Differential read-out architecture for CMOS ISFET microsystems

V.P. Chodavarapu, A.H. Titus and A.N. Cartwright

The operation of a pH (H^+ ion concentration) sensitive ion-sensitive field-effect transistor (ISFET) microsystem with a sensitivity of 40–45 mV/pH is demonstrated. This system has two identical ISFETs as the inputs to a pair of ISFET operational transconductance amplifiers (IOTAs) arranged in a novel differential architecture. The IOTAs have different sized *p*-MOSFET load transistors that enable pH sensitive operation without any post-fabrication processing or material deposition. The CMOS ISFET chip is fabricated in an unmodified 1.5 μm commercial process.

Introduction: The ISFET, first described by Bergveld in the early 1970s [1], has been used extensively for physiological measurements in biomedical applications. Commonly applied pH sensitive layers for ISFETs include SiO_2, Si_3N_4, Al_2O_3, Ti_2O_5, and SnO_2. Si_3N_4 and SiO_2 are the only materials used extensively in CMOS technology. SiO_2, however, suffers from severe instability and hydration. Hence, Si_3N_4 is the preferred choice because of its resistance to hydration, good sensitivity, long term stability, and CMOS compatibility. Typically, a differential ISFET configuration requires ISFETs with different pH sensitivities. Fabrication of ISFETs with sensing layers other than Si_3N_4 or SiO_2 requires some post-processing deposition [2, 3]. Here, we present a novel approach for developing a CMOS compatible differential ISFET configuration with Si_3N_4 as the only pH sensitive layer and that requires no post-processing deposition.

Specifically, a pH sensitive CMOS ISFET chip is presented as shown in the schematic of Fig. 1. The CMOS ISFET chip uses a differential setup of two IOTAs that have the ISFETs integrated as the input stage. The principle of operation of the IOTA is described elsewhere [4]. In the approach presented here, both the IOTAs have identical ISFETs, but the pH sensitivity of each IOTA differs according to the size of the *p*-MOSFET load in the IOTA. That is, the two IOTAs have different responses to the same pH change, similar to a differential setup of two ISFETs with different pH sensitivities. Hence, different sensitivities on a single chip are achieved without post-processing by sizing properly the *p*-MOSFET loads in the two IOTAs.

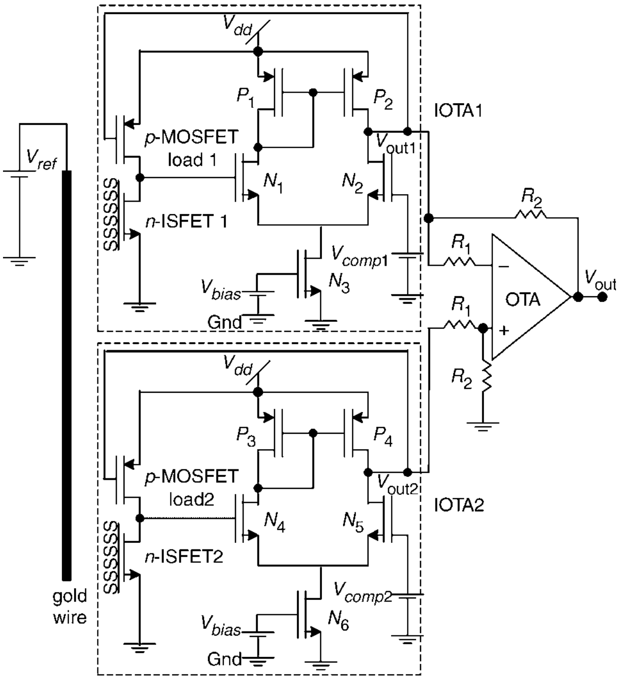

Fig. 1 *Schematic diagram of CMOS ISFET microsystem*

Dotted boxes show the architecture of the CMOS ISFET chip. N1–N6 are *n*-MOSFETs and P1–P6 are *p*-MOSFETs

System design: The CMOS ISFET used in this work is an *n*-channel device and has a linear design structure as proposed by Bausells *et al.* [5], with an electrically floating gate electrode 'stack' consisting of (from lowest to highest) a polysilicon layer, two metal layers, and a PEVCD-grown Si_3N_4 passivation layer, which acts as the pH sensitive layer. Note that PECVD-grown Si_3N_4 has a response of about 40–45 mV/pH. In the work reported here, the IOTAs are biased in the saturation region. Under this condition, and considering the IOTA1 in Fig. 1, the expression for the output voltage (V_{out1}) is given by (1) [4], where V_{Tn} is the threshold voltage of the ISFET and depends on the pH of the electrolyte; the offset voltage, V_{DC1}, and the amplification factor, a, are set by the device dimensions, circuit parameters and foundry process parameters:

