The targeting limits of transcranial electrical stimulation

Marom Bikson
The City College of New York

Lucas Parra, Jacek Dmochowski, Anli Liu, Greg Kronberg, Abhishek Datta, Dennis Truong, Niranjan Khadka, Dennis Truong, Louis Zannou, Zeinab Esmaeilpour, Nigel Gebodh, Belen Lafon, Gozde Unal, Mohamad Rad, Andy Huang, Asif Rahman, Mark Jackson, Devin Adair, Mahima Sharma,

UR Medicine, Del Monte Institute for Neuroscience. Oct 25, 2019

Disclosure

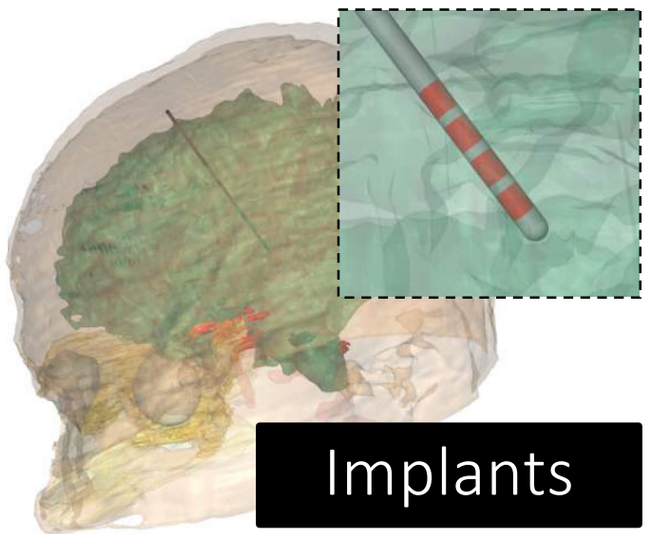
The City University of New York: Patents on brain stimulation.
Soterix Medical: Produces tDCS and High-Definition tDCS.
Boston Scientific: Neuromodulation Scientific Advisory Board
GlaxoSmithKline (GSK): Life Science Scientific Advisory Board
Mecta
Halo Neuroscience: Scientific Advisory Board

Support

NIH (NIMH, NINDS, NCI, NIBIB) – *BRAIN Initiative*, NSF, Grove Foundation, Harold Shames, CCNY Fund, 21st Century Fund, "X"

Slides and References @MaromBikson

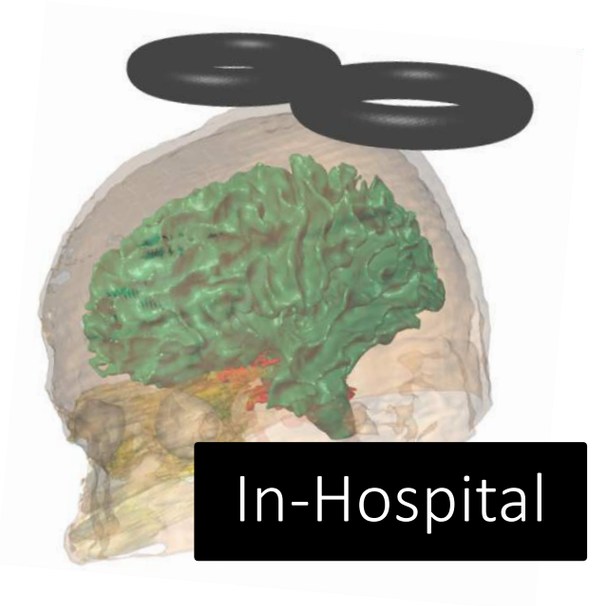
What defines neuromodulation technologies is how energy is delivered to what target



Implants

Deep Brain Stimulation (DBS)

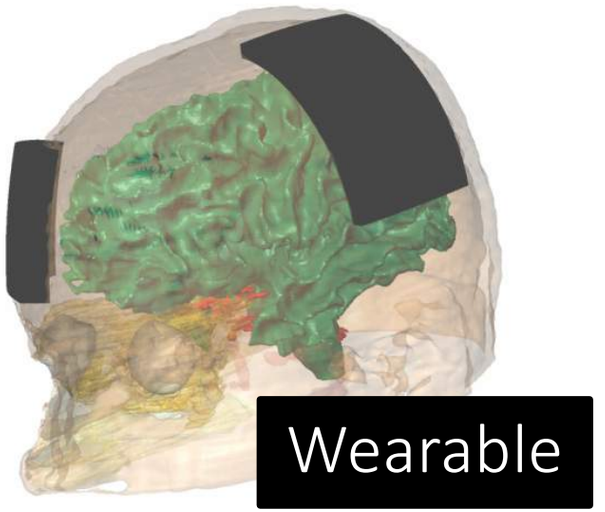
Spinal Cord Stimulation (SCS)



In-Hospital

Transcranial Magnetic Stimulation (TMS)

Electroconvulsive Therapy

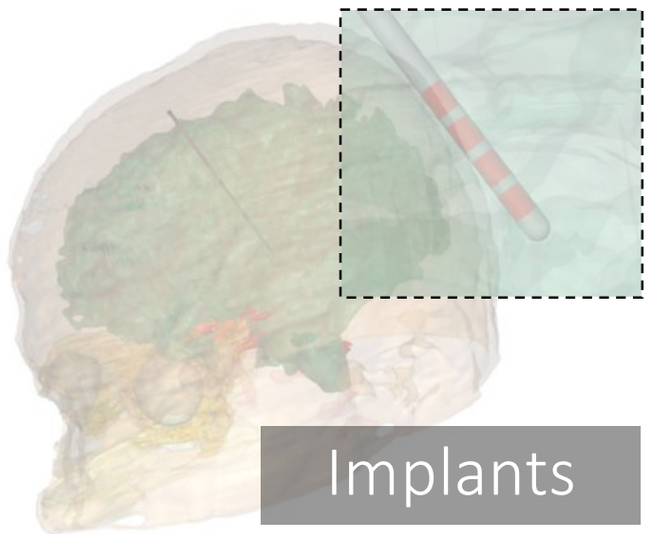


Wearable

Transcranial Electrical Stimulation (tES)

Transcranial Direct Current Stimulation (tDCS)

What defines neuromodulation technologies is how energy is delivered to what target



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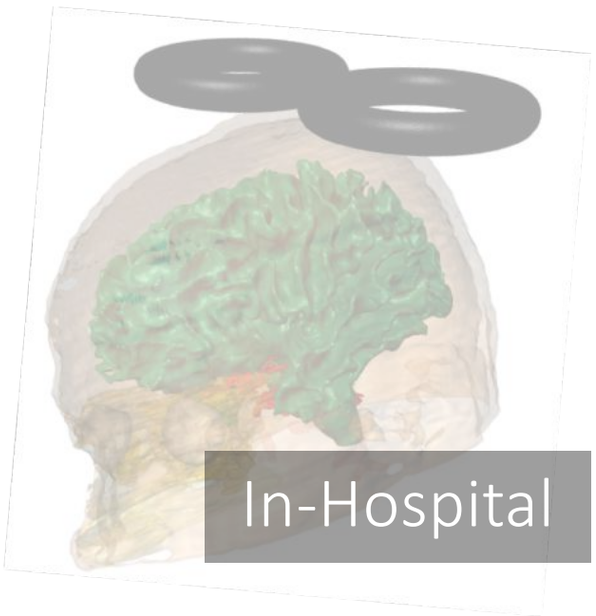

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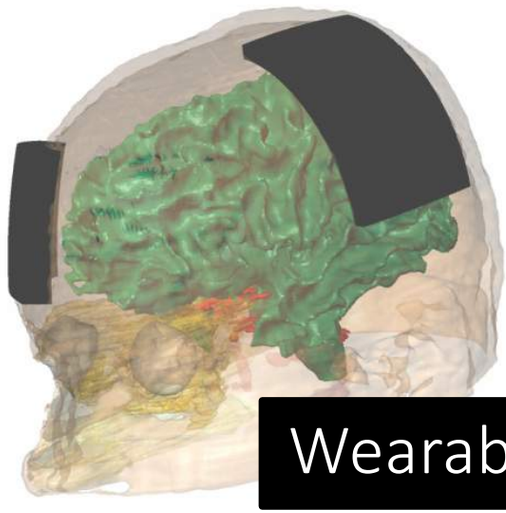
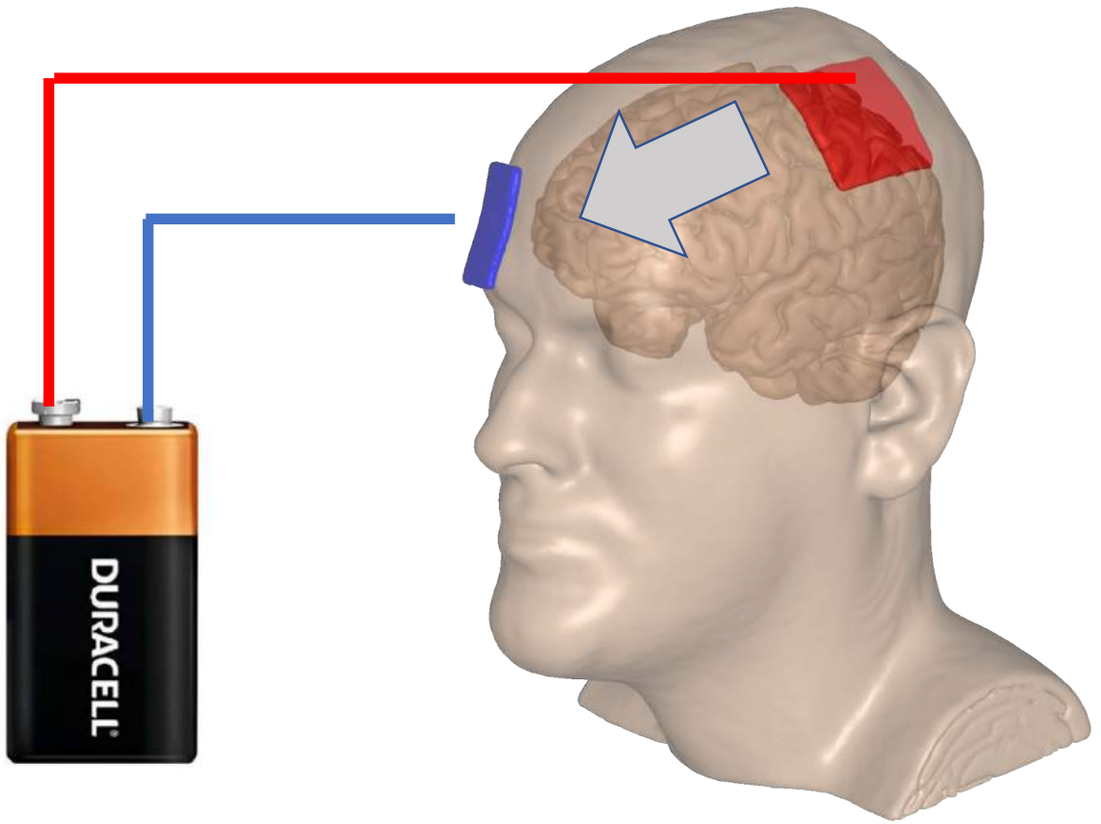


