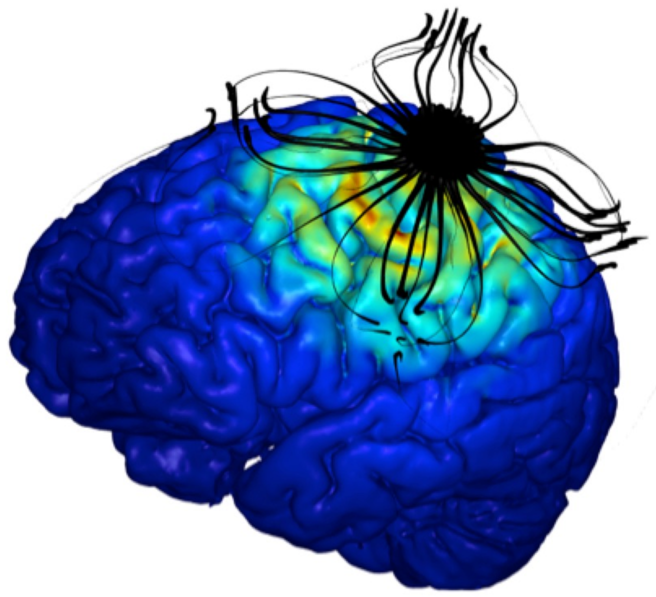
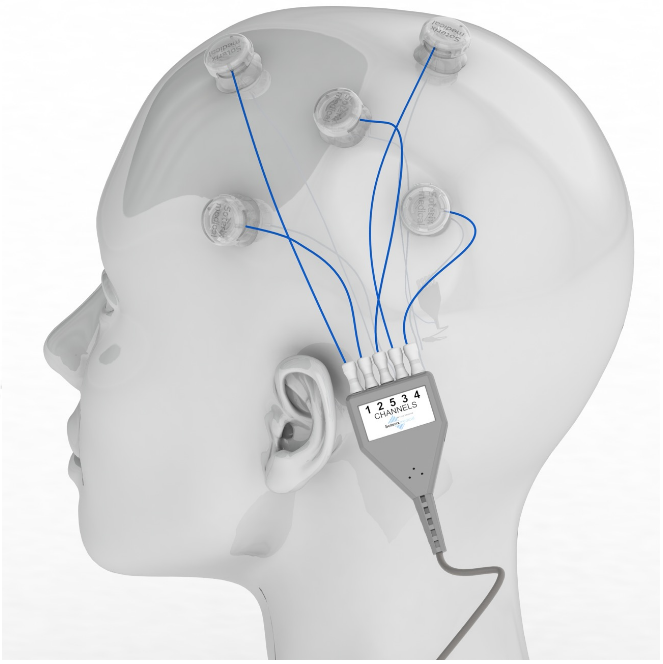
Optimizing brain targeting with High-Definition tDCS

Marom Bikson

Egas Caparelli-Daquer, Eric Wasserman, Dylan Edward, Mar Cortes, Lucas Parra, Jacek Dmochowski, Asif Rahman, Niranjan Khadka, Dennis Truong,, Zeinab Esmaeilpour, Gregory Kronberg, Nigel Gebodh, Belen Lafon, Mohamad Rad, Leigh Charvet, Abhishek Datta





Disclosure

The City University of New York holds patents on brain stimulation with MB as inventor. MB has equity in Soterix Medical Inc. MB consults, received grants, assigned inventions, and/or served on the SAB of SafeToddles, Boston Scientific, GlaxoSmithKline, Biovisics, Mecta, Lumenis, Halo Neuroscience, Google-X, i-Lumen, Humm, Allergan (Abbvie), Apple, Ybrain, Ceragem, Remz. MB is supported by grants from Harold Shames and the National Institutes of Health: NIH-NIDA UG3DA048502, NIH-NIGMS T34 GM137858, NIH-NINDS R01 NS112996, NIH-NINDS R01 NS101362, and NIH-G-RISE T32GM136499.

Slides and References
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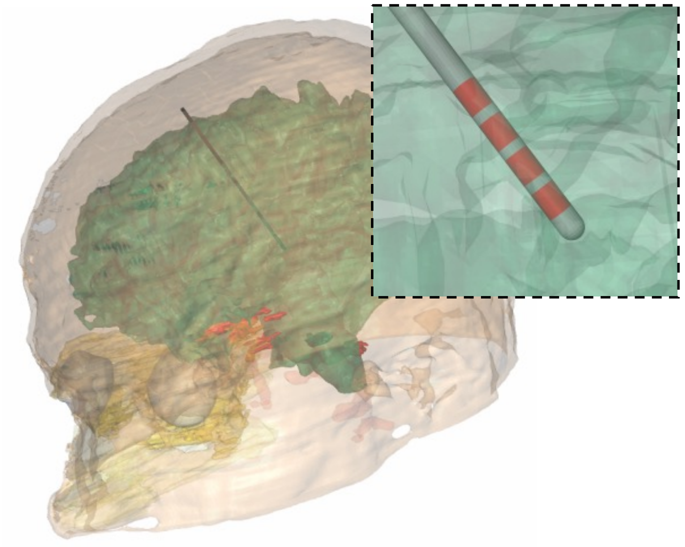
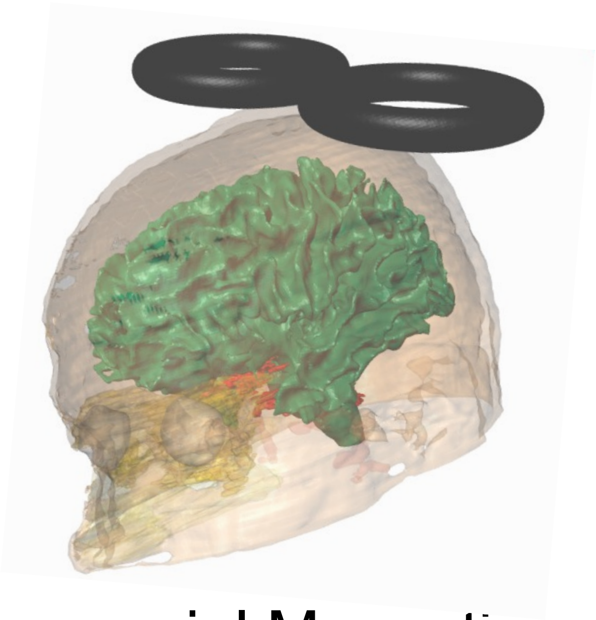
Direction matters.

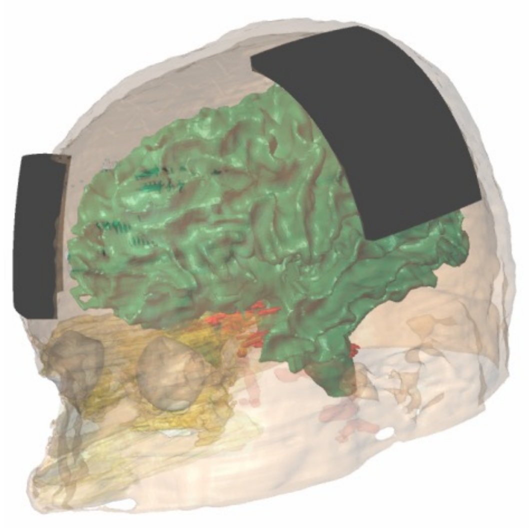
Which neuromodulation technique is the lowest cost, lowest risk, and most deployable?



Deep Brain Stimulation (DBS)



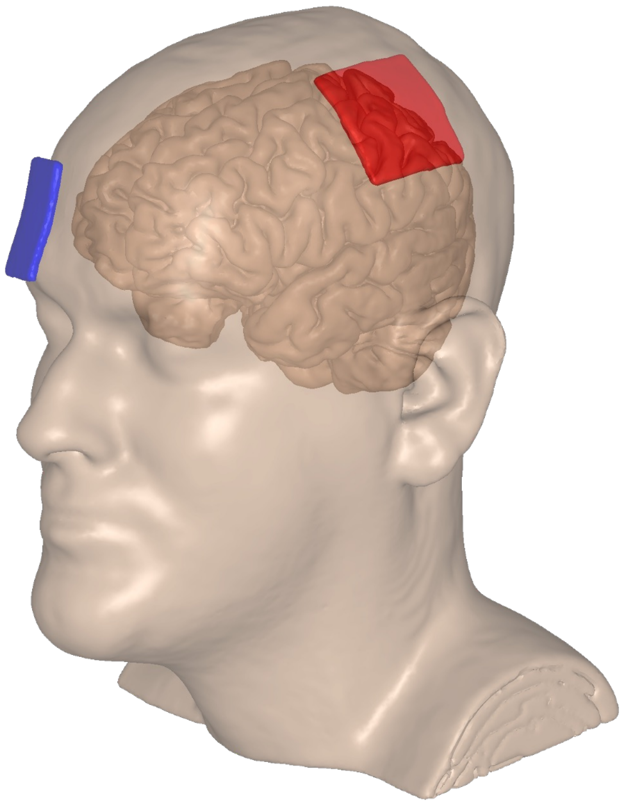
Transcranial Magnetic Stimulation (TMS)



Transcranial Direct Current Stimulation (tDCS)

Which neuromodulation technique produces the most targeted brain stimulation?

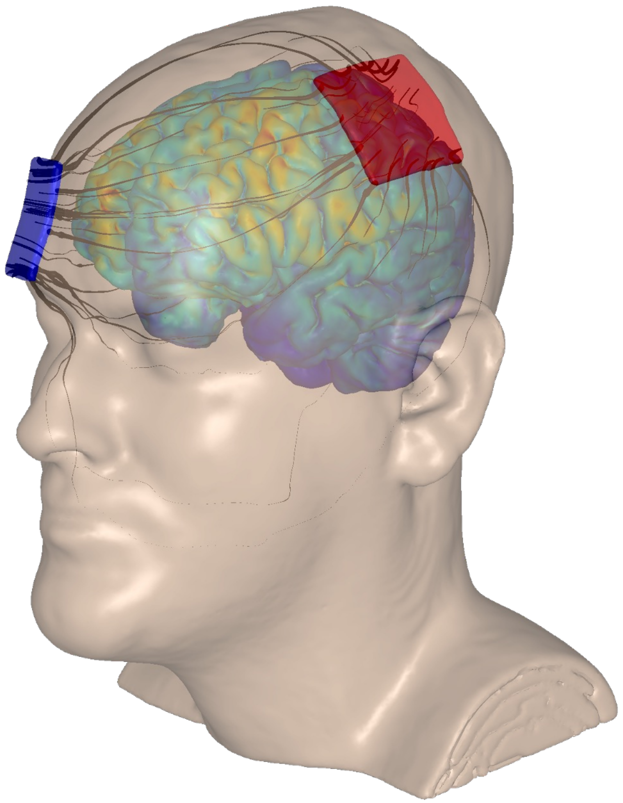
Conventional tDCS



Simulation of brain current flow

Datta et al. Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad. *Brain Stimulation*. 2009

Conventional tDCS



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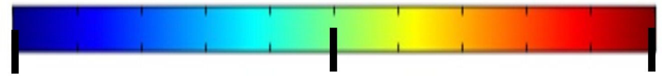

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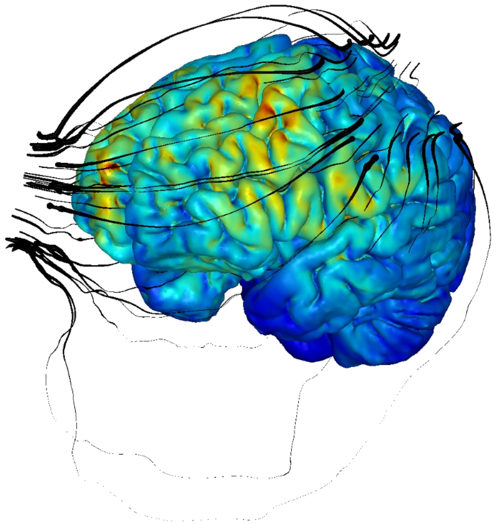

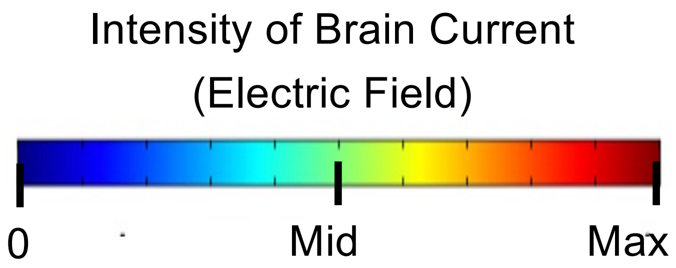

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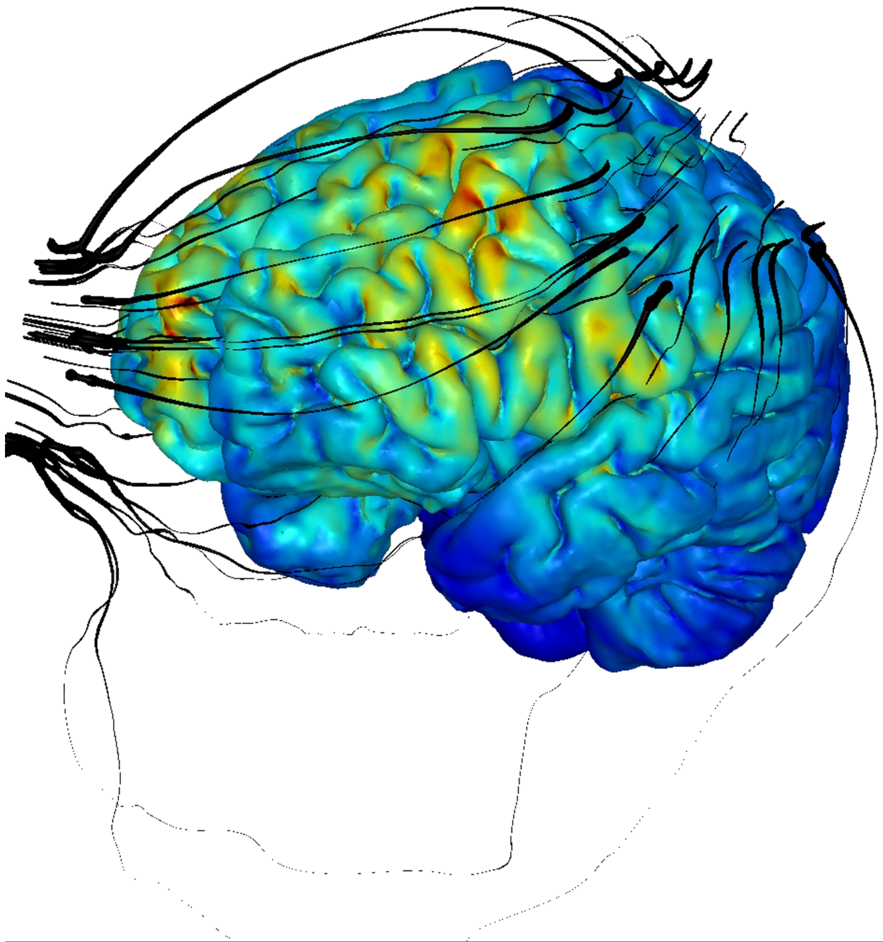
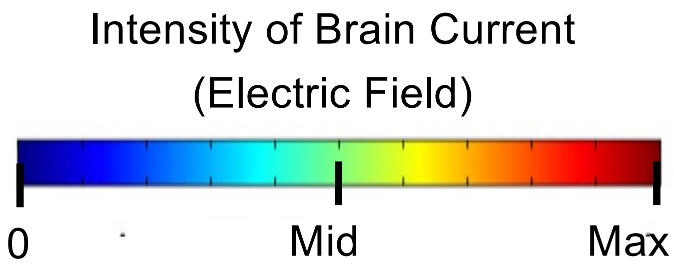




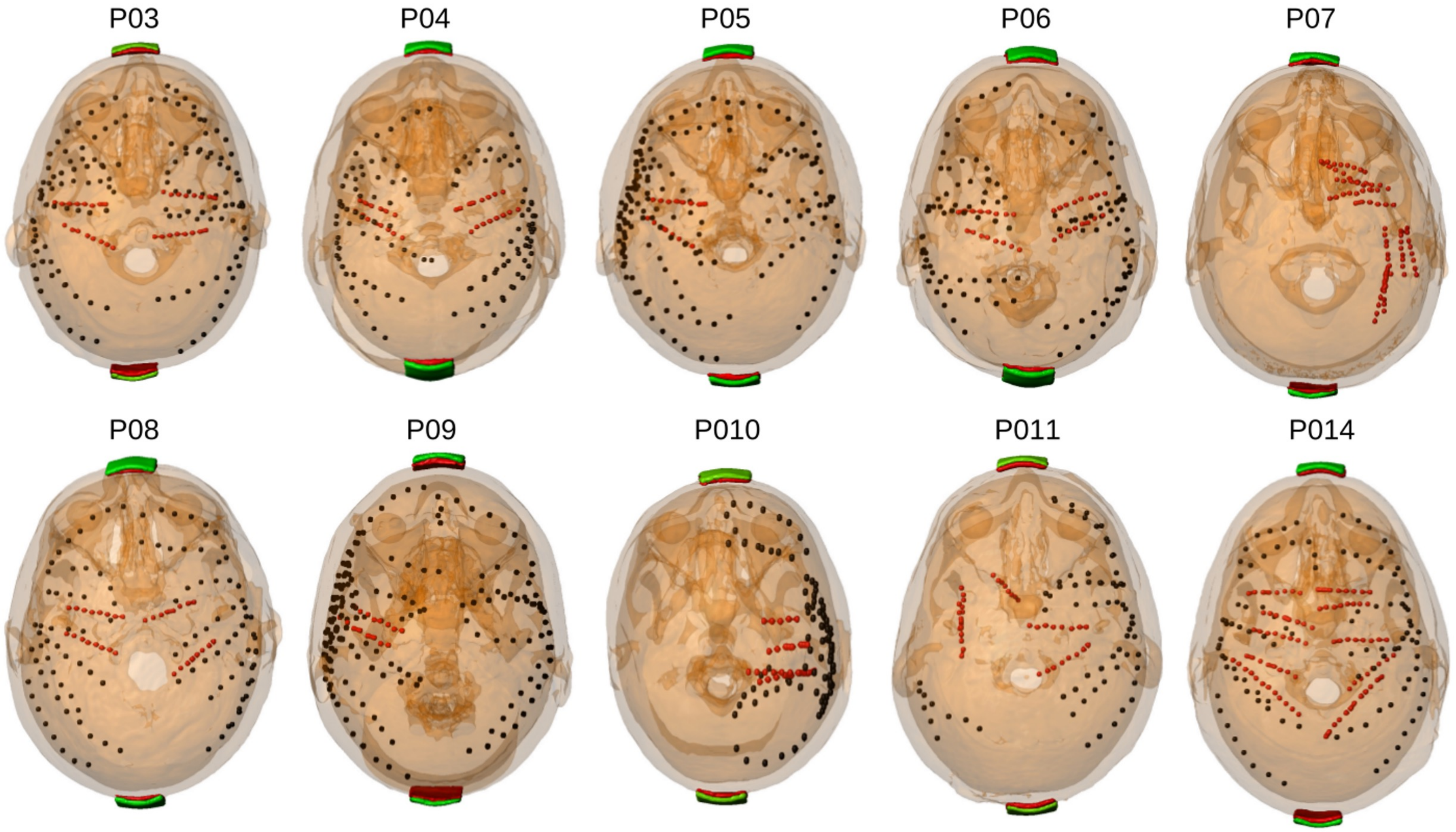
Simulation of brain current flow

Datta et al. Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad. *Brain Stimulation*. 2009

Recordings inside the human brain confirm conventional tDCS is diffuse.

Intra-cranial voltages during transcranial electrical stimulation:

Experimental recordings with subject specific MRI-derived models.



Huang et al. Measurements and models of electric fields in the human brain during tES. *Elife* 2017

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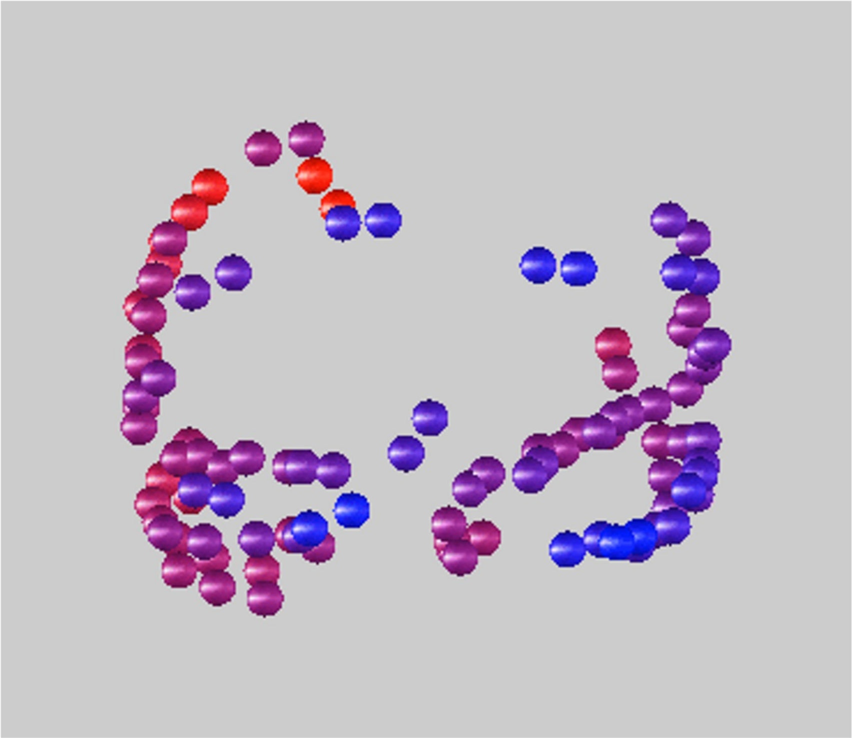
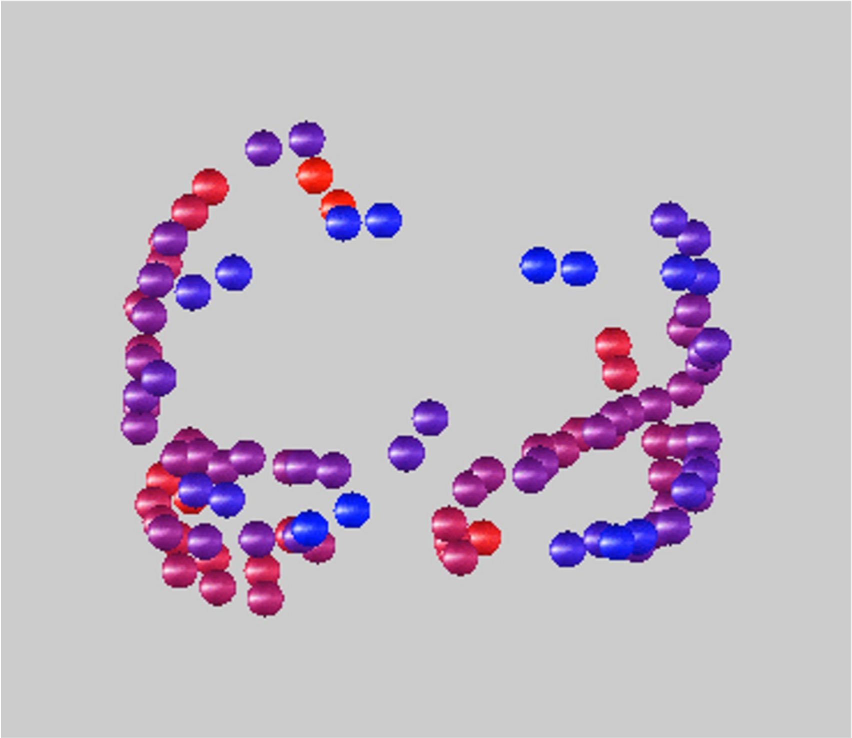


