Chapter 1
Introductory Issues

1.1 Ion-Selective Electrodes: What are These?

When I give a course in ion-selective electrodes, I normally ask my students in the very beginning of the first lecture: did you ever measure pH? Almost always, even if these are young first-year students, their answer is “yes.” Indeed, the most common and most frequently used ISE, the glass pH electrode, is familiar to nearly everybody who is doing chemistry, biology, in many branches of technology in industry, in agriculture, in environmental monitoring, and in various other activities. Thus, most of us know at least a little bit about ISEs and, more generally, about chemical and also physical sensors.

In this book, we will try to look at ISEs and related devices in a systematic way.

Ion-selective electrodes became routinely used analytical tool, and sometimes we even miss to realize the relation between ISEs and other kind of sensors. It may be therefore useful to outline briefly what is sensor and what kinds of sensors we currently know.

Normally, we call such measuring devices which transform the measured property into another kind of signal, mostly, an electrical signal which can be transmitted and registered by some instrument, as sensors. From this point of view, a traditional thermometer is not a sensor because we check the temperature by our own eyes, looking at the height of the mercury bar. However, a thermometer based on a thermocouple can be considered sensor. Sensor is a device which somehow gives a signal of the current state of the ambient, and if this state changes, the signal also changes. This happens due to some changes in the sensor caused by the changes in the environment. This we call “sensor response.”

Thus, for a sensor, we always have an input signal, a property which we wish to quantify, and an output signal which we can somehow register, see Fig. 1.1.

The input signal can be, for example, mass, pressure, temperature, humidity. The respective sensors are called “physical sensors.” Relatively modern kind of physical sensors comprise accelerometers used in automotive industry. For chemical sensors, the input signal is the chemical composition of the media with which the sensor is in contact. These can be liquid or gaseous samples, and also some semi-solid samples like soils. The output signal can be of the electrical nature:

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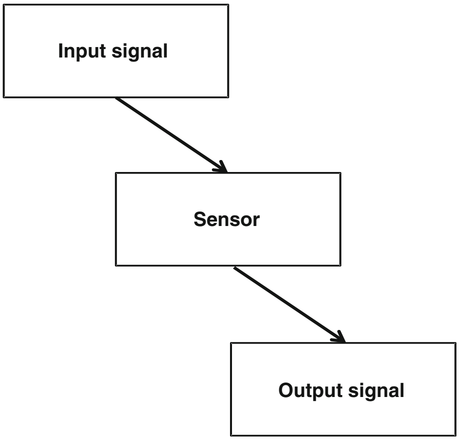

Fig. 1.1 Basic principle of sensing: sensor accepts an input signal and transforms it into an output signal

voltage, current, capacitance—and then, we denote the respective devices as electrochemical sensors. The output signal can be also the optical density, in optical sensors (optodes), or oscillation frequency, in sensors based on quartz crystal microbalances, or in acoustic sensors (surface wave or bulk wave acoustic sensors).

In this book, we will deal with ion-selective electrodes which comprise an important class of electrochemical sensors, giving potentiometric signal. Ideally, the potential of an electrode obeys equation below, known as the Nernst equation:

$$\varphi = \varphi^0 + \frac{RT}{z_I F} \ln a_I \tag{1.1}$$

In the Nernst equation, φ is the electrode potential, φ^0 is the so-called standard value of the potential, a_I is the activity and z_I is the charge number of the target analyte, R is the gas constant, T is the absolute temperature, and F is the Faraday constant. The electrode gains its standard potential value when $a_I = 1$.

One cannot measure a potential of an individual electrode, the measurable quantity is always the electromotive force (EMF), the difference between the potentials of two electrodes immersed into a solution, see Fig. 1.2, left side. A pair of electrodes immersed into a solution makes the so-called galvanic cell (galvanic element).

If one of the electrodes (the so-called indicator electrode) in the galvanic cell obeys the Nernst equation, while the potential of the other electrode (reference electrode) is constant (see Sect. 2.4), the EMF follows the equation below:

$$E = E^0 + S \log a_I. \tag{1.2}$$

Here, E is the measured EMF, E^0 is the standard EMF value at $a_I = 1$, and S is the response slope. Ideally, the slope is $S = \mathrm{d}E/\mathrm{d} \log a_I = 2.3026\, RT/F$.[1] At 25 °C, the ideal value of the slope is $S_{25} = 59.18/z_I$ mV. Equation (1.2) represents

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[1] Coefficient 2.3026 appears because in practical use of ISEs we always plot EMF against decimal logs instead of natural logs, and $\ln 10 = 2.3026$.

