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# Selective stimulation and neural recording on peripheral nerves using flexible split ring electrodes

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ABSTRACT

Reliable neural interfaces between peripheral nerves and implantable devices are at the center of advanced neural prosthetics and bioelectronic medicine. In this paper, selective sciatic nerve recording and stimulation were investigated using flexible split ring electrodes. The design enabled easy and reliable implantation of active electrodes on the sciatic nerve with minimal pressure on the nerve, but still provided good electrical contact with the nerve. Selective muscle stimulation was achieved by varying the stimulation configuration of the four active electrodes on the nerve to produce different muscle activation patterns. In addition, partially evoked neural signals were also recorded from the nerve using a transverse differential bipolar configuration, demonstrating differential recording capability. In addition, we showed that the quality of the neural signals recorded by the split ring electrode was higher than recordings from a commercial cuff electrode in terms of signal-to-noise ratio (SNR). Overall, our data shows that this flexible split ring electrode could be effective in neuromodulation in the future.

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## 1. Introduction

Recording from and stimulating peripheral nerves is an area of increasing importance, especially for restoring control of paralyzed limbs or for dexterous control of advanced bionic limbs [1,2]. Due to many physiological and anatomical difficulties in accessing small nerves, the precise targeting and modulation of neural signals in the peripheral nervous system (PNS) has remained a grand challenge. The most challenging thing is to develop implantable flexible neural interfaces that can be closely attached to nerves for long-term use without causing damage, while reliably maintaining high-resolution recording and stimulation, while targeting only the signals that elicit desired effects without altering other functionalities [2,3].

Numerous neural interfaces have been previously proposed and developed, such as extra-neural (cuff and FINE) [4–6], intrafascicular (LIFE and TIME) [7–9], penetrating (USEA) [10–12], regenerative electrodes [13–15]. Of these four types of electrodes, extra-neural electrodes have been most broadly used for clinical applications, thanks to their non-invasive approach and easy implantation. However, low signal-to-noise ratio (SNR) for neural recording is still a major challenge since decreasing the cuff diameter to improve signal quality can lead to increased risks of nerve damage over a long period of time [4]. Other ways of improving the signal quality involve the use of bipolar or tripolar electrode configurations, which work best when the electrodes can be separated by at least 20 mm [16]. This greatly increases the length of the cuffs, which increases the possibility of causing foreign body responses, biomechanical issues, and difficulty in implanting on small nerves for long-term use [17,18]. Recently, new extra-neural approaches with flexible materials fabricated using microfabrication technologies have shown promising results for recording and stimulating nerves by achieving close contact with nerve surfaces without applying too much pressure to the nerve [19–22]. In addition, flexible split ring electrodes were reported for neural recording in a previous study [22]. However, selective stimulation and high-quality neural recording have not yet demonstrated. Also, the configuration that was used in the previous study, was limited in that the reference electrode, located on the outer ring of

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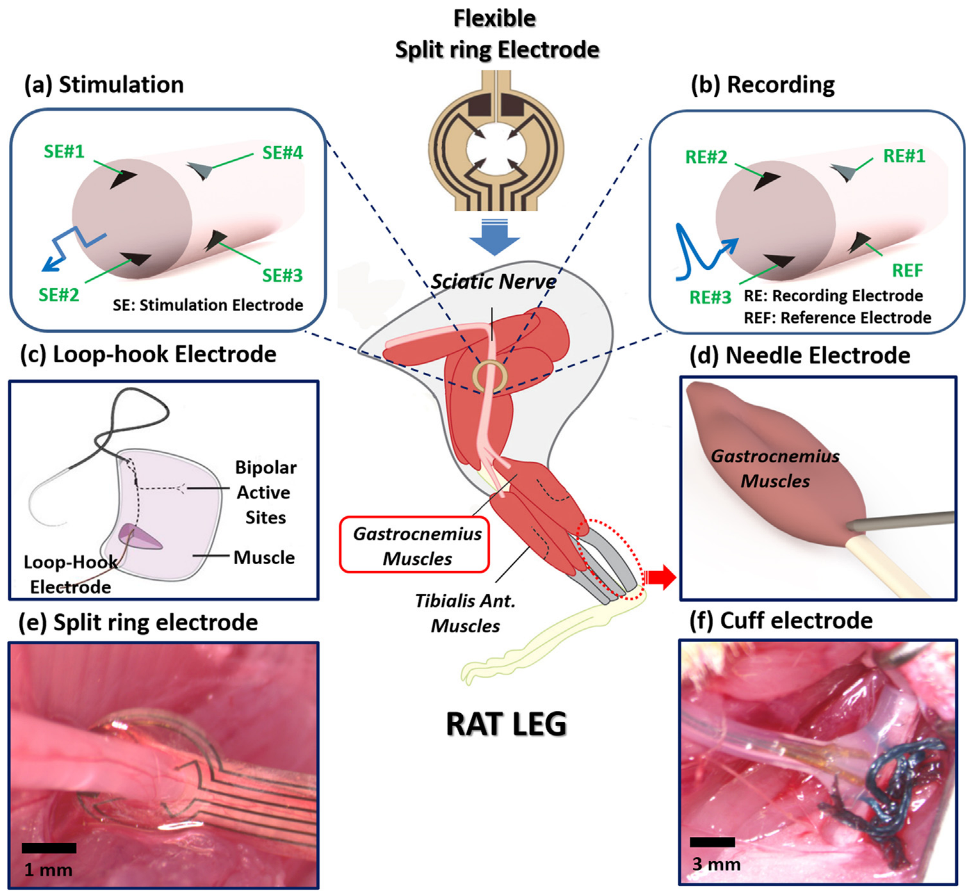


