Molecular simulation of the morphology and viscosity of aqueous micellar solutions of sodium lauryl ether sulfate (SLE\textsubscript{n}S)

Stavros D Peroukidis\textsuperscript{1}, Dimitris G Mintis\textsuperscript{2}, Ian Stott\textsuperscript{3} and Vlasis G Mavrantzas\textsuperscript{1,4,}\textsuperscript{*}

\textsuperscript{1} Department of Chemical Engineering, University of Patras and FORTH-ICE/HT, GR 26504 Patras, Greece
\textsuperscript{2} Computation-Based Science and Technology Research Center, The Cyprus Institute, Nicosia 2121, Cyprus
\textsuperscript{3} Unilever Research and Development Port Sunlight, Bebington CH63 3JW, United Kingdom
\textsuperscript{4} Particle Technology Laboratory, Department of Mechanical and Process Engineering, ETH Zürich, CH-8092 Zürich, Switzerland

\textsuperscript{*} Author to whom any correspondence should be addressed.
E-mail: vlasis@chemeng.upatras.gr and vlasisom@mat.ethz.ch

Keywords: molecular simulation, SLES, surfactants, micelle, molecular dynamics

Abstract
In a recent contribution, we introduced a new approach for the quantitative prediction of the micellar morphology of aqueous solutions of ionic surfactants based on coarse-grained MARTINI-type simulations followed by reverse-mapped all-atom (AA) molecular dynamics (MD) ones, using as a model system sodium dodecyl sulfate. We make use of the same approach in the present work to study the micellar structure of aqueous solutions of sodium lauryl ether sulfate (SLE\textsubscript{n}S) with the chemical structure CH\textsubscript{3}(CH\textsubscript{2})\textsubscript{11}(OCH\textsubscript{2}CH\textsubscript{2})\textsubscript{n}OSO\textsubscript{3}Na with a fixed number \(n\) of ethoxyl (EO) groups per surfactant molecule (\(n = 1, 2, 3\)). These surfactants are used in a wide range of industrial applications, particularly in personal and home care products, but a quick literature survey proves that a systematic study of their microstructure, micellar morphology, and equilibrium transport properties is missing. Our simulations provide predictions for the mean aggregation number of such monodisperse SLE\textsubscript{n}S solutions which are found to be in very good agreement with experimental data already reported in the literature. They also show that for a given total surfactant concentration, SLE\textsubscript{n}S molecules with a smaller number \(n\) of EO groups form, on average, larger micelles. From the reverse-mapped AA MD simulations we also compute the zero shear rate viscosity of the solution whose value is found to increase as its total concentration in SLE\textsubscript{n}S molecules increases (for a given \(n\)) or as the number \(n\) of EO groups in the surfactant increases (for a given concentration).

1. Introduction

Surfactants are amphiphilic molecules capable of reducing the surface tension of liquids due to their strong absorption at the liquid–air interface [1–5]. This very important property has its origin in the molecular characteristics of surfactants which are molecules composed of a hydrophilic head and a hydrophobic tail, the latter disfavoring contacts with water. As a result, they find numerous usages as the key components of detergents or as wetting and foaming agents or emulsifiers in many applications (pharmaceutical, mineral oil, health and personal care industry, etc) [1–5].

Among the most widely used anionic surfactants are the sodium dodecyl sulfate (SDS) (also known as sodium lauryl sulfate), and the sodium lauryl ether sulfate (SLES). Both of them are essential ingredients of liquid formulations for home and personal care products [1]. SLES, in particular, finds applications in formulations where a high degree of thickening is sought. It is characterized by good solubility, high biodegradation, and favorable hard-water resistance. It is rather inexpensive and facilitates ease of production and formulation [6]. SDS, on the other hand, exhibits low solubility while the final cosmetic formulation is characterized by low degree of thickening. It has also been reported that SDS may cause skin irritation [7]. SLES molecules contain a hydrophilic sulfate group, a fixed number of ‘semi’-hydrophilic
ethoxyl (EO) groups, and a hydrophobic hydrocarbon tail. Their general chemical formula is \( \text{CH}_3(\text{CH}_2)_m(\text{OCH}_2\text{CH}_2)_n\text{OSO}_3\text{Na} \), where \( m \) denotes the number of methylene (\( \text{CH}_2 \)) and \( n \) the number of EO groups. For practical applications, SLES molecules with \( n = 1–3 \) and \( m = 11 \) are typically used (see, for example, [8–17]).

Despite their importance, a literature survey reveals a rather limited number of computational [18] and experimental [11, 19–21] studies of the phase behavior and morphology of these surfactants, even for single-component SLES aqueous solutions. This might be explained by the fact that single-component SLES surfactants are time consuming to prepare in large scale; thus, mixtures of SLES molecules are typically employed, because of their lower cost and better performance characteristics compared to single-component ones [22].

In aqueous solution, SLES molecules self-assemble to form micelles. Experimental studies [11, 19, 20, 23] consider that spherical micelles are formed at the first critical micelle concentration (CMC), which typically shifts to lower values as the number of EO groups in the surfactant increases [24]. However, the surface tension exhibits the opposite trend, implying that the surfactant becomes less surface active as the number of EO groups increases [24]. We understand that, overall, the micelle size and the CMC of aqueous solutions of SLES depend strongly on both the number of EO groups [24] and the length of the hydrocarbon chain [25].

