

Using a Combination of Experimental and Mathematical Method To Explore Critical Micelle Concentration of a Cationic Surfactant

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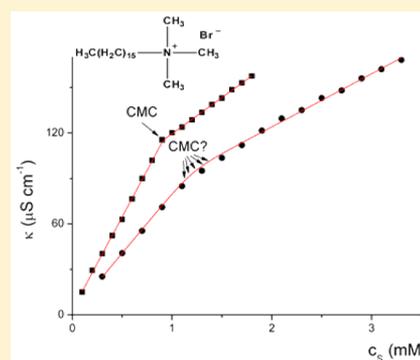
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S Supporting Information

ABSTRACT: An undergraduate electrical conductivity measurement experiment in a physical chemistry lab and basic fitting procedures are presented that allow a characterization of micellar system of hexadecyltrimethylammonium bromide (cetyltrimethylammonium bromide, CTAB) in binary mixture of water and acetonitrile (ACN) as a cosolvent (10%, v/v) at 30.0 °C. Conductivity–concentration data were processed by inbuilt function of ORIGIN software to attain the values of critical micelle concentration by method of integration. Acquiring the data-fitting skills that are developed through the addition of a computational tool to a conventional electrical conductometry experiment has a general significance for its applications to more complex upper-level experiments with the aim to process data and perform fast calculations and graphics.



KEYWORDS: Upper-Division Undergraduate, Physical Chemistry, Laboratory Instruction, Hands-On Learning/Manipulatives, Instrumental Methods, Colloids, Micelles, Conductivity

Surfactants¹ (a contraction of the term *surface-active agent*) are amphiphilic compounds comprising distinct polar (hydrophilic or liophobic “head”) and nonpolar (liophilic or hydrophobic “tail”) sections in their molecules. Molecules (monomers) of surfactant form aggregates over a narrow range of concentration called the critical micelle concentration (CMC).

Experimental techniques for CMC determination were the subject of certain articles^{2–9} in this *Journal*. However, all those articles do not deal with the CMC determination of nonaqueous surfactant media.

DETERMINATION OF CMC

Conventional Procedure

Attending the elective course of Colloid Chemistry during the second year of Integrated Academic Studies in Belgrade, pharmacy students have already learned to manage CMC determination by a simple procedure called Williams’ method.¹⁰ Since this method is based on determining the crosspoint between premicellar and postmicellar region of the specific conductivity (κ), versus surfactant concentration (c_s) curve (κ/c_s), i.e., solving the linear equations corresponding to those κ/c_s regions, students also learn to use plotting and linear fitting tools of ORIGIN software.

The conventional procedure is common for aqueous surfactant solutions¹¹ because κ/c_s shows small “width” of transition

and an abrupt change in CMC region. Nevertheless, the addition of co-solvents in aqueous surfactant solution, frequently leads to an increase in degree of micelle ionization (α), and consequently to a weak curvature in vicinity of CMC, making the precise determination of CMC difficult.¹¹ Thus, conventional procedure is inappropriate for CMC determination of ionic surfactant in nonaqueous media such as mixed organic solvent systems or in mixed state with the nonionic surfactants.

Advanced Method

Being aware that micellar systems have versatile uses in pharmaceutical and cosmetics products which contain variety of excipients that could influence the CMC, some students were interested in learning an advanced method that overcomes all the difficulties of CMC determination. Accordingly, we formed a group of interested students who applied the procedure described in this paper by using the fitting tool of ORIGIN software.

The mathematical procedure proposed to solve CMC determination difficulties is Carpena’s et al.¹² method, consisting of a nonlinear curve fit of $\kappa-c_s$ raw data. This procedure is based on

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the assumption that the first derivative of specific conductivity, κ with respect to c_s is a Boltzmann type sigmoidal function:

$$\frac{d\kappa}{dc_s} = p_2 + \frac{p_1 - p_2}{1 + e^{(c_s - c_0)/\Delta c}} \quad (1)$$

where p_1 (p_2) is the asymptotic value for small (large) values of surfactant concentration (horizontal asymptote), c_0 (CMC) is center of sigmoidal curve (central point of the transition), and Δc is the width of the transition (fitting parameter, i.e., the time constant, which is directly related to the independent variable range, where the sudden change of κ occurs).

