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An Intrafascicular Electrode for Recording of Action Potentials in Peripheral Nerves

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We are developing a new type of bipolar recording electrode intended for implantation within individual fascicles of mammalian peripheral nerves. In the experiments reported here we used electrodes fabricated from 25 μm diameter Pt wire, 50 μm 90% Pt–10% Ir wire and 7 μm carbon fibers. The electrodes were implanted in the sciatic nerves of rats and in the ulnar nerves of cats. The signal-to-noise ratio of recorded activity induced by nonnoxious mechanical stimulation of the skin and joints was studied as a function of the type of electrode material used, the amount of insulation removed from the recording zone, and the longitudinal separation of the recording zones of bipolar electrode pairs. Both acute and short term (two day) chronic experiments were performed.

The results indicate that a bipolar electrode made from Teflon™-insulated, 25 μm diameter, 90% Pt–10% Ir wire, having a 1–2 mm long recording zone, can be used for recording of peripheral nerve activity when implanted with one wire inside the fascicle and the other lead level with the first lead, but outside the fascicle. No insulating cuff needs to be placed around the nerve trunk.

Keywords *— Neuroprosthesis, Peripheral nerve electrodes, Sensory recording.*

INTRODUCTION

Loss of mobility of the extremities is a frequent, debilitating sequel to spinal cord injury, head trauma, and stroke. In these instances, the neural pathways connecting the brain to the spinal cord nuclei innervating target muscles are interrupted, leaving the muscles innervated but unable to respond to command signals originating in the brain. In addition, such patients often lack sensory feedback from the area of the body below the lesion, even though the peripheral sensory nerves are still intact and functional. Unlike peripheral nerves, which can regenerate to reestablish connections after injury, central nervous tissue does not normally regenerate in the human body.

While much work is being done in the area of spinal cord reconstruction (9), no

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method has yet proven useful in reestablishing pathways in the spinal cord. Meanwhile, prosthetic devices may provide a promising means to bridging this gap in communication (5,6). Functional electrical stimulation (FES) of neuromuscular tissue to produce movement or sensation has reached the clinical stage in many research centers: upper extremity FES has been used to restore key and pinch grasp in paraplegics (16), and lower extremity FES has shown promise for restoring walking (10,14,18).

Before present techniques of FES can move out of the experimental laboratory to a clinically accepted therapy, a number of significant improvements are needed. Among them are: (a) reliable implantable electronics and electrodes; (b) larger numbers of independent command channels for volitional control; and (c) somatosensory and proprioceptive or kinesthetic feedback. The work described in this paper is directed toward developing an implantable electrode system and insertion technique which can serve for chronic recording of several channels of sensory nerve activity.

The electrodes are patterned after a recording method demonstrated by Janssens *et al.* (8), but are designed to be reliably implanted within single fascicles of peripheral nerves on a chronic basis. Since each fascicle innervates a restricted, well localized set of peripheral receptors (19), our electrode system has the potential of being able to relay information about specific events within a localized receptive area back to an FES controller. Of particular interest are signals from cutaneous mechanoreceptors, which provide information about objects contacting the skin, and proprioceptors, which provide information about joint position and movement.

METHODS

Electrode Construction

Electrodes were fabricated from 25 μm diameter, Isonel insulated, Pt wire, 50 μm diameter, Teflon insulated, 90% Pt–10% Ir wire and 7 μm diameter carbon fibers wound together and coated with insulating varnish. The electrode design is shown in Fig. 1. The desired length of insulation was removed from a zone approximately 20 mm back from the end of the wire or carbon strands by heating it, between appropriately spaced heat sinks made from 30 gA needles, in a small flame. The terminal end of the electrode was then attached with cyanoacrylate adhesive to a 50 μm diameter, tungsten needle which had been previously sharpened by electrochemical etching in a dilute solution of KNO_2. This procedure is referred to as the single wire technique.

In some of the experiments, an alternate method was used in which an insulated carrier wire is glued to the tungsten needle. One or two electrodes, with insulation removed only at their ends, were wrapped around this lead wire starting approximately 2 cm behind the needle. We refer to this method as the lead wire technique. This design allowed better control over the length of insulation removed, but the addition of a lead wire increases the potential damage done to the nerve on insertion. Since this technique has a current path only at the tip of the wire, it was also used to test the effect of having two current paths (the zone of removed insulation and the cut end of the wire when the needle is removed) in the single wire technique. Several electrodes made using the single wire technique were compared to lead wire electrodes with the same nominal exposure length. The recording properties of these two types of electrodes were statistically indistinguishable, indicating that the exposure at the cut end of the single wire electrode does not significantly affect its performance.

