Packaging Design for Implantable Microstimulator

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Abstract

Implantable biomicrosystems for restoring neuromuscular functions have gained more attention for studying the characteristics of various types of neural interfaces. In our previous study, we have developed a microprocessor-based microstimulation system by using the surface mount device (SMD) components on printed circuit board (PCB) and stimulating electrodes, prepared for implantation into animal on neuromodulation studies. The aim of this study is to investigate the feasibility of packaging design of an implantable microstimulator. In current study, Micro Electro Mechanical System (MEMS) fabrication process for microassembly and interconnection on flexible polyimide substrates was employed to integrate microstimulator circuitry and nerve cuff electrodes as an implantable biomicrosystem for peripheral nerve applications to achieve a module package. The flexible mechanical structure design of microstimulator is more suitable for module design and implantation purposes. Dam-and-fill process was applied to seal the module, which was later encapsulated with medical grade silicone rubber for biocompatible package. The implantable microstimulator measured at 4 cm in diameter and 8 mm in height with cuff electrode interconnected to it. Finally, *in-vitro* experiment in the normal saline has confirmed that it is feasible to employ dam-and-fill encapsulation and medical-grade silicone rubber to package the biomicrosystem for a period of 30 days. The microstimulator is undergoing *in vivo* tests through the implantation of implantable microstimulator for stimulating rabbit's sciatic nerve.

***Keywords*:** Hermetic packaging, Implantable microstimulator, BioMEMS, Biomicrosystem, Polyimide

Introduction

Research has shown that modulated stimulating current can activate the residual but intact sensory or motor nerves in order to generate sensation or functional movements. Therefore, using electrical stimulation to generate the artificial action potential, resembling real action potential is widely applied to innervate the dysfunctional organs. Among various applications, functional electrical stimulation (FES) has been employed to restore the deprived motor or sensory functions. For example, FES has been applied for movement control of paralyzed patients with spinal cord injury (SCI), in case that the peripheral nerves and muscles remain intact but lose the ability to activate them voluntarily. Among various FES applications, implantable microstimulator has been designed to be placed closely to the stimulation site and in an attempt to obtain more sophisticated movements.

In a boarder aspect, the implantable microstimulator can be considered as an actuator type of biomicrosystem. Currently, biomicrosystem including actuators, sensors or integration of them might utilize well-developed technology currently used in integrated circuits (IC) industry. As implantable biomicrosystems become more complicated, MEMS technology has been increasingly applied for developing implantable biomedical devices. These advanced microtechnologies generate new opportunities for the development of active implants that go beyond the design of current implantable devices. These microimplants demand a high level of device miniaturization without compromising on design flexibility and biocompatibility requirements. However, there are a number of difficulties, including miniaturization in size, low power, functional versatility, and stable and biocompatible packaging. More and more research groups are leaning to apply the micro-fabrication technology for the implantable or wearable/portable biomedical devices.

In general, a biomicrosystem consists of signal transduction and processing units, and the electromechanical packaging. The purpose of packaging is to provide mechanical support, electrical interconnection, and protection to the internal circuitry from all possible attacks from mechanical and environmental sources. In common with IC packaging,

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Table 1. Physical properties of Durimide 7320

	Cured polyimide Durimide 7320	Units
Tensile Strength	215	MPa
Tensile Elongation	85	%
Young's Modulus	2.5	GPa
Glass Transition Temperature	285	°C
Coefficient of Thermal Expansion	55	ppm/°C
Dielectric Constant @1MHz 0~50% RH	3.2~3.3	
Dielectric Strength	345	V/μm
Dissipation Factor @1MHz 0~50% RH	0.003~0.008	
Density	1.39	g/cc

