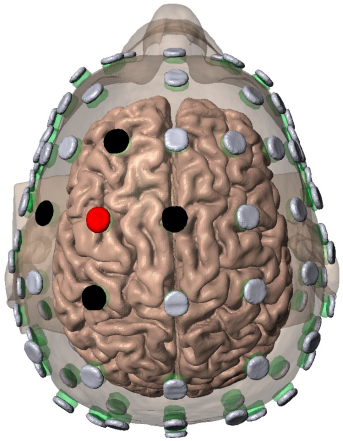
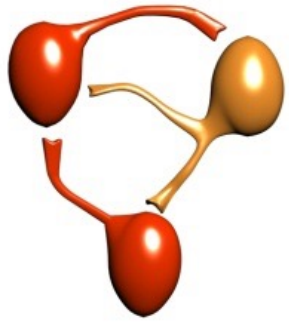
Technology and fundamentals of tACS



GGL section "Neurosciences" seminar on Transcranial Alternating Current Stimulation (tACS Lab Rotations in Gießen)

July 22, 2021



Marom Bikson

Lucas Parra, Dennis Truong, Abhishek Datta, Davide Reato, Asif Rahman, Belen Lafon, Thomas Radman, Preet Minhas, Yu Huang, Mahtab Alam, Alexander David, Ole Seibt, Zeinab Esmaeilpour, Jacek Dmochowski, Nigel Gebodh

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$ NIH, NSF, Epilepsy Foundation, Wallace Coulter Foundation, DoD (AFOSR)

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 serves on the SAB of Boston Scientific, GlaxoSmithKline, Biovisics, Mecta, Halo Neuroscience, X, i-Lumen, Biovisics, Humm.

Supported by grants from the National Institutes of Health: R01NS101362, R01NS095123, R01NS112996, R01MH111896, R01MH109289, UG3DA048502 (MB)

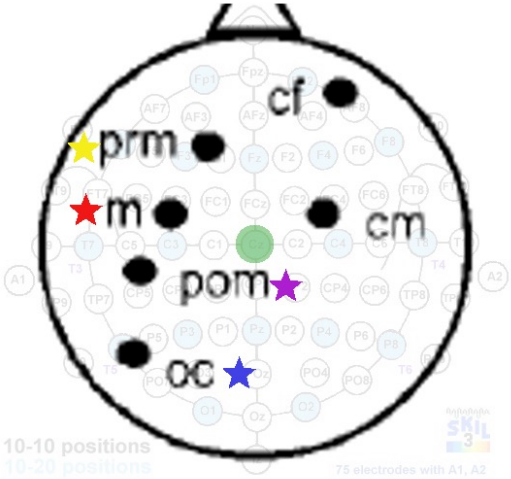
Slides @MaromBikson

References: NeuralEngr.Org

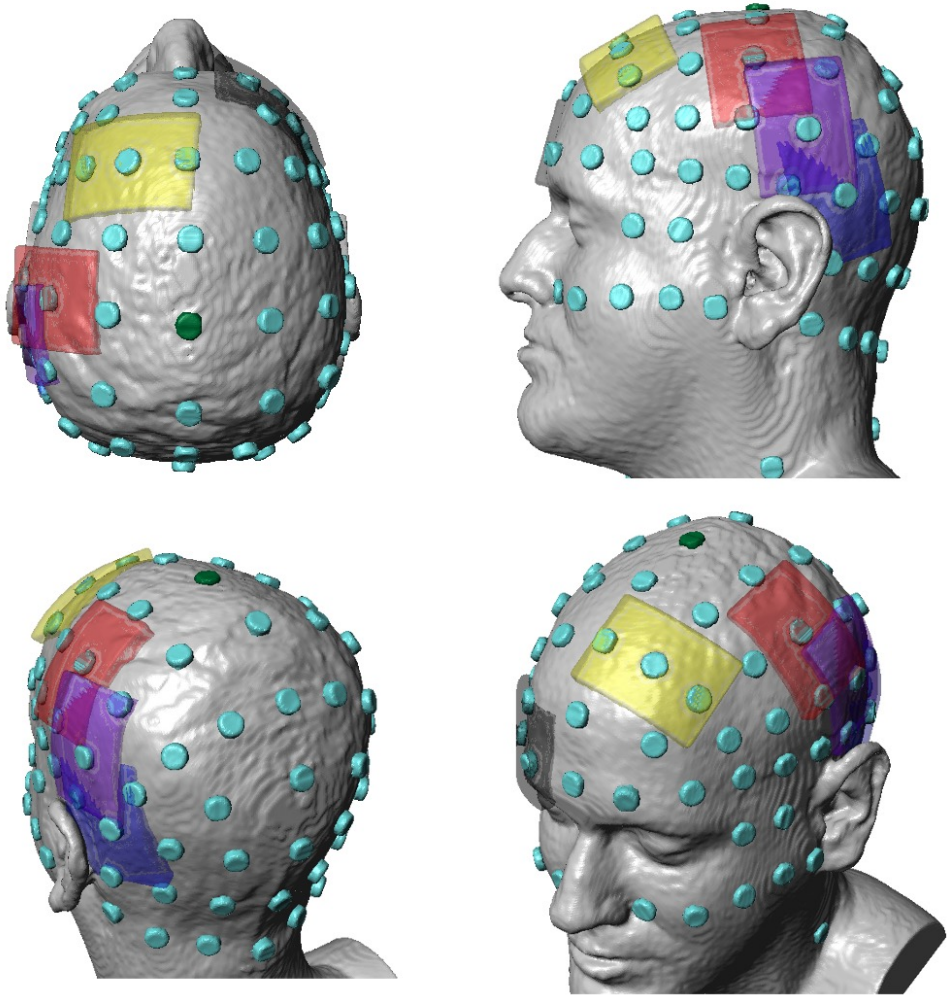
tACS dose: It's not one thing

Dose per Peterchev 2012

1) Electrode montage (electrode position) determines brain current flow patten.

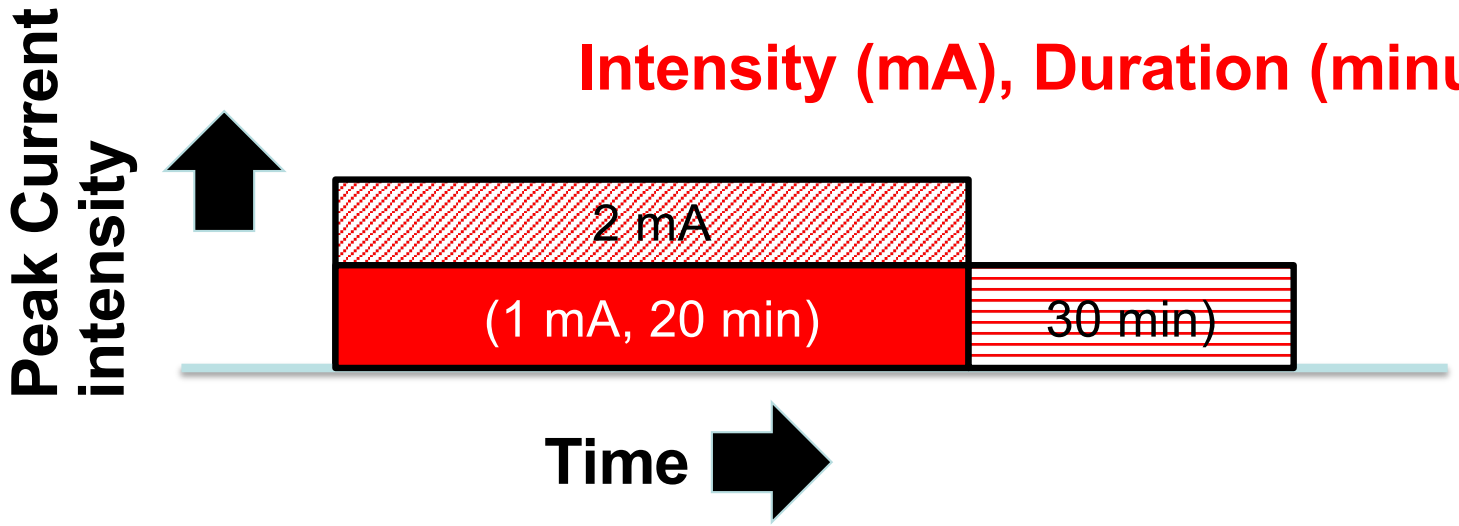


Contralateral Forehead:	AF8
PreMotor:	F1
Motor:	C3
PostMotor:	CP5
Occipital:	P7

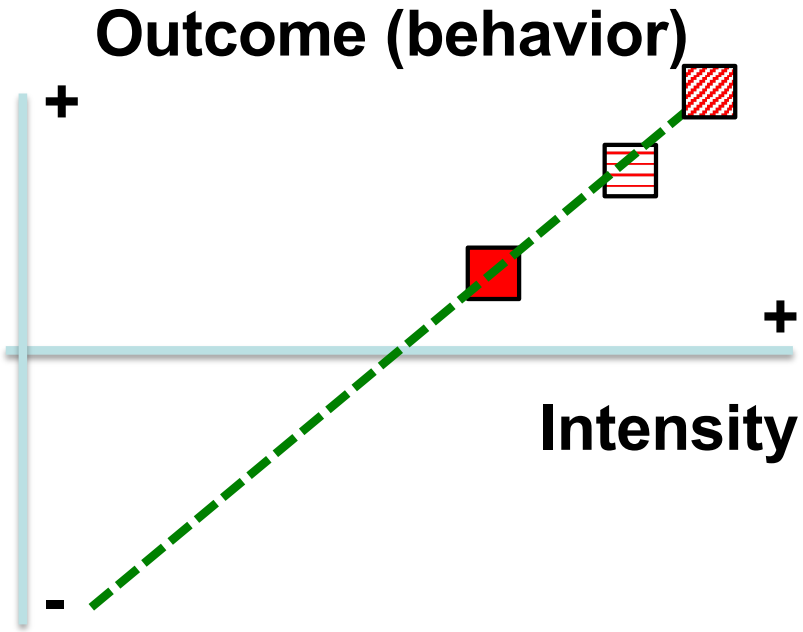


2) With **Sinusoid Waveform** (frequency, duration, intensity) determines neuromodulaion

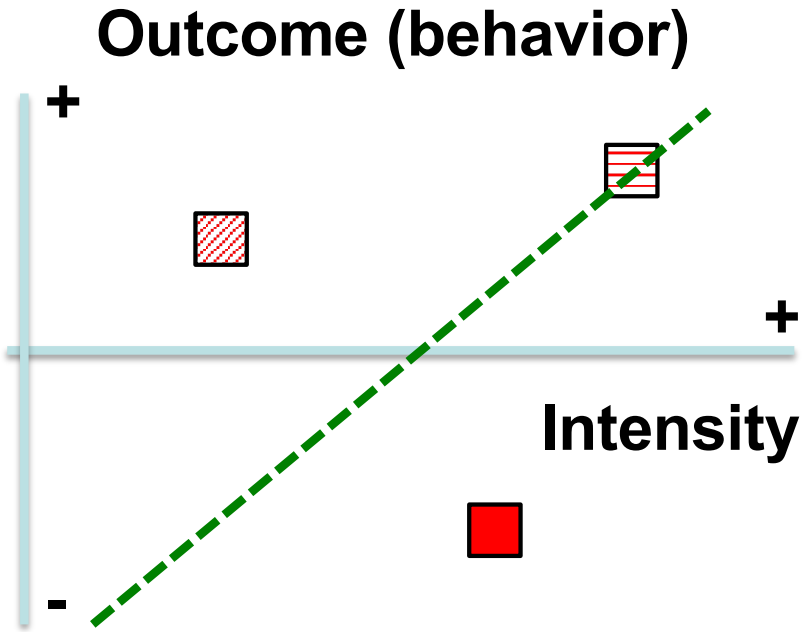
tACS dose: Waveform Intensity and Duration



Linear dose-reponse



None-Linear (Not monotonic) dose-reponse



tACS dose: Waveform Frequency

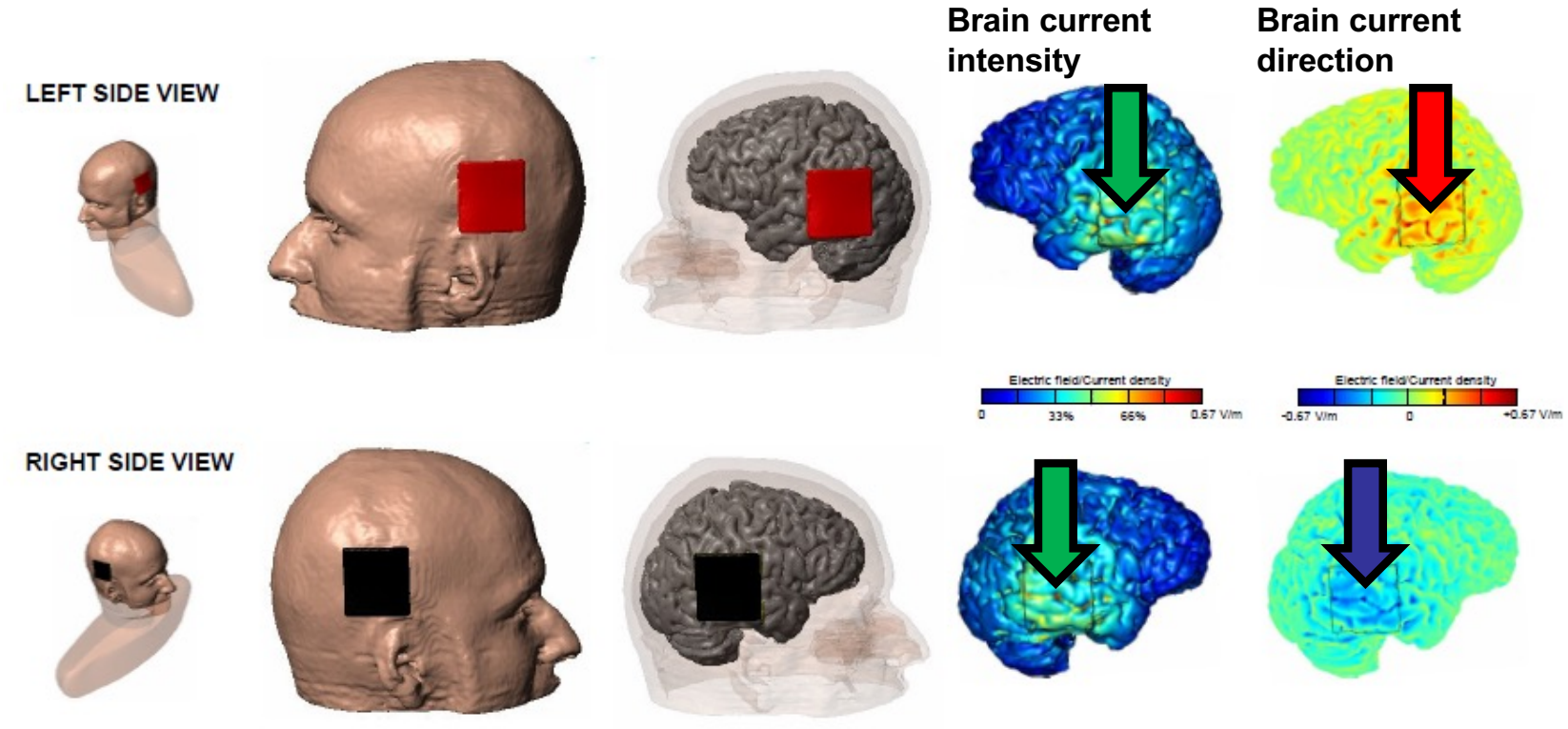
Frequency

- **The use of an AC waveform produces outcomes distinct from DC waveform, and moreover the effects of AC stimulation are frequency specific.**

- **(?) AC stimulation that matches the frequency of an endogenous oscillation preferentially modulates that oscillation, and specifically boosts it.**

