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Computer optimization in ion chromatography

II. A systematic evaluation of linear retention models for anions

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ABSTRACT

Extensive retention data for non-suppressed ion chromatography of anions have been acquired for 17 analytes (halides, oxohalides, nitrite, nitrate, sulfite, sulfate, bisulfite, thiosulfate, phosphate, thiocyanate, carbonate, acetate and oxalate) on three stationary phases (Waters IC Pak A, Hamilton PRP-X100 and Vydac 302.IC 4.6) using 7 eluent types (benzoate, phthalate, hydroxide, carbonate/bicarbonate, gluconate/borate, *p*-toluenesulfonate and phosphate). These retention data are used to assess the validity of retention models which predict a linear relationship between the logarithm of solute capacity factor and the logarithm of the activity of the eluent competing anion. The linearity of these plots is uniformly good, but the slopes differ markedly from those predicted from theory. When the eluent contains two competing anions, neither the dominant equilibrium approach nor the effective charge approach give reliable prediction of the slopes. Optimization of one eluent parameter at a time (*e.g.* the concentration of the competing anion in the eluent) can be successful if the slope of the retention plot is determined by measurement of analyte retention times at two eluent compositions falling at the extremes of the range of eluent compositions under consideration. An example of this "end points" method is provided, in which the concentration of a phthalate eluent is optimized.

INTRODUCTION

Computer optimization procedures have been applied extensively in liquid chromatography and one of the most successful of these applications has been the computer-assisted selection of mobile phase composition in reversed-phase liquid chromatography. Despite this success, computer optimization techniques have found only limited usage in ion chromatography (IC).

The most important parameter to be considered in an optimization procedure is the chromatographic selectivity; that is, the ability of the chromatographic system to differentiate between two solutes. In IC there are several variables which can be used to change chromatographic selectivity. These can be divided into two classes, namely, hardware variables (*e.g.* stationary phase composition, ion-exchange capacity, temperature and detection method) and eluent variables (*e.g.* the nature and

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concentration of the competing ions, and the pH). Whilst hardware variables must be taken into consideration in the initial selection of the chromatographic system to be used, it is often more appropriate to select a specific combination of these variables and to then concentrate on modifying the eluent composition.

We have recently reviewed the use of computer optimization in IC [1] and we have shown that two distinct approaches exist. The first of these is the algorithmic method, in which a suitable searching algorithm, such as the Simplex procedure, is applied to the optimization of a designated number of experimental variables until the separation is optimized. This approach is time consuming due to the large number of experiments required, but has the attributes that no theoretical insight into the chromatographic retention mechanism is necessary, and that several experimental parameters can be optimized simultaneously.

The second approach to optimization involves the modelling of solute retention over a specified range of experimental parameters (called the "search area"). The aim is to enable the retention time of any solute to be determined for any eluent composition within the search area. That is, solute retention times are derived from the retention model and are used to calculate the optimal eluent composition. The model used may be *experimental* or *theoretical.* Experimental models fit measured retention times to a mathematical equation, which is then used to calculate retention times for any desired eluent composition within the search area. The accuracy of this calculation is generally dependent on the number of data points used to define the retention equation, and the geographic distribution of these data points over the search area. Accurate calculation of retention times results only when the number of measured data points is large, so that the use of experimental models normally requires considerable exploration. On the other hand, theoretical models use an abstract understanding of retention behaviour to predict solute retention times over the designated search area. This prediction can be made solely on the basis of theory, but it is more usual to perform a small number of experiments using eluent compositions from within the search area and to then base predictions on these measured points.

All chromatographic techniques are relatively slow to produce data, especially when the composition of the mobile phase is varied. The reason for this is that the stationary phase must become fully equilibrated with the new mobile phase before reliable retention data can be measured. Relatively slow equilibration to changes in eluent composition is a characteristic of ion-exchange chromatography in general, and IC in particular. It therefore becomes desirable to restrict the number of experiments performed in an optimization process, and to this end, a reliable theoretical model would be preferable. In this paper, we provide a detailed evaluation of the suitability of simple, linear retention models as predictive tools for the retention of anions in non-suppressed IC. Our goal in performing this evaluation is to determine if any linear retention model can be used with confidence in a theoretical optimization strategy for IC.

THEORY

Linear retention models for IC

Consideration of fundamental equilibrium and chromatographic theory enables a retention equation for IC to be derived. The full derivation of this equation has been presented earlier by several authors [2–4], and when applied to the ion-exchange equilibrium between a solute anion, A^{x-}, and an eluent anion, E^{y-}, the final equation takes the form:

$$\log k'_A = \frac{1}{y}\log K_{A,E} + \frac{x}{y}\log\frac{Q}{y} + \log\frac{w}{V_m} - \frac{x}{y}\log[E_m^{y-}] \tag{1}$$

where k'_A is the capacity factor for a solute A^{x-}, $K_{A,E}$ is the ion-exchange selectivity coefficient for the solute and eluent, Q is the ion-exchange capacity of the stationary phase, w is the weight of stationary phase used in the column, V_m is the volume of mobile phase existing in the column, x is the charge on the solute anion, y is the charge on the eluent anion, and $[E_m^{y-}]$ is the concentration of the eluent ion in the mobile phase.

Although shown for the case of anion-exchange, eqn. 1 applies also to cation-exchange [5].

Some of the terms in eqn. 1 are constant for a particular column and type of mobile phase, so that under these conditions, eqn. 1 can be simplified to:

$$\log k'_A = \text{Constant} - \frac{x}{y}\log[E_m^{y-}] \tag{2}$$

Eqn. 2 predicts that a linear relationship exists between log k'_A and log $[E_m^{y-}]$, with a slope of $-x/y$. The literature of IC abounds with examples in which measured retention data obtained with eluents containing a single type of eluting ion are shown to produce linear plots with approximate agreement between the predicted and measured slopes. The only caveats which apply are that activity effects should be considered for eluents in which the ionic strength is sufficient to give activity coefficients less than unity, and that ions carrying a charge greater than 2 give slopes which are less than the theoretical value. The latter aspect can be rationalized by considering that the low ion-exchange capacities of typical IC stationary phases would make it improbable that a polyvalent ion will closely approach a stoichiometric number of exchange sites.

Problems arise with the above linear retention model when there are two or more eluent ions present, as typified by the use of phthalate eluents at pH values where both the singly charged hydrogen phthalate ion (HP^-) and the doubly charged phthalate ion (P^{2-}) co-exist. In these cases, experience shows that the linearity of the retention plots is maintained, but to predict the theoretical slope of the plot, an appropriate value of eluent charge must be inserted into the equation. Two possibilities exist; the first is to assume that the eluent ion with the higher charge dominates solute elution and the lesser charged eluent species can be disregarded, whilst the second possibility is to calculate a weighted average charge on the eluent ion by considering the concentrations and charges on each eluent species. The former will be referred to as the *dominant equilibrium approach*, and the latter as the *effective charge approach*. The effective charge on the eluent can be calculated according to:

$$y = \alpha_1 + 2\alpha_2 + 3\alpha_3 + \ldots + n\alpha_n \tag{3}$$

where α_n is the mole fraction of eluent species carrying a charge of n^-. When the effective charge approach is used, the total eluent concentration, C_E, replaces the $[E_m^{y-}]$ term in eqn. 2.

EXPERIMENTAL

Instrumentation

The liquid chromatograph consisted of a Millipore Waters (Milford, MA, U.S.A.) M6000A pump, a WISP M712 autoinjection unit, two six-port column switching valves and a Model M730 data module. The chromatographic columns were housed in a Waters temperature control module and were maintained at a constant 35 ± 0.1°C to minimize the effects of temperature fluctuations on analyte response [6]. The operating temperature was lowered to 25 ± 0.1°C for the Hamilton PRP-X100 column when used with eluents having a pH greater than 8. Two detectors were used throughout this study, these being a Waters M430 conductivity detector and a Waters M450 variable-wavelength UV detector. The conductivity detector was used wherever possible because of its wide applicability, but in cases where the background conductance of the eluent was high (especially with the phosphate and carbonate/bicarbonate eluents), the UV detector was also utilised. The UV detector was set at a wavelength of 195 nm, since it has been shown that a large majority of the anions studied show absorbance at this wavelength [7].

