31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Design and Fabrication of Neural Implant with Thick Microchannels based on Flexible Polymeric Materials

Samia. Benmerah, Stéphanie P. Lacour (IEEE Member), Edward. Tarte

***Abstract*—Mechanical guidance can be used to provide a supporting structure through which and onto which regenerating axons can grow. The dimensions of the mechanical guide need to be suitable to support regenerated axon outgrowth and vascularisation. In this paper, we present the design and fabrication process of a three-dimensional (3D) device comprising a bundle of parallel (100µmx100µm) microchannels with embedded electrodes. This device can be used as a 3D electrode interface for peripheral nerve repair. The skeleton of the device is entirely made of flexible polyimide films. Gold microelectrodes and microchannels of photosensitive polyimide are patterned directly on polyimide substrates. After fabrication, the 2D electrode channel array is rolled into a 3D channel bundle that fits the anatomy of the peripheral nerve. Samples are rolled and inserted into 1.5mm inner diameter tube.**

I. Introduction

WHEN the peripheral nerve is injured, the distal part of the nerve that is disconnected from their cell body degenerates while its proximal section still connected to the cell bodies in the dorsal and ventral ganglion roots, regenerates. When the gap between the two nerve endings is short, a direct tension free suture constitutes the best chance for good functional recovery [1]. However, when the gap between the nerve endings does not allow for a direct suture, an artificial bridge, in the form of hollow tube whose internal diameter matches nerve's diameter, can be used. Because of the huge number of axons in a single nerve, regenerating fibers are often misrouted to the wrong receptor cells, resulting in poor functional recovery [2]. In cases where the functional recovery post the lesion is not achieved or when there is complete amputation of the limb, finding a method for extracting neural signals and identifying the regenerating fibres would be very useful. The extracted and processed signals could then be used to drive muscle simulators or supply input signals to prosthetic limb.

Recording extracellular signals from myelinated axons is challenging as the amplitude of the recordable signal is small (a few µV) and depends heavily on how close the recording electrodes are to the nodes of Ranvier. Accurate positioning of electrodes in such circumstances is extremely challenging as one can not predict where the nodes of Ranvier will be located on the regenerating axons [3]. A way of solving this problem was recently reported by Fitzgerald et al. They found that confinement of axons in microchannels removes the dependence of the recorded extracellular signal amplitude on the proximity of a node of Ranvier [4]. In brief, the microchannels act as axonal signal amplifiers where the axons' confinement in the insulating channels increases the electrical resistance of the extracellular medium leading to an amplification of the recordable extracellular potential [3]. We believe confinement of the regenerating axons into microchannels will not only provide mechanical guidance but also will allow axonal extracellular signals to be reliably recorded.

We have already reported that two dimensional (2D) arrays of microchannels, ranging in width from micrometers to hundreds of micrometers and few micrometers in height, can provide good mechanical guidance for neurites *in vitro* [5].

We have also investigated the electrical properties of microchannels for recording and stimulating nerve fibres through an *in vitro* study. Action potentials of nerve fibres, inserted through long channels with diameters ranging from 90 to 130µm, were reliably recorded and efficiently stimulated [3].

In this paper we present how we are integrated those findings into a three dimensional electrode interface which is designed as a three dimensional bundle of closed 100µmx100µm square microchannels hosting gold microelectrodes. The design of the individual microchannels not only simply provides mechanical guidance to regenerating axons but also enables the reliable recording of signals from myelinated axons through embedded electrodes. The implants are produced using polyimide films and planar microfabrication technology. The extreme flexibility of the polyimide films, allows the 2D array of microchannels to be rolled and inserted into a suitable silicone tube whose diameter matches that of the nerve. This produces a 3D bundle of parallel microchannels with embedded microelectrodes designed to withstand the rolling without any mechanical fracture hence no electrical failure.

