Optimized Multifocal transcranial Current Stimulation: DLPFC and MC solutions

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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 $\lambda \cdot \mathbf{n}$, where **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.

Based on this rapid E-field simulator, we have built an optimization system, StimWeaver, where optimal montages can be defined and found [3].

In the following, we have optimized the match of the Electric field normal to the cortical surface (i.e., parallel with pyramidal neurons) with the target characteristics.

The generalization of the proposed method to the case of tACS is non-trivial, even though the process for calculation of electric fields for low frequencies (< 1 kHz) is essentially the same as for tDCS. That is, if E(x) is electric field the solution to a DC current for a particular montage and currents, then E(x,t) = E(x)cos(2πtf) is the solution to the analogous AC case in which each current is multiplied by cos(2πtf). The real difficulty here lies in the choice of a physiological meaningful optimization problem.

Current studies show that support of brain activity involves the orchestrated oscillatory activity of different and spatially separated brain regions. Indeed, a major challenge for neuroscience today is to map and analyze the spatio-temporal patterns of activity of the large neuronal populations that are believed to be responsible for information processing in the human brain. Phase or amplitude synchronization may relate different functional regions operating at the same or different frequencies via cross-frequency synchrony. In principle, tACS is potentially capable of acting on such natural rhythms in brain networks through the process of resonance. Devices such as Starstim already allow for the simultaneous multisite stimulation of different cortical regions with specific frequencies and relative phases as well as the recording of EEG data from the same electrode locations.

In order to configure properly a multisite monochromatic tACS montage (i.e., one using a single tACS frequency), EEG or MEG data can be used to define the target frequency as well as a target cortical map. The latter could be obtained, e.g., using EEG tomography or cortical mapping algorithms with EEG data filtered at the appropriate frequency band. Closed- loop implementations where the EEG data is used to optimize stimulation parameters can easily be envisioned, with applications such as epilepsy.

In what follows we provide some examples of montages optimized with Neuroelectrics' proprietary system, StimWeaver, to stimulate specific target areas using Starstim (Neuroelectrics), proving that a multichannel setup with Neuroelectrics' Pi (PISTIM) electrodes offers more focality and versatility than the classical bipolar montages using sponge electrodes.

In all the examples, the objective function in the multichannel stimulation optimization problem is to excite the target area (via the component of the electric field orthogonal to the cortical surface E_n) while providing in other cortical locations (non- target) an E_n magnitude lower than 0.1 V/m. In the optimization problem, a penalty is imposed associated to values of $|E_n|$ above this value in the non-target with the goal of limiting the effects outside the target area.

In more detail, the parameters of the problem are:

- Stimulation type: tDCS
- Electric field in target area: 0.25 V/m excitatory
- Electrode type: PISTIM (π cm^2 Ag/AgCl gel electrode)
- Max current any electrode: 2 mA
- Max total injected current: 4 mA
- Max number of electrodes: 8
- Positions: 10-10 international system cap

The standard safety constraints apply: the maximal injected current into the brain at any given time is below 4 mA.

Check our white paper on safety of tCS for more information about safety of small Pistim electrodes.

Left dorsolateral prefrontal cortex

We provide here a comparison between a standard bipolar montage and a multichannel montage analysis for excitatory stimulation of the left dorsolateral prefrontal cortex (DLPFC or BA46), a typical target for treatment in depression.

The typical old-fashioned bipolar montage to target the DLPFC consists on placing the anodal electrode on the left DLPFC (F3) and the cathode over right DLPFC (Figure 1) or, sometimes, over the contralateral supraorbital region (Figure 2).

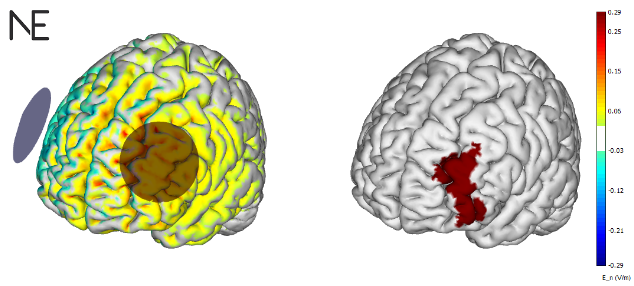

Figure 1. Bipolar montage targeting DLPFC: F3 anode vs F4 cathode using 25 cm^2 sponge electrodes. The figure on the left displays the normal component of the electric field. The one on the right displays the target BA46.

