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Light Guide Array Structure for Spatial Resolution Improvement of Implantable Image Sensor

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1. Introduction

Imaging of neural activities in a brain is one of the important methods to elucidate brain functions. Recently, brain activities have been observed vigorously by functional magnetic imaging (fMRI) and positron emission tomography (PET) [1, 2]. Optical imaging methods are also important because of their high spatial or temporal resolution. It is expected that optical imaging in a deep brain with high spatial resolution would be a powerful tool for observing neural activities. In order to realize it, we have proposed and developed implantable devices based on complementary-metal-oxide-semiconductor (CMOS) image sensors for *in-vivo* imaging. As an example, we implanted the device in a mouse brain and observed fluorescence in a stained hippocampus [3]. In our previous experiments, the spatial resolutions were lower than those expected from the pixel sizes although fluorescent images were successfully obtained. This is because it is difficult to implement a lens in such implantable devices due to limitation of dimensions and low index difference between optical glasses and cerebrospinal fluid.

In this paper, we propose a light guide array (LGA) plate for improving the spatial resolution of implantable imaging device. A Si plate with hole array is prepared and embedded on an image sensor as a LGA plate. Improvement of spatial resolution is demonstrated.

2. Light Guide Array Plate

Concept

Figure 1 shows the structure of LGA plate, which is a Si plate with through-holes. Light emission from fluorescent samples and sensitivity of image sensor are almost omnidirectional, so that the spatial resolution decreases significantly as the spacing between a fluorescent sample and the sensor increases. Through the LGA plate, only vertically incident light is transmitted and the other is filtered out. Therefore, each pixel of the image sensor receive only fluorescence above it. It results in suppression of the resolution reduction by spacing.

In order to reduce invasiveness, the dimensions of implantable device for *in-vivo* imaging should be as small as possible. The planar dimension of the proposed LGA structure is almost the same as that of the pixel array of the image sensor. The thickness of the LGA plate is a few hundreds of microns when the spacing between the device and the observed area is sub-millimeters.

Fabrication

Figure 2(a) is a photograph of LGA plate by a scanning electron microscopy (SEM). The LGA plate is made of Si. Circular through-holes with a diameter of 12.5μm are fabricated by using deep reactive ion etching (D-RIE) process. The thickness of the Si substrate is 60 μm and the aspect ratio of the holes is approximately 5. The holes are aligned in a lattice grid and the period is 15 μm, which corresponds to twice of the pixel size of image sensor combined with the LGA plate. A magnified SEM photograph of the through-hole is shown in Fig. 2(b). It should be note that there are sidewall scallops. It is expected that this structure is effective to reduce the angled incident light received by the image sensor.

The fabricated LGA plate was embedded onto an image sensor, which is based on a 3-transistor active pixel sensor and fabricated using a standard 0.35-μm 2-poly 4-metal standard CMOS process. The pixel size is 7.5 μm × 7.5 μm

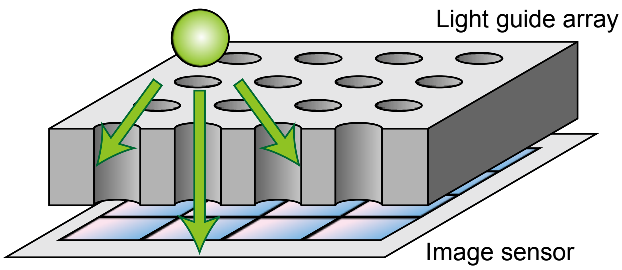

Fig. 1 Concept of light guide array structure..

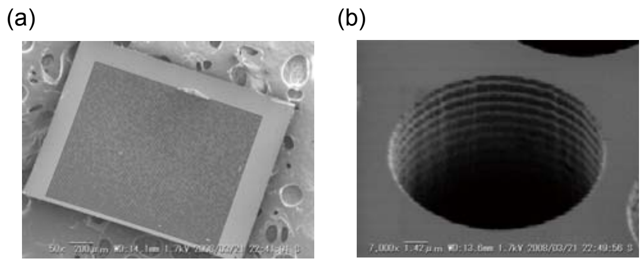

Fig. 2 SEM photograph of (a) a LGA plate, and (b) a hole in the plate.

