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Potentiometric Ion Sensors

Johan Bobacka,*[,†] Ari Ivaska,[†] and Andrzej Lewenstam[‡,§]

Åbo Akademi University, Process Chemistry Centre, c/o Laboratory of Analytical Chemistry, Biskopsgatan 8, FI-20500 Turku-Åbo, Finland;
Faculty of Material Science and Ceramics, AGH-University of Science and Technology, Al. Mickiewicza 30, PL-30059 Cracow, Poland; and
Åbo Akademi University, Process Chemistry Centre, c/o Center for Process Analytical Chemistry and Sensor Technology (ProSens),
Biskopsgatan 8, FI-20500 Turku-Åbo, Finland

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1. Introduction

Potentiometric ion sensors or ion-selective electrodes (ISEs) are an important subgroup of electrochemical sensors.[1−3] ISEs are characterized by small size, portability, low-energy consumption, and low cost, which are attractive features concerning practical applications. ISEs based on polymeric membranes containing neutral or charged carriers (ionophores) are available for the determination of a large number of inorganic and organic ions, as described in detail, about a decade ago, in extensive reviews.[4,5] However, during the past decade, the chemical sensing abilities of ISEs have been improved to such an extent that it has resulted in a "new wave of ion-selective electrodes".[6,7] This can be attributed to several important findings, such as the considerable improvement in the lower detection limit of ISEs, new membrane materials, new sensing concepts, and deeper theoretical understanding and modeling of the potentiometric response of ISEs. The aim of this review is to highlight some of these modern topics in the field of potentiometric ion sensors. This review is focused on recent achievements since the beginning of this millenium and emphasizes the results from the last 5 years (2002−2006). Section 2 gives a critical overview, placed in a historical perspective, on the theory of the potentiometric response, including classical equilibrium models as well as advanced nonequilibrium models. Section 3 deals with recent advances in the field of solid-contact ISEs, emphasizing the application of conducting polymers as ion-to-electron transducers. Recent developments in the area of miniaturized ISEs, including aplications in flow analysis, life science, and biology, are discussed in section 4. Finally, the new wave of ISEs is commented on in section 5. We hope that the issues discussed will illustrate the great possibilities offered by modern ISEs and encourage further innovations in the rapidly expanding field of chemical sensors in the years to come.

2. Theory of Potentiometric Response

The response of potentiometric ion sensors, i.e., ion-selective electrodes (ISEs) and/or ion-sensitive sensors (ISSs) (i.e., sensors with solid-state contact made of, e.g., conducting polymer film), is a complex time-dependent phenomenon that depends on the electroactive material (membrane/film) and the bathing solution as well as the membrane|solution interface and their composition, thermodynamic, and kinetic properties. All these features are the subjects of the theoretical modeling of the response. Modeling in the ion-sensors area serves two roles.[8] One *classical* role is in supporting the practitioner (the user of sensors) with very basic principles

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* Corresponding author. E-mail: johan.bobacka@abo.fi. Phone: +358 2 215 3246. Fax: +358 2 215 4479.
[†] Åbo Akademi University, Process Chemistry Centre, c/o Laboratory of Analytical Chemistry.
[‡] AGH-University of Science and Technology.
[§] Åbo Akademi University, Process Chemistry Centre, c/o Center for Process Analytical Chemistry and Sensor Technology (ProSens).

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Johan Bobacka was born in 1962 in Larsmo, a small village on the west coast of Finland. He received his M.Sc. degree in chemical engineering in 1988 and his Ph.D. degree in analytical chemistry in 1993 from Åbo Akademi University. The Ph.D. work on “Electrochemical characteristics of poly(3-octylthiophene) film electrodes” was performed under the supervision of Professor Ari Ivaska and Professor Andrzej Lewenstam. During the years 1994–1997, Johan Bobacka worked as a research scientist at Kone Instruments Corporation (now Thermo Fisher Scientific), and since 1997, he is a Docent in electroanalytical chemistry at Åbo Akademi University. He was a senior researcher (1997–2001) and Academy of Finland Research Fellow (2001–2006) at the Laboratory of Analytical Chemistry, which is part of the Åbo Akademi Process Chemistry Centre (Finnish Centre of Excellence 2000–2011). At present, Johan Bobacka is Professor of Analytical Chemistry at Åbo Akademi University (2006–2009). His current fields of interest include electroanalytical chemistry, process analytical chemistry, chemical sensors, conducting polymers, and electrochemical impedance spectroscopy, with special emphasis on the development of potentiometric ion sensors based on conducting polymers.

Ari Ivaska was born in 1946 in Kuopio, Finland. He received his M.Sc. degree in chemical engineering in 1971 and his Ph.D. in analytical chemistry in 1975 at Åbo Akademi University, Finland. The Ph.D. thesis “Potentiometric titration of weak acids and their binary mixtures” was supervised by Professor Erkki Wänninen. Ari Ivaska did his post doc in 1978/79 at Chelsea College, University of London, England, and 1982/83 at Northwestern University Evanston, Illinois, U.S.A. He also worked as UNESCO expert at UNICAMP in Brazil, 1980/81. In 1985/86, he worked at the research centre of Neste Company in Finland and was nominated to the Chair of Analytical Chemistry at Åbo Akademi University in 1987. He has been as visiting Professor at University of Washington, Seattle, U.S.A., in 1991/92 and 1996/97 and the spring term 2003 at University of Wollongon, Australia. He is the head of the Process Analytical Group at the Åbo Akademi Process Chemistry Centre nominated to the Centre of Excellence in research by the Academy of Finland for 2000–2011. Ari Ivaska is currently the director of the Research Institute of the Åbo Akademi University Foundation. His fields of interest are electroanalytical chemistry, process analytical chemistry, electroactive materials in general, and metal ions in the paper and pulp chemistry.

Andrzej Lewenstam obtained his Ph.D. (1977, supervisor prof. A. Hulanicki) and his DSc (1987) from Warsaw University and since 1990 he has been a Professor. Currently he is Professor of Sensor Technology at Åbo Akademi University and Director of the Center for Process Analytical Chemistry and Sensor Technology ‘ProSens’ at this University, Professor in Chemistry, AGH University of Science and Technology, Cracow, and Adjunct Professor in Chemical Engineering, Laval University, Quebec, Canada. Since 2006, he is a chairman of the Working Group on Selective Electrodes and Biosensors of the International Federation of Clinical Chemistry (IFCC). His current fields of interest are chemical sensors and biosensors, clinical chemistry, membrane potential and biomimetics, conducting polymers, hydrometallurgy, and mathematical modelling, as well as methodology of chemistry and philosophy of Science. He is the author of approximately 200 papers in chemistry and philosophy of Science and 20 patents and is a member of the editorial board of 4 international journals.

of sensor response to help the application and to support quantitative measurement by simple equations. Another *advanced* role is to provide a fundamental understanding of the sensor response for those interested in electrochemical theory as the forefront of sensor technology, by helping to map electric potential and concentration changes in space and time. Related to these two roles are a few levels of modeling generality and/or idealization, as schematically shown in Figure 1.

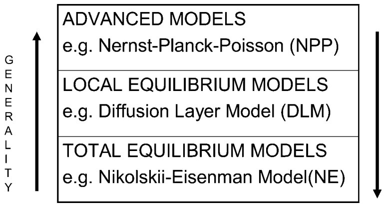


Figure 1. Methodology used in models of potentiometric ion-sensors response.

Classical models are more idealized to (intentionally) avoid mathematical, numerical, and computational difficulties stemming from solving nonlinear equations, inherent to advanced models. Classical models are easier to comprehend and to be presented and are the subject of many papers.[1−7] However, the use of advanced models is the only way to achieve a fundamental understanding (often nonintuitive) of a sensor response. The main reason is that the classical models disregard migration and, therefore, do not provide adequate space and time-dependent characteristics of sensor response, whereas the advanced models do, as shown in Figure 2.

Summarized below are the recent advances in the present quantitative theory of potentiometric ion sensors in contrast to more classical approaches. In all the models considered here, the potentiometric ion sensor is represented by the following scheme: sample|ion-sensitive membrane/film|internal contact (e.g., solution, gel, solid contact).

In all the models discussed, it is assumed that the potentiometric response is modeled under open-circuit conditions (under *the zero-current condition*). Furthermore, the sensor is made of separate, homogeneous, ionically conducting phases that form well-defined, flat interfaces; the

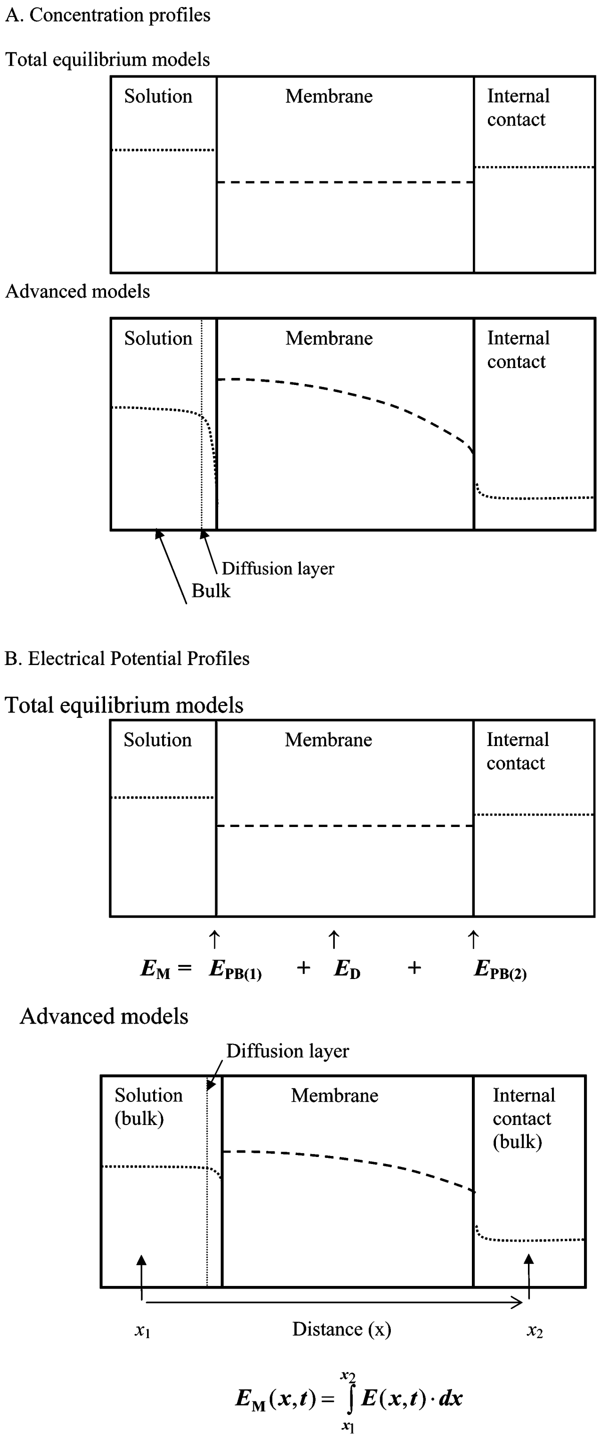


Figure 2. Schematic presentation of differences between total-equilibrium and advanced models: (a) concentration profiles and (b) electrical potential profiles.

interfaces are unblocked for ionic charge-transfer processes (faradaic currents), which applies to both ISEs and ISSs (see section 3.5); also, the sensor's phases are characterized by standard chemical potentials of the components and ionic mobilities invariant in space and time. It is also assumed that the only driving forces for ion-fluxes are gradients in ion concentrations and in electric potentials (the gradients perpendicular to the sensor surfaces (1D formulation)) and that the pressure and temperature in the modeled system are constant and solvent flow (osmotic effects) is ignored.

It should be mentioned that, although the models presented here refer to pure ion-exchanger membranes (solid state, glass, and plastic), they also apply to the membranes where complexation/association processes should be taken into account, e.g., the neutral carrier-based membranes.

2.1. Total-Equilibrium Models (Classical Models)

In all the classical models, the electric potential (E_M) of an ion sensor is represented by the sum of a boundary potential (E_{PB}) at the sample|ion-sensitive membrane (film) boundary (PB) and by the diffusion potential inside the membrane or film (E_D). The constant added includes the potential at the internal interfaces (internal contact).

$$E_M = E_{PB} + E_D + \text{constant} \tag{1}$$

(For simplicity in the equations below, it is arbitrarily assumed that constant = 0.)

In the classical modeling of the response of ion sensors, two possibilities are considered—one recognizes diffusion potential, while the other disregards it. These two approaches are presented below.

2.1.1. Phase-Boundary-Potential Approach

The phase-boundary-potential model is based on two idealizing assumptions:

(1) The phase-boundary potential at the sample|membrane interface (phase boundary) governs the membrane response, i.e., $E_M = E_{PB}$. Migration effects in the membrane are ignored, which means that the kinetic parameters of all the charged species involved, i.e., all ionic mobilities, are equal. Consequently, the diffusion potential is ignored, which formally means that $E_D = 0$, i.e., the electroneutrality in the membrane, except of the boundary, is assumed (*the electroneutrality assumption*). [On some occasions, the diffusion potential is assumed to be $E_D \neq 0 = \text{const}$ (*the pseudoelectroneutrality assumption*) and, in this way, is disregarded.]

(2) Electrochemical equilibrium is assumed at the sample|membrane interface; difference in chemical potential for any ion able to transfer the interface is balanced by a difference of the inner electrical potentials E_M (E_M is called the equilibrium potential). Additionally, it is assumed that the electric potentials and the concentrations of ions in the phases in contact are independent of the distance (except of the phase boundaries) and of time; there are no ion concentration drops in the respective phases over distance (*the total-equilibrium assumption*).

The two assumptions specified above provide grounds for implementing Guggenheim's concept of the electrochemical potential, $\tilde{\mu}_i$,[9]

$$\tilde{\mu}_i = \mu_i + z_i F\varphi = \mu_i^0 + RT\ln(a_i) + z_i F\varphi \tag{2}$$

where μ_i is the chemical potential in the phase (μ_i^0 under standard conditions), z_i is the ion valency, a_i is the single free ion activity, φ is the electric (inner) potential in the phase, and R, T, and F are the universal gas constant, the absolute temperature, and the Faraday constant, respectively.

Using further idealizing assumptions, namely, that only an ion "*i*" can transfer through the interface (*the ideal perm- and ion-selectivity assumptions*); the ion transfer is fast and reversible (*the infinite kinetics assumption*); the phases in contact are not only of distinctly different chemical properties but are immiscible (*the ideal immiscibility assumption*); the convention for a single ion activity instead of a mean ionic activity (e.g., by using Debye−Hückel theory and convention) is adopted and it is assumed that the single ion activity (a_i) in each phase is equal to its concentration (c_i) (*the ideal phase assumption*); and there is no flux of solvent through the membrane/film (*the solvent impermeability assumption*), it is possible to employ Guggenheim's concept to derive E_{PB} as a function of c_i.

