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## Review

# Control of separation selectivity in capillary zone electrophoresis of inorganic anions

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### Abstract

The control of the separation selectivity of anions in capillary zone electrophoresis is critically reviewed. Selectivity effects arising from the chemical environment of the analyte (that is, the pH, surfactant content and organic modifier content of the background electrolyte and the presence of complexing species) are shown to be more significant than those arising from physical effects, such as the sampling mode and the separation conditions. In general, the effects on separation selectivity exerted by these parameters are quite subtle, so that control of selectivity in capillary electrophoresis of inorganic anions is often quite difficult. Some practical limitations to selectivity control are highlighted and possible areas that can be studied in the future for selectivity variation are suggested. © 1999 Elsevier Science B.V. All rights reserved.

**Keywords:** Reviews; Selectivity; Buffer composition; Inorganic anions

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## 1. Introduction

Pioneered by Jorgenson and Lukacs [1–5], capillary zone electrophoresis (CZE) is gaining widespread use as a separation technique. Features like short separation time, high efficiency and sample throughput, minimal consumption of reagents and background electrolyte (BGE), high resolving power, minute sample requirement, and minimal sample pre-treatment make CZE attractive for the determination of ionic solutes in a wide range of matrices.

The separation by CZE of anions in simple solutions is relatively straightforward. However, for solutions with extremes of pH, high ionic strength, and a high disparity in concentration between analytes, separation with full resolution can be difficult, especially when the analytes have similar mobilities [6–8]. In such cases, the simplest and usually first course of action is dilution. Dilution however may not be a panacea for all cases as components present at lower concentrations can be diluted to below the limit of detection. To achieve a desired (optimised) separation, alteration of separation selectivity can be a better alternative.

The aim of this article is to review methods which may be used for the control of separation selectivity of anionic solutes using CZE, especially with reversed electroosmotic flow (EOF). EOF reversal is necessary to achieve rapid and efficient separation of anions. Selected separations will be used to illustrate some of the selectivity effects. Where appropriate, some of the practical limitations will be discussed.

### 1.1. Selectivity

Selectivity is the ability of an analytical technique to differentiate between analytes, and in the case of CZE is concerned with the migration order of analytes. For CZE, selectivity has been defined as the relative difference in effective electrophoretic mobilities between adjacent anions [9,10]. Selectivity

has also been expressed in terms of relative migration times [11].

### 1.2. Basic theory

To control selectivity, a basic appreciation of the underlying parameters governing separation is essential. The main forces governing anion migration include those of forward motion due to the applied electric field ( $F_1$ ), friction ( $F_2$ ) due to the resistance of the BGE, retardation ( $F_3$ ), and relaxation ( $F_4$ ) [12].  $F_3$  and  $F_4$  are considered as having negligible effects on the migration of inorganic anions [13]. At steady-state when the anions have reached a finite migration rate,  $F_1 = F_2$  and the migration rate follows Stoke's law (Eq. (1c)).

$$F_1 = Q_{\text{anion}}E \quad (1a)$$

$$F_2 = f_c \nu_{\text{anion}} = 6\pi r \eta \nu_{\text{anion}} \quad (1b)$$

$$\nu_{\text{anion}} = \frac{Q_{\text{anion}} \cdot E}{6\pi r \eta} = m_{\text{eff}}E \quad (1c)$$

where  $Q$  = charge,  $E$  = field strength,  $f_c$  = frictional resistance of the BGE,  $\nu$  = velocity,  $r$  = hydrodynamic radius of anion,  $\eta$  = viscosity of the BGE, and  $m_{\text{eff}}$  = effective mobility of anion. Eq. (1c) is limited to rigid spherical anions separated in free-solution [12,14].

For the widely used fused-silica capillaries under "normal" conditions (pH  $\geq$  2, detector at cathode), the EOF vector is to the cathode and bulk electrolyte flow moves in a direction opposite to the electrophoretic migration of anionic analytes. This can lead to long separation times. To shorten the separation time, a cationic surfactant [15–20] such as tetradecyltrimethylammonium bromide (TTAB) is normally incorporated into the BGE to reverse the EOF. With the EOF altered, anions migrate to the anode according to Eq. (2a) [21]. The mobility of the anion is defined by Eq. (2b) [22].

$$v_{\text{anion}} = \frac{(m_{\text{EOF}} + m_{\text{anion}})}{1} \cdot \frac{V_{\text{applied}}}{L_{\text{total}}} \quad (2a)$$

$$m_{\text{anion}} = \frac{2}{3} \frac{\epsilon_0 \epsilon_r \zeta E}{\eta} \quad (2b)$$

where  $m$  = electrophoretic mobility,  $V_{\text{applied}}$  = applied separation voltage,  $L_{\text{total}}$  = total length of capillary,  $\epsilon_0$  = permittivity of vacuum,  $\epsilon_r$  = dielectric constant of the BGE, and  $\zeta$  = zeta potential at the anion–BGE interface. The factor of 2/3 in Eq. (2b) can be omitted when the double-layers do not overlap [22].

Eqs. (1a)–(1c), (2a), (2b) show some of the parameters that can be controlled to effect selectivity changes. In “normal” CZE, the general migration order is cations, neutral compounds, slightly polar analytes, and anions [15,21]. For co-EOF CZE, the migration order is reversed, and for anionic solutes in particular, the general sequence is hydroxide, inorganic anions, carbonate, and organic acids [15]. Migration orders can be predicted according to equivalent ionic conductances [17,23–27] (Eq. (3)) or aqueous charge-to-radius ratios [15,25]. In practice however, migration orders do not always follow equivalent ionic conductance values [16].

$$m_{\text{abs}} = \lambda_0^* F^{-1} \quad (3)$$

where  $m_{\text{abs}}$  = absolute ionic mobility,  $\lambda_0^*$  = limiting equivalent ionic conductance at infinite dilution, and  $F$  = Faraday constant.

### 1.3. Standard conditions

To discuss and contrast variation of separation selectivity, it is instructive to have a “standard” or “typical” separation with the associated conditions to act as a reference point. Noting that; (i) most anions have poor UV-absorbing characteristics, (ii) it is necessary to reverse the EOF, typically with a cationic surfactant, to achieve rapid separation, (iii) bare fused-silica capillaries are of most common use, (iv) at  $\text{pH} \geq 8$ , most of those anions which are weakly acidic are negatively charged, and (v) chromate is the most widely used BGE or probe for typical inorganic anions, the separation shown in Fig. 1 will be used as the “standard” for this review.

## 2. Selectivity effects arising from chemical parameters

Chemical parameters governing selectivity are essentially those having an impact on the size and charge (i.e., charge-to-mass ratio) of anions. These parameters can be subdivided into (i) the anion and its nature, (ii) the chemical environment, and (iii) complexation and additives.

### 2.1. Nature of the analyte

The electrophoretic mobility [28] of an analyte anion plays a major role in separation selectivity. Mobility in turn depends on the nature of the anion and its chemical environment. In terms of the analyte itself, parameters such as  $\text{p}K_a$  (or  $\text{p}K_b$ ) [21], hydrophobicity, Stoke’s radius, effective charge, effective size and shape are important factors [16,23,29–34]. Molecular orientation and aspect ratio<sup>1</sup> also govern electrophoretic mobility and selectivity, especially for non-spherical polyions [14]. “Spherical” analytes are unaffected by orientation effects [14]. Anions having very high mobilities (such as arsenic species) can be separated without EOF reversal [27] and migrate in the opposite order compared to the same analytes separated with EOF reversal. This offers a means of controlling the selectivity in relation to some of the common inorganic anions.

The form in which an anion exists (and therefore its mobility and selectivity) depends largely on the pH of the BGE [21,24]. Changes in selectivity are pronounced when the  $\text{p}K_a$  of an analyte matches or nears the pH of the BGE [35]. Weak acids and bases are best separated using a pH at or near their dissociation constants ( $\text{p}K_a$  or  $\text{p}K_b$ ) [6]. This effect is pronounced for anions like carbonate [16] and phosphate, whilst some anions, such as vanadate, have been observed to give multiple peaks as a function of pH and BGE type [36].

Analytes having similar electrophoretic mobilities are difficult to resolve in CZE (e.g., Ref. [8]) unless advantage is taken of other characteristics of the anion, e.g., the migration order of thiosulfate can be altered markedly by taking advantage of its polaris-

<sup>1</sup>Represented by the symbol  $\emptyset$ , it is mathematically defined as  $(L/2R)^{-1}$  where  $L$  = solute length and  $R$  = solute radius [14].

