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A CMOS Image Sensor Having Stacked Photodiodes for Lensless Observation System of Digital Enzyme-linked Immunosorbent Assay (ELISA)

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Abstract

A CMOS image sensor having stacked photodiodes was fabricated using 0.18 µm mixed signal CMOS process. The stacked photodiodes consist of N+ / P-well / Deep-NW / P-sub. P-well and P-sub are shorted to ground. By monitoring the voltage of N+ and Deep-NW individually, we can observe two monoclonal colors simultaneously without any color filters. Therefore the sensor is suitable for fluorescent imaging especially contact imaging such as lensless observation system of digital enzyme-linked immunosorbent assay (ELISA).

1. Introduction

Enzyme-linked immunosorbent assay (ELISA) is a diagnosis method used for early stage detection of cancers and other diseases. Recently, digital ELISA was proposed to achieve higher sensitivity [1-5]. In a conventional digital ELISA system, a fluorescence microscope system is used for observing fluorescence from micro-reaction chambers. In order to distribute the diagnosis system widely in clinical practice, we have proposed a compact observation system (Fig. 1) which consists of a CMOS image sensor, an interference filter and a femto-liter size reaction chamber array [6].

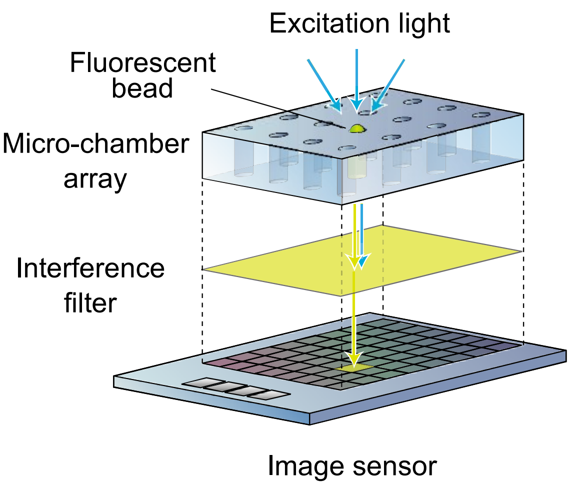

Fig. 1 Schematic diagram of lensless digital ELISA system.

However, high intensity of leaked excitation light is a problem. We should pick up small fluorescence signal out of the leaked excitation light. If the CMOS image sensor recognizes color, we can improve the specificity of digital ELISA. Stacked photodiodes are suitable way of color detection for this application because they have no color filters and color information is gathered in one position unlike the Bayer color filter sensors [7,8].

In this work, we have designed and fabricated a CMOS image sensor having stacked photodiodes and measured the sensitivity of the stacked photodiodes using LEDs as light sources. The wavelengths of LEDs are 470nm and 525nm which imitate excitation and emission light respectively.

2. Design and fabrication

We used 0.18 µm CMOS process for mixed signal applications. The process has deep N type well which isolates P type well from silicon substrate. We have designed pixel having stacked photodiodes by using the deep N type well. The cross-sectional structure and the layout are shown in Fig. 2. In digital ELISA, distinction between excitation and emission light is essential but full color imaging is not necessary. Thus we use only two stacked photodiodes (PD1

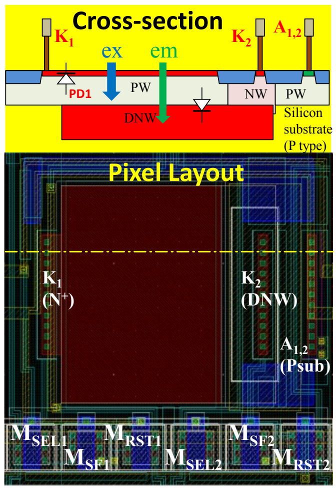

Fig. 2 Cross-section and the layout of a pixel of the CMOS image sensor having stacked photodiodes.

and PD2), so that the number of transistors in the pixels are reduced compared to the full-color sensors [7]. The less number of transistors helps to enlarge the fill factor of the photodiodes and to improve the sensitivity. The both photodiodes are monitored from N-type cathode while the both anodes are shorted to ground. In addition, the sensor in this work needs no bias modulation unlike the filter-less fluorescence detection sensor using photogate structure [9]. Therefore read-out circuit can be simplified. The circuit diagram of the pixel is shown in Fig. 3.

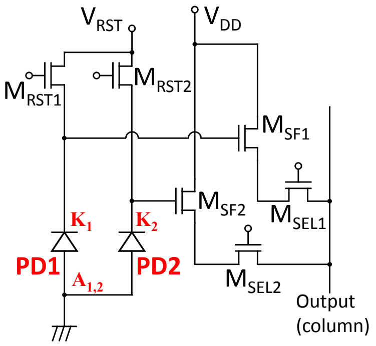

Fig. 3 Circuit diagram of the pixel.

3. Measurement results

LEDs were used as light sources for simulating fluorescence observation. Sensitivities of PD1 and PD2 were measured under 470nm and 525nm LED lights through ground glass diffuser so that uniform and stable illumination onto the image sensor was achieved. The measurement results are shown in Fig. 4 (470nm) and Fig. 5 (525nm).

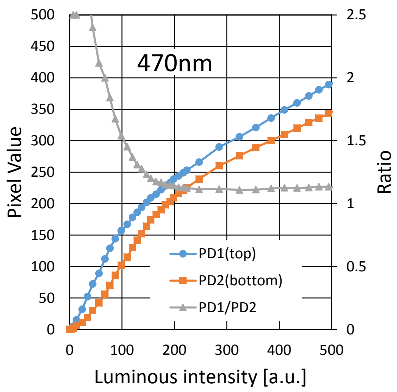

Fig. 4 Sensitivity of PD1 and PD2 and the ratio (@470nm).

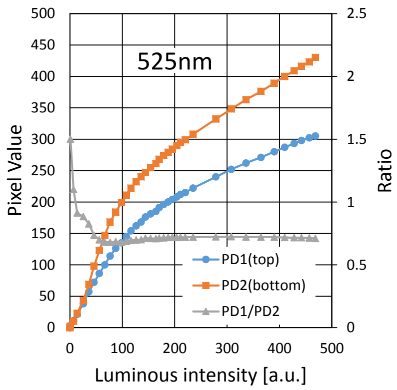

Fig. 5 Sensitivity of PD1 and PD2 and the ratio (@525nm).

The sensitivity of PD1 is higher than PD2 under 470nm illumination. On the other hand the sensitivity of PD1 is lower than PD2 in the case of 525nm. For both cases, the ratio of PD1 and PD2 sensitivities stay constant under relativity high light intensity. From the results, it is possible to detect the ratio of excitation and emission lights during fluorescence observation in digital ELISA.

The specification of the CMOS image sensor is summarized in Table I.

Table I Specifications of the CMOS image sensor

Technology		0.18-µm mixed signal CMOS process
Supply voltage		1.8V (Digital) / 3.3 V (Analog)
Pixel	Type	3-transistor active pixel sensor
	Size	15 µm × 15 µm
Photodiode type		Stacked photodiodes PD1 (top): N^+-Pwell PD2 (bottom): Pwell-Deep Nwell

4. Conclusions

We have designed and fabricated a CMOS image sensor having stacked photodiodes and measured the characteristics of the stacked photodiodes. The stacked photodiodes can distinguish excitation and emission lights during fluorescent reaction. This image sensor can improve the specificity of digital ELISA.

Acknowledgements

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