Optimization of multifocal transcranial current stimulation for weighted cortical pattern targeting from realistic modeling of electric fields

Giulio Ruffini - Neuroelectrics Corporation / Starlab

Overview

- Motivation: MtCS (Multichannel tCS/tES)
- Using MtCS for more focal stimulation
- Using MtCS to target networks
- How to define targets
- Future

Hive project

Can we use non-invasive tech for brain-to-brain communication?

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RESEARCH ARTICLE

157,306 VIEWS | 1 CITATION | 8 SAVES

Conscious Brain-to-Brain Communication in Humans Using Non-Invasive Technologies

Carles Grau, Romuald Ginhoux, Alejandro Riera, Thanh Lam Nguyen, Hubert Chauvat, Michel Berg, Julià L. Amengual, Alvaro Pascual-Leone, Giulio Ruffini

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Brain Stimulation

journal homepage: www.brainstimjrnl.com

Original Research

Effects of transcranial Direct Current Stimulation (tDCS) on cortical activity: A computational modeling study

Behnam Molaee-Ardekani [a,b], Javier Márquez-Ruiz [c], Isabelle Merlet [a,b], Rocio Leal-Campanario [c], Agnès Gruart [c], Raudel Sánchez-Campusano [c], Gwenael Birot [a,b], Giulio Ruffini [d], José-Maria Delgado-García [c], Fabrice Wendling [a,b,*]

From Oscillatory Transcranial Current Stimulation to Scalp EEG Changes: A Biophysical and Physiological Modeling Study

Isabelle Merlet[1,2*], Gwénaël Birot[1,2], Ricardo Salvador[3], Behnam Molaee-Ardekani[1,2], Abeye Mek
Aureli Soria-Frish[4], Giulio Ruffini[4], Pedro C. Miranda[3,5], Fabrice Wendling[1,2]

Original article

Transcranial Direct Current Stimulation Effects in Consciousness

Efthymios Angelakis, PhD[a, b], Evangelia Liouta, MSc[a, b], Nikos Andrea
MD[a, b], Periklis Ktonas, PhD[a], George Stranjalis, MD, PhD[a, b], Damianos E. S

Available online 11 September 2013

Transcranial direct-current stimulation modulates synaptic mechanisms involved in associative learning in behaving rabbits

Javier Márquez-Ruiz[a], Rocio Leal-Campanario[a], Raudel Sánchez-Campusano[a], Behnam Molaee-Ardekani[b,c], Fabrice Wendling[b,c], Pedro C. Miranda[d], Giulio Ruffini[e], Agnès Gruart[a], and José María Delgado-García[a,1]

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The electric field in the cortex during transcranial current stimulation

Pedro Cavaleiro Miranda [a,b,*], Abeye Mekonnen [a], Ricardo Salvador [a], Giulio Ruffini [c]

MtCS- Desired Features (2008)

- **Stimulate:**
  - Controlled - safe - multi-site stimulation (frequencies, intensities, phase relationships control)
  - Independent control of each electrode
  - Use EEG like electrodes (more focal)
- **Measure:**
  - Dual use electrodes (Stimulation and EEG)
  - Measure while stimulating
- **Visualize and adapt:**
  - Simulate E-fields
  - Provide EEG features online, visualization and feedback
  - Provide data services

HIVE - EU FET OPEN Project (2008-2012)

StarStim 8Ch system in a nutshell

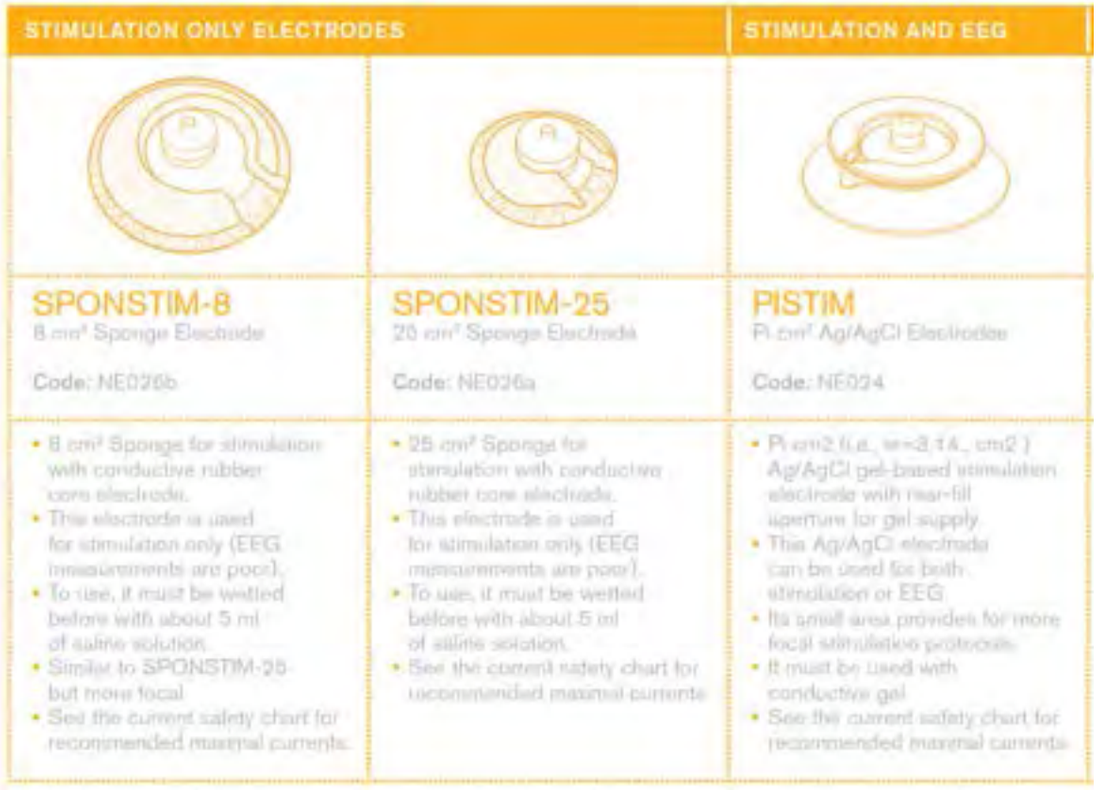
Multi-channel, wireless and programmable tCS
- Stimulate using up to 8 electrodes
- Current-controlled tDCS, tACS, tRNS, Sham
- Allows flexible electrode placement based on the EEG 10-10 system
- Independent current control at each electrode

Dual use electrodes for stimulation and EEG monitoring
- Stimulate and record at the same site using the same electrodes
- Monitor EEG during tDCS – our stimulator circuit is very quiet

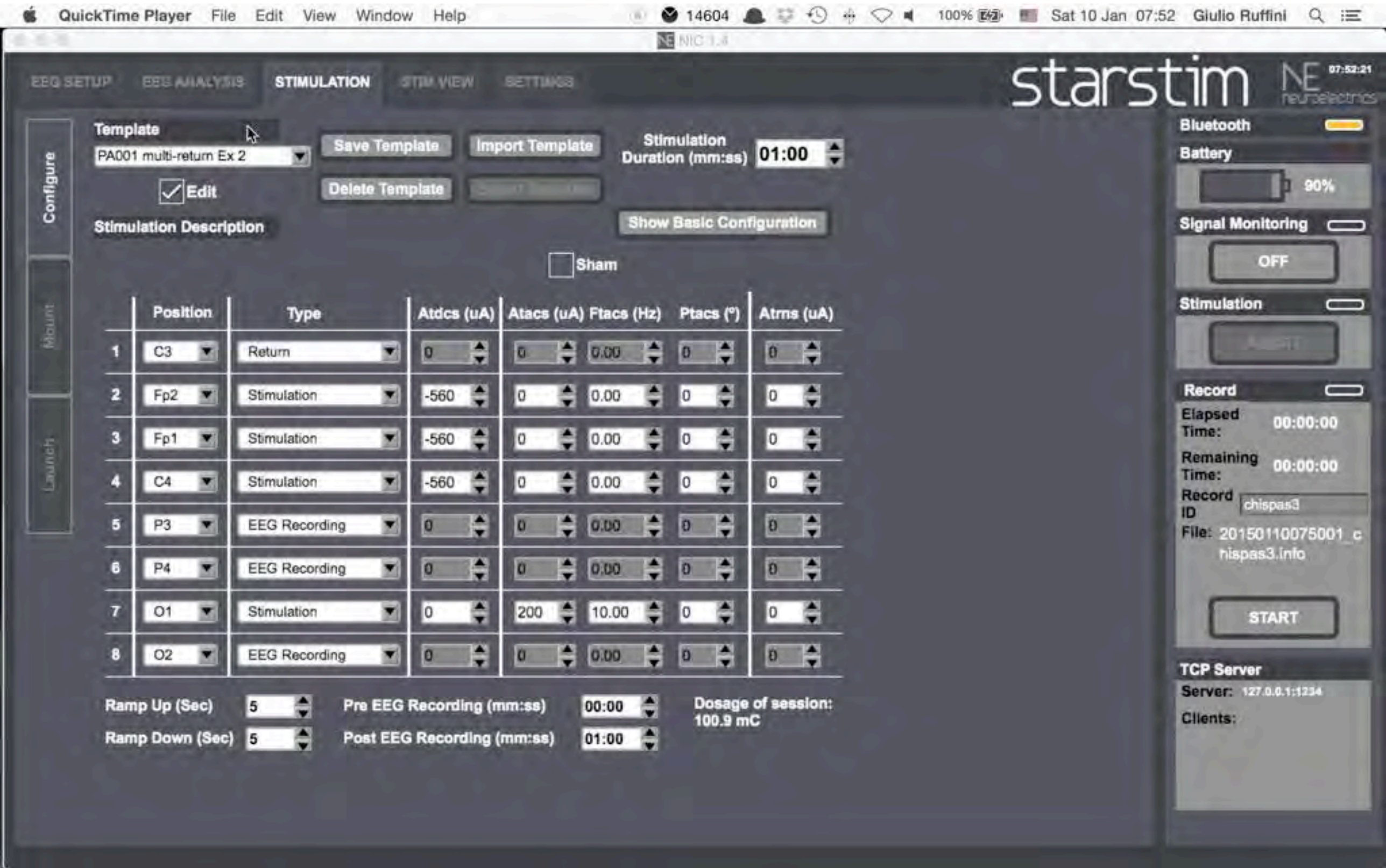
EEG 10-10 cap for precise positioning of elecrodes

A wireless wearable concept for fast and easy setup
- AMobile stimulation and recording away from the clinic or lab
- Quick setup
- 3D accelerometer + SD card
- USB rechargeable Li-Ion battery

Intuitive user application
- User friendly protocol programming and sequencing
- Provide on-line visualization of EEG features
- Simulate generated electric fields associated with tCS
- Cloud connected / home use
- Programmatic control with Matlab API



Implemented!



