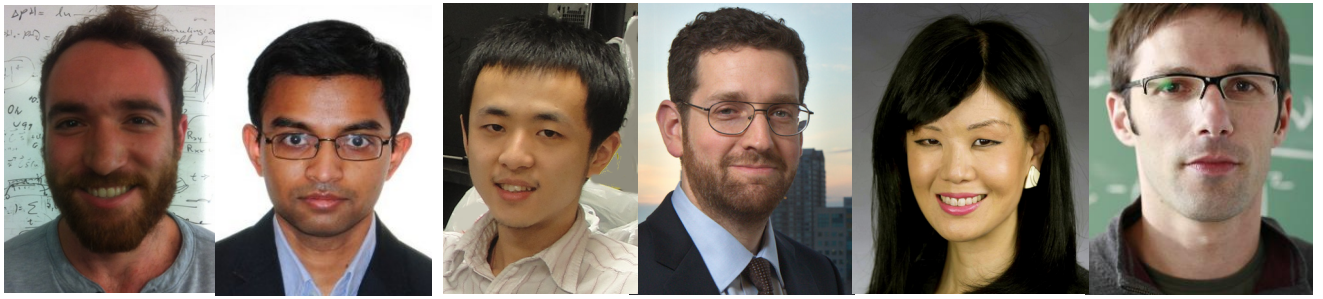
Synaptic plasticity mechanisms explain the specificity of DCS



Greg Kronberg | Asif Rahman | Yu Huang | Marom Bikson | Anli Liu NYU | **Lucas Parra**

Biomedical Engineering
City University of New York

NIH, September 2016

Disclosure

Lucas Parra is co-founder of Soterix Medial Inc. and co-inventor in patents held by the CCNY. The goal of these efforts is to make High-Definition tDCS broadly available.

