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A new type of ionophore for ion-selective field-effect transistors[†]

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Summary — A phthalocyanine subunit functionalized with three crown-ether macrocycles and one paraffinic side chain terminated with a carboxylic group has been used for grafting the surface of the gate insulator of a field-effect transistor. This type of structure has been chosen to favor nonlinear ion complexations as previously demonstrated in solution. The chemical means used to graft and substitute the silica surface are described. The effect of various cations (Na^+, K^+, Cs^+, Ca^{2+}, Ba^{2+}) on the characterics of the ion-selective field-effect transistor (ISFET) is described. A model previously reported in the literature has been used to rationalize the results.

field-effect transistor / ion titration / alkali cation / alkaline earth cation

Résumé — Un nouvel ionophore pour transistors à effet de champ. *Une phtalocyanine substituée par trois éther-couronnes et une chaîne paraffinique terminée par un groupe carboxylique a été utilisée pour fonctionnaliser la surface d'une grille de transistor à effet de champ. Ce type d'unité moléculaire devrait favoriser la complexation non-linéaire de cations à la surface du transistor, comme c'est le cas en solution. L'effet de divers cations (Na^+, K^+, Cs^+, Ca^{2+}, Ba^{2+}) sur les caractéristiques du transistor est décrit. Un modèle précédemment publié dans la littérature a été employé pour exploiter les résultats expérimentaux.*

transistors à effet de champ / titrage d'ions / ion alcalin / ion alcalino-terreux

Introduction

The field-effect transistor is omnipresent in the field of microelectronics. Following Bergveld's work in 1970, field-effect transistors have also been applied to the detection of protons [1] or ions [2-7].

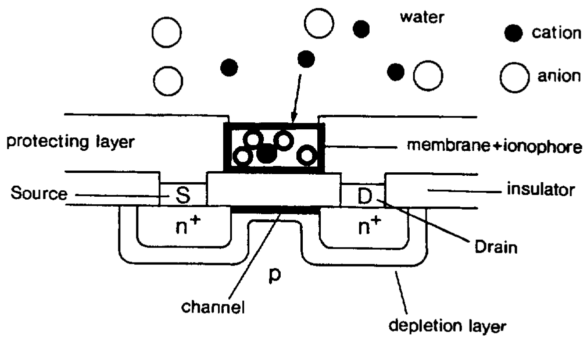


Fig 1. Schematic representation of an ion-selective field-effect transistor (ISFET) (partly reproduced from ref 8).

The advantages of using such devices are numerous: (i) the microtechnology used for fabricating field-effect transistors is now well mastered and of low cost; (ii) the quantity of active molecular material (membrane and ionophore) needed is extremely small (less than 1 mg) and allows the use of highly sophisticated molecular compounds; (iii) the sensitivity of the device is exceptionally high (10^{13}–10^{14} ions per cm^2 at the gate insulator surface); and (iv) the source-to-drain distance is of the order of 2–20 μm and permits the fabrication of miniaturized devices and the use of very small volumes of analyte.

It has recently been shown that crown-ether-substituted lutetium bisphthalocyanines yield nonlinear complexation processes of ions in behalf of two independent cooperativity effects favoring the formation of aggregates [9, 10]. It was therefore tempting to study the nonlinear binding process at the surface of an ISFET. A functionalized crown-ether-substituted phthalocyanine could be used for such a purpose [11]. It was also necessary to find a reliable way to covalently link the ionophore on the ISFET. These steps will be detailed in the next sections but a schematic representation of the final device is given in figure 2.

[†] Dedicated to Prof Raymond Weiss.