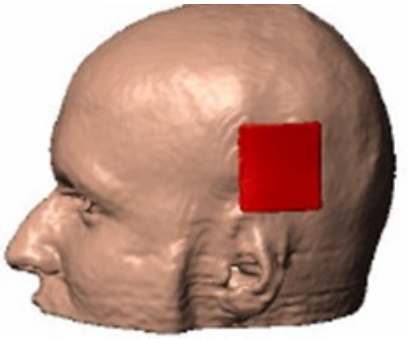
tDCS current flow : anode and cathode

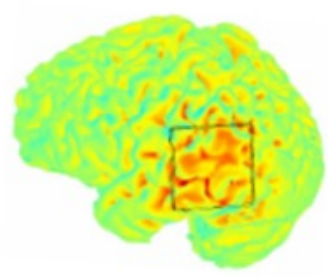
- Two pad electrodes placed on head and connected to DC current stimulator.
- Current passed between ANODE(+) and CATHODE(-)
- DC CURRENT FLOW across cortex.
- Current is INWARD under ANODE and OUTWARD under CATHODE



MRI derived computational model

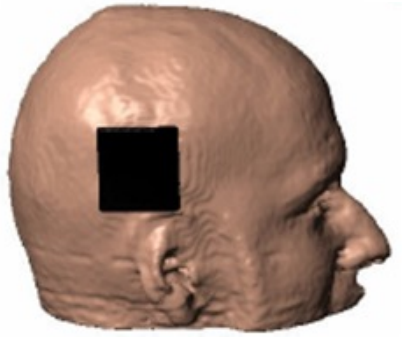
tDCS current flow : anode and cathode

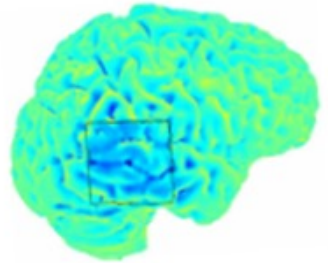




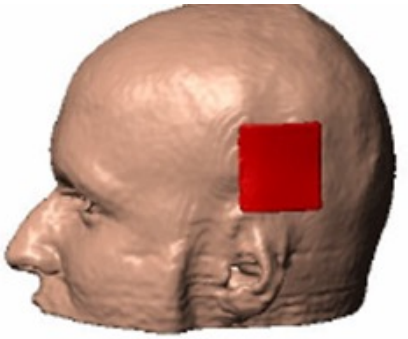
Current flow

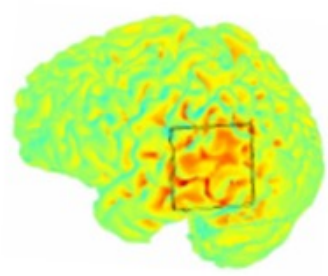
outward inward





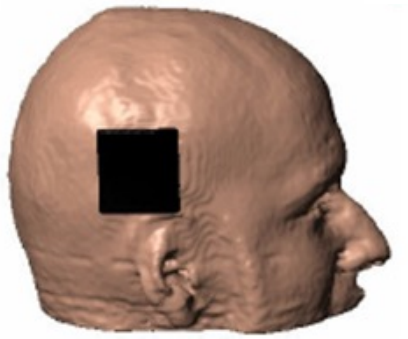
tDCS current flow : anode and cathode

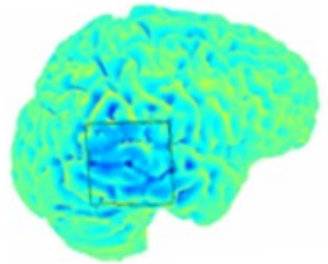




Current flow

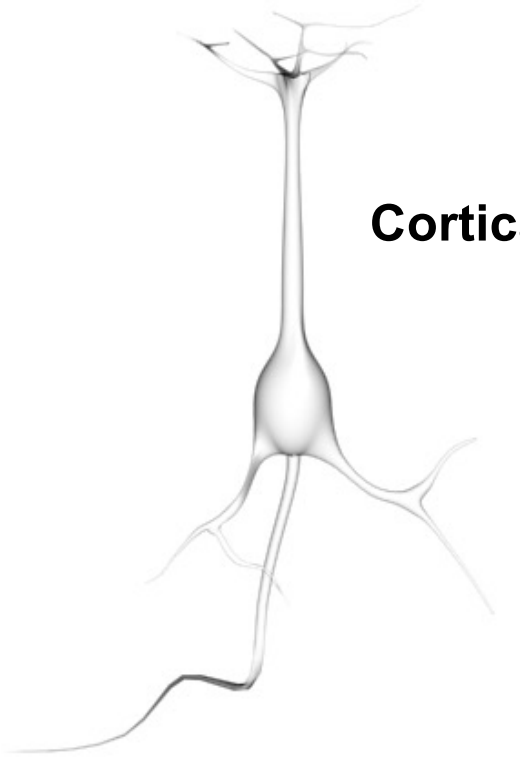
outward inward





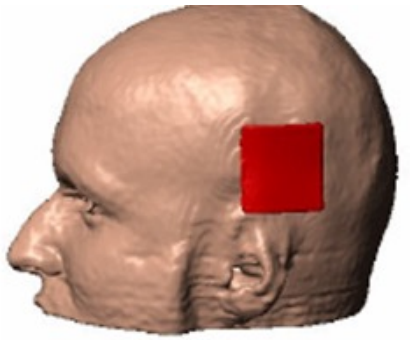
Electrode

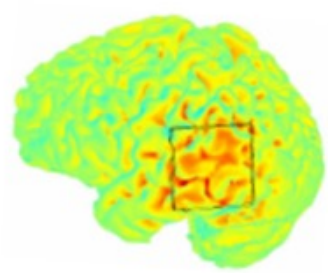
Head Surface



Cortical Neuron

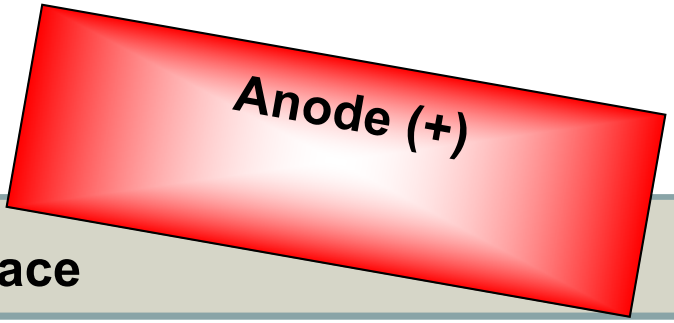
tDCS current flow : anode and cathode





Current flow

outward inward



Head Surface

Current Flow

Hyperpolarized cell compartments

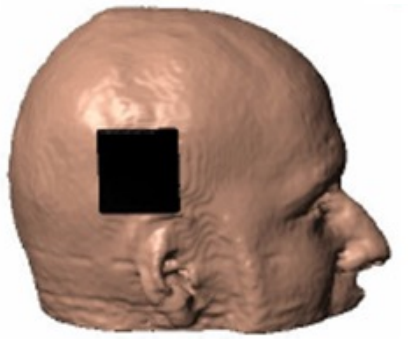
Depolarized cell compartments

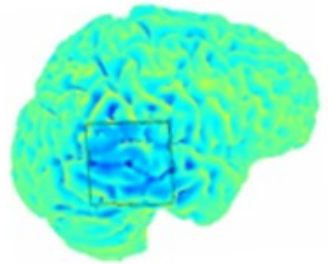
? Increased Excitability / Plasticity

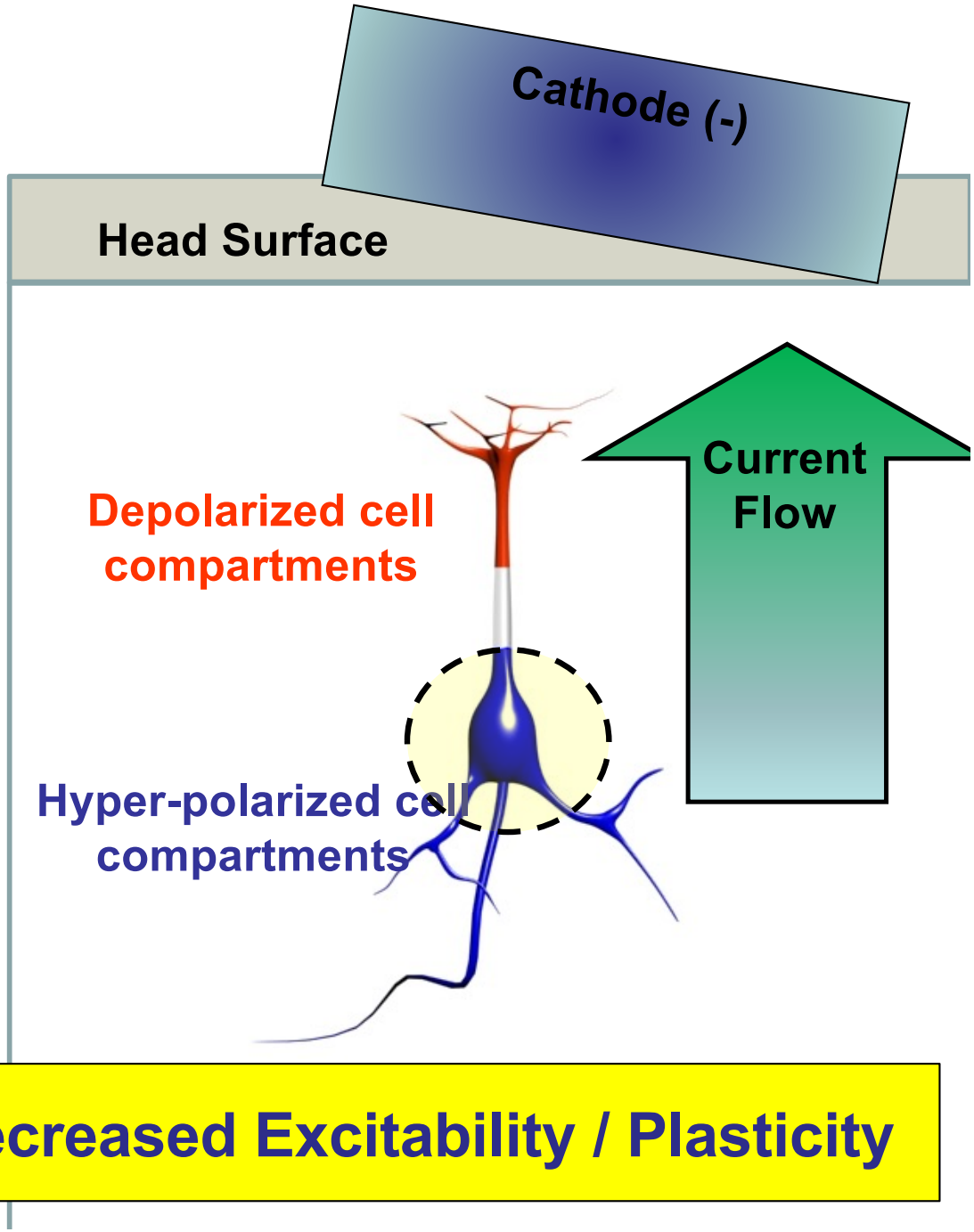
tDCS current flow : anode and cathode

Current flow

outward inward



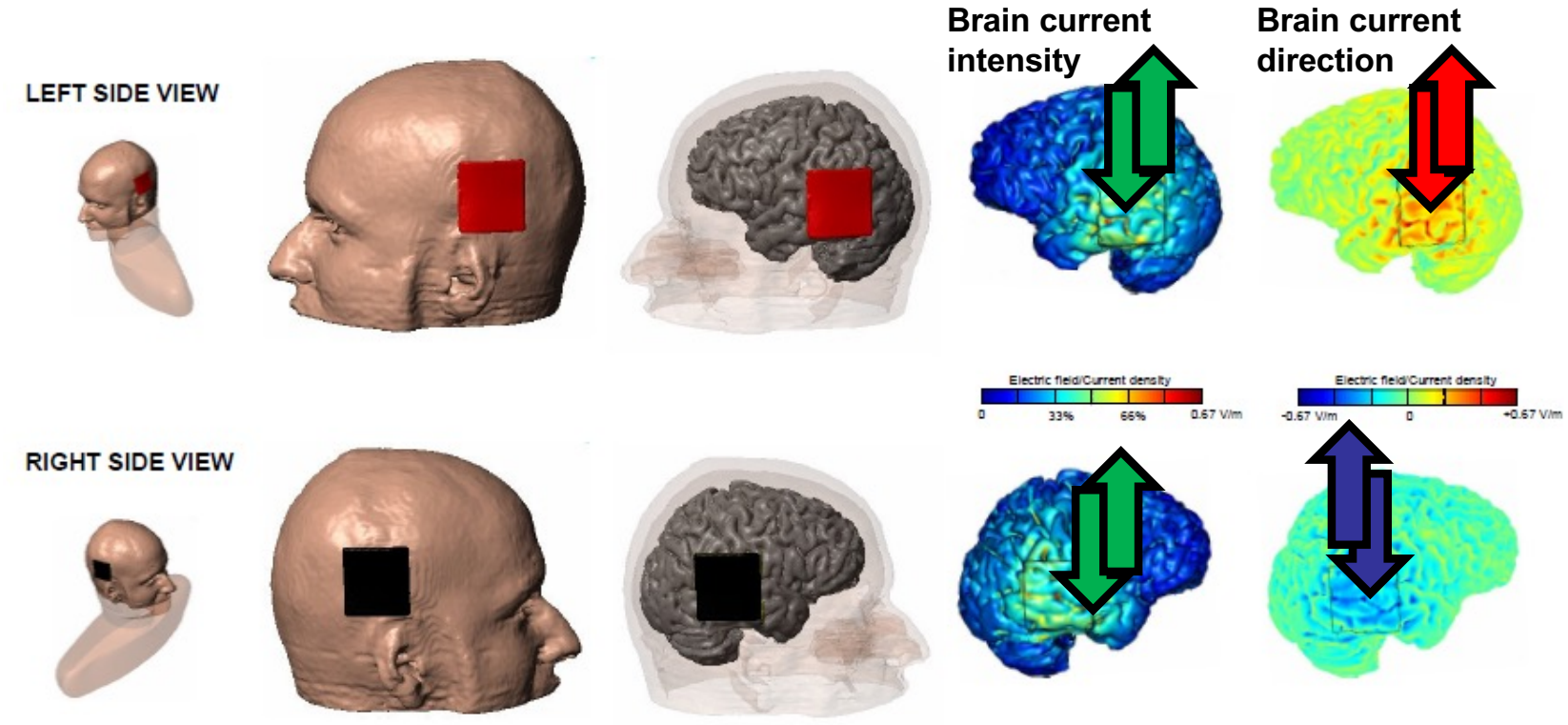




? Decreased Excitability / Plasticity

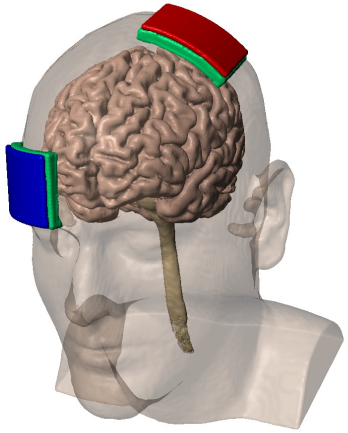
tACS current flow : alternating direction

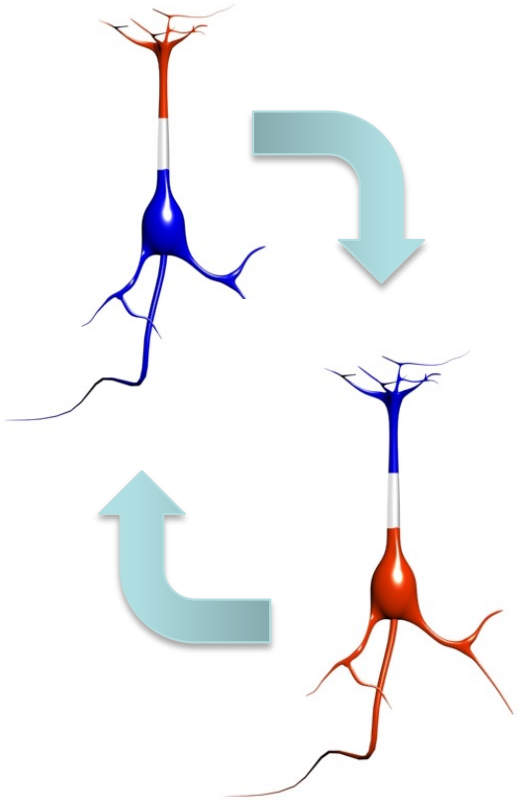
- Two pad electrodes placed on head and connected to AC current stimulator.
- At any given instant, current passed from ANODE(+) and CATHODE(-)
- AC CURRENT FLOW across cortex as ANODE and CATHODE alternate.

