

Full Length Research Paper

Molecular dynamics simulation of sodium dodecyl sulfate in the presence of bovine carbonic anhydrase: Behavior of water

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Accepted 16 August, 2011

The subject of this study is on the effect of sodium dodecyl sulfate (SDS) on water properties. We have studied the structure and dynamic behavior of water at different concentrations of sodium dodecyl sulfate in the presence of bovine carbonic anhydrase (BCA) by means of molecular dynamics simulation. The water oxygen to SDS oxygen radial distribution function, the relative frequency of water hydrogen forming none, 1 and 2 hydrogen bonds, and the diffusion constant of water were used to analyze water behavior. The results indicated different effects of SDS on the behavior of water in the absence and presence of BCA.

Key words: Hydrogen bond, diffusion constant, radial distribution function, molecular dynamics simulation.

INTRODUCTION

The SDS/water mixture is an interesting system both in terms of practical and fundamental points of view. Practical aspects are related to the particular properties of this system, such as the ability to denature proteins (Housaindokht et al., 1993; Housaindokht and Moosavi-Movahedi, 1994; Housaindokht et al., 2002; Housaindokht et al., 2005), the large scale use of SDS for cleaning purpose, the use of SDS to solubilize hydrophobic components of various tissues and cellular structures (Jones, 1992). The fundamental aspects are related with both the structure and dynamic behavior of the water molecules (Idrissi et al., 2004).

Generally, molecular dynamics simulations enable investigation of dynamics and conformational changes of biological macromolecules can yield information that is not available through any other means (Housaindokht et al., 2008a, 2008b).

A number of studies on SDS/water mixtures in atomic detail have been published, aimed at studying details of interactions (Bruce et al., 2002a, 2002b; Sammalkorpi et al., 2007). Bruce et al. (2002) used 5 ns explicit atom

molecular dynamic simulation of 60 monomer sodium dodecyl sulfate containing 7579 water molecules and indicated that penetration of water into the micelle was restricted to head group region. Sammalkorpi et al. (2007) studied molecular dynamics simulation of SDS with explicit water molecules. They showed that there is a structural transition for the surfactant aggregates brought upon by change in temperature. Bruce et al. (2002) used molecular dynamics simulation to investigate counter ion behavior in SDS/water mixture and showed that a long equilibrium time (one nanosecond) is required to achieve a stable distribution of counter ions. Molecular dynamics simulations were also used to study the effects of SDS on protein structure (Psachoulia et al., 2006; Braun et al., 2004; Wymore et al., 1999).

In this work, we have used molecular dynamics simulation to study the water behavior in SDS/water mixture in nine different concentrations of SDS in the presence of bovine carbonic anhydrase.

MATERIALS AND METHODS

All calculations were carried out using gromacs 3.3.1 package (Lindahl et al., 1995) and grooms 96 force field (van Gunsteren et al., 1996). The molecular dynamics (MD) simulations were performed by using periodic boundary conditions. In carrying out

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Table 1. Overview of studied systems.

Title	Number of water molecules	Number of SDS
Box1	9965	0
Box2	9951	4
Box3	9947	8
Box4	9943	12
Box5	9939	16
Box6	9935	20
Box7	9931	24
Box8	9927	28
Box9	9923	32

this performance, 9 cubic simulation boxes were defined with the dimensions of $7 \times 7 \times 7 \text{ nm}^3$. BCA (pdb entry: 1v9e) was placed in the center of the boxes. Then the boxes were filled with appropriate number of water molecules. In filling these boxes, the protein was overlaid by equilibrated simple point charge (SPC) water boxes. Components of simulation boxes for the given systems are listed in Table 1. In order to neutralize the system, the appropriate number of Na^+ ions was added to each box. 40 molecules of glycine and 5 molecules of Tris were added to each simulation box. According to Katherine et al. (2005), the aim of adding glycine and Tris molecules is to prepare buffer solution with pH = 8.3. A steepest-descent algorithm was performed to minimize the energy of each system and to relax the water molecules.

Molecular dynamics simulation for each system was performed in two stages. In the first stage, position-restrain simulation was conducted in which the atoms of the protein molecule were held fixed, whereas the water molecules were free to move around so that they would reach the equilibrium state. In the second stage, each system is simulated with a time step of 2 fs. LINCS algorithm was employed to fix the chemical bonds between the atoms of the protein and SETTLE algorithm in the case of water molecules (Hess et al., 1997). The atoms in the system were given initial velocities according to Maxwell-Boltzmann distribution at 300°C. To maintain a constant temperature and pressure for various components during simulations, the Berendsen coupling algorithm was used (Berendsen et al., 1984) for each component of the system with the relaxation times of 0.1 and 0.5 ps, respectively. Since the systems involve many positive and negative charges, PME algorithm was applied to estimating the electrostatic interactions. In this algorithm every atom interacts with all atoms in the simulation box and all of their images in an infinite number of identical copies surrounding the main box. Therefore, satisfactory results are produced from the electrostatic interactions (Danciulescu et al., 2004; de Oliveira and Freitas, 2005).