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The electric field in the cortex during transcranial current stimulation

Pedro Cavaleiro Miranda [a,b,*], Abeye Mekonnen [a], Ricardo Salvador [a], Giulio Ruffini [c]

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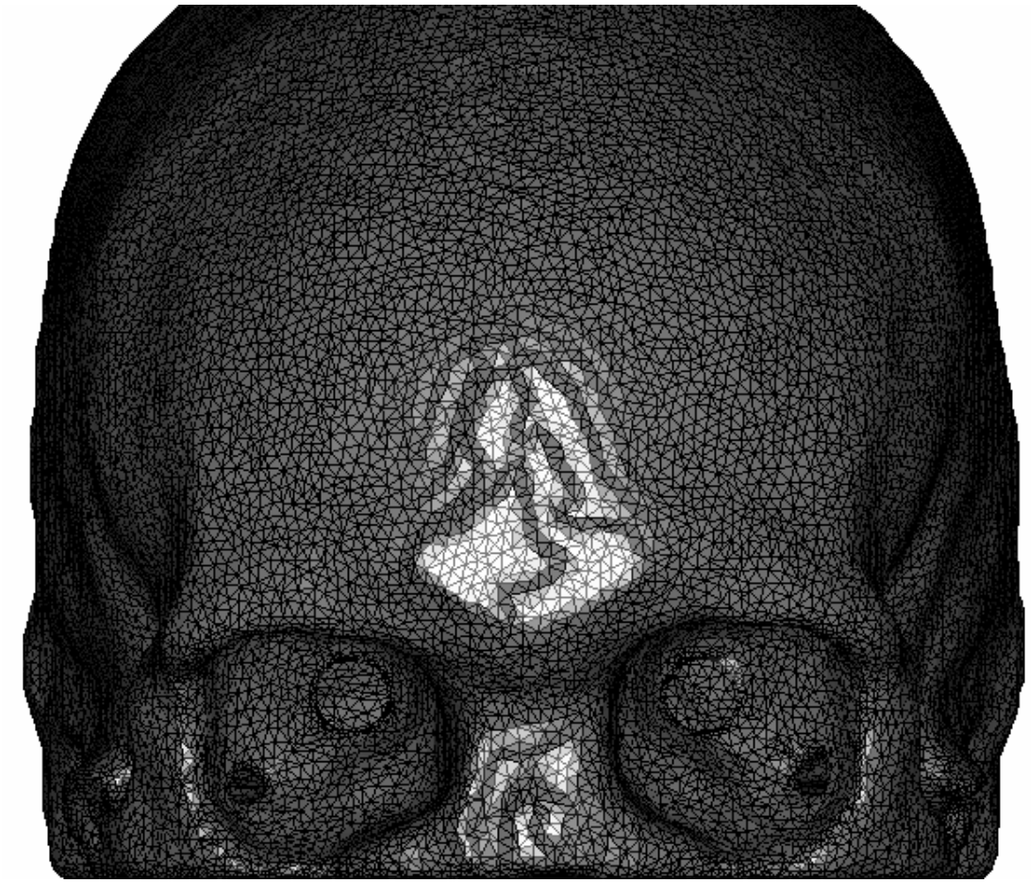
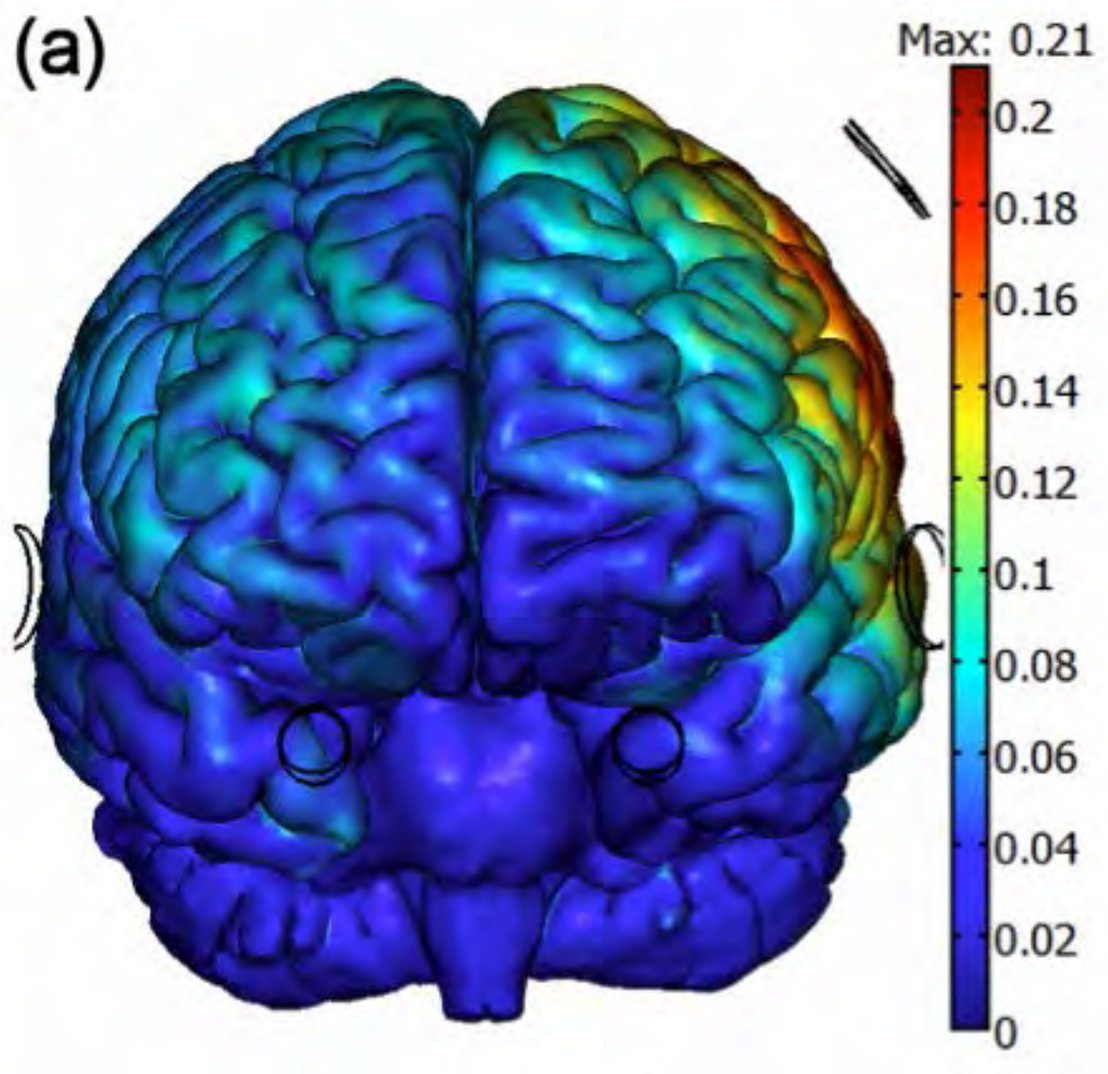
ABSTRACT

The electric field in the cortex during transcranial current stimulation was calculated based on a realistic head model derived from structural MR images. The aim of this study was to investigate the effect of tissue heterogeneity and of the complex cortical geometry on the electric field distribution. To this end, the surfaces separating the different tissues were represented as accurately as possible, particularly the cortical surfaces. Our main finding was that the complex cortical geometry combined with the high conductivity of the CSF which covers the cortex and fills its sulci gives rise to a very distinctive electric field distribution in the cortex, with a strong normal component confined to the bottom of sulci under or near the electrodes and a weaker tangential component that covers large areas of the gyri that lie near each electrode in the direction of the other electrode. These general features are shaped by the details of the sulcal and gyral geometry under and between the electrodes. Smaller electrodes resulted in a significant improvement in the focality of the tangential component but not of the normal component, when focality is defined in terms of percentages of the maximum values in the cortex. Experimental validation of these predictions could provide a better understanding of the mechanisms underlying the acute effects of tCS.

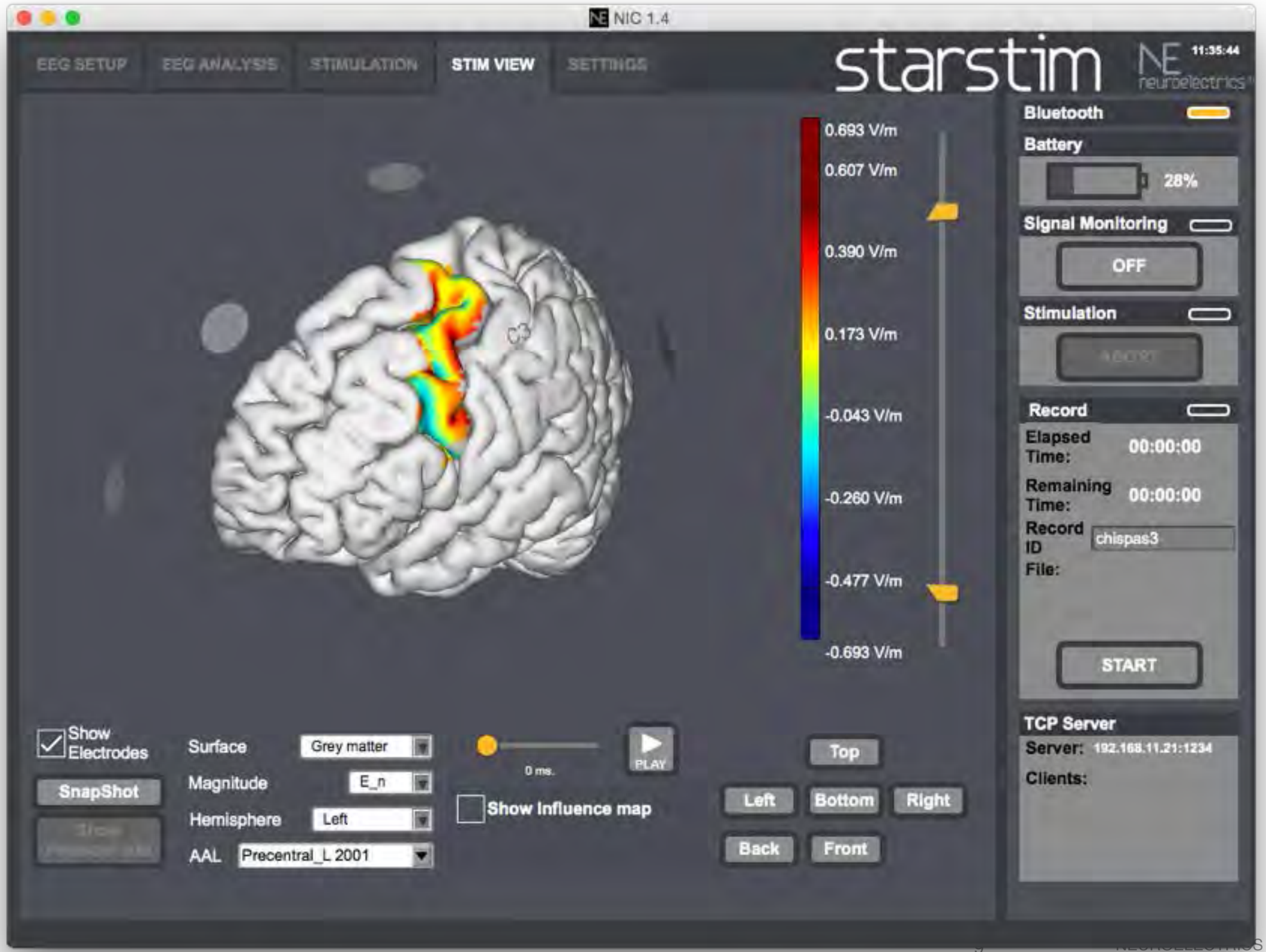
5-layer FEM / Poisson's equation: electric fields





The realistic FE model is shown in Fig. 1. The mesh contains 2.2×10^6 tetrahedral second order Lagrange elements. The surface mesh representing the GM–CSF interface contains 1.5×10^5 triangles with an average area of 1.2 mm^2 and an average edge length of 1.7 mm. The FE model is also in MNI space.

