

High-resolution head model of transcranial direct current stimulation: A labeling analysis*

Chris Thomas, Yu Huang, Paula Cristina Faria, and Abhishek Datta

Abstract— The ability of transcranial direct current stimulation (tDCS) to produce lasting polarity-specific modulatory effects continues to drive use both in research and clinical domains. Computational models of tDCS over the years have provided valuable insight on the current flow pattern and magnitude of electric field induced in the cortex. However, induced cortical values are usually not systematically quantified for different brain subcomponents that allow further investigation into the relevant contribution of these distinct regions. This information is of significant interest given different subcomponents of the brain contribute to different functions that ultimately underlie net outcomes. Thus given a particular stimulation response and the current flow pattern, one can potentially infer results in relation to current flow in different compartments (regions affected/spared, magnitude, etc.) The aim of this study is to determine tDCS induced electric field/current density using a high resolution head model incorporating a brain parcellated into 17 notable gyri and 10 sub-cortical regions. We consider both conventional tDCS and High Definition (HD)-tDCS electrode montages. The induced electrical field in each parcellated brain region is computed and compared across the two montages.

Findings indicate that maximum electrical field is induced in the precentral gyrus for both the montages considered. As expected, the current flow pattern using the HD-tDCS montage considered is more restricted- both spatially and depth-wise. The conventional tDCS montage results in deeper current flow with sub-cortical structures subject to as much as 47-95% of the current flow in the upper cortical regions. For the HD montage, electric field in the subcortical structures drop to 12-32% of the values induced in the upper regions. Incorporation of labeled human head models may guide rational electrode design and optimization of tDCS by providing more detailed and systematic information.

I. INTRODUCTION

Transcranial Direct Current Stimulation (tDCS) is a non-invasive technique that modulates underlying cortical activity using weak currents in a polarity-specific fashion [1]. It is well tolerated, easy to administer, cost effective, can be applied in a home setting, and allows adjunctive use/pairing with other interventions to potentially enhance outcomes. Clinical tDCS has shown promising beneficial effects for a

host of neurological and neuropsychiatric conditions and for stroke rehabilitation [2]. While tDCS effects depend on several factors, including on-going brain state, stimulation timing with respect to task [3], the induced cortical electric field (EF) intensity and its spatial extent play a central role in the efficacy of the technique.

Conventional tDCS using two large electrode pads (typically 5x5 cm) is considered to result in widespread diffuse current flow. However, conventional tDCS can induce biologically relevant EF in deeper regions including sub-cortical areas [4-7]. Modeling efforts have indicated that EF induced in inner cortical and sub-cortical-structures have comparable magnitude to the cortical surface [8]. This is corroborated by imaging studies revealing widespread changes in regional cerebral blood flow in both cortical and subcortical areas [9]. High-Definition (HD) tDCS is a variation of the conventional approach that employs arrays of smaller sized electrodes. These arrays allow flexibility to deliver optimized current flow in an application-specific manner- by imposing constraints like intensity, focality, etc. A simple and common realization of HD application is a ‘4X1 ring’ montage that allows adjusting the ratio of spatial versus depth focality by simply adjusting the ring diameter. Studies involving tDCS either adopt the conventional approach or the HD approach depending on the need for wide versus more targeted flow.

It continues to be important to have a detailed understanding of tDCS current flow to understand which brain regions are affected/spared and by how much. The aim of this study is to quantify the induced EF across the entire brain- segregated into different labeled components. This would facilitate not only relating outcomes to regions receiving considerable versus attenuated flow but to also determine optimized electrode montage to target/avoid specific regions [10]. tDCS studies are commonly planned by having a intended target, likely a “gyrus of interest” and are administered by positioning the active electrode on scalp directly coinciding over the gyrus. In addition, it is known that tDCS current flow is significantly influenced by the gyri / sulci anatomy resulting in EF peaks or “hotspots” at discrete cortical locations. This study incorporates a brain parcellated into 17 notable gyri facilitating individual analysis through each of the structures. Furthermore, current flow patterns through deeper subcortical structures are also of interest as the pathophysiology of many neurological and neuropsychiatric conditions are mediated by these structures. The head model considered therefore includes 10 subcortical regions in addition to the aforementioned gyri regions.

Several previous MRI-derived head models have been used to compute tDCS induced EF. In this study, we perform the first systematic study quantifying current flow in a

*Research supported by NIH 5R44NS092144.

