

Accurate Continuous Monitoring of pH and Blood Gases Using FET-based Sensors Operating in the Amperometric mode

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Abstract— The capacity of ion-selective and the Gas-sensitive field effect transistors (FETs) to serve as low-power sensors, operating in the amperometric mode for accurate continuous monitoring of pH and blood gases, is evaluated. A stand-alone current-mode topology is employed in which a constant bias is applied to the gate with the drain current serving as the measuring signal. In the amperometric mode, the static sensitivity of a FET-based sensor given by the product of the FET transconductance and $\partial V_{TH}/\partial[M]$, the sensitivity of the threshold voltage of the device, V_{TH} to the concentration of the measurand, M can be increased by adjusting the device design parameters. Compared with voltage-mode operation (e.g. in the feedback mode in ISFETs), current-mode topologies offer the advantages of small size and low power consumption. However, the ion-selective FET (ISFET) and the Gas-sensitive FET (GasFET) exhibit a similar drift behavior imposing a serious limitation on the accuracy of these sensors for continuous monitoring applications irrespective of the mode of operation. Given the slow temporal variation associated with the observed drift behavior of these devices a post-processing technique, which involves monitoring the variation of the drain current over short intervals of time, allows extraction of the measuring signal in presence of drift. Rigorous analytical validation of the method is presented for GasFET operation in the current mode. Moreover, the correction algorithm is verified experimentally using a Si_3N_4 -gate ISFET operating in the amperometric mode to monitor pH variations ranging from 3.5 to 10.

Keywords: *Amperometric; Continuous monitoring; Current mode; Drift; GasFET; Gas Sensor; ISFET; Instability; pH Sensor*

I. INTRODUCTION

The health care system will encounter a major challenge in the near future due to the ageing of population. Biomedical sensors will potentially be able to address this challenge by providing the ability to monitor important body functions as part of preventive medical practices or by serving as an enabling technology for telemedicine to reduce healthcare costs. The pH-sensitive ion-selective field effect transistor (ISFET) and the hydrogen-sensitive, catalytic metal-insulator-semiconductor field effect transistor (MISFET) gas sensor

represent two prevalent sensors with important biomedical applications belonging to the general class of FET-based sensors. In 1970 ISFET was introduced [1] as a solid state device linking the chemical sensitivity exhibited by a membrane with the field-sensing capability of a FET. A hydrogen-sensitive gas sensor compatible with integrated circuit (IC) technology was introduced in 1975 using a catalytic metal, namely palladium, as the gate metal of an MOS transistor [2]. FET-based sensors offer such advantages as small size, robustness, and low cost over sensors relying on conventional chemical electrode technology such as the glass pH-meter. While commercially available electrodes are small enough for *in vivo* applications, their fragility and relatively high manufacturing cost represent significant disadvantages precluding their utilization for biomedical applications. In contrast, FET-based sensors can be manufactured using the CMOS IC technology, which not only provides the level of miniaturization necessary for installation of FET-based biosensors in catheter tips, but also offers the tremendous cost advantage resulting from batch fabrication.

Biosensors generally employ potentiometric or amperometric modes of electrochemical transduction to convert a given biological interaction into an electrical signal. The response of a potentiometric biosensor is obtained through measurement of the potential difference between a reference electrode and a transducing electrode as a function of analyte concentration. In contrast, the response of an amperometric biosensor corresponds to current versus concentration variations. The response of the FET-based biosensors can be represented either by variations of the threshold voltage or those of the drain current as a function of the concentration of the analyte of interest. For example, in the popular potentiometric mode of ISFET operation, commonly known as the feedback mode, a constant drain current is maintained through application of negative feedback via the reference electrode, allowing measurement of the equilibrium interfacial potential as a function of the ion concentration. In the current mode of sensor operation, however, the FET-based sensor can be operated as a stand-alone device by applying a constant

potential to the gate electrode, sparing the need for integration of several operational amplifiers, with their high transistor counts, to maintain a constant drain current. This permits a significant reduction in the size and complexity of the sensor system. In addition, with the omission of the power-hungry operational amplifiers the amperometric mode of operation represents a viable option for low-power applications.

