An Integrated ISFETs Instrumentation System in Standard CMOS Technology

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Abstract—This paper describes an integrated ISFETs instrumentation system in a 0.18 μm 1-poly-6-metal CMOS process. The chip is able to compute the average of CMOS ISFETs' threshold voltages by using an averaging array employing global negative current feedback. In addition, neither reference voltage nor current is required to set up the sigma-delta modulator because the internal signal is converted and processed in the frequency domain. The chip operates at 3.3 V for the analog blocks and the digital input/output blocks, and at 1.8 V for the core digital logic. It achieves 8 bits accuracy under 80 μW static power consumption. The die area is 2.6 mm^2 .

Index Terms—Averaging, CMOS ISFET, current feedback, current feedback opamp, frequency modulator, ISFET, ISFETs array, log domain, sigma-delta modulator, VCO.

I. INTRODUCTION

ION-SENSITIVE field effect transistors (ISFETs), which were invented by Bergveld [1], are solid-state hydrogen ion (pH) sensors in silicon technology. An ISFET is similar to a field effect transistor (FET) which has a gate, source, drain, and bulk terminals. In contrast to the FET, however, an ISFET's gate comprises an exterior ion-sensitive membrane together with a reference electrode, usually as a silver/silver chloride electrode system. By modifying the chemical composition of the membrane, different chemical sensors such as glucose sensors or DNA sensors [2], [3] are mass producible in commercial CMOS processes at low cost. In the past 10 years, research has focused on integrating ISFETs into a CMOS substrate for experimental [4], portable [1], and implantable [5] applications. One of the drawbacks in these applications is the removal of the polysilicon layer in order to leave the gate oxide of the ISFET in direct contact with the chemical solution. This modification is not compatible with standard CMOS fabrication processes.

Recently, research has explored another direction in what is known as floating-electrode CMOS ISFETs [6], [7]. The CMOS ISFETs are formed by joining a transistor's polysilicon gate with all the metal layers and vias all together. The chip passivation layer, which is a layer of silicon nitride on top of silicon dioxide, becomes the ion-sensitive membrane. Since silicon nitride is amphoteric [1], [6], it can donate or accept positive hy-

drogen ions. When a silicon nitride is hydrolyzed and charged in an electrolyte, there are equal but opposite charged ions accumulated in the electrolyte just above the surface of the silicon nitride, and those ions are arranged by the electrochemical double layer capacitor [1]. In Nernstian responses, the voltage developed in the double layer capacitor can reach 59 mV in response to a unit change in pH at room temperature [1]. Silicon nitride has shown a sub-Nernstian sensitivity of 45–56 mV/pH [8]. By setting up a reference electrode's voltage to define the electrolyte potential, the electrical potential across the double layer capacitor can change the drain current of the ISFET. Thus, there exists a possibility of making chemical sensors in standard CMOS technology, but the potential creates an issue: variations of threshold voltages [6], [7]. Variation occurs as there are undefined trapped charges in the passivation layers, floating metals, and intra-layers dielectric where these charges all contribute to the computation of the threshold voltages. The situation is similar to the trapped charges found in the gate oxide of MOSFETs. In an extreme case, Hammond *et al.* reported that their p-typed ISFETs had threshold voltages of -5 V [9]. This is a big problem in biasing the ISFETs under a 3.3 V power supply.

There are few other problems in using this solid-state pH sensor in practice. For instance, ISFETs exhibit short term and long term drifts [10]. Thus, it needs a dedicated algorithm to counteract the drifts. ISFETs also show hysteresis, and recalibration is required for each new experiment. Nevertheless, the possibility of implementing specific functions on a CMOS chip to compensate those ISFETs' performance can produce accurate and precise pH measurements in micro- or nano-scale.

