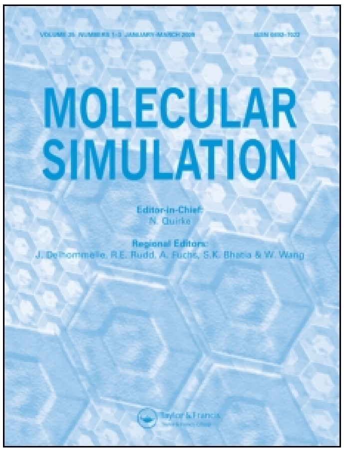

Molecular Simulation
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713644482

Molecular Dynamics Investigation of the Lamellar Liquid-Crystal D-Phase in the Octylammonium Chloride/Water System

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To cite this Article Tobias, Douglas J. and Klein, Michael L.(1996) 'Molecular Dynamics Investigation of the Lamellar Liquid-Crystal D-Phase in the Octylammonium Chloride/Water System', Molecular Simulation, 16: 4, 219 — 228
To link to this Article: DOI: 10.1080/08927029608024076
URL: http://dx.doi.org/10.1080/08927029608024076

Molecular Simulation, 1996, Vol. 16, pp. 219–228
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MOLECULAR DYNAMICS INVESTIGATION OF THE LAMELLAR LIQUID-CRYSTAL D-PHASE IN THE OCTYLAMMONIUM CHLORIDE/ WATER SYSTEM

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(Received November 1994, accepted July 1995)

The two-component cationic surfactant system octylammonium chloride/water (20/80 mole percent) has been investigated by molecular dynamics simulations using an intermolecular force field taken from the literature. The multi-lamella bilayer structure is demonstrated to be stable over a nanosecond molecular dynamics trajectory and to possess physical characteristics in reasonable accord with available experimental data. The results are sufficiently encouraging that further studies of this system seem warranted.

KEY WORDS: Octylammonium chloride/water, liquid crystal, D-phase.

1 INTRODUCTION

The lyotropic liquid crystalline phases of mixtures of amphiphilic molecules and water are of great fundamental and technological interest. Although the complex phase equilibria in many of amphiphile/water systems have been quantitatively described, the microscopic picture that is necessary to understand the relationship between the intermolecular interactions and the phase behavior has only recently begun to emerge with the help of computer simulations. Most of the atomistic simulation work to date has focused on anionic surfactants and zwitterionic phospholipids. The cationic surfactants have received relatively little attention. Until now, only the monolayer (Böcker *et al.* 1992; Tarek *et al.* 1994) and aqueous micellar phases (Böcker *et al.* 1994) of the tetraalkylammonium halides have been studied. In this paper we report the results of a molecular dynamics (MD) simulation of a lamellar phase of the octylammonium chloride/water binary system (Ekwall *et al.* 1968; Wärnheim *et al.* 1987).

2 SIMULATION SETUP AND METHODOLOGY

The simulated system consists of a water/surfactant mole ratio of 80/20, corresponding to the system studied experimentally by Wärnheim *et al.* (1987). There are 64 octylammonium chloride molecules and 256 water molecules in a 33.4 Å × 33.4 Å × 24.4 Å box, with three-dimensional periodic boundary conditions (see Fig. 1). In the chosen geometry, the hydrocarbon chains of molecules in different monolayers interact at the bilayer center through the periodic boundary conditions in the direction normal to the headgroup/water interface (the z-direction). The simulation cell dimensions were chosen to match the interlamellar repeat distance (24.4Å) and surface area/molecule (34.5 Å^2) measured by Wärnheim *et al.* (1987).

The initial configuration of each half of the bilayer was constructed by placing 32 octylammonium ions on a 4×4 body-centered square lattice with $a = 8.343$Å. A slab of 320 water molecules with appropriate x and y dimensions was placed at the center of the central simulation cell and 64 of the water molecules were selected at random and replaced with chloride ions. Each monolayer was then arranged with its headgroups facing the water slab with the planes of nitrogen atoms at $\pm$ 7 Å.

