

# MD Simulation of a Solvated Dodecylphosphocholine Micelle.

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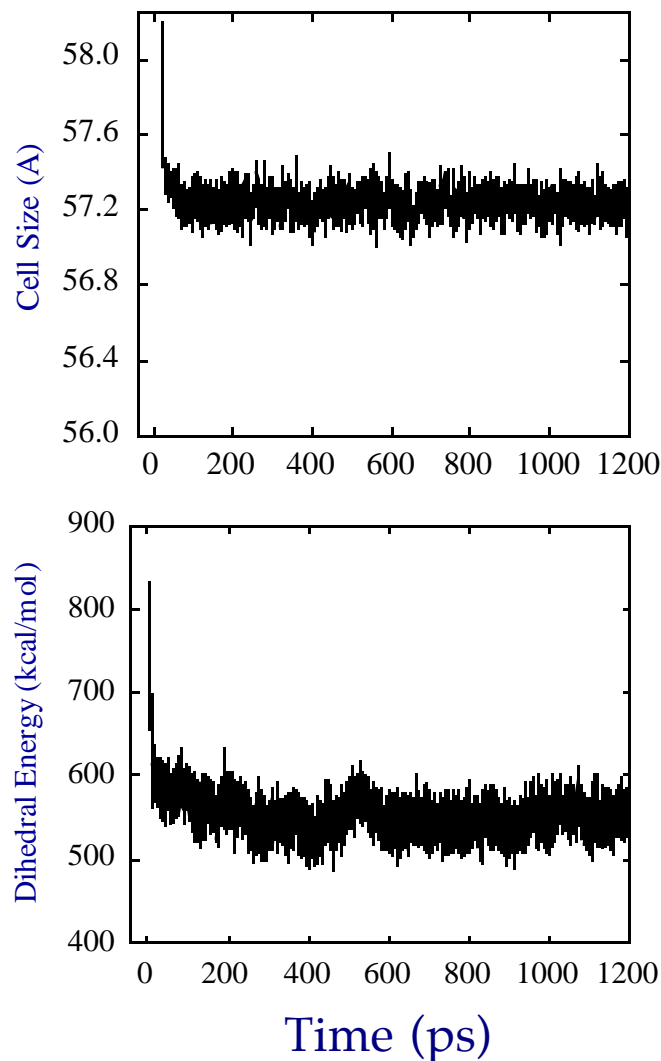
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## Introduction

The existence of a polar headgroup/water interface, and the separation of hydrophobic and hydrophilic regions of a micellar system has been utilized extensively as a model for biological membranes. Many experimental techniques, most notably, nuclear magnetic resonance (NMR) and fluorescence spectroscopy, are used in the study of peptides and proteins with micelles. The dodecylphosphocholine (DPC) and the sodium dodecylsulfate (SDS) micelle are currently the most frequently used membrane mimics for studies of peptide/membrane interaction by high resolution NMR techniques. Molecular dynamics (MD) simulations have been used to investigate the size, shape, hydration and dynamics of micelles. MD simulations have also been performed of peptides partitioned into the SDS micelle (see Poster #211). It is therefore of interest to have a simulated model of the DPC micelle to compare with the SDS micelle and lipid bilayers in MD studies of peptide-micelle interactions. The analysis of a 1.02 nanosecond MD simulation of a solvated DPC micelle is presented. This analysis includes the equilibration of the system, the shape, water penetration, conformational distribution of the hydrocarbon chains, and dynamics of the micelle.