**Fig. 1.** Schematic diagram of the experimental setup. Schematic diagram of the implaned flexible split ring electrode on the sciatic nerve for (a) stimulation and (b) recording. (c) Schematic diagram of an intra-muscular loop-hook bipolar electrode implanted in either the tibialis anterior or gastrocnemius muscles. (d) Schematic diagram of subdermal electrical stimulation of the hind limb using a needle electrode. Picture of the implanted (e) flexible split ring electrode and (f) commercial cuff electrode (Microprobe Inc., Gaithersburg, MD, USA) on the sciatic nerve in rats.

the device, had difficulty making contact with the nerve during the recording experiment. This required the addition of an external reference electrode. As a result, a modified recording configuration had to be tested before moving to chronic implantations.

In this paper, we tested the use of flexible split ring electrode for selective stimulation of the sciatic nerve, which were confirmed by different corresponding muscle activation patterns. In addition, we also performed neural recordings on the rat sciatic nerve using a transverse differential bipolar configuration (Fig. 1). A commercial cuff electrode was also implanted on the sciatic nerve to confirm the recording setup, and to act as a benchmark for the flexible split ring electrode (Fig. 1f).

## 2. Experimental

The flexible split ring electrode consisted of two layers of biocompatible polyimides with Au/Pt electrodes sandwiched in a split ring-shaped geometry. The detailed fabrication procedure is described in the Supplementary Material (Fig. S-1).

Characterization of an electrochemical interface is of paramount importance for neural recording and stimulation. Electrodes with lower impedance are better suited for both stimulating and recording electrodes [23,24]. Also, if charge delivery capacity (CDC) is poor, high current amplitudes will be required for the activation of the nerves, which may also causes nerve damage or delamination of the electrodes surface [25]. The electrochemical characterization of the split ring electrode was conducted to evaluate the device. The detailed procedure is described in the Supplementary Materials (Fig. S-2). The mean impedance of one sensing Pt electrode was 6.25 kΩ at 1 kHz, which was 7 times lower than Au electrodes (Fig. S-2b). This impedance is reasonably low, and thus suitable for neural recording, which is generally preferred to be lower than 10 kΩ [19]. Also, it shows a small capacitive phase angle at low frequencies, which indicates capacitive impedance (Fig. S-2c). The mean charge delivery capacity was 3.13 $mC/cm^2$. Also, the mean cathodic charge storage capacity (CSCc) was 2.4 $mC/cm^2$ indicated by the cathodic area of the CV plot (Fig. S-2d). These values are comparable to materials used previously in the literature for neural stimulation [26,27]. The results demonstrate that the Pt split ring electrode can be used for *in vivo* recording and stimulation experiments.

The other experimental procedures such as implantation, physiological characterizations and statistical analysis are described in the Supplementary Material.

