Modelling of cations retention in ion chromatography with methanesulfonic acid as eluent

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Abstract

The two retention models, the linear solvent strength model (LSS) and the quadratic relationship, in addition to artificial neural network (ANN) approach, were compared in their ability to predict the retention behaviour of common cations (Li, Na, NH_4, K, Mg and Ca) in isocratic ion chromatography using the methanesulfonic acid (MSA) eluent. Over wide variations in the MSA concentration, the quadratic model shows a quite good prediction power. LSS can be used only for monovalent cations and in the proximity of the experimental design point. ANN fails to predict the retention for the data not included in the training set. To find the optimal conditions in the experimental design, the normalized resolution product as a chromatographic objective function was employed. The optimum MSA concentration in the eluent on a Dionex CS12 column was found to be 18 mM, with the total analysis time of less than 10 min.

Keywords: computer-assisted optimization, ANN, MSA, IC, resolution.

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Ion chromatography (IC) has become a routine analytical method for the determination of inorganic anions with lots of applications in various fields. High selectivity of IC is a function of the eluent composition, nature of analytes and stationary phases at which separation occurs [1]. Eluent composition is a parameter which is the most commonly used for manipulating the retention and detection of solute ions [2]. The optimal eluent composition can be selected by using computer-assisted interpretive optimization approach [3]. This approach is increasingly used in chromatographic separations due to better quality of the results and time savings [4–6]. Selection of a suitable retention model is the first step in a computer-assisted interpretive optimization approach. The predictive ability of the used retention model is the key in the successful optimization procedure.

The linear solvent strength (LSS) model is the most widely applied model in the optimization of IC separations [3,7,8]. According to the LSS model, the retention factor, k, of a solute is related to the solvent composition, E^y, by:

$$\log k = C_1 - (x/y)\log E^y \qquad (1)$$

where x is the charge on the analyte anion, y is the charge on the eluent anion and C_1 is a constant. Eq. (1) predicts a linear relationship between the logarithm of

the retention factor and the logarithm of the eluent concentration.

Several quadratic models have been proposed [9––11]:

$$\log k^{'} = A + B\log E^y + C(\log E^y)^2 \qquad (2)$$

where the model parameters A, B and C can be calculated numerically by solving a set of equations:

$$A = (V_i/RT)(\delta_o - \delta_w)^2 \qquad (3)$$

$$B = -(2V_i/RT)(\delta_w - \delta_o)(\delta_w - \delta_i) \qquad (4)$$

$$C = (V_i/RT)\left[(\delta_w - \delta_i)^2 - (\delta_s - \delta_i)^2\right] + \ln(n_s/n_m) \qquad (5)$$

where δ is the solubility parameter, i, s, o and w indicate the solute, stationary phase, organic modifier and water, respectively. V_i is the molar volume of a solute, R is the gas constant, T is the absolute temperature and n_m and n_s are number of moles of solute in the mobile (m) and stationary (s) phases.

The models for the prediction of retention times for isocratic and gradient elution have also been built with artificial neural networks (ANN) [1,12–14]. This model offer attractive possibilities for providing non-linear modeling and optimization in IC when the underlying mechanisms are very complex. An ANN consists of many pathways and nodes organized into a sequence of layers. Initially, a learning phase is defined in which each of the input parameters are applied to a processing element. The weights between these parameters are adjusted until the output (the retention

parameter) is correct. The system can then be applied to unknown parameters.

In this work, the retention behavior of six cations (lithium, sodium, ammonium, potassium, magnesium and calcium) has been studied using interpretive optimization approach. The effect of the eluent concentration on the retention factors of cations was studied using MSA as the eluent. The quadratic model was applied in conjunction with objective function (total resolution) analysis and computer simulation of chromatograms. The retention modeling of cations by ANN has also been evaluated.

