Fascicular Selectivity in Transverse Stimulation with a Nerve Cuff Electrode: A Theoretical Approach

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▪ **ABSTRACT**

The performance of cathode-anode configurations in a cuff electrode to stimulate a single fascicle in a nerve trunk has been investigated theoretically. A three-dimensional volume conductor model of a nerve trunk with four fascicles in a cuff electrode and a model of myelinated nerve fiber stimulation were used to calculate the recruitment of 15 μm fibers in each fascicle. The effect of a monopole, a transverse bipole (anode opposite the cathode), and a narrow transverse tripole (guarded cathode) in selectively stimulating 15 μm fibers in each fascicle has been quantified and presented as recruitment curves. It is predicted that selective fascicle stimulation is advanced most by stimulation with a bipole in a plane perpendicular to the axis of the nerve trunk. Monopoles and conventional longitudinal tripoles perform less well, as does a longitudinal tripole with an additional "steering" anode. Apart from transverse bipolar stimulation an additional anode may be used to maximally fit the area of excitation to the topography of the fascicle to be recruited. As compared to monopolar and longitudinal tripolar stimulation, the slope of the recruitment curves in transverse bipolar stimulation is reduced considerably, thus allowing improved fine tuning of nerve (and thus force) recruitment. Another advantage of this method is a minimal number of cable connections to the cuff electrode. The cost of the improved selectivity is an increased stimulation current. ▪

KEY WORDS: computer modeling, multifascicular nerve, nerve stimulation, nerve cuff electrode, spatial selectivity.

INTRODUCTION

An important aspect of neuroprosthetic implants for motor control is the possibility to activate any specific muscle by peripheral nerve stimulation. This generally requires the stimulation of a single fascicle in a nerve trunk without stimulating other fascicles (1,2). Although electrically induced stimulation can be achieved with a variety of electrode types (3,4), stimulation with a nerve cuff electrode with multiple contacts is of particular relevance for the (spatially) selective activation of a nerve fascicle. These cuff electrodes should fit snugly around the nerve, as spiral nerve cuffs do (5).

Stimulation pulses were initially applied by longitudinal tripoles (central cathode with an anode

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Neuromodulation, Volume 6, Number 4, 2003 258–269

on either side) because it was believed that this configuration would confine fiber recruitment mainly to the nerve region on the side of the active tripole. The additional application of an anodal "steering" current by a contact located opposite the cathode has been shown to substantially improve the spatial selectivity (6–11). Although somewhat different experimental methods were used (Grill and Mortimer (7) and Sweeney et al. (9,10) used a transverse "steering" current with constant amplitude, Goodall et al. (11) used a fixed percentage of the cathodal current as the transverse current, and Veraart et al. (6) varied both the amplitudes and the ratio of the longitudinal and transverse currents), all studies led to the conclusion that increasing the transverse current component improves fascicle selectivity. It was also shown that a spiral nerve cuff with four longitudinal tripoles can selectively activate individual fascicles of a nerve trunk with any arbitrary position of the contacts with respect to the fascicles (6–8).

To analyze which aspects of the cathode-anode configurations used in these empirical studies are most relevant to secure a high fascicle selectivity we previously simulated various simple configurations by a computer model, representing a cuff electrode around a nerve trunk consisting of a single fascicle (12). In the study presented here we investigated whether the conclusions from this previous study would hold for a more realistic model as well. This model has a nerve trunk consisting of four fascicles with epineural tissue in between and is based on the transverse geometry of a rabbit's sciatic nerve.

The empirical studies, in which longitudinal tripoles were used in combination with a "steering" anode (6,7,9–11), suggest that the transverse component of the anodal current advances spatial selectivity more than the longitudinal components. Because the sum of the anodal currents equaled the cathodal current, an increasing percentage of transverse current automatically reduced the percentage of longitudinal current and increased the spatial selectivity performance. The results of several modeling studies in which a cuff electrode was placed around a monofascicular nerve trunk, predicted that a monopole and a longitudinal tripole have similar selectivity performances (9,12,13). These results suggest that the effect of a longitudinal current component on spatial selectivity is marginal, as do the preliminary results of an experimental study on the cat sciatic nerve by Tarler and Mortimer (14). The modeling study by Chintalacharuvu et al. (13) suggests that the small difference in spatial selectivity obtained in monopolar and longitudinal tripolar stimulation is most likely due to the rather large distance between the cathode and the anodes (5 mm). Adding a transverse "steering" current to both a monopolar and a longitudinal tripolar model configuration resulted in a substantially improved spatial selectivity (9,12).

These results led us to the hypothesis that a transverse bipole (anode opposite the cathode) would provide a better selectivity than a longitudinal tripole with an additional "steering" anode. The selectivity performance of the two configurations was calculated in a monofascicular nerve trunk model (12). The results predict that the transverse bipole, actually providing a 100% "steering" current, gives a better spatial selectivity than a lower percentage of "steering" current complemented by a longitudinal current. On the analogy of spinal cord stimulation (15), the performance of a transverse (narrow) tripolar configuration (a cathode and the adjacent contacts in the transverse plane as anodes) was modeled as well. It was concluded that this configuration with anodal currents each being 50% of the cathodal current would provide an even better spatial selectivity than the transverse bipole (12).

In addition to the predicted superior spatial selectivity performance of these simple bipolar and tripolar configurations in a single transverse plane, a significant technical advantage of these configurations is the threefold reduction of the number of contacts and cables as compared to a set of (generally four) longitudinal tripoles. This combination of functional and technical advantages led us to investigate whether the favorable selectivity performance of transverse configurations as predicted for a monofascicular nerve trunk (12) would exist in a multifascicular nerve model as well. Although this study was focused on stimulation with monopoles, bipoles, and (narrow) tripoles, a few other transverse configurations have been modeled as well. In addition, the dependency of the spatial selectivity performance on the position of the contacts in relation to the position of the fascicles has been investigated.