The work presented here was funded by NIMH and NINDS

Clinical perspective on mechanism of tDCS

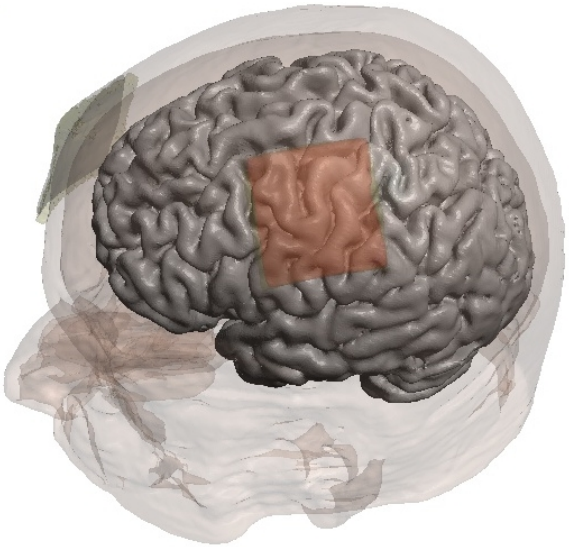
Cathode (-)
decreased
excitability

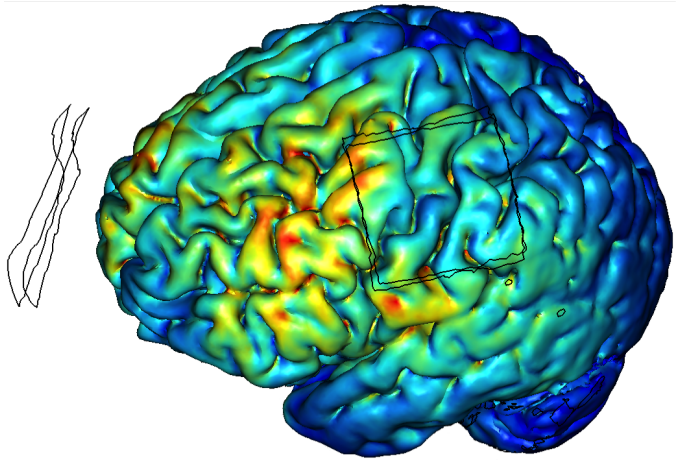
Anode (+)
increased
excitability

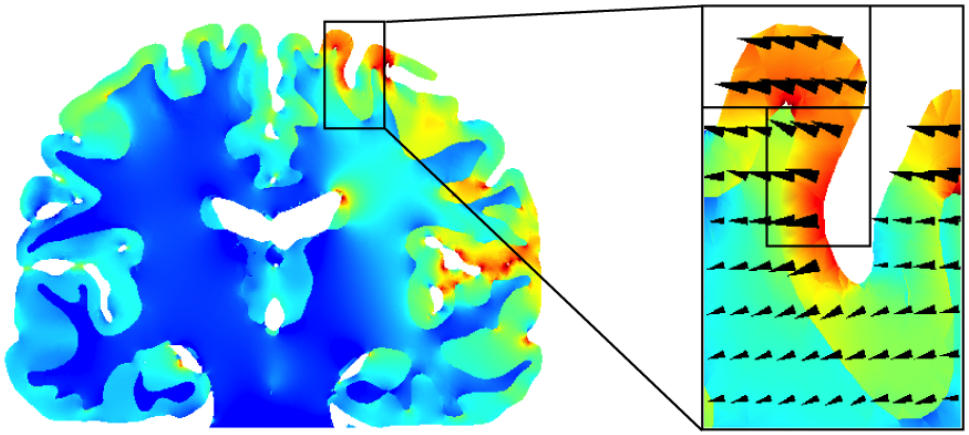
Perhaps too simplistic

Detailed models of current flow

Marom Bikson



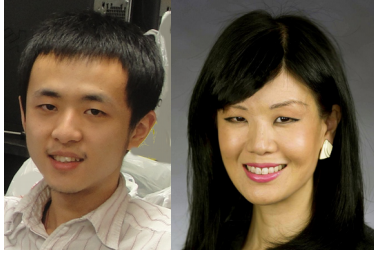




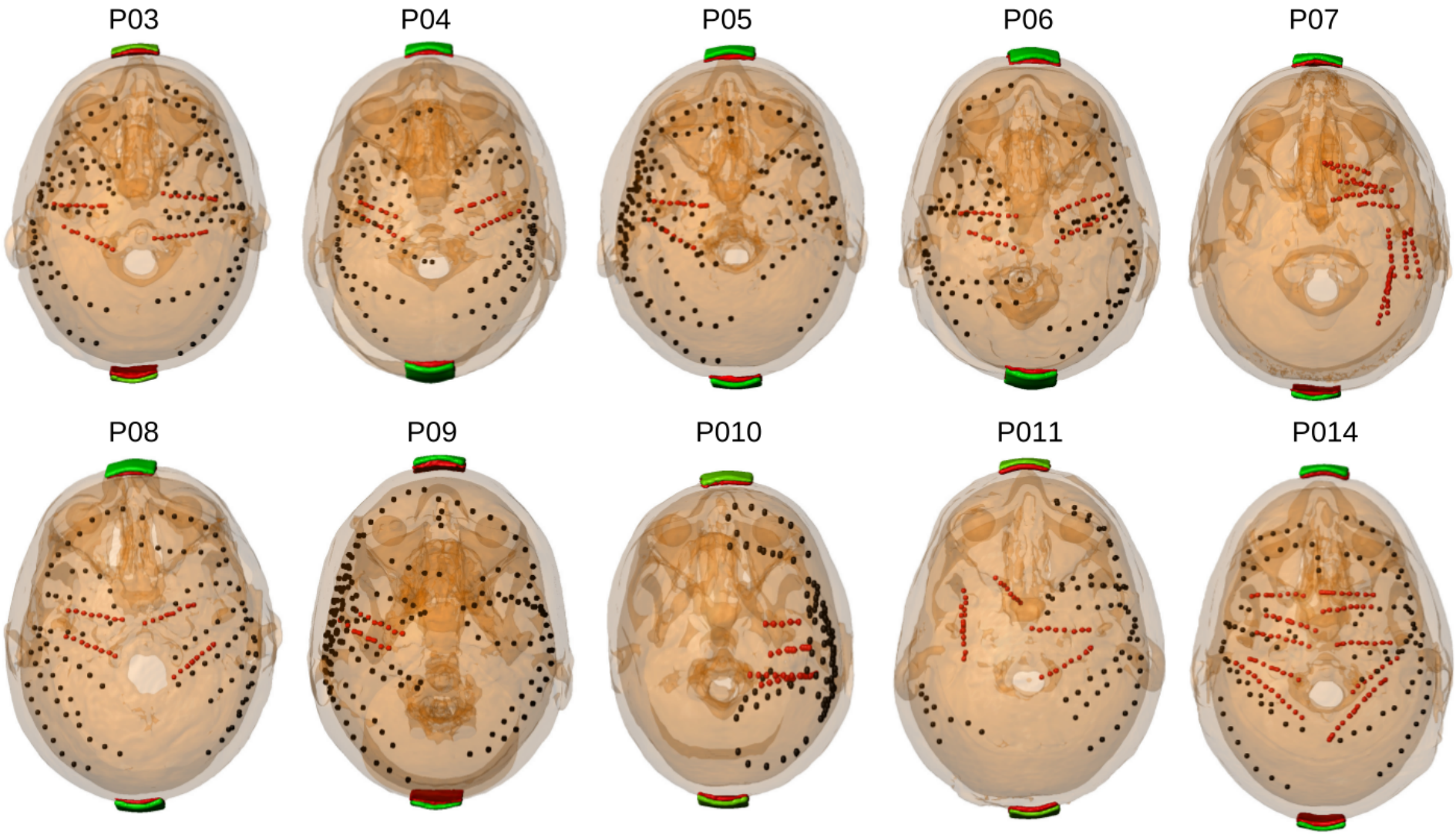
- Maximum not always under the electrode
- Polarity inevitably mixed