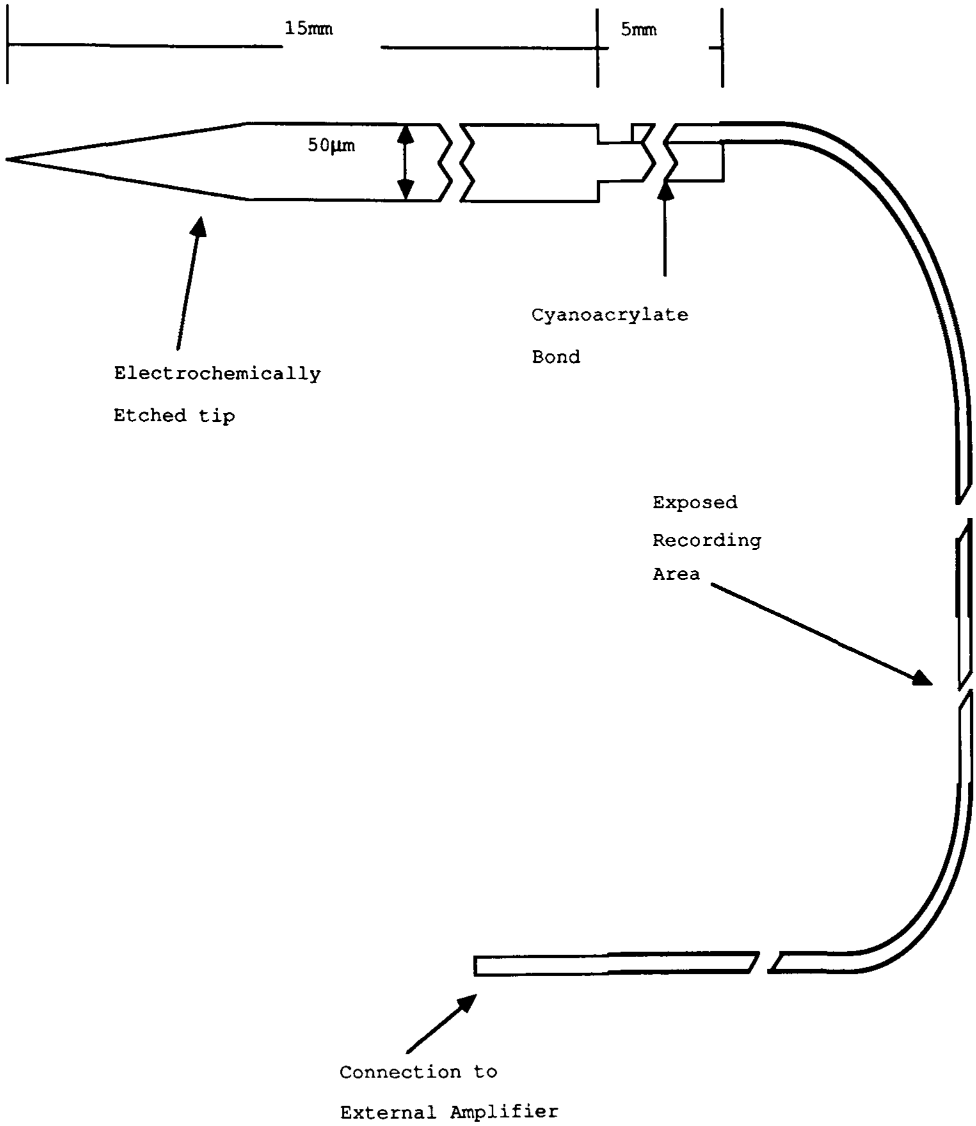

FIGURE 1. Schematic diagram of an intrafascicular electrode and its insertion micro-needle. The electrode is made of either insulated Pt–Ir wire or carbon fibers. Insulation is removed from an area about 20 mm behind the distal end of the wire to provide a recording zone. The distal end of the wire is then bonded to a sharpened tungsten needle with cyanoacrylate adhesive. Insulation is removed from the proximal end of the wire to allow connection to a high gain amplifier.

Approximately 1 cm of insulation was removed from the proximal ends of the electrodes to allow for attachment to recording equipment. Impedance measurements were made to confirm that the proper length of insulation for recording had been exposed. The Pt wire electrodes had properties expected from the analyses of wire electrode materials made by others (3,21).

Animal Preparation

Rats were anesthetized with an intraperitoneal injection of sodium pentobarbital (40 mg/Kg). Supplementary injections were given as needed to maintain the animals in an areflexic state. Body temperature was controlled with a heated plate. Both legs were shaved and an incision was made along the thigh from the sciatic notch to the knee. The hamstring muscles were separated and held open to expose the sciatic nerve. Under 25× magnification, fine forceps were used to tease away the epineurium from the largest fascicle of the sciatic nerve for approximately 1.5 cm. The perineurium of the fascicles was not damaged during this procedure.

For implantations in cats, similar procedures were used except that the surgery was done under aseptic conditions, and the ulnar nerve in the upper arm, rather than the sciatic, was exposed.