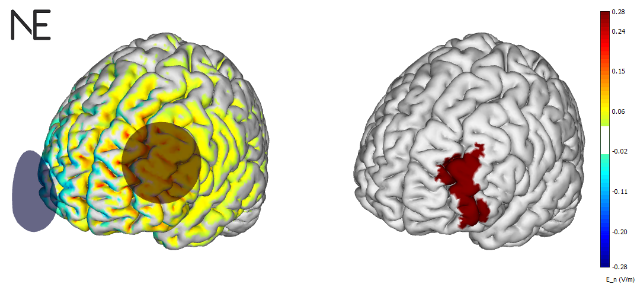

Figure 2. Bipolar montage targeting DLPFC: F3 anode vs Fp2 cathode using 25 cm^2 sponge electrodes. The figure on the left displays the normal component of the electric field. The one on the right displays the target BA46.

In contrast, the multifocal montage shown in Figure 3 has been optimized using StimWeaver and using 8 Pi-electrodes with Starstim. Note the improved focality with respect to the target and compare it to standard bipolar montage. See Figure 4 for further details.

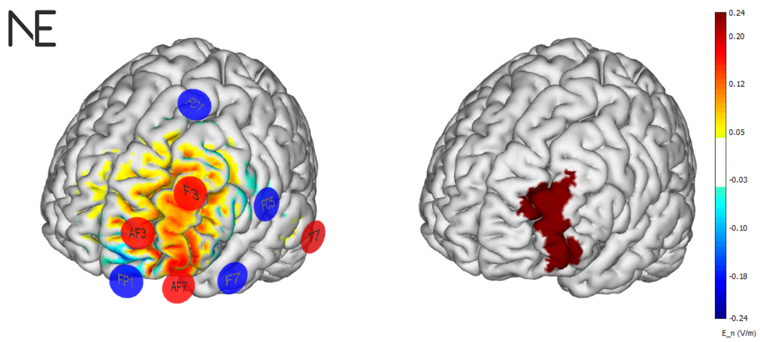

Figure 3. Multichannel montage targeting DLPFC optimized using StimWeaver and using 8 Pi electrodes with Starstim. The figure on the left displays the normal component of the electric field. The one on the right displays the target BA46.

The currents per electrode optimized solution (for excitatory effects on target) are:

AF3: 636 uA
AF7: 1996 uA
F3: 655 uA
F7: -782 uA
FC1: -307 uA
FC5: -431 uA
FP1: -2000 uA
T7: 233 uA