Datta, *Brain Stimulation*, 2009
Rahman, J Physiology, 2013

Model validation in human

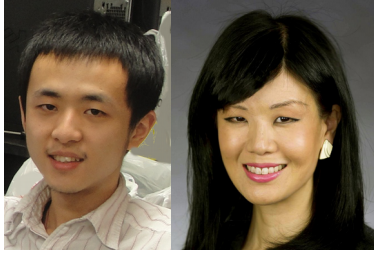


Yu Huang Anli Liu



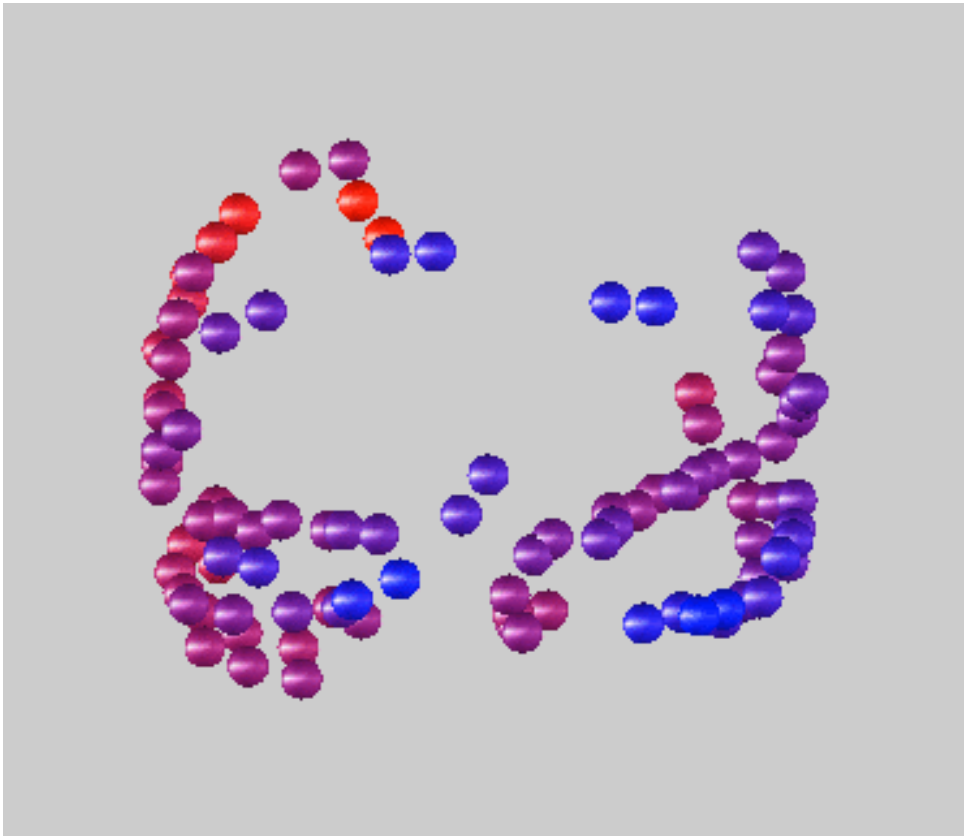
Huang, Liu,...Parra, *eLife*, in revision

