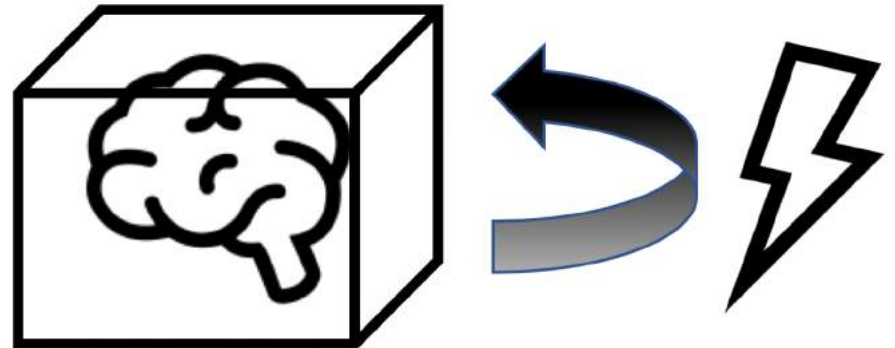


# Personalized Neuromodulation: Reading the Brain to Write the Brain

**Marom Bikson**

Lucas Parra, Jacek Dmochowski, Abhi Datta, Dennis Truong, Niranjan Khadka, Dennis Truong, Louis Zannou, Zeinab Esmailpour, Nigel Gebodh, Belen Lafon, Tianhe Zhang, Rosana Esteller, Brian Kopell, Brad Hershey, Gozde Unal, Mohamad Rad, Andy Huang



2019 joint meeting **Neuromodulation: The Science and NYC Neuromodulation**,  
Session 1: New Engineering of Neuromodulation & Brain Machine Interfaces  
Oct 4, 2019, Napa, California.

## **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

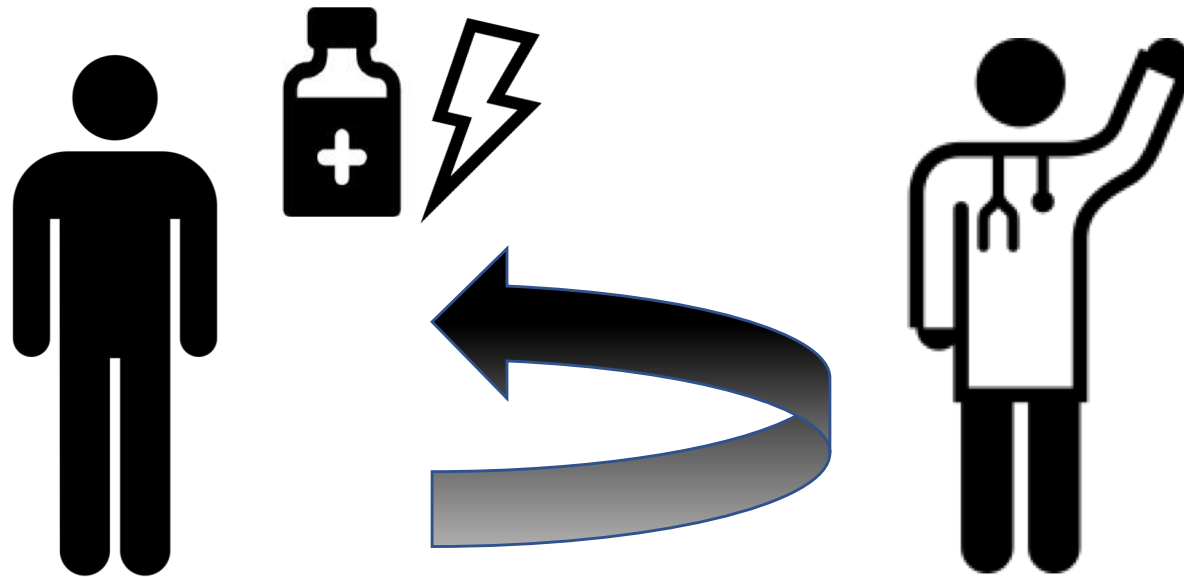
## **Support**

NIH (NIMH, NINDS, NCI, NIBIB) – *BRAIN Initiative*, NSF, Grove Foundation, Harold Shames, CCNY Fund, 21<sup>st</sup> Century Fund, “X”

Slides and References @MaromBikson



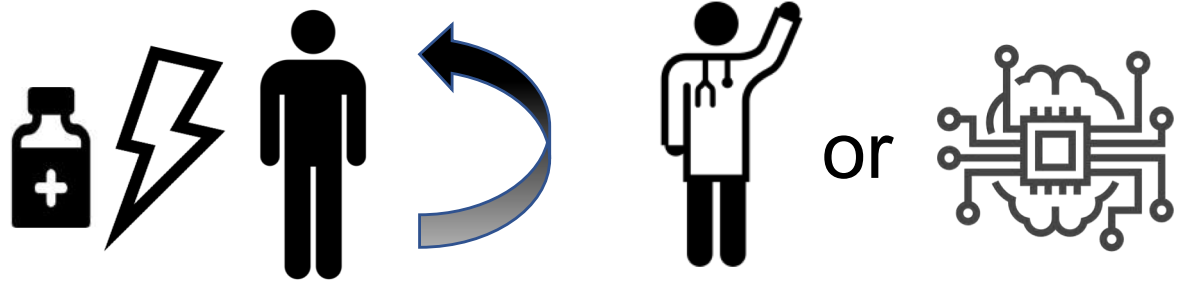
## Neuromodulation is individualized



Dose is titrated (on the scale of device design, clinical trials, individual treatment, responsive stimulation)

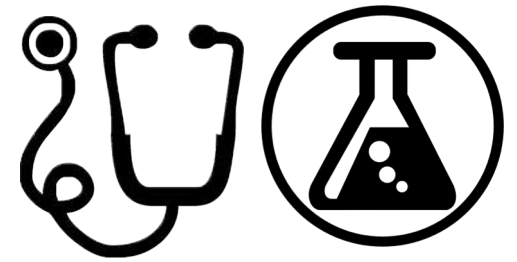
## Dose titration

- A) Open-loop
- B) Closed-loop



based on

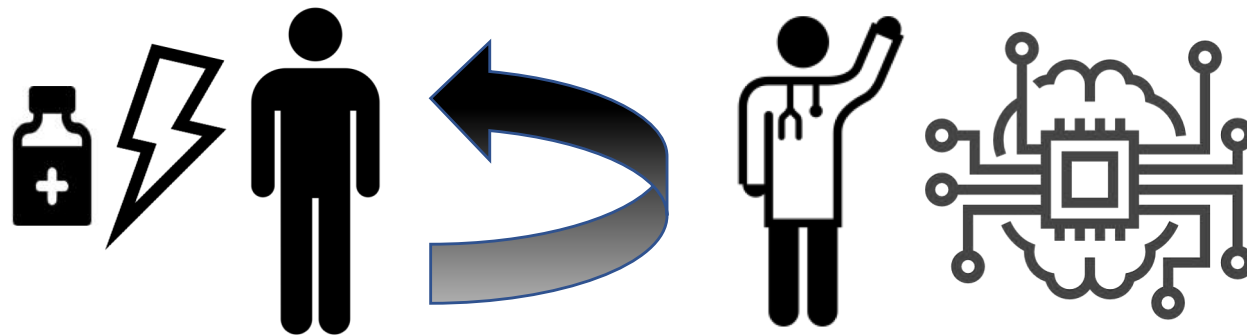
- 1) Clinical endpoints
- 2) Biomarker of treatment response
- 3) Biomarker of target engagement



