Dissipative particle dynamics (DPD) simulation of a lipid bilayer

Introduction to computer simulation, Spring 2010

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Introduction

In this project dissipative particle dynamics (DPD) simulations will be performed in order to model a single component lipid bilayer in water. The simulated lipids will have various designs. From the simulations structural information on the lipids and the entire lipids bilayer is obtained as well as the surface tension of the lipid bilayer is measured and interpreted.

DPD simulation specifications

All the simulations in this project are performed in a simulation box of size $(32r_0)^3$, r_0 being the diameter of the simulation beads. The simulations consists of 20,000 time points, but since the system has to equilibrate the first 10,000 points are discarded (in this period the temperature reaches a defined value of 1), and only the last 10,000 time points are used in the analysis. During this period an average value is obtained every 100 time points to get a total of 100 independent points that are finally used to obtain a single average number. The integration time for the last 10,000 time points is 0.01.

Three different kinds of beads are defined; water beads (W), head beads (H) and tail beads (T). The two latter ones are used to construct lipid molecules as described in the subsections below. The dissipative force parameter is set to $\gamma_{ij}=4.5\sqrt{m_0 k_B T/r_0^2}$ between bead i and j independent of the kind of beads. The dissipative force parameter also sets the random force parameter ζ_{ij} because of their interconnectivity (see Groot & Warren). The conservative force parameter a_{ij} between identical beads are 30 for H-H, 10 for T-T and 25 for W-W (all in units of k_BT/r_0^2). Between different kinds of beads the repulsions are larger; between H and W it is only slightly larger ($35k_BT/r_0^2$), increasing to $50k_BT/r_0^2$ between H and T, and the largest repulsion is between W and T ($75k_BT/r_0^2$) to mimic the different degrees of hydrophobicity of the beads.

In the lipids the preferred bond lengths are all $0.5r_0$ independent of the type of beads connected, and the bond constant (Hookean spring constant) is set to 128 for all bonds. The preferred angle between the bonds is 0°, while the bending stiffness is 15.

The density of beads per square unit volume is $\rho r_0^3=3$. This number is used together with the box size to determine the number of lipids in the simulation and the fraction of lipid molecules and water beads in the simulation. For a bilayer oriented along the z-axis with box lengths L_x, L_y and L_z (in units of r_0) the number of lipids, N_L, is given by:

$$N_L = 2\frac{L_x L_y}{A/N}$$

A/N being the required projected area per lipid molecule in the initial state, and the factor 2 coming from the fact that there are two lipid leaflets in a bilayer. The fraction of lipid molecules is then given by:

$$Fraction\ of\ lipids = \frac{n_w N_L}{\rho L_x L_y L_z + N_L(n_w - n_L)}$$

n_w and n_L are the number of beads in the water "molecules" (this is 1) and the lipid molecules (this depends on the design of the lipid), respectively.

I would like to apologize for the lack of consistency in the use of units.

Linear lipids

First, a lipid bilayer composed of a short chained linear lipid (DLPC; 12 carbons) and a long chained linear lipid (DSPC; 18 carbons) is compared. Each bead in DPD typically represents 3-4 chemical groups. In this problem the acyl chain with 12 carbons will be represented by 4 T, while the 18 carbon chain will be represented by 6 T. In this way the ratio of the number of carbons versus the number of beads is kept constant. The head groups are the same in the two systems and will be represented by 3 H. The T chains are associated with different H adjacent to each other, giving the following structures; H-HT_4-HT_4 ($H_3[T_4]_2$) and H-HT_6-HT_6 ($H_3[T_6]_2$). A number of water molecules will be represented by a single W (this means e.g. that hydrogen bond are not specifically allowed). A schematic representation of the simulated molecules is shown in Figure 1.

