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# Variability of selectivity coefficients of ionophore-based ion-selective membranes: description using multispecies approximation

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*Description of the response of ionophore-based ion-selective electrode membranes using multispecies approximation is briefly discussed. It is shown that the variability of selectivity coefficients of a given membrane with variation of concentrations of ions in aqueous solution is intrinsic feature of ionophore-based membranes. Advantages of multispecies approximation over apparently rigorous thermodynamic description are analyzed.*

## Introduction

Ion-selective electrodes (ISEs) constitute oldest and most matured type of chemical sensors [1–3]. ISEs are able for transduction of a chemical signal (concentration of an analyte in a sample) into a potentiometric signal: electromotive force of a cell including an ISE and a suitable reference electrode. Because of these advantages, ISEs became widely used in various applications: in clinical chemistry (blood, serum, urine, and saliva), in environmental, agricultural, and foodstuff samples (natural and waste water, soil, vegetables, fruits, wines, milk, meat), and in process analytical chemistry.

In many cases ISEs can be used for direct analysis without any pretreatment of the sample, and also for continuous monitoring, for on-line and in-line analysis. On the other hand, the usage of ISEs in a sample "as is" – i.e. without a pretreatment of the sample, demands high selectivity and reproducibility of the sensor response. Therefore, the ISEs must be tuned to comply with the concrete analytical task. The optimization of the membrane composition constitutes the main part of this tuning, although in some cases the optimization of the internal reference system can be even more important [4–5].

Nowadays, highly selective neutral and charged ionophores are known for a large number of analytes [3,6]. Introducing novel even better ionophores became more and more difficult task. Thus, the optimization of the membrane can be achieved rather by tailoring its composition via combination of various known ionophores in the most proper concentrations, than by synthesizing novel ionophores.

For such tailoring an advanced theory of membrane response is required. Most of known theories of ionophore-based membranes are sufficiently incomplete, that is only some limiting cases (like full dissociation or strong association of electrolytes in membranes) can be treated quantitatively [1,2]. Normally, it is arbitrarily assumed that some kind of species strongly predominate in membranes, even if the experimental conditions, i.e. the compositions of samples vary in a wide range. Sometimes only the boundary contribution to the overall membrane potential is considered, and the selectivity is then treated in terms of only equilibrium constants, while the differences of the mobilities of the species in membranes are neglected [2,7].

A rather fundamental theory based on simultaneous consideration of Nernst-Plank and Poisson equations has been proposed recently [8,9]. This theory allows for simulation of an ISE response and of migration of species in the membrane in real time and space. Being very general in principal, this masterpiece theory, as yet, is confined to relatively simple systems without complicated ion-to-ionophore complexes in membranes.

Ions and ionophores strongly interact in membranes. In addition, membranes are not really homogeneous: it is known that membranes extract water from solutions, and this water forms droplets (micelles) in the organic phase [10,11]. Therefore, from thermodynamic point of view, ionophore-based solvent polymeric ISE membranes are very complicated systems. Probably, this is why there are only a few attempts of rigorous thermodynamic description of ISEs [12,13].

In this paper we will consider the theory of ionophore-based ion-selective membranes based on a simple, but effective approximation, which we call multispecies approximation [14–16]. This is essentially chemical approach which takes into account the interactions between various species in real membranes. Thus, the non-ideality of these complicated systems is described

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in terms of complexation and association of ionic and nonionic species in the membrane phase. The idea of multispecies approach was already discussed and successfully applied for a number of real systems [17–20]. Here, we will focus on the variability of selectivity coefficients of ISEs because this issue is important for analytical applications. Also, we will compare multispecies approximation with apparently more rigorous thermodynamic description of ISE membranes presented in [12,13].

## Theory

The multispecies approximation relies on the following assumptions: 1) membrane/solution interface is at equilibrium; 2) association of electrolytes in membranes is incomplete and different for different membranes and ions; 3) ion-ionophore complexes of different stoichiometry are present in membranes simultaneously. These assumptions are consistent with numerous electrochemical experiments [21–26]. The approach takes into consideration free ions, the respective complexes with neutral ionophores, ion-pairs (and triplets, if applicable), and with ionic sites (charged ionophores, ion-exchangers).

The extra-thermodynamic assumptions in the model are the following: 1) the list of the species taken into consideration is adequate; 2) activity coefficients of the species can be different from 1, but are the same across the whole membrane; 3) all equilibrium constants, although expressed via concentrations, are considered true constants; 4) individual mobilities of ions are constant. Indirect evidence favoring assumption 2) was obtained in [27]: the steady state concentration profiles of species across membranes were linear, although the linearity must be fulfilled for activity profiles. Hence, activity coefficients of species were virtually constant in membranes studied in [27].

