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# Selectivity Behavior and Multianalyte Detection Capability of Voltammetric Ionophore-Based Plasticized Polymeric Membrane Sensors

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**The current response features of voltammetric ion-selective polymeric membranes doped with neutral ionophores in view of practical sensor development are elucidated. The membranes are designed to extract ions only under applied external potentials and interrogated by normal-pulse voltammetry and pulsed amperometry. They contain two polarizable interfaces to avoid loss of lipophilic ions at the sample side and to maximize the available potential window. A simple theoretical model is developed that describes the observed current at the end of an uptake pulse to the applied membrane potential, which is the sum of both boundary potentials (at the sample and inner electrolyte side) and the membrane internal *iR* drop. The results describe how the selectivity of the resulting sensor must be dependent on the applied potential. Evidently, the role of the applied potential is akin to incorporating lipophilic cationic and anionic sites with potentiometric ionophore-based membranes, which are well known to considerably affect membrane selectivity and to define the charge type of the assessed ions. This has important implications for sensor design, as the applied cell potential can be used to tune sensor selectivity. Theory also explains the role of the inner electrolyte on sensor behavior. A maximum measuring range is expected with ions in the inner electrolyte that are difficult to extract into the membrane. This corresponds to Kihara's experimental results and contrasts to common ion-selective electrode practice, where a salt of the analyte ion is normally present in the inner electrolyte. Separate and mixed solution experiments with membranes containing the sodium-selective ionophore *tert*-butyl calix[4]arene tetramethyl ester and the lithium ionophore ETH 1810 agree very well with theoretical expectations. Multianalyte detection capability with a single sensing membrane is demonstrated in a selectivity-modifying pulsed amperometric detection mode, where each applied voltage yields a different practical selectivity of the sensor. The sensor is altered from being sodium to potassium selective as the magnitude of the applied potential is repetitively varied within the pulse sequence. The sensors show high long-term stability under continuous measuring conditions over 15 h.**

Since the end of the 1960s, ion-selective electrodes have continued to be an important development in analytical chemistry. Polymer membrane ion sensors in particular find extensive practical applications, especially in clinical and environmental chemistry. Polymeric membranes that contain extremely selective ionophores are being used successfully in potentiometric and optical-sensing schemes, and sensors for over 60 different analytes have been reported with this technology so far.[1,2] Unfortunately, it is still difficult to design sensors with adequate selectivity for a number of ions, especially anions. Voltammetry or pulsed amperometry as an alternative transduction principle may offer a direct control of the ion extraction process into polymeric membranes, fully driven by an externally applied potential. Since the applied potential is an additional instrumental tool that can be used to control these devices, a higher or a more tunable selectivity could be obtained than in traditional systems.

The general goal of the research presented here is the development and characterization of voltammetric counterparts of ionophore-based ion-selective electrodes, with no alteration of the polymeric material used with traditional ISEs. The composition of these membranes is however different from that of potentiometric ISEs. With potentiometric membranes, the polymer is doped with a lipophilic ion exchanger to spontaneously uptake hydrophilic counterions from the sample. The resulting ion-exchange properties are known to render the membrane permselective. In contrast, voltammetric membranes are not doped with such ion-exchanger sites since the applied potential must be responsible for the ion uptake of the membrane. Instead, they contain a high concentration of inert lipophilic salt such as tetradodecylammonium tetrakis(4-chlorophenyl)borate (ETH 500), which is present in excess of the neutral ionophore. This keeps the resistance of the membrane comparably low by creating mobile ions in the membrane bulk. In addition, the cations and anions of this salt may provide the necessary counterions of the sample ions extracted under the influence of the applied potential.

On the other hand, these electrodes also distinguish themselves from classical voltammetry at the interface of two immiscible electrolyte solutions (ITIES), which today develops from a traditionally fundamental research area[3−10] to an area that targets the development of practically relevant detection devices.[11−18]

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Since ion diffusion is much slower in solvent polymeric membranes than in organic liquids, the current response is normally dependent on the mass transport of ions in the membrane, not in the contacting aqueous phase. This is evidenced in a lack of stir effect on the current response at moderately high concentrations.[19] This important characteristic also affects the way these membranes are interrogated. In accordance with Senda's work on ITIES,[20] these membranes must be measured with pulsed amperometry or, if the magnitude of the applied voltage is varied, with normal-pulse voltammetry.[21] Intermittent reconditioning periods, where the membrane is held at voltages that lead to near-complete back-extraction of the ions into their aqueous solutions, guarantee reproducible current responses during the short pulses where voltages are applied that lead to ion uptake into the membrane. Otherwise, a continuous uptake process will lead to a monotonic increase of the Nernst diffusion layer thickness in the ion-selective membrane, which results in drift and irreproducible behavior.[17,18,22] While normal-pulse voltammetry is known to be beneficial for voltammetry at ITIES, it is here essential because the membrane responds differently.

With traditional ITIES membranes, concentration polarizations at the internal interface were often avoided by using a common ion in both phases.[18] Frequently, the neutral salt added to the membrane was tetrabutylammonium tetrakis(4-chlorophenyl)-borate, which had a backside aqueous contact with a solution containing tetrabutylammonium chloride. However, the tetrabutylammonium ion can easily exchange with another sample cation if the membrane contains a neutral ionophore that strongly complexes the latter. Indeed, potentiometric studies have documented that valinomycin-based plasticized poly(vinyl chloride) membranes prefer potassium and tetrabutylammonium ions to about the same extent,[23] making an ion-exchange process unavoidable in contact with tetrabutylammonium-free potassium samples. Consequently, in view of practical sensor design, it is advisable to follow the approach taken by Kihara and co-workers, who have studied membranes with two polarizable interfaces.[24−26] The membranes here contain an extremely lipophilic salt such as tetradodecylmethylammonium tetrakis(4-chlorophenyl)borate, and an additional ionophore, and are backside contacted with a simple electrolyte such as sodium or potassium chloride.[22] In that case, uptake of sample cations must normally be coupled to either extraction of cations of the lipophilic salt or counterions of intrinsic impurities from the membrane to the inner side or uptake of anions from the inner electrolyte to the membrane backside.[25,26] Only at very low currents will it be possible that the known 10−200 $\mu$M[27−29] anionic impurities of poly(vinyl chloride) may contribute to the observed current by expelling their counterions into the contacting solution. Expelling cations of the lipophilic membrane salt added to the membrane is also made difficult if both the anion and cation of this salt are extremely lipophilic, as used in this work.[22] Therefore, at moderate currents, uptake of inner electrolyte anions into the membrane is here the most favorite process. Consequently, an applied membrane potential ideally forces the extraction of electrolyte into the membrane, with each type of ion being extracted from opposing sides of the membrane. This process leads to current flow across the membrane and can be accurately modeled.

The work presented here should not be confused with earlier attempts by Nieman, who proposed to use traditional ion-selective membranes in a so-called bipolar pulse conductivity mode, without the apparent need for an external reference electrode.[30] Sandifer established convincingly that such claims cannot be supported.[31] Again, the membranes discussed here are not traditional ion-selective membranes in that they contain ideally no ion-exchanger sites.[32] The concentration of hydrophilic ions in the membrane bulk is therefore always assumed to be very small, and the applied pulse sequence is also different from that proposed by Nieman, who performed conductivity measurements rather than ion transfer voltammetry.