## 3. Results and discussion

### 3.1. Device design

The split ring electrode design attempts to reduce the risk of nerve compression by using flexible polyimide tips, so that it allows for good electrical contact with the epineurium of the nerve (instead of penetrating or wrapping it), but without excessive pressure on the nerve. The split ring electrode consist of an open ringed structure of 1.3 mm inner diameter, and tips of 500 μm inner diameter, while the outer diameter is 2.5 mm, so it can fit

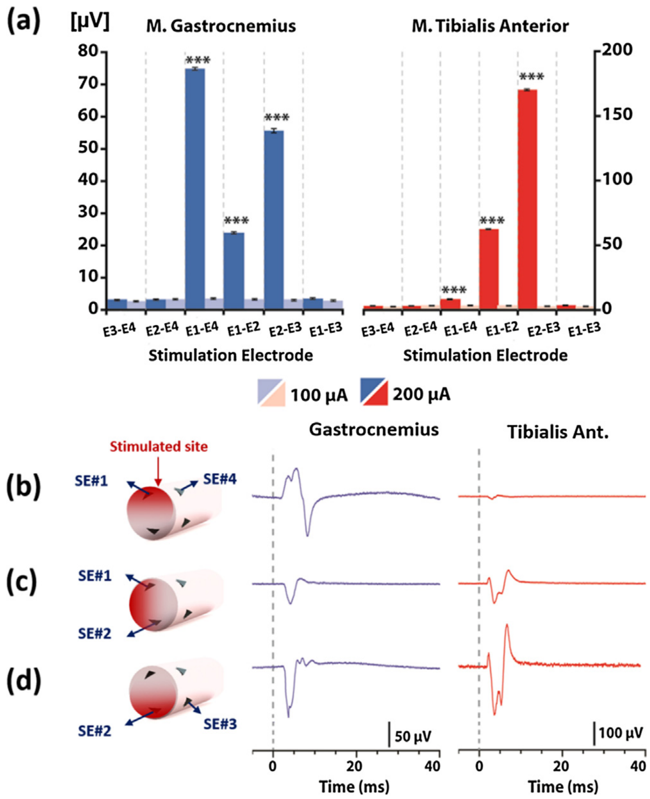


**Fig. 2.** (a) This plot shows the evoked compound muscle action potential (CMAP) in the Gastrocnemius (blue) and Tibialis Anterior muscles (red) as a function of electrode pairs from a single monophasic 20 μs pulse with stimulation currents of 100 (light color) and 200 μA (dark color) (n = 3). The CMAP recordings from the Gastrocnemius and Tibialis Anterior muscles are shown as a function of electrode pairs in (b) SE#1-#4, (c) SE#1-#2, and (d) SE#2-#3, respectively, using a single monophasic 20 μs pulse with currents of 200 μA. (To view the colors in this figure, the reader is referred to the web version of this article.)

a nerve with a diameter of 0.9–1.3 mm. Four triangular bendable 8500 $\mu m^2$ equidistant sensing electrodes protrude from this ring (Fig. S-3, inset). The split ring enables easy implantation by slotting the nerves into the ring after opening the split part (Fig. S-3).

### 3.2. Selective stimulation

Selective stimulation of the sciatic nerve was conducted while recording compound muscle action potentials (CMAPs) of the Gastrocnemius (GM) and Tibialis Anterior (TA) muscles to characterize the relationship between muscle activation and contact location. At lower stimulation current amplitudes (less than 100 μA), none of the paired contacts could elicit detectable CMAPs. As the current amplitude increased, the muscle activation patterns corresponding to each of the contact pairs appeared. CMAPs were evoked (along with the flexion or extension of the leg) using electrode pairs Stimulation Electrode (SE)#1-#4, SE#1-#2, and SE#2-#3 starting from stimulation currents of 200 μA (Fig. 2a). The electrode pair SE#1-#4 activated the GM muscle, but activation of the TA muscle was negligible (Fig. 2b). This indicated that the fascicles inside the sciatic nerve, which controlled the GM muscle, were closer to the positions of electrodes SE#1-#4. For the electrode pair SE#1-#2, the amplitude of CMAPs from the TA muscle was 2.5 times higher than those from the GM muscle (Fig. 2c). This suggested that the activation of fascicles under the electrode pair SE#1-#2 activated both muscles. The electrode pair SE#2-#3 activated the TA muscle 3 times more strongly than the GM muscle, suggesting preferential activation of the nerve fibers innervating the TA muscle compared to the GM muscle (Fig. 2d). The rest of the electrode pairs were not able to stimulate the muscles effectively until much higher levels of currents of approximately 1 mA. With stimulation amplitudes greater than 1 mA, all electrode pairs elicited muscle contractions, but the muscle activation pattern of each electrode pair became indistinguishable. The results showed that different motor fascicles were activated by different electrode pairs, thereby demonstrating selective stimulation of the sciatic nerve to activate GM and TA muscles by the flexible split ring electrode at low stimulation currents (200 μA). This low level of stimulation corresponded to 4 nC/Phase, which is an acceptable range for human applications [1].

