

Long-Term Neuroelectric Signal Recording from Severed Nerves

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Abstract—Six recording electrode units were implanted around the severed sciatic nerves of rabbits immediately after an axotomy was performed. *Voluntary* and *involuntary* motor neuroelectric signals (including individual action potentials) were recorded from the surface of the severed nerve for as long as 142 days after implantation, the average duration being 64 days. In order to study the course of the limited duration of the signal detection, a stimulation electrode was implanted around the sciatic nerve proximal to the lesion; evoked neuroelectric signals were recorded throughout the length of the experiment. The impedance of the recording electrode was also measured throughout the length of the experiment. The behavior of the above parameters, combined with histological observations, indicated that nerve degeneration accounted for the deterioration of signal detection.

INTRODUCTION

AN electrical interface for detecting voluntary neuroelectric signals from severed peripheral nerves could provide an effective path for activating and controlling various devices that behave in accordance with an amputee's wishes. This application appears promising in light of recent work by Lichtenberg and De Luca [13] which indicates that during electrical stimulation, signal patterns detected from the surface of a nerve can be associated with functionally distinct groups of nerve fibers inside the nerve.

Early in the investigation, an attempt to record volitional neuroelectric signals was carried out by a team¹ of physicians and engineers on a patient with a below-elbow amputation. The patient agreed to have surgical intervention under local anesthesia after he had been instructed to perform certain motions in the intact hand controlled by the median, ulnar, and radial nerves, respectively, and had practiced them extensively. He had also practiced "thinking" of performing the identical motions in the ablated hand. At the time of surgery, all three nerves were isolated from the surrounding tissues at the end of the amputated stump. Platinum wire loops were

placed around each of the isolated nerves to serve as electrodes. The patient was asked to think about executing the hand and finger motions normally controlled by the median, ulnar, and radial nerves. With the nerves suspended in air, signals generated from the nerves were recorded simultaneously with the subject's verbal descriptions of the intended motions. Although this experiment was not in itself entirely objective, the results were sufficient to indicate that a more detailed investigation on animals should be instituted.

The first task was to develop a suitable electrode that could be implanted near a nerve. There are a number of approaches one might pursue in developing such an electrode. However, in all cases a suitable recording electrode unit should have: 1) a stable mechanical bond with the nerve, 2) an acceptable signal-to-noise ratio, and 3) the means of excluding the concurring myoelectric signals from adjacent muscles. The design of such an electrode presents a basic problem; it must be placed close to the nerve with the least possible physical damage and with minimal physiological restrictions to the nerve.

Our first approach was to introduce tungsten microprobes into the severed end of sciatic nerves in cats and rabbits. However, mechanical problems concerning the stability of the electrodes and associated nerve damage made them undesirable for long-term implantation. In the next approach, two stainless steel rings were placed inside a Silastic thin-wall tube. The unit was implanted over one or two fasciculi of the severed medial gastrocnemius nerve that had been separated by microdissection. Neuroelectric signals of physiological origin were recorded for approximately 10-15 h after implantation; then nerve conduction ceased. All of these implants resulted in severe necrosis of the enclosed nerve fibers, most likely due to damage to the blood supply caused during the separation of the fasciculi. However, Hoffer *et al.* [9] have demonstrated that this approach may yield more positive results if a more careful and sophisticated microdissection technique is employed to separate the fasciculi.

It was then decided that a less traumatic approach should be pursued. An investigation was begun to develop a cuff electrode that would surround the complete perimeter of a severed nerve. The information reported in this paper is a continuation of our work described in previous publications [3]-[5]. Recently, other investigators have also implanted cuff electrodes around peripheral nerve trunks [8], [16]-[18], [20]-[22], and around separate nerve fiber bundles [9], [14]. In all the latter cases, the nerves were continuous with their target muscle at the time of implantation.

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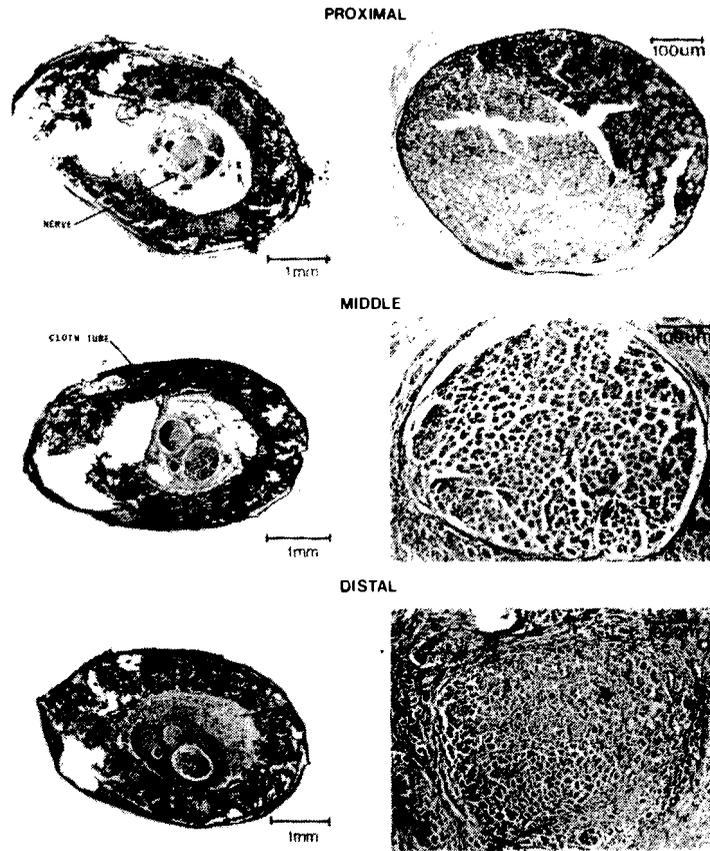


Fig. 1. The left column presents cross sections taken 12 mm (proximal), 8 mm (middle), and 3 mm (distal) from the point of severance of the nerve that has been surrounded by a Teflon cloth tube for 67 days and stained with Masson's Trichrome. A progressive increase in the amount of connective tissue and a progressive decrease in the amount of fatty tissue between the cloth tube and the nerve can be seen from the proximal section to the distal section. The right-hand column presents a magnified view of the enclosed nerve obtained from adjacent sections and stained with Periodic Acid-Schiff. The state of the nerve becomes progressively worse from the proximal section to the distal section.

