Transverse tripolar stimulation of peripheral nerve: a modelling study of spatial selectivity

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Abstract—*Various anode–cathode configurations in a nerve cuff are modelled to predict their spatial selectivity characteristics for functional nerve stimulation. A 3D volume conductor model of a monofascicular nerve is used for the computation of stimulation-induced field potentials, whereas a cable model of myelinated nerve fibre is used for the calculation of the excitation thresholds of fibres. As well as the usual configurations (monopole, bipole, longitudinal tripole, 'steering' anode), a transverse tripolar configuration (central cathode) is examined. It is found that the transverse tripole is the only configuration giving convex recruitment contours and therefore maximises activation selectivity for a small (cylindrical) bundle of fibres in the periphery of a monofascicular nerve trunk. As the electrode configuration is changed to achieve greater selectivity, the threshold current increases. Therefore threshold currents for fibre excitation with a transverse tripole are relatively high. Inverse recruitment is less extreme than for the other configurations. The influences of several geometrical parameters and model conductivities of the transverse tripole on selectivity and threshold current are analysed. In chronic implantation, when electrodes are encapsulated by a layer of fibrous tissue, threshold currents are low, whereas the shape of the recruitment contours in transverse tripolar stimulation does not change.*

Keywords—*Electrical nerve stimulation, Nerve cuff electrode, Transverse tripolar stimulation, Spatial selectivity, Peripheral nerve, Computer modelling*

1 Introduction

FUNCTIONAL ELECTRICAL stimulation (FES) is a technique to restore motor functions in patients with paralysis caused by central neurological deficits. To produce muscle activation resulting in 'normal' motor behaviour, independent control of motor neuron pools, innervating different muscles or muscle groups having different functions, is necessary. The nerve fibres of a single motor neuron pool are usually clustered in a single fascicle of a peripheral nerve, especially in its distal parts (SUNDERLAND, 1978). Therefore electrode devices stimulating a single fascicle in a selective way are needed.

For selective stimulation of peripheral nerve fascicles, different types of electrode have been developed, e.g. intraneural wire and silicon electrodes (RUTTEN *et al.*, 1991; YOSHIDA and HORCH, 1993), epineural electrodes (THOMA *et al.*, 1989) and multiple-contact nerve cuff electrodes (VERAART *et al.*, 1993). Cuff electrodes are relatively easy to construct and implant and types have been developed that appear to be safe for chronic use (NAPLES *et al.*, 1988). Therefore the development of cuff electrode configurations for achieving spatially selective stimulation is of particular relevance.

SWEENEY *et al.* (1990) have shown, both by numerical modelling and experiments on the cat's sciatic nerve, that pulses applied by dot electrodes aligned as a longitudinal tripole restrict excitation to a superficial nerve trunk region more successfully than does just a monopolar dot electrode. When stimulation pulses are applied with a longitudinally aligned tripole with a central cathode and an additional 'steering' anode opposite the cathode, the transverse current from the 'steering' anode should restrict the region of excitation even more to an area close to the cathode and therefore improve spatial selectivity. It was shown by modelling (SWEENEY *et al.*, 1990; CHINTALACHARUVU *et al.*, 1991) and experiments (SWEENEY *et al.*, 1990) that a transverse current indeed improves the spatial selectivity obtained by both monopolar and tripolar electrode configurations.

VERAART *et al.* (1993) developed a 12-contact spiral nerve cuff electrode to test combinations of a longitudinal tripole and 'steering' anode. Rather than choosing a single value for the transverse 'steering' current (SWEENEY *et al.*, 1990; CHINTALACHARUVU *et al.*, 1991), they determined experimentally that maximum selectivity was achieved by modulation of the amplitudes of both the (simultaneous) longitudinal and transverse currents.

SWEENEY *et al.* (1995) and GRILL and MORTIMER (1996) did experiments with longitudinal tripoles and an additional 'steering' anode in a nerve cuff, where the amplitude of the steering current was set constant at either 0, 45 or 90% of the

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transverse threshold. Both groups showed that steering current increased the spatial selectivity.

The same electrode configuration was used in experiments by GOODALL et al. (1996), but here the transverse current was a fixed percentage of the cathodal current. They showed that spatial selectivity was maximised when the transverse current was a high proportion of the total current. Accordingly, this suggests that 100% transverse current would result in maximum spatial selectivity. In that case, the two anodes from the longitudinal tripole are effectively eliminated.

When using a cathode and just one anode at the opposite side of the nerve, the net direction of the current is perpendicular to the nerve fibre axes, and threshold currents for fibre activation are increased considerably, compared with stimulation with a longitudinal tripole (RANCK, 1975; SWEENEY et al., 1990). When the (longitudinal) anodes only give a small percentage of the cathodal current, or no current at all, anodal block of large fibres by these anodes is not possible anymore. Therefore a combination of position selective activation and fibre size selective activation seems impossible using this approach (GOODALL et al., 1996). For this reason, we have focused this study primarily on position selective activation, although fibre size selectivity was analysed as well.

Fig. 1 shows the fascicular organisation of the tibial nerve of a cat. As the nerve consists of fascicles of a more or less round shape, we wish to obtain recruited areas with a similar shape. In modelling spinal cord stimulation, it was shown that a transverse tripolar electrode configuration (patented) might successfully be used for selective stimulation of median dorsal column fibres, by 'shielding' the fibres in the lateral parts of the dorsal columns (STRUIJK and HOLSHEIMER, 1996). It was shown that, with this transverse configuration, the recruited area in the dorsal columns was narrower than with stimulation with a longitudinal configuration.

