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Novel Thin Film Cuff Electrode for Neural Stimulation

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Abstract

One approach to reestablish disabled functions or to treat chronic diseases of patients is the electrical stimulation of nerves. This requires, in addition to special stimulator electronics, a dedicated electrode in close contact with the specific nerve. We present a new type of spiral self-sizing nerve cuff electrode capable of selective activating specific regions of a nerve trunk. The cuff consists of eight active contacts produced by technologies taken from microelectronics. A platinum metalization for contacts and connection wires was made on a sandwich flexible bi-layer polyimide foil substrate embedded in a biocompatible insulation (silicone). With such a design wrap thickness under 40μm were obtained. The spiral-like arrangement of the cuff placed around the nerve trunk allows a tight cuff to nerve contact without penetrating the nerve. The miniaturized active contact area along with the increased number of electrodes imply a highly spatial selectivity together with the need for a high charge transfer. Therefore we are focusing our research on alternative coatings like iridium oxide which promises to enable high current densities. The electrode's design, requirements and production are described.

1. INTRODUCTION

Electrical stimulation of the nervous system can be one satisfying way to help people who are paralyzed or impaired by stroke, head or spinal cord injury as long as restoration of damaged functions by regeneration of the nervous system remains theoretical. Specific applications include stimulating upper and lower extremities for functional movement [1], the peroneal nerve for footdrop compensation [2], and the phrenic nerve for respiratory control [3]. Recent and future recording and stimulation applications require refined and specific electrodes as well. Complex neural electrodes and systems will only be accepted when they run reliable and consistent for the lifetime of an impaired individual.

Several different types of stimulating nerve electrodes prepared in different manners have been reported on, e.g. intracortical electrode array [4], [5], epineural electrodes [6], intrafascicular silicon electrodes [7], multiple contact nerve cuff electrodes [8], and intrafascicular wire electrodes [9]. One special type for long-term applications is the cuff electrode. Since the first report about recording peripheral nerve signals using cuff electrodes in 1974 by Hoffer [10], the interest on such implants grew, especially for providing chronic neural information during functional movement [11]. Cuff electrodes have been produced by fixing tiny platinum sheets between differently stretched silicone sheets in a fine craftsman fashion and applied for chronic implantation [12], [8]. However, the disadvantages of all these electrodes are the large thickness and the limited number of contacts needed for stimulation and the inelastic and difficult "hand-made" structure of the cuff. So there is still a need for new cuff designs that can, for example control multiple motor functions through selective stimulation of the axons in a nerve trunk. Apart from the peripheral nerve stimulation there are other conceivable applications for cuff electrodes, e.g. stimulation of optic nerve for visual sensations, for use in bladder implants or chronic disease treatment of patients. Visual prostheses as retinal implants have been developed which are attached directly to the retina to replace damaged photoreceptors [13], [14], [15]. Another possible way to artificially elicit visual sensations in blind individuals shown by Veraart et. al. is the stimulation of the optic nerve [16], [17].

Presumably between five to ten active contacts over the nerve diameter are needed for selective nerve stimulation as has been shown by computer simulations [18]. Also by using computer simulations different stimuli parameters, e.g. biphasic or monophasic, might be tested. The specific design, like the alignment and shape of the active contacts and the cuff shape alike have a large influence on the current density respectively the charge density required for stimulation [18], [19], [20]. Technology taken from microelectronics serves as a powerful tool for manufacturing nerve cuff electrodes. When using microelectronics methods with its very good accuracy and reproducibility, a wide range of different simulated designs and materials can be quickly realized and tested.

In this paper we present a flexible thin film implantable nerve cuff electrode for neurostimulation with improved mechanical closure mechanism. We focus on the design of peripheral nerve cuffs and the development of serial manufacturing techniques. A thin and flexible polyimide foil acts as a substrate. Polyimides with their high thermal and chemical stability and low gas permeability and vapor transmission rates are widely used as flexible substrates for bioapplications [21], [22]. Platinum, the most commonly used noble material for neural stimulation is applied for metalization [23]. However, the miniaturization step enabling small active contacts leads to the requirement of high current densities. Such miniaturized platinum contacts may exceed the estimated reversible charge injection limits [24], [25]. Metal degradation, corrosion and final delamination are the consequences. For some applications it is necessary to transfer high charge densities in a reversible way to stimulate the cell membrane. Since the current density obtained by iridium oxide is higher than that of platinum, we added an additional electroactive iridium oxide layer by electrochemical deposition on the platinum base layer as an active surface. Manufacturing steps and the special cuff closure mechanism with the polyimide sandwich structure are presented and are a promising alternative to present commercially available implantable neuroelectrodes.

