Using "Prosurfactants" to Enhance Rates of Delivery of Surfactants

Craig A. Rosslee, Constantine Khripin, Theresa M. D. Foley, and Nicholas L. Abbott
Dept. of Chemical and Biological Engineering, University of Wisconsin-Madison, Madison, WI 53706

A strategy for accelerating the rate of transport of surfactant within a system by delivering the surfactant as a precursor to the surface-active state ("prosurfactant") and subsequently transforming it to a functional form (surfactant) is reported. An increase in the overall rate of transport of a redox-active surfactant across a polycarbonate membrane containing pores with a diameter of 10 nm is demonstrated. This redox-active molecule, which is molecularly dispersed in aqueous solutions in its oxidized state (prosurfactant), but assembles into globular micellar aggregates (R_h = 5 nm) in its reduced state (surfactant), was rapidly transported across the membrane in its oxidized state to a concentration of 0.2 mM. Subsequent delivery of ascorbic acid (a reducing agent) by diffusion through the same membrane led to reduction of the oxidized precursor and formation of surfactant and micelles. The sequential delivery of the prosurfactant and then transforming agent resulted in a greater than sixfold increase in the overall rate of delivery of surfactant as compared to a procedure in which the surfactant was diffused across the membrane. These observations are compared to calculations based on hindered diffusion through cylindrical pores. © 2004 American Institute of Chemical Engineers
AIChE J, 50: 708–714, 2004
Keywords: prosurfactant, redox, transport, hindered diffusion

Introduction

Surfactants are used in a range of products and processes because they spontaneously assemble at interfaces and within the bulk of solutions to form micro- and nanostuctures (Hiemenz and Rajagopalan, 1997). Many of these applications occur out of equilibrium, and thus control of the dynamic properties of surfactant-based systems is a topic of substantial importance. In this regard, the tendency of surfactants to adsorb at surfaces as well as to form micellar aggregates in bulk solution can slow the dynamics of surfactant systems through effects on mass transport. Micellar aggregates diffuse slowly compared to single molecules, and the adsorption of surfactants onto surfaces can deplete the bulk concentration of surfactant (particularly when dealing with transport through porous media). In this article, we explore the potential use of "prosurfactants" to accelerate the rate of transport of amphiphilic molecules. Similar to prodrugs, which are pharmacologically inert chemical derivatives that can be converted *in vivo* to active drug molecules to exert a therapeutic effect (Sinkula and Yalkowsy, 1975; Stella et al., 1985), we use the term "prosurfactants" to refer to molecules that can be delivered as a precursor to the surface-active state and are subsequently transformed to a functional (surface active and self-associating) form. In this article, we report the use of a prosurfactant system based on a redox-active surfactant to increase the rate of transport of surface-active species between two volumes of solution separated by a membrane with nanometer-sized pores. We view this system as a model system with which to demonstrate the use of prosurfactants to accelerate mass transport. Because mass transport plays a central role in phenomena such as dynamic surface tensions, penetration of surfactants into porous media, and formation of emulsions, we believe the principles reported in this article are relevant to a range of applications of surfactants.

The diffusion of surfactant molecules and their aggregates

Correspondence concerning this article should be addressed to N. L. Abbott at abbott@engr.wisc.edu.

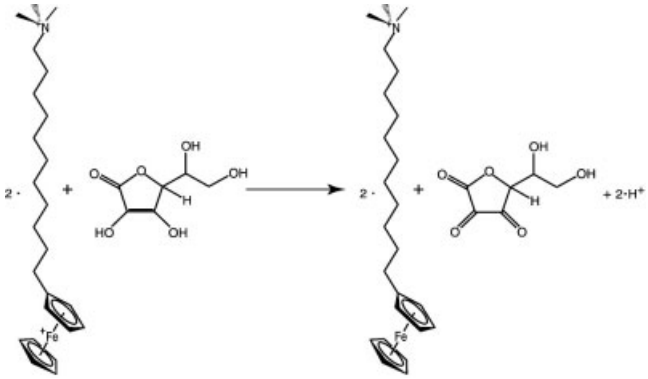

Figure 1. Reaction scheme showing oxidized (11-ferrocenylundecyl)trimethylammonium bromide (prosurfactant) being reduced by ascorbic acid (transforming agent) to form (11-ferrocenylundecyl)trimethylammonium bromide (surfactant).

through membranes has been the subject of several past studies. These studies have focused on the effects of surfactant aggregation state (Krovvidi et al., 1984), pore size (Johnson et al., 1987), surfactant type (ionic vs. nonionic) (Johnson et al., 1989), membrane charge, and solution ionic strength (Kuo et al., 2001) on the rate of surfactant diffusion. These studies have found that diffusion of the aggregate is slowed ("hindered diffusion") (Anderson and Quinn, 1974) when the pores and aggregates are of similar size. These studies also found that repulsive electrostatic interactions between ionic surfactants and charges immobilized on the walls of the pores can act to partition the aggregates from the pore, thus reducing the concentration driving force for diffusion (Smith and Deen, 1983). Alternatively, electrostatic interactions can drive adsorption of surfactants to form assemblies that coat the inside surface of the pore, thereby reducing the effective pore radius (Bisio et al., 1980) available for the transport of surfactant.

