modified GROMACS version tailored for pressure field calculations was used along with the standard GROMACS version 4.5 to calculate the pressure profile and surface tension in the CG simulated systems (Ollila et al. 2009; Hess et al. 2008). Pressure calculations were based on virial pressure relations (Lindahl and Edholm 2000; Ollila et al. 2007a, b; Schofield and Henderson 1982; Goetz and Lipowsky 1998). The applied add-on to the GROMACS package uses the technique described in Lindahl and Edholm (2000) along with the Irving and Kirkwood (1950) convention of contour choice. Though the pressure and stress profile calculation for CG employs the Harasima (1958) convention, it has been shown that the contour choices of both Irving-Kirkwood and Harasima yield consistent results for planar bilayers (Perozo and Rees 2003; Sonne et al. 2005).

It should be mentioned, however, that the stress profile of monolayers and bilayer in these liquid phase systems is the negative of the calculated pressure profile.

Step 4: Surface Tension Calculations

The surface tension of a layer between z_1 and z_2 corresponding to the bottom and top heights, respectively, of either a bilayer or a monolayer can be calculated from the pressure tensor according to the formula

$$\gamma = -\int_{z_1}^{z_2} [P_{\mathrm{L}}(z) - P_{\mathrm{zz}}(z)]\mathrm{d}z$$

in which P_{zz} is the normal component of the pressure tensor, and P_{L} is the lateral pressure, which is equal to $(P_{xx} + P_{yy})/2$. The integrand of γ is traditionally referred to as the lateral pressure (Rowlinson and Widom 1982).

Step 5: Calculation of First Moment of Pressure

The first moment of the lateral pressure is related to the elastic properties between z_1 and z_2 via

$$c_0 k = \int_{z_1}^{z_2} (z - z_0)[P_L(z) - P_{zz}(z)]dz$$

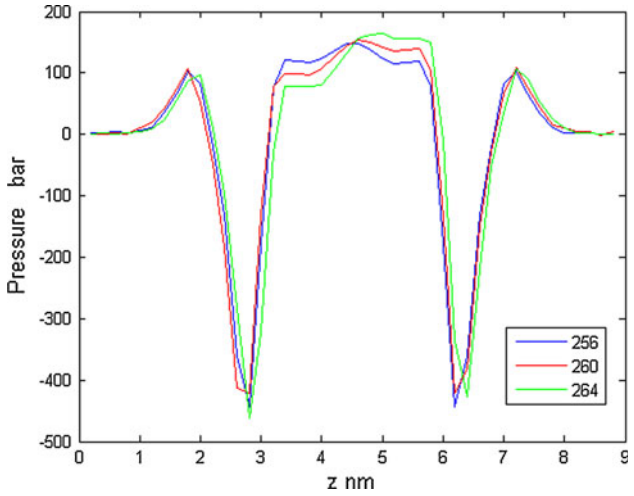

Fig. 2 Lateral pressure profile of lipid bilayer system comprising 256 phospholipids as the reference system and two developed systems including four and eight additional phospholipids in top leaflet. Changes of pressure are sensible for systems with four and eight POPC molecules

where c_0 denotes the spontaneous curvature with respect to a pivotal plane z_0 and k is the bending modulus (Safran 1994).

Results and Discussion

We studied the effect on the physical properties of a biological system when prototypes with properties exactly the same as the initial phospholipids are embedded in it. The reference system is a bilayer consisting of 256 POPC molecules. The physical properties were calculated four times, in four conditions: conditions in which one, two, four, and eight phospholipids were added, in that order, in the top monolayer. The results are presented below.