EXPERIMENTAL

Determination of cations by ion chromatography (IC) method has been achieved using a Dionex DX-300 ion chromatograph (Dionex, Sunnyvale, CA, USA). The instrument consists of an advanced gradient pump and a CDM-3 conductivity detector. The employed analytical separation columns was a Dionex IonPac® – CS12A cation exchange column. A cation Self Regenerating Suppressors (CSRS 300) was used. The injected volume was 20 µL. The separation of cations was carried out at a flow rate of 1.0 mL/min. Dionex Peaknet 5.1 software was employed for instrument control, data collection and processing. A Spectra-Physics model AS3500 autosampler was used for the direct programmed injection of samples. The retention times of cations were measured at the nine eluent concentrations evenly distributed within the range of 5–45 mM MSA to make the experimental design and study the retention behavior.

Working mixture was prepared from individual stock solutions (1.0 mg/mL) of six cations obtained from AccuStandard (New Haven, CT, USA). This mixture was diluted appropriately in Milli-Q water to prepare the solution of different concentration for each cation:

lithium 1.0 mg/L, sodium, ammonium and potassium 1.5 mg/L, magnesium and calcium 2.0 mg/L. Milli-Q system (Millipore Co., Bedford, MA, USA) processed water (18 MΩ/cm) was used for these experiments.

The estimation of model parameters was performed using Mathcad 2000 software (MathSoft Inc., USA).

RESULTS AND DISCUSSION

Interpretative optimisation

Retention behavior of six cations can be modelled using Eq. (2) and evaluated by measuring retention data at varying concentration of MSA in a range of 5.0-45 mM MSA, *i.e.*, at the three levels: 10, 25 and 40 mM. Then, each cation is studied at nine eluent concentrations (5.0, 10, 15, 20, 25, 30, 35, 40 and 45 mM) to obtain nine retention values for each ions. The data from this runs are fitted to Eq. (2) for all six analytes, using each of the eluent compositions in the data set, to predict retention data. Non-linear regression fitting was employed for the parameter estimation [12]. The experimental and calculated retention parameters for each eluent composition and the sum of squares of deviation (SSE) are summarized in Table 1. It is evident that a good agreement between experimental and calculated retention times has been obtained.

The percentage-normalized difference (d, %) between the measured and predicted retention times for a particular cation was calculated from the results shown in Table 1 ($d = (t_{R,exp} - t_{R,pred}) / t_{R,exp}$). The highest d values were observed for late eluting cations at the highest eluent concentrations. In general, all of the d values are less than 10% with an average value which is less than 2% for any cation.

Eq. (2) predicts a quadratic relationship between the retention factor and the concentration of the

Table 1. Experimental and calculated capacity factors for different eluent compositions and the sum of squares of deviation (SSE); a – retention factor from experimentally obtained chromatograms; b – retention factors obtained from calculated chromatograms

Analyte						k						SSE
Lithium	a	8.000	4.543	3.481	3.136	2.741	2.556	2.420	2.173	2.086		0.041
	b	7.985	4.613	3.547	3.022	2.708	2.501	2.353	2.244	2.160		
Sodium	a	10.938	5.926	4.395	3.840	3.272	3.062	2.852	2.605	2.457		0.034
	b	10.933	5.970	4.454	3.718	3.283	2.996	2.792	2.641	2.525		
Ammonium	a	14.000	7.407	5.358	4.605	3.877	3.580	3.309	2.975	2.827		0.042
	b	14.005	7.447	5.450	4.481	3.906	3.525	3.254	3.051	2.893		
Potassium	a	20.840	10.704	7.519	6.210	5.173	4.778	4.272	3.951	3.630		0.040
	b	20.819	10.666	7.602	6.121	5.244	4.663	4.247	3.935	3.692		
Magnesium	a	99.457	23.309	10.790	6.877	4.988	4.160	3.506	3.000	2.765		0.372
	b	99.450	23.028	11.168	7.091	5.156	4.063	3.373	2.903	2.566		
Calcium	a	136.642	31.395	14.111	8.679	6.136	5.025	4.160	3.494	3.136		0.678
	b	136.707	31.020	14.570	8.971	6.333	4.800	3.932	3.305	2.865		
MSA, mM		5.0	10	15	20	25	30	35	40	45		

