

Supplementary Information

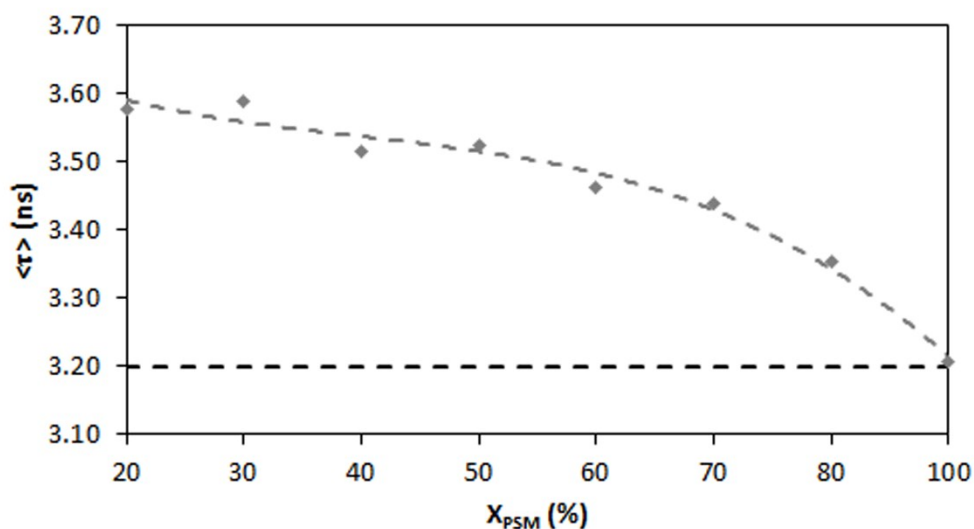


Figure S1. Intensity-weighted average fluorescence lifetime of Humulin® containing *m*-cresol 100 μM in the absence (black line) and in presence of LUV (POPC/PSM binary mixtures with molar proportions indicated in Materials and Methods) (gray line). The dotted lines are merely guides for the eye. All experiments were performed at room temperature.

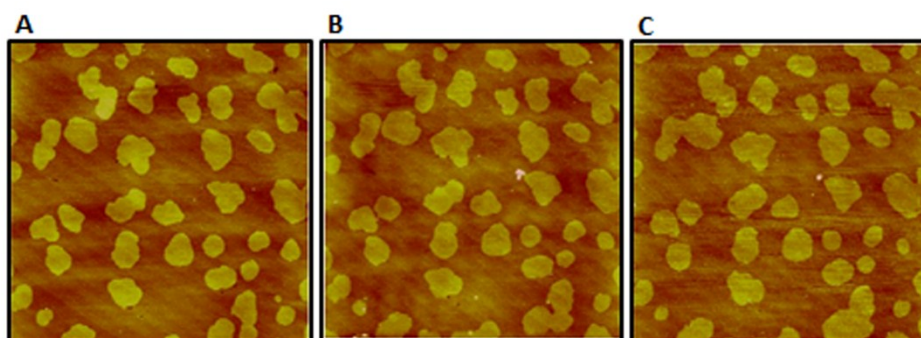


Figure S2. AFM topographic images of an SLB composed of DOPC/PSM/Chol (40:40:20 mol:mol:mol) deposited on mica in the beginning of the scanning (A), 1h (B) and 2h (C) after scanning the surface. The images were obtained in a liquid cell at room temperature. The image corresponds to an area of $20 \times 20 \mu\text{m}^2$. $Z = 7\text{nm}$.

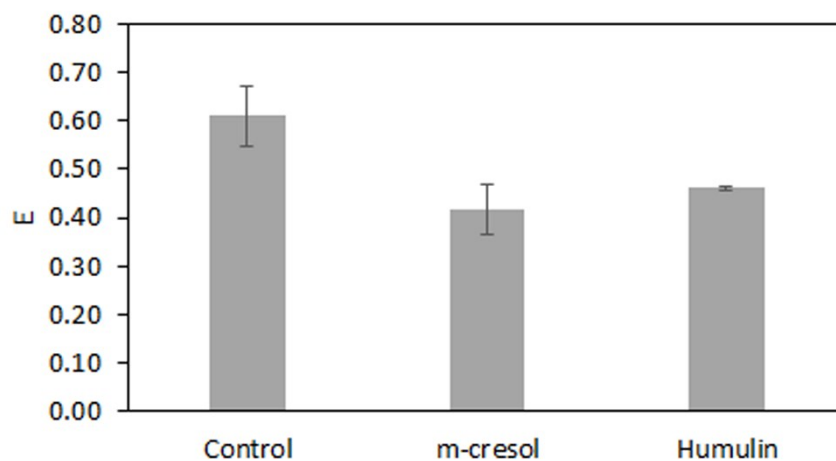


Figure S3. Efficiency of FRET between the donor/acceptor pair NBD-DPPE/Rhod-DOPE in the absence and in presence of pure *m*-cresol 30 μ M and *m*-cresol 1 mM from Humulin®. Measurements were performed in presence of LUV containing POPC/SM/Chol ternary mixtures with molar proportions 48.5/29.3/22.2 at room temperature.

