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Voltammetric Ion-Selective Electrodes for the Selective Determination of Cations and Anions

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A general theory has been developed for voltammetric ion sensing of cations and anions based on the use of an electrode coated with a membrane containing an electroactive species, an ionophore, and a supporting electrolyte dissolved in a plasticizer. In experimental studies, a membrane coated electrode is fabricated by the drop coating method. In one configuration, a glassy carbon electrode is coated with a poly(vinyl chloride) based membrane, which contains the electroactive species, ionophore, plasticizer and supporting electrolyte. In the case of a cation sensor, ionophore facilitated transfer of the target cation from the aqueous solution to the membrane phase occurs during the course of the reduction of the electroactive species present in the membrane in order to maintain charge neutrality. The formal potential is calculated from the cyclic voltammogram as the average of the reduction and oxidation peak potentials and depends on the identity and concentration of the ion present in the aqueous solution phase. A plot of the formal potential versus the logarithm of the concentration exhibits a close to Nernstian slope of RT/F millivolts per decade change in concentration when the concentration of K^+ and Na^+ is varied over the concentration range of 0.1 mM to 1 M when K^+ or Na^+ ionophores are used in the membrane. The slope is close to $RT/2F$ millivolts for a Ca^{2+} voltammetric ion-selective electrode fabricated using a Ca^{2+} ionophore. The sensor measurement time is only a few seconds. Voltammetric sensors for K^+ , Na^+ , and Ca^{2+} constructed in this manner exhibit the sensitivity and selectivity required for determination of these ions in environmentally and biologically important matrixes. Analogous principles apply to the fabrication of anion voltammetric sensors.

The determination of cation and anion concentrations in seawater, river water, drinking water, biologically important fluids (blood, urine), and other liquid media is commonly required for quality control or for medical or environmental reasons.¹ Potentiometric ion-selective electrodes (ISE) are commonly employed

for the routine monitoring of ions.^{2,3} In polymer membrane ISEs, an ionophore that binds strongly to the ion of interest but relatively weakly to other potentially interfering ions is dissolved in a polymer (poly(vinyl chloride), PVC) supported water immiscible organic solvent (plasticizer), together with other additives, such as an ion exclusion agent (e.g., potassium tetrakis(4-chlorophenyl) borate). High ion selectivity is achieved predominantly by the binding properties of the ionophore. Under ideal conditions, a potential difference, ΔE , between the ISE and reference electrode is generated by the Donnan potential⁴ present at the water/membrane interface. Under equilibrium conditions, ΔE is related to the activity and hence concentration of the target ion in the aqueous phase by the Nernst–Donnan equation.

Voltammetry is also a widely used technique for trace organic and inorganic analysis. This analysis method is based on the use of a current–potential relationship generated by an electron transfer process. Voltammetry therefore operates under kinetically controlled conditions associated with current flow, rather than equilibrium conditions that apply to potentiometric ISE measurements. A vast array of literature is available on voltammetric detection of electroactive cations and anions at dropping mercury (polarography) and solid electrodes.^{5,6} In the sensor area, the highly selective chronoamperometric detection of glucose is extraordinarily common.⁷ However, reports on compact voltammetric based ion sensors for nonelectroactive ions are relatively rare.

Voltammetric ion sensing devices based on the principle of facilitated ion transfer across the externally polarized interface of two immiscible electrolyte solutions^{8–11} have been reported. This approach may be coupled with ion chromatographic separation

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to achieve cation detection under both steady state¹² and transient state¹³ conditions or with ionophores to achieve the required selectivity.¹⁴ Most voltammetric ion sensors of this kind reported to date are associated with cation detection. However, in the past few years, several groups have described voltammetric anion sensors based on the same principle.^{15–22}

Recently, Bond and co-workers²³ have reported that the peak potentials from a voltammogram of adhered microparticles of tetracyanoquinodimethane (or tetrathiafulvalene) adhered to an electrode surface depended on the cation (or anion) concentration in the aqueous electrolyte solution. Furthermore, tetracyanoquinodimethane-tetrathiafulvalene microparticles adhered to an electrode will respond in a similar manner to both cations and anions.²⁴ This approach again provides a different concept for voltammetric ion sensing, although the selectivity toward different ions is not large. The principle of this sensor is based on the need for charge neutralization to be achieved at the solid phase when a neutral solid is converted to a cationic (or anionic) solid. Marken and co-workers used a related approach, which is based on the use of a redox liquid, *N,N,N',N'*-tetrahexylphenylenediamine microdroplets modified electrode as an anion sensor,²⁵ while Scholz and co-workers have used hexacyanoferrate based composite electrodes as cation sensors.²⁶

Of specific relevance to a new ion sensing concept described in this article is the report by Scholz and co-workers^{27–32} that well-defined voltammograms may be obtained via use of water immiscible organic solvents containing dissolved electroactive

species that are adhered to an electrode surface. When these chemically modified electrodes are placed in contact with an aqueous electrolyte solution, ion (cation or anion) transfer will occur across the aqueous–organic solvent interface in order to achieve the charge neutrality required when an electroactive species in the organic phase is oxidized (or reduced) during the course of the voltammetric experiment. In principle, the oxidized (or reduced) form of the electroactive species can also transfer into the aqueous phase. However this unwanted process could be made thermodynamically unfavorable by careful choice of the redox active species and organic solvent. Scholz et al used the reversible potential obtained from a voltammogram to provide information on the transfer potential of the partitioning ion and hence the free energy of ion transfer.^{27–32} Girault et al. have also inverted the phases, extracting nonelectroactive species from an organic phase into an aqueous membrane phase containing an electroactive species.³³ The research groups of Amemiya^{34,35} and Bakker³⁶ have both reported a related technique by controlling ion transfer into a PVC membrane using voltammetry of an underlying conducting polymer.

In this article, we show that the concept of high selectivity for ionophore based ISEs^{2,3,37–40} and the approach of Scholz and co-workers^{27–32} can be combined to provide a new form of voltammetric ion selective electrode (VISE). Significantly, sensors based on this concept provide a rapid measurement time, require only small sample volumes, and achieve the high selectivity normally associated with potentiometric ISEs and with the same Nernstian sensitivity.