C. Thomas is with Soterix Medical, Inc. New York, NY 10001 USA (Phone: 888-990-8327 E-mail: cthomas@soterixmedical.com).

Y. Huang is with Soterix Medical, Inc. (E-mail: yhuang@soterixmedical.com) and with City College of New York, NY 10031 (Email: andypotatohy@gmail.com)

P.C. Faria is with Polytechnic Institute of Leiria, Portugal (E-mail: paula.faria@ipleiria.pt)

A. Datta is with Soterix Medical, Inc. New York 10001 USA, (E-mail: adatta@soterixmedical.com) and with City College of New York, NY 10031 USA (E-mail: adatta@ccny.cuny.edu).

parcellated brain including 27 regions. We evaluate both the classic M1-SO pad and the 4X1 HD electrode configurations. We quantify the EF induced in the different labeled areas and plot the electric field on example regions.

II. METHODS

The original MRI (ID: 100_S_1286) was acquired from the Alzheimer's Disease Neuroimaging Initiative (ADNI) project, and the corresponding labeled scan was acquired from Neuromorphometrics Inc. [11]. The label set included 136 color labels, split into structures located in the left and right hemispheres, along with other subcortical structures and inter-cranial cavities. To simplify the model, right and left halves were combined. The labeled gyri were reduced to 17 notable gyri of interest [12]. Likewise, the labeled subcortical structures were combined into masks resulting in the 10 regions of interest.

The steps for generating forward models while preserving resolution of MRI input data are based on extensive prior work by our group [13-15]. These involve:

- 1) Segmentation of MRI data into tissue categories (e.g. skin, skull, etc.) using a combination of automated and manual tools. The label set was used to further parcellate the brain.
- 2) Stimulation electrodes created as Computer-aided design (CAD) files are then positioned within the skin mask to model the electrode configurations of interest:

- a) M1-SO: Electrodes (5x5 cm) positioned over C3 (M1) and Fp2 (or right supraorbital) region per EEG convention simulating the classic motor cortex tDCS

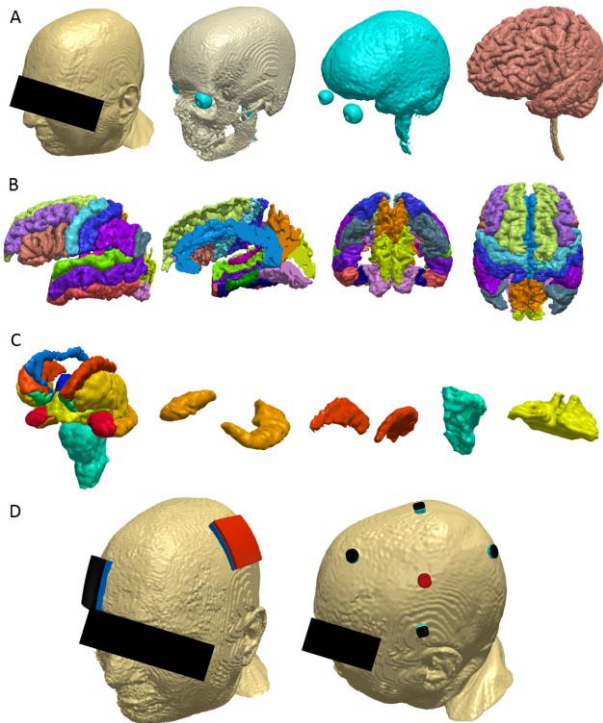


Figure 1. A. Segmentation masks of a sample subject. B. Segmentation masks of the 17 notable gyri (see full list in Table I). C. Segmentation masks of the 10 sub-cortical regions (side, medial, frontal and top views). A subset was plotted separately for better clarity (Orange: Hippocampus; Red: Caudate; Green: brain stem and yellow: ventral DC). D. Electrode montages considered: M1-SO (left) and 4X1 (right).

montage [1]. The M1 electrode was treated as anode while the SO electrode was treated as cathode.

- b) 4X1 HD ring centered at C3: Disk electrode (12 mm diameter) positioned at C3 with four additional disk electrodes arranged in a circular fashion around C3 (C5, F3, Cz, P3).

The square electrodes were made up of a bottom saline layer and a top electrode layer simulating typical sponge tDCS administration. The disk electrodes were made up of a bottom gel layer and a top electrode layer simulating typical HD administration.

- 3) Generation of accurate finite element (FE) meshes with a high quality factor.