However, regardless of whether a current-mode or a voltage-mode topology is employed, threshold voltage instability commonly known as drift, has presented a serious impediment to utilization of ISFET and GasFET for continuous monitoring of pH and blood gases. In both devices drift is typically characterized by a relatively slow, unidirectional temporal variation in the threshold voltage and, hence, in the drain current of FET in the absence of changes in the measurand of interest (e.g. concentration of the ion or partial pressure of gas). This phenomenon precludes utilization of ISFET and the GasFET for *in vivo* continuous monitoring due to the narrow physiological range associated with the plasma pH and blood gases. Continuous monitoring of blood pH during surgery, for example requires stabilities better than 0.002pH/hour, which is equivalent to maximum drift rate of 0.12mV/hour assuming that the ISFET exhibits an ideal Nernstian response with a slope of -61.8 mV/pH at a temperature of 37 °C, the normal body temperature. The typical long-term drift rate of pH-sensitive ISFETs at neutral pH is on the order of several tenths of a millivolt per hour. To date a physical model for drift in GasFETs, which is capable of accounting for experimental drift data quantitatively, has not been advanced. On the other hand, a deterministic physical model providing an accurate, quantitative description of the dynamics of the nonlinear drift behavior exhibited by Si₃N₄-gate and Al₂O₃-gate pH-sensitive ISFETs [3],[4] has been proposed.

Adopting a suitable strategy to counteract sensor drift in the amperometric mode allows realization of low-power sensor operation in the current mode. Unlike approaches relying on device-level implementations [5], analytical methods for correction of drift involving post-processing of the measuring signal [6] cannot compensate drift in real time. Nevertheless, analytical approaches represent cost-efficient solutions, which can be readily implemented within the framework of healthcare computing systems. In this work a post-processing method for correction of drift in FET-based sensors operating in the amperometric mode is developed, which relies on windowing of the drain current over short sampling time intervals. Analytical validation of the method is presented for GasFET operation in the current mode and the method is verified experimentally by monitoring step changes in pH in the 3.5-10 range using a Si₃N₄-gate ISFET biased in the triode region.

II. ANALYTICAL METHOD FOR CORRECTION OF DRIFT

In this section the proposed post-processing method for correction of drift is analytically validated for a GasFET. The analytical approach followed herein is also applicable to an ISFET by considering the sensitivity of the threshold voltage to the given ion.

In a GasFET biased in the amperometric mode the differential of the drain current can be expressed as the sum of the differential of the measuring signal, $dI_{D_{Gas}}$ and the differential of the drain current arising from drift, $dI_{D_{Drift}}$:

$$dI_D = dI_{D_{Gas}} + dI_{D_{Drift}} \quad (1)$$

where $dI_{D_{Gas}}$ represents the differential change in the drain current arising from the changes in the partial pressure of the gas e.g. H₂. Over sufficiently short intervals of time, Δt , $dI_{D_{Gas}}$ and $dI_{D_{Drift}}$ are given by

$$dI_{D_{Gas}} = \frac{\partial I_D}{\partial P_G} \cdot dP_G \cong \frac{\partial I_D}{\partial P_G} \cdot \frac{dP_G}{dt} \quad (2)$$

$$dI_{D_{Drift}} \cong \frac{\partial I_D}{\partial t} \cdot \Delta t \quad (3)$$

where P_G represents the partial pressure of the gas. Given the relatively low value of the long-term drift rate in a typical GasFET, the variation in the drain current due to drift $\frac{\partial I_D}{\partial t}$ can become negligible for a GasFET exhibiting a high amperometric sensitivity $\frac{\partial I_D}{\partial P_G}$ and/or experiencing a high rate of change in the partial pressure of the gas, $\frac{dP_G}{dt}$. That is, given

$$\frac{\partial I_D}{\partial t} \ll \frac{\partial I_D}{\partial P_G} \cdot \frac{dP_G}{dt} \quad (4)$$

