An optical / potential / voltammetric multifunctional CMOS image sensor for on-chip biomolecular / neural analytical applications

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Abstract

We have developed an on-chip image sensor with target applications of on-chip biomolecular and neural imaging. The sensor pixel can sense not only intensity of incident light, but also on-chip electric potential. The light shield structure on the pixel circuit was used as a sensing electrode. Once the passivation layer on the sensing electrode was removed, one can perform on-chip voltammetric measurement, which will be a powerful solution for on-chip biosensing applications. To realise the on-chip voltammetric measurement, we used a column reset line as a current path. Basic characteristics of the sensor was characterized in either optical / potential image sensor operation or optical / voltammetric image sensor operation.

1. Introduction

In the last decade, on-chip bio-sensing and bio-assay technologies using LSI-based intelligent sensors have been attracting a lot of interests and expectations. Measuring bioscientific targets (DNAs, proteins, neural cells, etc.) with on-chip configurations, there are three major approaches to take. One is optical sensing (imaging) [1], another is potential sensing with capacitively coupled electrodes [2], and the other is voltammetric analysis with conductive electrodes [3]. In the present work, we designed a novel image sensor with all the three sensing functions. We designed an optical/electric multifunctional-sensing pixel and columnar circuitry to achieve the optical / potential / voltammetric triple imaging functions.

2. Sensor design

Fig. 1 shows concept of the two kinds (potential and voltammetric) of on-chip electric imaging implemented on the present CMOS image sensor. Fig. 2 shows micrographs and Table 1 shows specifications of the fabricated sensor. Fig. 3 shows schematic and layout of the optical / electric multifunctional-sensing pixel designed for the multifunctional CMOS image sensor. The pixel consists of two sets of reset / readout circuits of 3-Tr APS. For optical sensing, conventional 3-Tr APS is implemented. On the other hand, in the electric sensing part of the pixel, the sensing node (cathode) of the PD in APS was replaced with a sensing electrode. The sensing electrode was formed with the top metal layer. As fabricated, the sensing electrode is covered with passivation layers of the standard LSI structure. The sensor is used as a capacitively-coupled on-chip potential image sensor. Since the pixel was designed with parallel output configuration, the optical and electric sensing functions can be simultaneously operated.

The sensing electrode has a reset transistor (M_4). Without the reset transistor for the electrode, the potential sensing function suffers from residual charge in the electrodes as large offset in pixel characteristic [4]. The reset line for the electrode is also used to establish a current path in voltammetric imaging function.

Fig. 4 shows schematic of columnar circuitry of the sensor. The columnar circuitry consists of two sets of a columnar load unit and a pmos source follower for optical and electric columnar signal lines, respectively. Each load unit has both nmos and pmos loads. Switching the applied voltage on pixel (**Vdd_Pixel** in Fig. 3(a)), and biasing pmos and nmos loads appropriately, the pixel amplifier transistor (M_2, M_5) can be operated in both source follower and common source mode.

To implement the voltammetric function on the sensor, not only voltage sensing path, but also a current supply path and current sensing circuitry are required. As noticed previously, the current path between the columnar circuitry and pixel is established with the reset line. In order to use the sensing electrode for voltammetric measurement, a voltage follower with resistance feedback is configured in each column. The current injected through the sensing electrode into measured object is estimated from a difference between input and output voltages of the sensing amplifier.

As shown in Fig.4, the sensor has four output channels for (1) PD level, (2) electrode potential, (3) input monitor for the amplifier, and (4) output of the amplifier. The 4-channel configuration enables to simultaneously operate the optical and electric imaging function. Furthermore, in voltammetric imaging operation, the potential of the electrode can be monitored via the output channel (3). The voltage difference between columnar circuit and sensing electrode due to the parasitic resistances in columnar **V1** line and transistors can be compensated owing to this feature.

