Distinguishability of Functionally Distinct Evoked Neuroelectric Signals on the Surface of a Nerve

BYRON K. LICHTENBERG AND CARLO J. DE LUCA, SENIOR MEMBER, IEEE

Abstract—**This paper describes initial experiments to determine the feasibility of recording functionally distinct neuroelectric signals from the surface of the rabbit's sciatic nerve. A cuff electrode assembly was constructed; it consisted of two planar arrays, each having four wires equally spaced around the circumference of the electrode. The electrode assembly was placed on the sciatic nerve proximal to the popliteal fossa. A hook electrode was placed on six branches of the sciatic nerve in turn, just proximal to each branch's insertion into a leg muscle. Stimulation of the nerve branches was used to evoke signals in the sciatic nerve.**

Analysis of the signal amplitudes recorded from the sciatic nerve after different nerve branch stimulation showed significant differences. The signals evoked by stimulation of the peroneal nerve were almost always distinguishable from the signals evoked by stimulation of the extensor nerves. Signals evoked by stimulation of the various extensor branches showed distinguishability at reduced levels of significance. After functional distinguishability of nerve signals was demonstrated, the electrical centers of activity of the stimulated fibers were mapped for cross sections of the sciatic nerve. The resulting loci correlate reasonably well with anatomical data describing the location of the nerve fibers.

INTRODUCTION

THE objectives of this paper were 1) to record functionally distinct, evoked neuroelectric signals from the surface of the sciatic nerve of a rabbit, and 2) to utilize these signals to map the relative positions of fiber bundles within the sciatic nerve.

Sunderland [1] and Bardeen [2] have presented anatomical evidence for the spatial localization within a major human nerve trunk of fibers from a specific branch of that trunk. These investigators have shown that fibers from a specific branch tend to group in a few funiculi and that there is coherence of these fibers even at sections close to the nerve roots. Theoretical calculations [3] suggest that, if this coherence exists, there should be measurable changes in the nerve's surface potential as different nerve branches are stimulated. Other investigators [4] have demonstrated that contraction of different muscles in the leg of a rabbit can be effected by stimulation at different points around the sciatic nerve circumference.

De Luca [5], De Luca and Gilmore [6] and others [7]-[10] have shown that it is possible to implant electrodes around peripheral nerves for extended periods of time. Further studies should investigate whether chronically implanted electrodes can detect more than one functionally distinct neuroelectric signal; the applications of such findings could include controlling multiple-degrees-of-freedom prostheses or bridging damaged nervous tissue.

Manuscript received October 31, 1977. This work was supported in part by the Liberty Mutual Insurance Company, the Whitaker Professorship in Biomedical Engineering at the Massachusetts Institute of Technology, and the Fannie and John Hertz Foundation.

B. K. Lichtenberg is with the Department of Aeronautics and Astronautics, Massachusetts Institute of Technology, Cambridge, MA 02139.

C. J. De Luca with the Children's Hospital Medical Center, Boston, MA 02115.

METHODS

Equipment

A cuff electrode assembly was constructed of a Dacron knit cloth surrounded by a Silastic tube glued to the cloth. A slit along the length of the cuff allowed insertion of the nerve. The complete assembly can be seen in Fig. 1(a). The sciatic nerve inside the cuff can be seen in Fig. 1(b). The length of the cuff was approximately 10 mm (chosen for mechanical considerations) and the inside diameter was 2.3 mm. This diameter was slightly smaller than the average diameter of the sciatic nerve of rabbits weighing 3 to 4 kg so the cuff would fit snugly around the nerve. Eight 0.076 mm diameter 90 percent platinum-10 percent iridium Teflon-coated wires were woven through the Dacron cloth and terminated on the inside surface of the cloth cuff with uninsulated wire endings positioned with cross sections parallel to the wall of the tube [see Fig. 1(c)]. The cuff was mounted on the plastic support which contained the connectors joining the wires from the cuff to the FET preamplifiers. In order that the electrode assembly could be accurately moved along the nerve, the plastic support was attached to a precision drive unit which had a travel of 2.3 cm.

The arrangement of the wires permitted two different recording configurations: 1) circumferential differential and 2) longitudinal differential. The circumferential differential recordings were made by subtracting the potentials detected by two adjacent wires in one cross-sectional plane. For example, $V1$ was obtained by subtracting the potential detected by wire 2 from the potential detected by wire 1. Similarly, $V2$ was obtained by subtracting the potential detected by wire 3 from the potential detected by wire 2. In this manner, four circumferential recordings were obtained from four wires. The four longitudinal differential recordings were made by subtracting the potentials detected by the two wires similarly oriented in different cross-sectional planes. For example, $V1$ was obtained by subtracting the potential detected by wire 1 in one plane from the potential detected by wire 1 in the other plane [see Fig. 1(c)]. A needle electrode placed in the muscles of the thigh was used as a ground reference.

The electrode assembly was connected to four preamplifiers which had a common-mode rejection ratio of 94 dB at 60 Hz.