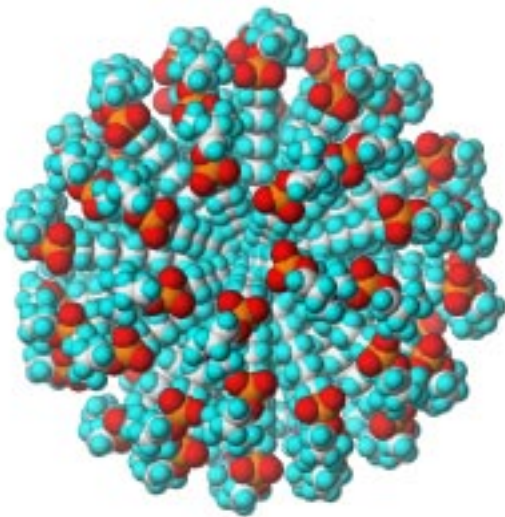
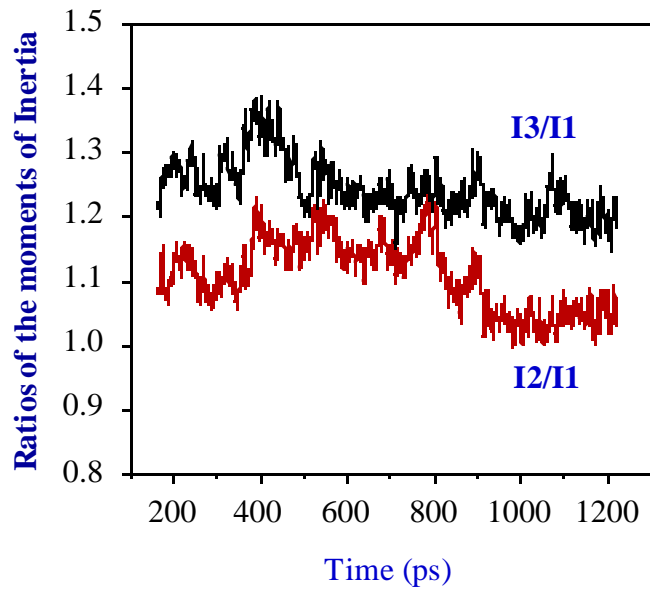
## *Molecular Dynamics Simulation Methods*

The CHARMM all22 force field was used for the lipids in which the parameters for the phosphocholine head group were combined with the parameters for the dodecyl tail of dodecylsulfate to create a dodecylphosphocholine monomer. The TIP3P model was used for water. The final system consisted of 60 DPC monomers and 5,294 water molecules for a total of 19,362 atoms. The system was equilibrated for 160 ps (140 ps in the NPT ensemble). The production simulation was performed for 1.06 nanoseconds in the NPT ensemble. The volume of the simulation cell as well as the dihedral energy, vdW and electrostatic energy all equilibrated rapidly.

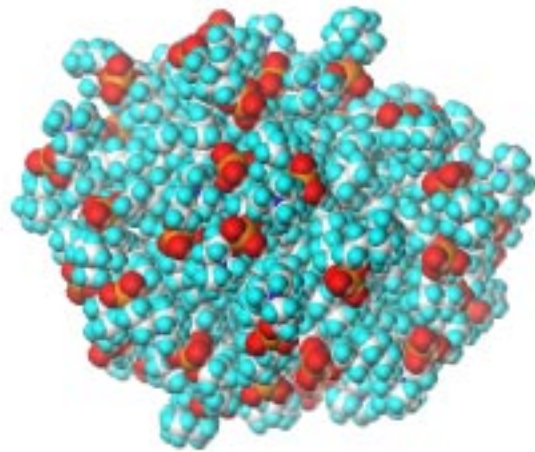


## Micelle Shape

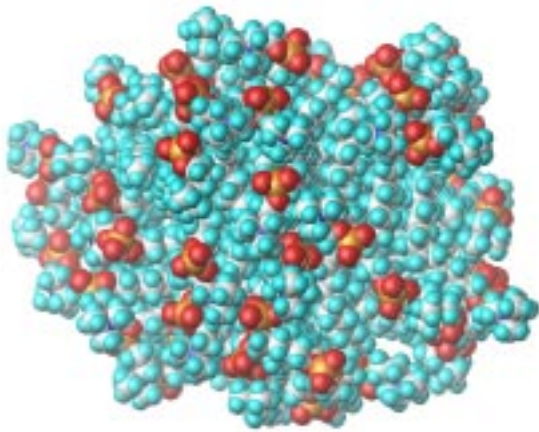
The average moments of inertia of the DPC micelle over the 1.02 ns simulation are in the ratio of 1.24: 1.11: 1 indicating the deviation from spherical shape to that of a prolate.



