Design of a Micro-Electrode Cell for Programmable Lab-on-CMOS Platform

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***Abstract*—This paper presents a programmable lab-on-CMOS (LoCMOS) with micro-electrode cell array. Array structure is suitable for programmable like CMOS VLSIs. In order to improve the utilization, each micro-electrode cell is composed of actuation and sensing circuit. In addition, a CMOS-compatible extended drain MOSFET (EDMOS) is adopted under a 3V supply. This LoCMOS platform is composed of 1,800 microelectrodes with exploiting EDMOS to enable droplet actuations. Through its field programmability, the chip can successfully perform all microfluidic operations, droplet moving/cutting/mixing on a 2-dimenional microelectrode cell array. Implemented in 0.35um standard CMOS process, the LoCMOS platform demonstrates microfluidic functions and droplet detection. Measured results show successfully for actuation and real-time droplet location sensing.**

***Index Terms*—Lab-on-chip, microfluidics, lab on CMOS**

I. Introduction

Over several decades, lab-on-a-chip (LoC) is broadly used in many bio-medical applications, which provides rapid and scalable assays on a single chip. Especially in point-of-care (POC) applications, it is necessary to have more personalized medical treatment and health care with LoCs. Microfluidic biochips are one of the most important categories in LoCs. A digital microfluidics (DMF) system has been developed to perform a set of Electrowetting-on-dielectric (EWOD)-based microfluidic operations for some particular bioassays by fixed-size electrodes arranged in a certain pattern [1], [2]. EWOD refers to physics describing electrical forces from an electric field between a droplet and an electrode [3]. As DMF-based chips find more applications, their complexity is significantly increased according to the trend of multiple and concurrent assays on the chip, as well as more sophisticated control for resource management.

As CMOS technology keeps improving, more and more complicated functions allow to be integrated on a single chip. As a result, several LoCs based on CMOS technology, called lab-on-CMOS (LoCMOS), have been developed. As compared to conventional DMF-based LOC, electrical and electrochemical sensors have been developed and fabricated by CMOS process to replace optical absorbance measurement instrumentation [4], [5]. A dielectro-phoresis (DEP)-based LoCMOS has been proposed to actuate bio-objects with DEP cage [6]. In [6], actuators are implemented by microelectrodes to produce force due to electrical field. However, sensors in the presented works occupy large die area such that the utilization of DMF operation region is limited. In addition, in order to speed up the analyses of bioassays, the force of actuation should be enhanced.

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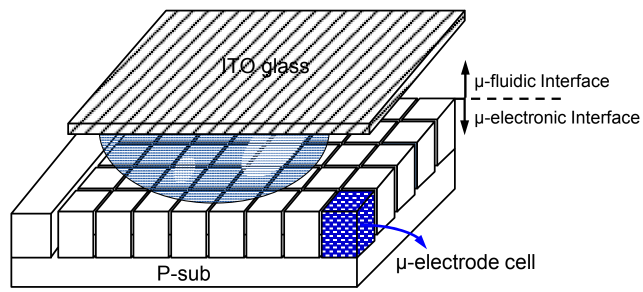

Fig. 1. The physical cross-section of the proposed lab-on-CMOS platform.

In this paper, we develop a programmable LoCMOS platform with microelectrode cells that include both functions of microfluidic droplet actuations and sensing. Fig. 1 illustrates the overview of the system structure of the proposed LoCMOS platform. The top drawing shows the physical structure for microfluidic operations, where a droplet is sandwiched in a bi-planar EWOD structure with hydrophobic layers between microelectrodes and Indium Tin Oxide (ITO) glass. Bonding pads and wires are minimized and placed on left side to increase region of the top plate and DMF utilization. The middle drawing between micro-fluidic and micro-electronic interfaces is droplet location and the microfluidic operation region. In this LoCMOS platform, the microelectrode cell integrates actuation circuit and a part of sensing circuit to improve microfluidic operation region. Besides, the proposed LoCMOS is demonstrated in standard

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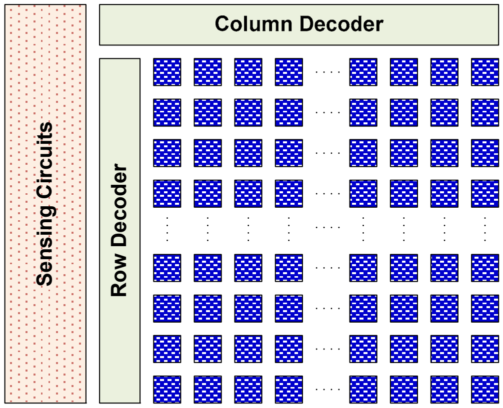

Fig. 2. The proposed programmable LoCMOS array structure.

