

# Structure and Dynamics of Cholic Acid and Dodecylphosphocholine-Cholic Acid Aggregates

Abdallah Sayyed-Ahmad, Lenard M Lichtenberger and Alemayehu A Gorfe\*  
Department of Integrative Biology and Pharmacology, The University of Texas Health  
Science Center at Houston, Houston, Texas 77030, USA

\*Corresponding Author

[Alemayehu.G.Abebe@uth.tmc.edu](mailto:Alemayehu.G.Abebe@uth.tmc.edu)

Phone: 713-300-753

Fax: 713-500-7444

## S1. Analysis

The VMD software<sup>1</sup> and in-house scripts were used for visualization and for most of the trajectory analysis. The following reaction coordinates and order parameters were used to characterize the structure and thermodynamics of the CA and DPC-CA micelles.

### a. CA aggregate identification and characterization

First, an empirical criterion for identifying CA micellar aggregates was defined as follows. Two CA molecules are considered to be in the same aggregate if the distance between their  $C_{18}$  atoms is less than 10 Å, or if they are hydrogen bonded (defined using a distance cutoff of 3.0 Å and an angle cutoff of 30°). Different cut-offs and visual inspection confirmed that these criteria faithfully capture CA aggregates seen in the simulations. Second, the internal organization of the primary CA aggregates was characterized by examining the orientation of the CA rings with respect to the radial direction from the center of mass for each aggregate size. This is achieved by computing the angle  $\varepsilon$  between the vectors  $A_{n_{\text{center}}} \rightarrow C_{13}$  and  $C_{18} \rightarrow C_{13}$  ( $A_{n_{\text{center}}}$  is the center of mass of an aggregate of size  $n$ ). The probability distributions of  $\varepsilon$  for each aggregate size provide information on the pattern of the radial organization of the CA aggregates. In particular,  $0^\circ < \varepsilon < 90^\circ$  would indicate that the hydrophobic faces of the CA molecules are pointing towards the core of the aggregate while  $90^\circ < \varepsilon < 180^\circ$  indicates the opposite.

The thermodynamic properties of the CA aggregates were studied based on the weight average and the number average aggregation numbers,  $N_w$  and  $N_N$ , which are calculated as

$$N_w = \frac{\sum_{n>1} n^2 A_n}{\sum_{n>1} n A_n} \quad (1)$$

and

$$N_N = \frac{\sum_{n>1} n A_n}{\sum_{n>1} A_n} \quad (2)$$

$A_n$  is the number of CA micellar aggregates consisting of  $n$  CA molecules. The more  $N_w$  and  $N_N$  differ, the higher the size polydispersity of the aggregates<sup>2,3</sup>.

### b. DPC-CA micelle identification and characterization

Since there is no unique way to unambiguously determine what constitutes a DPC-CA micelle, a criterion needs to be defined empirically. Here DPC-CA micelle is defined as the DPC micelle, which remained intact throughout all the simulations, plus all CA molecules whose  $C_{18}$  or  $C_{19}$  atom is within 4 Å of any DPC atom. Tests with different cut-offs and visual inspection confirmed that this criterion captures all CA molecules adsorbed onto the DPC micelle.

CA and DPC molecules aggregate to minimize the exposure of their hydrophobic side and tail to water, respectively. Change in the total solvent accessible surface area (SASA) is thus a good measure of the extent to which CA and DPC molecules aggregate. SASA was determined by rolling a probe sphere of radius 1.4 Å over the surfaces of all solute atoms (i.e. CA and DPC). Another measure for the structure, stability and size of the DPC-CA micelle as well as for the convergence of the MD simulations is the radius of gyration of the mixed micelle,  $R_{\text{gyr}}$ , defined as

$$R_{\text{gyr}} = \frac{1}{N_{\text{tot}}} \sqrt{\sum_{i \in \text{DPC-CA}} (r_i - r_c)^2}, \quad (3)$$

where  $N_{\text{tot}}$  is the total number of atoms in the DPC-CA micelle and  $r_i$  is the distance of atom  $i$  from the micelle geometric center ( $r_c$ ).

