Design and Packaging of an Implantable CMOS Neural Imaging and Interface Device

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Abstract

We present a CMOS image sensor device for neural imaging and interfacing. The sensor device is post-processed using MEMS microfabrication technique to enable backlit illumination. Pt electrodes are formed on the device for electrical stimulation of neurons. A specially developed packaging technique, which includes a color filter that increases the signal-to-noise ratio for on-chip fluorescence imaging, was used. In vivo experiments inside the mouse hippocampus verifies the use of the device for simultaneous imaging and electrical stimulation.

I. Introduction

Microfabrication techniques combining MEMS and CMOS technologies have recently been demonstrated to be an attractive platform for the development of many bioimaging and biosensing devices [1], [2]. While devices fabricated using CMOS technology have been shown to be capable of a host of sensing parameters like photons, pH, temperature, ion, and force, postprocessing with MEMS micromachining technologies enable these devices to be deployed to its intended application. Examples of these devices for medical and scientific research include, brain recording chips, camera pills, smart microdialysis chips, and artificial retinal prosthesis [3] – [6].

We have been working on a new neural imaging approach based on CMOS image sensors. In the past, we have demonstrated capability of contact imaging in vivo for discerning the time course of serine protease activity inside the mouse hippocampus [7]. The advantage of using a CMOS imaging device is high imaging resolution offered by this technology. Apart from imaging, the capability for electrical stimulus and recording is another advantage. A device that is capable of imaging and also electrical interface will enable simultaneous physiological and imaging experiments to be performed, promising new approaches for the study of the brain.

In this work, we developed a new CMOS image sensor device with embedded Pt electrodes. This new device is realized by a combination of sensor design and microfabrication techniques. We have also incorporated illumination light sources and chemical delivery onto the device thus realizing a single minimally invasive neural imaging and interface device.

II. CMOS Sensor Chip

The CMOS chip is specially designed for imaging the mouse brain (Fig. 1). The imaging element consists of an array of 3-transistor active pixel sensors. The sensor circuit schematic is shown in Fig. 2. To reduce the number of input-output pads, row and column scanners, instead of decoders were utilized. Also, the output signal is read-out serially from a single output pad. Four independent electrodes are strategically located within the imaging array to provide electrical stimulus and recording inside the mouse hippocampus. To minimize injury during insertion into the brain, the contact area in front of the chip is hyperbolically curved. Next, we designed backlit vias onto the sensor to enable backlit illumination from a LED light source. This will enable a more uniform light distribution on the image sensor, and also eliminate the use of excitation light filters. The chip was fabricated using standard 0.35 μm CMOS process.

III. MEMS Postprocessing and Packaging

In order to use the device for in vivo imaging, a special postprocessing and packaging process has been developed. The process flow is shown in Fig. 3. First, an Al etch mask for etching the backlit vias was patterned onto the backside of the chip. The backlit vias were etched using the DRIE Bosch process. The chip was etched until the passivation layer was reached. This layer is transparent to the illumination light from the LED (wavelength 365

nm). Next, the LED was attached to a flexible preprinted polyimide substrate by means of flip-chip bonding. The post-processed chip was then attached on top of the LED. A filter which has cut-off wavelength below 400 nm was spin coated onto sensor surface. This special filter is used to block off the LED light but allow higher wavelengths to pass through hence increasing the signal-to-noise ratio of fluorescence light. A YAG laser was used to ablate the sites coated with filter for subsequent wire bonding. The input-output pads were wire-bonded to the polyimide substrate, followed by formation of a platinum (Pt) bump electrodes onto the embedded Al electrode. Finally, the device was sealed in a transparent epoxy and a needle was attached for injection of chemical inside the brain.

IV. Device Characteristics

Fig. 4 (a) shows the packaged device without filter coating. When a single LED under the device was turned on, illumination light was observed from the backlit vias. This was captured by the image sensor device as shown in Fig. 4 (b). Also, the difference between images in free space and inside a brain phantom, prepared with 6.6% skim milk mixed uniformly inside 1% wt agarose gel, was observed. AMC fluorophore (absorbance peak: 380 nm, fluorescence peak: 460 nm) was mixed into the phantom and fluoresce when illuminated with light from the LED.

The device was used for fluorometric measurement of AMC inside the brain phantom. From the measurement result shown in Fig. 5 (a), a minimum AMC concentration of 10 μM was successfully detected. The characteristics of the Pt electrodes were determined by impedance measurement inside phosphate-buffered solution. Fig. 5 (b) shows the measured result as compared to conventional stainless steel (SS) 100 μm diameter electrodes commonly used for electrical stimulation inside the mouse brain. The result shows that the Pt electrodes perform comparably to that of conventional SS electrodes.

