

8.3.2.1 General terms relevant to ion-selective electrodes

Activity, Activity coefficient and Concentration

See sections 1.3.8, 1.3.10 and 3.3.

Calibration plot

This is a plot of the cell emf, E (i.e. the galvanic potential difference measured between the ion-selective electrode and the external reference electrode of a given ion-selective electrode cell assembly (ion-selective electrode combined with an identified external reference electrode) vs. the logarithm of the single ionic activity (concentration) of a given species. For uniformity, it is recommended that the cell emf is ascribed to the ordinate (vertical axis) with the more positive potentials at the top of the graph and that p_{aA} (-log activity of the measured species A) or p_{cA} (-log concentration of the measured species A) is ascribed to the abscissa (horizontal axis) with increasing activity or concentration to the right.

Comment: The cell potential (cell emf) is composed of interfacial and bulk potential differences established across the *membrane*, *reference electrodes* and *junctions* if present (see below). When referring to the potential difference at an ISE membrane interface, or across the ISE membrane including the bulk and two interfaces, the terms interfacial potential difference and ISE or membrane potential difference should be used to distinguish a portion of the cell potential difference (emf) under study.

Combination electrode

An ion-selective electrode and an external reference electrode combined in a single sensor, thereby avoiding the need for a separate external reference electrode.

Detection limit

A calibration plot of typical shape is shown in Fig. 8.3.2.1. By analogy to definitions adopted in other fields, a limit of detection is defined as the concentration at which, under specified conditions, the cell potential, E , deviates from the average value in region I by a multiple of the standard error of a single measurement of the cell potential in this region. The multiple selected depends on a statistical significance level selected. The fundamental difference in the nature of ISE potentiometry (their logarithmic response) as compared to linear methods, justifies another type of definition of detection limit. For the sake of practical convenience, a simpler (and more convenient) definition is recommended. The practical lower limit of detection may be taken as the activity (or concentration) of

substance A at the point of intersection of the extrapolated linear mid-range and final low concentration level segments of the calibration plot, as shown in Fig. 8.3.2.2.

For electrodes that become insensitive to high ionic activities, or the slope of the curve changes its sign, an upper limit of determination may be taken as the activity (or concentration) of A at the point of intersection of the extrapolated mid-range linear segment and the limiting high activity response.

Comment: The reliability of the detection limit data, determined by the cross point method, is illustrated in Fig. 8.3.2.2. The reliability depends on:

1. The standard deviation of a single potential measurement in both linear regions (it need not be the same in the Nernstian and concentration-independent regions);
2. The number of data points taken into account to determine the parameters of the linear sections;
3. The concentration range used to determine the parameters of the linear sections.

Based on the reliability conditions presented above, beside the experimental conditions (i.e., composition of the solution, the history and preconditioning of the electrode, stirring rate, etc.) used for the determination of the detection limit, also the details of the measured data, (e.g., number of measurements, standard deviation of a single measurement, etc.) and of the evaluation method, should be given. However, the description of the experimental conditions and the evaluation method offers only a possibility to reproduce the data, but is not helpful in the comparison of data collected under different conditions. Accordingly, the experimental conditions and the evaluation method should also be standardized if possible. The following recommendations are suggested for the determination of the lower detection limit:

1. The potential data used for the determination of the detection limit should be measured at least three times: from low to high, high to low and low to high concentrations again.
2. Data used to determine the linear sections of the plot should be collected from a concentration range two orders of magnitude higher, and two orders of magnitude lower, including the concentration of the cross point. A minimum of five data points in both regions should be taken within this concentration range to determine the parameters of the linear sections.
3. The parameters of the determined linear sections should be given with their standard deviations.
4. Besides the most probable values of the detection limits (DL_{mean}), the confidence interval should be given as well (DL_{min} , DL_{max}).

5. If the determination of data points below the detection limit is difficult, (too long response time, too bad reproducibility, etc.) a line parallel to the abscissa should be drawn through the mean data point obtained for solution of the lowest concentration, instead of fitting a line through some data in the curved region of the calibration plot. The detection limit should be determined similarly as above, only the data DL_{max} should be given as detection limit as $DL < \text{numerical value} \pm \text{standard deviation}$.

