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Modeling Deep Brain Stimulation: Point Source Approximation vs. Realistic Representation of the Electrode

Tianhe C Zhang and Warren M Grill

Department of Biomedical Engineering, Duke University

Abstract

Deep brain stimulation (DBS) has emerged as an effective treatment for movement disorders; however, the fundamental mechanisms by which DBS works are not well understood. Computational models of DBS can provide insights into these fundamental mechanisms and typically require two steps: calculation of the electrical potentials generated by DBS and, subsequently, determination of the effects of the extracellular potentials on neurons. The objective of this study was to assess the validity of using a point source electrode to approximate the DBS electrode when calculating the thresholds and spatial distribution of activation of a surrounding population of model neurons in response to monopolar DBS. Extracellular potentials in a homogenous isotropic volume conductor were calculated using either a point current source or a geometrically accurate finite element model of the Medtronic DBS 3389 lead. These extracellular potentials were coupled to populations of model axons, and thresholds and spatial distributions were determined for different electrode geometries and axon orientations. Median threshold differences between DBS and point source electrodes for individual axons varied between -20.5% and 9.5% across all orientations, monopolar polarities, and electrode geometries utilizing the DBS 3389 electrode. Differences in the percentage of axons activated at a given amplitude by the point source electrode and the DBS electrode were between -9.0% and 12.6% across all monopolar configurations tested. The differences in activation between the DBS and point source electrodes occurred primarily in regions close to conductor-insulator interfaces and around the insulating tip of the DBS electrode. The robustness of the point source approximation in modeling several special cases--tissue anisotropy, a long active electrode, and bipolar stimulation--was also examined. Under the conditions considered, the point source was shown to be a valid approximation for predicting excitation of populations of neurons in response to DBS.

1. Introduction

Deep brain stimulation (DBS) is a surgical therapy involving electrical stimulation of the thalamus, basal ganglia, or other subcortical structures. It has emerged as an effective procedure to treat movement disorders such as Parkinson's disease and essential tremor and shows promise for the treatment of epilepsy, drug-resistant depression, and obsessive compulsive disorder (Kringelbach *et al* 2007). However, the fundamental mechanisms by which DBS works are currently not known, and even the cellular-level effects of stimulation, such as excitation, inhibition, and block, remain unclear (McIntyre and Grill 2000). The neural response to DBS is dependent on myriad factors including electrode geometry, the electrical properties of surrounding tissue, and stimulation parameters (Kuncel and Grill 2004), and computational modeling is a tool that can be used to determine the effects of DBS on neurons.

Determining the effects of DBS on surrounding neurons requires two steps: first, calculation of the extracellular potentials generated in the tissue by the DBS electrode, and second, determining the effects of these potentials on neurons. Extracellular electrical potentials can be calculated using an analytical expression by approximating the DBS electrode as a point source, or the potentials can be calculated numerically using a realistic model of the stimulation electrode and the extracellular environment. The analytical point source approximation is fast and easy to implement, and earlier studies using the point source approximation have revealed key insights into the response of neural elements to electrical stimulation (McIntyre and Grill 1999, McIntyre and Grill 2000). In addition, faster, more efficient approximations are useful when estimates of the volume of tissue activated are needed, but computational resources are unavailable or inaccessible, such as during device programming. However, this simpler model neglects the geometry of the electrode, which could affect neural activation thresholds. Numerical solutions that account for the geometry of the electrode and the properties of the surrounding tissue offer more realistic depictions of the potentials generated by DBS (e.g., Butson and McIntyre 2005). As a result, they are more effective at predicting the specific populations affected by stimulation and likely have utility in delineating differences between activation of neurons targeted for the desired clinical effect and activation of non-target neurons that produce unwanted side effects (Miocinovic *et al* 2006), including symptom exacerbation (Cooper *et al* 2008). However, they are computationally expensive, more challenging to implement, and time-consuming to operate.

The objective of the present study was to determine whether a point source approximation is a valid representation of the DBS electrode when calculating the number and spatial distribution of neurons activated around the electrode. The effects of stimulation polarity, axon orientation, tissue anisotropy, electrode geometry, and monopolar vs. bipolar stimulation on the differences between the two representations of the electrode were quantified. Under the conditions examined, the point source approximation was valid for the prediction of the input-output properties describing activation of a population of neurons. The findings of this study will aid in simplifying future computational modeling studies of DBS and facilitate the development of optimal stimulation parameters. Some preliminary results were previously reported in a conference paper (Zhang and Grill 2009).

