A New Integration Method for Mounting and *in vivo* Handling of Sub-mm Flexible Cuff Electrode

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Abstract: Electrical stimulation of peripheral nerves is commonly used in both research and clinical fields. Cuff electrodes are one possible interface between nerves and the stimulation microsystem. Among cuff electrodes, flexible, polyimide-based devices have been demonstrating good and consistent results for the past 15 years. Regarding mounting and mechanical stability of flexible electrodes for *in vivo* trials, improvements are still due. A new concept aiming at the integration of polyimide-based devices in an elastic handling structure was developed. By taking advantage of PDMS elasticity and moulding, this new integration method provides surgeons with the ability to move and to rotate the cuff minimizing nerve-electrode contact and, consequently, nerve damages. A 9 parts stainless steel mould was designed and fabricated to allow integration of polyimide electrode arrays together with the PDMS mounting structure and a print circuit board. Furthermore, with the fabricated mould it is possible to achieve a final cylindrical channel with diameter of 800 µm, as well as handling strips to open and close the cuff.

1 INTRODUCTION

Electrodes are a key component in neural engineering applications, being used as both actuators and sensors, i.e. to excite neural tissue by electrical stimulation or to record bioelectrical signals from it. Therefore, implantable electrodes work as interfaces between neural prostheses and the biological tissue. Among others, potential applications of implantable electrodes for neural electrical stimulation range from restoration of walking (Gustafson et al., 2010) to vagal nerve stimulation (e.g., epilepsy treatment or heart rate control) (Connor et al, 2012)and bladder management in incontinence (Rijkhoff et al, 1997).

Geometrical configuration and dimensions of electrodes are strongly dependent on the size and morphology of target nerves. For cylindrical shaped nerves (e.g., sciatic nerve, vagus nerve) electrodes made of flexible substrates are a good solution because they can be wrapped around the nerve. Usually, this is made by means of cuff electrodes (Veraart et al, 1993). Cuff electrode diameters range from hundreds of micrometers (Rodrigues et al, 2012) to few milimeters. During the last two decades, improvements in the variety and in the complexity of electrodes for neural stimulation have provided new solutions in new applications fields (e.g., vagus nerve stimulation in epislepsy treatment (Englot et al., 2011, or the FINE electrode for walking restoration (Schiefer et al., 2008). Many of these clinical improvements were enabled through the development of micromachining technologies.

Polyimide-based electrodes have been demonstrating good and consistent results for the past 15 years. Polyimides have become an important and widespread used material for flexible electrodes due to its good adhesion to metals, long lifetime and low rate of water retention. Electrodes made of polyimide usually consist of a thin-film metallization sandwiched between two layers of polymer. Thin, uniform layers of polymer are achieved by means of pouring polyimide on the substrate followed by spinning. Therefore, the total thickness of a flexible, polyimide-based electrode is lower than 30 µm and *in vivo* handling conditions require a protective layer between the polyimide and the biological surrounding tissues.

Biomedical microsystems must fulfil different requirements for acute and chronic implantation. When using cuff electrodes for electrical stimulation of peripheral nerves, three of these requirements are:

1) a reliable method for cuff opening and closing (without damaging the nerve), 2) a mechanical, thus electrical, stable microsystem and 3) to protect the thin polyimide layers from potential damages when *in vivo*. In the present work, we these three practical challenges were addressed by designing and fabricating an elastic mounting structure. The fabricated mould with which it is possible to achieve the embedment of flexible electrode, silicon chip and the print circuit board (PCB) is presented. The used silicone is PDMS, a very used material in microfluidics and bio-MEMS applications, because it is easy to mould and biocompatible.

2 MATERIALS AND METHODS

2.1 Mounting Structure Design and Materials

Our goal is to build a system to allow integration of a flexible cuff electrode in an elastic mounting structure, thus providing surgeons and physicians with a tool to rotate or/and to move the electrode array along the nerve. The target nerve in our research is the rat vagus nerve – a cylindrical shaped nerve with a diameter of approximately 600 μm.