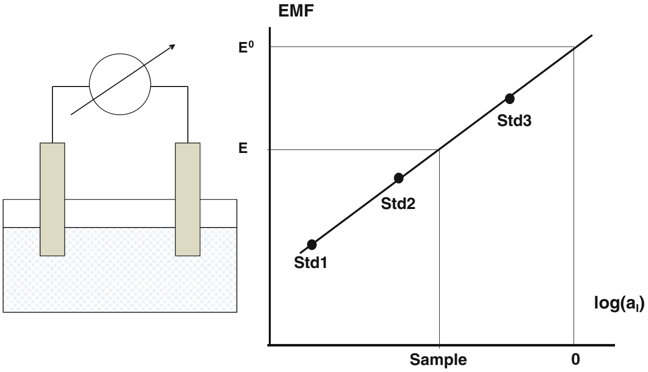

Fig. 1.2 Galvanic cell with two electrodes immersed into solution (*left*) and electrode calibration (*right*)

the practical form of the Nernst equation providing for some possible non-ideality of the response of the indicator electrode as well as that of the reference electrode. This is why instead of the ideal value $RT/z_I F$, the practical experimental slope $S = \mathrm{d}E/\mathrm{d} \log a_I$ appears in Eq. (1.2).

The values of E^0 the standard potential and S the slope are not *a priory* known. Therefore, one has to relate the measured signal (EMF) to the concentration (strictly activity) of the target analyte. This is made by performing calibration of the electrode, in fact, of the whole galvanic cell, using a series of standard solutions with known composition. Figure 1.2 (right side) illustrates a 3-point calibration procedure followed by the measurement of the activity of the analyte in the sample. First, the electrodes are immersed in several standard solutions (three in this example). The EMF values are measured, and in the respective 2D plot a line is obtained by linear regression. Ideally, it should be a straight line; therefore, it is recommended to use at least 3 standards to see whether it is true. The slope must be close to $RT/z_I F$ although it often deviates from this number in about 0.2–2 mV.

Once the calibration curve is obtained, and the calibration parameters: E^0 the standard EMF value and S the slope are known, one can use the electrode as measuring tool. The electrodes are now immersed into sample solution, and the measured EMF value delivers the value of the activity of the target analyte:

$$a_I = 10^{\frac{E-E^0}{S}}. \tag{1.3}$$

One can see that the values of interest: the activity and therefore also the concentration of the analyte are exponentially dependent on E the EMF measured in the sample, E^0 the standard EMF value and S the slope. Thus, the stability of the calibration curve of the electrode is of crucial importance. Normally, the slope is much better stable and reproducible than the individual EMF value. Bearing this in mind, we obtain from Eq. (1.2) the relative error of the analyte activity value:

$$\frac{\mathrm{d}a_I}{a_I} \approx S\mathrm{d}E. \tag{1.4}$$

The commonly used unit for the EMF measurements with ISEs is mV. An error of 1 mV in the EMF measurement translates into 4 % relative error in the concentration of a univalent analyte and into 8 % relative error for a divalent analyte. Normally, EMF values are registered with error significantly lower than 1 mV. Anyhow, the accuracy of the direct measurements with ISEs is relatively low. For better accuracy of analysis, the EMF values must be registered with precision of 0.1 and even 0.01 mV. On the other hand, Eq. (1.4) shows that the relative error of the analysis with ISEs remains constant within the whole linear range of the response, covering also diluted samples. This is a big and nearly unique advantage of the potentiometric analysis because in most of other analytical techniques, the relative error gets significantly increased along dilution of the sample.

