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An Implantable Neural Stimulator for Intraspinal MicroStimulation

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***Abstract*—This paper reports on a wireless stimulator device for use in animal experiments as part of an ongoing investigation into intraspinal stimulation (ISMS) for restoration of walking in humans with spinal cord injury. The principle behind using ISMS is the activation of residual motor-control neural networks within the spinal cord ventral horn below the level of lesion following a spinal cord injury. The attractiveness to this technique is that a small number of electrodes can be used to induce bilateral walking patterns in the lower limbs. In combination with advanced feedback algorithms, ISMS has the potential to restore walking for distances that exceed that produced by other types of functional electrical stimulation. Recent acute animal experiments have demonstrated the feasibility of using ISMS to produce the coordinated walking patterns. Here we described a wireless implantable stimulation system to be used in chronic animal experiments and for providing the basis for a system suitable for use in humans. Electrical operation of the wireless system is described, including a demonstration of reverse telemetry for monitoring the stimulating electrode voltages.**

I. Introduction

Restoration of motor and sensory control using electrical stimulation of the spinal cord is being considered as a means of compensating for spinal cord injury in several laboratories [1-3]. Using metal electrodes, electrical currents can be strategically used to activate pools of spinal cord neurons with spatial-temporal patterns that mimic the normal biological systems for motor and sensory functions. In our research, IntraSpinal MicroStimulation (ISMS) is being investigated for restoration of walking. Miniature metal wire electrodes are placed within the spinal cord with the intent of providing pulses of electrical stimulation that can stimulate paralyzed leg muscles and evoke a walking pattern. The control of the gait-like movements can be enhanced using feedback control from sensor nerves that provide information about the limb position and contact with the ground.

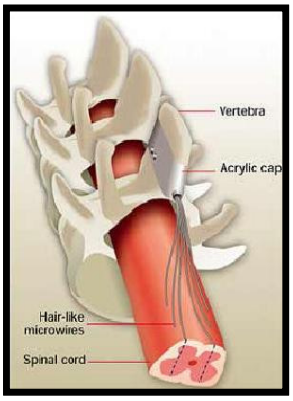

Figure 1. Depiction of IntraSpinal MicroStimulation (ISMS) using microwires implanted within the spinal cord. The microwires are inserted through the dorsal surface of the cord and the exposed tips target the ventral horn. The wires are fixed to the dura mater with cyanoacrylate glue and subsequently anchored to the spinous process of the L3 or L4 vertebra with dental acrylic.

The ISMS approach has a number of distinct advantages over other methods for spinal stimulation:

1) The implant surgery can be quite limited in extent, because the relevant length of the spinal cord controlling the legs is only 3 cm in cats and 5 cm in humans.

2) Stimulation through individual ISMS microwires can activate groups of muscles in organized synergies (e.g., whole limb extensor, flexor, forward, or backward movements), so relatively few stimulating channels can produce an appropriate gait pattern.

3) The evoked muscle contractions tend to be fatigue-resistant, providing prolonged periods of stable and maintained force levels

4) ISMS produces graded muscle contractions, thus allowing for finer control of the generated forces than that obtained with peripheral forms of electrical stimulation.

Our research is motivated by the need to place a multitude of intraspinal electrodes within the cord as a means of restoring locomotion. Our intent is to access both motor and sensory neurons in order to implement a closed loop control system in which biological sensory information is used to control the gait cycle. Here we describe an implantable wireless 16-channel stimulation device for use in chronic

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animal experiments that is specifically designed for ISMS use.

II. Animal Experimental Description

In a recent experiment we used ISMS in conjunction with an external tilt sensor (accelerometer) placed upon the hind leg of a cat. Figure 2 shows the intraspinal microwires electrodes implanted within the lumbosacral region.

Following the ISMS microwire implantation and fixation, as shown in Figure 3, the cat's spinal cord was stimulated to produce a gait-like pattern.

For this acute experiment, connections to the electrodes were made via a hardwired transcutaneous connection. In our present experimental regime this has limited the duration

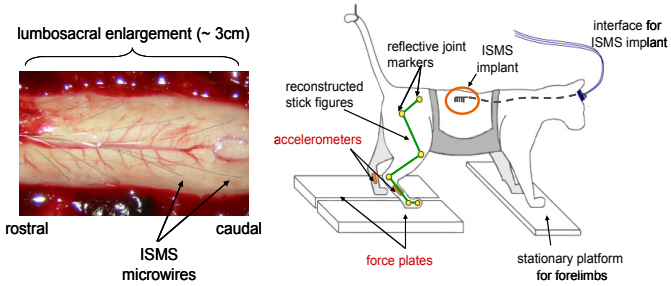

Figure 2 (left) – ISMS wires implanted within the lumbosacral region.