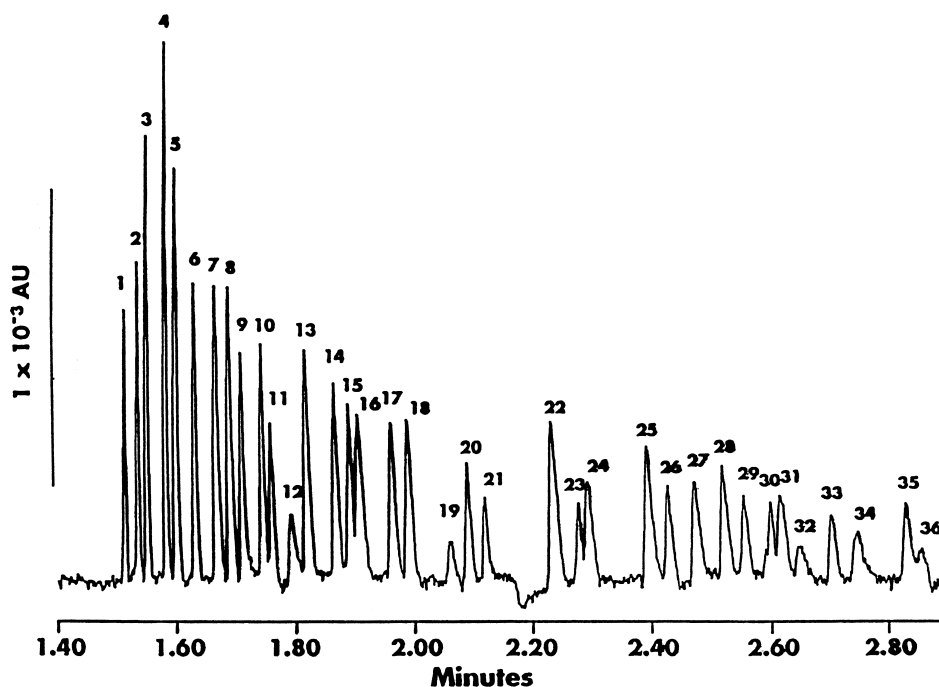


Fig. 1. “Standard” separation of anions by co-EOF CZE using indirect UV detection. Conditions: the BGE comprised 5 mM chromate and 0.5 mM Waters OFM Anion-BT at pH 8.0. Injection was by electromigration at 1 kV for 15 s. The separation voltage was  $-30$  kV and the wavelength was 254 nm. Solute identities: 1=thiosulfate, 2=bromide, 3=chloride, 4=sulfate, 5=nitrite, 6=nitrate, 7=molybdate, 8=azide, 9=tungstate, 10=monofluoracetate, 11=chlorate, 12=citrate, 13=fluoride, 14=formate, 15=phosphate, 16=phosphite, 17=chlorite, 18=glutarate, 19=*o*-phthalate, 20=galactarate, 21=carbonate, 22=acetate, 23=chloroacetate, 24=ethanesulfonate, 25=propionate, 26=propanesulfonate, 27=DL-aspartate, 28=crotonate, 29=butyrate, 30=butanesulfonate, 31=valerate, 32=benzoate, 33=L-glutamate, 34=pentanesulfonate, 35=D-gluconate and 36=D-galacturonate. Reproduced with permission from Ref. [16].

able character by promoting ion-pairing effects with the BGE surfactant through variation of the concentration of surfactant (e.g., Ref. [16]). Although outside the scope of this review, separation under an MECC [37–40] environment is another selectivity option, particularly for solutions containing anions and neutral species.

## 2.2. Chemical environment

### 2.2.1. Hydrogen ion concentration

The pH of either the sample or BGE impacts significantly on anion selectivity. The effect of the pH of the BGE has been studied extensively (e.g., Refs. [27,30–32,34,36,41–45,45–49]), but studies on the effect of sample pH on separation selectivity are limited. The probable reason could be the assumption that the BGE concentration is  $\geq 1000$ -times greater than the sample [50] and would

therefore have an overriding influence on the behaviour of the analyte anions. However, many of the BGEs used for the separation of inorganic anions are unbuffered, so that samples which are naturally buffered samples (e.g., seawater) will not show the same separation selectivity as standard solutions. Recently, samples containing anionic selenium species were adjusted to between pH 3 and 8 before injection and separation selectivity effects were studied [51].

Variation of the pH of the BGE is a common way of controlling selectivity and has been studied and applied extensively (e.g., Refs. [6,9,16,24,28,34,35,41–48,52–55]). Selectivity changes are obvious at or near the  $pK_a$  or  $pK_b$  values of the analytes [6,16,21,35,43,44,46–48,54–57] where charge transitions occur and changes to the effective charge and charge-to-mass ratios take place. As expected, selectivity changes using pH variation resemble a titration

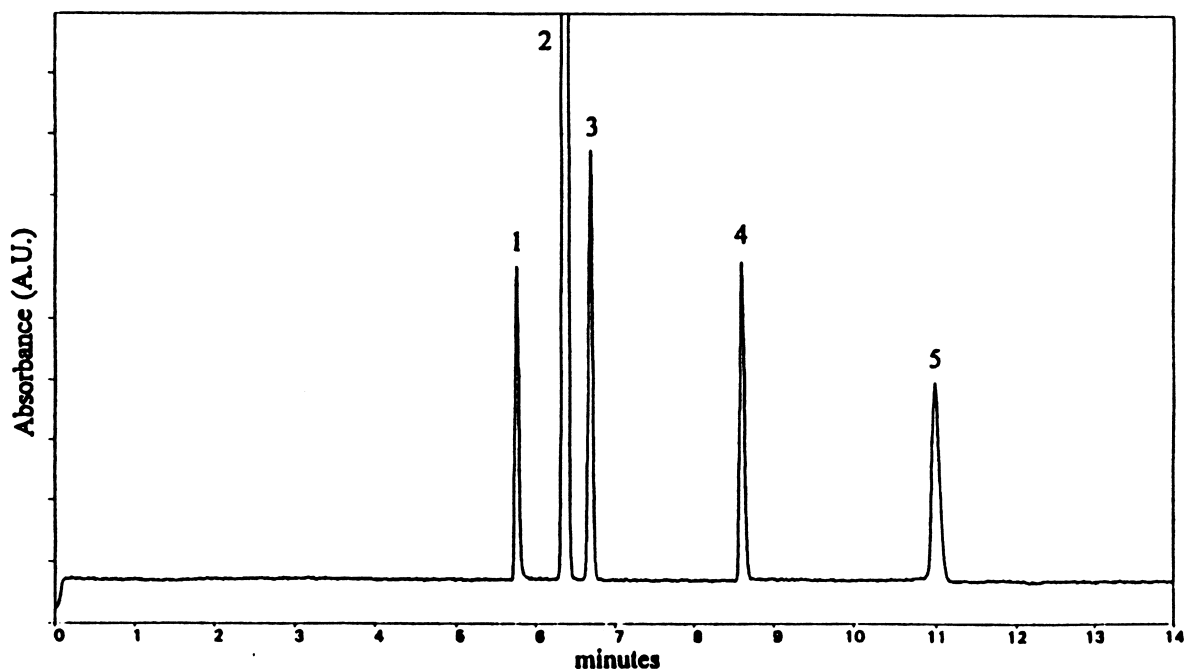


Fig. 2. Separation of inorganic anions in perchloric acid (pH 2.4) without using surfactants to reverse the EOF. UV<sub>214 nm</sub> detection was used. Anions: 1=iodide, 2=nitrate, 3=thiocyanate, 4=periodate and 5=iodate. Adapted and reprinted with permission from Ref. [34].

curve [16]. Recently, Thornton and Fritz [34] have shown that anions can be separated at sufficiently acidic pH without the aid of surfactants (Fig. 2). The selectivity in this case was based purely on electrophoretic mobilities. Under acidic conditions and using mixed BGEs, Pianetti et al. [33] separated phosphonic acid species according to size differences. Groh and Bächmann [36] have shown that the effect of pH depends on the anion and the BGE, e.g., vanadate gave two peaks with 1,2-dihydroxybenzene-3,5-disulfonic acid (Tiron) but only one peak with other BGEs. The two peaks, whose ratio varied with pH, were attributed to interaction of the analyte with Tiron [36]. Morin et al. [44] have used pH variation to speciate arsenic anions. Fluoride and phosphate at disparate levels are difficult to resolve using the “standard” BGE because they have similar mobilities [58–62]. Taking advantage of the weakly acidic nature of the phosphate and by incorporating a small amount of butan-1-ol in the BGE to prevent precipitation, the pH of the common chromate–TTAB BGE was lowered to  $\leq 7.5$  [63]. Fluoride could then be fully resolved from phosphate and

carbonate (Fig. 3). Using this approach,  $800 \mu\text{g ml}^{-1}$  phosphate and  $1 \mu\text{g ml}^{-1}$  fluoride can be baseline resolved [63]. The variation of pH and its effect is also a function of the BGE composition, e.g., ion-exchange plays a part in the separation selectivity of anions when poly(1,1-dimethyl-3,5-dimethylpyrrolidiniumbenzoate) (cationic polymer) is present in the BGE [45].