Columns

Three anion-exchange columns were used. A Waters IC Pak A (50 × 4.6 mm I.D.) column packed with 10 μm functionalised polymethacrylate with an ion-exchange capacity of 0.03 mequiv./ml. A Vydac (The Separations Group, Hesperia, CA, U.S.A.) 302 IC 4.6 (250 × 4.6 mm I.D.) column packed with 10 μm functionalised silica with an ion-exchange capacity of 0.10 mequiv./g. A Hamilton (Reno, NV, U.S.A.) PRP-X100 (150 × 4.1 mm I.D.) column packed with functionalised 10 μm polystyrene–divinylbenzene copolymer with an ion-exchange capacity of 0.19 mequiv./g.

The three columns were connected in parallel and housed in the temperature controlled oven. Two manually operated column switching valves were used to direct the eluent flow through the desired column. All three columns could therefore be equilibrated with the same eluent, as required.

Eluents

For each eluent used in this study, a stock solution of approximately 100 m*M* was prepared by dissolution of an accurately weighed amount of the appropriate analytical grade reagents in pure water. Working eluents were prepared daily by dilution of a suitable volume of the stock solution to approximately 900 ml, followed by adjustment of the pH (where necessary) by the dropwise addition of 0.1 *M* LiOH, using a magnetic stirrer. The solution was then made up to volume (1 l) and the pH measured accurately using an Activon (Sydney, Australia), Model 101 mV/pH meter with a glass electrode. Finally the solution was passed through a Millipore solvent clarification apparatus using 0.45-μm membrane filters and degassed in an ultrasonic bath before use.

The actual eluent compositions used are given in Tables II–VIII. The general preparation of these eluents was as follows:

Benzoate eluents. The stock solutions were prepared from sodium benzoate.

Carbonate/bicarbonate eluents. The stock solutions were prepared from sodium carbonate and sodium bicarbonate, mixed in the appropriate proportions.

Gluconate/borate eluents. The stock solution was prepared by dissolving 16 g sodium gluconate, 18 g boric acid and 25 g sodium tetraborate in 1 l of pure water. The working eluents were prepared by combining the appropriate aliquot of stock solution with glycerol solution (10 ml, 25%), acetonitrile (120 ml, UV grade), followed by dilution to 1 l.

Hydroxide eluents. The stock solution was prepared by dissolving AR grade LiOH in pure water under an inert atmosphere of argon. Working eluents were prepared under argon by dilution of an appropriate aliquot of the stock solution, with the concentration of OH^- being determined by titration with standardized HCl. During use, these eluents were maintained under an atmosphere of nitrogen to limit the absorption of carbon dioxide.

p-Toluenesulfonate eluents. The stock solutions were prepared from *p*-toluenesulfonic acid.

Phthalate eluents. The stock solutions were prepared from either potassium hydrogen phthalate or, where the mobile phase was to be buffered at a pH of 4.0 or below, from phthalic acid.

Phosphate eluents. The stock solutions were prepared from sodium dihydrogen phosphate.

Analytes

The analytes (see Table I) were prepared as 1000 ppm stock solutions by dissolving the appropriate amount of the sodium salt in pure water in a volumetric flask. A working standard (100 ppm) of each analyte was prepared daily by dilution of the stock solution. Where the retention time of the analyte being studied was found to occur in the water dip or the solvent front peak, a fresh standard was prepared by

TABLE I

ANALYTES, ELUENTS AND COLUMNS USED IN THIS STUDY

Anions: F^-, Cl^-, Br^-, I^-, ClO_3^-, BrO_3^-, IO_3^-, NO_2^-, NO_3^-, HSO_3^-, SO_3^{2-}, SO_4^{2-}, $S_2O_3^{2-}$, SCN^-, phosphate, carbonate, oxalate and CH_3COO^-.

Eluent	Column		
	Hamilton PRP-X100	Vydac 302 IC 4.6	Waters IC Pak A
Benzoate	Yes	Yes	Yes
Carbonate/bicarbonate	No	No	Yes
Gluconate/borate	Yes	No	Yes
Hydroxide	No	No	Yes
p-Toluenesulfonate	Yes	Yes	Yes
Phthalate	Yes	Yes	Yes
Phosphate	Yes	No	Yes

TABLE II

RETENTION TIMES FOR ANIONS USING BENZOATE ELUENTS ON THREE COLUMNS (HAMILTON PRP-X100, VYDAC 302 IC 4.6 AND WATERS IC PAK A)

	Hamilton				Vydac							Waters			
Concentration (m*M*):	2.00	3.00	4.00	5.00	2.38	2.66	3.53	4.49	4.67	5.88	7.71	2.99	3.99	4.99	5.99
pH:	6.4	6.4	6.4	6.4	4.0	4.0	4.0	4.0	4.0	4.0	4.0	6.4	6.4	6.4	6.4
Fluoride	3.06	2.26	1.69	1.39	–	–	–	–	–	–	–	3.21	2.85	2.42	2.15
Chloride	3.88	2.83	2.08	1.75	12.69	9.69	7.50	–	6.99	4.69	3.85	5.37	4.46	3.61	3.23
Bromide	5.26	3.75	2.76	2.32	15.47	11.75	9.01	7.68	8.45	5.54	4.46	8.10	6.65	5.47	4.75
Iodide	13.74	9.49	6.38	4.69	27.10	20.06	15.21	–	14.23	8.87	6.89	23.66	18.62	14.37	12.91
Chlorate	7.06	4.98	3.51	2.78	15.72	11.84	9.14	–	8.58	5.60	4.51	8.81	7.01	5.74	4.99
Bromate	3.98	2.89	2.16	1.80	–	8.91	6.94	6.04	–	4.47	3.69	4.59	3.86	3.24	2.85
Iodate	2.80	2.11	1.61	1.46	9.18	7.15	5.63	–	5.34	3.75	3.16	2.85	2.55	2.20	1.95
Nitrite	4.30	3.12	2.29	1.90	14.26	10.86	–	–	7.80	5.28	4.29	6.92	5.57	4.61	4.00
Nitrate	5.88	4.18	2.95	2.36	–	13.28	10.18	–	9.49	6.13	4.90	10.09	8.05	6.55	5.68
Bisulfite	–	–	–	–	–	8.24	–	–	6.02	4.37	3.69	–	–	–	2.36
Sulfite	38.18	17.66	7.78	4.54	–	–	–	57.14	–	–	13.91	41.33	28.34	18.51	13.29
Sulfate	36.88	18.81	7.06	5.01	–	–	–	57.97	41.46	25.10	13.98	42.42	28.85	18.80	13.50
Thiosulfate	65.34	31.61	10.68	8.56	–	–	–	77.87	–	33.14	18.13	79.56	51.76	32.89	23.81
Phosphate	5.58	3.66	1.76	1.54	–	13.68	–	11.13	10.28	–	–	5.49	5.49	4.59	3.35
Thiocyanate	–	–	–	–	–	30.48	23.15	19.37	–	13.25	10.08	–	–	–	–
Acetate	3.06	2.30	1.80	1.55	–	3.66	–	3.16	3.09	2.84	2.59	3.24	2.87	2.46	2.17
Oxalate	78.15	18.86	–	9.93	–	–	–	–	–	–	–	–	–	–	–
System	42.56	–	26.90	–	–	–	–	–	–	–	–	–	–	–	–
Void vol. eq.	0.75	0.77	0.81	0.83	1.65	1.65	1.65	1.65	1.65	1.65	1.65	0.77	0.78	0.79	0.80

dilution of the stock solution in the eluent being used. The limited stability of the bisulfite ion in aqueous solutions [8] required that the standards containing this ion also contain a preservative. In the low pH eluent studies the bisulfite ion was preserved by the addition of formaldehyde to give a final concentration in the sample of 0.2% (v/v). Under these conditions, the bisulfite ion is chromatographed as the hydroxymethanesulfonate ion.