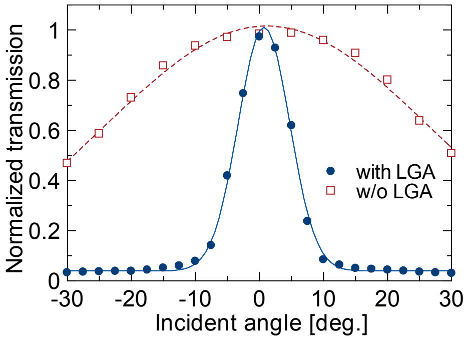

Fig. 3 Normalized transmission of output signal from the image sensor as a function incident angle.

and the number of pixel is 176 × 144. The LGA array was aligned to the pixel array as illuminating light from a halogen lamp and observing the acquired image by the image sensor. At the optimum position, the LGA array was glued to the image sensor by a UV curing resin.

3. Imaging Results

Transmission Dependence on Incident Angle

By embedding the LGA plate, the incident angle of light detected by the image sensor is restricted. Collimated light is launched into the image sensor and the detected signal as a function of incident angle was measured. The light source is a halogen lamp. With the LGA plate, the full width at half maximum (FWHM) of transmission peak is reduced drastically. This indicates that the incident angle is successfully restricted by the LGA plate.

The FWHM for the image sensor with the LGA plate is 9.5 deg, which corresponds to resolution of 15 μm with the spacing between the device and the observed area of approximately 180 μm. Without the LGA plate, the FWHM is approximately 60 deg. The spatial resolution of 15μm is obtained only up to the spacing of 26 μm.

Observation of Fluorescent Beads in the Water

In order to demonstrate improvement of spatial resolution by the LGA plate, we performed imaging of fluorescent beads (Fluoresbrite® YG Microspheres, Polysciences, Inc.) in the water. Figure 4(a) shows a schematic of experimental setup. The image sensor and a blue light emitting diode as an excitation light source were located on a polyimide substrate. In order to filter out the excitation light, a green filter layer with a thickness of 2μm is applied onto the image sensor. The device is waterproofed with a 100 μm- thick epoxy resin layer

Figures 4(b) shows the images of fluorescent beads by the devices with and without the LGA plate. The diameter of fluorescent bead is 42μm. The beads were spread on the device. The potential spatial resolution of the image sensor is sufficiently high because the pixel size is 7.5 μm × 7.5 μm. The image without the LGA plate indicates that the spatial resolution is reduced due to the epoxy resin layer. On the other hand, in the image with the LGA plate, the diameter of the fluorescent bead is approximately 4 holes of the LGA. These results shows that the spatial resolution is

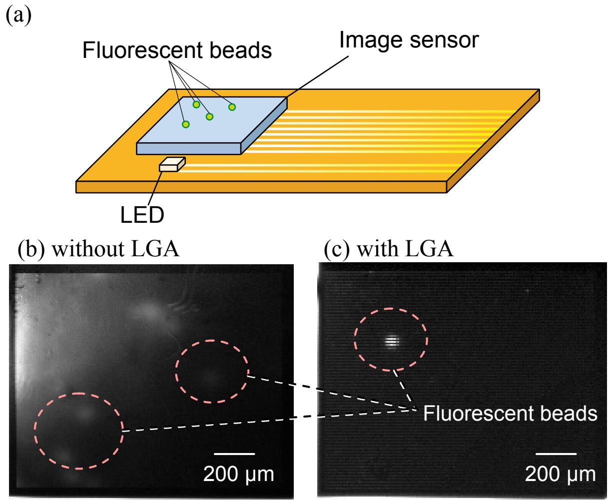

Fig. 4 (a) Experimental setup for imaging of fluorescent beads. The images obtained by the image sensor (b) without and (c) with the LGA plate.

improved by the LGA plate.

In addition, the image contrast is also improved with the LGA array. This is because the excitation light detected by the image sensor without the LGA plate is not negligible although the LED is located at the side of the sensor and the device has the green filter layer. The LGA plate eliminates the angled incident light, so that the intensity of excitation light detected by the image sensor is reduced and the extinction ratio of the excitation light and fluorescence is increased. By this effect, the contrast of *in-vivo* imaging would be improved.

3. Conclusions

We proposed and demonstrated a Si-based LGA plate for implantable imaging device. With the LGA plate, the incident angle of detected light is restricted. The imaging experiment shows that the LGA is effective to improvement of the spatial resolution and the contrast of fluorescent image.

Acknowledgements

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