This paper attempts to answer the question whether a pulsed amperometric sensing mode offers distinct advantages over traditional potentiometry with plasticized PVC membranes containing ionophores. Special attention is devoted to the selectivity of these membrane sensors and whether the applied potential can be used as an additional experimental tool to enhance or tune the selectivity. Recent experiments have suggested that the selectivity can be tuned to some extend by the magnitude of the applied potential.[18] While well-founded theoretical treatments on the current−potential behavior of ionophore-assisted ion-transfer reactions have been described,[33,34] no theory has so far been developed to address the issue of selectivity of amperometric plasticized polymeric membrane sensors.

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## THEORY

The theory discussed here primarily aims at presenting the main response features of ionophore-based pulsed amperometric sensors in a simple way, to offer a rather qualitative, yet intuitive, description of the observed sensor behavior. A separate paper deals more rigorously with the diffusion kinetics in such membranes,[35] which is primarily used to optimize the working conditions of the voltage pulse sequence applied to these membranes.[21] Upon the application of a discrete potential pulse, ions are transferred from the sample and inner electrolyte solution into both sides of the ion-selective membrane. A theoretical treatment of this process involves therefore the analysis of two individual boundary potentials and the potential drop across the membrane bulk. This paper specifically takes into account the presence of an electrically neutral ionophore in the membrane which selectively mediates the extraction of one ion. As noted in previous work,[18,36−38] discrete potential pulses are applied to the membrane which are followed by stripping voltages to effectively renew the surface composition of the sensing membrane. It is therefore assumed that toward the end of each voltage pulse, where the current is sampled, the thickness of the diffusion layer in the membrane is always identical. This allows substantial simplifications of the theoretical treatment.

It is well established that the membrane potential $E_M$ may be subdivided into two phase boundary potentials and a membrane internal potential, the so-called $iR$ drop, according to the segmented potential model:

$$E_M = E_{PB} + E_{PB}' + iR_{bulk} \qquad (1)$$

where $E_{PB}$ and $E_{PB}'$ are the phase boundary potentials at the sample and inner electrolyte side, respectively, and $i$ and $R_{bulk}$ are the observed current and the bulk resistance of the membrane, respectively. The current $i$ is here limited by the diffusion of extracted ions from the organic-phase boundary to the bulk of the membrane phase, rather than diffusion within the aqueous-phase boundary layer. This is mainly due to the small diffusion coefficients in plasticized polymers and the relatively high sample concentrations. The current is therefore dependent on the phase-boundary concentrations of all extracted ions, the diffusion coefficients in the membrane $D$, the exposed membrane surface area $A$, and the Nernst diffusion layer thicknesses $\delta$ in the membrane phase.[22,33] Because of the lack of available experimental data, complexed and uncomplexed cations are here assumed to have equal membrane diffusion coefficients $D$(org). The expected current can now be described as follows:

$$i = AFD([I^+]-[I^+]_{pb} + [IL^+]-[IL^+]_{pb} + [J^+]-[J^+]_{pb} + [JL^+]-[JL^+]_{pb})/\delta \qquad (2)$$

where $[I^+]_{pb}$, $[IL^+]_{pb}$, $[J^+]_{pb}$, and $[JL^+]_{pb}$ are the concentrations of free and complexed primary ions $I^+$ and interfering ions $J^+$ at the phase boundary of the organic phase in contact with the sample. Concentrations without subscript are membrane bulk concentrations. Ion-selective membranes are here chosen where the concentrations of these ions in the membrane bulk are much smaller than the surface concentrations. In this case, eq 2 simplifies to

$$i = -AFD([I^+]_{pb} + [IL^+]_{pb} + [J^+]_{pb} + [JL^+]_{pb})/\delta \qquad (3)$$

This theoretical treatment does not provide information on the magnitude or time-dependent behavior of the Nernst diffusion thickness. However, having constant $\delta$ values for varying potentials is likely justified here since the current is sampled after a fixed time interval toward the end of each uptake potential pulse, after which an appropriately long stripping period is applied. For every cation extracted at the sample side, an anion must be simultaneously extracted at the inner electrolyte−membrane side (denoted with a prime) to satisfy electroneutrality. As described earlier,[22] a membrane containing a salt of highly lipophilic cations and anions cannot expel membrane cations into the inner contacting solution, which would otherwise also satisfy electroneutrality. Since the extracted anion $A^-$ is assumed to remain uncomplexed by the ionophore, this charge balance requirement can be written as

$$[A^-]_{pb}' = [I^+]_{pb} + [IL^+]_{pb} + [J^+]_{pb} + [JL^+]_{pb} \qquad (4)$$

Alternatively, therefore, the current may equally be described by the flux of extracted anions at the inner membrane side:

$$i = -AFD[A^-]_{pb}'/\delta \qquad (5)$$

Again, eq 5 assumes that the membrane bulk concentration of $A^-$ is essentially zero at all times. The boundary potential at the sample−membrane interface is known to be a direct function of the activity of any ion $I^+$ in both boundary regions, written here for monovalent cations:

$$E_{PB} = \frac{RT}{F}\ln\frac{k_I a_I(\mathrm{aq})}{\gamma_I[I^+]_{pb}} = s\log\frac{k_I a_I(\mathrm{aq})}{\gamma_I[I^+]_{pb}} \qquad (6)$$

where $a_I$ and $[I^+]_{pb}$ are the activity and concentration of uncomplexed $I^+$ in the aqueous- and organic-phase boundary, respectively, $\gamma_I$ is the activity coefficient of $I^+$ in the organic phase, $k_I$ is a direct function of the standard chemical potential difference of $I^+$ in both phases, and $R$, $T$, and $F$ are the gas constant, the absolute temperature, and the Faraday constant. An applied potential forces the extraction of ions from the sample into the membrane to satisfy eq 6. An analogous equation is formulated for any interfering ion $J^+$:

$$E_{PB} = s\log\frac{k_J a_J(\mathrm{aq})}{\gamma_J[J^+]_{pb}} \qquad (7)$$

In the following, activity coefficients in the membrane phase are assumed to be constant and included in the respective $k_I$ values.

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The boundary potential at the second interface is obtained by inserting eq 4 into the appropriate phase boundary potential equation, here formulated for monovalent anions:

$$E_{\mathrm{PB}}' = \frac{RT}{F}\ln\frac{k_{\mathrm{A}}a_{\mathrm{A}}(\mathrm{aq})'}{[\mathrm{A}^-]_{\mathrm{pb}}'} = s\log\frac{k_{\mathrm{A}}a_{\mathrm{A}}(\mathrm{aq})'}{[\mathrm{I}^+]_{\mathrm{pb}} + [\mathrm{IL}^+]_{\mathrm{pb}} + [\mathrm{J}^+]_{\mathrm{pb}} + [\mathrm{JL}^+]_{\mathrm{pb}}} \quad (8)$$

For membranes containing a lipophilic ionophore, the complex formation constant $\beta_{\mathrm{IL}}$ for the complexation of primary ions is introduced as

$$\beta_{\mathrm{IL}} = [\mathrm{IL}^+]/[\mathrm{I}^+][\mathrm{L}] \quad (9)$$

and, in complete analogy, for the complexation of interfering ions

$$\beta_{\mathrm{JL}} = [\mathrm{JL}^+]/[\mathrm{J}^+][\mathrm{L}] \quad (10)$$

For simplicity, only 1:1 complexes are here assumed between ionophore and cation. At the phase boundary, the total ionophore concentration, $L_{\mathrm{T}}$, relates to the free concentration of ionophore, [L], and the concentration of the complexes with the following mass balance:

$$L_{\mathrm{T}} = [\mathrm{L}]_{\mathrm{pb}} + [\mathrm{IL}^+]_{\mathrm{pb}} + [\mathrm{JL}^+]_{\mathrm{pb}} \quad (11)$$

