33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Recording Sensory and Motor Information from Peripheral Nerves with Utah Slanted Electrode Arrays

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Abstract—**Recording and stimulation via high-count penetrating microelectrode arrays implanted in peripheral nerves may help restore precise motor and sensory function after nervous system damage or disease. Although previous work has demonstrated safety and relatively successful stimulation for long-term implants of 100-electrode Utah Slanted Electrode Arrays (USEAs) in feline sciatic nerve [1], two major remaining challenges were 1) to maintain viable recordings of nerve action potentials long-term, and 2) to overcome contamination of unit recordings by myoelectric (EMG) activity in awake, moving animals. In conjunction with improvements to USEAs themselves, we have redesigned several aspects of our USEA containment and connector systems. Although further increases in unit yield and long-term stability remain desirable, here we report considerable progress toward meeting both of these goals: We have successfully recorded unit activity from USEAs implanted intrafascicularly in sciatic nerve for periods up to 4 months (the terminal experimental time point), and we have developed a containment system that effectively eliminates or substantially reduces EMG contamination of unit recordings in the moving animal. In addition, we used a 100-channel wireless recording integrated circuit attached to implanted USEAs to transmit broadband or spike-threshold data from nerve. Neural data thusly obtained during imposed limb movements were decoded blindly to drive a virtual prosthetic limb in real time. These results support the possibility of using USEAs in peripheral nerves to provide motor control and cutaneous or proprioceptive sensory feedback in individuals after limb loss or spinal cord injury.**

I. Introduction

THE upper and lower limbs and digits exhibit high innervation densities, thereby allowing fine motor control and high-resolution, multi-modal sensory input. Consequently, to restore motor and sensory function effectively after limb loss or spinal cord injury, peripheral nerve interfaces will need to record from and stimulate a large number of different sites in a highly selective manner. For example, because residual nerves remain viable after limb amputation, recordings obtained from motor fibers could provide natural, intuitive control signals for a highly dexterous prosthetic arm. Similarly, after spinal cord injury, recordings from sensory fibers could provide cutaneous and proprioceptive information that could be used to evoke percepts (e.g., via stimulation of somatosensory cortex) or to provide local feedback control of motor systems. These first-order requirements strongly imply the need for multiple intrafascicular electrodes whose active tips closely abut small subsets of motor or sensory nerve fibers.

A leading example of such a neural interface is the Utah Slanted Electrode Array (USEA) [1]. Among its advantages, the USEA provides ~100 independent sites of stimulation and recording; a high degree of selectivity; and ease of implantation [1-7]. The 100 microelectrodes are spaced 400 μm apart on a 10 x 10 grid, with lengths from 0.5 to 1.5 mm. A single USEA thus provides almost complete coverage of both the width and depth of the cat sciatic nerve. The USEA provides highly selective stimulation and recording for multiple different motor and sensory fibers in cat hindlimb nerves [1-6], and, more recently, in monkey arm nerves [8]. A similar Utah Electrode Array (UEA) with equal-length electrodes has been used successfully for years in motor cortex of paralyzed humans [9], and has been implanted chronically in the median nerve of one individual without pain or loss of hand function [10].

The seminal work of Branner, Normann et al. [1] first examined chronic USEAs and containment systems (to protect and stabilize the array) in cat sciatic nerve. These important initial studies demonstrated that long-term USEA implants are relatively benign, and cause little or no behavioral locomotor deficits. The ability to evoke motor responses was also maintained. However, in general it was not possible to record single units long term, and recordings were contaminated by electromyographic (EMG) activity during movement. Additional challenges included large, rapid drops in electrode impedances, and failure of connectors and electrodes (perhaps due to broken lead wires), particularly in early implant systems.

Here we report substantial progress toward addressing these remaining challenges, including in particular the ability to obtain long-term, EMG-free unit recordings from USEAs implanted in cat sciatic nerve. Further, to demonstrate their functional utility, we recorded neural signals via a 100-channel wireless integrated circuit [11], and used the wirelessly transmitted spike-threshold data to drive a virtual prosthetic limb in real time [12].

Manuscript received April 15, 2011. This work was supported in part by NIH/NINDS contract N01-NS-4-2362, NIH/NINDS grant 1R01NS064318-01A1, and DARPA contract N66001-06-C-8005.

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II. METHODS

A. USEA, Containment System, and Transcutaneous Connector

1) USEAs: USEAs were manufactured as in previous work [1], with modifications including sputtered iridium oxide film (SIROF) electrode tips, Parylene-C electrode insulation, wirebonding, and lead-wire insulation. Four near-corner long electrodes with large exposed tips and low impedances converged to common bus and served as an additional on-array electrical reference.