Multispecies approximation allows for calculation of the actual composition of a membrane (concentrations of all the individual species) as a function of the total composition of the membrane, and the compositions of aqueous solutions, provided the necessary data are given. The latter are partition coefficients, ion-ionophore stability constants, and association constants for ion-pairs and triplets. If the membrane includes L neutral ionophore, $R^-$ (or $R^+$) exchanger sites, and $S^+$ ($S^-$) co-exchanger, the equations to be solved are the mass balances for the neutral ionophore, the sites, and the co-exchanger, and also the electroneutrality condition of the membrane bulk:

$$C_L^{tot} = C_L + \sum_{n=1}^{k}\sum_{q=0}^{z} nC_{IL_nR_q} + \sum_{n=1}^{k}\sum_{q=0}^{1} nC_{JL_nR_q} + \sum_{n=1}^{k}\sum_{q=0}^{1} nC_{SL_nR_q} \quad (1)$$

$$C_R^{tot} = C_R + \sum_{n=0}^{k}\sum_{q=1}^{z} qC_{IL_nR_q} + \sum_{n=0}^{k} C_{JL_nR} + \sum_{n=0}^{k} C_{SL_nR} \quad (2)$$

$$C_S^{tot} = \sum_{n=0}^{k}\sum_{q=0}^{1} C_{SL_nR_q} \quad (3)$$

$$C_R = \sum_{n=0}^{k}\sum_{q=0}^{z} (z-q)C_{IL_nR_q} + \sum_{n=0}^{k} C_{JL_n} + \sum_{n=0}^{k} C_{SL_n} \quad (4)$$

$$C_J = C_I\left((a_J k_J)^z / a_I k_I\right)^{1/z} \quad (5)$$

In the equations above, n stands for the stoichiometry of $IL_n^{z+}$ ion-ionophore complexes and q for the stoichiometry of $IL_nR_q^{(z-q)+}$ associates, C is concentration of the respective species, $k_I$, $k_J$ – ionic distribution coefficients [1]. It is assumed that n varies between 0 (uncomplexed species) and some integer k, and q varies from 0 (dissociated species) to z. Superscript "tot" denotes total concentration of the component. Total concentrations are under control when the membrane is prepared. The system of the equations above is solved by objective function method. The objective function is defined by Eq. (6) being the sum of discrepancies of the total concentrations of the ionophore, of the sites, and of the co-exchanger:

$$\Phi = \left(\frac{C_L^{tot} - C_L^{comb} - C_L}{C_L}\right)^2 + \left(\frac{C_R^{tot} - C_R^{comb} - C_R}{C_R}\right)^2 + \left(\frac{C_S^{tot} - C_S^{comb} - C_S}{C_S}\right)^2 \quad (6)$$

The superscript "comb" denotes sums of all species but the free. When Eqs. (1–5) are solved, i.e. the individual species concentrations are known, $E_b$ boundary potentials can be calculated by Eq. (7), and the differential of $E_d$ diffusion potential by Eq. (8):

$$E_b = E^{mem} - E^{aq} = -\frac{\left(M_I^{0,mem} - M_I^{0,aq}\right)}{z_I F} - \frac{RT}{z_I F}\ln\frac{C_I}{a_I} \quad (7)$$

$$dE_d = -\frac{RT}{F}\frac{\sum_I z_I U_I dC_I}{\sum_I z_I^2 U_I C_I} \qquad (8)$$

The methods of the integration of Eq. (8) are described in [14,16–18] in detail.

The equations above, together with the specially written computer program which allows numerical solution thereof, constitute the model for computer simulation of ISE membrane response [14–18].

## Results and discussion

Modeling in multispecies approximation allows for tracing the impact from various factors to membrane response. In particular, the dependence of the selectivity of ionophore-based membranes on their composition was thoroughly discussed in [14–16,18]. Especially interesting seem non-monotonous changes of selectivity with the increase of the content of neutral ionophore. This kind of behavior allows obtaining ISEs selective to two different ions using the same ionophore [14,28]. Another interesting consequence from the theory relates to the dependence of the selectivity of a given ISE on the composition of aqueous solution, if the selectivity is calculated by Nikolsky equation:

$$E = E^0 + \frac{RT}{F}\ln\left(a_I + K_{IJ}^{Nik} a_J\right) \qquad (9)$$

It is well known that the values of selectivity coefficients depend on the measurement conditions, typically $K_{IJ}$ apparently "improves" with the increase of $a_J/a_I$ [29,30]. One of the reasons of this variability is the contamination of samples with primary ions from the membrane. Thus, obtaining reproducible values of selectivity coefficients requires either special protocols of measurements [31], or fluxes of primary ions outwards the membrane must be suppressed [5].

