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Why tDCS models cannot be trusted yet?
A simulation study

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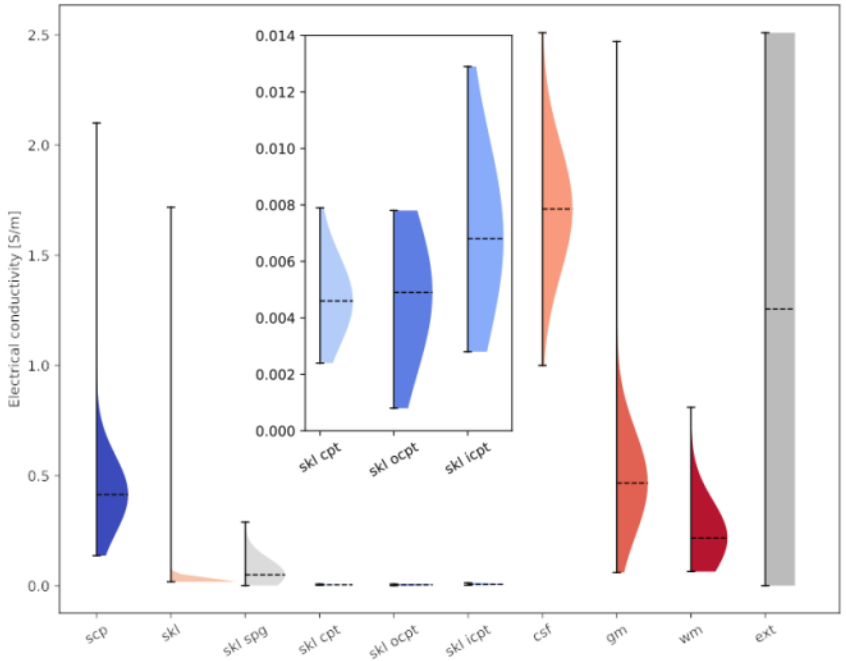
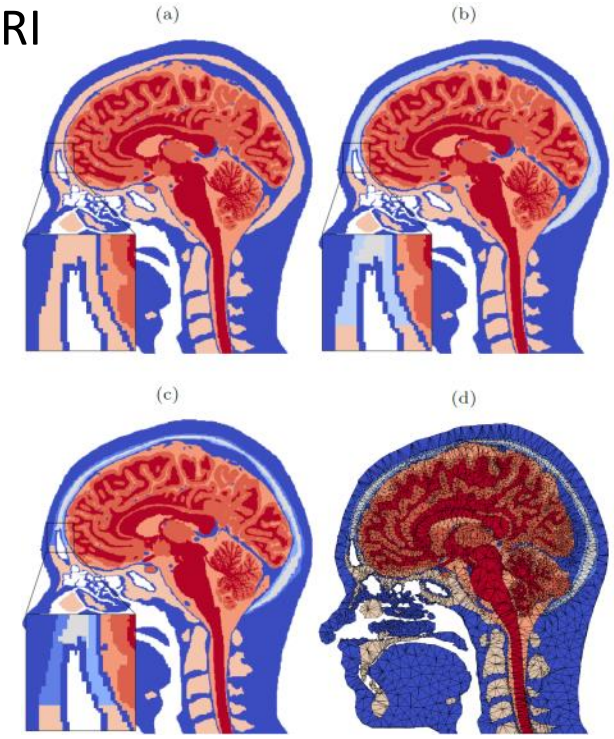
shamo, Stochastic HeAd MOdelling

Calculate forward problem solution for **EEG** and **tDCS**

- build FEM head model(s), based on segmented MRI
- consider stochastic variable for conductivity σ





