

Ionophore-Based Ion-Selective Electrodes in Non-Zero Current Modes: Mechanistic Studies and the Possibilities of the Analytical Application

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Abstract—This mini review briefly describes (i) literature data on the non-zero current measurements with ionophore-based ion-selective electrodes (ISEs) aimed at fundamental studies of the mechanism of their potentiometric response, and (ii) the data on the possibilities of analytical applications of ISEs in voltammetric and constant potential chronoamperometric/coulometric modes, in particular the K⁺ ion assay in blood serum with the sensitivity of 0.1%. A special attention is paid to the basics of voltammetry and chronoamperometry/coulometry with the ionophore-based ISEs, and to how and why these methods differ from the classical voltammetry and coulometry.

Keywords: ion-selective electrodes, ionophores, chronopotentiometry, impedance, voltammetry, constant potential chronoamperometry/coulometry

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Ion-selective electrodes (ISEs) with solvent-polymeric membranes containing neutral and charged ionophores have been used as potentiometric sensors for quantification of a wide range of analytes already for several decades [1–8]. During this period of time the non-zero current mode of measurements with ISEs was mostly limited to fundamental studies of the mechanism of the electrode response and the origin of its selectivity [9–15], or to improve the detection limits [16–18] and/or the sensitivity of ISEs, in particular for polyion sensing [19–23]. Until the year 2010, analytical applications of ISEs in non-zero current mode were scarce. However, in recent years practical use of ISEs by techniques like voltammetry, amperometry, coulometry and chronopotentiometry have become increasingly popular.

In this review we focus on non-zero current measurements with ISEs with ionophore-based solvent-polymeric membranes. We do not discuss here data obtained with purely liquid systems—interfaces between two immiscible electrolyte solutions because the latter make a separate piece of science, for a review see [24]. This mini review contains a brief description of mechanistic studies of the ISEs, a discussion on the use of ISEs in voltammetric mode, and also in chronoamperometric and coulometric modes.

STUDIES OF THE MECHANISM OF THE ISE POTENTIOMETRIC RESPONSE BY NON-ZERO CURRENT MEASUREMENTS

Most theoretical descriptions of the ISE membrane potential and selectivity employ the equilibrium approach according to which the selectivity coefficients to the primary ion over the interfering ion(s) are proportional to the ratios of the respective ion-ionophore complex formation constants [2, 5, 6, 25–27]. Camman advocated the kinetic approach suggesting the selectivity coefficients are proportional to the ratios of the standard exchange current densities of the competing ions [9–11].

Ion-ionophore complex formation constants can be measured potentiometrically using membranes containing the ionophore of interest and a chromoionophore [28, 29], or (and this method is more reliable) by the measurements of the potentials of the segmented sandwich membranes [15, 27, 30–35]. The sandwich potential method also allows for estimation of the association constants of ion pairs and triplets in the ISE membranes [36, 37].

The exchange current densities at the interface between the sensor phase (membrane) and the aqueous solution were estimated, primarily, by means of the electrochemical impedance measurements [9–15, 38, 39]. Measurements of the exchange current densities at ISEs are tricky. In fact, the measured values represent the interfacial charge transfer resistances. The

latter are by several orders of magnitude lower than the membrane bulk resistances because the resistivity of the ISE membranes is ca. $10^5 \Omega \text{ m}$. It is therefore difficult to resolve the charge transfer resistances connected in series with the membrane bulk.

This is why there are only a limited number of reports containing reliable values of the exchange currents at ISEs [11, 13, 15, 39]. To the best of our knowledge there is only one report on the ion-ionophore complex formation constants and exchange current densities measured in parallel, with the same membranes [15]. The study was performed with Li^+ -selective electrodes based on a Li^+ ionophore. The complex formation constants were measured by the segmented sandwich membrane technique, and the exchange current densities by the impedance method. Interestingly, the selectivity coefficients to Li^+ over K^+ and Na^+ ions correlate almost equally well with both the equilibrium and the kinetic data.

Pulse methods (primarily current pulse method: chronopotentiometry) are suitable for measurements of the membrane bulk resistance as well as the polarization curves η vs. time [40]. These curves, normally, comprise superposition of a decaying exponent and a concentration polarization proportional to a square root of time:

$$\eta = i \left[R \left(1 - e^{-\frac{t}{RC}} \right) + N\sqrt{t} \right], \quad (1)$$

$$N = \frac{2RT}{F^2\sqrt{\pi}} \left(\frac{1}{c_+\sqrt{D_+}} + \frac{1}{c_-\sqrt{D_-}} \right). \quad (2)$$

Here η is the polarization, i is the polarizing current density, t is time, R is the polarization resistance, c is the capacitance connected in parallel with R . Sometimes these values can be attributed to the interfacial charge transfer resistance and to the capacitance of the electrical double layer at the membrane/solution interface, however, this is hardly generally true. The N factor is determined by c_+ and c_- —the concentrations of the ionic species, and D_+ , D_- —the diffusion coefficients of these species in the membrane. By these measurements it is sometimes possible to estimate the association degree of the ion-ionophore complexes with ion-exchanger in the membranes as well as the diffusion coefficients of the species [32, 37, 41]. However, the reliability of these estimations is limited due to a large number of simplifications in derivation of Eq. (1).

