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The study of sodium dodecyl sulfate self-assembly behavior at three different concentrations in the presence and absence of lysozyme: Molecular dynamics simulation approach

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ABSTRACT

In this work, aggregation behavior of sodium dodecyl sulfate (SDS) at three different concentrations and in the presence and absence of lysozyme was studied using molecular dynamics simulation. The range of surfactant concentrations we have studied is from the concentration below the critical micellar concentration (CMC) to far above it. The abundance of self-assembled surfactant structures within this concentration range and in the absence and presence of protein was calculated. Based on the results provided, self-aggregation behavior of SDS above and below the CMC and as well as in the presence and absence of enzyme is different so that over this concentration and in the presence of protein, the number of surfactant monomers decreased and most surfactants have a tendency to contribute in aggregates. However, the aggregation number of formed clusters grew in the absence of protein. In addition to these pointed results, the effect of concentration from the structural point of view was investigated, and observations indicated that concentration increase did not create remarkable changes in β-sheet content whereas it had a tremendous impact on helices and acted as a structure breaking. Therefore, it reduced the helical content of protein and on the other hand; it increased the percentage of random coils.

1. Introduction

Industrial production of soaps which was an unavoidable consequence of the nineteenth century's chemical revolution was a good starting point for the dominance of surfactants over the other industries such as textile, food, agriculture, cosmetic and pharmaceutical industries [1–3]. Until now, it is more than a century that the aggregation behavior of these unique molecules in different environments has drawn the attention of many researchers (see the review of Otzen [1]). In other words, because of this fact that surfactants play an important role in protein denaturation so understanding their behavior and also protein–surfactant interactions can be a key step to answer this question: what "really" happens when proteins encounter surfactants?

Lysozyme is a small globular enzyme/protein that has a molecular mass of 14.3 kD, and consists of 129 amino acids, and 18 and 12 cationic and anionic residues respectively. It has a helical content of 30% and β-sheet content of 10%. Moreover, it is stabilized by four disulfide bridges, which are located between 127-6, 30-115, 80-64 and 97-76 residues. The interior surface of lysozyme usually is hydrophilic, and its isoelectric point is at pH = 11.0 [4]. This protein has high natural abundance, and it can be found in secretions of the animals' lacrimal glands, in nasal mucus, gastric secretions, and egg white [4], and it has been known as a major factor in breaking the bacterial protective cell walls down, as well. Therefore, it is a key element to fight and protect against certain infections [5].

Without a shadow of doubt, in many cases, lysozyme can be used as a model system to understand the underlying principles of the structure, function and dynamics of protein folding [4–7].

As interesting as lysozyme may be, surfactants like SDS count as a strong denaturant and are widely used for the separation, purification and analysis of protein [7]. Thus, the interaction of lysozyme–surfactant is an enormous topic which has been the subject of many different studies and is investigated by a wide range of experimental techniques such as, CD, IR [6] and UV, fluorescence, and dynamic light scattering [7]. In spite of this fact that the use of experimental methods has been quite broad in scope and application, unfortunately, they have their limitations [8]. A lot of work has been done on the amphiphilic systems by different experimental techniques like NMR, EPR, light scattering, fluorescence and neutron diffraction [9–12]. However, this feature that surfactant self-assembling occurs in a nanosecond time scale and nanometer length scale makes practical investigations difficult [13]. Fortunately, nowadays, due largely to the explosion of technology leading to dramatic development of computer power and algorithmic advances, molecular dynamics simulation (MDS) has become a valuable tool to

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Table 1
Overview of studied systems and simulation detail. The cross mark and check mark in this table were used to indicate the absence and presence of lysozyme, respectively.

Title	Dimensions of box (nm^3)	Number of SDS	Span time of simulation (ns)	Number of water molecules	Lysozyme
System A	7*7*7	10	50	6988	×
System B	7*7*7	60	50	6108	×
System C	7*7*7	100	50	5430	×
System D	7*7*7	10	50	6315	✓
System E	7*7*7	60	50	5469	✓
System F	7*7*7	100	50	4791	✓

study for such systems [14,15]. This effective technique by providing a clear microscopic picture paved the way for collecting information about dynamic and structural properties, which is difficult to obtain from experiments [8,16].

Waymor et al. studied a system of 60 dodecyl phosphocholine (DPC) molecules by a 1.2 ns constant pressure MD simulation and obtained information about structure and dynamics of this system. They also observed that the interaction between water and micelle surfactant's head group mostly occurs through the head groups and arises from positively charged choline groups and the negatively charged phosphate groups with hydrogen and the oxygen atoms of water; their obtained results are in good agreement with NMR relaxation's data [8].