The term "Ion-selective electrodes" reflects the capability of ISEs to discriminate between ions. Ideally, an ISE responds to only one kind of species in a mixed sample. Of course, the real-world electrodes show only limited selectivity. For decades, the glass pH electrode appeared the most selective. Some of glass electrodes work at pH 12 or even 14, that is, sustain huge excess of sodium and other electrolytes: up to 10^{12} or 10^{14} times. More recently, it was shown that some ionophore-based and solid state ISEs show even higher selectivity if the measurements are performed under certain protocols (see Chap. 3 for details). The selectivity of an ISE to, for example, I^+ ions in the presence of J^+ ions is quantified with the so-called selectivity coefficient: the parameter K_{IJ} in the Nikolsky equation [1]:

$$E = E^0 + S\log(a_I + K_{IJ}a_J). \tag{1.5}$$

Here, I^+ ions are the target analyte, the so-called "primary" or "main" ions, while J^+ ions are normally called "interfering" ions. Obviously, the smaller K_{IJ} value the smaller is the whole interference effect caused by J^+ ions, and the ISE is closer to the ideal case: primary ions only give impact on the electrode response. The term "selectivity coefficient" is therefore a bit confusing: high selectivity of the response requires low selectivity coefficient. However, everybody who works with ISEs are used with this terminology and suggestions to rename the selectivity coefficient into "interference coefficient" did not get support.

The physical nature of the selectivity coefficient, how exactly it depends on the ISE membrane composition and the nature of the competing ions, is very different for different kinds of membranes. More sophisticated equations have been suggested for more accurate description of the ISE response in mixed solutions. However, Eq. (1.5) remains the most widely used, partly due to its simplicity.

1.2 Brief Survey of the ISE Applications

Normally, analysis with ISEs does not require pretreatment of the sample, more of this, in line and in vivo measurements are possible offering great opportunities for continuous monitoring in clinical, industrial, and environmental applications. Unlike other analytical techniques, measurements with ISEs provide with data on the activity of the analyte. In many cases, this is a critical advantage because the Gibbs free energy (and other thermodynamic potentials) is characterized by activity rather than by concentration. Therefore, the activity of the analyte provides with the data whether the respective chemical process will or will not occur spontaneously. This knowledge is especially useful in industry. Both ISEs themselves and the instrumentation for measuring the potentiometric signal are inexpensive and easy in use, not requiring high-skilled operator. The power consumption for the measurements is low. This is why ISEs became so widely used in practice. Table 1.1 presents some examples of the applications of ISEs.

Examples presented in Table 1.1 illustrate the variety of the ISEs applications. Clinical analysis with ISEs appears the most important. A number of companies produce automatic clinical analyzers which measure dozens of parameters, blood electrolytes among them. Human homeostasis requires a very narrow window for the pH: approx. 7.44 ± 0.05. The normal level of the potassium ions concentration is 4.5 mM, it may be about 1 mM higher or lower, and these deviations indicate several various disorders including those related to cardiovascular system. Sodium

Table 1.1 Some applications of ion-selective electrodes

Branch of activity	Typical samples	Typical analytes
Clinical analysis	Blood serum, plasma, whole blood, saliva, urine, lymph	pH, K^+, Na^+, Ca^{2+}, Li^+, Cl^-, Mg^{2+}, HCO_3^-
Agricultural industry	Soil, vegetables, fruits, milk, meat	pH, NO_3^-, K^+, NH_4^+, Ca^{2+}, Cl^-, Na^+
Industrial manufacturing	Metal plating solutions, paper bleaching solutions, fertilizers	pH, Cu^{2+}, Ag, Au, NO_3^-, Ca^{2+}, K^+, Na^+ NH_4^+
Environmental monitoring	Natural, industrial, waste waters, soil, plants, human and animal tissues	pH, Pb^{2+}, Hg^{2+}, Cu^{2+}, NO_3^-, ionic and nonionic surfactants
Pharmaceutical industry	Medical drugs, liniments, mixtures	Biologically active amines, alkaloids, acids
Food industry	Juices, beverages, dough, pastry, wine	pH, Ca^{2+}, NO_3^-, CH_3COO^-
Power stations	Cooling water	pH, Na^+
Control of gases in air	Air in chemical factories	NH_3, NO_2, "acidic" gases
Control of enzymatic activity	Medical and biological liquids and tissues, pesticide polluted soils and plants	Enzymes, substrates, enzyme inhibitors

comprises the main cationic electrolyte in blood; its normal concentration value is about 140 mM/l. The control of lithium is especially important for patients suffering from manic-depressive psychosis. In the cases of calcium and magnesium, ISEs provide unique information because the clinically-relevant information can be extracted from the concentration of the free (not complexed) Ca^{2+} and Mg^{2+} ions. Other techniques like atomic absorption show only total content of these ions which is about 2 times higher than the free ion concentration. Less frequently performed but also important is analysis of electrolytes in saliva, urine, and lymph.

