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Multi-channel neural signal stimulating module and *in-vivo* experiments

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Abstract: The module for function electrical stimulation (FES) of neurons is designed for the research of the neural function regeneration microelectronic system, which is an in-body embedded micro module. It is implemented by using discrete devices at first and characterized *in vitro*. The module is used to stimulate sciatic nerve and spinal cord of rats and rabbits for *in-vivo* real-time experiments of the neural function regeneration system. Based on the module, a four channel module for the FES of neurons is designed for 12 sites cuff electrode or 10 sites shaft electrode. Three animal experiments with total five rats and two rabbits were made. In the *in-vivo* experiment, the neural signals including spontaneous and imitated were regenerated by the module. The stimulating signal was used to drive sciatic nerve and spinal cord of rats and rabbits, successfully caused them twitch in different parts of their bodies, such as legs, tails, and fingers. This testifies that the neural function regeneration system can regenerate the neural signals.

Key words: microelectrode; neural function regeneration; function electrical stimulation; neural signal channel; stimulation

Usually, nerve regeneration is a significant subject of neurobiology. Neuropathists and chirurgeons use biologic methods to help nerve-injured patients. There are two available methods. One is to activate the neurons at the damaged point to grow through guidance channels to connect the upper and lower nerve stumps again. Such a biological method is feasible for an injured periphery nerve, but difficult for injured central nerve fibers such as a spinal cord. The other method is to replant organs. But as far as almost all of the possible injuries to central neural systems, the biologic methods are still in a phase of development. The most hopeful approach may be to use stem cells. But there has been little practical progress toward clinical applications. Therefore, our research team has proposed an idea to recover the function of the central neural system, using microelectronic techniques to create an in-body embedded module which bridges the interrupted signal channels of a nerve fiber.

The in-body embedded module is a neural function regeneration system[1–4], as shown in Fig. 1, which consists of a group of detecting microelectrodes for neural signal detection, one microelectronic system chip, and a group of microelectrodes for function stimulation. It can be used in two opposite directions. One is in the direction from the upper neuron to the lower neuron and is responsible for regeneration of the motor nerves' signals. The other is in the inverse direction and is responsible for regeneration of the senses' signals. By this method, the interrupted neural signals can be regenerated.

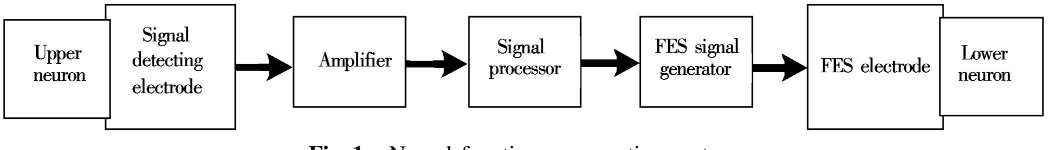

Fig. 1 Neural function regeneration system

This microelectronic system includes an amplifier, a signal processor, and an FES circuit to generate neural signals[2–3]. On the terminal of the neural stump, the neural functions are detected by the detecting electrodes. The detected signals are amplified up to a suitable amplitude, and to be processed so as to filter out the noise[4]. Then, the processed signals are used to control the generation of the required FES sig-

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nals. Finally, the FES signals are applied to the stimulating microelectrodes which connect to another neural stump. Thus, the interrupted signal channel is rebuilt.

1 Circuit Consisting of Discrete Devices

According to the neural function regeneration system, the circuit of the FES signal generator must amplify the electrical signals from the signal processor up to an adequate amplitude, so that the FES signal can be used to drive the stimulating electrodes. The load of the circuit is the shaft microelectrode or the cuff microelectrode which contacts with nerve bundles. So, the microelectrode and the resistance of the nerve bundle will be first discussed.

1.1 Microelectrodes and impedance of nerves

Several types of microelectrodes can be used for neural signal detection and stimulation[5-6]. Among them, two types of microelectrodes were selected for our *in-vivo* experiments: the shaft microelectrode and the cuff microelectrode[7].