RESULTS AND DISCUSSION

Selection of analytes, eluents and stationary phases

In order to systematically evaluate the suitability of linear retention models for predicting solute retention times, an experimental design was formulated to permit the acquisition of extensive retention data for a variety of anions, eluents and stationary phases. Table I shows the scope of this study. The range of analytes covers most of the common inorganic anions, and includes some species (such as phosphate, oxalate, carbonate and nitrite) which show changes in form as the pH is altered. Similarly, the eluents cover most of those commonly used in non-suppressed IC and include those which can be expected to show prominent pH effects (such as phthalate, benzoate, carbonate/bicarbonate and phosphate). The stationary phases are representative of the three main types of substrate used in columns for non-suppressed IC, namely silica, polystyrene–divinylbenzene and polymethacrylate. It was necessary to impose some limitations concerning the various combinations of eluents and stationary phase that could be used. For example, high pH eluents were unsuitable for use with the silica based column. Table I details the combinations of eluents and stationary phases that

TABLE III

RETENTION TIMES FOR ANIONS USING CARBONATE ELUENT ON A WATERS IC PAK A COLUMN

Concentration (m*M*):	0.49	0.99	1.49	1.49	1.99	1.98	2.49	2.48	2.99	2.98
pH:	10.3	8.5	8.5	10.3	8.5	10.3	8.5	10.3	8.5	10.3
Fluoride	3.85	7.75	5.76	3.09	4.60	2.46	4.01	2.26	3.70	2.01
Chloride	6.03	12.11	9.47	4.91	7.49	3.94	6.51	3.58	6.01	3.15
Bromide	10.66	24.06	17.42	9.60	13.71	7.14	11.83	6.61	10.86	5.61
Iodide	30.09	53.02	38.62	27.37	26.72	21.31	21.91	18.82	20.56	16.23
Chlorate	11.18	26.68	19.41	10.31	14.99	7.64	12.93	7.07	12.01	6.02
Bromate	5.37	12.61	9.30	4.51	7.33	3.46	6.35	3.34	5.90	2.92
Iodate	3.04	7.42	5.14	2.61	3.72	2.13	3.27	2.00	3.48	1.81
Nitrite	7.95	18.03	13.12	7.77	10.38	5.81	8.92	5.42	8.43	4.64
Nitrate	12.73	26.65	19.72	11.93	15.02	8.65	12.92	8.01	13.35	6.82
Bisulfite	4.20	9.76	7.24	3.53	5.70	2.84	4.98	2.51	4.64	2.32
Sulfite	41.90	49.35	37.34	29.77	24.47	16.81	20.14	14.42	18.97	10.41
Sulfate	42.16	51.51	34.59	29.78	24.08	16.82	19.43	14.39	18.41	10.41
Thiosulfate	79.16	–	139.98	54.25	82.93	30.60	61.32	27.23	53.05	18.97
Phosphate	36.75	51.05	32.14	23.90	20.62	13.60	16.64	11.49	18.33	8.45
Thiocyanate	57.73	57.33	40.73	50.58	29.83	40.94	24.79	38.32	23.02	20.47
Acetate	3.59	8.92	6.22	3.09	5.53	–	4.16	2.30	4.10	–
System	9.23	–	–	7.06	–	5.28	–	4.65	–	3.86
Void vol. eq.	0.85	0.81	0.79	0.85	0.80	0.86	0.80	0.84	0.81	0.86

were employed. Since retention times for each analyte were measured in triplicate, more than 8500 data points were acquired in this study.

Retention data

The retention times collected for the anions using the various combinations of eluents and stationary phases are presented in full in Tables II–VIII. It should be noted that some of the solutes were either unretained or were retained too strongly on the column to be eluted within a reasonable period of time (*i.e.* 4 h). In these cases, retention data are not shown. Tables II–VIII comprise a comprehensive database which will be used for the evaluation of further retention models in subsequent papers in this series.

Applicability of linear retention models

Plots of log k'_A *versus* $\log\{E_m^{y-}\}$ were prepared (where { } represents activity), in accordance with eqn. 2, for each combination of analyte, eluent and stationary phase. In each case, the points were fitted to a line of best fit using a linear regression analysis technique, giving correlation coefficients of 0.98 or higher. The observed slopes of these plots are presented in Tables IX–XV, together with theoretical slopes calculated using both the dominant equilibrium approach and the effective charge approach. These Tables show that neither of the above-mentioned approaches shows good agreement with the observed slopes.

TABLE IV

RETENTION TIMES FOR ANIONS USING GLUCONATE/BORATE ELUENTS ON TWO COLUMNS (HAMILTON PRP-X100 AND WATERS IC PAK A)

	Hamilton					Waters				
Concentration (m*M*)[a]:	1.10	1.46	1.83	2.20	2.56	1.10	1.46	1.83	2.20	2.56
pH:	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5
Fluoride	2.15	1.90	1.70	1.63	1.47	2.05	1.78	1.58	1.51	1.49
Chloride	4.37	3.75	3.27	3.07	2.72	3.40	2.85	2.48	2.30	2.30
Bromide	11.15	10.72	8.22	7.33	6.73	5.16	4.29	3.71	3.40	3.35
Iodide	–	–	–	–	–	14.23	11.59	9.77	8.90	8.93
Chlorate	26.71	24.24	23.03	17.87	17.70	5.71	4.69	4.05	3.70	3.66
Bromate	5.98	5.09	4.63	4.41	3.81	3.03	2.52	2.26	2.11	2.07
Iodate	2.11	2.07	1.74	1.54	1.46	1.82	1.62	1.60	1.17	1.07
Nitrite	6.39	5.69	4.89	4.78	4.00	4.15	3.51	3.04	2.79	2.76
Nitrate	17.30	12.56	13.09	11.86	9.91	6.05	5.06	4.33	4.02	3.85
Sulfite	30.03	20.50	15.04	12.92	10.13	14.29	9.52	6.88	5.67	5.15
Sulfate	30.60	20.57	14.80	12.55	10.10	14.29	9.53	6.89	5.61	5.08
Thiosulfate	–	72.10	–	57.03	29.83	30.08	19.90	14.17	11.36	9.91
Carbonate	2.80	2.41	2.11	1.97	1.76	2.61	2.23	1.96	1.83	1.72
Phosphate	17.05	13.62	8.77	7.20	6.02	10.19	6.73	5.03	4.18	3.75
Acetate	2.42	2.41	2.05	1.88	1.67	2.06	1.85	1.68	1.57	1.51
Oxalate	–	–	–	–	–	–	–	–	7.38	5.24
System	–	–	–	–	–	–	–	–	4.12	–
Void vol. eq.	0.77	0.82	0.81	0.83	0.82	0.90	0.89	0.88	0.89	0.91

[a] Refers to gluconate.

TABLE V

RETENTION TIMES FOR ANIONS USING HYDROXIDE ELUENT ON A WATERS IC PAK A COLUMN

Concentration (m*M*):	1.02	2.05	2.76	4.60
pH:	11–12	11–12	11–12	11–12
Fluoride	6.22	3.81	2.92	2.04
Chloride	10.38	5.63	4.31	2.89
Bromide	15.92	7.88	6.15	4.01
Iodide	45.09	19.82	15.62	9.65
Chlorate	14.57	8.14	6.38	4.13
Bromate	8.36	4.95	3.85	2.61
Iodate	5.32	3.31	2.68	1.92
Nitrite	11.82	6.75	5.22	3.43
Nitrate	16.83	9.19	7.23	4.64
Bisulfite	6.94	4.18	3.30	2.29
Sulfite	–	44.84	30.60	11.64
Sulfate	74.05	47.98	31.43	11.91
Thiosulfate	230.76	96.83	55.85	23.30
Carbonate	57.72	23.81	19.50	8.63
Phosphate	63.58	29.08	18.94	9.40
Thiocyanate	64.57	32.62	25.02	17.03
Acetate	5.42	3.24	3.07	2.08
Oxalate	60.86	26.04	20.77	9.05
System	–	36.20	23.59	10.63
Void vol. eq.	0.91	0.91	0.91	0.91

The data shown in Tables IX–XV were subjected to statistical analysis to determine the reliability to which retention times could be predicted. In each case, the retention time for a particular analyte, eluent and stationary phase combination, obtained at the lowest eluent concentration, was used as the basis for the prediction of other retention data. The plot of log k'_A *versus* $\log\{E_m^{y-}\}$ was assumed to be linear and the theoretical slope derived from either the dominant equilibrium approach or the effective charge approach was used to predict retention times at other eluent concentrations. The predicted and observed retention times were then compared using a paired data Student's *t*-test. The *t*-test was also applied to the retention times calculated using the slope of the line of best fit. Table XVI gives a summary of the *t*-test statistics and shows the percentage success of predicting retention times at the 95% confidence level.

From Table XVI it can be seen the success rate is variable, but the following trends emerge. First, prediction is most successful when the eluent contains a single competing anion (*e.g.* benzoate or phthalate at pH 4). Second, the effective charge approach gives slightly better prediction of retention times than the dominant equilibrium approach for eluents containing two competing anions (*e.g.* phthalate at pH 5). Third, neither the dominant equilibrium approach nor the effective charge approach can be considered to provide sufficient reliability in predicting solute retention times to permit their use as a theoretical model for optimization in IC.