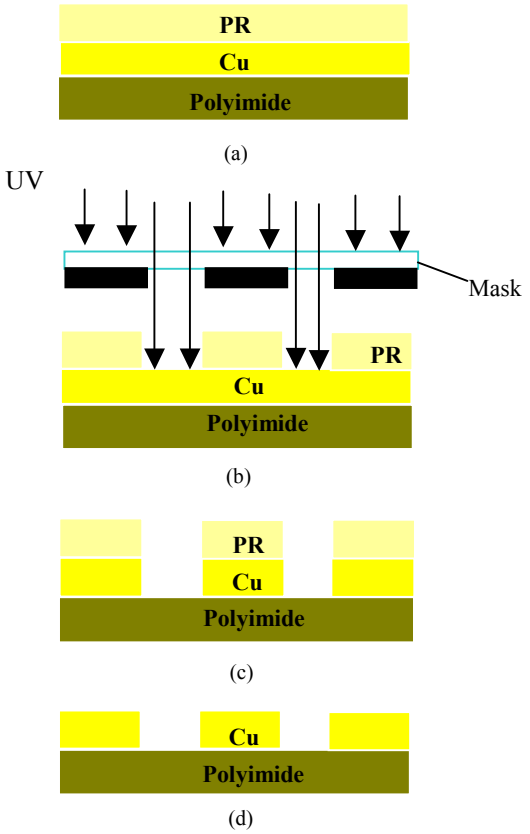


Figure 1. Schematic diagram of the fabrication process for RF circuitry.

one of the major roles of packaging is to ensure structural stability for the biomicrosystem. Successful packaging design requires the knowledge and detailed understanding of package and material issues, the behavior of the device and its reliability. On the other hand, biocompatible packaging requires accomplishing those required by microelectronics packaging, with additional requirements to expose the device for direct contact with human tissue. Thus, one of the fundamental differences between microsystem and IC packaging is that the microsystem generally interacts with the implanted environment. An implantable device could induce immune reaction when it is implanted into human body. To achieve hermetic packaging with biocompatible materials for biomicrosystem is urgently required to protect the implantable devices from hostile environment that could damage the normal function of the microsystem in the package. Hermetic and biocompatible packaging for an implantable device not only prevents the microsystem from corrosive environment to ensure the normal operation of the device but also can reduce the damage of tissue surrounding the implanted site. In addition, hermetic packaging for implantable biomicrosystem is a critical factor in commercialization of biomicrosystems.

Among varied packaging technologies, anodic bonding and Microflex techniques have been recently developed for packaging and feedthrough layout for glass and polymer substrates, respectively. Anodic bonding technology is used for bonding glass to polysilicon substrate [1-6]. To form a permanent bond between the glass capsule and polysilicon substrate, Najafi *et al.* developed a single-channel implantable microstimulator for functional neuromuscular stimulation [7], which can be implanted near the individual target through a gauge-12 hypodermic needle. Another approach for fabrication of glass capsule of microstimulator is BION1[8-12]. The whole device was packaged into a glass capsule, made of Borosilicate glass (Kimble N51A), to avoid the penetration of body fluid. The interconnection between internal circuitry and electrode was connected by Ta feed-through. The glass capsule packaging technology requires Infrared CO2 laser and YAG laser. In addition to bonding technology for glass substrate, polymer-based biocompatible packaging has long been a popular approach for implanted device. Recent development of Micro-Flex Interconnection (MFI) technology[13-16] has been used to interconnect flip-chip and electronic devices for implantable device. MFI technology mainly utilized lithography technique to generate a piece of thin-film layer on polyimide substrate to provide contact area between silicon wafer and aluminum. A rivet-like bump is used to electrically and mechanically interconnect the components and contact area. The distance between two contact areas could be less than 100 μm.

The aim of the study is the biocompatible packaging design of our previously developed implantable microstimulator [17]. Our strategy is to apply off-the-shelf technology to design an implantable microstimulator with flexible mechanical structure. MEMS technology is employed to integrate the implantable microstimulator with cuff electrodes on the polyimide substrate. The silicon rubber is selected as a candidate for the packaging material. Furthermore, silicon rubber serves as the biocompatible interface between living tissues and microstimulator due to its biocompatibility and easy process.

