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Sensors and Actuators B xxx (2004) xxx–xxx
SENSORS AND ACTUATORS B CHEMICAL
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A neural probe process enabling variable electrode configurations

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Received 1 July 2003; received in revised form 1 July 2003; accepted 7 October 2003

Abstract

Up till now, silicon neural probes have been produced using fixed lithographic mask sets, which is straightforward but inflexible and costly with respect to redesigns for small production volumes. We demonstrate a method to vary the recording site distribution on neural probes with a maskless finishing process. The concept is based on the use of direct write laser lithography (DWL) in one mask layer, thus, enabling on-demand processing of wafers with semi-custom designs at a reasonable cost and lead time. We use the DWL to define windows in the top isolation layer of the device, thus, selecting which electrodes, out of a standardised electrode array, should be active. In addition the active electrode area can be varied. The concept is evaluated using a 64-site neural probe design and manufacturing process. Impedance characterisation is made on active and inactive electrodes and on electrodes with varying active area. The results show ~15 times lower impedance for active compared to inactive electrodes at 1 kHz, which is considered sufficient for signal discrimination.

Keywords: Direct write lithography; Microelectrode; Neural probe; Impedance characterisation

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1. Introduction

Micro system technology is well suited to batch-fabricate neural probes with multiple electrodes, intended for recording or stimulation in neural tissue. A wet silicon-etch-based process was demonstrated early [1], and later a combination of wet silicon etching and a p^{++} diffused etch stop was used to define fork-like probe shapes [2]. Neural probes with on-chip integrated circuitry were also demonstrated [3,4]. In a later approach, a combination of patterned deep reactive ion etching (DRIE) of the wafer front side, and blank wet silicon etching of the back side was used to shape the probes [5]. An all-dry silicon-etch-based process where the buried oxide layer of a silicon-on-insulator (SOI) wafer acts as an etch stop was demonstrated in [6]. Two-dimensional arrays of recording electrodes, distributed on fork-like silicon probe structures are the most common approach, but the distribution of the recording sites on the tips of a ’pin-cushion’ structure has also been shown [7].

However, a fundamental problem is that the desired spatial electrode distributions often differ between different neuroscience experiments. Neural probes that are available today are designed according to specifications from specific scientific user groups, or offered as fixed standard designs. A commercial setting, on the other hand, prohibits custom made designs for individual researchers due to the associated costs and lead times. In this paper we report on a concept to generalise the probe design and modify the production process, so that relatively fast on-demand processing of a limited number of wafers with semi-custom/semi-standard probe designs will be possible.

2. Basic concepts and design

The basic features of our probe structure are illustrated in Fig. 1. From a user perspective or from the anatomical requirements respectively, the main design parameters of the neural probes are: (1) the electrode site centre-to-centre (c/c) distance a, (2) the shaft c/c distance b and (3) the shaft length L, see Fig. 1.

The parameters a and b define a two-dimensional array of electrode sites at which individual recordings or stimulations can take place. To limit the design space a standardised electrode grid seems necessary. After analysis of several previous probe designs made to user requirements, we suggest a standardised 8 × 32 coordinate “snap grid” with $a = 50\,\mu\text{m}$ and $b = 250\,\mu\text{m}$. The grid then defines 256 possible positions for the electrode sites, see Fig. 2. However,

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doi:10.1016/j.snb.2003.10.009