In the study presented in this paper a cuff model with six contacts, equally spaced over its inner circumference, and a nerve trunk with four fascicles were used. It was assumed that nerve fibers of the same caliber are uniformly distributed within each fascicle and that the largest fibers have the same caliber (15 μm) in all fascicles. The analysis has therefore been restricted to the recruitment of 15 μm motor nerve fibers, because under these assumptions and under identical stimulation conditions the nerve region in which smaller fibers are recruited is always covered by a larger region of recruited 15 μm fibers (when the stimulus is submaximal) (12). Furthermore, all fibers had their central node of Ranvier in a plane centered at the cathode. Randomization of the nodal positions would result in an increased mean stimulation threshold, but will not change the recruited area significantly (12).

MATERIALS AND METHODS

The computer model used in this study consists of two parts: a three-dimensional volume conductor model of a nerve containing four fascicles and surrounded by a cuff electrode and a model of a myelinated nerve fiber. In the volume conductor model, a numerical method was used to solve the steady state potential distribution resulting from stimulation by a particular anode-cathode configuration. Subsequently, this potential distribution was applied to the nerve fiber model to calculate the threshold current for excitation of the fiber. The models and computational algorithms have been extensively described in previous work (12,16,17).

In Fig. 1, a transverse section which includes the contacts (Fig. 1A,B) and part of a longitudinal section (Fig. 1C) of the volume conductor model are presented. In Fig. 1D, the nerve cuff electrode around the nerve is shown. The nerve model (23 mm long), based on a transverse section of a rabbit's sciatic nerve, contained four fascicles with (equivalent circle) diameters of 0.32, 0.37, 0.46, and 0.87 mm. Although the thickness of the perineurium roughly equals 5% of the diameter of the fascicle (1), the perineurium layers of all fascicles were given a thickness of 50 μm, according to the minimum grid size in the model. The layer of saline between the nerve and the cuff had also a thickness of 50 μm. The space between the fascicles was filled with epineurium. The cylindrical insulating cuff (2 mm inner diameter, 0.25 mm thick, 10 mm long) surrounding the nerve had six contacts on its inner surface (0.5 mm wide and 1.0 mm long), equally spaced in a transverse plane. The electrode geometry was determined by the following parameters: number of contacts (sufficient spatial resolution), contact size (avoiding high current densities), and contact distance (avoiding high stimulation currents), as investigated in a previous modeling study (12). The cuff was surrounded by saline and the outermost layer of the model was a low-conductivity boundary layer. The potential at the border of the model was set to zero to represent a distant ground. The compartmental conductivities used in the model are the same as in Deurloo et al. (12) and are presented in Table 1. All compartments were isotropic, except for the fascicles.

To discretize the volume conductor model, a rectangular grid was used. Grid sizes varied from 50 μm to 3 mm with the smallest values near the contacts (see Figs. 1B,C). The number of grid points was 175616 ($56 \times 56 \times 56$). The potential distribution was calculated by solving the discretized Laplace equation, using a Red-Black Gauss-Seidel iterative method with variable overrelaxation (16).

Each contact was modeled as a group of constant current point sources (at grid points) having the same voltage. The initial currents from each point source being part of a cathode or an anode were identical, but during the iterative calculation of the potential distribution the current was redistributed among the point sources to meet the constraints that all points of a contact are at the same potential and the total current of a contact is kept constant. The currents at the different points of a contact were roughly equal, except at the edges, where the currents were slightly higher than at other points (18).

The calculated potential distribution was applied to the model of a myelinated nerve fiber to determine the threshold current for excitation of the fiber as a function of its position in the nerve model. Only fiber models of 15 μm diameter were applied in this study, since these are almost the largest motor nerve fibers in mammals. The effect of considering multiple size nerve fibers is adressed in the Discussion. A McNeal-type cable model for stimulation of a myelinated nerve fiber

