Colloid & Polymer Science Colloid Polym Sci 271 : 745–754 (1994)

On the interpretation of solubilization results obtained from semi-equilibrium dialysis experiments

S. D. Christian[§]), E. E. Tucker[§]), J. F. Scamehorn[¶]), and H. Uchiyama

Institute for Applied Surfactant Research, The University of Oklahoma, Norman, Oklahoma USA
[§]) Department of Chemistry and Biochemistry, The University of Oklahoma, Norman, Oklahoma USA
[¶]) School of Chemical Engineering and Materials Science, The University of Oklahoma, Norman, Oklahoma USA

Abstract: The interpretation of intramicellar solubilization data obtained from semi-equilibrium dialysis (SED) experiments is described, and methods are presented for determining equilibrium constants for the solubilization of organic species by aqueous surfactant solutions as well as activity coefficients of both the organic solute and the surfactant within the micelle. The solubilization equilibrium constant of an organic solute in an aqueous micellar solution (K) is defined as the ratio of the mole fraction of organic solute in the micellar "pseudophase" (X) to the concentration of the unsolubilized monomeric organic solute in the aqueous phase (c_0). Expressions compatible with the Gibbs–Duhem equation are used to represent the concentration dependence of activity coefficients of both the solubilizate and surfactant in the micellar pseudophase; the analysis leads to calculated values of the concentrations of free and intramicellar surfactant and organic solute in both compartments of the equilibrium dialysis cell. Solubilization equilibrium constants for many amphiphiles are well correlated by the simple expression $K = K_0(1 - BX)^2$, where B is an empirical constant and K_0 is the limiting value of K as X approaches 0.

Key words: Solubilization – surfactant activity – dialysis – surfactant thermodynamics – semi-equilibrium

Introduction

Equilibrium dialysis has been used for many decades in binding studies [1–3], including investigations of the solubilization of organic solutes by aqueous surfactant micelles. The technique and principles underlying the method are quite simple: a solution containing a macromolecule (e.g., a protein or other soluble polymer) and a solute that binds to the polymer is placed in one compartment of the dialysis cell and the pure solvent (including added electrolytes, if required) is placed in the other. A membrane having a molecular weight cut-off (MWCO) value small enough to prevent transfer of the macromolecule separates the two compartments. After a suitable equilibration period, both the permeate (in solution not containing the added macromolecular species) and the retentate (the solution containing the macromolecule) are analyzed to determine the equilibrium concentrations of the small molecular solute. If necessary, the retentate is analyzed to determine the final concentration of the large molecular species (which may differ from the initial concentration owing to influx of solvent into the retentate or leakage of the macromolecule into the permeate). Assuming that the small molecule reaches equilibrium, and neglecting the presence of any of the macromolecular species in the permeate compartment, one ordinarily equates the concentration of organic in the permeate compartment to that of the "free" organic species in the retentate, and thereby infers the concentration of "bound" organic solute by *difference*.

Precisely the technique described in the preceding paragraph has been used to estimate the extent of binding or solubilization of organic solutes by surfactant micelles, neglecting complications caused by leakage of the surfactant into the permeate compartment [4–8]. Unfortunately, in such experiments, the concentration of surfactant in the permeate compartment (after equilibration periods of 20 to 24 h) usually somewhat exceeds the critical micelle concentration (CMC) [9], indicating that micelles are able to form in the permeate, and suggesting that some of the organic solute in the permeate compartment will be bound to or solubilized by the micelles. Thus, the simple interpretation of equilibrium dialysis data – in which the total concentration of the organic solute in the permeate is equated to the concentration of free molecules of the solute – is subject to considerable error. The presence of bound organic molecules in the permeate must be accounted for in order to infer reliable values of solubilization partition or binding coefficients.

Work from our laboratories has led to the development of a modified equilibrium dialysis method, which we refer to as "semi-equilibrium dialysis" (SED), and which differs from conventional equilibrium dialysis primarily in the mathematical analysis of data [9–23]. Studies of numerous organic solute/surfactant micelle systems indicate that corrections for the presence of micellar surfactant and solubilized organic solute in the permeate compartment are particularly important when binding constants between the micelles and the organic solute are large or when the surfactant has large values of the CMC. It is the purpose of the present article to indicate how data are obtained and analyzed to infer solubilization equilibrium constants under a wide range of conditions.

Description of the method

Figure 1 indicates the arrangement of the two compartments of an equilibrium dialysis cell. In our studies of surfactant solutions, we have utilized cells having compartments containing approximately 5 ml of solution, and employing regenerated cellulose membranes (MWCO = 6000 dalton). Initially, a solution containing surfactant and organic solute (e.g., 0.100 M hexadecylpyridinium chloride (CPC) and 0.025 M *p*-chlorophenol) is placed in the retentate compartment, and pure water is placed in the permeate. If replicate cells are assembled and loaded with the same retentate solution, results can be obtained corresponding to arbitrary periods varying from a few hours to several days. Typically, plots of the concentration of CPC and organic solute in the permeate vs. time will resemble those shown in Fig. 2. The total concentration of CPC in the permeate, [CPC], reaches a value near the CMC at approximately 6 to 10 h, and increases slowly thereafter; it would literally require years for the concentrations of CPC to reach the same value in both compartments. Similarly, the concentration of organic solute in the permeate, [O], rises rapidly at first and then less rapidly after 8–10 h. When careful measurements of the organic concentration are made, it is determined that [O] continues to increase in proportion to the increase in total concentration of CPC [9, 24]. Strictly speaking, neither component reaches thermodynamic equilibrium, because the presence of more and more CPC micelles in the permeate causes an increasing concentration of the organic solute to be extracted into that compartment. But it seems appropriate to describe the situation obtaining in the cell, after equilibration time of at least 16 h, as being that of semi-equilibrium, in which the organic solute is present at any instant in both compartments *at the same thermodynamic activity* (or monomer concentration). In