By using eq 2 for each phase, for the condition of electrochemical equilibrium between the phases ($\tilde{\mu}_i = \bar{\tilde{\mu}}_i$) and by recognizing that they are chemically distinctively different ($\mu_i^0 \neq \bar{\mu}_i^0$), after separation of electrical and chemical terms, one immediately arrives at a Nernstian-like equation for the electrical potential difference at the ion−sensor interface,

$$E_{\mathrm{M}} = E_{\mathrm{PB}} = \frac{RT}{z_iF}\ln k_i + \frac{RT}{z_iF}\ln\frac{c_i}{\bar{c}_i} \tag{3}$$

where c_i denotes the concentration of an ion i in the solutions (in mol/dm^3) and the barred symbol denotes the membrane/film phase, and k_i is an ion-partition constant defined as $k_i = \exp\{(\mu_i^0 - \bar{\mu}_i^0)/RT\}$, where μ_i^0 and $\bar{\mu}_i^0$ are standard chemical potentials of ion i in the respective phases.

The theoretical models of the ion-sensor responses exploiting Guggenheim's PB concept started with the paper by Nikolskii.[10] The author considered the contact of a pH-sensitive glass membrane with the bathing solution containing the main ions ($i = \mathrm{H}^+$) and the monovalent interfering ions ($j = \mathrm{Na}^+$) and obtained the equation for ion-sensor response in the form

$$\begin{aligned} E_{\mathrm{M}} = E_{\mathrm{PB}} = \frac{RT}{z_iF}\ln k_i + \frac{RT}{z_iF}\ln\frac{c_i}{\bar{c}_i} = \frac{RT}{z_iF}\ln k_i + {} \\ \frac{RT}{z_iF}\ln\left(\frac{c_i(\bar{c}_i + \bar{c}_j)}{\bar{c}_i(\bar{c}_i + \bar{c}_j)}\right) = \frac{RT}{z_iF}\ln k_i + \frac{RT}{z_iF}\ln\left(\frac{c_i + \dfrac{c_i\bar{c}_j}{\bar{c}_i}}{\bar{c}_i + \bar{c}_j}\right) = \\ \frac{RT}{z_iF}\ln k_i + \frac{RT}{z_iF}\ln\left(\frac{c_i + K_{i,j}c_j}{\bar{c}_i + \bar{c}_j}\right) = \mathrm{const} + \frac{RT}{z_iF}\ln(c_i + K_{i,j}c_j) \end{aligned} \tag{4}$$

where $K_{i,j}$ used in the derivation above is the equilibrium constant

$$K_{i,j} = \frac{k_j}{k_i} = \frac{c_i\bar{c}_j}{c_j\bar{c}_i} \tag{5}$$

for the ion-exchange reaction,

$$\overline{i^+} + j^+ \rightleftarrows i^+ + \overline{j^+} \tag{6}$$

and $\bar{c}_i + \bar{c}_j = \mathrm{const}$ (the bar means the ions are in the membrane phase). Nikolskii was aware that including potentials arising from the different mobilities of ions in the membrane is a complex mathematical task, which was completed three decades later by Eisenman.[11]

2.1.2. Total-Membrane-Potential Approach

Eisenman abrogated the idealizing assumption that $E_{\mathrm{D}} = 0$ and extended Nikolskii's eq 4 for $E_{\mathrm{D}} \neq 0$ in the membrane. He considered different membrane types, i.e., solid-state, glass, and membranes containing ion-exchangers and neutral ligands. He considered cases with and without association between ions in the membrane. Eisenman's modeling made under classical assumptions of a total equilibrium yielded, for most cases considered, the equations in the form first obtained by Nikolskii. For instance, the equation for the fully dissociated ion-exchanger case was derived in the form

$$\begin{aligned} E_{\mathrm{M}} = E_{\mathrm{PB}} + E_{\mathrm{D}} = {} \\ \frac{RT}{z_iF}\ln k_i + \frac{RT}{z_iF}\ln\frac{c_i}{\bar{c}_i} + \frac{RT}{z_iF}\ln\left(\bar{c}_i + \frac{\bar{u}_j}{\bar{u}_i}\bar{c}_j\right) = \\ \frac{RT}{z_iF}\ln k_i + \frac{RT}{z_iF}\ln\left[\left(\frac{c_i + K_{i,j}c_j}{\bar{c}_i + \bar{c}_j}\right)\left(\bar{c}_i + \frac{\bar{u}_j}{\bar{u}_i}\bar{c}_j\right)\right] = \\ \mathrm{const}' + \frac{RT}{z_iF}\ln\left(c_i + \frac{\bar{u}_j}{\bar{u}_i}K_{i,j}c_j\right) \end{aligned} \tag{7}$$

where $\bar{u}_i$ and $\bar{u}_j$ are the ion mobilities for i^+ and j^+ ions, respectively. If $\bar{u}_i = \bar{u}_j$, then eq 7 is identical to eq 4.

As is shown above, both the Nikolskii and the Eisenman models provided strict analytical derivations of equations, possible for equal charges of the main and interfering ions (e.g., 1:1, 2:2). These models were later applied on many occasions to describe the response all kinds of ion sensors (for review, see refs 4 and 5).

Analytical derivation of the above equations for unequal charges ($z_i \neq z_j$) in the frame of the total-equilibrium approach is impossible.[12−15] To cover such cases, a case-by-case approach for each nonequal charges is used and relatively complex formalisms with implicit methods of equation solving are employed. They are based on additional ad hoc assumptions, such as ignoring the changes in concentration of the main ion in the membrane. Some ad hoc formal stratagems are employed as well, e.g., using the same mathematical equation to bind two independent variables depicting the primary ion, one representing the primary ion activity in the sample without interference from the other sample ions and the other representing the primary ion activity in the mixed sample.[4,5,16] In this situation, to cover the cases of unequal charges while keeping the total-equilibrium assumption valid, the semiempirical equations, in a similar form to eqs 4 and 7, were postulated, as shown below.

2.1.3. Semiempirical Equations

The semiempirical equations reflect the emphasis on the practical applications of ion-selective membrane electrodes. As a result of the arbitral decision of IUPAC, it was postulated to merge and extend the previously mentioned eqs 4 or 7 in the form of a general equation for all ion-selective electrodes and ion sensors, covering all charges of ions. This equation is known today as the Nikolskii−Eisenman (NE) equation (for simplicity given below for one interfering ion).[17]

$$E_{\mathrm{M}} = \mathrm{const}' + \frac{RT}{z_iF}\log(c_i + K_{i,j}^{\mathrm{pot}}c_j^{z_i/z_j}) \tag{8}$$

This equation can be further extended to include the low detection limit (L) of the ion sensor:[18]

$$E_M = \text{const}' + \frac{RT}{z_i F}\log(c_i + K_{i,j}^{\text{pot}} c_j^{z_i/z_j} + L) \qquad (9)$$

Both parameters $K_{i,j}^{\text{pot}}$ and L are constitutive for analytical practice and theoretical modeling. Theoretical modeling attempts to help predict their values, and, if it occurs, to show the evolution of the response for different concentrations of main vs interfering ions, over a period of time.

2.1.4. Comments on Model Benefits and Drawbacks of Total-Equilibrium Models

The predominant way of modeling under total-equilibrium PB models is to ignore the diffusion potential without any formal (mathematical) justification, despite the reports on its significance even under total equilibrium.[15,19,20] A typical way of ignoring E_D in the PB models is formulated verbally, not mathematically, e.g., by saying that "by the end of the 1980s, it started to become clear that subtle effects of ionic mobilities in ISE membranes may be typically ignored without a significant loss in accuracy".[21] What is overlooked in the argument just cited is the fact that ignoring diffusion potential means arbitrarily placing and affixing the membrane potential at the phase boundary only and—at the same time—justifying an uncritical use of the boundary-potential concept.

Interestingly, this practice remains in contrast with well-balanced criticism of the phase-boundary approach by the inventors of this concept. Namely, according to Guggenheim, "the conception of splitting the electrochemical potential $\tilde{\mu}_i$ of an ion i into the sum of a chemical term μ_i and an electrical term $z_i F\varphi$ has no physical significance; for one can assign an arbitrary value to φ for some point in each medium and this will for the ions of each type i determine μ_i, so as to give $\tilde{\mu}_i$, the value which determines all the physical processes involving ions of type i".[9] Nikolskii added to Guggenheim by saying that his model "involves some difficulties, for in this case one deals with thermodynamically undefined variables, interface potential differences, diffusion potentials, and the activities of single ions".[22]

The advantage of the total-equilibrium PB models lies in their simplicity. Characteristic of the phase-boundary modeling is that it considers ion complexion/association equilibria in a membrane in a similar way to solution chemistry and to coupling the membrane chemistry with that of the bathing solution via a pivotal phase boundary, eq 3. This methodology provides similar flexibility, as known from the complex formation theory, in considering many ion-equilibria and complex formation constants, the mass conservation, and the charge balance (electroneutrality) equations.

Therefore, the methodology used in the total-equilibrium modeling has value: delivering the basic theoretical support and formal instrumentation needed for the practical applications of sensors, while offering an intuitive but essential understanding of the principles underlying sensor response. For these reasons, this modeling has been used extensively to provide a simple semiquantitative description of most ion-selective electrode related experiments and has assisted every period of development in the ion-sensor technology. The modeling was, and still is, applied in ion-selective electrodes[4,5] and conducting polymer ion sensors, including the sensors with a solid contact.[23−25]

The major drawbacks of the total-equilibrium models relate directly to the idealizations used; i.e., to the counterfactual assumption that all individual mobilities in the membrane are equal. This allows the migration effects ($E_D = 0$) to be ignored and the assumption that (i) the electroneutrality condition is valid even in the proximity of the phase boundary, (ii) the concentrations of primary and interfering (and their complexes) as well as oppositely charged sites in the layers adjacent to the membrane/film surface are equal to those in the respective bulks, and (iii) the ion-transfer rates are infinite (see Figure 2).

Primarily, assuming that the systems modeled are at total equilibrium leaves us with the sensor response interpretation that the electric potential, sensitivity, and, in particular, selectivity coefficients and detection limit are time-independent. The consideration in the total-equilibrium models that the sensor response is time-independent contradicts numerous time-dependent empirical reports in the field of potentiometric sensors, especially those delivered by the nonequilibrium potentiometry, such as the lowering of the detection limit by using transmembrane fluxes, which are time-dependent.

2.2. Local-Equilibrium Models (Diffusion-Layer Models)

In these models, called the diffusion-layer models (DLMs), the local equilibrium at the sensor interfaces is assumed (*the local equilibrium assumption*). (It means that eqs 3 and 7 as well as eqs 8 and 9 apply by substitution of the bulk concentration of ions by respective surface concentrations.) Additionally, it is assumed that the concentration of ions in the membrane phase and contacting phases are dependent on the distance but are independent of time, i.e., the sensor system is at steady state, or are dependent on time by diffusion of ions to/from membrane|solution interface(s) controlling the equilibration rate.

The need to extend the time-independent thermodynamic modeling as described above was already noticed some decades ago, owing to the observations of variable and time-dependent selectivity in the case of ion sensors with solid-state and plastic membranes.[26−28] The problem of selectivity changes with time is still an issue of significant interest in the area of bio-ion-sensitive membranes/films.[29] Sokalski et al.'s recent discovery of lowering the detection limit due to transmembrane fluxes gave an impetus to the consideration of ion fluxes[30] and resulting concentration gradients in the theoretical modeling using the DLM frame.

The diffusion-layer model (DLM) was first introduced by Lewenstam,[31] and was continued in a number of papers,[28,31−37] to model changes of selectivity coefficients with concentrations and time. This model is based on the assumption of local equilibrium at the solution|membrane interface, and consequently, a starting point in DLM are eqs 3 and 4 with surface (local) concentrations instead of bulk concentrations. The model assumes steady-state ion fluxes given by linear concentration gradients between the interface(s) and respective bulks, and it assumes constant and time-independent diffusion layers in the "local" areas.

In DLM, the time-dependent response (for ions of equal charges and an ignored detection limit) is obtained by using a pivotal parameter "$s(t)$" called the surface coverage or site filling factor, characterizing the distance of the system under local equilibrium from total equilibrium over time (t), which is defined as[29,33,35−37]

$$s(t) = \frac{\overline{c_{j0}}(t)}{\overline{c_{i0}}(t) + \overline{c_{j0}}(t)} = \frac{K_{i,j} c_{j0}(t)}{c_{i0}(t) + K_{i,j} c_{j0}(t)} \qquad (10)$$

Here, the barred concentrations refer to ion concentrations in the membrane or film surface at time t, and the sum $\bar{c}_{i0}(t) + \bar{c}_{j0}(t)$ is equal to $\bar{c}_{ib}$, where $\bar{c}_{ib}$ is the concentration of the main ion in the bulk of the membrane. The concentrations without bars $c_{i0}(t)$ and $c_{j0}(t)$ are the solution ion concentrations on the membrane surface at time t.

Assuming a constant diffusion-layer thickness with linear concentration changes in the diffusion layers (the Nernst approach) for any response time, and by coupling the ion fluxes (J_i,J_j) from/to the interface by virtue of mass conservation, one obtains

$$J_j = \frac{n_{\text{tot}}}{A}\frac{\mathrm{d}s(t)}{\mathrm{d}t} = D_j\frac{c_j - c_{j0}(t)}{10^3\delta} = D_i\frac{c_{i0}(t) - c_i}{10^3\delta} = -J_i \quad (11)$$

where A is the electrode surface area (m^2), n_{tot} is the number of active exchangeable sites occupied by the i and j ions (mol) on the membrane surface, and δ is the diffusion-layer thickness (m).

By combining eqs 5, 7, and 10 rewritten in local concentrations and eq 11, one further obtains

$$E_{\text{M}}(t) = \text{const} + \frac{RT}{F}\ln\frac{[1 - s(t)]K_{i,j} + s(t)\frac{\bar{u}_j}{\bar{u}_i}K_{i,j}}{K_{i,j}[1 - s(t)] + \frac{D_j}{D_i}s(t)}\frac{\left(c_i + \frac{D_j}{D_i}c_j\right)}{\bar{c}_{ib}} \quad (12)$$

where the const is the term including contributions independent of the concentration of the ions i and j; D_i and D_j are the diffusion coefficients of the primary ion and interfering ion in the aqueous diffusion layer (m^2 s^{-1}), respectively; and $\bar{u}_i$ and $\bar{u}_j$ represent the ionic mobilities of ions in the membrane phase (m^2 s^{-1} V^{-1}).