Pressure Field Profile of a Lipid Bilayer in the Presence of Additional Phospholipids in One of the Monolayers

The lateral pressure profile in a lipid membrane is the result of internal forces that act in the direction of the membrane plane in the different regions of the lipid bilayer. The integrated lateral pressure profile across the membrane, however, should vanish to ensure mechanical stability and satisfy the equilibrium condition. Nevertheless, the profile may display different behaviors in different regions in the membrane due to a variety of interactions whose relative

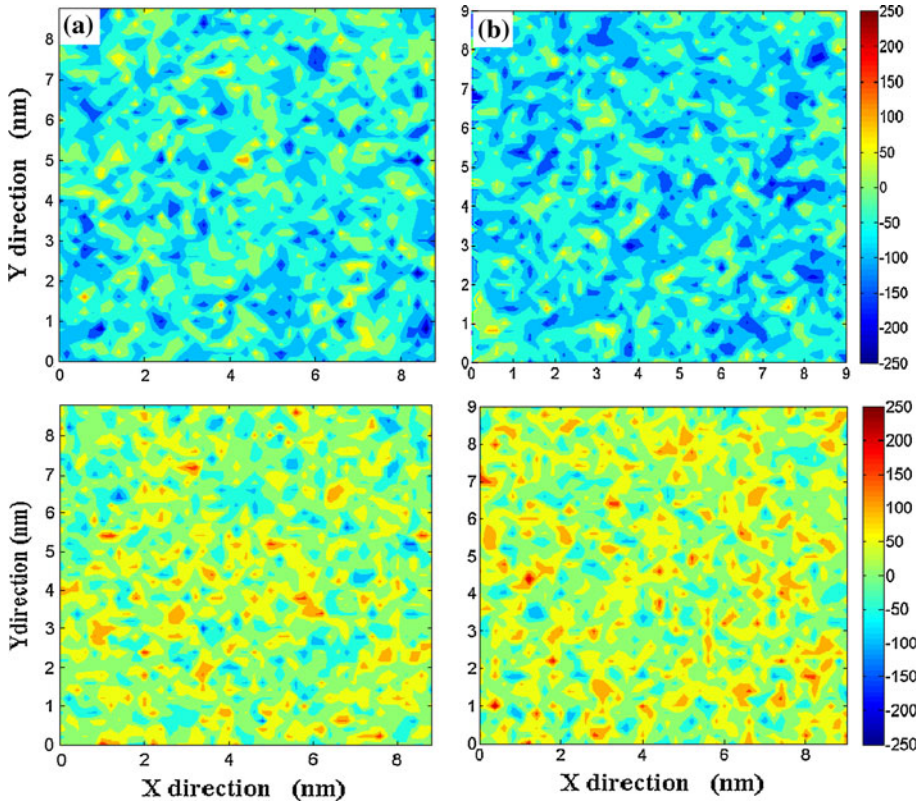

Fig. 3 Surface tension (mN/m) contour map for systems comprising 260 and 264 POPC molecules. *Top row* shows results for top leaflets, and *bottom row* shows results for bottom leaflets: **a** 260 POPCs, **b** 264 POPCs