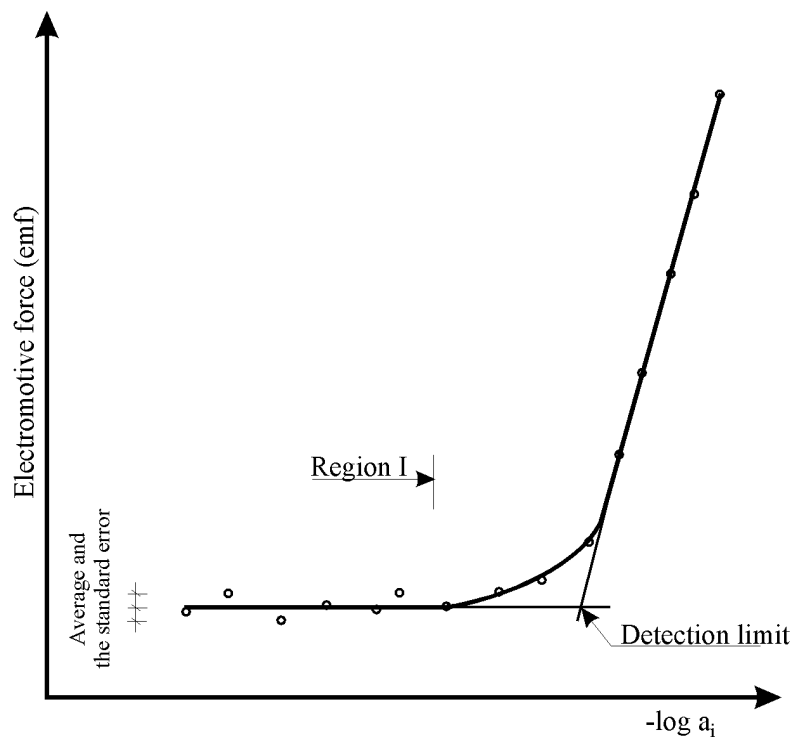


Fig. 8.3.2.1 Calibration plot of an ion-selective electrode.
(a_i denotes the single ion activity of the primary ion, i .)

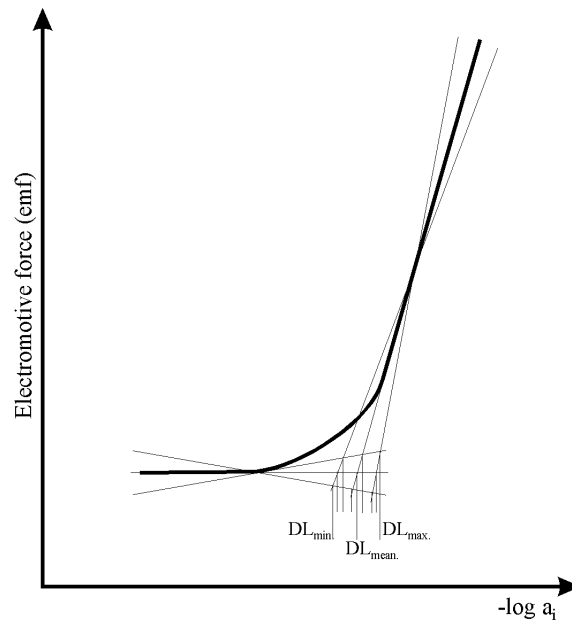


Fig. 8.3.2.2 Determination of the detection limit (DL) of ion-selective electrodes.
(DL_{mean} is the most probable value of the DL determined from the cross point of the lines fitted to the linear segments of the emf vs. $\log a_i$ curve where a_i denotes the single ion activity of the primary ion, i . DL_{min} and DL_{max} are the lowest and highest concentration values determined as DL

taking into account the minimum and maximum slope values (95% confidence values) of the lines fitted to the experimental data.)

