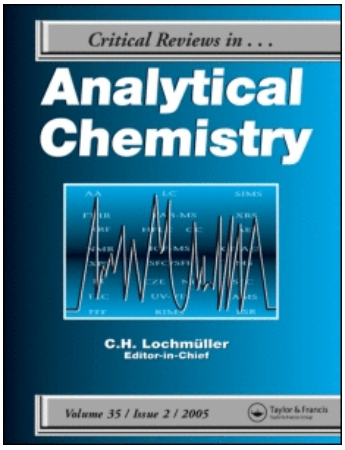

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Electrochemical Detectors for Ion Chromatographic Analysis: A Critical Review

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ELECTROCHEMICAL DETECTORS FOR ION CHROMATOGRAPHIC ANALYSIS: A CRITICAL REVIEW

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I. INTRODUCTION

The internal construction characteristics of detectors are not the only considerations influencing the quality of detection methods. As can be seen from Table 1, virtually all modules of a chromatographic system contribute to the overall performance of detectors.

Table 1 lists only those factors pertinent to electrochemical detection and is therefore incomplete. The improvements in detection limits for inorganic anions which led to the inception of ion chromatography (IC) as an analytical method were in fact derived chiefly from factors external to the detection system. The introduction of suppressors in 1975[1] was the inital step in the development of suppressed ion chromatography (SIC). Improvements in column technology allowing the use of stationary phases with lower ion-exchange capacity[2,3] made the subsequent evolution of single column ion chromatography (SCIC) possible. Further improvements of electrochemical detectors have followed more or less as a consequence of these two major technological breakthroughs. In this review, we maintain a corresponding perspective; developments of detection methods are discussed as they occurred, prompted by improvements of various modules in the ion chromatographic systems.

Electrochemical methods of detection have been reviewed[4-9] several times in the recent past. So far, the concept of these reviews has always been to discuss electrochemical detection as it relates to the whole domain of liquid chromatography. Correspondingly, conductometry has almost always received less attention than the electrolytic techniques since the main impetus for the expansion of electrochemistry into high performance liquid chromatography (HPLC) was the introduction of amperometric methods for the detection of neurotransmitters.[10] The nearly concurrent introduction and rapid development of IC as a methodology within liquid chromatography have so far failed to influence the focus of the reviewers. From the point of view of numerous users of IC, a critical review of electrochemical methods as they relate to this field is thus a long overdue undertaking.

At least two different definitions of IC are currently in use. This term was introduced in 1975

Table 1
FACTORS INFLUENCING ELECTROCHEMICAL DETECTION

Component	Parameter	Influences
Eluent	Chemical composition	Background conductance Proper conditions for electrode reactions pH value to generate the most conductive form for an ion
	Temperature	Conductance, electrode currents, and potentiometric response change with temperature Temperature control improves baseline noise and drift for all electrochemical methods
Injector	Injection volume	Direct injection or trace enrichment on a precolumn Contribution to band spreading
Column	Column chemistry	Proper conditions for electrode reactions must be achieved without an influence on separation The ion-exchange capacity must be fine-tuned to a specific separation problem; large capacities permit large concentration ratios (excesses) of sample components to be dealt with, but a post-column device for signal enhancement is required; low capacities do not require use of post-column devices
	Separation efficiency	Increases in separation efficiency lead to better signal-to-noise ratios
	Selectivity	At extreme concentration ratios of two incompletely resolved peaks, a change in selectivity leads to improved detection limits
Post-column reactors	Conductivity suppressors	
	Conductivity enhancement	See corresponding sections in this review
	Addition of electroactive compounds to enable indirect amperometric detection	Appropriate electrode reaction leading to a high background signal without compromising the reproducibility of the detection
Detectors	Principle	Conductometry, amperometry, voltammetry, potentiometry
	Electronics	Quality of signal processing, time constants
	Cell design	Cell geometry, number of electrodes, electrode materials
	Linearity of response	
Recording device	Analog	Quality of signal connections, time constant
	Digital	A/D convertor characteristics, rate of data acquisition

and was used to describe the chromatographic analysis of inorganic ions, and throughout its early years IC was concerned chiefly with the determination of inorganic anions. It has gradually become the most efficient technique for the detection of these species. Today, after more than 10 years of development, the technique embraces a much wider range of solutes and separation methods and an overlap with alternative liquid chromatographic methods currently exists. In its updated version, the definition of IC includes any liquid chromatographic procedure used for the determination of ionic and ionizable solutes. In this review, we conform with this more extensive second definition of IC and, together with the detection of inorganic anions and cations, we also discuss the detection of some organic compounds that are ordinarily not considered as ionic, e.g., catecholamines, carbohydrates, azo dyes, etc.

II. CONDUCTIVITY DETECTION

James and co-workers[11] are usually credited[4,5] with the first report on the use of conductivity as a method for the detection of ions in the eluate from a chromatographic column. Between 1951 and 1975, about ten additional reported applications of this technique can be found in the literature.[12-22] In that period of time, conductometry had been generally considered to be a simple and quite useful technique which lacked sensitivity and was therefore used chiefly for preparative scale chromatography rather than for trace level detection. Introduction of post-column signal enhancement devices[1] and the use of improved columns[2,3] a few years later brought about dramatic changes in the scope of applications. Conductometric detection has now become the preferred tool for the determination of trace concentrations of ionic compounds.

In the next two sections, we discuss the first successful attempts to increase the sensitivity of conductometric detection by the employment of post-column signal enhancing devices. We also review an alternative approach that achieves similar sensitivity improvements by an appropriate change in column technology. A discussion of the developments in electronics and detector design, occurring simultaneously with the introduction of post-column signal enhancers, and of improved columns follows.

A. Post-Column Enhancement of the Conductance Signal

The high concentration of ionic species in the eluents required for elution of ions from ion-exchange materials was the main cause for the lack of sensitivity of conductivity detection in the time period between 1951 and 1978. Detector signals resulting from separated ions were dominated by the large value of background conductance from the mobile phase.

In the first successful attempt to overcome this obstacle to sensitive conductometric detection, Small et al.[1] introduced a post-column signal-enhancing device called a chemical suppressor. In the initial stages of its development, this device consisted of a second column connected in series with the separator column. The suppressor column was packed with ion-exchange material of opposite charge to the material in the separator column. For example, in order to achieve sensitive detection of anions after their separation on an anion-exchange packing inside the separator column, cation-exchange material was placed in the suppressor column. The experimental arrangement and an example of a suppression reaction are given in Figure 1. Several other typical eluents allowing the suppression of the conductivity background in chemical suppressors are shown in Table 2. Sodium phenoxide was used as an eluent in the initial experiments with chemical suppression,[1] but because of its tendency to poison the separator columns, this eluent has gradually lost its importance[24] and for this reason is not included in Table 2.

Packed column suppressors of the same type as shown in Figure 1 have several disadvantages. The most important drawback is the requirement to regenerate the suppressor after only several hours of use. In the case of anion separations, the cation-exchange groups originally in the hydrogen form become progressively converted to the sodium form as a result of their suppression reaction with the sodium carbonate-bicarbonate eluent. After total exhaustion of the sulfonic groups, the suppression reaction will no longer occur and a strong increase of the background conductance signal will be recorded. Another difficulty is derived from the ability of undissociated aliquots of weak acids (HNO_2 and H_2CO_3 in Figure 1) to penetrate past the functional groups of the suppressor material.[25,26] This results in a decrease of peak heights for the dissociated anions (NO_2^-, HCO_3^-). The magnitude of such a decrease is dependent on the degree of exhaustion of the cation-exchange material in the suppressor column.[25] The retention of carbonic acid in the pores causes the negative system peak due to this species to change its position with increasing exhaustion of the suppressor material.[25,26] The constantly changing position of a negative system peak makes reliable quantitation of the positive peaks for separated anions rather difficult.

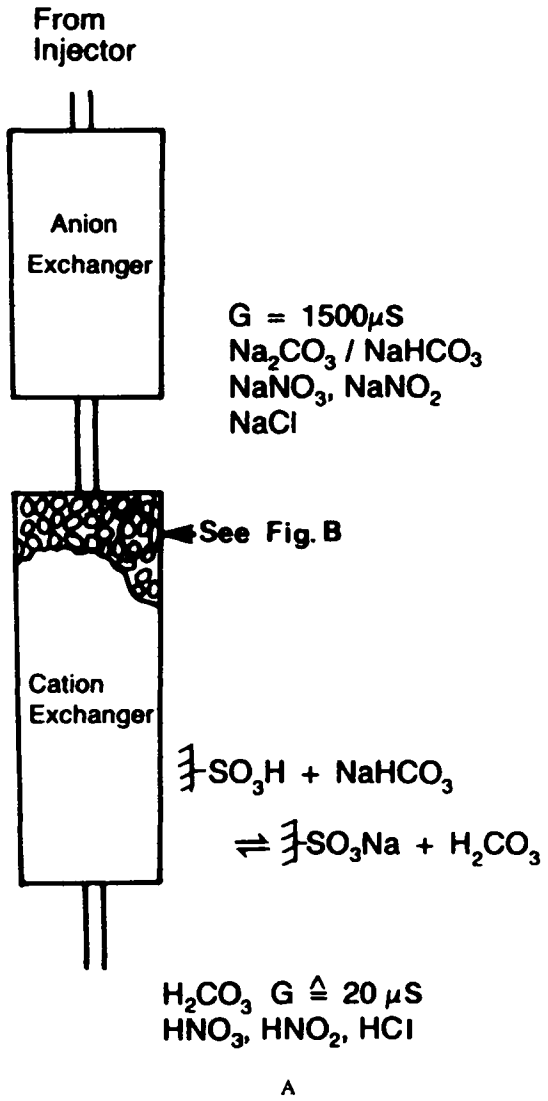


FIGURE 1. Cation-exchange column as a suppressor of the background conductance before the detection of anions. (A) Change of background condutance and the corresponding chemical equilibrium occurring in a carbonate eluent after a separation of anions. (B) Ion-exclusion processes influencing the detection of anions after chemical suppression. (See Table 3).

The recognition of these problems led to subsequent development of more sophisticated suppressor devices. At present, the furthest developed commercially available version of a post-column signal-enhancing device is the micromembrane suppressor (MMS). The principles of suppression on fiber and flat sheet membranes are illustrated in Figure 2, and a typical chromatogram obtained with the help of MMS is given in Figure 3. Table 3 summarizes this continuing development and lists the most important advantages and disadvantages of the signal-enhancement devices as they are known from practical experience or reported in the literature.

Various additional reports[36-39] on diverse aspects and possible improvements of signal enhancers occurring in recent years has led to the conclusion that development has yet to reach

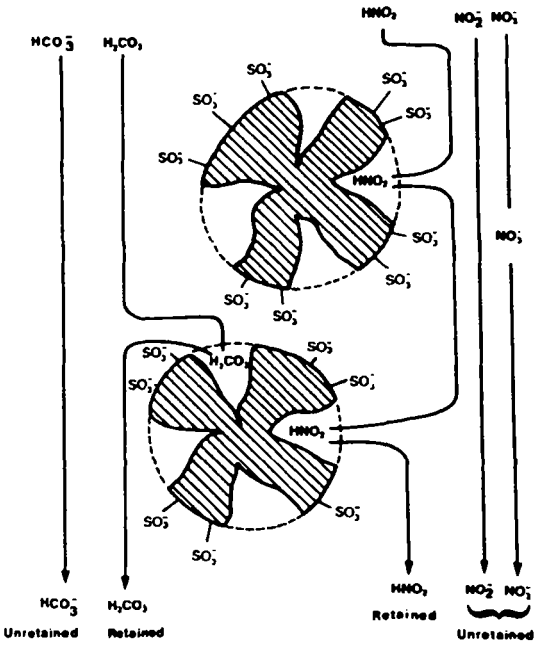


FIGURE 1B.

Table 2
TYPICAL ELUENTS USED IN SUPPRESSED ION CHROMATOGRAPHY[23]

Eluent	Species separated	Product of suppression	Typical regenerant used in membrane-based suppressors
$Na_2B_4O_7$	Anions	H_3BO_3	H_2SO_4
NaOH	Anions	H_2O	H_2SO_4
$NaHCO_3/Na_2CO_3$	Anions	H_2CO_3/HCO_3^-	Dodecyl benzene sulfonic acid
Protonated phenylenediamine	Cations	Phenylenediamine	KOH
HCl	Cations	H_2O	Tetramethylammonium hydroxide

a final stage. Significant improvements in the extra-detector post-column signal enhancement can be expected in the future.

B. Column Modifications Leading to Improvements in Conductivity Detection

The following expression has been derived to describe the conductance change in the detector cell during the elution of a peak from the column as a function of a change in sample concentration,[40,41]

$$\Delta G = \Delta(G_{sample} - G_{eluent}) = \frac{(\lambda_{E^+} + \lambda_{S^-}) \cdot \alpha_S - (\lambda_{E^+} + \lambda_{E^-})\,\alpha_E \cdot \alpha_S}{10^{-3}\,k} \cdot \Delta C \qquad (1)$$

In Equation 1, G is the conductance in μS; λ is the limiting equivalent conductance of eluent cation (E^+) and anion (E^-) or of the sample anion (S^-) in μS cm^2 equiv^{-1}; α describes the fraction of the eluent or sample that is ionized; k is the cell constant in cm^{-1}; and C_S is the normality of the sample anion.

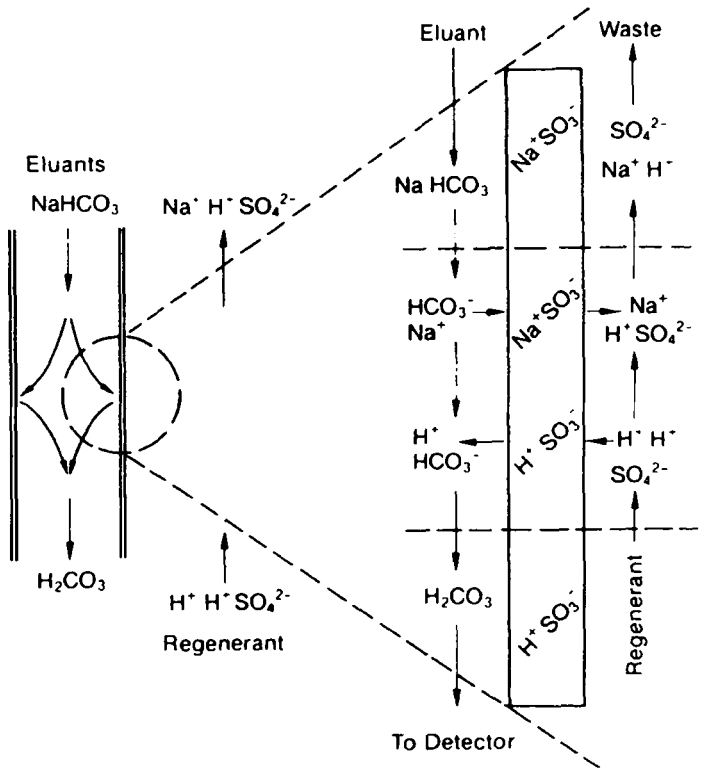


FIGURE 2. Chemical suppression and continuous regeneration in membrane-based anion suppressors. (Reproduced from Weiss, J., *Handbuch der Ionenchromatographie*, VCH Verlagsges., Weinheim, Federal Republic of Germany, 1985, chap. 3. With permission.)

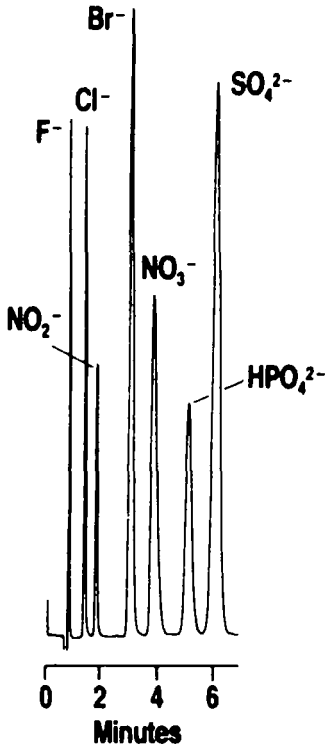
Using a simplified form of Equation 1, it can be shown that the sensitivity of detection ($\Delta G/\Delta C$) is affected predominantly by the difference between the limiting equivalent conductances λ_{E^-} and λ_{S^-}:

$$\frac{\Delta G}{\Delta C_S} = \frac{\lambda_{S^-} - \lambda_{E^-}}{10^{-3}\,k} \tag{2}$$

The limits of detection are, on the other hand, influenced jointly by the value of sensitivity and by the level of noise, which is a function of the background conductance, temperature, and pressure:

$$\text{Detection limit} = f\{\Delta G/\Delta C_S, \text{noise}(G_E, T, P)\} \tag{3}$$

As discussed in the previous paragraph, improvement in detection limits can be achieved by suppression of the conductance background G_E. Equations 1 to 3 help to better understand the underlying processes behind conductivity suppression, e.g., in carbonate-bicarbonate eluents. By removing sodium ions from the eluent, which under practical conditions is achieved with varying degrees of efficiency, the value of G_{eluent} in Equation 1 is decreased. At the same time, an increase in G is also derived from the ionization change in the mobile phase. The term λ_{E^-} in Equation 1 no longer corresponds to $\lambda_{CO_3^{2-}} + \lambda_{HCO_3^-}$ and is equal only to $\lambda_{HCO_3^-} \cdot \alpha_E$. The total



Concentrations

Anion	PPM
F^-	1
Cl^-	2
NO_2^-	3
Br^-	10
NO_3^-	10
HPO_4^{2-}	10
SO_4^{2-}	15

FIGURE 3. Typical chromatogram obtained with an anion membrane suppressor. (Courtesy Dionex Corporation.)

contribution of the carbonate is then futher reduced by the low value of α_{E^-} in the solution of carbonic acid appearing at its natural pH.

Employment of suppressor devices is not the only method available to increase the magnitude of the ΔG term. As demonstrated in 1979 by Gjerde et al.,[2,3] conductometric detection also can be improved by the utilization of low conductance eluents in conjunction with low ion-exchange capacity columns (1 to 150 μequiv/g). Several eluents for each of the newly developed columns were shown to give high values of ΔG by virtue of small equivalent conductances of their eluting anions.

The eluent conductance, G_{eluent}, is given by:

$$G_{eluent} = \frac{(\lambda_{E^+} + \lambda_{E^-}) \cdot C_E \cdot \alpha_E}{10^{-3}\, k} \qquad (4)$$

As indicated in Table 4, some eluent-column combinations in SCIC enabled sensitivity similar to that obtained with SIC to be reported as early as 1981.[41,42]

A chromatogram obtained using the benzoic acid eluent is shown in Figure 4. Very soon after this initial breakthrough in SCIC, another approach to better sensitivity was demonstrated by Okada and Kuwamoto,[43] who used potassium hydroxide eluent for separation and detection of weakly retained anionic species.

The negative value of sensitivity for the KOH eluent in Table 4 results from the negative deflection of the chromatographic peaks. A typical chromatogram of anions in this eluent is compared in Figure 5 with a conventional (direct conductivity detection) separation obtained

Table 3
POST-COLUMN SIGNAL ENHANCERS, 1975—1988

Device	Advantages	Disadvantages
Column suppressors (see Figure 1)	Suppresses the background conductance	Need to be periodically regenerated Changing position of system peaks dependent on the degree of exhaustion of $-SO_3H$ sites The peak height for weakly dissociated ions changes constantly Suppression reaction causes the signal for weak acids to decrease — true also of fiber and membrane suppressors
Hollow-fiber suppressor[25-28] (see Figure 2)	Suppresses the background conductance Shows no ion-exclusion related effects Continuous regeneration	Mechanically unstable, unable to withstand large back-pressures from detector cells To prevent peak spreading the fibers must be filled (e.g., with glass beads)[28] Regenerant often able to penetrate into the eluent
Flat sheet membrane suppressor[29]	The same as the hollow fiber suppressor Mechanically stable Large surface area and resulting high ion-exchange capacity make gradients possible	Plugging of the narrow passageways Pump or gas pressure required to force the regenerant through the device Leaking at high back pressures Incomplete suppression reactions leading to undesirable artifacts in conductivity detection[30] (see Section II.D)
Reverse suppressors[31,32] (column or membrane)	Enhances conductance signals for weakly dissociated ions	Same as column or membrane suppressors Signal sensitivity for strongly ionized ions is decreased
Two-step signal enhancement[33]	The first step is the same as in reverse suppression In the second step, the weakly dissociated solute is replaced by OH^-	As with all signal enhancing devices, the additional module between the column and detector increases the complexity of the system Similar criteria should be applied as in the selection of post-column reactors, i.e., use only if a simpler system is not avaliable

with a phthalate eluent. Note that the ratio of the peak heights for nitrate ($\lambda_{s^-} = 71$) agrees well with the ratio of sensitivities for phthalate and KOH in Table 4.

The less-than-optimal conductivity response for weakly ionized species in SIC has been known for some time. Reverse suppressors and other signal-enhancing configurations have been proposed to deal with this problem (see Table 3). In KOH eluents and on low capacity separators (30 μequiv g^{-1}),[44] the same characteristic of weak ionization leading to difficulties elsewhere allows for ultra-sensitive detection of anions of weak acids. Silicate, which does not exist in an ionic and conductive form below pH 9, is appreciably ionized in 2 m*M* KOH ($pK_1\ H_2SiO_3 = 9.7$, pH of 2 m*M* KOH = 11.3) and can be used as an example (see Figure 6).

The utilization of high background eluents for indirect conductometric detection (negative $\Delta G/\Delta C$) is made possible by instruments capable of electronic suppression of the noise contributed by high conductance backgrounds. In such instruments, the linear increase of noise with increasing background conductance (conductance of noise in Figure 7) is prevented by an appropriate processing of the signal before it is sent to a recording device. Although the actual fluctuations of the conductance are increasing, a slight decrease of the noise of the recorded

Table 4
BACKGROUND CONDUCTANCE AND SENSITIVITY IN SUPPRESSED AND NONSUPPRESSED ELUENTS

Eluent	Concentration (m*M*)	G_{eluent} (μS)[1] before suppression	G_{eluent} (μS) after suppression	$\Delta G/\Delta C_i \times 10^3$
Na_2CO_3 / $NaHCO_3$	3.0/2.0	20.9	0.63	12.7
Benzoic acid	1.0	2.8	NA	10.0
Potassium phthalate, pH 7.0	0.20	1.4	NA	1.0
KOH	2.0	16.5	NA	−3.9

Adapted from Gjerde, D. T. and Fritz, J. S., *Anal. Chem.*, 3, 2326, 1981.

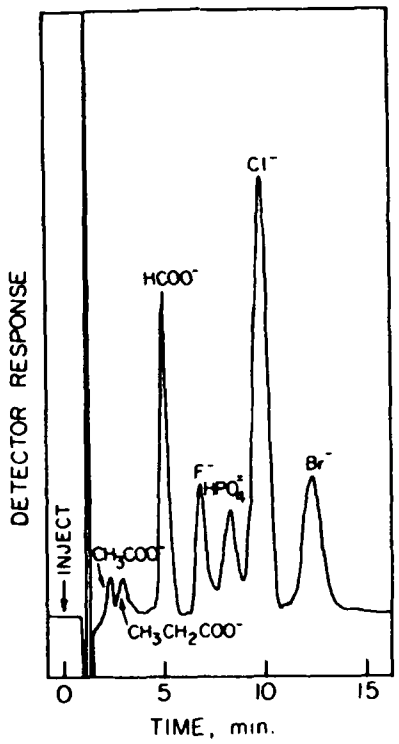


FIGURE 4. Separation and detection of 9.2 ppm acetate, 30 ppm propionate, 9.4 ppm formate, 7.2 ppm fluoride, 12.2 ppm phosphate, 8.4 ppm chloride, and 9.8 ppm bromide using 1 m*M* benzoic acid as a high-sensitivity eluent. Sensitivity setting: 1 μS full scale. Column: XAD-1 resin, 23 μequiv/g, 20- to 25-μm particle size. (Reproduced from Gjerde, D. T. and Fritz, J. S., *Anal. Chem.*, 53, 2324, 1981. With permission.)

signal (volts of noise in Figure 7) is actually observed for increased conductance backgrounds within a certain range. Dependencies of this kind can be easily verified for each detector type prior to its use with highly conductive mobile phases. With instruments giving the same rate of increase of noise in the output signal as in the measured conductance signal, the same detection limit as demonstrated in Figure 6 cannot be expected. A more detailed discussion of the design of conductivity detectors is given in a later section.

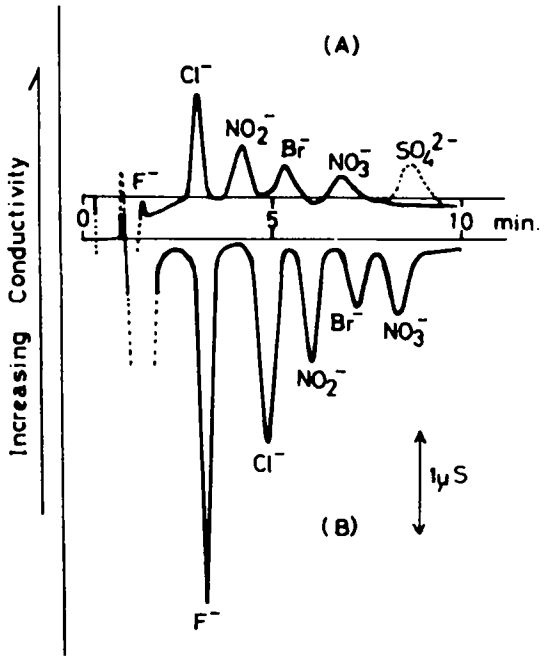


FIGURE 5. Direct and indirect conductometric detection. All anions at 5 ppm, 100 μl were injected. (A) Eluent, 1 m*M* potassium biphthalate adjusted to pH 6. (B) Eluent, 2 m*M* potassium hydroxide. Column: TSK-GEL IC-620a; flow rate: 1 ml/min. (Reproduced from Okada, T. and Kuwamoto, T., *Anal. Chem.*, 55, 1001, 1983. With permission.)

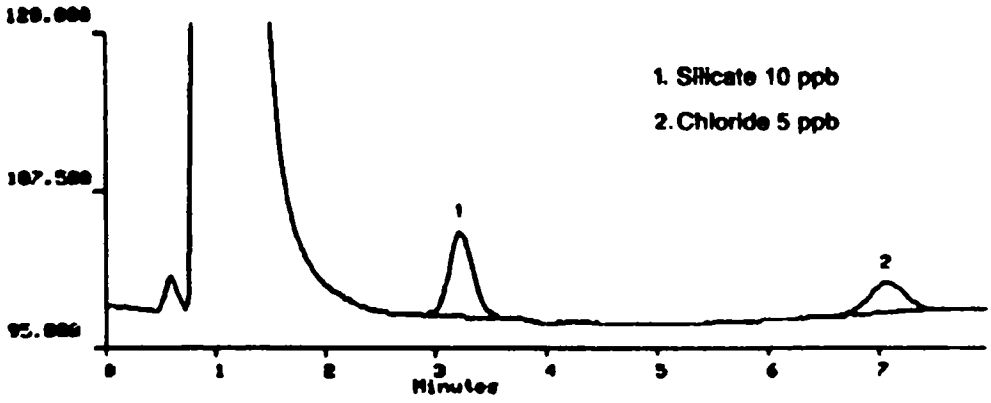


FIGURE 6. Indirect conductometric detection of silicate and chloride. Eluent: 2.0 m*M* potassium hydroxide; column: Waters IC PAK A; flow rate: 1.2 ml/min.