Bobačka proposed chronopotentiometric test aimed at fast estimation of the quality of solid contact ISEs [42]. The polarization curve allows prediction whether the chosen combination of (1) the electronically conducting substrate (e.g. glassy carbon), (2) the transducer layer (most often a conducting polymer or a carbon-based material with a large area) and (3) the sensor membrane, is promising in terms of the ISE

potential stability over time. This study, obviously, was of an academic and also of a practical importance.

According to the current views on the mechanism of the potentiometric response of ISEs, within the Nernstian response range the bulk resistance of ISE membranes must be constant. Obviously, co-extraction of the electrolyte from solution results in decrease of the membrane bulk resistance, however in this case ISE potentials deviate from the Nernst law. Replacement of the primary ions by interfering ions may cause changes of the membrane bulk resistance if this replacement entails a change in the association degree of the membrane electrolyte. Again, such a replacement results in the deviations from the Nernstian response up to the complete loss of the sensitivity to the primary ion. However, indications exist on the non-constancy of the ISE membrane bulk resistance within the Nernstian response range [15, 43]. Furthermore, the variation of the bulk resistance of K^+ -selective membrane was utilized in the development of a conductometric sensor for K^+ ions [43].

A systematic study of the bulk resistance of Ca^{2+} , K^+ , Cd^{2+} and NO_3^- ISE membranes performed by means of chronopotentiometric and impedance measurements revealed the following trend: the bulk resistance of the membranes under study was roughly constant over the range of the concentration of the respective electrolyte from 0.1 to 0.001 M, and increased significantly along with the further dilution [44–47]. Furthermore, the major part of the change (90–95% of the whole effect) occurs in a few minutes after the change of the concentration [44, 45, 47]. It was found that the bulk resistance of the membranes correlates with water uptake registered gravimetrically [47, 48]. It is known that water in membranes forms droplets with minimal size ca. 16 nm, and these droplets are non-uniformly distributed in the ISE membranes: the surface layers are enriched in water [49–52]. Originally, these data were obtained with the use of additions of colored salts [49, 50] or chromoionophores [51, 52]. Recently these data were confirmed directly by means of ATR-FTIR imaging of the profiles of polyvinylchloride (PVC), plasticizer 2-nitrophenyloctyl ether (oNPOE) and water in Cd^{2+} -selective membranes. It was shown that most of water in membranes is located within 50 μm from the membrane surface, and at depths of 150 μm water was not detected [48]. It was suggested that water droplets in membranes hamper the diffusion of lipophilic ion-ionophore complexes and ion-exchangers because lipophilic species are confined to the coherent organic phase in the membrane, and have to bypass the water droplets, so their average path length increases. Thus, the concentration of the species in the organic phase of the membrane is constant ensuring the Nernstian response of the ISE, while the resistance increases along with the increased sorption of water [48, 53].

It may appear that these findings are of only academic interest. It was shown, however, that water uptake and the bulk resistance of ISE membranes actually depends on the ionic strength of the solution, or on the total concentration of ions, rather than on the concentration of the respective primary ion [53]. This offers a prospect of measurements of not only activities but also of concentrations of ions by the same sensor. An ISE, in the potentiometric (zero-current) mode delivers data on the activity of the analyte, and measurements of its resistance allows for the estimation of the ionic strength of the sample. Once the latter is known, the activity can be re-calculated into the concentration by means of e.g. the Debye–Hückel theory.