[*] Correspondence and reprints

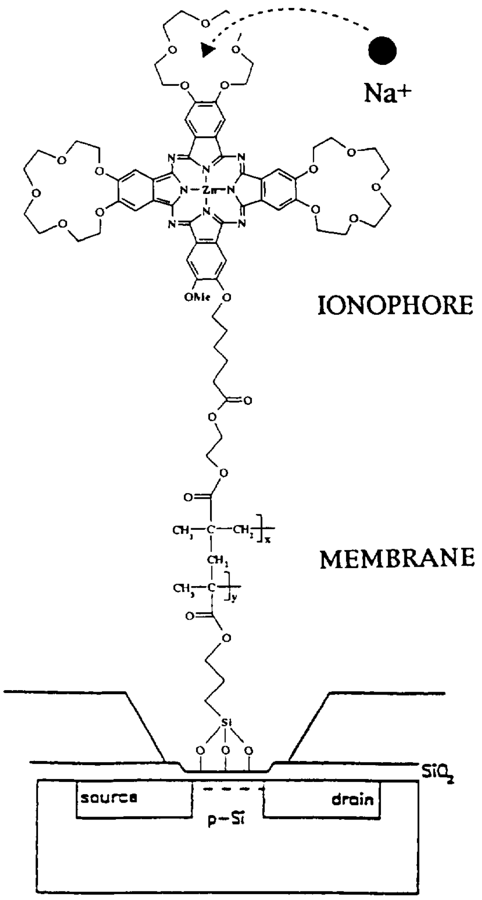


Fig 2. Schematic representation of the ISFET fabricated in the present study. The various parts are not reproduced on the same scale (drawing inspired from the stained glass window of Jesse's family tree, XIIth century, Cathédrale basilique de Saint-Denis).

The following sections will describe the synthesis of the membrane linked to the ISFET grid, the linkage of the crown-ether-substituted ionophore and the responses of the device in presence of ions.

ISFET

The ISFET used in the present study was designed at the Centre interuniversitaire de microélectronique (CIME). The process is closely related to the steps used in MOS technology [12] (fig 3).

Functionalization of the gate insulator surface

The gate silica must be first activated to increase the number of silanol groups ≡Si-OH present at the surface. This is achieved by a saturated solution of bichromate in which is added concentrated sulfuric acid (1 mL saturated solution of $K_2Cr_2O_7$ for 19 mL concentrated sulfuric acid). The gate insulator of the ISFET is treated for 3 min with the previous mixture, rinsed 3 min in ultrapure water and then left in ultrapure water for 18 h. The device was then dried in a stream of nitrogen. Under these conditions approximately 10^{14} silanol groups per cm^2 are obtained at the surface.

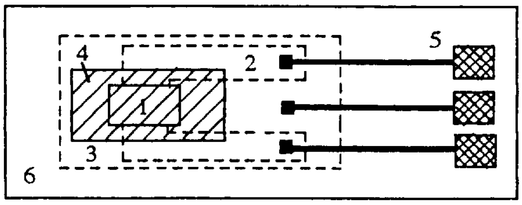
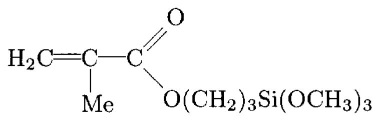


Fig 3. A simplified view of the FET used; 1: gate insulator (SiO_2 900 Å); 2: source and drain (diffusion n^+); 3: insulating layer (p^+); 4: membrane deposited; 5: connection plugs (Al); 6: silicon wafer (p).

The functionalization is then achieved by using the commercially available 3-(trimethoxysilyl) propyl methacrylate (Aldrich).



$$H_2C{=}C(Me){-}C({=}O){-}O(CH_2)_3Si(OCH_3)_3$$

This molecule is well known as an efficient reactant towards silanol groups of silica surface (see for example reference [5]). However, the classical representation of the linking (as shown in fig 2) is probably not correct since the density of 10^{14} silanol per cm^2 leads to a mean distance between silanol groups of 10 Å. A more satisfactory representation of the grafted surface is given in figure 4.

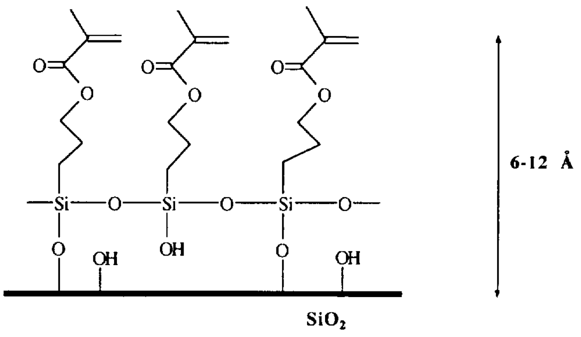


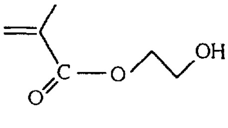
Fig 4. Representation of the grid silica grafted with the trimethoxysilane derivative.

The silanization is achieved by putting the silica layer in a solution containing 10% (w:w) trimethoxysilane derivative and 0.5% ultrapure water in toluene (SDS). The reaction was carried out for 4 h under reflux. The FET was then washed with acetone and dried in a stream of nitrogen.