RESULTS AND DISCUSSION

Effect of SDS on water structure

Radial distribution function (RDF)

RDF analysis is a common procedure to describe the average structure of liquids, because of the complexity of spatial distribution of molecules on the liquid phase; it is difficult to obtain the RDF from scattering experiments. It is accepted that RDF obtained from oxygen atom

interactions are useful to understand the structure of liquids (de Oliveira and Freitas, 2005).

To analyze the water-head group interaction, water oxygen to SDS oxygen radial distribution function were calculated over last 4 ns of the simulations at 2 ps intervals in the of different concentrations of SDS and the results are shown in Figures 1 to 8. Three oxygen atoms of SDS linked to sulfur atom was considered as head group oxygen and one oxygen atom linked to the alkyl chain was considered as main chain oxygen. According to these figures, it can be seen that the magnitude of peaks for head group oxygen is higher than those of main chain oxygen. It should be noted that the RDFs are normalized so that the difference in magnitude is not simply due to the fact that there are three terminal oxygen atoms on the head group and there is only one main chain oxygen atom. Position of the first peak in RDF diagram is different for main chain oxygen and head group oxygen. Obtained results reveal that SDS monomers cannot extend into water appropriately so that the main chain oxygen would be at different distance from water molecule as head group oxygen. The latter result in contrast to those results reported by Bruce et al. (2002), in which the correspondence RDFs from simulation of SDS/water mixture in the absence of protein were analyzed. Thus, it seems that bovine carbonic anhydrase behavior of water molecules in SDS/water mixture has been changed.

Water-water hydrogen bonds

The number of hydrogen bonds per water molecule is a useful metric to study the effects of solute on water structure, and it can show that subtle difference cannot be seen in other ensemble-averaged properties (Daggett, 2006). The hydrogen bond is analyzed using either energetic or geometric criteria (de Oliveira and Freitas, 2005). Van der Spoel et al. (2006) studied the thermodynamics of hydrogen bonding in hydrophobic media and reported that geometric criterion reproduced experimental data. We employed a geometrical criterion with a maximum donor-acceptor distance of 0.35 nm and

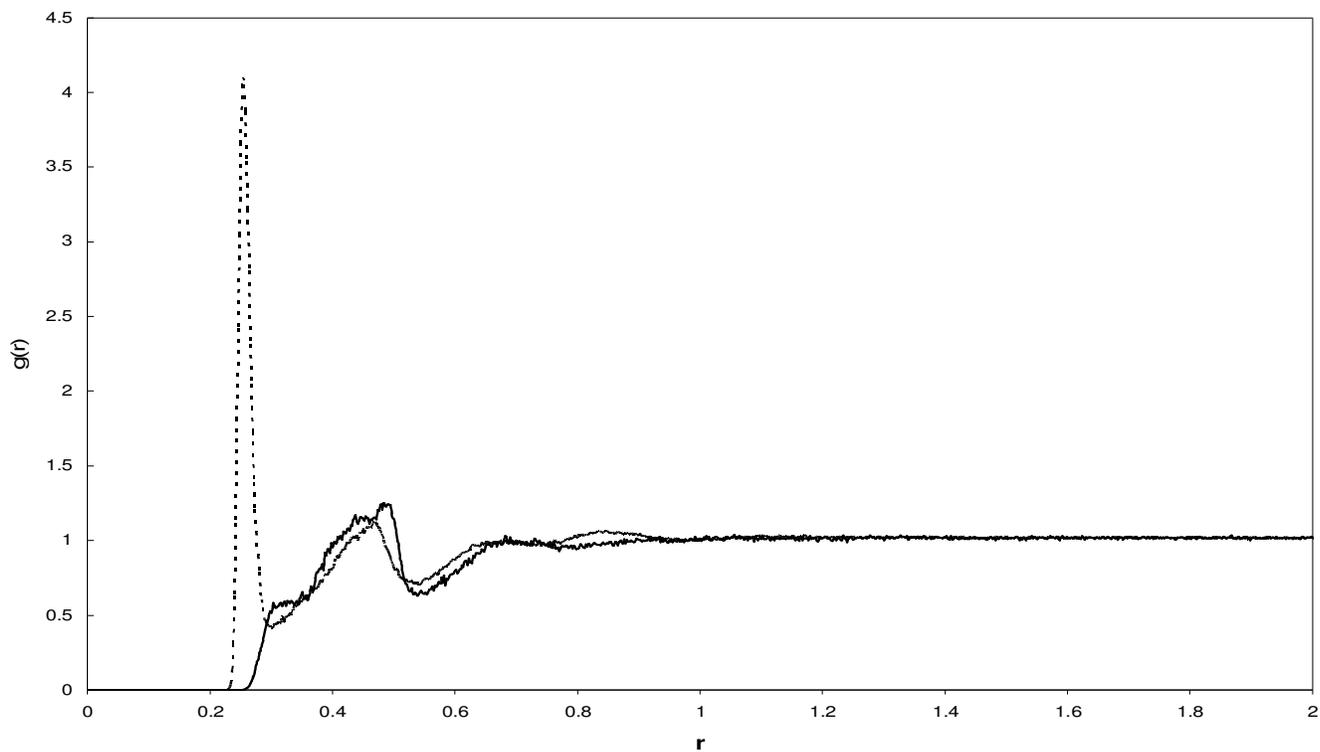


Figure 1. Water oxygen to SDS oxygen radial distribution function in the presence of 4 SDS molecules. Head group F = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