0018-9294/79/0400-0228$00.75

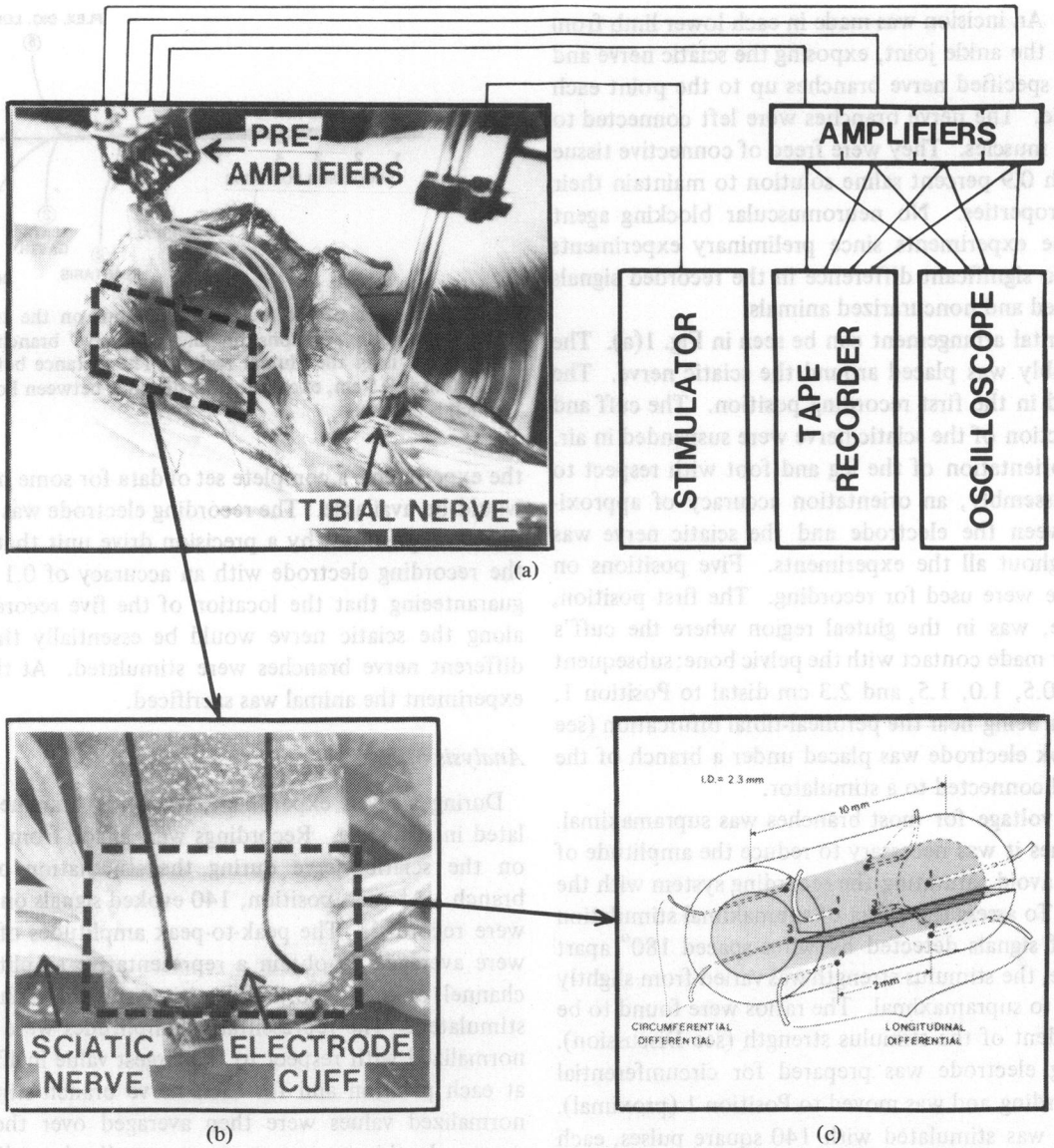


Fig. 1. Experimental arrangement and equipment used: (a) View of the dorsal part of a rabbit lower limb with the recording electrode placed around the sciatic nerve. The stimulating hook-electrode is placed on the tibial nerve. (b) Enlargement of the recording cuff-electrode area. (c) Details of the electrode contact arrangement in the cuff. An example of each type of recording configuration (longitudinal differential and circumferential differential) is also shown.

The outputs of the preamplifiers were cascaded with buffer amplifiers whose outputs were displayed on a four channel oscilloscope and recorded on an FM tape recorder. The system bandwidth was set at 10 Hz to 10 kHz.

Electrode Impedance

The impedance between each pair of electrode wires for each channel was measured in a 0.9 percent saline solution. One of the two wires in each pair was grounded to the measuring system. A signal generator was connected across the electrode leads through a 4.55 kΩ resistor. Two channels of an oscilloscope were connected to either side of the resistor and the ground through a high impedance (500 MΩ, 5 pF) preamplifier. The output of the signal generator was set to give a sinusoidal signal with a peak-to-peak amplitude of 1 mV. The amplitude and phase of the two voltages on the oscilloscope were measured at 2.5 kHz. These measured values were used to calculate the magnitude and phase of the electrode impedance. Other work done in our laboratory has shown the neuroelectric signal frequency spectrum to have a bandwidth of up to 7.5 kHz with a peak in the range of 2 to 2.5 kHz. Values of impedance for the different channels were found to range from 4.8 to 7.4 kΩ. Since the electrodes were connected in series with preamplifiers of much greater impedance (500 MΩ in parallel with 5 pF), no significant amplitude distortion was caused by the relatively small differences in impedance among the different channels.

Animal Preparation and Recording Procedure

Six white New Zealand rabbits (3 to 4 kg) were anesthetized with ethyl carbamate (1.6 g/kg) and shaved on the rear legs, hindquarters, neck and ears. A tracheotomy was performed to facilitate breathing. Normal body temperature was maintained throughout the experiment. The animals were placed in a

prone position. An incision was made in each lower limb from the hip joint to the ankle joint, exposing the sciatic nerve and each of the six specified nerve branches up to the point each entered a muscle. The nerve branches were left connected to the appropriate muscles. They were freed of connective tissue and coated with 0.9 percent saline solution to maintain their physiological properties. No neuromuscular blocking agent was used in the experiments since preliminary experiments demonstrated no significant difference in the recorded signals between curarized and noncurarized animals.

The experimental arrangement can be seen in Fig. 1(a). The electrode assembly was placed around the sciatic nerve. The cuff was located in the first recording position. The cuff and the enclosed section of the sciatic nerve were suspended in air. By fixing the orientation of the leg and foot with respect to the electrode assembly, an orientation accuracy of approximately 2° between the electrode and the sciatic nerve was achieved throughout all the experiments. Five positions on the sciatic nerve were used for recording. The first position, described above, was in the gluteal region where the cuff's proximal border made contact with the pelvic bone; subsequent positions were 0.5, 1.0, 1.5, and 2.3 cm distal to Position 1, the last position being near the peroneal-tibial bifurcation (see Fig. 2). A hook electrode was placed under a branch of the sciatic nerve and connected to a stimulator.

The stimulus voltage for most branches was supramaximal. However, at times it was necessary to reduce the amplitude of the stimulus to avoid saturating the recording system with the evoked signal.[1] To assess the effect of submaximal stimulation on the ratios of signals detected by wires spaced 180° apart around the nerve, the stimulus strength was varied from slightly above threshold to supramaximal. The ratios were found to be almost independent of the stimulus strength (see Discussion).

The recording electrode was prepared for circumferential differential recording and was moved to Position 1 (proximal). A nerve branch was stimulated with 140 square pulses, each having a duration of 0.05 ms, with a repetition rate of 20 pulses/s. Signals detected by the recording electrodes were stored on the FM tape recorder. This procedure was repeated for the other four recording positions on the sciatic nerve. Then the recording electrode was changed to the longitudinal differential configuration and the recording procedure was repeated for all the positions. Six nerve branches were stimulated in the following order: peroneal, plantaris, lateral gastrocnemius, tibial, flexor digitorum longus, and soleus (see Fig. 2). It was decided to record from all five positions while stimulating a given nerve branch rather than record from one position while sequentially stimulating all six nerve branches for the following reasons. First, due to the traumatic nature of the experiments, it was prudent to isolate and stimulate the superficial nerve branches first. In order to expose the deep branches (tibial, flexor digitorum longus, and the soleus) it was necessary to resect the medial and lateral gastrocnemius, and the soleus muscles. Second, if the animal were to die during

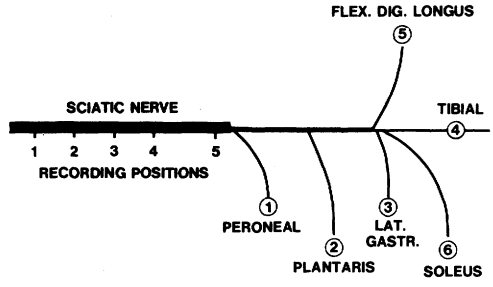


Fig. 2. Schematic of the recording positions on the sciatic nerve and the stimulating positions on the six nerve branches. Recording Position 1 is in the gluteal region. The distance between recording positions is 0.5 cm, except for the distance between Positions 4 and 5, which is 0.8 cm.

the experiment, a complete set of data for some nerve branches would be available. The recording electrode was moved to the different positions by a precision drive unit that could locate the recording electrode with an accuracy of 0.1 mm, thereby guaranteeing that the location of the five recording positions along the sciatic nerve would be essentially the same when different nerve branches were stimulated. At the end of the experiment the animal was sacrificed.