Model validation in human

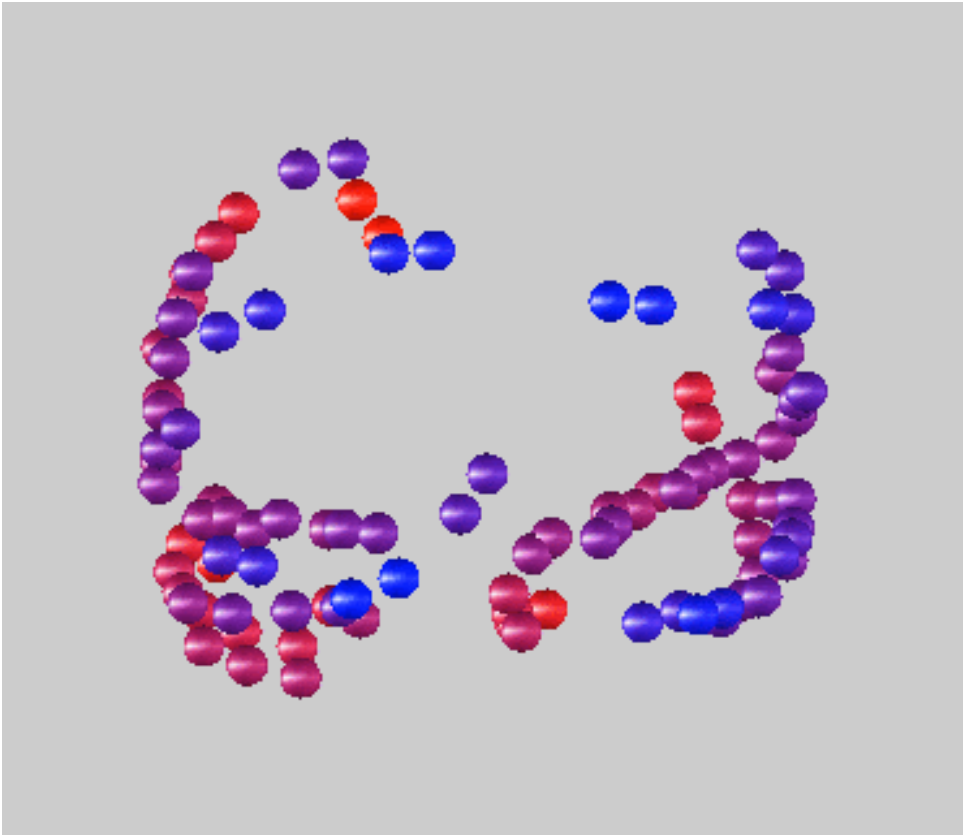


Yu Huang Anli Liu

Recording (Volts)



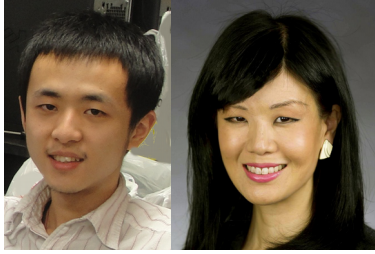
Model (Volts)



