

Chemically modified ion-sensitive field-effect transistors: elimination of the liquid junction potential in a double sensor flow-injection analysis cell

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Abstract

A flow-through cell was designed that can be used for flow-injection analysis with two chemically modified ion-sensitive field-effect transistors (CHEMFETs) in close proximity. This offers the possibility of a differential measurement without influence of the liquid junction potential. The differential signal of a potassium- and a sodium-selective CHEMFET responded in a Nernstian manner and selectively towards potassium in an excess (fixed) concentration of sodium. A highly lead-selective CHEMFET was used in the same flow cell in combination with a potassium-selective CHEMFET.

Keywords: Flow injection; Ion selective electrodes; Sensors; Ion-sensitive field effect transistors; Lead; Potassium

Selective chemical recognition of ionic species by neutral receptor molecules is the important feature in chemical sensors and field-effect transistors (FETs) are very attractive transducers of this chemical recognition because of their fast response time and in situ impedance transformation. The attachment of a polymeric membrane in which the receptor molecule is embedded to the gate oxide chemically modifies the FET into a selective potentiometric sensor for several ions (CHEMFET). The proposed new architecture of the CHEMFET [1] offers several advantages. First, the membrane can be chemically [2,3] anchored to the surface of the gate oxide. Further,

the influence of CO₂ on the CHEMFET response can be eliminated by the introduction of an intermediate buffered hydrogel layer [4,5]. Moreover, this hydrogel stabilizes the potential developed in the sensing membrane. The incorporation of calixarene-based receptor molecules in the membrane of such a CHEMFET has led to accurate sensors for the selective detection of potassium [1], sodium [6] and several heavy metal ions [7] in aqueous solution.

The relatively high drift rate of the ion-sensitive field-effect transistor (ISFET) can be circumvented when CHEMFETs are used in flow systems [8,9]. Several workers have reported the application of multiple ion sensors or arrays of ion sensors [10–12]. This paper, however, describes the use of two CHEMFETs in a differential arrangement where one CHEMFET functions as a reference for the other. Moreover, the flow-through cell, in which these are used, is

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constructed in such a way that the two CHEMFETs are positioned in such close proximity that the sample plug will cover both of them simultaneously. This effectively eliminates the interference of the liquid junction potential between the sample and the carrier solution from the differential measurements. Earlier designs [9] served as a basis for this cell, because of the easy interchangeability of the CHEMFETs. The first experimental results of measurements with potassium- or lead-selective CHEMFETs (with a sodium- or potassium-selective reference CHEMFET, respectively) in this cell design are presented.

EXPERIMENTAL

Chemicals

Ethylene glycol dimethacrylate (EGDMA) (Merck-Schuchardt), 2-hydroxyethyl methacrylate (HEMA) (Merck-Schuchardt) and 2,2-dimethoxy-2-phenylacetophenone (Janssen Chimica) were used. Poly(vinylpyrrolidone) (PVP) with

an average molecular weight of 360 000 (Janssen Chimica) and poly(vinyl chloride) (PVC) of high molecular weight (Janssen Chimica) were used. Valinomycin, sodium ionophore III, bis(1-butylpentyl) adipate (BBPA), bis(2-ethylhexyl) sebacate (DOS), 2-nitrophenyl octyl ether (*o*-NPOE) and potassium tetrakis(4-chlorophenyl)borate (KTCPB) were obtained from Fluka. The synthesis of the lead-sensitive tetrathioamidecalix[4]arene (**1**; see Fig. 4) was described previously [7]. Tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone ketyl before use. The alkali metal salts used were of analytical-reagent grade (Merck-Schuchardt) and solutions were prepared with doubly distilled, deionized water.