The thickness of the layer was separately checked by depositing the trimethoxysilane on a silicon wafer under the same conditions. The thickness was determined by ellipsometry; it was found to be between 6 and 12 Å for the organic layer. Such a value is expected from the molecular parameters of the grafted silane derivative.

Photopolymerization

The grafted silica surface is copolymerized under irradiation with 2-hydroxyethyl methacrylate (HEMA), Aldrich:



HEMA

A mixture of HEMA, polyvinylpyrrolidone ($\overline{M}_W$ = 300 000 g/mol) and methanol (20:1:19 w:w) was used and deposited on the FET by spin coating. The HEMA originally contained 4% (w:w) of 2-dimethoxy-2-phenylacetophenone (Janssen), which acts as a photoinitiator. UV irradiation under nitrogen at 365 nm with a mercury lamp for 2 min allows us to obtain the polymerized film at the desired position (fig 5).

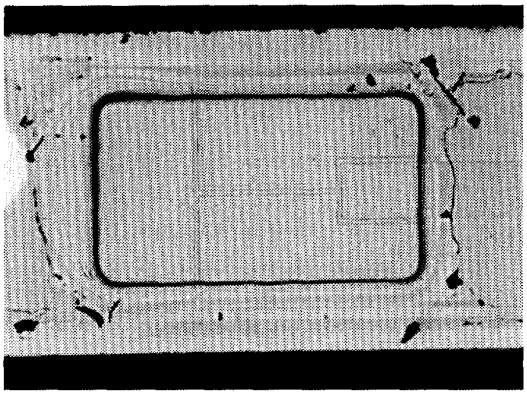


Fig 5. Membrane deposited between the source and the drain (thickness: 1.7 μm). (Scale: 2.2 cm per 500 μm).

The planarity of the membrane has been checked (Talystep) showing a larger thickness (30%) over a small fraction of the perimeter. The membrane could easily be made thinner (0.1–0.3 or 0.5–0.7 μm) by diluting the spin coating mixture with methanol (twofold or fivefold).

Covalent linking of the ionophores

The above membrane contains hydroxyethyl moieties, which can be reacted with various functional groups. A carboxylic acid group was chosen to form an ester linkage in the present case (fig 2).

A concentrated solution of the crown-ether phthalocyanine ionophore (5×10^{-3} M) in a mixture $CHCl_3$/MeOH (2:1) was used to impregnate the membrane. The excess of reactant was removed by washing it with pure chloroform. The quantity of substituted phthalocyanine deposited was checked by visible absorption spectroscopy on a glass slide which was treated under exactly the same conditions as the field-effect transistor. The spectrum shows two peaks at 636 and 676 nm corresponding to the dimeric (or aggregated) and monomeric species, respectively. The extinction coefficients of the monomeric (ε_{676} = 205 000 dm^3 mol^{-1} cm^{-1}; ε_{636} = 19 500) and dimeric (ε_{676} = 36 000; ε_{636} = 160 000) forms of $(15C5)_4PcZn$ are known [13]. This yields a proportion of 70% dimer and 30% monomer (m:m).

The covalent coupling was achieved by introducing the impregnated membrane in toluene in the presence of 1,3-dicyclohexylcarbodiimide (DCC) under reflux for 18 h. Under these conditions the substituted phthalocyanine was not soluble. It is worth noting that the quantity of toluene which diffuses within the membrane is negligible whereas CH_2Cl_2, MeCN or MeOH lead to a significant swelling of the membrane. The presence of DCC is essential for obtaining an irreversible grafting of the dye. The green coloration of the organic layer remained stable after DCC treatment and washing with $CHCl_3$/MeOH (2:1), $CHCl_3$ or pure MeOH. The layer which had not been treated with DCC shows an almost complete discoloration under the same conditions. The visible absorption spectra after DCC treatment were approximately the same as before the reaction coupling.