Acidity and salinity of soils, suitable concentrations of nitric, amino, and potassium fertilizers are quantified with the respective ISEs. These electrolytes often have to be controlled also in various agricultural products. Many ions must be monitored in industrial manufacturing. Among these are gold and silver which are present in industrial solutions mostly as anionic complexes, and therefore present in Table 1.1 without charge. Toxic heavy metals, pH, nitrate, surfactants are of interest for the environmental control. Dozens of ionic drugs of pharmaceutical relevance are measured with the respective ISEs. Food industry also needs tools for ions control, while pipelines in cooling systems of power stations are sensitive to the pH and to minute quantities of salt. One can see that the pH is always present among other electrolytes to measure, and therefore, the glass pH electrode, the oldest among all chemical sensors, remains, probably, the most important and most demanded.

Although ISEs are, rigorously speaking, ion sensors, one can use them in special devices: gas and biosensors. Earlier, these devices constituted a large branch of the ISE application. Currently, ammonia gas sensors based on the Severinghaus principle[2] and enzyme-based urea ISEs are still in use. However, other analytes used to be measured by gas and biosensors based on ISEs are measured by sensors with other work principles. Therefore, this application of ISEs is not discussed in this book.

1.3 ISEs Classification by the Membrane Type: Glass, Crystalline, Polymeric Membrane ISEs

ISEs are normally classified by the membrane material, although one can group them according to construction or other feature. The oldest group of ISEs is those with glass membranes. These are mostly silicate glasses and electrodes for the pH measurements. However, sometimes also boric and phosphorous glasses also are in use. On the other hand, there are glass membranes for Na^+, K^+, Li^+, and Ag^+ assay. Among these, only Na^+ glass electrodes are really practical. Glass electrodes are described in Chap. 5.

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[2] Change of the analyte gas concentration causes change of pH in a thin aqueous film on a surface of a glass pH electrode, and in this way the analyte concentration is measured.

Crystalline electrodes can be subdivided into those with polycrystalline and with monocrystalline membranes. The latter kind is represented by F^-—selective electrode with membrane made of LaF_3 monocrystal doped with EuF_2. Other crystalline electrodes have polycrystalline membranes containing mixtures of low-soluble silver salts like $Ag_2S + AgX$ ($X^- = Cl^-$, Br^-, I^-, SCN^-, CN^-). These ISEs are suitable for assay of the respective X^- ions and also S^{2-}. Other group of polycrystalline membranes contains mixtures of Ag_2S with low-soluble metal sulfides: $Ag_2S + MeS$ ($Me^{2+} = Pb^{2+}$, Cd^{2+}, Cu^{2+}, and Hg^{2+}). Similar compositions doped with B, Al, Ga, Ge, Sn, As, Sb, Bi compounds allow obtaining amorphous chalcogenide glass membranes. Crystalline and chalcogenide glass ISEs are described in Chap. 6.

ISEs with polymeric membranes containing ionophores comprise the most numerous group of electrodes. Ionophores are neutral or charged species selectively binding ions. This selectivity of association or complexation makes the basis for the potentiometric selectivity of the respective ISEs. The large variety of selective ionophores makes the main basis for the variety of selectively assayed analytes. Among these are various inorganic and organic cations and anions, ionic surfactants, it is possible to make ionophore-based ISEs sensitive to nonionic species like nonionic surfactants and some phenols.

Among the polymers used in ionophore-based membranes, polyvinylchloride is the most widely used although some other polymers became more and more popular. ISEs with polymeric membranes containing ionophores are described in Chap. 4.

The materials for the ISE membranes change over time. For years heterogeneous membranes were in use, containing low-soluble salts dispersed in polyethylene or other inert polymers, or membranes made of ion-exchange resins. Now these ISEs belong to the past. On the other hand, it was very recently suggested to modify gold nano-filters with adsorbed ionophores and make ISEs in this very novel way [2].