CHEMFET

The ISFETs were fabricated as described previously [2], but because of the new flow cells [9] the detailed structure of the ISFET was changed. The external dimensions were enlarged from 1.2 × 3.0 mm to 3.0 × 5.0 mm and the number of contact pads was reduced from three to two by

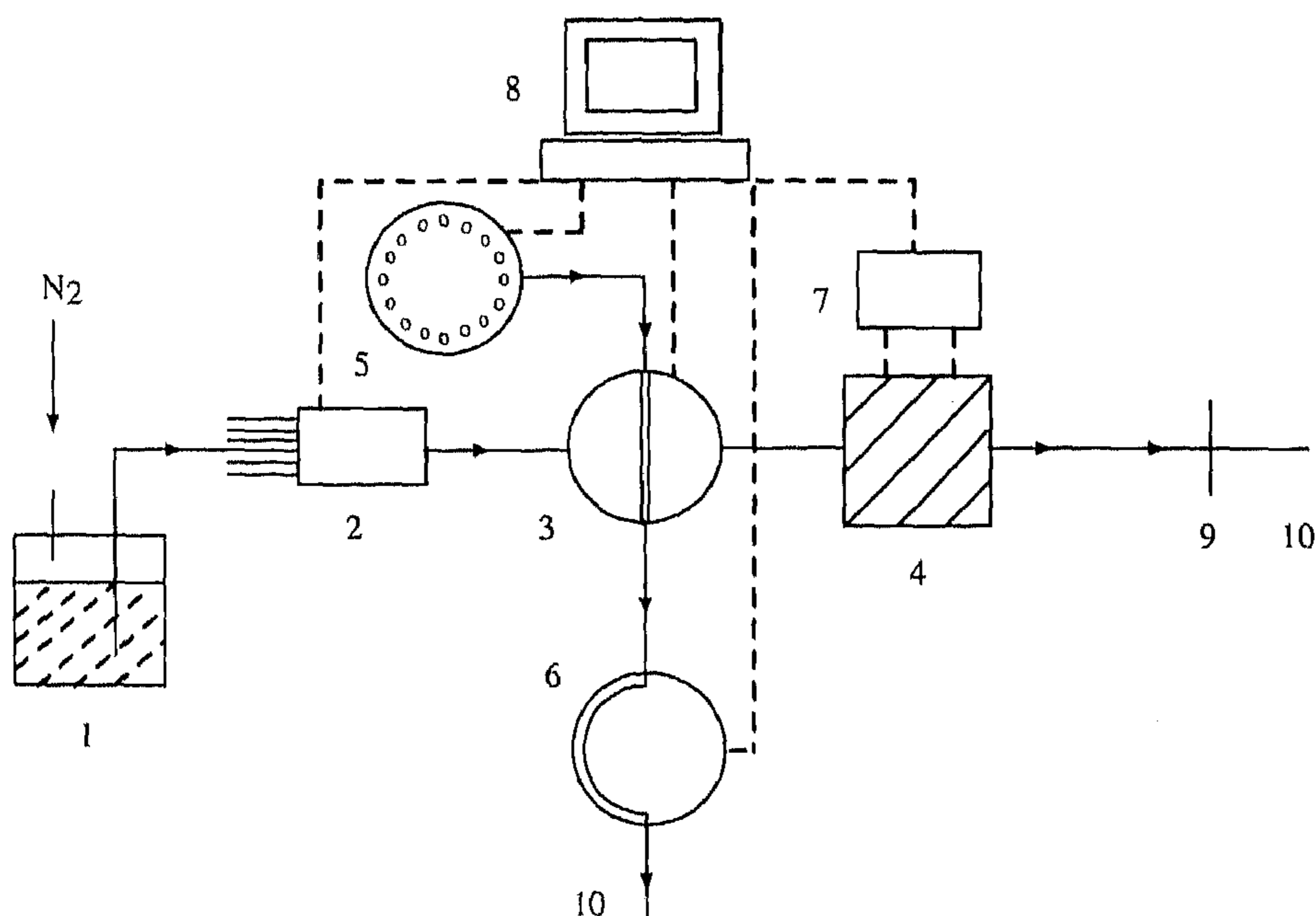


Fig. 1. Schematic diagram of the flow-injection system: 1 = carrier solution; 2 = six-way valve; 3 = injection valve; 4 = flow cell; 5 = autosampler; 6 = peristaltic pump; 7 = ISFET amplifier; 8 = Apple IIGS computer; 9 = saturated calomel (pseudo)reference electrode; 10 = waste.

connecting the source and the bulk internally. The size of the contact pads is 1.0×1.25 mm. Such an ISFET can be used in flow cells without traditional wire bonding and encapsulation with epoxy resin [9].

