Electronic Supplementary Material (ESI) for Nanoscale.

The Aggregation of Striped Nanoparticles in Mixed Bilayers - Supplementary Information

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Computing the Line Tension (γ) between the Phases of the Mixed Bilayer

To measure the effects of the interaction between the NP and the bilayer composition, we have utilized the decomposition of the the stress tensor contributions. Previous studies into the effect of NPs on the line tension in mixed bilayers were limited to hydrophobic NPS - *dissipative particle dynamics* (DPD) studies by Cheung[1] showed that hydrophobic NPs can ease the line tension between the demixed phases. However, such a decomposition is not unique in general, leading to an ambiguity in the definition of the stress tensor, particularly for multibody potentials. While some bulk mechanical properties of the membrane can readily be obtained experimentally or computationally, such as the area, compressability or the bending elastic moduli, other important mechanical features, such as the stress state within the bilayer or in the vicinity of an inclusion, are not as easily accessible. The stress contributions were calculated by averaging over a n $\times$ n grid of the simulation box, and the contribution from the lipid components were isolated. The stress tensor calculation used the *Irving-Kirkwood-Noll* (IKN) Theory, which implements the decomposition of the forces on molecular species inside the bilayer through a *central force decomposition* (CFD) approach.[2,3] The direct appli-

cation of the point-wise stress requires a well-sampled system. This is a requirement which by definition, cannot be obtained by molecular simulation techniques. However, Hardy used a time-dependent approach to calculate the stress tensor. Despite the clear issues regarding the methodology, this method remains the most robust way to measure the normal and shear stress imposed upon and by the lipid and other heterogeneous components within this mixed bilayer system. Each *gridmesh* style stress tensor can be divided into the following contributions of each MARTINI CG atom:

$$\sigma(x) = \sigma^K(x) + \sigma^V(x) \tag{1}$$

$$\sigma^K(x) = -\frac{1}{N_T}\sum_{i=1}^{N_T}\left[\sum_{\alpha} m^\alpha w(x; r_i^\alpha - x) v_i^\alpha \otimes v_i^\alpha\right] \tag{2}$$

$$\sigma^V(x) = \frac{1}{2N_T}\sum_{i=1}^{N_T}\left[\sum_{\alpha,\beta(\neq\alpha)} f_i^{\alpha\beta} \otimes r_i^{\alpha\beta} B(x; r_i^\alpha, r_i^\beta)\right] \tag{3}$$

Where m^α, r^α, v_i^α and $f_i^{\alpha\beta}$ represents the masses, positions, velocities and the pairwise forces of CG beads α and β for each time step i, respectively, over the total number of time steps N_T. $w(x; y)$ represents a weighted spatial distribution function. From the expression of the Hardy stress tensor, it is possible to measure the virial form of stress and therefore, the total pressure inside the molecular system. By visualising the bilayer and the line tension contribution together, we can estimate the effect on the raft interface. To estimate the line tension (γ) in this simulation, we computed the stress tensors in the lateral (x, y) and normal (y) planes to the bilayer. From this, the lateral pressure term can be denoted as:

$$P_L = (-\sigma_{xx} + \sigma_{yy})/2 \tag{4}$$

while the pressure normal to the bilayer plane can be represented as:

$$P_N = -\sigma_{zz} \tag{5}$$

Hence, from these values, γ is computed as:

$$\gamma = \frac{1}{2}(P_N - P_L)L_z L_{par} \tag{6}$$

The normal and lateral stress contributions were decomposed into the contributions from the following sources - velocity, electrostatic (coulombic), VdW, angles and bond potentials. In the MARTINI forcefield, the dihedral component is under the CG procedure. To effectively estimate the line tension, each stress tensor component was averaged over the domain interface tangent plane and the difference near the domain boundary was measured the effective line tension.

Cholesterol absent DPPC-4NP simulation

To establish the aggregating properties of NPs in the absence of the cholesterol, we ran an additional 5 μs simulation with a 30 $\times$ 30 nm^2 DPPC bilayer with 4 NPs. The snapshots of the simulation are shown in Figure S1. The average length of the DPPC molecules around the NPs is shown in Figure S2.

Equilibrium properties

To establish that we have reached equilibrium regarding the mixed bilayers, we measured the following parameters - the volume (V), pressure (P), energy (E) and the temperature (T) of the simulations. This is shown in Figure S3.

