Why transcranial direct current stimulation (tDCS) models cannot be trusted yet? A simulation study.

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Introduction:

Transcranial direct current stimulation (tDCS) has gained increased interest over the past decades due to its affordability, ease of use and wide range of applications. Yet, its lack of consistency and reproducibility is concerning. A potential solution to improve the method is to tailor the stimulation for each subject based on individual measurements and models. Such model requires accurate information about the geometry of the tissues composing the head of the subjects, their electric properties and the electrode montage.

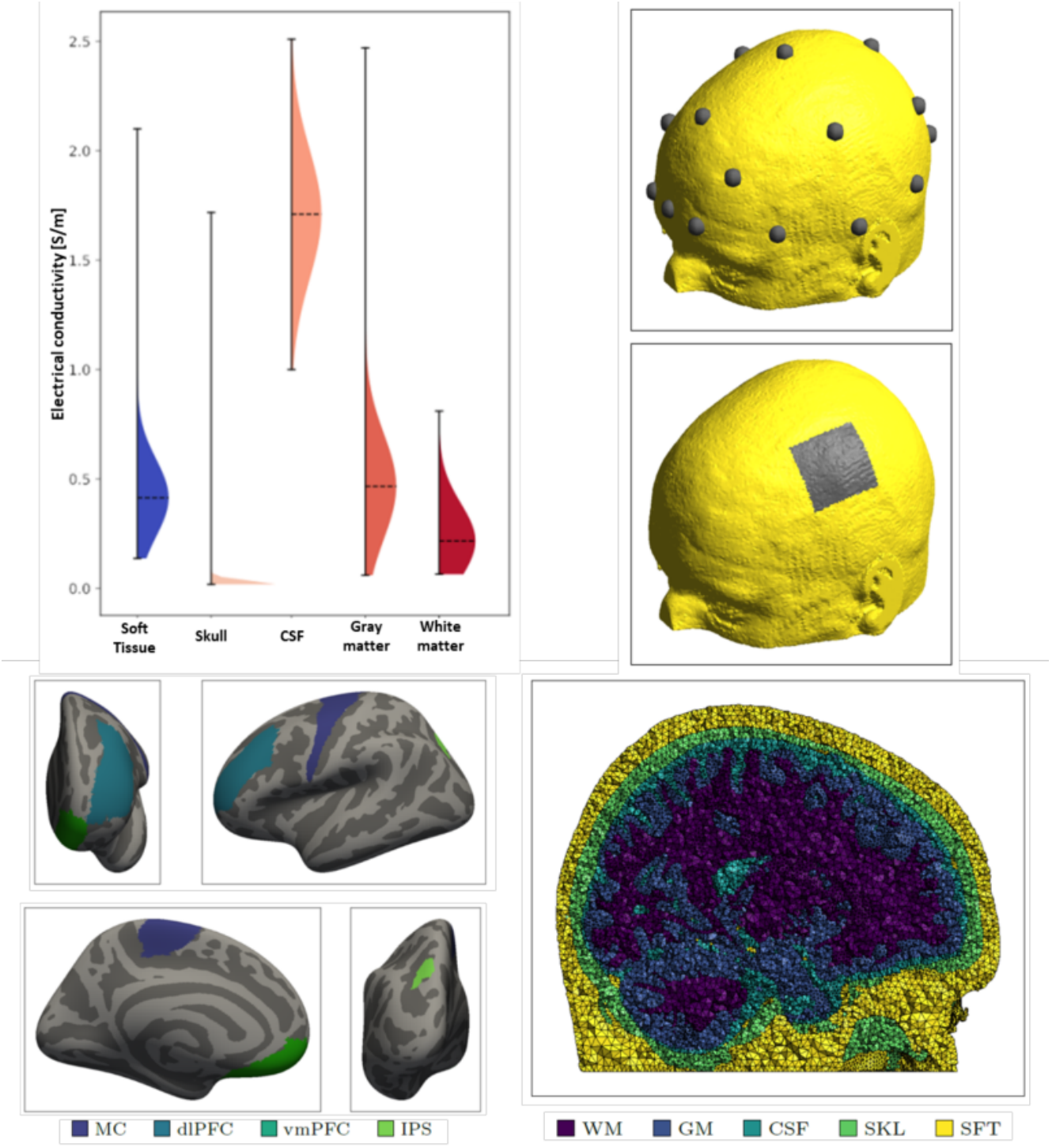
Here we explore the sensitivity of such models with respect to two factors (anode placement & conductivity values) with simulated data.

