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## STUDENT PAPER

### Effect of Permittivity on Temporal Interference Modeling

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#### Summary

Temporal interference (TI) is a recent development to target deep brain areas using transcranial alternating current stimulation (tACS). This technique is under investigation to estimate its ability to provide non-invasive deep brain stimulation. Modeling studies are carried out to study it and estimate the potential of the method. However, the modeling is commonly performed using quasi-static approximation together with purely ohmic tissues. Here is studied the impact of neglecting the capacitive effect of tissues, and so their permittivity, to estimate the electric field (EF) in deep brain areas. The results show a relative error below 10% at the brain level, demonstrating a good approximation using purely ohmic tissues for this purpose.

#### Introduction

Transcranial current stimulation (tCS) has demonstrated some potential as a non-invasive brain stimulation (NIBS) technique and offers portability while being low cost as compared to transcranial magnetic stimulation. Its safety profile has also been studied and shown [Bikson et al., 2016]. While it is well studied for either direct or alternating currents, temporal interference (TI) is a quite new technique that could enable tCS to target deeper regions of the brain [Esmaeilpour et al., 2021; Grossman et al., 2017]. It relies on the delivery of higher frequencies (in the kHz range) currents with a small frequency difference. These two signals are then interacting potentially in deep brain areas where beatings occur with a low-frequency amplitude designed for neural stimulation. Since the neuron membrane acts as a low-pass filter, only the low-frequency envelope stimulates the neurons at the beating frequency ( frequency difference of the two stimuli) [Beatrice Barra et al., 2020].

Modeling studies are performed to study the focality, specificity, and parameters of this promising approach. It is usually done by performing numerical methods such as finite element

methods. This method enables one to solve Maxwell's equations on numerical domains. In tCS, and TI, human head models, built with magnetic resonance images, are commonly used to predict and calculate the EF [Antonenko et al., 2019; Huang et al., 2016]. Most numerical studies about tCS are performed using QSA which is a good approximation at frequencies used for this purpose (<10kHz) [Plonsey and Heppner, 1967]. However, an additional approximation is implicitly used: the tissues are considered purely ohmic. This is mainly due to the fact that tCS was first mainly used with direct current and so in the static case where only resistive effect remains. However, using harmonic signals, the tissues exhibit a capacitive effect due to their permittivity which could change the impedance and affect the EF distribution, depending of the frequency[Wagner et al., 2014]. Indeed, the permittivity of biological materials can be significant at low frequencies [Foster and Schwan, 1989; Gabriel et al., 1996a]. The question of whether the contribution of the permittivity could change the magnitude and the focality of TI has not been yet tackled. It could be relevant to increase the accuracy of predictions made by numerical modeling. The present study aims to provide some insight into how the permittivity can affect the TI stimulation depending on relative permittivity values.

## Methods

TI stimulation modeling was implemented in a 3D head geometry from the SimNIBS example dataset [Thielscher et al., 2015; Windhoff et al., 2013] consisting of the full head model of the ICBM152 model [Fonov et al., 2011]. The model consists of the five main tissues used in tCS modeling such as scalp, skull, cerebrospinal fluid (CSF), grey matter (GM), and white matter (WM). The dielectric properties of these tissues were obtained by the Cole-Cole model reported by S. Gabriel [Gabriel et al., 1996a; Gabriel et al., 1996b] at the stimulation frequency ( $f=1\text{kHz}$ ). Stimulating electrodes were modeled as cylinders of 0.4 cm thickness on the scalp, consisting of the conductive gel layer between the scalp and electrodes. Four of these were built and placed on the P7, P8, FT7 and FT8 positions of the 10-10 electrode system [Klem et al., 1999]. This placement was studied in [Esmaeilpour et al., 2021; Huang and Parra, 2019] and took for comparison.

The purely ohmic approximation will be called static approximation since it basically assumes to solve the static or stationary equation consisting in the Laplace equation on the electric potential ( $\nabla \cdot (\sigma \nabla V) = 0$ ,  $V$  being the electric potential and  $\sigma$  electrical conductivity) over the domain. The more general case taking into account the capacitive properties of tissues will be called quasi-static (QS) approximation and still consists of solving the Laplace equation on the electric potential but with a complex conductivity and so complex values of potential ( $\nabla \cdot ((\sigma + j\omega\epsilon) \nabla V) = 0$ ,  $\epsilon$  being the permittivity and  $\omega$  the angular frequency), considering harmonic signals. A Dirichlet boundary condition was assigned to the ground electrodes ( $V = 0$ ) while a

Robin boundary condition was assigned to the other associated electrode ( $\int \mathbf{J} \cdot d\mathbf{S} = I_0 = 2 \text{ mA}$ ;  $V = V_{\text{ref}}$ ,  $\mathbf{J}$  being the current density). The remaining boundaries were set as insulating boundary conditions ( $\mathbf{J} \cdot \mathbf{n} = 0$ ). The two equations were solved over the geometrical domain using COMSOL Multiphysics. Each was solved for each couple of stimulation electrodes independently (P7-FT7 and P8-FT8). Then the two results for each electrode couple were transformed from frequency to time domain by Fourier transform and superposed using linearity of Maxwell's equations (especially of the Laplace equation) to compute the resulting EF during TI.