A hydrogel [4] was applied on the gate oxide of the ISFET by photopolymerization of a mixture of EGDMA, HEMA, PVP, water and photoinitiator in a ratio of 0.4:100:10:40:4 (w/w). The hydrogel was anchored chemically to the gate oxide via surface silylation [4] and had dimensions of $800 \times 15 \times 15$ μm .

The whole device was soaked in a 100 mM solution metal chloride for 1 h and subsequently the excess of solution was removed with a tissue. The potassium-sensitive membranes were made by dissolving a 10% mixture of valinomycin (2–3 wt.%), KTCBPB (50–60 mol% with respect to valinomycin), DOS (65 wt.%) and PVC (32 wt.%) in THF. The sodium-sensitive membranes were made by dissolving a 10% mixture of *N,N,N',N'*-tetracyclohexyl-1,2-phenylenedioxydiacetamide (sodium ionophore III) (1–2 wt.%), KTCBPB (50–60 mol% with respect to sodium ionophore III), BBPA (65 wt.%), and PVC (33 wt.%) in THF. The lead-sensitive membranes were made by dissolving a 10% mixture of the calix[4]arene 1 (2 wt.%), KTCBPB (0.8 wt.%), *o*-NPOE (64.8 wt.%) and PVC (32.4 wt.%) in THF. A droplet of the membrane solution was applied to the poly-HEMA-covered ISFETs and the solvent was allowed to evaporate overnight. The response of the modified ISFETs was measured with a source and drain follower-type ISFET amplifier (Electro Medical Instrumentation, Enschede, Netherlands) in a constant drain-current mode ($I_d = 100$ μA), with a constant drain-source potential ($V_{ds} = 0.5$ V) [13]. The differential signal from two ISFET amplifiers was recorded with an Apple IIGS computer with the use of a 12-bit analogue-to-digital converter (DIGILOG, Enschede, Netherlands).

Double sensor flow-through cell

General. The flow-injection analysis (FIA) system has been reported previously [9] and was used with minor adjustments (Fig. 1). The carrier solution (1) is propelled through the double sen-

sor flow cell by nitrogen pressure. The PTFE tubing supplying the carrier solution was of 0.8 mm i.d. The sample (V_1) of 220 μl is injected with a rotary valve (3) (Rheodyne Model 5020) into the carrier solution. In order to minimize the dispersion of the sample the distance between the injection valve and the detector [8] was as short as possible and the connector of the injection valve was mounted directly on the cell (4). The flow cell was equipped with two CHEMFETs which are measured differentially with respect to a saturated calomel electrode (9) [8,14] which is placed downstream, near the waste (10). Thus, one of the CHEMFETs functions as the reference of the other CHEMFET.

In one series of experiments the potassium-selective CHEMFET was measured with respect to the sodium-selective CHEMFET. In these experiments the concentrations of potassium used were 0.01, 0.1 and 10 mM in 100 mM NaCl. The flow-rate was 1.3 ml min^{-1} . In other experiments a potassium-selective CHEMFET functioned as a reference for the lead-selective CHEMFET. The concentrations of lead used were 0.01, 0.1 and 1 mM in 100 mM KCl. All aqueous solutions were buffered [1×10^{-3} M $\text{Mg}(\text{OAc})_2\text{-HCl}$, pH 4]. The flow-rate was 1.1 ml min^{-1} . Corrections for the activity of the salts were calculated by the extended Debye–Hückel approximation given by Meier [15].

Automation of the FIA set-up. The FIA system consisted of an autosampler (5), a peristaltic pump (6), a six-way valve (2) to select different carrier streams, an injection valve (3) and the double sensor flow-through detector (4). The operation of this system was fully automated with an Apple IIGS computer (8) equipped with a 12-bit ADC and parallel and serial interface cards to control the FIA molecules. A schematic diagram of the set-up is given in Fig. 1.