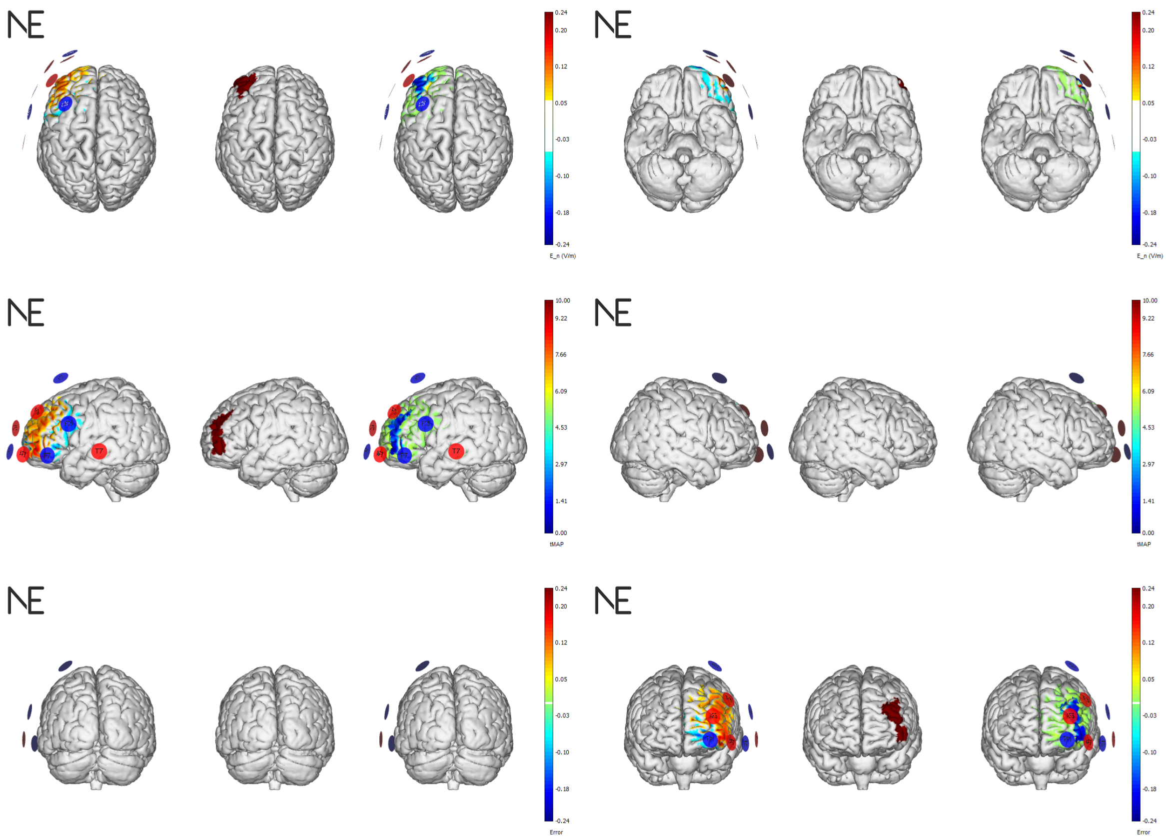

Figure 4. Different views of the multichannel montage targeting DLPFC optimized using StimWeaver and using 8 Pi electrodes with Starstim. For each set of three displays, the Electric field is displayed in the first plot, the target area is displayed in the second plot and error related to no intervention is displayed in the third plot.

Figure 5. We provide here a screenshot of the configuration panel in NIC (Neuroelectrics Instrument Controller software) to configure Starstim with the parameters for the multichannel optimized montage targeting DLPFC.

Superior Motor Cortex

We provide here a comparison between a standard bipolar montage and a multichannel montage analysis for excitatory stimulation of the motor area, a typical target for stroke rehabilitation.

A stroke that affects the cerebral cortex may have a wide range of effects depending on the location of the lesion. The clinical strategies for treating stroke typically involve stabilization of the patient, preservation of function in the brain area and adaptation of the patient to diminished function. There are some hints that electrical stimulation of the brain may in itself promote recovery or preservation of brain tissue [4], although to date a relatively small number of published studies have focused on improving specific functions through the use of single or repeated sessions of anodal stimulation.

The main motivation behind the use of non-invasive brain stimulation for stroke recovery is to support relearning of compromised abilities by enhancement of pathologically-reduced cortical excitability and activity, directly by excitability-enhancing brain stimulation of the lesioned area, and/or indirectly, by reducing excitability of the non-lesioned contralateral hemisphere – since this has inhibitory connections with the lesioned one [5]. Specifically, the respective excitability enhancements are thought to promote relearning of functions by enhancing learning-related long-term potentiation (LTP) (which is the likely physiological basis of learning and memory formation [6]) and via this mechanism promote recovery.

A typical bipolar montage using large, traditional sponges will result in large affected areas by the stimulation, as shown in Figure 6. An alternative is to put the cathode electrode over the "contralateral supraorbital region" (Figure 7). Again, we see large effects over widespread areas of the cortex, and the resulting high Error Relative to No Intervention (ERNI) as compared to the optimized 8-electrode montage (Table 1).