Although the polydispersity in the length of the hydrocarbon segments (and in the number of EO groups) complicates the analysis between chemical structure and final material properties of commercial SLES, polydisperse mixtures are preferred (as already discussed) due to the simple and inexpensive procedures followed to prepare them. On the contrary, homogenous (monodisperse) suspensions of SLES are preferred when better control over safety, stability and efficacy of the final product is needed, such as in biomedical applications or related ones [26–29]. Commercial SLES aqueous solutions follow the general principles of self-organization typical of anionic surfactants with their morphological and rheological properties being significantly dependent on the total concentration of the surfactant, the concentration of the salt added, the presence of co-surfactants, and the temperature. For example, adding salt to aqueous SLES solutions leads to a rapid increase in the size of the micelles, which, in turn, affects rheological properties (causing, e.g., a sharp increase in the viscosity of the solution by several orders of magnitude [22, 30]). A significant decrease in the first and second CMC (where a conformational transition from spherical to elongated micelles occurs) has been reported for mixtures of SLES and cocamidopropyl betaine [10]. In shampoos and body wash applications, mixtures of SLES and co-surfactants are commonly preferred for better performance with respect to specific criteria (sufficient foam, pleasant appearance, etc) [1].

As mentioned above, despite the appreciable amount of computational and experimental reports in the literature on the phase behavior of SDS (which can be considered as a limiting case of SLES with zero EO groups), the corresponding number of studies on SLES (both experimental and computational) is rather limited. To the best of our knowledge, the only systematic computational study of micellar solutions of single-component SLES surfactants (containing one, two or three EO groups) has been the recent one by Panoukidou et al [18] on their phase behavior in the context of the dissipative particle dynamics (DPD) method.

From a design point of view, developing efficient computational methodologies that could address self-organization and micellar formation as a function of surfactant concentration accounting directly for the specific molecular characteristics would be highly welcome. Being able to directly predict the size and shape of the micelles formed as a function of composition and detailed molecular features of the formulation, and connecting this microstructure with transport properties (e.g. zero shear rate viscosity) would help introduce specific design rules for the final liquid formulation to have the desired properties.

Recently, we made a big step forward towards such a direction through the implementation of a new simulation methodology consisting of three main steps: (a) coarse-grained (CG) molecular dynamics (MD) simulations based on the MARTINI forcefield (FF) [31, 32] with slightly modified parameters to afford the formation of large micelles; (b) reverse mapping of the final self-assembled CG configuration into an all-atom (AA) one; and (c) re-equilibration of the resulting AA configuration using a detailed force field (such as the CHARMM36 FF [33–35]) capable of fine-tuning micelle size and final morphology. The work allowed us to study the micellar structure of aqueous SDS solutions and predict their size and equilibrium transport properties (zero shear rate viscosity and diffusivity) as a function of the concentration of solution in SDS molecules. In the present study, we extend this very promising methodology to solutions of SLES molecules. To check the capabilities of the methodology, we restrict ourselves to strictly monodisperse (i.e. single-component) aqueous \( \text{CH}_3(\text{CH}_2)_m(\text{OCH}_2\text{CH}_2)_n\text{OSO}_3\text{Na} \) solutions with a fixed value of \( m \) equal to 11 (\( m = 11 \)) and different values of \( n \) (\( n = 1, 2 \) or 3), denoted from now on as SLE\( n \)S. The approach will allow us to directly observe on the computer the formation of micelles to their correct size and make important predictions for the physicochemical properties (viscosity and diffusivity) of the resulting solution as a function of its concentration in SLE\( n \)S molecules and number \( n \) of EO groups in the surfactant.
The rest of our paper is organized as follows: In section 2, we review our computational approach. In section 3, we present detailed results for the micellar morphology of the model SLEnS solutions studied here and their key physicochemical properties. The paper concludes with a summary of the major findings and a brief discussion of future plans in section 4.

2. Methods

2.1. Computational approach

As already mentioned, our computational approach follows closely the strategy already reported in a recent contribution for the simulation of micellar solutions of SDS molecules, and entails three steps: first, we introduce a CG model for SLEnS by slightly modifying certain parameters of the corresponding MARTINI FF [31, 32] to allow the formation of rather big micelles. Large simulation cells are utilized in this phase of our work containing a few hundred thousands of interacting sites (beads). In the initial configuration, the surfactant molecules are placed randomly in the simulation cell. The CG MD simulations are performed in the isothermal–isobaric (NPT) ensemble for several microseconds of simulation time and lead to well equilibrated micellar configurations. In the second step, an AA configuration is built from the final CG one through a reverse mapping scheme that restores the atomistic structure in each SLEnS molecule from the known positions of the beads in the corresponding CG structure. Compared to the CG configuration, the reverse-mapped AA one (water molecules and sodium ions being included) contains one order of magnitude more interacting sites (i.e. more than 2 millions). In the third phase, the generated AA configuration is subjected to an AA MD simulation in the NPT ensemble using the generalized CHARMM36 FF [33–35]. Despite the exceedingly large number of interacting sites contained in the simulation cell, the mean aggregation number equilibrates rather quickly (within a few tens of nanoseconds, ns) to a value which is smaller than that of the CG model and which remains stable in the course of the simulation. The reason why the average micelle size decreases in the course of the MD simulation is due to the spontaneous dissolution (breakup) of some large micelles to smaller ones. Therefore, a prerequisite for the success of the method is that the CG model gives micelles that are larger than the ‘true’ ones at the conditions of the computational experiment, since the subsequent short AA simulations do not allow (in general) for micelle fusion. In the next paragraphs, these three building blocks of our computational approach are described in somewhat more detail.

