Selectivity and Stoichiometry Boosting of β-Cyclodextrin in Cationic/Anionic Surfactant Systems: When Host–Guest Equilibrium Meets Biased Aggregation Equilibrium

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Cationic surfactant/anionic surfactant/β-CD ternary aqueous systems provide a platform for the coexistence of the host–guest (β-CD/surfactant) equilibrium and the biased aggregation (monomeric/aggregated surfactants) equilibrium. We report here that the interplay between the two equilibria dominates the systems as follows. (1) The biased aggregation equilibrium imposes an apparent selectivity on the host–guest equilibrium, namely, β-CD has to always selectively bind the major surfactant (molar fraction > 0.5) even if binding constants of β-CD to the pair of surfactants are quite similar. (2) In return, the host–guest equilibrium amplifies the bias of the aggregation equilibrium, that is, the selective binding partly removes the major surfactant from the aggregates and leaves the aggregate composition approaching the electroneutral mixing stoichiometry. (3) This composition variation enhances electrostatic attractions between oppositely charged surfactant head groups, thus resulting in less-curved aggregates. In particular, the present apparent host–guest selectivity is of remarkably high values, and the selectivity stems from the bias of the aggregation equilibrium rather than the difference in binding constants. Moreover, β-CD is defined as a “stoichiometry booster” for the whole class of cationic/anionic surfactant systems, which provides an additional degree of freedom to directly adjust aggregate compositions of the systems. The stoichiometry boosting of the compositions can in turn affect or even determine microstructures and macroproperties of the systems.

1. Introduction

1.1. Host–Guest Equilibrium and Selectivity. The synthesis of crown ethers and subsequent studies on their selective ligation of alkali metal cations have led to the flourishing development of host–guest chemistry, which was recognized by the award of the Nobel Prize in Chemistry in 1987.1 The selectivity of a host to different guests always plays a central role in host–guest chemistry due to its great importance in compound separation, molecular recognition, and construction of supramolecules, to name a few.2 In this context, J. E. Trend et al. gave an impressive example by solving a stubborn clinical problem of assaying blood K+ ions over Na+ ions, and the binding with K+ will trigger the fluorescence emission of its chromophore portion. Consequently, the emission intensity is proportional to [K+] even in the presence of highly excess Na+, allowing for specific determination of K+ concentrations.

In the above case and other typical cases, the host–guest equilibrium can be described by the classical solution-phase model

$$\text{Host} + \text{Guest} \rightleftharpoons \text{Complex}$$

where the binding constant \( K^b = \left[\text{Complex}\right]/\left[\text{Host}\right][\text{Guest}] \) for dilute solutions. The magnitude of \( K^b \) reflects the matching degree of a host–guest pair. When two guest species are presented, the selectivity of the host to one guest is exclusively governed by the ratio of binding constants (\( S_{\text{Guest}} = K^b_{\text{Guest}}/K^b_{\text{Guest}} \)). This simple situation could, however, be complicated by the emergence of a coexisting equilibrium, which may raise issues concerning the adequacy of the simple solution-phase model and the dependence of selectivity on binding constants.

1.2. Biased Aggregation Equilibrium in Cationic/Anionic Surfactant Systems. Recently, cationic/anionic surfactant systems4 have attracted increasing attention because of their advantages in synergism,5 spontaneous formation of vesicles,6 and aggregate polymorphism.7 The above features, especially the aggregate polymorphism, are closely related to surfactant compositions in aggregates. With the compositions approaching...
the electroneutral mixing stoichiometry, electrostatic attractions between the oppositely charged head groups increase, transforming the aggregates into less-curved ones (typically in a micelle-to-vesicle-to-precipitate sequence). The aggregate transformations, in turn, greatly influence macroproperties of the solutions such as absorbance, viscosity, and phase separation. In this sense, the aggregate composition is a deterministic parameter for this kind of system.

Several theories were successfully developed to model aggregation equilibria in mixed surfactant systems. The Rubingh theory, a handy and broadly applicable one among them, treats a mixed surfactant solution as two pseudophases, where the monomeric surfactant aqueous phase is in equilibrium with the aggregated surfactant phase. Meanwhile, it introduces an interaction parameter \( \beta \) to describe the nonideal mixing of different surfactants in the aggregation phase. This theory was proven to be quite effective for cationic/anionic surfactant systems because \( (1) \) aggregation numbers of such systems are usually very large, ensuring the validity of the pseudophase separation assumption and \( (2) \) electrostatic attractions between oppositely charged head groups are properly quantified by the interaction parameter \( \beta \). As theoretically predicted and experimentally determined, nonstoichiometric cationic/anionic surfactant systems are characterized by a great bias in the aggregation equilibrium, that is, the charged aggregates considerably prefer the countercharged, minor surfactant (molar fraction < 0.5) over the cocharged, major one (molar fraction > 0.5) due to electrostatic reasons. The bias causes aggregate compositions to deviate from bulk compositions by getting close to electroneutral mixing.

1.3. Host–Guest Equilibrium versus Biased Aggregation Equilibrium. CDs are donut-like oligosaccharides with hydrophobic cavities and hydrophilic outer surface. The hydrophobic cavities allow CDs to include various surfactants with high binding constants. The hydrophilic outer surface leads to the fact that the surfactant/CD complexes disfavor forming aggregates and are quite dissolvable in water. Many efforts were devoted to the relation between the structure of surfactants (such as Gemini, bola, and double-chain surfactants) and the structure of CDs (such as \( \alpha \)-, \( \beta \)-, \( \gamma \)-, and modified CDs). Most of the work was performed in CD/single surfactant systems, whereas little work was conducted on CD/mixed surfactants systems. For example, \( \beta \)-CD prefers the fluorinated surfactant in a fluorinated/hydrogenated surfactant mixture due to size matching.