ISEs IN VOLTAMMETRIC MODE: FUNDAMENTAL STUDIES AND THE POSSIBILITIES OF THE ANALYTICAL APPLICATION

Voltammetry with electrochemically active analytes at electrodes made of an electronic conductor (a noble metal or a carbon-based material, with a non-modified or a modified surface) assumes a RedOx reaction at the interface between the electrode and aqueous solution [54]. The bulk resistances of the electrode and of the solution do not hamper the measurements. The ISE membranes are typically high-resistant, and with these objects the implementation of voltammetric measurements is much more difficult. Due to a high Ohmic resistance of the membranes, common ISEs with membranes with thicknesses of 0.2–0.7 mm show no current peaks in the cyclic voltammetric (CV) mode and behave like high-ohmic resistors. Horvai managed to obtain peaks in CV curves with PVC membrane plasticized with oNPOE and containing chlorides of tetrahexylammonium or tetraphenylarsonium, when these cations were present in the aqueous phase [55]. Apparently, Horvai's membranes were low-resistant due to high concentrations of chlorides of tetrahexylammonium or tetraphenylarsonium in the membrane phase. Petrukhin's group reported on voltammetric measurements of NH_4^+ ion using different calixarenes as neutral ionophores and potassium tetrakis(p-Cl-phenyl) borate (**KCITPB**) as ion-exchanger in oNPOE. The sensor phase was low-resistant because of the lack of PVC, so the system consisted of liquid phases [56].

Few other examples of successful voltammetric measurements with relatively thick membranes refer to fundamental electrochemical studies. By means of square wave voltammetry with PVC membranes Serna measured the standard ion transfer potentials of dialkylimidazolium and alkylpyridinium cations from water to oNPOE [57]. Very important results were obtained by the Amemiya's group regarding the mechanism of the ion transfer across the interface between

the ISE membrane and aqueous solution. It was shown by the CV measurements that Ag^+ , K^+ , Ca^{2+} , Ba^{2+} and Pb^{2+} ions form complexes with the respective neutral ionophores directly at the membrane/solution interface, in contrast with the thermodynamically equivalent two-step mechanism based on the simple transfer of an ion from water to membrane followed by its complexation in the membrane bulk [58].

Use of thin membranes facilitates the voltammetric measurements with ISEs and makes them more suitable for the analytical applications. The lack of the mechanical robustness of thin membranes made of plasticized PVC calls for the so-called solid contact construct of the electrode when the sensor membrane is either drop-cast or spin-coated on a solid substrate, and there is no internal aqueous solution [2, 5, 6].

Voltammetric measurements of electroactive species of clinical relevance, and especially in real samples e.g. blood are often problematic due to the fouling of the electrodes. Lindner's group performed a systematic study of glassy carbon electrodes modified with plasticized PVC membranes similar to those used in potentiometric ISEs [59]. It was shown that PVC-coating drastically diminished fouling of the sensors. The selectivity also was improved due to the difference in partition coefficients of the hydrophobic analytes and hydrophilic interferences between sample and PVC membrane. Successful measurements were performed of a number of analytes (the limits of detection, DL values, μM are shown in brackets): amitriptyline (0.03), aripiprazole (0.009), citalopram (0.008), propofol (0.03), rapamycin (0.003), sertraline (0.13) and zortress (0.01). Besides the practical results, a detailed theoretical consideration of the factors influencing selectivity and sensitivity of the measurements was also presented.

The Bond's group developed Na^+ , K^+ and Ca^{2+} voltammetric ISEs with membranes with thicknesses of less than 1 μm and containing tetracyanoquinodimethane as electrochemically active species. In the case of a cation sensor, ionophore facilitated transfer of the target cation from the aqueous solution to the membrane phase occurs in the course of the reduction of the electroactive species present in the membrane to maintain charge neutrality [60]. Functionalized cationic [6] helicenes were used for Na^+ ion detection with an ISE containing Na^+ ionophore [61] and for CO_3^{2-} detection with an ISE based on ionophore selective to CO_3^{2-} anion [62] in the same role as electroactive species maintaining the charge neutrality.

The presence of electroactive species in the ISE membrane may cause sensitivity to RedOx species in samples, which is obviously non-desirable. Circumventing this disadvantage relies on the use of conducting polymers (CPs) as transducer layers between an electronically conducting substrate (most often glassy carbon) and an ionically conducting sensor mem-

brane. In these voltammetric ISEs, when an ion is transferred from the aqueous solution to the membrane or vice versa, the charge neutrality is maintained by the respective oxidation or reduction of the CP, and transfer of the dopant ion between the CP and the membrane layers. In this case there is no need for an electroactive species to be present in the membrane. The decisive results in these studies have been achieved by the Amemiya's and the Bakker's groups.