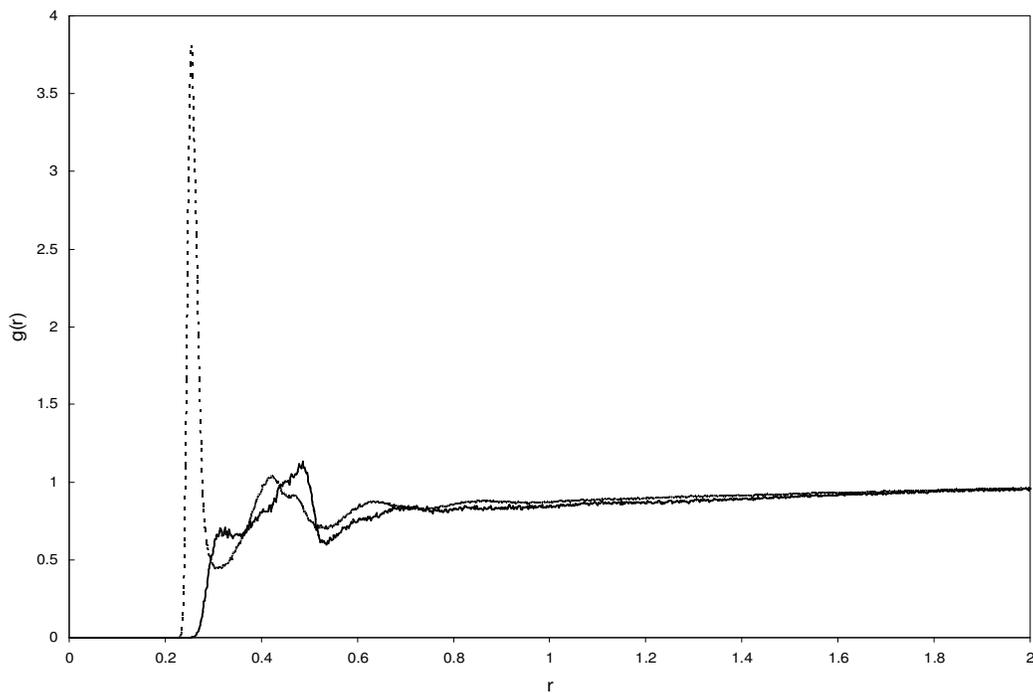


Figure 2. Water oxygen to SDS oxygen radial distribution function in the presence of 8 SDS molecules. Head group oxygen = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

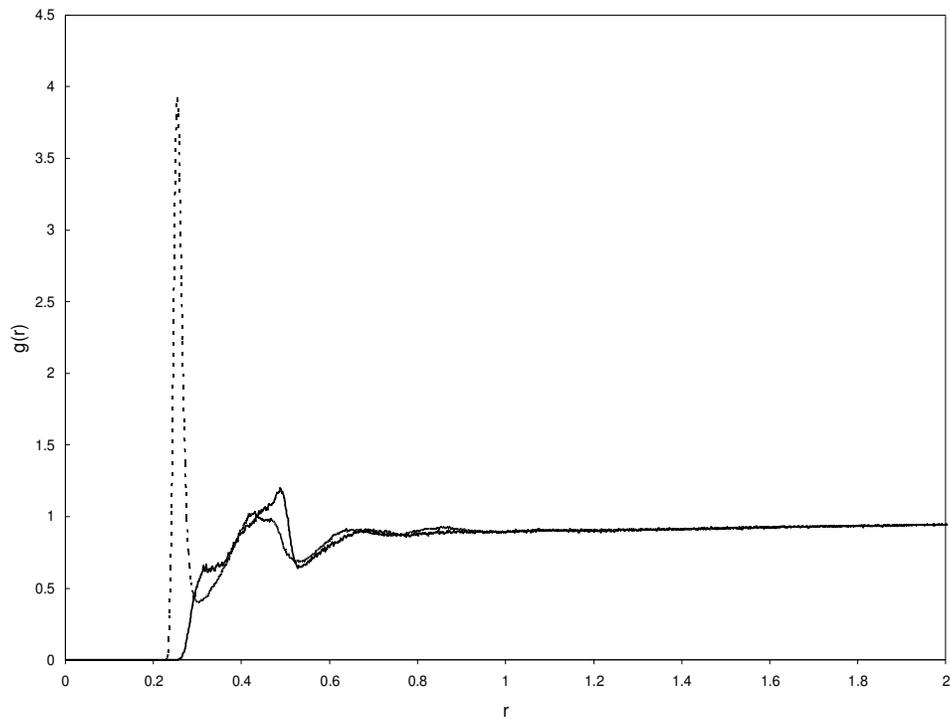


Figure 3. Water oxygen to SDS oxygen radial distribution function in the presence of 12 SDS molecules. Head group oxygen = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

