

The New Wave of Potentiometric Ion Sensors

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Abstract: Potentiometric selectivities and lower detection limits of ion-selective electrodes have been dramatically improved through better design of the electrodes. Ion-selective electrodes may now compete with the most sophisticated techniques of ultratrace activity determinations.

Keywords: Detection limits · Ion-selective electrodes · Selectivity · Trace-level measurements · Zero-current ion fluxes

1. Introduction

The field of ion-selective electrodes (ISEs) has matured over more than three decades. A few years ago, it seemed to have achieved its zenith [1][2]. In some areas, especially in clinical chemistry [3–5], it is being applied with success all over the world but in others, such as in environmental analysis, it has been less successful until now. For a long time, the notion persisted that the lower detection limits and selectivities of ISEs are rather restricted [6]. This view has radically changed over the last few years. It has become clear that lower detection limits and selectivity characteristics are better by up to six or more orders of magnitude than previously thought [7][8]. A brief review of the main improvements is given here together with several emerging new sensing possibilities based on a more fundamental understanding of the processes occurring in the sensor membranes.

2. The Problem: Biased Selectivities and Lower Detection Limits with Conventional Ion-Selective Electrodes

It is well established that the response of ISEs is a direct function of ionic activities in the sample and membrane phases at the phase boundary [1][9][10]. Based on correctly determined potentiometric selectivity coefficients [11], the EMF can be exactly predicted from ion activities [10][12]. The basic problem which, for decades, has led to the belief that selectivities and lower detection limits are generally insufficient, is that these activities near the phase boundaries do not exactly match those in the bulk phases. This is a consequence of concentration gradients and concomitant ion fluxes occurring in the membrane. In the traditional setup, with the back of the membrane in contact with the inner electrolyte solution containing a salt of the primary ion, the concentration profile of these ions decreases toward the sample and their ion fluxes induces their concentration to be higher near the outer membrane surface (Fig. 1, left). At low primary ion activities in the sample, such as during trace measurements or selectivity determinations, a flux-determined primary ion concentration of about 10^{-6} M defines the EMF [13–15]. As a consequence, lower detection limits of about 10^{-6} M and best selectivity coefficients above 10^{-4} – 10^{-5} have been reported for decades [6]. In contrast, recent results show that lower detection limits down to 10^{-8} – 10^{-12} M and selectivity coefficients better than 10^{-15} are feasible [8][16].

3. Reducing Transmembrane Ion Fluxes for Trace Analyses

Ion-selective membranes must have ion-exchange capabilities [1][9]. If uncharged ionophores are used, a salt with a lipophilic counterion is incorporated into the membrane as ion exchanger, e.g. a tetraphenylborate for cation-selective electrodes. Its concentration defines the amount of primary cations present in the membrane. However, small deviations from this amount may occur through two processes (see Fig. 1, top): coextraction of the primary cation together with its counteranion from the inner solution into the membrane [17] and ion exchange between primary and interfering ions at the sample side [13]. The thus generated concentration polarization is usually extremely small, typically less than 0.1% of the total concentration of the ion exchanger [16]. This tiny effect is, however, sufficient to induce fluxes generating an approximately micromolar concentration in the aqueous boundary layer near the membrane and, thus, to dictate the ISE response at submicromolar sample activities. The spectacular improvement of lower detection limits was first achieved in 1997 [18][19] when we found that these gradient generating effects could be counterbalanced by using an inner solution with a very low, buffered concentration of primary ions (Fig. 1, center). Subsequent theoretical [13][16][20][21] and experimental [14][16][22] studies revealed, however, that the solution to this problem is not so simple. If the above-mentioned gradient generating effects are overcompensated, a primary