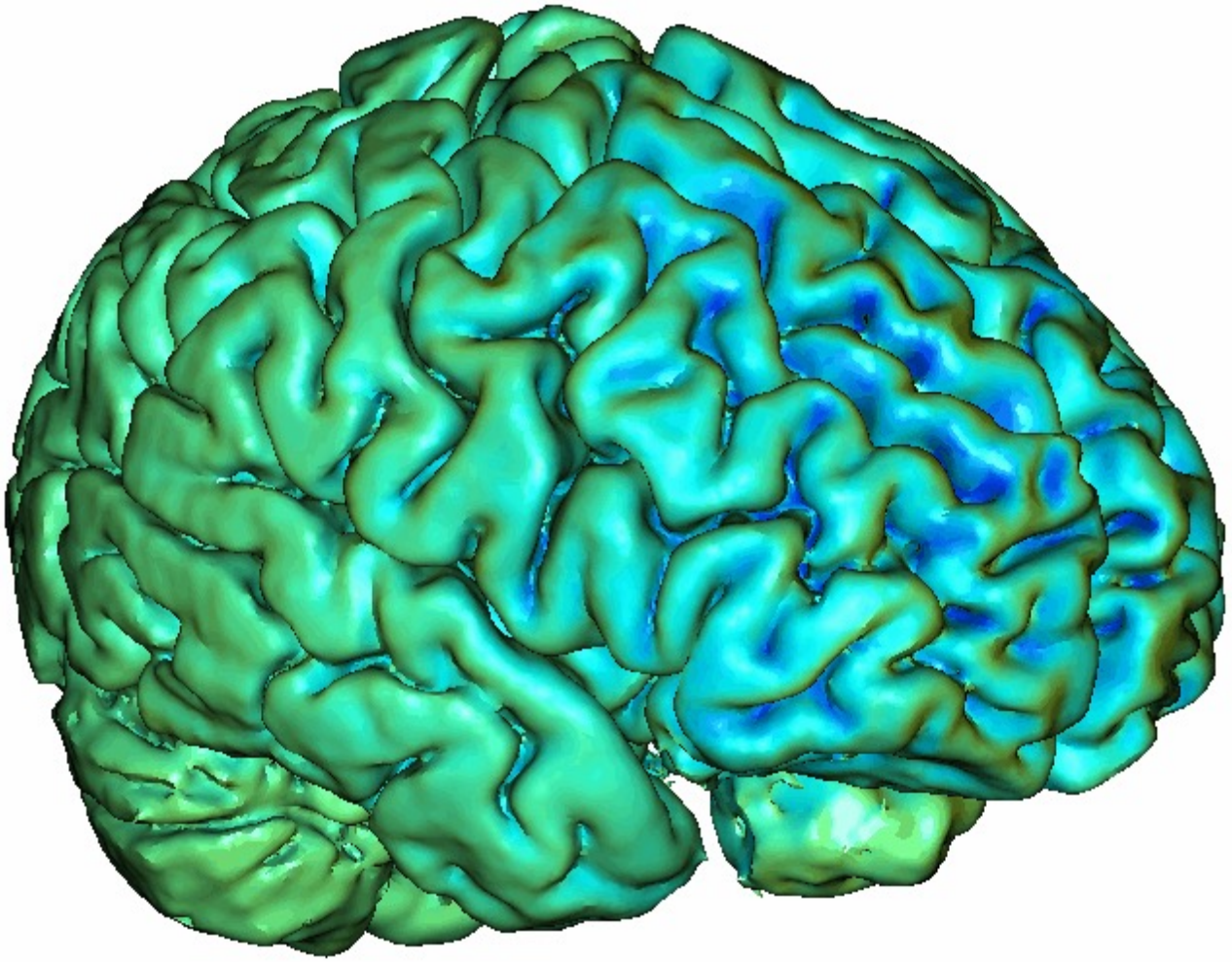


MRI derived computational model

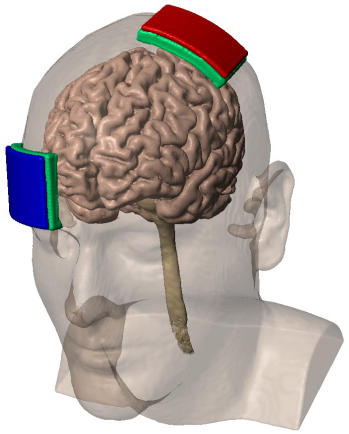
tACS current flow : alternating direction

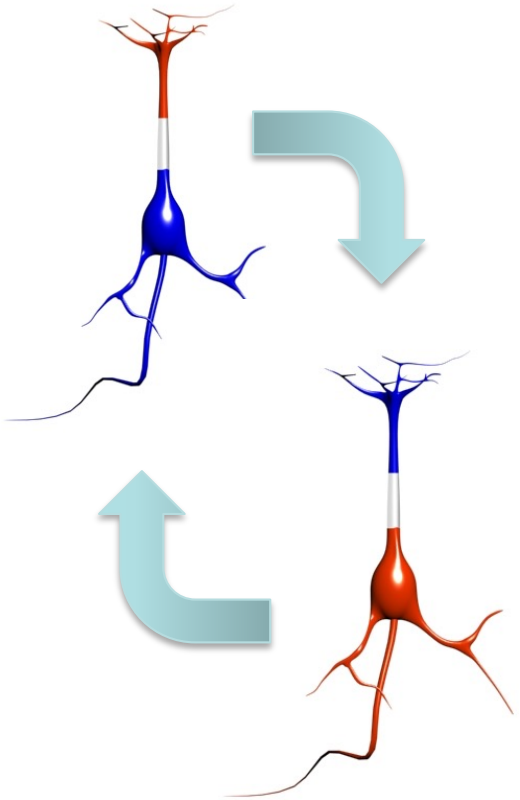


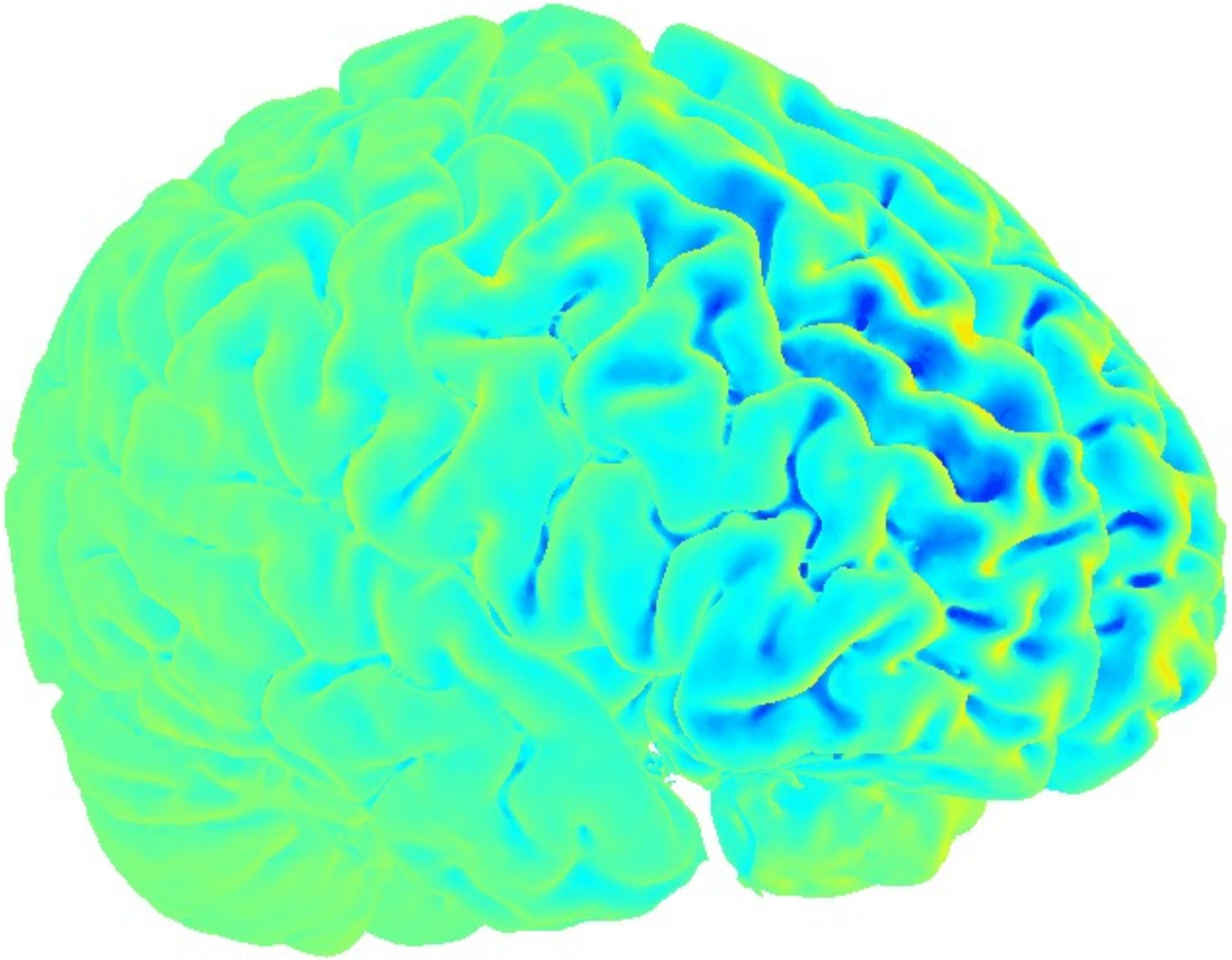




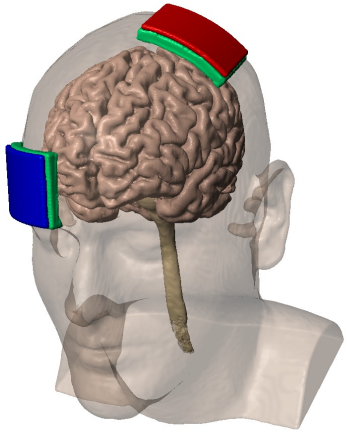
tACS current flow : alternating direction

