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A Multisensor Readout Circuit with a Multiplexed Pulse-signal Output

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1. Introduction

For several decades, much attention has been paid to silicon-based biosensors in the field of bio-analytical applications due to their favorable characteristics, such as sensitivity, speed, miniaturization, and low cost. This interest is evident in the numerous studies that have monitored biological events such as antigen-antibody binding, and enzyme-substrate reactions using these silicon-based biosensors [1]. Among these, the ion-sensitive field-effect transistor (ISFET) is one of the most popular electrical biosensors and has been introduced as the first miniaturized silicon-based chemical sensor. The ISFET, traditionally referred to as a pH sensor, has been used to measure ions concentrations (H^+ or OH^-) in a solution, causing an interface potential on the gate insulator, which acts as a sensing membrane for H^+ ions. The device, a modified metal oxide semiconductor field effect transistor (MOSFET) [2-5], had no gate electrode so that the gate oxide was exposed to a chemical analyte into which the device was immersed. Variations in the ion concentration of the analyte gave a Nernstian response in the electrochemical potential at the surface of the oxide that was in turn measured as a change in the threshold voltage of the MOSFET [3,4].

Numerous biosensors were established on the basis of theoretical development of ISFET technology. ISFET biosensors have widely been used in biosensing research, including the progress of the enzyme-immobilized FET which detects H+ ion concentration, the DNA (deoxyribonucleic acid)-modified FET based on DNA hybridization detection, and the cell-based FET for cell metabolism sensing or the measurement of extracellular potential. Spiegel et al. presented an extended gate field effect transistor (EGFET) [6]. An extended metal electrode, on which a sensing film is coated, is interconnected to the polysilicon gate of a MOSFET. With the topology, the sensing area can be increased and is not constrained by gate size.

In the biomedical area, a particularly important measurement has been that of pH since it is an important indicator of gut function. The pH values of human blood, urine, and saliva are also an important indicator of health. A more robust candidate for pH-value measurement is the ISFET. Performance drift resulting from temperature variation drift is also an important issue for a majority of sensors. In this work, a monolithically integrated CMOS multi-sensor was implemented to detect pH value, urea, temperature.

2. Experiments and Discussions

The extended gate electrode is an exposed top-layer metal and a native alumina film on the aluminum metal is used as a sensing membrane for H^+ ions. Under the fixed biasing voltage of an external Ag/AgCl reference electrode, which is dipped into the analyzed solution with the sensing chip, the floating gate of the ISFET really has an effective gate voltage $V_{G,eff}$. The $V_{G,eff}$ is related to the concentration of H^+ ion, which absorbs on the native alumina film. The pH-value sensing chip was fabricated by the TSMC 0.35μm CMOS process. The sensing area is 300μm×300μm.

The designed CMOC multi-biosensor has two ISFETs and one set of bipolar junction transistors (BJTs), and can detect pH values, urea and temperature by multiplexed selection. Fig. 1 shows the oscillation-type pH-ISFET readout circuit consisting of one voltage-to-current converter and one current-control oscillator. Every ISFET is one of input differential transistor pair of the operational amplifier in the voltage-to-current convertor. The operational amplifier has a simulated gain of 78.6dB with a phase margin of 75.6°. The oscillator is composed of two comparators, an SR-latch, two inverters, and a current-sinking circuit. The current-sinking circuit consists of a voltage-to-current converter and a current mirror. The converter transfers the $V_{G,eff}$ of the ISFET into a current and then controls the sinking current of the two inverters through the current mirror. Fig. 2 shows the temperature sensor, in which the output voltage V_{sen}, i.e. V_{EB}, decreases linearly with increasing temperature under a bandgap-reference biasing current.

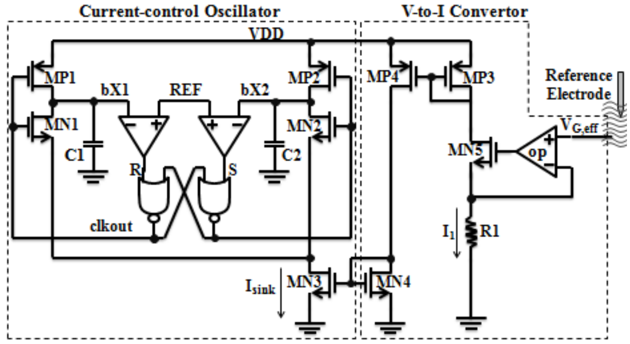

Fig. 1 Oscillation-type pH-ISFET readout circuit.