BACKGROUND

In a previous study [6], two series of experiments were performed to investigate the effects of Dacron and Teflon knitted cloth tubes on an enclosed severed nerve. The first series investigated the influence of the thickness and porosity of the cloth and that of the duration of the implantation; the second series studied the effects of the ratio of cloth tube diameter to nerve diameter.

Examinations of histology slide preparations revealed that connective tissue growth and tissue reaction around the cloth tube were quite similar to those reported from studies investigating the behavior of Dacron and Teflon vascular grafts [1], [27]. The external tissue increased in thickness up to the fifth day, when the thickness appeared to stabilize. The connective tissue was found to be progressively thicker around cloth tubes of increasing coarseness. Connective and fatty tissues invaded the space between the nerve and cloth tube. This was noted as early as three days after implantation. With increasing time, the cellular component of the connective tissue separated from the augmented collagen fibers. Within two weeks, the cellular component was restricted to the area adjacent to both sides of the cloth tube wall. With additional time, the collagen fiber matrix became more dense, and the cellular lining of the tube wall became thinner.

These developments stabilized part of the nerve with respect

to the surrounding tube and external tissue. This was achieved because: 1) the internal and external connective tissue fibers joined through the interstitial spaces of the cloth, 2) the connective fibers interwove with the yarn of the cloth, and 3) the collagen fibers or fat cells of the internal tissue appeared well bound to the epineurium of the enclosed nerve as seen in Fig. 1. The binding of the internal and external tissues reduced the relative movement between recording electrodes and the enclosed nerve. This is a requirement for obtaining faithful and consistent neuroelectric signals.

Fig. 1 shows typical cross-sectional views along a nerve-tube unit as seen 12 mm (proximal), 8 mm (middle), and 3 mm (distal) from the point of severance, along with the expanded cross-sectional views of the nerve (taken from adjacent-histological sections). It can be seen that the state of the nerve progressively degraded from the proximal sections to the distal sections. This retrograde degeneration is consistent with the results of other investigators [19], [24]. The distal sections typically contained relatively few intact axons and a substantial neuroma formation. The state of the nerve was not directly correlated to the duration of implantation. Some severed nerves deteriorated within a month, while in others, the proximal and middle nerve sections remained relatively healthy (i.e., contained more than 50 percent intact axons) for as long as 681 days after tube implantation.

ELECTRODE CONSTRUCTION

The procedure for this study used two types of electrodes—a recording electrode unit and a stimulation electrode unit. Both types of electrode units have four constituent parts—a cable, a transcutaneous device, a cloth support structure, and recording or stimulation contacts. The precursor of this cuff-type electrode was originally reported by De Luca *et al.* [5] in 1974, and by De Luca and Gilmore [4] in 1976.

The Recording Electrode Unit

The preferred design of the cloth tube for the purpose of supporting recording electrode wires requires a compromise. Ideally, to record the largest possible signals outside the nerve, the electrode contacts should be placed as close as possible to the nerve surface. On the other hand, a previous histological investigation [6] indicated that a relatively tight-fitting tube causes severe nerve damage. To reduce this damage, the cloth tube diameter should be sufficiently large to accommodate the enclosed nerve during the post-axotomy edema.

The cable of the current version of the recording electrode was formed from six Teflon-coated stranded wires (Medwire 10 IR 9/49T) helically wound around 2-0 surgical silk suture. Each wire was formed with 9 strands of 28 μm diameter, 90 percent Pt-10 percent Ir, having a total coated diameter of 130 μm . The entire cable was encased in medical grade Silastic. The six wires in the cable formed three pairs of electrode contacts (three channels) which were located on the inner surface of the cloth tube. Approximately 5 mm of the Teflon insulation was removed from the distal end of each wire so that the exposed wire surface formed the electrode contact area. The proximal ends of the six wires in the cable were soldered to a seven-pin connector (Microtech ER7 5-4H) cemented in the center portion of a biocarbon device from Bentley Laboratories, Inc. This formed a transcutaneous bacterial seal and housed the connector. The underside of the biocarbon device was covered with a thin coat of Silastic adhesive.

The cloth tube was constructed from knitted Dacron fabric having a thickness of 0.2 mm and a water porosity of 10 000 ml/min/cm² (at 1 atm). The length was 28 mm and the inside diameter of the tube was 3.5 mm. Based on information from an earlier investigation [6], the inside diameter was chosen to be approximately 0.8 mm greater than the average diameter of the sciatic nerve in the popliteal fossa region of the rabbits that were used.

Four of the electrode units were constructed with three pairs of electrode contacts woven into the cloth and bonded 0.5 mm above the surface of the fabric with Silastic adhesive. This arrangement placed the exposed surfaces of the electrodes in intimate contact with the surface of the nerve. The proximal and distal electrode contacts of each pair were located 5 mm from the respective ends of the tube. This arrangement positioned the recording contacts over the portion of the nerve in which at least 50 percent of the fibers have been shown to retain structural integrity after axotomy. (See Fig. 1.) The electrode pairs were spaced so that they were situated 120° apart on the circumference of the finished tube. The fabric patch with the attached electrode contacts was then shaped

into a tube, and the mating edges were bonded together with Silastic adhesive. The silk suture strain relief was secured to the cloth tube with Silastic adhesive. Two additional recording electrode units were similarly constructed, but they only contained one pair of electrode contacts.

Covers with sealed ends to be placed over the electrode unit were constructed with Silastic elastomer (Dow Corning 382). Their inside diameter was equal to the outside diameter of the cloth tube. The inside wall of the covers was lined with support ridges that assisted in centering the cloth tube within the insulating cover. The distal ends of the Silastic covers were sealed.

The entire assembly may be seen in Fig. 2.

The Stimulation Electrode Unit

The cable of the stimulation electrode was formed from a shielded Teflon-coated, two-conductor, stranded stainless steel cable (Cooner Wire Company AS633-2-SSF). Approximately 10 mm of the Teflon insulation was removed from the distal end of each of the wires forming two exposed contact surfaces. The proximal ends of the wires were soldered to a four-pin connector (Microtech DR-4S-4) cemented in the center portion of another biocarbon device. The structural component of the stimulation electrode was formed from a 25 mm \times 15 mm piece of knitted Dacron fabric folded in half. The wire cable was placed at the centerline of the fold and bonded to the fabric with Silastic adhesive. The exposed contact wires were bent at right angles to the cable and woven into one of the halves of the folded fabric spaced apart by 5 mm. The end of each wire was covered with Silastic adhesive.