The potential energy function used in the calculations was of the CHARMM form (Brooks *et al.* 1983). We employed the so-called "polar-H" model in which only polar hydrogen atoms (those attached to oxygen or nitrogen) are explicitly represented, and nonpolar hydrogens are implicitly represented through the heavy atoms to which they are attached (*i.e.* a methyl group is considered a single "extended atom"). For the octylammonium ions we used the potential parameters for the lysine sidechain from the PARAM19 protein parameter set (Reiher 1985). We used the SPCE/E parameters for water (Berendsen *et al.* 1987) and the OPLS parameters for the chloride ions (Buckner and Jorgensen, 1989). The Ewald method (Allen and Tildesley, 1989) was used to compute all of the electrostatic interactions in the infinite, periodic (multilamellar) system. The minimum image convention (Allen and Tildesley, 1989) was employed to calculate the van der Waals interactions and the real-space part of the Ewald sum with simple truncation at 11 Å. Long-range corrections (Allen and Tildesley, 1989) to account for the truncated van der Waals interactions were included in the energies and pressures.

After constructing the system according to the prescription above, the energy of the system was minimized with respect to the chloride and water positions using steepest descent minimization. Then, the positions of all but the hydrocarbon chain atoms were fixed, and a 2 ps simulation was performed at a temperature of 1000 K to randomize the chain conformations with the z dimension of the cell set to 100 Å. The z dimension was then set to 34 Å and a series of minimization and 2 ps dynamics runs was performed at 293 K with all atoms free, reducing the z dimension by 2Å in each subsequent run, until the desired z dimension (24.4 Å) was reached. The resulting configuration was used to initiate a 1200 ps MD simulation. A timestep of 2 fs was used in all dynamics calculations. With the exception of the properties related to the conformations of the hydrocarbon chains (i.e. gauche populations and segmental order parameters), which appeared to converge only after the first half of the simulation, the potential energy and all of the structural properties reported below appeared to converge within the first 100–200 ps.

This simulation was performed at a constant temperature of 293 K by using the Nosé-Hoover chains method (Martyna *et al.*, 1992), with separate thermostats coupled to the octylammonium ions, water molecules, and chloride ions. The equations of motion were integrated with a Verlet-like algorithm (Ciccotti and Ryckaert, 1986), and the SHAKE algorithm was used to constrain the lengths of bonds involving hydrogen methods. The fictitious masses of the thermostat variables were chosen according to the prescription of Martyna *et al.* (1992) with timescales of 0.5 ps, and the Nosé-Hoover chain length was five.

One criterion that can be used to judge the suitability of the chosen potential parameter set is to compare the average pressure computed from the constant volume simulation to the pressure under which the experimental data used to set up the simulation was measured (~ 1 atmosphere). If the potential is reasonable, these pressures should be equal. The average pressure from the simulation is -182 ± 630 atmospheres, with average components of -153 ± 818, -223 ± 806, and -171 ± 1044 atmospheres in the x, y, and z directions, respectively. Although the magnitude of the pressure is appreciable, it is actually quite small for a system containing ions and/or hydrogen bonded molecules. Moreover, the components are

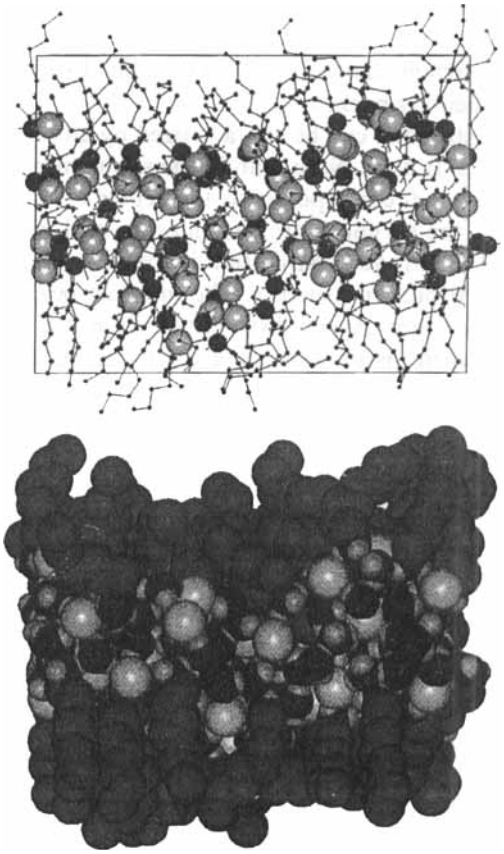

Figure 1 Two views of the octylammonium chloride/water system after 1000 ps MD simulation: (a) ball and stick representation with the nitrogen and chloride atoms enlarged and the central simulation cell outlined in red; (b) spacefilling representation. The coloring scheme is: C, gray; N, green; O, red, H, white; Cl, yellow. See color plate I.

practically equal, indicating that the pressure in the system is essentially isotropic. Thus, we would expect only a very small, isotropic compression of the system if the volume was allowed to adjust to ambient conditions.