The quantity of phthalocyanine linked to the polymeric membrane can be estimated by assuming that the extinction coefficients are the same in the membrane as in solution. It must be additionally assumed whether or not the dye is homogeneously dispersed within the membrane (e = 1.7 μm). This case will be considered together with a superficial (e = 20 Å) derivatization.

$$A(\lambda) = (\varepsilon_D C_D + \varepsilon_M C_M)e$$
$$(\lambda = 636\ ;\ 676\ \text{nm});\ e = 1.7 \times 10^{-4}\ \text{cm or}\ 2 \times 10^{-7}\ \text{cm}$$

In this way, the total concentration of phthalocyanine derivatives ($C_{TOT} = 2C_D + C_M$) is calculated to be 7 M for a superficial functionalization over 20 Å and 8×10^{-3} M for a homogeneous reaction. These concentrations must be compared with the density of hydroxy groups in the starting material. From the density of the polyhydroxyethylmethacrylate (1.313 g/cm^3) and the molecular weight of the monomeric unit (130.1 g/mol), a concentration of approximately 10 mol of hydroxy groups per liter can be calculated. This means that, in the case of a homogeneous linkage, one of the 1250 hydroxy groups had reacted. If the reaction is postulated to occur over 20 Å, the hydroxy groups are almost completely functionalized by the phthalocyanine moiety.

By considering only hydroxy groups at the membrane surface, a density of $(\mathcal{N}C/1000)^{2/3} = 3.3 \times 10^{14}/\text{cm}^2$ is found. This is the same order of magnitude as for silanol groups.

Deposition of the protecting layer

The final device is obtained by depositing a protecting layer (see fig 1) to avoid short circuits between the connection wires of the source and the drain and the analyte. This has been carried out using an epoxy resin (Epotecny E708) which is deposited manually.

Modelization of the ISFET

In this work, the site-binding-theory model has been modified to take into account the presence of a surface-grafted ionophore [14]. In this model only surface states as shown schematically in figure 6 are taken into account.

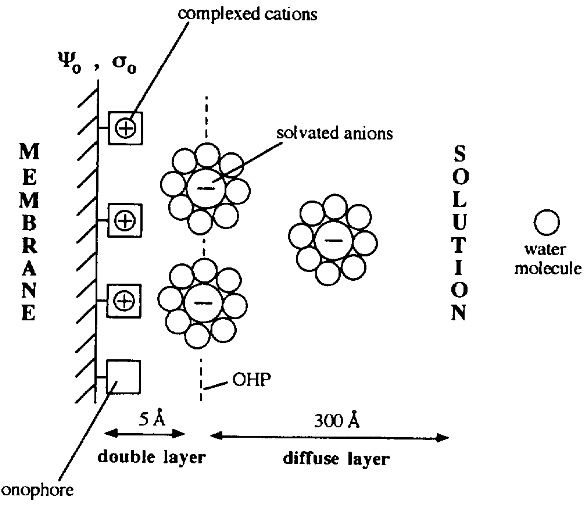


Fig 6. Chemical species present at an interface between a membrane grafted with an ionophore and an aqueous medium containing an electrolyte. OHP: outer Helmholtz plane (corresponding to the closest approach of solvated anions); diffuse layer: distribution of the counterions following a Boltzmann distribution; σ_o: excess of positive charges (coulomb/cm^2) at the surface with corresponding surface potential Ψ_o.

A preliminary equilibrium is postulated in which a certain amount of cation M_s^+ can enter the outer Helmholtz region:

$$M_s^+ = M^+ \exp\left(-q\Psi_o/kT\right)$$

$$q = 1.6 \times 10^{-19}\ \mathrm{C},\ k = 1.38 \times 10^{-23}\ \mathrm{J/K}$$

The cation approach is however prevented by the repulsive surface potential Ψ_o. Then:

$$N_{\mathrm{TOT}} = (\mathrm{L})_{\mathrm{surf}} + (\mathrm{LM}^+)_{\mathrm{surf}}$$

where L and LM$^+$ are the surface densities of the free ligand and the complex, respectively.

$$\sigma_o = q(\mathrm{LM}^+)_{\mathrm{surf}}$$

The concentration of cation within the solution is related to the stability constant K, ionophore/ligand, via the equations:

$$K = \frac{(\mathrm{LM}^+)_{\mathrm{surf}}}{(\mathrm{L})_{\mathrm{surf}}(\mathrm{M}_s^+)} - \log\,(\mathrm{M}^+)$$
$$= \log K + \frac{1}{\ln 10}\left[\ln\left[\frac{\mathrm{q}N_{\mathrm{TOT}}}{C_{\mathrm{dl}}\Psi_o} - 1\right] - \frac{\mathrm{q}\Psi_o}{\mathrm{kT}}\right]$$

C_{dl} is the capacity of the double layer (taken to be around 20 μF/cm^2 [17]):

$$\sigma_o = C_{\mathrm{dl}}\Psi_o$$

More than one ionic species may be postulated to be present at the membrane surface. The corresponding model may easily be deduced from the above considerations [14].