eluent. In Fig. 1, the experimental data for all analyzed cations were plotted as log *k versus* log [MSA] using the quadratic model (solid line) and the LSS model (dotted line). A good agreement of the retention data for all cations is obtained for quadratic model, while the LSS model was found to overestimate the experimental data. In both cases, the worst fit was obtained for the lowest MSA concentration, 5.0 and 10 mM, especially for magnesium and calcium. According to Tyteca *et al*. [5] and Madden et al. [15] the linear model is only an approximate one, with a good predictability of retention data only if the isocratic experiments include the extremes of the eluent conditions to be studied. This study revealed that the LSS model has bad prediction power for divalent cations.

The prediction powers of the applied quadratic model were further tested and the results are shown in Fig. 2. High retention coefficients obtained for calcium and magnesium can be explained by high retention times at low MSA concentrations. The calculated retention coefficients were plotted against the measured retention coefficients and a good agreement was obtained. The slope and intercept of the line were close to one (1.0002) and zero (−0.0073), respectively, with a correlation coefficient of 0.9999. Strong linear relationship means that there is no significant difference between the values of the predicted and measured retention coefficient and no systematic error is present in optimized quadratic retention model for all cations [16].
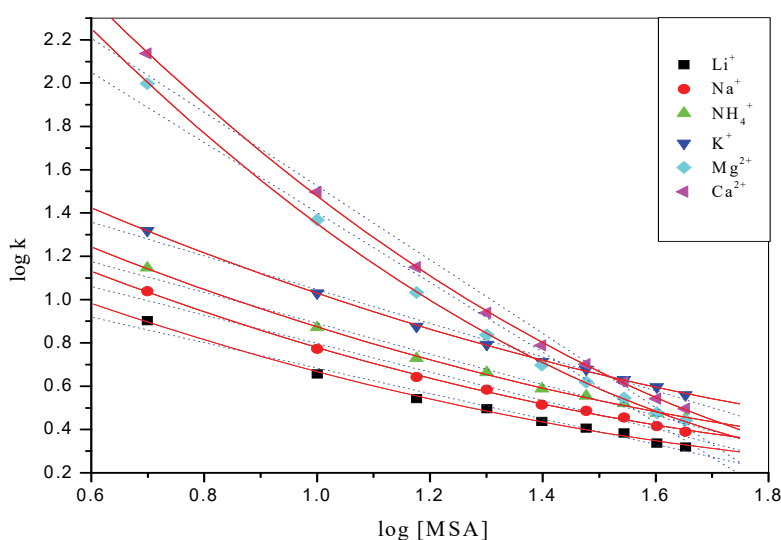

Figure 1. Retention relationships for all six analyzed cations plotted as log k versus log [MSA] using quadratic model (solid line) and LSS model (dotted line).
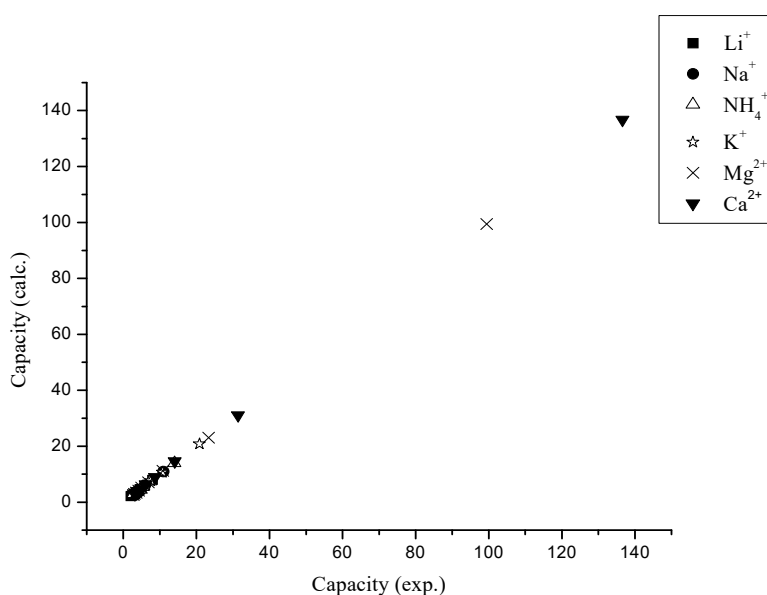