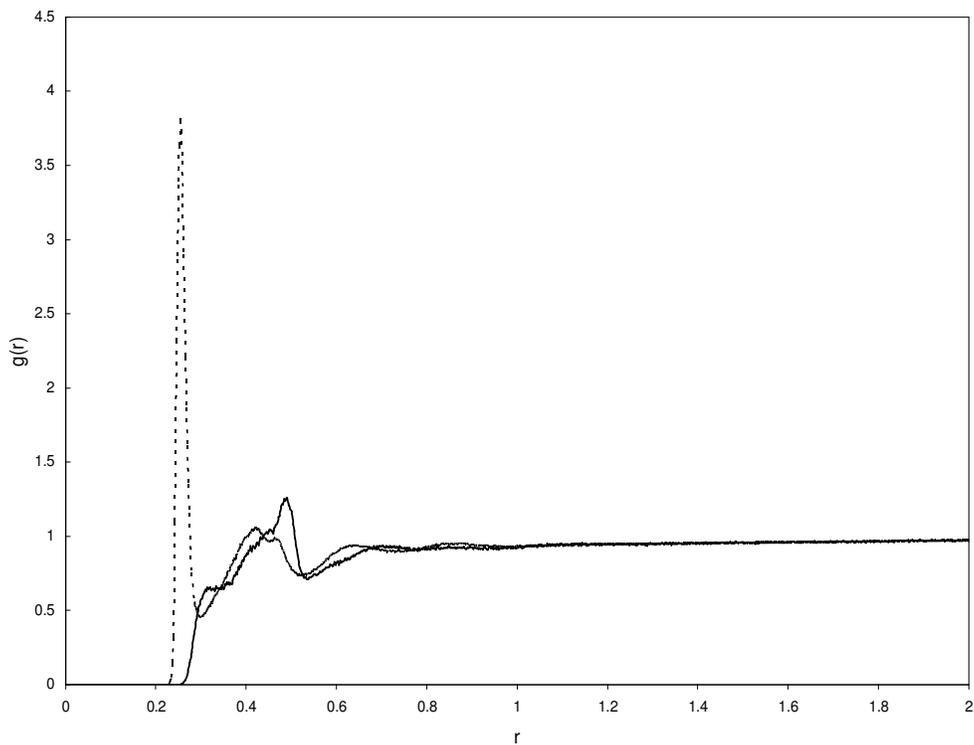


Figure 4. Water oxygen to SDS oxygen radial distribution function in the presence of 16 SDS molecules. Head group oxygen = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

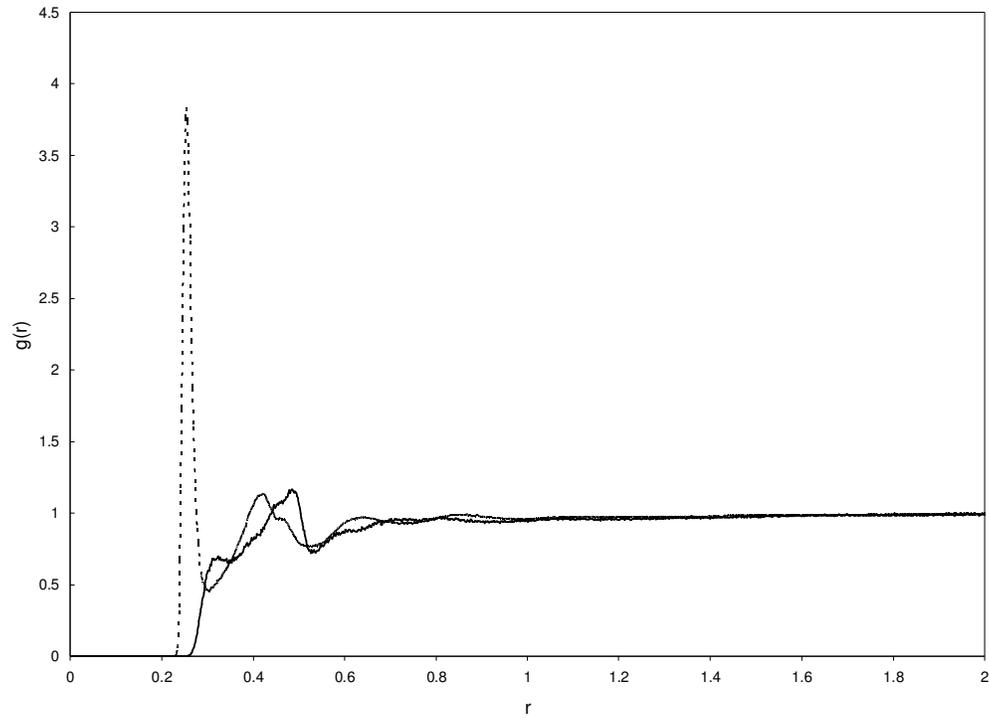


Figure 5. Water oxygen to SDS oxygen radial distribution function in the presence of 20 SDS molecules. Head group oxygen = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