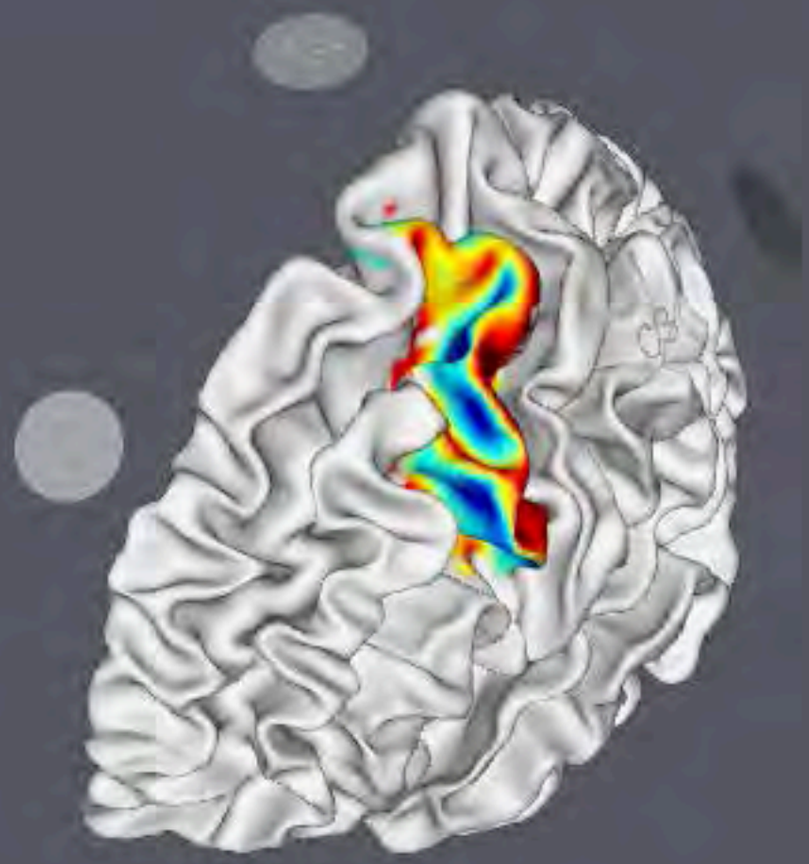
Visualizing the E field



NIC 1.4

EEG SETUP | EEG ANALYSIS | STIMULATION | STIM VIEW | SETTINGS

starstim neuroelectrics 11:38:07



0.686 V/m
0.600 V/m
0.386 V/m
0.171 V/m
-0.043 V/m
-0.257 V/m
-0.471 V/m
-0.686 V/m

Bluetooth

Battery 27%

Signal Monitoring

OFF

Stimulation

ABORT

Record

Elapsed Time: 00:00:00

Remaining Time: 00:00:00

Record ID: chispas3

File:

START

TCP Server

Server: 192.168.11.21:1234

Clients:

Show Electrodes

SnapShot

Show Precuneal info

Surface: Grey matter / White matter

Magnitude: E_n

Hemisphere: Left

AAL: Multiple

0 ms.

PLAY

Show Influence map

Top

Left | Bottom | Right

Back | Front

Transcranial Current Brain Stimulation (tCS): Models and Technologies

Giulio Ruffini, Fabrice Wendling, Isabelle Merlet, Behnam Molaee-Ardekani, Abeye Mekonnen, Ricardo Salvador, Aureli Soria-Frisch, Carles Grau, Stephen Dunne, and Pedro C. Miranda

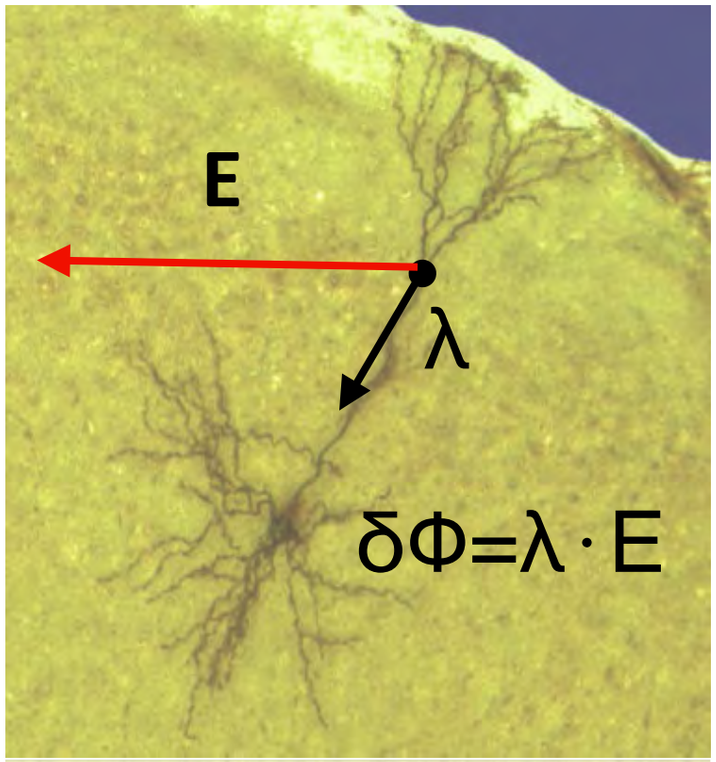
Today, the basic mechanism for interaction in transcranial Current Stimulation (tCS) is thought to be through the coupling of electric fields to elongated form-factor neurons such as pyramidal cells. The role of other types of neurons (e.g., interneurons such as basket cells) or other brain cells, such as glia, is not well understood.

Physically, the external electric field forces the displacement of intracellular ions (which move to cancel the intracellular field), altering the neurons internal charge distribution and as a result modifying the transmembrane potential difference. For a long, straight finite fibre with space constant λ in a homogeneous electric field, the transmembrane potential difference is largest at the fibre termination, with a value that can be approximated by $\lambda \cdot \hat{n}$, where $\hat{n}$ is the unit vector defining the fibre axis. This is an expected first-order result, with a spatial scale provided by the membrane space constant and directions by field and fibre orientation [1].

Thus, a necessary first step in understanding the effects of tCS is to determine the spatial distribution of the generated electric vector field in the brain [2]. For this reason we have developed at NE a software to model electric fields for our multi-channel stimulation system, StarStim.

First order model: “lamba-E” + coherent receptors + Hebb

$$\vec{\lambda}(x) = \lambda(x)\hat{n}(x)$$



- **λ** points from tree to axon termination
- First order effect from dot product of E and λ
- Units of $\delta\Phi = E \cdot \lambda$ are Volts

$$s(E_c(x)) = f(\vec{\lambda}(x) \cdot E_c(x))$$

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Transcranial Current Brain Stimulation (tCS): Models and Technologies

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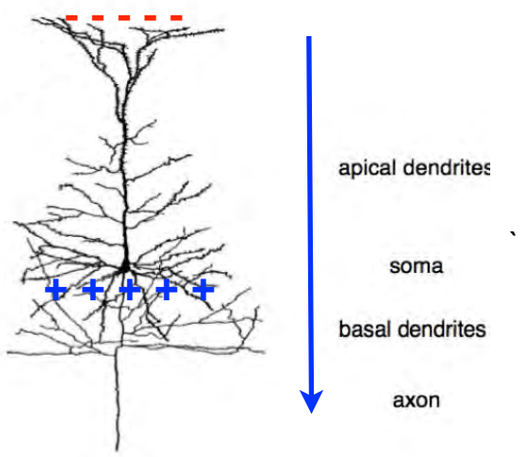
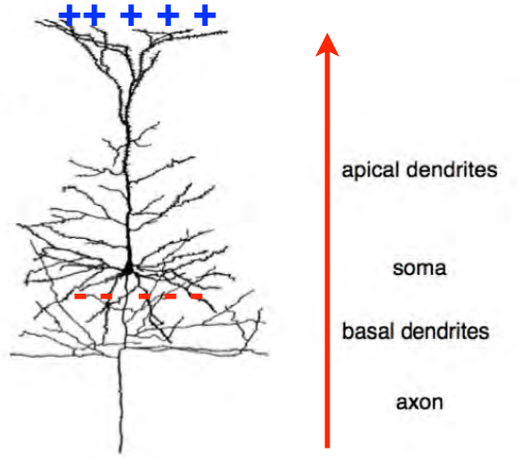


Electric field: Excitatory

Figure 5: Pyramidal cell structure (from [Bower:2003aa]). The outer cortical boundary is on top.



Electric field: Inhibitory

Figure 5: Pyramidal cell structure (from [Bower:2003aa]). The outer cortical boundary is on top.