The aim of this work is to illustrate a microwatt power instrumentation circuit with CMOS ISFETs for handheld instruments. The need for a low power application is very important so as to save batteries' life and to minimize any heat generation due to the electrical power dissipation. Constant temperature minimizes the change in the sensitivity to pH, as ISFETs are sensitive to temperature. Besides, the instrumentation circuit should be able to cope with the uncertainties of the threshold voltages while achieving a satisfactory signal-to-noise ratio for its output. Section II presents the strategy used in the instrumentation. Section III describes the CMOS ISFETs in 1-POLY-6-METAL (1P6M) CMOS process and its array implementation. Section IV discusses how the ISFETs array can be adapted into current feedback opamp topology to yield an averaging amplifier. Section V analyzes the microwatt power log domain voltage controlled oscillator which controls the ultimate linearity to the system. Section VI shows the chip measurement results, and Section VII draws a conclusion.

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Fig. 1. Open loop first order sigma-delta modulator employing FM.

II. CHIP ORGANIZATION

Popular high precision data converters, like SAR converters or integrating analog-to-digital converters, are very good for converting physical analog signals into electronic digital signals. The operation of such converters usually needs a stable reference, either a voltage or current source, to do data comparison and conversion. With negative feedback, the converter can produce an accurate digital representation. These kinds of converters, however, are not suitable for use with CMOS ISFETs readout circuits, as CMOS ISFETs suffer undefined threshold voltages. The difficulty in applying the Nyquist rate data converters involving CMOS ISFETs is determining the right level of the reference value. In an extreme case when the ISFET's threshold voltage is very large, the reference voltage will be too small to turn on the device such that the converter cannot function properly. Therefore, a referenceless converter such as the a first order sigma-delta modulator using frequency modulated intermediate values [11] might be better suited in ISFET-based applications.

The sigma-delta modulator shown in Fig. 1 consists of the frequency modulator, the phase quantizer, and the phase subtracter. The input signal $x(t)$ is frequency modulated according to the following equation:

$$\varphi(t) = 2\pi \int_{-\infty}^t (f_c + k \cdot x(\tau)) d\tau \quad (1)$$

where f_c is the modulator's free running frequency, and k is the gain of the frequency modulator. Thus, the phase content of the modulator embeds signal $x(t)$ which is under integration. After the phase quantization stage, the quantized phase will be subtracted. This restores back signal $x(t)$. On the contrary, the quantization noise q_n is differentiated once, so this noise will be first order noise-shaped.

In circuit implementation, a D-flip-flop will be used as the phase quantizer, and the phase subtraction is done by counting the difference of the sum of the previous zero crossing by its current sum. Nevertheless, when the sampling frequency is over twice that of the maximum FM frequency, a D-flip-flop can do the counting, whereas the subtraction can be done using an XOR gate. Hovin [11] has shown that the linear relationship between discrete Y_n and continuous $x(t)$ is

$$Y_n = T_s (f_c + k \cdot x(t)) + q_n - q_{n-1} \quad (2)$$

assuming that $1/T_s \gg k \cdot x(t)$, and T_s is the sampling time, q_n is the quantization noise at time n , while q_{n-1} is the previous quantization noise at time $n - 1$. Equation (2) reveals that the

digital output Y_n contains the analog input $x(t_n)$ with a gain factor of $T_s k$, whereas the quantization noise is first-order differentiated. In the frequency domain, the quantization noise is shaped by +20 dB/decade. The whole data conversion does not require any voltage or current reference; it just requires a stable clock. Note that the linearity of this data converter is solely dependent on the gain of the frequency modulator.

The signal to quantization noise ratio (SQNR) of this modulator can be represented as [11]

$$\text{SQNR} = 20 \log \left[\frac{SR_o}{2\sqrt{2}} \right] - 10 \log \left[\frac{\pi^2}{36} \frac{1}{\text{OSR}^3} \right] \quad (3)$$

where SR_o is the full signal output range, which is equal to the amplitude of the analog baseband signal times the gain of the frequency modulator divided by the sampling frequency. OSR is the oversampling ratio between the sampling frequency to two times the maximum baseband frequency. One efficient way to increase the SQNR is by increase the gain of the frequency modulator, subjected to the constraint that the maximum frequency of the intermediate FM signal has to be less than half of the sampling frequency. Otherwise, signal aliasing will occur.