Herein, we attempt to realize the coexistence of the host–guest and biased aggregation equilibria in cationic surfactant/anionic surfactant/\( \beta \)-cyclodextrin (\( \beta \)-CD) ternary aqueous systems. In a recent paper, we reported that addition of \( \beta \)-CD to nonstoichiometric cationic/anionic surfactant systems will result in growth of surfactant aggregates, typically from micelles to vesicles. This observation is in contrast to the well-accepted “aggregate-breaking” effect of CDs, thereby promoting us to unveil its origin. In this work, a thermodynamic model is established to describe the cationic surfactant/anionic surfactant/\( \beta \)-CD ternary aqueous systems, the validity of which is confirmed by surface tension, pulse-gradient spin–echo nuclear magnetic resonance (PGSE-NMR), and isothermal titration calorimetry (ITC) measurements. We find that the \( \beta \)-CD-induced aggregate growth is a direct consequence of the combination of the host–guest and biased aggregation equilibria. The biased aggregation equilibrium imposes an apparent selectivity on the host–guest equilibrium by forcing \( \beta \)-CD to selectively bind the major surfactant. The host–guest equilibrium, in return, amplifies the bias of the aggregation equilibrium by facilitating the depletion of the major surfactant from the surfactant aggregates. Concomitantly, the aggregate composition gets closer to the electroneutral mixing stoichiometry. Eventually, the composition variation leads to the aggregate growth, as we recently observed. Due to its remarkable effect on aggregate compositions, \( \beta \)-CD could be a promising additive to control cationic/anionic surfactant systems.

2. Experimental Section

2.1. Materials. Dodecyltriethylammonium bromide (DEAB) was prepared by reactions of 1-bromododecane with triethylamine, followed by recrystallizing five times from ethanol/acetone. \( ^1 \)H NMR: \( \delta \) 3.32 (q, 6H), 3.18 (t, 2H), 1.69 (m, 2H), 1.30 (m, 27H), 0.90 (t, 3H) ppm. Elementary analysis: found N 3.90%, C 60.95%, H 11.60%; calculated N 4.00%, C 61.70%, H 11.51%. Sodium dodecyl sulfate (SDS, 99%) was purchased from Acros Organics Co. and used as received. The purity of the surfactants was verified by the absence of minima in their surface tension curves (see the Supporting Information). \( \beta \)-Cyclodextrin (\( \beta \)-CD) was purchased from Sinopharm Chemical Reagent Co. with a water content of 14%. For NMR diffusion measurements, we dehydrated \( \beta \)-CD powder by heating it at 80 °C for 2 h before preparing its D2O solution. Otherwise, \( \beta \)-CD was used without further treatment. D2O (99.9%) was purchased from Cambridge Isotope Laboratories Inc. Water (H2O) was redistilled from potassium permanganate.

2.2. Surface Tension. Surface tension \( \gamma \) measurements were conducted using the drop volume method at 25.0 °C. In a typical surface tension–surfactant concentration curve, three regions can be identified; region I, the surface tension slightly changes with the surfactant concentration; region II, a steep, linear decline; region III, an abrupt leveling at the critical aggregation concentration (CAC) where \( \gamma \) reaches its minimum, \( \gamma^{CAC} \). The surface tension is related to the surfactant concentration by the Gibbs adsorption equation

\[
d\gamma = -RTd\Gamma \ln C
\]

where the Gibbs adsorption amount \( \Gamma \) is a surface excess quantity denoting the number of moles of the surfactant adsorbed per unit area at the surface, \( R = 8.314 \) J mol\(^{-1}\) K\(^{-1}\), and \( T \) is the absolute temperature. In region II (also known as the saturated adsorption region), the linear decline indicates that \( \Gamma \) reaches its maximum (\( \Gamma^* \)) and keeps constant.

Figure 1. The experimental surface tension curve of the SDS/DEAB (molar ratio 3/1) system upon dilution.
performed on a Bruker 400 NMR spectrometer at 25 °C. Samples were prepared using D2O as the solvent. For molecules, signal intensity is given by

\[ I = I_0 \exp(-D \lambda^2 G^2 \delta^2 (\Delta - \delta/3)) \]  

where \( I \) is the observed intensity, \( I_0 \) the intensity without the gradient pulse, \( D \) the diffusion coefficient of the molecules, \( \lambda \) the magnetogyric ratio of protons, \( G \) the gradient strength, \( \Delta \) the time interval, and \( \delta \) the duration time of the gradient pulse. A LED bipolar pulse sequence was used here, where \( G \) was changed from 0 to 32 G/cm, \( \delta \) was set as 6 ms, and \( \Delta \) was typically chosen as 300 ms. For DEAB and SDS, the peaks at ~3.2 and 3.9 ppm were selected, respectively. For all of the samples, single-exponential decays of the echo amplitude were always observed, indicating that the exchanges of the species between different states are rapid with respect to the NMR time scale. Figure 2 displays three representative decays (intensity versus \( U, U = \lambda^2 G^2 \delta^2 (\Delta - \delta/3) \)) of the SDS signal in different systems, all of which are clearly single-exponential. Fitting of the data to eq 3 will yield the diffusion coefficient \( D \). The PGSE-NMR measurements in this work serve to determine concentrations of surfactants in monomeric, complexed, and aggregated states, where diffusion coefficients of surfactants in the two former states need to be preobtained. For SDS, DEAB, and their complexes with β-CD, their diffusion coefficients are preobtained from control experiments and are listed in Table 1.