TABLE VI

RETENTION TIMES FOR ANIONS USING PHOSPHATE ELUENTS ON TWO COLUMNS (HAMILTON PRP-X100 AND WATERS IC PAK A)

	Hamilton														
Concentration (m*M*):	1.98	2.96	4.00	4.00	3.93	4.84	6.00	8.00	7.84	10.00	9.77	15.00	20.00	25.00	30.00
pH:	10.0	10.0	5.0	7.2	10.0	10.0	7.2	5.0	7.2	5.0	7.2	5.0	5.0	5.0	5.0
Fluoride	1.75	1.50	3.91	1.85	1.35	1.30	1.41	1.44	—	1.08	1.34	—	—	—	—
Chloride	3.12	2.66	8.55	3.02	2.39	2.27	2.66	8.02	2.44	7.01	2.18	5.48	4.82	4.18	3.74
Bromide	7.14	5.93	23.04	6.93	5.27	5.00	6.16	19.89	5.58	17.44	5.35	13.15	11.62	9.91	8.72
Iodide	—	—	—	—	47.70	36.70	48.26	170.90	47.54	108.40	38.69	—	—	76.60	75.02
Chlorate	12.52	10.55	51.63	14.77	9.09	8.37	9.20	30.75	8.80	24.70	10.99	18.81	15.88	9.82	13.24
Bromate	5.70	4.92	17.74	5.17	4.32	4.07	4.98	16.30	4.40	14.07	4.05	11.01	9.37	8.10	7.17
Iodate	1.74	1.55	5.58	1.76	1.41	1.34	1.55	3.96	1.42	3.44	1.36	2.80	2.48	2.19	1.99
Nitrite	4.66	4.02	16.01	4.54	3.55	3.32	4.09	13.41	3.65	12.02	3.52	9.48	8.13	7.04	6.21
Nitrate	10.76	8.91	35.82	9.59	7.69	7.12	8.60	25.86	7.91	23.64	—	17.77	15.28	14.93	12.63
Bisulfite	2.34	2.02	7.47	5.03	1.81	1.72	3.57	5.70	2.84	5.26	2.37	4.21	3.68	3.23	2.89
Sulfite	—	—	—	—	—	—	22.05	—	13.50	—	—	—	—	—	—
Thiosulfate	44.76	31.25	—	39.50	18.64	19.26	28.23	—	21.07	—	18.32	—	—	—	—
Acetate	2.36	2.03	6.90	2.45	1.83	1.74	2.14	5.59	1.63	4.94	1.82	4.03	3.60	3.26	3.01
Oxalate	12.70	11.58	—	—	9.49	8.09	57.31	—	44.89	—	—	—	74.53	41.59	41.11
System	31.65	25.51	31.06	11.58	20.47	—	9.84	31.02	8.64	28.35	12.57	19.66	16.18	12.83	10.34
Void vol. eq.	0.79	0.79	0.75	0.80	0.79	0.79	0.80	0.74	0.80	0.76	0.80	0.76	0.78	0.76	0.76

	Waters											
Concentration (m*M*):	2.00	3.99	3.99	5.84	6.00	8.00	7.83	8.00	10.02	9.78	15.04	19.99
pH:	10.0	7.2	10.0	7.2	10.0	5.0	7.2	10.0	5.0	7.2	5.0	5.0
Fluoride	—	1.90	1.45	1.65	1.27	—	1.46	—	—	1.31	—	—
Chloride	3.45	3.27	2.86	3.08	2.43	10.12	2.76	2.02	8.45	2.57	6.73	5.89
Bromide	6.26	6.48	5.83	5.94	4.64	23.35	5.51	3.47	19.22	4.94	14.78	12.94
Iodide	24.58	25.84	19.71	23.26	17.57	103.43	21.03	11.94	84.37	6.32	65.65	56.76
Chlorate	7.21	7.39	6.18	6.82	5.07	27.03	6.08	3.80	20.62	5.62	17.36	12.94
Bromate	3.05	3.00	2.67	2.80	2.26	9.63	2.61	1.84	7.92	2.34	6.52	5.39
Iodate	1.61	1.52	1.50	1.49	1.28	3.69	1.44	1.16	3.22	1.28	2.73	2.31
Nitrite	5.01	5.08	4.31	4.61	3.61	17.58	4.25	2.74	14.27	3.79	11.83	9.61
Nitrate	8.62	8.64	7.38	8.01	6.12	35.78	7.29	4.39	29.30	6.58	21.62	18.30
Bisulfite	2.25	2.16	2.02	2.06	1.72	6.13	1.93	1.43	5.19	1.76	4.22	3.63
Sulfite	—	9.24	6.09	8.43	4.62	84.50	5.76	—	—	4.42	—	—
Thiosulfate	24.59	22.84	16.75	16.95	11.33	—	13.09	6.15	—	11.04	—	—
Thiocyanate	47.72	54.39	43.33	32.04	36.30	220.40	—	24.90	169.20	—	143.00	126.11
Acetate	1.85	1.78	1.78	1.76	1.45	3.84	1.66	1.35	3.41	1.47	2.79	2.44
Oxalate	8.95	—	7.41	—	6.34	—	—	—	113.22	6.91	—	—
System	17.13	2.03	14.01	2.18	4.07	29.50	1.90	6.61	21.01	1.63	17.78	13.16
Void vol. eq.	0.83	0.80	0.83	0.80	0.83	0.80	0.80	0.83	0.80	0.80	0.80	0.80

End-points approach

The data listed in Tables IX–XV give linear plots and this linearity is further confirmed in Table XVI which shows that the success rate (using *t*-statistics) obtained when the observed slope is used to calculate retention times was 100%. However, this

TABLE VII

RETENTION TIMES FOR ANIONS USING PHTHALATE ELUENTS ON THREE COLUMNS (HAMILTON PRP-X100, VYDAC 302 IC 4.6 AND WATERS IC PAK A)

	Hamilton								
Concentration (m*M*):	1.00	1.00	1.00	2.00	2.00	2.00	4.00	4.00	4.00
pH:	4.0	5.0	6.0	4.0	5.0	6.0	4.0	5.0	6.0
Fluoride	2.96	2.10	1.65	2.02	1.52	0.81	1.45	1.37	0.82
Chloride	4.02	2.61	2.16	2.60	1.82	1.65	1.75	1.41	1.33
Bromide	5.14	3.41	2.94	3.25	2.32	2.19	2.11	1.69	1.70
Iodide	11.16	7.95	8.00	6.60	5.18	5.71	4.01	3.36	4.11
Chlorate	6.65	4.57	4.36	3.97	2.99	3.15	2.50	2.08	2.39
Bromate	3.93	2.62	2.26	2.49	1.85	1.74	1.75	1.42	1.40
Iodate	2.97	1.85	1.58	1.97	1.43	1.26	1.41	1.17	1.11
Nitrite	4.40	2.92	2.45	2.80	2.04	1.86	1.97	1.52	1.49
Nitrate	5.91	3.82	3.47	3.54	2.62	2.52	2.32	1.87	1.93
Sulfite	39.21	13.94	8.31	14.10	6.26	4.26	5.60	3.02	2.42
Sulfate	39.37	14.15	8.35	14.07	6.29	4.30	5.58	3.04	2.42
Thiosulfate	71.81	23.32	14.08	23.47	10.01	6.97	8.93	4.54	3.70
Phosphate	3.01	1.96	2.01	2.01	1.49	1.51	1.39	1.20	1.22
Acetate	2.13	2.01	1.81	1.95	1.66	1.45	1.67	1.45	1.23
Oxalate	53.78	13.54	8.96	–	6.36	5.04	4.04	3.66	3.40
System	55.00	43.33	–	46.00	22.96	–	30.00	13.64	–
Void vol. eq.	0.71	0.74	0.77	0.75	0.78	0.79	0.78	0.83	0.81