The modulator discussed above will be mapped to the proposed ISFET instrumentation system as shown in Fig. 2, together with its corresponding chip layout plot.

The BIAS GEN shown in Fig. 2 generates bias voltages for the ISFET averaging array, a front-end interface to an array of 64 ISFETs. Note that the ISFETs in Fig. 2 are located on the bottom right region as a rectangular matrix in the layout plot. The ISFET averaging array produces output signals which contain pH signal, which is equivalent to $x(t)$ as shown in Fig. 1. One of these outputs can be directly monitored via the output port VOUT, or they can be used to bias the on-chip voltage-controlled oscillator (VCO). The output of the VCO can be measured directly through the output port FM, and it also goes directly to the D-flip-flop for phase quantization and subsequent phase subtraction. The signal SD is a digital output representation of the input pH.

III. CMOS ISFETS ARRAY IMPLEMENTATION

In this work, an unmodified CMOS process is pursued in making p-typed ISFETs. On the silicon side, the process connects the polysilicon gate layer of a pMOS to all the available six metal layers with vias. These metals are electrically floating in the intra-chip dielectric, as shown in Fig. 3. The topmost chip passivation layer, which is silicon nitride, is used as a pH sensing layer. Depend on the pH of a chemical solution, silicon nitride can absorb or donate hydrogen ions, so it can be positively or negatively charged. Due to the electrostatic nature

Fig. 2. Functional diagram and chip layout of the integrated CMOS ISFETs instrumentation system.

Fig. 3. Cross-section of the CMOS ISFET in 1P6M CMOS process.

of this charged surface, equal but opposite charges are accumulated over the solution in microscopic layers. The charged silicon nitride and the opposite charged layers in the solution

form the electrochemical double layer capacitor. The voltage developed in this double layer capacitor is dependent on the amount of charges, so it is pH-dependent. When a reference

Fig. 4. A SEM image showing the ISFET in its top layer.

electrode is available to define the solution potential, the pH-dependent voltage across the double layer capacitor can modulate the potential at the passivation layer, which in turn modulates the channel current beneath the gate oxide of the transistor. Thus, the drain current of the device can be modulated by pH.

The scanning electron microscope (SEM) image displayed in Fig. 4 helps to illustrate the appearance of the CMOS ISFET over the chip's passivation layer. Note that the rectangular blocks surrounding the ISFET have no effect at all. They are just the same passivation layer covering the top metal fillings.

A reference electrode plays a very important role in forming a complete electrical potential with the ISFET through an electrolyte. In this work, an external Ag/AgCl reference electrode was used because it has an exceptional stable potential difference between the silver wire and the solution [12]. Therefore, any solution potential can be set up by applying a voltage bias to the reference electrode. When the solution potential goes down to a certain threshold, the p-typed ISFET will be turned on. As a result, the ISFET outputs current accordingly.

The value of the threshold is equal to the threshold voltage of the ISFET. A simplified model to relate ISFET's threshold voltage can be formulated as [1]

$$V_{th} = K + 2.3\alpha U_{TpH} \quad (4)$$

where the constant K , which is pH independent, cannot be determined accurately because of the trapped charges. The impact of the trapped charges [6] in the passivation layer cannot be found out in advance. In fact, there are variations of the threshold voltages in ISFETs, with extreme values of up to 7 V in n-typed ISFETs [7].

One possible solution to reduce the impact of the trapped charges is the use of an array. An ISFETs averaging array, which can compute the mean of the samples' threshold voltages, is able to reduce the impact of the variation of the ISFETs' threshold voltages by generating an average one. For instance, this work used 64 samples of p-typed ISFETs in an array configuration. The mean of the 64 samples was assumed to be -0.7 V, while the standard deviation was assumed to be 0.4 V. Fig. 5(a) shows

Fig. 5. (a) 64 ISFETs in a normal distribution. (b) Simulated current–voltage transfer characteristics of 64 ISFETs under the same bias conditions and the same aspect ratio.

Fig. 6. A SEM image showing the ISFETs arrays.

the threshold voltage distribution of the 64 samples based on the aforementioned statistical properties, while Fig. 5(b) shows the current–voltage transfer characteristics in $0.18 \mu\text{m}$ technology.