After separation of the variables $s(t)$ and t and integrating within time limits, t to $t = +\infty$, and corresponding s limits, $s(t)$ and s_{eq}, it is possible to obtain a function binding $s(t)$ and t,

$$\left[K_{i,j} - \frac{D_j}{D_i}\right]s(t) - K_{i,j}\frac{c_i + \frac{D_j}{D_i}\cdot c_j}{c_i + K_{i,j}c_j}\ln\left(1 - \frac{s(t)}{s_{\text{eq}}}\right) = (c_i + K_{i,j}c_j)Ct \quad (13)$$

with $C = D_jA/n_{\text{tot}}\delta \times 10^{-3}$ and where t is a time (s), 10^{-3} is a unit conversion factor (dm^3 to m^3), and s_{eq} is given by

$$s_{\text{eq}} = \frac{\bar{c}_{j0}(t \rightarrow \infty)}{\bar{c}_{i0}(t \rightarrow \infty) + \bar{c}_{j0}(t \rightarrow \infty)} = \frac{K_{i,j}c_j}{c_i + K_{i,j}c_j} \quad (14)$$

where $\bar{c}_{i0}(t \rightarrow \infty)$ and $\bar{c}_{j0}(t \rightarrow \infty)$ represent the ion concentration in the membrane phase at the interface at steady state and/or at total equilibrium (for both cases, $\mathrm{d}s(t)/\mathrm{d}t = 0$). In this way, in the DLM, potential is connected to time.

The DLM, in contrast to total-equilibrium models, contains time as a model parameter. The time is introduced ad hoc to describe attaining of total equilibrium (i.e., equilibration) via diffusion-controlled ion transport. The DLM predicts that the selectivity coefficient $K_{i,j}^{\text{pot}}$ changes during the equilibration process (i.e., in the measurement) as a function of $s(t)$ and, thus, with time (t).[33-37] According to DLM, the value of the selectivity coefficient $K_{i,j}^{\text{pot}}$ can vary between two limiting values—one for a short response time dictated by the ion-transport properties in solution,

$$K_{i,j}^{\text{pot}}(t \rightarrow 0) = \frac{D_j}{D_i} \approx 1 \quad (15)$$

and the other at steady state and/or total equilibrium, where $K_{i,j}^{\text{pot}}$ is characterized exclusively by the membrane-related parameters and expressions known from total-equilibrium models, eqs 4 and 7. In the DLM, eqs 4 and 7 are limiting cases for $t \rightarrow \infty$:

$$K_{i,j}^{\text{pot}}(t \rightarrow \infty) = K_{i,j} \text{ (for } E_{\text{D}} = 0) \text{ or } K_{i,j}^{\text{pot}}(t \rightarrow \infty) = \frac{\bar{u}_j}{\bar{u}_i}K_{i,j} \text{ (for } E_{\text{D}} \neq 0) \quad (16)$$

The above prediction given by eq 15 is of great practical importance in applications of ion sensors because it predicts that the sensor response for short readout times is characterized not by the equilibrium selectivity as given by eq 16 but by ion transport and the selectivity given by eq 15. In consequence, if it occurs, the electrode senses "equally" the main and interfering ions. This prediction resulted in important practical benefits that are also of interest today. It was, for instance, used to kinetically discriminate strong interferences by short readout times ($t \rightarrow 0$)[38,39] or, alternatively, to benefit from the measurements of strong interferents, such as heparin on chloride ISE. The latter is realized by taking advantage of $K_{\text{Cl,heparin}}^{\text{pot}} \approx 1$ and using the response to the interfering (heparin) translated "1:1" into the signal of the main (chloride) ions.[40,41] DLM was also used to interpret nonmonotonic transients in ion-sensor response[36] and for interpretation of long-term drifts in sensors in which a thin aqueous layer is formed between the membrane and the substrate electrode.[42]

DLM was used successfully to demonstrate that the poor apparent selectivities and detection limits have a common origin in the increased (vs bulk) surface concentrations of the main ion.[43-46] In consequence, it was shown for the first time that, using the ion sensors in the regime of nonequilibrium response, induced as a result of the ion-complexation processes, both true (unbiased) selectivity coefficients[44,46] and much lower detection limits for solid-state membranes can be achieved.[45]

In 1999, Sokalski et al.[47] used the DLM frame to interpret the effect of lowering of the detection limit for plastic membranes by analyzing transmembrane ion fluxes in a symmetric solution/membrane/(internal) solution system. In this formulation of DLM, the diffusion potential is ignored, the fluxes of ions are treated under steady state, and the concentrations of all species are assumed to change linearly within the diffusion layers, i.e., in the adjacent solution layer and over the membrane. Ion-exchange as well as co-extraction processes are considered to analyze the low detection limits. The model in this form provides a possibility to analytically find an equation for the detection limit (L) vs different model parameters, especially the concentrations of ions in the internal solution and membrane, but not vs time. An important outcome of this interpretation is reflected in the equation that allows the calculation of the steady-state surface concentration of the main ion, which dictates the low detection limit for (plastic) membranes:

$$c_{i0}(t \rightarrow \infty) = c_i + \frac{\bar{D}_i \delta}{D_i d} [\bar{c}_{i0}(t \rightarrow \infty) - \bar{c}_{id}(t \rightarrow \infty)] \qquad (17)$$

The above equation indicates that adjusting the composition of the internal solution (i.e., by keeping low free main ion concentration due to ion complexation and optimizing vs the membrane selectivity, the interfering ion concentration in the internal solution or the solid-contact film), the membrane thickness (d), the diffusion coefficient of in the membrane ($\bar{D}_i$), the thickness of the diffusion layer in the sample (δ), and the diffusion coefficient in the sample (D_i) plays an essential role in forming an ISS response in the concentration range close to the low detection limit, as shown schematically in Figure 3.

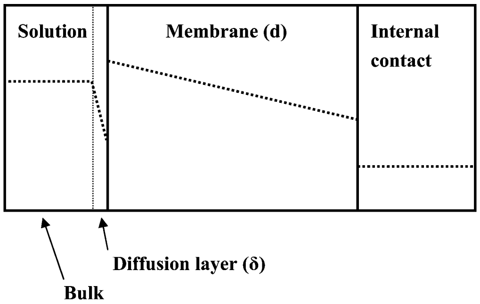


Figure 3. Schematic presentation of the concentration profile of the main ion influencing the lower detection limit.

Predictions from this version of DLM are better visualized by the graphical representations of the ISS responses instead of using rather complicated algebraic equations (see Figure 4). In fact, the application of a simple commercial equation solver (e.g., Mathcad) and its graphical tools proved to be quite feasible.[47]

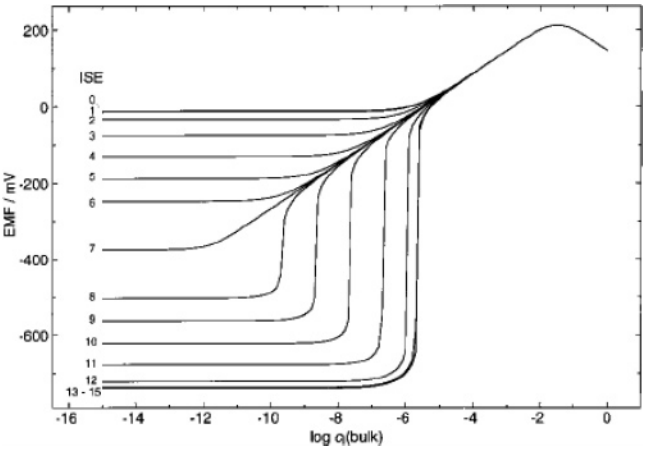


Figure 4. Calculated EMF functions for a series of ISEs having the same membrane but different primary ion concentrations, c_i in the internal solution, from 1 to 10^{-15} M in the inner solution. Curves are labeled with the corresponding negative logarithm.[47]

The observation of Sokalski et al. on the lowering of the ISS detection limit,[30] and its mathematical modeling by DLM, heralded a new chapter in exploring the power of potentiometric sensors under local equilibrium, as proved by a number of papers (for recent review, see ref 48).

2.2.1. Comments on Model Benefits and Drawbacks of DLM Models

The DLM allows the sensor response to be theoretically modeled in a way that was not possible for total-equilibrium models; it allows modeling of the variation in the selectivity vs time and the effect of lowering the detection limit under steady state to be interpreted.

From the theoretical point of view, the advantages of DLM-type modeling do not compensate for the drawbacks already known in the total-equilibrium models, as explained above. However, by extending the power of the total-equilibrium concepts, DLM, in a relatively simple way, can truly support practical advances in nonequilibrium potentiometry, since it exploits close-to-the membrane and trans-membrane fluxes for comprehensive analytical benefits. One possible application of DLM is by assuming the invalidity of steady state for concentration ($\partial c_i(x,t)/\partial t \neq 0$) and employment of the second Fick's law for ions treated as neutral species, as shown very recently.[49]

The main problem of the nonequilibrium potentiometry is in finding a "niche of stability" for the reproducible analytical readouts in a variety of matrixes and in time. The models presented so far are overidealized and not able to answer the basic questions, especially important in the case of lowering the detection limit: what is the role of the membrane, its thickness and dielectric constant, in shaping the sensor response? Similarly, how are other important questions to be answered, such as the following: How do the different diffusibilities of ions and ion-exchange rates influence the signal? When can the subtle effects of ionic mobilities in ISE membranes be ignored without a significant loss in accuracy? What are the bulk-to-bulk concentration and potential changes over time? Finally, how can the signal be stabilized if the sensor works in a nonequilibrium regime in different matrixes? All these questions call for a new "upper floor" approach in theoretical modeling, namely, for the advanced nonequilibrium models, which are described below.

2.3. Advanced Nonequilibrium Models

A fundamental difference between the advanced nonequilibrium models and the (total or local) equilibrium models is in abandoning of two constitutive conditions, the electroneutrality and (total or local) equilibrium condition. It is possible to do so, owing to the admission of charge separation from the Poisson equation and the finite ion-transfer rates described by the appropriate heterogeneous ion-transfer rate constants.

Modeling of the nonequilibrium potentiometric response of the ion-sensitive sensors requires employment of explicit space and time domains, which provide the platform for a set of relevant thermodynamic, extrathermodynamic, and kinetic data. This platform may be constructed by use of the Nernst−Planck and Poisson equation system (NPP)[50] or by a similar system that is an appropriate and rich enough tool to encompass the ion-sensor response. The first implementation of the NPP to model nonequilibrium (non-steady-state) response of ion sensors was recently reported by Sokalski and Lewenstam[51] and in the contributions that followed.[52−54]

The NPP equation system allows calculations of the electric potential difference and concentration profiles as a function of space and time for the conventional sensors with internal solution or for the sensors with solid internal contacts. In contrast to the total-equilibrium and diffusion-layer models, the NPP model does not require any arbitral splits of the membrane potential into phase boundaries and diffusion-potential terms (compare Figure 2). Additionally, it does not use idealizing assumptions of the total and/or local equilibrium and the electroneutrality conditions. The

NPP model applies for different membrane and film-based ISSs and for ions of every charge, without the need for a case-by-case approach as known from the previous models, described earlier.[4,13]

In the NPP model, multilayers and adjacent (diffusion) layers are admitted. The membrane and the bathing solution(s), or films in contact, may have a thickness and dielectric permittivity of choice. The membrane may contain unequally mobile and/or immobile charged and uncharged sites/ligands. Ions of any charge can be considered in the charge-transfer and transport processes. Different degrees of association between extracted ions and sites and ligands in the membrane are permissible. Furthermore, the gradient of the chemical potential of the solvent across the membrane and convective flows are allowed. In the present formulations of the NPP model, all activity coefficients in the membrane are assumed to be one, ion extraction is described by the first-order rate constants, and the 1D geometry is used.

The core of the NPP model is that ion fluxes in space (x) and time (t) are described by the Nernst−Planck equation,

$$f_i(x,t) = -D_i\left[\frac{\partial c_i(x,t)}{\partial x} - z_i c_i(x,t)\left(\frac{F}{RT}\right)E(x,t)\right] \tag{18}$$

where $f_i(x,t)$ is the flux of the ith ion, $c_i(x,t)$ is the concentration of the ith ion in space point x and time t, $E(x,t)$ is the electric field, D_i is the diffusion coefficient of the ith ion, and z_i is the charge of the ith ion, as in the models discussed above.

In order to solve eq 18, two additional equations are used to relate $f_i(x,t)$, $c_i(x,t)$, and $E(x,t)$. The first choice is the law of mass conservation:

$$\frac{\partial c_i(x,t)}{\partial t} = -\frac{\partial f_i(x,t)}{\partial x} \tag{19}$$

The second is the Poisson equation, rewritten for the total current density (I) as

$$I(t) = F\cdot\sum_i z_i\cdot f_i(x,t) + \epsilon\cdot\frac{\partial E(x,t)}{\partial t} \tag{20}$$

where ϵ is the dielectric permittivity.

In the calculations, the Chang−Jaffe boundary conditions are used,

$$\begin{aligned} f_{i0}(t) &= \overrightarrow{k}_i\cdot c_{i,bL} - \overleftarrow{k}_i\cdot c_{i0}(t) \\ f_{id}(t) &= -\overrightarrow{k}_i\cdot c_{i,bR} + \overleftarrow{k}_i\cdot c_{id}(t) \end{aligned} \tag{21}$$

where f_{i0}, f_{id}, c_{i0}, and c_{id} are the fluxes and concentrations at $x = 0$ and $x = d$ (where d is membrane thickness), respectively; $\overrightarrow{k}_i$ and $\overleftarrow{k}_i$ are the forward and backward rate constants, respectively, and their ratio is a partition coefficient; and $c_{i,\mathrm{bL}}$ and $c_{i,\mathrm{bR}}$ are the concentrations in the bathing solutions on the left (L) and right side (R) of the membrane, respectively.

The system of nonlinear partial differential equations 18, 19, and 20 is solved to obtain the resolution in space and time by the finite-difference[51−54] or finite-element method.[55] Some authors stress the complexity of these procedures.[21] We do not share this opinion; to the contrary, the implementation and access are simple when using appropriate commercial platforms.