With benzoic acid and potassium hydroxide being relatively weak eluents capable of separating only the weakly retained monovalent species within a reasonable amount of time, the search for additional suitable eluents for SCIC had to be continued. Elution of strongly retained species is achieved either by mass action, using an ion with a lower charge than the solute and at a relatively high concentration, or by increasing the eluent charge and employing a lower concentration. Frequently, a combination of the two approaches is utilized, e.g., in the case of polyvalent polyphosphonates,[45] where a relatively high concentration of hydrogen ions (10 to

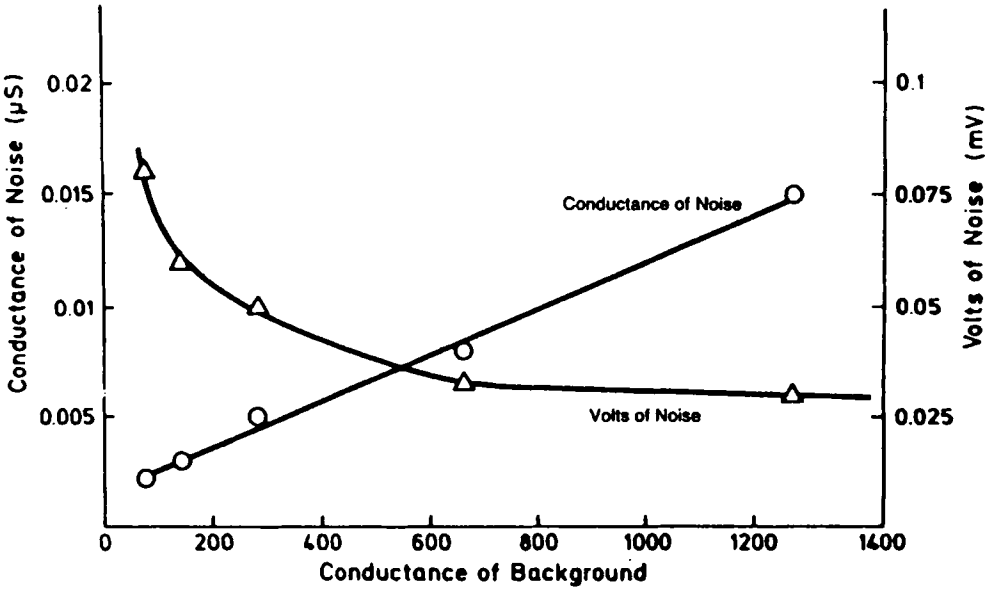


FIGURE 7. Dependence of baseline noise on background conductance of the eluent. Aqueous KCl solutions of conductances 75, 141, 285, 669, and 1270 μS were used at appropriate detector settings. The noise in terms of voltage is the value measured on a 10-mV recorder. (Reproduced from Haddad, P. R. and Jandik, P., in *Ion Chromatography*, Tarter, J. G., Ed., Marcel Dekker, New York, 1987. With permission.)

20 m*M*) in the nitric acid eluent suppresses the ionization of the polyphosphonate anions and keeps these species in their monovalent or less-than-monovalent form. The weakly ionized solute anions are then eluted by the mass action of the nitrate ion. However, hydrogen ion concentrations above 10 m*M* make sensitive detection by conductivity impractical. An increase in conductance is also observed in going from a singly charged eluent such as benzoate (1 m*M* lithium benzoate, G_{eluent} = 110 μS) to a triply charged eluent such as trimesate and keeping molar concentration constant for higher eluting strength (1 m*M* lithium trimesate pH = 8.5, G_{eluent} = 330 μS).

An increase in the number of charges on the eluting anion does not always have to lead to an increase in the background conductance. If the Walden rule in Equation 5 is combined with the expression for electrochemical mobility u_i in Equation 6, then the relationship shown in Equation 7 results, which describes the dependence of equivalent conductance on the ionic radius r.

$$u_i \cdot \eta = \frac{z_i \cdot e}{6 \cdot \pi \cdot r} = \text{constant} \tag{5}$$

In Equation 5, η is the viscosity of the medium in Poise, r is the ionic radius in cm, z_i is the number of charges, and e is the electronic charge. u_i is given by Equation 6.

$$u_i = \lambda_i / F \tag{6}$$

where F is Faraday's number in C/equiv and

$$\lambda_i = \frac{e \cdot F \cdot z_i}{\eta \cdot r} \tag{7}$$

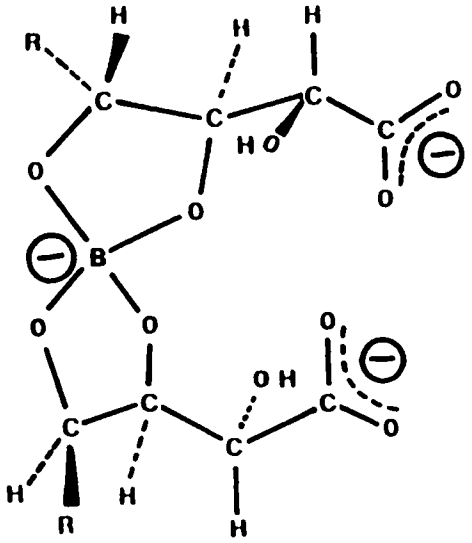


FIGURE 8. Proposed structure of the borate-gluconate eluent. R: $C_2H_5^-$. (Adapted from Erkelens, C., Billiet, H. A. H., deGalan, L., and deLeer, E. W. B., *J. Chromatogr.*, 404, 67, 1987. With permission.)

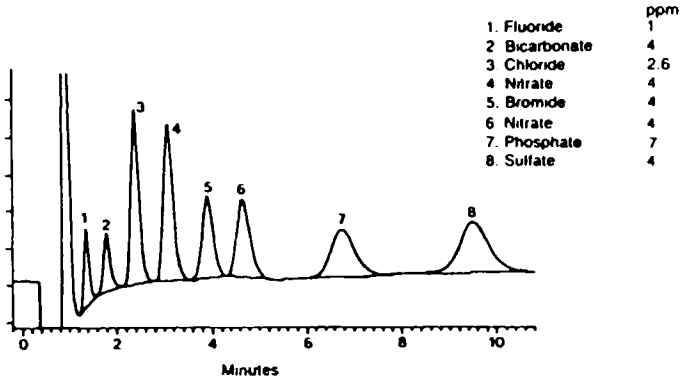


FIGURE 9. Chromatogram of eight common inorganic anions obtained with the 1-m*M* borate-gluconate eluent. Column: Waters IC PAK A; flow rate: 1.2 ml/min; 100 µl standard was injected.

From Equation 7, an inverse proportionality exists between the equivalent conductance λ_i and the size of the eluting ion as given by the ionic radius r. If an ion can be found in which the increase in z_i is counterbalanced by the increase in ionic radius, and if the same ion exhibits the desired eluting properties, then the corresponding mobile phase can be expected to possess a background conductance which is comparable to that of much weaker eluents with a lower number of charges. This principle has been applied in the borate-gluconate[46] eluent, which is usually prepared by mixing gluconic acid with an excess of boric acid and adjusting the resulting mixture to pH 8.5 with potassium or lithium hydroxide. According to recent reports,[47,48] the eluting species in the borate-gluconate eluent has been identified as a complex anion carrying three negative charges (Figure 8). A typical chromatogram obtained with the borate-gluconate using conductivity detection is shown in Figure 9. A typical background conductance reading

at 35°C for 1 m*M* borate-gluconate is about 220 μS for a cell constant of approximately 1 cm^{-1}. This compares favorably with eluents made up from anions having negative charges in the range between one and two, such as 1 m*M* benzoate (ca. 120 μS) and 1 m*M* phthalate at pH 6 (ca. 160 μS).

However, borate-gluconate eluents have been shown to function properly only on polyacrylate-based anion-exchange columns. Anion-exchangers with a different backbone material composition, such as styrene-divinylbenzene copolymers, cannot be used with this eluent. *p*-Hydroxybenzoate has been found to produce a similar separation on styrene-divinylbenzene anion-exchangers as that obtained with borate-gluconate on polyacrylate anion-exchangers.[49] In summary, it can be said that the optimization of eluent-column combinations has brought about similar improvements in conductometric detection as those achieved by the introduction of post-column signal-enhancing devices.

A further characteristic of separator columns which influences the levels of detection is the chromatographic efficiency, given by the number of theoretical plates, N.

$$N = k(V_R/w)^{0.5} \tag{8}$$

where V_R is the retention volume in ml, w is the peak width in ml, and k is a proportionality coefficient with a magnitude dependent on the method used to evaluate the peak width w. For example, if w is measured at half the peak height, then k = 25.

Equation 9[50] can be used to derive a relationship between the peak height (h) and N, as given in Equation 10.

$$\frac{C_{max}}{C_o} = \frac{V_o(N/2\pi)^{0.5}}{V_R} \tag{9}$$

where V_o is the injected volume of sample, C_o is the original concentration of solute injected, and C_{max} is the concentration of solute at the peak maximum.

$$h = B \cdot C_{max} = \frac{BV_oC_o(N/2\pi)^{0.5}}{V_R} \tag{10}$$

where B is the sensitivity coefficient defined as the slope ($\Delta h/\Delta C$) of the conductometric calibration plot.

Currently, efficiencies for the majority of ion chromatographic columns fall into the range of 500 to 8000 theoretical plates. As determined by Equation 10, a fourfold increase of peak heights results if a moderately efficient column (N = 500) is replaced by one of highest separation efficiency (N = 8000). This very significant contribution to overall sensitivity of detection is easily overlooked.

C. Development of Electronic Circuitry and Flow-Through Cells for Conductivity Detection

1. Introduction

Conductivity measurements in liquid samples rely on the application of an electric current between two electrodes with the objective of inducing a translational motion of ionic species in the measured solution. The amount of charge that is transported in this process is then interpreted as a measure of concentration.

Utilization of alternating currents prevents Faradaic removal of electroactive ions by their oxidation or reduction at the electrodes. This was recognized as early as 1897 by Kohlrausch,[51]

who developed the first conductivity-measuring technique using alternating current of ca. 10^3 Hz. In some ion chromatographic detectors and most conductivity meters, Kohlrausch's circuitry is still found today.

In each new design of electronic circuitry for conductivity detection, proper consideration has to be given to the amplitude and frequency of the utilized alternating current.

Its amplitude must not be sufficiently high to cause any thermal effects or significant chemical reactions in the measured sample. Too low an amplitude leads to unnecessary decreases in the sensitivity of measurement. The suitable range of frequencies for conductivity measurements has been established to be between ca. 50 Hz to ca. 10^5 Hz. Below 50 Hz or at unmodulated flow of electrons and ions, the extent of chemical change in the sample may render interpretation of transferred currents impossible. Electrochemical reactions at the electrodes and the resulting redox currents make possible the amperometric and voltammetric detection discussed later in this review. The objective of all conductance measurements is to resolve the electrolytic conductance from other contributions to the transfer of charge through a liquid sample.

As the frequency of the alternating current increases, the counterionic environment gradually loses its capability to rearrange itself according to the changed position of the central ion. At certain concentration-dependent frequencies, small (ca. 2.8%) increases in conductance will result from such phenomena (Debye-Falkenhagen Effect[52]). With further increasing frequencies, ions become gradually unable to transfer all of the energy imposed on them into translational motion due to their limited mobility (several orders of magnitude less than that of electrons). Other phenomena such as distortion of counterionic atmosphere or polarization resulting in the formation of dipoles will become predominant.[53] At this point, the dielectric properties of the sample determined by the degree of dipole reorientation contribute strongly to the measurement. Since our concern in this review is exclusively with the detection of ions, measurements close to or above such frequencies are not included in the discussion. For information on permittivity detectors or on contactless conductivity cells, the reader is referred to other more general reviews of electrochemical methods.[4-8]

The diagram of a Wheatstone bridge for conductivity measurement, along with the representation of substitution elements of the conductivity cells (Figure 10), clearly shows the difficulties involved in the balancing of the ratio arms of such a bridge circuit. Electrolyte resistance R_x (which we attempt to measure) is connected in series to the double-layer capacitance C_s caused by the local ordering of ions at the electrode surfaces. Faradaic impedances in parallel to R_x and C_s are caused by the depletion of the double layers by the redox reactions of ions at electrode surfaces. As a result, the capacitance C_s is partially short-circuited. Indeed, in real systems, it may not be possible at all to separate the double-layer effects from the Faradaic processes. Electrochemically active ions, if present, may begin to react at the electrode before the double layer is fully established. Therefore, the Faradaic processes are best represented by a frequency-dependent (nonlinear) resistance or impedance.

Just as there are no ideal gases or solutions, the components of a real detector will always remain somewhat short of optimum. As a consequence, there will be in the cell a resistive path parallel to the measured resistance R_x (see Figure 10). The influence of this parallel path on the measurements of R_x is described as the Parker effect; its magnitude usually increases in significance with increasing frequencies, thus imposing yet another threshold to the increase of applied frequencies of the alternating current. Another effect which is difficult to avoid is the RC-type connection between the electrolytic cell and the ground. This disturbance was analyzed originally by Mysels, and it is generally concluded that this element has to be accounted for at all resistances higher than 10^5 Ω,[54] i.e., under conditions frequently encountered in ion chromatographic detection. Other frequency-dependent influences on the linearity of conductivity response are the lead and parallel capacitances, which reflect signal distortions in the leads and elsewhere in the detector system. As with the Parker and Mysels effects, this contribution to the measured signal also increases with frequency.

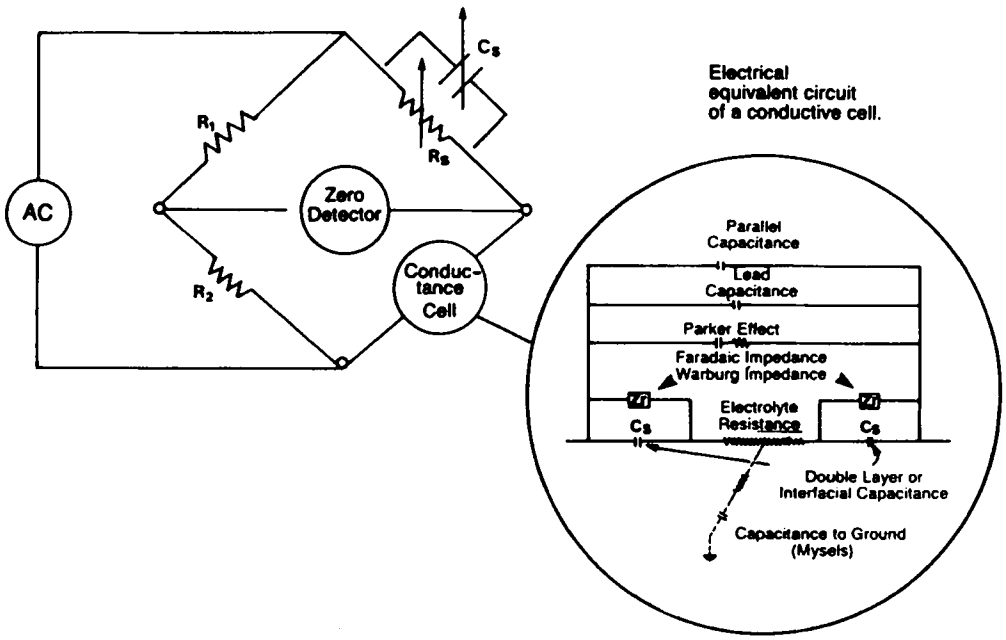


FIGURE 10. AC condutance bridge and an electrical equivalent circuit of a conductance cell. (Adapted from References 52 and 61.)

The relative magnitudes of these disturbing effects vary from sample to sample and also with different instruments. These noted disturbances notwithstanding, the measurement of conductances in static samples has developed into a high art. This was made possible predominantly by the contributions of Jones and co-workers in the 1930s.[55-59] The dynamic conditions of chromatographic detection further multiply the complications of conductance measurement. The original liquid chromatographic conductivity detectors[19,60,61] with Wheatstone bridge-type electronics had to utilize two or more cells to cover the broad range of conductances. The problems with the linearity of response were frequent and difficult to avoid.

The two important refinements of ion chromatographic methodology discussed in the previous two sections have provided impetus for the improvement of the design of conductivity detectors. Today, the majority of detectors of this type utilize one of the more advanced versions of electronics and cell design, based either on the application of bipolar pulse techniques[62-65] or derived from the four-contact measurement of electrolytic conductance.[63,66]

2. Bipolar Pulse Technique for Conductivity Detection

The bipolar pulse technique was first described by Johnson and Enke[61] in 1970. The original paper also contains a treatise on the limitations of the AC conductance bridges available at that time. The technique consists of applying two consecutive voltage pulses of equal amplitude and pulse width, but of opposite polarity, to a cell and then measuring the cell current precisely at the end of the second pulse.[61,63] The time-potential plots at several different points in a typical bipolar pulse detector circuit are presented in Figure 11.

The reader will notice a certain analogy with pulsed amperometric and voltammetric methodologies which are discussed later in this review. In each case, the modulated potential excitation is utilized in order to avoid distortion of the measured entity (oxidation or reduction currents in amperometry and voltammetry; electrolytic conductance in conductometry) by disturbing elements (capacitances, impedances) in the detector cells. Both approaches make use of the observation that the magnitude of the disturbances is time-dependent and that by sampling the signal at a well-chosen and narrow time interval the majority of interferences can be

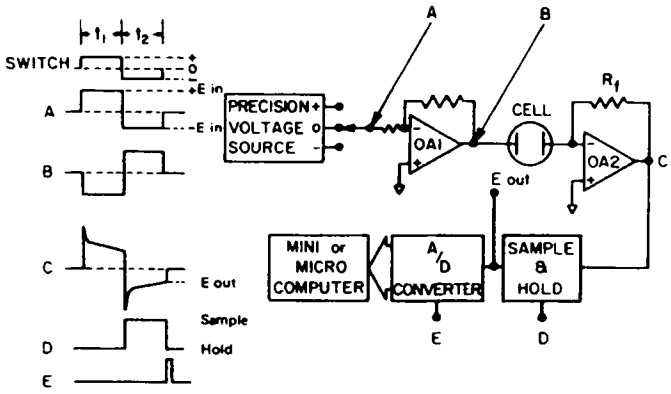


FIGURE 11. Bipolar pulse conductance measurement system. (From Holler, F. J. and Enke, C. G., in *Laboratory Techniques in Electroanalytical Chemistry*, Kissinger, P. T. and Heineman, W. R., Eds., Marcel Dekker, New York, 1984, 235. With permission.)

eliminated. Johnson and Enke were able to demonstrate that at the end of the interval t_2 in Figure 11 all parallel and serial capacitances of the electrical equivalent circuit of a conductivity cell (Figure 10) no longer influence the cell current i_{cell}. From the equations,

$$i_{cell} = E_{out}/R_f \tag{11}$$

$$R_s = E_{in}/i_{cell} \tag{12}$$

the electrolytic conductance (G) free of Faradaic and other distortions can be calculated as the reciprocal value of R_s:

$$G = 1/R_s = E_{out}/E_{in} \cdot R_f \tag{13}$$

The terms E_{out}, R_f, R_s, E_{in}, and i_{cell} are explained in Figure 11.

Several variations of this measuring principle have been demonstrated. In one approach, a bipolar current pulse is applied and the potential is sampled at the end of the second pulse.[67] In a somewhat related application, Svoboda and Marsal[68] achieved a linear dynamic range over six orders of magnitude by application of a square wave potential and by continuous measurement of the resulting voltage using logarithmization circuitry. In this work, additional attention also was given to the design of a low-volume conductometric cell (Figure 12). The reported minimum detectable concentrations with this instrument were of the order of 10^{-6} *M*.

In a convincing demonstration reported in 1981, Keller[62] connected a homemade bipolar pulse detector in series with a suppressor and an AC conductance bridge-type of detector from a commercial source (Figure 13). He was able to show that the sensitivity of the bipolar pulse detector in a nonsuppressed mode exceeded that of the conventional detector placed in series after a chemical suppressor. In the time period following this report, bipolar pulse conductivity detectors have been introduced by several manufacturers.[23,69-72]

3. Four-Electrode Conductivity Detector

The technique represents a modification of the four-contact measurement of resistances or electrolytic conductance. Two- and four-contact (two-electrodes vs. four-electrodes) measurements of solid and liquid resistances are compared in the following paragraph and in Figures 14 to 16.

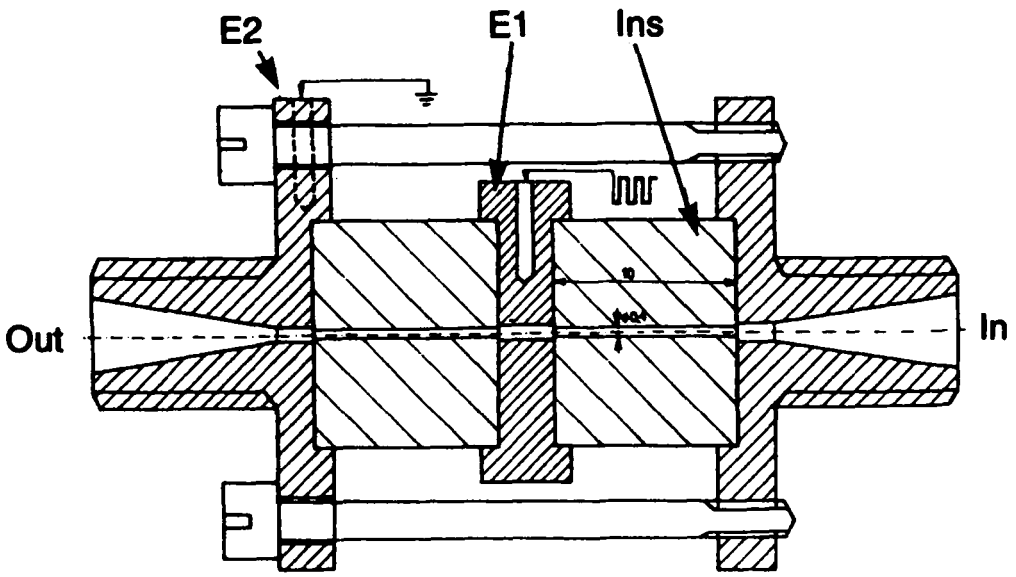


FIGURE 12. Low internal volume conductometric cell. E1 and E2 are the measuring electrodes; Ins designates a PTFE isolator; the modulated voltage is applied to the electrode E1; the internal cell volume is approximately 3 µl. (Reproduced from Svoboda, V. and Marsal, J., *J. Chromatogr.*, 148, 111, 1978. With permission.)

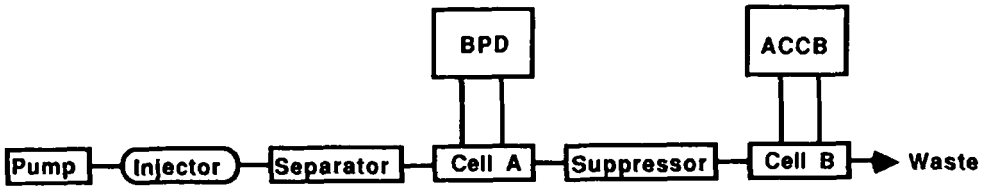


FIGURE 13. Comparison of sensitivities of two types of conductivity detectors. BPD, bipolar-pulse electronics module; ACCB, AC conductivity bridge; cell A, Wescan 219-900; cell B, Dionex Model 10. (From Keller, M., *Anal. Chem.*, 53, 344, 1981.)

The simplest practical arrangement for the evaluation of resistances of solid resistors is shown in Figure 14. The two (A and B) probes are attached to the unknown resistor by means of alligator clips or pressed against it manually. The unknown resistance, R_u, is then calculated from a comparison of two current values I_1 (probes A, B short circuited) and I_2 (configuration as in Figure 14).[63] Depending on the material characteristics of the contact interfaces or on the value of the measured resistance R_u, the contact resistances R_{c1} and R_{c2} may or may not be negligible. Also, the contact resistances may fluctuate if the probes are held manually. To avoid such difficulties caused by varying contact resistances, the four-contact resistance measurement was developed (Figure 15). In this arrangement, leads and contacts supplying the current are separated from the contacts probing the voltage drop across the resistor.

Since only an infinitesimal current (I_2) now flows through the probing circuit, the values of $I_2 \cdot R_{c1}$ and $I_2 \cdot R_{c2}$ can be neglected for all practical purposes. Relative difficulties of measurement of liquid and solid resistivities can be explained for example by comparing Figures 10 and 14. The only complication with solid samples is the influence of contact resistances R_{c1} and R_{c2}. On the other hand, measurements of liquid samples can be complicated by a multitude

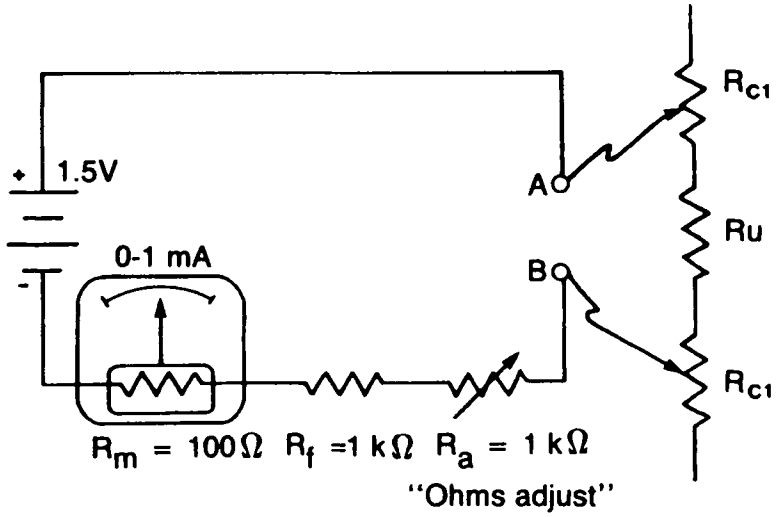


FIGURE 14. Simple two-contact measurement of a resistance. With the points A and B short circuited: $R_a + R_{c1} + R_{c2} = 0$. $R = R_m + R_f + R_a$ and $I_1 = 1.5/R$. With the probes applied to R_{c1} and R_{c2}, $R_u = R_{c1} + R_{c2} + R_a$ and $I_2 = I_1 \times R/R_u + R$. The unknown resistance is then $R_u = (I_1/I_2 - 1) \times R$. (Adapted from Holler, F. J. and Enke, C. G., in *Laboratory Techniques in Electroanalytical Chemistry*, Kissinger, P. T. and Heineman, W. R., Eds., Marcel Dekker, New York, 1984, 235.)

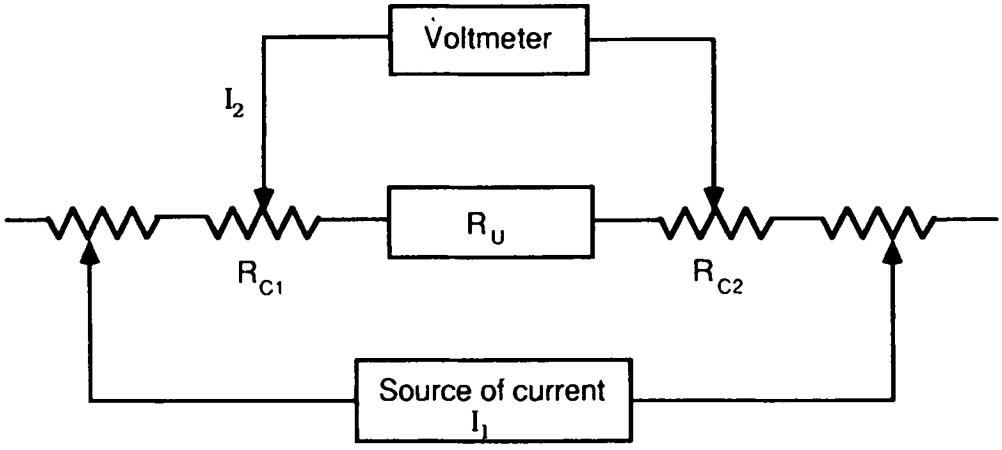


FIGURE 15. Four-contact measurement of resistances. $I_1 \gg I_2$.

of interferences that are represented by the electrical equivalent circuit of a conductivity cell in Figure 10. Most of these disturbances observed with the AC conductance bridges can be attributed to the fact that the same two electrodes through which the voltage is applied are also used as the measuring electrodes. In direct analogy to the four-contact measurements of solid resistances, the electrodes applying the potential or current to liquid samples can be separated from those used for the measurement (Figure 16).

