

# 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. Each **model requires accurate information** about the geometry of the tissues composing the head of the subjects, their electric properties and the electrode montage.

**Aim of the study:** Exploring the sensitivity of such models with respect to two factors (anode placement & conductivity values) with simulated data

## Methods

### Model building

- 20 BrainWeb virtual subjects [1]
- reduced to 5 tissue classes (WM, GM, CSF, skull, and soft tissues), to build individual finite element models (FEM)
- Reference conductivity profile for the 5 tissues as "weighted mean" from [2]
- 4 regions of interest (ROIs) as targets: MC, dlPFC, vmPFC, IPS;
- 5x5 cm<sup>2</sup> patch electrodes placed according to the 10-20 EEG system and 4 target regions
- 2 mA current injected at the anode and cathode as a reference (i.e. 0V).

### Sources of variability

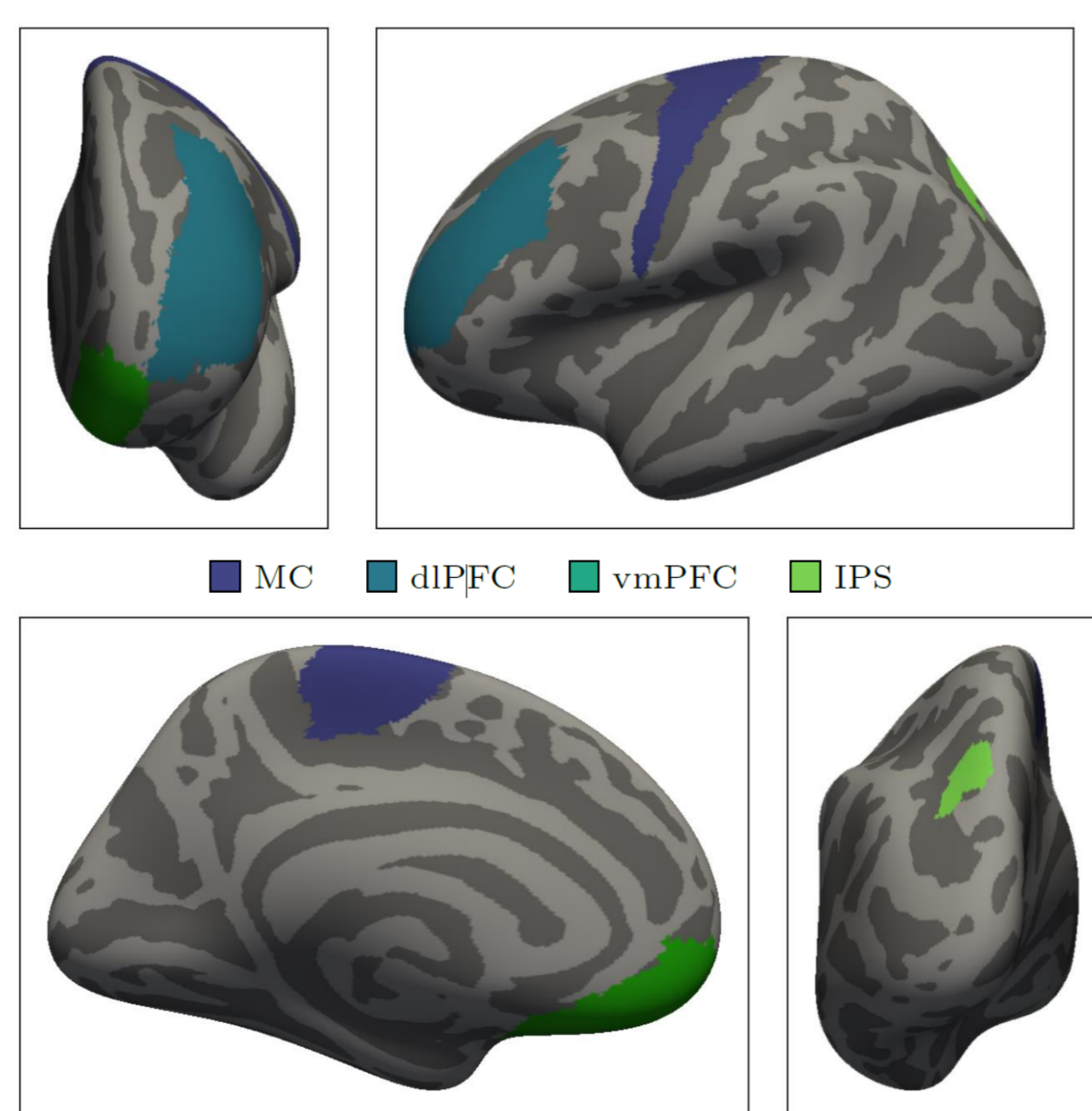
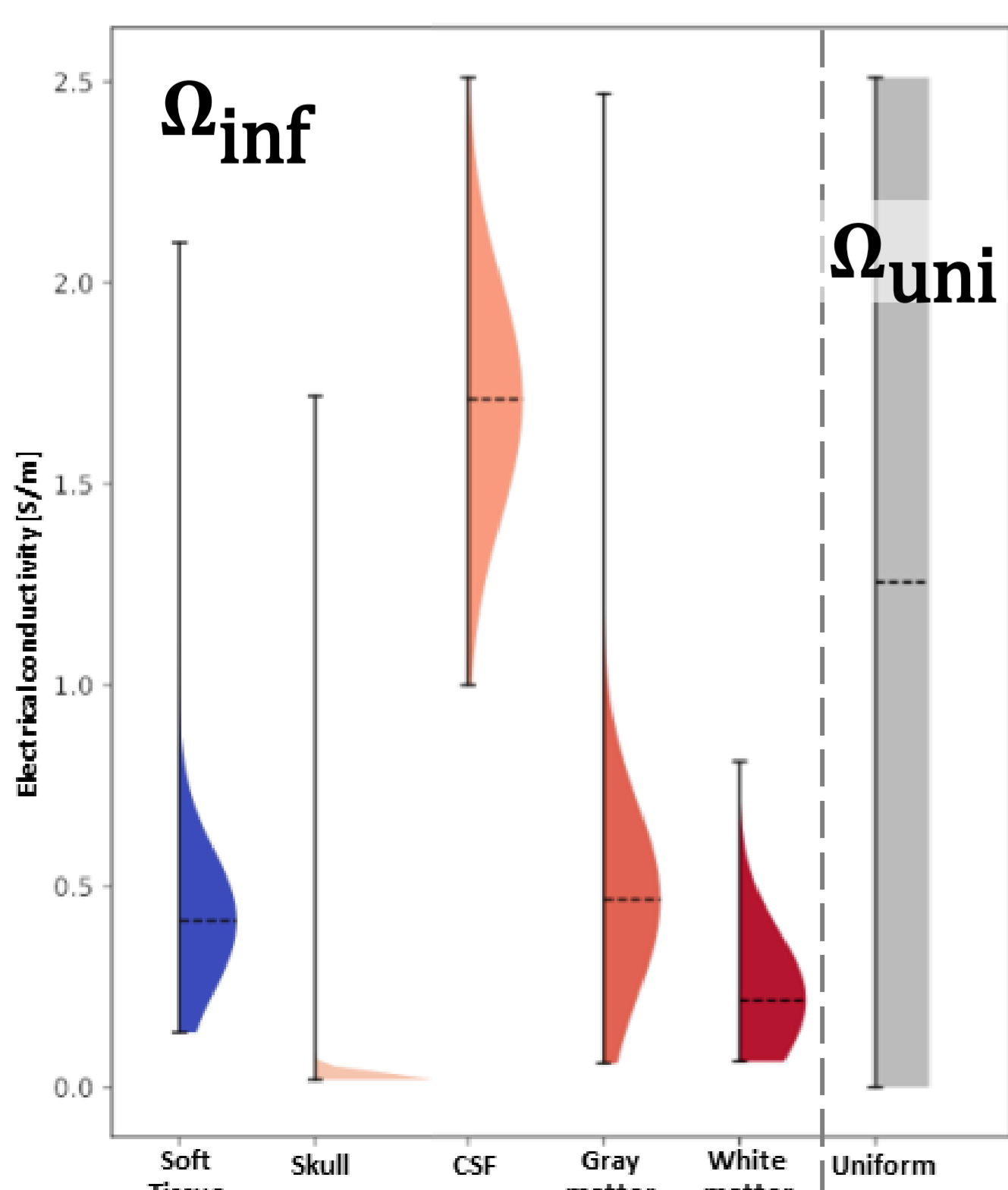
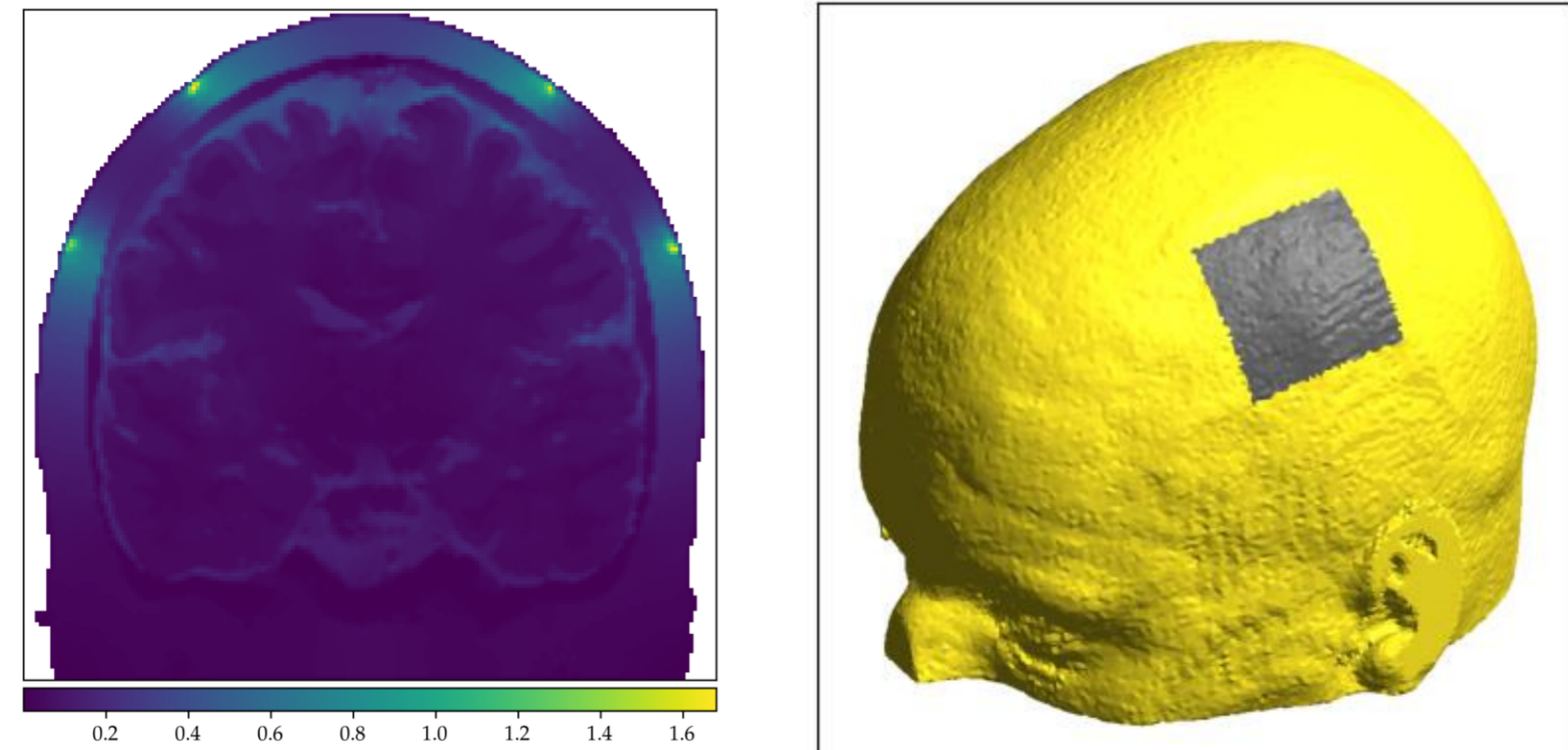
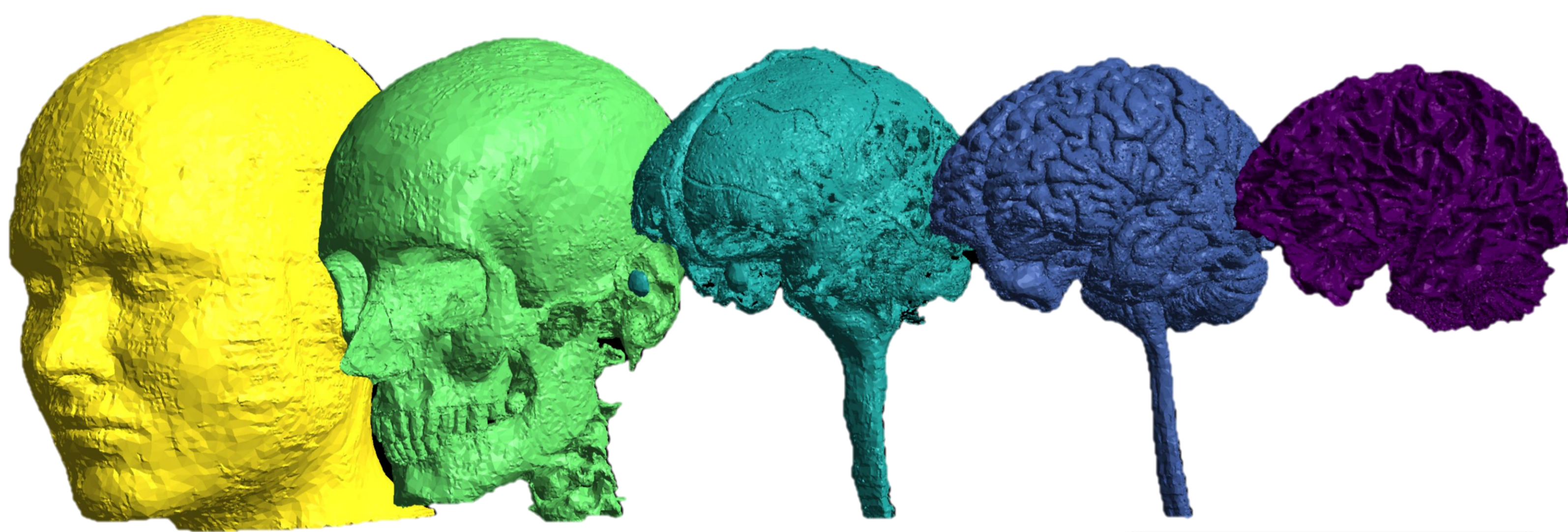
- bipolar or unipolar (only MC and dlPFC) montages → 6 montages
- anode was either correctly centred, or displaced by 1 cm in 4 directions (anterior, posterior, central or lateral) → 5 electrodes setup
- pick 20 random conductivity profiles, sampled [3] from uniform conductivity distribution,  $\Omega_{uni}$  + reference → 21 profiles