METHOD

Surgical Procedure

Six recording electrode units were implanted around the left sciatic nerve of six New Zealand white rabbits weighing 3.5-4 kg. A stimulation electrode was implanted proximal to the recording electrode on the same nerve in four of the animals.

An aseptic surgical procedure was used. The animals were anesthetized. An incision was made in the left popliteal fossa and the sciatic nerve was located and freed of its surrounding connective tissue with the epineurium left intact. The peroneal, tibial, and sural divisions of the sciatic nerve were cut with ophthalmological scissors. The location of the axotomy was chosen with no particular regard to the structure of the blood supply on the surface of the nerve. A 6-0 braided silk suture was secured to the epineurium of each division. The nerve trunk was then gently pulled into the sterile tube of the recording electrode using the attached suture until the distal edge of the tube was immediately adjacent to the cut end of the nerve. It was secured in place by tying the suture on the nerve to the electrode tube. The Silastic insulating cover was fitted over the tube. The nerve and tube were then arranged in an unobtrusive position in the popliteal fossa. The stimulation electrode was placed around the nerve approximately 5 cm proximal to the recording electrode. The transcutaneous carbon-button connectors were installed subcutaneously through separate small incisions around the area of the left thigh, and all four incisions were closed. The leg and foot were bandaged to reduce abrasion during the remainder of the experiment. At the termina-

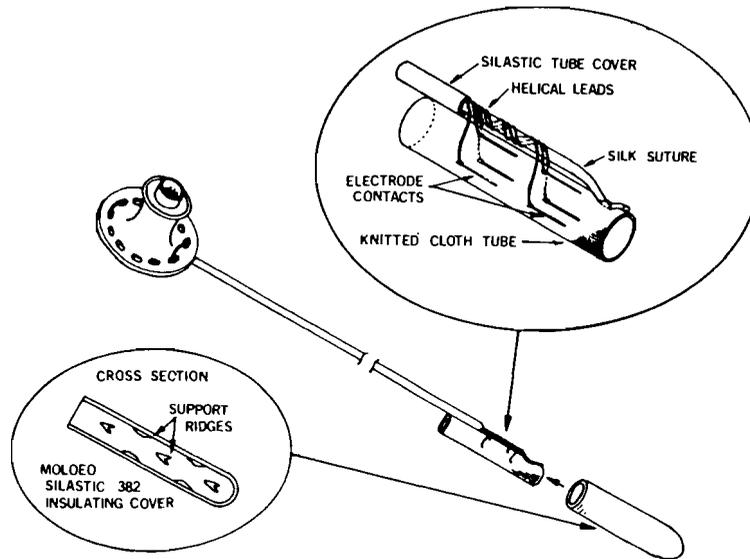


Fig. 2. Schematic diagram of recording electrode unit.

tion of the experiment, the recording electrode-nerve unit was surgically removed, and a histological analysis was performed.

Signal Recording and Analysis Procedure

Signals detected by the recording electrode were passed through differential preamplifiers having an input impedance of $500\text{ M}\Omega$ and 5 pF and a bandpass of 200 Hz – 10 kHz . The animal was electrically grounded via the transcutaneous bio-carbon device.

Voluntary neuroelectric (motor) signals were elicited by allowing the rabbit to hop about at will. Involuntary neuroelectric (motor) signals were elicited by: 1) tapping the rabbit on the right side of the chest wall, thereby initiating a reflex response in the left limbs for maintaining stability; or 2) lifting and holding the rabbit in an off-balance position and allowing only the left limb to support the body weight. Evoked neuroelectric signals were elicited by supramaximally stimulating the proximal section of the left sciatic nerve with a train of square pulses having a duration of 0.05 ms and a repetition rate of 20 pulses/s . All the neuroelectric signals were recorded on an FM tape recorder, prefiltered at 200 Hz – 8 kHz , and digitized.

Electrode Impedance Measurements

The impedance between each pair of electrode wires for each channel of two electrode units was measured while the units remained implanted in the animals. One of the two wires of each electrode pair was grounded to the measuring system. A sinusoidal signal with a peak-to-peak amplitude of 1 mV was introduced across the electrode leads. The amplitude and phase of the two voltages on the oscilloscope were measured at 20 Hz , 100 Hz , 1 kHz , 10 kHz , and 50 kHz .

RESULTS

General Results

The history of the neuroelectric signal recordings made from all the electrode units is presented in Fig. 3. A successful recording of the evoked signal is represented by a broken bar, and a successful recording of a voluntary motor signal is represented by a solid bar. Each time an evoked signal was recorded, an

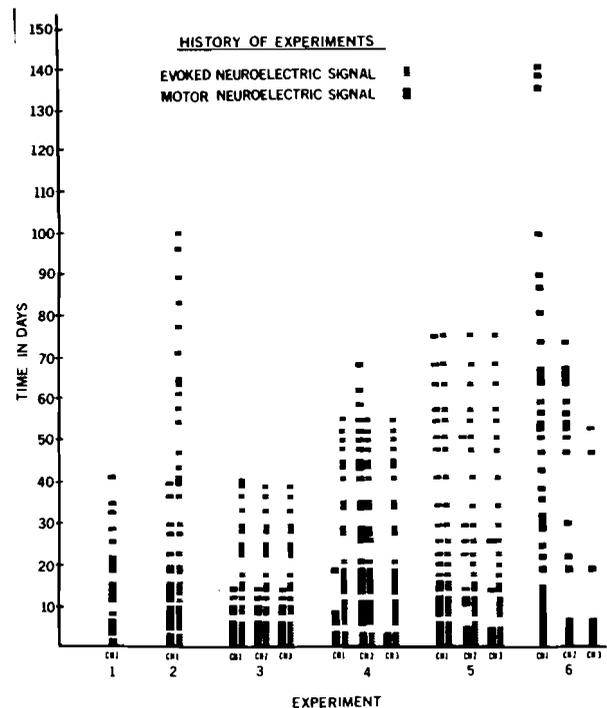


Fig. 3. History of the detected evoked neuroelectric signals and the voluntary motor neuroelectric signals of all the implanted units. In experiments 1 and 6, stimulation electrodes were not implanted, and thus, no evoked neuroelectric signals were recorded in these two experiments. Two of the experiments (1 and 4) were terminated due to wire breakage.

attempt was made to record voluntary motor signals. Hence, if no recording of voluntary motor signals is indicated on the date that an evoked signal was recorded, it signifies an unsuccessful recording attempt. Note that in several cases, the voluntary signal could not be recorded during a particular session, but was recorded during a subsequent session. This situation typically occurred when the rabbit would not attempt to use its left limb while hopping or supporting itself in the upright position. Experiments 1 and 4 were terminated due to a wire breakage in the recording electrode units. The remainder of the experiments was terminated because the voluntary motor signals could no longer be recorded.