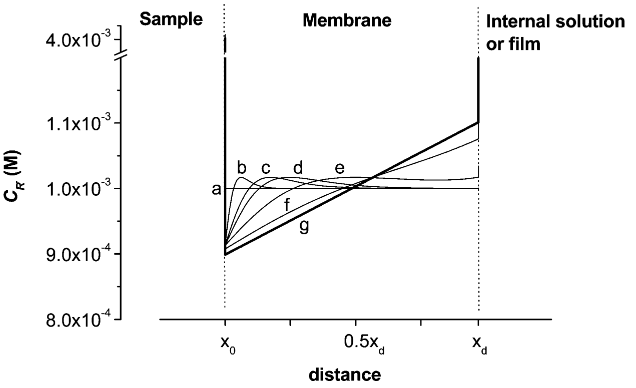


Figure 5. Time-dependent concentration profiles for site R$^-$ ([i^+] = 10^{-4}, [j^+] = 10^{-3}, $\bar{D}_i/\bar{D}_j = 0.5$, $K_{i,j} = 0.1$, and $\bar{R}_{\mathrm{TOTAL}} = 10^{-3}$). Curves a−g show profiles after the following: (a) 4 × 10^{-4}, (b) 1.64, (c) 13.1, (d) 26.2, (e) 104.8, (f) 420, and (g) 13 440 s (steady state).[50]

2.3.1. Comments on the Benefits and Drawbacks of the Advanced Model

The total-equilibrium and diffusion-layer models are merely special cases (concretizations) of the NPP model. In a strict formal (mathematical) sense, all that is predicted by the PBMs and DLMs can be obtained from the NPP model by deduction (as shown in Figure 11 and discussed below). Of course, in simple, theoretical cases and routine laboratory practice, the full use of NPP is not necessary. (While admitting this, it should be emphasized that the argument repeatedly given by some authors in favor of phase-boundary models (PBMs),[21] namely, that, in the NPP, the knowledge of individual mobilities of relevant ions and their transfer rates at the phase boundary is required, is not in contrast to the phase-boundary models. Actually, in the PB models, as was shown above, even stronger assumptions are used, i.e., that the rate constants are infinite and all individual mobilities are equal.) However, for modeling of time-dependent processes, in cases of suspected nonlinearities, and for someone working with sensors under nonequilibrium, as happens in the case of fast readout times or in lowering the detection limit, the NPP approach or a similar theoretical tool *is a must*. The reason is simple: as the model from the “upper floor”, the NPP model provides hard numerical facts instead of verbal declarations and unproven intuitions, so often made by advocates of simple modeling.

The NPP approach has already provided novel insights and numerical answers to problems in ISE practice that have been intriguing for decades and which the DLM and PB models were unable to describe: the concentration and potential profiles over equilibration time and even under steady state (or equilibrium) revealed striking nonlinearities (see Figure 5), shown for R$^-$, which in the PB and DLM models is assumed to be not dependent on distance (x) and time (t). It was presented that the contribution of the so-called diffusion potential prior to equilibrium is significant and varies with time (Figure 6), and in consequence, prediction of NPP and PB models for the same conditions can be strikingly different (Figure 7): In fact, the overall linearity of the calibration curves depends on the distance from the steady state or equilibrium in the sensor system, and even under steady state may be significantly influenced by migrational effects (Figure 8). (For simplicity, these

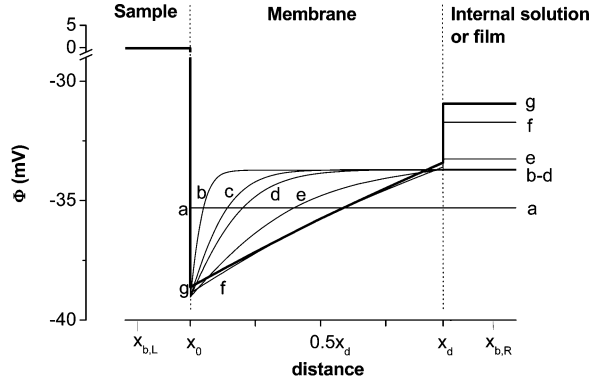


Figure 6. Time-dependent and distance-dependent potential profiles, calculated as $\varphi(x,t) = \int E(x,t)\,\mathrm{d}x$. Total membrane potential is $E_M(x,t) = \int_{x_{b,L}}^{x_{b,R}} E(x,t)\,\mathrm{d}x$, where $x_{b,L}$ and $x_{b,R}$ are the points in the bulk of bathing sample solution (on the left, L) and internal solution/film (on the right, R). Curves a−g show profiles after the following: (a) 4×10^{-4}, (b) 1.64, (c) 13.1, (d) 26.2, (e) 104.8, (f) 420, and (g) 13 440 s (steady state).[52]

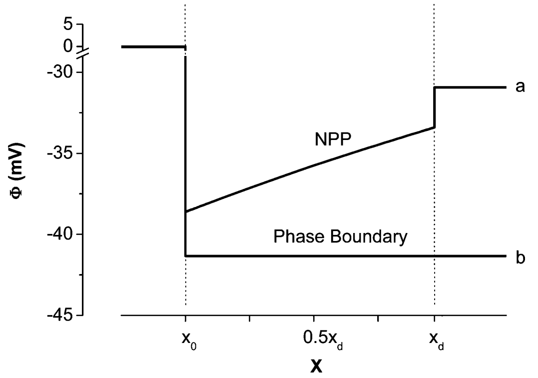


Figure 7. Comparison of the (a) steady-state NPP potential profile from Figure 6 with that presumed by (b) the phase-boundary model.[52]

effects are shown here schematically; for numerical details, see refs 52 and 53.)

Furthermore, the NPP model shows unequivocally that the concentration profile of the species confined in the membrane phase (the oppositely charged sites) can dramatically change over the membrane distance along with highly nonlinear (and thus "nonintuitive") profiles. For this reason, a strict electroneutrality condition, represented by the distance-independent charge-balance equation, used in PB models[16,21] is expedient to allow binding of opposite charges in the membrane boundary but is clearly inadequate.[53,55]

Recent results from use of the NPP model allowed the analysis of concentration profiles with time for membranes bathed by strongly interfering ions (a chloride-sensitive membrane bathed with perchlorates),[53] as illustrated in Figure 9, where the theoretical prediction and experimental results are compared.

In the same work, selectivity changes as a function of time were examined, which had been inaccessible for the total-equilibrium model (PB model) and only partially accessible to the diffusion-layer model (DLM). Moreover, the access to spatial distributions of ions and the electric potential vs distance during equilibration time allows inspection of the underlying reasons for selectivity coefficient changes and their magnitudes.[53,54]

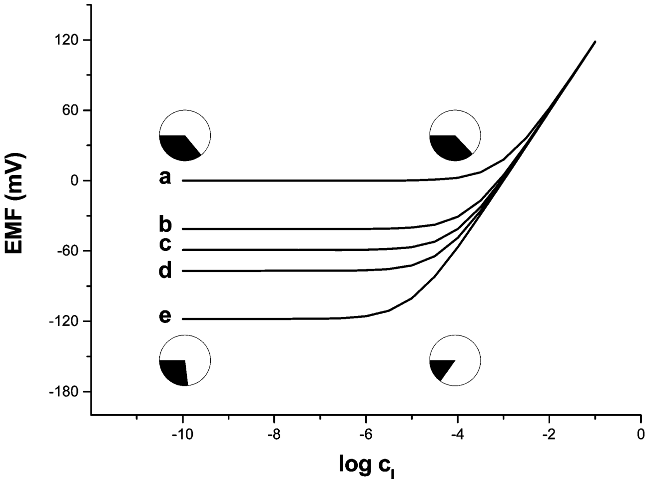


Figure 8. Calibration curves in the presence of primary ($[i^+] = (10^{-10}$ to 10^{-1} M)) and interfering ($[j^+] = 10^{-3}$ M) ions calculated according to the NPP model (other data as in Figure 5). Pie charts express contributions of phase-boundary potential (E_{PB}) (white) and inner membrane (diffusion) potential (E_d) (black) for the outermost calibration curves ($D_i/D_j = 0.1$ or 10) at $[i^+] = 10^{-4}$ and $[i^+] = 10^{-10}$ M, $K_{i,j} = 0.1$ The curves correspond to the following diffusion coefficient rations ($\bar{D}_i/\bar{D}_j$): (a) 0.1, (b) 0.5, (c) 1, (d) 2, and (e) 10.[52]

A similar methodology was used in the numerical analysis of the detection limit due to the transmembrane ion fluxes, to find the parameters important for its evolution and stabilization over a period of time. The NPP model allows numerical analysis of the important role of transmembrane ion fluxes—as well as the appearance of the electric potential drops at one interface (sample|membrane) or at two interfaces (sample|membrane and membrane|internal contact interfaces)—in shaping the effect of the lowering of the detection limit.[55,56] Consequently, for the first time, the significant influence of ion transport (diffusion), distribution and rate parameters, ion charges, dielectric constant, and thickness of the membrane are predicted. The NPP approach provides realistic concentration profiles as a function of time, which previously could only be addressed by the DLM, assuming linear concentration drops (compare Figure 3 and Figure 10a). In addition, the NPP model provides the profile of the electric potential in space and time (Figure 10b), which, according to the DLM (being a steady-state model), cannot be modeled. There is no doubt that enhanced sensitivity of measurements under nonequilibrium may be paid for by a decreased reliability of the results.

Thus, an important and so far untouched question concerning the influence of the diffusion potential and its variation from sample-to-sample and over readout time, which may unfavorably and in an uncontrolled manner influence the precision of measurements with ISSs, can now be considered. Demonstrably stable and reproducible measurements have not yet been convincingly achieved. However, via the nonequilibrium model (NPP), a comprehensive analysis of this problem will soon be presented.[56] The inevitable conclusion is that the NPP offers a novel tool for solving a number of, up until now, inaccessible problems in nonequilibrium potentiometry.

The NPP is, by far, more general than the DLM and PB models, with the latter being special cases of the NPP, as shown in Figure 11. The relationship between these potentiometric models is characteristic of empirical sciences, for instance, relativistic mechanics and its special case, classical mechanics (even if we have ample confirmation from everyday routines in contrast with relativistic theory). For

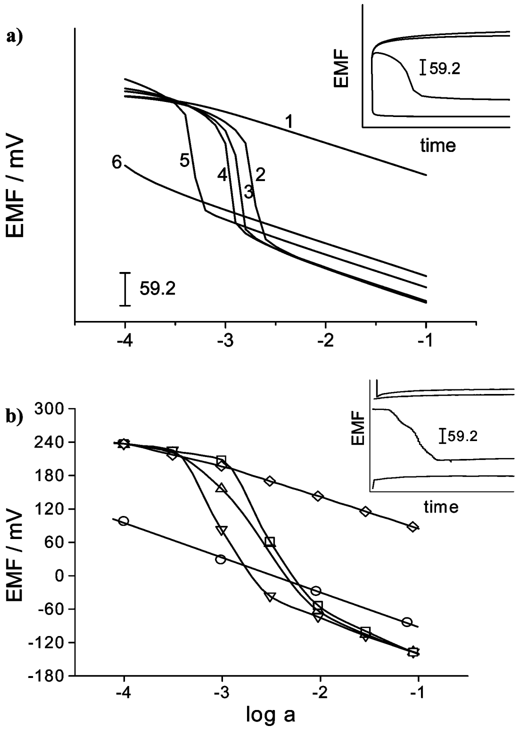


Figure 9. Theoretical and experimental calibration curves for ion-exchanger electrode chloride ISS.[53] (a) Calibration curves calculated for membrane conditioned in i^- and j^- for solutions of (1) j^- (5 min), (2) i^- (5 min), (3) i^- (15 min), (4) i^- (30 min), and (5) i^- (60 min), and (6) calibration curve obtained with a membrane conditioned in i^- for a solution of i^- (60 min). i is the preferred ion, and j is the discriminated ion. The inset shows the EMF time dependence for an ISE conditioned in discriminated ion for 10^{-4}, 10^{-3}, 10^{-2}, and 10^{-1} M, in order from top to bottom. (b) Calibration curves obtained with a membrane conditioned in Cl^- for solutions of (◇) Cl^- (5 min/conc.), (□) ClO_4^- (5 min/conc.), (△) ClO_4^- (15 min/conc.), (▽) ClO_4^- (30 min/conc.). Calibration curve obtained with a membrane conditioned in ClO_4^- for a solution of (○) ClO_4^- (60 min/conc). ClO_4^- is the preferred ion, and Cl^- is the discriminated ion. The inset shows the EMF time dependence for an ISE conditioned in Cl^- for 10^{-4}, 10^{-3}, 10^{-2}, and 10^{-1} M in order from top to bottom.

this reason, the theoretical value of the NPP is unquestionable.

To summarize, there is currently no doubt that, according to a hierarchy of the generality of the models discussed, the NPP approach provides clear added value, with regard to both nonequilibrium response and characteristics of the steady state of potentiometric ion sensors. The NPP also allows assessment of the migrational effects, finite kinetics, and permittivity of the membrane, none of which can be accessed via more idealized models because of their limited dictionaries and formalisms, as shown in Table 1.

Additionally, Table 1 shows that, although the NPP itself has its own intrinsic idealizations and limitations and shares common idealizing assumptions and parameters with the DLM and NE, it is simply more powerful. This again reflects the process of the cumulation of knowledge, which is well-known for empirical sciences.[8]

A new chapter in modeling on the level of the generality dictated by the NPP has now been breached, and questions insurmountable for the simpler DLM and PB models can now be answered. There is a list of problems concerning ISE/ISSs to be addressed, as well as many technical possibilities to be investigated. In 2D and 3D, modeling of fluxes through nanotubes and biological channels is still under development. Assumptions such as those listed above, i.e., equating activities and concentrations, uncoupled fluxes, complex-forming processes in the membrane, higher-order rate equations, influence of the electric field on ion-transfer rates, e.g., by extending the Chang−Jaffe boundary conditions in a form of Butler−Volmer conditions, must all be considered. (The latter condition admits the influence of the electric field on rate constants; although this is formally and programwise a simple extension as will be shown shortly,[54] the problem of the ion-transfer mechanisms is still controversial and open.[57−59]) Furthermore, the variability of the dielectric constant along the membrane distance and at the interfaces needs to be considered, and finally, increasing the library of transport parameters in the membranes and films relevant to sensor technology needs to be recognized.[60] These are just some examples of the interesting problems requiring further theoretical work on the assumed "level" of approximation and experimental verification.[55,56]

Present applications of ion sensors in the nonequilibrium regime, and the need for proper theoretical support, show that understanding of the response mechanism of potentiometric sensors is a new and open challenge. Without ignoring the achievements and power of the earlier classical or diffusion-layer models, a call for advanced modeling is nonetheless unquestionable.