**The only treatment reason to use biomarker or closed-loop is to accelerate dose titration.**

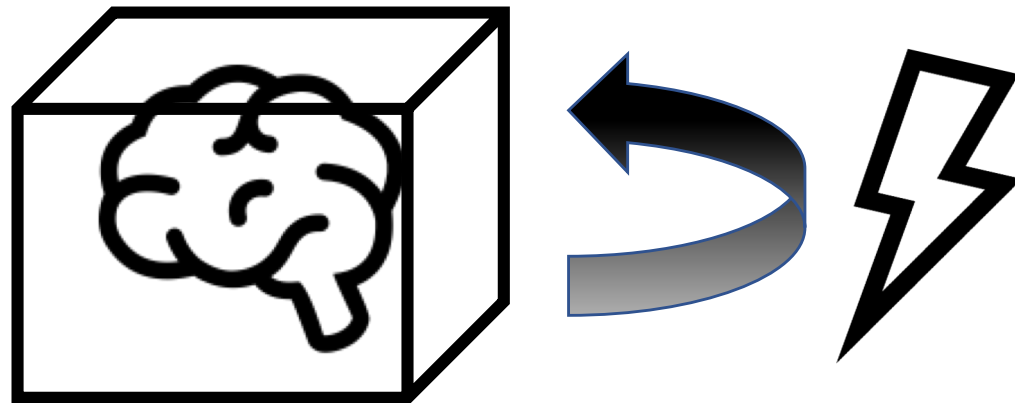
How we titrate (optimize) is the hypothesized mechanism of action

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# Neuromodulation is leading our understanding of normal brain function and pathology

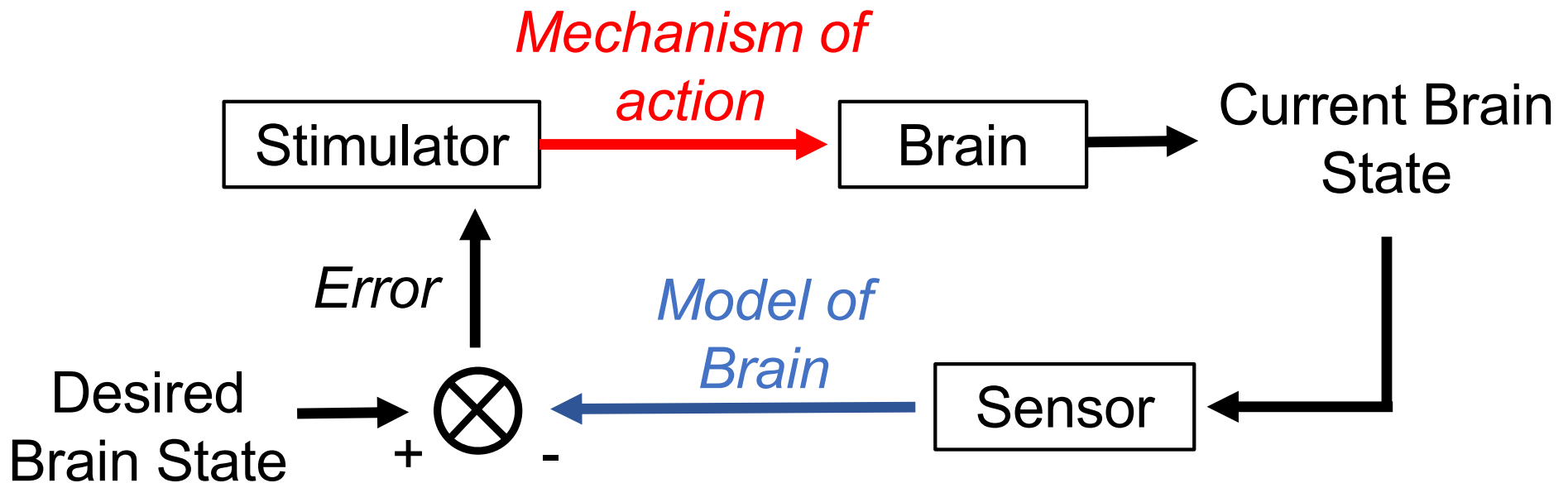
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When characterizing (complex systems) a method to perturb the system is required

# When biomarker is brain state

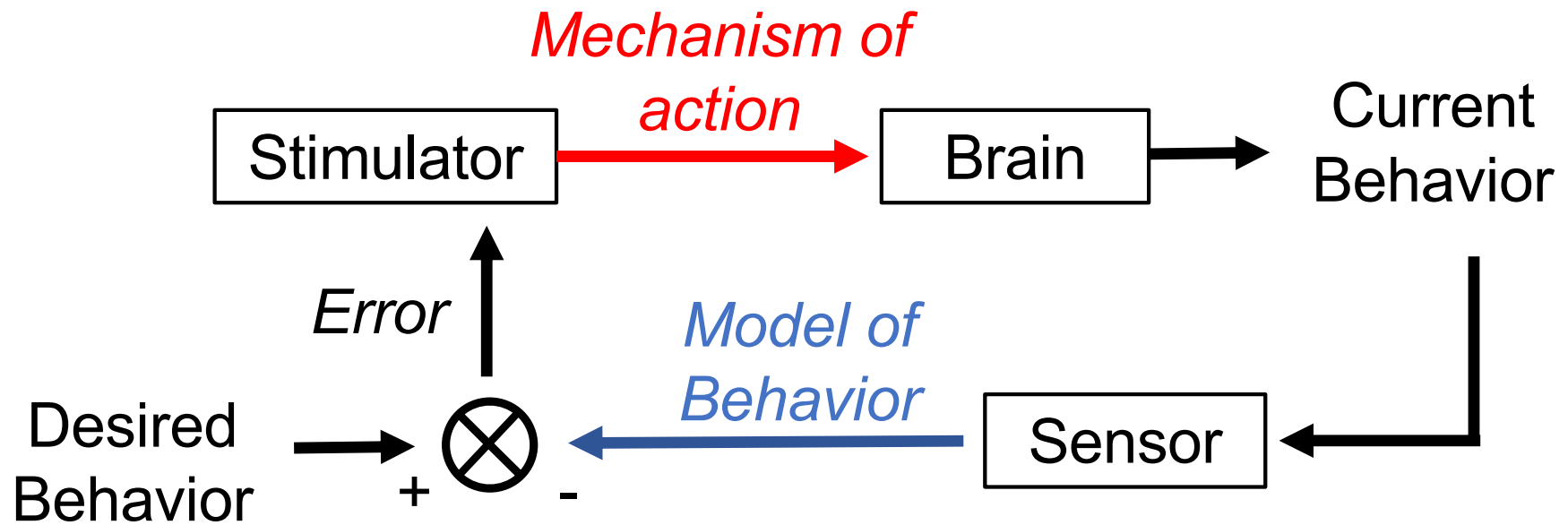
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- Electrophysiology uses neuromodulation tech [electrode]
- BCI: when there is “intent”