Electrode Insertion

While applying a slight amount of tension to one fascicle with the use of a nerve holder, the electrode needle was held with a pair of forceps, pierced through the perineurium and threaded distally along the fascicle for about 1 cm. The tungsten needle was then pushed out through the perineurium and pulled distally until the exposed recording area of the electrode was centered inside the fascicle.

The tungsten insertion needle was removed by cutting the electrode wire 5 mm beyond the point where it exited the fascicle. Silk suture was used to tie the proximal end of the electrode to neighboring connective tissue, stabilizing the electrode position while recordings were made. The skin was closed with two or three sutures, restoring the nerve to its natural environment. No insulating material was placed around the nerve. The proximal end of each electrode was attached to a preamplifier and the animal was electrically grounded through a 25 gA needle placed under the skin several centimeters from the recording site.

Recording Setup

The electrodes were capacitively coupled to a high impedance (100 MΩ) differential amplifier and bandpass filter with half power points of 400 and 6000 Hz. The total amplification of the system was 10^4. The signal was displayed on an oscilloscope, fed to an audio monitor, and recorded on an AM tape recorder.

Electrode impedance was measured, *in vivo*, with a 1 KHz constant current sine wave source applied to the electrode. The current was kept in the nano amp range to prevent damage to the nerve fibers.

Measures of Signal-to-noise Ratio

Four measures were used to quantify the signal-to-noise ratio of the recorded signal.

Amplitude. Figure 2 shows a typical nerve recording at slow sweep speed. Activity in the nerve was induced by alternately squeezing the paw of the rat for one second and then releasing the paw for one second. The ratio of the amplitude of the signal during stimulation divided by the amplitude in the absence of stimulation was used as one measure of signal-to-noise.

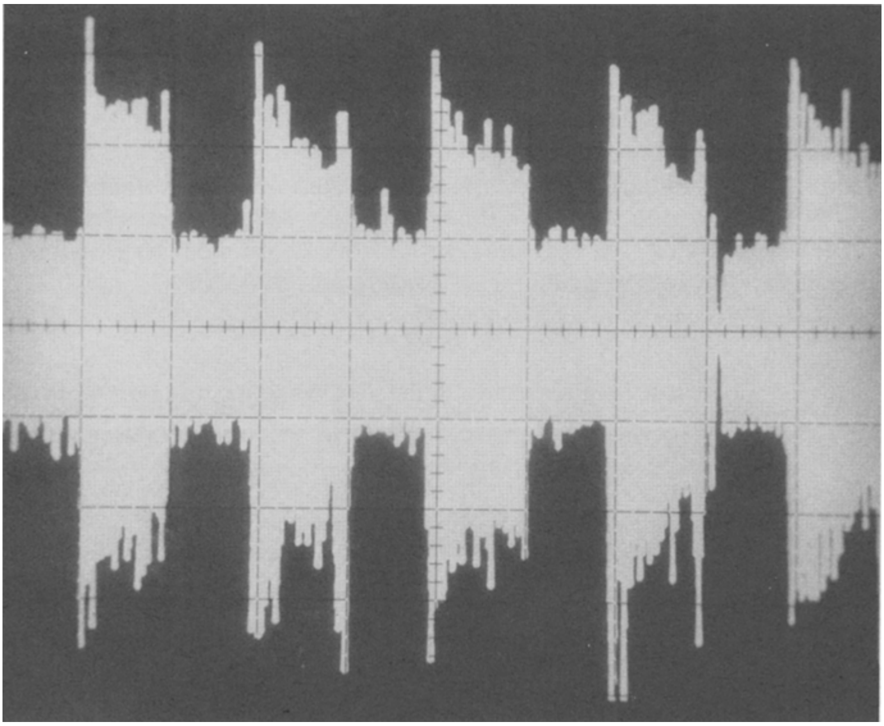

FIGURE 2. Oscillograph of neural activity recorded with an electrode placed in a single fascicle of the rat sciatic nerve. Periods of squeezing the paw were alternated with equal duration periods in which the leg was not stimulated. Scales: 1 sec/div and 10 μv/div (including preamplifier gain).

Pulse counting. A trigger level was set so that in the absence of stimulation between 0 and 5 nerve impulses per second exceeded the level of the trigger. This background level of activity was compared to the number of pulses per second that exceeded the threshold when the paw was mechanically stimulated. This measure is dependent on both the number of active nerve fibers and their rate of firing.

Fourier analysis. The tape recorded signal was digitized and analyzed with a fast Fourier transform (FFT) program which sampled 256 points at a rate of 5120 Hz. Ten transforms each were made for periods of stimulation and periods of rest, converted into voltage spectra, and an average spectrum was constructed from these ten spectra. Signal-to-noise ratio was measured by taking the area of the average spectrum during stimulation and dividing it by the area of the average spectrum during no stimulation. A value of 1 represents no difference in the spectral amplitudes, and a ratio of 2 means that the signal was twice as large during stimulation as it was in the absence of stimulation.