Manuscript received April 7, 2009. This work was supported by EPSRC-MR Basic Technology Program under the Grant EP/C52330X on "Bioelectronics Interfaces for Peripheral Nerve Repair" and a University Research Fellowship from the Royal Society awarded to SPL.

S. Benmerah is doing her PhD, at the University of Birmingham, which is partially sponsored by the school of Engineering, Edgbaston, Birmingham, B15 2TT, UK. (Email: sxb288@bham.ac.uk).

S. P. Lacour, is with the University of Cambridge, Nanoscience Centre, 11 JJ Thomson Avenue, Cambridge CB3 0FF, UK (Email: spl37@cam.ac.uk). She is now a University Research Fellow of the Royal Society and is coordinating a multidisciplinary team that develops compliant bio-electronic implants for nerve repair. She is also a research fellow of King's College in Cambridge

E. J. Tarte is with the University of Birmingham at the School of Engineering and Physical Sciences, Edgbaston, Birmingham B15 2TT, UK (Email: e.tarte@bham.ac.uk).

We first present the design considerations that lead us to choose the dimensions of the implant, such as channels size, length, and then describe the complete fabrication process of this polymeric implant. Then we detail the fabrication and assembly process of our 3D electrode implants.

II. Implant Design

Polyimide was chosen as the base material for the implant because of its biocompatibility, flexibility, and the availability of photo-sensitive polyimides which can be processed a one-step photolithography. The biocompatibility of the polyimides was evaluated and confirmed through both *in vitro* and *in vivo* studies [3], [6].

The three dimensional implant consists of concentric rolled layers of microchannels with embedded microelectrodes. The implant is made of four layers fabricated using polyimides and planar microfabrication technology. The first layer is the substrate film which is the structural base for the rest of the implant layers. The second layer is the microelectrode metallic layer. The third layer is the encapsulation film which electrically insulates the electrodes from each other and only exposes the recording sites. The fourth layer is that of the channel and is patterned so that the electrodes are exposed in the middle of the channels. The two dimensional implant is then rolled and inserted into a silicone tube of a suitable diameter.

The dimensions of the microchannel required for maximum regeneration were decided based on the result of axonal regeneration as a function of microchannel dimensions. These include the channel cross-sectional area which chosen to be 100µmx100µm and the spacing of the channels set to 50µm. The thicknesses of the substrate and the insulation layers decide on the vertical placement of the microelectrodes inside the microchannels. These thicknesses were selected to be 25µm and 5µm respectively. These thicknesses ensure that the strain on the microelectrodes in the rolled structure remain low (<< 1%) and does not lead to mechanical fracture of the microelectrodes.

A. The dimensional parameters of Microchannels

The channel dimensions were selected based on the regeneration results through a set of prototype implants investigated in a series of studies detailed in [3]. We have previously evaluated axon outgrowth through two dimensional arrays of polyimide microchannels as a function of channel width, spacing, and pitch *in vitro*. The channels were prepared by casting polyimide on a silicon mould to form the arrays [5]. It was found that the efficiency with which axons enter the channels is maximal when microchannels are wide (>30 µm), and when the array transparency (the channel width to pitch ratio) is at least 50%.

A further study evaluated the *in vivo* axon outgrowth and vascularisation through silicon and PDMS microchannels in order to investigate the effect of channel dimensions (channel width, height, length and channel spacing) on regeneration. Channels with the 100µmx100µm cross-sectional area supported the biggest number of myelinated axons. It was also found that regeneration through long channels (with length greater than 2mm) can be supported because blood vessels, which provide oxygen and the necessary nutrients, also grow with the regenerating tissue into the channels [3].

B. Design of electrode placement

Encasing axons in a microchannel provides signal enhancement. We found that the extracellular signal reaches its maximum amplification at the centre of the channel and decays at the channel ends [4]. For this reason the recording electrodes were placed halfway through the channels' length.