EXPERIMENTAL SECTION

Chemicals. The electroactive species, decamethylferrocene (DMFc, 97%), 1,1'-dimethylferrocene (DiMFC, 97%), 7,7,8,8-tetracyanoquinodimethane (TCNQ, 98%), and tetrabutylammonium hexacyanotetramethylcyclopropane (TBAHCTMCP), the ionophores, valinomycin, bis[(benzo-15-crown-4)-4'-ylmethyl]pimelate (K ionophore II), 2-dodecyl-2-methyl-1,3-propanediyl-bis [N-(5'-nitro(benzo-15-crown-5)-4'-yl) carbamate] (BME 44), dibenzo-18-crown-6 (DB18C6, 98%), bis[(12-crown-4)methyl] dodecylmethylmalonate (Na ionophore VI), [4,5-dimethyl-3,6-diethoxy-1,2-phenylene]-bis(mercury-trifluoroacetate) (ETH9009), 5, 10, 15, 20-tetraphenyl-21*H*,23*H*235 porphyrin manganese(III) chloride (Mn(III)TPPCL), 4,5-bis-[*N'*-(butyl)thioureido]-2,7-di-*tert*-butyl-9,9-dimethylxanthene), *N,N,N',N'*-tetracyclohexyl-3-oxapentanediamide (ETH129), calcimycin (A23187), tricyclohexyltin chloride, and tridodecylmethylammonium chloride, the membrane plasticizers, bis(1-butylpentyl) decane-1,10-diyl diglutarate (ETH469), 2-nitrophenyl octyl ether (NPOE), bis(2-ethylhexyl) sebacate, and bis(1-butylpentyl) adipate, high molecular weight poly(vinyl chloride), the supporting electrolytes tetrabutylammonium tetraphenylborate (TBATPB), tetraheptylammonium tetraphenylbo-

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rate (THATPB), and KPF₆ (98%) were all purchased from Sigma-Aldrich and used as received. The modular podand, 1,3,5-tris(3-((ferrocenylmethyl)amino)pyridiniumyl)-2,4,6-triethylbenzene hexafluorophosphate, [PD][PF₆]₃, was prepared as described in the literature.^{41,42} Aqueous supporting electrolytes KCl, NaCl, KNO₃, CaCl₂, NaClO₄, (NH₄)₂SO₄, Na₂HPO₄, and NH₄Cl (all BDH, analytical grade purity) and tetrahexylammonium perchlorate (THAClO₄, Alfa) were used as received. Tetrahydrofuran (THF) analytical grade from BDH was distilled, as nondistilled or stabilized forms of THF will form peroxides that are able to react with TCNQ resulting in a brown solution that inhibits VISE function. Tetrabutylammonium hexafluorophosphate (Bu₄NPF₆) was recrystallized as described previously.⁴³ Structures of some ionophores used are shown in Figure 1S in the Supporting Information. Triply distilled water or water obtained from a MiniQ purification system (resistivity ≥ 18 MΩ cm) from Millipore Corp. was used to prepare aqueous electrolyte solutions.

Instrumentation, Electrodes, and Procedures. Voltammetric experiments were undertaken in a conventional three-electrode cell with BAS 100B (Bioanalytical Systems) or Autolab PG-STAT100 (ECO-Chemie) electrochemical workstations or a home-built potentiostat controlled by LabVIEW with automatic peak detection software. The working electrodes were 1.5 or 3.0 mm diameter glassy carbon (GC) (IJ Cambria). The reference electrode was either Ag/AgCl (3 M NaCl) for K⁺ and Ca²⁺ or Ag/AgCl (saturated or 3 M KCl) for Na⁺ sensing experiments. The counter electrode was a Pt wire.

The drop coating method was used to prepare the modified GC electrode used for ion sensing. A typical composition used for the coating solution was 1 mL of PVC solution (0.15 g of PVC dissolved in 8 mL of THF), 37.5 μL of plasticizer (nonvolatile organic solvent) containing 2.5 mM electroactive species, 25 mM ionophore (10 mM for the less soluble ionophores), and 10 mM TBATPB or THATPB for cation sensors or 25 mM THAClO₄ for anion sensors. A small volume (less than 1 μL, resulting in a film less than 1 μm thick and hence preventing polarization of the electrode/membrane interface and diffusion effects at 100 mV s⁻¹) of the coating solution was introduced onto the GC working electrode surface using a micropipet. The modified electrode was then left in the air for about 5 min to ensure complete evaporation of THF occurs prior to sensor use. The multicomposite PVC film on the electrode surface that consists of polymer, supporting electrolyte, plasticizer, electroactive species, and ionophore or other combinations is designated as the membrane phase (see Figure 2S in the Supporting Information). The GC working electrode was polished with a 0.3 μm Al₂O₃ (Buehler) slurry, washed successively with water and acetone, and finally dried with tissue paper, prior to addition of the membrane coating. All experiments were conducted at ambient temperature (20 ± 1 °C).

In the presence of light, a color change from green to brown is observed in the coating solution at room temperature after several hours, although the voltammetric response is not sensitive to this effect. No color change is detected in the absence of either TBATPB or TCNQ, so it is assumed to arise from a reaction between TCNQ and TPB.⁴⁴

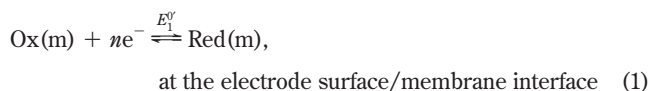
CHOICE OF MEMBRANE MATERIALS

Ionophores that are employed in potentiometric ISEs were chosen to ensure selective transfer of the target ion from the aqueous solution into the membrane. The role of the supporting electrolyte is to increase the membrane conductivity and therefore should be soluble in the membrane plasticizer and have a very low solubility in water. For a cation selective electrode, the transfer of the anion of the supporting electrolyte into the aqueous phase must be less favorable than the transfer of the target aqueous cation into the membrane. If this condition is achieved, the Donnan potential across the membrane/water interface is governed by the target cation. Similarly for an anion sensor, the transfer of the supporting electrolyte cation into the aqueous phase has to be less favorable than the transfer of the target anion into the membrane.

The electroactive species must undergo a reversible electrode reaction in the membrane, and its neutral and charged forms must be hydrophobic so that they both remain in the membrane during the course of ion sensing measurements. The electroactive species should also be stable for at least the time required to undertake experiments when dissolved in the membrane. Furthermore, the voltammetric response needs to be in a suitable potential range for ion sensing and to avoid the need to remove oxygen. The plasticizer is a water immiscible, nonvolatile organic solvent used to dissolve the supporting electrolyte, ionophore, and electroactive species and to provide a homogeneous, flexible membrane with the polymer, which in this case is PVC.

