Supplementary Information

Computer investigations of influences of molar fraction and acyl chain length of lipids on the nanoparticle-biomembrane interactions

Yang Li*
School of Biomedical Engineering, Tianjin Medical University
Tianjin 300070, P. R. China

1 Phospholipid molecules models

As the major component of biological membranes, two kinds of zwitterionic phosphatidylcholine (PC) lipids were used here, including dipalmitoyl-phosphatidylcholine (DSPC) and dipalmitoyl-phosphatidylcholine (DPPC). The acyl chain length of PCs ranges from 16 carbon atoms in DPPC to 18 carbon atoms in DSPC. In view of the relatively large length and time scales of the biological phenomenon in our simulations, MARTINI coarse grained (CG) force field was employed for the time effectiveness and its ability to reproduce experimental properties of various lipid dynamics and some kinds of polymer as well[1, 2, 3]. In the standard MARTINI model, both acyl chains of DSPC and DOPG lipids consists of five CG beads; the acyl chain of a DPPC lipids consists of four CG beads; one acyl chain of a POPG molecule consists of five CG beads, and the other acyl chain of a POPG consists of four CG beads (Figure 1). Force field parameters and further information on the CG phospholipid model can be found in the original paper of MARTINI force field[2].

2 Properties of two lipid bilayers

The DSPC/DOPG and DPPC/POPG lipid bilayer were modeled in the simulation for investigating the influence of acyl chain length of lipids on the perturbation of a NP on the membrane. Two mixed membranes were constructed with a same PC/PG mixed

*Corresponding author: liyang@tijmu.edu.cn

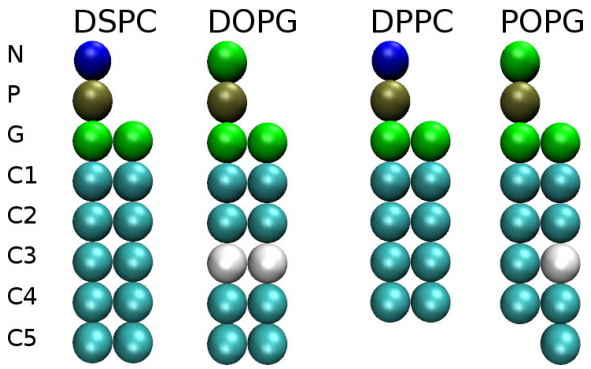

Figure 1: Coarse grained models of phospholipid molecules in MARTINI force field.

ratio 5:1. Some quantitative parameters, including the thickness of the membrane(Figure 2) and area per lipid (Figure 3), are listed in Table 1 as a comparison between the two bilayers of DSPC/DOPG and DPPC/POPG.

Table 1: Properties of two lipid bilayers

	DSPC/DOPG	DPPC/POPG
thickness (nm)	4.83 ± 0.03	4.07 ± 0.04
area per lipid (nm^2)	0.606 ± 0.010	0.632 ± 0.011

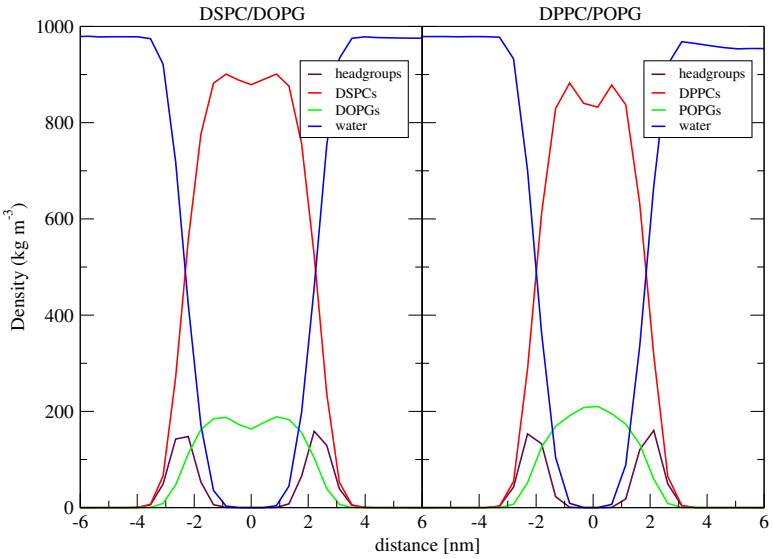

Figure 2: Projected density profiles in the x–z plane for different components in the DSPC/DOPG and DPPC/POPG membranes respectively.