# When biomarker is behavior

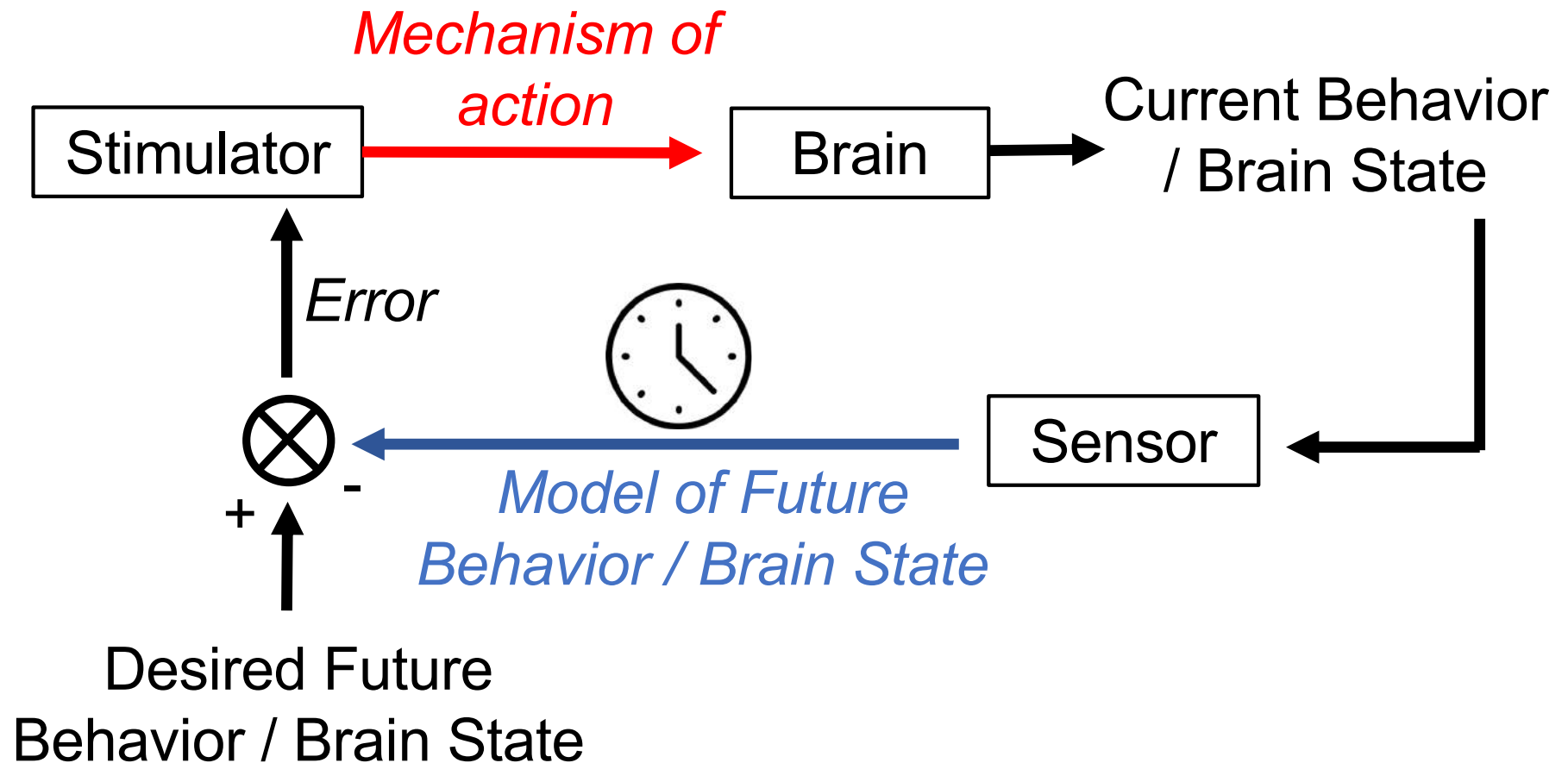
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# Forecasting with Biomarker

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## Invasive



- Focal
- Chronic:  
acute mechanisms

## Non-invasive



- Not focal
- Out-patient:  
plastic mechanisms

Invasive



- ~~Focal~~
- ~~Chronic:~~  
acute mechanisms

Non-invasive

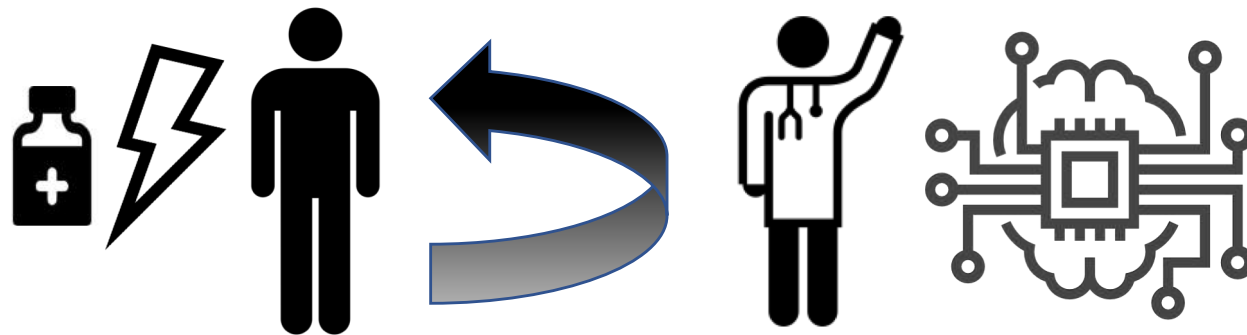


- ~~Not focal~~
- ~~Out-patient:~~  
plastic mechanisms

- Model driven design
- Circuit neuromodulation
- Bioelectronic medicine
  - Wearables
  - Closed-loop
- Brain-state dependent