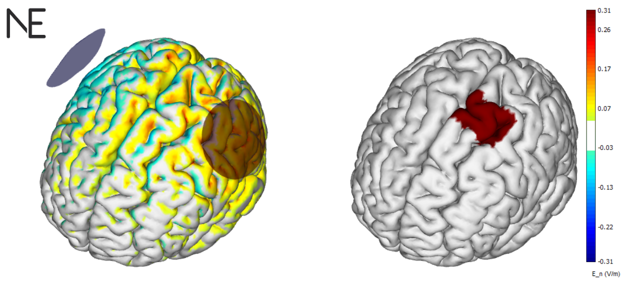

Figure 6. Bipolar montage targeting motor cortex with anode in C3 vs cathode in C4 using 25 cm^2 sponge electrodes. The figure on the left displays the normal component of the electric field. The one on the right displays the target area.

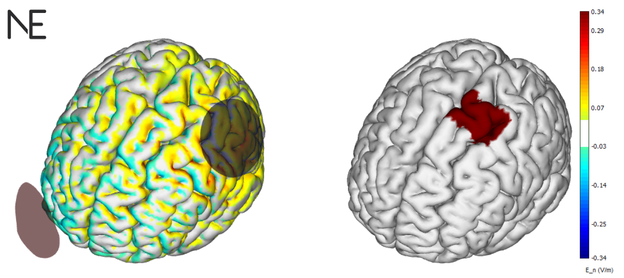

Figure 7. Bipolar montage targeting motor cortex with anode in C3 vs cathode in FP2 using 25 cm^2 sponge electrodes. The figure on the left displays the normal component of the electric field. The one on the right displays the target area.

A modern multifocal montage optimized with StimWeaver and targeting only the left hemisphere (i.e., trying to avoid stimulation of other sites) is shown in Figure 8. Note the improved focality with respect to the target and compare it to standard bipolar montages. See Figure 9 for further details.

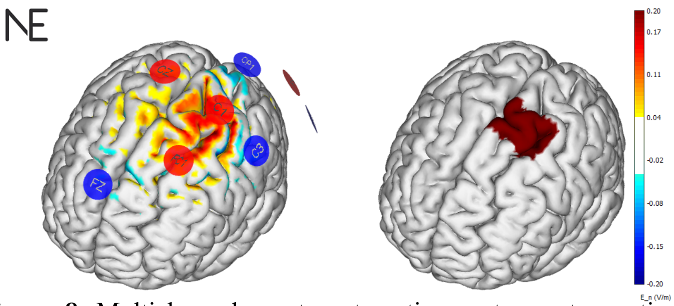

Figure 8. Multichannel montage targeting motor cortex optimized using StimWeaver and using 8 Pi electrodes with Starstim. The figure on the left displays the normal component of the electric field. The one on the right displays the target area.

The currents per electrode in optimized solution (for excitatory effects on target sites) are:

C1: 1389uA
C3: -673uA
CP1: -977uA
FC1: 160uA
FZ: -377uA
P3: 425uA
PO7: -159uA
Cz: 212uA

