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Review

Detection techniques in ion analysis: what are our choices?

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Abstract

Trends in detection techniques for ion analysis by ion-exchange chromatography and capillary zone electrophoresis are reviewed. Special attention is paid to conductivity, UV–Vis absorbance, amperometric and potentiometric detection, mass spectrometry (including inductively coupled plasma MS and atmospheric pressure ionization MS) and post-separation reaction detection. Applications reported within the last few years are summarized.

Keywords: Reviews; Detection, LC; Detection, electrophoresis; Organic acids; Inorganic anions; Inorganic cations

Contents

1. Introduction

Nowadays, the term ion analysis covers the determination of low-molecular-mass inorganic and organic ions by ion chromatography (IC) or by capillary electrophoresis (CE). Both techniques have developed into high-performance separation techniques that complement each other. Nevertheless, the power of IC and CE depends on the availability of appropriate detectors. Although universal detection by a bulk property detector based on conductivity measurements is still the preferred mode for routine

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work in IC, new applications have called for the development of advanced detection techniques that might provide more information about the identity, the structure or the elemental composition of the analytes. In CE, further improvements in detection might even be the most important challenge in the development of methods useful for routine work. The present review intends to cover the trends in detection techniques observed within the last few years and to highlight important applications. It should be pointed out that the review will not include pre-separation derivatization procedures, because such applications often lead to separation conditions that are no longer typical for ion analysis in the strict sense.

IC includes a variety of separation modes like ion-exchange chromatography (IEC), ion-exclusion chromatography, ion-pair chromatography or chelation ion chromatography. In this paper, the discussion will be restricted to IEC, which seems to be the currently most widely applied separation mode. The discussion of ion analysis by CE will be restricted to the mode of capillary zone electrophoresis (CZE) as the most important electrophoretic technique in ion analysis.

A characteristic of both IEC and CZE is the fact, that during the separation process analyte ions displace co-ions (these are the ions of the same charge in the mobile phase or in the carrier electrolyte). Therefore, when analyte ions pass through the detector, this volume of mobile phase or carrier electrolyte will contain an increased concentration of analyte ions and at the same time a decreased concentration of the co-ions. The detection signal depends on the difference between a property of the analyte ion and a property of the co-ion (in the worst case, this difference can even be zero). This displacement process can be characterized by the transfer ratio TR, which represents the number of moles of co-ions displaced by one mole of analyte ions. In IEC, TR is simply the ratio of the charge numbers z of the analyte ion A and the co-ion C of the mobile phase (in order to fulfil electroneutrality):

$$\mathrm{TR}_{(\mathrm{IEC})} = \frac{z_\mathrm{A}}{z_\mathrm{C}} \tag{1}$$

(for highly charged ions, z is not necessarily the formal charge number but may be lower because for steric reasons not all of the charged functionalities of the ions may be able to interact simultaneously with the stationary phase).

In CZE, the transfer ratio is not only governed by the law of electroneutrality but also by Kohlrausch's Regulating Function. This leads to the fact that TR not only depends on the charge numbers of analyte ions and co-ions but also on the electrophoretic mobilities μ of analyte ion A, co-ion C and counter-ion X in the carrier electrolyte:

$$\mathrm{TR}_{(\mathrm{CZE})} = \frac{z_\mathrm{A}}{z_\mathrm{C}} \cdot \frac{\mu_\mathrm{C}}{\mu_\mathrm{A}} \cdot \left(\frac{\mu_\mathrm{A} + \mu_\mathrm{X}}{\mu_\mathrm{C} + \mu_\mathrm{X}} \right) \tag{2}$$

Keeping these characteristic behaviors of IEC or CZE systems in mind, it is straightforward to calculate the response for most of the commonly used detection techniques.

2. Conductivity detection

2.1. Non-suppressed conductivity detection

In IEC, the change in conductivity G during the elution of an analyte ion depends on the difference in ionic equivalence conductances λ of analyte ion A and mobile phase co-ion C and is directly proportional to the analyte concentration c_A:

$$\Delta G_{(\mathrm{IEC})} = \frac{(\lambda_\mathrm{A} - \lambda_\mathrm{C}) c_\mathrm{A} \alpha_\mathrm{A}}{10^{-3} K} \tag{3}$$

where α_A and K stand for the degree of dissociation of the analyte and the cell constant of the detector, respectively. To obtain low baseline noise, a low-conductivity mobile phase at a low concentration is advantageous (provided that it exhibits a reasonable elution strength); in this case, the term $\lambda_\mathrm{A} - \lambda_\mathrm{C}$ becomes positive (direct detection). Typical mobile phases encountered in non-suppressed conductivity detection of anions include salts of aromatic carboxylic acids, salts of aliphatic carboxylic acids, salts of aromatic or aliphatic sulfonic acids or polyol–borate complexes. Mobile phases for cation separations include strong inorganic acids (in this case the term $\lambda_\mathrm{A} - \lambda_\mathrm{C}$ becomes negative, which means an indirect detection mode), salts of aliphatic or aromatic amines or complex-forming organic acids and their salts.

In CZE, non-suppressed conductivity detection is somewhat more complex with respect to both instrumental set-up and mathematical treatment. A commercially available instrumentation is based on a disk-ring double electrode for conductivity measurements positioned at the end of the separation capillary [1]. The signal is – similar to IEC – dependent upon the differences in ionic equivalence conductances λ of analyte ion and carrier electrolyte co-ion. Unfortunately, maximizing this difference is problematic, as peak shapes in CZE will deteriorate when the electrophoretic mobilities μ (that is λ divided by the Faraday constant) of analyte ion and co-ion are not similar. Therefore, a compromise is necessary when choosing a suitable carrier electrolyte. The signal also depends on the transfer ratio given in Eq. (2). Assuming monovalent ions only, the following equation has been derived for an analyte anion A [2]:

$$\Delta G_{(\mathrm{CZE})} = \frac{c_A F \cdot \left\{ \mu_X \cdot \left[1 - \frac{\mu_C(\mu_A + \mu_X)}{\mu_A(\mu_C + \mu_X)} \right] - \mu_C \cdot \frac{\mu_C(\mu_A + \mu_X)}{\mu_A(\mu_C + \mu_X)} + \mu_A \right\}}{10^{-3} K} \quad (4)$$

Most applications reported so far deal with co-ions of lower mobility than the analyte ions (direct detection). In such cases, Eq. (4) would suggest that ΔG is increased when the mobility of the co-ion is decreased and the mobility of the counter-ion is increased. Nevertheless, a high detector response does not necessarily guarantee an optimum result; instead, a high signal-to-noise ratio is desired. Assuming that baseline noise is directly proportional to the conductivity of the carrier electrolyte, the term ΔG divided by G of carrier electrolyte must be maximized. The corresponding calculations reveal that both co-ion and counter-ion should have a low mobility [2] to obtain the lowest detection limits. The zwitterionic Good's buffers proved to be suitable carrier electrolytes for a number of separation problems. A compilation of applications can be found in Table 1.

2.2. Suppressed conductivity detection

Eluent conductivity suppression was one of the main new ideas at the introduction of IC in 1975. This detection principle involves in the case of anion separations the use of eluents like sodium hydroxide or carbonate–hydrogencarbonate buffers. Such electrolytes can be converted into species of low conductance like water or H_2CO_3 after exchanging the cations of the eluent for hydrogen ions by a suitable cation-exchange device (analogous principles can be exploited for cation separations). For a sodium hydroxide eluent, the change in conductivity during analyte elution after suppression will entirely arise from the ionic equivalence conductances of the analyte ion and an equivalent amount of H_3O^+:

$$\Delta G_{(\mathrm{IEC})} = \frac{(\lambda_{H_3O^+} + \lambda_A) c_A \alpha_A}{10^{-3} K} \quad (5)$$

A comparison of Eqs. (3) and (5) clearly indicates that suppressed conductivity detection leads to enhanced sensitivity (generally by an order of magnitude).