Fig. 1 shows a schematic of the proposed mounting structure plus schematic of integrated system and a 2-D view of the flexible electrode. In order to have enough room for the nerve a central channel with a diameter of 800 μm is designed – the cuff mounting channel. A cuff sustaining ring is designed with 3 mm in order to have a minimum amount of elastic material around the flexible polyimide. It keeps the cuff closed during implantation but also allows an easy opening. Handling strips allow positional adjustments during *in vivo* experiments, as shown in fig. 2. Re-positioning of electrode array around the nerve can be done by using tweezers for cuff opening. As the handling strips are released, cuff goes back to its original closing position, taking advantage of PDMS elasticity. Besides integration of polyimide electrode, the mounting structure was also designed to protect wire bonding (from chip to PCB), to integrate PCB and a connector (fig. 1B). A good alignment between the micro-fabricated electrode and the mounting structure is crucial, as the electrode array is designed to be wrapped around the cuff mounting channel. To facilitate the alignment between electrode and mounting structure, 4 guiding holes (1.05 mm in diameter each) were included in the polyimide layer (fig. 1C).
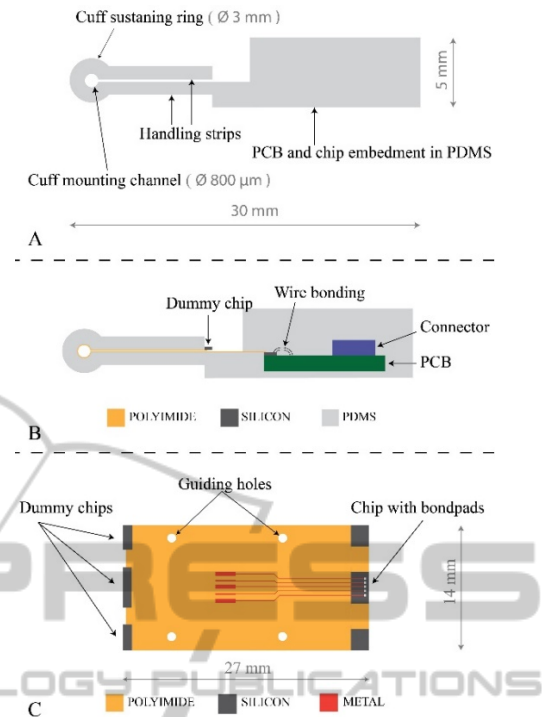

Figure 1: A. Cross section view of elastic mounting structure. B. Schematic of integrated microsystem. C. Top view of polyimide electrode array.

To fabricate the elastic mounting structure, a mould consisting of 9 main parts was designed and fabricated. Then, polydimethylsiloxane (PDMS, Sylgard 184, Dow Corning) was poured and cured inside the mould. Sylgard 184 consists of two parts: elastomer and curing agent. These two parts were mixed at 10:1 ratio (10 parts of elastomer - 1 part of curing agent), very well mixed and degassed. For the curing of PDMS, a short period of 30 min at 65 ºC was used.
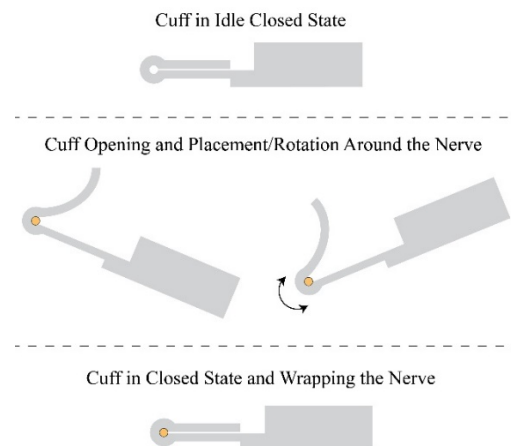

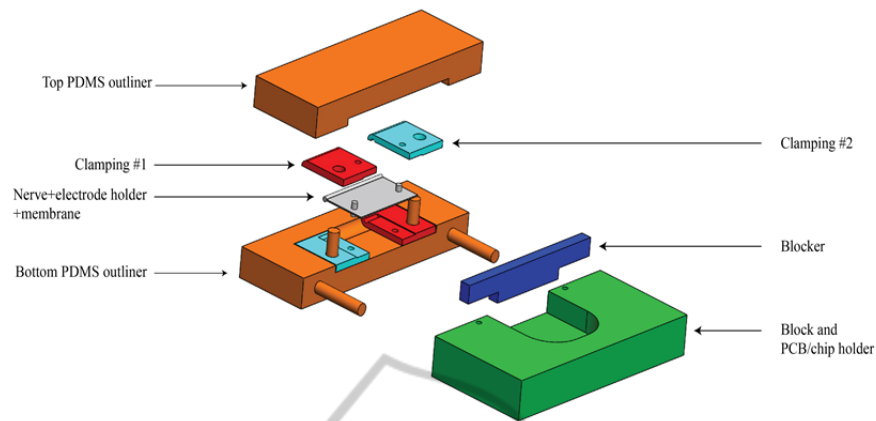Figure 2: Operational states of the elastic mounting structure.