This measurement technique has been further developed and utilized in one of the detectors for SIC[73] (Figure 17). The variable AC current generator (ACG) controlled by a differential amplifier (DA1) supplies a sinusoidal measuring current to the outer two electrodes of the cell

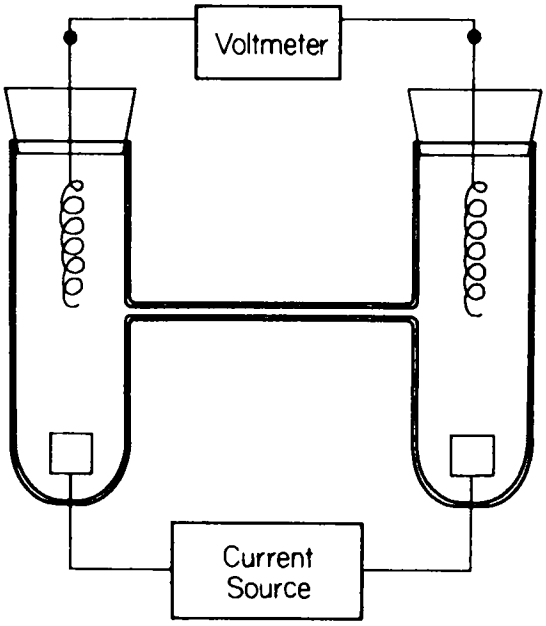


FIGURE 16. Four-contact measurement of electrolytic conductance. (Reproduced from Holler, F. J. and Enke, C. G., in *Laboratory Techniques in Electroanalytical Chemistry*, Kissinger, P. T. and Heineman, W. R., Eds., Marcel Dekker, New York, 1984, 235. With permission.)

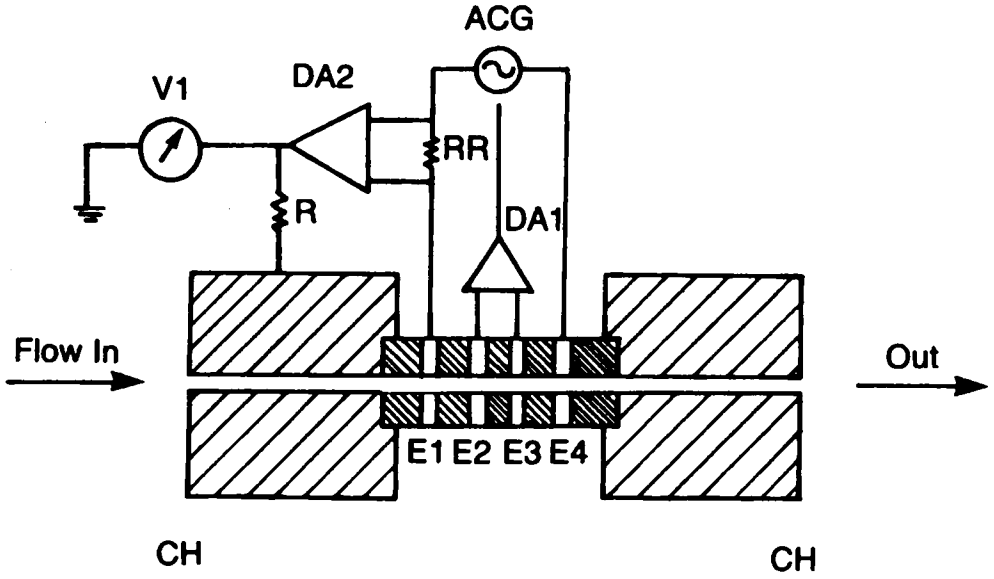


FIGURE 17. Four-electrode conductometric cell. See text for explanation of the symbols. (Reproduced from Baba, N. and Housako, K., U.S. Patent 4,462, 962, 1984.)

(E1, E4). The inner two electrodes (E2, E3) are connected to the input terminals of the DA1 which forces the current generator to maintain a constant potential drop between E2 and E3. Similarly, as in the four-contact measurements of solid resistances, only a negligible current

flows in the loop defined by E2, E3, and DA1. The Faradaic impedancies, and the serial and parallel capacitances, are thus largely excluded from the measurement. As the DA1 forces the ACG to increase or to decrease the current flow in response to the varying values of conductances between E2 and E3, the value of the potential across the range resistor (RR) will also vary. The amplifier (DA2) senses these variations and applies them in the form of a proportionate analog signal to the voltmeter V1. In this manner, the conductivity of the liquid through the cell is indicated. The cell holder (CH) is connected to ground and at the same time through the resistor (R) to the output of the amplifier (DA2). The cell holder thus serves as a guard electrode against effects described by Mysels and co-workers[54] in their work with conductance bridges.

The stability of the signal coming from this simple and robust detector is further increased by effective insulation and thermal control of the entire conductivity cell. The four-electrode instrument described earlier has been found to be particularly useful for indirect conductivity detection in SCIC. The dependence of baseline noise on background conductance for this detector is discussed in one of the preceding sections and is illustrated in Figure 7.

4. Additional Remarks on the Design of Conductivity Cells

As in the case of almost all other components of current (1987) ion chromatographic systems, the search for the optimum design of conductivity cells is still continuing. Efforts are in progress to reduce the size and the internal volume of the cells in order to minimize peak spreading and to improve the compatibility of the cells with microbore columns[74,75] or electrokinetic separation methods.[76] Two different patents[66,77] were granted for cells allowing the simultaneous use of fluorometry, UV absorption, and conductance for liquid chromatographic detection.

At least two reports[78,79] have been published proposing the simultaneous or sequential use of the same cell for permittivity and conductance measurements. However, in the simultaneous utilization of the two techniques, frequencies in the MHz range are generally used. As discussed, conductivity detection of ions becomes more difficult under these conditions, and as a consequence, this type of instrument cannot be recommended for sensitive detection in IC.

D. Theoretical Considerations in Conductometric Detection

A disturbing influence of temperature fluctuations on both the detection limits and the reproducibility of conductivity detection has been reported for suppressed[80,81] and nonsuppressed[83,84] IC. Jenke and Pagenkopf[82] achieved 10- to 20-fold improvements in detection limits after insulating the separator column and other exposed components of a single column system. Along with these improvements in sensitivity, the reproducibility (% RSD) for the majority of analyzed anions was also improved. In two other reports,[80,81] desired detection limits could be attained only after the separator and suppressor columns were immersed in a waterbath at 27.5 ± 0.1°C.

Sorensen and Glass[84] have recently evaluated four of the most common equations describing the temperature dependence of electrolytic conductance in solutions:

$$G_{25} = G_t(\eta_t/\eta_{25})^{K1} \quad (14)$$

$$G_{25} = G_t[1 + K_2(25\text{-}t)] \quad (15)$$

$$G_{25} = G_tK_3(25\text{-}t) \quad (16)$$

$$G_{25} = G_t/[1 - K_4(25\text{-}t)] \quad (17)$$

Utilizing literature data for conductances of KCl[85] and comparing these with values calculated from Equations 14 to 17, the best agreement between calculated and measured conductances was found for Equation 14. A plot of the difference between the measured and

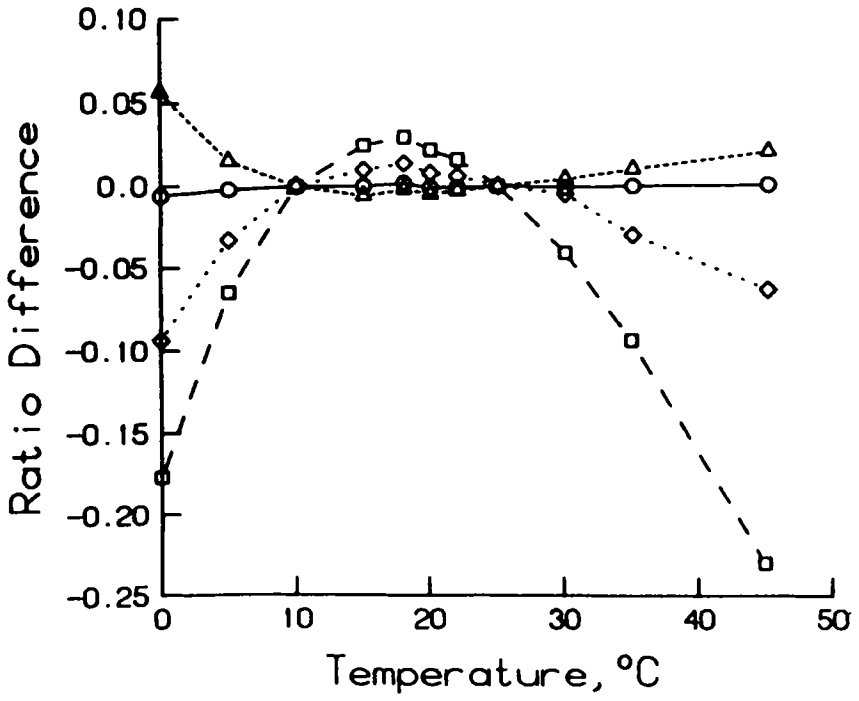


FIGURE 18. Difference between calculated and literature conductance ratios for KCl at several temperatures: (o) Equation 14, (□) Equation 15, (◊) Equation 16, (Δ) Equation 17. (Reproduced from Jenke, D. R. and Pagenkopf, G. K., *Anal. Chem.*, 54, 2603, 1982. With permission.)

calculated values of the parameter (G_{25}/G_t) at several temperatures was made for each of the four equations (Figure 18). This figure shows that the popular rule-of-thumb calculation (as described by Equation 15),[86] which estimates a 2% conductance change for each degree of temperature change, holds well only in a very narrow temperature range between 10 and 25°C. Outside this range, this calculation may be in error by as much as 25%.

The published list of K_i values[84] is not sufficiently extensive to allow Equations 14 and 4 to be applied to the full range of eluents used for suppressed and nonsuppressed IC. With reliable values of water viscosities being given in the literature,[87] the availability of K_i data for a wider range of anions and cations would for the first time permit exact predictions of temperature-induced baseline fluctuations.

In recent years several workers[88-90] have investigated the deviations from linearity observed with conductivity detection carried out in chemically suppressed eluents. If inorganic anions are analyzed, the main constituents of the suppressor eluate are acids of different acidic strength. As determined by the principle of chemical suppression, the acid H_nL generated from the eluent is always relatively weak and dissociates according to:

$$H_nL \Leftrightarrow H_{n-1}L^- + H^+ \qquad (18)$$
$$pK > 3$$

Most of the analyte anions which can be analyzed successfully by means of SIC are salts of strong acids and are converted in the suppressor to their corresponding acid, as described by Equation 19:

$$H_nX_i \Leftrightarrow H_{n-1}X_i^- + H^+ \qquad (19)$$
$$pK < 1$$

A significant complication arises from the following reaction which may occur in the separated zones for each of the anions.

$$H_nX_i + H_{n-1}B^- \Leftrightarrow H_{n-1}X_i^- + H_nB \quad (20)$$

Correspondingly, the conductance of the background will undergo significant changes during the transport of a strongly acidic peak zone of an anion X_i^- from the suppressor through the detector cell.

Two groups of authors have attempted to elucidate the phenomena related to such changes in the baseline occurring during the elution of a peak. van Os and co-workers[88,89] have derived an equation relating the concentration of the analyte with the conductometric response under conditions encountered in suppressed conductivity detection of anions. The authors claim that their equation makes linear calibration possible in the range 0 to 40 ppm. A Fortran program which performs the necessary calculations is available upon request.[89]

A somewhat similar equation was derived by Doury-Berthod and co-workers[90] for a strong acid $H_mX^{(n-m)}$ eluting in a mobile phase containing weakly acidic anions L^{2-} and HL^-:

$$\begin{aligned}\Delta G = 1000/k \{&[(n - m')(\lambda^\circ_H + \lambda^\circ_{[1/(n-m')]Hm'X})(1 - \alpha_- - \alpha_+) + \\ &(n - m' - 1)(\lambda^\circ_H + \lambda^\circ_{[1/(n-m'-1)]Hm'+1X})\alpha_+ + \\ &(n - m' - 1)(\lambda^\circ_H + \lambda^\circ_{[1/(n-m'-1)]Hm'+1X})\alpha_- - \\ &(n - m)(\lambda^\circ_H - \lambda^\circ_{HL})[1 - \beta/2)]\alpha]\Delta C - (\lambda^\circ_H - \lambda^\circ_{HL})(\alpha - \alpha_E)C_E\}\end{aligned} \quad (21)$$

where m describes the number of protons, n is the original number of charges on the anion increased by the dissociation of m′ protons (n-m′), β is the fraction of $H_mX^{(n-m)}$ anions exchanged in the separator with eluent ions L^{2-}, $\alpha_+\alpha_-$ are the dissociation coefficients of two different ionic forms of $H_mX^{(n-m)}$, α_E is the dissociation coefficient of H_2L, and C_E is the concentration of the eluent.

For a case where a single anionic species of the polybasic anion $H_{m'}X^{(n-m')}$ predominates, Equation 21 can be rewritten as follows:

$$\Delta G = (n - m')B\Delta C + A\alpha[C_E - (n - m)[1 - (\beta/2]\Delta C] - A\alpha_E C_E \quad (22)$$

where

$$A = \frac{1000}{k}(\lambda^\circ_H + \lambda^\circ_H);$$

$$B = \frac{1000}{k}(\lambda^\circ_H + \lambda^\circ_H + \lambda^\circ_{[1/(n-m')]Hm'X});$$

$$\begin{aligned}\alpha = [&-(n - m')\Delta C - K_a + \{[(n - m')\Delta C + K_a]^2 + \\ &4K_a[C_E - (n - m)[1 - \beta/2)]\Delta C]\}^{1/2}]/2[C_E - (n - m)[1 - m)[1 - (\beta/2)]\Delta C];\end{aligned}$$

$$\alpha_E = [-K_a + (K_a^2 + 4K_aC_E)^{1/2}]/2C_E$$

By substituting a more extensive form of the elution law than that given in Equation 10 into Equation 22, the three major contributions to the height of a chromatographic peak at any moment during its elution can be expressed:

$$\Delta G = G_I + G_{II} - G_{III} \quad (23)$$

where G_I is the contribution to ΔG by the sample anion $H_{m'}X^{(n-m')}$; G_{II} is the conductometric contribution of the species HL^-; and G_{III} is the conductance of the unperturbed eluent at concentration C_E.

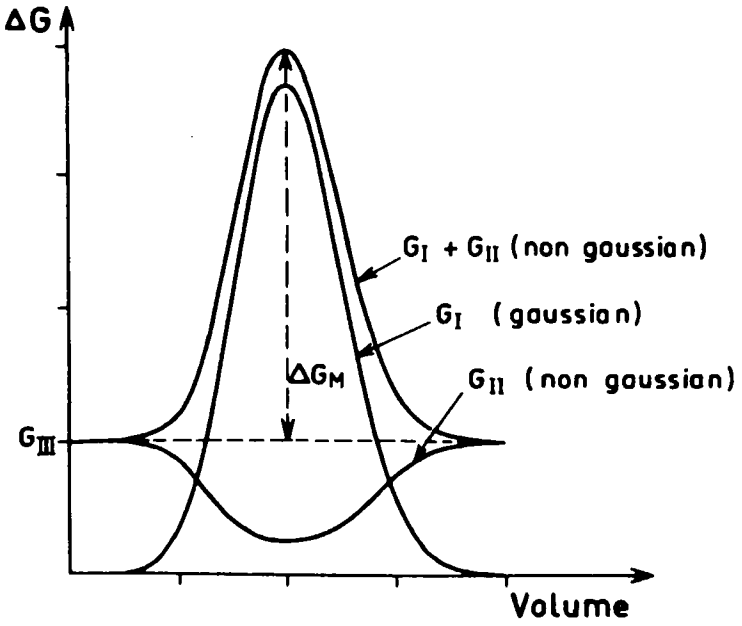


FIGURE 19. Three contributions to the shape of a peak in the suppressed ion chromatographic detection. See Equations 24 to 26. (Reproduced from Doury-Berthod, M., Giampoli, P., Pitsch, H., Sella, C., and Poitrenaud, C., *Anal. Chem.*, 57, 2257, 1985. With permission.)

$$G_I = (n - m')BdC_o \cdot \exp[-N(V - V_R)^2/2VV_R] \quad (24)$$

$$G_{II} = A\alpha[C_E - (n - m)[1 - (\beta/2)]dC_o \cdot \exp[-N(V - V_R)^2/2VV_R] \quad (25)$$

where $d = \frac{V_o}{V_R}\left(\frac{N}{2\pi}\right)^{1/2}$

$$G_{III} = A\alpha_E C_E \text{ (Note: identical with Equation 4)} \quad (26)$$

With the help of Equation 23, a point-by-point modeling of the shape of a conductance peak obtained by the suppressed technique becomes possible. An example obtained using arbitrary parameters is shown in Figure 19.

As determined by Equation 24, the contribution G_I describes the rise and fall of the conductance signal during the lifetime of a peak. The term G_{II} allows calculation of the fluctuations of the eluent background conductance during the development of the same peak. As the concentration of the strongly acidic sample reaches a maximum, the momentary effect of Equation 20 causes the background conductance ($G_{II} - G_{III}$) to be depressed to its minimum value. The third term G_{III} calculates the constant level of the background conductance in the absence of strong acids as observed outside of the eluting peak zones in the chromatogram.

It is clear from Figure 19 that the resulting peak shape given by $G_I + G_{II} - G_{III}$ is essentially non-Gaussian as a result of the very complex relationship between α and ΔC in Equation 22. As a consequence, all calculations assuming Gaussian peak shapes, such as Equation 8, may be erroneous if used for chromatograms generated using chemical suppression.

If it is desirable to use the peak height (h) at the peak maximum for calibrations, a relationship using this entity can be obtained by modification of Equation 23 to give:

$$h = (n - m')BdC_o - (A/2)dC_o\{(n - m') - K_a[(n - m') - (n - m)(2 - \beta)]/K_a^2 + 4K_aC_E)^{1/2} - (n - m')^2dC_o/2(K_a^2 + 4K_aC_E)^{1/2}\} \quad (27)$$

For very small values of C_o (the concentration of analyte in the sample to be injected), h approaches a limiting value (h_{lim}) given by:

$$h_{lim} = (n - m')BdC_o - (A/2)dC_o\{(n - m') - K_a[(n - m') - (n - m)(2 - \beta)]/(K_a^2 + 4K_aC_E)^{1/2}\} \quad (28)$$

At a high value of C_o, the baseline shift indicated by the term G_{II} is very pronounced, and Equation 27 becomes:

$$h'_{lim} = (n - m')BdC_o - A\alpha_E C_E \quad (29)$$

From Equation 28, h_{lim} can be expected to be proportional to C_o for low concentrations of injected anions. In higher ranges of concentration, the same linear relationship between h'_{lim} and C_o can no longer be expected. The theoretical trend of calibration curves in suppressed chromatography of ions can thus be represented by the two limiting forms of the peak height equation (Equations 28 and 29; Figure 20).

In the same report,[90] variations of nonlinear shapes of calibration diagrams of the type shown in Figure 20 are compared for three eluents of different acidity, namely, carbonate (pK = 6.37), benzoate (pK = 4.20), and phthalate (pK = 2.92). As concluded by Doury-Berthod et al.,[90] the linearity of calibration plots improves in going from carbonate to phthalate, but sensitivities (slopes) become gradually smaller. This theoretical trend was verified experimentally by the authors.

In respect to the investigations of the effect of various mobile phases on the linearity of calibration plots, the recent work by Tian and co-workers[30] overlaps with the above theoretical study. One part of their report describes the varying shapes of calibration plots in eluents with pK values between 6 and 12 (Figure 21). As in the previous model,[90] the slope of the calibration curve decreases with decreasing value of pK. However, the main focus was to investigate the effects of residual concentrations of sodium (as indicators of incomplete suppression of sodium carbonate or sodium hydroxide eluents) on the shapes of calibration plots. The reported background conductance of a sodium hydroxide eluent after passage through a MMS was about 13 μS.[29] This can be interpreted as a conductance corresponding to 50 μ*M* NaOH in the eluent after the suppression step. Results of calculations of the effect of such residual sodium concentrations on peak heights are shown in Figure 22A and B.

One of the practical consequences of the irregular shapes of the calibration plots is the impossibility to extrapolate detector response at lower concentration of a sample anion from data obtained at higher concentration ranges. As demonstrated for two different eluents, the proportionality of calibration failed at a value increasing with concentration of the residual sodium ions. This breakdown of the linear calibration relationship appeared in a less abrupt fashion in eluents of lower pK (Figure 22B). On the other hand, it was found in the same report that an eluent with higher pK provided a more extended linear range and greater sensitivity under conditions of ideal suppression where the concentration of residual sodium ions was zero. In a continuation of their investigations, Tian et. al.[30] tested an electrochemically operated suppressor[35] and reported improvements in residual levels of sodium in comparison with the furthest developed commercial version of the device.

In SCIC, the concentration and ionic properties of the eluent at typical pH values generally provide for sufficient buffering capacity to prevent any fluctuations of the background conductance from occurring. For the majority of cases in SCIC, the simple relationship shown in Equation 1 usually suffices to describe the relationship between the sample concentration and the magnitude of detector response.

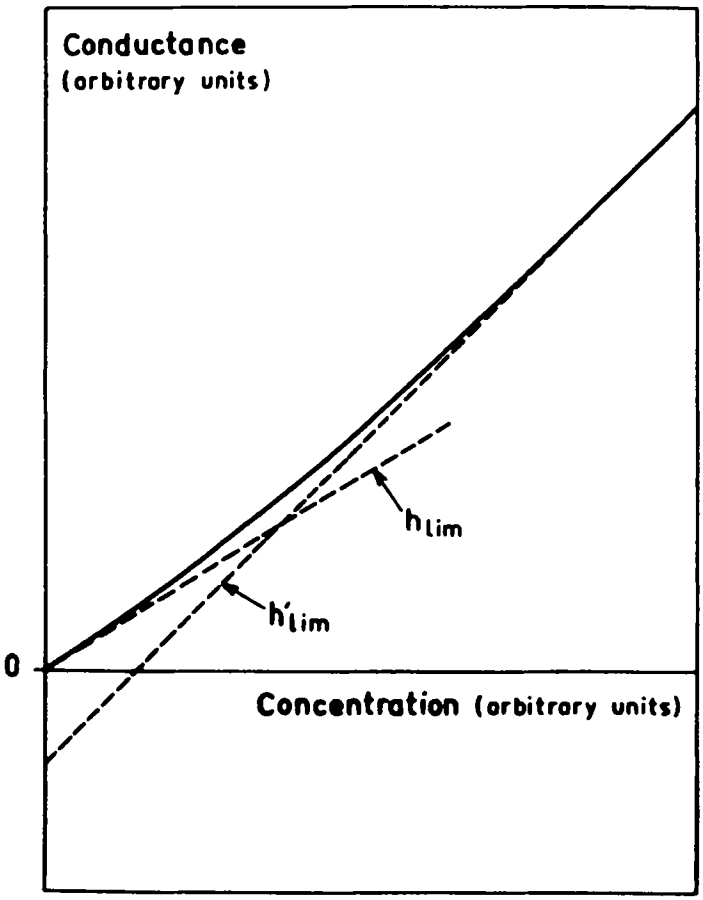


FIGURE 20. Nonlinear conductance-concentration dependence resulting from the two limiting forms of Equation 27. (Reproduced from Doury-Berthod, M., Giampoli, P., Pitsch, H., Sella, C., and Poitrenaud, C., *Anal. Chem.*, 57, 2257, 1985. With permission.)

In an interesting application of the principles originally developed for UV detection of weakly absorbing ions,[91] Wilson et al.[92] proposed a method of calibration of the response for conductivity detectors without having to use standard solutions of ions.

Applying equations similar to these derived for UV detection,[91] they arrive at:

$$C_x = (S_1C_2/S_a) + (S_2C_1/S_b) \quad (30)$$

$$\lambda_x = [\lambda_2(S_1S_bC_2/S_2S_aC_1) + \lambda_1]/[(S_1S_bC_2/S_2S_aC_1) + 1] \quad (31)$$

where C represents molar concentrations, S represents peak areas, and λ is equivalent conductance. The subscripts have the following meanings: 1 refers to the first eluent; 2 refers to the second eluent; a denotes the peak area of the anion of eluent 1 when eluted by eluent 2; b denotes the peak area of the anion from eluent 2 when eluted by eluent 1.

Equation 30 may be used for calculations of the concentrations of an unknown sample C_x after this sample has been injected into two different eluents of concentrations C_1 and C_2, provided that the values S_a and S_b were determined previously in a separate experiment. Using the data from the same set of experiments together with known values of equivalent conductances for

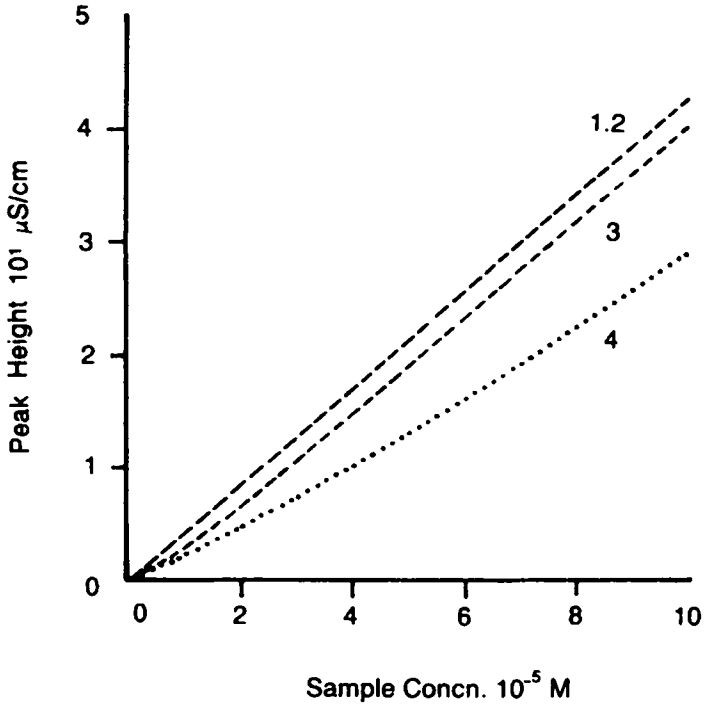


FIGURE 21. Values of pK of eluents in suppressed ion chromatography and the shapes of calibration plots. Curve (1) pK 12, curve (2) pK 10, curve (3) pK 8, and curve (4) pK 6. C_{N_a} is assumed to be zero (see the discussion in the text). The limiting equivalent conductance of chloride was used in the calculations of peak heights. (Reproduced from Tian, Z. W., Hu, R. Z., Lin, H. S., and Wu, W. L., 5th Int. Symp. on Ion Chromatogr., Sils Maria, October 1987. With permission.)