The Amemiya's group published several papers devoted to subnanomolar ion detection by stripping voltammetry with solid contact ISEs with membranes with thicknesses of ca. 0.7 μm . Gold electrodes modified with poly(3-octylthiophene) doped with perchlorate (POT- ClO_4) was spin-coated with a membrane containing PVC, oNPOE and tetradodecyl ammonium tetrakis(pentafluorophenyl)borate (TDDATFPB). By stripping voltammetry ClO_4^- anion was measured with the detection limit of 0.2–0.5 nM with the background of deionized water, commercial bottled water and tap water [63]. Gold electrodes modified with POT- ClO_4 or with poly(3,4-ethylenedioxythiophene) doped with tetrakis(pentafluorophenyl)borate (PEDOT-TFPB) and covered with thin membranes containing PVC, oNPOE and TDDATFPB were used for measurements of tetrapropylammonium and of hexafluoroarsenate with LOD of 0.1 nM [64]. In the case of the hexafluoroarsenate anion sensing the transfer of the analyte from the sample solution to the membrane is accompanied by oxidation of POT, and the TFPB $^-$ anion compensates the cationic charge of POT $^+$. On the contrary, the in the tetrapropylammonium cation sensing the analyte transfer from solution to membrane results in de-doping of PEDOT, so TFPB $^-$ compensates the tetrapropylammonium charge in the membrane layer. In the two cases above, the electrons flow from the CP layer to the metal, or vice versa, respectively. Stripping voltammetry was also used for measurements of K^+ and NH_4^+ ions at nanomolar levels with gold electrode modified with PEDOT-TFPB and spin-coated with a membrane containing valinomycin [65]. In the case of protamine (a heparin antidote), it was shown that the ISE signal is caused by reversible adsorption of protamine at the membrane/water interface, down to 0.038 $\mu\text{g}/\text{mL}$ [66]. The voltammetric mode of measurements allows for multiion detection: the same ISE is used to quantify several ions. In the course of the potential scanning, initially the ion selectively complexed by the ionophore (primary ion) is transferred to the membrane. Once the ionophore is exhaustively depleted, the primary ion is exchanged by the secondary favorable ion at more extreme potentials. In this way Na^+ ion peaks were obtained with ISE containing Na^+ -selective ionophore, and at more positive potentials the ISE also showed peaks related to the concentrations of Ba^{2+} or Sr^{2+} ions. With Li^+ ionophore in the membrane, the

ISE showed a peak of Li^+ ion and at more positive potentials a Ca^{2+} ion peak [67].

The opportunity to exploit the multianalyte ion detection with the same ISE was thoroughly studied by the Bakker's group [68, 69]. Unlike Amemiya's approach, the ISE membrane contained several ionophores, each facilitated the transfer of the respective ion from the sample solution phase to the ISE membrane phase. With ca. 300 nm thin membrane containing Li^+ and Ca^{2+} ionophores and deposited on top of POT- ClO_4 layer on glassy carbon, CVs with well-resolved peaks of Li^+ and Ca^{2+} ions have been obtained [68]. Similar ISE with a membrane containing Li^+ , Na^+ and K^+ ionophores allowed for simultaneous measurements of these three analytes over the range of 0.1 to 100 mM. In fact, nice peaks were obtained also for Mg^{2+} and Ca^{2+} ions when the respective ionophores were also presented in the membrane, however the respective peaks overlapped with those of Li^+ and Na^+ [69].

Importantly, the regularities of the voltammetry with electrodes (e.g. made of glassy carbon) and modified with a conducting polymer, covered, in turn, with a thin ionophore-based membranes are distinctly different from those of the classical voltammetry with electrodes without a membrane cover. In the classical voltammetry, the peak current, ideally, is proportional to the concentration of the analyte in the solution, and the peak potential is characteristic for a particular RedOx reaction which takes place at the interface between the electrode and the sample solution [54].

On the contrary, in the case of voltammetry with electrodes modified with a CP and covered with an ionically conducting membrane, the peak current does not depend on the concentration of the analyte in the sample, whereas the peak potential varies with the concentration of the solution. Furthermore, the peak potential depends on the activity of the analyte rather than on its concentration. We believe that these regularities deserve a special consideration presented below. The theory explaining these regularities was developed in the Bakker's group [68, 70, 71]. The essence of the theory is as follows.

Let us consider an electrode e.g. a glassy carbon rod (GC) modified with a layer of a conducting polymer, e.g. POT, which is presented in two forms: neutral (reduced) POT and oxidized POT $^+$. The CP layer, in turn, is covered with a thin ion-selective membrane. The membrane contains an ionophore selective to M^+ cation, and an ion-exchanger MR with a lipophilic anion R^- . The latter distributes between the CP layer, compensating the positive charge of POT $^+$, and the membrane layer compensating the positive charge of M^+ cation. It is assumed that the diffusion of species within the membrane and the CP can be neglected (the complications related to diffusion are considered elsewhere [70, 71]). It is also assumed that the electro-

chemical processes at the interfaces between the CP and the membrane and between the membrane and the solution are fast, so both interfaces are at electrochemical equilibrium even when an external potential is applied. Respectively, the interfacial potentials at the CP/membrane interface (E_p) and the membrane/solution interface (E_M) obey the Nernst equation with $S \cong 2.303RT/F$:

$$E_p = E_p^0 - S \log \frac{c_{\text{POT}}}{c_{\text{POT}^+}}, \quad (3)$$

$$E_M = E_M^0 + S \log \frac{a_M}{c_M}. \quad (4)$$

Terms E_p^0 , E_M^0 are determined by the standard chemical potentials of the species involved in the formation of interfacial electrical potentials, and are assumed constant. The values c_{POT} , c_{POT^+} , a_M , and c_M refer, respectively, to the concentrations of POT and POT^+ in the CP layer, the activity of M^+ in the aqueous solution, and the concentration of M^+ in the membrane. When the applied potential is scanned to more positive values the CP is oxidized, and an electron transfers from the CP layer to GC. The positive charge of the CP is compensated by the transfer of the exchanger anion R^- from the membrane layer to the CP layer. In turn, M^+ cation is released from the membrane to the aqueous phase. This is how current flows through such an ISE. For the external voltage E_{applied} we obtain:

$$E_{\text{appl}} = \text{Const} + E_p + E_M = E_p^0 + E_M^0 - S \left(\log \frac{c_{\text{POT}}}{c_{\text{POT}^+}} - \log \frac{a_M}{c_M} \right). \quad (5)$$

The term Const combines the contributions from the reference electrode, from the junction potential at the contact of the salt bridge with the solution, and from the potential at the interface between the CP and glassy carbon. These contributions are considered constant. The CP is confined to the CP layer, and the total concentration of the CP (whatever the form) in the CP layer is constant:

$$c_{\text{POT}}^{\text{tot}} = c_{\text{POT}} + c_{\text{POT}^+}. \quad (6)$$

Unlike the CP, the R^- anion is presented both in the CP layer and in the membrane layer, and the total quantity of R^- in the whole ISE is constant. Next, according to the Bakker' theory [68] we assume that either the volumes of the CP layer and the membrane layer, or their parts involved in the electrochemical processes are equal in size. Then for the total concentration of R^- we can write:

$$c_{\text{R}}^{\text{tot}} = c_M + c_{\text{POT}^+}. \quad (7)$$

Now the Eq. (5) can be re-written as follows:

$$E_{\text{applied}} - S \log a_M = \text{Const} + E_p^0 + E_M^0 - S \frac{(c_{\text{POT}}^{\text{tot}} - c_{\text{POT}^+}) (c_{\text{R}}^{\text{tot}} - c_{\text{POT}^+})}{c_{\text{POT}^+}}. \quad (8)$$

Using a following auxiliary parameter:

$$\alpha = 10^{\frac{E_{\text{applied}} - S \log a_M}{S}}, \quad (9)$$

and combining Eqs. (3) to (9) we obtain for c_{POT^+} :

$$\alpha c_{\text{POT}^+} = c_{\text{POT}}^{\text{tot}} c_{\text{R}}^{\text{tot}} - c_{\text{POT}}^{\text{tot}} c_{\text{POT}^+} - c_{\text{POT}^+} c_{\text{R}}^{\text{tot}} + c_{\text{POT}^+}^2. \quad (10)$$

The solution of this quadratic equation is as follows:

$$c_{\text{POT}^+} = \frac{(c_{\text{POT}}^{\text{tot}} + c_{\text{R}}^{\text{tot}} + \alpha) - \sqrt{(c_{\text{POT}}^{\text{tot}} + c_{\text{R}}^{\text{tot}} + \alpha)^2 - 4c_{\text{POT}}^{\text{tot}} c_{\text{R}}^{\text{tot}}}}{2}. \quad (11)$$

Finally, let us take into account that the applied potential is scanned over time t with the scan rate v starting from an initial value E_{initial} to more positive values:

$$E_{\text{applied}} = E_{\text{initial}} + vt. \quad (12)$$

Further results are simulated using the Bakker' theory for linear sweep voltammetry assuming $\text{Const} + E_p^0 + E_M^0 = 0$ and $E_{\text{initial}} = -0.5V$. The curves of the dependence of c_{POT^+} on the applied potential are shown in Fig. 1. The data refer to $c_{\text{POT}}^{\text{tot}} = 0.005\text{M}$ and $c_{\text{R}}^{\text{tot}} = 0.01\text{M}$, and to three values of the activity of the M^+ ion in the solution: 1, 10 and 100 mM.