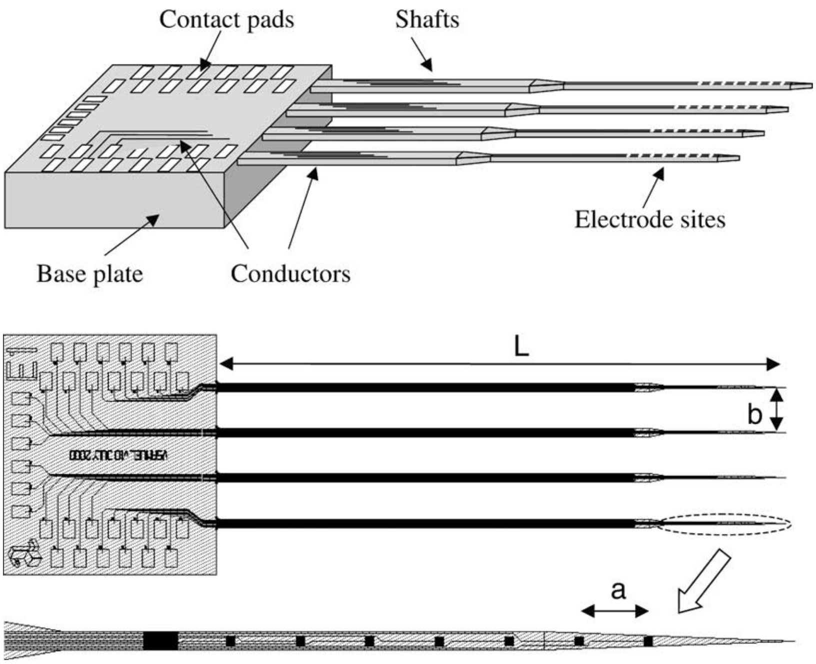

Fig. 1. Schematic illustration of a neural probe (top) and a CAD layout showing the design parameters *a*, *b* and *L* (bottom).

limitations on silicon area and shaft dimensions make 256 bond pads and conductor traces impractical. In our case, we have worked with 32 or 64 connected sites. In the case of 64 sites on a 256-point grid, we have found that 11 different main designs suffice to approximate most other permutations well enough. Multiple shaft lengths, *L*, could in principle also be implemented, but that would increase the design space. Experimental results have shown that a standard shaft

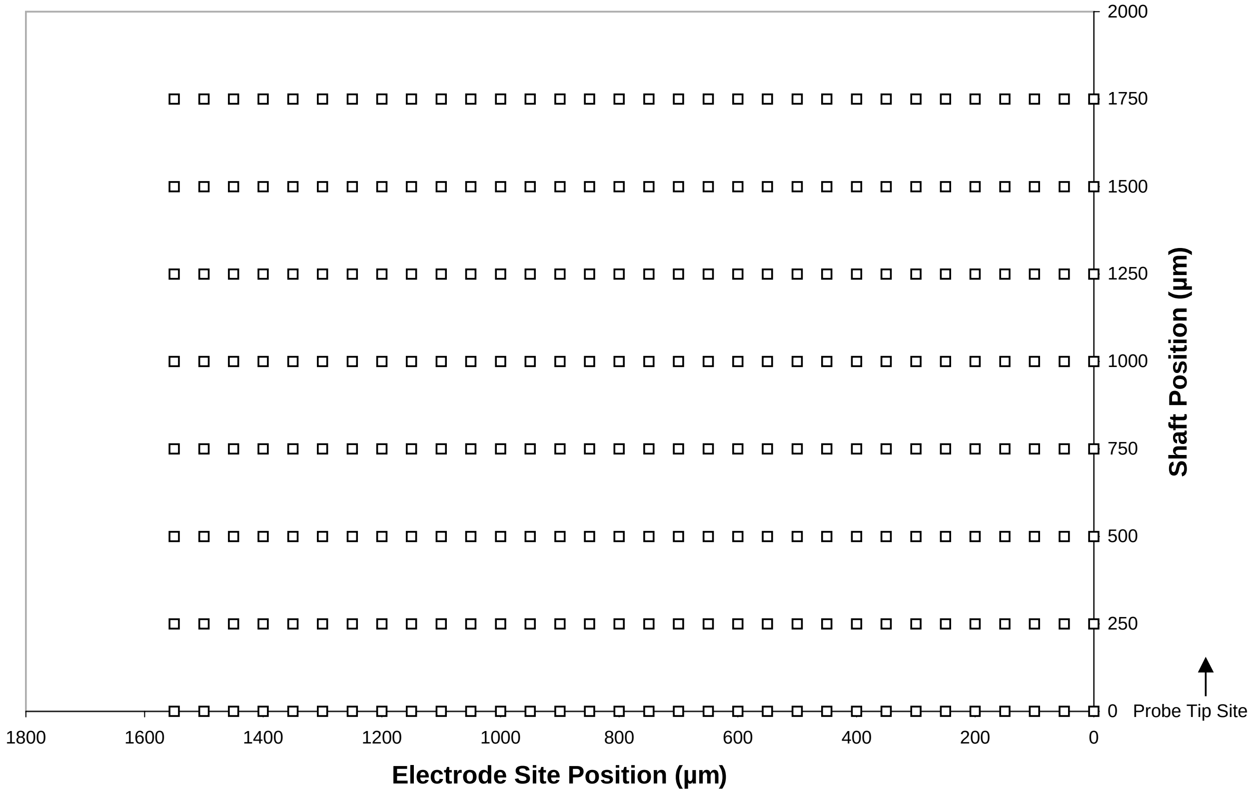

Fig. 2. A proposed snap grid for the electrode sites of a neural probe.