Motor Response

The electrode unit had the capability of detecting individual motoneuron action potentials when the level of activity within the nerve was low. The time duration of the action potentials ranged from 0.25–0.5 ms during the first week post-implantation, and increased to 0.4–0.6 ms after an implantation period of two months. No increase in the duration was noted after that time. A typical action potential of a motoneuron recorded while the animal made no observable movement can be seen in Fig. 4(a). The motoneuron fired at a rate of 9 pulses/s [Fig. 4(b)]. With an increasingly greater exertion by the animal, additional motoneurons were recruited and more action potential trains were recorded by the electrode, as can be seen in Fig. 4(c). As an increasing number of action potential trains were recorded, they were no longer distinguishable. The resulting superposition signal can be seen in Fig. 4(d).

Fig. 5(a) shows modulation of the voluntary motor signal amplitude detected by the recording electrode unit. This signal was obtained while the animal hopped during the 29th day of Experiment 4. Each burst of activity, indicated by the arrows, corresponds to a distinct hop. An example of the involuntary motor signal detected when the rabbit was tapped on the side of the chest wall contralateral to the limb containing the implanted electrode can be seen in Fig. 5(b). This signal was recorded on the 41st day of Experiment 4. Each burst corresponds to an individual tap and is an indication of the reflex reaction to counteract the slight displacement of the animal's body. When the animal was tapped on the ipsilateral side, no signal was observed.

The peak-to-peak amplitude of the neuroelectric signal recorded while the rabbit was hopping was plotted as a function of implantation time in Fig. 6. The bottom plot is an expansion of the data of the first 15 days. In the experiments where the electrode unit had three channels, the channel that detected the largest sustained amplitude of the signal was plotted. The peak-to-peak amplitude of the signal ranged from 68 to 7.2 μV , where it was no longer distinguishable from the system noise. Note that "day 0" corresponds to the day of the implantation. Although the values recorded on different days are not directly comparable, they do show an indication of the progression as a function of time. In five of the six experiments, there was an increase in amplitude of the signal during the first day after implantation. Subsequently, all the experiments demonstrated a common behavior—a rapid decrease in the amplitude of the signal up to the sixth day. Following this time, the amplitude fluctuated between 7.2 and 15 μV for five of the six experiments. Experiment 4 was the exception.

Fig. 7 displays the spectra of the signals obtained in Experiment 4. The larger of the two spectra in Fig. 7(a) was obtained from the neuroelectric signal recorded within 2 min of the prior signal when no apparent neuroelectric activity was detected by the electrode. This is the spectrum of the recording-system noise. The spectra of the neuroelectric signal and the recording-system noise intersect at approximately 7 kHz. Fig. 7(b) displays the spectra of the corresponding signals recorded 27 days post-implantation. Note that the shape of the frequency spectrum of the neuroelectric signal has changed;

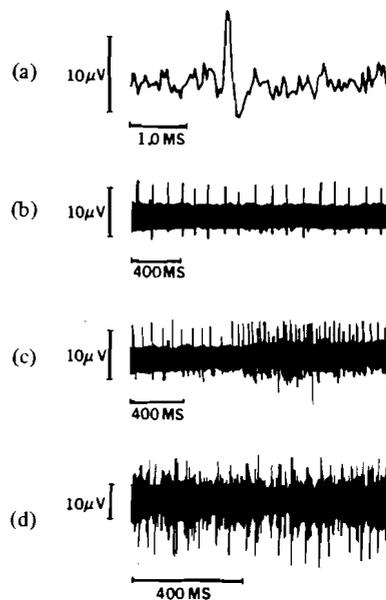


Fig. 4. Recruitment of motoneuron action potential trains detected on the surface of a nerve by the recording electrode unit 4. The neuroelectric signals of (a), (b), and (c) were recorded on the 17th day, and that of (d) on the 27th day post-implantation of the electrode unit. The signal was bandpass filtered at 1.2–8 kHz to eliminate the myoelectric signal from adjacent muscles.

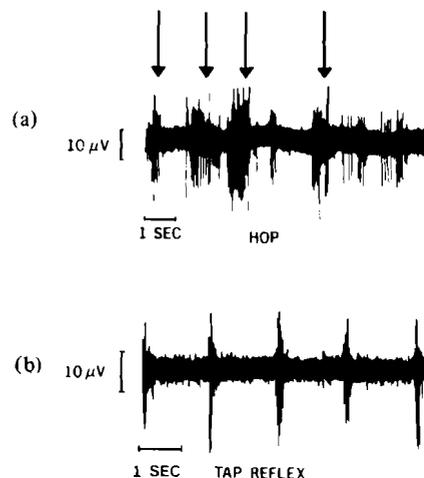


Fig. 5. (a) The neuroelectric signal detected from the severed sciatic nerve while the rabbit was hopping. The main bursts indicated by the arrows were associated with distinct forward propulsion movements. The remainder of the activity was associated with nonspecific movements of the limb containing the electrode unit. The signal was detected by the recording electrode unit 4 on the 29th day post-implantation. The signal was bandpass filtered at 1.2–8 kHz to eliminate the myoelectric signal from adjacent muscles. (b) The neuroelectric signal was detected in the severed sciatic nerve when the rabbit was tapped on the contralateral side of the chest wall. Each burst of activity represents a reflex response associated with a tap. The signal was detected by the recording electrode unit 4 on the 41st day post-implantation. The signal was bandpass filtered at 1.2–8 kHz.