2. METHODOLOGY

2.1. Spiral Cuff Design and Fabrication

Cuff electrodes were constructed by a lithographic technique. They were constructed as "self-sizing", that means the cuff is designed to self-wrap around the nerve trunk. Similar types of cuffs using different fabrication processes have been previously reported on [26], [27], [28], [29]. The spiral nerve cuff electrode, as shown in Fig. 1, was developed to be easily implanted on a nerve without fixing and protection by suture. The expandable cuff fully encloses the nerve without affecting its physiological functions. The close nerve contact allows low stimulus intensities and the consistent alignment of the active contacts, a selective and spatial stimulation, i.e. target axons at specific locations can be stimulated, while axons at other positions in the nerve trunk remain inactive.

A 12μm thick polyimide foil mounted on a stainless steel frame for better handling was used as substrate. For the following manufacturing process a sequence known in microelectronics as lift-off process was used. The frame mounted substrates are first ultrasonic cleaned in acetone and isopropanol and then rinsed with de-ionized water. A positive photo resist is spin coated onto the polyimide surface to a thickness of ~2μm and cured for 10 min at 100°C. After curing, the photo resist layer is exposed and developed using standard photolithography techniques.

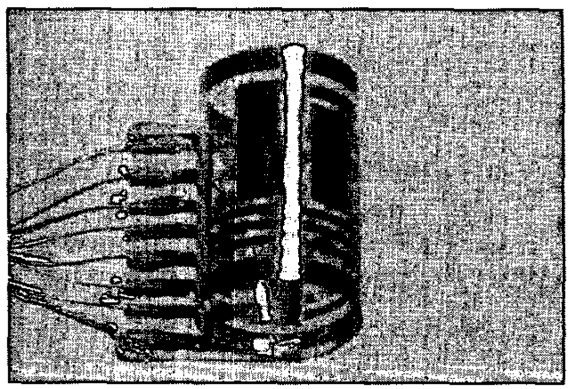

Fig. 1 The novel spiral nerve cuff electrode consisting of eight conductive segments in the fully closed state including connecting wires. Electrode structures on the transparent polyimide are seen .The cuff dimensions are: length of 6mm, an internal diameter of about 2.4mm, and a wrap thickness under 40μm.

The conducting layers are deposited in sequential steps. First a thin adhesive titanium (30nm) layer is electron-beam deposited after argon plasma cleaning. Next, an electrode of about 200nm platinum (iridium, gold etc. can be used as well) is evaporated in the same processing chamber. The final platinum electrode structure is obtained after a lift-off process in acetone. The active contacts areas are then protected by a thin adhesive film before the final silicone encapsulation is spun on. A silicone for biomedical purposes is applied, which has to be ramp cured at 25°C for 30 min, 75°C for 45 min and finally at 150°C for 2.5 hours. The electrode itself is then cut from the polyimide foil and the active contacts are coated with iridium oxide. This step will be described in the next chapter. A cross-sectional schematic of the manufacturing process is shown in Fig. 2. The structured electrode has now to be coiled into the cuff accurately to keep the "spring-like" characteristic. To realize this, another polyimide foil is bonded to the back using silicone glue. Before bonding, one side of the new foil is encapsulated and cured by the same procedure as described before. Such a bi-layer sandwich structure is coiled to the desired diameter.

