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Development of an ion chromatographic gradient retention model from isocratic elution experiments

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Abstract

When facing separation problems in ion chromatography, chromatographers often lack guidelines to decide a priori if isocratic elution will give enough separation in a reasonable analysis time or a gradient elution will be required. This situation may be solved by the prediction of retention in gradient elution mode by using isocratic experimental data. This work describes the development of an ion chromatographic gradient elution retention model for fluoride, chloride, nitrite, bromide, nitrate, sulfate and phosphate by using isocratic experimental data. The isocratic elution retention model was developed by applying a polynomial relation between the logarithm of the retention factor and logarithm of the concentration of competing ions; the gradient elution retention model was based on the stepwise numerical integration of the corresponding differential equation. It was shown that the developed gradient elution retention model was not significantly affected by transferring data form isocratic experiment. The root mean squared prediction error for gradient elution retention model was between 0.0863 for fluoride and 0.7027 for bromide proving a very good predictive ability of developed gradient elution retention model.

Keywords: Ion chromatography; Retention model; Gradient elution

1. Introduction

Ion chromatography (IC) can now be considered a well established technique for the analysis of ionic species and many standard organizations, such as ASTM, AOAC, ISO, etc., have regulatory methods of analysis based upon IC [1]. The technique is applicable to the determination of a wide range of solutes in many diverse sample matrices [2,3]. For routine analysis, isocratic elution is a preferred separation mode. Some reasons that may justify this prevalence are the lower cost, simpler instrumentation, and no need of column re-equilibration between consecutive injections. In practical utility of isocratic IC some compounds are scarcely retained whilst others elute under impractically long analysis times. A common solution to overcome such situations consists of increasing progressively the elution strength of the mobile phase as the analysis progresses (i.e. gradient elution), which expedites the elution of the most retained compounds. The most suited tools to obtain best separation conditions are interpretive optimizations, which substitute successfully trial and error approach. Several optimization software packages using interpretive methodologies have been developed [4–8], but some topics of gradient elution optimization still remain problematic.

The first step in optimization of the separation of a mixture is gathering, for each compound, information about its retention behavior. A large number of retention models were developed for isocratic elution ion chromatography [9–19]. For the theoretical models it was noted that as the complexity of the model increases, the accuracy and precision both increase, but also the level of knowledge requirements necessary to implement the model [20–22]. More complex theoretical retention models are capable to predict retention times with equal or greater accuracy and precision than the empirical end points model, but the low level of knowledge requirements and excellent ruggedness of the end points model make it superior for optimization calculations [22]. The artificial neural network retention models show the highest accuracy, precision and robustness [23–25] but more experimental data have to be used for modeling procedures then for any other model [26].

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The gradient elution retention model is harder to develop due to a fact that far more variables need to be modeled in order to present sufficient gradient combinations. The retention behavior of inorganic anions in relation with the slope of linear gradient elution curve [27,28] and starting time of gradient program [28] has been modeled by artificial neural networks. It is shown that artificial neural network gradient elution retention models have excellent accuracy and precision but gradient elution experimental data which has been used for modeling procedure cannot be used for modeling of various gradient programs. The one possibility to overcome that shortcoming is to use isocratic experimental data for gradient elution retention modeling. The methods for prediction of retention times under gradient conditions by using isocratic elution experimental data have already been described for reversed – phase HLPC separations [29,30], but – according to our best knowledge – never for IC. Therefore, we believed it was important to investigate the applicability proposed approach on other chromatographic methods – in this case ion chromatography.

This report concerns with the gradient elution retention modeling procedure of fluoride, chloride, nitrite, sulfate, bromide, nitrate and phosphate in ion chromatography. The retention information gathered from isocratic experimental design was used to process the gradient information by using fundamental integral equation (Eq. (6)) for gradient elution [29,30] in order to get maximal benefit for a subsequent optimization. The limitations associated to crossing the information between isocratic and gradient elution mode were studied. The way to overcome them is shown. The quality of prediction was evaluated by checking the uncertainty of the model.