Multispecies description allows revealing another (intrinsic) reason for the dependence of the selectivity on the experimental conditions. As presented in Fig. 1, even ideal Nernstian response in separate solutions of IX and JX does not guarantee constant value of selectivity coefficient in IX + JX mixed solutions. The modeling shows that the main reason for this dependence is the increase of the concentration of L free ionophore along the dilution of IX at constant background of JX due to the displacement of $I^+$ primary ions with $J^+$ interference in the membrane [14]. The additional reason comes from the difference in ion-site

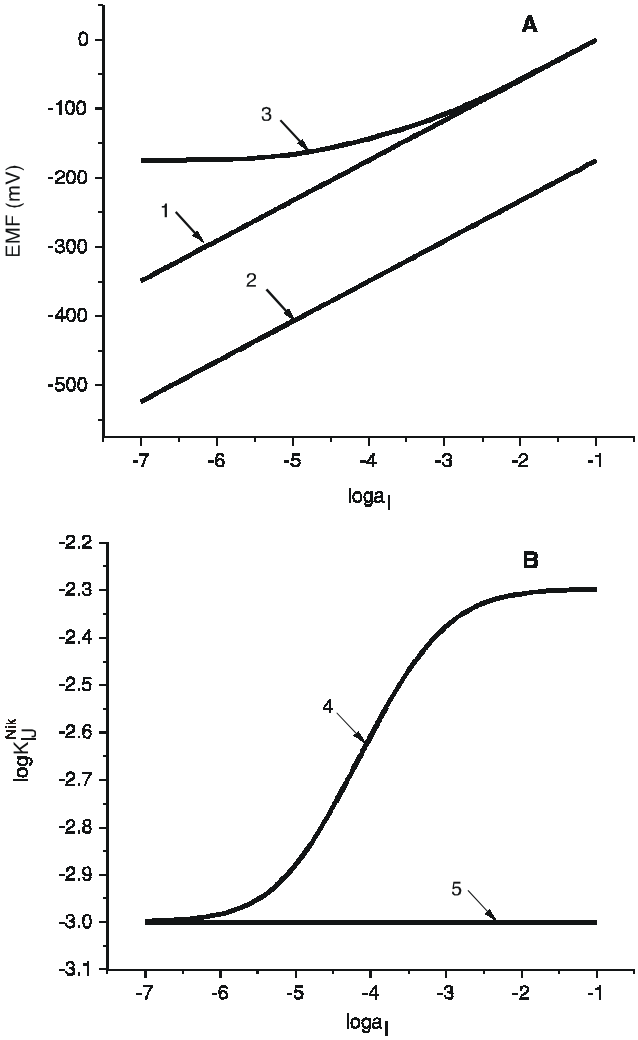


Fig. 1. Simulated EMF (A) and selectivity (B) curves for membrane with $k_J/k_I = 10^{-2}$, $K_{IR} = 10^{10}$ $M^{-1}$, and $K_{JR} = 10^8$ $M^{-1}$. The response: pure IX – curve 1, pure JX – curve 2, and mixed IX + 0.1 M JX – curve 3. The selectivity: Nikolsky selectivity coefficient calculated from the response in mixed solutions – curve 4, and Nikolsky selectivity coefficient calculated from the distance between curves 1 and 2 (like in separate solutions method) –horizontal line 5

association constants: when strongly associated species are replaced with less associated, the fraction of free $R^-$ gets increased [16,18]. Thus, the displacement of $I^+$ with $J^+$ becomes more and more unfavorable, and $K_{IJ}$ calculated by Nikolsky equation gets more and more "improved" with the decrease of $I^+$ ions activity in mixed solution. As a result, constant values for selectivity coefficients should be expected only for ions with similar affinity to the neutral ionophore in the membrane, and for low (or equal) affinity to sites, i.e. for strongly interfering ions. From practical point of view, the variability of selectivity coefficients hampers corrections for the interferences by Nikolsky equation.