Wearable

Transcranial Electrical Stimulation (tES)

Transcranial Direct Current Stimulation (tDCS)

Transcranial Direct Current Stimulation is a wearable brain stimulator that applied Direct Current (no pulses)



tDCS: transcranial Direct Current Stimulation

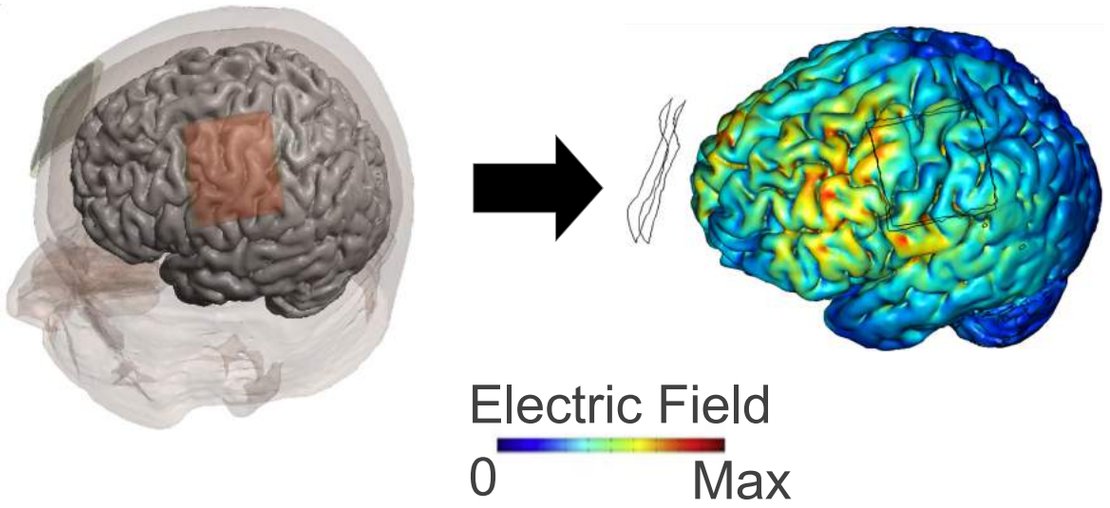
Cathode (-)
Electrode

Anode (+)
Electrode

2 mA
20 minute session

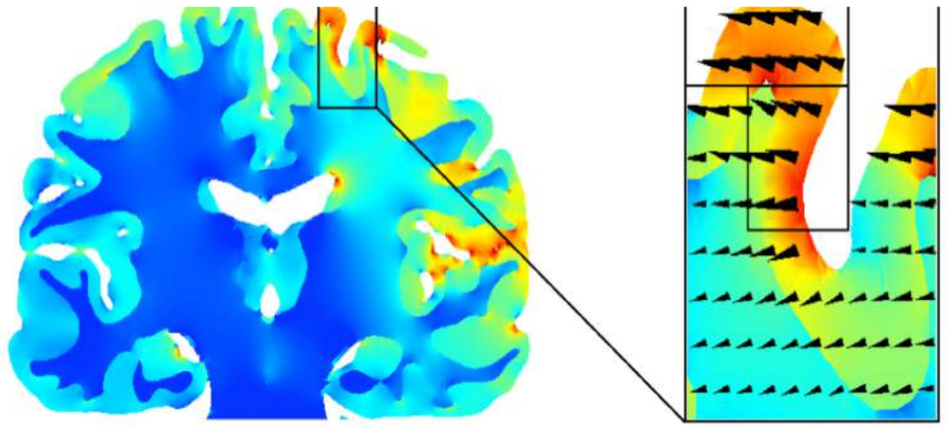
“Anodal” / “Cathodal”
refer to proximity of target

Computational models predict brain current flow (inside) during transcranial electrical stimulation (outside)



MRI-derived models with gyri-level precision.

Datta et al. Gyri-precise model of tDCS: Improved spatial focality *Brain Stim* 2009



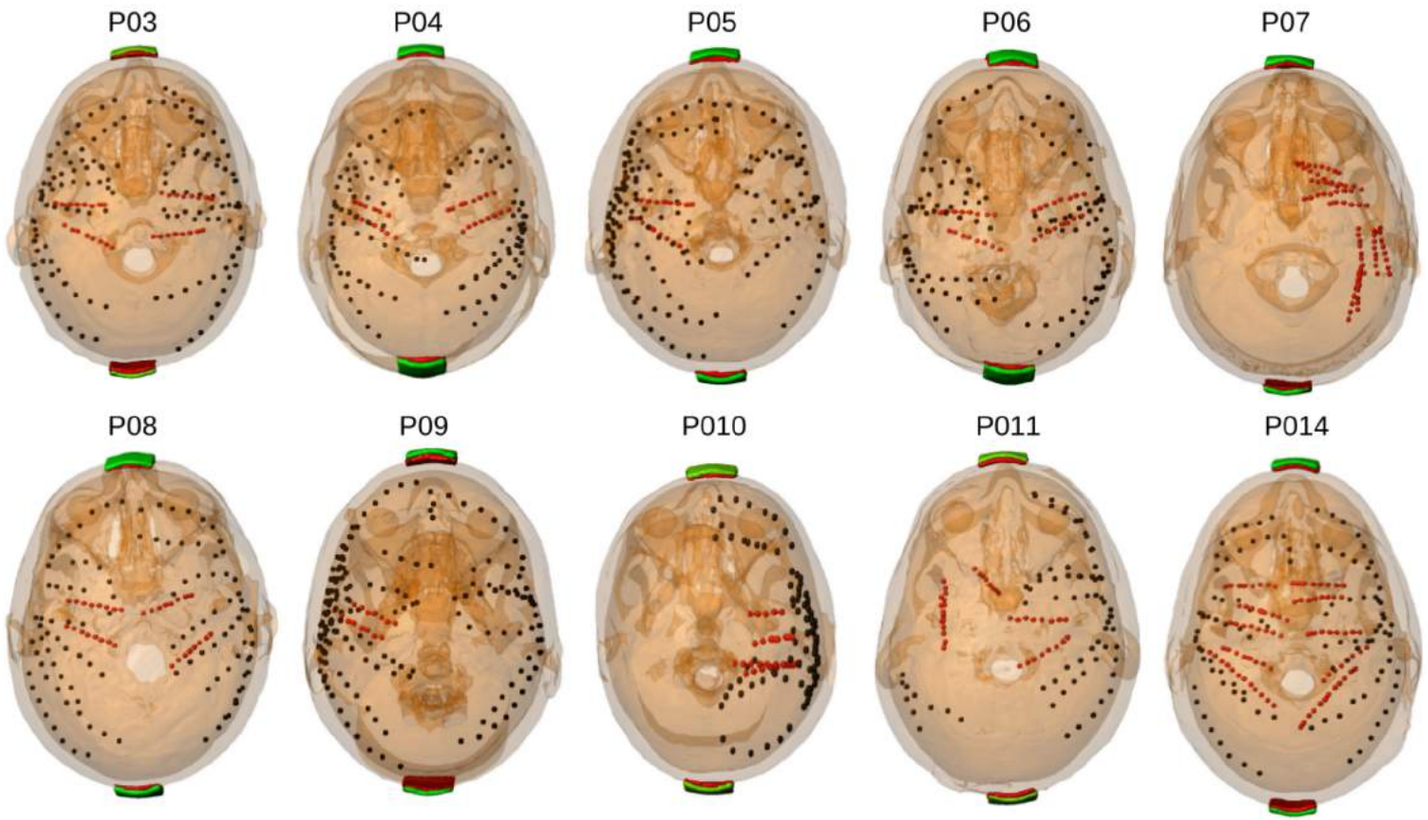
Sub-gyri level nuance in outcomes.

Rahman et al. Cellular Effects of Acute Direct Current Stimulation: Somatic and Synaptic Terminal Effects *J Physiol* 2014

Models of brain current flow have been validated (again and again)

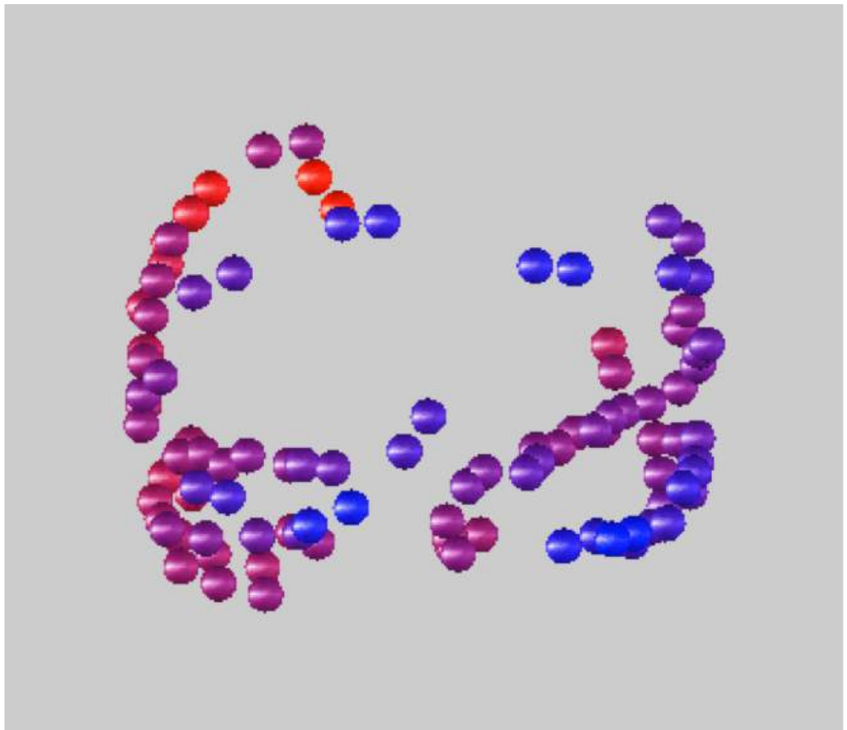
Intra-cranial voltages during transcranial electrical stimulation:

Experimental recordings with subject specific MRI-derived models.

