Atomistic Molecular Dynamics Simulations Of Spontaneous Aggregation Of Linoleic Acid Micelles In Water

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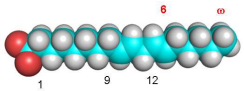
INTRODUCTION



LIN (an ω-6 fatty acid) (figure 1) in water can form various structures depending on the experimental parameters. For example, it has been shown that LIN aggregate into spherical micelles at pH = 11.5 aqueous solution/medium with NaOH [1]. Micelles of LIN molecules are also used as templates to construct metal nanoparticles [2] (figure 2) and despite the widespread interest in nanosciences their structure is not well documented. We have examined by MD the micellar structure of LIN micelle solvated in explicit water with the influence of the protocol (preformed vs. self-aggregated). The aggregates obtained by the two approaches are most often similar, but sometimes they can differ. To examine this aspect, we have performed two different MD of LIN micelle with 60 molecules at ambient conditions (P = 0.1 MPa and T = 300 K).

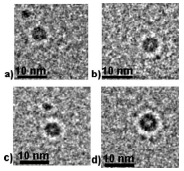


Figure 2. Cryo-TEM images of an aqueous sample of linoleate (10 mmol•L^{-1}) and silver ions (10 mmol•L^{-1}) irradiated with γ-rays up to 20 kGy. Taken from [2].

MODELISATION OF THE LINOLEIC ACID MICELLE

The aggregation number N for the micelle simulation was obtained with a geometric model. The linoleic acid molecule displays a carboxylate headgroup that presents a surface (S_h) close to the section of the CH_2- groups (21 Å^2). Considering the headgroups are at the micelle surface and if the micellar hydrophobic core contains only the alkyl chains (i.e. with x*N methyl groups, with $0 < x \leq 17$), we can write:

Volume and surface of the micelle:

$$V_m = NLS_h = \frac{4}{3}\pi R_M^3$$

$$S_m = (1+x)NS_h = 4\pi R_M^2$$

Where L is the total lipid length (23 Å), R_M the micelle radius and N the aggregation number, respectively. Combining the two expressions, we obtain:

$$3L = (1+x)R_M$$

Since the simulated micelle exhibits a significant amount of methyl groups at its surface, we can obtain f, fraction of hydrophilic surface over the micelle surface:

$$f = 1/(1+x)$$

We have tested different values of N (45, 60, 75 and 90) and compared the values obtained for R_M and *f*. Similar evolution along with the number of aggregation is found with best agreement for N=60 with an geometrical estimation of R_M=19.4 Å and *f*= 26.6%.

SIMULATIONS DETAILS

Two systems were constructed with two different approaches (i.e. "preformed" vs. "self-aggregated") containing 60 monomers of linoleic acid (LIN) molecule, 60 Na^+ and 9997 TIP3 water molecules each, corresponding to a detergent concentration of 0.3 M. The preformed micelle (called M60-P) was constructed with the packmol program [4]. For the self-aggregated system (M60-S), LIN and Na+ were randomly placed in a water cubic box (a = 69 Å). The resulting systems were minimized, equilibrated and subject to NPT (P = 0. 1 MPa and T= 300 K) molecular dynamics simulations with full electrostatics and periodic bound conditions using ORAC MD package [5]. We used the CHARMM27 force field for lipids with the default cis torsions parameters for the double bonds of the LIN molecule [6].

