Multiionophore-based solid-state potentiometric ion sensor as a cation detector for ion chromatography

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Abstract

A new solvent/polymeric multiion-selective membrane electrode is described for use as a flow-through detector in ion chromatography. Unlike conventional ion-selective membranes that utilize only one type of ionophore, the multiion-selective membranes incorporate several different ionophores. In this study, a $K^+/NH_4^+/Na^+/Ca^{2+}$ selective membrane has been prepared by incorporating four different neutral-carrier ionophores in a strongly adhesive polyurethane matrix. This membrane is cast on solid electrode surfaces, with no internal electrolyte solution, to form solid-state multiion sensors. The detection characteristics of the multiionophore membranes, which are controlled by the amounts and ratios of the ionophores they contain, are examined in a flow-injection arrangement. The sensors have been demonstrated in the target application, a flow-through ion chromatography system.

Introduction

High-performance ion chromatography is an attractive method for simultaneous multicomponent analysis of mixtures of anions and cations [1]. In most applications of ion chromatography, the conductometric method is used to detect eluting ions. The high temperature coefficients and limited detection capabilities of the conductivity detector have prompted efforts to implement spectrophotometric detection in ion chromatography [2]. The cost of spectrophotometric detection, however, makes ion chromatography very expensive. Another possible replacement for the conductivity detector is an inexpensive potentiometric sensor. Unlike conductometric or amperometric detectors, the response of potentiometric ion-selective electrode (ISE) detectors does not depend on the surface area of the electrode. This could allow further reduction in the detector cost through miniaturization.

Highly selective neutral-carrier-based solvent/polymeric ISEs are now routinely used as flow-through detectors for accurate and rapid determination of various ionic species, e.g., K^+, Na^+, Ca^{2+}, CO_3^{2-}, Cl^-, etc. [3–5]. However, direct application of such ISEs to ion chromatography systems does not allow the detection of different ions with comparable detectabilities. Recently, several researchers have attempted to employ neutral-carrier-based ISEs as flow-through cation detectors for ion chromatography [6–8]. In one effort to balance the detectability of different ions, several different cation ionophores (i.e., valinomycin, benzo-15-crown-5, nonactin, and tetranactin) were examined [6]. Of these neutral carriers, tetranactin was the least selective, so it was used to prepare a cation detector for ion chromatography [6, 7]. Another effort included the use of a less selective ionophore in conjunction with selection of an appropriate plasticizer [8].

This work presents a new approach for designing a neutral-carrier-based ISE detector for ion chromatography. Unlike conventional ion-selective membranes that utilize only one type of ionophore, this new solvent/polymeric ion-selective membrane incorporates several different neutral-carrier-type ionophores in order to provide the membranes with multiion selectivity. The response characteristics of the resulting membranes are controlled by the amounts and ratios of the ionophores incorporated in the membranes. In this work, valinomycin, nonactin, *N,N,N',N'*-tetracyclohexyl-3-phenylenedioxydiacetamide (ETH 2120), and *N,N,N',N'*-tetracyclohexyl-1,2-oxapentanediamine (ETH 129) were

employed to provide selectivities of the membranes for potassium, ammonium, sodium, and calcium, respectively. As a preliminary demonstration, a $K^+/NH_4^+/Na^+/Ca^{2+}$ selective membrane electrode was shown to detect eluting cations very well in ion chromatography.

Solid-state multiion sensors were fabricated by casting the multiionophore-doped polymer membranes on solid electrode surfaces with no internal electrolyte solution. Both macrosized and miniaturized silicon-based solid-contact ISE structures [9–12] were used in this study. Finally, the analytical utility of this inexpensive solid-state multiion sensor, made with a strongly adhesive polyurethane-matrix membrane [11, 13], was demonstrated in flow-injection arrangements.

Experimental

Reagents

Poly(vinyl chloride) (PVC), bis(2-ethylhexyl) adipate (DOA), potassium tetrakis(p-chlorophenyl)borate (KTpClPB), nonactin, N,N,N',N'-tetracyclohexyl-3-phenylenedioxyldiacetamide (ETH 2120), and N,N,N',N'-tetracyclohexyl-1,2-oxapentanediamide (ETH 129) were obtained from Fluka (Ronkonkoma, NY); valinomycin was purchased from Sigma Chemical Co. (St. Louis, MO). Hydroxylated PVC (a copolymer of vinyl chloride, vinyl acetate and vinyl alcohol (PVC/Ac/Al), 80/5/15 wt.%) was obtained from Scientific Polymer Products, Inc. (Ontario, NY), while Tecoflex polyurethane (SG-80A) was a product of Thermedics, Inc. (Woburn, MA).

