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Monolithic Capillary-Based Ion-Selective Electrodes

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Poly(styrene-*co*-divinylbenzene)-based monolithic capillaries of an inner diameter of 200 μm and a length of 2–5 mm have been used to construct Ca^{2+} -, Ag^{+} -, and Na^{+} -selective electrodes. The membranes consist of a solution of ionophore and ion exchanger in bis(2-ethylhexyl) sebacate or 2-nitrophenyl octyl ether, which are used as plasticizers in conventional PVC-based membranes. With capillaries of low porosity, the potentiometric responses down to 10^{-8} – 10^{-9} M solutions do not depend on the composition of the internal solution, which indicates a strong suppression of transmembrane ion fluxes. Thus, no tedious optimization of the inner solution is required with monolith ISEs. The lower detection limits of Ag^{+} - and Ca^{2+} -ISEs are comparable to the best ones obtained earlier with optimized inner solutions. Additionally, a monolithic Na^{+} -selective ISE has been obtained exhibiting a lower detection limit of 3×10^{-8} M Na^{+} . With monolithic capillaries of higher porosity and fused-silica GC capillaries, the transmembrane flux effects are noticeable but still significantly smaller than with conventional PVC membranes.

Potentiometry is usually termed as a method involving zero-current measurements, which means that the measuring current of the order of 1–100 fA is negligible in practice. Until recently, ion flux effects were, therefore, not considered to be relevant in ion-selective electrode (ISE) membranes.^{1,2} However, in the past few years, it has been established that this view is not correct if the sample ion concentrations are $\leq 10^{-6}$ M. In such situations, zero-current transmembrane ion fluxes^{3–5} play a decisive role because they alter the composition of the sample near the sensor surface. In conventional polymeric membrane electrodes, for example, they were found to bring about a micromolar concentration increase in this layer, which was considered to be the attainable lower detection limit of ISEs in the absence of ion buffers. Today, it is well established that the driving force of such

fluxes is either the coextraction of primary ions together with their counterions from the inner solution^{5,6} or their exchange by interfering ions on the sample side of the membrane.^{7–10} Spectacular improvements of the lower detection limit and the selectivities, which are also biased by ion fluxes, have been achieved by strongly reducing the primary ion activity of the internal solution.¹¹ The thus induced partial exchange of primary ions by interfering ones in the inner surface layer of the ISE membrane decreases the transmembrane concentration gradient. Another possibility is the compensation of zero-current ion fluxes by applying an external current.^{12–14} During the past few years, lower detection limits in the range of 10^{-8} – 10^{-12} M have been reported for a series of cations and anions (for reviews, see, e.g., refs 15–17). It must be noted that because of the very conservative definition of the potentiometric lower detection limit,¹⁸ these values are higher by ~ 2 orders of magnitude than they would be according to the usual definition in analytical chemistry.^{17,19}

Transmembrane ion fluxes in both directions, i.e., toward the inner and the outer (sample) solutions, give rise to a biased ISE response, because of either increasing or reducing the analyte concentration in the sample near the membrane surface. Since the composition of an optimal inner solution, which would fully eliminate concentration gradients and concomitant ion fluxes, is different for each kind of sample, ion flux effects cannot be totally suppressed by optimizing the inner solution. Therefore, various further means have been introduced to reduce these ion fluxes. For steady-state conditions, the transmembrane concentration

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gradient of primary ions is related to the (biasing) concentration gradient within the sample by the ratio of mass-transfer coefficients, $q = D_m d_{aq} / D_{aq} d_m$, with D as the diffusion coefficients in the membrane (m) and aqueous solution (aq) and d as the thickness of the diffusion layers of the corresponding phases.^{7,9,10,20} Successful measures for reducing transmembrane ion fluxes have included a decrease in D_m (by increasing the PVC content in the membrane,²¹ covalently attaching the ionophore to the polymer matrix,^{22,23} or incorporating lipophilic particles in the membrane²⁴), an increase in d_m ,²¹ and a decrease in d_{aq} (flow-through system,²¹ wall-jet system,¹² rotating electrode²⁵). More recently, ISEs were described with a solid internal contact, i.e., without an inner solution, which also showed similar or better lower detection limits than conventional electrodes with optimized inner solutions.^{26,27}

Recently, monolithic capillaries have been introduced as attractive chromatographic columns.^{28,29} They contain a porous polymer rod as the stationary phase prepared inside the capillary. Superior chromatographic performances are achieved owing to the elimination of the interstitial volume and increase in mechanical stability. Stationary phases are either silica-based or organic polymers including acrylates and styrene-based polymers.^{30,31}

In this work, for the first time, we investigate the use of monolithic columns based on poly(styrene-*co*-divinylbenzene)^{31,32} as matrixes of ISE membranes. The resulting ion-selective electrodes are characterized in terms of their lower detection limit, selectivity behavior, and response times.