Grignard *et al.*, https://github.com/CyclotronResearchCentre/shamo

shamo, Stochastic HeAd MOdelling

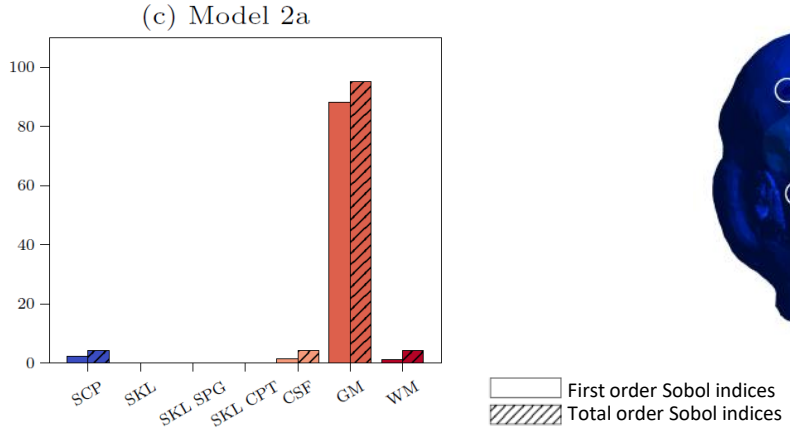
- Use *getDP* to solve the FEM problem, given conductivity values σ
- Build surrogate model to explore the N-D conductivity space.
- Sensitivity analysis with Sobol indices based on scalar $m(\sigma)$

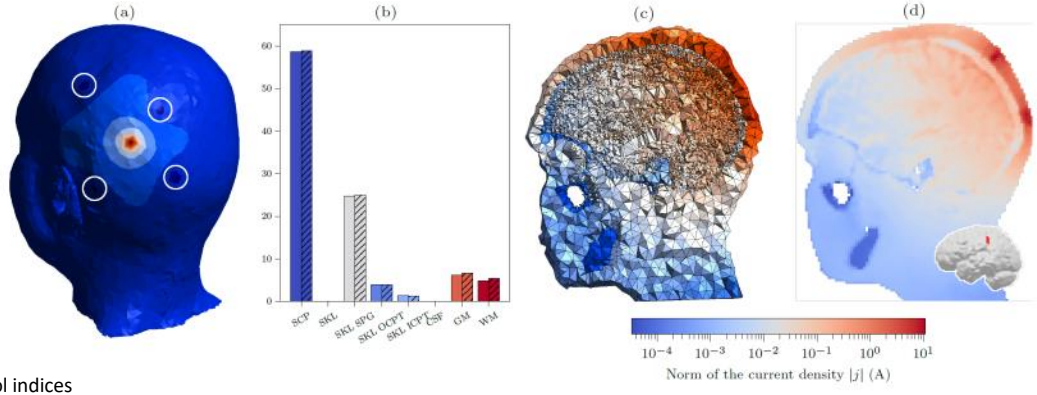
EEG forward solution, sensitivity of the whole leadfield

$$m(\sigma) = \left\| L(\sigma) - L_{\text{ref}} \right\|_F$$

tDCS current density, sensitivity in target region of interest

$$m(\sigma) = \text{mean}(\|j\|_2)_{\text{ROI}}$$





Grignard *et al.*, https://dx.doi.org/10.1007/s12021-022-09574-7

tDCS issues?

Low response rate (~50%) ➔ Potential causes?

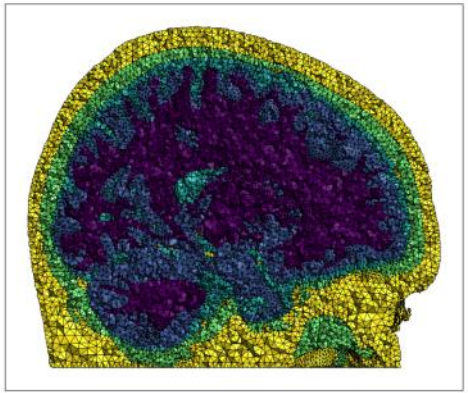
- Subject variability?
  - Function vs. anatomy
- Target region actually stimulated?
  - How do we know ?
- Head model?
  - subject‘s anatomy
  - electrodes positioning
  - tissue properties