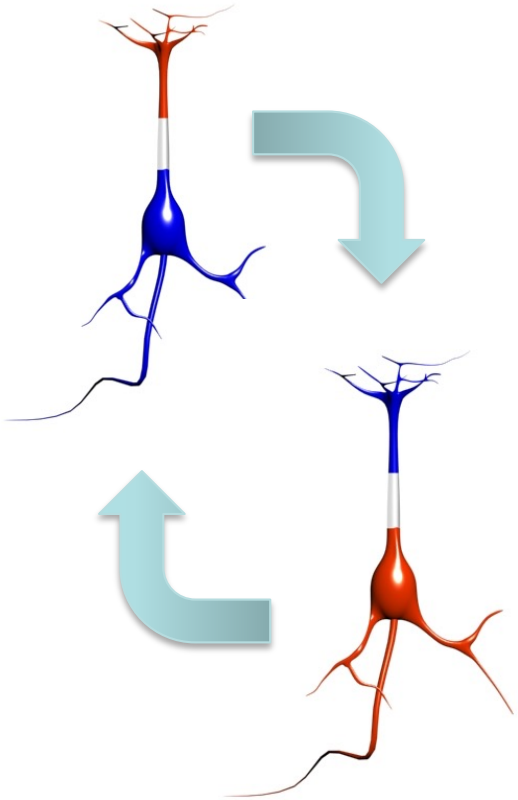


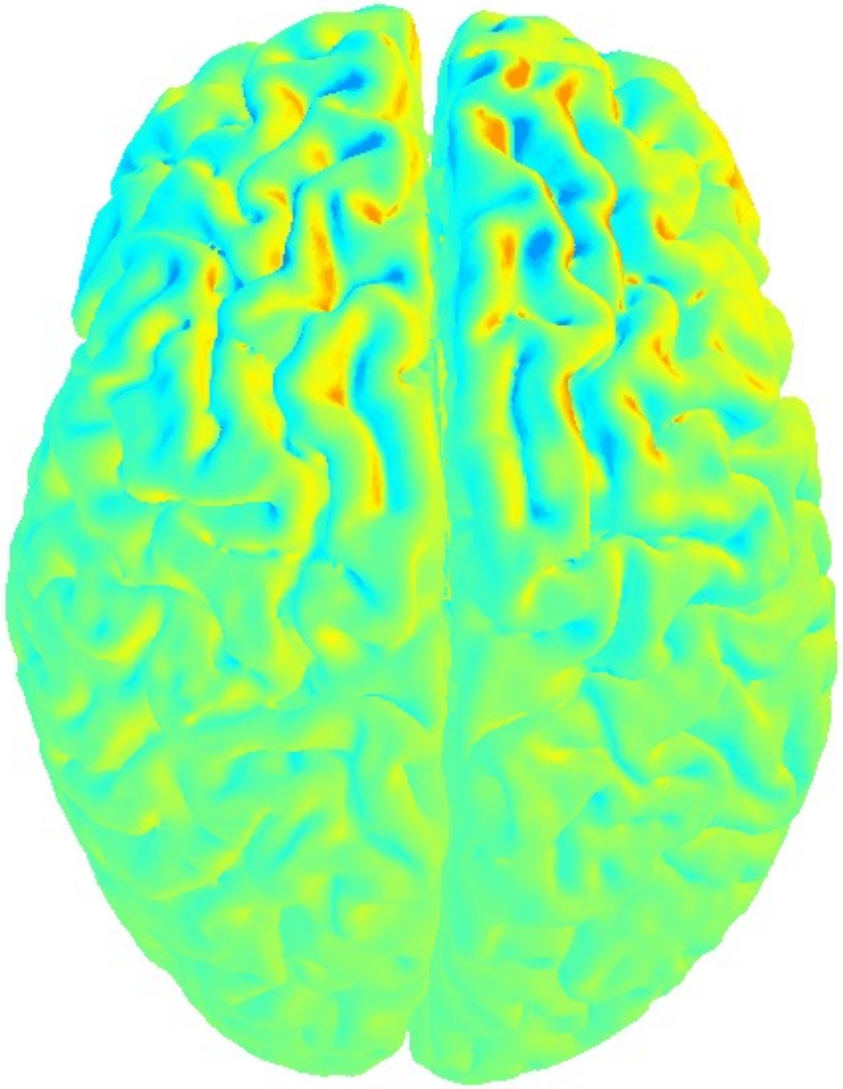




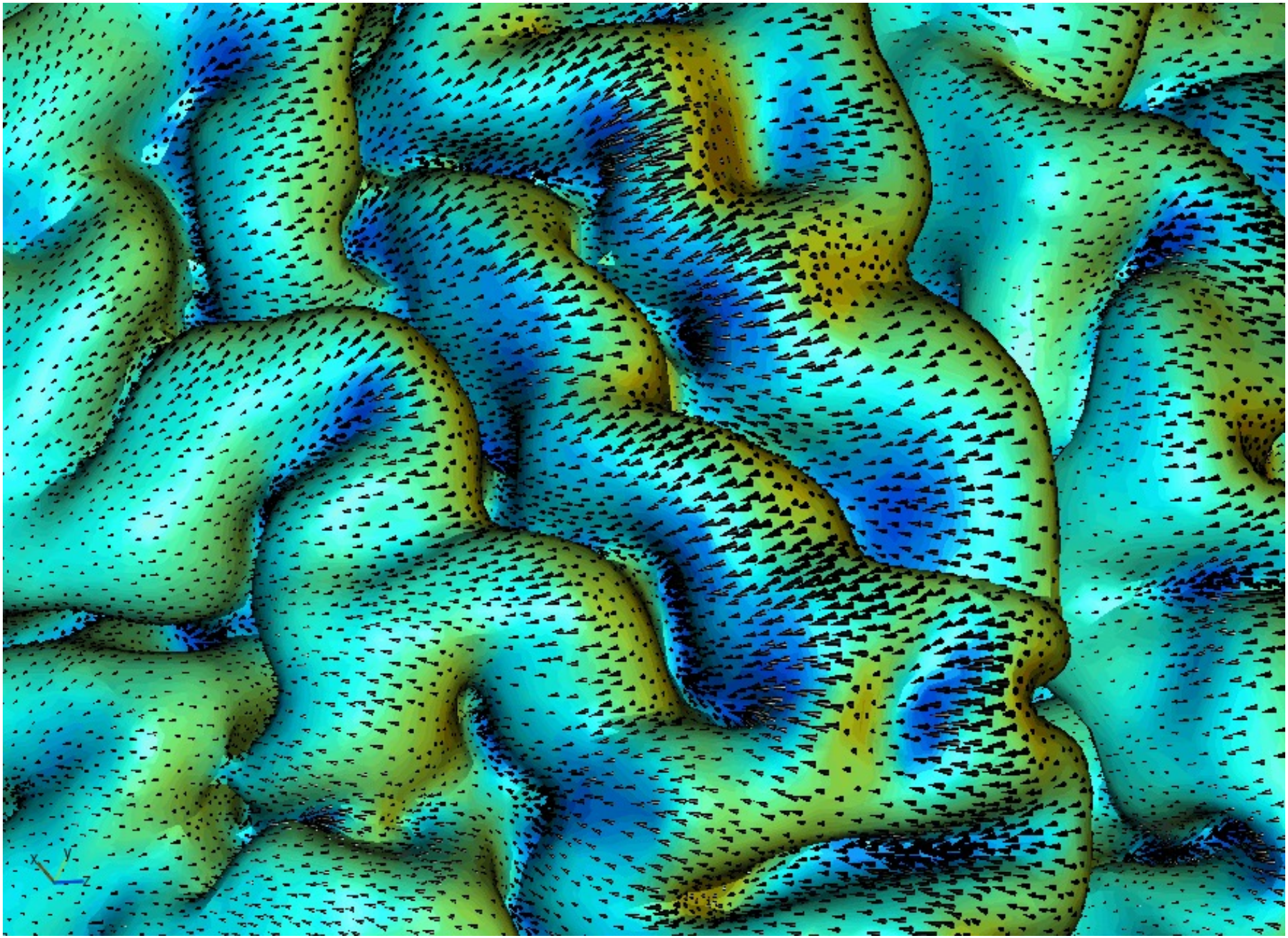
tACS current flow : alternating direction





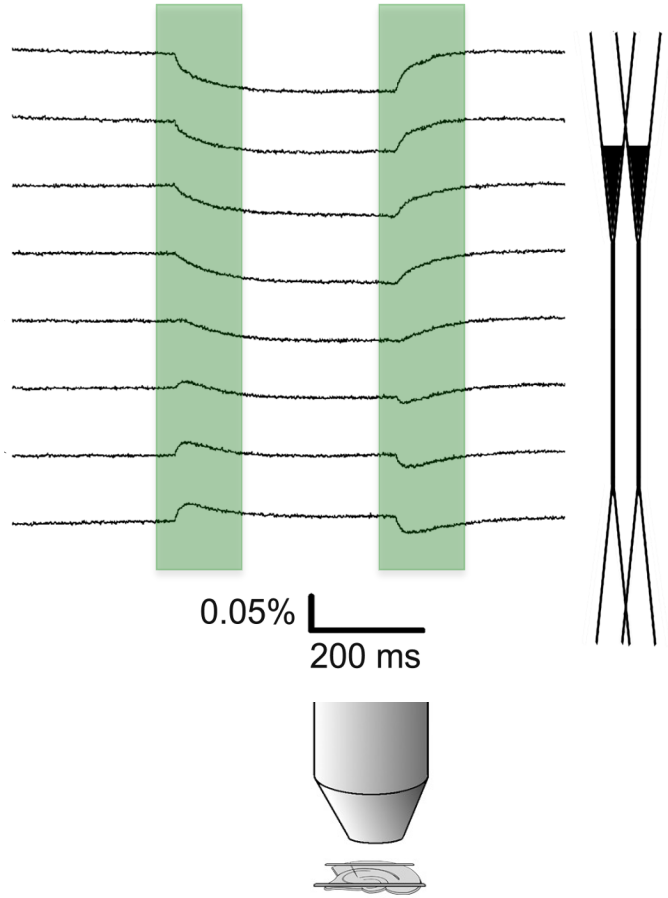


tACS current flow : alternating direction

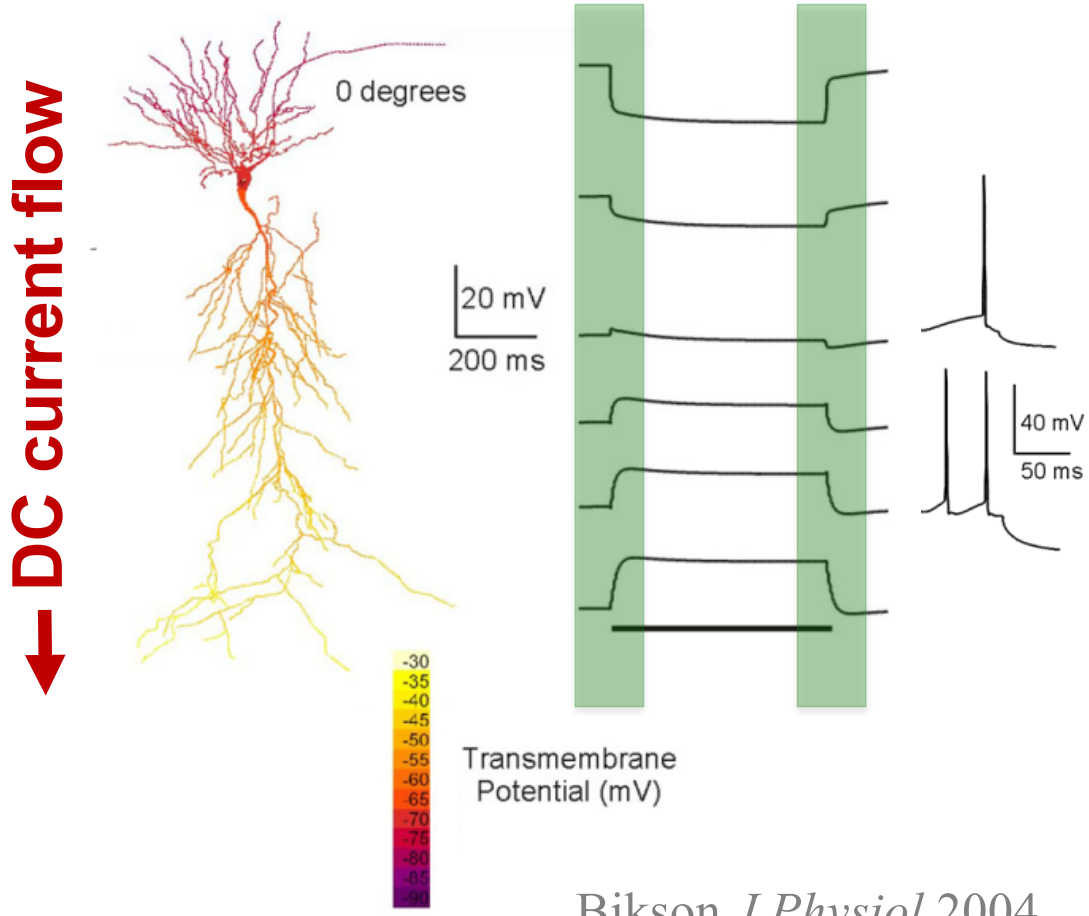


Neuron Polarization during DCS

Optical Mapping with voltage sensitive dyes



Multi-compartment neuronal modelling



Bikson *J Physiol* 2004

Soma Polarization by electric field has a time constant (~20 ms)

Chakraborty *Cerebral Cortex 2018*

Axon Polarization by electric field has a time constant (~5 ms)

tACS dose: Waveform

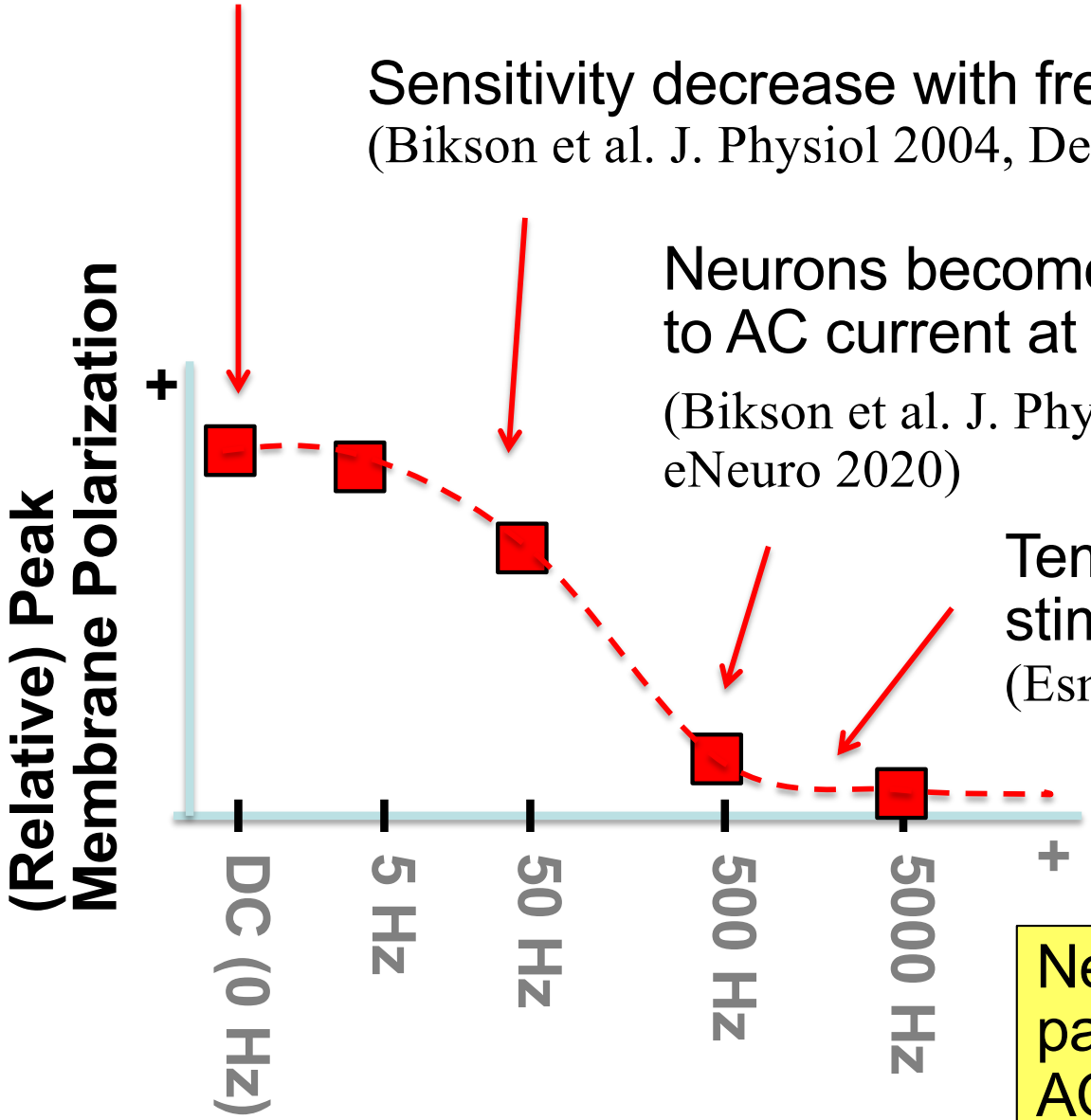
Maximum polarization at DC is 0.15 mV per mA current
(Bikson et al. J. Physiol. 2004, Radman et al. Brain Stim. 2009)

Sensitivity decrease with frequencies >20 Hz
(Bikson et al. J. Physiol 2004, Deans et al. J Physiol 2007)

Neurons become insensitive "transparent" to AC current at >500 Hz

(Bikson et al. J. Physiol 2001. Esmaeilpour et al. eNeuro 2020)

Temporal interference stimulation is kHz modulated
(Esmaeilpour et al. Brain Stim 2020)