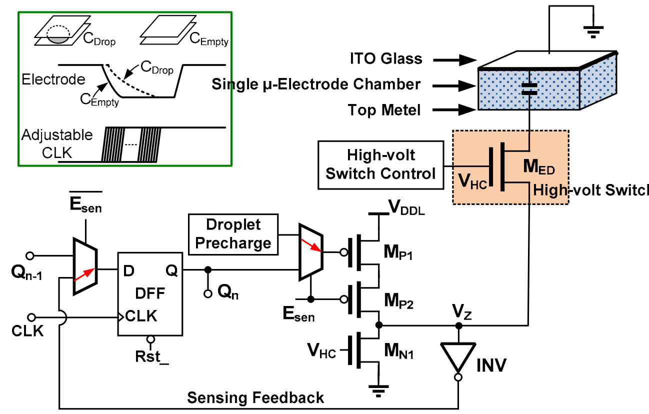

Fig. 3. Circuit diagram of the sensing circuit in the proposed microelectrode cell.

low-voltage CMOS process. In order to significantly increase avalanche breakdown voltage, we exploit the high-voltage switch with the compatible EDMOS.

The rest of the paper is organized as follows. Section II introduces the proposed programmable LoCMOS platform and circuit operations of our microelectrode cell. In addition, design of the compatible EDMOS is presented. Section III presents the simulation and experimental results. Finally, the conclusions are given in Section IV.

II. PROPOSED PROGRAMMABLE LOCMOS PLATFORM AND MICRO-ELECTROED CELL

In Sec. II, we have four subsections. First of all, the proposed programmable LoCMOS array structure is introduced. The array is mainly composed of microelectrode cells. Next, sensing and actuation of the microelectrode cell and design of the compatible EDMOS are presented.

A. *Programmable lab-on-CMOS architecture*

The proposed LoCMOS platform is composed of an array of identical micro-electrode cell served as a microfluidic unit component, sensing circuits and column/row decoders, as shown in Fig. 2. Array-based structure features regular design which fosters a better development path for the systematic top-down design for DMF. Besides, based on the array structure, the LoCMOS can be easily programmed to perform EWOD microfluidic operations, such as droplet creating, moving, cutting, and mixing. In addition, as compared to computer-aided design (CAD) tools, the programmable LoCMOS also likely develop along the advances of future DMF developments.

In comparison with conventional LoCs, the LoCMOS platform achieves various functions without area penalty due to standard CMOS process. According to different design requirements, different array structures can be selected for this 2-D microelectrode array, such as column/row control to have high-speed operations. On the other hand, to have minimum I/O pins and to increase scalability, a daisy-chain control structure is designed.

In recent CMOS VLSIs, marching algorithms and scanned chain are well developed for testability. As a result, array structure of the LoCMOS is very suitable for developing testability. In our design, calibration of each microelectrode cell is developed to test functionality of flip flops and high voltage switch accordingly. Also, test patterns of microfluidic operation can be developed to check aging of hydrophobic layer or height of ITO glass.

B. *Sensing circuit in the micro-electrode cell*

In conventional DMF systems, microscope is used to observe location of the droplet. The proposed microelectrode cell provides a real-time feedback control loop to sense the droplet location and ensure that all droplets are in scheduled routes[7], [8]. Our droplet location map reduces cost and accurately reflects the position of the droplet. Fig. 3 shows the design of the sensing circuit where M_{P1}, M_{P2} and M_{N1} present a driver and M_{ED} is the high-voltage switch. INV shows the sense amplifier to detect signal at node V_Z. The parasitic capacitors with drop/without drop in the microelectrode chamber are defined C_{Drop}/C_{Empty}, respectively. In the location sensing mode, droplet precharge circuit generates a period of pulse to charge the parasitic capacitor between ITO and top metal. Then, M_{N1} is turned on to discharge the parasitic capacitor. Depending on the different capacitance, the INV outputs different edges and delivers to a flip flop. The flip flop senses the output of INV with adjustable clock signal. A digitally adjustable delay-chain is designed for calibration of adjustable sensing clock, which is not included in a microelectrode cell, as shown as sensing circuit in Fig. 2. Finally, a certain code corresponding to the time duration generated by this capacitance change is stored in microelectrode array.

