A Miniature Imaging Device Using a Self-Reset Image Sensor for Hemodynamic Imaging

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Abstract—In this study, we developed a miniature imaging device with high effective signal-to-noise ratio, which can measure a weak signal with a relatively high offset such as the intensity signal of transmitted light as a result of blood flow change. In the image sensor pixel, a self-reset circuit is implemented in order to avoid pixel saturation. The effective SNR is higher than photon shot noise limit of a normal image sensor pixel architecture. We performed a blood flow imaging experiment by using the fabricated device and demonstrated a function of hemodynamic imaging.

I. Introduction

Hemoglobin concentration of blood flow is one of the important signals to observe brain activity [1-3]. It can be detected optically, but its variation is so weak that relatively high intensity illumination is required to obtain clear image. In that case, the photon shot noise is dominant. Thus, an image sensor with high full-well capacity is required. It is easy to achieve such a high full-well capacity by increasing pixel area. However, it is not suitable for implantable imaging devices to observe mouse a brain under freely moving conditions [4-6].

In our previous works, we proposed to use an implantable self-reset CMOS image sensor to obtain high effective SNR under such a high intensity illumination condition [7-9]. The concept of implantable image sensor is shown in Fig. 1. The sensor is very small and directly implanted in a living body. The sensor device does not have any lens. Thus, its pixel should be as small as observation targets such as blood vessel or neural cells. Our proposed self-reset sensor achieves effectively high full-well capacity by avoiding pixel saturation using an in-pixel comparator to self-reset. Thus, we have realized the effective signal-to-noise ratio over 60 dB that is required for hemodynamic imaging.

However, the noise level after self-resetting was approximately 3-dB higher in comparison with the photon shot noise limitation. This is because the sensor was mounted on a flexible printed circuit board and any other parts were on it. However, the self-reset should be finished in short time (< a few tens of nsec). In this study, we designed and fabricated a miniature device using a self-reset sensor that can be mounted on the head of an adult mouse. In order to realize stable operation and noise reduction, external EMI filters are equipped on the device.

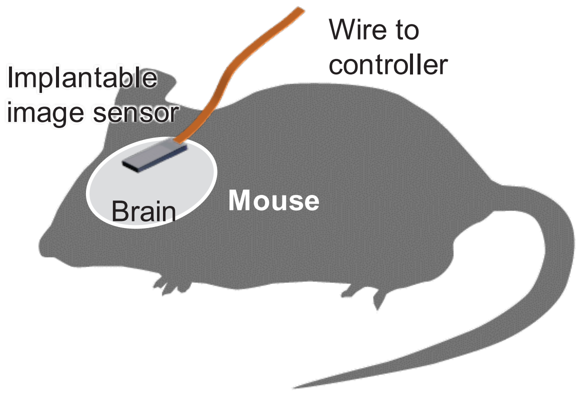

Fig.1. Concept of implantable image sensor for mouse brain imaging.

II. Self-Reset Image Sensor

A self-reset image sensor pixel has a comparator and resets itself when the number of accumulated charges exceeds the threshold. Thus, pixel saturation reset can be avoided. Ideally, the noise increase by self-resetting is similar to that by external pixel reset. The total noise of self-reset pixel is approximately described as:

$$\sigma_{SELFRST} \cong \sqrt{(\sigma_{SN}^2/FWC+1)\sigma_{RST}^2+\sigma_{SN}^2} \cong \sigma_{SN}\sqrt{\sigma_{RST}^2/FWC+1}\,, \quad (1)$$

