

GROMACS Coarse-Graining Workshop

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Tutorial Wed 28: MARTINI Lipids

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1 Topology files and system setup

Unpack the martinilip.tar.gz. It contains the required MARTINI topology files, mpd-files, and the gro-files to start from:

- dspc.top
- dspc_bilayer.gro
- dspc_single.gro
- em.mdp
- md.mdp
- martini_v2.0_lipids.itp
- martini_v2.1.itp
- water.gro

You can find more on the MARTINI force-field plus some additional topology files at the MARTINI homepage.

We will begin with self-assembling a DSPC (distearoyl-phosphatidylcholine) bilayer from a random configuration of lipids and water in the simulation box. First, create this random configuration of 128 DSPC's starting from a single DSPC molecule:

- `genbox -ci dspc_single.gro -nmol 128 -box 7 7 7 -try 100 -o 128_noW.gro`

Next, minimise the system...

- `grompp -f em.mdp -c 128_noW.gro -p dspc.top -maxwarn 10`
- `mdrun -v -c 128_minimised.gro`

...add 6 CG waters (i.e., 24 all-atom waters) per lipid...

- `genbox -cp 128_minimised.gro -cs water.gro -o waterbox.gro -maxsol 768`

...and minimise again:

- `grompp -f em.mdp -c waterbox.gro -p dspc.top -maxwarn 10`
- `mdrun -v -c minimised.gro`

2 Self-assembly of a DSPC bilayer

Now, you are ready to run the self-assembly MD simulation. About 25 ns should suffice.

- `grompp -f md.mdp -c minimised.gro -p dspc.top -maxwarn 10`
- `mdrun`

This might take ca. 25 min on a dual core machine.

Check whether you got a bilayer. If yes, check if the formed membrane is normal to the z-axis (i.e., membrane in the xy-plane). If the latter is not the case, rotate the system accordingly (with `editconf`). In case you did not get a bilayer at all, continue with the pre-formed one from `dspc_bilayer.gro`.

Continue the simulation for another 15 ns at zero surface tension (switch to semi-isotropic pressure coupling).

3 Analysis

From the latter simulation, calculate properties such as

- area per lipid
- bilayer thickness
- lateral diffusion of the lipids

In general, for the analysis, you might want to discard the first few ns of your simulation (equilibration time).

3.1 Area per lipid

To get the area per lipid, you can simply divide the area of your simulation box (Box-X times Box-Y from `g_energy`) by half the number of lipids in your system.¹

3.2 Bilayer thickness

To get the bilayer thickness, use `g_density`. You can get the density for a number of different functional groups in the lipid (e.g., phosphate and ammonium headgroup beads, carbon tail beads, etc) by feeding an appropriate index-file to `g_density` (make one with `make_ndx`; you can select, e.g., the phosphate beads by typing “a P*”). The bilayer thickness you can obtain from the distance between the headgroup peaks in the density profile.

Compare your results to those from small-angle neutron scattering experiments (Balgavy et al., *Biochim. et Biophys. Acta* 2001, 1512, 40-52):

- thickness = $4.98 \pm 0.15\text{nm}$
- area per lipid = $0.65 \pm 0.05\text{nm}^2$

3.3 Lateral diffusion

Before calculating the lateral diffusion, remove jumps over the box boundaries (`trjconv -pbc nojump`). Then, calculate the lateral diffusion using `g_msd`. Take care to remove the overall center of mass motion (`-rmcomm`), and to fit the line only to the linear regime of the mean-square-displacement curve (`-beginfit` and `-endfit` options of `g_msd`). To get the lateral diffusion, choose the “-lateral z” option.

¹Note that this might not be strictly OK, because the self-assembled bilayer might be slightly asymmetric in terms of number of lipids per monolayer, i.e., the areas per lipid are different for the two monolayers. However, in a first approximation, we will ignore this here.

4 Other bilayers: unsaturated tails, headgroups

Next, investigate the effect of changes in the lipid tails and in the headgroups on the properties of the bilayer. We will i) introduce a double bond in the lipid tails, and ii) change the lipid head groups from PC to PE.

4.1 Unsaturated tails

To introduce a double bond in the tail, we will replace the DSPC lipids DOPC (compare the MARTINI topologies of these two lipids). A simple way is to open the confout.gro from the last DSPC simulation with your favorite text editor and to search-replace all "DSPC" by "DOPC". Replace DSPC by DOPC in your .top and .mdp files as well, and grompp does the rest for you (you can ignore the "atom name does not match" warnings of grompp).

4.2 Changing the headgroups

Starting again from the final snapshot from the DSPC simulation, change the head groups from PC to PE. Again, an easy way to do so is to search-replace DSPC by DSPE in the .gro, .top, and .mdp files, and run grompp.

For both new systems, run 15-ns MD simulations and compare the above properties between the three bilayers (DSPC, DOPC, DSPE). Do the observed changes match your expectations? Why/why not? Discuss.

5 Refine CG parameters based on AA simulation

A little more "advanced" exercise, still to be added.