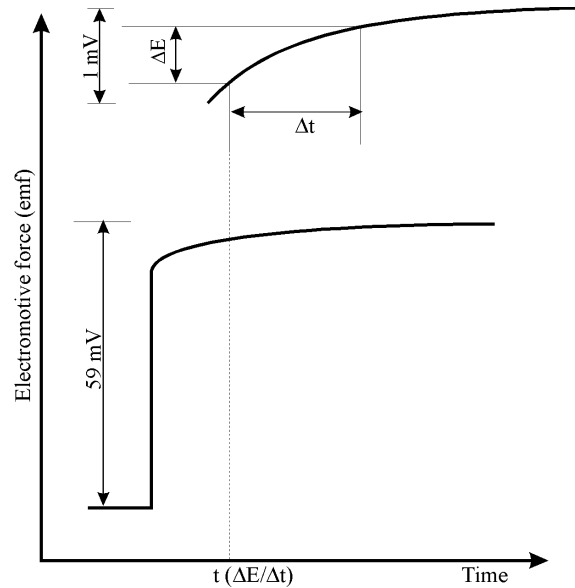


Fig. 8.3.2.3 Definition and determination of response time $t_R(\Delta E/\Delta t)$, i.e., the time which elapses between the instant when an ion-selective electrode and a reference electrode (i.e., ISE cell) are brought into contact with a sample solution (or at which the activity of the ion of interest in a solution is changed) and the first instant at which the emf/time slope ($\Delta E/\Delta t$) becomes equal to a limiting value selected on the basis of the experimental conditions and/or requirements concerning the accuracy (e.g., 0.6 mV/min).

Drift and standard deviation

Drift is the slow non-random change with time in the emf of an ion-selective electrode cell assembly maintained in a solution of constant composition and temperature. The determination of the drift is carried out by a linear curve fitting on the data set collected in a given period of time in a solution of constant composition and temperature. The slope of the emf vs. time line is called drift. The random potential deviations around the line define the standard deviation of the measured potential data.

Hysteresis and reproducibility

Hysteresis or *electrode memory* occurs when there is a potential difference between the emf first measured in solution A of certain concentration and that of a second

measurement in the same solution after exposing the electrode to solution A of different concentration. The systematic error of hysteresis is generally in the direction of the concentration of the solution in which the electrode was previously immersed. Hysteresis is thought to be a kinetic process. Reversible responses are expected if sufficient time is allowed for the system to return to its initial conditions.

Reproducibility is the standard deviation of emf data collected in a series of emf measurements in solutions of different concentrations, after removal and washing and/or wiping of the electrodes. If a distinct hysteresis occurs, the reproducibility is poor. Successive emf measurements in solution A, lead to determination of drift and reproducibility, but not of hysteresis.

Interfering substance (interference)

This may be any substance, other than the ion being determined, whose presence in the sample solution affects the measured emf of a cell. Interfering substances or interferences fall into two classes: "electrode/electrochemical" interferences and "chemical" interferences. Examples of the first class include:

- (a) Substances whose response is similar to that of the ion being determined, and whose presence generally results in an apparent increase in the activity (or concentration) of the ion to be determined (e.g., Na^+ for the Ca^{2+} electrode).
- (b) Electrolytes present at a high concentration that give rise to appreciable liquid junction potential differences or results in a significant decrease of the determined substance activity coefficient, or incipient Donnan exclusion failure.

The second class, of "chemical" interferences, includes:

- (c) Species that interact with the ion being determined, so as to decrease its activity or apparent concentration. Then the true activity is determined (e.g., CN^- present in solution for determination of Ag^+), but a considerable gap occurs between the activity and concentration of the ions, even in very dilute solutions. Under these conditions the determination of ion concentration may be difficult.
- (d) Substances interacting with the membrane itself, blocking thus the surface or changing its chemical properties (e.g., organic solvents in case of the liquid or poly(vinyl chloride) (PVC) membrane electrodes), are grouped as interferences or electrode poisons.

