
**Separation Science and Technology**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

# MODELING SOLUTE TRANSPORT IN MICELLAR LIQUID CHROMATOGRAPHY

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Online publication date: 23 October 2002

**To cite this Article** Baltus, Ruth , Lavine, Barry K. and Ritter, Jason(2002) 'MODELING SOLUTE TRANSPORT IN MICELLAR LIQUID CHROMATOGRAPHY', Separation Science and Technology, 37: 15, 3443 — 3464
**To link to this Article: DOI:** 10.1081/SS-120014436
**URL:** http://dx.doi.org/10.1081/SS-120014436

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SEPARATION SCIENCE AND TECHNOLOGY
Vol. 37, No. 15, pp. 3443–3464, 2002

# MODELING SOLUTE TRANSPORT IN MICELLAR LIQUID CHROMATOGRAPHY

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## ABSTRACT

To better understand the causes of reduced efficiencies in micellar liquid chromatography (MLC), a mathematical model that includes both solute–stationary phase and solute–micelle interactions has been developed. Solute mass transfer between mobile and stationary phases and kinetic limitations within the stationary phase are incorporated in the model equations. Equilibrium is assumed between the micelles and the surfactant monomer in the bulk solvent of the mobile phase as well as for the solute distributed between the micelles and the mobile phase solvent. It is also assumed that only free surfactant is found in the pores of the alkyl-bonded phase since the micelles are larger than the typical stationary phase pore sizes. The increase in mobile phase dispersion due to partitioning of the solute between the micelle and the bulk solvent is incorporated in this model.

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DOI: 10.1081/SS-120014436
0149-6395 (Print); 1520-5754 (Online)

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Solution of the solute mass balance equations developed for the mobile phase, the pores of the silica gel, and the surface of the stationary phase yields an explicit expression for the number of plates as a function of the physical and chemical parameters governing the kinetics and transport in MLC separations. An examination of changes in predicted plate numbers with different mobile phase conditions helps to understand the observed efficiencies with MLC systems.

Model predictions were compared to experimental observations from a series of vanillin compounds injected onto a BDS-$C_{18}$ column with mobile phases containing different concentrations of sodium dodecyl sulfate. This comparison showed that an equilibrium model provides a reasonable prediction of the number of plates for all of the solutes considered. However, the experimental results for vanillin, isovanillin, and coumarin indicate that stationary phase kinetics also play a minor role in column efficiency. The results from this analysis suggest that it is the secondary equilibrium between micellar and bulk mobile phases, which is the primary contributor to band broadening in MLC.

*Key Words*: Micellar liquid chromatography; Column efficiency; Band broadening; Mathematical modeling



## INTRODUCTION

The use of aqueous micellar solutions as mobile phases in reversed phase liquid chromatography (RPLC) was first demonstrated by Armstrong and Henry.[1] They called this new technique pseudophase or micellar liquid chromatography (MLC). Since the first report by Armstrong and Henry, a number of articles have appeared in the chemical literature focusing on the advantages of MLC relative to conventional RPLC, and these advantages can include reduction in hazardous wastes, ability to simultaneously separate charged and neutral compounds, and unusual selectivities for a variety of compounds due to the ability of the micelles to compartmentalize and organize compounds at the molecular level.

Compartmentalization of organic compounds at the molecular level by micelles has also been used to great advantage in the development of sensitive fluorescence detection schemes in MLC.[2,3] Fluorescence is enhanced by

micelles because the environment of the micelle is generally of higher viscosity, which decreases the freedom of movement, thereby, shielding the compound from collision-induced radiationless decay. The enhanced quantum yields and greater fluorescence intensities that occur with micellar mobile phases can be attributed to micelle solubilization, which protects the excited singlet state.

In spite of these advantages and the fervor of its proponents, this separation technique has not seen widespread application because MLC tends to be less efficient than conventional RPLC. Dorsey et al.[4] were the first to address this problem. They believed that the reduction in column efficiency was due to slow mass transfer, which arose principally from poor wetting of the stationary phase. Dorsey et al. demonstrated that chromatographic efficiency in MLC could be improved by adding a small amount of propanol, 3% by volume, to the mobile phase. Yarmchuk et al.[5] on the other hand, attributed the lower efficiency of ionic micellar mobile phases to poor mass transfer between the micelle and the stationary phase, with the micelle exit rate constant being the limiting factor for hydrophobic solutes. Borgerding and Hinze[6] concluded that poor mass transfer within the stationary phase itself, resulting from adsorption of surfactant onto the alkyl-bonded phase is responsible for the low efficiencies observed in MLC. They demonstrated that addition of an alcohol, such as isopropanol, to a nonionic micellar solution can reduce the amount of surfactant adsorbed onto the stationary phase, resulting in a more efficient separation. In contrast to what has been reported by other workers, Bailey and Cassidy[7] reported in a study on band broadening in MLC that the improvement in solute mass transfer, which can occur upon addition of propanol to an SDS micellar solution is probably due to changes in the structure of the micelles, and not mass transfer effects related to the loading of surfactant onto the bonded phase.