2. Methods

2.1. Calculation of Extracellular Potentials

Extracellular potentials were calculated using either a geometrically accurate model of the DBS electrode or an idealized point source electrode. A three-dimensional model of the clinical electrode was created using the finite element method with dimensions based on the Medtronic DBS 3389 electrode (Minneapolis, MN). The electrode model consisted of four cylindrical conductive contacts ($\sigma=4 \cdot 10^6$ S/m) 1.27mm in diameter and 1.5mm in height separated by insulating bands ($\sigma=1 \cdot 10^{-10}$ S/m) 0.5mm in height, as well as an insulating hemispherical tip with radius 0.635mm beginning 1.5 mm below electrode zero (Figure 1). The electrode was positioned in a homogeneous, isotropic volume conductor with a conductivity of $\sigma=0.2$ S/m (Ranck 1963). The volume conductor was modeled as a box measuring 6 cm by 6 cm by 6 cm using Dirichlet boundary conditions ($V=0$) on the sides and a constant voltage boundary condition (1V) at the active electrode(s). The model was implemented using COMSOL Multiphysics (Comsol Inc., Stockholm, Sweden) and meshed using an adaptive algorithm that produced smaller elements near the electrodes and larger elements at the boundaries of the volume conductor; a total of 54425 tetrahedral elements were generated in the mesh.

The generalized form of Laplace's equation was solved using an algebraic multigrid preconditioner and a conjugate gradient solver to determine the potentials (V) throughout the modeled volume:

$$\nabla \cdot \sigma \nabla V = 0 \quad (1)$$

Current density distributions within the model were calculated from potentials using Ohm's Law:

$$J = -\sigma \nabla V \quad (2)$$

The total current delivered by an active electrode was determined by integration of the current density over the outer boundaries of the volume conductor. The model was refined by either individually doubling the volume by increasing the length of the edges of the tissue box or doubling the mesh resolution by increasing the number of mesh elements. This procedure was continued until extracellular potentials within the region of interest (i.e., within 3 mm of the electrode) or total current flowing out of the electrode did not change by more than 5% versus the previous refinement iteration.

Extracellular potentials generated by a point source located at the origin and delivering current I_0 to a homogeneous, isotropic medium of conductivity σ were calculated at the location of nodes of Ranvier given by (x, y, z) using equation (3):

$$V(x, y, z) = \frac{I_0}{4\pi\sigma \sqrt{x^2 + y^2 + z^2}} \quad (3)$$

A point source approximations of each electrode configuration was made by positioning a point source at what would have been the geometric center of the respective DBS electrode contact. Extracellular potentials due to bipolar point source stimulation were calculated using superposition.

2.2. Population Model of Myelinated Axons

Neural excitation by the extracellular potentials was calculated using a population of model myelinated nerve fibers. A cable model of a 2.5 μm diameter myelinated axon (Sweeney *et al* 1987) was implemented in NEURON (Version 6.1, Hines and Carnevale 1997) to quantify the response of a population of neurons to extracellular stimulation. Each node of Ranvier was modeled as a single electrical compartment connected to other nodes via a series resistance, and to the extracellular medium by a parallel circuit consisting of a voltage-gated sodium channel, a linear leakage conductance, and a membrane capacitance with parameters derived from voltage clamp recordings of mammalian myelinated axons (Chiu *et al* 1979). Internodal lengths were 100 times the axon diameter, and the diameter of the Node of Ranvier was 0.7 times the axon diameter (Rushton 1951). Populations of 100 axons oriented 0° (parallel), 30°, 60°, and 90° (perpendicular) with respect to the central axis of the DBS electrode (Figure 1), were randomly distributed in the volume conductor such that no axon passed through the region occupied by the realistic electrode. Thus, the same populations could be used to analyze both the point source and realistic DBS electrode. The closest distance between the axon and the geometric center of the electrode was between 0.7 mm and 3 mm. Central node locations were randomized such that the distance between the central node and the plane corresponding to the closest point between the axon and the electrode center varied between 0 and 0.5 internodal lengths. Potentials at each node of

Ranvier were calculated from the potentials at the FEM grid points using 4-point cubic interpolation. Thresholds to excite axons in response to 100 μ s duration rectangular monophasic pulses were calculated to within 1% using a binary search algorithm.