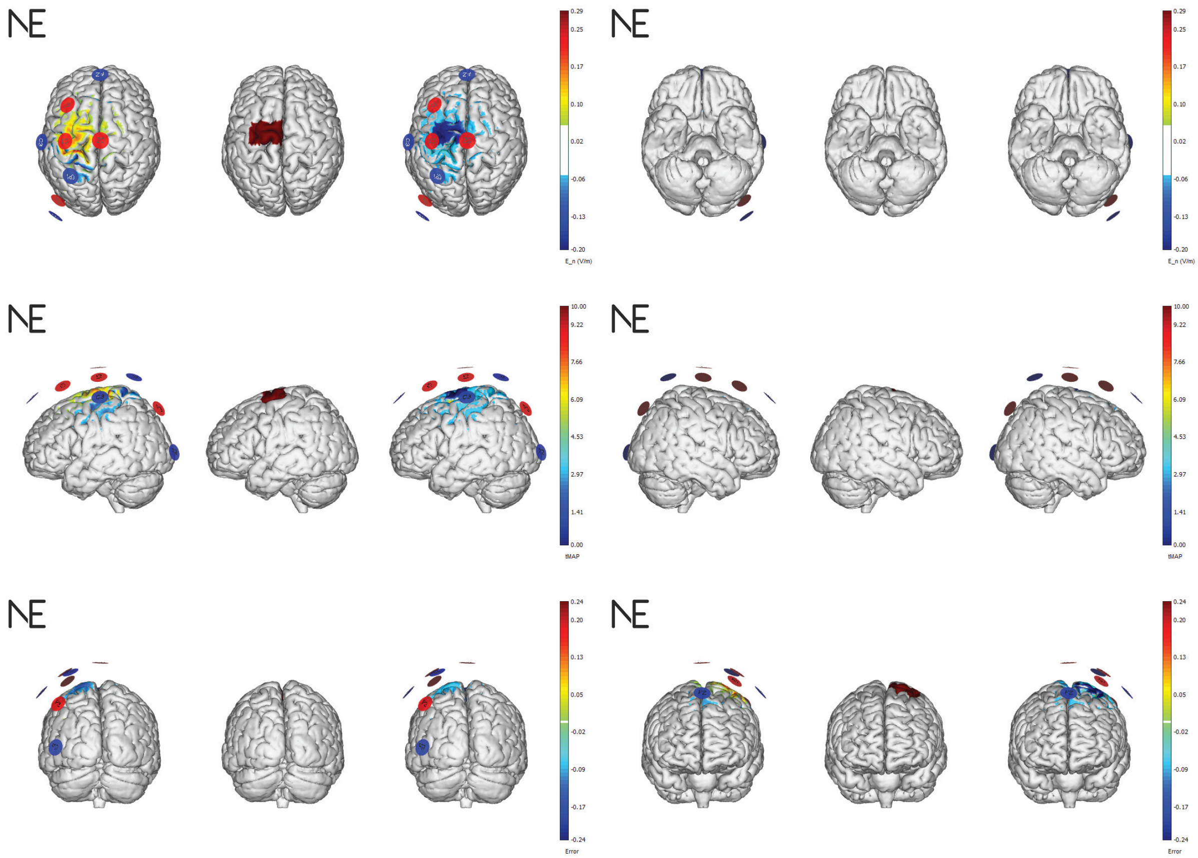

Figure 8. Different views of the multichannel montage targeting motor cortex optimized using StimWeaver and using 8 Pi electrodes with Starstim. For each set of three displays, the Electric field is displayed in the first plot, the target area is displayed in the second plot and the error relative to no intervention is displayed in the third plot.

Figure 9. We provide here a screenshot of the configuration panel in NIC (Neuroelectrics Instrument Controller software) to configure Starstim with the parameters for the multichannel optimized montage targeting the motor cortex.

Discussion

In the following table we provide a montage comparison for some bipolar and multifocal target maps. The overall quality of the solutions is quantified by the related weighted cross correlation coefficient (WCC) of target map and electric field (a number between −1 and 1), and the electric field on the target and non-target areas.

Target area	Type of montage	Number of channels	Electrodes	Current (mA)	WCC	Average E_n on target (mV/m)	Average E_n on non-target (mV/m)
DLPFC	Bipolar F3-FP2	2	25cm^2 sponge	1mA	0,232	47,3	-0,2
	Bipolar F3-F4	2	25cm^2 sponge	1mA	0,228	49,3	-0,3
	NE multifocal	5	Pistim	1mA	0,505	58,6	-0,2
				2mA	0,520	59,4	-0,1
	NE multifocal	8	Pistim	1mA	0,534	60,6	0,1
				2mA	0,552	70,8	-0,2
Superior Motor Cortex	Bipolar C3-FP2	2	25cm^2 sponge	1mA	0,075	16,9	-0,2
	Bipolar C3-C4	2	25cm^2 sponge	1mA	0,031	6,8	-0,2
	NE multifocal	5	Pistim	1mA	0,415	35,5	-0,3
				2mA	0,417	39,9	-0,3
	NE multifocal	8	Pistim	1mA	0,422	39,0	-0,3
				2mA	0,425	42,0	-0,2

The higher WCC and E_n on target areas for the NE multifocal montages with 5 and 8 channels prove the improvement in focality as compared with the traditional bipolar ones.

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