The structure of a model peptide in the presence of micelles studied by means of molecular dynamics simulations

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Introduction

Micelles are regarded as biomimetic structures due to their ability to form separated hydrophobic and hydrophilic regions, thus resembling one of the main structural features of biological membranes. It is generally argued that biological molecules may orient themselves with respect to the micellar interface, maximizing the interactions of their polar groups with surfactants headgroups and molecules near the interface (*e.g.*, water and counterions), while at the same time their apolar moieties would remain buried within the aggregates, a region pictorially described in most textbooks as a small liquid hydrocarbon droplet.

We report below the preliminary results obtained from the first 10 ns of a molecular dynamics simulation of one serine 16-mer peptide in a concentrated micellar system. We have recently reported a theoretical study of the structure and dynamics of this model peptide in water and ethylene glycol, an additive that stabilizes the peptide secondary structure with respect to the water solution.[1]

Results and Discussion

We have employed a large model system, comprising nine sodium octanoate micelles (the surfactant concentration was *ca.* 1 mol L^{-1}). The number of aggregates increased during the first 5 ns of the trajectory and then remained in the range from 14 to 18 clusters, although as much as 23 aggregates were eventually observed. During the last 5 ns, the aggregation number distribution presented three populations, consistent with previous simulations.[2] Nearly all molecules were found either into small micelles with aggregation numbers N = 7-17 (62% of the molecules) or into larger micelles with N = 19-30 (37% of them). These figures may lead to the conclusion that smaller aggregates would play a more important role, but they are short lived as compared to the larger aggregates, which are stable in the timescale spanned by the simulation.

As regards the peptide structure, we have found RMSD values for the whole peptide and RMSF values for the individual serine units that are consistent with those obtained for the peptide in pure water. Thus we have not identified any significant stabilization of the secondary structure of the model peptide. These observations might lead us to the conclusion that the peptide is not interacting favorably with the micelles, but further investigations show this is not the case. For instance, the potential energy between octanoate molecules and the peptide decreases continually (*ca.* 1200 kJ mol^{-1} during the first 10 ns of the trajectory), indicating that more favorable configurations were attained as the simulation proceeded. On the other hand, the potential energy between water molecules and the peptide increased by the same amount. Thus it seems more likely that water molecules have been partially replaced by the anions and that this replacement had little or no effect on the structural stability of the peptide.

A more detailed picture of the system interactions may be obtained from the radial distribution functions. Serine has a hydrophilic OH group attached to its lateral chain, along with polar N, H and O atoms forming the peptide bond, all of them potentially forming hydrogen bonds with each other and with water or octanoate molecules. Our major finding was that octanoate molecules were not significantly hydrogen-bonded to the peptide. They were instead interacting with the peptide N-terminal region, mostly by means of their hydrophobic atoms (methyl and methylene groups).

Conclusions

We presented an atomic level description for the behavior of a serine 16-mer peptide in the presence of anionic micelles. The molecular dynamics simulation did not indicate that serine residues interact directly with the octanoate anions by means of hydrogen bonds. Instead, octanoate hydrophobic sites interact with serine methylene groups.

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