3 RESULTS AND DISCUSSION

3.1 Bilayer structure

In Figure 1 we show two views of the system after 1000 ps of dynamics. The Figure shows that the bilayer structure is preserved, but the interface with the water is broad and rough, with appreciable water and ion penetration into the hydrocarbon region. The penetrating chloride ions appear always to be associated with, albeit sometimes behind, the headgroups. Most of the penetrating water molecules appear to be associated with the headgroups, chloride ions, or in clusters with each other, although they are occasionally isolated in the hydrocarbon region. As there are only four water molecules per ion, the chloride ions often find themselves in contact with each other. The hydrocarbon chains appear to be quite disordered and, in the space filling representation, densely packed.

The average bilayer structure can be characterized by atomic density distributions along the bilayer normal (z axis). Note that, in the simulation cell, the bilayer center is at $z = \pm 12.2$ Å, and $z = 0$ corresponds to the center of the interlamellar region. The density profiles of the carbon, nitrogen, chloride, and water oxygen atoms are shown in Figure 2a. The nitrogen distribution is roughly symmetric with two peaks indicating a well-defined bilayer structure. The nitrogen peaks are broad and have a large overlap with the water oxygen distribution. Thus, the bilayer/water interface is very diffuse. The oxygen distribution shows that the density of water molecules between the lamella is significantly less than the bulk water density (0.033 Å^{-3}), and the water molecules penetrate completely through the bilayer. The chloride ion distributions are slightly peaked on the water side of the nitrogen peaks, indicating a small preference for association with the headgroups at the surface of the bilayer. The chloride ions also penetrate deeply into the bilayer, although not as much as the water molecules. The value at the maxima in the carbon atom density, $\sim 0.032\text{Å}^{-3}$, is slightly greater than the density of carbon atoms in liquid octane, 0.030Å^{-3}, at 293 K (Small 1986). There is a relative minimum in the carbon density at the bilayer center (the so-called "methyl trough"), indicating less than complete interpenetration of the hydrocarbon chains from the two monolayers. This has been observed in electron density profiles from X-ray diffraction studies of phospholipid bilayers (Simon *et al.* 1992), as well as in simulations of lipid bilayers (Damodaran *et al.* 1992; Wilson and Pohorille, 1994). The carbon atom density profile in Figure 2a shows that the carbon atoms are occasionally found in the middle of the water layer. The density profiles of the individual carbon atoms in Figure 2b show that it is primarily the first carbons (attached to nitrogen) in the chains, but also the second the third carbons, that make it to the middle of the system. In fact, the first three carbon have nonzero densities throughout the system. The broad distributions of all of the carbon atoms are evidence that the hydrocarbon chains are highly disordered.