### Model estimations

- solve the 12600 (20x5x6x21) FEM simulations with Shamo [4]
- calculate the electric field  $e$  (V/m) over the head volume
- each simulation summarized by the "average magnitude of  $e$ " (AME) in the ROIs targeted in each model
- interpolate (GPR) results for another 20 "informed" conductivity profiles  $\Omega_{inf}$  using a truncated normal distribution [2]

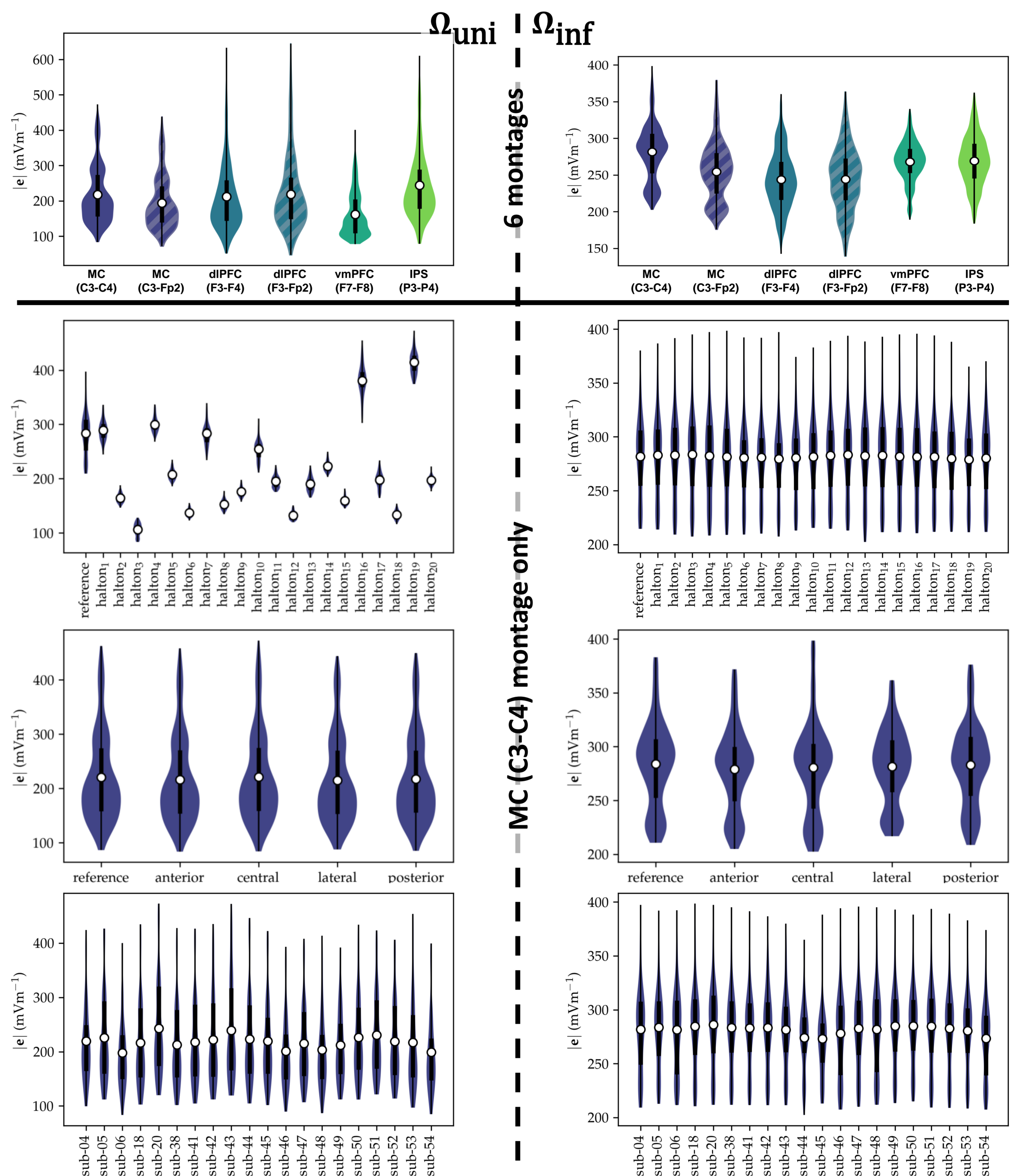
### Statistics

- Bayesian generalized linear mixed effects models [5] to assess the effect of the 2 factors of interest: anode placement and conductivity profile
- Check 95% overlap of "highest density interval" (HDI) and the "region of practical evidence" (ROPE) [6], with boundaries set to  $\pm 1 \cdot \text{std}(AME)$ .