Suppressors consist of columns packed with the appropriate ion-exchange material or of continuously operating ion-exchange membrane devices. Protons (or hydroxide ions) necessary for the suppression reaction can also be generated by the electrolysis of water (''electrolytic suppressors''). A detailed description of suppressor devices has been given in an earlier review on detectors in IC [10] so that no further discussion seems necessary at this point.

A highly innovative device for eluent generation as well as eluent conductivity suppression has recently been developed by Small and Riviello [11]. They called this new principle ''ion reflux''. Fig. 1 demonstrates the fundamental ideas of this approach. The main part is (for anion separations) a cation exchanger in the potassium form held between two porous electrodes. If a voltage is applied to the electrodes and at the same time water is pumped through the column with the anode being the inlet side, then hydronium ions generated at the anode by the oxidation of water will migrate into the cation exchanger, thereby replacing potassium ions towards the cathode. At the cathode, the reduction of water will lead to the formation of hydroxide ions, so that a solution of potassium hydroxide will come out of the column (see Fig. 1A). If we do the same experiment with water pumped through the column from the cathode to the anode, then the generated potassium

Table 1
Recent examples for non-suppressed conductivity detection in CZE[a]

Analytes	Carrier electrolyte	Sample	Ref.
Sulfur-containing anions	50 m*M* CHES, 35 m*M* LiOH (capillary rinsed with CTAB)	Water and waste water	[3]
Inorganic anions and organic acids	50 m*M* TAPSO, 32 m*M* arginine, 0.15 m*M* TTAOH, pH 8	Electrodipcoats	[4]
Phosphonic acids	30 m*M* MES, 30 m*M* histidine, 0.7 m*M* TTAOH, pH 6.5	Nerve agent degradation products in environmental samples	[5]
Inorganic and organic acids	7.5 m*M* 4-aminobenzoic acid, 0.12 m*M* TTAB, pH adjusted to 5.75 with histidine	Beer	[6]
Chloride, nitrate, sulfate	100 m*M* CHES, 40 m*M* LiOH (capillary rinsed with CTAB)	Rain water	[7]
Inorganic anions	100 m*M* CHES and 40 m*M* LiOH–2-propanol (92:8, v/v), pH 9.3, 80 μ*M* spermine	Lung airway surface fluid	[8]
Sodium, potassium, calcium, magnesium	100 m*M* MES, 100 m*M* histidine, 20 m*M* α-hydroxyisobutyric acid, pH 5.6	Lung airway surface fluid	[8]
Arsenic and selenium species	50 m*M* CHES, 20 m*M* LiOH, pH 9.4 (capillary rinsed with CTAB)	Water	[9]

[a] Abbreviations: CHES = 2-(*N*-cyclohexylamine)ethanesulfonic acid; CTAB = cetyltrimethylammonium bromide; TAPSO = 3-[*N*-tris(hydroxymethyl)methylamino]-2-hydroxypropanesulfonic acid; TTAOH = tetradecyltrimethylammonium hydroxide; MES = 2-(*N*-morpholino)-ethanesulfonic acid; TTAB = tetradecyltrimethylammonium bromide.

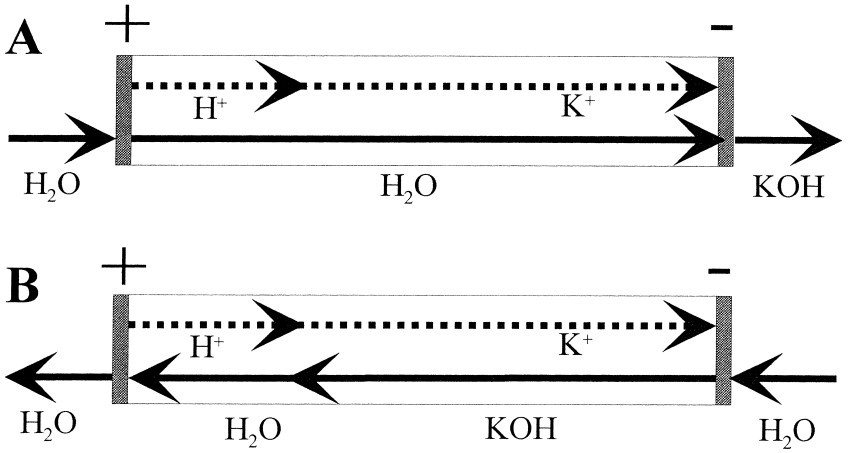

Fig. 1. Flows within a cation-exchange bed held between two porous electrodes. Broken lines: migration of ions; full lines: flow of pumped mobile phase. (A) Water pumped from anode to cathode; (B) water pumped from cathode to anode (adapted from Ref. [11]).

hydroxide will be transported back through the column and will finally reach a zone of cation-exchange material in the hydronium form. In this zone the typical suppression reaction of potassium hydroxide into water will occur (see Fig. 1B). If a cation-exchange material is used that also carries anion-exchange latex particles, then an anion separation system is created that can generate the mobile phase KOH, can do the separation of anions and can suppress the mobile phase for conductivity detection within one and the same device. Small and Riviello also described another device based on the same principle that can be used as eluent generation and suppression system in combination with a conventional external column [11].

A general problem in suppressed IEC can be the fact that sensitivity will be poor when the product from suppression exhibits a small degree of dissociation, such as in the case of very weak acid anions (e.g., silicate, cyanide). A way around this problem has been described by Sjögren and Dasgupta [12,13], who introduced two-dimensional conductivity detection. In this approach, NaOH is utilized as the mobile phase and converted to water in a conventional suppressor with subsequent measurement of conductivity. Afterwards, the suppressed mobile phase enters a microscale electrolytic NaOH generator and a second conductivity detector, which records the decrease in the NaOH background signal in the analyte zones (regardless of the strength of the analyte acid). This technique combines the advantages of both suppressed and non-suppressed conductivity detection and provides some information on peak identity according to the signal ratio from the two detectors, which depends on the pK_a value of the analyte.

A different approach to conductivity detection of very weak acid anions in IEC is the use of incomplete suppression as demonstrated by Huang et al. [14], or the conversion of the weak acids back to their sodium salts using a second micromembrane device [15].

Suppressed conductivity detection has also been applied for CZE separations by Dasgupta and coworkers [16,17]. The detection device consists of a tubular cation-exchange membrane (for anion separations), housed in a reservoir of dilute acid regenerant solution, attached to the end of the separation capillary; the conductivity detection electrodes are positioned in a capillary following the suppression (see Fig. 2). In this arrangement the detector is decoupled from the electric field of separation. Typical carrier electrolytes which are compatible with conductivity suppression and at the same time match the mobilities of low-molecular-mass analytes include sodium tetraborate, sodium glycinate or sodium carbonate [18]. Detection limits at the level of 1 μg/l have been reported.

