Extended Abstracts of the 2009 International Conference on Solid State Devices and Materials, Sendai, 2009, pp675-676

Actuation of Magnetic Beads on a CMOS chip for Biological Applications

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1. Introduction

Prevention of pandemic diseases requires a large scale screening. Immuno-assay with magnetic beads is one of candidates of such a screening since it can be done on a chip with relatively simple scheme [1,2].

One of authors had reported Immuno-assay on a standard CMOS chip [3]. However all the steps of an assay were done on a chip wirelessly, it required external magnetic field to manipulate and detect magnetic beads.

The aim of this paper is to provide mean to handle magnetic beads on a chip itself so that we can have an even simpler assay set up.

2. General Instructions

A CMOS chip in a size of 2.5 mm by 2.5 mm was designed and fabricated on a 180 nm standard CMOS process with five metal layers as seen in Fig. 1. It has two sets of sixteen parallel electrodes in the top metal layer and the second to the top for generation of magnetic field. These two are placed in orthogonal to each other. The electrodes has four variations in the size, 3 μm/3 μm, 5 μm/5 μm, 10 μm/10 μm and 25 μm/25 μm in line and space. Simplified construction of the electrodes is shown in Fig. 2. When the chip has a pair of opposite directional currents in each layer, a magnetic field between the pair is similar to which is given by a one-turn coil. The choice of electrodes can change the size and position of the magnetic field. Therefore, it enables to drive magnetic beads arbitrarily. To set

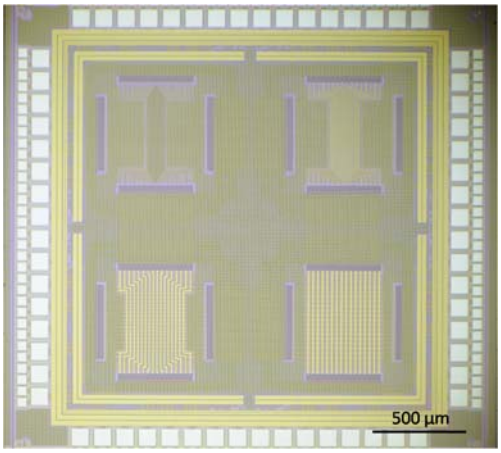

Fig. 1 Micrograph of the fabricated device.

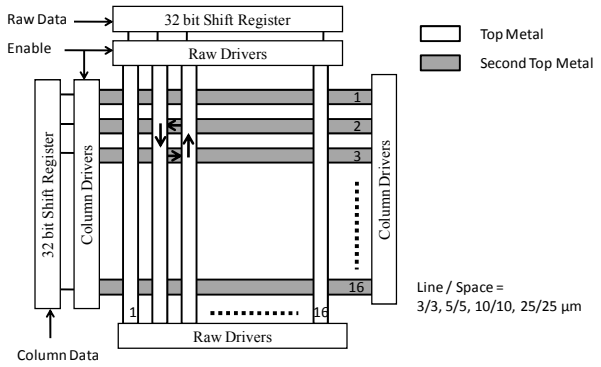

Fig. 2 Simplified structure of the chip.

the direction of the currents on the electrodes, driver circuits are attached to each end of each electrode. And each driver is controlled by 32-bit shift register.

The chip is designated for 1.8 V power supply. Drivers are consisted by large pass transistors, in the size of length / width = 0.18 μm/50 μm and connect the end of electrodes to either VDD or Gnd. The power supply of the pass transistor circuit it separated from the logic circuit to measure the current which goes through the electrodes.

3. Peripheral Circuit

A peripheral circuit with a microcontroller is designed to provide sequential control signals to the chip. A programmable System-on-Chip CY8C29466, by Cypress Semiconductor, set the configuration of currents on a chip through Raw and Column data as shown in Fig. 3. Each time when *Enable* turns to low, System-on-Chip read out

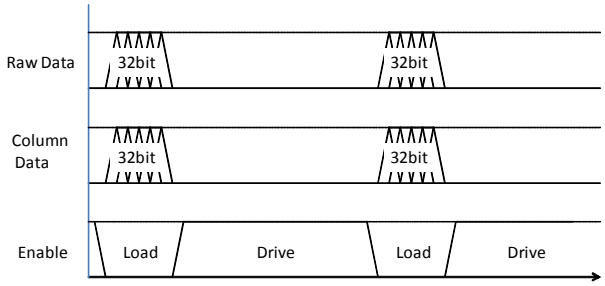

Fig. 3 Data feed from the System-on-Chip.

programmed data and loads it to the chip out.

