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Flexible Multi-Electrode Array with Integrated Bendable CMOS-Chip for Implantable Systems*

N. Winkin and W. Mokwa

Abstract— **Micro-electrodes and micro-electrode arrays (MEAs) for stimulating neurons or recording action potentials are widely used in medical applications or biological research. For medical implants in many applications like brain implants or retinal implants there is a need for flexible MEAs with a large area and a large number of stimulation electrodes. In this work a flexible MEA with an embedded flexible silicon dummy CMOS-chip facing these challenges has been designed, manufactured and characterized. This approach offers the possibility by connecting and addressing several of these MEAs via a bus system, to increase the number and the density of electrodes significantly. This paper describes the design and fabrication process. Results on the mechanical and electrical behavior will be given and possible improvements for medical applications by this novel approach will be discussed.**

I. Introduction

Micro-electrodes and micro-electrode arrays (MEAs) for stimulating neurons or recording action potentials are widely used in medical applications or biological research. In a variety of medical implants like cochlear implants, retinal implants or deep brain stimulators micro-electrodes are essential. Especially for retinal implants due to the curvature of the eye and the mechanical sensitivity of the retina it is necessary that these MEAs are flexible. Looking to retinal implants that had been implanted into humans up to now the diameter of the electrode array is in the range of 6 mm [1-3]. By this, the visual field is very limited. Wide field retinal prostheses must have a diameter of more than 10 mm corresponding to a visual field greater than 34° [4]. Another challenge is the number of stimulation electrodes. The highest electrode number shows the Argus II implant with 60 electrodes on a flexible polyimide substrate [5]. The 60 electrodes are connected to the control electronics via metal lines and wires. Looking to wide field retinal implants and to an enhanced resolution it is necessary to increase the number of stimulation electrodes of these systems significantly. Chader, Weiland and Humayun forecast an electrode count of 1000 in 2014 [6]. Such high numbers of electrodes can no longer be connected via metal lines or wires to the electronics. It is necessary to have the electronics very close to the stimulation electrodes. This approach is implemented in the subretinal implant of the Retina Implant AG in Germany. This implant has 1500 pixels with integrated electronics [2]. Electrodes and electronics are on a single silicon chip having a size of 3 mm x 3 mm. This system is non flexible and has only a small visual sight. A purely optical subretinal approach was introduced by Palanker [7]. The system has an array of silicon islands that are connected via flexible silicon membranes. Photodiodes on top of the islands could be activated by infrared light from the outside in such a way that stimulation currents were generated. Flexible high density arrays have been developed for mapping brain activity [8]. In this development very thin silicon membranes (260 nm) were used for realization of transistors. The transistors and the circuitry are built in a complex non standard process so that it is not possible to use standard state of the art CMOS.

In our approach state of the art CMOS-chips can be used. We propose a flexible intelligent implantable MEA-system with high electrode count and wide visual sight. This is shown schematically in figure 1. CMOS-chips providing the stimulation currents are brought onto a flexible polyimide substrate in close proximity to stimulation electrodes that are on this substrate. One stimulator chip controls a certain number of electrodes. All chips are connected to each other via a bus system. By this, the number of connection lines can be very small. In order to be flexible the silicon chips have to be thinned below 20 µm. In this way, the whole system remains flexible and due to the bus system the number of electrodes can be adapted to the application.

In this paper the design and the fabrication of such a "flexible intelligent electrode" and results on mechanical and electrical properties are presented.

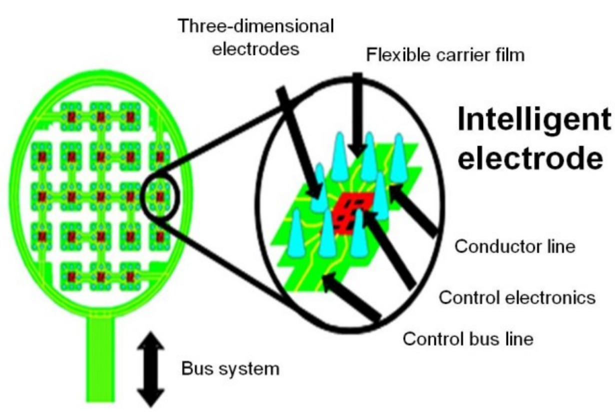

Fig. 1: Flexible micro-electrode array with distributed control electronics and distributed electrodes.