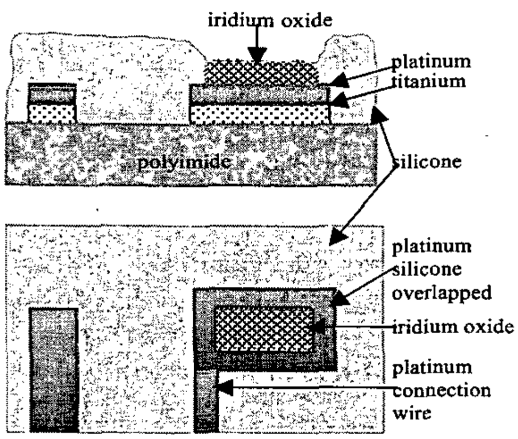

Fig. 2 Schematic view (not necessarily to scale) of the multilayer configuration used in the manufacture of a cuff electrode. A single active contact pad, partially overlapped by silicone to avoid polyimide / tissue contact and a silicone covered connection wire are shown.

After a drying process of the inlying silicone layer, the shear forces of the silicone keep the cuff in shape and give the required "spring-like" characteristic. The external wires are bonded with a silver paste and finally covered by silicone. Typically, cuff diameters between 1mm and up to 6mm can be reliably produced. Smaller diameters do not offer the required space to place a satisfying number of active contacts.

2.2. Iridium Oxide Coating

In the present study iridium oxide has been electrochemically deposited as an active coating. A normal tree-compartment glass cell was used, incorporating a platinum counter electrode and a saturated calomel electrode (SCE) as reference. Several substrates prepared as described before by electron-beam deposited iridium or platinum metal on either silicon wafer or polyimide foil have been used. Both metals, platinum and iridium are widely used in biomedical applications for many years. Iridium(IV)-chloride bound in a stable oxalic acid complex and dissolved in water served as electrolyte. The recipe for preparation is described elsewhere [30]. Substrates are first ultrasonic cleaned in acetone and isopropanol and then rinsed with de-ionized water. Before deposition, electrolytic cleaning is done by using cathodic current.

Cyclic voltammetry, often used in analytical electrochemistry is employed for iridium oxide deposition onto metals at room temperature. For better comparison, all samples were coated in the same manner using a potential cycling in the range between –300 and 800mV with a scan rate of 100mV/s.

3. RESULTS

3.1. Special Features of the Cuff

In order to achieve a reliable long-term interface to the nervous system, several requirements have to be met. Most important is the material selection. This nerve cuff electrode is based on widely used materials for implantations and bioapplications. This small dimension device creates much less disturbance in the surrounding tissue than conventional cuff electrodes. The contact design significantly improves the possibility for selective and spatial stimulation.

The special "spring-like" design of the cuff allows an easy implantation without having to suture it to the nerve. The flexible and very thin structure with the overall wrap thickness of 40μm minimizes considerably the weight of the electrode. This is of great importance to reach the stable and close contact without penetrating the nerve. Furthermore, long-term pressure impact, postoperative swelling or blood circulation disturbance of the nerve affected by cuff pressure is reduced or might even be completely prevented.

Position shifts and failure of the system due to breakage is avoided by such a flexible and light construction. The direct nerve contact results also in low power dissipation due to short pathways of the current which will cause lower stimulation currents to trigger off the action potentials. A high spatial selectivity is achieved by the configuration of eight active contacts uniformly distributed over the nerve perimeter. Each contact can be separately used for specific current contour manipulation. The number of contacts is chosen to match the number of output channels of commercial available stimulators.

3.2. Topography of Iridium Oxide

Iridium oxide coatings currently made by cyclic voltammetry show a high feasibility for application in neural stimulations. The adherence to thin iridium and platinum metals deposited on a silicon wafer or polyimide foil in specific thickness ranges is excellent. The settings of the deposition parameters, potential range, sweep rate, cycle number, temperature or even substrate precleaning have a significant impact on the final coating characteristics and depend strongly on the thickness of the metalization. A sweep rate of 100mV/s with potential range between –300 and 800mV applied at room temperature resulted in an uniform and smooth surface. The resulting thickness is controlled by the number of cycles. Cycle numbers around 100 turned out to be a good compromise between thickness (around 60nm) and adherence of the layer. Lower cycle numbers led to thin and "soft" layers with a low density, while higher numbers left a rough and cracked unusable surface. The same effect can be seen by expanding the potential range. Potentials above 850mV yielded in a strong and steep linear increase of the current to very high values (in the range of few mA) which resulted in diffusion restriction or even oxygen evolution. Fig. 3 shows an AFM picture of an optimized, smooth and dense layer with a roughness of about 15nm. It should be emphasized that the z-scale in the AFM picture is in the nm range. Single hemispheres can be seen with diameters up to 200nm.

