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Review

Electrochemical detection methods in capillary electrophoresis and applications to inorganic species

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Abstract

The three electrochemical detection methods in capillary electrophoresis, namely conductometry, amperometry and potentiometry, are discussed and compared to the more common optical detection methods. The principles of each method and their implementations are detailed and reported applications to inorganic species are reviewed.

Keywords: Electrochemical detection; Detection, electrophoresis; Reviews; Inorganic anions; Metal cations

Contents

1. Introduction

Detection in capillary electrophoresis (CE) is commonly carried out using optical means (absorption and fluorescence). Electrochemical means in the form of conductometry, amperometry or potentiometry are an attractive alternative, which, however, has been explored comparatively little. This is in interesting contrast to ion-chromatography, the other and older general method for ion determination, which mainly employs conductivity detection and where optical methods are seldom used. Perhaps,

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this is even more surprising when one considers that optical detection is made more difficult in capillary electrophoresis because of the smaller cell volumes and the fact that many ions cannot be detected directly by optical means. The explanation for this situation may be twofold. Firstly, it is fairly easy to adapt absorption detectors, as widely used in high-performance liquid chromatography (HPLC), for capillaries. Many CE instrument manufacturers appear to have gone this route and have incorporated existing detectors into their CE equipment. Secondly, the applied high separation voltage is an intrinsic interference in electrochemical detection. In the early days, elaborate schemes were employed to overcome this difficulty. In recent years, it has, however, become evident that, with the correct design of the system, this does not have to be a problem.

Common to all three variants of electrochemical detection means is the fact that they are intrinsically simpler than the optical methods. An electrical signal is obtained directly without the involvement of an intermediate physical parameter, such as radiation intensity in optical methods. The detector hardware consists of three or fewer small electrodes and some fairly simple electronic circuitry, whereas for optical detection, a light source, monochromator, optical detectors and focussing optics are necessary. In optical methods, the cell volume directly affects the signal via the optical pathlength and, for this reason, the capillary diameters always should be as large as possible. For electrochemical detection, the cell size (sample volume) has only a direct bearing in conductivity measurements. In amperometry, the signal is related to the area of the working electrode, the size of which will be limited by the available sample volume. For potentiometric detection, the signal is completely independent of the sensor size and, therefore, of the cell volume and capillary diameter. Optical methods, on the other hand, have the advantage of providing complete electrical isolation of the detector from the separation voltage applied to the capillary.

Conductivity detection can be regarded as a universal method, while amperometric detection is restricted to electroactive species and potentiometric detection is not possible for certain small ions with multiple charges. Very low detection limits have been reported for amperometric detection. Optical absorption and fluorescence measurements are also restricted to species that show the respective properties. For this reason, indirect optical methods are often used in which the displacement of a sensed auxiliary agent by the analytes is monitored (forced by the requirement to have overall charge neutrality). This approach may also be used for electrochemical detection methods when the analyte species cannot be sensed directly. Chemical derivatization of the analyte in order to impart detectability is another possible approach. Neither of these means is ideal, however, as indirect detection only allows a narrow dynamic concentration range and derivatization adds to the complexity of the method. In practice, the choice of the detection method should perhaps, in the first instance, exploit an intrinsic property for direct sensing and, secondly, be based on the achievable and required detection limits. A compromise may have to be found when several species are to be determined as not all may have the same set of detectable properties.

Other reviews on electrochemical detection in capillary electrophoresis are available [1–5].

2. Conductometric detection

2.1. Principle

Here the ability of ions to conduct charge in solution is exploited. The current produced between two electrodes when applying a voltage is measured and, according to Ohm's law, yields the resistance or the conductance of the electrolyte solution. In order to suppress the influence of any redox reaction taking place at the electrodes, conductometric measurements are usually carried out by employing a.c. voltages at a frequency of typically 1 kHz. If higher frequencies are used, it is possible to employ electrodes that are not in contact with the solution, but attached outside the sample cell [6]. The conductance of a solution (L) is dependent on the electrode area (A), their distance (l), the concentration (c) of the charge carriers and their mobility (λ) in the electric field, according to Eq. (1):