All other chemicals used were analytical-reagent grade. Standard solutions and buffers were prepared with deionized water.

Ion-selective membranes

Preparation of polymer-matrix membranes

PVC- and polyurethane (PU)-based ion-selective membranes were prepared by incorporating a given amount of ionophore(s) into PVC or PU/(PVC/Ac/Al) (80/20 wt.%) matrices as described previously [11]. In this study, varying amounts of ionophores (nonactin, valinomycin, ETH 2120, and ETH 129) and lipophilic additive (KTpClPB), 66 mg of PVC or PU/(PVC/Ac/Al), and 132 mg of DOA were dissolved in 1.0 ml tetrahydrofuran (THF) for casting in a 22 mm (i.d.) glass ring for use in conventional electrode bodies, or for casting directly on the solid-state electrodes.

Evaluating potentiometric response and selectivity

The electrochemical properties of the membranes were evaluated in conventional ion-selective electrodes. For all types of membranes, after cure, 5.5 mm diameter disks were cut out and placed in Phillips electrode

bodies (IS-561) (Glasblaserei Möller, Zurich). For multiion-selective electrodes, an aqueous mixture of NaCl, KCl, NH_4Cl, and $CaCl_2$ (0.1 mol l^{-1} each) was employed as the internal filling solution. The external reference electrode was an Orion sleeve-type double-junction Ag/AgCl electrode (model 90-02). Electrodes were connected through a high-impedance amplifier to an IBM AT-type computer equipped with an analog-to-digital converter, or through a Fisher Accumet model 157 electrode switch box to a Fisher Accumet model 620 pH–mV meter (Romulus, MI).

Static-mode potentiometric measurements

Initial potentiometric evaluation of membranes of various compositions was conducted by employing a static arrangement. The calibration data were obtained from additions of standard solutions to 200 ml of background electrolyte (0.05 mol l^{-1} Tris-HCl, pH 7.2) at room temperature. The solutions were magnetically stirred throughout and equilibrium potentials were recorded. Selectivity coefficients were determined by the separate solution method [14].

Flow-injection measurements

A large volume wall-jet cell was used to evaluate the performance of the multiion-selective membrane electrodes in a flow-injection analysis mode [15, 16]. A Phillips electrode body was fitted with a special flow cap for use as a flow-through detector in a large volume wall-jet configuration. An Orion Ag/AgCl reference electrode and the working multiion-selective electrodes were placed in a large beaker of reagent buffer (0.05 mol l^{-1} Tris-HCl, pH 7.2). Teflon tubing (0.012 in i.d.) connected the flow cap to the injection valve. A peristatic pump (Ismatech model 7331-00, Zurich) and a Rheodyne four-way rotary valve (model 7125) equipped with a sample loop completed the flow-injection setup. For these studies, 150 μl of various cation standard or mixture solutions was injected into a buffer stream (7.5 ml min^{-1}) of 0.05 mol l^{-1} Tris-HCl, pH 7.2. The standards were prepared with the same buffer solution. The e.m.f. values were recorded every 0.1 s at room temperature, using the high-impedance amplifier/analog-to-digital converter setup described in the previous section.

Ion chromatography

Chromatographic measurements were carried out using a pump (model 200; Scientific Systems, State College, PA) for HPLC, a sample injector (model 7125; Rheodyne, Inc., Cotati, CA) with a 250 μl sample loop, and a cation exchange column (ION-210; Interaction Chemicals, Mountain View, CA). The eluent used was 0.05 mol l^{-1} Tris-HCl, pH 7.2 solution. Potentiometric detection was done using the large volume wall-jet

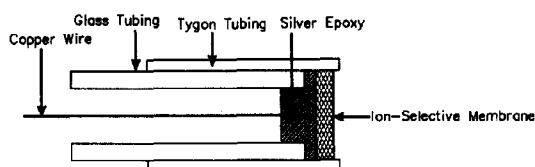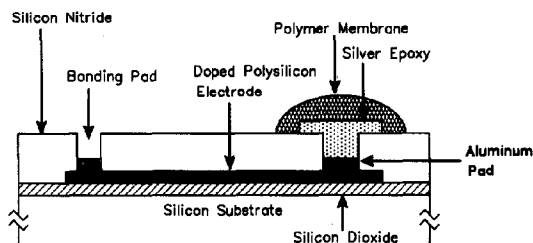Fig. 1. Schematic drawing of the macrosized polymer-coated solid-contact ISE.