3. Characteristics of the fabricated multifunctional imager

Imaging functions with the optical and electrical multifunctional pixel was demonstrated. The sensor and wires in a ceramic package were molded with epoxy resin. A water droplet was placed on the sensor surface and two tungsten electrodes were placed in the water. The tips of the tungsten electrodes are placed on the sensor surface. Fig. 5 shows (a) experimental setup, (b) optical image, and (c) potential image taken with the present sensor. Potentials of the two

electrodes were set as 0V (left), and 3V(right). The potential images were taken without removing the passivation layer. Thus, the image is taken under capacitively-coupled potential sensing mode. In Fig. 5 (a), two electrodes with shadows on the sensor were observed. In the optical image (Fig. 5 (b)), two shadows of the electrodes were observed. In the potential image (Fig. 5 (c)), potential distribution in water evoked by the electrodes were imaged.

In order to extend the sensor functionality and enable the voltammetric imaging mode, the passivation layer of the sensor should be removed. Reactive ion etching process can be used for the removal of the passivation layers. However, using the potential imaging function, the removal of the passivation layers can be performed more correctly and safely. At first, the top passivation layer (silicon nitride) was removed with RIE process. Then the silicon oxide layer on the sensing electrodes was etched with diluted HF (or buffered HF) solution. During the etching process, the sensor is operated in potential sensing mode, and potential of the HF solution is pulled up at 3.0V.

Fig. 6 shows *in situ* observation of the removal process of the passivation layer. At first, the potential sensing function is in capacitive coupling mode, and it turns conductive coupling mode as the passivation layer is etched away. The removal of the passivation layer on the sensing electrode can be observed as a drastic change of the pixel value. At the last stage of the Fig. 6, all the pixels exposed to the etching solution turns into conductive coupling mode.

Fig. 7 shows a typical current measurement characteristic of the column operational amplifier for voltammetric measurements. The feedback resistance was 10kOhm. The measurement was performed using a current source which was directly connected to the V1 line. We confirmed that the column amplifier is correctly working and current injected through V1 line can be measured with an acceptable linearity for voltammetric measurements used in electrochemical applications.

Acknowledgements

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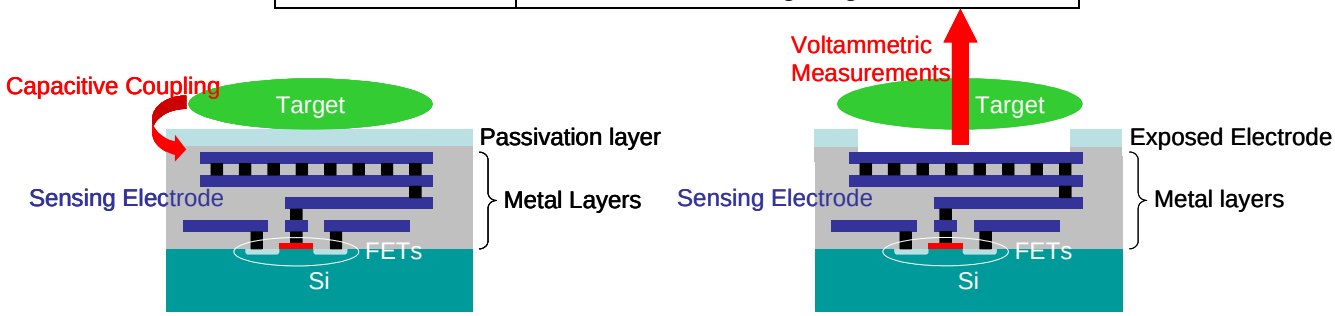
Table 1: Specifications of the multifunctional sensor

Technology	0.35 μm 2-poly, 4-metals standard CMOS
Functions	Optical imaging Potential imaging (capacitive / conductive coupling) Voltammetric imaging (conductive coupling)
Chip size	3980 μm x 4080 μm
Array size	320 x 240
Pixel size	7.5 μm x 7.5 μm
PD area (Fill factor)	10.8 μm^2 (19.2 %)
Electrode area	38 μm^2
Readout	Analog voltage



(a) Potential sensing (capacitive coupling) (b) Voltammetric sensing (conductive coupling)

Fig. 1: Two kinds of on-chip electric sensing: potential (capacitive coupling) and voltammetric imaging.