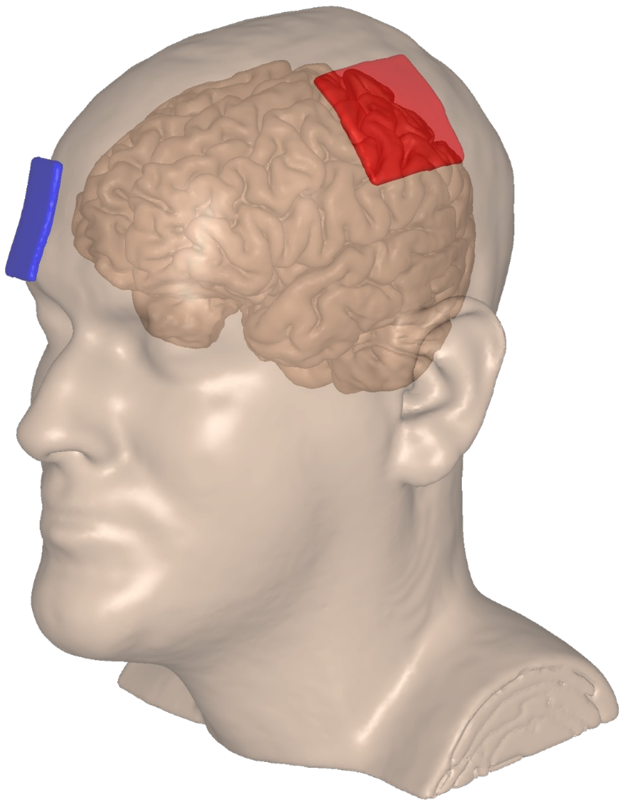
Recording (Volts)



Model (Volts)

Huang et al. Measurements and models of electric fields in the human brain during tES. *Elife* 2017

Conventional tDCS



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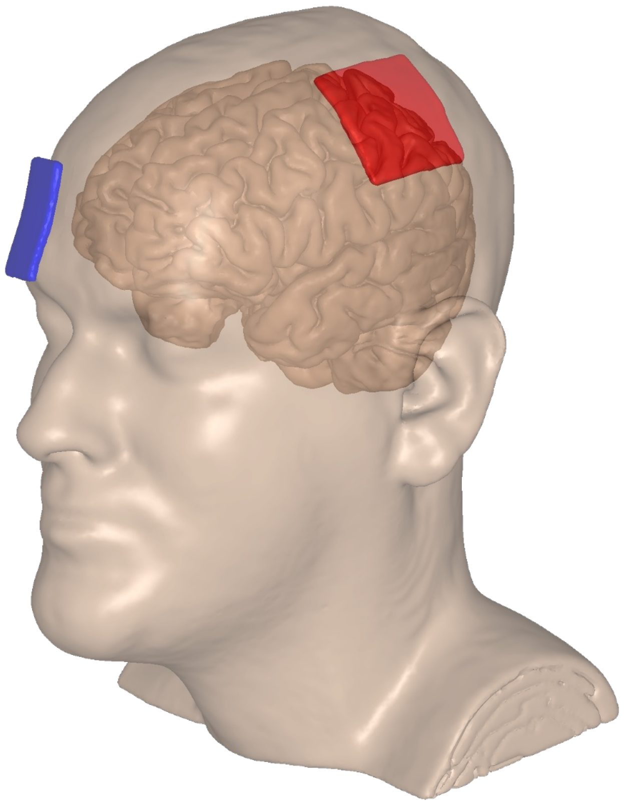
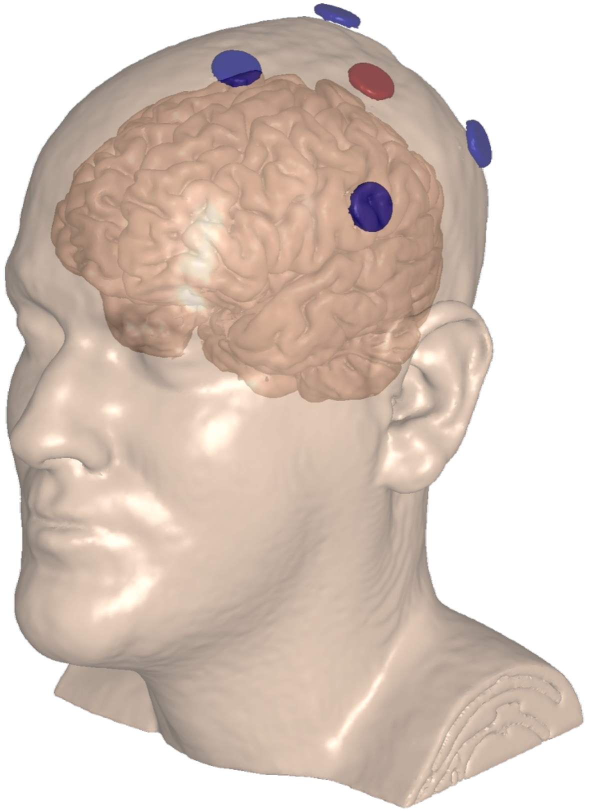


Simulation of brain current flow

High Definition tDCS



Datta et al. Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad. *Brain Stimulation*. 2009

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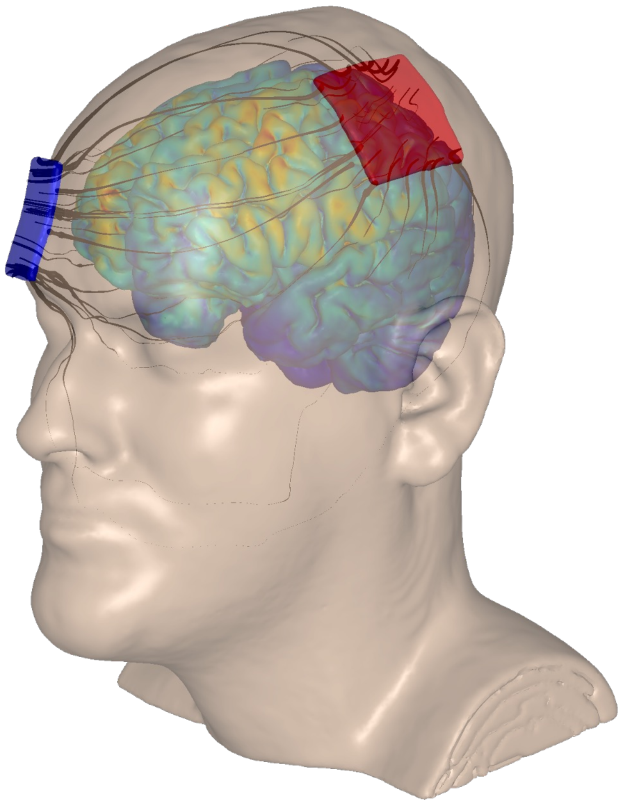

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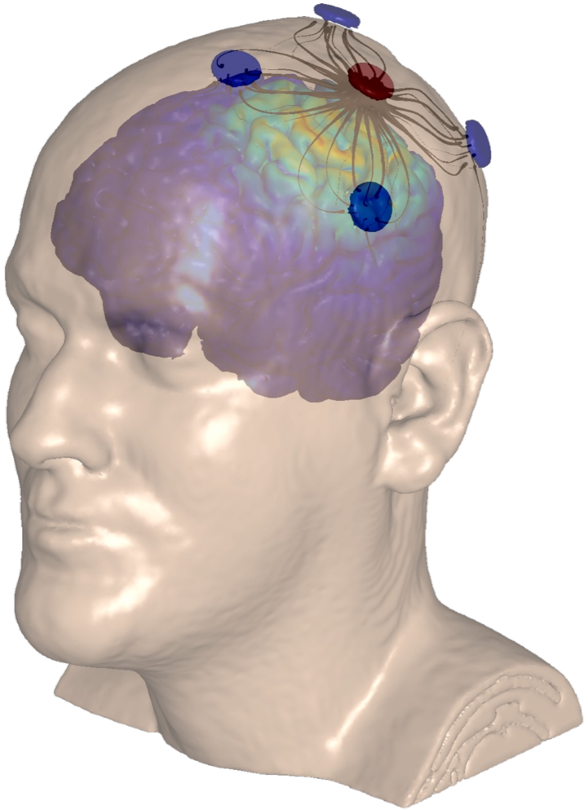

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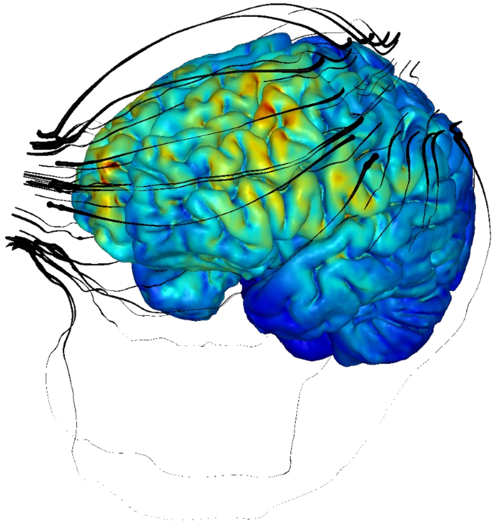
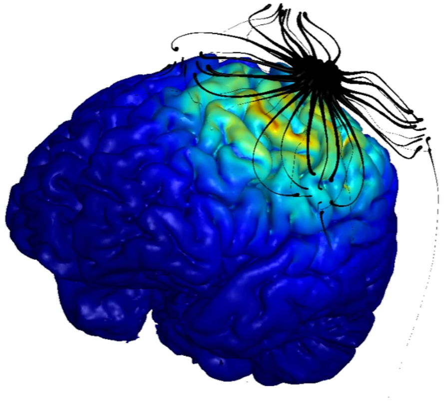
Conventional tDCS

High Definition tDCS





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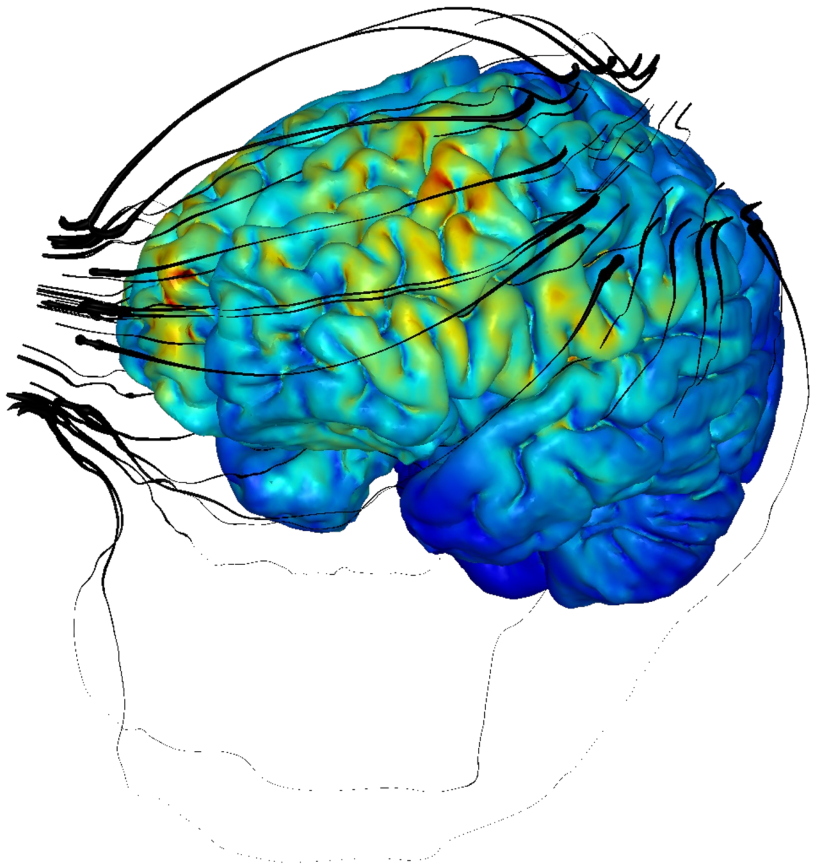

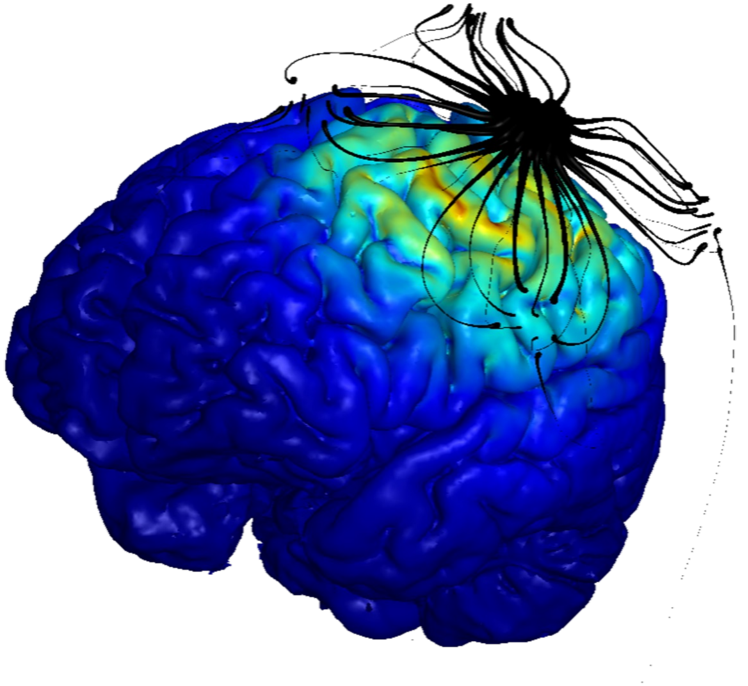

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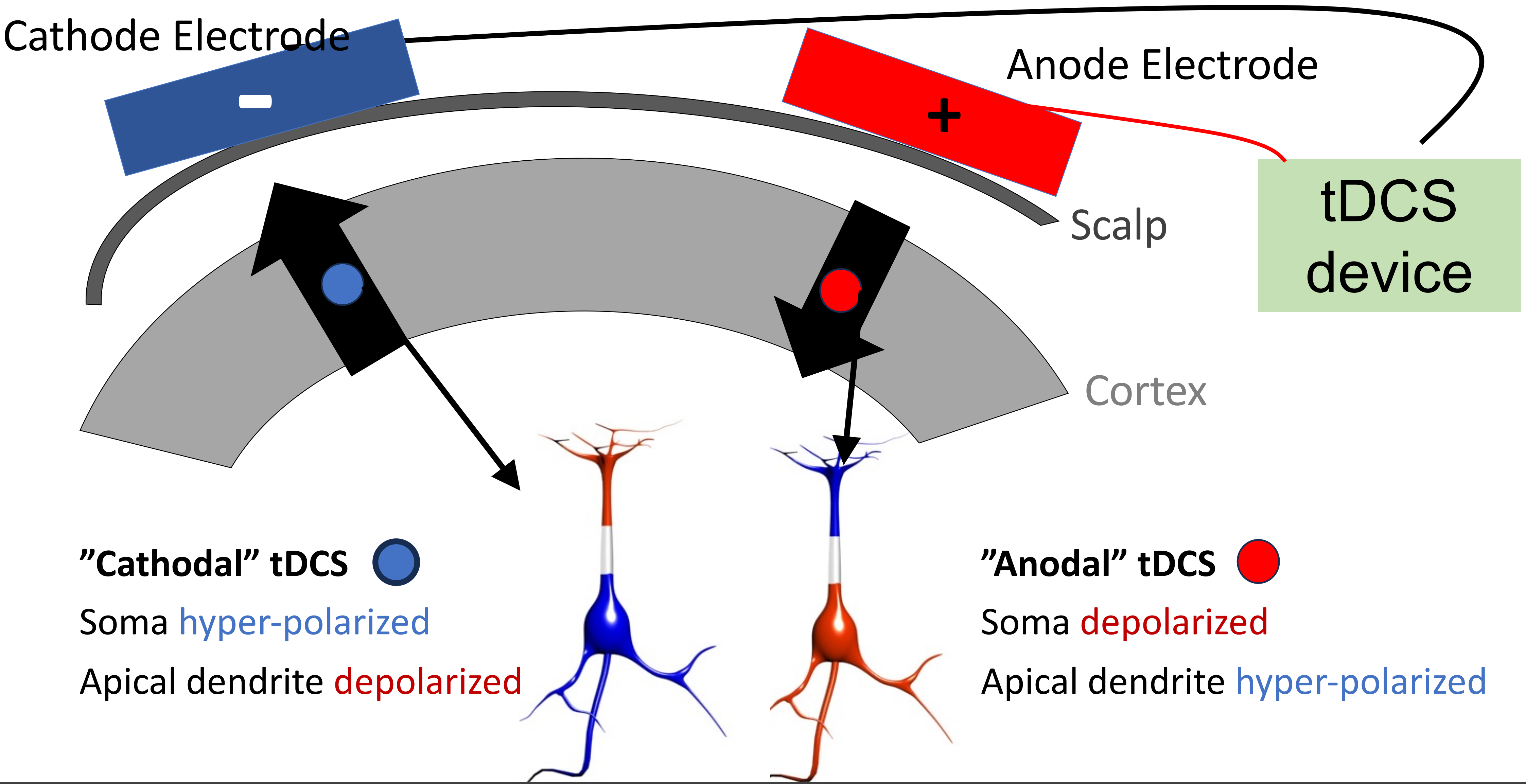
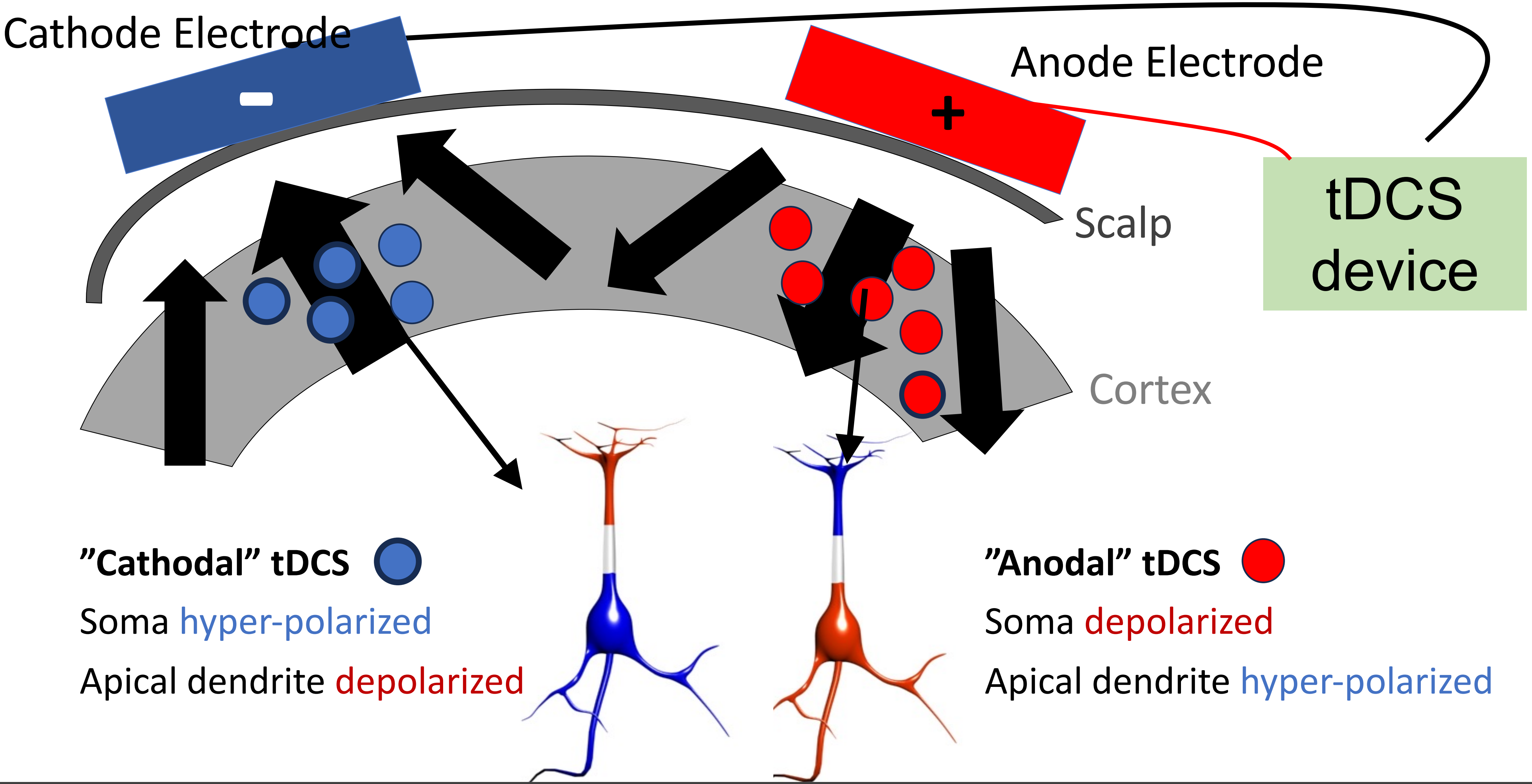


Radman et al. Role of cortical cell type and morphology in subthreshold and suprathreshold uniform electric field stimulation in vitro. . Brain Stimulation. 2009



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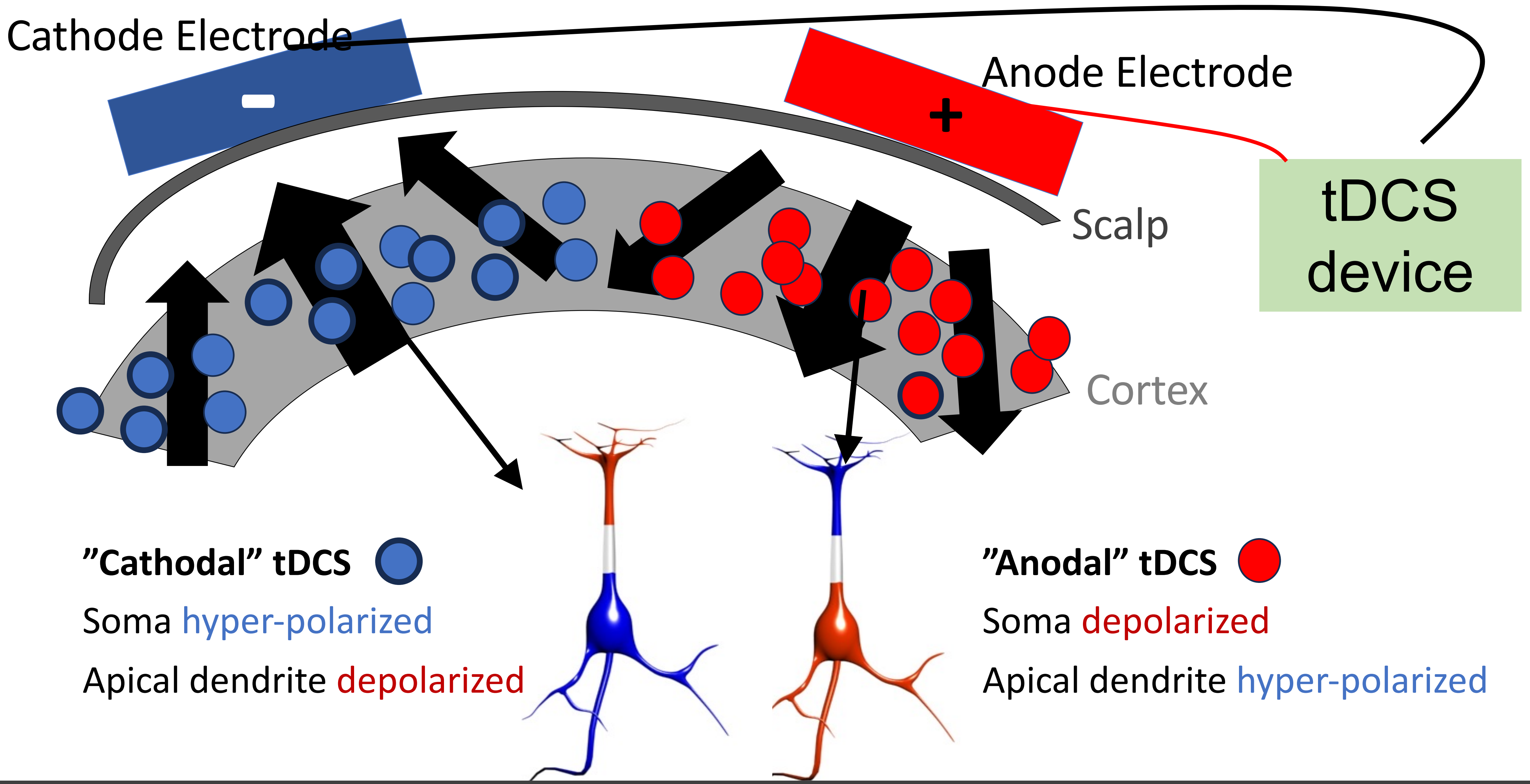