1.4 Brief History of ISEs

The history of ISEs started in the beginning of the XX century (1906) when Cremer [3] noticed that the potential of a glass membrane depends on the pH of the solution. On the basis of this observation, Haber and Klemensienwicz invented glass pH electrode in 1909 [4]. However, these electrodes only got wide use much later when Beckman in 1936 started commercial production of glass pH electrodes and pH meters. At about the same time, Nikolsky published his article devoted to the theory of the glass electrode response [1] with the derivation of the Nikolsky equation and coined the term “selectivity constant.” Nikolsky considered the ion exchange between the glass phase and the aqueous phase, this was his crucial idea. Later on, this particular version of the Nikolsky theory was called “the simple theory of the glass electrode.” This simple theory considered all ion-exchange sites in glass equal to one another with respect of the ability to dissociate and neglected the diffusion potential within the glass membrane phase. In 1950s, Nikolsky and Shultz published a series of papers inventing what they called "the generalized theory of the glass electrode" [5, 6]. The generalization was done in two distinctively different respects. One was rather formal introducing "partial" activity coefficients for species in the membrane. The other one accounted for different dissociation degree for different ionogenic groups in glass. In early 1960s, Shultz and Stefanova for the first time considered the glass electrode potential as "membrane potential," that is, containing not only boundary potential drops but also the diffusion potential within the membrane [7]. Eisenman (who himself made enormous contribution to the theory and practice of ISEs) edited an excellent book devoted to the then state of the art in glass electrodes for the pH and alkali metal sensing [8].

By early 1960s, the progress in ISEs was almost exclusively connected to glass electrodes. In 1961, Pungor invented ISEs with heterogeneous membranes: low-soluble salts dispersed in a polymer (polyethylene) matrix [9]. The second half of the 1960s was the time of several breakthrough inventions. Frant and Ross in 1966 proposed fluoride electrode with membrane of monocrystalline LaF_3 doped with EuF_2 [10]. In the same year, Simon invented first ISE with liquid membrane containing a neutral ionophore (at that time called carrier or ligand) [11]. This was potassium-selective electrode with nonactin as the ionophore. Later on, it turned out that nactins are more selective to ammonium cations, while valinomycin is much more suitable for K^+-ISEs. Eisenman published a book devoted to various aspects of natural cell membranes and their artificial models [12]. In 1967, Ross proposed first Ca^{2+}-ISE with liquid membrane containing organophosphorous charged ionophore [13]. Also in 1967, Bloch, Shatkay and Saroff published their pioneering work devoted to ISEs with plasticized polyvinylchloride membranes [14]. The plasticizer imparts to the elasticity of the membrane and, in the same time, acts as solvent for ionophores. Moody and Thomas [15] also contributed very much to this basic principle of the ionophore-based ISEs, which until now remains highly relevant. Durst published a book summarizing the achievements in the theory and practice of ISEs made by the early 1970s [16]. The book consists of chapters written by the world-leading scientists in the field.

Bergveld in 1970 invented ion-selective field effect transistors [17]. These devices effectively combine ion-selective membrane with semiconductor unit enhancing the signal. Rapid evolution in the field of ISEs lasted until the late 1970s. At that time, a number of excellent books [18–22] have been published devoted to the theory, development and applications of ISEs. By early 1980s, ISEs became mature. At that time, Morf published his fundamental book on the principles of the ISEs [23] which for years became a kind of handbook for those who were involved in this branch of science and technology.

New impetus for the ISEs studies, in particular for those based on ionophores, was given by Bakker in mid-1990s when apparently well-established concepts were re-examined, and many turned out being inaccurate or even incorrect. The results of this re-addressing were summarized in two excellent reviews published by Pretsch, Bakker and Bűhlmann in late 1990s [24, 25]. Review [24] is primarily devoted to the theory of ionophore-based sensors: ISEs and optodes, and review [25] summarizes known ionophores in the course of their selectivity to a given analyte. In analogy with the so-called electronic nose based on array of gas sensors, Vlasov invented "electronic tongue": an array of ISEs with limited selectivity in combination with sophisticated software [26]. This system is capable of providing with qualitative and quantitative information of the composition of various kinds of rather complicated real samples.

Another breakthrough achieved in the late 1990s was made by Sokalski and referred to the sensitivity of ISEs in strongly diluted solutions [27]. Efforts aimed at measurements with electrodes in nano- and sub-nanomolar concentration range became the mainstream in the ISE research and application in the beginning of the XXI century. At that time, it also became clear that ISEs are not necessarily pure potentiometric sensors, that is, applied only under zero current conditions. More of this, polarized electrodes showed certain advantages over classical ISEs for a number of practical tasks [28–30]. A large success in theoretical description of ISE potential in real time and space was achieved in early 2000s [31–34] in Lewenstam group. Recently, the fundamentals of ISEs, together with that of other kind of sensors, were described by Janata [35].

