Effects of Free Fatty Acid Inclusion in a DMPC Bilayer Membrane

Free fatty acids in biomembranes have been proposed to be a central component in several cellular control and regulatory mechanisms. To elucidate some fundamental elements underlying this, we have applied molecular dynamics simulations and experimental density measurements to study the molecular packing and structure of oleic acid (HOA) and stearic acid (HSA) in fluid bilayers of dimyristoylphosphatidylcholine (DMPC). The experimental data show a small but consistent positive excess volume for fatty acid concentrations below 10 mol %. At higher concentrations the fatty acids mix ideally with fluid DMPC. The simulations, which were benchmarked against the densitometric data, revealed interesting differences in the structure and location of the fatty acids depending on their protonation status. Thus, the protonated (uncharged) acid is located rather deeply in the membrane with an average position of the carboxy group near the second carbon segment of the lipid chains with a typical end-to-end distance of 16–18 Å. This structure of the fatty acid brings about a rather tight lateral packing in the mixed membrane and a moderate ordering and hence stretching of the lipid chains. Deprotonation of the fatty acids is associated with a pronounced movement of their carboxy group to a more hydrated position at the membrane interface and a lateral expansion driven by the mutual repulsion of the anions. These changes increase both the disorder and the degree of interdigitation of the lipid chains, and they make the membrane thinner by 2–3 Å.