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ELECTROCHEMICAL DETECTION IN LIQUID FLOW ANALYTICAL TECHNIQUES: CHARACTERIZATION AND CLASSIFICATION

(IUPAC Technical Report)

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Electrochemical detection in liquid flow analytical techniques: Characterization and classification

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Abstract: Liquid flow analytical techniques are classified, and definitions are provided of flow-injection analysis, segmented flow analysis, flow titration, continuous monitoring, liquid chromatography, and capillary electrophoresis. Electrochemical detection and flow-through detection cells are characterized with respect to the surface and bulk detection. The detector performance is discussed in terms of its principal analytical parameters, such as detection limit and dynamic concentration range, as well as its dynamic characteristics, such as the response time, sampling frequency, transport lag, and long-term stability. Moreover, different detection modes are critically evaluated, including both potentiostatic and galvanostatic techniques. Factors influencing sensitivity and detection limit, which include electronic and hydrodynamic approach, are also discussed. Different detector designs are critically reviewed, and the special features of electrochemical detectors for flow analytical techniques are emphasized.

CONTENTS

1.   INTRODUCTION

Recent decades have witnessed an extensive development of automation in chemical analysis. This automation was stimulated by the need for rapid analysis of increased numbers of analyte samples in clinical, pharmaceutical, and environmental chemistry, and by the demand for the continuous monitoring of different analytes in industrial processes [1] and the natural environment. A significant part of these modern approaches of automated chemical analysis is based on liquid flow analytical techniques operating under hydrodynamically controlled conditions. These techniques comprise those involving separation, for instance, liquid chromatography (LC) or electromigration techniques, or those carried out without separation, like flow analysis (FA). In the latest stage of this development, the automated flow analytical systems are being miniaturized and both FA and separation techniques are becoming integrated with microfabricated sensors to reduce the necessary sample size, analysis time, and reagent consumption [2–4].

Various types of detection modes are applied to flow analytical techniques [5], and electrochemical detection is one that is most commonly used. Microfabrication technologies make the integration of handling microliter volumes of liquid and electrochemical detection especially advantageous. Thanks to the inherent features of electroanalytical techniques, and the versatility of the detector design, electrochemical detection meets most of the requirements of flow analysis. The high sensitivity and wide linear dynamic concentration range of electrochemical detectors is often incidental to superb selectivity. In principle, the flow analytical manifold (the layout of the flow analytical technique) is simplified if a highly selective electrochemical detection mode is applied. Flow analytical techniques involving in-flow separation (e.g., LC [6–8], capillary electrophoresis [9,10], microdialysis [11], etc.), chemical transformation, and/or preconcentration [12] remain, however, important because of the limitations of electrochemical detection and because there is only a limited number of selective detectors of sufficient sensitivity.

Since the early 1970s, a large number of papers has been published on different liquid flow analytical techniques [5,13,14]. The flow analysis database on the World Wide Web [15,16] (<http://www.FIA.unf.com> and <http://www.flowinjection.com/>) lists more than 10 000 references. In 1994, IUPAC classified the analytical methods based on flowing media and defined flow analytical systems, component parts, and terms for describing their performance [17]. Then, fundamentals of analytical aspects of chemical process control were discussed in 1999 [18] and information essential for characterizing a flow-based analytical system has been provided in 2002 [19]. The aim of the present report is to extend the existing, recommended, and consistent terminology to electrochemical detection and detectors used in flow analytical techniques with a brief critical overview of the currently used electrochemical flow-through detectors.

2.   CLASSIFICATION OF LIQUID FLOW ANALYTICAL TECHNIQUES

In flow analytical techniques, a liquid analyte sample, or an aliquot of it, is moved by the flowing stream from the place of sampling to the waste (or back to the sampling area in case of recirculation) through the spatially separated stages of the analysis process. Flow analytical techniques involve dispersion, i.e., the broadening of a discrete analyte zone during its travel through the flow-through system. The detection of the analyte is accomplished under hydrodynamically controlled flow conditions. The present report is built on the IUPAC report on the "Classification and definition of analytical methods based on flowing media" [17].

2.1   Flow analysis

Flow analysis (FA) is recommended in refs. [20] (the "Orange Book", Chap. 7.2) and [21] as the generic name for all analytical techniques that are based on the introduction, processing, and detection

of liquid samples in flowing media. The sample processing may involve sample transport, in-flow separation, chemical reaction, heat treatment, etc., under diffusion and/or convection dispersion conditions. Therefore, the term *flow analysis* may be considered as an equivalent to *controlled dispersion analysis*. *Flow analysis* modes are classified according to (i) the basic character of the flow, which is either continuous or segmented and (ii) the method of sample introduction, which can be continuous or intermittent.

2.2   Segmented flow analysis

The term *continuous flow analysis* (CFA) was introduced by Skeggs [22,23] for the air-segmented flow analysis, and the CFA acronym has been widely accepted ever since. However, the terms *segmented flow analysis* (SFA) and *segmented flow analysis with sample aspiration* (SFASA) have also been used. In the present report, the term *segmented flow analysis* (SFA) is recommended because it clearly identifies the method among the other FA methods and unambiguously defines the basic character of the flow.

The features of segmented flow analysis are:

(i)   The liquid stream is segmented by bubbles of air or another gas with the aim of separating subsequent samples and avoiding the broadening of the discrete analyte zones (i.e., sample dispersion). It helps to maintain stable flow conditions, suppresses the sample carryover, and facilitates the mixing of sample with reactants in liquid segments.

(ii)   The sample is introduced by aspiration into the carrier liquid stream.
   •   Chemical reaction of an analyte in the sample is often facilitated by mixing the sample with a reactant to produce a derivative suitable for detection.
   •   Spectrophotometric and electrochemical detection are most frequently used.
   •   Generally, a steady-state signal is used for determination of the analyte concentration. The precision and accuracy of the steady-state methods are much less sensitive to fluctuations in the recorded signal compared to those where the quantitative evaluation is based on a transient value.

2.3   Flow-injection analysis

Flow-injection analysis (FIA) implies a nonsegmented FA in which the liquid analyte and/or reagent is injected into a nonsegmented flowing stream of inert or reacting carrier solution (often called carrier solution) and the analyte, reagent, or a chemical reaction product is detected downstream [24–30]. Injection means forming a well-defined zone of the analyte or reagent sample within the analyzer channel, where the zone disperses in a controlled manner on its way toward and through the detection cell. For injecting a small volume of the sample as a narrow plug, mechanical injection valves (rotary valves and, in the early history of FIA, syringes) or hydrodynamic injection techniques are utilized. Both can be made as volume- or time-based injections or a combination of the two. The concentration profile of the analytes entering the detection cell (i.e., the dispersion of the detected species) depends upon the mode of the sample introduction, the flow parameters, and the geometry of the FIA channel situated between the sampling point and the detection site (often called the reaction or dilution section). Therefore, a symmetric or asymmetric peak-shaped transient signal (rather than a steady-state plateau) is obtained as the detection signal. The extent of sample dispersion determines the analysis frequency (or throughput), i.e., the number of analyses per time unit.