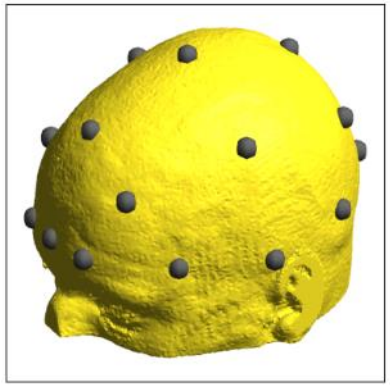
Wiethof *et al.*, https://doi.org/10.1016/j.brs.2014.02.003

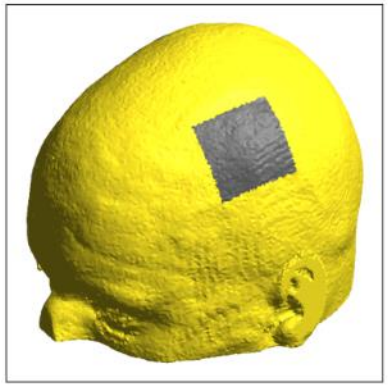
tDCS models

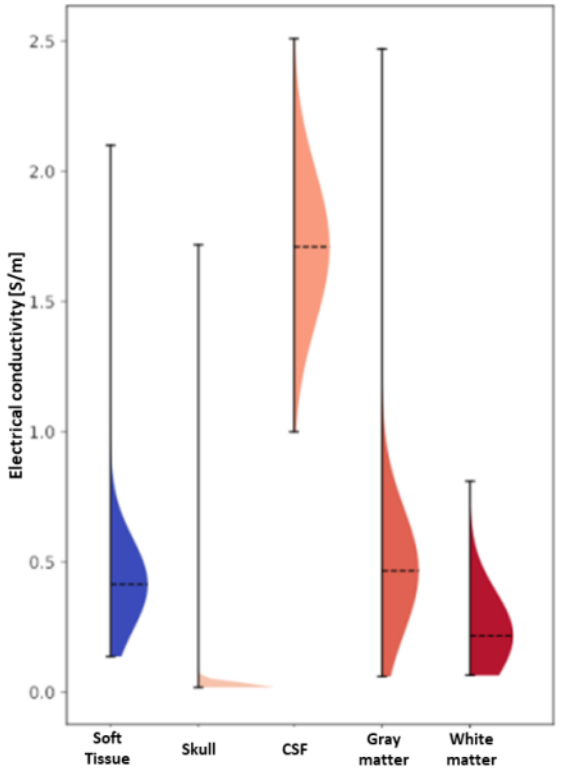
Calculate forward problem solution for **tDCS**

- build FEM head model(s), based on
  - segmented MRI
  - electrode position
- solve forward problem, based on
  - tissue properties, conductivity value or distribution
  - injected current









McCann *et al.*, https://doi.org/10.1007/s10548-019-00710-2

Models, many models…

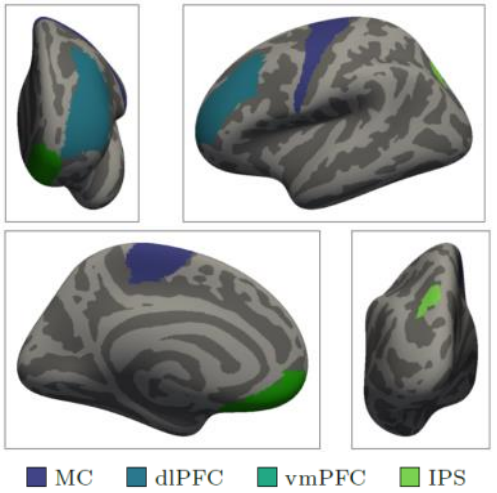
Consider

- 4 target regions ⟶ MC, dlPFC, vmPFC, IPS
- 6 montages (4 bipolar + 2 unipolar), according to the 10-20 EEG system