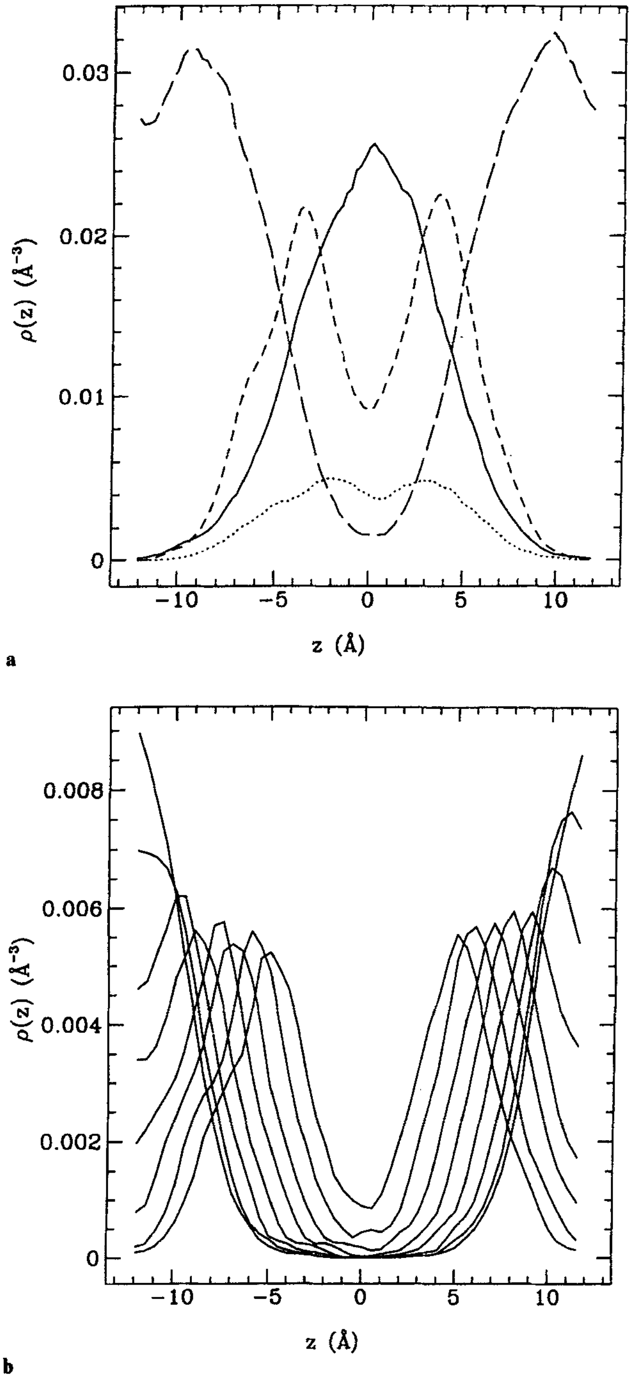

Figure 2 Atomic density profiles along the bilayer normal (z axis): (a) carbon (long dash), nitrogen (short dash), chloride (dot), and water oxygen (solid); (b) carbon atom densities plotted separately according to position in the chain.

Using the difference between the interlamellar spacing, 24.4 Å, and the separation between the maxima in the peaks of the nitrogen atom densities in Figure 2a namely, 7.3 Å, we estimate the bilayer thickness to be 17.1 Å. This value may be compared with the estimate of Wärnheim *et al.* (1987), which depends on whether the chloride ion volume is ascribed to the bilayer or the water. The former choice gives 16 Å and the latter gives 17.5 Å for the bilayer thickness. According to the present simulation, the latter choice appears to be in more reasonable agreement with the supposition of Wärnheim *et al.* From the full width at half maximum of the water density, we estimate the thickness of the water layer to be 8.8 Å. Wärnheim *et al.* estimated the water thickness as the difference between the interlamellar spacing and the bilayer thickness, *e.g.* assuming no overlap between the water and bilayer, obtaining either 8.4 Å or 6.9 Å depending on where the chloride ions are assumed to be. The latter value goes with the bilayer thickness that best fits the simulation result, but it is much lower than our estimate because, according to the simulation results in Figure 2a, there is significant overlap between the water and bilayer regions.

3.2 Headgroup structure and solvation

To gain insight into the association of the ammonium headgroups and the chloride counterions with each other and with the water molecules, we have calculated various pair correlation functions. In inhomogeneous systems such as the one studied here, the g(r) functions do not have to go to one at long distances as they do in homogeneous systems (Friedman 1985). There is a broad, split first peak in the N—N $g(r)$ extending out almost to 10 Å. Integration of this peak gives a coordination number (number of neighbors) of 6.5. To elucidate further how these neighbors are distributed, we have followed the procedure outlined by Tarek *et al.* 1994. In this way, we established that the observed split speak in the N—N $g(r)$, centered around $r = 5$ Å, arises primarily from nearest neighbors in the same plane as a given headgroup, although there is a substantial contribution from neighbors with smaller in-plane separations and displaced in the z-direction.

