A Compact Deep Brain Stimulation System for Animal Experiments

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Abstract

The implantable brain stimulation system is a powerful tool for animal behavioral experiments in neuroscience studies. Even though the stimulation systems are commercially available for clinical applications such as deep brain stimulation and cochlear implant systems, due to the large size of the system, it has been difficult to apply them to the small animals such as rodents. In the present study, we propose a novel, low cost, and small-sized implantable brain stimulation system exclusively for animal studies using state-of-the-art technologies of polymer thin-film processes. The implemented system comprises a silicone elastomer-encapsulated stimulation circuit and a liquid crystal polymer (LCP)-based electrode array. The encapsulated stimulator is 22~23 mm in diameter and 5 mm in thickness including a LCP-based planar coil for both power delivery and data telemetry. These sizes of the internal device are designed to be small enough to be mounted onto the rat skull. The stimulation parameters (channel selection, current level, frequency, pulse duration, and polarity) can be determined by the external controller via the inductive coil link. The results of the operation test are equivalent to those with the previous percutaneous system. In addition, compared to the conventional implantable stimulation systems with metal packages, the fabrication procedures of the LCP-based system is relatively simple and low-cost due to batch processes. These LCP-based technologies for micro-fabrication and packaging will contribute to the advance in development of implantable stimulation systems for neuroscience research as well as neural prostheses.

Keywords: brain stimulation, compact implantable system, electrical stimulation

Introduction

Recently, several studies have employed the electrical stimulation on the animal models of neurological diseases to develop a new therapeutic method or to verify the mechanisms. [1] To date, most of these studies have been performed with the external stimulation system with percutaneous connection to the implanted electrodes. [2-3] However, this approach prevents the free behaviors of the animal and gives rise to the risk of infection migrating along the connection wires [4-5]. The battery-powered system like commercial implantable pulse generators (IPG) for clinical applications can circumvent these issues. However, it still has the limitations due to the large size of the battery and the limited lifespan [6]. For these reasons, a compact implantable system with wireless power delivery could be an ideal solution for animal experiments. Moreover, considering the large number of samples in animal experiments, it is desired that the system is composed of inexpensive off-the-shelf components for low-cost fabrication [6]. The batch process like roll-to-roll (R2R) technology will be a good method to reduce the fabrication cost.

We propose compact deep brain stimulation (DBS) systems exclusively for small animal experiments. In the present study, we employed liquid crystal polymer (LCP) as a substrate of stimulating
electrodes [7-8]. The proposed system can be implanted onto the brain without any wired connection to the external system because both of the power and data are wirelessly delivered to the implanted system via an inductive-coil link. The electrode array is designed to deliver 4 channel stimulation currents. The system builds upon the devices reported previously [4, 7-8].

**Materials and Methods**

**LCP-based Electrode Array**

LCP has biocompatibility, high stability in aqueous environments [7-9]. Moreover, it also has controllable stiffness via thickness control because LCP is composed of stiff and flexible monomers. The film-type LCP (FA/CT, Kuraray, Tokyo, Japan) is used in this study which is adaptable to the low cost R2R process. In this study, we fabricated a LCP-based deep brain stimulation electrode array using the LCP process established in previous studies [7-8]. This LCP process includes metal (gold) micro patterning, laser micromachining, and thermal press bonding [7-9]. As shown in Fig. 1, the designed electrode has 4 channels stimulation sites for bipolar stimulation and holes for electrode fixation with dental cement and screws.

**Receiver Coil and Stimulation IC**

As shown Fig. 1, internal devices consists of a current stimulator based on a customized IC components (AMS technology, Austria) on a circular 2 layer circuit board (20 mm in diameter). The LCP-based planar coil (20 mm in diameter, 0.2 mm thickness) with 24 turns wirelessly received the RF-modulated signal. The power voltage is established through a combination of rectifier and regulating circuitry, and the data is extracted through a envelop detector from external device [11]. Using the LCP lamination process, it is available to develop a multi-layered planar coil to increase the number of turns of the coil. The customized IC was designed to control stimulation electrode channels (one pair of channels is needed for bipolar stimulation), select the stimulation polarity (monopolar/bipolar; the global reference wire has to be implanted for the monopolar stimulation strategy), stimulation current amplitude (0~10.23 mA), pulse frequency (20~230 Hz), and duration of biphasic current (0~630 μsec) via a wireless telemetry.

**Silicone Elastomer Encapsulation**

To provide biocompatibility and protection against body fluids, the system was coated with silicone elastomer (MED-6215, NUSIL, Carpinteria, CA, USA), which is known to be biocompatible for long term human applications [10]. During the animal behavioral tests (4 ~ 8 weeks), this silicone elastomer encapsulation provided the sufficient hermeticity.
External Device

As shown in Fig. 1, the external device controls the stimulation parameters and supplies the power to the ICs of the internal devices. The external device consists of power and data transmission circuits with Class-E amplifier and touch screen interface (M.I.Tech, Gyeonggi-do, Korea). It sends PWM (pulse width Modulation) data signals via a 2.5 MHz radio link for parameter setting of the internal device. During stimulation and resting periods, the external device sends a high signal (1; 5V high) for power supplying to the internal system. Both sides were tuned with capacitors for matching the Q factor.

Operation Test

The functionality of the implemented system was verified. The electrode impedance was measured with impedance analyzer (Solartron 1260/1287, AMETEK, UK) using the 3-electrode configuration-Ag/AgCl reference electrode, Pt counter electrode, and the fabricated LCP-based 4 channels electrode as working electrodes. The electrical stimulation pulse was measured at the two selected electrode sites connected through a 1 kohm resistor using an oscilloscope (TDS3000C, Tektronics, Beaverton, OR, USA).

Results

The overview of the developed system was shown in Fig 2. 50 electrode arrays were fabricated from a 4-inch wafer-sized LCP substrate. As shown in Fig. 2 (B), the electrode site has gold square surface (300 \( \mu \)m ×300 \( \mu \)m). The magnitude of the electrode impedance was 4.7 ± 1.1 k\( \Omega \). The charge storage capacity for electrical stimulation was 10.86 ± 6.86 \( \mu \)C/cm².

The efficiency of power delivery was in the range of 20–30 % with 20 mm air gap between a transmission coil and a receiving planar coil. It was also confirmed that the internal device correctly decoded the received data and injected pertinent stimulation current signals as shown in Fig. 3.

The packaged stimulator was 22–23 mm in diameter and 5 mm in thickness. This size is suitable as a rodent head mountable device.

Discussion

The results showed that the suggested polymer-based compact implantable animal brain stimulation systems are fully functional after the fabrication procedure. The efficiency of power delivery via inductive link is considerable to the conventional implanted device which has the power source outside. The implanted system was successfully controlled by the external device.

We could get a number of electrodes from a 4 inch wafer-sized LCP film. This suggests that the fabrication of LCP-based brain stimulation system can be low-cost because the conventional hand-made electrode arrays are expensive. The LCP-based DBS electrode is designed to have a relatively low impedance to prevent the stimulation limitation caused by the compliance voltage during current injection and sufficient charge storage capacitance for current injection to the target tissues of cells [12]. Furthermore, the suggested system could be applicable to various neural stimulation experiments.

Conclusion

We suggested a polymer (LCP and silicone...
elastomer)-based compact implantable animal deep brain stimulation system with wireless control and power delivery. We believe this system will contribute to the advance in neuroscience research requiring in vivo neural stimulation. Animal experiments with these systems will be performed in the near future.

References


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