Analysis of Data

During a given experiment, six nerve branches were stimulated in sequence. Recordings were made from five positions on the sciatic nerve during the stimulation of each nerve branch. At each position, 140 evoked signals on each channel were recorded. The peak-to-peak amplitudes of these signals were averaged to obtain a representative amplitude for each channel, at each recording position and for each nerve branch stimulated. The representative amplitudes were subsequently normalized with respect to the largest value in all the channels at each position and for each nerve branch stimulated. The normalized values were then averaged over the five experiments. In this manner, a mean normalized amplitude for each channel at each of the five recording positions and for each of the six nerve branches stimulated was obtained. At each position and for each channel, Duncan's multiple range test[2] was used to indicate statistically significant differences in the means as a function of the nerve branch stimulated.

In order to use the potentials recorded on the circumference of a nerve trunk to map the positions of the electrical centers of activity, it is necessary to know the voltage decrement function. Clark and Plonsey [11] have derived equations describing the potential fields inside and on the surface of a nerve trunk. They assumed a cylindrical nerve trunk and an infinite isotropic medium outside the trunk. The source was assumed to be a cylindrical eccentric "active" fiber in the nerve trunk. Values needed for their equations include the active fiber's radius and position within the nerve, the active fiber's transmembrane potential, the nerve's radius, and the following electrical parameters of the nerve: the sheath capacitance and conductivity, the conductivity of the external medium, the conductivity of the inactive fiber area and the average radial

[1] It should be made clear that saturation was not due to the stimulus artifact. Evoked signal amplitudes of over 400 μV saturated the tape recorder; the stimulus artifact never reached this level.

[2] The computer program used was BMD 07V multiple range tests.

interstitial conductivity of the inactive part of the nerve trunk. In a more recent study, Plonsey [12] has treated the case of anisotropic media, which are defined as having different *average* values for radial and longitudinal conductivity. He has shown that the equations remain essentially unchanged.[3]

To calculate the potential on the circumference of a nerve trunk, Clark and Plonsey [11] used electrical parameters obtained from various published studies; for the radial interstitial conductivity, however, they assumed a value of 2.5 ℧/m, about one-half that of a sea water bathing medium. With these values, their calculations showed a 1.1 percent change in amplitude between voltages detected at two opposite points 180° apart on the nerve's surface. Our data show typical voltage changes of 70 percent. The predictions of the model can be reconciled with the experimental data by reducing the average radial interstitial conductivity from 2.5 ℧/m to approximately 0.01 ℧/m. This parameter has the most effect on the ratio of potentials recorded on the nerve's surface. In fact, no other parameter could be modified sufficiently to yield the ratios observed experimentally. As can be seen, this change represents a 250 fold reduction in the value for radial interstitial conductivity from that assumed by Clark and Plonsey. Tasaki [13] measured the radial interstitial conductivity and found an average value of 0.01 ℧/m (approximately 50 times smaller than the longitudinal interstitial conductivity). Therefore, although the results of Clark and Plonsey's simulation differ from the experimental results, it appears that the only discrepancy is due to their choice of an improper value for the average radial conductivity.

The equations derived by Clark and Plonsey [11] were used to calculate the potential along the radius inside the nerve trunk. The calculated values were then fitted with a linear regression curve of $v = k/d$ (v is the voltage measured at a distance d from the source and k is a constant). This approximation of the voltage decrement function was fitted with a regression coefficient of 0.97.

The above calculations assume that a large volume conductor surrounds either a single fiber or a nerve trunk. Stein and Pearson [14] have discussed the effects on signal amplitude of locally restricted extracellular space such as one might find in a cuff electrode. Their calculations, although interesting, are only valid for one unmyelinated fiber inside the cuff. They attempt to incorporate the effects of other fibers but assume that the extracellular potential anywhere on a cross section of nerve trunk is constant. Marks and Loeb [15] extended the work of Stein and Pearson to a myelinated fiber located eccentrically inside an anisotropic nerve trunk. They showed that Stein and Pearson's equations were also valid for these conditions, but that the constant potential on a cross section of the nerve trunk should be replaced with a weighted average potential. Although technically taking into account radial anisotropy, the use of a weighted average is actually the use of a constant, and is, therefore, essentially Stein and Pearson's assumption of a constant potential everywhere on a cross section of the nerve trunk. It appears extremely difficult, if not impossible, to calculate accurate extracellular potentials due to the interactions of a number of active and passive fibers within a nerve trunk.

In the same paper, Marks and Loeb examined the relationship of extracellular potentials to the position of a node, or nodes, of Ranvier inside a cuff electrode. They concluded that for tube lengths (electrode spacing) in excess of 2 nodes of Ranvier, the position of the nodes inside the tube has virtually no effect on the amplitude and only a minimal effect on the waveform of the recorded extracellular potential.

With a known voltage decrement function, it is possible to use evoked signals recorded from the surface of a nerve trunk to locate the electrical center of activity inside the nerve trunk. Two assumptions are required: 1) the nerve trunk can be treated as an isotropic medium and 2) the center of electrical activity of the active fibers can be considered as a point source. From Fig. 3 the following equations can be written relating the signals recorded at four different positions around the nerve to the center of activity. The four longitudinal differential signals were considered to represent monopolar signals recorded at one cross section of the nerve. Since a k/d decrement function has been established, $V3/V1 = d1/d3 = A$ and $V2/V4 = d4/d2 = B$. With a normalized radius of the nerve equal to 1, the following equations can be obtained:

$$y^2 + (1 - x)^2 = d1^2 \quad \text{and} \quad y^2 + (1 + x)^2 = d3^2;$$

hence,

$$(d1/d3)^2 = A^2 = \frac{y^2 + (1 - x)^2}{y^2 + (1 + x)^2} \quad \text{and}$$

$$(d4/d2)^2 = B^2 = \frac{x^2 + (1 + y)^2}{x^2 + (1 - y)^2}.$$

The solutions of the above quadratic equations are

$$x = C \pm [C^2 - (y^2 + 1)]^{1/2} \qquad \text{where } C = \frac{1 + A^2}{1 - A^2}$$

and

$$y = \frac{-DC \pm C[D^2(C^2 - 1) - C^2]^{1/2}}{C^2 + D^2} \qquad \text{where } D = \frac{1 + B^2}{1 - B^2}.$$

There are four roots to these equations, but only one is the actual solution. Since it is known that the source of the signals must be inside the nerve, any root outside the nerve boundary could be immediately discarded. The remaining roots had to be substituted into the equations to find the solution.