According to Carpena et al. a direct integration of eq 1 yields

$$\kappa = \kappa(0) + p_1 c_s + (p_2 - p_1) \Delta c \ln \left(\frac{1 + e^{(c_s - c_0)/\Delta c}}{1 + e^{-c_0/\Delta c}} \right) \quad (2)$$

where $\kappa(0)$ is the value of specific conductivity when c_s is 0, p_1 and p_2 are the slopes obtained in the premicellar and postmicellar segments; other symbols in eq 2 retain their mentioned meanings. Although some authors^{12,13} suggest that $\kappa(0)$ is the value of specific conductivity when c_s equals 0, we consider that it is the integration constant since the eq 2 is obtained by performing the integration of a Boltzmann type sigmoidal function (eq 1).

MATERIALS AND METHODS

Cetyltrimethylammonium bromide (Merck, Germany) and acetonitrile (Sigma-Aldrich) were used without any pretreatment. Different CTAB concentrations (0.3–3.3 mM) were prepared.

The conductivity measurements were carried out using a digital conductivity meter HI8820N (Hanna instruments, Portugal) with the uncertainties $\pm 0.5 \mu\text{S cm}^{-1}$, and with the matching HI7684W probe that used the 4-ring method. Calibration was done with different concentration of solutions of KCl prior to the experiment.

All measurements were conducted in glass vessel, $V \approx 100$ mL (Metrohm Model 876-20). Circulating water bath (Series U, MLW, Friel, Germany) was used to control temperature within uncertainties of ± 0.2 °C.

For processing all experimental data software package OriginPro 9.0 (OriginLab Corporation, US) was used.

HAZARDS

Solutions should be prepared in a fume hood while using safety goggles and gloves due to eye, skin and respiratory toxicity of CTAB and acetonitrile. Afterward, they should be placed into a glass container labeled as “flammable waste”.

RESULTS AND DISCUSSION

In this study, CMC determination approach recently proposed by Carpena et al.¹² was applied on the example of CTAB in binary mixture ACN–water (10%, v/v) at 30.0 °C. This micellar system was chosen due to its weak curvature around the CMC region of κ/c_s curve (Figure 1). Experimentally obtained data were fitted to the eq 2 by using nonlinear fitting tool of the ORIGIN software.

To help students to overcome this fitting procedure, a scheme of all included steps was prepared (Figure 2). After the OriginPro 9.0 was started and the experimental data was put in (step A1, Figure 2), Williams' method²⁷ was applied to experimental points in order to determine the CMC (step A2, Figure 2).

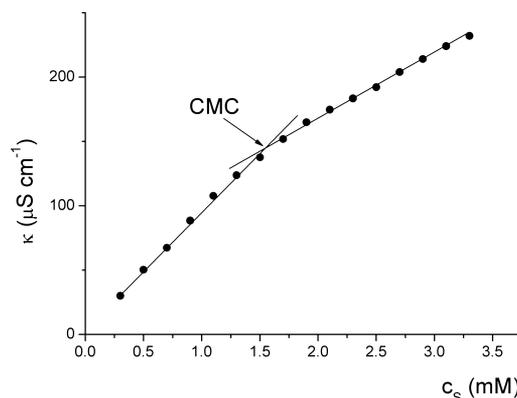


Figure 1. Specific conductivity (κ) versus CTAB concentration (c_s) in a mixture acetonitrile–water (10%, v/v) at 30.0 °C. The arrow denotes the critical micelle concentration (CMC) determination by Williams' method.

In our case, two linear equations were obtained (Figure 1): $\kappa = 4.55 (\pm 2.29) + 91.04 (\pm 2.32) c_s$ ($r^2 = 0.9984$, $p < 0.001$) and $\kappa = 69.01 (\pm 2.05) + 49.78 (\pm 0.80) c_s$ ($r^2 = 0.9991$, $p < 0.001$) for premicellar and postmicellar region, respectively. Solving these equations for c_s , CMC value of $1.56 (\pm 0.23)$ mM was obtained.

