SENSITIVITY CONTROL OF ISFETs BY CHEMICAL SURFACE MODIFICATION

A VAN DEN BERG, P BERGVELD, D N REINHOUDT and E J R SUDHOLTER

Department of Electrical Engineering and Laboratory of Organic Chemistry, Twente University of Technology, P O Box 217, 7500 AE Enschede (The Netherlands)

(Received May 30, 1985, accepted in revised form October 17, 1985)

Abstract

The response of ISFETs (ion-sensitive field-effect transistors) to concentrations of ions, especially H^+ ions, is determined by the type of gate surface. Both the number of active surface sites and (proton) association and dissociation constants influence the sensitivity.

In the case of a chemically-modified gate surface, a new surface is formed, which generally has a different sensitivity.

It is shown that the original pH response of the gate oxide can be either lowered or increased, depending on the reactivity of the added groups. In general, coverage with apolar groups and reduction of the number of sites result in a lower pH response, while addition of basic or acidic groups as well as an increase of active sites give a higher pH response.

Using the extended site-dissociation model, which describes the behaviour of a surface composed of two types of sites, theoretical curves for surface potential *versus* pH are calculated. Measurements with chemically-treated SiO_2 and Ta_2O_5 ISFETs confirm the theoretical expectations. The conclusion has been drawn that by a proper choice of chemical treatment, both the point of zero charge (pzc) and the pH-insensitive range can be changed.

1 Introduction

Since the introduction of the ISFET (ion-sensitive field-effect transistor) in 1970 by Bergveld [1], many theoretical and experimental studies have been published describing the behaviour of this chemically sensitive electronic device. The commonly accepted model to account for the pH sensitivity of the ISFET is the site-dissociation model, which was first proposed by Yates *et al* [2], and later applied to ISFETs by Siu and Cobbold [3] and Bousse [4]. It has been shown that the pH response of an ISFET with an inorganic gate material can be described in terms of proton dissociation and association constants and the number of reactive sites on the

gate surface The behaviour of gate surfaces such as SiO_2 , Al_2O_3 , Si_3N_4 and Ta_2O_5 has been experimentally verified and can be accounted for by this theory [4 - 8]

For some applications of the ISFET, for example the development of a REFET (Reference FET), or an ISFET-based ion sensor, it is necessary to change the specific characteristics of the surface

The literature concerning REFETs describes various processes for obtaining a completely pH-insensitive surface [9 - 11] Using a standard procedure that is compatible with both semiconductor technology and organic chemistry, it would be possible to create a large variety of ion sensors The modification may be carried out by bonding of ionic molecules to this surface or by incorporating ionophores in a layer that renders the surface pH insensitive Hitherto the major problem in obtaining such structures has been the attachment of the pH-insensitive layers to the gate surface, resulting in bad long-term stability The main reason for this lies in the fact that the original gate surface in most cases contains hydrophilic OH groups, to which a hydrophobic layer has to be attached

Therefore we have investigated modifications of the inorganic gate surface with several coupling agents The original gate surfaces studied were Ta_2O_5 and SiO_2 SiO_2 is particularly interesting because

(i) Many experimental results have been described in the literature concerning the chemical modification of silica gel (*e.g.*, in liquid chromatography) and glass fibres (in polymer chemistry)

(ii) SiO_2 has a relatively low pH sensitivity (less than Nernstian), which might be convenient for REFET development

(iii) Because of its non-Nernstian behaviour, the pH response can be made more or less sensitive, thus allowing experimental confirmation of theoretical considerations and calculations

It must be noted, however, that compared with Al_2O_3 , Ta_2O_5 and Si_3N_4 , an SiO_2 gate surface has the disadvantage of a relatively large hysteresis [12, 13] Since such a hysteresis is absent with Ta_2O_5 as a gate oxide, we have also included this modification

2 Theory

2.1 Theory for single-site inorganic gate surfaces

The generally accepted model for ISFET behaviour in aqueous solutions is the site-dissociation model [2 - 4] This model considers the reversible surface reactions that take place at the gate of the ISFET Generally, the H^+ and OH^- ions in solution determine the response of the ISFET (the so-called potential-determining ions) There are two equivalent approaches to calculating the surface charge σ_0 , corresponding to a potential difference ψ_0 between the gate surface and the bulk solution Both models consider the dissociation and association of amphoteric sites, which can be written in the form of two dissociation reactions

The most commonly used model is based on the equilibrium between surface OH groups and H^+ ions *located directly near the surface*, H_s^+ . We can write the following equations

where $A-OH_2^+$, $A-OH$ and $A-O^-$ represent positive, neutral and negative surface sites respectively, and $[A-OH_2^+]$, $[A-OH]$ and $[A-O^-]$ are the numbers of sites per surface area. Note that we have replaced the H_s^+ activity by $[H^+]_s$, the surface concentration. The activity coefficient is included in the dissociation constants. We have to use the Boltzmann equation to correlate $[H^+]_s$ to the bulk concentration of H^+ ions ($[H^+]_b$)

$$[H^+]_s = [H^+]_b \exp(-q\psi_o/kT) \quad (3)$$

with q = elementary charge, k = Boltzmann's constant, T = temperature and ψ_o = potential difference between surface and bulk solution ($\psi_o = \psi_s - \psi_b$) generated by the surface charge

The surface charge density is easily calculated from

$$\sigma_o = q\{[A-OH_2^+] - [A-O^-]\} = q[A-OH] \left\{ \frac{[H^+]_s}{Ka_1} - \frac{Ka_2}{[H^+]_s} \right\} \quad (4)$$