2) Connectors: In the previous chronic USEA study [1], each array was wired to 36 pins of two 40-conductor connectors mounted on the animal's back. Here the USEA was wired to a custom-designed printed circuit board (PCB) attached to a single Tucker-Davis Technologies 96-pin ZIF-Clip connector. The PCB and a protective titanium shell were mounted outside the animal atop a surface-treated medical-grade titanium transcutaneous post, shaped as a rounded 5 mm by 20.5 mm rectangle. The post attached to a bone plate screwed to the femur. The height from the bone to the bottom of the flange holding the PCB and shell was approximately 18 mm, which was sufficient to traverse intervening muscle and to clear the outer surface of the skin.

3) *Containment system.* The array containment system for chronic preparations consisted in part of a 19 mm x 13 mm gold-wire screen (#52 gold mesh, Alfa Aesar, Ward Hill, MA) whose edges had been coated with Parylene-C to prevent unraveling of the screen and to minimize snagging on tissue. The screen was attached via a lead wire to the connector shell, which served as electrical ground.

B. Surgery

Four purpose-bred adult cats with chronic USEA implants were used. One additional acute preparation was used for the wireless recording and neural decode experiment.

Two different surgical methods were used for chronic implants. In the one-stage procedure, all devices were implanted in the same surgery. In the two-stage procedure, the bone plate for subsequent connector attachment was first screwed to the femur, and the animal subsequently was allowed to recover for over one month prior to USEA implantation in the second surgical stage. This recovery period was intended to promote greater osseointegration prior to the connector's being subjected to external torques.

Animals were maintained on isoflurane anesthetic with mechanical ventilation. The sciatic nerve of the left hindlimb was exposed as previously described [1-3]. The chronic connector was attached to the bone plate, and the containment system screen was laid flat under the nerve prior to high-speed insertion of the USEA into the nerve. The USEA was lightly glued to the nerve with veterinary-grade cyanoacrylate tissue adhesive. The USEA and nerve were then lightly covered with Kwik-Cast, a two-component silicone elastomer. The containment system screen was closed prior to elastomer curing, and additional Kwik-Cast used to fill voids and to cover screen edges. The lead wires from the array to the connector followed a U-shaped course that did not cross any joints.

C. Post-Surgical Physiological and Behavioral Testing

The four chronically implanted animals were followed for a period of one month (n = 1), two months (n = 1), and four months (n = 2) respectively, at which time the animal was sacrificed for quantitative histological analyses (data to be reported separately).

Four physiological measures were obtained in post-surgical tests, initially at frequent (sometimes daily) intervals, and subsequently at successively longer intervals. First, impedance measures were taken using a custom-built automated impedance tester [13] that provided estimates of the true tip impedance, independent of possible shunting to other electrodes. Second and third, unit recordings were obtained both when the animal was anesthetized (which presumably revealed sensory discharges), and when the animal was awake and moving (which presumably revealed motor as well as sensory discharges). To test the ability of the containment system to serve as an electrical shield to block contamination of neural recordings by myoelectric signals, recordings were obtained with either the on-array reference electrodes (within the containment system shield), or with conventional off-array reference wires (outside the containment system shield). Fourth, we measured the ability of the USEA to evoke motor responses, as monitored via fine-wire EMG electrodes (data to be reported separately).

We also periodically assessed the animals' locomotor behavior.

D. Wireless Recordings and Real-Time Neural Decodes

Neural data were recorded via an INI-R5 (Integrated Neural Interface, Recording, version 5) or INI-R6 integrated circuit [11]. The INI chips were packaged in a quad flat pack (QFP) with up to 16 lead wires attached via a connector to a 100-electrode USEA implanted acutely (n = 1 cat, 1 session) or chronically (n = 2 cats, 3 sessions) in cat sciatic nerve. Both INI chips are wireless low-power integrated circuits that receive power and commands inductively, and return wide-band neuronal and spike-threshold crossing data via digital radio-frequency telemetry. Cat ankle rotation, produced by the experimenter in anesthetized animals, was monitored via a goniometer. A neural decode based on wirelessly recorded neural data was used to predict joint angle and to drive a prosthetic limb in parallel in real time. Correlation coefficients and RMS error were used to assess how closely the neural decode algorithm predicted movements of the biological limb.

III. RESULTS

Most importantly, unit activity was successfully recorded using USEAs implanted intrafascicularly in sciatic nerve for periods up to 4 months (the terminal experimental time point), and the containment system effectively eliminated or substantially reduced EMG contamination of unit recordings in the moving animal. In addition, neural signals obtained

wirelessly during imposed limb movements were decoded blindly to drive a virtual prosthetic limb in real time.