One can see that, essentially, these are titration curves. Indeed, when external potential is applied, and current flows, the CP is oxidized. Gradually, the whole POT transforms to POT^+ . The applied potential, to a constant value, equals $E_p + E_M$, and E_M obeys the Nernst law. Therefore, the tenfold change in the activity of the analyte in the solution results in $2.303RT/F$ mV change in the E_M value. Thus, at the same value of the applied potential the E_p is in $2.303RT/F$ less positive, and the oxidation of POT in the course of the potential sweep lags accordingly. The curve therefore shifts to more positive potentials.

Current is the derivative of the charge over time. Therefore, the current curves must be the differential titration curves. The current peaks originate from the fact that in the inflection point of the titration curve the derivative is maximal. The results simulated for the same system as above are presented in Fig. 2.

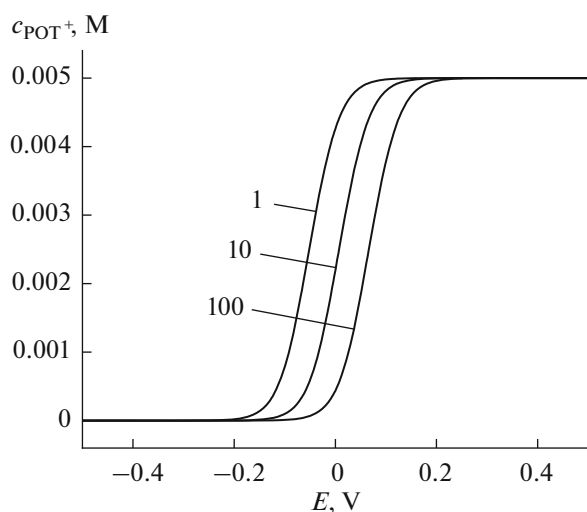


Fig. 1. The curves of the dependence of c_{POT^+} on the applied potential, $c_{\text{POT}}^{\text{tot}} = 0.005 \text{ M}$, $c_{\text{R}}^{\text{tot}} = 0.01 \text{ M}$, and a_{M} equals 1, 10 or 100 mM.

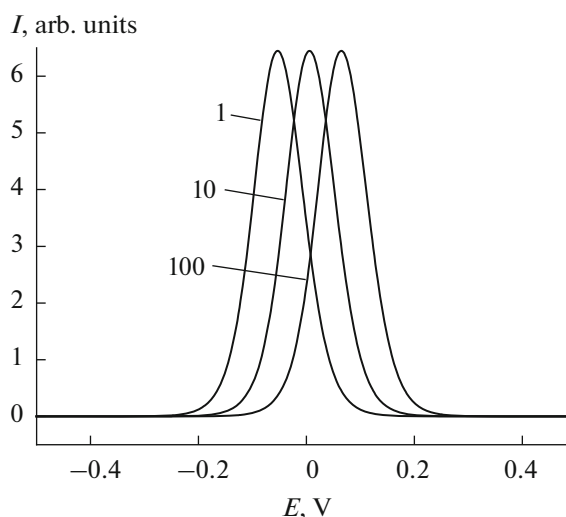


Fig. 2. Current curves simulated for $c_{\text{POT}}^{\text{tot}} = 0.005 \text{ M}$, $c_{\text{R}}^{\text{tot}} = 0.01 \text{ M}$, and a_{M} equals 1, 10 or 100 mM. Scan rate is 100 mV/s.

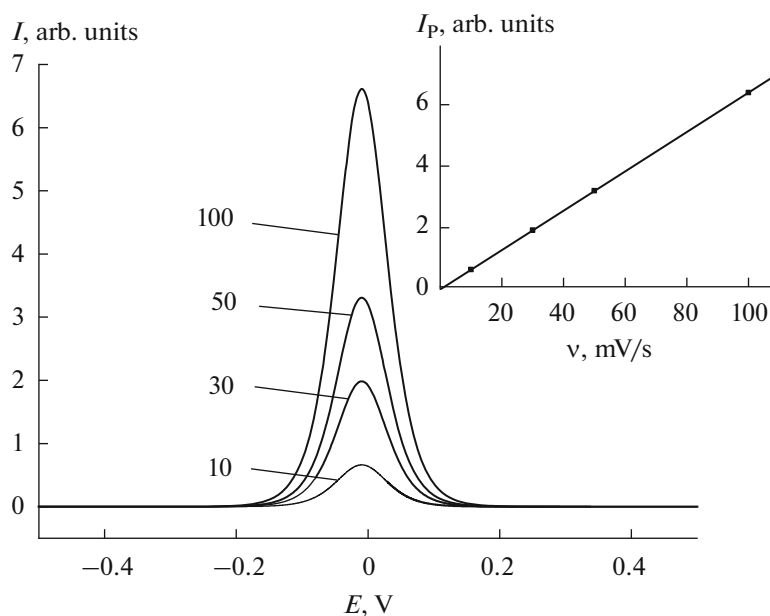


Fig. 3. The dependence of current on the applied potential at scan rates 10, 30, 50 and 100 mV/s, for the case $c_{\text{POT}}^{\text{tot}} = 0.005 \text{ M}$, $c_{\text{R}}^{\text{tot}} = 0.01 \text{ M}$ and $a_{\text{M}} = 10 \text{ mM}$. Inset: the peak current vs. the scan rate.

