

Development of chemically modified ISFETs as durable sensors for continuous flow measurements

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Abstract

An ion sensing device based on an ISFET is described for horticultural applications. Encasing problems are circumvented by using a new packaging technique based on backside-contacted ISFETs. It is shown that an increased lifetime of the selectivity determining membrane can be achieved by covalently anchoring the ionophore to the membrane matrix.

Introduction

Ion sensors based on field-effect transistor technology (ISFETs) are promising devices for application in biomedical and analytical chemistry, as well as in environmental and process monitoring. Especially membrane-based ion-selective sensors (CHEMFETs) offer the flexibility of changing the ion selectivity by altering the membrane constituents. Using supramolecular chemistry to design and synthesize receptor molecules that selectively recognize ionic guest species, the ion selectivity of the sensor can be tuned [1]. Widespread use of these sensors is, however, restricted due to the limited lifetime under continuous flow conditions [2]. The lifetime of a CHEMFET is determined by the rate of leaching out of the electroactive components from the membrane into the aqueous phase, the rate of detachment of the sensing membrane from the FET surface and the packaging of the device. Approaches to solve these problems, necessary to make a multi-ion sensor system for continuous control of the irrigation water composition in greenhouses, are presented.

Sensor architecture and measurement set-up

For application of a CHEMFET in an aqueous environment only the gate area is allowed to come into contact with the analyte solution in order to prevent the occurrence of a CHEMFET response from leakage currents between bulk, source or drain and reference

electrode. Usually this is achieved by encapsulating the CHEMFET in epoxy or other resins [3]. However, the sensing membrane and resin can cause compatibility problems in the long term use of such a sensor, resulting in detachment of the sensing membrane. The packaging problem can be solved by using a plastic housing in which the electrical contacts of a backside-contacted CHEMFET are isolated from the solution by means of O-rings as shown in Fig. 1. Moreover, the housing allows the construction of a multi-ion flow-through cell by connecting individual casings adjacent to each other [4].

A pH-sensitive FET can be modified to sense other ions like potassium or calcium by applying an ion-