A. General

As in previous work [1], USEA implants appeared behaviorally benign. Cats showed little or no signs of locomotor deficits shortly after recovery from surgery. They used the implanted hindlimb fully in a weight-bearing manner. The cats ignored the transcutaneous connector, which ironically proved slightly problematic in that they would bump into objects with the connector during locomotion, subjecting it to mechanical stress. Although the small sample sizes preclude definitive conclusions, the two-stage implants, in which the bone plate was first implanted separately to allow time for osseointegration, were mechanically more stable than the one-stage implants, both of which loosened at the bone attachment site. In one case, we repaired the loosened connector with bone cement, and it remained stable for months thereafter.

B. Physiological Metrics

Improvements were obtained on multiple physiological metrics, compared with previous work [1].

Electrode impedances were reasonably stable across time. A small rise in impedance occurred immediately after implantation, presumably because tissue impedances were higher than impedances of saline test solutions. Impedances then stabilized for several weeks or months thereafter (Fig. 1). In most cases there was little apparent lead-wire or electrode breakage evidenced by impedances > 2 Mohm.

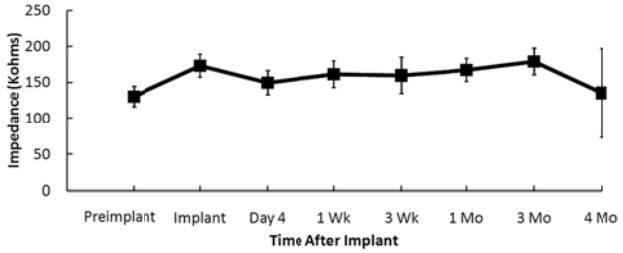

Fig. 1. USEA electrode impedances (mean ± SEM) remained relatively stable across time. Day 0 to 1 month, $n = 4$; at 3 and 4 months, $n = 2$.

Long-term single- and multiple-unit recordings were obtained on multiple electrodes in each animal (Figs. 2 and 3). Shortly after implantation, 40 ± 7 (mean ± standard error of the mean, SEM) units were recorded in response to cutaneous stimuli or experimenter-imposed movement of the limb in anesthetized animals. Presumably, many electrode tips that did not show neural activity resided in extrafascicular space. There was a modest drop in unit activity over the course of the first week. Thereafter, the number of units recorded stabilized or increased for a period of weeks or months, till animal sacrifice. Later implant systems showed more unit recordings than early systems.

To examine the ability of the containment system to shield neural recordings from contamination by myoelectric activity, we also recorded from awake, moving animals. In conjunction with use of on-array references, the shield dramatically reduced contamination by EMG (Fig. 3). Recordings in awake animals showed a greater number of units than did recording in anesthetized animals, indicating that USEAs recorded motor as well as sensory discharges.

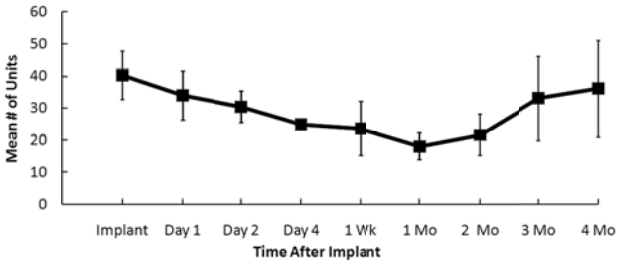

Fig. 2. The number of units recorded by USEAs chronically implanted in sciatic nerve was maintained for several months (the terminal experimental time point). At 2 months, $n = 3$; otherwise, n's as indicated in Fig. 1.

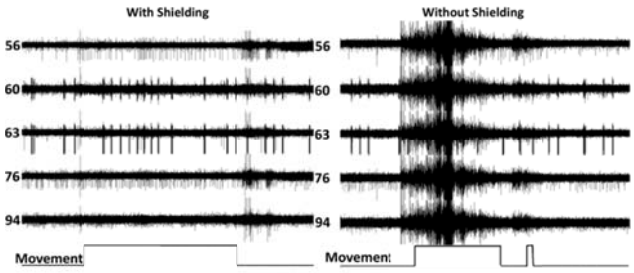

Fig. 3. EMG-free chronic recordings from sciatic nerve in the behaving cat. Left: Recordings obtained using the on-array reference within the containment-system shield were nearly entirely free of EMG contamination even during movement (bottom marker trace). Right: In contrast, recordings obtained with reference wires outside the containment-system shield showed large myoelectric signals common to all channels, obscuring the neural signals. Traces show recordings from different USEA electrodes.