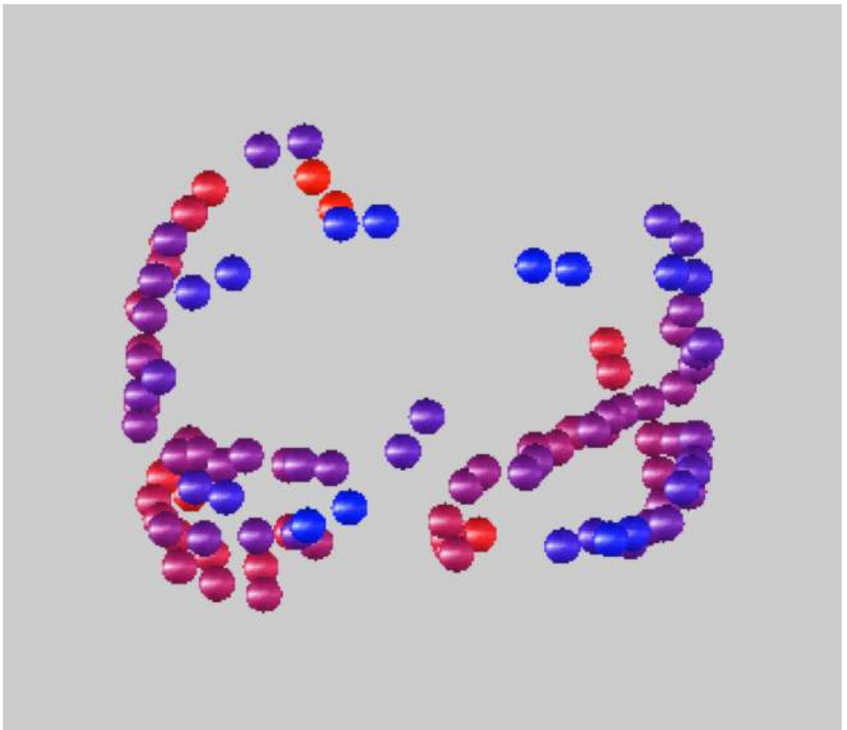


Huang et al. Measurements and models of electric fields in the human brain during tES. *Elife* 2017

Models of brain current flow have been validated (again and again)



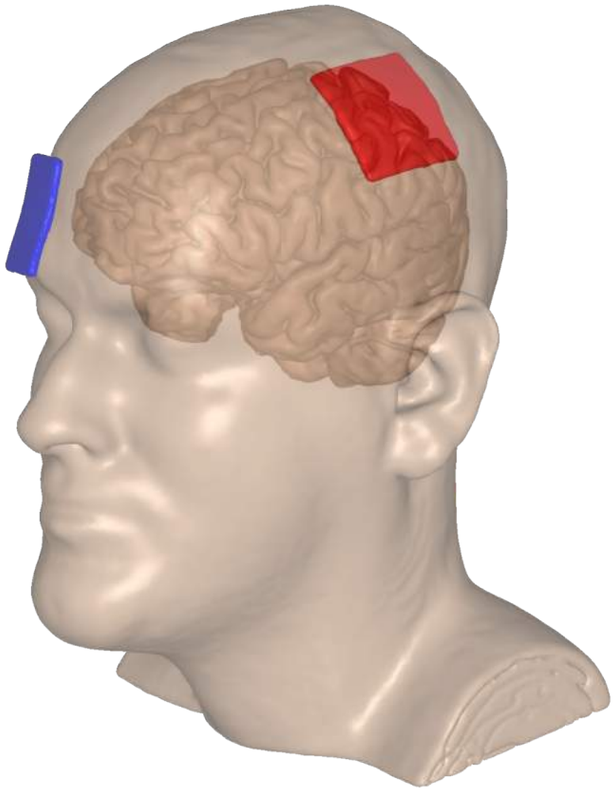
Recording (Volts)



Model (Volts)

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

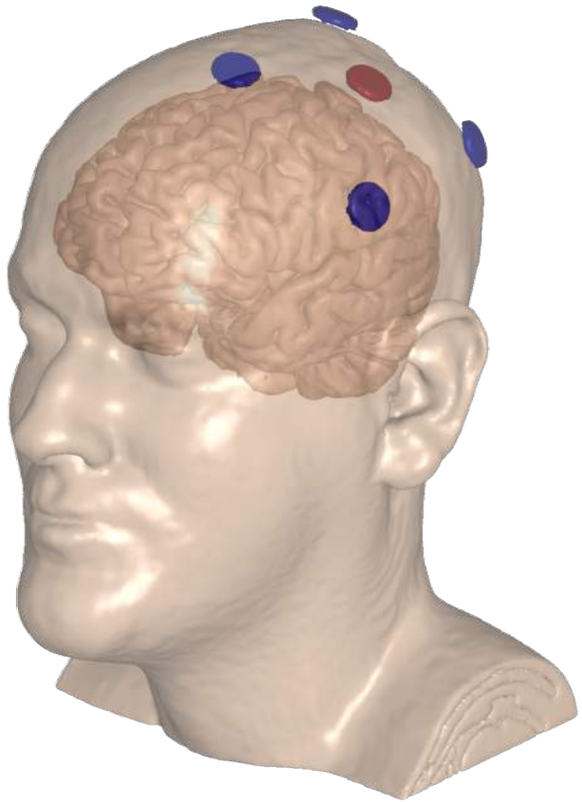
tDCS / tACS (pad electrode)



M1-SO tDCS montage

Anatomical MRI derived models of current flow

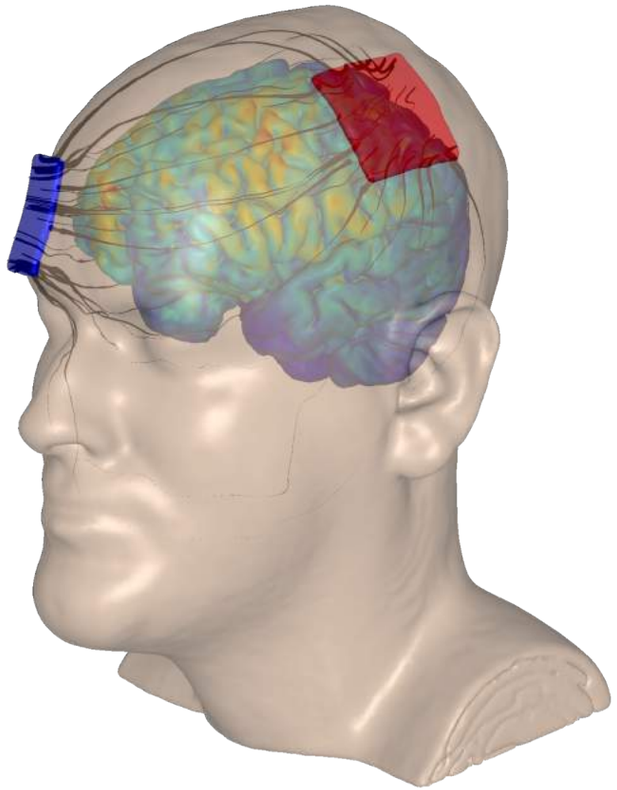
High Definition tDCS / tACS



4x1 HD-tDCS montage

Datta et al. Gyri-precise model of tDCS: Improved spatial focality *Brain Stim* 2009

tDCS / tACS (pad electrode)



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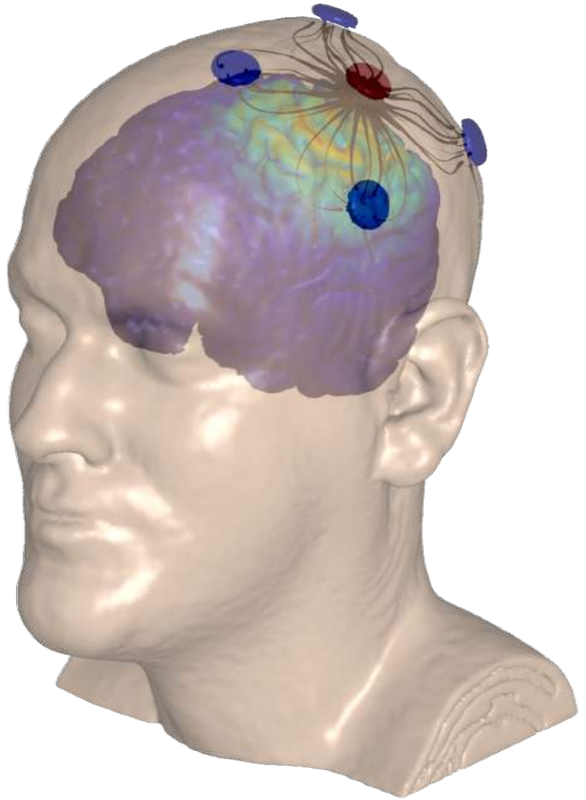

