# Mechanical properties of POPC lipid vesicle determined using molecular dynamics simulations

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Abstract

To describe behaviour and functions of lipid bilayers it is necessary to understand their mechanical nature. The elasticity of lipid bilayer is believed to play important role in cell functioning. Molecular dynamics simulations have been extensively used to investigate mechanics of a lipid bilayer, however, due to the computational limitations, those simulations have been usually calculated on flat patches of the membrane. Because those simulations did not account for the effect of curvature on lipid bilayer properties, we performed full-atomistic simulation of 20 nm in diameter POPC vesicle. The mechanical properties were determined using spherical harmonics analysis and Helfrich continuum model.

*Keywords: molecular dynamics, mechanical properties, lipid bilayer, POPC, bending rigidity coefficient*

## 1. Introduction

An essential part of any living cell - a lipid bilayer - serves as a scaffold for many biochemical processes. In order to understand its complex behaviour it is necessary to quantitate precisely its physical properties including, often overlooked, mechanics. The lipid bilayer elasticity is believed to play an important role in cell functioning impacting endomembrane trafficking within the cell volume. Furthermore complex dynamics of the lipid bilayer influences processes occurring in various time scales. Bending rigidity coefficient is a parameter defined as an energy cost required to bend the lipid bilayer. Due to its small value (from 20 up to 150 times of Boltzmann energy) it is impossible to measure it directly. To this end molecular dynamics (MD) simulations, among other methods, can be used to study membrane bending rigidity. Such analysis was successfully carried out on flat lipid bilayer systems with variety of analytical approaches [4]. Recently, MD simulations of lipid vesicles with sizes greater that 20 nm have been calculated using coarse-grained force fields [1]. However the use of coarse-grain approach limits the flexibility of modelled particles therefore introducing approximation, which may influence the outcome of the computational experiment. To address those issues, we present in this paper, and to our knowledge for the first time, an advanced mechanical analysis of full-atomic POPC lipid vesicle system.

## 2. MD Simulation and analysis

### *2.1. Molecular Dynamics*

The full-atomic simulations were performed using NAMD [5] program with CHARMM36 force field under NPT conditions. The 20 nm vesicle consists of 3637 united atom POPC lipid models (1521 lipids in inner leaflet and 2116 in outer one) [3] hydrated with 748344 TIP3P water molecules giving a final simulation box of 30 $nm^3$. Three dimensional periodic boundary conditions were applied in the simulations. Initial area per lipid (APL) was assumed to be in average 70 $Å^2$, which is slightly higher that reported literature values. APL was adapted in that manner accounting for the effect of vesicle's curvature. Specifically, the value of APL was set to be equal to 66.5 $Å^2$ and 73.5 $Å^2$ for inner and outer leaflets, respectively. The example of a modelled system is presented in Figure 1.

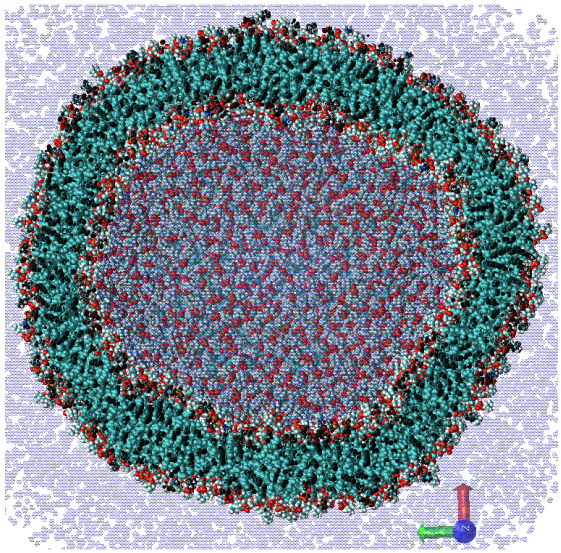


Figure 1: Snapshot from simulation of all-atom POPC vesicle system used for membrane mechanical properties analysis.

Simulations were analysed for the last 12 ns of the total 31 ns run. Six selected parameters were monitored including; vesicle radius, thickness of the lipid bilayer, and mean values and standard deviations of both inner and outer leaflet) in order to determine the optimal time for analysis starting point (Figure 2).

