

Position-Selective Activation of Peripheral Nerve Fibers with a Cuff Electrode

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Abstract—The degree of spatial selectivity which can be obtained with longitudinal dot tripoles in an insulating cuff was quantified in terms of the overlap between fiber populations activated by different tripoles. Previous studies have failed to take into account the relative influences of transverse current and longitudinal current on position-selective activation, and furthermore have not controlled for the differing sensitivities of large and small nerve fibers to electrical stimuli. In this study, these factors were taken into account. Transverse current from an anode positioned opposite the stimulating cathode was found to improve spatial selectivity, and selectivity was enhanced when the ratio of transverse current to longitudinal current was increased. Large fibers were excited before small fibers, irrespective of fiber position, indicating a combination of position and size selectivity.

I. INTRODUCTION

POSITION-SELECTIVE activation of nerve fibers within a nerve or nerve bundle is of interest in functional electrical stimulation (FES) for several reasons. It may be desirable to selectively activate fascicles which innervate different muscles in order to control motor functions. If a nerve innervates a single muscle, position-selective stimulation can be used to activate several subsets of fibers within the nerve in a cyclical manner, thereby maintaining a desired overall stimulus frequency while reducing the stimulation frequency (and thus fatigue) for each subset of fibers [4], [6], [7]. It is possible to produce position-selective stimulation with extraneural “dot” electrodes in an insulating cuff. Recent simulations [1], [8] and experimental work [3], [8], [9] indicate that spatial selectivity with this type of electrode can be improved by providing a transverse current from an anode opposite the stimulating cathode (thus favoring activation of fibers close to the cathode). This technique has been assessed experimentally by measuring the force recruitment of muscles innervated by different fascicles of the stimulated nerve. Various combinations of transverse and longitudinal current result in differential activation of muscles innervated by different fascicles [3], [9]. However, the relative influences of transverse and longitudinal current on muscle recruitment is not clear. Furthermore, because the different muscles may not be innervated by fibers of the same diameters,

the experimental results do not allow a distinction to be made between differences in recruitment due to fiber position and differences due to fiber diameter (i.e., preferential activation of larger fibers).

We investigated the nerve recruitment properties of stimulation with a cuff electrode containing a longitudinal dot tripole plus transverse anode, by measuring the compound action potential (CAP) from the stimulated nerve. With this recording technique it is possible to differentiate between the activity of large and small nerve fibers, so that size and position selectivity can be distinguished. Position selectivity was quantified in terms of the overlap between nerve fiber populations activated by different tripoles, by measuring the decrease in neural response when one population was activated during the refractory period of the other population, similar to the approach described by Rutten *et al.* [5] and Yoshida and Horch [10].

II. METHODS

Experiments were performed on six New Zealand white rabbits weighing 2.5 to 3.5 kg. Anesthesia was induced with hypnorm and maintained with a mixture of O₂ and N₂O (1:2) and 1.5–2.5% isoflurane. Measurements were made in only the left tibial nerve in two of the experiments, and in both the left and right tibial nerves in the other four experiments. An incision was made on the lateral side of the hind leg and the sciatic nerve was exposed. The peroneal and tibial branches were separated and the tibial branch was bound proximally. An oil pool was formed in the upper leg and a bipolar hook electrode was positioned for recording CAP's from the tibial nerve. Neural signals were differentially amplified (gain 6000) and filtered (50-Hz notch filter and a bandpass filter with cutoff frequencies of 75 Hz and 12 kHz) and digitized at 51.2 kHz. Several centimeters of the tibial nerve were exposed at the ankle, for placement of the stimulating cuff electrode. The incision at the ankle was closed after electrode implantation to maintain a moist environment around the nerve and stimulating electrode. The stimulating electrode is illustrated in Fig. 1. It consisted of a cylindrical, 1.25-mm inner diameter silicone rubber cuff in which 12 platinum contacts were arranged in four longitudinal tripoles. A longitudinal slit in the cuff allowed the electrode to be fit around the nerve, while a rubber flap over the slit improved the closure. Contacts had a length of 1.0 mm and were spaced 3 mm apart (edge to edge) in the longitudinal direction, and were 0.5-mm wide and spaced 0.48 mm apart about the circumference of the cuff. In each tripole, the central contact served as a cathode, and the