- 4) Resulting meshes are then imported into a FE solver and respective electrical conductivities assigned (in S/m): skin (0.465); skull (0.01); CSF (1.65); gray matter (0.276); white matter (0.126); air ($1e-7$); electrode ($5.8e7$); sponge (1.4); gel (0.3) [3]. The relevant boundary conditions are then imposed: 1 mA at the active (anode) electrode, ground condition at the reference (cathode) electrode(s) and all other external surfaces treated as insulated. The standard Laplacian equation is solved using appropriate numerical solver and tolerance settings

The EF induced in each of the notable gyri and the subcortical structures were determined for each montage. Since tDCS protocols are typically planned by positioning the active electrode “over region of interest”, the induced EF value at regions directly underneath the active electrode is logically of more interest. Since current flow is expected between the electrodes as well, we generated EF plots on the regions encompassing central regions and regions anterior to it, namely: precentral, postcentral, superior frontal, middle frontal, and inferior frontal gyri respectively. We also generated EF plots on representative subcortical structures (Figure 2). For each of the structures considered, we determined the maximum, mean and standard deviation of induced EF for both the left and right hemispheres (Table I). The percentage decrement of the induced EF in a given subcortical region was determined relative to the value induced in the precentral gyrus - the intended cortical target of the chosen electrode configurations (Table II).

III. RESULTS

The current flow due to the M1-SO montage as shown in several prior studies is widespread and was evident by substantial current flow not only in the left hemisphere but also in the right hemisphere. Of all the gyri regions analyzed, the maximum EF was induced on the precentral gyrus (0.276 V/m) which is expected given the proximity to the M1 electrode. On the contrary, the current flow due to the 4X1 HD montage is confined to regions defined by the ring perimeter and therefore reflected by EF restricted to the left precentral and left postcentral areas (Figure 2 right). Some current flow was observed in the frontal gyri regions but limited to the area immediately adjacent to the precentral gyri. Similar to the M1-SO montage, the maximum EF for the 4X1 montage was induced on the precentral gyrus (0.257

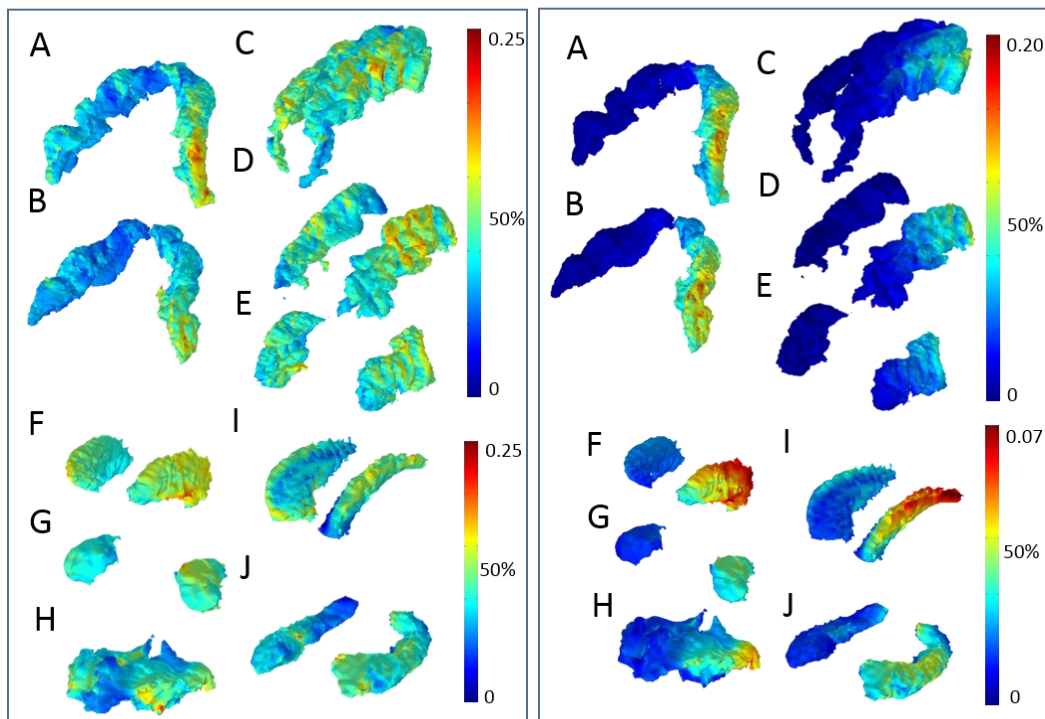


Figure 2. Induced electric field magnitude plots for the C3-SO (left) and the 4X1 (right) configurations. A through E denote representative notable gyri. F through J denote representative subcortical structures. A: precentral; B: postcentral; C: superior frontal; D: middle frontal; E: inferior frontal; F: putamen; G: amygdala; H: ventral DC; I: caudate; J: hippocampus