In addition, the order parameter for lipid molecules were calculated as a measure of lipids packing (Figure 4). It is given by $S_{zz} = \frac{1}{2}\langle 3\cos^2\theta_i - 1\rangle_i$, where θ_i is the tilt angle between the bilayer normal (lying along the z direction) and the molecular axis which connects the neighboring atoms $i-1$ and $i+1$, and $\langle\cdot\rangle_i$ denotes an average over all of the atoms in the lipid. The extremum values of S_{zz} are 1 and -0.5, corresponding to a perfectly ordered state and a conformation perpendicular to the membrane normal,

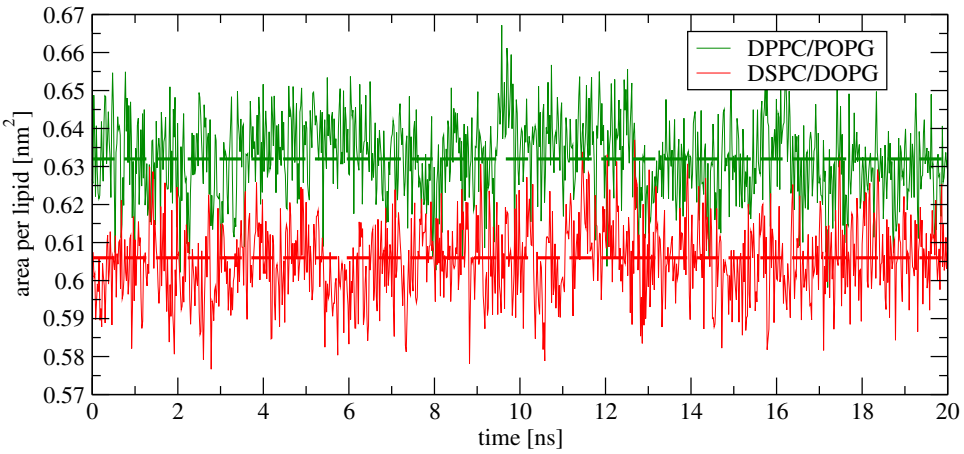

Figure 3: Area per lipid of the DSPC/DOPG and DPPC/POPG membranes.

respectively, and lack of order is characterized by $S_{zz} = 0$[4]. These structural parameters of the lipid bilayer mentioned above were obtained from the equilibrium stage of the trajectory.

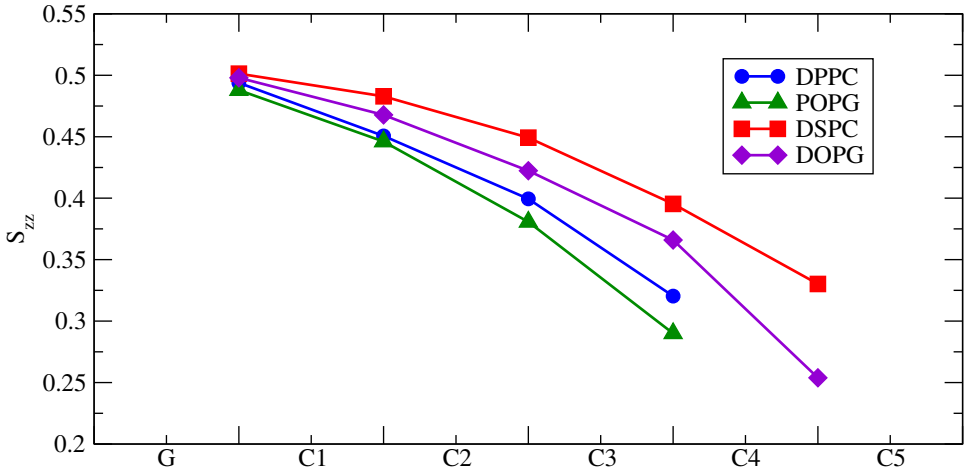

Figure 4: Order parameters of DSPC, DOPG, DPPC, and POPG lipid molecules.

3 Umbrella sampling windows

Umbrella sampling approach was employed to obtain the potential of mean force (PMF) as a energetic function of moving a POPG lipids cluster along the normal direction of the membrane to the water. A series of separate biased simulations were performed for 6 ns per simulation window in which the headgroups of lipids were restrained to a given distance from the center of the bilayer by a harmonic restraint on the z-coordinate only. The force constant of 2500 kJ mol^{-1} nm^{-2} was used with a spacing of 0.1 nm between the centers of the biasing potentials to ensure the overlapping of the z histograms between adjacent umbrella sampling windows. Overlapping of the z histograms between adjacent umbrella sampling windows for different pulled lipids clusters are shown as follow.