2.4   Flow titration

Flow titration (FT) is an FA technique in which a reagent solution (i.e., the titrant) is added to the carrier solution containing the analyte sample according to a predetermined reagent concentration (mass

flow) vs. time program. The reagent addition can be executed intermittently or continuously using volumetric methods, controlled dispersion, or in situ reagent generation (e.g., by coulometry) [31–35]. The course of the titration is followed with flow-through detection cells situated downstream in the flow system. One or two complete titration curves are recorded in a single experiment, and the location of the equivalence point or pair of equivalence points is used for the quantitative evaluation depending on the program of reagent generation.

2.5 Continuous monitoring

Continuous monitoring (CM) is an FA technique in which continuous sampling and sample processing is carried out in a nonsegmented liquid flow with or without continuous reagent addition. Laboratory and industrial process monitors belong in this group. The SFA, FIA, and FT techniques are also widely used in the process analytical chemistry. A basic difference between CM and the group of techniques utilized for analyzing discrete samples (SFA, FIA, and FT) consists in that SFA, FIA, and FT mimics automated batch analyses. Consequently, a separate time scale must be adopted for each sample, with $t = 0$, defined by the sample injection, which is especially important in kinetic analyses.

2.6 Liquid chromatography

Liquid chromatography (LC) is a primary analytical separation technique, which implies mainly column liquid chromatography [36]. In LC, the sample is injected into a mobile liquid phase, which is fed to a column packed with a stationary phase. The sample components are separated on the basis of differences in their distribution between stationary and mobile phase. All liquid chromatography techniques, including the *high-performance liquid chromatography* (HPLC) technique, operate under hydrodynamically controlled conditions. In LC, the analyte dispersion arises primarily from the processes occurring in the column, i.e., (i) slow distribution of the analyte between the mobile and the stationary phase, (ii) convection of the analyte due to local turbulences of the tortuous liquid flow paths through the stationary phase, and (iii) axial diffusion. In this respect, LC is basically different from FA where dispersion is determined by the geometry of the flow channel and flow velocity. LC is designed for separation of the sample components. To attain the highest possible resolution of the component zones, the dispersion in all parts of the LC apparatus should be suppressed as much as possible.

2.7 Capillary electrophoresis or capillary zone electrophoresis

Capillary electrophoresis (CE) or capillary zone electrophoresis (CZE) separates charged analytes on the basis of differences in their migration speeds in an electric field. From the point of view of the detection, the main difference from LC are a much flatter speed profile, governed by the electroosmotic flow, in the running electrolyte and the effect of the strong electrostatic field on electrochemical measurements which impose special demands with respect to the placement of the voltammetric electrodes.

3. ELECTROCHEMICAL DETECTION UNDER FLOW-THROUGH CONDITIONS

3.1 Characteristics of electrochemical detection and detectors

A flow-through electrochemical detector consists of a detection cell and the electronic circuitry required for the cell operation and for monitoring, recording, and processing the detector signal. The detector signal depends on the electroanalytical technique selected for detection.

The *flow-through detection cell* monitors the concentration (mass)-time profile of the analyte in the FA system. There are several types of flow-through detection cells. Each type is characterized by parameters such as the length, diameter, and shape of its detection channel, which determine the char-

acter of the liquid flow under the given experimental conditions (laminar or turbulent, as described by the Reynolds number) and the predominant mode of the mass transport within the cell (diffusional or convectional, as described by the Péclet number). More detailed discussion is provided, e.g., in [37]. All these parameters then describe the detection cell contribution to the overall dispersion of the zones of samples.

In FA systems, the detection cell is located at a distance (L) downstream from the sampling point. Depending on how the detector is probing the dispersed sample zone, the detection cell measures the average concentration, C_{av}, over the detection channel cross-section, or the local concentration, C_L, at the surface of the sensing probe. The sensing probe can be located at the detection channel wall or in its center [37]. Since practical detection cells have a finite length in the direction of the flow, they may average the concentration over a certain length of the channel.

There are two kinds of cross-sectional average concentrations, namely, the cross-sectional mean concentration, C_m, and the bulk concentration, C_b, which are defined as:

$$C_m = \frac{\int_q C_L dq}{\int_q dq} = \frac{\int_q C_L dq}{q} \tag{1}$$

and

$$C_b = \frac{\int_q u C_L \, dq}{\int_q u \, dq} = \frac{\int_q u C_L \, dq}{F_m} \tag{2}$$

where:

q is the cross-section of the detection channel,
u is the local linear liquid speed,
F_m is the volume flow rate, and
C_L is the local analyte concentration at distance L.

The mean concentration, C_m, corresponds to the local concentration averaged over the detection channel cross-section, whereas the bulk concentration, C_b, is the cross-sectional average concentration weighted by the local speed. (C_b is proportional to the flux of solute across the detection section per time unit). If there is no cross-sectional change in the concentration then, obviously, the local and mean concentrations are equal. Noticeably, the integral in the numerator of eq. 2 is equal to the rate at which the analyte is passing through the detection channel, in mole per second.

In practical FIA systems, it is extremely important that the cross-sectional variations in the analyte concentration, C, can effectively be minimized. In this respect, the design of the tube, most notably the coiling of the flow line, the disruption of the flow pattern at the entrance of the detection cell, the connectors (fittings), and sharp bends are of utmost importance. However, if cross-sectional inhomogenities of concentrations are not eliminated at the detection cell entrance, commonly used detectors will measure different concentration averages.

A surface detector, i.e., *a local, point,* or *non-integrating detector*, is a detector with which a local concentration in close proximity of the detector's sensing surface is measured. For successful operation of the local concentration detection cell, radial distribution of the analyte must be reproducible and rigorously described.

A bulk concentration detector, i.e., an *average-concentration (mean value)* or *integrating detector*, is a detector which measures the cross-sectional average concentration weighted with the local velocity, i.e., the average concentration in the whole volume of the detection cell (channel).

Comment: Bulk concentration detection cells usually contribute much more to the overall sample dispersion than local concentration or cross-sectional average detection cells and, therefore, they are recommended to be placed last in the sequence of detection cells if several detection cells are utilized in series.

The bulk concentration of the analyte, C_b, i.e., a ratio of the number of moles of a solute to the volume of the carrier solution, can be measured, for example, by cutting the experimental flow channel at a distance $l = L$ and analyzing aliquots of the solution collected in sampling cups. This measurement process led to an alternative name of the bulk concentration: the *cup mixed value* whose usage is archaic and, therefore, discouraged.