there is a considerable decrease in low-frequency components and the spectrum peaks at approximately 2 kHz. There is also a new peak at approximately 200 Hz. The latter peak represents the presence of a myoelectric signal that was also detected as the time of implantation progressed. The frequency components of the myoelectric signal may also be seen in the spectrum of the recording-system noise obtained during the same recording session. The separate and distinct contributions of the

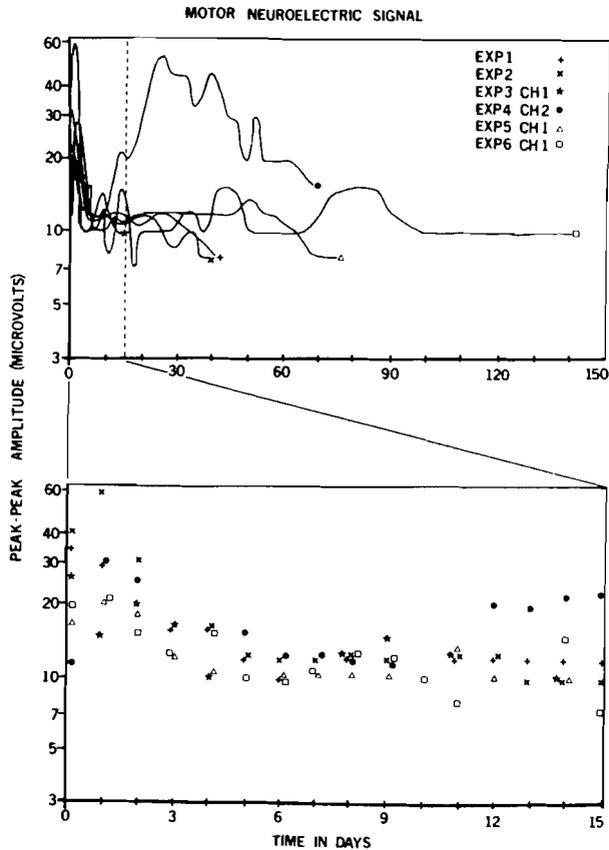


Fig. 6 The peak-to-peak amplitude of the voluntary motor neuroelectric signal as a function of implantation time. The bottom plot presents an expanded time scale over the first 15 days.

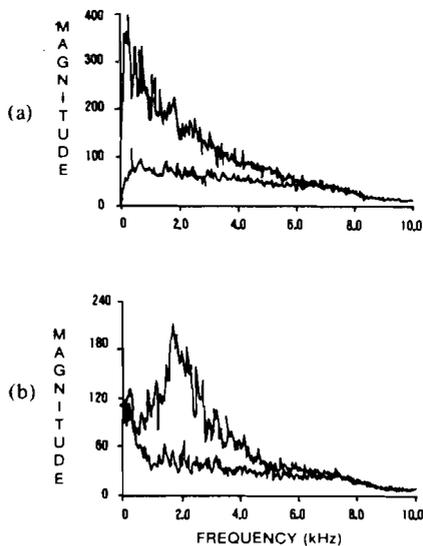


Fig. 7. (a) The frequency spectrum of the neuroelectric signal (higher amplitude) and the system noise (lower amplitude) recorded from channel 2 of unit 4 on the second day post-implantation. (b) The spectra of the corresponding signals recorded from the same channel on the 27th day post-implantation. In both cases, the signals were recorded with a bandwidth of 200 Hz–8 kHz.

myoelectric and neuroelectric signals to the frequency spectrum were verified by obtaining the spectra of voluntarily elicited signals obtained from a lightly anesthetized rabbit before and after crushing the enclosed nerve. These spectra are presented in Fig. 8.

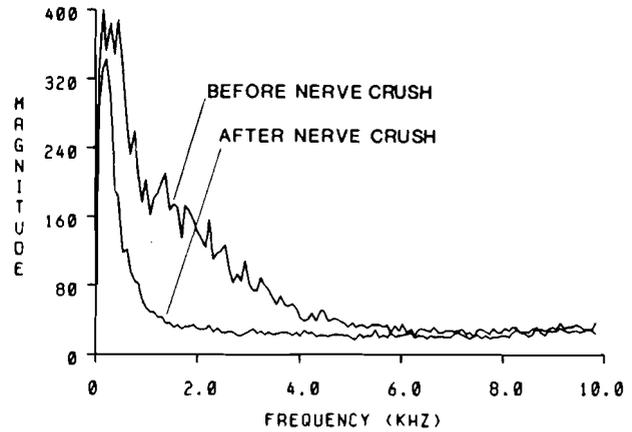


Fig. 8. The frequency spectra of the voluntarily elicited signal detected by the electrode unit implanted around a severed sciatic nerve. The spectrum with the greater energy content was obtained during normal recording procedures, whereas the spectrum with the lesser (and lower) frequency content was obtained after the sciatic nerve had been crushed proximal to the recording electrode unit.

Electrode Impedance

The time history of the impedance magnitude of the electrode pair of channel 1 in Experiment 6 is presented in Fig. 9. The data obtained from the unit in Experiment 5 were similar. These measurements were all taken at 1 kHz. The magnitude varies between 1.5 and 2.5 k Ω . These results are somewhat similar to those of Stein *et al.* [23], who performed comparable measurements.

Evoked Response

During the first few days post-implantation, the detected compound action potential evoked by the stimulation electrode was predominantly biphasic with a relatively high-amplitude and short-duration initial phase and a relatively low-amplitude and long-duration second phase. As the implantation time progressed, the compound action potential remained biphasic with the two phases approaching equality in amplitude and duration. Examples of the compound action potentials may be seen in Fig. 10. The first peak of the compound action potential occurred approximately 0.6 ms after the stimulus artifact, indicating that the compound action potential was the result of the direct stimulation 5 cm proximally. No monosynaptic reflex activity was seen in the evoked response. This would be expected to occur 2–3 ms after the stimulus artifact, the reason being that any reflex response induced by the centrifugally stimulated afferent fibers (particularly the Ia) would be cancelled out with the activity of the antidromically stimulated α motoneurons. This "collision" occurs when the nerve is supramaximally stimulated, as was the case in these experiments. This situation is comparable to that which is commonly observed when one attempts to elicit H-reflexes. Therefore, changes in the detected compound action potential reflect changes within the nerve and the tissue surrounding the nerve and electrode unit. Note that as the implantation time progressed, the latency increased indicating that an average conduction velocity of the nerve fibers decreased.