Ionic-strength or/and pH adjustment solution

These are solutions of high ionic strength which are added to sample or calibration solutions before measurements in order to bring them to the same ionic strength. Often a fixed pH solution or buffer controls the hydrogen ion activity as well as ionic strength. Additionally, complexing agents and other components are often added to minimize the effects of certain interferences.

Ion-selective electrode (ISE)

This is an electrochemical sensor, based on a thin selective membrane or film as recognition element and is an electrochemical half-cell equivalent to other half-cells of the zeroth (inert metal in a redox electrolyte), 1st, 2nd and 3rd kinds. These devices are distinct from half-cells that involve electrode redox reactions (electrodes of zeroth, 1st, 2nd and 3rd kinds), although they often contain a 2nd kind electrode as the “inner” or “internal” reference electrode. The potential difference response (i.e., that of ISE versus outer reference electrode potentials) is its principal component, of the Gibbs energy change associated with permselective mass transfer of ions (e.g., by ion-exchange, solvent extraction or some other mechanism) across a phase boundary. The ISE must be used in conjunction with a reference electrode (i.e., “outer” or “external” reference electrode) to form a complete electrochemical cell. The measured potential difference (ISE versus outer reference electrode potentials) is linearly dependent on the logarithm of the activity of a given ion in solution.

Comment: The term “ion-specific electrode” is not recommended. The term “specific” implies that the electrode does not respond to additional ions. Since no electrode is truly specific for one ion, the term “ion-selective” is recommended as more appropriate. “Selective ion-sensitive electrode” is rarely used term to describe an ion-selective electrode. “Principal” or “primary” ions are those for determination of which an electrode is designed. It is never certain that the ISE is more sensitive to the “principal” ion than to interferences, e.g., nitrate ISEs.

Ion-selective electrode cell

An ion-selective electrode in conjunction with a reference electrode is an ISE cell. Generally, the cell contains two reference electrodes, “internal” and “external”, and a selective thin film or membrane as the recognition/transduction element. However, besides this conventional type of cell with solution contact on both sides of the membrane there are ISE cell arrangements with wire contact to one side of the membrane (all solid state and coated wire types).

Conventional notation of the cell is:

outer ref. | test solution | membrane | internal ref.

or

outer ref. | test solution | ion-selective electrode

and the measured cell emf, E (right electrode potential minus left electrode potential) is described with the Nicolsky-Eisemann equation:

$$E = \text{constant} + \frac{2.303RT}{z_A F} \lg[a_A + K_{A,B}^{\text{pot}} a_B^{z_A/z_B} + K_{A,C}^{\text{pot}} a_C^{z_A/z_C} + \dots]$$

Terms in this equation are defined in section 8.3.2.3.

Typically internal components of an ISE include solvent, pH buffer, salt of the sensed ion, and soluble salt of anion in equilibrium with the internal reference electrode of 2nd kind. Also high-stability internal reference electrodes based on an inert metal electrode and a reversible redox couple are common.

Isopotential point

For an ion-selective electrode cell, there is often a particular activity of the determined ion for which the emf of the cell is independent of temperature. That activity, and the corresponding potential difference, defines the isopotential point. The specification of the ISE and outer reference electrode must be described.

Comment: When an isothermal cell is used with identical “internal” and “external” reference electrodes, the isopotential point is the activity of sensed ions for which zero net membrane potential is measured, e.g., sensed ion activity is the same in the inner and outer (test) solution. Slopes of calibration plots for different cell temperatures are different, but intersect at a common activity point. Cells with temperature gradients are not recommended.

Membrane

This general term refers to a continuous layer, usually consisting of a semi-permeable (solid or liquid) material, with controlled permeability. The membrane separates the internal components of the ISE from the test solution. It covers solid electric conductor, such as carbon or an inert metal, or separates two electrolyte solutions. This latter case is the most typical for an ISE. The membrane of an ion selective electrode is responsible for the emf response and selectivity of the ISE.

Comment: Membranes of sensor electrodes are thought to be practically homogeneous, but an actual membrane may contain inhomogeneous regions, often at surfaces, depending on the materials and preparation methods used. Inhomogeneous regions may include polymer regions with low and high local density of charged sites. Surface regions of plasticized liquid membranes often are low in charged sites and high in plasticizer or exuded impurities.