Most electrochemical detectors, such as amperometric and potentiometric detectors, are surface detectors. A coulometric detector with a porous working electrode, being a bulk concentration detector, is an exception. Successful operation of a surface detector requires reproducible radial concentration distribution. Therefore, the mixing block design of the flow manifold must ensure effective and reproducible radial mixing. In addition, a proper detector channel design must warrant the effective transport of electroactive species to the electrode surface for successful application of these detectors in flow analysis.

With electrochemical detectors, the detection signal may originate from:

- a cumulative property of the flowing liquid (solution), which is determined by the overall composition of the solution, e.g., conductivity, high-frequency impedance, permittivity (measurement of bulk property), or
- a specific property of the flowing liquid, related to the activity or concentration of a particular component in the flowing liquid, e.g., the potential of an ion-selective electrode, ISE, or the electrolytic current flowing through an amperometric working electrode (measurement of a selective property of the system).

The design of the flow-through detection cell influences the overall performance characteristics of the detector. The detection cell design is a part of the optimization of the FA system for a given analytical problem [38]. The possible goals of the optimization are: (i) high sample throughput, (ii) small sample volumes and low reagent consumption, (iii) high precision and accuracy, (iv) high sensitivity and low detection limit (little dilution), (v) low equipment and operational costs, etc. In LC and CE detection, the primary goal is minimization of the detector contribution to the analyte zone dispersion. It is always important to clearly determine the relative importance of the optimization goals because all these goals are difficult to attain simultaneously. However, there are some essential parameters both for the flow-through detection cell design and operation, which should be considered in all FA applications:

- effective volume of the detection channel (for LC, it should not be larger than one-tenth of the peak volume, as determined by the peak variance analysis),
- response time of the working or indicator electrode or the detection cell,
- well-defined hydrodynamic conditions, and
- user friendliness (versatility and simple handling).

Additional requirements may arise with regard to the generation of the detection signal, e.g., the need to use a special electrode material for the desired sensitivity, reproducibility and/or selectivity, suppressed passivation phenomena, etc.

3.2   Characteristics of the detector performance

Electrochemical detectors used for flow analytical techniques are characterized by the following operational parameters.

3.2.1 Principal analytical parameters

3.2.1.1 Sensitivity

Sensitivity (S) is defined as the change in the detector signal (ΔR) divided by the change of analyte concentration (ΔC) or mass (Δm). ΔR is the difference between the observed steady-state (R_{ss}) or transient (R_t) signal and the background (R_{bg}) signal when the analyte concentration in the cell changes by ΔC ($\Delta R = R_{ss} - R_{bg}$ or $\Delta R = R_t - R_{bg}$). The sensitivity is obtained from the slope of the linear part of the calibration plot.

For linear sensors:

$$S = \frac{\Delta R}{\Delta C} \text{ or } S = \frac{\Delta R}{\Delta m} \qquad\qquad (3)$$

while for logarithmic sensors:

$$S = \frac{\Delta R}{\Delta \lg C} \qquad\qquad (4)$$

Comment: The measured response of a detector contains the detector response to the analyte and, generally to a lesser extent, to the other components of the flowing carrier solution. The analyte concentration independent part of the detector response signal is called the background signal (R_{bg}) or, in flowing systems, the baseline signal. The background signal value is measured in the absence of the analyte. It does not contain chemical information on the analyte, and it is subtracted from the detector response signal measured in the presence of the analyte. Noise is a random fluctuation in both the detector and background signal due to external events. It is inherent in the combination of instrument and method.

Major components of the background (or baseline) signal are as follows:

- detector response to electrochemically active impurities in the carrier solution (in the flowing liquid)
- high-frequency noise, primarily line noise
- low-frequency noise with frequencies similar to the variations in the detection signal
- spikes (random pulses of the measured quantity) caused by, e.g., signals related to air bubbles in the flow channel, fluctuation of the power voltage, or electrostatic discharge
- drift (slow, non-random, one-directional changes in the detector signal with time in a carrier solution of constant composition); it is determined as the slope of the base line signal vs. time. Temperature changes can be a cause of drift.

3.2.1.2 Limit of detection

Limit of detection (LOD) or *minimum detectable value*, in agreement with general definitions in refs. [20] (Orange Book, Chaps. 2.4, 8.3.2.1, 12.4.1, and 18.4.3.7) and [21], is expressed in electrochemical detection under flow-through conditions as a concentration (C_{LOD}), or quantity (q_{LOD}) and derived from the smallest measurable net signal (R_{LOD}), that can be determined with reasonable certainty based on a statistical basis. It is defined by the analyte concentration which yields a detector signal (R_{LOD}) equal to the background signal (R_{bg}) plus a multiple (k) of the standard deviation of the blank signal, s_B:

$$R_{LOD} = R_{bg} + ks_B \qquad\qquad (5)$$

The limit of detection (limit of the determination) in concentration units is given by:

$$C_{LOD} = ks_B/S \qquad\qquad (6)$$

The multiple k depends on the adopted statistical significance level.

Below the LOD, the detector signal is independent of the analyte concentration. It is very important to avoid confusing the limit of detection of a technique with its sensitivity.

3.2.1.3 Dynamic concentration range

In accord with a similar definitions in ref. [20] (Orange Book, Chaps. 4.2., 8.3.2.1, and 9.2.4.5), *dynamic concentration range* is a concentration interval in which a change in the analyte concentration results in a change of the detector signal. If the concentration dependence of the detection signal is described as:

$$R = SC^x \tag{7}$$

the dynamic concentration range is the concentration interval for which $x \neq 0$. The *linear dynamic concentration range* is the part of the dynamic concentration range for which $x = 1$. In the linear dynamic concentration range, the intensity of the signal is directly proportional to the concentration of the species producing the signal.

The concentration dependence of the detection signal for logarithmic sensors is defined as:

$$R = constant + S \lg C \tag{8}$$

3.2.1.4 Selectivity

Selectivity of a sensor (detector) expresses quantitatively the extent of interference by substances other than the analyte. It is characterized by the *selectivity coefficient*, which defines the ability of a sensor to distinguish a particular analyte species from others (e.g., a particular ion from other ions). The selectivity coefficient and its determination is defined by IUPAC [20] (Orange Book, Chaps. 8.3.2.1 and 9.2.5.5) and selectivity coefficient data for ISEs are listed in IUPAC technical reports and textbooks [39–41].