The peak current is determined by the rate of the oxidation of POT to POT^+ . This depends on the scan rate but does not depend on the composition of the solution. Therefore, the peak current does not depend on the sample composition.

One can ask: where is the factor of the nature of the RedOx reaction gone? It is not gone: if we replace one CP, e.g. POT, with another one, e.g. PEDOT, the curves shown in Figs. 1, 2 will be shifted.

Since the current is determined by the rate of the oxidation of POT to POT^+ i.e. by the scan rate, one can expect linear dependence of the current (including the peak current) on the scan rate, as illustrated in Fig. 3. This is analogous to classical voltammetry when the process is limited by the reaction rate at the electrode.

The theoretical predictions were nicely confirmed with the experimental data [66–71].

ISEs IN A CONSTANT POTENTIAL
(CHRONO)AMPEROMETRIC
AND COULOMETRIC MODES

Ion-selective coulometry has been invented by the Bobacka's group [72–76]. In fact, current is recorded, and charge is obtained by the integration of current over time. Large improvement of the sensitivity makes the main advantage of this method over the zero-current potentiometry: 0.1% instead of 1–5% [76]. The electrodes comprised glassy carbon rods with electrochemically deposited CP poly(3-octylthiophene) doped with poly(styrenesulfonate) (PEDOT-PSS) layer covered with a drop-cast or spin-coated plasticized PVC membrane. The membrane thickness was ca. 5–10 μm i.e. thicker than for the voltammetric measurements but much thinner than in the zero current potentiometry. Initially, the studies were limited to K^+ -selective ISEs [72–74, 76]. Later, it was shown that the method can be also applied for the quantification of Ca^{2+} and Ba^{2+} ions [77], Cl^- [75] and NO_3^- [78].

The idea of the method is as follows. The potential of an I^{z_i} -selective electrode as a whole is kept constant artificially by a potentiostat, whereas the boundary potential at the interface between the ISE membrane and solution responds to the changes of the I^{z_i} ion activity in solution according to the Nernst law. The discrepancy between an artificially fixed overall potential of the ISE and the changes in the boundary potential is compensated by spontaneous current flow across the electrode. In the very first moment after the change of the solution composition, the respective change of the boundary potential at the membrane/solution interface is compensated by the Ohmic drop, primarily on the membrane bulk because the resistances of the CP layer, of the GC substrate, and of other parts of the cell are significantly lower. The current flow results in oxidation or reduction of the CP, and in the respective changes of the potentials at the membrane/CP and the CP/substrate interfaces. This potential change contributes to the compensation of the aforementioned discrepancy, and the current decays over time. During this process, the CP layer capacitance is re-charging, and the charge value can be obtained by integration of the current over time.

The theory of the chronoamperometric and coulometric responses of the ISEs assumes that the ISE can be represented by a resistor (membrane) and a capacitor (CP layer) connected in series [75]. The respective equation for i_t current flowing across the ISE at a time t after an abrupt change of the activity of I^{z_i} ion changes from a_i^{ini} initial to a_i^{fin} final value can be written as follows:

$$i_t = \frac{RT}{z_i F} \ln \frac{a_i^{\text{ini}}}{a_i^{\text{fin}}} \frac{1}{R} e^{-\frac{t}{R_{\text{mem}} C_{\text{pol}}}} \quad (13)$$

Here R_{mem} is the membrane resistance, and C_{pol} is the capacitance of the CP layer. The respective charge Q_t accumulated by the time t is described as follows:

$$Q_t = \frac{RT}{z_i F} \ln \frac{a_i^{\text{ini}}}{a_i^{\text{fin}}} c_{\text{pol}} \left(1 - e^{-\frac{t}{R_{\text{mem}} C_{\text{pol}}}} \right) \quad (14)$$

The driving force of the current flow and of the charge accumulation is the change of the activity of the respective ion in solution. This is why this type of coulometry delivers the information on the activity, not on the concentration of ions, in contrast with classical coulometry when the current is set by a galvanostat.