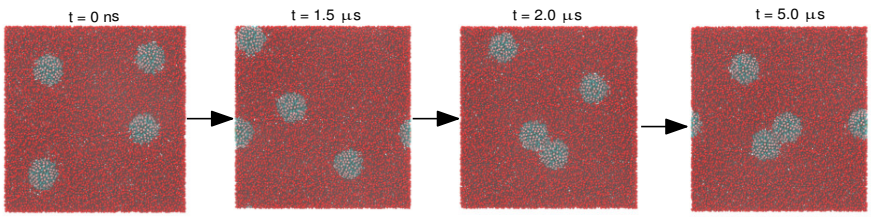

Figure S1: Simulation snapshots of the cholesterol-absent DPPC simulations with 4 NPs over 5 μs

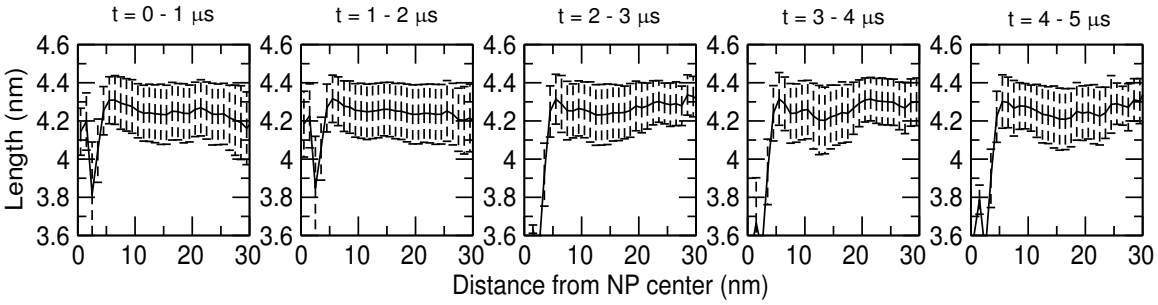

Figure S2: Averaged thickness of DPPC around the cholesterol-absent DPPC simulations with 4 NPs over 5 μs