2.2. Building blocks of the computational approach

2.2.1. CG (MARTINI-based) model

The CG model for SLEnS used in our work is based on the MARTINI FF [31, 32]. According to this, each SLEnS molecule consists of three tails (C1) beads, a number n of EO beads, and the sulfate (COSO3) or head (Qa) group. A negative charge of $-1 \, \text{e}$ is assigned to the Qa bead. The three different types of beads represent on average five, four, and three heavy atoms (oxygen, sulfur, carbon, or combinations thereof) together with the hydrogen atoms chemically bonded to them (see figure 1). Also employed are water beads (W or P4) each one representing four water molecules (the solvent), and hydrated sodium ion beads (Na or Q4) with a positive charge of $+1 \, \text{e}$ accounting for counterbalance ions. In the model, electrostatic interactions are computed using the Particle Mesh Ewald summation method [36] with the value of the relative permittivity $\varepsilon_r$ equal to 18. The value $\varepsilon_r = 18$ for the relative permittivity was determined through a trial-and-error procedure by running several test MD simulations at different $\varepsilon_r$ values and choosing the one that provides the best comparison to the limited experimental data found in the literature for the mean aggregation number (namely, the average number of surfactant molecules per micelle in the solution) at the same temperature and concentration conditions. This can be seen in figure S3 of the supporting information (available online at stacks.iop.org/JPMATER/4/044001/mmedia). Intra-molecular interactions, on the other hand, were specified by following the methodology described on the web page [37] of the MARTINI FF, based on matching the CG bond-stretching and bond-angle bending distribution functions for various parametrizations of the bonded potentials with the corresponding ones derived from an atomistically detailed model (the reference model). The same parameterization for intra- and inter-molecular potentials were applied to the entire family of SLEnS, with the exception perhaps of a bond-bending angle, as described in the supporting information to this manuscript. The full functional form of the modified MARTINI FF adopted in our simulations is provided in section S1 of the supporting information.

With the modified MARTINI-based CG potential, long MD simulations were performed in the NPT statistical ensemble at temperature $T = 300$ K and pressure $P = 1 \, \text{atm}$ using the GROMACS [38–40] software (version 4.6.7). To keep the temperature and pressure fixed, the Berendsen [41] thermostat and barostat were used. The equations of motion were integrated with the velocity–verlet algorithm, with a time step $\Delta t = 20 \, \text{fs}$. The simulations lasted approximately $5 \, \mu\text{s}$.
2.2.2. Reverse mapping

The resulting, fully equilibrated CG configuration at the end of the NPT MD simulation of the previous section was mapped to an AA configuration by extending the methodology reported in [17] for SDS molecules to SLE\textsubscript{n}S molecules. The methodology involves several intermediate steps, all of which are described in figure 2 for the case of the SLE\textsubscript{2}S molecule. In the figure, different types of beads are represented with different colors and denoted with different numbers. Let the set \{\(r_1, r_2, r_3\)\} denote the positions of the tail beads, the set \{\(r_4, r_5\)\} the positions of the EO beads, and \(r_6\) the position of the head bead in the molecule. We also denote as \(r_{ij} = r_i - r_j\) the vector connecting bead \(i\) with bead \(j\). The AA configuration is then built according to the following steps (see also figure 2).

1. First, we construct an all-trans configuration of eight carbon atoms in the positions of the first and second tail beads, exactly as described in [17].
2. Next, we build the atoms of the sulfate group in the place of the head bead. Initially, we define the position of an oxygen atom, denoted as Ot, through \(r_{Ot} = r_6 + r_{56}\hat{r}_{56}\) with \(r_{56}\) being equal to 0.45 times the distance between the EO and the head bead. This serves to place (in a next step) the nearest carbon atom (the one directly bonded to Ot) while avoiding overlaps. The rest of atoms on the sulfate head are built as described in [17].
3. In a third step, we construct the oxygen atom for each EO bead; we denote this as O\textsubscript{EO}. This is built around the center of the \(j\)-th EO bead with its position vector specified according to \(r_{OEO} = r_j + r_{ij}\hat{r}_{ij}\) with \(r_{ij}\) denoting the distance between a previous bead \(i\) and the next bead \(j\). In addition, for each EO group, a pair of carbon atoms is built whose positions are between the two oxygen atoms of two successive EO beads or (in the case of the last EO bead) between the oxygen atom of the EO bead and the Ot atom of the sulfate group. The construction of this pair is accomplished iteratively as follows:
   (a) We first construct a pair of carbon atoms, namely the dimer C\textsubscript{I}EO−C\textsubscript{II}EO, whose bond length is given by \(l_{C_{I}EO−C_{II}EO} = 0.12 \text{ nm} + \Delta l \cdot (\text{rand} - 0.5)\) with \(\Delta l = 0.05 \text{ nm}\) and ‘rand’ a random number in the interval \([0, 1)\). The center-of-mass of the dimer is randomly placed inside the sphere centered at EO bead position \(r_j\) with radius \(r_{sphere} = 0.12 \text{ nm}\) and a \(C_{I}EO − C_{II}EO\) bond vector that is randomly oriented in space. To accept the dimer just constructed, the distance of the carbon atoms of the dimer from the two oxygen atoms on the two successive EO beads should be less than \(R_{max} = 0.20 \text{ nm}\) (i.e. slightly greater than the length of the carbon–carbon bond) and clearly larger than 0.12 nm (approximately equal to the carbon–oxygen bond length). If this condition is satisfied, then the configuration is accepted, otherwise the iteration starts again from (a).
4. Then, we construct four carbon atoms in a ‘coil’ configuration at the position of the third tail bead, exactly as described in [17].
5. The construction of the AA configuration is completed by adding the hydrogen atoms.
6. Steps 1–5 are repeated for all SLE\textsubscript{n}S molecules in the simulation cell for the given CG micellar configuration.
7. The reversed-mapped AA configuration is completed by further inserting (randomly) the water molecules and the sodium ions.