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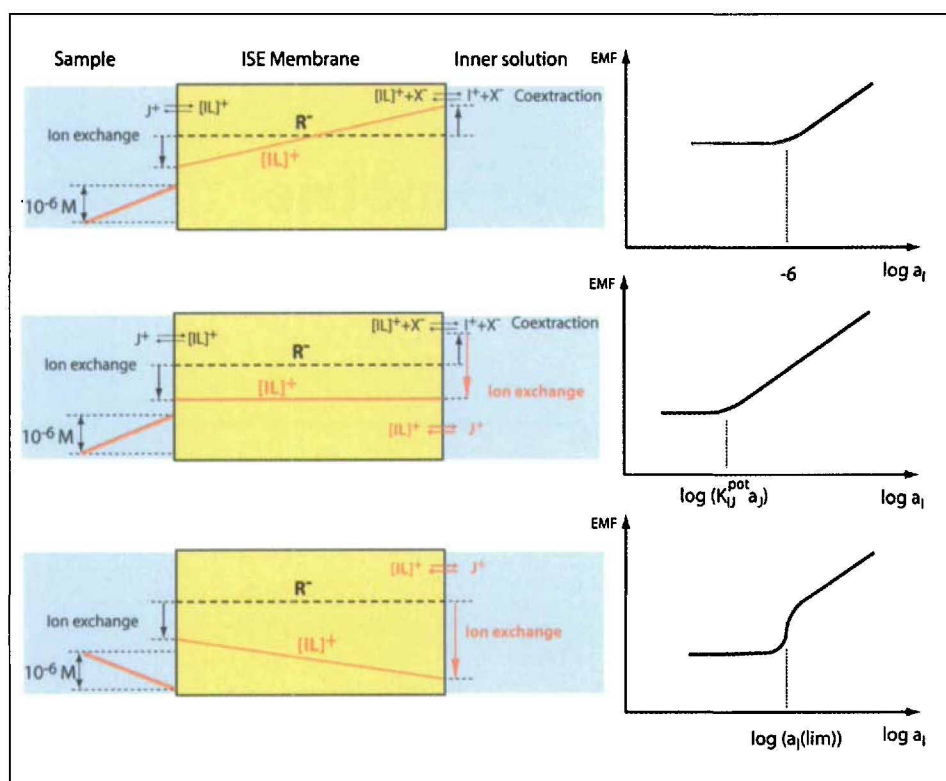


Fig. 1. Left: Schematic representation of the processes influencing the lower detection limit of an ISE based on a ionophore (L) forming 1:1 complexes with the primary (I^+) and interfering ions (J^+). Initially, the total cationic concentration is defined by the amount of ion exchanger (R^-) in the membrane. Concentration gradients are generated by coextraction of I^+ with X^- from the inner solution into the ISE membrane (right side) and by ion exchange of I^+ by J^+ on the sample side (left side). These gradients typically induce a concentration of 10^{-6} M in the aqueous surface layer, which dictates the lower detection limit of the sensor (see right part of the Fig.). Center: Idealized situation where the gradient generating effects are counterbalanced by using an appropriate inner solution, which leads to an optimal lower detection limit defined by the selectivity coefficient K_{IJ}^{pot} of the ISE (center right). A concentration profile decreasing toward the inner solution induces a step-like response at the activity $a_i(lim)$, where the extent of concentration reduction by this ion flux approaches the total sample concentration (typically near 10^{-6} M with conventional ISEs; bottom right).

ion flux takes place toward the inner solution. At submicromolar sample concentrations, this causes the membrane surface layer to be depleted of analyte, which induces a step-like potential change. Below the limiting concentration, the ISE no longer responds to the analyte (Fig. 1, bottom). The idealized situation shown in Fig. 1 (center) is only valid for exactly matching concentrations of sample and inner solution and any sample change will induce ion fluxes in either direction. The underlying effects are fully understood by now [13][16][20][21] and the model predictions have been validated by experiment [14–16][22]. Two strategies are required for a rugged submicromolar ISE response behavior, *i.e.* the adjustment of concentration profiles to a typical sample activity and the reduction of membrane permeability to make the response function insensitive to small deviations from the ideal situation.

Potentiometric selectivity coefficients are directly related to ion-exchange equilibria between the aqueous sample and the organic membrane phase [11][23–26]. Therefore, they allow exact prediction of the ion concentrations in a membrane of known composition in equilibrium with the adjacent sample phase [10][12][21]. To match the concentrations on both sides of the membrane, selectivity values can then also be used to predict the required composition of the inner solution [16][27]. With highly se-

lective membranes, the required partial ion exchange can only be achieved when the concentration of primary ions is low. Initially, it was kept constant at a low level with the help of ion buffers such as EDTA or NTA [14][19]. More recently, it was shown that the method can be extended to ions for which no adequate complexing agents are known (*e.g.* alkali metal ions or anions) by adding an ion exchanger resin to the inner solution [28]. Another possibility is to compensate ion fluxes by applying small external currents [29].

Any means that reduce ion fluxes in the membrane or increase them in the unstirred aqueous layer will extend the linear response range of ISEs toward lower activities. Independent of the concentration polarization across the membrane, there are various possibilities to reduce its permeability. As expected from theory [20] and shown by experiments, the increase in the thickness or polymer content of the membrane [22], the decrease in the concentration of the ion exchanger [22][27], or the covalent immobilization of the ionophore to a polymer [30–32] are beneficial.

