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Performance of ultra-high-density microelectrode arrays

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Abstract

Imaging the electrical output activity of biological cells is important to gain an understanding of how cell networks process information. This has implications for the understanding of brain processing, such as that performed by the retina in encoding the visual scene. The performance and electrical quality of a state-of-the-art high-density 519-microelectrode array, that recorded simultaneously from hundreds of live retinal output cells (ganglion cells) is reported on. The fabrication process for these devices has been optimised and their electrical characteristics examined. The electrode arrays typically exhibit an impedance of ~200 kΩ at 1 kHz and the RMS noise of the whole recording system is 7 μV with a signal to noise ratio of 20:1. With a view to direct stimulation of retinal ganglion cells, a low impedance $Z = 300\,\text{k}\Omega$ iridium oxide interface capable of delivering large currents $Q_{\text{cap}} = 4\,\text{mC/cm}^2$ to cells was also developed.

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1. Introduction

Being an approachable neural network, unlike most regions of the brain, the retina is of great scientific interest. It has a planar, layered structure allowing it to be coupled to a 2D detector from which light, its natural stimulus, can then be focused on to the input photoreceptor cells [1]. Additionally, an understanding of retinal processing is crucial to research groups world wide who are attempting to build a retinal prosthesis aimed at curing some forms of blindness [2].

Historically, to gain an understanding of the neural code used by the retina to communicate the visual scene, signals were recorded from retinal tissue on a single cell basis. However, results from multi-neuronal recordings have shown that neurons do not act as independent sources of information but instead signal in a connected fashion [3]. In order to study the connectivity of these retinal neurons large-area microelectrode arrays are needed to record signals from hundreds of retinal ganglion cells simultaneously. The arrays are placed in an electronic readout system that contains low-noise pre- and post-amplification circuitry. Ref. [4] provides a more detailed account of the system. Arrays with 61 electrodes spaced by 60 μm were initially fabricated. To further study cell connectivity, these devices were superseded by a larger area coverage 60 μm spacing 512-electrode array. In order to study certain classes of smaller-sized cells (OFF-small ganglion) in more detail, however, a higher density array of 519 electrodes with 30 μm inter-electrode spacing has been developed [5,6].

More recently, studies have been focused on the stimulation of retinal cells via arrays of microelectrodes, aiming to fully understand retinal cell functions. Since a current substantial enough to stimulate cells must be supplied an alternative electrode material must be found to platinum black, whose charge capacity is not sufficient [7].

2. Recording microelectrode arrays

In this section, the design of the state-of-the-art 30 μm spacing 519-electrode array is detailed. The optimised process for the fabrication of this device is also described.

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2.1. Array design

Devices are fabricated onto 4-in. glass wafers sputtered with 150 nm of indium tin oxide (ITO), a semiconductor exhibiting transparency. This is an essential property of these arrays as it enables both accurate placement of the biological tissue over the electrodes before the experiment and observations to be made from either side of the tissue during experiments. At the centre of each device, which measures 3.2×3.2 cm, there exists an array of 519, 5 μm diameter electrodes with inter-electrode spacing of 30 μm covering an area of 0.4 μm^2. These connect to outer bond pads by ITO tracks with a 1 μm minimum width. Fig. 1 shows various magnifications of these arrays.

2.2. Array fabrication

A process was originally developed where a combination of photo- and electron beam-lithography were used to pattern the ITO for the 519-electrode device [6]. A new process was realised, however, which utilises only electron beam lithography for the transfer of the pattern, improving the quality of the device (no wire alignment required) and the efficiency of its production. The procedure is described in the following section.