Initial Construction of DPC micelle with methylene chains in an all trans configuration

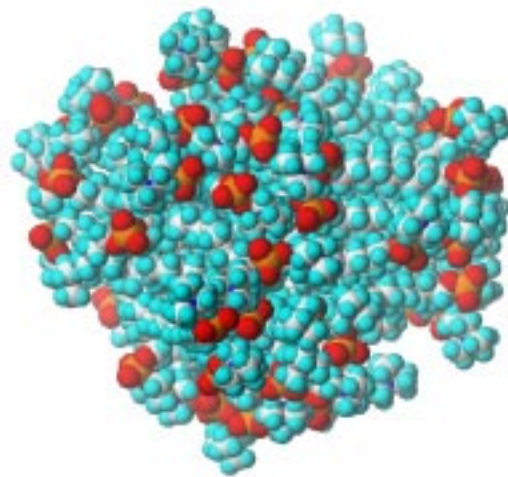


200 ps  
Equilibration to a prolate ellipsoidal shape



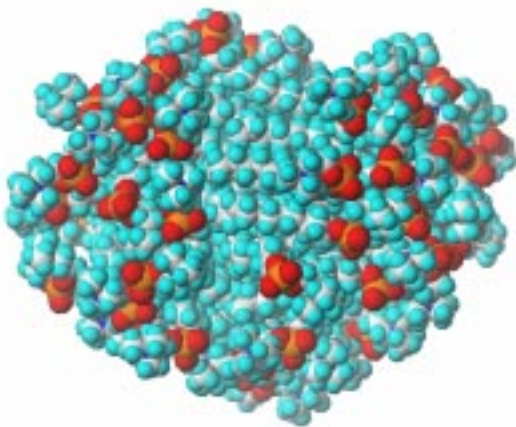
400 ps

A few lipids orient on the surface  
of the micelle



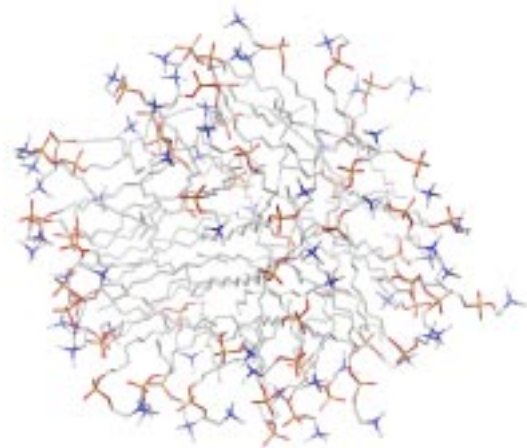
700 ps

Formation of a bilayer-like  
arrangement of some lipids



900 ps

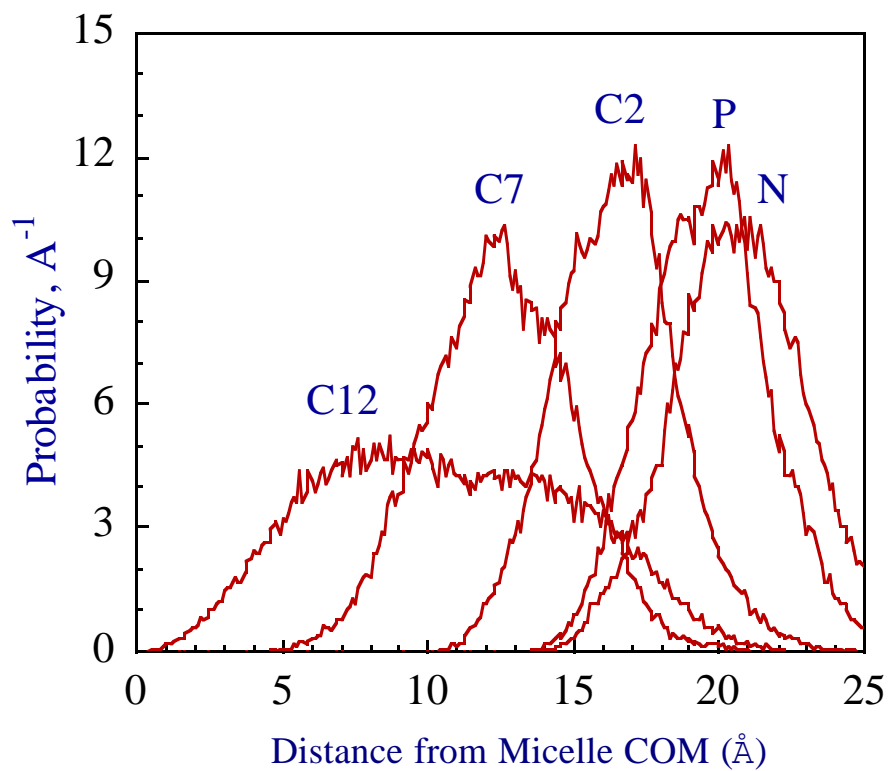
Observation of hydrophobic areas  
on the surface of micelle