Dynamic pH changes have been used to manipulate selectivity [6,7,35,64–68] employing  $\text{H}^+$ , ligands,  $\text{OH}^-$ , counter-ions, or co-ions. The pH change can be effected using pulsing effects [67], step changes (e.g., Refs. [68,69]) or gradient variations [64–66,70]; and can be done manually or automatically with computer control [7]. Although most of the above methods involving non-step pH variation were performed on analytes (e.g., proteins) other than common inorganic anions, this approach has also been applied to the separation of weak organic acid anions [6,7,35].

A practical aspect to be noted is that although at high pH the  $\text{OH}^-$  ion performs a cleaning and surface re-generation role [28], care should be exer-

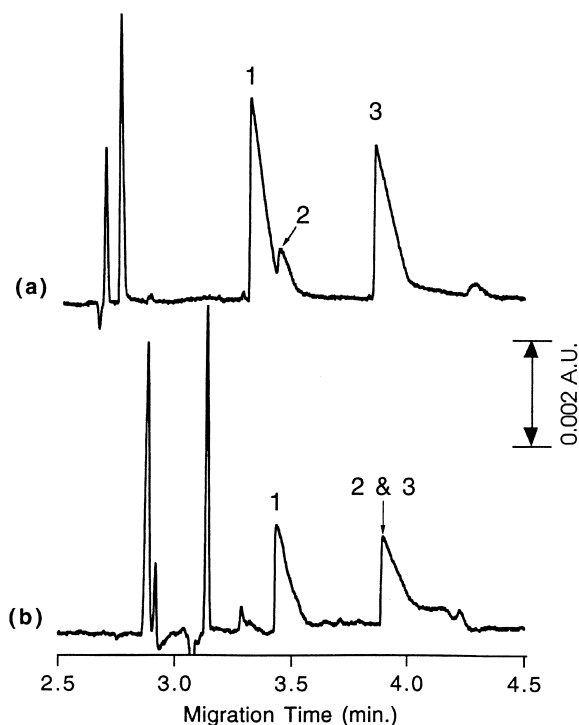


Fig. 3. Separation of fluoride from phosphate in toothpaste. Conditions: (a) the BGE had 0.5 mM TTAB and 5 mM chromate at pH 8.7. Sampling was in the hydrostatic mode (10 cm for 30 s) and detection was in the indirect mode at 254 nm. Separation voltage was  $-20$  kV. The capillary was of fused-silica [60 cm (52 cm to detector)  $\times$  75  $\mu$ m I.D.]. (b) The pH of the BGE was 7.5 and it contained 2.5 mM TTAB, 5 mM chromate and 5% (v/v) butan-1-ol as BGE additive. Other conditions were as in (a). The toothpaste sample was prepared as described in Ref. [63]. Anions: 1 = fluoride, 2 = phosphate and 3 = carbonate. Adapted and reprinted with permission from Ref. [63].

cised as pH extremes can be detrimental to bare capillaries [54]. The baseline can be noisy at extreme pH values. Also, interference from carbonate due to  $\text{CO}_2$  absorption by the BGE at high pH can be a problem [71] and the quantification of carbonate using such BGEs will therefore be unreliable [72]. At high pH for the chromate BGE system, migration time precision is poor for hydroxide and carbonate. Finally, it should be noted that practical considerations can limit the accessible pH range, e.g., precipitation occurs at  $\text{pH} < 10$  for BGEs with vanadate and TTAB [17], and at  $\text{pH} < 8$  for BGEs with TTAB and chromate [63].

### 2.2.2. Electroosmotic flow modifiers

To rapidly separate anions by CZE, cationic surfactants (or EOF modifiers) are included in the BGE to reverse the EOF flow so that it moves in the same direction as anions. The presence of the surfactant offers a further opportunity for the manipulation of selectivity in CZE (e.g., Ref. [16]). The use of EOF modifiers has been reviewed recently [73]. The effect of cationic surfactant EOF modifiers on the separation selectivity of inorganic anions has been studied widely (e.g., Refs. [6,9,16,21,48,74–79]). The type of cationic surfactants used include TTAB (e.g., Refs. [16,17,27,57,74,80–84]) patented as Nice-Pak OFM Anion BT [72,85] or CIA-Pak OFM Anion BT [48,86–88], tetradecyltrimethylammonium hydroxide [48,81,84], dodecyltrimethylammonium bromide [57,89], cetyltrimethylammonium bromide [6,8,21,55,57,62,84,90], hexamethonium bromide or hydroxide [27,83,84,91–95], decamethonium bromide [27], diethylenetriamine [57,92], tributylhexadecylphosphonium bromide [27], tertiary amines (e.g., triethylamine [96]), and benzyltrimethylammonium bromide [97].

Cationic polymers or polyelectrolytes like hexadimethrine or polymethobromide [84,98–100], poly(1,1-dimethyl-3,5-dimethylenepiperidinium (PD-DPi) chloride, bromide, chromate [100,101] or benzoate [45], poly(1,1-dimethyl-3,5-dimethylpyrrolidinium) chromate, [(diethylamino)ethyl]-dextran chromate [100], and poly(1,1-dimethyl-3,5-dimethylpyrrolidinium chloride [45] have also been used to alter separation selectivity of inorganic anions [45,98,100]. Hexadimethrine and polydiallyldimethylammonium bromide have been used to control the selectivity of mono- and dibasic organic acids [102,103]. Cationic polymers [45,100,101] (Fig. 4) exhibit different separation selectivities to those of cationic surfactants (Figs. 1 and 3). Ion-exchange [100,101] and steric effects associated with the bulk of the polyelectrolyte and/or reduced charged density with the polymer [100] have been noted as possible causes for selectivity changes.

In choosing a surfactant, the detection mode and detection wavelength are important variables; for example benzyltrimethylammonium bromide is UV active and would interfere with indirect UV detection. Also, the surfactant counter-ion can interfere

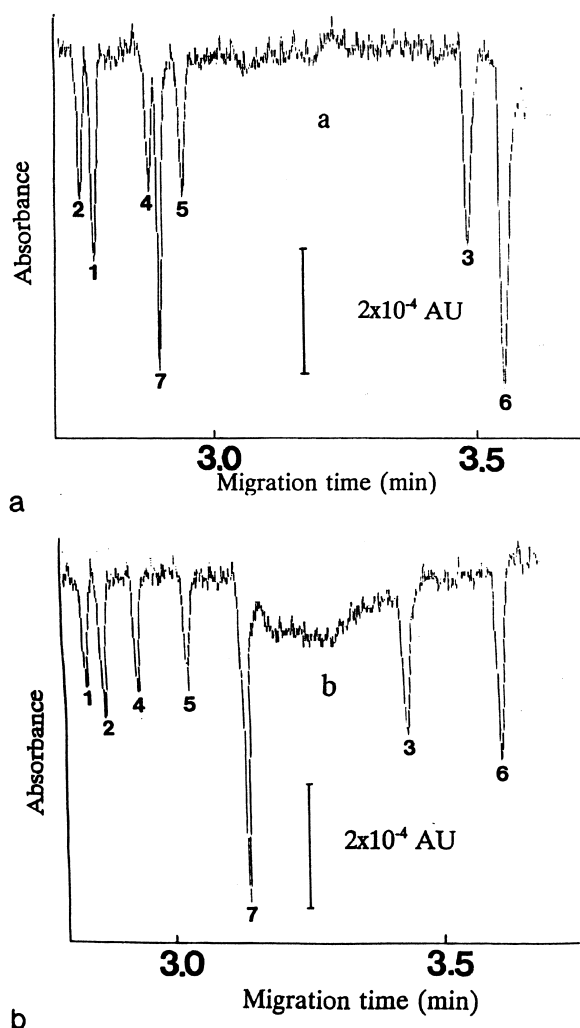


Fig. 4. Effect of cationic polymer (PDDPi-chromate) on anion selectivity. Conditions: The BGE was chromate-based. (a) 0.02% (w/v), and (b) 0.14% (w/v), respectively, of PDDPi-chromate. Anions: 1=bromide, 2=chloride, 3=fluoride, 4=nitrite, 5= nitrate, 6=phosphate and 7=sulfate. Reprinted with permission from Ref. [100].

in the separation [101]. It has been shown that the system peak induced by the bromide present in TTAB interferes with thiosulfate determination, whereas the same surfactant in the hydroxide form does not interfere [85]. Precipitation of surfactants with certain BGEs at given pH values has been noted in Section 2.2.1.