The selection of the fitting equation or putting it in (the integrated form of Boltzmann type sigmoid, eq 2), together with setting the number of iterations to maximum value constitute the step A3 (Figure 2). This precedes choosing the initial and boundaries values of fitting parameters (step A4, Figure 2). The values of the parameters previously obtained by the step A2 (Figure 2) were the initial parameters set for all further fitting steps: $p_1 = 91.04$, $p_2 = 49.78$, CMC = 1.56 mM and $\kappa(0) = 4.55$, while boundaries values were set to $\pm 10\%$ of the initial p_1 , p_2 and CMC value, or even more because they do not have influence on the obtained fits values. Nevertheless, this observance could not be applied to both $\kappa(0)$ and Δc boundaries values. Unlike the other parameters, $\kappa(0)$ experienced great relative change by following the fitting procedure within a certain range of Δc , and this is why its boundaries were set in a wide range, from negative to positive values, i.e., from -5 to 5 .

It should be noted that in step A5, Figure 2, Δc value was fixed during fitting so you get a number of fitting sets, each for a different Δc value. We have to examine a number of fits for different Δc values in a wide range in order to find the one that corresponds to such a weak curvature presented in Figure 1. So we took $\Delta c = 0.01$ as the lowest reasonable value to start fitting and continued to examine fits by increasing Δc and its boundaries for a certain increment following the fitting procedure (steps B1 and C1, Figure 2).

After selection of all initial and boundaries values of p_1 , p_2 , CMC, $\kappa(0)$ and Δc (steps A1–A5), students accessed the fitting itself (step A6, Figure 2). As a result, but depending on whether fit converged or not, there were two possibilities to proceed fitting: (1) in the case of convergence, Δc was increased for a smaller increment, for example 0.0025 (step B1, Figure 2) in order to find the CMC with a higher reliability and (2) in the case of divergence, Δc was increased for a higher increment, for example 0.01 (step C1, Figure 2). In both occasions, fitting was performed again (steps B2 and A6, Figure 2) after setting the new Δc value. The convergence was reassessed after each performed fitting session (steps B3 and A7, Figure 2).