2.4. Isothermal Titration Calorimetry (ITC). Calorimetric measurements were conducted with a TAM 2777-201 microcalorimetric system (Thermometric AB, Jarfalla, Sweden) at 25.00 °C. A 1 mL stainless steel sample cell was initially loaded with the titrant solution, and the titrant solution was injected into the sample cell via a 250 µL Hamilton syringe controlled by a 612 Thermometric Lund pump. The system was stirred at 50 rpm with a gold propeller. For the calibration constant of ITC measurements, please see the Supporting Information. The observed heat was obtained by integration over the peak of each injection in the plot of heat flow \( P \) against time \( t \). For \( Q^{\text{obs}} \), the dilution heat \( Q^{\text{dilution}} \) always contributes, and this contribution needs to be corrected. The \( Q^{\text{dilution}} \) was evaluated from control experiments and was subtracted from \( Q^{\text{obs}} \), giving the dilution-corrected heat \( Q \). This \( Q \) was then weighted by the mole number of the added titrant, giving \( \Delta H \) in kJ mol\(^{-1}\).

First, ITC was employed to determine binding constants of SDS/β-CD and DEAB/β-CD. Figure 3 gives the \( \Delta H \) curves for

![Image](image_url)
the titrations of a β-CD (12 mM) aqueous solution into SDS (2 mM, below its CMC) and DEAB (2 mM, below its CMC) aqueous solutions, respectively. The software Ligand Binding was used to fit the curves to a 1:1 surfactant/β-CD model. The fitting yielded binding constants $K^b_i$ and enthalpy changes in the transfer of surfactant $i$ from monomeric to complexed states $\Delta H^m_{i-\beta-CD}$ (or equivalently, the complexation enthalpy $\Delta H^k_{i-\beta-CD}$), which are listed in Table 1.

Second, ITC was used to obtain enthalpy changes in the transfer of surfactants from aggregated to monomeric states $\Delta H^m_{i-\beta-CD}$. A SDS (5 mM) or DEAB (2 mM) aqueous solution was titrated into a SDS/DEAB (4/1 mM) aqueous solution. These titrations involve the transfer of surfactant molecules from monomeric to aggregated states, a reverse of the objective process ($\Delta H^m_{i-\beta-CD} = -\Delta H^m_{i-\beta-CD}$). After accounting for the fraction of the transferred surfactant molecules, we can obtain $\Delta H^m_{i-\beta-CD}$ as listed in Table 1.

3. Thermodynamic Model

Consider a given aqueous mixture of surfactant 1, surfactant 2, and β-CD, where their respective bulk concentrations are $C_1$, $C_2$, $C_{\beta-CD}$, and $C_{\beta-CD}$ (eqs 5 and 9). In a 1:1 surfactant/β-CD binding model, the host–guest equilibrium is governed by

$$K^b_1 = \frac{C^a_1}{C^m_1 C^m_{\beta-CD}}$$

(4)

where $K^b_1$ is the binding constant of β-CD to surfactant 1 ($i = 1$ or 2) and $C^m_1$, $C^a_1$, and $C^m_{\beta-CD}$ are the concentrations of the $i$/β-CD complex, monomeric (uncomplexed and unaggregated) $i$, and free (uncomplexed) β-CD, respectively. The mass balance of β-CD gives

$$C^m_{\beta-CD} + C^a_1 + C^a_2 = C^m_{\beta-CD}$$

(5)

It is reasonable to use the ratio of $C^a_1$ weighed by $C_1$ to measure the apparent selectivity of β-CD to 1, $S_a$, which yields

$$S_a = \frac{C^a_1 C^2_2}{C^a_2 C^2_1} = \frac{K^b_2 C^m_2}{K^b_1 C^m_1 C^2_1}$$

(6)

$$S_a = 1/S_1$$

(7)

Clearly, $S_a \gg 1$, $S_a \ll 1$, and $S_a \approx 1$ correspond to a high selectivity to 1, a high selectivity to 2, and a low selectivity, respectively. Moreover, this selectivity $S_a$ will depend on the nature of a specific binary surfactant mixture and the amount of added β-CD (i.e., $C^m_{\beta-CD}$). To eliminate the effect of $C^m_{\beta-CD}$, we define the initial selectivity $S^*$ in the limit of $C^m_{\beta-CD} \rightarrow 0$, that is

$$S^* = \lim_{C^m_{\beta-CD} \rightarrow 0} \frac{C^a_1 C^2_2}{C^a_2 C^2_1} = \lim_{C^m_{\beta-CD} \rightarrow 0} \frac{K^b_2 C^m_2}{K^b_1 C^m_1 C^2_1}$$

(8)

If $C_1 <$ critical aggregation concentration (CAC), the mass balance of surfactant 1 is given by

$$C^m_1 + C^a_1 = C_1$$

(9)

and the mixed system can be fully described by the host–guest equilibrium (eq 4) and the mass balances of β-CD and surfactants (eqs 5 and 9). At the limit of $C^m_{\beta-CD} \rightarrow 0$, $C^a_1$ is practically 0, $C^m_1 = C_1$, and the selectivity $S^*_1$ simply reads

$$S^*_1 = K^b_1/K^b_2$$

(10)

In this case, the selectivity $S^*_1$ is identical to the classic selectivity that exclusively depends on binding constants.