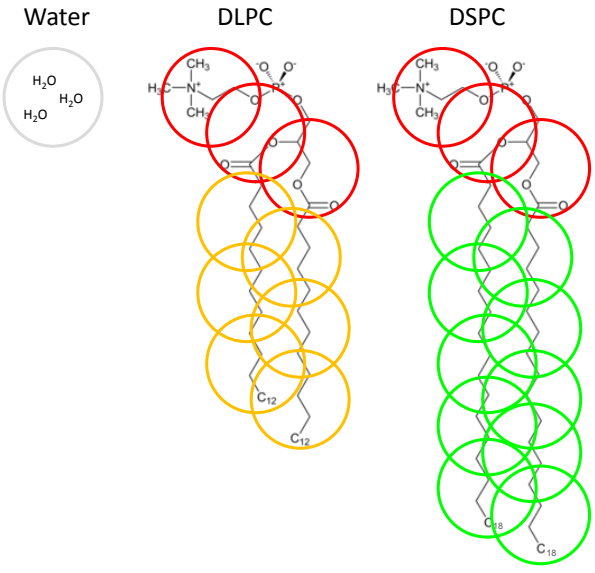

Figure 1. Bead representation of simulated lipids. Schematic representation of the molecules in the simulation modeling DLPC ($H_3(T_4)_2$) and DSPC ($H_3(T_6)_2$) lipid bilayers in water.

Representative examples of bilayers consisting of 1638 $H_3[T_4]_2$ lipids (left) and 1556 $H_3[T_6]_2$ (right) lipids are shown in Figure 2.

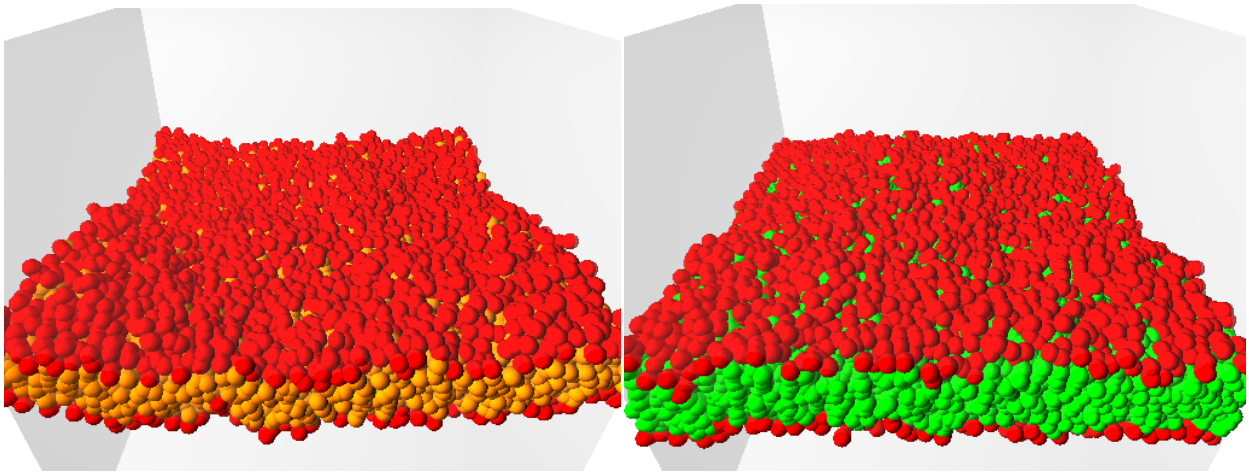

Figure 2. Bilayer snapshots. Snapshots of bilayers containing 1638 $H_3[T_4]_2$ lipids (left) and 1556 $H_3[T_6]_2$ lipids (right), at their zero surface tension points.

For DLPC the projected area per lipid molecule is A/Nr_0^2=1.25 making the bilayer close to the tension-free state with $\sigma r_0^2/k_bT$=0.015511+/-1.788928. The lipid end-to-end length is 2.599883r_0+/-0.00884r_0, while the lipid bilayer thickness is 3.684574r_0+/-0.01082r_0.

The surface tension of the DSPC bilayer is also close to zero; $\sigma r_0^2/k_bT$=0.06852+/-1.518054, however, the projected area per lipid molecule is A/Nr_0^2=1.316407. The lipid end-to-end length is 3.520996r_0+/-0.010982r_0, whereas the lipid bilayer thickness is 4.889799r_0+/-0.0008626r_0.