THEORY

Basic Principles. For a voltammetric ion sensor consisting of an ion-selective membrane deposited on a solid surface such as glassy carbon (Figure 2S), two major processes, described by eqs 1 and 2, are relevant for the case of cation sensing



where Ox and Red are the oxidized and reduced forms of the electroactive species, respectively and Cat refers to a cation. The m and aq in parentheses refer to the membrane phase and aqueous phase, respectively. E_1^0 is the formal potential of the redox active species present in the plasticizer; n is the number of electrons transferred in the electron transfer process; ΔG is the free energy represented for convenience as E_2^0 , which represents the formal potential (derived from free energy terms) of the target cation that is transferring from

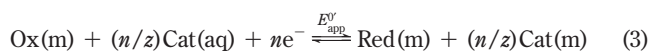
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the water phase into the membrane. On the basis of eqs 1 and 2, the total reaction occurring at the voltammetric ion sensor can be written as



where E_{app}^0 is the apparent reversible potential; z is the cation charge. A coefficient of n/z is used in the equation in order to satisfy the charge neutrality requirement. Under equilibrium conditions, a Nernst equation of the form shown in eq 4 applies

$$\begin{aligned} E &= E_{\text{app}}^0 + \frac{RT}{nF} \ln \frac{c_0 c_{\text{ca}}^{(n/z)}}{c_{\text{r}} c_{\text{cm}}^{(n/z)}} \\ &= E_{\text{app}}^0 + \frac{RT}{nF} \ln \frac{c_0}{c_{\text{r}}} + \frac{RT}{zF} \ln \frac{c_{\text{ca}}}{c_{\text{cm}}} \end{aligned} \quad (4)$$

where c_0 and c_{r} are the concentrations of oxidized and reduced forms of the redox active species present at the electrode/membrane interface, respectively; c_{cm} and c_{ca} are the concentrations of the free target cation at the membrane and aqueous sides of the membrane/water interface, respectively.

Quantitative Analysis. In the situation where the electrode reaction is reversible and the electrochemically facilitated transfer of the target cation across the interface is the most favorable ion transfer process (from both the thermodynamic and kinetic perspectives), the potential difference between the working and reference electrodes, $E(t)$ (E is time, t , dependent on voltammetric experiments), is governed by the following equation:

$$E(t) = E_1^0 + \frac{RT}{nF} \ln \frac{c_0}{c_{\text{r}}} + E_2^0 + \frac{RT}{zF} \ln \frac{c_{\text{ca}}}{c_{\text{cm}}} \quad (5)$$

Only the $z = n = 1$ case is considered for convenience in the following discussion; the Supporting Information should be consulted for details of cases with any other combinations of z and n .

Under conditions where diffusion within the membrane is insignificant, the electron transfer process may be regarded as fully surface confined and hence c_{cm} equals its bulk value, c_{m} . If the concentration of the target cation in the aqueous phase is high relative to that in the membrane or diffusion in the aqueous phase is much faster than in the membrane phase (highly probable since the viscosity of water is significantly lower than for the plasticizer), the concentration of the target ion at the water/membrane interface will be maintained at the bulk aqueous phase concentration so that $c_{\text{ca}} = c_{\text{b}}$, where c_{b} is the bulk aqueous solution concentration of the target cation. Under these conditions, c_{m} can be related to the total concentration of the target ion in the membrane (free and complexed forms) according to the reaction scheme given in eq 6 for the case of a 1:1 complex formed between the charged cation Cat(m) and an ionophore L(m),



where K is the equilibrium constant and is solvent dependent. As both E_2^0 and K depend on the plasticizer, a carefully chosen plasticizer can also enhance the selectivity of the ion sensor.

The ionophore is introduced into the membrane in order to make the transfer of the cation selective and the most favorable ion transfer process which otherwise need not be the case. If the complexation process (eq 6) is assumed to be at equilibrium on the voltammetric time scale, then

$$c_{\text{cm}} = c_{\text{CatL}}/(c_{\text{L}}K) \quad (7)$$

where c_{CatL} and c_{L} are the concentrations of CatL(m) and L(m), respectively. Since the concentration of L(m) is in a large excess and the sum of the concentration of Cat(m) and CatL(m) must equal c_{r} in order to satisfy the charge neutrality requirement, it follows that

$$c_{\text{cm}} = c_{\text{r}}/(c_{\text{L}}K + 1) = K'c_{\text{r}} \quad (8)$$

where $K' = 1/(c_{\text{L}}K + 1)$ is a constant. Substitution into eq 5 gives

$$\begin{aligned} E(t) &= E_1^0 + \frac{RT}{F} \ln \frac{c_0}{c_{\text{r}}} + E_2^0 + \frac{RT}{F} \ln \frac{c_{\text{b}}}{K'c_{\text{r}}} \\ &= E_3^0 + \frac{RT}{F} \ln \frac{c_0}{c_{\text{r}}} + \frac{RT}{F} \ln \frac{c_{\text{b}}}{c_{\text{r}}} \end{aligned} \quad (9)$$

where $E_3^0 = E_1^0 + E_2^0 - RT(\ln K'/F)$.

In a linear sweep voltammetric experiment, $E(t)$ is related to the starting potential E_{start} and the scan rate ν by the expression

$$E(t) = E_{\text{start}} - \nu t \quad (10)$$

A related equation applies for an oxidation component of a cyclic voltammogram.⁴⁵ Combining eqs 9 and 10 gives

$$E(t) = E_{\text{start}} - \nu t = E_3^0 + \frac{RT}{F} \ln \frac{c_0}{c_{\text{r}}} + \frac{RT}{F} \ln \frac{c_{\text{b}}}{c_{\text{r}}} \quad (11)$$

which can be rearranged to give the ratio of c_0/c_{r} as

$$\begin{aligned} \frac{c_0}{c_{\text{r}}} &= \frac{c_0}{c_{\text{redox}} - c_0} \\ &= \exp \left\{ \frac{F}{RT} \left[E(t) - (E_3^0) - \frac{RT}{F} \ln c_{\text{b}} + \frac{RT}{F} \ln (c_{\text{redox}} - c_0) \right] \right\} \\ &= (c_{\text{redox}} - c_0)(c_{\text{b}})^{-1} \exp \left[\frac{F}{RT} (E(t) - E_3^0) \right] \end{aligned} \quad (12)$$

where c_{redox} is the total concentration of redox active species (both reduced and oxidized forms) in the membrane. Equation 12 can be rearranged to give

$$\frac{x}{(1-x)^2} = \frac{c_{\text{redox}}}{c_{\text{b}}} \exp \left[\frac{F}{RT} (E(t) - E_3^0) \right] \quad (13)$$

This relationship may be solved as a quadratic equation in the usual way to give

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$$x = \frac{2 + y - \sqrt{y^2 + 4y}}{2} \quad (14)$$

where

$$y = 1 / \left\{ \frac{c_{\text{redox}}}{c_b} \exp \left[\frac{F}{RT} (E(t) - E_3^0) \right] \right\} \quad (15)$$

The Faradaic current, i , for a surface confined process is given by⁴⁶

$$i = FAc_{\text{redox}}l \frac{dx}{dt} \quad (16)$$

where l is the thickness of the membrane phase. Combining eqs 14 and 16 allows the current to be calculated as

$$i = \frac{F^2 A \nu c_{\text{redox}} l}{RT} y \left(0.5 - \frac{y + 2}{2\sqrt{y^2 + 4y}} \right) \quad (17)$$

The derivative of i with respect to $E(t)$ when it equals zero provides the values of the peak current and peak potential. Since $(\partial i / \partial E(t)) = (\partial i / \partial y)(\partial y / \partial E(t))$ and $(\partial y / \partial E(t))$ is nonzero according to eq 15, the y value when $(\partial i / \partial y)$ is equal to zero is related to the peak position. Consequently, according to eq 15, the peak potential, E_p , can be obtained with this y value. According to eq 15, E_p is independent of l but is a function of c_L and K (both of them affect E_3^0) and is linearly dependent on $\ln c_b$ and $\ln c_{\text{redox}}$ with a slope of RT/F . It should also be noted that x is not equal to 0.5 at the peak potential, as expected for the case when the potential difference across the membrane/water interface is constant. In practice, the average values of the measured peak potentials associated with the oxidative and reductive components of cyclic voltammograms, E_m^0 , plotted versus $\ln c_b$ is recommended for calibration purpose in order to minimize complications introduced by the presence of uncompensated resistance.