2.3. Contactless conductivity detection

Designing conductivity cells compatible with the

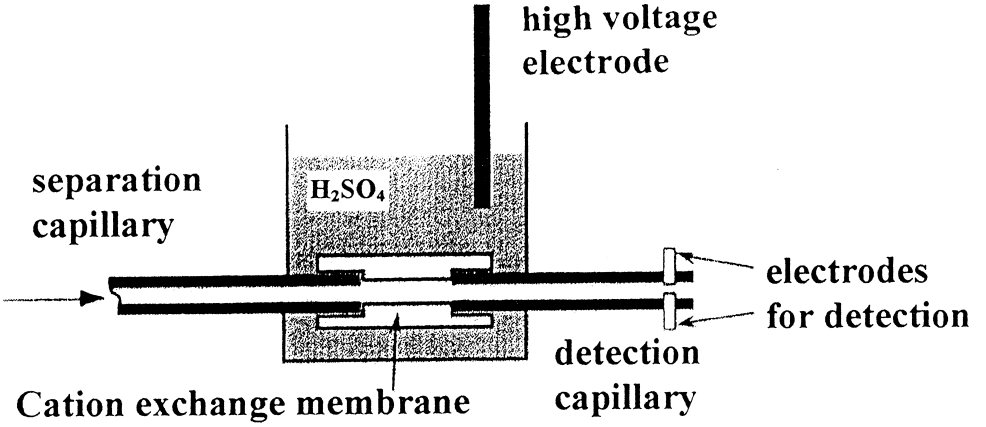

Fig. 2. Design of a cell for suppressed conductivity detection in CZE.

small inner diameters of capillaries used in CZE is not a simple task. Therefore, contactless conductivity detection with the electrodes positioned at the outside of the capillaries can have significant advantages. Recently, Zemann and co-workers [19,20] reported a contactless capacitively coupled conductivity detector for CZE separations of low-molecular-mass anions and cations. It simply consists of two cylindrical electrodes that are slipped onto the separation capillary with a gap between the two electrodes of 1–2 mm. In combination with an oscillator, each of the two electrodes acts as a capacitor; the gap between the electrodes acts as resistor depending on the conductivity of the migrating zone. A similar design has also been described in a recent paper of da Silva and do Lago [21]. Suitable carrier electrolytes and detection limits are similar to those in conventional non-suppressed conductivity detection. In addition to the contactless detection mode with two electrodes, Kaniansky et al. [22] developed a design with four electrodes, that was used for CZE separations in capillaries of 300 μm I.D. The performance of this detector with capillaries of inner diameters of 50–75 μm seems not yet fully investigated.

3. UV–Vis absorbance detection

In UV–Vis absorbance detection, the change of the absorbance A during elution of an analyte ion is governed by the differences of the molar absorptivities ϵ of analyte ion and co-ion in the mobile phase or carrier electrolyte.

The following equation can be derived in IEC for a fully dissociated analyte:

$$\Delta A = \left(\epsilon_A - \frac{z_A}{z_C} \epsilon_C \right) c_A d \tag{6}$$

with d being the path-length of the detector. For direct UV–Vis detection, ϵ_C should be zero; UV–Vis transparent mobile phases include alkane sulfonic acids and their salts, phosphate buffers, sodium perchlorate and similar electrolytes that allow the direct UV detection of anions such as bromide, iodide, bromate, iodate, nitrite, nitrate, chromate, carboxylic acids and some others.

A more universal mode is indirect UV–Vis detection, for which a wavelength should be chosen where ϵ_A is zero and ϵ_C high. Frequently used mobile phases for anion separations are composed of aromatic carboxylic or sulfonic acids and their salts; for cation separations, Cu(II) salts, Ce(III) salts or protonated aromatic amines are appropriate. Both direct and indirect UV–Vis detection are well-established techniques in IC so that no further discussion seems necessary within this paper.

In CZE, an equation similar to Eq. (6) can be derived, which differs just in the term representing the transfer ratio:

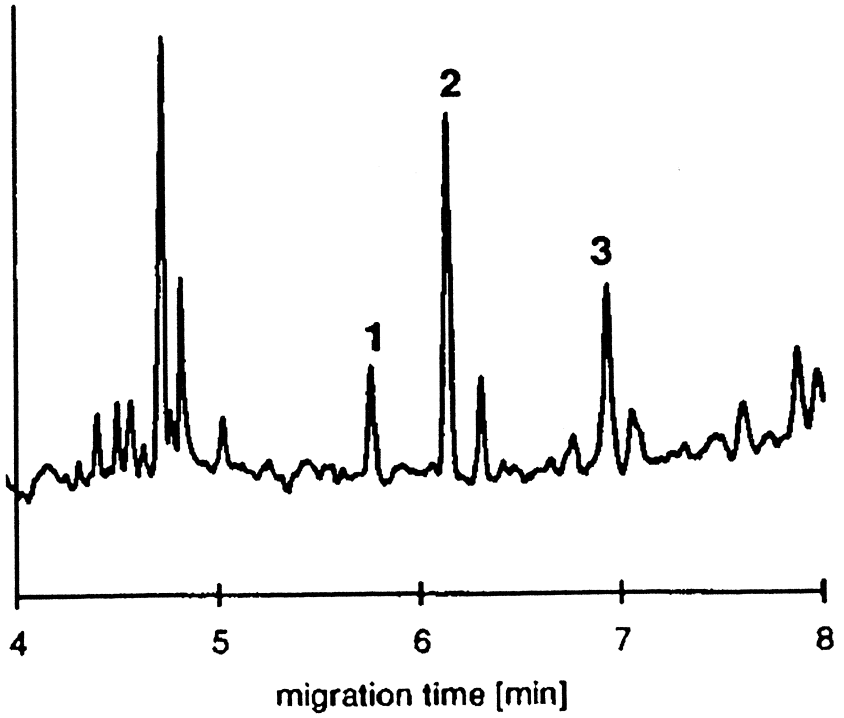

Fig. 3. Electropherogram for the determination of fermenting acids in a grass silage sample extract with direct UV detection at 185 nm. Carrier electrolyte: 50 m*M* NaH_2PO_4, containing 0.5 m*M* tetradecyltrimethylammonium bromide, pH 5.6. Peaks: 1=acetic acid; 2=lactic acid; 3=butyric acid. Concentration range: 10–70 mg/l (reproduced from Ref. [23] with permission).

$$\Delta A = \left[\epsilon_A - \frac{z_A}{z_C} \cdot \frac{\mu_C}{\mu_A} \cdot \left(\frac{\mu_A + \mu_X}{\mu_C + \mu_X} \right) \cdot \epsilon_C \right] c_A d \qquad (7)$$

Contrary to IC, direct UV detection at very low wavelengths such as 185 nm is often feasible in CZE. An example is given in Fig. 3 which shows the direct UV detection of fermenting acids even in very complex matrices such as silage samples [23].

Indirect UV–Vis detection in CZE requires a careful choice of the carrier electrolyte. On the one hand, the co-ion must have a high molar absorptivity; on the other hand, the mobility of the co-ion must be as close as possible to the mobility of the analyte ions in order to ensure optimum peak shapes. Suitable carrier electrolytes for inorganic anions are chromate or pyromellitate, whereas a range of aromatic carboxylates and aromatic sulfonates have been reported for organic acids, phosphates, phosphonates and various other analytes. A comprehensive compilation of carrier electrolytes for indirect photometric detection has recently been done by Doble and Haddad [24,25]. Although most work with indirect UV–Vis detection is done in a wavelength range between 200 and 300 nm, also some highly absorbing dyes like bromocresol green and indigo-tetrasulfonate have been investigated as carrier electrolytes in the visible range [26].