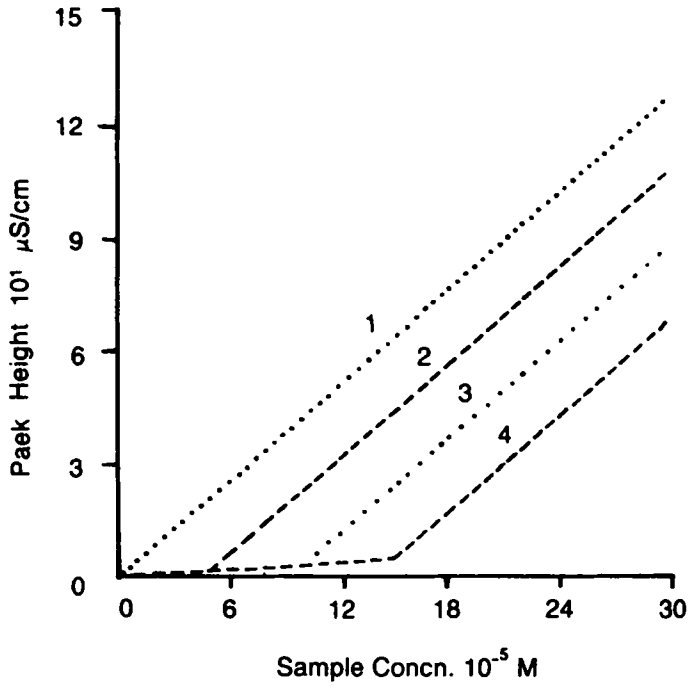
eluent anions, the equivalent conductance for an unknown solute can be calculated from Equation 31.

For similar calibrations without the use of standards in SIC, the authors recommend use of a third column, which in the case of anion separations could be an anion-exchanger in the chloride form. All anions eluting from the suppressor after their separation on the separator column would thus be exchanged for chloride inside the third column. The number of equivalents of chloride indicated by a detector calibrated with a standard solution of chloride would thus correspond to an equal number of equivalents of the analyzed anion.

E. Typical Applications of Conductivity Detection in Ion Chromatography

The rapid expansion of IC has been reflected by a steadily growing number of books.[23,40,44,93,94] Because of this significant expansion, it has now become difficult to compile a complete list of applications of IC in which conductivity detection is used. Rather than by a long listing of different applications, the present status of conductivity detection may be better described by a presentation of its application to a few selected classes of ions. For the purposes of this review of applications, we have elected to subdivide ionic compounds into four categories: strong cations, weak cations, strong anions, and weak anions.

Analysis of anions of strong inorganic acids has been the mainstay of IC with conductivity detection since the beginning of the method in the years between 1975 and 1979. Detection limits for anions achievable by direct injection vary from anion to anion and according to the separation mode, eluent, and applied variety of the conductometric method. Generally, it can be said that



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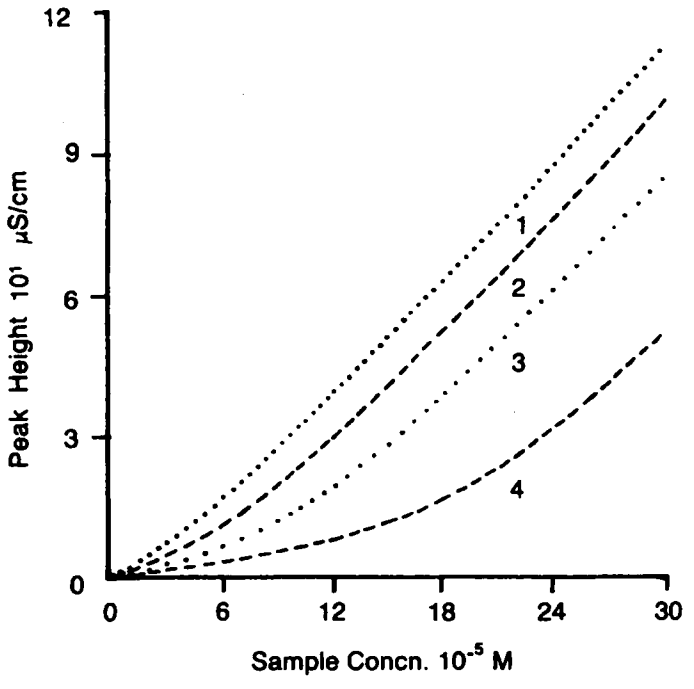


B

FIGURE 22. Calibration plots in suppressed ion chromatography: effect of residual sodium concentration in two different eluents. (A) pK = 10. (B) pK = 12. (Reproduced from Tian, Z. W., Hu, R. Z., Lin, H. S., and Wu, W. L., 5th Int. Symp. on Ion Chromatogr., Sils Maria, October 1987. With permission.)

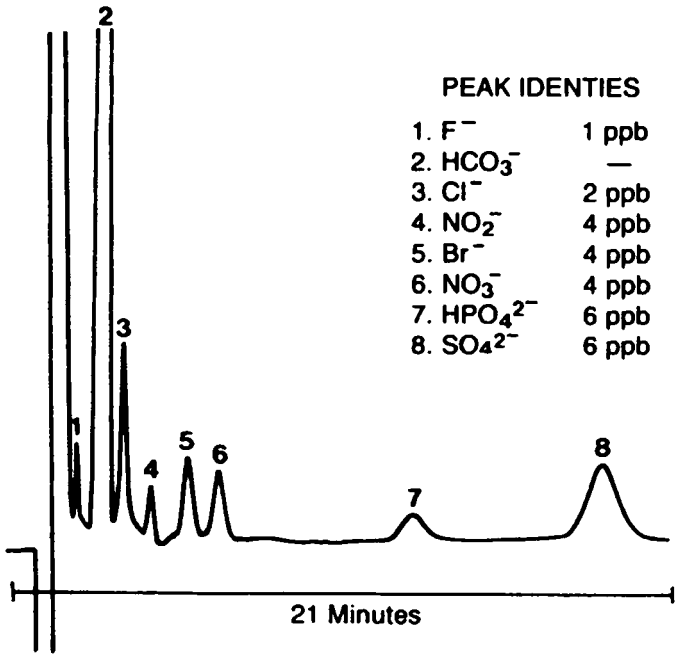


FIGURE 23. Trace levels of anions determined using trace enrichment; 20 ml of the sample preconcentrated on a precolumn. Column: Waters IC PAK A; eluent: 1 m*M* borate-gluconate; flow rate: 1.2 ml/min; conductivity detector: Waters M430.

values between 50 to 100 ppb can be detected in both suppressed and nonsuppressed conductivity methods without any need for preconcentration.

Examples of chromatograms of strong anions were given in Figures 3 and 9. With suitable sample preconcentration, the minimal detectable concentrations can be found in the lower half of the ppt range, the real limits being imposed more by sample handling considerations than by the sensitivity of detection. A chromatogram of low levels of anions obtained using preconcentration is presented in Figure 23.

A definite strength of conductivity detection arising from its character as a bulk property technique is its utility for speciation after separation, e.g., of different anionic forms of the same element. Speciation of anions of sulfur, phosphorus, and chlorine are documented in Figures 24 to 26.

Detection of partially ionized inorganic and organic acids has always presented a challenge for conductivity detection. In the suppressed method, the reduction of the background conductance leads simultaneously to the suppression of ionization of analyzed weak acids. This renders their detection by conductivity very difficult. In SCIC, the sensitivity of detection is impaired for any ion whose coefficient of dissociation differs from unity under the chosen chromatographic conditions (see Equation 1). For the detection of boric acid, as an example of a weakly ionized inorganic acid, two approaches have been proposed in SIC. An early attempt[95] utilized addition of a polyfunctional alcohol to the eluent, with detection of the borate as a strongly ionized complex similar to that in Figure 8. Alternatively, it is also feasible to apply one of the reverse suppression techniques,[23] as indicated in Figure 27. In the case of boric acid, detection by refractive index has been shown to be superior to any version of conductivity detection.[96]

A somewhat similar situation is encountered in the detection of cyanide. Amperometric detection provides sensitivity exceeding that of all conductance methods for cyanide.[97,98] Sillinger[99] improved the response for cyanide using oxidation by hypochlorite. The cyanide was

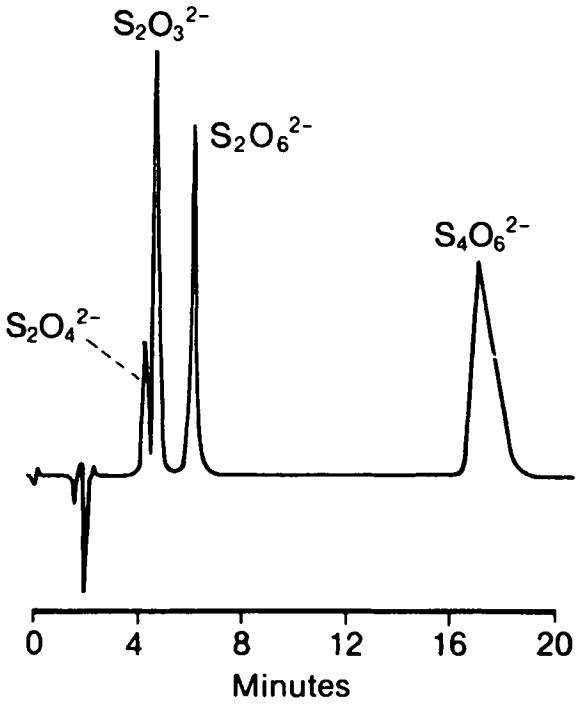


FIGURE 24. Separation and detection of several sulfur-containing anions. Column: Dionex MPIC-NS1; eluent: 2 m*M* tetrabutyl ammonium hydroxide, 1 m*M* sodium carbonate, 20% acetonitrile; 50 µl of sample was injected; concentrations: thiosulfate 20 ppm, dithionate 50 ppm, and tetrathionate 100 ppm; detection: suppressed conductivity. (Reproduced from Weiss, J., *Handbuch der Ionenchromatographie*, VCH Verlagsges., Weinheim, Federal Republic of Germany, 1985, chap. 3. With permission.)

oxidized to cyanate prior to injection of the sample into the ion chromatographic system. Less than 10 ppb of cyanide could then be detected by conductivity (Figure 28). In an analogous approach, Fritz and co-workers[100] detected iodide as a product of the reaction between cyanide and iodine.

The sensitivity of nonsuppressed conductivity detection for carboxylic acids has been shown to improve with decreasing concentration of eluents used in ion-exclusion separations[101] (Figure 29). An example of conductivity detection applied to carboxylic acids is given in the upper chromatogram of Figure 30, while the lower trace shows that strong anions can be separated and detected simultaneously with carboxylic acids if an appropriate column-switching scheme is chosen for the analysis. One of the few possible examples of coupled systems in which two conductivity detectors are utilized for two simultaneous separations is shown in Figure 31. In this diagram, a preconcentration module is connected to the two systems in order to increase the sensitivity of the technique into the ppt range as required for routine analyses in the power and semiconductor industries.[101] Due to the extremely large differences of equivalent conductances for protons on one hand and monovalent alkaline cations on the other, indirect single-column conductivity detection surpasses the sensitivity attainable by the suppressed conductivity approach (Figure 32A and B).

Suppressed detection of cations also suffers from problems similar to those encountered with weakly ionized acids. According to the following equilibrium:

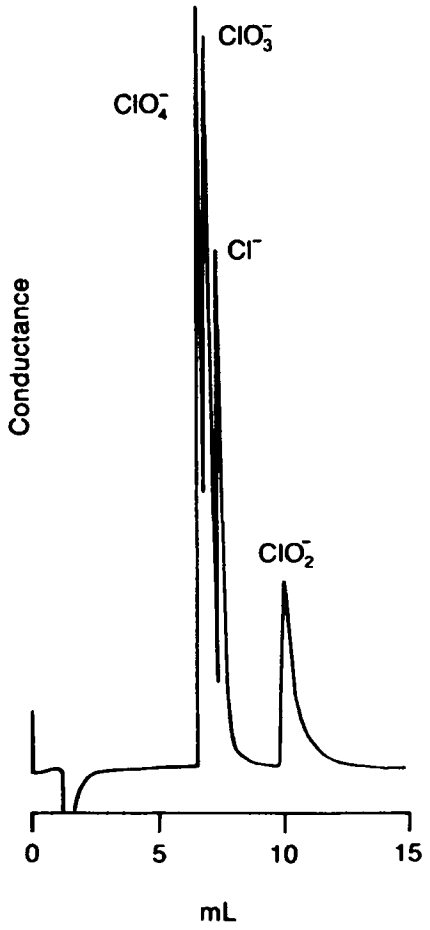


FIGURE 25. Speciation of chlorine oxyanions. Column: Spherisorb A5Y; eluent: 0.5 m*M* orthophosphoric acid; flow rate: 1 ml/min; detection: nonsuppressed conductivity. (Reproduced from Schmitt, G. L., Ph.D. thesis, The University of Iowa, Iowa City, 1985.)

$$R_3NH^+ + OH^- = R_3N + H_2O \quad (32)$$

a hydroxide form of suppression considerably decreases the conductivity response for protonated amines. As a solution to this problem, it has been recommended[102] that the borate form of suppression be used since this deprotonates the amines to a lesser degree. Nitric acid eluents enable sensitive detection of fully protonated amines in the nonsuppressed method.[40]

Conductivity detection of divalent metals[103-105] represents a simpler and often preferable approach in comparison with methods utilizing post-column reactions in conjunction with UV detection (Figure 33). It should, however, be applied only for samples with uncomplicated matrices such as purified water samples in the power and semiconductor industries. For more difficult matrices such as seawater or brines, post-column derivatization[106] is preferred.

The use of coupled systems has also been demonstrated for simultaneous analysis of anions and cations using conductivity detection[107] (Figure 34). Several authors[108-110] have published

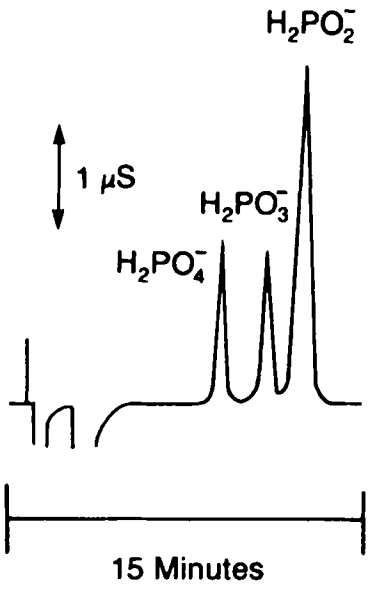


FIGURE 26. Speciation of oxyanions of phosphorus. Column: Waters IC Anion SW; eluent: 2 m*M* tartaric acid; flow rate: 1.2 ml/min; detection: nonsuppressed conductivity; 50 μl of a standard containing 20 ppm of each of the anions was injected.

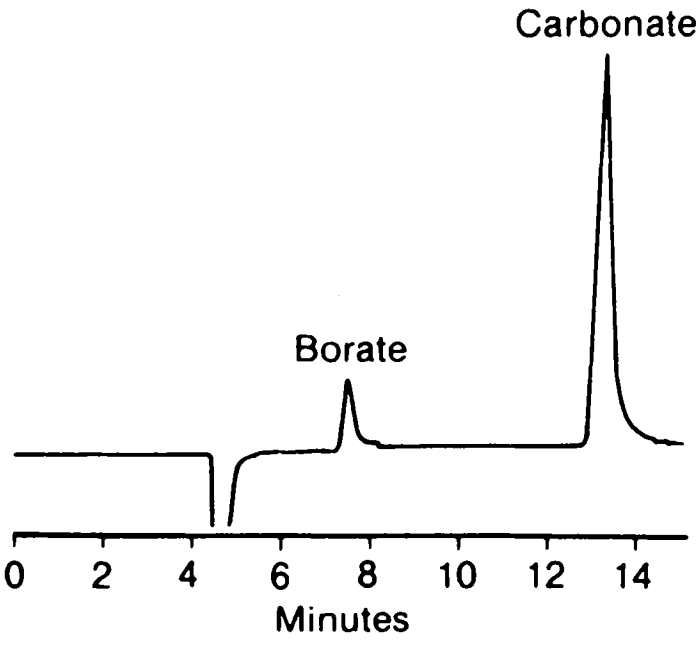


FIGURE 27. Detection of borate using a membrane suppressor. Column: Dionex HPICE-AS1; eluent: 1 m*M* octanesulfonic acid; regenerant: 10 m*M* ammonium hydroxide; detection: suppressed conductivity; 50 μl of a standard containing 10 ppm borate and 50 ppm carbonate was injected. (Reproduced from Weiss, J., *Handbuch der Ionenchromatographie*, VCH Verlagsges., Weinheim, Federal Republic of Germany, 1985, chap. 3. With permission.)

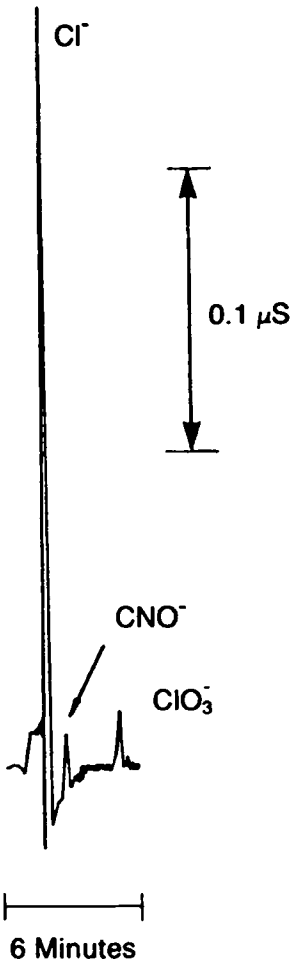


FIGURE 28. Indirect detection of cyanide after its oxidation to cyanate. Column: Dionex HPIC-AS4A; eluent: 0.75 m*M* sodium bicarbonate, 2.2 m*M* sodium carbonate; regenerant: 20 m*M* sulfuric acid; detection: suppressed conductivity. (Reproduced from Sillinger, P., *Plating Surf. Finishing*, 72, 82, 1985. With permission.)

reports on simultaneous detection of anions and cations using just one conductivity detector in series with a single separator column. An example of such work is given in Figure 35.

In what may have come as a surprise to many observers, at least two methods[111,112] have been demonstrated which allow the utilization of conductivity detectors after elution performed by a concentration gradient. In SIC, the combination of gradient elution and conductivity detection was made possible by the introduction of a flat sheet, large area suppressor having a large ion-exchange capacity.[29] This large ion-exchange capacity permitted continuous suppression over a wide eluent concentration range, e.g., 0.5 m*M* KOH up to 100 m*M* KOH (Figure 36). In SCIC, the conductivity change during gradient elution can be minimized by a proper adjustment of the conductances of the eluents used at the start and finish of the gradient run. One way to achieve this for anion gradients is to choose cations of higher equivalent conductance for the weaker anionic eluent and less conductive cations are used in the stronger eluent. The change of conductance occurring with properly adjusted eluents can be reduced to several μS and the corresponding small baseline shift is fully eliminated by a computerized baseline subtraction (see Figure 37).

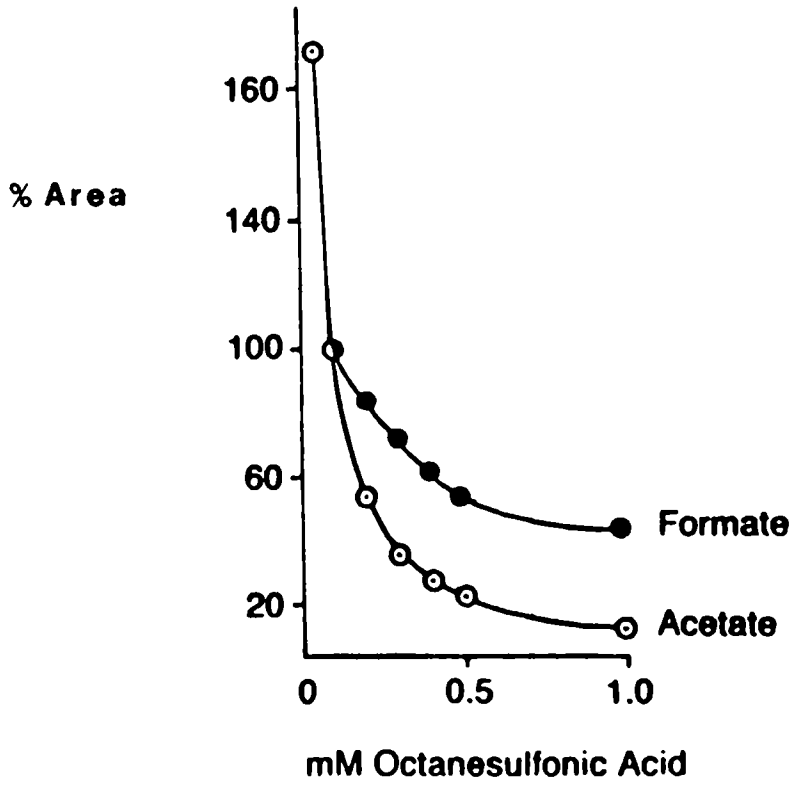


FIGURE 29. Conductivity detection after a separation by ion-exclusion. Sensitivity of the conductometric response increases with the decreasing concentration of the eluent. Peak area at 0.1 m*M* of octane sulfonic acid is regarded as 100%.[107]

III. AMPEROMETRIC AND VOLTAMMETRIC DETECTORS

A. Introduction

The detectors discussed in this section differ from those discussed in the other sections by a current which flows as the analyte bolus passes through the detector cell. Usually this current results from an electron-transfer (Faradaic) process; thus, an electrochemical reaction must occur at the surface of the working electrode of the cell. The rate of such a heterogeneous reaction can be influenced by many factors, including the nature of the analyte, the material and condition of the working electrode, the electrode potential, the mobile phase, and the flow patterns within the cell. There are many different types of amperometric and voltammetric detectors, each with its advantages and disadvantages. When the pressures of the marketplace enter into the picture, some distortion results and the situation can be extremely confusing to the nonspecialist. It is one aim of this review to help minimize the confusion.

B. Nomenclature

Nomenclature in electrochemistry has been a problem for a long time. With the advent of electrochemical detection in flowing streams, new factors have been mixed with traditional electrochemistry and some researchers are entering the area without a background in electrochemistry and its nomenclature. There is no uniform set of definitions. All that can be done here is to describe how the terms are used in this review and to point out some alternative terms that the reader might encounter in other publications.

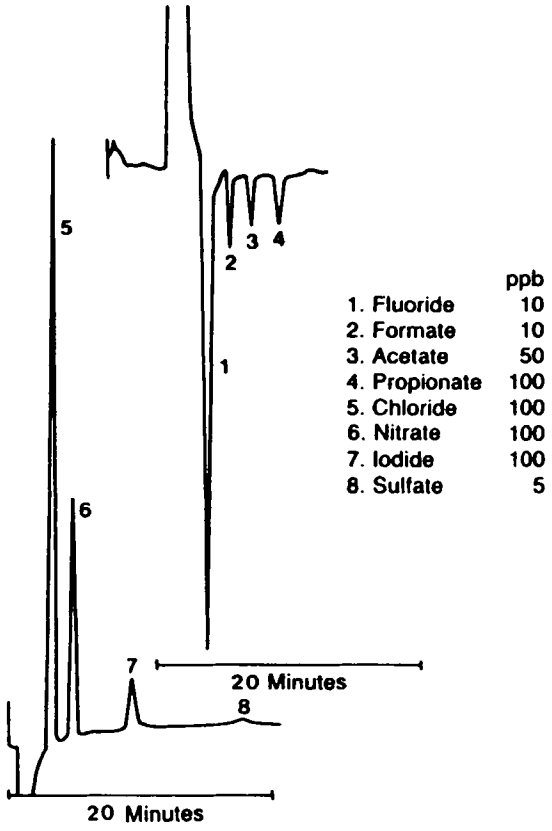


FIGURE 30. Simultaneous analysis of trace concentrations of weak and strong acid anions. Detection: nonsuppressed conductivity. Upper chromatogram — column: Waters Ion Exclusion; eluent: 1 m*M* octanesulfonic acid. Lower chromatogram — column: Waters IC PAK A; eluent: 3 m*M* sodium octanesulfonate.[107]

1. Amperometric Detector

The most common type of electrochemical detector is the amperometric detector in which the cell current is recorded while the working electrode is held at a constant potential. Sometimes this detector is named a DC amperometric detector. Other authors might refer to this as a voltammetric detector if a solid electrode is used, or as a polarographic detector if a dropping mercury electrode is used. However, amperometry entails the measurement of current at a fixed potential, while voltammetry and polarography entail the measurement of current as a function of potential.

Usually, only a small fraction of the analyte bolus undergoes an electrode reaction in the cell and is sensed. However, some cell designs lead to almost complete reaction of the analyte bolus. Such detectors are correctly named high-efficiency amperometric detectors, but often are named coulometric detectors. In such cells, the current is measured and is rarely integrated to obtain the coulombs as implied by the name coulometric.

Recently, there has been growing interest in amperometric detection with the potential stepped to other potentials between measurement cycles. The most common reason for the potential steps is to clean and reactivate the electrode surface. The term pulsed amperometric detection (PAD) is becoming accepted for this technique (Figure 38A).

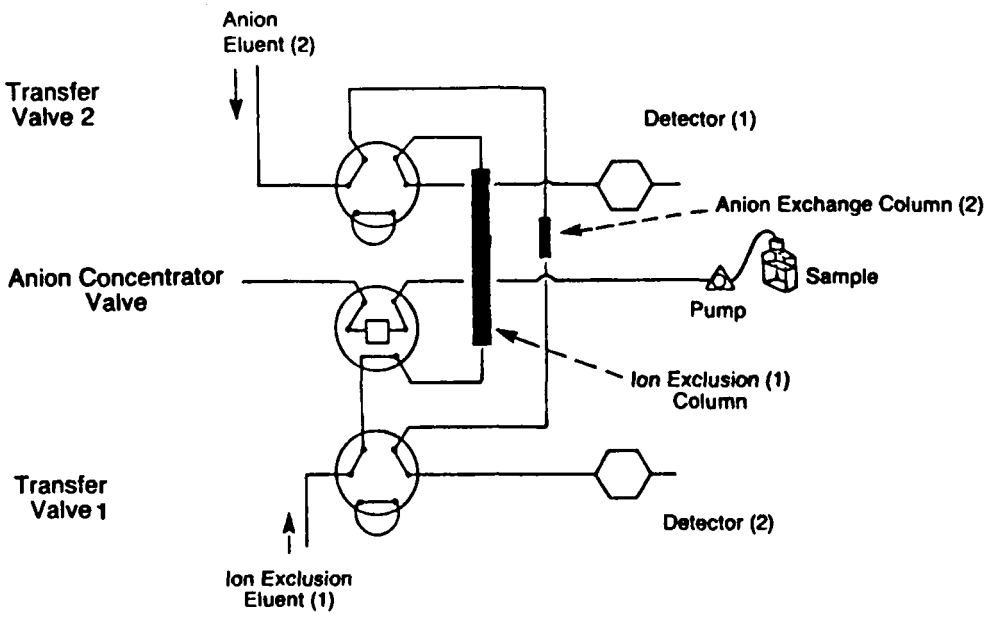


FIGURE 31. Schematic diagram of an instrument for coupled ion-exclusion and anion-exchange chromatography. Detectors (1) and (2) are Waters M 430 conductivity monitors. The sample preconcentration for both separation modes is carried out on a precolumn connected to the anion concentrator valve.