The δ relative overestimation of the sought $a_I$ corrected for $a_J$ by Nikolski equation with constant $K_{IJ}$=0.001 (this value would be obtained from the data presented in Fig. 1 by separate solution method), provided $a_J$ is known or measured separately, is as follows:

| log $a_I$ | -1 | -2 | -3 | -4 | -5 | -6 | -7 |
|---|---|---|---|---|---|---|---|
| δ (%) | 0.4 | 4 | 32 | 147 | 322 | 405 | 531 |

Although curves 4 and 5 in Fig. 1B approach one another at low $a_I$, they still don't coincide. This is why the relative overestimation increases monotonously with the decrease of $a_I$.

We will turn now to the comparison between multispecies approximation and more rigorous thermodynamic description of the membrane potential given by Hall [12]. By means of irreversible thermodynamics and statistical mechanics, an equation was derived which must be true for membranes with fixed or mobile sites in the steady state. Seemingly, only one extra assumption is introduced: Hall's theory is confined to systems with only minor degree of displacement of the primary ions with the interference, and this degree is not specified. Unfortunately, this assumption devaluates Hall's theory, as will be shown below.

According to Hall's theory, Nikolsky equation must be correct for the interference between monovalent ions, i.e. the selectivity coefficient calculated according to Nikolsky equation must be constant. For divalent primary ions and monovalent interference, the correct equation must be that proposed by Buck [32]:

$$E = E^0 + \frac{RT}{F}\ln\left(a_I^{1/2} + K_{IJ}^{Buck} a_J\right) \qquad (10)$$

However, it is well known that neither Nikolsky, nor Buck equation satisfy the experimental data in the sense

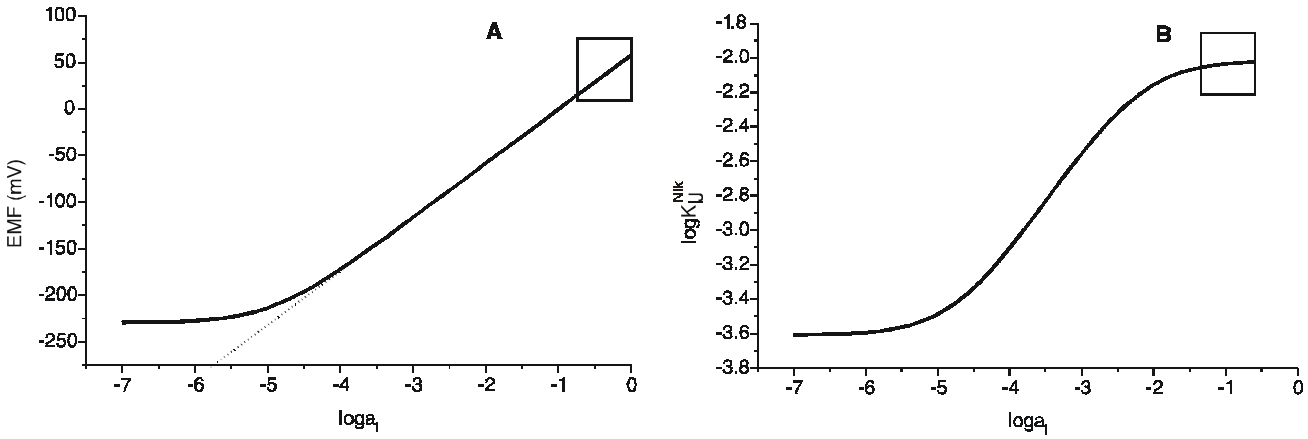


Fig. 2. Simulated EMF (A) and selectivity (B) curves for membrane with $k_J/k_I = 10^{-1}$, $K_{IR} = 10^6$ M$^{-1}$, and $K_{JR} = 10^3$ M$^{-1}$, in mixed IX + JX solutions with constant background 0.1 M JX. The open rectangle shows Hall's domain of the response, the dashed line shows ideal Nernstian response