Although the statistics are estimated pessimistically, some observations can be made in Fig. 5. First, the 64 samples approximate a normal distribution whose mean is close to -0.7 V. Second, there are fewer samples whose threshold voltages are in the extreme values. Fig. 5(a) shows the threshold voltages from -1.7 V to 0.2 V; the range is about 1.9 V. As a result, the drain current of the samples can be much different, given the same bias condition. In simulation, when the reference electrode is driven by -2 V, there are about $700 \mu\text{A}$ differences in the samples, which all have the same aspect ratio.

An added advantage of an array implementation is the increase of the surface area to volume ratio over the passivation layer, which can also be visualized by looking at the SEM image in Fig. 6. The longer rectangular blocks represent the passivation layer of the ISFETs array. In this 3-D view, the effective area to volume ratio of the ion-sensitive membrane increases by splitting up a big ISFET into a number of smaller ISFETs. The array is expected to help speed up the chemical equilibrium between the hydrogen ions in the chemical solution and the silicon nitride layer.

Fig. 7. 64 pH-ISFETs averaging array using a global current feedback.

IV. ISFETs ARRAY INCORPORATED IN CURRENT FEEDBACK TOPOLOGY

To minimize the impact of the samples' variation of threshold voltages, the ISFETs array described in the previous section has been formatted to compute averages. One of the solutions to bringing up average is employing global negative current feedback as shown in Fig. 7 [13].

Note that $ISFET_1$ to $ISFET_{64}$ are biased by the constant current source I_o to form source follower systems. The choice to use p-type ISFETs is in order to eliminate the back gate effect by shorting the ISFETs' source terminals to their individual substrates. The gate length of the ISFETs is $2 \mu\text{m}$, at which level their channel length modulation parameter is determined to be 0.04 V^{-1} after empirical extraction of the on-chip devices. Hence, the channel length modulation effect is also negligible. Therefore, the drain current of the ISFETs operating in a weak inversion region can be modeled as [14]

$$i_k = 2n \left(\frac{w}{L} \right) \mu_p C_{ox} U_T^2 \exp \left(\frac{v_{sg,k} + V_{th,k}}{nU_T} \right), \quad k = 1 \dots 64 \quad (5)$$

where μ_p is the mobility factor, C_{ox} is the gate oxide capacitance, $U_T = KT/q$ is the thermal voltage, n is the subthreshold slope factor, and V_{th} is the threshold voltage of the ISFETs, which is pH dependent.

Since all the ISFETs are biased by the current source I_o , and the remote gate voltage is driven by V_{ref} , any change in the pH of the solution will cause a change in the source terminal voltage v_x , which can be evaluated by rearranging (5):

$$v_{x,k} = V_{ref} - V_{th,k} + nU_T \left(\frac{i_k}{2n \frac{w}{L} \mu_p C_{ox} U_T^2} \right) \quad (6)$$

By lumping all constants to C , the summation of v_x can be represented by the summation of the threshold voltages of the ISFETs as in (7):

$$\text{or} \quad \sum_k v_{x,k} = \sum_k C_k - \sum_k V_{th,k} \quad (7)$$

Summing all the ISFET's drain currents i_k , where they are under small signal representation, i_k can be expressed as

$$\sum_k i_k = \sum_k \left[\frac{v_{x,k}}{R_g} + \frac{v_{x,k} - v_{out}}{R_f} \right] \quad (8)$$

Referring back to Fig. 7, all the ISFETs' drain currents are mirrored and conveyed to the high impedance cascode node Z_t via M0 to M4. Subsequently, they are all buffered to the output node v_{out} .

$$\left(\sum_k i_k \right) Z_t = v_{out} \quad (9)$$

Solving (7), (8), and (9) together and assuming $Z_t \gg R_f$, v_{out} can be expressed as

$$v_{out} = \left(1 + \frac{R_f}{R_g} \right) \frac{\sum_k (C_k - V_{th,k})}{64} \quad (10)$$

Equation (10) reveals that the output of the amplifier is equal to the closed loop gain of $1 + R_f/R_g$ times the average of the IS-

Fig. 8. (a) Transient simulation, and (b) DC simulation of the 64 pH-ISFETs averaging array. The thicker line represents the output of the 64 pH-ISFETs averaging array, while the thinner lines represent 64 single-input current feedback amplifiers.