One should be cautious when using carrier electrolytes with more than one co-ion (multiple co-ion electrolytes), since such a composition generally leads to system peaks that may (or may not) interfere with the analyte peaks. A carrier electrolyte with n co-ions will lead to $n-1$ system peaks. Qualitatively speaking, in a system with two co-ions a system peak will be created by a vacancy of that co-ion with the greatest difference in mobility relative to that of the analyte ion. On the other hand, an analyte will displace preferentially that co-ion with the closest mobility match. Various mathematical treatments of systems with multiple co-ion carrier electrolytes have

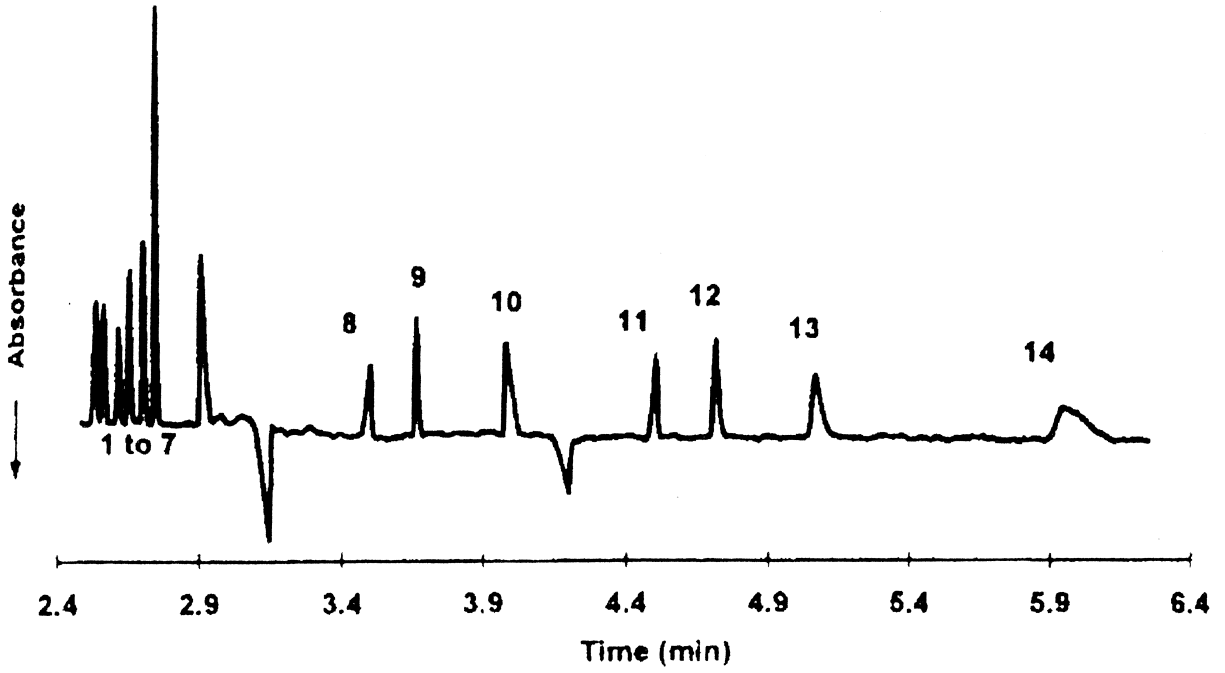

Fig. 4. Electropherogram obtained with three co-ions. Carrier electrolyte: 5 m*M* chromic acid, 5 m*M* phthalic acid, 10 m*M* benzoic acid, 60 m*M* diethanolamine, 0.5 m*M* tetradecyltrimethylammonium hydroxide, pH 9.2. Indirect detection at 254 nm. Peaks: 1=bromide, 2=chloride, 3=iodide, 4=nitrite, 5=nitrate, 6=sulfate, 7=chlorate, 8=phosphate, 9=carbonate, 10=ethanesulfonate, 11=butanesulfonate, 12=pentanesulfonate, 13=hexanesulfonate, 14=heptanesulfonate (reproduced from Ref. [28] with permission).

been reported in the literature. In this paper it may be sufficient to draw the attention to a recent publication of Mikkers [27], who gave a relatively simple model that can adequately describe peak shapes, location of peaks or peaks widths of analyte and vacancy peaks.

Multiple co-ion carrier electrolytes with co-ions of significantly different mobilities may be beneficial when mixtures of analytes with widely varying mobilities are to be separated [28]. In this case, fast analytes will displace the fast co-ion and slow analytes the slow co-ion, thereby maintaining good peak shapes throughout the whole electropherogram. A typical example is given in Fig. 4.

It can be interesting to use indirect UV detection in series with conductivity detection and to do a direct comparison of the two techniques. A typical carrier electrolyte for anions compatible with both modes is 4-aminobenzoic acid adjusted with histidine to a pH between 5 and 6. Fig. 5 shows the separation of inorganic anions and carboxylic acids in a beer sample. Obviously, highest sensitivity is achieved by conductivity detection for fast migrating analytes, whereas slowly migrating analytes give a better response in the indirect UV detection mode.

4. Amperometric detection

Amperometric detection is based on oxidation or reduction of an analyte at a working electrode held at a potential that is high enough to initiate the oxidation or reduction process. The electric current resulting from this electrochemical reaction serves as the analytical signal and is directly proportional to the concentration of the electrochemically active analyte. Generally, amperometric detection is carried out in a direct mode, that is the use of an electrochemically non-active co-ion in the mobile phase or carrier electrolyte.

The potential applied to the working electrode may be constant during the time of separation or it may be applied in a pulsed mode. Triple-pulse and

related waveforms are often applied when the electrode surface gets deactivated by products of the electrochemical reaction. In this case, the successive application of a measuring potential, a cleaning potential and a conditioning potential in a repetitive way (typical frequency 1 to 2 Hz) can lead to a stable response. Typical applications of this detection mode are carbohydrates or amino acids under alkaline conditions. For metal ion detection, a bipolar waveform may be of advantage; metal ions are reduced to the metallic state at the first potential and reoxidized at the second potential, which is the measuring potential. Finally, even cyclic voltammetry waveforms may be used yielding quantitative information via the reduction/oxidation potentials of the analytes.

Constant-potential amperometric detection at carbon, platinum or silver electrodes has been used in IC as a detection technique complementary to conductometric and photometric detection since the early developments of this separation technique. Applications (usually in the oxidative mode) include ions like nitrite, bromide, iodide, sulfite, thiosulfate, thiocyanate, cyanide or arsenite (for applications see also an earlier review on IC detection [10]). Some efforts have been spent on the development of new electrode materials for analyte ions generally non-active at conventional electrodes. One interesting approach is the use of conducting polymers like polypyrrole or polyaniline [29]; with a certain potential applied, an oxidative current will flow in the presence of anionic analytes that can counterbalance the positive sites generated in the oxidation process of the polymer. Another approach is the detection based on ion-transfer reactions across the interface between two immiscible electrolyte solutions (ITIES); Lee and Girault [30] have developed a detector that uses the organic phase as a gel which

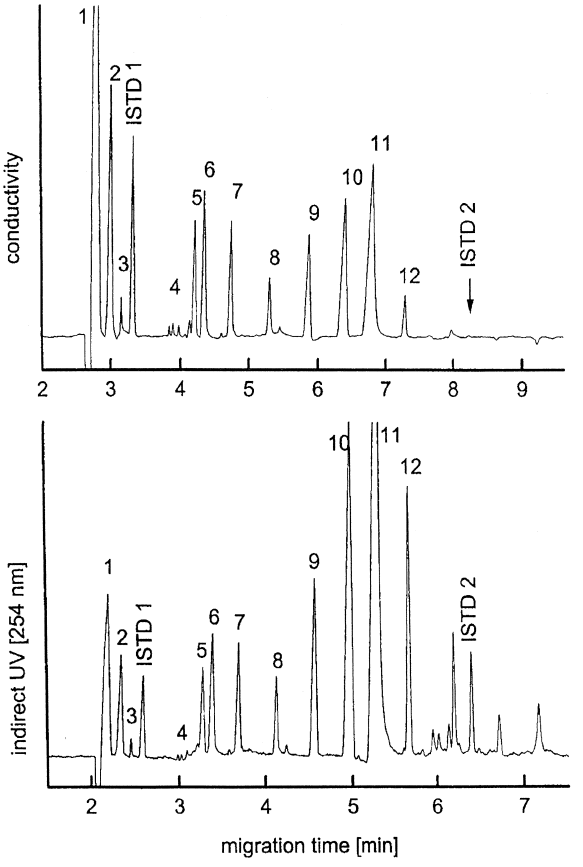

Fig. 5. Electropherogram obtained for a diluted beer sample using conductivity detection (upper part) and indirect UV detection at 254 nm (lower part). Carrier electrolyte: 7.5 m*M* 4-aminobenzoic acid containing 0.12 m*M* tetradecyltrimethylammonium bromide, pH adjusted to 5.75 with histidine. Peaks: 1=chloride, 2=sulfate, 3=oxalate, 4=formate, 5=malate, 6=citrate, 7=succinate, 8=pyruvate, 9=acetate, 10=lactate, 11=phosphate, 12=pyroglutamate, ISTD=internal standard (reproduced from Ref. [6] with permission).