Fig. 2. Cross-sectional view of a solid-state electrode.

electrode design described in the previous section. The potentiometric detector was connected to an Accumet pH–mV meter (model 925; Fisher Scientific, Romulus, MI), and analog outputs were recorded on a strip-chart recorder (Fisher Recordall Series 5000).

Solid-state sensors

The macrosized polymer-coated solid-contact ISEs (see Fig. 1) were fabricated using the silver epoxy test structure described previously [10, 11]. Multiion-selective sensors were prepared by applying one drop of 1.0 mol l^{-1} SiCl$_4$ to the silver epoxy surface then casting 50 μl of the PU-based multiionophore membrane casting solution and evaporating the solvent overnight.

The solid-state electrodes were fabricated as described previously [9, 12], with screen-printed silver epoxy electrode contacts. These solid-state electrodes (see Fig. 2 for cross section) model a single electrode site on the integrated chemical sensors made by our group [18, 19]. Solid-state multiion-selective sensors were prepared by casting the PU-matrix multiionophore membrane on top of the silver epoxy electrode contact. These multiion-selective solid-state electrodes were fitted to a modified flow cap for use as a flow-through detector in a wall-jet flow-injection system.

Results and discussion

Initially, we employed three different ionophores, valinomycin, nonactin and ETH 2120, in order to evaluate the use of multiple ionophores in multiion-selective membrane electrodes. These neutral-carrier-type ionophores provide the membranes with potassium, ammonium, and sodium selectivities, respectively. We sys-

tematically demonstrated that the response characteristics of the resulting membranes can be controlled by the amount and ratio of the ionophores incorporated into the PVC membrane matrices [16].

Several different amounts of ETH 129 were further incorporated in the K$^+$/NH$_4^+$/Na$^+$ ion-selective membrane formulation to induce selectivity towards the calcium ion. Figure 3 illustrates the response peaks obtained by injecting 150 μl of cation standard solutions (10^{-3} mol l^{-1} each) into the wall-jet flow-injection system as described in the Experimental section. The membranes were prepared by incorporating active components into 66 mg of PVC and 132 mg DOA. The response peaks for the K$^+$/NH$_4^+$/Na$^+$ ion-selective membrane are shown in Fig. 3(A). Three other combinations of ionophores and lipophilic additive, as listed in Table 1, were tested to evaluate the relationship between the amount of each ionophore used and the membrane response. As we expected, the response to various ions is a function of the amounts of ionophore and lipophilic additive. Membrane B has the same amount of ETH 2120 (Na$^+$ ionophore), but adds ETH 129 (Ca^{2+} ionophore), and has increased amounts of nonactin and valinomycin. Compared to the Na$^+$ response, the Ca^{2+}, NH$_4^+$ and K$^+$ responses are increased (see Fig. 3(B)). The formulation of membrane C maximizes the response to the four ions (note 10 mV bars). Figure 3(D) illustrates the response of a typical ETH 129-based single ionophore membrane exhibiting a significant response only towards the calcium ion. It is clear that the selectivity of the membrane can be controlled by varying the types and amounts of ionophores incorporated.
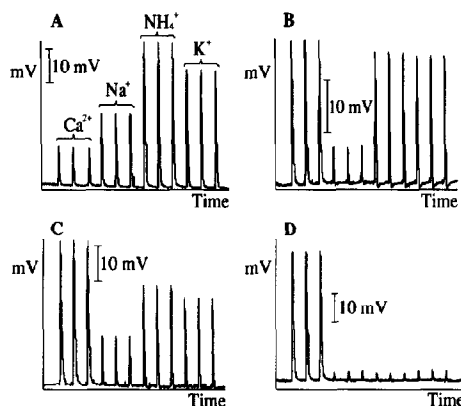

Fig. 3. Potentiometric flow-injection response peaks for 1.0 mmol l^{-1} of Ca^{2+}, Na$^+$, NH$_4^+$ and K$^+$ obtained with ion-selective membrane electrodes doped with: (A) 0.04 mg valinomycin, 0.07 mg nonactin, and 4 mg ETH 2120; (B) 0.2 valinomycin, 0.33 mg nonactin, 4 mg ETH 2120, 0.5 mg ETH 129, and 0.2 mg KTpClPB; (C) 0.1 mg valinomycin, 0.16 mg nonactin, 8 mg ETH 2120, 0.3 mg ETH 129, and 0.12 mg KTpClPB; (D) 2 mg ETH 129 and 0.8 mg of KTpClPB.