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LINOLEIC MICELLE SELF-ASSEMBLY

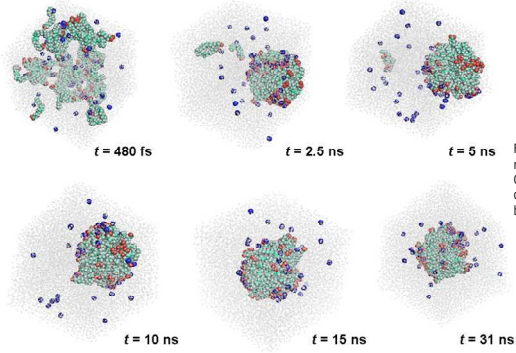
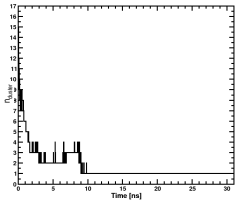
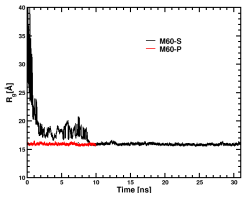
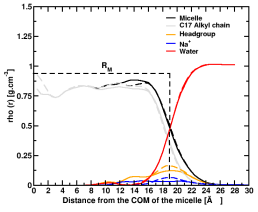


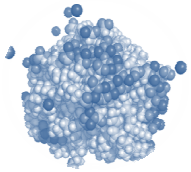
Figure 3. Aggregation process of a LIN monomers into a micelle versus time. LIN and Na^+ molecules are drawn in CPK style while water is represented as grey lines. Carbon, oxygen, hydrogen and ions are in magenta, red, white and blue colors, respectively

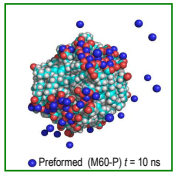
COMPARISON BETWEEN THE SELF-ASSEMBLED AND PREFORMED MICELLE

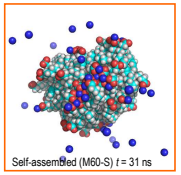












- Micelle aggregation process is fast: < 10 ns (hydrophobic effect) with two stages: a fast and a slow periods
- During the fast stage LIN clusters collapse, fragment and collapse.
- At t = ~2.5 ns, a micelle is formed with ~57 - 58 monomers of LIN molecules and it takes ~ 7.5 ns to form a complete and stable micelle with all the lipids. A similar kinetic behavior was also found by other authors (such as Marrink et al. 2000)

The figures and the table show that the self-aggregated and preformed micelles have a similar size, shape and microstructures. With the micelle radial profiles $\rho(r)$ one can estimate the micellar radius (RM). The values of R_M for the both are around 19.0 ± 0.5 Å, close to the value obtained from the geometrical model (19.4 Å) or with $R_M=(5/3)^{0.5}R_g$ (20.6 ± 0.1 Å)

System	a/c	R_M (Å)	f (%)	$n_{hg\text{-}OW}$
Geom. Model	-	19.4	26.6	-
M60-S	1.24	20.6	28.0	3.8 -3.9
M60-P	1.23	20.6	26.5	3.8 –3.9

Table 1. Summary of the structural parameters calculated from the last 20 ns (M60-S) and 10 ns (M60-P). a/c is the average ratio between the major and minor semi-axes lengths obtained from the inertia tensors. RM is the effective average radius $(5/3R_g)^{0.5}$ of the micelle. *f* is the average fraction of hydrophilic surface over the micelle surface calculated with the Voronoi surface. $n_{hg\text{-}ow}$ is the hydration number of the LIN headgroup.

CONCLUSIONS

- Spontaneous aggregation of LIN monomers into a micelle is fast (driven by the hydrophobic effect): < 10 ns and undergoes two stages with a fast and a slow period at t < ~2.5 ns and ~2.5 ns < t < 10 ns of the run, respectively.
- The self-aggregated micelle has a stable structure after 10 ns of simulation and has similar structure than to the preformed one.
- The two micelles have a slightly ellipsoidal shape (a/c=1.2) and a similar microstructure.
- Dimension of the two micelles (20 Å) is close to the size obtained from the geometrical model (19.4 Å)
- The micellar surfaces are mainly hydrophobic with 73 % of their surface covered by the LIN tails in agreement with the geometric model (73.4 %)
- Na^+ ions are restricted in the polar layer of the micelle and interact with 2 - 3 LIN headgroups.