In the conventional linear sweep voltammetric studies of surface confined reversible one-electron transfer processes, the potential difference used as the driving force for the electron transfer reaction, $E_{\text{et}}(t)$ is the same as the applied potential, $E(t)$ in the absence of uncompensated resistance. Under this

situation, a voltammogram with the expected^{46,47} peak width at half-height, $W_{1/2}$, value of 89 mV at 20 °C can be obtained (see the dashed line in Figure 1). However, in the present situation, $E_{\text{et}}(t) \neq E(t)$ due to the presence of a potential difference across the membrane/water interface. In this case, a voltammogram with a smaller peak current (only about 68.6% of that associated with the conventional one) and broader peak width ($W_{1/2} = 129$ mV instead of 89 mV) is predicted (solid line of Figure 1) due to the deviation of $d(E_{\text{et}}(t))/dt$ from $d(E(t))/dt$ (Figure 1b) as a result of the partitioning of the aqueous cation into the membrane phase that is needed to achieve charge neutralization. However, the oxidative and reductive components of a cyclic voltammogram are still expected to be symmetrical so that the oxidation and reduction peak potentials are still identical.

RESULTS AND DISCUSSION

Cation Sensors. Voltammetric sensors based on the above principles have been fabricated for K^+ , Na^+ , and Ca^{2+} cations. They have a rapid measurement time and are highly selective at the levels required for determination of these cations in biologically and environmentally important matrixes. Importantly, under conditions of cyclic voltammetry, they produce a reversible potential based on the average $(E_p^{\text{red}} + E_p^{\text{ox}})/2$ of the reduction E_p^{red} and oxidation E_p^{ox} peak potentials, which is linearly dependent on $\ln c_b$.

K^+ Sensor. A cyclic voltammogram of a K^+ sensor containing a membrane fabricated from 2.5 mM TCNQ, 25 mM valinomycin, and 10 mM TBATPB dissolved in the plasticizer, NPOE with PVC as the base-polymer, is presented in Figure 2a when 0.1 M KCl is present in the aqueous phase. TBATPB is used as the supporting electrolyte because the transfer of TPB^- from the membrane phase to the aqueous phase is thermodynamically unfavorable.⁴ Many of the voltammetric characteristics observed for this system are those predicted theoretically for a one-electron $\text{TCNQ}^{0/\bullet-}$ surface-confined process. However, the slightly larger than predicted ΔE_p value of 40 mV and $W_{1/2}$ value of ~ 130 mV obtained at a scan rate of 100 mV s^{-1} suggest that a small diffusion controlled component contributes to the voltammetry. Importantly, the voltammetry is stable over multiple cycles and with respect to the sensing requirement, $E_m^0 = (E_p^{\text{red}} + E_p^{\text{ox}})/2$ is independent of the scan rate within experimental error over the range of 10 mV s^{-1} to 1 V s^{-1} when the concentration of aqueous KCl is 0.1 M. In conventional ISEs where an ion partition equilibrium is established, the response

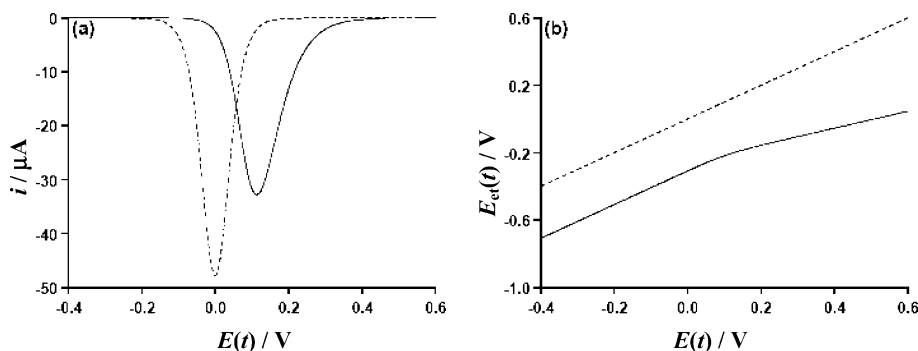


Figure 1. (a) Theoretical linear sweep voltammograms calculated for a conventional surface confined process (---, $E_3^0 = 0$)⁴⁶ and a surface confined process involving ion transfer across a phase boundary (—, $E_3^0 = -0.2$ V and use of eqs 15 and 17). $T = 293$ K, $A = 1 \text{ cm}^2$, $\nu = 0.1 \text{ V s}^{-1}$, $c_{\text{redox}} = 5 \text{ mM}$, $c_b = 1 \text{ M}$, and $l = 1 \text{ } \mu\text{m}$; (b) the relationship between $E_{\text{et}}(t)$ and $E(t)$ for the two models considered in part a.

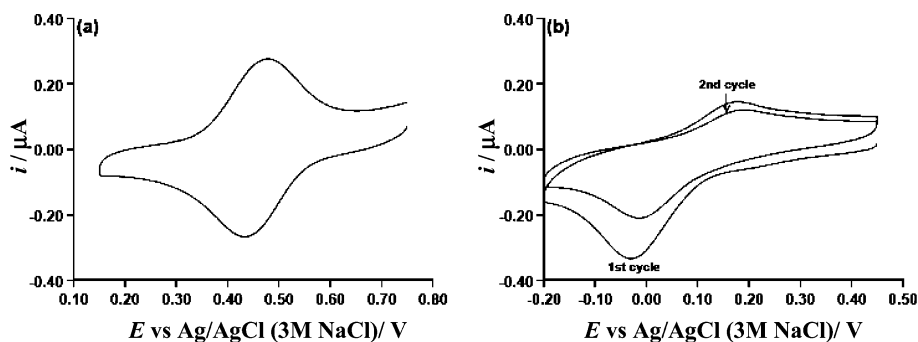


Figure 2. Voltammogram obtained at a scan rate of 0.1 V s^{-1} (a) for a voltammetric K^+ sensor (NPOE plasticizer used in the membrane, which contains 2.5 mM TCNQ, 25 mM valinomycin, and 10 mM TBATPB) in contact with 0.1 M KCl aqueous electrolyte solution; (b) the same as for part a but in the absence of valinomycin.