TABLE 1. Membrane additives for Fig. 3

Membrane formulation	Ionophore and lipophilic additive content				
	ETH 129 (mg)	ETH 2120 (mg)	Nonactin (mg)	Valinomycin (mg)	KTpClPB (mg)
A	0	4	0.07	0.04	0
B	0.5	4	0.33	0.2	0.2
C	0.3	8	0.16	0.1	0.12
D	2	0	0	0	0.8

The $K^+/NH_4^+/Na^+/Ca^{2+}$ ion-selective membrane C was further evaluated in the wall-jet flow-injection system by injecting different concentrations (10^{-5}, 10^{-4}, and 10^{-3} mol l^{-1}) of calcium, sodium, ammonium, and potassium ions, respectively (Fig. 4). It is apparent that, unlike most single ionophore-based ISEs, the multiple ionophore detector achieved comparable sensitivities towards all cations injected.

Figure 5 shows typical ion chromatograms obtained by using ISE detectors with (A) a multiple ionophore membrane and (B) a nonactin-based single ionophore membrane. While the ION-210 cation exchange column is intended for the separation of transition metal ions, we successfully employed this column to separate several monovalent alkali metal cations, including sodium, ammonium, and potassium ions. Potentiometric detection was carried out with the wall-jet flow-injection system. The chromatograms were obtained by injecting 250 μl of a mixture containing several different monovalent cations in an equal concentration of 0.25 mmol l^{-1} with 0.05 mol l^{-1} Tris-HCl, pH 7.2 buffer as the eluent at a flow rate of 2.5 ml min^{-1}. As can be seen from Fig. 5, the multiple ionophore ISE detector exhibited detection capabilities superior to those of the nonactin-based detector.
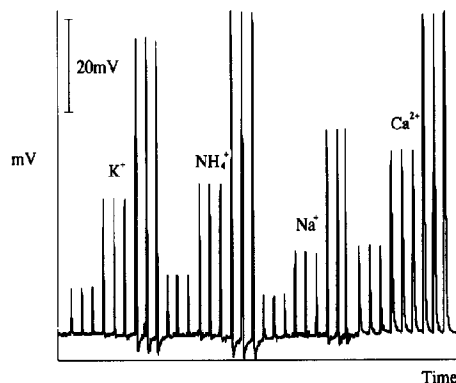

Fig. 5. Ion chromatograms obtained for the injection of 250 μl of a mixture containing 0.25 mmol l^{-1} of lithium, sodium, ammonium, and potassium chlorides using ISE detectors; (A) $K^+/NH_4^+/Na^+/Ca^{2+}$ selective multiple ionophore membrane electrode; (B) nonactin-doped single ionophore membrane electrode.

In this work, we employed both the macrosized and miniaturized solid-contact ISE structure previously described [9–12] to examine the feasibility of adapting our multiionophore membranes to our solid-state chemical sensor technology [12, 18, 19]. The silver epoxy solid contact of the macrosized test structure [10, 11] was coated with the PU/(PVC/Ac/Al)-matrix membrane doped with multiple ionophores (valinomycin, nonactin, ETH 2102, and ETH 129). The resulting multiion-selective solid-state electrode was evaluated as a flow-through cation detector in the wall-jet flow-injection system. The multiion selectivity of the sensor was demonstrated, as shown in Fig. 6.

Finally, a miniaturized, solid-state, multiionophore sensor was fabricated with a strongly adhesive polyurethane-matrix membrane following the method previously reported [9, 12]. The screen-printing mask dimensions of the silver epoxy sites of the miniature solid-state electrodes were 750 μm squares. Figure 7, taken with the miniature sensor, can be compared to Fig. 6; the miniature sensor has less noise and greater response. As seen in the data of Fig. 8, this inexpensive multiionophore sensor performed very well in detecting a variety of eluting cations in a flow-through system.