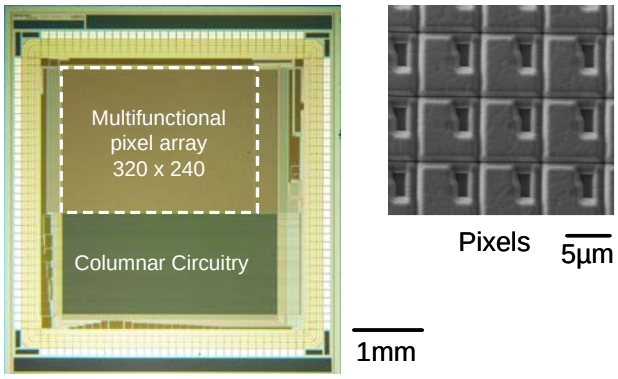


Fig. 2: Micrographs of the fabricated multifuncional image sensor.

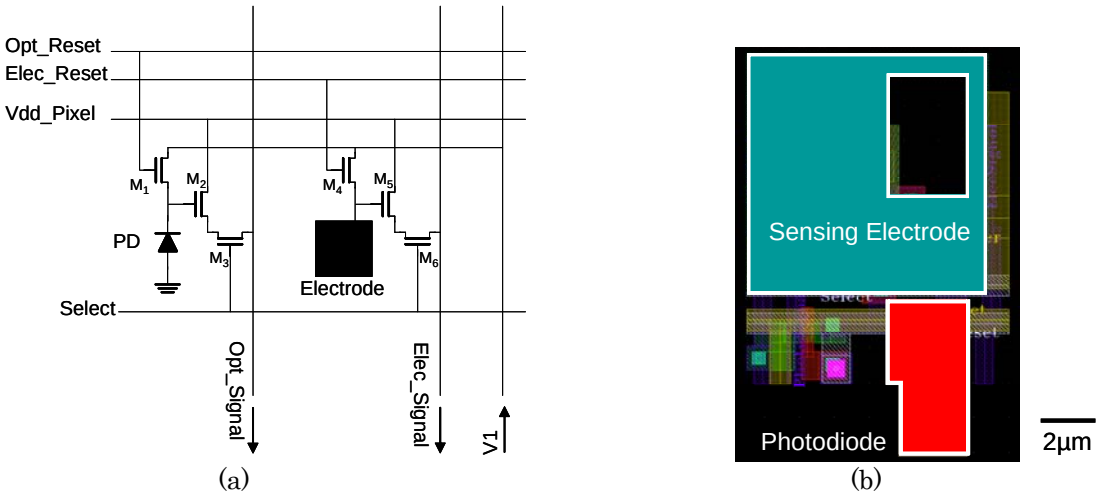


Fig. 3 (a) Schematic and (b) layout of the optical / electric multifunctional pixel.

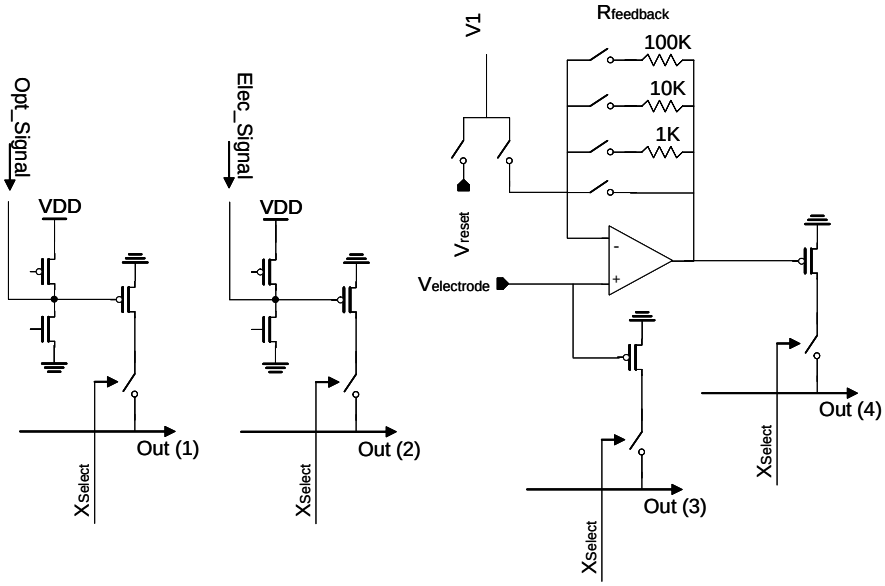


Fig. 4: Schematic of columnar circuitry of the optical / potential / voltammetric image sensor