Clearly, there is disagreement among workers concerning the reason(s) for the reduced efficiencies evidenced in MLC. While the addition of a medium chain length alcohol such as propanol to a micellar mobile phase has been shown to improve column efficiency significantly, the presence of an alcohol in the mobile phase can also affect the retention mechanism by shifting the equilibrium of the solute away from the stationary phase and the micelle and toward the bulk aqueous phase.[8] In addition, the presence of alcohols[9,10] will influence the properties of the micelles in these so-called hybrid mobile phases, but it is not clear to what extent, thereby, complicating the interpretation of plate count data. Hence, there is a limit to the information that can be garnered about the underlying cause of the reduced efficiencies in MLC from experiments involving alcohol-containing micellar solutions.

To better understand the causes of reduced efficiencies in MLC, it is necessary to develop a mathematical model to describe band broadening. The model should include terms for both solute–stationary phase and solute–micelle interactions. For this reason, we have developed a model for MLC that

incorporates solute mass transfer between the mobile and the stationary phase, kinetic limitations within the stationary phase, and assumes equilibrium between the micelles and the surfactant monomer in the bulk solvent of the mobile phase as well as for solute distributed between the micelles and the surrounding bulk solution. The model assumes that only free surfactant is found in the pores of the alkyl-bonded phase since the micelles are larger than the typical stationary phase pore sizes.[11] The increase in solute dispersion that occurs because solute in the mobile phase is partitioned between the micelle and the bulk solvent is incorporated in this model. Solution of the solute mass balance equations developed for the mobile phase, the pores of the silica gel, and the surface of the stationary phase yields an explicit expression for the number of plates as a function of the physical and chemical parameters governing the kinetics and transport in MLC separations. In this paper, we report results from model predictions and compare predicted changes in plate number to those observed experimentally.



## EXPERIMENTAL

### High Performance Liquid Chromatographic Measurements

All high performance liquid chromatographic (HPLC) measurements were made with a Perkin–Elmer Tridet HPLC system (Norwalk, CT) equipped with a 254 nm ultraviolet detector. The analytical column used was a BDS-HYPERSIL-$C_{18}$ ($4.6 \times 100\,mm^2$) purchased from Keystone Scientific, Inc. (Bellefonte, PA). For MLC, a silica guard column was placed between the injector and the pump to saturate the mobile phase with silicates, thereby, minimizing dissolution of the column packing. All HPLC measurements were performed at a flow rate of 1 mL/min.

The dead volume of the column was determined by injecting different solutions such as methanol, methanol–water, or water onto the columns. Dead volume measurements obtained for micellar mobile phases were comparable to the values obtained for methanol–water mobile phases. This volume, approximately 1 mL was used in all $k'$ calculations. The $k'$ values reported in this study were averages of at least triplicate determinations. Deviations in individual capacity factor values were never greater than 5%.

### Materials

The alcohol mobile phase modifier used in this study, 1-propanol was purchased from Fisher (Pittsburgh, PA). The choice of 1-propanol was based on

literature studies that have shown it to be effective in improving column efficiency in MLC. Sodium dodecyl sulfate (SDS) was purchased from BDH Chemicals (Poole, BH15 1TD, England). Prior to use, SDS was purified by dissolving it in ethanol followed by addition of charcoal to the solution. The supernatant was then recrystallized with ice. The surfactant SDS was chosen because it has been used in hundreds of MLC studies, and because the dynamics of SDS micelles has been studied more extensively than for most other micellar systems.

All mobile phases were prepared using doubly distilled water and were twice filtered with 0.45 $\mu$m pore size Varian Nylon-66 filters to remove particulate matter. Each mobile phase solution was degassed for 5 min and then percolated through the column at a flow rate of 1 mL/min for approximately 120 min to ensure reproducible solvation of the stationary phase by the mobile phase.

The vanillin compounds, which constituted the test solutes (see Fig. 1), were obtained from Aldrich (Milwaukee, WI) and Sigma (St. Louis, MO) and were used as received. Stock solutions of the test solutes ($1 \times 10^{-2}\,M$) were prepared with methanol (HPLC grade) and were then diluted to the appropriate

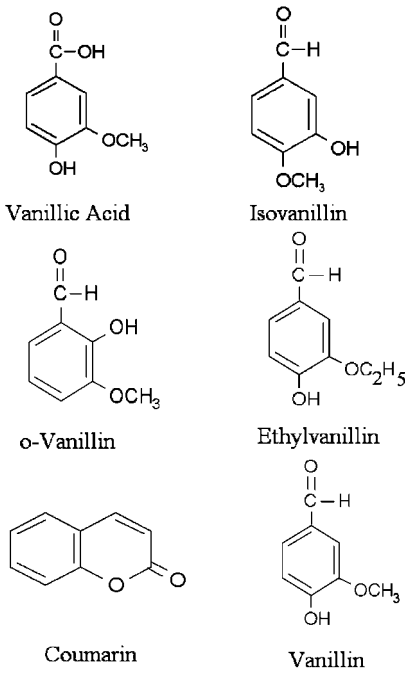


***Figure 1.*** Vanillin compounds.

working concentration ($5 \times 10^{-4}\,M$) using doubly distilled water. Because the vanillin compounds are somewhat hydrophilic, the BDS C-18 column will weakly retain them, which is why it was necessary to use water as a solvent to prepare each test solute. If a stronger solvent such as methanol were used to prepare the test solutes, the compounds would not have been deposited onto the head of the column as a sufficiently thin plug during sample injection, with the net result being increased band broadening.