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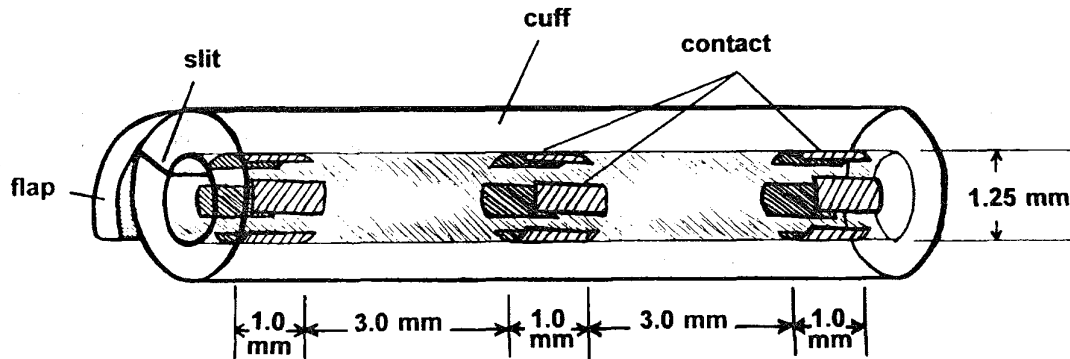


Fig. 1. Stimulating electrode.

outer two contacts served as anodes. This tripolar arrangement minimized the flow of current outside the insulating cuff. The contact opposite the central cathode of the tripole (i.e., the cathode of the opposite tripole) was used as an anode for passing transverse current. The sum of the anodal currents balanced the cathodal current. In general, equal currents were passed through the two outer anodes; however, if necessary the balance of current between the two anodes was adjusted to prevent the formation of a virtual cathode (which caused excitation that could be detected as an early peak in the CAP). A ground electrode was placed in a muscle, distant from the stimulation site. Stimuli consisted of 100 μ s rectangular current pulses with a 100 μ s exponentially decaying tail, generated by an HP 3245A Universal Source.

The excitation threshold was determined for each tripole (with or without a transverse anode). The current was then increased until the first peak of the CAP, which corresponds to the population of large, easily activated fibers, had reached its maximum. The rabbit tibial nerve contains fibers of up to 15 μ m in diameter; the distribution is bimodal, one peak ranging from about 2 to 6 μ m with a maximum at 3.5 μ m, and the other from about 6 to 15 μ m with a maximum at 9 μ m (R. Hoekema, personal communication). The first peak of the CAP presumably corresponds to fibers in the 6–15- μ m range. Two tripoles positioned on opposite sides of the cuff were selected (referred to as tripole 1 and tripole 2), and a stimulus pulse sufficient to produce a response amplitude of about 75% of the maximum response was delivered, first with tripole 1 and then with tripole 2. The second pulse was given after a delay which varied between 200 and 1000 μ s, and the interval at which the response to the second stimulus was smallest (i.e., at which the nerve was most refractory) was identified. The stimulation protocol shown in Table I was delivered using various current pulse amplitudes between the excitation threshold and the amplitude which produced the maximum large-fiber response. To ensure that the CAP's produced by the two tripoles were of similar amplitudes, the amplitudes of the current pulses delivered with tripole 1 and tripole 2 were held at a constant ratio equal to the ratio of the excitation thresholds for the two tripoles (these were typically similar, but not identical). The 16 responses to each stimulus level were averaged. The protocol was carried out with transverse currents of 0, 40, and 70% of the cathodal current. Due to the amount of time required,

TABLE I
STIMULATION PROTOCOL

	Tripole 1	Tripole 2
(1)	16 pulses at 1/s	—
(2)	—	16 pulses at 1/s
(3)	16 pulses at 1/s	16 pulses at 1/s, with pulse delivered to Tripole 2 during refractory period for fiber activated by Tripole 1
(4)	16 pulses at 1/s	—
(5)	—	16 pulses at 1/s

Channel 2 stimulus amplitude = (Channel 1 stimulus amplitude) \times (Channel 2 Threshold/Channel 1 Threshold).

the protocol was not carried out with all transverse current levels in each nerve. A 0% transverse current was used with 13 different tripoles, a 40% transverse current was used with 11 tripoles, and a 70% transverse current was used with 10 tripoles.