The relatively high error bars for surface tension reflects the variance in the 100 measurements between time point 10,000 and 20,000. The fact that the lipid end-to-end lengths are significantly more than half the total bilayer thickness is a bit surprising, since we are at the zero surface tension point, but it must somehow reflect that the lipids from the different leaflets overlap in the hydrophobic core of the membrane, or that the lipids are tilted in the membrane. The DSPC membrane in Figure 2 (right) is quite planar as expected, whereas the DLPC membrane seems to wobble a bit. This is unexpected because of the zero surface tension.

In Figure 3 the surface tension as a function of the area per lipid in the simulations is plotted.

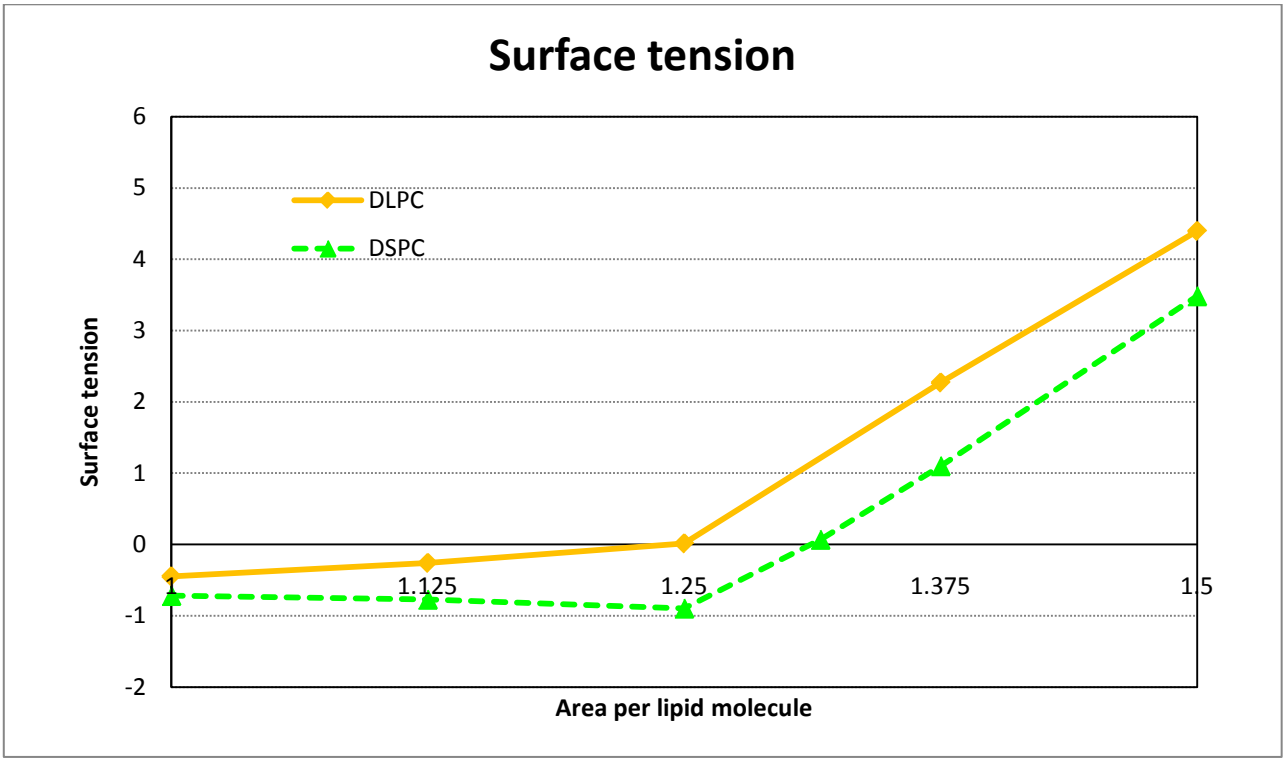

Figure 3. Surface tension as a function of the projected area per lipid. The DLPC molecule data is plotted in solid orange (squared points), whilst the DSPC lipid data is plotted as a dotted green line (triangular points).