$$V_{out1} = V_{DC1} - \frac{V_{Tn}}{\sqrt{a}} \qquad (1)$$

In the current design, the ISFETs are the same size ($W/L = 400/40$, where W is the width and L is the length of the MOSFET in μm), but the two IOTAs have different dimensions for their *p*-MOSFET load which produces a different amplification factor, a. Thus, IOTA1 and IOTA2 have a different sensitivity for the same change in pH. To improve device matching, the *p*-MOSFET loads have the same length, but their widths are different: $W/L = 250/10.4$ for IOTA1 and $W/L = 600/10.4$ for IOTA2. The output voltage of the microsystem (V_{out}) is given by (2), where G is the gain of the operational amplifier (OTA, National—LF356 N), and V_{DC} is the offset voltage set to the difference between the offset voltages of IOTA1 and IOTA2. Equation (3) relates the change in the output voltage of the microsystem to the change in the pH of the electrolyte. The simulated output for the two IOTA circuits is shown in Fig. 2. IOTA1 has a sensitivity of 50 mV/pH and IOTA2 has a sensitivity of 30 mV/pH:

$$V_{out} = G \cdot (V_{out1} - V_{out2}) = G \cdot \left[V_{DC} - V_{Tn} \left(\frac{1}{\sqrt{a_1}} - \frac{1}{\sqrt{a_2}} \right) \right] \qquad (2)$$

$$\Delta V_{out} = G \cdot \Delta V_{Tn} \left(\frac{1}{\sqrt{a_1}} - \frac{1}{\sqrt{a_2}} \right) \qquad (3)$$

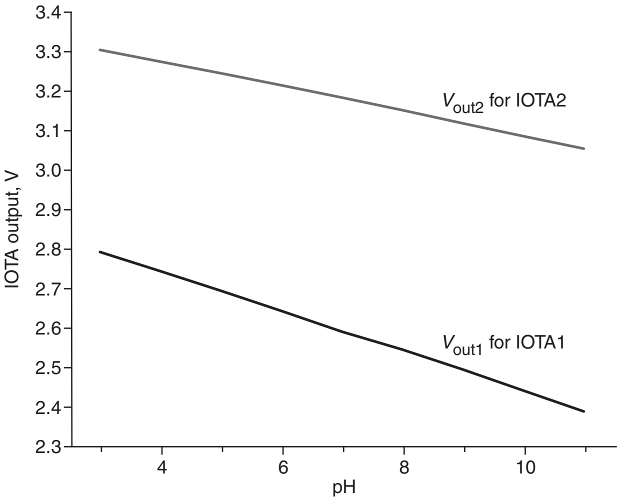

Fig. 2 *Plot of sensitivities of IOTA1 and IOTA2 from simulation*

Experimental results and discussion: The 4.84 mm^2 ISFET sensor chip is fabricated using the AMI 1.5 μm CMOS process available through MOSIS and packaged in a 40-pin DIP. The chip is covered with an insulating adhesive with only the ISFET gate region exposed to the electrolytes. A plastic sample chamber with an integrated gold metal electrode, used as a quasi- or pseudo-reference electrode, is attached to the sensor chip. The sensor chip works with a 5.0 V DC power supply and consumes 4 mW of power.

For the microsystem, V_{ref}, the reference voltage applied to the gold electrode is set to 5.0 V, V_{bias} is set at 0.9 V and the gain, G, of the OTA is set at 2.25. The gain of the OTA can be adjusted as needed. Fig. 3 shows the response of the CMOS ISFET microsystem for 2.0 ml phosphate buffer solution (pH 6.85) with measured quantities of 1.5 M HCl added at regular intervals of time without stirring at room temperature. The pH of the solutions is measured using a conventional glass electrode (Orion 720A) calibrated with two standard buffer solutions of pH 4.0 and 7.0. The microsystem has a sensitivity of

40–45 mV/pH in the pH range of 3–11. Following (3), the measured results are in agreement with the system design, with gain, G, of the OTA set at 2.25 and the differential pH sensitivity between the two IOTAs being 20 mV/pH, as noticed from the simulation results.

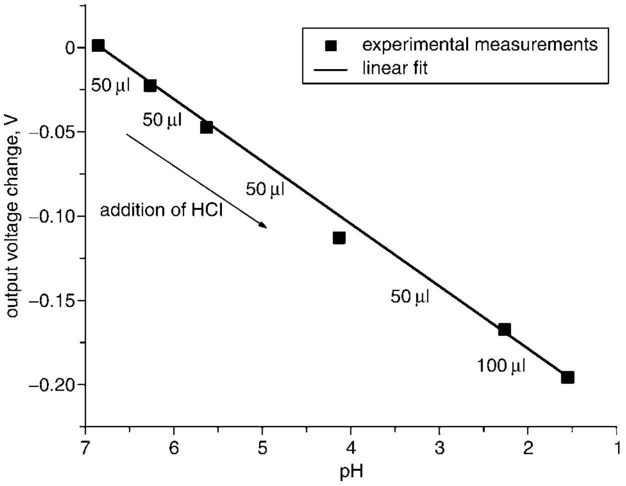

Fig. 3 *CMOS ISFET microsystem output response*

Change in output voltage is measured from 'zero' output (starting with phosphate buffer solution at 6.85 pH). Quantity of HCl added is also shown in microlitres (µl).

Conclusion: We have designed, fabricated and tested an integrated pH sensitive CMOS ISFET microsystem. The microsystem is compact, low-cost, low-power and is fabricated using commercial CMOS or volume production processes without any significant post-processing deposition.

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