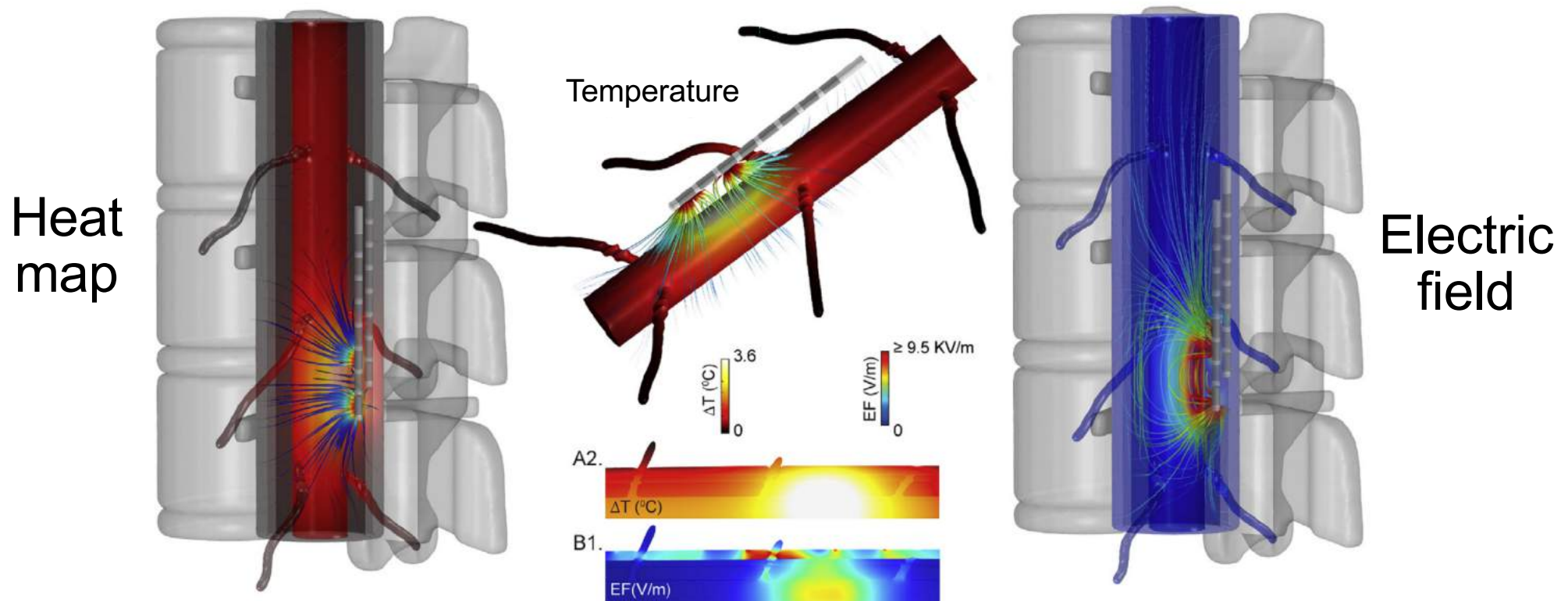
How we titrate (optimize) is the hypothesized mechanism of action

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# Heating mechanism of kHz (high density) SCS / DBS

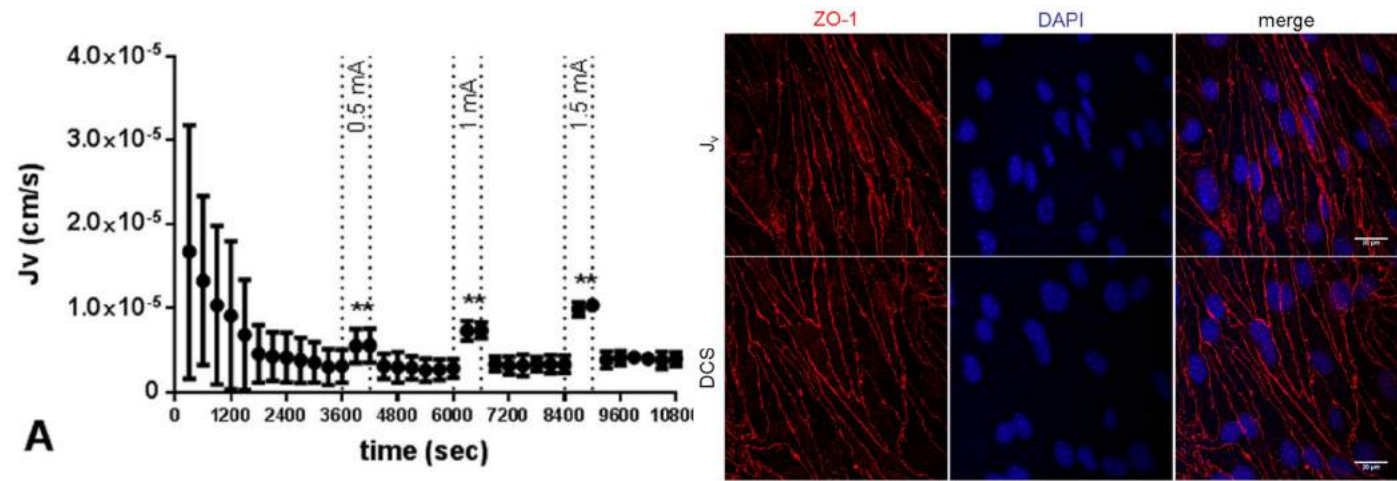
Optimize based on power, not pulse shape or frequency



Zannou et al. Temperature increases by kilohertz frequency SCS. *Brain Stim* 2019

# Novel cellular targets of tDCS / DBS

Coupled Neuro-Vascular Hypothesis of Neuromodulation  
Optimize for BBB modulation with biomarker

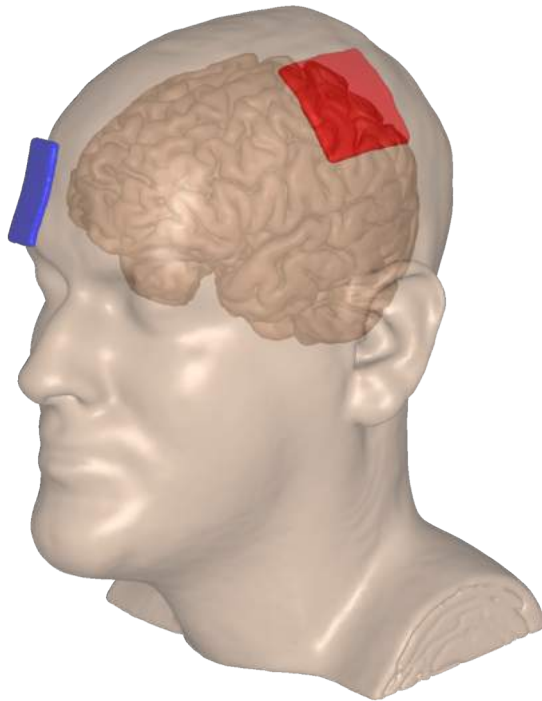


Lopez-Quintero et al. DBS-relevant electric fields increase hydraulic conductivity of in vitro endothelial monolayers. *J Neuro Engr.* 2010