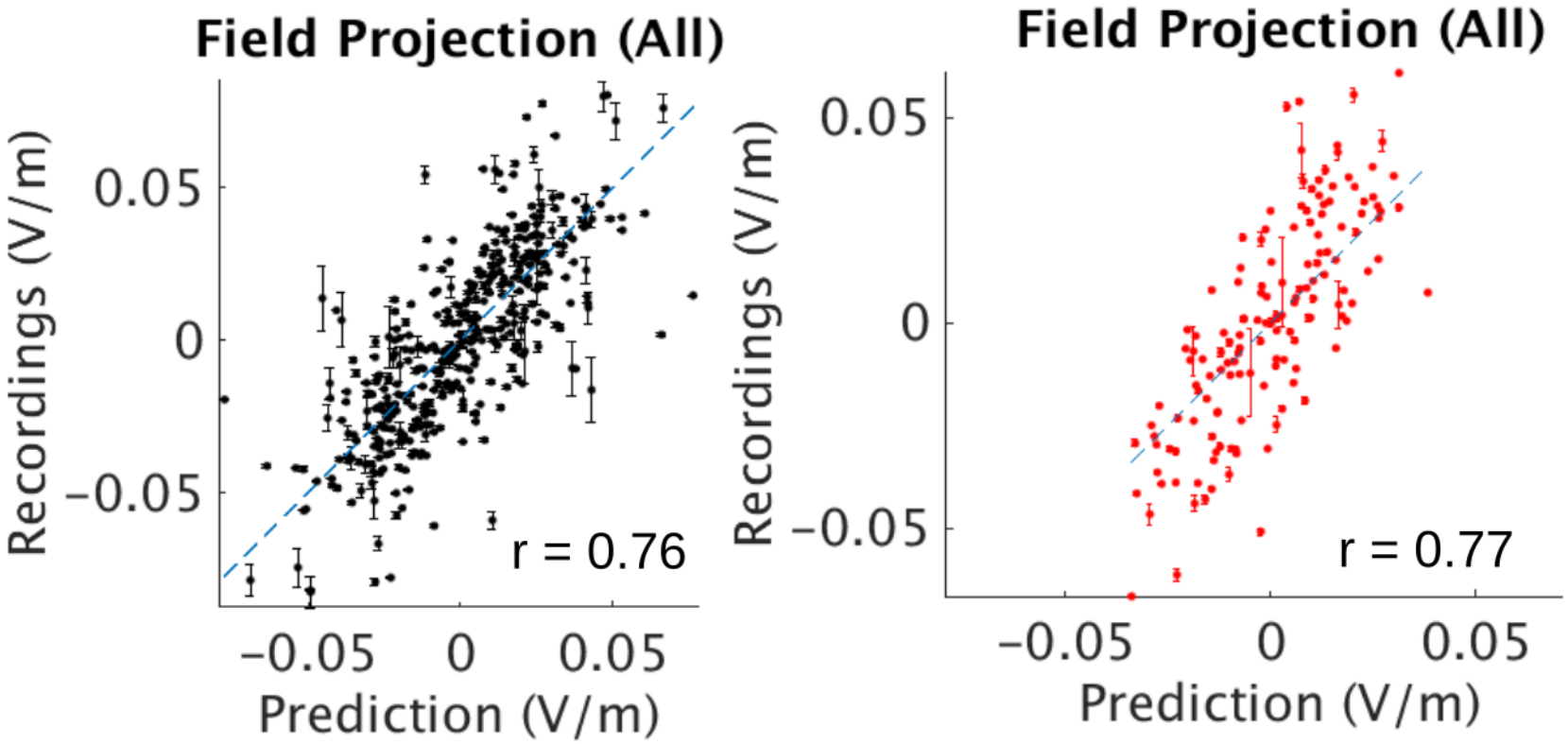
- Individual head anatomy is important

Huang, Liu,...Parra, *eLife*, in revision

Acurate prediciton of distribution