To compare voltage stimulation by the DBS electrode with current stimulation by the point source, a conversion factor was calculated by determining the current delivered by the DBS electrode when the active contact(s) were set to 1 V using surface integration of the current density. Thresholds calculated in volts using the DBS electrode model were then converted to currents via direct multiplication by the conversion factor.

3. Results

3.1. Realistic Model Geometry vs. Point Source Approximations: Extracellular Potentials

The validity of using the point source approximation to calculate the extracellular potentials generated by DBS was quantified. Square grids with side lengths of 6 mm, centered on the origin and containing points equally spaced 0.02 mm apart, were created and oriented parallel and perpendicular to the electrode. The differences in potentials generated with the point source and DBS electrodes were calculated at each point on these grids (Figure 2). The percent errors between point source and DBS electrode calculated potentials ranged from -29.8% to 18.4% (r.m.s. error = 0.0298 V, 9.82%); deviations between calculated potentials were greatest at points near conductor-insulator interfaces and near the insulating tip of the realistic electrode. However, when the viewing axis was parallel to the electrode, near-field effects were less apparent, and errors ranged from -12% to -3% (r.m.s. error = 0.0263 V, 7.75%).

3.2. Realistic Model Geometry vs. Point Source Approximation: Response to Monopolar Stimulation

Input-output curves of the percent of the population of axons activated as a function of the stimulation amplitude were calculated using the point source and DBS electrodes. Figure 3 shows the input-output curves of axons of various orientations in response to anodic and cathodic stimulation for three monopolar electrode configurations. Anodic thresholds were consistently higher than cathodic thresholds; the average current required to activate 50% of the axon in a population using anodic stimulation was greater than the current required using cathodic stimulation by a factor of 4.5 using the point source approximation and 4.1 using the DBS electrode. Although the thresholds for anodic stimulation and for axons oriented more parallel to the electrode calculated with the DBS electrode were slightly lower, the input-output curves calculated with the point source approximation were remarkably similar to those predicted by the realistic models for all monopolar configurations.

Differences in input-output properties between the two representations of the electrode were visualized by plotting the percentage of axons activated by point source stimulation against the percentage activated by the DBS electrode as the stimulus intensity was progressively increased to activate an increasing proportion of axons in the population (Figure 4). The percentage of axons activated as predicted by the point source approximation correlated well with that activated by the DBS electrode, and the deviation of the percentage of axons activated and the percentage of axons which would have been activated if the DBS and point source electrode were identical (percent deviation) varied from -9% to 12.4% for anodic stimulation and from -8.0% to 8.0% for cathodic stimulation across all stimulation amplitudes and monopolar configurations tested.

Differences between the thresholds for individual axons calculated with the point source electrode and DBS electrode were quantified across electrode contact and polarity (Figure 5). The median error for cathodic stimulation ranged from -5.7% to 0.7% across all

orientations and monopolar configurations. Median errors were greater for anodic stimulation than for cathodic stimulation and ranged from -20.7% to 9.5% . Outliers were defined as axons with differences in threshold that exceeded 1.5 times the interquartile ranges above or below the median threshold difference. Most outliers in populations of axons perpendicular to the electrode were located underneath the insulating tip of the DBS electrode for both anodic (6/10 outliers) and cathodic stimulation (12/22 outliers). For both groups of outliers, the DBS electrode predicted larger excitation thresholds than the point source approximation. Similar trends were observed for activation of populations of axons with a diameter of $5\ \mu\text{m}$ oriented perpendicular and parallel to the electrode axis (median errors -13.0% to 2.8% , with similar outliers trends), suggesting that these trends were not sensitive to fiber diameter. A previously published sensitivity analysis also indicated that these differences were not sensitive to monophasic stimulus pulse durations between $10\ \mu\text{s}$ and $500\ \mu\text{s}$ (Zhang and Grill, 2009).

3.3 Realistic Model Geometry vs. Point Source Approximation: Special Cases

3.3.1. Tissue Anisotropy—The effect of tissue anisotropy on activation was assessed by quantifying the response of axons oriented perpendicular and parallel to the electrode axis in an anisotropic medium, where the axis of higher conductivity was parallel to the axon orientation. The conductivity along this axis was set to 5 times ($1.0\ \text{S/m}$) or 10 times ($2.0\ \text{S/m}$) the conductivity along the perpendicular axes ($0.2\ \text{S/m}$) (Nicholson 1965, Tuch et. al. 2001). The thresholds calculated with the DBS electrode were consistently lower than those calculated with the point source approximation across all orientations and polarities examined (median errors: -22.2% to -3.7% ; Figure 6(a)), and percent deviations in the population model never exceeded 16% .