The experimental system described in this article revolves around the use of ferrocene-containing surfactants. Past studies (Saji et al., 1985a, b; Gallardo et al., 1995; Takeoka et al., 1995) have reported that micelles formed by cationic surfactants containing a ferrocenyl moiety can be reversibly disassembled into monomers by oxidation of the electrically neutral ferrocene to the ferrocenium cation. The structure of one surfactant of this type (11-ferrocenylundecyl)trimethylammonium bromide (FTMA), is shown in Figure 1. In dilute solutions, FTMA assembles into globular micellar aggregates (R_h = 5 nm) in its reduced state [critical micelle concentration (CMC) of 0.1 mM in 0.1 M Li_2SO_4, pH 2], but remains singly dispersed in its oxidized state (for concentrations $<$30 mM, at least) (Gallardo et al., 1995). Measurements of surface tensions at bulk concentrations near the CMC of reduced FTMA indicate that FTMA reduces the surface tension of aqueous solutions by $\sim$22 mN/m, whereas oxidation of the FTMA leads to recovery of the surface tension of the surfactant-free solution of electrolyte. In this article, we exploit the oxidized species as a prosurfactant. We use it to test the hypothesis that we can enhance the overall rate of transport of a surfactant across a nanoporous membrane by first diffusing the prosurfactant (oxidized form of FTMA) across the membrane, and then diffusing a transforming agent across the membrane [a reducing agent that reduces oxidized FTMA to FTMA (Figure 2)]. Whereas the study reported in this article is based on sequential delivery of a redox-active prosurfactant and a reducing agent, by predelivering the transforming agent or by utilizing other modes of transformation [light (Shin and Abbott, 1999) or electrochemistry (Gallardo et al., 1995)], it should also prove possible to exploit the use of prosurfactants in a number of different situations.

Materials and Methods

Materials

(11-Ferrocenylundecyl)trimethylammonium bromide (FTMA) was used as received from Dojindo Corp. (Gaithersburg, MD). Lithium sulfate monohydrate and ascorbic acid were purchased from Aldrich (Milwaukee, WI). Ascorbic acid and surfactant solutions were prepared using 0.1 M Li_2SO_4 (pH 2). The electrolyte solutions were prepared using lithium sulfate monohydrate in high-purity deionized water (R = 18.2 MΩ/cm, γ = 72.0 mN/m at 25°C). Sulfuric acid was used to lower the pH to 2. Surfactant solutions were prepared daily. Commercial

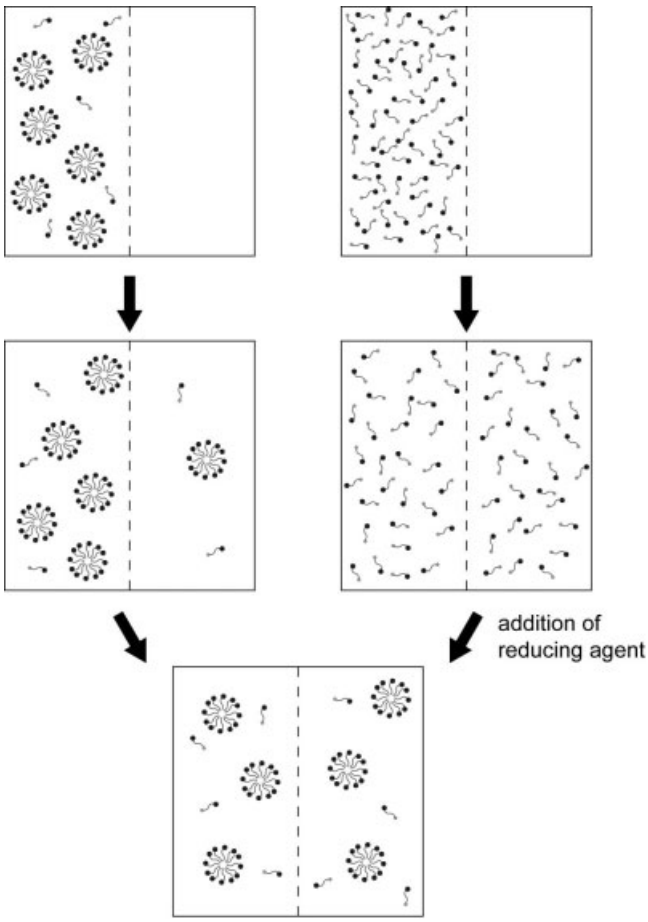

Figure 2. Two surfactant delivery pathways.

In the first route, micelles and monomers of surfactant slowly diffuse through a membrane. The second route shows that this process can be expedited by first diffusing the prosurfactant and subsequently delivering a transforming agent that converts the prosurfactant into surfactant, resulting in formation of micelles.

polycarbonate membranes (Poretics, Livermore, CA) with a pore radius of 8–10 nm and pore density of 6×10^8 pores/cm^2 were used as received. The membranes were supplied with poly(vinylpyrrolidone) (PVP) adsorbed to the surface of the membrane to promote the wetting of aqueous solutions.