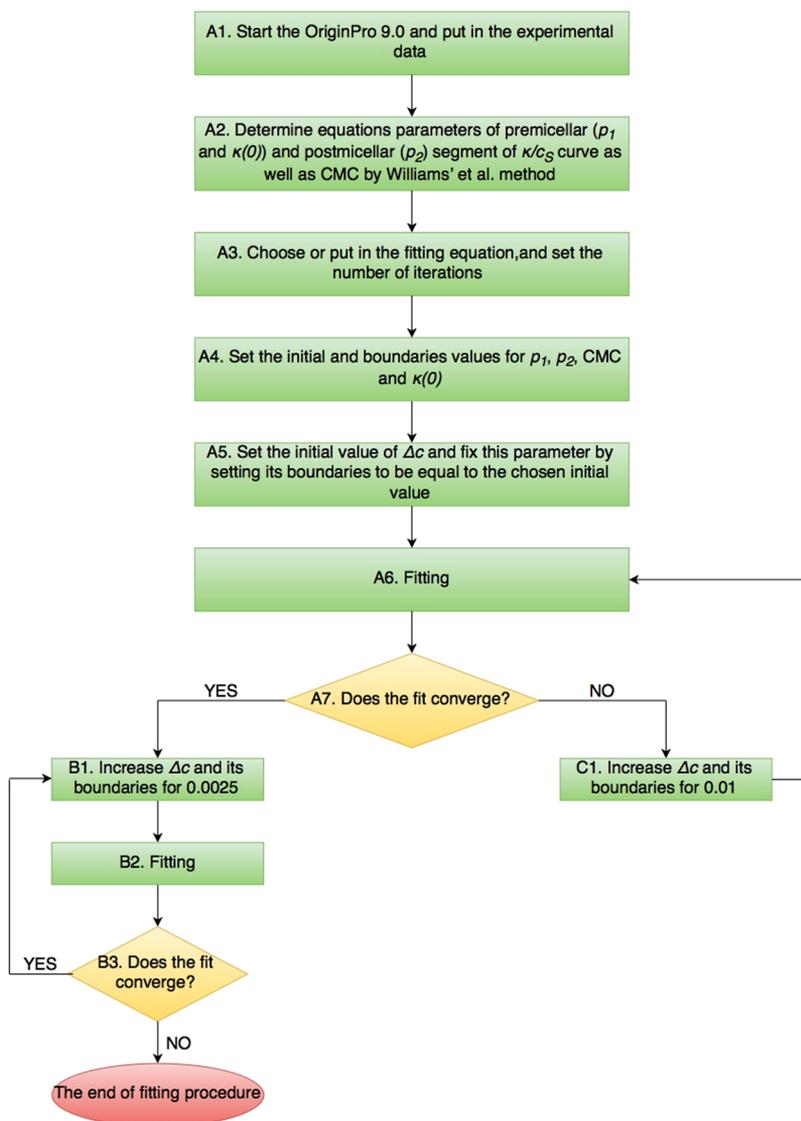


Figure 2. Schematic representation of applied fitting procedure by Carpena's et al. method.

After performing a number of fitting sessions there were two regions of Δc values to notice: the one where fit did not converge despite the maximum value of iterations set (0.01–0.20) and the other where fit did converge (0.21–0.32). Initial values of Δc were increased until the point of disconvergence was reached again (for $\Delta c = 0.3225$).

After performing all of the above examinations, students asked the question: "Which fit is chosen and declared as a "true" one?"

For this purpose, students were introduced to OriginPro 9.0 output report containing parameters for statistical analysis: coefficient of determination (r^2), reduced chi-square (red. χ^2), and standard deviation of the obtained CMC (SD_{CMC}). Since $r^2 > 0.999$, whether fit converged or not, it was not considered as a crucial parameter when deciding which fit to choose. On the other hand, particular significance was given to the red. χ^2 , as previously described by some authors,¹⁵ since it reflects the convergence of both input and output data (eq 3).

$$\text{red. } \chi^2 = \frac{\sum_{i=1}^N [\kappa_i - \text{approx. } \kappa_i]^2}{N} \quad (3)$$

where N is the number of experimental points, κ_i and $\text{approx. } \kappa_i$ are the experimental and approximate conductivity at a given total surfactant concentration, respectively.

With the aim to precisely determine the CMC value students analyzed dependence of red. χ^2 on Δc (Figure 3a) for Δc in the interval for which fit converged (0.21–0.32). There were three regions to notice in the plot red. $\chi^2/\Delta c$ (Figure 3a): the first where red. χ^2 slightly decreased with the increase of Δc ($0.2100 \leq \Delta c \leq 0.2175$, region I, Figure 3a), the second where red. χ^2 values were constant ($0.2200 \leq \Delta c \leq 0.2375$, region II, Figure 3a) as well as the third where those values further increased ($\Delta c > 0.2375$, region III, Figure 3a).

Since the best convergence between input and output data was shown for Δc values from range 0.2200–0.2375 (region II, Figure 3a), students further analyzed dependence of obtained standard deviation of CMC (SD_{CMC}) on Δc (Figure 3b) for this region. Obviously, values of SD_{CMC} were more than acceptable (<5% of the value of CMC obtained for a certain fit). Moreover, for $\Delta c > 0.2375$, values of SD_{CMC} increased (Figure 3b).

