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Generalized model of electromigration with 1:1 (analyte:selector) complexation stoichiometry: Part I. Theory

Pavel Dubský*, Ludmila Müllerová, Martin Dvořák, Bohuslav Gaš

Charles University in Prague, Faculty of Science, Department of Physical and Macromolecular Chemistry, Prague, Czech Republic

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ABSTRACT

The model of electromigration of a multivalent weak acidic/basic/amphoteric analyte that undergoes complexation with a mixture of selectors is introduced. The model provides an extension of the series of models starting with the single-selector model without dissociation by Wren and Rowe in 1992, continuing with the monovalent weak analyte/single-selector model by Rawjee, Williams and Vigh in 1993 and that by Lelièvre in 1994, and ending with the multi-selector overall model without dissociation developed by our group in 2008. The new multivalent analyte multi-selector model shows that the effective mobility of the analyte obeys the original Wren and Row's formula. The overall complexation constant, mobility of the free analyte and mobility of complex can be measured and used in a standard way. The mathematical expressions for the overall parameters are provided. We further demonstrate mathematically that the pH dependent parameters for weak analytes can be simply used as an input into the multi-selector overall model and, in reverse, the multi-selector overall parameters can serve as an input into the pH-dependent models for the weak analytes. These findings can greatly simplify the rationale method development in analytical electrophoresis, specifically enantioseparations.

1. Introduction

Selectors have the ability to separate structurally highly related analytes (including enantiomers) with similar mobilities or neutral compounds that would otherwise co-migrate in the (capillary zone) electrophoresis (CZE). For this ability, the interactions between the selectors and the analytes are intensively studied and several models of electromigration under the complexation have been introduced in the CZE theory. The most relevant seems the models assuming 1:1 (selector:analyte) complexation stoichiometry. Although the 1:1 stoichiometry is not guaranteed in general, it results from experimental studies that this is a preferred stoichiometry for many complexes, namely with cyclodextrins, the popular selectors in CZE [1,2].

Under these circumstances, the analyte–selector equilibrium is established as

$$\mathrm{A} + \mathrm{S} \rightleftharpoons \mathrm{AS} \qquad K'_{\mathrm{AS}} = \frac{[\mathrm{AS}]}{[\mathrm{A}][\mathrm{S}]} \tag{1}$$

where A and S represent the free analyte and the free selector in the solution, respectively, AS is the analyte–selector complex, K'_{AS} is the (ionic-strength apparent) complexation constant and the terms in the square brackets, $[\cdot]$, stay for the concentrations. The selector is supposed to be in a high excess over the analyte, so that the complexation does not consume a significant portion of its total concentration, c_{S}. Thus the approximation of

$$[\mathrm{S}] = c_{\mathrm{S}} \tag{2}$$

is generally applied. If an analyte is present in numerous forms among which equilibria much faster compared to the electrophoretic movement exist, its effective mobility becomes

$$\mu_{\mathrm{eff}} = \sum \alpha_i \mu_i \tag{3}$$

where α_i are the molar fractions of the individual forms of the analyte and μ_i are their respective electrophoretic mobilities. Using this relationship, the effective mobility of an analyte under complexation results as published by Wren and Rowe in 1992:

$$\mu_{\mathrm{eff}} = \frac{\mu_0 + \mu_{\mathrm{AS}} K'_{\mathrm{AS}} c_{\mathrm{S}}}{1 + K'_{\mathrm{AS}} c_{\mathrm{S}}} \tag{4}$$

where μ_0 is the electrophoretic mobility of the free analyte and μ_{AS} is the mobility of the analyte–selector complex. The relation (4) can be used to predict separation characteristics such as

* Corresponding author at: Charles University in Prague, Faculty of Science, Albertov 2030, CZ-128 40 Prague 2, Czech Republic. Tel.: +420 221 951 296.
E-mail address: dubsky@natur.cuni.cz (P. Dubský).

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the effective mobility difference, selectivity and resolution. This is advantageously utilized in analytical chemistry for the rationale method development and optimization [1–5].

The shortcoming of the model (4) is its limitation to the single analyte form interacting with the single selector (as we will further refer to as the S_AS_S system). In reality, the analytes are often weak acids or bases that undergo dissociation equilibria coupled with the complexation. Rawjee, Williams and Vigh partially overcome this limitation in 1993 by extending the model to monovalent weak acidic and basic analytes [6,7]. The theoretical work of this group finally resulted in the "charged resolving agent migration" (CHARM) model, which relates the physical characteristics of the monovalent weak acidic/basic analyte to the fundamental separation characteristics, such as the selectivity and the resolution [8].

Lelièvre et al. [9] has adopted a different strategy, and showed that the effective mobility of the monovalent week acidic/basic analyte can be formally expressed in terms of the simple S_AS_S model (4):

$$\mu_{\mathrm{eff}} = \frac{\mu_0^{\mathrm{pH}} + \mu_{\mathrm{AS}}^{\mathrm{pH}} K'^{\mathrm{pH}}_{\mathrm{AS}} c_S}{1 + K'^{\mathrm{pH}}_{\mathrm{AS}} c_S} \tag{5}$$

with

$$K'^{\mathrm{pH}}_{\mathrm{AS}} = K'_{\mathrm{HAS}} \frac{K'_{a,\mathrm{HAS}} + [H_3O^+]}{K'_{a,\mathrm{HA}} + [H_3O^+]} \tag{6}$$

$$\mu_0^{\mathrm{pH}} = \frac{K'_{a,\mathrm{HA}} \mu_{A^-} + [H_3O^+]\mu_{\mathrm{HA}}}{K'_{a,\mathrm{HA}} + [H_3O^+]} \tag{7}$$