C. Wireless Recordings

Consistent with earlier work [11, 12], both the INI-R5 and INI-R6 chips successfully recorded unit activity from USEAs in sciatic nerve, and operated in an entirely wireless mode. Commands were successfully sent via a wireless inductive link; spike threshold levels were set wirelessly and independently on multiple amplifiers; and low-noise recordings of nerve discharges and spike-threshold crossings were transmitted and received wirelessly from multiple electrodes (Fig. 4). Noise levels approached 6 µV RMS, which was near the theoretical limit of 5 µV recorded in benchtop experiments. These results represent the first *in-vivo* use of the INI-R6 chip.

D. Neural Decode and Control of the VIE arm

A "training set" of neural and behavioral data was used to develop an off-line optimal linear estimator of the ankle angle through multivariable linear regression of the neuronal firing rates. The neural decode utilized wireless recordings and spike-threshold crossings on up to 16 different amplifiers. The decode described the actual joint angles very accurately (e.g., $r = 0.99$).

We next cross-validated this algorithm on a "test set" of new data to predict changes in joint angle of the cat ankle

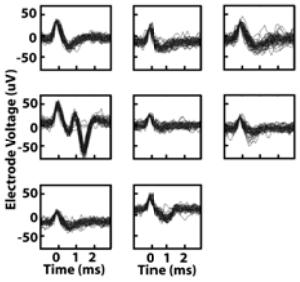

Fig. 4. Units recorded wirelessly via eight different INI-R5 amplifiers, each connected to a different electrode of a USEA implanted in sciatic nerve. Digitized neural data were transmitted and received wirelessly (15.7 kS/s) from one selectable INI-R5 amplifier at a time, and subsequently analyzed to extract spike waveforms. Figure is a composite.

from neural discharges, and used the predictions to control elbow flexion of a prosthetic limb in a virtual integration environment. These two operations were performed simultaneously, in real time. The movements of the virtual arm closely tracked the movements of the biological limb (Fig. 5), indicating that the sensory discharges could be used to accurately determine joint angle. The neural decode was conducted "blind"; i.e., did not depend on separate information to delineate trial start or stop, and it provided continuous analog control, rather than using a nominal classifier approach. Previously, UEA recordings from dorsal root ganglia have been used with off-line decodes to predict cat hindlimb position [14]. The present results represent the first real-time control of a virtual prosthetic arm via discharges recorded wirelessly from peripheral nerve.

IV. Discussion

Although further increases in unit yield and long-term stability remain desirable, the present results support the possibility of using USEAs in peripheral nerves to provide motor control and cutaneous or proprioceptive sensory feedback in individuals after limb loss or spinal cord injury.

Several factors may have contributed to the improved physiological metrics, relative to earlier work [1]. Improved USEA and lead wire insulation may have reduced previously seen drops in impedance, and, together with SIROF tips, improved unit recording capabilities. The containment system electrical shield, in conjunction with on-array references, minimized contamination of neural signals by myoelectric activity, and together with the silicone elastomer and tissue adhesive, provided mechanical stability for the array and minimized connective tissue ingrowth. The bone-mount connector allowed lead wires to avoid crossing moving joints, thereby reducing wire bending and potential breakage. The two-stage surgical approach allowed greater osseointegration and connector stability. Finally, the high-density 96-pin connectors provided access to almost all 100 USEA electrodes.

The ability to use chronic recordings of nerve discharges to predict and control joint angles provides further evidence that the long-term recordings provide functionally useful signals. The successful development and implementation of wireless technologies presage further enhancements of long-term reliability and performance.

Neural interfaces may be implanted for decades in clinical use. It therefore will be important to demonstrate viability

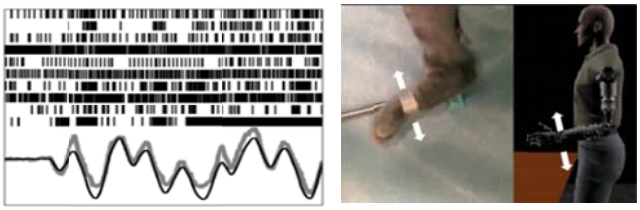

Fig. 5. Wireless decode of ankle joint angle. Left, top traces: Spike threshold crossings from 10 channels telemetered wirelessly from INI-R5. Bottom traces: Actual ankle joint angle (thin black line), together with joint angle predicted in real time by the neural decode algorithm (thick grey line) (r = 0.93, RMS error = 13.7°). Right: The predicted joint angle was then used to drive a virtual prosthetic limb in real time.

lasting many years. The improvements reported here represent important progress toward that goal.

Acknowledgment

We thank Richard Normann for discussions and advice, and Florian Solzbacher, Loren Reith, Prashant Tathireddy, and Trevor Taylor for improvements to USEAs.

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