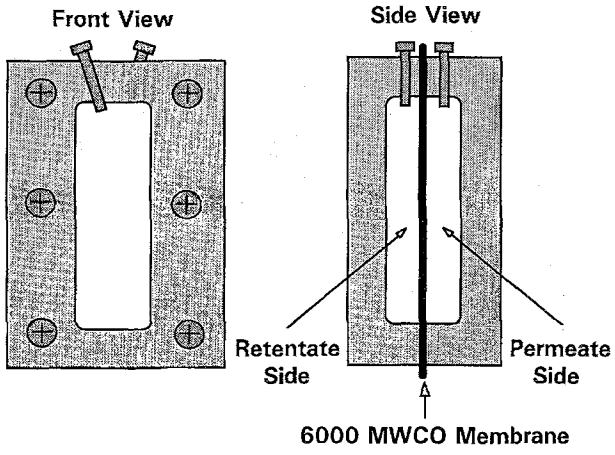

Fig 1. Representation of the Semi-Equilibrium Dialysis (SED) Cell

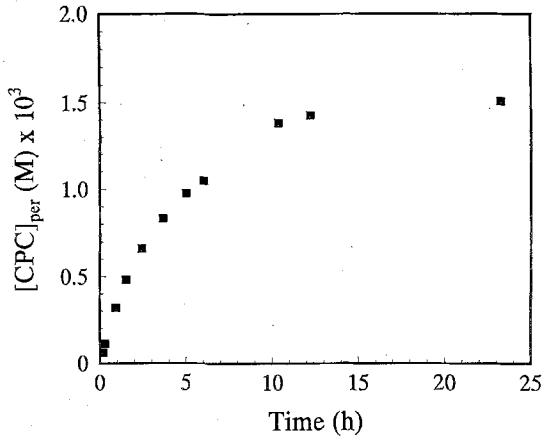

Fig. 2a. Transfer of *n*-hexadecylpyridinium chloride through membrane for an initial concentration of 0.2265 mol/l in the retentate solution

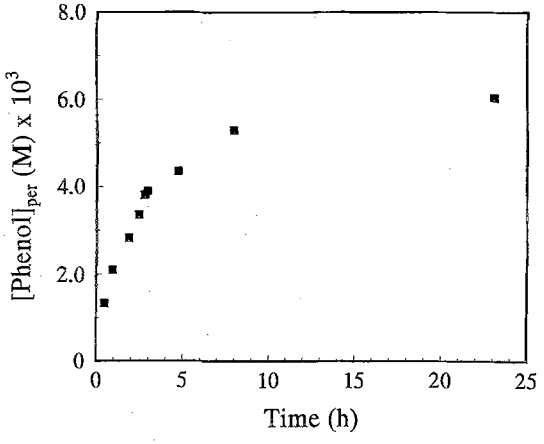

Fig. 2b. Transfer of phenol through membrane for an initial concentration of 0.0122 ml/l in the retentate solution.

the following section, we describe methods used to analyze data (collections of $[O]_{per}$, $[CPC]_{per}$, $[O]_{ret}$, and $[CPC]_{ret}$) to infer values of equilibrium extent of solubilization of the organic component in the micelles present in either compartment. In these symbols, brackets [ ] denote total or analytical concentrations and the subscripts per and ret indicate permeate and retentate compartments.

Mathematical analysis of data

The total concentration of surfactant in either compartment may be expressed as

$$[CPC] = c_{CPC,\,monomer} + [CPC]_{mic}\,, \tag{1}$$

Where $c_{CPC,\,monomer}$ and $[CPC]_{mic}$ denote concentrations of surfactant in monomer and micellar forms, respectively. Similarly, the total concentration of organic solute in either the permeate or the retentate solution can be written

$$[O] = c_0 + [O]_{mic}\,, \tag{2}$$

where c_0 is the concentration of monomeric organic solute and $[O]_{mic}$ is the concentration of organic solute associated with surfactant micelles. Now the assumptions made in the SED method imply that c_0 will be the same in both compartments (neglecting medium effects on the activity coefficient of the organic solute in monomeric form in the two compartments). By applying Eq. (2) to both the retentate and permeate, we can write:

$$\begin{aligned}[O]_{ret}/[O]_{per} &= \{c_0 + [O]_{mic,\,ret}\}/\{c_0 \\ &\quad + [O]_{mic,\,per}\} \\ &= [1 + [O]_{mic,\,ret}/c_0]/[1 \\ &\quad + [O]_{mic,\,per}/c_0]\,. \end{aligned} \tag{3}$$

