Modeling of Some Calorimetric and Spectropolarimetric Titration Data

Jurij Lah* and Gorazd Vesnaver

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, 1000 Ljubljana, Slovenia

Microcalorimetric and spectropolarimetric titrations were used to investigate micellization of cationic surfactants and binding of netropsin to dodecameric DNA duplex. For description of both processes, model functions containing linear and non-linear parameters were derived. Model analysis was based on a weighted (multi)linear regression and a standard »Simplex« procedure. Close investigation of the interplay of adjustable parameters has shown that a proper choice of the model function can significantly reduce the correlations between parameters. Values of physical properties (enthalpy changes, apparent equilibrium constants...) obtained from such curve modeling are in very good agreement with the corresponding values obtained by other methods. Equations and the calculation procedure reported here could be easily generalized and used for the description of some other concentration dependent properties in similar systems.

Key words: calorimetry, CD-spectropolarimetry, thermodynamics, micellization, surfactant, binding, drug, DNA.

INTRODUCTION

Thermodynamic characterization of any process that takes place in a solution is very important for understanding the properties of each solution constituent. One of the aims of thermodynamic studies is to obtain precise values of equilibrium constants and changes of thermodynamic quantities (enthalpies, entropies).[1,2] There are fundamentally different approaches to obtaining these data, hard modeling and soft modeling. According to the

* Author to whom correspondence should be addressed. (E-mail: jurij.lah@uni-lj.si)

hard modeling approach, also used in this work, a given process is described thermodynamically in terms of an appropriate physical model. The corresponding model function usually contains two or more correlated parameters. It is known that the more parameters such a model function contains the better the agreement with experimental data is achieved. Often, the qualitative information about the correlations between parameters,[3] which is crucial for such treatment of data, is left out of reports. Therefore, our results (thermodynamic parameters) are presented also with the corresponding correlation matrixes.[4] The aim of this work is in no way to present a well-known hard modeling approach, but to show possible new applications of this kind of analysis to describe thermodynamically two entirely different solution systems.

Surfactant aggregates (micelles) and drug-DNA complexes are often studied systems in the field of physical chemistry and biochemistry.[5–8] In this study, a high sensitivity titration calorimetry[9] was employed to observe micellization of undecylpyridinium bromide ($C_{11}PyBr$) in aqueous solution. The model function for this process was derived from the expression for the surfactant partial molar enthalpy, $\bar{H}_2$, based on the mass-action model. Since this is the first such description of calorimetric titration of a ionic surfactant solution in water, the behavior of all six model parameters was precisely investigated. Three of them can be derived directly from experimental data and the other three can be obtained by a regression procedure. Such data treatment gives values of the critical micellization concentration, c.m.c., the enthalpy of micellization, ΔH_{ab}, and the aggregation number, a, which are in excellent agreement with the corresponding values obtained by other methods.[10–12]

CD-spectropolarimetry[2] was applied to study the binding of antibiotic netropsin (Net) to the dodecameric DNA duplex d(GTTAGTATATGG)·d(CCATATACTAAC). Differential CD-titration curves measured at two different wavelengths were modeled using the Beer-Lambert and mass-action law. The model function, which describes the binding of two Net molecules to two independent binding sites on the DNA duplex molecule, contains four adjustable parameters. The characteristic apparent binding constants K'_{11} and K''_{11} obtained by curve fitting are in very good agreement with the corresponding K'_{11} and K''_{11} values obtained from UV-melting experiments.[13]

EXPERIMENTAL

Materials

Undecylpyridinium bromide ($C_{11}PyBr$) was synthesized from the corresponding 1-bromoalkanes and pyridine,[14] and purified by repeated recrystallization from acetone.

DNA duplex d(GTTAGTATATGG)·d(CCATATACTAAC) was prepared from the corresponding single strands that were synthesized using the standard cyanoethyl-phosphoramide chemistry.[15] The molar (decadic) absorption coefficients of the single-stranded oligomers were determined by phosphate analysis.[16] Dodecameric DNA duplex was obtained by mixing the appropriate single strands in 1:1 molar ratio. Its molar (decadic) absorption coefficient (ε_{260}(duplex) = 165×10^3 cm^2 mmol^{-1}) was determined in buffer solution (10 mmol dm^{-3} Na-Cacodylate, 100 mmol dm^{-3} NaCl and 1 mmol dm^{-3} Na$_2$EDTA; pH = 6.9) at 260 nm and 25 °C.[17] This buffer solution was also used in our Net to DNA binding experiment.

