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Self-Assembling Flexible 3D-MEAs for Cortical Implants

Abstract: Flexible Multi Electrode Arrays (MEAs) for neural interfacing reduce the mechanical mismatch between the soft brain tissue and the electrode arrays allowing accurate signal recordings and neural stimulation while reducing inflammatory responses. Many standard manufacturing processes of MEAs are designed for planar structures and the production of three-dimensional structures is challenging. In the present study, shaft structures with one to two circular gold microelectrodes (10 – 20 μm), each on a base polyimide (PI) substrate, were investigated. We describe a fabrication method, with which shafts made from bi-layer PI flip into the third dimension, which is a first step towards spontaneous assembly of electrodes in flexible 3D MEAs for neuroelectronic applications. A lift-up of the shafts was achieved by the contraction of a second PI layer and a steady nitrogen flow during polycondensation. This shrinking PI was structured in pits with a width of 5 – 600 μm . We achieved lift-up angles of up to 42 degrees. The shaft structures can be hardened and later be used for neural implantation experiments.

Keywords: flexible MEAs, Polyimide, polycondensation shrinkage, self-assembling electrodes

<https://doi.org/10.1515/cdbme-2021-2091>

Figure 1: Light microscope image (a) and SEM-image (b) of 0.5 mm and 1.5 mm long shafts with 50 μm pits and two circular microelectrodes in a MEA-design

1 Introduction

The visual cortex is a part of the central nervous system in the cerebral cortex. Electrical stimulation at the cortex can evoke phosphenes and is therefore a starting point for restoring visual sensory perception. To reduce the required stimulation current and the signal strength to record, close contact to the individual neurons is necessary [1]. Therefore, penetrating electrodes with a length of 1 to 2 mm are a promising approach [2-4]. Implants made of rigid materials such as platinum or silicon generally elicit a higher inflammatory response after implantation than flexible implants made of PI or Parylene-C [2]. Therefore, the development of three-dimensional MEAs on flexible substrates is of great interest [5]. In addition, a primary goal is to intrinsically induce the raising of the three-dimensional structures, to avoid the additional use of external actuation, as done by Soscia and co-workers [6] and to design the flexible structures in such a way that they are easily implantable an implantation robot [7]. Thermal shrinkage could already be shown as a useful actuator principle in other studies with solid and flexible structures [8, 9].

To fabricate self-assembling three-dimensional MEAs, a thermal polycondensation-based process was used and integrated into the process flow of planar electrodes on PI. The PI (PI2611, HD Microsystems™, New Jersey, United States), which shrinks by about 40% during polycondensation, creates a bending and is lifting up shaft structures with embedded electrodes from the x-y plane into the z-direction. To enhance this bending, the PI was patterned in pits that were structured into the upper PI layer. The functionality of this process has

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already been demonstrated with stiff silicon substrates [5] and shorter (~500 µm) PI shafts [6]. In our study, the substrate material and the shrinking actuator material were both flexible and had to be cured at 400°C in a nitrogen atmosphere for polycondensation. Nitrogen gas flow during imidization was the major influencing factor for the lift-up angle. Furthermore, the influence of different pit sizes was investigated to analyse the influence of the actuator material on the lift-up behaviour. The influence of the pit size and number of pits as analysed by different simulations and subsequently served as the basis of the mask design for the lithography processes. During the fabrication of the MEAs, a high density of electrodes and the largest possible lift-up angle of the individual electrode shafts should be achieved. Figure 1 shows a light microscopy and a scanning electron microscopy (SEM) image of the fully cured, upright structures.