2.2.1. Electron beam lithography

To create a reflective layer by which the electron beam writer can form an accurate height map, 100 nm of titanium is evaporated onto the ITO surface. A consequence of a poor height map is the possibility of stitching errors (misalignment of successive writing fields resulting in a mismatched pattern). This is coated with a 200 nm layer of electron sensitive Shipley UVIII resist, chosen for its low dosage exposure (25 $\mu m/cm^2$) resulting in a reduction in the time taken to fully expose this large area pattern. Before exposure, the resist is baked at 130 °C for 60 s. The newly developed procedure involves dividing the electron beam write into two matrices. Replacing the previous use of photolithography for larger features, the first matrix is written using a 300 nm electron-beam spot to pattern the outer array (minimum feature size of 10 μm). The second matrix exposes the resist with a 112 nm beam spot allowing the central region of the device to be patterned (minimum feature size of 1 μm). The effect of using a larger spot for the outer regions is reduction of write time. The smaller spot, which is essential for 1 μm resolution exposure would take significantly longer to write large feature sizes, creating a less cost effective process. The exposed resist is post-baked at 135 °C and developed in CD-26, each for 60 s. The uncovered titanium is removed using a $SiCl_4$ reactive ion etch (RIE). Removal of the now exposed ITO is achieved by a selective CH_4/H_2 reactive ion etch. Until this stage of fabrication, RIE techniques have been used to obtain high-resolution, anisotropic profiles. To etch the remaining titanium, however, a $H_2O_2/NH_3/H_2O$ chemical wet etch is employed as neither a high-resolution or anisotropic etch is required. It is very selective, however, so long etch times can be used to ensure 100% titanium removal without damaging the ITO, a consequence of RIE.

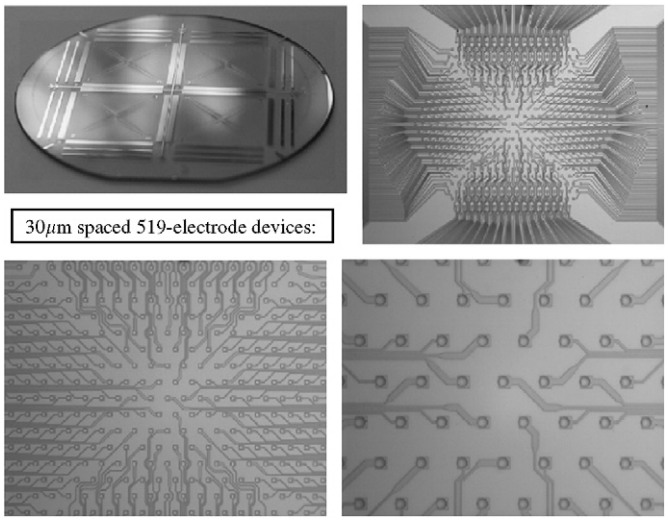

Fig 1. Images of fabricated 519-electrode arrays. Top left: wafer on which 4 devices are patterned. Top right: Hexagonal array of electrodes. Bottom left: Increased magnification of hexagonally close packed electrodes. Bottom right: 5 μm diameter holes in passivating silicon nitride over electrodes.

2.2.2. Photolithography

A 1.5 μm, high-quality insulating layer of Si_3N_4 is PECVD (plasma-enhanced chemical vapour deposition) deposited onto the sample. An SF_6 RIE is used to etch holes in the insulation to electrically expose the electrodes and bond pads [6]. The final fabrication step is to sputter a 1 μm layer of aluminium onto the bond pads. This provides a good surface for the wire bonding of the array to readout electronics.

2.3. Platinisation

To reduce the resistivity of the cell–electrode interface, a porous material called platinum black is formed over the 5 μm diameter ITO electrodes. This is necessary since typical retinal pulses have an amplitude of around only 1 mV. Platinising the electrodes not only reduces the electrodes' impedances but is also an effective method of identifying broken channels. Platinum black satisfies two essential conditions: it has a low resistivity and is biocompatible. It is formed by applying a current to each electrode through an electrolytic solution of platinic chloride:lead acetate:RO water. Due to the fragile nature of electrochemistry, variations in environment, particularly surface or solution contamination, can greatly affect the conditions required for success. For this reason, applied current densities are found to vary approximately between 4 and 7 $nA/\mu m^2$.