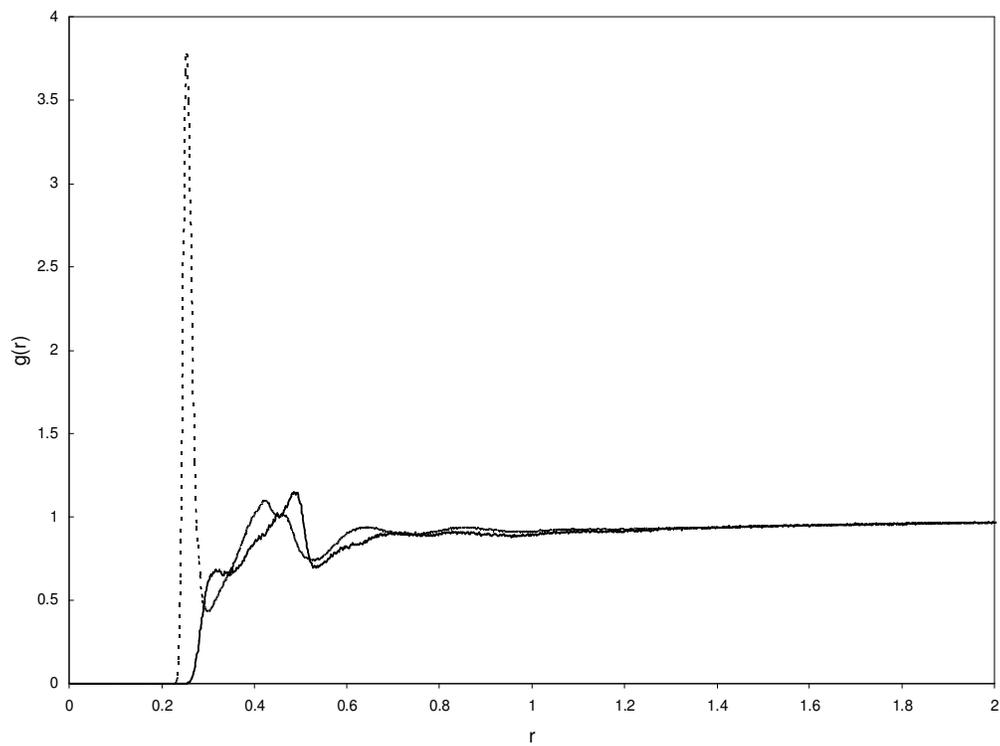


Figure 6. Water oxygen to SDS oxygen radial distribution function in the presence of 24 SDS molecules. Head group oxygen = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

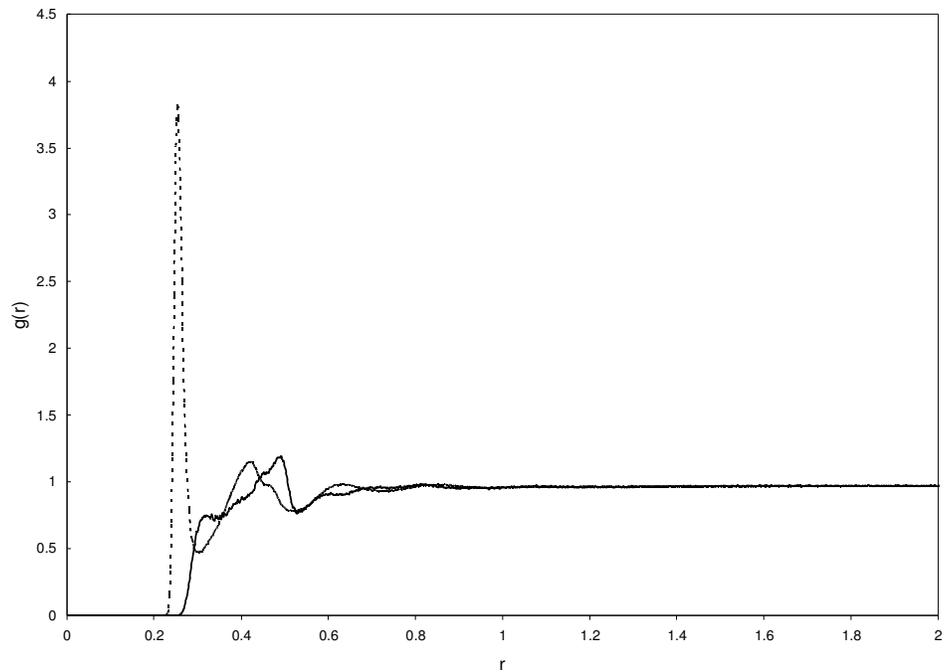


Figure 7. Water oxygen to SDS oxygen radial distribution function in the presence of 28 SDS molecules. Head group oxygen = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