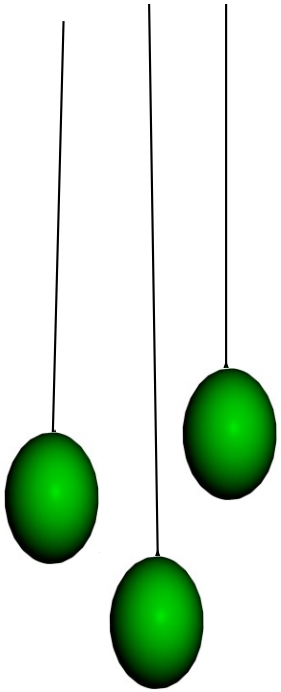


Neurons membranes are low-pass filters for polarization by AC currents

tACS mechanisms: Neuromodulation

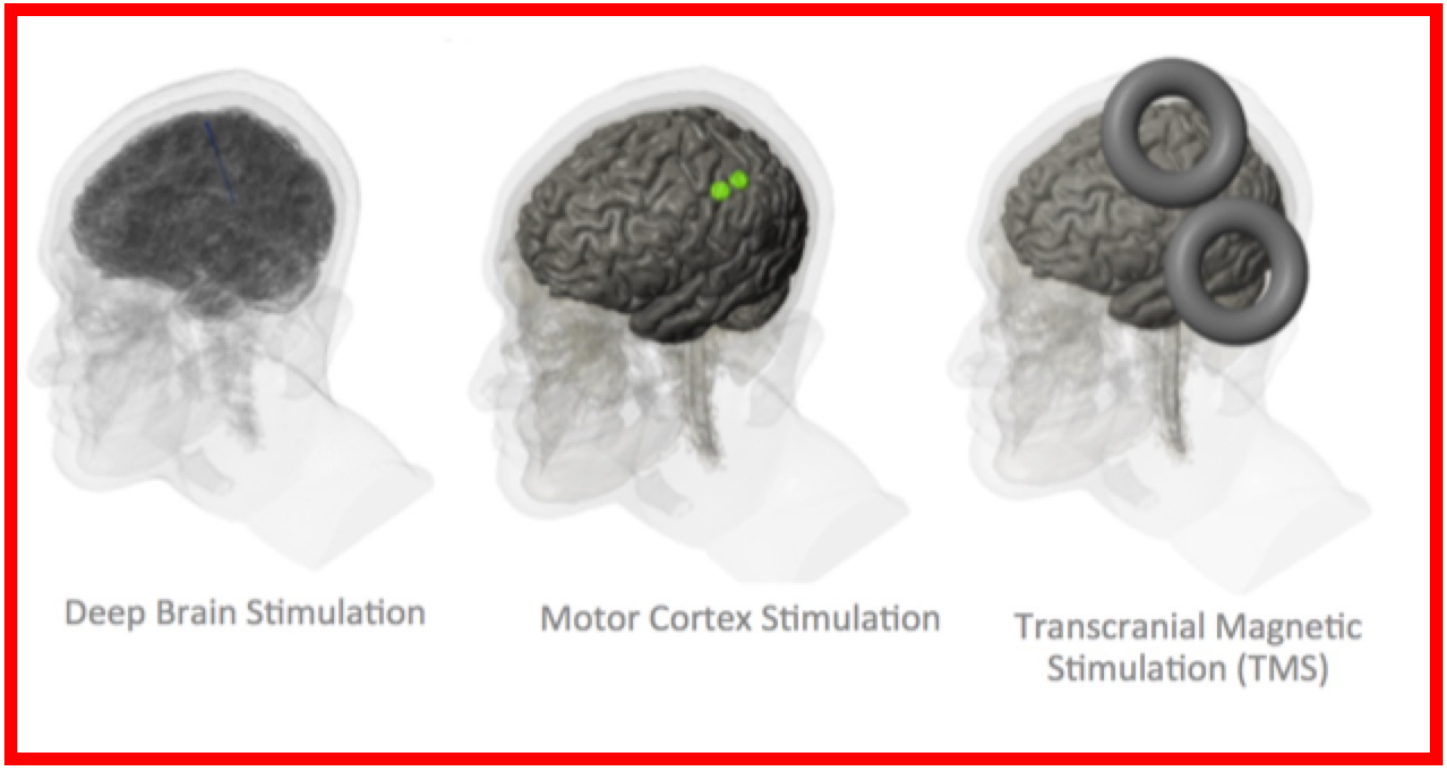
High-intensity Pulses

Low-intensity AC



Over-driving a
neural network

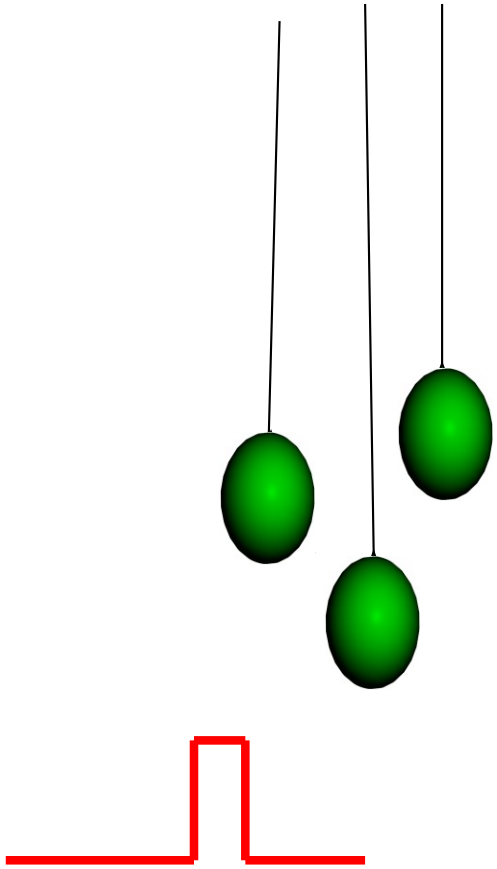
Nuance comes from dose
(pulse frequency, shape):
leading to non-linear changes



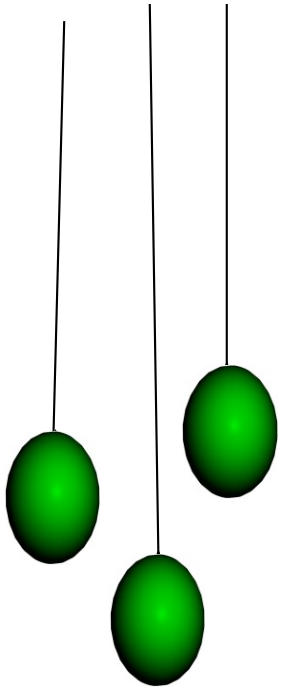
tACS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network



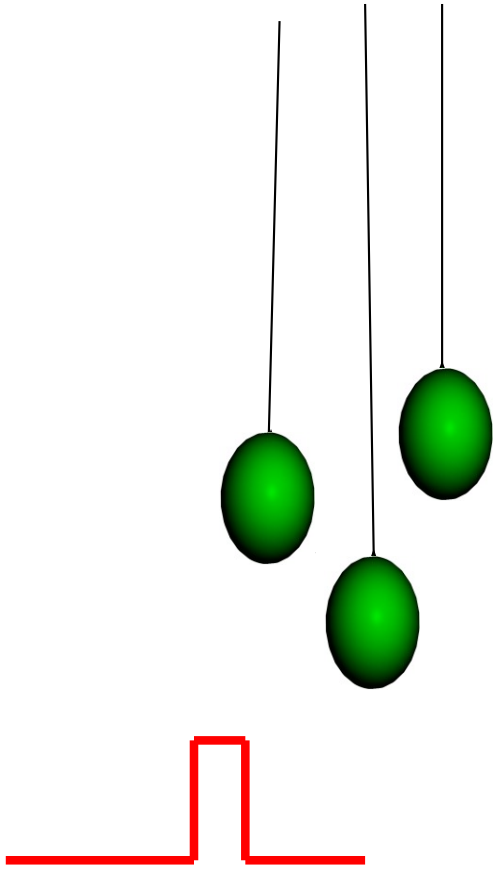
Low-intensity AC



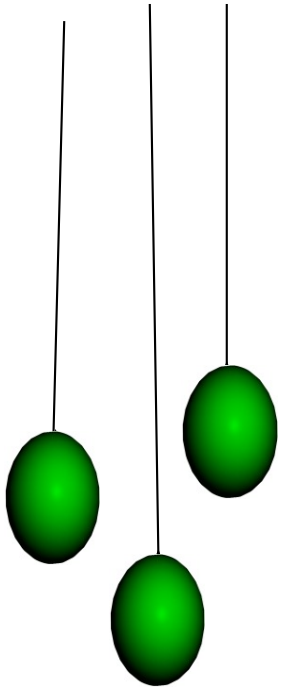
tACS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network



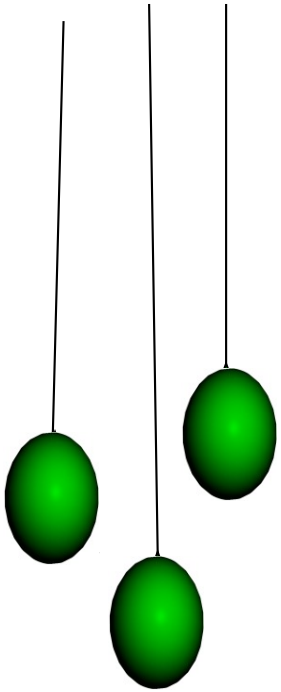
Low-intensity AC



tACS mechanisms: Neuromodulation

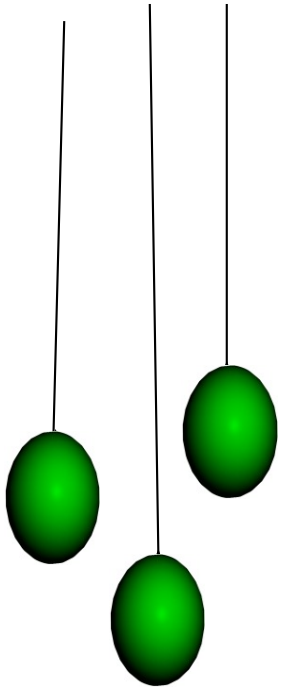
High-intensity Pulses

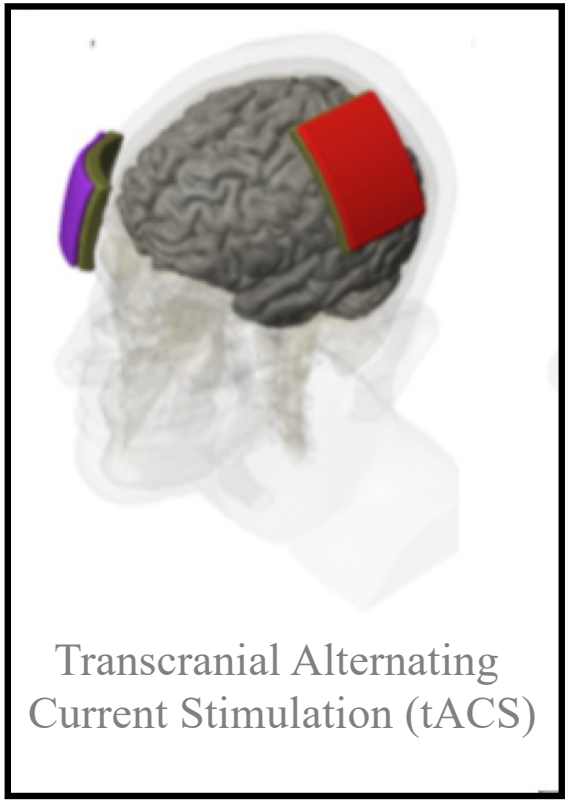
Over-driving a neural network



Low-intensity AC

Interacting with specific activity in a neural network

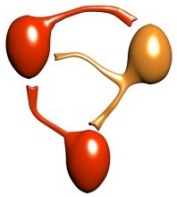


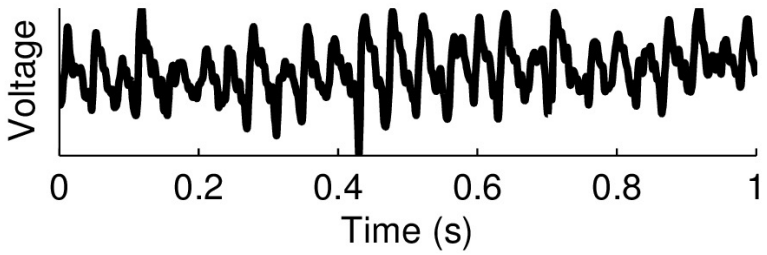


Transcranial Alternating Current Stimulation (tACS)

Direct Current Stimulation of Network Oscillations

Network Gamma Activity

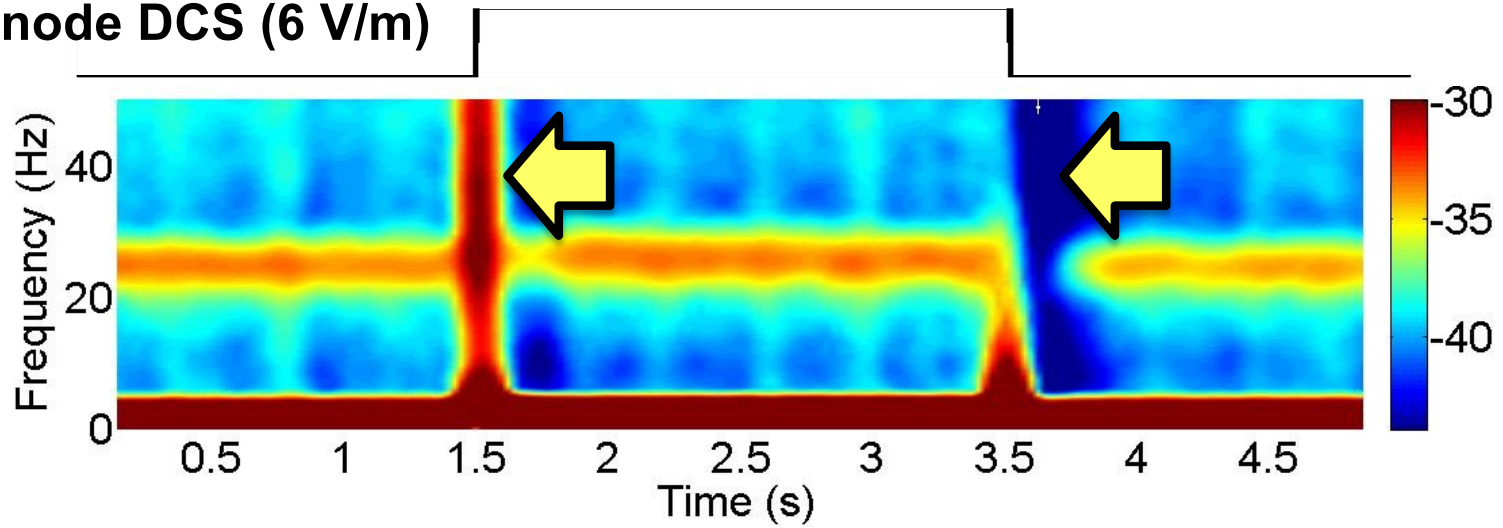




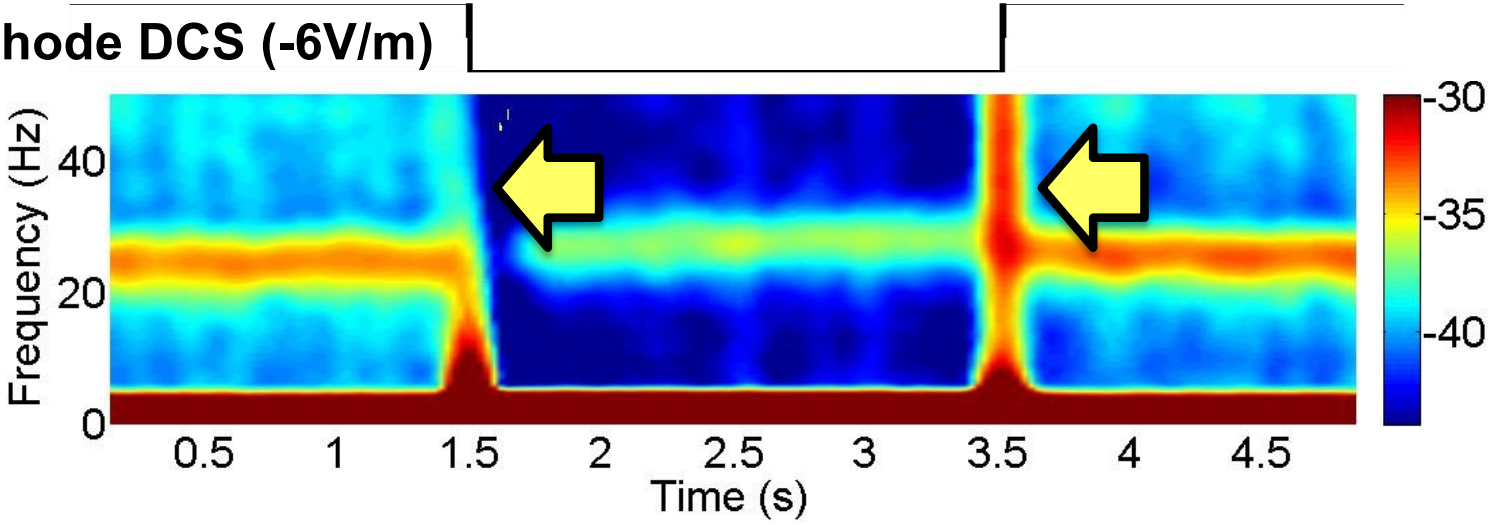
Brain Slice + Computational Model

Reato *J. Neurosci* 2010

Anode DCS (6 V/m)

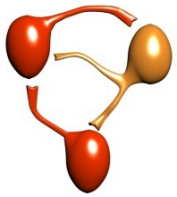


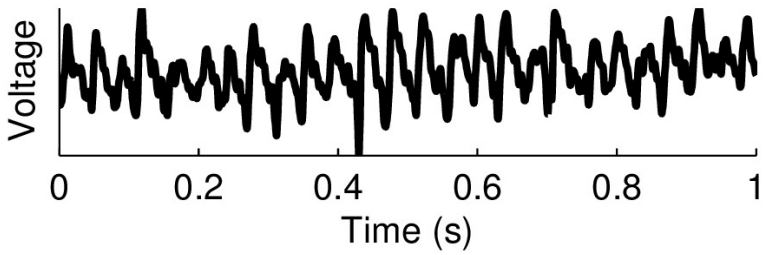
Cathode DCS (-6V/m)



