MD Simulations of Micelles Formation in $C_{12}E_x$ Solutions

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Since the dawn of polymeric micelles application as drug delivery systems in the late 1980s [1], numerous polymer self-assemblies have been extensively investigated, designated to deliver various substances including: low-molecular-weight anticancer drugs, contrast/imaging agents, proteins, etc. Promising building blocks of drug delivery containers are deemed nonionic surfactants of the poly(ethylene glycol) alkyl ethers C_nE_m.

One of the purposes of the present study is to derive from first principles calculations and test molecular mechanics parameters for such ethers to be used in subsequent all-atom simulations. Monomers and dimers with two different types of periphery, which are short-chain prototypes of the amphiphilic surfactant $C_{12}E_x$, were used as model systems. The geometry of low-energy conformers is optimised (PBE and MP2) in vacuum and in implicit solvent. Validation of the derived parameters provided the comparison between the thermodynamic parameters obtained from MD simulations (Amber99/NPT/300 K) of diethyl ether and the existing experimental data.

On the other hand, the stability of the pre-aggregates is determined, which are supposed to exist in aqueous solution before the actual micelles assembly, and to assess the aptitude to their formation. All-atom and coarse-grained molecular dynamic simulations (NPT/293 K) of two molecules of each species in explicit water (TIP4P) with PBC applied were carried out to estimate the mutual orientation and the interaction between the surfactants in the dimers. The derived force field parameters for the ether groups were used for this aim. The structural aspects of the amphiphilic organization in aqueous medium from the simulation data with the MARTINI CG force field for surfactant concentrations are discussed.

[1] K. Kataoka, G.S. Kwon, M. Yokoyama, T. Okano, Y. Sakurai, J. Control. Release 24 (1993) 119