GRILL and MORTIMER (1996) did experiments with longitudinal tripoles in a spiral nerve cuff electrode, with a 'steering' anode at a transverse angle of 90° from the cathode. They showed that this configuration can be used to modify the region of excitation by hyperpolarising the nerve fibres near the adjacent 'steering' anode. In the study presented here, we analysed theoretically the capability of transverse tripolar electrode configurations in a cuff to activate selectively nerve fibres in a nerve trunk close to the cathode, and we compared the results with those obtained with other configurations.

Because the shape of the excitation area and the magnitude of the threshold current depend on the sizes of the contacts and their separations, the influences of these parameters on spatial selectivity and threshold current were analysed theoretically.
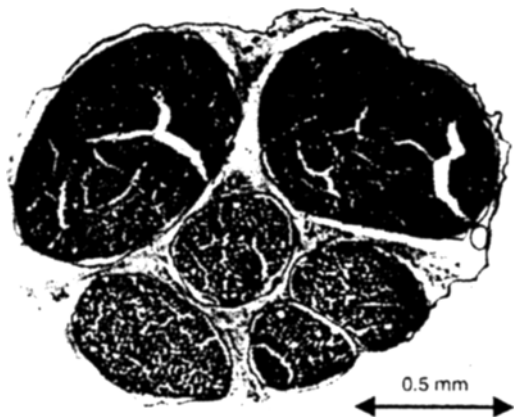

Fig. 1   Transverse section of cat tibial nerve

The capability of a nerve cuff electrode to stimulate a specific area of the nerve also depends on the electrical conductivities of the tissues in and around the nerve trunk. The precise values of the conductivities of the perineurium and epineurium, however, are not known from the literature. Moreover, the thicknesses of these layers may vary among nerves. Electrodes implanted chronically become encapsulated by a layer of fibrous tissue. The formation of this layer results in a significant increase in the load impedance (GRILL and MORTIMER, 1994). The presence of fibrous tissue may thus alter the shape and magnitude of the electric field generated in the nerve and thus modify the region of tissue activated by stimulation. Therefore the influences of the electrical conductivities of several tissues were analysed as well.

A computer model was used that calculates both the electric potential distribution generated by a cuff electrode and the responses of myelinated nerve fibres to this field. Through simulation of the effects of various geometric and electrical parameters on the behaviour of the nerve fibres, a better understanding of these effects was obtained. The results of the modelling study are presented in this paper.

2 Methods

A two-part computer model, developed by STRUIJK et al. (1992) and modified by GOODALL et al. (1995) so that current sources instead of voltage sources can be used, was applied for the simulations.

The first part is a 3D volume conductor model of a monofascicular nerve. A transverse section and a part of a longitudinal section of the model are shown in Fig. 2. The model used in this study comprises a nerve segment with a length of 23 mm and a diameter of 1.9 mm, surrounded by a 50 μm layer of perineurium, a 50 μm layer of epineurium, a 50 μm saline layer and a cylindrical insulating cuff. The cuff had an inner diameter of 2.2 mm and was 0.25 mm thick and 11.0 mm long. A rectangular grid of variable size was used: grid spacings ranged from 50 μm in the transverse plane for the nerve trunk, perineurium, epineurium and saline layer and 125 μm in the z-direction, to 400 μm (transverse plane) and 4 mm (z-direction) in the periphery of the model. Each electrode contact was modelled as a current source, placed on the inner surface of the cuff. Saline was outside the cuff. The outermost layer of the model was a low-conductivity boundary layer, and the potential at the border of the model was set to zero to represent a distant ground. The conductivities used for the different compartments of the volume conductor model are listed in Table 1. Only the nerve bundle's conductivity was assumed to be anisotropic.

In this model, the steady-state potential distribution, resulting from stimulation by any particular contact configuration, was obtained by applying a finite difference method using Taylor series and solving the resulting set of linear equations by a red–black Gauss–Seidel iteration, with an over-relaxation coefficient adjusted by the speed of convergence (STRUIJK et al., 1992). Thereby, the initial currents from each point source of a cathode or anode were identical, but during the iterative calculation of the potential distribution the current was redistributed among the point sources to meet the constraint that all points of a contact were at the same potential (and the total current of a contact was kept constant).

The second part of the computer model calculates the threshold current for excitation of a myelinated nerve fibre as a function of its calibre and its position within the fascicle. This was done with a nerve fibre model based upon that used by McNEAL (1976). Instead of using the Frankenhaeuser–Huxley equations, describing the non-linear nodal membrane
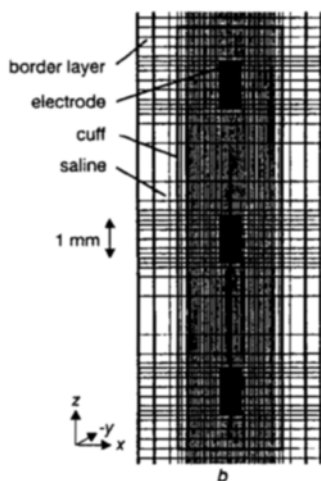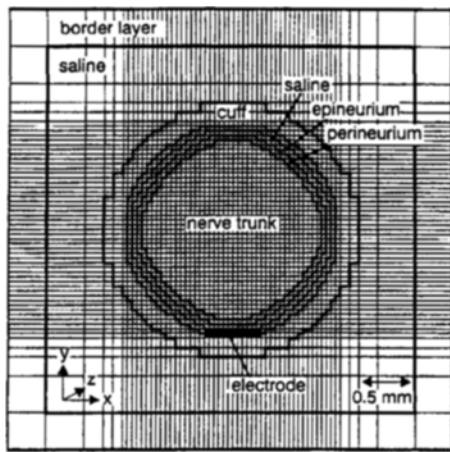
Fig. 2 *Sections of volume conductor model: (a) mid-transverse section (x-y-plane); (b) part of longitudinal section (x-z-plane)*

behaviour of frog myelinated nerve fibres, the equations of CHIU *et al.* (1979), based on experimental data from rabbit myelinated nerve fibres and adapted to a temperature of 37°C (SWEENEY *et al.*, 1987; STRUIJK *et al.*, 1992), were implemented in all Ranvier nodes of the nerve fibre. Because the threshold stimulus to excite a nerve fibre varies with the nodal position with respect to the cathode, the central node of a fibre model was always placed at a longitudinal position in the 3D model, corresponding to the centre of the cathode.