3. Solid-Contact ISEs

Elimination of the internal filling solution from conventional ISEs results in solid-contact ISEs (ISSs), which are more durable and easier to miniaturize than their conventional counterparts. However, in order to obtain solid-contact ISEs with stable electrode potential, it is necessary to have sufficiently fast and reversible ion-to-electron transduction in the solid state without any contribution from parasitic side reactions.[61] Research and development of solid-contact ISEs had already started in the beginning of the 1970s with the invention of the coated-wire electrode (CWE), which indeed represents a simple and robust design.[62] The main drawback of the CWE is obviously the poor potential stability resulting from the blocked interface that forms between the purely electronic conductor (metal) and the purely ionic conductor (ion-selective membrane). Solid-contact ISEs with improved potential stability have, therefore, been produced by utilizing electroactive materials showing mixed electronic and ionic conductivity that serve as ion-to-electron transducers between the electronic conductor and the ion-selective membrane.[61] Among the electroactive materials available today, electroactive conjugated polymers (conducting polymers) have emerged as one of the most promising ion-to-electron transducers for solid-contact ISEs.[63−66]

Other approaches to solid-contact ISEs involve the use of Ag/AgCl,[67] Ag/AgCl/hydrogel,[68] redox-active self-assembled monolayers,[69,70] Prussian Blue,[71] carbon-based composites,[72,73] Ag-based composites,[74] and Ag/AgCl/porous carbon loaded with ionophore and plasticizer that resulted in a solid-contact Pb^{2+}-ISE with an impressive lower limit of detection below 10 pM.[75]

3.1. Conducting Polymers

The discovery and development of conjugated polymers that can be made electronically conducting by partial oxidation (p-doping) or reduction (n-doping) has had a great

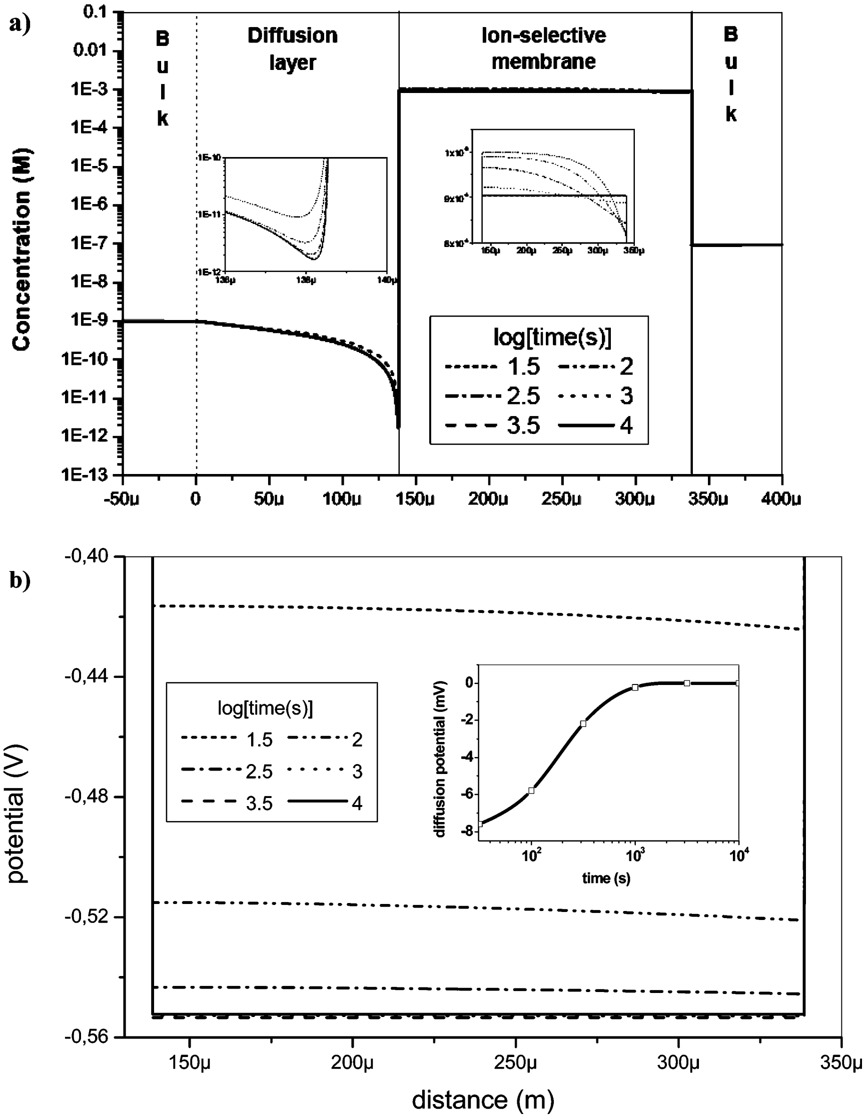


Figure 10. Calculated by NPP, the main ion concentration (a) and the electrical potential changes in space and time (b).[54] $c_{iL} = 10^{-9}$, $c_{iR} = 10^{-7}$, $\bar{c}_{jL} = 10^{-7}$, and $\bar{c}_{jR} = 10^{-1}$; $\bar{c}_i = \bar{c}_{R^-} = 10^{-3}$ (mol/dm^3); $D_i = 10^{-9}$ and $D_j = 10^{-8}$ and $\bar{D}_i = 10^{-11}$ and $\bar{D}_j = 10^{-10}$ (m^2/s); $\bar{k}_{i,l} = \bar{\bar{k}}_{i,l} = 1$; $\bar{k}_{i,l} = 10^{-7}$ and $\bar{k}_{i,l} = 1$ (m/s), L and R denote the left and right sides of the membrane. Diffusion potential is calculated at 1 μm distance from the interfaces in the interior of the membrane.

impact on several fields of science and technology, which naturally goes far beyond the scope of this review.[76−84] However, it should be mentioned here that conducting polymers have been applied in a large variety of chemical sensors and several reviews have been published on this topic.[63−66,85−114] A few of these reviews focus entirely on the application of conducting polymers in potentiometric sensors.[63−66,92,97,114] Although conducting polymers have been known in the field of potentiometric ion sensors since the 1980s, development is still continuing.

Conducting polymers have some key features that are useful when applied as ion-to-electron transducers in solid-contact ISEs. Conducting polymers are electronically conducting materials that can form an ohmic contact to materials with a high work function, such as carbon, gold, and platinum, which ensures a proper electronic (ohmic) contact. Conducting polymers can be deposited on the electronic conductor by electropolymerization of the monomer or by solution-casting of the soluble conducting polymer, which gives some flexibility in the manufacturing process. Conducting polymers are electroactive materials with mixed electronic and ionic conductivity, which means that they can transduce an ionic signal into an electronic one in the solid state. Furthermore, the properties of conducting polymers can be tailored via functionalization, e.g., by covalent bonding of side groups to the conjugated polymer backbone and by immobilization of functional doping ions. These are important features that make conducting polymers suitable as solid contacts in combination with conventional ion-selective membranes.[63]

In this type of solid-contact ISE, where the conducting polymer is coated with a conventional ion-selective membrane, the ion-selectivity is determined mainly by the ion-selective membrane, which allows the utilization of various ionophore-based polymeric membrane formulations that are available.[4,5] Recent progress in the area of ISEs such as the lowering of the detection limit toward the picomolar level,[30] enabling potentiometric trace-level analysis,[6] gives an additional impetus for the development of solid-contact ISEs with improved analytical performance. Conducting polymer-based solid-contact materials are boosting "the new wave of ion-selective electrodes".[7]

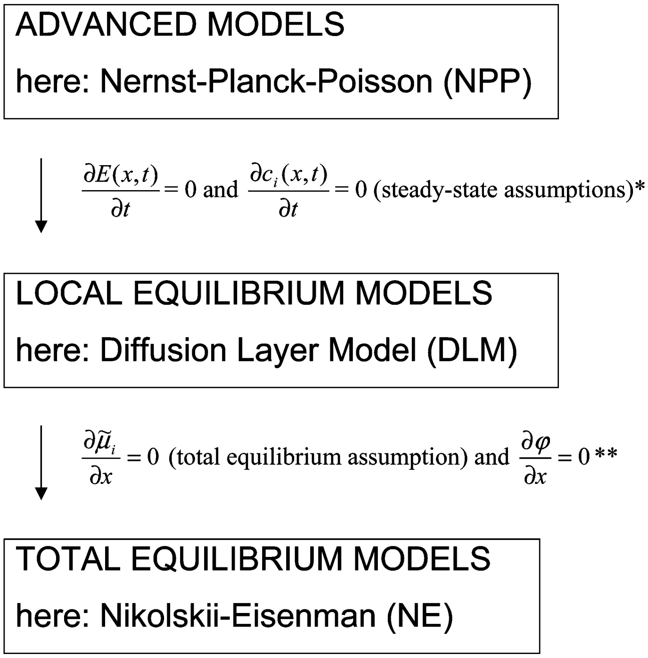


Figure 11. Interrelation between models in potentiometry. (*) The condition reads as follows: there is no change in electric field strength and concentration of ions over time in the system sample/membrane/internal contact (solution or film). (**) The condition reads as follows: there is total equilibrium over distance in the system sample/membrane/internal contact (solution) or film, i.e., electrochemical potential of each special along x is constant; additionally, electrical potential over distance in each phase, and in consequent concentrations of each species, are contact except the phase boundaries.

3.2. Conducting Polymers as Solid Contact

Over the past few years, the analytical performance of ISEs where conducting polymers are used as ion-to-electron transducers (solid-contact ISEs) has been dramatically improved. Solid-contact ISEs for determination of both inorganic and organic ions were constructed by using conducting polymers as the ion-to-electron transducers. Of particular interest is the lowering of the detection limit down to the nanomolar level. The conducting polymer materials were based mainly on electropolymerized or chemically polymerized derivatives of pyrrole (Figure 12), thiophene (Figure 13), and aniline (Figure 14).

3.2.1. Polypyrroles

Polypyrrole was already used as an ion-to-electron transducer in solid-contact ISEs in the beginning of the 1990s[115] and is frequently still used for the same purpose today. Recent developments were focused on improving the fabrication techniques and the analytical performance of such solid-contact ISEs.

Polypyrrole was found to be useful as a solid contact in planar ISEs.[116,117] A critical comparison of conducting polymer- and hydrogel-based solid contacts in K^+-ISEs showed that polypyrrole doped with potassium hexacyanoferrate results in solid-contact K^+-ISEs with better long-term potential stability than those based on the hydrogel contact.[118]

Polypyrrole doped with Tiron was used as a solid contact in Ca^{2+}-ISEs.[119−121] Since Tiron complexes Ca^{2+}, the detection limit of such ISEs was found to be as low as 10^{-9} M. Similar detection limits were obtained for a Pb^{2+}-ISE using polypyrrole doped with hexacyanoferrate as a solid contact when the electrode was used in a flow-through cell.[122] The detection limit of Cl^--ISEs based on polypyrrole as the solid contact could be lowered by more than 3 orders of magnitude when applying an anodic current that compensated the Cl^- leakage from the ion-selective membrane (due to self-discharge of polypyrrole).[123] The influence of spontaneous charge-transfer processes of polypyrrole on the linear response range and selectivity of Ca^{2+}-ISEs using polypyrrole as a solid contact was studied.[124] Galvanostatic polarization of solid-contact ISEs was found to offer some control of the ion flux through the electrode and, consequently, could be used to lower the detection limit.[125,126] Interestingly, K^+-ISEs based on methacrylic/acrylic membranes in combination with polypyrrole as the solid contact resulted in K^+-ISEs with both improved detection limit (below 10^{-6} M) and excellent stability.[127] These results show that polypyrrole-based solid-contact ISEs with polymeric ion-selective membranes are promising also for low-concentration measurements.

Polypyrrole doped with tetraphenylborate was used as a solid contact in K^+-ISEs in order to have well-defined ion transfer between the conducting polymer and the ion-selective plasticized poly(vinyl chloride) (PVC)-based membrane.[128] Polypyrrole doped with different anions was also employed as a solid contact in pH electrodes based on polymer membranes containing tertiary amine ionophores.[129] The physicochemical properties of polypyrrole can be significantly influenced by the doping ion, which offers possibilities of improving, e.g., adhesion of polypyrrole to the ion-selective membrane. This is well-illustrated by the use of polypyrrole doped with cobalt bis(dicarbollide) ions as the solid contact in pH-, Cu^{2+}-, and K^+-selective microelectrodes.[130−132] Furthermore, a composite of polypyrrole and Nafion was applied as the solid contact in pH electrodes based on glass membranes.[133,134] Polypyrrole was used as an ion-to-electron transducer also in solid-contact ISEs for determination of oxytetracycline hydrochloride and methacycline hydrochloride, which are antibiotics belonging to the tetracycline family.[135,136]

Poly(1-hexyl-3,4-dimethylpyrrole), which is soluble in tetrahydrofuran (THF), was used as a solid contact in carbonate-selective ISEs based on a silicone rubber membrane.[137,138] Solution-processable conducting polymers offer some additional flexibility in the electrode manufacturing process, when compared to electropolymerization.

3.2.2. Polythiophenes

Poly(3-octylthiophene) (POT) was the first one of the polythiophenes to be used as a solid contact in ISEs.[139] More recently, solution-cast films of POT on screen-printed gold substrates and on platinum (silicon-based substrates) were evaluated as solid contacts in miniature Cl^--ISEs.[140,141] Improved analytical performance was obtained by using an additional adhesive layer (3-aminopropyltriethoxysilane) between the screen-printed gold electrode and the POT film, while there was no significant difference between PVC and polyurethane (PUR, Tecoflex) used as the ion-selective membrane matrices.[140,141]

Pb^{2+}-ISEs were constructed by using solution-cast POT as the solid contact to a Pb^{2+}-selective membrane based on poly(methylmethacrylate)/poly(decylmethacrylate) (MMA/DMA).[142] POT is highly lipophilic, which helped to prevent the formation of an internal water layer between the solid contact and the ion-selective membrane. Interestingly, the solid-contact Pb^{2+}-ISE showed a much faster response at low

Table 1. Principles of the Models in Potentiometry

model	parameters used (model dictionary)	main assumptions	main benefits of model application in potentiometry (current state)
advanced models here, Nernst−Planck−Poisson (NPP)	$E_M(x,t)$ $c_i(x,t)$ $\bar{c}_i(x,t)$ $\vec{k}_i$ and $\overleftarrow{k}_i$ (including $K_{i,j}$) x (including δ, d) D_i, $\bar{u}_i$ ϵ t	(1) general assumptions (see p 5); zero-current, no pressure and temperature gradients, no solvent flow, no convection (2) membrane homogeneous and flat, ionically conducting (3) one-dimension (1D) (4) infinite dilution/ideal phase (activities = concentrations) (5) sharp border between phases (6) permittivity = const over distance in each phase[a] (7) no flux coupling[a]	time- and space-dependent electrode response, selectivity, and low detection limit, access to membrane physicochemical properties (e.g., migrational effects, permittivity), finite charge-transfer rates
local-equilibrium models here, diffusion-layer model (DLM)	$E_M(t \rightarrow \infty)$ c_{i0}, $\bar{c}_{i0}$, $K_{i,j}$ δ, d D_i, $\bar{u}_i$ t (?)	(1) as in NPP (1−5) (2) electroneutrality (3) infinite rate constants (4) local equilibrium (5) steady state (limited access to time and space domains) (6) linear concentration changes over distance; electrical potential changes only at the phase boundaries	electrode response, selectivity, and low detection limit under steady state
total-equilibrium models here, Nikolskii−Eisenman (NE)	E_M c_i, $\bar{c}_i$ $K_{i,j}$ u_i (?)	(1) as in DLM (1−3) (2) total equilibrium (3) constant concentrations and electrical potentials in each phase except of phase boundaries	time-independent electrode response, selectivity, and low detection limit; access to chemical binding processes in the membrane

[a] 6 and 7 specific for NPP.

