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EFFICIENCY OF ENDONEURAL STIMULATION WITH 5- TO 24-FOLD MULTIELECTRODES

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Abstract – Optimal selective stimulation of nerve with endoneurally (intrafascicularly) inserted multi-micro-electrodes means that each electrode activates, with its own threshold stimulation current, as few distinct motoneurons as possible, preferibly only one. If the latter is the case, the efficiency of a multi electrode is 100%. However, neighbouring electrodes may control the same motor fiber(s), as there are generally more fibers than electrodes and because the position of fibers is largely unknown. In that case, efficiency is less than 100%.

This paper reports on experiments in rat peroneal nerve with 5- and 24-fold wire multi micro electrode arrays. The threshold force of the twitch recruitment curve of the corresponding EDL muscle was used to monitor nerve activation. It was found that on average the threshold force efficiency was 0.48 = 48 %. After re-inspection of the data, taking into account that neighbouring electrodes have a higher probability to activate the same motor units, in contrast to distant electrodes, the average efficiency even rises to 81 %.

For several reasons, threshold forces do not correspond to motor unit forces, implying that the threshold-force-efficiency can not be regarded as motor-unit-efficiency.

INTRODUCTION

In artificial electrical stimulation, if selective contact of one-electrode-with-one-fiber is to be obtained, one has to bring an electrode close to one of the nodes of Ranvier of a fiber. This can only be achieved, in a 'random' population of fibers, if one uses a sufficiently redundant number of electrodes in the nerve.

For example, the peroneal nerve of the rat controls four muscles. One of these is the Extensor Digitorum Longus (EDL) muscle, with about 70 motor units [11]. Assuming a random topology for the position of the EDL motor fibers in the fascicle, and with realistic dimensions for fiber and nerve fascicle, one calculates that for the selective control of 10-20 fibers a number of 128 electrodes will be sufficient. For sufficient redundancy, control of all 70 fibers would then imply the need for a multiple of 128 electrodes.

In practice, a multi-micro-electrode with hundreds of electrodes would be difficult to produce, even with microfabrication technology [1,2,3,4,5].

To get insight into the selectivity that can be obtained with existing micro electrode arrays, experiments with 5- and 24-fold wire-arrays were performed in rat peroneal nerve. (Earlier we have compared these array data with single wire electrode data, showing that much of the recruitment data of both methods compare favourably well [10]).

Selectivity can best be studied by evaluation of the overlap of the stimulus space of a particular electrode by that of its neighbours, as a function of stimulus level [5]. However, this method is too time consuming in case of many electrodes. Therefore, we have measured the stimulated threshold force per electrode. If a neighbouring electrode has a different threshold force, one may assume that a different motoneuron has been adressed, or a different combination of a few motoneurons.

From the threshold force data one now derives the efficiency E of the multi electrode, i.e. the ratio of distinct threshold forces, adressed by the electrodes, and the total number of electrodes in the device.

$$\text{Efficiency} \qquad E = N_{\text{distinct thresholds}} / N_{\text{electrodes}}$$

METHODS

Acute experiments were conducted on male Wistar rats (3 - 8 months old, 300 - 500 g weight) maintained under sodium pentobarbital anesthesia. Both tendons of the extensor digitorum longus (EDL) muscle of the right hind leg were cut. To ensure isometric conditions the proximal tendon was mechanically fixed and the distal tendon connected to an isometric force transducer. The peroneal branch (which innervates the EDL muscle) of the exposed sciatic nerve was prepared free. Care was taken to avoid water condensation on the nerve.

After positioning the animal, an Ag/AgCl reference electrode was inserted into the gastrocnemius muscle. A hook electrode was placed around the common peroneal nerve, and supramaximal stimuli were applied in order to determine the optimal twitch length (OTL, i.e. the length of the muscle where twitch force is maximal) and the initial maximum twitch-contraction force of the EDL muscle. The hook electrode was then removed.

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The common peroneal nerve was now placed on a support table and an incision was made using a pair of tweezers and an ophthalmic knife. The incision was directed along the longitudinal axis of the nerve and long enough to allow easy insertion of a wire multi electrode array (WMEA). Push-out of the endoneurium was observed in approximately 75 % of the incisions made. A one-dimensional 5-channel array and a two-dimensional 24-channel array were used, consisting of 5 rows of 1 electrode and 6 rows of 4 electrodes, respectively. The individual electrodes in the arrays were 25 µm-diameter NiCr wires insulated with a 4 µm Karma coating (California Fine Wire Co., Grover City, CA). Only the tip (obliquely cut, see Figure 1) was uninsulated, resulting in an effective electrode area of about 2800 μm^2 and electrode impedance of about 1 MΩ at 1 kHz. Interelectrode spacing was 120 µm.