EXPERIMENTAL SECTION

Reagents. Poly(vinyl chloride) (PVC), bis(2-ethylhexyl)sebacate (DOS), 2-nitrophenyl octyl ether (*o*-NPOE), sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (NaTFPB), potassium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate, the Ag⁺ ionophore, *O,O'*-bis[2-(methylthio)ethyl]-*tert*-butylcalix[4]arene, the Ca²⁺ ionophore, *N,N*-dicyclohexyl-*N',N'*-dioctadecyl-3-oxapentaneamide (ETH 5234), the Na⁺ ionophore 4-*tert*-butylcalix[4]arene tetraacetic acid tetraethyl ester, and tetrahydrofuran (THF) were Selectophore products from Fluka AG (CH-9471 Buchs, Switzerland). Aqueous solutions were prepared with freshly deionized water (>18.0 MΩ cm, specific resistance) obtained with a NANOpure reagent-grade water system (Barnstead, CH-4009 Basel, Switzerland). The salts NaNO₃, NaCl, Ca(NO₃)₂, CaCl₂, NH₄NO₃, and KCl were of

Suprapur grade from Merck (Darmstadt, Germany); AgNO₃ puriss p.a. was obtained from Fluka. For the preparation of monolithic capillaries, acetonitrile (HPLC gradient grade), divinylbenzene (synthesis grade), methanol (HPLC gradient grade), and styrene (synthesis grade) were obtained from Merck, THF (99.9%, anhydrous, inhibitor free) was from Sigma-Aldrich (Steinheim, Germany). Styrene and divinylbenzene were distilled before use. Azobisisobutyronitrile (synthesis grade) and decanol (synthesis grade) were purchased from Fluka.

Monolithic Capillaries. Capillaries filled with porous, monolithic poly(styrene-*co*-divinylbenzene) were prepared according to the following protocol.³¹ Briefly, polyimide-coated fused-silica capillary tubing of 350-μm o.d. and 200-μm i.d. (Polymicro Technologies, Phoenix, AZ) was silanized with 3-(trimethoxysilyl)-propyl methacrylate (Sigma-Aldrich, St. Louis, MO) according to the procedure published in ref 33 in order to ensure immobilization of the monolith on the capillary wall. For preparing the monoliths of low porosity, the silanized capillary was filled with a mixture of styrene (50 μL), divinylbenzene (50 μL), decanol (130 μL), THF (20 μL), and azobisisobutyronitrile (10 mg/mL). The polymerization mixture for the monoliths of high porosity contained 50 μL of styrene, 50 μL of divinylbenzene, 135–150 μL of decanol, and 10 mg/mL azobisisobutyronitrile. The mixture was polymerized at 70 °C for 24 h. Subsequently, the capillaries were flushed extensively with acetonitrile before preparing the ISE membranes. The specific permeabilities B_0 of the monoliths of low porosity measured with water and acetonitrile were 2.9×10^{-15} and 3.5×10^{-15} m,^{2,32} indicating only slight swelling in organic solvent due to the high degree of cross-linking in the poly(styrene-*co*-divinylbenzene) copolymer. The specific permeabilities of the monoliths of high porosity were about 8–12 times higher as compared to the monoliths of low porosity.