### 3.3. Neural recording with transverse differential bipolar configuration

To investigate the quality of the neural recordings from the split ring electrode, the transverse differential bipolar configuration was used in *in vivo* experiments in this study. The compound neural action potentials (CNAPs) evoked by the subdermal electrical stimulation of the hind limb in rats (Fig. 1d) were recorded by three sensing electrodes and one reference electrode, which were transversally positioned on the nerve (Fig. 3). This transverse differential bipolar configuration provided several advantages; 1) it enabled the direct comparison of recording amplitudes among the sensing electrodes, 2) the implantation required a much smaller lateral space compared to the conventional cuff electrodes, and 3) reduced the need for complicated signal processing procedures and calculations for evaluating selectivity. The subdermal stimulation primarily excited sensory receptors, evoking the activation of relevant fascicles inside the sciatic nerve. The clear CNAPs from the three sensing electrodes were recorded using stimulation currents of 2 mA, which is shown in Fig. 3. As shown in Table 1, the mean amplitudes of the CNAPs were 33.7, 91.5, and 36.1 μV for Recording Electrode (RE) #1, #2, and #3, respectively. The mean latencies of the peak were 0.2 ms for all cases. The nerve conduction velocity (NCV) was calculated to be 35 m/s, which is consistent with values reported in the literature [19]. The mean noise level from the three sensing electrodes was measured as 7.4 μV, showing a SNR of 13 (SNR is based on absolute peak value/95th percentile noise value) on RE#2 (Fig. 3a). Even though direct comparisons of the SNR with other studies are difficult due to the different experimental conditions (e.g. the size and material of the recording electrode, where the electrode was implanted, and the type of CNAPs), this SNR value is again quite consistent with those reported in the literature [21]. The recorded amplitudes on RE#2 were the highest among all the electrodes, possibly indicating that the fascicles activated by the subdermal stimulation were closest to RE#2. The recorded amplitudes on RE#3 were slightly higher than those on RE#1, but the difference was negligible, indicating that the fascicles close to RE#1 or RE#3 were also slightly activated by the sebdermal stimulation, but they were negligible compared with the fascicles close to RE#2 (Fig. 3b, c). This indicates that using the transverse differential bipolar configuration, the flexible split ring electrode was able to distinguish subtle differences in the activation of the nerve fibers in the sciatic nerve.

### 3.4. Acute recording using commercial Pt cuff electrode

To verify the recording setup and the condition of the sciatic nerve, as well as to compare with the recording result from the split ring electrode, a commercial cuff electrode was also tested under the same recording setup after the previous recording experiment (Fig. 1f). The evoked CNAPs were recorded with a stimulation current of 1.5 mA, and were saturated with a stimulation current of 2.5 mA (Fig. S-4). The mean amplitude was 67.2 μV, and mean noise level was 13.2 μV, showing a SNR of 5.3 when stimulated with a current of 2 mA. It was 2 times lower SNR than that by the