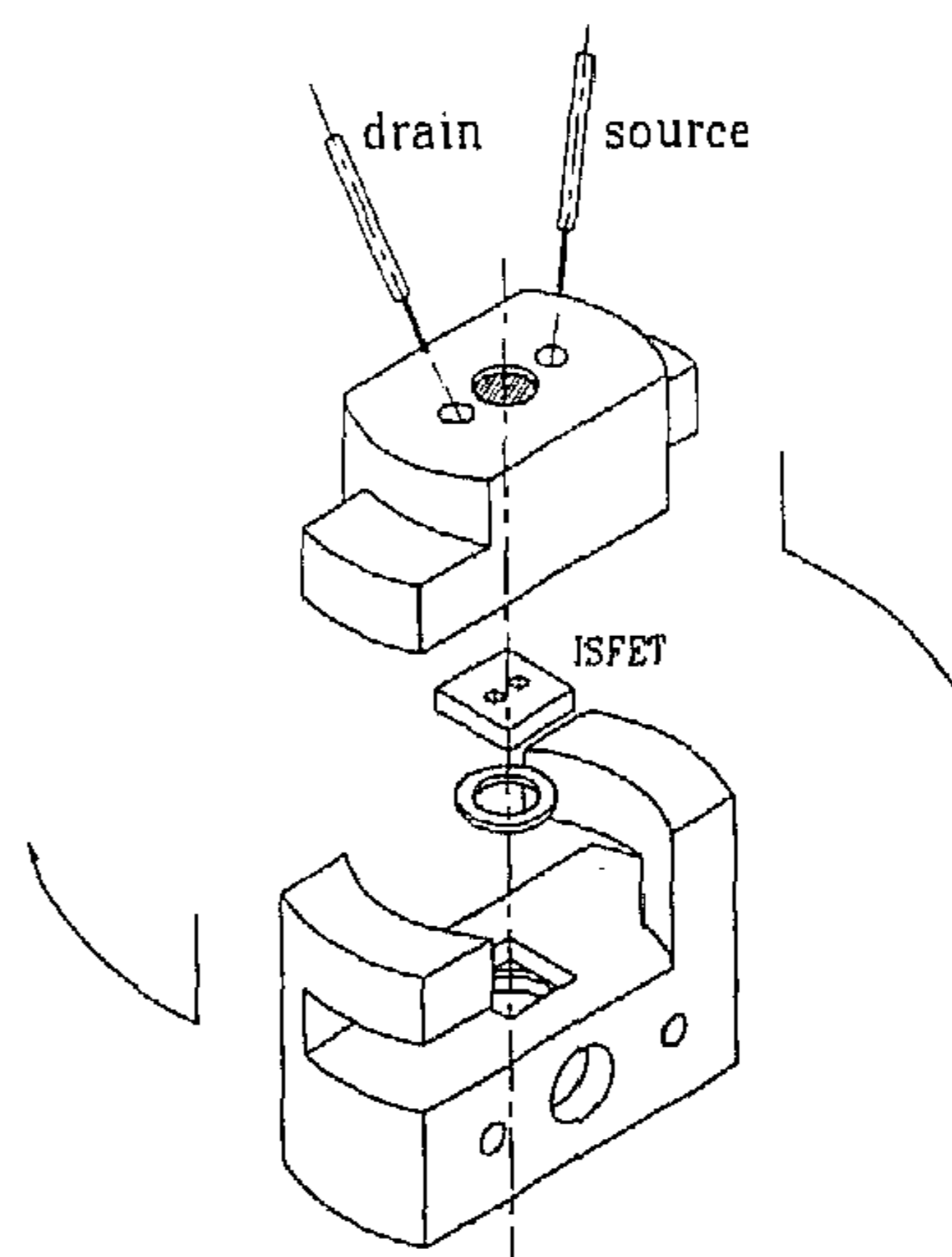


Fig. 1. Schematic drawing of the packaging.

sensitive membrane on top of the gate oxide. The membrane initially employed for these CHEMFETs consists of a mixture of PVC, plasticizer, suitable ionophore and anionic sites. However, a drawback of such an architecture is that under continuous flow conditions the physically attached membrane system will detach from the FET surface. Moreover, these CHEMFETs show a response towards carbon dioxide [5]. We have solved these problems by introducing a polyHEMA hydrogel between the sensing membrane and the gate area of the FET. By methacrylation of silanol groups at the gate surface, using methacryloxypropyl trimethoxysilane, photochemical anchoring groups are introduced with which the polyHEMA layer can be covalently attached to the gate. This polyHEMA hydrogel, conditioned in a suitable pH buffer, prevents the occurrence of a carbon dioxide response [6]. Using methacrylate-modified polysiloxanes as sensing membranes, photochemical anchoring of this membrane to the FET surface is achieved with IC technology compatible techniques. In addition, the covalent attachment of the methacrylate-modified polysiloxanes to the polyHEMA hydrogel layer can be achieved by prior methacrylation of hydroxyl groups at the polyHEMA surface using methacryloyl chloride. The procedure is schematically depicted in Fig. 2.

For the introduction of ion selectivity, the polyHEMA hydrogel is covered with a polysiloxane membrane that contains an ionophore and an anionic site which are added before photopolymerization. Good response and selectivity for potassium, calcium, sodium and heavy metal ions have been demonstrated with this architecture [7]. Under continuous flow conditions, however, the electroactive ionophore and borate leaches out of the membrane, thereby gradually changing the sensor selectivity and sensitivity in time [2, 8]. To improve the long term stability of the sensor we have modified the ionophore by linking it to a methacrylate group which allows the covalent entrapment of the ionophore in the crosslinking polysiloxane matrix during photopolymerization and thus prevents leaching out of this component.