A fourth measure of signal-to-noise was obtained by looking at the difference between the stimulated and unstimulated spectra, choosing the octave band that encompassed the peak of this difference spectrum, and taking the ratio of the spectral amplitudes only within this octave band.

All four measures gave qualitatively and statistically similar results. Therefore, only the data from method three, wide-band Fourier analysis, is presented here.

Exposure Length

The lead wire technique was used to study the effect of exposure length since it allowed for the most accurate control of recording zone dimension. Exposed lengths of 0, 0.25, 0.5, 0.75, 1.0, 2.0, and 4.0 mm were used, where 0 mm corresponds to the cut end of the wire. Ten electrodes, made from 25 μm diameter Pt wire, were studied for each exposure length.

Electrode Size and Material

Electrodes with 1 mm long recording zones were made from Teflon®-insulated, 50 μm diameter, 90% Pt–10% Ir wire and from twisted sets of 5 strands of 7 μm carbon fibers (Hercules Inc.) insulated with Epoxylite®. The properties of these electrodes were compared to those of 1 mm exposure electrodes made from the 25 μm Pt wire.

Bipolar Separation

Pairs of 25 μm diameter, Pt wire electrodes with 1 mm recording zones were used to construct bipolar electrodes. These were inserted with the lead wire technique. Four series of animals were implanted with these bipolar electrodes, with the longitudinal spacing between the recording zones set at 1, 2, 3, and 4 mm, respectively. Another group of animals had one lead of the bipolar pair placed inside the fascicle and the other placed directly adjacent, but outside the fascicle. This latter system allows for only a single wire to be threaded into the fascicle while still affording the benefits of bipolar recording.

Histology

Electrodes were implanted in one of the ulnar nerves of each of two cats and left in place for 48 hours, a time long enough for acute damage and inflammatory reactions to be seen histologically (12). The other ulnar nerve in each animal was exposed and manipulated as if inserting an electrode, but no implant was made. The animals remained anesthetized, and nerve signals were recorded at 18, 24, 36, and 48 hours post implantation. After two days, the cats were perfused with Palay's solution, the nerves were removed and prepared for light microscopy by the University of Utah Histology Lab (Palay's solution: a 0.1 M PO_4 buffered solution of glutaraldehyde and paraformaldehyde).

RESULTS

Exposure Length

As expected, electrode impedance is inversely related to the amount of insulation removed (Fig. 3). Beyond 4 mm there is little reduction in electrode impedance within the range of feasible recording zone lengths.

Figure 4 shows the frequency spectrum of the neural signal when the paw was being stimulated, when the paw was at rest, and the difference between these two sig-