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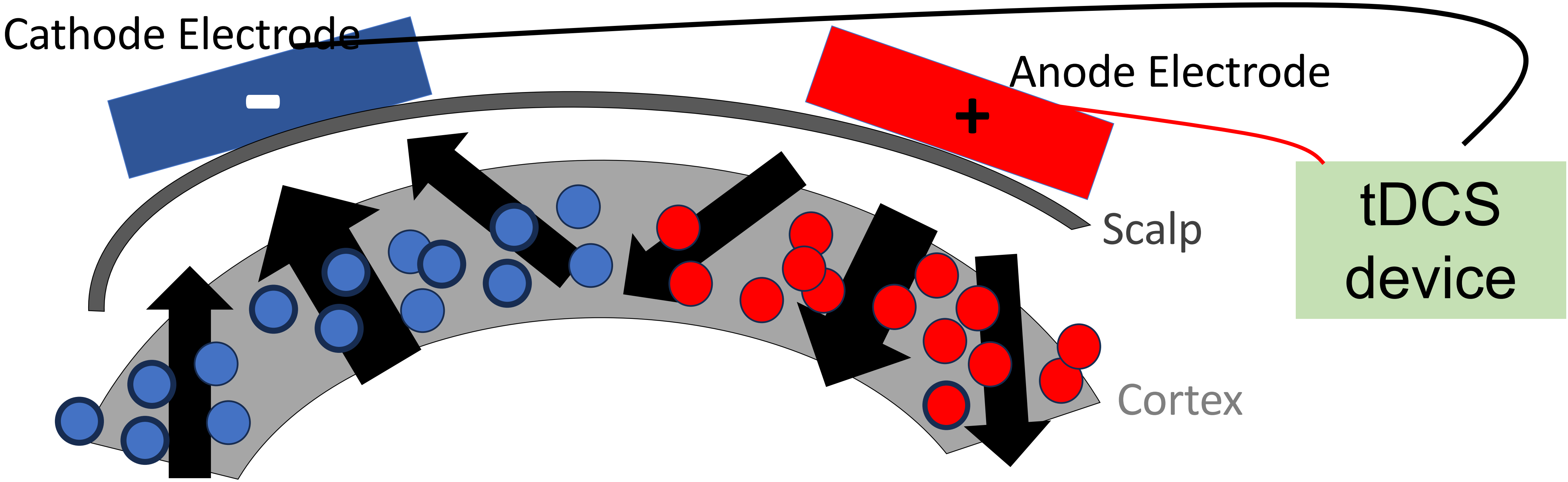
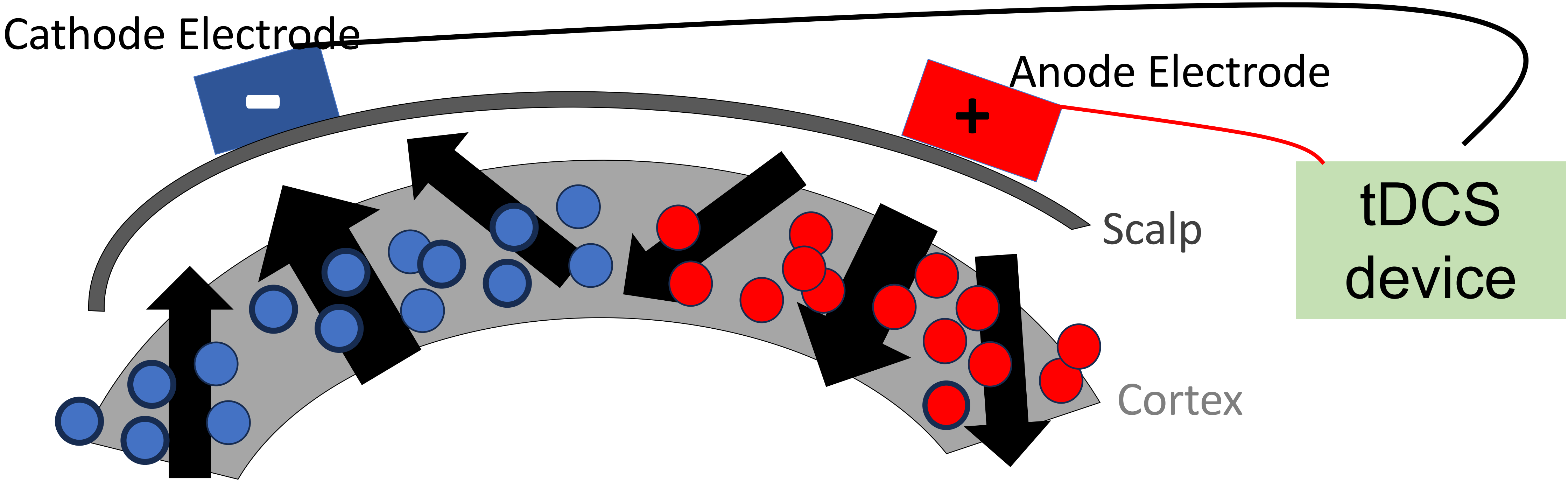
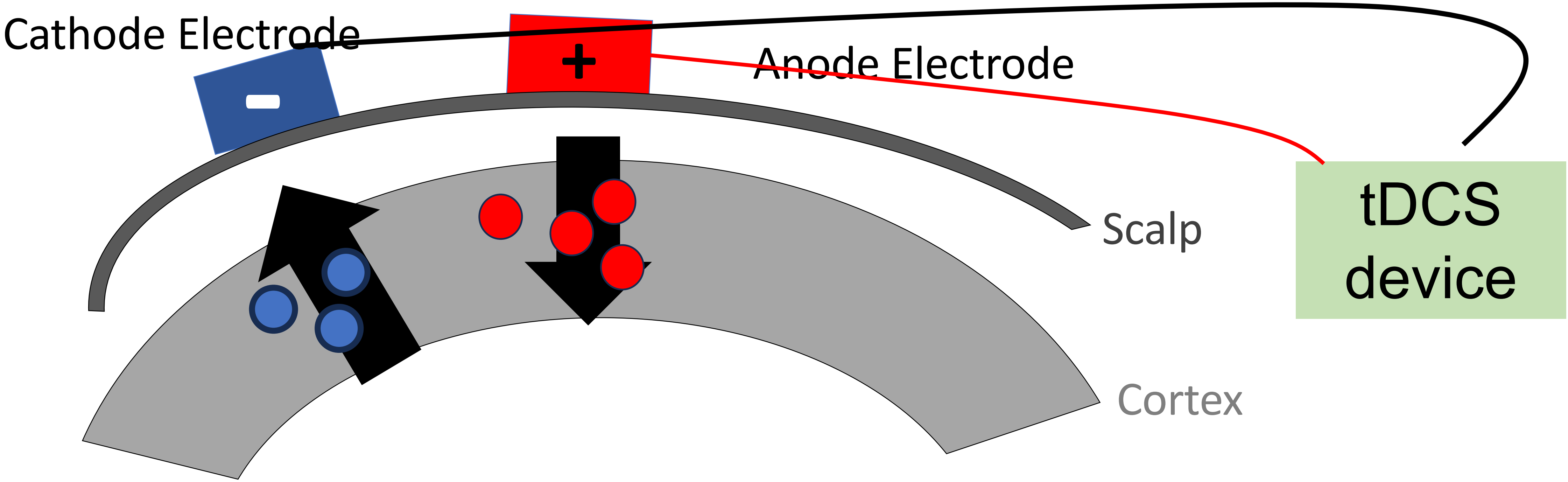


tDCS with two large electrodes leads to diffuse current flow and stimulation.



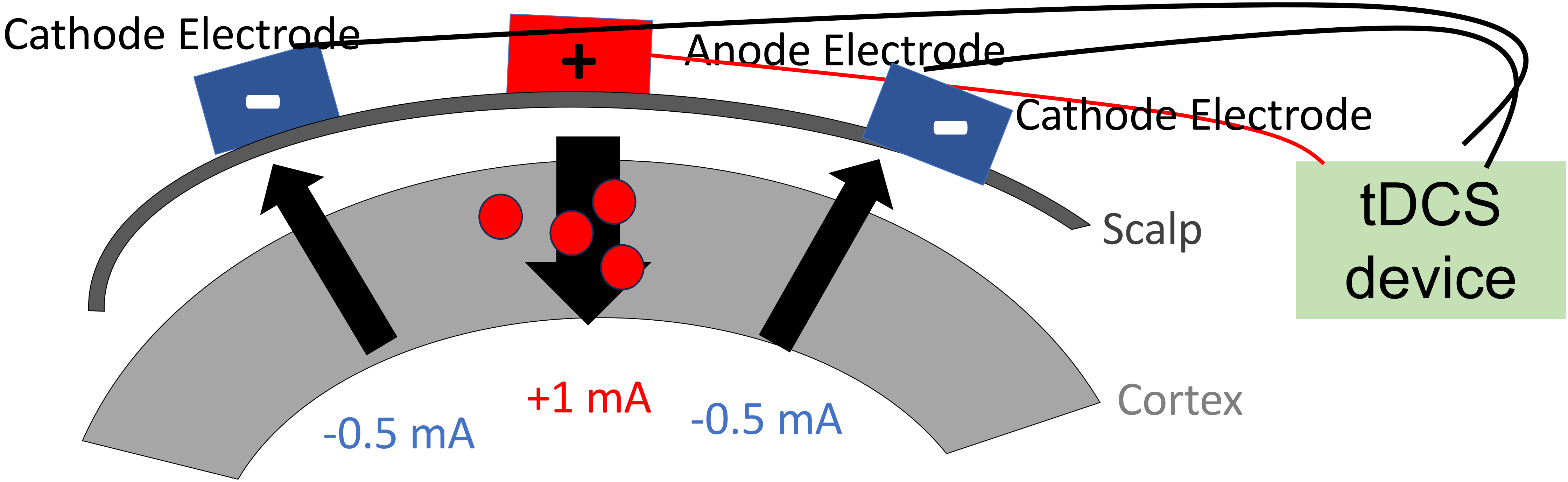
Smaller electrodes called “High Definition” (HD).

Making electrodes small does not in itself make stimulation focal. Current must still travel between electrodes.

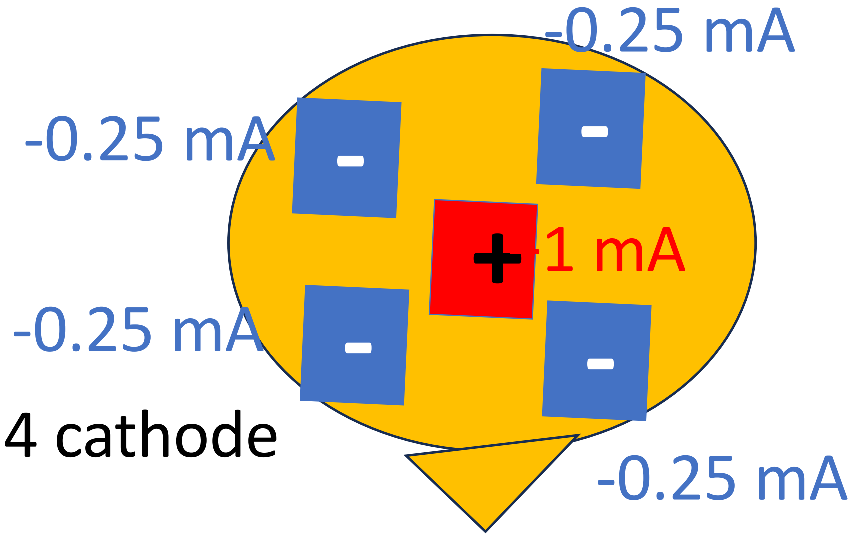


Make electrodes small (High Definition) and moving them closer together make current focal.

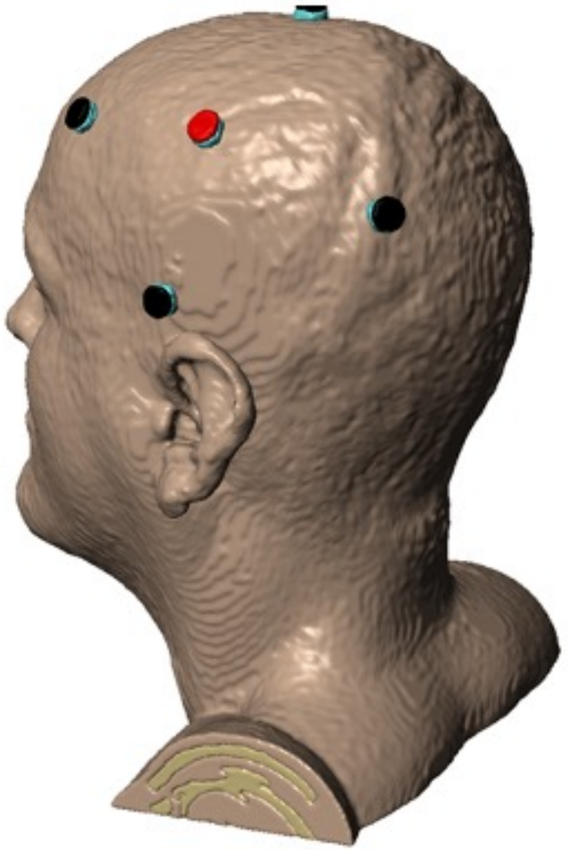
With two electrodes you have an anodal and cathodal regions.



Adding more “return” cathodes, makes the cathodal weaker. Leaving anodal strong.



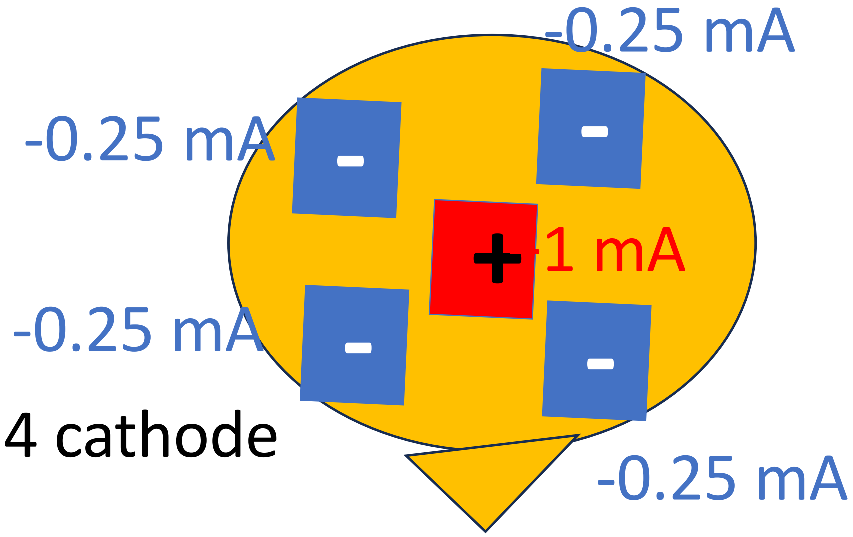
1 center anode x 4 cathode
4x1-HD-tDCS



Cathode Electrodes (-0.25 mA)

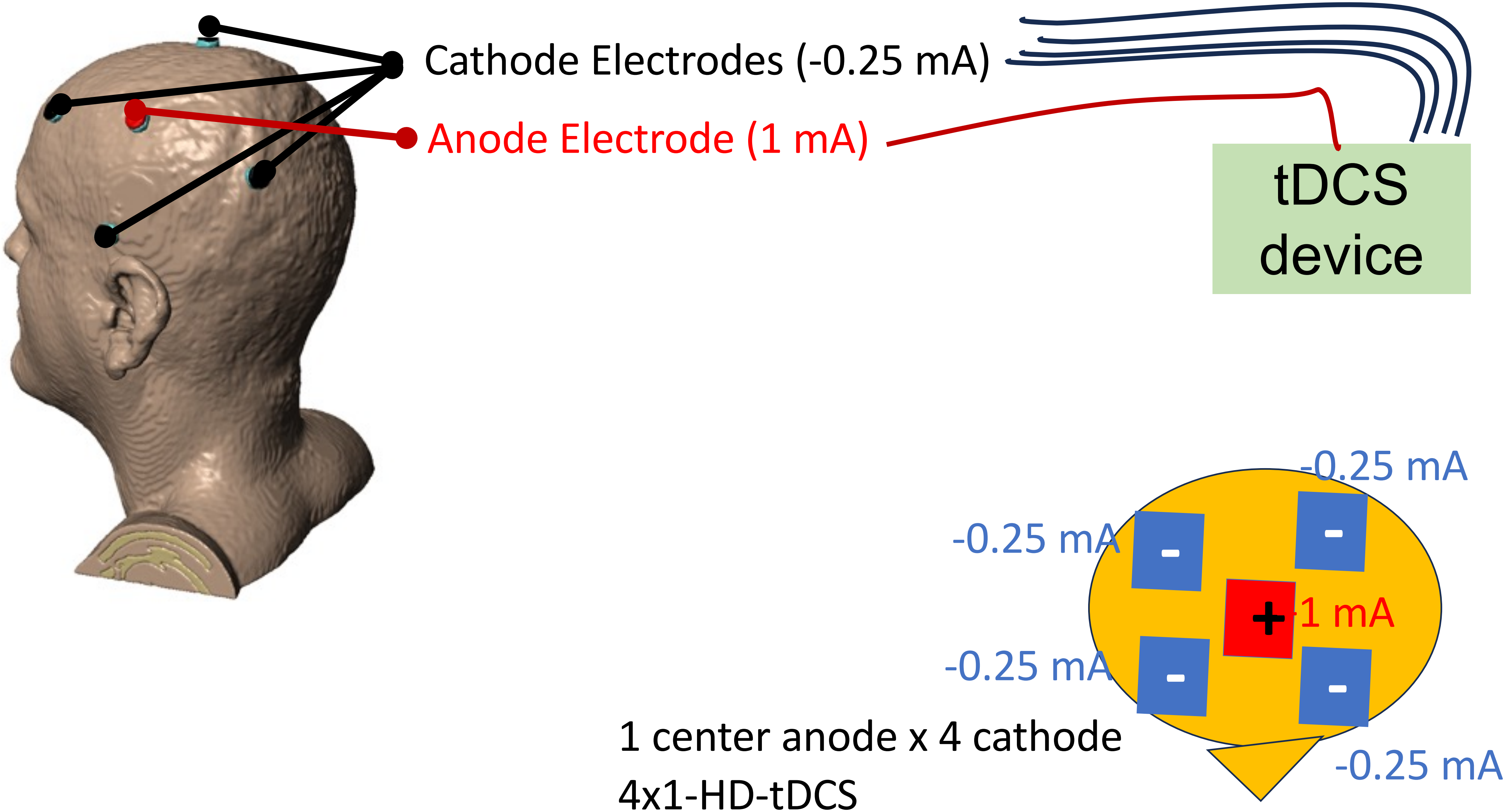
Anode Electrode (1 mA)

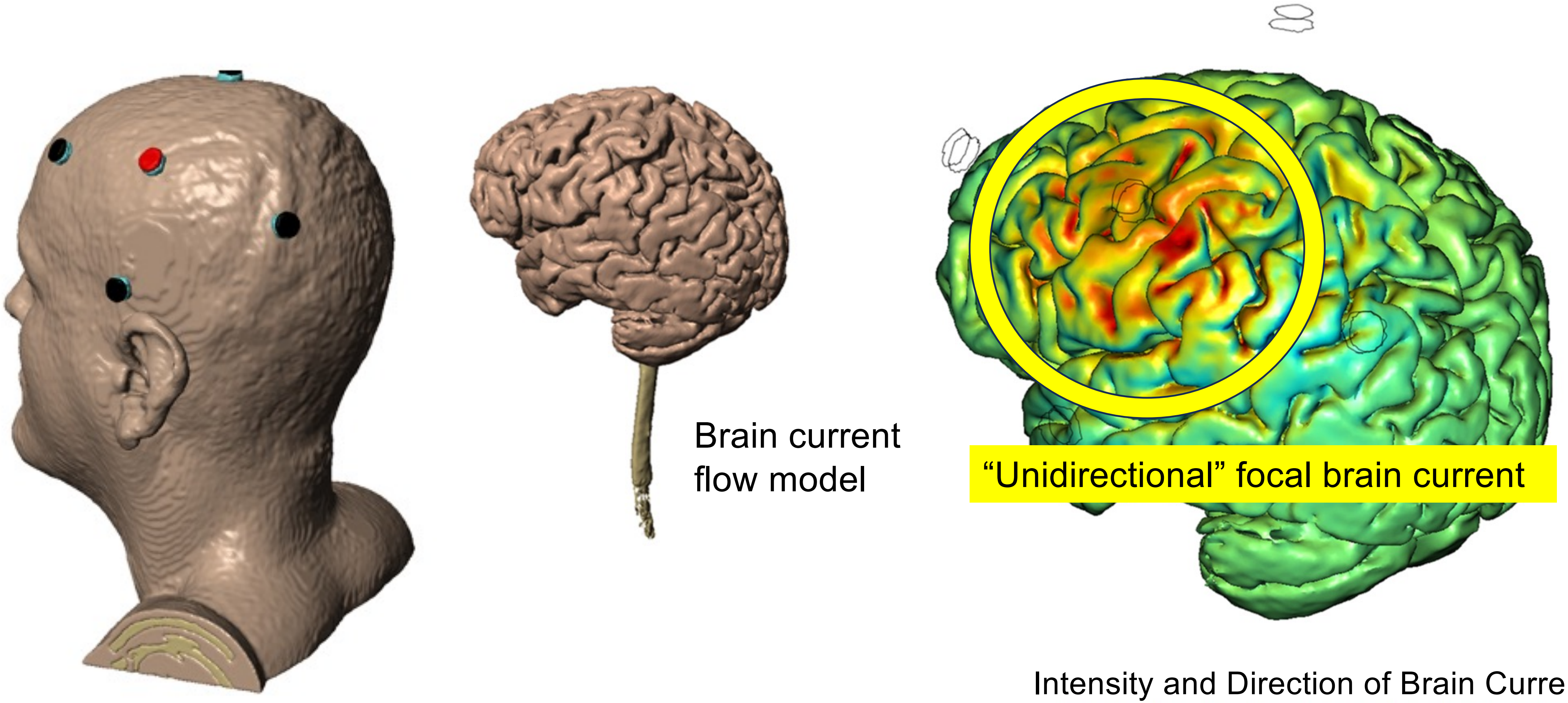
tDCS device



1 center anode x 4 cathode

4x1-HD-tDCS

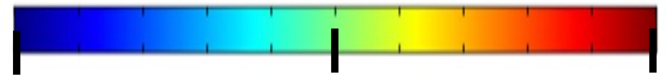

Cathode Electrodes (-0.25 mA)
Anode Electrode (1 mA)
tDCS device
-0.25 mA
-0.25 mA
+
1 mA
-0.25 mA
-0.25 mA
1 center anode x 4 cathode
4x1-HD-tDCS



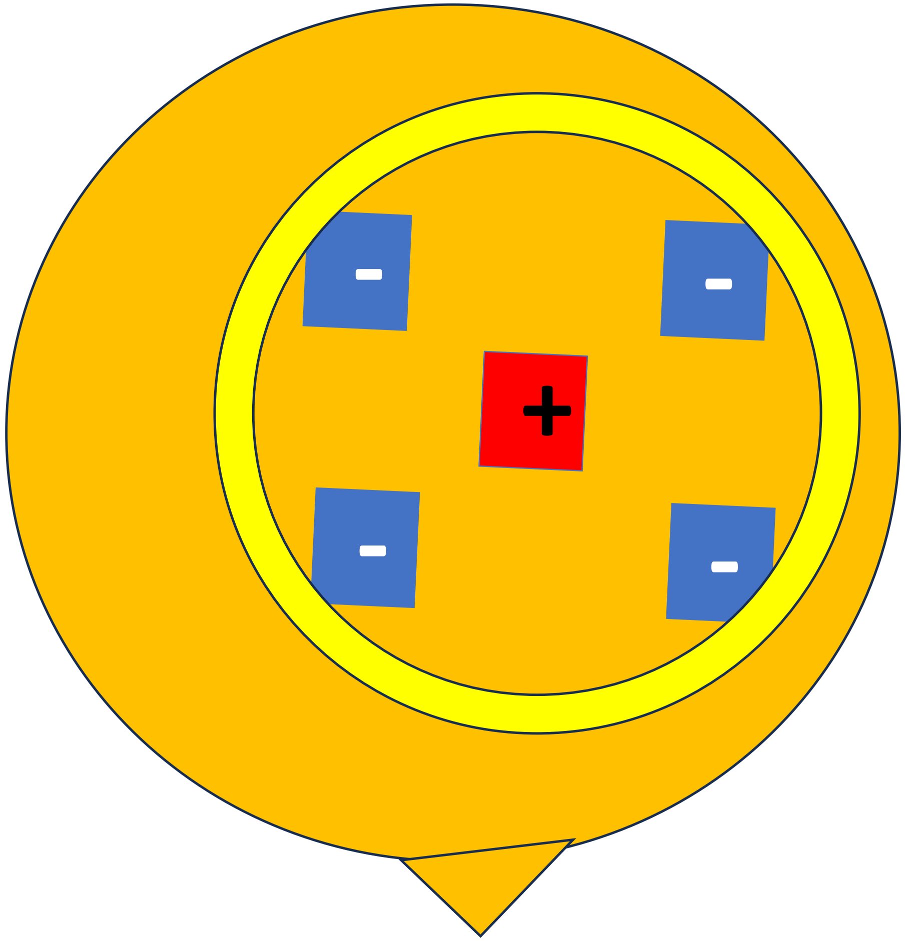
1 center anode x 4 cathode: 4x1-HD-tDCS

Cathode Electrodes (-0.25 mA) Anode Electrode (1 mA)

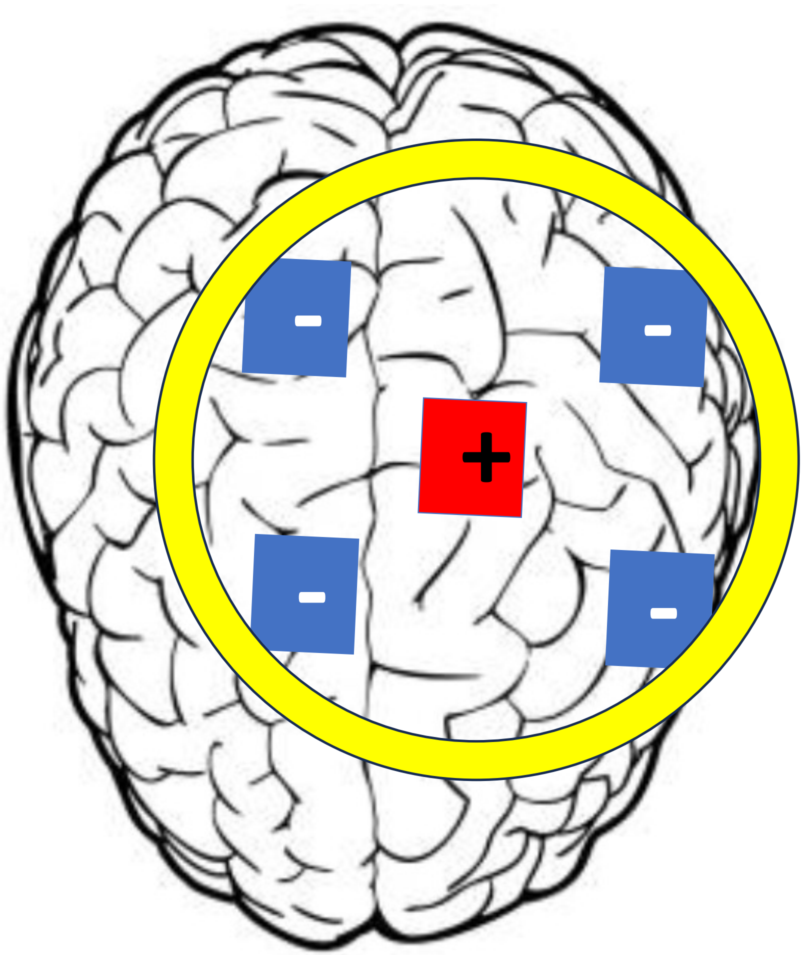
Intensity and Direction of Brain Current



Villamar et al. Focal modulation of the primary motor cortex in fibromyalgia using 4×1-ring high-definition transcranial direct current stimulation (HD-tDCS). *Journal of Pain*, 2013



The outer electrodes form a ring.
The area of brain targeted is inside the ring.