Figure 3: Exploded view of designed mould parts. Identification of each part by a label name.

2.2 Mould Design and Material

To realize the elastic mounting structure using PDMS, a mould composed of 9 different parts was designed using Solidworks 2013. Fig. 3 shows an exploded view of the 9 parts of the mould. The design was made in order to achieve the following characteristics: 1) leak tight, 2) easy assembly/disassembly and 3) straightforward mounting of flexible electrode using the 4 guiding holes. Due to PDMS viscosity in its uncured stage, gaps higher than 20 µm between mating parts can origin a leak. So then, tolerances were kept as high as 10 µm. Few pillars were introduced to align mould parts and 2 mounting pillars (1 mm in diameter) were designed specifically for the alignment of the flexible electrode, by using the 4 guiding holes. These 2 mounting pillars are the smaller ones in the clamping parts (fig. 4).

Clamping parts fix the flexible electrode wrapped around the 'Nerve+electrode holder+membrane' part. This clamping mechanism is responsible for alignment of flexible electrode in the mounting structure.

Thickness of handling strips (1 mm) is given by the thickness of clamping parts, as shown in fig. 4 and shaping of the cuff sustaining ring is given by circular grooves in Top and Bottom PDMS outliner parts. PDMS moulded by 'Block and PCB/chip holder' part sustains the PCB and protects the chip and the wire bonding area.

Stainless steel was chosen as material for the moulding fabrication because of its high stiffness (which reduces risks of breakage during cleaning) and also because it is easy to clean by acetone and isopropanol.

'Nerve+electrode holder+membrane' part is composed by 2 independent parts: 1) a 200 µm sheet
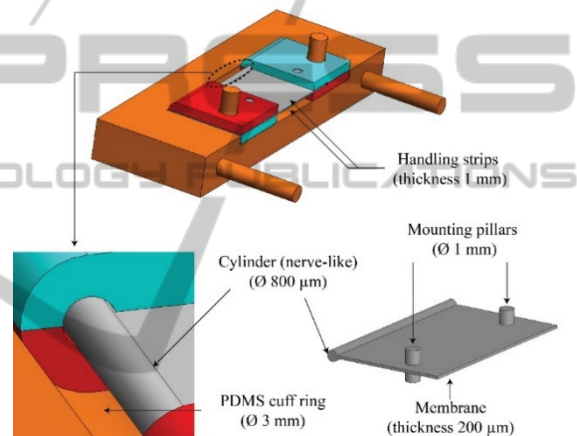

Figure 4: Close-up of the clamping mechanism to mount the flexible electrode.

of stainless steel with holes made by electrical discharge machine (EDM): membrane and 2) a cylinder with diameter of 800 µm coupled to the membrane. These two parts are coupled together by a longitudinal groove all along the cylinder, where the membrane mates. This groove is also made by EDM using a wire of 100 µm in diameter.

The mounting pillars are not solder to the membrane. Also the grooves in the clamping parts were made by EDM. All the other parts were made by normal milling machines.

Fig. 5 depicts the final assembly of the mould. All parts mate together. PDMS can be poured inside, before adding the 'Top PDMS outliner' part, to check for possible air bubbles. And it is also be poured after mating all parts together, to make sure that silicon, wire bonding and PCB are protected.
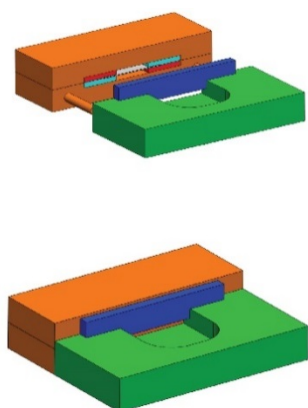
Figure 5: Final assembly of mould.