Anode	Cathode	ROI	Bipolar	Unipolar
C3	C4	MC	■	□
C3	Fp2		□	■
F3	F4	dlPFC	■	□
F3	Fp2		□	■
F7	F8	vmPFC	■	□
P3	P4	IPS	■	□

Simulated variability

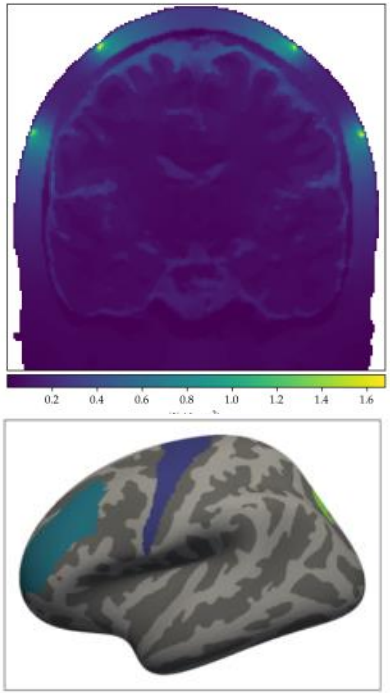
- 20 virtual subjects ⟶ different anatomy
- electrodes (5x5 cm2 patches)
  ⟶ centered + anode misplaced by 1cm in 4 directions
- 5 tissues classes (WM, GM, CSF, skull, and soft tissues)
  ⟶ 1 reference + 20 random conductivity profiles



➔ **6 x 5 x 20 x 21 = 12600 models!**

BrainWeb, https://brainweb.bic.mni.mcgill.ca/anatomic_normal_20.html

Model output & summary variable



Inject 2 mA at anode, in all 12600 models:

- whole brain current density j (mA/m^2) & electric field e (mV/m)
- per ROI, average absolute values $|e|$

Note:

- Uniform $[\min \max]$ vs. informed $G(\mu, \sigma)$ conductivity values
- tDCS effectivity ➔ lower bound ~ 0.5mV/mm = 500mV/m

Opitz *et al.*, https://doi.org/10.1038/srep31236

Conductivity distribution

(a) Ω_{uniform}

Sim.	Electrical conductivity ($\mathrm{S\,m^{-1}}$)				
	WM	GM	CSF	SKL	SFT
1	0.1385	0.4170	1.2831	1.2670	1.0792
2	0.2063	1.2204	2.0381	1.5099	1.4718
3	0.2741	2.0237	1.6606	0.0876	1.8644
4	0.3418	0.6848	2.4156	0.3304	0.3726
5	0.4096	1.4881	1.0472	0.5732	0.7652
6	0.4773	2.2915	1.8022	0.8161	1.1578
7	0.5451	0.2385	1.4247	1.0589	1.5504
8	0.6129	1.0419	2.1797	1.3017	1.9430
9	0.6806	1.8452	1.2359	1.5446	0.4511
10	0.7484	0.5063	1.9909	0.1223	0.8437
11	0.0769	1.3096	1.6134	0.3651	1.2363
12	0.1447	2.1130	2.3684	0.6079	1.6289
13	0.2124	0.7741	1.1416	0.8508	2.0215
14	0.2802	1.5774	1.8966	1.0936	0.1527
15	0.3480	2.3807	1.5191	1.3364	0.5453
16	0.4157	0.0898	2.2741	1.5792	0.9379
17	0.4835	0.8931	1.3303	0.1570	1.3305
18	0.5513	1.6964	2.0853	0.3998	1.7231
19	0.6190	0.3575	1.7078	0.6426	0.2312
20	0.6868	1.1609	2.4628	0.8854	0.6238
21	0.2167	0.4660	1.7100	0.0160	0.4137