	Vydac								
Concentration (m*M*)	1.00	1.00	1.00	2.00	2.00	2.00	4.00	4.00	4.00
pH:	4.0	5.0	6.0	4.0	5.0	6.0	4.0	5.0	6.0
Chloride	10.92	6.34	5.05	6.84	4.51	3.49	4.63	3.33	2.70
Bromide	13.20	7.85	6.77	8.15	5.43	4.13	5.30	3.75	3.02
Iodide	22.49	14.36	15.45	13.30	9.29	6.90	7.91	5.53	4.30
Chlorate	13.26	7.96	7.12	8.27	5.53	4.15	5.41	3.90	3.07
Bromate	9.97	5.83	4.67	6.36	4.27	3.32	4.52	3.20	2.65
Iodate	8.07	4.37	3.29	5.30	3.50	2.83	3.86	2.96	2.41
Nitrite	11.93	7.55	6.43	7.57	5.28	3.97	5.10	3.70	2.95
Nitrate	14.59	8.82	6.90	8.93	6.04	4.53	5.81	4.05	3.21
Sulfite	48.00	35.63	19.22	54.35	17.18	8.56	22.90	8.12	4.40
Sulfate	48.00	35.42	18.52	53.40	17.17	8.61	22.68	8.13	4.42
Thiosulfate	86.40	55.76	29.32	70.61	22.48	11.26	28.05	10.01	5.33
Phosphate	10.02	5.59	4.84	6.35	4.03	4.05	4.51	4.03	3.23
Acetate	3.83	4.40	3.73	3.27	3.76	3.28	2.76	2.98	2.70
Oxalate	37.45	27.63	21.81	24.00	22.63	12.26	18.00	12.34	5.96
System	48.00	39.55	–	24.00	–	–	18.00	12.34	–
Void vol. eq.	1.45	1.62	1.78	1.60	1.68	1.75	1.52	1.79	1.87

TABLE VII (*continued*)

	Waters								
Concentration (m*M*):	1.00	1.00	1.00	2.00	2.00	2.00	4.00	4.00	4.00
pH:	4.0	5.0	6.0	4.0	5.0	6.0	4.0	5.0	6.0
Fluoride	3.76	2.07	1.67	2.29	1.42	1.26	1.69	1.27	1.15
Chloride	6.26	3.93	3.61	3.99	2.53	2.29	2.70	1.94	1.85
Bromide	9.81	8.10	6.53	6.25	4.12	4.07	3.96	2.97	2.92
Iodide	28.14	28.13	23.18	17.58	12.79	13.60	10.42	9.35	8.95
Chlorate	10.43	6.81	5.69	6.83	4.67	4.26	4.07	3.15	3.37
Bromate	5.18	3.26	2.66	3.62	2.38	2.08	2.29	1.76	1.74
Iodate	3.16	2.11	1.66	2.29	1.56	1.32	1.86	1.28	1.07
Nitrite	7.91	5.37	5.26	5.03	3.70	3.25	3.22	2.57	2.35
Nitrate	11.85	9.14	8.83	7.72	6.26	5.29	4.73	3.75	3.61
Sulfite	53.60	17.19	10.44	24.62	8.27	5.63	10.74	4.21	2.85
Sulfate	53.28	17.92	10.62	24.29	8.05	5.72	10.76	4.10	2.81
Thiosulfate	109.77	34.00	18.68	–	14.62	9.36	16.71	7.10	5.14
Phosphate	3.43	2.23	2.10	2.14	1.61	1.55	2.45	1.26	1.30
Acetate	1.69	1.98	1.92	1.36	1.55	1.50	1.08	1.29	1.31
Oxalate	36.39	22.20	15.84	17.30	10.04	6.99	7.33	4.63	3.50
System	35.00	26.78	–	22.00	15.86	–	12.00	9.72	–
Void vol. eq.	0.72	0.65	0.77	0.65	0.68	0.60	0.66	0.76	0.71

success rate is of limited practical value in optimization procedures since it can be attained only after retention data are measured for at least 5 points across the search area. As stated earlier, acquisition of these data would be a time consuming process.

One possible compromise between the theoretical approaches (*i.e.* the dominant equilibrium and the effective charge methods) and the experimental technique is to define the slope of the retention plot by measuring retention data at the extremes of the search area. Retention times for eluent compositions which are intermediate between the measured points could then be calculated by assuming linearity of the retention plot. This method can be termed the "end points" approach. The success rate for this approach is shown in Table XVI, from which it can be seen that the end points method is certainly more successful than either of the theoretical methods and so can be considered more appropriate for use in an optimization routine for IC. The main advantage of this method is that only two experiments are necessary to permit prediction of solute retention times for any eluent composition in the search area.

Optimization of eluent composition using the end points approach

A limited optimization of the separation of a mixture of inorganic anions using the "end points" approach was performed. The optimization strategy employed has been described in detail earlier [1]. Since this approach enables one parameter to be optimized at a time, only the concentration of the competing ions in the eluent was optimized. Phthalate eluents at pH 5.0 were employed since at this pH value, both the singly and doubly charged forms are present. Two initial experiments were performed in which retention times for each solute ion were obtained at two limiting eluent concentrations, namely 1 m*M* and 4 m*M*. This defined the search area of eluent

TABLE VIII

RETENTION TIMES FOR ANIONS USING *p*-TOLUENESULFONATE ELUENTS ON THREE COLUMNS (HAMILTON PRP-X100, VYDAC 302 IC 4.6 AND WATERS IC PAK A)

	Hamilton				Vydac				Waters			
Concentration (m*M*):	1.00	2.00	3.00	4.00	2.00	3.00	4.00	5.00	2.00	3.00	4.00	5.00
pH:	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Fluoride	2.74	1.85	1.52	1.32	—	—	—	—	3.54	2.74	2.35	1.96
Chloride	4.15	2.34	1.80	1.57	6.45	5.15	4.04	3.55	6.88	4.59	3.70	3.14
Bromide	4.81	2.77	2.15	1.79	6.97	4.99	4.07	3.59	10.02	6.89	5.74	4.61
Iodide	9.30	5.66	4.03	3.31	8.76	5.92	4.50	3.96	29.04	19.65	14.91	12.68
Chlorate	6.18	3.45	2.53	2.13	6.97	5.24	4.09	3.61	10.69	7.21	6.03	4.92
Bromate	3.85	2.26	1.75	1.52	6.55	4.74	3.88	3.46	5.54	3.93	3.33	2.77
Iodate	2.98	1.85	1.61	1.44	6.34	4.76	3.82	3.41	3.56	2.64	2.29	1.95
Nitrite	4.03	2.53	1.98	1.71	7.42	5.14	4.14	3.56	7.66	5.56	4.65	3.71
Nitrate	5.41	3.08	2.28	1.95	7.52	5.53	4.27	3.76	12.40	8.47	6.75	5.64
Bisulfite	—	1.70	—	—	—	—	—	—	—	—	2.44	—
Sulfite	9.99	7.77	5.08	3.51	75.23	38.94	16.43	13.85	60.75	26.70	16.77	11.16
Sulfate	9.70	7.71	5.06	3.52	81.87	34.21	16.51	13.99	59.29	26.87	16.18	11.25
Thiosulfate	38.73	14.08	8.45	5.17	92.85	66.54	20.89	14.36	114.57	48.97	32.25	19.38
Phosphate	2.95	1.98	1.43	1.53	10.14	7.07	5.41	4.10	3.42	2.62	2.24	1.86
Thiocyanate	—	12.49	—	—	—	—	—	—	—	—	30.49	—
Acetate	1.97	1.80	1.61	1.39	3.40	3.20	2.94	2.49	1.64	1.66	1.50	1.28
Oxalate	8.43	6.08	3.85	—	74.17	—	—	11.68	—	49.40	17.73	8.04
System	10.63	9.45	10.66	—	36.00	28.10	18.30	13.88	41.70	42.54	18.81	12.10
Void vol. eq.	0.75	0.82	0.88	0.93	1.47	1.58	1.66	1.70	0.74	0.75	0.77	0.72

TABLE IX

OBSERVED AND PREDICTED SLOPES OF LOG *k'* *VERSUS* LOG{BENZOATE} PLOTS FOR ANIONS ON THREE COLUMNS (HAMILTON PRP-X100, VYDAC 302 IC 4.6 AND WATERS IC PAK A)