Cancel et al. Direct current stimulation of endothelial monolayers. *Sci Reports* 2018

# Focal transcranial electrical stimulation

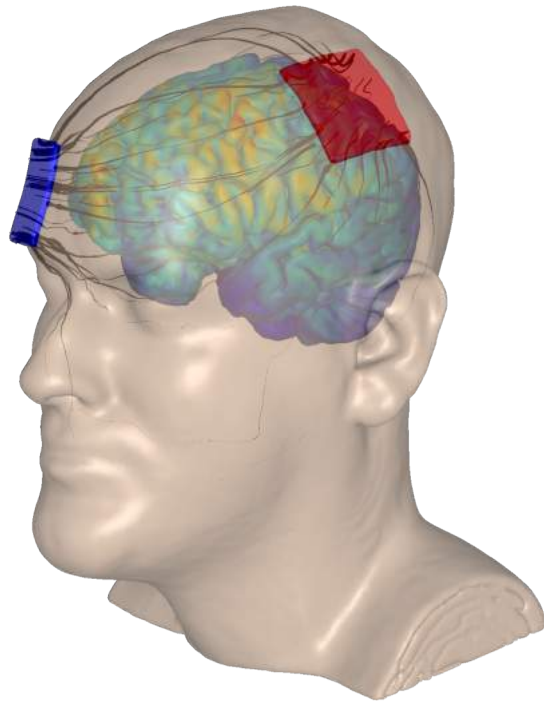
# tDCS / tACS



Experimentally-  
verified Anatomical  
MRI derived models  
of current flow

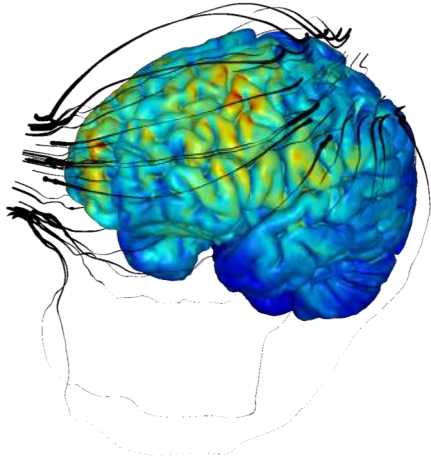


# tDCS / tACS



Experimentally-  
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MRI derived models  
of current flow

# tDCS / tACS

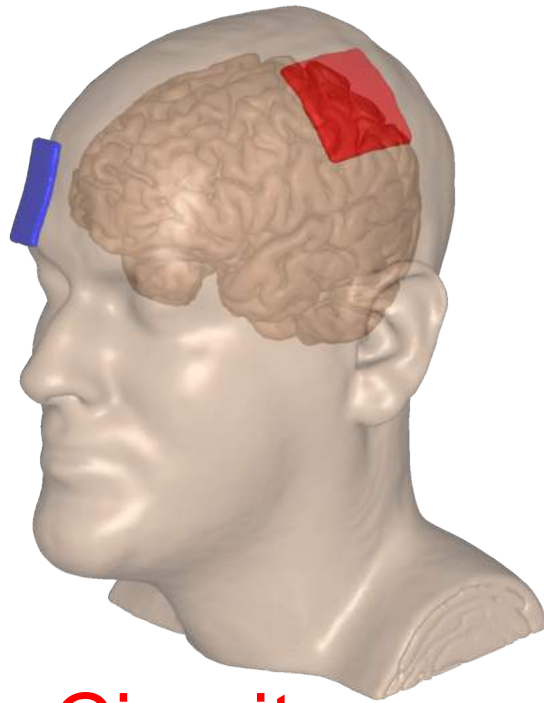


**Circuit  
therapeutics**



Experimentally-  
verified Anatomical  
MRI derived models  
of current flow

# tDCS / tACS

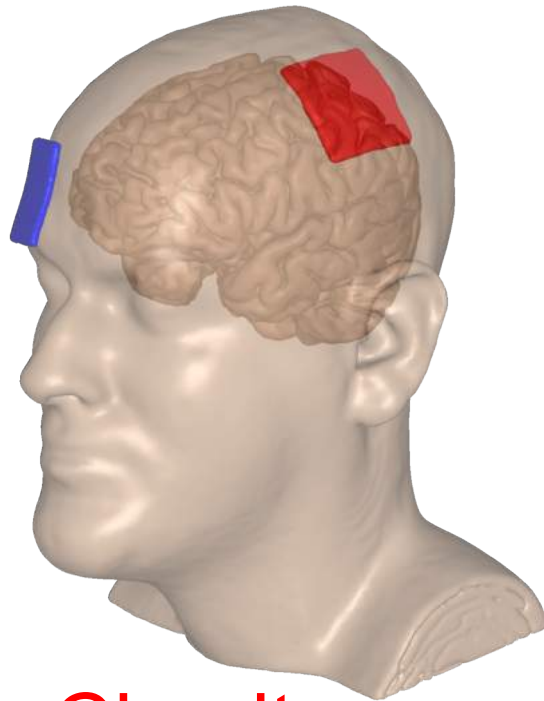


Circuit  
therapeutics



Experimentally-  
verified Anatomical  
MRI derived models  
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## tDCS / tACS