The required selectivity of a potentiometric sensor is a function of the acceptable relative error, *P* %, in the determination of the primary ion concentration due to interference. It can be expressed as

$$K_{A,B}^{pot} = \frac{C_{A,min}}{C_{B,max}} \frac{P}{100} \tag{9}$$

where:

- $K_{A,B}^{pot}$ is the *selectivity* coefficient of the potentiometric indicator electrode for the interfering ion, B, relative to the primary ion, A;
- $C_{A,min}$ is the *lowest expected* concentration of the primary ion, A;
- $C_{B,max}$ is the *highest* expected concentration of the interfering ion, B; and
- *P* is the relative allowed error in determination of the primary ion, A, due to interference from ion, B.

The selectivity of the sensor depends on the selectivity of the signal generating reaction (i.e., the recognition element part of the sensor). Recommended methods for measuring and reporting potentiometric selectivity coefficients are presented in IUPAC documents [39–43], while for amperometric detectors selectivity is discussed in refs. [44,45].

> *Comment*: The selectivity coefficients of potentiometric ISEs can be biased by minute ionic fluxes of primary ions from the sensing membrane. Biased selectivity coefficients can be recognized by the concentration dependence of the experimentally determined selectivity coefficient values [46].

3.2.1.5 Repeatability and reproducibility

Repeatability and reproducibility are defined by the International Organization for Standardization (ISO 3534-1) [47]. The repeatability and reproducibility of flow-through electrochemical detectors are determined similarly to other sensing devices according to the IUPAC recommendations [20,39].

The *reliability* of flow-through electrochemical measurements is expressed in the same way as for any other measurements, i.e., in terms of the precision and accuracy, obtained by well-known statistical methods in accord with similar definitions in refs. [20,48].

3.2.2 Dynamic characteristics

The dynamic characteristics of flow-through detectors reflect their ability to monitor concentration variations with time. The transient response of the detector after a stepwise change in the analyte concentration can be characterized by a mathematical expression of the transient function, from which the response time is derived, corresponding to a preselected point of a detector signal vs. time curve. The **response time** is most commonly defined by the time required for the detector signal to attain a given percentage of a new, steady-state value upon a stepwise concentration change of the analyte [49]. The response time is dependent on the detection cell geometry, the flow parameters, the response mechanism of the detector electrode, and, to a smaller extent, on the time constant of its electronic circuitry, if it is designed to respond rapidly and not to smooth the signal for noise reduction. In FA systems, the large sampling frequency sensors with short response time are required. It is important to make a distinction between the response time of a sensor and a whole electrochemical cell.

3.2.2.1 Sampling frequency or sample throughput

Sampling frequency or *sample throughput* is the number of measurements in an FA system in a given period of time without any significant interference by the preceding samples. It depends on the design of the complete FA system including the applied methods, the detection cell, and the electrochemical sensor. However, the sampling frequency is not equivalent to the number of test samples that can be analyzed per unit time because, in practical analysis, regular calibration with standard samples in combination with cleaning cycles using washing solutions is essential. Moreover, it is quite usual to evaluate the results from the average of several repeated measurements [17].

3.2.2.2 Residence time

Residence time is the time of passage of the analyte through the detection channel. In practical FA systems, the type of flow is described by the residence time distribution curve, or by the mean residence time (the inflection point of the curve), which reflects the various times that each component of flowing liquid resides within the flow-through detection cell [5]. Shorter residence times are advantageous because they diminish undesired merging of signals from closely spaced analyte zones. On the other hand, however, longer residence times may improve the measuring sensitivity, e.g., in coulometric detectors.

In FA systems, the time required to bring the detected species from the sample introduction site to the detection site is called *transport lag* or *hold-up time*, or *dead time of the detector*. The total time needed for the analysis of a single sample in an FA manifold is the sum of the transport lag and residence time, i.e., the transport lag is a parameter of primary importance for FA.

3.2.2.3 Long-term stability

Long-term stability is characterized by the drift and residual standard deviation of the detection signal in a solution of constant flow rate, composition (concentration), and temperature.

3.2.3 Detection modes

Electrochemical detection techniques are based on the measurement of electrical properties of a solution of the analyte (the sample). The measured properties are determined by the sample composition and the selected electroanalytical techniques (Table 1), which are defined in ref. [20] (Orange Book, Chaps. 8.5.1–8.5.4). Examples of the electroanalytical techniques used are:

- galvanostatic techniques, in which the potential difference of two electrodes is measured at controlled current;
- potentiostatic techniques, in which the current flowing through the electrochemical cell is measured at controlled external potential;

- potentiometric techniques, in which the potential of the indicator electrode is measured at zero current; and
- conductometric techniques, in which the impedance of the electrochemical cell is measured.

The measured parameters can depend on time, the liquid movement (forced flow, stirring, or rotation of the electrode), the composition of the sample matrix and the electrode surface conditions (changes in active surface area, surface chemical modification [37,50–52], and coverage, etc.).

Table 1 Electroanalytical techniques commonly used for measurements in flow analysis.

Parameter controlled	Quantity measured	Name of techniques
$I = 0$	$E = f(a)$	Ion-selective potentiometry
$I = 0$	$E = f(V_{titr})$	Potentiometric titration
E	$I = f(E, C_b)$	Steady-state voltammetry and polarography (dc); amperometry and biamperometry
E	$I = f(V_{titr})$	Amperometric and biamperometric titration
I	$E = f(I, C_b)$	Chronopotentiometry, bipotentiometry
$E(t)$	$I_{ac} = f(E, t, C_b)$	Transient polarographic and voltammetric techniques (mainly ac, square-wave, pulse, and differential pulse techniques)
E	$Q = \int_0^t I \, dt = f(m)$	Constant-potential coulometry
I	$Q = It = f(m)$	Constant-current coulometry (coulometric titration)
I_{ac} or I_{dc}	$G = f(C_b)$	Conductometry
I_{ac} or I_{dc}	$G = f(V_{titr})$	Conductometric titration
W_v	$G = f(C_b)$	High-frequency impedance measurements
	$B = f(C_b)$	
	$Y = f(C_b)$	

3.2.3.1 Potentiostatic techniques

In *potentiostatic techniques*, the potential of the working electrode is controlled according to a predetermined program or it is maintained at constant value vs. the potential of the reference electrode. The electric current, flowing through the electrochemical cell at the controlled working electrode potential, is measured. In amperometry, the potential of the working electrode is kept constant (stepped to a certain value or sequence of values, generally in the limiting current region) and the current is measured as a function of the composition of the solution in the cell, e.g., as the reagent mass transfer rate changes during titrations in flow-though electrochemical detectors. Changes in the flow rate of the solution (or the rotation speed with rotating disk working electrodes), in the active area and activity of the working electrode (through changes in the chemical composition or coverage limiting the mass transport) influences the measured signal.

3.2.3.2 Galvanostatic techniques

In *galvanostatic techniques*, the electrical current flowing through the electrochemical cell is maintained at constant level or it is controlled according to a predetermined program (current step, pulse, ramp, or staircase, etc.) and the potential of the working electrode is measured vs. the potential of the reference electrode.