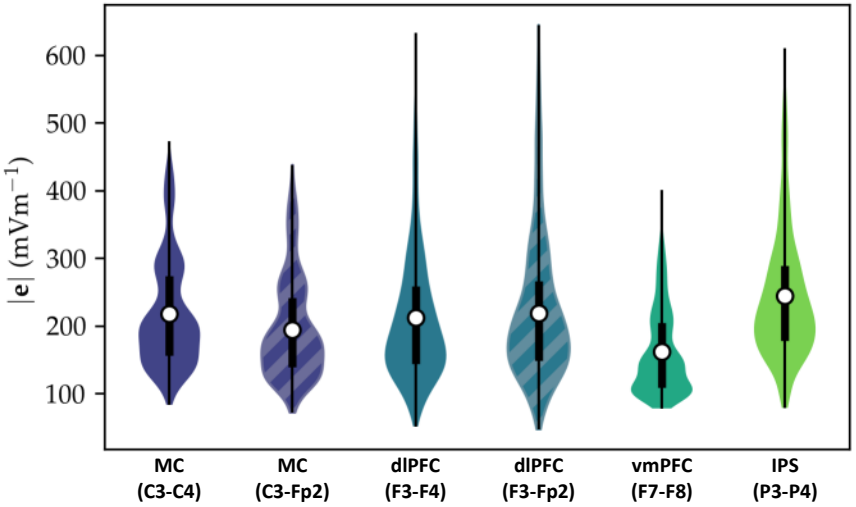
(b) Ω_{norm}

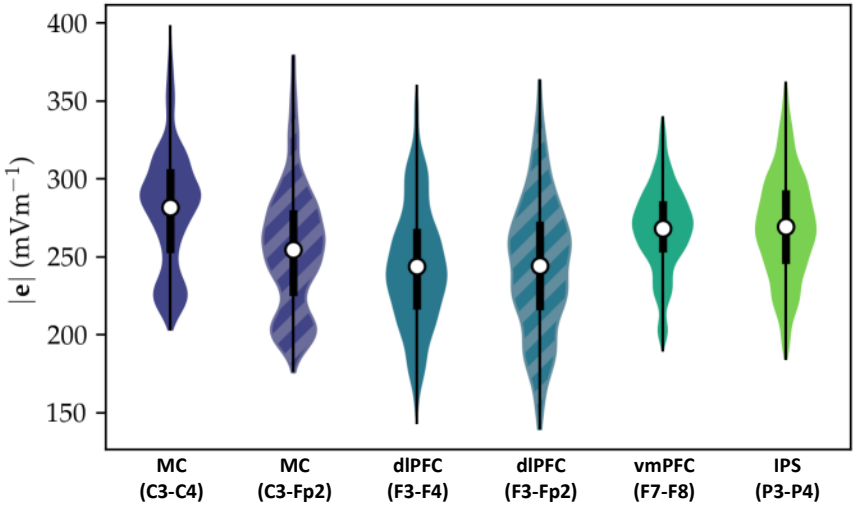
Sim.	Electrical conductivity ($\mathrm{S\,m^{-1}}$)				
	WM	GM	CSF	SKL	SFT
1	0.1458	0.2527	1.6971	0.03828	0.2323
2	0.3291	0.4688	1.8497	0.0463	0.2877
3	0.2346	0.6878	2.0570	0.0191	0.3327
4	0.4950	0.3353	1.3702	0.0223	0.3729
5	0.0801	0.5333	1.5745	0.0257	0.4110
6	0.2679	0.8177	1.7266	0.0294	0.4490
7	0.1800	0.1796	1.8836	0.0337	0.4888
8	0.3737	0.4262	2.1236	0.0392	0.5329
9	0.1337	0.6291	1.4216	0.0480	0.5862
10	0.3160	0.2827	1.6065	0.0195	0.6636
11	0.2238	0.4901	1.7563	0.0227	0.1585
12	0.4600	0.7228	1.9199	0.0262	0.2381
13	0.1083	0.3593	2.2213	0.0299	0.2921
14	0.2912	0.5557	1.0746	0.0344	0.3365
15	0.2020	0.8982	1.4738	0.0401	0.3764
16	0.4106	0.0871	1.6434	0.0499	0.4144
17	0.1574	0.3898	1.7926	0.0200	0.4526
18	0.3430	0.5869	1.9681	0.0232	0.4926
19	0.2456	0.2308	1.2363	0.0267	0.5372
20	0.5485	0.4547	1.5123	0.0305	0.5919
21	0.2167	0.4660	1.7100	0.0160	0.4137

Table S2: Sets of electrical conductivities used for the different simulations ($\mathrm{S\,m^{-1}}$). The 20 first combinations have been drawn using a quasi-random Halton sequence on the ranges described in Table 3 and the 21-th uses the recommended values for all the tissues.