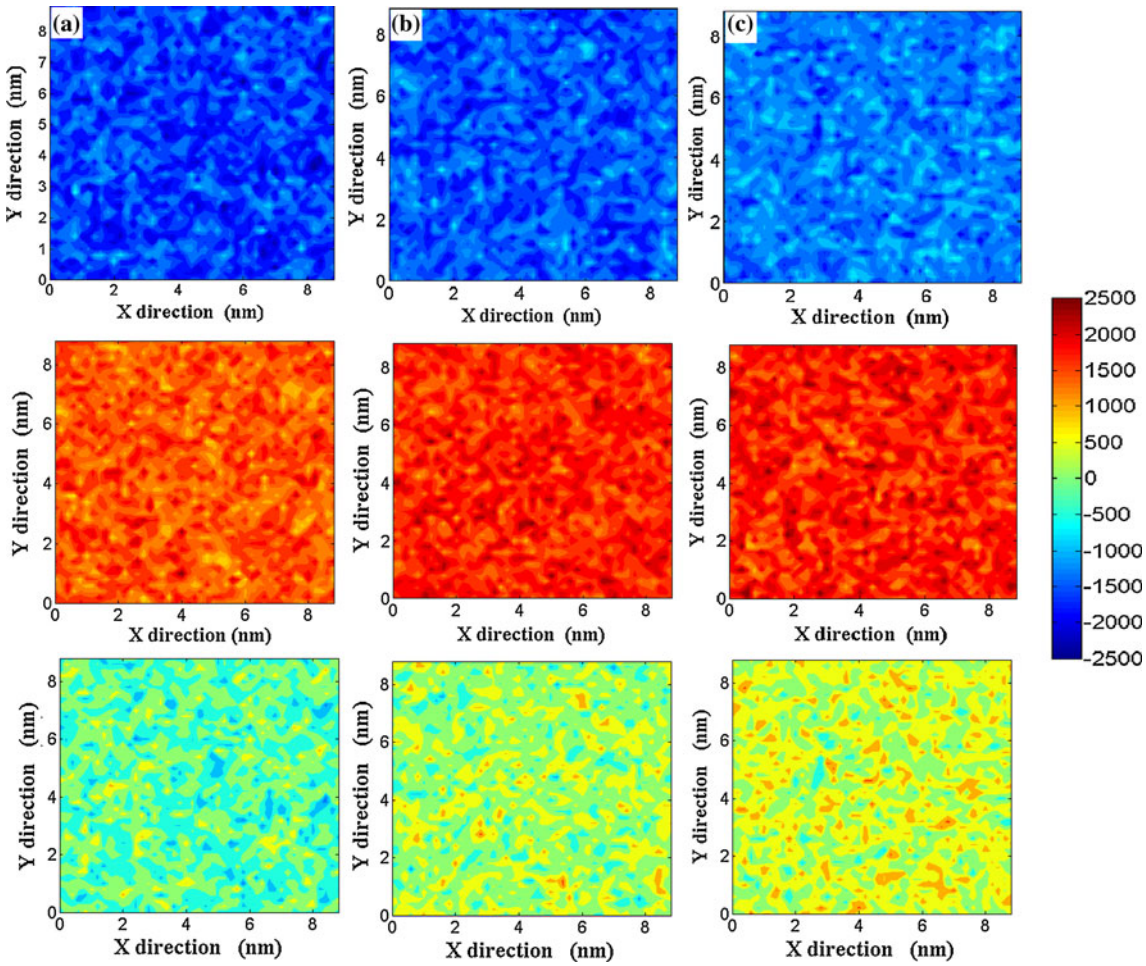

Fig. 4 Plot of first moment of lateral pressure (10^{-13} J/m) for simulated system comprising 256, 260 and 264 POPC–molecule phospholipids. *Top row* shows result for top leaflets, *middle row* shows results of bottom leaflets and *bottom row* shows results for the bilayers in each case: **a** 256, **b** 260 and **c** 264 POPCs

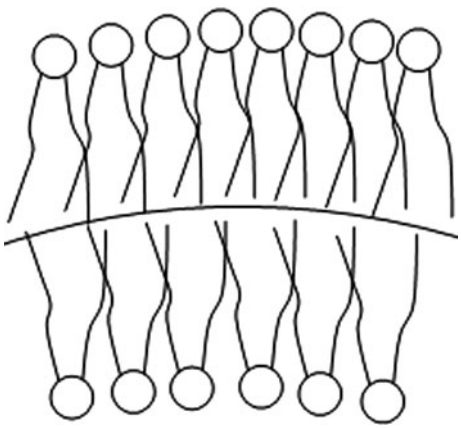

Fig. 5 The anticipated curvature of nanobiolipid membrane as a result of asymmetry in phospholipid density

importance varies across the membrane. Usually, the lateral pressure profile can be divided in three different parts: (1) a repulsive contribution in the hydrophilic headgroup region as a result of electrostatic and steric interactions and repulsion of hydration; (2) an attractive contribution from the interfacial energy between the water and the lipid phases, which works to minimize the surface area; and (3) a repulsive contribution inside the membrane originating from steric interactions between hydrophobic acyl chains (Israelachvili et al. 1980; Israelachvili 1985; Marsh 1996). Together these forces have been suggested to create a nonuniform lateral component of local pressure inside the lipid bilayer whose details may vary considerably from one system to another (Marsh 1996; Seddon and Templer 1995; Ollila et al. 2007a, b).