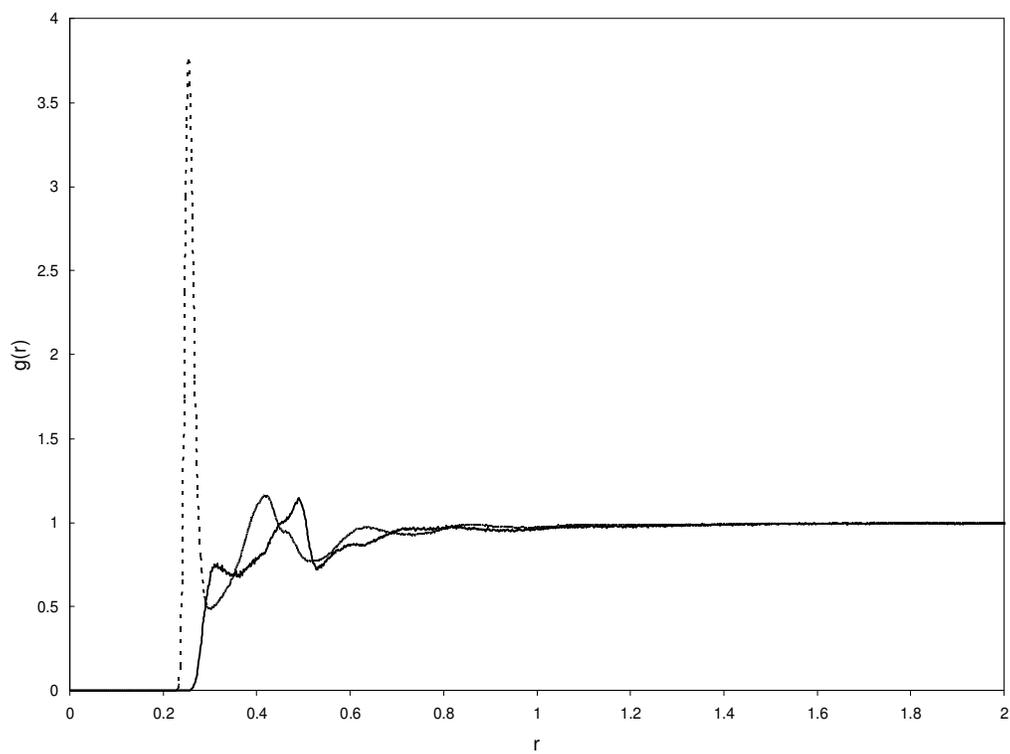


Figure 8. Water oxygen to SDS oxygen radial distribution function in the presence of 32 SDS molecules. Head group oxygen = O_{1-3} (dashed line) and main chain oxygen = O_4 (solid line).

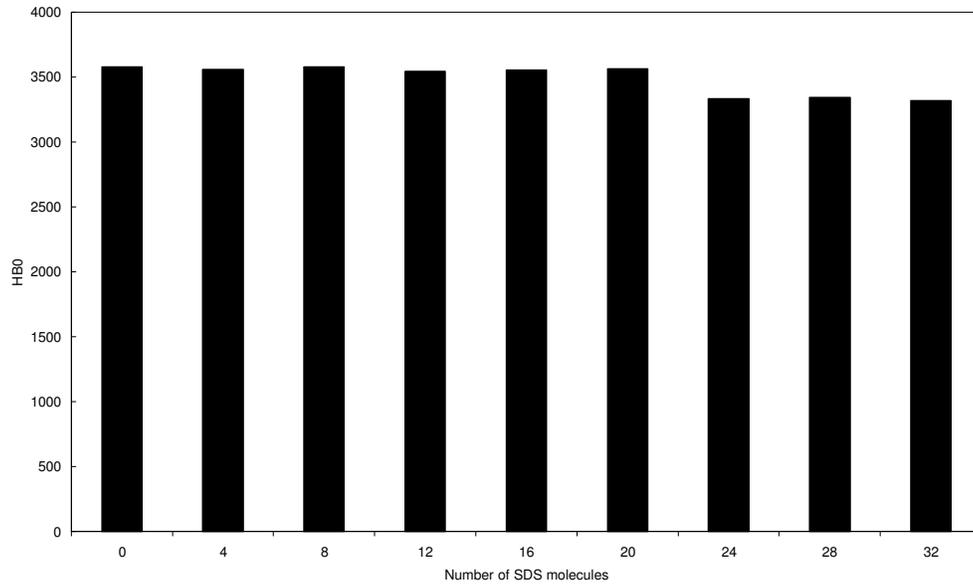


Figure 9. HB0 values versus number of SDS molecules. HB0 is the relative frequency of water hydrogen forming none hydrogen bond.