Results, 6 montages

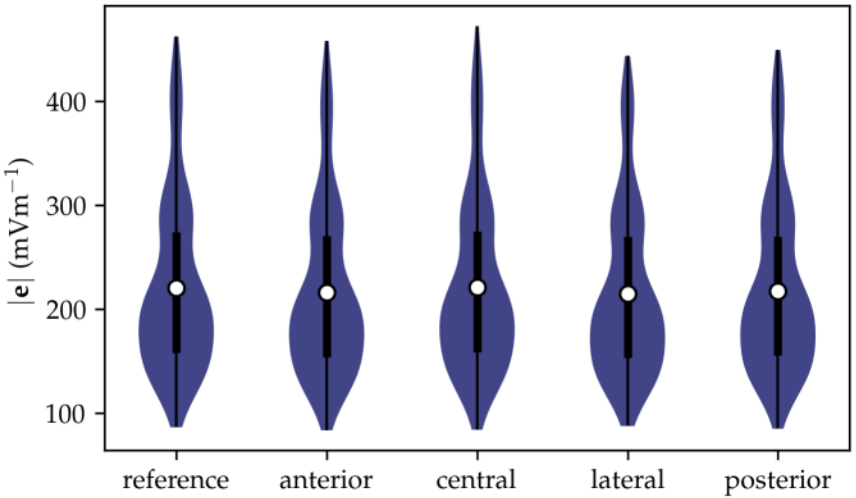
- Uniform $[\min \max]$ (left) vs. informed $G(\mu, \sigma)$ (right) conductivity values

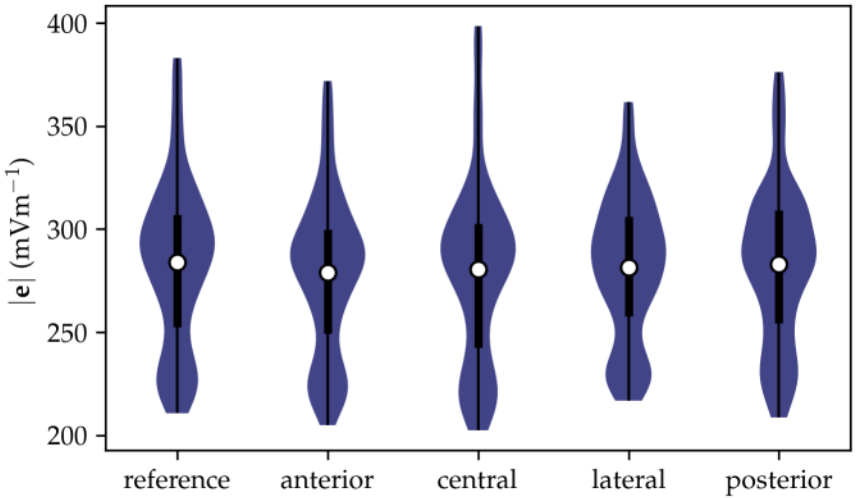




Results, MC target only

- Effect of electrode positioning (ref. & 1cm displacement)