### *2.2. The determination of the bending rigidity coefficient.*

Mechanical analysis was performed using protocol from Braun and Sachs [1], which consists of three main stages. First,

This work was possible thanks to financial support from National Science Centre (grants numbers 2015/19/B/NZ7/02380 and 2016/21/N/NZ1/02767).
Calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl/en), grant No. 274

the location of each lipid was determined, using as a reference point the following; for the lipid head-group the location of the

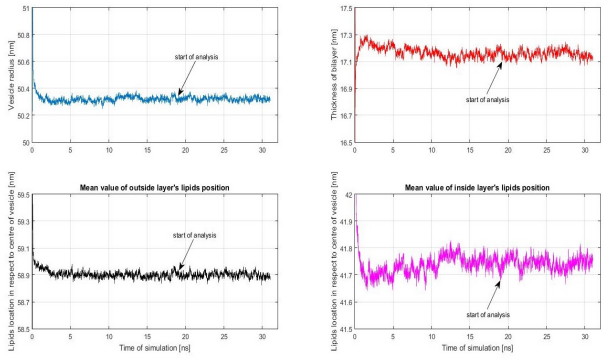
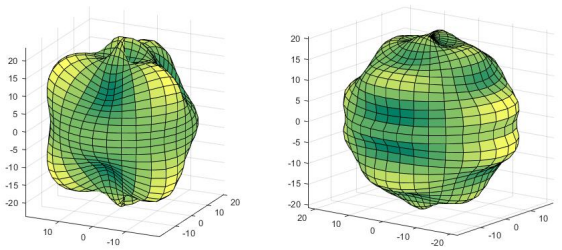



Figure 2: Selected four parameters used to determine the equilibrium state of a vesicle, ie. radius of vesicle, thickness of lipid bilayer and mean values of inner and outer bilayer leaflet.

phosphorus atom and for lipid tail - the mid-point of 16th carbon atoms in each of both tails. Next the Spherical Harmonics Analysis (SPHA) was performed in order to integrate parameters from the atomistic system with the Helfrich continuum model. Since spherical harmonics are standing waves on vesicle surface, it is possible to represent the surface as a linear combination of spherical harmonics with degree (l) and order (m). Figure 3 illustrates two examples of calculated wave patterns. The surface harmonics were determined based on Equation 1, where $a_{lm}$ are the spherical harmonic coefficients, angles θ and ϕ represents the position on the vesicle surface and $Y_{lm}$ are the spherical harmonics basis functions. Basis functions can be expressed as a matrix of Legendre polynomials *P*.

$$f(\theta,\varphi) = \sum_{l,m} a_{lm} Y_{lm} = \sum_{l,m} a_{lm} \overline{P}_l^m (cos\theta) e^{im\varphi} \tag{1}$$



l=4, m=2 l=8, n=2

Figure 3: Spherical Harmonics Analysis (SPHA) decomposes vesicle surface into a series of standing waves with degree (l) and order (m).

Obtained spherical harmonic coefficients were translated to mechanical properties using Helfrich continuum model for undulations on a sphere expressed by Equation 2, where $k_B$ is Boltzmann constant, $k_c$ is bending rigidity coefficient and T is temperature.

$$|a_{lm}|^2 = \frac{k_B T}{k_C[l^2(l+1)^2 - 2l(l+1)]} \tag{2}$$

## 3. Results and Discussion

Figure 4 shows the power spectra of squares of spherical harmonics coefficients fitted with the Helfrich continuum model as determined for POPC vesicle. The model was fitted to 45th mode. Obtained value of bending rigidity coefficient was equal to 17.8 times $k_BT$, which corresponds to $7.3 \cdot 10^{-20}$ J. This result agrees with literature data [2].

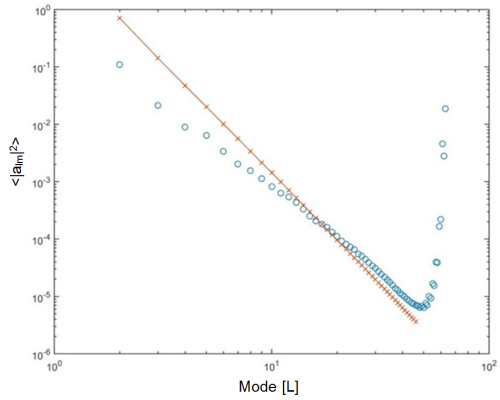



Figure 4: Power spectra of squares of spherical harmonic coefficient calculated for POPC vesicle fitted with $k_c$ model (Equation 2).

## 4. Conclusions

The simulation protocol for the determination of the bending rigidity coefficient for a coarse-grain system, using Helfrich equation, has been successfully tested on full atomistic system. The calculated value of he bending rigidity coefficient for DOPC vesicle agrees with these present in the literature Simulation of whole vesicle, instead of small 2D bilayer fragments, takes into account curvature effects and provide potentially more reliable results. Presented 3D simulation system opens the possibility to study the effect of the membrane asymmetry on its mechanical properties the possibility not available with 2D simulation system. Using atomistic molecular dynamics as a method to determine bending rigidity coefficient allows analysing furthermore other structural parameters such as bilayer thickness and area per lipid (in respect to outer and inner layer).

## References

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