3 RESULTS

Some of fabricated parts are shown in fig. 6 and fig. 7. In fig. 6 it is emphasized the 200 μm thick membrane sandwiched in between the 4 clamping parts. Fitting pillars to mate different parts are also visible as well as the simmetry of the entire mould, which is import to achieve a stable and working mounting structure. Also, low roughness of the fabricated stainless steel parts is important to avoid air bubbles inside PDMS.
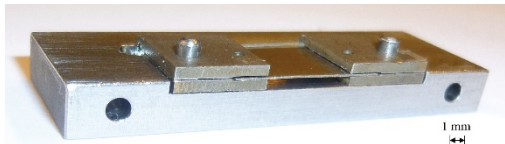

Figure 6: Some of the fabricated parts. Membrane is 200 μm.

In fig. 7, 'Bottom PDMS outliner', 2 clamping parts and the 'Nerve+electrode holder+membrane' part are shown. The cylinder of the former part is well aligned with the grooves in the clamping parts. Also the cylinder (nerve-like) is well aligned with the grooves in the 'Bottom PDMS outliner', which contributes for a good alignment of the flexible electrode with PDMS cuff ring.

The 200 μm thick membrane could be very well fitted in the mounting pillars, which also contributed for a good alignment. In our first trials, PDMS was poured before placing the 'Nerve+electrode holder+membrane' which led to less air bubbles in the final moulded mounting structure.

In fig. 8, the part 'Nerve+electrode holder+membrane' is shown in detail. To prevent damages (like bending) to the membrane it has to be handled by tweezers. And also to prevent the stick
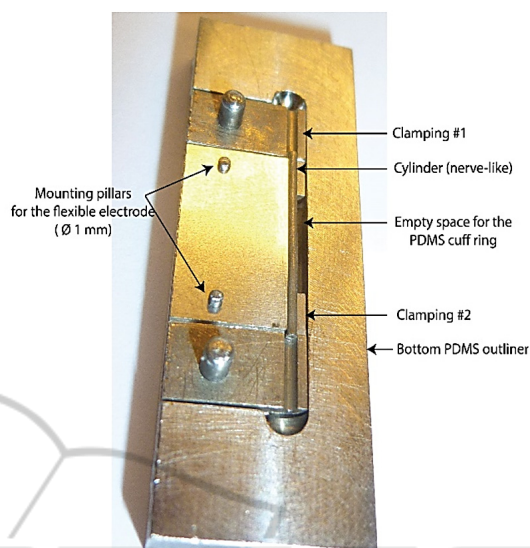

Figure 7: Alignment of cylinder (nerve-like) with the clamping parts and with the groove for the PDMS cuff ring.

and the membrane to detach from each other.

After few moulding iterations, we have not seen any signs of reactions between the mould parts and the PDMS. We also report that, acetone and isopropanol are good cleaning agents for the stainless steel parts after PDMS moulding. However, if between moulding iterations cleaning is not well done in all small features, some residues might prejudice the next procedure.

3.1 Elastic Mounting Structure

In fig. 9 it presented one mounting structure after being moulded and removed from the mould. It is in the closed idle state, so the two handling strips are closed and the cuff channel can be seen in the bottom part of the figure. Total width is about the diameter of a euro-cent coin, while the length is slighty bigger.

In fig. 11, it is shown a cuff opening technique by using a tweezer. It is possible to open the cuff just by pulling the handling strip, so without using high force. This is important to: 1) preserve, in a future prototype, good adhesion between the flexible polyimide electrode and the elastic mounting structure and 2) cuff position around the nerve can be adjusted without damaging the nerve.