In this book, I tried to describe the basics of the measuring with ISEs, the state of the art in ISEs with different types of membranes (with special emphasis on the ionophore-based ISEs), and some modern trends in the ISE research and application. Ion-selective field effect transistors (ISFETs) are not discussed here.

References

1. B.P. Nikolsky, Acta Physicochim. URSS, 1937, 7, 597.
2. G. Jagerszki, A. Takacs, I. Bitter, R.E. Gyurcsanyi, Angew. Chem. Int. Ed. 2011, 50, 1656.
3. M. Cremer, Z. Biol. 1906, 47, 562.
4. F. Haber, Z. Klemensienwicz, Z. Phys. Chem., 1909, 65, 385.
5. B.P. Nikolsky, M.M. Shultz, Russ. J. Phys. Chem., 1953, 27, 724 (Russ.).
6. B.P. Nikolsky, M.M. Shultz, Russ. J. Phys. Chem., 1962, 36, 1327 (Russ.).
7. O.K. Stefanova, M.M. Shultz, E.A. Materova, B.P. Nikolsky, Herald of St.Peterburg Univ., 1963, 4, 93 (Russ.).
8. G. Eisenman (ed), Glass electrodes for hydrogen and other cations. Principles and practice. M. Dekker, New York., 1967.
9. E. Pungor, E. Hollos-Rokosinyi, Acta Chem. Hung., 1961, 27, 63.
10. M.S. Frant, J.W. Ross, Science, 1066, 154, 1553.
11. Z. Stefanac, W. Simon, Chimia, 1966, 20, 436.
12. G. Eisenman (ed) Membranes, 1-2, M. Dekker, N.Y., 1972/1973.
13. J.W. Ross, Science, 1967, 156, 1378.
14. R. Bloch, A. Shatkay, H.A. Saroff, Biophys. J., 1967, 7, 865.
15. G.J. Moody, R.B. Oke, J.D.R. Thomas, Analyst, 1970, 95, 910.
16. R. Durst (editor) Ion-selective electrodes, NBS special publication 314, 1969.
17. P. Bergveld, IEEE Trans. Biomed. Eng., 1970, 17, 70.

18. N. Lakshminarayanaiah, Membrane electrodes, Academic Press, NY, San Francisco, London, 1976.
19. H. Freiser (ed), Ion-selective Electrodes in Analytical Chemistry, Plenum Press, N.Y., 1978.
20. B.P. Nikolsky, E.A. Materova, Ion-selective Electrodes, Khimia, 1980, 239 p. (Russ.).
21. K. Cammann, Das Arbeiten mit ionenselektiven Electroden, Springer, Berlin, 1973.
22. J. Koryta, K. Stulik, Iontove-selectivni electrody, Acadeia, Praha (1984).
23. W.E. Morf, The principles of Ion-selective Electrodes and of Membrane Transport, Akademiai Kiado, Budapest, 1981.
24. E. Bakker, P. Bühlmann, E. Pretsch, Chem. Rev., 1997, 97, 3083.
25. P. Bühlmann, E. Pretsch, E. Bakker, Chem. Rev., 1998, 98, 1593.
26. A.V. Legin, A.M. Rudnitskaya, Yu.G. Vlasov, C. Di Natale, F. Davide, A. D'Amico, Sens. Act. B, 1997, 44, 291.
27. T. Sokalski, A. Ceresa, T. Zwickl, E. Pretsch, J. Am. Chem. Soc., 1997, 119, 11347.
28. E. Lindner, R.E. Gyurcsanyi, R.P. Buck, Electroanalysis, 1999, 695.
29. A. Shvarev, E. Bakker, Anal. Chem., 2003, 75, 4541.
30. M.A. Peshkova, T. Sokalski, K.N. Mikhelson, A. Lewenstam, Anal. Chem., 2008, 80, 9181.
31. T. Sokalski, A. Lewenstam, Electrochem. Commun., 2001, 3, 107.
32. T. Sokalski, P. Lingenfelter, A. Lewenstam, J. Phys. Chem., 2003, 107, 2443.
33. J. Bobacka, A. Ivaska, A. Lewenstam, Chem. Rev., 2008, 108, 329.
34. T. Sokalski, W. Kucza, M. Danielewski, A. Lewenstam, Anal. Chem., 2009, 81, 5016.
35. J. Janata, Principles of Chemical Sensors, Springer, 2009, 395 p.