$$L = \frac{A}{l} \sum \lambda_i c_i \quad (1)$$

The mobility of ions is a function of their size (radius of hydrated ion) and the number of charges, incidentally, this is the same property that is exploited for the electrophoretic separation of the ions. Conductometric measurements are therefore not selective and, as stand-alone methods, these are limited to circumstances where the overall sample composition is well known. The fact that all ions give a response in conductometry is on the other hand exactly what is required for detection in a separation method for ions and, for this reason, conductometric detection is widely used in ion-chromatography [7]. This feature on the other hand also leads to a response to any background ion, such as those required as an eluent in ion-chromatography or as pH- and ionic strength buffer in capillary electrophoresis and the counter ions (of opposite charge) to the analyte ion. For the latter reason, the conductivity equation has to include the summation term in all cases. A high background conductivity may compromise the detection limit for the analyte species. So-called suppressed detection methods are therefore used for ion-chromatography in which the background ions are removed from the stream before detection takes place. It is also noteworthy that the cell's dimensions enter the equation via the electrode area and distance and, therefore, the cell volume affects the measured signal.

2.2. Implementations

In early capillary zone electrophoresis and isotachophoresis systems, use was made of so-called potential gradient detection [8–11]. Here, the solution potential in the detection region brought about by the application of the electric field is sensed with a single electrode or a pair of inert electrodes. The voltage drop over the separation capillary is not uniform if the conductivity varies (with sample zones). As this is a function of the conductivity, this can be viewed as a clever means of sensing this property without the need for applying a measuring signal. It may be expected, however, that such an arrangement is more prone to inherent noise than the normal AC mode of conductivity measurements (the added complication of needing to apply a signal should be offset easily by the inherent discrimination against electrical noise). Perhaps for this reason the method did not find wider acceptance. AC conductivity detection was introduced by Everaerts and Verheggen [8]. In the early studies, relatively large bore separation channels and capillaries were used and the detector electrodes were placed ahead of the terminal electrolyte chamber directly into the separation channel. This arrangement is illustrated in Fig. 1A. The two detector electrodes are ideally arranged directly opposite and perpendicular to the separation channel in order to avoid sensing any potential gradient in the channel. With careful design of the AC detector electronics, it should also be possible to discriminate against the DC field or low frequency fluctuations thereof. In a first report on conductivity detection with modern silica capillaries by Huang et al. [12], two small holes were laser drilled into the separation capillary for inserting the two detector electrodes. Simplified end-column detectors were later introduced [13]. This latter arrangement consists of an electrode mounted in the wall-jet arrangement directly at the outlet of the capillary and a second ground electrode located at a distance in the

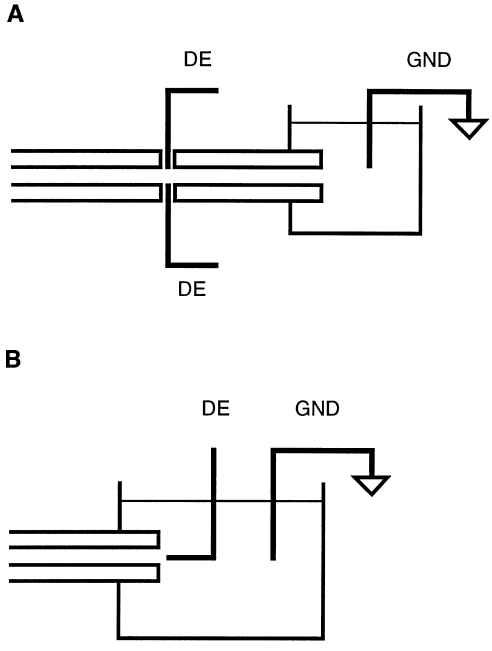

Fig. 1. A.c. conductometric detection. (A) An earlier system with two detector electrodes (DEs) in-line, electrically independent of electrophoretic ground (GND). (B) A later system with a single detector electrode used against electrophoretic ground.