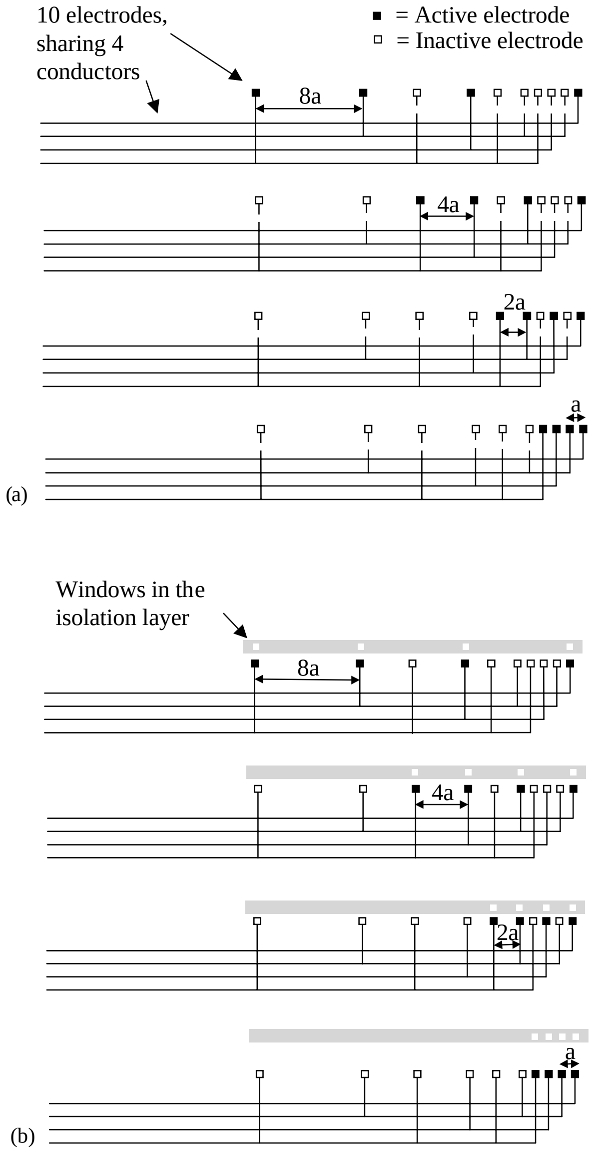

Fig. 3. Example showing how 10 electrodes can share four conductors. By activating/deactivating the appropriate electrodes, four different site distances (*a*, 2*a*, 4*a* or 8*a*) can be implemented. The controlling element can be placed (a) in the electrode–conductor interface or (b) in the electrode–tissue interface.

length of 7–8 mm would be a good compromise for most end users.

The number of conductors on each shaft is limited by the shaft width and conductor line width. The shaft width should be kept as small as possible to minimise tissue damage. The number of conductors, in turn, limits the number of possible electrode sites. To have several electrodes connected to the same conductors is, thus, a way to make efficient use of the available space. Fig. 3 illustrates how different patterns of electrode sites could be activated, starting from a common configuration of electrodes and conductors. The electrodes could in principle be activated/deactivated either by controlling the electrode/conductor interface (Fig. 3a) or by controlling the electrode/tissue interface (Fig. 3b). Activation/deactivation of the electrodes could be realised e.g. by designing fuses that can be blown by a high current [8], by laser cutting [9] or ultra-sonic cutting of conductors, laser destruction of link insulators [10], or by selective opening of windows in the isolation layer on top of the electrodes.