Accordingly, this region was set for determination of the relative standard deviation of both, the CMC (RSD_{CMC}) and α (RSD_α), since this micellar quantity was crucially dependent on

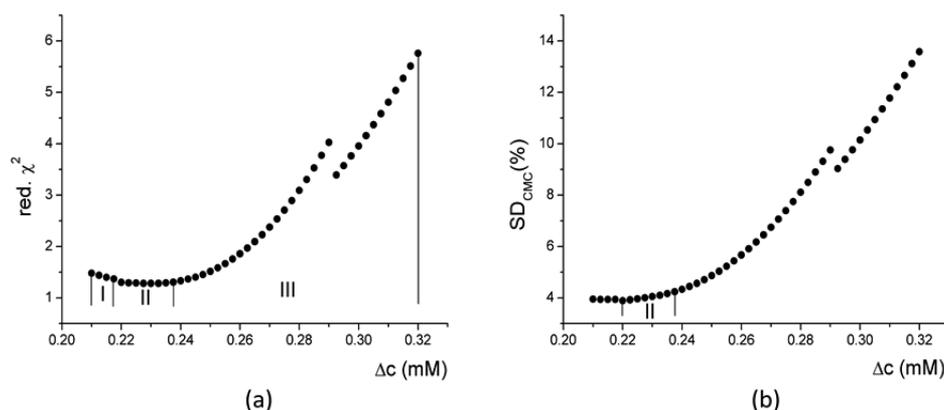


Figure 3. Dependence of (a) the reduced chi-square ($\text{red. } \chi^2$) coefficient and (b) the standard deviation of CMC (SD_{CMC}) on the initial values of the width of transition (Δc). I, II and III denote regions in which values of $\text{red. } \chi^2$ change in different manner.

Table 1. Distribution of Some Fitting Results Obtained within a Certain Width of Transition Range

Δc , mM ^a	CMC, mM ^b	α (p_2/p_1) ^c	$\text{red. } \chi^2$ ^d	SD_{CMC} , % ^e
0.2200	1.450	0.493	1.301	3.89
0.2225	1.449	0.492	1.293	3.92
0.2250	1.449	0.492	1.288	3.96
0.2275	1.448	0.492	1.284	4.00
0.2300	1.448	0.491	1.282	4.05
0.2325	1.448	0.491	1.283	4.10
0.2350	1.448	0.491	1.290	4.16
0.2375	1.449	0.492	1.307	4.24

^aWidth of transition, Δc . ^bCMC, critical micelle concentration; the relative standard deviation of the CMC (RSD_{CMC}) = 0.05%. ^cDegree of micelle ionization, α ; the relative standard deviation of α (RSD_α) = 0.14%. ^dReduced chi-square. ^eStandard deviation of CMC determination.

Δc also. Obtained RSD_{CMC} and RSD_α are 0.05% and 0.14%, respectively (Table 1), so any of both CMC and α (p_2/p_1) value obtained when Δc in the range 0.2200–0.2375 can be chosen.

APPLICATION TO CLASSROOM

The discussed laboratory experiment was performed by a test group of students attending the second year of Integrated Academic Studies of Pharmacy in Belgrade as trial experimental exercise for elective course of Colloid Chemistry. The students' activities were performed in two practical classes: (1) the first, experimental, involving the collection of data obtained by conductometric measurements of examined micellar system and (2) the second, computational, involving mathematical analysis of the obtained raw data using computer software OriginPro 9.0.

At the first class, after instructor made a 30 min introduction to background information on micellar systems, conductivity and Kohlrausch's law, a group of 16 students was divided into four smaller groups, each consisting of four students. Each group worked with four solutions and had 30 min per a solution to complete its preparation and conductivity measurement (detailed procedure given in the Supporting Information material).

At the second class, instructor introduced students to advanced method of CMC determination and its use by the fitting tools of OriginPro 9.0. Students were expected to perform Williams' method on their own, while fitting by Carpena's et al. method was realized with help of instructor, complying with

Box 1. Fitting Issues Regarding Carpena's Model

1. Carpena's fitting equation (eq 2) consists of five fitting parameters. Accordingly, why four parameter fitting was used?

It is recommended to use four parameter fitting since the width of transition (Δc) is the only parameter whose value cannot be predicted by any other simpler method.

2. Why fix the width of transition (Δc) value?

If Δc value was not fixed, OriginPro would give only one data fitting set after fitting session, i.e., one CMC value as a result which decreases reliability of method. The idea is to find more data fitting sets, i.e., more CMC values and choose a very narrow range where CMC can be found with appropriate reliability.