## Results

- Overall very weak current flow/electric field throughout the head volume
- AME distribution all target regions & montage, with conductivity random sampling, ranges from 47.2 to 644.2 mV/m and from 139.2 to 398.5 mV/m, for  $\Omega_{uni}$  and  $\Omega_{inf}$
- effect of a 1cm placement error, according to conductivity profile, on AME in the ROIs
  - ✓ with  $\Omega_{uni}$ , HDI and ROPE do overlap to some extent → no decision can be made
  - ✓ with  $\Omega_{inf}$ , little overlap → significant effect of electrode placement
- effect of conductivity profiles on AME in the ROIs
  - ✓ with  $\Omega_{uni}$ , majority of the 95 % HDI completely outside the ROPE → significant influence of uncertainty on the conductivity of the tissues
  - ✓ with  $\Omega_{inf}$ , mainly overlap → no or undecided effect.



Distribution of the AME, estimated with 20  $\Omega_{uni}$  (left column) and  $\Omega_{inf}$  (right column) 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).

## Conclusion

tDCS is expected to generate an induced transmembrane potential of around 0.5 mV in the neurons of the ROI [7] but

- the values we obtain, considering  $r=1\text{mm}$ , are at most of the same order of magnitude but can be up to 20 times smaller.
- the uncertainty on the electrical conductivity makes it practically impossible to assess the stimulation effect in the ROI + using any standard values could potentially yield biased results.

More results and code are available in [8].

[1] BrainWeb: 20 Anatomical Models of 20 Normal Brains [https://brainweb.bic.mni.mcgill.ca/anatomic\\_normal\\_20.html](https://brainweb.bic.mni.mcgill.ca/anatomic_normal_20.html)  
 [2] McCann, H., Pisano, G. & Beltrachini, L. (2019) 'Variation in Reported Human Head Tissue Electrical Conductivity Values'. Brain Topogr., 32, 825–858. <https://doi.org/10.1007/s10548-019-00710-2>  
 [3] Halton, J.H. (1960) 'On the efficiency of certain quasi-random sequences of points in evaluating multi-dimensional integrals.' Numer.Math., 2, 84–90. <https://doi.org/10.1007/BF01386213>  
 [4] Grignard, M., Geuzaine, C. & Phillips, C. (2022) 'Shamo: A Tool for Electromagnetic Modeling, Simulation and Sensitivity Analysis of the Head.' Neuroinform., 20, 811–824. <https://doi.org/10.1007/s12021-022-09574-7> and <https://github.com/CyclotronResearchCentre/shamo>  
 [5] Yarkoni, T., & Westfall, J. (2016). 'Bambi: A simple interface for fitting Bayesian mixed effects models.' OSF preprint. <https://doi.org/10.31219/osf.io/v7sn>  
 [6] Kruschke, J.K., Liddell, T.M. (2018). 'The Bayesian New Statistics: Hypothesis testing, estimation, meta-analysis, and power analysis from a Bayesian perspective.' Psychon. Bull. Rev., 25, 178–206. <https://doi.org/10.3758/s13423-016-1221-4>  
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 [8] Grignard, M., Geuzaine, C., Hansenne, M., Majerus, S., & Phillips, C. (2022). 'Why tDCS models cannot be trusted yet? — A simulation study.' Eprint/Working paper <https://orbi.uliege.be/z268/294662> and <https://github.com/CyclotronResearchCentre/BrainWeb-tDCS>