

Sensitivity of TMS-Induced Electric Fields to the Uncertainty in Coil Placement and Brain Anatomy

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Abstract— A computational framework for statistically characterizing electric (E-) fields generated during transcranial magnetic stimulation (TMS) is presented. The framework combines a high dimensional model representation (HDMR) technique with a quasi-static finite-difference (QSFD) simulator to obtain statistics of E-fields due to uncertainty in the TMS setup and patient’s brain anatomy. Application of the proposed computational framework shows that E-fields induced by TMS are highly sensitive to the position and orientation of TMS coils, as well as the size of patient’s brain.

I. INTRODUCTION

TMS is a non-invasive method used in psychiatry and in neuroscience research for stimulating neuronal tissue. During TMS, coils located near the scalp and driven with low-frequency current pulses generate magnetic fields that induce E-fields and eddy currents inside the conductive brain tissue. If E-field inside a neuron exceeds a specified threshold, the neuron will depolarize its membrane leading to an action potential and thus affecting brain function. This trigger mechanism allows studying causal links between stimulated cortical region and observable behaviors. That said, the location, volume, and depth of the stimulated cortical region often are strongly affected by the uncertainty in the TMS setup (e.g. the position and orientation of TMS coils), as well as the uncertainty in patient’s brain anatomy (e.g. the permittivity, conductivity, and size of the patient’s brain).

This paper presents a computational framework for statistically characterizing E-fields (and thereby, the regions stimulated during TMS), given the uncertainty in TMS setup and patient’s brain anatomy. The proposed framework leverages HDMR expansions [1] to approximate E-fields (and hence, their statistics) that are potentially affected by a large number of random variables, i.e., the variables that parameterize the above uncertainties. The HDMR expansions allow generating surrogate models of E-fields via series of iteratively constructed component functions involving only the most significant random variables. The component functions of HDMR expansions are approximated via a multi-element probabilistic collocation (ME-PC) method described in [2, 3]. While approximating each component function, a QSFD simulator [4] is used to compute E-field values at integration/collocation points specified by the ME-PC method.

Upon the generation of accurate surrogate models of E-fields, the classical Monte-Carlo (MC) method is used to compute the statistics of E-fields while accounting for the probability density functions (PDFs) of the random variables. The proposed framework was applied to the statistical characterization of E-fields inside a three-sphere head model and a cortical region of a MRI-derived head model targeted during TMS therapy.

II. FORMULATION

Assume uncertainties in TMS setup and brain anatomy are parameterized by an N_{dof} -dimensional random vector $\mathbf{x} = [x_1, x_2, \dots, x_{N_{\text{dof}}}]$, $\mathbf{x} \in \Omega = \prod_{i=1}^{N_{\text{dof}}} \Omega_i$, and each random variable x_i , $i = 1, \dots, N_{\text{dof}}$, is mutually independent and distributed with a PDF across $\Omega_i = [a_i, b_i]$. Let $F(\mathbf{x})$ represent an observable (e.g., the E-field on a point in cortical region), which is typically a complicated function of \mathbf{x} and can only be evaluated by a deterministic simulator. In principle, the statistics of $F(\mathbf{x})$ can be obtained by applying MC, which requires evaluation of $F(\mathbf{x})$ for many samples of \mathbf{x} . That said, MC method converges very slowly and becomes impractical when each deterministic simulation performed to compute $F(\mathbf{x})$ is CPU-intensive. To circumvent this difficulty, we apply the MC method to the surrogate model (i.e., approximate representation) of $F(\mathbf{x})$ generated using HDMR expansion, which approximates $F(\mathbf{x})$ via component functions as [1]

$$F(\mathbf{x}) = F_0 + \sum_{i_1=1}^{N_{\text{dof}}} F_{i_1}(x_{i_1}) + \sum_{i_1 < i_2}^{N_{\text{dof}}} F_{i_1 i_2}(x_{i_1}, x_{i_2}) + \sum_{i_1 < i_2 < i_3}^{N_{\text{dof}}} F_{i_1 i_2 i_3}(x_{i_1}, x_{i_2}, x_{i_3}) + \dots + F_{12 \dots N_{\text{dof}}}(x_1, \dots, x_{N_{\text{dof}}}) \quad (1)$$

Here, F_0 is the zeroth-order component function which is constant over Ω ; $F_{i_1}(x_{i_1})$ denotes a first-order component function that represents the individual contribution of x_{i_1} to $F(\mathbf{x})$; $F_{i_1 i_2}(x_{i_1}, x_{i_2})$ denotes a second-order component function that reveals the combined contribution of x_{i_1} and x_{i_2} to $F(\mathbf{x})$; the remaining terms in (1) are higher order combined contributions of random variables to $F(\mathbf{x})$. The representation in (1) can be constructed using the cut-HDMR method [1], which expresses the component functions in terms of observable values on lines, planes, and hyperplanes (i.e. cuts) in Ω . The observable values on cuts are approximated using the adaptive ME-PC method [2, 3], which requires the

evaluation of $F(\mathbf{x})$ on collocation/integration points using the QSFD solver described in [4]. The HDMR expansion in (1) and its advantage can be best described by an example. Assume $N_{\text{dof}} = 3$; the expansion in (1) can be written explicitly as

$$F(\mathbf{x}) = F_0 + F_1(x_1) + F_2(x_2) + F_3(x_3) + F_{12}(x_1, x_2) + F_{13}(x_1, x_3) + F_{23}(x_2, x_3) + F_{123}(x_1, x_2, x_3). \quad (2)$$

Assume that $F(\mathbf{x})$ consists of a constant term and monomials, i.e., $F(\mathbf{x}) = 2 + x_1^4 + x_2^4 + x_3^4$. The component functions F_0 , $F_1(x_1)$, $F_2(x_2)$, and $F_3(x_3)$ in (2) are needed to approximate $F(\mathbf{x})$ while the remaining ones in (2) are redundant and should be excluded from the HDMR expansion. Including only the “most significant” component functions in HDMR expansion significantly reduces the computational cost of surrogate model generation. An iterative scheme described in [5, 6] is used to incorporate the most relevant component functions in the HDMR expansion.