The second approach is a more fundamental one, as described by Yates *et al* [2]. It considers the equilibrium between the $A-OH$ sites at the surface and the H^+ ions in *the bulk solution*

with the following thermodynamic equations

$$\mu_{A-OH_2^+}^\circ + kT \ln \nu_{A-OH_2^+} = \mu_{A-OH}^\circ + \mu_{H_b^+}^\circ + kT \ln \nu_{A-OH} + kT \ln a_{H_b^+} - q\psi_o \quad (7)$$

$$\mu_{A-OH}^\circ + kT \ln \nu_{A-OH} = \mu_{A-O^-}^\circ + \mu_{H_b^+}^\circ + kT \ln \nu_{A-O^-} + kT \ln a_{H_b^+} - q\psi_o \quad (8)$$

where μ_i° and ν_i are the standard chemical potential and number of sites per surface area of species i respectively, and $a_{H_b^+}$ is the H^+ activity in the bulk. Now the dissociation constants Ka_1' and Ka_2' are defined as follows

$$Ka_1' = \exp\left(\frac{\mu_{A-OH_2^+}^\circ - \mu_{A-OH}^\circ - \mu_{H_b^+}^\circ}{kT}\right) \quad (9)$$

$$Ka_2' = \exp\left(\frac{\mu_{A-OH}^\circ - \mu_{A-O^-}^\circ - \mu_{H_b^+}^\circ}{kT}\right) \quad (10)$$

and the surface charge density is given by

$$\begin{aligned}\sigma_0 &= q(\nu_{\text{A-OH}_2^+} - \nu_{\text{A-O}^-}) \\ &= q\nu_{\text{A-OH}} \left[\frac{a_{\text{Hb}^+} \exp(-q\psi_0/kT)}{Ka_1} - \frac{Ka_2}{a_{\text{Hb}^+} \exp(-q\psi_0/kT)} \right]\end{aligned}\quad (11)$$

Equation (11) is essentially equivalent to eqn (4) and with eqn (3) it is easily found that $Ka_1' = Ka_1$ and $Ka_2' = Ka_2$. The main advantage of the latter description is that it is immediately clear that Ka_1 and Ka_2 are real thermodynamic constants, *independent of the ionization state of the surface*.

This ionization dependency of pKa is nevertheless reported in the literature for SiO_2 [14, 15]. In these cases we suppose that the electric potential is included in the definition of pKa , but it is in our opinion incorrect and confusing to use pKa in this way.

The interface potential ψ_0 actually measured with an ISFET is related to the surface charge density σ_0 using the Gouy-Chapman-Stern theory [4]

$$\psi_0 = \frac{2kT}{q} \sinh^{-1} \left\{ \frac{\sigma_0}{(8\epsilon_r\epsilon_0kTC)^{1/2}} \right\} + \frac{\sigma_0}{C_H} \quad (12)$$

where $\epsilon_r\epsilon_0$ = dielectric constant of the solvent, C_H = capacity of the Helmholtz layer and C = ionic concentration in solution. Equation (12) can be simplified if we keep in mind that the total number of sites per unit area, N_s , for an SiO_2 surface equals approximately $5 \times 10^{14}/\text{cm}^2$ [4], so that for a fully ionized surface $\sigma_{0,\text{max}} = qN_s \approx 10^{-4} \text{ C/cm}^2$. This means that, using a concentration $C = 0.1 \text{ M}$, the argument of the $\sinh^{-1}$ function is $\approx 2.5 \times 10^{-7}$, so that the function can be replaced by its argument. The resulting term is defined as the diffuse layer capacity C_d

$$C_d = \frac{\sqrt{8\epsilon_wkTCq}}{2kT} \quad (13)$$

From eqn (12) it can be seen that the series connection of this diffuse layer capacity C_d and the Helmholtz layer capacity C_H determines the surface potential ψ_0 generated by the surface charge density σ_0 .

At sufficiently high ionic concentrations ($C \geq 0.1 \text{ M}$), $C_d \geq 130 \mu\text{F/cm}^2$ and with values for C_H reported between 10 and $40 \mu\text{F/cm}^2$ [16], for which a value of $20 \mu\text{F/cm}^2$ is usually taken, we conclude that C_d can be neglected. We remark that this simplification is only allowed at higher ionic concentrations, and that we do not consider the case of a very low charge density in which the semiconductor charge influences the response, as was investigated by Matsuo [17].

To complete the model we have added an equation for the total number of sites per unit area to eqns (11) and (12)

Fig 1 ψ_o -pH curve for Nernstian (1) and non Nernstian (2) surfaces

	N_s	Ka_1	Ka_2
1	10^{15}	10^{-6}	10^{-8}
2	10^{15}	10^{-3}	10^{-11}

$$N_s = \nu_{A-OH} + \nu_{A-O^-} + \nu_{A-OH_2^+} \quad (14)$$

Now the relation between ψ_o and $\text{pH}(-\log a_{H^+})$ can be calculated

Figure 1 shows typical ψ_o -pH curves. For a good interpretation we have to introduce and define the following terms

(a) pH_{pzc} point of zero charge, pH at which the net amount of surface charge is zero ($\nu_{A-O^-} = \nu_{A-OH_2^+}$). It is easily shown that $\text{pH}_{pzc} = (\text{pKa}_1 + \text{pKa}_2)/2$

(b) Nernstian behaviour we define a linear pH curve of 55 - 60 mV/pH as Nernstian behaviour

(c) Reactive surface a surface is called reactive if the surface groups are easily ionized

All curves that can be calculated in this way are determined by the values of Ka_1 , Ka_2 and N_s . This means that if we want to change the characteristics of a gate surface, we have to change these parameters. Therefore we will examine below the influence of Ka_1 , Ka_2 and N_s on the calculated ψ_o -pH curve