Fig. 4. Potentiometric flow-injection response obtained for the injection of 150 μl of 0.01, 0.1 and 1.0 mmol l^{-1} cation standards using an ion-selective membrane electrode doped with valinomycin, nonactin, ETH 2120, and ETH 129.
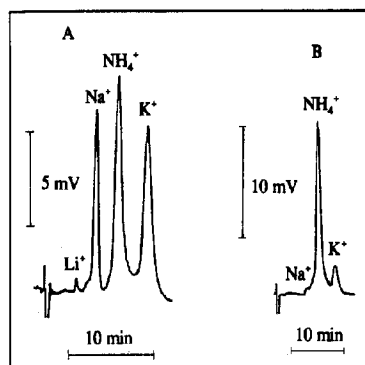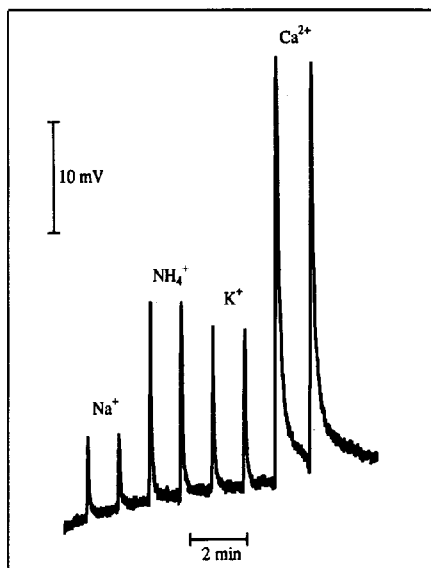
Fig. 6. Potentiometric flow-injection response peaks for 0.1 mmol 1^{-1} of Na^+, NH_4^+, K^+, and Ca^{2+} obtained with a macrosized solid-contact electrode coated with a multiionophore PU-matrix membrane.
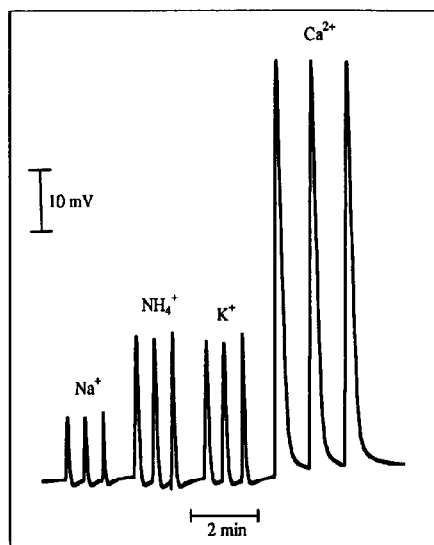

Fig. 7. Potentiometric flow-injection response peaks for 1.0 mmol 1^{-1} of Na^+, NH_4^+, K^+, and Ca^{2+} obtained with a miniaturized solid-contact electrode coated with a multiionophore PU-matrix membrane.

The linear range for both the macrosized and miniature solid-contact sensors having membranes as described above is approximately 5×10^{-5}–1×10^{-1} mol 1^{-1}. The slopes are: 43.7 mV decade^{-1} for potassium; 46.6 mV decade^{-1} for ammonium; 43.1 mV decade^{-1} for sodium; and 28.5 mV decade^{-1} for calcium. Limits
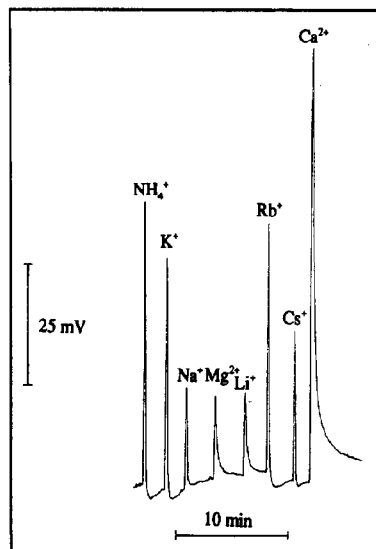

Fig. 8. Flow-injection response obtained for the injection of 50 μl of 1.0 mmol 1^{-1} metal ion standards using a miniaturized, solid-state, multiionophore sensor.

of detection are: 9.8×10^{-6} mol 1^{-1} for potassium; 8.6×10^{-6} mol 1^{-1} for ammonium; 1.7×10^{-5} mol 1^{-1} for sodium; and 9.0×10^{-6} mol 1^{-1} for calcium. The reproducibility of these characteristics in the multiion membranes seems to be a function only of our ability to control the exact quantities of ionophores incorporated into the membrane phase, just as is the case in conventional single ionophore membranes.

