1

MODELING OF RELATIONS BETWEEN IONIC FLUXES AND MEMBRANE POTENTIAL IN ARTIFICIAL MEMBRANES

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1.1 INTRODUCTORY CONSIDERATIONS

A membrane can be regarded as a phase, finite in space, which separates two other phases and exhibits individual resistances to the permeation of different species (Schlögl's definition cited in [1]). The membranes can be of different thickness, from thin used typically for biological and artificial bilayers (in the range of a few nanometers) to relatively thick (hundreds of micrometers) used typically in ion-selective electrodes. A particular case is a membrane separating two electrolyte solutions, where ions are transferable species. In such a case, different modes of ion transport are possible: (i) Brownian motion; (ii) diffusion, resulting from concentration gradient; and (iii) migration as transport under the influence of an electrical field.

A general prerequisite related to the presence of charged species is electroneutrality condition of the membrane. However, even if electroneutrality is held on a macroscopic scale, charge separation effects appear, mainly at membrane/solution interfaces, resulting in the formation of potential difference. Taking into account possible chemical and electrical forces present in the system, assuming for simplicity one-dimensional

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transfer along the x-axis only, the flux of ion "i," J_i, across the membrane can be described as

$$J_i = -kU_i c_i \frac{\partial \bar{\mu}_i}{\partial x} \tag{1.1}$$

where k is a constant; U_i, c_i, and $\bar{\mu}_i$ are electrical mobility, concentration, and electrochemical potential of ion "i," respectively; and x is the distance from the membrane/solution interface. Using a well-known definition of electrochemical potential and assuming that the activity of ion "i" is equal to the concentration, this equation can be transformed to

$$J_i = -kU_i c_i \left(\frac{RT \partial \ln c_i}{\partial x} + z_i F \frac{\partial \varphi}{\partial x} \right) \tag{1.2}$$

with φ as the Galvani potential of the phase.

Since mobility, U_i, is a ratio of the transfer rate, v, and potential gradient ($\partial\varphi/\partial x$), while the flux under influence of the electrical force is $J = vc$, it follows from Equation (1.2) that $k = 1/|z_i|F$. Taking then into account the Einstein relation, concerning diffusion coefficient, $D_i = U_i RT/|z_i|F$, Equation (1.2) can be rewritten as

$$J_i = -D_i \left(\frac{\partial c_i(x,t)}{\partial x} + \frac{z_i F}{RT} c_i(x,t) \frac{\partial \varphi(x,t)}{\partial x} \right) \tag{1.3}$$

This is the Nernst–Planck equation, relating the flux of ionic species, "i," to gradients of potential and concentration, being generally functions of distance, x, and time, t.

The Nernst–Planck equation is a general expression describing transport phenomena in membranes. Unfortunately, as differential equations deal with functions dependent on distance and time, solving of this equation is neither easy nor straightforward. However, under some conditions, simplifications of this equation are possible.

(i) For the equilibrium case, summary fluxes of all ionic species are zero, $J_i = 0$. In such a case,

$$\frac{\partial \ln c_i}{\partial x} = -\frac{z_i F}{RT} \frac{\partial \varphi}{\partial x} \tag{1.4}$$

After rearrangement and integration across the whole membrane (of thickness d), the well-known form is obtained:

$$\varphi_R - \varphi_L = \Delta\varphi_{mem} = \frac{RT}{z_i F} \ln \frac{c_R}{c_L} \tag{1.5}$$

where R and L refer arbitrarily to "right" and "left" hand side (membrane/solution interface) and c_R and c_L are solution concentrations at "right" and "left" interfaces.

This equation describing a membrane potential, $\Delta\varphi_{\mathrm{mem}}$, is equivalent of the typical Nernst equation.

(ii) For the case of a neutral substance, $z_{\mathrm{i}} = 0$, or in the absence of electrical driving force $(\partial\varphi/\partial x) = 0$, the Nernst–Planck equation reduces to Fick's equation, describing diffusional transport:

$$J_{\mathrm{i}} = -D_{\mathrm{i}}\left(\frac{\partial c_{\mathrm{i}}}{\partial x}\right) \tag{1.6}$$

Solutions of the Nernst–Planck equation can be more easily obtained for the steady state, when the ionic fluxes $J_{\mathrm{i}} = \mathrm{const}$ and a time-independent version of the equation can be used. In this case, the Nernst–Planck equation can be applied to calculate potential difference in the membrane for given values of concentrations and mobilities. However, this procedure also requires integration, which can be difficult in some cases. Therefore, additional approximations are often used [2, 3]. The most known and used solutions are the Goldman and Henderson approximations.

1.1.1 Goldman Approximation and Goldman–Hodgkin–Katz Equation

This approximation assumes linearity of potential gradient across the membrane (i.e., constant electrical field in the membrane). This approximation is usually applicable to thin biological membranes, where charge prevails only in the surface areas of the membrane. In such a case, the derivative $(\partial\varphi/\partial x)$ can be approximated by the term $(\varphi_{\mathrm{R}} - \varphi_{\mathrm{L}})/d$ leading to the simplified Nernst–Planck equation:

$$J_{\mathrm{i}} = -\left(D_{\mathrm{i}}\frac{\partial c_{\mathrm{i}}}{\partial x} + \frac{z_{\mathrm{i}}F}{RT}c_{\mathrm{i}}\frac{\varphi_{\mathrm{R}} - \varphi_{\mathrm{L}}}{d}\right) \tag{1.7}$$

Under constant field condition, a steady state is practically obtained ($J_{\mathrm{i}} = \mathrm{const}$) and the Goldman flux equation can be derived:

$$J_{\mathrm{i}} = \frac{z_{\mathrm{i}}FD_{\mathrm{i}}(\varphi_{\mathrm{R}} - \varphi_{\mathrm{L}})}{dRT} \cdot \frac{c_{\mathrm{i}}(\mathrm{R}) - c_{\mathrm{i}}(\mathrm{L})\exp\left(-(z_{\mathrm{i}}F(\varphi_{\mathrm{R}} - \varphi_{\mathrm{L}}))/RT\right)}{\exp\left(-(z_{\mathrm{i}}F(\varphi_{\mathrm{R}} - \varphi_{\mathrm{L}}))/RT\right) - 1} \tag{1.8}$$

In the absence of transmembrane potential, $\varphi_{\mathrm{R}} - \varphi_{\mathrm{L}} \sim 0$, this equation simplifies to the well-known diffusion equation in a steady state.