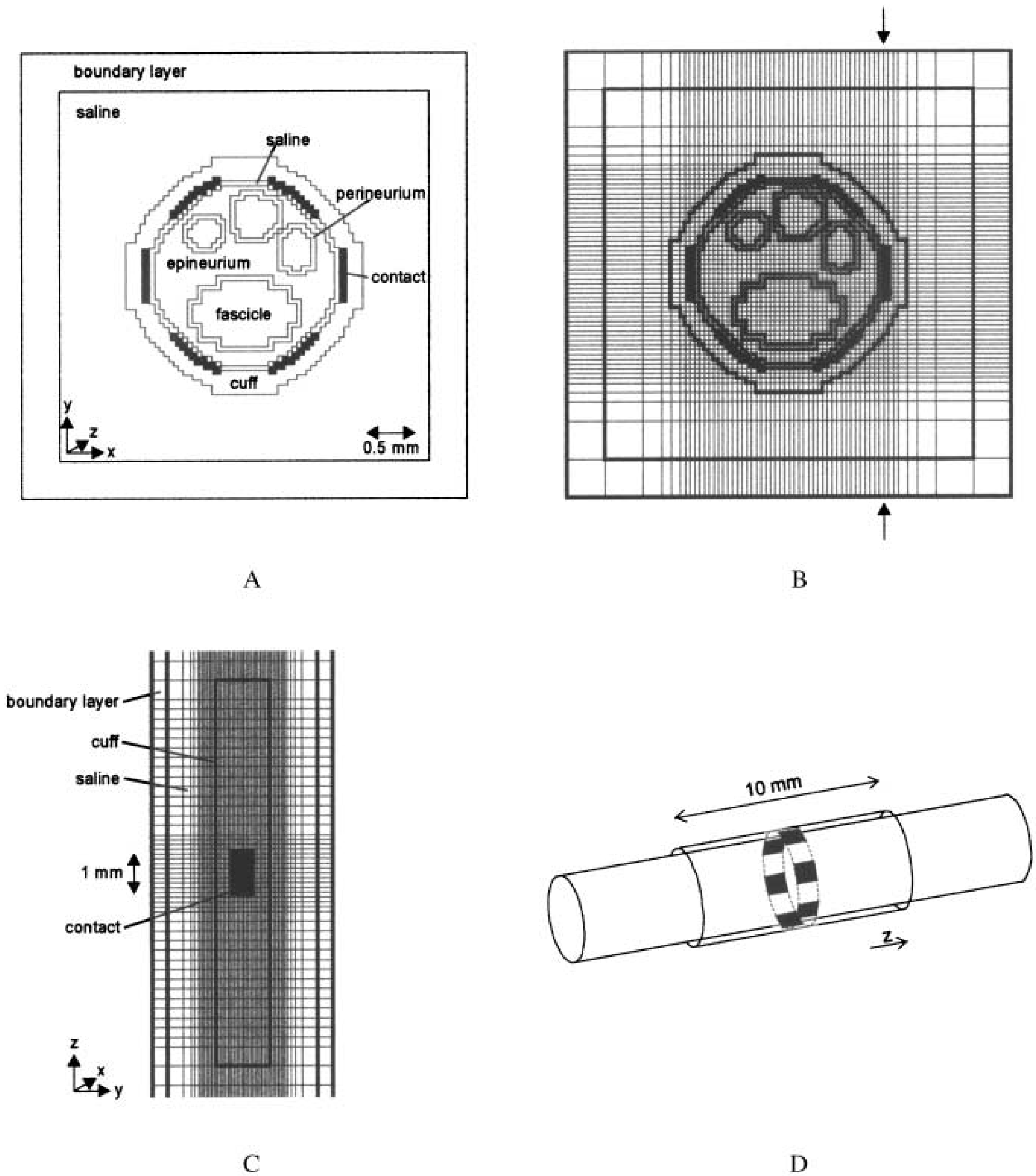

Figure 1. Three dimensional volume conductor model (A–C) of a nerve with cuff (D). A) Transverse (X–Y) section without grid; B) transverse section with grid; C) portion of longitudinal (Y–Z) section with grid (position of Y–Z plane indicated by arrows in B); D) cuff electrode around a nerve.

was used (19). In all nodes of Ranvier of the fiber, the membrane parameters as determined experimentally by Chiu et al. (20) and adapted to body temperature (37 °C) (16,21) were implemented. The position of the fiber along the z-axis was defined such that the central node of Ranvier was centered under the cathode. The internodal distance was 1.5 mm.

The threshold current was defined as the minimum stimulation current resulting in a 50 mV depolarization of the membrane of the node at three internodal distances apart from the central node, thus indicating the presence of a propagating action potential. Threshold currents were calculated at stimulation with a 100 μs duration, rectangular pulse, and three different contact combinations: a monopole, a transverse (wide) bipole, and a transverse (narrow) tripole. In case of monopolar (cathodal) stimulation, the border of the model served as the distant anode. In addition,

Table 1. Conductivities of the Volume Conductor Model Compartments (12)

Model compartment	Conductivity σ ($\Omega^{-1}m^{-1}$)
Boundary	0.02
Saline	2.0
Cuff	0.0008
Epineurium	0.008
Perineurium	0.00336
Fascicle	0.08 (σ_x, σ_y) 0.5 (σ_z)

a few other transverse configurations have been modeled (see Results).

Within each fascicle a 15 μm nerve fiber in the z-direction was defined at each grid point in the *x-y* plane. For several stimulation currents it was calculated how many nerve fibers were activated within each fascicle. These numbers were normalized to the total number of nerve fibers (at grid points) in the corresponding fascicles (100%). These normalized values represent the fraction of 15 μm nerve fibers recruited in each fascicle as a function of the stimulation current. The slope of the recruitment curves (in percentage of recruitment per μA) was calculated by using the least-squares method to fit the interval of the recruitment curve between 0 and 100% (both points not included) or between 0 and maximum percentage recruitment (if less than 100%) to a linear approximation.

RESULTS

Selectivity Performance in Mono-, Bi-, and Tripolar Stimulation

To compare the selectivity performances of the monopole, the transverse bipole and the transverse tripole, the fraction of recruited 15 μm nerve fibers in each fascicle of the model as given in Fig. 1 was determined for each contact configuration as a function of the cathodic current. This was done for each contact as a cathode, as is shown in Fig. 2 (c1 as cathode in Fig. 2A, c2 as cathode in Fig. 2B, etc.). The graphs in the first, second, and third column are for the monopole, the transverse bipole, and the transverse tripole, respectively. For the transverse tripole with c4 as the cathode, over 2.2 mA was necessary to activate the lowest threshold fibers. Because this current is extremely high (compared to the values in the other graphs), the graph for the transverse tripole was omitted in Fig. 2D and instead a picture of the central part of the nerve model was included, showing the position of the contacts in relation to the fascicles. The numbers of fibers (at grid points) in fascicles 1–4 are 20, 49, 30, and 201, respectively.

Stimulation currents for the monopole were small compared to the values needed for the other two configurations. The mean current to stimulate the fiber with the lowest threshold (closest to the cathode in Fig. 2A-F) was 37.3 ± 7.3 μA (mean ± SD). With all six contacts it was possible to stimulate all fibers in all four fascicles completely with less than 100 μA. The slope of the recruitment curves was steeper than for the other two configurations (see Table 2).

The mean current to stimulate the fiber closest to the cathode with the transverse bipole was 2.1 ± 0.4 times higher than for the monopole. Recruitment curves were less steep (see Table 2), and therefore stimulation currents to obtain 100% recruitment of a fascicle were considerably higher than with the monopole. For c1 to c4 as the cathode, approximately twice as much current as for the monopole was needed to obtain 100% recruitment of the lowest threshold fascicle, and for c5 and c6 as the cathode, about 5.5 times as much current was needed. Approximately 50% of all fibers of the nerve could be stimulated at most with the bipolar configuration.

With the transverse tripole the mean current to stimulate the fiber closest to the cathode was 5.4 ± 2.3 times higher than for the monopole. Depending on which contact was used as the cathode, only part of the fibers in one fascicle (c5 and c6), all fibers in one fascicle (c1), or all fibers in one fascicle and part of the fibers in a second fascicle (c2 and c3) were stimulated. The slopes of the recruitment curves were generally small (see Table 2).