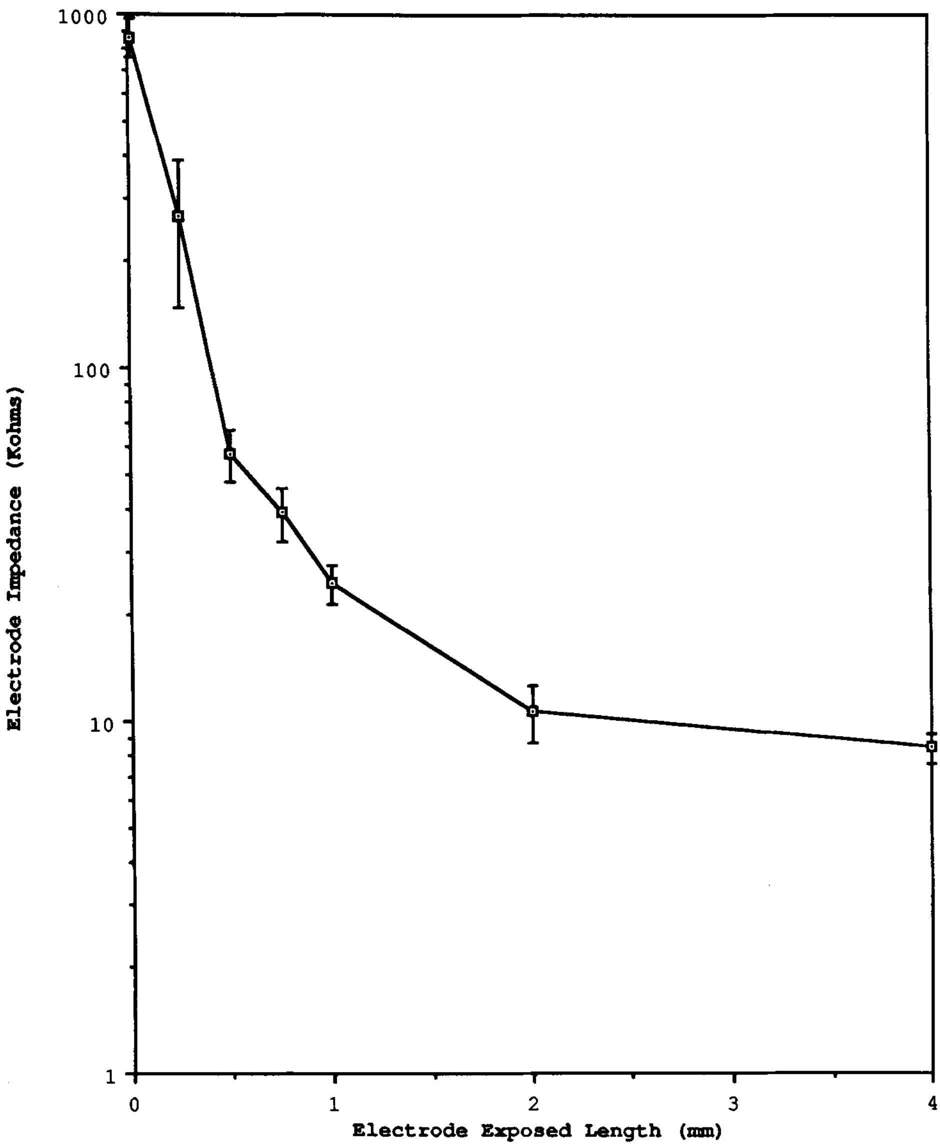

FIGURE 3. Semi-logarithmic plot of electrode impedance as a function of the length of insulation removed from the recording zone of 25 μm diameter Pt wire electrodes. Shown are means and standard deviations for measurements from 10 different electrodes. Similar curves are obtained with 50 μm diameter Pt–Ir wire (when adjusted for the increase in surface area) and C fiber electrodes.

nals. The signal was recorded with a 25 μm Pt wire, bipolar electrode with 1 mm of insulation removed. The reference member of the bipolar pair was placed outside the fascicle. The peak of both the stimulated and the difference spectra occurs between 750 and 1500 Hz. There is a small but significant ($p < 0.001$) increase in signal-to-noise ratio using just the octave band between 750 and 1500 Hz compared to the full 20 to 2560 Hz band of the recorded signal.