If $C_1 \geq$ CAC, the aggregation equilibrium emerges, and the surfactant mass balance is expressed by

$$C^m_1 + C^a_1 + C^a_2 = C_1$$

(11)

where $C^a_1$ is the concentration of 1 in the mixed aggregates. Within the pseudophase separation model, the balance between chemical potentials of 1 in monomeric and aggregated states reads

$$\mu^m_1 + RT \ln(C^m_1/55.5) = \mu^a_1$$

(12)

where $\mu^m_1$ is the standard chemical potential of monomeric 1, 55.5 the molar concentration of water, and $\mu^a_1$ the chemical potential of 1 in the mixed aggregation phase. According to the Rubingh theory, the mixed aggregation phase is treated as a regular solution, leading to

$$\mu^a_1 = \mu^m_1 + RT \ln(f^a_1 x_1)$$

(13)

where $\mu^m_1$ is the standard chemical potential of 1 in its own pure micelles, $f^a_1$ the activity coefficient of 1 in the mixed aggregation phase, and $x_1$ the mole fraction of 1 in the mixed aggregation phase ($x_1 = C^a_1/(C^a_1 + C^a_2)$). Then, $\mu^m_1$ is correlated to the critical micelle concentration of 1, $C_{MC1}$, and $\mu^m_1$ by

$$\mu^m_1 + RT \ln(C_{MC1}/55.5) = \mu^a_1$$

(14)

Combining eqs 12, 13, and 14, one obtains

$$C^m_1 = C_{MC1} f^a_1 x_1$$

(15)

Here, a dimensionless parameter $\beta$ is introduced to correlate $f^a_1$ and $x_1$ by

$$f^a_1 = \exp(\beta(x^a_1)^2)$$

(16)

$$x^a_1 = \exp(\beta(x^a_1)^2)$$

(17)

where $\beta$ is the interaction parameter of the two surfactants and represents a net energy difference between the mixed (1 + 2) aggregation phase and the pure (1 or 2) micellar phases. Now the ternary 1/2/β-CD aqueous mixture can be described by the host–guest (eq 4) and aggregation (eqs 15–17) equilibria as well as the β-CD (eq 5) and surfactant (eq 11) mass balances.
At the limit of $C_{\beta,CD} \to 0$, the combination of eqs 8, 15, 16, and 17 gives

$$S_i^T = \lim_{C_{\beta,CD} \to 0} \frac{K_{\beta,CD}^b C_M^i x_i^2 C_2}{K_{\beta,CD}^b C_M^i x_i^2 C_1} \exp(\beta((x_i^2)^2 - (x_i^1)^2))$$

$$= \frac{K_{\beta,CD}^b C_M^i x_i^2 C_2}{K_{\beta,CD}^b C_M^i x_i^2 C_1} \exp(\beta((x_i^2)^2 - (x_i^1)^2))$$

(18)

in which $x_i^m$ is the molar fraction of $i$ in the aggregates without $\beta$-CD addition (i.e., $C_{\beta,CD} = 0$).

It is worthy noting that 1) this model can be modified to account for systems involving 1:2 surfactant/$\beta$-CD complexation by re-establishing the complexation equilibria (in a 1:2 manner) and relevant mass balances, (2) $\beta$-CD here can be replaced by any member from the CD family, and (3) although this work focuses on cationic/anionic surfactant mixtures, this model is, in principle, operative for any other binary surfactant mixtures.

4. Results

In this section, several conclusions that can be directly drawn from the thermodynamic model are listed, and the correctness of them is experimentally checked in SDS/DEAB/$\beta$-CD systems. In the studied SDS/DEAB/$\beta$-CD systems, the molar ratio of SDS/DEAB was always selected to be 3/1 to avoid an equimolar ratio because a SDS/DEAB equimolar mixture is not stable and will precipitate over 1 to 2 weeks. A partial phase diagram of the SDS/DEAB system is presented in the Supporting Information.

4.1. Low Selectivity at $C_T < CAC$. For $C_T < CAC$, the aggregation equilibrium is not yet raised, and the selectivity is simply governed by binding constants. The thermodynamic model suggests quite low selectivity for SDS/DEAB/$\beta$-CD ($C_T < CAC$) systems, which is not surprising since the binding constants of $\beta$-CD to SDS and DEAB are almost identical. The initial selectivity is always 0.91, and the apparent selectivity is even closer to 1 (Figure 4a) for mixtures of SDS/DEAB (molar ratio 3/1 and $\beta$-CD). The above prediction is tested by surface tension measurements, in which SDS/DEAB/$\beta$-CD solutions are diluted against $\beta$-CD buffers (the surfactant molar ratio is constant at 3/1, and $C_{\beta,CD}$ is kept at 3, 6, or 10 mM). The experimental results are shown as scatters in Figure 4b, while the predicted lines are obtained as follows. In the presence of $\beta$-CD, the effective total surfactant concentration related to the surface tension is actually the sum of monomeric surfactant concentrations. The Gibbs adsorption equation (in integral form, in the saturated adsorption region) then reads

$$\gamma - \gamma^{CAC} = -\Gamma^\infty RT \ln(C_{SDS}^m + C_{DEAB}^m - \ln \text{CAC})$$

(19)

The $C_{SDS}^m$ and $C_{DEAB}^m$ can be readily calculated according to the predicted selectivity for a given solution. The $\gamma^{CAC}$, $\Gamma^\infty$, and CAC are determined from a $\beta$-CD-free control experiment (see the Experimental Section and Table 1). The consistency between the experimental and predicted results validates our thermodynamic model and the deduced low selectivity for the SDS/DEAB/$\beta$-CD ($C_T < CAC$) systems.