V. In vivo Verification

Preliminary experiments in vivo have been performed inside the mouse brain. The device was inserted into the Schaffer collateral region of the hippocampus and pulse stimulus currents of various intensities were applied. A separate recording electrode placed at the CA1 region was used to record the postsynaptic neural potential. The recorded signals are shown in Fig. 6. From this experiment, it is concluded that the device can be used for on-chip electrical stimulation of the neuron cells.

Acknowledgement

The funding for this work was kindly sponsored by the Semiconductor Technology Academic Research Center (STARC) and the Ministry of Education, Culture, Sports, Science and Technology, Japan.

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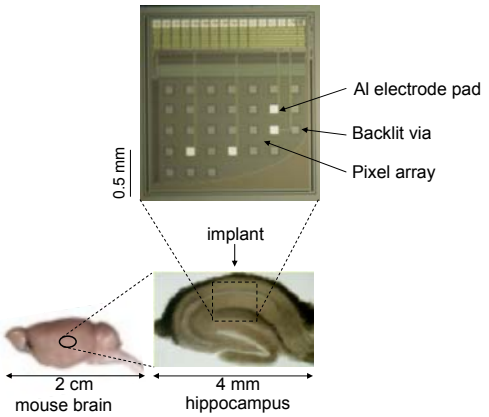

Technology		0.35 μm std. CMOS 4M2P
Operating voltage		3.3 V
Chip size		2 mm x 2.2 mm
Image pixel	type	3-transistor APS
	number	224 x 164
	size	7.5 x 7.5 μm²
Photodiode	type	Nwell-Psub
	size	19.75 μm²
Backlit via	size	85 x 85 μm²
	number	26
Electrode	size	90 x 90 μm²
	number	4
Image sensor output		Serial analog voltage

Fig. 1 CMOS image sensor device compared to the mouse hippocampus. The chip specification is tabulated on the right

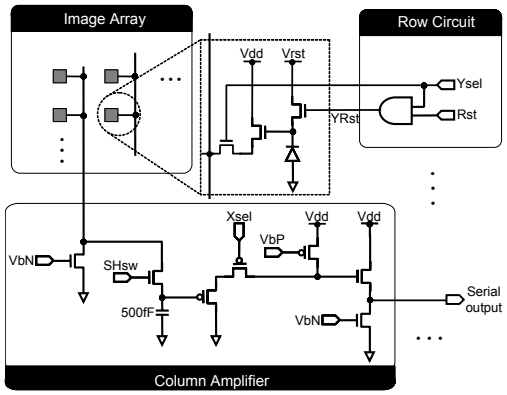

Fig. 2 Schematic of the sensor circuit showing the imaging array, and column and row circuits.

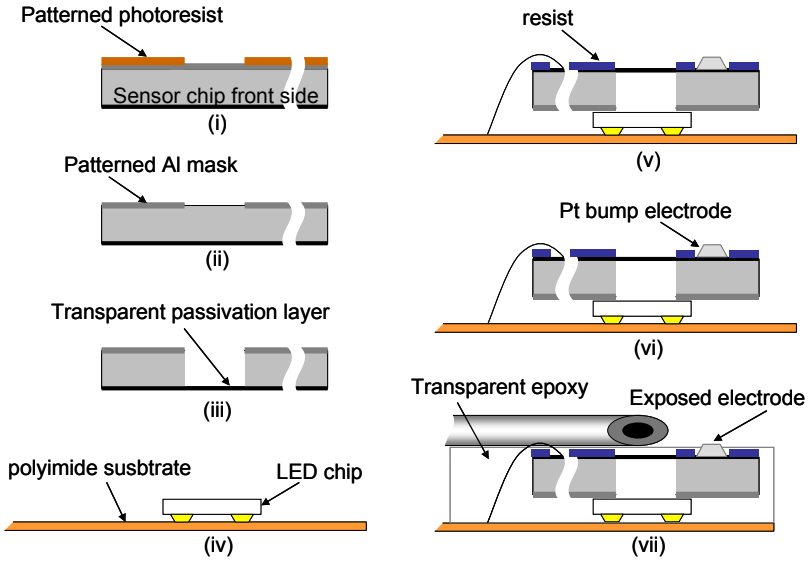

Fig. 3 Post-process and packaging flow of the CMOS device. (i) Sputter Al and pattern photoresist on backside of chip, (ii) wet-etch Al as mask for DRIE, (iii) deep reactive ion etch backlit via and sensor outline (Bosch process), (iv) flip-chip bond LED onto polyimide substrate, (v) attach sensor chip on top of LED and spin coat filter resist, (vi) laser-assisted ablation of resist at bond sites followed by wire bonding of input output pads and forming Pt bump onto Al electrodes, (vii) seal with transparent epoxy and precision laser cut out final shape. An injection needle is attached onto the device for chemical delivery.