Concentration measurements

Concentrations of surfactant and ascorbic acid were determined by using a Cary 1E spectrophotometer (Varian, Walnut Creek, CA) to measure the absorption spectrum of solutions at wavelengths between 190 and 900 nm. Samples were analyzed in 1-mL quartz cuvettes with a path length of 10 mm (Fisher, Pittsburgh, PA), and the concentrations calculated using a numerical fitting procedure reported previously (Rosslee and Abbott, 2001). Whereas concentrations of FTMA and oxidized FTMA were measured simultaneously in solution, the concentration of ascorbic acid could only be measured in the absence of surfactant (due to overlap of adsorption spectra). Thus, all measurements of the flux of ascorbic acid through the membrane were performed using surfactant-free solutions.

Transport measurements

Measurements of the rates of transport of surfactants and reducing agents were performed using a glass diffusion cell (Figure 3). The cylindrical diffusion cell consisted of two glass chambers separated by a nanoporous membrane and a rubber gasket. The rubber gasket was prepared from high-grade viton rubber (McMaster-Carr, Chicago, IL) that was placed between chamber α and the nanoporous membrane. Chamber β was filled first with aqueous 0.1 M Li_2SO_4. The experiment was initiated when chamber α was filled with the species whose transport rate was to be measured. Both chambers were stirred vigorously with one-quarter-inch magnetic stir bars. The stir bars were prevented from striking the membrane by placing magnets outside of the diffusion chamber. One-milliliter samples were periodically removed from chamber β, and surfactant and ascorbic acid concentrations were measured with the spectrophotometer. Immediately following each measurement, the samples were returned to chamber β. The flux of each species through the membrane was determined by performing a least-square fit on each plot of concentration vs. time, multiplying the slope by the receiving volume ($\sim$13.3 mL), and dividing by the area of the membrane (5.3 cm^2).

Light scattering

The hydrodynamic diameters of micelles formed by FTMA were determined using quasi-elastic light scattering (90° angle) (Brown, 1996). A Brookhaven Instruments BI-200SM light-scattering apparatus with a BI-9000AT digital autocorrelator (Brookhaven Instruments Corporation, Holtsville, NY) was utilized. Samples were thermostated at 25 $\pm$ 0.1°C and data were analyzed using the method of cumulants (Koppel, 1972). All solutions were filtered twice with 0.22 μm filters (Millipore S.A., Molsheim, France) before measurement. Three types of samples were characterized: a 3-mM FTMA solution, a 3-mM oxidized FTMA solution that was prepared using a standard electrochemical cell (see below), and a 3-mM FTMA solution that was formed by the chemical reduction of a 3-mM electrochemically oxidized FTMA solution by using an excess of ascorbic acid.

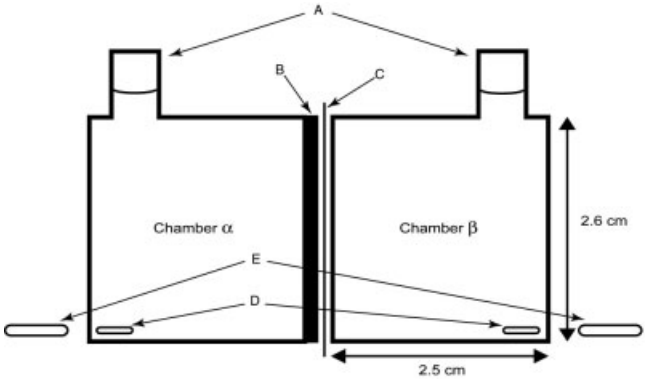

Figure 3. The diffusion cell.

The cell consists of (A) two glass chambers, between which a (B) rubber gasket and (C) membrane are clamped. (D) Two stir bars are present inside the chambers and (E) two are outside the chambers. The chambers are bound together with two rubber bands (not shown).

Electrochemical oxidation

Oxidized FTMA samples were prepared by oxidizing solutions of FTMA in an electrolysis cell (Bioanalytical Systems, West Lafayette, IN) at 0.4 V vs. a saturated calomel electrode (SCE). The counter electrode was separated from the solution being oxidized by a salt bridge so as to prevent reduction of the surfactant solution at the counter electrode. Samples were oxidized until the current decreased by three orders of magnitude from the initial current. The surfactant solutions were stirred during the process of oxidation. We confirmed by using light-scattering measurement (see above) that oxidation of FTMA by this procedure led to solutions that did not contain measurable aggregates of surfactant.

