

## Chemically modified field-effect transistors for measurement of ion activities in aqueous solution

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**During the last decade a growing need for miniaturized sensors for the (on-line) detection of low concentrations of ions in aqueous solution has emerged. These sensors can provide direct information for localisation of environmental pollution and can be applied in water quality monitoring, biomedical analysis and biomonitoring. The chemical sensor system must replace the current methods of discontinuous sampling followed by analysis in the laboratory.**

Until now such miniaturized sensor systems of sufficient stability have not been fully developed for the majority of analytes and analysis must be carried out with conventional techniques, eg chromatography, atomic absorption and emission spectrometry and various wet analytical techniques. However, the innovative technology in semiconductor materials, micro-engineering, and molecular engineering shows great promise for the fabrication of microsensors by IC technology. Solid state pH-sensors based on ion-sensitive field effect transistors (ISFETs) are already commercially available and it is expected that these will be followed by chemically modified field effect transistors (CHEMFETs) capable to detect activities of various ionic species in solution.

### ■ The architecture of CHEMFETs

CHEMFETs are chemically modified field effect transistors designed for the selective detection of ions in aqueous solution. Basically, the CHEMFET is a special modification of the ion sensitive field effect transistor (ISFET), which shows sensitivity for the activity of hydrogen ions in solution [1]. A field effect transistor (FET) is a potentiometric sensor which measures the conductance between source and drain (the gate) of a semiconductor as a function of an electrical field perpendicular to the gate

oxide surface (fig 1). In contact with an aqueous solution, the state of ionisation of the surface SiOH groups of a SiO<sub>2</sub> gate oxide in a aqueous solution determines the surface potential and therefore the source-drain current in the transistor. A change in pH of the solution will produce a change in surface potential which can be measured by the change in conductance of the transistor. In practice, the source-drain current is kept constant (100  $\mu$ A) by modulation of the potential between reference electrode and bulk of the semiconductor. Typical pH responses thus obtained are 37-40 mV/pH unit.

Important advantages of ISFETs compared to conventional pH electrodes are

their small size (typically, 1.2 X 3 mm), very fast response time, robustness, and low output impedance which makes special shielding of wiring not necessary. Moreover, ISFETs can be produced in large quantities at potential low costs.

Application of the field effect transistor principle for the detection of ionic species other than protons, requires the introduction of selectivity for these species above the gate area of the transistor. This can be achieved by deposition of an ion-selective membrane on top of the gate of the FET. The response to the activity of the analyte ions in solution is then caused by the development of a membrane potential above the gate of the semiconductor which modulates

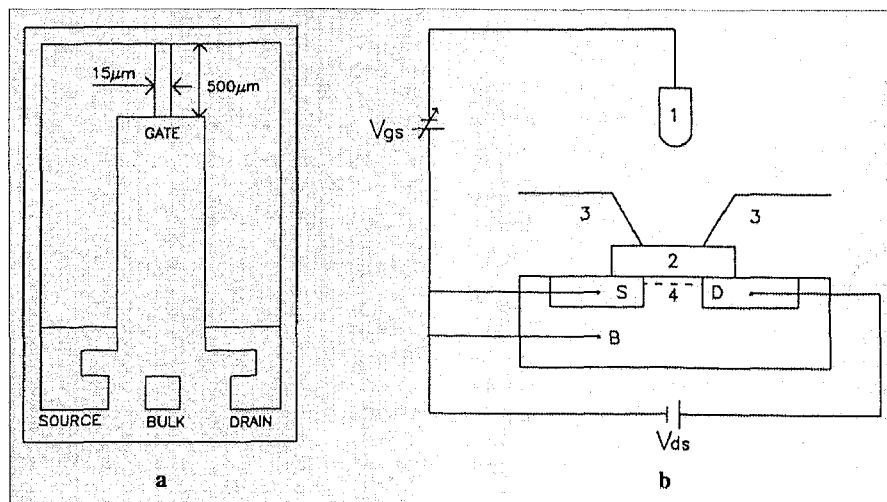


Fig 1. Schematic representation of (a) a top view of an ISFET, and (b) a cross-section of an ISFET in a measuring system. 1, reference electrode; 2, gate oxide; 3, insulating resin; 4, channel; S, source; D, drain; B, bulk.