This relationship is strictly only exact at currents well below the limiting current. At currents approaching the limiting current where ionophore is depleted by the complexation process with extracted cations, diffusion of ionophore from the membrane interior to the surface and diffusion/migration of complexed ionophore from the surface to the bulk may change the total concentration of ionophore at the surface relative to the membrane bulk. Migration is here minimized by the use of a high concentration of lipophilic salt in the membrane, which significantly exceeds the concentration of ionophore. If complexed and uncomplexed ionophore diffuse at the same rate, no change in $L_{\mathrm{T}}$ is expected from its bulk value. Since no experimental data on the diffusion coefficients of free and complexed ionophore are available at this stage, equal diffusion coefficients are assumed, for which case the model must be adequate. For other cases, a kinetically more exact approach must be applied to model this region. After assuming appropriate values for $k_{\mathrm{I}}$, $k_{\mathrm{J}}$, $\beta_{\mathrm{IL}}$, $\beta_{\mathrm{JL}}$, $L_{\mathrm{T}}$, $a_{\mathrm{I}}(\mathrm{aq})$, and $a_{\mathrm{J}}(\mathrm{aq})$, the five unknowns $[\mathrm{I}^+]_{\mathrm{pb}}$, $[\mathrm{IL}^+]_{\mathrm{pb}}$, $[\mathrm{J}^+]_{\mathrm{pb}}$, $[\mathrm{IL}^+]_{\mathrm{pb}}$, and $[\mathrm{L}]_{\mathrm{pb}}$ in the five eqs 3 and 8−11 may be solved as a function of varying extracted anion concentrations at the inner side, $[\mathrm{A}^-]_{\mathrm{pb}}$. For the same $[\mathrm{A}^-]_{\mathrm{pb}}$, eq 5, and assumed values for $A$, $F$, $D$, and $\delta$, the current $i$ can be calculated. Equations 6 and 8 can then be solved to obtain the values for both phase-boundary potentials. These values are inserted into eq 1, together with the assumed bulk membrane resistance, $R$, to give the membrane potential $E_{\mathrm{M}}$ as a function of the current $i$:

$$E_{\mathrm{M}} = iR_{\mathrm{bulk}} + s\log\frac{-k_{\mathrm{A}}a_{\mathrm{A}}'}{i\delta/AFD} + s\log\left\{-2k_{\mathrm{I}}a_{\mathrm{I}}\left(a_{\mathrm{I}} + \frac{k_{\mathrm{J}}}{k_{\mathrm{I}}}a_{\mathrm{J}}\right)\left(\beta_{\mathrm{IL}}a_{\mathrm{I}} + \frac{k_{\mathrm{J}}}{k_{\mathrm{I}}}\beta_{\mathrm{JL}}a_{\mathrm{J}}\right)\Big/\left(a_{\mathrm{I}}^2(\beta_{\mathrm{IL}}(i\delta/AFD + L_{\mathrm{T}}) + 1) + \frac{k_{\mathrm{J}}}{k_{\mathrm{I}}}a_{\mathrm{I}}a_{\mathrm{J}}(1 + \beta_{\mathrm{JL}}(L_{\mathrm{T}} + i\delta/AFD)) - \sqrt{a_{\mathrm{I}}^2\chi}\right)\right\}$$

$$\text{with}\quad \chi = -4\left(a_{\mathrm{I}} + \frac{k_{\mathrm{J}}}{k_{\mathrm{I}}}a_{\mathrm{J}}\right)\left(\beta_{\mathrm{IL}}a_{\mathrm{I}} + \frac{k_{\mathrm{J}}}{k_{\mathrm{I}}}\beta_{\mathrm{JL}}a_{\mathrm{J}}\right)i\delta/AFD + \left\{a_{\mathrm{I}}(1 + \beta_{\mathrm{IL}}(L_{\mathrm{T}} + i\delta/AFD)) + \frac{k_{\mathrm{J}}}{k_{\mathrm{I}}}a_{\mathrm{J}}(1 + \beta_{\mathrm{JL}}(L_{\mathrm{T}} + i\delta/AFD))\right\}^2 \quad (12)$$

The phase labels in eq 12 are omitted. This equation is drastically simplified for a number of cases. If the ion extraction process is not mediated by any ionophore, for example, with currents well above the limiting current, the mixed ion response is obtained by simplifying eq 12 to obtain

$$E_{\mathrm{M}} = iR_{\mathrm{bulk}} + s\log\frac{k_{\mathrm{I}}k_{\mathrm{A}}a_{\mathrm{A}}'}{(i\delta/AFD)^2} + s\log\left(a_{\mathrm{I}} + \frac{k_{\mathrm{J}}}{k_{\mathrm{I}}}a_{\mathrm{J}}\right) \quad (13)$$

Evidently, the last logarithmic term is formulated in complete analogy to the Nicolskii equation for potentiometric ion sensors.[39] The selectivity is dictated by the relative lipophilicity of the sample ions ($k_{\mathrm{J}}/k_{\mathrm{I}}$). For a given current, the membrane potential depends on the sample activity according to the Nernst equation if no interference is observed.

If instead the concentration of uncomplexed ions can always be neglected relative to that of complexed ions, as with currents below the limiting current where ionophore saturation occurs, eq 12 reduces to

$$E_{\mathrm{M}} = iR_{\mathrm{bulk}} + s\log k_{\mathrm{I}}k_{\mathrm{A}}\beta_{\mathrm{IL}}a_{\mathrm{A}}' + s\log\frac{L_{\mathrm{T}} + i\delta/AFD}{(i\delta/AFD)^2} + s\log\left(a_{\mathrm{I}} + \frac{\beta_{\mathrm{JL}}k_{\mathrm{J}}}{\beta_{\mathrm{IL}}k_{\mathrm{I}}}a_{\mathrm{J}}\right) \quad (14)$$

As in potentiometry,[39] the selectivity now depends on the ratio of the complex formation constants, as well as the relative lipophilicities of the ions. In addition, changes in the complex formation constant and single ion lipophilicities also have a profound effect on the overall membrane potential. Unlike in potentiometry, the absolute value of the formation constant of the ion−ionophore complex, the single-ion lipophilicities and the membrane composition influence the membrane potential. In this respect, voltammetric ion-selective electrodes reveal a great deal of information about the binding properties of ionophores in the membrane, which in potentiometry can only be achieved with dedicated experiments.[40]

## EXPERIMENTAL SECTION

**Reagents.** The salts, acids, and membrane components tetradodecylammonium tetrakis(4-chlorophenyl)borate ($\mathrm{TDDA}^+$

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TpClPB$^-$) and sodium tetrakis[3,4-bis(trifluoromethyl)phenyl]-borate (NaTFPB), the lithium ionophore ETH 1810 ($Li^+$-ionophore III), *o*-nitrophenyl octyl ether (NPOE), high molecular weight poly-(vinyl chloride) (PVC), and tetrahydrofuran were purchased in the highest quality available from Fluka Chemika-Biochemika (Ronkonkoma, NY). The ionophore *tert*-butyl calix[4]arene tetramethyl ester was obtained from Professor S. Harris (Dublin, Ireland). Aqueous solutions were prepared by dissolving the appropriate salts in Nanopure-purified distilled water.

**Membrane Preparation.** Ion-selective electrode membranes (~200 $\mu$m thick) were solvent cast in complete analogy to preparations of traditional ion-selective electrode membranes by dissolving PVC and NPOE (1:2 by weight), 10 wt % of the inert salt TDDA$^+$TpClPB$^-$, and 10 mmol/kg of the ionophore in 1.5 mL of tetrahydrofuran, pouring the solution into a glass ring fixed onto a microscope glass slide, and evaporating the solvent overnight.[41] Membranes for potentiometry contained 10 mmol/kg sodium ionophore and either 5.0 or 15 mmol/kg NaTFPB as lipophilic anionic sites.

