Integrated Current Readout Circuit and DMFET Array for Label-Free Detection of Cancer Marker

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Abstract—**This paper describes a current readout platform designed for dielectric modulated field effect transistor (DMFET) arrays to detect a prostate cancer marker without labeling. A chip of 16 DMFET array has been fabricated as a biosensor cartridge. Standard 0.35μm CMOS technology has been used to fabricate the readout circuit which includes a current integrator and a 10-bit single-slope analog-to-digital converter (ADC). The prostate cancer marker has been successfully detected by monitoring a change of DMFET current with aid of the fabricated readout circuitry.**

Keywords: label-free, biosensor, readout, current integrator

I. INTRODUCTION

In ubiquitous era, portable biomedical systems and point-of-care testing are becoming more important for disease prevention and health promotion. Integrating biosensors with the readout circuitry gives the advantages of miniaturization for the purpose of portable applications and human body implantation. It was reported that the specific binding of biomolecules changed the dielectric constant in a vertical nanogap underneath the gate then modulated the threshold voltage (V_T) of a field effect transistor (FET) [1]. This paper introduces a circuit integrated readout platform for the cartridge-like DMFET array.

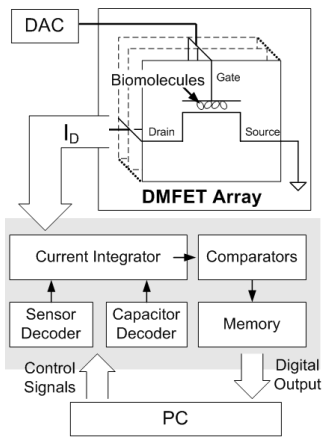

Figure 1. A functional block diagram of overall system.

II. OPERATIONAL PRINCIPLES

A. DMFET Operation as a Biosensor

Fig. 1 shows a functional block diagram. The DMFET array has been fabricated and utilized as a biosensor. It has a vertical nanogap between the gate electrode and the gate oxide surface [1]. Specific binding of biomolecules in the nanogap changes its gate dielectric constant then it results in threshold voltage (V_T) shift. Various kinds of biomolecules can be detected by using DMFET without labeling process.

B. Readout Circuit Design

To detect V_T shift, the drain current (I_D) has been measured with the readout circuit fabricated by standard 0.35μm CMOS technology. Schematic of the readout circuit is shown in Fig. 2. A current integrator consists of a folded-cascode amplifier (FCA) and feedback capacitors (C_F) [2]. Both terminals of feedback capacitors are initially set to the reference voltage (V_{REF}) controlled by signal Reset. Sample signal starts charging or discharging C_F by I_D of the DMFET. While integrating current in the C_F, 10-bit binary code counter values are loaded to a 10-bit SRAM cell array [3]. As soon as the voltage of the node $V_{INTEGRATION}$ reaches V_{HIGH} or V_{LOW}, $Write_{SRAM}$ goes low by two comparators and an AND gate. At that moment, the SRAM memories latch the counter values. From the latched values in the memories, I_D can be obtained through simple calculation.

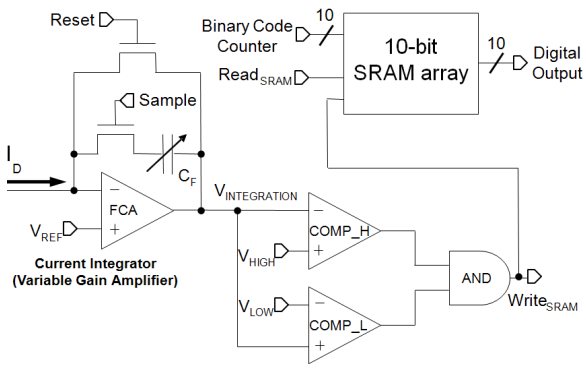

Figure 2. Schematic of the integrated current readout circuit.

