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Development of a CMOS-based Neural Imaging and Interface Device

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1. Introduction

CMOS technology is increasingly being applied to develop devices for medical and life science research. One important application is the imaging of the brain to study its functions [1]. We have been developing CMOS neural imaging tools which are capable of real time in vivo imaging of the intact brain at arbitrary depths [2-3]. In our previous work, we have successfully demonstrated functional imaging inside the intact brain using a CMOS imaging device. In this work, we combine CMOS and MEMS technologies to develop a next generation device incorporating an imaging array and electrodes onto a single minimally invasive neural imaging and interface device.

2. CMOS Imaging and Interface Device

Sensor Chip

A single device that is capable of simultaneous imaging and electrophysiological experiments will add another dimension to our understanding of the brain functions. This is helpful for the study of various brain disorders such as Parkinson's disease or epilepsy. Using standard 0.35 μm CMOS process, we have designed and fabricated a sensor chip for imaging and electrical interfacing with the mouse hippocampus. It consists of electrodes strategically located on an image sensor array as shown in Fig. 1. To reduce cross-talk between the image sensor operation signals and the electrode signals, the metal interconnections are separated from each other on different layers. The chip specification is listed in Table 1 while its schematic is shown in Fig. 2.

Postprocessing and Packaging

In order to perform on-chip fluorescence imaging, we integrated excitation light sources in the form of LEDs located under the sensor chip. A checkered pattern of backlit vias were included onto the sensor to enable the LED light to propagate through the sensor and illuminate the biological tissue in contact with the sensor front surface. A novel process was developed to postprocess the sensor chip and package it for invasive imaging. The process 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 transparent passivation layer was reached. The LEDs (peak wavelength 365 nm) were attached to a flexible preprinted polyimide substrate by flip-chip bonding. The postprocessed 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. Pt bumps were formed onto the exposed Al electrode. Finally, the device was sealed in a transparent epoxy and a needle was attached for injection of chemical inside the brain.

3. Verification Experiments

Fluorescence Imaging

The fluorescence imaging capability of the device was evaluated by using a brain phantom. The brain phantom has similar optical transmittance to the mouse brain within the 365 to 460 nm wavelength range. 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 signal level from the image array was plotted as a function of the AMC concentration as shown in Fig. 4.

Electrical Interfacing

We tested the capability of the embedded Pt electrodes for stimulation in vivo. The packaged device was inserted until the Pt electrodes reached the Schaffer collateral. An external 100 μm W electrode was used as the recording electrode. A typical recorded signal response is shown in Fig. 5. These result verify that the on-chip Pt electrodes can inject sufficient stimulus current to induce normal synaptic response at the CA1 region.

4. Conclusion

We have developed a CMOS imaging device for simultaneous fluorescence and electrical interfacing with the mouse brain. Further work using the device for in vivo experiments is underway.

Acknowledgements

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References

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Table 1 Specification of CMOS sensor chip.

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 (non-rectangular)
	size	7.5 x 7.5 μm^2
Photodiode	type	Nwell-Psub
	size	19.75 μm^2
Backlit via	size	85 x 85 μm^2
	number	26
Electrode	size	90 x 90 μm^2
	number	4
Image sensor output		Serial analog voltage

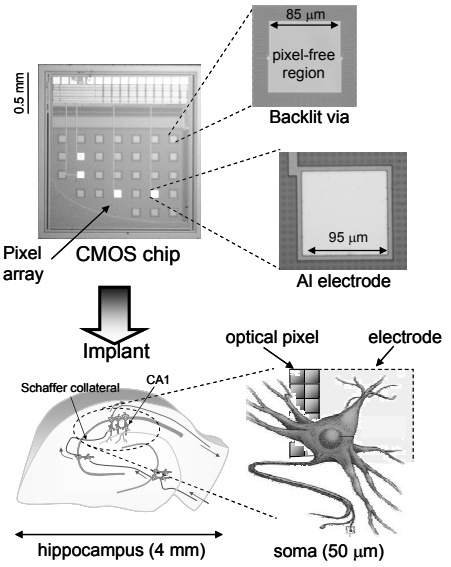

Fig. 1. Dedicated CMOS sensor chip for in vivo imaging and interfacing with neurons of the mouse hippocampus.