With an additional on-chip gold electrode for immobilization of urease enzyme, a pH-ISFET can be used to detect urea concentration. Urease is one kind of enzyme that can decompose the urea and generate OH^-. The reactant OH^- would change the pH value of solution. Fig. 3 shows the oscillation-type CMOC multi-biosensor readout circuit. Three voltage-to-current convertors, in which the positive terminal of input differential transistor pairs is a H^+-sensitive floating gate electrode or is connected to the output terminal of the temperature sensor, are multiplexed to a current-control oscillator by a set of selection lines.

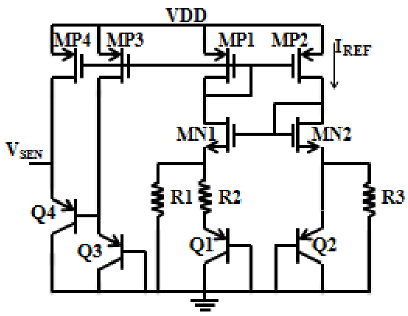

Fig. 2 Temperature sensor biased by a bandgap reference current.

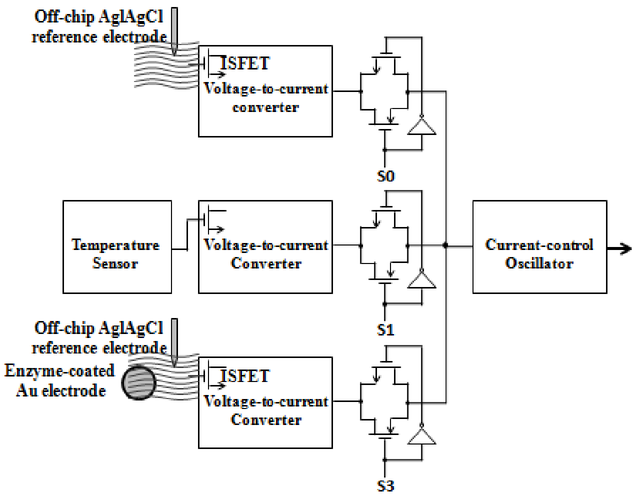

Fig. 3 CMOC multi-biosensor using multiplexed selection .

The chip is tested under 3V supply voltage. Fig. 4 shows the plot of the measured output oscillation frequency versus temperature. The output frequency varies linearly with temperature. Sensing sensitivity is about 0.55kHz/ºC with R^2 values of linear regression of 0.9999. Temperature errors range from -0.16 ºC to 0.14 ºC in the tested temperature range. Because the temperature sensor is for biomedical applications, tested solution or used enzymes will be destroyed under higher temperatures higher than 60 ºC. Fig. 5 shows the measured output oscillation frequency for the solution of several pH values by taking the average of the last three measured frequencies for every pH values. The output frequency varies linearly with the pH value. Sensing sensitivity is about -2.44kHz/pH with R^2 values of linear regression of 0.9947. The experiment for urea sensing is proceeding. It can be expected that the good linearity still exists for the urea detection.

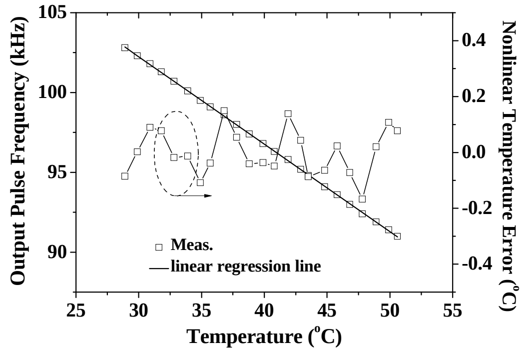

Fig. 4 shows the plot of the measured output oscillation frequency versus temperature.

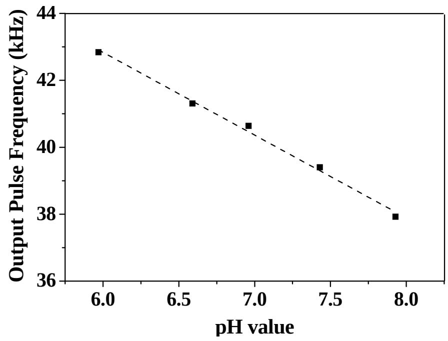

Fig. 5 shows the measured output oscillation frequency for the solution of several pH values.

3. Conclusions

An oscillation-type CMOS multi-sensor readout circuit for the detection of pH-value, urea, and temperature has successfully been designed. ISFETs are used to detect pH values and urea concentrations in solutions. BJTs are used to detect temperature. The linearity of output frequency versus pH value and temperature is up to 0.995 or higher value. The thinner native alumina can be applied to test the solution with pH value ranging from 6 to 8 at least, but the pH-ISFET is still suitable for humans because the normal pH values are about 7.34~7.45, 5~8, and 6.35~6.85 for human blood, urine, and saliva, respectively.

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