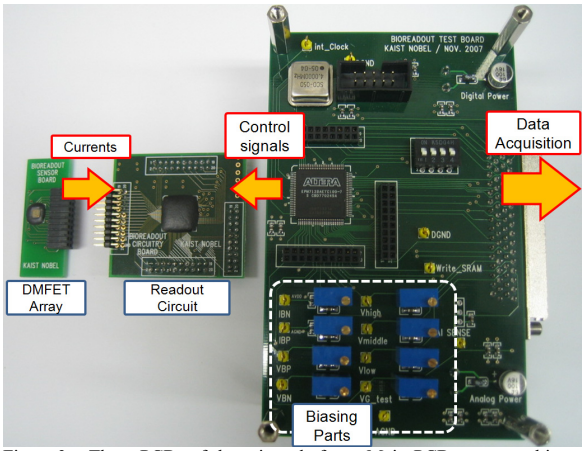

Figure 3. Three PCBs of detection platform. Main PCB generates biases for circuitry and connects this platform to a computer. The other two PCBs are for the readout circuitry and the DMFET array.

III. Experimental Results

Detection platform consists of three printed circuit boards (PCBs) as shown in Fig. 3. As a biosensor cartridge, 16 DMFET array had been fabricated and mounted on a discrete PCB. In an array form, it is possible to collect more statistical data in a short time. Additionally, repetitive analyses can be realized by replacing DMFET array cartridges.

Prostate specific antigen (PSA) has been detected to verify the functional operation of the integrated system. To immobilize PSA antibody (Ab) [4] on the gate oxide surface in the nanogap of the DMFET, it was reacted with 1wt% of trimethoxysilane aldehyde in ethanol for 2 hours, washed with copious ethanol, and heated at 120°C for 30min. Antibody solution of 100μg/ml had dropped on the DMFET array, reacted for 4 hours, and washed with phosphate buffer solution (PBS) and deionized water sequentially. Finally antigen (Ag) solution of 100μg/ml had been introduced as a droplet, and I_D was measured after 4-hour-reaction and subsequent washing. Fig. 4 shows the current monitoring results of every step at a fixed gate voltage. The gain of the current integrator can be selected by changing the feedback capacitor as the input current varies. In addition, detectable current range and the resolution can be adjusted by changing the counting speed of the binary counter. Statistical data of I_D in the array are plotted in Fig. 5.

IV. Conclusions

In this work, a tumor marker for the prostate cancer has been successfully detected with aid of a cartridge-like DMFET array chip and a circuit integrated readout platform. The readout circuit consists of a current integrator and a 10-bit single-slope ADC. Specific binding of PSA Ab and Ag has successfully detected by monitoring a change of the drain current in the DMFETs originating from dielectric constant change in the nanaogap.

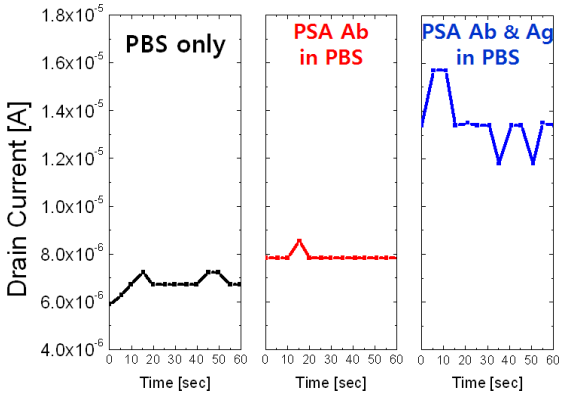

Figure 4. Real time current monitoring data at a fixed gate voltage of 3V for one minute. Because the gate dielectric costant of DMFET changes by binding of PSA Ab and Ag in the nanogap, V_T decreases and I_D increases.

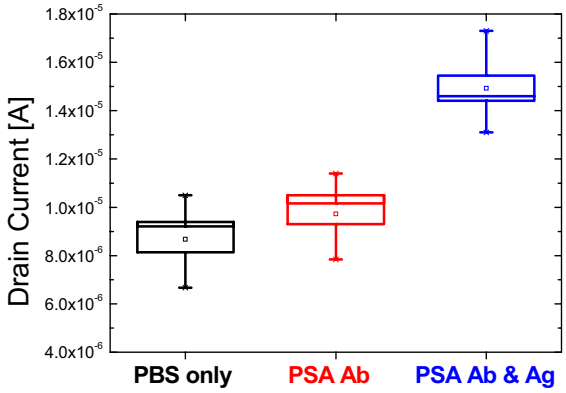

Figure 5. Statistical data of the DMFET array using the current readout platform. Both concentrations of PSA Ab and Ag are 100μg/ml. Time-averaged drain currents are measured for every single DMFET at a gate voltage of 3V.

Acknowledgment

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References

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