After insertion into the nerve, the WMEA was allowed to settle for approximately 30 minutes. Then, rectangular depolarizing current pulses of 100 µs duration were generated by a home-built, computer-controlled stimulator. For each electrode in the array a series of stimuli was applied with amplitudes increasing from subthreshold to supramaximal. Stimulus current step size was 0.1 µA or 0.2 µA; maximum stimulus current varied from 30 µA to 100 µA. Stimulus repetition rate was 1 Hz (this low rate avoids fatigue effects). The elicited twitch-contraction forces were measured, one for each stimulus amplitude. Recruitment curves were constructed off-line by determining the peak values of the series of twitch forces.

Twitch forces were measured using a Model 373 Isometric Force Transducer (Harvard Apparatus Company, Inc., Millis, MA). The sensitivity of this transducer is 2 mV/mN over a range of 4.9 - 1078 mN; accuracy is 1.25 mN. The force signal was amplified two times and filtered (0 - 500 Hz, 50 Hz notch), and then sampled at 2 kHz. The overall resolution of the force measurement system was 0.31 mN/bit.

At the end of the experiment, the electrode array was carefully removed from the nerve and the quality of insertion visually assessed. We generally found that the electrode array was firmly attached to the nerve and the electrodes were clearly positioned inside the fascicle. In approximately 17 % of the cases, however, the array had not been inserted properly and the electrodes had not entered the fascicle. These experiments were excluded from further analysis. A total of eight experiments remained.

Figures 1, 2 and 3 show the 24-electrode device, the positioning and numbering of electrodes in the fascicle and a sample of 4 out of 24 recruitment curves of one experiment. The lowest force on each curve is the threshold force.

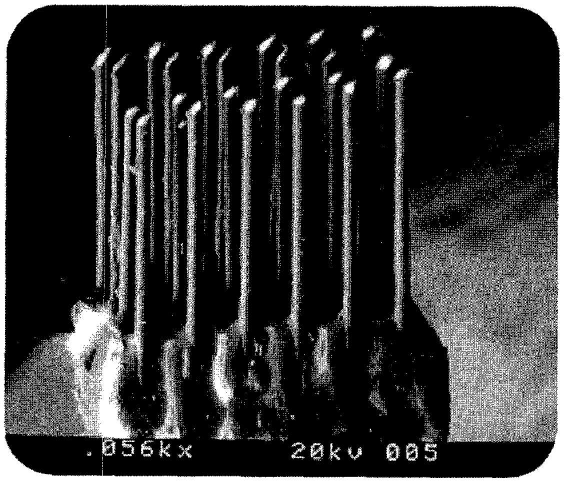


Figure 1. Two dimensional wire multi micro electrode array, consisting of 24 wires, insulated except at the tip, interdistance 120 micrometer.

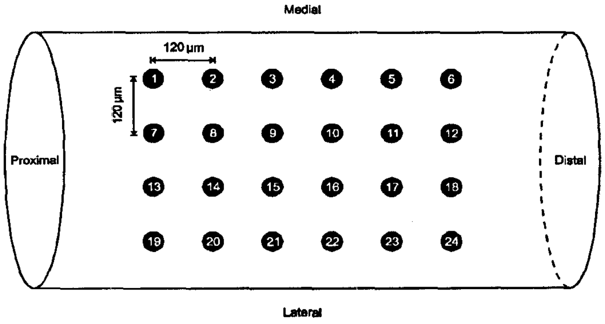
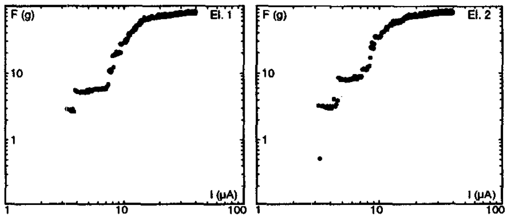


Figure 2. Sketch showing how a 6×4 two-dimensional electrode array, (electrodes are numbered 1 to 6 on the upper row etc. until no. 24 right below), is inserted into the nerve fascicle. The electrodes are separated from each other by 120 µm. Fascicle diameter is 500 µm.