Table 1   Conductivities of compartments of volume conductor model

Model compartment	Conductivity σ, Ω^{-1} m^{-1}
Boundary	0.02[a]
Saline	2.0[b]
Cuff	0.0008[c]
Epineurium	0.008[d]
Perineurium	0.00336[e]
Fascicle	0.08 (σ_x, σ_y)[f]
	0.5 (σ_z)[f]

[a] (value selected to give good representation of distant ground)
[b] (GEDDES and BAKER, 1967)
[c] (value selected to represent an insulator)
[d] (GOODALL *et al.* (1995))
[e] (calculated according to FRIESWIJK *et al.* (1997))
[f] (VELTINK *et al.* (1989)).

With this model, the transmembrane potential in a fibre, induced by the potential distribution in the volume conductor, was calculated against time. The threshold stimulus for excitation of a fibre was defined as the stimulus current that caused the transmembrane potential at the most easily excited Ranvier node (generally the node centred under the cathode) to be depolarised by 50 mV. This depolarisation occurred only during an action potential.

The occurrence of an action potential was also examined at nodes at some distance from the cathode, because propagation of action potentials in nerve fibres close to the cathode might be blocked at high stimulation currents (the blocking threshold being defined as the lowest current above the excitation threshold at which an action potential would fail to be conducted to the end of the fibre). At high-stimulation currents, action potentials might be generated near an anode as well (RANCK, 1975).

The model implementation for spinal cord stimulation has been validated on the basis of clinical data (STRUIJK *et al.*, 1993*b*). The model was verified by comparing the potential distribution with an analytically obtained solution (STRUIJK *et al.*, 1993*a*). A detailed description of the model has been given by STRUIJK *et al.* (1992, 1993*b*).

The response to a standard rectangular current pulse with a pulsewidth of 350 μs was calculated, with both large (15 μm) and small (5 μm) nerve fibres modelled. The geometric fibre parameters are given in Table 2. The electrical fibre parameters have been presented by STRUIJK *et al.* (1993*b*). Recruitment contours were plotted in a transverse section of the model corresponding to the centre of the cathode. These lines are the loci of all positions at which a fibre model with a specific diameter was just reaching threshold at a specified stimulus current. All fibres of this diameter in the area between the cathode and the recruitment contour are then excited. Sample points for the recruitment lines were taken at intersections of the gridlines and halfway in between. The simulation program runs on an HP 700 workstation. Solving the potential distribution in a model takes ~2 h, whereas a recruitment contour is generated in a few seconds.

3 Results

3.1 Electrode configurations and recruitment contours

Recruitment contours, calculated in models with a geometry and conductivities as described in Section 2, and five different electrode configurations, were compared in the following way. At three fixed positions in front of the centre of the cathode, at 0.3, 0.5 and 0.7 mm distance (see markers in Fig. 3*a*), the threshold current needed to excite a 15 μm fibre was calculated, and subsequently the corresponding recruitment contour was calculated. These contours, together with the corresponding (cathodal) currents, are shown in the mid-transverse sections of the models for the following configurations: a single cathode (Fig. 3*a*), a longitudinal tripole (central cathode) (Fig. 3*b*), a longitudinal tripole with additional anode opposite the cathode (Fig. 3*c*), a transverse bipole (Fig. 3*d*),

Table 2 Geometric fibre parameters

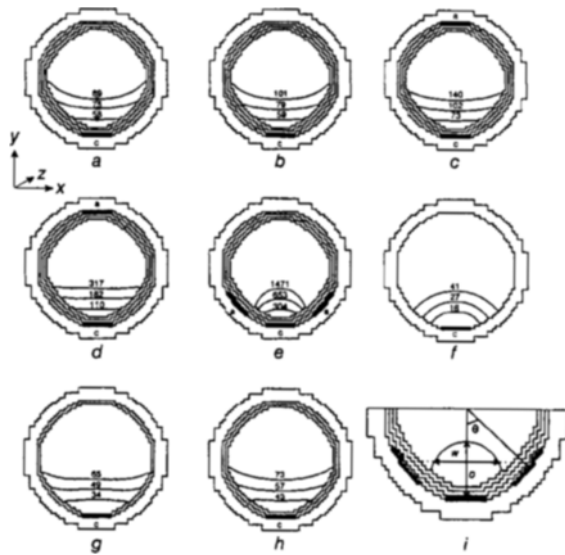|	Small	Large
Fibre diameter	5 μm	15 μm
Axon diameter	3 μm	9 μm
Nodal length	1.5 μm	1.5 μm
Internodal length	0.5 mm	1.5 mm
Fibre length	22 mm	21 mm
Number of nodes	45	15

Fig. 3 *Recruitment contours showing excitation regions in the nerve trunk; corresponding threshold currents are given (cathodal current in μA), c = cathode, a = anode; (a)–(e) Complete nerve model: (a) single cathode; (b) longitudinal tripole (central cathode); (c) longitudinal tripole with additional anode opposite cathode providing 40% of total anodal current; (d) transverse bipole; (e) transverse tripole. (f)–(h) Single cathode: (f) anisotropic nerve trunk; (g) anisotropic nerve trunk surrounded by saline; (h) anisotropic nerve trunk surrounded by epineurium and saline. (i) Definition of parameters*

and a transverse tripole (Fig. 3e). The contacts were 0.5 mm wide (x-direction) and 1.0 mm long (z-direction). The contact separation used for the longitudinal tripoles was 3.0 mm. In all simulations, except the monopolar one, the cathodal current equalled the sum of the anodal currents, so that no net current left the inside of the cuff. When two anodes were used (Figs. 3b and e), each one gave 50% of the cathodal current.