This simple modeling allows us to semiquantitatively determine the influence of the two main parameters, the association constant K and the number of binding sites at the surface N_{TOT}, on the curves, giving the surface potential Ψ_o as a function of the concentration of cations in the solution.

The limiting value of 59 mV per tenfold increase in concentration for the curve Ψ_o vs $-\log$ (M$^+$) can only be obtained for a sufficiently high density of binding sites (fig 7).

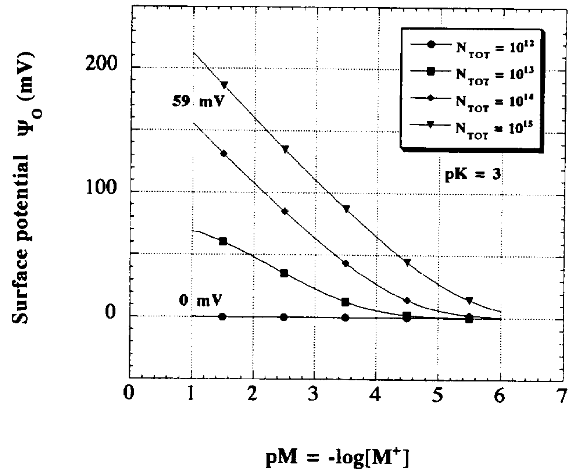


Fig 7. Surface potential (Ψ_o) as a function of the logarithm of the concentration of cations (pM) for different values of the density (number per cm^2) of binding sites N_{TOT}. The association constant K is taken to be 10^3.

The association constant K will also influence the concentration threshold at which the variation of the ion concentration is detected; a higher association constant yields a lower detection limit (fig 8).

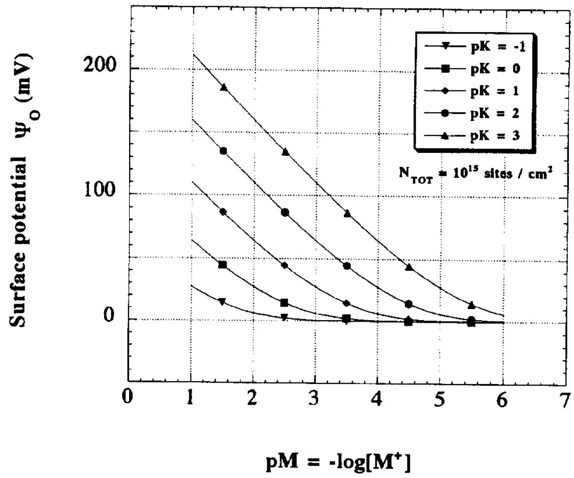


Fig 8. Surface potential Ψ_o as a function of the logarithm of the cation concentration for different values of the association constants $\log K = \mathrm{p}K$. The number of surface binding sites is considered to be constant (10^{15} sites/cm^2).

It can be concluded that a surface density of binding sites higher than $10^{13}/\mathrm{cm}^2$ and an association constant grafted ionophore/cation of at least 10^3 are required to obtain well-behaved devices.

Experimental determination of the performances of the ISFET

The determinations have been carried out in such a way that the source-to-drain current I_{DS} and the source-to-drain voltage V_{DS} are maintained constant by varying V_s:

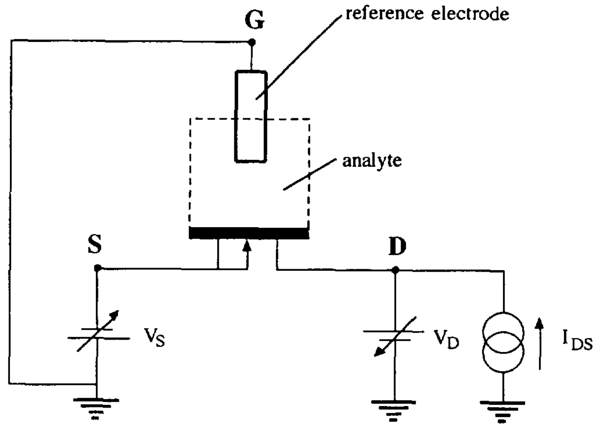


Fig 9. Electrical circuit used to measure the characteristics of the ISFET.