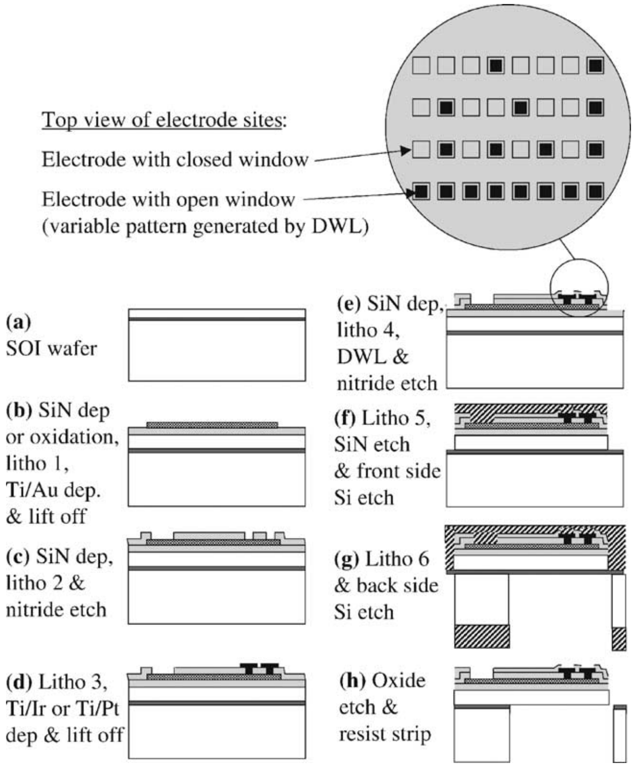

Fig. 5. Schematic cross-section of the neural probe fabrication process (not to scale). In step (e) windows are selectively exposed with DWL and opened in a reactive ion etch.

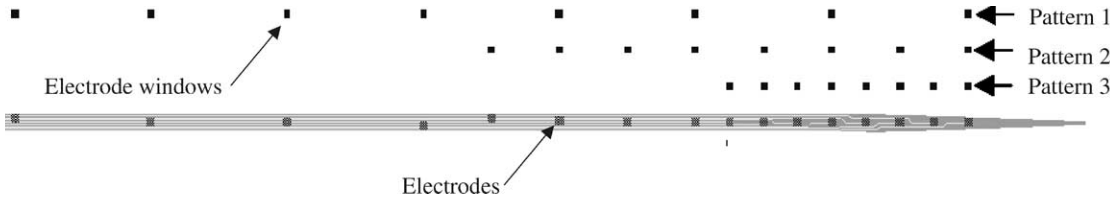

Fig. 4. CAD design of a probe shaft with 16 sites. The shaft can be programmed to three different site distances (50, 100 or 200 μm), see patterns above the shaft.

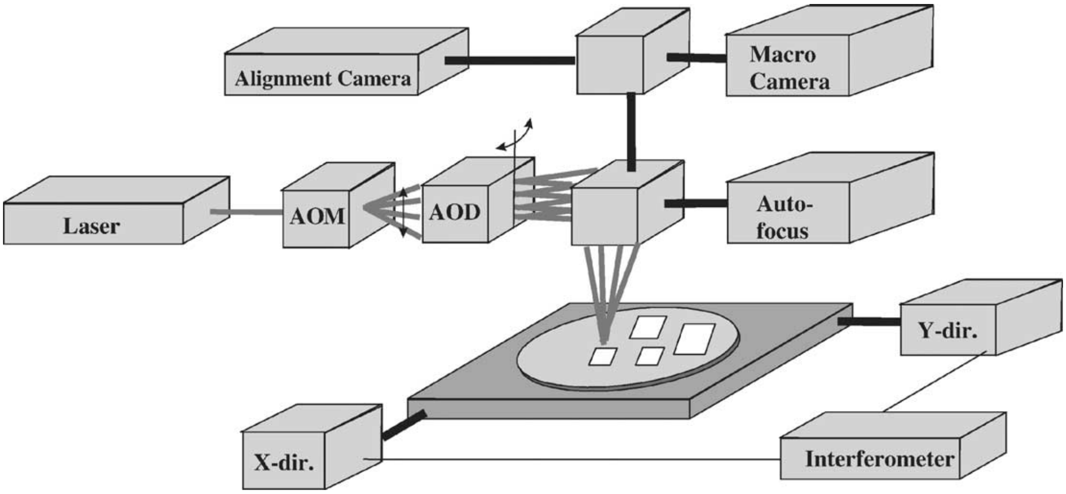

Fig. 6. Schematic illustration of the DWL working principle.

We found the electrode window approach a straightforward way to proceed. A sample CAD-design of an electrode window "programmable" probe is shown in Fig. 4, illustrating three different electrode distributions with eight active sites on a shaft with 16 electrodes sharing eight conductors. Although selective opening of electrode windows in principle could be accomplished by a large set of conventional glass/chrome masks, this would be expensive and inflexible. Instead we used a programmable direct write laser lithography (DWL) machine to define the electrode window mask layer. The general drawback of DWL is its low throughput, as it works in a scanning mode. This application seems, however, ideally suited for DWL, as only one mask layer needs to be written and the complexity of the pattern is limited. The other mask layers are still defined by conventional step-and-repeat projection lithography. Additional design alternatives made possible by the DWL lithography technique are e.g. to vary the size of the electrode windows and to program each shaft, within the same probe, to different electrode configurations.