time is the time elapsed from the instant the electrode is inserted into the solution to when the steady state potential is within 1 mV. There is no formal definition of a response time for a VISE; however, varying the time between electrode insertion and measurement ideally has no influence on the VISE measurement time, as no ion transfer should occur prior to the measurement. The measurement time can therefore be controlled by the voltammetric scan rate, allowing a potential measurement in seconds. In comparison, potentiometric ISEs may require considerably longer times to achieve the required equilibrium value. A close to Nernstian dependence on K^+ concentration is found in the KCl concentration range of 0.1 mM to 1 M. Thus, a slope of $54 \pm 2 \text{ mV}$ per decade change in concentration is obtained for a calibration plot of E_m^0 versus $\log_{10}[\text{K}^+]$.

Uncompensated resistance (R_u) influences the voltammetric response when only dilute concentrations of KCl are present in the aqueous solution phase. However, measurement of the E_m^0 value as $(E_p^{\text{red}} + E_p^{\text{ox}})/2$ compensates for this effect. Furthermore, ohmic (iR_u) distortion can be avoided by addition of an inert supporting electrolyte. iR_u problems in the measurement of K^+ in biologically or environmentally important samples are unlikely to be significant because of the presence of high salt concentration usually associated with these matrixes.

In the absence of the ionophore, a nonsymmetrically shaped voltammogram is obtained at the much more negative E_m^0 potential of 74 mV (Figure 2b). A much larger peak-to-peak separation is now also observed. These features suggest that the kinetics of K^+ transfer across the aqueous/membrane interface is slow and that the solubility of K^+ in the membrane has been reduced. Moreover, the peak currents now decrease during the course of cycling of the potential, which implies that partial loss of electrogenerated $\text{TCNQ}^{\bullet-}$ occurs by dissolution into the aqueous phase, in addition to the transfer of K^+ into the membrane. Consistent with the hypothesis that transfer of both K^+ and $\text{TCNQ}^{\bullet-}$ govern the potential across the aqueous/membrane interface is the low slope of only 37 mV per decade change in concentration that is obtained for a calibration plot of E_m^0 versus $\log_{10}[\text{K}^+]$ in the absence of the ionophore. Furthermore, without ionophore and if 20 mM THAClO_4 is used instead of TBATPB as the supporting electrolyte in the membrane phase, then E_m^0 becomes independent of the aqueous

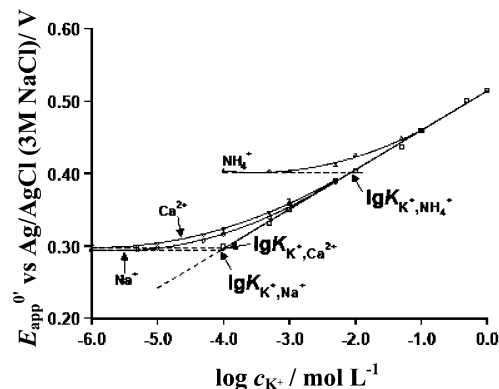


Figure 3. Determination of the selectivity coefficients for the K^+ sensor using the fixed interference concentration method. The calibration curve for K^+ sensor (\square) is obtained by varying the concentration of KCl in the absence of interfering ions. The interference curves are obtained with 1 M Na^+ (\circ), NH_4^+ (Δ), or Ca^{2+} (∇). The membrane composition is the same as described in the caption for Figure 2a.

ous KCl concentration in the range of 10 mM to 1 M, since the reversible transfer of ClO_4^- is now the favored ion transfer process.

In the absence of the redox active TCNQ, only nonreversible voltammetric processes are detected at potentials near the solvent/electrolyte potential window limit. Such voltammetric responses are ill-defined and nonreproducible and hence not suitable for ion sensing purposes. Thus, in the form of the voltammetric ion selective electrode we have developed, the presence of a reversible redox active species in the membrane phase is critical to the generation of a well-defined and highly reproducible voltammogram in a convenient potential range.

A recent study by Bakker et al.⁴⁸ has examined the methods for determining the selectivity coefficients, K_{ij} , for polymer membrane ISEs, and they have demonstrated the pitfalls that can be associated with such measurements. In this article we have adopted one of the IUPAC recommended³ methods for the determination of the VISE selectivity coefficients. This is the fixed interference method which is employed in Figure 3.

The selectivity coefficient, K_{ij} , of a sensor for ion i , in the presence of interfering ion j , can be determined using eq 18 at constant ionic strength, when concentrations are used instead of activities.

(47) Zhang, J.; Guo, S.-X.; Bond, A. M.; Honeychurch, M. J.; Oldham, K. B. *J. Phys. Chem. B* **2005**, *109*, 8935–8947.

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$$E_m^{0'} = E_i^{0'} + s \log_{10} [c_i + K_{ij} c_j^{z_i/z_j}] \quad (18)$$

where s is the slope of a $E_m^{0'}$ versus $\log_{10} c_i$ plot in the absence of interfering ion, j , and c_i and c_j are the concentration of ions i and j , respectively.

The intersection of the plot of $E_m^{0'}$ versus $\log_{10} c_i$ obtained for solutions containing only the primary ion i with that for solutions containing the primary ion and a high concentration of interfering ion j gives the value of $\log_{10} K_{ij}$. In this present study, the concentration of the interfering ion was fixed at 1 M and the concentration of the primary ion was typically varied from 10^{-3} mM to 0.1 M in order to maintain constant ionic strength. Na^+ , NH_4^+ , and Ca^{2+} were chosen as examples of interfering ions, since they are usually present at significant concentrations in blood or water samples. Typical concentrations of these ions found in blood are summarized in Table 1.

For the K^+ sensor in the presence of interfering ions Na^+ , NH_4^+ , and Ca^{2+} , selectivity coefficients calculated as $\log_{10} K_{ij}$ were -4.05 , -2.07 , and -3.97 , respectively. This implies that the voltammetric K^+ sensor should have sufficient selectivity to determine K^+ in blood samples even though this fluid contains a large excess of Na^+ (Table 1). The $\log_{10} K_{ij}$ values calculated using the fixed interference method are similar to values of -4.07 , -2.04 , and -3.98 obtained from the separate solution method,³ which is based on eq 19,

$$\log_{10} K_{ij} = \frac{E_{m,j}^{0'} - E_{m,i}^{0'}}{s} \quad (19)$$

where $E_{m,i}^{0'}$ and $E_{m,j}^{0'}$ are the measured formal potential of the sensor in solutions containing either ion i or j with equal concentration, respectively, and s is the slope of the $E_{m,i}^{0'}$ versus $\log_{10} c_i$ curve.