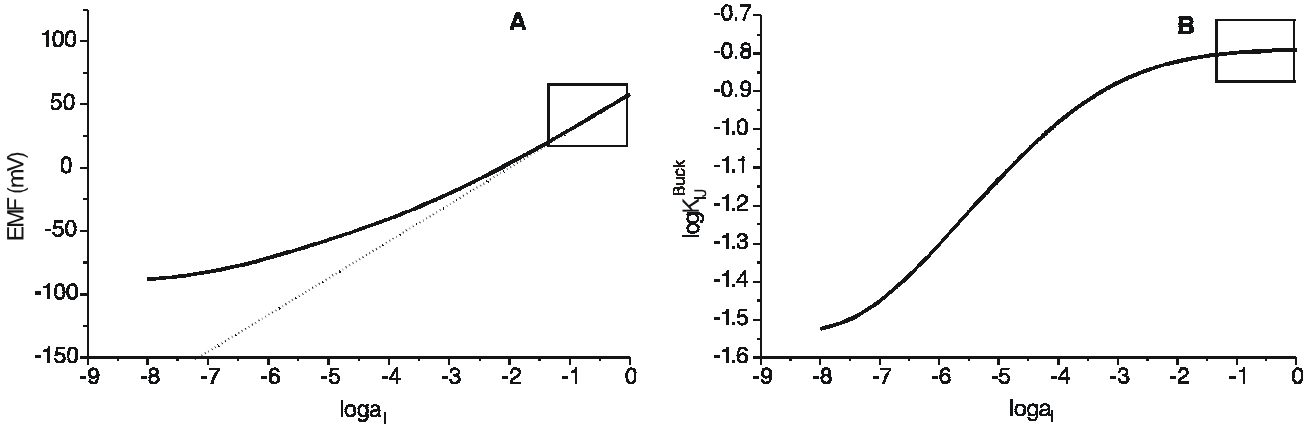


Fig. 3. Simulated EMF (A) and selectivity (B) curves for membrane with $k_J/k_I = 10^{-1}$, $K_{IR} = 10^6$ M$^{-1}$, $K_{IRR} = 10^9$ M$^{-1}$, and $K_{JR} = 10^3$ M$^{-1}$, in mixed $IX_2$ + JX with constant background 0.1 M JX. The open rectangle shows Hall's domain of the response, the dashed line shows ideal Nernstian response

of constant selectivity coefficients, and more complicated equations were introduced [33,34].

Our model calculations (see Fig. 2) show that $K_{IJ}^{Nik}$ depends on the composition of aqueous solution. For differently charged ions, the situation is analogous: $K_{IJ}^{Buck}$ is not constant, see Fig. 3. As it was already mentioned, the variability of selectivity coefficients is well known experimental fact. Thus, the proposed model which includes extra-thermodynamic assumptions is in better agreement with experimental data than apparently strict theory proposed by Hall.

Now, we will try to understand how can this happen. Let's consider mixed solutions with variable activity of $I^+(I^{2+})$ primary ions ($a_I$) and constant activity of $J^+$ interference ($a_J$). When $a_I$ is high, the degree of the displacement of primary ions with the interference is very low, and $C_I$ – the concentration of primary ions in the membrane remains practically constant. The calculated ISE response in these solutions is almost Nernstian, and the deviations from linearity are very small, see Fig. 2A and 3A. The respective values of $\log K_{IJ}^{Nik}$ and $\log K_{IJ}^{Buck}$, indeed, remain constant, in agreement with Hall's theory (Fig. 2B and 3B). This part of the response curve we will call "Hall's domain". Outside this domain, with the decrease of $a_I$, the calculated selectivity coefficients vary significantly. At high excess of $J^+$, the selectivity coefficients, again, produce a plateau. According to the model calculations, these two plateau values can be different in 1 order of magnitude, or even more.

It is important that the deviations of the calculated response from the ideal Nernstian values in Hull's domain do not exceed 0.5 mV. In practical measurements, the inaccuracy is about 0.3–1 mV. Therefore, deviations within 1 mV are practically "unseen" in real experiment. On the other hand, deviations higher than 1 mV, which can be registered for sure, belong to the domain with variable values of $\log K_{IJ}^{Nik}$ and $\log K_{IJ}^{Buck}$. Thus, Hull's theory fits only the domain where the deviations from Nernstian response do not exceed the experimental noise. Obviously, this is that domain of "low degree of displacement" which was not specified by Hall [12].

Another approach also proposed by Hall [13] allows evading any extra thermodynamic assumptions within the whole range of ISE response. He invented a procedure of measurements with a number of ISEs. This procedure, in principal, allows for analysis of any certain sample. However, the procedure does not yield data on the selectivity, and therefore gives no heuristic treatment to characterize the sensors. Thus, multispecies approximation, currently, is more efficient than thermodynamic description proposed in [12,13].

## Conclusions

Description of ISEs with ionophore-based membranes in multispecies approximation elucidates the intrinsic reason for the variability of selectivity coefficients with changes of the measurement conditions. Multispecies approximation, although cannot be realized in explicit formulas and requires numerical computer simulations, is an efficient alternative to either oversimplified equations, or to apparently strict thermodynamic description.

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