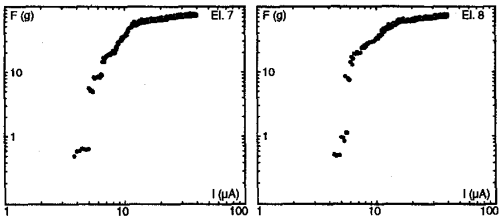


Figure 3. Twitch force recruitment curves of rat EDL muscle stimulated by a 24-fold 2D electrode array, electrode spacing is 120 μm. Scales are log-log. Vertical scale ranges from 0.1 to 100 grams, horizontal from 1 to 100 μA. Only 4 curves of a 24-fold WMEA experiment are shown. See [6,7,8,9] for more detail.

RESULTS

Table 1 shows the threshold currents and forces for one of the experiments, with a 24-fold WMEA. Threshold forces have been grouped in 2.5 mN wide bins, starting at the 5.0 +/- 1.25 mN bin. Bin width and start-bin values follow from the accuracy and threshold of the force transducer, 1.25 mN and 4.9 mN respectively (see methods section). In this experiment 11 distinct threshold forces have been measured, resulting in an efficiency

$$E = 11/24 = 0.46 = 46\ \%.$$

However, closer inspection of these data yields a higher efficiency, called E'. For example, analysis of the first bin in Table 1 reveals three longitudinally neighboring electrode pairs (viz. electrodes 4-5, 7-8, and 15-16). The third bin contains one such pair (viz. electrodes 9-10). This suggests that these bins may actually contain four (7-3) and two (3-1) (small groups of) motor units, respectively, thereby increasing the efficiency E for this particular experiment from the previously calculated 11/24 = 0.46 to

$$E' = 20/24 = 0.83 = 83\ \%.$$

Table 1. Threshold forces and associated threshold currents for experiment g (cf. Table 2). The electrodes are ordered according to increasing threshold forces. Forcces are classified into 2.5 mN-wide bins as imposed by force-transducer accuracy. Efficiency = 11/24 = 0.46; After re-analysis, see text, efficiency E' = 20/24 = 0.83.

Bin limits (mN)	Electrode no.	Threshold current (μA)	Threshold force (mN)
5.0 ± 1.25	5	6.0	5.024
	7	3.8	5.024
	8	4.4	5.204
	15	4.0	5.383
	4	5.5	5.623
	23	7.2	5.742
	16	6.0	5.981
7.5 ± 1.25	12	4.7	7.417
	17	5.6	7.537
	24	10.8	7.656
	20	4.2	8.015
	3	4.7	8.494
12.5 ± 1.25	10	7.2	11.960
	19	5.6	12.140
	9	4.1	12.260
15.0 ± 1.25	11	2.5	14.000
	18	3.6	16.030
25.0 ± 1.25	22	4.5	24.580
27.5 ± 1.25	21	5.1	27.570
30.0 ± 1.25	1	3.3	29.130
32.5 ± 1.25	2	3.2	32.360
37.5 ± 1.25	13	4.9	38.700
50.0 ± 1.25	14	3.7	50.360
52.5 ± 1.25	6	7.7	52.400

Table 2 summarizes the efficiencies E and E' for the total set of 8 experiments. On average the efficiency E = 48%, rising to E' = 81% after a re-analysis of the data.

Table 2. Summary of efficiencies E and E' in all eight experiments. Number of electrodes : N_{el}.

Experiment	E	E'	N_{el}
a	0.80	1	5
b	0.40	0.80	5
c	0.60	0.80	5
d	0.42	0.79	24
e	0.50	0.88	8
f	0.47	0.71	17
g	0.46	0.83	24
h	0.21	0.64	14
Average	0.48	0.81	

DISCUSSION

The lowest force that could be measured by the force transducer was 4.9 mN (0.5 gram). However, motor unit forces in the EDL muscle can be as low as 0.1 gram, implying that we 'missed' the smallest motor unit forces. Therefore, we are not able to express our force thresholds in terms of motor units (single ones or combinations). Nevertheless, considering the maximum force of the EDL, about 90 grams, and the reported number and distribution of motor units in this muscle, 69 +/- 11 [11], the lower limit of 0.5 gram is still very acceptable [10].

The efficiency of a multi electrode should not be taken as the only absolute measure for successful array performance. It should always be considered together with the number of electrodes in the array, the statistical distribution of position of fibers in the fascicle and the specific use of the array for muscle control. For example, the 5-electrode arrays in table 2 score about as well as the 24-fold arrays and this should not be misinterpreted. The absolute number of distinctly adressed threshold forces is very different in both cases ! The efficiency being about equal in both groups simply means that the interelectrode spacing is equal. The number of 5, 8, 17 or 24 electrodes still undersamples the distribution of fibers in the fascicle: the arrays are away from being redundant.

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