Netropsin-HCl (Net) from Boehringer Mannheim GmbH was used without further purification. Its concentration in solution was determined spectrophotometrically at 25 °C using the molar (decadic) absorption coefficient: $\varepsilon_{296} = 21.5 \times 10^3$ cm^2 mmol^{-1}.

Titration Microcalorimetry

The heat effects resulting from mixing aliquots of titrant solution from the syringe with the solution (solvent) in the titration cell were measured using a multi-channel heat-leakage TAM 2277 calorimeter from Thermometric AB, Sweden (Figure 1A). A volume of 2 cm^3 of triple-distilled water was titrated at 25 °C by a surfactant solution placed in a 0.250 cm^3 syringe. Surfactant concentration in the syringe was about 20-times higher than its c.m.c. The reference cell of the microcalorimeter was filled with distilled water and the instrument was calibrated by means of a known electrical pulse.

Circular Dichroism (CD)-spectropolarimetry

CD spectra were measured in an AVIV Model 62A DS spectropolarimeter (Aviv Associates, Lakewood, N.J.) equipped with a thermoelectrically controlled cell holder and a cuvette of 1 cm path length. CD-titration was conducted at 20 °C by incrementally injecting $(2.5–20) \times 10^{-3}$ cm^3 aliquots of Net solution into a 2 cm^3 of 5 µmol dm^{-3} DNA duplex solution in the same buffer. After each injection, the CD spectrum was recorded between 220 and 400 nm and normalized to 1 mol dm^{-3} single strand concentration.

MODELING

Mass-action Model

Every step in multiple equilibria of interacting species A and B can be described according to the mass-action approach by the following formulas:

$$a\text{A} + b\text{B} \rightleftharpoons \text{A}_a\text{B}_b; \qquad K_{ab} = \frac{[\text{A}_a\text{B}_b]}{[\text{A}]^a[\text{B}]^b} \ , \qquad (1)$$
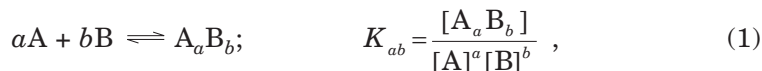
where K_{ab} represents the apparent equilibrium binding constant of formation of complex A_aB_b from a molecules of species A and b molecules of species B while quantities in the square brackets are the equilibrium concen-

trations of components participating in the equilibrium presented in Eq. (1). To connect this model with the experimental data, a measured physical property, F, was expressed as a sum of concentration dependent contributions, f, of individual components involved in the equilibrium process described by Eq. (1):

$$F = f_A + f_B + \sum_{a,b} f_{AB} \ .$$

(2)

Calorimetric Titration Curve

In a titration calorimetry experiment the measured property is the heat effect, q_i, that results from each injection of titrant solution into the titration cell. This heat effect, which depends on the total amount of the solute in the titration cell, n_2, is usually given as the enthalpy change, $\Delta H(n_2)$, expressed per mol of added titrant

$$F = \frac{q_i}{\Delta n_2} = \Delta H(n_2) = \frac{(H_i - H_{i-1})}{\Delta n_2} - \frac{H_a}{\Delta n_2} \ ,$$

(3)

where H_i and H_{i-1} represent enthalpies of solution in the measuring cell after i-th and (i-1)-th injection, respectively, while H_a represents the enthalpy of the added aliquot of titrant solution and Δn_2 is the amount of solute added per injection. As Δn_2, is very small, Eq. (3) simplifies into:

$$\Delta H(n_2) = \left(\frac{\partial H_i}{\partial n_2} \right)_{n_1,P,T} + \text{const.} = \overline{H}_2 + \text{const.} \ ,$$

(4)

where $\overline{H}_2$ is the solute partial molar enthalpy in the solution in the titration cell.