**Experimental Setup.** The ion-selective electrode membrane, a 6-mm-diameter disk, was cut with a cork borer from the parent membrane and incorporated into a Philips electrode body (IS-561, Glasbläserei Möller, Zurich, Switzerland). The inner electrolyte for the ion-selective electrode consisted of 0.1 M NaCl or 0.1 M KCl (for sodium electrodes) and 0.1 M KCl (for lithium electrodes) and was contacted by an internal Ag/AgCl electrode. The electrodes were conditioned in a solution identical to the inner filling solution overnight before measurement. All membrane electrode potential measurements were performed at laboratory ambient temperature (21.5 ± 0.5 °C) vs a double-junction Teflon sleeve Ag/AgCl reference electrode (Ingold, Wilmington, MA). The ion-selective electrode served as the working electrode and a high surface area Ag/AgCl electrode (WPI, Sarasota, Florida) as the counter electrode in a galvanic cell of the type

Ag, AgCl | NaCl || membrane || sample |
1 M LiOAc | KCl | AgCl, Ag

The pulsed amperometric measurements were performed with a AFRDE5 Pine potentiostat (Pine Instruments, Grove City, PA) controlled by LabView 3.1 software (National Instruments, Austin, TX) on a Macintosh computer equipped with a 12-bit data acquisition board (PCI-1200, National Instruments). A low-pass filter was used to reduce high-frequency noise. The current was stepped between at least two selected potentials, and the data were acquired at 10 Hz to keep the data volume low. Sampled currents were obtained as the last reading of each uptake pulse. Titrations were performed by adding aliquots from a 1 M stock solution to unstirred pure water samples.

Zero-current electrode potential measurements were performed at laboratory ambient temperature in unstirred salt solutions versus a Ag/AgCl reference electrode with a 1 M LiOAc bridge electrolyte, as described.[41]

## RESULTS AND DISCUSSION

The theory developed above describes the basic current response characteristics of ion-selective solvent polymeric membranes doped with an ionophore upon the application of a discrete voltage pulse. It mimics the actual experiment where ions extracted during any previously applied voltage pulse are forced to partition again into the contacting aqueous solutions, thereby avoiding memory effects and ensuring that the effective diffusion layer thicknesses in the membrane remain invariant at various applied potentials. Without any applied potential, the concentration $[IL^+]_{pb}$ in the membrane-phase boundary region must be small. Values are chosen that mimic PVC−NPOE membranes containing the calix[4]arene ionophore as closely as possible ($k_Ik_A = 10^{-14.5}$, $a_I = a_A = 0.07$ M, $\beta_{IL} = 10^{10.3}$, and $L_T = 0.01$ M). While the coextraction constant ($k_Ik_A$) was estimated from the upper detection limit of a valinomycin electrode in PVC−NPOE,[42] the apparent stability constant was determined experimentally for the tetraethyl ester derivative of this ionophore in PVC−NPOE,[43] by taking into account that the ionophore here forms complexes that are 25 times weaker than valinomycin[43] and that sodium is ~40 times less lipophilic than potassium with PVC−NPOE.[44] With this system, therefore, 0.5% of the ionophore is predicted to be spontaneously present in its complexed form because of coextraction of $I^+$ and $A^-$ from the sample. This leaves ~99% of the ionophore free for potential-mediated extraction, which appears to be adequate. This simple calculation may be used to discuss some important features of voltammetric PVC-based ion sensors. First, ionophores that induce spontaneous electrolyte coextraction (Donnan failure) in traditional ion-selective electrodes are also not suited for voltammetric ion-selective electrodes since it renders the membrane−sample interface nonpolarizable. In practice, such a situation would show an essentially featureless ohmic response region, as with potentiometric membrane electrodes that are doped with an ion exchanger.[22] Second, the mechanism of assisted ion transfer discussed here is mainly applicable in the current range where the ions extracted by the applied potential significantly exceed the concentration of ions that are spontaneously extracted by coextraction from the sample.

Figure 1 shows calculated current responses of a membrane containing an $I^+$-selective ionophore in 0.100 M sample solutions of $I^+$ and $J^+$, respectively, calculated according to eq 12. The interference $J^+$ is assumed to bind more weakly to the ionophore ($\beta_{JL} = 10^{-4}\,\beta_{IL}$), but to be more lipophilic than $I^+$ ($k_J = 10^2\,k_I$). Other chosen parameters are a complex formation constant $\log\beta_{IL} = 10.3$ (again as determined experimentally), $R_{bulk} = 10^4\ \Omega$, and $AFD_I(\text{org})/\delta = 3 \times 10^{-3}$ A M$^{-1}$, and, as above, $L_T = 0.01$ M, $\log\beta_{IL} = 10.3$, and $k_Ik_A = 10^{-14.5}$. At negative applied potentials, sample cations and inner electrolyte anions are transferred into the organic phase, while at positive potentials, sample anions and inner electrolyte cations are extracted (latter curves not shown). It is known experimentally from Kihara that such membranes show approximately double potential windows relative to experiments on membranes with a classical nonpolarizable internal interface.[24−26] According to Figure 1, the ionophore-mediated extraction starts to occur at moderately negative potentials. The observed current appears to reach a saturation plateau around −600 mV, with predicted currents around $-3 \times 10^{-5}$ A. At more extreme applied potentials, the magnitude of the current again increases. In this

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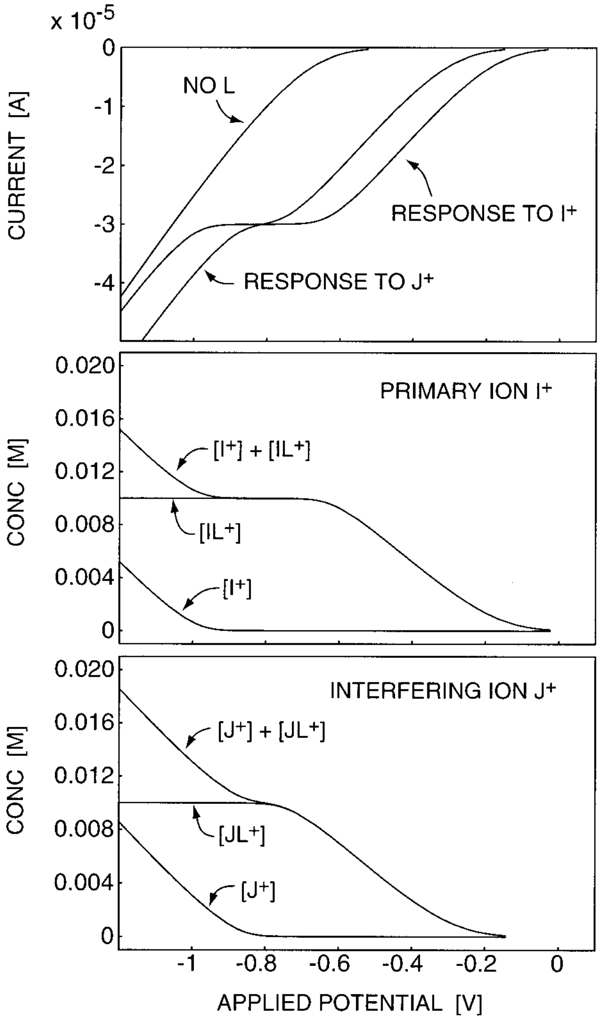