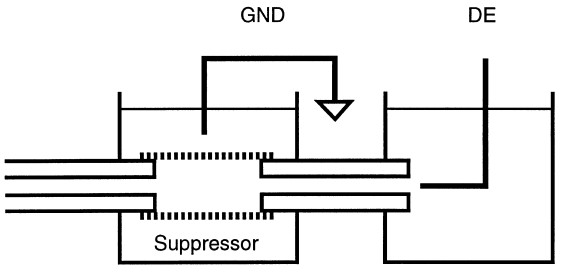

Fig. 2. Conductometric detection with a chemical suppressor. Electrophoretic ground is in the container with the suppressant solution. The conductivity may be measured at the end of the column against this ground (as shown) or with a separate two-electrode system.

buffer container, as illustrated in Fig. 1B. Here, the conductivity is measured against the electrophoretic ground. The conductivity signal will largely arise at the capillary outlet where the detector electrode is located due to the much larger cross-section of the fluid around the counter electrode. This geometry also leads to an immediate loss of the electric field outside the capillary end. The only commercial instrument with electrochemical detection that appears to be available presently incorporates such an end-column conductivity cell [14].

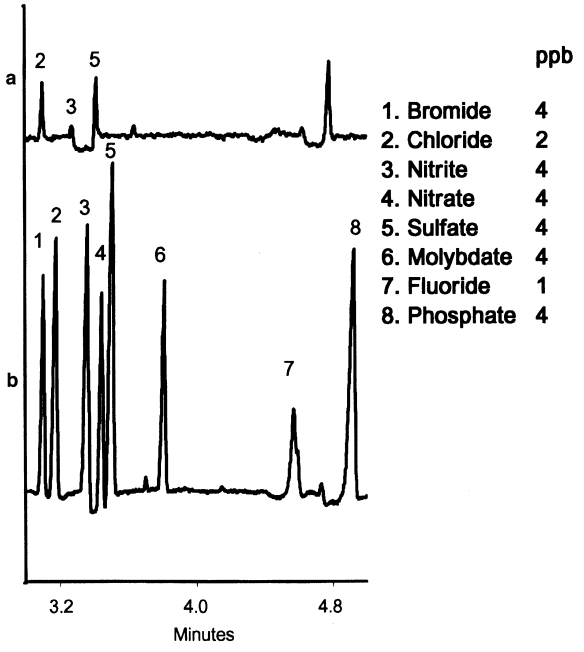

Fig. 3. Electropherogram using conductivity detection for an anion standard mixture of low concentrations determined by sample-stacking (reproduced with permission from Ref. [14]).

Detection limits for normal conductivity detection and non-stacking sample injection are relatively high, being typically 10^{-5} mol/l. The suppressed detection technique allows the detection of concentrations as low as 10^{-7} mol/l [15–18]. Background buffer ions are removed by using weak acids or bases that are rendered non-ionic when in contact with an ion-exchanger membrane, delivering protons or hydroxide ions. To achieve this in capillary electrophoresis without excessive band broadening, a tube of the ion-exchanger material with similar dimensions is attached to the separation capillary ahead of the detector cell, as illustrated in Fig. 2. While lower levels can be determined, the implementation is more complicated than non-suppressed conductivity detection and poses limitations on the choice of the buffer employed.

A different approach to lowering the detection limit is the use of sample-stacking methods, and concentrations below 1 ppb have been determined [14,19,20]. An electropherogram for a low ppb standard mixture is given in Fig. 3 to illustrate this technique. Sample stacking is, however, only possible with samples of low ionic strength and the use of internal standardization may be necessary to obtain adequate precision.

A contactless conductivity detector cell has also recently been described. Two tubular electrodes are placed over the capillary and coupling to the detection volume is achieved capacitively by applying an a.c. field of 40 kHz [21]. The construction of this cell is very simple and allows combination with a second detector. Limits of detection appear to be comparable to normal end-column detection.

3. Amperometric detection

3.1. Principle

Amperometric detection relies on oxidation or reduction of the analyte species on a working electrode. The method is therefore not as universal as conductivity detection, as only electroactive species are accessible. On the other hand, very low detection

limits can be achieved. Generally in amperometry, the measured current (i) is related to the electrode area (A), the number of electrons exchanged (n), Faraday's constant (F), the diffusion coefficient (D), the thickness of the diffusion layer (δ_N) and the concentration of the species (c).