Materials and Methods

Ideally, an implantable biomicrosystem has to fulfill different requirements for a long-term implantation. There is no degeneration should occur in physiologic environment. All

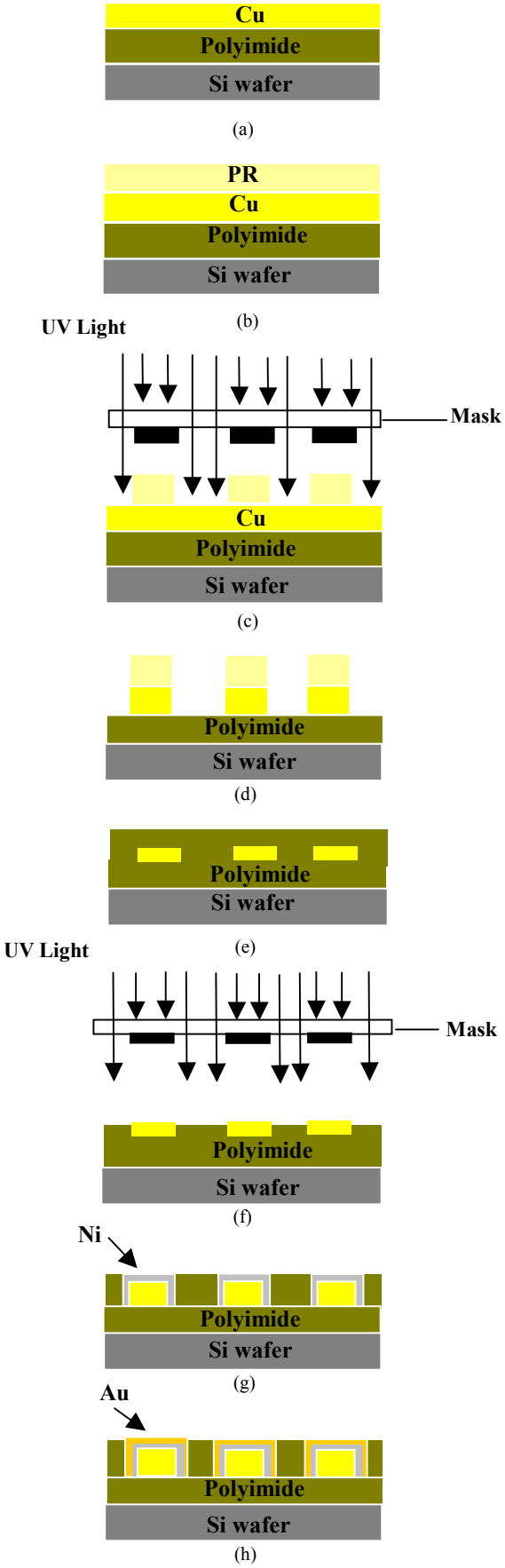


Figure 2. Fabrication process for stimulation electrodes.

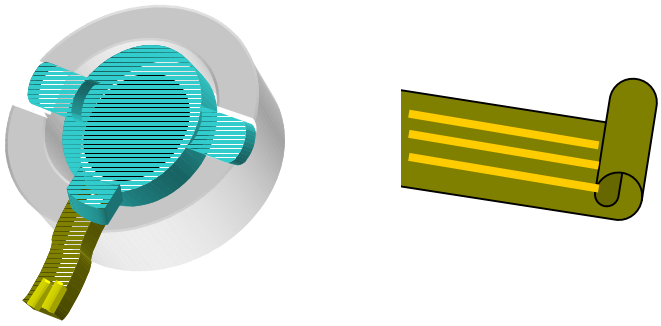
parts of a biomicrosystem not only have to be stable in the human body but also have the flexible mechanical geometry. For the development of highly flexible, ultra-light weighted implantable biomicrosystem, we choose polyimide (Durimide 7320) as substrate. The polyimide-based printed circuit boards are micromachined, on which SMD such as resistor, capacitors and ICs are mounted. Compared to other silicon-based substrate such as silicon oxide and silicon nitride, polyimide equipped with similar insulation resistance and dielectric strength at a lower density and a higher flexibility (Table 1). In addition, polyimide substrate can easily be processed with standard clean-room fabrication processes.