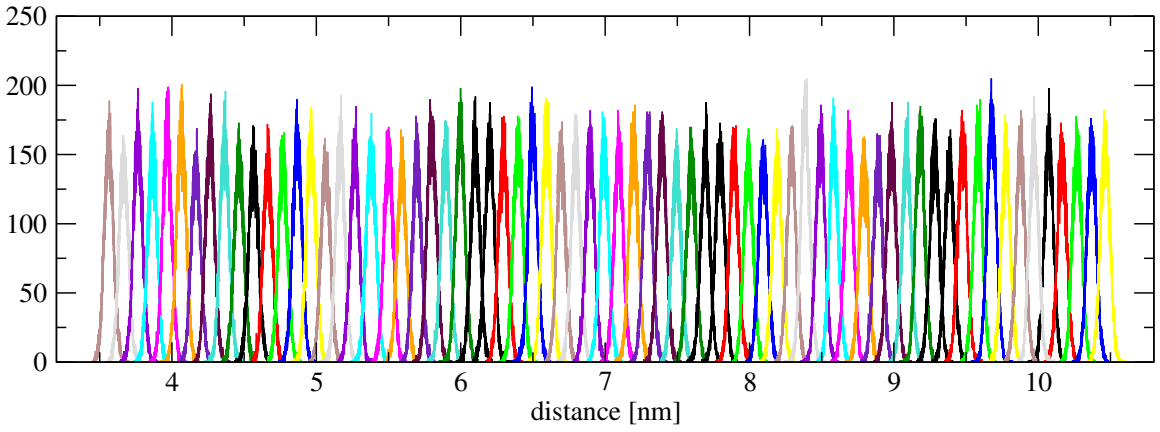

Figure 5: Overlapping of the z histograms between adjacent umbrella sampling windows for the PMF of one pulled lipid.

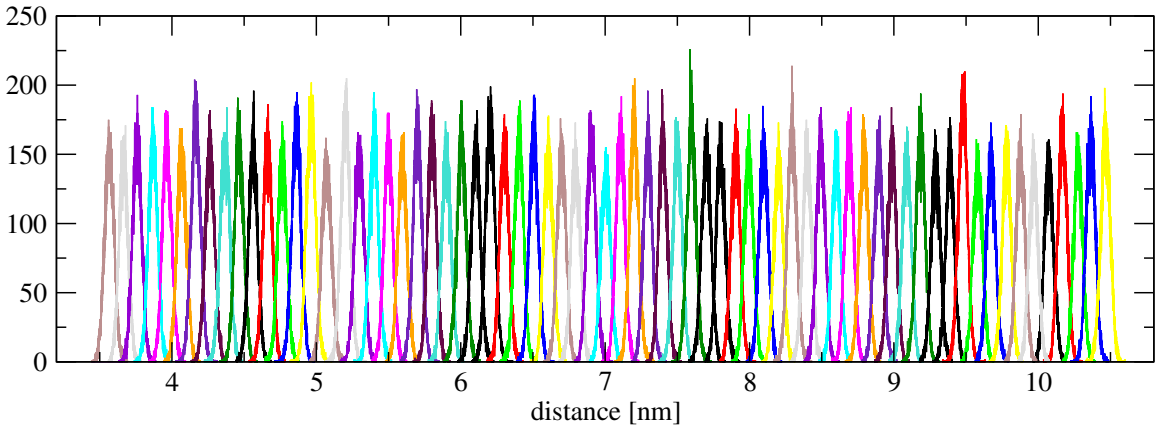

Figure 6: Overlapping of the z histograms between adjacent umbrella sampling windows for the PMF of 3 pulled lipids.

References

[1] Siewert J. Marrink, Alex H. de Vries, and Alan E. Mark. Coarse grained model for semiquantitative lipid simulations. *J Phys Chem B*, 108(2):750–760, 2004.

[2] Siewert J. Marrink, H. Jelger Risselada, Serge Yefimov, D. Peter Tieleman, and Alex H. de Vries. The martini force field: coarse grained model for biomolecular simulations. *J Phys Chem B*, 111(27):7812–7824, 2007.

[3] Siewert J. Marrink and D Peter Tieleman. Perspective on the martini model. *Chem. Soc. Rev.*, 42(16):6801–6822, Aug 2013.

[4] Yang Li and Ning Gu. Thermodynamics of charged nanoparticle adsorption on charge-neutral membranes: a simulation study. *J. Phys. Chem. B*, 114(8):2749–2754, Mar 2010.