2.2.3. AA model

The AA MD simulations with the reverse-mapped configurations are carried out with the GROMACS [38–40] software (version 4.6.7) in the NPT statistical ensemble at temperature \(T = 300 \text{ K}\) and pressure \(P = 1 \text{ atm}\) using the Nosé–Hoover [42, 43] thermostat and the Parrinello–Rachman [44] barostat to...
maintain temperature and pressure, respectively, fixed to their prescribed values. In our simulations, we utilized the generalized, explicit-atom CHARMM36 FF for all intra- and inter-molecular interactions between SLE\textsubscript{n}S molecules and counterions, along with the SPC/E model \cite{45} for water which is included in the CHARMM36 FF \cite{33–35} library for the description of solvent interactions. Our choice of the SPC/E model \cite{45} for water was motivated by its ability to provide more accurate predictions of the diffusion coefficient and viscosity (compared, for example, to the TIP3P model \cite{46} which is also compatible with the CHARMM36 FF). As it will be discussed further below, the choice of the water model (SPC/E or TIP3P) \cite{45,46} does not affect the predictions of our methodology for the mean aggregation number of micelles. The reverse-mapped AA simulations lasted up to about 60 ns.

3. Results and discussion

3.1. CG simulations

Each SLE\textsubscript{n}S system was simulated at two different values of the total surfactant concentration \(c_T=0.064\) and 0.107 M, both of which were above the first CMC of the three surfactants, approximately equal to 3.7, 2.6, and 2.2 ± 0.2 mM for SLE1S, SLE2S, and SLE3S, respectively \cite{24}.

As we have already mentioned in section 1, experimental data for single-component SLE\textsubscript{n}S solutions are scarce; nevertheless, we could come across a few studies in this regime of concentrations from which we got some data to compare the predictions of our simulations with. For the systems at the lower concentration, the (cubic) simulation cell had an edge length of \(\sim 27.5\) nm and contained 800 SLE\textsubscript{n}S molecules, while for the systems at the higher concentration, the simulation box had an edge length of \(\sim 27.9\) nm and contained 1400 SLE\textsubscript{n}S molecules. In all cases, the SLE\textsubscript{n}S molecules were initially placed randomly in the simulation cell. The large size of the simulation cells utilized was necessary not only in order to avoid any finite system size effects but also to make sure that a large number of micelles form for better statistics. Additional details regarding the simulation cells can be found in section S1 of the supporting information to this manuscript.

The formation of micelles and their size in the course of the simulation (either with the CG or with the AA FF) was quantified by computing the distribution function \(P(k)\) of the number \(k\) of SLE\textsubscript{n}S molecules per aggregate. Details about the calculation of \(P(k)\) are provided in section S2 of the supporting information. From the computed \(P(k)\) distributions in the equilibrated part of the simulation trajectory we also computed the mean aggregation number \(\langle k \rangle\). For the simulations with the CG model, it was found that for both concentrations \(c_T\) studied, three to four microseconds of simulation time were sufficient for \(\langle k \rangle\) to reach steady-state values (see section S3 of the supporting information to this manuscript). Initially (e.g. within the first few hundreds of nanoseconds), we observed the formation of relatively small micelles; at later times, these initially small micelles were seen either to fuse together or to attract additional SLE\textsubscript{n}S molecules, thus further increasing in size. Eventually, rather large micelles formed. Simulation predictions for the average value \(\langle k \rangle\) in the state of thermodynamic equilibrium as a function of total surfactant concentration \(c_T\) for all three different SLE\textsubscript{n}S surfactants investigated are depicted in figure 3. Data from experimental measurements are also reported in the figure for direct comparison. Typical configurations obtained from the CG and AA simulations are provided in figures 4 and 5, respectively.

We observe that for each one of the three SLE\textsubscript{n}S systems studied, the size of micelles increases with increasing value of \(c_T\). The MD predictions for \(\langle k \rangle\) from the modified MARTINI FF for SLE3S and SLE2S are...
in very good agreement with the experimental data. For SLE1S, we could not find any experimental data in the literature in the range of concentrations simulated here to compare our simulation results to; however, we were able to spot some $<k>$ values at concentrations between 0.04 and 0.06 M which we also report in figure 3 (the filled square symbols). According to our simulations, the value of $<k>$ for SLE1S is equal to 119 at 0.064 M which should be compared with the value of 79 at 0.06 M from experiments. Overall, however, the lack of independent and systematic experimental data on single-component SLE$nS$ surfactants does not allow us to draw safe conclusions regarding the exact variation of $<k>$ with $c_T$. The variation of $<k>$ with $c_T$ will be revisited in section 3.3 below where we will discuss the corresponding predictions from the more detailed and accurate AA simulations.

Another important finding from the simulations with the CG model is that the mean aggregation number of the micelles increases as the number of EO groups in the SLE$nS$ molecule decreases from three to one, keeping the total surfactant concentration constant. This is consistent with the experimental measurements of Anachkov et al [11] according to which SLE$nS$ molecules with a smaller number of EO
groups form larger micelles (for the same total surfactant concentration). A similar tendency has been reported by Zana and Weill [47] for the family of non-ionic surfactants C$_n$H$_{2n}$EO$_n$ with $n = 6, 8$ or $9$, where the mean aggregation number was found to increase as the number of EO groups was decreased. It also agrees with the DPD simulations of [18] where a mesoscopic model was employed for SLES molecules with some small amount of salt also added.