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Nadine Winkin is with the RWTH Aachen University, Institute of Materials in Electrical Engineering 1, D-52074 Aachen, Germany (corresponding author to provide phone: 0049-24180-27769; fax: 0049-24180-22392; e-mail: winkin@iwe1.rwth-aachen.de).

Wilfried Mokwa is with the RWTH Aachen University, Institute of Materials in Electrical Engineering 1, D-52074 Aachen, Germany (e-mail: mokwa@iwe1.rwth-aachen.de).

II. Design and Fabrication

A. Design

During the development phase, a dummy stimulator chip was used to optimize the integration into the polyimide. This silicon chip has aluminum pads on top as shown in figure 2. Pad dimensions and spacings are identical to those of the CMOS-stimulator chips, used in the epiretinal implant of Rössler et al. [3]. The five pads on the left side are used for connecting the CMOS-chip to external electronics, the 25 pads on the right side are intended for connecting the stimulation electrodes.

To obtain the desired flexibility of the dummy CMOS-chips, they have to be thinned to thicknesses below 20 µm. These thinned dummy chips, the gold conductor lines to the electrodes and 25 electrodes are integrated into a polyimide carrier and encapsulated with parylene. In the following, this structure is called "Flex-MEA" (figure 3). It will act as the basic unit for the "flexible intelligent electrode".

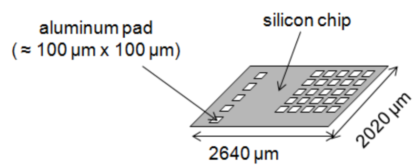

Fig. 2: Dummy stimulator chip (schematic).

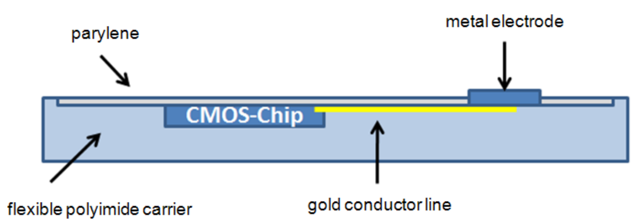

Fig. 3: Schematic view of the cross section of the Flex-MEA.

B. Fabrication

The first fabrication step is the preparation of a polyimide base structure. A silicon wafer is first coated with 50 nm titanium, 1 µm aluminum and 150 nm titanium. The first titanium coating serves as an adhesion layer for the aluminum. The second titanium protects the aluminum from unwanted etching attacks during subsequent processing steps. The aluminum itself serves as a sacrificial layer to separate in a final step the finished Flex-MEA from the wafer. Photo sensitive liquid polyimide "PI 2611" (HD MicroSystems Inc.) was spin-coated onto the metal layer. The "PI 2611" has excellent biocompatibility and biostability [9]. Depending on the number of revolutions per minute, different layer thicknesses between 1 µm and 11 µm can be produced within one step. Greater thicknesses of the polyimide layer can be formed by alternating coating and bake-out steps. A layer thickness of 5 µm was used for the base structure of the Flex-MEA. After photolithography and wet chemical patterning, polyimide carriers with a size of 7000 µm x 7000 µm x 5 µm were defined. Next, the polyimide base structure (1. PI) had to be cured entirely. This is done in an oven at temperatures around 350°C to 400°C under nitrogen atmosphere. After this curing step the polyimide is resistant to most solvents, acids and bases.

Then a second polyimide layer (2. PI) with a thickness of 25 µm was deposited. After photolithographic and wet chemical patterning, a trench of about 2790 µm x 2170 µm was created in this thick polyimide layer.

In a next step the silicon chip was thinned to 20 µm. Thinning is conducted on a lapping machine and stopped when a thickness of 50 µm is reached. The thickness is further reduced to 20 µm by dry-etching with sulfur hexafluoride. Then the thinned dummy stimulator chip was placed into the trench, centered and fixed in the trench with just two polyimide drops "on top" as shown in figure 4. The thickness of the drops does not increase the total thickness because a third PI-layer is spin coated on top to planarize the surface. This additional PI-layer can be seen in figure 5.