III. NUMERICAL RESULTS

The proposed framework was used to statistically characterize the magnitudes of the E-fields generated inside a three-sphere head model [Fig. 1(a)]. The head model consists of three-concentric spheres (or layers) that represent the brain, skull, and skin tissues from innermost to outermost. The head model is excited by a Figure-8 coil centered at $(0, 0, 10.2)$ cm, positioned perpendicular to the z -axis, and driven with a current varying at a rate of $8 \text{ kA}/\mu\text{s}$. Five parameters characterize the uncertainty in brain anatomy and TMS setup ($N_{\text{dof}} = 5$): the conductivities of the brain σ_{brain} , the skull σ_{skull} , and the skin σ_{skin} , and the position of the coil along the x - and y - directions, C_x and C_y , (i.e., $\mathbf{x} = [\sigma_{\text{brain}}, \sigma_{\text{skull}}, \sigma_{\text{skin}}, C_x, C_y]$). The random variables are assumed to be uniformly distributed in ranges $[a_i, b_i]$, $i = 1, \dots, 5$; $[0.3825, 0.5175] \text{ S/m}$, $[0.0425, 0.0575] \text{ S/m}$, $[0.3825, 0.5175] \text{ S/m}$, $[-1, 1] \text{ cm}$, and $[-1, 1] \text{ cm}$, respectively. The observables are the magnitudes of E-fields computed at 121 points selected on a Cartesian grid centered at $(0, 0, 6.5)$ cm; the points on grid are positioned 0.3 cm apart from each other [Fig. 1(b)]. The proposed method required 680 deterministic simulations to generate surrogate models of observables with average L-2 norm error of 2.16×10^{-4} . Using the surrogate models, the means and standard deviations of observables are computed when $\mathbf{x} = [\sigma_{\text{brain}}, \sigma_{\text{skull}}, \sigma_{\text{skin}}, C_x, C_y]$ [Figs. 1(c)-(d)]. In addition, standard deviations of observables are obtained when $\mathbf{x} = [C_x, C_y]$ [Fig. 1(e)], and $\mathbf{x} = [\sigma_{\text{brain}}, \sigma_{\text{skull}}, \sigma_{\text{skin}}]$ [Fig. 1(f)], respectively. Apparently, the uncertainty in coil position significantly affects the E-fields while the effect of the uncertainty in tissue conductivity to the E-fields is negligible. These results are consistent with the results obtained when MRI-derived head models were used instead of three-sphere model. The statistics of the E-fields

inside MRI-derived head models showed that the coil orientation and the patient’s brain size have even more significant effect on E-fields. The statistics were also useful to draw the following conclusions for the use of TMS in experimental and clinical settings: (i) Uncertainty in coil position and orientation may reduce the response rates of TMS depression therapy. (ii) When MRI-guided neuronavigation is available, the practitioners should favor targets on the crest of a gyrus to obtain maximal stimulation. (iii) An increasing scalp-to-cortex distance reduces the magnitudes of E-fields on the surface and inside the cortex.

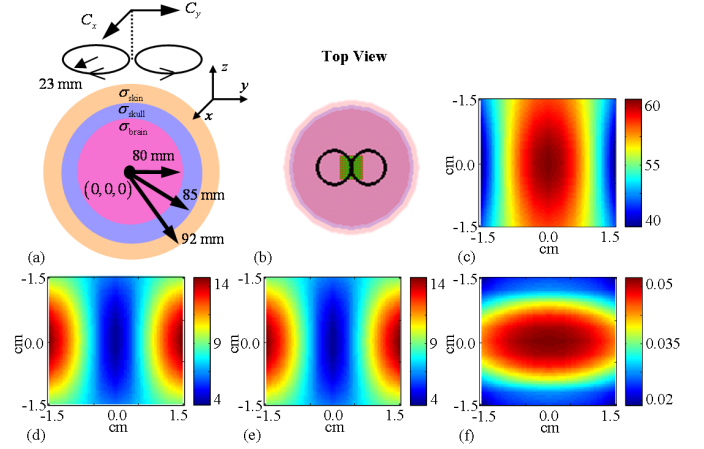


Fig. 1 (a) The geometry of the three-sphere head model with the Figure-8 coil. (b) The Cartesian grid under the coil. The statistical moments of the E-fields’ magnitudes (in V/m): (c) the means and (d) standard deviations when $\mathbf{x} = [\sigma_{\text{brain}}, \sigma_{\text{skull}}, \sigma_{\text{skin}}, C_x, C_y]$; the standard deviations when (e) $\mathbf{x} = [C_x, C_y]$ and (f) $\mathbf{x} = [\sigma_{\text{brain}}, \sigma_{\text{skull}}, \sigma_{\text{skin}}]$.

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