Fig. 11 represents the peak-to-peak amplitude of the evoked compound action potentials as a function of implantation time. In all cases there is a sharp decrease of the amplitude

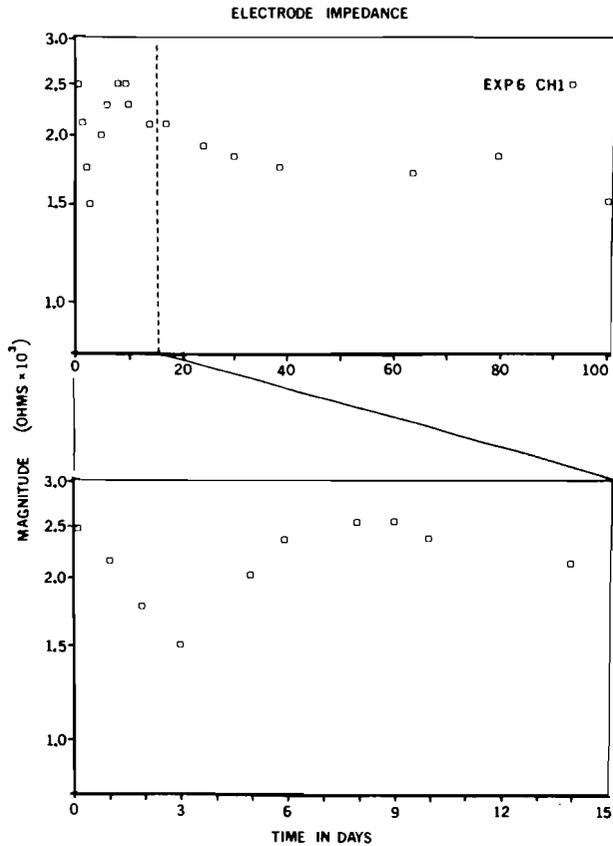


Fig. 9. Magnitude of the differential electrode impedance of channel 1 in unit 6 as a function of implantation time. The bottom plot presents an expanded time scale over the first 15 days. The measurements were made at 1 kHz.

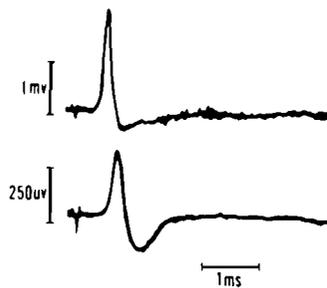


Fig. 10. Compound action potentials recorded during Experiment 4, two days after implantation (top), and 20 days after implantation (bottom). The relatively smaller pulse on the extreme left represents the stimulus artifact.

during the first six or seven days post implantation, and a slower rate of decrease beyond that time. This decrease in the evoked signal coincides with that observed in the voluntary signal shown in Fig. 6. The peak-to-peak amplitude of the evoked compound action potential ranged from approximately 0.3 to 10 mV.

In attempting to explain why both the evoked and motor signals were of such a surprisingly low amplitude, an acute preparation was arranged for measuring the effect of shunting of the electrodes by the external media. Fig. 12 presents the frequency spectra of supramaximally evoked compound action potentials recorded by the electrode unit implanted around a severed tibial nerve, with varying amounts of the nerve being in contact with the underlying muscle tissue and interstitial

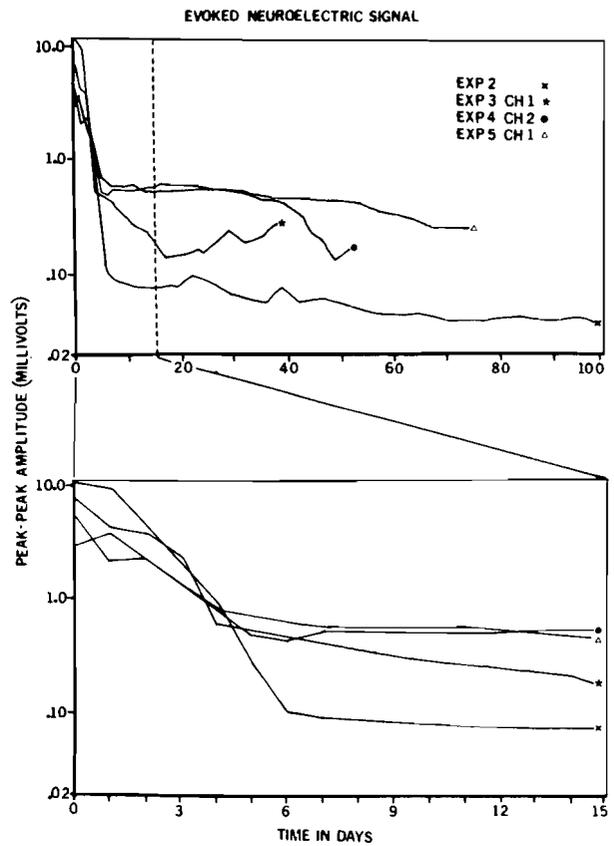


Fig. 11. The peak-to-peak amplitude of the evoked neuroelectric signals as a function of implantation time. The bottom plot presents an expanded time scale over the first 15 days.

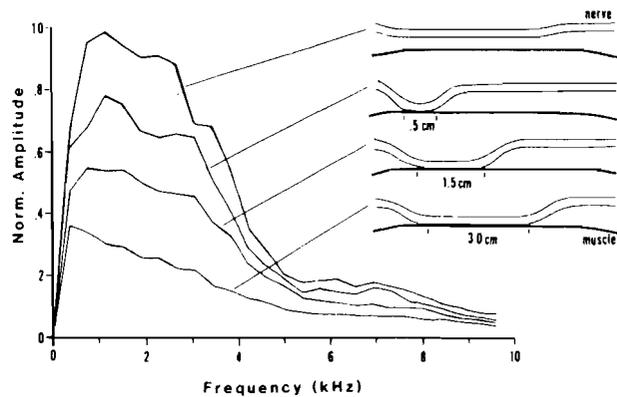


Fig. 12. Spectra of the neuroelectric signal obtained while varying amounts of nerve segments were in contact with the underlying muscle tissue and surrounding interstitial fluid.

fluid. The length of the contact surface varied from 0 to 3 cm. A measurement was also taken (but not presented in Fig. 12) with the whole length of the nerve and electrode implant being in contact with the underlying muscle and surrounding fluid. The results were essentially the same as those with 3 cm contact length. The plots in Fig. 12 strongly indicate that the inevitable electrical shunting of the surrounding tissues and fluids play a major role in decreasing the amplitude of the recorded neuroelectric signal.