Next, we assume that the ratios $[O]_{mic,\,ret}/c_0$ and $[O]_{mic,\,per}/c_0$ in Eq. (3) are both equal to $\kappa[CPC]_{mic}$, where $[CPC]_{mic}$ is the micellar concentration of CPC in the corresponding compartment (either retentate or permeate) and the proportionality constant κ is a partition coefficient for the organic species between the "bulk" aqueous solution and the intramicellar "pseudophase". (The reasonable assumption is made that κ is the same on both sides of the membrane.) By making the substitution $[O]_{mic}/c_0 = \kappa[CPC]_{mic}$, we can rearrange Eq. (3) to obtain:

$$\begin{aligned}\kappa = \{&[O]_{ret} - [O]_{per}\}/\{[O]_{per}[CPC]_{mic,\,ret} \\ &- [O]_{ret}[CPC]_{mic,\,per}\}\,. \end{aligned} \tag{4}$$

Of the four concentration terms in Eq. (4), both $[O]_{ret}$ and $[O]_{per}$ are directly measurable, and $[CPC]_{mic,\,ret}$ is in most experiments practically equal to the total concentration of CPC in the retentate. The remaining term, $[CPC]_{mic,\,per}$

causes the major difficulty in the calculation of κ. When κ is less than about 1000 M^{-1}, complications caused by the presence of micelles of [CPC] in the permeate are less important, and it is usually possible to make good estimates of the effects of total concentrations of the organic solute and CPC on the relative concentrations of surfactant monomers and micelles in the permeate compartment. The Appendix to this paper summarizes methods in which the Gibbs–Duhem equation is applied to components within the micelle in order to infer values of the concentrations of monomeric and micellar species in the permeate. These procedures also yield values of the activity coefficients of both the organic solute and the surfactant in the intramicellar pseudophase.

Solubilization equilibrium constants and solute activity coefficients

The partition ratio, κ, was defined in the preceding section as $[O]_{mic}/\{c_0[CPC]_{mic}\}$. This constant may also be thought of as a mass action equilibrium constant for the reaction O (in bulk aqueous solution) + CPC (in micellar form) = O (in micellar form); κ has been interpreted in this way in many studies of the solubilization of organic solutes by surfactant micelles [25–32]. However, for many purposes it is more convenient to define an equilibrium constant by the equation

$$K = [O]_{mic}/\{c_0([CPC]_{mic} + [O]_{mic})\} = X/c_0 , \quad (5)$$

where X is the mole fraction of the organic solute in the micelles. Using the logic of the SED method, X should be the same in the permeate and retentate solutions, because both K and c_0 are constant for a given intramicellar composition (again neglecting any effects of differences in the media on the activity of the organic species) [9–12]. K and κ are simply related by the equation $K = (1 - X)\kappa$. A major research goal in our laboratory has been to determine how K (or κ) depends on X for given solutes; plots of K vs X are referred to as "solubilization isotherms" [33].

One advantage of defining an equilibrium constant, K, by Eq. (5) is that this constant is closely related to the activity coefficient of the organic solute in the "intramicellar solution". A commonly used model for micellar solutions is one in which the monomers and micelles of the surfactant are assumed to form separate *pseudophases* that in many ways resemble co-existing liquid and vapor phases; the micellar phase is treated as analogous to the liquid phase and the monomer phase as analogous to the vapor phase. For sparingly soluble compounds, the activity of the solute in the micellar phase is usually equated to c_0/c_0^0, where c_0^0 is the saturation concentration of the organic solute in water (or in the electrolyte solution being employed). Thus, knowledge of the concentration of organic monomers in the bulk aqueous phase provides a measure of the escaping tendency of the organic component from the micellar phase. If the intramicellar solution were ideal, c_0/c_0^0 would simply be equal to X, and the solution would be said to obey Raoult's law.

One can define an activity coefficient for the organic solute by the equation

$$\gamma_0 = \text{solute activity}/X = (c_0/c_0^0)/X , \quad (6)$$

where values of $\gamma_0 > 1$ characterize solutions deviating positively from Raoult's law; values of $\gamma_0 < 1$ imply negative deviations, and $\gamma_0 = 1$ defines an ideal solution [19–21]. γ_0 is simply interpreted as the relative volatility of the solute O; the value of γ_0 is a direct measure of the escaping tendency of the solute from the micelle, compared to its escaping tendency from a solution obeying Raoult's law. For example, the activity coefficient for cyclohexane in CPC micelles at $X = 0.1$ is approximately 3 [24], and this implies that cyclohexane has three times the volatility from the micellar phase that it would have from an ideal solution in which $X = 0.1$. What is impressive about the value of the activity coefficient in this system, however, is not the fact that it is greater than 1, but that it is so much smaller than the activity coefficient of cyclohexane in water, a constant having a value on the order of 10^5. This comparison makes it clear that the intramicellar environment is many orders of magnitude "more hospitable" to cyclohexane than pure water itself. By combining Eqs. (5) and (6), we obtain the relation

$$\gamma_0 = 1/(Kc_0^0) , \quad (7)$$

which relates the relative escaping tendency of organic solutes from the micelle (on the basis of

pure component standard states) to both the solubilization equilibrium constant and the solubility of the solute in water.