3.3.2 DBS Electrode Length—The effect of electrode contact size was assessed by comparing predictions between the point source approximation and a realistic model of the DBS 3391 electrode (radius = 0.635mm , height = 3mm). Differences in predicted thresholds were small for anodic stimulation and cathodic stimulation when axons were oriented perpendicular to the electrode. Under these conditions, median errors ranged from -7.1% to -0.2% (Figure 6(b)), and percent deviations in the population model never exceeded 11% . However, the realistic model predicted substantially higher thresholds (median error: 64.8% ; Figure 6(b)) and less population activation (maximum difference vs. point source: -33%) for axons oriented parallel to the electrode axis undergoing cathodic stimulation. These large differences suggest that the point source is not an appropriate approximation for this larger electrode contact.

3.3.3 Bipolar Stimulation—The validity of the point source approximation of bipolar stimulation was also analyzed. Differences between thresholds were generally small, and median errors ranged from -2.5% to -0.1% across all orientations tested. Outliers in axons perpendicular to the DBS electrode were primarily confined to the region between the two active electrodes (8/15 outliers). In axons parallel to the electrode, outliers were located within $1\ \text{mm}$ of the central axis (10/11 outliers). For these cases, the DBS electrode predicted smaller excitation thresholds than the point source approximation (Figure 6(c)). However, predictions of the percentage of the axon population activated by the point source and realistic model were similar across the range of stimulation amplitudes and orientations tested.

3.4. Patterns of Activation: Realistic Model Geometry vs. Point Source Approximation

Input-output curves enabled quantitative comparisons of the *number* of axons activated with the point source approximation and the DBS electrode, but they did not enable comparison of the *spatial distribution* of activated axons. Therefore, we generated threshold contours by

interpolation of thresholds for activation of individual axons distributed on a 0.1 mm by 0.1 mm grid within 3 mm of the geometric center of the electrodes (excluding the region occupied by the realistic electrode) either perpendicular or parallel to the electrode axis (Figures 7 and 8). The shape and magnitude of the threshold contours generated by the point source and DBS electrodes were similar, especially in the bipolar case, and the greatest differences lay near conductor/insulator interfaces, around the inactive contact, and below the insulating tip of the DBS electrode.

To quantify the differences in the spatial distribution of activation between the point source and DBS electrodes, we calculated the total cross-sectional area of tissue activated as a function of the stimulation amplitude for monopolar (cathodic) and bipolar geometries (Figure 9) for axon orientations perpendicular and parallel to the electrode. Cross-sectional planes over which areas were calculated were perpendicular to and included all axons in the population being examined. The cross-sectional areas activated by the point source and DBS electrode were quite similar, and differences between the point source and DBS electrode did not exceed 2 mm² across all geometries tested. The largest difference was observed for monopolar cathodic stimulation of axons perpendicular to the electrode, for which the point source predicted 1.87 mm² more tissue activated than the DBS electrode (10.33%) with a 9 mA stimulus. This difference reflected the increased amplitudes required to activate neurons underneath the insulating tip of the electrode (Figure 7).

