Molecular Simulations of Dodecyl-β-Maltoside Micelle in Water: Headgroup Conformation and the Force Field Parameters

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INTRODUCTION

During the last decades, alkyl-glucosides detergents have been involved in membrane protein extraction experiments, as they are capable to readily solubilize large membrane proteins complexes. Among these detergents Dodecyl-β-maltoside (DDM) is one of most used. DDM has two anomers: one with a linear conformation (α) and one with a right angle bend between the headgroup and the alkyl tail (β). The α-anomer is less soluble than the β one and is not commonly used in membrane protein solubilisation with some notable exceptions, e.g. bacterial E.Coli Nar/Hþ antiporter.

Experiments show that this simple difference in the headgroup conformation changes the micelle properties. Little is known about the influence of the surfactant conformation on the micelle internal structure and hydration properties. To examine these aspects, we performed molecular dynamics (MD) simulation on the micelles of the α-DDM and β-DDM anomers, in standard thermodynamics conditions and using different force fields [1].

FORCE FIELD PARAMETRIZATION

• Atomic charges calculations for glycolipid for the GLYCAM force field (GLYCAM06)

Computations of the atomic RESP charges for the two DDM anomers were performed with the R.E.D program version IV [2] using the different steps described in the left figure. This procedure ensures that the compatibility with the GLYCAM force field is respected.

• Optimizations of Torsion angles for the ether link of the glycolipid for CHARMM (CHARMM-Opt):

Ethoxy tetrahydropran (Et-THP) was used as a model compound to parameterize ether-linked hexopyranosides. Both α and β substituted anomers were used in the study. THP parameters were those previously developed in the context of hexopyranosides [3]. The missing bond, angle, dihedral, Lennard-Jones, and partial charge parameters of the ether group were taken from those of the methoxy-THP[4] and of the linear ether[5]. QM MP2/cc-pVTZ/MP2/6-31G(d) / QM scans for both α and β anomers were performed (φ=O1=O=C2, O1=C2, H=C2, O=C2). Our new parameter set can be used in association with the CHARMM force field.

REFERENCES

[6] Kuttel et al. [7], from now on called CHARMM-K. Alky chains were modeled using the alkane parameters of Klauda et al.[8]. Long range electrostatics were treated using particle mesh Ewald. TIP3 model was used for the water. Equilibration was carried out in NVE and NPT ensembles using the Nose-Hoover thermostat [9] and the Parrinello and Rahman[10] barostat at 1·297 K and P=0.1015 bar. Trajectories were obtained during 14 ns. We performed six simulations with two sizes of micelles containing 75 α-DDM and 132 β-DDM monomers. The size of the system was of 47000 and 67000 atoms for the α and β anomers, which includes water. Initial pre-assembled micelles were generated using the Packmol program.

CONCLUSIONS

The average radial density profiles, p(r), with respect to the micelle center of mass of the n=0 Å show that the 6 micelles differ mainly on the localization of the outermost (GlCA) and the innermost (GlGB) glucose unit of the maltose head.

The average relative population in trans and gauche+ (60°) and gauche- (60°) of the dihedral angles of the alky chain (in grey) and ether link (in blue) show differences mainly in the ether link. The distribution maps of the φ, ψ, glycosidic dihedral angles (φ,ψ,ψo) of the maltose head for the α-DDM (α-C') and β-DDM (β-f) micelles are located at -40°, 25° ± 10°. Due to sterical constraints on the headgroup at the micelle surface, this region differs from that found for maltose in water (-50°, -30°) ± 20° [11].

The translational diffusion of the water at the micelle surface is 7-10 times slower than that of TIP3 bulk water (D=2.8 ps) due to the entrapment of the water at the micelle interface and to the formation of water-solvent hydrogen bonds. This behavior depends only slightly on the headgroup conformation.

• Newly developed force fields parameters for glycolipids within the CHARMM and GLYCAM frameworks have been developed. They have been tested by performing MDs of DDM micelles of the two anomers.
• Comparison of the MD between the three force fields show differences in the headgroup due to the different conformation of the maltose head.

HYDRATION WATER DYNAMICS