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the conductivity in the ISFET channel. ISFETs of which the gate is covered with a plasticized PVC membrane containing the potassium-selective natural ionophore valinomycin give a Nernstian response of 59 mV/decade upon variation of the potassium concentration in the analyte solution.

However, the above described sensor construction has no long-term stability. Upon prolonged contact with the aqueous solution the physically adsorbed membrane comes loose from the semiconductor surface and the plasticizer and ionophore are slowly leaching out from the membrane. In addition, such sensors show interfering pH sensitivity (and carbon dioxide sensitivity) due to the uncontrolled ionization of the surface silanol groups of the gate oxide.

Much research has been done by our group to improve ion selectivity and lifetime of chemically modified field effect transistors. We have solved the problem of pH and carbon dioxide interference by placing a buffered hydrogel layer (polyhydroxyethylmethacrylate, polyHEMA) in between the gate oxide and the sensing membrane which keeps the dissociation of the surface silanol groups constant [2]. A next step in our sensor development was the development of a stable sensing membrane which could be deposited over the polyHEMA layer. The limited lifetime observed with physically adsorbed PVC membranes showed that it was necessary to bind the sensing membrane chemically to the semiconductor surface in order to obtain a sensor with a long lifetime. Moreover, the electroactive components (*ie* the ion receptors and the ionic sites) in the sensing membrane must be prevented to leach out from the membrane. This can also be achieved by covalent attachment of these components to the membrane matrix.

## ■ Development of durable ion sensing membranes

An ion sensing membrane which is suitable for long-life CHEMFETs must fulfill a number of requirements: i) the sensing membrane must be an elastomer (glass transition temperature  $\leq 0^\circ\text{C}$ ) in order to keep mobility of charged species in the membrane; ii) the membrane must be hydrophobic, but with sufficient conductivity to obtain fast response times; iii) ionic sites with charge opposite to the analyte ion must be present in the membrane or allowed to be added in order to obtain sufficient permselectivity for the analyte ions and to increase the membrane conductivity; iv) the membrane matrix must allow chemical attachment of receptor molecules and ionic sites in order to prevent leaching out of these components; and v) all chemical binding steps must occur by photopolymerisation in order to make sensor fabrication compatible with IC-technology.

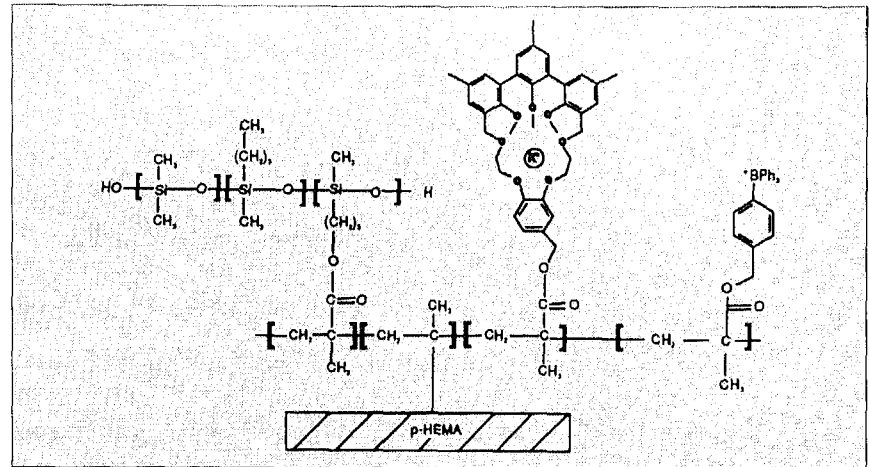


Fig 2. Schematic representation of a polysiloxane sensing layer covalently attached to a polyHEMA layer.