Influence of Ka_1 on the ψ_o -pH response

The effect of an increase and decrease of Ka_1 by a factor of 10^3 has been calculated for Nernstian and non-Nernstian surfaces (Fig 2). In the case of a *non-Nernstian* surface, the part of the curve at $\text{pH} < \text{pH}_{pzc}$ ('acidic branch') is shifted 3 pH units towards lower pH values if Ka_1 is increased. If Ka_1 decreases, the acidic branch is shifted in the opposite direction. The pH_{pzc} (pH at which $\psi_o = 0$) is shifted -1.5 and +1.5 pH units respectively (Fig 2). The influence on a *Nernstian* surface depends on its reactivity. When Ka_1 is increased or decreased at a *reactive* surface, the response remains Nernstian and the whole curve (and pH_{pzc}) is shifted -1.5 or +1.5

Fig 2 Influence of the Ka_1 value on the ψ_o -pH response of a non-Nernstian surface

	N_s	Ka_1	Ka_2
1	10^{15}	10^{-3}	10^{-11}
2	10^{15}	10^{-0}	10^{-11}
3	10^{15}	10^{-6}	10^{-11}
-	10^{15}	10^{-3}	10^{-8}

pH units. When the surface is *less reactive* however, then for an increase of Ka_1 the acidic branch is lifted downwards over 3 pH units and the pH_{pzc} is shifted 1.5 pH unit towards lower pH, resulting in a non-Nernstian curve (Fig 2, broken line). In the case of a decrease of Ka_1 the acidic and basic branches are both shifted 1.5 pH unit towards higher pH, and the response remains Nernstian.

Influence of Ka_2 on the ψ_o -pH response

Because calculations made with the amphoteric sites dissociation model give symmetrical ψ_o -pH curves around pH_{pzc} [4], the effect of increasing Ka_2 a thousand-fold on the 'basic' branch of the ψ_o -pH curve is similar to the effect of a decrease of Ka_1 on the 'acidic' branch. A thousand-fold decrease of Ka_2 corresponds to a thousand-fold increase of Ka_1 in the same way.

Influence of N_s on the ψ_o -pH response

The number of sites per unit area, N_s , largely influences the calculated ψ_o -pH responses. In practice the upper limit of N_s in oxides lies around $10^{15}/\text{cm}^2$, due to bonding distances in oxides. Only if more than one atomic layer contributes to the formation of surface charge, as was assumed by Akiyama *et al* for ZrO_2 [5] and discussed by Bousse *et al* for SiO_2 [12], are larger values possible. Therefore, in our calculations we only investigated the influence of a lower value of N_s on Nernstian and non-Nernstian surfaces. Figure 3(a) shows the effect of the change of N_s from 10^{15} to 10^{14} , 10^{13} and 10^{12} sites/ cm^2 respectively, in the case of a *Nernstian* surface. We see

Fig 3 (a) Influence of N_s value on the ψ_o -pH response of a Nernstian surface

	N_s	Ka_1	Ka_2
1	10^{15}	10^{-6}	10^{-8}
2	10^{14}	10^{-6}	10^{-8}
3	10^{13}	10^{-6}	10^{-8}
4	10^{12}	10^{-6}	10^{-8}

Fig 3 (b) Influence of N_s value on the ψ_o -pH response of a non-Nernstian surface

	N_s	Ka_1	Ka_2
1	10^{15}	10^{-3}	10^{-11}
2	10^{14}	10^{-3}	10^{-11}
3	10^{13}	10^{-3}	10^{-11}
4	10^{12}	10^{-3}	10^{-11}

that with $N_s = 10^{14}/\text{cm}^2$ the response is still linear, but the slope is decreased from 58 to 56 mV/pH, at lower values of N_s (10^{13} and $10^{12}/\text{cm}^2$), we find a saturation effect at $\text{pH} > \text{pH}_{\text{pzc}} + 3$. In Fig 3(b) the calculated effects for the same values of N_s at a *non-Nernstian* surface are shown. Now we see that changing N_s from 10^{15} to $10^{14}/\text{cm}^2$ results in a shift of both the 'acidic'

and 'basic' branches over 1 pH unit away from pH_{pzc} . Again we find the saturation effect at N_s values of 10^{13} and $10^{12}/\text{cm}^2$. We note that a change of N_s does not affect the position of the pH_{pzc} .

Conclusions

From the previous calculations we can conclude that an increase in Ka_1^{-1} , Ka_2 and N_s leads to a shift from non-Nernstian to Nernstian behaviour. The values of these parameters required to obtain a slope of 55 mV/pH at pH_{pzc} can be calculated using the sensitivity parameter β as introduced by Bousse [4]. He showed that at pH_{pzc} the slope of the curve is given by $59\beta/(\beta + 1)$ (mV/pH), with

$$\beta = \frac{(2q^2 N_s) \left(\frac{Ka_2}{Ka_1} \right)^{1/2}}{C_H k T}$$

Using $C_H = 20 \mu\text{F}/\text{cm}^2$, we find that for a minimum slope of 55 mV/pH, $\beta > 14$ is required, which corresponds to

$$N_s \left(\frac{Ka_2}{Ka_1} \right)^{1/2} > 2.15 \times 10^{13} \text{ cm}^{-2}$$

It is obvious that a pH-insensitive surface requires lower values of Ka_1^{-1} , Ka_2 and N_s . If we want to displace the pH-insensitive region, which lies around pH_{pzc} , towards higher values only Ka_2 should be decreased, while for a shift towards lower pH values Ka_1^{-1} should be made smaller.

In practical situations, however, it is difficult to control these parameters independently.

A possible way to change the values of Ka_1^{-1} and Ka_2 is to bind sites with other Ka_1^{-1} and Ka_2 to the original sites (chemical modification). However, in this way N_s will generally also be changed. This is because it is unlikely that all the original sites disappear, it is clear that now at least two types of sites give rise to a surface charge. Therefore we have to extend the theory for such a compound surface using a *two-site dissociation model*.