Results

Characterization of surfactant solutions

The use of oxidized FTMA as a prosurfactant required that we be able to reduce the oxidized FTMA by using a chemical reducing agent (without side reactions and formation of precipitates). To determine if this was possible, we examined solutions of FTMA, oxidized FTMA, and oxidized FTMA reduced with ascorbic acid by using quasi-elastic light scattering. Aqueous solutions containing 3 mM FTMA (0.1 M Li_2SO_4, pH 2) were measured to contain aggregates with hydrodynamic diameters of 5.3 $\pm$ 1 nm and a diffusion coefficient of $9 \pm 1 \times 10^{-7}$ cm^2/s. This result is consistent with past studies (Saji et al., 1985a). After electrochemical oxidation, no aggregates were detected in the 3-mM oxidized FTMA solutions. We utilized ascorbic acid (vitamin C) as the reducing agent in all of our experiments. As shown in Figure 1, one mole of ascorbic acid will reduce two moles of oxidized FTMA. We chose ascorbic acid because it reduced oxidized FTMA to FTMA at pH 2.0 and did not interfere with our ability to measure the concentrations of FTMA and oxidized FTMA using UV-visible spectrophotometry. While the oxidized FTMA solutions were blue in color, both the FTMA and the

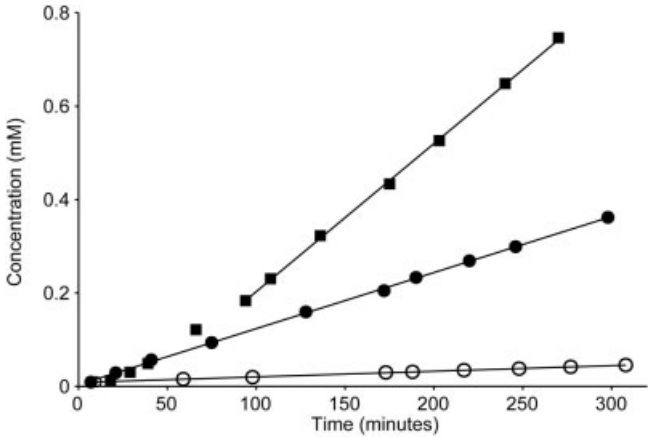

Figure 4. Concentration of (○) FTMA, (●) oxidized FTMA, and (■) ascorbic acid in 0.1 M Li_2SO_4 in chamber β plotted as a function of time. Chamber α initially contained 3 mM FTMA, 3 mM oxidized FTMA, or 0.016 M ascorbic acid in 0.1 M Li_2SO_4.

oxidized FTMA reduced with ascorbic acid were yellow in color. UV-visible spectroscopy also indicated that ascorbic acid reduces oxidized FTMA to FTMA. Reduction of the oxidized FTMA solution with 3 mM of ascorbic acid (1.5 mM excess: Figure 1) led to formation of aggregates with hydrodynamic diameters of 5.2 ± 1 nm. Thus, reduction of oxidized FTMA solutions by using ascorbic acid leads to aggregates of FTMA that are indistinguishable from those present prior to the cycle of electrochemical oxidation and chemical reduction.

Measurement of rates of transport of reduced and oxidized species across a nanoporous membrane

The rate of transport of oxidized FTMA (prosurfactant) and FTMA (surfactant) across the nanoporous membrane was determined by filling chamber α with either a 3-mM FTMA or oxidized FTMA solution containing 0.1 M Li_2SO_4 and chamber β with a solution of 0.1 M Li_2SO_4. Both solutions were stirred. The concentrations of both FTMA and oxidized FTMA in chamber β, measured as a function of time, are shown in Figure 4.

Figure 4 shows that the concentrations of both FTMA and oxidized FTMA increase as a linear function of time, with an intercept ($t = 0$) passing through the origin. By using the slopes of the linear plots in Figure 4, we calculated the macroscopic fluxes of the FTMA and oxidized FTMA across the membrane to be $5.04 \pm 0.04 \times 10^{-8}$ moles/s · m^2 and $5.01 \pm 0.04 \times 10^{-7}$ moles/s · m^2, respectively.

Next, we repeated the experiment just described using a higher rate of stirring to ascertain whether a concentration boundary layer near the membrane was a significant source of resistance to the transport of either FTMA or oxidized FTMA (Hou et al., 2000). We determined that a doubling of the stirring rate had no effect on the rate of transport of either species, indicating that the primary source of resistance to transport was the membrane itself and not a concentration boundary layer near the membrane.

In conclusion, the flux of oxidized FTMA (prosurfactant) across the nanoporous membrane was measured to be 10 times greater than that of FTMA (surfactant). This difference in flux was due solely to differences in the transport rates of the surfactant and prosurfactant across the membrane, and not to concentration boundary-layer effects. In the discussion presented below, we interpret this difference in flux using a simple model of diffusive transport through membranes.