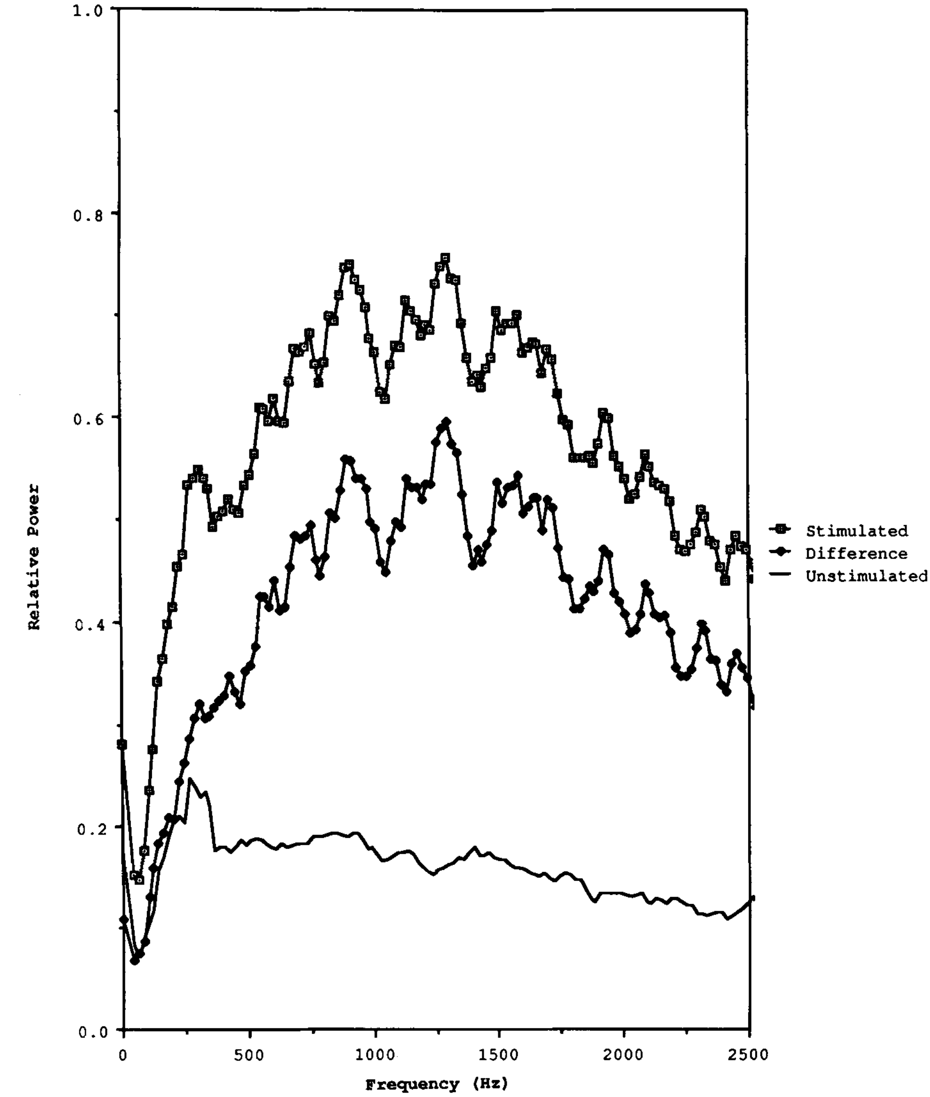

FIGURE 4. Power spectra of recordings of sensory nerve activity during (open symbols) and in the absence of (bottom trace) mechanical stimulation of the foot, and their difference spectrum (filled symbols). Each point is the average of ten recordings made from 25 μm diameter Pt wire, bipolar implants with 1 mm exposure. One wire was inside the fascicle while the second wire was outside the fascicle. Frequencies below 400 Hz were attenuated by the preamplifier filter characteristics.

The effect of changing recording zone length on signal-to-noise ratio is shown in Fig. 5. Student's t-test showed that there was no statistically significant difference in signal-to-noise ratios for exposure lengths between 0.5 and 4.0 mm, but that these lengths had significantly ($p < 0.05$) higher ratios than recording zone lengths below 0.5 mm. The optimal length appears to be around 1 mm.

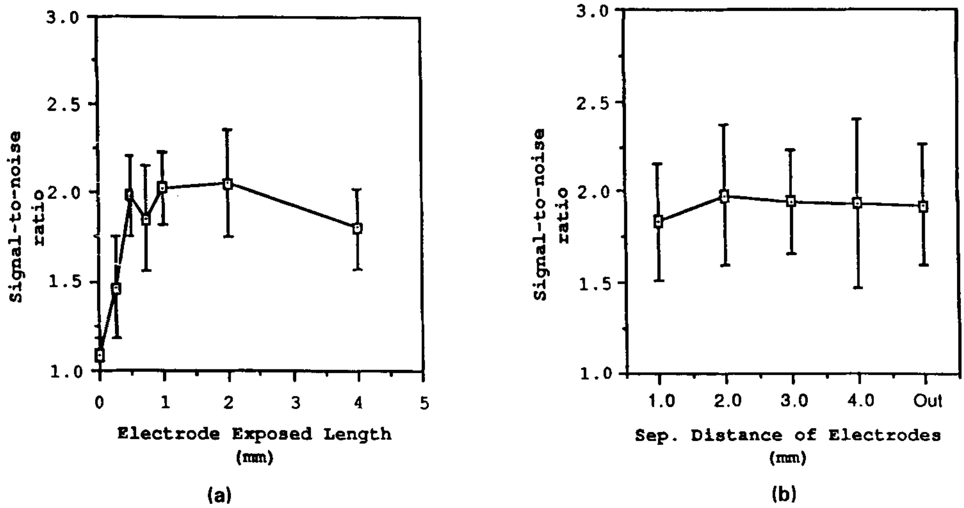

FIGURE 5. Signal-to-noise ratio as a function of (a) recording zone length and (b) longitudinal separation between recording zones of bipolar electrodes. Each point is the mean (with standard deviation) for 10 different experiments using 25 μm diameter Pt electrodes implanted in rat sciatic nerve fascicles. A length value of 0 mm refers to the cut end of the wire, and OUT refers to bipolar pairs in which one member of the pair was placed outside the fascicle, but level with the implant.

Electrode Size and Material

The average impedance of the 50 μm diameter wire electrodes with 1 mm of insulation removed was 9.8 kΩ. This decrease in impedance compared to that of 25 μm wires with 1 mm exposure (mean of 25.0 kΩ) was expected because surface area is proportional to electrode diameter. The carbon filament electrodes (which had a diameter around 35 μm) had a mean impedance of 23.9 kΩ for 1 mm exposures. This value was statistically indistinguishable from the mean value for 25 μm Pt wire electrodes.

The only difference in recording properties between these three types of electrodes that reached statistical significance ($p < 0.05$) by Student's t-test was a slightly lower average signal-to-noise ratio for carbon fiber electrodes (1.69) than for 25 μm Pt electrodes (2.02).

Bipolar Separation

Figure 5 also shows the relationship between the longitudinal separation of the recording zones in bipolar electrodes and the signal-to-noise ratio. OUT indicates that one electrode was placed outside the fascicle directly adjacent to the recording electrode inside the nerve. There was no statistically significant difference in signal-to-noise ratio as a function of separation: although the amplitude of the recorded signal increased with increasing separation, the noise level also increased proportionally, leaving the ratio of the two roughly constant.