Fabrication of circuitry and stimulation electrode

The fabrication processes were divided into two major parts: fabrication of circuitry for microstimulation and stimulating electrodes. Figure 1 depicts the fabrication process for the circuitry of microstimulator. In the first step, a piece of polyimide substrate with a layer of cooper plated on it was spun with photoresist (Shipley S1818) (Fig.1 (a)) by using spin coater and was baked on a hot plate. IA well-defined mask was applied to exposure process to pattern desired circuitry on the photoresist and then the device was put in the specific developer (Fig.1 (b)). Finally, the device was etched in Ferric Chloride liquid with heated stirred bath at 45^{o}C (Fig.1 (c)) and was removed photoresist by Acetone (Fig.1 (d)).

The process for fabrication of stimulation electrode is similar to that of microstimulator circuitry. A layer of polyimide with a layer of copper film plated on was attached onto a silicon wafer, which served as a support structure during the process (Figure 2 (a)). A layer of photoresist was spun onto the copper layer (Figure 2(b)) to pattern the electrode (Figure 2 (c)) using a designed mask. The copper etchant was applied to the next step (Figure 2 (d)). A layer of polyimide was then spun on it to act as an insulation layer (Figure 2 (e) with stimulating site opened by polyimide etchant (Fig. 2 (f)). At last, the nickel and gold layer were subsequently plated on to the copper layer by electroless gold plating (Fig. 2 (g) and Figure 2 (h)).

While bare copper tracks can be etched to high precision, the poor corrosion properties of the metal make it undesirable for practical applications. In the presence of moisture, air, or chlorine, bare copper is readily tarnished which would make it unsuitable for subsequent soldering, other assembly operations. Bare copper tracks could also induce toxicity when it is implanted into human body. However, a proper remedy demands an additional protective plating of more resistant metals such as nickel and gold. The gold was chosen for plating for its excellent conduction capability and corrosion resistance. Gold plating, although relatively expensive, is a well-established technology developed over the past several decades. There are a number of proprietary formulations for applying a thin coating of gold all over the copper traces of a circuit by simple immersion in a hot solution. Electroless plating of nickel and gold on the copper feed-throughs which is a convenient and inexpensive process is adopted in this study. Electroless plating is an autocatalytic process in which



(a) (b)

Figure 3. (a) Integration of electrode and wireless transmission circuitry. (b) Thermal forming process for forming stimulating electrode.

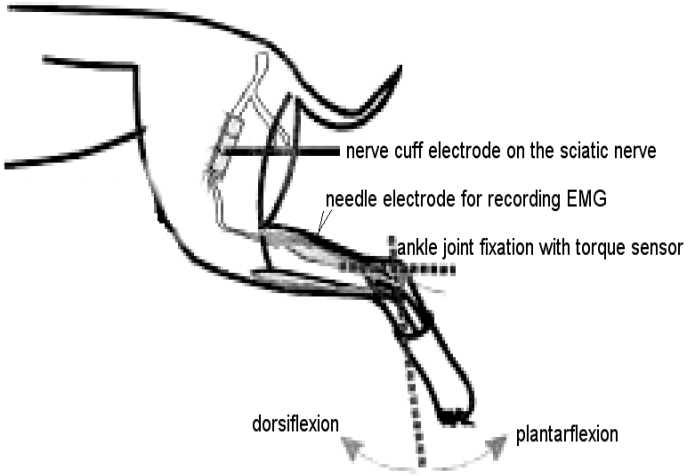


Figure 4. Schematic illustration of the implantation site and recording torque sensor.

the metal being deposited serves to catalyze the reaction. Such a deposit is suitable for corrosion protection or for wire bonding purposes.