To investigate the global structure of the DPC-CA micelle, the moment of inertia tensor,  $\mathbf{I}$ , was calculated as

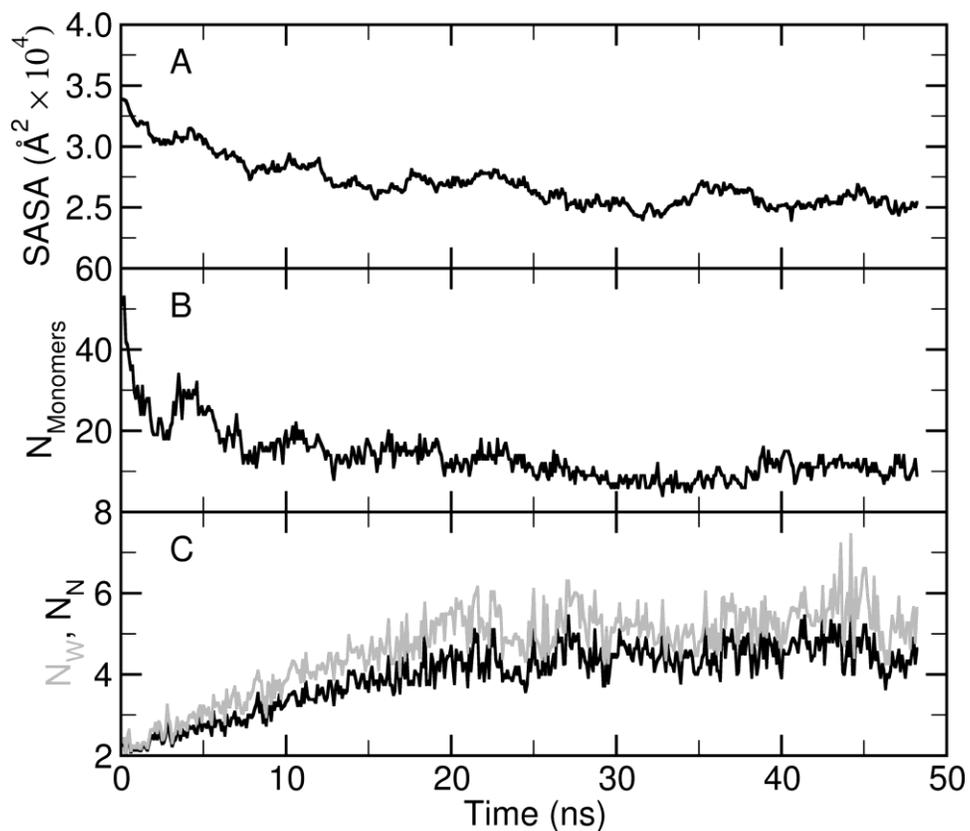
$$\mathbf{I} = \sum_{k=1}^{N_{\text{tot}}} \begin{bmatrix} y_k^2 + z_k^2 & -x_k y_k & -x_k z_k \\ -x_k y_k & x_k^2 + z_k^2 & -y_k z_k \\ -x_k z_k & -y_k z_k & x_k^2 + y_k^2 \end{bmatrix}. \quad (4)$$

The three principal moments of inertia of the DPC-CA micelle ( $I_1$ ,  $I_2$  and  $I_3$ ) are then determined by diagonalizing  $\mathbf{I}$ . This transformation is a rotation of  $\mathbf{I}$  so that the principal axes coincide with the Cartesian coordinate axes.  $I_1$ ,  $I_2$  and  $I_3$  are the ordered eigenvalues of  $\mathbf{I}$  (i.e.  $I_1 \geq I_2 \geq I_3$ ) and describe the size of the micelle in each of the three principal directions.