Results

Distinguishability of Recorded Signals

Experiments were numbered by taking the identification number of the rabbit and following it by an R or L, designating either the right or the left lower limb (e.g., the experiment on the left lower limb of the second rabbit would be 2L). Each rabbit lower limb was considered a separate experiment. Due to the traumatic nature of the experiments and length of recording sessions (2 to 3 h per leg), most experiments did not

[3]The only change involves a transformation of coordinates and a scale factor.

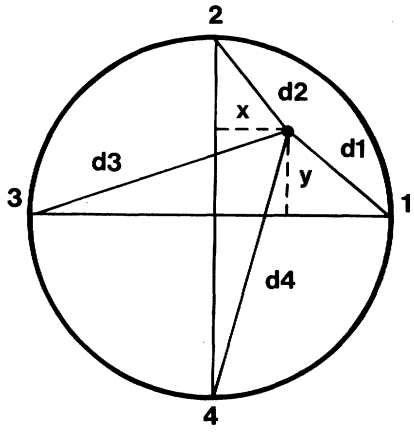


Fig. 3. Schematic of an idealized cross section of the sciatic nerve. Points 1, 2, 3, and 4 represent the longitudinal differential signals recorded at one position; x and y describe the location of the center of electrical activity; $d1$, $d2$, $d3$, and $d4$ represent the distances from the center of activity to the respective electrode. This representation was used to develop equations relating the location of the center of electrical activity to the 4 longitudinal differential signals recorded at one position (see text).

yield a complete set of data. At times the death of the animal or pressure-induced constriction blocks rendered the evoked signals unusable. When the recorded waveform changed noticeably from waveforms recorded during the beginning of an experiment, or if a conduction block became evident, that particular experiment was terminated. Therefore, out of ten experiments only five complete sets of data were recorded (Table I). A complete set of data consisted of circumferential and longitudinal differential recordings at all five recording positions for each of the six nerve branches stimulated. Due to problems with the longitudinal recording mode, only three voltages around the circumference at each recording position were available during experiment 3R and subsequent experiments. This constituted a complete set of information since only three of the four voltages around the nerve are sufficient to locate a point source within the nerve.

The circumferential differential signals have two major characteristics of interest: 1) their peak-to-peak amplitudes (mean value of 39 μV) are lower than the corresponding peak-to-peak amplitudes of the longitudinal signals (mean value of 104 μV) and 2) their waveforms vary noticeably depending on recording position and stimulation site. Fig. 4(a) shows the four channels of circumferential differential information recorded at Position 3 during stimulation of the plantaris branch in Experiment 1L. In Fig. 4(b), the recording position has been changed to 5 (1.3 cm distal to Position 3) with all other parameters remaining the same. Notice the change in amplitude, waveform, and phase relationships dependent only on the recording position on the sciatic nerve. Because such obvious phase and amplitude changes occurred in the circumferential differential data, these data were analyzed first.

Two problems were encountered in determining the phase polarity of the circumferential differential signals. First, the peaks of the signals in a group of four voltages did not always occur at the same time. Second, because the waveforms varied between biphasic and triphasic, it was difficult to consistently classify the phase relationships between channels at different recording positions.

TABLE I
RECORDING CONFIGURATIONS ARE CIRCUMFERENTIAL DIFFERENTIAL (C) AND LONGITUDINAL DIFFERENTIAL (L). (NOTE THAT A COMPLETE SET OF RECORDING COULD NOT ALWAYS BE OBTAINED.)

DATA COLLECTION

Stimulated Nerve	Recording Configuration	EXPERIMENT 1L	2L	2R	3L	3R	4L	4R	5L	5R	6L
Peroneal Nerve	C	X	X	X	X	X					
	L	X	X	X	X						X
Plantaris Nerve	C	X	X	X	X	X					
	L	X	X	X	X		X				
Lat. Gast. Nerve	C			X	X	X	X			X	
	L		X	X	X	X	X				
Tibial Nerve	C		X	X	X	X	X				
	L		X	X	X		X	X			
Flex. Dig. Longus Nerve	C		X		X	X		X	X		
	L	X			X	X		X			X
Soleus Nerve	C		X	X	X	X	X				
	L		X	X	X		X	X			

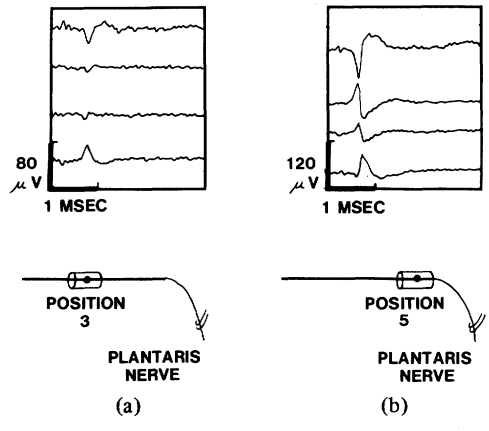


Fig. 4. Sample of the circumferential differential data recorded during Experiment 1L. (a) Four channels ($V1$ at the top, $V4$ at the bottom) recorded at Position 3 while the plantaris nerve was stimulated. (b) Same as (a), except the recording position has been changed to Position 5 (1.3 cm distal to Position 3). Note the change in amplitudes and phase relationships. These data indicate that the location of the center of electrical activity is moving inside the nerve as a function of the recording position.

The longitudinal differential signals did not present the problems of the circumferential differential signals. The amplitudes were uniformly larger than those of the circumferential signals, and all the signals in one data set (with a few exceptions)[4] had the same waveform. Fig. 5(a) and (b) show the four channels of longitudinal data recorded at Positions 3 and 4 while stimulating the plantaris nerve branch during Experiment 1L. Notice that the phase relationships remain almost constant, with only minor changes in the waveform, but with significant changes in the amplitudes.

Duncan's multiple range test on the means of the normalized circumferential data showed that there was statistical distinguishability between the means of the normalized ampli-

[4]The only changes in waveform were between biphasic and triphasic (see Discussion).

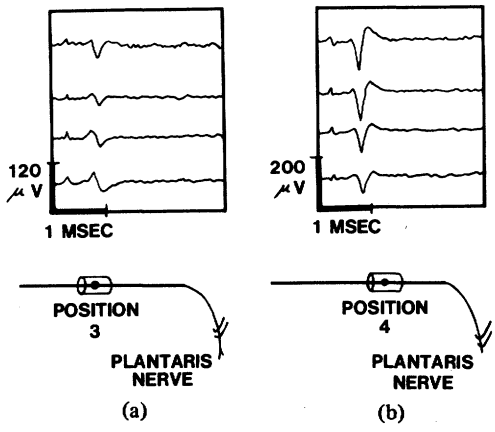


Fig. 5. Sample of the longitudinal differential data recorded during Experiment 1L. (a) Four channels ($V1$ at the top, $V4$ at the bottom) recorded at Position 3 while stimulating the plantaris nerve. (b) Same as (a), except that the recording position has been changed to Position 4 (0.5 cm distal to Position 3). Note the change in amplitudes with constant phase relationships. These data indicate that the location of the center of electrical activity is moving inside the nerve as a function of recording position.