The main parameters involved in the grid-to-source voltage V_{GS} are:

$$V_{GS} = \Psi_{SiO_2} - \Psi_o + c^{st}$$

Ψ_o: surface potential; Ψ_{SiO_2}: potential across the dielectric. The constant includes V_{ref}, V_{el}, V_{dif} and other parameters. V_{ref}: electrode potential; V_{el}: ohmic drop in the electrolyte; V_{dif}: potential of the diffuse layer. V_s is the voltage measured experimentally and, with the electrical circuit taken in figure 9:

$$V_s = -V_{GS}$$

When the concentration of electrolytes within the solution is varied, the potentials V_{ref}, V_{el}, V_{dif} and Ψ_{SiO_2} are considered to remain constant, whereas Ψ_o and V_{GS} vary. In the procedure used here, I_{DS} and V_{DS} are constant whereas V_s is varied. First, the properties of the membrane grafted with the phthalocyanine ionophore have been compared with the unsubstituted polyhydroxyethyl methacrylate membrane (fig 10).

The ISFET without ionophore does not show any response up to a concentration of 10^{-2} M; it then seems that anions (rather than cations) are incorporated in the membrane since $\Delta V_s < 0$.

Another series of experiments was carried out at pH 8.1 (fig 11).

By fitting the experimental points with the equation relating $-\log(M^+)$ with f (K, N_{TOT}, Ψ_o), the values of the density of binding sites (N_{TOT}) and the complexation constants (K) may be estimated (table I).

The complexation properties of the benzo-15-crown-5 subunit in various solvents are known [15] (table II).

By comparing with the association constants found with the ISFET, it seems that the polymeric membrane furnishes the ionophore with a medium intermediate between water and methanol. This can be deduced from the magnitude of the binding constant but also from the Na^+/K^+ selectivity which is null in water and significantly in favor of Na^+ in

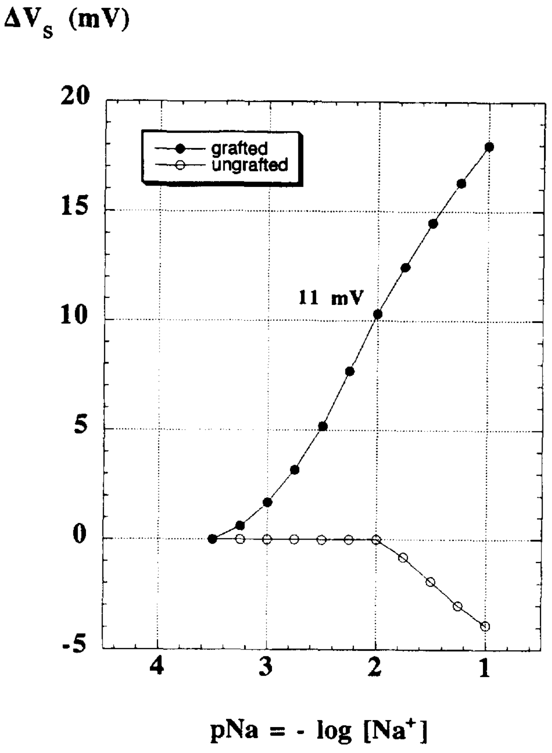


Fig 10. Variations of V_s as a function of the concentration of NaCl in water (buffer HCl/tris-(hydroxymethyl) aminomethane 10^{-3}M; pH = 6.7). Saturated calomel reference electrode. Membrane: 0.1–0.3 μm, I_{DS} = 100 μA, V_{DS} = 0.5 V (no reference ISFET).

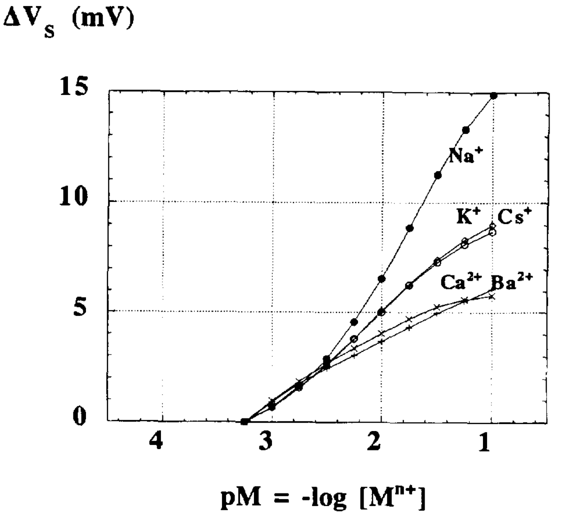


Fig 11. Variations of V_s as a function of the addition of NaCl, KCl, CsCl, $BaCl_2$ and $Ca(NO_3)_2$ in water. Buffer pH: 8.1 HCl/tris-(hydroxymethyl) aminomethane 10^{-3} M. Membrane thickness 0.1–0.3 μm. Platinum counter-electrode. I_{DS} = 100 μA; V_{DS} = 0.5 V. Values determined by using an ungrafted ISFET for reference.