The ionophores in these membranes will leach at different rates, with the membrane lifetime being determined by the one that leaches most rapidly. Based on the lipophilicity values of valinomycin, nonactin, ETH 2120, and ETH 129 previously reported, membranes incorporating these ionophores will have lifetimes of more than six months even under continuous flowing conditions. Therefore, the lifetime of the solid-state electrodes will more likely be determined by limitations in membrane adhesion rather than by ionophore leaching. As stated earlier, these membranes were formulated to adhere strongly to the surface of the solid-state sensors [13]. We have tested variations of single-ionophore polyurethane-based membranes soaking in test solution for one month, and found nearly constant slope and absolute temperature variations of less than 120 mV over this period [17].

Several ion chromatography applications would benefit from the availability of these reliable low-cost/ disposable passive chemical sensors that could be used with portable instrumentation. To satisfy many present and future applications, these chemical sensors could include integrated circuitry. This would improve the sensor signal-to-noise ratio; provide temperature com-

pensation of the sensor response; and allow the sensor to interact with a host controller, which could make real-time decisions that would result in the initiation of actuator-driven control sequences, resulting in a complete chemical-sensing system. For example, Fig. 9 is a photomicrograph of a batch-fabricated chemical multisensor chip. The four solid-contact ion-selective electrode sites (Ca^{2+}, pH, NH_4^+, and K^+) directly connect to on-chip silicon-on-insulator (SOI) CMOS operational amplifier buffers. Similarly, Fig. 10 is a photomicrograph of an SOI CMOS chemical multisensor chip with four ion-selective electrode sites (Na^+, Ca^{2+}, pH, and K^+), a programmable gain stage, 14 user-programmable read-out modes, a 12-bit analog-to-digital converter, temperature sensor, and an RS-422 serial communication interface. Both of these active chemical sensors (which vary in complexity) were fabricated with a standard manufacturing sequence, which utilizes the screen-printing technology previously developed by our research group [18, 19]. Now that the functionality of these new multiion-selective membranes has been demonstrated, they could be screen-printed onto sensors with on-chip electronics using our existing manufacturing technology.
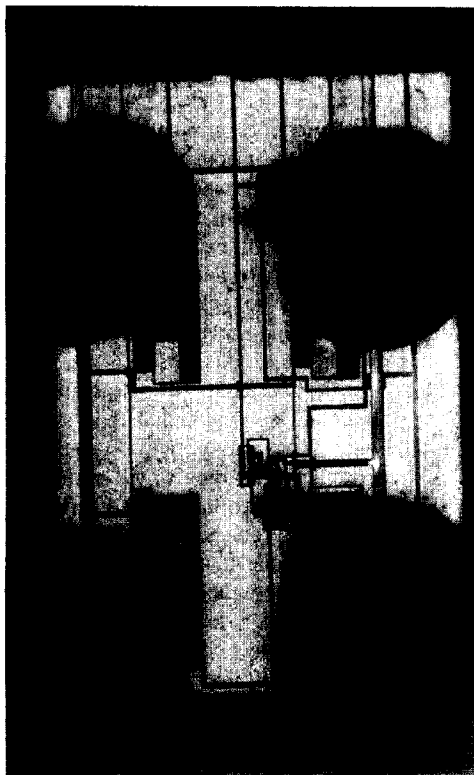

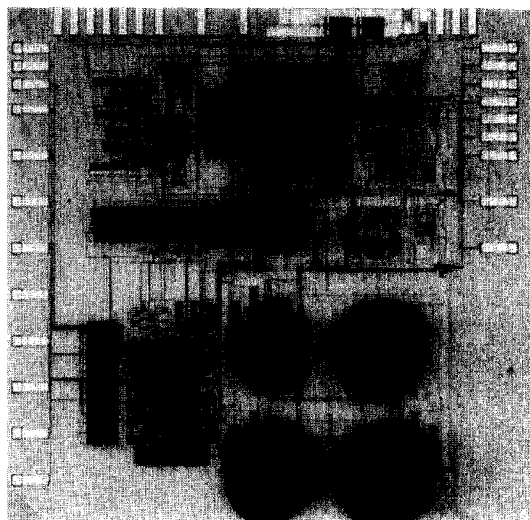Fig. 9. Photomicrograph of an active chemical multisensor chip. The total die size is 1.7 mm×2.5 mm (from [18, 19]).