2.2 Theory for a chemically modified surface (two-site model)

We assume that the surface obtained after chemical modification consists of a (mono)layer of new sites which partly covers the original surface sites. For convenience we represent the newly-formed sites by $A_2\text{—OH}$, although this is not correct for CH_3 groups or NH_2 groups, for example.

Figure 4 gives a schematical representation of the new surface. In order to be able to describe the operational mechanism of this compound layer, we make the following assumptions:

(a) The additional sites have an amphoteric character, with dissociation constants K_2a_1 and K_2a_2 . Note that calculations made with extremely

Fig 4 Schematical representation of a surface composed of two types of sites

low $K_2a_1^{-1}$ and K_2a_2 can account for the case of coverage with apolar groups that are hardly ionized (We usually take a value of $K_2a_1^{-1} = K_2a_2 = 10^{-30}$ for these cases)

(b) With the chemical treatment only one extra type of site is introduced ($A_2\text{--OH}$) that contributes significantly to the surface charge

(c) Both original and additional sites are at the same electrical potential

(d) The chemical nature of the residual original sites ($A_1\text{--OH}$) is not influenced by the modification

(e) If the added groups are not amphoteric but acidic (or basic), then we take $K_2a_1^{-1}$ (or K_2a_2) = 10^{-30} in the calculations

Under these conditions the site dissociation can be extended to a *two-site dissociation model*. Now, the surface charge is generated by sites 1 and 2 and eqn (11) is extended to

$$\begin{aligned} \sigma_0 &\approx q(\nu_{A_1\text{--OH}_2^+} + \nu_{A_2\text{--OH}_2^+} - \nu_{A_1\text{--O}^-} - \nu_{A_2\text{--O}^-}) \\ &= q \left\{ \nu_{A_1\text{--OH}} \left[\frac{a_{H_b^+} \exp(-q\psi_o/kT)}{K_1a_1} - \frac{K_1a_2}{a_{H_b^+} \exp(-q\psi_o/kT)} \right] + \right. \\ &\quad \left. + \nu_{A_2\text{--OH}} \left[\frac{a_{H_b^+} \exp(-q\psi_o/kT)}{K_2a_1} - \frac{K_2a_2}{a_{H_b^+} \exp(-q\psi_o/kT)} \right] \right\} \end{aligned} \quad (15)$$

and the total number of sites 1 and 2 per unit area is given by

$$N_{s1,2} = \nu_{A_1,2\text{--OH}} + \nu_{A_1,2\text{--OH}_2^+} \quad (16)$$

In this case, calculations of ψ_o -pH curves cannot be made directly, especially if saturation effects are taken into account. We now have to use an implicit relation between ψ_o and pH ($-\log a_{H_b^+}$) with $[H^+]_s$ as a variable. To get some insight into the effects of chemical modifications on the pH response, we will discuss some simulations made with this model.

Chemical modification with unreactive groups

It is clear that if only unreactive sites that do not interact with protons are introduced, the surface charge density is determined only by the $A_1\text{--OH}$ sites that are left. The resulting effect is a decrease of N_{s1} , similar to that discussed already (Fig 3(a) and (b)).

Chemical modification with reactive groups

The results shown in Fig 2 indicate that it is possible to improve the behaviour of a non-Nernstian surface towards a Nernstian response by adding acidic or basic groups. Figure 5 shows results of the calculated effect of

Fig 5 Effect of covering a non-Nernstian surface with reactive acidic groups

	N_{s1}	$K_1 a_1$	$K_1 a_2$	N_{s2}	$K_2 a_1$	$K_2 a_2$
1	10^{15}	10^{-3}	10^{-11}	0	—	—
2	10^{14}	10^{-3}	10^{-11}	9×10^{14}	10^{30}	10^{-9}
3	10^{13}	10^{-3}	10^{-11}	9.9×10^{14}	10^{30}	10^{-9}

90% and 99% coverage of a surface with $N_{s1} = 10^{15}/\text{cm}^2$, with sites that have $K_2 a_2 = 10^2 K_1 a_2$. We find an increase in pH response at higher pH values. It can also be seen that if only one type of site (in this case acidic) is added, it is not recommended to cover too many original sites, since then saturation occurs at lower pH values. Addition of basic instead of acidic sites gives comparable results due to symmetry effects, as discussed above. The best way to derive a Nernstian pH response would be to cover partially a surface that is relatively acidic (or basic) with relatively basic (or acidic) sites, with $K_2 a_1 \ll K_1 a_1$ ($K_2 a_2 \gg K_1 a_2$). In the case of SiO_2 as a starting material, this means coverage with sites that have $K_2 a_1 \ll 10^2 \approx K_1 a_1$. In Fig 6, curve 3, we show the calculated ψ_o -pH response of a surface that consists of 50% Si-OH sites ($N_{s1} = 2.5 \times 10^{14}/\text{cm}^2$) and 50% Al-OH sites ($N_{s2} = 5 \times 10^{14}/\text{cm}^2$) (values for $N_{s1,2}$ and the dissociation constants are taken from Bousse [4]). We observe that in this case the compound surface gives a linear pH response with a Nernstian slope. We notice, however, that the practical disadvantages of such a modification are not considered.

Conclusions

If a pH-insensitive surface is desired (REFET), it is necessary that less than 0.01% of the original sites is left uncovered (Fig 3(a)) and that the added sites have sufficiently small values of Ka_1^{-1} and Ka_2 in order to give no contribution to the surface charge density σ_0 (Fig 2).

Since the first condition seems very hard to fulfill with monolayer coverage, it is more realistic to achieve such a reduction in the number of original sites by coverage with a thin film consisting of at least several molecular layers. The second condition then prescribes the properties of this thin film.