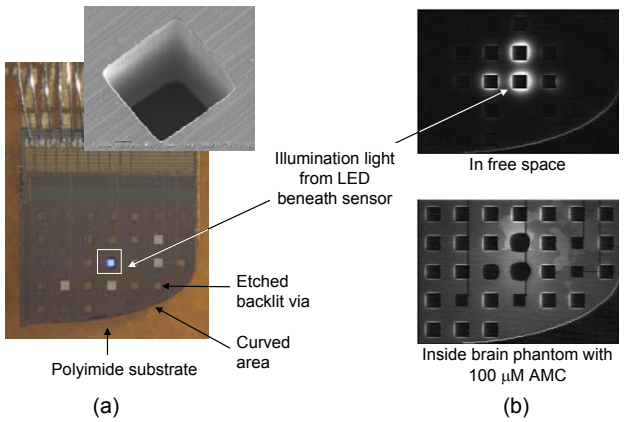

Fig. 4 (a) Photograph of fully post-processed and packaged sensor chip showing illumination from the LED underneath the chip. Inset shows a backside etched via. (b) Captured image from the image sensor chip in free space (upper) and inside a brain phantom (lower).

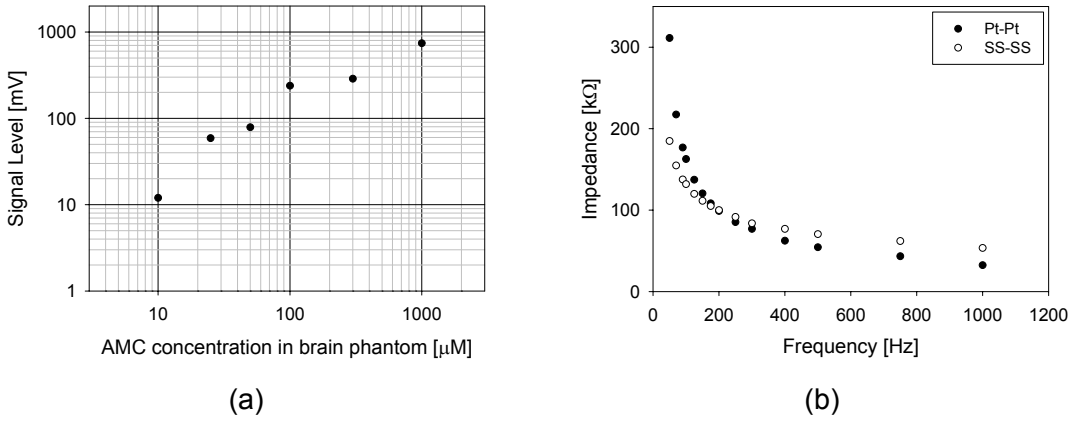

Fig. 5 (a) Fluorometric measurement at various AMC concentration levels inside a brain phantom. (b) Impedance spectrum of the Pt electrodes compared to standard SS electrodes.

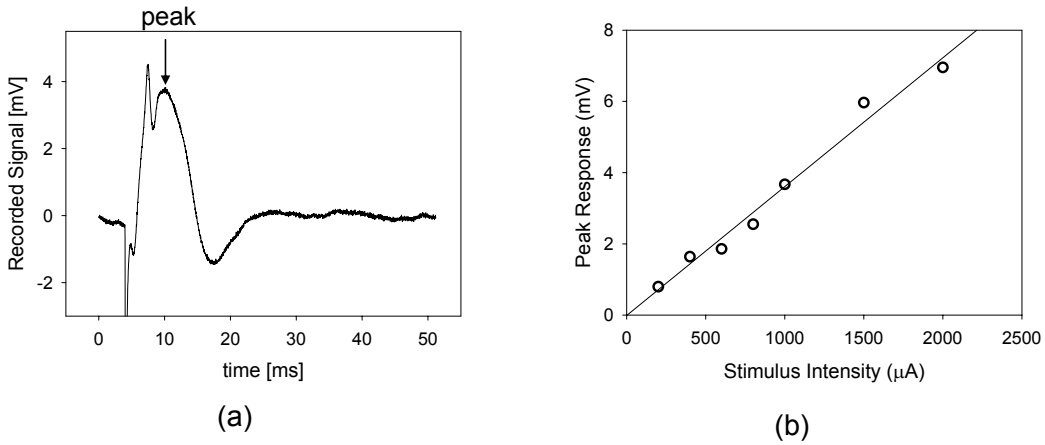

Fig. 6 (a) Typical recorded signal from single pulse stimulation. (b) Recorded peak amplitude is a linear function of input stimulus current intensity.