The effect of the length of alkyl chain on the

surfactant on separation selectivity of inorganic anions has been studied by Buchberger and Haddad [77]. Fig. 5 shows the selectivity trends for dodecyltrimethylammonium bromide (DTAB) (12 C), TTAB (14 C) and cetyltrimethylammonium bromide (CTAB) (16 C), and reveal that the selectivity changes were pronounced for thiocyanate and iodide. These anions showed an increase in relative migration time (RMT) with increasing size of the alkyl group on the surfactant, whilst other (more hydrophilic) anions showed decreased relative migration times with increasing size of the alkyl chain. The observed changes in migration order for the polarisable anions can be attributed to formation of ion-pairs [16,23,77,79,104–106] with the surfactant. Alternatively, ion-exchange effects between the analytes and the surfactant have also been suggested as a further mechanism for the observed selectivity [77].

Cetyltrimethylammonium ions ( $\text{CTA}^+$ ) in the bromide, chloride and hydrogensulfate forms have been used to investigate the effect of surfactant counter-anion on separation selectivity, but no significant changes in selectivity were recorded [107]. Nevertheless, appropriate choice of EOF modifier counter-anion is essential to avoid interference since it is this ion that produces the “system peak” [92], e.g., the use of  $\text{CTA}$ -chloride would be inappropriate for the separation of anions in samples like urine and tap water because of the inability to quantify chloride in such samples.

The concentration of cationic surfactant in the BGE can influence the selectivity. The following concentration ranges of TTAB have been reported; 0.2–0.8 mM [77], and 0.5–5 mM [16,107]. At concentrations above the critical micelle concentration (CMC), chromatographic partitioning effects with the micelle also play a part in the separation. Although MECC is useful for “neutral” solutes, separation of anions under an MECC environment has been shown [39,40,108,109]. At concentrations less than the CMC, ion-pairing is the predominant mechanism which influences separation selectivity [16,23,79,104]. Ion-pairing (or ion-association) is an equilibrium effect and the theory relating to it has been derived by Kaneta et al. [104], at least for monovalent anions. Ion-pairing effects are pronounced for polarisable or lipophilic anions [16,79,106]. Variation of the concentration of tetra-

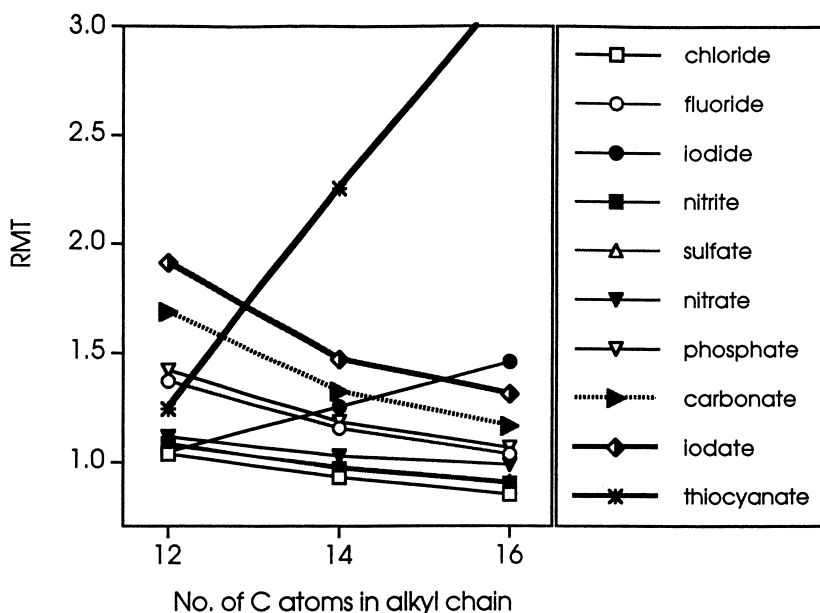


Fig. 5. Effect of alkyl chain length of quaternary ammonium bromide surfactants on anion selectivity. Conditions: 2.5 mM surfactant, 5 mM chromate and pH  $8.5 \pm 0.1$ . Sampling was in the hydrostatic mode (10 cm for 30 s) and indirect UV at 254 nm was used for detection. Separation voltage was  $-20$  kV applied across a 60 cm (52 cm effective length)  $\times$  75  $\mu$ m I.D. fused-silica capillary. Key: RMT=relative migration time (to the system peak), 12 C=DTAB, 14 C=TTAB and 16 C=CTAB. The anion concentrations in  $\mu$ g ml $^{-1}$  were: chloride=20, bromide=10, fluoride=10, iodide=20, nitrite=5, sulfate=8, nitrate=12, (hydrogen)phosphate=16, iodate=20 and thiocyanate=8. Reproduced with permission from Ref. [77].

decyltrimethylammonium hydroxide in the BGE has been shown to affect selectivity [85]. The major change in migration order of anions like thiosulfate has been attributed to their hydrophobicity and formation of ion-pairs, and to the presence of micelles [85]. The reversal of migration order between nitrite and sulfate with increasing surfactant concentration has been indicated as being due to a greater ion-association between the sulfate and the surfactant [84], and the same argument has been used for the selectivity change between chloride and bromide at  $\geq 6$  mM CTAB [84] or  $\geq 0.5$  mM TTAB. Although most studies have involved step changes in concentration of surfactant, a concentration gradient (using CTAB) has also been used to manipulate separation selectivity of anions [6,59].

Variation of the concentration of cationic polymers yields a selectivity [45,100,101] that is different to that of cationic surfactants [16,77]. For instance, the migration order of sulfate is altered markedly with rising polymer concentration and the likely cause for this has been suggested as ion-exchange [100,101]

(see Fig. 4). In contrast, cationic surfactants do not induce significant changes in the selectivity of sulfate with increasing concentration [16,77]. Also, steric effects associated with the bulk of the polyelectrolyte and/or reduced charged density with the polymer have been noted as possible causes for selectivity changes [100]. Changes in selectivity with concentration of the polymer have been noted for organic acids and again was attributed to ion-pairing [102,103].

A further means to manipulate selectivity is to mix two or more surfactants together and to seek a selectivity in the mixed surfactant system that differs from that obtained using the two component surfactants individually as the EOF modifier. This approach has been reported for binary mixtures of dodecyltrimethylammonium bromide (DTAB) and TTAB [110,111]. Selectivity changes were evident for chloride, nitrite and fluoride as a function of total surfactant concentration and the molar ratios of the surfactants. Binary mixtures of cationic surfactants were used to simultaneously separate over 10 anions



in Bayer liquor in 4 min [111]. Control of selectivity with binary cationic mixtures also has the advantage of improving anion resolution. This is illustrated in Fig. 6, in which a standard mixture separated using BGEs with single 2.6 mM DTAB (Fig. 6a) and 2.6 mM TTAB (Fig. 6b) suffered from poor resolution of bromate and nitrite from their respective adjacent anions. By using a BGE containing a binary mixture of 2.6 mM each of DTAB and TTAB, the problems noted above were eliminated (Fig. 6c).