TABLE III

STATISTICAL DISTINGUISHABILITY OF THE MEANS OF THE NORMALIZED LONGITUDINAL DIFFERENTIAL AMPLITUDES USING DUNCAN'S MULTIPLE RANGE TEST. DIFFERENCES IN THE MEANS ARE PRESENTED FOR THREE DIFFERENT LEVELS OF SIGNIFICANCE. THE MEANS OF THE SIGNALS ARE CODED ACCORDING TO NERVE BRANCH STIMULATED: 1 = PERONEAL NERVE, 2 = PLANTARIS NERVE, 3 = LAT. GAST. NERVE, 4 = TIBIAL NERVE, 5 = FLEX. DIG. LONGUS NERVE, 6 = SOLEUS NERVE.

CIRCUMFERENTIAL DIFFERENTIAL DATA

	LEVEL OF SIGNIFICANCE		
	$p \leq 0.01$	$p \leq 0.05$	$p \leq 0.10$
Position 1			
V1		1 from 5, 6 3 from 5	1 from 5, 6 3 from 5
V2	1 from 4	1 from 3, 4	1 from 2, 3, 4, 5, 6
V3		1 from 4, 5	1 from 2, 3, 4, 5
V4		1 from 2, 4, 5, 6	1 from 2, 3, 4, 5, 6
Position 2			
V1	1 from 5	1 from 4, 5, 6 3 from 5	1 from 2, 4, 5, 6 3 from 4, 5, 6
V4			1 from 2, 4
Position 3			
V1		1 from 5	1 from 2, 4, 5 3 from 5
V3		1 from 4, 6	1 from 2, 3, 4, 6
Position 4			
V2	1 from 4	1 from 2, 4, 6	1 from 2, 3, 4, 5, 6
V3		3 from 2, 4	1 from 2, 4 3 from 2, 4
Position 5			
V2			1 from 4
V3		1 from 6	1 from 4, 6
V4	1 from 3, 4, 5, 6	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6

tudes of the evoked signals from the peroneal nerve and the means of the normalized amplitudes of the evoked signals from the various extensor nerve branches (Table II). These differences, however, were not at the high levels of significance found in the longitudinal data. For example, in distinguishing between the means (on the various channels) of the normalized circumferential differential amplitudes of the evoked signals from the peroneal nerve and the means of the normalized

TABLE II

STATISTICAL DISTINGUISHABILITY OF THE MEANS OF THE NORMALIZED CIRCUMFERENTIAL DIFFERENTIAL AMPLITUDES USING DUNCAN'S MULTIPLE RANGE TEST. DIFFERENCES IN THE MEANS ARE PRESENTED FOR THREE DIFFERENT LEVELS OF SIGNIFICANCE. THE MEANS OF THE SIGNALS ARE CODED ACCORDING TO NERVE BRANCH STIMULATED: 1 = PERONEAL NERVE, 2 = PLANTARIS NERVE, 3 = LAT. GAST. NERVE, 4 = TIBIAL NERVE, 5 = FLEX. DIG. LONGUS NERVE, 6 = SOLEUS NERVE.

LONGITUDINAL DIFFERENTIAL DATA

	LEVEL OF SIGNIFICANCE		
	$p \leq 0.01$	$p \leq 0.05$	$p \leq 0.10$
Position 1			
V1	1 from 2, 3, 4, 5, 6 1, 5 from 2, 3, 4, 6	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6
V2		1 from 2, 3, 4, 5, 6 1, 2, 3 from 4, 5, 6	1, 2 from 3, 4, 5, 6 2, 3, 4 from 1, 5, 6
V3			1 from 2, 3, 4, 5, 6 3 from 1, 2, 4, 5, 6
Position 2			
V1	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6
V2	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6
Position 3			
V1		1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6
V2	1 from 2, 3, 4, 5, 6 4 from 1, 2, 3, 5, 6	1 from 2, 3, 4, 5, 6 1, 3 from 2, 4, 5, 6	1 from 2, 3, 4, 5, 6 1, 3 from 2, 4, 5, 6
V3	5 from 1, 2, 3, 4, 6 3 from 1, 2, 4, 6	2, 3, 4, 6 from 1, 5 1, 2, 4, 6 from 3, 5 1, 4, 5 from 2, 3, 6	2, 3, 4, 6 from 1, 5
Position 4			
V1	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6
Position 5			
V1	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6
V2		1 from 2, 3, 4, 5, 6	1 from 2, 3, 4, 5, 6

amplitudes of the evoked signals from the various extensor nerve branches, the following results can be seen (Table II). At Position 1, all four channels show distinguishability ($p \leq 0.05$). In addition, some distinguishability can be seen between the means of various extensor nerves on the various channels (e.g., Position 2, $V1$; and Position 4, $V3$).

Duncan's multiple range test on the means of the longitudinal data (Table III) indicated that these data were much more consistent than the circumferential data. For example, at every recording position, the means of the normalized amplitudes of the evoked signals from the peroneal nerve can be distinguished from the means of the normalized amplitudes of the evoked signals and from the extensor nerves on at least one channel at a level of significance of $p \leq 0.01$. In addition, distinguishability among the means of the normalized amplitudes of the evoked signals from various extensor nerves is demonstrated. For example, the data of Position 3, channel 2, show that the means of the normalized amplitudes of the evoked signals from the tibial nerve branch can be distinguished from all other means at $p \leq 0.01$. Similarly, on channel 3, the means of the normalized amplitudes of the evoked signals from the flexor digitorum longus nerve branch can be distinguished from all others at $p \leq 0.01$. Other comparisons can be made at lower levels of significance. At $p \leq 0.10$, the means of the normalized amplitudes of the evoked signals from the plantaris, lateral gastrocnemius, and tibial nerves can be distinguished from all other means at Position 1, channel 2.

Fig. 6 is a plot of the normalized longitudinal differential amplitudes of the four recording channels for one experiment (2R). The plot is a point plot with the symbols connected for

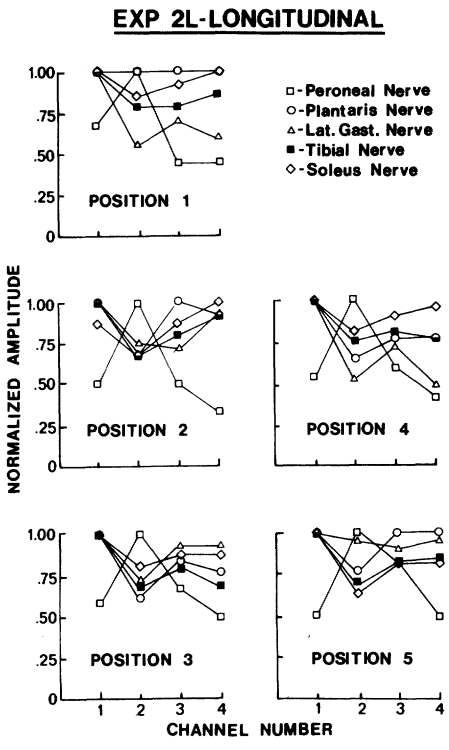


Fig. 6. Normalized longitudinal differential amplitudes of all recording positions during Experiment 2L. The plot is a point plot with the symbols connected for legibility. Note the striking difference between the evoked signals from the peroneal nerve and those from the extensor nerves. Also, there are significant differences among the evoked signals from the extensor nerves. For example, at Position 4, the signals from the lateral gastrocnemius nerve are different not only from the signals from the peroneal nerve, but also from the signals from the other extensor nerves.