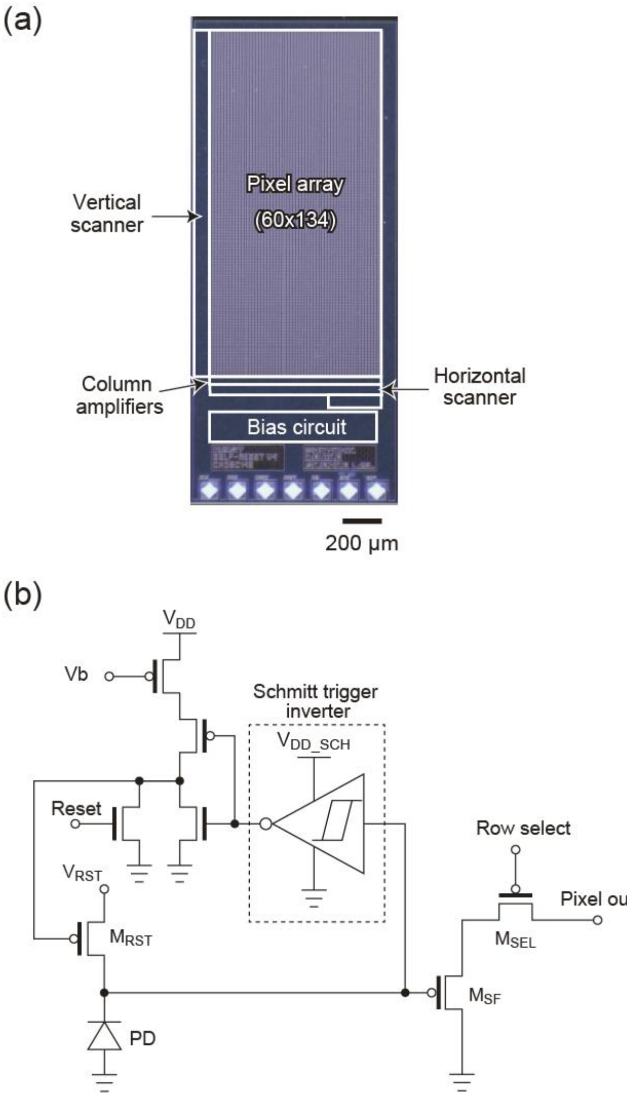

Fig.2. (a) Micrograph of the self-reset image sensor. (b) Schematic of pixel circuit.

TABLE I. SPECIFICATION OF THE SELF-RESET IMAGE SENSOR

Process	AMS 0.35-μm 2-poly 4-metal standard CMOS
Chip size	1.1 × 3.0 mm
Pixel number	60 × 120
Pixel type	3-Tr active pixel sensor with self-reset circuit
Self-reset circuit	4-Tr Schmitt trigger inverter
Pixel size	15 μm × 15 μm
Photodiode	n-well / p-sub
Number of transistors / pixel	11
Fill factor	29%

where FWC is the full-well capacity of the pixel, σ_{SN} and σ_{RST} are the shot noise and the reset noise, respectively. This suggests that the additional noise from self-resetting is not considerable if the reset noise is much smaller than the full-well capacity.

Figure 2(a) shows the micrograph of the self-reset image sensor used in this work. Table I is the specification of the sensor. It is fabricated by using AMS 0.35-μm 2-poly 4-metal standard CMOS process. The pixel size is 15 μm × 15 μm. The fill factor is 29%. The pixel has no counter for the self-resetting number because our purpose is to observe intensity changes with high effective signal-to-noise ratio. The size of the self-resetting circuit is smaller than other self-reset pixels reported before [10, 11]. In addition, if it is allowed to obtain frames with different exposure times, high dynamic image can be reconstructed [12].

Figure 2(b) shows the schematic diagram of the pixel. The pixel is based on a normal 3-Tr active pixel sensor architecture [13]. To implement a self-reset function, a 4-Tr Schmitt trigger inverter is used as a comparator. It does not require any reference voltages. Thus, a simple and small pixel circuit is realized. One of the disadvantages is variation of self-resetting threshold between pixels. However, it is not a significant issue because our purpose is to observe the signal difference between frames. The Schmitt trigger inverter is driven by low voltage (1.4-2.0V) to reduce its through current. The output is boosted and used as a self-reset signal.

III. MINIATURE SELF-RESET IMAGING DEVICE

We fabricated a miniature self-reset imaging device for hemodynamic imaging of a mouse brain surface. In our

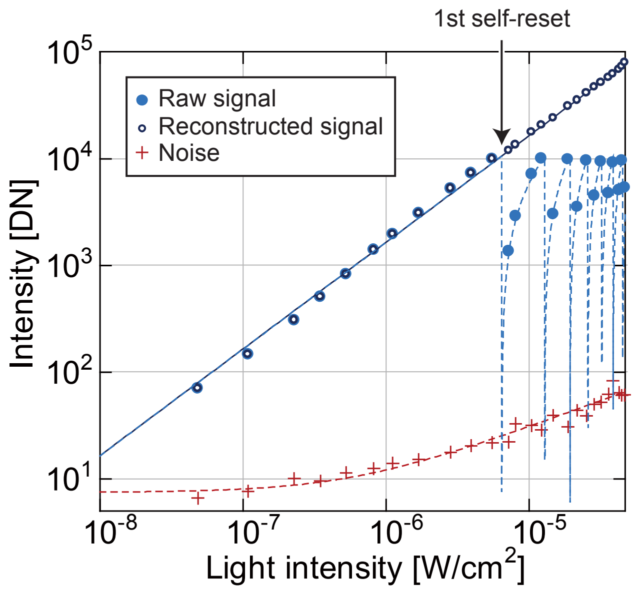

Fig. 3. Signal and noise intensities of the self-reset pixel as functions of light intensity.