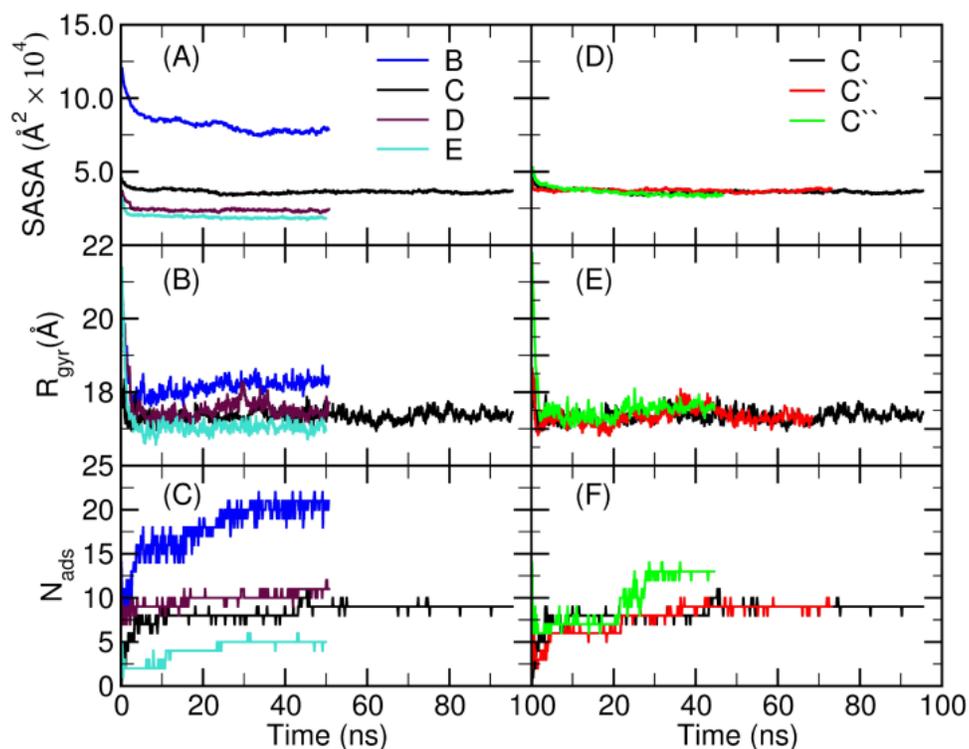
## Literature Cited

- (1) Humphrey, W.; Dalke, A.; Schulten, K. *Journal of Molecular Graphics* **1996**, *14*, 33.
- (2) Lazaridis, T.; Mallik, B.; Chen, Y. *The Journal of Physical Chemistry B* **2005**, *109*, 15098.
- (3) Nagarajan, R.; Wang, C.-C. *Langmuir* **2000**, *16*, 5242.