We have developed sensing membranes which meet these requirements based on polysiloxanes. Good response characteristics are obtained with a copolymer composed of dimethylsiloxane, cyanopropylsiloxane (for modulation of the polarity of the membrane), and methacryloxypropylsiloxane (enabling covalent linkage of receptor and ionic sites) [3]. Synthetic receptor molecules and anionic sites containing photopolymerisable side groups were developed and incorporated into the polysiloxane membrane. Covalent attachment of polysiloxane to the polyHEMA layer is achieved by prior methacrylation of part of the hydroxyethyl groups of polyHEMA. Subsequent photopolymerisation yields a stable polymer network in which all membrane components are covalently anchored. A sche-

matic representation of the architecture of the sensing layers on top of the field effect transistor for a potassium-selective CHEMFET is given in figure 2.

In figure 3 the response characteristics are given of a potassium-selective CHEMFET based on polysiloxane copolymer in which the methacrylated potassium receptor is covalently bound by photopolymerisation, and to which tetraphenylborate is added as anionic sites. Due to the covalent linkage of the ionophore, leaching out from the membrane matrix is prevented and a stability of several months for the sensor in flow cells is obtained. In contrast, membranes with the same ionophore but without covalent attachment lose their activity quickly.

Currently we are also investigating the effects of covalent binding of the

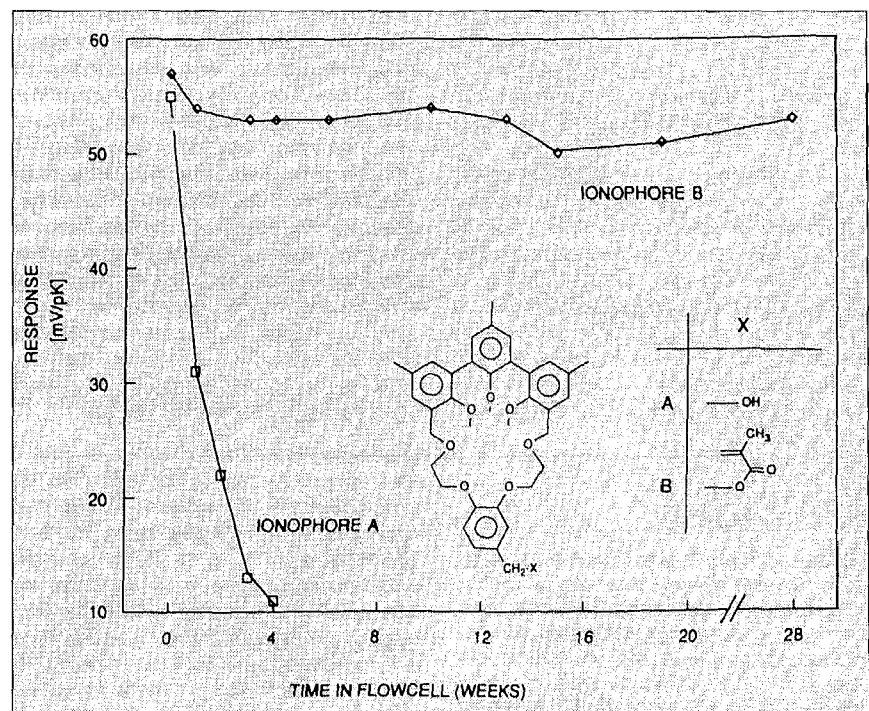
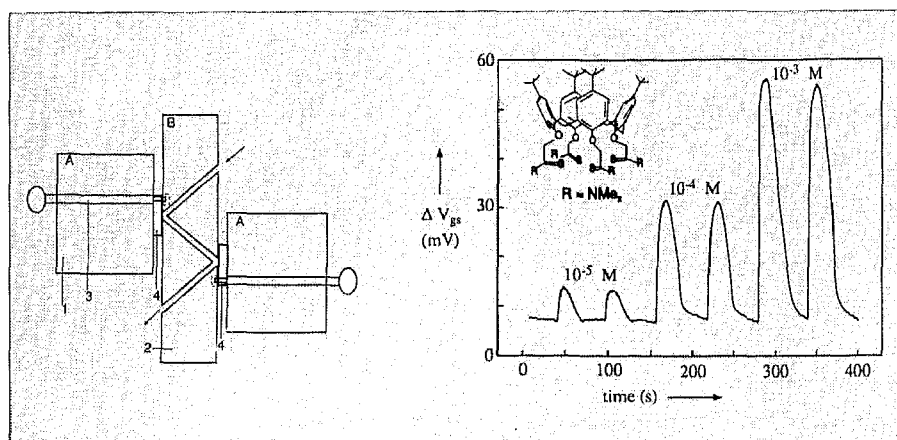


Fig 3. Sensor response characteristics in time.