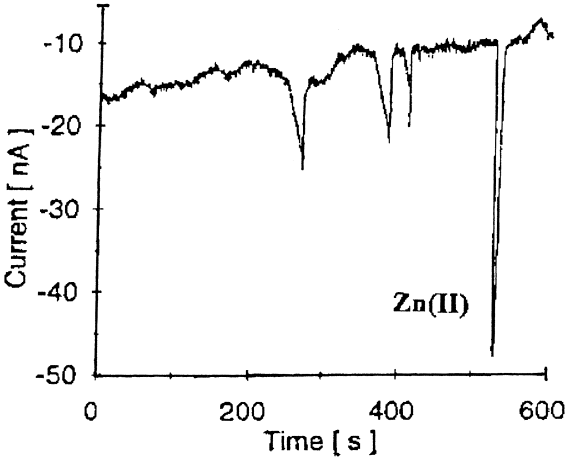

Fig. 6. Electropherogram for the trace determination of zinc in a snow sample with amperometric detection using a gold electrode and a bipolar potential. Electrode potential: −800 mV for 72 ms and 100 mV for 144 ms with data collection at 100 mV (reproduced from Ref. [32] with permission).

allows the use for detection of monovalent cations after conventional IC separation.

Amperometric detection in CZE is a less straightforward approach. Many applications have been done with detection cells that had been decoupled from the high electric field used for the separation process. Such a design is similar to the cell design used for suppressed conductivity detection (see Fig. 2) except for the fact that the ion-exchange membrane between separation and transfer capillary is replaced by a porous membrane that allows the passage of electric current but not of carrier electrolyte; furthermore, the vial containing the separation voltage electrode is filled with carrier electrolyte.

In recent years, amperometric CZE detection has more and more been done without decoupling the detection electrode. When capillaries with inner diameters of less than 50 μm are used, the detection electrode can be positioned directly at the end of the separation capillary without major interferences from the high electric field. A cell design that meets many requirements of routine applications with respect to reliability has been reported by Gerhardt et al. [31]. Such a cell design has also been used for metal ion separations and fast cyclic voltammetry waveforms and multiple-step waveforms at gold and platinum electrodes (see Fig. 6); detection limit improvements down to 10^{-8} *M* were possible [32,33]. Copper electrodes have found some interest for detection of sugars and organic acids [34].

5. Potentiometric detection

IEC or CZE with potentiometric detection using ion-selective electrodes (ISEs) enables the selective determination of selected analytes even in complex matrices. One should take into account that a high selectivity of an ISE may be a distinct disadvantage, because the information obtained in combination with a separation technique might be just the same as the information obtained in flow-injection analysis. Therefore, it may make sense to use detectors with

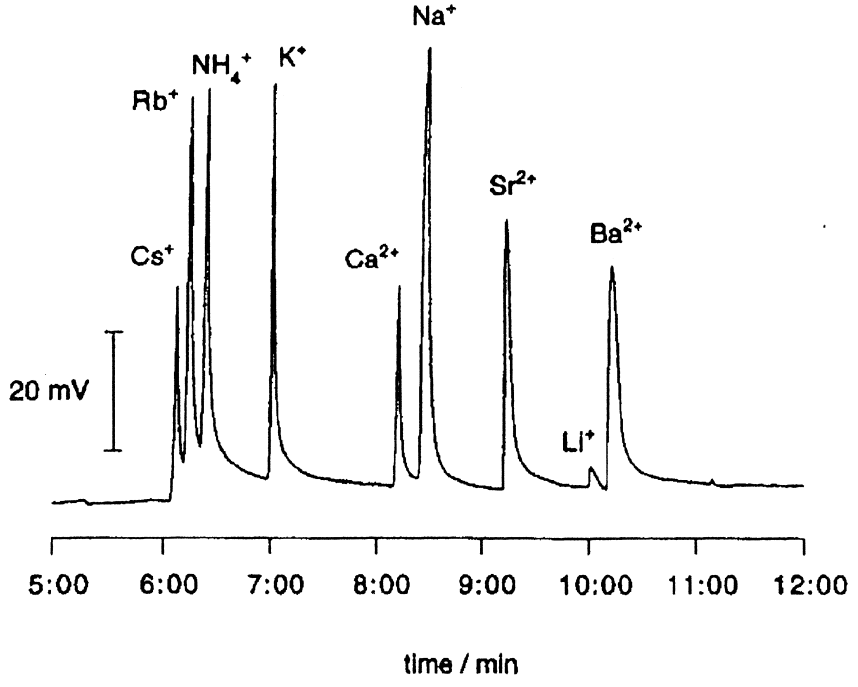

Fig. 7. Electropherogram of alkali and alkaline earth ions using potentiometric detection at a PVC electrode containing potassium tetrakis(4-chlorophenyl)borate. Carrier electrolyte: 10 m*M* magnesium acetate, 2 m*M* 18-crown-6, pH 4.7 (reproduced from Ref. [43] with permission).

Table 2
Recent examples for potentiometric detection in CZE

Analytes	Electrode material	Ref.
Alkali and alkaline earth metal ions	PVC containing *N,N,N′,N′*-tetracyclohexyl-oxybis(*o*-phenyleneoxy)diacetamide or tetrakis(4-chlorophenyl)borate	[42,43]
Inorganic anions	PVC containing 5,10,15,20-tetraphenyl-21H-23H-porphin manganese(III) chloride	[42]
Sulfonic acids	PVC containing tridodecylmethylammonium chloride	[44]
Amines	PVC containing tetrakis(4-chlorophenyl)-borate	[44]
Organic acids	PVC containing a quaternary ammonium salt or a macrocyclic pentamine	[45]
Carboxylic acids	Polycarbonate polymer containing a conducting phenylene vinylene trimer and iodine	[46]
Amino acids	Metallic copper	[40]
Inorganic anions and sulfonates	Metallic copper	[41]

ISEs in series with more universal detection techniques or to use ISEs with intentionally reduced selectivities so that they respond to a wider range of analytes rather than to a single species.

The response and selectivity of an ISE can be described by the Nikolsky–Eisenman equation:

$$E = E^0 + \frac{RT}{z_A F} \cdot \ln\left(a_A + \sum K_{A/i} a_i^{z_A/z_i}\right) \quad (8)$$

with A being the analyte ion and i the interfering ion; $K_{A/i}$ is the selectivity coefficient.