Analysis of SED data to obtain solubilization constants

As noted above, at semi-equilibrium the mole fraction of organic solute in the surfactant micelle should be the same in the micelllar pseudophase on either side of the dialysis membrane; this implies that the dependence of γ_0 and γ_{CPC} (the activity coefficient of CPC in the micelle) should also be the same in the permeate as in the retentate solution. In the retentate solution, at surfactant concentrations exceeding a few hundredths molar, the fraction of CPC in the monomeric form is almost negligible. One can relate the CMC of the solution (which is the same as the concentration of surfactant in monomeric form) to the concentration of free counterion (Cl^-) by the equation [34]

$$\log(\mathrm{CMC}) = -0.658 \log[Cl^-] - 5.02 . \quad (8)$$

This result implies that at total concentrations of surfactant greater than 0.01 M, less than 4% of the surfactant is in monomeric form. However, in the permeate solution, the total concentration of Cl^- is only on the order of 1 mM, so it is necessary to consider the fraction of the surfactant in both monomeric (CP^+) and micellar forms.

By applying Eqs. (1) and (2) to both the permeate and retentate solutions, and using the activity coefficient of the CPC to relate the monomer and micellar concentrations of the surfactant in each compartment, one obtains the set of equations:

$$\begin{aligned}
[\mathrm{CPC}]_{per} &= c_{CPC,\,monomer,\,per} + [\mathrm{CPC}]_{mic,\,per} \\
&= \gamma_{CPC}(1 - X)\mathrm{CMC}_{per} + [\mathrm{CPC}]_{mic,\,per} \\
[\mathrm{CPC}]_{ret} &= c_{CPC,\,monomer,\,ret} + [\mathrm{CPC}]_{mic,\,ret} \\
&= \gamma_{CPC}(1 - X)\mathrm{CMC}_{ret} + [\mathrm{CPC}]_{mic,\,ret} \\
[\mathrm{O}]_{per} &= c_0 + \{X/(1 - X)\}[\mathrm{CPC}]_{mic,\,per} \\
[\mathrm{O}]_{ret} &= c_0 + \{X/(1 - X)\}[\mathrm{CPC}]_{mic,\,ret} \quad (9)
\end{aligned}$$

which involve the known concentrations $[\mathrm{CPC}]_{per}$, $[\mathrm{O}]_{per}$, $[\mathrm{O}]_{ret}$, and $[\mathrm{CPC}]_{mic,\,ret}$. By solving the first two of Eqs. (9) for $[\mathrm{CPC}]_{mic,\,per}$ and $[\mathrm{CPC}]_{mic,\,ret}$, and substituting these expressions into the equations for $[\mathrm{O}]_{per}$ and $[\mathrm{O}]_{ret}$, one obtains:

$$[\mathrm{O}]_{per} = c_0 + \{X/(1 - X)\}\{[\mathrm{CPC}]_{per} - \gamma_{CPC}(1 - X)\mathrm{CMC}_{per}\}$$

and

$$[\mathrm{O}]_{ret} = c_0 + \{X/(1 - X)\}\{[\mathrm{CPC}]_{ret} - \gamma_{CPC}(1 - X)\mathrm{CMC}_{ret}\} \quad (10)$$

Equations (10) involve four known concentrations $\{[\mathrm{O}]_{per}, [\mathrm{CPC}]_{per}, [\mathrm{O}]_{ret}$, and $[\mathrm{CPC}]_{ret}\}$and the two known values of the CMC (CMC_{per} and CMC_{ret} calculated from Eq. (8), as well as the unknowns c_0, X, and γ_{CPC}. Therefore, it is clear that one additional equation relation among the three unknowns must be found if the experimental results of the SED method are to be analyzed to obtain all of the required species concentrations and the intramicellar mole fraction of surfactant and organic solubilizate. The additional relationship is in fact a form of the Gibbs–Duhem equation, applied to interrelate the activity coefficients of CPC and O within the micelle [10–12, 17, 19–21, 35]. Equations analogous to those employed in treating nonideal solutions of nonelectrolytes are employed to represent the dependence of γ_{CPC} and γ_0 on X and hence to analyze collections of data obtained through ranges of relative concentrations of organic solute and CPC in SED experiments. Fortunately, at low values of X, the activity coefficient of the surfactant in the micelles remains close to unity (its limiting value as its mole fraction in the micelle approaches 1), so for many purposes, γ_{CPC} can simply be ignored in Eqs. (10), making it possible to solve these equations to obtain values of $c_{CPC,\,monomer,\,per}$, c_0, and X.

In numerous applications of the SED method to study the solubilization of polar solutes in ionic surfactant micelles, it has been found that the equation

$$K = K_0 (1 - BX)^2 \quad (11)$$

quite accurately represents the dependence of the solubilization equilibrium constant on intramicellar composition [19–21, 23]. In the limit as X goes to zero, K approaches K_0, the value of the solubilization constant in the limiting (Henry's law) region. The parameter B in equation 11 can be related to constants in the Langmuir equation,

fitted to data by assuming that the polar head group of the solute occupies an "adsorption site" near the ionic exterior of the micelle. The value of B uniquely determines the dependence of γ_{CPC} on X. Fortunately, values of B in the range 1 to 2 are commonly found for polar solutes, and for particular classes of organic compounds the value of B can be estimated to predict values of γ_{CPC} for use in Eqs. (10) [19, 21, 23]. Thus, the preliminary evaluation of SED data can be done quite simply, without performing a Gibbs–Duhem analysis of complete sets of SED results.