C. *Actuation circuit in the micro-electrode cell*

In our programmable LoCMOS, descriptions of DMF applications are translated into a set of microfluidic operations, which includes managing the types of

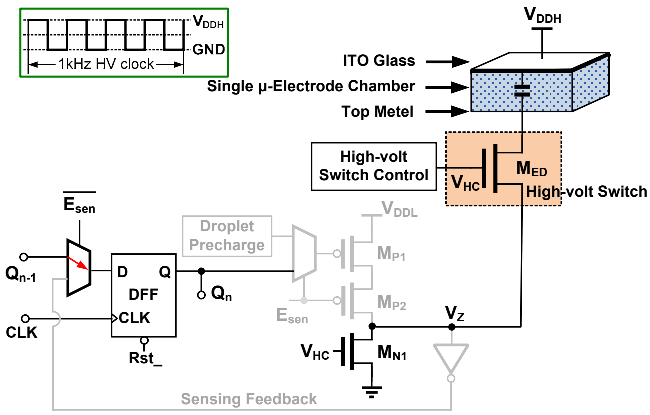

Fig. 4. Circuit diagram of the actuation circuit in the proposed microelectrode cell.

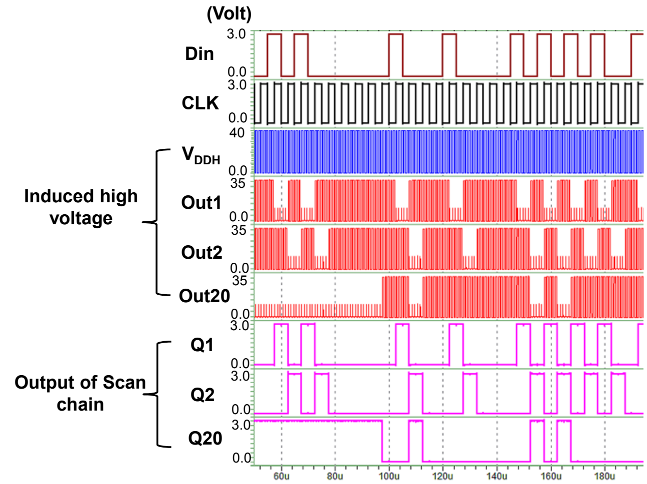

Fig. 6. Simulated waveforms of the proposed LoCMOS.

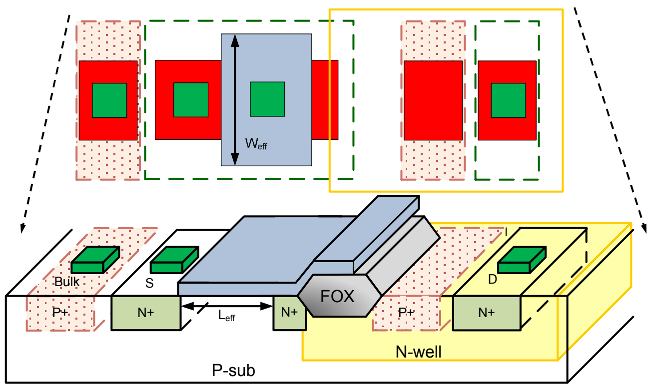

Fig. 5. Physical layout and cross section of the proposed EDMOS.

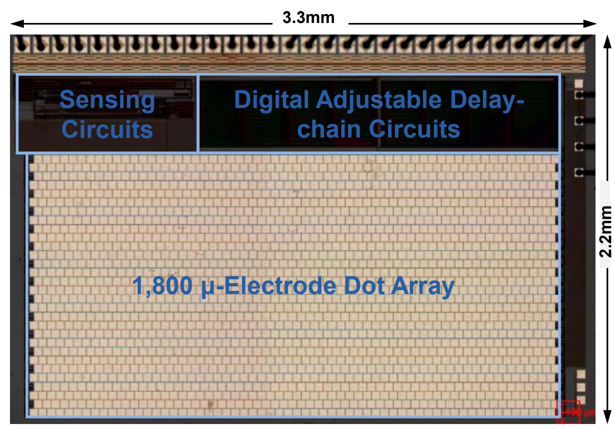

Fig. 7. Die photo the proposed LoCMOS.

microfluidic operations (moving/cutting/mixing) and timing sequences in software expressions. Fig. 4 shows actuation circuit in the micro-electrode cell. In the DMF actuation mode, each control sequence is stored into the D flip-flop (DFF), where Q_n shows the stored value. Then, V_{HC} controls M_{N1} and M_{ED}. Once control signal V_{HC} is low, the high-voltage switch M_{ED} is turned off, the 1 kHz high voltage on the top ITO glass plate is enabled and drivers perform the next actuation cycle. As compared to current LoC design techniques all using high-voltage process, our design uses standard low voltage CMOS process for well scalable and the increasing integration and complexity. In order to achieve high break-down voltage of 25V, a compatible EDMOS is designed as the high-voltage switch, which is present in detail in the next subsection. The actuation cycle is typically greater than 100ms and the control window is designed to be less than 10ms.

D. Design of a compatible high-voltage EDMOS

The programmable LoCMOS is fabricated in standard low-voltage CMOS process. However, the conventional NMOS behaves breakdown when V_{DS} rises to around 12-13V. The force due to 12V electrical field is not good enough to EWOD-based LoCMOS. Therefore, a compatible EDMOS is exploited, which significantly increases avalanche breakdown voltage [9]. As a result, the programmable LoCMOS can then actuate droplets smoothly.