Figure 3 (right) – Following implantation of the ISMS microwires, the cat is placed in a harness and suspended over a split-belt treadmill with indwelling force plates. A miniature accelerometer was placed on the cat's leg to provide a mock sensory feedback signal

of the experiments to a maximum of 36 hours. To overcome this limitation and assess the viability of a chronically implanted device in humans, we have designed a wireless implantable stimulator suitable for use in chronic animal experiments.

III. Experimental Methods – Stimulator Design

For the acute experiments, a 16-chanel custom-built stimulator module was controlled by MatLab code via an RS-232 connection to the stimulator. This stimulator module contains a custom application-specific-integrated-circuit (ASIC) named the V6 stimulator, as originally designed by the Illinois Institute of Technology and now produced by Sigenics, Inc (Chicago, IL) [4].

A wireless version of this ASIC was developed for experimental animal use, called the V6WTA, and specifically adopted to the needs of ISMS. It was fabricated using the CX08 (0.8micron) bi-Cmos process of XFab (Lubbock, Texas, USA). The ASIC measures approximately 4.5mm x 4.5mm.

Increasingly, it is becoming understood that metal electrodes used for stimulation must be maintained within certain electrochemical limits in order to avoid deterioration of the metal surface and damage to the surrounding neural tissue. Controlling the cathodic and anodic voltage excursions during stimulation pulsing is crucial to preserving the electrochemical integrity of the electrode. Measurements of the voltage excursions can be used to determine to what extent the electrode has been driven beyond the acceptable electrochemical limit commonly known as the "Water Window." For an electrode to operate safely, the total polarization must remain within the water window.

The V6 ASIC automatically controls the voltage excursion through the use of compliance limits on the constant-current electrode drivers.

The V6WTA stimulator ASIC is the core electronic component of the ISMS implantable neural stimulator device. The ASIC connects to 16 stimulator electrodes. Each stimulator electrode has its own independent electronic drive channel, which may be controlled and observed through the communication interface portion [5] of the IC device.

Figure 4 shows an architectural block diagram of the ASIC. The "antenna" interface is a wire-wound coil inductor that is coupled to an extracorporeal magnetic transmitter. A full-wave rectification power supply module is comprised of upper BJTs and lower cross-coupled NFET transistors. The antenna interface contains an FSK demodulator module that decodes data sent to the ASIC via 120kB/sec FSK modulation of the Class-E transmitter. The demodulated data is sent to the state machine for decoding and packeting into electrode driver commands. The commands are loaded into the individual stim drive channel modules that provide the constant-current stimulus electrode drive. Voltage and current monitoring circuits can be switched on to any channel and sent to the analog-digital converter (ADC). The output of the ADC is processed by the reverse telemetry transmitter which creates subcarrier modulation on the antenna coil. All electronic circuitry is contained within the ASIC. The only required external components are two capacitors, one for resonating the antenna coil, and one to act as a power supply filter for the internally regulated 5VDC supply.

Table 1 shows the basic operational parameters for the ASIC. The ASIC supports both a reference electrode and a counter electrode (via two separate pads) The reference electrode presents a high input impedance node that is used for true electrochemical measurements of the electrode voltage and for creating the current driver compliance supplies. For the ISMS application, the reference pad is tied to the counter electrode pad within the implantable package module. Doing so will ensure that the voltage differential between the electrodes and the counter electrode will be maintained at a known value.