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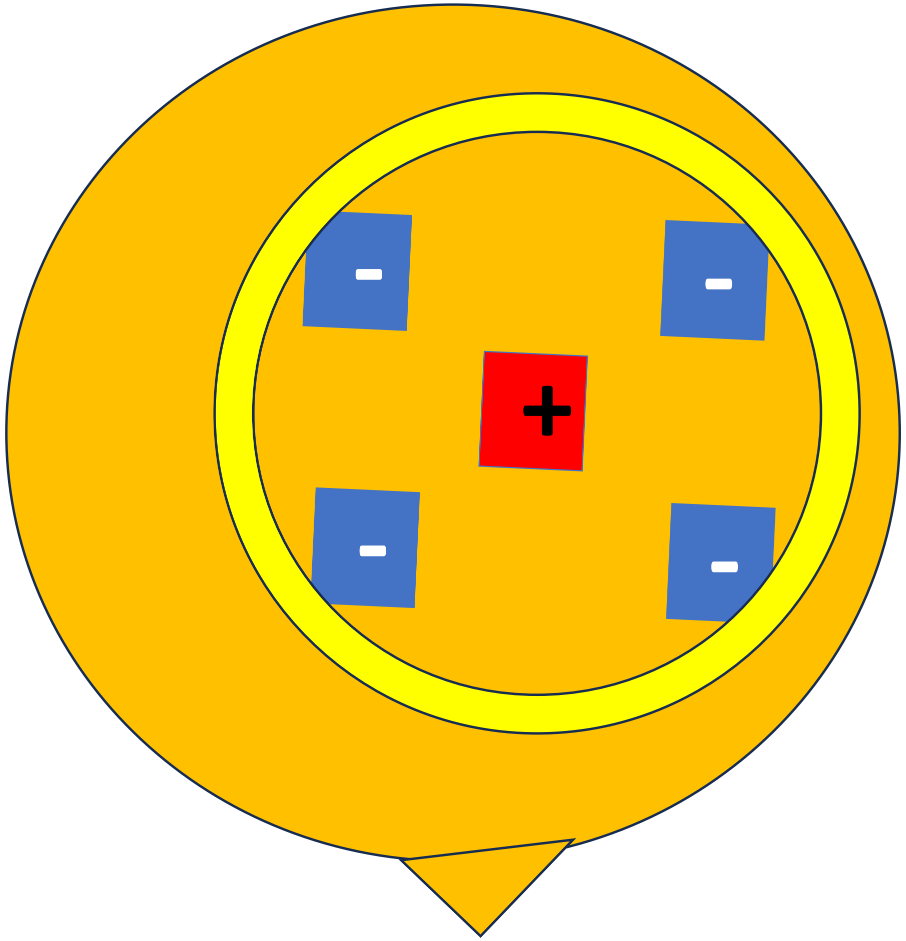

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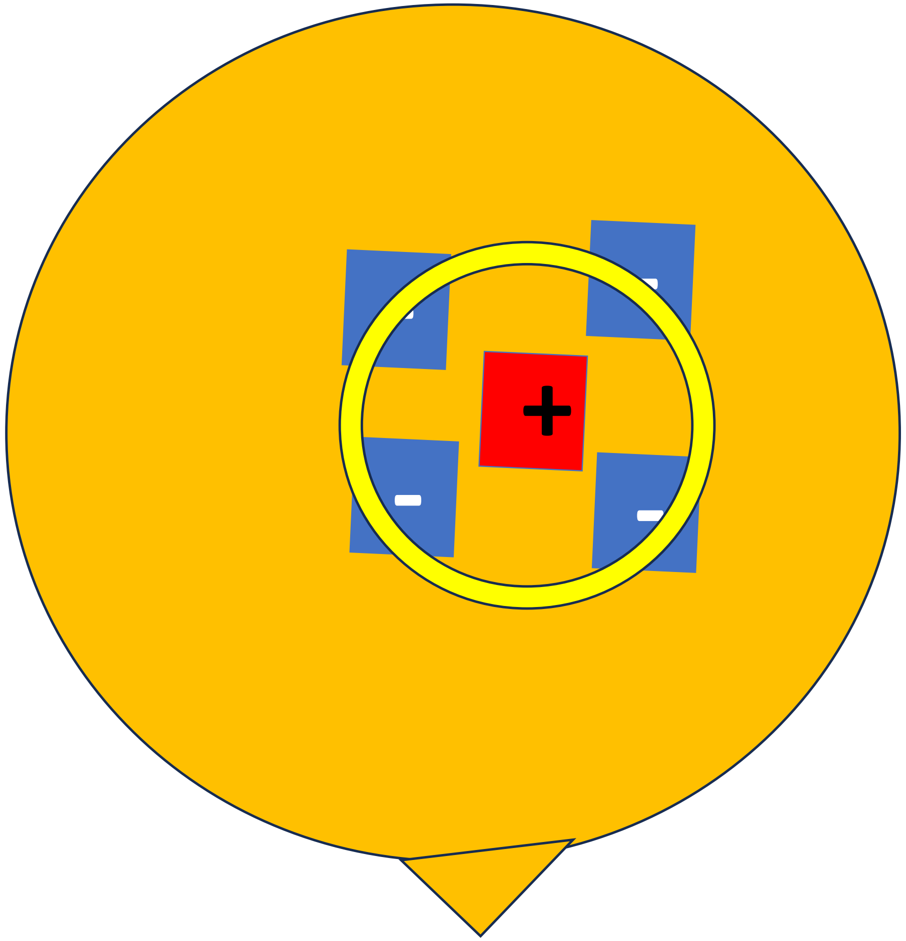
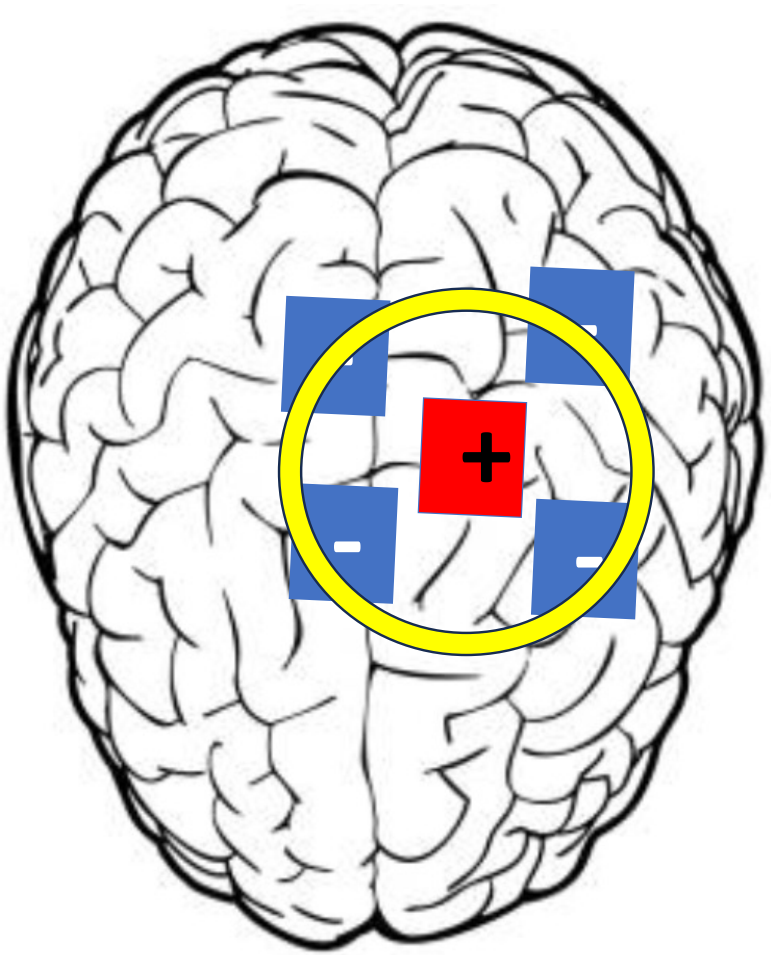


Making the ring small focuses brain targeting.

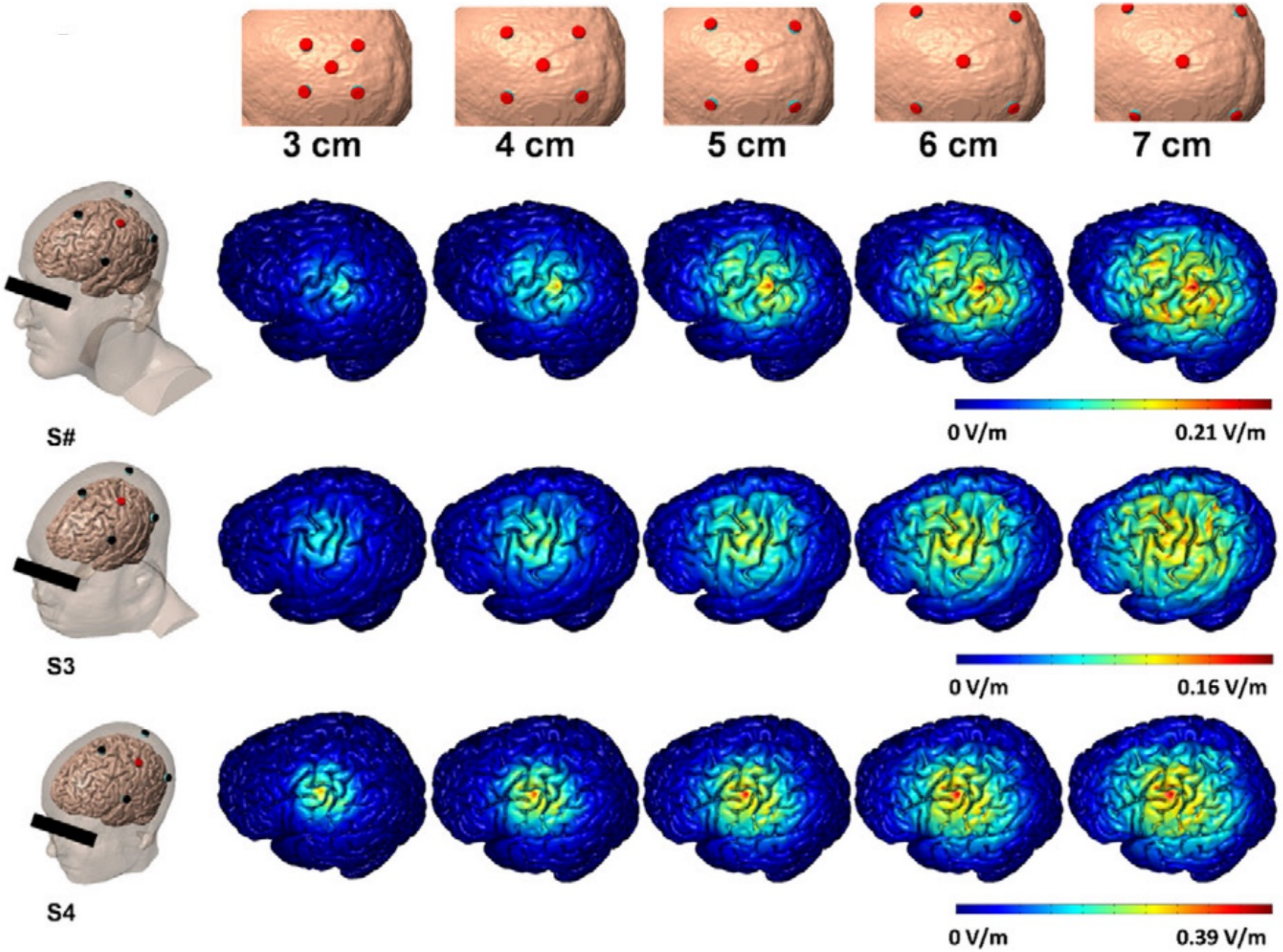


Making the ring small focuses brain targeting.

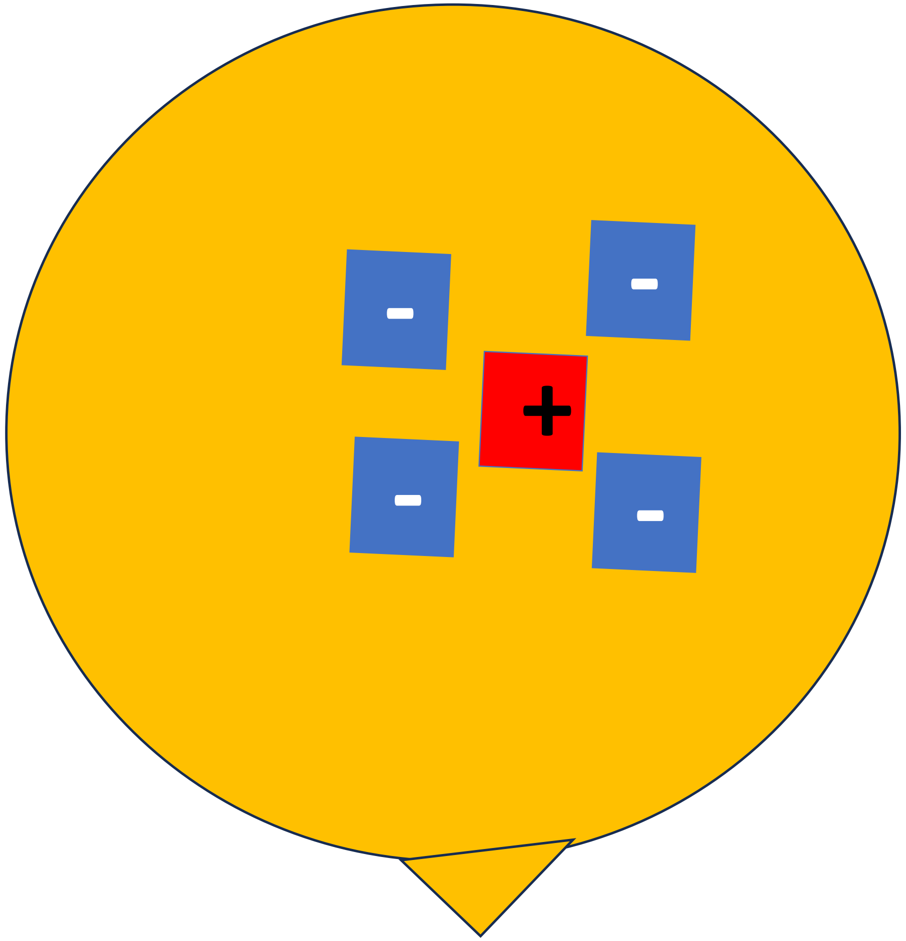
However, the intensity of current in the brain also decreases.

More focal.
Reduced intensity.

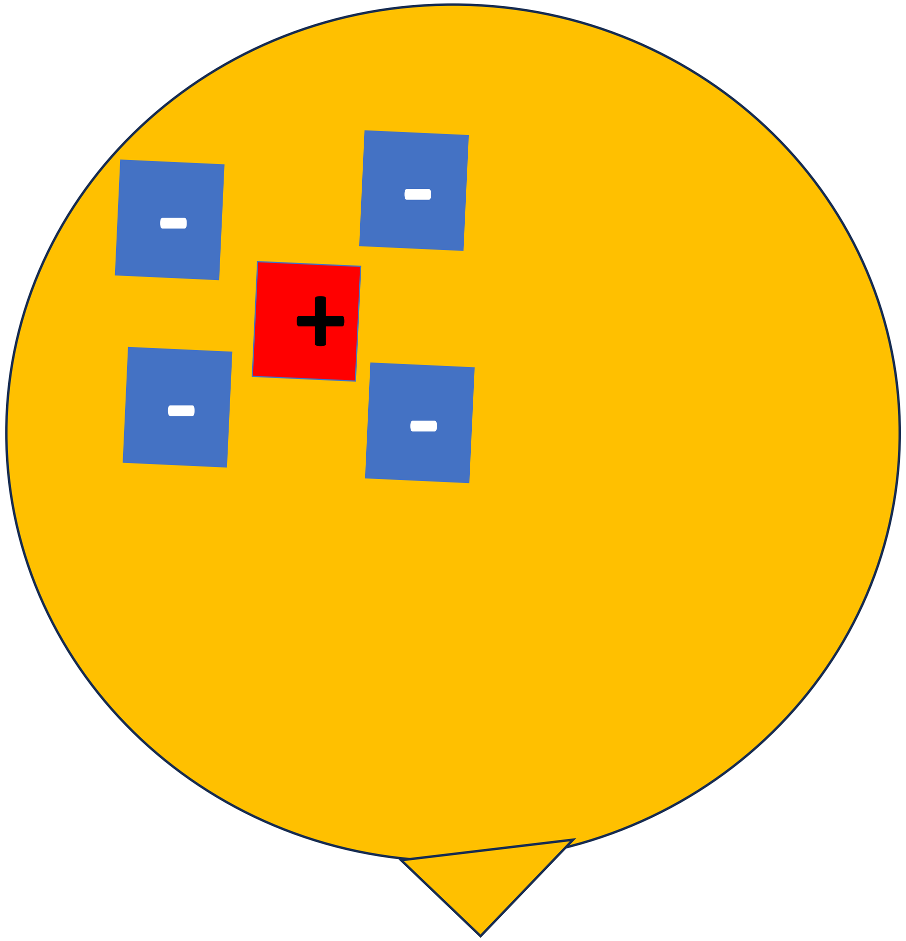
Reliably inside ring.



Alam et al. Spatial and polarity precision of concentric high-definition transcranial direct current stimulation (HD-tDCS). Physics in Medicine and Biology, 2016



Any cortical region
can be targeted.