Then contact holes were processed to open the aluminum pads. 30 nm chromium and 100 nm gold were evaporated onto the whole wafer to serve as a plating base. Hereafter, a resist mask that defines the pads, gold conductor lines and electrode-areas was applied. Then 3 µm of gold was electroplated. The resist mask was removed with acetone and the plating base was etched away wet chemically. The gold pads and gold surfaces of the electrodes finally remained as shown in figure 6.

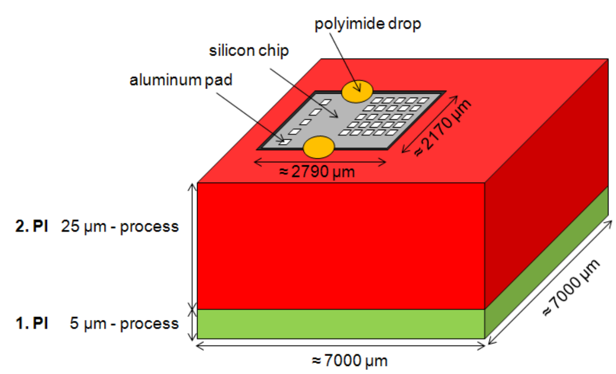

Fig. 4: Fixing the dummy stimulator chip with two polyimide drops.

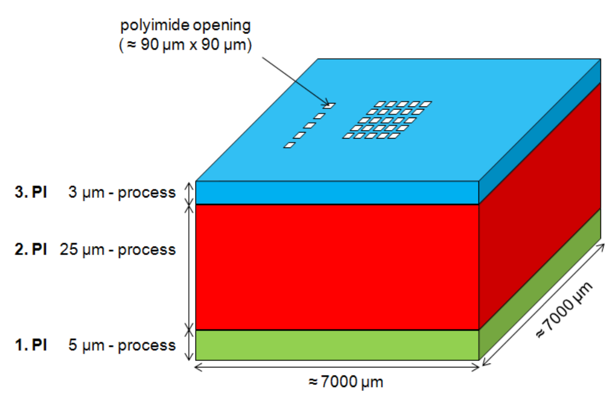

Fig. 5: Embedding the dummy stimulator chip into polyimide.

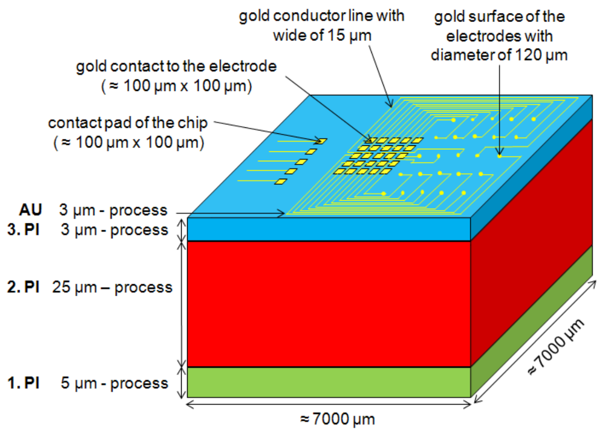

Fig. 6: Contacting the dummy stimulator chip to the gold surfaces of the electrodes.

The electrodes were then coated in a lift-off process with iridium oxide by reactive sputtering of iridium in an oxygen atmosphere. Iridium oxide is biocompatible and biostabile [10] and is used worldwide by many research groups, since it is adequate for stimulations of neurons with a charge delivery capacity of more than 95 mC/cm^2 after electrochemical activation [11]. The iridium oxide is a highly porous material. To block a corrosion of the gold surfaces sputtered platinum (Pt) with a thickness of 150 nm was used as an intermediate layer. After lift-off, the iridium oxide electrodes remained.

For electrical isolation parylene C (PA) was used (figure 7). It was deposited from the gas phase with a thickness of 3.5 µm. Electrode openings of 100 µm diameter were obtained by reactive dry etching afterwards. Parylene C is widely used as coating material for medical applications.