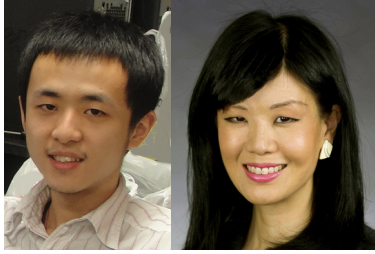
Yu Huang Anli Liu



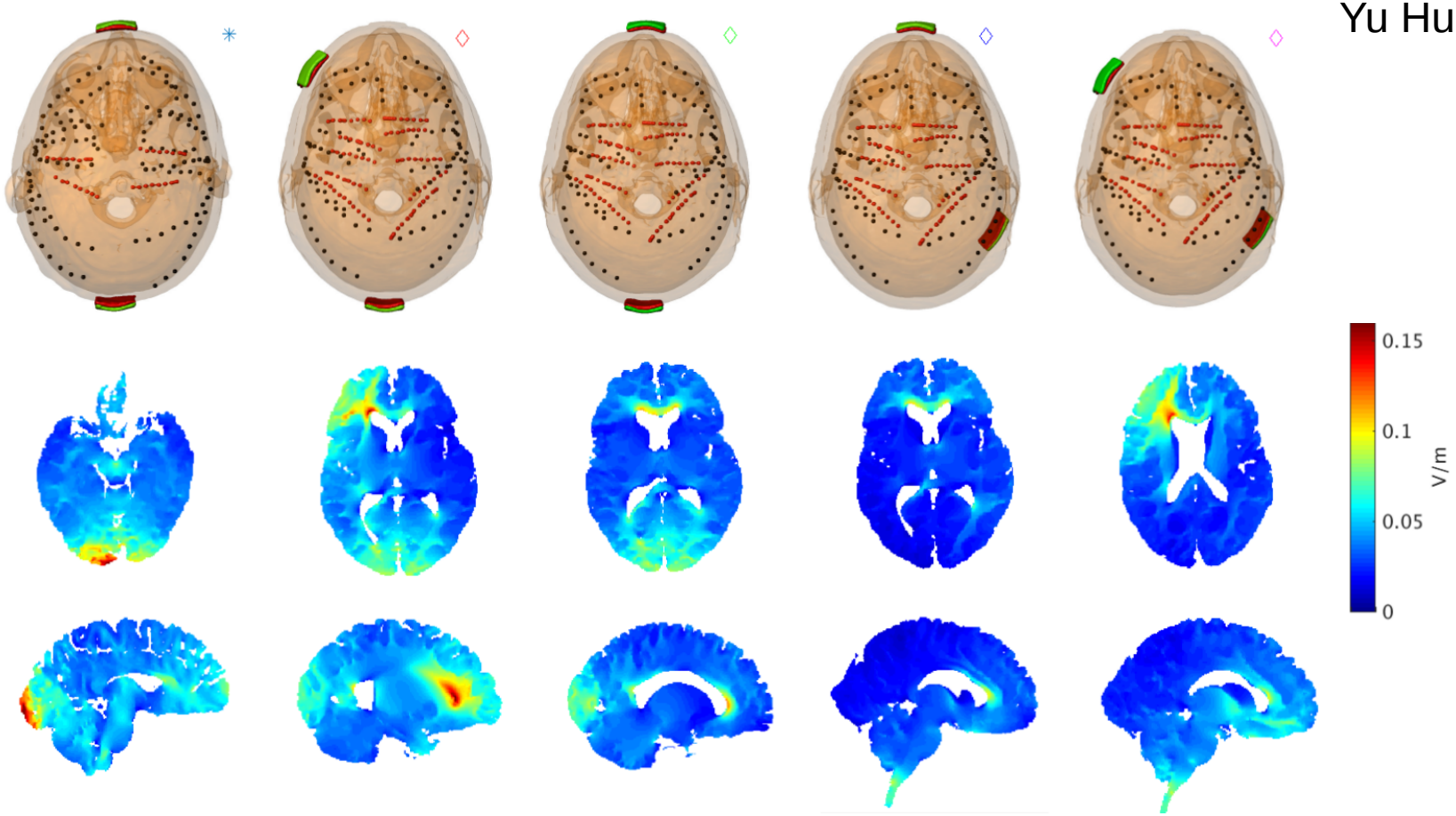
- Magnitude estimates of existing models generally too high