Fig. 10. Photomicrographs of a programmable chemical multisensor chip. The die size is 5.8 mm×6.0 mm; the circuit includes 4917 transistors (from [18, 19]).

Conclusions

We have developed miniature multiionophore-based solid-state potentiometric ion sensors that are well suited for use as ion chromatography detectors. This approach brings the high selectivity and low detection limits of neutral carrier ionophores to ion chromatography. Detectabilities for the ions of interest are matched by using the correct ratios of ionophores. The small size of the sensors means that little ionophore is needed, and the detectors can be inexpensive. They will be especially useful in situations where a small detector is necessary, such as in capillary ion chromatography. A multiion sensor selective to calcium, sodium, ammonium, and potassium has been successfully demonstrated as a detector for eluting cations in ion chromatography.

Acknowledgements

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Geun Sig Cha received his B.S. degree from Korea University in 1977 and his Ph.D. in analytical chemistry from the University of Michigan in 1989. He continued his research at the University of Michigan as a joint research fellow in the Departments of Chemistry and Electrical Engineering and Computer Science until January, 1991. He is now a professor of analytical chemistry in the Department of Chemistry at Kwangwoon University, Seoul, Korea. His current research interest involves the development of new ion- and bioselective membrane electrodes and the design of enzyme-linked competitive and non-competitive binding assay methods.

Marek Trojanowicz obtained his M.Sc., Ph.D. and D.Sc. (1981) degrees in the Department of Chemistry, University of Warsaw. He is an author of over 130 scientific papers and patents in the field of electroanalysis, flow analysis, chromatography, and biosensors and a book on automation in chemical analysis. He is currently a professor of analytical chemistry in the Chemistry Department, University of Warsaw, head of the Laboratory for Flow Analysis and Chromatography and scientific secretary of the Committee for Analytical Chemistry of the Polish Academy of Sciences. He has been a visiting professor at the University of Michigan (USA) and Pontifical Catholic University of Rio de Janeiro (Brazil).

Dong P. Liu received her B.S. degree in chemistry from the University of Science and Technology of China in 1986. In 1989, she received her M.S. in medicinal chemistry from Beijing Medical University. She received her Ph.D. degree in electro-analytical chemistry at the University of Michigan in 1994, under the guidance of Professor Mark E. Meyerhoff, and is now employed at Ciba Corning.

Howard D. Goldberg received his B.S. degree in electrical engineering from Lehigh University in 1987. He received his M.S. (1989) and his Ph.D. (1993) in electrical engineering, with an emphasis on solid-state electronics, from the University of Michigan. His Ph.D. work was concerned with improving the reliability and lifetimes of solid-contact potentiometric chemical sensors, as well as the development of a new mass-

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Robert W. Hower received his B.S. and M.S. degrees in electrical engineering from the University of Michigan in 1992. Robert is presently working on his Ph.D. in electrical engineering under the guidance of Professor Richard B. Brown. His Ph.D. work is focused on the mass fabrication of multi-site integrated electro-, bio-, and opto-chemical sensors.

Richard B. Brown received B.S. and M.S. degrees in electrical engineering from Brigham Young University in 1976. From 1976 to 1981 he worked in computer design as Vice-President of Research and Development at Holman Industries, Oakdale, CA, and then Manager of Computer Development at Cardinal Industries, Webb City, MO. Richard received an electrical engineering Ph.D. at the University of Utah in 1985. His Ph.D. work was in the area of solid-state chemical sensors, which included development of a custom MOS fabrication process and integration of multiple transducers with analog and digital circuitry. In September 1985, he joined the University of Michigan Department of Electrical Engineering and Computer Science faculty. He has been instrumental in shaping the VLSI program and introducing a uniform set of electronic CAD tools into the curriculum. His areas of current research are high-speed digital integrated circuits and solid-state sensors.