Concurrent transport of FTMA and oxidized FTMA across nanoporous membrane

Past studies have shown that, in some instances, surfactants will adsorb to the pore walls of membranes, thereby reducing the effective pore radius (Bisio et al., 1980). The membranes used in our experiments were supplied with a poly(vinylpyrrolidone) (PVP) coating to render them hydrophilic. At low pH, PVP is protonated, thus establishing a positive surface charge (Kuo et al., 2001). This charge will likely prevent the adsorption of both FTMA and oxidized FTMA. However, to test for possible adsorption of surfactant within the pores, a mixture containing 1.5 mM FTMA and 1.5 mM oxidized FTMA in 0.1 M Li_2SO_4 was placed in chamber α and an aqueous solution of 0.1 M Li_2SO_4 was placed in chamber β. We sought to determine if the flux of oxidized FTMA was influenced by the presence of FTMA (or visa versa). Samples were removed from chamber β at 20-min intervals and the concentrations of FTMA and oxidized FTMA were determined using UV-visible spectroscopy (as described in the "Methods" section). The concentrations of both species in chamber β as a function of time are shown in Figure 5. From the results shown in Figure 5, the flux of FTMA was calculated to be $1.8 \pm 0.7 \times 10^{-8}$ moles/s · m^2 and the flux of oxidized FTMA was $2.6 \pm 0.04 \times 10^{-7}$ moles/s · m^2. By normalizing the fluxes by the concentration of each species in chamber α, we can compare the results with those obtained earlier when diffusing each species separately through the membrane. The apparent velocities of FTMA and oxidized FTMA across the membrane were $1.68 \pm 0.01 \times 10^{-5}$ m/s and $1.67 \pm 0.01 \times 10^{-4}$ m/s, respectively, when diffused separately across the membrane, and $1.17 \pm 0.48 \times 10^{-5}$ m/s and $1.72 \pm 0.02 \times 10^{-4}$ m/s, respectively, when diffused together. Because the apparent velocity of oxi-

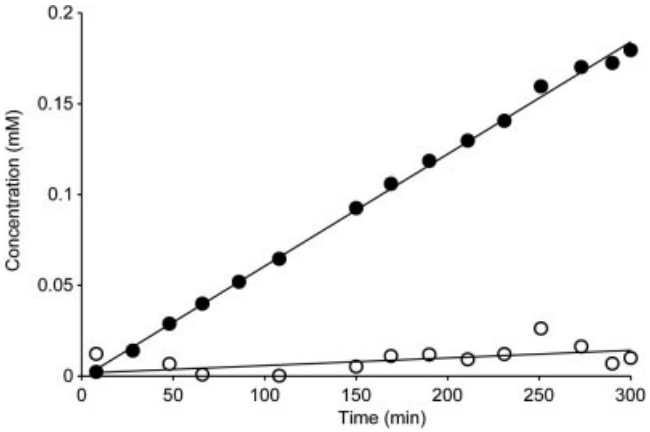

Figure 5. Concentration of (○) FTMA and (●) oxidized FTMA in chamber β plotted as a function of time following placement of a 50:50 mixture of 3 mM FTMA and 3 mM oxidized FTMA into chamber α.

dized FTMA was unaltered by the presence of FTMA, we conclude that adsorption of FTMA to the pore walls is not responsible for the differences in the fluxes between FTMA and oxidized FTMA. We note that the apparent velocity of FTMA appears to decrease slightly in the presence of oxidized FTMA. This effect may be due to the influence of oxidized FTMA on the state of aggregation of FTMA in bulk solution.

Measurement of transport of reducing agent across membrane

We next measured the flux of ascorbic acid across the membrane. The flux of ascorbic acid across the membrane was measured by placing a 16-mM ascorbic acid solution containing 0.1 M Li_2SO_4 in chamber α and a 0.1 M Li_2SO_4 solution in chamber β. One-milliliter samples were removed from chamber β at 20-min intervals. The concentration of ascorbic acid in the samples was determined by using UV-visible spectroscopy. Figure 4 shows the concentration of ascorbic acid in chamber β plotted as a function of time. While at short time the concentration of ascorbic acid in chamber β does not appear to increase linearly with time, at longer times it does. We speculate that the nonlinear behavior at short times is due to adsorption of ascorbic acid on the oppositely charged membrane. By fitting to the linear portion of the data, the flux of ascorbic acid was determined to be $1.33 \pm 0.01 \times 10^{-6}$ moles/s $\cdot$ m^2.

By dividing the measured flux of ascorbic acid by the concentration driving force and then comparing this result with the same calculation reported earlier for oxidized FTMA, it is evident that the apparent velocity of oxidized FTMA is roughly twice that of ascorbic acid ($1.67 \pm 0.01 \times 10^{-4}$ m/s and $8.3 \pm 0.08 \times 10^{-5}$ m/s for oxidized FTMA and ascorbic acid, respectively). This result is surprising because the diffusion coefficient of ascorbic acid in water (1×10^{-5} cm^2/s) (Shamim and Baki, 1980) is roughly twice that for oxidized FTMA in water (4.5×10^{-6} cm^2/s) (Saji et al., 1985a).