There are some practical limitations to the use of surfactants in manipulating anion selectivity. CTAB and TTAB are disadvantaged by limited solubility and formation of insoluble ion-associates with some

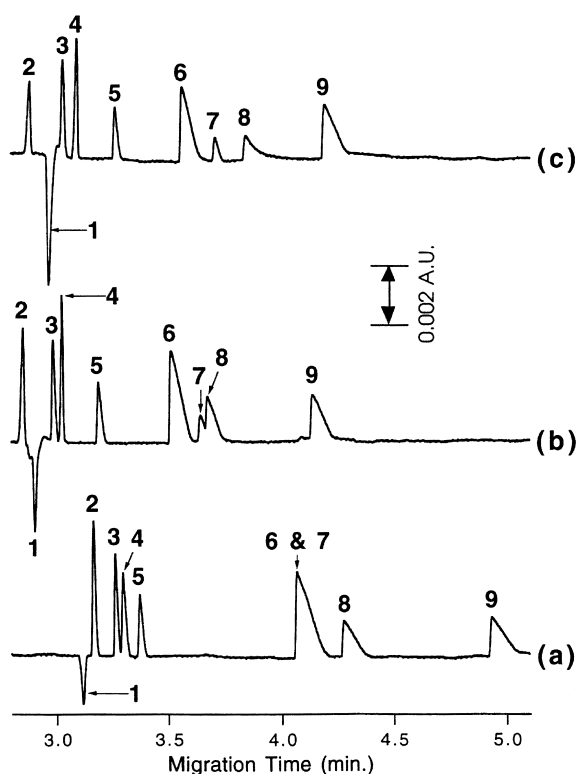


Fig. 6. Comparison of separations using DTAB and TTAB singly and as binary mixtures. Conditions: (a) 2.6 mM DTAB, 5 mM chromate and pH 9.1. Sampling was in the hydrostatic mode (10 cm for 30 s) and indirect UV at 254 nm was used for detection. Other conditions were as in Fig. 5. (b) 2.6 mM TTAB. Other conditions as in (a). (c) BGE had 2.6 mM TTAB and 2.6 mM DTAB. Other conditions were as in (a). Anions: 1=system (bromide), 2=chloride, 3=nitrite, 4=sulfate, 5=nitrate, 6=fluoride, 7=bromate, 8=phosphate and 9=carbonate.

BGE components. The useful pH range can also be limited due to precipitation effects.

### 2.2.3. Background electrolyte

For the indirect detection mode employed widely for CZE of inorganic anions, the co-ion is known as the probe or visualising agent [112] and is the anion present in the highest concentration [92] in the BGE. Atamna et al. [53] have studied the role of the BGE counter-cation and its influence on selectivity (at least for dansylated amino acids) and have noted that although migration time increased with cation size, significant selectivity changes were not demonstrated under the conditions used. Acetate BGEs increased the mobility of *p*- and *m*-aminobenzoic acids in the order lithium < sodium < potassium as the counter-cation [113]. This was unexpected and in disagreement with the observations of Atamna et al. [53]; and a satisfactory explanation is yet to be found [113]. Sodium phosphate and potassium phosphate did not afford selectivity changes [43]. Lithium nitrate and sodium nitrate were used for the simultaneous separation of chloride and sulfate in nitric acid-digested concrete [114] but no migration sequence changes were seen. It is generally considered that migration orders are rarely affected by changes in probe type [25].

Some of the carrier anions (or probes) used in CZE are shown in Table 1. It is noted that adenosine-5'-triphosphate [55] was used to separate polyphosphate and polycarboxylate anions. 2,6-Naphthalene-dicarboxylate and chromate showed different selectivities for anions [125]. With naphthalene sulfonate, the di-form performs best compared to the mono- and tri-forms, but selectivity changes achieved were minor [126].

The probe can be chosen to suit given anionic solutes, e.g., *p*-hydroxybenzoate for slowly migrating anions, phthalate for anions with intermediate mobility and chromate for very mobile anions [19]. The choice will also depend on the sample pH, acid-base dissociation constants of analytes, degree of ionisation required for resolution, sensitivity, available detection method, chromophoric properties of the anion(s), desired separation efficiency, precipitation with other BGE components, etc. The choice of probe can affect selectivity by allowing the detection of given anions and not others, e.g., 8-

Table 1  
Some carrier ions used in CZE for the separation of anionic solutes

Carrier	Ref.	Carrier	Ref.
Acetate	[41]	Methanesulfonic acid	[121]
Adenosine-5'-triphosphate	[55]	Molybdate	[91]
<i>p</i> -Anisate	[25]	2,6-Naphthalenedicarboxylate	[125]
Benzoate/benzoic acid	[17,74,76]	Mono-, di- and tri-naphthalene sulfonates	[126]
Borate or tetraborate	[11,41,43,115,116]	Nicotinic acid	[74]
Carbonate	[41,43]	Nitrate	[41,77,114]
Chloride	[45,77,85]	Nitrite	[41]
Chromate <sup>a</sup>	e.g., [16,27,45,57,72,77] [83,86,88,91,99,100] [101,117–120]	Perchloric acid	[34]
Citrate	[41]	Phosphate <sup>d</sup>	[41,43,47,53]
1,2-Dihydroxybenzene-3,5-disulfonic acid <sup>b</sup>	[36]	Phthalate	[25,57,90] [119,127]
Formic acid	[121]	Pyromellitic acid <sup>e</sup>	[25,49,57,83] [92,93,120,122]
Glycinate	[43]	Salicylate	[25,91]
Hydrochloric acid	[34]	Sorbic acid	[76]
Hydroxybenzoate	[19,57,90]	Sulfate	[48,77,128]
Hydroxyisobutyric acid <sup>c</sup>	[121]	Sulphosalicylic acid	[74]
8-Hydroxyquinoline-5-sulfonic acid	[122]	Thiocyanate	[129]
Imidazole	[123]	Trimesate	[17]
Iodide	[124]	Vanadate	[17]
Mellitate	[25]		

<sup>a</sup> Most common carrier in CZE.

<sup>b</sup> Also known as Tiron.

<sup>c</sup> Commonly known as HIBA

<sup>d</sup> In its various forms

<sup>e</sup> Also known as 1,2,4,5-benzenetetracarboxylic acid.

hydroxyquinoline-5-sulfonic acid allows the detection of eight organic acids whereas 1,2,4,5-benzenetetracarboxylic acid detects only four under the same conditions [115]. Fig. 7 shows the effect on separation selectivity of chromate, trimellitate, nitrate and tetraborate as probes. At the same concentration and pH, a possible cause for the changes to the observed migration behaviour of iodide and thiocyanate is the effect of ionic strength (e.g., trimellitate was titrated with NaOH from pH~2 to 9.5). A subtle but important change in migration order was noted for nitrate and a change in migration order for bromate occurred with tetraborate. Recently, it was shown that selectivity can be altered for anionic complexes by changing electrolytes from phosphate to perchlorate [95]. This effect is indicated to be due to ion-pairing.

Combined probes [imidazole–nitrate; Cu(II)–ethylenediamine–nitrate] have been used to separate

inorganic anions and metals simultaneously [123]. Similar separations have been achieved by Beckers et al. [130]. A homologous series of alkylphosphonic acids was separated using borate–phenylphosphonic acid BGE [33]. Other binary combinations of borate with sorbic acid or benzoic acid were also. Under the conditions used, the charge of the each of the analytes was identical and the separation selectivity was based on differences in size [33]. Mixed or multiple BGEs (e.g., HIBA and methanesulfonic acid, and HIBA and formic acid) have also been used by other workers [121]. Mixed BGEs of  $\epsilon$ -aminocaproic acid–2-hydroxyphenylacetic acid,  $\epsilon$ -aminocaproic acid–mandelic acid,  $\beta$ -alanine–mandelic acid, and  $\beta$ -alanine–hippuric acid were used for the separation of organic acid anions in the serum of critically ill children [131]. Although multiple BGEs can improve peak symmetry, ill defined peaks can occur in the region between the mobilities of the

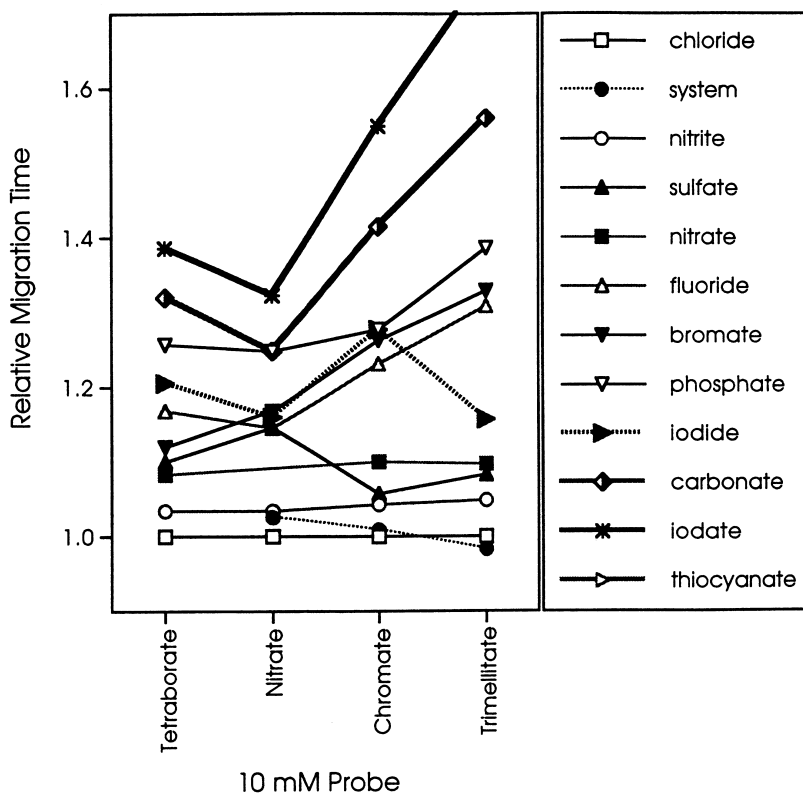


Fig. 7. Effect of probe type on anion selectivity. All probes were 10 mM in concentration. Conditions: All BGEs were 2.5 mM in TTAB at pH  $8.96 \pm 0.13$ . The detection was in the indirect mode at 254 nm for chromate and trimellitate; and 214 nm for tetraborate and nitrate. Other conditions were as in Fig. 5. All times have been normalised to that of chloride. The anions were in the concentration range of 5–12  $\mu\text{g ml}^{-1}$ .