Analysis of SED data to obtain slubilization constants – a specific example

Qualitative information about the solubilization of *p*-chlorophenol (O) by CPC micelles was presented in an earlier section. Let us now consider how SED measurements for a specific experiment might be interpreted. We suppose first that a value of K is sought corresponding to a value of X (the mole fraction of *p*-chlorophenol in the micelles) equal to approximately 0.2. Assume that we set up the SED cell with 0.050 M CPC and 0.013 M *p*-chlorophenol in the retentate, with the expectation that the major fraction of each solute will remain in the retentate compartment at equilibrium. With such a starting solution, it might be found that at semi-equilibrium (after 20 h) the values of the four measured concentrations would be:

$$[CPC]_{per} = 0.00123\ M,\ [CPC]_{ret} = 0.0425\ M\ ,$$

$$[O]_{per} = 0.000467\ M,\ \text{and}\ [O]_{ret} = 0.0104\ M\ .$$

All four concentrations could be obtained by uv spectrometry, using absorbances measured at multiple wavelengths and correcting for the overlap of the absorption bands of CPC and *p*-chlorophenol. Note that both $[CPC]_{ret}$ and $[O]_{ret}$ are smaller than their starting values and that the decreases in these concentrations exceed the small concentration of each compound that transfers into the permeate compartment. The apparent loss of these solutes from the retentate occurs because some water is transferred from the permeate into the retentate compartment owing to osmotic pressure, but the effect does not cause any experimental problems or complicate the analysis of data *provided* analytical determinations of the two solutes are obtained for both compartments.

In performing preliminary calculations, it is convenient to utilize Eqs. (10) assuming: a) that the activity coefficient of CPC in the micelles is unity; b) that the term $\gamma_{CPC}(1 - X)CMC_{ret}$ can be neglected in comparison with $[CPC]_{ret}$; and c) that X can be estimated from the known final concentrations of O and CPC in the retentate (i.e., neglecting monomer concentrations in the retentate compartment). With these assumptions, $X \sim 0.0104/(0.0104 + 0.0425) = 0.19$ and the estimated value of $\gamma_{CPC}(1 - X)CMC_{per}$ is $(1 - 0.19)0.00078\ M = 0.00063\ M$, where 0.00078 M is the value of the CMC obtained from Eq. (8), using the approximate value of the free chloride concentration, $[Cl^-] = 0.00123$ M. Therefore, the concentration of CPC in the micelles in the permeate is calculated to be 5.01×10^{-4} M and the concentration of O in micelles in the permeate is $\{X/(1 - X)\} \times 5.01 \times 10^{-4}\ M = 1.19 \times 10^{-4}$ M. Therefore, the estimated value of c_0 is $4.67 \times 10^{-4}\ M - 1.19 \times 10^{-4}\ M = 3.48 \times 10^{-4}$ M.

Employing the value of c_0 just calculated, it is possible to refine the calculations illustrated in the previous paragraph, utilizing an improved value of X and if necessary accounting for the fact that γ_{CPC} is not precisely equal to one. Thus, the molarity of micellar *p*-chlorophenol in the retentate is almost exactly equal to 0.0104 M – 0.0003 M, so that a better estimate of the mole fraction of *p*-chlorophenol in the micelle is $X = 0.0101/(0.0101 + 0.0424) = 0.192$. (A very tiny correction for the concentration of monomeric CP^+ in the retentate has also been applied.) Now, utilizing the previous observation that the value of B (in Eq. (11) is equal to 1.3 ± 0.1 for the mono- and dichlorophenols [19], one can use the value of X and this estimated value of B to calculate an approximate value of the activity coefficient of CPC in the micelle (see Appendix). This leads to the estimate $\gamma_{CPC} = 0.94$, so that the improved estimate of the concentration of CPC in monomeric form in the permeate is $0.94 \times 0.808 \times 0.000964 = 0.000729$ M and the concentration of CPC in micellar form is 0.00123 M – 0.000729 M = 0.000501 M. Finally, the concentration of O in the micelles is $0.000501\ M \times 0.192/0.808 = 0.000119$ M and $c_0 = 0.000467\ M - 0.000119\ M = 0.000348$ M.

Additional iterations can be performed, but the derived value of c_0 will not change significantly unless a revised value of B is employed. An exact solution Eqs. (8–11) yields X and c_0 values differing by less than 0.5% from the values calculated here.

Using the values of c_0 and X just inferred, one can calculate

$$K = X/c_0 = 0.192/0.000348\ \text{M} = 552\ \text{M}^{-1}$$

in reasonable agreement with the value of K reported previously at $X \sim 0.2$.

When SED measurements covering a range of X values have been obtained for a given surfactant/solubilizate system, it is possible to use a nonlinear least squares curve-fitting method to derive values of K_0 and B in Eq. (11) and thereby obtain the best values of these parameters [19–22]. By using equations derived in the preceding sections, one can then infer values of γ_{CPC}, γ_0, and K as functions of X. Moreover, as an additional check on the consistency and scatter of the experimental results, K values corresponding to each of the individual SED experiments can be calculated from Eq. (4) (which is multiplied by $1 - X$ to convert κ into K). This type of calculation requires using the least squares value of B (deduced from the entire collection of SED data) to calculate values of $[CPC]_{mic,per}$ and hence K from the measured concentrations of the two solutes determined in each separate SED experiment. Figure 3 illustrates data plotted in this way for the system CPC/*p*-chlorophenol; the smooth curve is consistent with Eq. (11), using $B = 1.25 \pm 0.03$ and $K_0 = 786 \pm 49$, and the points denote individual values of K calculated from Eq. (4), utilizing the procedure described in the preceding paragraphs. Note that the individual K values can be calculated from the separate data sets, provided a reasonable estimate of B is available.