Eq. (4) can be used as a basis for the thermodynamic analysis of micellization process assuming that it occurs in a two-state manner. Using this assumption, the micellization of a 1:1 cationic surfactant occurring in an aqueous salt free solution can be described in terms of the mass-action approach (Eq. 1) where A represents the monovalent surfactant ions in the monomeric form, B the corresponding monovalent counterions and A_aB_b the micellar aggregate of surfactant monomers with an effective charge of (a-b). It has been shown that the partial molar enthalpy of surfactant in a salt free aqueous solution can be expressed as[11]

$$\overline{H}_2 = \overline{H}_A + \overline{H}_B + \Delta H_{ab} \left(\frac{\partial n_{ab}}{\partial n_2} \right)_{n_1,P,T} \ ,$$

(5)

where $\overline{H}_A$ and $\overline{H}_B$ are the partial molar enthalpies of free surfactant ions and the corresponding counterions, respectively, n_{ab} is the amount of surfactant ions in the micellar form, n_2 is the total amount of surfactant ions ($n_2 = n_A + n_{AB}$) and ΔH_{ab} is the enthalpy of micellization defined as

$$\Delta H_{ab} = \overline{H}_{ab} - \overline{H}_A - (b/a)\overline{H}_B, \tag{6}$$

where $\overline{H}_{ab}$ represents the partial molar enthalpy of surfactant ions in the micellar form. By combining Eqs. (4) and (5), an expression for the measured quantity, $\Delta H(n_2)$ is obtained, which includes the enthalpy of micellization, ΔH_{ab}, and may be considered as an example of Eq. (2)

$$\Delta H(n_2) = (\overline{H}_A + \overline{H}_B + \text{const.}) + \Delta H_{ab}\left(\frac{\partial n_{ab}}{\partial n_2}\right)_{n_1,P,T}. \tag{7}$$

Thus, by fitting the model calorimetric titration curve (Eq. 7) to the experimental one, the determination of the ΔH_{ab} values becomes possible. Since the experimental titration process includes titration of surfactant solution at concentrations below and above c.m.c., the model titration curve must be able to cover different surfactant behavior in these two regions. Below c.m.c. where $(\partial n_{ab} / \partial n_2)_{n_1,P,T} = 0$, the $(\overline{H}_A + \overline{H}_B)$ contribution can be derived from the expression for the surfactant chemical potential. Using the Gibbs-Helmholtz relation and Guggenheim approximation for the surfactant mean activity coefficient,[18] one obtains that

$$\overline{H}_A + \overline{H}_B = \overline{H}_2^o + 2RT^2\left(\frac{A'\sqrt{[A]_T}}{1+\sqrt{[A]_T}} + B'[A]_T\right), \tag{8}$$

where $[A_T]$ is the total surfactant concentration, A' and B' are the temperature derivatives of parameters A and B in Guggenheim's expression for the surfactant's mean activity coefficient and $\overline{H}_2^o$ is the partial molar enthalpy of surfactant in its standard state. Above c.m.c., it is assumed that, due to small changes in concentrations of A and B ions, the $(\overline{H}_A + \overline{H}_B)$ contribution remains constant and equal to its value at c.m.c. The derivative, $(\partial n_{ab} / \partial n_2)_{n_1,P,T}$, expressed in terms of the total surfactant concentration $[A]_T$ and the corresponding micellar concentration $[A_aB_b]$ can be obtained for given parameters a and b from the apparent equilibrium constant K_{ab} (Eq. 1)

$$\left(\frac{\partial n_{ab}}{\partial n_2}\right)_{n_1,P,T} = \frac{a[u+g]}{1+a[u+(b/a)g]}, \tag{9}$$

where

$$u = \frac{\alpha}{1-\alpha}, \quad g = \frac{(b/a)\alpha}{1-(b/a)\alpha}, \quad \alpha = \frac{n_{ab}}{n_2} = \frac{a[A_a B_b]}{[A]_T} \quad .$$

CD-titration Curve

Physical property, F, used for modeling the Net binding to DNA (Eq. 2) was defined as the differential molar ellipticity at a given wavelength, $\Delta[\Theta]_\lambda$,

$$F = \Delta[\Theta]_\lambda = [\Theta]_\lambda - [\Theta]_{\lambda, DNA} \;, \tag{10}$$

where $[\Theta]_\lambda$ is the measured molar ellipticity at any titration point and $[\Theta]_{\lambda, DNA}$ is the corresponding molar ellipticity of the pure DNA (the first titration point). It was assumed that the DNA duplex (A) molecule has two independent sites available for Net (B) molecules, each with its characteristic binding constant ($K_{11}^{'}$ and $K_{11}^{''}$) and that for any formed Net-DNA complex ($(AB)^{'}$, $(AB)^{''}$, (AB_2)) the molar ellipticity is an ideal concentration property (Beer-Lambert law is obeyed). Taking into account that Net itself is not CD-active, one obtains:

$$\Delta[\Theta]_\lambda = \frac{1}{[A]_T}\left[\Delta[\Theta_{11}^{'}]_\lambda [AB]^{'} + \Delta[\Theta_{11}^{''}]_\lambda [AB]^{''} + \Delta[\Theta_{12}]_\lambda [AB_2] \right] \;, \tag{11}$$

where $[AB]^{'}$ is the concentration of 1:1 Net-DNA complex with Net bound to the first binding site, $[AB]^{''}$ is the concentration of 1:1 Net-DNA complex with Net bound to the second binding site and $[AB_2]$ is the concentration of 2:1 Net-DNA complex. $\Delta[\Theta_{11}^{'}]_\lambda$, $\Delta[\Theta_{11}^{''}]_\lambda$, and $\Delta[\Theta_{12}]_\lambda$, represent the corresponding differential molar ellipticities and $[A]_T$ is the total DNA duplex concentration.

Calculation Procedure

For a complete description of the above mentioned titration curves one must, in addition to linear parameters, visible directly from the model functions, calculate concentrations of all solution components that contribute to the measured signal. For these calculations, stochiometric factors (a, b) and equilibrium binding constants (K_{ab}) must be known. Then, for known total concentrations of A, $[A]_T$, and B, $[B]_T$, the system of two non-linear equations

$$[A]_T = [A] + a\sum_b [A_aB_b] \quad \text{and} \quad [B]_T = [B] + \sum_b b\,[A_aB_b] \tag{12}$$

can be solved iteratively (a or $b > 1$). Evidently, a, b and K_{ab} enter the model functions as non-linear parameters. For this reason, they can be obtained from the non-linear fitting procedure based on the minimization of the χ^2-function defined as:

$$\chi^2 = \sum_i \left(\frac{F_i^{\text{exp}} - F_i^{\text{mod}}}{\Delta F_i^{\text{exp}}} \right), \tag{13}$$

in which F_i^{mod} is the value of the model function at point i, F_i^{exp} is the value of the experimentally measured property at point i and ΔF_i^{exp} is the corresponding error in F_i^{exp}. By choosing values of non-linear parameters and solving systems of equations (Eq. 12) one can obtain linear parameters using weighted (multi)linear regression.[19] Applying the »Simplex« method[19] (with linear procedure as a subroutine) for the minimization of χ^2, one can finally improve initial guesses of nonlinear parameters to obtain their best values. The mean-square deviations (errors) of the parameters are calculated as square roots of the diagonal elements, c_{kl}, of the covariance matrix, $\boldsymbol{C}$, which was obtained by inversion of the curvature matrix, $\boldsymbol{\alpha}$. The elements of $\boldsymbol{\alpha}$, α_{kl}, are given by simplified relation:[19]

$$\alpha_{kl} = \frac{\partial^2 \chi^2}{\partial A_k \partial A_l} \cong \sum_i \frac{1}{(\Delta F_i^{\text{exp}})^2} \left(\frac{\partial F_i^{\text{mod}}}{\partial A_k} \frac{\partial F_i^{\text{exp}}}{\partial A_l} \right), \tag{14}$$

where A_k and A_l are the fitting parameters. The qualitative information about the correlation between A_k and A_l is obtained as the element of correlation matrix, q_{kl}, defined as:

$$q_{kl} = \frac{c_{kl}}{\sqrt{c_{kk}c_{ll}}} . \tag{15}$$

RESULTS AND DISCUSSION

Calorimetric Titration of $C_{11}PyBr$

If the individual heat bursts $\Delta H(n_2)$ (Eq. 3), accompanying each injection of the highly concentrated titrant solution into the titration cell, are plotted against the total surfactant concentration, $[A]_T$, in the titration cell, a typical sigmoidal curve with an inflection point at the surfactant's c.m.c., emerges (Figure 1B). Below c.m.c. this curve describes the concentration dependence of the heat effects caused predominantly by the demicellization of micelles

injected into solution while above c.m.c. it mainly reflects the dilution of micelles added at each injection. Following the Philips criterion,[5] critical micellization concentration, c.m.c., was obtained as the concentration at which $(\partial^2 \Delta H(n_2) / \partial [A]_T^2)_{c.m.c.} = 0$.