The systems discussed above (Fig. 1) consist of a traditional ISE containing an internal electrolyte. One can expect that ISEs without an inner solution should have better lower detection limits. Such systems have been known since 1971 [33][34] but their long-term stability is

not sufficient. One of the sources of instabilities, the lack of a well-defined redox couple between membrane and metal electrode, was successfully eliminated by several authors [35–37]. More recently, we have used Au with a lipophilic redox-active monolayer as the inner contact [38]. In the course of these studies, it turned out that also the lipophilicity of this inner layer is essential for a good performance of the ISE; if it is too low, a thin aqueous layer forms between membrane and metal, which may cause long-term drifts owing to a kind of memory effects [39][40]. As expected, we have found that with our setup, the lower detection limit of the ISE is greatly improved [30][32].

4. What Are the Limits?

Within only four years after achieving the first breakthrough, the general applicability of the new concept has been realized for a series of ISEs [8] (for a selection, see Fig. 2). Although their lower detection limits are by far better than could have been thought a few years ago, it was also important to show that they can be used for trace level analyses of real samples. In environmental assays, submicromolar activities must be measured in the presence of interfering ions at millimolar activities so that a sufficiently high selectivity of the sensors is prerequisite. Fortu-

nately, also in this respect, ISEs perform a lot better than widely believed for a long time. This was first shown by Bakker with a special measurement protocol [41][42]. Today, it is clear that the same ion flux processes in the membrane/sample phases biased the lower detection limits and the measured selectivities. Unbiased values of selectivity coefficients are now obtained with ISEs having optimized lower detection limits. They are often better by many orders of magnitude than those previously reported in the literature and selectivity coefficients $\leq 10^{-10}$ are regularly observed [8] with the best polymeric membrane ISEs.

The applicability of ISEs to trace level measurements in environmental samples was shown recently [27]. The membrane was optimized to exhibit a rugged behavior and a sufficient (albeit not the best possible) lower detection limit 10 times better than the action limit demanded by the US Environmental Protection Agency. Comparison with ICP-MS proved that our activity determinations are correct [27].

The best achievable lower detection limit of potentiometric sensors is not yet known. If ion flux effects can be reduced further, it is likely that not the selectivities but other factors, *e.g.* the potential measuring technique, will set the limits. There is, however, no doubt that these in-

expensive and simple devices can compete with the most sophisticated methods of analysis.

5. Making Use of Transmembrane Ion Fluxes for Special Applications

The essential goal of the research presented above is to eliminate, as far as possible, ion fluxes through the ISE membrane. As a side effect of our efforts, various cases have been found where one can take advantage of strong ion fluxes toward the inner compartment of the ISE. Earlier, Meyerhoff *et al.* made use of ion fluxes inducing nonequilibrium responses with polyion sensors [43–45]. Because of the depletion of analyte near the membrane surface, such ISEs are not adequate for submicromolar activity measurements (Fig. 1, bottom). However, they are best suited for determining thermodynamic selectivity coefficients [11][14] [28]. A prerequisite for such measurements is that each ion to be measured is potential-determining, *i.e.* that it replaces the primary ion in the boundary layer of both phases [11]. The steady flux of primary ions toward the inner compartment helps to achieve this condition. Another interesting application is that in some cases ISEs, which clearly respond to ion activities, can be used to measure total

concentrations. In the presence of complexing agents in the sample, the total fluxes to and from the membrane surface, and thus the free ion activities, depend on the total concentrations [46]. Strong ion fluxes may also be beneficial in potentiometric titrations because, by lowering the initial concentration before reaching the end point, they can induce potential steps at the end point that are significantly larger than those thermodynamically predicted for the equilibrium case (Fig. 3, [47]). In a further application, we showed that the step-like response of ISEs with a strong inward ion flux (Fig. 1, bottom) can be used as a kind of chemical amplification. A pair of such electrodes showing slightly different positions of the potential step induce, within a narrow activity range, a peak-like response that is >1000 times larger than the potential change found with a conventional ISE [48]. Since the step-like response of such ISEs strongly depends on ion fluxes near the membrane surface, it is expected that any chemical reaction in the surface layer of the membrane would also induce large potential shifts. Potentiometric measurements with a kind of marker ion could then be used to detect such surface reactions. Means for the selective surface immobilization of chemical recognition elements are currently under investigation [49].