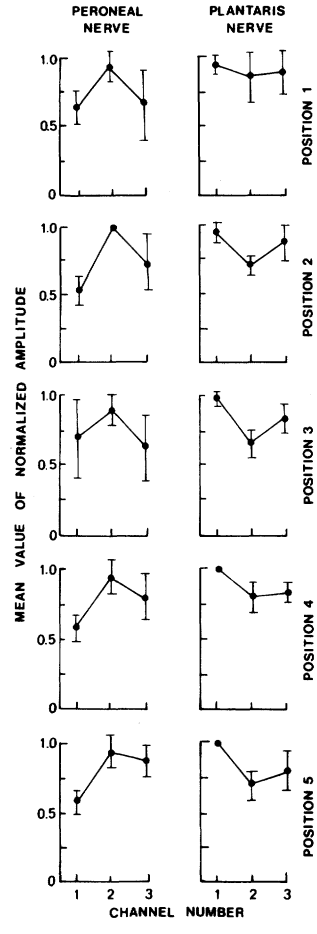


Fig. 7. Mean ($N = 5$) and standard deviation of the normalized amplitudes recorded during stimulation of the peroneal nerve and the plantaris nerve. The plots are point plots with the means connected for legibility. The data from only two of the six stimulated nerves are shown. The variance shown is representative of the variance calculated for the other four plots not presented here. The repeatability (as shown by the variance) between experiments is acceptable considering the inherent biological variability among rabbits.

legibility. The flexor digitorum longus nerve branch was not stimulated during this particular experiment. Fig. 6 shows that at all five recording positions evoked signals from the peroneal nerve branch are distinctly different from evoked signals from the extensor nerve branches. In addition, there is some distinguishability among the various extensor evoked signals, especially at Position 1. Even though the recording sessions lasted for 2 to 3 h, there is no evidence of a relationship between the amplitudes of the recorded signals and the stimulation order.

Fig. 7 indicates the consistency of the data obtained from five rabbits. Note that after Experiment 3R, only three longitudinal differential channels were recorded. This figure shows the means ($N = 5$) and standard deviations for the normalized longitudinal signals recorded during stimulation of the peroneal and plantaris nerves. The plots are point plots with the means connected for legibility. The data from only two of the six stimulated nerve branches are shown. The variance shown in Fig. 7 is representative of the variances calculated for the other four plots not presented here. The variance is a measure of the consistency between experiments and recording positions.

Mapping the Center of Activity

The circumferential differential data were initially thought to be useful for mapping the approximate locations of the center of activity of the different active fiber groups within the sciatic nerve trunk because of two characteristics. First, the circumferential differential recordings were made at one cross section of the nerve, reducing any errors due to fiber migration or changes in the longitudinal conductivity of the nerve trunk. Such errors might appear in the longitudinal data because these data are obtained by subtracting the signals detected at cross sections 2 mm apart. Second, there appeared to be more phase information in the circumferential differential data than in the longitudinal differential data. However, as noted before, the phases of the circumferential data were found to be difficult to classify and were not useful in determining the location of the active fibers.

The longitudinal data were satisfactory for mapping the approximate centers of activity of the stimulated nerve branches. Fig. 8 shows the results of Experiments 1R, 2L, 2R, 3L. Recall from Table I that not all nerve branches could be stimulated during each experiment. These diagrams represent a cross section of the sciatic nerve. The center of activity for each nerve branch stimulation is mapped by a line joining a nerve branch symbol (recording Position 1) to a series of dots

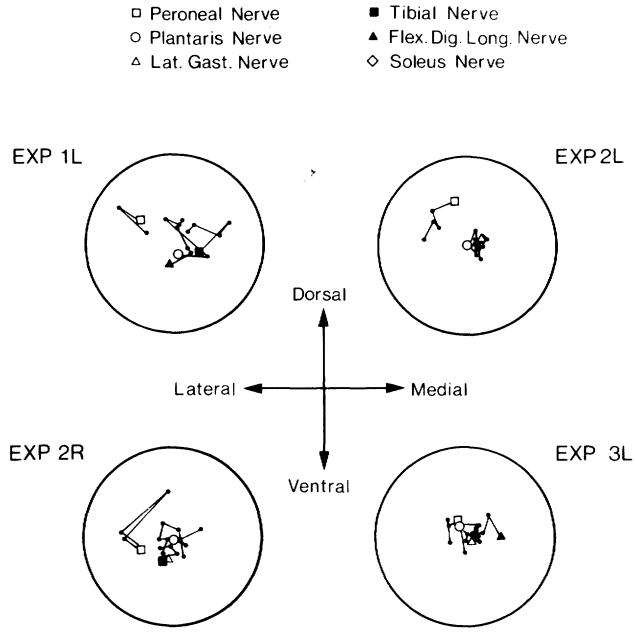


Fig. 8. Location and displacement of the electrical centers of activity during four different experiments. The large symbol indicates the location at recording Position 1 and the small dots indicate the location at the other recording positions. The circles indicate the cross-sectional boundary of the nerve. Note the lateral position of the peroneal nerve during 3 of the 4 experiments.

(recording Positions 2–5). Distinguishability among evoked signals of the various nerve branches is thus shown graphically. An anomaly was noted in Experiment 2R. At Position 3, the peroneal nerve's center of activity jumped from a lateral to a dorsal location and at Position 4 it returned to the lateral location. At this point, the nerve appears to have twisted. But this would have occurred only if the nerve had been removed from the electrode and then replaced in it. If this had been done, one would expect to see the twist show up at Positions 4 and 5 also. Since Positions 4 and 5 appear to be compatible with Positions 1 and 2, the only apparent explanation is that the nerve fibers do migrate. In Experiment 2L, the centers of activity rotate slightly as the recording electrode progressed from proximal to distal positions. In the other experiments there is no such clear-cut trend. For the most part, the centers of activity of the extensor nerve fibers are grouped together with a definite separation from that of the peroneal nerve, whose fibers tend to be located laterally. The centers of activity of the extensor nerve fibers occasionally moved between quadrants, but only a few large migrations are noted.