2. Retention modeling

The retention behavior of given solute was described by establishing a polynomial relationship between the logarithm of the retention factor, k, and the logarithm of the concentration of KOH in mobile phase. The quadratic dependence was used:

$$\log k = a_0 + a_1 \log c(\mathrm{KOH}) + a_2[\log c(\mathrm{KOH})]^2, \tag{1}$$

where a_i are regression coefficients with characteristic values for a given ion chromatographic system. The optimal values of the model parameters a_i were found for each anion by minimizing the mean square deviation of calculated and experimental isocratic data.

Like many other processes with variable parameters, gradient elution chromatography may be described, in principle, either by differential or by integral equations. In this work we were trying to describe the final (integral) retention times of solutes, t_g, in terms of some measurable properties (retention factor, k, void time of a column, t_0). Hence, the integral equation seemed to be the reasonable choice. The final integral equation takes the following general form:

$$F(t_g, k, t_0) = 0, \tag{2}$$

although it may be given in any arrangement suitable for numerical solving.

In developing the integral model it is crucial to assume that the void time of a column is constant for the selected column and for the fixed flow rate. A starting point for the development of integral equation may be the definition equation of retention factor in isocratic chromatography:

$$k[c] = \frac{t_g - t_0}{t_0}, \tag{3}$$

where k is the function of eluent composition, expressed, e.g. by the concentration of competing ion c. This equation is easily rearranged to take the following form:

$$t_0 = \frac{1}{k[c]}\{(t_g - t_0) - (t_0 - t_0)\}, \tag{4}$$

where the term given in curved brackets is a common solution of the time integral, as shown in:

$$t_0 = \frac{1}{k[c]} \int_{t_0 - t_0}^{t_g - t_0} \mathrm{d}(t - t_0) = \frac{1}{k[c]} \int_0^{t_g - t_0} \mathrm{d}t. \tag{5}$$

Upon the inclusion of the time-independent term $k[c]$ within the time integral, one may easily switch to the gradient elution result by allowing for the temporal variation of c:

$$t_0 = \int_0^{t_g - t_0} \frac{\mathrm{d}t}{k[c(t)]} \tag{6}$$

The last equation is the desired integral equation for gradient elution ion chromatography. The gradient elution time of a solute can be found by splitting the integral in small isocratic time steps:

$$\begin{aligned} t_0 &= \int_0^{t_g - t_0} \frac{\mathrm{d}t}{k[c(t)]} = \int_0^{t_1} \frac{\mathrm{d}t}{k[c(t)]} + \int_{t_1}^{t_2} \frac{\mathrm{d}t}{k[c(t)]} \\ &\quad + \cdots + \int_{t_{i-1}}^{t_1} \frac{\mathrm{d}t}{k[c(t)]} + \int_{t_i}^{t_{i+1}} \frac{\mathrm{d}t}{k[c(t)]} \end{aligned} \tag{7}$$

$k[c]$ can be assumed constant for each step and t_0 can be approximated to:

$$\begin{aligned} t_0 &\approx \frac{t_1}{k_{0,1}} + \frac{t_2 - t_1}{k_{1,2}} + \cdots + \frac{t_i - t_{i-1}}{k_{0,1}} + \frac{t_{i+1} - t_i}{k_{i,i+1}} \\ &= I_{0,1} + I_{i,i+1} = I_{0,i+1} \end{aligned} \tag{8}$$

$$k(c)_{i,i+1} = \frac{k[c(t_i)] + k[c(t_{i+1})]}{2} \tag{9}$$

where I represents the approximate cumulative integral. The approximate value of the cumulative integral is calculated stepwise; it is expected to increase in due course of the integration procedure and it will eventually exceed the fixed t_0-value on the left-hand side of Eq. (8) at some $t_g - t_0$-value. This is illustrated schematically in Fig. 1. Now, by applying the simple similarity of triangles (or linear interpolation formula) one comes to:

$$\frac{t_0 - I_{0,i}}{(t_g - t_0) - t_i} = \frac{I_{0,i+1} - I_{0,i}}{t_{i+1} - t_i} \tag{10}$$