Methods:

We used anatomical information from 20 BrainWeb virtual subjects [1], reduced to 5 tissue classes (WM, GM, CSF, skull, and soft tissues), to build individual finite element models (FEM). Four regions of interest (ROIs) were targeted (MC, dlPFC, vmPFC, IPS) with a bipolar or unipolar (only MC and dlPFC) montages (6 experiment altogether) with electrodes (5x5 cm2 patches) placed according to the 10-20 EEG system and target region. The anode was either correctly centred, or displaced by 1cm in 4 directions (anterior, posterior, central or lateral), leading to 30 models per subject. The reference conductivity profile for the 5 tissues were set as the "weighted mean" values in [2]. Another set of 20 conductivity profiles, Ωuni, were uniformly sampled, with a quasi-random Halton sequence[3], over the value ranges reported in [2]. Then we used Shamo [4] to solve the 12600 (20x30x21) FEM simulations and calculate the electric field e (V/m) over the head volume, for a current of 2 mA injected at the anode and and cathode acted as a reference (i.e. 0V). Each simulation was summarized by their "average magnitude of e" (AMe) in the ROIs targeted in each model. Additionally, using Gaussian Process Regressors, we interpolated for another 20 conductivity profile Ωinf, using a truncated normal distribution [2], i.e. more informed profiles than the broad "worst case" Ωuni.

Finally Bayesian generalized linear mixed effects models, as implemented in BAMBI [4], were used to assess the effect of the 2 factors of interest (anode placement and conductivity) for each experiment. To decide whether a parameter has a significant effect on the AMe,

we looked at the overlap of the 95 % "highest density interval" (HDI) and the "region of practical evidence" (ROPE) [6]. Here the boundaries of the ROPE are set to +/-.1*std(AMe).



(Top left) Tissue conductivity value distribution (from [2]); (top right) 10-20 electrode system & C3-C4 anode-cathode set up; (bottom left) the 4 target ROIs; (bottom right) finite element model for 1 subject.

·Modelling & parameters of interests

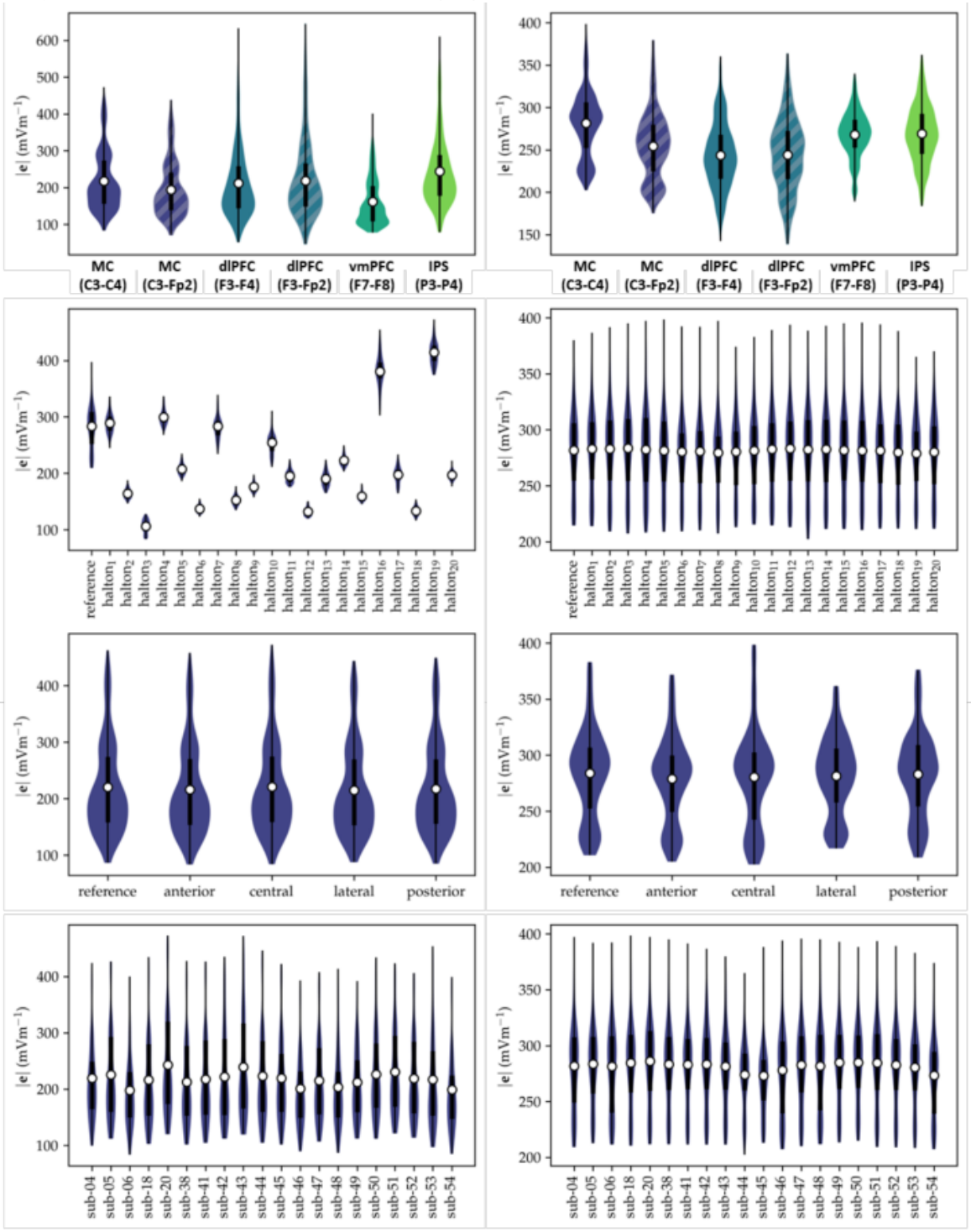
Results:

The overall distribution of the average magnitude of e in the target region for each montage, with either the uniformly or informedly conductivity random sampling, ranges from 47.2 to 644.2 mV/m and from 139.2 to 398.5 mV/m, respectively, as displayed in Fig. 2 top row.

Looking at the effect of a 1cm placement error on the AMe in the ROIs: with the Ωuni conductivity profiles, HDI and ROPE do overlap to some extent, so no decision can be made. On the contrary, with the Ωinf conductivity profiles, electrode placement has significant effect of AMe in the ROIs.

Looking at the effect of conductivity profiles, the majority of the 95 % HDI computed on Ωuni fall completely outside the ROPE, meaning that the uncertainty on the conductivity of the tissues has a significant influence on the electric field computed in the ROI. With the Ωinf conductivity profiles, the trend is reverse, with no or undecided effect.

See Fig. 2 for results observed with the motor cortex (MC) AMe distributions. More results and code are available in [7,8].



Distribution of the mean electric field **e** magnitude, estimated with 20 Ω_{uni} (left) and Ω_{inf} (right) conductivity profiles: for the 6 ROIs & montages (1st row); then for the "MC (C3-C4)" set up only across 21 conductivity profiles (2nd row), 5 anode positions (3rd row), and 20 subjects (4th row).

·All the main results.

Conclusions:

tDCS is expected to generate an induced transmembrane potential of around 0.5 mV in the neurons of the ROI [9]. Still the values we obtain, considering r=1mm, are at most of the same order of magnitude but can be up to 20 times smaller. Moreover, the uncertainty on the electrical conductivity makes it practically impossible to assess the stimulation effect in the ROI and using any standard values could potentially yield biased results.

Brain Stimulation:

Non-invasive Electrical/tDCS/tACS/tRNS
TDCS [1]

Modeling and Analysis Methods:

Other Methods [2]

Neuroinformatics and Data Sharing:

Informatics Other

Keywords:

Computing
Modeling
Other - brain stimulation, tDCS, tissue connectivity, electrode position, sensitivity, effect size

[1|2]Indicates the priority used for review

Abstract Information

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

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Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Not applicable

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Not applicable

Please indicate which methods were used in your research:

Structural MRI
Computational modeling
Other, Please specify - tDCS

Which processing packages did you use for your study?

Other, Please list - Shamo, getDP

Provide references using author date format

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