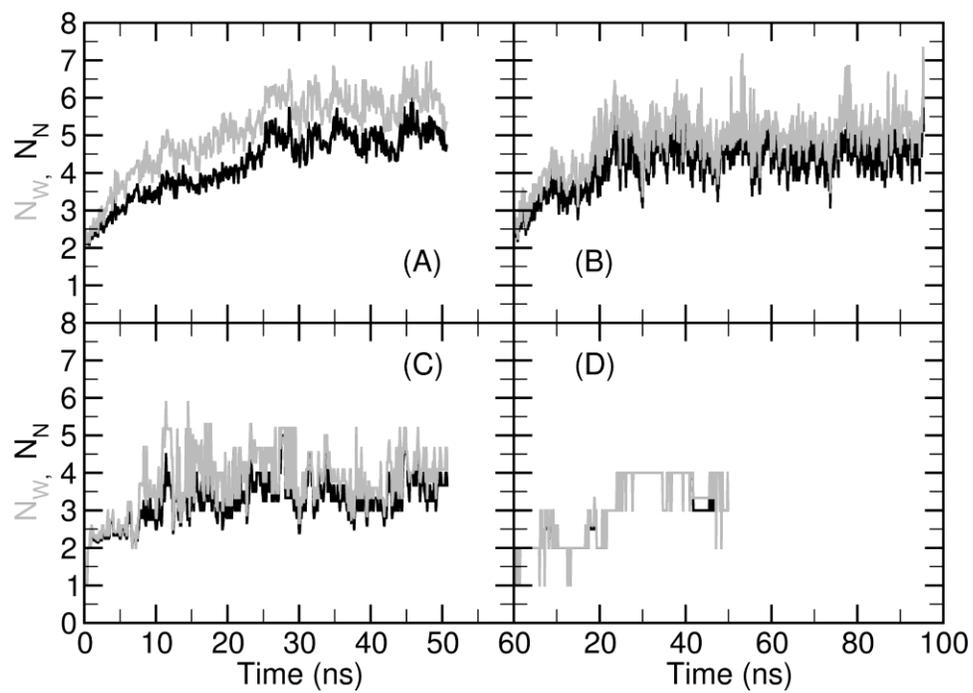
## S2. Supplementary Figures



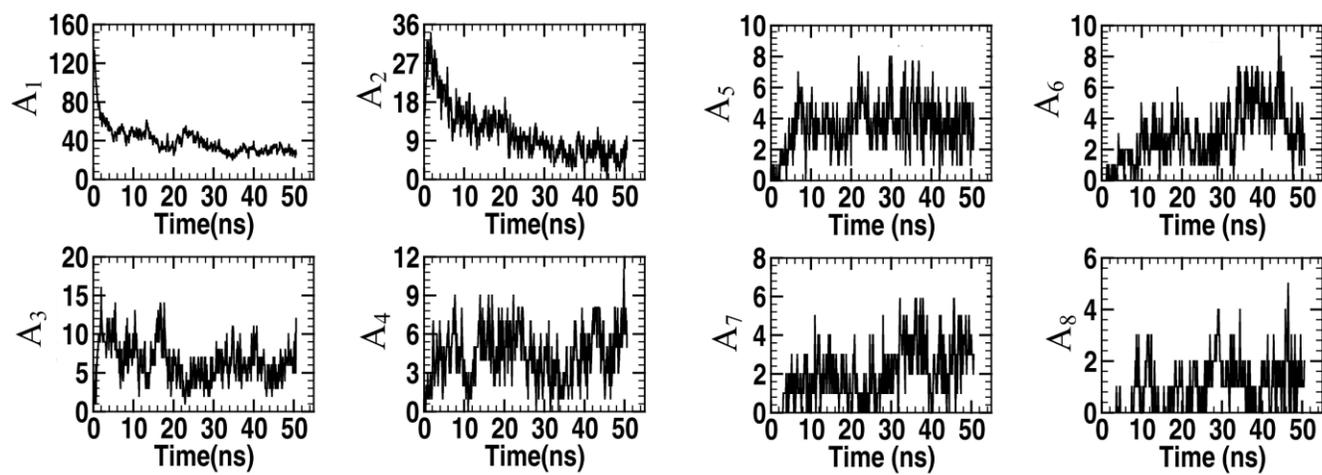
**Figure S1:** Time evolution of various structural parameters during the simulation of pure CA. (A) Solvent accessible surface area (SASA), (B) number of CA monomers ( $N_{\text{Monomer}}$ ) and (C) the weight average ( $N_W$ ) and number average ( $N_N$ ) aggregation numbers.



**Figure S2:** Time evolution of the structural parameters used to monitor the formation of a DPC-CA micelle during simulations B, C, D and E. (A) and (D) Solvent-accessible surface area (SASA), (B) and (E) radius of gyration ( $R_{\text{gyr}}$ ) and (C) and (F) number of CA monomers adsorbed onto the DPC micelle ( $N_{\text{ads}}$ ). The SASA plotted here measures the overall behavior of the solutes (DPC and CA) in the system, and therefore contain information on both CA self-aggregation as well as their adsorption onto the pre-formed DPC micelle. It could also be modulated to some degree by the slight deformation of the DPC micelle upon CA adsorption. (A), (B) and (C) present results from simulations B, C, D and E while (D), (E) and (F) describe results from simulations of 1:1 DPC:CA mixtures at different initial organization and total volume (simulations C, C' and C'').



**Figure S3:** The weight average ( $N_w$ ) and number average ( $N_n$ ) aggregation numbers as a function of time for simulations B, C, D and E, respectively.



**Figure S4:** Time evolution of the number of CA monomers and aggregates of size 2 to 8 as identified from simulation B.