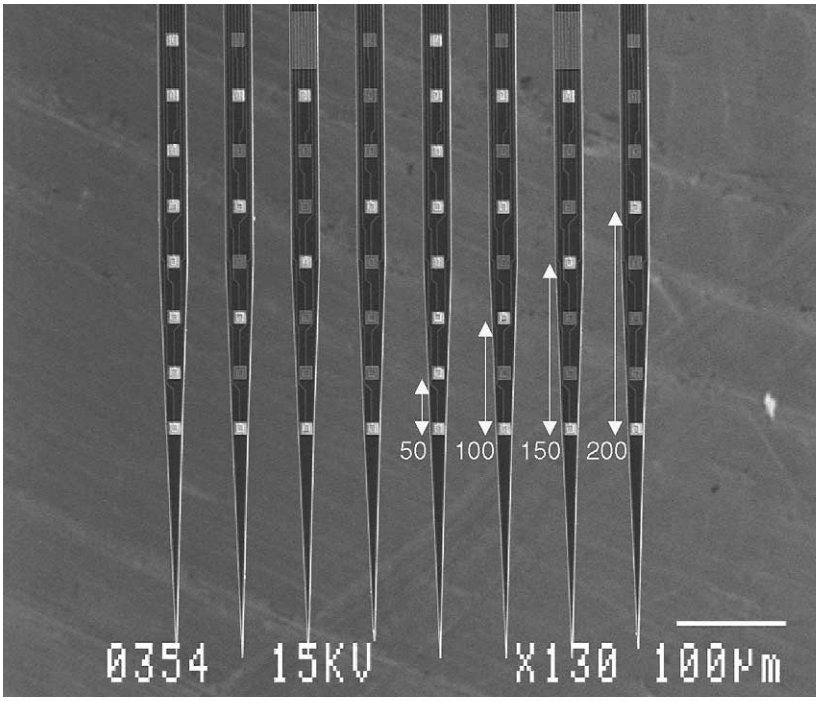

Fig. 7. Scanning electron micrograph showing selectively opened electrode windows in the Si_3N_4 layer on a 64-site probe. Bright squares are opened windows. Distances shown are in micrometer.

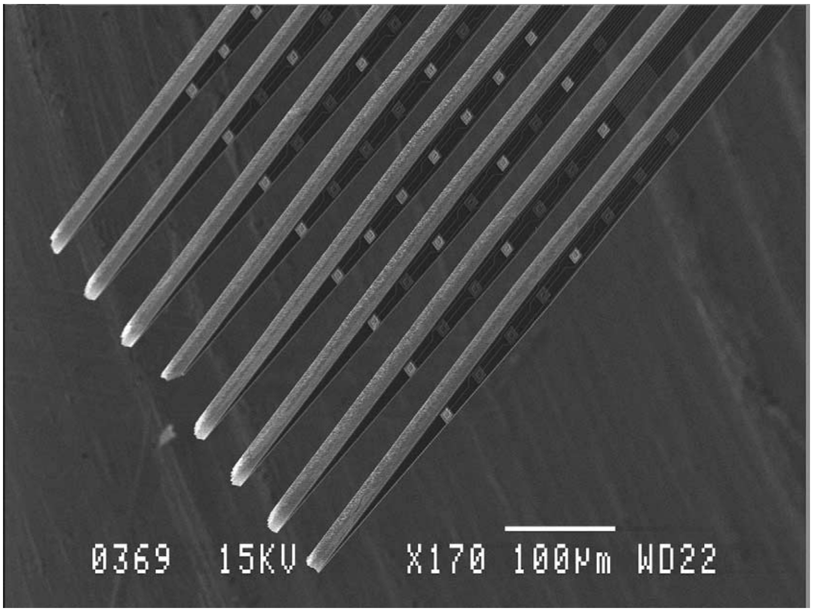

Fig. 8. Scanning electron micrograph showing the 64-site probe with opened and closed windows from a side view.