2. Voltammetric Detector

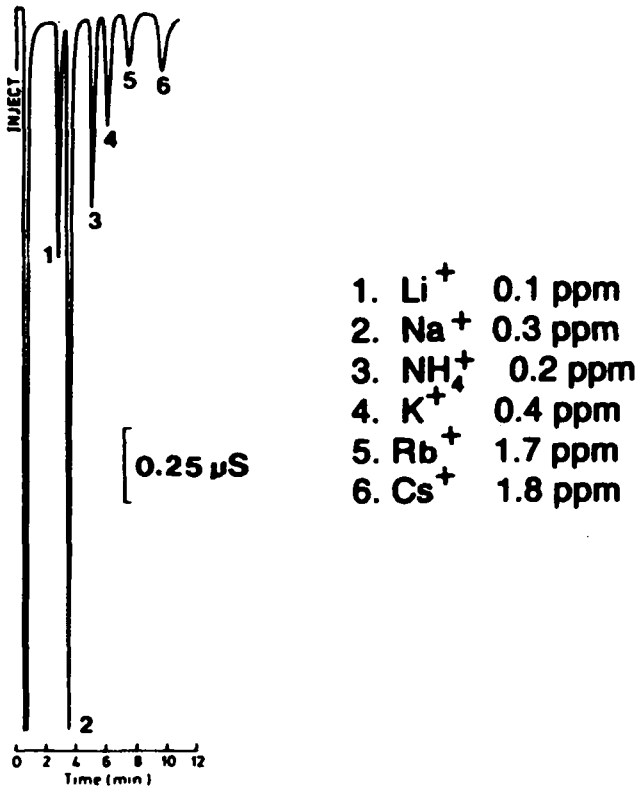
Voltammetry entails the measurement of current as the potential is changed in some prescribed manner. With such a detector, current is measured at more than one potential. There are several ways of obtaining multipotential current information and some of these are discussed later. The similarity and difference between amperometric and voltammetric detectors are elaborated in the following sections on cells and instrumentation.

C. Mobile Phases

Mobile phases for use with electrochemical detectors require some special considerations in addition to the chromatographic considerations. The mobile phase should not undergo an electrode reaction at the potential of detection, should provide a conduction path for the ionic current between the electrodes, and should be of such nature as to enhance the electrochemical reactivity of the analyte. In some cases the mobile phase can enhance the selectivity of the detection by inhibiting the electrode reactions of possible interferences in the sample.

It is commonly thought that these requirements for the mobile phase limit the use of amperometric detection to reverse-phase isocratic chromatography. However, recent work by Gunasingham et al.[113] has shown application to normal-phase gradient chromatography, and Khaledi and Dorsey[114] have demonstrated amperometric detection in gradient micellar chromatography. Other workers have demonstrated voltammetric detection with reversed-phase gradient elution.[115]

Chromatographers are so familiar with the mobile phases that have been developed for use with UV detection that they tend to use them for amperometric detection regardless of their electrochemical properties. For example, methanol has much higher background currents at positive potentials than acetonitrile and should not be used in such cases. HPLC-grade solvents have been processed to remove UV-absorbing impurities which might be of no importance for amperometric detection.



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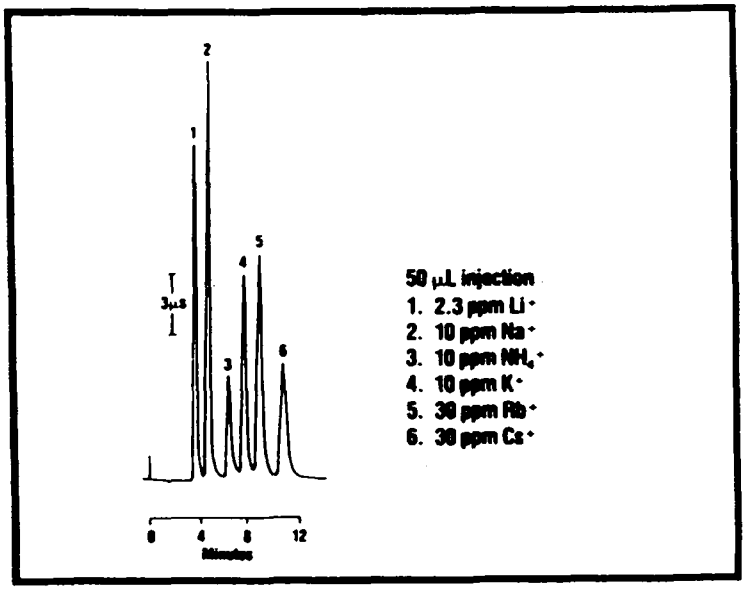


B

FIGURE 32. Comparison of suppressed and nonsuppressed conductometric detection of monovalent cations. (A) Nonsuppressed detection — column: Waters IC PAK C; eluent: 2 m*M* nitric acid; 8 µl of a standard was injected. (Reproduced from Haddad, P. R. and Jandik, P., in *Ion Chromatography*, Tarter, J. G., Ed., Marcel Dekker, New York, 1987. With permission.) (B) Suppressed detection — column: Dionex HPI -CS3; eluent: a linear HCl gradient; 50 µl was injected. (Courtesy Dionex Corporation.)

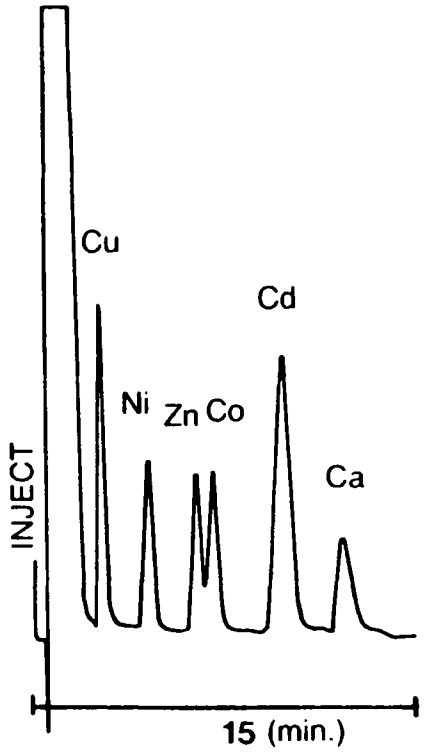


FIGURE 33. Conductometric detection of divalent metals. Column: Waters IC cation; eluent: 3.5 m*M* ethylenediamine, 10 m*M* citric acid; detection: nonsuppressed conductivity; 100 µl of a solution containing 5 ppm of all separated cations was injected.

D. Electrode Material

Amperometric detection may be accomplished through an oxidation reaction (anodic) or a reduction reaction (cathodic) at the working electrode. Some analytes can be oxidized readily, others reduced readily, and some can undergo both oxidation and reduction. In theory, the selection between oxidation or reduction is controlled by the potential for the experiment. However, the identity of the electrode material is very important, and it is usually necessary to select a cell, or at least an electrode, based on whether oxidative or reductive detection is to be performed.

For reduction reactions, the electrode material of choice has been, and remains, mercury. The primary reasons for this choice are the high overpotential for the reduction of hydrogen ion, the formation of amalgams with many metals, and the ease of replacement of mercury-drop electrodes. In this day of environmental and health concerns, many workers would like to avoid mercury because of its toxicity. We believe this is an overreaction; whereas the toxicity of mercury and its compounds is very real, reasonable care is adequate to prevent problems. Pertinent information can be obtained from the material safety data sheet provided by the supplier of the mercury.

The second electrode material of choice for reduction detection is carbon in one of its several forms (glassy carbon, pyrolytic graphite, carbon fiber, reticulated vitreous carbon, or carbon paste). The overpotential for hydrogen ion reduction is considerably lower on carbon than on mercury, leading to a more restricted range of reduction potentials. In addition, any solid

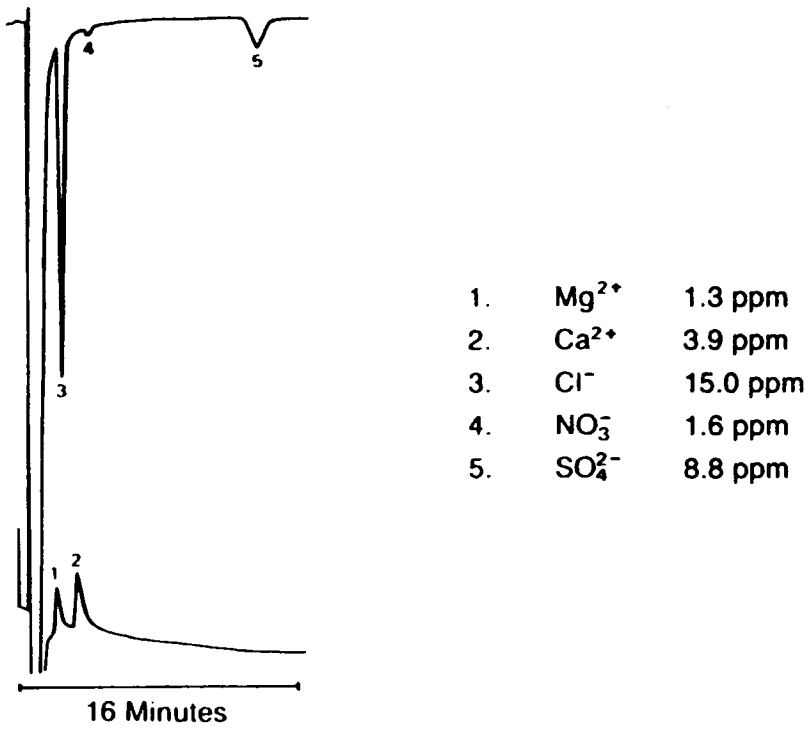


FIGURE 34. Nonsuppressed conductometric detection in the simultaneous detection of anions and cations. Upper chromatogram — column: Waters IC PAK A; eluent: 3 m*M* sodium octanesulfonate. Lower chromatogram — column: Waters IC PAK C; eluent: ethylenediamine to which octanesulfonic acid was added to adjust the pH to 6; 100 µl was injected. (Reproduced from Jones, W. R., Heckenberg, A. L., and Jandik, P., *J. Anal. Pur.*, 1, 68, 1986. With permission.)

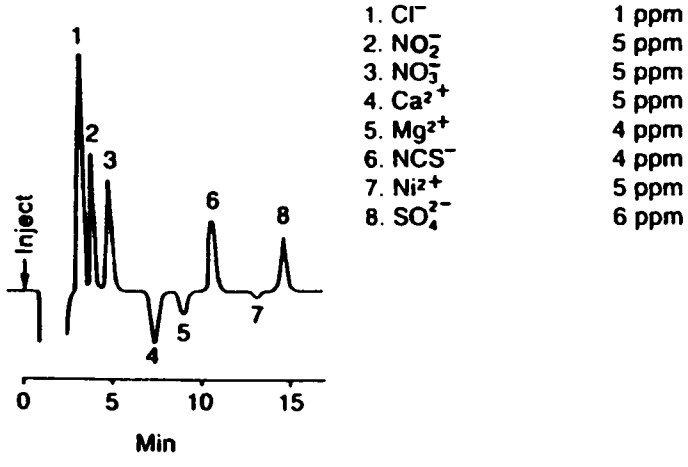


FIGURE 35. Simultaneous determination of anions and cations using only one column. Column: TSK IC Anion SW; eluent: 1 m*M* EDTA at pH 6.0; detection: nonsuppressed conductivity. Peak identities: 1 = 5 ppm chloride, 2 = 5 ppm nitrite, 3 = 5 ppm nitrate, 4 = 5 ppm calcium, 5 = 4 ppm magnesium, 6 = 4 ppm isothiocyanate, 7 = 5 ppm nickel, and 8 = 6 ppm sulfate. Flow rate: 1 ml/min. (Reproduced from Matsushita, S., *J. Chromatogr.*, 312, 327, 1984. With permission.)

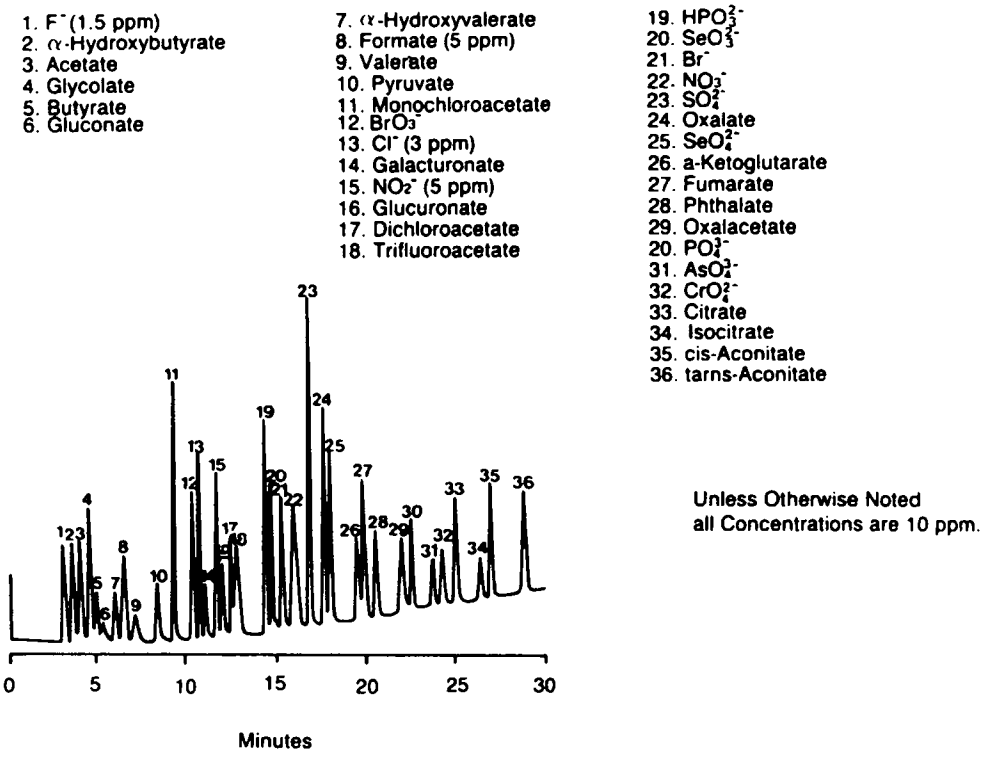


FIGURE 36. Suppressed conductometric detection after a gradient separation. Column: Dionex HPIC AS5A; eluent: 25 to 100 m*M* NaOH gradient. (Courtesy Dionex Corporation.)

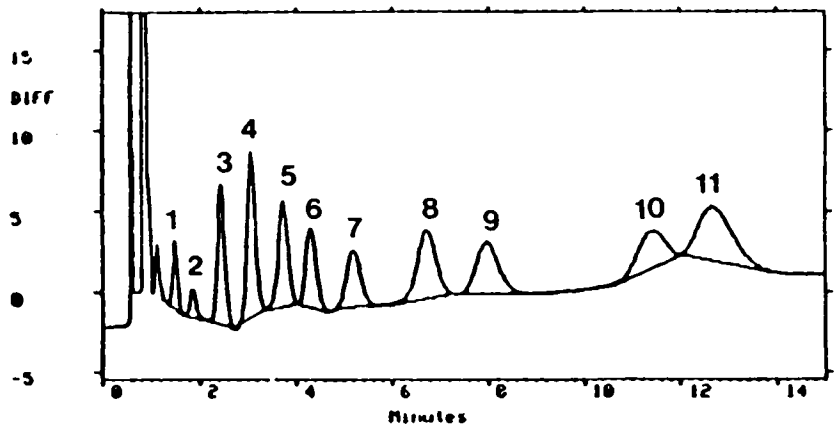


FIGURE 37. Isoconductive gradient and nonsuppressed conductometric detection. Column: Waters IC PAK A; eluent: 0.7 to 2 m*M* borate gluconate gradient. Peak identities: (1) 1 ppm fluoride, (2) 2 ppm carbonate, (3) 4 ppm chloride, (4) 4 ppm nitrite, (5) 4 ppm bromide, (5) 4 ppm nitrate, (7) 6 ppm phosphate, (8) 4 ppm sulfate, (9) 4 ppm oxalate, (10) 10 ppm chromate, (11) 10 ppm molybdate. 100-µl standard mixture was injected. (Courtesy Waters Division of Chromatography.)

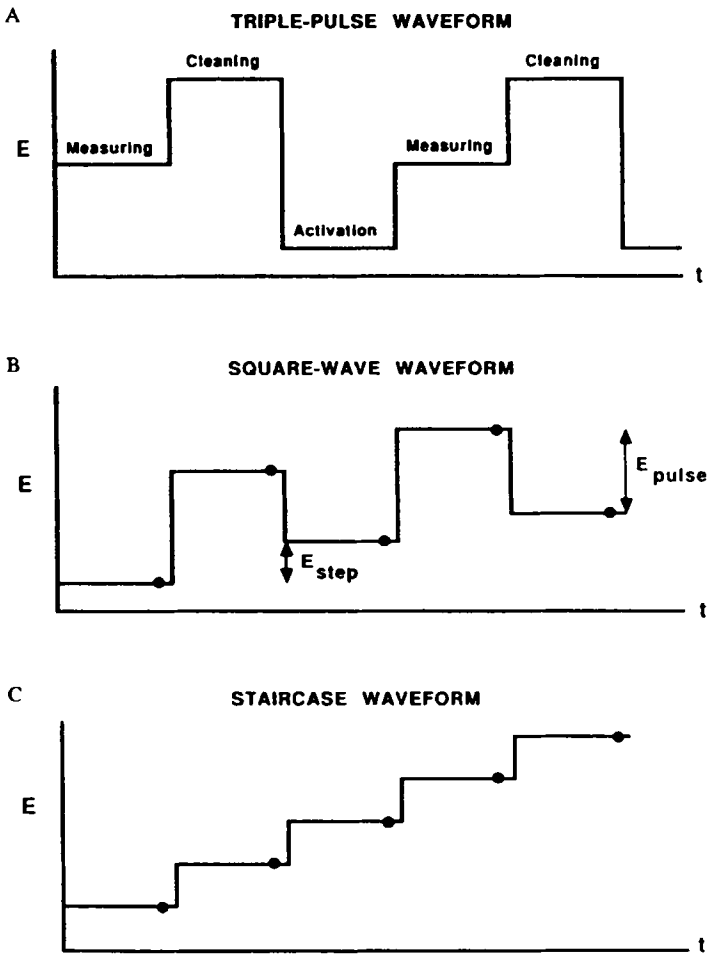


FIGURE 38. Three most frequently used modulations of the applied potential in amperometric and voltammetric detection. (A) pulsed amperometric detection — PAD; (B) square wave voltammetry; (C) staircase voltammetry.

electrode is susceptible to surface fouling and such electrodes are inherently more difficult to replace or recondition than a mercury-drop electrode. Electrodes of platinum, gold, or silver have such low overpotentials for the reduction of hydrogen ions that they are seldom suitable for reduction reactions.

The choice among electrode materials for oxidation reactions is more difficult than for reduction reactions since there are more alternatives and none is as clearly outstanding as mercury is for reduction reactions. The use of mercury for oxidation reactions is limited because it is so easily oxidized itself ($Hg \rightarrow Hg_2^{2+}$ or Hg^{2+}).

The early favorite was carbon paste in which powdered graphite is suspended in some inert binder such as mineral oil. Such a paste can be prepared easily and pressed into an electrode holder. Since only a small portion of the surface area is graphite, background currents are very low. However, the binder is attacked by most organic solvents, so this type of electrode is almost restricted to aqueous systems. Newer versions of this electrode use more stable binders such as Kel-F,[116] but these are more difficult to renew.

At present, the most commonly used electrode material is glassy carbon, which is very hard, impervious to organic solvents, and can be repolished easily. The primary problem with this material, as with all solid electrodes, is a gradual loss of response as the surface becomes coated

with contaminants from the solution or reaction products. Other forms of carbon-based electrodes, such as carbon fibers and reticulated vitreous carbon, have been used in specialized cell designs discussed later.

Metal electrodes, such as platinum and gold, have not been in favor because of their marked tendency to adsorb materials on their surfaces with a rapid deterioration of analyte response. The recent development of pulsed cleaning and activation (see later) has resulted in a resurgence of interest in these electrodes and more use of them can be expected in the future.

There are a number of cases in which a metal electrode actively enters into the electrode reactions of anions. The basic principle is that the anion forms a complex ion with the cation produced by the oxidation of the metal electrode and thereby makes possible the oxidation of the electrode at a potential lower than possible in the absence of the anion. For example, silver electrodes can be used for the detection of cyanide, halides, sulfite, and thiosulfate.[117-119] In the same way, mercury can be used to detect many anions and copper can be used to detect amino acids.[120]

Of increasing importance are catalytic reactions for detection. In some cases, the clean metal surface exhibits catalytic activity, but more frequently an oxide layer serves as the catalyst or the surface is modified by reaction or adsorption. For example, adsorption of iodine on platinum makes possible the detection of chromate,[121] nitrate and nitrite,[122] and carbohydrates are detected at platinum and gold by surface-catalyzed anodic dehydrogenation followed by oxide-catalyzed surface cleaning and reactivation.[123] Formation of surface oxide catalyzes the direct anodic detection of amino acids and many sulfur compounds.[134]

E. Potential Window

The range of electrode potentials accessible in any given experiment is named the potential window. In order to detect a given analyte, its electrode reaction must occur within the range of the potential window. The potential window is limited in both the positive and negative direction by the electrode material or by the mobile phase. For example, in the positive direction (oxidation reactions), mercury oxidizes at about +0.2 V vs. saturated calomel (SCE) and limits the window in that direction. However, if platinum is the electrode material, the oxidation of the mobile phase, either solvent or electrolyte, limits the potential region which can be pH dependent. In the negative direction, the reduction of hydrogen ion usually limits the window and this can be a function of pH, solvent system, or overpotential, which is, in turn, a function of the electrode material. Figure 39 shows the potential ranges for the oxidation of various inorganic and organic compounds for which suitable potential windows can be found.

F. Cell Types

Electrochemical cells for use with flow streams have been classified as flow by, in which the eluent flows parallel to the surface of the working electrode; flow through, in which the eluent winds through a tortuous path between surfaces of the working electrode; and flow at, in which the eluent impinges perpendicularly onto the surface of the working electrode.

1. Thin-Layer Cell

The most common cell type is the flow-by, as illustrated in Figure 40. This cell appears to be a direct descendent of the familiar IR sandwich cell. A thin spacer between two rigid blocks establishes the thickness, width, and length of the flow channel. Early cells of this type had the working electrode mounted flush in one of the rigid sides of the thin-layer flow channel and both the counter electrode and the reference electrode were mounted downstream in another compartment. Newer designs have the counterelectrode positioned on the opposite side of the thin-layer flow channel from the working electrode and, in some cases, even the reference electrode is positioned in the same compartment. These changes result in greatly improved electrochemical performance because the electrical resistance of the cell is much lower and the

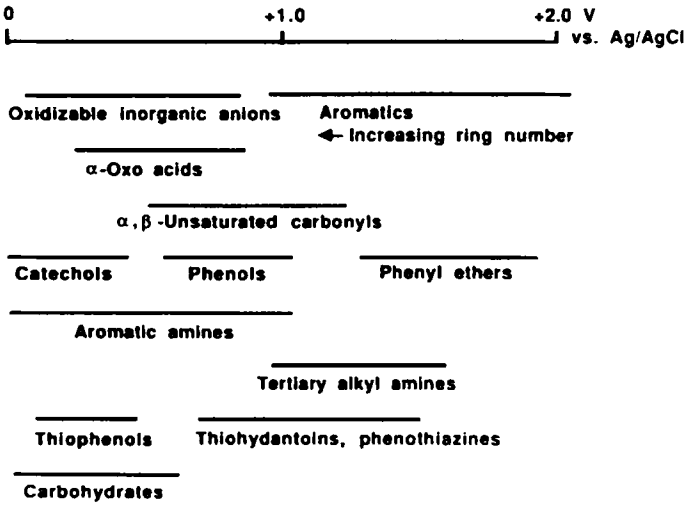


FIGURE 39. The potential windows. Ranges of potentials for the oxidation of various compounds and functional groups are shown.

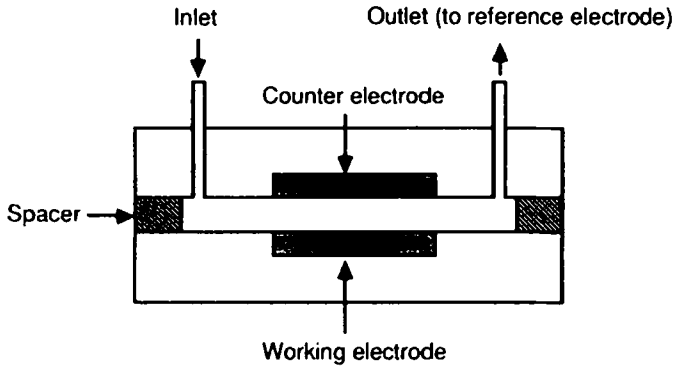


FIGURE 40. Thin-layer cell.

potential control is improved. The advantages of the thin-layer cell are simplicity of design and the ease with which the cell can be taken apart for refinishing of the electrode surface. The following equation for the cell current is predicted on the basis of a simple model for the thin-layer cell:[124]

$$i = 1.467nFCA(D/h)^{2/3}(U_v/d)^{1/3} \quad (33)$$

where i is the current in amperes, n is the number of electrons in the electrode half-cell reaction equation, F is the Faraday constant, A is the electrode area in cm^2, D is the diffusion coefficient in $cm^2 s^{-1}$, h is the channel thickness and d the channel width in cm, U_v is the volume flow rate in $cm^3 s^{-1}$, and C is the analyte concentration in mol cm^{-3}.

However, the work of Roe[125] indicates that the current does not continue to increase indefinitely with increased flow rate in real cells. The article by Moldoveanu and Anderson[126] should be consulted for a more detailed theoretical analysis. Also, see the discussion following for a comparison to other cell designs.

2. Tubular Cell

A second type of flow-by cell is the design with a tubular working electrode arranged so that the effluent flows down the center of the tube. The counter and reference electrodes are usually mounted downstream from the working electrode. The theoretical response for this cell is given by:[122]

$$i = 5.43nFC(DL)^{2/3}U_v^{1/3} \quad (34)$$

All terms are as defined for Equation 33, except L, the length of the working electrode in cm. Thus, in this cell, like the thin-layer cell, the response should have a one-third power dependence on the flow rate. One disadvantage of this cell, compared with the thin-layer cell, is that it is quite difficult to refinish the surface of the working electrode. When the response of this cell deteriorates, it is common to simply dispose of the old electrode and install a new one.

3. High-Efficiency Cell

If the electrode of a flow-by cell is made long enough, the portion of analyte undergoing electrode reaction will approach 100%. However, such a high-efficiency (coulometric) detector can be made much more compact by use of a flow-through electrode. Such an electrode can be made from a packed bed of small particles or from a porous plug of electrode material (e.g., reticulated vitreous carbon). The theoretical equation for the response of these cells is[125]

$$i = nFCU_v \quad (35)$$

An alternate form of Equation 35 is a statement of Faraday's Law:

$$Q = nFC^*V = nFM \quad (36)$$

where Q is the coulombs of electricity from the analyte in the injected volume V, C* is the concentration injected, and M is the moles of analyte injected. The integrated current Q can be an absolute measure of the analyte in the sample bolus; the only calibrating constants are an integer, n, and the universal constant, F. It is apparent that the current in such a cell is more sensitive to flow rate than in a flow-by cell, but that the integrated current Q is independent of flow rate.