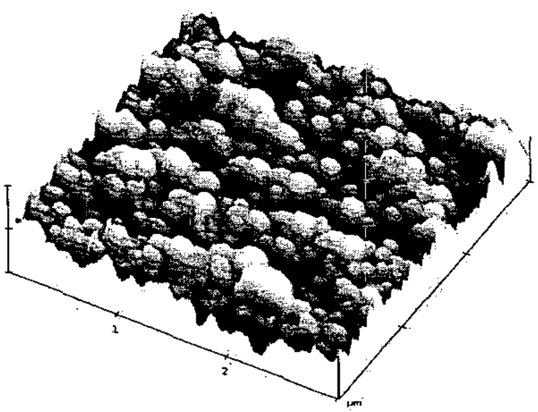

Fig. 3 AFM micrograph of an iridium oxide coated platinum surface. Z-scale 50nm, layer roughness of about 15nm on average.

3.3. Impedance Measurements

The reason for the low impedance of iridium oxide is the electroactive property of this material. Electroactive materials form a redox system, the applied potential connected with changes in oxidation states causes reversible proton incorporation into the layer. This is associated with a charge transfer across the interface between electrode and electrolyte, so-called phase boundary, resulting in increased current flow which decreases the interfacial impedance [30]. Other option to increase the capacity is an increase of the frequency and the enlarging of the electrodes' surface area by sintering, etching, or creation of fractal structures.

All impedance measurements were done in a standard phosphate buffered saline solution (PBS). Fig. 4 shows clearly the decreased impedance of iridium oxide compared to platinum and iridium in the frequency range below 100 Hz. This strong decrease can be explained by the electroactive behavior. For iridium and platinum electrodes capacity values of

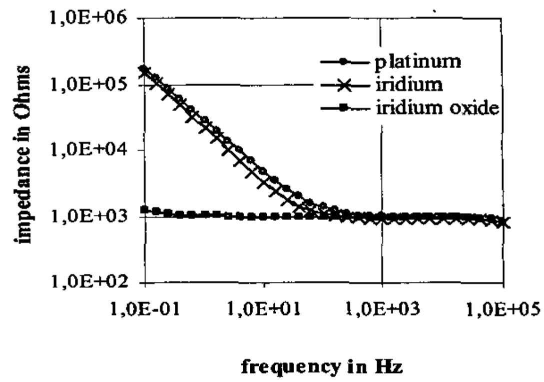

Fig. 4 Impedance spectrum of platinum, iridium and iridium oxide coated electrode, measured in a PBS solution.

about 15µF/cm² were achieved, while the iridium oxide coating increased the capacity up to 3,6mF/cm². For metals deposited on a silicon wafer, slightly lower capacity values were achieved as compared to polyimide substrates. This can be attributed to the roughness characteristic of polyimide. The impedance of iridium oxide electrodes stays low even for very low frequencies below one Hertz. That means that for example sensory systems based on iridium oxide can detect very low biosignals without distortions which reduces signal losses to a minimum value.

4. CONCLUSION

A thin-film nerve cuff electrode for neural stimulation was described. The implantable device is manufactured using common microelectronics techniques like contact photolithography, physical vapor deposition, and lift-off process, composed of platinum or iridium metalization with active contacts reinforced by iridium oxide. The iridium coating lowers significantly the interfacial impedance which enhances the capability for neural applications.

An insulating bi-layer polyimide foil serves as a flexible substrate with an optimum adjustment to the nerve shape. In addition, the self-sizing characteristics enhance the secure implantation. The flexibility of the cuff can automatically size itself to the nerve without occluding the blood flow. An additional silicone layer serves as passivation. Mechanical, electrical, and biological characteristics of the implant supports the assumption that this nerve cuff electrode can be a candidate for extended neuroimplant applications and not only for peripheral nerves.

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