Sample responses from one of the experiments are shown in Fig. 2. The response produced by the second tripole during the refractory period of the first tripole [Fig. 2(d)] was determined by subtracting the response to the first tripole activated alone [Fig. 2(a)] from the response produced by the two tripoles activated in sequence [Fig. 2(c)]. The peak-to-peak amplitude of each response was determined, and further analysis was performed on this amplitude measure. In order to enable comparison and averaging of the results of all experiments, the stimulus currents were normalized to the threshold current in each experiment, while the responses were normalized to the maximum response. In order to average the normalized recruitment curves from different experiments, data points at uniformly spaced multiples of the excitation threshold were determined by linear interpolation from the experimental data (which were not at the same multiples of the excitation threshold for all experiments).

III. RESULTS

The responses to the same stimuli given at the beginning and at the end of the protocol were the same, indicating that the responses were stable over time, i.e., the nerve fibers did not accommodate or fatigue during stimulation. This does not, of course, imply that the muscle response would also

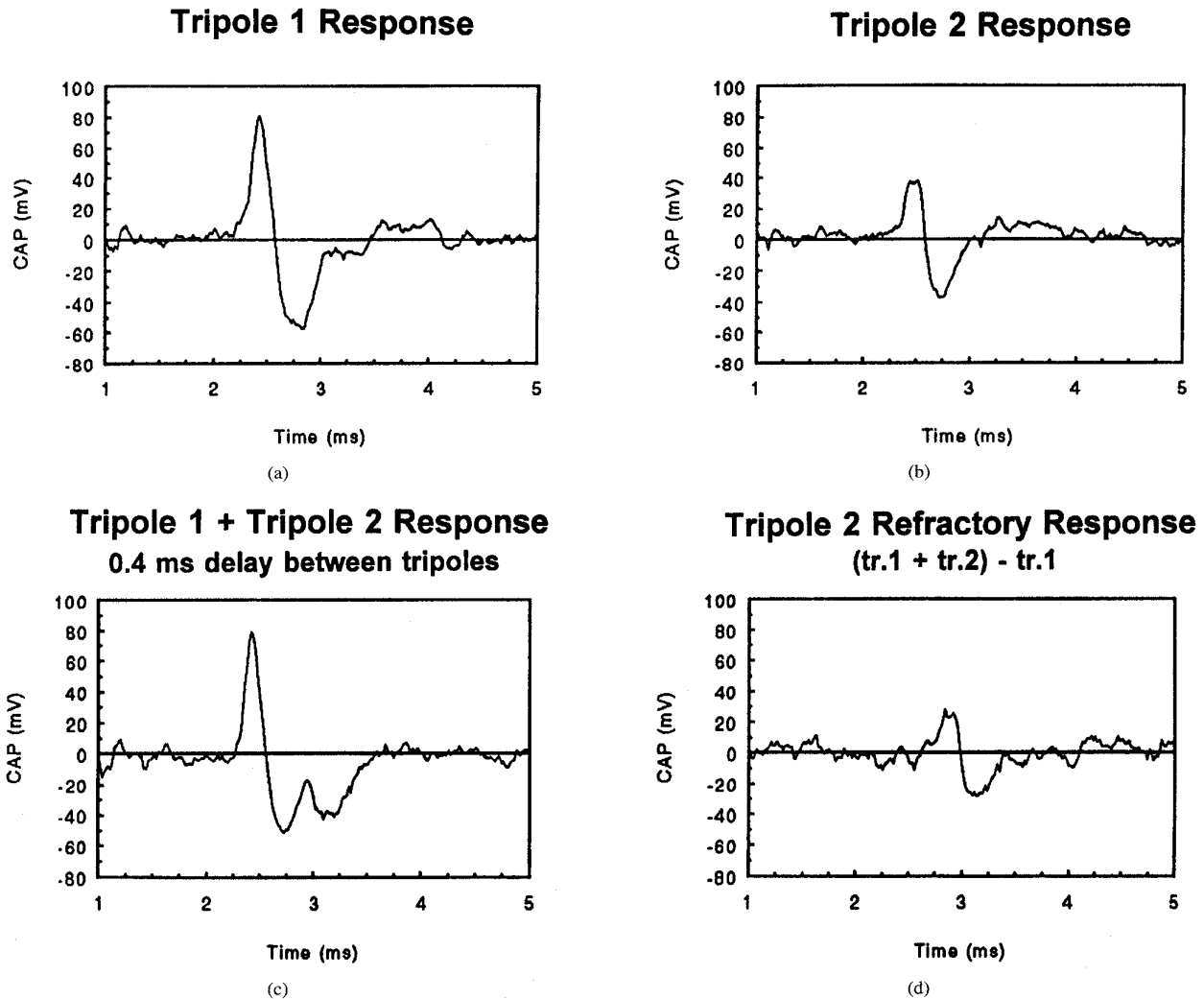


Fig. 2. Compound action potentials produced by stimulation with (a) tripole 1, (b) tripole 2, (c) tripole 1 followed by tripole 2 after a delay of 400 μ s, and (d) the response to stimulation with tripole 2 during the refractory period of tripole 1, calculated by subtracting the trace in (a) from the trace in (c). A transverse current of 40% was used. The stimulus pulses were 65 μ A and 97.5 μ A through tripoles 1 and 2, respectively (1.6 times the corresponding excitation thresholds).