### Procedure

The Foley–Dorsey method[12] was used to compute the number of theoretical plates:

$$N_{\text{exp}} = \frac{41.7(t_r/W_{0.1})^2}{B/A + 1.25} \tag{1}$$

where $t_r$ is the retention time, $W_{0.1}$ is the peak width at 10% peak height, and the ratio $B/A$ accounts for the peak asymmetry. Although there are many methods available for the calculation of chromatographic efficiency, Bildingmeyer and Warren[13] and Berthod[14] have shown that the Foley–Dorsey equation is the most accurate manual method for plate count calculation. Because the Foley–Dorsey equation for plate count corrects for the asymmetry in skewed peaks, reliable chromatographic figures of merit can be obtained from tailing peaks using this method.



## MATHEMATICAL MODELING

### Model Equations

Our representation of a single stationary phase particle in MLC and the accompanying transport and kinetic steps important in this separation are shown in Figs. 2 and 3. This pictorial description was adapted for MLC from a similar scheme presented for conventional liquid chromatography by Horvath and Lin.[15] In our model, solute is found in one of the four regions: (1) within the micelle in the mobile phase, with concentration $C_{\text{micelle}}$, (2) in the bulk solvent of the mobile phase outside of the micelle with concentration $C_{\text{mobile}}$, (3) within the pores of the stationary phase with concentration $C_p$, and (4) adsorbed onto the stationary phase surface with concentration $C_s$. With the exception of $C_s$, all concentrations are defined as moles of solute per volume. The surface concentration $C_s$ is defined as moles of solute adsorbed per surface area. It is

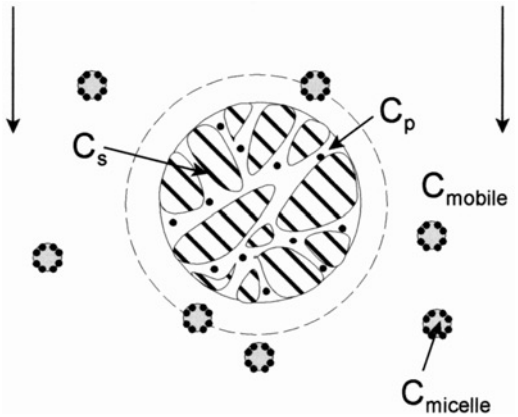


***Figure 2.*** Schematic picture of a stationary phase particle illustrating the four regions where solute can be found in MLC. The dashed line surrounding the particle represents the stagnant boundary layer.



assumed that the pores of the stationary phase are smaller than a typical micelle so that only free surfactant is found within the stationary phase. The concentration of micelles in the mobile phase is described by the volume fraction of micelles in the interstitial volume, $\beta$. This is related to the molar concentration of added surfactant as described later in this paper. The fact that solute is found in the interstitial space both as free solute and solubilized in the

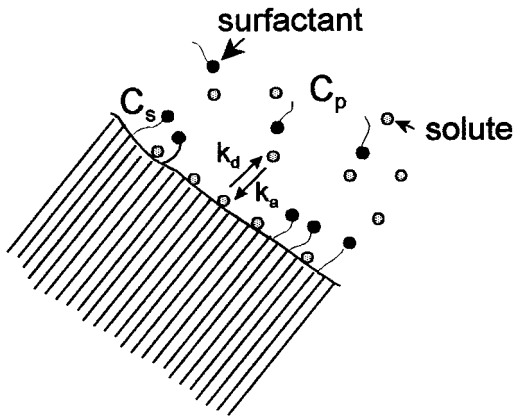


***Figure 3.*** Schematic picture of the intrapore surface in the stationary phase.

micelles is incorporated in the solute mass balance written for the interstitial space:

$$\frac{\partial}{\partial t}[(1-\beta)C_{\text{mobile}} + \beta C_{\text{micelle}}] + u\frac{\partial}{\partial z}[(1-\beta)C_{\text{mobile}} + \beta C_{\text{micelle}}]$$
$$= \frac{\partial^2}{\partial z^2}[D_{\text{mobile}}(1-\beta)C_{\text{mobile}} + D_{\text{micelle}}\beta C_{\text{micelle}}]$$
$$- \frac{6}{D_p}\frac{1-\varepsilon_c}{\varepsilon_c}k_e[C_{\text{mobile}} - C_p|_{r=D_p/2}] \quad (2)$$

where $D_{\text{mobile}}$ is the dispersion coefficient of unbound solute and $D_{\text{micelle}}$ is the dispersion coefficient of micelle-solubilized solute (i.e., the dispersion coefficient of micelles), $u$ is the fluid velocity in the interstitial space, $D_p$ is the particle diameter, $\varepsilon_c$ is the column porosity (interstitial volume/column volume), and $k_e$ is the mass transfer coefficient characterizing solute transport from the mobile phase into the stationary phase through the boundary layer depicted by the dashed line in Fig. 2. It is assumed in this model that the unbound solute and micelle can sample the same interstitial space.