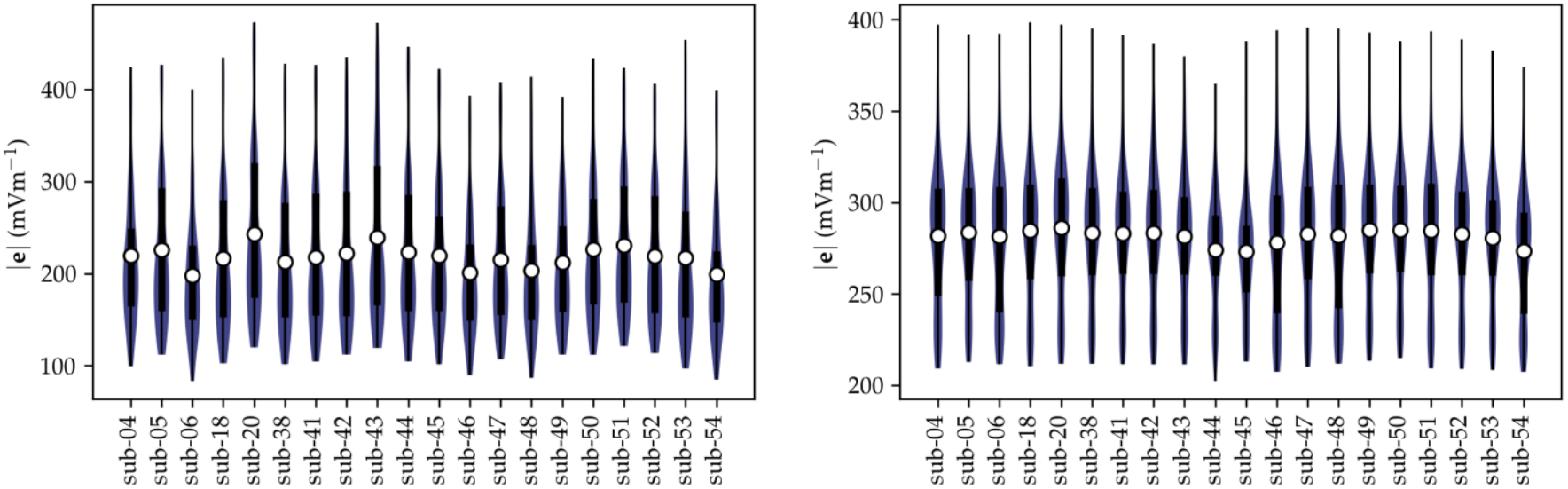




Uniform [min max] (left) vs. informed $G(\mu, \sigma)$ (right) conductivity values