Mask Name	M1/SO (V/m)						4x1 C3 (V/m)					
	Max		Mean		Standard Deviation		Max		Mean		Standard Deviation	
	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
Angular Gyrus	1.90E-01	8.92E-02	6.95E-02	4.82E-02	1.87E-02	5.53E-03	2.03E-01	1.07E-01	8.38E-02	1.13E-02	2.16E-02	1.38E-02
Cingulate Gyrus	1.95E-01	1.83E-01	7.81E-02	7.36E-02	1.93E-02	2.02E-02	6.87E-02	3.99E-02	1.97E-02	1.30E-02	7.31E-03	3.39E-03
Cuneus	9.11E-02	9.33E-02	4.63E-02	4.48E-02	8.77E-03	7.02E-03	3.52E-02	3.57E-02	1.64E-02	1.12E-02	3.58E-03	2.47E-03
Fusiform Gyrus	1.79E-01	1.67E-01	6.75E-02	6.02E-02	1.37E-02	1.68E-02	4.20E-02	1.41E-02	1.70E-02	7.44E-03	4.10E-03	1.06E-03
Inferior Frontal Gyrus	2.56E-01	2.42E-01	1.11E-01	1.02E-01	1.99E-02	2.03E-02	1.32E-01	7.28E-02	4.32E-02	8.98E-03	1.78E-02	6.72E-03
Inferior Temporal Gyrus	1.49E-01	1.39E-01	7.89E-02	5.69E-02	1.25E-02	1.49E-02	5.16E-02	3.18E-02	2.02E-02	7.68E-03	6.83E-03	3.05E-03
Lingual Gyrus	1.16E-01	1.09E-01	5.15E-02	4.18E-02	1.08E-02	8.12E-03	4.47E-02	2.71E-02	1.42E-02	9.92E-03	3.74E-03	2.14E-03
Middle Frontal Gyrus	2.50E-01	2.25E-01	1.14E-01	1.00E-01	2.27E-02	1.96E-02	1.56E-01	2.92E-02	4.48E-02	7.71E-03	2.39E-02	2.90E-03
Middle Temporal Gyrus'	2.25E-01	2.07E-01	8.67E-02	5.62E-02	1.47E-02	1.15E-02	1.11E-01	8.30E-02	3.21E-02	8.06E-03	1.12E-02	6.05E-03
Parahippocampal Gyrus	2.75E-01	2.20E-01	8.86E-02	7.96E-02	1.75E-02	2.01E-02	4.68E-02	3.65E-02	1.86E-02	1.01E-02	5.37E-03	3.02E-03
Postcentral Gyrus	2.66E-01	1.69E-01	1.01E-01	6.77E-02	2.63E-02	1.28E-02	2.06E-01	8.10E-02	8.50E-02	1.28E-02	2.36E-02	1.03E-02
Precentral Gyrus	2.76E-01	1.89E-01	1.06E-01	7.56E-02	2.65E-02	1.53E-02	2.57E-01	3.65E-02	7.85E-02	1.01E-02	2.57E-02	4.16E-03
Precuneus	1.39E-01	1.04E-01	5.69E-02	4.84E-02	1.20E-02	7.73E-03	7.71E-02	3.63E-02	2.28E-02	1.45E-02	7.13E-03	3.26E-03
Superior Frontal Gyrus	2.37E-01	2.51E-01	1.09E-01	1.04E-01	2.08E-02	2.65E-02	1.42E-01	4.04E-02	3.98E-02	1.24E-02	2.24E-02	5.74E-03
Superior Temporal Gyrus	1.71E-01	1.12E-01	9.62E-02	5.89E-02	1.78E-02	9.89E-03	1.34E-01	1.79E-02	4.38E-02	7.08E-03	1.91E-02	1.58E-03
Supramarginal Gyrus	2.35E-01	1.81E-01	1.00E-01	6.26E-02	2.04E-02	1.28E-02	2.03E-01	1.07E-01	8.38E-02	1.13E-02	2.16E-02	1.38E-02
Transverse Temporal Gyrus	1.87E-01	1.47E-01	1.02E-01	7.00E-02	2.25E-02	1.26E-02	1.03E-01	2.20E-02	4.27E-02	9.57E-03	1.54E-02	2.02E-03
Accumbens Area	1.30E-01	1.73E-01	8.16E-02	1.18E-01	1.17E-02	1.96E-02	3.10E-02	1.76E-02	1.66E-02	1.27E-02	2.66E-03	1.89E-03
Amygdala	1.91E-01	1.43E-01	1.16E-01	9.26E-02	1.95E-02	1.19E-02	5.16E-02	1.73E-02	2.78E-02	1.20E-02	5.33E-03	1.79E-03
Brain Stem	2.86E-01	1.79E-01	6.20E-02	6.80E-02	2.26E-02	1.88E-02	3.59E-02	2.51E-02	1.18E-02	9.56E-03	4.31E-03	2.19E-03
Caudate	1.92E-01	1.92E-01	1.01E-01	1.14E-01	2.77E-02	2.09E-02	9.65E-02	3.24E-02	3.53E-02	1.78E-02	1.47E-02	4.09E-03
Corpus Callosum	2.44E-01	1.94E-01	9.28E-02	8.75E-02	3.92E-02	2.74E-02	4.70E-02	3.77E-02	2.41E-02	1.94E-02	6.63E-03	4.82E-03
Hippocampus	2.64E-01	2.39E-01	1.00E-01	8.25E-02	2.18E-02	2.37E-02	8.11E-02	3.86E-02	2.77E-02	1.23E-02	7.29E-03	3.08E-03
Pallidum	1.76E-01	1.44E-01	1.13E-01	9.97E-02	1.31E-02	7.75E-03	5.65E-02	2.05E-02	3.44E-02	1.49E-02	7.26E-03	1.38E-03
Putamen	2.07E-01	1.86E-01	1.30E-01	1.08E-01	1.95E-02	1.69E-02	7.42E-02	2.24E-02	4.31E-02	1.60E-02	1.16E-02	2.30E-03
Thalamus Proper	1.94E-01	1.77E-01	8.17E-02	7.57E-02	2.08E-02	1.81E-02	5.77E-02	4.16E-02	2.26E-02	1.40E-02	8.96E-03	3.93E-03
Ventral DC	2.43E-01	2.30E-01	9.50E-02	9.61E-02	3.34E-02	2.38E-02	8.35E-02	3.46E-02	2.06E-02	1.18E-02	1.13E-02	3.04E-03