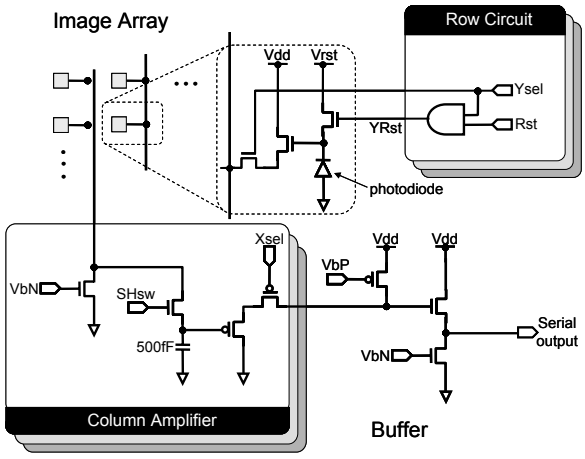

Fig. 2. Schematic of the sensor circuit showing the imaging array, and column and row circuits.

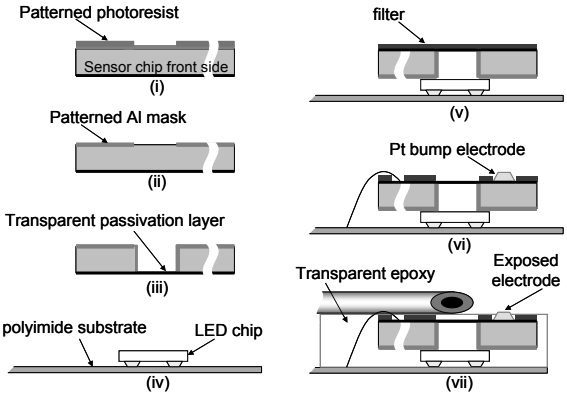

Fig. 3. Post-processing of the sensor chip and packaging process flow of the device. (i) Sputter Al and pattern photoresist on back-side of chip, (ii) wet-etch Al as mask for DRIE, (iii) deep reactive ion etch backlit via and sensor outline (Bosch process), (iv) flip-chip bond LED onto polyimide substrate, (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.

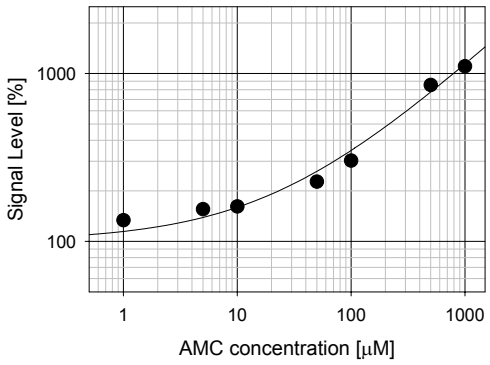

Fig. 4. Fluorescence signal as a function of AMC concentration (background level is normalized to 100%).

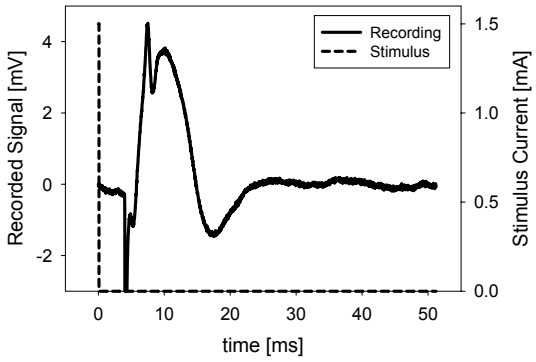

Fig. 5. Typical in vivo recorded signal after single pulse (100 μs) stimulation from the Pt electrodes.