FETs' threshold voltages. Simulation was done using a $0.18 \mu\text{m}$ technology in Cadence Virtuoso Spectre circuit simulator. Fig. 8 illustrates the simulation results of 64 single-input current feedback amplifiers, and a 64 pH-ISFETs averaging array, all configured in a closed loop gain of one. All the ISFETs were sized by the same aspect ratio and subjected to the same current bias. Their threshold voltages followed the normal distribution of a mean -0.7 V and a standard deviation of 0.4 V , like what is described in Section III. Fig. 8(a) plots the output voltage versus reference electrode voltage. Even though some of the individual curves saturate toward the power supply voltage, the output of the 64 pH-ISFETs averaging array, which emerges as the thicker line situated in the middle of all the curves, extends the linearity range. In fact, the curve is roughly equal to the mean of all the 64 samples. Fig. 8(b) plots the output voltage of the amplifiers in real time with a reference electrode voltage of $2 + 0.1 \times \sin(2\pi 100t) \text{ V}$. Some of the curves saturate to the power supply voltage, while some other curves follow the sinusoids with different offsets. However, the output of the 64 pH-ISFETs averaging array, shown as the thicker line, does not appear distorted at all; the extreme samples have no significant effect on the aggregate average.

Fig. 9. Simulated frequency spectrum of one ISFET input and 64 ISFETs inputs configured in current feedback opamp topology.

The advantage of using averaging not only reduces the impact of the variations of ISFETs' threshold voltages on the bias point, but also it improves the signal-to-noise ratio to the system [15]. The same schematic set up was done on the transient simulation, but the bias of the reference electrode is $1.4 + 0.1 \times \sin(2\pi 100t) \text{ V}$ now. This bias ensures that all the outputs stay in the linear region of the amplifiers. Finally, the simulated data was transferred to Matlab for evaluating their individual power spectral density (psd) so that their spectral characteristics can be compared. In Fig. 9, there are two spikes located at 100 Hz; they are corresponding to the baseband signals. Besides, the noise floor of the one-input current feedback amplifier is about 15 dB higher than the 64 pH-ISFETs averaging array. This verifies that the signal-to-noise ratio of the averaging system increases as the sample size of the averaging increases.

Depending on the trapped charges in the passivation layers as well as in the floating metals, it is not easy to implement a single ISFET or even an array of ISFETs on-chip because it is difficult to bias ISFETs with predefined operating point. Therefore, a closed loop gain of one in the ISFETs averaging array was employed in this work to allow headroom for the amplifier to work in the linear region. In order to add amplification to the proposed instrumentation system, a frequency modulator was used; the frequency modulator will be discussed next. Finally, the power consumption will not be a stringent issue as most of the transistors are biased with sub-nano-amps in the weak inversion region.

V. LOG DOMAIN VOLTAGE-CONTROLLED OSCILLATOR

The VCO shown in Fig. 1 should ideally be operating as a simple harmonic oscillator, whose transfer function can be represented by the Laplace equation:

$$\frac{Y(s)}{X(s)} = H(s) = \frac{w_o^2}{s^2 + w_o^2} \quad (11)$$

where w_o is the frequency of oscillation, and s is a complex variable. A simple harmonic oscillator, such as an LC oscillator, can be designed with a high quality factor (high Q) such that its

phase noise is minimized [16], [17]. In this work, an operation of CMOS in the weak inversion region was exploited again to synthesize a microwatt power log domain oscillator. The attractiveness of this VCO is that both its Q value and its frequency of oscillation are tuned independently by two bias currents. It will also be shown that the oscillator is very linear to its controlled current, which can be adjusted by the pH.