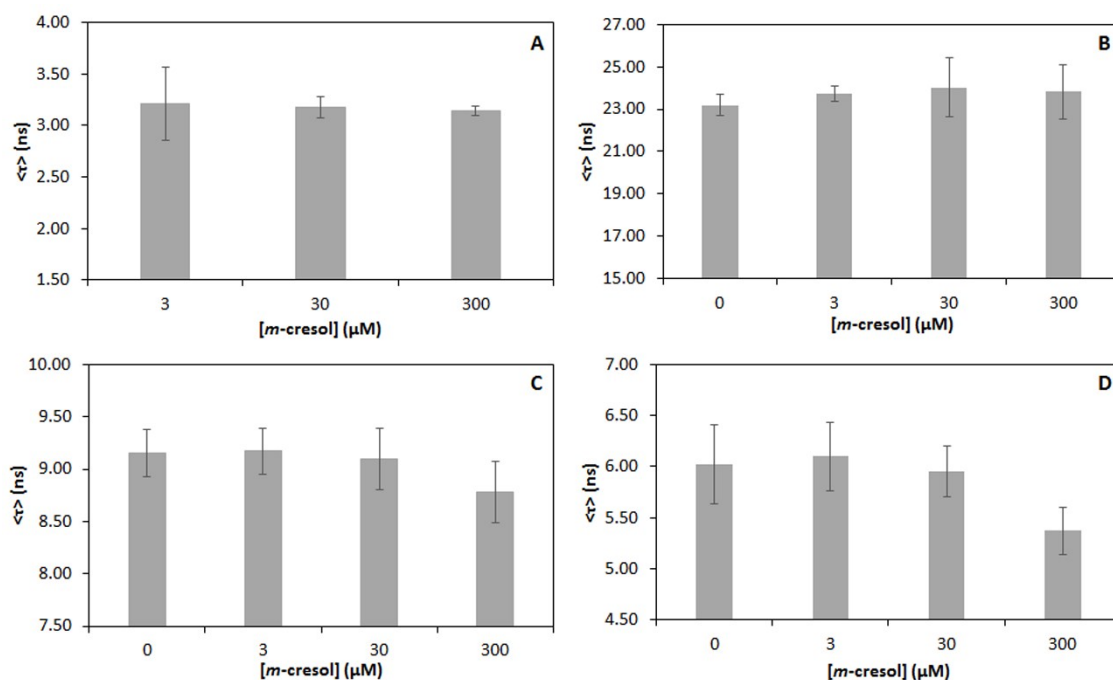


Figure S4. Interaction of *m*-cresol with LUV of DOPC/PSM/Chol with molar proportions 40/40/20, corresponding to a l_o fraction of 40 mol% at room temperature assessed by fluorescence spectroscopy. Intensity-weighted average fluorescence lifetime of *m*-cresol 3 μM , 30 μM and 300 μM (A); *t*-PnA (B), NBD-DPPE (C) and NBD-DOPE (D), in the absence and in the presence of *m*-cresol 3 μM , 30 μM and 300 μM . The intensity-weighted fluorescence lifetimes of *m*-cresol in the presence of LUV are quite similar to those measured in presence of the mixture POPC/PSM/Chol (Figure 4 – B in the main text). Regarding the fluorescent probes, the intensity-weighted fluorescence lifetimes of *t*-PnA remain unchanged, even in presence of *m*-cresol 300 μM , as observed for the lipid system containing POPC (Figure 6 in the main text). The intensity-weighted fluorescence lifetimes of NBD-DPPE and DOPE also follow the same trend in presence in both lipid systems, being almost undetectable for NBD-DPPE (Figure 5 – A), while for NBD-DOPE, a small but significant decrease is detectable for larger *m*-cresol concentrations. Overall, these experiments reinforce our conclusions about the *m*-cresol interaction with lipid bilayer. The comparison was made with the mixture POPC/PSM/Chol (48.5/29.3/22.2 mol/mol/mol) which has 36 mol% l_o fraction.