have remained stable (the stimulus rate of one pulse per second would most likely have produced fatigue in the muscle fibers); however, the goal of the present study was to evaluate neural response, and muscle response was not measured. The maximum large fiber response was reached when the stimulus amplitude was three to four times the excitation threshold. The small fiber response typically began to appear after the larger fiber response had reached its maximum, but we limited our investigation to the large fiber response, since we were primarily interested in investigating spatial selectivity of fibers of similar diameters. The maximum large fiber responses produced by the two tripoles were typically the same, indicating that the maximum response represented activation of all large fibers in the nerve.

The interval at which the nerve was most refractory varied somewhat among experiments but was always between 400 and 750 μ s, which is consistent with the values reported by Rutten *et al.* [5] and Yoshida and Horch [10]. The amplitude of the response to stimulation with one tripole increased

gradually as the stimulus was increased, and levelled out at the maximum response, as shown in the Fig. 3. When a stimulus was delivered with one tripole during the refractory period induced by the other tripole, the response amplitude initially increased as the stimulus amplitude was increased, but began to decrease after the stimulus exceeded some level, eventually returning to zero (lower curve, Fig. 3). The recruitment curve for the tripole activated first was unaffected, so the decrease in the response to the stimulus delivered during the refractory period was presumably due to overlap of the populations of fibers activated by the two tripoles. The recruitment curves thus began to differ when the areas of the nerve activated by the two tripoles began to overlap.

The mean current and percent activation (i.e., percentage of maximal response) at which overlap began for transverse currents of 0, 40, and 70% of the cathodal current are shown in Table II. Also shown are mean excitation thresholds for each transverse current level. The largest fibers in the nerve were excited first, so excitation thresholds for the nerve corresponded

