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Integrated Photodiode DNA Identification System for Genetic Chip Applications

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1. Introduction

With the progress of the Human Genome project [1], there is a tremendous demand for efficient instrument for analyzing DNA-encoded information. The difficulties in handling the vast amount of information contained in DNA molecules can be resolved by using microelectronic technologies to convert the biological or chemical responses to an electrical signal and perform analysis in the electrical domain with the well-developed signal processing techniques [2]. This paper describes the methodology to integrate bio-material with conventional silicon based material and their identification process by photodiode based CMOS imaging.

2. Attaching DNA probes onto Silicon Fixture

The DNA detection process involves attaching a known sequence of DNA strend (or probe) corresponding to an ingredient (such as the DNA of a bacteria) onto the silicon based fixture. Afterward, a sample (say the blood of a patient) is applied to the probes and if a match is found, the matched DNA will be attached to the fixture (referred as hybridization). By introducing an optical label to the DNA sample to be detected, the amount of fluorescence emitted by the sample remains on the silicon fixture indicated the quantity of the ingredient to be detected. The result can be captured by a photo-diode arrays and analyzed by signal processing techniques. Such system is shown in Fig. 1. The first step to achieve integration between the bio-material to the silicon fixture.

The detection procedure is illustrated in Fig. 2. It starts with surface cleaning with strong acid which attack most of the metal used in silicon processing. Therefore, conventional photodiode fabrication process has to be modified to incorporate more inert metal such as gold and platinum. In our experiment, gold is used as the contact electrode. After the cleaning, the surface is treated with a solution composed of 1:4:3000 of H_2O_2: MPTS (3-mercaptopropyl trimethoxysilane): 2-propanal for 30minutes at 100°C to form the self-assembly layer. Afterword, DNA probe with known sequence is attached to the MPTS layer (immobilization). Experimental result shows that the DNA probes can only be attached to silicon dioxide but not polysilicon or silicon nitride. As a result, all surface has to be passivated by silicon dioxide to act as a buffer material. The DNA samples with optical labels are then applied to silicon chip and the entire chip is incubated in a custom-made hybridization chamber in a water bath at 55°C for 2 hours.

The DNA attachment is studied by Atomic Force Microscopy (AFM) after each step and result is shown in Fig. 3, indicating the successful incorporation of MPTS layer, DNA probes and the hybridization of DNA material onto the silicon chip.

3. Detection with photodiode

However, the observation requires optical filters which are difficult to be integrated in a CMOS process and also the filter material is not compatible with the bio material. As a result, a silicon photodiode was used as a natural optical filter to amplify the emitted signal from the optical label without the need of using color filters as in most of the currently available CCD detection system. The spectral response of the photodiode is calibrated and shown in Fig. 4. A sharp transition is observed at a wavelength around 380nm. The absorption and emission spectrum of the optical label used (Texred) is shown in Fig. 5. To achieve a maximum difference in the measured current from the photodiode, a laser that provides radiation at a wavelength of 325nm is used. The excitation spectrum is not located at the wavelength for maximum absorption of optical label. However, it utilizes the natural filter of the photodiode to effectively filter off the background signal, and thus, the necessity of adding an optical filter is removed. The measured photodiode current from the photodiode is shown in Fig. 6, indicates that matched and unmatched DNA sample has been successfully detected.

4. Conclusion

A CMOS photodiode system form DNA identification has been demonstrated. In order to incorporate the DNA material onto the silicon based material, minor modification to the photodiode fabrication process to incorporate inert metals is necessary. Nevertheless, the microelectronic-based identification provides a revolutionary approach for DNA identification.

Acknowledgments:

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Reference:

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[2] L. Kricka, et. al., Journal of IFCC, vol. 6, no. 2, p. 59, 1994

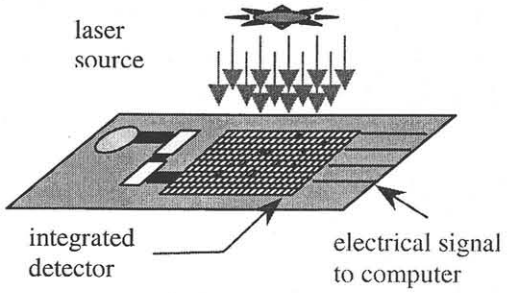

Fig.1. Illustration of a photodiode array based DNA identification system

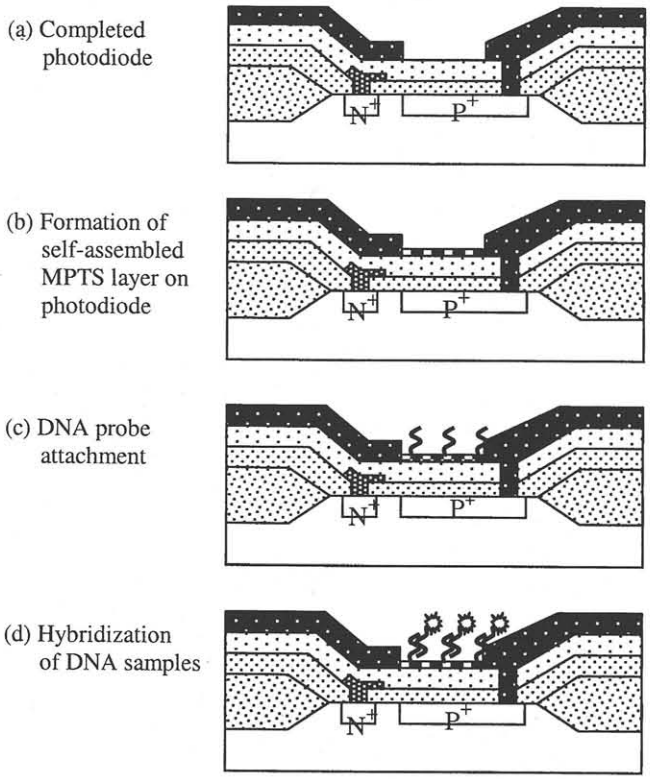

Fig.2. Sequence of DNA identification process after photodiode fabrication.