The N—Cl $g(r)$ displays a sharp first peak at about 3.5 Å (slightly less than the sum of the Cl and N van der Waals radii) arising from chloride ions that are in contact with the headgroups. Integration of this peak gives a coordination number of 1.7, implying that the chloride ions are shared amongst the headgroups. To determine more precisely the location of the ions with respect to the headgroups, we have computed the function $g(R,Z)$, defined by Böcker *et al.* (1992) where Z is the displacement away from a nitrogen atom along a vector pointing from the nitrogen atom to the first carbon in the chain, and R is the distance perpendicular to the vector. We find that the first peak in N—Cl $g(r)$ arises from chloride ions in front of the headgroups (toward the hydrogen atoms) and the second peak from chloride ions behind the headgroups (toward the first carbon in the chain). Moreover, the most closely associated ions are off to the side (not directly in front) of the headgroups, where they are shared.

The N—O $g(r)$ has a sharp first peak corresponding to water molecules hydrogen bonded to the headgroups. The first two peaks are at the same distance as those in the N—O $g(r)$ from a simulation of an isolated methylammonium ion in water (Jorgensen and Gao, 1986). Integration of the first peak gives a coordination number of 3.0, which is about 50% less than the value for the isolated ion because of competition between the chloride ions and water molecules for association with the headgroups. The $g(R, Z)$ for the oxygen atoms, not shown, is very similar to that of the chloride ions. The distributions of the chloride ions and water oxygen atoms around the headgroups are, thus on the average, essentially the same.

While discussing the snapshots of the system above (Fig. 1), we noted that there appeared to be many instances of chloride ion contact pairs. Indeed, the Cl—Cl $g(r)$, has its first peak centered at $r = 5$ Å, which is roughly equal to twice the van der Waals radius of the OPLS chloride ion. It is also approximately the location of the minimum corresponding to contact ion pairs in the potential of mean force between OPLS chloride ions in water (Buckner and Jorgensen, 1989).

3.3 *Hydrocarbon chain structure*

We can compute many properties from the simulation to characterize the structure of the hydrocarbon chains. One measure of the hydrocarbon chain structure that is directly accessible experimentally is the deuterium order parameter, S_{CD}, defined by (Seelig and Seelig, 1980):

$$S_{\mathrm{CD}} = (1/2)[\langle 3\cos^2\theta_{\mathrm{CD}}\rangle - 1], \tag{1}$$

where θ_{CD} is the angle between a CD bond and the bilayer normal (z axis), and the angular brackets denote an average over CD bonds and time. The S_{CD} values can span the range between $-1/2$, which corresponds to full order in the plane of the bilayer, and 1, which corresponds to full order along the bilayer normal; the value $S_{\mathrm{CD}} = 0$ corresponds to isotropic orientation. We constructed the CD vectors and computed the order parameters from the positions of the extended-atom carbons over the second half of the simulation by assuming a CD bond length of 1.10 Å, a DCD angle of 108°, and by assuming that the DCD plane bisects the CCC angle and the the CCC plane bisects the DCD angle. The simulation results are compared in Figure 3 to those measured by Wärnheim *et al.* (1987). Qualitatively, the agreement is good: for the most part, both the simulation and experimental order parameters decrease as a function of methylene number, counting away from the headgroup, and the relatively small changes in the experimental S_{CD} on going from carbon two to three and carbon four to five are reproduced in the simulation results. However, there are some notable differences: the simulations predict too much order in the first three carbons and slightly too little in carbons six and seven. The deviations between the simulated and the experimental order parameters could reflect deficiencies in the potential used to model the hydrocarbon chains (for example, the lack of explicit H atoms), incomplete sampling of slow chain motions (Pastor and Venable, 1993), or both.

To further characterize the chains, we have investigated the fraction of gauche conformations versus C—C bond number. The gauche populations are fairly constant at about 18% throughout the chain except for at the second and last bonds, where the populations are about 23%. The greatest fraction of gauche conformations occurs in the last bond of the chain. There is also an increase in the gauche population at the second bond relative to the middle of the chain. A similar effect was seen a simulation of