4.2. High Selectivity toward the Major Surfactant at $C_T > CAC$. With $C_T > CAC$, the combination of the host-guest and aggregation equilibria dominates the systems. For the SDS/DEAB/$\beta$-CD systems, the thermodynamic model generally gives high selectivity of $\beta$-CD to the major surfactant regardless of the similarity between $K_{SDS}^\beta$ and $K_{DEAB}^\beta$. Specifically, Figure 5a–c shows the predicted binding behavior of $\beta$-CD in the SDS/DEAB (15/5 mM) system upon addition of $\beta$-CD. The concentration of complexed SDS ($C_{SDS}$, the red curve in Figure 5a) is almost proportional to $C_{\beta,CD}$, whereas the concentration of complexed DEAB ($C_{DEAB}$, the red curve in Figure 5b) is always close to 0, qualitatively revealing a high selectivity to SDS ($S_{SDS}$). The quantitative value of $S_{SDS}$ shows a maximum of ∼140 at $C_{\beta,CD} = 0$ mM (i.e., the initial selectivity $S_{SDS}^{\infty}$) and undergoes a progressive decrease to ∼25 (still >1) at $C_{\beta,CD} = 5$ mM (the black line in Figure 5c). The figures further manifest that (1) the added $\beta$-CD will bind the major surfactant SDS with a high selectivity, partly removing the excess SDS from aggregates (the green line in Figure 5a), (2) the concentration of DEAB in aggregates $C_{DEAB}$ is not affected (the green line in Figure 5b), and (3) the net effect is clearly the shift of the aggregate composition toward 1:1 electroneutral mixing (the blue curve in Figure 5c).

These predictions are examined by PGSE-NMR measurements. Figure 5d demonstrates the observed diffusion coefficients of tetramethylsilane (TMS), DEAB, and SDS with the addition of $\beta$-CD to the SDS/DEAB (15/5 mM) solution. TMS is added to the solutions to label the diffusion coefficient of the surfactant aggregates $D^a$. Because the strongly
hydrophobic TMS will be fully solubilized into the aggregates, \( D^\text{a} \) is simply given by \( D^\text{a} = D^\text{obs} \). As shown in Figure 5d, the aggregates diffuse more slowly with \( \beta\text{-CD} \) addition, in line with the previously observed \( \beta\text{-CD} \)-induced aggregate growth. The \( D^\text{obs} \) and \( D^\text{SDS} \) are related to the concentrations of SDS or DEAB in different states by the n-state exchange model. The validity of this model in this case is confirmed by the fact that the echo amplitude of SDS or DEAB always follows single-exponential decays (Figure 2). In the n-state exchange model, the observed diffusion coefficient of surfactant \( i \) (i = DEAB or SDS) is a concentration-weighed average of the diffusion coefficients in different states

\[
D_i^\text{obs} = \left( C_i^m D_i^m + C_i^c D_i^c + C_i^a D_i^a \right) / C_i
\]  

where \( D_i^m \) and \( D_i^c \) are the diffusion coefficients of \( i \) in monomeric and complexed states, respectively, and can be obtained from separate experiments (see the Experimental Section and Table 1). According to this equation, the mass balances of \( \beta\text{-CD} \) and surfactants (eqs 5 and 11), and the complexation equilibrium (eq 4), we experimentally determined \( C_i^m \), \( C_i^c \), and \( C_i^a \), which are shown as scatters in Figure 5a−c. Obviously, the experimental data is in good agreement with the predicted data, verifying the highly selective binding to SDS and the approaching of 1:1 electoneutral mixing.

The thermodynamic model and its predictions are further evaluated by ITC measurements, where a \( \beta\text{-CD} \) (5 mM) solution is titrated into a SDS/DEAB (4/1 mM) solution. The experimental result is that \( \Delta H = \sim -12 \) kJ/mol, while predicted data are generated by the following procedure. When a \( \beta\text{-CD} \) solution is titrated into a SDS/DEAB (\( C_t > C_{\text{CAC}} \)) solution, the dilution-corrected heat \( Q \) for each injection can be divided into four parts

\[
Q = Q_i^{m\rightarrow c} + Q_i^{c\rightarrow m} + Q_i^{a\rightarrow c} + Q_i^{c\rightarrow a}
\]

where \( Q_i^{m\rightarrow c} \) and \( Q_i^{c\rightarrow m} \) (i = SDS or DEAB) are the heats due to the transfers of \( i \) from water and the aggregates to \( \beta\text{-CD} \) cavities, respectively. Equation 21 can be expressed by molar enthalpy changes

\[
\Delta H \Delta n_{\beta\text{-CD}} = \Delta H_i^{m\rightarrow c} n_i^{m\rightarrow c} + \Delta H_i^{c\rightarrow m} n_i^{c\rightarrow m} +
\Delta H_i^{a\rightarrow c} n_i^{a\rightarrow c} + \Delta H_i^{c\rightarrow a} n_i^{c\rightarrow a} = \Delta H_{\text{SDS}}^{m\rightarrow c} (-\Delta n_{\text{SDS}}) +
\Delta H_{\text{DEAB}}^{m\rightarrow c} (-\Delta n_{\text{DEAB}}) +
\Delta H_{\text{DEAB}}^{a\rightarrow c} (-\Delta n_{\text{DEAB}}) +
\Delta H_{\text{DEAB}}^{c\rightarrow a} (-\Delta n_{\text{DEAB}})
\]