2 Materials and Methods

2.1 Manufacturing

The fabrication of the self-assembling PI structures with gold microelectrodes is shown in Figure 2. An approximately 5 µm thick PI layer was spin-coated onto a 4" silicon (Si) wafer with a silicon oxide layer and cured at 400 °C in a nitrogen atmosphere. A 30-nm-thin chromium adhesion promoter layer and a 100 nm thin gold layer were then deposited. Photoresist (AZ®5214E, Microchemicals GmbH, Ulm, Germany) was deposited on the metallization to wet-chemically pattern the electrode structures and bond pads using aqua regia and acid chromium etch. Then photoresist was removed with acetone. Subsequently, the second PI layer with the same thickness was spin coated. After soft baking, the shaft and pit structures were wet-chemically patterned into the PI using the AZ®5214E photoresist. The layer was then cured at 400 °C under nitrogen atmosphere. In a next photolithographic step, the shaft structures were defined in an approximately 30-µm-thick resist (AZ®40XT, Microchemicals GmbH, Ulm, Germany). The shaft structures were etched into the PI of the first layer down to the silicon wafer by reactive ion etching (RIE) with oxygen and sulphur hexafluoride (150 mTorr, 300 W, 50 sccm O₂, 2 sccm SF₆). The pits were filled with another PI layer and also wet-chemically patterned. Subsequently, the PI sandwich was manually peeled off the wafer. Finally, the curing was performed at 400 °C in a nitrogen atmosphere (10 liters/min flow rate) in two different holders that either used the gas-flow to support the lift-up process or shielded the film from the gas flow (Fig. 3). The lift-up height of the shafts was measured

with a distance meter (ND 221 B, Heidenhain, Traunreut, Germany) and the lift-up angles were determined via equation 1.

$$\alpha = \sin^{-1} \left(\frac{\text{height}}{\text{length}} \right) \quad (1)$$

Three chrome masks were designed for the various lithography steps. One of them reproduced the metallization (lead and contact areas) for the chrome-gold layer. The second one structured the pits and the third one structured the shafts and opened the electrode contact areas. The shafts were between 200-µm- and 1500-µm-long, the pits were between 5 µm and 600-µm-long. Up to 10 pits were patterned on one shaft. Furthermore, we tested how the shafts behave with different sizes of metallization below the pits and between the two PI layers. A total of 42 chips were processed on a 4" wafer.

Figure 2: Processing steps: a) Si-wafer with SiO₂-Layer, b) first unstructured cured PI-layer, c) wet-chemical structured chrome-gold-metallization, d) second wet-structured (shafts and pits) and cured PI-layer, e) dry etching of shaft-structures in first PI-layer, f) wet-structured PI in pits, g) manual release foil from wafer, h) curing of the last PI-layer

2.2 Simulation

To investigate the influence of the different pit lengths and geometries on the bending, a static-mechanical simulation was performed using COMSOL Multiphysics (COMSOL Inc., Stockholm, Sweden) for finite element analysis. This identified the components of the pit geometry that had the greatest influence on the bending. To simplify the model, the 150 nm thin metallization is not considered because of the small degree moment of area compared to the much thicker 10 µm PI-layers, which is decisive for the determination of the bending stiffness. Possible internal stresses in the PI due to environmental effects were also not considered. Contraction of the PI in the pits was introduced into the model as thermal expansion with 40%. The results of this simulation formed the

basis for the selection of different pit geometries, which were subsequently validated in the experiments. The simulation results predicted that the angle is larger for longer pits (Fig. 4) and that multiple small pits have a bigger resulting angle than one long pit. Therefore, several pit geometries and combinations were considered in the mask design instead of only single large pits.

Figure 3: Holders for the last curing step of the PI-foils in the oven. a) Holder 1 with nitrogen gas flow supporting the lift-up mechanism, b) Holder 2: shielding the foil from the nitrogen flow, c) schematic drawing of the nitrogen flow through the PI in holder 1

2.3 Statistical Analysis

For statistical evaluation of the results the software of SPSS (IBM Deutschland GmbH, Ehningen, Germany) was used. To test the normal distribution of the samples, a Kolmogorov-smirnov test was performed with a significance level of 5%. Subsequently, statistical Man-Whitney tests are performed to test the equality of different samples in the case of non-normally distributed samples, also with a significance level of 5%.