To test this concept, a polyHEMA-covered, methacrylated backside-contacted ISFET was conditioned for 12 h in a citrate buffer solution of 0.1 M KCl (pH 4.0) and subsequently a solution consisting of 1 wt.% ionophore A or B (Fig. 3), 3 wt.% 2,2'-dimethoxy-2-phenylacetophenone, 40 mol% potassium tetrakis(4-chlorophenyl) borate and 96 wt.% polysiloxane (a copolymer of (cyanopropyl)methyl-, dimethyl- and (methacryloxypropyl)methyl-siloxane) in dichloromethane was applied on top of the polyHEMA-modified ISFET. After drying and UV irradiation under a flow of nitrogen,

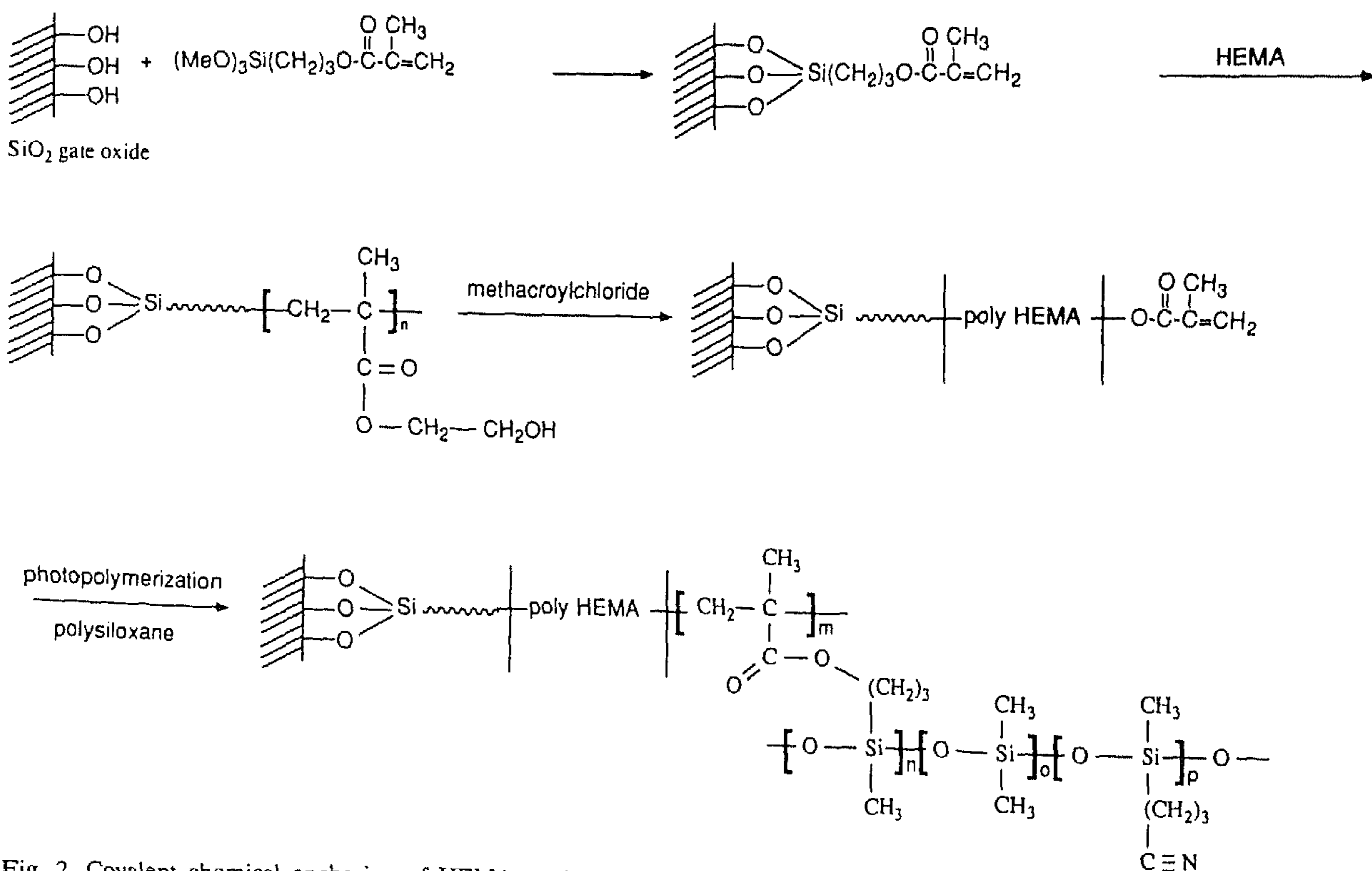


Fig. 2. Covalent chemical anchoring of HEMA to the ISFET gate oxide (top), methacrylation of polyHEMA layer (middle) and photochemical anchoring of polysiloxane (bottom).