In this study, the pressure tensor was calculated for all CG simulated systems and the corresponding reference system. The lateral pressure profile for the reference system is symmetric and shows a similar trend, exhibiting a global maximum in the middle of the bilayer and a deep minimum around the middle of each leaflet (Fig. 2). In addition, two local maxima are present at the lipid–water interfaces.

Figure 2 also shows the corresponding lateral pressure profiles for the systems with four and eight additional

phospholipids. Clearly, the introduction of an extra POPC molecule leads to an increase in the lateral pressure within the corresponding leaflet and a decrease of that in the other leaflet. For systems with one and two additional phospholipids the variation in pressure is insignificant, but upon adding four and eight POPC molecules a change of pressure is clearly observed. Interestingly, in our case, the symmetry of the maximum in the middle of the bilayer is broken, which leads us to conclude that, based on what is observed in this phenomenon, the change in the lateral pressure profile is dissimilar for each monolayer.

Behavior of Surface Tension of the Bilayer Membrane's Different Leaflets in the Presence of Additional Phospholipids in One Leaflet

For all simulated systems the surface tension is zero, as predicted from the simulation situations: NPT ensemble with one bar reference pressure. The surface tension contour in the membrane plane is plotted for each of the bilayer leaflets for 260- and 264-POPC systems (Fig. 3). As is clearly seen, the surface tensions in the top and bottom monolayers in each case are equal in magnitude but have opposite singes. The top leaflets have a negative sign, and the bottom ones have a positive sign.

Behavior of First Moment of Lateral Pressure in the Presence of Additional Phospholipids in One of the Leaflets

Dissimilar lateral pressure in the bilayer leaflets results from changes in the contributing internal forces. The higher pressure in the top leaflet implies that this layer thermodynamically has a greater tendency to decrease the area with respect to the upper leaflet. As a consequence, spontaneous curvature is anticipated to emerge in the membrane. To quantify this phenomenon the first moment of lateral pressure was calculated (Fig. 4). This parameter gives the relation between lateral pressure and the elastic properties of the lipid membrane. Average values of first moment (kc_0) for 256-POPC for the top and bottom leaflets are $(-1{,}521.012 \pm 0.5) \times 10^{-13}$ and $(1{,}521.621 \pm 0.5) \times 10^{-13}$ J/m, respectively, whereas for 260-POPC the top and bottom leaflets are $(-1{,}413.26 \pm 0.5) \times 10^{-13}$ and $(1{,}778.76 \pm 0.5) \times 10^{-13}$ J/m. Finally, 264-POPC values for the top and bottom leaflets are $(-1{,}213.73 \pm 0.5) \times 10^{-13}$ and $(1{,}799.92 \pm 0.5) \times 10^{-13}$ J/m, respectively. The asymmetric behavior of different monolayers is observable as a result of the presence of additional phospholipids in the top leaflet. Experimental values for k for different lipid bilayers vary in the range of $(0.1–6) \times 10^{-19}$ J (Marsh 2006). In the presence of additional phospholipids, using experimental lower and upper values of k for bilayer, the spontaneous curvatures, c_0, varies between 0.04433 and 2.6 nm^{-1} for 260-POPC and between 0.07666 and 4.6 nm^{-1} for 264-POPC bilayer. In real membranes the spontaneous curvature parameter would lead to a curved membrane surface and/or a redistribution of lipids between the two leaflets. The employed periodic boundary condition prevents the anticipated curvature from being fully observed. The anticipated curvature of asymmetric lipid bilayer may be imagined as shown in Fig. 5.

Conclusion

This work presents an approach to study the effect of additional phospholipid insertion in one leaflet of a lipid bilayer by computation of the mechanical properties of the membrane. A CG MD simulation was used to calculate the resulting lateral pressure, surface tension, and first moment of lateral pressure. The results of the CG MD and pressure tensor calculation show that the presence of additional phospholipids leads to an asymmetric modulation of the mechanical properties of the membrane. Also, it has been observed that the change in phospholipid density in one leaflet affects the unperturbed leaflet as well. This asymmetric behavior, which results from changes in the contribution of intermolecular forces, may lead to formal effects.