ISEs reported for use in IEC and CZE generally respond to both the analyte ion and the co-ion according to Eq. (8). It may seem a matter of philosophy whether we look at the co-ion as the interfering ion or we look at the co-ion as the ion primarily establishing an equilibrium at the electrode surface and the analyte ion acting as the interfering ion. Unfortunately, the Nikolsky–Eisenman equation may lead to somewhat different results for these two points of views [35]. Without going into further details, treating the analyte ions as the interfering ions would lead to the following change in the potential E during passage of the sample zone through the detector (TR is the transfer ratio):

$$\Delta E = \frac{RT}{z_C F} \cdot \ln \frac{a_C - a_A \cdot \mathrm{TR} + K_{C/A} a_A^{z_C/z_A}}{a_C} \quad (9)$$

Potentiometric detection has found only limited use in routine IEC. Recent publications in this field include papers of Isaldik and Asan [36,37], who used poly(vinyl chloride) (PVC) membrane electrodes for anion or cation separations. The active component of the membrane was a hydrophobic quaternary ammonium salt for detection of anions or a crown ether for detection of cations. Poels et al. [38] employed a conducting oligomer electrode prepared from a mixture of phenylene vinylene trimer with a polycarbonate host polymer and iodine; it was applied to the detection of organic acids.

Potentiometric detection may have some benefits in CZE. Eq. (9) does not include the area of the electrode so that the response should not depend on the size of the electrode. This means that microelectrodes (that are fully compatible with the small dimensions of the separation capillaries in CZE) can be used without sacrificing sensitivity. Several applications reported so far have been based on PVC membranes containing various ionophores. A typical example is given in Fig. 7. Such electrodes have also proved to be suited for portable CZE instruments [39]. In addition, copper electrodes have been used for potentiometric detection of amino acids and various anions in CZE [40,41], but in this case the detection mechanisms are more complex and the signal is no longer independent of the size of the electrode. A list of examples for potentiometric detection is given in Table 2.

6. Detection by emission of light

The measurement of the emission of light in the UV–Vis range includes atomic emission spectrometric (AES) detection as well as fluorescence detection. Luminescence detection would be another technique based on light emission; it is generally performed in a post-column reaction mode so that it will be discussed only later.

The majority of AES detection techniques in ion analysis are based on an inductively coupled plasma (ICP) source. Within the last 2 or 3 years, there had been a significant decrease of papers dealing with AES detection. This is mainly due to the fact, that mass spectrometry (MS) with an ICP source has become available to an increasing number of users; the superior sensitivity of ICP-MS in comparison with ICP-AES has favored the replacement of AES by MS. Therefore, in this paper no further discussion of AES detection will be given.

Analytes with native fluorescence are rare in ion analysis. Alternatively, fluorescence detection can be performed in the indirect mode with mobile phases or carrier electrolytes containing a fluorescent component to provide a fluorescent background signal. Some applications have been reported in CZE with carrier electrolytes such as quinine sulfate [47], 6-aminoquinoline [48], or Ce(III) [49] for cation separations and 2,5-dihydroxybenzoate [49], fluorescein [50–52] or flavin mononucleotide [53] for anion separations. However, sensitivities are worse than those that can be expected in the direct detection mode.

7. Mass spectrometric detection

Two different modes of MS are of major importance for detection in IC and CE. On the one hand, MS with ICP ionization serves as an element-selective detector. On the other hand, atmospheric pressure ionization (API) interfaces to MS can be used to obtain structural information about the analytes.

7.1. ICP-MS detection

The flow-rates of mobile phases in IC are in the order of 1 ml/min which is compatible with conventional sample introduction systems for ICP consisting of pneumatic nebulization and spray chamber. The relatively poor efficiency of transport from conventional nebulizers to the plasma can be improved by use of hydraulic high-pressure nebulizers, direct injection nebulizers or ultrasonic nebulizers. Generally, these sample introduction systems are well established, commercially available and can be used routinely for coupling with IC. Instrumental details relevant for IC–ICP-MS can also be found in a recent review of Sutton and Caruso [54].

Due to its high sensitivity, ICP-MS coupled to IC has become one of the most powerful techniques for speciation analysis in biological fluids, food, environmental samples and various other matrices. Furthermore, the combination of chromatographic separation with the ICP-MS interface is advantageous in those cases where matrix elements may form polyatomic ions that interfere with the signal of the analytes so that ICP-MS alone is no longer really element-selective. A range of examples for the successful hyphenation of IEC with ICP-MS is listed in Table 3. In Fig. 8, a chromatogram is given for the detection of arsenic species in urine.

When coupling CZE to ICP-MS, one has to take into account that the nebulizers of the ICP interface are generally not compatible with the flow-rates generated by the electroosmotic flow. A make-up buffer at the end of the capillary can solve this problem and also serves as the contact to the electrode for the separation voltage. Both pneumatic nebulizers (conventional concentric and cross-flow nebulizers, high-efficiency nebulizers, microconcentric nebulizers, direct injection nebulizers, oscillating capillary nebulizers) and ultrasonic nebulizers have been used. Reviews on different interfaces for CZE–ICP-MS can be found in the recent literature [84,85]. If analytes can be transformed into volatile hydrides (arsenic, selenium and some others), a nebulizer can be avoided; unfortunately, the post-capillary reagent addition and gas–liquid separation makes the instrumentation quite complex. Table 4 summarizes some recent applications of CZE–ICP-MS. The technique is still quite new and many of the papers published so far have focussed primarily on the optimization of the interface and not on the analysis of real samples. Nevertheless, CZE–MS will have its due place in metal speciation analysis.

7.2. API-MS detection

API interfaces can be based on atmospheric pressure chemical ionization (APCI) or on electrospray ionization (ESI) including pneumatically-assisted ESI (ion spray). API-MS detection for IEC and CZE is generally done in the ESI (ion spray) mode.

Table 3
Recent examples for ICP-MS detection in IEC

Element	Analyte species	Sample	Ref.
As	As(III), As(V), arsenobetaine, methylarsonic acid, dimethylarsinic acid	Fish tissue	[55]
As	As(III), As(V), arsenobetaine, arsenocholine, methylarsonic acid, dimethylarsinic acid, trimethylarsine oxide, tetramethylarsonium	Dogfish muscle, mushrooms, seepage water	[56,57]
As	As(III), As(V), arsenobetaine, arsenocholine, methylarsonic acid, dimethylarsinic acid	Mung been seedlings	[58]
As	As(III), As(V), arsenobetaine, methylarsonic acid, dimethylarsinic acid	Urine	[59]
As	As(III), As(V), arsenobetaine, arsenocholine, methylarsonic acid, dimethylarsinic acid	Urine, earthworm extract, groundwater	[60]
As	As(III), As(V), methylarsonic acid, dimethylarsinic acid	Soil and sediment	[61]
As, Se	As(III), As(V), Se(IV), Se(VI), methylarsonic acid, dimethylarsinic acid	Mixtures of fly ash with organic waste	[62]
As, Se, Sb	As(III), As(V), Se(IV), Se(VI), Sb(III), Sb(V), methylarsonic acid, dimethylarsinic acid, selenomethionine	Standards	[63]
As, Cr	As(III), As(V), Cr(VI)	Drinking water	[64]
Br	Bromate	Drinking water	[65–67]
Br	Bromate, haloacetic acids	Drinking water	[68]
Br	Bromide, bromate	Drinking water	[69]
Br, I	Bromate, iodate	Drinking water	[70]
Cl, Br, I	Chloride, chlorite, chlorate, perchlorate, bromide, bromate, iodide, iodate	Drinking water	[71]
Cr	Cr(III), Cr(VI)	Standard reference material	[72]
Cr	Cr(III), Cr(VI)	Waste water	[73]
S	Sulfur-containing inorganic anions	Standards	[74]
Se	Se(IV), Se(VI), trimethylselenonium, selenomethionin	Standards	[75]
Se	Se(IV), Se(VI), selenocystine, selenomethionine	Standard reference material (White Clover)	[76]
Se	Se(IV), Se(VI), selenocystine, methylselenocysteine, selenomethionine, allylselenocysteine	Vegetables	[77]
Lanthanides	Lanthanide ions	Irridiated tantalum	[78,79]
Lanthanides and actinides	Lanthanide and actinide ions	Uranium	[80]
Sb	Sb(III), Sb(V), trimethylstiboxide	Standards, surface water, soil extracts	[81,82]
Sb	Sb(V), trimethylantimony dichloride	Seepage water, sewage sludge	[83]