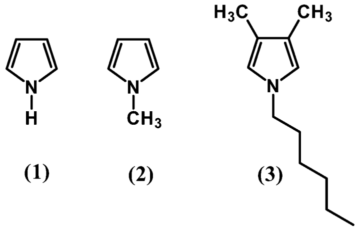

(1) (2) (3)

Figure 12. Pyrrole-based monomer units of polymers applied as ion-to-electron transducers in solid-state ISEs over the past few years: (1) pyrrole, (2) *N*-methylpyrrole, and (3) 1-hexyl-3,4-dimethylpyrrole.

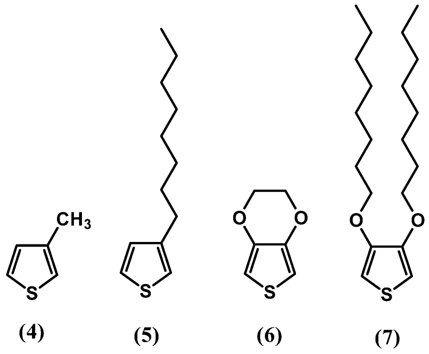
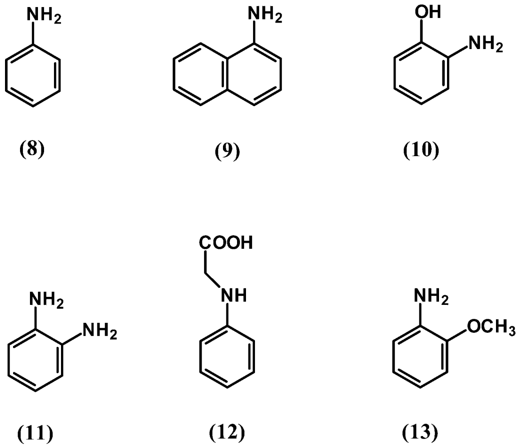

(4) (5) (6) (7)

Figure 13. Thiophene-based monomer units of polymers applied as ion-to-electron transducers in solid-state ISEs over the past few years: (4) 3-methylthiophene, (5) 3-octylthiophene, (6) 3,4-ethylenedioxythiophene, and (7) 3,4-dioctyloxythiophene.


(8) (9) (10)

(11) (12) (13)

Figure 14. Aniline-based monomer units of polymers applied as ion-to-electron transducers and/or in solid-state ion-selective electrodes over the past few years: (8) aniline, (9) α-naphthylamine, (10) *o*-aminophenol, (11) *o*-phenylenediamine, (12) *N*-phenylglycine, and (13) *o*-anisidine.

concentrations and even a slightly better detection limit ($10^{-9.3}$ M) compared to the corresponding liquid-contact ISE. This has resulted in renewed interest in POT as a solid-contact material in ISEs. The use of solution-cast films of undoped POT as a solid contact together with plasticizer-free acrylate-based ion-selective membranes resulted in a number of solid-contact ISEs (Ag^+, Pb^{2+}, Ca^{2+}, K^+, I^-) with detection limits close to the nanomolar (10^{-9} M) range.[143,144] Solution-cast POT was found to be a very suitable solid-contact material also for Ca^{2+}-ISEs utilizing conventional PVC-based ion-selective membranes, showing, in addition, a low detection limit.[145] However, the long-term potential stability of solid-contact NO_3^--ISEs based on POT as a solid contact was found to be somewhat inferior to conventional NO_3^--ISEs with internal filling solution.[146]

The potential stability of solid-contact K^+-ISEs was found to correlate well with the bulk redox capacitance of the conducting polymer, as shown by using poly(3,4-ethylenedioxythiophene) (PEDOT) as a solid-contact material.[147] This can be understood when considering that the transduction of an ionic signal into an electronic one via the redox reaction of a conducting polymer results in charging/discharging (doping/undoping) of the conducting polymer layer. From this point of view, chronopotentiometry was found to be a convenient and fast experimental method to evaluate the potential stability of solid-contact ISEs.[147]

PEDOT is highly electroactive and shows good environmental stability in its oxidized (p-doped) form. Consequently, PEDOT has been studied rather intensively as a solid-contact material in recent years. PEDOT doped with poly(styrene sulfonate) (PSS), i.e., PEDOT(PSS), was applied as an ion-to-electron transducer in solid-contact ISEs for various ions, including K^+,[147,148] Ag^+,[149,150] Na^+,[151] Cs^+,[151] Ca^{2+},[152] and some aromatic cations (*N*-methylpyridinium, bupivacaine).[153,154] The potential of solid-contact K^+-ISEs based on PEDOT as a solid contact was found to be less sensitive to O_2 and CO_2 (pH) compared to those based on polypyrrole.[147,148] A small-volume radial flow cell for solid-contact ISEs using PEDOT(PSS) as a solid contact was also described.[155] The solid contacts were prepared by electropolymerization of the 3,4-ethylenedioxythiophene monomer and by solution casting of the commercially available aqueous dispersion of PEDOT(PSS) (Baytron P). Solution-cast films of PEDOT(PSS) (Baytron P) were applied as the solid contact also to screen-printed gold substrates.[106] The water-solubility of the solution-cast PEDOT(PSS) film was decreased by ionic cross-linking with multicharged cations (Mg^{2+}, Ca^{2+}, $Fe^{2+/3+}$, or $Ru(NH_3)_6{}^{2+/3+}$) before application of the plasticized PVC-based K^+-selective membrane.[156] Recently, PEDOT was applied as the solid contact in newly designed microcavity-based solid-contact ion-selective microelectrodes.[157]

PEDOT doped with hexacyanoferrate was used as the solid contact in Cu^{2+}-ISEs.[158] The improvement in the detection limit was attributed to spontaneous accumulation of Cu^{2+} in the solid contact, causing an influx of Cu^{2+} ions at the ion-selective membrane/solution interface.[158] The detection limit and stability of Pb^{2+}-ISEs using PEDOT(PSS) as a solid contact was found to be influenced by the presence of interfering ions in the conducting polymer layer.[159] Furthermore, by using soluble poly(3,4-dioctyloxythiophene) (PDOT), which is more lipophilic than PEDOT, it was possible to show the importance of the ion content of PDOT when used as a solid-contact layer.[160]

All-plastic disposable Ca^{2+}-ISEs and K^+-ISEs were prepared via solution-casting of PEDOT/PSS (Baytron P) and plasticized PVC-based membranes on plastic substrates.[161] Here, the PEDOT/PSS worked both as the ion-to-electron transducer and as the electronic contact. The same approach was used also for Cu^{2+}-ISEs where the leakage of primary ions from the membrane was eliminated as indicated by a super-Nernstian response for Cu^{2+} activities below 10^{-4} M.[162]

Poly(3-methylthiophene) (PMT) doped with BF_4^- and modified with EDTA as a complexing agent was used as the solid contact in Ca^{2+}-ISEs for low-level concentration measurements.[163] The Ca^{2+}-ISEs showed a super-Nernstian response for Ca^{2+} activities below 10^{-5} M, indicating an influx of Ca^{2+} ions to the ion-selective membrane as a result of complexation of Ca^{2+} with EDTA present in the solid contact.[163]

3.2.3. Polyanilines

Solution-cast polyaniline (PANI) was used as a solid contact in miniature Cl^--ISEs.[141] The analytical performance of these solid-contact Cl^--ISEs was found to be similar to those based on POT as a solid contact.[141]

Electrosynthesized PANI was applied as a solid contact in ISEs based on plasticized PVC-based ion-selective membranes. Good overall analytical performance was obtained for such solid-contact ISEs selective to pH[164] and Tl^{3+}.[165] The stability of the PANI solid contact in K^+-ISEs based on plasticized PVC was studied by using UV−visible spectroscopy. Partial conversion of PANI from its conducting emeraldine salt form to its nonconducting emeraldine base form was found to take place during long-term measurements (1−3 months) but not during short-term measurements (4 days).[166]

Different derivatives of polyaniline, including poly(α-naphtylamine), poly(*o*-aminophenol), poly(*o*-phenylenediamine), and poly(*N*-phenylglycine), were used as solid contacts in plasticized PVC membrane-based ISEs for determination of various organic compounds of pharmaceutical importance, including dimedrol,[167] chlordiazepoxide,[168] propranolol,[169] papaverine,[170] amiodarone,[171] and dopamine.[172] The potential stability of some of the solid-contact ISEs was evaluated by current reversal chronopotentiometry,[168,171,172] a method used earlier for K^+-ISEs based on PEDOT as the solid contact.[147]

3.3. Conducting Polymers Dissolved in the Ion-Selective Membrane

Solid-contact ISEs, where the conducting polymer is dissolved in the ion-selective membrane, were initially called single-piece electrodes.[173] Since the conducting polymer is dissolved in the ion-selective membrane, it can influence the selectivity of the electrode.

Solid-contact Li^+-ISEs based on plasticized PVC containing 1% (w/w) PANI protonated (doped) with bis(2-ethylhexyl) phosphoric acid were studied.[174] The solid-contact Li^+-ISEs showed the same dynamic response range as the conventional ISE with internal solution. However, the presence of PANI in the ion-selective membrane increased the H^+ interference, due to the pH sensitivity of PANI.[174]

PANI protonated (doped) with phosphoric acid dihexadecyl ester was used both as an ion-to-electron transducer and as a pH-sensitive component in plasticized PVC-based membranes.[175] Membranes containing 50% (w/w) PANI and 50% plasticized PVC showed the best pH sensitivity among those studied. Interestingly, the emeraldine salt−emeraldine base transition of PANI was facilitated by lipophilic cations and hindered by lipophilic anions added to the membrane. However, the analytical performance of these pH electrodes was slightly inferior to that of electrochemically synthesized PANI.[175]

Solid-state ISEs for determination of linear alkylbenzenesulfonates were constructed by using plasticized PVC membranes containing 5% (w/w) electrochemically synthesized polypyrrole doped with dodecylbenzenesulfonate.[176] Here, polypyrrole worked both as an ion-to-electron transducer and as an anion-exchanger for alkylbenzenesulfonate anions.

Solid-state K^+-ISEs were prepared by using plasticized PVC membranes containing 2% (w/w) polypyrrole, PANI, or poly(*o*-anisidine) that were doped (protonated) with diesters of sulfosuccinic acid.[177] The membranes were solution-cast on planar silver electrodes. The resulting solid-contact K^+-ISEs showed comparable selectivity with the corresponding hydrogel-contact K^+-ISEs. However, the presence of the conducting polymer, especially polypyrrole, in the ion-selective membrane improved the reproducibility and repeatability of the response. The signal stability of this type of solid-contact K^+-ISE containing 2% (w/w) polypyrrole doped with di(2-ethylhexyl)sulfosuccinate was improved when the membrane was cast on a gold substrate instead of silver,[178] which can be related to the higher work function of gold compared to silver. The presence of polypyrrole in the membrane did not influence the ion-selectivity in this case.

3.4. Conducting Polymers as Sensing Membranes

Solid-state ion-selective electrodes based on immobilization of ion-recognition sites in the conducting polymer membrane represent a research area of great potential. Over the past few years, the main focus has been on conducting polymers that contain ion-recognition sites in the form of immobilized doping ions.[24] Covalent binding of ion-recognition sites to conducting polymers was already suggested in the 1980s.[179] Covalent binding of ion-recognition sites to the conducting polymer backbone allows integration of the ion-recognition sites and the ion-to-electron transducer even within the same (macro)molecule, which may be of great importance for the construction of durable micro- and nanosized ion sensors in the future. However, the synthesis of such functionalized monomers and their polymerization is relatively demanding.

A solid-state Zn^{2+}-ISE based on electrochemically synthesized polypyrrole doped with tetraphenylborate was developed.[128,180] The selectivity coefficients ($\log K_{Zn,j}$) determined by the fixed interference method were as follows: $j = Ca^{2+}$ (−2.7), Mg^{2+} (−2.1), Pb^{2+} (−1.6), Ni^{2+} (−0.6), and Co^{2+} (−0.6).[128,180]

Solid-state ISEs for different cations (Ca^{2+}, Mg^{2+}, Cu^{2+}, and Zn^{2+}) based on electrochemically synthesized polypyrrole doped with metal-complexing ligands were further developed.[181,182] In addition to metal-complexing groups, the ligands contain sulfonate groups that compensate for the positive charge of the oxidized (p-doped) polypyrrole backbone. The effects of chemical (soaking) and electrochemical (oxidation/reduction) conditioning on the potentiometric sensitivity and selectivity of polypyrrole doped with metal-complexing ligands were studied in detail.[181,182]

Polypyrrole doped with adenosine triphosphate (ATP) was found to give a near-Nernstian response to Ca^{2+} and Mg^{2+}, and the response was not influenced by Na^+.[183] It was suggested that the polypyrrole doped with ATP can be used as artificial membranes in order to model ATP-mediated processes of real biological membranes.[183] Furthermore, there was a correlation between the film topography and the potentiometric response of PEDOT doped with ATP, which was sensitive to Ca^{2+} and Mg^{2+}.[184] Smoother films generally showed a more stable and faster potentiometric response than the rougher ones.[184] Polypyrrole and PEDOT doped with heparin were also found to give a near-Nernstian response to Ca^{2+} and Mg^{2+}, and the response was not influenced by Na^+ or K^+.[185] The response remained unchanged even after 1 year of soaking, indicating the high stability of this type of electrode.[185]

A solid-state pH electrode were developed by using electrochemically synthesized polypyrrole doped with cobalt bis(dicarbollide).[186] The electrode showed a quasi-Nernstian response (−50 mV/pH unit) and a linear range from pH 3 to 12. Electrodeposited polymers based on various monomers containing amino groups (1,3-diaminopropane, diethylenetriamine, pyrrole, *p*-phenylenediamine, and aniline) were studied as pH sensors, showing a linear response in the range from pH 2 to 11.[187] Polypyrrole-based pH sensors were miniaturized.[188] Electrochemically synthesized PPy doped with bicarbonate was applied as a pH electrode in a Severinghaus CO_2 sensor.[189] Electrochemically synthesized polypyrrole doped with dodecylsulfate (DS^-) was used for the development of a tubular solid-state ISE for determination of DS^- in a flow-injection analysis system.[190]