# Micro total analysis systems ( $\mu$ TAS)



**Fig 4.** a. Side view of the detailed structure of a double sensor flow cell: 1,2, perspex; 3, contact wires; 4, CHEMFETs. b. Response of this flow cell containing a  $\text{Pb}^{2+}$ - and a  $\text{K}^+$ -selective CHEMFET in differential measurement of injections of  $220 \mu\text{l}$  of  $\text{PbCl}_2 + 100 \text{ mM KCl}$  in a carrier flow of  $10^{-6} \text{ M PbCl}_2 + 100 \text{ mM KCl}$ .

ionic sites in the membrane matrix. Our first results show that this additional step elongates the lifetime of the sensors still further. After 40 weeks of exposure in a continuous water stream 60% of the sensors retained a good response, whereas of those with only the ion receptor covalently linked 25% were still functioning. However, the yield of well functioning CHEMFETs of longevity is not satisfactory yet for large scale production and our effort is directed to further improvement of this yield.

## Development of ion-selective receptor molecules

In principle, the above described CHEMFET architecture is generally applicable for the detection of charged species which can build up a membrane potential. The selectivity of the membrane for a particular ion is largely determined by the kind of ion receptor incorporated in the membrane. An important part of our sensor research is directed to the design and synthesis of ion receptor molecules which have a high selectivity towards common interfering ions and can be chemically bound to the membrane matrix. Especially versatile in this respect are calix[4]arenes as molecular building blocks. These cyclic tetramers of phenols and formaldehyde offer a unique possibility to orient ligand groups by functionalisation of the phenolic oxygens. In

the cone conformation of calix[4]arene these ligands are oriented on the same side of the molecule. Moreover, these molecules have a high lipophilicity which gives them a high affinity for the membrane phase. Using these building blocks, highly selective receptors have been developed for potassium [4], sodium [5], some heavy metal ions [6], and a number of other cations. The structure of one calixarene derivative, selective for lead ions is shown in the graph in figure 4b.

## CHEMFETs in flow injection analysis

An important aspect for the practical application of ISFETs and CHEMFETs is a reliable packaging, which completely isolates the device, except the ion-sensitive part above the gate from the contacting solution. This can be done by encapsulation of the devices with insulating polymers (epoxy resin, silicone rubber) or, alternatively, by mounting them in specially designed flow cells. An example of the latter is described in [7].

One of the remaining problems in the application of ISFETs and CHEMFETs, the relatively high drift, can be overcome by using a flow injection system. In flow injection analysis (FIA) the sample solution is injected into a carrier solution which is in permanent contact with the sensor. Due to their small size and fast response CHEMFETs are excellently suitable for this technique.

We have developed a flow cell in which two CHEMFETs are measured differentially with respect to a (pseudo) reference electrode [6]. In this set-up one of the CHEMFETs is selective for a cation present in a constant concentration in the carrier solution and the second CHEMFET is selective for the ion to be detected. The schematic picture of the flow cell is given in figure 4a. Figure 4b shows the Nernstian response obtained with this flow cell, incorporating a potassium selective CHEMFET and a lead selective CHEMFET, upon injection of different lead concentrations in a carrier stream of  $0.1 \text{ M KCl}$ . Implementation of this differential measurement system in a micro total analysis system is currently part of our investigations.

## Acknowledgments

The results described in this paper are a part of work on chemically modified field effect transistors in our department over a period of several years. We thank all colleagues and coworkers, several of whose names appear in the references, for their valuable contribution to this work.

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