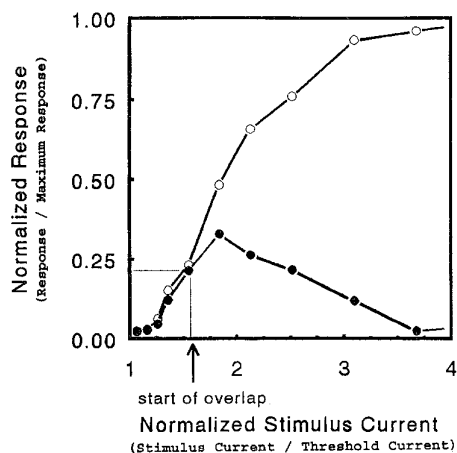


Fig. 3. Nerve recruitment curves. The upper curve was obtained from stimulation with one tripole (with 40% transverse current). The lower curve was obtained when each stimulus was preceded (by 400 μ s) by a stimulus of comparable amplitude from a tripole on the opposite side of the nerve. An arrow indicates the stimulus amplitude at which the fiber populations activated by the two tripoles begin to overlap. Stimulus current is normalized with respect to the excitation threshold and response amplitude is normalized with respect to the maximum response of the nerve.

to large fiber excitation thresholds. The 40% transverse current produced a statistically significant increase in the current and percent activation at which overlap began compared to the case where 0% transverse current was used. The 70% transverse current produced a significant increase in percent activation and current at which overlap began compared to both 0% and 40% transverse currents. Significance was determined using a single-ended Student's *T* test. *p* values are shown in Table II. The amplitude of the second response continued to increase with increasing current even after the start of overlap, presumably for as long as additional large fibers lying outside the area activated by the first tripole were recruited. Average recruitment curves are shown in Fig. 4. The normal (nonrefractory) 40% recruitment curve was significantly lower than the normal 0% recruitment curve, with $p \leq 0.005$, between normalized stimulus current levels of 1.75 and 3.0 (Student's *T*-test). The normal 70% recruitment curve was significantly lower than the normal 0% recruitment curve, with $p \leq 0.005$, between normalized stimulus current levels of 1.5 and 3.25. The 40% and 70% curves differed significantly only between stimulus current levels of 2.0 and 2.5 ($p \leq 0.1$). The refractory recruitment curves differed somewhat as a function of transverse current. For the 0% refractory curve versus the 40% refractory curve, $p \leq 0.1$ from 2.0 to 4.0; for the 0% curve versus the 70%, $p \leq 0.01$ from 1.75 to 4.0; and for the 40% curve versus the 70% curve, $p \leq 0.1$ from 1.75 to 3.75, except at 2.25 where the difference is not significant. These differences presumably reflect the fact that the percent transverse current alters the shape of not only the area recruited by the first stimulus, but as a consequence also the shape of the area recruited during refractory stimulation.

A selectivity index (defined as the ratio of the response produced by stimulation with the second tripole during the refractory period of the first, to the response produced by stimulation with the second tripole alone) is plotted as a

function of normalized stimulus current in Fig. 5. A selectivity index of one indicates that the fiber populations activated by the two tripoles are distinct, while a smaller value indicates an overlap between the populations. A selectivity index greater than one was obtained at low stimulus levels (at and slightly above the excitation threshold), indicating that the refractory response was greater than the normal response at that stimulus level. This was presumably due to a few fibers which were not activated by the first stimulus, but which were sufficiently depolarized that they were activated by the second stimulus. The selectivity index obtained with a 40% transverse current was significantly higher than the selectivity index obtained with a 0% transverse current for normalized stimulus currents of 1.5 and above ($p \leq 0.05$ from 1.5 to 2.0, $p \leq 0.001$ from 2.25 to 4.0; Student's *T*-test). The selectivity index obtained with a 70% transverse current was significantly higher than the selectivity index obtained with a 0% transverse current for normalized stimulus currents of 1.25 and above ($p \leq 0.005$ at 1.25, $p \leq 0.0005$ from 1.5 to 4.0). The selectivity index obtained with a 70% transverse current was significantly higher than the selectivity index obtained with a 40% transverse current for normalized stimulus currents of 1.0 and above ($p \leq 0.05$, except at 2.75 through 3.25, where $p \leq 0.1$). The average increase in selectivity index obtained with a 40% transverse current was 0.25 ± 0.08 ; with a 70% transverse current an average increase of 0.45 ± 0.04 (averaged over normalized stimulus currents of 1.25 to 4.0; $n = 12$) as compared to 0%.