Figure 2. Predictive ability calculations for optimized quadratic model of six cations.

The essential part of chromatographic separation study is the selection of an appropriate response function which requires a clear definition of the goal of the process. Many different criteria have been suggested in the literature [17–19] to quantify chromatograms.

The normalized resolution product (*r*) criterion, chosen here, is described by the following equation:

$$r = \prod_{i=1}^{n-1} \{R_{Si,i+1} / [(n-1)^{-1} \sum_{i=1}^{n-1} R_{Si,i+1}]\} \qquad (3)$$

where *n* is the number of peaks, $R_{S\,i,i+1}$ is the resolution between peaks *i* and *i*+1, and *r* is the product of all resolution values, each parted by the average resolution. This criterion gives a value of one to a chromatogram if the resolution between all pairs of peaks is the same, and zero for the chromatogram with at least one peak fully overlapped. This criterion allows the selection of an optimum mobile phase. The normalized resolution product for the separation of six cations was shown in Fig. 3. Several maximums were observed, the main maximum corresponding to 18 mM MSA was selected as the optimum because of the maximum value of the resolution product and satisfactory retention times. Each minimum corresponds to a peak reversal. On increasing the MSA contents the resolution worsened, because the compounds with the greater elution strength appeared close to the beginning of the chromatogram.

Based on the above results, the next step was design to calculate of chromatogram for any point on the curve (Fig. 3). Exponentially Modified Gaussian (EMG) equation [20] was used for calculation. Also, for selected eluent compositions (18 mM MSA), real chromatogram were obtained by injecting the mixture of analyzed cations. In Fig. 4 the calculated and the measured chromatogram of a lithium, sodium, ammonium, potassium, magnesium and calcium mixture are presented. By comparison of these chromatograms, high matching degree was obtained for retention time, peak shape and resolution, which confirms the high predictive power of the applied model.
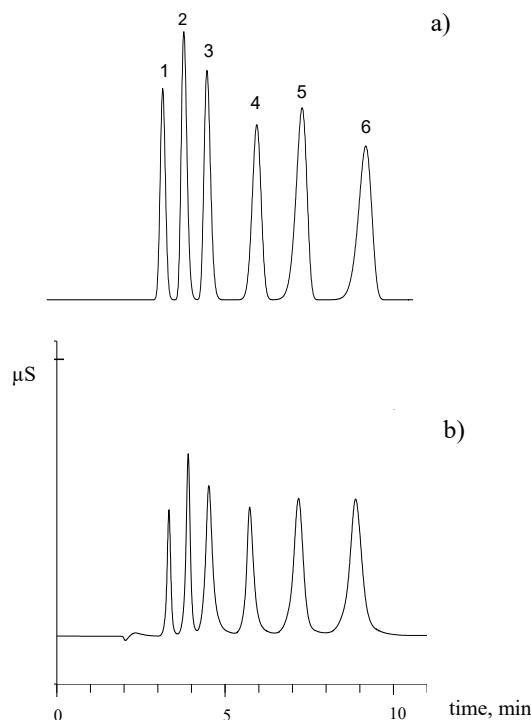

Figure 4. Chromatograms (predicted (a) and obtained (b)) for six cations at 18 mM MSA: (1) lithium, (2) sodium, (3) ammonium, (4) potassium, (5) magnesium and (6) calcium.

