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A 3D microelectrode array to record neural activity at different tissue depths

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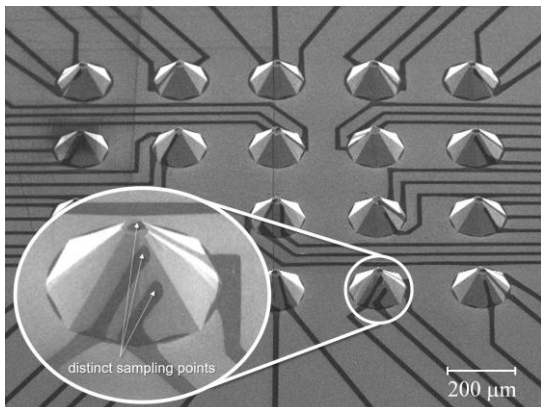
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Introduction

In vitro study of high-level neurobiological systems requires three-dimensional (3D) neuronal cultures [1]. Measuring responses along all three spatial dimensions is critical to record electric activity inside 3D neuronal models, such as organoids and other 3D brain tissue constructs. However, this lies beyond the capacity of 2D microelectrode arrays (MEAs) [2]. We present planar arrays of 3D micro-pyramids, whereby each micro-pyramid supports multiple, electrically distinct and vertically stacked microelectrodes. The 3D microarrays were produced by wafer-scale micromachining and assembled onto printed circuit boards (PCBs) conforming to MEA readout standards.

Theory and Experimental procedure

3D MEAs (Fig. 1) were fabricated on 4" Si wafers. The truncated micro-pyramids were obtained by timed anisotropic wet etching (25% TMAH + Triton solution) of the Si substrate using lithographically defined hard masks that allowed precise selection of crystallographic directions. After thermal growth of a 270 nm-thick SiO₂ passivation layer, a 40 nm/200 nm-thick Ti/TiN layer was sputtered and lithographically patterned to define the electrically independent electrodes. On each pyramid, vertically stacked and distinct sampling points were defined at the tip of each electrode by lithographic patterning of a thin polyimide layer. The wafer was saw diced into 2 by 2 cm² chips that were finally glued and wire-bonded to square PCBs with 60 peripheral contact pads [2].



Results and Discussion

Wet anisotropic etch of the Si substrate yielded ~100 μm-high truncated pyramids with octagonal base and ~46° slope facet as by design (Fig. 1). The etching left a smooth surface on the facets of the micro-pyramids. The smallest metal tracks patterned on the slanted facets were 15 μm-wide with minimal inter-track gap of 5 μm. Multiple geometries and configurations of the microelectrodes were defined, as will be shown in the full presentation.

Figure 1: SEM micrograph of a 3D array of 60 microelectrodes. Each micro-pyramid in the array is ~85 μm-high and features three distinct and vertically stacked microelectrodes (see inset).

Conclusion

We fabricated 3D MEAs able to record electric tissue activity at multiple, distinct and vertically resolved points. Metal interconnects with features as small as 15 μm across the slanted and smooth facets of Si micro-pyramids were defined by single lithographic steps. The Si chips were assembled onto PCBs compatible with standard MEA measurement setups. By virtue of these innovative 3D MEAs we expect to be able to measure responses of 3D neuronal networks from hiPSC-derived cortical neurons cultured within biogel matrices or as brain organoids.

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