Huang, Liu,...Parra, e*Life*, in revision

Can reach deep targets



Yu Huang Anli Liu

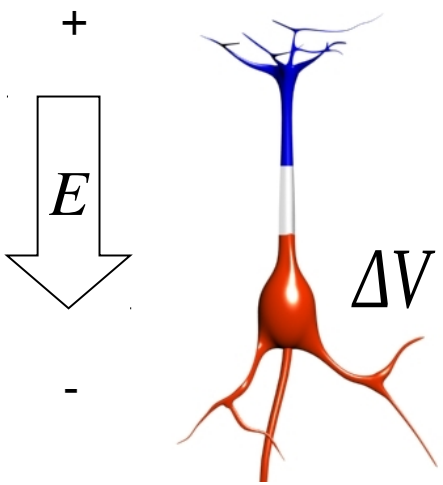


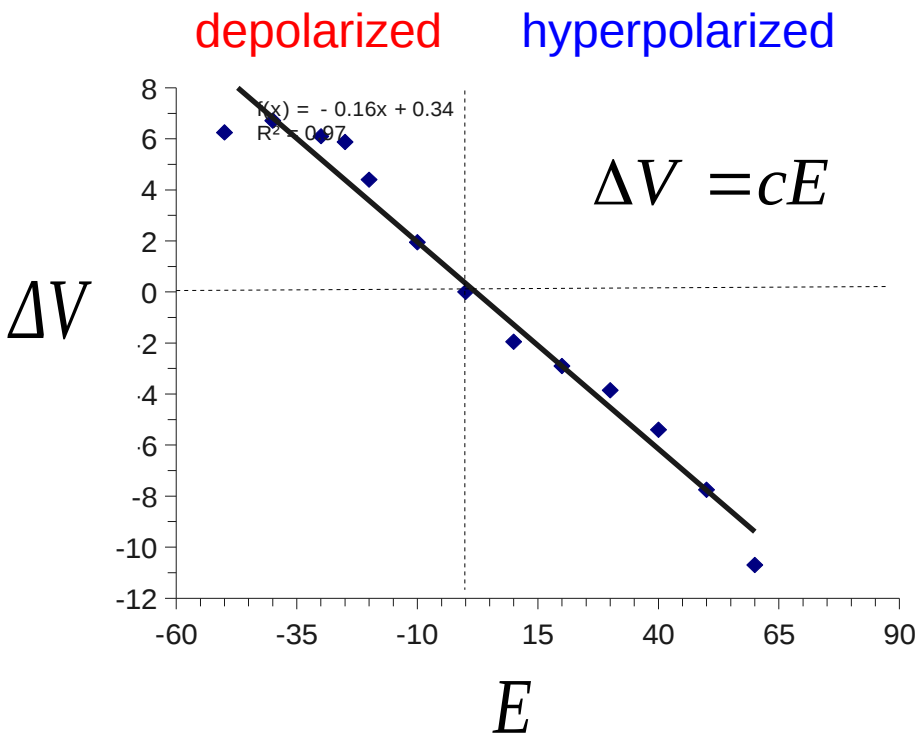
- Maximum cortical stimulation for 2mA → 0.5 V/m
- Deep targets next to CSF can be equally strong

Huang, Liu, Lafon, Friedman, Dayan, Wang, Bikson, Devinsky, Parra, Measurements and models of electric fields in the in vivo human brain during transcranial electric stimulation, *eLife*, in reversion, October 2016