Referring back to (11), the Laplace equation representing the simple harmonic oscillator can be transformed to one of its state space equivalent [18]:

$$\begin{cases} \dot{X}_1 = w_o X_2 - w_o X_1 \\ \dot{X}_2 = w_o X_2 - 2w_o X_1 + w_o U \\ Y = X_1 \end{cases} \quad (12)$$

where X_1 and X_2 are the internal state variables, and U and Y are the input and output, respectively. This set of linear state space equations can be manipulated into a set of exponential state space nodal equations [19], which can reveal the specific circuit topology of the log domain oscillator. The synthesis procedure is as follows.

First, the following exponential state variable mappings are defined:

$$\begin{cases} X_1 = I_1 \exp\left(\frac{V_1}{nU_T}\right) \\ X_2 = I_2 \exp\left(\frac{V_2}{nU_T}\right) \\ U = I_u \exp\left(\frac{V_u}{nU_T}\right) \end{cases} \quad (13)$$

The above mappings are analogs to a MOSFET's drain current in a weak inversion region as listed in (5).

$$i_D = 2n \left(\frac{w}{l}\right) \mu_n C_{ox} U_T^2 \exp\left(\frac{v_{gs} - V_{th}}{nU_T}\right)$$

Or in short, $i_D = I_s \left(\frac{v_{gs}}{nU_T}\right)$

Thus, (13) is processing in a current mode domain where the state variables, input, and output are all current. Next, the following assignments are chosen:

$$\begin{cases} I_o = nCw_o U_T \\ I_1 = I_o \\ I_2 = I_s \\ I_u = \frac{I_s^2}{I_o} \end{cases} \quad (14)$$

Using (13) and (14), the linear state space (12) could be transformed to the following nonlinear KCL equations:

$$\begin{cases} C\dot{V}_1 = I_s \exp\left(\frac{V_2 - V_1}{nU_T}\right) - I_o & (15a) \\ C\dot{V}_2 = I_o - 2\frac{I_o^2}{I_s} \exp\left(\frac{V_1 - V_2}{nU_T}\right) + I_s \exp\left(\frac{V_u - V_2}{nU_T}\right) & (15b) \\ Y = I_o \exp\left(\frac{V_1}{nU_T}\right) & (15c) \end{cases}$$

To realize (15) in terms of circuit implementation, Table I employs possible circuit building blocks [18]. Note that the nMOS devices have a triple well option so that their source terminals and the bulk terminals can be tied together individually to minimize the back gate effect.

TABLE I
CIRCUIT BUILDING BLOCKS TO REALIZE EQUATION (15)

Equation 15a
Equation 15b
Equation 15b supplementary
Equation 15c

A complete schematic is shown in Fig. 10. It consists of the 64 pH-ISFETs averaging array, the voltage-to-current converter, and the log domain oscillator.

The pH dependent signal I_o is set by connecting the ISFETs averaging array with the external resistor R_{ext} configuring in closed loop gain of one. I_o is equal to:

$$I_o = \frac{V_{out}}{R_{ext}} \quad (16)$$

The value of Q and the frequency of oscillation can also be deduced from Fig. 10 [20]. They are:

$$\begin{cases} \frac{w_n}{Q} = \frac{I_q - 2I_o}{nC U_T} \\ w_n = \frac{\sqrt{3I_o^2 - I_o I_q}}{nC U_T} \end{cases} \quad (17)$$

If $I_q = 2I_o$ (which is the ideal case of a simple harmonic oscillator)

$$\begin{cases} Q \rightarrow \infty \\ w_n = \frac{I_o}{nC U_T} = \frac{V_{OUT}}{nR_{ext} C U_T} \end{cases} \quad (18)$$

Simulations investigated the bias current I_q on the Q value of the VCO. The Q value can be inferred by looking at the phase change in the VCO's open loop configuration. The faster the phase changes at its frequency of oscillation, the higher the Q is. Equivalently, the phase noise of the VCO is minimized when

Fig. 10. Schematic diagram showing the log domain vco. The signal I_o is determined by the V-I converter consisting of the ISFETs averaging array and the external resistor R_{ext} .