The shaft electrode can reduce mechanically induced traumatization of spine nerves due to its flexibility, light-weight, and small dimensions. Another superiority of the shaft electrode is that its contact sites contact to the nerves closely so that the FES signal can be directly applied to the nerves. When a shaft electrode was inserted into the spinal cord, one contact site of the electrode was contacted directly to one neuron or several neurons, so, when a stimulating signal was applied to the contact site, the animal would twitch its body in a specific part which had relationship with the specific area of the spinal cord. The shaft electrode was designed on both front and back sides with five sites on each side; the 10 contact sites have a diameter of 0.01 mm. So, it can reduce insertion trauma at a given number of electrode sites. The constructional drawing and the photo of the shaft electrode are shown in Fig. 2.

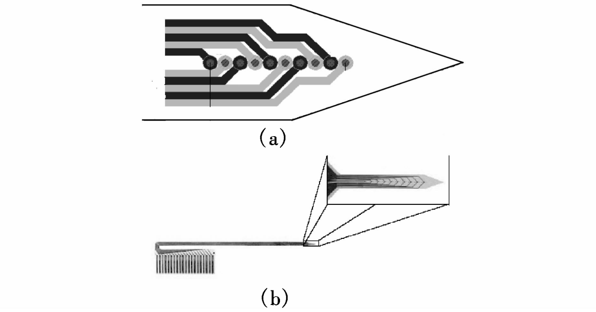

Fig. 2 Shaft microelectrode. (a) Constructional drawing; (b) Photo

The cuff electrode is superior to others due to its causing less damage to the nerve bundles and the safe implantation in the organism for a long time. Thus, two cuff microelectrodes of a medium size were chosen in our *in-vivo* experiments to detect and stimulate sciatic nerve and spine cord in rats and rabbits. The cuff electrodes have a circumferential shape after implementation. The 12 contact sites have a diameter of 0.3 mm. The constructional drawing of an unfurled electrode and the photo of four samples in a naturally furling state are shown in Fig. 3.

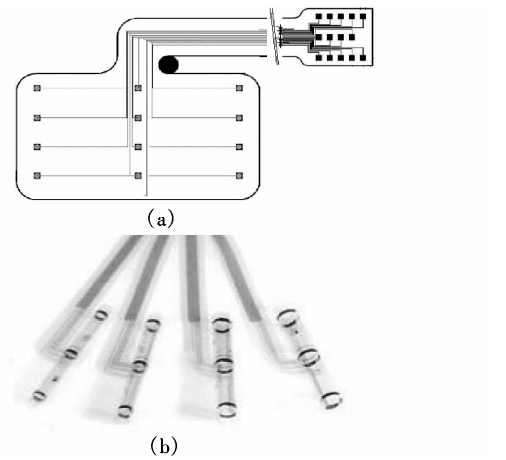

Fig. 3 Cuff microelectrode. (a) Constructional drawing; (b) Photo of four samples in a naturally furling state

For the circuit design of the FES signal generator, the load performance is important[8]. Experiments have shown that the impedance of a cuff electrode contacted on nerve bundles is about several kilo ohms. The impedance of a shaft electrode which was inserted into the spinal cord has a similar value.

1.2 Circuit of single channel FES signal generator

An FES signal generator will be used to stimulate the shaft electrode which was inserted into the spinal cord, or to stimulate the cuff electrode which contacts nerve bundles. The circuit consists of a pre-amplifier and a post-amplifier; it generates two signals with 180° phase difference with each other. The diagram of the circuit structure is shown in Fig. 4.

The first stage of the amplifier whose gain is invariable is an inverting amplifier including an opera-

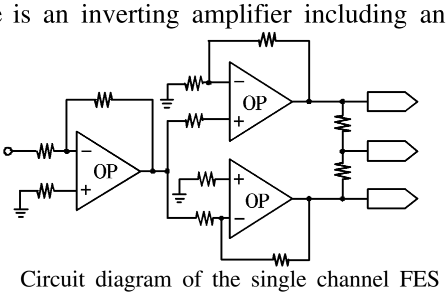

Fig. 4 Circuit diagram of the single channel FES signal generator

tional amplifier and three resistors. The function of the first stage is to amplify the input signal to sufficient amplitude. The second stage consisting of two amplifiers can generate two signals with 180° phase difference. This stage is used to amplify the signal further so as to obtain a high enough voltage to drive the microelectrode.