The low frequency envelope was then extracted taking the module of the Hilbert transform of the EF at each point. The relative error between the static and QS (SQS) approximation of this envelope was then computed as  $\eta_{\text{SQS}} = |\mathbf{E}_{\text{Stat}} - \mathbf{E}_{\text{QS}}|/|\mathbf{E}_{\text{QS}}|$ . The metrics of interest were calculated on the brain since it is the region where occurs the stimulation and where the modeling should be as accurate as possible. Then the associated distribution was computed using tetrahedron volumes as weights and their average values

## Results and Discussion

2D Maps of the SQS relative error in the brain are shown in Figure 2. It shows some local regions where the SQS relative errors are higher, especially localized at boundaries with CSF where the brain geometry is sharper. The distribution of  $\eta_{\text{SQS}}$  and its cumulative distribution function are shown in Figure 3. The distribution is localized below the 10% values. The 95<sup>th</sup>, 97.5, and 99<sup>th</sup> quantiles were assessed and are respectively 5.35%, 7.32% and 10.47%. This demonstrates a good approximation at least in brain tissues at 1kHz with these values of permittivity.

## Conclusion

This study addressed the quantification of the error induced by neglecting the permittivity in the TI stimulation modeling. Our results show that the relative error is relatively low with a 99<sup>th</sup> quantile at 10.47% in the brain with the Cole-Cole model. It shows a good agreement with results considering purely ohmic medium with some higher errors distributed close to brain to CSF boundaries. However, considering the relatively low computational cost of adding permittivity contribution during modeling, this error could be avoided using reliable permittivity measurements together with conductivity ones.

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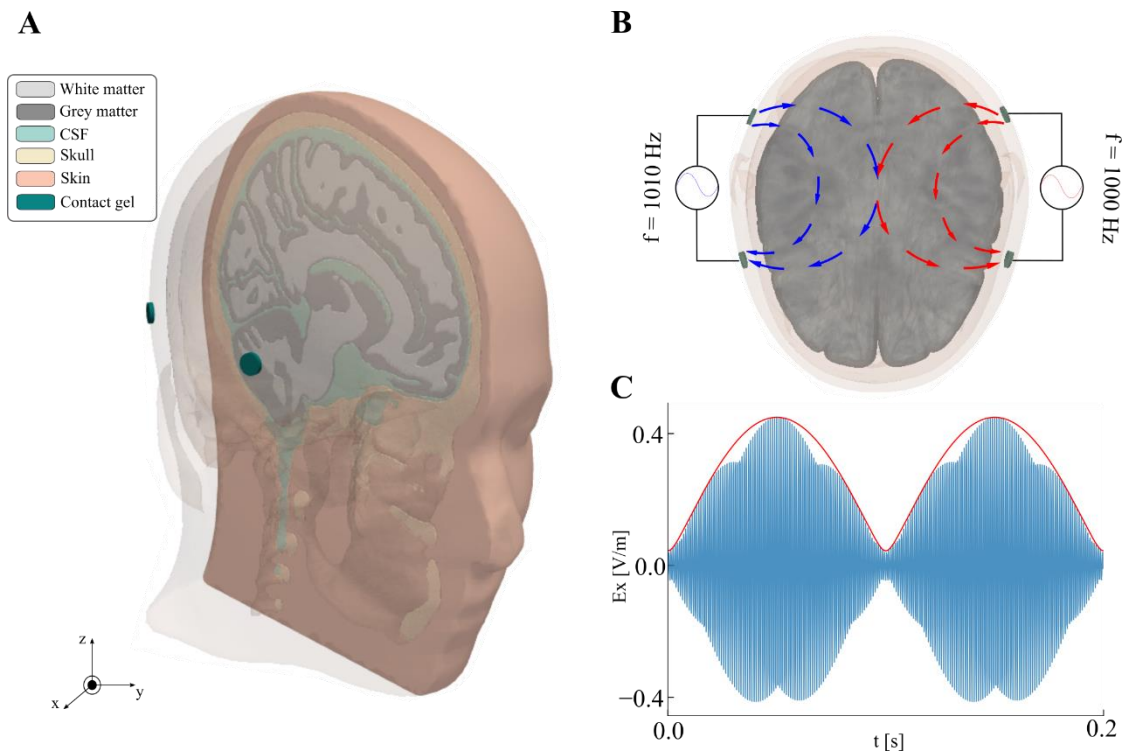


Figure 1. Problem formulation. A: Head model geometry with the five main tissues. B: Top view of the model with schematics of the set-up and electric field representation. C: Example of the electric field (x component) time course (light blue) and its envelope (red).