We also computed the radius of gyration $R_g$ of the micellar aggregates formed by calculating the eigenvalues of the corresponding radius-of-gyration matrix [48, 49] and the results (table 1) confirm that the size of the micelles increases as the number of EO groups decreases. According to the CG MD simulations, and for the range of concentrations examined here, the shape of the micelles observed in the case of SLE3S and SLE2S is spherical; in the case of SLE1S, on the other hand, it appears that spherical micelles coexist with elongated or rod-like ones. In general, the shape of micelles can be classified according to the value of the so called relative shape anisotropy (or asphericity) parameter $A$ [48, 49] which takes values between 0 and 1. Values of $A$ close to 0 indicate a spherical micelle while values of $A$ close to 1 indicate a rod-like micelle. For both SLE3S and SLE2S, the value of $A$ from the CG model is less than 0.2 implying mostly spherical micelles. On the other hand, for SLE1S, there exists an appreciable subpopulation of non-spherical micelles (about 15% for $c_T = 0.064$ M, and about 27% for $c_T = 0.107$ M) characterized by values of the asphericity parameter $A$ greater than 0.2 pointing to the presence of a good number of non-spherical micelles (compare, for example, figures 4(a)–(c)). More details regarding the shape of the micelles formed in the case of the three different SLENs systems studied here can be found in section S4 of the supporting information to this manuscript.

Overall, it is very pleasing that the proposed CG model offers a satisfactory (qualitative and quantitative) description of the micellar structure of SLENs surfactants. The agreement, in particular, between simulation and experimental data on the variation of the mean aggregation number of the micelles formed with total surfactant concentration is quite remarkable. Moreover, the model makes the important prediction that the size of the micelles formed is closely related to the number of EO groups present in the molecule; according to this, the mean aggregation number increases by decreasing the number of EO groups in the chain, keeping the total surfactant concentration constant. In the next section, we will check if these conclusions are supported from the more detailed, and more accurate, AA simulations.

### 3.2. Reverse-mapped structures

The reverse-mapped AA configuration that is built from the CG one purely on geometric criteria consists of more than 2 millions of interacting sites and may contain excessive atom–atom overlaps. This is corrected by performing a potential energy minimization for each reverse-mapped AA configuration. This procedure does not bring about any changes in the morphology (i.e. size and shape of the micelles) of the configuration. This is illustrated in figure 6 showing together an equilibrated CG configuration and the respective reverse-mapped AA one.

### 3.3. AA simulations

For each SLENs system, the generated AA configuration was used to perform a fully-atomistic MD simulation in the NPT ensemble at the same conditions of temperature and pressure ($T = 300$ K, $P = 1$ atm) as in the corresponding CG simulation. The AA simulations were carried out with the GROMACS [38–40] software using the generalized CHARMM36 FF [33–35] for SLENs molecules and the SPC/E model [45] for water molecules. Each one of the three SLENs systems ($n = 1, 2, 3$) was simulated at two different concentrations, a small one equal to $c_T = 0.064$ M (corresponding to 800 surfactant molecules in a simulation cell of edge length approximately equal to 27.5 nm), and a larger one equal to $c_T = 0.107$ M (corresponding to 1400 surfactant molecules in a simulation cell with edge length approximately equal to 27.9 nm). We report more details about the AA simulations of this phase of our work in section S5 of the supporting information to this manuscript. In the course of these AA simulations, the mean aggregation number was observed to reach quickly from the very first nanosecond of the simulation (figure 7) a constant

| System   | $c_T$ (M) | $R_g$ (nm) |
|----------|-----------|------------|
| SLE1S    | 0.064     | 2.39 ± 0.70|
| SLE1S    | 0.107     | 2.36 ± 0.40|
| SLE2S    | 0.064     | 1.94 ± 0.22|
| SLE2S    | 0.107     | 2.03 ± 0.27|
| SLE3S    | 0.064     | 1.82 ± 0.22|
| SLE3S    | 0.107     | 1.97 ± 0.18|
Figure 6. Characteristics snapshots from the simulations with the SLE2S system: (a) the CG configuration, and (b) the reverse-mapped AA one.

Figure 7. Mean aggregation number $<k>$ as a function of simulation time from the AA MD simulations of the SLE$n$S systems (with $n = 1, 2$ and 3) at two different concentrations $c_T$. Value which hardly changed after that. To confirm this, we extended some of these AA MD simulations to 60 ns, and no change was observed in the value of $<k>$.

MD-predicted mean aggregation numbers $<k>$ from the AA simulations as a function of SLE$n$S concentration are shown in figure 3. Additional details are provided in section S6 of the supporting information. For SLE3S and SLE2S, these values are very close to the corresponding ones from the CG model. Apparently, for these surfactants (SLE3S and SLE2S), the micelles generated by the CG model did not break to smaller micelles, which is very good since these $<k>$ values were already quite close to the corresponding experimental data. This is especial so for the case of SLE3S for which the value of the mean micelle size coincides practically with the one reported from experiments [11]. In contrast to SLE2S and SLE3S, in SLE1S the relatively large micelles formed in the course of the CG MD simulations were observed to break down to smaller ones, resulting in smaller $<k>$ values by approximately 15% for the lower and by 25% for the higher surfactant concentration studied, bringing simulation and experimental values much closer to each other. The breakage of large micelles occurs within one or two nanoseconds of simulation time from the beginning of the MD simulation, and is accompanied by a re-organization of molecules within the new micelles, without significant exchange of surfactants between micelles taking place. This is illustrated in figures 8(a)–(d). Several test MD simulations with different starting reverse-mapped AA configurations yielded practically identical $<k>$ values, thus proving that the above behavior was not a coincidence but a robust result (see below).