(1) can be written as

$$dI_D \cong dI_{D_{Gas}} \quad (5)$$

In the amperometric mode of operation constant voltages V_{GS} and V_{DS} are applied to the gate and drain electrodes of the GasFET respectively, and the source electrode is maintained at the ground potential. If the GasFET is biased in the triode region of operation, the drain current is given by [7]

$$I_{D_{lin}} = \left(\mu C_{ins} \frac{W}{L} \right) \left[(V_{GS} - V_{TH_{GasFET}}) V_{DS} - \frac{1}{2} V_{DS}^2 \right] \quad (6)$$

where μ represents the surface mobility of electrons in an n -channel GasFET, C_{ins} denotes the gate insulator capacitance per unit area, $V_{TH_{GasFET}}$ designates the threshold voltage of the GasFET and finally W and L are the width and the length of the GasFET respectively. The threshold voltage of the GasFET can be expressed as [7]

$$V_{TH_{GasFET}} = V_{FB0} - \Delta\Psi - \frac{Q_D}{C_{ins}} - \frac{Q_I}{C_{ins}} + 2\phi_F \quad (7)$$

where ϕ_F designates the Fermi potential determined by the bulk doping concentration, $\Delta\Psi$ represents the changes in the work function resulting from absorption of gas atoms at the metal-insulator interface, and V_{FB0} denotes the flatband voltage of the MOS system, which depends on the dopant density in the semiconductor, as well as the characteristic work function of the specific metal used in a metal-based GasFET, e.g. palladium in the Pd-MOS of Lundstrom [2].

To derive the current-mode response of the GasFET to variations in the partial pressure of the gas, the amperometric sensitivity of the device, S_A can be determined as

$$S_A = \frac{\partial I_D}{\partial P_G} = \left(\frac{\partial I_D}{\partial V_{TH_{GasFET}}} \right) \left(\frac{\partial V_{TH_{GasFET}}}{\partial P_G} \right) \quad (8)$$

Noting the definition of the FET transconductance, $g_m = \frac{\partial I_D}{\partial V_{GS}} = -\frac{\partial I_D}{\partial V_{TH_{GasFET}}}$, (8) can be written as

$$S_A = \frac{\partial I_D}{\partial P_G} = -g_m \left(\frac{\partial V_{TH_{GasFET}}}{\partial P_G} \right) \quad (9)$$

In a metal-based work function gas sensor such as the Pd-MOS, the sensitivity of the threshold voltage to the gas concentration, $\frac{\partial V_{TH_{GasFET}}}{\partial P_G}$ can be modeled based on the Sieverts' law. Specifically, for a diatomic gas, G_2 if the association and dissociation of the gas atoms represent the only surface reactions occurring we can write:



where G represents the dissolved gas atom. The equilibrium constant for the reaction is given by $K_{eq} = [G]^2/[G_2]$, where $[G]$ and $[G_2]$ represent the molar concentrations in moles/m³ of the absorbed gas atoms and of the diatomic gas respectively. Therefore, assuming validity of the ideal gas law $P_G = N_{av}kT[G_2]$ with N_{av} , k and T denoting the Avogadro's number, the Boltzman's constant and the absolute temperature respectively, $[G]$ can be expressed as:

$$[G] = \sqrt{\frac{K_{eq}P_G}{N_{av}kT}} \quad (11)$$

The contribution to the threshold voltage of the surface dipole potential $\Delta\Psi$ resulting from absorption of gas atoms at the interface is given by [2]

$$\Delta\Psi = \frac{N_s p}{\epsilon_0} \quad (12)$$

where N_s designates the area density of the gas atoms absorbed on the surface of the metal at the metal-insulator interface, p represents the dipole moment of the absorbed gas atom, and ϵ_0 is the permittivity of vacuum. Assuming a uniform distribution for the dissolved gas atoms in the metal, N_s can be estimated as