ISE Membranes and Electrodes. The membrane solution for the conventional Ca²⁺-ISE contained Ca²⁺ ionophore (17.2 mmol kg⁻¹, 1.38 wt %), NaTFPB (5.27 mmol kg⁻¹, 0.47 wt %), DOS (65.4 wt %), and PVC (32.7 wt %). Composition of membrane cocktail for monolithic Ca²⁺-ISEs: Ca²⁺ ionophore (16.83 mmol kg⁻¹, 1.35 wt %), NaTFPB (5.14 mmol kg⁻¹, 0.46 wt %), and DOS (98.2 wt %). For capillary Ca²⁺-ISE: Ca²⁺ ionophore (14.72 mmol kg⁻¹, 1.18 wt %), NaTFPB (5.46 mmol kg⁻¹, 0.49 wt %), DOS (93.2 wt %), and PVC (5.1 wt %). For monolithic Ag⁺-ISE: Ag⁺ ionophore (15.05 mmol kg⁻¹, 1.20 wt %), NaTFPB, 4.68 mmol kg⁻¹, 0.41 wt %), and *o*-NPOE (98.4 wt %). For monolithic Na⁺-ISE: Na⁺ ionophore (14.44 mmol kg⁻¹, 1.43 wt %), NaTFPB (5.31 mmol kg⁻¹, 0.48 wt %), and *o*-NPOE (98.1 wt %).

The membrane components for conventional ISEs (typically 300 mg of total mass) were dissolved in THF (2.0 mL) during ~1 h and poured into a glass ring fixed on a glass support to obtain a standard membrane of ~200-μm thickness. After overnight evaporation of the solvent, 5-mm disks were punched from the mother membrane, glued with THF/PVC slurry to a plasticized PVC tubing, and fixed mechanically to a 1000-μL polyethylene (PE) pipet tip. The membrane components for monolith ISEs (typically 300 mg of total mass) were dissolved in THF (2.0 mL) during ~1 h, and the solvent was evaporated under vacuum. The monolithic capillaries were fixed mechanically in PE pipet tips and filled under

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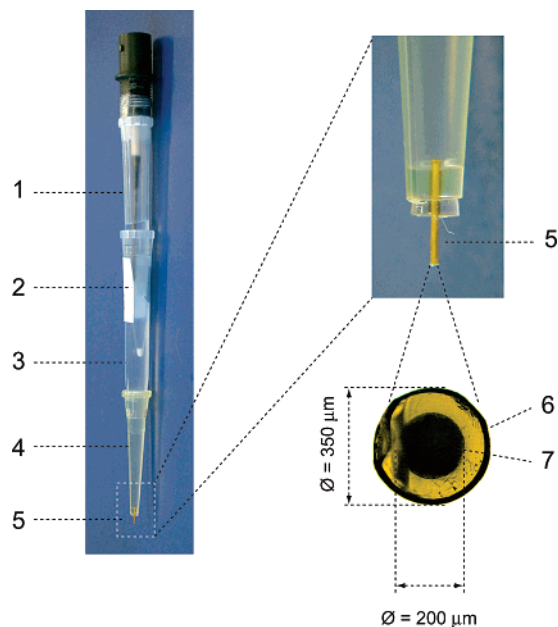


Figure 1. Construction of ISEs based on monolithic capillaries: inner reference electrode Ag/AgCl (1), second inner filling solution (2), diaphragm (3), inner filling solution (4), monolithic capillary (5), Kapton layer (6), and ISE membrane (7).

vacuum with membrane cocktail (Figure 1). A syringe was used to fill the fused-silica capillaries (RP18 GC capillary, J&W Scientific, Folsom, CA) with the membrane cocktail that contained a little THF. After overnight evaporation of the solvent, pieces of the filled capillary were cut under the microscope and fixed in PE pipet tips in the same way as the monolithic capillaries (Figure 1).

Inner filling solutions: for Ca^{2+} -ISEs, 10^{-1} M CaCl_2 or 5×10^{-2} M Na_2EDTA , pH 9.0; for Na^+ -ISEs, 10^{-3} M NaCl , and for Ag^+ -ISEs, 10^{-10} M AgNO_3 . The second inner filling solution, connected to the first one through a diaphragm, consisted of 10^{-3} M NaCl contacting the Ag/AgCl inner reference electrode. The capillary and monolith ISEs were first conditioned for 48 h in solutions of higher concentrations (in 10^{-5} M CaCl_2 , 10^{-4} M NaNO_3 , or 10^{-4} M AgNO_3) and then several days at lower concentrations (10^{-6} M NaNO_3 , 10^{-8} M CaCl_2 , or 10^{-8} M AgNO_3).