Discussion

Distinguishing the Evoked Signals

As noted in the Methods section, not all nerve branches were stimulated supramaximally. At times it was necessary to reduce the stimulus level to about 60 percent of supramaximal. The lowest stimulation level used was approximately three times greater than the threshold level. To assess the changes in voltage ratios as a function of stimulus level, recordings from the sciatic nerve were made while varying the stimulus levels of the peroneal and soleus nerves. Stimulation of the peroneal nerve was applied at two different levels (60 percent of supramaximal and supramaximal). Recordings were made from Positions 2 and 4 on the sciatic nerve. At each of these positions the voltage ratios $V1/V3$ and $V2/V4$ were computed. The coefficient of variation (standard deviation/mean) was calculated for each ratio at each position and used as a measure of variation in the voltage ratios as a function of stimulus level. At Position 2, the coefficient of variation for $V1/V3$ was 3.7 percent and for $V2/V4$, 2.2 percent. At Position 4, the coefficient of variation for $V1/V3$ was 0 and for $V2/V4$, 0.4 percent. For the soleus nerve, the stimulus was varied from slightly above threshold to supramaximal in five equal increments. Recordings were made from Position 1 on the sciatic nerve. As explained in the results, only three channels were recorded. The coefficient of variation for $V1/V2$ was 6.0 percent and for $V1/V3$, 2.8 percent. Because of the low coefficients of variation it can be concluded that the voltage ratios, obtained from slightly above threshold to supramaximal stimulation, are representative of values obtained with supramaximal stimulation.

The amplitudes of the circumferential differential data were lower than those of the longitudinal differential data due to the configurations used in obtaining the signals. The circumferential signals were obtained by subtracting the potentials recorded from two adjacent wires located on the same cross-sectional plane of the nerve. Since the recorded signals reached their peak amplitudes at the same time, the difference between them was small. The longitudinal differential signals were obtained by subtracting the potentials recorded from two wires, one in each of two planes spaced 2 mm apart longitudinally. In this case, since the recorded signals reached peak amplitudes at two different times, the difference between the potentials was greater than that between potentials in the circumferential differential signals.

As noted in the data analysis section, Marks and Loeb [15] showed that the extracellular potential as a function of a node position inside the cuff was virtually constant as long as the electrode spacing was equal to approximately two nodes of Ranvier. The electrode used in this study had a spacing of 2 mm, and the average internode distance is on the order of 1.1 mm [16]. Therefore, no significant changes in amplitude or waveform were associated with changes in the positions of the nodes inside the cuff.

There are three possible explanations for the changing waveforms. First, the theoretical work done on extracellular potentials of a single axon by van Rotterdam [17] could be applicable to the case of compound action potentials. Van Rotterdam developed a mathematical model to predict the extracellular potential as a function of radial and longitudinal distance from the initiation point of the action potential. In particular, he calculated the extracellular potential along a length of axon corresponding approximately to one internodal length in the large diameter fibers in the peroneal nerve of a rabbit. Van Rotterdam's calculations predicted an extracellular phase change from biphasic to triphasic and back to biphasic as a function of radial and longitudinal distance from the node of

Ranvier. Occasionally, similar behavior was seen in the waveforms of the longitudinal differential data. Since approximate internodal distance for large fibers in the peroneal nerve is 1.1 mm [16], the distance between recording positions in this study (5 mm) traverses approximately 4 nodes of Ranvier. Thus, van Rotterdam's calculations cannot be used to predict the phase anomalies in the data, but they can help to explain their presence. A second possible explanation for the changing waveforms is that a change in the conduction velocity within the recording region could alter phase relationships. A third possibility could be that the signal source might be distributed within the nerve trunk instead of being a point source. In fact, Sunderland [1] showed there were usually 2 or 3 funiculi that carried fibers from one nerve branch.

The distinguishability of evoked signals associated with the different nerve branches can be interpreted as a measure of the coherence of the active fibers inside the sciatic nerve. The results of Tables II and III show that the statistical distinguishability does change at the different recording positions. Table II (circumferential) shows that distinguishability is greatest at Positions 1 and 5, whereas Table III (longitudinal) shows that distinguishability is small at Positions 2 and 4 and greater at Positions 1 and 3. Sunderland [1] also noted that bundles from various identifiable fiber groups sometimes spread out and then regroup during their proximal progression.

The data showed some inherent consistency, but also some variability. The general consistency indicates the inherent anatomical arrangement of nerve fibers inside the sciatic nerve. The variability can be due to anatomical variation and experimental errors. Anatomical variations include the nonhomogeneity of the sciatic nerve epineurium and variations in the fiber arrangement within the sciatic nerves of different rabbits. Experimental errors include induced changes in the cross-sectional shape of the sciatic nerve from its noncircular shape to the circular shape of the electrode, and varying amounts of blood and interstitial fluid accumulating between the cuff and the nerve during the recording procedure. Fluid and tissue between the nerve and recording electrodes could cause significant shunt impedance variation along the epineurium. However, the variances shown in Fig. 7 and Tables II and III indicate that there is some inherent repeatability at the same positions along the sciatic nerve among experiments. Therefore, the variability of the longitudinal sheath resistance (although present) does not significantly distort the voltage measurements.

The primary result is that in every experiment evoked signals recorded from stimulation of the peroneal nerve (innervating flexor muscles) could be distinguished from evoked signals of the other five nerve branches (innervating extensor muscles). In several cases some of the extensor nerve branches could be distinguished from each other (see Fig. 8).

A final point to consider in determining the distinguishability of the evoked signals from different nerve branch stimulations is the difference between antidromic stimulation of a nerve branch and physiological initiation of motor activity. The expected voltage patterns during a motor command will not be identical to the patterns recorded during these experiments. The electrical stimulation employed in this investigation excites both sensory and motor fibers. However, Sunderland [1] has demonstrated that for many of the nerve branches in man, sensory and motor fibers are in different funiculi. Consequently, voluntary signals of motoneuron origin would probably be more localized. However, their amplitude will be considerably lower than that of the evoked signals detected in this study. Further work is required to demonstrate if the functionally distinct motor neuroelectric signals of physiological origin can be detected from the surface of a nerve.

Mapping the Centers of Activity

The lateral location of the center of electrical activity of the peroneal nerve fibers correlates reasonably with the physical location of these active fibers within the nerve trunk [18]. The physical location of the extensor nerve fibers have not been mapped for the rabbit sciatic nerve, but studies in man [2] have shown that they are located more medially. Fig. 8 also shows, in a different form, that stimulation of the peroneal nerve is distinguishable from stimulation of the extensor nerve branches in each experiment. In contrast to the nerves in the human arm, there are only a few funiculi in the region near the peroneal-tibial bifurcation of the rabbit sciatic nerve. Therefore, small movements of the center of activity of fibers associated with a given nerve branch imply that these fibers are moving within a funiculus; whereas, large movements of the center of activity imply that the fibers are moving between funiculi.