Voltammograms obtained using other K^+ ionophores or plasticizers were analogous to that shown in Figure 2a. In all cases, a close to Nernstian relationship was obtained when the K^+ concentration was varied over the range of 0.1 mM to 0.1 M. A summary of the performance of K^+ sensors with different membrane compositions in the presence of 0.1 M K^+ , Na^+ , NH_4^+ , or Ca^{2+} is shown in Table 2. Data show that, as expected, for the facilitated ion transfer across two immiscible liquid/liquid interfaces,^{8,9} the measured formal potential depends on the identity of the ion, the plasticizer, and ionophore. Moreover, the selectivity of the K^+ sensor also depends on the nature of both the plasticizer and the ionophore. Thus, a K^+ sensor that uses DB18C6 as an ionophore or ETH469 as a plasticizer, as alternatives to valinomycin and NPOE, respectively, are less selective to K^+ based on eq 19 and the $E_m^{0'}$ data contained in Table 2.

The lower detection limit of the VISE has not been determined, as a linear calibration curve was obtained over the desired analyte concentration range. However, similar limitations to the lower

Table 2. $E_m^{0'}$ Values Found for K^+ Voltammetric Sensors As a Function of Membrane Composition, in the Presence of 0.1 M Aqueous Chloride Solutions^a

membrane composition	$E_m^{0'}/\text{V}$ vs Ag/AgCl			
	K^+	Na^+	NH_4^+	Ca^{2+}
recommended ^b	0.460	0.240	0.330	0.245
DB18C6 ^c	0.260	0.145	0.165	0.115
ETH469 ^d	0.335	0.160	0.210	0.155

^a $\nu = 0.1 \text{ V s}^{-1}$. ^b Recommended membrane composition for a K^+ sensor based on valinomycin is 2.5 mM TCNQ, 25 mM valinomycin, 10 mM TBATPB in NPOE, and other constituents mentioned in the Experimental Section. ^c The composition is 2.5 mM TCNQ, 10 mM ionophore DB18C6, 10 mM TBATPB in NPOE, and other constituents mentioned in the Experimental Section. ^d The composition is 2.5 mM TCNQ, 25 mM valinomycin, 10 mM TBATPB in ETH469, and other constituents mentioned in the Experimental Section.

detection limit as seen in conventional potentiometric ISEs are expected, such as the supporting electrolyte lipophilicity and the presence of impurities. Other factors specific to the VISE are the electroactive species lipophilicity and its formal potential. Furthermore, it has been assumed that the interfacial concentration of the target ion in the aqueous phase will remain at its bulk value during the course of the voltammetric experiment. This will apply when the concentration of the target ion in the aqueous phase is sufficiently high, compared to the concentration of electroactive species in the membrane, after taking into account the differences in the viscosity of the two phases. Reducing the electroactive species concentration would require less target ion to transfer into the membrane as a counterion and result in a decrease in the lower detection limit. However, the use of dc voltammetry would result in an unfavorable Faradaic to background current ratio. Use of more sensitive techniques such as pulse voltammetry, Osteryoung square wave voltammetry, or Fourier transformed ac voltammetry should minimize this issue.^{46,49} These techniques may also reduce the voltammetric peak width, increase the sensor accuracy, and allow direct measurement of the formal potential at the peak potential. However, these techniques are more expensive to implement, an important issue for low cost, portable analyzers.

Na^+ Sensor. The membrane for the Na^+ sensor was fabricated as for the K^+ VISE except that 25 mM Na^+ ionophore VI, dissolved in NPOE, was used. This ionophore facilitates the transfer of Na^+ from the aqueous media into the membrane without detectable loss of TCNQ^{*-} occurring during the course of a voltammetric experiment. The voltammetric response obtained when this sensor is in contact with 0.1 M NaCl is shown in Figure 4. An even more symmetrically shaped voltammogram ($\Delta E_p = 38 \text{ mV}$, $W_{1/2} = 131 \text{ mV}$) is obtained than for the K^+ sensor, and $E_m^{0'}$ is independent of scan rate over the range of 10 mV s^{-1} to 1 V s^{-1} and film thickness (Figure 5). A close to Nernstian slope of $56 \pm 2 \text{ mV}$ per decade concentration

Table 1. Typical Composition of Blood Sample^{51,53}

ion	K^+	Na^+	Ca^{2+}	NH_4^+
concentration	3.6–5.0 mM	135–145 mM	2.25–288 mM	2.22–6.93 μM

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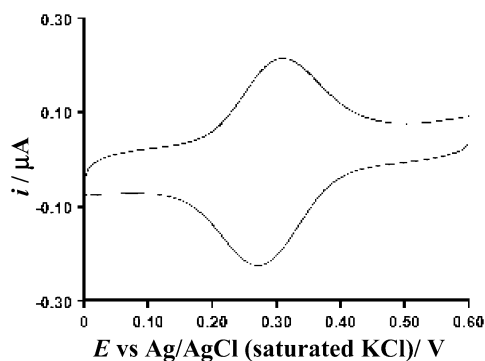


Figure 4. Voltammogram obtained at a scan rate of 0.1 V s^{-1} for a voltammetric Na^+ sensor (NPOE plasticizer containing 2.5 mM TCNQ, 25 mM Na^+ ionophore VI, and 10 mM TBATPB) in contact with 0.1 M NaCl aqueous electrolyte solution.

change of Na^+ was found for the concentration range of 0.1 mM to 1 M. The selectivity of this voltammetric Na^+ sensor using the fixed interference concentration method is shown in Figure 6 and gave $\log_{10} K_{ij}$ values with respect to interfering ions K^+ , NH_4^+ , and Ca^{2+} of -1.69 , -2.39 , and -2.98 , respectively. These selectivity values are very similar to values determined for Na^+ ISEs.⁵⁰ This implies that it should be possible to use this voltammetric Na^+ sensor for the determination of Na^+ in blood samples, which contain a dominant concentration of Na^+ (Table 1).

The use of 10 mM TBAPF₆ instead of TBATPB as the supporting electrolyte in the membrane phase resulted in a decrease in the sensitivity over the range of 1 mM to 1 M with a reduction in slope to 23 mV per decade concentration change of Na^+ since the reversible transfer of PF₆[−] to the aqueous phase competes with the Na^+ transfer.