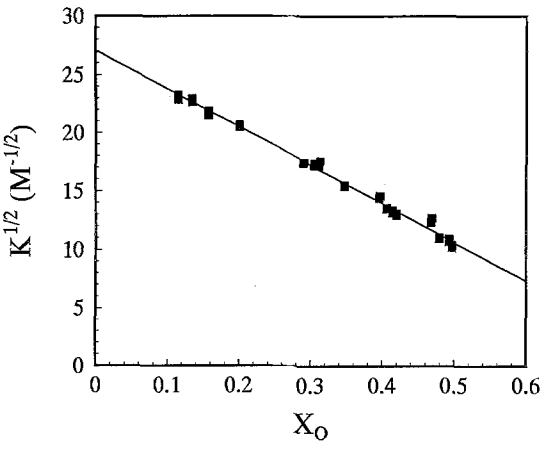

Fig. 3. Dependence of the square root of solubilization equilibrium constants for *p*-chlorophenol in hexadecylpyridinium chloride micelles on intramicellar mole fraction of solute. Data taken from ref. 23.

Summary

The semi-equilibrium dialysis method appears to be one of the most general techniques available for obtaining complete solubilization isotherms. In work of the greatest precision, the method requires determination of the concentrations of surfactant and organic solubilizate in both compartments of the dialysis cell; however, in many applications it is only necessary to analyze the permeate, inferring the concentrations of the solute components in the retentate by difference. For most systems, a 16- to 20-h equilibration time seems adequate, and the assumption that organic solutes can reach equilibrium with respect to the solutions on both sides of the membrane seems to be justifiable. Although a variety of surfactants and organic solubilizates have been investigated using the method, considerably more research needs to be done to map out the behavior of surfactant/organic solute systems. In addition, the SED method can be used for determining the extent of binding of monovalent and multivalent counterions to ionic micelles [37] and for studying the Donnan expulsion of ions having the same charge as the micelles [16].

Note added in proof: A recent publication describes a modified SED method, in which surfactant concentrations well above the CMC are added to both compartments of the dialysis cell [42]. The new technique simplifies calculation of the relative concentrations of micellar and nonmicellar species in both compartments.

Appendix

In order to interpret results of SED experiments to obtain information about the extent of

solubilization of organic solutes by surfactant micelles, Eqs. (10) must be solved simultaneously to infer the values of the unknowns c_0, X, and γ_{CPC}. These variables represent, respectively, the concentration of monomeric organic solute, the mole fraction of the organic solute in the micelle, and the activity coefficient of the surfactant in the micelle. Values of c_0, X, and γ_{CPC} are taken to be the same in both compartments of the dialysis cell, corresponding to the assumed *semi-equilibrium* condition. To complete the analysis of data, it is necessary to assume one or another mathematical model for expressing the dependence of γ_{CPC} on X. Several possible functional relationships for $\gamma_{CPC}(X)$ are treated explicitly here, starting with the simplest assumption that γ_{CPC} is always equal to unity, and proceeding to more complicated forms in which the activity coefficients of surfactant and organic solute in the micelle vary according to parametric equations consistent with the Gibbs–Duhem equation.

A. Ideal solution model

The simplest thermodynamic model for the mixing of components within a surfactant micelle is the pseudophase equivalent of Raoult's law. When it can be assumed that Raoult's law is obeyed, γ_{CPC} is set equal to unity, and Eqs. (10) are solved explicitly for X and c_0. Such an assumption has been shown to be valid for binary surfactant mixtures containing quite similar surfactants – for example, mixture of the anionic soaps and alkylsulfates having similar hydrophobic chain lengths [36]. Moreover, even in the ordinarily more complex intramicellar mixtures of surfactant and organic solute, the value of γ_{CPC} at small values of X will not vary much from unity, because the solvent activity coefficient tends to approach the value $\gamma = 1$ *tangentially* (on a plot of γ vs X) as $X \to 0$ [35].

B. Activity coefficient expansions consistent with the Gibbs–Duhem equation

Numerous algebraic expressions have been used to relate activity coefficients of components in binary nonelectrolyte mixtures to the mole fraction of these components in the liquid phase. General type relationships applying to a solvent (component 1) and a solute (component 2) are:

$$\ln \gamma_1 = X^2(A_1 + B_1X + C_1X^2 + \cdots)$$

and

$$\ln \gamma_2 = (1 - X)^2(A_2 + B_2X + C_2X^2 + \cdots), \quad (12)$$

where X refers to the mole fraction of the solute and the coefficients $A_2, B_2, C_2, \ldots$ can be expressed as known functions of $A_1, B_1, C_1, \ldots$ by applying the Gibbs–Duhem equation. If all of the constants except A_1 and A_2 can be neglected, it can be shown that these two parameters must be equal. Mixed micellar systems for which $A_1 = A_2$ may be said to obey the Rubingh model [38] or the one-parameter Margules model [39]; such systems have also been termed *regular solutions*, although this terminology is usually inappropriate as applied to nonideal mixed micelles [40]. A regular solution model had been applied previously to describe the concentration dependence of the activity coefficient of a polar solute in a nonionic surfactant micelle [41].