When the sciatic nerve was stimulated, the stimulus also traveled up the nerve into the spinal cord, and a reflex volley propagated down other nerves that innervate some of the

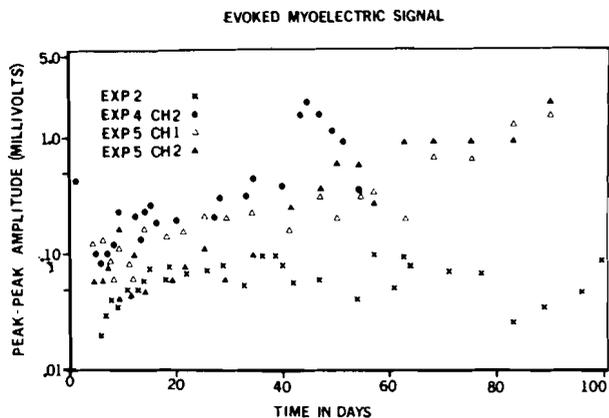


Fig. 13. The peak-to-peak amplitude of the evoked myoelectric signal as a function of implantation time.

thigh muscles. Hence, a myoelectric signal was present in the muscles surrounding the recording electrode unit. The peak-to-peak amplitude of some of the myoelectric signals recorded during evoked-signal sessions is presented in Fig. 13. After six or seven days post-implantation, all the recording electrode units detected the myoelectric signal, and its amplitude increased as a function of implantation time.

DISCUSSION

The implant procedure used in this investigation represents a worst case approach in that the electrode was attached to the severed nerve immediately after axotomy, and the implant was located at the distal end of the severed nerve. This paradigm was specifically chosen in order to mimic the electrode implantation during a limb amputation. Numerous alternative approaches are possible, and it is very likely that better results would have been attained if less traumatic procedures had been employed, e.g., implanting the electrode more proximal to the severed end of the nerve. Recently, Davis *et al.* [2] implanted cuff electrodes around peripheral nerves of cats, and in some cases were able to record evoked compound action potentials for approximately one year. They employed a less traumatic procedure, where the electrode was implanted around the intact nerve and the axotomy was performed 20 days later. However, it should be noted that the amplitude of the compound action potentials detected in our experiments is similar to that reported by Davis *et al.* [2]. Furthermore, our experiments were terminated when the motor signal was no longer available. The evoked neuroelectric signal would have been detectable for a considerably longer period of time.

The bandwidth of the neuroelectric signal recorded with the electrode unit described in this paper is considerably greater than that of the myoelectric signal. The frequency spectra shown in Fig. 7(a) and (b) have distinctly different shapes. The shape in Fig. 7(a) is characteristic of the neuroelectric signal recorded during the first two weeks. The spectrum shape in Fig. 7(b) is characteristic of the neuroelectric signal for the remainder of the implantation time. In the latter case, there is a pronounced decrease of the frequency components of the neuroelectric signal below 2 kHz. The shape of the frequency

spectrum of bioelectric stochastic processes such as neuroelectric and myoelectric signals is sensitive to the shape of the constituent action potentials (LeFever and De Luca [12]). Apparently, after two weeks, action potentials with longer time courses (lower frequency components) that contribute to the neuroelectric signal are not present. However, further work is needed to provide a more concrete explanation.

The spectra of Fig. 7(b) also contain the frequency components of the concurring myoelectric signal detected by the recording electrode. Note that the frequency components of the myoelectric signal are limited to the lower end of the spectrum with no substantial overlap with the frequency components of the neuroelectric signal. The distinction between the biological sources of the two peaks in the spectra was confirmed by the data in Fig. 8. These spectra were obtained from voluntarily elicited motor signals recorded from a lightly anesthetized rabbit before and after crushing the nerve enclosed by the electrode. Hence, in the latter case, no neuroelectric signal would be present. However, the contribution of the myoelectric signals from adjacent muscles persists and contributes to the low-frequency (<800 Hz) end of the spectrum only. This is clear evidence that the energy in the frequency spectrum above 800 Hz is, in fact, exclusively due to the neuroelectric signal. This separation of myoelectric and neuroelectric signal bandwidth is in agreement with the observations of De Luca and Gilmore [4] in curarized animals. The insulating Silastic cover sufficiently reduces the amplitude of the myoelectric signal so that the magnitude of the myoelectric frequency spectrum is of the same order as that of the neuroelectric frequency spectrum. Therefore, a simple filter can be used to separate the two signals.

The cuff-type electrode is capable of detecting motoneuron action potential trains from a nerve. Fig. 4(a)-(d) present evidence of motoneuron recruitment detected during an increasing effort on the part of the rabbit. The particular signals presented in Figs. 4 and 5 contain only neuroelectric signals. The signals were bandpass filtered at 1.2-8 kHz to eliminate the myoelectric signal which was at times present after the sixth day. In preparations somewhat similar to those of this study, Govrin-Lippman and Devor [7] found that in some cases, sensory fibers in the neuroma at the severed end of the sciatic nerve in rats continuously discharged spontaneously. This behavior was not seen during the sessions in which the recordings of Figs. 4 and 5 were obtained. The single action potential train displayed in Fig. 4(b) was observed to stop firing completely during the recording session. Furthermore, the trace of the involuntary neuroelectric signal response in Fig. 5(a) contains substantial periods of quiescence.

The amplitude of the neuroelectric signal can be modulated as seen in the signals displayed in Fig. 5(a) which were detected while the rabbit was hopping. This behavior is reminiscent of that seen in the myoelectric signal. This detectable modulation of the signal recorded from the surface of the nerve presents interesting possibilities for using the neuroelectric signal to control external devices such as prostheses. Many of the current versions of myoelectrically-controlled prosthetic devices, such as the "Boston Elbow" [11], [28], employ the

amplitude modulation of the myoelectric signal recorded with surface electrodes to control the prosthesis.