When equilibrium is assumed between mobile and micelle phases, we can eliminate $C_{\text{micelle}}$ from Eq. (2) using the equilibrium constant, $K_2 = C_{\text{micelle}}/C_{\text{mobile}}$ yielding

$$\phi\frac{\partial C_{\text{mobile}}}{\partial t} + u\phi\frac{\partial C_{\text{mobile}}}{\partial z} = [(1-\beta)D_{\text{mobile}} + \beta K_2 D_{\text{mobile}}]\frac{\partial^2 C_{\text{mobile}}}{\partial z^2}$$
$$- \frac{6}{D_p}\frac{1-\varepsilon_c}{\varepsilon_c}k_e[C_{\text{mobile}} - C_p|_{r=D_p/2}] \quad (3)$$

where $\phi = 1 - \beta + K_2\beta$ and has a value of 1 when there are no micelles. This equilibrium assumption seems reasonable because of the relatively short length scales involved in transport to the micelle compared to the length scales for diffusion into the stationary phase. The mass balance developed for the solute within the stationary phase is:

$$\varepsilon_i\frac{\partial C_p}{\partial t} + \frac{S_p}{V_p}\frac{\partial C_s}{\partial t} = \frac{\varepsilon_i D^o_{\text{solute}}}{r^2}\left[\frac{\partial}{\partial r}\left(r^2\frac{\partial C_p}{\partial r}\right)\right] \quad (4)$$

where $\varepsilon_i$ is the particle porosity and is included because the intrapore concentration ($C_p$) is based on pore volume and $S_p/V_p$ is the internal surface area per particle volume. The infinite dilution molecular diffusivity ($D^o_{\text{solute}}$) is used in the intraparticle diffusion term because it is assumed that solute is sufficiently small so that there is no hindrance to transport within the pores. The reversible

adsorption of solute to the stationary phase surface is assumed to follow first-order kinetics for both adsorption and desorption:

$$\frac{\partial C_s}{\partial t} = k_a C_p - k_d C_s \tag{5}$$

Equation (5) is a standard Langmuir adsorption/desorption kinetic expression written with the additional assumption that solute loading is sufficiently low at all times so that the number of available sites for adsorption does not change as the solute moves through the column. In MLC, it is expected that there will be free surfactant adsorbed to the stationary phase and it is reasonable to assume that the amount of adsorbed surfactant will be uniform throughout the column. However, the amount of adsorbed surfactant (and, therefore, the adsorption rate constant, $k_a$) is expected to change with different mobile phase conditions. The initial and boundary conditions used with Eqs. (3)–(5) are

$$t = 0 \quad C_{mobile} = C_p = C_s = 0 \tag{6}$$

$$z = 0 \quad C_{mobile}/C_f = H(t) - H(t - t_f) \tag{7}$$

$$z = \infty \quad C_{mobile} = 0 \tag{8}$$

$$r = 0 \quad \frac{\partial C_p}{\partial r} = 0 \tag{9}$$

$$r = D_p/2 \quad \varepsilon_i D^o_{solute} \frac{\partial C_p}{\partial r} = k_e[C_{mobile} - C_p] \tag{10}$$

where $H(t)$ is the Heaviside step function used to describe solute injection over a time period $t_f$ and $C_f$ is the solute concentration of the injected solution. Because solute transport is primarily convective, other axial boundary conditions give essentially the same results.[16]

Equations (3)–(5), subject to the conditions in Eqs. (6)–(10) were solved using the method of Laplace transforms. This was done by first solving Eq. (5) for $L(C_s)$:

$$L(C_s) = \frac{k_a}{s + k_d} L(C_p) \tag{11}$$

where $L(C_s)$ and $L(C_p)$ are the Laplace transforms of $C_s$ and $C_p$, respectively, and $s$ is the frequency. Equation (11) was substituted in the Laplace transform of Eq. (4) and this was then solved for $L(C_p)$ using the boundary conditions in Eqs. (6)

and (7):

$$L(C_p) = L(C_{mobile})\frac{D_p k_e}{2\varepsilon_i D^o_{solute}}\frac{1}{r}\sinh\left(\sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left[\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right]}\,r\right) \times \left(\sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left(\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right)} \times \cosh\sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left(\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right)} + \left(\frac{D_p k_e}{2\varepsilon_i D^o_{solute}} - 1\right) \times \sinh\sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left(\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right)}\right)^{-1} \quad (12)$$

where $L(C_{mobile})$ is the Laplace transform of $C_{mobile}$. Equation (3) was then solved by substituting $L(C_p)$ from Eq. (12) in the Laplace transform of Eq. (3). The solution can be expressed as:

$$L(C_{mobile})|_{z=L} = L(C_{mobile})|_{z=0}\, G_{column}(s) \quad (13)$$

where $L(C_{mobile})|_{z=0}$ is the Laplace transform of the step function input:

$$L(C_{mobile})|_{z=0} = [1 - \exp(-st_f)]/s \quad (14)$$

and $G_{column}(s)$ is the transfer function describing transport and kinetics in the column:

$$G_{column}(s) = \exp\left[\frac{Pe}{2} - \sqrt{\frac{Pe^2}{4} + \frac{sLPe\psi}{u}}\right] \quad (15)$$

with

$$Pe = \frac{uL}{(1-\beta)D_{mobile} + \beta D_{micelle}}\phi \quad (16)$$

and

$$\psi = 1 + \frac{6(1-\varepsilon_c)}{D_p \varepsilon_c \phi}\frac{k_e}{s} \times \left[1 - \frac{D_p k_e}{2\varepsilon_i D^o_{solute}} \sinh \sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left(\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right)} \times \left(\sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left(\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right)} \times \cosh \sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left(\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right)} + \left(\frac{D_p k_e}{2\varepsilon_i D^o_{solute}} - 1\right) \times \sinh \sqrt{\frac{sD_p^2}{4\varepsilon_i D^o_{solute}}\left(\varepsilon_i + \frac{S_p/V_p k_a}{s+k_d}\right)}\right)^{-1}\right] \quad (17)$$

A fast Fourier transform algorithm can be used to numerically invert the frequency domain solution to the time domain and generate elution profiles.[17] However, our objective in this study was to examine the effect of changes in mobile phase chemistry on column efficiency and to compare predicted changes to those observed experimentally. The column efficiency is quantified experimentally by the number of theoretical plates computed using the Foley–Dorsey method [Eq. (1)]. The number of plates can be predicted by determining moments of the elution profile directly from the solution in the frequency domain.