The program to control the FIA equipment and to register the signal from the detector and its amplifier (7) was written in the computer language FORTH [16–18], which is very suitable for this type of real-time programming. A full measurement cycle consists of the choice of a sample via the autosampler, pumping of the sample into the rotary injection valve, injection of the

sample into the carrier stream and registration of the ISFET amplifier signal via the ADC. Processing of the acquired data was performed in a Lotus spread sheet program.

Construction. The cell consists of three Perspex blocks, A (two) and B (Fig. 2). Part A is a Perspex block (1) ($24 \times 24 \times 20$ mm) equipped with two pairs resilient hooks (3) for the electrical contact. These hooks, via a spring, press at the surface of the contact pads of the CHEMFET (4), whose reverse side is on the Perspex surface.

In this way the gate of the CHEMFET is positioned in the centre of the Perspex block which is marked with a cross engraved in the Perspex [9]. Part B of the cell is a rectangular Perspex block (2) ($85 \times 24 \times 10$ mm) in which a Z-shaped flow channel of 0.5 mm i.d. is drilled. Each of the wedges of the Z reaches the exterior of the rectangular block. At those two points the gate of a CHEMFET is positioned via block A. In this way a Z-type flow cell is formed without a dead volume in the cell. Consequently, the volume of solution between the two CHEMFETs is

very small ($3 \mu\text{l}$). The cell is sealed by gently pushing block A to B with a lever. The inherent plasticity of the PVC membrane ensures a water-tight closure of the cell.

RESULTS AND DISCUSSION

An electrochemical cell without any liquid junction is possible when in the experimental set-up the reference electrode is replaced with a second ion-selective electrode, selective towards an ion other than the primary ion [19,20]. Analogously, if two CHEMFETs in an FIA experiment are in contact with the same sample, the possible liquid junction potential will have no influence on the differential signal. In this experimental set-up one of the CHEMFETs is the reference of the other. This can only function if one of the CHEMFETs is a reference FET or is selective towards only one type of ion of which the activity is constant in all samples. The latter situation was