1.3 Simulation and test results

The single channel FES signal generator circuit is simulated by means of the software of Electronically Workbench (EWB). The maximum gain of the circuit is about 60 dB, with a bandwidth of more than 10 kHz. The phase difference of two output signals is 180°. Under a power supply of 12 V, the maximum output signal amplitude on a 10 kΩ load is more than 11 V. The circuit can work very well when power supply changes from 3 to 15 V. The simulation results testify that the circuit can generate the desired signals.

The circuit is also tested by using a function signal generator, Agilent 33220A, an adjustable power supply, and a double-trace oscillograph. The test results are similar to the simulation ones and prove that the circuit can offer a high enough voltage to stimulate nerve bundles. Because the circuit will be integrated to a small one by using CMOS technology and will be implanted into animal's body, lower supply voltage and lower power consumption is very important to the circuit[9-10]. The circuit is tested under power supply voltages of 3.3 V and 5 V which are standard supply voltages of CMOS ICs. The maximum output signal amplitudes on a 10 kΩ load are about 2.7 V under a supply voltage of 3.3 V, and 4.7 V under a supply voltage of 5 V.

1.4 Four channels FES signal generator module

Based on the single channel FES signal generator above, a four-channel FES signal generator module is implemented. Fig. 5 shows the photo of its PCB. The size of the PCB is 30.3 cm × 12.7 cm.

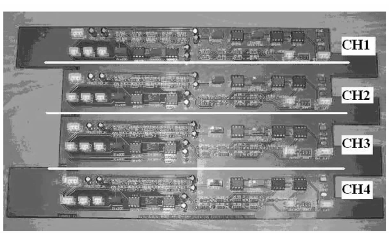

Fig. 5 Photo of four-channel FES signal generator module

2 Animal Experiments

Three animal experiments have been made by using two rabbits and five rats. The neural signals were imitated by an arbitrary wave generator, Agilent 33220. The bioelectrical signals received from the nerves of the experimental animals were recorded by a four channel oscillograph of Agilent 54624A.

A photo of the animal experiments which were made on a rat's sciatic nerve is shown in Fig. 6.

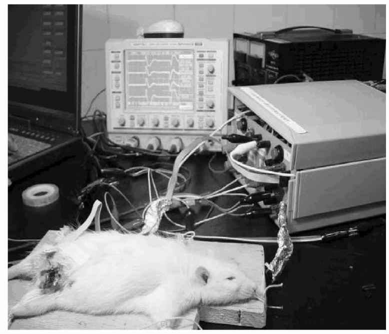

Fig. 6 Photo of the *in-vivo* experiments on a rat's sciatic nerve

An experiment was made by using a shaft electrode which was inserted into the spinal cord[11] of a rat. The sites of the shaft were inserted into the motor nerve area of the spinal cord by accurate location. So, the sites of the shaft electrode contacted directly to the motor nerve. Two sites of the shaft electrode were used for one stimulating channel. There were four channels in the shaft electrode except for two sites which were not used. The driving signal had a frequency of 1 to 4 Hz, generated by Agilent 33220. When the FES signal was applied to different channels, the rat showed different motoric reactions. This is because the different areas of the motor nerve take charge of different parts of the animal's body. In the experiment, for example, the rat moved its left crus, right crus, tail, and even the different fingers in left foot when the FES signal was applied to different channels.

For the cuff electrode, one group was also as one signal channel consisting of three sites, so the cuff electrode includes four channels which could be used to stimulate the sciatic nerve of a rat. The imitated neural signal generated by Agilent 33220 had a frequency of 1 to 4 Hz, which was sent to the FES signal generator to generate the desired signal. One channel of the cuff electrode was used as a stimulating channel; the other three channels of the cuff electrode were used to monitor the reacting signal. The monitored signals were observed and recorded by the four channel Agilent oscillograph 54624A. Fig. 7 shows a group of the waveforms from four channels. Among them, A1 is the stimulating signal, A2 to A4 are monitored signals by the other three channels. In this experiment, the rat moved its crus when the FES signal was applied to the sciatic nerve. It is testified that the FES signal generator can generate desired stimulating signals.