To examine the effect of the water model used in the AA simulations on the size of the micelles formed, we repeated some of these simulations using two different models, the SPC/E [45] and the TIP3P [46], both starting from the same reverse-mapped AA configuration. In all cases, the $<k>$ values came out to be the same, independent of the type of water model used. This is a pleasing result, because it proves that our approach is robust and reliable; and that the very good agreement with experimental data is not fortuitous but the result of a systematic and well-planned methodology. Again, the most important finding from both the CG and AA models is that by decreasing the number of EO groups in the SLE$n$S surfactant for the same surfactant concentration, the value of $<k>$ increases and, thus, larger micelles are formed. As already mentioned above, a similar tendency has been observed experimentally [47] for the non-ionic surfactants of the chemical type $C_{12}H_{25}EO_n$ (with $n = 6, 8$ and 9) where the mean aggregation number was found to
Figure 8. Typical system configurations (sodium ions and water molecules are omitted for clarity) from the AA MD simulation with SLE1S at $c_T = 0.107$ M: (a) the very initial (at $t = 0$ ns) reverse-mapped structure, (b) an early-time structure (at $t = 0.2$ ns) where some dissolution of large micelles has already occurred, (c) still an early-time structure but at a later time ($t = 1.7$ ns) where dissolution of large micelles had been completed, and (d) the final ($t = 50$ ns), and fully equilibrated structure.

| System  | $c_T$ (M) | $R_g$ (nm) | $\eta_0$ (cP) |
|---------|-----------|------------|--------------|
| SLE1S   | 0.064     | 1.72 ± 0.22| 0.76         |
| SLE1S   | 0.107     | 1.80 ± 0.21| 0.79         |
| SLE2S   | 0.064     | 1.63 ± 0.21| 0.80         |
| LE2S    | 0.107     | 1.72 ± 0.20| 0.91         |
| SLE3S   | 0.064     | 1.57 ± 0.17| 0.82         |
| SLE3S   | 0.107     | 1.70 ± 0.17| 1.15         |

reduce by increasing the number of EO groups. This shows the importance of the EO group on the morphological properties of the solutions, even without the presence of the anionic sulfate group.

The average shape of the micelles formed in the three different cases (SLE1S, SLE2S, and SLE3S) was examined by computing the relative anisotropy (asphericity) parameter $A$ [48, 49]. In general, we found that $A$ takes small values, less than 0.2, characteristic of nearly spherical micelles (for more details see section S7 of the supporting information to this manuscript). Nevertheless, as the number of EO groups increases (i.e. as we go from SLE1S to SLE2S, and then to SLE3S) keeping the concentration constant, $A$ takes even smaller values. This indicates that shape anisotropy (deviation from the spherical shape) becomes more pronounced as the number of EO groups along the chain decreases. However, the small values of $A$ computed in all cases (less than 0.2) suggest that micelles with rod-like shape are not present in the solutions. This is also confirmed in the snapshots shown in figures 5(a)–(c). On the contrary, the CG MD simulations had indicated the formation of some highly anisotropic micelles for SLE1S (figure 4(a)).

We have also quantified the size of the micelles by computing their radius of gyration $R_g$ and the results are displayed in table 2. Calculated $R_g$ values range from 1.57 to 1.72 nm at $c_T = 0.064$ M, and from 1.70 to 1.80 nm at concentration $c_T = 0.107$ M. For both concentrations examined, $R_g$ exhibits a small increase (albeit not significant) as the number of EO groups increases.

A few important remarks are in order here regarding our three-step simulation methodology. First, it is important to note that the actual time for micelles to self-assemble from individual surfactants is much longer than the time to re-equilibrate micelle size starting from a reverse-mapped pre-equilibrated CG configurations. The latter mechanism consists of two different stages: a very short one (on the order of a few nanoseconds) involving the breaking of several large micelles, and a longer one (ranging from a few tens up to a few hundreds of nanoseconds) wherein individual surfactant molecules are exchanged between the micelles already formed leading to further adjustment of micelle size. According to our simulations, this second mechanism does not affect considerably the final size of the micelles. Micelle breakup during the very first nanoseconds of the AA simulation is the dominant mechanism, bringing quickly the size of micelles formed close to their final values. The second mechanism through exchange of individual surfactant molecules (which is a slower process) makes only a secondary contribution. Second, the quality of the
predictions from the reverse-mapped AA simulations can be increased by running several of them (after converting many different pre-equilibrated CG configurations to AA ones), and averaging. For SLE1S, such an approach gave the results that are summarized in table 3.

Based on these, the updated values for the mean aggregation number of SLE1S are \( <k> = 89 \pm 7 \) at \( c_T = 0.064 \) M, and \( <k> = 120 \pm 7 \) at \( c_T = 0.107 \) M, which have to be compared to the respective values of \( <k> = 101 \) and \( <k> = 112 \) for the two concentrations from the corresponding single MD runs (figure 1) for this system. Third, the predictions form the CG MD simulations for the structural properties reported in table 1 should be taken with some caution because of the approximate character of the corresponding simulations. Much more reliable are the results from the short AA–MD simulations, despite their short duration (and thus the neglect of contributions from the surfactant exchange mechanism already discussed above). It is reassuring, however, that the CG simulations provide qualitatively correct results.