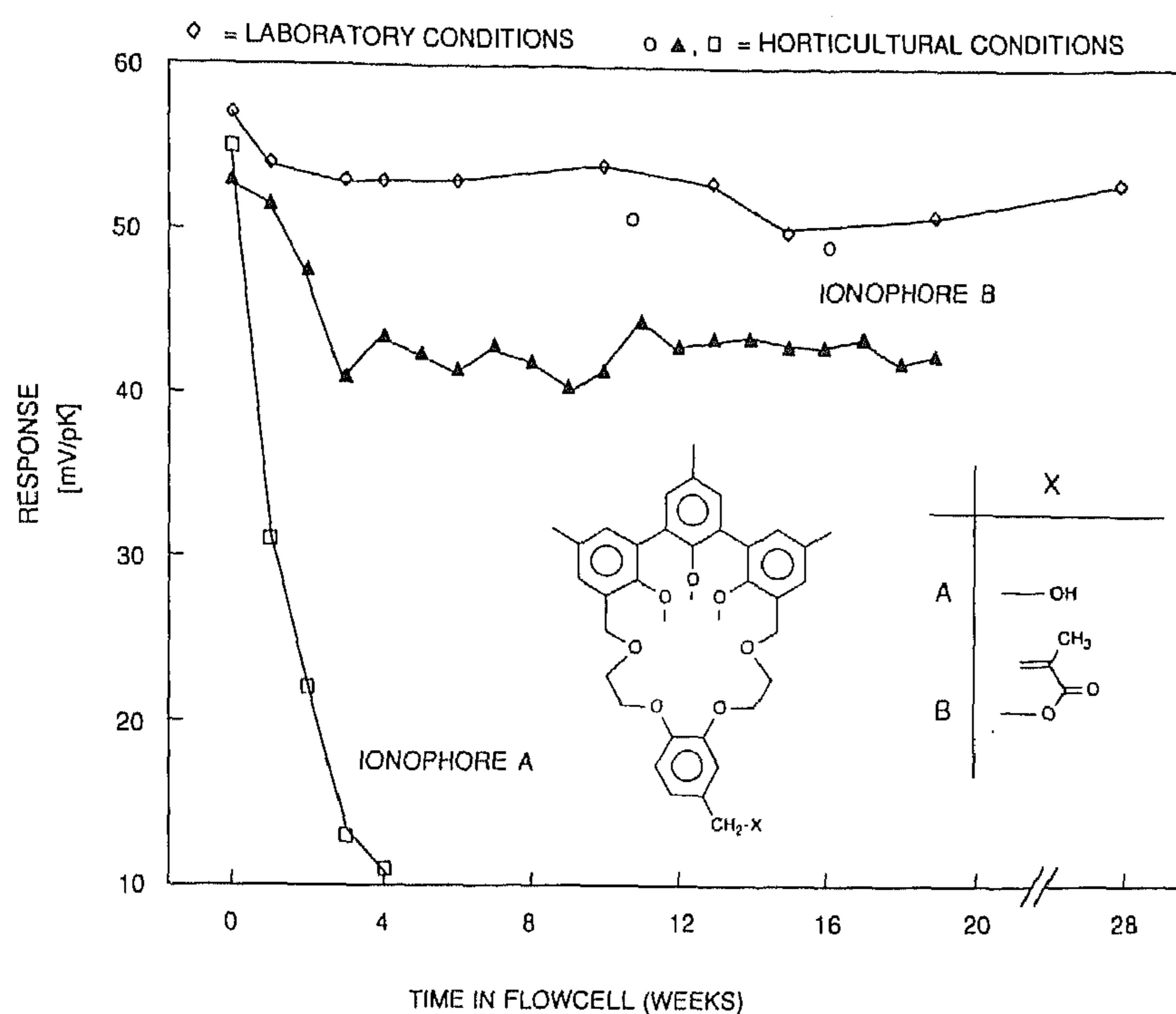


Fig. 3. Response of potassium sensors under continuous flow conditions using a free potassium ionophore (A, horticultural conditions) and a polysiloxane-bound potassium ionophore (B, laboratory and horticultural conditions). Also shown is the response using KCl-NaCl solution (O) under horticultural conditions.