Because the separation and movements of the center of activity (especially for the extensor nerve fibers) appear small, a sensitivity analysis was done to correlate the movement of the center of activity to a given amplitude change in the voltages around the nerve circumference. The sensitivity analysis was computed for two different cases. First, the initial center of activity was taken to be at a distance $0.25r$ from the center, along a line between the center of the nerve and one of the recording positions. A 5 μV change in amplitude was easily detectable. This change corresponds to approximately 5 percent with respect to the mean longitudinal differential amplitude (104 μV). This increment in amplitude moved the center of activity from $0.25r$ to $0.36r$. In the second case the initial position was taken to be a distance of $0.25r$ from the center along a line inclined 45° to the first line. In this case the center of activity was assumed to move along the line inclined 45°. A 5 μV increment moved the center of activity from $0.25r$ to $0.29r$. Therefore, a 5 percent change in the amplitude of the signal (which is easily detectable) indicates that the center of activity has moved only a small distance.

Conclusion

This study has shown that it is possible to detect functionally distinct evoked neuroelectric signals from the surface of the rabbit sciatic nerve. Better distinguishability of neuroelectric signals is obtained with differential electrodes located along the length of the nerve than those located around its circumference. Distinguishability always existed between the amplitude of the evoked signals obtained by stimulation of the

peroneal nerve branch (flexor) and that of the evoked signals obtained by stimulation of the extensor nerve branches. In addition, some distinguishability also existed between the amplitudes of the evoked signals obtained by stimulation of different extensor nerve branches.

The variances of the means of the normalized amplitudes of the evoked signals imply that there is some consistency between rabbits. This consistency indicates the inherent anatomical arrangement of nerve fibers inside the sciatic nerve.

Acknowledgment

The authors wish to thank L. D. Gilmore for his assistance in performing the experiments. Thanks are also due to R. Schumann and R. A. Campanelli for their computer programming assistance, and to Prof. R. W. Mann for his advice throughout the project.

References

[1] S. Sunderland, "The intraneural topography of the radial, median and ulnar nerves," *Brain*, vol. 68, pp. 243–299, 1945.

[2] C. R. Bardeen, "Development and variation of the nerves and the musculature of the inferior extremity and of the neighboring regions in man," *Amer. J. Anat.*, vol. 6, pp. 259–384, 1906–1907.

[3] R. R. Rothchild, Decoding electrical artifact from large nerve bundles *"in vivo,"* Sc.D. thesis, Massachusetts Inst. Tech., Cambridge, MA, 1973.

[4] D. R. McNeal and J. Haughey, "Annual report of progress, December 1973 to November 1974," Rehabil. Eng. Cent., Rancho Los Amigos Hospital, Downey, CA, p. 24, 1975.

[5] C. J. De Luca, "Control of upper-limb prostheses: A case for neuroelectric control," *J. Med. Eng. Tech.*, vol. 2, pp. 57–61, 1978.

[6] C. J. De Luca and L. D. Gilmore, "Voluntary nerve signals from severed mammalian nerves: long-term recordings," *Science*, vol. 191, pp. 193–195, 1976.

[7] I. Ninomiya, Y. Yonezawa, and M. F. Wilson, "Implantable electrode for recording nerve signals in awake animals," *J. Appl. Phys.*, vol. 41, pp. 111–114, 1976.

[8] H. Schad and H. Seller, "A method for recording autonomic nerve activity in unanesthetized, freely moving cats," *Brain Res.*, vol. 100, pp. 425–430, 1975.

[9] G. Sell, G. Schauf, Ch. Gerlach, H. A. Küster, and Marquardt, "Ableitung und Analysen von Neurosignalen aus dem peripheren Nervensystem mit dem Ziel der Nutzung zur mehrkanaligen Prothesensteuerung," *Z. Orthop.*, vol. 114, pp. 94–98, 1976.

[10] R. B. Stein, D. Charles, L. Davis, J. Jhomandas, A. Mannard, and T. R. Nichols, "Principles underlying new methods for chronic neural recordings," *Can. J. Neurol. Sci.*, vol. 2, pp. 235–244, 1975.

[11] C. Clark and R. Plonsey, "The extracellular potential field of the single active nerve fiber in a volume conductor," *Biophys. J.*, vol. 8, pp. 842–962, 1968.

[12] R. Plonsey, "The active fiber in a volume conductor," *IEEE Trans. Biomed. Eng.*, vol. BME-21, pp. 371–381, 1974.

[13] I. Tasaki, "A new measurement of action currents developed by single nodes of Ranvier," *J. Neurophysiol.*, vol. 27, pp. 1199–1205, 1964.

[14] R. B. Stein and K. G. Pearson, "Predicted amplitude and form of extracellulary recorded potentials from unmyelinated nerve fibers," *J. Theor. Biol.*, vol. 32, pp. 539–558, 1971.

[15] W. B. Marks and G. E. Loeb, "Action currents, internodal potentials, and extracellular records of myelinated mammalian nerve fibers derived from node potentials," *Biophys. J.*, vol. 16, pp. 655–668, 1976.

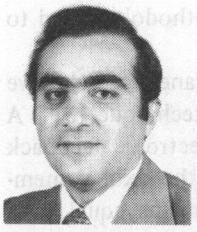
[16] A. D. Vizoso and J. Z. Young, "Internodal length and fiber diameter in developing and regenerating nerves," *J. Anat.*, vol. 82, pp. 110–134, 1948.

[17] A. van Rotterdam, "A discrete formulation for the computation of extracellular potentials," *Kybernetik*, vol. 12, pp. 223–228, 1973.

[18] L. H. Hyman, *Comparative Vertebrate Anatomy*. Chicago, IL: University of Chicago Press, 1943.

Byron K. Lichtenberg received the B.S. degree from Brown University, Providence, RI, the M.S. degree from the Massachusetts Institute of Technology, Cambridge, and expects to complete the Ph.D. degree at the Massachusetts Institute of Technology, in 1979.

He served in the USAF for four years as a Fighter Pilot, during which time he completed a tour in Southeast Asia. His master's thesis investigated some basic neurophysiology with applicability to prothesis control. His Ph.D. dissertation is involved with ground-based experiments as a part of an overall series of vestibular experiments which have been accepted for the Spacelab I shuttle mission planned for 1981. He is currently a Payload Specialist crew member training for the Spacelab I flight.



Carlo J. De Luca (S'64–M'70–SM'77) was born in Italy in 1943. He received the B.A.Sc. degree in electrical engineering from the University of British Columbia, Vancouver, Canada, in 1966, the M.Sc. degree in electrical engineering from the University of New Brunswick, Fredericton, Canada, in 1968, and the Ph.D. degree in biomedical engineering from Queen's University, Kingston, Canada, in 1972.

He currently holds the following appointments: Research Associate in Orthopaedic Surgery at Children's Hospital Medical Center, Boston, MA; Associate in Orthopaedic Surgery (Anatomy) at Harvard Medical School, Cambridge, MA; Adjunct Associate Professor at Boston University, Boston, MA; Project Director, Liberty Mutual Insurance Company Research Center, Boston, MA; Lecturer at Massachusetts Institute of Technology, Cambridge; and Research Member at Harvard–MIT Division of Health Science and Technology, Cambridge. His research interests are in the areas of detection, analysis and applications of myoelectric and neuroelectric signal. He is the author of approximately 40 scientific publications in these areas.