3. Which Δc start value is recommended when operating with ionic surfactant in aqueous media micellar systems?

Since those systems have a sharp width of transition, recommended to use is Δc value lower than suggested in this paper, e.g., Δc start 0.0025.

4. Is $\text{red. } \chi^2$ value really the best way to determine "the best data fitting set"?

It is the fact that this statistical parameter has its uncertainties regarding degrees of freedom for nonlinear models and can be affected by sample size, but in case of proposed way of Carpena's fitting, it was shown that, unlike coefficient of determination (r^2) which did not change through fitting procedure, $\text{red. } \chi^2$ was also affected by Δc value and showed the best convergence of data for a certain range of Δc values.

the scheme given in Figure 2 and referring to Box 1. Students worked in pairs, each examining the convergence for eight values of Δc (the first pair worked in Δc range 0.01–0.08, the second one in range 0.09–0.16, etc.) and this activity took 15 min. This term consisted of 3 periods (30 min per period): introductory lecture, fitting procedure and analyzing obtained data in order to precisely determine the CMC followed by Williams' and Carpena's methods comparison presented in Box 2.

PEDAGOGY

Students showed a very good understanding of importance of the precise CMC determination since they had been familiar with micellar systems and their practical usage in pharmacy during the Colloid Chemistry course. Thus, this experiment

Box 2. Uncertainties Regarding Williams' and Carpena's et al. Method

Williams' method		Carpena's et al. method
$p_1 = 91.04 \pm 2.32$ SD(%) = 2.55%	$< 5\%$	$p_1 = 98.46 \pm 3.51$ SD(%) = 3.56%
$p_2 = 49.78 \pm 0.80$ SD(%) = 1.61%	$< 5\%$	$p_2 = 48.38 \pm 1.33$ SD(%) = 2.74%
CMC = 1.56 ± 0.23 SD(%) = 14.74%	$< 5\%$	CMC = 1.448 ± 0.059 SD(%) = 4.05%
$*b_1 = 4.55 \pm 2.29$ SD(%) = 50.33% *premicellar region y-intercept value		$\kappa(0) = 0.55 \pm 1.80$ SD(%) = 330.51%

Although Carpena's et al. method shows higher reliability in CMC determination, both Carpena's et al. and Williams' method show great uncertainty regarding y value when $c_s = 0$. This fitting parameter corresponds to integration constant in Carpena's et al. method and to premicellar region y -intercept value in Williams' method. Namely, since Carpena's model is obtained by mathematical operation of integrating, its inherent part is an integration constant ($\kappa(0)$) that represents just an arbitrary constant whose value depends on premicellar region slope value (p_1), at first place, but also on other model's coefficients values. As regarding to Williams' method, the premicellar region y -intercept value depends on number of points chosen for linear fitting in premicellar region. Also, this parameter's values show great relative changes comparing to other fitting parameters values and all of the above constitutes source of such a great uncertainties for both models.

helped them to improve their knowledge by learning how to choose the right method for CMC determination according to a certain micellar system. For this purpose, some formulations of cosmetics and pharmaceutical products available at Serbian market were represented to students and they were asked to suggest the method of CMC determination for each of them. These questions highly motivated students for further scientific investigation through learning to perform an advanced method for CMC determination by using computer software which makes this task faster and easier to perform.

When asked to bring their impressions, students told that although at first sight Carpena's fitting function had seemed hard to overcome, they revealed that it had been easy to use and understand when having an appropriate computer software allowing the usage of nonlinear fitting tool.

CONCLUSION

Designing these integrated colloidal chemistry–computational trial lab experiments, we wanted to assess the benefits of acquainting students to the concepts of electrochemical experimental techniques and manipulation with conductivity-concentration raw data using computer software. After this exercise, students were able to compare, contrast and apply both conventional and integration method in order to precisely determine CMC of the examined micellar system. Thus, we got strong evidence in favor of introducing the

discussed experiment into the Colloid Chemistry curriculum for the next year.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available on the ACS Publications website at DOI: 10.1021/acs.jchemed.5b00913.

Instructor notes; instructions for students; tasks to work out (PDF, DOCX)

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Notes

The authors declare no competing financial interest.

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