As mentioned above, the main advantage of the coulometric readout is a drastic increase of the sensitivity of the analysis. This is achieved by increasing the capacitance of the conducting polymer layer between the sensor membrane and the substrate, see also Eq. (14) [76]. The sensitivity to a change of the analyte ion concentration of 0.1% relative to the initial value was demonstrated, the coulometric mode of measurements allows resolving 0.1 mM changes of K^+ ion concentration in blood serum sample containing 4.4 mM K^+ [76]. Here the concentration instead of activity is discussed because the ionic strength of the samples was constant. From the sensitivity viewpoint the coulometric mode is by far superior to the classical potentiometric readout where the sensitivity of the ISE response to species I^{z_i} is limited by the value of the Nernst factor $RT/z_i F$.

On the other hand, coulometric measurements require a relatively long time to accumulate the signal. From this point of view, the use of the current value instead of that of charge, as the analytical signal, may be advantageous [79]. However, a change of the solution composition requires time. This produces uncertainty on the real time value which corresponds to $t = 0$ in Eqs. (13), (14). Furthermore, the signal measured during the procedure of the solution change is noisy due to the respective manipulations and stirring. Because of this, the current value at $t = 0$ cannot be measured accurately. In contrast, the sensitivity of the value of the accumulated charge to the uncertainty about $t = 0$ is, obviously, very much less. Therefore, charge, and not current, is typically used as the analytical signal in such measurements.

Adding a commercially available electronic capacitor in series with the ISE allows for drastic reduction of the coulometric response time [80] although on cost of the sensitivity of the measurements. This approach: use of a capacitor in series with the electrode makes it possible to perform coulometric mea-

measurements with classical ISEs with an internal solution and an internal electrode, e.g. Ag/AgCl [81].

Another approach aimed at shortening the response time in coulometric measurements relies on fitting the current/time and charge/time curves to the theoretically expected equations: Eqs. (13), (14) [82]. The study was fulfilled with valinomycin-based K⁺-ISE as model system, and it was shown that Eqs. (13), (14) not always allowed for successful fitting of the experimental curves. It was concluded that the current flow across the ISE membrane results in concentration polarization. To account for this, Eqs. (13), (14) were modified by adding the Cottrellian term yielding [82]:

$$i_t = \frac{RT}{z_I F} \ln \frac{a_I^{\text{ini}}}{a_I^{\text{fin}}} \left[\frac{1}{R_{\text{mem}}} e^{-\frac{t}{R_{\text{mem}} c_{\text{pol}}}} + \left(\frac{N}{2}\right) t^{-1/2} \right], \quad (15)$$

$$Q_t = \frac{RT}{z_I F} \ln \frac{a_I^{\text{ini}}}{a_I^{\text{fin}}} \left[c_{\text{pol}} \left(1 - e^{-\frac{t}{R_{\text{mem}} c_{\text{pol}}}} \right) + N t^{1/2} \right]. \quad (16)$$

The N factor is dependent on A_E —the ISE cross-section area, c_I —the concentration of the ionic species in the membrane, and D_I —their diffusion coefficient: $N = 2FA_E D_I^{1/2} c_I (\pi^{1/2} t^{1/2})^{-1}$ [83]. It was confirmed experimentally that current and charge at any time t are linearly dependent on the logarithm of the ion activity in solution (or of the ion concentration if the ionic strength is constant) [82]. This result is consistent with Eqs. (13)–(16) and thus further confirms the theory. From the practical viewpoint this means that the linear dependencies of the current and of the charge on the analyte ion activity (taken at a certain time) can be used as calibration plots. This allows for a cutoff: waiting for a total decay of current and, respectively, for a complete saturation of charge is not needed. In this way K⁺ ion concentration was measured in serum samples using calibration with model solutions with constant ionic strength of 145 mM.

The Karyakin's group showed that the amperometric measurements at a constant potential are especially suitable in a flow injection mode. Screen-printed carbon electrode modified with boronate-functionalized polyaniline or Prussian Blue and lactate oxidase was successfully used in amperometric detection of lactate in human sweat [84]. Rigorously speaking, these data do not refer to ionophore-based membranes. However, promising results were obtained also with K⁺-selective and Na⁺-selective ISEs (glassy carbon/PEDOT-PSS/PVC membrane) in flow injection amperometric measurements at a constant potential [85].

The ion-selective ionophore-based membranes, traditionally, were used in analysis only under an equilibrium or a steady-state conditions, in the potentiometric ISEs or optodes. Non-zero current measure-

ments were used only for the studies of the mechanism of the response of these sensors. Currently, however, the ionophore-based membranes are increasingly applied for an analysis under non-steady conditions when a current flows across the sensor. These new modes of the measurements: voltammetry, and the constant potential chronoamperometry and coulometry allow for multianalyte measurements with a sole sensor, and for a significant improvement of the sensitivity of the analysis. Without doubt, we will see further development of these techniques in near future.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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