The recorded neuroelectric signals showed some distinct trends during the time course of the experiments. The behavior of the peak-to-peak amplitude of the signals detected by the recording electrode units can be interpreted as having two distinct phases. The first phase occurs from the time of implantation to the sixth or seventh days. The second phase spans the time from the seventh day to the time that a motor neuroelectric signal was no longer detected. In interpreting the changes in amplitude of the detected signals, it must be remembered that both the motor signals (voluntary and involuntary) and the evoked signals will be affected by at least two characteristics of the nerve-electrode unit: 1) the electrical properties of the tissues that grow between the enclosed nerve and the recording electrode, and 2) the physiological properties of the enclosed nerve. In addition, the detected motor signals will depend on the willingness of the rabbit to cooperate in the execution of the movements, as well as on the disposition of its central nervous system for processing and integrating voluntary and involuntary commands in the presence of limited sensory information supplied by the severed sciatic nerve. The effect of a loss of sensory input does not appear to be critical in experiments of this kind, in view of investigations by Taub *et al.* [25] and Taub and Berman [26], who found that following both unilateral and bilateral forelimb deafferentiation, monkeys were able to use their limbs adaptively in conditioning experiments and in locomotion.

Phase 1: During the first six or seven days, there is a sharp decrease in the peak-to-peak amplitude of the voluntary motor signal and of the evoked signal as seen in Figs. 6 and 11. At the same time, almost no myoelectric signal is detected (see Fig. 13). The decrease in the amplitude of the evoked signal limits the cause of this decrease to changes in the sciatic nerve or the recording electrode unit. The initial corresponding decrease in magnitude of the electrode impedance during the first three days further indicates that the amplitude of the neuroelectric signal is due in part to the decreasing impedance between the two electrode contacts. Although the relationship between the externally recorded evoked neuroelectric signal and the impedance measurements is complex and depends on several variables, the initial decrease of impedance is likely due to shunting from the interstitial fluid which invades the space between the recording electrode contacts. (The degree in which shunting by tissue and interstitial fluid can reduce the amplitude of the neuroelectric signal was verified by the observations in Fig. 12.) After the third or fourth day, the connective tissue and fatty tissue ingrowth between the enclosed nerve and the inside wall of the recording electrode unit displaces the accumulated fluid (see Fig. 1). This reduces the shunting across the electrode contacts and results in an increased electrode impedance (see Fig. 9).

Some of the decrease in the amplitude of the evoked neuroelectric signal noted during the first week may be due to the degeneration process. However, the amount of degeneration which occurs during this time interval is unlikely to account for the tenfold decrease in the amplitude of the evoked neuro-

electric signal seen in Fig. 11. Luttges *et al.* [15] recorded compound action potentials evoked at maximal stimulation levels from the degenerating segment of ligated mice sciatic nerves. The nerves were exposed and the signals were recorded with bipolar tungsten electrodes. They noted little change in the peak-to-peak amplitude of the compound action potential from the second to the tenth day post ligation, although several electrophoretic parameters indicated substantial degeneration. In view of this finding, it is likely that the neuroelectric signal amplitude decrease during the first week is mostly due to invasive tissue growth in the space between the enclosed nerve and the inside wall of the tube supporting the recording electrode contacts.

Phase 2: During the second phase, i.e., past the seventh day, the peak-to-peak amplitude of the evoked signals recorded in Experiments 4 and 5 continued on a near constant level and then declined, whereas that of Experiments 2 and 3 continuously decreased at a slower rate. During this time, the magnitude of electrode impedance continuously decreased. The behavior of the impedance shown in Fig. 9 is not reflected in the behavior of the amplitude of the evoked neuroelectric signal recorded from the same channel of the same electrode unit. The continuous decrease of the amplitude of the neuroelectric signals recorded from Experiments 2 and 3 may be interpreted as indicating a continuous degeneration process occurring in the nerve fibers. On the other hand, in Experiments 4 and 5, the augmented decline of the evoked neuroelectric signal at days 40 and 53 flags a possible later acceleration of nerve fiber degeneration. This interpretation is supported by the evidence in Fig. 10. As the implantation time progressed, the latency of the evoked compound action potential increased. This is a manifestation of a general decrease in the conduction velocity of the nerve fibers, which is in turn an indication of possible degeneration. Inspection of histology slides prepared (at the termination of each experiment) from the section of the sciatic nerve enclosed in the electrode unit revealed substantial nerve fiber degeneration. Hoffer *et al.* [10] also reported evidence of a similar progressive nerve degeneration. Their results further indicated that approximately 45 days post axotomy, myelinated sensory fibers presented a more accelerated degeneration process than the myelinated motor fibers.

During the second phase, the amplitude of the motor neuroelectric signal ranges between 7.2 and 15 μV , with the exception of the results of Experiment 4 where the amplitude soars to 50 μV before decreasing. Conceivably, in this case, the recording electrode was fortuitously in close proximity with some active nerve fibers within the nerve. Lichtenberg and De Luca [13] have shown that the neuroelectric signal detected on the surface of a peripheral nerve with this type of recording electrode may have a fourfold variation, depending on its location with respect to the active nerve fibers.

The results of the experiments performed in this study point towards a continual degeneration process which renders a sufficient number (not necessarily all) of the nerve fibers near the distal end of a severed nerve incapable of conducting action potentials. Experiments involving less traumatic implantations are in progress. Special emphasis will be placed on minimizing

the damage to the blood supply of the nerve, and minimizing the external mechanical forces on the nerve-electrode unit.

CONCLUSION

This study has shown that it is possible to construct an electrode unit which chronically detects neuroelectric signals from the surface of severed peripheral nerves. The presence of the electrode unit appears to aggravate the degenerative process which typically occurs after axotomy, but this does not preclude motor neuroelectric signals (voluntary and involuntary) and evoked signals from being detected near the severed end of the nerve. To date, the longest duration of successful recordings of motor neuroelectric signals that have continued to propagate down a nerve after axotomy has been 142 days. The observed motor neuroelectric signals ranged from single action potentials to graded superposition patterns with characteristics similar to the myoelectric signal.

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