Fig. 11. Simulated open loop VCO's phase spectrum under different I_q .

Fig. 12. Simulated VCO's phase noise under different I_q .

a maximum Q is attained. These relationships are illustrated in Figs. 11 and 12.

Fig. 13. Chip microphotograph.

Fig. 11 shows the open loop phase response of the VCO. When the value of the bias current $I_q = 1 \mu\text{A}$, it has the steepest slope at frequency = 150 kHz where the phase is zero degree. All the other I_q shows non-optimal Q to the system. Fig. 12 shows the phase noise of the VCO in closed loop, and it reveals that the phase noise is the lowest when $I_q = 1 \mu\text{A}$.

VI. MEASUREMENT RESULTS

Fig. 13 shows the chip microphotograph. The ISFETs array is located in the region in the lower right of the rectangular matrix. The die area is 2.6 mm^2 .

A. ISFETs Averaging Array Measurements

First, the electrical properties of the ISFETs averaging array are characterized before investigating the chemical behavior. A DC voltage was swept to the off-chip reference electrode; in this case it was Ag/AgCl. The reference electrode was used to provide a stable interfacial potential between the electrode and its

Fig. 14. Measured output voltage of the ISFETs averaging array against the reference electrode's voltage.

Fig. 15. Measured output characteristics against pH of the ISFETs averaging array.

surrounding chemical solution. In this way, a complete electrical potential can be set up from the electrode down to the chip's substrate. Next, a Keithley Model 6430 Source Meter was used to sweep the DC voltage on the electrode from 0.1 V to 1.8 V in 0.1 V increments. It was also used to measure the leakage current of the reference electrode. The Source Meter is a good indicator for detecting the leakage current of the ISFETs array. Fig. 14 plots the measured output voltage of the ISFETs averaging array. The result indicates a gain error of less than 1% in the 1.7 V output range, which covers more than the full scale range of pH from 1 to 14. The measured reference electrode's leakage current for the whole sweep range is less than 10 nA in absolute value.

To characterize the pH sensitivity of the averaging array, the chip was tested against three chemical buffer solutions: pH = 4, 7.4, and 10. The measurements are displayed in Fig. 15. About 37 mV/pH sensitivity is recorded in this readout; the value is slightly lower than the reported values: 45–56 mV/pH in silicon

Fig. 16. Measured pH response of the ISFETs averaging array.

nitride. Finally, real time pH responses were obtained by exposing the array in N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid (HEPES) at pH = 7.6 for an hour. Then, 200 μ L 0.05 M H_2SO_4 was added at $T = 200$ s, 600 s, 1000 s, and 1400 s. The results are displayed in Fig. 16. There are four obvious step changes over the window, which verifies the basic performance of the ISFET averaging array. The strong point of this averaging array is that there is no CMOS post-processing involved. The power consumption of this averaging array is 66 μ W approximately.

B. Log Domain VCO

Recall from Section V that the frequency sensitivity of the log domain VCO can be controlled by the external resistor R_{ext} . A 10 M Ω external resistor was used for the test chip, and it generates a bias current I_o about 100 nA at 1 V output. An Agilent Model 4395A Spectrum Analyzer was used to estimate the frequency details of the VCO, and one of the results is shown in Fig. 17. Apart from this frequency spectrum, the VCO gain characteristic is also important because the linearity of the VCO establishes the linearity of the overall instrumentation system. A DC voltage of 0.1 V incremental sweep across the reference electrode was carried out, and the corresponding output frequency was recorded. These results are displayed in Fig. 18, which shows that the VCO's gain is very linear to the controlled voltage range from 0.5 V to 1.9 V. The power consumption of this VCO is below 10 μ W over the entire input sweep.

C. Total System

A 500 kHz sampling clock was chosen to fit the proposed instrumentation system, and the measurements were logged by an oscilloscope from LeCroy. With reference to the signals associated in the instrumentation as shown in Fig. 2, a snapshot of the transient response showing the sampling clock (clk), the frequency modulated signal (FM), and the one bit sigma-delta signal (SD) is displayed in Fig. 19. The same figure shows two internal signals A and B, which were assembled to supplement the functional performance of the sigma-delta modulator. This set of results is based on what the sinusoidal voltage acted on

Fig. 17. Measured power spectrum of the log domain VCO when $V_{ref} = 1.4$ V.