Next, the finished Flex-MEA was separated from the silicon wafer. First, the 150 nm titanium was etched between the individual structures. Then the entire sacrificial aluminum layer was etched and the Flex-MEAs were detached from the carrier wafer. Finally, remaining titanium was etched away. During this etching process, the structures were protected with a resist. A photograph of the finalized Flex-MEA is shown in figure 8.

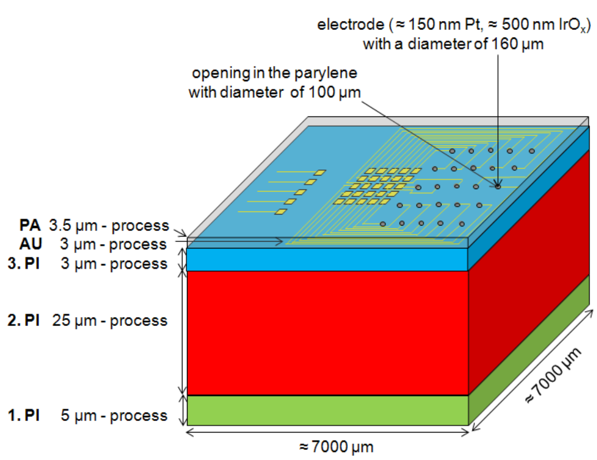

Fig. 7: Flex-MEA (schematic).

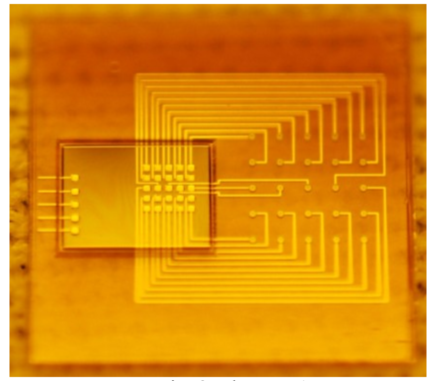

Fig. 8: Flex-MEA.

III. Experimental Results

To proof the robustness of the gold conductor lines against mechanical stress, a modified design of the Flex-MEA was fabricated. This design adds 5 gold conductor lines connecting the 5 control pads on the left side with 5 electrode pads on the right side as shown in figure 9. 10 additional pads facilitate the measurement of the electrical resistances of these 5 conductors with the four probes measurement method during mechanical stress.

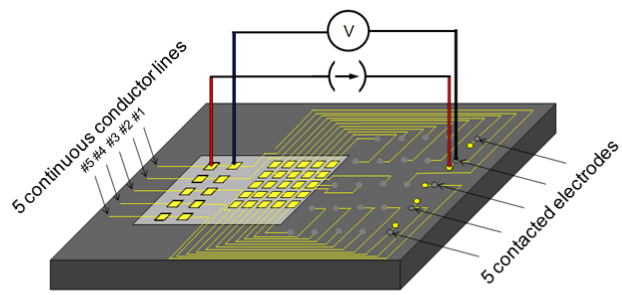

Fig. 9: Modified Flex-MEA.

Bending tests were performed with five of these modified Flex-MEAs. For this, seven semi-cylinders with different diameters of 22 mm, 19 mm, 16 mm, 13 mm, 10 mm, 7 mm, and 4 mm were fabricated. For the mechanical stress tests, the Flex-MEAs were bent around these semi-cylinders, thus ensuring well reproduced bending diameters.

The tests started with the largest diameter of 22 mm (typical size of a human eyeball). Up to 50 deflections were repeated. The electrical resistance of each of the gold conductor lines was measured after 1, 25, and 50 repetitive deflections.

Representative of all five conductor lines, the electrical resistances for conductor #3 of micro-electrode array #1 are plotted against the number of iterated deflections in figure 10. These results are comparable with those of the other conductor lines and micro-electrode arrays. Additionally, the resistance values were measured as a function of the bending diameter. Just a single deflection was executed for each diameter starting with 22 mm and iterating the measurement for the smaller bending diameters in decreasing order. The results for conductor #3 are plotted in figure 11.