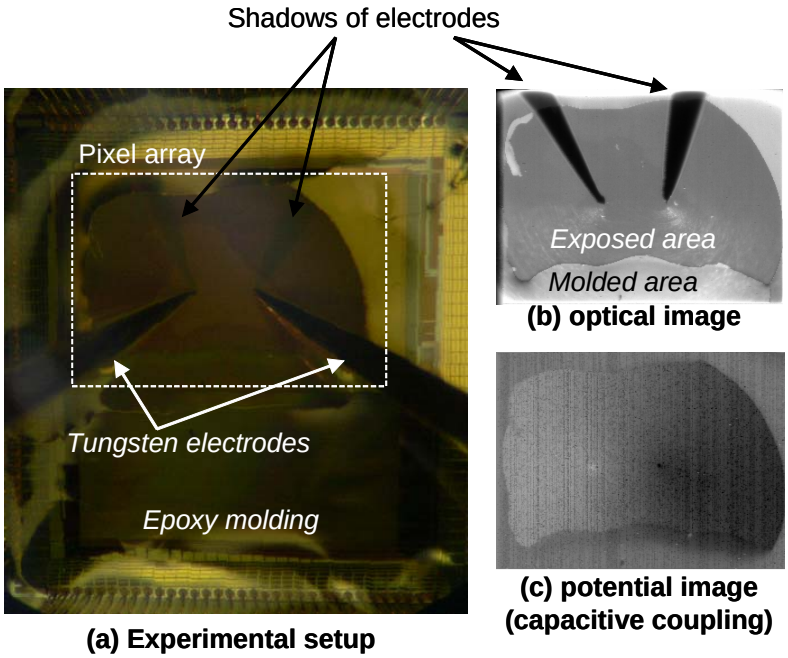


Fig. 5: (a) Experimental setup (b) optical image, and (c) on-chip potential (capacitive coupling) image of two electrodes in water. Potentials of the two electrodes are 0V(left) and 3V(right).

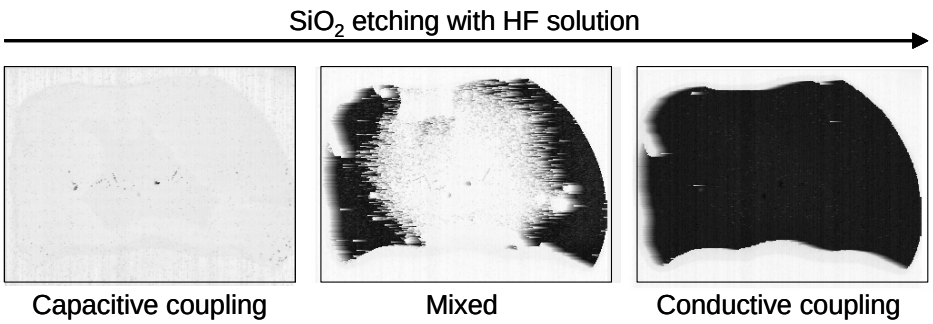


Fig. 6: Transition of the potential measurement mode from capacitive coupling to conductive coupling in etching process of SiO_2 passivation layer. Potential of the HF solution was kept at 3.0 V.

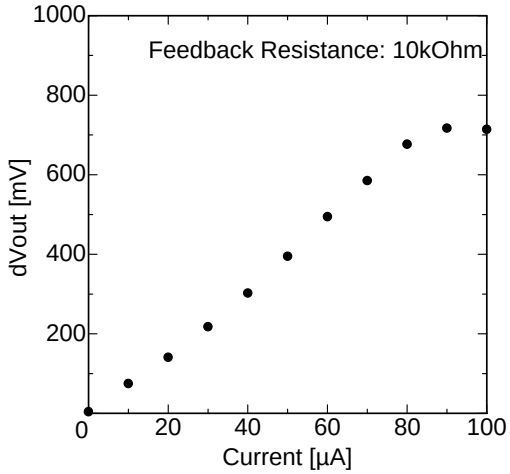


Fig. 7: Current measurement characteristic of the column operational amplifier for voltammetric measurements. The feedback resistance was 10kOhm