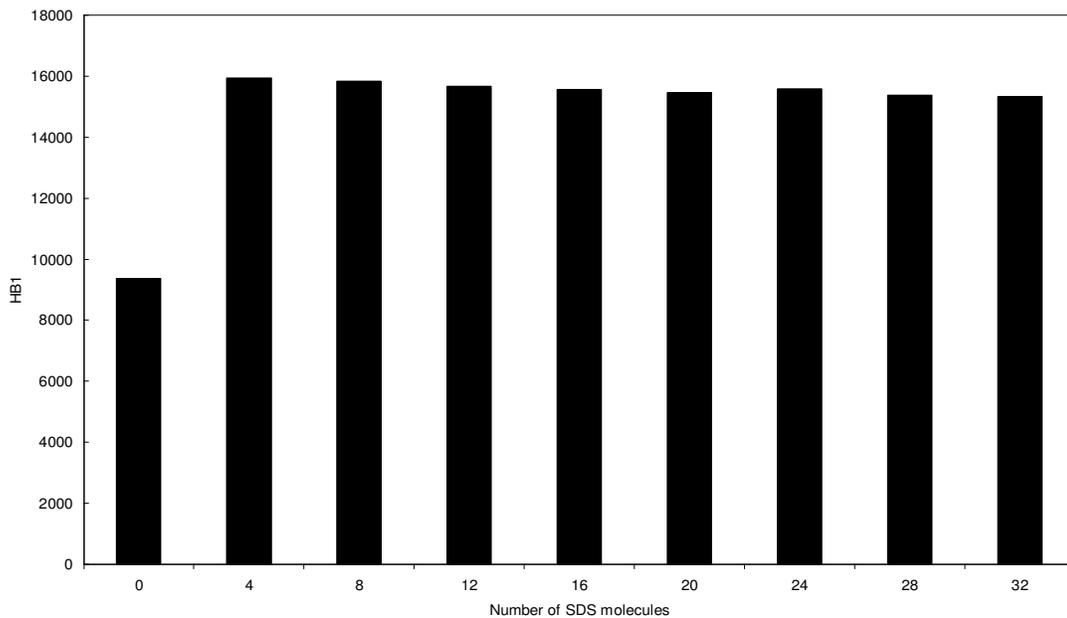


Figure 10. HB1 values versus number of SDS molecules. HB1 is the relative frequency of water hydrogen forming one hydrogen bond.

donor-hydrogen-acceptor angle of 30° . We found hydrogen of water molecules forming none, one and two hydrogen bonds in the absence and presence of various concentrations of SDS, and the results are shown in Figures 9 to 11. It is observed that for the presence of 12 SDS molecules, the relative frequency of water hydrogen

forming two hydrogen bonds is greater than the correspondence values in other conditions. This observation reveals that the structure of water tends to obtain its best tetrahedral structure (consider that two hydrogen bonds per hydrogen atom of water molecule is equal to four hydrogen bonds per water molecule). The number of

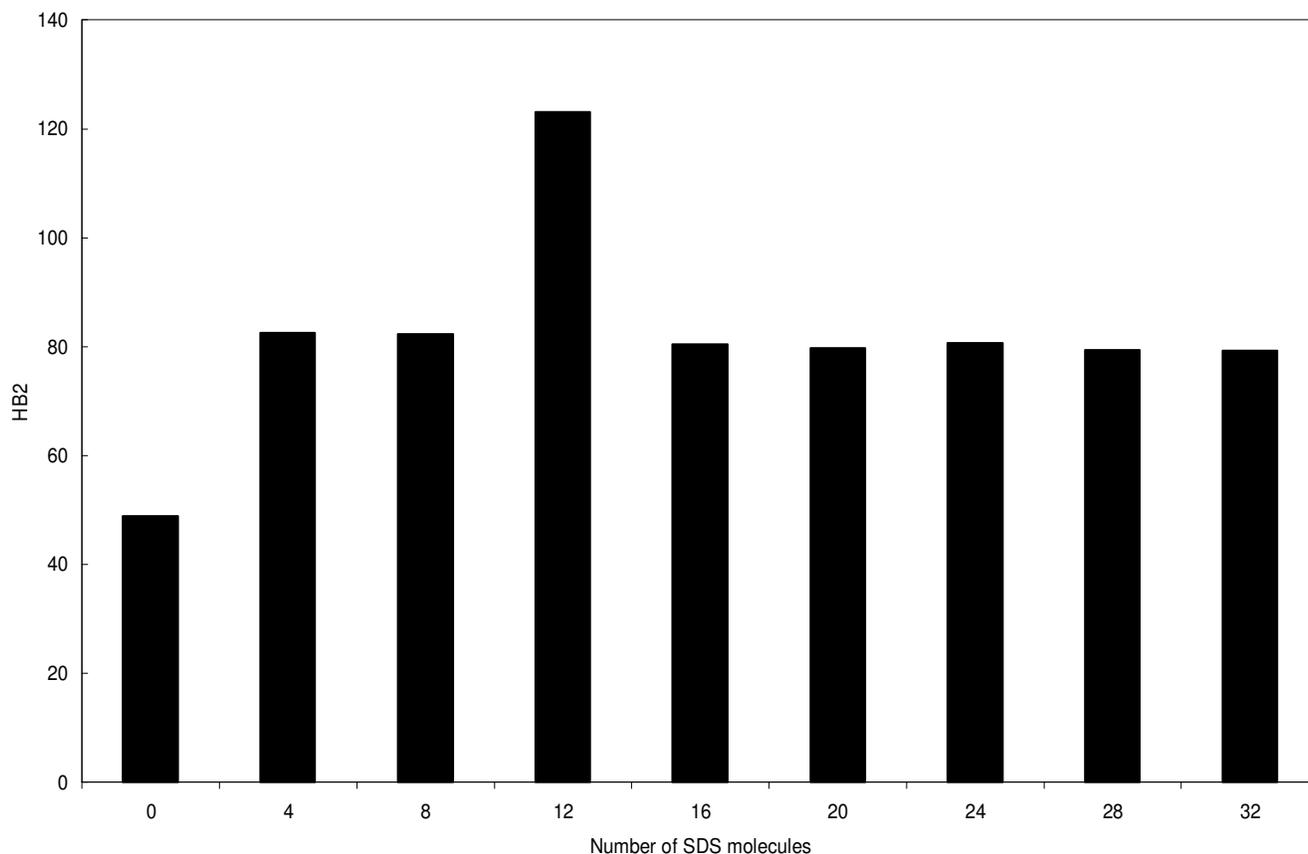


Figure 11. HB2 values versus number of SDS molecules. HB2 is the relative frequency of water hydrogen forming two hydrogen bonds.

hydrogen atom with one hydrogen bond is about three times greater than the number of hydrogen atom with no hydrogen bond. Thus, in the presence of SDS, the structure tends to become better defined.