EMF Measurements. Measurements were performed with a 16-channel electrode monitor (Lawson Labs Inc., Malvern, PA) in magnetically stirred solutions at ambient temperature (21–23 °C). The calibration curves were taken by successive dilution. Data were recorded during the last minute of the time period when the drifts were $\leq \pm 1$ mV/h. Activity coefficients were obtained from the Debye–Hückel approximation, and EMF values were corrected for liquid-junction potentials with the Henderson equation. Sample pH values were determined with a Metrohm glass electrode (No. 6.0133.100, Metrohm AG, CH-9010 Herisau, Switzerland). The reference electrode was a Metrohm double-junction Ag/AgCl reference electrode (No. 6.0729.100) with 3 M KCl as reference electrolyte and 1 M NH_4NO_3 as bridge electrolyte.

Selectivity Measurements. Prior to selectivity measurements, the ISEs were conditioned in 10^{-2} M solutions of the most discriminated ions for 1 d. For each ion, a calibration curve was recorded and the selectivity coefficients were determined according to the separate solutions method.

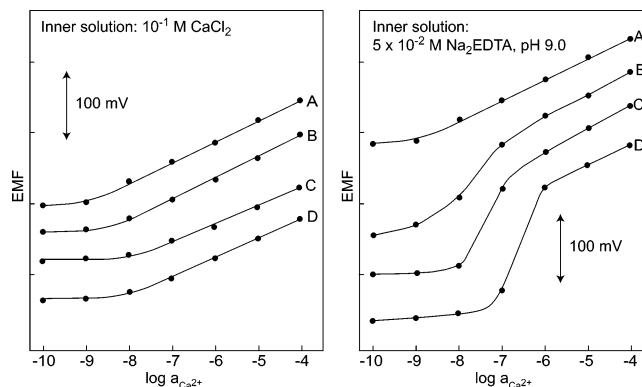


Figure 2. Calibration curves for Ca^{2+} -selective membrane electrodes having two different inner solutions. The ISEs were based on (A) monolith of low porosity (i.d., 200 μm , no PVC), (B) monolith of high porosity (i.d., 200 μm , no PVC), (C) open tubular capillary column (i.d., 200 μm , 5% PVC), and (D) conventional membrane (o.d., 5 mm, 33 wt % of PVC). The responses were recorded by successive dilutions with a background electrolyte of 10^{-4} M NaCl at pH 6.2.

RESULTS AND DISCUSSION

During the past years, tremendous advances have been achieved with potentiometric measurements in the submicromolar concentration range.^{15,16} Based on a theoretical model, the steady-state^{7,9,10} and transient potentiometric responses of ISEs³⁴ are well understood even in the presence of zero-current transmembrane ion fluxes. Various techniques of reducing the adverse effects of such fluxes have been successfully tested recently (see introduction). Some of them, such as the covalent immobilization of membrane components^{22,23} or rotating electrode potentiometry,²⁵ are, however, demanding or not generally applicable. Therefore, a simple method is desirable that would allow constructing ISEs with low detection limits in a straightforward manner. As a novel technique in these lines, we here apply monolithic capillaries as membrane matrix. The usual components of ISE membranes, i.e., the ionophore and ion exchanger, are dissolved in a solvent (which is used as a plasticizer in conventional PVC membranes) and filled into a 3–5-mm-long piece of a monolithic capillary mounted in a pipet tip (Figure 1). We compare the behavior of such ISEs having monoliths of two different porosities (high, low; see Experimental Section) and similar open tubular capillaries with that of conventional PVC-based ISE membranes.

In Figure 2, the calibration curves are given for the above-mentioned four types of membranes investigated with two kinds of inner solutions. On the left, they are shown for 10^{-1} M CaCl_2 , which is known to induce a slight coextraction of CaCl_2 from the inner solution to the membrane,⁸ and, thus, a transmembrane concentration profile decreasing toward the sample. The concomitant Ca^{2+} flux is responsible for the less than optimal lower detection limit of the conventional ISE (D). With the monolithic capillary of low porosity (A), the lower detection limit is better by ~ 1 order of magnitude. On the other hand, 5×10^{-2} M Na_2EDTA at pH 9.0 as inner solution (Figure 2, right) brings about an almost quantitative exchange of Ca^{2+} with Na^+ in the inner membrane surface layer. In this case, the concentration profile in the ISE membranes strongly decreases toward the inner solution, and the corresponding Ca^{2+} flux depletes the sample near the membrane surface, which induces an apparently super-Nernstian response of the conventional membrane (D) below 10^{-6} M