3.2.4 *Factors influencing sensitivity and detection limits*

The detection limit is determined by the signal-to-noise (S/N) ratio. The S/N ratio of electroanalytical techniques can be improved electronically and hydrodynamically.

3.2.4.1 Electronic approach

In voltammetry, a variable potential excitation signal is imposed upon an electrochemical cell. The waveform of the excitation signal and the sampling pattern of the measured current determine the sensitivity and detection limit of the technique. The different potential pulse techniques typically improve the detection limit of the electroanalytical detection modes by decreasing the noise, i.e., the detrimental effect of charging current.

> *Comment*: Modulation of the excitation signals does not eliminate charging current. However, the influence of the charging current on the results can be suppressed by selecting optimal sampling time(s) or phase angle. The contribution of charging current to the measured signal can be accounted for by background current correction (off-line subtraction) or by applying a differential cell with twin electrodes (on-line subtraction) and by charge injection method (i.e., electronic compensation of the charging current). In these methods, it is assumed that the working electrodes are perfectly matched and that the background current is identical in the presence and absence of the electroactive species. Errors in the assumptions limit the power of these compensation methods.

3.2.4.2 Hydrodynamic approach

In flow-through voltammetric techniques, the S/N ratio is increased and the detection limit is improved through the increased mass transfer rates. It is called the *hydrodynamic approach* for improving the S/N ratio. An increase in the flow rate increases the signal (faradaic current), while the background current changes less as its main component is the charging current, which is flow-independent.

In principle, the electrode signal in potentiometry is flow-rate independent. However, the detection limits of potentiometric sensors are improved in flowing solutions [53,54]. The surface concentrations often deviate from the concentrations in the bulk of the sample solution due to minor ionic fluxes from or into the sensing membrane. In flowing solutions, these concentration differences are minimized and the theoretical detection limits are approached.

The flow-through electrochemical detection cells differ in their cell and electrode geometries. In the most common arrangements, the flow is either parallel to the electrode surface (e.g., thin-layer cells), perpendicular to the electrode surface (e.g., wall-jet cells) or the liquid passes through a tubular, annular, reticulated, or porous electrode cell [37,55]. The most frequently used working electrode materials are carbon (e.g., glassy carbon, pyrolytic graphite, carbon paste), or noble metals, such as gold and platinum, or silver. These materials are used mainly for oxidizable analytes. But for reducible analytes, mercury and amalgams are frequently used as the working electrode materials. Mercury electrodes used in flow-through cells are most often a hanging or static mercury drop, dropping mercury, or mercury film (e.g., amalgamated gold) electrodes. The most common electrode geometries are disks, rings, spheres, hemispheres, cylinders, or tubes.

Electrochemical flow-through detection cells are frequently used in LC. The small effective cell volume (from a few μl with standard packed columns to less than a nl with capillary columns) of the electrochemical flow-through cells avoids undue band-broadening and guarantees excellent detection limits. The electrical current or potential changes reflect changes in the composition of the eluent as a function of time. During the passage of the sample through an amperometric detector, a small fraction of the analyte is lost, i.e., oxidized or reduced at the surface of the working electrode. By increasing the electrode area, nearly 100 % conversion can be achieved, which is utilized in coulometric detectors. In coulometric detectors, the current is much larger compared to amperometric detectors, but there is no improvement in the S/N ratio or the detection limit due to the concomitant increase in noise.

3.3   Flow analytical techniques based on electrochemical detection

Most of the known electroanalytical techniques (potentiometry, voltammetry including pulsed amperometry, coulometry, and conductometry) are available for detection in flow analytical techniques (Table 1) [20,56].

Symbols and abbreviations: a, analyte activity in the bulk of the solution; C_b, analyte concentration in the bulk of the solution; E, electrode potential (against a reference electrode); $E(t)$, electrode potential as a function of time; I, current; I_{ac}, alternating current; I_{dc}, direct current; m, analyte mass; Q, electric charge; t, time; V_{titr}, volume of the titrant; W_v, energy of radiofrequency electromagnetic radiation; G, conductance; B, susceptance; Y, admittance.

3.4   Detection cell design

Electrochemical detection based on voltammetry is most important and most widely applied in both FA and LC. The design of most common voltammetric electrodes used in flow-through electrochemical detectors and the relevant signal vs. concentration relationships are compiled in Table 2. A wider range of designs, also including potentiometric and impedance cells, and their detailed discussion, can be found in ref. [37]. Some general properties of electrochemical detectors and their comparison with flow detectors based on other principles are discussed in Section 3.5.

3.5   Special features of electrochemical detectors for flow analytical techniques, their critical evaluation and comparison with the properties of other common detectors

Electrochemical detection under hydrodynamically controlled conditions reveals certain characteristic features:

1. The shear forces of the flowing liquid continuously clean the surface of the indicator or working electrode. Consequently, in flow analytical techniques the electrochemical and/or mechanical regeneration of the working electrode surface with intensive washing, solution or solvent switching, potential cycling, etc. are generally less crucial when compared to batch electroanalytical techniques.
2. The continuously streaming carrier solution removes reaction products (voltammetric electrodes) and impurities leached from the electrode (potentiometric electrodes), and conditions the working or indicator electrode. With flow-through potentiometric detection cells, the carrier solution often contains the primary ion at low concentrations for well-defined and stable potential, which is essential for high-precision direct measurement.
3. The convective transport of an analyte and/or a reactant reduces response time and improves the detection limit compared to batch-type measurements with pure diffusion transport [57].
4. Differences in the response rate for the primary and interfering ions, in case of potentiometric detectors, can improve the selectivity under flow analytical conditions.
5. Since the reference electrode can be located downstream with respect to the working or indicator electrode, it gives great flexibility in the reference electrode selection and design as well as the salt bridge composition.
6. Microelectrodes and microelectrode arrays bring about additional advantages for flow measurements [50], such as:
    -   ability of operating in solutions with very low conductivity
    -   suppressed signal dependence on the liquid flow rate due to high mass transport rate generated by efficient spherical or semispherical, nonlinear diffusion
    -   fast establishment of a steady-state signal which permits the use of rapid-scan voltammetric techniques in combination with flow analytical techniques and generates three-dimensional recordings (time/potential/intensity)
    -   continuous replenishment of the diffusion layer with analytes during the passage of the solution over a microelectrode array (an increase of detectability)