$$i = -AnFD\frac{c}{\delta_N} \quad (2)$$

A prerequisite is that the applied potential is sufficiently positive or negative to induce oxidation or reduction of the analyte species, respectively. The concentration in the bulk of the solution in this process is usually not significantly altered by the electrode reaction in amperometry. For the small cell volumes in capillary electrophoresis, this may no longer be true and near complete bulk electrolysis may take place. Such methods are generally known as coulometry but the delineation between the methods is blurred in the present application. The fraction of analyte consumed in the detection electrode reaction is often expressed as the coulometric efficiency. A high coulometric efficiency is desirable as this relates to the sensitivity of the detection. Pulsed amperometric detection (PAD) is employed when the system is not stable at a fixed applied potential (e.g. through accumulation of reaction products on the electrode surface). In these schemes, the electrodes are cleaned frequently by first applying a high positive potential in which the products and the electrode surface itself are oxidized. This is followed by a negative potential for reducing the electrode surface back to the pure metal and then the actual working potential. Different electrode materials may need to be employed to suit the analytes to be determined. For the determination of many metal cations, mercury wetted electrodes have proven useful. Mercury has a wide cathodic potential window and, also, reduction products are amalgamated, leaving the electrode surface relatively unperturbed. Amperometry usually requires the use of a potentiostat with three electrodes: working, counter and reference. The method is selective for electroactive substances and, with the correct choice of background electrolyte, no baseline signal is obtained. The electrode area enters the equation and the signal is therefore dependent on the size of the electrode and, thus, of the cell. On small electrodes, however, the diffusion pattern is improved, which at least partially offsets this current limitation.

3.2. Implementations

Amperometric detection in capillary electrophoresis was introduced in 1987 by Wallingford and Ewing [22]. A fused-silica capillary of 75 μm internal diameter was used. This was fractured approximately 5 cm from the detector end in order to form a porous joint at which the ground electrode for the applied high voltage was positioned. The detector consisted of a carbon fibre electrode inserted into the end of the capillary with the aid of a micromanipulator under a microscope. Together with a small conventional reference electrode and a counter electrode, the working electrode was connected to a conventional three-electrode potentiostat. In some cases, a two-electrode potentiostat was used instead [23]. The arrangement with the capillary joint is illustrated schematically in Fig. 4A. The grounded porous glass joint in the capillary serves to effectively isolate the detector's electronics from the applied electrical field and current and the electroosmotic pressure serves to propel the analytes past the joint to the detector end. Several modifications to and simplifications of this arrangement were subsequently reported. Different approaches to the fabrication of the joint were proposed [24–26]. It was also shown by Huang et al. [13] that, for capillaries of small diameter (5 μm I.D.), the resulting smaller current through the capillaries did not pose an interference in amperometric detection and the porous joint was not necessary. The use of these very narrow capillaries enabled the sampling of single cells for the detection of electroactive neurotransmitters [27]. It was later found that capillaries of diameters up to 50 μm could be used without a joint [28]. The detector electrode is then kept at a small distance from the capillary end in order to minimize the interference from the electrophoretic current. This approach is illustrated in Fig. 4B. It relies on the fact that the electric field and current density drop readily outside the end of the capillary, as the cross-section of the conducting electrolyte solution is drastically enlarged. The smaller the diameter of the capillary and the greater the distance of the detector electrode from the capillary end are, the larger is the suppression of the

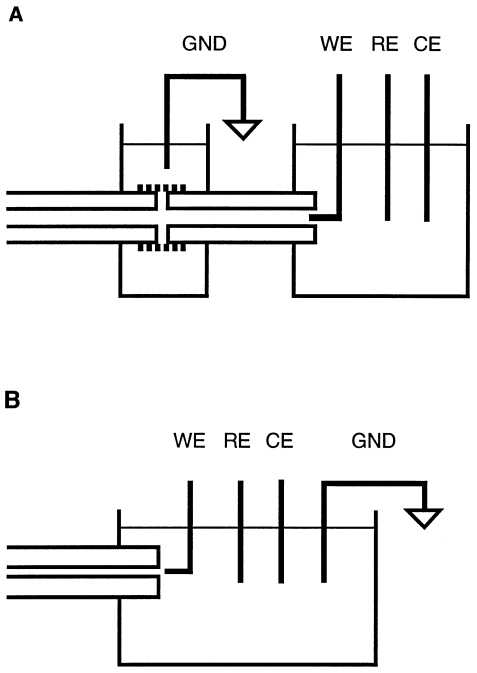

Fig. 4. Amperometric detection. (A) An earlier system used with capillaries with I.D. >approx. 50 μm. This capillary is grounded ahead of detection with a three- (or two-) electrode potentiostat. WE=working electrode, RE=reference electrode, CE=counter electrode. The working electrode can be inserted into the capillary (on-column detection). (B) A system that can be used with capillaries with I.D. <approx. 50 μm. The working electrode needs to be outside the capillary (end-column detection). The capillary end may be etched conically.