Sequential delivery of prosurfactant and reducing agent

As stated earlier, this study was driven by the hypothesis that sequential delivery of oxidized FTMA and then ascorbic acid (reducing agent) would lead to a higher overall rate of delivery of FTMA to chamber β than direct delivery of FTMA. To test this hypothesis, we performed the experiments shown in Figure 6. Figure 6 shows the measured concentrations of FTMA and oxidized FTMA in chamber β as a function of time. This experiment was performed by first filling chamber α with a solution of 3 mM oxidized FTMA containing 0.1 M Li_2SO_4 and chamber β with a solution of 0.1 M Li_2SO_4. Approximately 180 min after filling the chambers, the concentration of oxidized FTMA in chamber β was measured to have increased linearly with time to a concentration of 0.2 mM. Next, 1 mL of an aqueous solution of 0.2 M ascorbic acid was introduced to chamber α, resulting in the transformation of all the oxidized FTMA in chamber α to FTMA. The excess ascorbic acid diffused through the membrane, thus reducing the oxidized FTMA in chamber β. Within approximately 80 min of the addition of ascorbic acid, all of the oxidized FTMA in chamber β had been reduced to FTMA.

Inspection of Figure 6 reveals that sequential delivery of oxidized FTMA and then ascorbic acid leads to the presence of

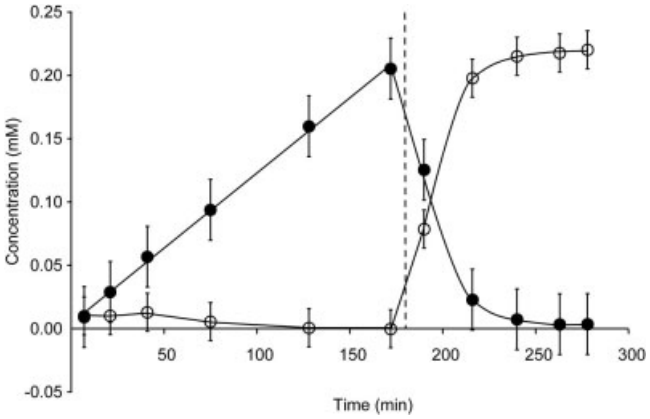

Figure 6. Concentration of (○) FTMA and (●) oxidized FTMA in chamber β plotted as a function of time.

The α chamber initially contained 3 mM oxidized FTMA. Ascorbic acid was added to chamber α at 180 min (indicated by the dashed line).

0.2 mM FTMA in chamber β in only 260 min. In contrast, inspection of Figure 4, and extrapolation to 0.2 mM of FTMA, reveals it would have taken ~1660 min to achieve the same concentration of FTMA in chamber β by direct diffusion of FTMA. These results, when combined, demonstrate a roughly 6.5-fold increase in the overall rate of delivery of FTMA (surfactant) across the nanoporous membrane by sequential delivery of oxidized FTMA (prosurfactant) and reducing agent (ascorbic acid).

Discussion

The strategy that we report in this article to enhance the rate of mass transport of surfactant across a nanoporous membrane is effective because the rate of transport of the prosurfactant is much higher than the surfactant. Specifically, our experimental results reveal that the flux of FTMA and oxidized FTMA differ by a factor of 10 at a concentration of 3 mM. Here we consider in more detail the likely origins of this difference in flux. First, we present a simple model of bulk mass transport of FTMA and oxidized FTMA. Second, we consider the possible effects of hindered diffusion through the nanopores of the membrane.

In bulk solution, the diffusive flux of species A can be calculated as

$$N_{Az} = D_A \frac{\partial c_A}{\partial z}, \tag{1}$$

where N_{Az} is the flux of species A in the z-direction, D_A is the diffusion coefficient of species A, and c_A is the concentration of species A (Cussler, 1997). For a solution containing monomeric surfactant and aggregates with an overall concentration of surfactant of C_b, the monomer concentration in solution is $C_m = CMC$ and the micelle concentration in solution is

$$C_M = \frac{C_b - CMC}{n}, \tag{2}$$

where CMC is the critical micelle concentration, and n is the aggregation number of the micelles. By assuming steady-state diffusion, the total flux of surfactant is

$$N_{total} = N_m + n \cdot N_M, \tag{3}$$

where N_m is the flux of monomers, and N_M is the flux of micelles. Thus

$$N_{total} = D_m \frac{CMC}{\Delta z} + D_M \frac{C_b - CMC}{\Delta z}, \tag{4}$$

where D_m and D_M are the diffusion coefficients of the monomers and micelles, respectively, and Δz is a length in the z-direction. In contrast, if the surfactant does not aggregate (i.e., is below its CMC), then the flux of surfactant is

$$N_{total} = D_m \frac{C_b}{\Delta z}. \tag{5}$$

By using the fact that reduced FTMA has a CMC of 0.1 mM, whereas oxidized FTMA does not aggregate, and by using the fact that micelles of FTMA have a bulk diffusion coefficient of $9 \pm 1 \times 10^{-7}$ cm^2/s, whereas monomers (in both the oxidized and reduced forms) have a diffusion coefficient of $4.5 \pm 0.5 \times 10^{-6}$ cm^2/s (Saji et al., 1985a), we use Eqs. 4 and 5 to calculate that the flux in a 3-mM solution should be 4.5 ± 0.8 times greater for oxidized FTMA than reduced FTMA. In contrast, the results shown in Figure 4 indicate that the flux of a 3-mM solution of oxidized FTMA is 10 times greater than that of FTMA through a 10-nm membrane. Thus, it appears that the bulk diffusion coefficients cannot account for the differences in the fluxes of FTMA and oxidized FTMA across the membrane.