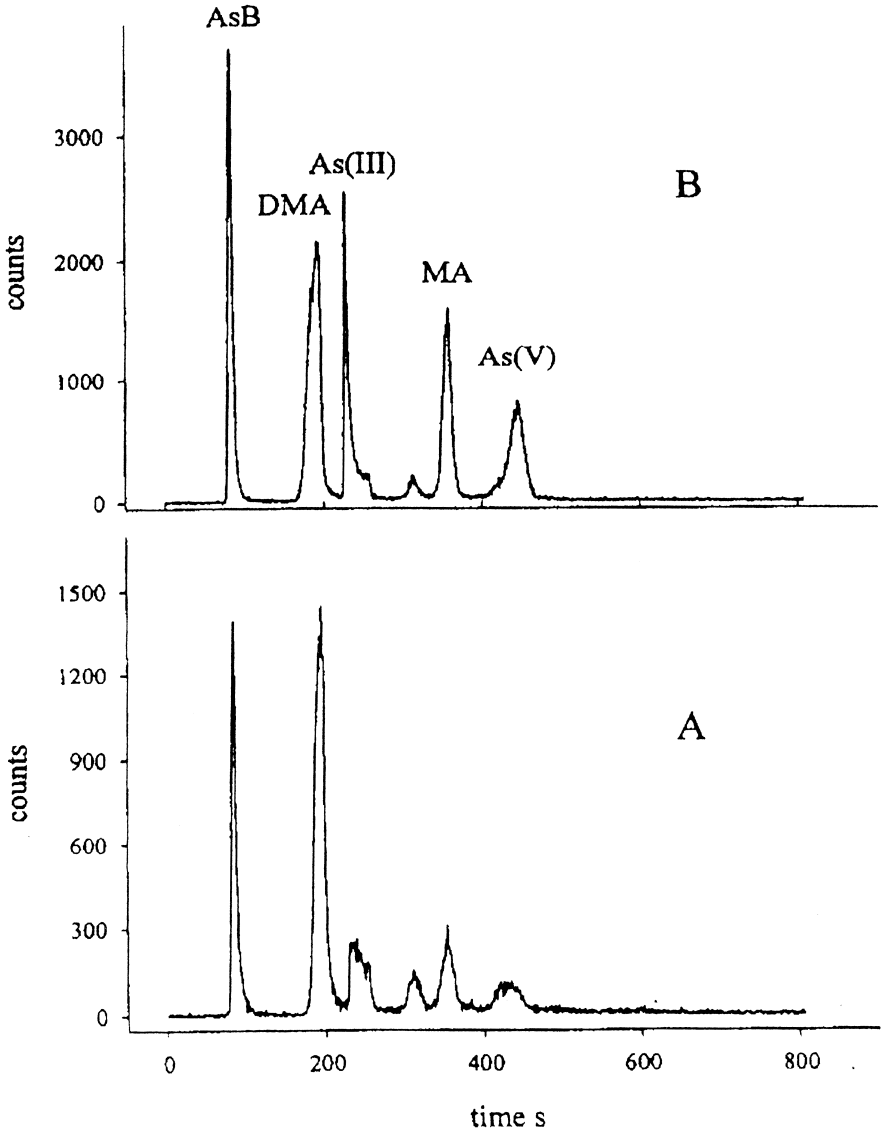

Fig. 8. Chromatogram of a urine sample (after consumption of mussels) using ICP-MS detection. (A) Sample not spiked, (B) sample spiked with arsenobetaine (AsB), dimethylarsinic acid (DMA), As(III), methylarsonic acid (MA) and As(V) (5 μg As/l each) (reproduced from Ref. [59] with permission).

If non-suppressed IEC is used, the choice of the mobile phase is strongly influencing the sensitivity of ESI detection. Especially the kind and concentration of the electrolytes in the eluent affects baseline noise and may be a reason for inefficient transfer of analyte ions from the liquid eluent to the gas phase in the ESI interface which usually results in low sensitivity. Good results have been obtained with mobile phases like ammonium nitrate [95], ammonium sulfate [96] or ammonium citrate [97]. Nevertheless, significantly lower detection limits are possible if IEC is carried out in the suppressed mode (identical to suppressed conductivity detection). A direct comparison of suppressed and non-suppressed mode revealed a 10-fold improvement in sensitivity for oxyhalides [97]. Applications of API-MS de-

Table 4
Recent examples for ICP-MS detection in CZE

Analyte	Type of sample	Ref.	Remarks
Platinum species	Aqueous extracts of soil	[86,87]	
As(III), As(V), methylarsonic acid, dimethylarsinic acid	Drinking water	[88,89]	On-line hydride generation
As(III), As(V), methylarsonic acid, dimethylarsinic acid, arsenobetaine, arsenocholine	Sewage sludge	[90]	
Se(IV), Se(VI)	Drinking water	[88]	On-line hydride generation
Se(IV), Se(VI), selenomethionine, selenocystine, selenocystamine, selenium carrying glutathione	Standards, milk, serum	[91,92]	
Sb(III), Sb(V), methylated Sb	Fouling and sewage sludge	[93]	
Iodide, iodate, thyroxine, triiodothyronine	Serum, urine	[94]	

Table 5
Recent advances of API-MS detection in IEC

Analyte	Mode	Type of sample	Ref.	Remarks
Chlorite, chlorate, bromate, iodate	Non-suppressed	Drinking water	[95,96]	Tandem MS
Chlorate, bromate, iodate	Suppressed	Drinking water	[97]	
Methylphosphate, methylsulfate	Suppressed	Agricultural chemicals	[98]	
Methylphosphate, methylsulfate, *S*-methylphosphoramido-thionate, *O*,*S*-dimethyl-phosphorothionate	Suppressed	Agricultural chemicals	[99]	
Glyphosphate, aminomethylphosphonic acid, EDTA, diacetonketogulonic acid	Suppressed	Ground and surface water	[100]	
Inorganic anions	Suppressed	Standards	[101]	
Lactate, glycolate, chloride, formate, sulfate, oxalate	Suppressed	Pharmaceutical samples	[102]	

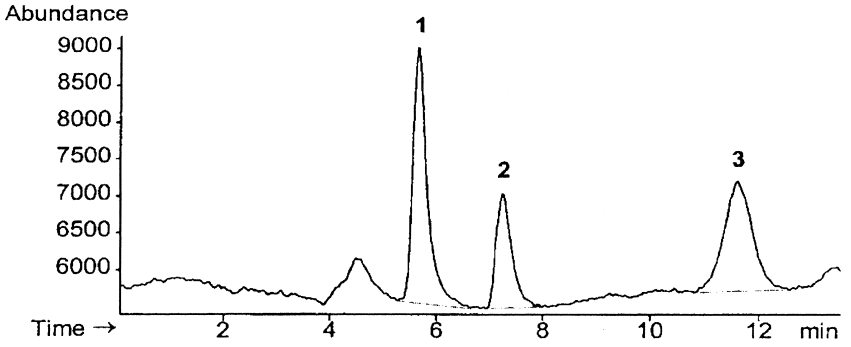

Fig. 9. Chromatogram of oxyhalides with ESI-MS detection. Peaks: 1=iodate, 2=bromate, 3=chlorate (5 μg/l each) (reproduced from Ref. [97] with permission).

tection in IEC are summarized in Table 5 and a typical example for trace analysis of oxyhalides is given in Fig. 9. Other commercially available interfaces have been investigated such as the particle-beam interface for detection of inorganic anions and aminopolycarboxylic acids [103] or the thermospray interface for detection of compounds like alkyl phosphates [98], but their importance has remained limited compared to ESI.