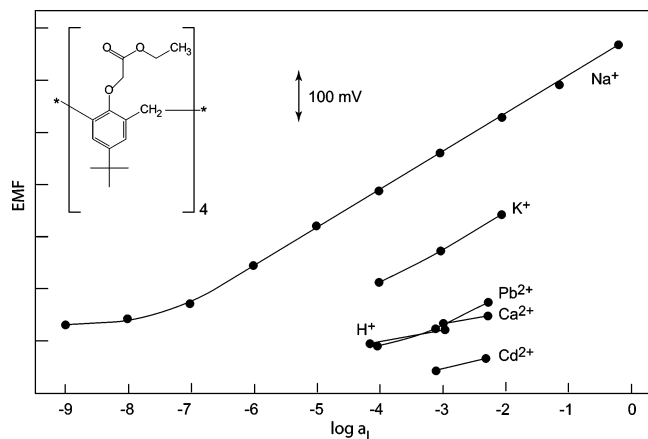


Figure 3. Calibration curves obtained for primary and interfering ions with a Na^+ -selective monolith ISE.

Ca^{2+} . On the contrary, this inner solution has virtually no effect on the response of the monolith ISE of low porosity (A). The fact that the response curves A with the two inner solutions are practically identical indicates that ion flux effects above the observed lower detection limit of 10^{-9} M Ca^{2+} are not relevant with this membrane. The ISEs with the monolith of high porosity (B) and the open tubular capillary (C) show intermediate responses with both inner solutions. Note that none of the two inner solutions are optimal for trace analytical measurements. They were selected here to demonstrate the different sensitivity of the investigated membranes to transmembrane concentration gradients.

Except for H^+ , potentiometric selectivity coefficients, $K_{\text{Ca},\text{J}}^{\text{pot}}$, were somewhat superior for the monolith ISEs than for the conventional membranes (H^+ , $-2.6/-3.5$; Na^+ , $-4.1/-3.9$; K^+ $-4.4/-3.9$ for monolith and conventional ISEs, respectively). Based on the Na^+ and H^+ selectivities, the static lower detection limit,¹⁰ i.e., in the absence of ion fluxes, should be $\sim 10^{-12}$ M Ca^{2+} . This is much lower than the value obtained with the monolith ISE of low porosity (2×10^{-9} M, curves A) so that the release of primary ions from the membrane into the sample is still a relevant process at this concentration. A quantitative estimate of the change in ion fluxes in monolith ISEs relative to those in conventional ISE membranes can be obtained from the position of the super-Nernstian step, $a_{i,\text{step}}$, which is directly proportional to the effective diffusion coefficient of the ions in the membrane.⁹ Since with the monolith of low porosity, such a step response is not visible, it must be $\leq 10^{-9}$ M, i.e., lower by at least 3 orders of magnitude with the monolith than with conventional membranes.

Due to the high degree of cross-linking of the organic monolith and the low swelling in organic solvents, we can assume that the porous structure is mostly retained upon filling the pores with the ionophore solutions. The ohmic resistance of the monolith ISE (A) was 1.6 G Ω as compared to 5.0 M Ω for the conventional ISE (D). Since the surface of the conventional membrane is ~ 400 times larger and its thickness ~ 25 times smaller than those of the monolithic capillary ISEs, an increase in the resistance of the latter by a factor of $\sim 10^4$ is expected purely because of the different geometries. On the other hand, the absence of PVC in the monolith ISEs and its low amount in the open tubular capillary should decrease it by a factor of ~ 10 – 100 .³⁷ This rough estimate would account for the difference in the resistance of the monolith and conventional ISEs.