In our design, a compatible EDMOS is developed to improve avalanche breakdown. Physical layout and cross section of the proposed EDMOS is shown in Fig. 5. Several layout techniques are adopted. The P+ field ring technique is adopted to form high resistive path and improve the corresponding drain breakdown voltage. In addition, field oxide (FOX) is also used to create further buffer region for channel and drain. In addition, extended N+ region with N-well increases the resistivity of the turned-on path. Although both of P+ field ring and extended N+ region techniques degrade the capability of driving current, according to the sensing requirement, the ON-current is designed for 60uA. As compared to a conventional MOS, the proposed EDMOS not only keeps its current capability, but also shows higher immunity against breakdown even at V_{DS}=25V and V_G=0V. The characteristics EDMOS are simulated by TCAD 2-D simulator.

III. Discussions and Simulation Results

Fig. 6 shows the simulated transient waveforms where simulator HSPICE is based on BSIM4 model (level =54). The

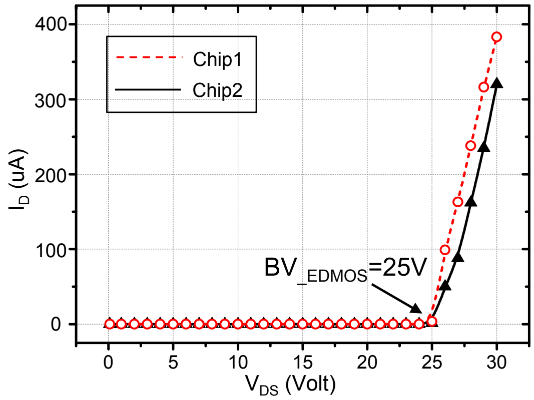

Fig. 8. Measured results of the EDMOS.

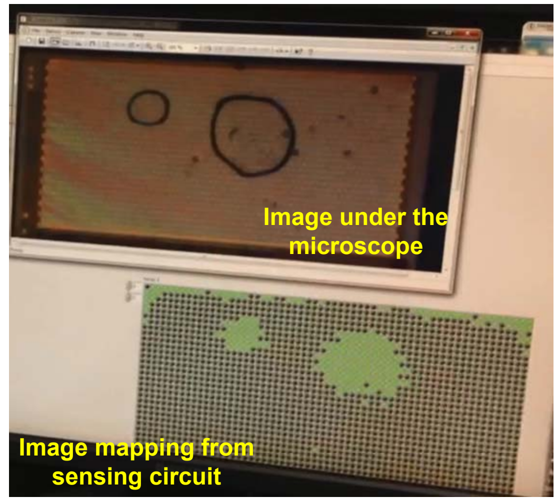

Fig. 9. Demo system of the proposed LoCMOS.

array structure here selects the daisy-chain architecture. The input sequence is scanned into a DFF array. V_{DDH} is set at 40V and we can find out the induced output voltage is around 40V. The degradation is due to the charge sharing of the other parasitic capacitance. Fig. 7 shows the die photo, in which wall brick is used in physical layout for better activation capability. The whole chip is implemented in 0.35um 4-Metal CMOS process, which contains a 60 × 30 microelectrodes (each microelectrode cell size: 50 × 50 um).

Fig. 8 shows the measured results of two EDMOS test chips. Note that the breakdown voltage is around 25V on chip1 and chip2, respectively when the high-voltage square wave is applied on ITO glass. Besides, the turned-on current is around 60uA, which fits the sensing requirement. Finally, microfluidic operations such as moving and cutting can be functioned and are shown in Fig. 9. Accordingly, results of real-time location mapped by sensing circuit are also demonstrated. As shown in the figure, location mapped by a sensing circuit is as the same shape as the image from a micro scope.

IV. CONCLUSIONS

This paper has described a programmable lab-on-CMOS (LoCMOS) with micro-electrode cell array. As compared to CMOS VLSIs, array structure is suitable for programmable and CAD tools. The proposed micro-electrode cell is composed of actuation and sensing circuits so as to improve the utilization. In addition, a CMOS-compatible EDMOS is adopted for low voltage standard process. This programmable LoCMOS is with totally 1,800 microelectrodes with exploited EDMOS to enable droplet actuations Through its field programmability, the chip can successfully perform all microfluidic operations, droplet moving/cutting/mixing on a 2-dimenional microelectrode dot array. Implemented in 0.35um standard CMOS process, the programmable LoCMOS demonstrates microfluidic functions and droplet detection Measured results show that programmable LoCMOS is very suitable for biomedical assays.

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