probes. Best separation was achieved by using a triple mixture having HIBA, methanesulfonic acid, and formic acid [121]. Mixed chromate–borate BGEs were used to resolve the chloride isotopes [132]. Mixed L-histidine and 2-[N-morpholino]ethanesulfonic acid (His/MES) BGEs were used for the separation (with conductivity detection) of anions in wines and juices [133]. His/MES BGEs can be used for both anion and cation separation.

Caution needs to be exercised in selecting BGEs. Some BGEs are toxic and should be avoided, e.g., NaCN and sodium phenate [129]. Compatibility with the detection mode is another vital consideration, e.g., sodium tetraborate and other suppressible BGEs are compatible with suppressed conductivity detection [129]. Pyromellitic acid cannot be used with TTAB as a white precipitate forms [57].

Chromate-based BGEs with various surfactant

concentrations have been studied for their effects on anion selectivity [16,77,117]. The chromate concentration ranges studied include 2.5–15 mM [117], 1–7 mM [77], 3–9 mM [16], 2–8 mM [27], and 2–15 mM [107]. Although selectivity changes will depend on the nature of the anions, subtle changes were noted for iodide, nitrite [77], sulfate [16,27,77] and nitrate [16,27]. With most of the above studies, 0.5 mM surfactant was used. Only minor selectivity changes were noted for inorganic anions using chromate as carrier anion [16,77,107,117]. The migration order for sulfate and chloride was reversed with increasing concentration of BGE [127]. Similarly, thiosulfate (and other divalent anions) was retarded more than monovalent anions with increasing probe concentration [91] and the cause for this has been suggested as shifts in the solvation equilibrium [91,134]. For anions demonstrating marked selectivi-

ty changes with variation of the concentration of chromate, Jimidar and Massart [117] have indicated that migration order changes were due to ion-exchange partitioning effects. This means that anions are in equilibrium with the surfactant as ion-pairs [16,79,104,106,117]. The equilibrium between the anions and the surfactant is a competitive process; and the introduction of more chromate ions displaces the iodide and thiocyanate from their “less” charged ion-pair form with TTAB. Their release effectively yields ionic species of “higher” effective charge, which will migrate faster, resulting in the selectivity changes noted above. Harrold et al. [129] varied tetraborate from 2–10 mM and achieved migration order changes for fluoride and phosphate. This was suggested as being due to the different rates at which mobilities change with changing BGE concentration or ionic strength [129]. Increasing phosphate concentration altered the selectivity of anions with a charge of  $\geq 2$ , and has been ascribed to the well-known dependence of mobility on ionic strength which is more pronounced for higher charged anions [46].

It is noteworthy that at 5 mM chromate (the “typical” concentration used in CZE), the migration order for the  $-1$  charged halide anions does not follow trends expected from charge-to-mass ratios (assuming other variables are identical) where the expected order is fluoride, chloride, bromide and iodide. The actual migration order shows fluoride behaving anomalously. This can be explained as being due to the highly electronegative nature of fluoride [135], which has a tendency to form structures through hydrogen-bonding, so that in an aqueous BGE, its small size allows it to acquire a relatively higher hydration volume [136]. This means that the effective charge:mass ratio of the electronegative fluoride entity is lower, thereby resulting in the anomalous behaviour. The possible formation of donor–acceptor complexes with silicon atoms [137] at the capillary surface can be a factor contributing to reduced fluoride migration rate. In methanol, the migration sequence of halides is iodide > bromide > chloride > fluoride. On the other hand, in water without surfactants, the order is reversed [126].

Whilst some selectivity effects arise from changes in the concentration of the BGE, there is no quantita-

tive advantage in using ever increasing concentrations of chromate because peak area and height responses plateau off at high levels [117]. This is attributable to the limitation defined by the linear dynamic range of the UV detector. Generally, resolution is better at higher chromate concentration as EOF is reduced [28] but at the expense of increased migration time [12,21,138–140].

#### 2.2.4. Organic solvents

Whilst there is large amount of published work on selectivity effects in aqueous media [24], separation of inorganic anions by CZE in non-aqueous media is largely unexplored. Non-aqueous media can allow for manipulation over a wider operational pH range than aqueous systems and may also be useful in ionic species present in a hydrophobic matrix [5]. Solvents also reduce sorption of hydrophobic substances onto capillary walls, and reduce Joule heat [141].

Solvation is a common way of controlling selectivity [9,45,98] through changes in the hydration volume [43,92,142,143] or dissociation ( $pK$ ), which in turn alter the charge-to-mass ratio of the solute. The influence of organic solvents on selectivity has been reviewed by Sarmini and Kenndler [143]. Solvation changes can be effected by the addition of organic solvents to the BGE, either as single solvents or as mixtures. Solvents used in CZE include methanol [43,45,77,92,98,126,144–147], acetonitrile [28,43,45,77,98,99,144,145], tetrahydrofuran [77,144,145], ethylene glycol, acetone [77], ethanol [45,98,144,145], 2-propanol [98,144,145,148], butan-1-ol [149], propan-1-ol [98], dimethylformamide, tetrabutylammonium hexafluorophosphate [126], and dioxane [145].

The type and concentrations of organic solvents used vary widely and the choice will depend on the effect of the solvent on detection, baseline noise, miscibility, volatility, carrier electrolyte, etc. Salimi-Moosavi and Cassidy [126] used up to 98% (v/v) methanol and 100% dimethylformamide (DMF), and recorded significant changes in migration order, e.g., chloride which migrated first or second in aqueous BGEs migrated in fourth position with 98% methanol. For lipophilic anions, the change in selectivity was more pronounced, e.g., in a mixture with six anions, thiocyanate went from migrating last in aqueous systems to migrating second with 98%

methanol [126,150]. Solvation and hydrophobicity of anions have been suggested as the features influencing selectivity in the above study [126]. In addition, the nature of the organic solvent was shown to influence selectivity through ion-association [126], i.e., the migration order for protic solvents like methanol was different from aprotic solvents like DMF as a result of H-bonding effects on ion-association. Organic solvents can also influence the selectivity of solutes by partially suppressing the interaction between the solutes and the surfactant [98].