Ca^{2+} Sensor. To confirm the generality of the principle established for the fabrication of voltammetric cation sensors, the possibility of sensing the biologically important Ca^{2+} cation was investigated.⁵¹ For this purpose, 25 mM Ca^{2+} ionophore, ETH 129, was used in NPOE in order to facilitate the transfer of Ca^{2+} into the membrane during the course of the reduction of TCNQ. Otherwise the membrane composition was the same as for the K^+ sensor. The voltammetric response obtained for this sensor in contact with 0.1 M aqueous CaCl_2 is shown in Figure 7a. The almost symmetrical shaped voltammogram ($\Delta E_p = 41 \text{ mV}$ and $W_{1/2} = 127 \text{ mV}$) implies that a one-electron TCNQ^{0/•−} surface confined process remains dominant but with a small diffusional component still being present. In keeping

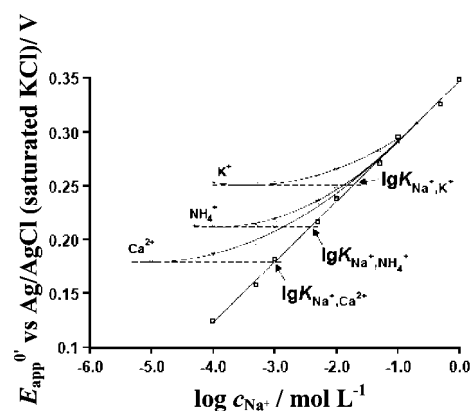


Figure 6. Determination of the selectivity coefficients for the Na^+ sensor using the fixed interference concentration method. Calibration curve for Na^+ sensor (\square) is obtained by varying the concentration of NaCl in the absence of interfering ions. The interference curves are obtained with 1 M K^+ (\circ), NH_4^+ (Δ), or Ca^{2+} (∇). The membrane composition is the same as described in the caption for Figure 4.

with that expected for the 2+ charged Ca^{2+} cation, the Nernst slope was found to be $29 \pm 1 \text{ mV}$ per decade change in concentration in the range of 0.1 mM to 0.25 M (Figure 7b). This slope dependence on cation charge confirms the sensor response obeys many of the features established for a classical potentiometric ion sensor.^{2,3,37–40} The E_m^0 data for Ca^{2+} and interfering K^+ , Na^+ , and NH_4^+ cations are summarized in Table 3. The fact that E_{app}^0 obtained in the presence of 0.1 M CaCl_2 is far more positive than when other cations are present at the same concentration indicates that the Ca^{2+} sensor is highly selective for Ca^{2+} (see eq 19). Calcimycin was also tested as a calcium ionophore, but it has a very low formation constant (β_{II}) and seemed to bind Ca^{2+} so poorly that the TCNQ^{0/•−} reduction process was not shifted until Ca^{2+} concentrations in excess of 0.1 M were present and the cyclic voltammetry showed poorly defined peaks.

Anion Sensors. Attempts to fabricate a chloride sensor were made by preparing a membrane containing anion selective ionophores, such as ETH9009, Mn(III)TPPCl, 4,5-bis-[N'-(butyl)thioureido]-2,7-di-*tert*-butyl-9,9-dimethylxanthene), tricyclohexyltin chloride, and tridodecylmethylammonium chloride, and also a modular podand^{41,42} along with plasticizers such as NPOE, bis(2-ethylhexyl) sebacate, and bis(1-butylpentyl) adipate. The electroactive species used in the anions sensors were DMFc or DiMFC, and THAClO₄ or THATPB were used as the supporting electrolyte in the membrane (THA⁺ should remain in the

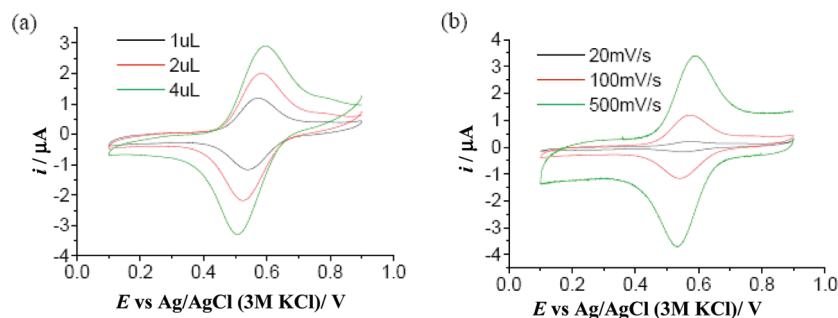


Figure 5. Cyclic voltammetry of a thin film with 20 mM Na ionophore VI in 0.1 M NaCl varying (a) film thickness (applied droplet volume) at a scan rate of 100 mV s^{-1} and (b) scan rate with a $1 \mu\text{L}$ coating solution droplet. Otherwise, the membrane composition is the same as described in the caption for Figure 4.

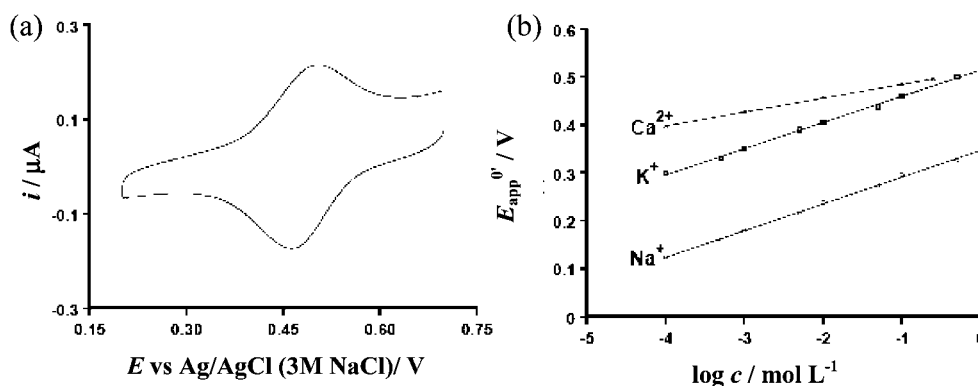


Figure 7. (a) Voltammogram obtained at a scan rate of 0.1 V s^{-1} for a voltammetric Ca^{2+} sensor (NPOE plasticizer containing 2.5 mM TCNQ, 25 mM ETH 129, and 10 mM TBATPB) in contact with 0.1 M CaCl_2 aqueous electrolyte solution. (b) Calibration curves of K^+ , Na^+ , and Ca^{2+} sensors (see captions for Figures 2, 4, and 7a for the membrane compositions of these sensors).

Table 3. E_m^0 Values (vs Ag/AgCl (3 M NaCl)) Obtained for a Voltammetric Ca^{2+} Sensor in the Presence of 0.1 M Aqueous Chloride Solutions ($v = 0.1 \text{ V s}^{-1}$)

ion	Ca^{2+}	K^+	Na^+	NH_4^+
E_m^0/V	0.484	0.228	0.255	0.237

membrane⁴ during the course of the oxidation of DMFc, DiMFc, or TBAHCTMCP).

4,5-Bis-[*N*-(butyl)thioureido]-2,7-di-*tert*-butyl-9,9-dimethylxanthene) (20 mM) in the membrane at a high concentration of Cl^-

gave symmetrical shaped voltammetric peaks on both the forward and reverse scans, but at lower concentrations of Cl^- the reduction process was very broad (Figure 8a). Also, the sensitivity of the electrode was only 26.9 mV per decade change in Cl^- concentration from 0.01 to 1 M.