Table 1. Potentiometric Selectivity Coefficients, $\log K_{\text{Na},\text{J}}^{\text{pot}}$ and Response Slopes (in Parentheses, mV/decade) Obtained with the Separate Solution Method for the Na^+ -Selective Monolith ISE Compared with Results Published Earlier for *o*-NPOE/PVC⁴² and Poly(methyl methacrylate)/Poly(decyl methacrylate) (MMA–DMA) Membranes⁴³

ion J	monolith ^a	<i>o</i> -NPOE/PVC	MMA–DMA
H^+	-4.8 ± 0.4 (42.4)	-2.2	
Li^+		-2.5	-3.8 ± 0.1 (45.6)
K^+	-2.7 ± 0.1 (55.2)	-2.0	-2.8 ± 0.1 (56.9)
Mg^{2+}		-2.9	-4.3 ± 0.1 (30.0)
Ca^{2+}	-6.0 ± 0.1 (30.7)	-2.6	-4.9 ± 0.1 (28.6)
Cd^{2+}	-6.5 ± 0.1 (25.3)		
Pb^{2+}	-5.6 ± 0.1 (29.6)		

^a Values obtained from four measurements. Slope for Na^+ : 59.2 mV/decade (in the range of 10^{-2} – 10^{-7} M Na^+).

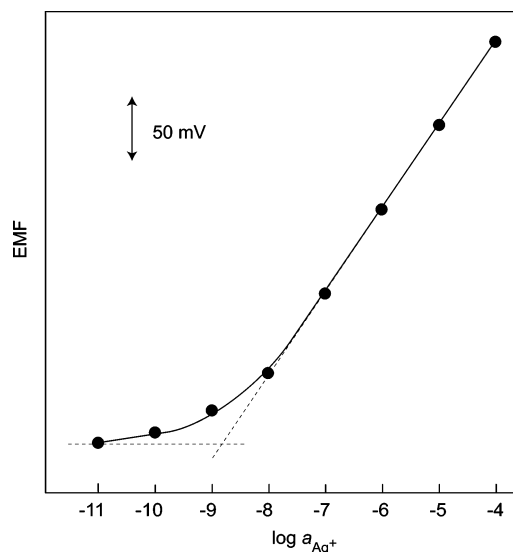


Figure 4. Calibration curve for a Ag^+ -selective monolith ISE.

As a second test, the Na^+ -selective ionophore, 4-*tert*-butylcalix-[4]arene tetraacetic acid tetraethyl ester,³⁸ was used in a monolith ISE. The calibration curve (Figure 3) indicates a lower detection limit of 3×10^{-8} M Na^+ , which represents the first example of a Na^+ -ISE with submicromolar detection limit. Note that this was achieved with 10^{-1} M NaCl as inner solution. In this case too, the detection limit is still not so good as that expected (10^{-11} M at pH 6.2) in the absence of ion fluxes on the basis of the selectivity coefficients (cf. Table 1). Except for H^+ (slope, ~ 40 mV/decade), close to Nernstian responses were obtained for the discriminated interfering ions too. Thus, the selectivity coefficients are not biased by ions released from the membrane. This is also reflected by comparing these selectivities with those found earlier with an *o*-NPOE/PVC membrane, where the values were much worse, especially for the strongly discriminated interfering ions, H^+ and Ca^{2+} (see Table 1).

As a further example, the response of a Ag^+ -selective monolith ISE is shown in Figure 4. With 10^{-10} M AgNO_3 as inner solution,

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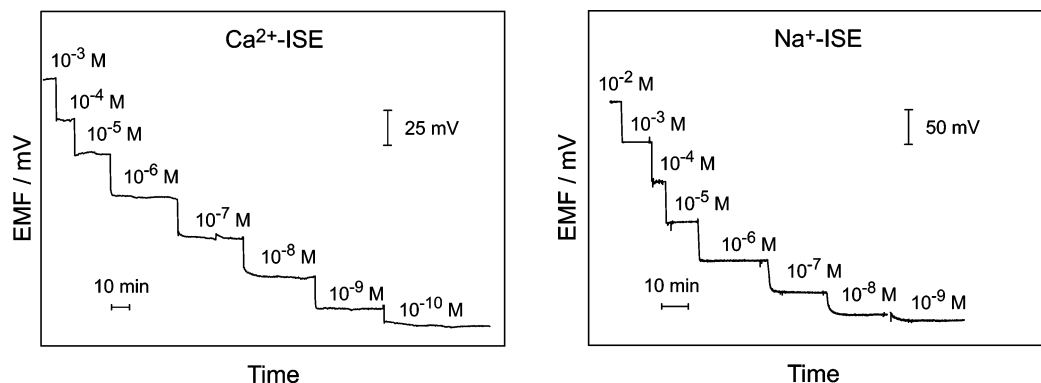


