Scalable Sensor Array Platform for Analysis of Quantal Transmitter Release Events

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Principal Investigator: Manfred Lindau
User: Meng Huang

Affiliation: School of Applied and Engineering Physics, Cornell University
Primary Source of Research Funding: National Institutes of Health
Contact: ML95@cornell.edu, mh2236@cornell.edu
Primary CNF Tools Used: ABM contact aligner, Unaxis 770 Deep Si etcher, AJA sputter deposition system

Abstract:
Neuronttransmitters 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:
Neuronttransmitters 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 chip has a die dimension of around 3 mm × 4 mm. Therefore, direct spin coating of photoresist on the chip will leave a severe side effect and distort the pattern, especially for the viscous SU-8. Here, we fabricate a silicon wafer holder for the chips for better handling and pattern transfer. First, SPR220-7.0 resist is spin coated on the wafer at 3000 rpm for 30s followed by a 90s soft bake. Then, it is exposed using ABM contact aligner to transfer the pattern (exact dimension of the die but with 50 µm margin) on it as a mask layer for etching. After the post exposure bake and development in 726MIF, the wafer is etched using Unaxis 770 deep silicon etcher to make a 250 µm deep well for the chip to fit in.

The CMOS sensor chip is fabricated at MOSIS by On Semiconductor C5F/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.

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. Finally, 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. The round shape rather than the original square shape of the electrode opening is beneficial for cell trapping (Figure 2). Microcontact printing of poly(L-lysine) and poly(ethylene glycol) will be performed for promotion and resistance of cell adhesion. The product was tested with 350 µM Dopamine solution and the dopamine molecule diffusion can be observed from the current level of each pixel on the chip (Figure 3). Live cell amperometry recordings also show clear and clean amperometric spikes (Figure 4).

The device is able to measure multiple cells in parallel, facilitating the experiment in terms of time and efforts.

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