IV. DISCUSSION

We have shown that transverse current changes the recruitment pattern obtained during stimulation with tripolar cuff electrodes. With increasing transverse current, the slope of the normalized recruitment curve decreased, while the normalized percent activation at which fiber populations activated by separate tripoles began to overlap increased. Transverse current increased the selectivity index over a wide range of stimulus amplitudes, not only raising the (normalized) stimulus level at which the index became less than one, but also causing the index to decrease more slowly as more fibers were recruited.

When a tripole was used without transverse current, overlap began when only 10% of the nerve was activated. The most plausible explanation for overlap occurring at this seemingly low activation level is that each tripole activates fibers around the periphery of the nerve (a layer of Ringer's solution between the nerve and the cuff could allow current to spread around the nerve). When transverse current is used, fibers near the transverse anode would be hyperpolarized, and fibers closer to the cathode would be depolarized and activated. Simulations performed by Chintalacheruvu *et al.* support this hypothesis; they show that if no transverse current is used, fibers tend to be recruited around the periphery of the nerve, while with a transverse current, fibers are recruited primarily on the side of the nerve closest to the cathode [1]. If fibers are excited closer to the cathode, there will be less overlap between the fiber groups activated by different cathodes. This presumably accounts for our finding that as we increase the ratio of

TABLE II
CURRENT AND ACTIVATION LEVELS AT WHICH OVERLAP BEGIN

	0% Transverse Current*		40% Transverse Current*		70% Transverse Current*	
Threshold (μ A)	68		95		173	
	normalized current**	percent activation***	normalized current**	percent activation***	normalized current**	percent activation***
mean	1.18	10.0	1.53	20.7	1.77	37.5
s.d.	0.14	6.6	0.38	16.7	0.44	20.9
n	13	13	11	11	10	10
significance	a, b	d, e	a, c	d, f	b, c	e, f

*Percent transverse current = (transverse current) \times 100/(cathodal current)
 **normalized current = (current at which overlap begins)/(excitation threshold)
 ***percent activation = percent of maximal response at which overlap begins
 Values labeled with the same letter (in the row labeled significance) are significantly different with the following p values:
 a, b, e: $p < 0.005$
 d, f: $p < 0.05$
 c: $p < 0.2$
 Student's T-test, single-ended.

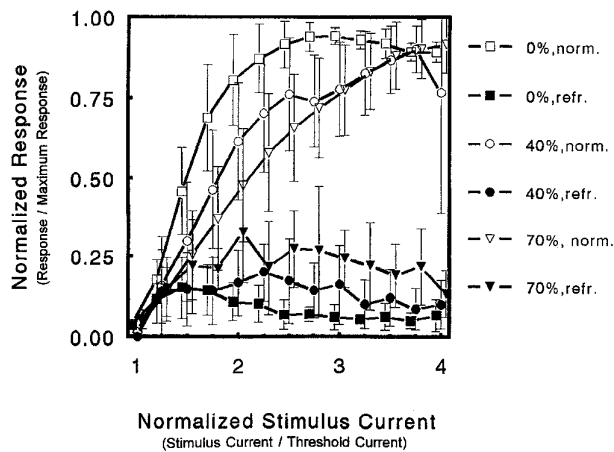


Fig. 4. Normalized, averaged recruitment curves obtained by independent stimulation (upper curve) and stimulation during the refractory period of an opposing tripole (lower curve). Transverse currents of 0%, 40%, and 70% were used. Error bars indicate standard deviation.