3 Results and Discussion

The simulation showed that larger pits produce a larger angle of incidence, but the increase of the angle becomes smaller with increasing size of the pits (blue stars in Fig. 4). This assumption could not be confirmed in the experimental surveys. In each case, 12 shafts with a length of 1500 μm and different lengths of pits (40 – 200 μm) were analysed and no significant difference between the measured angles of the shafts with the 40 μm and the 200 μm pits was observed (boxplots in Fig. 4). The mean values of the lift-up angles were 16.2 deg and 17.1 deg for the two samples, respectively. Statistical analysis revealed that there was no significant

difference between the two samples (Table 1, Table 2). The general influence of the PI on the angle was then further analysed. During the final curing step, the films were clamped in a holder that deliberately used the nitrogen flow in the oven to blow the shafts in the lift-up direction. Alternatively, a holder that suppressed the air flow was used. The results of the two holders were compared and showed that the shafts achieve a significantly larger angle under the influence of the nitrogen flow (10 l/min). Regardless of the pit size, the influence of the PI was analysed in comparison to the influence of the nitrogen flow. Three sets of lift-up angle data were analysed. All data were taken from 1500 μm long shafts. One of the samples ($n=240$) measured shafts were baked with PI in the pits but without the influence of the nitrogen flow. In addition, one sample ($n=320$) with shafts without PI in the pits and one sample ($n=320$) with PI in the pits, both baked with nitrogen flow, were analysed. The samples with PI baked with and without nitrogen gas flow showed a significant difference with a large effect. The samples with and without PI both baked with nitrogen flow show a significant difference with a medium effect.

Table 1: Values of the Kolmogorov-Smirnov test for normal distribution: all significances under 5% show, that all the probes were not normally distributed

Data	Nr. of Values	Mean value [°]	Significance
40- μm pits	19	17.1°	0.02
200- μm pits	19	16.2°	0.018
With PI in holder b)	240	3.45°	1.69e-8
No PI in holder a)	320	12.69°	9.91e-16
With PI in holder a)	320	17.32	5.71e-8

Table 2: Values of the Mann-Whitney-Test to test the significant equality of the two samples for 40- and 200- μm -wide pits, the two samples that were cured with PI in holder a) or holder b) and the two samples that were cured with or without PI

Data	Rank sum	Significance	Effect
40- μm pits	367.0	0.919	0.019
200- μm pits	374.0		
With PI in holder b)	162.68	2.1e-5	0.63
With PI in holder a)	368.87		
no PI in holder b)	267.37	3.5e-13	0.28
With PI in holder b)	373.63

Figure 4: Results from simulation (blue stars) and measured results from 108 shafts with pits between 40 μm and 200 μm pits (black boxplots with median and red crosses for outliers)

The mean values of the lift-up angles were 3.45 deg for the sample with PI without nitrogen flow and 12.69 deg (without PI) and 17.32 deg (with PI) for the two samples in nitrogen flow. Therefore, we can state that the influence of the nitrogen flow was very large and therefore cannot be neglected. With an optimised holder or a homogeneous gas flow in the furnace, our self-assembling method could possibly be improved. The smaller influence of the PI compared to the simulation results may be due to inappropriate processing steps. Due to the isotropic behaviour of the PI during wet development, there was no clear edge closure and the PI in the pits did not fill the entire cavity. In addition, reduced adhesion of the PI to the metal or underlying PI could result in reduced force transmission and in smaller lift-up angles.

4 Conclusion

This proof-of-concept study demonstrated that it is generally possible to create self-assembling 3-dimensional shafts with microelectrodes for neural stimulation on a flexible polymer basis. The design allows the fabrication of MEAs with a large number of three-dimensional microelectrode structures without external actuation. In our future studies, we will investigate the influence of the bending process on the electrical properties of the microelectrodes and utilize them in neuronal implantation experiments.

Author Statement

Research funding: Hans Hermann Voss Stiftung 2020/2021 project “Epiretinales Stimulator-Array”, Conflict of interest: Authors state no conflict of interest.

Figure 5: Left boxplot shows angles measured from foils with PI in pits and cured shielded from nitrogen flow, middle boxplot shows angles from shafts without PI in pits and cured under nitrogen flow environment and the right boxplot shows the angles measured from shafts with PI in pits and with nitrogen flow during curing. All measurements were from 1500 μm long shafts with pit-length between 20 and 200 μm .

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