Biocompatible packaging for microstimulator

Glob top and dam-and-fill are two common liquid encapsulation techniques used in IC industry. In glob top encapsulation, a volume of material is deposited on top of a component. The material flows downwards, covering the component. There is no border around the material. In this study, the dam-and fill technique is applied to encapsulate the internal circuit. The dam-and-fill is a two-step encapsulation processes, including the dispensing of higher-viscosity encapsulant around the component to form a dam and the fill of dam with a lower-viscosity material. After dam-and-fill encapsulation, the implantable device is coated with a layer of biocompatible material, silicon rubber (Nusil^{TM} 1137). The encapsulation process is accomplished within a custom-made Teflon mold. The cuff electrode was undergone thermal-forming to produce the cuff shape structure, as shown in Figure 3.

Both *in vitro* and *in vivo* experiments were performed to evaluate the hermeticity and reliability of implants. The function of the biomicrosystem is evaluated by transmitting commands from external coil and generating the stimulating current from the implanted module. The implantable microstimulator was encapsulated with dam-and-fill encapsulant and silicone rubber, which was later placed in the normal saline solution for *in vitro* test. The stimulus is measured through a 1kΩ load connected to the output of stimulating electrodes when it is placed in normal saline solution for *in-vitro* evaluation. After *in-vitro* test, the microstimulator is implanted around rabbit's sciatic nerve for initial *in vivo* experiments. After implantation, the microstimulator is magnetic coupled to stimulate the sciatic nerve from which a torque device is used to measure the reactive torque, as shown in Figure. 4.

Results

Fabrication Process for Circuitry and Stimulation Electrode

Figure 5 illustrates the mask for microstimulator circuitry as well as that for stimulating electrode. The design of integrating the microstimulator circuitry and electrode in separating modules but they can be connected through the designed connection pads. This design is flexible and suitable for future module design of varied types of stimulating electrodes in various animal experiments.