Various specific forms of Eq. (12) have been applied to fit semi-equilibrium dialysis results for micellar mixtures and solutions of organic solutes in micelles, consistent with the assumptions of the pseudophase equilibrium model [10]. Relations of the type

$$\ln \gamma_1 = X^2[A - B/2 + (B - 2C/3)X + CX^2]$$

and

$$\ln \gamma_2 = (1 - X)^2(A + BX + CX^2) \quad (13)$$

are obtained in the three-parameter case, where the Gibbs–Duhem equation has been used to relate the coefficients in expressions for $\ln \gamma_1$ and $\ln \gamma_2$. Equation (13) has been included in a nonlinear least squares analysis of sets of SED data obtained throughout a range of X values to infer best values of the parameters K_0, A, B, and C. (This formulation of course reduces to the one-parameter Margules model if B and C are both equal to 0.) Although this type of analysis may be required if extensive and accurate SED data are available, for most purposes it is probably adequate to fit data to somewhat simpler mathematical models.

C. Alternative one- and two-parameter models consistent with the Gibbs–Duhem equation

The SED method and other techniques have been used to obtain equilibrium isotherms for numerous polar amphiphiles solubilized by surfactant micelles. These solutes contain a polar head group and a more or less bulky hydrophobic "tail"; they tend to solubilize with the head group localized in the outer polar or polar/ionic region of the surfactant micelle, and with the hydrophobic tails extending toward the micellar interior. Solutes such as aliphatic alcohols, phenols and chlorinated phenols, carboxylic acids, and many other similar species are known (or assumed) to solubilize in this way.

Lee et al. have shown that data for numerous systems of amphiphiles solubilized by ionic micelles are well represented by the simple equation.

$$K = K_0(1 - BX)^2 \tag{11}$$

in which K_0 is the limiting binding constant for the solute (as $X \to 0$) and B is a parameter related to the number of sites occupied by a molecule of the amphiphile at the micellar surface. The limiting linear form of Eq. (11) that applies as $X \to 0$ is consistent with the Langmuir equation, but the equation also predicts that K vs X plots will be concave upward (as is almost invariably observed for polar solutes) at larger values of X. When the simple model equation $K = K_0(1 - BX)^2$ is applied, it can be shown that the Gibbs–Duhem equation implies that

$$\ln \gamma_{CPC} = 2[B\ln(1 - X) - \ln(1 - BX)]/(1 - B)\,. \tag{14}$$

Thus, only the value of the dimensionless parameter B is required to predict values of the activity coefficient of the surfactant at any chosen value of X. The results of extensive solubilization studies have shown that B is practically constant for given classes of amphiphilic solutes, so that values of the surfactant activity coefficient can usually be predicted quite reliably by Eq. (14).

A more general two-parameter extension of Eq. (14) has also been used, for cases in which the dependence of K on X is more complicated than predicted by Eq. (12). Thus, the equation

$$K = K_0(1 - AX)(1 - BX) \tag{15}$$

can be fitted to solubilization isotherms (K vs. X) which are either concave upwards or concave downward [22, 23]. The equation involves the two dimensionless parameters, A and B, but these constants are not simply related to the parameters in the Langmuir equation. Nonetheless, Eq. (15) is readily integrated, using the Gibbs–Duhem equation, to derive a two-parameter equation for $\ln \gamma_{CPC}$, analogous to Eq. (14).

$$\ln \gamma_{CPC} = [A\ln(1 - X) - \ln(1 - AX)]/(1 - A) + [B\ln(1 - X) - \ln(1 - BX)]/(1 - B) \tag{16}$$

Equation (16) has been used to fit solubilization isotherms for systems in which K exhibits either a maximum or a minimum as X is varied in the range 0 to 0.6.

D. Choice of models for fitting SED results

In the specific example given in the text for calculating K from SED data, it was indicated that an initial value of unity could be chosen for the activity coefficient of the surfactant, so that Eqs. (10) could be solved simultaneously to obtain preliminary estimates of c_0 and X. If B (in Eq. (11)) can be estimated from results for similar solutes, the B value and the provisional value of X can be used to obtain an improved value of the activity coefficient of the surfactant (using Eq. (14)). Ordinarily this procedure will lead to derived values of K and X that are as accurate as can be justified, given the inevitable uncertainties in the analytically determined concentrations of species in both compartments of the equilibrium dialysis cell.

In more elaborate studies, K values can be determined by the procedure outlined in the previous paragraph, and the parameters in Eq. (11) can be estimated from the dependence of K on X. It is convenient to plot $\sqrt{K}$ vs X, obtaining $\sqrt{K_0}$ as a limiting value and estimating B from the slope of the plot, which can be shown to be equal to $-B\sqrt{K_0}$. If necessary, a nonlinear least squares method may be employed to fit all of the SED data for a given system to models consistent with Eqs. (11) and (13) or Eqs. (15) and (16). It is ordinarily quite useful to employ the resulting equations for $\ln \gamma_{CPC}$ to

obtain point by point estimates of K and X, so that the individual points and the fitted curve can both be represented on the plot of K vs X, indicating the scatter of experimental results and the goodness of fit of the model to the entire adsorption isotherm.

Acknowledgments

The authors appreciate the financial support of the Office of Basic Energy Sciences, Department of Energy, contract DE-FG05-87ER13678, National Science Foundation grant CBT 8814147, University of Nevada-Reno, contract 90-09, an Applied Research Grant from the Oklahoma Centers for the Advancement of Science and Technology, and the Center for Waste Reduction Technologies of the American Institute of Chemical Engineers, Agreement No. N12-N10. In addition, they gratefully acknowledge the assistance of industrial sponsors of the Institute for Applied Surfactant Research, including Kerr-McGee Corporation, E. I. Du Pont de Nemours & Co., and ICI Chemicals.