4. Discussion

The objective of this study was to quantify the differences in neural excitation thresholds between a point source approximation and a geometrically realistic model of a DBS electrode. The point source and realistic models predicted similar activation thresholds for axons located within 3 mm of the active electrode. Differences in thresholds of individual axons were greatest in regions close to specific geometric features of the realistic electrode, including the insulating tip, conductor-insulator interfaces, and in the vicinity of an inactive contact (Figures 7, 8). Activation of an axon in response to an extracellular field is driven by the second spatial derivative of the extracellular potentials along the neuron - the activating function - (Rattay 1989), and the activating function was most different near these specific geometries or at electric discontinuities. For example, the insulating tip at the base of the electrode shields the region directly underneath the electrode from current flow; this has the effect of creating a “notch” in the values of $\Delta^2 V / \Delta x^2$ for axons positioned underneath the electrode (Figure 7). In contrast, current density is greatest at the conductor/insulator interfaces on the stimulation electrode (Rubinstein *et al* 1987), and these discontinuities generate larger activating functions (Wei and Grill 2005). Similarly, the inactive electrodes, which are not present in the point source model, act as secondary sources that distort the spatial distribution of potentials and thus the activating functions of nearby axons. Near field effects due to inactive electrode contacts distorted the activating function at the depolarized flanking nodes during anodic stimulation of axons oriented at 30° and 0°. This effect and the observation that action potential initiation due to anodic stimulation occurs at a depolarized flanking node in proximity to the nearest inactive electrode contact resulted in greater variability in anodic stimulation thresholds. Tissue anisotropy further amplified these distortions, resulting in larger differences between thresholds predicted with the realistic model and the point source approximation. However, these near-field effects rapidly diminished as electrode to neuron distance increased, and both input-output curves and assessments of overall population behavior (e.g., parametric plots, threshold contours) were strikingly similar between the point source and DBS electrodes.

Despite differences in thresholds between individual model axons, the responses of populations of axons (i.e., input output curves) were generally similar for the point source

and DBS electrodes. The differences in the proportion of model axons activated at the same intensity of stimulation were less than 16% across most electrode geometries, axon orientations, and stimulus polarities for monopolar and bipolar stimulation. These findings can be reconciled by observing that axons activated at lower thresholds were offset by other axons activated at higher thresholds when considering activation of a population. Near-field effects on the threshold of individual axons due to the geometry of the electrode were most pronounced close to the electrode and resulted in both larger and smaller thresholds than those predicted from the point source. These deviations canceled each other out when considering activation of a population of axons, and the point source and DBS electrodes activated a similar number and spatial extent of axons at the same stimulation intensities.

Only one electrode geometry - DBS 3391 electrode, cathodic stimulation, axons parallel to electrode - could not be reasonably approximated by the point source. This is the case because the longer DBS 3391 electrode produced an elliptical isopotential contour in contrast to circular isopotential contours produced by the point source or the shorter electrode. The isopotential contours generated by the DBS 3391 electrode caused the potentials along the nodes of Ranvier of parallel axons passing close to the electrode to be quite similar (i.e. a smaller activating function) where the point source predicted a peak (i.e. a larger activating function), resulting in higher thresholds for parallel axons than predicted by the point source. This finding indicates that the validity of the point source approximation is sensitive to electrode geometry, and it represents a case where the point source approximation should not be used to predict regional activation in response to electrical stimulation.

The primary implication of these results is that under the conditions tested, the use of simpler, more easily implemented models gave results similar to those generated using complex, computationally expensive models. Although differences in individual axon threshold predictions exist, it is clear that clinical efficacy requires activation of a critical volume or number of neurons (McIntyre *et al* 2004b, Kuncel *et al* 2007). However, several general limitations of this study should be considered when determining the appropriate model to implement for computational studies. First, for most simulations, the tissue medium was modeled as a homogeneous, isotropic volume conductor. This assumption is supported by recent studies showing that gray matter regions in the brain have relatively uniform electrical properties (Logothetis *et al* 2007) and that anisotropy and inhomogeneity do not have a substantial effect on the volume of tissue activated by DBS (Miocinovic *et al* 2009). Additionally, our simulations of anisotropy indicated that the point source approximation could reasonably predict trends in population activation in an anisotropic medium. However, tissue inhomogeneity within and outside of the stimulated nucleus (Grill 1999) and effects from tissue encapsulation (Grill and Mortimer 1994) may still influence the actual volume of tissue activated in response to a stimulus pulse (Butson *et al* 2007). As well, the quasistatic approximation was employed when calculating extracellular potentials. Although the quasi-static approximation has been shown to be valid for neural stimulation (Bossetti *et al* 2008), previous studies suggest that tissue capacitance can influence the volume of tissue stimulated (Butson and McIntyre 2005). Furthermore, clinical DBS systems employ biphasic pulses whose temporal profiles are filtered by the capacitive component of the electrode-tissue interface impedance (Butson and McIntyre 2005). Thus, near-field effects in the region of the realistic electrode, especially around conductor/insulator interfaces where current densities are highest (Rubinstein 1987), may be more pronounced, resulting in larger errors between thresholds predicted by the point source approximation and realistic models.