Direct Current Stimulation of Network Oscillations

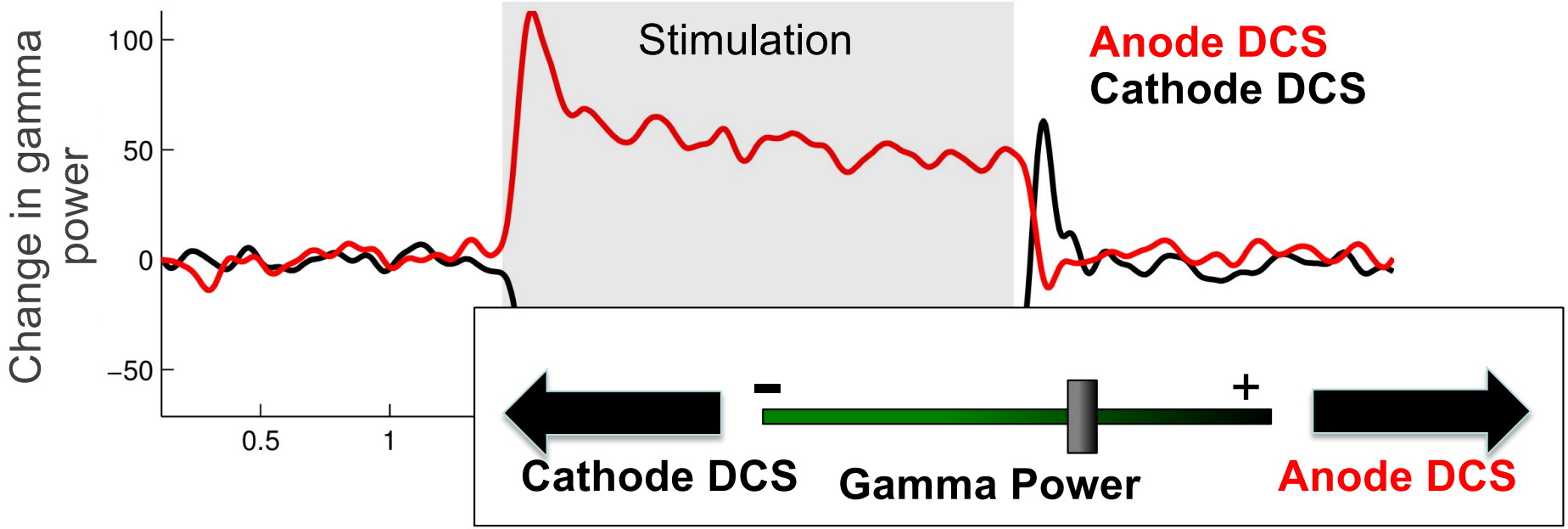
Network Gamma Activity





Brain Slice + Computational Model
Reato *J. Neurosci* 2010

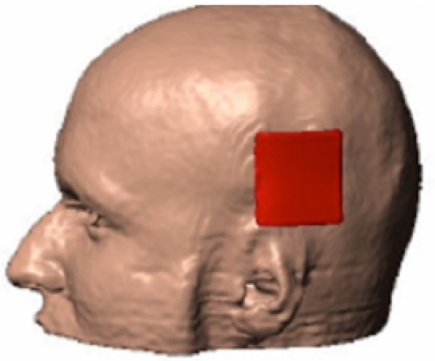
- **Boost (anode) or suppress (cathode) <u>ongoing</u> gamma oscillations**



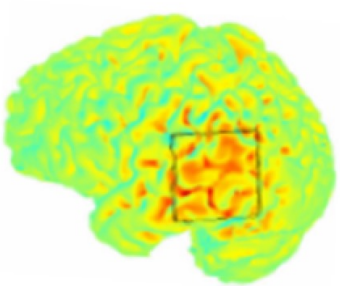
- **Gamma oscilations are a substrate for neuronal function / plasticity (learning)**

tDCS / ACS applied adjunct to cognitive therapy / rehabilitation / training

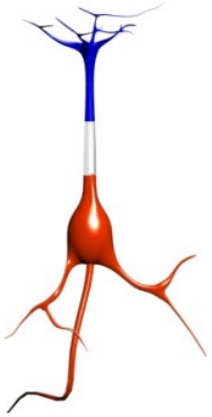
? Mechanism of tACS: Origins of Specificity



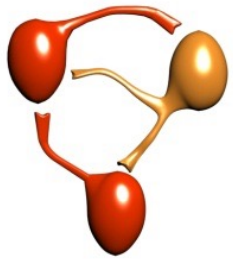
tACS



AC Current flow



AC cell polarization



Enhance of ongoing activity (oscillations)

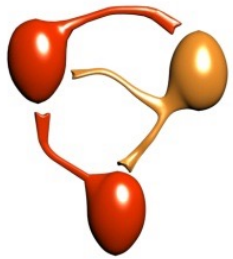
+

Subject training (therapy)

- Cellular substrate to enhance learning / adjunct therapy
- Task-specific facilitation: "Functional Targeting"
- tACS as a general tool to promote functional changes / neuroplasticity

- **Can a "simple" intervention modulate brain function?**
- **How is specificity of action achieved?**

? Mechanism of tACS: Origins of Specificity

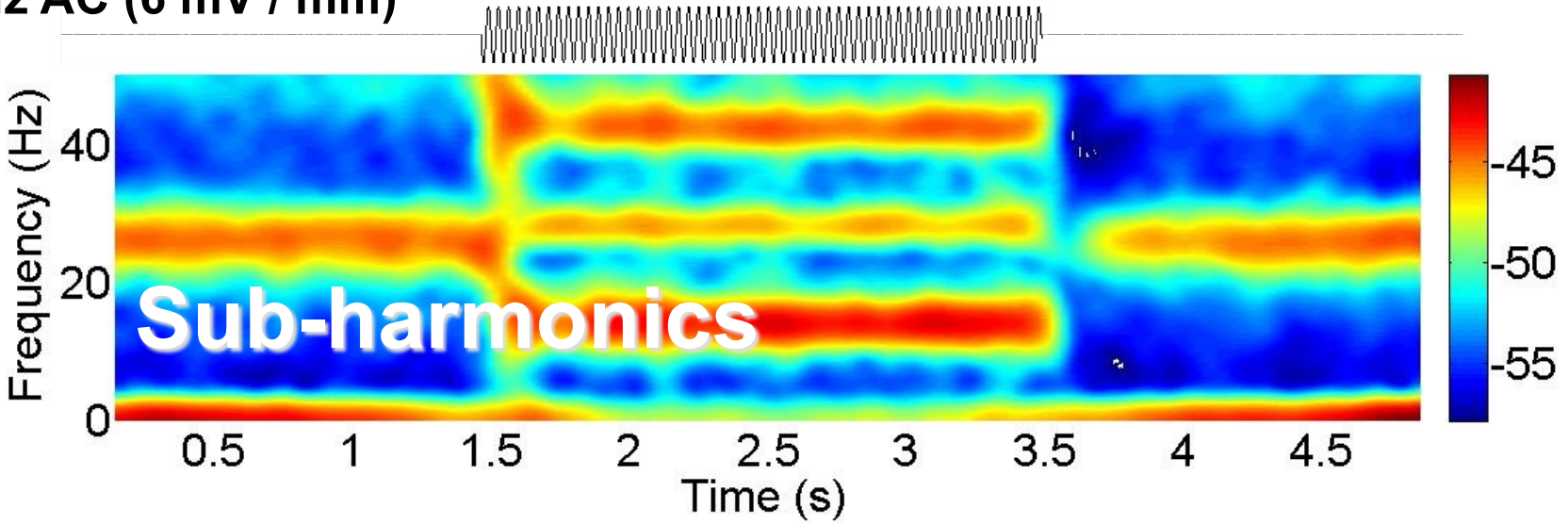


Enhance of ongoing activity (oscillations)

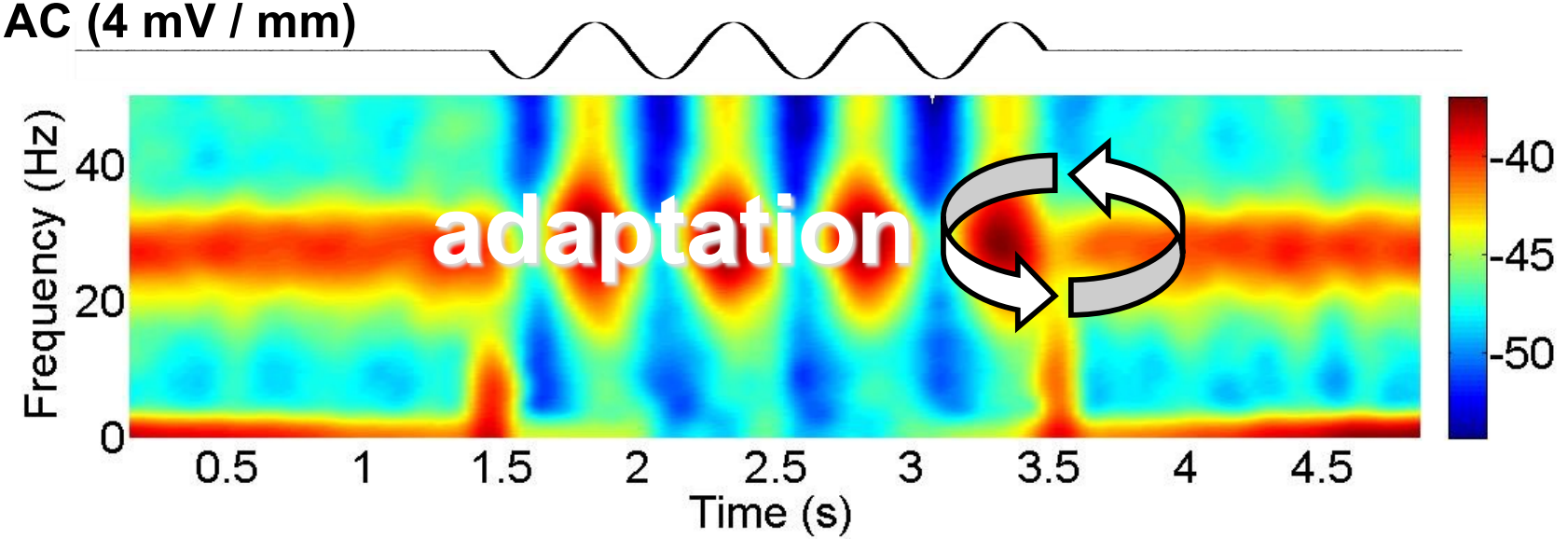
Complex AC stimulation of oscillations

Complex AC stimulation of oscillations

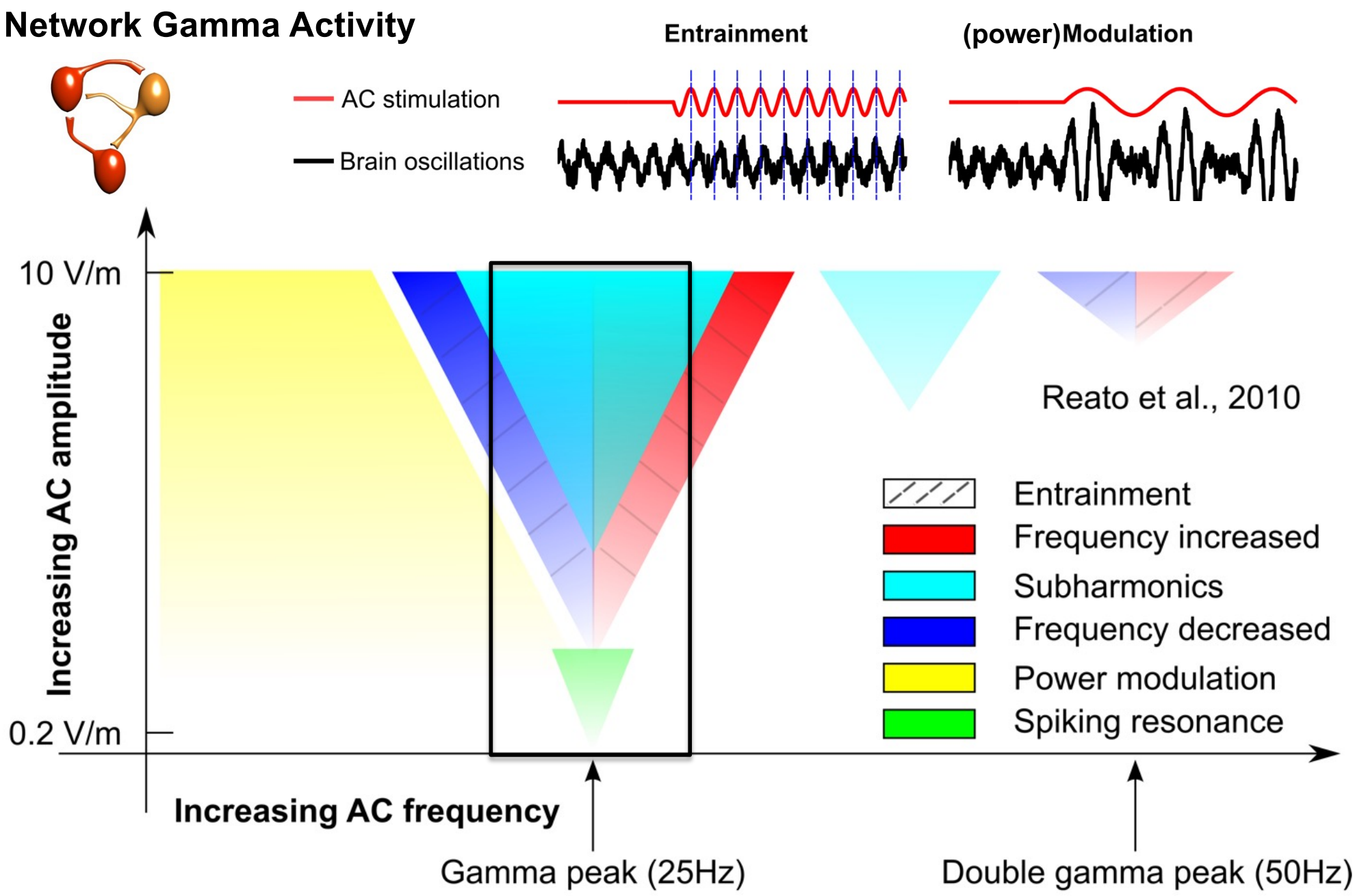
28 Hz AC (6 mV / mm)



2 Hz AC (4 mV / mm)

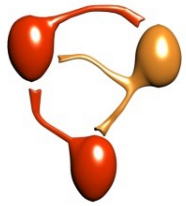


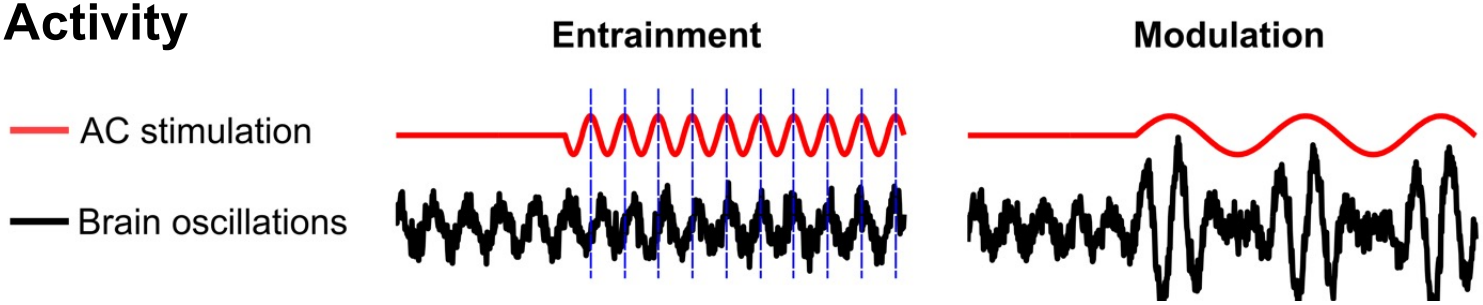
Alternating Current Stimulation of Network Oscillations