The \( \Delta n_{\beta\text{-CD}}, \Delta n_{\text{SDS}}, \Delta n_{\text{DEAB}} \), and \( \Delta n_{\text{DEAB}} \) are molar changes of corresponding species in the titrand solution during an injection, where the last four molar changes are predictable for a given \( \Delta n_{\beta\text{-CD}} \). Noteworthily, the transfer of surfactant \( i \) from aggregates into \( \beta\text{-CD} \) cavities can be conceptually broken down into two steps, the transfer of \( i \)
from the aggregates to water and then to β-CD cavities, which leads to

\[ \Delta H^\text{m-c} = \Delta H^\text{m-m} + \Delta H^\text{m-c} \] (23)

The \( \Delta H^\text{m-m} \) and \( \Delta H^\text{m-c} \) can be determined from separate experiments (see the Experimental Section and Table 1), eventually enabling the prediction of \( \Delta H \). The predicted \( \Delta H \) is \(-11.4 \text{ kJ/mol} \), consistent with the experimental data.

Taken together, the PGSE-NMR and ITC measurements confirm the validity of the present thermodynamic model and identify the high selectivity toward SDS for the SDS-rich SDS/DEAB systems. As to DEAB-rich SDS/DEAB systems, high selectivity is, not surprisingly, quite low. The situation gets complicated for the SDS/DEAB mixture, where the two equilibria coexist and are coupled through the bridging of surfactant monomers. Before the discussion on how the combination of the two equilibria dominates the systems, we attempt to clarify the bias of the aggregation equilibrium, which always plays a central role in nonstoichiometric cationic/anionic surfactant systems with or without the presence of β-CD. The bias is that the aggregation of the minor surfactant is much more preferred than that of the major surfactant even if the two surfactants are of close CMCs. This is reasonable considering that the net charge of the aggregates will favor the countercharged, minor surfactant and repel the cocharged, major surfactant electrostatically. In the case of the SDS-rich SDS/DEAB mixture, the bias is evidenced by the remarkable difference in the aggregation enthalpy changes (\(-20 \text{ kJ/mol} \) for DEAB, favored; \(-0.1 \text{ kJ/mol} \) for SDS, disfavored) as well as by the β parameter of \(-13 \).

As a result of the bias, there is a tendency for the aggregates to deplete all of the excess part of the major surfactant and to finally reach electroneutral mixing stoichiometry. In the absence of β-CD, the major surfactant can be solely depleted into water, an environment that disfavors the hydrophobic moiety of the surfactant and that can only accommodate a limited amount of the major surfactant. In the presence of β-CD, the major surfactant can also be depleted in β-CD cavities, an environment quite comfortable with the hydrophobic moiety of the surfactant. Therefore, β-CD has to accept the major surfactant, the less aggregatable and more available one, although β-CD may exhibit no preference to the major or minor surfactants on its own. In this context, the bias gives rise to a kind of apparent \( K_w \)-independent host–guest selectivity. Considering the high binding constants of β-CD to surfactants, the β-CD cavities can act as efficient vessels for the depleted major surfactant molecules. Upon the addition of β-CD, an increasing amount of the major surfactant is removed from the aggregates to β-CD cavities, leaving the aggregate composition approaching electroneutral mixing stoichiometry. The approaching to electroneutrality promotes transitions of aggregates into low-curved ones, which answers for the recently observed β-CD-induced aggregate growth.14 The above description is summarized in Scheme 1.20,21

On account of its influence on aggregate compositions, β-CD is defined as a stoichiometry booster for nonstoichiometric cationic/anionic surfactant systems. This stoichiometry boosting effect is further profiled in a contour map (Figure 6) for SDS/DEAB/β-CD systems, where \( x_{SDS} \) (the aggregate composition; its value is denoted by different colors) is predicted according to input values of \( x_{SDS} \) (the bulk composition) and \( C_{β-CD} \). Along the y axis, the relation between \( C_{β-CD} \) and \( x_{SDS} \) at a constant \( x_{SDS} \) is demonstrated. Taking \( x_{SDS} = 0.8 \) as an instance, one observes the approach of \( x_{SDS} \) to the 1:1 stoichiometry (from