Figure 1. Theoretical separate solution normal-pulse voltammetric current responses for an ion-selective membrane containing a neutral ionophore, calculated from eq 12. The two lines in the upper plot are the current responses for a sample containing either the analyte ion or a lipophilic interfering agent that complexes the ionophore more weakly. Line labeled with “no L”: expected current response for $I^+$ without any ionophore in the membrane. The lower plots show the corresponding phase-boundary concentrations of complexed and uncomplexed ions at the sample side for both situations, calculated from eqs 3 and 11.

potential region, the magnitude of the applied phase-boundary potential is sufficiently large so that the concentration of extracted $I^+$ in the membrane starts to exceed the available concentration of ionophore (see bottom curves in Figure 1). The membrane therefore begins here to behave as an ionophore-free membrane.[22] This behavior should have significant implications for the selectivity characteristics of the membrane. Indeed, the curve in Figure 1 for the current response toward a more lipophilic interference $J^+$ shows that the selectivity of the membrane is dependent on the magnitude of the applied potential. At positive applied voltages, the responses toward both solutions are identical since both samples contain the same anion, which governs the current response of the membrane under those conditions (curves not shown). At negative potentials, the response toward $J^+$ is initially suppressed relative to $I^+$, owing to the high binding selectivity of the ionophore. As the current response to $I^+$ begins to saturate around −600 mV, the response to $J^+$ in the same region is continuously increasing since, in a separate solution experiment, a sufficient concentration of ionophore is still available to mediate the extraction of this interference. At more extreme potentials, the current response to $J^+$ starts to become larger than the one to $I^+$ after reaching a very small saturation region around −800 mV as well. From here on, the sensor is essentially selective for $J^+$ since this cation is more lipophilic than $I^+$. According to theory, therefore, the magnitude of the applied potential indeed dictates the sensor selectivity to a large extent. Smaller applied voltages give smaller current responses but take better advantage of the embedded ionophore for sensing selectivity. Figure 2 shows mixed ion response curves that were also calculated according to eq 12. The upper plot models the response to varying concentrations of sodium (here equal to $I^+$ in the theory) in a potassium ion background (equal to $J^+$), while the lower plot shows the expected response to varying potassium concentrations in a sodium ion background solution. Indeed, it is expected that the sensor will show orthogonal selectivity depending on whether the membrane is held at electrochemical conditions where the ionophore mediates the ion extraction process.

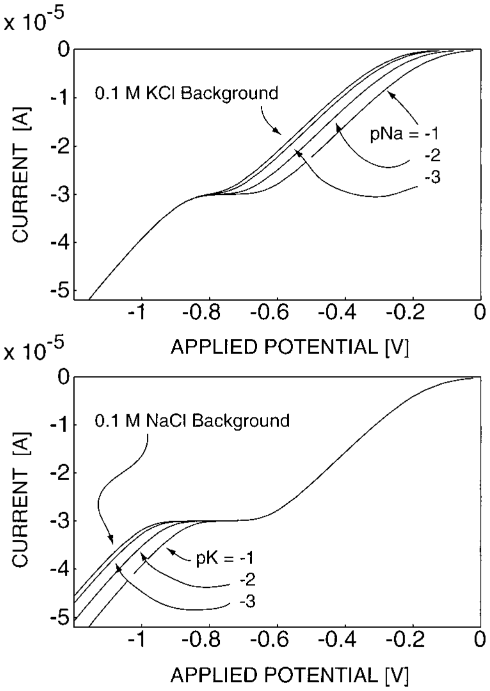

Figure 2. Theoretical mixed solution normal-pulse voltammetric current response for the same system shown in Figure 1, but with the indicated ion concentrations in a constant background of a competing electrolyte.

The theory was confirmed with a PVC−NPOE membrane containing the sodium ionophore *tert*-butyl calix[4]arene tetramethyl ester. Figure 3 shows the observed current response of a typical normal-pulse voltammetric experiment with this membrane. Individual voltage pulses were incrementally decreased from 0.0 to −1.0 V. Between each 1-s uptake pulse, a 10-s baseline potential at 0.0 V was applied to ensure an effective stripping of the ions from the membrane between each uptake pulse. The figure shows that the observed current toward the end of each stripping pulse decreases to near-zero values, as required to ensure effective membrane renewal. For data analysis, only the last data point of each uptake pulse is sampled (shown here as filled circles). It is

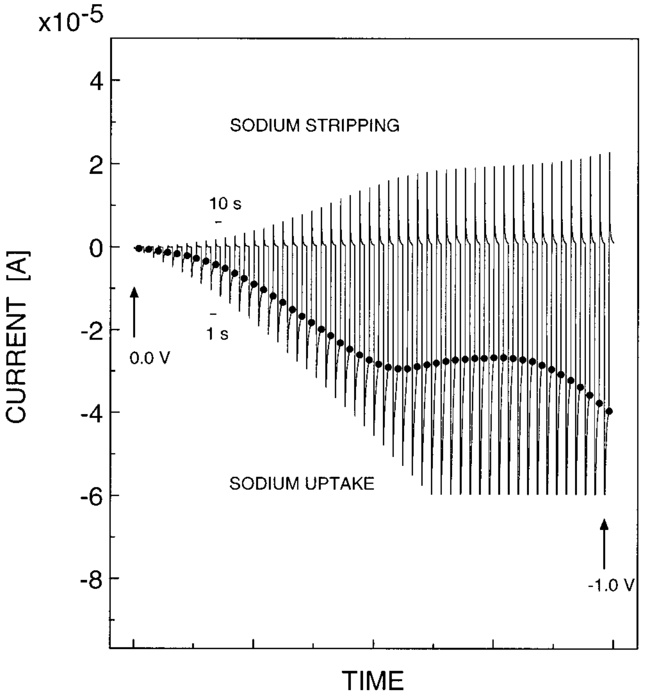

Figure 3. Experimental normal-pulse voltammetric current response for a membrane containing the sodium-selective calix[4]arene ionophore. The applied potential is pulsed from 0 to −1.0 V, in 25-mV increments. Between every 1-s uptake pulse, a 10-s stripping pulse at 0 V is applied. For visibility reasons, stripping current data are condensed by a factor of 10. The current is sampled at the end of each uptake pulse (shown as filled circles) to give quantitative pulsed amperometric response data.

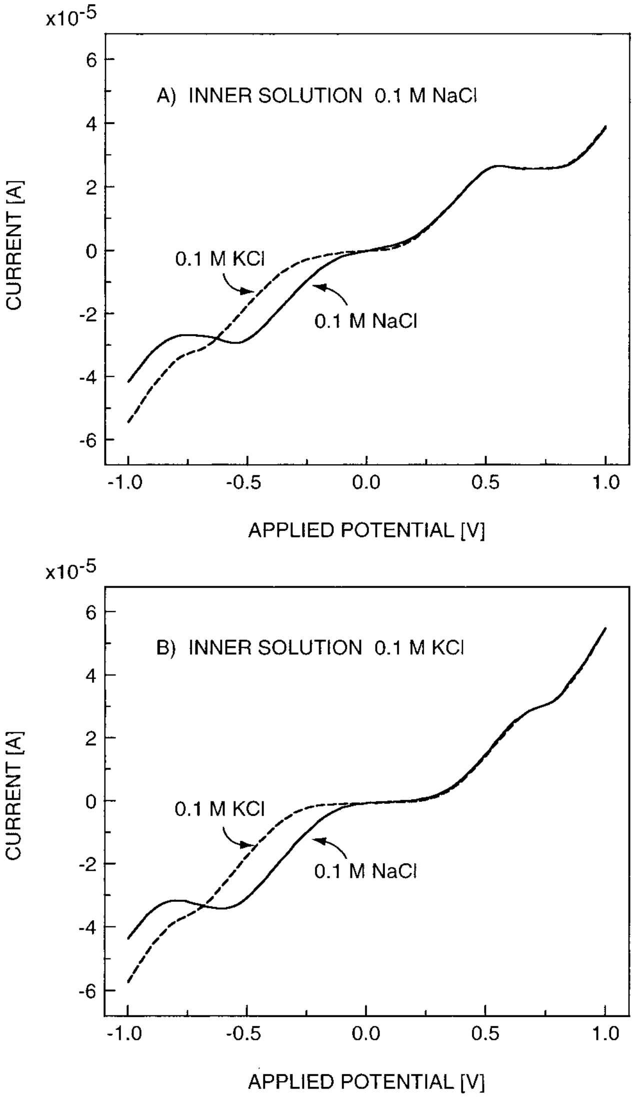

Figure 4. Observed normal-pulse voltammetric response for a calix[4]arene ionophore-containing membrane and either 0.1 M NaCl or 0.1 M KCl in the sample and (A) 0.1 M NaCl and (B) 0.1 M KCl in the inner electrolyte solution. The current data are sampled as shown in Figure 3.