A correlation between the spontaneous charging/discharging processes and the potentiometric detection limit of conducting polymers, such as polypyrole, poly(*N*-methylpyrrole), and PEDOT, was found.[191] Furthermore, the potentiometric detection limit for electrosynthesized PEDOT(PSS) could be lowered to $10^{-6}-10^{-7}$ M by polarization with a small cathodic current that prevented cation leakage from the polymer film into the solution. However, similar to most nonfunctionalized conducting polymers, PEDOT itself showed low selectivity.[192]

Solid-state Ag^+-ISEs based on polypyrrole and PEDOT doped with sulfonated calixarenes (and resorcarenes) were developed.[193,194] The response mechanism was studied for Ag^+-ISEs based on PEDOT doped with hexabromocarborane.[195] Pretreatment of these electrodes by cyclic voltammetry in KNO_3 solution was found to improve the potentiometric response to Ag^+.[195] Electrochemically mediated doping/templating by repeated oxidation/reduction in $AgNO_3$ solution was employed to enhance the potentiometric Ag^+ response of polypyrrole that was synthesized by electropolymerization of pyrrole in the presence of Eriochrome Blue−Black B.[196] Even undoped poly(3-octylthiophene) (POT) was found to give a selective potentiometric response to Ag^+, indicating that Ag^+ interacts with the polythiophene backbone (sulfur atoms, π-electrons).[197]

Electrochemically overoxidized polypyrrole (OPPy) gave a potentiometric response to alkali and alkaline earth metal cations, albeit with low selectivity.[198] Overoxidation was suggested to result in oxygen-containing groups acting as "hard" Lewis bases that form complexes with hard cations, while the redox interference was simultaneously decreased because of the lower electronic conductivity of overoxidized polypyrrole.[198]

Novel electropolymerized films based on some functionalized polyanilines, polypyrrole,s and amino heterocyclic compounds were studied as solid-state ISEs for determination of anions, such as amino acids and ascorbic acid.[199] In fact, oxidized (p-doped) conducting polymers are inherently suitable for anion sensors because of the polycationic backbone.[199] A very simple procedure for manufacturing of a solid-state NO_3^--ISE by electrosynthesis of polypyrrole doped with NO_3^- on a pencil lead was described.[200] Similarly, PEDOT doped with ClO_4^- worked very well as ClO_4^- sensors with similar selectivity as commercial ClO_4^--ISEs.[201] Following the same approach, polypyrrole doped with valproate was found to give a well-functioning valproate sensor.[202]

Solid-state Cl^--ISEs based on chemically synthesized undoped POT containing trihexadecylmethylammonium chloride (THMACl) ions were studied.[203] In contrast to tridodecylmethylammonium, the more lipophilic trihexadecylmethylammonium cation required the addition of a plasticizer (2-nitrophenyloctyl ether, *o*-NPOE) to the POT film in order to give a functioning Cl^--ISE with the following composition: 35% (w/w) POT, 23% (w/w) THMACl, and 42% (w/w) *o*-NPOE.[203]

Solid-state Cu^{2+}-ISEs were developed by using electrosynthesized undoped polycarbazole and polyindole as sensing membranes.[204] However, these electrodes showed a severely super-Nernstian response to Cu^{2+} at concentrations higher than 10^{-4} M.

A solid-state pH nanoelectrode was constructed by electrodeposition of PANI onto an ion-beam conically etched carbon fiber with a tip diameter of ca. 100−500 nm.[205] The pH electrode gave a slope of ca. −60 mV/pH unit in the linear pH range of 2.0−12.5. The selectivity coefficients (log $K_{H,j}$) were around −12 with respect to K^+, Na^+, Ca^{2+}, and Li^+, which is comparable to conventional glass pH electrodes. A solid-state pH microelectrode based on PANI electrodeposited on a microband electrode was used for in situ pH measurement of the self-oscillating Cu(II)−lactate system.[206]

The pH sensitivity of PANI and its derivatives was found to depend on the substituent and the doping anion incorporated in PANI during electropolymerization.[207,208] The best pH response was obtained for PANI doped with chloride, while *N*-substituted PANI showed no pH sensitivity, because the *N*-substituent hindered the emeraldine salt−emeraldine base transition.[207,208]

A solid-state ISE for determination of dodecylsulfate (DS^-) was prepared by using electrochemically synthesized PANI doped with DS^-. The DS^--ISE showed a Nernstian response to DS^- in the linear range from 10^{-9} to $10^{-5.5}$ M. The electrode showed relatively high selectivity to DS^-, with the strongest interference being observed from dodecylbenzenesulfonate (DBS^-) (log $K_{DS,DBS} \approx -2.2$).[209] Alternatively, when PANI was electrosynthesized in the presence of DBS^- as the doping anion, the electrode became selective to DBS^- (e.g., log $K_{DBS,DS} \approx -2.2$) with a Nernstian response to DBS^- in the linear range from $10^{-5.3}$ to $10^{-2.4}$.[210]

The potentiometric response of PANI toward aniline based on the formation of charge-transfer complexes between aniline (donor) and the oxidized form of PANI (acceptor) was explained theoretically.[211] The theory could also explain the potentiometric response of other similar sensor materials to aromatic amines, pyrrole, and phenols.[211]

A novel approach for the potentiometric detection of saccharides using poly(aniline boronic acid) was presented.[212] The detection was based on pK_a changes of the poly(aniline boronic acid) resulting from boronic acid−diol complexation.

3.5. Comments on the Ion-to-Electron Transduction Process

Not only solid-state ISEs/ISSs but also conventional ISEs with internal filling solution (and reference electrodes as well) are asymmetric systems, because ions do not enter electronic equipment used to measure the potential. At some point, there is a transduction of the ionic signal into an electronic signal via a reversible redox reaction. In the case of a conventional Ag/AgCl electrode in contact with chloride ions, the reversible redox reaction involves the Ag/Ag^+ redox couple, as follows:

$$Ag + Cl^- \rightleftharpoons AgCl + e^- \tag{22}$$

The ion-to-electron transduction is completely analogous for other electroactive materials, such as conducting polymers.[63−65] Since the electrode contains a finite amount of redox-active material, the electrode has a finite redox capacitance (*C*).[147] For a given constant current (*i*), there will be a change in the electrode potential (*E*) with time (*t*):

$$\frac{\Delta E_C}{\Delta t} = \frac{i}{C} \tag{23}$$

Additionally, the electrode resistance (*R*), including all time-independent resistances of the electrode, will give a constant potential shift:

$$\Delta E_R = iR \tag{24}$$

Equations 23 and 24 represent the simplest possible case that neglects diffusion/migration processes in the ion-selective membrane and the ion-to-electron transducer. However, this simple *RC* model was verified experimentally and is used mainly to conceptualize the ion-to-electron transduction process in ISEs.[147,213]

In practical potentiometric measurements, the current (*i*) of the high-impedance voltmeter is small enough so that ($\Delta E_C/\Delta t$) and ΔE_R can be neglected. In contrast, currents induced by electrical noise may be significant enough to influence the potential. Furthermore, miniaturization of electrodes tends to decrease *C* and increase *R*, resulting in lower potential stability. This is valid for conventional ISEs with internal filling solution as well as for solid-contact ISEs. The same reasoning is also true for ion-selective electrodes with a completely blocked interface (coated-wire electrodes) where the redox capacitance is replaced by a double-layer capacitance. Consisely, the potential stability of coated-wire electrodes should improve by increasing the contact area between the ion-selective membrane and the electronic contact, because of the increase in the double-layer capacitance.

The conjugated polymers so far used as ion-to-electron transducers can be divided into two main groups of materials based on their redox capacitance, which is related to the oxidation level (degree of p-doping) of the conjugated polymers. POT represents a conjugated polymer with a relatively high oxidation potential, and therefore, it has a very low degree of p-doping under ambient conditions. This means that POT has a low electronic conductivity and a low redox capacitance under ambient conditions. On the contrary, PPy, PEDOT, and PANI represent conjugated polymers that are relatively stable in their highly oxidized (p-doped) state, showing high electronic conductivity and high redox capacitance. On the basis of the magnitude of the redox capacitance, highly p-doped conducting polymers, such as PPy, PEDOT, and PANI, should, therefore, be more suitable as ion-to-electron transducers compared to POT. However, this is not the complete account, partly because there may be electrochemical side reactions taking place in parallel with the main ion-to-electron transduction process. Such parallel reactions may be due to the presence of, e.g., O_2, CO_2, and H_2O that can reach the solid contact, even if it is coated with a polymeric ion-selective membrane. Side reactions due to redox couples in the solution are, of course, more likely to play a role when conducting polymers are dissolved in the ion-selective membrane and especially when conducting polymers are used as sensing membranes.

Electrochemical side reactions that change the redox state of the conducting polymer will not only influence the electrode potential but also cause a flux of ions into or out of the conducting polymer, which may, for example, influence the detection limit of the ISE. This is likely to happen in the case of highly p-doped conducting polymers that are electroactive in a broad potential range. PEDOT is known to be less sensitive to CO_2 and pH compared to PPy and PANI. However, similar to other highly p-doped conducting polymers, PEDOT is also sensitive to redox interference, which results in long-term potential drift. Regardless, the higher the redox capacitance, the smaller is the potential change for a given current and ion flux, i.e., for a given rate of an electrochemical side reaction or a given applied current that compensates for such a side reaction (chronopotentiometry). Simply expressed, this means that a high capacitance stabilizes the potential of the solid contact itself but does not eliminate the ion flux associated with side reactions. The above discussion suggests that a high capacitance is only a partial solution to the stability problem. It would be of utmost importance to have a conducting polymer (or any other electroactive solid material) with a high redox capacitance (in a narrow potential range) that would not participate in any side reactions at all.

However, even in the absence of electrochemical side reactions, there may be ion-exchange processes between counterions of a highly p-doped conducting polymer and ions in the ion-selective membrane (in the case of solid-contact ISEs) or solution (in the case where the conducting polymer is used as a sensing membrane). Such ion-exchange processes depend on the selectivity of the ion-selective membrane and the solid-contact materials. Even salt formation at the interface between the conducting polymer and the ion-selective membrane is possible, depending on the solubility of the ions present in the two phases. The presence of water at the interface leads to an unwanted situation resembling the conventional liquid-contact ISE where the conducting polymer plays the role of an internal reference electrode in contact with a very small volume of internal filling solution, the ion composition of which can easily change with time.

As mentioned previously, POT has a low redox capacitance and a low electronic (and ionic) conductivity. This means that the potential of POT is more sensitive to current flow than PPy, PEDOT, and PANI. However, because of its low conductivity, POT is less electroactive and may not participate in side reactions to the same extent as the highly p-doped conducting polymers. Additionally, POT has a low content of ions and is relatively lipophilic, which prevents the accumulation of water and salt inside the solid contact. In the case of solid-contact ISEs, the compatibility between the material used as a solid contact and the plasticizer (and polymer) used in the ion-selective membrane is a key issue that has not been studied thus far. Furthermore, leakage of plasticizer, ionophore, and additives to the solution may become a serious problem in the case of miniaturized ISEs based on plasticized polymer membranes.

It is interesting to note that low detection limits for several ions were achieved by using POT as a solid contact together with plasticizer-free acryl-based ion-selective membranes. This indicates that POT may be a good alternative as a solid-contact material, despite its low redox capacitance, if the main target is to reach a low detection limit. In contrast, POT is expected to be more sensitive to external electrical noise compared with the highly doped conducting polymers.

The above discussion focused on ion-to-electron transducers based on conducting polymers, because these materials have been extensively studied for many years and they appear to be very promising. Conducting polymers make it possible to fabricate, e.g., all-plastic ISEs[161] and pH nanoelectrodes.[205] However, recent results indicate that excellent potential stability (potential drift ca. 11.7 μV/h) can be achieved by using three-dimensionally ordered macroporous carbon as the solid contact.[214] Despite the relatively complicated manufacturing procedure, this latter approach is indeed very promising. In this case, the large contact area between the ion-selective membrane and the electronically conducting carbon material should result in a large double-layer capacitance that would stabilize the potential. Further characterization of this type of solid-contact ISE by, e.g., electrochemical impedance spectroscopy may provide important fundamental information concerning the ion-to-electron transduction process of solid-contact ISEs.

Consequently, which material is the best ion-to-electron transducer? The above discussion indicates that the choice of conducting polymer or any other material used as an ion-to-electron transducer must be done on a case-to-case basis. Requirements, such as analytical performance, mechanical durability, lifetime, fabrication methods, and cost of the ion sensor, have to be considered. Finding a solid material that fulfills all possible requirements of a good ion-to-electron transducer for all possible applications is really a great challenge.

4. Miniaturized ISEs

4.1. Conventional Microelectrodes

Ion-selective microelectrodes are used in many different applications from life sciences to environmental control. There are several reviews, books, and sections of books dedicated to this topic, e.g., by Purves,[215] Ammann,[216] and Takahashi et al.[217]

Microelectrodes based on the concept of micropipets have already been used for a longer time, especially in life-science applications.[218] Two different pipet electrodes, one as the indicator electrode and the second as the reference electrode, have been used, as well as the construction of a double-barreled micropipet electrode. The pipets have to be silanized before applying the ion-selective cocktail into the pipet. An improved method for this procedure was described recently.[219] There is also a patent for the apparatus and method to selectively induce hydrophobicity in a single barrel of a multibarreled ion-selective microelectrode.[220]

Scanning electrochemical microscopy (SECM) is a technique where ion-selective microelectrodes have found wide areas of application and where the advantages are the micrometer dimensions, selectivity, and low detection limit.[221] pH probes based on an antimony microdisk electrode[222] or a H^+-sensitive liquid membrane have been used in pH-microscopy where pH profiles have been measured in corrosion studies[223,224] or in measuring biological activities.[225,226] The technique has also been applied to study many other kinds of surfaces and processes.[227,228] A novel type of solid-contact ammonium-selective microelectrode was recently constructed for SECM measurements.[229] Double-barreled chloride-selective microelectrode were used to map in situ Cl^- ion distribution in localized corrosion systems.[230]

There are also microelectrodes for some "not-so-common" ions. A new Schiff's base was synthesized and tested as the ionophore for yttrium ions in an ion-selective microelectrode.[231] That sensor was tested in complexometric titration and direct determination of yttrium in dissolved yttrium−aluminum alloy samples.