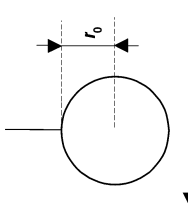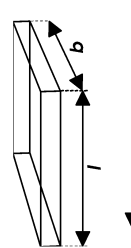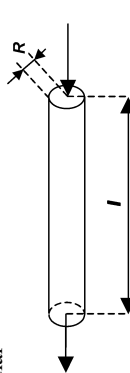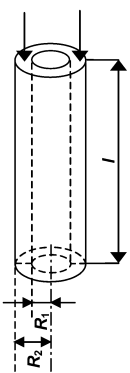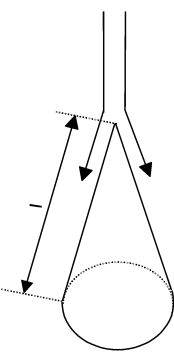**Table 2** Some important flow-through voltammetric electrode designs and limiting current characteristics* [37].
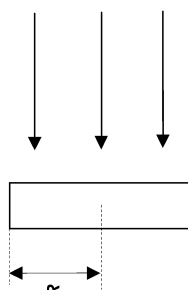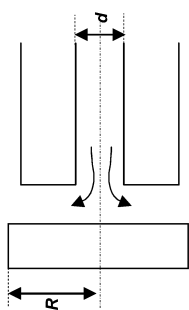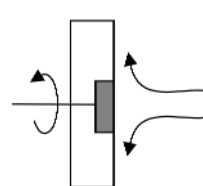
Electrode design	Limiting current equation		Notes	Ref.
Spherical	$I_{\lim} = 4\pi r_0 nFDC + knFr_0^2 D^{2/3} \nu^{-1/6} f^{1/2} C$	(10)	Turbulent flow; constant k is determined empirically	[59–61]
	$I_{\lim} = 0.85\, nFAD^{2/3} \nu^{-1/6} \upsilon^{1/2} l^{-1/2} C$	(11)	Laminar flow; f - frequency of solution stirring, $l = 2r_0/3$	[62]
Planar	$I_{\lim} = knFD^{2/3} \nu^{-1/6} \upsilon^{1/2} l^{1/2} Cb$	(12)	$k = 0.68$ (developing laminar flow); $k = 0.81$ (developing laminar flow); $k = 0.83$ (developing laminar flow)	[63–66]
	$I_{\lim} = 1.47\, nFD^{2/3} Cl^{2/3} F_{\mathrm{m}}^{1/3}$	(13)	Plate in a rectangular channel (thin-layer system), fully developed laminar flow	[67]
Tubular	$I_{\lim} = 2.01\, nFD^{2/3} \upsilon^{k} l^{2/3} R^{2/3} C$	(14)	$k = 0.33$ for laminar flow	[68,69]
Cylindrical in a narrow channel (annulus)	$I_{\lim} = 3.22\, nFC[\phi(z)]^{1/3} \dfrac{\pi^{2/3} l^{2/3} (R_2 - R_1) D^{2/3} F_{\mathrm{m}}^{1/3}}{2(R_2 - R_1)^{1/3}(R_2^2 - R_1^2)^{1/3}}$; $z = R_1 / R_2$ $\phi(z) = \dfrac{1-z}{z} \cdot \dfrac{0.5 - z^2/(1-z^2)\ln(1/z)}{[(1+z^2)/(1-z^2)\ln(1/z)]-1}$	(15)	Laminar flow	[70,71]
Conical	$I_{\lim} = 0.77\, nFAD^{2/3} \nu^{-1/6} \upsilon^{1/2} l^{-1/2} C$	(16)	Laminar flow	[72]

Table 2 (*Continued*).

Electrode design	Limiting current equation	Notes	Ref.
Disk with perpendicular flow of solution	(17) $I_{\text{lim}} = knFD^{2/3} v^{-1/6} \upsilon^{1/2} l^{1/2} RC$	$k = 3.27$ (only mass transport perpendicular to disk considered) $k = 3.02$ (nonuniformity of the flow pattern taken into consideration) l - characteristic dimension of the disk, $l = \pi R/2$	[73] [62]
Wall-jet and impinging-jet	(18) $I_{\text{lim}} = 1.38\, nFD^{2/3} v^{-5/12} F_{\text{m}}^{3/4} d^{-1/2} R^{3/4} C = 1.15\, nFD^{2/3} v^{-5/12} \upsilon^{3/4} d R^{3/4} C$ $F_{\text{m}} = \dfrac{\pi a^2 \upsilon}{4}$	The electrode diameter is much larger than the diameter of the liquid stream (wall-jet).	[62,74]
	(19) $I_{\text{lim}} = knFACD^{2/3} v^{-1/6} (\upsilon/l)^{1/2}$	The electrode diameter is smaller than that of the liquid stream (impinging-jet); A - electrode surface area; $l = \pi R/2$	[62]
Rotating disk (RDE)	(20) $I_{\text{lim}} = 0.62\, nFACD^{2/3} v^{-1/6} \omega^{1/2}$	A - electrode surface area ω: angular velocity (laminar flow)	[59,61,68, 75,76]

*All equations refer to reversible electrode processes.

- the possibility for simultaneous multicomponent analysis using a microelectrode array as a multichannel detector
- easy miniaturization for microcolumn LC and capillary electrophoresis.

When considering the typical properties of electrochemical detectors listed above, one may arrive to the following conclusions [58]:

- Electrochemical detectors are typical selective detectors whose application range is limited compared to the most common absorption spectrophotometric detectors. However, when the application is judiciously selected, they offer analytical parameters superior to other detection systems including mass spectrometry. The low- and high-frequency conductometric detectors are not selective per se, but their advantages appear selectively in ion chromatography and capillary electrophoresis where their analytical parameters for determination of primarily inorganic ions are superior to those of the common spectrophotometric detectors.
- Electrochemical detectors are simple in design and use, easy to miniaturize, and, moreover, they are cheap. However, their use requires certain knowledge and experience in electrochemistry, which unfavorably, contrasts with, e.g., the most common UV–vis spectrophotometric detectors. This requirement is often considered as a drawback, especially with voltammetric detectors. The electrochemical detector response depends on the transport of the analyte toward the electrode. This sensitivity to the flow parameters may induce some problems in certain applications. The electrochemical detection in capillary electrophoresis must compete with interference of the intense electrostatic field used for the separation.
- When properly used, voltammetric detectors provide enhanced measuring sensitivity and LOD values up to three orders of magnitude smaller compared to UV–vis spectrophotometric detectors. Noticeably, appreciable precision is maintained even for the lowest analyte concentrations (amounts). The advantage of truly coulometric detectors, i.e., those featuring 100 % electrochemical conversion of the analyte, consists in that they are absolute detectors.
- The selectivity of electrochemical detectors is their prominent advantage. The selectivity of electrochemical detectors can be modified or controlled through physico-(bio)chemical modification of the electrode surface. The sensor's selectivity can be tailored for a particular purpose [52]. The behavior and operational parameters of voltammetric detectors is in many respects similar to laser fluorescence detectors, but electrochemical detectors are more rugged. Advantageously, voltammetric detectors are sometimes substantially less sensitive to matrices of biological samples than spectroscopic detectors. This favorable feature often simplifies the required sample pretreatment.
- In some cases, voltammetric and especially potentiometric detectors may suffer from sluggish response, compared to spectroscopic detectors; however, this problem is less important when microelectrodes are utilized in electrochemical detectors.
- Voltammetric detectors offer many possibilities for multi-analyte (multi-channel) detection (microelectrode arrays with individually addressed microelectrodes in combination with chemometric data processing) and combination with other detection approaches (e.g., spectro-electrochemistry, or simultaneous electrochemistry and piezoelectric microgravimetry with the use of an electrochemical quartz crystal microbalance, etc.).