The preferred area per lipid is at the zero surface tension point where there is no stress in the membrane. By adding more lipids (lower area per lipid) the membrane loses its planar structure and start to fluctuate as shown for DLPC at $A/Nr_0^2=1$ in Figure 4. For fewer lipids (higher area per lipid) the packing becomes less dense and the surface tension builds up until at certain point, where a hole will be created in the membrane. This point was however not reached in these simulations.

For a certain surface tension the area per molecule is larger for the longer acyl chained lipid. This is in direct contradiction to previously published data by Shillcock & Lipowitz. Since the hydrophobic force is more pronounced for the longer chains it would be expected that these lipids where more closely packed and thereby would have a lower area per lipid compared to the shorter tailed lipid, which would have a greater tendency for the tail to move closer to the head groups creating a larger area per lipid for a certain surface tension. The results are therefore surprising and the reason for the discrepancy would have to be investigated further. By the things differing among the simulations are some of the force parameters and the time of the simulation.

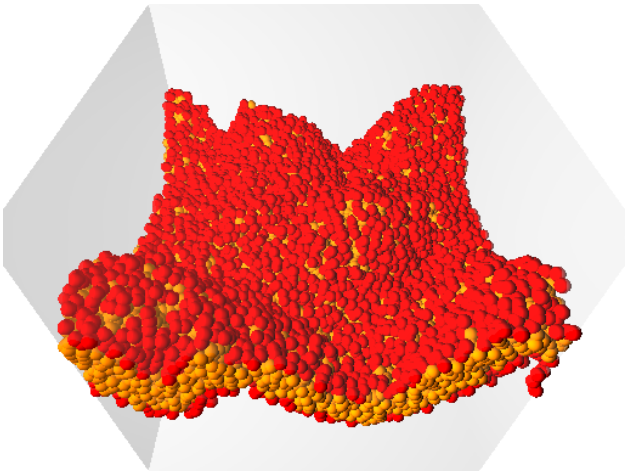

Figure 4. DLPC membrane at A/Nr_0^2=1. The lipids are so closely packed, that the membrane starts to wobble.

When the A/N is increased the lipid end-to-end distance varies only a little (data not shown), because the lipid is linearly stretched. The bilayer thickness, however, decreases for increased A/N () since the lipids now are allowed more space and does not need to be oriented along the z-axis.