4x1 HD-tDCS montage

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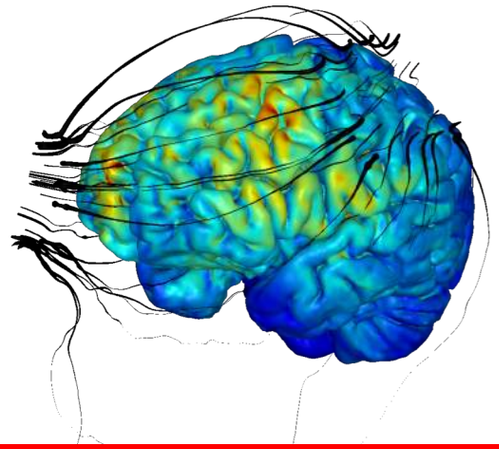
tDCS / tACS (pad electrode)

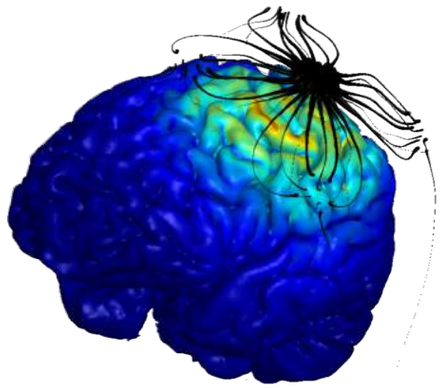


"Circuit Therapeutics" modulate multiple brain-node involved in disorder

M1-SO tDCS montage

Anatomical MRI derived models of current flow

High Definition tDCS / tACS

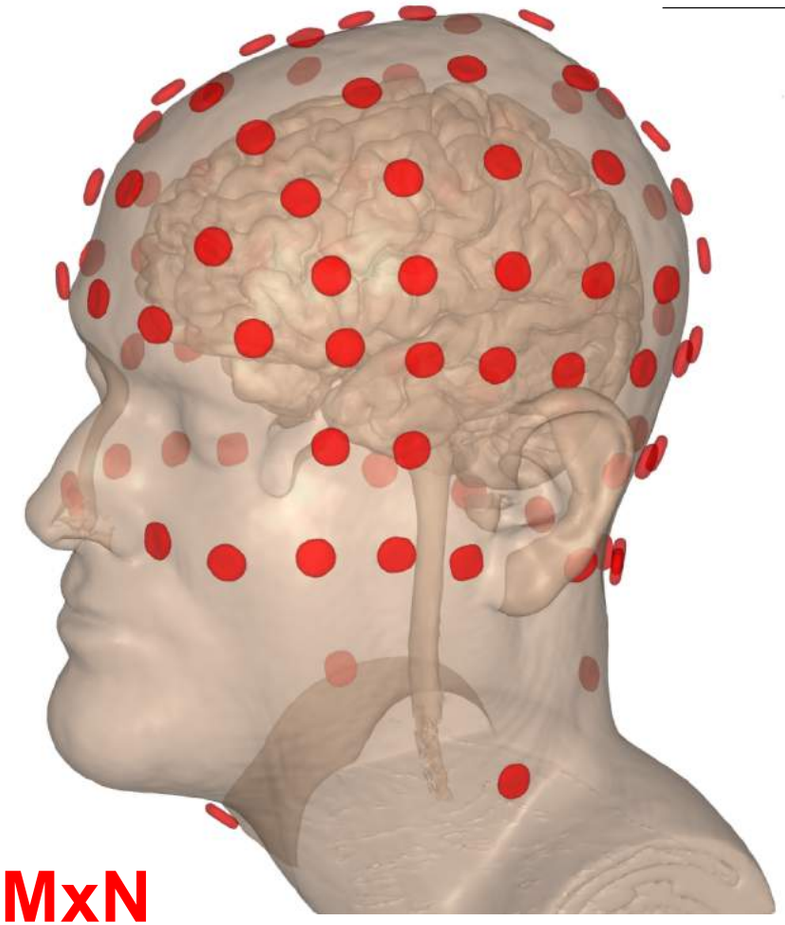


Non-invasive targeted arbitrary-waveform neuromodulation

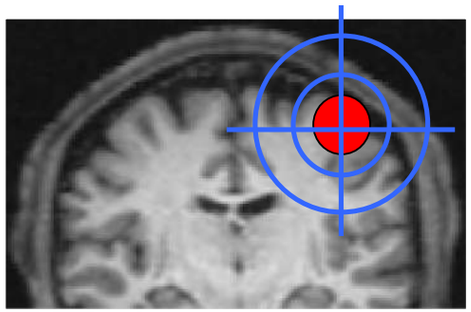
4x1 HD-tDCS montage

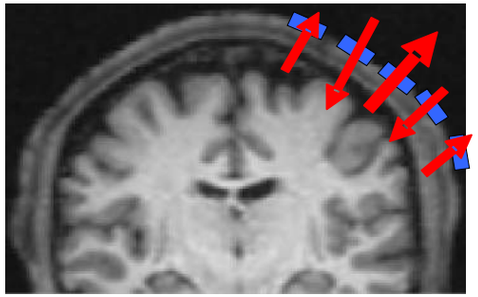
Datta et al. Gyri-precise model of tDCS: Improved spatial focality *Brain Stim* 2009

Pick a brain target: software provides optimized dose



MxN





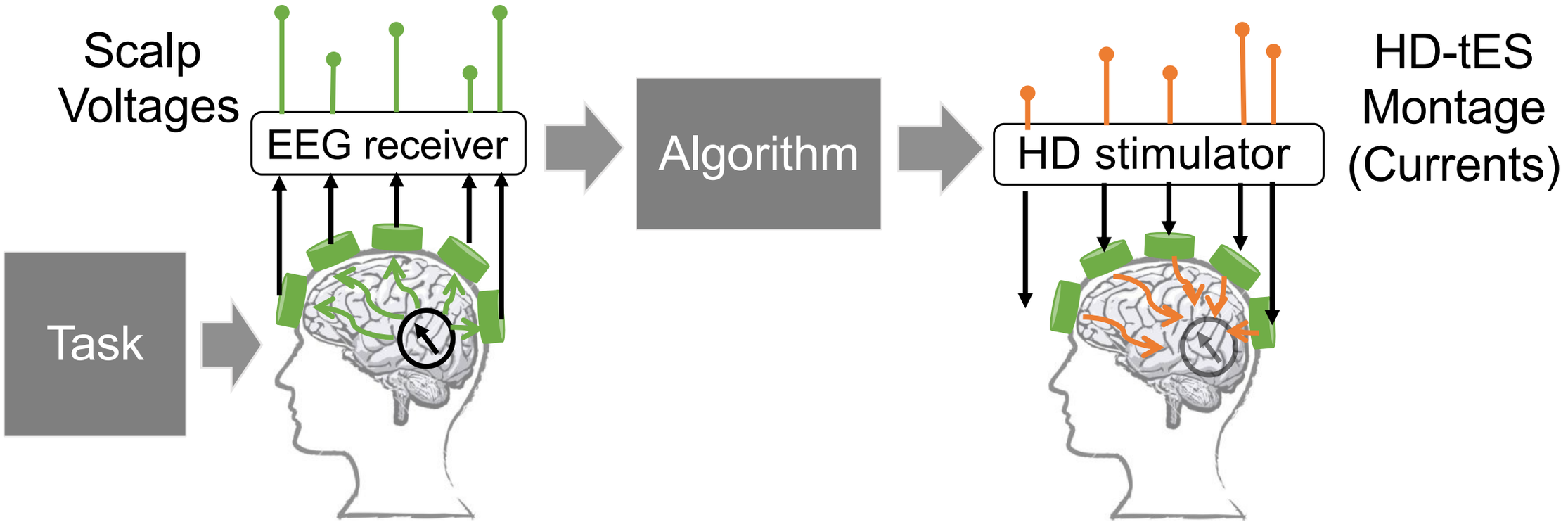
- ✓ Software allows target selected (HD) tES optimization
- ✓ Subject (MRI) specific (skull defect, brain injury, extremes of age, Zika..)
- ✓ Any waveform (DC, AC, pulsed, Interferential, ECT…)
- ✓ Multi-target, deep…

Dmochowksi et al. Optimized multi-electrodes stimulation. *J Neural Engr* 2011

EEG automatically and instantly “inverted” to optimal HD-tES

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

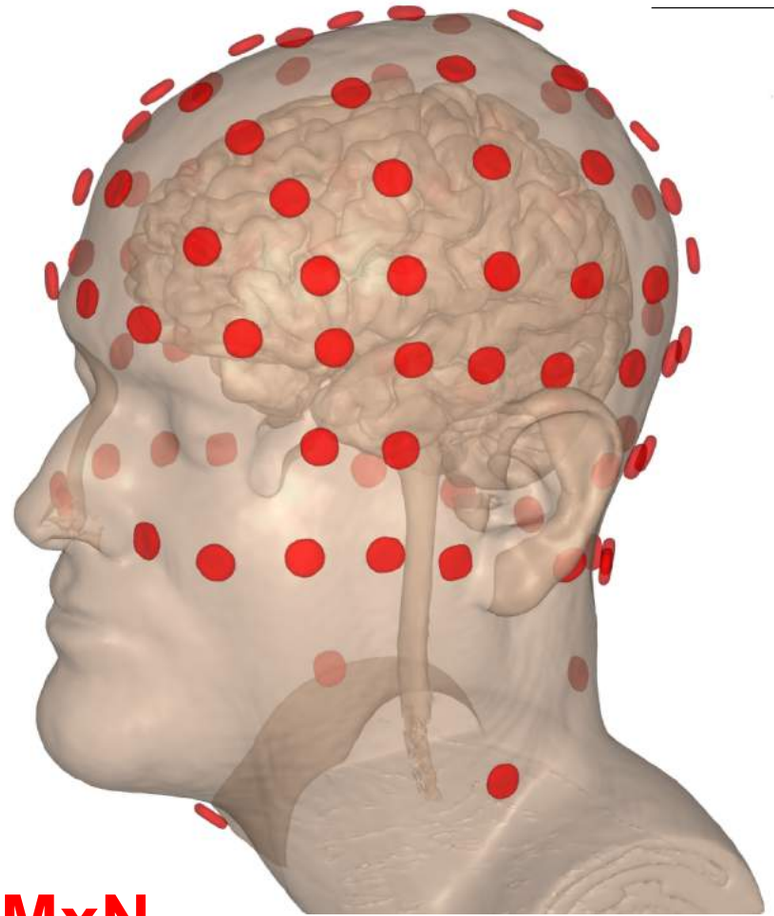
EEG automatically and instantly “inverted” to optimal HD-tES