Because the aggregates of FTMA and pores of the membrane have similar sizes, we consider here the possible role of hindered diffusion of the micelles across the membrane. The diffusion coefficient of a hard sphere in a cylindrical pore (D_p) relative to the diffusion coefficient of the same particle in free solution (D_∞) is given by the following expression (Bungay and Brenner, 1973)

$$\frac{D_p}{D_\infty} = \frac{6\pi}{K_t}, \tag{6}$$

where K_t is evaluated as

$$K_t = \frac{9}{4}\pi^2\sqrt{2}(1-\lambda)^{-5/2}\left[1 + \sum_{n=1}^{2}\alpha_n(1-\lambda)^n\right] + \sum_{n=0}^{4}\alpha_{n+3}\lambda^n, \tag{7}$$

where λ is the ratio of the sphere diameter to pore diameter, and the coefficients, a_n, can be found in a previous report (Bungay and Brenner, 1973).

In Eq. 6, D_p is the diffusion coefficient based on the concentration of particles in the pore. The intrapore diffusion coefficient based on the bulk concentrations of particles (D) is the product of D_p and the ratio of the concentration of particles in the pore relative to the concentration of particles in the bulk (Φ). When electrostatic interactions exist between the particle and the pore, Φ is given by the expression (Smith and Deen, 1983)

$$\Phi = \int_0^{1-\lambda} \exp\left[\frac{-E(\theta)}{\kappa T}\right] \cdot \theta \cdot d\theta, \tag{8}$$

where θ is the normalized distance from the center of a particle to the center line of the pore (normalized by the pore radius), and $E(\theta)$ is the electrostatic free energy of the particle relative to that in the bulk solution at the dimensionless pore position θ. If $E(\theta) = 0$ (that is, the particle experiences no electrical potential), then Eq. 7 becomes

$$\Phi = (1-\lambda)^2. \tag{9}$$

Thus, the intrapore particle diffusion coefficient for an uncharged hard sphere in an uncharged cylindrical pore based on the bulk concentration of particles is

$$D = D_\infty(1-\lambda)^2 \frac{6\pi}{K_t}. \tag{10}$$

For a globular micelle of FTMA with a diameter of 5 nm diffusing through a 10-nm pore, Eq. 10 leads to the prediction that the diffusion coefficient decreases from $\sim 9 \times 10^{-7}$ cm^2/s to $\sim 4 \times 10^{-8}$ cm^2/s. When applied to monomers of FTMA and oxidized FTMA (with estimated diameters of 2.5 nm), Eq. 10 predicts the diffusion coefficients to decrease from $\sim 5 \times 10^{-6}$ cm^2/s to $\sim 2 \times 10^{-6}$ cm^2/s. Solving Eqs. 4 and 5 with the adjusted diffusion coefficients, we calculate that the flux of a 3-mM solution should be $\sim$15 times greater for oxidized FTMA than for reduced FTMA. The results shown in Figure 4 indicate that the flux of a 3-mM solution of oxidized FTMA is 10 times greater than that of FTMA through a 10-nm membrane. Although the agreement between experiment and calculation is not exact, these results suggest that hindered diffusion likely plays a role in our experimental results. We emphasize that our calculation is approximate because we neglected the effects of electrostatic interactions and assumed that the micelles and monomers were hard spheres.

Whereas the work described in this article demonstrates that it is possible to increase the effective rate of transport of a surfactant through a membrane by utilizing a prosurfactant with a higher diffusion coefficient than the surface-active species, we believe that use of prosurfactants offers approaches to increase the rate of transport of surfactants through other complex media, such as biofilms and soils. In these systems, rates of transport of surfactants are limited by adsorption to the large surface areas present. By utilizing a precursor to the surfactant that does not adsorb to interfaces, this mechanism, which slows the delivery of surfactant, should be minimized. Finally, we note that mechanisms that convert prosurfactants into the surface-active species that rely on stimuli such as light also appear to be promising avenues for future investigation. Past studies have shown that surfactants that incorporate an azobenzene moiety undergo changes in size (Sakai et al., 1999) and/or

number density of aggregates (Shin and Abbott, 1999) upon illumination with either UV or visible light. A change in size and/or number density of aggregates should result in changes in the rates of transport of these species to interfaces (Shin and Abbott, 1999).

Conclusion

The transport of the redox-active surfactant, (11-ferrocenylundecyl)trimethylammonium bromide (FTMA), through a 10-nm polycarbonate membrane was measured with the surfactant in the reduced (aggregating) and oxidized states (nonaggregating). The flux of the surfactant in the reduced (surfactant) state was 10 times slower than in the oxidized state (prosurfactant). By sequentially transporting the oxidized surfactant (prosurfactant), and then a reducing agent, we were able to increase the effective transport rate of surfactant across the nanoporous membrane by a factor of 6. This result demonstrates the potential utility of delivering surfactants in precursor states (prosurfactants) and then transforming them to surface-active states after delivery.