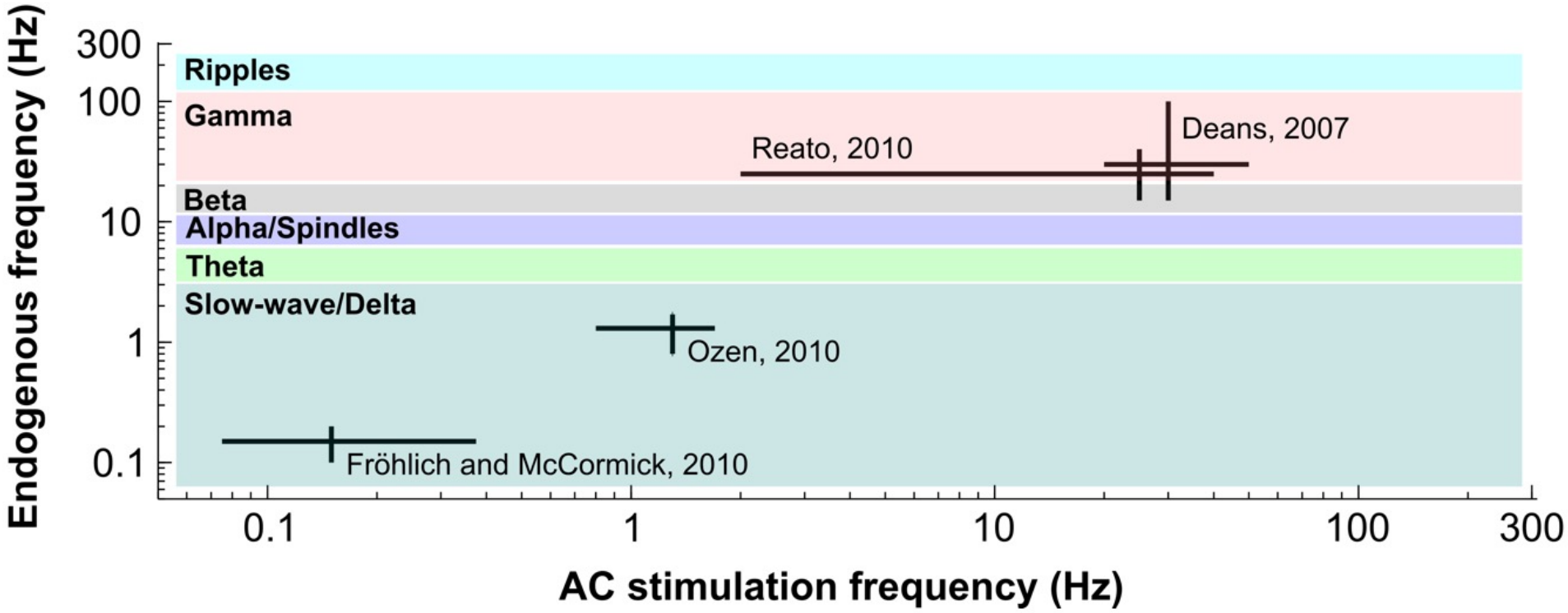


Alternating Current Stimulation of Network Oscillations

Network Gamma Activity

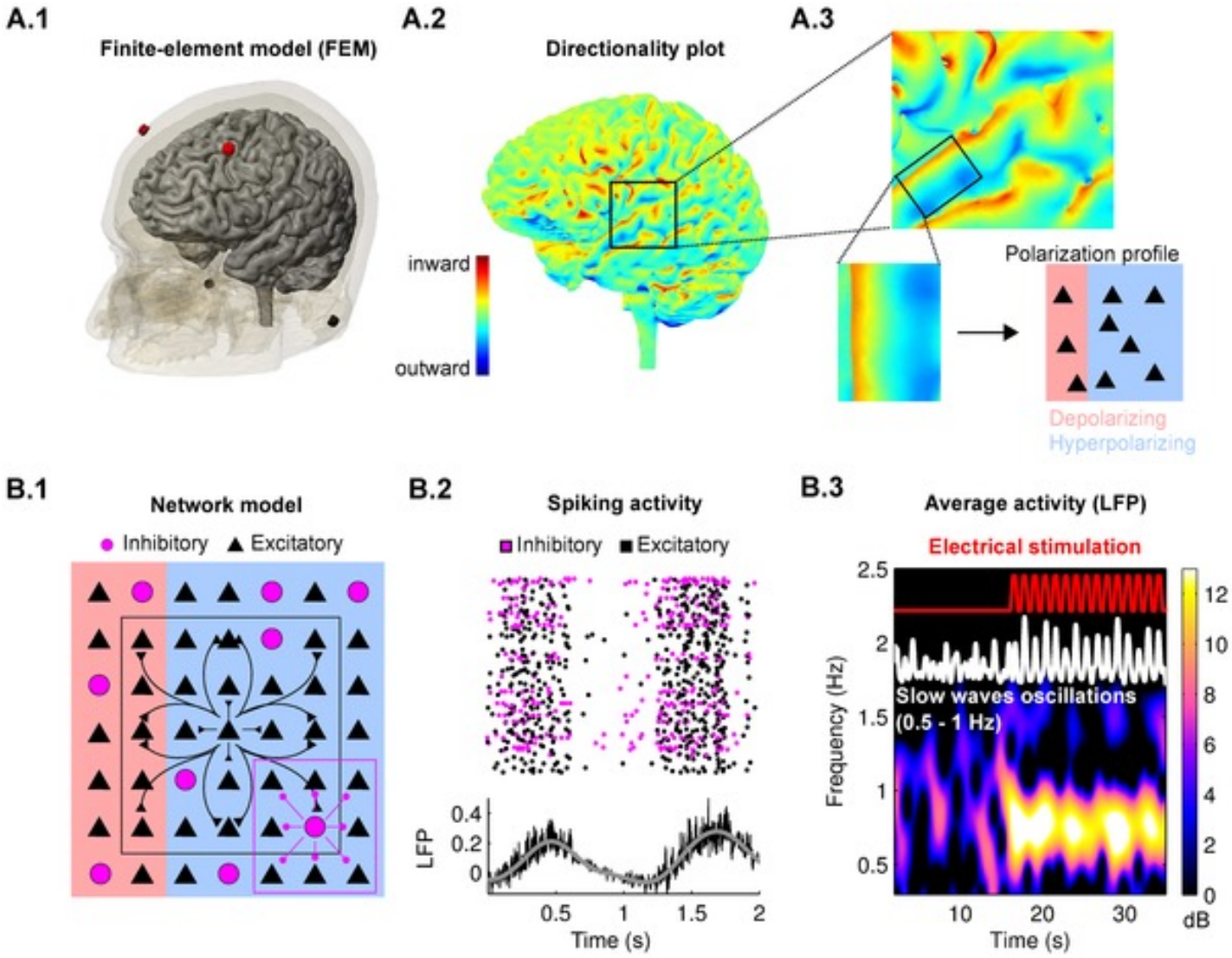






Reato et al. 2013 Frontiers of Human Neuroscience
Effects of weak transcranial Alternating Current Stimulation on brain activity
– a review of known mechanisms from animal studies.

tACS mechanisms: Neuromodulation

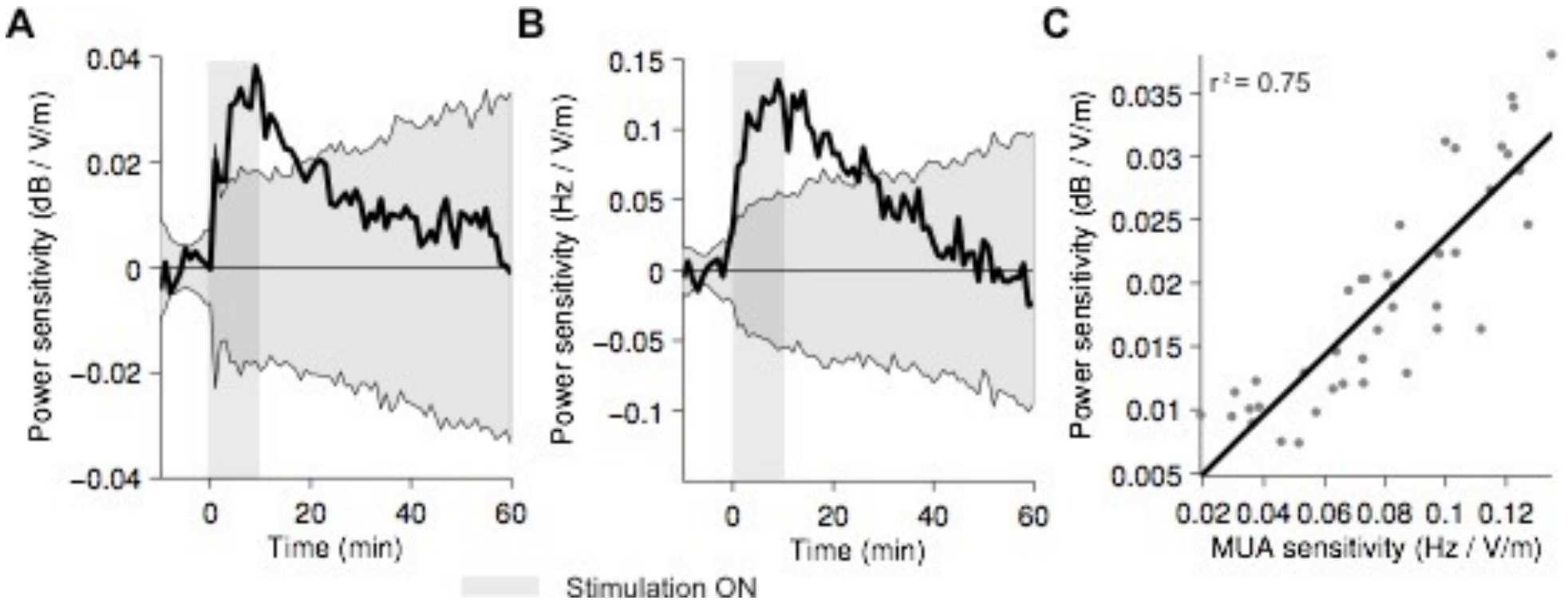


- Quantiative multi-scale models of tDCS modulated learning in sleep
- Full cellular to human behavior/learning integration

.

Reato et al. Plos Comput. Biol. 2013

tACS and plasticity



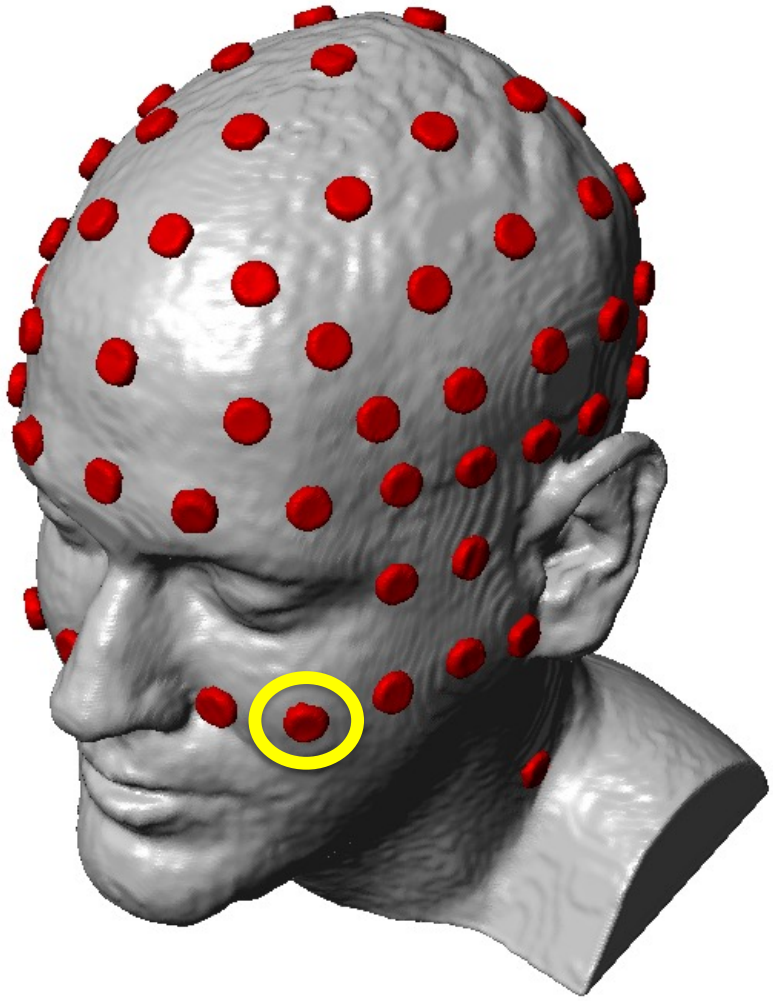
- Prolonged application of ACS produces cumulative changes in oscillation power and frequency.
- Prolonged application of ACS produces changes in oscillation power and frequency that outlast stimulation (~time of stimulation).
- Cellular and modeling analysis provides synaptic substrate for long-term changes.

Reato et al. J Neurophys 2015

Anatomical Specificity of HD-tES

Datta, Bikson, Alam

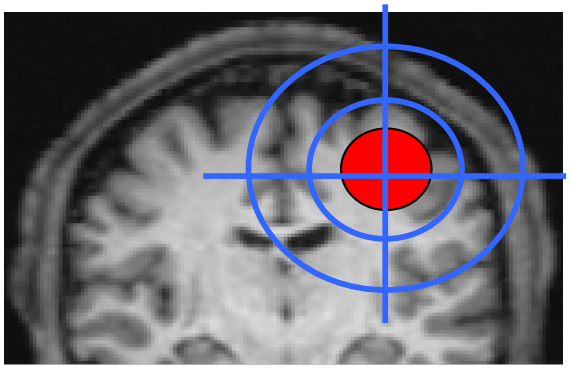
- High-Definition tES (HD-tES) array provides high degree of current flow control.
- Current at each electrode controlled to steer targeting
- Single non-invasive system with wide configurations: low-cost
- HD electrodes rated for 2+ mA peak, 22 min

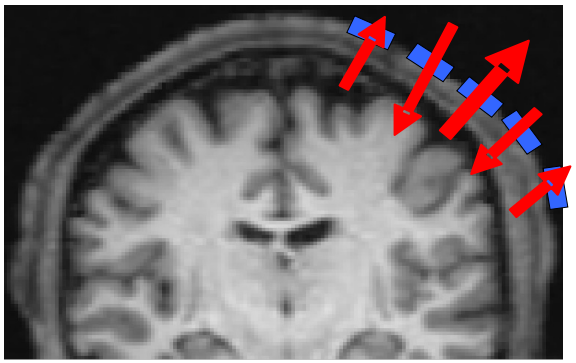


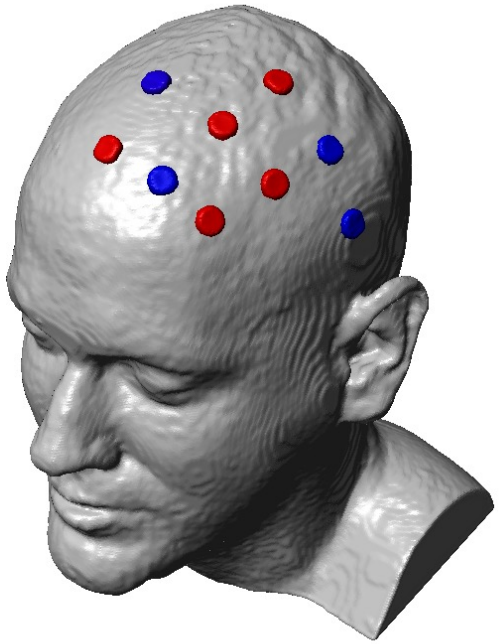
HD-tACS Optimization

- Given target and head anatomy: single "optimal" montage is close-form solution

Dmochowski
Bikson, Parra



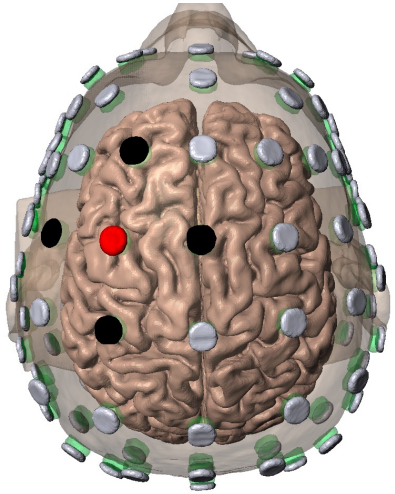




- Physican graphic user interface program
- One device, flexible dose
- Well tolerated (tDCS) + focal (TMS)