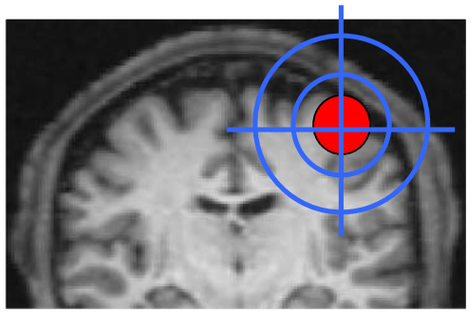
- Decades old “reciprocity” hypothesis, but with closed head model
- Activity guided targeting, does not require source localization

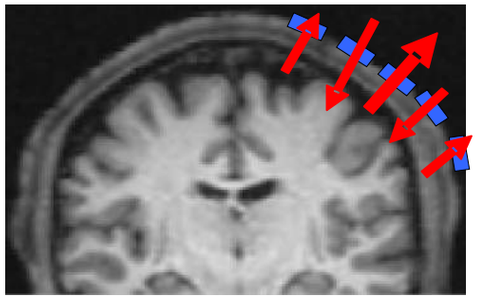
Dmochowksi et al. Optimal use of EEG recordings to target active brain areas with transcranial electrical stimulation. *Neuroimage* 2017

Pick a brain target (or don't): software provides optimized dose



MxN





a) Software allows subject and target specific (HD) tDCS optimization

b) Software allows for closed-loop stimulation based on EEG

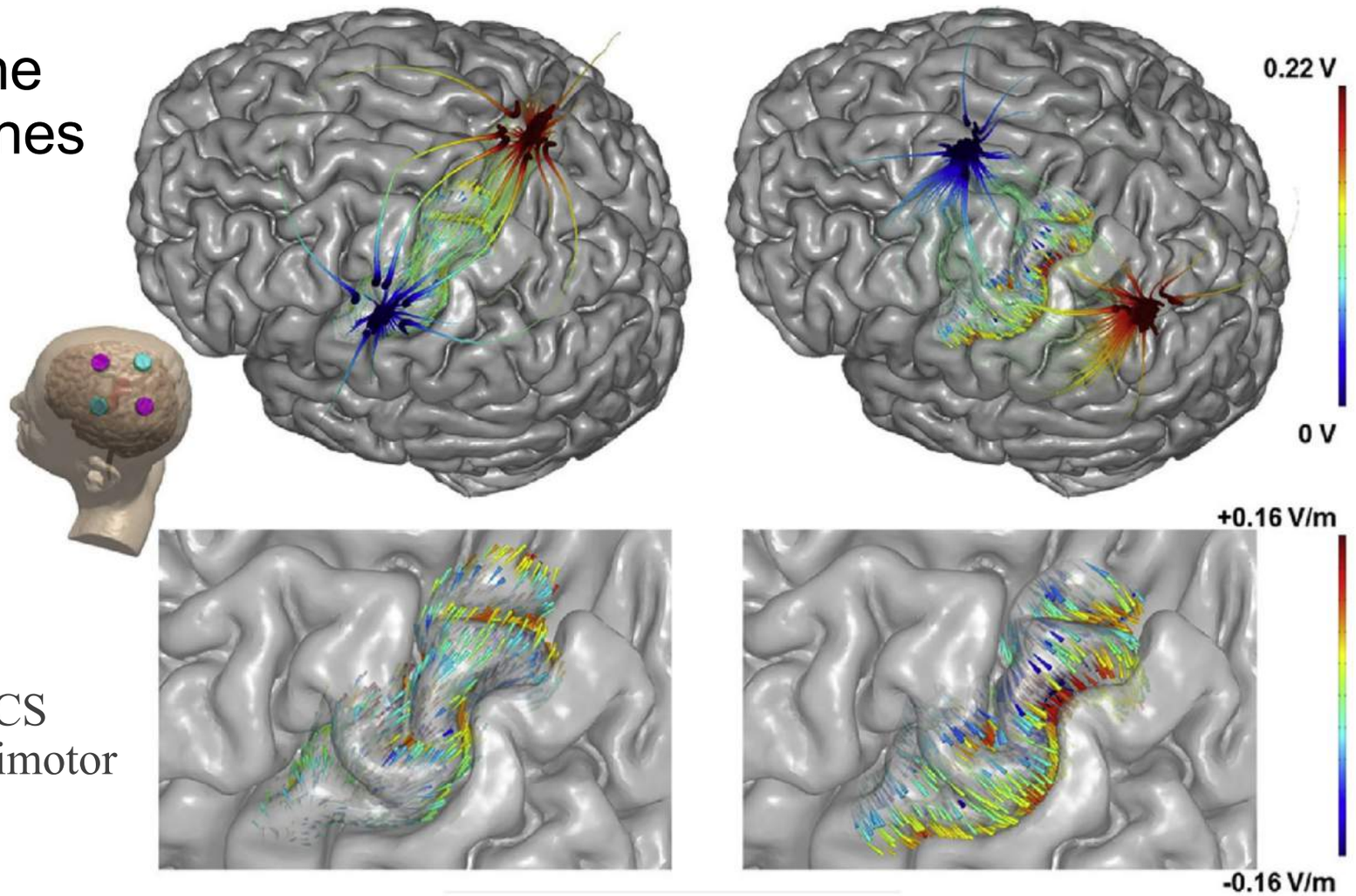
Dmochowksi et al. Optimized multi-electrodes stimulation. *J Neural Engr* 2011

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

Sub-gyri (pathway) level precision with bipolar HD-tDCS

Sub-gyri (pathway) level precision with bipolar HD-tDCS

Orientation of tDCS current flow across the motor cortex determines excitability changes measured by TMS, and behavior.



Rawji et al. tDCS changes motor excitability specific to orientation of current flow. *Brain Stim* 2018

Hannah et al. Direction of tDCS current flow in human sensorimotor cortex influences behavioural learning. *Brain Stim* 2019

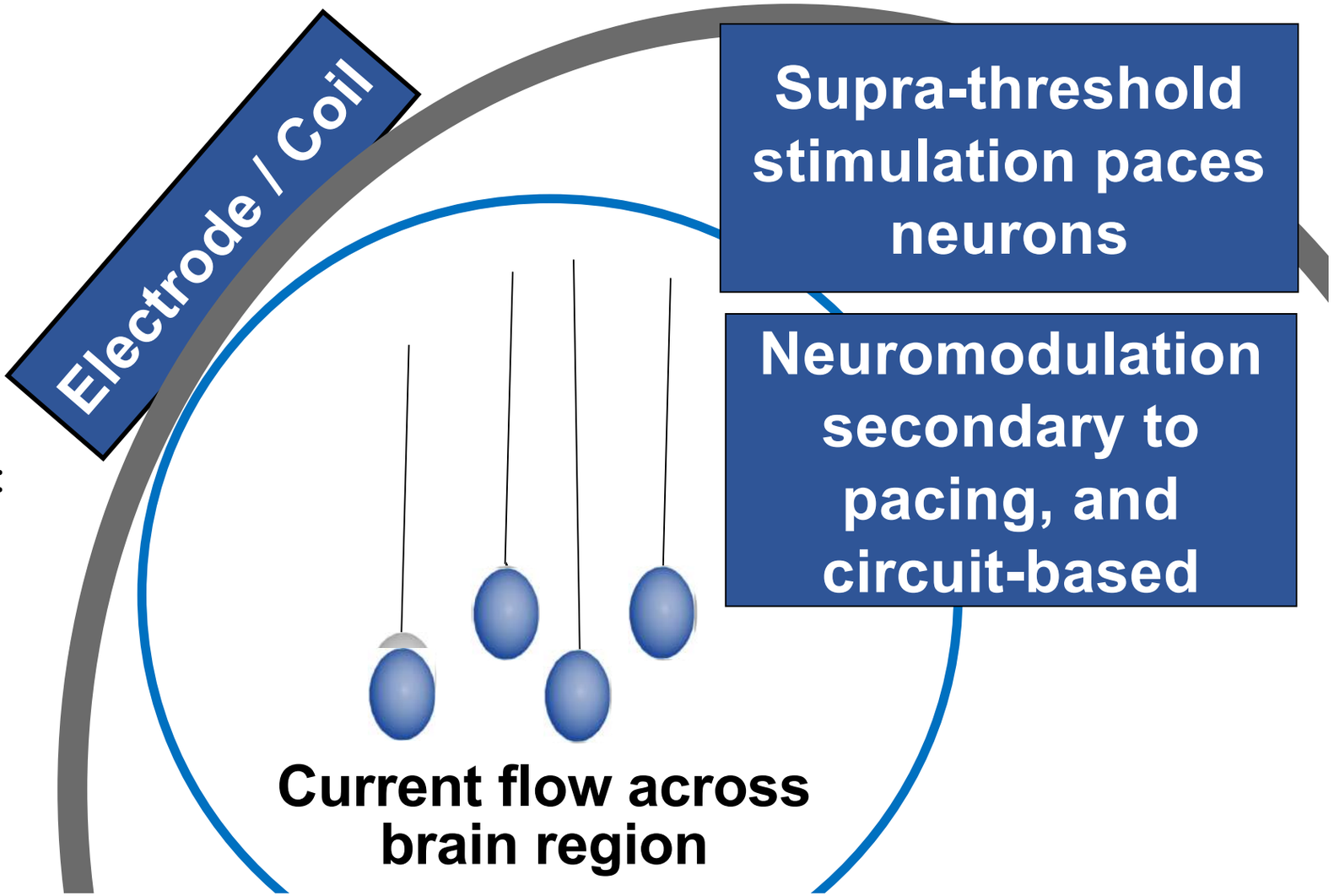
From Anatomical Targeting to Functional Targeting. tDCS / tACS are sub-threshold so modulate (target) ongoing activity.

Jackson et al. Animal models of transcranial DC stimulation: Methods and mechanisms. *J Physiol* 2016

Bikson et al. Effects DC electric fields on excitability in rat hippocampal slices in vitro. *J Physiol* 2014

From Anatomical Targeting to Functional Targeting. tDCS / tACS are sub-threshold so modulate (target) ongoing activity.