Both when stimulation is given monopolarly (Fig. 3a) or with a longitudinal tripole (Fig. 3b), the recruitment contours have a concave shape. A wide area of the nerve trunk at both sides of the cathode is then activated. The currents at the lowest recruitment line are almost the same, but the other two are increasingly higher with the longitudinal tripole. This means that the current is more restricted to the side of the nerve trunk where the contacts are. Reducing the tripolar contact spacing did not generally affect the shape of the recruitment contours; it only increased the threshold currents. When the longitudinal tripole consisted of a central dot cathode and two anodes each consisting of four dot electrodes equally spaced around the nerve, with the same length (1 mm) and the same longitudinal distance (3 mm), the recruitment contours became slightly more concave than in Figs. 3a and b, and slightly more current (7.5%) was needed (data not shown).

In Fig. 3c, the additional anode opposite the stimulating cathode provided 40% of the total anodal current. Fibres closer to this anode are now more difficult to activate, owing to the hyperpolarising effect of this anode. The recruitment contours are therefore less concave than in Figs. 3a and b, and the threshold currents have slightly increased. Increasing the current of the anode opposite the cathode to 70% of the total anodal current reduces the concavity even more (data not shown).

In Fig. 3d, the current of the anode opposite the cathode was increased to 100% of the cathodal current, thus representing a transverse bipole. As expected, the recruitment contours are now nearly straight lines, perpendicular to the cathode–anode axis. The threshold currents have further increased.

When a transverse tripole is used (Fig. 3e), the recruitment contours are convex. The excitation area is thus confined to a smaller area near the cathode, because the cathode and anodes are narrowly spaced. Threshold currents for fibre excitation are higher. The threshold current also increases rapidly as a function of fibre–cathode distance (see also Section 3.3).

The convex shape of the recruitment contours of the transverse tripole is thus caused by the positions of the contacts. To understand why the recruitment contours of the other configurations have a concave shape, simulations were done with a single cathode and three different models (Figs. 3f–h). In Fig. 3f, only a nerve trunk (anisotropic) was modelled, without the saline, epineurium and perineurium layers. The recruitment contours have a convex shape. An isotropic nerve trunk (not shown) resulted in the same shape. When the anisotropic nerve trunk is surrounded by a layer of well-conducting saline (Fig. 3g), the current spreads around the surface of the nerve trunk, resulting in slightly concave recruitment contours. This effect is more pronounced when a layer of epineurium is added (Fig. 3h). This layer, having a lower conductivity than the nerve trunk, reduces the current density penetrating the nerve trunk near the cathode and therefore increases the current density in the saline layer. This effect is even stronger when a layer of perineurium is added (Fig. 3a).

When cuff electrodes are chronically implanted, they become encapsulated by fibrous tissue. According to GRILL and MORTIMER (1994), this tissue has a conductivity $\sigma = 0.16 \ \Omega^{-1} m^{-1}$. Replacing the saline layer by a layer of fibrous tissue only produces a minor change in the shape of the recruitment contours of the transverse tripole (slightly more convex). The recruitment contours of the other electrode configurations in Fig. 3 become slightly convex (not shown).

Threshold currents and corresponding recruitment contours were also calculated for 5 μm fibres. The recruitment contours have almost the same shape as those in Fig. 3 (data not shown). With the single cathode (Fig. 3a), the threshold currents are approximately five times higher than for a 15 μm fibre, and this ratio decreases gradually to about three for the transverse tripole in Fig. 3e.

The above calculations predict that the transverse tripole is most able to activate selectively fibres in a region in front of the cathode. The properties of this transverse tripole will be further analysed in the following Sections.

3.2 Effects of transverse tripole geometry on threshold current and recruitment area

The influences of contact area and intercontact spacing of the transverse tripole on threshold current and spatial selectivity were further investigated. The parameters studied in this Section are defined in Fig. 3i: the angle Θ between the centres of the cathode and the anodes, the width W and the depth D of the recruitment contour. Suppose we want to activate a round nerve region, with a diameter of 0.55 mm, situated directly in front of the cathode. For that purpose, D is taken to be 0.7 mm (0.55 mm nerve + 50 μm perineurium + 50 μm epineurium + 50 mm saline), and W is measured at 0.45 mm from the central cathode (approximately the centre of the nerve region). W can be considered as an index for spatial selectivity. Ideally, W should equal the diameter of the nerve region ($W = 0.55$ mm).

