32 × 32 pH IMAGE SENSORS FOR REAL TIME OBSERVATION OF BIOCHEMICAL PHENOMENA

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Abstract: 32 × 32 pH image sensors were successfully fabricated by using the CCD/CMOS image sensor technique, and real time imaging of a chemical reaction and pH distribution was carried out for the first time. The pH variations by a chemical reaction are observed by 200 ms step (i.e. 5 flames per sec). The pH image sensor was able to take a pH image of mouse stomach successfully. It means that the novel image sensor can be applied to a biomedical and biochemical field.

Keywords: pH, two-dimensional imaging, image sensor

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1. INTRODUCTION

Conventionally, pH is measured on the supposition that a solution is a uniform concentration. The conventional solid-state-type pH sensor is ion-sensitive field-effect transistor (ISFET) [1]. If the distribution of biochemical phenomena can be obtained as a visible image in real time, the local variations in these will lead to a better understanding. The technique of this pH sensor is based on the principle of a charge-coupled-device (CCD) [2]. Recently, pH-ISFET array based on standard CMOS process was reported [3], but the pH-ISFET array sensor has not taken a pH image. Previously, we proposed and presented 10 × 10 arrayed pH imaging sensor [4]. However, it is not integrated scanning circuits and could not observe a pH distribution shape.

2. EXPERIMENTS AND RESULTS

The cross section and the operation mechanism of the charge-transfer-type pH sensor are shown in Fig. 1. The charge-transfer-type pH sensor consists of seven elements: an input diode (ID), an input control gate (ICG), an ion-sensing region, a transfer gate (TG), a floating diffusion (FD) region, a reset switch and a source follower circuit. The structure of the pH-sensing region is similar to that of an ISFET.

The pH image sensors were fabricated by the CCD/CMOS technology. The pH image sensor chip composed a 32 × 32 pixel arrays and the pH image sensor chip with waterproofed package is shown in Fig. 2(a), (b). The chip size is 8.0 mm × 7.4 mm. The size of a pixel is 130 μm square, and the sensing region is about 40 μm square.

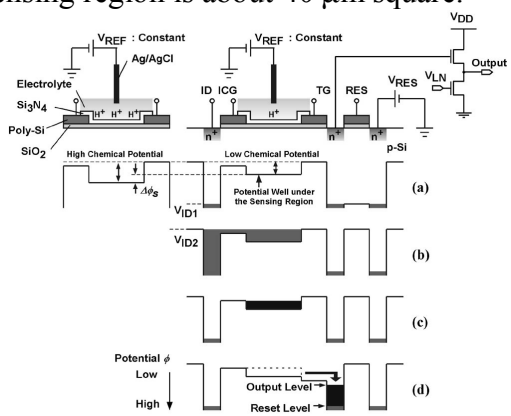
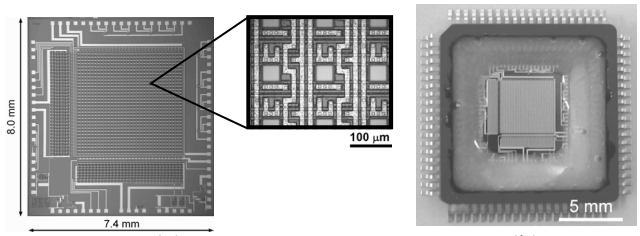


Fig. 1. The principle of conversion from pH to charge. (a) The clock cycle is initiated. The floating diffusion is reset. (b) The input diode is briefly pulsed from V_{ID1} to V_{ID2}. (c) The input diode is kept again V_{ID1}. (d) The transfer gate is turned on and the charge in the sensing region is transferred to the floating diffusion region.

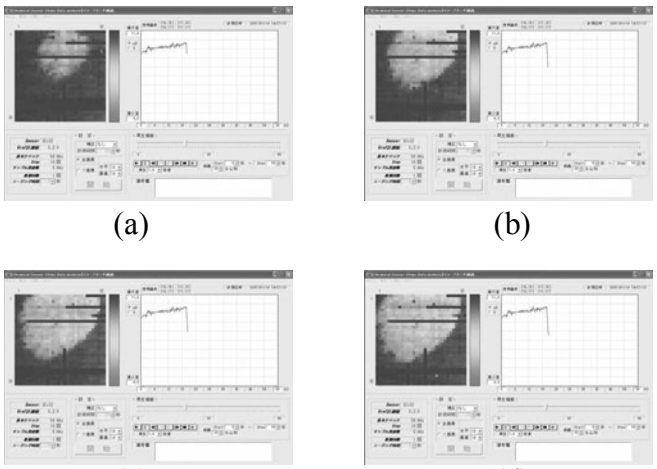
In Fig. 3, an imaging result of pH distribution variation is shown. The images were taken by 200 ms step (i.e. 5 flames per sec). At first, pH 9.2

buffer solution (70 µl) was filled on a pH image sensor, and pH 6.9 buffer solution (70 µl) was dropped in upper side of the chip. The pH distribution spread with time. It is shown that solution of pH 6.9 is diffused about 500 µm during 200 ms in this condition.



(a) (b)

Fig. 2. Photograph of the 32 × 32 pH image sensor chip. (a) pH image sensor chip. (b) Packaged pH image sensor chip.



(a) (b)

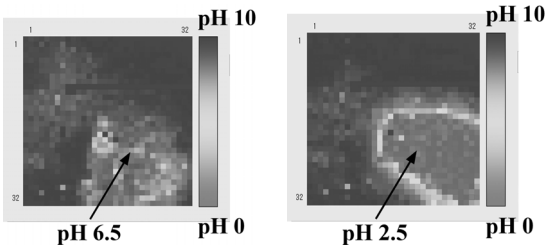
(c) (d)

Fig. 3. The images of variation of 2-D pH of solution with time. ((a-d) 200 ms step)

We took pH images of steamed rice and "SUSHI" rice as shown in Fig. 4 (a), (b). Rice was dropped in a buffer solution with pH 9.2. It is confirmed a shape of rice by pH in formations. The pH image from steamed rice shows pH 6.5. "SUSHI" rice shows about pH 2.5, because vinegar is contained in "SUSHI" rice.

Finally, we tried to observe a living related material. A stomach of mouse was set on the pH image sensor chip with PBS (Phosphate-Buffered Saline) solution (pH 7.4) as shown in Fig. 5. The place of the stomach is clearly confirmed and the pH of stomach indicates acid (about pH 5.5).

From these results, the novel image sensor can be applied to a biomedical and biochemical field.



(a) (b)

Fig. 4. The images of 2-D distribution of pH. (a) Steamed rice. (b)" SUSHI" rice.

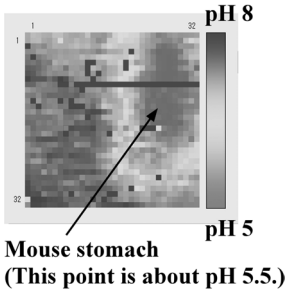


Fig. 5. pH image of mouse stomach.

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