Environmental measurement of ionic species with ion-selective microelectrodes is also an interesting application area. Several ions have been measured in pore water samples,[232] and a phosphate-selective microelectrode based on cobalt as the sensing material was used in studying a biological phosphorus removal process.[233]

By selecting an optimum composition for the inner reference solution, the detection limit of a calcium micropipet electrode could be lowered.[234] The calibration curve was found to be linear down to 10^{-8} M of Ca^{2+}.

Ion-selective microelectrodes were recently used in determination of extremely low levels of calcium, lead, and silver ions, 10^{-10} M in the presence of 10^{-5} or 10^{-6} M sodium ions.[235] It was possible to detect 300 attomol of those ions at a constant ionic background.

4.2. Solid-Contact Microelectrodes

During the past decade, microsensors have gained a widespread and increasing interest both by scientists, engineers, and people working with practical applications of these sensors. The collaboration between scientists and microtechnology engineers has been fruitful, leading to different manufacturing procedures for making both thin- and thick-film microelectrodes. New technologies enabling mass production of miniaturized ion-selective electrodes were reviewed.[236] The discussion concerned mainly applications in biology and medicine, but procedures to make thin- and thick-film microelectrodes were also reviewed.[236]

Most of the currently used microelectrodes are manufactured on solid substrates. Gold, silver, platinum, and different kinds of carbon materials are used. A recent review on advanced chemical microsensors deals with the design and performance of miniaturized chemical sensors based on Si transducers: ion-selective field effect transistors and solid-state electrodes.[67] Si nitride substrate with a polymeric solid contact was used in a miniaturized sodium-selective electrode.[237] Silicon substrate was also used in constructing a pH-sensitive microelectrode where the sensitivity is due to ion-selective PVC membrane on top of polypyrrole layer doped with cobalt bis(dicarbollide).[238] Pulsed-laser deposition is also a practical method for making solid-state micro-ion-selective electrodes. Cd^{2+} selective microelectrode was constructed by pulsed laser deposition (PLD) technique and using $CdSAgIAs_2S_3$ as the sensitive material.[239]

Screen-printing technology is a useful and practical way to produce solid-contact electrodes. A procedure to make an array of all-solid-state potassium selective electrodes on screen-printed gold substrates has been described.[156] Screen-printing technology was also used to produce thick-film Ag sulfide electrodes.[240] The performance of these strip sensors was comparable to those of conventional electrodes. Another way to make silver- and sulfide-selective electrodes is to etch the end of a silver wire to a sharp tip and then to insulate the wire except for the very end that then functions as the sensing part of the probe.[241] Even an all-solid-state potentiometric sensor for ascorbic acid was constructed based on this screen-printing technology.[73] Laser-ablation, screen-printing, and molecular-imprinting techniques were used in making nanoliter-volume vials with carbon and Ag/AgCl ring electrodes embedded in the sidewalls.[242] Polypyrrole was electropolymerized on the carbon rings with nitrate as the doping ion, and the vials were used in determination of nitrate in nanoliter samples. On the basis of earlier reports on anion-selectivity of polypyrrole, it is somewhat suprising how selective are the nitrate sensors that the authors have been able to produce by using nonfunctionalized polypyrrole. The main advantage of that system lies in the small sample size. Screen-printing technique is also used in making planar-form solid electrolyte modified Ag/AgCl reference electrodes.[243,244] Construction and design of this type of reference electrodes make them suitable for measurements in physiological samples and in flow analysis.

A novel method to make miniaturized solid-contact ion-selective electrodes has been presented.[157] The gold wire in a glass capillary was etched to form a microcavity in the electrode body. The gold disk electrode was then coated by electropolymerization with the conducting polymer poly(3,4-ethylenedioxythiophene) (PEDOT) doped with poly(4-styrenesulfonate) (PSS). Potassium- and calcium-selective microelectrodes were then made by filling the cavity with the corresponding ion-selective membrane. These microelectrodes were found to have similar potentiometric characteristics as conventional electrodes.

Solid-contact microelectrodes are suitable for use in harsh and remote environments. An exotic example of such an application is the use of a microelectrode array for measurement of ion concentrations in the Martian soil.[245] A prototype miniature array of polymer-membrane and solid-state ion-selective electrodes was developed to perform in situ analysis of soil samples for a number of ions. The array consisted of 27 microelectrodes for nine ions. Each electrode was in three replicates.[68]

Screen-printing technology has also been used in constructing miniaturized solid-contact electrodes for chloride ions. Either carbon or silver was used as the screen-printed substrate. The conducting polymers polypyrrole or polyaniline with an adhesive admixture of 3-aminopropyltriethoxysilane was placed on the substrate. The ion-selective PVC membrane containing the ion-exchanger for chloride (methyl-tri-*n*-tetradecylammonium chloride) was then placed on the conducting polymer film. This construction showed the same performance and stability as the conventional electrodes with inner reference electrode and solution.[116,246]

The potential stability of microfabricated potassium ion-selective electrodes with two types of solid contact was studied and compared.[118] Hydrogel and polypyrrole doped with potassium hexacyanoferrate(II)/(III) were used as the solid contact between the PVC-based potassium-selective membrane and the screen-printed silver or platinum substrates. The electrodes were incorporated into a flow-through cell where the measurements were conducted. The electrodes with the polypyrrole solid contact showed much higher potential stability than the electrodes with hydrogel contact.[118]

A microfabricated ion-selective microelectrode-array platform has been constructed and characterized.[247,248] The platform contained 24 micropipets individually filled with a Ca^{2+} selective membrane and was developed for in vitro intracellular measurements. Different chalcogenide glass-sensitive materials have also been used to make an array of miniaturized ion-selective electrodes.[249] It was demonstrated in that work that the sensor array allows the problem of an insufficient selectivity of single sensors to be overcome. A microsensor array of miniaturized solid-state ion-selective electrodes to analyze sweat samples for sodium, potassium, and chloride was developed for point-of-care diagnosis of cystic fibrosis.[250]

Miniaturized, planar ion-selective electrodes fabricated by thick-film technology were recently reviewed.[251] Different manufacturing procedures were discussed and screen printing was found to be a suitable technique because of its simplicity, low cost, high reproducibility, and efficiency in large-scale production. Thick-film technology was also demonstrated to be a proper method to produce ionophore-based ion-selective electrodes on inexpensive substrates. The analytical parameters of these electrodes were comparable with those of conventional electrodes. Miniaturized Ag, Ag/AgCl, or iridium oxide solid-state potentiometric sensors were used to measure the capacitance and the response time of the electrodes by an electrochemical time-of-flight method.[252,253]

4.3. Microelectrodes in Flow Analysis

Solid-contact ion-selective microelectrodes have many advantages when used in flow channels. They are robust and rather easy to fabricate and install. A miniaturized ion-selective Cu^{2+} electrode was developed for fluidic microsystems.[254] Cu was deposited on a silicon wafer and then converted to CuS by hydrogen sulfide. The electrode performed well in the system. The authors found differences in the adhesion of the CuS layer for Si, SiO_2, and Si_3N_4. An all-solid-state potassium microelectrode for flow analysis was developed for measurements in flowing solutions[177] as well as a nitrate sensor for determination of nitrates in wastewaters, fertilizers, and pharmaceuticals by the flow-injection analysis technique.[255] A small-volume flow cell was developed by incorporating all-solid-state electrodes.[155] Ca^{2+} and pH measurements were carried out in the Lab-on-Valve instrument by using all-solid-state microelectrodes.[152] Low-temperature cofired ceramic technology was used to construct continuous-flow analytical microsystems.[256] Ammonium- and nitrate-selective microelectrodes were incorporated in that microfluidic sysytem, allowing a complete on-chip integration for potentiometric detection. A microfluidic device was developed for measurement of pH as well as of Ca^{2+} and K^+ concentrations with in-channel-incorporated all-solid-state ion-selective electrodes.[257] Construction of different planar solid-state ion-selective microelectrodes as well as reference electrodes for flow analysis was recently discussed in an overview.[117]

4.4. Life Science and Biology Applications

The use of microelectrodes to investigate transportation of inorganic ions in plants has been reviewed.[258] The construction of multibarreled ion-selective microelectrodes for measurements in biological tissues was also reviewed.[259] It was also demonstrated how cell volume, membrane potential, and intracellular ion concentrations can simultaneously be determined by using potentiometric measurement with multibarreled ion-selective electrodes. A special study on the cell volume regulation mechanism of nerve cells by using multibarreled ion-selective microelectrodes was made.[260] Different requirements for the charge-exchange processes between a dielectric layer and the ions in the sample in ion-selective biosensors made on silicon were discussed in another study.[261] It was found that standard dielectric materials normally employed in microelectronics technology can be used in making ion-sensitive field-effect transistors and ion-selective microelectrodes for biosensing applications. Use of ion-selective microelectrodes and fluorescent dyes in measurement of intracellular pH has been compared and discussed.[262]

Ion-selective microelectrodes were used in plant physiology in studying the NH_4^+, H^+, and NO_3^- fluxes around the roots of plants[263] and their concentration profiles in nitrifying biofilms.[264] By using these electrodes, the authors were able to determine the source of nitrogen for a particular plant. The mechanism of pH homeostasis in Listeria monocytogens subjected to, e.g., acid stress was studied by using a pH microelectrode,[265] and ammonium transport across the plant cell membrane was measured with an ammonium-selective microelectrode.[266]

Ionized magnesium has been measured with an ion-selective microelectrode in physiological solutions,[267,268] and the release of ionized Ca from bones has been measured by a Ca-selective microelectrode.[269]

Ion-selective microelectrodes were also used in studying ion fluxes across cardiac membrane patches.[270] Potassium, calcium, sodium, and proton fluxes were measured, and the authors were, additionally, able to quantify those fluxes.

The effect of interfering ions in using ion-selective microelectrodes in biological applications has been discussed.[271] The kinetics of ion fluxes in some plant leaf and root tissues was determined by using ion-selective microelectrodes,[272,273] as was ion fluxes in bacteria.[274] Fluxes of H^+ and Ca^{2+} ions during the growth of a single-celled fungus were also studied by ion-selective microelectrodes.[275] Salicylate selective microelectrodes were even constructed for biological applications to measure fluxes of salicylate ions.[276]

Ion-selective electrodes are used in many biosensors to detect, e.g., ammonia or H^+ released in the enzymatic reactions involved in the detection procedure. Ion-selective microelectrodes are needed for miniaturization of such biosensors.[277]

Some of the main problems in using ion-selective microelectrodes are the slow response time and the susceptibility to noise because of the high electrical resistance of the convential micropipet electrodes (see section 3.5). These problems are especially crucial in biological in vivo measurements but can partially be overcome by using a concentric inner micropipet.[278] Response times in the order of a few ms were obtained for pH and Ca^{2+} electrodes used in extracellular measurements.

5. New Wave

During the past decade, the developments in the field of potentiometric ion sensors (ISEs) have been exceptionally fruitful. The discovery of the low detection limit in 1997 represents a major breakthrough in the field of ISEs.[30] Much research has been devoted to the design and optimization of liquid-contact ISEs to measure low ion concentrations.[234,235,279−285] The "new wave" of ISEs has unquestionably arrived.[6,7] The question is: where will it lead us in the future?

Solid-contact ISEs for trace-level analysis have already been demonstrated by several groups.[75,120−123,125,142−144,163] When such powerful ion sensors are combined with solid-state reference electrodes,[243,286−292] mass-producible miniaturized ion-sensor systems with unforeseen analytical capabilities are within reach. Deep theoretical understanding based on advanced modeling of the potentiometric response will definitely boost this development.

Parallel developments of plasticizer-free membranes,[293−304] covalently bound ionophores,[293,296,298,302,305−309] and charged sites[304] will enhance the durability of ion sensors. Other alternative membrane materials and construction principles add new tools for the future as well. Here, we would like to mention anion-sensitive epoxy resins,[310,311] membranes prepared by the sol−gel method,[312] polymer-supported liquid-crystal membranes,[313] polymer membranes located inside an electrochemically inert porous matrix,[314] monolithic capillary-based membranes,[284] and fluorous membranes with exceptionally low polarity.[315]

There are several other interesting developments that may have an impact on the future developments of ISEs. The so-called sandwich membrane method, which was actually introduced already in 1979, is a useful tool for studying complexation in real membranes.[316,317] Polycation-sensitive electrodes can be used to detect even polycationic dendrimers.[318] Highly lipophilic *closo*-dodecacarborane anions showing very weak ion-pair formation are promising alternatives to the commonly used tetraphenylborate derivatives as anionic additives in polymeric ion-selective membranes.[319] Under certain conditions, conventional ISEs with internal filling solution can be calibrated by varying the composition of the internal solution, which may be particularly useful in applications where the electrode cannot easily be removed from the sample (e.g., process control and in vivo measurements) during calibration.[320] A solvent-free method for making hot-pressed ion-selective membranes is an environmentally friendly approach that avoids the use of organic solvents.[321]

Application of a controlled current can be used to influence transmembrane ion fluxes and is an elegant approach toward lowering the detection limit of ISEs.[322,323] This method has also been applied to solid-contact ISEs using polypyrrole as the ion-to-electron transducer.[126] As discussed in section 3.5, highly p-doped conducting polymers with a high redox capacitance can simultaneously work as “source” and “sink” of electrons and ions without any significant change in potential if the magnitude of the applied current is sufficiently low. Therefore, chronopotentiometry may become a useful method to control transmembrane ion fluxes and detection limits of solid-contact ISEs. Under some conditions, current-reversal chronopotentiometry allows the equilibrium potential to be determined although the electrode is significantly polarized by the applied current.[213] Furthermore, a significant increase in sensitivity was achieved by imposing current pulses to the ISE, leading to the concept of so-called pulstrodes.[324] Being a fascinating research area in itself, the new wave of ISEs will most probably also result in new applications of potentiometric ion sensors in the future.

6. Conclusions

The response of potentiometric ion sensors, i.e., ion-selective electrodes (ISEs), is a complex time-dependent phenomenon that calls for advanced theoretical modeling in addition to classical equilibrium models. This is particularly important when ISEs are used in their nonequilibrium regimes, e.g., in order to reach low detection limits, which is intensively being explored all over the world. The prerequisites for obtaining solid-contact ISEs with stable potential are well-documented, and during the past decade, conducting polymers have gained widespread acceptance as ion-to-electron transducers in solid-contact ISEs. However, in spite of extensive research in this area, obtaining solid-contact ISEs with reproducible standard potentials is still a great challenge. Miniaturized versions of both conventional and solid-contact ISEs have been used in various applications. Cost-effective miniaturized ion-sensor systems with unforeseen analytical capabilities are within reach. Advances made by numerous research groups all over the world allow us to conclude that the future of potentiometric ion sensors looks very prospective indeed.

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