The apparent equilibrium constant of micellization, K_{ab}, was calculated according to the Philips criterion[5] from the c.m.c. value obtained directly from the experiment and from the values for the aggregation number, a, and the degree of the micelle ionization, $(1 - b/a)$, obtained by the iteration fitting procedure. This procedure, which involves five adjustable parameters $(\overline{H}_2^\circ + \text{const.}, B', \Delta H_{ab}, a, b/a)$, turns out to be highly problematic because the errors in these parameters may be too high and for some of them almost total reciprocal correlation $(q_{kl} \approx 1)$ has been observed. To avoid this problem, the number of adjustable parameters was reduced to two $(\Delta H_{ab}, a)$ while the parameters $(\overline{H}_2^\circ + \text{const.})$ and B' were obtained from the experimental titra-
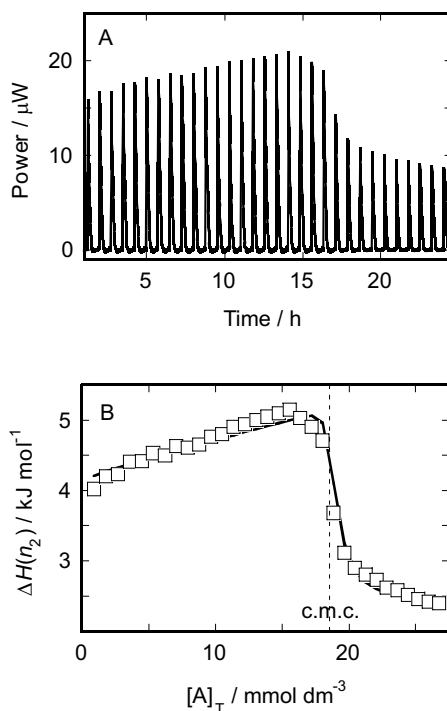

Figure 1. Typical calorimetric titration of the surfactant in water. 2 cm^3 of water was titrated with an aqueous solution of C$_{11}$PyBr (0.361 mol dm^{-3}) at 25 °C. Each peak corresponds to 5×10^{-3} cm^3 injection of the titrant solution (panel A); the corresponding experimental (□) and model (—) ($a = 37$, $b/a = 0.8$, $\Delta H_{ab} = -2.54$ kJ mol^{-1}) titration curves (panel B).

tion curve below c.m.c. and the degree of the micelle ionization $(1 - b/a)$ was taken from the literature.[12] The reason why the b/a value could not be determined from the described fitting procedure is that the shape of the model titration curve practically does not depend on the b/a value while it depends strongly on the a value alone (for $a \leq \approx 50$).[20] With the described method, the errors of the parameters of our interest (ΔH_{ab}, a) were 10–100 times reduced and the value of q_{kl} was lowered from 1 to 0.7. In performing the fitting procedure, a relative error of 5% was taken for each experimental titration point. Values of ΔH_{ab} (−2.54 ± 0.06 kJ mol⁻¹) and a (37 ± 7) are in very good agreement with the literature ones.[10–12] Furthermore, the ΔH_{ab} value is in good agreement with the corresponding ΔH_{ab} value obtained from the same data by the graphic extrapolation method.[20]

CD-spectropolarimetric Titration of DNA Duplex with Net

Binding of Net to the DNA duplex was characterized by measuring the induced CD spectra in the wavelength range between 220 nm and 400 nm (Figure 2A). The induced CD signal reflects the Net-duplex interactions within the Net-DNA complex and can therefore be used to monitor the Net-DNA binding events. To quantify the CD signal that results only from the bound drug, the DNA contribution (Figure 2A) was subtracted from the experimental CD data. Then, the differential CD-titration curves were produced as profiles of the thus obtained difference CD spectra at two different wavelengths, 275 nm and 309 nm (Figures 2B and 2C). Raw CD spectra of Net-DNA complexes (Figure 2A) show that only one or two molecules of Net ($b = 1$ or 2) are bound per one molecule of DNA duplex ($a = 1$). It is interesting that two distinctive binding modes of Net can be clearly seen only from the CD titration curve obtained at 275 nm and not from the corresponding titration curve obtained at 309 nm. To observe some possible differences in the thermodynamic parameters accompanying the binding of Net to DNA, both curves were analyzed by the presented model.

