A molecular investigation of partition behavior in the systems biomembrane/water and micelle/water

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Membranes and micelles are both anisotropic systems composed of amphiphile molecules (lipids and surfactants). The distribution of solvent molecules in biological membranes is important for the development of potential drugs, toxicological studies, and to understand metabolism. Micellar systems find application for example in the food industry, as drug delivery agents in the pharmaceutical industry, and in surfactant-based separation processes.

To reduce the number of time consuming and expensive experiments, theoretical methods to predict partition behavior in biomembrane and micellar systems are required. We are using molecular dynamics (MD) simulations to investigate these processes. Whereas for membranes the molecular structure needs careful consideration especially in the case of mixed lipid types, for micelles the structures need always special attention due to varying sizes and shapes [1,2]. MD simulations and the umbrella sampling method were carried out in order to obtain free energy profiles, leading to the preferential location and the partition coefficients of the investigated solute. Furthermore, drug influences on membrane phases were studied. In most cases good agreement between simulation and experimental results are found. MD simulations of surfactants were started from a random distribution (self-assembly) or from a pre-assembled micelle to investigate the influence of micelle structure on solute partitioning. The relatively new extension of COSMO-RS for membranes and micelles named COSMOmic [4] was also used and investigated for its applicability for an efficient calculation of partition behavior.

[1] D. Yordanova, I. Smirnova, S. Jakobtorweihen, *J. Chem. Theory Comput.* **2015**, 11, 2329–2340. DOI: 10.1021/acs.jctc.5b00026

[2] E. Ritter, D. Yordanova, T. Gerlach, I. Smirnova, S. Jakobtorweihen, *Fluid Phase Equilib.* **2016**, 422, 43–55. DOI: 10.1016/j.fluid.2016.03.006

[3] S. Jakobtorweihen, A. C. Zuniga, T. Ingram, T. Gerlach, F. J. Keil, I. Smirnova, *J. Chem. Phys.* **2014**, 141, 45102. DOI: 10.1063/1.4890877

[4] A. Klamt, U. Huniar, S. Spycher, J. Keldenich, *J. Phys. Chem. B* **2008**, 112, 12148–12157. DOI: 10.1021/jp801736k