Taking into account that the sum of individual ionic contributions to electrical current is zero (denoting the absence of applied external current),

$$\sum_{i=1}^{n} z_{\mathrm{i}}J_{\mathrm{i}} = 0 \tag{1.9}$$

further rearrangements are possible. For a simplified case of solution of ions of ±1 charge (e.g., Na^{+}, K^{+}, Cl^{-}), the equation describing the potential difference across the membrane (under steady-state conditions) can be obtained:

$$\varphi_R - \varphi_L = \frac{RT}{F}\ln\frac{D_{Na^+}c_{Na^+}(L) + D_{K^+}c_{K^+}(L) + D_{Cl^-}c_{Cl^-}(R)}{D_{Na^+}c_{Na^+}(R) + D_{K^+}c_{K^+}(R) + D_{Cl^-}c_{Cl^-}(L)} \tag{1.10}$$

It can be also assumed that ions take part in ion-exchange equilibrium, between the membrane and bathing electrolyte solution (sol) from the right or left hand side, (Eq. 1.11a) and (Eq. 1.11b), respectively:

$$c_i(R) = k_i c_i(\text{sol}, R) \tag{1.11a}$$

$$c_i(L) = k_i c_i(\text{sol}, L) \tag{1.11b}$$

with partition coefficients k_i of the species "i" between the solution and membrane phases. Then, introducing the permeability coefficient, P_i, $P_i = U_i k_i / |z_i| F d$, Equations (1.10) and (1.11) can be transformed to the Goldman–Hodgkin–Katz equation, expressing the membrane potential as a function of ion concentrations in bathing solutions on both sides of the membrane and partition (permeability) coefficients:

$$\varphi_R - \varphi_L = \frac{RT}{F}\ln\frac{P_{Na^+}c_{Na^+}(L) + P_{K^+}c_{K^+}(L) + P_{Cl^-}c_{Cl^-}(R)}{P_{Na^+}c_{Na^+}(R) + P_{K^+}c_{K^+}(R) + P_{Cl^-}c_{Cl^-}(L)} \tag{1.12}$$

This equation is applicable, for example, to describe resting potentials of biological membranes.

1.1.2 Henderson Approximation

This approximation assumes linear concentration gradient across the membrane, while the electrical field need not be constant [4]. This approximation is usually applied to describe diffusion (liquid junction) potentials, particularly for the case of ion-selective electrodes. This potential can be approximated by the equation

$$\Delta\varphi_{LJ} = -\frac{RT}{F}\cdot\frac{\sum z_i u_i (c_i(R) - c_i(L))}{\sum z_i^2 u_i (c_i(R) - c_i(L))}\ln\frac{\sum z_i^2 u_i c_i(R)}{\sum z_i^2 u_i c_i(L)} \tag{1.13}$$

where u_i is $U_i/|z_i|F$.

Membrane processes related to charge separation and transport of charged species concern both biological membranes in cell biology (or artificial membranes having significant importance in separation processes) and membranes used in electroanalytical chemistry, for example, in ion-selective electrodes. However, in contrast to similarity of physicochemical phenomena occurring in all membranes containing mobile charged species, the description related to biological or separation membranes is different from that applicable to membranes of ion-selective electrodes. Therefore, the considerations in the following were divided into two sections: (i) related to more general description typical for separation and biological membranes where typically the Nernst–Planck equation is applicable and (ii) related to membranes used in ion-selective electrodes. In case (ii), practical and historical conditions result in dominance of simple empirical equations for the membrane potentials; however, in the last decade, the role of a more general theory using the Nernst–Planck equation is increasing.

1.2 GENERAL CONSIDERATIONS CONCERNING MEMBRANE POTENTIALS AND TRANSFER OF IONIC SPECIES

1.2.1 Boundary and Diffusion Potentials

Separation membranes are important both in biology and various technological areas: fuel cells, dialysis, reverse osmosis, separation of mixtures components, etc. These membranes can be generally described as neutral or charged membranes. For the former class of membranes, size exclusion and specific chemical interactions are the main factors responsible for selective permeability, while for charged membranes with incorporated ionic sites, electrostatic interactions are of substantial significance.

For the charged membranes, the membrane potential, understood as a potential difference between two electrolyte solutions (of different concentration or/and composition) separated by the membrane, is an important parameter characterizing their properties [5]. Measurements of membrane potential offer also a straightforward method for studying transport processes of charged species. Due to difficulties in solving the Nernst–Planck equation in a general case, simplifications are used, as they were shortly described in the previous section.

In the discussion given in the following, only cases with no external current flow are considered. In the description of membrane potentials, mostly a simplified formalism is used, expressed in terms of classical model proposed by Sollner [6], Teorell, Meyer, and Sievers [7, 8]. This model postulates splitting the potential prevailing in the system into three components: boundary potentials on the membrane (left and right side)/bathing solution interfaces and membrane bulk diffusion potential resulting from different mobility of ionic species as well as ion-exchange reactions leading to inhomogeneities in the interior of the membrane. It should be noted that the Teorell–Meyer–Sievers theory is applicable to fixed-site membranes with one kind of monovalent cations and anions as transferable species. It can be not valid for liquid membranes, where ionic sites are mobile.

Boundary potentials are regarded as equilibrium potentials resulting from ion exchange on the interface between the charged membrane and solution. In the case of equilibrium, assuming that activity coefficients are equal to 1, the change of chemical potential of transferable ion, “i,” is equal to zero:

$$\Delta\mu_{\mathrm{i}} = 0 \tag{1.14}$$

The chemical standard potentials, $\mu_{\mathrm{i,m}}^{0}$ and $\mu_{\mathrm{i,s}}^{0}$, in the membrane and in the solution, respectively, can be different, determining the value of the distribution coefficient of species, “i” and k_{i}:

$$k_{\mathrm{i}} = \exp\left[\frac{-\left(\mu_{\mathrm{i,m}}^{0} - \mu_{\mathrm{i,s}}^{0}\right)}{RT}\right] \tag{1.15}$$

Then, assuming the existence of ion-exchanging sites in the membrane (unable to be released from the membrane), the boundary potential at a chosen membrane/solution interface can be represented by the Donnan potential, $\Delta\varphi_{\mathrm{D}} = \varphi^{\mathrm{m}} - \varphi^{\mathrm{s}}$ [9]:

$$RT \ln \frac{k_{\mathrm{i}} c_{\mathrm{i}}^{\mathrm{m}}}{c_{\mathrm{i}}^{\mathrm{s}}} + z_{\mathrm{i}} F \Delta\varphi_{\mathrm{D}} = 0 \tag{1.16}$$

where superscripts “m” and “s” relate to the membrane and solution phases, respectively.

The dependence of the Donnan potential on the electrolyte concentration in solution can be derived from Equation (1.16) taking into account electroneutrality condition in the membrane phase. In the case of a membrane with fixed ionic site concentration, X, and for 1:1 electrolyte (with cation M^{+} and anion A^{-}) of concentration c, assuming the absence of specific interactions of ions with the membrane components ($k_{\mathrm{i}} = 1$), the Donnan potential is expressed by equation [10]

$$\Delta\varphi_{\mathrm{D}} = \varphi^{\mathrm{m}} - \varphi^{\mathrm{s}} = \pm \frac{RT}{F} \ln\left[\frac{X}{2c} + \left(1 + \left(\frac{X}{2c}\right)^{2}\right)^{\frac{1}{2}}\right] \tag{1.17}$$

with sign “+” or “–” for anion- or cation-exchanging membrane, respectively.

From this equation, two limiting cases follow (Fig. 1.1). For dilute solutions, when $c \ll X$, the concentration of counterions in the membrane is practically equal to X (with negligible concentrations of coions, this is the so-called Donnan exclusion case), and the Donnan potential becomes a linear function of ln c with positive or negative Nernstian slope, for cation and anion exchanger, respectively. On the other hand, for high electrolyte concentrations, when $c \gg X$, concentrations of counter- and coions in the membrane are almost equal; the Donnan potential is independent of electrolyte concentration and close to zero (Donnan exclusion failure).

