Scalable Sensor Array Platform for Analysis of Quantal Transmitter Release Events

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Primary CNF Tools Used: ABM contact aligner, AJA sputtering system, Unaxis 770 deep silicon etcher, Aura 1000 resist stripper, YES Asher, YES image reversal oven

Abstract:

Neurontransmitters are released in a quantal event by fusion with membranes. We develop and fabricate a CMOS sensor array capable of parallel electrochemical detection of vesicle release events from chromaffin cells. To enable amperometry measurement, polarizable platinum electrodes are deposited on the Al/Cu metal contact on the CMOS chip by sputtering. SU-8 insulation layer is also applied to protect the surface structure of the chip and avoid incomplete coverage of the metal contact by shifting the position of the electrodes as well as form deep wells to trap cells. A silicon wafer with deep etched wells is used as holder for the CMOS chips for better handling and pattern transfer.

Summary of Research:

Neurontransmitters are released into the extracellular space in a process known as exocytosis [1]. The amperometry measurement provides precise details about the released transmitters in a single quantal event. However, amperometric spikes vary from cell to cell even under the same condition [2]. Therefore, a large number of measurements for vesicle release events must be performed to achieve a change in the mean value. Here, we present the CMOS IC sensor array capable of parallel amperometry measurement of vesicle release events and the post-fabrication to enable its functionality.

The CMOS sensor chip is fabricated at MOSIS by On Semiconductor C_5F/N. Polarizable electrode materials such as platinum are not offered in this process. Instead, Al/Cu metal contact are deposited to serve as interconnection of the chip. However, amperometry measurement requires polarizable electrodes for low noise current measurement as the oxidation current is usually on the order of pA. Hence, it is necessary to have a post-fabrication process in the CNF clean room to deposit platinum electrodes directly onto the Al/Cu metal contacts for amperometry measurement. AJA sputtering system is used to deposit Ti(60s)/Pt(500s) bilayer with 400w power on the electrode to have a uniform metal film as well as good side wall coverage.

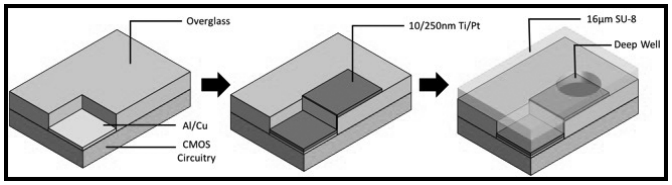

Figure 1: The geometry of shift electrode. The opening of the working area is redefined. In our case, one passivation SU-8 layer is applied with redefined shape (round) of the new opening for better cell trapping.

To avoid possible defect such as incomplete coverage of the Pt electrode, a shift electrode strategy is performed to redefine the position and shape of the working electrodes (Figure 1) [4]. The shifted electrodes also enable cell trapping by SU-8 deep wells. The patterned poly(L-lysine) in register with the electrodes will promote cell adhesion, while poly(ethylene glycol) is applied in between wells will resist cell adhesion [5]. Pt electrodes are deposited over the Al/Cu contact, but instead of just covering the contact window, they are extended to cover some part of the overglass. A 16 μm SU-8 2025 thick layer is fabricated on the surface of the CMOS chip. Deep wells with 20 μm in diameter are opened by general lithography at the redefined electrode position.

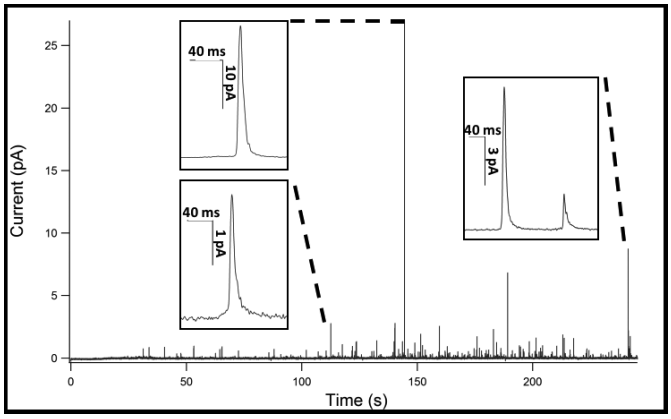

Figure 2: Amperometry recording at one pixel. Many amperometric spikes are observed, validating the function of the device.

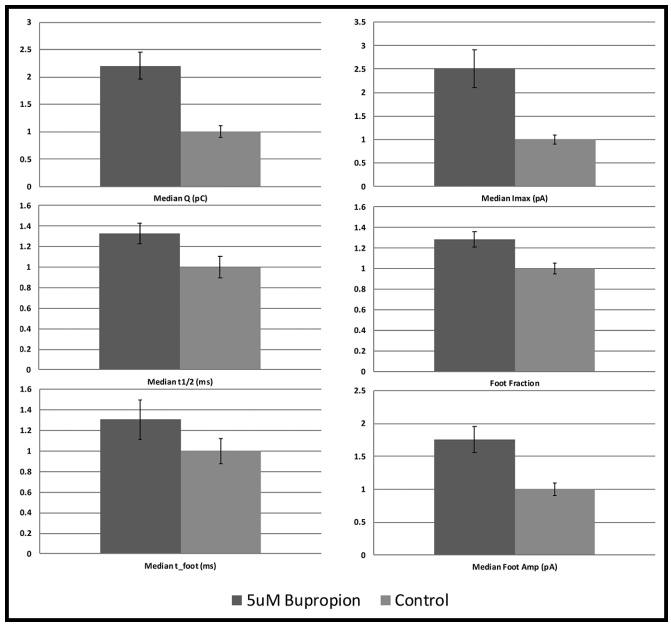

Figure 3: Comparison of various normalized amperometric parameters between the bupropion treated and the control group.

Microcontact printing of poly(L-lysine) and poly(ethylene glycol) will be performed for promotion and resistance of cell adhesion.

Previously we have demonstrated live cell recording on the device. Highly parallel amperometry measurement with low noise is shown in Figure 2 [6]. The device will significantly increase the efficiency of amperometry measurement.

To further utilize the advantages of the CMOS IC with deep wells, effects of several drugs and labels on the quantal release kinetics, such as bupropion, citalopram and FFN511, has been investigated. Figure 3 shows the results for the comparison of various amperometric parameters between the bupropion treated group and the control group. The results were collected from only four experiments from only four separate days, which would normally take weeks or months to get the statistical significance.

References:

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