The $k$th moment of the elution profile, $\mu_k$, can be determined from Eq. (11) using

$$\mu_k = \lim_{s\to 0}\left[-\frac{\partial^k}{\partial s^k} L(C)|_{z=L}\right] \quad (18)$$

Applying Eq. (18) to Eqs. (13)–(17) for $k = 0$ and 1 yields the following expression for the retention time, $t_r$:

$$t_r = \frac{\mu_1}{\mu_0} = \frac{L}{u}\left(1 + \frac{(1-\varepsilon_c)}{\varepsilon_c \phi} K_1\right) + t_f \quad (19)$$

where $K_1$ is the equilibrium constant describing solute equilibrium between

stationary and mobile phases:

$$K_1 = \frac{\varepsilon_i C_p + C_s S_p / V_p}{C_{mobile}} = \varepsilon_i + \frac{k_a}{k_d}\frac{S_p}{V_p} \tag{20}$$

The second equality in Eq. (20) results because it is assumed that there is no solute hindrance in the pores of the stationary phase so that $C_p = C_{mobile}$ at equilibrium. If pulse injection is assumed (i.e., $t_r - t_f \sim t_r$) and if $\beta \ll 1$, Eq. (19) can be rearranged to

$$\frac{t_r - L/u}{L/u} = k' = \frac{K_1(1-\varepsilon_c)/\varepsilon_c}{(1+\beta K_2)} \tag{21}$$

where $k'$ is the capacity factor. Examination of Eq. (21) shows that a plot of $1/k'$ vs. $\beta$ (which is related to surfactant concentration) should yield a straight line and the equilibrium constants $K_1$ and $K_2$ can be determined from the slope and intercept of that line. Equation (21) is in agreement with similar expressions developed by Armstrong and Nome[18] and by Arunyanart and Cline-Love[19] using equilibrium arguments.

Applying Eq. (18) to Eqs. (13)–(17) for $k = 2$ yields the following expression for the variance, $\sigma^2$:

$$\begin{aligned}\sigma^2 &= \frac{\mu_2}{\mu_0} - \left(\frac{\mu_1}{\mu_0}\right)^2 \\ &= \left(\frac{L}{u}\right)^2 \left[\frac{2}{Pe}\left(1 + \frac{(1-\varepsilon_c)}{\varepsilon_c \phi} K_1\right)^2 \right. \\ &\quad + \frac{2u}{L}\frac{(1-\varepsilon_c)}{\varepsilon_c \phi}\left((1+\varepsilon_i+K_1)^2\left(\frac{D_p^2/4}{15\varepsilon_i D^o_{solute}} + \frac{D_p/2}{3k_e}\right)\right. \\ &\quad \left.\left. + \frac{\varepsilon_i + K_1}{k_d}\right)\right] + \frac{t_f^2}{12}\end{aligned} \tag{22}$$

Examination of the values of the individual terms in Eq. (22) for a given system enables one to estimate the contributions of mobile phase dispersion, intrapore diffusion, mobile phase (boundary layer) diffusion, surface kinetics, and injection to the variance.

In the Foley–Dorsey method for determining the number of plates, the peak width at 10% of the peak height ($W_{0.1}$) is used to characterize peak breadth [Eq. (1)]. Our objective in this study was to examine the effect of changing mobile phase conditions on predictions of column efficiency and to compare those predictions to experimental observations. This comparison can be made quite easily by using the standard deviation, $\sigma$ as the characteristic of peak width

rather than $W_{0.1}$:

$$N_{\text{theor}} = \frac{t_r^2}{\sigma^2} \tag{23}$$

Because the peak width used to determine $N_{\text{theor}}$ and $N_{\text{exp}}$ are different, agreement between these values is not expected. However, if our model is accurately capturing the important phenomena governing these systems, we should expect agreement in the relative changes in $N_{\text{theor}}$ and $N_{\text{exp}}$ when mobile phase conditions are changed.

## Column Parameters

The average particle size of the C-18 packing material used in our column as reported by the manufacturer was 5 $\mu$m, and this value was used for $D_{\text{p}}$ in all calculations. The column porosity was determined by taking the ratio of the column dead volume (1 mL) to the total column volume (1.66 mL) to yield a value of 60%. The particle porosity depends upon surfactant concentration as well as the nature and amount of mobile phase modifier. Borgerding et al.[20] used nitrogen porosimetry to determine the cumulative pore volume of a C-18 stationary phase in equilibrium with a variety of mobile phases: pure water, 0.285 *M* SDS, and 0.285 *M* SDS with 5% solutions of various alcohol modifiers. Using this data, the following empirical prediction for the cumulative pore volume in C-18 has been developed:

$$V_{\text{pore}}(\text{cm}^3/\text{g}) = 0.279 - 0.5 \times [\text{SDS}] + a \times \text{wt\% alcohol} \tag{24}$$

where $a = 0.22$ for methanol, 0.36 for ethanol, 0.82 for 1-propanol, 1.26 for 1-butanol, and 1.56 for 1-pentanol. The density of C-18 modified silica has been reported by Cheng[21] to be 1.74 g/cm$^3$. Using this value, we have developed the following prediction for the internal porosity of the C-18 modified silica used in our experiments:

$$\varepsilon_{\text{i}} = \frac{1.74 V_{\text{pore}}}{1 + 1.74 V_{\text{pore}}} \tag{25}$$