During the fabrication of microstimulator circuitry and

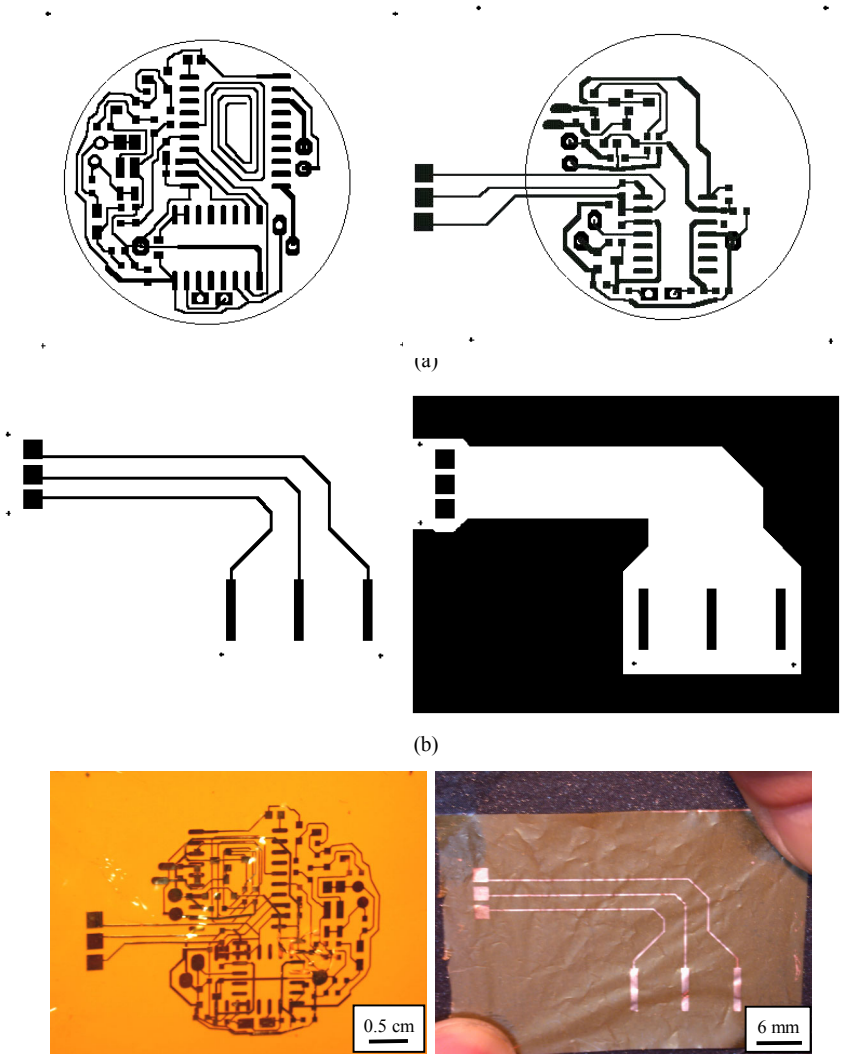


Figure 5. Masks for fabricating (a) transmission circuitry and (b) stimulating electrode. The optimized etching results for RF circuitry and stimulating electrode in (c).

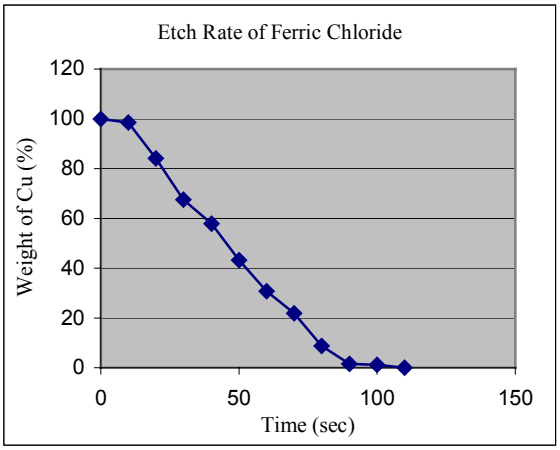
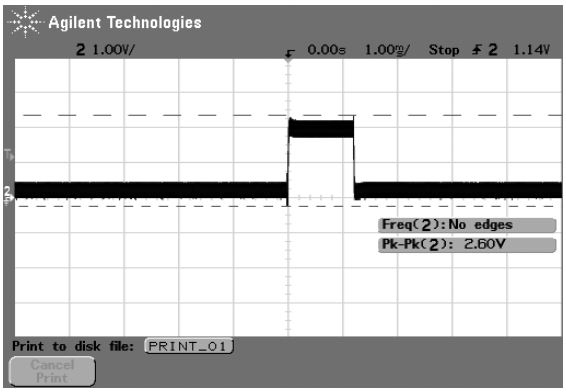


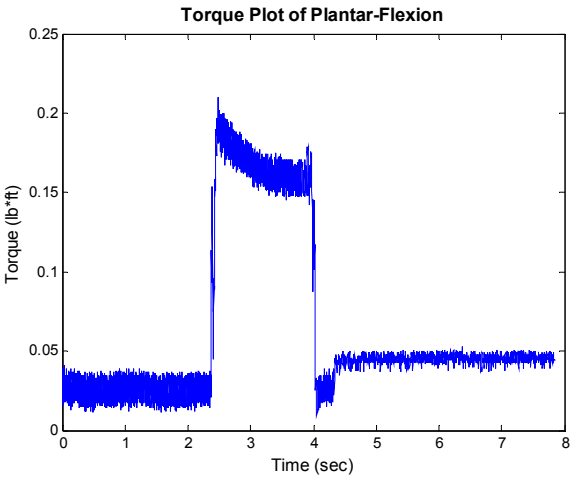
Figure 6. Etch rate of copper in ferric chloride solution.

stimulation electrode, copper photolithography and insulation layer photolithography are two crucial processing steps. Any failure in these processes might cause defects in the final produt. For copper photolithography, the temperature of $FeCl_3$ is heated to 40°C to increase etch rate. The etch rate is denoted by the quantity of copper dissolved in $FeCl_3$. The original weight of the sample, flexible film with copper layer, is 0.4778g. The plot of copper weight etch rates with etch time is shown in Figure 6. The copper weight decreases rapidly when etch time is less than 90 secs. When etch time exceeds 90 secs, etch rate decreases very slowly. According to the etch rate of Ferric Chloride, the appropriate etch time of RF circuit is about 6 minutes. There are several typical process failures in copper patterning process caused by over-etching or under etching because of the inappropriate process control on the etch rate, temperate control, or concentration. After the etch process is finished, there are always some unwanted residues on the sidewall or on the substrate surface. These undesired residues could be caused by insufficient etch time of the film. On contrary, over-etching could break the connecting wires or feedthroughs to the electrodes.