The rolling of the structure results in compressive strain in

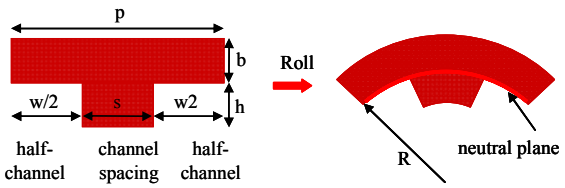

Fig. 1: T-shaped section in the implant structure before and after the rolling.

the inner rolls that may reach a few percents. The flexibility of the Polyimide layers allows them to withstand high strain but careful design needs to be implemented to protect the thin metal electrodes. If the metal film of the electrodes is overstrained, a mechanical fracture will result and lead to electrical failure. One way around this problem it to position the electrode layer at or as close as possible to the rolled structure's neutral plane where the bending strain is close to 0% [5]. This will protect the embedded electrodes from fracture caused by tight rolling of the structure. This is achieved by optimizing the implant parameters which include: the thickness of PI substrate (*b*) and the thickness of the insulation layer (*i*). Equation (1) calculates the position of the neutral plane in the T-shaped cross-section structure shown in Fig. 1.

$$y_{neutral} = \frac{pbh + 0.5pb^2 + 0.5sb^2}{pb + sh} \quad (1)$$

$$p = w + s$$

Where $y_{neutral}$, *p, b, h, s, w* are the neutral plane, the channel pitch, the substrate thickness, the channel height, the channel spacing and the channel width respectively [5]. Therefore, according to equation (1) and the process flow (to be described later), the electrodes will be placed at the

structure's neutral plane when: $y_{neutral} = h + i$ where i is

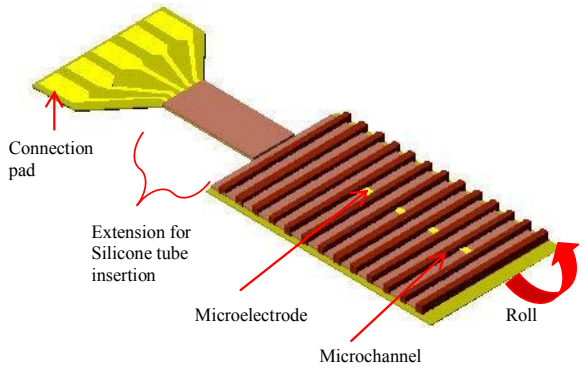

Fig.2: the design layout of the implant before rolling showing location of channels, electrodes and the connection pads and the extension to allow for silicone tube insertion.

the insulation layer's thickness. For example, with the required dimensions of 100µm channel height, 100µm channel width, 50µm channel spacing and an insulation layer thickness of 5µm , the substrate thickness should be 25µm.

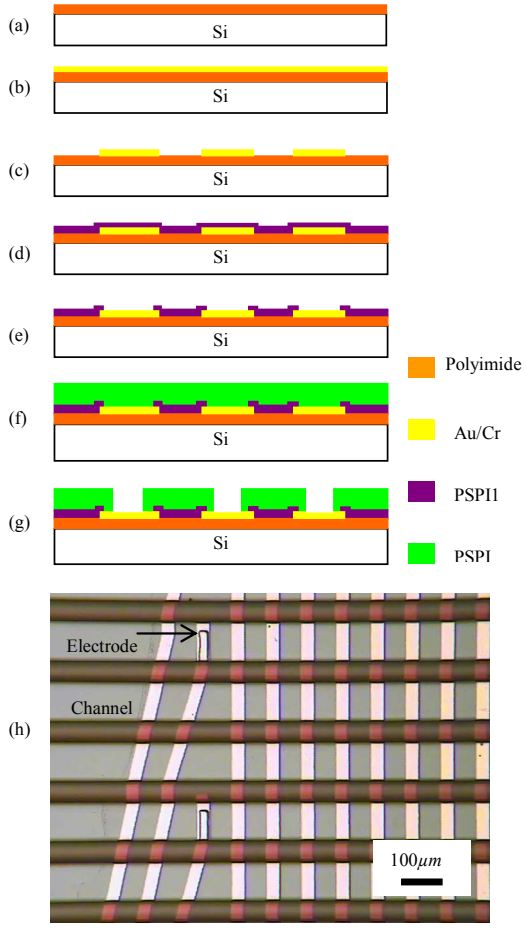

Fig. 3: (a) the fabrication process of the 2D micromicromicrochannel arrays with embedded electrodes. (b) An optical micromicromicrograph of an array of micromicromicrochannels with their embedded and exposed micromicromicroelectrode recording sites.