applied voltage and current. The capillary end may also be etched conically to achieve the best compromise between electrical interference on the detector on the one hand and coulometric efficiency and band broadening on the other [29]. It was also found that it was not essential to match the diameter of the disk electrodes with that of the capillary and acceptable performance could be achieved with electrodes that are several times larger than the diameter of the capillary [30]. When using a carefully designed cell, it was possible to align capillaries and detector electrodes permanently without the use of the hitherto employed micromanipulators and microscope [31,32], which is an important practical simplification in view of a more widespread acceptance of this detection method. In a different approach, a detector electrode was formed directly on the capillary end by sputter coating [33]. Amperometric detection is illustrated by the electropherogram of Fig. 5 with the determination of heavy metal ions using a mercury film electrode at a fixed applied potential. Typical detection limits for amperometry are 10^{-7} mol/l.

In a further development, the application of fast anodic stripping voltammetry as a detection method has been reported [34]. Here, the analyte is first preconcentrated on the electrode surface by reduction and determined via oxidation in an anodic potential sweep. Detection limits could be lowered by one–two orders of magnitude. The voltammogram yields further information on peak identity (similar to diode array detection for optical absorption) and the distinction between two comigrating (albeit normally well separable) metal ions was demonstrated. An interesting miniaturized device for which the separation channel and detection electrodes were fabricated with photolithographic patterning techniques, as known from the manufacturing of electronic integrated circuits, has also been presented recently [35].

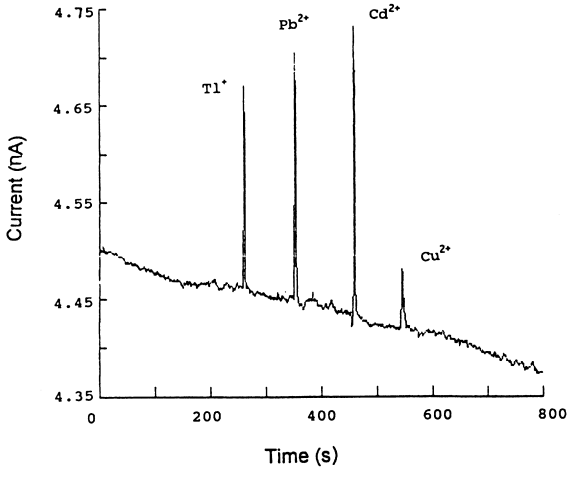

Fig. 5. Electropherogram using amperometric detection for heavy metals at concentrations ranging from 10^{-5} to 10^{-6} mol/l (reproduced with permission from Ref. [47]).

4. Potentiometric detection

4.1. Principle

Potentiometric detection is, as far as the electronic instrumentation is concerned, the simplest of the three methods, as only the measurement of a potential is required. Miniaturized ion-selective electrodes have been used as detectors. Ion-selective electrodes (ISEs) are usually employed as selective sensors for specific ions. However, no ISE is perfectly selective and, in practice, they all respond to a range of different ions and can therefore be used as detectors in separation methods. Their behaviour can be described with the extended Nernst equation, the Nicolsky-Eisenmann equation, in the following form. E is the potential measured against a reference, $E°$ is a constant, and R, T and F are the universal gas constant, temperature and Faraday's constant, respectively, and K and c are the selectivity coefficients and concentrations of species i of charge z, present.

$$E = E° + \frac{RT}{F} \ln\left(\sum_i K_i^{pot} c_i^{1/z_i} \right) \quad (3)$$

The response to the ions is given by the selectivity coefficient, K. This value is usually related to the lipophilicity of the ion as, for the common liquid membrane electrodes, transfer into a non-polar phase is part of the response mechanism. This means that the larger the ion and the lower its charge, the greater the response of the electrode. Detectability increases with the lipophilicity of the ion. Modifications to this pattern can be obtained by including ionophores in the ion-selective membrane that modify this underlying behaviour. For this detection method, the signal is truly independent of detection volume, but the construction of ion-selective microelectrodes on the scale of the diameters of capillaries used in electrophoresis is not an easy task.