These cells have a higher conversion efficiency and a concurrent increase in cell current for a given amount of analyte (i.e., sensitivity). However, there has been considerable controversy in the literature about the relative merits of these cells, and the matter is still not resolved.

The important factor for an electrochemical detector is not sensitivity (i.e., current response for amount injected), but rather limit of detection, i.e., is the mass, moles, or concentration of analyte at which the response is two (or three) times the standard error of the baseline (baseline noise). There are several sources for baseline noise, and their relative importance varies with the type of detector. It is even possible that different noise sources might prevail in a single detector under different operating conditions. Common sources of baseline noise are the electronics, the cell flow, and surface reactions of the electrodes.

A comparison of Equations 33 and 35 indicates that the thin-layer cell (flow by) develops less current than the flow-through cell, but that the flow-through cell is more sensitive to changes in flow rate. This means the relative performance of the thin-layer cell would worsen with increasing electronic noise in the system, whereas the flow-through cell would be more affected by a change in flow pulsations. Therefore, the type of system noise present is an important influence upon the performance of a cell.

Many workers have reported that baseline noise is approximately proportional to the surface area of the electrode. Since the high-efficiency amperometric detector obtains its high efficiency

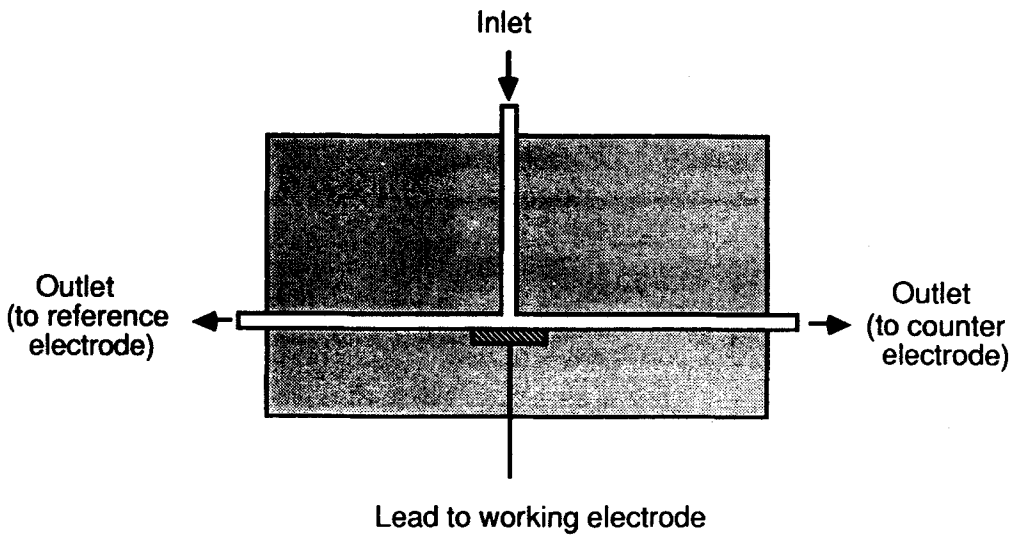


FIGURE 41. Constrained wall-jet cell.

by increasing the electrode area, it is readily seen that the increased efficiency is offset, to some extent, by the increased baseline noise. Flow-through cells are usually designed so that a large excess of surface area is available in order to accommodate the largest expected sample and to allow for loss of active surface by fouling. The question still under dispute is whether or not the efficiency increases more or less than the noise with increases in the electrode area. The answer to this question will determine whether the limit of detection improves or deteriorates.

Regardless of the ultimate resolution of the question of limits of detection in amperometric detection, certain attributes of the high-efficiency cell are clear. The cells are well suited for screening and clean-up applications where electroactive interferences in the sample or mobile phase are reacted before the bolus reaches the detector cell. On the other hand, these cells are not well suited to applications in which the electrode potential is swept or stepped rapidly because the large surface area has a large double-layer capacitance associated with it.

4. Wall-Jet Cell

The flow-at cell is exemplified by the wall-jet cell illustrated in Figure 41. The theoretical response equation for this cell is[127]

$$i = 1.38nFCD^{2/3}v^{-5/12}U_v^{3/4}a^{-1/2}R^{3/4} \quad (37)$$

where v is the kinematic viscosity, R is the radius of the working electrode in cm, and a is the inside diameter of the jet in cm. Equation 37 predicts that the response should increase by the three-fourths power of the flow rate. However, most workers have found an experimental dependence to the one-third power as for a thin-layer cell. It is now recognized that this discrepancy is caused by the way in which the cell is constructed. The true wall-jet cell (Figure 42), which responds in accord with Equation 37, has a jet internal diameter, a, smaller than the radius of the working electrode, R, and a sufficient gap between the tip of the jet and the electrode such that the tip does not interfere with the reflected flow from the electrode surface. Such cells are named unconstrained wall-jet cells or large-volume wall-jet cells.[127-129]

Early wall-jet cell designs attempted to minimize the cell volume by drilling the inlet jet through a solid block located very close to the working electrode (Figure 41). Such a design, now called a constrained wall-jet cell, results in interference of the reflected flow, which is deflected

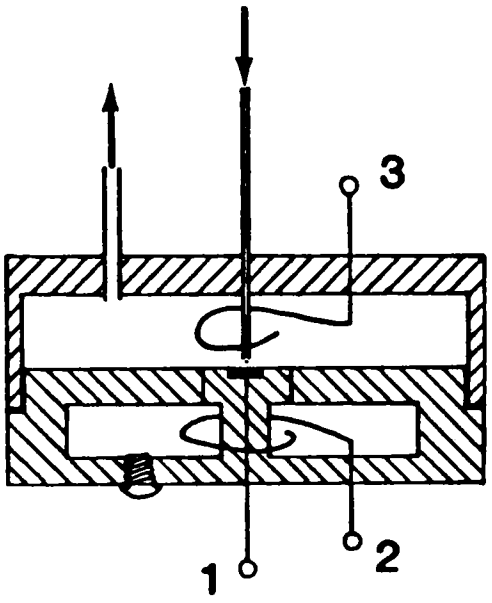


FIGURE 42. Unconstrained (large volume) wall-jet cell. (1) Working electrode; (2) reference electrode; (3) counter electrode. The arrows indicate the direction of the flow. (Reproduced from Berger, T. A., U.S. Patent 4,496,454, January 29, 1985.)

to a path parallel to the working electrode. Thus, such cells are effectively thin-layer cells with radial flow patterns and respond in accord with Equation 33.

An important aspect of the wall-jet design is that the effective volume of the cell is much smaller than the volume of the compartment in which the working electrode is located. The effective volume is hydrodynamically limited to a thin layer over the surface of the electrode. After leaving this limited volume, the effluent is mixed with the solution in the relatively large volume of the cell and the bolus has essentially lost its identity by the time it exits the cell. Thus, the wall-jet cell can be used in series with other cells, only if the wall-jet is the last cell in the sequence.

A second aspect of the wall-jet design, evident from Equation 37, is the much higher dependence on flow rate than for the flow-by designs. This aspect follows from the more efficient transport of analyte to the surface of the electrode and results in a higher ratio of current-to-electrode area, or current density, than for the other cells. Since noise is usually found to be proportional to electrode area, increased current density should lead to an improved signal-to-noise ratio and a more favorable limit of detection. This increased dependence on flow rate means, however, that this cell design is more susceptible to flow pulsations and therefore requires more care in the selection of the pumping system.

Two other aspects of the wall-jet design deserve comment. In Equation 37, it can be seen that the ratio of electrode radius to jet diameter is a more important factor than electrode radius alone. Thus, this cell should be appropriate for miniaturization to make it compatible with microbore columns without significant loss of concentration limits of detection and with greatly improved mass limits of detection. Also, the relatively small size of the working electrode results in a small double-layer capacitance and, therefore, a much shorter time constant for the cell. Thus, this cell is well suited to those applications in which the electrode potential will be changed rapidly, such as for PAD and voltammetric detection.

The reviewers do not know of any true wall-jet cells with solid electrodes available commercially at this time. The EG&G PARC Model 310 mercury electrode stand and flow cell is essentially a wall-jet design if the original jet diameter is used with a large mercury drop. An improved version of the 310, in a metal cabinet for shielding, has recently been introduced as the model 420.

5. Micro Cell

Recent articles by White et al.[130,131] and Goto and Shimada[132] describe detector cells formed by inserting a short lenth of a single carbon fiber into the outlet end of an open-tubular or a packed microbore column. The reference and counter electrodes were mounted in an external cavity with a resulting high cell resistance. No theoretical response equations were given.

G. Instrumentation

The instrumentation required to control the detector cell and record response data varies from very simple analog instrumentation for amperometric detection to rather sophisticated computer-controlled instrumentation for voltammetric detection.

While it is possible to obtain satisfactory results under favorable circumstances with amperometric detection using two-electrode cells and a battery to supply the applied potential, most amperometric detectors use line-powered instrumentation, comprised of operational amplifiers, to control the potential of the working electrode of a three-electrode cell in the presence of high resistance solutions and varying current levels. Such instruments are inherently more noisy than simple battery-operated instruments, but the low-frequency response required for the DC signals allows the use of heavy damping (long time constants) which filters out the noise.

The overall instrument contains analog circuits to control the potential of the electrode and other analog circuits to measure and process the cell current. The name potentiostat is sometimes used for the overall instrument or may be used to refer to the control circuits only. The current output is usually fed to a strip-chart recorder which also acts as a noise filter. Such instruments are no more complicated than the ubiquitous pH meter.

PAD requires rapid changes of electrode potential in a reproducible, repetitive manner and the measurement of current at a specific, timed point in this cycle (Figure 38A). The control circuits must be capable of rapid response and therefore are inherently more susceptible to the propagation of noise than those used with a simple amperometric detector. This problem is not too serious with PAD because the current-measuring circuits do not require rapid response and usually incorporate long time-constant filters.

One approach to obtaining a flexible, easy-to-use instrument is to use a digital computer to generate the potential values and timing sequence (Figure 43). The digital representations of the potentials are converted to analog signals by a digital-to-analog converter (DAC). The analog output signals, proportional to the cell current, are converted back to digital by an analog-to-digital converter (ADC) and fed back to the computer for storage, processing, and display. A danger inherent in this approach is that digital computers are prone to inject digital noise into the analog control circuits. Post-run analysis and printout of the data are additional advantages of this type of instrumentation.

Voltammetric detection requires more complex instrumentation than PAD. Not only is the potential changed rapidly in this case, but the current measurement also must be made rapidly and repeatedly as the potential is swept or stepped through the voltammogram (Figure 38), which rules out the use of long time-constant filtering. In addition, so many data points are generated that a strip-chart (or X-Y) recorder is not a suitable readout device. There does not appear to be any good alternative to a computer-controlled system as described here. The principles of such instrumentation are well established, but the design of such instrumentation, while achieving a satisfactory signal-to-noise ratio, is a serious challenge. Careful attention to

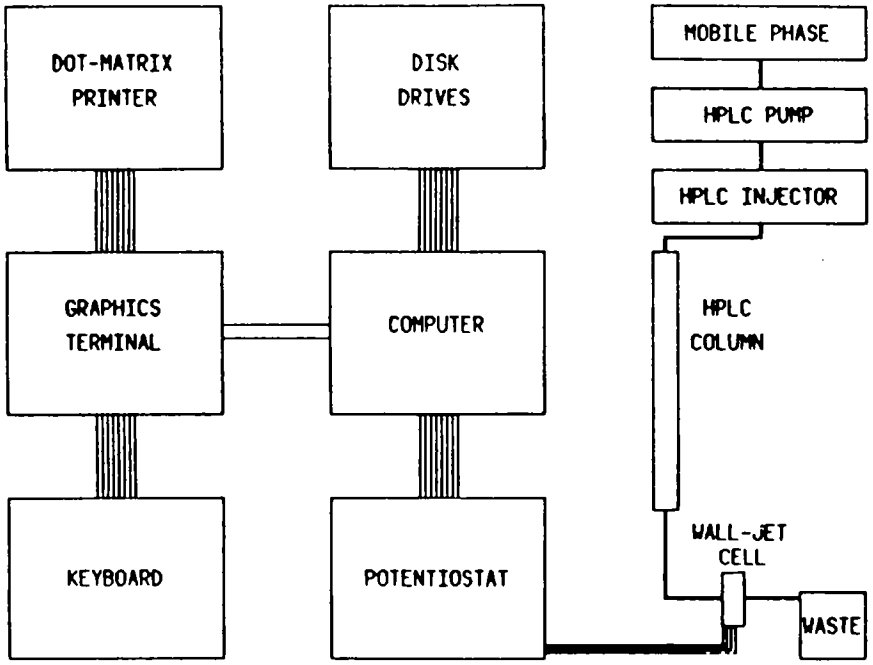


FIGURE 43. Block diagram of a computer-controlled detector system connected to a simple chromatograph. (Reproduced from Reardon, P. A., O'Brien, G. E., and Sturrock, P. E., *Anal. Chim. Acta*, 162, 175, 1984. With permission.)

the elimination of noise sources in the instrument, and post-run computer (digital or mathematical) filtering of the acquired data, are both important.[133]

H. Detection Modes

1. Amperometric Detection

By far the most common mode of detection is amperometric detection in which the working electrode of the cell is kept at a constant potential and the cell current is monitored continuously and recorded. Almost all commercial detectors are designed for and restricted to this mode of detection. The virtues of this mode of detection are obvious: it is simple to use, inexpensive, and capable of excellent limits of detection for certain classes of analyte. Control of the electrode potential allows some degree of selectivity. However, selectivity is quite limited since any material capable of an electrode reaction at any potential up to the potential of operation will result in a response from the detector. Optimum electrode potentials are usually determined empirically during method development, but may be deduced from voltammograms.

The most serious problem with amperometric detection is a gradual loss of sensitivity. To understand the nature of this problem, it must be appreciated that an amperometric detector is a reaction detector with a heterogeneous electrochemical reaction occurring at the interface between the electrode and the solution. In some cases, reaction products can accumulate and adhere to the surface of the electrode, thus blocking the surface and hindering further reaction. In other cases, the surface of the electrode can undergo slow deterioration. The sensitivity must be carefully monitored by frequent injections of a standard and, when response has deteriorated to an unacceptable level, the cell must be reconditioned by replacing or polishing the working electrode.

2. Pulsed Amperometric Detection

One reason for the development of PAD was to provide a means of preventing the slow

deterioration of response prevalent in simple amperometric detection. Adsorbed products of the electrode detection reaction may be desorbed or oxidatively removed by pulsing the working electrode to an extreme positive potential (Figure 38A). The oxidation of these materials may be by direct electron transfer or indirectly by the generation of chemical oxidants from the solution. Electrodes of platinum or gold are essentially unaffected by such pulsing, but graphite electrodes can be damaged if the potential is too positive. After the cleaning pulse, the electrode may be returned directly to the potential for detection or passed through an intermediate potential for reduction of surface sites on the electrode or possibly for adsorption of the analyte.[123,128]

A second reason for using PAD is the possible electrode reaction and detection of otherwise nonreactive analytes because of an activated electrode surface, which may occur due to the cycling of potentials. An excellent example of this is the catalytic oxidation of carbohydrates at a platinum or gold electrode. From their recent research, Johnson and co-workers report several classes of analytes, previously thought to be undetectable, that can be detected by PAD.[123,134]

At this time, there are two commercial detectors that feature PAD capability: the triple-pulse detector from Dionex Corporation and the Model 400 from EG&G Princeton Applied Research.

3. Detection with More Than One Working Electrode or Cell

Several modes of detection using more than one working electrode have been developed in recent years.[135] The working electrodes may be housed in a single cell or in a series of cells. The potential for each working electrode must be controlled individually by the instrument, which is either two or more potentiostats or a combined instrument known as a bipotentiostat. Care must be taken to minimize interaction among the control circuits for the working electrodes.

High-efficiency cells are often used as a screening cell in front of a second cell which performs the actual detection. The screening cell may be set to a lower potential than the detection cell so that it effectively removes by reaction those interferences which react at its lower potential. An alternate approach is possible when the analyte can undergo electrode reaction in both the forward and reverse directions, but interferences can only react in the forward direction. In such cases, the screening cell is set to the higher potential and reacts everything in the forward direction; then the detector cell selectively reacts the analyte in the reverse direction without interference. Also, such high-efficiency screening cells may be used before the injector to remove electroactive impurities from the mobile phase.

Valuable information can be obtained from two cells or two working electrodes even when the first electrode is not of the high-efficiency type. In such cases, the second electrode responds to reaction products of the first electrode and thereby helps to identify or characterize the material being detected.

Another mode of detection involves two working electrodes which may be operated in parallel positions in the same cell but at different potentials. The current responses from the two cells can be overlayed or differenced. This approach is valuable in determining the reaction potentials of analytes and in determining peak purity. A problem inherent in this approach is the uncertainty in the relative sensitivities of the two electrodes due to the condition and effective areas of the electrodes and their positioning in the flow stream.

At present, the most extensive use of multiple working electrodes is the instrumentation from Environmental Science Associates (ESA) for determination of catecholamines.[136] In this system, a number of high-efficiency cells are connected in series, with each cell controlled by its own potentiostat. The first cell is set to oxidize all components of the injected mixture, and each successive detector cell is operated at an increasingly negative potential to reduce a range of products from the first cell.

4. Voltammetric Detection

An alternative to the ESA multicell approach is voltammetric detection in which the potential of a single working electrode is swept or stepped to various potentials and the cell current

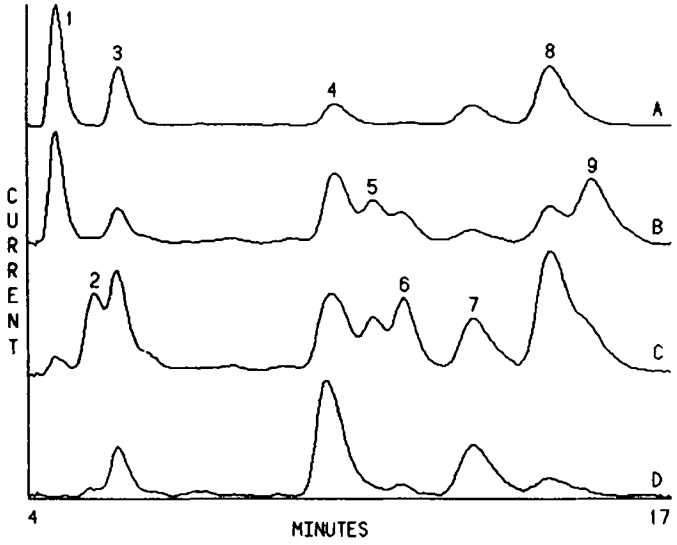


FIGURE 44. Multipotential chromatogram of a mixture of nitrophenols. (1) 2,6-dinitrophenol (75 ng); (2) unknown impurity; (3) 2,4-dinitrophenol (128 ng); (4) *p*-nitrophenol (150 ng) and 2,3-dinitrophenol (120 ng); (5) *m*-nitrophenol (150 ng); (6) 2,5-dinitrophenol (98 ng), (7) 3,4-dinitrophenol (128 ng); (8) 2,4-dinitro-*o*-cresol; (9) *o*-nitrophenol (150 ng). Mercury working electrode; column: reverse phase; eluent: methanol containing acetate buffer. See Reference 139 for complete conditions. (A) –0.25 V, (B) –0.39 V, (C) –0.48 V, (D) –0.61 V. (Reproduced from Scanlon, J. J., Flaquer, P. A., Robinson, G. W., O'Brien, G. E., and Sturrock, P. E., *Anal. Chim. Acta*, 158, 169, 1984. With permission.)

measured as a function of potential (Figure 38). This approach was demonstrated by Buchanan and Bacon in 1967 for the detection of copper, lead, cadmium, and zinc following separation by ion-exchange chromatography.[137] The techniques and instrumentation have been extended and refined by a number of researchers since that time. At present, there is no commercial instrumentation available for voltammetric detection. Unfortunately, there is considerable confusion generated by the incorrect use of the term voltammetric detection to refer to amperometric detection at a solid electrode.

The advantages of voltammetric detection are obvious when it is realized that voltammetric detection is the electrochemical analog of the multiwavelength photodiode-array detector (Figures 44 and 45). The voltammetric information can be used to help identify analytes and to check for chromatographic peak purity. In addition, the voltammetric information can serve as a guide for the development of a procedure for a routine amperometric detection. Finally, mathematical deconvolution of coeluted peaks is possible, thus it is sometimes unnecessary to perfect the complete chromatographic separation of an analyte system.

The relative limits of detection for voltammetric detection vs. amperometric detection are highly dependent on the nature of the reaction, the analyte, and the electrode. For reduction reactions on mercury, the limits of detection of the two techniques are comparable, while for oxidation reactions, the limits of detection for amperometric detection are about two orders of magnitude lower than for voltammetric detection.[138] This difference is due primarily to the larger potential-dependent background currents at solid electrodes which reach equilibrium very slowly after a change in potential compared with the much smaller background currents on mercury electrodes, which are largely capacitance and decay rapidly following a change in potential.

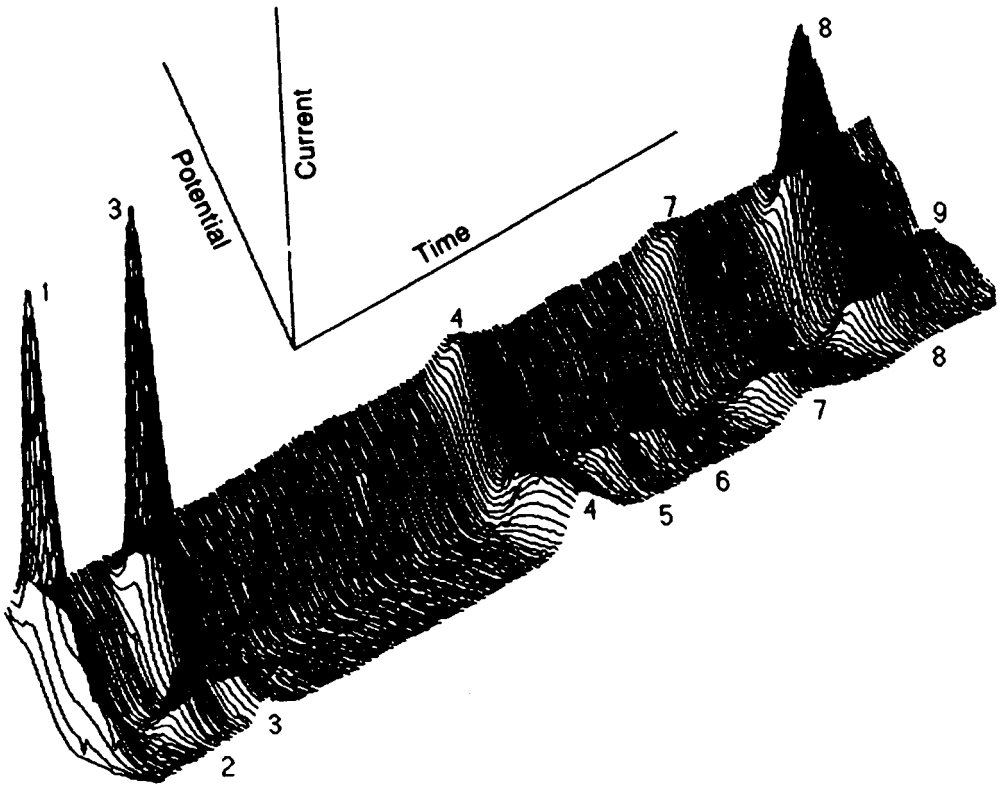


FIGURE 45. Voltammetric 3-D chromatogram of nitrophenols. Data are from the same experiment as in Figure 44. (Reproduced from Scanlon, J. J., Flaquer, P. A., Robinson, G. W., O'Brien, G. E., and Sturrock, P. E., *Anal. Chim. Acta*, 158, 169, 1984. With permission.)

Several papers report limits of detection for square-wave voltammetric detection with the EG&G PARC model 310 electrode stand and flow cell as below 1 ng injected with a chromatographic column 4.6 × 150 mm.[139-141] Unpublished work using the newer EG&G PARC model 420, with a single mercury drop for the entire chromatogram, resulted in an estimated limit of detection well below 100 pg injected.

Since electrochemical detectors are concentration dependent, it is important to distinguish between mass limits of detection and concentration limits of detection when considering limits of detection for electrochemical detectors. For example, the concentration limits of detection reported for catecholamines by Owens et al.[138] are approximately an order of magnitude lower than those reported by White et al.[130,131] and two orders of magnitude below those of Goto and Shimada.[132] However, the mass limits of detection in White's work are much lower than those of Owens due to the miniature open-tubular column and low volume flow rates used by White.

It is interesting to note that all three of these papers[130,132,138] on the oxidative voltammetric detection of catecholamines made use of background subtraction while most of the papers on reductive voltammetric detection did not require background subtraction. This is another manifestation of the larger background currents on solid electrodes than on mercury. Figure 46 illustrates the relative magnitudes of the background and analyte currents for the oxidation of norepinephrine on platinum. In such a situation, it is necessary to lower the gain of the current amplifiers to keep the output within the dynamic range of the amplifiers, thus resulting in only a very small difference between the two curves and a very poor signal-to-noise ratio and a poor limit of detection. A constant-potential chromatogram, extracted from the differences of background and a series of analyte voltammograms as in Figure 46, is shown in Figure 47.

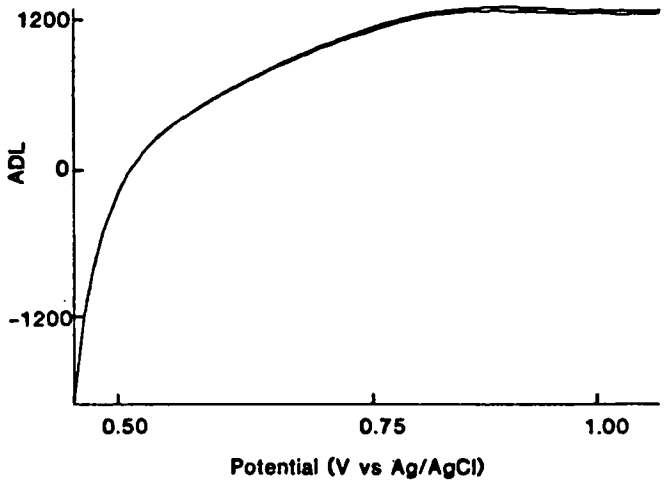


FIGURE 46. Staircase voltammograms of 75 ng of norepinephrine and of a blank. (ADL is analog-to-digital level). Platinum working electrode in an unconstrained wall-jet cell.

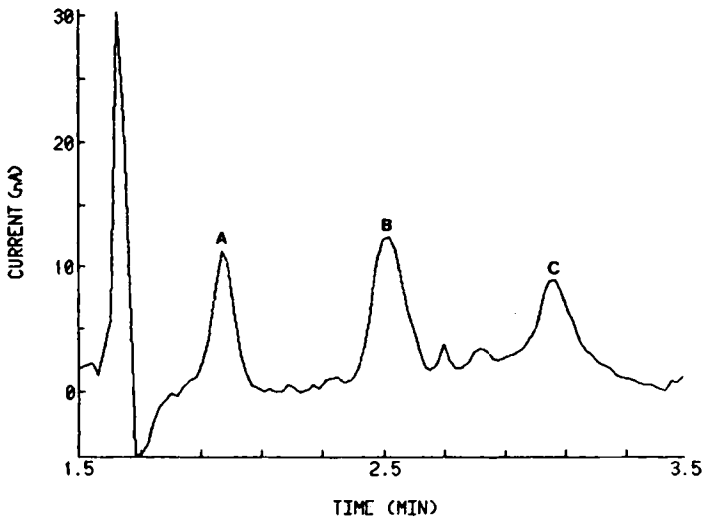


FIGURE 47. Chromatogram of catecholamine standards at 0.90 V vs. Ag/AgCL resulting from electronic processing of staircase voltammograms similar to those shown in Figure 46. (A) Norepinephrine, 6.1 ng; (B) epinephrine, 8.4 ng; (C) dopamine, 4.9 ng. Column: reverse phase; eluent: 5% acetonitrile, 95% aqueous 50 m*M* citrate buffer at pH 5.2 with an addition of 1m*M* EDTA; flow rate: 0.8 ml/min. (Reproduced from Owens, D. S., Johnson, C. M., Sturrock, P. E., and Jaramillo, A., *Anal. Chim. Acta*, 197, 249, 1987. With permission.)