The surface area per particle volume ($S_{\text{p}}/V_{\text{p}}$) of the stationary phase used in our experiments was estimated using the BET surface area reported by Borgerding et al.[20] The BET area was found to be dependent upon both the SDS concentration as well as the type of alcohol modifier added to the mobile phase. Using their data, the following empirical expression was developed:

$$S_{\text{p}}/V_{\text{p}}(\text{cm}^{-1}) = 1.74 \times 10^{-4}(1 - \varepsilon_{\text{i}})[121 - 217.5[\text{SDS}] + b \times \text{wt\% alcohol}] \tag{26}$$

where $b = 80$ for methanol, 180 for ethanol, 420 for 1-propanol, 580 for 1-butanol, and 760 for 1-pentanol.

## Mobile Phase Parameters

The volume fraction of micelles in the mobile phase, $\beta$ was estimated using the partial specific volume of surfactant (0.862 mL/g for SDS[22]) and its molecular weight after first subtracting the critical micelle concentration (CMC) from the concentration of the added surfactant (0.008 $M$ for SDS):

$$\beta = 0.862 \times 288/1000([\text{SDS}] - 0.008) \tag{27}$$

All solutes used in this study were relatively small. Therefore, the molecular diffusivity for all solutes was estimated to be $10^{-5}$ cm$^2$/sec. The diffusion coefficient of SDS micelles was estimated to be $10^{-6}$ cm$^2$/sec, based on data reported by Weinheimer et al.[23] This value is the reported diffusion coefficient of SDS in a solution with concentration just above the CMC, which should represent micelle diffusion rather than an average of unbound surfactant and micelle diffusion.

The dispersion coefficients $D_{\text{mobile}}$ and $D_{\text{micelle}}$ were estimated using

$$D_i = \frac{uD_p}{2}\left[\frac{uD_p}{D_i^o}\right]^{1/3} \tag{28}$$

where $i$ represents free solute or micelle and $D_i^o$ is the diffusivity of i. Equation (28) is the mobile phase dispersion term in the Knox equation for estimating plate heights in gas and liquid chromatography.[24]

The equilibrium constants $K_1$ and $K_2$ were determined from experimental measurements of capacity factor ($k'$) for systems with mobile phases containing different surfactant concentrations as described following Eq. (21). The experimental results used to generate these values have been previously reported.[26]

## Kinetic Parameters

The mass transfer coefficient characterizing solute transport from the mobile phase to the stationary phase surface, $k_e$ was estimated using a correlation developed by Ohashi et al.:[25]

$$Sh = \frac{k_e D_p}{D_{\text{solute}}^o} = 2 + 0.51\left[\left(\frac{1200(1-\varepsilon_c)(\varepsilon_c u)^3}{D_p Re\, \varepsilon_c}\right)^{1/3}\left(\frac{D_p^{4/3}}{\nu}\right)\right]^{0.6} Sc^{1/3} \tag{29}$$

where the Reynolds number is defined using the superficial velocity ($\varepsilon_c u$).

With our chromatographic measurements, it was not possible to independently determine the adsorption and desorption rate constants, $k_a$ and $k_d$. As noted earlier, the equilibrium constant $K_1$ was determined from a plot of $1/k'$ vs. $\beta$ and this is related to the ratio of these rate constants as shown in Eq. (20). In our analysis, we have selected the adsorption rate constant to be a free parameter and determined the value of $k_d$ for a given value of $k_a$ using our experimentally determined $K_1$ and Eq. (20). In this paper, we will examine the effect of changing $k_a$ on the sensitivity of our predicted plate numbers to changing mobile phase conditions. In the future, we plan to perform frontal analysis chromatography in order to experimentally measure $k_a$ and $k_d$ values.

## RESULTS AND DISCUSSION

We begin with an examination of the effect of adsorption kinetics and surfactant concentration on the column efficiency. A comparison of the number of plates for orthovanillin, as predicted from our model, as a function of the adsorption rate constant for solutions with different SDS concentration is shown in Fig. 4. These results show a sigmoidal dependence of $N_{theor}$ on $k_a$ and show

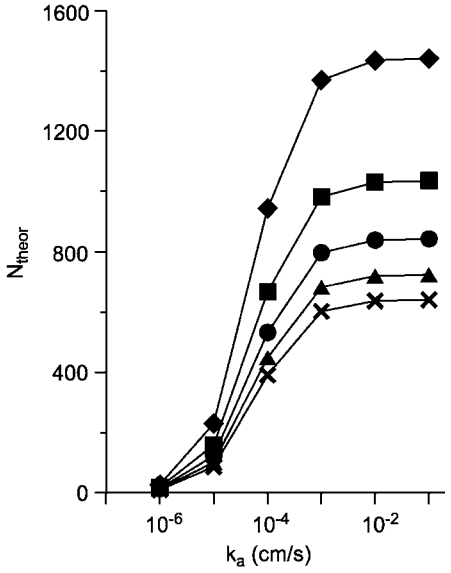


***Figure 4.*** The number of plates predicted from the model as a function of adsorption rate constant for orthovanillin solutions with different SDS concentration: ◆ 0.01 *M* SDS, ■ 0.02 *M* SDS, ● 0.03 *M* SDS, ▲ 0.04 *M* SDS, × 0.05 *M* SDS.

little effect on $N_{theor}$ when $k_a > 0.01$ cm/sec. The asymptote at large $k_a$ gives us the upper equilibrium limit for each system. The other vanillin compounds also show a similar sigmoidal dependence with the equilibrium limit reached at $k_a \sim 0.01$ cm/sec.