evident that the current response within one voltage pulse decreases, which is mainly due to the steadily increasing diffusion layer thickness in the membrane.[38] Current readings, as the filled circles shown in Figure 3, are therefore acquired under computer control at fixed intervals to yield reliable values for a practical application of such sensors.

Panels A and B of Figure 4 show the sampled uptake current response for 0.100 M NaCl and 0.100 M KCl sample solutions, respectively. As predicted by theory (see above), the resulting current at positive applied potentials is identical for both sample solutions since the same sample anion is extracted into the membrane in both situations. In Figure 4A, the current response reaches an intermediate saturation plateau around $3 \times 10^{-5}$ A. The chloride ions extracted from the sample are not expected to bind the sodium-selective ionophore, but the inner electrolyte for Figure 4A contains sodium ions. For every chloride anion extracted at the sample side, a sodium ion is extracted at the inner electrolyte side to maintain membrane electroneutrality. Consequently, the extraction of chloride is mediated by the presence of sodium at the inner side. As all ionophore molecules become saturated with sodium at the inner side, which occurs at around +500 mV, the extraction of chloride can no longer be mediated and the current remains approximately constant in this region. The limiting current region is not perfectly flat as predicted by theory, which may be due to incomplete stripping of previously extracted ions from the membrane. This would diminish the concentration of available free ionophore in the polymer and lead to a smaller current than expected by the idealized theory. If the inner electrolyte composition is altered to 0.1 M KCl, the chloride response occurs at more positive potentials and a smaller saturation plateau is observed (Figure 4B). Potassium ions bind more weakly with the ionophore but possess a higher intrinsic lipophilicity relative to sodium. This has important implications for the design of pulsed amperometric ionophore-based membrane electrodes with two polarizable interfaces. A maximum potential window is observed with an inner electrolyte that is difficult to extract into the membrane (KCl in this case). This is contrary to common ion-selective electrode practice, where a relatively large concentration of the analyte ion is often present to ensure a well-defined inner phase boundary potential.[42]

For the measurement of the two different NaCl and KCl samples shown in Figure 4A, the current responses are only different for negative applied potentials and again follow theoretical predictions (see Figure 1). As observed from the normal-pulse voltammetric data shown in Figure 4A, the selectivity of the membrane is initially high for sodium ions. This is expected, given that this calix[4]arene ionophore embedded in potentiometric sensing membranes induces a high preference of sodium over potassium by ~3 orders of magnitude.[45] When the membrane is pulsed to more negative potentials, the selectivity pattern reverses and the membrane starts to prefer $K^+$ over $Na^+$. Similar experimental effects were observed earlier by Sawada et al. with lithium-selective membrane electrodes, where lithium selectivity decreased with increasing applied potentials.[18] According to theory, this preference must be due to the higher lipophilicity of potassium over sodium ions. In ionophore-free potentiometric sensing membranes based on PVC−NPOE, potassium is indeed preferred over sodium by nearly 2 orders of magnitude.[44] In potentiometric sensors, the selectivity of one given sensor cannot be altered by instrumental means. Similar selectivity changes can, however, be accomplished with a number of individual membranes that contain a given ionophore by altering the concentration of embedded lipophilic ionic sites.[46,47] These sites normally dictate, through the electroneutrality requirement, the concentration of total extracted sample ions in the membrane. The concentration of these added sites has an important selectivity modifying effect that can be used to optimize the selectivity of potentiometric membrane electrodes.[46] For monovalent analyte cations, the site concentration must ordinarily be smaller than 100% of the ionophore concentration and defines the concentration ratio of uncomplexed to complexed ionophore in the membrane. If the site concentration significantly exceeds the ionophore concentration, a selectivity pattern similar to that of an ionophore-free membrane is observed, which is normally not desired. This was here validated experimentally for the present system with potentiometric experiments on analogous membranes containing the same concentration of ionophore, but with 5.0 and 15 mmol $kg^{-1}$ lipophilic anionic sites (sodium tetrakis[3,4-bis(trifluoromethyl)phenyl]borate) instead of the inert lipophilic salt ETH 500. Indeed, 0.15 M NaCl solutions showed 153 mV higher potential values for the membrane containing 5 mmol $kg^{-1}$ anionic sites (50 mol % relative to the ionophore concentration) relative to a KCl sample of the same concentration. This is consistent with the horizontal potential shift observed in Figure 4 in the current range of −10 to −20 $\mu$A and indicates that the sensor selectivity is dictated by the ionophore. Instead, the second potentiometric membrane with excess ionic sites relative to ionophore preferred potassium over sodium by 101 mV, showing that the ionophore no longer contributes to the sensor selectivity. This is in agreement with the horizontal potential shift observed in Figure 4 at −40 $\mu$A. Clearly, with amperometric sensors, it is the magnitude and direction of the observed current that assumes the selectivity modifying role of the ionic sites in potentiometric ion-selective electrodes. If ion diffusion in the membrane phase is rate limiting, and the free and complexed ions have similar diffusion coefficients in the membrane phase, the current is directly proportional to the total concentration of extracted ions at the organic phase boundary (see eq 2). Therefore, a single voltammetric sensor interrogated with a suitable pulse sequence can accomplish variations in selectivity that would, with potentiometric sensors, require an array of sensors, each with a different content of anionic or cationic sites. Potentials (and therefore currents) of opposite sign lead to the uptake of sample counterions, akin to the incorporation of ion-exchanger sites of opposite charge sign with potentiometric membranes. This versatility seems to be a striking advantage of voltammetric over potentiometric ionophore-based sensors.