The major solvent in polyimide is driven out to turn the liquid state polyimide into polyimide film around 126°C. The temperature was set to be the soft bake temperature. In order to



(a)



(b)

Figure 7. (a) The monophasic stimulus output for stimulating. (b) The torque generated by plantar-flexion.

evaporate the solvent out of polyimide slower and to prevent the possible formation of surface defects (pin-hole), the soft baking process was performed in two steps, starting at 70°C and increasing to 120°C. To be well fit to peripheral nerve, the patterned stimulating electrode is heated up to the transition temperature of polyimide and then quenches to remain the cuff shape.

Biocompatible Packaging for microstimulator

Both i*n-vitro* and *in-vivo* tests are performed by placing implantable microstimulator in normal saline solution and implanting it onto rabbit's sciatic nerve, respectively. The stimulus is measured and recorded once a day to evaluate the normal function of microstimulator. Figure 7 (a) shows the recorded stimulation pulse while placed the microstimulator module in normal saline. The longest lasting microstimulator survived in normal saline for a period of 30 days. Later, the microstimulator is implanted around the sciatic nerve. The function of implanted microstimulator was tested from the reactive torque via the electrical stimulation. The torque is measured during *in-vivo* stimulation for plantar-flexion movement, as shown in Figure 7 (b). The torque is measured under a constant current of 280μA for pulse duration of 2 sec and 60Hz monophasic stimulus after received commanded from the external transmitter.

Discussion and Conclusion

The implantable microstimulator with flexible mechanical structure has been fabricated by MEMS technique on polyimide substrate. MEMS technique is mainly employed to fabricate wireless transmission circuitry and stimulating electrode. Although the prototype of microstimulator has been successfully fabricated, its size measuring at 4 cm in diameter and 8 mm in height is still rather bulky after packaging. Our current research is in attempt to extract the dies of chip and perform system in package (SIP) approach to minimize the size of implanted device.

Among varied polymer materials, polyimide has been proven to be biocompatible [18] which can be used as substrate and carrier for SMD components and stimulating/ sensing electrodes and interact with living tissue. In this study, thermal-forming characteristic of polyimide is employed to form cuff-shape electrode. The cuff-shape structure can be easily processed by heating polyimide up to its glass transition temperature (T_g) which can form a cuff shape permanently.

The *in-vitro* and *in-vivo* tests have been evaluated for both hermeticity and reliability. The reliability of the microstimulator has been performed through the acute *in vivo* evaluation when we applied it on the rabbit's sciatic nerve. The *in vivo* evaluation can be considered as an initial step for long-term chronic implantation. Further studies are needed to closely investigate the biocompatible properties of packaging materials.

In conclusion, we have developed a fabrication process and packaging technology for flexible, lightweight implantable biomicrosystem, which could be used on microstimulator for animal experiments. The monophasic stimulus, generated by the internal circuitry and the stimulation on rabbit's sciatic nerve was performed. We conclude that our packaging approach generally meets the basic requirements of flexible mechanical structure and biocompatible packaging to interface with neural system. The standardization of interface between transmission circuit and electrode for module packaging could offer viable opportunities for varied neuromodulation animal studies using implanted microstimulator.

Acknowledgement

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References

[1] J. V. Arx, B. Ziaie, M. Dokmeci, and K. Najafi, "Hermeticity Testing Of Glass-silicon Packages With On Chip Feed Throughs," presented at The 8th International Conference on Solid-State Sensors and Actuators, 1995.