These results predict poorer efficiency as SDS concentration is increased for a fixed value of $k_a$. This trend is expected because of the increase in mobile phase dispersion, which is caused by an increase in the micelle concentration of the system. However, experimental observations have shown that plate number for a particular solute does not always decrease with increasing surfactant concentration.[7] To explain these observations using our model requires one to assume that $k_a$ must change as surfactant concentration changes. The general understanding of micellar systems indicates that the concentration of free surfactant in a micellar solution is expected to stay fixed at the CMC when surfactant concentration is changed (as long as the system remains above the CMC). As depicted in Fig. 3, it is believed that surface kinetics are controlled by the amount of surfactant adsorbed onto the stationary phase. Therefore, if the free surfactant concentration does not change, one does not expect the surface kinetics ($k_a$) to change. However, this general understanding of micellar systems may not apply in the presence of the stationary phase. In fact, Berthod et al. have shown that SDS monomer continues to adsorb onto a C-18 alkyl bonded phase at concentrations in excess of the CMC.[27] If this is indeed the case, then it is necessary to assume that $k_a$ for a solute will increase when additional surfactant is adsorbed onto the stationary phase surface in order to predict an increase in plate number with increasing surfactant concentration. Clearly, there is still a considerable lack of understanding of solute–stationary phase interactions for mobile phases containing surfactant.

Because the parameter used to characterize peak breadth when determining the number of plates experimentally and theoretically was different, we cannot directly compare the measured to the predicted number of plates. As an alternative, we have selected the system with SDS concentration of 0.05 $M$ as a basis and scaled the other results relative to this basis. A comparison of the ratio of $N$ for each micellar mobile phase to $N$ for 0.05 $M$ SDS for experiment and theory are shown in Fig. 5 for vanillin and in Fig. 6 for ethylvanillin. We have selected the results for these two solutes because they generally represent the behavior observed for all of the compounds investigated. It should be noted that the scale on the $y$ axis is different in these two figures.

The vanillin data for 0.02, 0.03, and 0.04 $M$ SDS are in close agreement with the theoretical prediction for $k_a = 1 \times 10^{-6}$ cm/sec, which suggests that lower column efficiencies for this system can probably be attributed in some measure to slow stationary phase kinetics. However, the experimental results are not significantly different than the equilibrium prediction, indicating that one of the primary contributors to band broadening in this system is likely the secondary

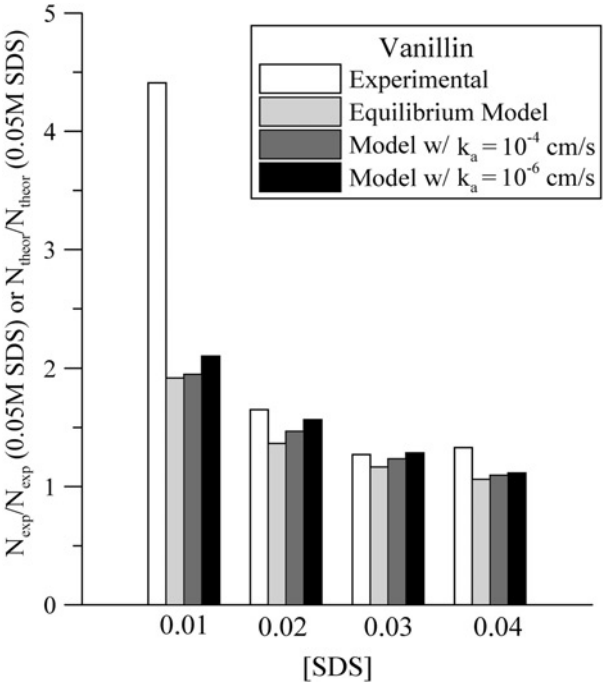


***Figure 5.*** Ratio of the number of plates to the number of plates for [SDS] = 0.05 *M* as a function of SDS concentration for vanillin. Similar trends were observed for isovanillin and coumarin.



equilibrium that comes into play with MLC. The kinetic factors appear to play only a minor role. As for the large discrepancy between the predicted and experimental value of *N* for 0.01 *M* SDS, the mathematical model developed for band broadening in MLC assumes that aggregation number and geometry of the micelles do not change as a result of solute interaction with the surfactant assembly. This assumption may not hold true near the CMC of the surfactant for compounds that strongly interact with the SDS micelles. Trends similar to those presented in Fig. 5 for vanillin were observed when comparing observed and predicted ratios for isovanillin and coumarin with changing SDS concentration.