3. Fabrication process

We have previously presented a fabrication process for neural probes based on double-sided deep reactive ion etching of silicon-on-insulator substrates and shown the manufacture of 32-site [6] as well as 64-site recording probes [11]. We used our 64-site probe process, to show a proof of concept of the "on-demand" fabrication principles described above. During the process flow shown in Fig. 5, we routed some wafers into a side-track at step (e). The resist-coated wafers were exposed in a DWL machine (Heidelberg Instruments DWL 2.0) followed by development and reactive ion etching (RIE) of the Si_3N_4. This resulted in differently spaced and sized electrode windows in the passivation Si_3N_4 layer. For cost reasons the concept was shown in the electrode window definition only, whereas the conductor pattern remained in the form of individual connections to each site.

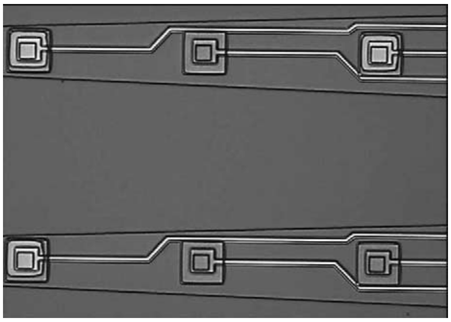

Fig. 9. Photomicrograph of three opened and three closed electrode windows.

The DWL machine (see Fig. 6) uses standard CAD files (GDSII) as raw input data. The light source is a HeCd laser ($\lambda = 442$ nm, $\sim$70 mW). An acousto-optic modulator (AOM) splits the laser beam into 30 parallel beams. Each beam is modulated on/off according to the data pattern and an acousto-optic deflector (AOD) scans the beams 200 µm in the *x*-direction, at the same time as the wafer is moved in the *y*-direction. An interferometer controls the wafer position relative the laser beam.

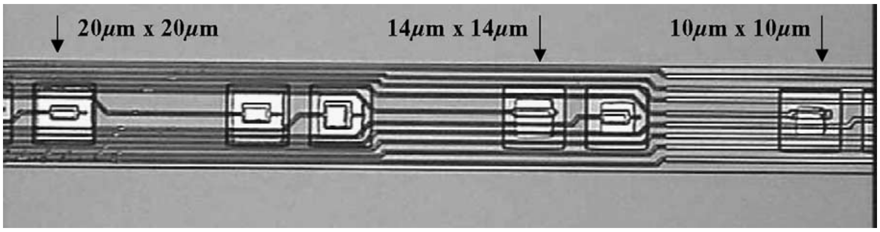

Fig. 10. Photomicrograph of selectively opened electrode windows with varying size. The window side lengths are 20, 18, 16, 14, 12 and 10 µm from left to right.

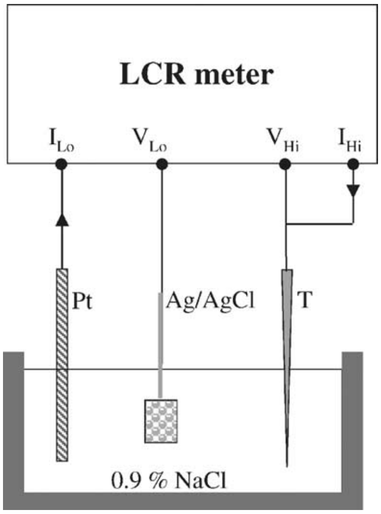

Fig. 11. Setup for three-point impedance measurements. T = device under test (neural probe).

If a large number of wafers will be exposed in the DWL, the process time can be reduced if the contact pad windows on the base plate (see Fig. 1) are exposed using conventional lithography, and only the electrode windows are exposed in the DWL.

4. Results

Figs. 7 and 8 show scanning electron microscope (SEM) images of a neural probe where the electrode distance is varied by selective opening of windows in the top Si_3N_4 layer using DWL and RIE. Fig. 9 shows a close-up of three opened and three closed windows. The platinum metal area is 12 μm × 12 μm with a 10 μm × 10 μm widow area (mask dimensions). In Fig. 10 selective opening of windows with different sizes is demonstrated. The underlying platinum electrode recognised by its outline in Fig. 10 is 22μm × 22 μm. The alignment between stepper lithography and DWL worked well. DWL alignment targets can be included in the stepper CAD design in order to minimise process difficulties.