Taking into account the various stimulation waveform modes, charge recovery modes, counter electrode offset

modes, and electrode offset bias, there are effectively 3 useful and/or safe stimulation modes:

- Biphasic, cathodic (or anodic) first charge-balanced waveform where the electrode is maintained at a bias of 0V relative to the reference electrode between pulses. The compliance supply for the two phases source or sink current up to a maximum voltage drop of ±2.5V.
- Monophasic, cathodic (or andodic) first charge-balanced waveform where the electrode is maintained at a bias of 0V relative to the reference electrode between pulses. The compliance supply for the current driver can sink current up to a maximum voltage drop of 2.5V. Charge recovery is performed by a 20 µA current source that returns the electrode to its 0V bias following the pulse.

parameter	symbol	min	nom	max	unit
Power Carrier Frequency	Fc		500		kHz
FSK Frequency Deviation	Fd	2		4	%
anodic current (3.1)	Ia	<0.01		63.5	µA
cathodic current (3.1)	Ic	<0.01		63.5	µA
electrode drive current increment (3.2)	I_{LSB}		0.5		µA
stimulation pulse duration (3.3; 3.4)	Tw	32		928	µs
pulse duration increment (3.3; 3.4)	Tw_{LSB}		64		µs
inter-phase delay (3.4)	Td		32		µs

Table 1 – Basic operational parameters of the V6WTA ASIC

note 3.1: Minimum anodic and cathodic currents are the "off-state" leakage current of the electrode drive circuitry.

note 3.2: Electrode drive current is set by a 7-bit digital value; the electrode drive DAC is guaranteed monotonic over all codes.

note 3.3: The timing of stimulation pulses (duration and inter-phase interval) is determined by counting cycles of the power carrier. Changes in the power carrier cycle period will result in proportional changes in the timing characteristics of stimulation pulses. The measurements given in this table assume a nominal 500 kHz power carrier frequency.

note 3.4: The duration of stimulation pulses is set by a 4-bit value. The mapping from the 4-bit binary value N to pulse duration is given by the equation: 64us * N – 32us.

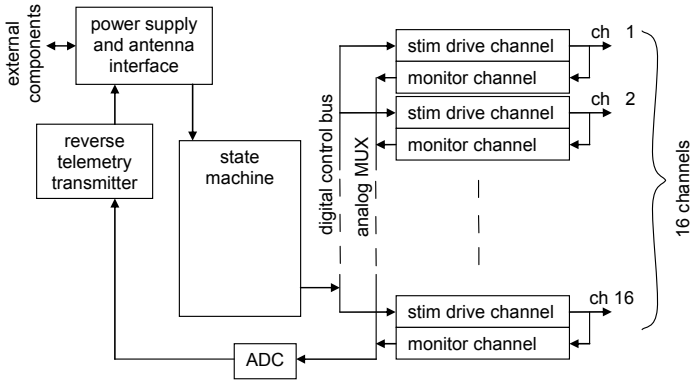

Figure 4 - Block diagram of the V6WT stimulator IC device. Arrows show the direction of information flow, without any indication of information format.

- Monophasic, cathodic first charge-balanced waveform where the electrode is maintained at a bias of +0.6V relative to the reference electrode between pulses. The compliance supply for the current driver can sink current up to a maximum voltage drop of 5V. (The device operates in the "Shift Counter Mode", and cannot support any of the other modes listed above, on any of the electrodes, unless power is removed and reapplied to the device.) Charge recovery is performed by a 192 µA current source that returns the electrode to its +0.6 V bias following the pulse.

For each of the modes, charge recovery is assured because during the interpulse interval the electrode is returned to the its pre-stimulus voltage. The latter of these three modes is specifically designed to accommodate the bias-demands of AIROF electrodes. Stimulation frequency limits are not part of the ASIC, per se. Since each pulse is controlled by the extracorporeal telemetry controller (TC), with a maximum command rate of 125kb/sec, for 33-bit commands, one pulse on any channel can be initiated every 264usec.

The reverse telemetry data link is carried by phase modulation of a carrier signal at an integer fraction of the power carrier frequency. Reverse data channel symbols are LR and HR, carrying reverse-channel information corresponding to logic 0 and 1, respectively. The LR and HR symbols are transmitted by binary phase-shift keying (BPSK) on a carrier frequency of Fc / 8.