From a physics point of view, the most important result of our work is the prediction (both from the CG and the short AA simulations) that the mean aggregation number decreases with increasing number of ethoxy groups along the surfactant. As already mentioned, Zana and Weill [47] had reported a similar observation for aqueous solutions of alkyl poly(oxyethylene glycol) where the mean aggregation number was found to decrease as the number of ethylene oxide groups in the surfactant was increased. Such a size dependence can be explained by considering that an increase in the number of ethoxy groups increases the hydrophilic character of the molecule, thus also its tendency to dissolve in the solvent, implying the formation of micelles with a smaller size. If this is accompanied by an increase in the total number of micelles or not is something that deserves further analysis. Moreover, SDS surfactants can be considered as a special case of SLEnS corresponding to \( n = 0 \). And from our earlier work [17], we recall that at the same total surfactant concentration, SDS micelles are characterized by mean aggregation numbers that are comparable to those of SLEnS. Thus, an explanation in terms of the degree of hydrophilicity of the surfactant seems plausible (SDS molecules are even less hydrophilic than SLE1S ones) although a more detailed analysis should have considered additional factors such as the number of aggregates, the number of free surfactants, the relative flexibility of the molecules, and the degree of intermolecular packing inside micelles which may very well depend on the relative length of hydrophobic tails and hydrophilic heads. We hope to carry out such an analysis in the future.

### 3.4. Solution viscosity from the AA simulations

From the AA MD simulations we also deduced the zero-shear rate viscosity \( \eta_0 \) of the investigated solutions by resorting to the Green–Kubo formalism [50]. The methodology involves the integration in time of the autocorrelation function \( P_{\alpha\beta} (\alpha \text{ and } \beta \text{ denote any of the } x, y \text{ and } z \text{ components of the Cartesian coordinate system}) \) of the off-diagonal elements of the pressure tensor and computing the average of the three contributions from the \( P_{xy}, P_{xz} \text{ and } P_{yz} \) elements. The results obtained are reported in table 2. Our simulations indicate a strong correlation of the zero shear rate viscosity with the concentration of the solution in surfactant molecules, as well as with the number of EO groups per molecule. More specifically, the viscosity increases: (a) as the total concentration in SLEnS molecules increases (keeping the number of EO groups the same), and (b) as the number of EO groups in the surfactant increases (keeping the surfactant concentration constant).

It would be interesting to check if there exists a possible correlation between the zero shear rate viscosity and the underlying organization of micelles in the solution. To this, we computed the radial pair correlation function of the micelles’ centers-of-mass (com) \( g_{\text{com}} (r) \), and the results can be seen in figure 9. From the calculated \( g_{\text{com}} (r) \) curves we can draw the following observations: (a) the minimum distance between the micelles’ centers-of-mass decreases somewhat as the concentration of the solution increases (keeping the number of EO groups constant); (b) the inter-micellar distance increases (although not considerably) as the number of EO groups in the surfactant decreases (keeping the solution concentration constant), and (c) the characteristic peaks on the curve tend to decrease in amplitude and broaden somewhat in width as the
number of EO groups decreases (keeping the concentration of the solution in surfactants constant).
Observation (a) helps us interpret the slight increase in the value of the zero shear rate viscosity with increasing surfactant concentration (within the given family). Observations (b) and (c) indicate that, with decreasing number of EO groups in the surfactant, the corresponding solutions become more dilute as far as the number of micelles formed per unit volume is concerned. In addition, the actual geometrical size of the micelles does not change significantly (table 2) despite that their mean aggregation number increases. It is therefore the presence of micelles with a smaller number of EO groups per chain that are similar in shape but present in a lower concentration that can explain the slight decrease in the zero-shear rate viscosity at the same total concentration of the solution in SLES molecules.

4. Discussion and conclusions

We have studied the micellar structure and zero shear rate viscosity of strictly monodisperse, dilute aqueous micellar solutions of SLE\(n\)S with the chemical formula CH\(_3\)(CH\(_2\))\(_{11}\)(OCH\(_2\)CH\(_2\))\(_n\)OSO\(_3\)Na with \(n = 1, 2\) and 3 using a recently introduced computational approach involving CG MARTINI-type of simulations followed by reverse-mapped AA ones [17]. Even with the CG model, the MD predictions for the mean aggregation number (average size of micelles in the solution) are in favorable agreement with available experimental data for SLE2S and SLE3S, and in reasonably good agreement for SLE1S. The CG simulations further indicate that the mean aggregation number in such monodisperse (i.e. single-component) SLE\(n\)S solutions increases as the number of EO groups in the surfactant decreases (while keeping the concentration of the solution in surfactants the same).

An attractive feature of our approach is that in our simulations, the AA simulations are started from configurations fully pre-equilibrated with the CG model, rather than from a completely random distribution of surfactants in the cell. We have avoided to perform brute force AA MD simulations, since exceedingly long simulation times would be needed to correctly describe the fusion of smaller micelles into larger ones; the CG model accelerates this process by generating relatively large micelles, although not necessarily of the correct size (as, for example, found in experiments).

The detailed AA simulations with the generalized CHARMM36 FF [33–35] lead to micelles of equal or smaller size than those obtained from the CG model, since many of the pre-existing big micelles in the simulation cell quickly break down to smaller ones. In particular, in the simulations with SLE1S, smaller micelles are observed while in the simulations with SLE2S and SLE3S, the mean aggregation numbers remain practically the same between CG and AA simulations.

Our simulations confirm that the mean aggregation number is strongly related to the total surfactant concentration in the solution and the number of EO groups. In particular, for a given concentration, the mean aggregation number increases with decreasing number of EO groups per surfactant. This observation deserves to be explored experimentally more systematically and carefully, especially in light of the rather limited number of experimental investigations currently in the field. We hope that our initiative to address single-component systems can motivate a more systematic experimental study of these systems.