We designed implants with 20 electrodes, which are evenly distributed across the central layers of the rolls and located all at the centre of their channel. The extension shown in Fig. 2 allows for the insertion of Silicone tube on either sides of the implant while allowing the contact pads to be accessible. Two lengths are chosen for the implants; short implants are 2.5mm long, and long implants are 4mm long.

III. IMPLANT FABRICATION

A. Material

Implants are fabricated using nonphoto-definable and photo-sensitive polyimide (PSPI) materials. Polyimide (PI), Pyralin2611, is supplied by HD Microsystems, and the Photo-definable Durimides (7505 & 7020) are supplied by Fujifilm. Pyralin 2611 PI is widely used in neuro-prosthetic implants because of its suitable properties in biomedical applications. These properties include biocompatibility, low water uptake, good thermal stability and electrical insulation properties. Durimides PSPI, on the other hand, are photo-definable polyimides and, hence, can be patterned photolithographically. The biocompatibility of Durimides has been proven *in vitro* and is being evaluated in *vivo*. The microelectrodes are made of patterned gold films which are thermally evaporated on the substrate.

B. Fabrication process

The 3D polymeric implant with embedded microelectrodes is fabricated following the process flow presented Fig. 3. The recording sites of the microelectrodes are incorporated into the microchannels and exposed in the target channel through windows in the insulation layer. The electrodes are accessible through contact pads which are used to connect the implant to IC circuitry.

The substrate is prepared by spinning the PI2611 on a silicon wafer Fig. 3a. Two spins are required to reach the 25µm thick substrate. The first PI spin is to produce a thin substrate layer which adheres well to the carrier wafer to allow for subsequent processing but can also be easily peeled off to release the device. The second PI spin brings the substrate thickness to the required value. The samples are fully cured after each spin at 350 C in N2 environment. An adhesion promoter is used to enhance adhesion between the two spins of the substrate and prevent delamination.

The metallic thin layer, which consisted of an adhesive Chromium layer with a thickness of 5nm and a Gold film with a thickness of 175 nm, is thermally evaporated on the PI substrate and patterned using photolithography Fig. 3b-c. Because of the toxicity of Chromium, Titanium adhesive layer will be used instead in future devices.

Electrode leads are encapsulated by a 5µm thick PSPI layer made of durimide 7505 PSPI Fig. 3d-e. The window openings in this encapsulation layer form 30µm×100µm recording sites and 0.3mmx1mm contact pads for connection

to off-board electronics.

The 100µm thick PSPI layer is prepared by spinning durimide 7020 at a suitable speed Fig. 3f-g. After pre-baking the layer at a very slow and smooth temperature ramp, the layer is exposed and developed to define the microchannel

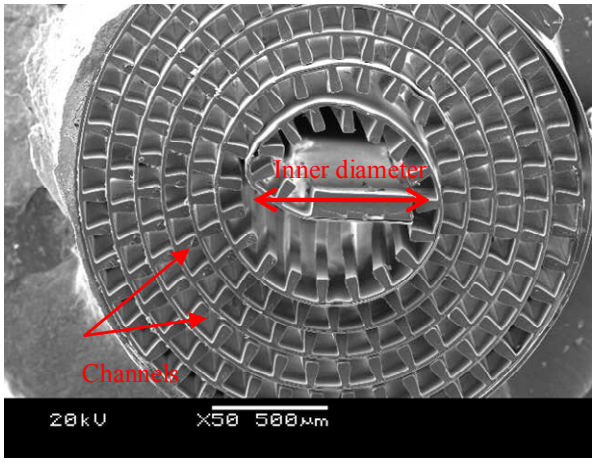

Fig. 4: An SEM of the 3D implant obtained by rolling the 2D channel array and then inserted into a silicone tube.