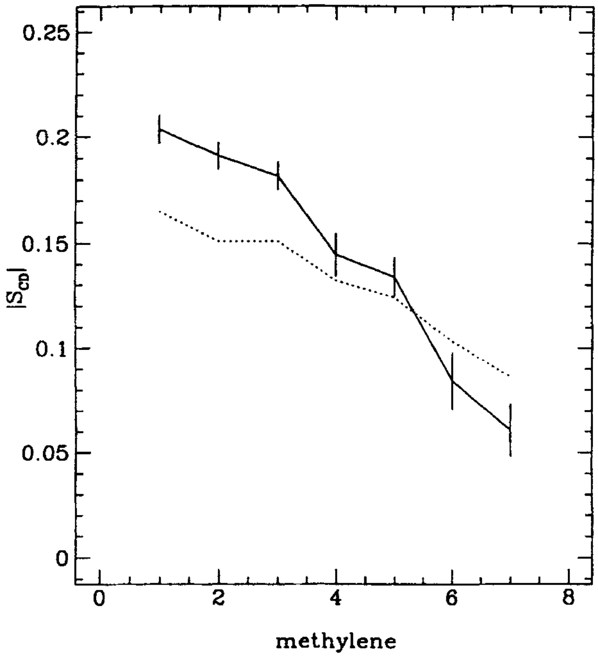

Figure 3 Deuterium order parameter as a function of methylene number (counting from C_1, the carbon attached to nitrogen) from the present simulation (solid line) and the experimental measurements of Wärnheim *et al.* (dots). The error bars on the simulation results were calculated as the standard deviations of averages evaluated over five blocks of 100 ps.

a Newton black film composed of sodium dodecylsulfate molecules (Gamba *et al.* 1992). Comparing the present results to the gauche populations of about 0.3 calculated from a recent simulation of liquid octane at 293 K (Tobias *et al.* 1996), we conclude that the hydrocarbon chains in the bilayer are quite disordered, but not as much as in a neat alkane liquid of comparable chain length. We reach the same conclusion after comparing the C—C $g(r)$ from the bilayer simulation to that from the octane simulation of Tobias *et al.* (1996): the first peak in the bilayer C—C $g(r)$ is higher, reflecting more organized packing of the hydrocarbon chains in the bilayer compared to in the liquid alkane.

3.4 Dynamics

On the simulation timescale ($\sim$1 ns), all of the components of the bilayer system are mobile in all three spatial directions, but the primary mobility is in the plane of the bilayer. Molecular graphics analysis of the trajectories indicated that none of the headgroups, water molecules, or chloride ions made complete excursions through one bilayer into another in the multilamellar system during the nanosecond time scale of the simulation.

To quantify the dynamics in the plane of the bilayer, we have calculated the center-of-mass mean-squared-displacements in the xy plane as a function of time. The Einstein relation (Friedman 1985) has been used to estimate a diffusion coefficient

1.0×1.0^{-6} cm^2/s for the octylammonium ions at a surface area/molecule of 34.5 Å^2. This value may be compared with lateral diffusion coefficients 2.7×10^{-6} and 5.2×10^{-6} for decanoate and decanol, respectively, calculated for surfactant molecules in a sodium decanoate/decanol bilayer at a surface area/molecule of 23.4 Å^2 (Egberts and Berendsen, 1988) and the values 1.9×10^{-6} and 4.8×10^{-6} at surface areas/molecule of 44 and 65 Å^2, respectively, from simulations of tetradecyltrimethylammonium bromide monolayers at the air/water interface (Tarek *et al.* 1994). Typical errors in the diffusion coefficients are 20%.

The lateral diffusion coefficient calculated for water is 6.2×10^{-6}cm^2/s. This value is about four times smaller than that of bulk SPC/E and real water (Berendsen *et al.* 1987), and is comparable to the values for water in the vicinity of the decanol headgroups and in the middle of the bilayer from the simulation of the decanoate/decanol system by Egberts and Berendsen (1988). For the chloride ions the calculated diffusion coefficient is 1.8×10^{-6} cm^2/s.

4 CONCLUSIONS

We have shown that it is relatively straightforward to carry out reliable and instructive simulations of concentrated cationic surfactant solutions on a desk-top workstation. Minor discrepancies between the simulation and experimental data likely reflect the inadequate treatment of the hydrocarbon chains and possibly the neglect of polarization interactions between the surfactant, ions and water (Shelley, 1992). Nevertheless, the present investigation sufficiently encouraging that it would be profitable to extend the investigation and explore the behavior three-component cationic systems.

Acknowledgements

This work was supported by grants from the National Institutes of Health (GM 40712) and The Procter and Gamble Company. We would like to thank Dr. Robert Laughlin for suggesting that we investigate the octylammonium chloride/water system.

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