When using c1 or c3 as the cathode, all fibers of a single fascicle can be recruited selectively with all three configurations. In Fig. 2A (c1 as cathode), only 45 μA is necessary to activate all fibers in fascicle 3 (indicated as $I_{100\%\text{-fascicle3}}$) with monopolar stimulation. The fibers in this fascicle can only be stimulated selectively in a very small current window because at only 11% above $I_{100\%\text{-fascicle3}}$ fibers in fascicle 2 already start to be

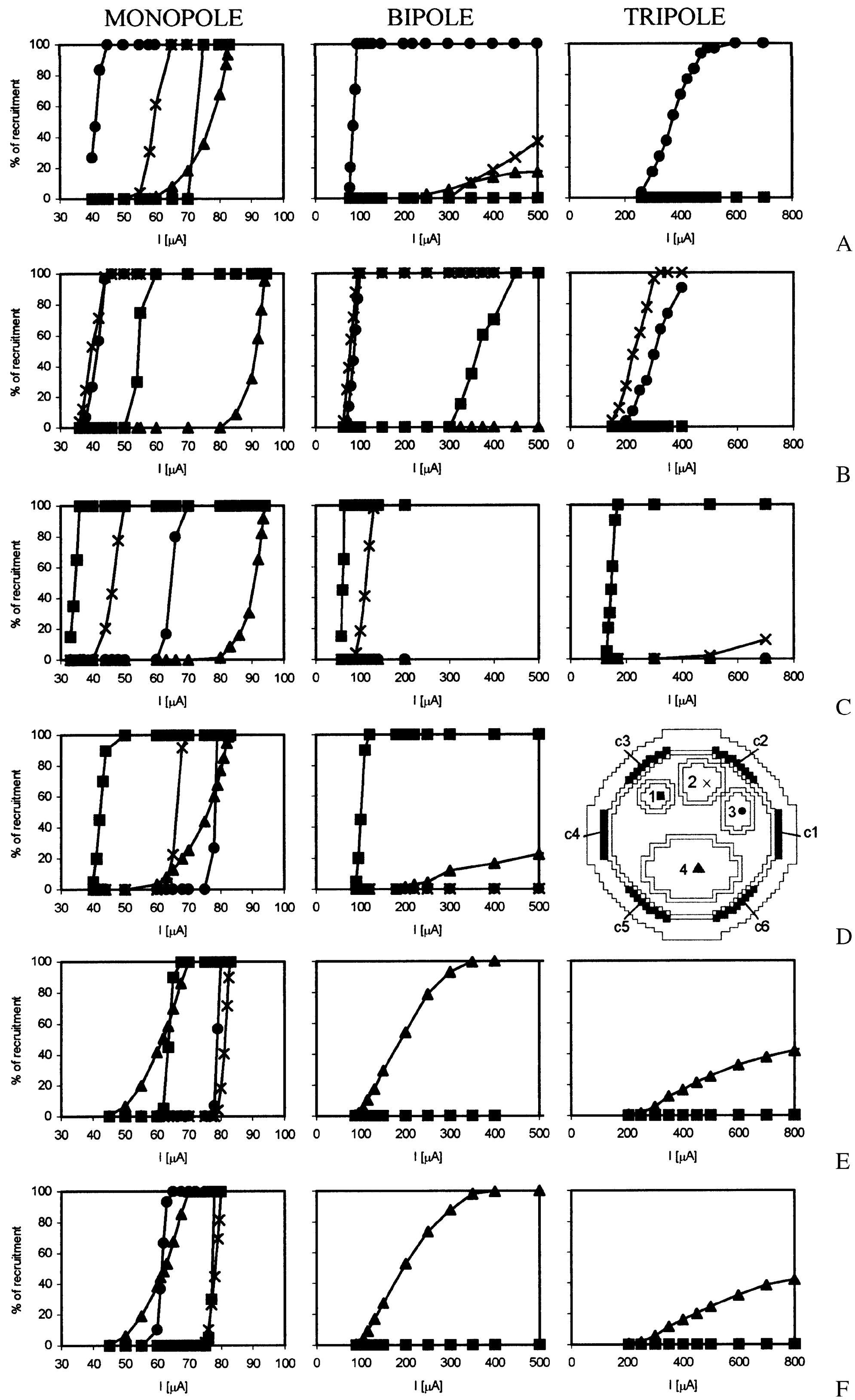

Figure 2. Recruitment of 15 μm nerve fibers in each fascicle (in percentage) as a function of cathodic current: A) c1 as cathode; B) c2 as cathode; C) c3 as cathode; D) c4 as cathode; E) c5 as cathode; F) c6 as cathode. first column: monopolar, second column: transverse bipolar, third column: transverse tripolar stimulation; ■ fascicle 1, × fascicle 2, ● fascicle 3, ▲ fascicle 4.

Table 2. Slopes (in Percentage of Recruitment per μA) of the Recruitment Curves in Figs. 2A–F[a]

Fascicle	Monopole	Bipole	Tripole
A			
1	70	–	–
2	11.22	0.13	–
3	22.8	5.24	0.39
4	3.74	0.03	–
B			
1	45	0.76	–
2	11.88	3.12	0.63
3	15	3.24	0.46
4	9.24	–	–
C			
1	25	8.33	2.75
2	14.29	2.43	0.05
3	21.11	–	–
4	6.64	–	–
D			
1	22	4.34	–
2	17.99	–	–
3	46.66	–	–
4	4.26	0.05	–
E			
1	28.33	–	–
2	24.64	–	–
3	50	–	–
4	3.79	0.42	0.07
F			
1	40.79	–	–
2	18.13	–	–
3	28	–	–
4	3.67	0.36	0.08

[a] "–" indicates that none of the 15 μm fibers had been recruited within the range of currents applied.

recruited. For the bipole (Fig. 2A, column 2), $I_{100\%\text{-fascicle3}} = 95\ \mu A$ and at 263% of $I_{100\%\text{-fascicle3}}$ fibers in the next fascicle (4) start to be recruited. With the tripole (Fig. 2A, column 3) only fibers in fascicle 3 are stimulated selectively up to 100% recruitment (up to at least 700 μA). Similar results are obtained with c3 as the cathode (Fig. 2C).

With c4 as the cathode (Fig. 2D), however, stimulation of just a single fascicle (fascicle 1) was only possible with the bipole. The stimulation current to recruit all fibers in fascicle 1 with the monopole ($I_{100\%\text{-fascicle1}} = 50\ \mu A$) is equal to the current at which fibers in fascicle 4 start to be recruited. More than 2.2 mA is needed to stimulate a few fibers in fascicles 1 and 4 with the tripole (not shown). Both fascicles are recruited at the same current.