Supra-threshold stimulation (TES, TMS, ECT…)

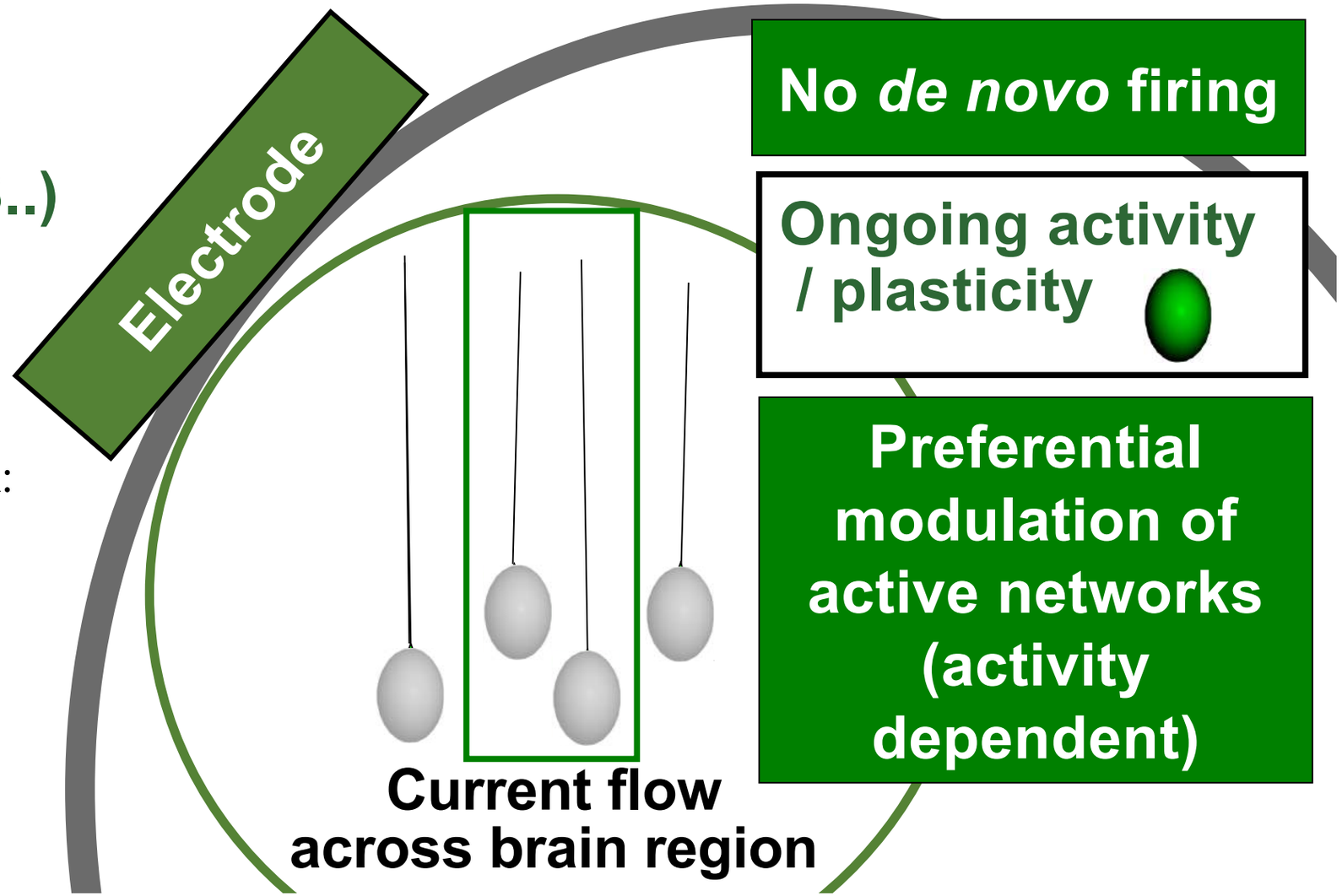


Jackson et al. Animal models of transcranial DC stimulation: Methods and mechanisms. *J Physiol* 2016

Bikson et al. Effects DC electric fields on excitability in rat hippocampal slices in vitro. *J Physiol* 2014

From Anatomical Targeting to Functional Targeting. tDCS / tACS are sub-threshold so modulate (target) ongoing activity.

Sub-threshold stimulation (tDCS, tACS, tRNS..)



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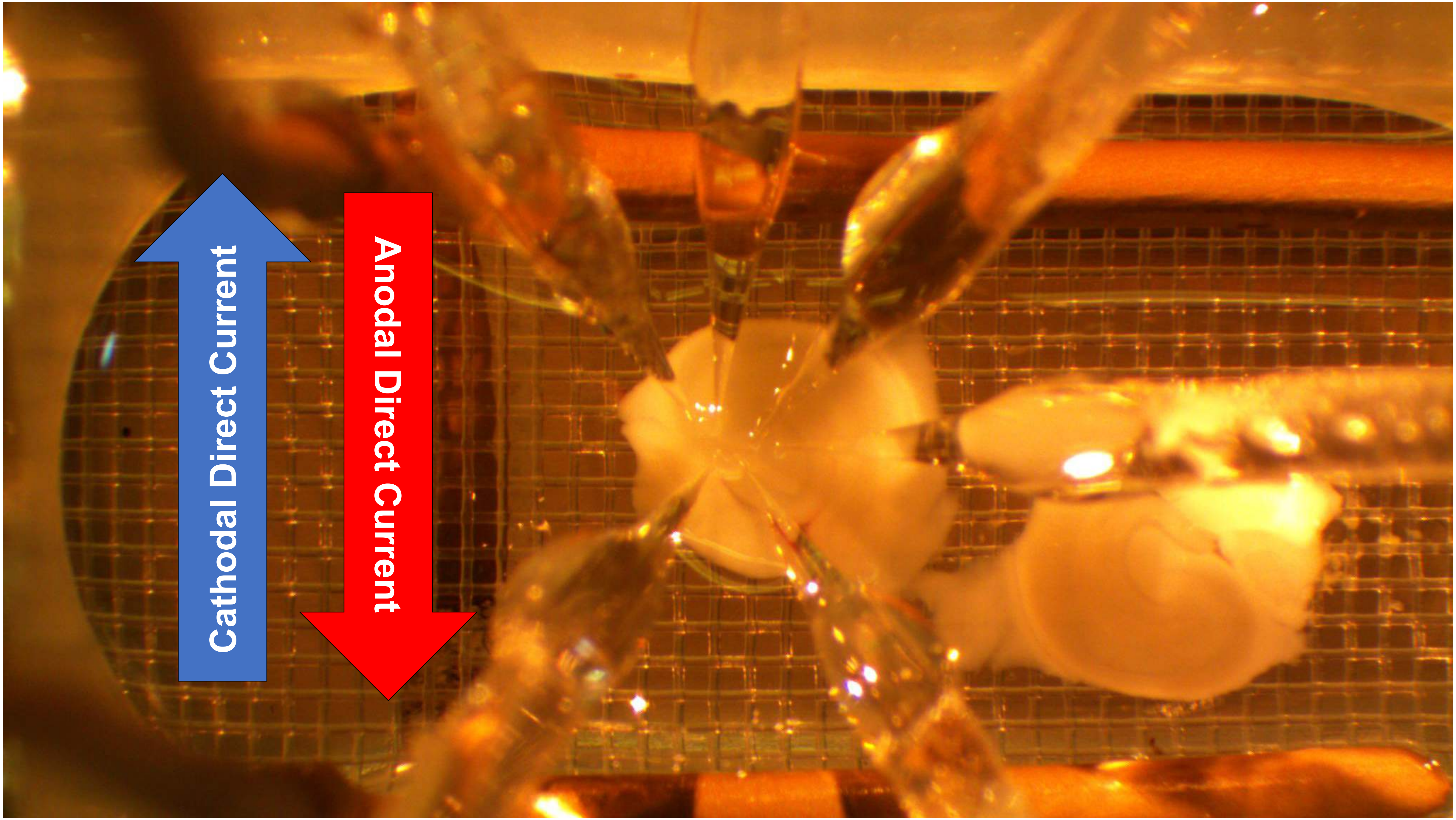
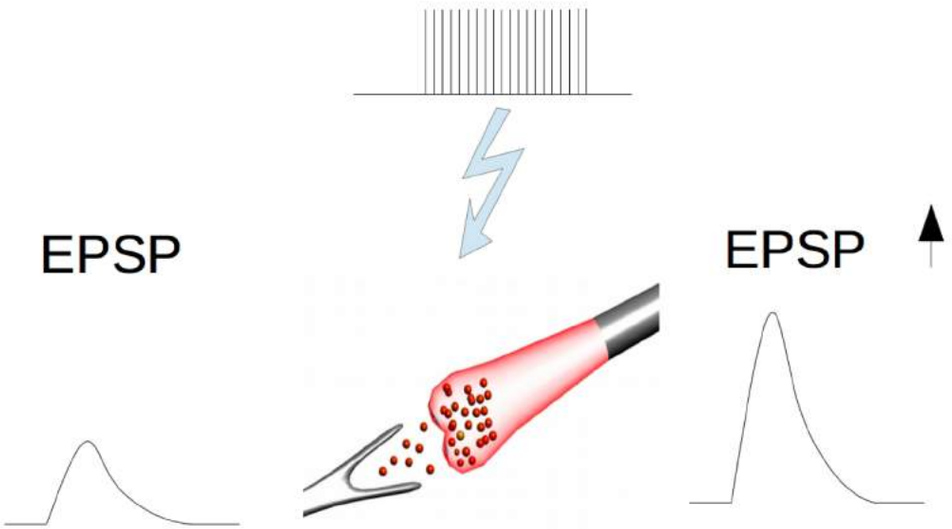
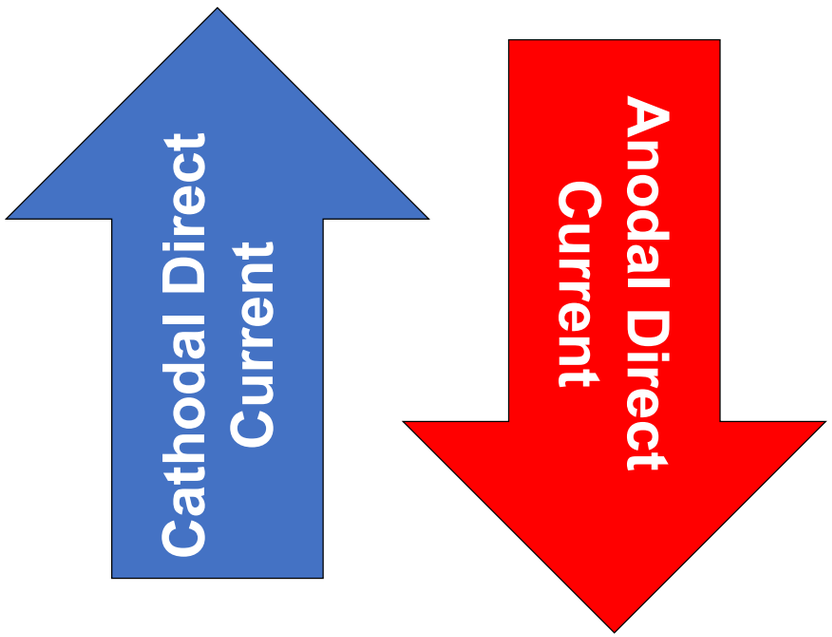