A voltammogram obtained for another membrane composition using ETH9009 as the ionophore is shown in Figure 8b. In this case, the oxidative peak current is larger than the reductive peak current and both decrease significantly with cycling of the potential. This result suggests that sparingly soluble electrogen-

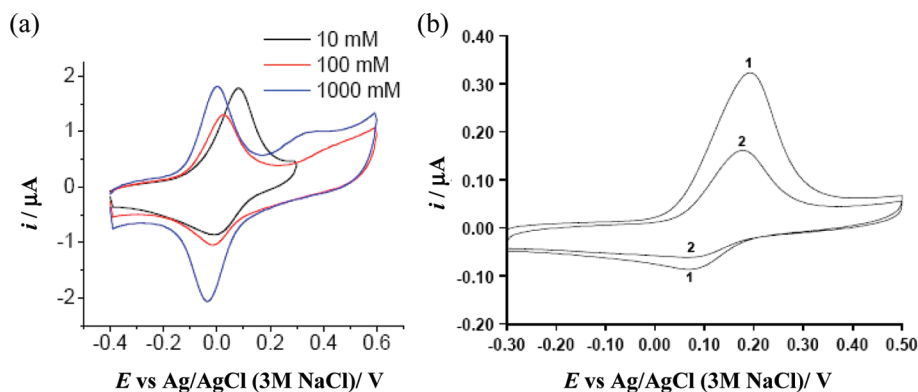


Figure 8. Voltammograms obtained at a scan rate of 0.1 V s^{-1} for voltammetric Cl^- sensors formed from NPOE plasticizer containing 2.5 mM DMFc and (a) 20 mM 4,5-bis-[*N*-(butyl)thioureido]-2,7-di-*tert*-butyl-9,9-dimethylxanthene and 25 mM THATPB in contact with varying concentrations of KCl aqueous electrolyte solution (b) 10 mM ETH 9009 and 25 mM THAClO_4 in contact with 0.1 M NaCl aqueous electrolyte solution.

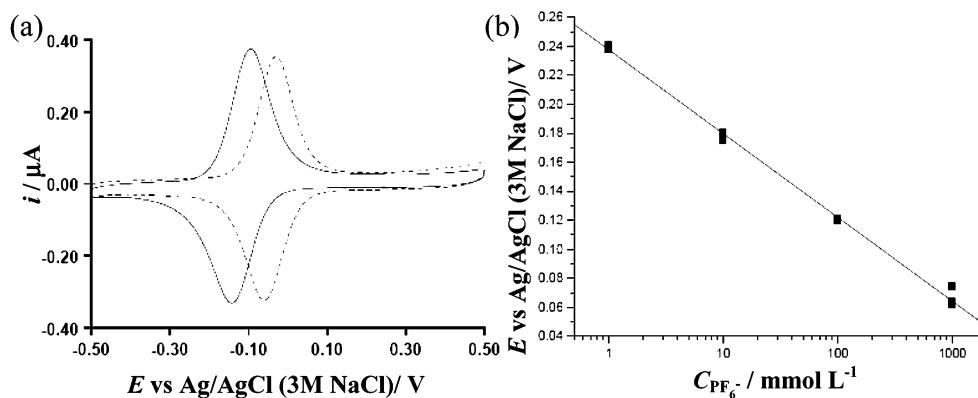


Figure 9. (a) Voltammogram obtained at a scan rate of 0.1 V s^{-1} for a voltammetric sensor (NPOE plasticizer containing 5 mM DMFc and 25 mM THAClO_4) in contact with 0.1 M NaClO_4 (---) or 0.1 M KPF_6 (—) aqueous electrolyte solution. (b) Calibration curve for the PF_6^- ion.

erated DMFc⁺ transfers into the aqueous phase during the course of the voltammetric experiments. Furthermore, essentially identical voltammograms to the one in Figure 8 were obtained in the absence of ionophore in the membrane or if 0.1 M electrolyte solutions of (NH₄)₂SO₄, KNO₃, or Na₂HPO₄ were used instead of 0.1 M NaCl. Moreover, the E_m^o data obtained are independent of the concentration of NaCl. These results suggest that Cl⁻ transfer into the membrane solvent facilitated by chloride ionophore does not occur on the voltammetric time scale and that charge neutralization by transfer of DMFc⁺ from the membrane into the aqueous phase is implied to be the preferred process. Similar results were obtained by varying the ratio of supporting electrolyte and ionophore. This rules out the lack of free ionophore for the interfacial complexation reaction due to the possible strong complexation reaction between the ionophore and Cl⁻. Potentiometric sensing of Cl⁻ and nuclear magnetic resonance (NMR) measurements suggest that ionophore complexation with Cl⁻ is thermodynamically favorable.^{2,3,37–42} Consequently, the lack of facilitated Cl⁻ transfer process under voltammetric conditions most likely arises from a kinetic limitation in the anion binding process.⁵² However, facilitated anion (including Cl⁻) transfer on the voltammetric time scale has been reported with other ionophores in the electrochemical studies employing conventional externally polarized water/oil interfaces.^{15–22}

The principles described enable sensors to be fabricated for less hydrophilic anions, such as ClO₄⁻ and PF₆⁻, as the transfer of these anions into the membrane, even without an ionophore being present, is both thermodynamically and kinetically favorable (Figure 9a). In both cases, a close to Nernstian dependence on ClO₄⁻ or PF₆⁻ concentration is found in the

range of 0.1 mM to 1 M in the sense that a slope of 56 ± 3 mV per decade change in concentration is obtained for a calibration plot of E_m^o versus log₁₀[ClO₄⁻] or log₁₀[PF₆⁻] (Figure 9b).

CONCLUSIONS

Voltammetric cation sensors that have the sensitivity and selectivity required for the detection of K⁺, Na⁺, and Ca²⁺ in blood have been fabricated by employing the principle of facilitated ion transfer that accompanies an electron transfer process in a membrane phase containing a redox active species, supporting electrolyte, ionophore, and plasticizer components. Anion sensors may be constructed on the same principle provided the binding between the anion and anion ionophore is sufficiently rapid. Only one ionophore (4,5-bis-[*N'*-(butyl)thioureido]-2,7-di-*tert*-butyl-9,9-dimethylxanthene)) showed any sensitivity to Cl⁻ concentration, but it was non-Nernstian. In the case of anions such as ClO₄⁻ or PF₆⁻, it has been shown that a sensor can be fabricated without using an ionophore.

ACKNOWLEDGMENT

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SUPPORTING INFORMATION AVAILABLE

General quantitative analysis, ionophore structures, and VISE schematic. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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