Final moulded structure showed a good overal mechanical stability and also a good opening and closing procedures due to PDMS elasticity after being cured.
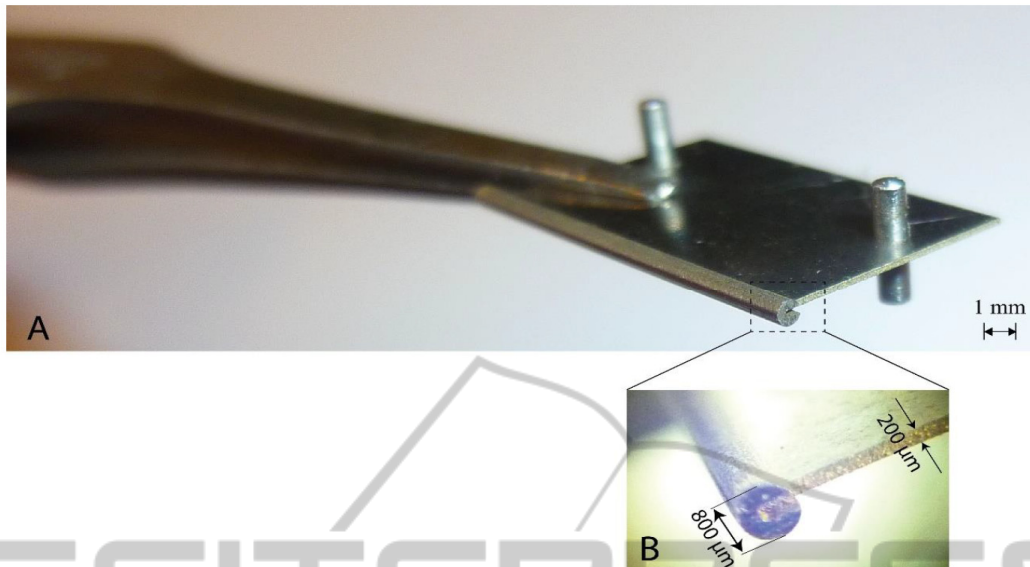
Figure 8: A. Close up view of the 'Nerve+electrode holder+membrane' part. B. Microscopic image of the slot made by EDM to join membrane and stick together.
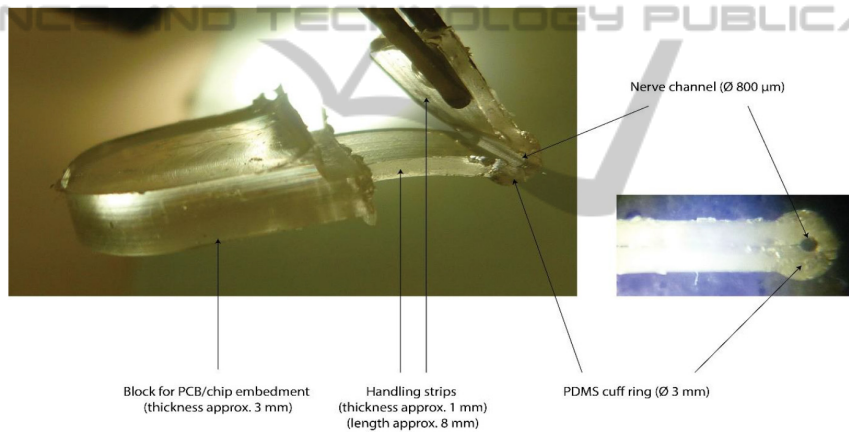

Figure 10: Left: Elastic mounting structure in its open state. Right: close up of the nerve (cuff) channel when the structure is in its closed state.
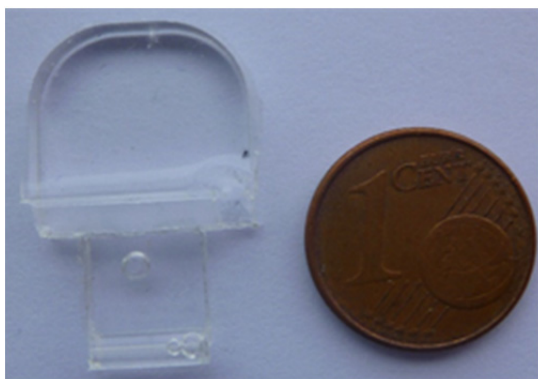

Figure 9: Moulded mounting structure (without integrated flexible electrode and PCB).

4 CONCLUSIONS AND FUTURE WORK

A mould made of stainless steel was fabricated. The presented mould is used to realize an elastic structure which is a useful tool for implantation of a cuff electrode around a nerve. Gometrical features of the elastic structure were based on anatomical and surgical constraints faced during *in vivo* tests in the rat vagus nerve.

The integration of a flexible electrode in the moulding step is under study. The final goal is to achieve a fully embedded system for electrical stimulation of the rat vagus nerve.

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