It is easy to show that by substituting $[AB]'$ and $[AB]''$ with $K_{11}'[A][B]$ and $K_{11}''[A][B]$, respectively, the number of parameters can be reduced by one. The experimental data was fitted with the model function, including two linear parameters, A_1 and A_2 (e. g. $A_1 = (\Delta[\Theta_{11}']_\lambda K_{11}' + \Delta[\Theta_{11}'']_\lambda K_{11}'')/[A]_T$, $A_2 = \Delta[\Theta_{12}]_\lambda K_{11}' K_{11}''/[A]_T$), and two non-linear ones, K_{11}' and K_{11}''. Reasonable values of K_{11}' and K_{11}'' were determined from the differential CD-titration curve at 275 nm. For the CD-titration curve measured at 309 nm, we obtained similar values of K_{11}' and K_{11}'', only with higher errors. The main problem here was not the error itself, but large correlations ($q_{kl} \approx 1$) between the parameters $A_1 - K_{11}'$, $A_2 - K_{11}''$ and $A_1 - A_2$. For this reason, parameter A_1 in the model function was changed. Since K_{11}' ($\approx 10^9$ mol⁻¹ dm³) is about
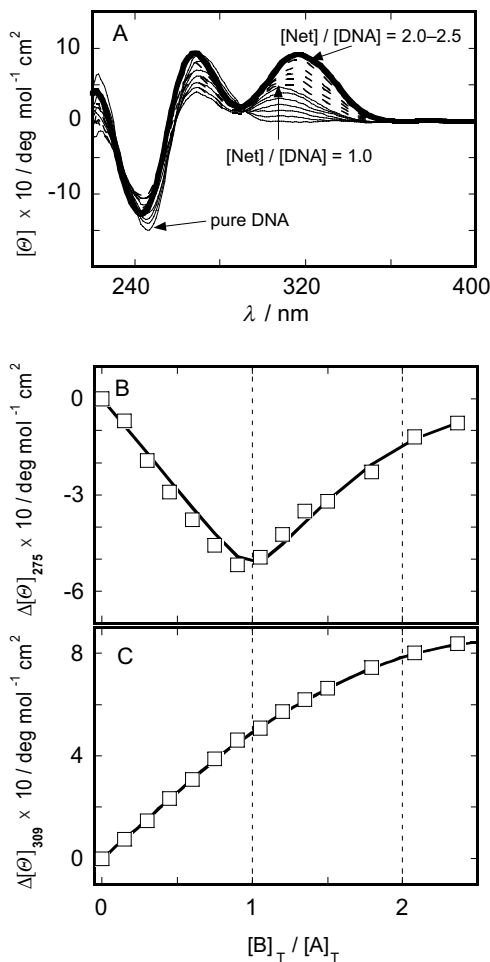
Figure 2. Induced CD spectra of the Net-DNA (B-A) complexes at a ligand/duplex ratio varying between 0 and 1 (—) and between 1 and 2.5 (– –) at 20 °C (panel A); the corresponding experimental (□) and model (—) differential CD titration curves measured at 275 nm (panel B) and at 309 nm (panel C).

two orders of magnitude higher than $K_{11}^{''}$ (10^6–10^7 mol^{-1} dm^3), the second term in A_1 can be neglected and A_1 becomes: $A_1 = \Delta[\Theta_{11}^{'}]_\lambda K_{11}^{'} / [A]_T$. With this new form of the model function, we obtained similar values of binding constants as with the unsimplified model function; however, the correlations (except between A_2 and $K_{11}^{''}$) were much lower.