4.2. Implementations

Potentiometric detection for cations with ion-selective microelectrodes was introduced in 1991 by Haber et al. [36] and further developed by Nann et al. [37,38]. Initially, microelectrodes that had been developed for physiological studies of single cells had been used. These consist of a glass capillary with a drawn out tip that is filled with a liquid membrane containing the ionophore. The back of the detector capillary contains an internal filling solution and a Ag/AgCl wire as an internal reference electrode. It was also found that, by conical etching of the capillary end, the electrical characteristics of the detection could be improved, as is the case for amperometric detection. In analogy to conventional measurements, a miniature reference electrode, again constructed from a drawn out capillary, containing a chloride electrolyte solution and a Ag/AgCl internal reference electrode to complete the measurement cell was used. This arrangement is illustrated in Fig. 6A. The tip of the microelectrode was aligned with the end of the capillary using a micromanipulator assembled under a microscope. The method was then extended to the detection of anions using anion-selective microelectrodes [39,40] and of amino acids

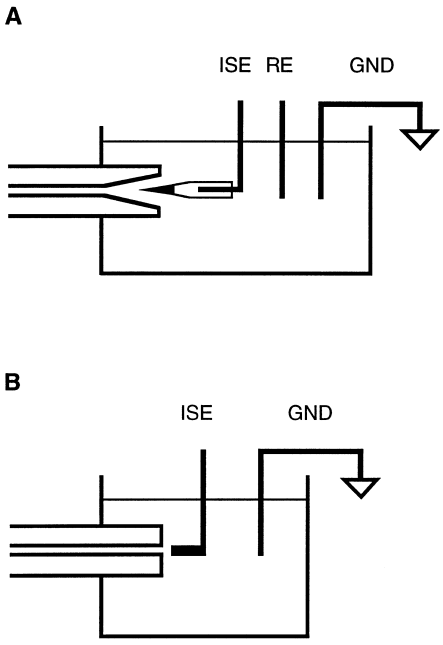

Fig. 6. Potentiometric detection. (A) An earlier system using micropipette electrodes. A conically etched capillary may be used with micropipette electrodes to achieve on-column detection. (B) A later system using wire-coated ion-selective electrodes. The reference electrode may be deleted as the electrophoretic counter electrode provides a sufficiently stable reference potential.

Table 1
Conductometric detection

Species	System	Detection limits	Reference
Alkali and alkaline earth cations and anions	Isotachophoresis, PTFE capillaries, 0.45 mm I.D., potential gradient and a.c. methods, in-line detector cell	–	[8]
Inorganic (and organic) anions	PTFE capillaries, 0.2 mm I.D., potential gradient detection	–	[10]
NO_3^-, Cl^- and SO_4^{2-} in drinking water	200×1×0.2 mm channel in polymer, potential gradient detection	Approx. 10^{-5} mol/l	[11]
Inorganic and organic anions	0.13 mm I.D. quartz capillaries, purpose-built in-line detector cell	Approx. 10^{-5} mol/l	[48]
Alkali metals	50–75 μm I.D. fused-silica capillaries, on-column detector (laser drilled holes for Pt wires), a.c. detection	Approx. 10^{-7} mol/l	[12]
Ca^{2+}, Na^+, Mg^{2+}, Ni^{2+} and Cd^{2+}	75 μm I.D. fused-silica capillaries, detector electrode pushed inside capillary end that has laser-drilled hole for eluent, a.c. detection	Approx. 10^{-5} mol/l	[49]
Anions	75 μm I.D. fused-silica capillary, Nafion tube suppressor with grounded electrolyte ahead of purpose-built a.c. detector cell	Approx. 10 ppb (suppressed)	[15]
Anions	75 μm I.D. fused-silica capillary, Nafion tube suppressor with grounded electrolyte ahead of purpose-built a.c. detector cell	Approx. 10^{-7} mol/l ($\leq$ 10 ppb) (suppressed)	[17]
Chloride, nitrate, sulfate, nitrite, fluoride and phosphate	Isotachophoretic preconcentration coupled with capillary zone electrophoresis in plastic tubes of relatively large bore	Sub-ppb with stacking	[19]