4. SYMBOLS AND ACRONYMS

4.1 List of symbols

a	activity
A	surface area; m^2
A	primary ion
b	width of a planar rectangular electrode; m
B	susceptance; S
B	interfering component
C	amount concentration; mol dm^{-3}
$C_{A,min}$	lowest expected concentration of the primary ion, A, in a potentiometric determination; mol dm^{-3}
C_{av}	average concentration; mol dm^{-3}
C_b	bulk concentration; mol dm^{-3}
$C_{B,max}$	highest expected concentration of an interfering ion in a potentiometric determination; mol dm^{-3}
C_{LOD}	minimum detectable concentration; mol dm^{-3}
C_L	local analyte concentration; mol dm^{-3}
C_m	mean concentration; mol dm^{-3}
ΔC	concentration change/difference; mol dm^{-3}
D	diffusion coefficient; $m^2\ s^{-1}$
E	electrode potential; V
$E(t)$	electrode potential as a function of time; V
f	frequency of solution stirring or electrode rotation; s^{-1}
F_m	volume flow rate; $dm^3\ s^{-1}$
F	Faraday constant; $96\,484.56$ C mol^{-1}
G	conductance; S
I	current; A
I_{ac}	alternating current; A
I_c	charging current; A
I_{dc}	direct current; A
I_{lim}	limiting current; A
I_{ss}	steady-state current; A
k	multiplication factor or constant
$K_{A,B}^{pot}$	potentiometric selectivity coefficient
l, L	distance; m
m	mass; kg
Δm	mass change/difference; kg
n	number of electrons per molecule oxidized or reduced
P	relative acceptable/allowed error in determination due to interference; %
q	cross-section of the detection channel; m^2
Q	electric charge; C
q_{LOD}	minimum detectable quantity; mol
r_0	spherical electrode radius; m
R	tubular or disk electrode radius; m
R_1	inner wall radius of a narrow channel cylindrical electrode; m
R_2	outer wall radius of a narrow channel cylindrical electrode; m
R_{bg}	background signal
R_{ss}	steady-state signal

R_t	transient signal
R_{LOD}	smallest measurable net signal
ΔR	detector signal change or difference
S	sensitivity
s_B	standard deviation of a blank signal
t	time; s
u	local linear liquid flow speed; m s^{-1}
υ	linear liquid flow speed; m s^{-1}
V_{titr}	titrant volume; dm^3
W_v	energy of radiofrequency electromagnetic radiation; J
Y	admittance; S
z	inner-to-outer radius ratio of a narrow cylindrical channel electrode; $z = R_1/R_2$
v	kinematic viscosity; m^2 s^{-1}
ω	angular frequency of rotation, $\omega = 2\pi f$; s^{-1}

4.2   List of acronyms

ac	alternating current
CE	capillary electrophoresis
CFA	continuous flow analysis
CM	continuous monitoring
CZE	capillary zone electrophoresis
FA	flow analysis
FIA	flow-injection analysis
FT	flow titration
HPLC	high-performance liquid chromatography
ISE	ion-selective electrode
LC	liquid chromatography
LOD	limit of detection
SFA	segmented flow analysis
SFASA	segmented flow analysis with sample aspiration
S/N	signal-to-noise ratio

5.   REFERENCES

1. A. M. Bond. *Anal. Chim. Acta* **400**, 333 (1999).
2. A. Manz, N. Graber, H. M. Widmer. *Sens. Actuators* **62**, 978 (1990).
3. D. J. Harrison, A. Manz, Z. Fan, H. Lüdi, H. M. Widmer. *Anal. Chem.* **64**, 1926 (1992).
4. G. Blankenstein and U. D. Larsen. *Biosens. Bioelectron.* **13**, 427 (1998).
5. J. Ruzicka and E. H. Hansen. *Flow Injection Analysis*, 2nd ed., John Wiley, New York (1988).
6. B. Oosterhuis, K. Brunt, B. H. C. Westerink, D. A. Doornbos. *Anal. Chem.* **52**, 203 (1980).
7. M. McEnery, A. M. Tan, J. Alderman, J. Patterson, S. C. O'Mathuna, J. D. Glennon. *Analyst* **125**, 25 (1999).
8. B. P. Solomon. *Curr. Separ.* **18**, 123 (2000).
9. T. J. O'Shea and S. M. Lunte. *Curr. Separ.* **14**, 18 (1995).
10. L. A. Holland and S. M. Lunte. *Anal. Communs.* **35**, 1H (1998).
11. M. I. Davies. *Anal. Chim. Acta* **379**, 227 (1999).
12. J. Lichtenberg, E. Verpoorte, N. F. de Rooij. *Electrophoresis* **22**, 258 (2001).
13. E. Pungor, Z. Fehér, G. Nagy, K. Tóth. *Crit. Rev. Anal. Chem.* **14**, 53 (1983) and **14**, 175 (1983).
14. G. Horvai and E. Pungor. *Crit. Rev. Anal. Chem.* **21**, 1 (1989).