This result clearly indicates that the second model function is more appropriate for obtaining »safer« values of the linear parameters A_1 and A_2 and the non-linear parameter $K_{11}^{'}$ whereas the first model function gives a

TABLE I

Linear parameters A_1 and A_2 and binding constants $K_{11}^{'}$ and $K_{11}^{''}$ for Net binding to DNA obtained by fitting the model function (Eq. 11) to the experimental differential CD-titration curves measured at two different wavelengths

	Value	Full correlation matrix			
		A_1	A_2	$K_{11}^{'}$	$K_{11}^{''}$
$\lambda = 275$ nm					
$A_1 / 10^8$ deg cm^{-1}	-1.14 ± 0.01	1.00	0.21	0.64	-0.28
$A_2 / 10^8$ deg cm^{-1}	0.11 ± 0.02	0.21	1.00	-0.22	-0.98
$K_{11}^{'} / 10^9$ mol^{-1} dm^3	0.6 ± 0.1	0.64	-0.22	1.00	0.18
$K_{11}^{''} / 10^6$ mol^{-1} dm^3	1.3 ± 0.2	-0.28	-0.98	0.18	1.00
$\lambda = 309$ nm					
$A_1 / 10^8$ deg cm^{-1}	1.02 ± 0.01	1.00	-0.09	-0.49	0.06
$A_2 / 10^8$ deg cm^{-1}	1.69 ± 0.05	-0.09	1.00	-0.66	-0.98
$K_{11}^{'} / 10^9$ mol^{-1} dm^3	2.1 ± 3.7	-0.49	-0.66	1.00	0.68
$K_{11}^{''} / 10^6$ mol^{-1} dm^3	6.7 ± 6.8	0.06	-0.98	0.68	1.00

The relative error of each experimental value, $\Delta(\Delta[\Theta]_\lambda)/\Delta[\Theta]_\lambda$, was estimated to be $\pm$ 1%.

more independent $K_{11}^{''}$ value. We also fitted parts of the CD-titration curves below and above [Net]/[DNA] ratio of 1 separately, but this procedure did not cause any further reduction of errors in the parameters nor a decrease in their correlations. The values of $K_{11}^{'}$ and $K_{11}^{''}$ obtained by such treatment of the CD data are in good agreement with the corresponding $K_{11}^{'}$ and $K_{11}^{''}$ values (9.0×10^8 mol^{-1} dm^3 and 1.8×10^6 mol^{-1} dm^3) obtained from our UV-melting experiments.[21]

CONCLUSIONS

Titration microcalorimetry and CD-spectropolarimetry are techniques that are often used in different fields of research. The application of these techniques was illustrated for two different processes: micellization of surfactant ions and drug binding to DNA. It was shown that by applying the hard modeling approach based on the mass-action law for both processes, the titration curves obtained by these two methods were successfully analyzed. Originally, the model functions contain more than four highly correlating parameters. In the case of the titration calorimetric study of the

micellization of $C_{11}PyBr$, where a description of the measured heat effect based on the $\bar{H}_2$ was employed, the errors and correlations between parameters were reduced by minimization of the number of adjustable parameters. On the other hand, analysis of the CD-titration data of Net-DNA complexes demonstrates that more reliable values of binding constants are obtained when a combined analysis of the different data sets (profiles at 275 nm and at 309 nm) in various model functions is performed. Values of thermodynamic parameters obtained by the described procedures are in very good agreement with the corresponding values obtained by other methods. By applying the »Simplex« method with the linear procedure as a subroutine, only the initial values of non-linear parameters have to be set. For this reason, when studying micellization or binding phenomena by the traditional hard modeling approach, the described calculation procedure may be more appropriate than the classical »Simplex« or Levenberg-Marquardt method.[19]

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SAŽETAK

Modeliranje nekih podataka kalorimetrijskih i spektropolarimetrijskih titracija

Jurij Lah i Gorazd Vesnaver

Micelizacija kationskih površinski aktivnih tvari i vezanje netropsina na dodekamernu dvostruku uzvojnicu DNA istraživani su primjenom mikrokalorimetrijskih, odnosno spektropolarimetrijskih titracija. Za opis oba procesa izvedene su modelne funkcije koje uključuju linearne i nelinearne parametre. Modelna analiza temeljila se na vaganoj (višestrukoj) linearnoj regresiji i standardnom simpleks-postupku. Potanko istraživanje međudjelovanja ugodivih parametara pokazalo je da se pravilnim izborom modelne funkcije mogu znatno reducirati korelacije između parametara. Vrijednosti fizikalnih svojstava (promjene entalpije, prividne konstante ravnoteže …) dobivene takvim modeliranjem krivulja vrlo se dobro slažu s odgovarajućim vrijednostima dobivenim drugim metodama. Jednadžbe i postupak računanja opisani u ovom radu mogu se lako prilagoditi za opisivanje nekih drugih, o koncentraciji ovisnih, svojstava u sličnim sustavima.