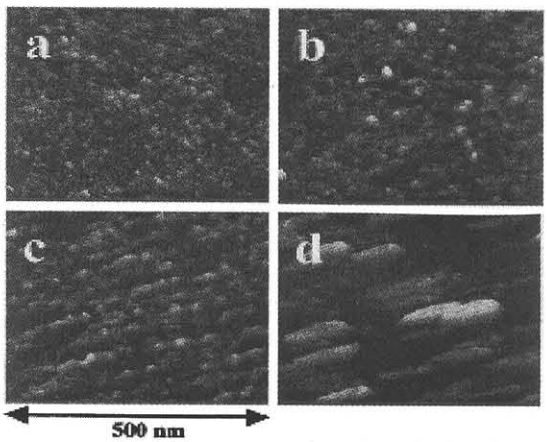

Fig.3. AFM measured SiO_2 surface after (a) cleaning; (b) formation of MPTS layer, (c) DNA probe attachment and (d) DNA sample applications

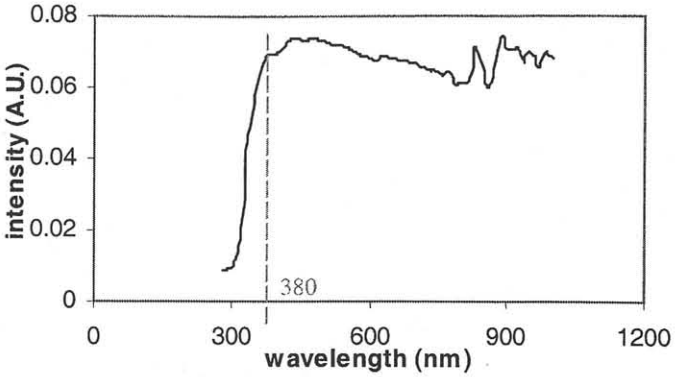

Fig.4. Spectral response of photodiode

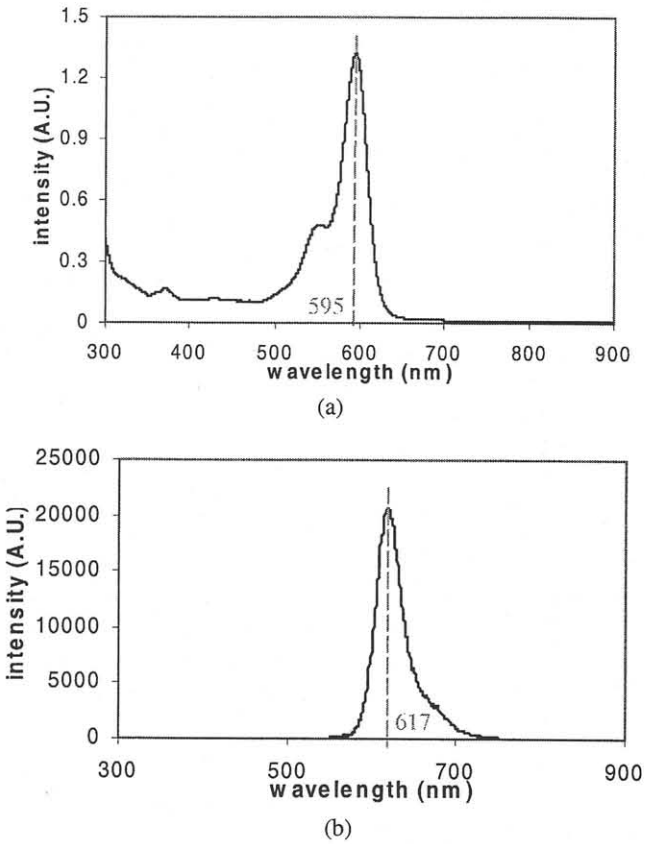

Fig.5. (a) absorption and (b) emission spectrum of the optical label used

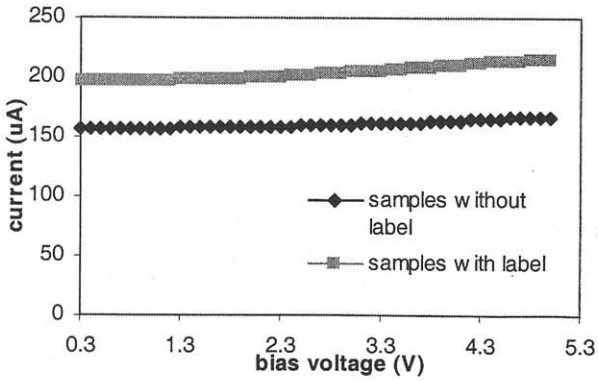

Fig.6. Measured photo current difference for the different samples with and without fluorescence signal