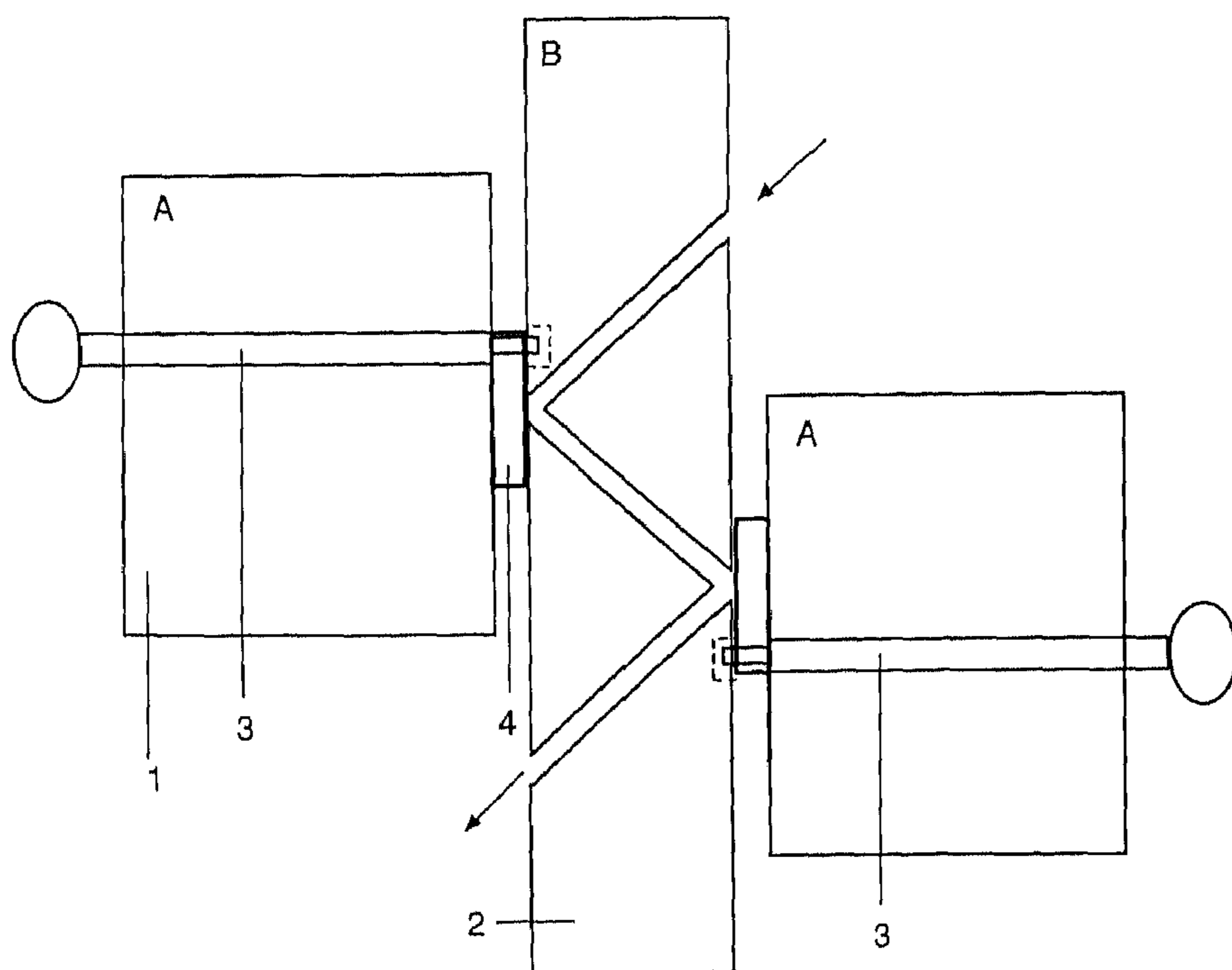


Fig. 2. Detailed structure (side view) of the double sensor flow-through cell: 1,2 = Perspex; 3 = contact wire (hook); 4 = CHEMFET.