[2] Y. T. Cheng, L. Lin, and K. Najafi, "Localized bonding with PSG or indium solder as intermediate layer," presented at The 12th IEEE International Conference on Micro Electro Mechanical Systems, 1999.

[3] Y. T. Cheng, L. Lin, and K. Najafi, "A hermetic glass-silicon package formed using localized aluminum/silicon-glass bonding," *Journal of Microelectromechanical Systems*, 10: 392 -399, 2001.

[4] B. Ziaie, J. A. Von Arx, M. R. Dokmeci, and K. Najafi, "A hermetic glass-silicon micropackage with high-density on-chip feedthroughs for sensors and actuators," *Journal of Microelectromechanical Systems*, 5:166 -179, 1996.

[5] Y. T. Cheng, L. Lin, and K. Najafi, "Fabrication and hermeticity testing of a glass-silicon package formed using localized aluminum/silicon-to-glass bonding," presented at the 13nth Annual International Conference on Micro Electro Mechanical Systems, 2000.

[6] T. J. Harpster and K. Najafi, "Long-term testing of hermetic anodically bonded glass-silicon packages," presented at The 15th IEEE International Conference on Micro Electro Mechanical Systems, 2002.

[7] B. Ziaie, M. D. Narkin, A. R. Coghlan, and K. Najafi, "A single-channel implantable microstimulator for functional neuromuscular stimulation," *IEEE Transactions on Biomedical Engineering*, 44:909-920, 1997.

[8] G. E. Loeb, F. J. R. Richmond, W. H. Moore, and R. A. Peck, "Design and fabrication of hermetic microelectronic implants," presented at The 1st Annual International Conference on Microtechnologies in Medicine and Biology, 2000.

[9] F. J. R. Richmond, G. E. Loeb, A. C. Dupont, S. D. Bagg, J. L. Creasy, C. Romano, and D. Romano, "Clinical trials of BIONs for therapeutic electrical stimulation," presented at The 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2001.

[10] J. Singh, R. A. Peck, and G. E. Loeb, "Development of BION technology for functional electrical stimulation: hermetic packaging," presented at The 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2001.

[11] P. R. Troyk, I. E. Brown, W. H. Moore, and G. E. Loeb, "Development of BION technology for functional electrical stimulation: bidirectional telemetry," presented at The 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2001.

[12] A. C. Dupont, S. D. Bag, L. Baker, S. Chun, J. L. Creasi, C. Romano, D. Romano, R. L. Waters, C. L. Wederich, F. J. R. Richmond, and G. E. Loeb, "Therapeutic electrical stimulation with bions: clinical trial report," presented at EMBS/BMES Conference, 2002.

[13] H. Beutel, T. Stieglitz, and J. U. Meyer, "Microflex: a new technique for hybrid integration for microsystems," presented at The Eleventh Annual International Workshop on Micro Electro Mechanical Systems, 1998.

[14] T. Stieglitz, H. Beutel, R. Keller, M. Schuettler, and J.-U. Meyer, "Flexible, polyimide-based neural interfaces," presented at The Seventh International Conference on Microelectronics for Neural, Fuzzy and Bio-Inspired Systems, 1999.

[15] T. Stieglitz, H. Beutel, R. Keller, and J.-U. Meyer, "Integrative design and hybrid assembly of a flexible retina implant system," presented at The First Joint of BMES/EMBS Conference, 1999.

[16] T. Stieglitz, M. Schuettler, and J.-U. Meyer, "Micromachined multichannel cuff electrodes for interfacing small nerves," presented at The First Joint of BMES/EMBS Conference, 1999.

[17] C. K. Liang, G. S. Yang, J. J. J. Chen and C. K. Chen, “A microcontroller-based implantable stimulation system with wireless power data transmission for animal neuromuscular experiments,” Journal of the Chinese Institute of Engineers, 26: 493-501, 2003.

[18] R. R. R. Jr., M. J. A., and R. W.M., "Polyimides as biomaterials: Preliminary biocompatibility testing," *Biomaterials*, 14: 627-635, 1993.