Artificial neural networks

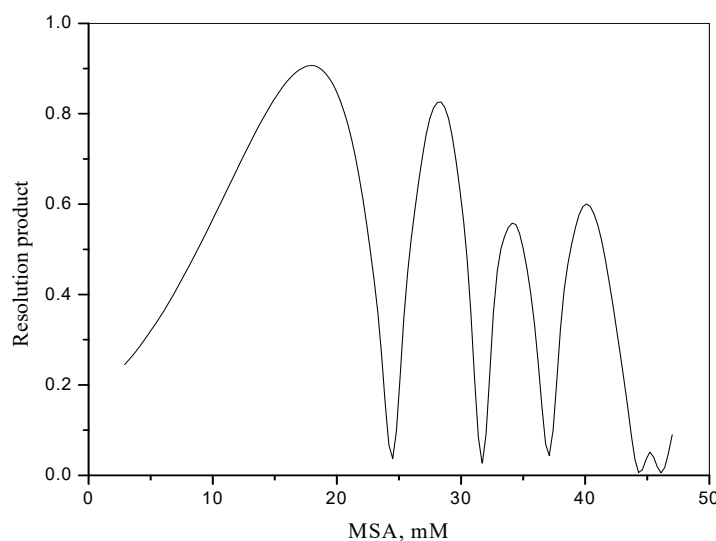Artificial neural networks could provide a lot of models for the prediction of retention times for both

Figure 3. Resolution product for six cations as a function of MSA.

isocratic and gradient elution. Only ANN has a capability to model the retention with no prior knowledge of the separation mechanism.

In this work, ANN was used to study the effect of variation of the concentration of MSA on the retention time of six cations in isocratic ion chromatography. The applied ANN model consists of an input layer with one nodes (the concentration of MSA), an output layer with six nodes (the cations retention times), and a hidden layer. The number of nodes in the hidden layer should be optimized using a trial and error approach.

To predict the retention data for six cations, the retention and trained ANN data were used. The prediction was done at the optimum MSA concentration of 18 mM obtained by interpretative optimization approach. Since the predictive power of ANN depends on the number of input experiments, we applied the same three-level experimental design for ANN training. The calculated and the measured retention data were compared in Table 2.

Table 2. Calculated and measured retention times (min) of six cations at optimum MSA concentration (18 mM) for one-variable models

Cation	Exp. values	Interp. model	ANN model
1. Lithium	3.47	3.48	3.49
2. Sodium	4.08	4.02	4.01
3. Ammonium	4.77	4.67	4.66
4. Potassium	6.26	6.12	6.06
5. Magnesium	7.56	7.44	7.02
6. Calcium	9.38	9.29	8.73

Graphical representation of the percentage normalized difference (*d*) between the observed and the predicted retentions is illustrated in Fig. 5.
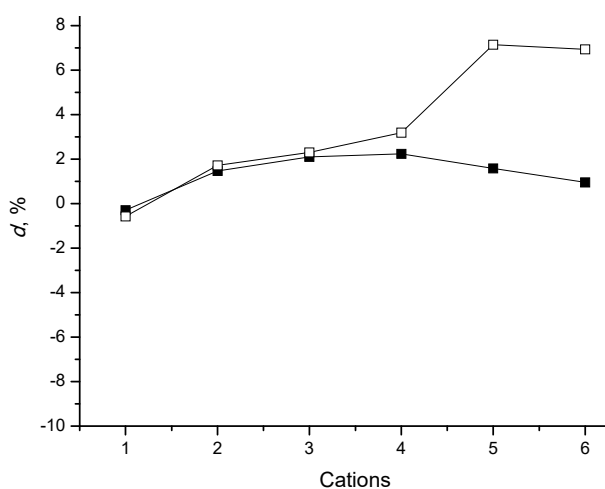

Figure 5. Normalized percentage differences between the measured and the predicted retention times for 6 cations for: (■) interpretative model and (□) ANN model. Cations identities as in Table 2.