Fig 6 Theoretical ψ_0 -pH response of SiO_2 and Al_2O_3 surfaces, and a surface consisting of 50% SiO_2 and 50% Al_2O_3

	N_{s1}	$K_1 a_1$	$K_1 a_2$	N_{s2}	$K_2 a_1$	$K_2 a_2$
1	5×10^{14}	10^2	10^{-6}	0	—	—
2	10^{15}	10^{-6}	10^{-10}	0	—	—
3	2.5×10^{14}	10^2	10^{-6}	5×10^{14}	10^{-6}	10^{-10}

If a large pH response is required, a partial coverage will give the best results. It depends on the value of the original pH_{pzc} whether acidic or basic sites should be added: a low pH_{pzc} requires addition of basic sites and a high pH_{pzc} addition of acidic sites.

Note that an increase in pH response can also be obtained by composing the whole gate of two types of sites, for example by ion implantation of Al in SiO_2 [18] or by mixed CVD (chemical vapour deposition), as Harame reported [19].

It should be emphasized that the simulations mentioned above give only theoretical possibilities and limitations of chemical surface modification. Practical difficulties such as chemical stability, drift and hysteresis caused by the original gate material, compatibility of the modification with semiconductor technology, etc. have so far been neglected.

3. Results and discussion

We carried out a number of reactions with SiO_2 - and Ta_2O_5 -gate ISFETs to investigate the behaviour of chemically treated gate materials and to verify the validity of the theory.

The last step in the fabrication process is in all cases a thermal annealing of the aluminium contacts at 450°C for 30 min under wet N_2 . Therefore we assume that the oxide surface is fully hydrolysed after fabrication.

3.1 Thermal treatment

It is known from the literature that in the case of a fully hydrated SiO_2 surface, the number of chemically bonded OH groups is around $5 \times 10^{14}/\text{cm}^2$ [20]. SiO_2 ISFETs heat treated in vacuum (see Section 4.1 treatment (a)) showed a lower pH response than fully hydrolysed ISFETs (Fig. 7). This is in qualitative agreement with the calculated decrease in pH response caused by a lowering of N_s (see Fig. 3(b)). However, when taking the usual values of $\text{p}K_{a1} = -2$ and $\text{p}K_{a2} = 6$ for SiO_2 [4], $N_s = 3 \times 10^{13}/\text{cm}^2$ gives the best agreement with the experimental data. This does not correspond with the data in Fig. 8, from which $N_s = 2 \times 10^{14}/\text{cm}^2$ is predicted after annealing at 500°C [20]. This discrepancy can be attributed to a decrease of the dissociation constant (K_{a2}) of SiOH groups, due to a change in chemical environment, which is much more apolar than in the case of a hydrolysed surface.

Fig. 7 Measured ψ_o -pH response of several treated SiO_2 surfaces. Treatments: $\square$, none, $\circ$, (a), ∇ , (a) + (b), $\blacktriangledown$, (a) + (c), $\blacksquare$, (a) + (d), $\triangle$, (a) + (f), $\bullet$, (e), $\blacktriangle$, (a) + (e).

Fig. 8 Number of silanol sites/ cm^2 as a function of temperature

3.2 Silylating agents

Silane coupling agents such as chlorosilanes and alkoxy silanes are well-known chemical compounds. They are frequently used as modifying agents in chromatography [21-23] or as coupling compounds between glass fibres and polymers [24, 25]. In both cases, the surface silanol ($\text{Si}_s\text{—OH}$) groups are changed into $\text{Si}_s\text{—O—Si—R}$ groups, where Si_s is a surface silicon atom, and R is an organic group. In contrast to this, however, there are only a few reports concerning the chemical treatment of semiconductor-oxide surfaces, especially SiO_2 , with such reagents. Haller [26] reports both the liquid phase and vapour phase reaction of silicon wafers with native

oxide with 3-aminopropyl-triethoxy silane (APS) He concluded that in the vapour-phase reaction a monolayer of 3-aminopropyl-silyl groups is obtained Jonsson found a similar result [27] Yanazawa [28] treated CVD-SiO₂ surfaces with trimethylchlorosilane (TMS) and hexamethyldisilazane (HMDS) and found that the surface was changed from hydrophilic to hydrophobic

Following the above results, we investigated the effect of a number of silane reagents on the chemical sensitivity of the gate surface under specified experimental conditions (see Section 4.1, treatments (b) - (f))

In Fig. 7 the effect of the different treatments on the pH response of SiO₂-gate ISFETs is shown We remark that all silylating reactions were preceded by the thermal treatment This was done in order to leave as few OH groups as possible unreacted, since steric hindrance by the attached groups prevents all the OH groups of a hydrolysed surface from reacting We see that treatments (b), (c), (d) and (f) give a comparable reduction of pH sensitivity, whereas (e) gives a rather high increase in pH response, especially with the hydrolysed SiO₂ ISFETs The shape of the curves recorded with silylated SiO₂ surfaces is quite different from that of bare SiO₂ This can be attributed to the fact that additional groups with different dissociation constants are formed However, this is unlikely since bounded methyl groups do not react with protons in the normal pH range studied (pH = 1 to pH = 14) Another explanation could be that the dissociation and association constants of the residual silanol groups are changed due to the apolar environment of the methyl groups The fact that the pH_{pzc} seems to be shifted towards higher pH values indicates that the proton-dissociation reaction of SiOH is relatively more hindered than the proton-association reaction

The increase in pH sensitivity found after reaction with APS (treatment (e)) is due to two factors First, the number of Si-OH groups is not decreased because of the silanol groups that are formed by hydrolysis of the ethoxy-silicon bonds in aqueous solution [25] Secondly, amino groups are introduced To estimate the p*K*_a of the protonated form, we may compare the group formed with different reagents [29] in Table 1