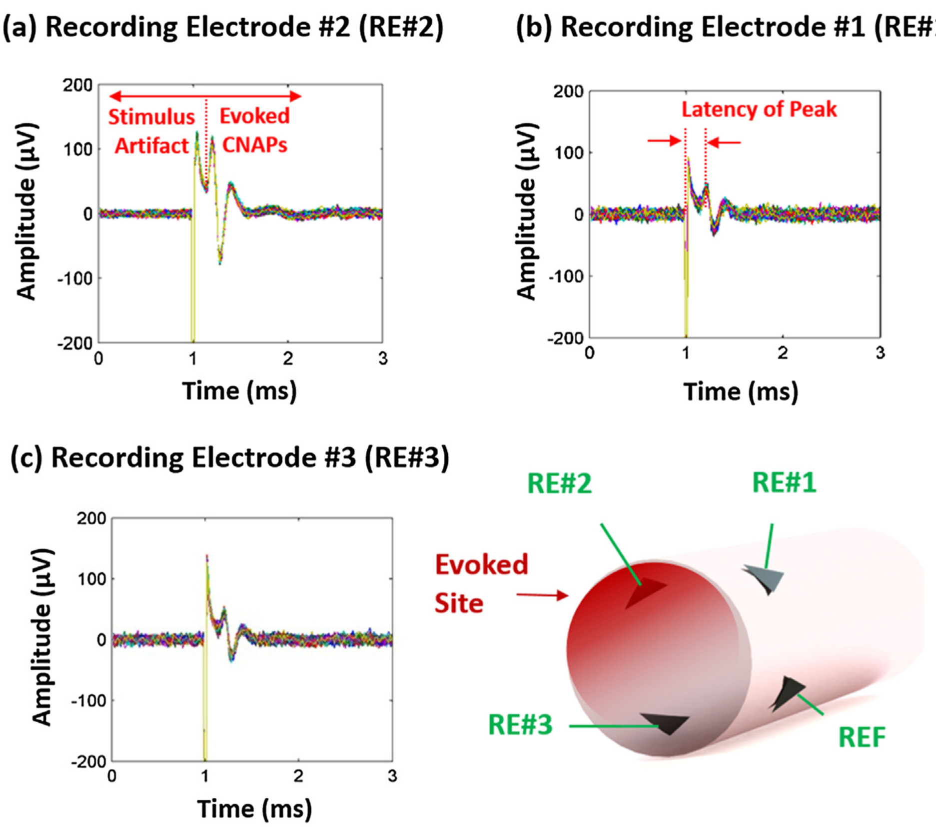


**Fig. 3.** The compound neural action potential (CNAP) recordings from (a) recording electrode #2 (RE#2), (b) recording electrode #1 (RE#1), and (c) recording electrode #3 (RE#3) from the sciatic nerve evoked by subdermal electrical stimulation in the hind limb. Schematic diagram of the transverse differential bipolar configuration with three sensing electrodes and one reference electrode on the sciatic nerve. Red color highlights the evoked fascicles inside the sciatic nerve. (To view the colors in this figure, the reader is referred to the web version of this article.)

**Table 1**
The recorded compound neural action potentials (CNAPs).

| | RE#1 | | RE#2 | | RE#3 | |
|---|---|---|---|---|---|---|
| | Amplitude [µV] | Latency [ms] | Amplitude [µV] | Latency [ms] | Amplitude [µV] | Latency [ms] |
| 1st Peak | 42.23 | 0.2 | 112 | 0.2 | 43.92 | 0.2 |
| 2nd Peak | −25.25 | 0.28 | −70.89 | 0.28 | −28.2 | 0.28 |
| 3rd Peak | 16.33 | 0.4 | 43.09 | 1.4 | 16.17 | 0.4 |
| Mean Amplitude | 33.74 | | 91.45 | | 36.06 | |

split ring electrode, which might be due to slightly larger size of the cuff compared to the diameter of the sciatic nerve. The split ring electrode, on the other hand, was able to make close contact with the nerve across a range of dimensions. Also, the larger space required for the cuff electrode resulted in higher latencies than those recorded by the split ring electrode since the cuff electrode had to be implanted on the proximal segment of the sciatic nerve due to its length (Fig. S-4). In comparison, the split ring electrode was implanted on the end of the sciatic nerve closer to the muscles, and as a result, recorded lower latencies than those from the cuff electrode. This reduced latency may be advantageous if a quick reaction to a stimulus is needed, for example, when a pain receptor is activated by a pin prick. In addition, the flexibility of the split ring electrode allows us to implant the electrode at any desired position on a nerve. These results using a commercial cuff electrode validated the recordings using the split ring electrode, but also highlighted the many advantages that the split ring electrode can potentially offer in neuromodulation and the control of advanced neural prosthetics.

## 4. Conclusion

Due to its unique design, split ring electrodes can be used for quick and easy implantation at any desired position on peripheral nerves, which is a powerful advantage for a neural interface used in physiological studies and neuromodulation applications. The results of the selective stimulation demonstrated that Gastrocnemius (GM) and Tibialis Anterior (TA) muscles were selectively activated by different pairs of active electrodes on a split ring electrode using a transverse bipolar configuration and stimulation currents of 200 µA. In addition, the results of the neural recordings demonstrated that small differences in evoked CNAPs could be distinguished using a transverse differential bipolar configuration. Also, we showed that the SNR of the CNAPs recorded by the split ring electrode was higher than those from commercial cuff electrodes. The results of the selective stimulation and recording demonstrated that the split ring electrode could be used to figure out the position of desired fascicles inside peripheral nerves, as well as high-resolution stimulation where there is a need to target only the nerve fibers that elicit desired effects without altering non-target functions. In summary, our results demonstrated that this electrode design shows promising possibilities for recording and stimulating nerves, and may be suited for neuroprosthetics and bioelectronic medicine in the future.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.snb.2016.09.127.

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