The Pt microelectrode impedance was characterised in 0.9% saline solution at room temperature, by 3-point-measurements with a HP 4284A Precision LCR Meter, a Pt counter electrode and a Ag/AgCl reference electrode, see Fig. 11. Fig. 12 shows the resulting impedance magnitude for active and inactive electrodes at different frequencies. As a reference, the impedance from a contact pad not connected to an electrode site is also shown. The impedance at 1 kHz is ∼15 times lower for opened compared to closed 10μm × 10 μm windows, which is considered sufficient for signal discrimination. If required, the closed window impedance can be further increased by employing a thicker Si_3N_4 passivation layer than the 4600 Å used in this experiment, and the open window impedance can be further decreased by electroplating Pt black onto the electrode surface [12,13].

Fig. 13 shows the magnitude of the measured impedance for different window areas. A reference line, representing a closed window over a 10 μm × 10 μm Pt electrode is included in the plot. Differently sized electrode window areas could provide a possibility to vary and tailor the trade-off between the signal-to-noise ratio and the spatial selectivity of the microelectrodes.

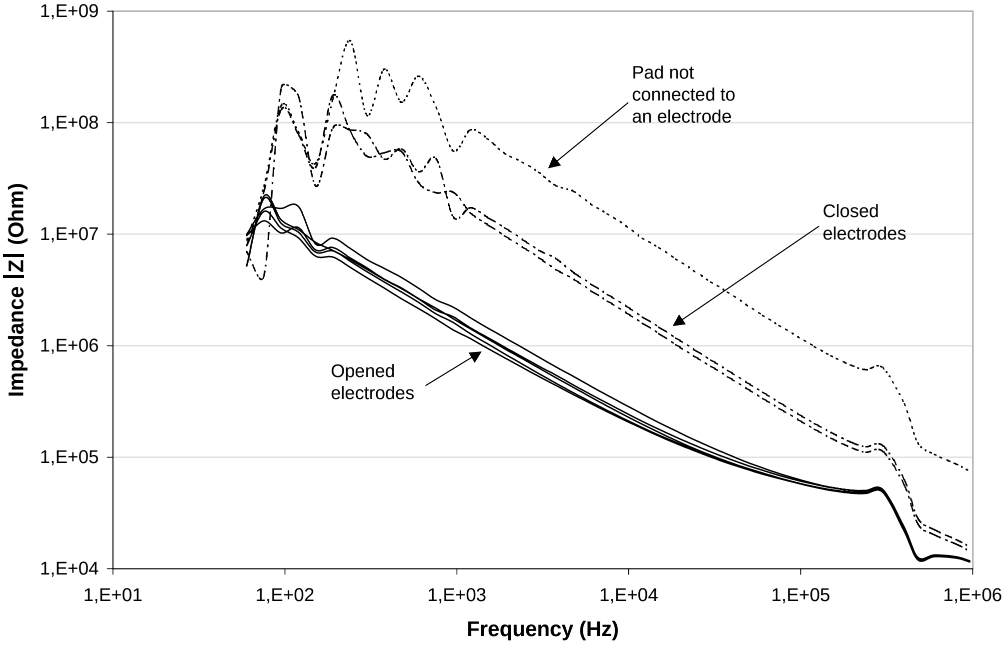

Fig. 12. Impedance magnitude vs. frequency for Pt electrodes in saline with closed and opened 10 μm × 10 μm windows.

