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High spatial resolution probes for neurobiology applications

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ABSTRACT

Position-sensitive biological neural networks, such as the brain and the retina, require position-sensitive detection methods to identify, map and study their behavior. Traditionally, planar microelectrodes have been employed to record the cell's electrical activity with device limitations arising from the electrode's 2-D nature. Described here is the development and characterization of an array of electrically conductive micro-needles aimed at addressing the limitations of planar electrodes. The capability of this array to penetrate neural tissue improves the electrode-cell electrical interface and allows more complicated 3-D networks of neurons, such as those found in brain slices, to be studied. State-of-the-art semiconductor fabrication techniques were used to etch and passivate conformally the metal coat and fill high aspect ratio holes in silicon. These are subsequently transformed into needles with conductive tips. This process has enabled the fabrication of arrays of unprecedented dimensions: 61 hexagonally close-packed electrodes, ~200 μm tall with 60 μm spacing. Electroplating the tungsten tips with platinum ensure suitable impedance values (~600 kΩ at 1 kHz) for the recording of neuronal signals. Without compromising spatial resolution of the neuronal recordings, this array adds a new and exciting dimension to the study of biological neural networks.

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1. Introduction

Planar arrays of electrically conducting microelectrodes have been applied to and widely used in the fields of neurobiology and life sciences. They have been very successful in allowing neurobiologists to study networks of cells, whether in the retina or in culture [1], through the position-sensitive recording of the cell's electrical activity.

However, these types of arrays have limitations in terms of making good electrical contact with neurons and also in terms of studying cells which have a 3-D distribution (such as those found in the brain). By studying and gaining a better understanding of how the brain and the central nervous system function at a cellular level, it may be possible to treat their disorders, such as epilepsy, Parkinson's disease, paralysis and deafness. A high-density readout system has been developed by adapting technology originally used in particle physics experiments [2]. The system enables spatially discrete recordings from tens of neurons simultaneously and is scalable to hundreds. The current state-of-the-art in these devices [3,4] have been used to successfully record signals in brain studies [5]. However, there is evidence from studies by Litke et al. [6] that a higher density (inter-electrode spacings of 30–60 μm) of electrodes improves spatial resolution of recordings significantly, allowing complete detection of neurons over the studied area of tissue. This paper describes the development of a semiconductor fabrication technology which is capable of realising high resolution and large-area bed-of-nails arrays of unprecedented dimensions. These arrays are characterised mechanically and electrically to qualify them for use in biological experiments.

2. Method

2.1. Device fabrication

The fabrication of these devices was carried out on 4-in. diameter, double polished silicon wafers at the Stanford Nanofabrication Facility, Stanford University. Fig. 1 shows a schematic of the fabrication process required to form the needles on a bed-of-nails array.

The process relies heavily on a deep reactive ion etch which allows extremely high aspect ratio, tapered holes (~11:1) to be etched in silicon. This is achieved via a technique called the Bosch process which alternates between two modes: an etch and a passivation step. Silicon is firstly plasma etched isotropically using sulfur hexafluoride (SF_6) and then passivated with Teflon (using C_4F_8). The directionality of the plasma etch removes the

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passivation layer from the bottom of the hole being etched but not the sidewalls. This results in a vertical etch profile through the silicon wafer at high aspect ratios. For these devices, the Bosch process is used to etch, in silicon, 280 μm deep tapered holes that are 25 μm in diameter at the base and with tips varying controllably in diameter from 10 μm down to sub-micron. A 1-μm-thick wet thermal oxide is grown on to wafer. This oxide later forms the insulating sidewalls of the needles.

Also critical to this process, is the conformal nature of the low pressure chemical vapour deposition (LPCVD) technique. It is used to line the hole sidewalls with ~0.5 μm tungsten (W) and, for mechanical strength, partially fill the holes with ~4 μm of polysilicon. Aluminium (Al) readout is patterned using a combination of optical lithography and reactive ion etching.

On the backside of the wafer, wet chemical etching of silicon in 25% tetra methyl ammonium hydroxide (TMAH) at 95 °C is used to expose the array of oxide and tungsten-coated holes as an array of needles. When the tips of the needles are exposed, a buffered hydrofluoric acid (BHF) solution is used to etch half the thickness of thermal oxide. Further etching of the silicon fully exposes the needles. The remaining oxide is removed from the tip (using BHF) to expose the LPCVD tungsten tip. It is important in this final silicon etch to leave ~100 μm of silicon to support the needles. Extra rigidity of the chip is achieved by bonding it to a custom cut 550-μm-thick support silicon substrate.