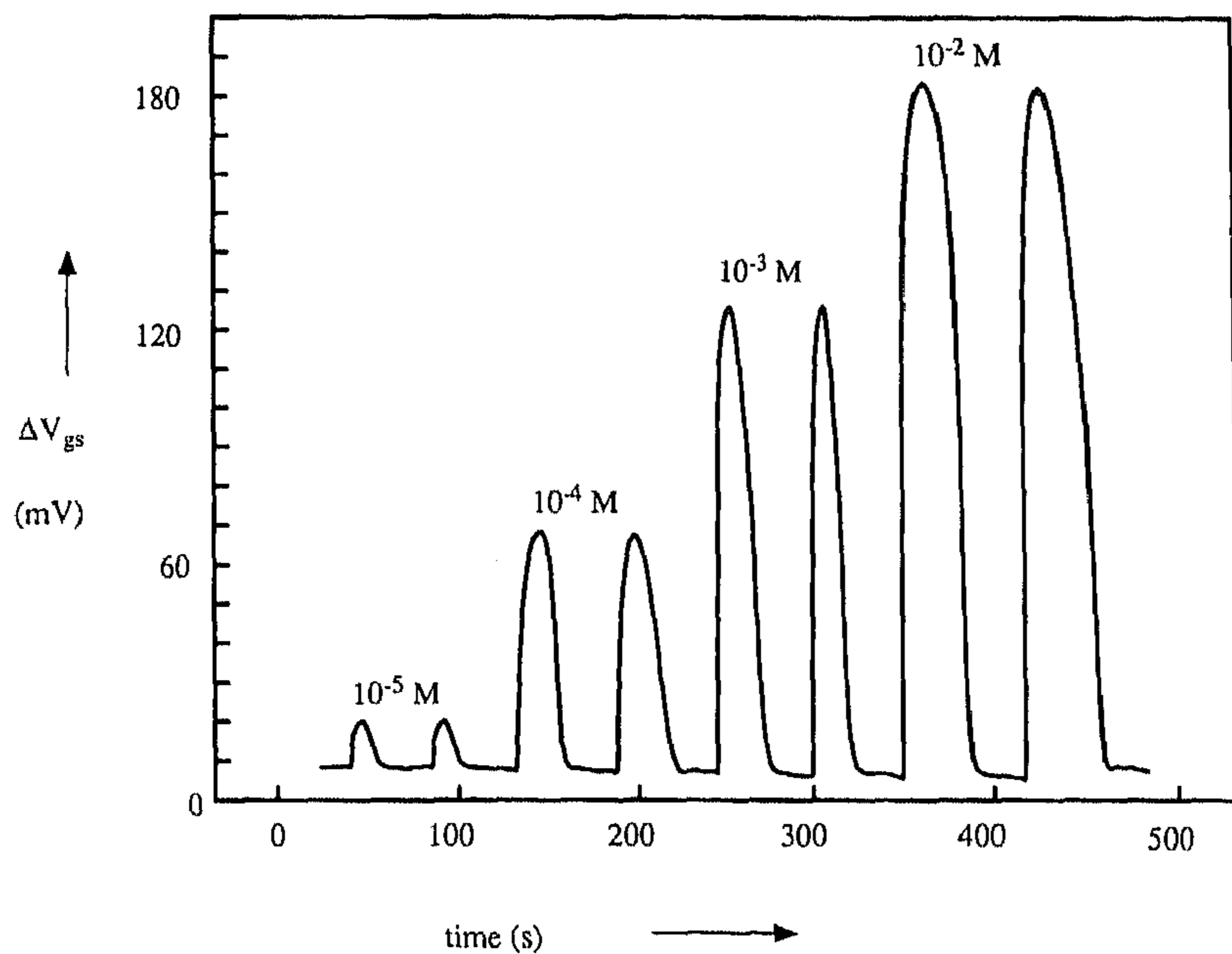


Fig. 3. Response of K^+ CHEMFET in the flow cell. Sodium reference CHEMFET. Carrier, 100 mM NaCl; injection, 1×10^{-5} – 1×10^{-2} M KCl + 100 mM NaCl; $V_i = 220 \mu\text{l}$; $Q = 1.3 \text{ ml min}^{-1}$.