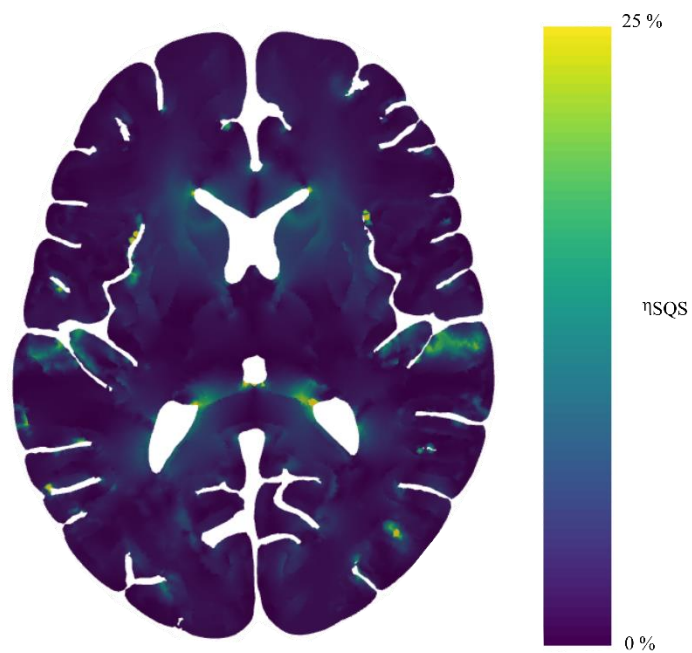
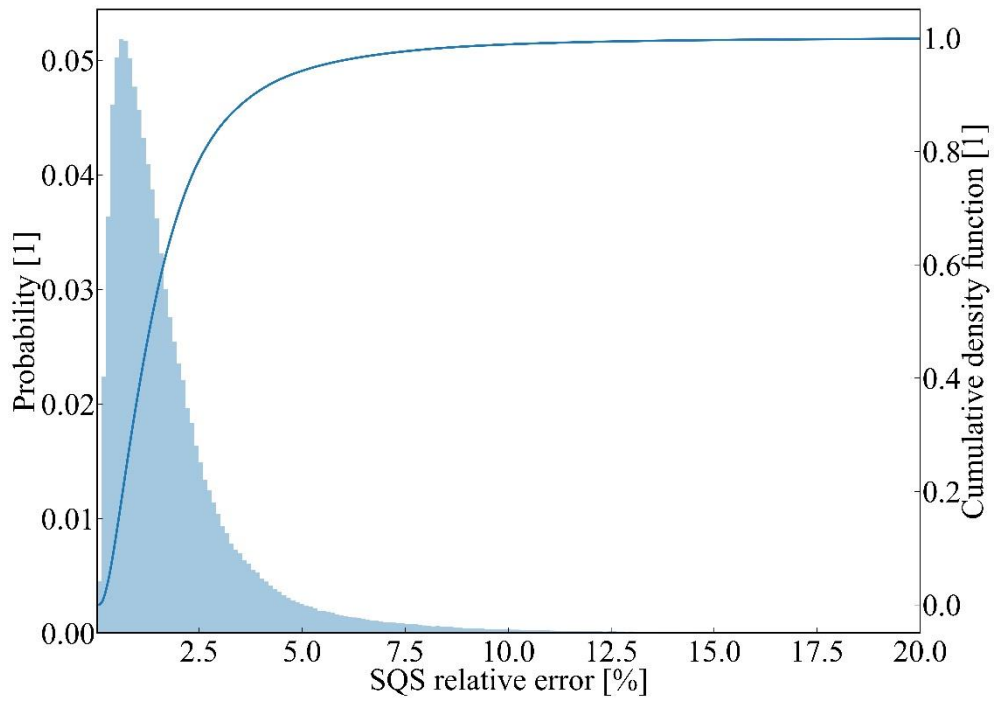


Figure 2. Slice of the 3D model to visualize the SQS relative error across the brain.



*Figure 3. SQS relative error distribution across the brain volumetric mesh. The y-left axis indicates the probability associated with the distribution in light blue. The y-right axis corresponds to the cumulative density function values.*