Table 1. Continued

Species	System	Detection limits	Reference
Atmospheric gases sampled directly into capillary electrophoresis instrument	75 μm I.D. fused-silica capillary, Nafion tube suppressor with grounded electrolyte ahead of new purpose-built a.c. detector cell	1 ppb (suppressed)	[16]
Potassium ions	Chemically deposited platinum electrode at capillary end as one electrode of a.c. cell	Approx. 10^{-8} mol/l	[50]
Alkali and earth alkali metals, transition metals, anions	Commercial end-capillary detector, non-suppressed	Approx. 20 ppb with stacking	[14]
Alkali, alkali earth and transition metals, anions	Contactless a.c. cell on 50 μm I.D. fused-silica capillary	200 ppb or higher	[21]
Anions	Commercial end-capillary detector, non-suppressed, use of internal standard with stacking	Sub-ppb with stacking	[20]

using a simple copper wire electrode [41]. In the latter method, the amino acids complex Cu ions formed at the surface of the wire and thus alter its potential. Several simplifications of the detection cell were possible. More rugged miniaturized ion-selective electrodes could be constructed by using the so-called coated-wire approach, which consists of a poly(vinyl chloride) (PVC) membrane in direct contact with a metal wire [42,43]. As for the other electrochemical detection techniques, a fixed cell for alignment of the separation capillary and the detector electrode could be constructed [44]. Furthermore, it was realized that the counter electrode used in the application of the electrophoretic voltage provided a sufficiently stable reference potential. It is therefore not necessary to use conventional reference electrodes [36,41,42]. A schematic representation of the thus simplified design of a potentiometric detector cell is shown in Fig. 6B. These improvements then allowed the construction of a robust portable instrument for CE with potentiometric detection [45]. Potentiometric detection is illustrated by the electropherogram of Fig. 7. 18-Crown-6 was included in the buffer to achieve the separation of K^+ from NH_4^+ and Cs^+ from Rb^+ and this was also found to lead to an increase in the sensitivity of the detector. Note that the peak shapes are typical for potentiometric detection and are caused by the logarithmic response of the detector, which accentuates low concentra-

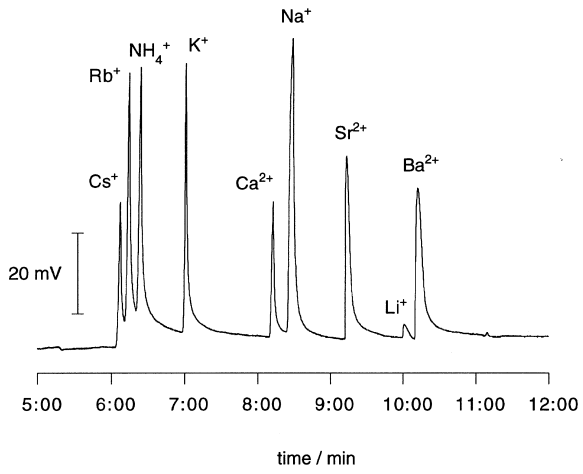

Fig. 7. Electropherogram using potentiometric detection for alkali and alkaline earth metal ions using a coated-wire ion-selective electrode. Concentrations ranged between 10^{-5} and 10^{-4} mol/l.

Table 2
Amperometric detection

Species	System	Detection limits	Reference
Tl^{+}, Pb^{2+}, Cd^{2+}, Cu^{2+}, NO_2^-	Mercury wetted carbon fibre microelectrode, aligned under microscope, purpose-built three-electrode potentiostat, fixed potential, 25 μm capillary without joint	Pb^{2+}: $2 \cdot 10^{-8}$ mol/l NO_2^-: 10^{-5} mol/l	[51]
Heavy metals	Carbon fibre, Au and Pt microelectrodes, some mercury wetted, aligned under microscope, purpose-built three-electrode potentiostat, fixed potential and pulsed detection, 10–25 μm capillary without joint	Between 0.6 and 2000 ppb	[47]
SCN^-, N_3^-, NO_2^-, Cl^-	Partially organic electrolyte, Pt microelectrode aligned under microscope, purpose-built three-electrode potentiostat, fixed potential detection, 25 μm capillary without joint	Between approx. 10^{-9} and 10^{-7} mol/l	[52]
Heavy metals	Au and Pt microelectrodes, pulsed amperometric detection, aligned under microscope, purpose-built three-electrode potentiostat, 10–25 μm capillary without joint	$0.2–20 \cdot 10^{-6}$ mol/l	[53]
NO_2^- and SO_2^- in raindrops	Au electrode in purpose-built off-column detector cell	$<10^{-7}$ mol/l with electrostacking	[54]
Hg^{2+}, Cd^{2+}, Cu^{2+} and alkyl mercury species	Au microelectrode, fixed potential detection, purpose-built three-electrode potentiostat, 50 μm capillary without joint, aligned under microscope	1–3 ppb	[55]
Heavy metals	Au and Pt microelectrodes, fast anodic stripping voltammetry, purpose-built three-electrode potentiostat, 25 μm capillary without joint, aligned under microscope	Approx. 10^{-8} mol/l	[34]