In Fig. 4a, the effects of Θ on W and threshold current I are shown for contacts with a contact area of 0.5 mm² (0.5 mm wide and 1.0 mm long). For each value of Θ, the threshold current $I(0.5 \ mm²)$ of a 15 μm fibre situated at $D = 0.7$ mm was calculated, and, for each I, the recruitment contour was calculated, and $W(0.5 \ mm²)$ was determined. As expected, the
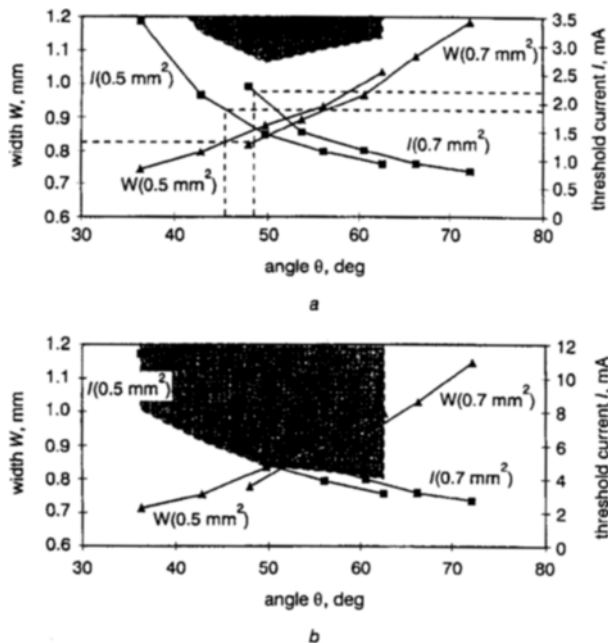
Fig. 4   *Width of recruitment contour W and threshold current I against anode–cathode angle Θ of transverse tripole; contact areas 0.5 or 0.7 mm²; (a) 15 μm fibre; (b) 5 μm fibre. Hatched areas indicate current range in which anodal excitation occurs (see Section 3.3). Dotted lines indicate currents needed to obtain W = 0.825 mm*

Fig. 5   *Threshold currents for 5 μm and 15 μm fibres (logarithmic scale) against distance to cathode D in (▲ and ×) longitudinal and (■ and ●) transverse tripole*

data show that a small Θ is related to a high I (most of the current flows from the anodes to the cathode through the saline layer) and a small W. At increasing Θ, I is reduced, whereas W is increased (more current penetrates the nerve bundle). The same calculations were made with contacts 0.7 mm wide instead of 0.5 mm wide and also 1.0 mm long (I(0.7 mm²) and W(0.7 mm²)), see Fig. 4a. Similar to the smaller contacts, a decreasing distance Θ leads to an increase in I and a reduction in W.

Fig. 4a shows that W = 0.55 mm and thus recruitment confined to the round nerve region cannot be obtained with the contact areas used. With smaller contact areas, W = 0.55 mm could presumably be obtained, but, in that case, the contacts need to be placed very close to one another (small Θ), and threshold currents would be very high. If we allow W to be 1.5 × 0.55 mm, a transverse tripole with 0.5 mm² contacts needs less current to obtain W = 0.825 mm (Θ = 45.4° and I = 1.88 mA) than a transverse tripole with 0.7 mm² contacts (Θ = 48.5° and I = 2.21 mA), as shown by the dotted lines in Fig. 4a.

Similar relationships were obtained for a 5 μm fibre instead of a 15 μm fibre (see Fig. 4b).

3.3 Effects of transverse tripolar stimulation on fibre recruitment

In the next series of simulations, the dependency of the threshold current I on stimulation depth D (Fig. 3i) and fibre diameter of the transverse tripole was calculated. In Fig. 5, the threshold currents for 5 μm and 15 μm fibres were calculated against the stimulation depth in front of the cathode (0.5 mm² contact area, Θ = 49.7°). As expected, the threshold currents increase considerably and progressively with fibre–cathode distance, and the threshold difference between small and large fibres increases as well, resulting in an increasing preferential activation of large nerve fibres.
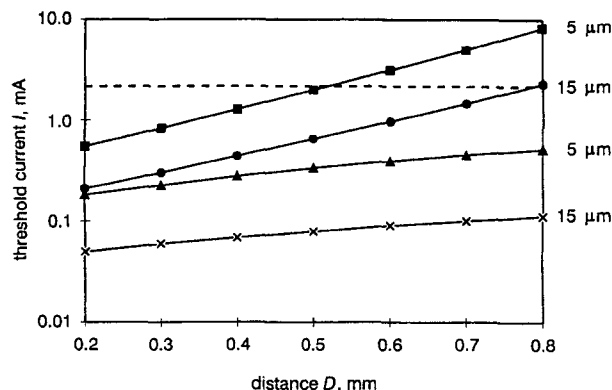
For comparison, the same calculations were made for the longitudinal tripole (configuration as in Fig. 3b) and included in Fig. 5. It is shown that the increase in threshold current for the transverse tripole is much larger than that for the longitudinal tripole. The diameter selectivity, defined as the threshold ratio of a 5 μm and a 15 μm fibre, is less for the transverse tripole (2.58 and 3.55 at D = 0.2 mm and 0.8 mm, respectively) than for the longitudinal tripole (3.67 and 4.60, respectively) (less 'inverse' recruitment).

Owing to virtual cathode/anode effects, an increasing current not only increases the area of recruited fibres near the cathode, but may also recruit fibres close to the anodes and block fibres close to the cathode. The probability of these
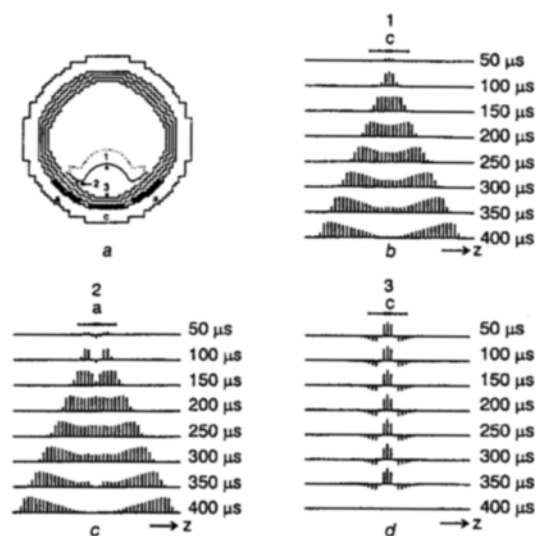