In contrast to the equilibrium state observed at the membrane/solution interface, in the membrane interior, similar equilibria are typically not observed. In this case, different rates of ion transfer in the membrane result in diffusion potential formation, necessary to maintain a zero current steady state [1].

In order to calculate exact values of the diffusion potentials, knowledge about concentration profiles of all species in the membrane is needed. However, for practical purposes, some approximations can be used; the most popular is the Henderson

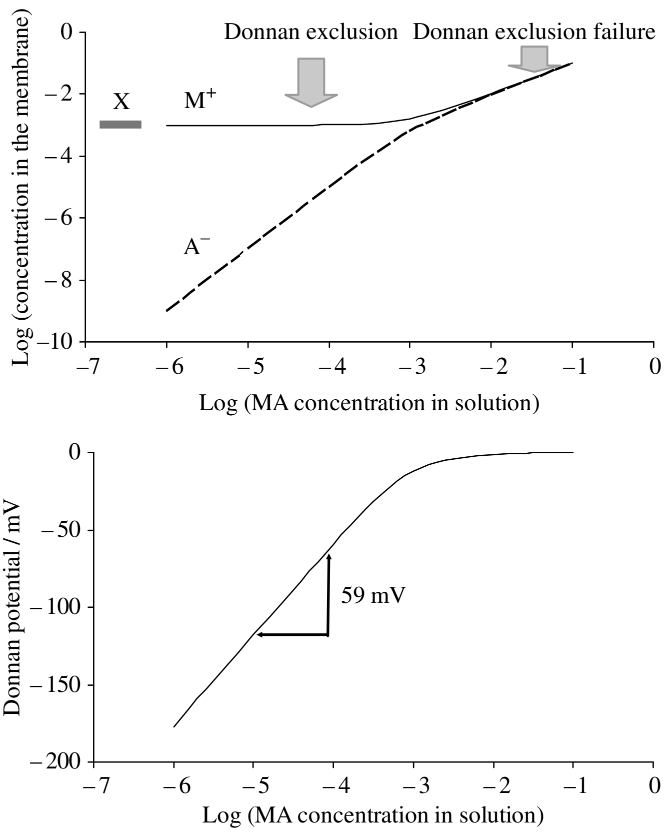

FIGURE 1.1 Dependence of M^+ and A^- ions concentrations in the membrane (top figure) and Donnan potential (bottom figure) on concentration of salt MA in solution, for cation-exchanging membrane with ion-exchange site concentration $X = 10^{-3}$ M.

approximation (see previous section). More advanced treatments are also available, for example, the Planck and Schlögl description is based on a given model of diffusion in the layer [1, 2], in contrast to the model of uniform mixing typical for the Henderson approach. However, the classical Planck approach is less convenient for practical applications than the Henderson approximation; thus, some simplifications facilitating calculations in terms of the Planck model have been proposed, and thus, iterative calculations method can be used [11]. A significant simplification of the Planck description is expected for the case of two equimolar solutions of 1:1 electrolytes, where the Planck equation simplifies to the Goldman equation. On the other hand, the Planck approach and the Goldman equation can be considered as special cases of a more general Teorell equation [7], applicable for any two classes of diffusing ions and for additional fixed sites in the membrane [1]. Assuming that all transferring ions have the same charge, the following equation for the diffusion potential can be obtained:

$$E_D = \frac{RT}{z_i F} \ln \frac{\sum u_i a_i(\mathrm{L})}{\sum u_i a_i(\mathrm{R})} \tag{1.18}$$

1.2.2 Application of the Nernst–Planck Equation to Describe Ion Transport in Membranes

Knowledge about transfer of ionic species in membranes is crucial from the point of view of some general issues concerning membrane potentials (without arbitrary and sometimes controversial splitting into boundary and diffusion potential) and practical applications of membranes in separation processes, dialysis, and selective transfer of charged species. This requirement is connected with the solution of a system of the Nernst–Planck equations for all ionic species, which can be transported in the membrane. Due to mathematical difficulties, calculation of ion fluxes or membrane potential accompanying ionic fluxes by solving the Nernst–Planck equation is usually connected with application of numerical procedures. Additionally, simplifying assumptions, as the aforementioned Henderson or Goldman approximations, are used. The proposed solution is related rather to the steady state (time-independent phenomena).

In 1954, Schlögl proposed a general solution of the Nernst–Planck equation under steady-state conditions, applicable also for thick membranes, for any number of transferring ions, and for fixed ionic sites [1, 12]. He proposed to divide diffusing ions into subgroups—so-called valency classes. For ion-exchanging membrane containing only one class of ions, the equation proposed here simplifies to the Goldman flux equation.

The first numerical solution of the Nernst–Planck equations coupled with the Poisson equation

$$\frac{\partial E(x,t)}{\partial x} = \frac{\rho(x,t)}{\varepsilon}; \;\; \rho(x,t) = F \cdot \sum_{i} z_i \cdot c_i(x,t) \tag{1.19}$$

that is, taking into account the existence of noncompensated charge, was proposed by Cohen and Cooley in 1965 [13] ($\rho(x,t)$ is the charge density, E is the electrical field, while ε is the dielectric permittivity). In this work, a solution of the Nernst–Planck–Poisson equations has been proposed, taking into account also time influence; however, this procedure was not explicit (nonpredictive). Authors have introduced a system of reduced units, often used in electrochemical simulations.

Sandifer and Buck [14] have extended this method, and then a significant progress has been achieved by Brumleve and Buck [15] who have discussed numerical solution both for steady-state and transient phenomena, for species with arbitrary valence, mobility, and interfacial charge transfer rate constants. These authors were using finite difference method and applied iterative Newton–Raphson method coupled with the Gaussian elimination to solve the nonlinear equations. This time also, some numerical procedures for solving the Nernst–Planck–Poisson equation systems have been proposed by other researchers outside the area of membrane physical chemistry and electrochemistry [16–18].

In 1984, Buck discussed critically limitations of the Nernst–Planck equation [19]. The first argument against this theory results from the macroscopic and smooth nature of the medium considered in the model. The second argument arises from the omission of “cross terms”—this means that the flux of any species is not only linearly related to its activity gradient but also to the corresponding gradients of other mobile species. Some alternatives and microscopic models have been discussed in terms of atomic properties. For instance, percolation theory [20] has been presented as complementary one to the Nernst–Planck model, as it provides values of transport parameters in terms of structure and composition. However, in contrast to their significant limitations, the Nernst–Planck equations are very useful, applicable to describe transport in solids, liquids, and gels [19].

On the other hand, the use of transport equations of linear nonequilibrium thermodynamics for the description of membrane transport is difficult owing to a large number of coefficients present in the equations; these coefficients are also functions of the composition of the solution being in contact with the membrane. Due to these difficulties, fundamental classical works of Staverman [21] or Kedem and Katchalsky [22, 23] are not used very often. Moreover, cross-coefficients should be also considered, but there are approaches neglecting some of these coefficients (e.g., [24]).