$$N_s = N_{av}[G]x_m \quad (13)$$

where x_m denotes the thickness of the metal. Note that the maximum value of N_s is on the order of 10^{19} m⁻² and corresponds to a metal-insulator interface with near saturation of absorption sites i.e., an interface with one hydrogen atom per palladium atom. Substituting the expression given by (11) for $[G]$, (13) can be written as

$$N_s = x_m \cdot \sqrt{\frac{N_{av}K_{eq}P_G}{kT}} \quad (14)$$

Substituting (14) into (12), the expression for $\Delta\Psi$ will be given by

$$\Delta\Psi = K_G \sqrt{P_G} \quad (15)$$

where $K_G = \left(\frac{x_m p}{\epsilon_0}\right) \sqrt{\frac{N_{av}K_{eq}}{kT}}$ is a temperature-dependent proportionality constant. Accordingly, using (15) the sensitivity is given by

$$S_A = -g_m \left(\frac{\partial V_{TH_{GasFET}}}{\partial P_G}\right) = -g_m \left(\frac{\partial V_{TH_{GasFET}}}{\partial \Delta\Psi}\right) \left(\frac{\partial \Delta\Psi}{\partial P_G}\right) = -g_m(-1) \left(\frac{K_G}{2\sqrt{P_G}}\right) = \frac{g_m K_G}{2\sqrt{P_G}} \quad (16)$$

Therefore, the transfer characteristics of the GasFET is nonlinear with the amperometric sensitivity depending on the partial pressure of the gas and the operating point of the FET. For an GasFET operating in the saturation region the sensitivity $S_{A_{lin}}$ can be written in terms of the device

transconductance $g_{m_{lin}} = \frac{\partial I_{D_{lin}}}{\partial V_{GS}} = \mu C_{ins} \frac{W}{L} V_{DS}$ as:

$$S_{A_{lin}} = \frac{g_{m_{lin}} K_G}{2\sqrt{P_G}} = \left(\frac{K_G}{2}\right) \left(\mu C_{ins} \frac{W}{L}\right) \left(\frac{V_{DS}}{\sqrt{P_G}}\right) \quad (17)$$

By substituting (3) into (6) following replacement of $\frac{\partial I_D}{\partial P_G}$ by

$S_{A_{lin}}$ we will have:

$$dI_D \cong S_{A_{lin}} dP_G \quad (18)$$

Integrating [the above eqn.] over the interval Δt we obtain

$$\int_t^{t+\Delta t} dI_D \cong \int_{P_G}^{P_G+\Delta P_G} S_{A_{lin}} dP_G' \quad (19)$$

Substituting the expression for $S_{A_{lin}}$ given by (17) into (19) yields

$$\Delta I_{D_{lin}} = I_D(t + \Delta t) - I_D(t) = K_G g_{m_{lin}} \left[\sqrt{P_G'} \right]_{P_G}^{P_G+\Delta P_G} = K_G g_{m_{lin}} (\sqrt{P_G + \Delta P_G} - \sqrt{P_G}) \quad (20)$$

Over short intervals of time, $\Delta P_G \ll P_G$, $\left[\sqrt{P_G'} \right]_{P_G}^{P_G+\Delta P_G}$ can be written as:

$$\sqrt{P_G + \Delta P_G} - \sqrt{P_G} = \sqrt{P_G} \left[\left(1 + \frac{\Delta P_G}{P_G}\right)^{1/2} - 1 \right] \cong \left[\left(1 + \frac{\Delta P_G}{2P_G}\right) - 1 \right] = \left(\frac{1}{2}\sqrt{P_G}\right) \Delta P_G \quad (21)$$

As a result (20) can be rewritten as

$$\Delta P_G = \frac{2\Delta I_{D_{lin}}}{K_G g_{m_{lin}} \sqrt{P_G}} \quad (22)$$