We have also found that the zero shear rate viscosity of aqueous SLE\(n\)S solutions increases with: (a) increasing number of EO groups (for the same total surfactant concentration), and (b) increasing surfactant concentration (for the same number of EO groups in the surfactant). Overall, the zero shear viscosity

![Figure 9](image-url)
decreases if the mean inter-micellar distance increases, and increases when inter-micellar correlations are enhanced.

From a methodological point of view, a potential drawback of our approach is that refinement of micelle size by converting pre-equilibrated CG configurations to AA ones and running short runs is not accompanied by significant surfactant exchange [51]. Moreover, the approach will presumably fail if the CG model gives micelles that are too small, since the AA simulations do not allow micelle fusion. One way to assess the accuracy and possible limitations of the method would be to compute the distribution of micelle sizes before and after refinement with the AA model, and check how different the latter is from the Gaussian distribution. Of course, for a population of sizes to obey a Gaussian or Gaussian-like distribution, a prerequisite is that the population analyzed be sufficiently large. Thus, we need to perform additional simulations in the near future with the AA model (starting from pre-equilibrated CG structures and reverse-mapping) for all SLEnt5 systems and concentrations studied here. Then, by comparing the breakage-induced micelle size distribution with the hypothetical ‘true’ Gaussian one will provide us with an assessment of the benefits and limitations of the method. In the literature, a way to get an accurate micelle size distribution is by using an umbrella sampling method as, for example, described by Yuan and Larson [52]. Applying this to the AA simulations of the present work will also be pursued.

Overall, our approach appears to be able to describe the structure and morphology of aqueous surfactant solutions quite well. We therefore hope that it can motivate additional studies in the future of other classes of surfactants that include e.g. non-ionic, gemini, or even bio-inspired structures [2, 4]. In the long term, it has the potential to lead to a robust computational framework for addressing structure-property relationships in formulations of industrial relevance by addressing polydisperse systems and new surfactants.

Data availability statement

The data that support the findings of this study are available upon reasonable request from the authors.

Acknowledgments

Financial support for this study has been provided by the FORCE (Formulations and Computational Engineering) project funded by the Horizon 2020 EC program under the NMBP-23-2016 call, with Grant Agreement Number 721027 (http://the-force-project.eu). We also acknowledge the Greek Research and Technology Network (GRNET) for generous allocation of computational time on the National HPC facility-ARIS, based in Athens, Greece, under projects HDevCG (pr008024) and PolyMplex_II (pr008042).

ORCID iD

Vlasis G Mavrantzas https://orcid.org/0000-0003-3599-0676

References

[1] Zana R and Kaler E W (eds) 2007 Giant Micelles Properties and Applications (Surfactant Science Series vol 140) (Boca Raton, FL: CRC Press)
[2] Zana R and Xia J (eds) 2004 Gemini Surfactants Synthesis, Interfacial and Solution-Phase Behavior, and Applications (New York: Marcel Dekker, Inc.)
[3] Holmberg K, Lönnson B, Kronberg B and Lindman B 2003 Surfactants and Polymers in Aqueous Solution 2nd edn (New York: Wiley)
[4] Esumi K and Ueno M (eds) 2003 Structure—Performance Relationships in Surfactants 2nd edn (New York: Marcel Dekker, Inc.)
[5] Goddard E D and Gruber J V (eds) 1999 Principles of Polymer Science and Technology in Cosmetics and Personal Care (New York: Marcel Dekker, Inc.)
[6] Cornwell P A 2018 A review of shampoo surfactant technology: consumer benefits, raw materials and recent developments Int. J. Cosmet. Sci. 40 16
[7] Bondi A M, Marks J L, Wroblewski L B, Raatikainen H S, Lenox S R and Gebhardt K E 2015 Human and environmental toxicity of sodium laurel sulfate (SLS): evidence for safe use in household cleaning products Environ. Health Insights 9 27
[8] Kekicheff P, Grabriedelmadelmont C and Ollivon M 1989 Phase diagram of sodium dodecyl sulfate–water system: a calorimetric study J. Colloid Interface Sci. 131 112
[9] Hammouda B 2013 Temperature effect on the nanostructure of SDS micelles in water J. Res. Natl Inst. Stand. Technol. 118 151
[10] Christov N C, Denkov N D, Kralchevsky P A and Ananthapadmanabhan K P and Lips A 2004 Synergistic sphere-to-rod micelle transition in mixed solutions of sodium dodecyl sulfate and cocamidopropyl betaine Langmuir 20 565
[11] Anachkov S E, Danov K D, Basheva E S, Kralchevsky P A and Ananthapadmanabhan K P 2012 Determination of the aggregation number and charge of ionic surfactant micelles from the stepwise thickening of foam films Adv. Colloid Interface Sci. 183 55
[12] Jusufi A, Hyninnen A P and Panagiotopoulos A Z 2008 Implicit solvent models for micellization of ionic surfactants J. Phys. Chem. B 112 13763
[13] Wang S H and Larson R G 2015 Coarse-grained molecular dynamics simulation of self-assembly and surface adsorption of ionic surfactants using an implicit water model Langmuir 31 1262
[50] Mintis D G, Dompe M, Kamperman M and Mavrantzas V G 2020 Effect of polymer concentration on structure and dynamics of short poly (N, N-dimethylaminoethyl methacrylate) in aqueous solution: a combined experimental and molecular dynamics study J. Phys. Chem. B 124 240

[51] Yuan F, Wang S and Larson R G 2015 Potentials of mean force and escape times of surfactants from micelles and hydrophobic surfaces using molecular dynamics simulations Langmuir 31 1336

[52] Yuan F and Larson R G 2015 Multiscale molecular dynamics simulations of model hydrophobically modified ethylene oxide urethane micelles J. Phys. Chem. B 119 12540