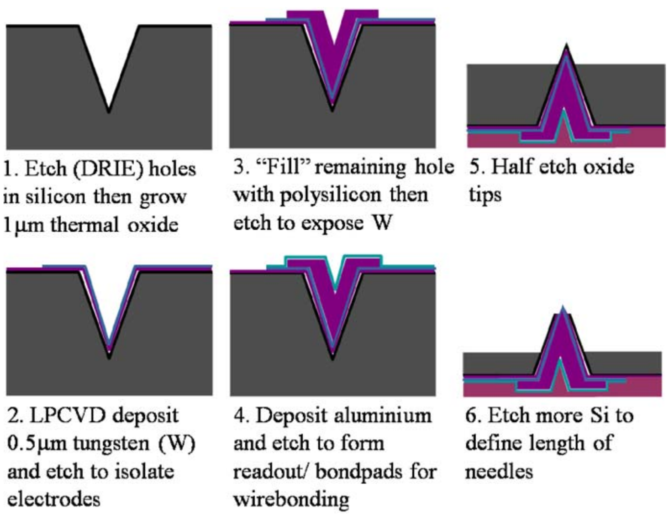

Fig. 1. Schematic of the process steps involved in the fabrication of high-density bed-of-nails type devices.

2.2. Electrical requirements

To successfully record action potentials from neurons, low impedance (<600 kΩ at 1 kHz) conducting sites are required. For large-area electrodes, this is easily achievable with smooth metal depositions. However, for smaller-area electrodes, as in this case ~55 μm^2, a platinum electroplating technique has been very successful in lowering the electrode impedance. By applying a current (4 nA/μm^2 [7]) to an electrode through 2% platinic chloride solution, platinum deposits form over the electrode in a granular structure. The nature of this platinum formation increases the electrode area, thereby reducing significantly the impedance of the electrode.

3. Results

This section shows results of the fabrication of these 3-D neural probes and details their mechanical and electrical properties.

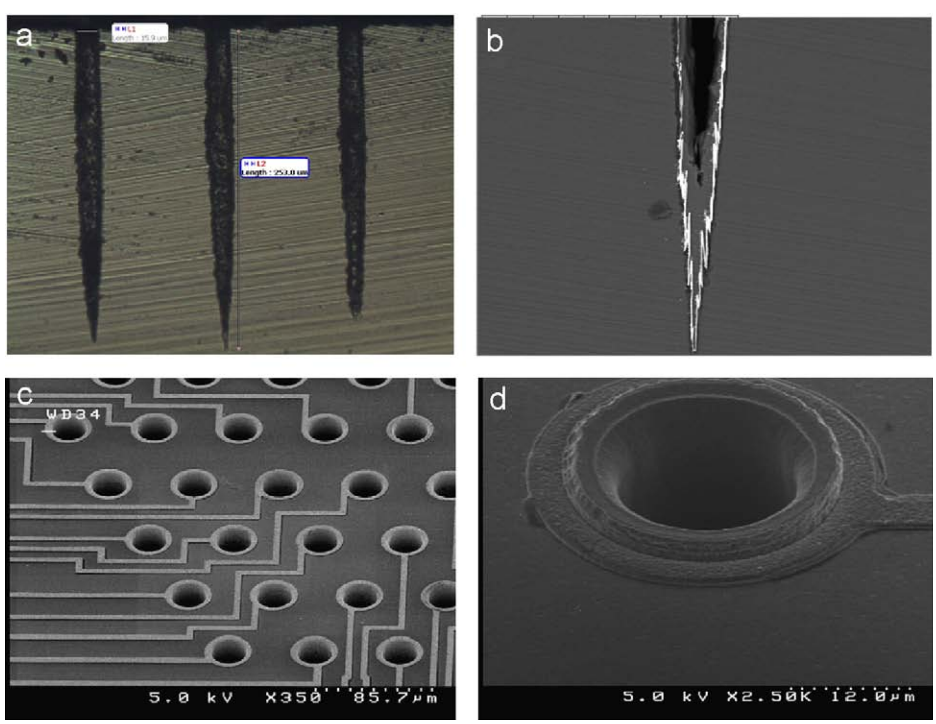

Fig. 2. Images of intermediate steps in the fabrication of bed-of-nails. Top left: cross-section of deep reactive ion etched holes in silicon, with 11:1 aspect ratio. Different depths are a consequence of cutting diagonally through the wafer. Top right: SEM image of W lined and polysilicon filled tip of hole. Bottom left: SEM of array of hexagonally close-packed holes with W readout. Bottom right: SEM image of one hole with polysilicon filling and Al readout.

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