Membrane sites

Membranes frequently contain built-in "fixed" charged sites (e.g., "immobile" $-\text{SO}_3^-$ group in polystyrenesulfonate), or intentionally added, hydrophobically trapped, "mobile" sites (e.g., tetraphenyl borate in plasticized poly(vinyl chloride)). Such membranes with charged sites are named *sited membranes*. Ions of opposite sign to that of immobilised or entrapped ions in the membrane are "counterions". Ions of the same sign as sites are "coions". Usually coions are present in minor quantities. Sited membranes are "permselective" to counterions, i.e., only counterions exchange into the membrane and therefore are mobile to certain extent in the membrane bulk.

Donnan exclusion and exclusion failure

Sited membranes contain counterions whose overall charge exceeds that of sites. The excess of counterion charge is compensated by co-ions. In addition to the gross electroneutrality condition, the salt partition equilibrium expression:

$$\frac{\bar{a}_+ \bar{a}_-}{a_+ a_-} = K$$

determines the activity of minority co-ion species. The bar activities are ionic species of the salt in the membrane. Nonbar terms are the activities of ionic species of the salt in the bathing electrolyte solution. If K is large, i.e., the site concentration is large and/or activities in the bathing solution are small then, almost the entire current is carried by counterions. This condition favours Donnan exclusion since co-ions are nearly absent in the membrane. However, if K is small, i.e., activities in bathing solution are large, then and/or site concentration is small, then large concentrations of co-ions can be in the membrane, in the ultimate zero-site limit, equivalent in charge to counterion concentration. This condition is Donnan exclusion failure.

There are two manifestations of salt diffusion through the membrane:

1. If the membrane is asymmetrically bathed, then salts diffuse through the membrane from high to low concentration sides.

2. If the membrane is symmetrically bathed, but a potential difference is applied across the membrane which separates the inner and outer reference electrodes (through a high impedance circuit, for example,) then current is carried by both counterions and co-ions.

Nernstian response

Nernstian response occurs when an ion-selective electrode responds according to "local" thermodynamic equilibrium, over a given range of activity (or concentration). For Nernstian response a plot of the potential difference of the ISE cell (ISE with an outer reference electrode) vs. the logarithm of the ionic activity of a given species (a_A) is linear with a slope of $2.303 RT/z_A F$ (59.16/ z_A mV per unit change of $p a_A$ at 298.15 K). Nernstian response implies ideal sensitivity, but not necessarily ideal selectivity since interfering ions may also give Nernstian response when present as the sole potential determining species.

Potentiometric selectivity coefficient, $K_{A,B}^{pot}$

It defines the ability of an ion-selective electrode to distinguish a particular ion, i.e., primary ion from others (interfering ions). The selectivity coefficient, $K_{A,B}^{pot}$, is determined by means of potential difference of the ion-selective electrode in mixed solutions of the primary ion, A, and interfering ion, B (Fixed Interference Method) or less desirable, in separate solutions of A and B (Separate Solution Method). The activities of the primary ion, A, and the interfering ion, B, at which $K_{A,B}^{pot}$ is determined should always be specified, as the value of $K_{A,B}^{pot}$ is defined by the modified Nikolsky-Eisenman equation (See 8.3.2.3). The smaller the value of $K_{A,B}^{pot}$ the greater the electrode's preference for the primary ion, A, as described below.

Comment: The terms *selectivity constant* and *selectivity factor* are sometimes used instead of *selectivity coefficient*. However, in order to standardize the terminology associated with ion-selective electrodes, the term selectivity coefficient is recommended, as is the fixed interference method for its evaluation (see section 8.3.2.3). This selectivity coefficient is not the same as the similar term used in separation science.

Range and span

A range of activity or concentration of cell response between the lower and upper detection limits is determined from a plot of the cell potential difference vs. the logarithm of primary ionic activity. The span is the corresponding potential range (in contrast to the activity range) determined by projecting the lower (initial) and the upper (final) concentration limits to the potential axis.