It was impossible to selectively recruit all fibers of a single fascicle with any configuration when c2 was used as the cathode (Fig. 2B). Fibers in fascicles 2 and 3 are recruited at almost the same stimulation current. With the monopole, recruitment starts at 36 μA (fascicle 2) and 38 μA (fascicle 3), and recruitment is 100% in both fascicles at 46 μA. The slight preference for fascicle 2 becomes more obvious in bipolar, and even more in tripolar stimulation.

The recruitment with c5 (Fig. 2E) and c6 (Fig. 2F) as the cathode is similar for each contact configuration. With the monopole, fibers in the large fascicle 4 start to be recruited first. With increasing current, fibers in a second, small fascicle (fascicle 1 in Fig. 2E and fascicle 3 in Fig. 2F) start to be recruited and all these fibers are recruited before all fibers in fascicle 4 are recruited. In contrast to monopolar stimulation, all fibers in fascicle 4 are recruited selectively in bipolar stimulation (at 400 μA), whereas fibers in fascicles 1, 2, and 3 are not recruited at all. With the tripole only about 40% of the fibers in fascicle 4 can be stimulated with a current not exceeding 800 μA.

Effect of Additional Anode on Selectivity

To investigate whether the selectivity of stimulation with c2 as the cathode could be improved, transverse bipolar stimulation with an additional adjacent anode (c1) was tested; anodal contacts c5 and c1 gave 40% and 60% of the total current, respectively. The results are shown in Fig. 3A. The stimulation currents lie in between the values for the transverse bi- and tripole (Fig. 2B, columns 2 and 3). See also Table 3A, presenting the stimulation currents needed to obtain 100% recruitment of fascicle 2 for all four configurations with c2 as the cathode. Only with adjacent steering (Fig. 3A) all fibers in fascicle 2 are stimulated selectively (at $110\% \times I_{100\%\text{-fascicle2}}$ fibers in fascicle 3 start to be recruited). If the anodal current ratio is 30%–70% instead of 40%–60%, the current window in which fibers in fascicle 2 can be stimulated selectively is increased, but stimulation currents are increased as well (data not shown). A further change of the anodal current ratio towards 0%–100% ("narrow" bipole) may improve the selectivity of stimulating fascicle 2 even more, but would increase the current as well (to similar values as in tripolar stimulation).

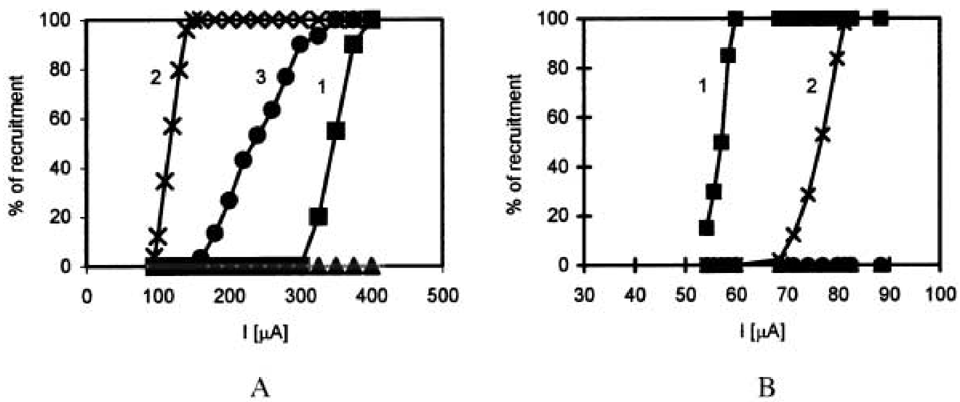

Figure 3. Recruitment of 15 μm nerve fibers in each fascicle (in percentage) as a function of cathodic current: A) transverse bipole with adjacent anode (c2 as cathode, anode c5 gives 40%, and anode c1 gives 60% of the total current); B) monopole with 90% transverse "steering" current (c3 as cathode, c6 and model border as anodes). ■ fascicle 1, × fascicle 2, ● fascicle 3, ▲ fascicle 4.

Table 3. Stimulation Currents to Obtain 100% Recruitment of 15 μm Fibers of the Lowest Threshold Fascicle

A. c2 as the cathode (Figs. 2B and 3A)	$I_{100\%\text{-fascicle2}}$ (μA)
Monopole	46
Transverse bipole	95
Transverse tripole	325
Transverse bipole with adjacent steering	150
B. c3 as the cathode (Figs. 2C and 3B)	**$I_{100\%\text{-fascicle1}}$ (μA)**
Monopole	36
Transverse bipole	65
Transverse tripole	170
Monopole with transverse steering	60

Similar to the anodal "steering" current experiments by Grill and Mortimer (7) and Sweeney et al. (9,10), stimulation with c3 as the cathode was simulated. The anodal current (at c6) was set at 90% of the bipolar threshold (I = 57 μA, see Fig. 2C, column 2) and an additional anodal current originating from the border of the model was given to compensate for the difference between the cathodal current at c3 and the anodal current at c6. In Fig. 3B, it is shown that the recruitment curves for fibers in fascicles 1 and 2 are in between the curves for the monopole and the transverse bipole (Fig. 2C, columns 1 and 2). See also Table 3B which presents the stimulation currents needed to obtain 100% recruitment of fibers in fascicle 1 for all four configurations with c3 as the cathode. The current at which fibers of the next fascicle (2) start to be recruited is $116\% \times I_{100\%\text{-fascicle1}}$ when 90% steering current was used, which is marginally higher than in monopolar stimulation ($113\% \times I_{100\%\text{-fascicle1}}$), but considerably less than in bipolar stimulation ($131\% \times I_{100\%\text{-fascicle1}}$).