Bruce et al. performed a 5 ns simulation of a water-solvated micelle containing 60 SDS monomers and evaluated some structural properties. They found that the lion's share of the water–micelle contact not only occurs via the head groups but also a significant portion of this kind of contacts occurs through the tails. In addition, all micellar structural quantities are stable during the simulation and micelle shape is not fully spherical [9].

Tieleman et al. simulated DPC micelles with different sizes, 40, 54 and 65 monomers in water. Their study focused on the effect of aggregation size on the micelle structure. They showed that the shapes of micelles composing 54 and 65 monomers are mostly spherical and discrimination between these micelles is difficult. The results of this study are compatible with those obtained by quasi-elastic light scattering and analytical ultracentrifugation [10].

Marrink et al. performed MD simulation of 54 DPC molecules in water at two concentrations above CMC (0.46 M and 0. 12 M). They observed that surfactant monomers aggregated into a worm-like micelle at the higher DPC concentration, whereas at lower concentration, they aggregate into a spherical micelle. Therefore, the shape of surfactant clusters has a connection with surfactant concentration [11].

Besides, such an approach provides insight into the effect of solvophilic interactions on micellar shape and micellar transformation [12]. Counter ion effects on the surfactant system properties, also, have been studied by computer simulations [13]. Although the studies mentioned above have rendered valuable information about different angles of the amphiphilic systems, it leaves much to be the desired answer to the remaining questions.

In the present work, MD simulation approach was used to investigate the behavior of SDS at the CMC and in surfactant solutions above and below the CMC and in the presence and absence of lysozyme as well. Our particular intent was to understand the manner of effect of SDS on the lysozyme structure in different conditions.

2. Simulation details

All MD simulations and subsequent analyses were carried out using gromacs 4.5.5 package [14]. Six simulation boxes with dimensions of $7 \times 7 \times 7$ nm^3 were defined. In three out of six boxes, the lysozyme was located in the center of the boxes. The crystal structure of lysozyme (PDB entry: 4D9Z) was taken from the protein data bank. Then, 10, 60 and 100 SDS molecules were placed uniformly randomly within the three boxes, including protein and three remained empty boxes, respectively. All simulation boxes were filled with simple point charge (SPC) [15] water. In order to neutralize the systems, an appropriate number of Na^+ ions were added to each box. The components of simulation boxes for the given systems are briefly listed in Table 1.

The OPLSAA force field was assigned for SDS and protein. Since the parameters of the OPLSAA for some molecules like SDS have not been incorporated within gromacs by default, these parameters were inserted manually. To do this, the geometry of SDS was optimized using DFT method. The calculations were performed with the Gaussian 03 [16] at the B3LYP/6-31G (d, p) [17–20] level of approximation. The optimized structure of SDS was depicted in Fig. 1.

The atomic partial charges of SDS were computed by CHELPG (CHarges from Electrostatic Potentials using a Grid based method) method [21]. To eliminate any undesirable contacts between atoms and also initial kinetic energy in the simulation boxes the energy was minimized by applying the steepest descent algorithm. Then, each of the defined systems was equilibrated in two stages, including 10 ns NPT and NVT simulations with temperature and pressure fixed at 300 K and 1 bar, respectively. To fix a constant temperature during the simulations, systems' components were coupled with V-rescale thermostat [22] in each of equilibration steps and molecular dynamics simulations. For each component of the systems PME algorithm [23] was applied to estimate the electrostatic interactions. LINCS algorithm [24] was employed to fix the chemical bonds between the atoms of the protein and SETTLE algorithm [25] in the case of solvent molecules. The simulations were run for 50 ns, and time step was 2 fs throughout the simulations.

3. Results and discussion

Due to the amphiphilic nature of surfactants, that is, they have a hydrophilic moiety and a hydrophobic moiety; these fascinating molecules can form multiple structures with different sizes above or near a critical concentration of surfactant (CMC). Aggregation numbers, N_{agg}, the number of surfactant molecules per micelle, closely associated

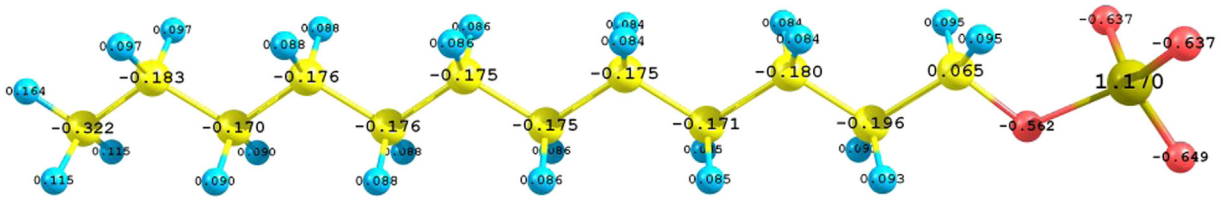

Fig. 1. Optimized structure of dodecyl sulfate molecule.