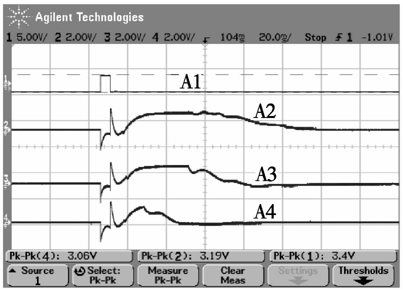

Fig. 7 Signals recorded during the *in-vivo* experiment

In these experiments, the smallest voltage of the FES signal was 0. 75 V and the smallest width of the signal pulse was 40 μs for the rat' s crus motion.

The neural function regeneration system was used to regenerate the neural signal by another *in-vivo* experiment on a rat' s sciatic nerve. One cuff microelectrode was connected to the upper position of the sciatic nerve of the rat; another cuff microelectrode was connected to the lower position of the same sciatic nerve. The 12 sites of the microelectrode were also divided into four group, and every group was a channel. The sciatic nerve was cut between the two microelectrodes. In the upper microelectrode, one channel was sent to the Agilent oscillograph 54624A to monitor the neural signal. One channel was used to detect the neural signals coming from the rat' s body by the detecting amplifier[4, 12]. The output of the detecting amplifier was sent to one channel of the FES signal generator module. The FES signal generated by the FES signal generator module was sent to one channel of the lower microelectrode. Another channel of the lower microelectrode was sent to the Agilent oscillograph 54624A, to monitor the regeneration of the neural signal. In this experiment, the neural signal including spontaneous and stimulating was detected by the detecting amplifier and regenerated by the FES signal generator module. This was recorded by the Agilent oscillograph 54624A as shown in Fig. 8. When we stop stimulating, the spontaneous neural signals coming from the rat' s body could also be detected by the detecting amplifier and regenerated by the FES signal generator module.

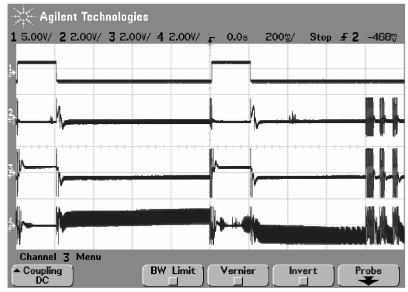

Fig. 8 Spontaneous and stimulating signals recorded during the *in-vivo* experiment

3 Conclusion

An FES signal generator module has been designed and implemented by using discrete devices at first. It can be used in a micro-electronic system of the neural function regeneration system. A module for four-channel FES signal generation was realized. It has been used to stimulate spinal cord and sciatic nerves of rats and rabbits for *in-vivo* experiments. The FES signal generator successfully caused reaction in different parts of the animals' bodies in the experiments, and different reactions have been observed. That the neural function regeneration system can regenerate neural signals was testified by the *in-vivo* experiment on a rat' s sciatic nerve.

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多通道神经信号激励模块的研制及其动物实验

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摘要:为了研究植入式神经功能再生微电子系统,设计了功能激励神经信号产生模块. 首先用分立器件设计并实现了体外应用的单通道功能激励神经信号产生模块,并将该模块成功应用于激励老鼠和兔子的坐骨神经和脊椎神经的神经功能再生微电子系统的动物试验. 在此基础上,设计了用于12 个电极点的卡肤电极或者 10 个电极点的剑状电极四通道神经信号激励模块. 用 5 只老鼠和 2 只兔子进行了 3 次坐骨神经和脊髓神经束活体动物试验. 试验中,功能激励神经信号产生模块再生了大鼠体内的自发神经信号和模拟的神经信号,模块所产生的信号使大鼠和兔子的腿部、尾巴甚至脚趾产生了相应的动作,验证了神经功能再生微电子系统的可行性.

关键词:微电极;神经功能再生;神经功能激励;神经信号通道;激励

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