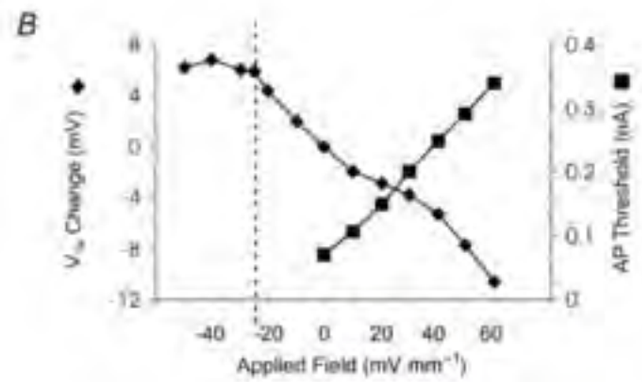
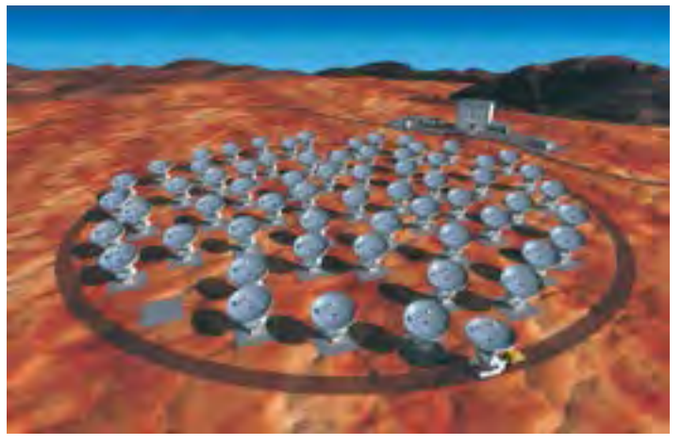
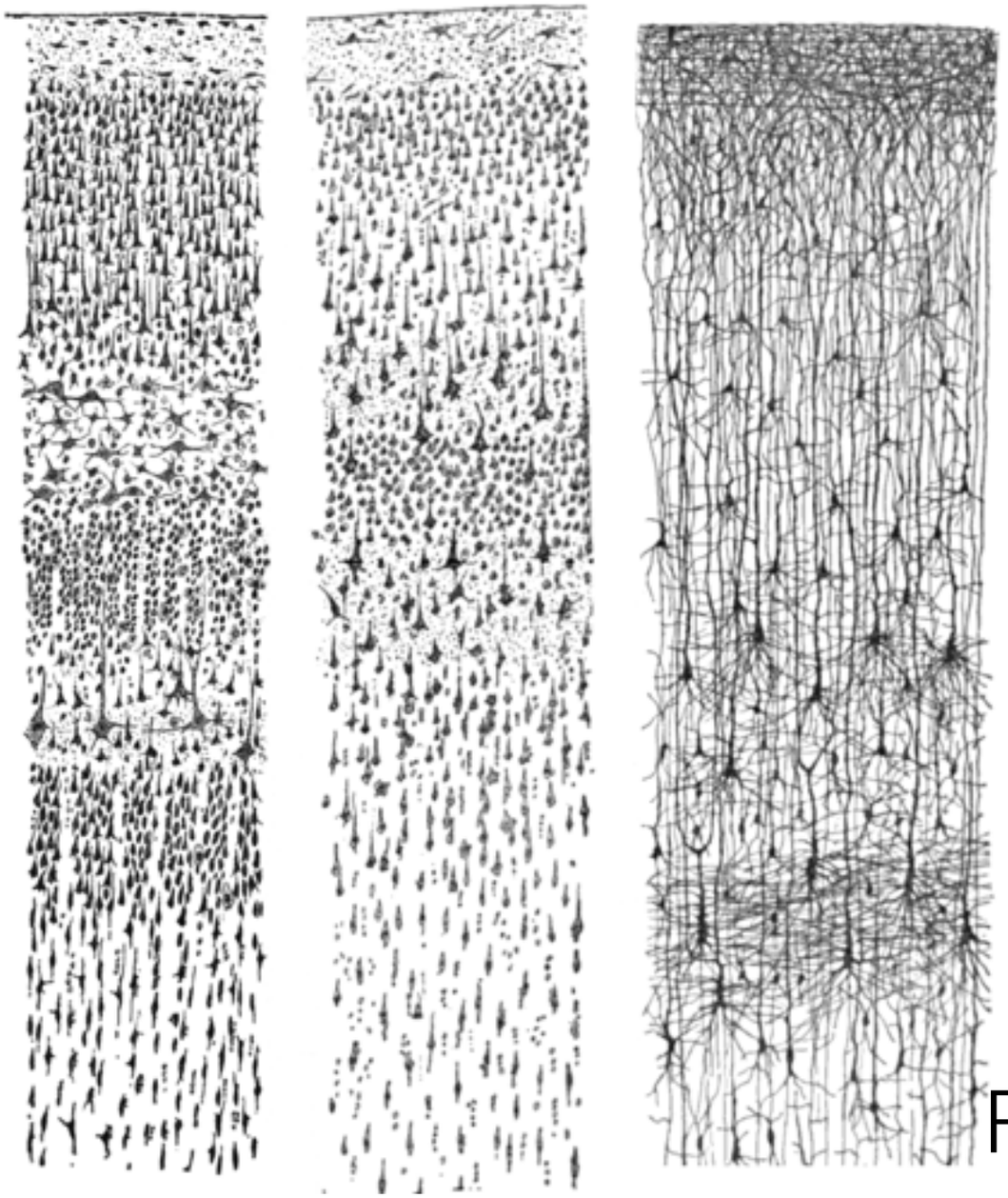
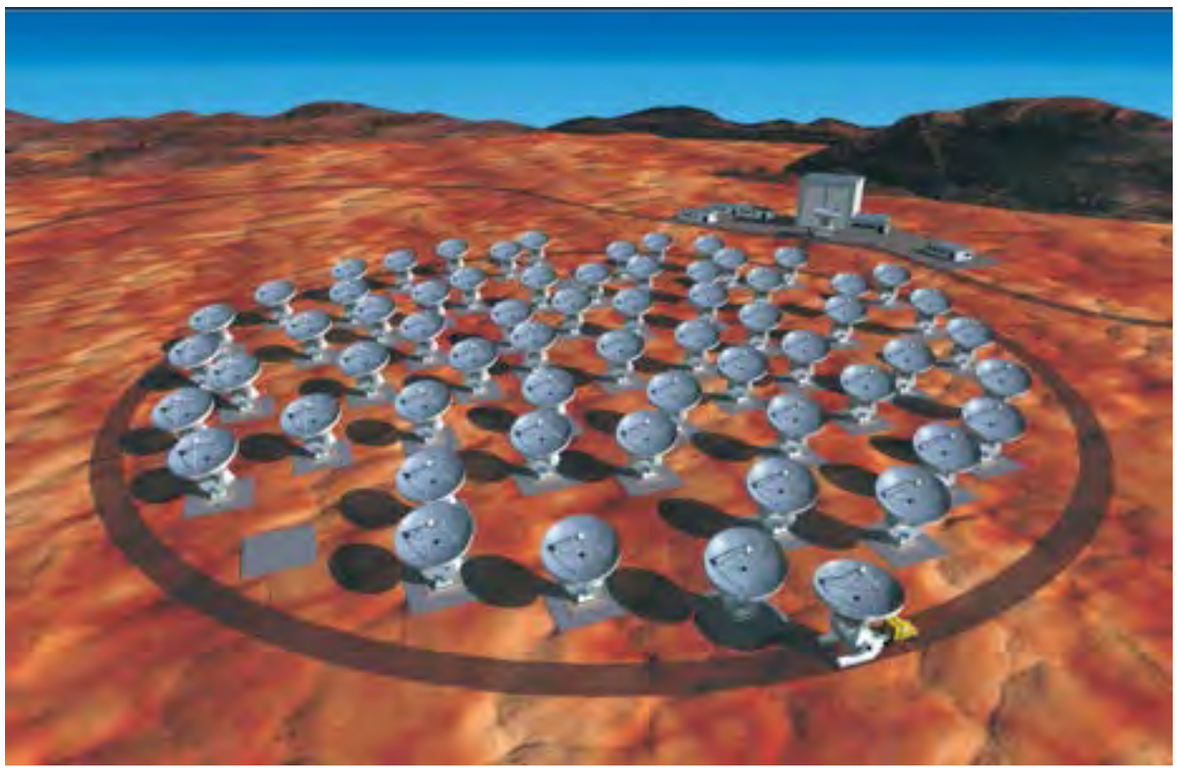


Figure 4: Excerpt from figure 7 of [Bikson:2004aa]. In this paper 'positive fields' are in the soma-to-dendrite direction. They are soma-hyperpolarizing, while 'negative' fields (which we have called 'orthodromic'), in the dendrite-



Coherence emission/ reception (EEG/tCS)



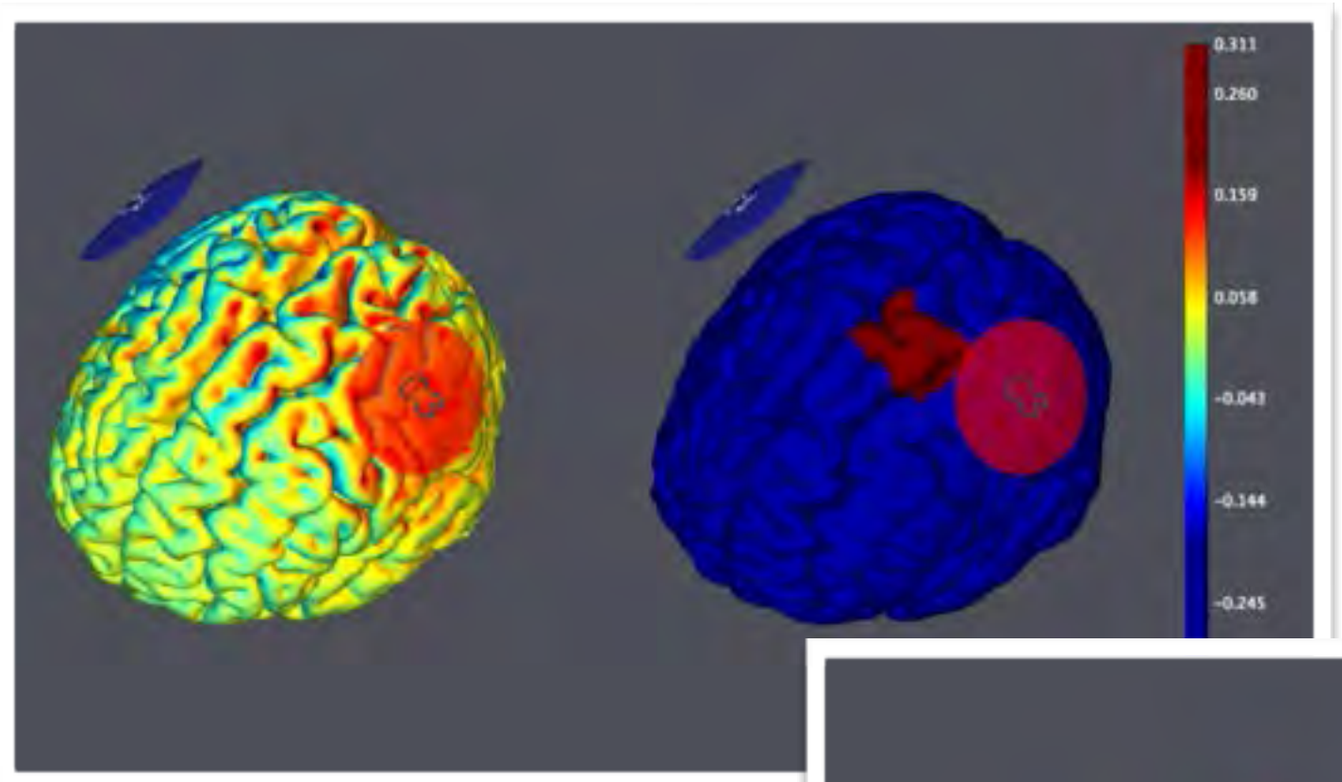


Ramon y Cajal

To optimize …

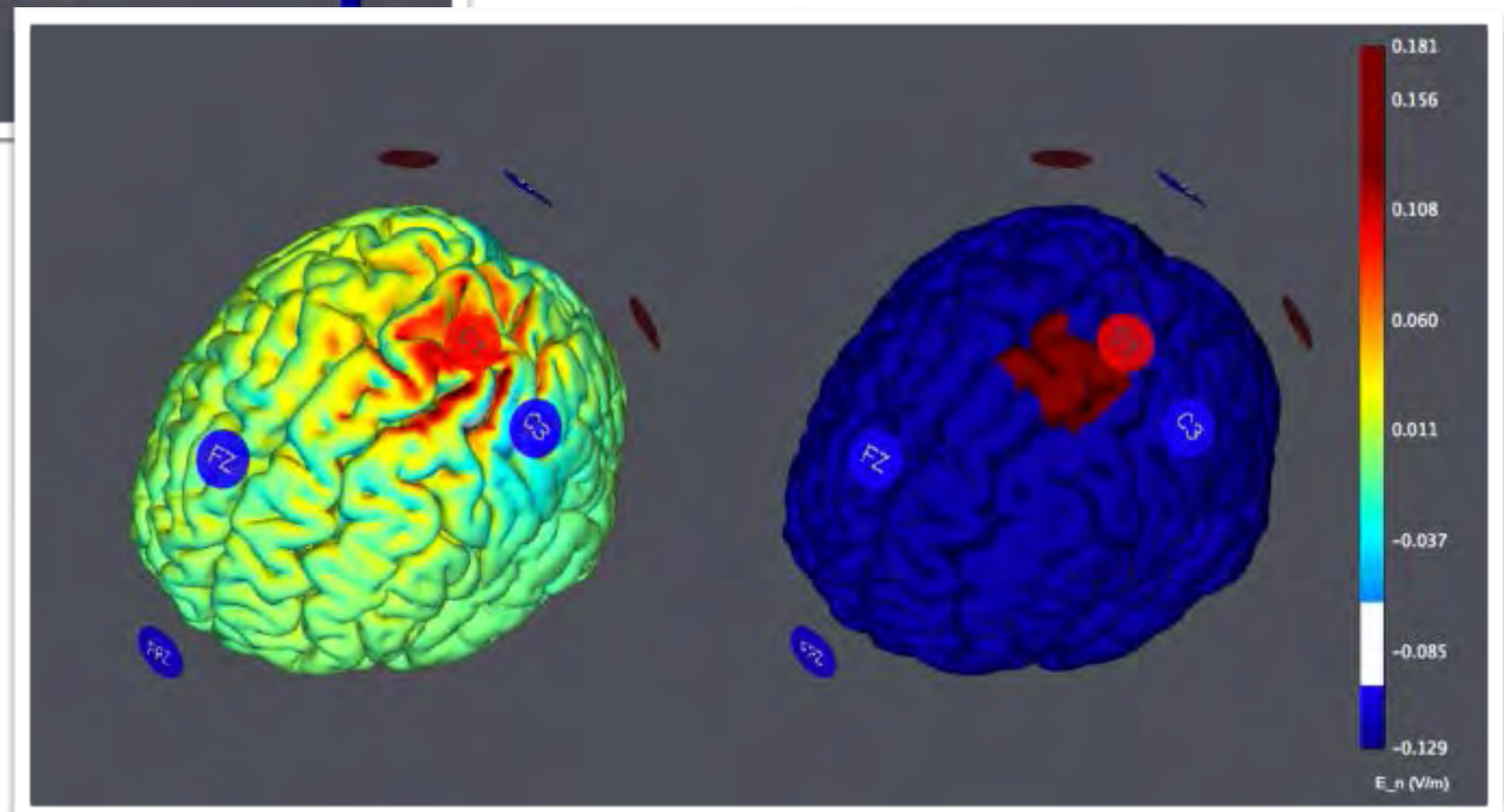
- Specify your target areas and E field targets
- Specify both what to affect and what to leave alone
- Weight your statements: give a weight map
- **Spec**: target map+weight map