Cathodal Direct Current
Anodal Direct Current

Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current Stimulation (DCS)

LTP from theta burst stim

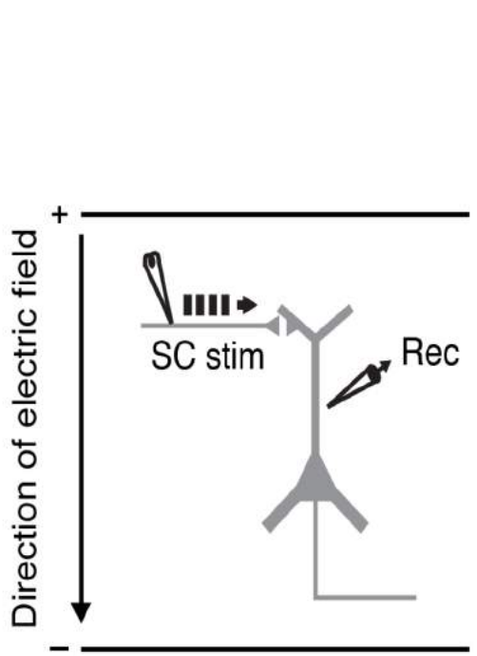


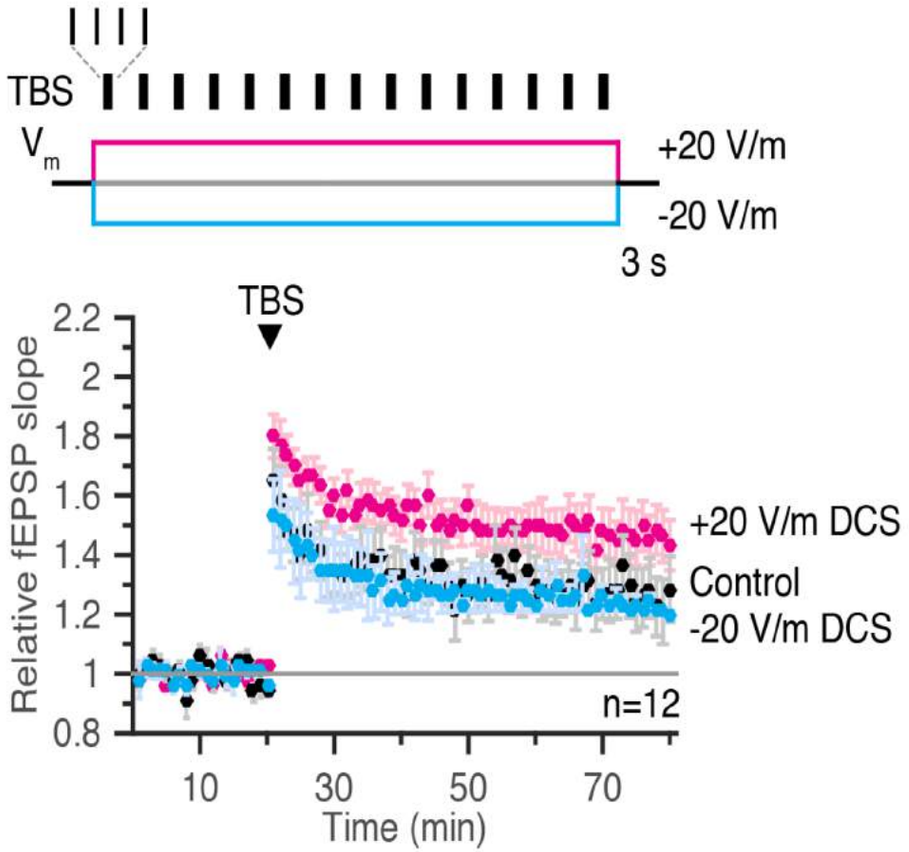
Cathodal or Anodal Direct Current Stimulation



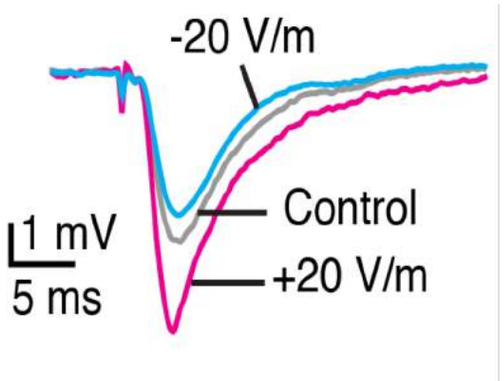
Kronberg et al. Direct current stimulation boosts Hebbian plasticity in vitro. *Brain Stim* 2019

Theta Burst Stimulation (TBS) generates LTP which is modulated by concurrent Direct Current Stimulation (DCS)



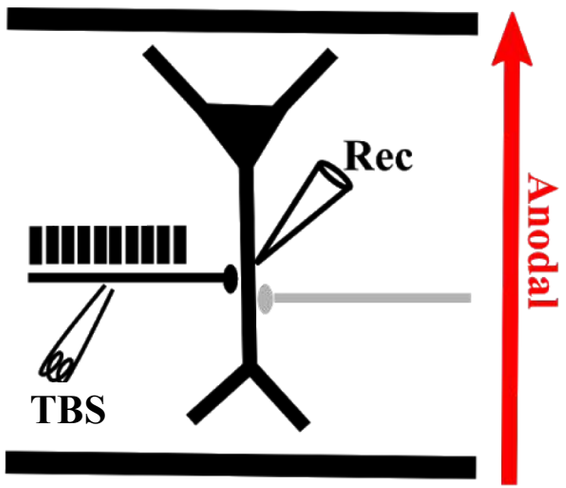


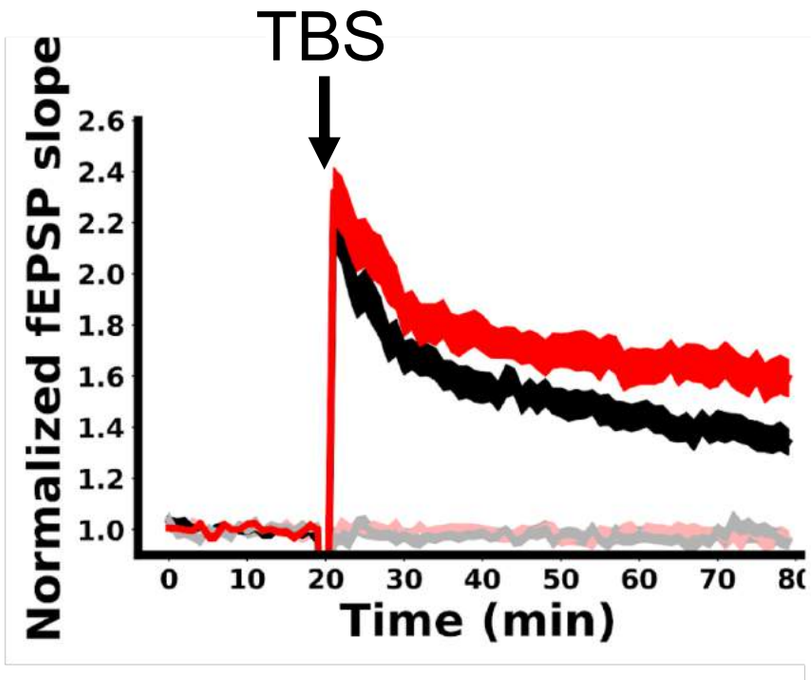
1 hour after TBS



Kronberg et al. Direct current stimulation boosts Hebbian plasticity in vitro. *Brain Stim* 2019