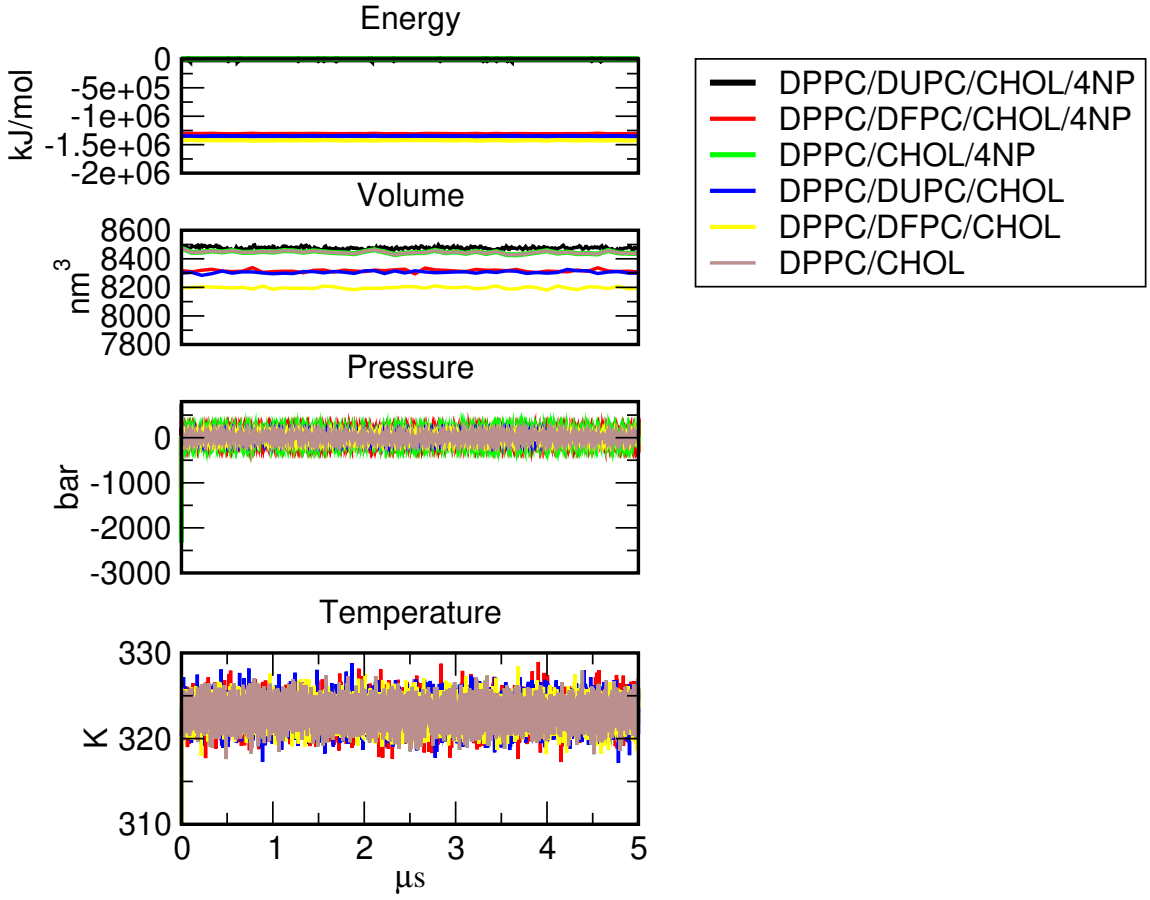

Figure S3: Measurements of the Energy, Volume, Pressure and Temperature over 5 μs

NP-absent Simulations

Figure S4 shows the snapshots of the NP-absent simulations over 5 μs simulation time.

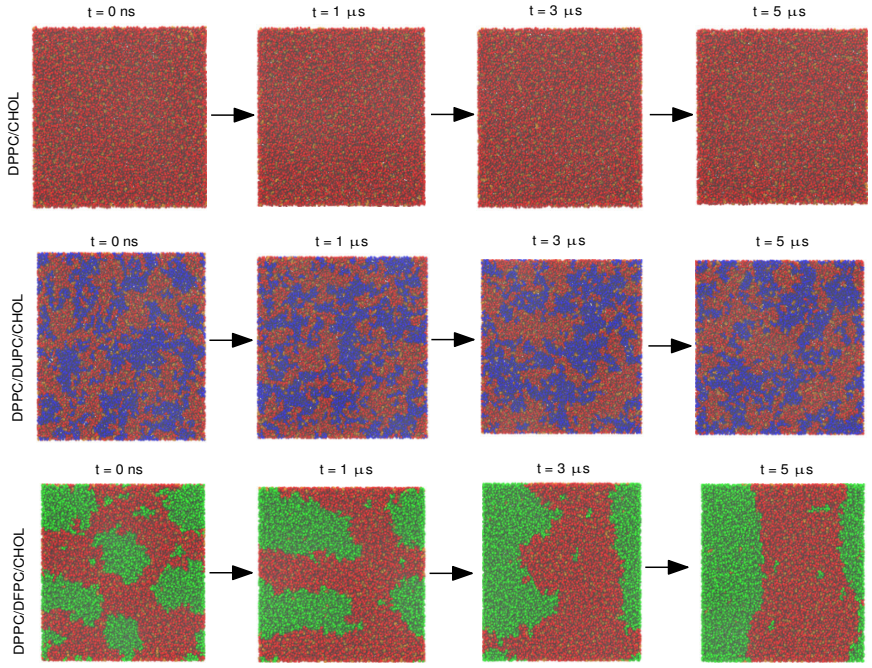

Figure S4: Snapshots of the simulations runs over 5 μs, for the DPPC/CHOL, DPPC/DUPC/CHOL and DPPC/DFPC/CHOL for the 30 $\times$ 30 nm^2 simulations

NP Topology Files

All GROMACS compatible files regarding the NP and its topology is included here: Striped NP topology

References

(1) Cheung, D. Aggregation of nanoparticles on one and two-component bilayer membranes. *Journal of Chemical Physics* **2014**, *141*, 194908.

(2) Vanegas, J. M.; Torres-Sànchez, A.; Arroyo, M. Importance of Force Decomposition for Local Stress Calculations in Biomembrane Molecular Simulations. *J. Chem. Theory Comput.* **2014**, *10*, 691 – 702.

(3) Torres-Sànchez, A.; Vanegas, J. M.; Arroyo, M. Examining the Mechanical Equilibrium of Microscopic Stresses in Molecular Simulations. *Phys. Rev. Lett.* **2015**, *114*, 258102.