Fig. 18. Measured VCO gain characteristics.

the reference electrode. Note that the signal SD is a direct result of an XOR operation between the internal signals A and B.

The power spectral density (psd) of the signal SD was estimated by Matlab from its 2^{16} samples using a Hanning window, and the results are displayed in Fig. 20. Fig. 20 (a) and (b) show the existence of the baseband signals, one at 100 Hz and the other at 500 Hz. On the other hand, the noise floors displayed in Fig. 20 exhibit a first order noise shaping at frequencies above 10 kHz. The SQNR is predicted to be about 45 dB, effectively representing 8 bits of information. The fact that the modulator can produce SQNR of more than 40 dB with the 500 Hz baseband signal suggests that the bandwidth of the system can occupy 1 kHz. From the above discussions and results, the referenceless sigma-delta modulator achieves 8 bits accuracy in less than 80 μ W.

Spectral analysis might not be a good way to evaluate the performance of the sigma-delta modulator against pH, as the pH of a chemical solution changes slowly in real time. Since

Fig. 19. Transient response showing the main input/outputs of the instrumentation system.

Fig. 20. Measured power spectral density. (a) Input: $1.4 + 0.12 \times \sin(2\pi 100t)$ V. (b) Input: $1.4 + 0.12 \times \sin(2\pi 500t)$ V. (c) Input: DC of 1.4 V.

the pH in a solution is almost constant in case of no chemical disturbance, the modulator will output bitstream data, whose average value in a given period of time is a scaled version of the FM's carrier frequency, as described by (2). Recall that the carrier frequency of the FM signal is dependent on pH, so the easy way to examine the relationship between pH and the output of the sigma-delta modulator is to evaluate the DC content of

Fig. 21. Measured transfer characteristic between the number of ones in the bitstream output and the pH input.

TABLE II
PERFORMANCE SUMMARY

Technology	0.18 μm 1 POLY 6 METAL CMOS
Supply Voltage	1.8V/3.3V
Chip Area	2.6 mm ²
Power Consumption	76 μW (excluding digital core and IO)
ISFET Size (W/L)	20 μm by 2 μm
Chemical Sensitivity	37 mV/pH (an average of 64 ISFETs)
Reference Electrode	Off chip
VCO gain	81 kHz/V (tunable by an external resistor)
Frequency Range	80 $\leftrightarrow$ 200 kHz
Accuracy	8 bits
Bandwidth	1 kHz
Sampling Frequency	500 kHz

the bitstream output. By evaluating the number of ones in the output of the sigma-delta modulator a 100 ms period, the DC value of the output could be roughly equivalent to the number of ones in the 100 ms period. However, the counting procedure is post-processed in Matlab.

The experiment consisted of testing the three pH buffer solutions, pH = 4, 7.42, and 10, in the chip again and counting the number of ones in the output of the sigma-delta modulator. The count began when the ISFETs' responses reach a steady state. The result is displayed in Fig. 21. The circle represents the measured number of ones, while the straight line represents the linear regression model. The data shows a good match between the digital output and the chemical input with less than 0.5% error in predicting the linear model.

Finally, a performance summary of the instrumentation system is listed in Table II.

VII. CONCLUSION

An integrated ISFETs instrumentation system in a standard CMOS process has been presented. The instrumentation regulates the undefined ISFETs' threshold voltages by using the averaging array, which is based on a global negative current feedback technique. Moreover, signal amplification is achieved in a frequency domain by employing the microwatt power VCO to

transform a baseband signal into a frequency modulated signal. The wide voltage tuning range together with the independent Q control makes the log domain VCO a good frequency modulator for use in the referenceless sigma-delta modulator. Finally, the sigma-delta modulator is able to perform a linear relationship between the pH input and the digital output, and it provides up to 8 bits accuracy under 80 μW power consumption.

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