Table I. Overall superficial binding site density and ligand-cation association constant for various salts in water.

	N_{TOT}[a] (*cm*$^{-2}$)	*log* K[b]
NaCl	2×10^{12}	1.75
KCl	1.2×10^{12}	2.1
CsCl	1.2×10^{12}	2.0
$Ca(NO_3)_2$	4.3×10^{11}	2.6
$BaCl_2$	4.1×10^{11}	2.3

[a] N_{TOT} is calculated for a purely superficial grafting and corresponds to the crown-ether moieties density.

[b] HCl/tris-(hydroxymethyl)aminomethane pH = 8.1, 10^{-3} M used as buffer.

Table II. Logarithm of the association constant (log *K*) for benzo-15-crown-5 in water and methanol (from reference 15).

Ion	*Solvent*	*log* K
Na^+	H_2O	0.40
	MeOH	3.37
K^+	H_2O	0.38
	MeOH	2.8
Cs^+	MeOH	1.91

MeOH; this is found both in solution and for the ISFET (fig 11). For these determinations the response of the grafted ISFET was compared to an ungrafted one and only the difference is reported.

The ISFET (grafted and ungrafted) are highly sensitive to pH changes. The use of buffer solutions and the comparison with an ungrafted ISFET is therefore an absolute necessity (fig 12).

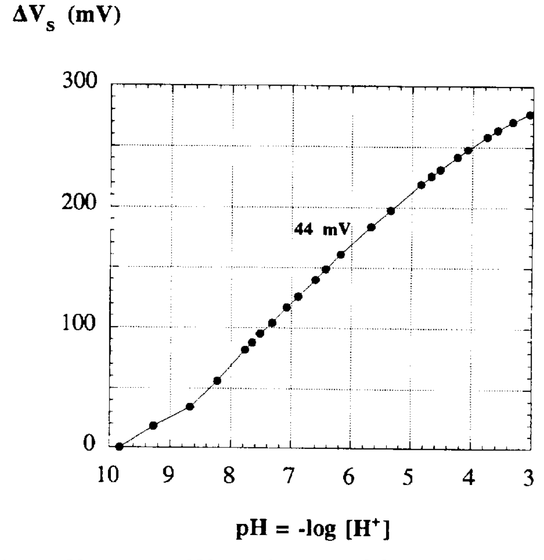


Fig 12. Variations of V_s as a function of the concentration of HCl added in tris-(hydroxymethyl)aminomethane 10^{-2} M. Saturated calomel electrode I_{DS} = 100 μA, V_{DS} = 0.5 V. Ungrafted membrane with no ISFET reference.

A slope of 44 mV per decade of proton concentration is detected in the pH range 3–10. This indicates a high concentration of ionizable groups at the silica surface. These arise from unreacted silanol groups of the silica surface or from the anchoring polysiloxane chain. The pH sensitivity for SiO_2 surfaces after sulfochromic treatment is 36 mV per pH unit [16]. By titration with CH_3Li, the corresponding silanol density has been shown to be 3.4 SiOH per nm^2 (see references mentioned in reference 16).

Conclusions

A new monofunctionalized phthalocyanine-based ionophore has been used for grafting the grid of field-effect transistors. The method used involves a photopolymerization process taking advantage of the current microelectronics technology. The ionophore bears three crown-ether moieties whose properties may be adjusted as a function of the type of cations complexed and the magnitude of the desired complexation constant. The grafted ISFET obtained in this way shows relatively satisfactory performances. As a comparison, functionalization of similar membranes with a simple carboxylic acid derivative of benzo-15-crown-5 yields almost no ion response under the same conditions. However, a strong pH dependence precludes a practical use for the moment. The interposition of polymeric protecting gel layers could be envisaged [5] but alternative ways are also possible by neutralizing the surface silanol groups [16].

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