	pH 4.0				pH 6.4					
Model:	Dominant equilibrium	Effective charge	Vydac		Dominant equilibrium	Effective charge	Hamilton		Waters	
			Observed slope	End points			Observed slope	End points	Observed slope	End points
Fluoride	–	–	–	–	–1.000	–1.000	–1.705	–1.703	–0.953	–0.946
Chloride	–1.000	–2.564	–1.334	–1.426	–1.000	–1.000	–1.515	–1.493	–1.033	–1.009
Bromide	–1.000	–2.564	–1.314	–1.411	–1.000	–1.000	–1.387	–1.367	–0.989	–0.982
Iodide	–1.000	–2.564	–1.297	–1.398	–1.000	–1.000	–1.486	–1.482	–1.045	–1.011
Chlorate	–1.000	–2.564	–1.311	–1.411	–1.000	–1.000	–1.452	–1.441	–1.040	–1.033
Bromate	–1.000	–2.564	–1.250	–1.239	–1.000	–1.000	–1.486	–1.474	–0.993	–0.987
Iodate	–1.000	–2.564	–1.325	–1.422	–1.000	–1.000	–1.488	–1.441	–0.942	–0.939
Nitrite	–0.880	–2.256	–1.302	–1.385	–1.000	–1.000	–1.482	–1.466	–1.040	–1.036
Nitrate	–1.000	–2.564	–1.250	–1.248	–1.000	–1.000	–1.494	–1.481	–1.035	–1.026
Bisulfite	–0.990	–2.538	–1.165	–1.148	–	–	–	–	–	–
Sulfite	–1.980	–2.538	–2.914	–2.914	–1.140	–1.140	–2.745	–2.721	–1.832	–1.821
Sulfate	–2.000	–5.128	–2.754	–2.932	–2.000	–2.000	–2.657	–2.547	–1.847	–1.834
Thiosulfate	–2.000	–5.128	–2.956	–2.956	–2.000	–2.000	–2.669	–2.508	–1.929	–1.911
Phosphate	–0.990	–2.538	–0.553	–0.612	–1.140	–1.140	–2.431	–2.283	–0.935	–0.979
Thiocyanate	–1.000	–2.564	–1.214	–1.202	–	–	–	–	–	–
Acetate	–0.150	–0.384	–0.741	–0.745	–0.980	–0.980	–1.440	–1.427	–0.939	–0.937
Oxalate	–1.380	–3.538	–	–	–1.990	–1.990	–2.489	–2.529	–	–
System	–	–	–	–	–	–	–0.815	–0.815	–	–

TABLE X

OBSERVED AND PREDICTED SLOPES OF LOG *k'* *VERSUS* LOG{CARBONATE} PLOTS FOR ANIONS ON A WATERS IC PAK A COLUMN

	pH 8.5				pH 10.3			
Model:	Dominant equilibrium	Effective charge	Waters		Dominant equilibrium	Effective charge	Waters	
			Observed slope	End points			Observed slope	End points
Fluoride	−0.500	−1.000	−0.832	−0.812	−0.500	−0.667	−0.521	−0.553
Chloride	−0.500	−1.000	−0.744	−0.719	−0.500	−0.667	−0.441	−0.468
Bromide	−0.500	−1.000	−0.796	−0.778	−0.500	−0.667	−0.387	−0.418
Iodide	−0.500	−1.000	−0.959	−0.901	−0.500	−0.667	−0.342	−0.370
Chlorate	−0.500	−1.000	−0.803	−0.776	−0.500	−0.667	−0.370	−0.400
Bromate	−0.500	−1.000	−0.802	−0.779	−0.500	−0.667	−0.425	−0.451
Iodate	−0.500	−1.000	−0.931	−0.839	−0.500	−0.667	−0.452	−0.483
Nitrite	−0.500	−1.000	−0.784	−0.757	−0.500	−0.667	−0.330	−0.363
Nitrate	−0.500	−1.000	−0.734	−0.671	−0.500	−0.667	−0.368	−0.396
Bisulfite	−0.500	−1.000	−0.813	−0.788	−0.500	−0.667	−0.460	−0.477
Sulfite	−1.000	−2.000	−0.985	−0.912	−1.000	−1.333	−0.783	−0.831
Sulfate	−1.000	−2.000	−1.036	−0.981	−1.000	−1.333	−0.787	−0.835
Thiosulfate	−1.000	−2.000	−1.502	−1.485	−1.000	−1.333	−0.782	−0.834
Phosphate	−1.000	−2.000	−1.090	−0.977	−1.000	−1.333	−0.842	−0.885
Thiocyanate	−0.500	−1.000	−0.905	−0.866	−0.500	−0.667	−0.456	−0.609
Acetate	−0.500	−1.000	−0.867	−0.836	−0.500	−0.667	−0.355	−0.388
System	–	–	–	–	–	–	−0.550	−0.588

TABLE XI

OBSERVED AND PREDICTED SLOPES OF LOG *k'* *VERSUS* LOG{GLUCONATE} PLOTS FOR ANIONS ON TWO COLUMNS (HAMILTON PRP-X100 AND WATERS IC PAK A) AT pH 8.5

Model:	Dominant equilibrium	Effective charge	Hamilton		Waters	
			Observed slope	End points	Observed slope	End points
Fluoride	−1.000	−1.000	−0.943	−0.980	−0.848	−0.832
Chloride	−1.000	−1.000	−0.825	−0.851	−0.754	−0.725
Bromide	−1.000	−1.000	−0.817	−0.759	−0.710	−0.690
Iodide	−1.000	−1.000	–	–	−0.658	−0.628
Chlorate	−1.000	−1.000	−0.627	−0.586	−0.713	−0.694
Bromate	−1.000	−1.000	−0.697	−0.750	−0.758	−0.755
Iodate	−1.000	−1.000	−1.048	−0.970	−2.074	−2.138
Nitrite	−1.000	−1.000	−0.720	−0.766	−0.725	−0.699
Nitrate	−1.000	−1.000	−0.686	−0.801	−0.700	−0.692
Sulfite	−1.960	−1.960	−1.430	−1.466	−1.434	−1.409
Sulfate	−2.000	−2.000	−1.471	−1.492	−1.457	−1.430
Thiosulfate	−2.000	−2.000	−1.426	−1.640	−1.455	−1.439
Phosphate	−1.960	−1.960	−1.519	−1.461	−1.460	−1.453
Acetate	−1.000	−1.000	−0.897	−0.886	−0.818	−0.824
Oxalate	−2.000	−2.000	–	–	−2.927	−2.927
Carbonate	−1.010	−1.010	−1.003	−1.035	−0.901	−0.914

TABLE XII

OBSERVED AND PREDICTED SLOPES OF LOG *k'* *VERSUS* LOG{HYDROXIDE} PLOTS ON A WATERS IC PAK A COLUMN AT pH 11–12

Model:	Dominant equilibrium	Effective charge	Waters	
			Observed slope	End points
Fluoride	−1.000	−1.000	−1.058	−1.058
Chloride	−1.000	−1.000	−1.070	−1.069
Bromide	−1.000	−1.000	−1.077	−1.079
Iodide	−1.000	−1.000	−1.103	−1.108
Chlorate	−1.000	−1.000	−0.983	−0.987
Bromate	−1.000	−1.000	−1.010	−1.013
Iodate	−1.000	−1.000	−1.003	−1.007
Nitrite	−1.000	−1.000	−1.000	−1.003
Nitrate	−1.000	−1.000	−0.987	−0.992
Bisulfite	−1.000	−1.000	−1.006	−1.008
Sulfite	−2.000	−2.000	−1.825	−1.797
Sulfate	−2.000	−2.000	−1.269	−1.296
Thiosulfate	−2.000	−2.000	−1.592	−1.593
Phosphate	−2.000	−2.000	−1.365	−1.367
Thiocyanate	−1.000	−1.000	−0.944	−0.939
Acetate	−1.000	−1.000	−0.893	−0.923
Oxalate	−2.000	−2.000	−1.333	−1.365
Carbonate	−2.000	−2.000	−1.329	−1.363
System	—	—	−1.650	−1.641

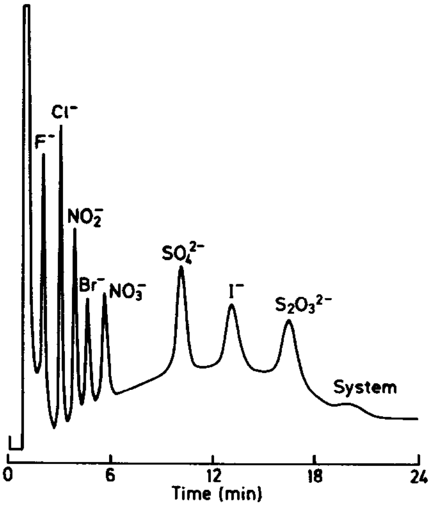

Fig. 1. Chromatogram obtained using the optimal mobile phase composition predicted by the end-points optimization strategy. Conditions: eluent, 1.74 m*M* phthalate at pH 5.0; column, Waters IC Pak A at 35°C; flow-rate, 1.0 ml/min; solute concentrations, Cl^-, Br^-, NO_2^-, NO_3^-, SO_4^{2-}, $S_2O_3^{2-}$ (all 10 ppm), F^- (20 ppm) and I^- (30 ppm); injection volume, 20 μl.