MacGillivray [25] has also proposed quasianalytical solutions of the Nernst–Planck equations for time-dependent phenomena in the form of asymptotic solutions based on assumptions consistent with reasonable experimental cases. This was analyzed on the example of studying instantaneous potential jump regarded as small compared to potential difference existing before the experiment (e.g., method of “voltage clamp”). MacGillivray [26] and later Seshadri [27] have analyzed also the problem of electroneutrality condition using perturbation theory resulting in the electroneutrality condition as a certain limiting case. It was found that the electroneutrality condition is a consequence of the Poisson equation when a certain dimensionless parameter, interpreted as a ratio of the Debye length and the membrane thickness, is small. It was also shown that under such assumption the Donnan equilibrium can be derived from the Nernst–Planck equation. Later, Mafé et al. [28] in their consideration have taken into account electrical and diffusional relaxation times as alternative to the approach with relation of Debye length to the membrane thickness.

Similar issues have been critically discussed by Kato [29] by relating also applicability of simplifying assumptions with ratio of Debye length to the membrane thickness. Castilla et al. [30] have used a network approach to obtain numerical solutions based on the Nernst–Planck and Poisson equations under non-steady-state conditions, in a liquid membrane. In this approach, the fluxes were regarded as currents in electrical circuits and diffusion or electrical field influences were regarded as circuit elements (resistors, capacitances), and electrical circuit simulation program has been used to simulate concentration profiles, ionic fluxes, and membrane potentials. Robertson et al. [31] have also used a model with hybrid network description, using a network simulation program (SPICE). This procedure was applied to describe ion transport in bilayer lipid membranes tethered to a gold electrode.

The most significant assumption concerning the charged membrane is homogeneous fixed-charge distribution. The role of charge distribution inhomogeneity has been taken into account by Mafé et al. [32] as well as by Tanioka and coworkers [33]. Tanioka et al. [33, 34] have shown that distribution of effective charge can be nonhomogeneous even in the membrane with homogeneous fixed-charge distribution, under conditions of ion-pair formation between counterions and fixed-charge groups.

Besides inhomogeneity in charge distribution, also, the role of surface and bulk parts of the membrane has been taken into account (e.g., [35, 36]). In the surface region, the conductivity results from mobile counterions compensating charge of fixed groups. In the central part, the conductive properties resemble those of the bathing solution. For this system, the results of modeling have been presented showing a clear difference between mechanisms typical for bulk and surface conductivity [37].

Takagi and Nakagaki [38] have analyzed two kinds of membrane asymmetry: with respect to the partition coefficient and with respect to the charge density. For the first case, when the ion concentration gradient within the membrane is larger than within a symmetric membrane, facilitated transport will take place. However, when the direction of the ion concentration gradient within the membrane is opposite to that expected from the concentration difference between two solutions separated by the membrane, the reverse transport will take place. In the case of charge density inhomogeneity, the difference in cation concentration between the two membrane surfaces is not equal to the difference in anion concentration. Here, facilitated or reverse ion transfer can take place. This model, with the Henderson assumption concerning the distribution of ionic components, has been applied to the aforementioned nonhomogeneous systems. Ion transfer against concentration gradient as a phenomenon related to the multi-ionic transport in a membrane has been discussed in other papers (e.g., [39, 40]). Ramirez et al. [41] have solved numerically the Nernst–Planck equations without invoking the Goldman assumption for the case of pH difference as the driving force for ions.

Chou and Tanioka [42, 43] have discussed the role of organic solvent presence resulting in ion-pair formation in the membrane between counterions and fixed-charge groups. The effective membrane charge densities and the cation-to-anion mobility ratios in the membrane were determined by a nonlinear regression method. This issue can be analyzed in terms of Donnan equilibrium taking into account effective charge concentration that is lower than the analytical one, due to interactions with membrane charged groups [44, 45].

The role of acid/base (amphoteric) properties of polymeric membranes composed of a weak electrolyte as well as acid/base properties of transferring species has been also considered, mainly in papers of Ramirez and Tanioka with coworkers [46–50]. Some papers proposed solutions without invoking simplifying approximation as Goldman constant field assumption [46–48]. The aforementioned, so-called continuous models capable of describing ionic transport in membranes with wide pores have been found useful for nanopore membranes [51] (being of special importance for biomembranes).

The Teorell, Meyer, and Sievers model (including Donnan potentials and diffusion potential in the membrane) was used to describe processes of nanofiltration [52], including also the extended Nernst–Planck equation and Gouy–Chapman theory [53]. Nanofiltration membranes have a cavity structure with pore sizes approximately 1–2 nm, where separation results mainly from size exclusion and electrostatic interactions. Hagmeyer and Gimbel [54] utilized the zeta potential measurements to calculate surface charges of nanofiltration membranes; this charge was then incorporated in a model based on the Teorell, Meyer, and Sievers theory, and the salt rejection effect by the membrane was described. Various models have been proposed to describe rejection mechanism for salts and charged organic species in nanofiltration membranes. These models are based mainly on the extended Nernst–Planck equation, and one of the most popular models is the Donnan steric pore model [55–58]. According to this approach, the membrane is considered as a charged porous layer, characterized by average pore radius, volumetric charge density, and effective membrane thickness. It is also assumed that partitioning effects are described taking into account steric hindrances and the Donnan equilibrium. The role of membrane porosity has been also discussed in papers of Revil et al. (e.g., [59, 60]). The proposed model was based on a volume-averaging approach applied to the Stokes and Nernst–Planck equations and uses Donnan equilibria. It can explain the influence of pore water behavior and water saturation on the diffusion coefficient of a salt in the membrane. As described in [61], selectivity of ion transport in nanopore systems was based on charge repulsion [62], size exclusion [63, 64], and polarity [65].

Nanopore membrane mimicking biological ion channels have been also adapted and developed for sensing purposes in chemical analysis ([66, 67] and review article [68]).

The description of transport phenomena and membrane potentials becomes more complicated in the case of bi-ionic systems, where an ion-exchange membrane separates two electrolyte solutions having the same coion but different counterions. In this case, diffusion processes result in appearance of multi-ionic system because the counterions will be present in both solutions. Many papers concentrate on potential measurements (e.g., [44]), and due to system complexity, analysis of transmembrane ionic fluxes is not often presented [69, 70].

Other more complicated systems are bipolar membranes. They consist of a cation-exchange layer in series with an anion-exchange layer. The models describing potential of such membranes are typically extension of the Teorell–Meyer–Sievers model of monopolar membranes [71–73], with application of the Nernst–Planck equation [74, 75].

1.3 POTENTIALS AND ION TRANSPORT IN ION-SELECTIVE ELECTRODES MEMBRANES

One of the most powerful and successful applications of artificial membranes permeable for ionic species are sensors or biosensors [76] and particularly ion-selective electrodes, where the membrane composition is responsible for sensor's sensitivity and selectivity. The recorded response is open-circuit potential, representing, under typical conditions, the membrane potential as a function of sample composition and concentration. This system and particularly the relation between membrane potential, ion concentrations, and fluxes, as in the case of other membranes, are described by the Nernst–Planck equation for a number of ionic species participating in transfer processes. A simplification/condition required for this class of sensors is the summary flux of ionic species (electrical current) equal to zero.

1.3.1 Equilibrium Potential Models

Taking into account all ionic mobile species, one obtains a system of nonlinear differential equations that cannot be solved analytically. Therefore, for practical purposes related to ISE applications, significant simplification of the rigorous Nernst–Planck protocol or even empirical or semiempirical equations are typically used.