Motor cortex target

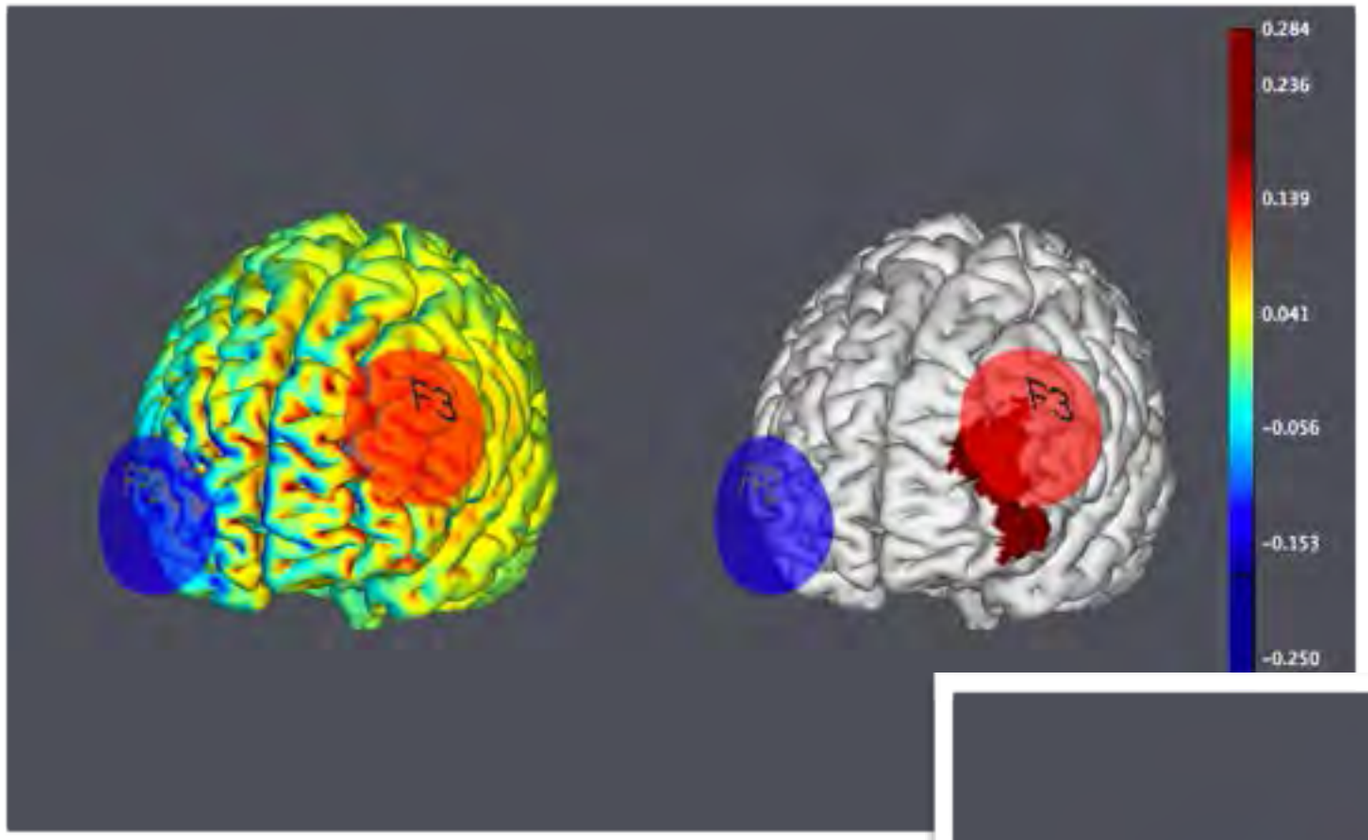


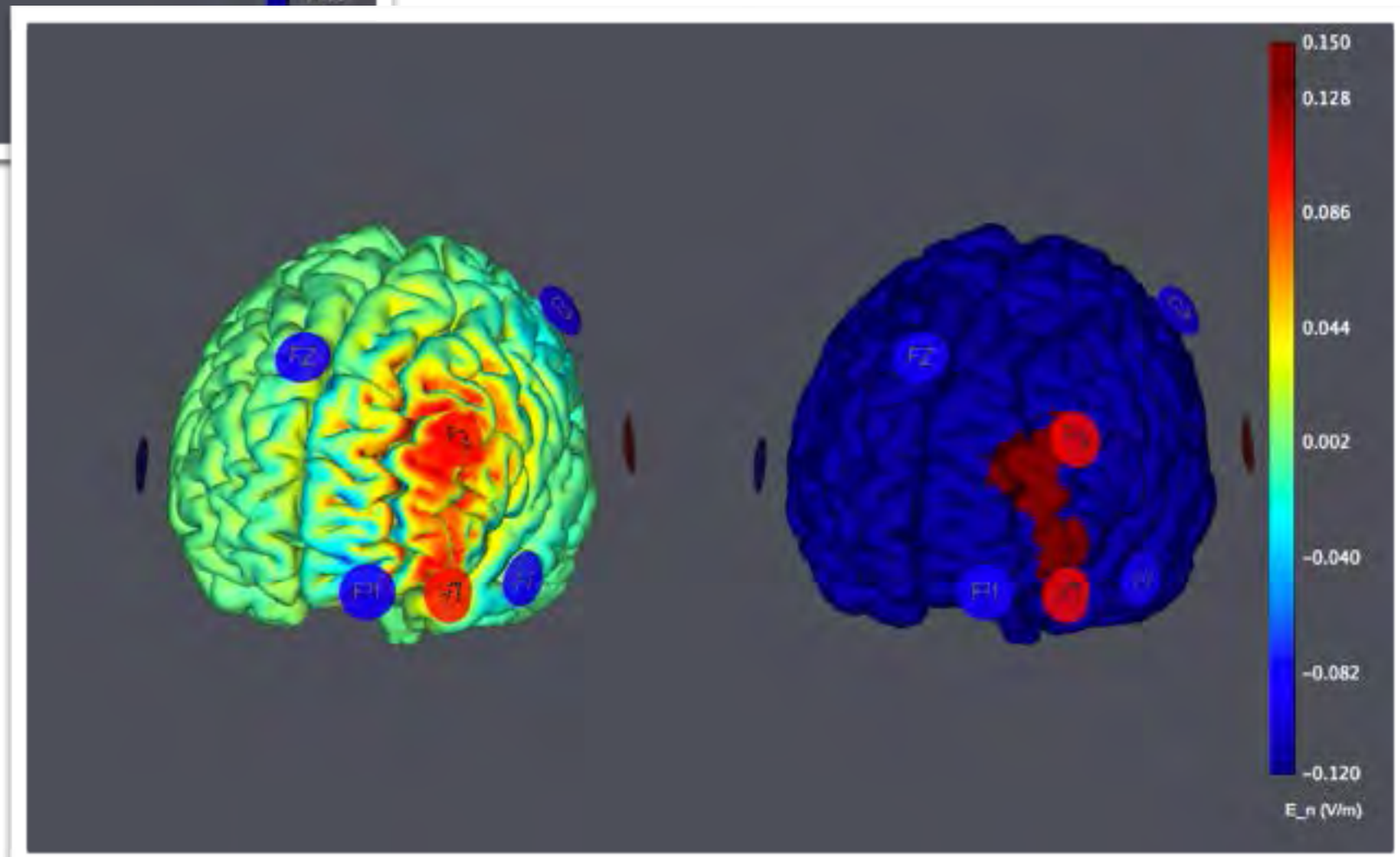
Target on the right
En component on left

