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The Development of Oligonucleotide Micro Array Detecting System

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1. Introduction

The theory of gene chip for detecting DNA is based on the hybridization with it's completely strands. Several methods have been develped using fluorescent labing for detection of DNA hybridization. But the optical system is very expensive and fluorescence will be quenched depending on the lifetime. Therefore, to develop an alternative method which can in situ monitor and rapidly detect is very important.

In this study, we describe an electrical method for detecting DNA hybridization on silicon chips. Chips are fabricated by standard photolithography process. A sensing chip is made of an array of interdigital metallic electrode pairs with the electrode spacing of 5 μm. The detection of DNA hybridization is implemented by measuring the capacitance between the two interdigital comb-shaped electrodes. A circuit board is subsequently designed to automatically measure individual capacitance from the array of electrode pairs. The success of this work could lead to the development of multi-purpose sensor to detect different DNA sequences in the future.

2. Experiment

Structure on silica substrate is formed by using standard photolithographic technologies. Fig 1 shows a schematic crosssection of a unit cell. Metal 1 is the row-line connection; metal 2 is the column-line connection, metal 3 is the one of interdigital electrodes for detecting capacitance. A BCB dielectric is inserted between metal 1 and 2 to reduce the overlay capacitance to increase the sensitivity from interdigital electrode capacitance.

Figure 2 shows the final biomolecular structure of hybridized DNA. A brief procedure for sample preparation is described. The chip surface is coated by DETA to form monolayer, which provides the connectivity with the amino-groups to be attached to SMPB. SMPB has an amine group, which can be attached to the 5' end of thiolated capture-DNA. The DNA hybridization processes in this investigation are designed as sandwich type. When a sample containing with a complementary sequence, the oligonucleotide probes will be hybridized with target strand and the extra gold particles are attached to the probes to increase sensitivity.

Fig. 3 shows the circuit for detecting the capacitances of individual sensors in the array chip. Multiplexers selected the array element to be measured. The measurement is performed and controlled automatically by a personal computer.

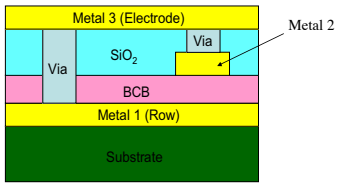


Figure 1 A unit cell of sensing chip structure

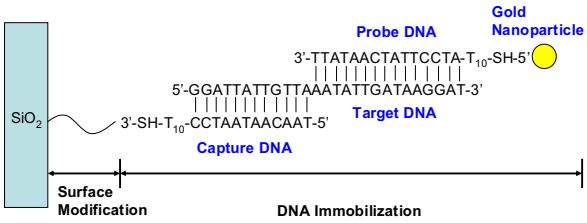
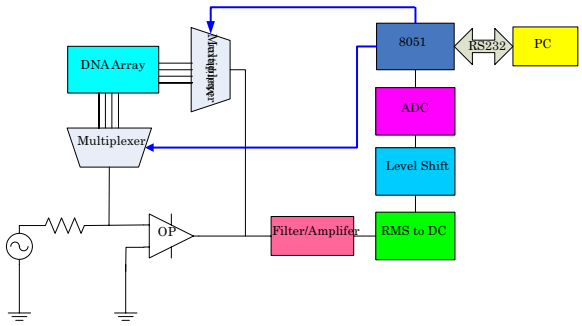


Figure 2 The biomolecular structure of hybridized DNA



strands

Figure 3 Block diagram of the hybridization detection circuit

3. Result and Discussion

Figure 4 shows the top-view photograph of an array of comb-shaped electrodes bonded on a PCB board. Array sensor with 144 electrode sensing units has been designed and tested. Figure 5 compares AFM morphology of surface for DNA hybridization and non-hybridization with deposition of gold nanoparticles. The result shows the different morphology on the chip surface and indicates the hybridization has succeeded and provided a different electric conductivity for capacitance measurement.

The measured capacitances of a 7×7 array is shown in Figure 7 for DNA hybridization and non-hybridization, respectively. In this study, the classification of

hybridization and non-hybridization is determined with a capacitance threshold of 30.1 pF. The hybridization chip demonstrates an average increase in the capacitance of ~ 20% than non-hybridization chip. This electrical measurement using interdigital electrode capacitance indicates an excellent alternative to the optical labeling method, not only integrated with semiconductor process but also reduce the cost.

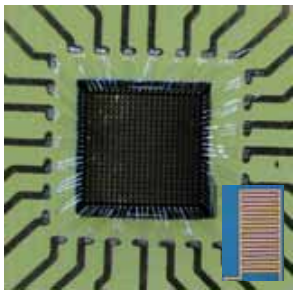


Figure 4 An array of sensing structure bonded on a PCB board. The inset is the interdigital electrodes.

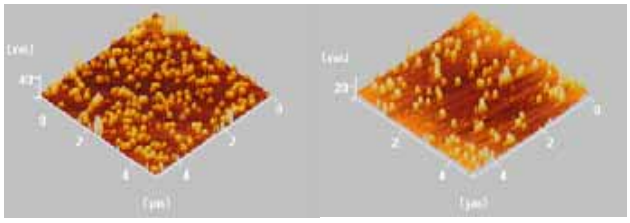


Figure 5 AFM images of the interelectrode area. The left is hybridization surface, and right is non-hybridization surface.

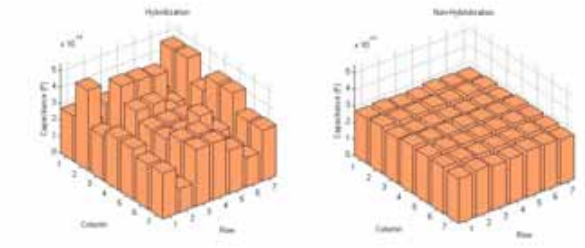


Figure 7 Measured capacitances of interdigital electrodes for hybridization and non-hybridization monitoring.

4. Conclusions

We have developed an array of interdigital electrode for detecting DNA hybridization. The experimental results show that the capacitance difference between the electrode pairs with hybridization and without hybridization could be up to 20 %, which presents a speedy way to detect the DNA hybridization without using optical labeling method. This idea can be further implemented in standard CMOS process with signal processing circuits to be a Si-based bio-chip.

5. References

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