Consequently, over sufficiently small sampling intervals, Δt , the variation of the drain current in the triode region basically corresponds to changes in the P_G , which allows extraction of the GasFET response in presence of drift over a given time interval (t_0, t_n) through summation of $\Delta I_{D_{lin}}$ values. Specifically, the change in P_G can be expressed as

$$P_G(t_n) - P_G(t_0) = \left(\frac{2}{K_G g_{m_{lin}}}\right) \sum_{k=0}^{k=n} \frac{\Delta I_{D_{lin}}(t_k \rightarrow t_{k+1})}{\sqrt{P_G(t_k)}} \quad (23)$$

where $\Delta I_{D_{lin}}(t_k \rightarrow t_{k+1}) = I_{D_{lin}}(t_{k+1}) - I_{D_{lin}}(t_k)$ denotes the change in the measuring signal over the sampling time interval $\Delta t = t_{k+1} - t_k$, with $n = \frac{t_n - t_1}{\Delta t}$ being the number of samples taken over the (t_1, t_n) interval. Note that the change in P_G over the given interval of time is obtained by summing the successive changes in pressure over the $t_k \rightarrow t_{k+1}$ intervals. Furthermore, since the sensitivity of the GasFET depends on the operating point, evaluation of the change in the partial pressure $P_G(t_{k+1}) - P_G(t_k)$ over the $(k+1)$ th interval requires that $P_G(t_k)$ be known. This implies that the initial pressure $P_G(t_0)$ must be determined based on calibrations in order to proceed with the monitoring process.

Similarly, in a pH-sensitive sufficiently small sampling intervals, Δt , the variation of the drain current in the triode region basically corresponds to changes in the pH, which allows extraction of the ISFET pH response in presence of drift over a given time interval (t_1, t_n) through summation of $\Delta I_{D_{lin}}$ values. Specifically, given the constant sensitivity of the device threshold voltage to pH in a H⁺-sensitive FET, the change in pH can be expressed as

$$pH(t_n) - pH(t_1) = \left(\frac{1}{S_{A_{lin}}}\right) \sum_{k=1}^{k=n} \Delta I_{D_{lin}}(t_k \rightarrow t_{k+1}) \quad (23)$$

where $\Delta I_{D_{lin}(t_k \rightarrow t_{k+1})} = I_{D_{lin}}(t_{k+1}) - I_{D_{lin}}(t_k)$ denotes the change in the measuring signal over the sampling time interval given by $\Delta t = t_{k+1} - t_k$, with $n = (t_n - t_1)/\Delta t$ being the number of samples taken over the (t_1, t_n) interval.

III. EXPERIMENTAL VERIFICATION

The method for correction of drift developed in section II is verified by conducting a pH monitoring experiment using a Si_3N_4 -gate pH -sensitive ISFET operating in the amperometric mode. In this section experimental details concerning device fabrication, characterization of ISFET drift and sensitivity, and the experimental procedure followed for monitoring step changes in pH is presented.

A. ISFET Fabrication

The n -channel Si_3N_4 -gate pH -sensitive ISFET used in the pH monitoring experiment was fabricated based on a metal-gate, p -well CMOS process by blocking formation of the metal gate using an additional masking step. The substrate material consisted of an n -type, (100) silicon wafer whose resistivity lied in the 4-6 Ωcm range. The p -well was defined by diffusion using boron as the dopant with a uniform concentration of 10^{16} cm^{-3} . Threshold voltage adjustment by ion implantation was not performed. The gate insulator was formed by a 110-nm layer of silicon nitride serving as the pH -sensitive insulator deposited by the LPCVD method over a 50-nm layer of thermally-grown silicon dioxide. The source and drain regions were defined by diffusion of phosphorous with a typical doping concentration of 10^{19} cm^{-3} . The drawn length and width of the gate were $15\mu\text{m}$ and $450\mu\text{m}$ respectively.