Effect of SDS on the dynamic behavior of water

The translational mobility of molecules is best described by the diffusion constant. Effects of SDS on the dynamic behavior of water were studied with aid of diffusion coefficient parameter. Diffusion coefficient was computed using Einstein's expression.

$$D = \lim_{t \rightarrow \infty} \frac{1}{2dt} \frac{1}{n} \sum_j^n \langle [x_j(0) - x_j(t)]^2 \rangle \quad (1)$$

Where d is the space dimension, n is the number of particles, $x(t)$ is the position of the particle at time t .

Diffusion coefficients of water were calculated in the absence and presence of various concentration of SDS, and it is shown in Figure 12. The obtained values for

diffusion coefficients in this work are comparable to that of previously mentioned results for water molecule (Bruce et al., 2002). For pure water the self-diffusion constant is $2.3 \times 10^{-5} \text{ cm}^2/\text{s}$, a value that is difficult to reproduce in simulations due to approximates applied in simple classical model and inadequate span time of simulation.

Conclusion

In the present study, we used 5 ns (45 ns in overall) molecular dynamics simulation to investigate the effects of SDS on the behavior of water in the presence of bovine carbonic anhydrase. The selection of bovine carbonic anhydrase for this study is particularly attractive for many reasons: (1) it is inexpensive and widely available, therefore, experimental studies are possible. (2) the structure of carbonic anhydrase is well defined (3) the mechanism of inhibition is fairly simple and well characterized (4) the interaction between bovine carbonic anhydrase and SDS are well documented (Gitlin et al., 2006; Bushmarina et al., 2001; Satoko et al., 2004; Saito et al., 2004; Leslie et al., 1981). The main conclusion of

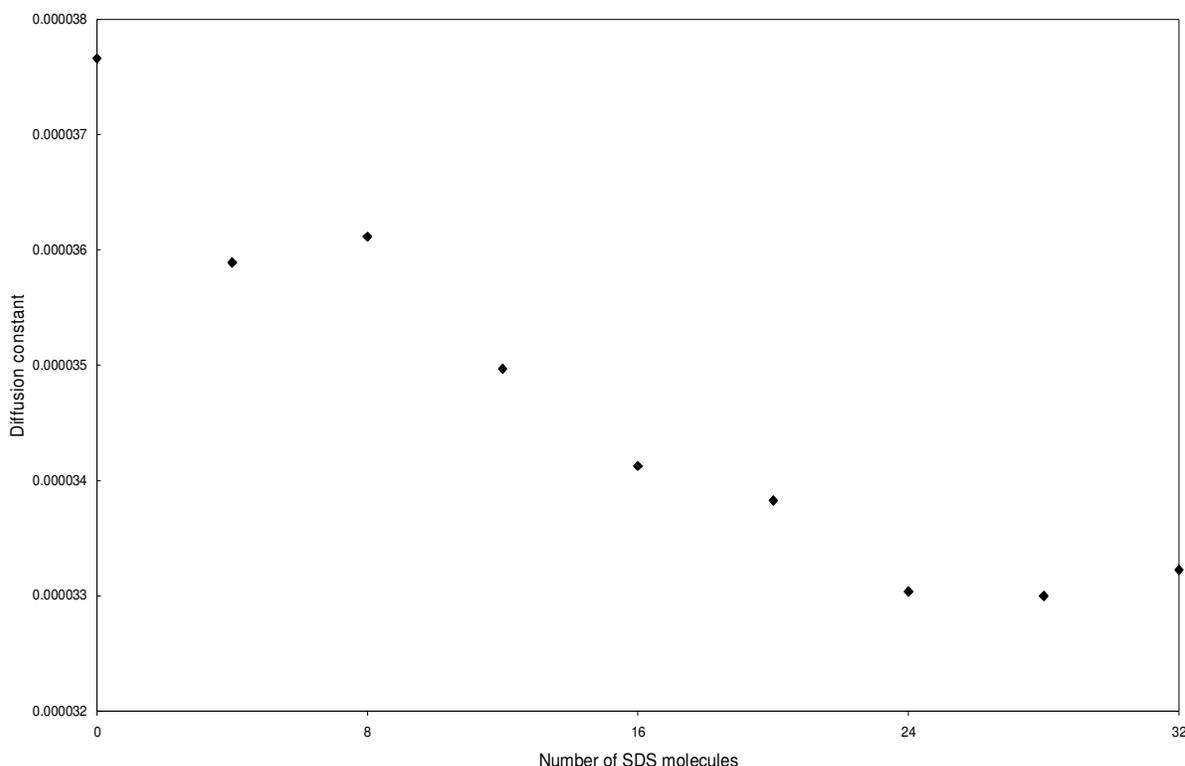


Figure 12. Diffusion constants (cm²/s) of water versus number of SDS molecules.

our study is that the effects of SDS on the behavior of water are different in the presence and absence of protein.

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