arrays. The processed wafer is cured at 350◦C in a N2 environment and then peeled of the carrier wafer. The two dimensional channel arrays are rolled up along the channel length and then placed in silicone tube to fix and support the 3D structure. Fig. 3h shows an array of 100µmx100µm sized microchannels with their embedded microelectrodes while Fig. 4 shows an SEM image of the rolled implant.

IV. Making The thick PI channels

A. *Spin coating speed and spin time*

To obtain a 100µm PSPI layer, the spin speed and the spin time were first varied to determine the values that can give the required layer thickness. It was experimentally found that a 100µm thick polyimide layer can be obtained by spinning at 300 RPM for 60 seconds.

B. *Pre-baking regime for 100µmx100µm channels*

During the pre-baking step, the solvent is partially evaporated from the polyimide to allow the photosensitive cross-linker to cross-link successfully during the exposure step. Making thick PSPI channels (100µmx100µm) requires a very slow and smooth ramp of temperature during the pre-baking step. If the temperature ramp is not slow enough, the evaporation rate of the solvent will be too fast leading to the formation of bubbles and shrinkage in the layer. In addition, a slow and smooth pre-baking step reduces the stresses within the film and prevents cracking during curing.

V. Conclusion

We have successfully updated the design and fabricated a polymeric 3D implant composed of large microchannels. The optimal dimensional parameters of the implant were determined through earlier in vitro and in vivo studies. This paper shows that we can make such devices using conventional planar microfabrication. The implants, made of polyimides, have 10,000µm^2 microchannel cross-section separated by 50µmx100µm wide polyimide walls. The substrate capping each channel in the roll is 25µm thick. The channels have a square cross-sectional area. Each implant is designed to fit a rat sciatic nerve (outer diameter of 1.5mm), and hosts a total number of 150 microchannels and 20 electrodes. The microelectrode recording sites are 30µmx100µm sitting on the PI substrate. We are now working on interfacing the implants with electronics, and evaluating nerve regeneration through those novel 3D channel bundle arrays.

References

[1] X. Navarro, E. Verdú, “Cell transplants and artificial guides for nerve repair, in: T. Herdegen, J. Delgado-García (Eds.), Brain Damage and Repair”, *Kluwer Academic Pub*, 2004, pp. 451–471.

[2] X. Navarro, T.B. Krueger, N. Lago, S. Micera, T. Stieglitz, P. Dario, “A critical review of interfaces with the peripheral nervous system for the control of neuro-prostheses and hybrid bionic systems”, *J. Peripher. Nerv. Syst.*, 2005, pp. 229–258.

[3] S. P. Lacour , J. J. FitzGerald , N. Lago, E. Tarte, S. McMahon, J. Fawcett[2] “Long microchannel electrode arrays: a novel type of regenerative peripheral nerve interface”, under review.

[4] J. FitzGerald, S. Lacour, S.McMahon, J. Fawcett, “Microchannels as axonal amplifiers”, *IEEE Trans. Biomed. Eng. 55*, 2008, 1136–1146.

[5] S. P. Lacour, R. Atta, J. J. FitzGerald, M. Blamire, E Tarte, J. Fawcett “Polyimide microchannel arrays for peripheral nerve regenerative implants”, *Sensors and Actuators A147*, Jun 2008, pp. 456-463..

[6] Y. Sun, S. P. Lacour, R. Brooks, N. Rushton, J. Fawcett, and R. Cameron, "Assessment of the biocompatibility of photosensitive polyimide for implantable medical device use," *Journal of Biomedical Material Research A,* pp. on-line, 2008