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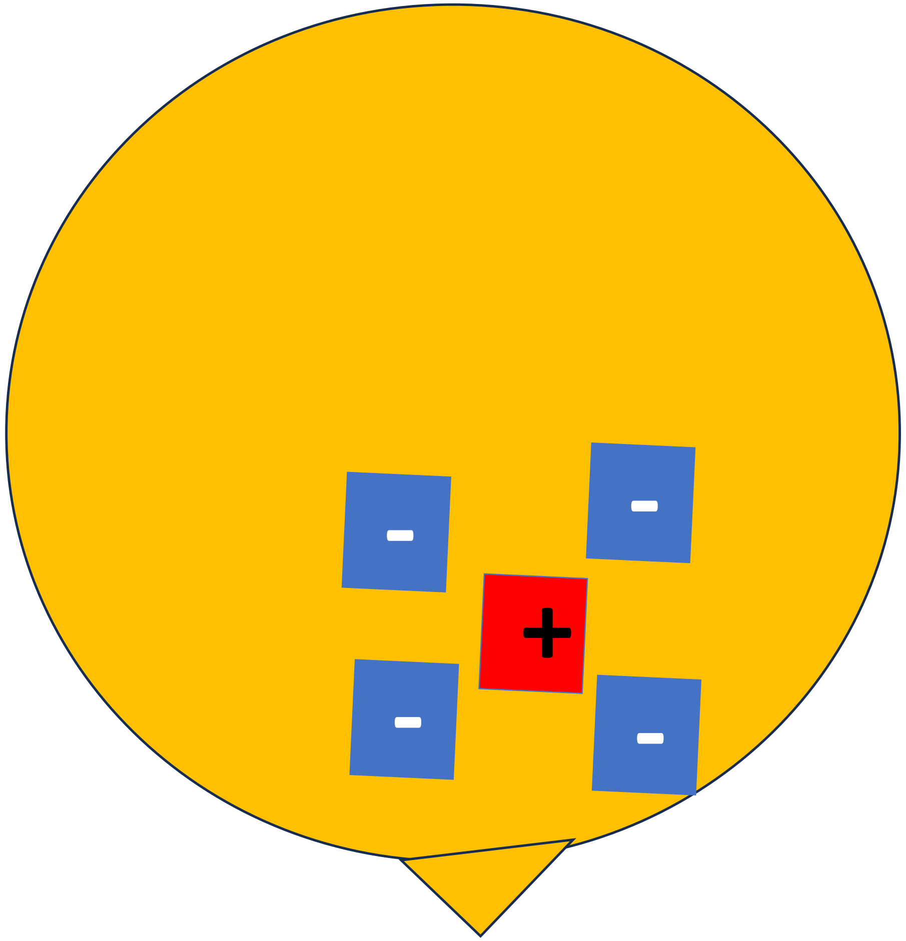

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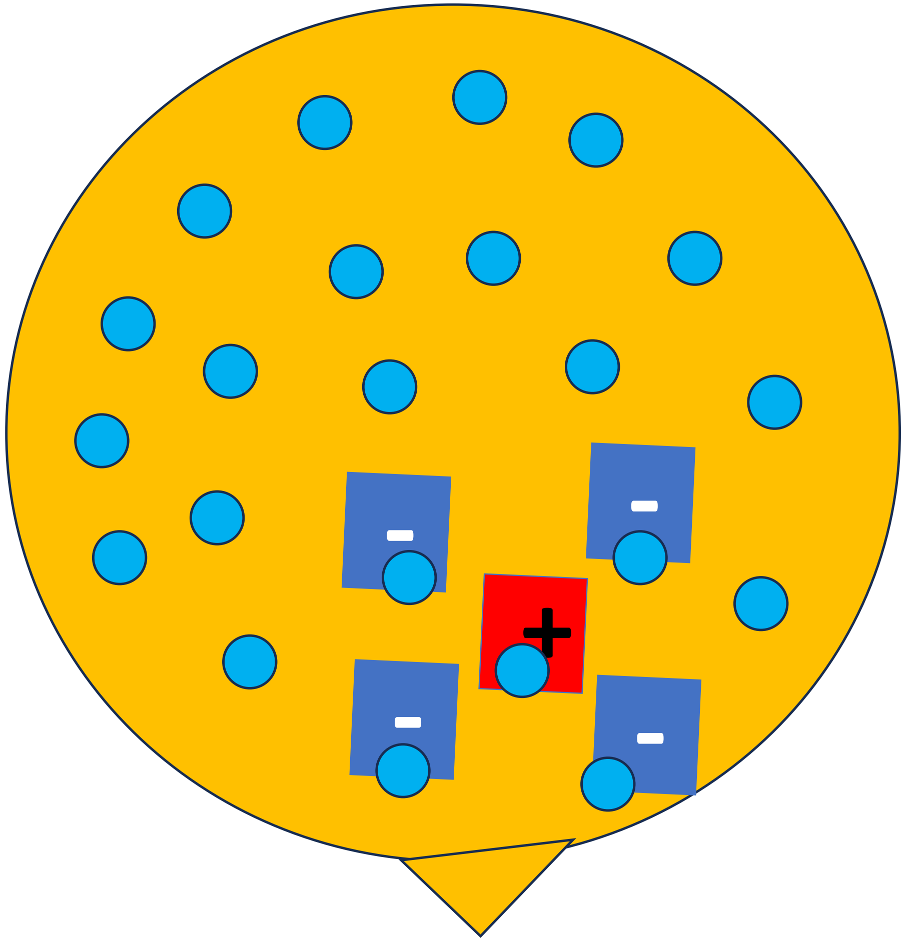
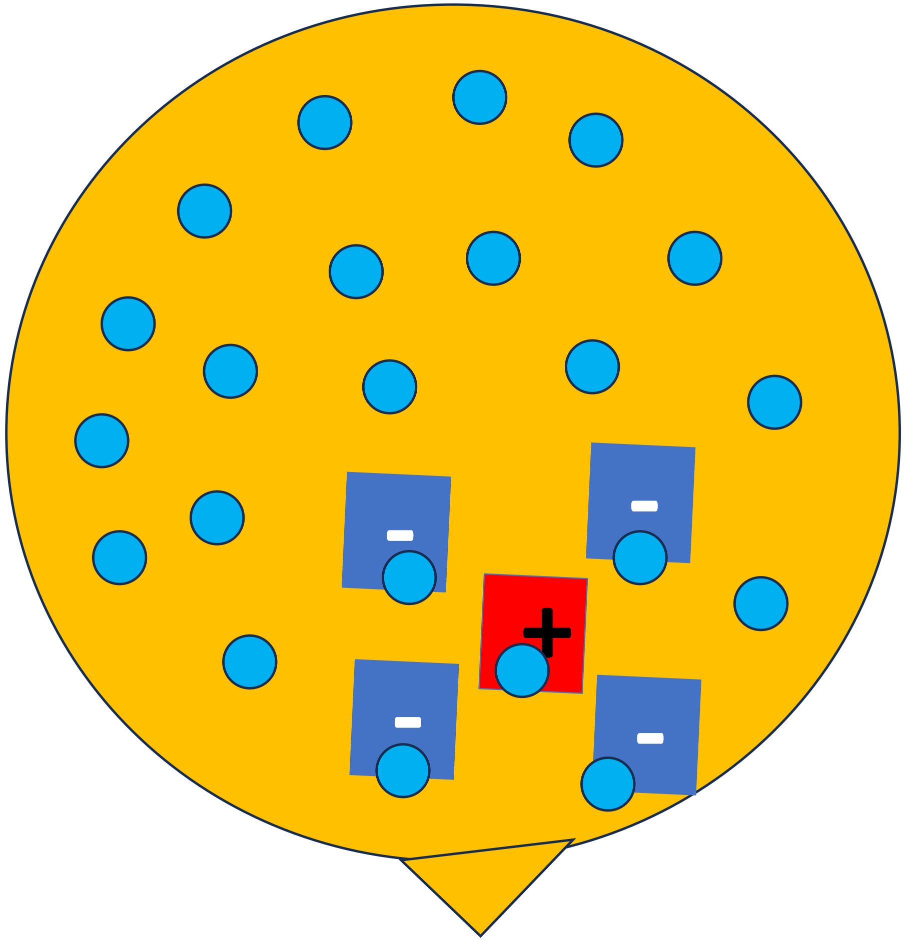
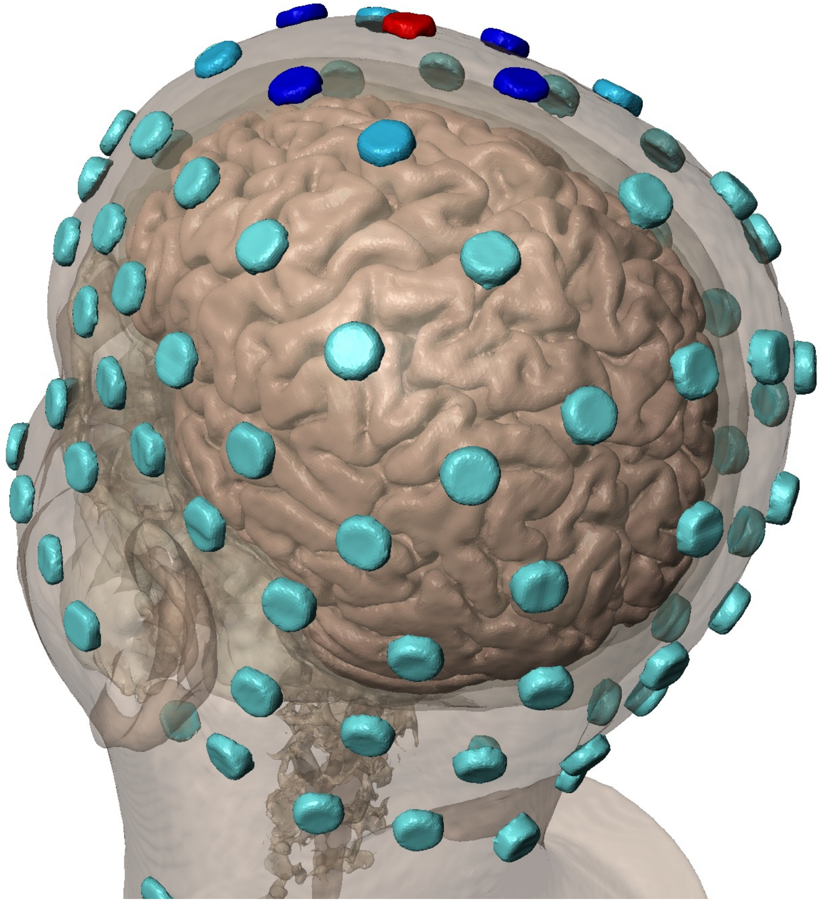


HD electrodes positioned according to EEG 10-10 system

Any cortical region can be targeted.

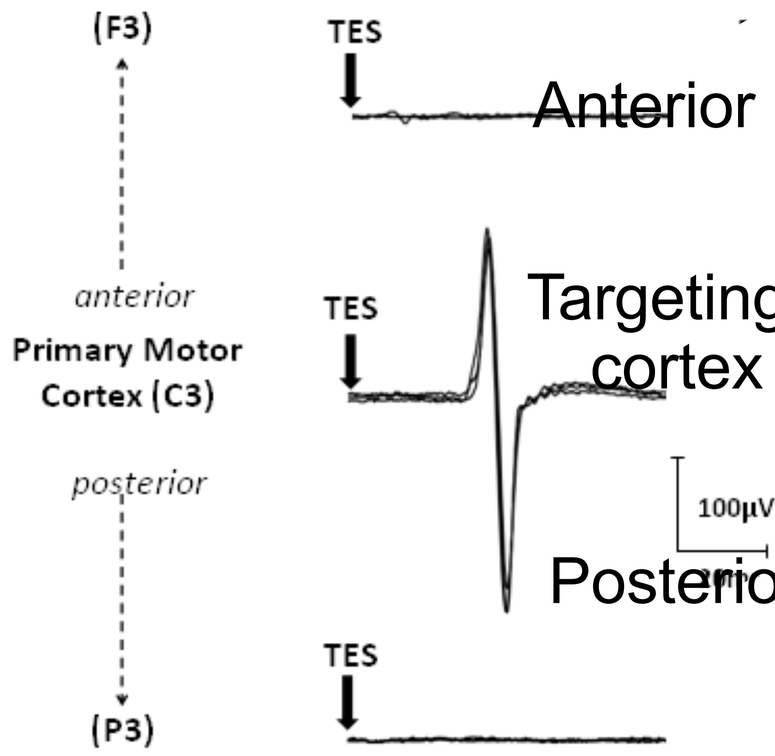


HD electrodes positioned according to EEG 10-10 system



4x1 HD electrodes

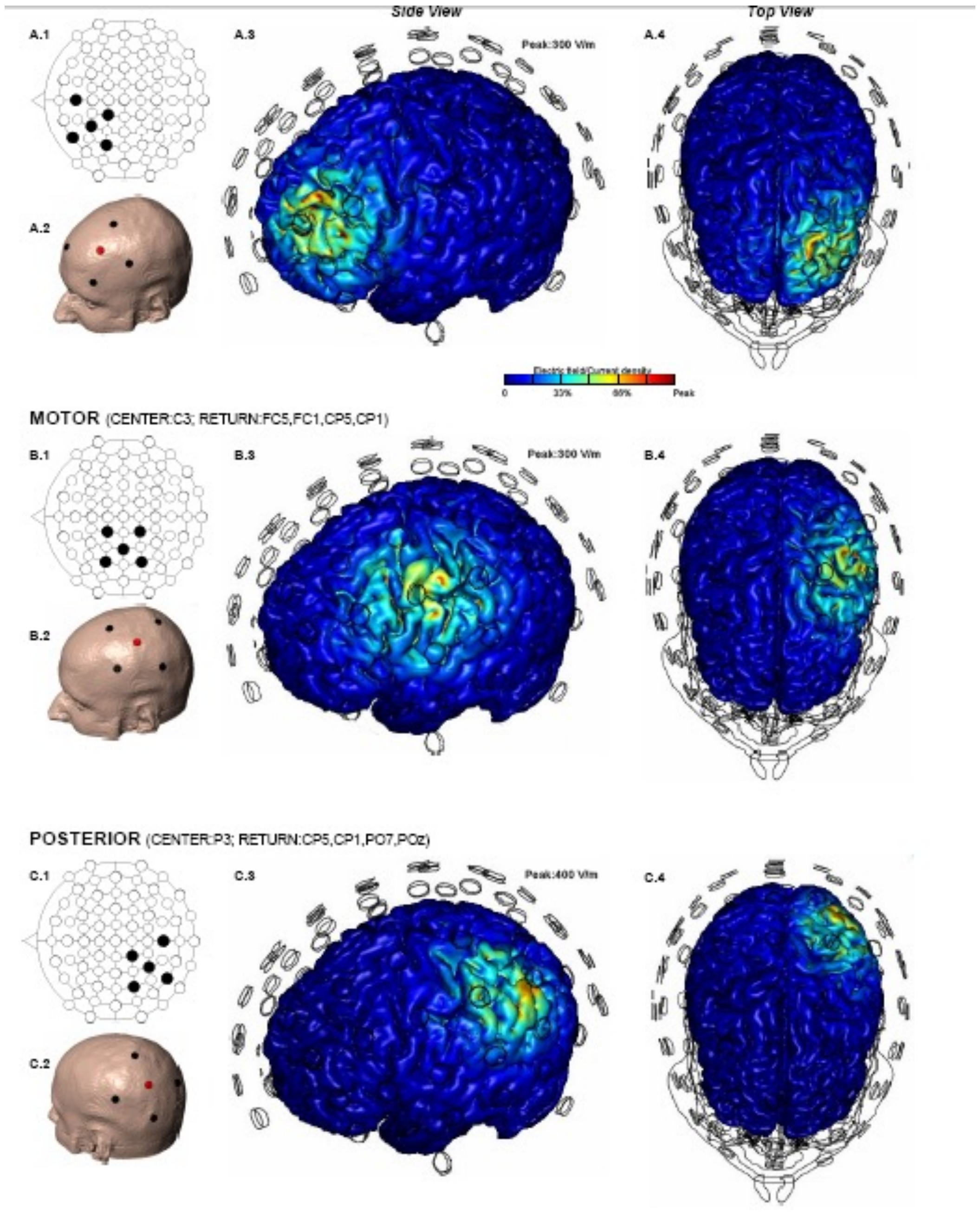
Using high-intensity (~1000 mA) pulse to trigger motor evoked potential (MEP)



Anterior (F3)

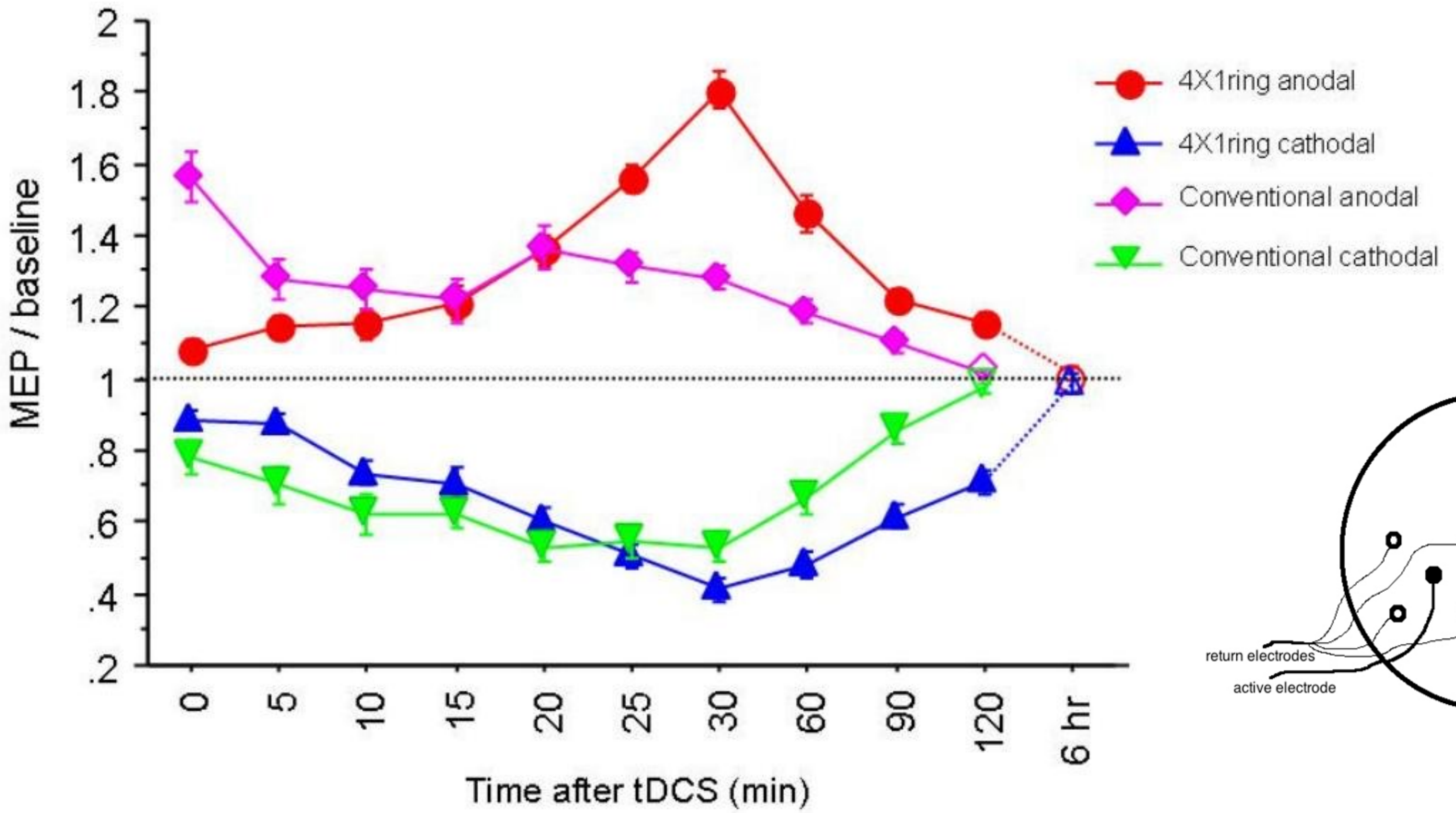
Targeting motor cortex (C3)

Posterior (P3)

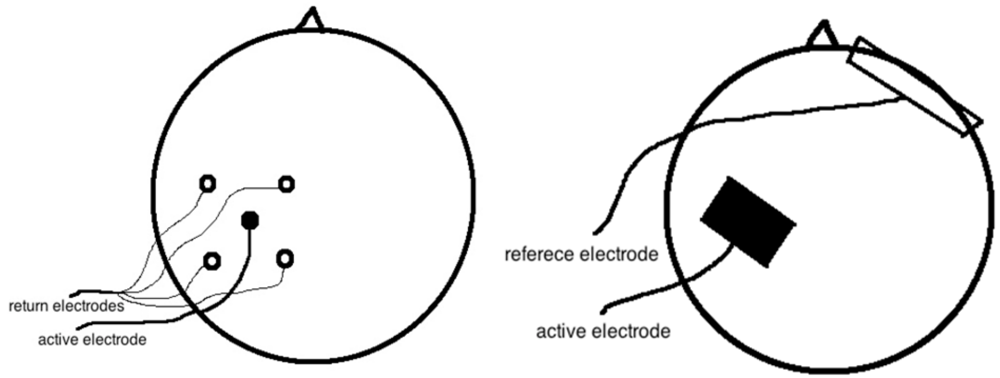


Edwards et al. Physiological and modeling evidence for focal transcranial electrical brain stimulation in humans. NeuroImage. 2013

- Human neurophysiology marker of “brain exctiability”: Transcranial Magnetic Stimulation evoked Motor Respone (MEP).
- After tDCS exctiability is modulated. Anode=UP, Cathode=DOWN.



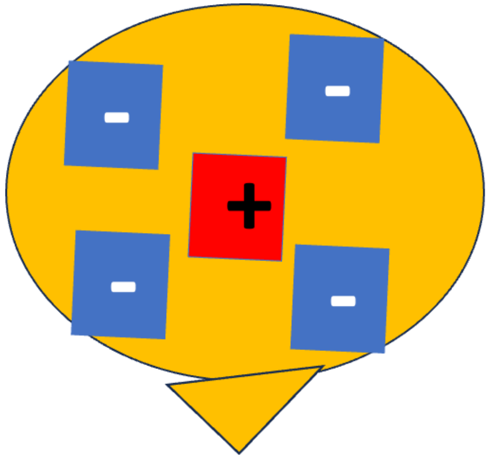
2 mA, 10 min 4x1 HD-tDCS: >2 hours excitability change



Kuo et al. Comparing cortical plasticity induced by conventional and high-definition 4×1 ring tDCS: A neurophysiological study. *Brain Stimulation*. 2013

4x1 HD-tDCS is a unique tool for low-intensity non-invasive focal cortical neuromodulation.

- A deployable and tolerated as tDCS. As focal as TMS. 'Unidirectional' neuromodulation.
- Causal role of brain regions in cognition.
- Clinical trials (increased efficacy).

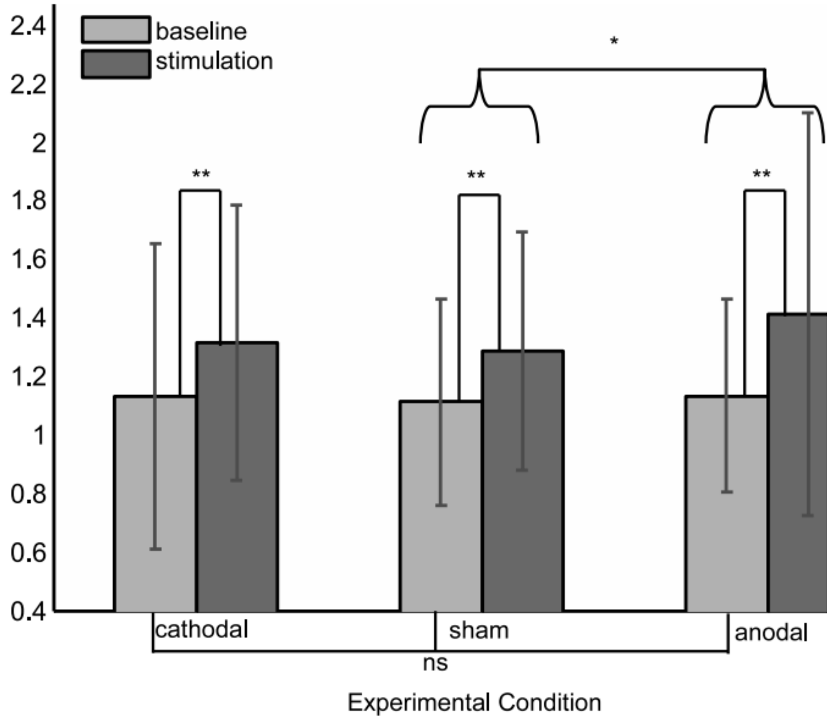


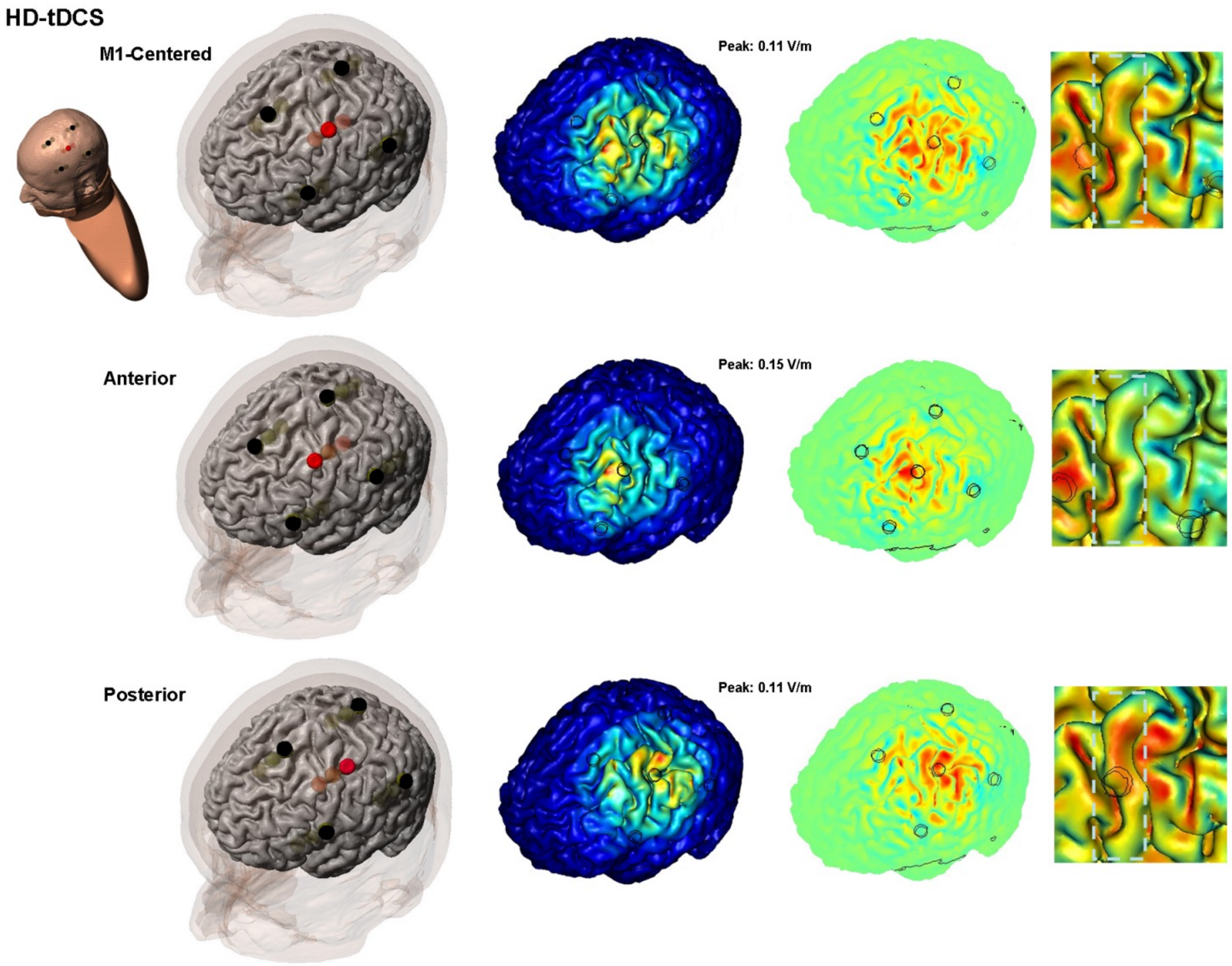
Santana et al. Non-invasive brain stimulation for fatigue in post-acute sequelae of SARS-CoV-2 (PASC). *Brain Stimulation*. 2023