These simplifications are based on the aforementioned model of Teorell, Meyer, and Sievers. Assuming then linear ion concentration profiles in the membrane, integration of the electrical field [5] results in the diffusion potential. Then, the Nernst–Donnan equations describing the ion-exchange equilibrium at membrane/ solution interfaces are added to obtain the membrane potential. In more general treatments, differential diffusion potential is integrated and the interfacial components can be added.

For practical purposes, the description of membrane potentials is usually based on a simple phase-boundary potential model. Within this approach, the membrane potential is equal to the equilibrium potential prevailing on the membrane/solution interface. Migration effects in the membrane were ignored, and thus, diffusion potential was assumed zero (or constant) (Fig. 1.2). Eisenman has extended this

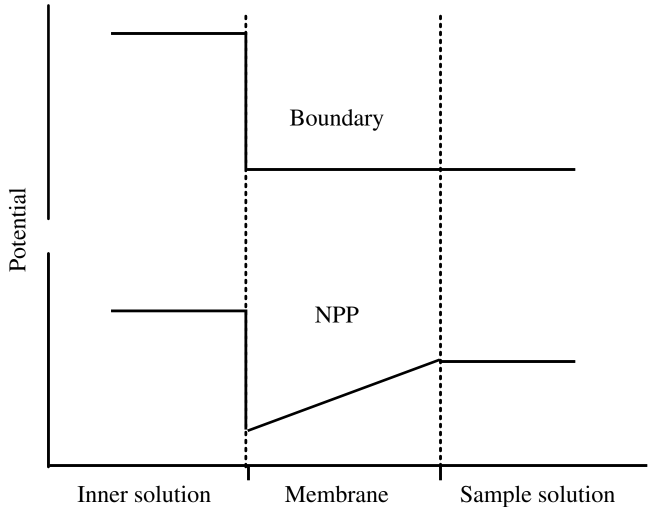

FIGURE 1.2 Comparison of (a) boundary potential profile and (b) approached steady-state Nernst–Planck–Poisson potential profile [77].

model also for nonzero diffusion potential (so-called total membrane potential approach).

Basing on works of Nicolsky and Eisenman, the IUPAC has recommended the semiempirical Nicolsky–Eisenman equation to describe the potential, E, of ion-selective electrode [78, 79]:

$$E = \text{const} + \frac{RT}{z_i F}\ln\left(c_i + K_{ij}c_j^{\frac{z_i}{z_j}}\right) \tag{1.20}$$

derived from separate Nicolsky and Eisenman models. In this equation, K_{ij} is the potentiometric selectivity coefficient for the interferent ion, j. This treatment was based on assumption that the membrane potential response is determined by the sample/membrane interface potential and electrochemical equilibrium prevails at this interface. Moreover, migration effects in the membrane are ignored by assumption that mobilities of all ionic species are equal, and thus, diffusion potential can be neglected.

This relatively simple phase-boundary (equilibrium potential) model is useful and sufficient under typical conditions, denoting ion concentration above 10^{-6} M, membranes saturated with primary ions, and fast ion-exchange processes. Significant advantages of this models have been summarized in a review of Bakker et al. [80], showing a series of its recent applications as a basis for understanding of membrane selectivity, applications of the so-called sandwich membrane method, theoretical advances in optimizing the lower detection limit of ISEs, understanding polyion sensors, potential drifts in the case of ISEs with solid contact (replacing the inner solution), as well as development of galvanostatic ISEs. The problem of selectivity in terms of phase-boundary model has been also discussed in other papers of Bakker et al. [81, 82].

1.3.2 Local Equilibrium Potential Model

However, under some conditions, this simplified description is not sufficient, especially when time-dependent or nonequilibrium phenomena appear. This can concern (i) membranes with low diffusion coefficient values (e.g., polyacrylate-based membranes), where uniform distribution of ions is not attained within reasonable experiment's time; (ii) diluted sample solutions, close to detection limits; (iii) very fast measurement protocols; and (iv) presence of thin membrane, thin transducer phases placed between the membrane and electrode support, or presence of thin aqueous layers between the membrane and support, characterized by significant alteration of their composition in course of measurements. In such cases, the role of transmembrane ion fluxes, under zero current conditions, can be no longer ignored. Moreover, some applications of ISEs directly explore ion flow, for example, determination of polyions as heparin or protamine [83], when the analyte ions are spontaneously accumulated in the membrane phase. Due to the influence of mass transport, the slope of potential versus logarithm of activity is higher than expected from the Nernst relation (concerning equilibrium conditions).

The evolution of models related to responses of ion-selective electrodes has been presented in [84]. Compared to the simple phase-boundary potential model, a more advanced description was offered by a local equilibrium model (or diffusion layer models (DLM)), where a local equilibrium at interfaces was assumed but concentrations of ions in the membrane and the contacting phases are dependent on the distance but are independent of time. Any source of ion fluxes is concentration gradient described by Fick’s law, that is, migration is ignored. Steady-state ion fluxes resulting from linear concentration gradients between the interface area and bulk are also assumed. Some cases with any number of ionophores and differently charged ions have been discussed [85].

Steady-state concentration profiles accompanying ion fluxes can be also used in the area of nonequilibrium potentiometry, where reproducible accumulation and depletion processes at ion-selective membranes may be used to gain analytical information about the sample [86].

The diffusion model has been developed to take into account the role of time, in contrast to the equilibrium potential model. The time was introduced to describe attaining of equilibrium via diffusion-controlled ion transport. The role of time can be, for example, reflected in changes of selectivity coefficients [87–90]. The selectivity coefficient (within the frame of this model) can change from the value typical for short times, when ion transport limitations are of crucial importance and the selectivity coefficient represents the ratio of diffusion coefficients of interferent and analyte ion. On the other hand, for a long time, when equilibrium is attained, the selectivity coefficient is the same as predicted by equilibrium potential model.

In 1999, Sokalski et al. [91] used this model to interpret lowering of the detection limit, taking into consideration ion fluxes in a system consisting of a plastic membrane bathed by two solutions. Assumptions of steady-state and linear concentration changes were used. This issue is described in detail in chapter 2 of this book.

Morf et al. [92–94]) have taken into account two monovalent ions (preferred and interfering one) assuming equal diffusion coefficients of these ions. A finite difference method was used in modeling ion fluxes. This approach was also extended assuming that diffusion coefficients can have different values and with other boundary conditions.

1.3.3 Model Based on the Nernst–Planck Equation

A more advanced description, compared to local equilibrium model, accommodates influence of electrical field, using the Nernst–Planck equation, and these approaches do not require equilibrium or steady state as well as electroneutrality condition.

A more rigorous description of phenomena occurring in charged membranes of ISEs can be based on pioneering works proposing first attempts to find numerical solutions of the Nernst–Planck equations, as papers published by Cohen and Cooley [13], Hafemann [95], and MacGillivray [25, 26]. The first important contribution relating numerical solving of the Nernst–Planck equation for the case of ion-selective electrodes, considering space-charge effects using the Poisson equation, has been published by Brumleve and Buck [15], where finite difference simulation method has been used. This method has been developed also by other authors, for example, Manzanares et al. [32, 96], Rudolph [97], Samson and Marchand [98], and Moya et al. (network simulation [99]).