ABLE XIII

BSERVED AND PREDICTED SLOPES OF LOG *k'* *VERSUS* LOG{PHOSPHATE} PLOTS FOR ANIONS N TWO COLUMNS (HAMILTON PRP-X100 AND WATERS IC PAK A)

	pH 5.0						pH 7.2	
odel:	Dominant equilibrium	Effective charge	Hamilton		Waters		Dominant equilibrium	Effective charge
			Observed slope	End points	Observed slope	End points		
luoride	−0.495	−0.990	−2.547	−2.640	–	–	−0.500	−0.667
hloride	−0.500	−1.000	−0.588	−0.518	−0.653	−0.662	−0.500	−0.667
romide	−0.500	−1.000	−0.583	−0.552	−0.674	−0.677	−0.500	−0.667
odide	−0.500	−1.000	−0.611	−0.700	−0.654	−0.664	−0.500	−0.667
hlorate	−0.500	−1.000	−0.946	−1.011	−0.774	−0.840	−0.500	−0.667
romate	−0.500	−1.000	−0.564	−0.524	−0.684	−0.715	−0.500	−0.667
odate	−0.500	−1.000	−0.740	−0.733	−0.690	−0.714	−0.500	−0.667
itrite	−0.495	−0.990	−0.576	−0.553	−0.668	−0.704	−0.500	−0.667
itrate	−0.500	−1.000	−0.590	−0.585	−0.757	−0.757	−0.500	−0.667
isulfite	−0.505	−1.010	−0.625	−0.615	−0.677	−0.693	−0.500	−0.667
ulfite	−1.000	−2.000	–	–	–	–	−1.000	−1.333
hiosulfate	−1.000	−2.000	–	–	–	–	−1.000	−1.333
hiocyanate	−0.500	−1.000	–	–	−0.576	−0.615	−0.500	−0.667
cetate	−0.315	−0.630	−0.565	−0.540	−0.673	−0.673	−0.500	−0.667
xalate	−0.930	−1.860	−1.609	−1.565	–	–	−1.000	−1.333
ystem	–	–	−0.660	−0.618	−0.838	−0.923	–	–

concentrations over which the optimization process would operate. The retention times of the solute anions at eluent concentrations throughout the search area were predicted by assuming linearity between log k' and log{eluent} (an assumption which has been justified throughout this work). A suitable optimization criterion [1] was then used to predict the eluent concentration providing the best separation of the anion mixture. The chromatogram obtained with this predicted concentration (1.74 m*M*) is shown in Fig. 1, from which it can be seen that resolution of all eight anions present in the mixture, and the system peak, was achieved. Table XVII shows the observed retention times for this eluent composition, together with those predicted from the linear retention model. The differences between these retention times are also listed in Table XVII, from which the correlation between predicted and actual retention times can be seen to be good. This further indicates the validity of the linear retention model which permits successful one-factor optimization using the "end points" approach to be achieved.

CONCLUSION

Simple linear retention models are of limited suitability for optimization in IC. Extensive retention data for a range of analytes, eluents and stationary phases demonstrate that plots of log k'_A *versus* log{E_m^{y-}} show good linearity, but the slopes of these plots are not in accordance with theoretical predictions. Linear models are therefore unreliable for use in theoretical optimizations unless the slopes of the

				pH 10.0					
Hamilton		Waters		Dominant equilibrium	Effective charge	Hamilton		Waters	
Observed slope	End points	Observed slope	End points			Observed slope	End points	Observed slope	End points
−0.781	−0.795	−0.841	−0.849	−0.500	−0.500	−0.734	−0.713	−0.831	−0.831
−0.546	−0.562	−0.382	−0.375	−0.500	−0.500	−0.523	−0.513	−0.545	−0.569
−0.359	−0.348	−0.340	−0.352	−0.500	−0.500	−0.471	−0.462	−0.485	−0.519
−0.474	−0.490	−1.430	−1.685	−0.500	−0.500	−1.251	−1.251	−0.492	−0.549
−0.436	−0.372	−0.346	−0.348	−0.500	−0.500	−0.500	−0.492	−0.515	−0.551
−0.355	−0.350	−0.384	−0.401	−0.500	−0.500	−0.465	−0.453	−0.534	−0.565
−0.639	−0.625	−0.410	−0.459	−0.500	−0.500	−0.625	−0.616	−0.604	−0.616
−0.393	−0.376	−0.384	−0.397	−0.500	−0.500	−0.489	−0.481	−0.525	−0.565
−0.329	−0.331	−0.333	−0.338	−0.500	−0.500	−0.521	−0.512	−0.520	−0.565
−1.158	−1.161	−0.370	−0.383	−0.500	−0.500	−0.592	−0.581	−0.583	−0.617
−1.520	−1.546	−0.959	−0.944	−1.000	−1.000	—	—	−0.807	−0.807
−0.954	−0.930	−0.872	−0.854	−1.000	−1.000	−1.313	−1.340	−1.010	−1.080
—	—	−1.378	−1.378	−0.500	−0.500	—	—	−0.433	−0.481
−0.704	−0.561	−0.388	−0.418	−0.500	−0.500	−0.573	−0.561	−0.509	−0.494
−0.982	−0.982	—	—	−1.000	−1.000	−1.000	−0.994	−0.348	−0.353
−0.017	0.105	−0.428	−0.438	—	—	−0.663	−0.670	−1.001	−0.748

TABLE XIV

OBSERVED AND PREDICTED SLOPES OF LOG k' *VERSUS* LOG{PHTHALATE} PLOTS FOR ANIONS ON THREE COLUMNS (HAMILTON PRP-X100, VYDAC 302 IC 4.6 AND WATERS IC PAK A)

Model:	pH 4.0							
	Dominant equilibrium	Effective charge	Hamilton		Waters		Vydac	
			Observed slope	End points	Observed slope	End points	Observed slope	End points
Fluoride	−0.435	−0.935	−1.041	−1.042	−0.792	−0.792	—	—
Chloride	−0.500	−1.075	−1.049	−1.049	−0.725	−0.726	−0.924	−0.923
Bromide	−0.500	−1.075	−1.030	−1.031	−0.737	−0.737	−0.940	−0.940
Iodide	−0.500	−1.075	−1.008	−1.008	−0.751	−0.752	−0.985	−0.985
Chlorate	−0.500	−1.075	−1.060	−1.060	−0.762	−0.763	−0.922	−0.921
Bromate	−0.500	−1.075	−1.026	−1.026	−0.728	−0.730	−0.870	−0.869
Iodate	−0.500	−1.075	−1.087	−1.087	−0.498	−0.498	−0.866	−0.864
Nitrite	−0.440	−0.946	−0.976	−1.976	−0.751	−0.752	−0.892	−0.891
Nitrate	−0.500	−1.075	−1.042	−1.042	−0.731	−0.732	−0.928	−0.927
Sulfite	−1.000	−2.150	−1.727	−1.727	−1.248	−1.249	−0.653	−0.657
Sulfate	−1.000	−2.150	−1.735	−1.735	−1.242	−1.243	−0.659	−0.664
Thiosulfate	−1.000	−2.150	−1.798	−1.798	—	—	−0.961	−0.964
Phosphate	−0.495	−1.064	−1.135	−1.136	−0.265	−0.262	−0.876	−0.875
Acetate	−0.075	−0.161	−0.445	−0.446	−0.598	−0.600	−0.555	−0.554
Oxalate	−0.690	−1.483	−2.295	−2.295	−1.262	−1.264	−0.661	−0.659
System	—	—	−0.565	−0.566	−0.810	−0.811	−0.867	−0.864

(*Continued on p. 56*)