Bahr-Hosseini et al. High-definition Cathodal Direct Current Stimulation for Treatment of Acute Ischemic Stroke: A Randomized Clinical Trial. *JAMA Network Open*. 2023

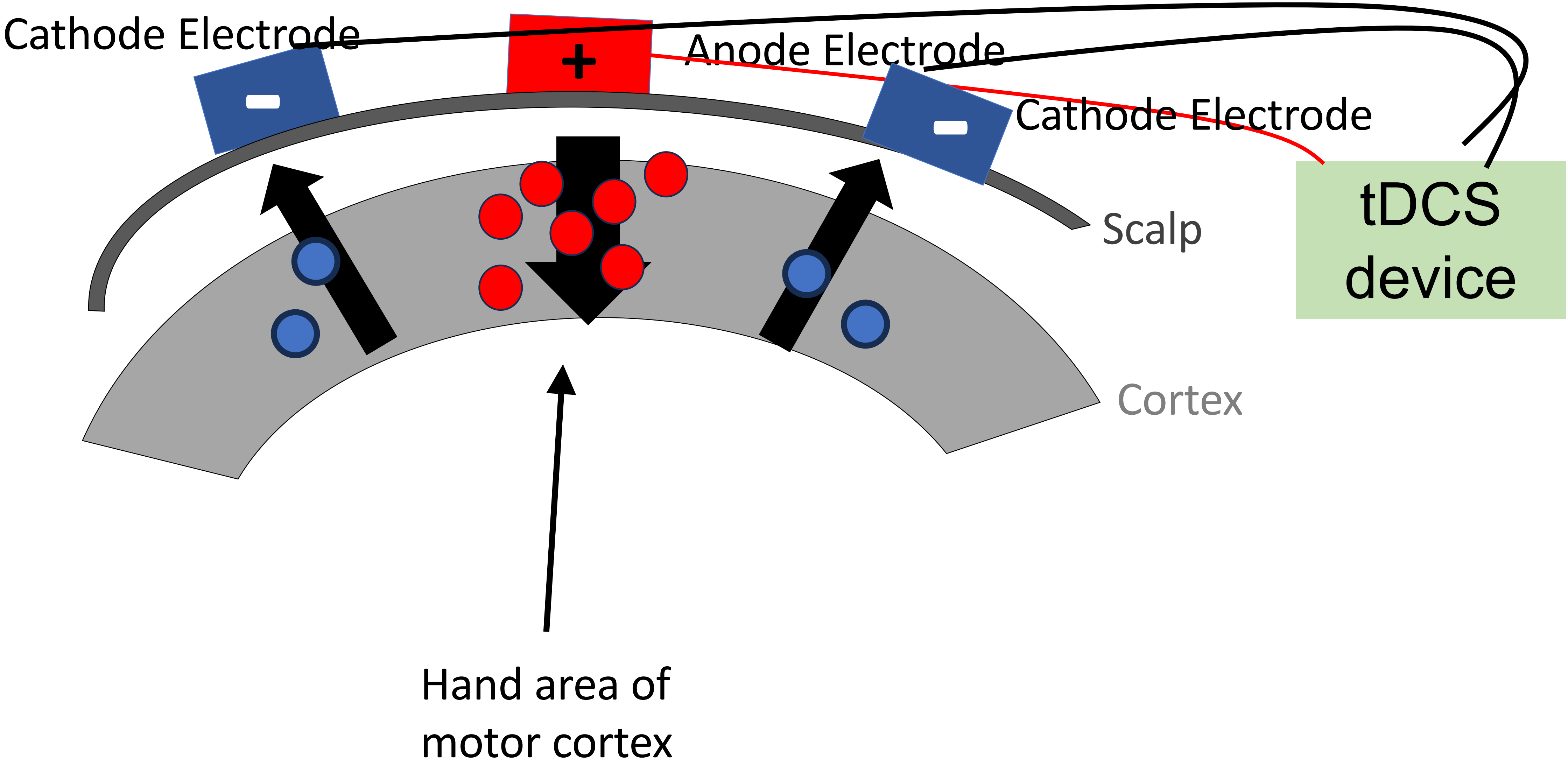
Andrade et al. Efficacy and safety of HD-tDCS and respiratory rehabilitation for critically ill patients with COVID-19 The HD-RECOVERY randomized clinical trial. *Brain Stimulation*. 2022

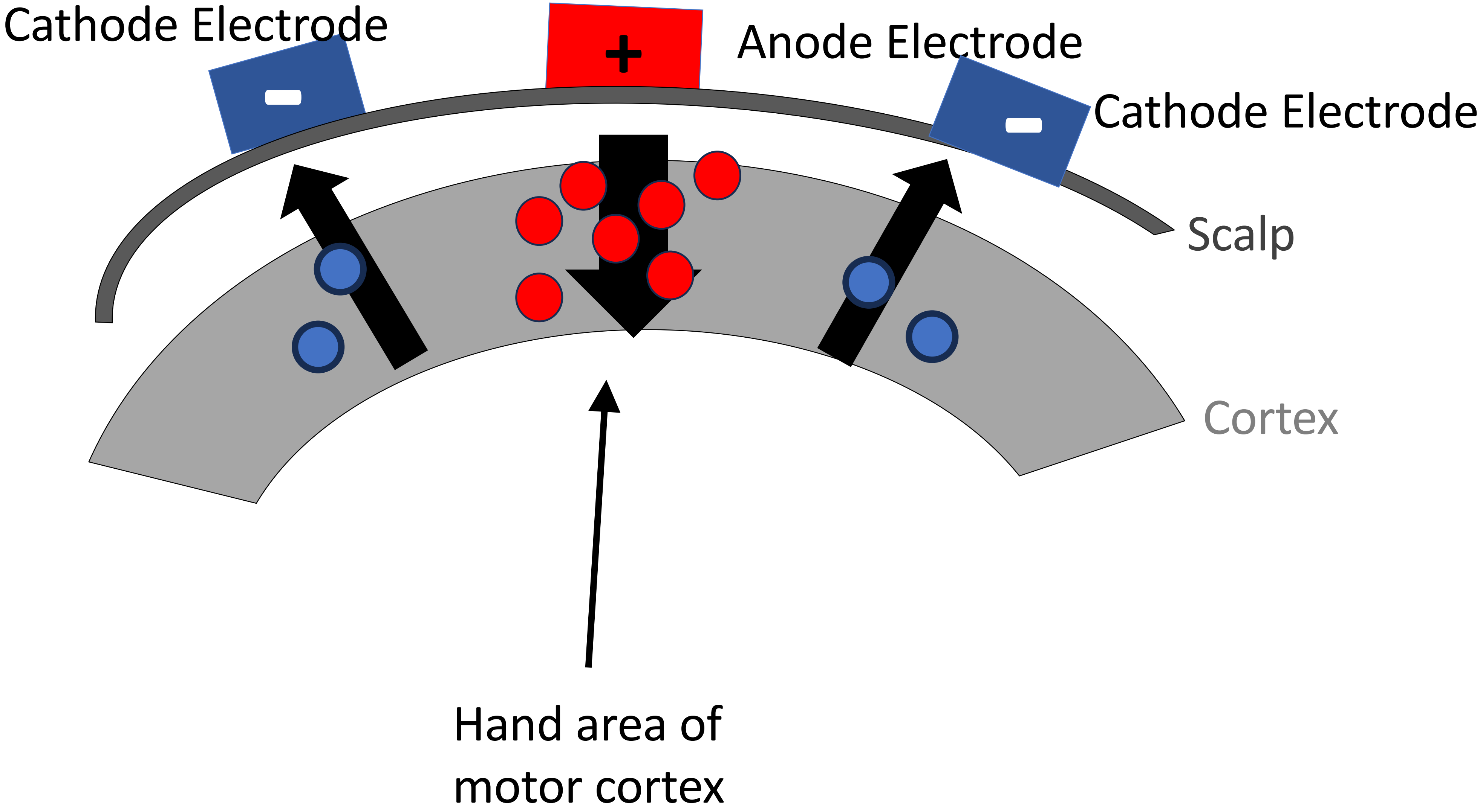
First trial of HD-tDCS on cortical excitability reported real but variable outcomes.

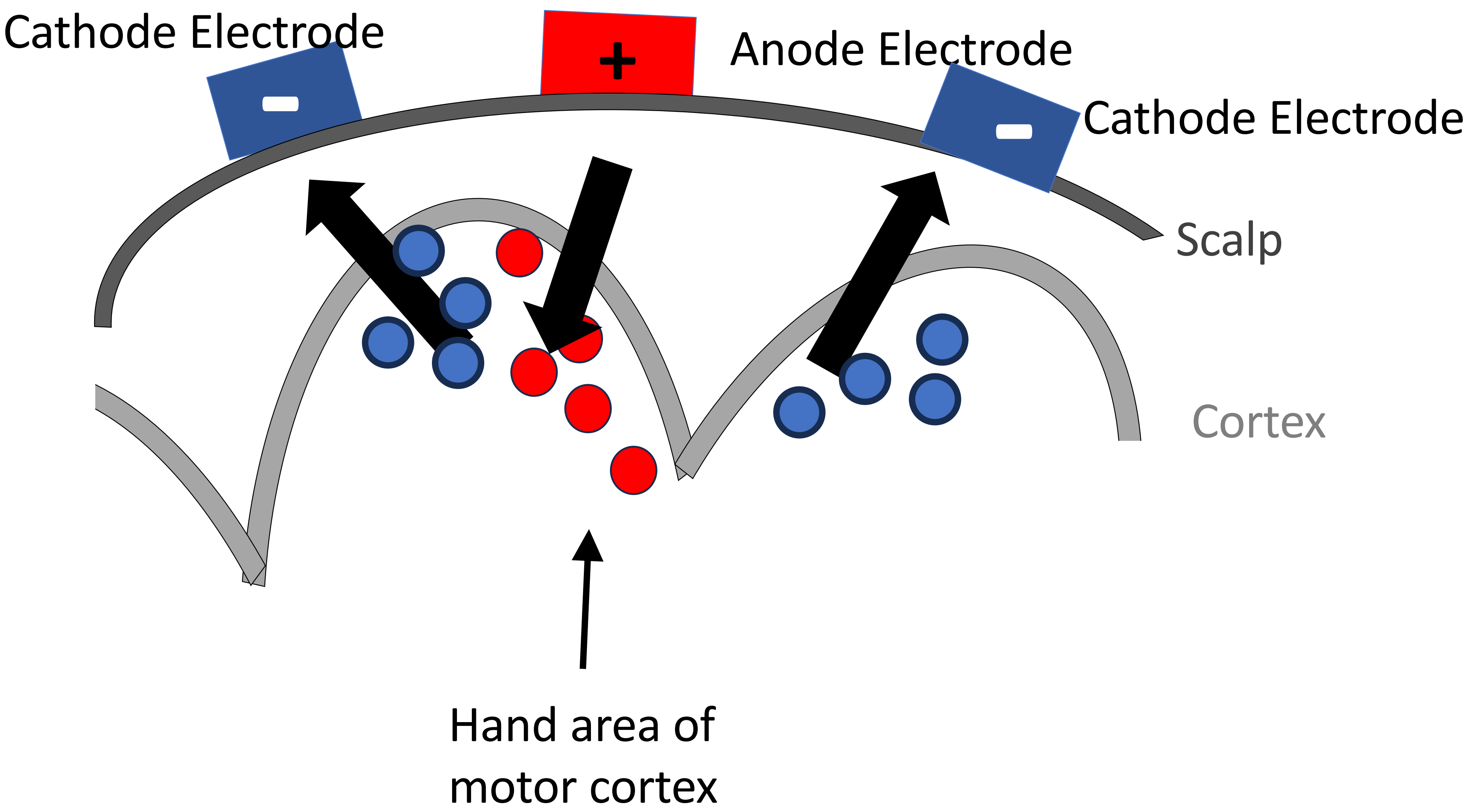




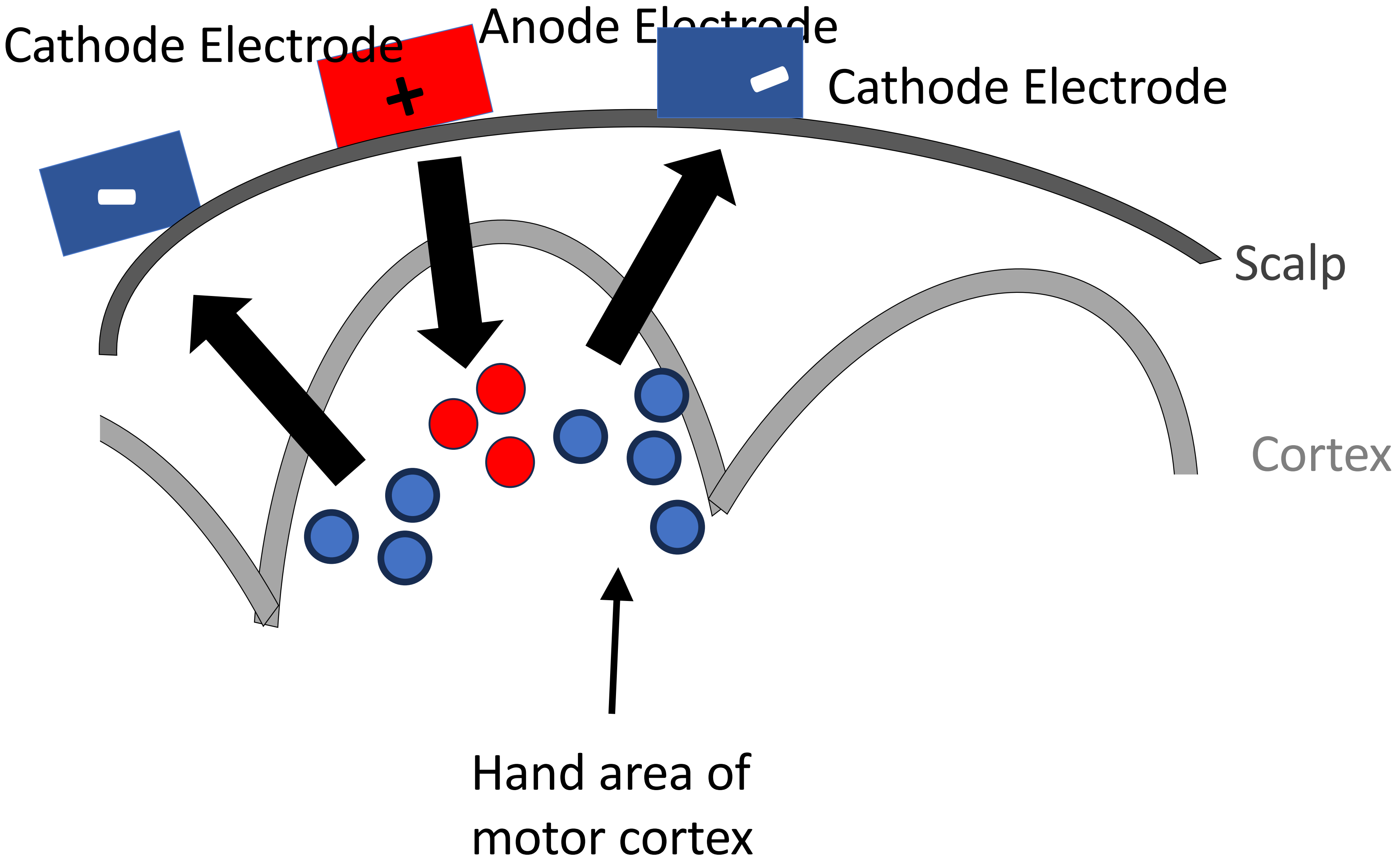
Caparelli-Daquer et al. A pilot study on effects of 4×1 high-definition tDCS on motor cortex excitability. *EMBS*. 2012


Cathode Electrode
Anode Electrode
Cathode Electrode
tDCS device
Scalp
Cortex
Hand area of motor cortex


Cathode Electrode
Anode Electrode
Cathode Electrode
+
Scalp
Cortex
Hand area of
motor cortex



Caparelli-Daquer et al. A pilot study on effects of 4×1 high-definition tDCS on motor cortex excitability. EMBS. 2012



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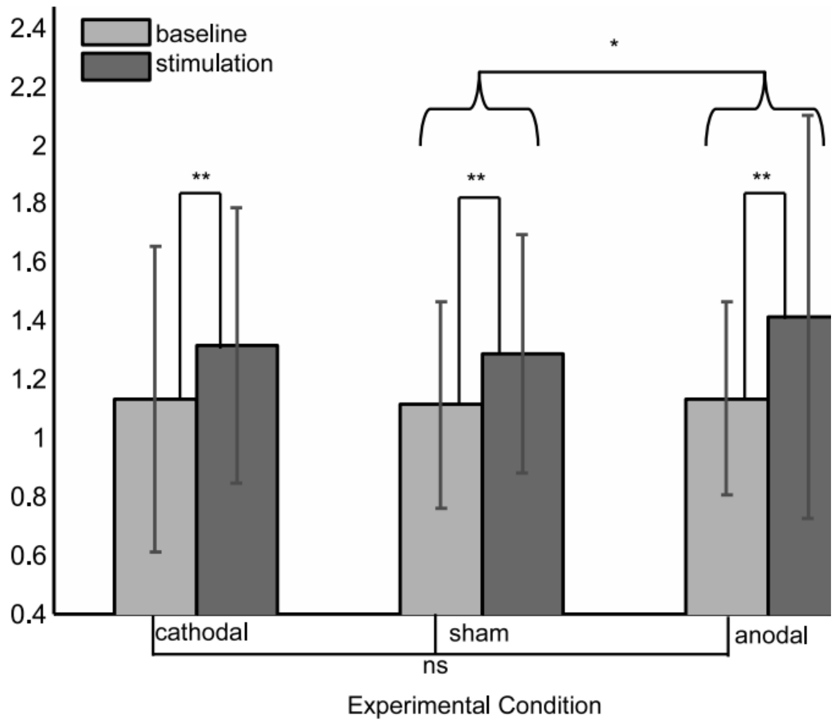

