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FS1c.8

EFFICIENT OPTIMIZATION OF TRANSCRANIAL TEMPORAL INTERFERENCE STIMULATION (tTIS)

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Abstract
For two decades, transcranial current stimulation (tCS) has been used to noninvasively influence brain function in healthy volunteers and clinical populations. Many positive results have been demonstrated with traditional tCS, but there are limitations to targeting and focality of the electric fields delivered to the target region. Additionally, tCS has only been used to modulate superficial brain regions. Transcranial temporal interference stimulation (tTIS) offers a potential solution to these limitations by combining two alternating currents to create an amplitude-modulated electric field that can peak deep in the brain. Positive results have been shown in rodents, and simulations in human models indicate the potential of tTIS for subthreshold neuromodulation similar to tACS, but with maximal effects in deep brain areas and greater focality. Because tTIS requires a non-convex and non-linear optimization method, existing tCS optimization methods do not apply. Previously proposed solutions for tTIS optimization included exhaustive search and reformulations of tCS methods. Since these optimizations can take hours to complete, these methods are inefficient for practical use in research or in the clinic. As an alternative, we propose to apply convex relaxations to the non-convex tTIS optimization problem, exploiting the mathematical model using tailored heuristics. We tested our approach on multiple realistic human head models with a large set of electrodes and target regions spread throughout the brain. The proposed method was able to find electrode current patterns that deliver maximal tTIS fields to any target in seconds. Optimization outcomes were evaluated on target region field strength, focality and efficiency, and compared to previously proposed methods. The results show that the optimal method depends on which of these metrics is prioritized and on the location of the target in the brain.
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HOW IMPORTANT ARE EXTRACEREBRAL BRAIN COMPARTMENTS FOR TES, TMS, AND ECT MODELING PREDICTIONS?

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Abstract
Extracerebral brain compartments comprise partitioning skull into outer table (cortical bone), diploë (cancellous or trabecular bone), inner table (cortical bone), three meningeal layers (dura, arachnoid, and pia mater tightly enclosing the brain) as well as partitioning scalp into several tissue types such as skin itself, muscle, and fat. At present, their accurate segmentation is difficult. However, meaningful results could be obtained by expanding the existing subject specific automated brain segmentation of major compartments using anatomical rules known from many prior extensive studies.
Extracerebral tissue types present additional conductivity interfaces which indeed distort transcranial stimulation fields, most notably the electric field. What is the order of this distortion for different modalities and targets? Although an approach exists which replaces this effect by modified conductivities of simpler models, this is true only for specific subjects/locations/montages where an approximate adjustment can be made via accurate numerical modeling of a particular problem.
Modeling tightly spaced thin layers of tissues is computationally expensive when using the finite element method (FEM) due to the requirement of an adequate volumetric mesh. To overcome this issue, we use the boundary element fast multipole method (BEM-FMM), which only requires the discretization of the surfaces. Furthermore, we extend the existing BEM-FMM algorithm by an automated adaptive mesh refinement mechanism. With this extension, we are able to determine accurate and self-converged results for the electric field with reasonable computational cost.
Our extensive modeling results reveal that the extracerebral brain compartments are less important for TMS but are quite important for TES and ECT dose predictions. There and for deeper targets, the electric field deviation could be on the order of 100%. Our method could be applicable to any head geometry with or without lesions, and also to tissues in the form of thin separate islands.
Research Category and Technology and Methods
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EFFECT OF REALISTIC DENSELY PACKED AXONAL ARBOR ON DBS ACTIVATING FUNCTION

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Abstract
The commonly accepted approach to modeling the activating function in brain stimulation (either DBS or TMS) assumes that the axonal/neuronal microscopic arbor is non-existing in the physical sense. The applied electric field is found via a macroscopic FEM solution in a homogeneous (or macroscopically anisotropic) medium and is then fed into the cable equation. The field resolution approaches the size of a finite element (~1 mm).
As a result, induced charges deposited on physically realistic curved membrane/myelin conductivity interfaces in response to an applied electric field are not included into consideration. These charges may alter the applied electric field and the activating function. Moreover, nearby axons and dendrites could “talk” to each other via capacitive coupling.
To estimate microscopic variations of the activating function, open-source data for precise modeling of axon microgeometry have been used. These data include intra-axonal space segmented from 3D scanning electron microscopy of the mouse brain genu of corpus callosum. The data were converted to accurate surface meshes for intracellular space and myelin with 302 axons packed in a dense ensemble and with ca. 20 million facets in total.
The boundary element fast multipole method was applied to accurately compute induced surface charge density subject to an applied electric field. The field of the induced charges was added to the applied field and the total activating function was found along every axon’s centerline.
Our results indicate that taking the physical structure of the arbor into account generally predicts higher values of the activating function as compared to the common approach. The average difference is no less than