the resulting CHEMFETs were mounted in the described flow cells. The CHEMFETs were operated in the constant current mode. The change in time of the sensor response under laboratory conditions was tested by titration with potassium chloride in a background electrolyte of 0.1 M magnesium chloride, at a flow speed of 1 ml/min, using a calomel reference electrode. Between titrations the sensors were stored in a recirculation system at a flow speed of 1 ml/min of 0.1 M magnesium chloride and 0.1 M potassium chloride. Under horticulture conditions, the sensor response is measured using a system that automatically switches with a flow speed of 3 ml/min between two calibration solutions. The first calibration solution contains a high concentration potassium chloride in combination with a low concentration of salts resembling an average horticultural solution, i.e., sodium, calcium, magnesium, sulfate, nitrate, phosphate. The second calibration solution contains a low concentration of potassium chloride in combination with a high concentration of mixed salts. Between these response measurements, filtered water from a greenhouse is passed through the flow cell at a rate of 3 ml/min.

For comparison, potassium-sensitive membranes, based on PVC and valinomycin with different plasticizers and anionic sites, were tested with respect to lifetime under horticultural and laboratory conditions. The mem-

branes were solvent cast on backside-contacted ISFETs with a conditioned polyHEMA layer.

In order to obtain insight in the efficiency of covalent linkage of the methacrylated ionophore in the polysiloxane matrix, separate extraction experiments were performed. Therefore, UV-cured membranes, composed of methacrylated polysiloxane, 2 wt.% of ionophore B (Fig. 3) and 3 wt.% of photoinitiator in addition to an extractable internal standard, were extracted with dichloromethane. Determination of the change in the ratio of the peak areas of ionophore and internal standard before and after photocuring by HPLC analysis gave the percentage of extractable ionophore and, therefore, a measure of the ionophore not bound to the polysiloxane matrix in the photopolymerization process. According to the HPLC analysis, 70 to 90% of the added ionophore B (Fig. 3) is bound to the polysiloxane matrix.

Results and discussion

Preliminary results of the approaches to increase the sensor lifetime under continuous flow measurements are shown in Fig. 3. Whereas a sensor equipped with a polysiloxane membrane containing the free potassium

ionophore (Fig. 3, A) almost immediately shows a steady decrease in response and is operational only two to three weeks under continuous flow conditions, the lifetime of a potassium sensor using the polysiloxane-bound ionophore will last at least 20 weeks (Fig. 3, B).

In Fig. 3 the sensors using a polysiloxane-bound potassium ionophore show a slight decrease in response in the first three weeks, after which there is a constant response level during the rest of the period.

In Table 1 a summary is given of the different lifetimes of the tested membrane systems. The lifetime is defined as that period in time whereby the response is above 50 mV/pK as measured using the calibration solutions. From Table 1 it is clear that for the PVC-based membrane systems lifetime depends not only on measurement conditions (flow, lab. or greenhouse) but also strongly on the membrane components used. Sensors with lipophilic constituents have a longer lifetime compared to the membranes with less lipophilic components. The phenomena indicate a strong leaching out of the membrane matrix of ionophore, anionic site and plasticizer. This is in agreement with the predictions of Simon and co-workers [2]. Furthermore, sensitivity drops eventually to zero, which can also be observed for the polysiloxane membranes with non-covalently bonded ionophore. In contrast, membranes whereby the ionophore is prevented from leaching out by covalently bonding maintain a certain response. Not shown in Fig. 3, but evident, is a small decrease in sensitivity occurring for these type of membranes during the first two days of the experiments (from 58 to 52 mV/pK) under horticultural conditions. After a couple of weeks this response drops to around 40 mV/pK. This drop in response is not observed under laboratory conditions. The first initial decrease can be explained by fast leaching out of the nonbonded ionophore, as indicated by our extraction