MtCS much more precise



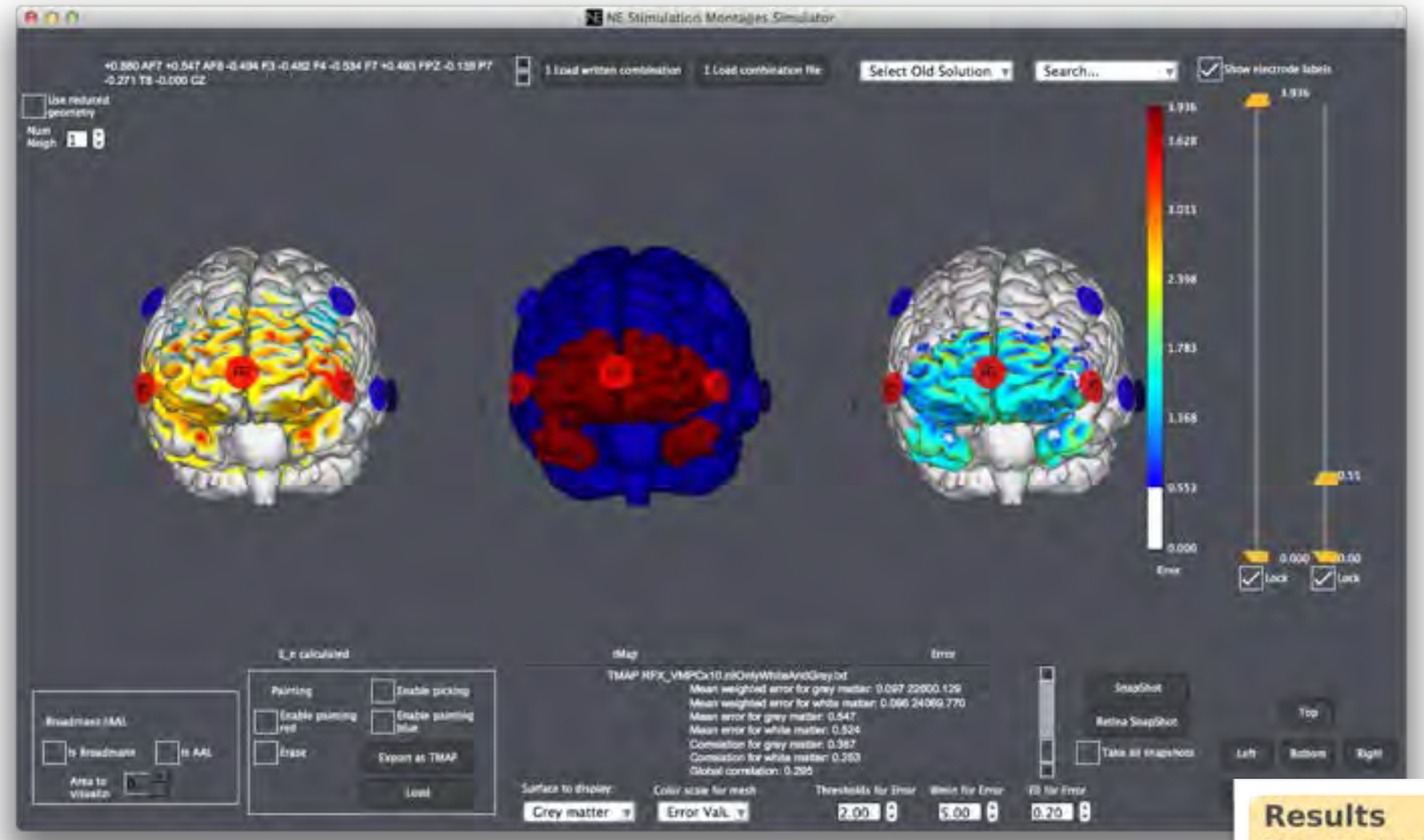
Prefrontal target



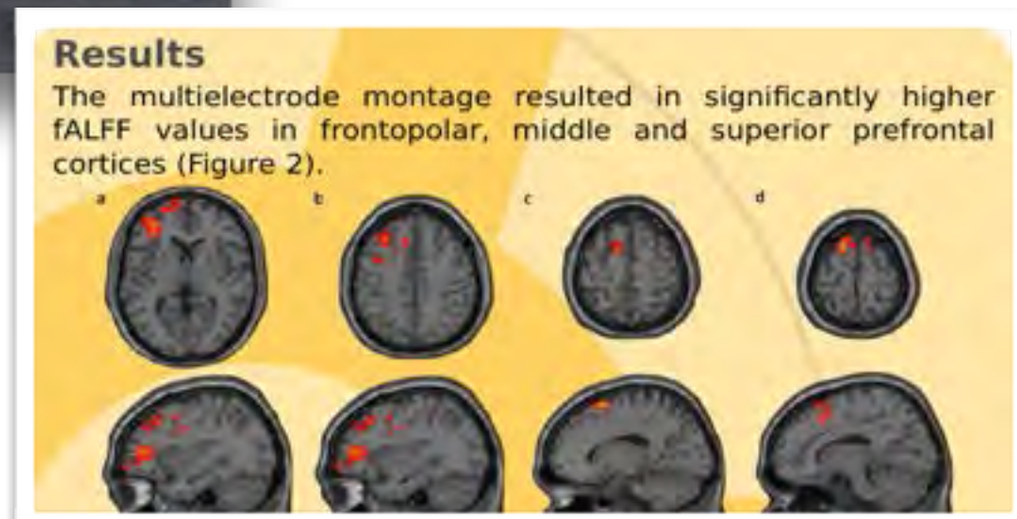


Optimized multielectrode tDCS modulates corticolimbic networks

G. Ruffini*[a,b], C. Martinez-Ruiz de Lara[c], I. Martinez-Zalacain[c], O. Ripolles[a], M. Subira[c], E. Via[c], G. Mitja[a], J. Munuera[e], J. M. Menchón[c,d], C. Soriano-Mas[c,d], Narcís Cardoner[c,d]



Work with N. Cardoner's group



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Optimization of multifocal transcranial current stimulation for weighted cortical pattern targeting from realistic modeling of electric fields

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NIBS
fMRI
PET
rs-fcMRI

ABSTRACT

Recently, multifocal transcranial current stimulation (tCS) devices using several relatively small electrodes have been used to achieve more focal stimulation of specific cortical targets. However, it is becoming increasingly recognized that many behavioral manifestations of neurological and psychiatric disease are not solely the result of abnormality in one isolated brain region but represent alterations in brain networks. In this paper we describe a method for optimizing the configuration of multifocal tCS for stimulation of brain networks, represented by spatially extended cortical targets. We show how, based on fMRI, PET, EEG or other data specifying a target map on the cortical surface for excitatory, inhibitory or neutral stimulation and a constraint on the maximal number of electrodes, a solution can be produced with the optimal currents and locations of the electrodes. The method described here relies on a fast calculation of multifocal tCS electric fields (including components normal and tangential to the cortical boundaries) using a five layer finite element model of a realistic head. Based on the hypothesis that the effects of current stimulation are to first order due to the interaction of electric fields with populations of elongated cortical neurons, it is argued that the optimization problem for tCS stimulation can be defined in terms of the component of the electric field normal to the cortical surface. Solutions are found using constrained least squares to optimize current intensities, while electrode number and their locations are selected using a genetic algorithm. For direct current tCS (tDCS) applications, we provide some examples of this technique using an available tCS system providing 8 small Ag/AgCl stimulation electrodes. We demonstrate the approach both for localized and spatially extended targets defined using rs-fcMRI and PET data, with clinical applications in stroke and depression. Finally, we extend these ideas to more general stimulation protocols, such as alternating current tCS (tACS).

Targeting a network: example

- Use a DBS target in depression therapy as a seed in rs-fcMRI
- Use the resulting correlation map on the cortex as target
- For excitation of deep target, seek to excite positive correlated regions and inhibit negatively correlated ones (or viceversa)
- Statistical significance of correlation used for weighting
- This approach can be used with other imaging techniques.

Fox et al 2012

ARCHIVAL REPORT

Efficacy of Transcranial Magnetic Stimulation Targets for Depression Is Related to Intrinsic Functional Connectivity with the Subgenual Cingulate

Michael D. Fox, Randy L. Buckner, Matthew P. White, Michael D. Greicius, and Alvaro Pascual-Leone

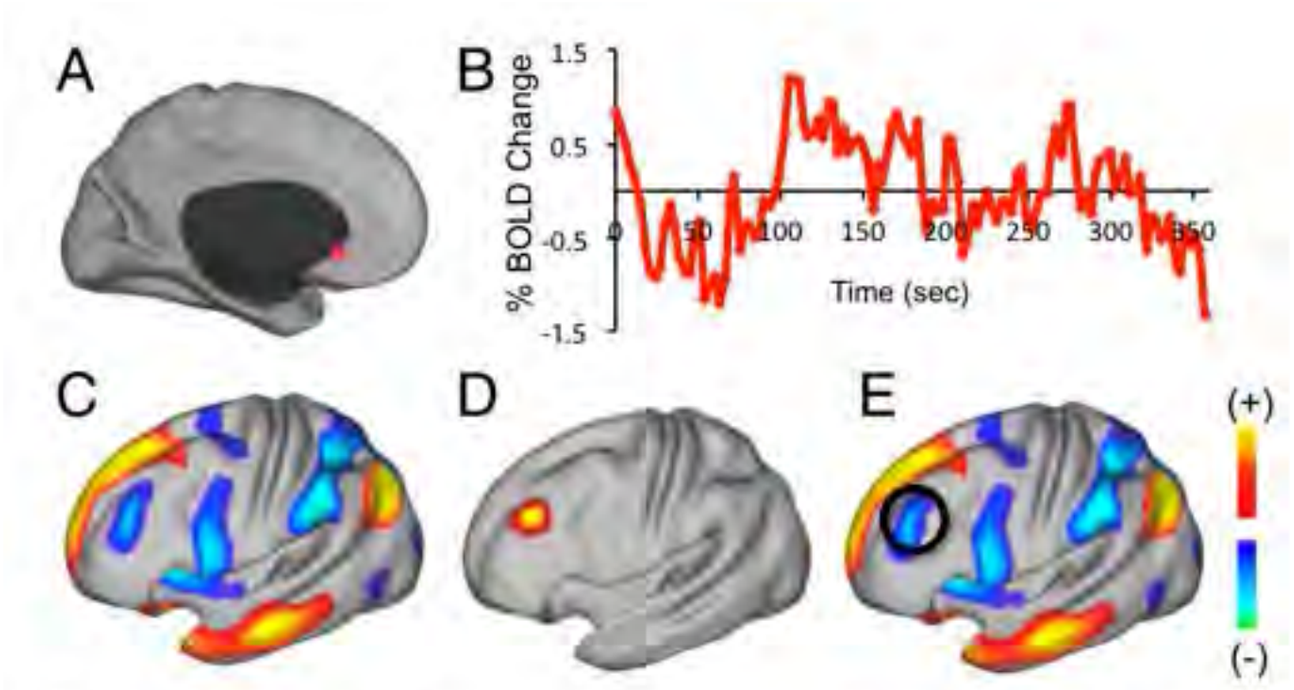
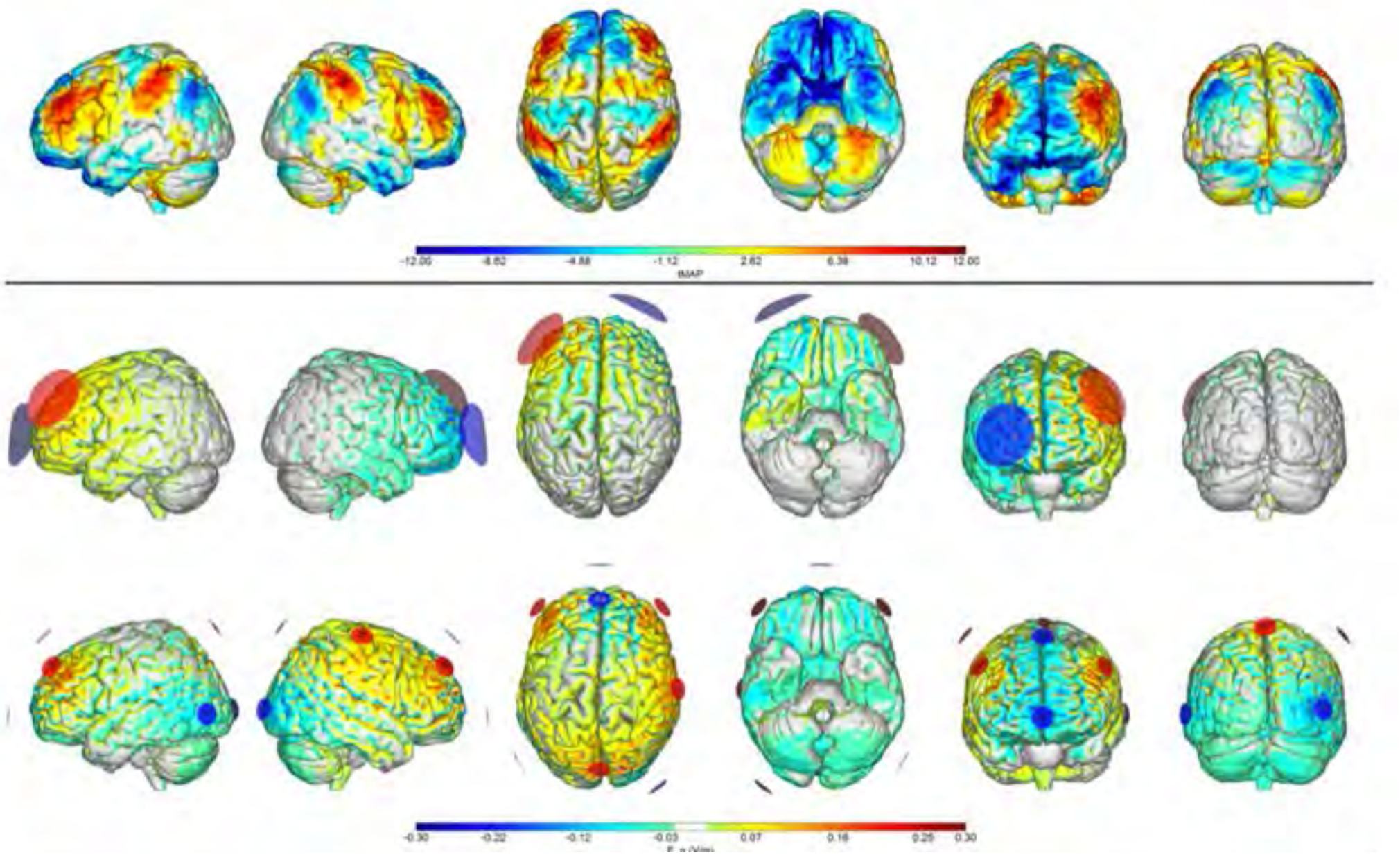


Fig. 1. Methodological approach for linking sites for invasive and noninvasive brain stimulation. (*A*) An ROI is created at a DBS site with reported efficacy for a given disease, in this case the subgenual cingulate for depression. (*B*) For each of 1,000 normal subjects, spontaneous modulations in the fMRI signal are extracted from this DBS ROI. (*C*) This time course is correlated with all other brain voxels and then averaged across subjects to create a DBS correlation map. (*D*) An ROI is created at the site where noninvasive stimulation is reported effective in the given disease, in this case the left DLPFC. (*E*) The site of noninvasive brain stimulation is illustrated on the DBS correlation map using a circle centered over the site.