TABLE 1
p*K*_a values of 'APS-like' reagents in H₂O

Reagent	p <i>K</i> _a
(C ₂ H ₅ O) ₃ -Si-CH ₂ -NH ₃ ⁺	8.4
(C ₂ H ₅ O) ₂ -Si-CH ₂ -NH ₃ ⁺ CH ₃	9.2
(C ₂ H ₅ O) ₁ -Si-CH ₂ -NH ₃ ⁺ (CH ₃) ₂	10.2

For the pure APS reagents a value of $pK_a \approx 9$ seems to be reasonable. This means that protonation of the anchored NH_2 groups will give a significant contribution to the surface charge density. However, if we calculate the pH response of this structure, a Nernstian response is found, with $pH_{pzc} = 7.5$. This means that in fact the pK_a value is much lower as a result of the interaction (hydrogen bonding) between the silanol hydrogen and nitrogen.

Evidence for the bonding of amino groups to the surface is found in the fact that at high electrolyte concentrations anion adsorption is found (ion exchange at protonated amino groups), whereas bare SiO_2 only shows cation adsorption (Table 2).

TABLE 2

$\Delta\psi_o$ due to ion adsorption from background electrolyte (BE) to 0.5 M of salts mentioned at pH = 2 (BE = 0.1 M NaCl, $[K^+]$, $[Cs^+]$, $[Li^+]$, $[NO_3^-] < 0.01$ M)

$\Delta\psi_o$ due to ion adsorption (mV)	KCl	NaCl	LiCl	CsCl	KNO ₃	NaNO ₃
SiO ₂	20	5	5	34	12	5
SiO ₂ + APS	-18	-18	-16	-20	-32	-30

To clarify the effect of adding relatively reactive sites, we have also introduced extra acidic sites at the surface. This was done by sulfonation of a polystyrene layer, anchored on the surface by treatment (g). The sulfonyl groups that are formed can be compared with p-toluenesulfonic acid ($pK_a = 1.34$ [30]), which means that these sites dissociate much more easily than SiOH sites with $pK_a = 6$. In Fig. 9 the measured responses of a polystyrene-covered ISFET and of the sulfonated form are shown. It is clear that the sensitivity increases significantly due to the strongly acidic sulfonyl groups, however, the steep slope at higher pH values is not well understood. It must be noted that when titrating the sulfonated polystyrene-covered ISFETs back with a solution of 0.1 M HCl and 0.1 M NaCl, a large hysteresis was observed, although the starting point at pH = 2 was reproducible.

In order to verify the presence of the polystyrene layer, we also carried out the reaction on bare SiO_2 . Now, no change in pH response was observed. In Fig. 9 the calculated effect of the addition of 10^{14} sites with $pK_{a2} = -1.34$ to a 99% covered SiO_2 surface is also shown. We can see that although the shape of the curve does not agree very well with the experiments, the increase in sensitivity is predicted.

In the case of Ta_2O_5 , which is known to exhibit Nernstian behaviour over the region pH = 2 to pH = 12 [5, 8], we have also carried out the reactions mentioned above. It appears that only coverage of the Ta_2O_5 ISFET with polystyrene reduces the pH sensitivity. Figure 10 shows the effect of this treatment. The sulfonation of the polystyrene layer on Ta_2O_5

Fig 9 Measured and theoretical ψ_0 -pH responses of a polystyrene-covered SiO_2 ISFET, and its sulfonated form Treatments $\times$, (a) + (b) + (g) + (h), $\circ$, (a) + (b) + (g)

	N_{s1}	$K_1 a_1$	$K_1 a_2$	N_{s2}	$K_2 a_1$	$K_2 a_2$
1	10^{13}	10^2	10^{-6}	0	—	—
2	10^{13}	10^2	10^{-6}	10^{14}	10^{+30}	22

Fig 10 Measured and theoretical ψ_0 -pH responses of treated Ta_2O_5 ISFETs Treatments $\square$, none, $\circ$, (a) + (b) + (g), $\times$, (a) + (b) + (g) + (h)

	N_{s1}	$K_2 a_1$	$K_1 a_2$	N_{s2}	$K_2 a_1$	$K_2 a_2$
1	10^{15}	10^{-5}	10^{-8}	0	—	—
2	10^{14}	10^{-5}	10^{-8}	0	—	—
3	10^{14}	10^{-5}	10^{-8}	10^{15}	10^{30}	22

was carried out under similar conditions as with SiO_2 . Although a distinction between bare Ta_2O_5 and Ta_2O_5 + sulfonated polystyrene cannot be made from the (Nernstian) pH response shown in Fig 10, we assume that as in the case of SiO_2 , the polystyrene has not yet been removed by this treatment. From these measurements we may conclude that the pH_{pzc} lies around

pH = 7. If we assume a site density of $10^{15}/\text{cm}^2$ and a coverage of 90%, a theoretical curve with $\text{p}K_{a1} = 5$ and $\text{p}K_{a2} = 8$ fits the experimental data well.

3.3 Conclusions

We investigated experimentally the effect of chemical surface modifications of SiO_2 and Ta_2O_5 ISFETs using several silylating agents. It was found that a thermal treatment or attachment of apolar inactive groups (e.g., methyl groups) reduces the pH response of the ISFET. This effect can be explained by a decrease in the number of sites. If acidic or basic groups are attached, however, we find an increase in pH sensitivity towards Nernstian behaviour. These effects can be explained qualitatively by the two-site site dissociation model. The derived results can be used to choose appropriate reagents for a pH-sensitive ISFET with Nernstian sensitivity, as well as to develop a REFET. Besides this, the theory prescribes which polymer materials are useful if we want to develop ion sensors based on ionophoric additives, such as crown-ethers, in a polymeric layer attached to the surface.