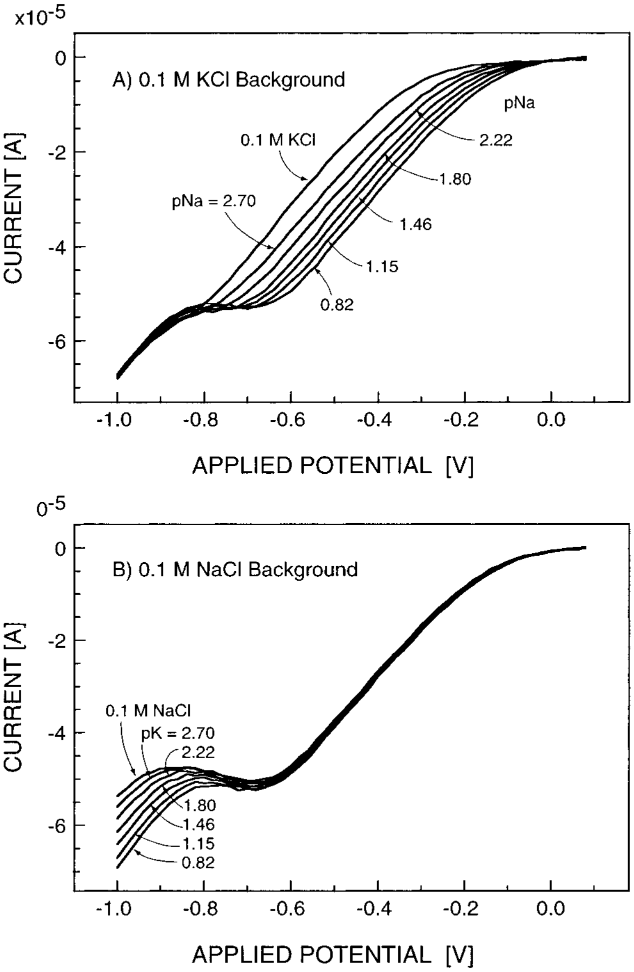

**Figure 5.** Observed normal-pulse voltammetric response in mixed sample solutions, demonstrating orthogonal selectivity at different potentials. (A) Varying NaCl concentrations in a 0.1 M KCl background and (B) varying KCl concentrations in a 0.1 M NaCl background. The logarithmic concentrations are indicated on the plot. The membrane electrode composition is as in Figure 4B.

The selectivity modifying effect of the applied membrane potential was further validated with mixed solution experiments. Figure 5 shows normal-pulse voltammetric responses of the calix[4]arene ionophore-containing membrane with a 0.1 M KCl inner electrolyte and 500-ms uptake and 10-s stripping times. Shorter uptake times lead to higher uptake current readings (see traces in Figure 3). In Figure 5A, NaCl concentrations were varied from $2 \times 10^{-3}$ to 0.15 M in a 0.1 M KCl background. As expected for a selective sensor, the response is directly dependent on the NaCl concentration at potentials less negative than −600 mV, at values before limiting current is observed. In the potential region where theory predicts extraction of uncomplexed cations (see Figure 2), variations in NaCl have no apparent effect on sensor response.

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Figure 5B shows the complementary experiment with variable KCl concentrations in a 0.1 M NaCl background. Variations in current are only observed beyond the limiting current region, around −1000 mV. The current is indifferent in the range where the previous experiment indicated strong NaCl selectivity. In contrast to most other voltammetric sensing systems, including metal electrodes, the magnitude of the potassium response appears to be independent of the presence of sodium in the sample (see also Figure 2). This indicates that potassium and sodium ions both have similar diffusion coefficients in the membrane phase and that the ionophore-mediated extraction region is competitive; i.e., if no sodium is present, potassium will extract until the ionophore is saturated (see Figure 4). This leads to a very similar background current for the potassium-selective response region. These experiments provide strong evidence of the analytical utility of voltammetric ion sensors based on plasticized polymer membranes.

Figure 6A illustrates the sensing selectivity for a membrane containing the sodium-selective ionophore determined in 0.1 M separate ion solutions of lithium, sodium, potassium, magnesium, and calcium chloride. All interferences are significantly rejected at potentials between 0 and −600 mV. This is again in agreement with the observed potentiometric selectivity of membranes containing the same sodium ionophore.[45] Magnesium and calcium appear to bind very weakly with the ionophore, and a very small observed limiting current region at less than $-1$ μA is likely associated with NaCl sample impurities. Lithium, on the other hand, is significantly stabilized by this ionophore, although the high hydrophilicity of this ion make it no serious interference here. Figure 6B demonstrates the response and selectivity behavior of a membrane containing an identical concentration of the lithium ionophore ETH 1810, which was previously characterized in ITIES by Shao et al.[48] A lithium-selective response is observed at moderately negative potentials. The relatively wide potential range with near-zero current response indicates that lithium does not form extremely strong complexes with this ionophore. A recent potentiometric study has suggested that the overall formation constant for the 1:2 complex of this ionophore with lithium is $\sim 6 \times 10^8$, which would ideally predict a ~420 mV positive potential shift owing to the presence of the ionophore in the membrane. While this estimate can only serve as a rough indication only, it is quite consistent with the lithium response curve at negative potentials shown in Figure 6B. The observed limiting current is about half as large as that observed for the sodium-selective membrane in Figure 6A. Since the ionophore is known to form 1:2 complexes with lithium, ionophore saturation will occur after extracting half the ions relative to membranes containing the calix[4]arene ionophore, which forms 1:1 complexes. Therefore, the limiting current has to be smaller here as well. Since KCl served as the inner electrolyte of the membrane electrode, and this ionophore apparently complexes potassium very weakly, no limiting current region is apparent for the anion uptake range at positive potentials.

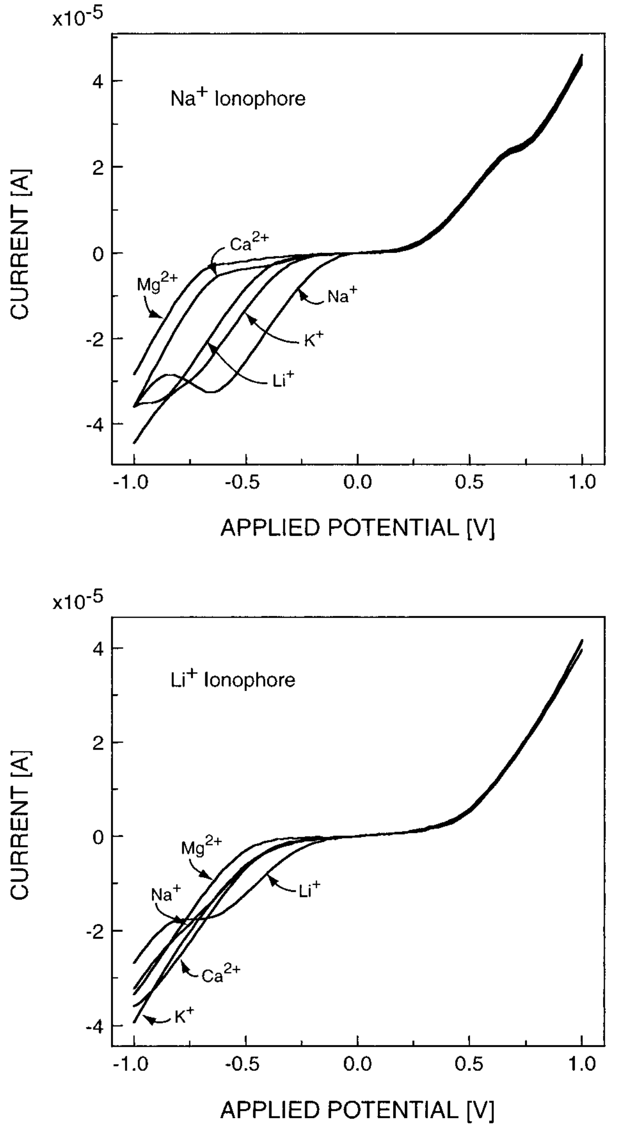

**Figure 6.** Separate solution normal-pulse voltammetric response curves for membranes containing (A) the sodium-selective ionophore *tert*-butyl calix[4]arene tetramethyl ester and (B) the lithium-selective ionophore ETH 1810, with 1-s uptake pulses and 10-s stripping pulses at 0 V. The inner electrolyte was 0.1 M KCl in both cases. Ion solutions contain 0.1 M of the chloride salt of the indicated ion.

