

Introduction: Motor cortex stimulation (MCS) is a promising clinical technique for treatment of chronic pain. However, optimization of the therapeutic efficacy is hampered since it is not known how electrically activated neural structures in the motor cortex can induce pain relief. Furthermore, multiple neural elements are present in the motor cortex such as cell bodies, dendrites and axons which are parallel or perpendicular to the cortical layers (figure 1). Which of these neural elements are immediately excited by the electrical pulses in MCS depends on positioning of anodal and cathodal electrodes and stimulation parameters. A proper insight on these effects would be useful for peroperative decision making on electrode positioning and for the interpretation of stimulation results after implantation. Computational modeling studies can help to identify the effects of electrical stimulation on cortical neural tissue, elucidate mechanisms of action and ultimately to optimize the therapy.

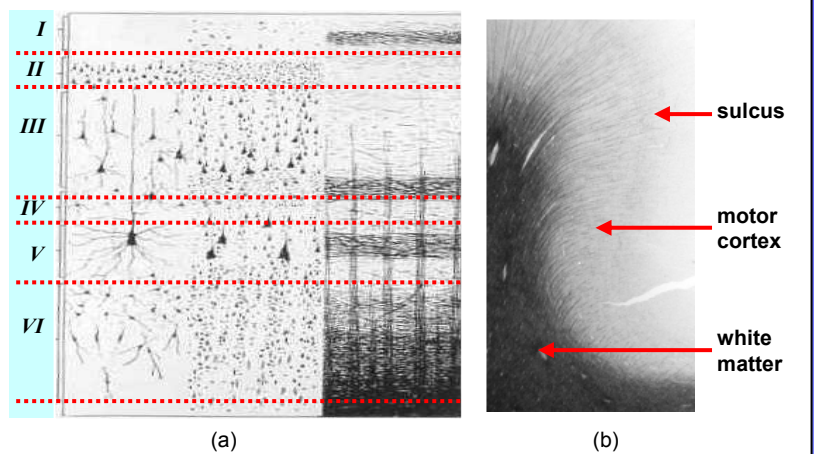


Figure 1: (a) Layered structure of motor cortex (laminae I-VI); cortical afferents from various parts of brain ascend and bifurcate into specific layers parallel to the cortical surface. Efferents from various laminae descend normal to the laminae. (b) Efferents of pyramidal neurons leave cortex into white matter below, creating 'fountain' of fibres in gyrus. In precentral gyrus laminae are parallel to electrode(s), in central sulcus laminae are normal to electrode(s).

Methods: The activation of neural elements in the precentral gyrus (PCG) and in the anterior wall and lip of the central sulcus (CS) was studied by:

- (1) Calculating the stimulus-induced electrical field using a realistic 3D volume conductor model (figure 2).
- (2) Simulation of the response of neural elements using compartmental neuron models including the axon, soma and dendritic trunk (figure 3,4).

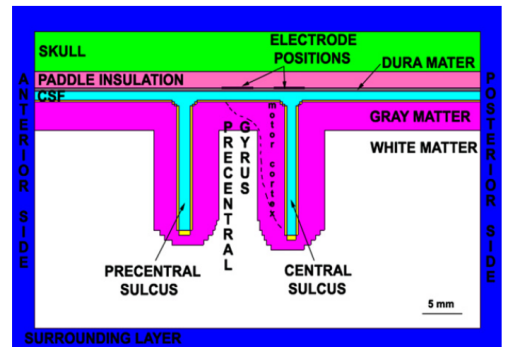


Figure 2: Anterior-posterior cross-section of the model. Model compartments are labeled. Electrode positions and approximate position of the motor cortex are indicated (see [3] for details).

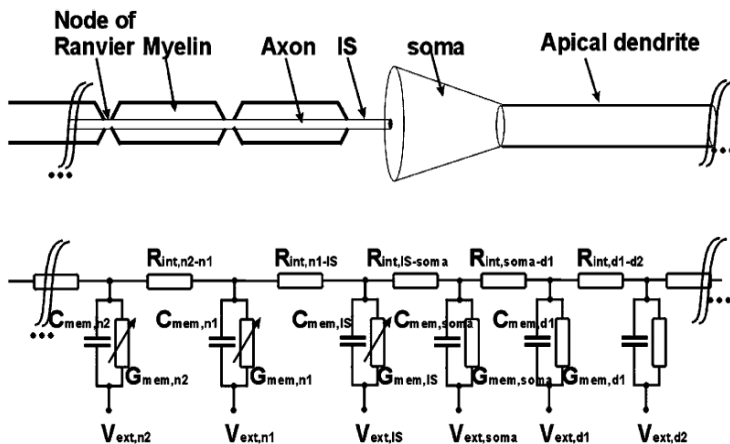


Figure 3: Geometry of the pyramidal neuron model. The soma is modeled as a frustum, apical dendrite as a cylinder. Electrical equivalent of the model for small signals is shown (see [1] for details)

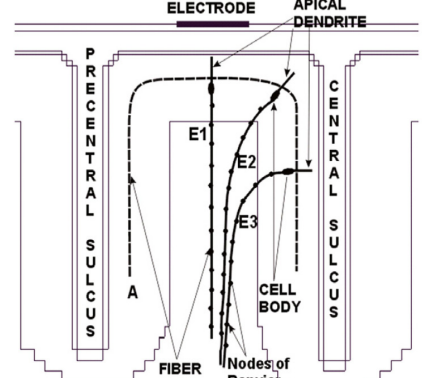


Figure 4: The full model contains a nerve fiber parallel to the cortical laminae ('A'), a neuron in the crown of the precentral gyrus ('E1'), a neuron in the lip of the central sulcus ('E2') and a neuron in the wall of the central sulcus ('E3').