4 Experimental section

4.1 Chemical treatments

(a) Thermal treatment

The ISFETs were heated to 500°C , $p = 5 \times 10^{-3}$ Torr in a quartz tube for 1 h. Then the system was cooled down to room temperature slowly (10–15 h), while the pressure was kept low. Finally the ISFETs were stored under dry argon.

(b) Trichlorovinylsilane (TVS)

The ISFETs were treated for 16 h in 5 ml refluxing dry toluene to which 0.5 ml TVS was added, at 90°C . During the reaction the reaction mixture was kept under dry N_2 . After the reaction was completed, the ISFETs were rinsed in toluene and ether, and stored under dry argon.

(c) Trimethylchlorosilane (TMS)

For the experimental conditions of the treatment with TMS we followed Yanazawa *et al.* [28]. Thus, the ISFETs were evacuated in a reaction vessel at 200°C , and exposed to TMS vapour for 1 h. The samples were subsequently stored under dry argon.

(d) Hexamethyldisilazane (HMDS)

Experimental conditions as in (c).

(e) 3-Aminopropyl-triethoxy silane (APS)

0.5 ml APS was added to 190 ml methanol and 10 ml H_2O . This gave a solution that is commonly used as a primer for polyimide deposition on semiconductor wafers. One droplet of this solution was placed on the

surface through a millipore filter ($0.2\ \mu\text{m}$), and the excess solution was removed by spinning at 4000 rpm. Finally the ISFETs were dried at $60\ ^\circ\text{C}$ for 1 h.

(f) t-Butyldimethylsilylchloride (TBDMS)

2g TBDMS was dissolved in 5 ml methylenechloride and added to the ISFETs. Then, 1 ml diisopropylethylamine was added, and the mixture was kept under dry N_2 at room temperature for 6 h. After reaction the ISFETs were rinsed with toluene and ether and stored under dry argon.

(g) Surface polymerization

To vinyl-substituted surfaces (treatment (b)) a polystyrene layer was attached by a radical initiated polymerization of styrene. First, the styrene was purified as in ref. 31. The polymerization reaction was in 3 ml dry toluene, to which 40 mg dibenzoylperoxide and 1 ml styrene were added. The solution formed was outgassed twice, and then brought to $90\ ^\circ\text{C}$ for 3 h under refluxing conditions. After reaction, the samples were rinsed in toluene and ether and stored under dry argon. Measurements of polystyrene layer thickness were carried out on treated oxidized silicon wafers. The oxide layer on these wafers was made in the same way as the gate oxide of the ISFETs. Layer thicknesses of $50 - 100\ \text{\AA}$ were measured with an ellipsometer (Applied Materials, Ellipsometer II), thus indicating that a thin polystyrene film was formed. In the thickness determinations we assumed a uniform refractive index for both SiO_2 and polystyrene.

(h) Sulfonation

Polystyrene-covered ISFETs were dipped in 98% H_2SO_4 at $120\ ^\circ\text{C}$ for 10 - 20 s. The maximum time was restricted by dissolution of the aluminium contacts.

4.2 Measurement of ψ_0 -pH curves

Surface potential against pH curves were recorded as follows. 10 ml solution containing 0.01 M citric acid, 0.01 M phosphoric acid, 0.02 M boric acid and 0.1 M NaCl was titrated with a solution of 0.1 M HCl + 0.1 M NaCl until $\text{pH} = 2$ was reached. A pH electrode calibrated with two standard buffers (Merck) and an ISFET was placed in this solution, which was stirred thoroughly. Then, a 0.1 M NaOH solution was titrated, and the surface potential differences were measured by a source and drain follower circuit, as described by Bergveld [32], with a drain current of $100\ \mu\text{A}$. All measurements were carried out in a dark grounded box at room temperature. Typical recording time for a scan from $\text{pH} = 2$ to $\text{pH} = 11$ was 20 min. After each measurement, the measurement cell was refilled with the starting solution, and ψ_0 was measured again. Only if the value of ψ_0 was reproduced within $\pm 10\ \text{mV}$ of the original value were the measured responses taken as data.

Acknowledgements

The authors wish to express their gratitude to the Twente Centre of Microelectronics (C M E T) for financial support of the ion-sensor research project