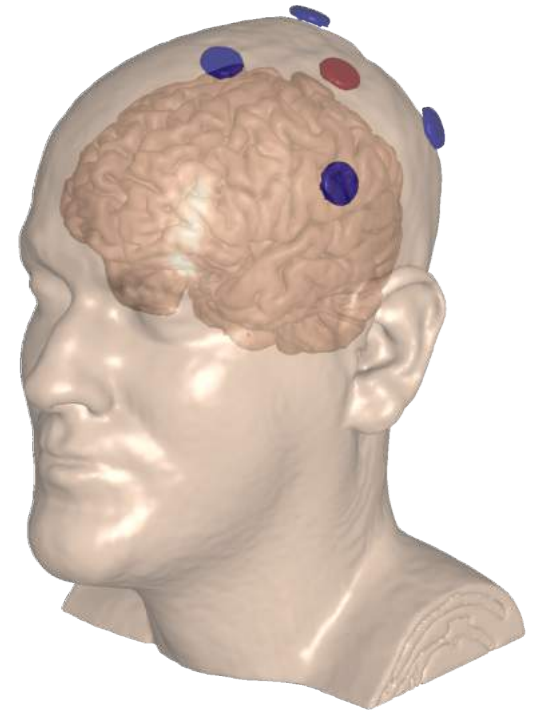


**Circuit  
therapeutics**

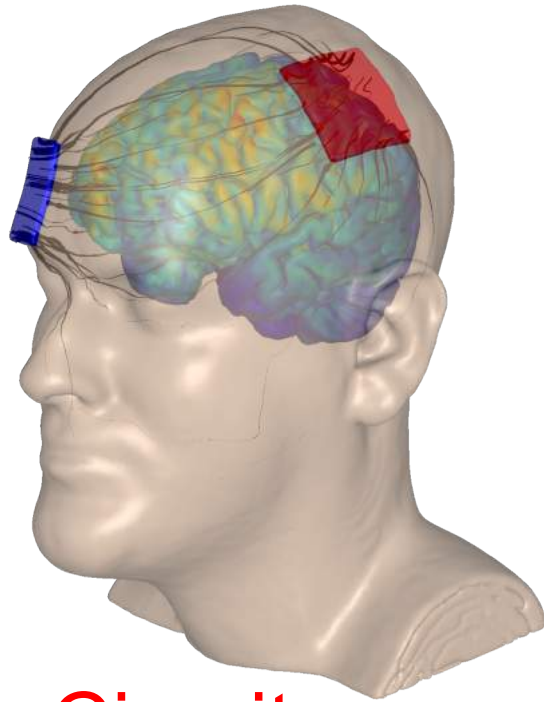
## High Definition tES



Experimentally-  
verified Anatomical  
MRI derived models  
of current flow



## tDCS / tACS

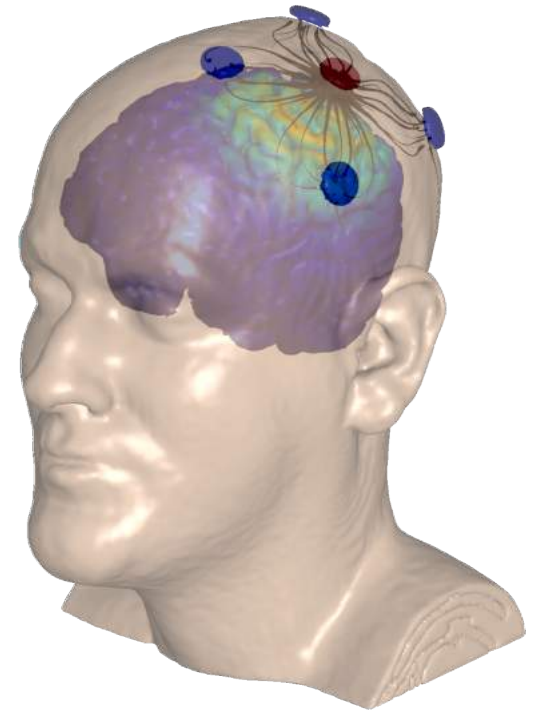


**Circuit  
therapeutics**

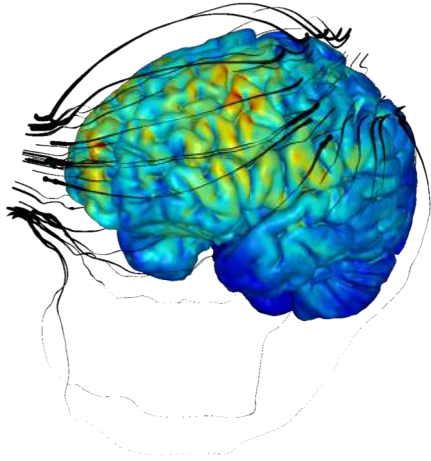
## High Definition tES



Experimentally-  
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## tDCS / tACS

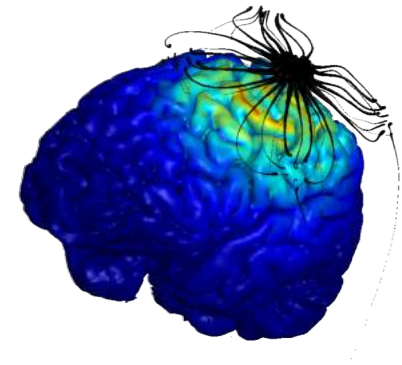


**Circuit  
therapeutics**

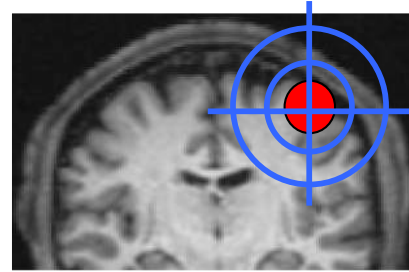
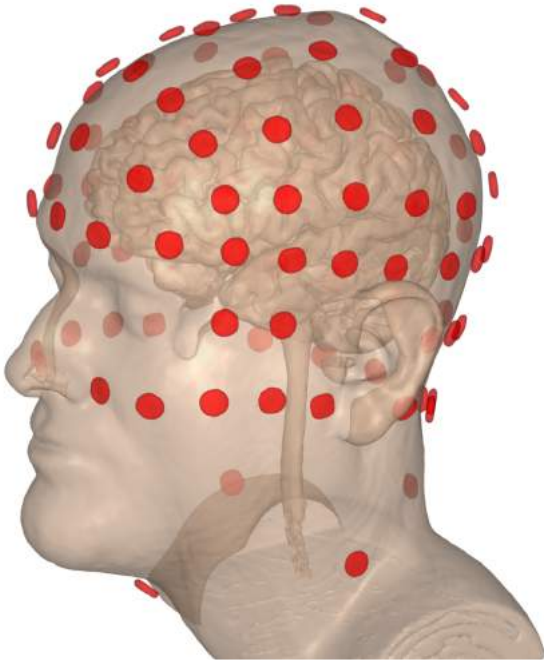
## High Definition tES



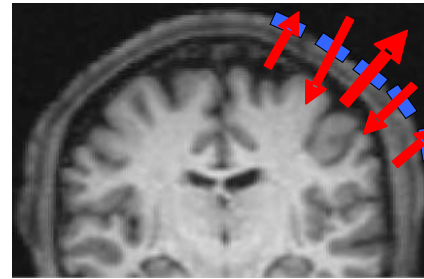
Experimentally-  
verified Anatomical  
MRI derived models  
of current flow