Effects of Anodal, Cathodal and Bipolar Stimulation

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Figure 5: Iso-current density lines in the xy-plane through centre of cathode for different thicknesses of CSF layer between electrode and cortex. From monopolar cathodal stimulation (1 V), 55 equidistant lines (5-60 $\mu\text{A}/\text{mm}^2$) are drawn. Thickness of CSF layer and load impedance are indicated in each plot

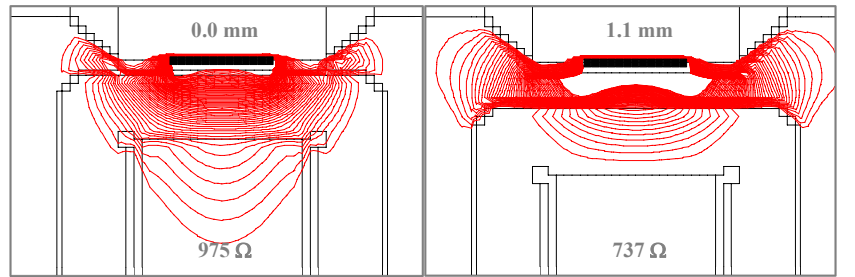
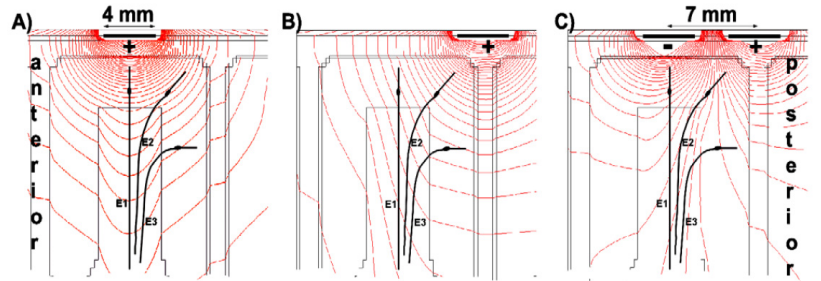


Figure 6: Iso-potential lines for a stimulus of 1 V: (A) anodal stimulation centered on PCG, (B) anodal stimulation centered on CS, (C) bipolar stimulation with cathode centered on PCG. Fifty iso-lines between 0.4 and 0.6 V in monopolar and 0.1 and 0.1 V in bipolar stimulation are shown (4.1 mV distance between lines).



Results: Excitation thresholds depend on geometry (figure 5), fiber orientation (figure 6) and diameters (figure 7). While neural elements perpendicular to the electrode surface are preferentially excited by anodal stimulation, cathodal stimulation excites those with a direction component parallel to its surface (figure 8). When stimulating bipolarly, the excitation of neural elements parallel to the bipole axis is additionally facilitated. The polarity of the contact over the precentral gyrus determines the predominant response. Inclusion of the soma-dendritic model generally reduces the excitation threshold as compared to simple axon model.

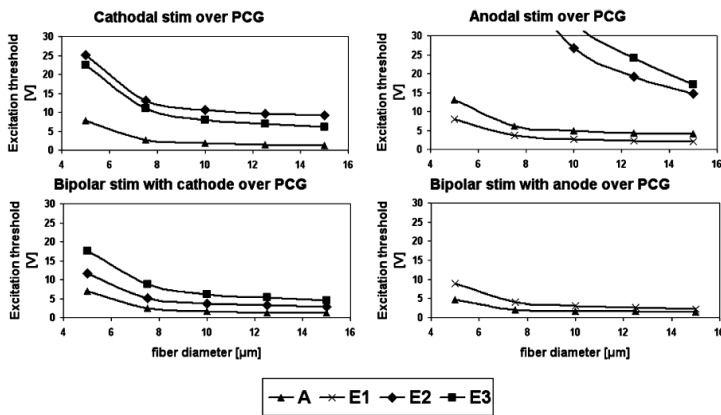


Figure 7: Excitation thresholds (V) of the 'A' fiber and 'E' neuron models (figure 4) when stimulated by the electrodes having different positions and polarities. The fiber diameter was varied in the range 5-15 μm .

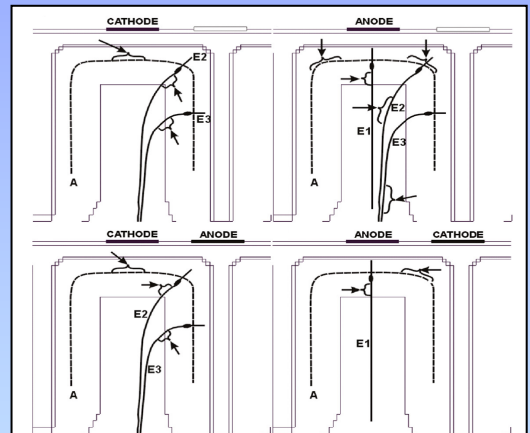


Figure 8: Sites of excitation in the 'A' fiber and 'E' neurons when stimulated by the electrodes having different positions and polarities. For each electrode configuration, only those neurons that are activated below 30 V are shown.

Conclusions: Electrode polarity and electrode position over the precentral gyrus and central sulcus have a large and distinct influence on the response of cortical neural elements to stimuli:

- (1) Cathodic and anodic stimulation at the same site results in the activation of different groups of local cortical nerve fibers
- (2) In bipolar stimulation both cathode and anode are active electrodes, selectively activating those axons which have the proper orientation in the cathodal and anodal field, respectively.

References

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3. Manola, L., et al., *Modelling motor cortex stimulation for chronic pain control: Electrical potential field, activating functions and responses of simple nerve fibre models*. Medical and Biological Engineering and Computing, 2005. **43**(3): p. 335-343.