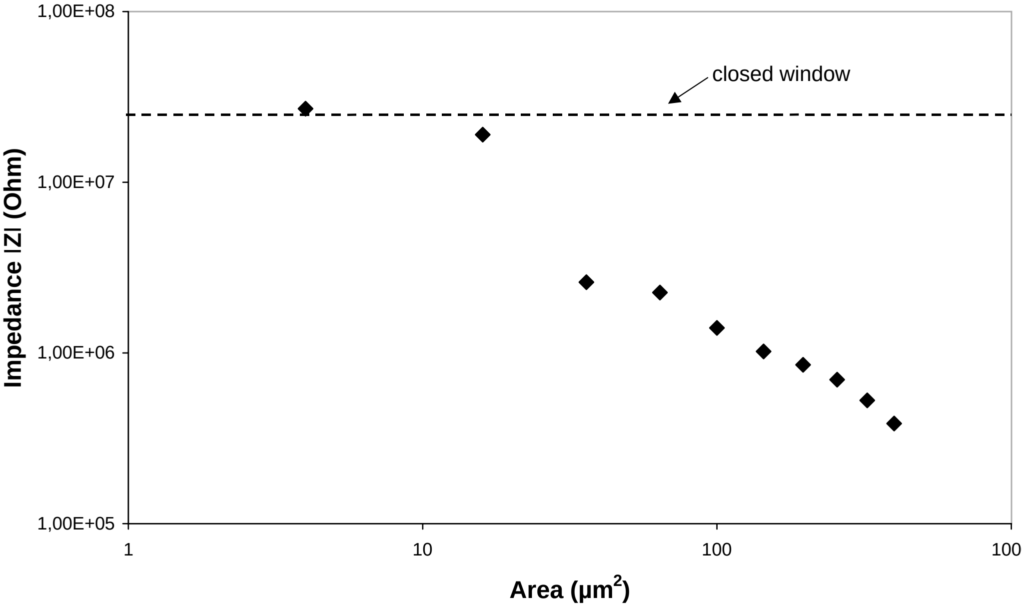

Fig. 13. Electrode impedance magnitude vs. window area for Pt electrodes at 1 kHz. The dashed horizontal line shows the impedance recorded with a closed window.

5. Conclusions

In this paper a concept for relatively fast and low-cost manufacture of semi-custom neural probes was presented. The concept is based on direct write lithography to selectively open windows in the insulating Si_3N_4 layer on top of the Pt electrode sites. We have showed how a large parameter space for neural probes can be covered and manufactured on-demand, without having to redesign the entire lithographic mask set for the probes. The principles were demonstrated in the manufacture and electrical characterisation of neural probes with differently spaced and sized electrode windows.

In the future this process could be used to prefabricate a stock of neural probe wafers up until the deposition of the final passivation layer (cf. Fig. 5). At the time of one or several customers' requests, one of the wafers would be patterned with a tailor-made electrode distribution corresponding to the customers' requirements and the remaining process could be finalised in relatively short time.

Acknowledgements

The authors wish to thank Sara Ahlberg, Sirpa Persson and Helena Strömberg for their skilled help with the device fabrication. We also thank Per Ericsson for help with the DWL software and Ken Yoshida, Aalborg University, for valuable advice on impedance measurements. The work was supported by the European Commission under contract no. IST-1999-10073.

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Biographies

Maria Kindlundh was born in Lund, Sweden, in 1974. After studies at Lund Institute of Technology, she received the MSc degree in engineering physics in 1999. In 1999 she was a consultant at Sigma Design and Development for 6 months. From 1999 she has been an employee at Acreo AB in the positions of scientist and project manager in the field of micro system technology (MST). Kindlundh's main research interests are in the field of MST devices for applications in biotechnology and biomedicine. Since 2000 she has worked in the Swedish part of the EU-funded project VSAMUEL. She has also worked with process development for optical and thermal MST devices, and since 2002 she has been project manager for the development of an integrated opto-electronic consumer gas sensor device.

Peter Norlin was born in Gävle, Sweden, in 1960. After studies at Uppsala University and the Federal Institute of Technology (ETH) in Zürich, he received the MSc degree in engineering physics from Uppsala University in 1986. Between 1986 and 1993 he was with the Swedish Institute of Microelectronics, Stockholm, Sweden, working first in the fields of power semiconductor devices and optical material characterisation, and later with micro system technology (MST). Between 1993 and 1999 he continued his MST-related work at the Industrial Microelectronics Centre (IMC) in Stockholm, and since 1999 he has been with Acreo AB, a Microelectronics and Optics Research Institute, in the position of senior scientist/project manager. Norlin's main research interests are in the field of MST devices for applications in biotechnology and biomedicine. He has been a project manager for several device development projects carried out in collaboration with major industrial partners. Since 2000 he has managed the Swedish part of the EU-funded VSAMUEL-project (development of multisite microelectrodes for neuroscience). In addition to his scientific work, Norlin has upheld a part-time position as corporate quality manager of Acreo.

Ulrich G. Hofmann received his diploma in physics 1993 and his PhD in biophysics 1996 from the Technical University of Munich, Germany. He stayed at the Abo Akademi, Finland, as an EU-fellow (HCM) and as Feodor-Lynen-fellow at the California Institute of Technology. Since 1999 he is research assistant at the Institute for Signal Processing of the University of Lübeck. He is the project coordinator and initiator of the VSAMUEL-project. His long-term research aims to interface brains with computers by multisite neuronal recordings, which consequently drives his interest to neuro- and micro-engineering, computational neuroscience and signal processing.