The effect of butan-1-ol on the selectivity of anions in a chromate–TTAB system was studied for the range 0–7% (v/v). Fig. 8 shows the separation of

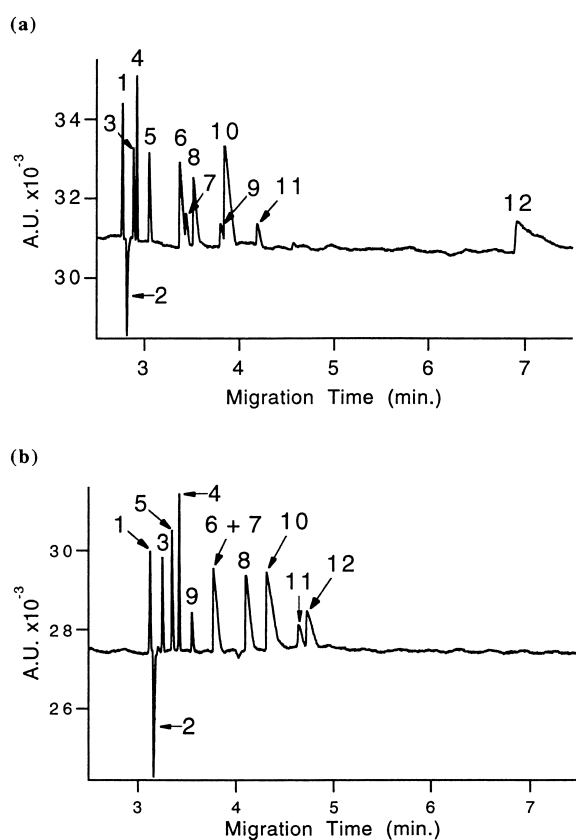


Fig. 8. Effect of butan-1-ol on separation time and resolution of anions in the standard mixture. Conditions: Both (a) 5 mM chromate, 2.5 mM TTAB at pH 8.0. Other conditions were as in Fig. 5. (b) As in (a) except the BGE had 5% (v/v) butan-1-ol. Anions: 1=chloride, 2=system peak, 3=nitrite, 4=sulfate, 5= nitrate, 6=fluoride, 7=bromate, 8=hydrogenphosphate, 9= iodide, 10=hydrogencarbonate, 11=iodate and 12=thiocyanate.

a model mixture at 0% (v/v) and 5% (v/v) of butan-1-ol. Major changes in selectivity occurred for iodide, thiocyanate and nitrate. For the polarisable anions, an increase in effective charge (charge-to-mass ratio) [126] due to suppression of the interaction with the surfactant monomer (ion-pair) is one possible cause [98]. Another possible cause is a reduction in ion-exchange interaction between the polarisable anions and the dynamically coated surfactant layer on the capillary surface which can act as an anion exchanger [77]. The change in selectivity for nitrate could have been due the selective destruction of the solvation shell [92,126,145,148] or changes in ion-association [126].

Using methanol in a BGE with PDDPi–chromate (see Fig. 4), selectivity changes for anions were ascribed to changes in anion solvation and dipole–anion interactions which are strong for protic solvents [45]. In contrast, selectivity control with acetonitrile in a BGE with PDDPi–chromate was different, and polyelectrolyte properties such as solvation and structural conformation may play a part in selectivity control [45]. Polyelectrolytes interact via hydrophobic effects to control the selectivity of anions [45].

The choice of solvent can be limited by the available detection method, e.g., methanol can be used in UV detection whereas solvents with appreciable UV absorption are unsuitable. Organic solvent-based systems can yield poor migration time precision due to the influence of electrolysis products that influence pH [126]. Precipitation occurs for methanol and acetonitrile at 65% and 35%, respectively, when PDDPi–chromate is used as the EOF modifier [45]. Butan-1-ol cannot be used above 7% (v/v) due to its limited solubility in water and interference with UV detection.

### 2.3. Complexation and additives

Complexation can be used to alter selectivity through the variation of charge, charge density, geometry, and hydrophobicity [129]. Vancomycin has great enantioselectivity for anionic solutes [151]. Poly(ethyleneglycol) has been used to alter the selectivity of benzoic acids through H-bonding effects [152]. Stathakis and Cassidy [119] have studied the influence of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -cyclodextrins (CDs) on

anion selectivity. The selectivity due to CD can be controlled further by changing the probe, e.g.,  $\alpha$ -CD/chromate yields a different migration order to that of  $\alpha$ -CD/phthalate [119].  $\beta$ -CD has also been used to control the selectivity of organic acid anions [122]. Resolution between nitrate and sulfate has been shown to be improved using  $\text{Ba}^{2+}$  to form ion-pairs [81], and  $\text{Ba}^{2+}$  has also been used to control the selectivity of carboxylic acid anions, with changes attributed to complexation between the cation and the carboxylate groups [122,129]. Negatively charged  $\text{Cu}^{2+}$  complexes of polyaminocarboxylic acids have been separated as a function of charge and size [153]. The selectivity of organic acids has been varied by complexation with  $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$  [154], and  $\text{Cu}^{2+}$  [153–155] in various BGEs.  $\text{Pb}^{2+}$  was added to the BGE to selectively influence the migration time of sulfate, ultimately enhancing the separation between sulfate and chloride [156].

### 3. Selectivity effects arising from instrumental parameters

#### 3.1. Method of detection

Whilst the discussion thus far has concentrated on the selectivity changes which can be generated in the separation process, selective detection also offers a means to discriminate between analytes, even when they are not separated. Electrochemical methods such as conductivity [74,129,133,157–159], amperometry [126], and potentiometry can be used for the selective detection of electroactive analytes. Nann and Simon [160] have used ion selective electrodes to detect KCl. Mass spectroscopy can be used to selectively detect anions or for anion speciation [161,162]. Anions exhibiting strong UV-absorbance at convenient wavelengths can be detected using direct UV spectroscopy, e.g., nitrate, nitrite, thiocyanate, thiosulfate and hydrosulfide at 214 nm [72,79,85]; arsenite and arsenate at 190 nm [27]; chloride at 185 nm [85,163]; polyaminocarboxylate anions at 290 nm [153]; iodate and periodate at 222 nm [27]; and thiosulfate, iodide, sulfide and molybdate at 229 nm [48]. The selective detection of UV

absorbing anions in the presence of other anions has been demonstrated for the common chromate–TTAB system by Jones [79]. As most inorganic anions have poor UV absorbing properties [18,23,76,92], indirect UV absorbance is most commonly used in CZE. Suppressed conductivity gives a different detection selectivity to that of UV detection [129,159,164] (Fig. 9).

#### 3.2. Sampling mode

Sample introduction by electromigration (e.g., Refs. [81,82,94,165,166]) offers a selectivity option where charged analytes are selectively injected and under given conditions, discrimination between charged analytes occurs [43]. The duration and field strength used for electromigration can be adjusted to selectively load only the more mobile anions.

#### 3.3. Voltage

Separation voltage defines the migration rate of anions but its use in controlling anion selectivity is rare. Although this may not be relevant for most inorganic anions, it is noted that the applied electric field strength affects the orientation of analytes within the applied field, with the mobility of rod-shaped solutes increasing with increased field [14].

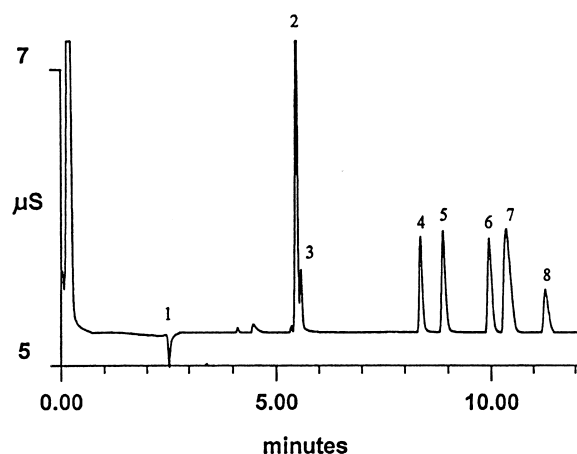


Fig. 9. Separation of anions employing capillary electrophoresis with suppressed conductivity detection. Peaks (all at  $1.0 \mu\text{g ml}^{-1}$ ): 1 = water dip, 2 = fluoride, 3 = phosphate, 4 = nitrate, 5 = nitrite, 6 = sulfate, 7 = chloride and 8 = bromide. Reprinted with permission from Ref. [116].

Additionally, the electric field can cause selectivity changes via Joule heat-induced pH changes [20,167] and shifts in ion-pair or ion-exchange equilibria. Influence of applied potential on the separation of inorganic anions has been studied, but no changes in migration order were reported [27,46]. The electrical field configuration and EOF alteration can be used to control selectivity. A six-component low-molecular-mass carboxylic acid mixture separated under “standard” conditions allowed for the detection of four, one and six peaks in different migration orders depending on the field and EOF direction [78].

Voltage variation (Fig. 10) was studied by the authors with a view to applying it to the analysis of iodide, iodate and thiocyanate in seawater. The BGE was made up to contain 0.56 M NaCl, thereby approximating the chloride content in seawater, and the detection was performed in the direct absorbance mode at 214 nm to selectively detect the above anions. The change in selectivity in Fig. 10 was almost certainly an indirect effect resulting from the applied voltage. It must be noted that iodide and thiocyanate are polarisable whilst iodate is not, so that iodide and thiocyanate participate in ion-pair formation with the CTA–chloride. Although the exact mechanism is presently unclear, the observed selectivity changes may arise from temperature induced ion-pairing effects [168].