The model axon included only a non-linear sodium conductance and a linear leakage conductance (Sweeney 1987). This model enabled relatively rapid calculation of the

response of a population to stimulation and is likely more accurate than estimates of the region of activation based solely on values of the activating function (Warman *et al* 1992, Moffitt *et al* 2004). However, more complex, multi-compartmental models which incorporate realistic membrane currents and channel kinetics (McIntyre *et al* 2002) may more accurately represent the response of human myelinated axons in the basal ganglia. As well, the modeled populations did not include other neural elements, and the response of local cell bodies (McIntyre *et al* 2004a) or presynaptic terminals (Grill *et al* 2007) might differ substantially from the response of passing axons. Previous computational studies have indicated that local cell bodies and axons of passage respond similarly to monophasic bipolar stimulation, but that differences exist in the response of these neural elements to monophasic monopolar stimulation (McIntyre and Grill 2000). Furthermore, presynaptic terminals are typically activated at lower thresholds, and stimulation of these terminals in the basal ganglia circuit may be directly related to tremor suppression (Anderson *et al* 2006, Gradinaru *et al* 2009).

5. Conclusions

Approximation of the DBS electrode as a point source is a valid simplification for the calculation of the number and spatial distribution of activation of a population of axons in response to DBS. Differences between individual thresholds, input-output behavior, and the spatial distribution of activation predicted by a point source and realistic model of the DBS electrode were quantified and shown to be small. The results of this study will aid in future computational studies and provide insights that may lead to more optimized DBS electrode designs.

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Figure 1.

Depictions of axon populations and electrode geometries that were tested. Axons were oriented 90° (a), 60° (b), 30° (c), and 0° (d) with respect to the electrode axis, and axons were seeded such that none passed through the region occupied by the realistic electrode. DBS electrode contacts were numbered in ascending order from the electrode closest to the tip (Electrode 0) to the electrode farthest away from the tip (Electrode 3). Stimulation geometries included 3 monopolar configurations (Electrodes 0, 1, 2) and one bipolar configuration (Electrodes 1, 2). In the bipolar configuration, the active contacts were set to equal amplitudes of opposite polarity.

Figure 2.

False color plots depicting extracellular potentials generated by point source and realistic (Electrode 0) modeling of DBS at 1V (and equivalent current for point source). Origin is defined at the geometric center of the active monopolar DBS electrode.

Figure 3.

Input-output curves showing the relationship between current delivered during stimulation (mA) and the percentage of the axon population activated. Plots are grouped by active monopolar electrode and stimulation polarity.

Figure 4.

Parametric plots mapping the relationship between the % of axons activated by the point source versus the % of axons activated by the DBS electrode with the parametric variable being the stimulation current amplitude. Plots are grouped by active monopolar electrode and electrode polarity.

Figure 5.

Box and whisker plots showing distribution of individual percent difference between thresholds determined using a monopolar point source electrode and the DBS electrode relative to point source thresholds. The center line of each box represents the median error while the lower and upper bounds of each box represent the lower and upper quartiles, respectively. Whiskers indicate 1.5 times the interquartile range; outliers are depicted by (+). The number of outliers is denoted above each respective box and whisker plot.

Figure 6.

Box and whisker plots showing distribution of individual percent difference between thresholds calculated when stimulating in an anisotropic medium (principal axis: 10x conductance) **(a)**, a long DBS 3391 electrode **(b)**, and a bipolar point source and a bipolar DBS electrode (Electrodes 1 and 2) relative to point source thresholds **(c)**. The center line of each box represents the median error while the lower and upper bounds of each box represent the lower and upper quartiles, respectively. Whiskers indicate 1.5 times the interquartile range; outliers are depicted by (+). The number of outliers is denoted above or below each respective box and whisker plot.

Figure 7.

False color filled contour plots indicating the range of activation thresholds due to monopolar cathodic stimulation of axons passing through distinct colored regions. Note that the volume occupied by the realistic electrode is excluded.

Figure 8.

False color filled contour plots indicating the range of activation thresholds due to bipolar stimulation of axons passing through distinct colored regions. Note that the volume occupied by the realistic electrode is excluded. In the perpendicular orientation, a red point denotes an anodic source and a blue point denotes a cathodic source.

Figure 9.

Plots of bulk spatial activation versus stimulus amplitude for monopolar, cathodic stimulation and bipolar stimulation. "Area activated" refers to the cross-sectional area in the planes shown traversed by activated axons.