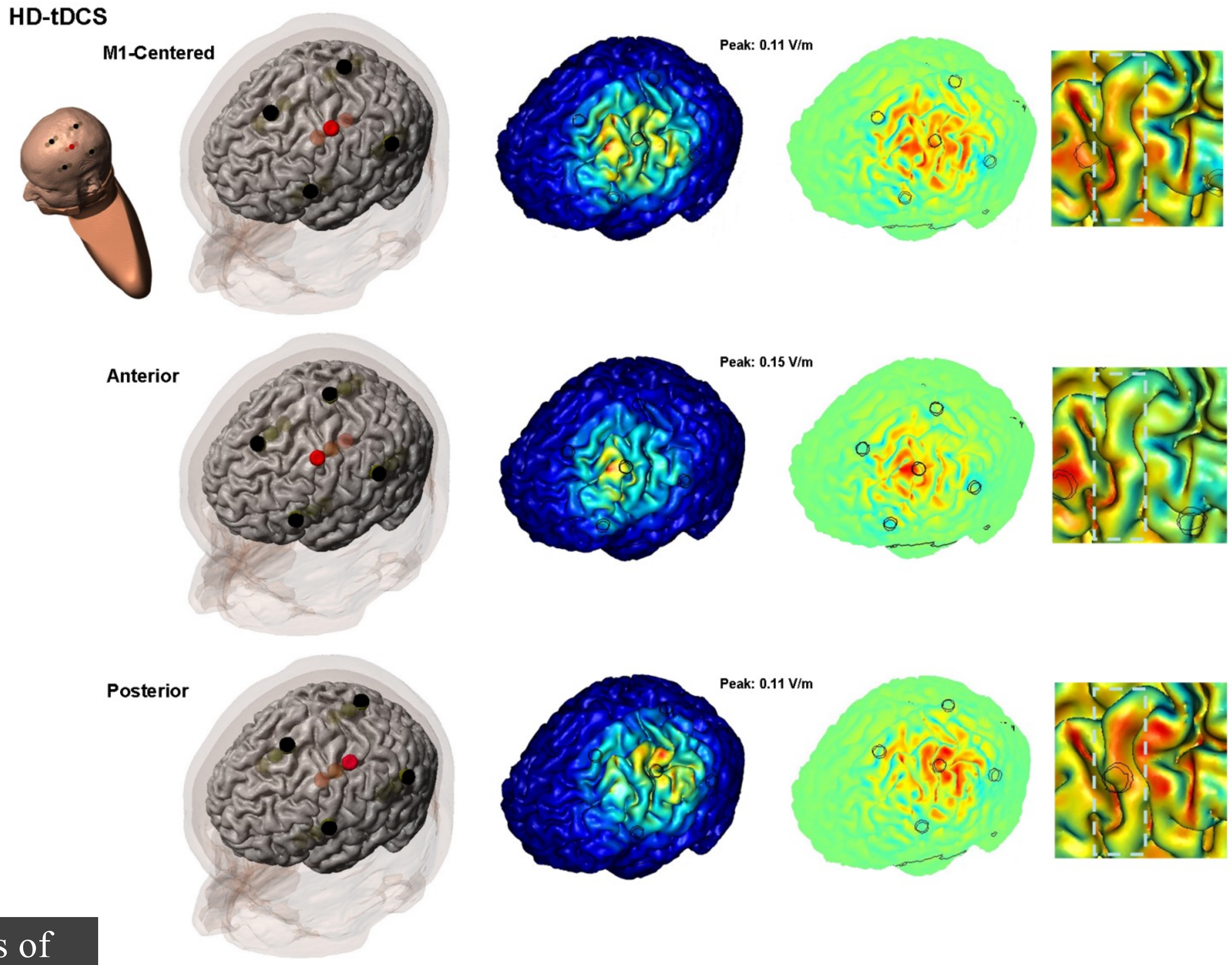

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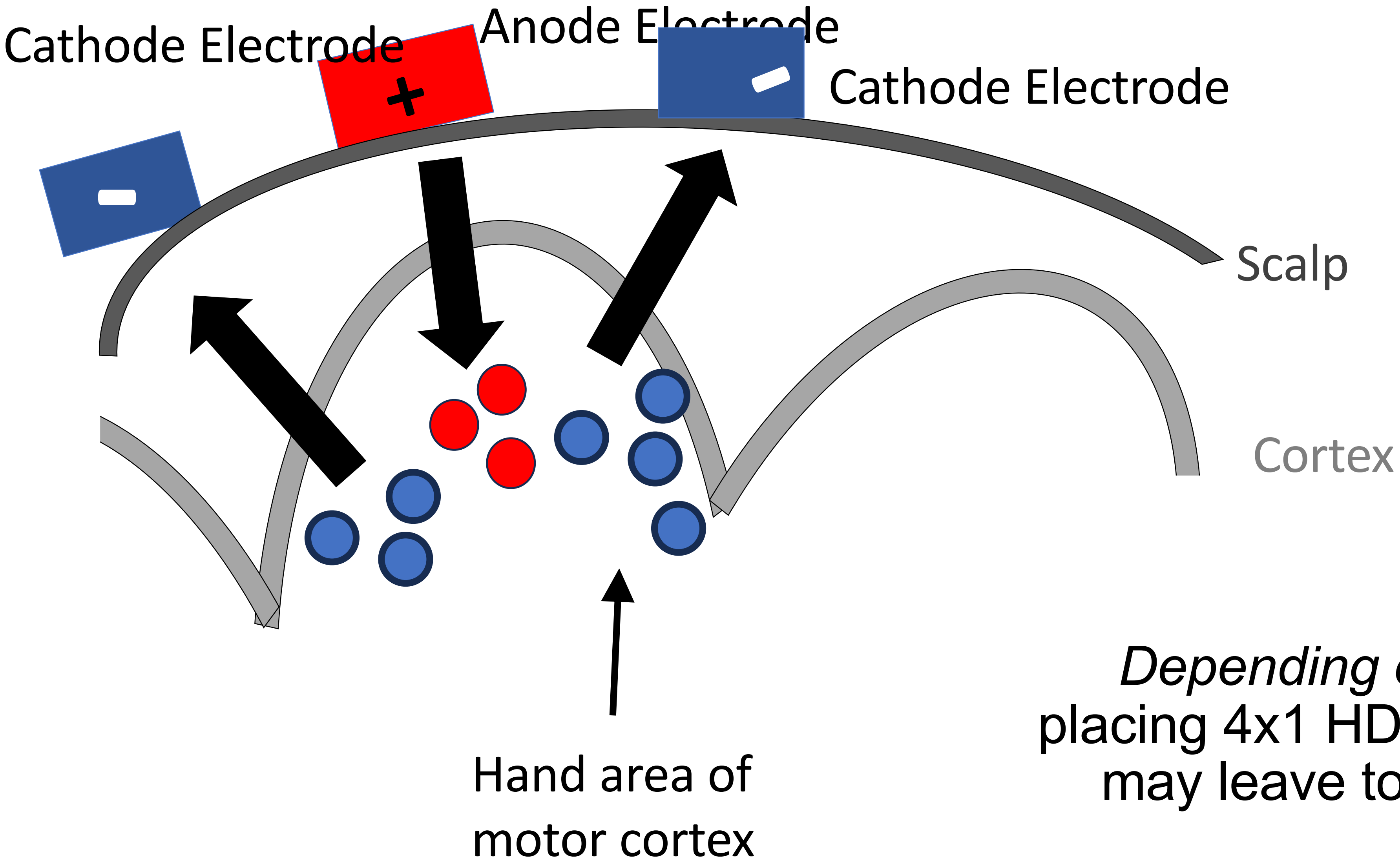
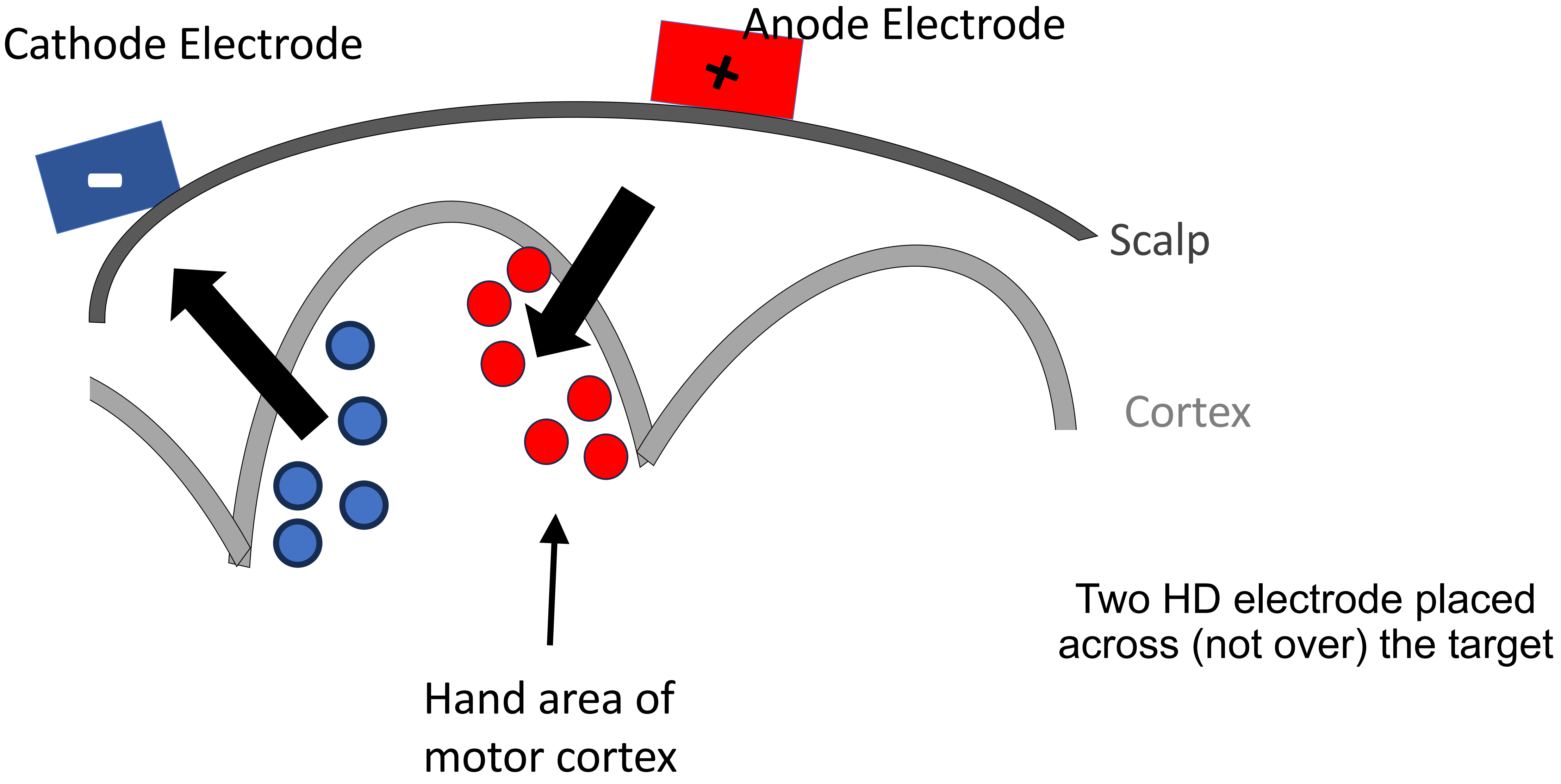
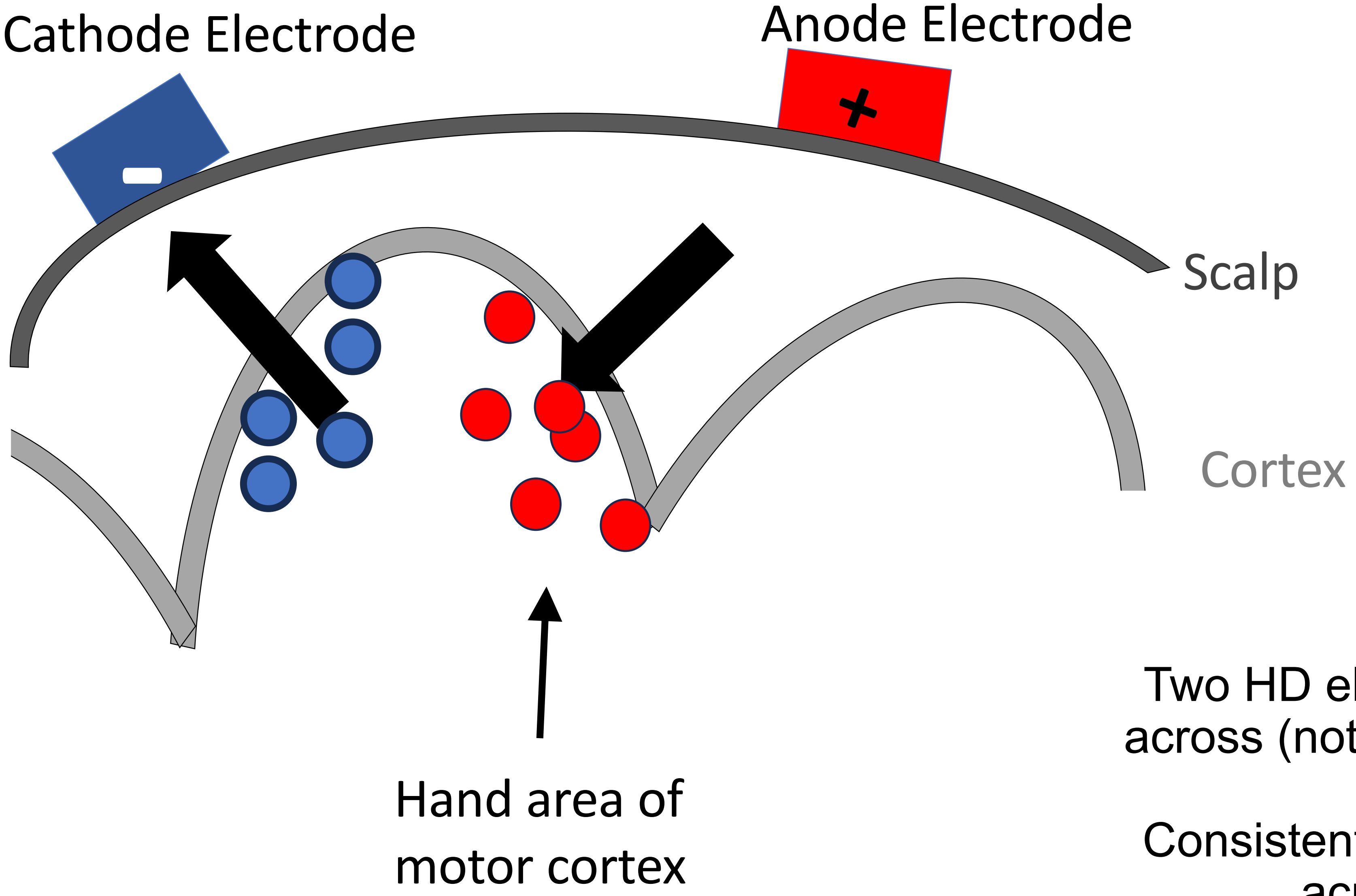


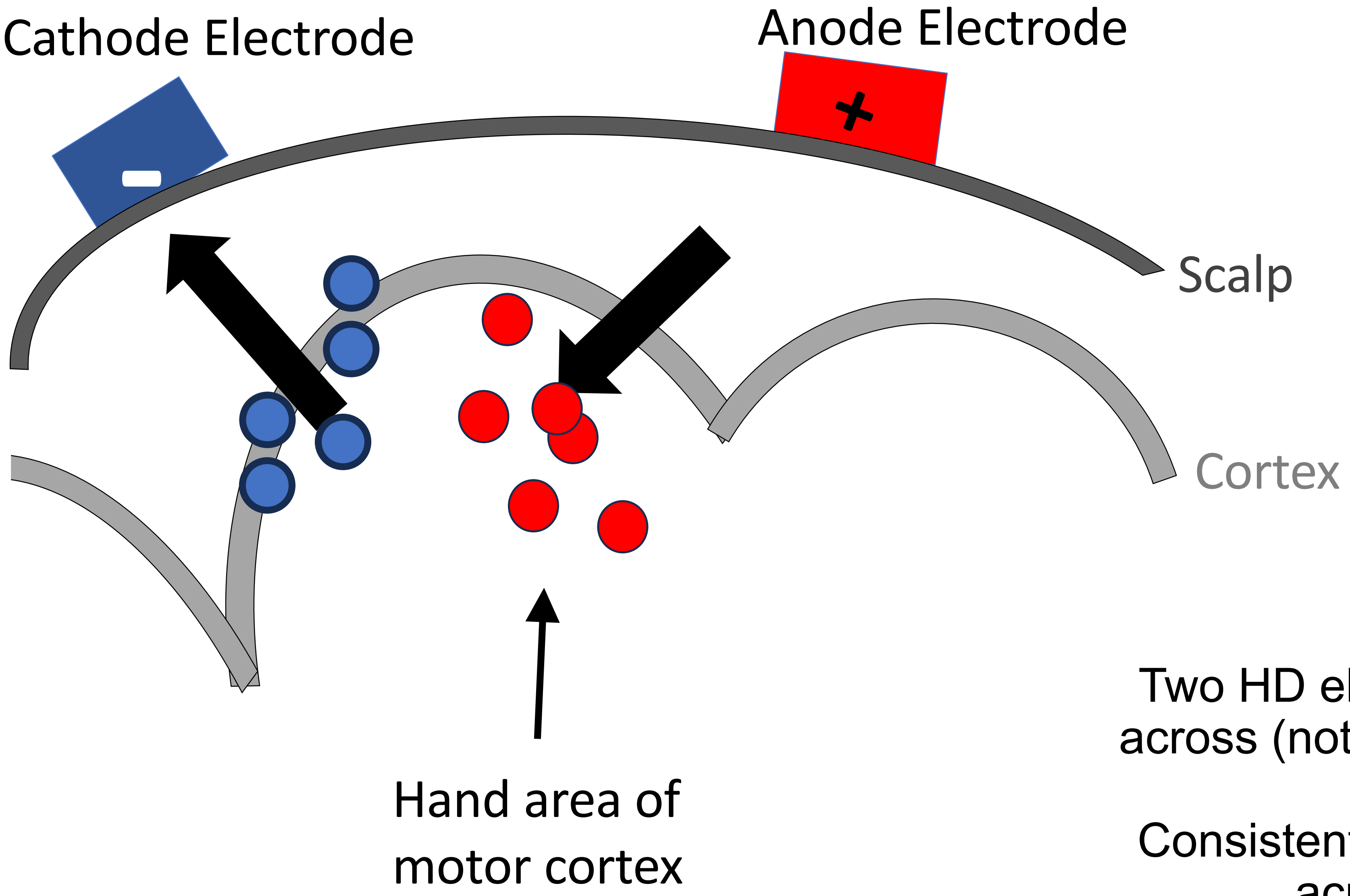
Depending on details,
placing 4x1 HD over a target
may leave to variability.


Cathode Electrode
Anode Electrode
-
+
Scalp
Cortex
Hand area of
motor cortex
Two HD electrode placed
across (not over) the target



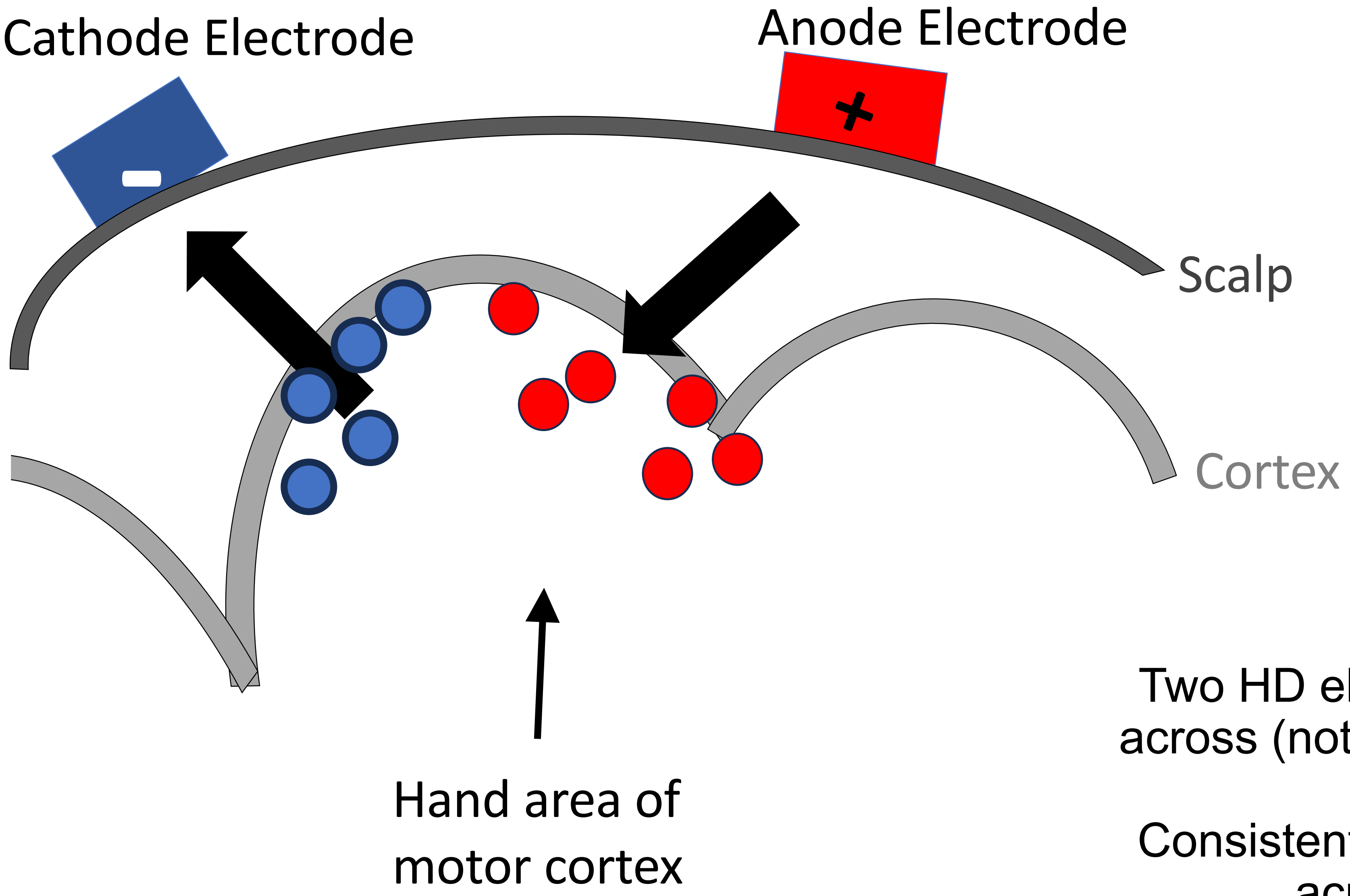
Two HD electrode placed across (not over) the target

Consistent polarity control across gyri



Two HD electrode placed
across (not over) the target

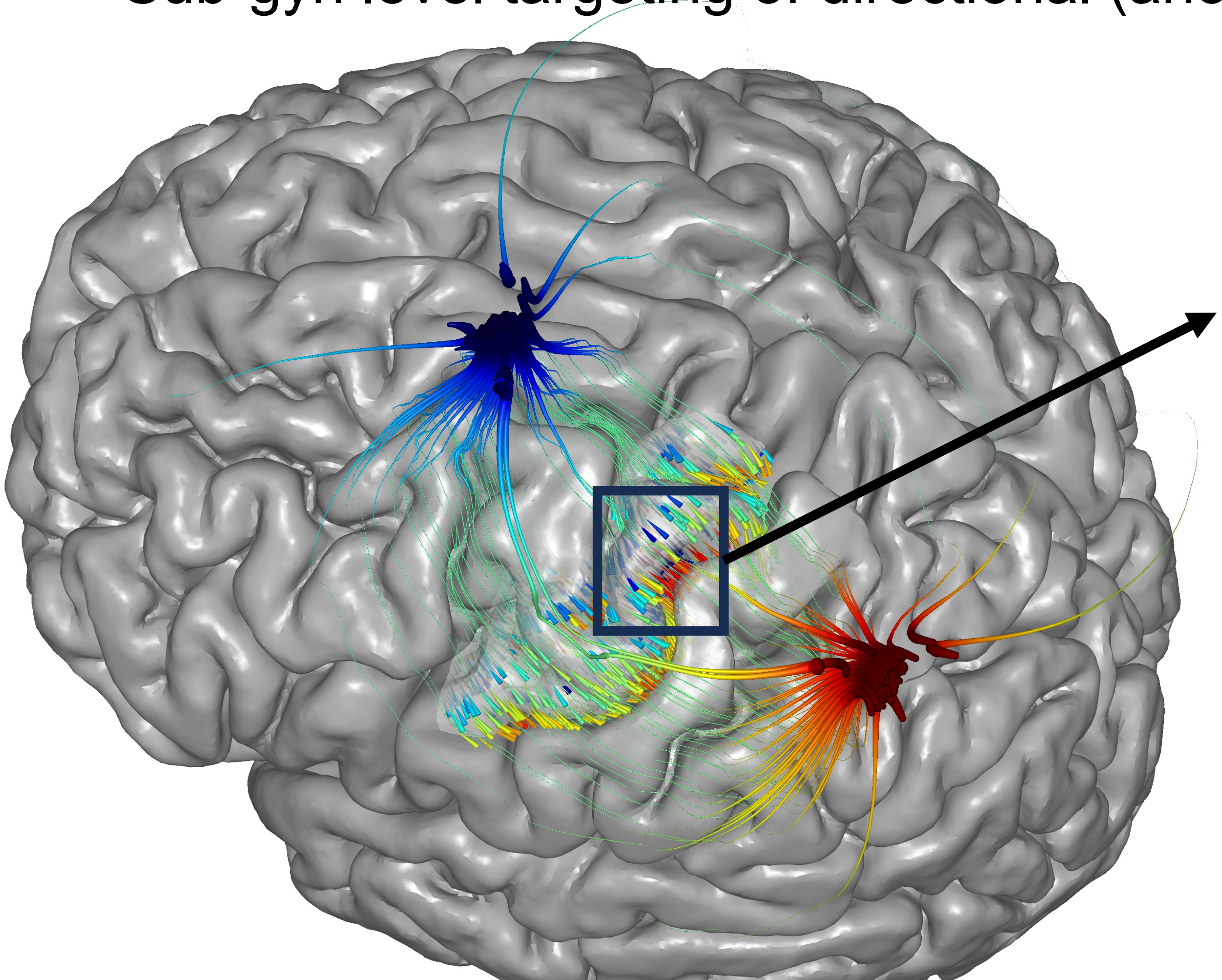
Consistent polarity control
across gyri

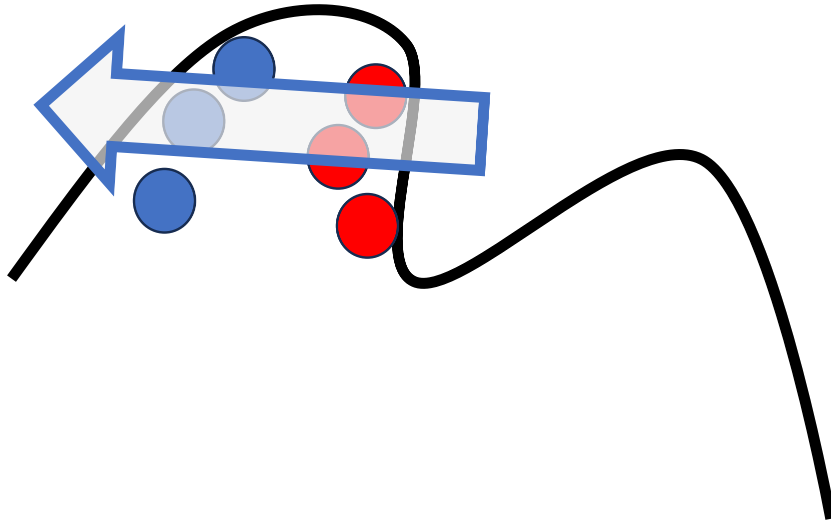


Two HD electrode placed across (not over) the target

Consistent polarity control across gyri

Sub-gyri level targeting of directional (anodal) modulation.