Distributed target map (depression SG seed /8Ch)

Classical:

Modern:



rs-fcMRI SG seed map	Traditional	0.11
	8 Channel	0.29
	27 Channel	0.31

Ruffini et al 2014

Fox et al 2014

Resting-state networks link invasive and noninvasive brain stimulation across diverse psychiatric and neurological diseases

Michael D. Fox[a,b,c,1], Randy L. Buckner[c,d,e], Hesheng Liu[c], M. Mallar Chakravarty[f,g], Andres M. Lozano[h,i], and Alvaro Pascual-Leone[a]

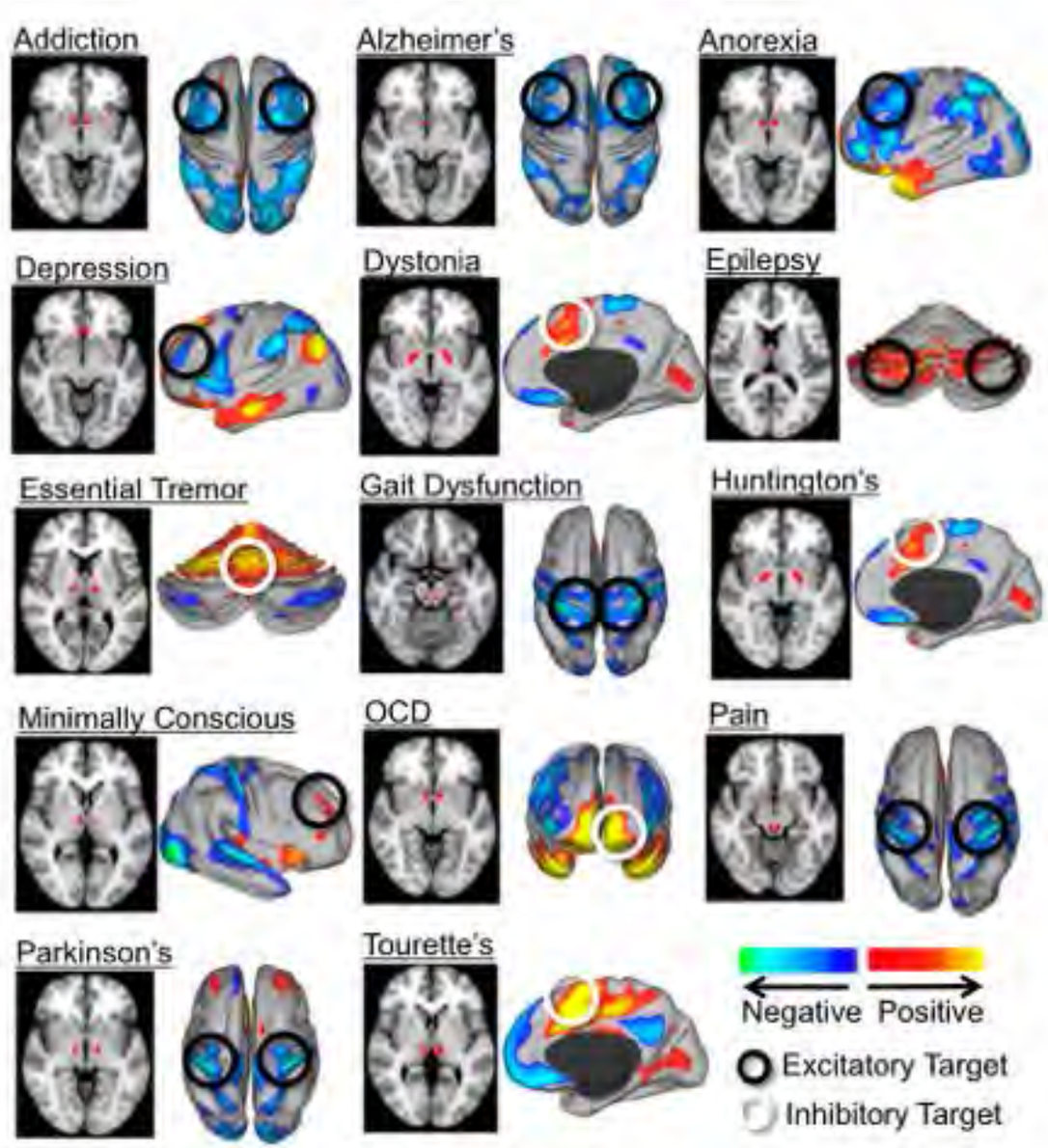
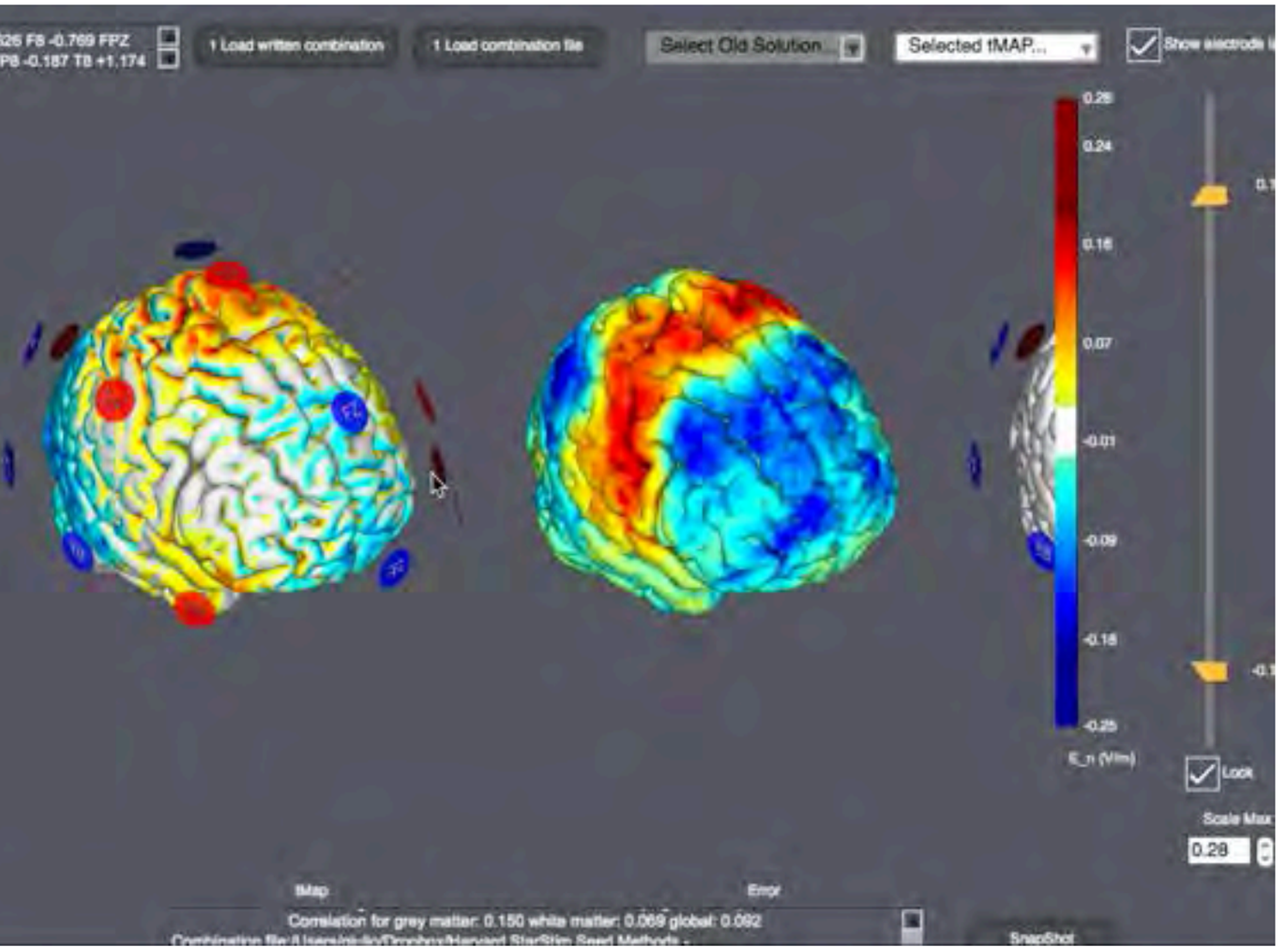


Fig. 2. Sites for invasive and noninvasive brain stimulation with the best evidence of therapeutic efficacy in each disease are functionally connected. For each disease, the site at which DBS is most effective is shown in red. Resting-state functional connectivity with this site is shown along with the correspondence to the site at which noninvasive stimulation is most effective in each disease (circles). Black circles indicate sites at which noninvasive excitatory stimulation (>5 Hz TMS or anodal tDCS) has been reported to be efficacious. White circles indicate sites where inhibitory stimulation (<1 Hz TMS or cathodal tDCS) has been reported to be efficacious.

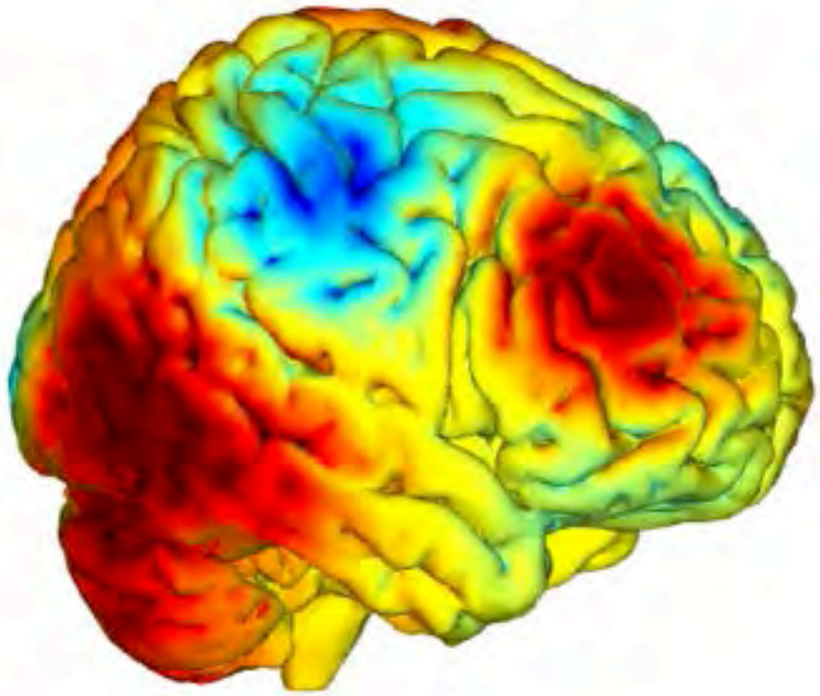
Optimized solution: Stimweaver



Using EEG for targeting

- Using EEG Cortical mapping to define targets for tCS (very consistent approach in terms of assumptions)
- E.g., for tACS: alpha band Eyes Closed EEG data: use EEG cortical activity to guide tACS locations +frequencies+ relative phases. Relative phases important!