1200 ps

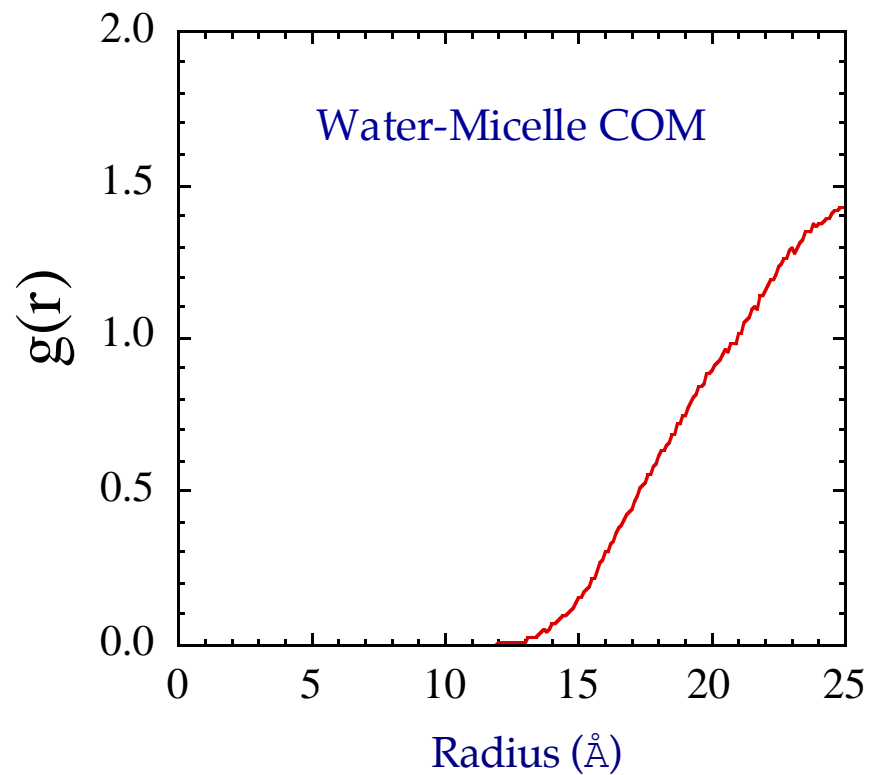
The prolate ellipsoid shape  
remains

The probability distribution from the micelle center-of-mass (COM) is shown below for respective atoms of DPC. By comparing the location and the width of the distributions of each carbon atom along the dodecyl chain, we observed that the rms average location of the carbon atom moves monotonically closer to the COM as one goes down the chain from the C1 position. Initially the change is about 1 Å per carbon atom, with the change accelerating as the end approaches. The width of the distribution along the chain shows a similar pattern of increasing towards the end of the chain.