Anodal DCS boost synapses with LTP but does not generate LTP in silent synapses

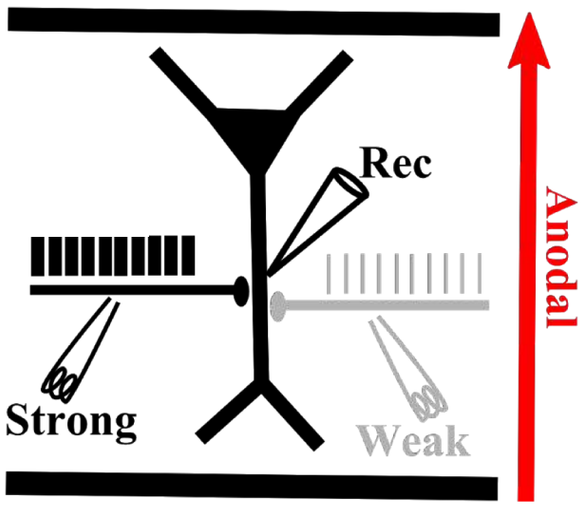


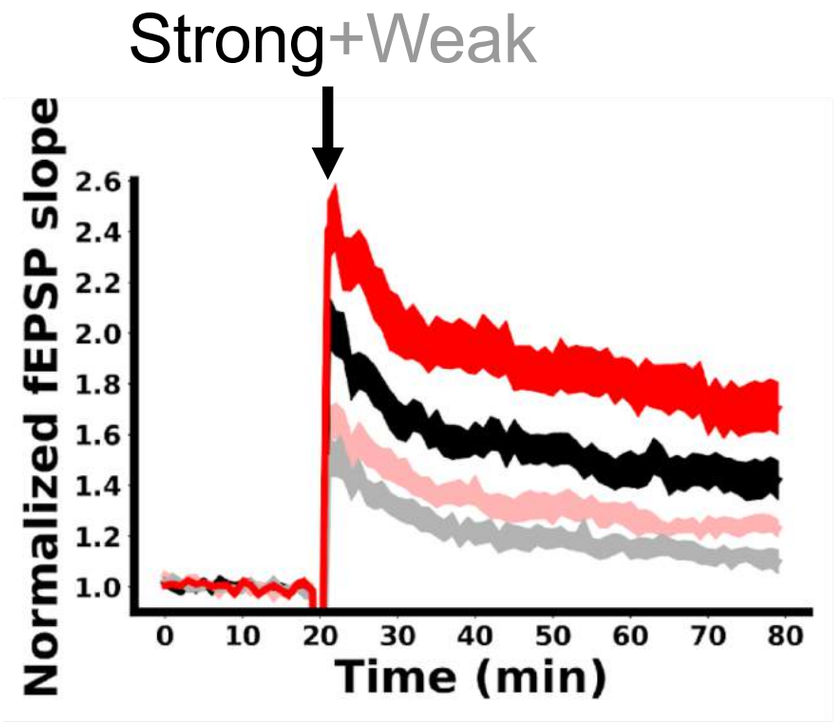


Only active synapse get benefit of tDCS: Functional Targeting.

Kronberg et al. Direct current stimulation boosts Hebbian plasticity in vitro. *Brain Stim* 2019

“Strong” stimulation induces LTP in “weakly” co-activated pathway. This **associative** effects is enhanced with DCS.

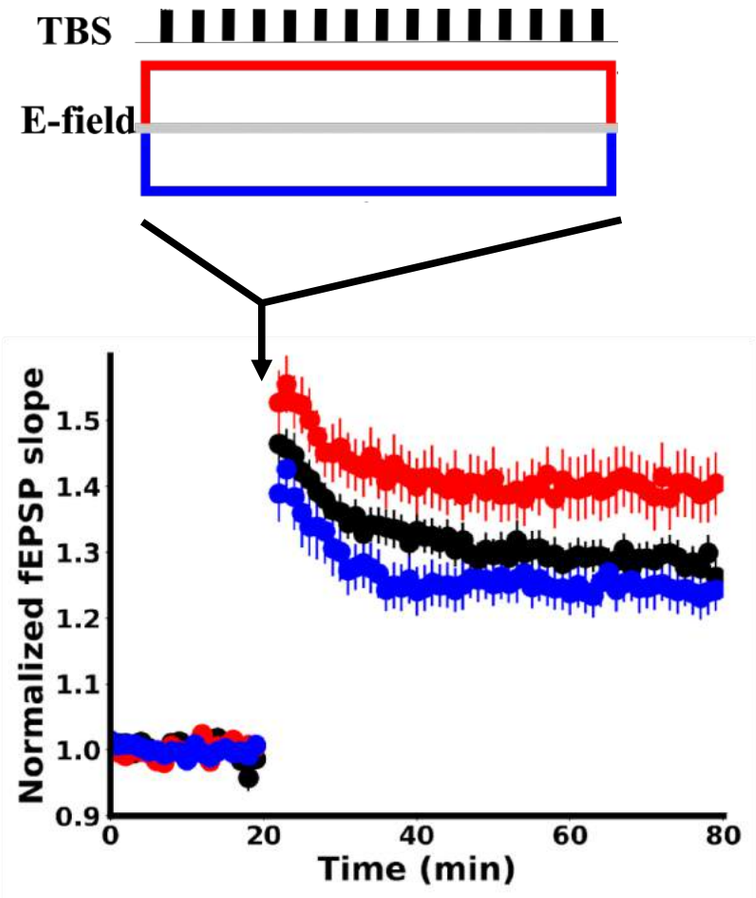


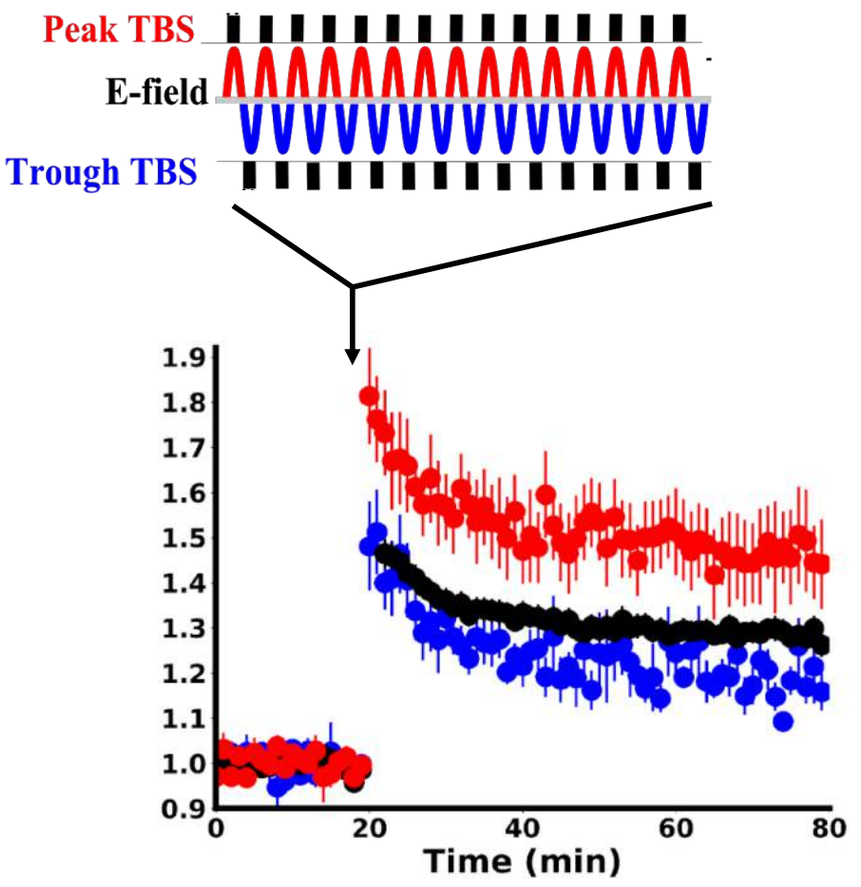


tDCS boosts Hebbian plasticity: Functional Targeting.

Kronberg et al. Direct current stimulation boosts Hebbian plasticity in vitro. *Brain Stim* 2019

Only “instant” electric field matters. As a result, AC stimulation (tACS) can produce net plasticity boost.





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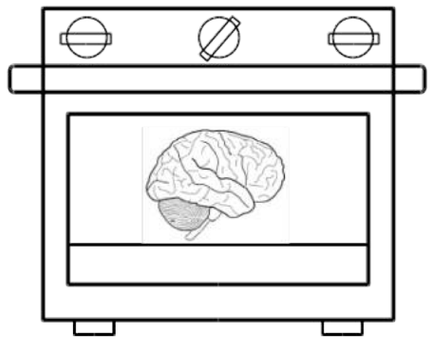
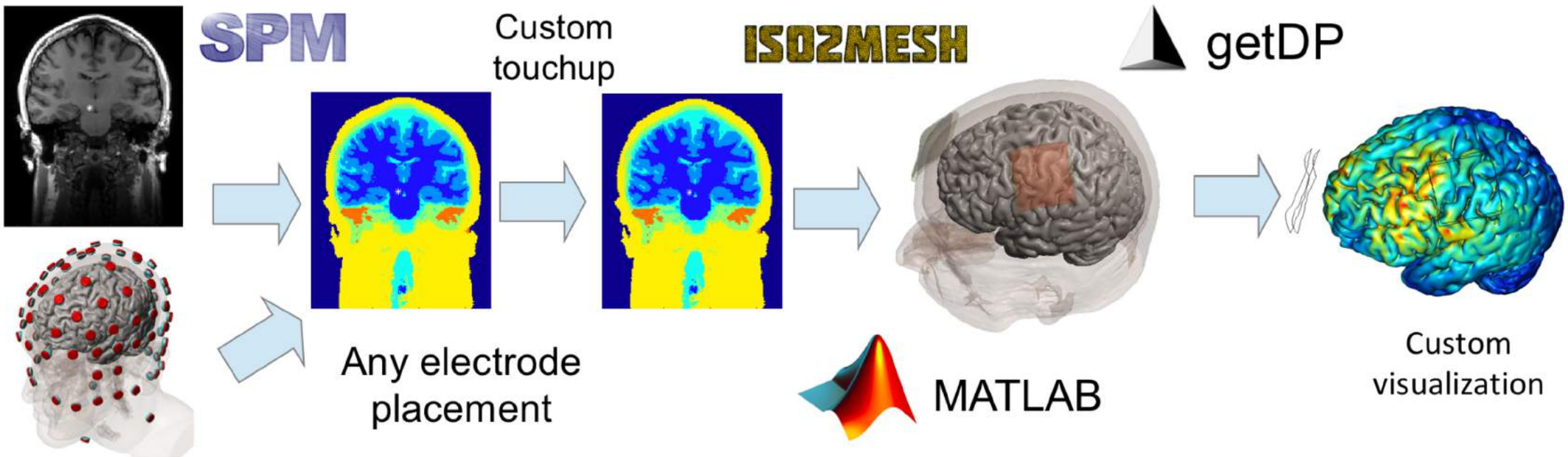
UR Medicine, Del Monte Institute for Neuroscience. Oct 25, 2019

Realistic vOlumetric-Approach-based Simulator for Transcranial electrical stimulation

ROAST



BRAIN initiative, NIMH. Free (Matlab), Open Source, One command line, validated outcomes.



Huang et al. ROAST -- a fully automated open-source pipeline, bioRxiv 217331, Nov 10, 2017

Targeting limited: Interferential Stimulation