experiments. The second can be explained by a slow leaching out of the anionic sites. This will lead to a reduced selectivity and an apparent low sensitivity using the calibration solutions [8]. The experiment under laboratory conditions using a titration to determine the sensitivity and the experiment with a solution containing only potassium chloride solutions under horticultural conditions (see Fig. 3) indicate that the sensitivity itself remains constant at about 52 mV/pK. Another indication that the leaching out of the anionic site is responsible for the reduced lifetime is the increase in lifetime by using a more lipophilic anionic site. We also measured a decrease in the potassium/sodium selectivity under laboratory conditions. From the experiments discussed above it is evident that both eliminating the plasticizer and anchoring the ionophore to the membrane matrix increases the lifetime of FET-based ion sensors. Experiments in which the anionic sites are chemically bonded to the membrane matrix are in progress to clarify further the observed phenomena.

Conclusions

An increased sensor lifetime under continuous flow conditions can be achieved using IC technology compatible techniques by combination of a special packaging of the CHEMFET which isolates it (except for the sensing part) from the aqueous solution, the application of a buffered hydrogel between sensing membrane and gate oxide of the CHEMFET, and the covalent anchoring of membranes and ionophore by photopolymerization.

References

- 1 D. N. Reinhoudt, Application of supramolecular chemistry in the development of ion-selective CHEMFETs, *Sensors and Actuators B*, 6 (1992) 179–185.
- 2 O. Dinten, U. E. Spichiger, N. Chaniotakis, P. Gehrig, B. Rusterholz, W. E. Morf and W. Simon, Lifetime of neutral-carrier-based liquid membranes in aqueous samples and blood and the lipophilicity of membrane components, *Anal. Chem.*, 63 (1991) 596–603.
- 3 N. J. Ho, J. Kratochvil, G. F. Blackburn and J. Janata, Encapsulation of polymeric membrane-based ion-selective field-effect transistors, *Sensors and Actuators*, 4 (1983) 413–421.
- 4 H. H. van den Vlekkert, U. H. Verkerk, P. D. van der Wal, A. van Wingerden, D. N. Reinhoudt, J. R. Haak, G. W. N. Honig and H. A. J. Holterman, Multi-ion sensing device for horticultural application based upon chemical modification and special packaging of ISFETs, *Sensors and Actuators B*, 6 (1992) 34–37.
- 5 E. J. Fogt, D. F. Untereker, M. S. Norenberg and M. E. Meyerhoff, Response of ion-selective field effect transistors

TABLE 1. Sensor lifetime experiments under horticultural conditions

Membrane composition ^a			Flow speed (ml/min)	Lifetime (h)
Ionophore	Polymer	Anionic site		
Val	PVC/DOS	Cl	2.6	< 50
Val	PVC/469	F	2.6	1000
3B	PSX	Cl	2.6	300
3B	PSX	F	2.6	1000
Val	PVC/DOS	Cl	0.4	250
Val	PVC/469	F	0.4	> 1500
3B	PSX	F	0.4	> 1500

^aVal=valinomycin; 3B=ionophore B (Fig. 3); 469=ETH469; PSX= methacryl, cyanopropyl-modified polysiloxane; F=potassium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate; Cl=potassium tetrakis(4-chlorophenyl) borate.

- to carbon dioxide and organic acids, *Anal. Chem.*, *57* (1985) 1995–2002.
- 6 E. J. R. Sudholter, P. D. van der Wal, M. Skowronska-Ptasinska, A. van den Berg, P. Bergveld and D. N. Reinhoudt, Modification of ISFETs by covalent anchoring of poly(hydroxyethyl methacrylate) hydrogel, *Anal. Chim. Acta*, *230* (1990) 59–65.
- 7 P. L. H. M. Cobben, Sensors for heavy metal ions based on ISFETs, *Thesis*, University of Twente, Enschede, 1992.
- 8 R. Eugster, P. M. Gehrig, W. E. Morf, U. E. Spichiger and W. Simon, Selectivity-modifying influence of anionic sites in neutral-carrier-based membrane electrodes, *Anal. Chem.*, *63* (1991) 2285–2289.