TABLE XIV (*continued*)

pH 5.0

Model:	Dominant equilibrium	Effective charge	Hamilton		Waters		Vydac	
			Observed slope	End points	Observed slope	End points	Observed slope	End points
Fluoride	−0.495	−0.779	−0.821	−0.828	−0.947	−0.946	–	–
Chloride	−0.500	−0.787	−1.021	−1.021	−0.937	−0.937	−0.968	−0.969
Bromide	−0.500	−0.787	−0.995	−0.995	−1.093	−1.092	−0.999	−1.000
Iodide	−0.500	−0.787	−0.924	−0.924	−1.050	−1.048	−1.053	−1.054
Chlorate	−0.500	−0.787	−0.982	−0.982	−0.876	−0.877	−0.955	−0.955
Bromate	−0.500	−0.787	−1.017	−1.018	−0.888	−0.889	−0.950	−0.951
Iodate	−0.500	−0.787	−1.035	−1.035	−0.942	−0.942	−0.761	−0.761
Nitrite	−0.495	−0.779	−1.004	−1.004	−0.887	−0.888	−0.981	−0.982
Nitrate	−0.500	−0.787	−0.953	−0.953	−0.954	−0.955	−1.002	−1.003
Sulfite	−1.000	−1.574	−1.522	−1.522	−1.370	−1.371	−1.415	−1.416
Sulfate	−1.000	−1.574	−1.525	−1.525	−1.431	−1.431	−1.410	−1.411
Thiosulfate	−1.000	−1.574	−1.528	−1.528	−1.444	−1.444	−1.578	−1.578
Phosphate	−0.500	−0.787	−1.042	−1.043	−1.030	−1.031	−0.537	−0.535
Acetate	−0.315	−0.496	−0.665	−0.665	−0.858	−0.859	−0.752	−0.754
Oxalate	−0.930	−1.464	−1.292	−1.291	−1.490	−1.491	−0.794	−0.797
System	–	–	−1.046	−1.045	−0.976	−0.977	−1.096	−1.096

pH 6.0

Model:	Dominant equilibrium	Effective charge	Hamilton		Waters		Vydac	
			Observed slope	End points	Observed slope	End points	Observed slope	End points
Fluoride	−0.500	−0.555	3.618	3.601	−0.500	−0.502	–	–
Chloride	−0.500	−0.555	−0.819	−0.819	−0.663	−0.664	−1.128	−1.129
Bromide	−0.500	−0.555	−0.746	−0.746	−0.694	−0.696	−1.205	−1.205
Iodide	−0.500	−0.555	−0.663	−0.663	−0.730	−0.732	−1.410	−1.410
Chlorate	−0.500	−0.555	−0.693	−0.693	−0.424	−0.426	−1.242	−1.242
Bromate	−0.500	−0.555	−0.778	−0.778	−0.414	−0.416	−1.084	−1.085
Iodate	−0.500	−0.555	−0.822	−0.822	−0.641	−0.645	−0.849	−0.851
Nitrite	−0.500	−0.555	−0.765	−0.765	−0.734	−0.736	−1.197	−1.198
Nitrate	−0.500	−0.555	−0.741	−0.741	−0.747	−0.749	−1.106	−1.107
Sulfite	−1.000	−1.111	−1.267	−1.267	−1.133	−1.136	−1.573	−1.574
Sulfate	−1.000	−1.111	−1.275	−1.275	−1.160	−1.164	−1.536	−1.537
Thiosulfate	−1.000	−1.111	−1.258	−1.258	−1.045	−1.047	−1.690	−1.690
Phosphate	−0.500	−0.588	−0.926	−0.927	−0.579	−0.582	−0.682	−0.684
Acetate	−0.475	−0.527	−0.753	−0.753	−0.448	−0.451	−0.721	−0.723
Oxalate	−0.990	−1.100	−0.957	−0.957	−1.273	−1.275	−1.301	−1.303

TABLE XV

OBSERVED AND PREDICTED SLOPES OF LOG *k'* *VERSUS* LOG{*p*-TOLUENESULFONATE} PLOTS FOR ANIONS ON THREE COLUMNS (HAMILTON PRP-X100, VYDAC 302 IC 4.6 AND WATERS IC PAK A) AT pH 4.0

Model:	Dominant equilibrium	Effective charge	Hamilton		Waters		Vydac	
			Observed slope	End points	Observed slope	End points	Observed slope	End points
Fluoride	−0.870	−0.870	−1.326	−1.375	−0.900	−0.897	–	–
Chloride	−1.000	−1.000	−1.368	−1.396	−1.041	−1.020	−1.300	−1.279
Bromide	−1.000	−1.000	−1.270	−1.309	−0.949	−0.949	−1.378	−1.370
Iodide	−1.000	−1.000	−1.093	−1.108	−0.973	−0.940	−1.511	−1.485
Chlorate	−1.000	−1.000	−1.255	−1.278	−0.945	−0.943	−1.377	−1.353
Bromate	−1.000	−1.000	−1.359	−1.389	−0.935	−0.929	−1.373	−1.361
Iodate	−1.000	−1.000	−1.210	−1.259	−0.918	−0.908	−1.364	−1.344
Nitrite	−0.880	−0.880	−1.198	−1.224	−0.913	−0.916	−1.477	−1.477
Nitrate	−1.000	−1.000	−1.267	−1.288	−0.961	−0.941	−1.404	−1.380
Sulfite	−2.000	−2.000	−1.073	−1.105	−1.947	−1.942	−2.329	−2.200
Sulfate	−2.000	−2.000	−1.046	−1.078	−1.929	−1.905	−2.382	−2.282
Thiosulfate	−2.000	−2.000	−1.251	−1.784	−1.981	−2.010	−2.536	−2.393
Phosphate	−0.990	−0.990	−1.209	−1.122	−0.940	−0.936	−1.585	−1.615
Acetate	−0.150	−0.150	−0.835	−0.887	−0.518	−0.515	−1.118	−1.178
Oxalate	−1.380	−1.380	−1.000	−1.037	−3.764	−3.759	−2.404	−2.404
System	–	–	−0.178	−0.159	−1.497	−1.414	−1.361	−1.341

TABLE XVI

SUMMARY OF *t*-TEST STATISTICS SHOWING PERCENTAGE SUCCESS OF PREDICTING RETENTION TIMES USING FOUR RETENTION MODELS

Column	Eluent	pH	Retention model			
			Dominant equilibrium	Effective charge	End points	Observed slope
Hamilton	Benzoate	6.4	93.3	93.3	100.0	100.0
	Gluconate/borate	8.5	35.7	35.7	100.0	100.0
	Phosphate	5.0	50.0	16.6	27.2	100.0
	Phosphate	7.2	53.8	53.8	80.0	100.0
	Phosphate	10.0	66.6	66.6	90.0	100.0
	Phthalate	4.0	78.6	92.8	–	100.0
	Phthalate	5.0	66.7	100.0	–	100.0
	Phthalate	6.0	73.3	73.3	–	100.0
	p-Toluenesulfonate	4.0	26.7	26.7	92.8	100.0
Vydac	Benzoate	4.0	42.8	7.1	91.6	100.0
	Phthalate	4.0	26.6	92.8	–	100.0
	Phthalate	5.0	92.8	100.0	–	100.0
	Phthalate	6.0	85.7	85.7	–	100.0
	p-Toluenesulfonate	4.0	30.7	30.7	85.7	100.0

(*Continued on p. 58*)

TABLE XVI (*continued*)

Column	Eluent	pH	Retention model			
			Dominant equilibrium	Effective charge	End points	Observed slope
Waters	Benzoate	6.4	100.0	100.0	100.0	100.0
	Carbonate/bicarbonate	8.5	18.7	25.0	93.7	100.0
	Carbonate/bicarbonate	10.3	68.7	6.2	93.7	100.0
	Gluconate/borate	8.5	6.6	6.6	13.3	100.0
	Hydroxide	11–12	66.6	66.6	94.1	100.0
	Phosphate	5.0	0.0	90.9	75.7	100.0
	Phosphate	7.2	38.4	15.4	64.3	100.0
	Phosphate	10.0	92.3	92.3	76.9	100.0
	Phthalate	4.0	100.0	85.7	–	100.0
	Phthalate	5.0	66.7	93.3	–	100.0
	Phthalate	6.0	100.0	100.0	–	100.0
	p-Toluenesulfonate	4.0	73.3	73.3	86.6	100.0
Times model was more than 90% successful			6/26	10/26	9/17	26/26

TABLE XVII

COMPARISON OF PREDICTED AND ACTUAL RETENTION TIMES OBTAINED FOR EIGHT ANIONS USING 1.74 m*M* PHTHALATE ELUENT AT pH 5.0 ON A WATERS IC PAK A COLUMN

Anions	Predicted retention time (min)	Actual retention time (min)	Difference (%)
F^-	1.78	1.80	1.12
Cl^-	2.77	2.81	1.44
Br^-	4.35	4.37	0.45
I^-	12.72	12.82	0.78
NO_2^-	3.60	3.62	0.55
NO_3^-	5.33	5.37	0.75
SO_4^{2-}	9.65	9.78	1.34
$S_2O_3^{2-}$	15.74	16.18	2.79

retention plots are determined by preliminary measurements of retention times at the extremes (end points) of the search area. Under these circumstances, successful optimization can be achieved.

Although the end points approach offers promise, it is limited in its utility since it can be applied to only one eluent parameter at a time. In order to optimize both the eluent concentration and pH, a more complex retention model is necessary. The multiple eluent species model [9] or its variants [10,11] may be suitable for this purpose, and we are currently undertaking a comprehensive evaluation of these models.

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