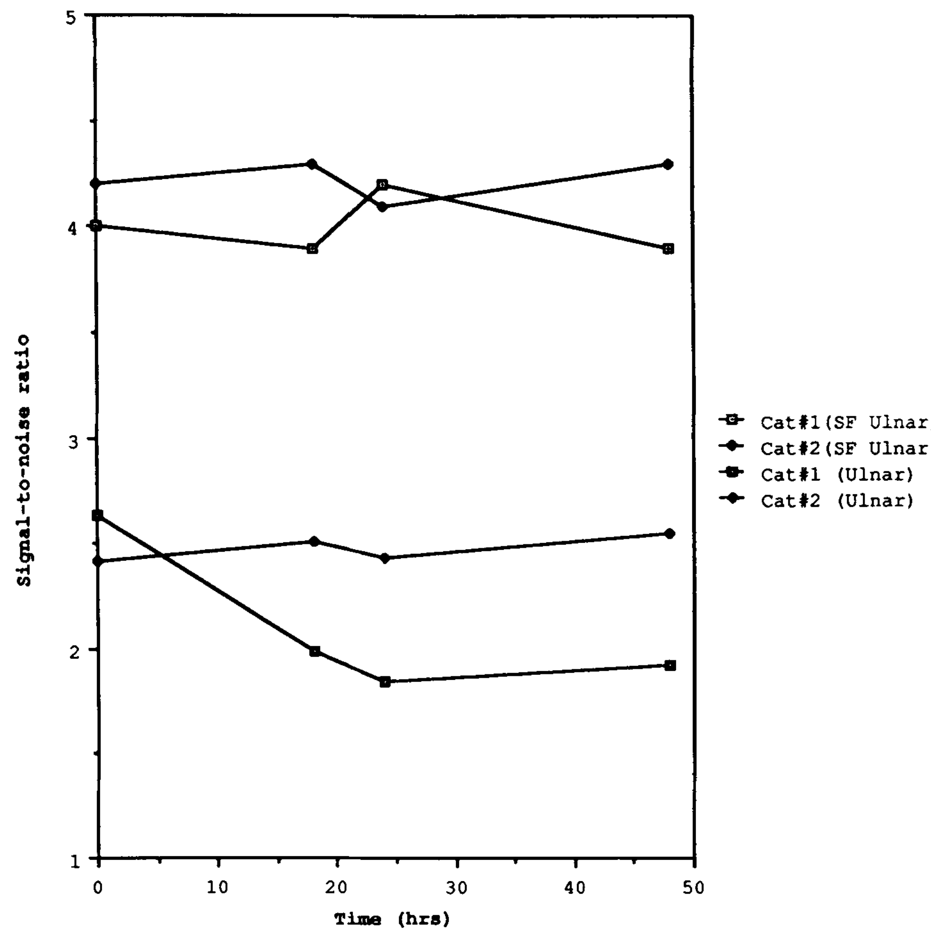

FIGURE 6. Signal-to-noise ratios (full bandwidth, Fourier component method) as a function of time for four electrodes implanted in two branches of the ulnar nerve of two cats. The cats were anesthetized for the duration of the observation period. Stimulation was provided by brushing the skin in the receptive area of the implanted fascicle. Recordings were made from 25 μm Pt, monopolar electrodes with 1 mm exposure.

Stability of the Signal-to-Noise Ratio

Electrodes were implanted in the ulnar nerve just above the elbow in two cats and recordings were made of evoked activity over a 48 hour period. The results are shown in Fig. 6. The signal-to-noise ratios of the recordings exhibited little or no decline during this time.

This data also showed an inverse relationship between fascicle diameter and signal-to-noise ratio: the large branch of the ulnar nerve produced a signal-to-noise ratio of about 2.5, while the smaller branch had a signal-to-noise ratio of about 4.0. A possible basis for this effect is presented in the Discussion.

Histology

No signs of inflammation, infection, or extensive mechanical trauma were seen in any of the implanted fascicles from the two cats described above, nor was there any evidence of neuronal degeneration or demyelination attributable to the presence of the electrode in any of the histological sections examined.

DISCUSSION

Expected Waveform and Amplitude of the Recorded Signal

The biophysical basis for our ability to record signals with this technique can be derived from the model describing extracellular potential fields surrounding an active nerve fiber developed by Clark and Plonsey (1,2) and waveform parameters for myelinated fibers supplied by Fitzhugh (4). This model predicts a peak extracellular potential of 26 μV for a single action potential recorded near the active fiber. The relatively high impedance of the perineurium causes this potential to decay less rapidly in the fascicle than would be expected in an infinite, isotropic conducting medium. The smaller the fascicle, the larger the potential will appear at a given distance from the fiber. Interestingly, the signals we recorded were about twice as large as predicted. One possible explanation for this finding is that the electrode wire provided a lower resistance pathway for current than the interstitial medium, and the presence of surrounding, myelinated nerve fibers increased the resistance to radial current flow, thereby increasing the potential from nearby fibers seen by the electrode.