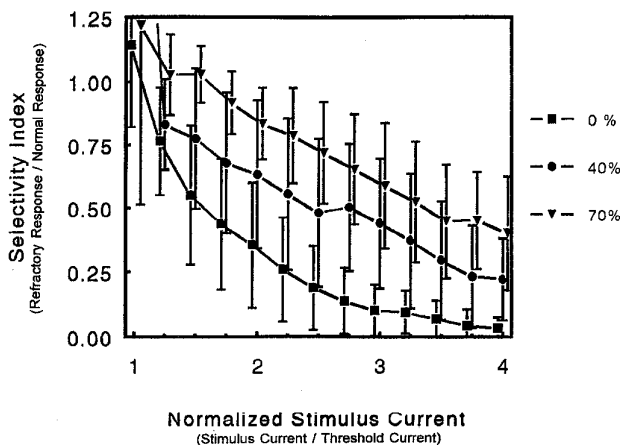


Fig. 5. Selectivity index (for definition see text) for 0%, 40%, and 70% transverse current plotted versus normalized stimulus current. A selectivity index of less than one indicates overlap between fiber populations activated by different tripoles. Error bars indicate standard deviation.

transverse current to cathodal current, the percent activation at which overlap begins also increases. Furthermore, as the proportion of anodal current flowing through the transverse anode is increased, fibers closer to the transverse anode are relatively more difficult to activate, due to the hyperpolarizing effect of the anode; this presumably explains the decrease in the slope of the normalized recruitment curve with larger transverse currents.

In our experiments, the transverse current was a fixed percentage of the cathodal current, and therefore, the shape of the potential field should have remained constant, with changes in current level simply producing a linear scaling of the potential field. In contrast, in other experimental work in this area, no fixed relationship was maintained between transverse and longitudinal current. Sweeney *et al.* used a constant transverse current and varied the longitudinal current [8], while Veraart *et al.* varied both transverse and longitudinal currents, but constructed recruitment curves using whichever current combination gave optimal selectivity at each force level, in a given experiment [9]. Like these authors, we conclude that the use of a transverse current improves spatial selectivity; however, the differences in experimental approach preclude more extensive comparison. We considered the use of a tripolar electrode arrangement plus a transverse anode within an insulating cuff. If the same contact configuration was used without an insulating cuff, a number of differences from our results could be expected. First of all, larger stimulus currents would have to be used to activate the nerve fibers, since a larger percentage of the current would flow to the surrounding tissue. Moreover, the electrical field around the nerve would be influenced by external electrical field fluctuations caused by, e.g., muscle contractions, and thus less readily controlled. The general effect of a transverse current would presumably be similar, that is, fibers would be excited closer to the cathode. However, from our results it is not possible to draw more specific conclusions about the use of transverse anodal current in the absence of an insulating cuff.

It appears that position selectivity is optimized when the transverse current is a high proportion of the total current; accordingly, maximum spatial selective stimulation would be

obtained by completely eliminating the anodes on either side of the cathode. Such an electrode design would, of course, preclude the use of anodal block to achieve size-selective activation. Furthermore, excitation thresholds would increase, which might be a drawback in implantable devices in which power consumption must be minimized.

All the large fibers in the nerve were activated before a detectable number of the small fibers were activated. Thus, it was possible to obtain position-selective stimulation of fibers between about 6- and 15- μm diameter. If the entire range of fiber diameters was considered, the larger fibers were more easily excited than the smaller fibers regardless of their locations, so that stimulation was diameter as well as position selective. It should be noted that selective activation of small fibers by anodal blocking of larger fibers, as described by Fang and Mortimer [2], is unlikely to occur, since currents at the outer anodes are relatively low.

V. CONCLUSION

The degree of spatial selectivity which we obtained with dot tripoles in an insulating cuff, with the use of a transverse current, should be useful for application in "carousel" stimulation (i.e., sequential activation of electrodes placed around the circumference of a nerve) for reducing fatigue in a homogenous group of nerve fibers. Spatial selectivity was improved by the use of a transverse current. For selectively activating particular fascicles in a nerve, in order to control the function of different muscles, it appears that this approach would provide relatively coarse control. A particular concern in applying this approach to activating different muscles is that the size distribution of the nerve fibers innervating the different muscles must be taken into account; we found that all large fibers in the nerve were activated before a significant number of the small fibers, so that position-selective stimulation would not be effective for activating a muscle innervated by small fibers. On the other hand, it could be useful to select between two muscles innervated by fibers in the same diameter range.

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