Effect of Contact Positions on Selectivity

The positions of the contacts in Fig. 1 were chosen arbitrarily. To investigate the effect of a different placement, the positions of all contacts were rotated 30° clockwise with respect to the nerve. In Fig. 4A, the new positions of the contacts are shown; c2 is now in between the previous positions of c1 and c2, opposite fascicle 3. The calculations with c2 as the cathode were repeated for the displaced c2 to see whether it would be possible to stimulate all fibers in fascicle 3 without stimulating any fibers in fascicle 2. The results are shown in Fig. 4B–D.

For all three configurations the selectivity performance was improved. The currents to stimulate the fiber closest to the cathode and the ratios of these thresholds are similar to the numbers mentioned in the first section of the Results. With the monopole (Fig. 4B), all fibers in fascicle 3 can be activated (at 41 μA) before any fiber in fascicle 2 is, but only for a very small current window (1 μA). With the bipole (Fig. 4C), all fibers in fascicle 3 are activated at 80 μA and recruitment of fibers in fascicle 2 starts at 90 μA. 190 μA is needed with the tripole (Fig. 4D) to stimulate all fibers in fascicle 3 and up to 500 μA not any fiber in the other fascicles is recruited. The slope of the recruitment curve of fascicle 3 (● in Fig. 4B–D) is steeper

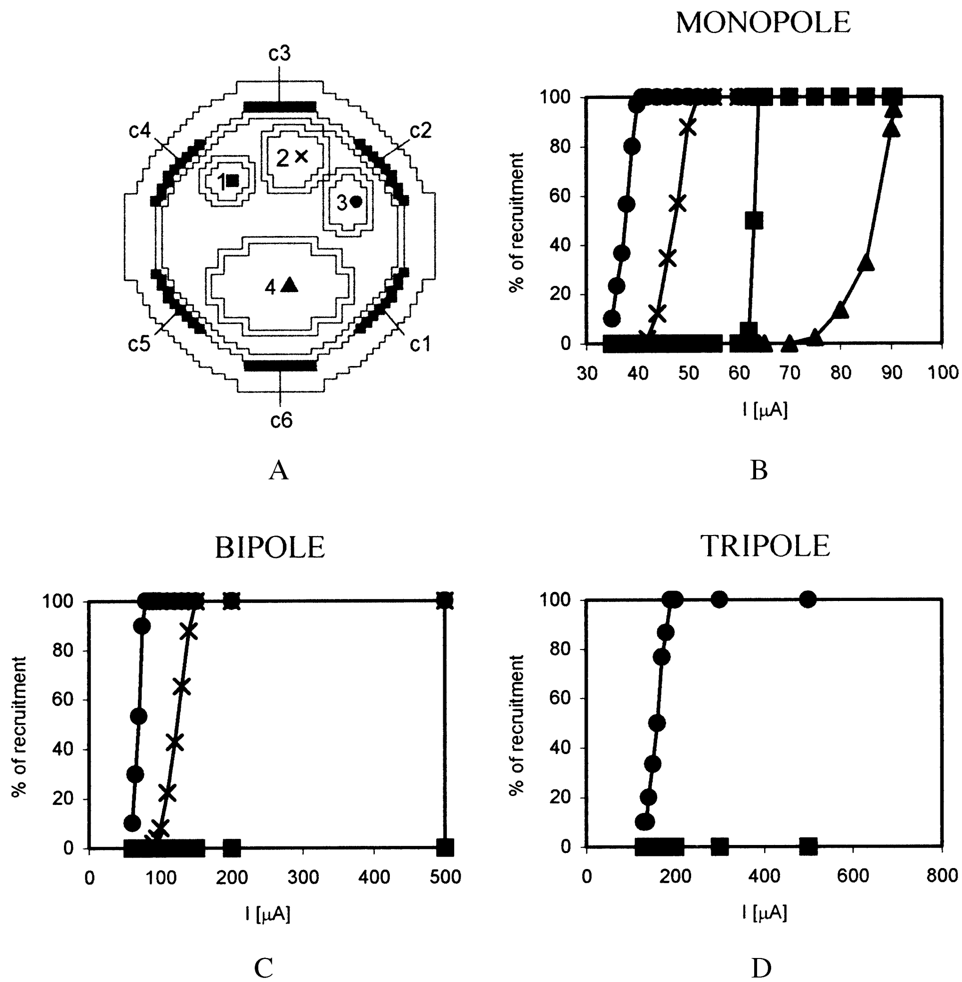

Figure 4. A) Transverse section of the central part of the volume conductor model with displaced contacts (rotated 30° clockwise with respect to Fig. 1). B–D) Recruitment of 15 μm nerve fibers in each fascicle (in percentage) as a function of cathodic current (c2 as cathode): B) monopolar, C) transverse bipolar, and D) transverse tripolar stimulation. ■ fascicle 1, × fascicle 2, ● fascicle 3, ▲ fascicle 4.

than in Fig. 2B for all three configurations, but the slope of the curve of fascicle 2 is less steep (× in Fig. 4B–D).

DISCUSSION

In this study, a computer model has been used to predict the spatial selectivity performance of monopolar and transverse bi- and tripolar stimulation of a nerve trunk with four fascicles in a nerve cuff electrode. It was investigated whether conclusions drawn by Deurloo et al. (12) regarding selective stimulation of a monofascicular nerve with various cathode-anode configurations were also valid for a multifascicular nerve. Instead of stimulating an almost round fiber bundle in the periphery of a uniform nerve trunk it has been investigated how each of four fascicles in a nerve trunk could be stimulated selectively.

Effect of Fiber Caliber

This study on fascicular selectivity was confined to the performance of 15 μm fibers. Since fibers of this caliber are almost the largest motor nerve fibers in mammals (22), the recruitment curves of almost all other motor fibers will be less steep and will be shifted to higher current levels. At a given stimulation current 15 μm fibers will thus be recruited up to a larger distance from the cathode than smaller fibers do. If the recruitment of 15 μm fibers is confined to (part of) a single fascicle, this will also be true for smaller fibers. Assuming that the fiber size distribution within a fascicle is (almost) uniform, the smaller fibers will be recruited in an even smaller part of that fascicle, covered by a larger recruited area of the 15 μm fibers. Although a 100% recruitment of the largest (motor) fibers in a fascicle can generally be obtained without recruiting fibers in another fascicle, a 100% recruitment of all (motor) fibers in a fascicle is generally not possible without activating (motor) fibers in neighboring fascicles. If each fascicle innervates a different muscle, a 100% force recruitment of a single muscle will not be possible without any recruitment of other muscles. Since the largest motor fibers have the largest contribution to muscle force ["size principle" (23)], the recruitment of only part of the smaller motor fibers in a fascicle will result in just a limited reduction of the maximum force obtainable by the corresponding muscle. The situation is more complicated when the size of the largest fibers is substantially different among fascicles.