Fig. 6   *(a) Excitation region for a (—) 5 μm fibre and (···)15 μm fibre for a transverse tripole (0.5 mm² contacts, Θ = 36.3°, D = 0.7 mm, I = 11.45 mA). (b), (c) and (d) Deviation of membrane potential from resting potential at each Ranvier node of a 5 μm fibre, positioned at markers 1, 2, and 3 respectively, in (a); (b) cathodal action potential initiation and propagation; (c) initiation by virtual cathodes; (d) propagation block by virtual anodes. 50 μs intervals after stimulus pulse initiation (350 μs pulsewidth); depolarisation is shown by upward bars, hyperpolarisation is shown by downward bars; at the top, the cuff and the position of the anode (a) or cathode (c) relative to the Ranvier nodes are shown*

virtual cathode/anode effects increases for the smaller angle Θ, which increases the threshold current considerably (see Fig. 4).

In Fig. 6a, the recruitment contour for the excitation of 5 μm fibres (solid line) is shown for a transverse tripole with 0.5 mm² contact areas, $\Theta = 36.3°$ and $D = 0.7$ mm. The current needed to excite these fibres at the contour is 11.45 mA (the dotted line shows the recruitment contour for 15 μm fibres at the same current). In Fig. 6b, the response of a 5 μm fibre at marker 1 (Fig. 6a) is shown against node position at 50 μs intervals after stimulus pulse initiation.

Depolarisation starts at the node right under the cathode, and adjacent nodes at both sides are depolarised successively. The excitation of fibres close to an anode is due to the virtual cathodes at both sides of the anode in the z-direction, as shown in Fig. 6c, where the response of a 5 μm fibre at marker 2 (Fig. 6a) is shown. Initially, the nodes right under the anode are hyperpolarised, and the depolarisation/excitation starts at both sides (virtual cathodes).

In Fig. 4b, the hatched area indicates the current range in which a 5 μm fibre, situated 0.2 mm in front of the centre of an anode (0.5 mm² contacts), is excited as a result of virtual cathodes. It is shown that, for small angles Θ, the current at which anodal excitation occurs is less than the cathodal threshold current for a 5 μm fibre at 0.7 mm distance in front of the cathode. For 15 μm fibres, the current at which anodal excitation occurs is higher than the cathodal threshold current for all angles Θ (0.5 mm² contacts), as shown by the hatched area in Fig. 4a. Anodal excitation of small fibres, widening the recruited area, can be avoided by restricting the current (deeper-lying small fibres cannot be excited anymore), or increasing the angle Θ (spatial selectivity will be less).

Fig. 6d shows the response of a 5 μm fibre at marker 3 (Fig. 6a). The nodes right under the cathode are depolarised, but the action potential does not propagate beyond the virtual anodes. In Fig. 5, the dotted line indicates the blocking threshold of a 5 μm fibre at $D = 0.2$ mm for the transverse tripole. Thus, 5 μm fibres up to $D = 0.2$ mm are blocked when excitation of 5 μm fibres has reached a depth $D = 0.52$ mm. The cathodal blocking effect does not occur when the pulse duration is significantly shorter than the duration of the action potential.

3.4 Sensitivity of threshold current to volume conductor model parameters

The precise values of the conductivities of perineurial and epineurial tissue are not known from literature. The conductivity of the perineurium was derived from WEERASURIYA et al. (1984), using the same calculation as FRIESWIJK et al. (1997). The conductivity of the epineurium was chosen higher than the perineurial conductivity, but of the same order (GOODALL et al., 1995). Because the thicknesses of these layers vary among nerves, it is not possible to predict accurately the value of threshold currents of fibres in a nerve by modelling alone.

The thickness of the perineurium roughly equals 5% of the diameter of the fascicle (SUNDERLAND, 1978). Because the minimum grid spacing in the model was 50 μm, both the perineurium and the epineurium layer were given a thickness of 50 μm. While the geometry of the model was kept constant, the conductivities of these layers were varied.

The same electrode configuration as in Fig. 3e was used (contact area = 0.5 mm², $\Theta = 49.7°$). For five conductivity values of the perineurium and the epineurium (0.25σ, 0.5σ, σ, 2σ and 4σ (with σ as in Table 1)) the threshold currents were calculated for a 15 μm fibre at $D = 0.7$ mm, as shown by the upper curves in Figs. 7a and b.
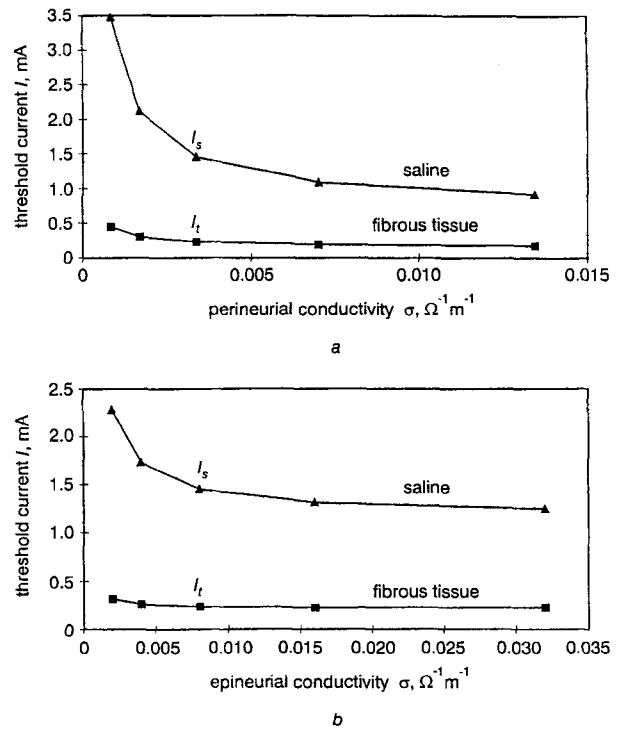