4. Experimental Results

The chip is wire bonded and covered with epoxy resin except the parallel electrodes area to avoid electrolysis. Magnetic beads those have a diameter of 4.5 μm, Dynabeads M-450 Tosylacitivated, by Invitrogen Dynal AS, was diluted 1 to 1000 by water. The solution contained 4×10^5 beads / ml and 50 μl was applied onto the chip. Suspended beads gradually settled onto the surface of the chip in the time scale of 10's of seconds. The sample was observed with a biological microscope, Nikon FN-1, with a ×60 water immersion objective lens.

Two of 1.8V power supplies are provided separately for both logic circuit and driver circuits. For this time, line and space of 5 μm/5 μm was chosen as the test platform and only electrodes in top layer were activated. System-on-Chip periodically repeated eight patterns of the current configuration. Pairs of opposite directional current are set and shifted in phase as Fig. 4 shows. With this set of pattern, the beads on the chip are expected to move toward right step by step.

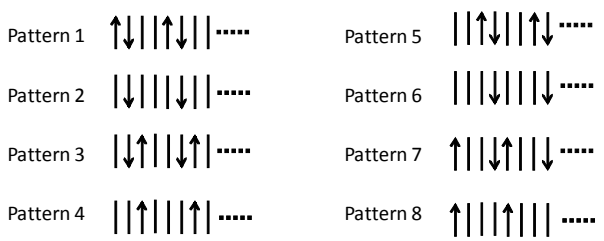

Fig. 4 Periodic repetition of current pattern.

The driver circuit drew 160 mA at 1.8 V while the logic consumed 14 μA.

Magnetic beads are pulled and caught by a magnetic field by the current and moved as the current pattern are shifted as seen in Fig.5. Not all of magnetic beads on the electrodes are actuated. This is supposed because of the surface affinity of the beads.

5. Conclusions

Magnetic beads on a standard CMOS chip were actuated by currents on electrodes on the chip. This will provide on chip beads manipulation which offers simple immuno-assay. Though all the electrodes are activated alternatively, some beads in the electrodes area were remained and weren't actuated. There is a need of increment of actuation current to provide arbitrary manipulation of the beads.

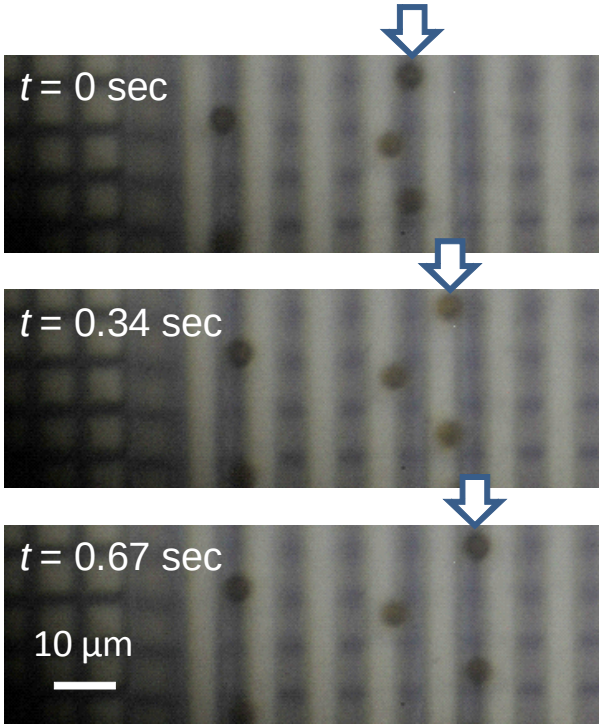

Fig. 5 Manipulation of the beads on the chip.

Acknowledgements

We would like to thanks to supports following.

Part of this work was supported by the Creation of Innovation Centers for Advanced Interdisciplinary Research Areas Program "Interdisciplinary Research on Integration of Semiconductor and Biotechnology", Ministry of Education, Culture, Sports, Science and Technology, Japanese Government.

The chip in this study has been fabricated in the chip fabrication program of VDEC, the University of Tokyo and Rohm Co.

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