Sokalski and Lewenstam [77, 100] have developed the method proposed by Brumleve and Buck [15] and have proposed a more advanced description useful to numerical solving the Nernst–Planck equations in the case of ion-selective electrodes. In this approach, diffusion and migration of ions were described by the Nernst–Planck equation, while electrical interactions of ionic species were expressed by the Poisson equation (Eq. 1.19).

These equations and the continuity equation (law of mass conservation) relating fluxes, f_i, and concentrations, c_i,

$$\frac{\partial c_\mathrm{i}(x,t)}{\partial t} = -\frac{\partial f_\mathrm{i}(x,t)}{\partial x} \tag{1.21}$$

formed a system of partial nonlinear differential equations that were solved numerically.

In all calculations, Chang–Jaffe boundary conditions expressing ion transfer kinetics were used:

$$\begin{aligned} f_\mathrm{i0}(t) &= \vec{k}_\mathrm{i} \cdot c_\mathrm{i,bL} - \overleftarrow{k}_\mathrm{i} \cdot c_\mathrm{i0}(t) \\ f_\mathrm{id}(t) &= -\vec{k}_\mathrm{i} \cdot c_\mathrm{i,bR} + \overleftarrow{k}_\mathrm{i} \cdot c_\mathrm{id}(t) \end{aligned} \tag{1.22}$$

where $f_\mathrm{i0}, f_\mathrm{id}$, c_i0, c_id are the fluxes and concentrations of the ith component at $x = 0$ and $x = d$ (d: membrane thickness), $\vec{k}_\mathrm{i}$ and $\overleftarrow{k}_\mathrm{i}$ are the forward and backward rate constants, and $c_{i,\mathrm{bL}}$ and $c_{i,\mathrm{bR}}$ are the concentrations in the bathing solutions at the left (L) and right (R) side of the membrane, respectively.

In the calculations, implicit finite difference method was used, and the resulting system of difference equations was solved using the Newton–Raphson method, expressed in the following form:

$$\mathbf{J}\left(\mathbf{x}^{(\mathrm{i})}\right)\Delta\mathbf{x}^{(\mathrm{i}+1)} = -\mathbf{F}\left(\mathbf{x}^{(\mathrm{i})}\right) \tag{1.23}$$

where $\mathbf{J} \equiv \nabla\mathbf{F}$, the Jacobian of $\mathbf{F}$.

The authors managed to avoid splitting the membrane potential into boundary and diffusion potential; it could be shown that both membrane/solution interfaces and the membrane bulk contribute to overall membrane potential. Therefore, analyses of membrane potential distribution and changes covered the whole membrane. The Planck and Henderson equations for liquid junction and the Nicolsky–Eisenman equations for membranes of ISEs were shown as specific cases of the Nernst–Planck–Poisson approach. The former equations give the same results as the general model but for infinite time.

This model can predict significant influence of ion transport (diffusion), distribution and rate parameters, ion charges, dielectric constants, and thickness of the membrane. This model provides also the profile of electrical potential in space and time, which according to DLM (a steady-state model) cannot be modeled. Thus, analyses of transient membrane potentials and its spatial distribution were possible.

The Nernst–Planck–Poisson model offers new solutions related to practical problems of work with ISEs. It can successfully describe concentration and potential profiles in the processes of electrode equilibration, for example, change of the shape of potential profiles in the membrane can be followed, showing approaching a linear dependence of potential on the distance from membrane surface (Fig. 1.2). Moreover, under steady-state conditions (or equilibrium), it can show nonlinearity for ion-exchanger sites, R^-, and migrational effects, which could not be predicted using earlier models (phase-boundary model or DLM). It can be shown that contribution of "diffusion" potential before equilibrium is significant and changes with time; moreover, it is dependent on the magnitude and relation of diffusion coefficients of primary, interfering ions and ion-exchanger sites (Fig. 1.3), and thus, predictions of the present and earlier models can be quite different. These effects are also reflected in the shape of potentiometric calibration plots. Linearity of such plots depends on the distance from the steady state or equilibrium state of the system. However, under steady-state conditions, the shape of the plots can be to some extent affected by diffusion potential.

This model has been later used to analyze time-dependent phenomena in the potentiometric response of ion-selective electrodes related to the role of transmembrane fluxes for the detection limit [101, 102] and selectivity of ISEs [103]. Particularly, it was possible to analyze concentration profiles with time for membranes conditioned

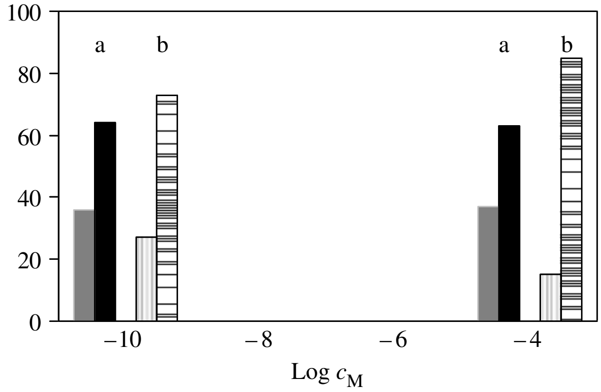

FIGURE 1.3 Contribution (in %) to boundary potential (black and horizontal lines) and inner membrane potential (grey and vertical lines) calculated according to the Nernst–Planck–Poisson model, for $[M^+] = 10^{-4}$ and $[M^+] = 10^{-10}$ M, in the presence of interfering ion ($[N^+] = 10^{-3}$ M) and in the presence of R^- anions in the membrane [77], for diffusion coefficients: (a) $D_M = D_R = 1 \cdot 10^{-7}$, $D_N = 1 \cdot 10^{-6}$ cm$^2 \cdot$s^{-1}; (b) $D_M = 1 \cdot 10^{-6}$, $D_R = D_N = 1 \cdot 10^{-7}$ cm$^2 \cdot$s^{-1}; $\overrightarrow{k}_M = \overleftarrow{k}_M = 10^{-1}$, $\overrightarrow{k}_N = 10^{-2}$, $\overleftarrow{k}_N = 10^{-1}$, for X^- anions $\overrightarrow{k}_X = X = 0$, $k_N/k_M = 0.1$.

in solutions of highly interfering ions. Moreover, selectivity changes with time could be effectively described. Following changes of concentration and potential in time enabled quantitative explanation of observed selectivity coefficients changes. This model was also used to explain the role of transmembrane ion fluxes and electrical potential drops for the detection limit, its changes, and stabilization in time.

Recently, Morf et al. have analyzed behavior of very thin membranes [104] (below 1 μm), which cannot be regarded as electroneutral phases (as bulk membranes), but they are distinct space-charge systems. The authors applied the theory based on the Nernst–Planck equation and Poisson relationship between space-charge density and electrical field gradient to analyze steady-state potentials and concentration profiles. Solid-contacted thin membranes exhibited sub-Nernstian response, while those contacting aqueous solutions on both sides showed a theoretical Nernstian slope.

Gyurcsanyi with coworkers [105] has applied the Nernst–Planck–Poisson equations to describe potentiometric responses of permselective gold nanopore membranes [61], using the surface charge density of nanopores as a fitting parameter.

Introduction of the Nernst–Planck equation to solve problems related to ion-selective electrodes has brought significant progress in the theoretical description and understanding of response mechanisms of potentiometric sensors. However, there are still problems that could be analyzed in the nearest future as, for example, modeling in 2- or 3-dimensional space, taking into account details of the membrane structure, changes of experimental parameters in dependence on location in the membrane, the role of the membrane inhomogeneity, the role of cross terms, and details of ion-exchange mechanisms.