The interpretative approach gives better results (*d* below 2%) for all the cations studied, while the predicted power of ANN is very bad for late-eluting cations (*d* about 7%). Although the ANN model does not require any mathematical form of the relationship between input and output data, the ANN needs more experimental input points than the interpretative method.

CONCLUSION

In this work the interpretative and the ANN models were used for the modelling of the retention of six common cations in isocratic ion chromatography. A good prediction of the effects of mobile phase factor, total concentration of MSA (5-45 mM), on the separation of cations by quadratic model was obtained. The experimental and calculated values of the retention times were found to be in a good agreement. The concentration of 18 mM of MSA was selected as the optimum mobile phase composition by normalized resolution product criterion. The predictive power of ANN was very limited for late-eluting cations.

Acknowledgements

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IZVOD

MODELOVANJE RETENCIJE KATJONA U JONSKOJ HROMATOGRAFIJI SA METANSULFONSKOM KISELINOM KAO ELUENTOM

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(Naučni rad)

Dva retenciona modela, model linearne jačine rastvarača (LSS) i kvadratni model, zajedno sa veštačkim neuronskim mrežama (ANN) su upoređivani u njihovoj sposobnosti da predvide retenciono ponašanje katjona (Li, Na, NH$_4$, K, Mg i Ca) u izokratskoj jonskoj hromatografiji sa metansulfonskom kiselinom (MSA) kao eluentom. Proučavan je uticaj varijacije koncentracije MSA na razdvajanje smeše katjona na Dionex CS12 koloni. Devet koncentracija eluenta, od 5,0, 10, 15, 20, 25, 30, 35, 40 i 45 mM, korišćeno je za optimizaciju razdvajanja smeše šest katjona i dobijeno je devet setova retencionih podataka. Kvadratni model je pokazao veliku sposobnost u predviđanju retencionog ponašanja sa odličnim slaganjem između izračunatih i izmerenih retencionih koeficijenata. Zavisnost teorijski izračunatih i eksperimentalno dobijenih retencionih koeficijenata je linearna sa korelacionim koeficijentom 0,9999 i nagibom 1,00. LSS model može da se koristi samo za monovalentne katjone. Za pronalaženje optimalnih uslova eksperimentalnog dizajna korišćen je normalizovani rezolucioni produkt. Dobijena optimalna koncentracija MSA u eluentu je 18 mM sa maksimalnom vrednošću rezolucije i zadovoljavajućim retencionim vremenom. Ukupno vreme analize je manje od 10 min. Na osnovu ovih rezultata dobijen je teorijski hromatogram. Takođe, za selektovanu optimalnu koncentraciju MSA od 18 mM, dobijen je i eksperimentalni hromatogram. Poređenjem ova dva hromatograma dobijeno je dobro slaganje u retencionim vremenima, obliku pikova i rezoluciji za sve analizirane katjone. Ovo potvrđuje efikasnost primenjenog kvadratnog modela. Retenciono ponašanje analiziranih katjona je takođe proučavano i primenom veštačkih neuronskih mreža. Primenom ovog modela, retenciono ponašanje katjona je takođe proučavano na optimalnoj koncentraciji MSA od 18 mM dobijenoj primenom interpretativnog optimizacionog modela. Poređenjem dobijenih retencionih vremena primenom ova dva modela, dobijeni su bolji rezultati interpretativnim pristupom za sve analizirane katjone (*d* < 2%), dok su korišćenjem ANN dobijeni lošiji rezultati za katjone sa dužim retencionim vremenom kao što su magnezijum i kalcijum (*d* oko 7%).