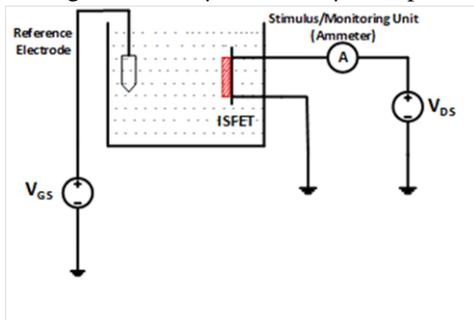


Figure 1. Set-up for characterization of drift in the amperometric mode

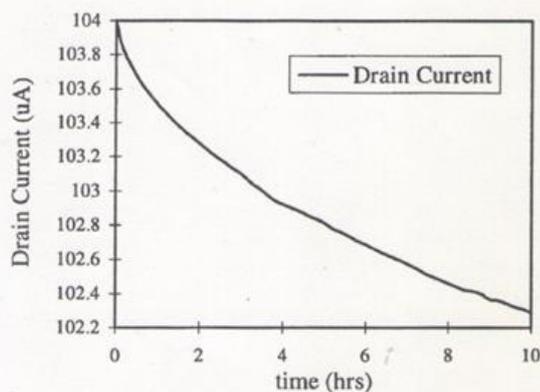


Figure 2. Si_3N_4 -gate pH -sensitive ISFET Drift Characteristics at $pH=7$

B. Drift Characterization and Sensitivity

The drift behavior of the Si_3N_4 -gate pH -sensitive ISFET used in the pH monitoring experiment was characterized in the amperometric mode at room temperature using the set-up shown in Fig. 1. The drift characteristics obtained at $pH=7$ for the Si_3N_4 -gate pH -sensitive ISFET used in the experimental verification of the proposed method is given in Fig. 2. The long-term drift rate for this device after exposure to a neutral buffer solution for 6 hours was measured to be minus $0.0975\mu\text{A}/\text{hour}$. The ISFET had been placed in the buffer solution for 12 hours before conducting the experiment. The threshold voltage of the ISFET was measured to be roughly 1.1V with the substrate grounded i.e. with no body bias. A gate voltage of $V_{GS}=2.1\text{V}$ was applied to the solution using a saturated calomel reference electrode to maintain the device in the triode region with the drain voltage set to $V_{DS}=0.2\text{V}$.

The amperometric sensitivity of the ISFET was determined by linear regression using standard buffer solutions of known pH as the slope of the calibration curve generated with an average of five measured drain current readings taken at each pH . Specifically, the amperometric sensitivity in the triode region at room temperature was determined to be $-4.23 \mu\text{A}/\text{pH}$ for the device employed to monitor the pH . The equivalent feedback mode sensitivity of the ISFET had been measured to be $42.9\text{mV}/\text{pH}$ at room temperature prior to use of the device in the monitoring experiment.

C. Continuous Monitoring of pH

Solutions with pH values of 3.5, 5.4, 7.0, 9.0, and 10.0 were obtained by adding 1M HCl or 1M KOH to a solution with 0.05M phosphate monobasic and 0.142M KCl concentrations. pH values were measured using the a Corning semimicrocombination pH probe and the Orion ResearchTM 601A pH meter with an accuracy of $\pm 0.01\text{pH}$ unit. A 0.142M concentration of KCl was used for the baseline solution in order to approximate plasma electrolyte concentration. However K^+ was used instead of Na^+ , since Si_3N_4 -gate pH -sensitive ISFETs are known to be sensitive to Na^+ ions. Addition of KOH altered the final osmolarity of K^+ by approximately 50mOsm.

Five beakers were prepared each of which contained one of the solutions with the given pH value. Following device calibration, the ISFET was arbitrarily exposed to each of the solutions for various time intervals. The resulting pH response was monitored by measuring the drain current at 30-second intervals. To estimate the change in the pH value the difference between the drain current immediately prior to transfer of the ISFET from the given solution and the drain current measured after transfer to the new solution was determined. The magnitude of the drain current difference divided by the measured device sensitivity represented the change in pH value. During the transfer the ISFET and the reference electrode were manually placed in the new solution within a 30-second time delay. No stirring was performed following transfer of the device to the new solution.