All modeled fibers had their central node of Ranvier in a plane centered at the cathode. Taking into account the actual distribution of the position of these nodes with respect to the cathode, threshold currents to activate fibers of any size will vary somewhat. In reality some overlap of the threshold current distributions corresponding to nerve fibers of slightly different calibers will exist. Moreover, stimulation of small fibers will be favored at low recruitment levels (24).

Monopolar vs. Transverse Bipolar Stimulation

In monopolar stimulation the current mainly spreads tangentially along the periphery of the nerve trunk, as for a monofascicular nerve (12,13). In Fig. 2A (column 1) for example, fibers in fascicle 2 start to be recruited before fibers in fascicle 4, even though fascicle 4 is closer to the cathode (c1). This happens because fascicle 2 is closer to the periphery of the nerve trunk than fascicle 4. In contrast, fibers in fascicle 4 start to be recruited before fibers in fascicle 2 when stimulating bipolarly (Fig. 2A, column 2). The effect of tangential current spread is also shown in Fig. 2E,F (column 1) where during the recruitment of fibers in nearby fascicle 4, fibers in a second, more distant fascicle start to be recruited as well (fascicle 1 in Fig. 2E and fascicle 3 in Fig. 2F). Whether fibers in a fascicle can be stimulated selectively by monopolar stimulation depends on the diameter of the fascicle and its position with respect to the cathode. But even fibers in a small fascicle directly in front of the cathode can only be stimulated selectively in a very small current window when neighbored by other fascicles (see Fig. 4B). Therefore, it is concluded that monopolar stimulation should generally not be used for the selective stimulation of a single fascicle. It can, however, be used for stimulation of the complete nerve at a low current (less than 100 μA in the model).

Deurloo et al. (12) predicted that with transverse bipolar stimulation of a monofascicular nerve, recruitment contours are almost straight lines perpendicular to the anode-cathode axis. This is approximately true for a multifascicular nerve as well. Transverse bipolar stimulation will therefore perform well in the selective stimulation of a large fascicle (4 in Fig. 2E,F, column 2). For smaller fascicles the recruitment curves are shifted apart and the range of currents in which the lowest threshold fascicle can be selectively stimulated is increased as compared to monopolar stimulation (see for instance fascicles 1 and 2 in Fig. 2C). In bipolar stimulation the slope of the recruitment curves is considerably reduced (see Table 2), which may be favorable for accurate muscle force control. Stimulation currents are, however, higher than in monopolar stimulation. About twice as much current is needed to stimulate the lowest threshold 15 μm fiber and 2–5.5 times as much, depending on the position and size of the fascicle, is needed to obtain 100% recruitment of the 15 μm fibers of the lowest threshold fascicle.

To simulate anodal "steering" experiments from literature (7,9,10), a transverse bipole was completed with a distant anode (the border of the model), thus providing similar recruitment properties as a longitudinal tripole (9,12–14). The "steering" anode, opposite the cathode, had a current of 90% of the transverse bipolar threshold. At complete recruitment of the 15 μm fibers in fascicle 1, the transverse "steering" current was 85% of the cathodal current, whereas the longitudinal component was only 15%. The selectivity obtained with this configuration is only marginally better than with just a monopole (116% and 113% $\times$ $I_{100\%\text{-fascicle1}}$, respectively) or a longitudinal tripole. In contrast, transverse bipolar stimulation results in an initial fiber recruitment in fascicle 2 at 131% $\times$ $I_{100\%\text{-fascicle1}}$. These results predict that transverse bipolar stimulation provides an improved fascicle selectivity as compared to a monopole, or a longitudinal tripole with or without an additional anodal "steering" current.

Transverse Bipolar vs. Transverse Tripolar Stimulation

Deurloo et al. (12) concluded that monofascicular nerve stimulation with a narrow transverse tripole is more selective than with a transverse bipole and other configurations. For a multifascicular nerve, however, a substantial improvement in selectivity in transverse tripolar stimulation as compared to transverse bipolar stimulation is not apparent. Moreover, due to the small cathode-anode separation, stimulation currents are considerably higher in tripolar than in bipolar stimulation. The current to stimulate the lowest threshold 15 μm fiber with a transverse tripole was, on average, 2.7 times higher than with a bipole. Therefore, a transverse (wide) bipole should generally be preferred over a transverse narrow tripole ("shielded cathode") to obtain fascicle selective stimulation.

MISCELLANEOUS

In real stimulation experiments, the size and the position of the fascicles with respect to the contacts is generally unknown. The likelihood of selectively stimulating a single fascicle will increase with the number of contacts to be used as a cathode. Therefore, a cuff electrode with many small contacts on its inner circumference is preferred. If a fascicle is in between two contacts, an additional anode near the cathode can be used to modify the region of excitation obtained with a transverse bipole, as shown in Fig. 3A. The additional anodal current "pushes" the region of excitation away. The use of an additional adjacent "steering" anode has been reported by Grill and Mortimer (7). When a cuff electrode has many contacts, intercontact spacings may be small. In this situation the use of adjacent contacts as a bipole should be avoided, as stimulation currents increase exponentially with reduction of their distance (12). Instead, one (inactive) contact should separate the cathode and the "adjacent" anode.

When using the methods discussed, centrally positioned fascicles cannot be stimulated selectively with a nerve cuff electrode (25). To overcome this problem, subthreshold depolarizing prepulses reducing the excitability of fibers close to the cathode (26,27) or supramaximal stimulation with ring electrodes causing anodal block in the periphery of the nerve trunk (28) might be used.