Results, MC target only

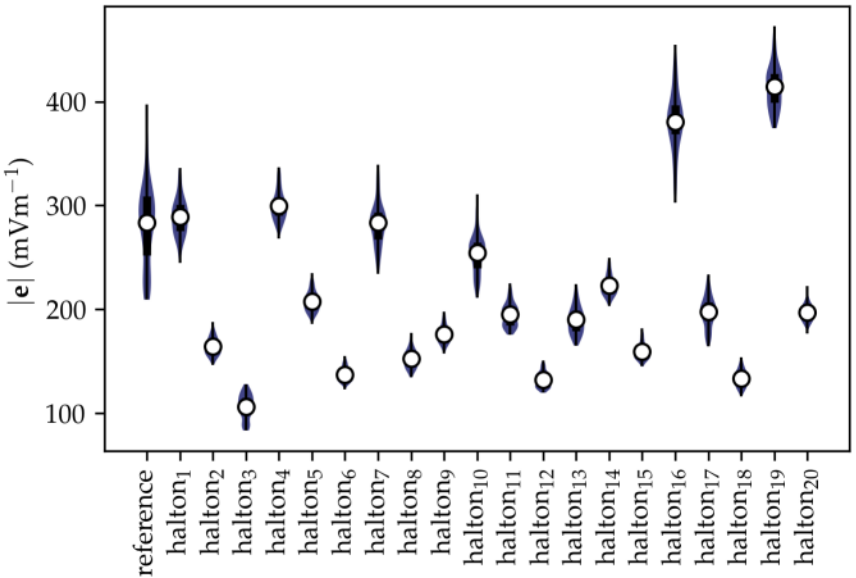
- Effect of different subjects anatomy

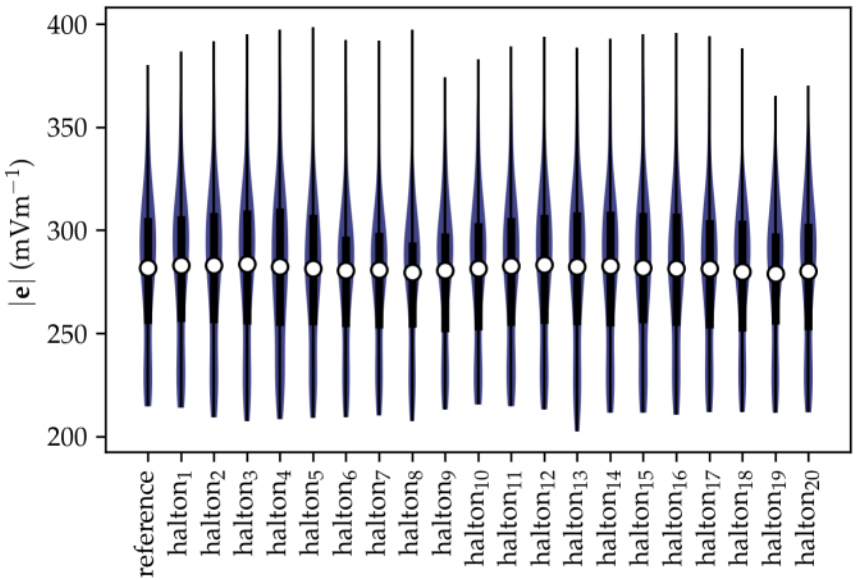


Uniform $[\min\ \max]$ (left) vs. informed $G(\mu, \sigma)$ (right) conductivity values

Results, MC target only

- Effect of conductivity profile variability





Uniform $[\min\ \max]$ (left) vs. informed $G(\mu, \sigma)$ (right) conductivity values

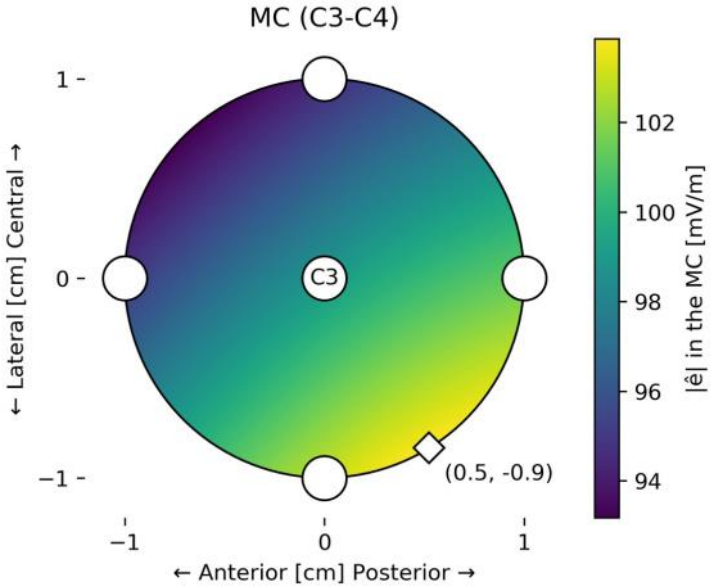
Discussion

- Sources of variance
  - Electrode positioning → small (but big electrodes)
  - Subject's anatomy → relatively small (but ~uniform population)
  - Conductivity → BIG (but smaller if informed)
- Conductivity vs. anatomy & electrodes
- Large $|e|$ value amplitude range
  → "sufficient to too small!"

Future…

Individualised setup

- measure (relative) tissue properties, e.g. with “magnetic resonance electric impedance tomography” (MREIT)
- adjust current intensity
- optimize electrode placement



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- M. Grignard et al., ‘Why tDCS models cannot be trusted yet? — A simulation study’. Pre-print. 2022. https://hdl.handle.net/2268/294662 Code on https://github.com/CyclotronResearchCentre/BrainWeb-tDCS

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