References

Anglin TC, Conboy JC (2008) Lateral pressure dependence of the phospholipid transmembrane diffusion rate in planar-supported lipid bilayers. Biophys J 95:186–193

Baoukina S, Marrink SJ, Tieleman DP (2010) Lateral pressure profiles in lipid monolayers. Faraday Discuss 144:393–409

Berendsen HJC, van der Spoel D, van Drunen R (1995) GROMACS: a message-passing parallel molecular dynamics implementation. J Comput Phys Commun 91:43–56

Bretscher MS (1972) Asymmetrical lipid bilayer structure for biological membranes. Nat N Biol 236:11–12

Canham PB (1970) The minimum energy of bending as a possible explanation of the biconcave shape of the human red blood cell. J Theor Biol 26:61–68

Cantor RS (1997) Lateral pressures in cell membranes: a mechanism for modulation of protein function. J Phys Chem B 101: 1723–1725

Cantor RS (1998) The lateral pressure profile in membranes: a physical mechanism of general anesthesia. Toxicol Lett 101: 451–458

Cantor RS (1999a) Lipid composition and the lateral pressure profile in bilayers. Biophys J 76:2625–2639

Cantor RS (1999b) The influence of membrane lateral pressures on simple geometric models of protein conformational equilibria. Chem Phys Lipids 101:45–56

Carrillo-Tripp M, Feller SE (2005) Evidence for a mechanism by which ω-3 polyunsaturated lipids may affect membrane protein function. J Biochem 44:10164–10169

de Kruijff B (1997) Lipids beyond the bilayer. Nature 386:129–130

Frank FC (1958) Liquid crystals. On the theory of liquid crystals. Discuss Faraday Soc 25:19–28

Frischknecht AL, Frink LJD (2006) Alcohols reduce lateral membrane pressures: predictions from molecular theory. Biophys J 91:4081–4090

Goetz R, Lipowsky R (1998) Computer simulation of bilayer membranes: self assembly and interfacial tension. J Chem Phys 108:7397–7409

Griepernau B, Bockmann RA (2008) The influence of 1-alkanols and external pressure on the lateral pressure profiles of lipid bilayers. Biophys J 95:5766–5778

Gruner SM, Shyamsunder E (1991) Is the mechanism of general anesthesia related to lipid membrane spontaneous curvature? Mol Cell Mech Alcohol Anesth 625:685–697

Gullingsrud J, Schulten K (2004) Lipid bilayer pressure profiles and mechanosensitive channel gating. Biophys J 86:3496–3509

Gurtovenko AA (2005) Asymmetry of lipid bilayers induced by monovalent salt: atomistic molecular dynamics study. J Chem Phys 122:244902

Harasima A (1958) Molecular theory of surface tension. Adv Chem Phys 1:203–212

Harries D, Benshaul A (1997) Conformational chain statistics in a model lipid bilayer: comparison between mean field and Monte Carlo calculations. J Chem Phys 106:1609–1619

Helfrich W (1973) Elastic properties of lipid bilayers: theory and possible experiments. Z Naturforsch C 28:693–703

Hess B, Kutzner C, van der Spoel D, Lindahl E (2008) GROMACS 4: algorithms for highly efficient, load-balanced, and scalable molecular simulation. J Chem Theory Comput 4:435–447

Irving JH, Kirkwood JG (1950) The statistical mechanical theory of transport processes IV. The equations of hydrodynamics. J Chem Phys 18:817–824

Israelachvili JN (1985) Intermolecular and surface forces. Academic, New York

Israelachvili JN, Marcelja S, Horn RG (1980) Physical principles of membrane organization. Q Rev Biophys 13:121–200

Kukol A (2009) Lipid models for united-atom molecular dynamics simulations of proteins. J Chem Theory Comput 5:615–626

Liang X, Mao G, Simon KY (2004) Mechanical properties and stability measurement of cholesterol-containing liposome on mica by atomic force microscopy. J Colloid Interface Sci 278:53–62