15. J. Ruzicka and E. H. Hansen. *Anal. Chem.* **72**, 212A (2000).
16. S. J. Chalk. *Talanta* **45**, 591 (1998).
17. W. E. van der Linden. *Pure Appl. Chem.* **66**, 2493 (1994).
18. J. F. van Standen. *Pure Appl. Chem.* **71**, 2303 (1999).
19. E. A. G. Zagatto, J. F. van Staden, N. Maniasso, R. I. Stefan, G. D. Marshall. *Pure Appl. Chem.* **74**, 585 (2002).
20. J. Inczedy, T. Lengyel, A. M. Ure. *Compendium of Analytical Nomenclature (definitive rules 1998)* (the "Orange Book"), 3rd ed., Blackwell Science, Oxford (1998).
21. A. D. McNaught and A. Wilkinson. *Compendium of Chemical Terminology: IUPAC Recommendations* (the "Gold Book"), 2nd ed., Blackwell Science, Oxford (1997).
22. L. T. Skeggs. *Am. J. Clin. Pathol.* **13**, 451 (1957).
23. L. T. Skeggs. *Anal. Chem.* **38**, 31A (1966).
24. G. Nagy, Z. Fehér, E. Pungor. *Anal. Chim. Acta* **52**, 47 (1970).
25. J. Ruzicka and E. H. Hansen. *Anal. Chim. Acta* **79**, 145 (1975).
26. D. Betteridge. *Anal. Chem.* **50**, 832A (1978).
27. E. Pungor, Z. Fehér, G. Nagy, K. Tóth, G. Horvai, M. Gratzl. *Anal. Chim. Acta* **109**, 1 (1979).
28. J. Ruzicka and E. H. Hansen. *Anal. Chim. Acta* **99**, 37 (1978).
29. J. Ruzicka and E. H. Hansen. *Anal. Chim. Acta* **114**, 19 (1980).
30. J. Ruzicka and E. H. Hansen. *Trends Anal. Chem.* **17**, 69 (1998).
31. B. Fleet and A. Y. Ho. *Anal. Chem.* **46**, 9 (1974).
32. G. Nagy, K. Tóth, E. Pungor. *Anal. Chem.* **47**, 1460 (1975).
33. G. Horvai, K. Tóth, E. Pungor. *Anal. Chim. Acta* **82**, 45 (1975).
34. J. Ruzicka, E. H. Hansen, H. Mosbaek. *Anal. Chim. Acta* **92**, 235 (1977).
35. A. U. Ramsing, J. Ruzicka, E. H. Hansen. *Anal. Chim. Acta* **129**, 1 (1981).
36. L. S. Ettre. *Pure Appl. Chem.* **65**, 819 (1993).
37. K. Štulík and V. Pacáková. *Electroanalytical Measurements in Flowing Liquids*, Ellis Horwood, Chichester (1987).
38. G. Horvai and E. Pungor. *Crit. Rev. Anal. Chem.* **17**, 231 (1987).
39. R. P. Buck and E. Lindner. *Pure Appl. Chem.* **66**, 2527 (1994).
40. Y. Umezawa. *Handbook of Ion-Selective Electrodes: Selectivity Coefficients*, CRC Press, Boca Raton, FL (1990).
41. Y. Umezawa, P. Bühlmann, K. Umezawa, K. Tohda, S. Amemiya. *Pure Appl. Chem.* **72**, 1851 (2000).
42. Y. Umezawa, K. Umezawa, P. Bühlmann, N. Hamada, H. Aoki, J. Nakanishi, M. Sato, K. P. Xiao, Y. Nishimura. *Pure Appl. Chem.* **74**, 923 (2002).
43. Y. Umezawa, P. Bühlmann, K. Umezawa, N. Hamada. *Pure Appl. Chem.* **74**, 995 (2002).
44. J. Wang. *Talanta* **41**, 857 (1994).
45. J. Wang, L. Chen, H. Wu. *Anal. Chim. Acta* **300**, 127 (1995).
46. E. Bakker, E. Pretsch, P. Bühlmann. *Anal. Chem.* **72**, 1127 (2000).
47. ISO 3534-1, *Statistics - Vocabulary and Symbols. Part I: Probability and General Statistic Terms* (1993).
48. L. A. Currie. *Pure Appl. Chem.* **67**, 1699 (1995).
49. E. Lindner, K. Tóth, E. Pungor. *Pure Appl. Chem.* **58**, 469 (1986).
50. K. Štulík, C. Amatore, K. Holub, V. Mareček, W. Kutner. *Pure Appl. Chem.* **72**, 1483 (2000).
51. R. A. Durst, A. J. Bäumer, R. W. Murray, R. P. Buck, C. P. Andrieux. *Pure Appl. Chem.* **69**, 1317 (1997).
52. W. Kutner, J. Wang, M. L'Her, R. P. Buck. *Pure Appl. Chem.* **70**, 1301 (1998).
53. E. Lindner, R. E. Gyurcsányi, R. P. Buck. *Electroanalysis* **11**, 695 (1999).
54. R. E. Gyurcsányi, É. Pergel, R. Nagy, I. Kapui, B. T. T. Lan, K. Tóth, I. Bitter, E. Lindner. *Anal. Chem.* **73**, 2104 (2001).

55. P. T. Kissinger and W. R. Heineman. *Laboratory Techniques in Electroanalytical Chemistry*, Marcel Dekker, New York (1996).
56. H. Freiser and G. H. Nancollas. *Compendium of Analytical Nomenclature, (Definitive Rules 1987),* (the "Orange Book"), 2nd ed., Blackwell Science, Oxford (1987).
57. E. Pungor, Zs. Fehér, M. Váradi. *Crit. Rev. Anal. Chem.* **9**, 97 (1980).
58. K. Štulík. *Electroanalysis* **11**, 1001 (1999).
59. V. G. Levich. *Acta Physicochem. USSR* **19**, 113 (1944).
60. V. G. Levich. *Acta Physicochem. USSR* **19**, 117 (1944).
61. V. G. Levich. *Acta Physicochem. USSR* **17**, 257 (1942).
62. H. Matsuda. *J. Electroanal. Chem.* **15**, 109 (1967).
63. V. G. Levich. *Discuss. Faraday Soc.* **1**, 37 (1947).
64. G. Wranglén and O. Nilsson. *Electrochim. Acta* **7**, 121 (1962).
65. H. B. Hanekamp and H. J. van Nieuwkerk. *Anal. Chim. Acta* **121**, 13 (1980).
66. K. Brunt and C. H. P. Bruins. *J. Chromatogr.* **172**, 37 (1979).
67. H. Matsuda. *J. Electroanal. Chem.* **15**, 325 (1967).
68. V. G. Levich. *Physicochemical Hydrodynamics*, Prentice Hall, Englewood Cliffs, NJ (1962).
69. R. Tijssen. *Anal. Chim. Acta* **114**, 71 (1980).
70. T. K. Ross and A. A. Wragg. *Electrochim. Acta* **10**, 1093 (1965).
71. J. A. Lown, R. Koile, D. C. Johnson. *Anal. Chim. Acta* **116**, 33 (1980).
72. J. Jordan, R. A. Javick, W. E. Ranz. *J. Am. Chem. Soc.* **80**, 3846 (1958).
73. S. L. Marchiano and A. J. Arvia. *Electrochim. Acta* **12**, 801 (1967).
74. J. Yamada and H. Matsuda. *J. Electroanal. Chem.* **44**, 189 (1973).
75. V. G. Levich. *Zh. Fiz. Khim.* **18**, 355 (1944).
76. V. G. Levich. *Zh. Fiz. Khim.* **22**, 575 (1948).