The Reverse Telemetry Data consists of a single 8-bit value representing the output of the ADC. The input to the ADC is switchable between a voltage monitor input and a current monitor input. The electrode voltage monitor input can be connected to one of the electrodes via software control. The current monitor measures the current through the counter electrode. One A/D sample is taken per stimulation pulse. The time at which the sample is taken is governed by a 14-bit counter that is reset upon receipt of the stimulation command. The counter counts up to a threshold value and, upon reaching that threshold value, triggers an A/D conversion. Thus, when viewed as a waveform, the reverse telemetry samples can be thought of a composite

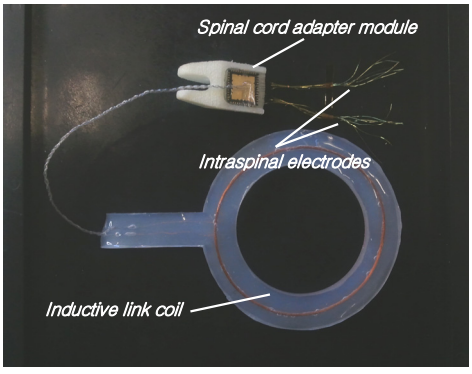

Figure 5 – Physical configuration of the ISMS implantable stimulator. The QFN package is contained withint Spinal cord adapter module

waveform having been sampled at 2 µs intervals.

Physically, as shown in Figure 5, the ASIC is contained within a standard ceramic QFN package, and the QFN package is contained within a custom-fabricated spinal cord adapter module, mimicking that shown in Fig 1.

IV. Experimental Data

Space does not permit detailed measurements of all the stimulator functional parameters. The demonstration of the reverse telemetry is of interest. Figure 6 shows the analog output of the extracorporeal receiver that is detecting the stimulator reverse telemetry.

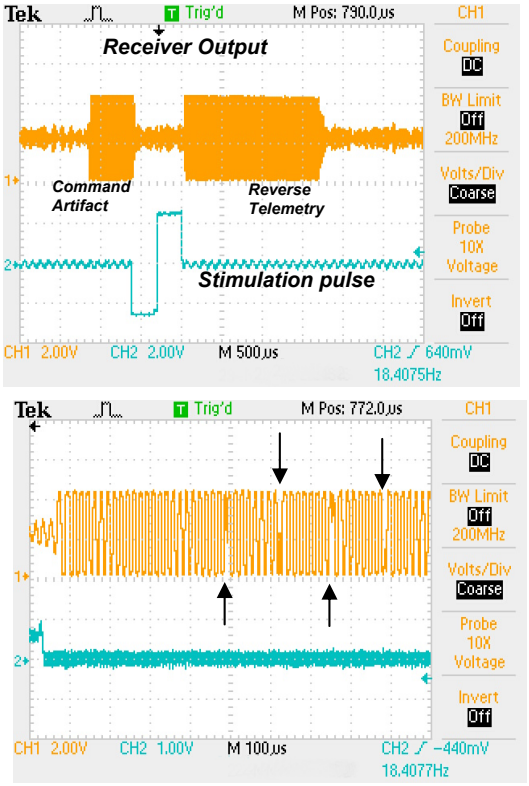

Figure 6 – Oscilloscope waveforms of the reverse telemetry showing the external receiver output following the application of the stimulus pulse

In the upper portion of Fig 6, it can be seen that the receiver is initially subjected to a command artifact caused by the forward FSK command modulation of the transmitter necessary to initial the stimulation pulse. The ADC sample is taken during the stimulation pulse, and then transmitted via the subcarrier reverse telemetry after the stimulation pulse is completed. This specific timing is used so that any droop of the stimulator DC power supply caused by the reverse telemetry does not corrupt the stimulation pulse. In the lower portion of Fig 6, the details of the phase shifts within the reverse telemetry signal can be seen at the locations of the bit changes.

V. Discussion

Physical fabrication of the implantable stimulator presented a challenge because the locations for the construction of the electronics module and the intraspinal electrodes are not the same. The stimulator electronics is fabricated at IIT, and the electrodes are fabricated at U of Alberta. It was necessary to devise a segmented assemlby procedure that allowed for attachment of the 16 electrodes and counter, as well as the final polymer encapsulation set at U of Alberta. A complex set of assembly fixtures was devised which are now ready for trial use. It is anticipated that the first chronic ISMS animal experiment will begin in the second half of 2012.

The software interface for the implantable stimulator needs to be compatible with that being currently used for the non-implantable V6-based stimulator. A customized GUI will be used for rapid collection of chronic electrode voltage and current waveforms at the onset of each chronic experimental session.

The data from the chronic experiments will form the design basis for an implantable system suitable for human use.

VI. Conclusion

An implantable neural stimulator for chronic ISMS animal experiments has been developed, tested, and is ready for use. The expectations are that the data from these first-ever chronic demonstrations of ISMS induced walking will be an important step towards the implementation of the ISMS method in humans.

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