References

1. Freifelder D (1982) In: Freeman WH et al (eds) Physical Biochemistry – Applications to Biochemistry and Molecular Biology, 2nd ed. San Francisco, p 675
2. Cantor CR, Schimmel PR (1980) In: Freeman WH (eds) Biophysical Chemistry Part III – The behavior of Biologial Macromolecules San Francisco, pp 1328–1339
3. Molyneux P (1984) In: Water-Soluble Synthetic Polymers: Properties and Behavior, Vol II. CRC Press, Boca Raton, Florida, pp 101–105
4. Patel NK, Kostenbauder HB (1958) J Am Pharm Ass Sci Ed 47:289
5. Kazmi SJA, Mitchell AG (1971) J Pharm Pharmacol 23:482
6. Mitchell AG, Brown KF (1966) J Pharm Pharmacol 18:115
7. Patel NK, Foss NE (1965) J Pharm Sci 54:1495
8. Patel NK, Foss NE (1964) J Pharm Sci 53:94
9. Christian SD, Smith GA, Tucker EE, Scamehorn JF (1985) Langmuir 1:564
10. Smith GA, Christian SD, Tucker EE, Scamehorn JF (1986) J Solution Chem 15:519
11. Higazy WS, Mahmoud FZ, Taha AA, Christian SD (1988) J Solution Chem 17:191
12. Bhat SN, Smith GA, Tucker EE, Christian SD, Scamehorn JF, Smith W (1987) I&EC RESEARCH 26:1217
13. Smith GA, Christian SD, Tucker EE, Scamehorn JF (1987) Langmuir 3:598
14. Christian SD, Scamehorn JF (1989) In: Scamehorn JF, Harwell JH (eds), Surfactant-Based Separation Processes. Marcel Dekker, New York, pp 3–28
15. Sasaki KJ, Burnett SL, Christian SD, Tucker EE, Scamehorn JF (1989) Langmuir 5:363
16. Christian SD, Tucker EE, Scamehorn JF, Lee B-H, Sasaki KJ (1989) Langmuir 5:876
17. Mahmoud FZ, Christian SD, Tucker EE, Taha AA, Scamehorn JF (1989) J Phys Chem 93:5903
18. Scamehorn JF, Christian SD, Tucker EE, Tan BI (1990) Colloid Surf 49:259
19. Lee B-H, Christian SD, Tucker EE, Scamehorn JF (1990) Langmuir 6:230
20. Uchiyama H, Christian SD, Scamehorn JF, Abe M, Ogino K (1991) Langmuir 7:95
21. Lee B-H, Christian SD, Tucker EE, Scamehorn JF (1991) J Phys Chem 95:360
22. Lee B-H, Christian SD, Tucker EE, Scamehorn JF (1991) Langmuir 7:1332
23. Lee B-H (1990) Ph.D. dissertation, The University of Oklahoma
24. Smith GA (1986) Ph.D. dissertation, The University of Oklahoma
25. Goto A, Endo F (1978) J Coll Interf Sci 66:26
26. Mukerjee P, Cardinal JR (1978) J Phys Chem 82:1620
27. Armstrong DW, Nome F (1981) Anal Chem 53:1662
28. Arunyanart M, Cline Love LJ (1984) Anal Chem 56:1557
29. Treiner C, Chattopadhyay AK (1984) J Coll Interf Sci 98:447
30. Sepulveda J, Lissi E, Quina F (1986) Adv Coll Interf Sci 25:1
31. Malliaris A (1987) Adv Coll Interf Sci 27:153
32. Hinze WL (1987) In: Hinze WL, Armstrong DW (eds) Ordered Media in Chemical Separations
33. Nguyen CM, Christian SD, Scamehorn JF (1988) Tenside Surfactant Detergents 25:6
34. Tipton R (1989) M.S. thesis, The University of Oklahoma
35. Christian SD, Tucker EE, Smith GA, Bushong DS (1986) J Coll Interf Sci 113:439
36. Corrin ML, Harkins WD (1947) J Am Chem Soc 69:683
37. Christian SD, Bhat SN, Tucker EE, Scamehorn JF, El-Sayed DA (1988) AIChE Journal 34:189
38. Rubingh DN (1979) In: Mittal KL (ed) Solution Chemistry of Surfactants, Vol 1. Plenum Press, New York p 337
39. Reid RC, Prausnitz JM, Poling BE (1987) In: The Properties of Gases and Liquids, fourth edition, McGraw-Hill, New York, p 256
40. Christian SD, Tucker EE, Scamehorn JF (1992) In: Holland, PM, Rubingh DN (eds) Mixed Surfactant Systems. ACS Symp Ser 501, Am Chem Soc, Washington D.C., pp 45–51
41. Mukerjee P (1971) J Pham Sci 60:1531
42. Uchiyama U, Christian SD, Tucker EE, Scamehorn JF (1993) J Phys Chem 97:10868

Received May 13, 1993;
accepted August 13, 1993

Authors' address:

Professor Sherril D. Christian
Department of Chemistry and Biochemistry
The University of Oklahoma
Norman, OK 73019
USA