Lindahl E, Edholm O (2000) Spatial and energetic-entropic decomposition of surface tension in lipid bilayers from molecular dynamics simulations. J Chem Phys 113:3882–3892

Lipowsky R, Grotehans S (1994) Renormalization of hydration forces by collective protrusion modes. Biophys Chem 49:27–42

Marrink SJ, de Vries AH, Mark AE (2004) Coarse grained model for semiquantitative lipid simulations. J Phys Chem B 108:750

Marrink SJ, Risselada HJ, Yefimov S, Tieleman DP, de Vries AH (2007) The MARTINI force field: coarse grained model for biomolecular simulations. J Phys Chem B 111:7812–7824

Marsh D (1996) Lateral pressure in membranes. Biochem Biophys Acta 1286:183–223

Marsh D (2006) Elastic curvature constants of lipid monolayers and bilayers. Chem Phys Lipids 144:146–159

Melzak KA, Bender F, Tsortos A, Gizeli E (2008) Probing mechanical properties of liposomes using acoustic sensors. Langmuir 24:9172–9180

Monticelli L, Kandasamy SK, Periole X, Larson RG, Tieleman DP, Marrink SJ (2008) The MARTINI coarse-grained force field: extension to proteins. J Chem Theory Comput 4:819–834

Mukhin SI, Baoukina S (2005) Analytical derivation of thermodynamic characteristics of lipid bilayer from a flexible string model. Phys Rev E Stat Nonlinear Soft Matter Phys 71:061918

Ollila S, Hyvönen MT, Vattulainen I (2007a) Polyunsaturation in lipid membranes—dynamic properties and lateral pressure profiles. J Phys Chem B 111:3139–3150

Ollila S, Rog T, Karttunen M, Vattulainen I (2007b) Role of sterol type on lateral pressure profiles of lipid membranes affecting membrane protein functionality: comparison between cholesterol, desmosterol, 7-dehydrocholesterol and ketosterol. J Struct Biol 159:311–323

Ollila OHS, Risselada HJ, Louhivuori H, Lindahl E, Vattulainen I, Marrink SJ (2009) 3D pressure field in lipid membranes and membrane–protein complexes. Phys Rev Lett 102:078101

Patra M (2005) Lateral pressure profiles in cholesterol-DPPC bilayers. Eur Biophys J Biophys Lett 35:79–88

Perozo E, Rees DC (2003) Structure and mechanism in prokaryotic mechanosensitive channels. Curr Opin Struct Biol 13:432–442

Rowlinson JS, Widom B (1982) Molecular theory of capillarity. Clarendon Press, Oxford

Safran SA (1994) Statistical thermodynamics of surfaces, interfaces, and membranes. Addison–Wesley, Reading

Schofield P, Henderson JR (1982) Statistical mechanics of inhomogeneous fluids. Proc R Soc Lond A Math Phys Sci 379:231–238

Seddon JM, Templer RH (1995) Structure and dynamics of membranes. Elsevier, Amsterdam, pp 97–160

Shillcock JC, Lipowsky R (2002) Equilibrium structure and lateral stress distribution of amphiphilic bilayers from dissipative particle dynamics simulations. J Chem Phys 117:5048–5061

Sonne J, Hansen FY, Peters GH (2005) Methodological problems in pressure profile calculations for lipid bilayers. J Chem Phys 122:124903

Szleifer I, Kramer D, Benshaul A, Gelbart WM, Safran SA (1990) Molecular theory of curvature elasticity in surfactant films. J Chem Phys 92:6800–6817

Terama E, Ollila S, Salonen E, Rowat AC, Trandum C, Westh P, Patra M, Karttunen M, Vattulainen I (2008) Distribution and dynamics of adamantanes in a lipid bilayer. J Phys Chem B 112:4131–4413

Venturoli M, Smit B (1999) Simulating the self-assembly of model membranes. Phys Chem Commun 10:45–49

Xiang TX, Anderson BD (1994) Molecular distributions in interphases: statistical mechanical theory combined with molecular dynamics simulation of a model lipid bilayer. Biophys J 66:561–572