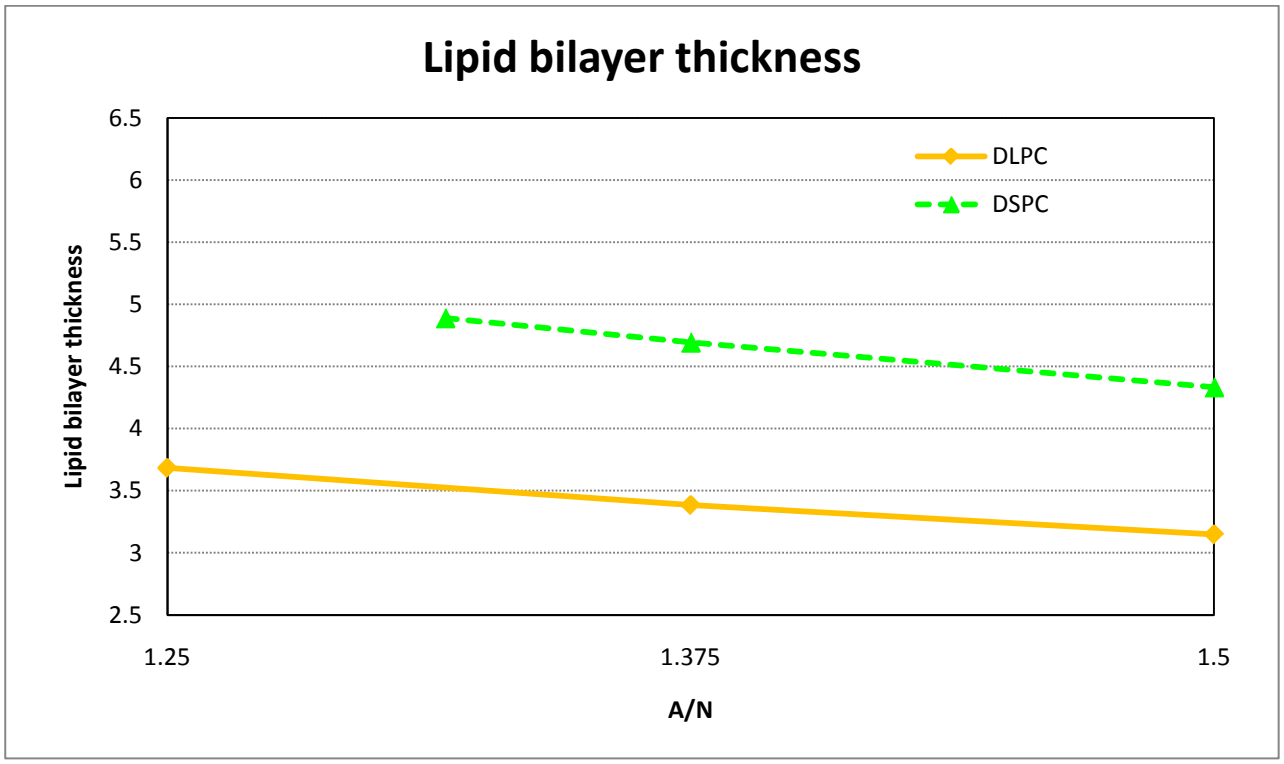

Figure 5. Lipid bilayer thickness as a function of the projected area per lipid. Data for the DLPC membrane is plotted in solid orange (squared points), while the DSPC membrane is plotted as a dotted green line (triangular points). Only the data with non-negative surface tension is plotted.

Non-linear lipids and increased lipid head repulsion

It is now investigated what influence increased H-to-H repulsion and a kink in one of the acyl chains has on the lipid bilayer. The increased repulsion would mimic a negative charge in the lipid head group, while the

kink would correspond to a double bond in one acyl chains. The head group repulsion is just simulated by increasing the conservative force parameter to 40 instead of 30. The kink is created by defining a new tail bead T_{kink} which has the same force parameters as T, but with a preferred angle between adjacent bonds of 60°. The lipid is designed such that the kink is at the very end of the lipid tail; $H\text{-}HT_4\text{-}HT_2\text{-}T_{kink}\text{-}T$, where the 60° angle is defined for the bonds $T\text{-}T_{kink}\text{-}T$. Other designs could give the same final lipid.

The perturbations are only run for a 4 T lipid and only at an area per lipid of $1.25r_0$, which was the zero tension point without kink or increased head repulsion. The influence of the changes on the surface tension, the lipid end-to-end length and the bilayer thickness are shown in Figure 6.