$$\mu_{\mathrm{AS}}^{\mathrm{pH}} = \frac{K'_{a,\mathrm{HAS}} \mu_{A^-S} + [H_3O^+]}{K'_{a,\mathrm{HAS}} + [H_3O^+]} \tag{8}$$

where μ_{A^-}, μ_{A^-S}, μ_{HA}, μ_{HAS}, K'_{A^-S} and K'_{HAS} are respectively mobilities of the free dissociated form of the analyte, its complex with the selector, the free protonated form of the analyte, its complex with the selector, and the (ionic strength apparent) complexation constant for the dissociated, and the protonated forms of the analyte. $K'_{a,\mathrm{HA}}$ is the (ionic strength apparent) acidic dissociation constant of the free analyte and $[H_3O^+]$ is the concentration of the hydroxonium cations. $K'_{a,\mathrm{HAS}}$ is the (ionic strength apparent) acidic dissociation constant of the analyte in the complex. Value of this dissociation constant is determined by dissociation constant of the free analyte and complexation constants of the protonated and deprotonated analyte forms, respectively:

$$K'_{a,\mathrm{HAS}} = K'_{a,\mathrm{HA}} \frac{K'_{A^-S}}{K'_{\mathrm{HAS}}} \tag{9}$$

This model shows that under the constant pH, the two (protonated and deprotonated) forms of the analyte act as a single analyte form with the pH-dependent parameters μ_0^{pH}, $\mu_{\mathrm{AS}}^{\mathrm{pH}}$ and $K'^{\mathrm{pH}}_{\mathrm{AS}}$. Later on, Mofadel et al. [10] expressed the parameters $K'^{\mathrm{pH}}_{\mathrm{AS}}$, μ_0^{pH} and $\mu_{\mathrm{AS}}^{\mathrm{pH}}$ for bivalent acids. We will further call this model (5) a "pH-overall model" and the parameters (6)–(8) "pH-overall parameters".

Somewhat opposite situation arises if a single analyte form (*e.g.* strong, fully deprotonated acid) interacts with a mixture of selectors, which is often encountered in practice [4,11–23]. Luire et al. [24] have first described the interaction of a single analyte with two selectors as a simple extension of Eq. (4) in 1994. This equation has then become a basis for further method optimization in the dual-selector systems, predominantly in enantioseparations [25]. Similarly to the pH-overall model, Kranack et al. [26] and later us [27] have shown that, effective mobility of an analyte (present in a single free form) interacting with a mixture of selectors can be expressed in a form of the S_AS_S Eq. (4):

$$\mu_{\mathrm{eff}} = \frac{\mu_0 + \mu_{\mathrm{AS}}^{\mathrm{M}} K'^{\mathrm{M}}_{\mathrm{AS}} c_{\mathrm{tot}}}{1 + K'^{\mathrm{M}}_{\mathrm{AS}} c_{\mathrm{tot}}} \tag{10}$$

with

$$K'^{\mathrm{M}}_{\mathrm{AS}} = \sum_{j=1}^{N} K'_{S_j} \chi_{S_j} \tag{11}$$

$$\mu_{\mathrm{AS}}^{\mathrm{M}} = \frac{\sum_{j=1}^{N} K'_{S_j} \mu_{S_j} \chi_{S_j}}{K'^{\mathrm{M}}_{\mathrm{AS}}} \tag{12}$$

where c_{tot} is the total concentration of the mixture of N selectors ($c_{\mathrm{tot}} = \sum_{j=1}^{N} c_{S_j}$), χ_{S_j} are fractions of the individual selectors in the mixture, K'_{S_j} and μ_{S_j} complexation constant and mobility of complex of each particular selector with the analyte, and μ_0 is the electrophoretic mobility of the free analyte. Eq. (10) demonstrates that the mixture of selectors of a constant composition, χ_{S_j}, which interacts with the single analyte form, acts as a single selector with an ostensible complexation constant and mobility of complex. We will further call this model "M-overall model" and the parameters (11) and (12) "M-overall parameters". Eq. (10) is applicable to virtually an unlimited number of selectors under the assumption (2). It is useful for describing migration of a single analyte under interaction with a commercial mixture of selectors [28] as well as for investigating separation characteristics, such as mobility difference and selectivity, as a function of mixture composition, namely in the dual selector mixtures [29].

The aim of this paper is to show that the dependence of the effective mobility of the analyte on the selector concentration can always be converted to the S_AS_S formula (4) whenever the various forms of the analyte interact with an arbitrary number of selectors, in 1:1 (analyte:selector) stoichiometry each. The "various forms" of the analyte are not necessarily specified, although the (de)protonated forms of acidic/basic analytes would certainly be of the prime interest. We will denote the systems where multiple forms of the analyte interact with multiple selectors as "M_AM_S systems". This paper focuses on a deep theoretical analysis of such systems. We provide the experimental investigation of the model elsewhere [30].

2. Theory and discussion

2.1. The generalized overall model

Let an analyte A exists in L various (yet not complexed) forms: $A_1, \ldots, A_i, \ldots, A_L$. Next, consider an arbitrary number of N selectors, $S_1, \ldots, S_j, \ldots, S_N$, present in the system. Finally, let every form of the analyte, A_i, undergo an interaction with each of the N selectors, in 1:1 ratio exclusively:

$$A_i + S_j \rightleftharpoons AS_{ij} \qquad K'_{ij} = \frac{[A_i][S_j]}{[AS_{ij}]} \tag{13}$$

where K'_{ij} is the (ionic strength apparent) complexation constant between the ith form of the analyte and the jth selector. Then, for the total (analytical) concentration of the analyte, c_A, it applies

$$c_A = \sum_{i=1}^{L} \sum_{j=0}^{N} [A_{ij}] \tag{14}$$