**Non-invasive  
electrical  
targeting**



Identify target



Select current  
per electrode

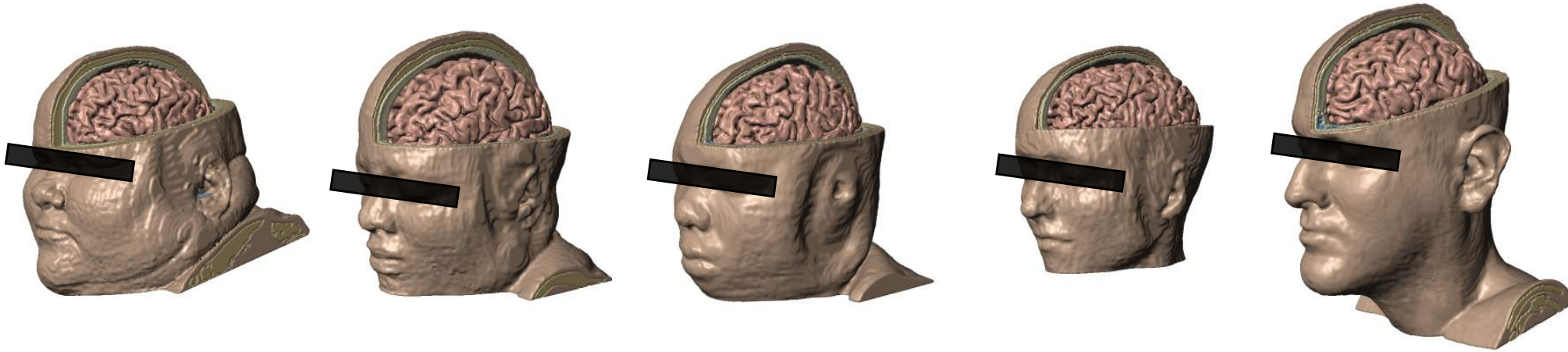
- Software steers currents to targeted brain regions
- Single programmable device and head-gear
- **Arbitrary / interacting waveforms**

Dmochowski JP, Datta A, Bikson M, Su Y, Parra LC. Optimized multi-electrodes stimulation increases focality and intensity at target. *J Neural Engr* 2011

Individualized transcranial electrical stimulation



## Individual Differences

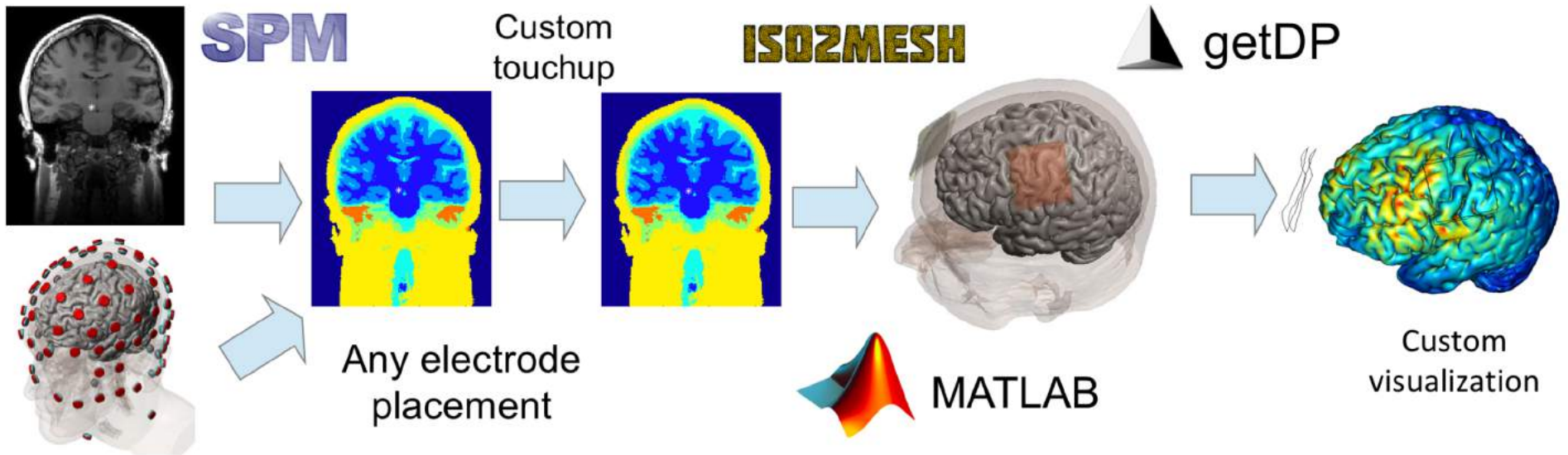
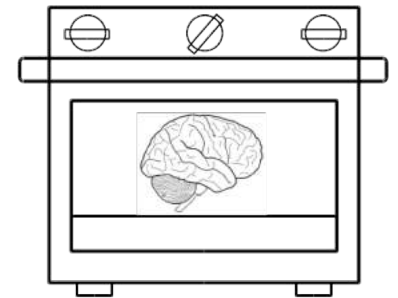


- Different anatomy → Different brain current flow.
- Including for atypical anatomy (neurodegenerative disorders, brain injury), extremes of age...
- **When applying the same dose across a population, aggregate response reflect individual variability.**