Fig. 7 *Threshold current I against (a) perineurial and (b) epineurial conductivity for a nerve surrounded by saline or fibrous tissue. $I_s = 1.47$ mA, $I_t = 0.23$ mA*

With the conductivity values of perineurium and epineurium as in Table 1, the threshold current was 1.47 mA (I_s). For small values of σ, higher currents are needed. Because the difference in conductivity between perineurium and fascicle is larger than the difference between epineurium and fascicle, the threshold current is more sensitive to changes in the perineurial conductivity. At a 16-fold increase of σ_{peri} and σ_{epi}, threshold currents are reduced to 26% and 55%, respectively. The influence of changing the conductivity values on the shape of the recruitment contours of the transverse tripole is minimal.

When cuff electrodes are chronically implanted, they will become encapsulated by fibrous tissue ($\sigma_{fibrous-tissue} = 0.16$ $\Omega^{-1}m^{-1}$ (GRILL and MORTIMER, 1994)). Therefore the modelled conductivity of the saline layer surrounding the nerve and cuff was changed into this fibrous-tissue conductivity, and the calculations were repeated, resulting in the lower curves in Figs. 7a and b.

With the conductivity values of perineurium and epineurium as in Table 1, the threshold current is now 0.23 mA (I_t). It is shown that the reduced conductivity of the layer between the cuff and the epineurium reduces the threshold currents by a factor of 5–8. Threshold currents are now less sensitive to variations in the conductivity of the perineurium and epineurium: they are reduced to 39% and 71% at a 16-fold increase of σ_{peri} and σ_{epi}, respectively.

If no saline layer or fibrous tissue layer is modelled in the transverse tripole, implying layers of perineurium and epineurium between fascicle and cuff electrode only, the values for the threshold current are reduced significantly and come close to the values for the single cathode (Fig. 3a). The same effect is seen when a cuff electrode with only a nerve trunk in it (no perineurium, no epineurium, no saline or fibrous tissue) is modelled. Therefore larger differences in conductivities of the nerve trunk and the surrounding layers result in higher

threshold currents. A saline layer (present in an acute experiment) is therefore less favourable than a layer of fibrous tissue having the same thickness (present in a chronic implant). A spiral cuff (NAPLES et al., 1988) in contrast to other cuff electrodes, reduces the saline layer thickness between nerve and cuff to a minimum.

4 Discussion and conclusions

The model applied in this study to investigate the position selectivity of nerve fibre stimulation obtainable by various anode–cathode configurations in a nerve cuff can only be used to predict changes in threshold currents and recruitment contours as related to changes in model parameters, and not their absolute values, unless precise data on the conductivities of the various tissues and their thicknesses at the site of stimulation are known.

A simple, monofascicular nerve, surrounded by layers of perineurium, epineurium and saline, was modelled. Preliminary results from simulations using a multifascicular nerve (four fascicles, each surrounded by a layer of perineurium and epineurium) showed that recruitment contours had a similar shape to that for the monofascicular model (unpublished data). Therefore it is expected that conclusions regarding selective stimulation of fibres in the periphery of a monofascicular nerve will be applicable to selective stimulation of small fascicles in the periphery of a multifascicular nerve or a spinal anterior root as well.

Several experimental and theoretical studies have been performed to test the spatial selectivity obtainable by a longitudinal tripole electrode configuration with a transverse 'steering' anode (SWEENEY et al., 1990, 1995; CHINTALA-CHARUVU et al., 1991; VERAART et al., 1993; GOODALL et al., 1996; GRILL and MORTIMER, 1996). In all these studies it was concluded that an additional transverse current improves the spatial selectivity of a longitudinal tripole. Our simulations show the same result.

SWEENEY et al. (1995), and GRILL and MORTIMER (1996) expressed the amplitude of the steering current as a percentage of the transverse (bipolar) threshold. In our simulations the transverse current was a fixed percentage of the cathodal current. Therefore the 40% transverse current used in Fig. 3c corresponds to 34% ($D = 0.3$ µm), 48% ($D = 0.5$ mm), and 66% ($D = 0.7$ mm) of the transverse threshold. 70% transverse current (discussed in Section 3.1 but not shown in Fig. 3) corresponds to 72, 115 and 170% of the transverse threshold, respectively. Because of the difference in definition of transverse current, the results cannot be compared quantitatively, but they do agree qualitatively.

GOODALL et al. (1996) already noted that spatial selectivity is optimised when the transverse current is a high proportion of the total current. As would be expected, an increase in the transverse current to 100% of the cathodal current (thus representing transverse bipolar stimulation) indeed gives the best spatial selectivity. However, we have shown theoretically that recruited areas are still rather wide, thus hampering the selective activation of a small (cylindrical) bundle of fibres in the periphery of a nerve. This could be the reason why SWEENEY et al. (1995) were not able to activate the soleus muscle selectively by sciatic nerve stimulation, which is, however, difficult to verify because they did not show cross-sections of the nerve at the site of stimulation.