TABLE I: Electric field values for the two configurations tested. For each gyri and sub-cortical structure, maximum (max), mean and the standard deviation was determined.

V/m) – again expected given the proximity of the region to the center electrode in the ring montage. For the M1-SO montage, the peak induced value in the subcortical regions with respect to the peak induced value in the precentral gyrus varied between 47% to 95% (barring the brain stem). Therefore in some subcortical regions like the hippocampus and ventral DC, the induced EF was found to be as

	Peak Subcortical/Peak Target			
	M1/SO		4X1 C3	
	Left	Right	Left	Right
Accumbens Area'	47.20%	62.82%	12.08%	6.86%
Amygdala'	69.08%	51.71%	20.12%	6.74%
Brain Stem'	103.58%	65.03%	13.99%	9.77%
Caudate'	69.42%	69.41%	37.62%	12.64%
Corpus Callosum'	88.27%	70.41%	18.31%	14.70%
Hippocampus'	95.57%	86.70%	31.63%	15.04%
Pallidum'	63.82%	52.11%	22.02%	7.98%
Putamen'	75.00%	67.56%	28.92%	8.72%
Thalamus Proper'	70.34%	64.03%	22.50%	16.23%
Ventral DC'	88.01%	83.25%	32.54%	13.47%

TABLE II: The decrement of the induced EF in a given sub-cortical structure in relation to value induced in target (precentral gyrus). The maximum or peak induced values are considered.

high as the values induced on the cortical surface. For the 4X1 montage, the variation of peak induced value in the subcortical regions with respect to the value induced in the precentral gyrus was 12% to 32%. This considerable drop in value is expected given the restricted and as a result superficial current flow pattern of the 4X1 montage. We also noted lower EF value variability in areas removed from the dominant current flow path (see standard deviation in right hemisphere structures). The variability in EF values for the M1-SO montage across most of the structures was overall higher given the widespread nature of the current flow.