# Realistic vOlumetric-Approach-based Simulator for Transcranial electrical stimulation

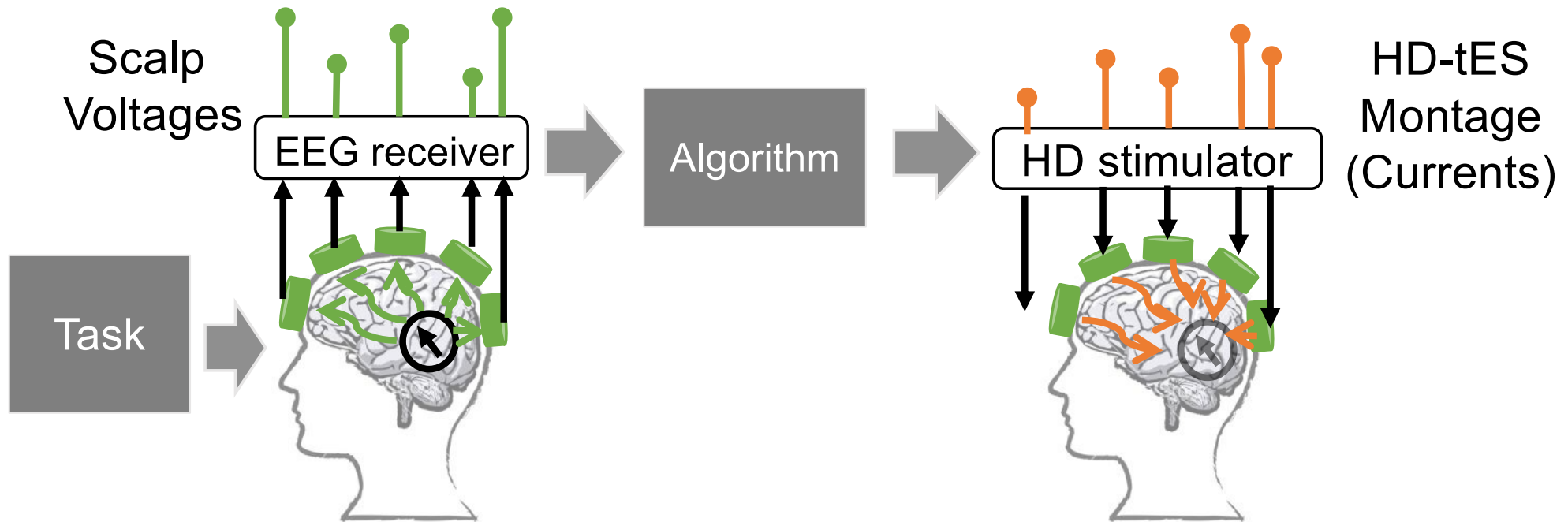
# ROAST

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

## 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

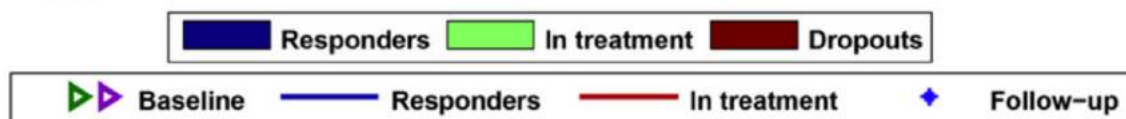
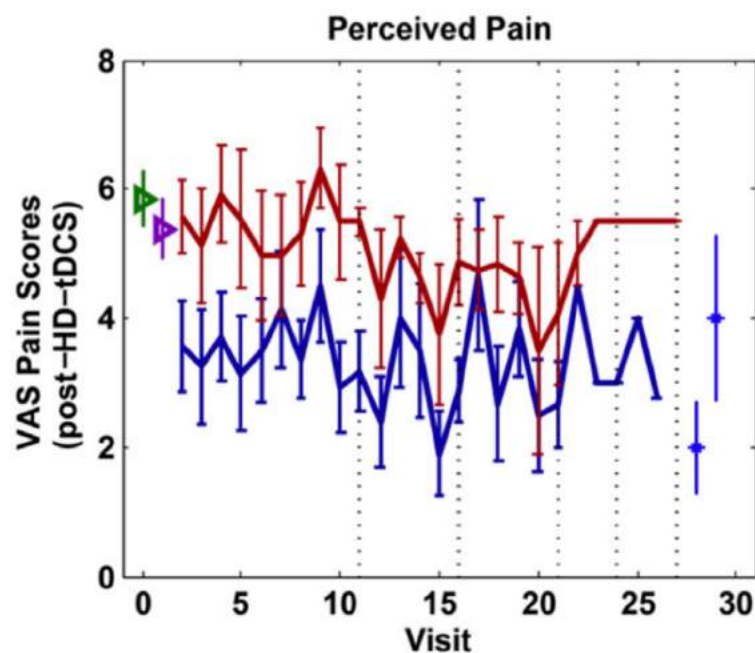
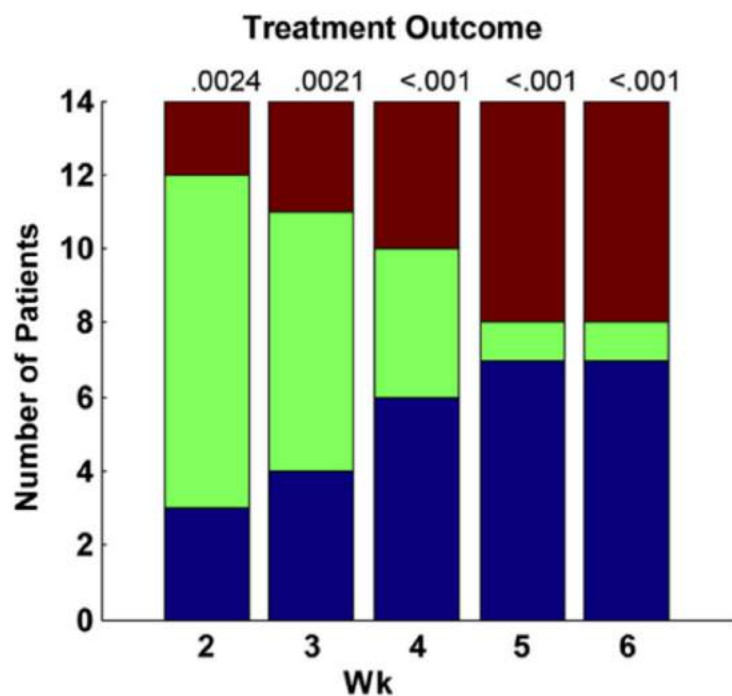
## Phase II (Harvard/Spaulding) **Fibromyalgia pain**

Daily in-clinic sessions of EEG Guided HD-tDCS, open label



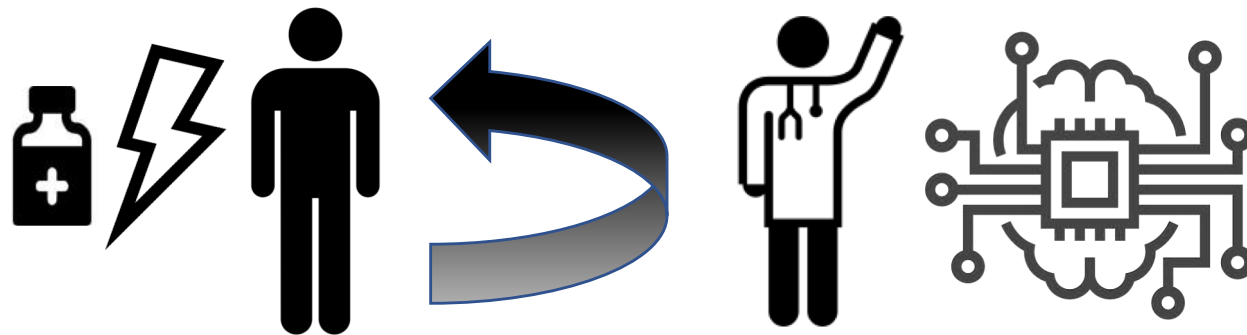
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How we titrate (optimize) is the hypothesized mechanism of action

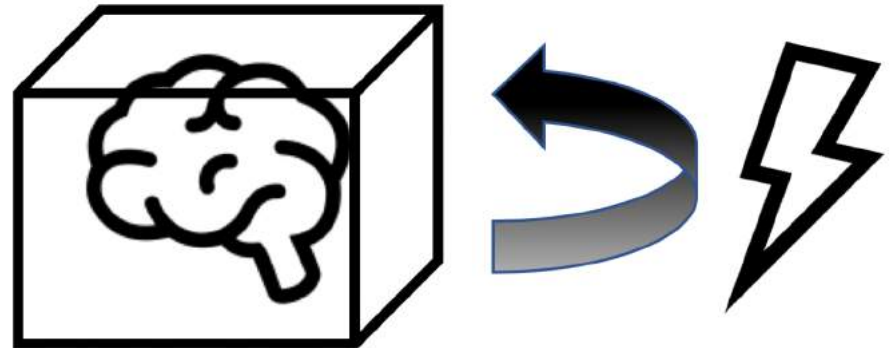
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