Further improvements can be expected through the use of a programmed current offset, an extension of the idea of the DC current offset which is used commonly in amperometric detection to permit use of higher recorder sensitivity.

I. Applications

IC applications of amperometric and voltammetric detection were reviewed recently by

Table 5
SELECTED APPLICATIONS OF AMPEROMETRIC AND VOLTAMMETRIC DETECTION IN ION CHROMATOGRAPHY

Species	Ref.
Amino acids	120, 142—148
Arsenite	149
Bromide	150, 151
Carbohydrates	123, 134, 152
Chloride	150, 151
Cyanide	150, 153—155
Iodide	150, 156—159
Nitrate	118, 122, 160, 161
Nitrite	118, 122, 160, 161
Sulfide	154, 155, 162
Sulfite	163, 164
Thiosulfate	118, 156, 165

Haddad and Jandik[44] in their Table 4 and the reader should consult this source for the older literature. Table 5 contains a partial listing of applications, mostly from the 1983 to 1987 literature. No attempt has been made to survey the voluminous literature of applications to HPLC, some of which can be considered to fall under the broad definition of IC.

A persistent problem in reduction detection is the interference from oxygen. The usual practice is to remove oxygen from the carrier stream by sparging the reservoir with an inert gas such as nitrogen or helium. Sometimes the carrier stream is heated or placed under vacuum to further facilitate the removal of oxygen. Oxygen present in the injected sample can be removed in a similar manner, but this is difficult with small sample volumes, especially if some other sample components are volatile. It has been pointed out that oxygen is retained on many chromatographic columns and that appropriate selection of the chromatographic conditions can resolve the interference. An alternative approach is the use of reverse-pulse voltammetry[166,167] in which the initial potential is such that oxygen is reduced (Figure 48). The measuring pulse is applied in the positive direction. Since oxygen is reduced irreversibly, it is not detected during the subsequent measuring pulse. Reversed-pulse polarography has been applied successfully to the detection of metals after separation on a cation-exchange column (Figure 49).

The selectivity of amperometric/voltammetric detection has been widely recognized. The potential use of three-dimensional voltammetric detection for the determination of low levels of environmentally important azo dyes is illustrated in Figure 50.

IV. POTENTIOMETRIC DETECTION

A. Principles

Potentiometry is the branch of electrochemical detection in which potential changes at an indicator electrode are measured with respect to a reference electrode, under conditions of constant current (usually zero) flow. The indicator electrode may be an ion-selective electrode (ISE), a reactive metallic electrode, or an inert electrode constructed of materials such as platinum or glassy carbon. Potentiometry has been widely applied to the determination of ionic species (particularly inorganic anions) in aqueous solution, generally through the use of ISEs, and for a number of years represented the most attractive approach to this analysis.

This period saw intensive development of ISEs which resulted in improvements to their detection sensitivity and also to their selectivity. While high selectivity is essential for the analysis of solutions containing interfering species, and also for potentiometric detection in flow-injection analysis applications, the resulting response to only a limited number of solutes

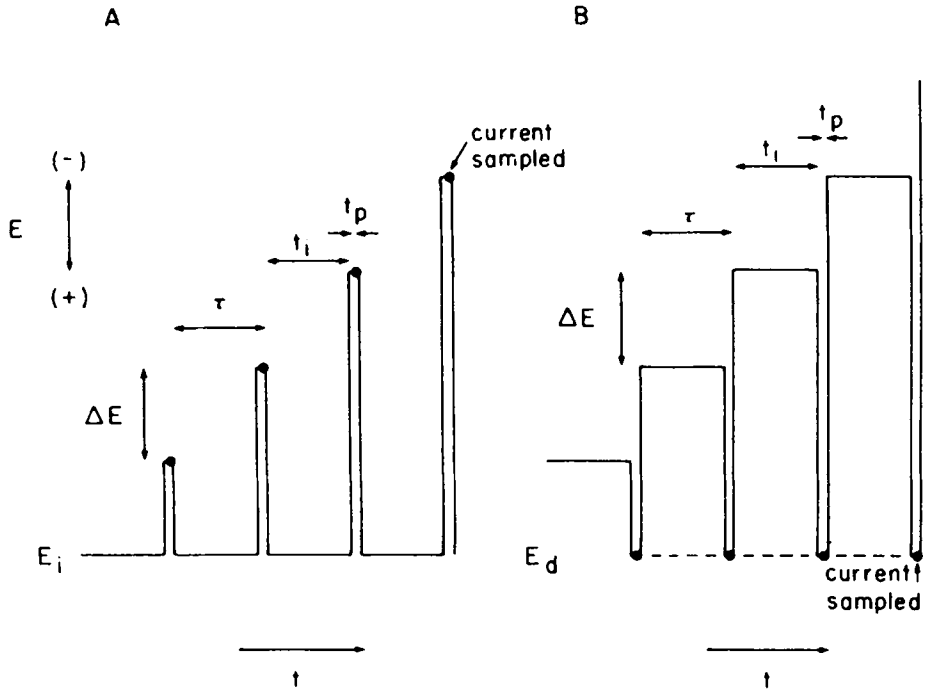


FIGURE 48. Pulse forms for reducible analytes: (A) normal pulse polarography; (B) reverse pulse polarography. (Reproduced from Hsi, T. and Johnson, D. C., *Anal. Chim. Acta*, 175, 23, 1985. With permission.)

can often represent a disadvantage when potentiometric detection is coupled with a chromatographic separation technique. In such cases, it is desirable that the detector show a more general response so that it can be applied to the detection of a wider range of solutes.

The main advantages of potentiometry conducted under conditions of zero current flow are that the indicator electrode does not participate in electrolysis reactions which could result in surface contamination of the electrode, and the ohmic resistance existing between the indicator and reference electrodes is not critical.[60] The latter factor permits the reference electrode to be placed remotely from the indicator electrode, provided that electrical contact between the two is maintained via the flowing solution. Despite these advantages, potentiometric detection has found only limited usage in IC, chiefly because of the selectivity considerations just discussed.

Further drawbacks existing with some indicator electrodes in flowing solutions are slow response and the poor baseline stability. This instability arises because the electrode potential is poorly defined under conditions where the concentration of the active solute ion is zero. It is therefore often necessary to stabilize the baseline electrode potential by addition to the mobile phase of a constant but low concentration of the active solute ion.

The response of an ion-selective indicator electrode can be expected to follow the Nernst equation:

$$E = \text{Const} + (2.303RT/nF) \log X \quad (38)$$

where E is the potential of the indicator electrode in volts; R, T, and F have their usual meanings; and X is the activity of the solute ion sensed by the electrode. The symbol n refers to the equivalents of electrons per mole of reaction (when a redox couple is involved), or the equivalents of charge per mole of analyte for a membrane electrode. When an inert indicator electrode is used to monitor a redox reaction, the same equation applies, except that X becomes the ratio of chemical activities of the oxidized to reduced forms of the redox couple. Equation

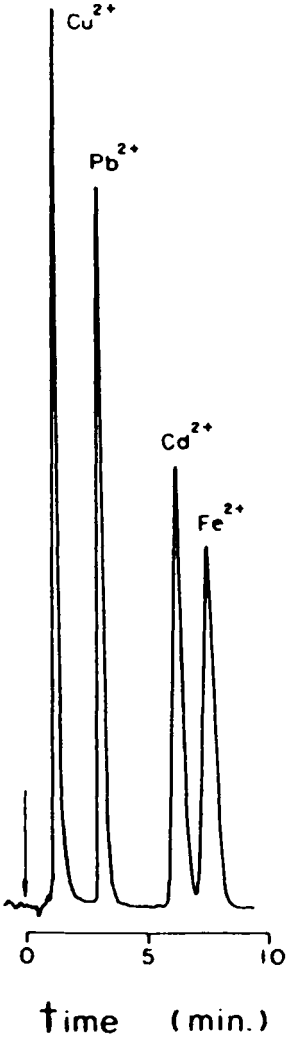


FIGURE 49. Reverse pulse polarography applied to the detection of metals. Column: Durrum DC-4A cation exchange; eluent: 0.25 *M* sodium hydrogentartrate at pH 4.0; detection potential: –0.80 V vs. SSCE; working electrode: PAR 310 mercury. (From Schultz, F. A. and Mathis, D. E., *Anal. Chem.*, 46, 2253, 1974. With permission.)

38 implies that for an ion-selective indicator electrode (which is the more common type), a logarithmic electrode response profile results as the activity of the solute ion is increased. This is often seen as a disadvantage of potentiometric detection, but as will be shown in the next section, linear response can also occur in the low concentration ranges typically encountered in chromatographic methods of analysis.

B. Instrumental Considerations

To enable potentiometric detection to be achieved, it is necessary that the indicator electrode

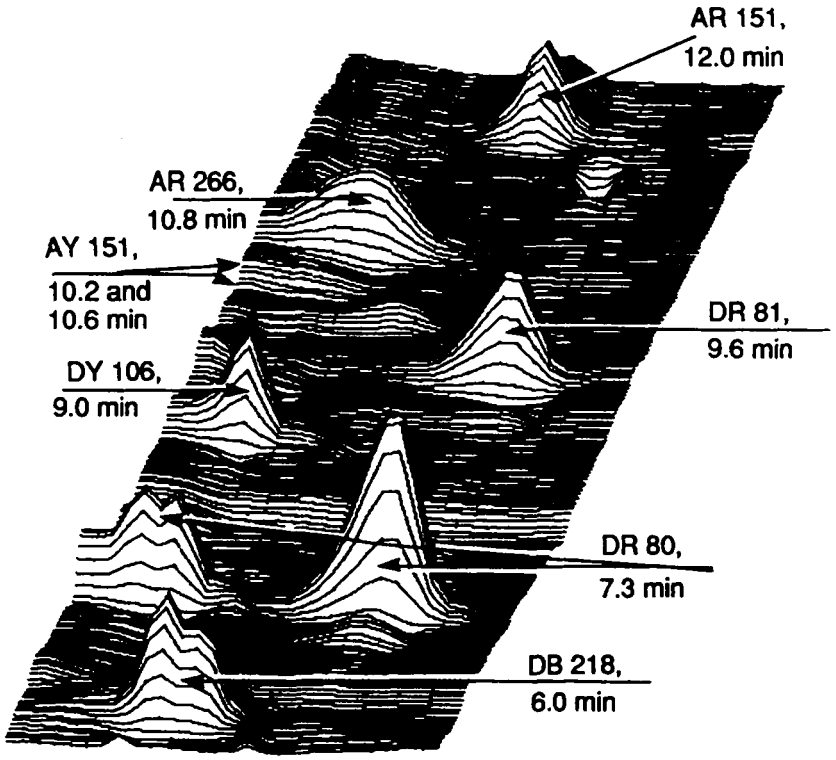


FIGURE 50. Polarographic 3-D chromatogram of a mixture of azo dyes. Abbreviations used to identify the peaks are standard and are explained in Reference 115. Column: C8 reverse phase; eluent: step-gradient from 100% pH 6.5 acetate buffer with 3 m*M* TBA perchlorate to 45% of the same buffer in methanol. The chromatogram was obtained after preconcentration of 25 ml of a sample containing 2.5 ppb AR151, 5 ppb DR81, 10 ppb AR266, 15 ppb DY106, 30 ppb DR80, and 20 ppb DB218.

(and often the reference electrode as well) be incorporated into a suitable flow-cell. For the maintenance of chromatographic efficiency, it is essential to minimize dispersion of the solute by placing the flow-cell close to the column outlet, by reducing flow turbulence in the cell, and by ensuring that the internal volume of the cell is as low as possible.

When cylindrical ISEs are used as indicator electrodes, the simplest flow-cell configuration is a flow cap designed to fit over the end of the electrode. A typical flow cap is illustrated in Figure 51A, and in the design shown, a small cavity of 5 µl volume, drilled into the inside bottom of the cap, serves as the detection chamber.[168] Most efficient operation of the electrode was achieved when the inlet stream was directed vertically onto the electrode surface and the entrapment of air bubbles was prevented when the outlet tube was oriented at 45°. When flow caps are used, the distance between the indicator and reference electrodes is generally large, and the electrical contact between the electrodes can be enhanced by inserting a platinum wire into the connecting tubing.[169] Cylindrical indicator electrodes can also be housed in a variety of alternative flow-cells, and two designs are shown in Figure 51b and c. Both cells are of very low volume (6 to 10 µl), provide for high linear flow velocities over the electrode surface to promote rapid electrode response,[170] and permit the indicator and reference electrodes to be placed in close proximity to each other.

Wire indicator electrodes are more easily accommodated into a flow-cell than cylindrical electrodes because of their smaller size, and the design of the flow-cell does not appear to exert a major influence on electrode performance. Figure 52 shows two flow-cells which are representative of published designs. The simple design in Figure 52a has a low volume (4 µl)

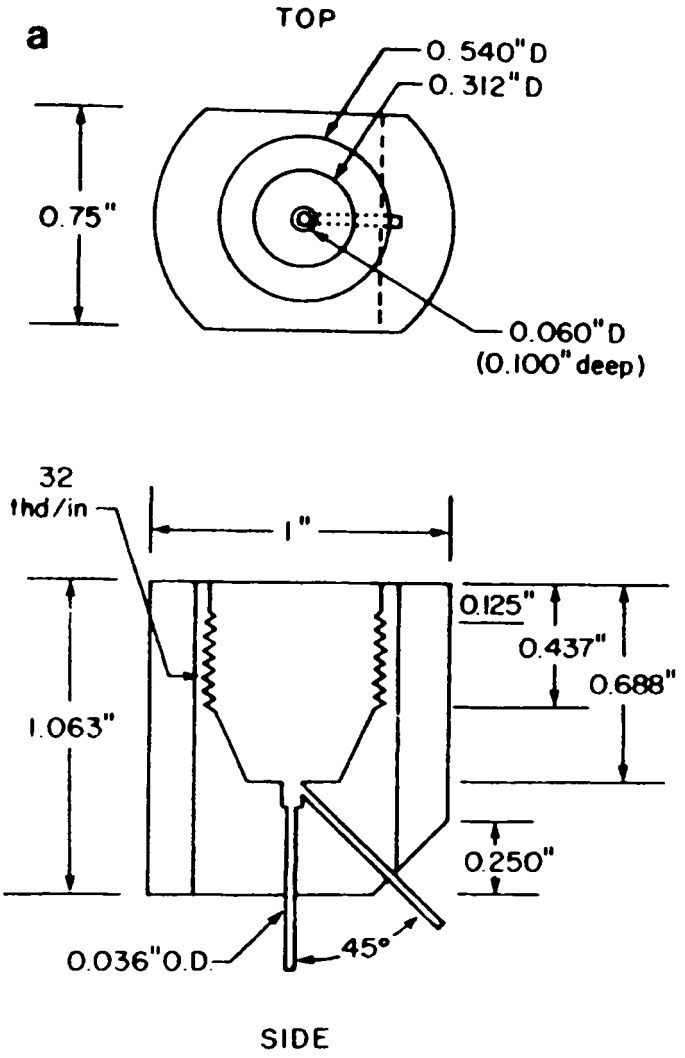


FIGURE 51. Typical flow-cell designs for cylindrical ISEs. (a) Flow cap; (b) and (c) electrode housing types. (Reproduced from References 168, 170, and 191. With permission.)

and permits easy removal and cleaning of the metallic copper wire indicator electrode,[171] while the flow-cell shown in Figure 52b[172] is more suited to indicator electrodes which do not require frequent treatment.

A membrane cell has been reported for potentiometric detection in IC.[173] This cell consists of an ion-exchange membrane which separates two chambers, each of which contains a reference electrode. The column effluent passes through one chamber while eluent is pumped through the second chamber. When a solute ion elutes into one chamber of the cell, and provided that the concentration of the solute is very small compared with that of the eluent, then the potential of the cell changes linearly with solute concentration.

As discussed previously, it is advantageous if a low background level of an electroactive solute is added to the eluent in order to give a stable baseline electrode potential. While this can be achieved by adding the solute ion to the eluent, this approach has a number of disadvantages. Samples with levels of the solute less than that present in the eluent will produce negative detector signals, while those with concentrations similar to this level cannot be analyzed. A

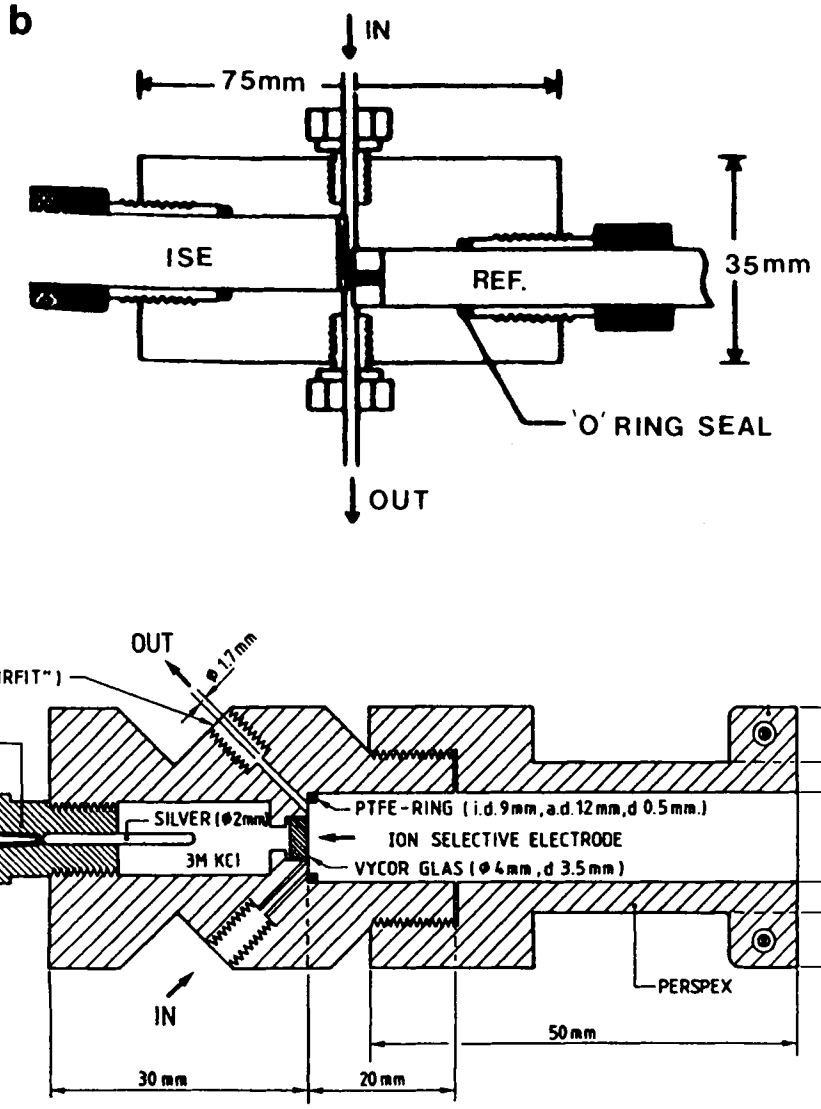


FIGURE 51 (continued)

concentric flow diffusion cell has been described[170] for the introduction of iodide ion to the effluent of an ion chromatographic column. This cell contained a length of hollow fiber dialysis tubing through which the column effluent was passed, while eluent containing 0.1 m*M* iodide was circulated around the exterior of the tubing with the aid of a peristaltic pump (Figure 53). Provided pressure fluctuations from the eluent pump were eliminated with a suitable pulse dampener, the rate of diffusion of iodide into the column effluent was constant.

C. Indicator Electrodes and Response Profiles

1. Ion-Selective Electrodes

Both solid state and membrane type ISEs have been employed as indicator electrodes in IC. The solid-state type has the advantage of rapid response in swiftly flowing streams in which the width of the diffusion layer at the electrode surface is minimal, but the selectivity is often too high for chromatographic applications. For this reason, potentiometric detection with solid-state electrodes finds most use when coupled with a more general detection method such as

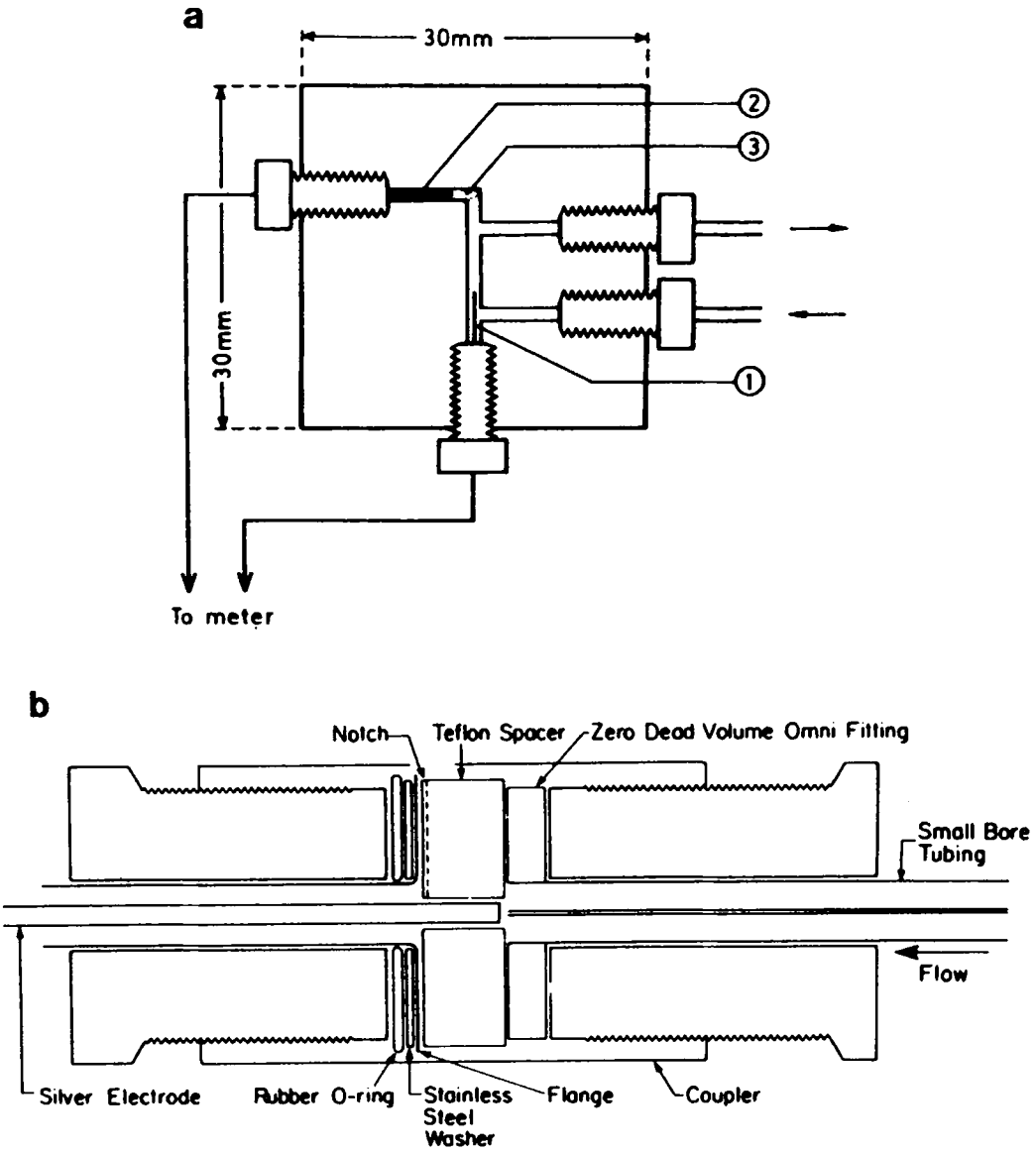


FIGURE 52. Typical flow-cell designs for wire indicator electrodes. (a) Copper wire electrode: (1) silver-silver chloride, (2) reference electode, (3) agar gel. (b) Cell for silver-silver chloride coated wire electrode. (Reproduced from References 171 and 172. With permission.)

conductivity. On the other hand, membrane electrodes are much less selective and are therefore more suited to chromatographic detection, but give slow response and show marked dependence on flow-rate. Wang et al.[174] have successfully improved the response time of a silver sulfide membrane electrode by coating the membrane surface with Nafion ion-exchange membrane, but this process adversely affected the sensitivity and linearity of the response.

Calibration plots of electrode potential vs. analyte concentration show either a linear or logarithmic relationship, depending on the concentration range studied. Under conditions where a background concentration of analyte is added to the eluent stream, detector response is usually Nernstian, according to the equation:[168]

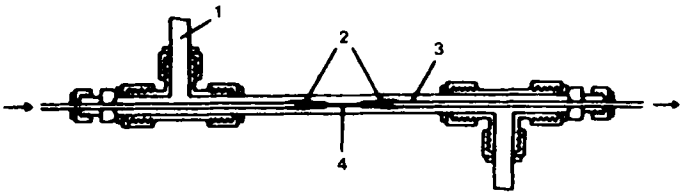


FIGURE 53. Concentric-flow diffusion cell for post-column addition of an electroactive species to the mobile phase. (1) External feed solution; (2) collars from heat-shrinkable plastic; (3) 1.6-mm O.D. polyethylene tubing transporting eluent; and (4) hollow-fiber dialysis tubing. (Reproduced from Butler, E. C. V. and Gershey, R. M., *Anal. Chim. Acta*, 164, 153, 1984. With permission.)

$$\text{moles } X^- \propto a_{X^-} = k(10^{E/0.0591} - 1) \quad (39)$$

where X^- is the analyte ion of activity a_{X^-}, k is the background concentration of analyte in the eluent, and E is the change in electrode potential observed on elution of the analyte. However, when the total analyte concentration at the electrode surface is very low, a linear relationship dependence on electrode potential may be observed.[170,175-177] That is, the detector is operating in the sub-Nernstian region.

A solid-state copper ISE has been used for the detection of non-UV-absorbing amino acids after post-column addition of 0.1 m*M* Cu(II) in acetate buffer.[169] Here, reaction with the eluted amino acids caused a reduction in the [Cu(II)] reaching the electrode and thus a change in potential, resulting in indirect detection. At low values of amino acid concentration and for high values of the stability constant for the copper-amino acid reaction, it can be shown that the potential change of the electrode is linearly proportional to the total amino acid concentration. This relationship was valid in practice provided formation of the 1:2 copper-amino acid complex was negligible.