Comment: The notion of span appears in the clinical literature, e.g., the normal span for K^+ in blood is a few millivolts which corresponds to the physiological activity range of the primary ion and interferences.

Reference electrode

An electrode which maintains a virtually constant potential with respect to the solution under the conditions prevailing in an electrochemical measurement, and which serves for monitoring, measurement or control of the potential of the indicator (or test) or working electrode.

Comment: In potentiometry, under zero current condition, the virtually constant potential difference is realized by assuring a constant composition solution in contact with the reference element, i.e., any electrode with small standard deviation can be used as a reference electrode (another ISE, electrodes of zero, 1st, 2nd or 3rd kind). However, practical reference electrodes are generally nonpolarizable electrodes of the second kind, constructed so that their electrolyte solutions serve as salt bridges to the solutions under investigation. "Double" junction reference electrodes are recommended when the reference electrolyte contains ions that interfere with primary ion measurement or react with components of the test solution.

Internal (or inner) reference electrode

This is a reference electrode which is incorporated inside an ion-selective electrode assembly.

Comment: Usually the reference electrode is a silver/silver chloride electrode in contact with a solution containing fixed concentrations of chloride and an ion which the electrode selective for. This solution is in contact with the ion-selective membrane.

Response time, t_R ; s

The time which elapses between the instant when an ion-selective electrode and a reference electrode (ISE cell) are brought into contact with a sample solution (or at which the activity of the ion of interest in solution is changed) and the first instant at which the slope of the cell potential vs. time plot ($\Delta E/\Delta t$) becomes equal to a limiting value selected on the basis of the experimental conditions and/or requirements concerning the accuracy (e.g., 0.6 mV/min). This concept is illustrated in Fig.8.3.2.1.3. In clinical applications (where the physiological activity range corresponds to a small potential span), a small slope e.g., 0.1 mV/min may be chosen, provided that the standard deviation of the response is smaller than the required slope.

Comment: The previously defined response times t_{95} (corresponding to the 95% change of the potential span) and t^* (to 1 mV from the steady value) require prior knowledge of steady-state E values that may not be available. These descriptive quantities underestimate practical response times of ion-selective electrodes in clinical applications where the total span may be smaller than 10 mV. The response time expressed in terms of $\Delta E/\Delta t$ (i.e., rate of cell potential variation with time) seems to be best defined, the best choice among the non-ideal options. It can be related to t_{95} and t^* through mathematical models, provided that the long-time potential determining processes are identified.

Standard addition or known addition method

This is a procedure for the concentration determination of an ion of interest in a test solution which consists of adding of known amounts of that species to the solution and recording the potential change of an ion-selective electrode cell. *Analyte addition* is a variation of this method. It uses sequential addition of the sample of unknown concentration to a standard solution while recording cell potential changes. A method of data treatment (which consists of plotting of the apparent concentration, as derived from the cell potential versus the volume of standard or reagent added to the sample) and the procedure is known as *Gran addition*.

Standard subtraction or known subtraction

This is a variation of the standard addition method. In this procedure changes in the cell potential are measured, resulting from the addition of a known amount of a species which reacts stoichiometrically with the ion of interest (e.g., a complexing agent) in order to determine the original activity or concentration of the ion.

"Suspension effect" or Pallmann effect

This effect occurs when ISEs are used in concentrated, space-filled suspensions while the external reference electrode remains in the supernatant (suspension-free) solution. The suspensions are specifically solvent-swollen ion exchangers or other materials, like soils and clays, that concentrate ions by adsorption and absorption. Space-filled, gravity-packed suspensions act like a second phase and form apparently an interfacial potential difference (pd) with respect to the supernatant. The measured ion activity in the suspension differs from the value in the supernatant by the interfacial potential difference and corresponds to a higher value approximating the activity inside the ion exchanger gel. The effect nearly disappears when the outer reference electrode is placed in the same region of the suspension as the sensor electrode. There are some changes in the junction potential differences of the reference electrode, between suspension and supernatant.