In conclusion, the results of this modeling study predict that fascicle selective stimulation is advanced most by stimulation with a cathode and one or two anodes in a plane perpendicular to the axis of the nerve trunk. Because nerve fibers are excited near the cathode, whereas currents from one or more anodes are used to maximally fit the area of excitation to the topography of the fascicle to be recruited, other anodal positions or anodal current ratios than those modeled in this study may be preferable under specific stimulation conditions. Finally, selectivity has its price: stimulation currents are higher than in conventional longitudinal tripolar stimulation, because the driving force of nerve fiber stimulation is related to the longitudinal current component (29).

REFERENCES

1. Sunderland S. *Nerves and Nerve Injuries*, 2nd edn. Churchill Livingstone: Edinburgh, 1978.
2. Brushart TM. Central course of digital axons within the median nerve of Macaca mulatta. *J Comp Neurol* 1991;311:197–209.
3. Naples GG, Mortimer JT, Yuen TGH. Overview of peripheral nerve electrode design and implantation. In: *Neural Prostheses, Fundamental Studies.* Prentice Hall: Englewood Cliffs, 1990: 107–145.
4. Mortimer JT, Agnew WF, Horch K, Citron P, Creasey G, Kantor C. Perspectives on new electrode technology for stimulating peripheral nerves with implantable motor prostheses. *IEEE Trans Rehab Eng* 1995;3:45–154.
5. Naples GG, Mortimer JT, Scheiner A, Sweeney JD. A spiral nerve cuff electrode for peripheral nerve stimulation. *IEEE Trans Biomed Eng* 1988;31:905–916.
6. Veraart C, Grill WM, Mortimer JT. Selective control of muscle activation with a multipolar nerve cuff electrode. *IEEE Trans Biomed Eng* 1993;40:640–653.
7. Grill WM, Mortimer JT. Quantification of recruitment properties of multiple contact cuff electrodes. *IEEE Trans Rehab Eng* 1996;4:49–62.

8. Grill WM, Mortimer JT. Stability of the input-output properties of chronically implanted multiple contact nerve cuff stimulating electrodes. *IEEE Trans Rehab Eng* 1998;6:364–373.

9. Sweeney JD, Ksienski DA, Mortimer JT. A nerve cuff technique for selective excitation of peripheral nerve trunk regions. *IEEE Trans Biomed Eng* 1990;37:706–715.

10. Sweeney JD, Crawford NR, Brandon TA. Neuromuscular stimulation selectivity of multiple-contact nerve cuff electrode arrays. *Med Biol Eng Comp* 1995;33:418–425.

11. Goodall EV, de Breij F, Holsheimer J. Position-selective activation of peripheral nerve fibers with a cuff electrode. *IEEE Trans Biomed Eng* 1996;43:851–856.

12. Deurloo KEI, Holsheimer J, Boom HBK. Transverse tripolar stimulation of peripheral nerve: a modelling study of spatial selectivity. *Med Biol Eng Comp* 1998;36:66–74.

13. Chintalacharuvu RR, Ksienski DA, Mortimer JT. A numerical analysis of the electric field generated by a nerve cuff electrode. *Proc Ann Int Conf IEEE Eng Med Biol Soc* 1991;13:912–913.

14. Tarler MD, Mortimer JT. Quantification of similarities in recruitment properties of monopolar and tripolar configurations. *Proc Ann Int Conf IEEE Eng Med Biol Soc* 1997;19:2000–2001.

15. Struijk JJ, Holsheimer J. Transverse tripolar spinal cord stimulation. theoretical performance of a dual channel system. *Med Biol Eng Comp* 1996;34:273–279.

16. Struijk JJ, Holsheimer J, van der Heide GG, Boom HBK. Recruitment of dorsal column fibers in spinal cord stimulation. *IEEE Trans Biomed Eng* 1992; 39:903–912.

17. Goodall EV, Kosterman LM, Holsheimer J, Struijk JJ. Modeling study of activation and propagation delays during stimulation of peripheral nerve fibers with a tripolar cuff electrode. *IEEE Trans Rehab Eng* 1995; 3:272–282.

18. Suesserman MF, Spelman FA, Rubinstein JT. In vitro measurement and characterization of current density profiles produced by nonrecessed, simple recessed, and radially varying recessed stimulating electrodes. *IEEE Trans Biomed Eng* 1991;38:401–408.

19. McNeal DR. Analysis of a model for excitation of myelinated nerve. *IEEE Trans Biomed Eng* 1976; 23:329–337.

20. Chiu SY, Ritchie JM, Rogart RB, Stagg D. A quantitative description of membrane currents in rabbit myelinated nerve. *J Physiol* 1979;292:149–166.

21. Sweeney JD, Mortimer JT, Durand D. Modeling of mammalian myelinated nerve for functional neuromuscular stimulation. *Proc Ann Int Conf IEEE Eng Med Biol Soc* 1987;9:1577–1578.

22. Boyd IA, Davey MR. Composition of peripheral nerves. E & S Livingstone Ltd.: London, 1968.

23. Dengler R, Stein RB, Thomas CK. Axonal conduction velocity and force of single human motor units. *Muscle Nerve* 1988;11:136–145.

24. Veltink PH, van Alsté JA, Boom HBK. Simulation of intrafascicular and extraneural nerve stimulation. *IEEE Trans Biomed Eng* 1988;35:69–75.

25. Veltink PH, van Veen BK, Struijk JJ, Holsheimer J, Boom HBK. A modeling study of nerve fascicle stimulation. *IEEE Trans Biomed Eng* 1989;36:683–692.

26. Grill WM, Mortimer JT. Inversion of the current-distance relationship by transient depolarization. *IEEE Trans Biomed Eng* 1997;44:1–9.

27. Deurloo KEI, Holsheimer J, Bergveld P. The effect of subthreshold prepulses on the recruitment order in a nerve trunk analyzed in a simple and a realistic Volume conductor model. *Biol Cybernetics* 2001;85:281–291.

28. Rijkhoff NJM, Holsheimer J, Koldewijn EL et al. Selective stimulation of sacral nerve roots for bladder control; A study by computer modeling. *IEEE Trans Biomed Eng* 1994;41:413–424.

29. Rattay F. Analysis of models for external stimulation of axons. *IEEE Trans Biomed Eng* 1986;33:974–977.