### 3.4. Temperature

Temperature variation is usually applied for the control of speed and efficiency of separation [35]. However, temperature control can be used for the in situ generation of pH changes [35] that in turn may be used to control selectivity. Whilst François et al. [27] and others [46] did not observe selectivity changes with temperature variation, Harrold et al. [129] have noted some effects of temperature on anion selectivity using tetraborate as the BGE. The dominant effect was a change in viscosity and mobility, and selectivity changes were observed for chloride and bromide [129]. A change in migration order between *m*- and *p*-aminobenzoic acids was reported by Nielen [113] who explained this observation on the basis of changes in chemical equilibria. Strong acid anions are fully ionised at pH 9.2 and should not show selectivity dependence on tempera-

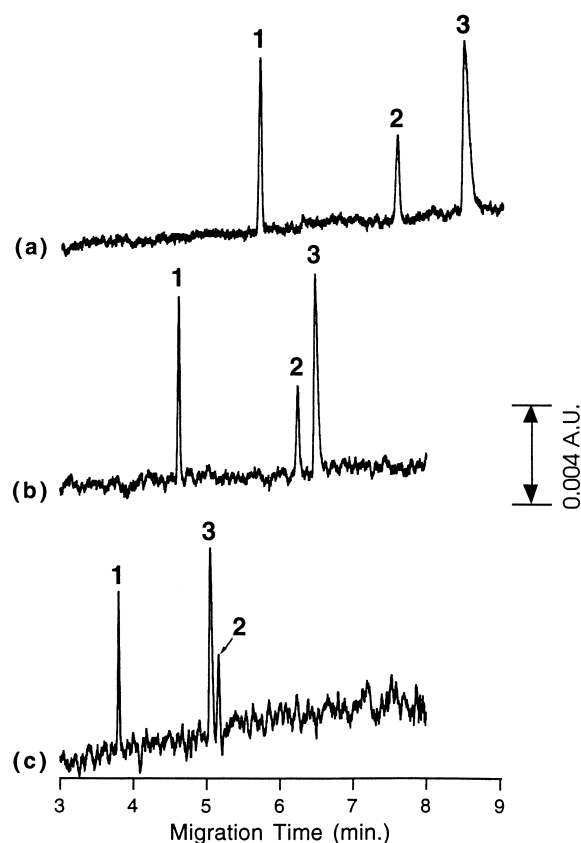


Fig. 10. Effect of applied voltage on separation selectivity of anions. Conditions: the BGE had 560 mM NaCl, 90 mM LiCl, 8 mM Tris, and 10 mM cetyltrimethylammonium chloride. The pH was unadjusted. Sampling was in the hydrostatic mode at 10 cm for 30 s. Separation was performed in a polyimide-coated fused-silica capillary measuring 60 cm (52 cm to detector)  $\times$  75  $\mu$ m I.D. Detection was performed in the direct mode at 214 nm. Separation voltage: (a) = -8 kV, (b) = -8.5 kV, and (c) = -9 kV. Anions (all 10  $\mu$ g ml<sup>-1</sup>): 1 = iodide, 2 = iodate and 3 = thiocyanate.

ture, but Harrold et al. [129] have noted otherwise and have indicated that the changes could be due the different rates at which the mobilities of anions change with temperature.

The temperature range available to be accessed is limited by the BGE composition (e.g., boiling point, and volatility of any solvent used), impact on viscosity which affects mobility, migration time precision, effect on detection, effect on sample (e.g., biological samples can be denatured), the capabilities of the instrument, effect on resolution (e.g., the

resolution between thiocyanate and molybdate can be worsened with increasing temperature [46]), etc.

#### 4. Selectivity effects arising from the capillary

The capillary can be bare, treated (bonded) [127,169], or packed, and can be made of pyrex borosilicate glass [4,5], fused-silica, glass, PTFE [5], poly(fluoroethylpropylene) [170], polyethylene, poly(vinyl chloride), polyfluorocarbon [167], and polypropylene [167,171]. Capillaries used in CZE are usually made of fused-silica [9] since this material has the best transparency and compatibility [12] with UV detection. At the present time, the majority of publications in CZE concerning the separation of inorganic anions involve the use of bare capillaries with a dynamic coating of cationic or other surfactants.

Bonded and packed capillaries (e.g., Refs. [41,77,169,172–176]) are being used increasingly in CZE. Although any effect on selectivity will depend on the nature of the bonded phase, treated capillaries can offer a wider accessible pH range [169] and the need for EOF reversal is negated [46,120,171,177]. Coated capillaries allow for the analysis of serum without the need for deproteination [131]. Selectivity as a function of normal distribution equilibria can be achieved by using packed (e.g., with ODS/C<sub>18</sub>) capillaries in the capillary electrochromatography (CEC) mode [173,174,178]. Packing can be tedious and difficult and expansion of CEC is subject to improvements in packing [174]. CEC also offers the possibility of utilising different stationary phases. A similar effect to CEC may be obtained by coupling an on-line liquid chromatography column to a CZE system as has been done for *rac*-terbutaline isomers [179].

Capillaries coated with linear polyacrylamide have been used for the determination of organic acids [131] and cross-linked polyacrylamide coatings have been used for the separation of inorganic anions [177]. Polypropylene capillaries have been employed to separate inorganic anions [171] but no migration order changes were apparent as compared to the “standard” system. Such capillaries have been found to give good migration time precision [46,120,171,173,177]. Poly(ethyleneglycol), dimethylpolysiloxane, and (cyanopropylphenyl)-

methylpolysiloxane coatings have used to separate anions [46] but no selectivity changes were reported. In a paper on the separation of oxo- and thiooxoarsenate species (arsenic speciation), it was shown that polyacrylamide-coated capillaries were suitable for the separation of arsenate and oxomonothioarsenate whereas the uncoated capillary was suitable for the separation of oxodithioarsenate and tetrathioarsenate [47]. Capillaries coated with poly(acryloylaminoethoxyethanol)- $\beta$ -D-glucopyranoside were used for the separation of organic acids complexed with divalent metal ions [154].

Packed or bonded capillaries have the potential to greatly expand the options available for selectivity manipulation of inorganic anions in CZE. The present limitations are the relatively poor stability of the bonded phase, physical seepage or bleeding of fillings, possible formation of bubbles when gels are used, and the relative difficulty and tediousness of preparation of the bonded or packed phases. Also, polyacrylamide gel coating in capillaries is unstable at alkaline pH [180] and batch-to-batch variation in gel characteristics results in variation of analyte mobility which may necessitate the use of internal standards [181]. Most organic solvents can be used with  $\beta$ -cyclodextrin packed capillaries with the pH range of 3.5–7.5, but suffer hydrolysis at pH values outside the indicated range [173]. Packed capillaries take relatively longer to equilibrate [173] and can be fragile [175]. Lastly, derivatisation can be an involved and elaborate process and “derivatised” capillaries are not widely available commercially.

#### 5. Miscellaneous selectivity effects

Other ways of altering the separation selectivity of anionic solutes include having different BGEs in the anodic and cathodic vials [139] which would introduce an isotachophoretic mechanism. Switching between co-EOF and counter-EOF modes of CZE affords different migration orders [182]. The selectivity of the copper–cyanide anion can be altered by including a small amount of cyanide in the BGE [95]. Hyphenated techniques can be employed as a means of introducing selectivity control, e.g., the use of on-line ion chromatography [179] as a sample preparation method, or on-line electro dialysis as has been shown for inositol phosphates [183].



## 6. Conclusions

Although it has been noted that selectivity manipulation in CZE can be achieved using a limited range of options [182,184], many practical separations can be performed through the judicious control of the parameters which have been discussed in this review. However, the control of selectivity and its application must be performed with an awareness of the practical limitations which exist for many of the parameters.

The option that is likely to expand the control of selectivity for anions in CZE is the use of stable bonded-phase and packed capillaries. Such capillaries offer both an electrophoretic and chromatographic distribution mechanism for control of selectivity. Organic solvents need further study, particularly involving mixtures. Binary and other combinations of cationic surfactants or polymers are likely to alter selectivity. The use of selective additives (complexation) offers room for further investigation: e.g., complexation of oxoanions with catechol or thiols [185]; chloride with acyclic ruthenium bipyridyl receptors [186]; and interaction of nitrate with  $\text{Th}^{4+}$  and nitron. Double- and triple-chain surfactants [187], neutral and zwitterionic surfactants and their mixtures, e.g., vancomycin and SDS, are further possibilities that have the advantage of minimal Joule heat generation [151,187]. Heparin and calixarenes could be applied to inorganic anions as their use has been demonstrated for other analytes [188,189].

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