In practice, recording an entire normal-pulse voltammetric scan may be prohibitively time-consuming. Dedicated single-pulse or multipulse sequences should be used for single or multianalyte detection purposes. This concept was tested by using the sodium-selective calix[4]arene-containing membrane with a 0.1 M NaCl inner electrolyte in an amperometric multipulse sequence, to take advantage of the selectivity tuning capability for continuous ion detection. Uptake pulses of −0.25, −0.40, and −1.00 V that lead to variable selectivity of the sensor were alternately applied in the sequence, each followed by a 10-s stripping pulse at 0 V. Figure 7 shows the continuously sampled current responses of the membrane to varying concentrations of potassium and sodium in the sample, obtained by using this multipulse method. The current responses for each discrete uptake potential are displayed in a dedicated titration plot, although the data shown in all three plots for a particular electrolyte were recorded simultaneously in the same titration experiment. One membrane controlled with an appropriate pulse sequence can therefore be used for the continu-

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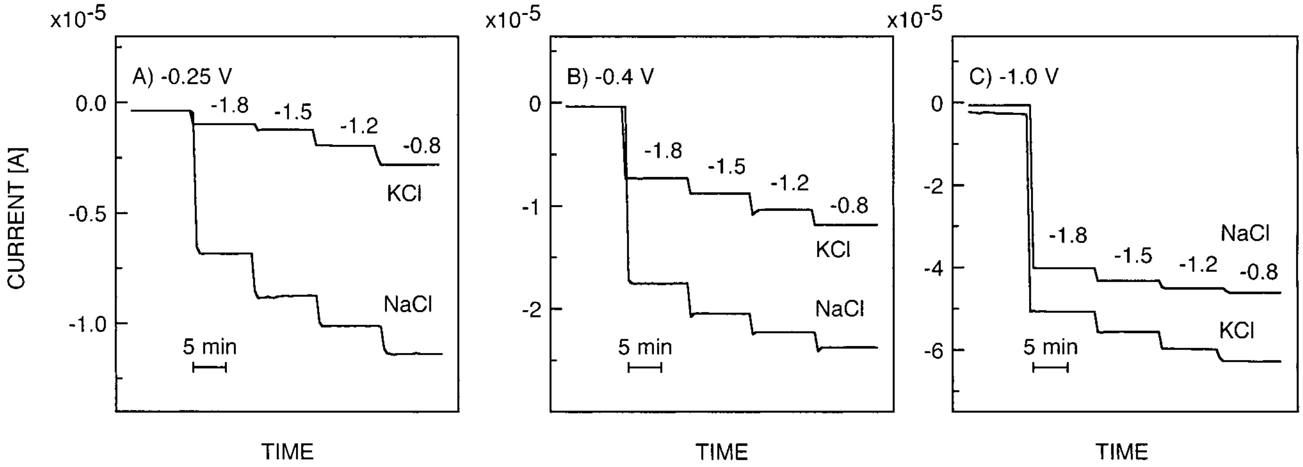

Figure 7. Pulsed amperometric response to varying sodium and potassium concentrations using a multipulse sequence, with the magnitude of the three different uptake potentials shown in the three plots. Between each 1-s uptake pulse, a 10-s stripping pulse at 0 V is applied. The membrane electrode is otherwise identical to the one shown in Figure 4B. The sample concentrations are given as logarithmic molar activities above the traces. All three plots were obtained simultaneously, and each corresponds to the indicated potential within the pulse sequence. The reversal in selectivity observed near-instantaneously with the same membrane shows that continuous multianalyte detection is possible.

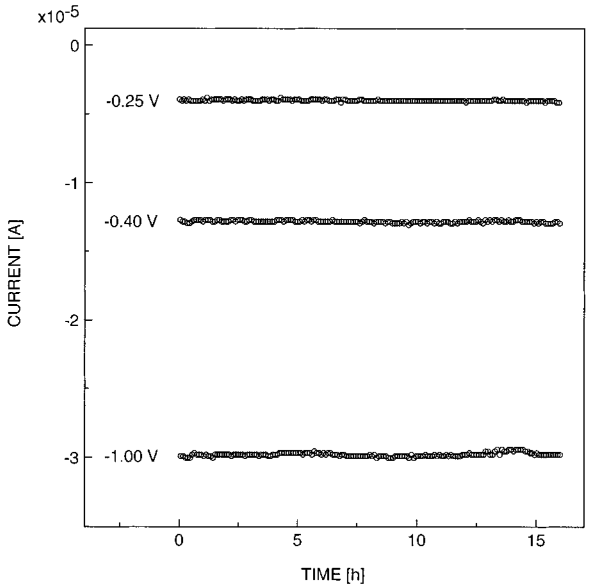

Figure 8. Continuous-pulsing experiment of a membrane electrode containing the sodium ionophore in contact with a 0.1 M NaCl sample over the course of 15 h. The membrane composition is identical to the one shown in Figure 4B. The same multipulse sequence as described in Figure 7 is used, with 100-s stripping times.

ous amperometric detection of more than one analyte. This concept could in principle be readily extended to the detection of anions by including positive uptake pulses in the potential sequence (see Figure 4).[22]

The feasibility of using the multipulse sequence as a stable continuous measuring mode was evaluated by choosing 100-s stripping times with otherwise the same multipulse sequence, with repetitive uptake pulses of −0.25, −0.40, and −1.0 V as discussed above. The 15-h-long continuous-pulsing experiment in contact with a 0.1 M NaCl sample is shown in Figure 8. The magnitude of the three different uptake currents remains stable over the entire time, with no apparent drift. An analogous experiment with short stripping times of just 10 s showed stable behavior for about 3−5 h.

The lower detection limits were not optimized with the membranes presented here. At very low sample concentrations, the diffusion of extracted ions within the organic membrane phase will likely be no longer rate limiting. In this case, depletion at the sample side will be encountered, and the sensor will function more akin to classical liquid−liquid extraction systems or reversible voltammetric metal electrodes. On the other hand, the same exact effect may turn out to be very beneficial in discriminating highly preferred, yet dilute interferences, where the current limited by mass transport in the aqueous phase is not sufficient to alter the response of the more concentrated analyte ion. The mechanism studied here, where the signal is entirely dependent on diffusion processes in the polymeric phase, may also prove to be valuable in view of bioanalytical and medical applications. Such a system could turn out to be more robust toward protein adsorption than traditional voltammetric electrodes. Such studies are beyond the scope of this paper, however, and will be topics of future research.

## CONCLUSIONS

Ion-selective electrodes can be successfully used in a normal-pulse voltammetric and multipulse amperometric detection mode for ion-sensing purposes. Membranes containing two polarizable interfaces are well understood. The use of electrolytes in the inner solution of the electrode that are discriminated by the membrane, such as hydrophilic anions and cations that bind weakly to the ionophore in the case of cation-selective electrodes, again widens the useful potential window. The selectivity of these sensors can be tuned by altering the magnitude of the applied potential, and individual separate and mixed solution calibration curves demonstrate this characteristic convincingly. This selectivity modifying effect is akin to using different concentrations of lipophilic ionic sites in potentiometric ion-selective electrode membranes. Therefore, sensing selectivity can be significantly altered by pulsing the membrane at different potentials. This is perhaps so far the most striking advantage of this transduction principle relative to classical potentiometric sensors. While the systems discussed here show variable selectivities that are certainly interesting, further research with ionophores that more strongly alter the membrane selectivity as a function of the available free ionophore concentration and with membranes containing more than one ionophore will be explored in view of practically relevant multianalyte detection applications. Such sensors may ultimately find use as tunable detectors in separation science, as inexpensive multianalyte sensors for special applications and as multianalyte probes in scanning electrochemical microscopy.

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