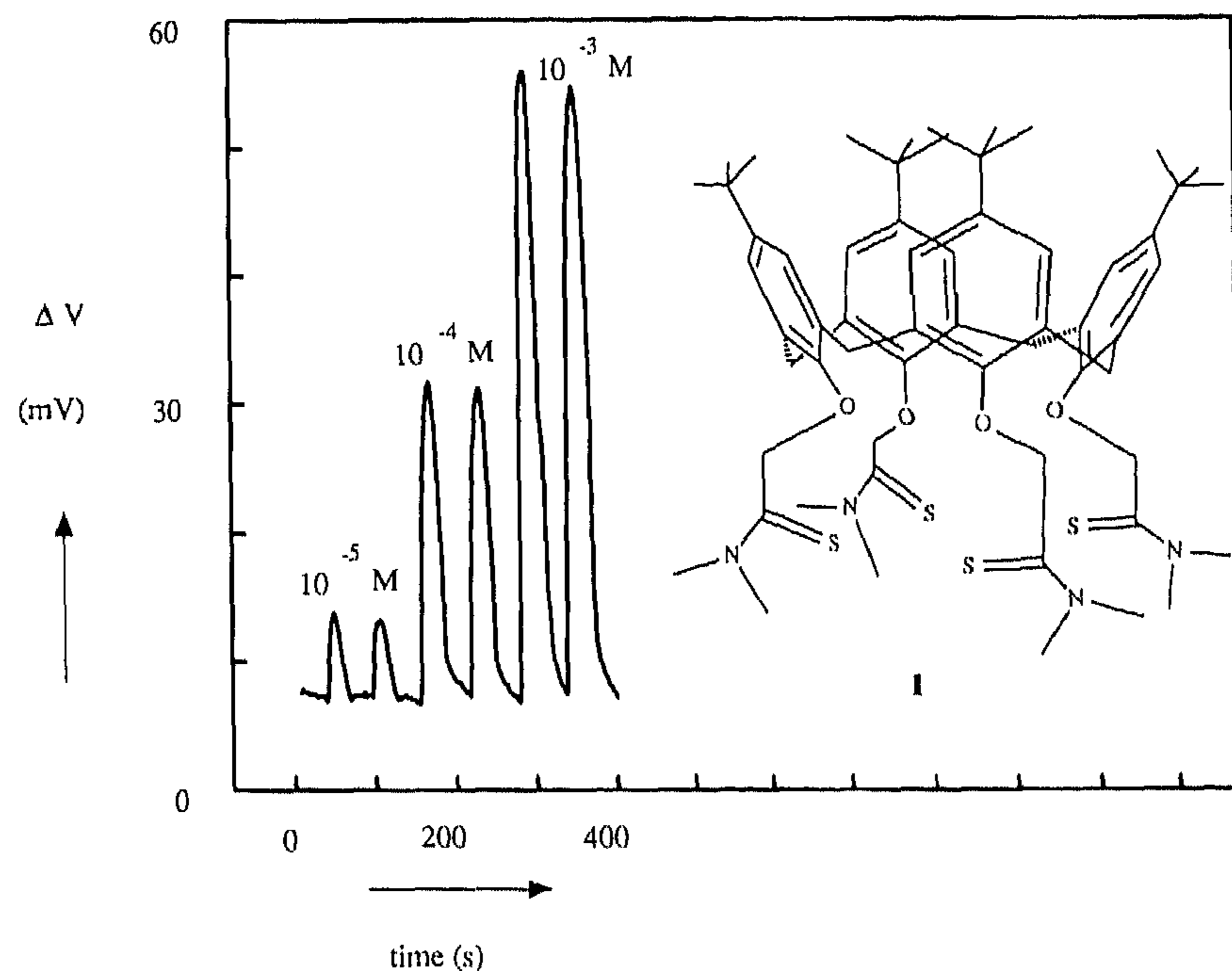


Fig. 4. Response of Pb^{2+} CHEMFET in the flow cell. Potassium reference CHEMFET. Carrier, 100 mM KCl; injection, 1×10^{-5} – 1×10^{-3} M $PbCl_2$ + 100 mM KCl; $V_i = 220 \mu\text{l}$; $Q = 1.1 \text{ ml min}^{-1}$. The structure of the highly lead-selective tetrathioamidecalix[4]arene (1) is shown.

tested experimentally in the new double sensor flow-through cell. In previous work only the experimental results of a potassium-selective CHEMFET in a V-type flow cell in combination with a saturated calomel reference electrode were reported [9]. Therefore, in the first experiment a combination of a sodium- and a potassium-selective CHEMFET was measured in the above-described flow-through cell. The sodium-selective CHEMFET consisted of a PVC–BBPA membrane with the ionophore *N,N,N',N'*-tetracyclohexyl-1,2-phenylenedioxydiacetamide. The potassium-selective CHEMFET was identical with those used before. The concentration of sodium was fixed at 0.1 mol l^{-1} . Thus, the sodium-selective CHEMFET functions as the reference FET of the potassium-selective CHEMFET.

The concentration of potassium was varied in the sample from 1×10^{-5} to $1 \times 10^{-2} \text{ mol l}^{-1}$. At a flow-rate (Q) of 1.3 ml min^{-1} a calibration run was performed with such a double sensor flow cell. The differential signal of the two CHEMFETs responded selectively and Nernstian (57 mV per decade) to the various potassium concentrations (Fig. 3). These results indicate that under the experimental conditions used, the double sensor flow-through cell and the flow-through cell and the flow-through cell described previously [9] are identical with respect to the performance of the CHEMFET.

For the detection of lead in the double sensor flow-through cell, a potassium- and a lead-selective CHEMFET were tested experimentally. The potassium-selective CHEMFET is based again on valinomycin as the ionophore. Tetrathioamide-calix[4]arene (1) is the ionophore in the lead selective CHEMFET. The concentration of potassium was fixed at 0.1 M.

The concentration of lead was varied in the sample from 1×10^{-5} to $1 \times 10^{-3} \text{ M}$. At a flow-rate (Q) of 1.1 ml min^{-1} a calibration run was performed with this double sensor flow cell. The differential signal of the two CHEMFETs responded selectively and in a Nernstian manner (ca. 25 mV per decade) to the various lead concentrations (Fig. 4).

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