Wassermann (NIH), George (MUSC), Fridriksson (MUSC), Edwards (Cornell), Nitsche (Goettingen)…

- Individualized
- Integration with EEG and monitoring*



NeuroImage 185 (2019) 408–424

Contents lists available at ScienceDirect

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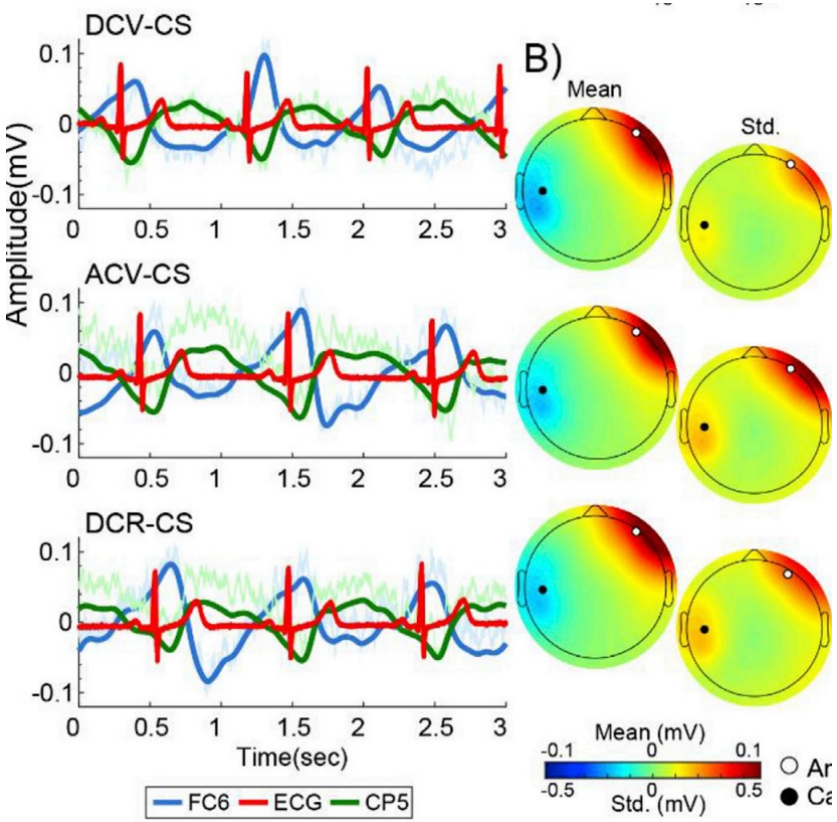
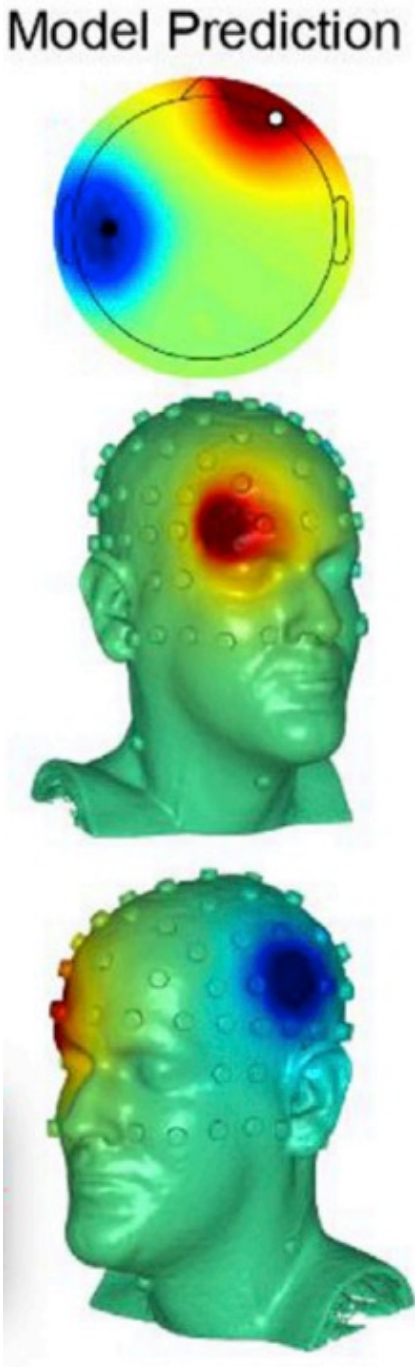
Inherent physiological artifacts in EEG during tDCS

Nigel Gebodh [a,**], Zeinab Esmaeilpour [a], Devin Adair [b], Kenneth Chelette [c], Jacek Dmochowski [a], Adam J. Woods [d], Emily S. Kappenman [e], Lucas C. Parra [a], Marom Bikson [a,b,*]



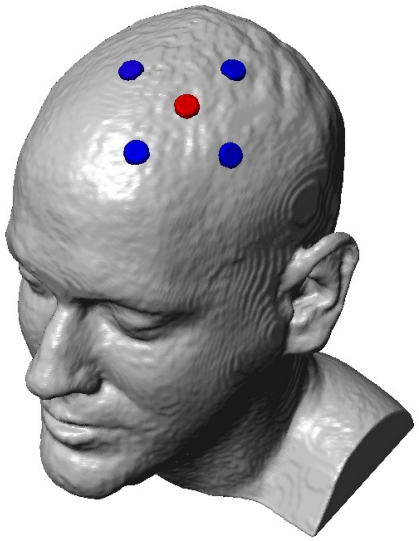


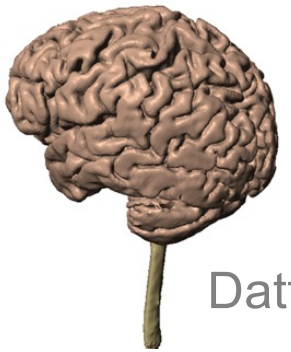
4x1 HD-tDCS

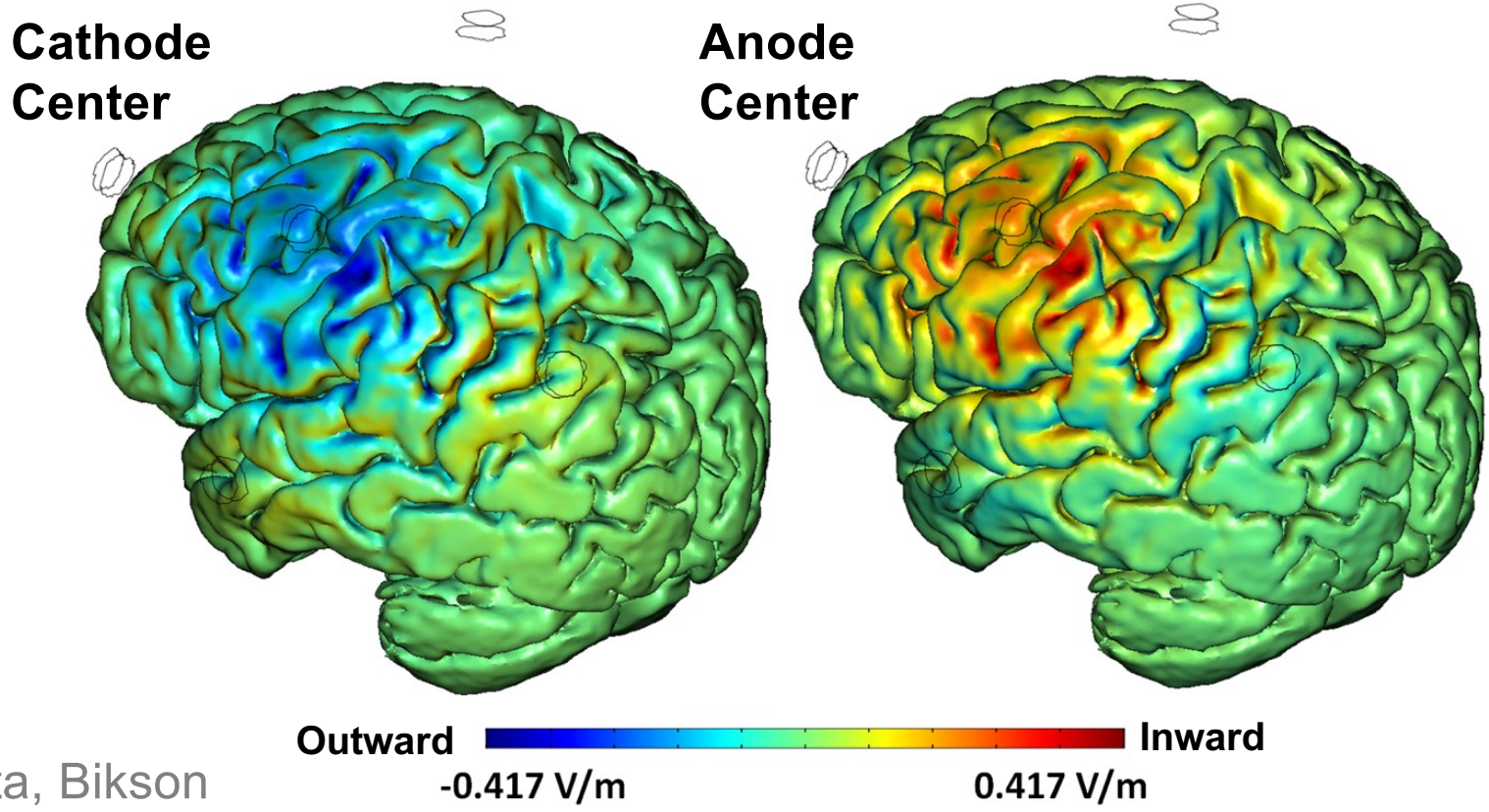
- 4x1 High-Definition tDCS (HD-tDCS) optimized for cortical targeting

4x1 HD-tDCS ”unidirectional”

- 4x1 High-Definition tDCS (HD-tDCS) optimized for cortical targeting
  - Center electrode determines polarity
    - ➢ Uni-directional modulation
  - Ring radius determines cortical focality
    - ➢ Skull resistivity is not the problem







Datta, Bikson

nature neuroscience

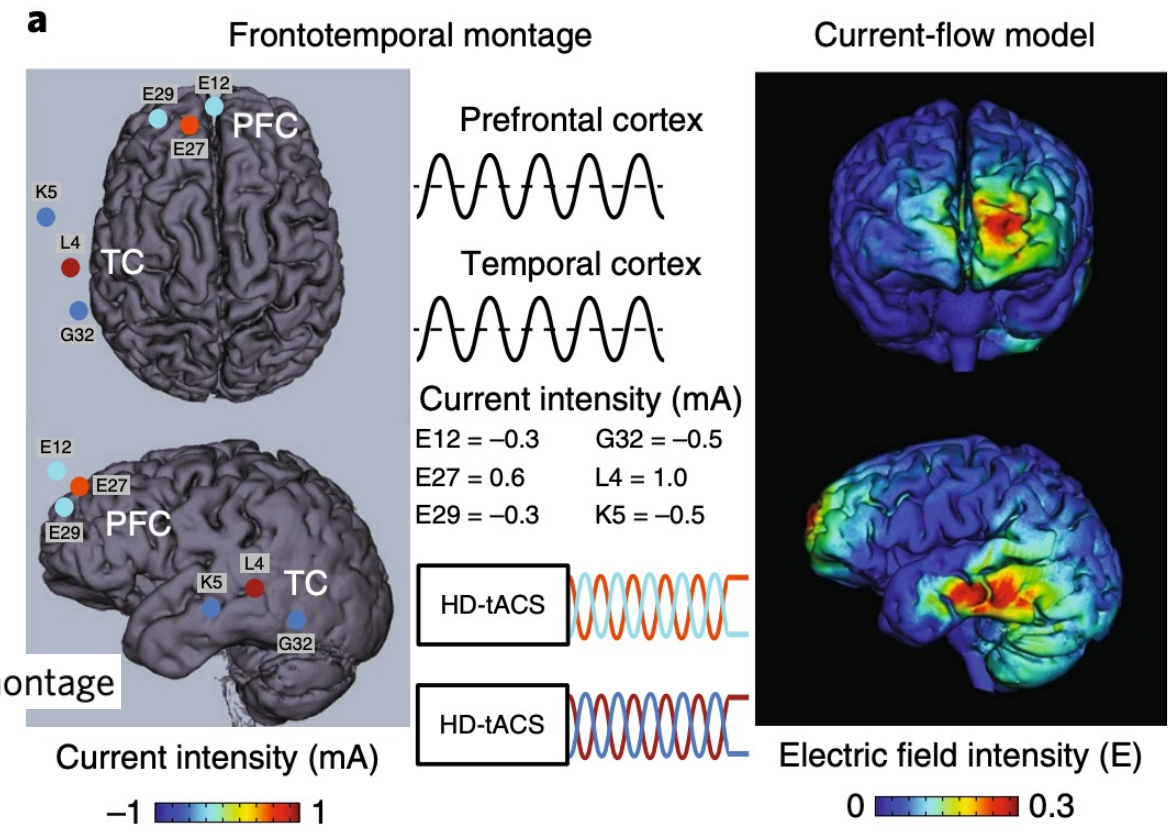
ARTICLES

https://doi.org/10.1038/s41593-019-0371-x

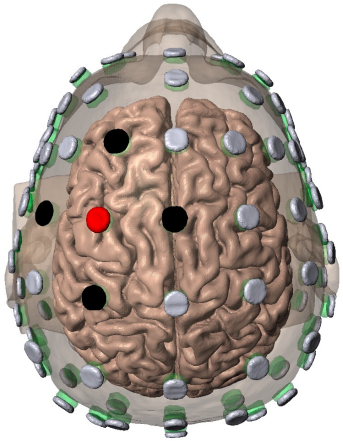
Working memory revived in older adults by synchronizing rhythmic brain circuits

Robert M. G. Reinhart * and John A. Nguyen

multifocal in-phase frontotemporal HD-tACS montage

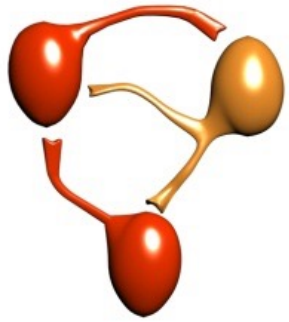


Technology and fundamentals of tACS



GGL section "Neurosciences" seminar on Transcranial Alternating Current Stimulation (tACS Lab Rotations in Gießen)

July 22, 2021



Marom Bikson

Lucas Parra, Dennis Truong, Abhishek Datta, Davide Reato, Asif Rahman, Belen Lafon, Thomas Radman, Preet Minhas, Yu Huang, Mahtab Alam, Alexander David, Ole Seibt, Zeinab Esmaeilpour, Jacek Dmochowski, Nigel Gebodh

Department of Biomedical Engineering, The City College of New York, New York, NY

$ NIH, NSF, Epilepsy Foundation, Wallace Coulter Foundation, DoD (AFOSR)