Figure 5. Time responses obtained with a Ca^{2+} -selective (left) and a Na^{+} -selective monolith ISE (right).

the lower detection limit of $2 \times 10^{-9} \text{ M Ag}^{+}$ is about the same as that obtained earlier for a liquid-contact ISE with optimized inner solution.¹⁰ Again, despite the suppressed ion fluxes, the lower detection limit of the monolith ISE is not better than that of the liquid-contact ISE with optimized inner solution. This suggests that not the transmembrane ion fluxes but other processes might be responsible for the observed lower detection limit.

The time responses of the Ca^{2+} and Na^{+} monolith ISEs are shown in Figure 5. They are fast despite the experimental procedure of successive dilutions starting at rather high concentrations. For example, a drift of $<0.4 \text{ mV/min}$ was obtained for the Ca^{2+} - and Na^{+} -ISE within 4 and 5 min, respectively. The corresponding response times for repeated alternate measurements of 10^{-4} and 10^{-6} M NaCl with the Na^{+} -ISE were <2 and <3.5 min for the higher and lower concentration, respectively. The responses of the Ag^{+} -ISE were slower by a factor of ~ 2 . At steady state, the drifts in 10^{-6} M solutions were $<0.01 \text{ mV/min}$ for both the Na^{+} - and the Ag^{+} -ISEs. The lifetime of monolith ISEs is at least of the order of months. The average potential drifts on the long term are not bigger than those for the short term.

At first glance, the monolith ISE might be confused with earlier approaches,³⁹ where microporous materials such as carbon saturated with the membrane components were used as internal contact of a membrane. However, in those cases, no internal solutions are present and thus no transmembrane fluxes to be suppressed may occur. Moreover, unlike in the present paper, the porous material was merely used as an internal contact but not as a sensing membrane. In a very recent paper on these lines, the lower detection limit of a Pb^{2+} -selective PVC membrane was investigated with such an internal contact.⁴⁰ The lower detection limits in samples without ion buffers was merely $10^{-7.3}$, i.e., less good by 2–3 orders of magnitude than the best solid or liquid contact Pb^{2+} -ISEs known so far.¹⁷

Compared with previously described ISEs for the same ions, ion flux effects were strongly suppressed in all investigated cases. Interestingly, however, the lower detection limits are not better than the best values obtained earlier with optimized inner solutions. They are significantly less good than expected from the selectivity values in the absence of ion fluxes (static detection limit).

Hence, they seem still to be determined by certain not yet identified processes that induce a slow release of primary ions from the membrane. Earlier, it was shown by the group of Bakker that the lipophilicity of the ion exchangers normally used is so high that simple leaching cannot account for the observed value.⁴¹ However, their slow decomposition might be a possible explanation for the fact that the detection limits are not even better than the observed values. Further improvements of the performance of monolith ISEs is expected once these processes are understood and can be controlled.

Even though the performance of the monolith ISEs is not superior to the best values obtained earlier with optimized systems, monolithic ISEs offer various significant advantages. For trace-level measurements, the inner solution of conventional liquid-contact ISEs must be optimized for each target application. Although this is a straightforward process,¹⁰ it is rather time-demanding because all relevant selectivity coefficients must be determined first. Since this is not required with the monolith ISEs, their development is much faster. Due to their small dimensions, it is also easy to reduce the sample volumes with monolith ISEs, which is an advantage if optimal detection limits in terms of absolute amounts are sought for.

CONCLUSIONS

We have demonstrated that lipophilic monolithic phases are attractive matrixes for ISEs. The lower detection limit and the selectivity behavior are, independently of the composition of the inner solution, about as good as those obtained with optimized liquid-contact ISEs. The tedious optimization of the inner solution is no longer required when developing an ISE for a target application. So far, it is not yet clear whether the use of porous monolithic capillaries is mandatory for achieving such a dramatic reduction of transmembrane ion fluxes. Currently, we are investigating the behavior of analogous rod-shaped membranes prepared by in situ polymerization in the presence of the required membrane components.

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