## *Micelle-Water Interactions*

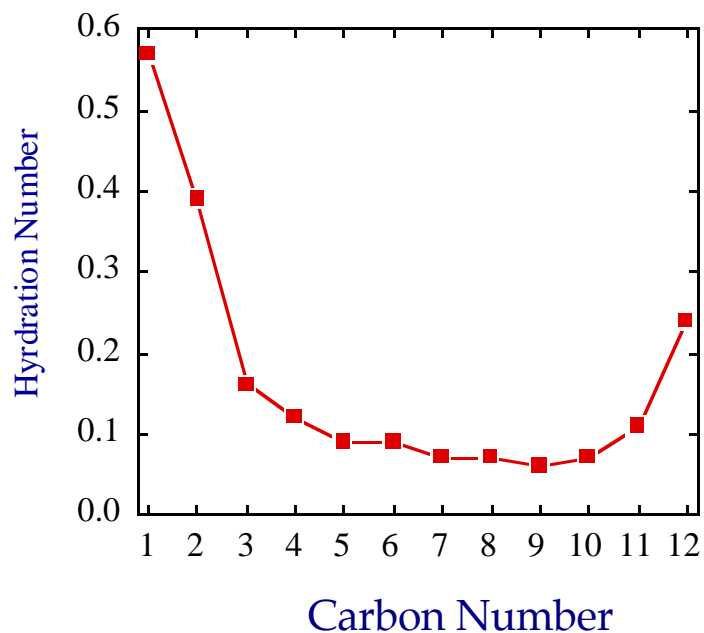
The extent of water penetration into micelles has been a much debated issue. The radial distribution function between the oxygen atoms of water and the micelle center of mass reveals that within 12 Å of the COM, the micelle interior is devoid of water. By comparing the water and carbon profiles from the micelle COM, our results show that the probability of finding water within the average position of C1 is quite small.



The hydration number of all the carbon atoms in the hydrocarbon chain were determined by integrating the probability distribution function between the respective carbon atom and the oxygen atoms of water out to 3.5 Å. The variation of the hydration number with the carbon positions qualitatively resembles the results of MacKerell (1995) for a SDS micelle though quantitatively we report higher values. This could be due to

1. the DPC being more anisotropic than the SDS micelle due to a larger headgroup which leads to higher conformational defects and larger water penetration
2. surface-lying lipids seen in the DPC micelle simulation
3. the difference in simulation time (1.02 ns vs. 120 ps) for the DPC micelle and SDS micelle respectively.

Our results also show the tendency for the end of the hydrocarbon chain to “swing” towards the interfacial region which leads to the increase in the C11 and terminal methyl group hydration.



## *Trans/gauche ratio from MD simulation of micelles*

The *trans/gauche* ratio was determined for the DPC micelle simulation and is compared to other reported values.

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Bond	DPC <sup>a</sup>	SDS <sup>b</sup>	LPE <sup>c</sup>
C1-C2	0.76	0.58	0.64
C2-C3	0.82	0.83	0.86
C3-C4	0.83	0.69	0.91
C4-C5	0.83	0.73	0.87
C5-C6	0.82	0.82	0.90
C6-C7	0.83	0.79	0.92
C7-C8	0.82	0.80	0.95
C8-C9	0.85	0.88	0.96
C9-C10	0.85	0.81	0.97
C10-C11	0.77	0.91	