IV. RESULTS AND DISCUSSION

The pH monitoring experiment performed to validate the method for correction of ISFET drift in the amperometric mode involved application of pH steps in the sequence indicated in Table I, the given sequence of step changes in the pH resulted in the variations of the ISFET drain current shown in Fig. 3. The resulting step changes in the drain current following exposure of the ISFET along with the reference electrode to a new solution represent the corresponding experimental pH transitions. After introduction of the ISFET and the reference electrode into the new solution the time required for the pH change to take effect and for the new value to stabilize was generally less than 30 seconds. The pH step amplitudes measured using the Orion 601A meter were compared, in the order of occurrence of the steps, with the corresponding amplitudes determined with the ISFET based on the proposed corrective scheme using (23). The results of this comparison are provided in Table I. As indicated, with the exception of large step changes in pH (i.e. $|\Delta pH| > 3$) and the 9.0→10.0 pH transition, the absolute value of the change in pH as determined based on the corrective scheme was within 0.2 pH units of that measured using the pH meter with the average relative error not exceeding 6.3%. The inaccuracies in estimation of large step changes in pH are due to errors resulting from the hysteresis phenomenon, which occurs when the pH is ramped up and down [8]. The inaccuracy associated with the 9.0→10.0 pH transition, on the other hand, is due to the large initial drift following exposure to high pH values, which occurs irrespective of the drift history at lower pH values.

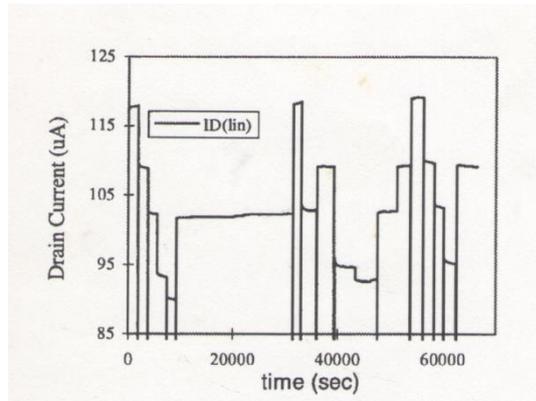


Figure 3. pH Response of the Si₃N₄-gate pH-sensitive ISFET

As noted in Section II, a relatively high sensitivity is a prerequisite to the application of the correction method described. Given the measured drift rate of 0.0975 μA/hour at pH=7 and the sensitivity of -4.23 μA/pH for the ISFET used in the experiment, the validity of the equivalent of the criterion given by (4) for an ISFET, namely $\frac{\partial I_D}{\partial t} \ll \frac{\partial I_D}{\partial pH} \cdot \frac{dpH}{dt}$, would be satisfied in an application such as cardiac surgery, where the pH changes of several tenths of pH unit can occur in a matter of minutes.

The drift behavior of hydrogen-sensitive palladium-gate MOSFETs is similar to that of pH-sensitive ISFETs exhibiting a relatively fast transient after the exposure of the sensor surface to gaseous medium followed by a significantly slower

long-term drift in the sensor output characterized by a random-looking evolution in time. In fact, the time dependence of drift in palladium-gate MOSFETs [2] is accurately described by the deterministic drift model accounting for instability in pH-sensitive ISFETs [3],[4]. The underlying mechanism of drift in catalytic metal-gate FETs can, therefore, be postulated to be associated with hopping and/or trap-limited dispersive diffusion within the amorphous material forming the gate insulator. Therefore, the proposed method for correction of drift, which has been experimentally verified using pH-sensitive ISFETs, is also applicable to FET-based gas sensors provided that the requirement given by (4) is satisfied.