FEM based cortical map of eyes closed spontaneous EEG data (alpha).



Red: inward, blue: outward oriented dipoles

OPEN ACCESS Freely available online

PLOS ONE

From Oscillatory Transcranial Current Stimulation to Scalp EEG Changes: A Biophysical and Physiological Modeling Study

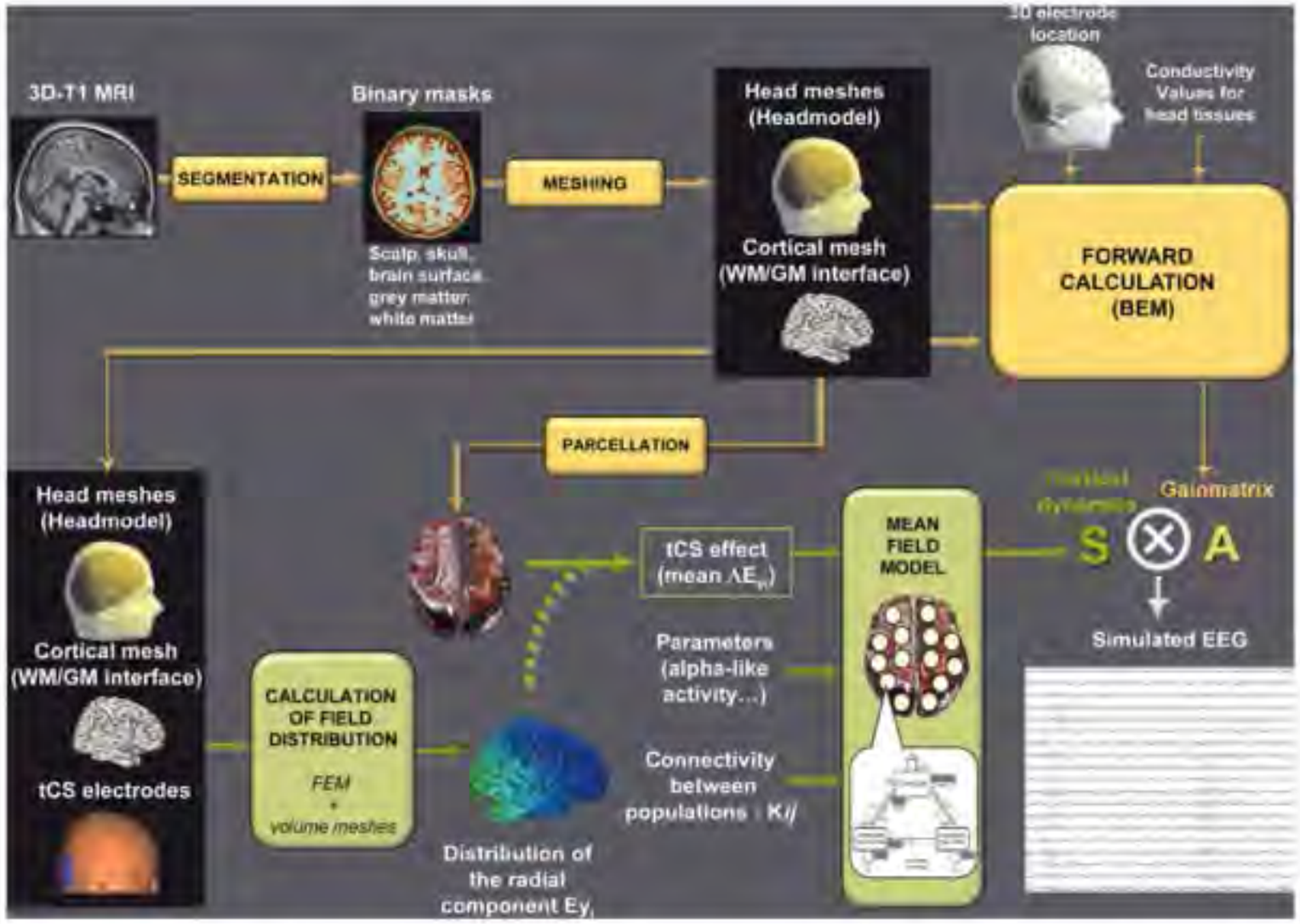


Figure 3. Simulation pipeline. 3D T1 MRI images are segmented into binary masks of the different head tissues in order to get meshes of the scalp, skull and brain surface (realistic head model) as well as of the white matter (WM)/grey matter (GM) interface. Unit dipoles are located at the barycenter of the triangles of this WM/GM mesh and set perpendicular to the triangle surface. This dipole layer over the cortex defines the source space. The forward problem is computed for each dipole using the Boundary Element Method (BEM) in order to get the leadfield matrix $\boldsymbol{A}$ that represents the contribution of each unit dipole of the mesh at each of the 19 scalp electrodes considered in our simulations (orange arrows in the pipeline). In order to get a physical model of the current distribution after tCS stimulation, surface meshes representing the boundaries between the different head tissues are transformed into volume meshes. In addition, virtual tCS electrodes are also represented into the model and can be placed at any scalp location (in our simulation protocol, we used PO9-PO10 location of the international 10–10 system). The electric field is calculated using the Finite Element Method (FEM) and the normal component of the field E_{y_i} is mapped on the surface mesh of the WM/GM interface. E_{y_i} values are then averaged over 66 macro-regions to get the 66 $\overline{E_{y_i}}$ coefficients representing the mean field effect during tCS. We used then a model of coupled neuronal populations, with parameters of each population being adjusted to generate alpha-like activity, and connectivity between populations being defined in order to account for the thalamic input. $\overline{E_{y_i}}$ coefficients can be added to the average membrane potential of pyramidal cells of each cortical neuronal population in order to mimic the de- or hyper-polarizing effect of the electric field and to get the resulting time-varying activities at the level of each cortical macro-region (green arrows in the pipeline). The resulting spatio-temporal source matrix $\boldsymbol{S}$ is multiplied by leadfield matrix $\boldsymbol{A}$ to get the simulated EEG data under tCS condition.
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Connecting stimulation and EEG response: modeling can help to guide and interpret tCS experiments.

hiVE HYPER INTERACTION VIABILITY EXPERIMENTS

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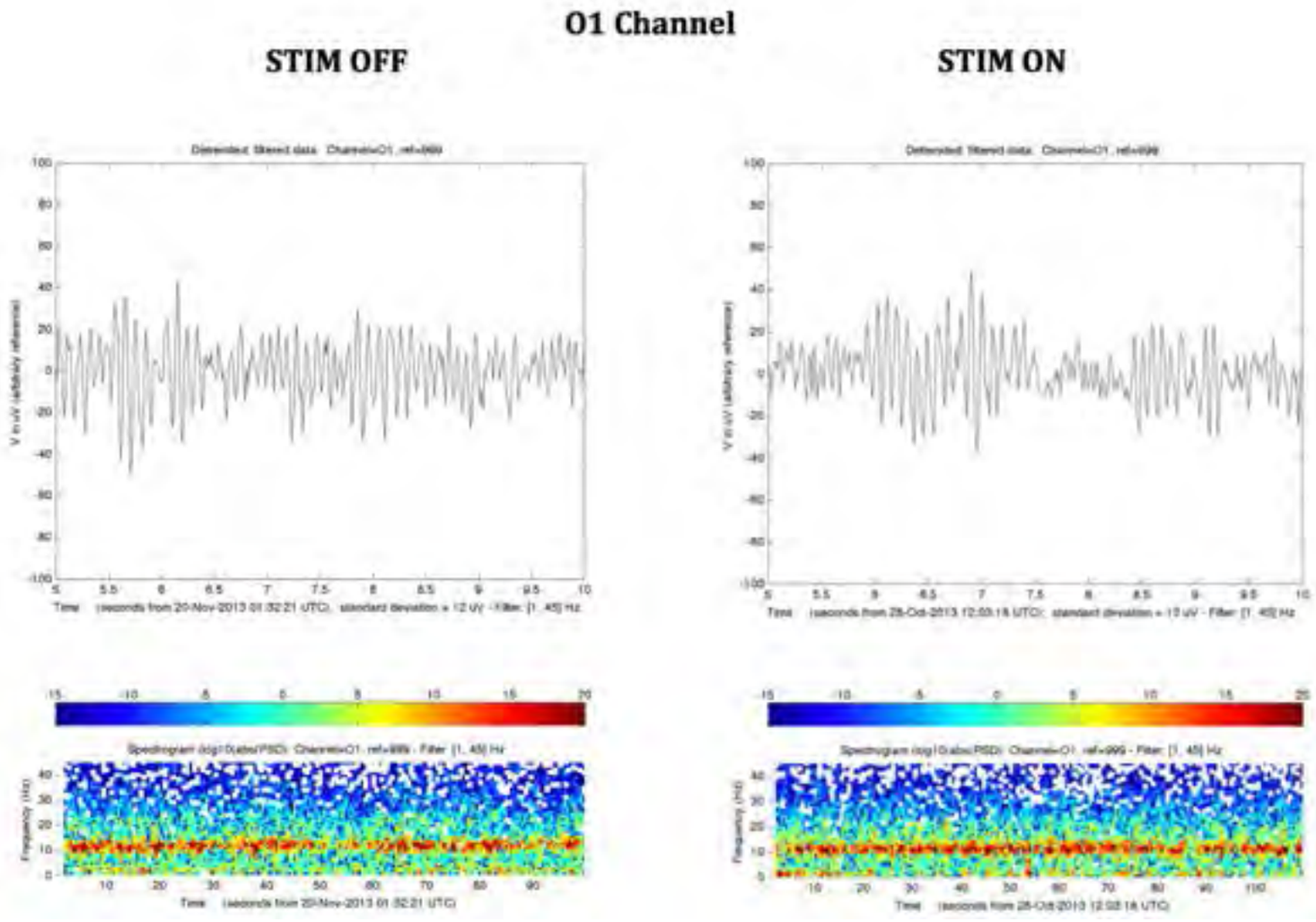
Closed loop stimulation is here (MatNIC)

- It is now possible to stimulate and record EEG concurrently with tDCS, and w. limitations, tACS
- Explore sequential stim/record protocols using the MatNIC Matlab API to control Starstim remotely and programatically
- Adjust stimulation parameters based on collected EEG data: now possible



Conclusions

- Models exist and represent the state of the art in our understanding what tCS produces physically. Explore them! They are not perfect but will be improved over time using the scientific method
- Targeted multielectrode montages offer the opportunity for more precise, meaningful stimulation: the technology is here
- Brain function is mediated by networks: let's go after them!
- Target maps can be defined in various ways:
  - Brodmann Areas or AAL; simple or multiple
  - rs-fcMRI
  - rs-fcEEG / ERPs / MEG
  - PET
  - …
- Technologies now offer the possibility of modeling/optimizing and - crucially - implementing advanced methods
- Approach is applicable to tACS and tRNS

Thank you for your attention!

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P. Miranda, F. Wendling, I. Merlet, B. Molaee-Ardekani, N.Birbaumer, C Grau, M. Nitsche, A Pascual-Leone, O. Ripolles, N. Cardoner, J. Marquez-Ruiz, R Salvador, D. Edwards, M Cortes, J. M. Delgado, A Gruart, M Berg, R. Ginhoux, A. Riera, D. Boratyn, L. Murray, A Soria-Frisch, S Dunne, ….