References

- 1 P Bergveld, Developments of ion-sensitive solid-state device for neuro-physiological measurements, *IEEE Trans Biomed Eng*, BME-17 (1970) 70
- 2 D E Yates, S Levine and T W Healy, Site-binding model of the electrical double layer at the oxide/water interface, *J Chem Soc, Faraday Trans*, 70 (1974) 1807
- 3 W M Siu and R S C Cobbold, Basic properties of the electrolyte-SiO₂-Si system Physical and theoretical aspects, *IEEE Trans Electron Devices*, ED 26 (1979) 1805
- 4 L Bousse, The chemical sensitivity of electrolyte/insulator/semiconductor structures, *Ph D Thesis*, Enschede, 1982
- 5 T Akiyama, Y Ujihira, Y Okabe, T Sugano and E Niki, Ion-sensitive field-effect transistors with inorganic gate oxide for pH sensing, *IEEE Trans Electron Devices*, ED 29 (1982) 1936
- 6 Y Ohta, S Shoji, M Eshahi and T Matsuo, Prototype sodium and potassium sensitive micro ISFETs, *Sensors and Actuators*, 2 (1982) 387
- 7 P T McBride, J Janata, P A Cante, S D Moss and C C Johnson, Ion-selective field effect transistors with polymeric membranes, *Anal Chim Acta*, 101 (1978) 239
- 8 A Fog and R P Buck, Electronic semiconducting oxides as pH sensors, *Sensors and Actuators*, 5 (1984) 137
- 9 S Tahara, M Yoshii and S Oka, Electrochemical reference electrode for the ion-selective field effect transistor, *Chem Lett* (1982) 307
- 10 M Fujihira, M Fukui and T Osa, Preparation of pH-insensitive Parylene gate for chemical modification, *J Electroanal Chem Interfacial Electrochem*, 106 (1980) 413
- 11 H Nakajima, M Esashi and T Matsuo, The cation concentration response of polymer gate ISFET, *J Electrochem Soc*, 129 (1) (1982) 141
- 12 L Bousse and P Bergveld, The role of buried OH sites in the response mechanism of inorganic-gate pH-sensitive ISFETs, *Sensors and Actuators*, 6 (1984) 65
- 13 N F de Rooij and P Bergveld, The influence of the pH on the electrolyte-SiO₂-Si system studied by ion-sensitive FET measurements and quasi-static C-V measurements, *Thin Solid Films*, 71 (1980) 327
- 14 D N Strahesko, V Strelko, V N Belyakov and S C Rubanik, Mechanism of cation exchange on silica gels, *J Chromatogr*, 102 (1974) 191
- 15 W G Trampusch and S G Weber, Effect of some amines on the ionic, dipolar and hydrogen bonding interactions between test solutes and support in reversed-phase liquid chromatography, *Anal Chem*, 56 (1984) 2567
- 16 S R Morrison, *Electrochemistry at Semiconductor and Oxidized Metal Electrodes*, Plenum Press, New York, 1980
- 17 T Matsuo and H Nakajima, Characteristics of reference electrodes using polymer gate ISFET, *Sensors and Actuators*, 5 (1984) 293
- 18 M T Pham and W Hoffmann, Ion-sensitive membranes fabricated by the ion beam technique, *Sensors and Actuators*, 5 (1984) 217
- 19 D Harame, personal communication
- 20 R K Iler, *The Chemistry of Silica*, Wiley, New York, 1978,
- 21 A C Zettlemoyer and H H Hsing, *J Colloid Interface Sci*, 58 (1977) 263
- 22 L Bokszanyi, D Liardon and E Kováts, Chemically modified silicon dioxide surfaces, *Adv Colloid Interface Sci*, 6 (1979) 95

- 23 D W Sindorf and G E Maciel, *J Am Chem Soc*, 105 (1983) 3767
- 24 S Navroij, S R Culler, J L Koenig and H Ishida, *J Colloid Interface Sci*, 97 (1984) 308
- 25 E P Plueddemann, *Silane Coupling Agents*, Plenum Press, New York, 1982
- 26 I Haller, Covalently attached organic monolayers on semiconductor surfaces, *J Am Chem Soc*, 100 (26) (1978) 8050
- 27 U Jonsson, G Olfsson, M Malmquist and I Ronnberg, *Proc 6th Int Conf on Thin Films, Stockholm, 1984*
- 28 H Yanazawa, H Utsugi, N Hashimoto and M Ashikawa, *Proc 6th Int Vac Congr*, 1974, p 753
- 29 D D Perrin, *Dissociation Constants of Organic Acids and Bases in Aqueous Solution*, Butterworths, London, 1965
- 30 A Albert and E P Serjeant, *The Determination of Ionization Constants*, Chapman and Hall, London, 1984
- 31 D D Perrin, W L F Armarego and D R Perrin, *Purification of Laboratory Chemicals*, Pergamon Press, New York, 1980
- 32 P Bergveld, The operation of an ISFET as an electronic device, *Sensors and Actuators*, 1 (1981) 17

Biographies

Albert van den Berg was born in Zaandam, the Netherlands, on September 20, 1957. He received his M S degree in (technical) Physics in 1983 from the Twente University of Technology. Since then he has been working on the ion sensor research project, which is being carried out in cooperation between the Biosensor Research Group and the Department of Organic Chemistry of the Twente University of Technology.

Piet Bergveld was born in Oosterwolde, the Netherlands, on January 26, 1940. He received the M S degree in Electrical Engineering (electronics) from Eindhoven University of Technology, Eindhoven, the Netherlands, in 1965, and the Ph D degree from Twente University of Technology, Enschede, the Netherlands, in 1973.

Since 1965 he has been a member of the Bio-information Group, Department of Electrical Engineering, Twente University of Technology. He is further a member of the Coordination Centre for Biomedical Engineering and a member of the Research Unit Sensors and Actuators of this University. In 1981 he became a member of the Semiconductor Group of the Foundation for Fundamental Research on Matter in the Netherlands.

The subject of his dissertation was the ion-sensitive field-effect transistor (ISFET) and the OSFET. He is involved in research on electronic measuring and stimulating methods in physiological systems, with special attention for *in vivo* biosensors. He lectures on biomedical instrumentation for graduate students of Twente University of Technology and medical personnel of affiliated hospitals.

In 1984 he was appointed as full professor in biosensor technology at the Twente University of Technology.

David N Reinhoudt was born in Wolfaartsdijk, the Netherlands, on September 18, 1942. He received his M S degree in Chemical Engineering (organic chemistry) from the Delft University of Technology in 1966, and his Ph D degree from the same institute in 1969 (with honours). From 1970 until 1975 he was research chemist at the Koninklijke/Shell Laboratories in Amsterdam (organic chemistry section). In 1975 he was appointed as professor in organic chemistry at the Twente University of Technology.

Ernst J R Sudholter was born in Hengelo, the Netherlands, on November 23, 1953.

He received his M S degree in Organic Chemistry from the University of Groningen in 1977, and his Ph D degree (*cum laude*) from the same University in 1981.

From 1981 until 1984 he was research chemist at the Koninklijke/Shell Laboratories in Amsterdam in the fundamental and process development departments. Since 1984 he has worked at Twente University of Technology on physical organic chemistry of surfaces and membranes.