TABLE I. COMPARISON OF MEASURED CHANGES IN pH

Transition Order	Measured Changes in pH		
	pH Meter	ISFET with correction	Relative Error (%)
1(3.5→5.4)	1.90	1.98	4.2
2(5.4→7.0)	1.42	1.60	12.7
3(7.0→9.0)	2.0	1.99	0.50
4(9.0→10.0)	1.0	0.59	41.0
5(10.0→7.0)	-3.0	-2.71	9.67
6(7.0→3.5)	-3.5	-3.70	5.70
7(3.5→7.0)	3.5	3.48	0.57
8(7.0→5.4)	-1.50	-1.48	1.33
9(5.4→9.0)	3.60	3.12	13.3
10(9.0→10.0)	1.0	0.44	56.0
11(10.0→7.0)	-3.0	-2.27	24.3
12(7.0→5.4)	-1.6	-1.52	5.0
13(5.4→3.5)	-1.9	-2.09	5.3
14(3.5→5.4)	1.90	2.07	8.94
15(5.4→7.0)	1.60	1.43	10.6
16(7.0→9.0)	2.0	1.83	8.50
17(9.0→5.4)	-3.6	-3.3	8.30

On the other hand, the main advantage gained by operating the ISFET in the feedback mode is that the variations in the potential of the reference electrode may represent the variations in the interfacial potential resulting from pH changes. Ideally, the variations in the reference electrode potential would represent a Nernstian response. This advantage, however, is only realized in the absence of variations stemming from drift, supply voltage, and temperature. A fixed operating point is maintained through application of feedback regardless of the source of variation. The feedback electronics, on the other hand, not only requires a higher component count, but also leads to significant static power dissipation. A typical ISFET measuring circuit employing feedback requires three operational amplifiers and the associated resistors and capacitors. In applications such as

telemetry requiring low-power integrated sensor systems, therefore, implementation of the feedback electronics may not justify the considerable additional costs involved. Although the measuring circuit employed in the current mode of ISFET operation is considerably simplified, direct application of the bias voltages to the reference electrode and the drain exposes the ISFET to the same sources of inaccuracies as those encountered in the feedback mode of operation. For example, the current-mode sensitivity of the ISFET is proportional to the gate insulator capacitance, whose variation with time has been identified as the origin of the threshold voltage drift [3],[4]. Therefore, supply-independent biasing, temperature compensation and correction or compensation of drift would still be required in the current mode of operation.

The proposed method has also been successfully applied to correct the threshold voltage drift in a Si₃N₄-gate pH-sensitive ISFET operating in the feedback mode [6]. In general, according to (4), the validity of the proposed method requires that the product of device sensitivity and the rate of change in analyte concentration be considerably larger than the drift rate.

On the other hand, while the ISFET sensitivity in the feedback mode is, to the first order of approximation, independent of bias and device geometry, the device sensitivity can be enhanced in an ISFET operating in the current mode by increasing the device transconductance. Therefore, for abrupt changes in pH (i.e. large values of dpH/dt) the proposed method is effective regardless of the mode of ISFET operation. In either mode of operation, however, the accuracy of the method can be improved by employing supply-independent biasing techniques and temperature compensation to render the device sensitivity independent of supply voltage and temperature variations.

V. CONCLUSION

Considering the similarity between the drift behavior of ISFETs and GasFETs a method for correction of instability in these FET-based sensors was proposed. This method was analytically developed for GasFETs and verified experimentally using a Si₃N₄-gate pH-sensitive ISFET operating in the current mode. The method was shown to be effective for applications such as continuous monitoring of

plasma pH in which changes in pH are within physiological limits regardless of the mode of ISFET operation. The proposed method can be generally applicable to correct sensor instability, if a drift signal is superimposed on the measuring signal. However, the requirement for the validity of this method is that the product of sensor sensitivity and the rate of change in analyte concentration be considerably larger than the rate of drift in the measuring signal.

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