2. Coated Wire Electrodes

Some very useful potentiometric detectors have been developed using coated wires as indicator electrodes. A simple example is a silver-silver chloride electrode prepared by treating a length of silver wire with hydrochloric acid;[176] however, any insoluble silver salt can be used as the coating material. The potential of the indicator electrode is given by:[176,178]

$$E = E^\circ_{Ag/Ag^+} + RT(\ln K_s - \ln a_{X^-}) \quad (40)$$

where K_s is the solubility product of the salt AgX used to coat the electrode and a_{X^-} is the activity of the analyte ion X^-. When the electrode is immersed in a flowing stream, a certain amount of the AgX salt dissolves from the surface, giving rise to a steady state concentration of Ag^+ and hence a stable background potential. A new potential is established if X^- is added to the flowing stream (e.g., by elution from the chromatographic column) since the concentration of free silver ions will change. The difference between the new electrode potential and the baseline value is governed by the added concentration of X^-. By analogy, low concentrations of other anions which form insoluble silver salts should also produce potential changes proportional to the concentrations in which they were added. Thus a potentiometric detector of this type should be capable of detecting a wide range of anions including halides, thiocyanate, and thiosulfate.

Lockridge et al.[172] have examined a number of coating materials such as AgCl, AgBr, AgI, Ag_3PO_4, Ag_2S, and AgSCN; when an eluent of sodium perchlorate was used, the AgCl and AgSCN-coated electrodes gave optimum response and repeatability. The coatings were produced by electrical oxidation of a silver wire in an aqueous solution of the selected anion for a period of 3 to 7 min. Electron microscopy of the coating showed a wide variation in particle size

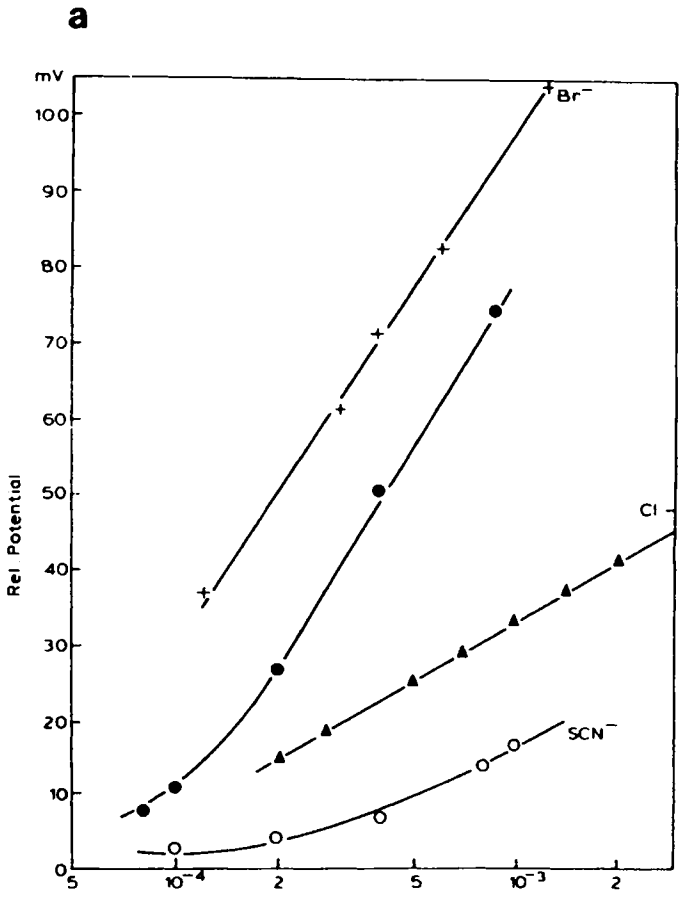
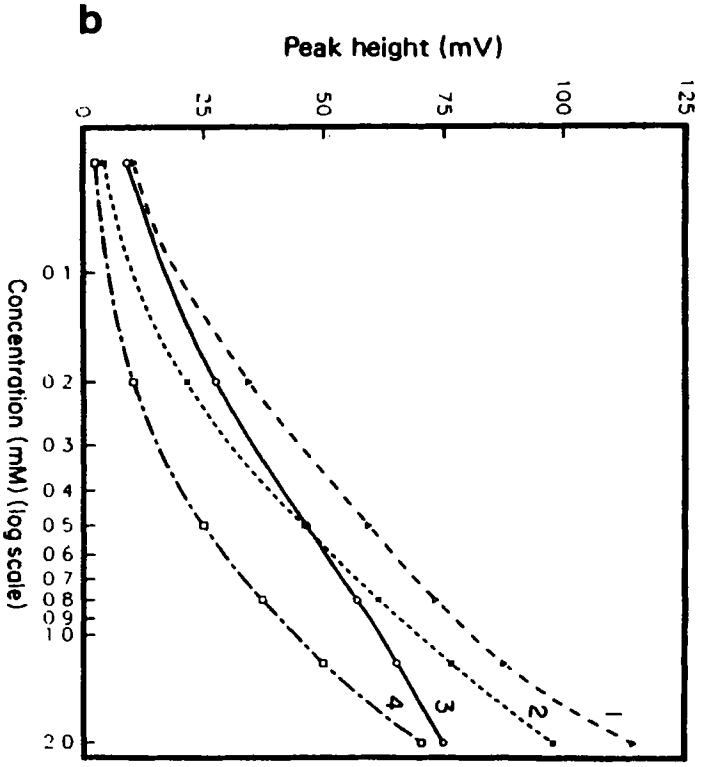


FIGURE 54. Calibration plots obtained with wire indicator electrodes. (a) Silver-silver salicylate-coated wire electrode; (b) silver-silver chloride-coated wire electrode; and (c) metallic copper electrode. (Reproduced from References 172, 178, and 186. With permission.)

for the precipitated layer, and with the exception of silver sulfide, coatings of smaller particle sizes were observed to have faster response kinetics in flowing solution. It was also found that newly prepared electrodes required conditioning by repeated immersion (and rinsing with water) in a solution containing 1 m*M* concentrations of each of the ions to be detected. When this conditioning process had been performed, the electrode surface was a composite of many silver salts covering the underlying layer of silver chloride precipitate.

The response of this type of electrode will again be dependent on the concentration of analyte injected and will also be influenced by the nature of the eluent used. Franks and Pullen,[176] when using a silver-silver chloride electrode with an acetate eluent, observed a linear relationship between electrode potential and analyte concentration for chloride in the sub-ppm range. Hershcovitz et al.[178] observed a Nernstian response with a silver-silver salicylate electrode for several anions in the 0.1- to 1-m*M* concentration range after separation with a salicylate eluent. On the other hand, Lockridge et al.[172] found the response of a silver-silver chloride electrode in a perchlorate eluent to be neither linear nor logarithmic. However, curvature of the logarithmic plot was sufficiently slight that the calibration was still useful for analytical purposes. Calibration plots obtained with coated-wire electrodes are shown in Figure 54a and b.

Potentiometric detectors based on coated-wire electrodes show peak shape dependent on the reequilibration kinetics of the precipitate film existing at the electrode surface. The response



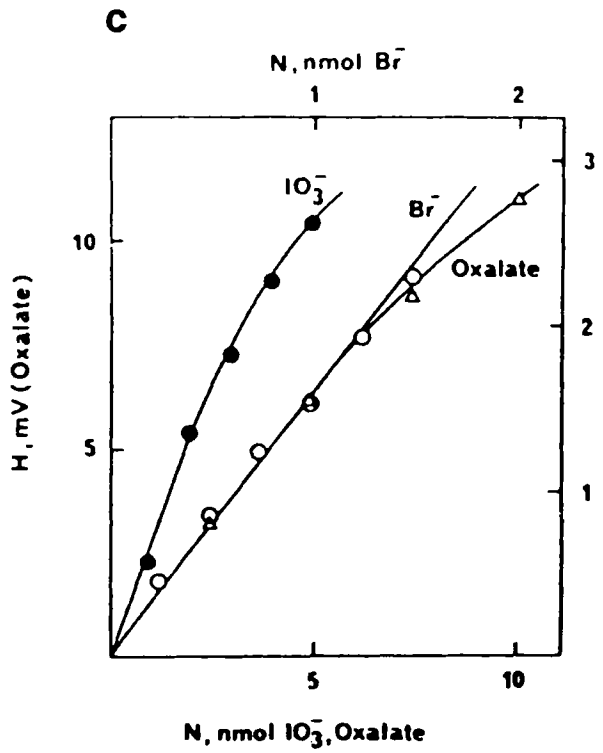


FIGURE 54 (continued)

profiles observed for these electrodes are also influenced by consumption of a small, but significant, proportion of the analyte as a necessary part of the detection process. This effect may be an explanation for the fact that response with these electrodes can vary from linear to logarithmic, with unexplained effects occurring most often at low concentration levels. Mass-transfer processes and surface kinetics therefore assume an important role for indicator electrodes which are based on insoluble silver salts, particularly when large-area electrodes are used in conjunction with microbore columns, and these factors merit further investigation.

3. Metallic Copper Elecrode

Metallic copper in the form of a wire or tube has been employed as an indicator electrode for IC and flow-injection methods.[171,179-190] When a metallic copper electrode is placed in a flowing stream of an oxygenated buffered eluent, copper ions (both cuprous and cupric) are formed at the electrode surface. Considering only the cupric ions and assuming that the buffer contains a species B which complexes Cu(II), the potential of the electrode may be described by the equation:[180]

$$E_1 = E^\circ_{Cu^{2+},Cu^\circ} + \frac{RT}{2F} \ln \frac{C_{Cu}^{II}}{\alpha_{Cu^{II}(B,OH)}} \quad (41)$$

where C_{Cu}^{II} is the total cupric ion concentation at the electrode surface and $\alpha_{Cu^{II}(B,OH)}$ is the side-reaction coefficient for the binding of cupric ions by component B and hydroxyl ion. If a copper-complexing ligand L now passes the electrode as an eluted peak, the new electrode potential is given by:

$$E_2 = E^\circ_{Cu^{2+},Cu^\circ} + \frac{RT}{2F} \ln \frac{C_{Cu}^{II}}{\alpha_{Cu^{II}(B,OH,L)}} \quad (42)$$

where

$$\alpha_{Cu^{II}(B,OH,L)} = \alpha_{Cu^{II}(B)} + \alpha_{Cu^{II}(OH)} + \alpha_{Cu^{II}(L)} - 2 \quad (43)$$

and the α values describe the side reaction coefficients for Cu(II) with the indicated components.

Under conditions where the complexation of cupric ions by the added ligand is much stronger than by the buffer component and hydroxyl ions, and a 1:1 complex is assumed between Cu(II) and L, then for constant pH and constant composition of the eluent it can be shown that the difference between E_1 and E_2 (i.e., the peak height H in volts) is given by:

$$H = \text{const} + \frac{RT}{2F} \log \frac{\beta_1 C_L}{D\alpha_{L(H)}} \quad (44)$$

where β_1 is the stability constant for the Cu(II)L complex, C_L is the total concentration of ligand L, D is the dispersion factor, and $\alpha_{L(H)}$ is the side-reaction coefficient for ligand protonation. A similar equation may be derived for complexation of the ligand with cuprous ions.

Thus, if a single stable compound (either a soluble complex or a precipitate) is formed by the solute ligand L with cuprous or cupric ions, a logarithmic relationship with Nernstian slope can be expected between the peak height H and C_L (or N, the total number of moles of solute injected). When several complexes are formed in comparable amounts, then a more complex

relationship can be predicted. Similarly, the above Nernstian relationship will not be followed for very small concentrations of injected ligand, and it can be shown that under these conditions the peak height is given by:[185]

$$H = \text{const} + \frac{RT\beta_1}{2FD\alpha_{L(H)}} N \quad (45)$$

A typical calibration plot is illustrated in Figure 54c.

Regardless of the response relationship applicable, the electrode potential is dependent on the concentration of copper ions which is, in turn, governed by a number of factors which are either constant over the period of the analysis or show variation. Factors of the former type include the oxygen content of the eluent and the flow-rate, while the chief variable factor is the changing concentration of the solute species. Several detection modes are possible and are summarized here:

1. If the eluted solute forms a *more* stable complex with copper ions than does the eluent ion, a local decrease in copper ion concentration will occur at the electrode surface, leading to a decrease in the electrode potential.
2. If the eluted solute forms a *less* stable complex with copper ions than does the eluent ion, a local increase in the copper ion concentration will occur at the electrode surface, leading to an increase in the electrode potential. This process assumes that an ion-exchange separation is being employed, so that solute ions replace an equivalent number of eluent ions in the mobile phase at the time of elution.
3. If the eluted solutes are strong oxidants and are able to oxidize the surface of the metallic copper electrode, a local increase in copper ion concentration will occur and the electrode potential will increase. Reducing solutes can also be detected by the reduction of cupric ions to cuprous and this will also result in an increase of the electrode potential due to the higher standard electrode potential of the Cu^+/Cu° couple (+0.520 V) compared with the Cu^{2+}/Cu° couple (+0.337 V).

A potentiometric detector employing a metallic copper indicator electrode can therefore function in a direct mode, wherein only copper-complexing ions are detected, or in an indirect mode in which only the eluent needs to show copper complexation properties. In addition, the direction of the measured peak can be used as a further means of identification of the eluted solute. This type of detector is the most widely applicable potentiometric detector in IC and is influenced by analyte consumption or surface kinetic effects to a lesser degree than other indicator electrodes, such as those based on insoluble silver salts.

D. Applications

One of the more commonly encountered applications of potentiometric detection in IC involves the use of a solid-state electrode for the detection of fluoride. This species elutes early in a chromatogram in which common anions such as halides, nitrite, nitrate, phosphate, and sulfate are separated. In many cases, it is difficult to discern the fluoride peak from the solvent front eluting at the column void volume and this provides strong justification for coupling potentiometric detection for fluoride with a general purpose detection mode such as conductivity.[191,192] Use of an iodide ISE for the analysis of iodide in seawater has also been reported.[170]

Chromatographic problems are encountered with the conductometric detection of anions of weak acids because these species are weakly retained unless the eluent pH is high, and they become partially or fully protonated after passage through the suppressor column. For these reasons, potentiometric detection is attractive, and the use of a silver sulfide membrane electrode

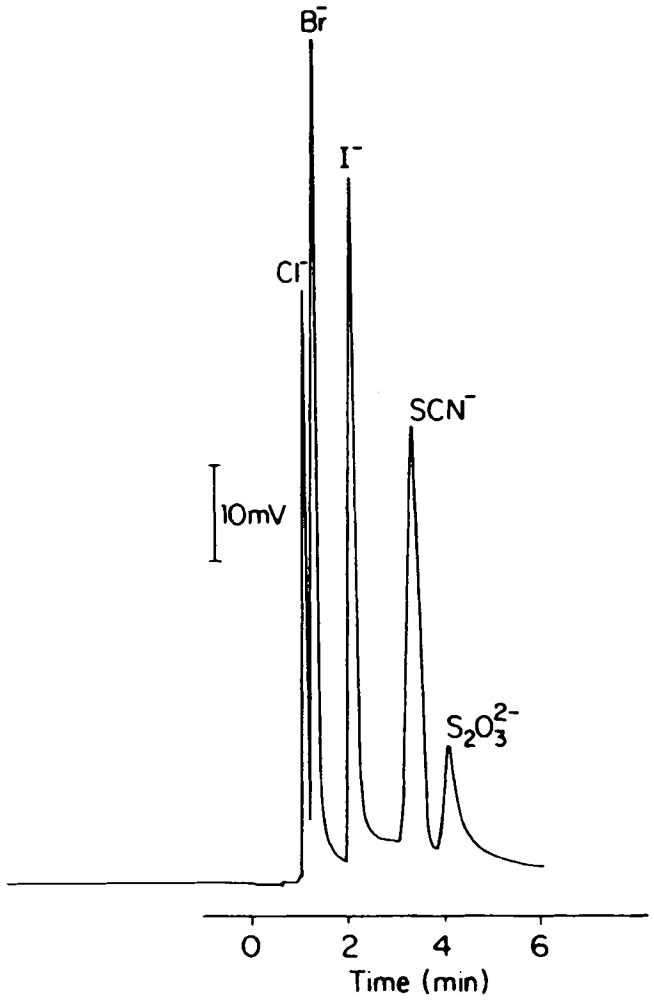


FIGURE 55. Gradient elution with potentiometric detection using a silver-silver chloride-coated wire indicator electrode. Eluent: 3.5 to 10.0 m*M* sodium perchlorate at 1.6 ml/min; injection volume, 20 µl; analyte concentrations, 1.0 m*M*. (Reproduced from Lockridge, J. E., Fortier, N. E., Schmuckler, G., and Fritz, J. S., *Anal. Chim. Acta*, 192, 41, 1987. With permission.)

has been reported for the detection of cyanide and sulfide.[174] Bromide, iodide, and thiocyanate did not present an interference, provided chromatographic conditions were chosen so that these ions did not co-elute with the analyte ions. A glass membrane electrode has been employed for the detection of carboxylic acids after ion-exchange separation,[193] and a liquid-membrane electrode of low selectivity has been successfully used for the analysis of nitrate and nitrite ions, as well as phthalate isomers.[168] Suzuki et al.[194] have described a homemade PVC matrix membrane electrode for the detection of monovalent cations. The polymer coating contained small quantities of active ligands such as valinomycin. A calcium liquid-membrane ISE has been applied to the determination of calcium using measurements of conductance rather than potential.[195] An instrument using the bipolar pulse method was employed for conductance measurements, and while the sensitivty of the electrode under these conditions was similar to that obtained when the electrode was operated in the potentiometric mode, the electrode response time was dramatically shorter for the conductance mode. The times required for the

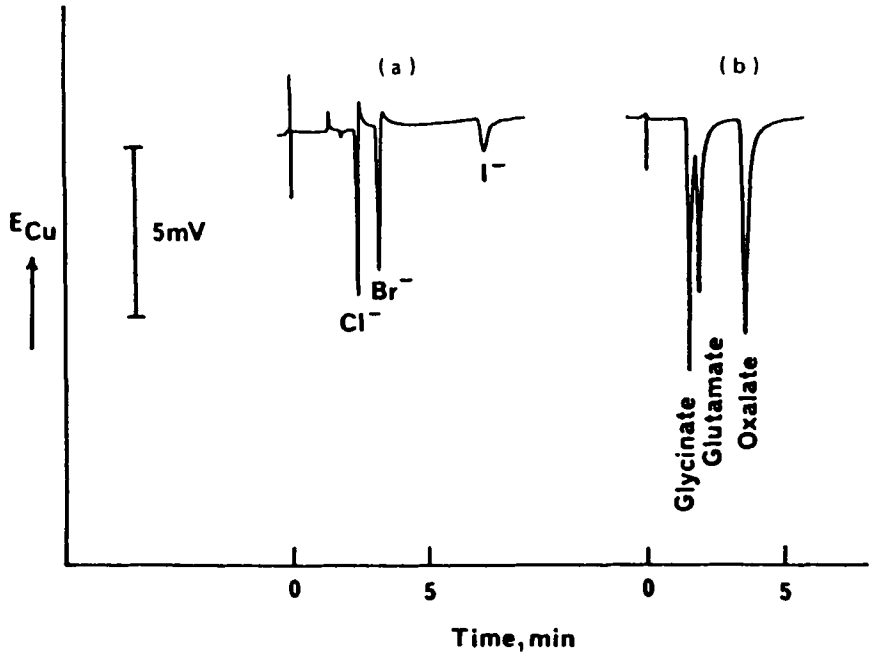


FIGURE 56. Chromatogram of species exhibiting direct response with a metallic copper electrode. Column: Vydac 302 IC 4.6; eluent: (a) 1 m*M* sodium tartrate at pH 3.2; (b) 1 m*M* potassium orthophosphate at pH 7. Injected amounts: (a) 0.5 to 50 nmol; (b) 5 nmol of each species. (Reproduced from Alexander, P. W., Haddad, P. R., and Trojanowicz, M., *Chromatographia*, 20, 179, 1985. With permission.)

electrode to reach 90% of total response were 10 ms and 4 to 5 s for the conductance and potentiometric modes, respectively. It is therefore likely that conductance measurements using ISEs could find wider application to ion chromatographic analysis.

Silver wire electrodes coated with insoluble silver salts have been applied to the detection of halide and pseudohalide (thiocyanate and thiosulfate) ions. A silver salicylate coating coupled with the use of salicylate ion for the ion-exchange separation has been suggested to provide a stable baseline potential,[178] whereas other authors[172,176] have found that a silver chloride coating is suitable when the eluent used does not form an insoluble silver salt. Under the latter conditions, the baseline potential of the electrode is not dependent on eluent concentration and this leads to the possibility of gradient elution with potentiometric detection. Figure 55 shows a chromatogram obtained using a silver-silver chloride indicator electrode with a linear concentration gradient of sodium perchlorate in the eluent.

A metallic copper indicator electrode housed in the flow-cell shown in Figure 52a has been widely applied in IC. Direct detection of copper-complexing solutes eluted with weakly complexing eluent ions has been reported for carboxylic acids, halides, and amino acids using eluents such as tartrate, phosphate, and phthalate, in both ion-exchange and ion-exclusion separation systems (Figure 56). Similarly, direct detection of oxidizing anions (iodate, bromate, and chlorate) and reducing species (ascorbic acid, hydrazine, and hydroxylamine) has been achieved (Figure 57). The high degree of selectivity offered by direct detection has proven to be advantageous in the determination of oxalate in urine where differentiation of oxalate from closely eluting excess sulfate is required. Use of the potentiometric detector enabled sample preparation to be confined to simple dilution and no interference from sulfate was observed.[189]

Indirect detection with a metallic copper indicator electrode has been applied to inorganic anions and some weakly complexing carboxylic acids (Figure 58), as well as alkaline earth and transition metal ions, provided that the eluent used for the ion-exchange separation showed appreciable copper complexation ability. Thus nitrite, nitrate, and sulfate are detectable in a

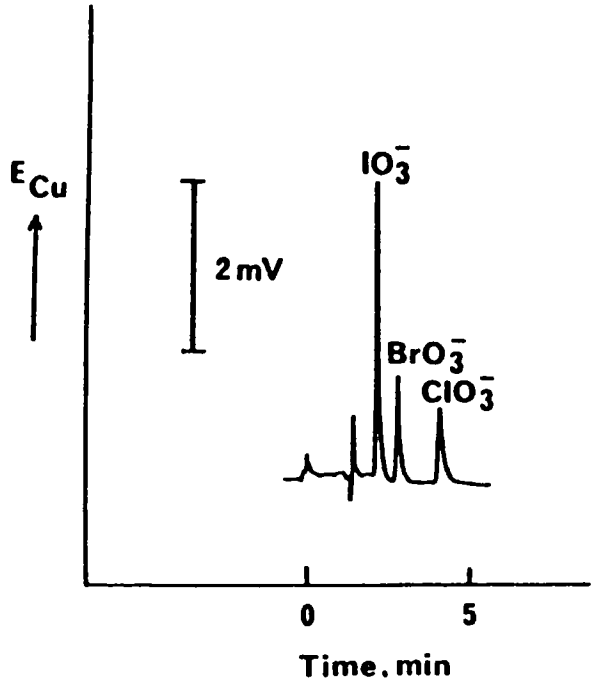


FIGURE 57. Chromatogram of oxidizing anions detected at a metallic copper electrode. Column: Vydac 302 IC 4.6; eluent: 20 m*M* sodium tartrate at pH 3.2; injected amounts: 1 to 100 nmol. (Reproduced from Alexander, P. W., Haddad, P. R., and Trojanowicz, M., *Chromatographia*, 20, 179, 1985. With permission.)

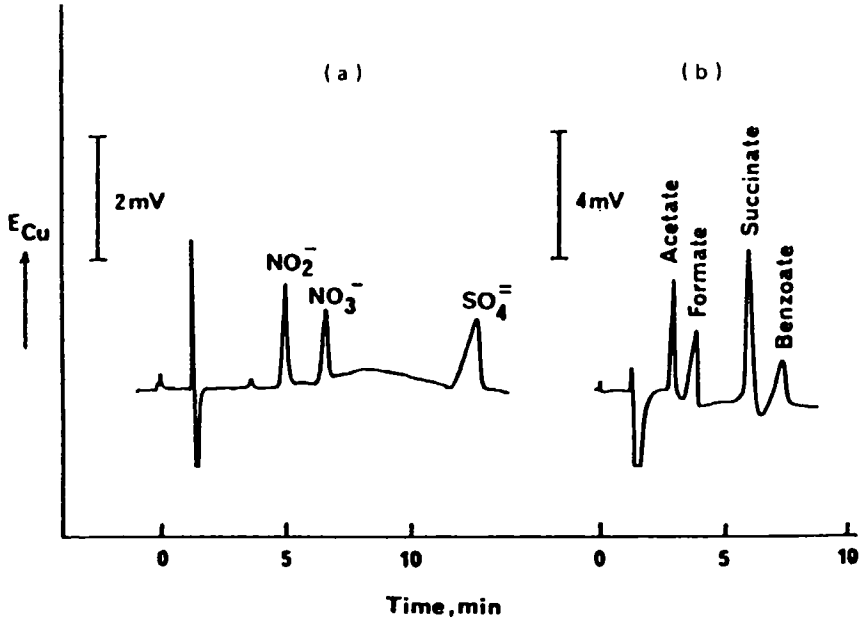


FIGURE 58. Chromatograms of inorganic and organic anions exhibiting indirect potentiometric response with a metallic copper electrode. Column: Vydac 302 IC 4.6; eluent: 2 m*M* potassium phthalate at pH 4.6 (a) or 4 (b); injected amounts: (a) 60 to 120 nmol and (b) 250 nmol of each species. (Reproduced from Alexander, P. W., Haddad, P. R., and Trojanowicz, M., *Chromatographia*, 20, 179, 1985. With permission.)

Table 6
APPLICATIONS OF POTENTIOMETRIC DETECTION IN ION CHROMATOGRAPHY

Indicator electrode	Separation mode	Species separated	Ref.
Nitrate-ISE	Ion-exchange	Nitrate, nitrite	168
Copper-ISE	Reversed-phase	Amino acids, diamines	169
Iodide-ISE	Ion-exchange	Iodide	170
Ag-AgCl	Ion-exchange	Halides, thiocyanate, thiosulfate	172
Nonselective membrane cell	Ion-exchange, ion-interaction	Sodium, lithium, fluoride, phosphate, acetate, sulfate	173
Ag_2S-ISE	Ion-exchange	Cyanide, sulfide	174
Ag-AgCl	Ion-exchange	Halides	176
Ag-Ag salicylate	Ion-exchange	Halides, thiocyanate	178
Metallic copper	Reversed-phase	Amino acids	179
Metallic copper	Ion-exchange	Alkaline earth ions	181
Metallic copper	Ion-exchange	Carboxylic acids	182
Metallic copper	Ion-exchange	Inorganic anions, iodate, bromate, chlorate	183
Metallic copper	Ion-exchange	Transition metal ions	185, 187
Metallic copper	Ion-exchange	Ascorbic acid, hydrazine, hydroxylamine	188
Metallic copper	Ion-exchange	Oxalate	189
Metallic copper	Ion-exclusion	Carboxylic acids	189
Metallic copper	Ion-exchange	Reducing carbohydrates	190
Fluorid -ISE	Ion-exchange	Fluoride	191, 192
Hg_2Br_2-ISE	Ion-exchange	Bromide	192
H^+-glass	Ion-exchange	Carboxylic acids	193
PVC matrix membrane electrode	Ion-exchange	Monovalent cations	194

phtahlate eluent, and alkaline earth and transition metal ions are detectable in an eluent comprising ethylenediamine and a complexing agent such as tartrate, citrate, or oxalate. Post-column addition of Cu(II) has been employed for the indirect potentiometric detection of reducing carbohydrates, using a metallic copper electrode and ion-exchange separation.[190] The ubiquitous complexation characteristics of copper enable a wide range of eluents to be used with the indirect detection mode, which suggests that this form of detection could be applied to almost any ion which can be separated by IC.

Table 6 summarizes the published applications of potentiometric detection in IC.

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