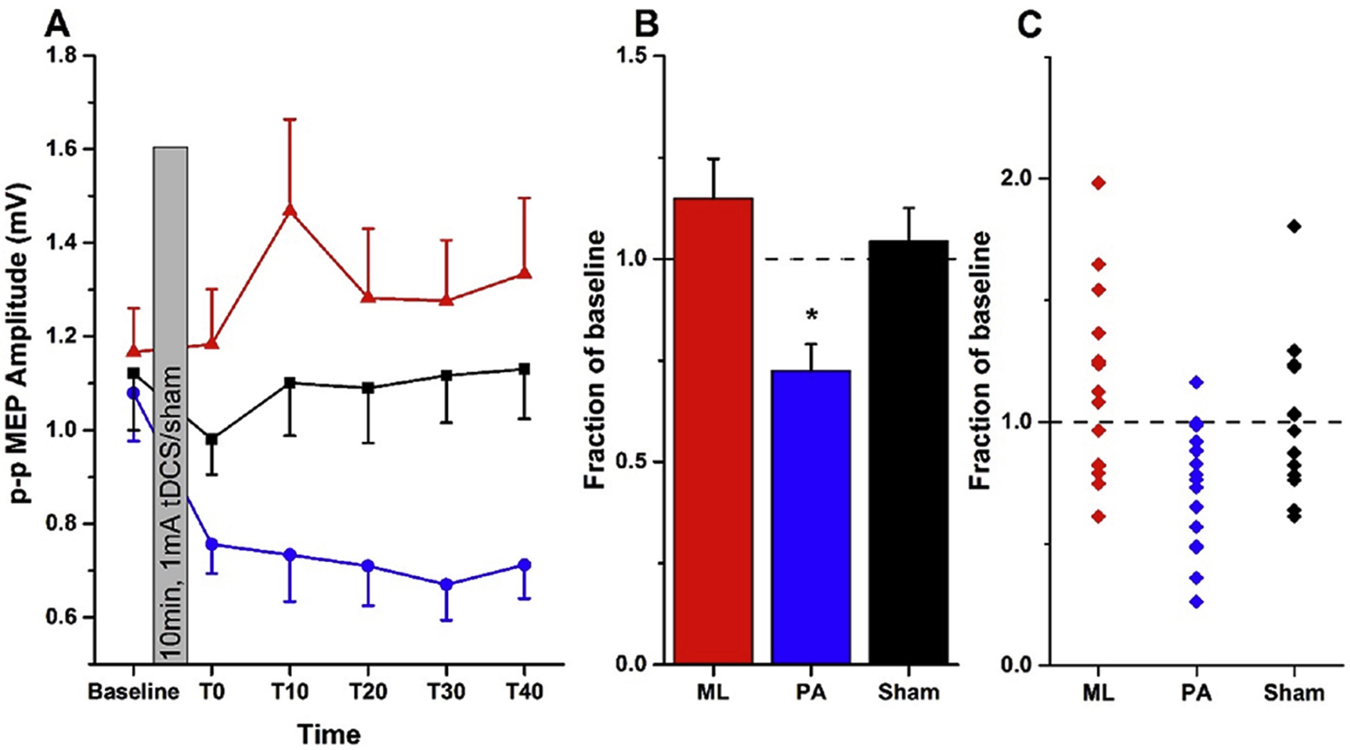


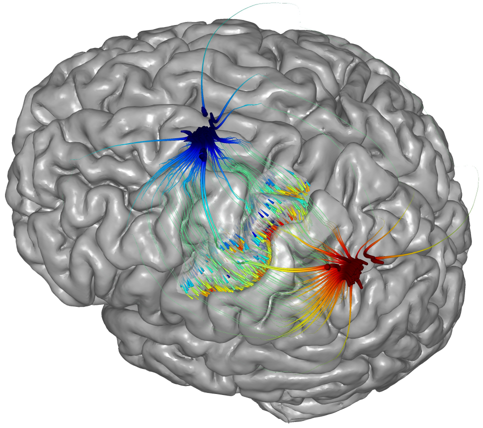


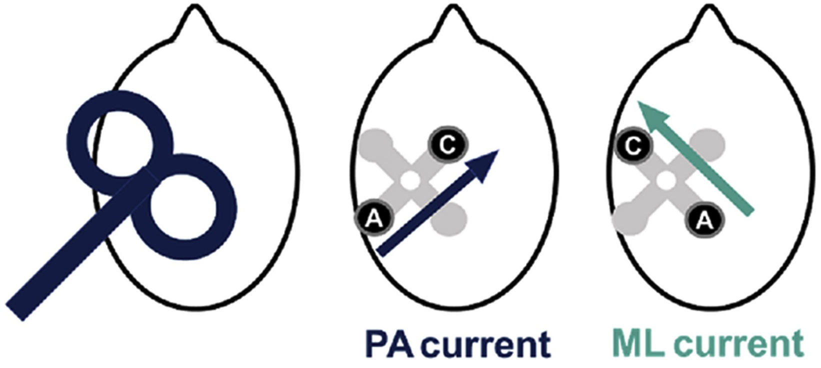
Two HD electrode placed across (not over) the target

Consistent polarity control across gyri

Rawji et al. tDCS changes in motor excitability are specific to orientation of current flow. *Brain Stimulation*. 2017







TMS is used a probe on motor excitability.

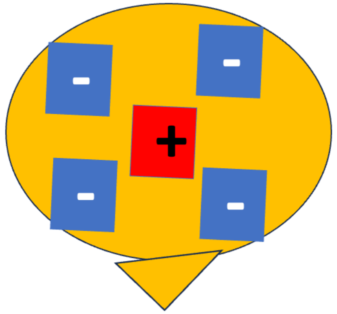
Orientation of two-electrode HD-tDCS varied.

Significant changes in cortical excitability - but highly direction specific .

Rawji et al. tDCS changes in motor excitability are specific to orientation of current flow. *Brain Stimulation*. 2017

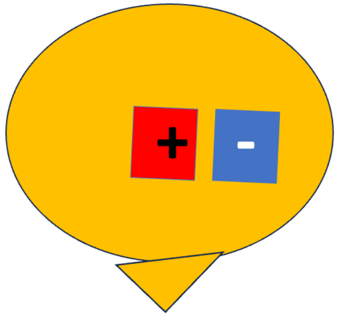
4x1 HD-tDCS is a unique tool for low-intensity non-invasive focal cortical neuromodulation.

- A deployable and tolerated as tDCS. As focal as TMS. ‘Unidirectional’ neuromodulation.
- Causal role of brain regions in cognition, Clinical trials (increased efficacy).



Two electrode (1x1) HD-tDCS, proximal placement across target, enhances directional control at gyri-walls

- High-resolution clinical neurophysiology.
- Clinical trials (increased efficacy)



DaSilva et al. The Concept, Development, and Application of a Home-Based High-Definition tDCS for Bilateral Motor Cortex Modulation in Migraine and Pain. *Frontiers in Pain Research*. 2022

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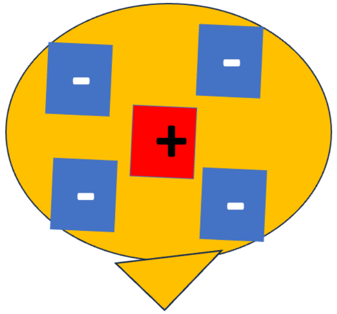

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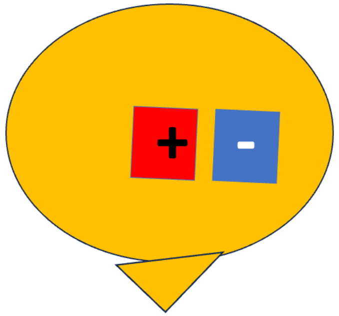
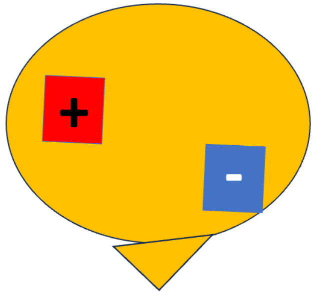
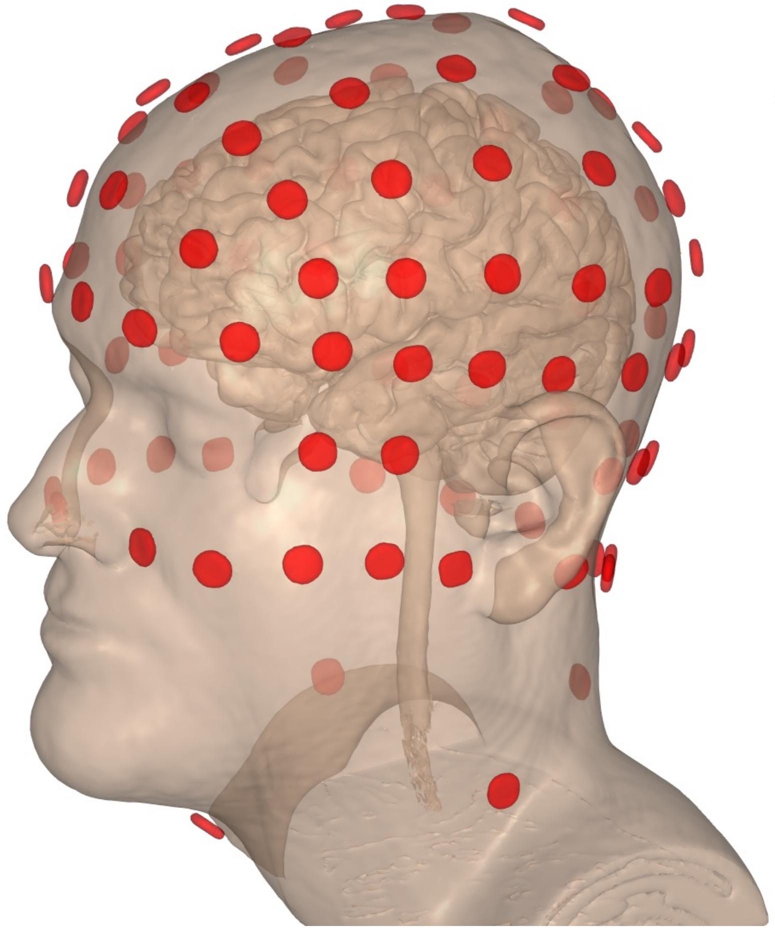


- High-resolution clinical neurophysiology.
- Clinical trials (increased efficacy)

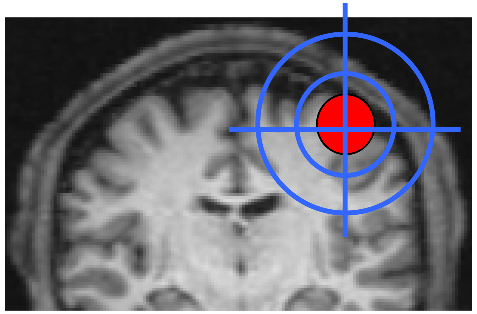
Two electrode (1x1) HD-tDCS with distant electrodes optimized direction intensity at target (at cost of reduced focality)



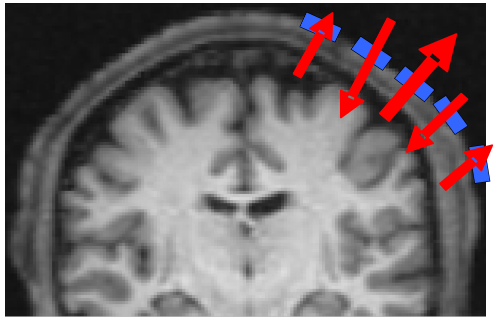
Dmochowski et al. Optimized multi-electrode stimulation increases focality and intensity at target. *Journal of Neural Engineering*. 2011



Multi-electrode (MxN) HD-tDCS



Pick target and indicate number of electrodes (2, 4, …)



Software automatically determined HD configuration

- Trade-off between maximum intensity and maximum targeting

Dmochowski et al. Optimized multi-electrode stimulation increases focality and intensity at target. *Journal of Neural Engineering*. 2011

4x1 HD-tDCS is a unique tool for low-intensity non-invasive focal cortical neuromodulation.

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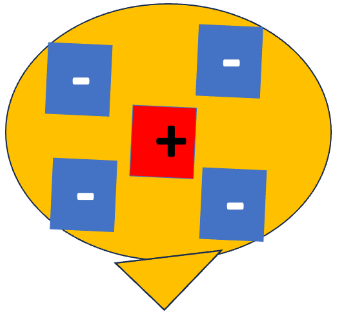

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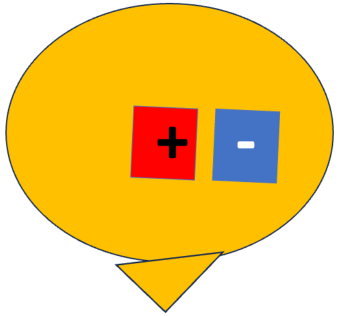
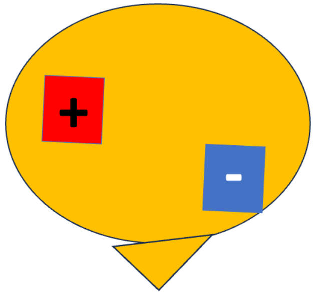
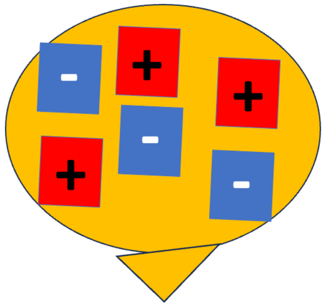


Two electrode (1x1) HD-tDCS with distant electrodes optimized (directional) intensity at target (at cost of reduced focality)



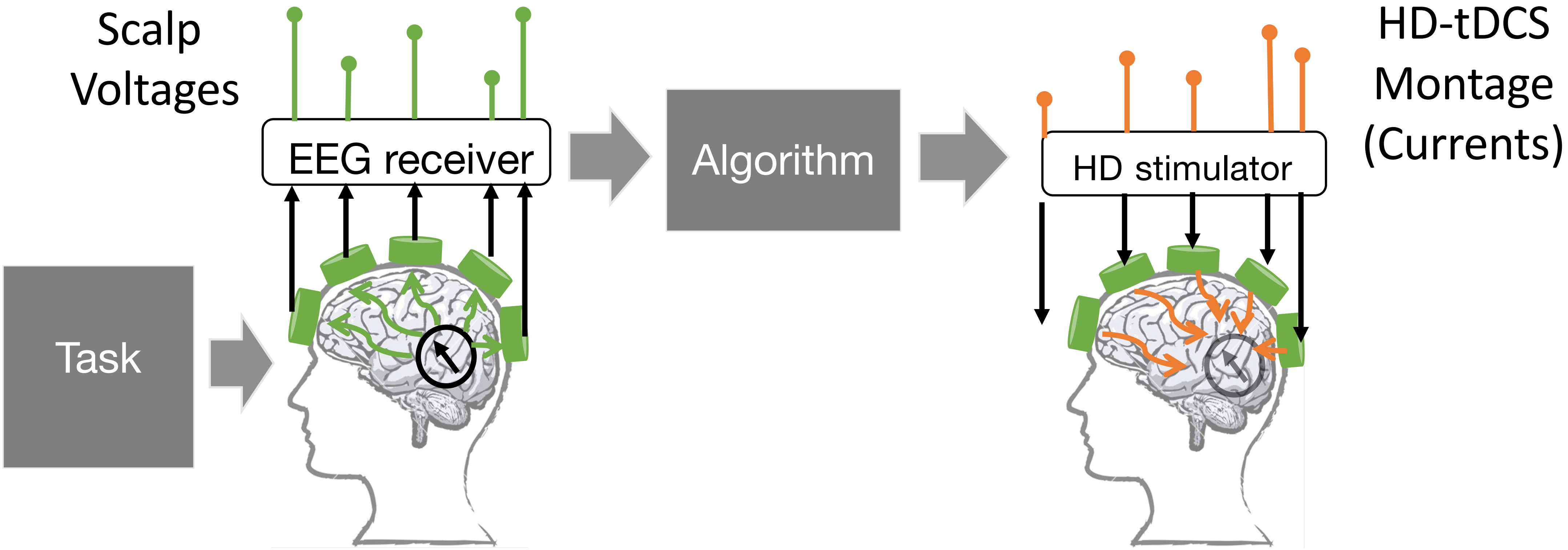
Multi-electrode (MxN) HD-tDCS algorithmically optimized to multi-target, deep target, high-intensity etc…



HD-tDCS can be combined with EEG.

Dmochowski et al. Optimal use of EEG recordings to target active brain areas with transcranial electrical stimulation. *NeuroImage*. 2017

EEG recordings can automatically guide HD-tDCS targeting.



Dmochowski et al. Optimal use of EEG recordings to target active brain areas with transcranial electrical stimulation. *NeuroImage*. 2017

- High-Definition tDCS (HD-tDCS) are different approaches that use small “High-Definition” (HD) electrodes.
- 4x1 HD-tDCS modulates any cortical region inside the ring in a “unidirectional” manner.
- A proximal (close) 1x1 HD-tDCS montage can be used for gyri-wall direction “targeting”.
- MxN montages can be optimized using software for intensity, deep stimulation, etc.

- Same montages can be used for HD-tACS : however, polarities are flipping in time.
- Conventional (pad) tDCS cannot be focal but can be application optimized, including directionality at gyri.

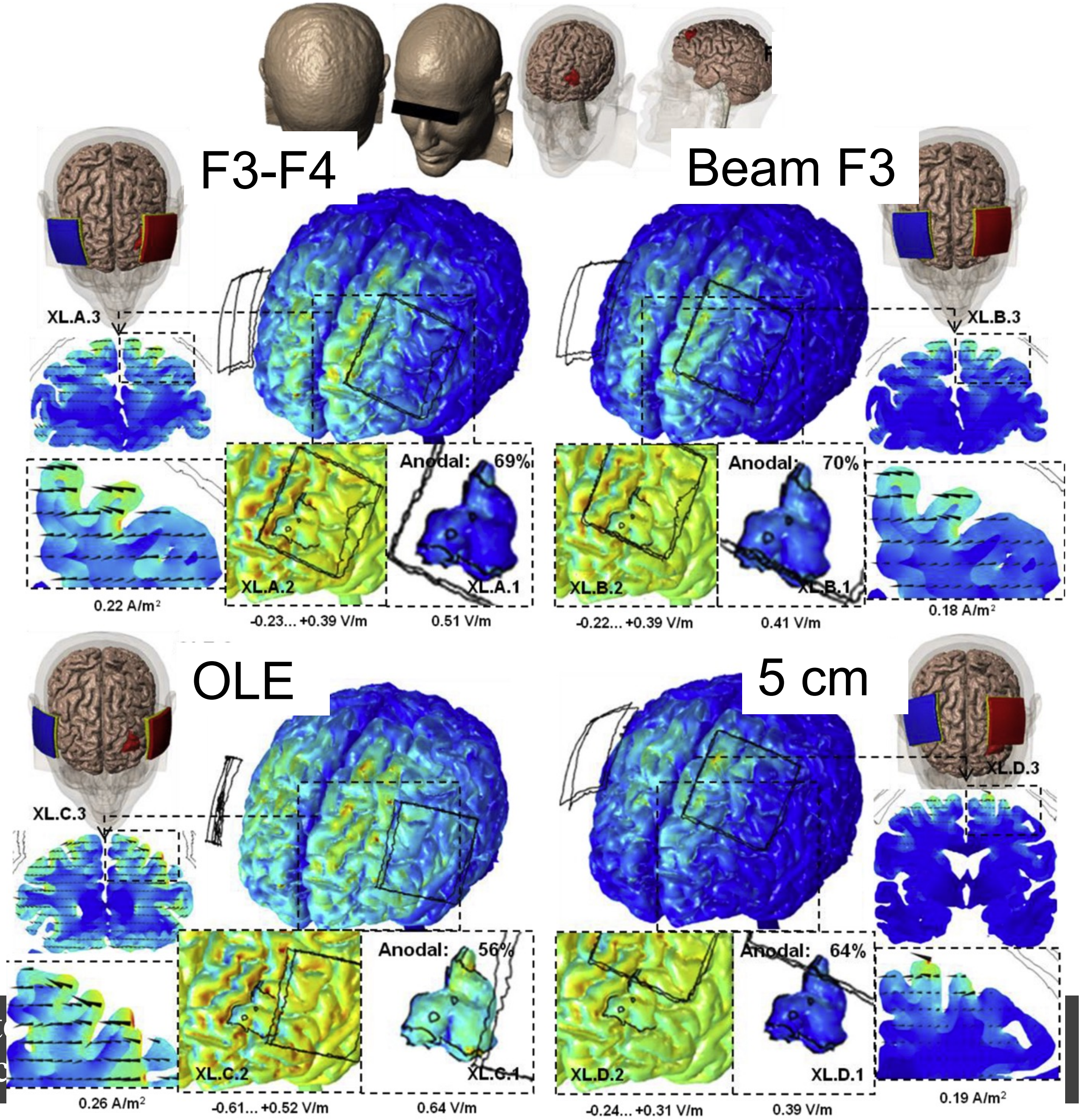
Direction Matters

Conventional (pad) tDCS optimization: Intensity and direction at ”target” gyri.

Target: Anodal left DLPFC

No MRI / No Neuronavigation

Electrodes placed automatically using fixed position head-gear



Seibt et al. The pursuit of DLPFC: Non-neuronavigat
symmetric bicephalic transcranial direct c

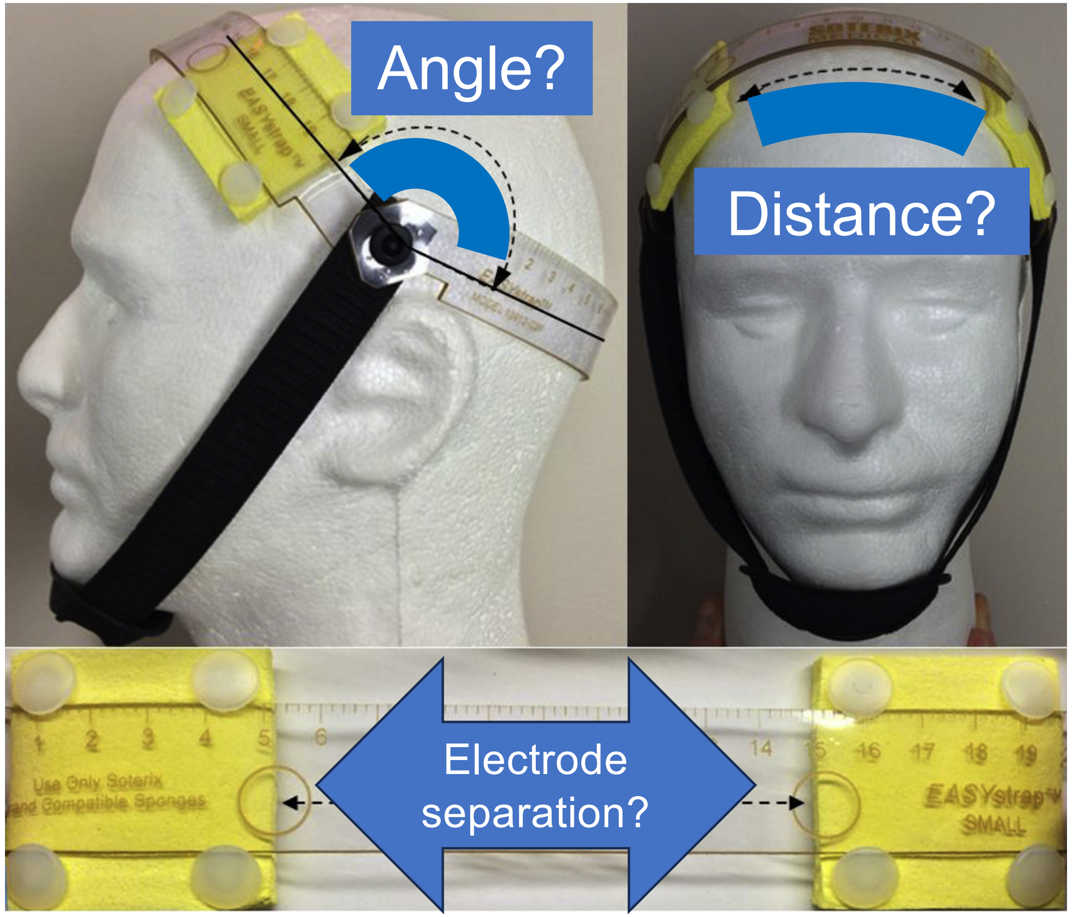
Conventional (pad) tDCS optimization: Intensity and direction at "target" gyri.

Target: Anodal left DLPFC

No MRI / No Neuronavigation

Electrodes placed automatically using fixed position head-gear

Omni-Lateral-Electrode (OLE) head-gear



Seibt et al. The pursuit of DLPFC: Non-neuronavigated methods to target the left dorsolateral pre-frontal cortex with symmetric bicephalic transcranial direct current stimulation (tDCS). *Brain Stimulation* 2015

Conventional (pad) tDCS optimization: Intensity and direction at ”target” gyri.

Target: Anodal left DLPFC

No MRI / No Neuronavigation

Electrodes placed automatically using fixed position head-gear

Omni-Lateral-Electrode (OLE) head-gear

The NEW ENGLAND JOURNAL of MEDICINE

Trial of Electrical Direct-Current Therapy versus Escitalopram for Depression

A.R. Brunoni, A.H. Moffa, B. Sampaio-Junior, L. Borrione, M.L. Moreno, R.A. Fernandes, B.P. Veronezi, B.S. Nogueira, L.V.M. Aparicio, L.B. Razza, R. Chamorro, L.C. Tort, R. Fraguas, P.A. Lotufo, W.F. Gattaz, F. Fregni, and I.M. Benseñor, for the ELECT-TDCS Investigators*

JUNE 29, 2017

of placebo minus escitalopram), so noninferiority could not be claimed. Escitalopram and tDCS were both superior to placebo (difference vs. placebo, 5.5 points [95% CI, 3.1 to 7.8; P<0.001] and 3.2 points [95% CI, 0.7 to 5.5; P=0.01], respec-

INTERVENTIONS

Anode and cathode electrodes were placed over the left and right dorsolateral prefrontal cortexes, respectively, with the use of the Omni-Lateral-Electrode system.[12] In a total of 22 sessions that

Seibt et al. The pursuit of DLPFC: Non-neuronavigated methods to target the left dorsolateral pre-frontal cortex with symmetric bicephalic transcranial direct current stimulation (tDCS). *Brain Stimulation* 2015

Optimizing brain targeting with High-Definition tDCS and conventional tDCS: Direction matters.

Marom Bikson