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<sup>a</sup> This work

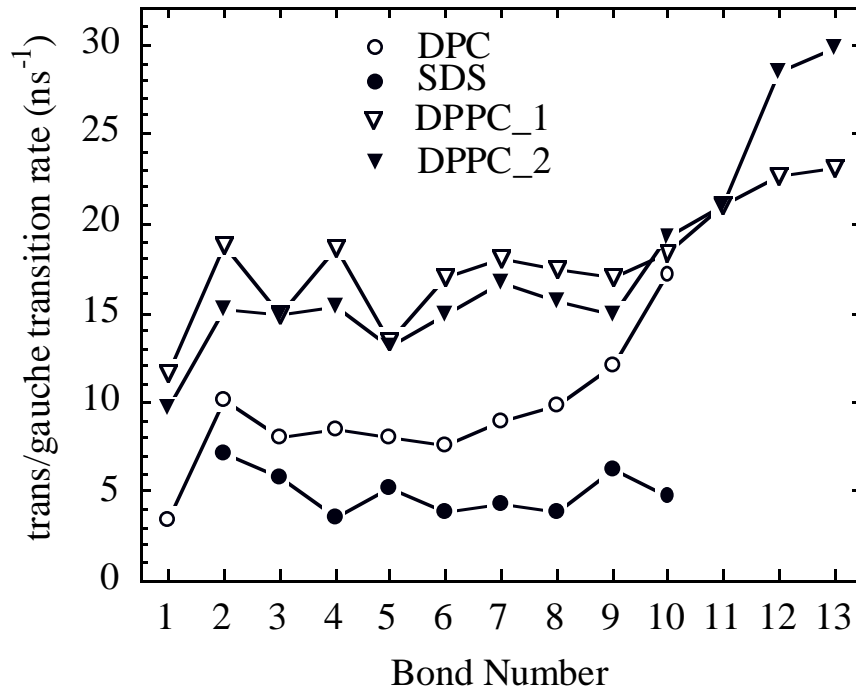
<sup>b</sup> A. Mackerell, 120 ps MD simulation of 60 monomer SDS micelle

<sup>c</sup> Wendeloski et al., 125 ps MD simulation of 85 monomer LPE micelle .

## Dynamics of the DPC micelle

### *Trans/gauche transition rate*

The *trans/gauche* transition rate is compared to those reported for the SDS micelle (MacKerell, 1995) and the two chains of DPPC in a lipid bilayer (Venable et al., 1993).



### *The time correlation function*

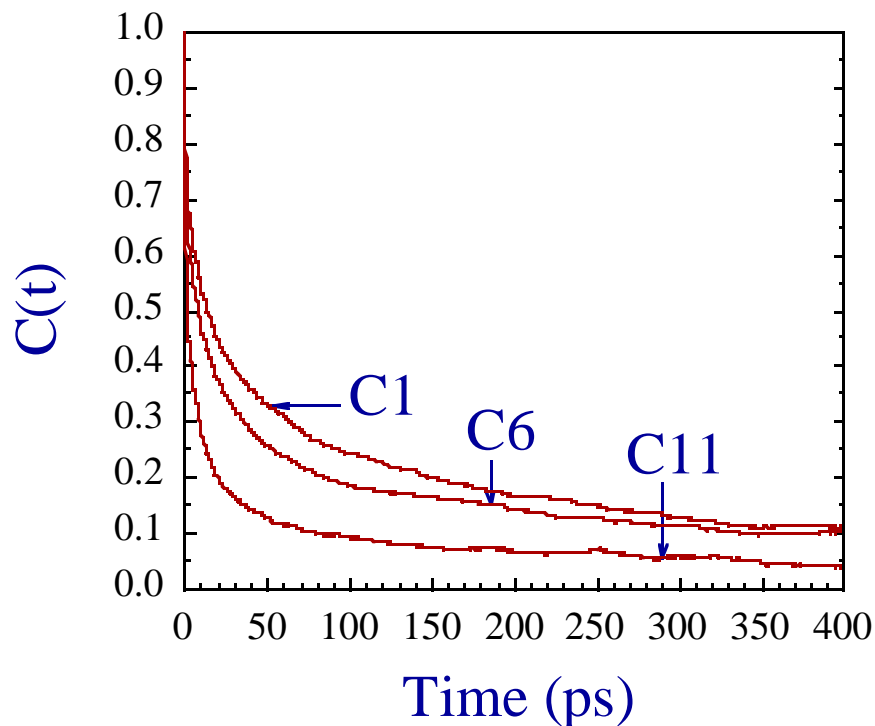
The time correlation function (tcf) of the C-H bond vector for each C-H bond on the hydrocarbon chain have been computed. The tcf for the C-H bonds are given by

$$C(t) = \langle P_2[\mu(t) \cdot \mu(0)] \rangle_t = 3/2 \langle [\mu(t) \cdot \mu(0)]^2 - 1 \rangle_t$$

where  $P_2$  is the second rank Legendre polynomial,  $\mu$  is a unit vector, and in the present case, representing the C-H (or C-D in deuterated lipids) bond vector in the laboratory frame and  $\langle \rangle_t$  represents the time (t) average.