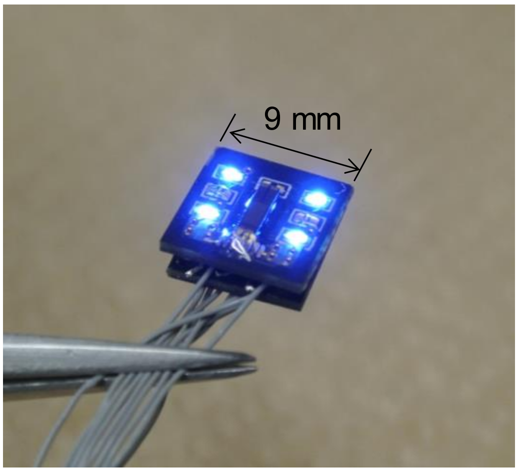

Fig. 4. Photograph of the miniature imaging device using a self-reset sensor

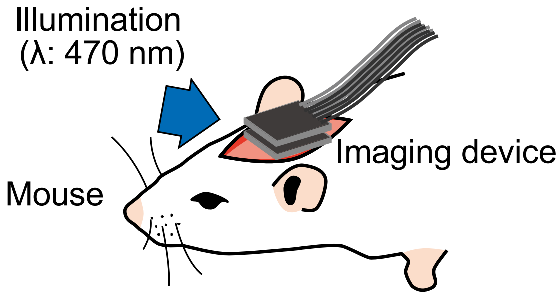

Fig. 5. Experimental setup of blood flow imaging on a mouse brain surface.

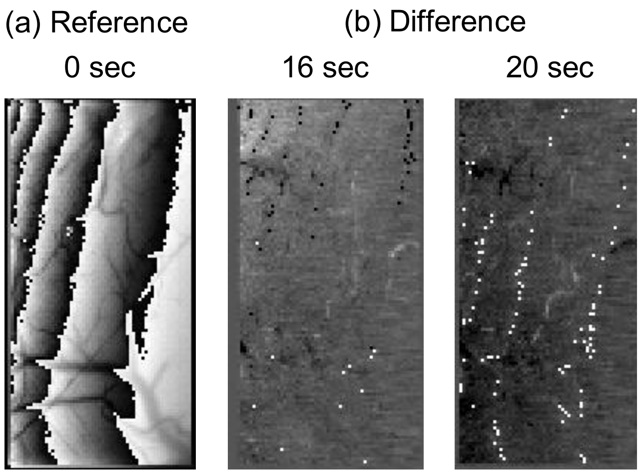

Fig. 6. Imaging results of mouse brain surface. (a) normal reference image. (b) difference images at 16 and 20 sec from 0 sec.

previous works, we mounted a small image sensor on a flexible substrate to make the device as small as possible. On the other hand, the present device is mounted on a rigid printed circuit board (PCB) with external parts in order to realize high stability and low noise characteristics. Figure 3 shows the photograph of the fabricated device. To reduce unwanted reflection and fluorescence from the PCB, matt matte black solder resist is used. EMI filters (Murata, MFM18PS) are used on the lines of the constant voltage such as VDD, V_{RST}, V_b in order to reduce instantaneous fluctuations of the voltages by self-resetting.

Figure 4 shows the signal and noise characteristics of the pixel. The wavelength of the irradiated light was 470 nm. The frame rate was set to 47 fps. The lines are fitted curves for the signal and noise. In our previous work [8], a gap of noise curve was apparently observed at the first self-resetting. In this result, the gap was reduced. From the ratio of the reconstructed signal and the noise, it can be estimated that the effective signal-to-noise ratio of the fabricated device is over 60 dB at maximum.

IV. Hemodynamic Imaging Demonstration

We demonstrated an experiment of blood flow imaging on the surface of a mouse brain by using the fabricated device. All the animal procedures were conducted in accordance with the animal care and experimentation guidelines of the Nara Institute of Science and Technology. Figure 5 shows the experiment setup. The sensor device has any lens optics. Thus, the device was contacted to the brain surface. In this experiment, an external blue LED light source (Thorlabs, M470L3) was used to make illumination intensity gradation. Figures 6 show the imaging results. The frame rate was set to 69 fps. The light irradiates from the left side. By self-resetting, the pixels do not saturate and a folded pattern is observed (Fig. 6a). In the difference images (Fig. 6b), flows of red blood cell can be observed as intensity changes. The noise intensity difference around the boundary of the self-reset number is small. It suggests that the stability of reset voltage is improved from our previous work [10]. On the boundaries of the self-reset number, some black or white spots are observed. However, it can be corrected because intensity change of hemodynamic image is much smaller than the difference between the black and white level.

V. Conclusions

We fabricated a miniature imaging device based on a self-reset image sensor and demonstrated hemodynamic imaging of mouse brain. By using external EMI filters, noise increase by self-resetting was reduced. The maximum effective SNR at the frame rate of 47 fps was over 60 dB. The hemodynamic imaging results also show that the noise increase by self-resetting is small and clear blood flow images were obtained.

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