The results presented in Fig. 6 for ethylvanillin show observed band broadening to be most closely predicted by an equilibrium model, a trend that was also observed for orthovanillin. These results suggest that the primary cause of band broadening for these two compounds is mobile phase dispersion caused by the secondary equilibrium introduced with the presence of micelles and that kinetic effects play an insignificant role for MLC with these two compounds. The

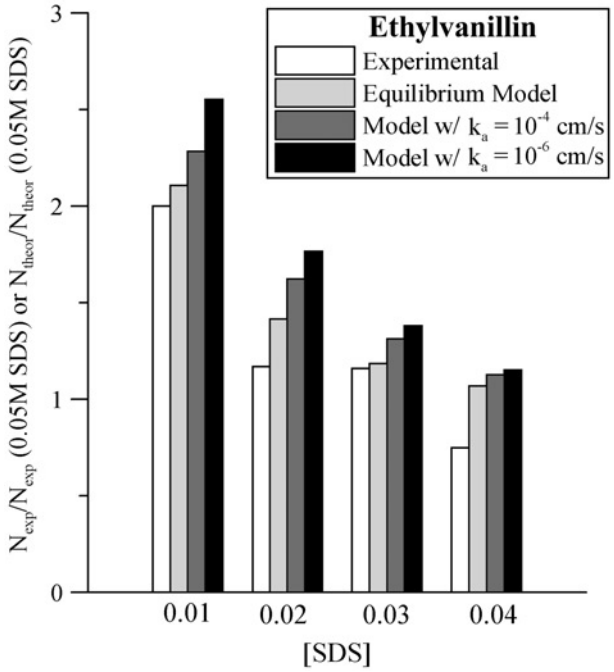


***Figure 6.*** Ratio of the number of plates to the number of plates for [SDS] = 0.05 *M* as a function of SDS concentration for ethylvanillin. A similar trend was observed for orthovanillin.



results displayed in Figs. 5 and 6 suggest that band broadening in MLC can primarily be explained using only equilibrium arguments, although stationary phase kinetics can also play a minor role for some systems. This would explain the disagreement among workers concerning the reason(s) for the reduced efficiencies evidenced in MLC.

To examine the effect of mobile phase modifiers on the efficiency of MLC separations, we have selected a base system of vanillin in 3% propanol without any surfactant. The ratio of the number of plates calculated from experimental elution profiles for each solute in 0.2 *M* SDS and 0.2 *M* SDS with 3% propanol to the number of plates calculated from the elution profile for vanillin in 3% propanol was determined. The adsorption rate constant value for the base system was then selected to be $10^{-4}$ cm/sec and $N_{theor}$ was calculated for this system using Eqs. (19), (22), and (24). The number of plates, $N_{theor}$ was then determined for the other mobile phases using different values for the rate constant, $k_a$. The rate constant for each solute in each

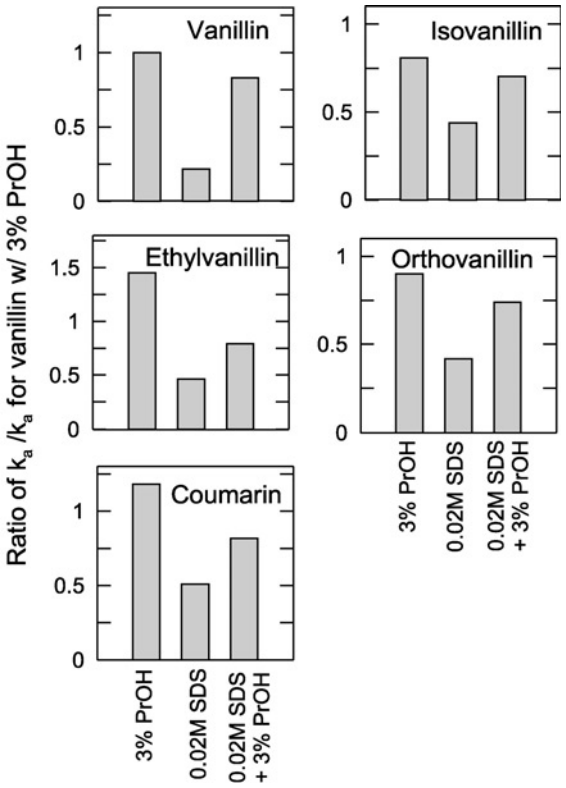


***Figure 7.*** Ratio of $k_a$ to $k_a$ for vanillin with 3% propanol mobile phase needed to predict the ratio of the number of plates ($N_{theor}/N_{theor}$ w/propanol) equal to that observed experimentally ($N_{exp}/N_{exp}$ w/propanol). A $k_a$ value of $10^{-4}$ cm/sec was selected for vanillin in 3% propanol.

mobile phase that yielded a ratio of $N_{theor}/N_{theor}$ for vanillin in 3% propanol identical to the experimentally observed ratio was then determined. The ratio of this value of $k_a$ to the value of $k_a$ for vanillin in 3% propanol ($10^{-4}$ cm/sec) is compared for each solute in the different mobile phases in Fig. 7. It is evident from Fig. 7 that adding propanol to the micellar mobile phase increases the value of $k_a$. This comparison supports Dorsey's argument that MLC is less efficient than conventional RPLC because of slow kinetics in the stationary phase. Adding 3% propanol by volume to the micellar mobile phase improves the wetting of the stationary phase, thereby, increasing the rate of solute adsorption to the stationary phase surface while maintaining the integrity of the micelles.

## ACKNOWLEDGMENTS

BKL acknowledges helpful discussions with J. Kratohvil and J. Dorsey. JR acknowledges financial support of the Office of Scientific Research (Bollings Air Force Base, Washington DC) through their Summer Graduate Research Program.

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Received September 2001
Revised April 2002