IV. DISCUSSION

This study systematically quantified the induced EF values in 27 different regions for the classic M1-SO montage and the 4X1 HD montage centered over the C3 location. While already demonstrated via actual experimental recordings [4-7], this label based modeling study also confirms that contrary to common perception, scalp applied tDCS using the M1-SO montage can generate electric fields deep inside the brain and the values in some regions are similar to the ones induced in the superficial cortical regions. Chhatbar et al. 2018 noted a value of 0.13 V/m in the thalamic / subthalamic region for 2 mA current injection using a bitemporal montage. While our model did not include a separate mask for subthalamic region, we observed a mean value of 0.08 V/m for 1 mA current injection (or 0.16 V/m for 2 mA). We therefore observe comparable magnitude but note that an exact match cannot be expected due to the consideration of a different individual dataset (not specific to the one who underwent experimentation), a different electrode montage, amongst other differences.

In summary, the incorporation of labeling information provides an opportunity to obtain detailed information of the relevant contribution of distinct regions- thereby allowing disentangling their individual role. This information is meaningful given the different role different brain regions play that ultimately fashion outcomes- whether it be behaviorally, clinically or physiologically. Computational forward models incorporating labeling analysis provide an systematic approach to both- plan/design optimal strategy targeting /or avoiding specific compartments as well as to relate stimulation outcome to individual label current flow.

ACKNOWLEDGEMENT

Data collections and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) (NIH Grant U01 AG024904) and Department of Defense (DOD) ADNI (DOD award number W81XWH-12-2-0012).

REFERENCES

- [1] Nitsche MA and Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol.* 2000 Sep 15;527 Pt 3:633-9.
- [2] Lefaucheur JP. Evidence-based guidelines on the therapeutic use of tDCS *Clin Neurophysiol* 2017;128:56-92
- [3] Woods AJ, Antal A, Bikson M, Boggio PS, Brunoni AR, Celnik P, et al. A technical guide to tDCS, and related non-invasive brain stimulation tools. *Clin Neurophysiol.* 2016 Feb;127(2):1031-1048.
- [4] Chhatbar PY, George MS. Evidence of transcranial direct current stimulation-generated electric fields at subthalamic level in human brain in vivo. *Brain Stimul* 2018; 11(4):727-733
- [5] Opitz A, Falchier A. Spatiotemporal structure of intracranial electric fields *Sci Rep* 2016;6:31236
- [6] Huang Y, Liu AA, Lafon B. Measurements and models of electric fields in the in vivo human brain during transcranial electric stimulation. *Elife* 2017;6
- [7] Ruhnau P. Sailing in a sea of disbelief: In vivo measurements of transcranial electric stimulation in human subcortical structures. *Brain Stimul* 2018;11(1):241-243
- [8] Dasilva AF tDCS-induced analgesia and electrical fields in pain-related neural networks in chronic migraine. *Headache.*
- [9] Lang N, Siebner H. How does transcranial DC stimulation of the primary motor cortex alter regional neuronal activity in the human brain?
- [10] Dmochowski JP, Datta A, Bikson M. Optimized multi-electrode stimulation increases focality and intensity at target. *J Neural Eng* 2011; 8(4): 046011
- [11] Caviness, V.S., Meyer J, Makris, Kennedy MRI-based topographic parcellation of human neocortex: an anatomically specified method with the estimate of reliability. *J Cogn Neurosci* 1996
- [12] Tallinen T. On the growth and form of cortical convolutions *Nature Phys.* 2016
- [13] Bikson M and Datta A. Guidelines for precise and accurate computational Brain Stimul. 2012 Jul;5(3):430-1.
- [14] DattaA, Truong D, Minhas P, Parra LC, Bikson M. Inter-Individual Variation during Transcranial Direct Current Stimulation and Normalization of Dose Using MRI-Derived Computational Models. *Front Psychiatry.* 2012;3:91.
- [15] Huang Y, Dmochowski JP, Su Y, Datta A, Rorden C, Parra LC. Automated MRI segmentation for individualized modeling of current flow in the human head. *J Neural Eng.* 2013;10(6):066004.
- [16] Sadleir RJ, Vannorsdall TD, Schretlen DJ, Gordon B. Transcranial direct current stimulation (tDCS) in a realistic head model. *Neuroimage* 2010; 1310-18