Literature Cited

Anderson, J. L., and J. A. Quinn, "Restricted Transport in Small Pores. A Model for Steric Exclusion and Hindered Particle Motion" *J. Biophys.,* **14**, 130 (1974).

Bisio, P. S., J. G. Cartledge, W. H. Keesom, and C. J. Radke, "Molecular Orientation of Aqueous Surfactants on a Hydrophobic Solid," *J. Colloid Interface Sci.,* **78**, 225 (1980).

Brown, W. Y. N., *Light Scattering Principles and Development,* Clarendon Press, Oxford (1996).

Bungay, P. M., and H. Brenner, "The Motion of a Closely-Fitting Sphere in a Fluid-Filled Tube," *Int. J. Multiphase Flow,* **1**, 25 (1973).

Cussler, E. L., *Diffusion, Mass Transfer in Fluid Systems,* Cambridge Univ. Press, Cambridge (1997).

Gallardo, B. S., M. J. Hwa, and N. L. Abbott, "In Situ and Reversible Control of the Surface Activity of Ferrocenyl Surfactants in Aqueous Solutions," *Langmuir,* **11**, 4209 (1995).

Hiemenz, P. C., and R. Rajagopalan, *Principles of Colloid and Surface Chemistry,* Dekker, New York (1997).

Hou, Z., N. L. Abbott, and P. Stroeve, "Self-Assembled Monolayers on Electroless Gold Impart pH-Responsive Transport of Ions in Porous Membranes," *Langmuir,* **16**, 2401 (2000).

Johnson, K. A., G. B. Westermann-Clark, and D. O. Shah, "Transport of Micelle-Solubilized Steroids Across Microporous Membranes," *J. Pharm. Sci.,* **76**, 277 (1987).

Johnson, K. A., G. B. Westermann-Clark, and D. O. Shah, "Diffusion of Charged Micelles Through Charged Microporous Membranes," *Langmuir,* **5**, 932 (1989).

Koppel, D. E., "Analysis of Macromolecular Polydispersity in Intensity Correlation Spectroscopy. Method of Cumulants," *J. Chem. Phys.,* **57**, 4814 (1972).

Krovvidi, K. R., A. Muscat, P. Stroeve, and E. Ruckenstein, "Transport of Monomer Surfactant Molecules and Hindered Diffusion of Micelles Through Porous Membranes," *J. Colloid Interface Sci.,* **100**, 497 (1984).

Kuo, T. C., L. A. Sloan, J. V. Sweedler, and P. W. Bohn, "Manipulating Molecular Transport Through Nanoporous Membranes by Control of Electrokinetic Flow: Effect of Surface Charge Density and Debye Length," *Langmuir,* **17**, 6298 (2001).

Rosslee, C. A., and N. L. Abbott, "Principles for Microscale Separations Based on Redox-Active Surfactants and Electrochemical Methods," *Anal. Chem.,* **73**, 4808 (2001).

Saji, T., K. Hoshiro, and S. Aoyagui, "Reversible Formation and Disruption of Micelles by Control of the Redox State of the Surfactant Tail Group," *J. Chem. Soc., Chem. Commun.,* **13**, 865 (1985a).

Saji, T., K. Hoshiro, and S. Aoyagui, "Reversible Formation and Disruption of Micelles by Control of the Redox State of the Head Group," *J. Am. Chem. Soc.,* **107**, 6865 (1985b).

Sakai, H., A. Matsumura, S. Yokoyama, T. Saji, and M. Abe, "Photochemical Switching of Vesicle Formation Using an Azobenzene-Modified Surfactant," *J. Phys. Chem. B.,* **103**, 10737 (1999).

Shamim, M., and S. M. A. Baki, "Diffusion Measurements in Aqueous L-Ascorbic Acid Solutions," *Aust. J. Chem.,* **33**, 1857 (1980).

Shin, J., and N. L. Abbott, "Using Light to Control Dynamic Surface Tensions of Aqueous Solutions of Water Soluble Surfactants," *Langmuir,* **15**, 4404 (1999).

Sinkula, A. A., and S. H. Yalkowsky, "Rationale for the Design of Biologically Reversible Drug Derivatives. Prodrugs," *J. Pharm. Sci.,* **64**, 181 (1975).

Smith, F. G., and W. M. Deen, "Electrostatic Effects on the Partitioning of Spherical Colloids Between Dilute Bulk Solution and Cylindrical Pores" *J. Colloid Interface Sci.,* **91**, 571 (1983).

Stella, V. J., W. N. Charman, and V. H. Naringrekar, "Prodrugs. Do They Have Advantages in Clinical Practice?" *Drugs,* **29**, 455 (1985).

Takeoka, Y., T. Aoki, K. Sanui, N. Ogata, M. Yokoyama, T. Okano, Y. Sakurai, and M. Watanabe, "Electrochemical Control of Drug Release from Redox-Active Micelles," *J. Controlled Release,* **33**, 79 (1995).

Manuscript received Dec. 26, 2002, and revision received June 26, 2003.