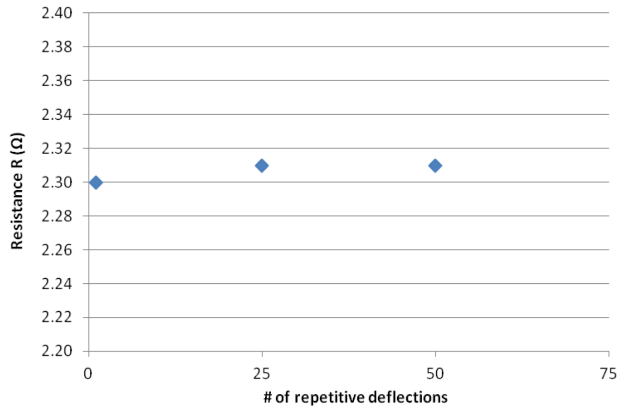

Fig. 10: Resistance of conductor #3 depending of the number of repetitive deflections at a cylinder diameter of 22 mm (micro-electrode array #1).

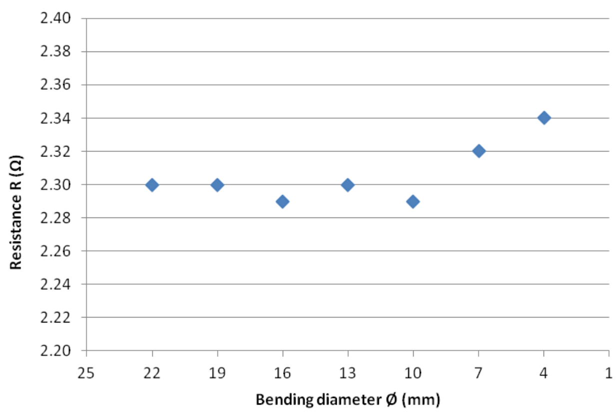

Fig. 11: Resistance of conductor #3 depending on the bending diameter for a single deflection per diameter (micro-electrode array #1).

Obviously, the gold conductor lines are not influenced by the deflection down to a diameter of 10 mm. The small increase of the resistance value for a diameter of 7 mm and 4 mm may indicate first effects due to mechanical stress. This correlates with the observation for micro-electrode array #4, the gold conductor lines #3, #4, and #5 were broken at the rim of the embedded silicon chip at a bending diameter of 4 mm (see figure 12). Along with these cut-offs, fracture traces on the embedded silicon chip have been observed.

In summary, the performed mechanical stress tests show, that the gold conductor lines are suitable for the integration in medical retinal implants.

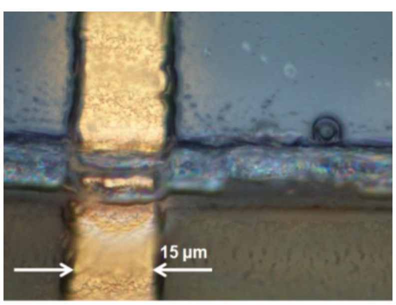

Fig. 12: Microscope picture of a broken gold conductor (micro-electrode array #4)

IV. Conclusion

A novel flexible multi-electrode array with embedded silicon chips has been manufactured and successfully tested. Measurements of the electrical resistances of the integrated conductor lines were carried out during mechanical stress. The results show, that the Flex-MEA metallization is not influenced by deflections, which are typical for retinal implants.

The presented results are relevant for cochlear implants and deep brain stimulators as well. Flexibility and softness produce a better interfacing to the human tissue for these applications too. In addition, a higher number of electrodes allows a more selective stimulation in a general sense. Finally, a decrease of the electrode size will be possible by using an appropriate coating increasing the charge delivery capacity [11]. Of course for these applications, techniques similar to the Seldinger technique have to be developed to place the flexible structures in the right position.

In a next step the dummy chips will be exchanged by CMOS-stimulator chips. Furthermore, the integration of three-dimensional electrodes is planned. Additionally, a further reduction of the total thickness of the micro-electrode array is intended to enhance the mechanical flexibility.

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