The tcf's show

- 1) an initial very fast decay to a value of 0.6-0.8 in less than 1 ps due to the fast vibrational and librational motions within the same (*trans* or *gauche*) state
- 2) followed by a slower decay (in the time scale of tens of ps) the rate of which depends on the carbon position in the expected fashion, *i. e.*, the decay becomes faster for positions closer to the tail of the chain due to *trans-gauche* isomerization and
- 3) a slow decay with time constant in nanoseconds as the slow process of reorientation of the whole micelle and the diffusion of lipid monomers over the micellar surface further reduce the tcf.



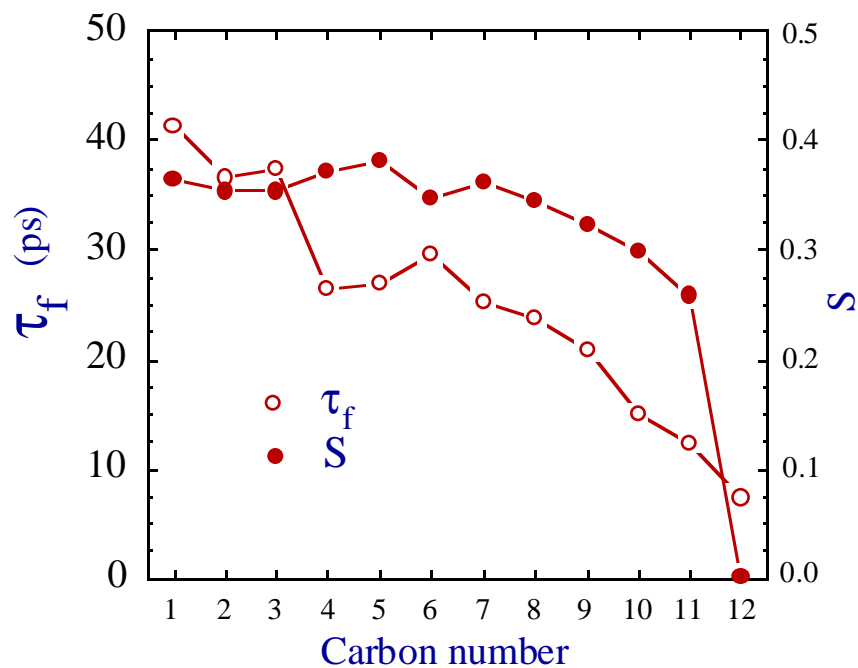
Functions of the following form are used to fit the tcf's where the  $a_i$ 's are constrained to be positive.

$$C(t) = \sum_i a_i \exp(-t/\tau_i) + S^2 \exp(-t/\tau_s) \quad (i = 1-3)$$

The fast correlation time  $\tau_f$  is then given by

$$\tau_f = (\sum_i a_i \tau_i) / (\sum_i a_i) \quad (i = 1-3)$$

The profile of the order parameter,  $S$ , versus carbon positions exhibits a plateau region from C1 to C8 before decreasing rapidly towards the end of the chain which is consistent with NMR relaxation measurements in other micelle systems. The values of  $\tau_f$  are in excellent agreement with those of other micelle systems experimentally.



## Conclusions

- 1) The average shape of the DPC micelle is a prolate ellipsoid for our constant pressure 1.22 nanosecond simulation. A simulation of over 100 ps seems necessary to develop the deviation from an initial spherical shape.
- 2) Water penetration into the micelle is limited. The average probability of finding water within the average position of C1 is quite small. Distinct hydrophobic and hydrophilic regions of the micelle are observed.
- 3) The time correlation functions for the C-H bonds obtained from this simulation rendered correlation times and order parameters that closely reproduce the salient features obtained experimentally for most micellar systems.

This work has been accepted to a Festschrift issue of the Journal of Molecular Structure.

Coordinate sets produced over the simulation are available at <http://www.missouri.edu/~chemwww/chemfaculty/wong.html>

This poster presentation is available in pdf format at <http://www.missouri.edu/~chemtw/pubs.html>

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