In CZE–ESI-MS, most often a make-up flow (sheath flow) in the range of several μl/min is added at the end of the separation capillary. This sheath flow allows the contact to the electrode of the separation voltage and generates adequate flow-rates for the interface; the composition of the sheath liquid can be chosen in a way that best conditions are established for the ionization process even in cases when a carrier electrolyte must be used that is not optimal for ESI. Several recent examples of this technique are summarized in Table 6.

8. Post-separation reaction detection

Post-separation reaction detection may be called a never-ending story. Again and again new chemical reactions have been adapted to the ion analysis instrumentation, thereby establishing unexpectedly powerful conditions for sensitive and/or selective detection. Although the post-separation derivatization is mostly used in combination with UV–Vis absorbance detection, other techniques like fluorescence or luminescence detection are also possible.

The instrumentation for post-column reaction (PCR) detection in IEC is relatively simple. The effluent from the column is mixed with the reagent

Table 6
Recent examples for ESI-MS detection in CZE

Analyte	Carrier electrolyte	Sheath liquid	Type of sample	Ref.
Haloacetic acids	10 m*M* ammonium acetate in methanol containing 12% acetic acid	2-Propanol–water (80:20) containing 0.1% triethylamine	Drinking and indoor pool water	[104]
Selenomethionine, selenocystine, selenocystamine	2...5% acetic acid	Methanol–water–acetic acid (85:10:5)	Standards	[105,106]
Carboxylic acids	4 m*M* pyromellitic acid, 4 m*M* naphthalene disulfonate, 2 m*M* diethylene triamine, 20% methanol	Same as carrier electrolyte	Standards	[107]
Phosphonic acids	5 m*M* sorbic acid, ammonia, pH 6.5	Pentanol	Standards, tap water	[108]
Inorganic cations	10 m*M* creatinine (or 10 m*M* ammonium acetate) with hydroxyisobutyric acid in 20% methanol, pH 4.5	2 m*M* ammonium acetate in 25% methanol, pH 6.8	Standards	[101]
Inorganic anions	2.5 m*M* pyromellitic acid in 20% methanol, pH 7.8	0.24 m*M* pyromellitic acid in 25% methanol, pH 7.8	Standards	[101]

by means of a T-piece; the reagent is delivered by a pump (that should have a low pulsation) or by pressure applied to the reagent bottle. Afterwards, a knitted PTFE capillary can serve as the flow-through reactor (and also as a mixing device); its length depends on the necessary reaction time. In cases where more than one reagent is needed for the post-column reaction, the instrumentation can be kept simple if one of the reagents can be a component of the mobile phase. Nevertheless, it must be kept in mind that post-column reagents in the mobile phase can gradually coat the stationary phase, thereby altering the chromatographic performance.

Among the most widely used reagents for post-column reactions in IEC are still 4-(pyridylazo)resorcinol (PAR) for the detection of transition metals and lanthanides and Arsenazo III for detection of lanthanides. Some interesting new reagents for PCR have been developed to meet the demands of sensitive detection of bromate (and other oxyhalides) in drinking water. Weinberg and co-workers [109,110] and Inoue at al. [111] described a method based on the conversion of oxyhalides into the tribromide ion by HBr and HNO_2 (detection wavelength 267 nm, detection limit 0.2 μg/l); Walters et al. [112] used chlorpromazine which is oxidized by bromate to an oxidized species detectable at 530 nm (detection limit 0.5 μg/l); Wagner et al. [113] employed *o*-dianisidine and obtained a detection limit of 0.1 μg/l (detection wavelength 450 nm); finally, Achilli and Romele [114] reported the reaction of bromate with a SO_2-reduced fuchsin solution with subsequent addition of HCl (wavelength 530 nm, detection limit 0.1 μg/l). This listing should just be a demonstration how new PCR methods have been developed on demand to meet the requirements of monitoring toxic compounds.

Post-column chemiluminescence detection in IEC is mainly based on the luminol–hydrogen peroxide system and can be applied to trace analysis of various metal ions. A recent example has been given by Gammelgaard et al. [115], who were able to determine Cr(III) and Cr(VI) with detection limits of about 0.1 μg/l.

In CZE, post-separation reaction detection is much less common than in chromatography [116]. One possible instrumental design is the free solution approach, in which the separation capillary ends in an electrolyte vessel containing the reagent. Analytes migrating out of the end of the capillary will mix with the reagent and can be detected right at the capillary outlet (provided the reaction rate is fast); generally, such a technique is restricted to fluorescence detection. This system can be improved if the separation capillary is inserted into a larger capillary, through which the reagent is delivered as a sheath flow. In another design, the separation capillary is coupled to a reaction capillary with a small gap (or

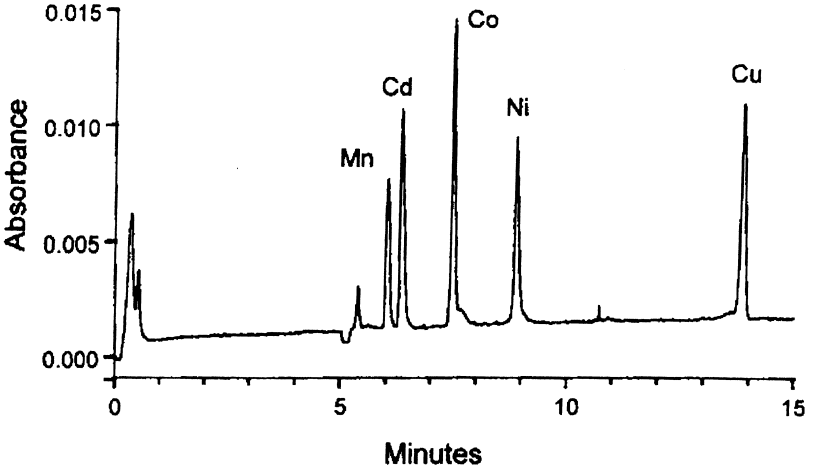

Fig. 10. Electropherogram of metal ions using post-capillary reaction detection with PAR. Carrier electrolyte: 5 m*M* oxalic acid, 10 m*M* ammonium phosphate, pH 8.6. Analyte concentrations 1 . . . 2 ppm (reproduced from Ref. [116] with permission).

porous tubing) between the two capillaries; the reagent can be fed into this gap by means of pressure.

The applicability of post-capillary reaction detection in CZE has been demonstrated with well-tried reagents for trace metal analysis like PAR with photometric detection [116] (see Fig. 10) or 8-hydroxyquinoline-5-sulfonic acid [117] with fluorescence detection. In addition, the luminol–H_2O_2 reaction has been used for chemiluminescence detection of metal ions like Co(II), Cu(II), Ni(II), Fe(III) and Mn(II) [118]. In an indirect format, amino acids have been detected due to the complexation of Co(II) which in the free from enhances the luminol–H_2O_2 reaction [119].

9. Conclusions

The developments in detection techniques for ion analysis have resulted in a variety of different devices from universal detectors like conductivity detection to element-selective or structure-selective detectors like MS. Reliability and robustness have increased over the years and fulfil the needs of users in routine work. Nevertheless, the research in the area of detection in ion analysis has not yet come to a standstill. Several interesting and sometimes exotic-looking detection principles can be found in the current literature, like condensation nucleation light scattering [120,121], bulk acoustic wave detection [122–126], or thermal lens detection [127–129] (to mention just a few). Some of these new developments may still be far away from general acceptance in ion analysis but should be kept in mind during problem-solving. System optimization in ion analysis will always include the art of choosing the most efficient tool from a broad range of detectors available.

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