Our recording electrodes integrate the potential field over their exposure length. Since the extracellular potential is biphasic, with a net area of zero due to the fact that both the source and sink move past the recording site as the action potential travels along the nerve, increasing exposure lengths beyond the wavelength of one phase will produce decreasing signal amplitudes with little change in noise level. Using published values of action potential durations and nerve fiber conduction velocities (13,20) to derive the active length of a single, myelinated axon action potential, we expect the maximum useful recording zone length to be about 7 mm. Conversely, because of the sharp increase in impedance, and hence noise level, with exposure lengths less than 0.5 mm, electrodes shorter than this will have poor signal-to-noise characteristics.

The frequency spectrum of the signal is dependent on the frequency components of the potential wave and the distance of the electrode from the nerve fiber. Action potentials in smaller nerve fibers have slower rise times and longer durations than those in large fibers. As the recording site is moved farther from the nerve fiber the spectrum shifts to lower frequencies (15). The peak energy components for potentials within the recording zone of our electrodes was near 1 kHz.

Exposure Length

The results of the exposure length experiments can best be explained by examining the relationship between exposure length, noise level, and signal level. The experimentally determined optimum exposure length of 1 to 2 mm lies on the flat portion of the impedance curve of Fig. 3 and is less than one quarter of the expected wavelength of the action potentials.

Electrodes of this length had a measured equivalent impedance, at 1 kHz, of about 25 kΩ. Comparison of the expected Johnson and instrumentation noise levels using these electrodes with the measured *in situ* noise level of 20 to 30 μV indicates that the predominant source of noise in this system is from background activity in the nerve.

Electrode Diameter and Material

The average signal-to-noise ratios for the 50 μm diameter wire electrodes did not differ significantly from those for the 25 μm wires. Although the larger wire is surrounded by more axons in its immediate vicinity due to its larger circumference, the amount of spontaneous background activity within the recording zone is also increased, so the signal-to-noise ratio stays roughly constant.

Although the carbon fiber recordings produced lower signal-to-noise ratios, we cannot conclude that the carbon fibers have less desirable recording properties. Proper insulation of carbon fiber electrodes is still the subject of some uncertainty, the benefits of Parylene notwithstanding (11). For these studies, we used epoxylite as an insulator. Tests in saline showed that there was measurable capacitive signal loss with this method even after four coats of insulation. With better insulation, we expect an improved signal-to-noise performance for carbon electrodes.

Taken together, these results favor a system composed of 25 μm diameter Pt or Pt–Ir wires with 1 mm recording exposures. If the 25 μm wire proves too fragile under chronic use, 50 μm wire could be used, although it will produce somewhat more damage to the nerve trunk due to its larger size. In the long run, development of better insulation for the carbon fiber electrodes may be the best path to follow since their excellent flex life makes them ideal candidates for long term implants. The ability to vary the size of the carbon electrode by the addition or subtraction of 7 μm strands is also a useful advantage.

Bipolar Electrode Configuration

The method of bipolar recording by placing one electrode outside the nerve directly adjacent to the recording electrode produced results similar to the condition where both electrodes were inside the nerve. This implies that damage to the nerve can be reduced, since only one electrode of the pair needs to be implanted.

Comparison with Cuff Electrodes

The most commonly used cuff electrode consists of a slit Silastic tube into which three platinum–iridium wires have been sewn in a circular manner (17). Variations on this theme have been developed in the past decade, including printed traces on polyester film (22). In all cases, the insulating cuff is wrapped around the nerve to provide a high impedance barrier between the recording zone and the body fluids. Our system is analogous in that we use the perineurium as an insulating cuff rather than a stiff, synthetic material which can damage the nerve. Cuff electrodes require careful sizing to avoid compromising the blood supply to the nerve. With intrafascicular electrodes, one size fits all. The post implantation swelling which occurs with any kind of implant, and which can compress the nerve in a cuff, is not a problem with our intrafascicular electrodes. However, implanting intrafascicular electrodes requires greater surgical skill.

A functionally more important difference between cuff and intrafascicular electrodes is the population of fibers from which activity is recorded. A cuff electrode records a weighted average of all the activity in the nerve branch around which it is placed, with large fiber activity dominating. An intrafascicular electrode records from a subset of the fibers in an individual fascicle (mapping of receptive areas during our recording sessions showed no measurable cross talk between fascicles), with proximity to the electrode being the dominant factor in what fibers contribute to a recording (Horch and Goodall, unpublished observations). Because of the somatotopic and functional grouping of fibers within a peripheral nerve fascicle (19), intrafascicular electrodes provide information about much more restricted receptive areas and receptor types than do cuff electrodes. That is, intrafascicular electrodes are more selective than cuff electrodes. An array of intrafascicular electrodes in a single nerve can provide several channels of information which would be mixed together with a cuff electrode.

SUMMARY

The system described in this report allows information about afferent nerve fiber activity to be extracted from peripheral nerves. The size of the implants is of the same order as the individual nerve fibers so that little damage is done on insertion. Future work will be directed toward developing this system into a totally implantable, peripheral nerve recording system capable of providing feedback control for functional neuromuscular stimulation.

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