1.4 SUMMARY

Ionic fluxes and membrane potentials are coupled by the Nernst–Planck equation. This equation is widely used to describe transport phenomena in biological and artificial membranes. In biological membranes, most often, the Goldman approximation is used, assuming constant electrical field in the membrane. Generally, for the description of transport processes in the membranes, also, numerical procedures were proposed, enabling transport description without invoking the Goldman assumption, taking into account, for example, acid/base equilibria, ion-pair formation, and inhomogeneity of charge distribution.

A significant area of membrane applications are potentiometric ion-selective electrodes. Although the nature of transport processes of charged species is similar as for biological membranes, usually, a different method of description prevails in the literature, based on simplified empirical description of boundary potentials (Nicolsky–Eisenman equation), resulting from ion-exchange equilibria on the membrane/solution interface. Additionally, diffusion potential can be taken into account, described usually by considering the Henderson approximation (linear concentration gradient). More advanced descriptions are also proposed as DLM and recently the most advanced approach based on the Nernst–Planck–Poisson equations, without splitting the membrane potential into boundary and diffusion potentials. The last theory is particularly useful to describe the phenomena in the case of, for example, dilute solutions, for short time scale of membrane potential measurements and for thin or highly resistive membranes.

REFERENCES

1. W.E. Morf, *Studies in Analytical Chemistry 2. The Principles of Ion-Selective Electrodes and of Membrane Transport*. Akadémiai Kiadó, Budapest, 1981.
2. J. Koryta, J. Dvorak, L. Kavan, *Principles of Electrochemistry*, Wiley, New York, 1993.
3. H. Ti Tien, A. Ottova-Leitmannova, *Membrane Biophysics. S Viewed from Experimental Bilayer Lipid Membranes (Planar Lipid Bilayers and Spherical Liposomes)*, Elsevier, Amsterdam, 2000.
4. P. Henderson. *Z. Phys. Chem.* 59, 118 (1907)
5. R.P. Buck, E. Lindner. *Acc. Chem. Res.* 31, 257 (1998).
6. K. Sollner. *Z. Elektrochem.* 36, 36 (1930).
7. T. Teorell. *Proc. Soc. Exp. Biol. Med.* 33, 282 (1935).
8. K.H. Meyer, J.F. Sievers. *Helv. Chim. Acta* 19, 649 (1936).
9. F.G. Donnan. *Z. Electrochem.* 17, 572 (1911).
10. K. Vetter. *Electrochemical Kinetics*, Academic Press, New York, 1967.
11. W.E. Morf. *Anal. Chem.* 49, 810 (1977).
12. R. Schlögl. *Z. Phys. Chem.* 1, 305 (1954).
13. H. Cohen, J.W. Cooley. *Biophys. J.* 5, 145 (1965).
14. J.R. Sandifer, R.P. Buck. *J. Phys. Chem.* 79, 384 (1975).
15. T.R. Brumleve, R.P. Buck. *J. Electroanal. Chem.* 90, 1 (1978).
16. A. de Mari. *Solid State Elektron.* 11, 1021 (1968).
17. G.D. Hachtel, R.C. Joy, J.W. Cooley. *Proc. IEEE* 60, 86 (1972).
18. J.W. Slotboom. *IEEE Trans. Electron Devices* ED-20, 669 (1973).
19. R.P. Buck. *J. Membr. Sci.* 17, 1 (1984).
20. S. Kirkpatrick. *Rev. Mod. Phys.* 45, 574 (1973).
21. A.J. Staverman. *Trans. Faraday Soc.* 48, 176 (1952).
22. O. Kedem, A. Katchalsky. *J. Gen. Physiol.* 45, 143 (1961).
23. O. Kedem, A. Katchalsky. *Trans. Faraday Soc.* 59, 1918 (1963).
24. S. Koter, W. Kujawski, I. Koter. *J. Membr. Sci.* 297, 226 (2007).
25. A.D. MacGillivray. *J. Chem. Phys.* 52, 3126 (1970).
26. A.D. MacGillivray. *J. Chem. Phys.* 48, 2903 (1968).
27. M.S. Seshadri. *Ber. Bunsenges. Phys. Chem.* 87, 666 (1983).
28. S. Mafé, J. Pellicer, V.M. Aguilella. *J. Phys. Chem.* 90, 6045 (1986).
29. M. Kato. *J. Theor. Biol.* 177, 299 (1995).
30. J. Castilla, M.T. Garcia-Hernández, A. Hayas, J. Horno. *J. Membr. Sci.* 136, 101 (1997).
31. J.W.F. Robertson, M.G. Friedrich, A. Kibrom, W. Knoll, R.L.C. Naumann, D. Walz. *J. Phys. Chem. B* 112, 10475 (2008).