tions. Detection limits for non-stacking sample injection are typically about 10^{-6} mol/l.

5. Applications to inorganic species

The literature on applications of the three detection methods to inorganic species is summarized in Tables 1–3. Note that the results are presented in historical order. The detection limits given are direct quotes from the original publications where available, in other cases, estimates were made from the data given. Overall, it is evident that, in comparison to organic species, the detection of inorganic species by electrochemical means has probably found even fewer applications. Conductometric detection, at least in principle, should work better for inorganic species because of the higher mobility of the small ions that directly affects the detection signal and the fact that suppression detection is not possible, with many organic species being weak acids or bases. Impressive results have indeed been achieved with

Table 3
Potentiometric detection

Species	System	Detection limits	Reference
Alkali and alkaline earth metals	Micropipette electrode, postcolumn, alignment under microscope	$<10^{-5}$ mol/l	[36]
Potassium ion, (dopamine)	Micropipette electrode, conically etched capillary end, alignment under microscope	–	[37]
Alkali and alkaline earth metals, (dopamine, histamine, imidazole), blood serum	Micropipette electrode, conically etched capillary end, alignment under microscope	$<10^{-5}$ mol/l	[38]
Anions	Micropipette electrode, conically etched capillary end, alignment under microscope, dynamically charge reversed-phase column	$5 \cdot 10^{-8}$ mol/l for ClO_4^-, higher for others	[39]
Anions	Micropipette electrode, conically etched capillary end, alignment under microscope	Approx. 10^{-7}–10^{-5} mol/l for electrokinetic injection without electrostacking	[40]
Alkali and alkaline earth metals, anions	Coated-wire electrode for improved lifetime and robustness, alignment under microscope	Approx. 10^{-7}–10^{-5} mol/l for electrokinetic injection without electrostacking	[43]
Alkali and alkaline earth metals	Coated-wire electrode, fixed cell without microscope, crown ether for improved separation	Approx. 10^{-7}–10^{-5} mol/l for electrokinetic injection without electrostacking	[44]

this technique. The shortness of the list for amperometry is noteworthy; this is the electroanalytical method that has found the most usage for the detection of organic species. Amperometric detection should be possible and should be a useful method for most transition metals and for some electroactive anions (composite anions such as nitrogen- and sulphur-containing species). In contrast, alkali and alkali earth metals are not accessible to amperometric detection. Potentiometric detection methods have been reported mainly for inorganic species, as this is the usual domain of ion-selective electrodes, but, as recent reports show, it can also be used for organic species [42,46]. A disadvantage in the application to inorganic ions is the poor selectivity for most multiple charged ions.

6. Conclusions

A trend to more simple cell arrangements is evident for all three modes of electrochemical detection. On-column electrode arrangements, which are generally difficult to construct, have given way to more simple end-column detectors. This is partly made possible by the use of capillaries of small diameter, which reduces the interference from the applied electrophoretic potential and current. Whereas for optical detection, diameters of 75 and 100 μm are the norm, for electrochemical detection, capillary sizes of 25 or 50 μm are more common. Alignment with micromanipulators on a microscope stage has been replaced by fixed cells. This progress in detector design is expected to lead to the more widespread application of electrochemical detection to inorganic species. In particular, conductivity detection promises to be a useful general method, with a performance that is at least as good as that of indirect optical absorption detection. Smaller, and less expensive, instruments can be constructed when employing electrochemical detection.

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