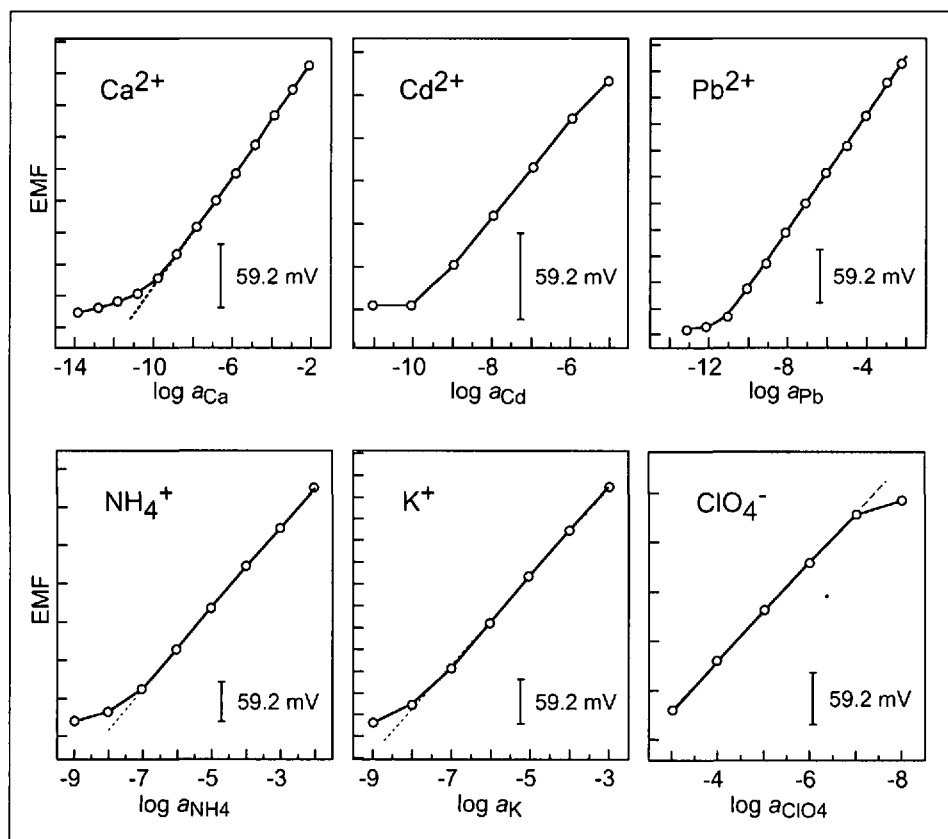


Fig. 2. Response functions of some ISEs exhibiting specially good lower detection limits [8].

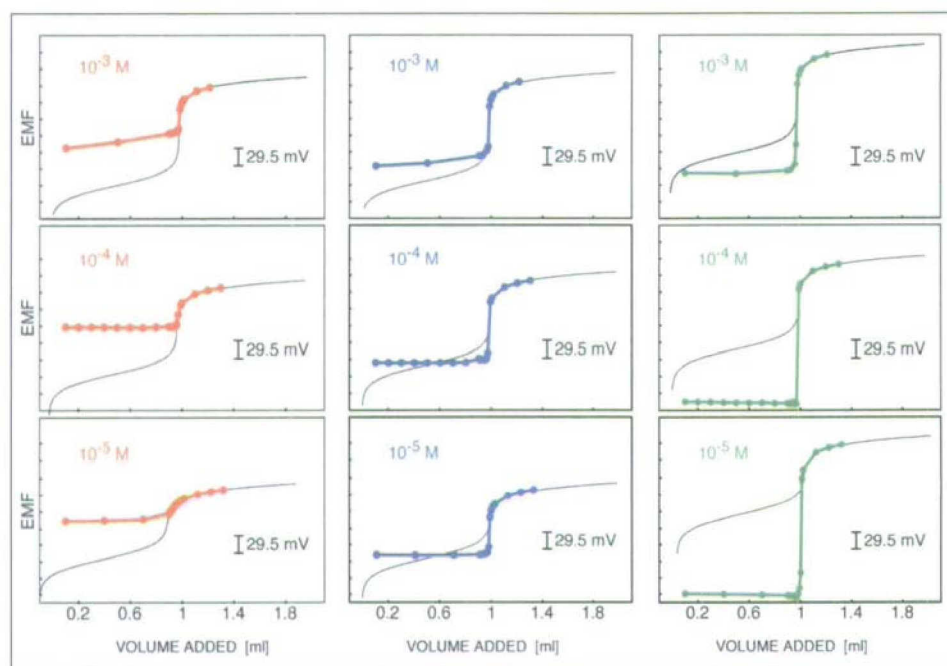


Fig. 3. Titration of the indicated concentrations of EDTA with $\text{Pb}(\text{NO}_3)_2$ at pH 4.5, monitored with the three types of ISEs schematically described in Fig. 1. Theoretical curves for the equilibrium situations are drawn in black. Red (conventional ISE): At low added amounts of Pb^{2+} , its concentration in the phase boundary layer is too high, which causes a cut-off of the titration curve and too small potential changes at the end point. Blue: With the optimized ISE, the cut-off is smaller and the end point better. Green: The ISE with ion uptake induces a larger EMF change at the end point than theoretically expected for the equilibrium situation. The improvement of the end point detection is, however, limited to cases where the concentration of Pb^{2+} beyond the end point is so high that the ion uptake by the membrane is negligible [47].

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