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**Figure 6.** Predicted contour map for SDS/DEAB (\( C_T = 10 \text{ mM} \)) and β-CD mixed systems: \( x_{SDS} \) against the surfactant composition in bulk solution (\( x_{SDS} \)) and against \( C_{β-CD} \).
cyan via green to yellow) with the C\textsubscript{β-CD} increase. Along the x axis, the connection between x\textsubscript{3SDS} and x\textsubscript{DS} at a constant C\textsubscript{β-CD} is displayed. For β-CD-free samples (C\textsubscript{β-CD} = 0), x\textsubscript{DS} is basically determined by input x\textsubscript{3SDS} (i.e., their values are close); x\textsubscript{3SDS} falls in the near-stoichiometry region (0.45–0.55, magenta) only for x\textsubscript{DS} from 0.43 to 0.56. However, for samples with C\textsubscript{β-CD} = 5 mM, x\textsubscript{3SDS} shows a strong resistance to variations of x\textsubscript{3SDS}: x\textsubscript{3SDS} remains near stoichiometry for a highly broadened range of x\textsubscript{3SDS} from 0.27 to 0.72. This figure clarifies two equivalent features of stoichiometry boosters, (1) altering aggregate compositions to stoichiometry for samples at a fixed bulk composition as well as (2) resisting variations of bulk compositions and maintaining aggregate compositions near stoichiometry for samples at a fixed total bulk concentration. These features manifest that the stoichiometry booster is analogous to a pH buffer which always adjusts the ratio of H\textsuperscript{+}sto stoichiometry for samples at a fixed total bulk concentration.

5.2. Factors that Affect the Initial Selectivity at C\textsubscript{T} > CAC.

These factors will be evaluated one by one in terms of eq 18, which is rewritten here for convenience

\[ S^*_T = \frac{K^b_{\text{CMC1}} x^{a0}_{\text{DS}} C_T}{K^b_{\text{CMC1/CMC2}}} \exp(\beta((x^{a0}_{\text{DS}})^2 - (x^{a0}_{\text{T}})^2)) \]  

As listed in Table 2, for a mixture of cationic/anionic surfactants with equal tails, both K\textsuperscript{1}/K\textsuperscript{2} and CMC\textsubscript{1}/CMC\textsubscript{2} are close to 1. As for a mixture of cationic/anionic surfactants with unequal tails, K\textsuperscript{1}/K\textsuperscript{2} and CMC\textsubscript{1}/CMC\textsubscript{2} is close to 1, as well due to a “compensation effect” between K\textsuperscript{1}/K\textsuperscript{2} and CMC\textsubscript{1}/CMC\textsubscript{2}. This compensation effect is understandable since surfactants with longer tails (more hydrophobic) are easier to bind with β-CD (higher K\textsuperscript{b}) and to aggregates (lower CMC). Thus, the two terms can hardly contribute to the initial selectivity.

The dependence of S\textsubscript{T} on x\textsuperscript{a0} is plotted by predicted curves in SDS/DEAB systems (Figure 7). For the SDS-rich systems (x\textsuperscript{DS} or x\textsubscript{3SDS} > 0.5), S\textsubscript{T} is larger than 1 and increases abruptly with the composition moving from 0.5 to 1. As for the DEAB-rich systems (x\textsuperscript{DS} or x\textsubscript{3SDS} < 0.5), S\textsubscript{T} is lower than 1 and decreases precipitously upon shifting the composition from 0.5 to 0. Alternatively, the poorer the selectivity to SDS, the better the selectivity to DEAB (S\textsubscript{DEAB} = 1/S\textsubscript{T}). It is also noticeable that the deviation of a x\textsubscript{3DS} curve from the x\textsubscript{3SDS} curve is aggravated by C\textsubscript{T} decrease, which is associated with the fact that, in nonstoichiometric cationic/anionic surfactant systems, aggregate compositions always depart farther from bulk compositions (i.e., gets closer to 1:1) with C\textsubscript{T} decrease. Overall, the selectivity exhibit near-exponential dependence on the aggregate composition.

As for the interaction parameter β, it measures the net energy difference between the mixed and unmixed systems within the regular solution theory. For a binary surfactant mixed system, (1) negative β reveals that the two surfactants are more aggregatable when they are mixed than on their own, that is, they form mixed aggregates in a synergistic way, (2) positive β reveals that the two surfactant are less aggregatable when they are mixed than on their own, that is, they form mixed aggregates in an antagonistic way, (3) zero β reveals that the two surfactant form mixed aggregates in an ideal way, and (4) the magnitude of β reflects the degree of synergism or antagonism. Cationic/anionic surfactant systems are generally of negative β values less than −10 because the aggregation of the mixture is greatly synergized by the strong electrostatic attractions between oppositely charged surfactant head groups. Other binary surfactant systems like cationic/cationic, anionic/anionic, and ionic/nonionic ones are of β values between 0 and −5 due to the lack of significant aggregation synergism. As clearly shown in Table 2, all of the cationic/anionic surfactant systems have highly negative β values and exhibit conspicuously high selectivity (S\textsubscript{T} ≈ 10\textsuperscript{3} or 10\textsuperscript{4}) for x\textsuperscript{a0} = 0.3 or 0.7, whereas a cationic/anionic system with β = 0 displays no appreciable selectivity (S\textsubscript{T} ≈ 1). For different cationic/anionic surfactant mixtures, a larger absolute value of β corresponds to a higher selectivity value. The above results reveal that β is the leading parameter in eq 18 and that the electrostatic attractions between cationic and anionic surfactants are of the greatest importance to the initial selectivity.