32. J.A. Manzaranes, S. Mafé, J. Pellicer. *J. Phys. Chem.* 95, 5620 (1991).
33. R. Yamamoto, H. Matsumoto, A. Tanioka. *J. Phys. Chem. B* 107, 10615 (2003).
34. H. Matsumoto, R. Yamamoto, A. Tanioka. *J. Phys. Chem. B* 109, 14130 (2005).
35. K. Kontturi, S. Mafé, J.A. Manzaranes, L. Murtomäki, P. Viinikka. *Electrochim. Acta* 39, 883 (1994).
36. N.P. Berezyna, N. Gnusin, O. Dyomina, S. Timofeyev. *J. Membr. Sci.* 86, 207 (1994).
37. S. Mafé, J.A. Manzaranes, P. Ramirez. *Phys. Chem. Chem. Phys.* 5, 376 (2003).
38. R. Takagi, M. Nakagaki. *J. Membr. Sci.* 27, 285 (1986).
39. P. Schwahn, D. Woermann. *Ber. Bunsenges. Phys. Chem.* 90, 773 (1986).
40. M. Higa, A. Tanioka, K. Miyasaka. *J. Membr. Sci.* 37, 251 (1988).
41. P. Ramirez, A. Alcaraz, S. Mafé. *J. Membr. Sci.* 135, 135 (1997).
42. T.-J. Chou, A. Tanioka. *J. Phys. Chem. B* 102, 7198 (1998).
43. T.-J. Chou, A. Tanioka. *J. Membr. Sci.* 144, 275 (1998).
44. N. Lakshminarayanaiah. *Transport Phenomena in Membranes*, Academic Press, New York, 1969.
45. S. Mafé, P. Ramirez, A. Tanioka, J. Pellicer. *J. Phys. Chem. B* 101, 1851 (1997).
46. P. Ramirez, S. Mafé, A. Tanioka, K. Saito. *Polymer* 38, 4931 (1997).
47. P. Ramirez, A. Alcaraz, S. Mafé. *J. Electroanal. Chem.* 436, 119 (1997).
48. M. Kawaguchi, T. Murata, A. Tanioka. *J. Chem. Soc. Faraday Trans.* 93, 1351 (1997).
49. P. Ramirez, A. Alcaraz, S. Mafé, J. Pellicer. *J. Membr. Sci.* 161, 143 (1999).
50. I. Uematsu, T. Jimbo, A. Tanioka. *J. Colloid Interf. Sci.* 245, 319 (2002).
51. P. Ramirez, S. Mafé, A. Alcaraz, J. Cervera. *J. Phys. Chem. B* 107, 13178 (2003).
52. H. Matsumoto, Y.-Ch. Chen, R. Yamamoto, Y. Konosu, M. Minagawa, A. Tanioka. *J. Mol. Struct.* 739, 99 (2005).
53. J. Garcia-Aleman, J.M. Dickson. *J. Membr. Sci.*, 235, 1 (2004).
54. G. Hagmeyer, R. Gimbel. *Sep. Pur. Technol.* 15, 19 (1999).
55. W.R. Bowen, A.W. Mohammad, N. Hilal. *J. Membr. Sci.* 126, 91 (1997).
56. D. Vezzani, S. Bandini. *Desalination* 149, 477 (2002).
57. A.W. Mohammad, M.S. Takriff. *Desalination* 157, 105 (2003).
58. A. Szymczyk, C. Labbez, P. Fievet, A. Vidonne, A. Foissy, J. Pagetti. *Adv. Colloid Interface Sci.* 103, 77 (2003).
59. P. Leroy, A. Revil, D. Coelho. *J. Colloid Interface Sci.* 296, 248 (2006).
60. A. Revil, D. Jougnot. *J. Colloid Interface Sci.* 319, 226 (2008).
61. G. Jagerszki, A. Takacs, I. Bitter, R.E. Gyurcsanyi. *Angew. Chem. Int. Ed.* 50, 1656 (2011).
62. C.R. Martin, M. Nishizawa, K. Jirage, M. Kang, S.B. Lee. *Adv. Mater.* 13, 1351 (2001).
63. K.B. Jirage, J.C. Hulteen, C.R. Martin. *Science* 278, 655 (1997).
64. K. Motesharei, M.R. Ghadiri. *J. Am. Chem. Soc.* 119, 11306 (1997).
65. E.D. Steinle, D.T. Mitchell, M. Wirtz, S.B. Lee, V.Y. Young, C.R. Martin. *Anal. Chem.* 74, 2416 (2002).
66. M. Sugawara, K. Kojima H. Sazawa, Y. Umezawa. *Anal. Chem.* 59, 2842 (1987).
67. H. Minami, M. Sugawara, K. Odashima, Y. Umezawa, M. Uto, E.K. Michaelis, T. Kuwana. *Anal. Chem.* 63, 2787 (1991).

68. R.E. Gyurcsanyi. *Trends Anal. Chem.* 27, 627 (2008).
69. L. Dammak, C. Larchet, V.V. Nikonenko, V.I. Zabolotsky, B. Auclair. *Eur. Polym. J.* 32, 1199 (1996).
70. S. Mokrani, L. Dammak, C. Larchet, B. Auclair. *New J. Chem.* 23, 375 (1999).
71. N. Lakshminarayanaiah. *Equations of Membrane Biophysics*, Academic Press, New York, 1984.
72. F. Helfferich. *Ion Exchange*, McGraw-Hill, New York, 1962.
73. A. Higuchi, T. Nakagawa. *J. Membr. Sci.* 32, 267 (1987).
74. P. Ramirez, S. Mafé, J.A. Manzaranes, J. Pellicer. *J. Electroanal. Chem.* 404, 187 (1996).
75. T.-J. Chou, A. Tanioka. *J. Colloid Interf. Sci.* 212, 293 (1999).
76. E. Lindner, R. Gyurcsányi, R.P. Buck. Membranes in electroanalytical chemistry: Membrane-based chemical and biosensors. in *Encyclopedia of Surface and Colloid Science*, Marcel Dekker, New York, 2002.
77. T. Sokalski, P. Lingenfelter, A. Lewenstam. *J. Phys. Chem. B* 107, 2443 (2003).
78. K.N. Mikhelson. *Ion-Selective Electrodes*, Springer, Berlin, Heidelberg, 2013.
79. IUPAC. *Pure Appl. Chem.* 66, 2527 (1994).
80. E. Bakker, P. Bühlmann, E. Pretsch. *Talanta* 63, 3 (2004).
81. E. Bakker, E. Pretsch, P. Bühlmann. *Anal. Chem.* 72, 1127 (2000).
82. E. Bakker. *J. Electroanal. Chem.* 639, 1 (2010).
83. B. Fu, E. Bakker, J.H. Yun, V.C. Yang, M.E. Meyerhoff. *Anal. Chem.* 66, 2250 (1994).
84. J. Bobacka, A. Ivaska, A. Lewenstam. *Chem. Rev.* 108, 329 (2008).
85. W.E. Morf, M. Badertscher, T. Zwickl, N.F. de Rooij, E. Pretsch. *J. Phys. Chem. B* 103, 11346 (1999).
86. K. Tompa, K. Birbaum, A. Malon, T. Vigassy, E. Bakker, E. Pretsch. *Anal. Chem.* 77, 7801 (2005).
87. A. Hulanicki, A. Lewenstam. *Anal. Chem.* 53, 1401 (1981).
88. A. Hulanicki, A. Lewenstam. *Talanta* 29, 661 (1982).
89. W.E. Morf. *Anal. Chem.* 55, 1165 (1983).
90. A. Lewenstam, A. Hulanicki, T. Sokalski. *Anal. Chem.* 59, 1539 (1987).
91. T. Sokalski, T. Zwickl, E. Bakker, E. Pretsch. *Anal. Chem.* 71, 1204 (1999).
92. W.E. Morf, E. Pretsch, N.F. de Rooij. *J. Electroanal. Chem.* 602, 43 (2007).
93. W.E. Morf, E. Pretsch, N.F. de Rooij. *J. Electroanal. Chem.* 614, 15 (2008).
94. W.E. Morf, E. Pretsch, N.F. de Rooij. *J. Electroanal. Chem.* 633, 137 (2009).
95. D.R. Hafemann. *J. Phys. Chem.* 69, 4226 (1965).
96. J.A. Manzaranes, W.D. Murphy, S.S. Mafé, H. Reiss. *J. Phys. Chem.* 97, 8524 (1993).
97. M. Rudolph. *J. Electroanal. Chem.* 375, 89 (1994).
98. E. Samson, J. Marchand. *J. Colloid Interface Sci.* 215, 1 (1999).
99. A.A. Moya, J. Horno. *J. Phys. Chem. B* 103, 10791 (1999).
100. T. Sokalski, A. Lewenstam. *Electrochem. Commun.* 3, 107 (2001).
101. T. Sokalski, W. Kucza, M. Danielewski, A. Lewenstam. *Anal. Chem.* 81, 5016 (2009).

102. J.J. Jasielec, T. Sokalski, R. Filipek, A. Lewenstam. *Electrochim. Acta* 55, 6836 (2010).

103. P. Lingenfelter, I. Bedlechowicz-Sliwakowska, T. Sokalski, M. Maj-Żurawska, A. Lewenstam. *Anal. Chem.* 78, 6783 (2006).

104. W.E. Morf, E. Pretsch, N.F. de Rooij. *J. Electroanal. Chem.* 641, 45 (2010).

105. I. Makra, G. Jagerszki, I. Bitter, R.E. Gyurcsanyi. *Electrochim. Acta* 73, 70 (2012).