Biophysical Journal, Volume 99

Supporting Material

Title: Partitioning of Lipids at Domain Boundaries in Model Membranes

Authors: Lars V Schafer and Siewert Jan Marrink

Partitioning of Lipids at Domain Boundaries in Model Membranes: Supporting Information

Lars V. Schäfer and Siewert J. Marrink

Equilibration of lateral composition. It is crucial that the simulation time is long enough to allow the lipids to sample the entire bilayer patch, in particular also including the (bulk of the) L_o domain, in which diffusion is slowed down as compared to the L_d domain. To test the convergence of our simulations with respect to the

lateral composition, we separately analyzed each 2-μs interval from the last 8 μs of the simulation. Figure S1 shows the POPC number density profiles obtained for one leaflet of the bilayer containing 40 POPC lipids (20 per monolayer); similar results were obtained for the other leaflet and for PLiPC and LysoPC.

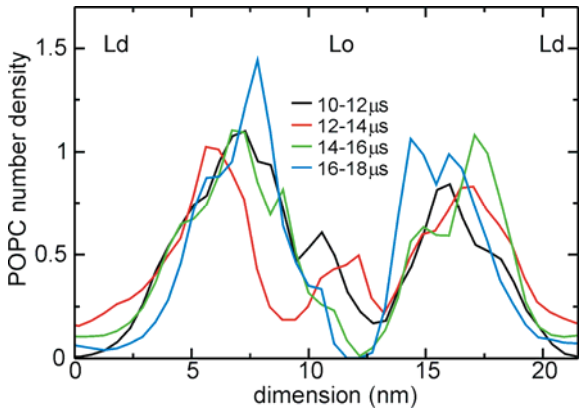

Figure S1. POPC number densities along dimension perpendicular to domain boundary interface, obtained from different time intervals of the simulation.

Initially, the 2 mol-% of the 4th component were inserted into the L_d domain. Thus, an important test is to check whether these molecules actually visit the bulk of the L_o domain during the simulation. The profiles in Figure S1 show that some POPC lipids are indeed temporarily located in the bulk of the L_o domain. Already between 10–12 μs simulation time, a few POPC lipids are located in L_o, whereas no POPC is located in the bulk of the L_d domain during that time interval (black curve). From 12–14 μs (red curve), some POPC molecules re-enter the bulk of the L_d domain, yet some POPC also remains in the bulk of L_o. Towards the end of the simulation, all POPC lipids have left the bulk of the L_o domain, and the density almost exclusively peaks at the domain boundary interfaces (green and blue curves).

The convergence of the composition profiles is understandable from the observed lateral diffusion coefficients of the PC lipids, which range from $12 \cdot 10^{-8}$ cm^2 s^{-1} in the bulk of the L_d domain to $2.5 \cdot 10^{-8}$ cm^2 s^{-1} in the bulk of the L_o domain.(1) For the interpretation of these diffusion coefficients, one has to keep in mind that they were obtained using a factor of 4 to convert simulation time to real time, as obtained by comparing to experimental diffusion coefficients (1). In the present study, scaling of the simulation time was not required, because we did not calculate dynamic properties. All reported times are thus simulation times. To carefully estimate the root mean square distance sampled by the lipids in the membrane plane during the 18 μs of simulation time, we also assume the same conversion factor 4, and, furthermore, the slow diffusion coefficient of $2.5 \cdot 10^{-8}$ cm^2 s^{-1} (observed in the bulk of the L_o domain). This yields a distance of 27 nm, which is larger than the lateral dimensions of the simulated bilayer patch (ca. 21.5 x 21.5 nm).

Line tension. The line tension σ was obtained from the bulk pressures measured during the simulations. For an interface along the X-dimension, it can be calculated according to $\sigma = \frac{1}{2}\left\langle L_Y L_Z \left(P_{YY} - P_{XX}\right)\right\rangle$, where < > denotes an ensemble average, L_Y and L_Z are the box dimensions along the Y and Z dimensions, respectively, and P_{YY} and P_{XX} the respective pressure tensor components perpendicular and parallel to the interface. The factor ½ accounts for the fact that there are 2 interfaces in the simulation system. Statistical errors were obtained by analyzing the block averages of the pressure components as a function of block size, as implemented in the g_analyze tool of Gromacs (2). Note, the line tensions reported in this study are bilayer line

tensions, whereas the fluctuation analysis carried out in Ref. (1) yielded the line tension per monolayer, i.e., $\sigma/2$.

1. Risselada, H. J., and S. J. Marrink. 2008. The molecular face of lipid rafts in model membranes. *Proc. Natl. Acad. Sci. USA* 105:17367-17372.
2. Hess, B. 2002. Determining the shear viscosity of model liquids from molecular dynamics simulations. *J. Chem. Phys.* 116:209-217.