**Conclusion**

In this work, we systematically investigated the cationic surfactant/anionic surfactant/β-CD ternary aqueous systems.
thermodynamic model was developed to describe the systems, the validity of which was verified by surface tension, PGSE-NMR, and ITC measurements. It is found that these systems are dominated by the interplay between the host—guest and aggregation equilibria. The aggregation equilibrium in nonstochiometric cationic/anionic surfactant systems is inherently biased, in which the aggregates tend to deplete the excess part of the major surfactant to reach electroneutrality. The bias will force the added β-CD to selectively accept the major surfactant even if the binding constants of β-CD to the two surfactants are similar. The apparent host—guest selectivity is of considerably high value and of an “abnormal” origin, that is, in contrast to “normal” selectivity governed by the difference in binding constants, the present “abnormal” selectivity arises from the strong electrostatic attractions between cationic and anionic surfactants. Since the binding constants between β-CD and surfactants are generally high, the selective binding will efficiently remove the major surfactant (a part of its excess) from the aggregates to β-CD cavities. This behavior leaves the aggregate composition approaching the electroneutral mixing stoichiometry and thus amplifies the bias of the aggregation equilibrium. The approaching of electroneutrality causes the aggregates to be transformed into less-curved ones, as we observed in a recent work. Furthermore, β-CD is defined as a stoichiometry booster for the whole class of cationic/anionic surfactant systems, which provides an additional dimension to directly tune aggregate compositions. Because the aggregate composition is a central parameter of the cationic/anionic surfactant systems, which can profoundly affect the systems at both microscopical and macroscopical levels, the stoichiometry booster, β-CD, is envisioned to be a promising and powerful additive to control this kind of system.

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Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>concentration</td>
</tr>
<tr>
<td>C_i, C_i^*, and C_i^m</td>
<td>concentration of surfactant i in bulk solution, concentrations of surfactant i in aggregated, complexed, and monomeric states, respectively</td>
</tr>
<tr>
<td>C_g-CD</td>
<td>concentration of β-CD in bulk solution</td>
</tr>
<tr>
<td>C_g-CD^*</td>
<td>concentration of free (uncomplexed) β-CD</td>
</tr>
<tr>
<td>CAC</td>
<td>critical aggregation concentration of a surfactant mixture</td>
</tr>
<tr>
<td>CMC_i</td>
<td>critical micelle concentration of surfactant i</td>
</tr>
<tr>
<td>D</td>
<td>diffusion coefficient</td>
</tr>
<tr>
<td>D_{iobs}</td>
<td>observed diffusion coefficient of surfactant i</td>
</tr>
<tr>
<td>D_{i} and D_{i}^m</td>
<td>diffusion coefficients of surfactant i in complexed and monomeric states, respectively</td>
</tr>
<tr>
<td>ΔH_{i}^{f-m}, ΔH_{i}^{f-c}, and ΔH_{i}^{m-c}</td>
<td>enthalpy changes in the transfer of surfactant i from aggregated to monomeric, from aggregated to complexed, and from monomeric to complexed states, respectively</td>
</tr>
<tr>
<td>S_i and S_i^a</td>
<td>apparent and initial selectivity of β-CD to surfactant i</td>
</tr>
<tr>
<td>K_i</td>
<td>binding constant of β-CD to surfactant i</td>
</tr>
<tr>
<td>Q_{vdw}, Q_{dilution}, and Q_{obs}</td>
<td>dilution-corrected heat, dilution heat, and observed heat, respectively</td>
</tr>
<tr>
<td>Q_{i}^{h-c} and Q_{i}^{m-c}</td>
<td>heats due to the transfers of i from water and the aggregates to β-CD cavities, respectively</td>
</tr>
</tbody>
</table>

\[ R \] gas constant
\[ T \] absolute temperature
\[ \beta \] interaction parameter in mixed aggregates
\[ \gamma \] surface tension
\[ \Gamma \] surface tension at CAC
\[ \Gamma^m \] Gibbs adsorption amount
\[ \mu_i^{\Theta} \] standard chemical potential of surfactant i in mixed aggregates
\[ \mu_i^{ab} \] chemical potential of surfactant i in its own pure micelles and in monomeric states, respectively
\[ \chi_i \] molar fraction of surfactant i in bulk solution
\[ \chi_i^c \] molar fraction of surfactant i in mixed aggregates
\[ \chi_i^{mc} \] molar fraction of surfactant i mixed aggregates without β-CD addition

Supporting Information Available: Figures S1—S4. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes


(20) Actually, the Le Chatelier principle also predicts that β-CD will form more complexes with the surfactant at a higher concentration. According to this principle, one might intuitively expect the difference to be similar to the difference in concentrations of the two surfactants. In the present case (SDS/DEAB 15/5 mM), it was found that the selectivity of β-CD to SDS over that to DEAB is ∼100:1, much larger than the ratio of concentrations of SDS and DEAB, 3:1. Therefore, the interplay between the host–guest and biased aggregation equilibria is within the frame of the Le Chatelier principle, yet they are not exactly the same. In addition, the present thermodynamic model can predict the exact value of the selectivity, whereas the Le Chatelier principle cannot.

(21) Recently, it has been established that β-CD can form aggregates with diameters ∼200 nm above 3 mM by itself; see: (a) Bonini, M.; Rossi, S.; Karlsson, G.; Almgren, M.; Nostro, P. L.; Baglioni, P. *Langmuir* 2006, 22, 1478. (b) Rossi, S.; Bonini, M.; Nostro, P. L.; Baglioni, P. *Langmuir* 2007, 23, 10959, and references therein. However, in the present case of SDS/DEAB/β-CD solutions, most of β-CD will form complexes with SDS or DEAB, and the complexes will not aggregate, as evidenced by the diffusion coefficient of the complexes (measured by PGSE-NMR).