At low current levels, all electrode configurations are able to activate selectively fibres close to the cathode. At higher current levels, the current mainly spreads tangentially along the periphery of the nerve trunk with most configurations and thus activates a wide area at both sides of the cathode. Conversely, we have shown that stimulation with a transverse tripole gives convex recruitment contours and is therefore most suitable to activate selectively a cylindrical or oval bundle of fibres in the periphery of the nerve, even at higher current levels. HOLLE et al. (1984) used four epineural electrodes equally spaced around the nerve in their 'roundabout' stimulation system. By periodic change of the electrode combinations used for stimulation, they were able to activate different fibre groups alternately. They stimulated with $\Theta = 90°$, which is too large to limit stimulation of fibres in a tangential direction.

The same applies to GRILL and MORTIMER (1996), who performed experiments with a longitudinal tripole with a 'steering' anode at a transverse angle of 90° from the cathode. In this way, they were able to modify the region of excitation. This method can be used, for example, when the area that has to be excited is not lying directly in front of the cathode but a little to one side. In transverse tripolar stimulation, this can be achieved by using asymmetrical stimulation (different anodal currents), as in spinal cord stimulation (STRUIJK and HOLSHEIMER, 1996).

A similar theoretical comparison of different electrode configurations and tissue conductivities in and around the nerve trunk has been performed by CHINTALACHARUVU et al. (1991). Their simulations are qualitatively in accordance with ours. A quantitative comparison, however, was not possible, owing to different geometries and conductivities in both models. The authors suggest that the concave shape of the recruitment contours of a single cathode or a longitudinal tripole with a transverse 'steering' current is caused by the anisotropy of the nerve trunk. We have shown that the concave shape is primarily caused by the inhomogeneities introduced by the layers surrounding the nerve trunk. In transverse tripolar stimulation, this effect is cancelled and the shape is reversed into a convex one, due to the shielding effect of the close anodes.

In contrast to a longitudinal tripole, the main current flow in transverse bi- or tripolar stimulation is perpendicular to the orientation of the nerve fibres, whereas the driving force of fibre stimulation is related to the longitudinal current component (RATTAY, 1986). Therefore transverse tripolar stimulation necessitates more current for fibre excitation. As higher currents are used, virtual cathode/anode effects may complicate fibre recruitment.

Changing the contact spacing of the transverse tripole has a relatively large influence on the threshold current and the width of the recruitment contour. To obtain a narrow recruited area, the contact area and intercontact spacing need to be small, and threshold currents and current densities will be high. The charge requirements for a transverse tripole are higher than for conventional cuff electrode configurations. For example, to excite the 15 µm fibre at $D = 0.7$ mm in Fig. 3e ($I = 1.471$ mA) would require 103 µC cm^{-2}. This value exceeds the estimated reversible charge injection limits of platinum electrodes (24–74 µC cm^{-2} for charge-balanced pulses), with the potential risk of electrode corrosion or tissue damage (ROBBLEE and ROSE, 1990). If, however, iridium oxide-coated electrodes are used, this charge requirement of 103 µC cm^{-2} is much smaller than the estimated reversible charge injection limits (1000–3000 µC cm^{-2} for charge-balanced pulses). Moreover, for the example given above, unfavourable circumstances have been assumed: the smallest electrode surface (0.5 mm^2), a saline layer in the cuff instead of fibrous tissue, a long excitation pulse (350 µs) and a relatively large fascicle ($d = 1.9$ mm).

The lack of selective activation of centrally positioned fascicles with a nerve cuff electrode has already been noted by VELTINK et al. (1989). The current study shows that, with transverse tripolar stimulation, deeper-lying fibres cannot be activated selectively, because the threshold current to excite fibres increases rapidly against fibre–cathode distance. This basic problem can be overcome by the use of subthreshold depolarising pre-pulses, which generate a transient decrease in neural excitability and thus an increase in the threshold for stimulation by a subsequent stimulus pulse. In this way, an inversion of the threshold current–distance relationship can be obtained, which allows selective stimulation of nerve fibres distant from the electrode, as shown both theoretically and experimentally by GRILL and MORTIMER (1995, 1997).

We have also shown that, for the transverse tripole, the threshold ratio of small and large fibres is lower than for all other configurations (less 'inverse' recruitment). When taking into account the actual positions of Ranvier nodes with respect to the cathode, stimulation of small fibres is favoured even more at low recruitment levels (VELTINK et al., 1988). The central node of the fibres was always placed at the centre of the cathode. Simulations with the transverse tripole with the central node offset by one-half of one internodal length show that the threshold current is higher, but the shape of the recruitment contours does not change significantly.

Nerve cuff electrodes are intended for chronic use in human FES applications. The electrodes then become encapsulated by a small layer of fibrous tissue. GRILL and MORTIMER (1994) noted that the growth of encapsulation tissue might modify the region of tissue activated by stimulation. Simulations with fibrous tissue instead of saline predict that the shape of the recruitment contours in transverse tripolar stimulation will not change significantly, only the threshold currents will be lower by a factor of 5–8. In reality, the difference in thresholds might be less, owing to a saline layer (between nerve and cuff) that is smaller than we modelled (50 μm), whereas a realistic fibrous tissue layer approximately fits the modelled layer. The present study also indicates that fewer electrodes are needed than in the 12-contact spiral nerve cuff of VERAART et al. (1993). In the case of transverse tripolar stimulation, only one row of contacts is needed. The number of contacts, presumably between five and ten, depends on the diameter of the fibre bundle to be activated.

Transverse tripolar cuff electrodes will thus activate bundles of fibres in the periphery of a nerve trunk in a more selective way than other electrode configurations do. Threshold currents for fibre excitation will be higher than in other cuff electrode configurations, as, generally, stimulation current increases with improving spatial selectivity. These predictions on transverse tripolar stimulation will have to be validated in animal experiments.

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