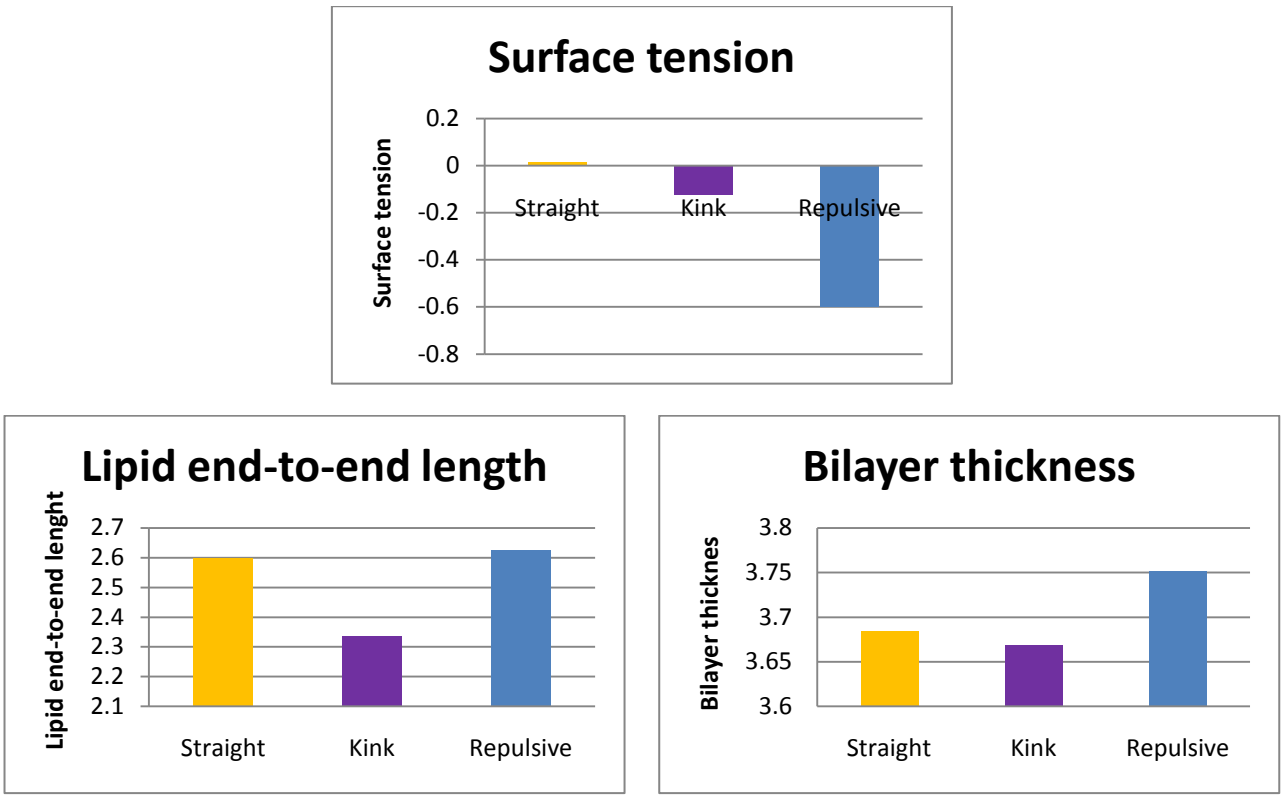

Figure 6 Data at A/Nr_0^2=1.25 for 4 bead tailed straight lipids, kinked lipids and lipids with increased head-to-head repulsion. Top: surface tension. Middle: Lipid end-to-end length. Bottom: Bilayer thickness.

The surface tension is slightly decreased for the kinked lipid, which would need a higher A/N to sustain the same surface pressure since the kink forces the lipid to take up more space. However, since the tail is short the effect is not that pronounced. The increased head-head repulsion forces the lipids further apart or here, as the area is held constant, decreases the surface tension.

The kink shortens the lipid end-to-end length, while it is not changed for increased head-to-head repulsion. Both results are expected.

The bilayer thickness increases slightly for the increased repulsion, but since the surface tension is negative and the membrane has started to fluctuate (not shown) this quantity is less well defined.

Conclusion

A bilayer of lipids of various kinds has been modeled. When comparing the influence of lengths of the lipid tails is was found in contradiction to previous results that the zero tension point was located at higher projected area per lipid molecule for longer tails. The reason for this has to be investigated further. When adding a kink in the lipid or increasing the head-to-head repulsion it was found that the surface tension was lowered for constant area per molecule. This was in agreement with the expectations.

Literature

1. Julian C. Shillcock & Reinhard Lipowsky, Equilibrium structure and lateral stress distribution of amphiphilic bilayers from dissipative particle dynamics simulations, Journal of Chemical Physics, 117, 10, 2002. (Shillcock & Lipowsky)
2. Robert D. Groot & Patrick B. Warren, Dissipative particle dynamics: Bridging the gap between atomistic and mesoscopic simulation, Journal of Chemical Physics, 107, 11, 1997. (Groot & Warren)