Fields polarize the membrane linearly

Marom Bikson

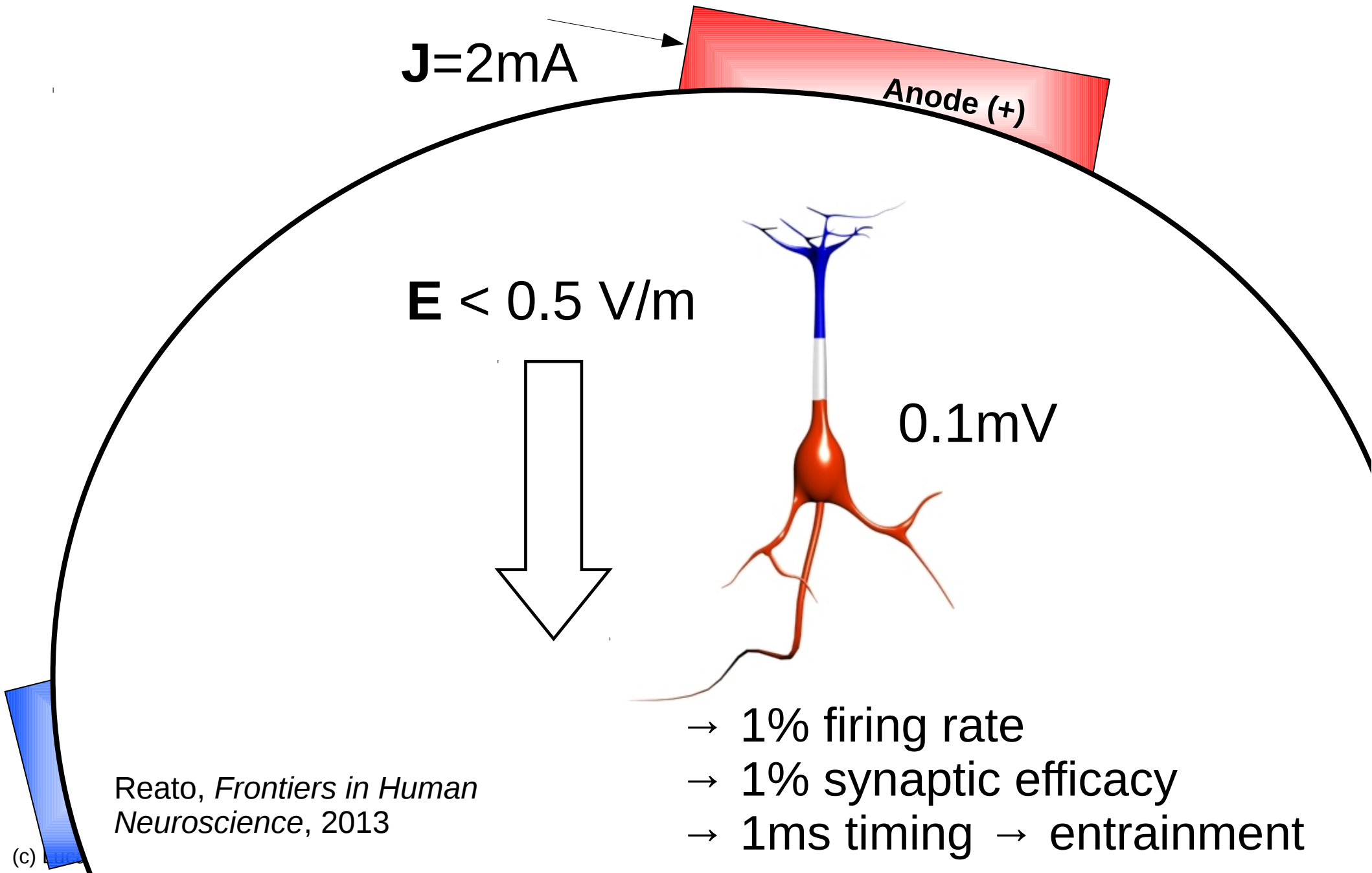




Somatic membrane susceptibility: $c = 0.1 \frac{\mathrm{V}}{\mathrm{V/m}}$

Bikson et al. J Physiol (2004) 9

Transient effects – summary

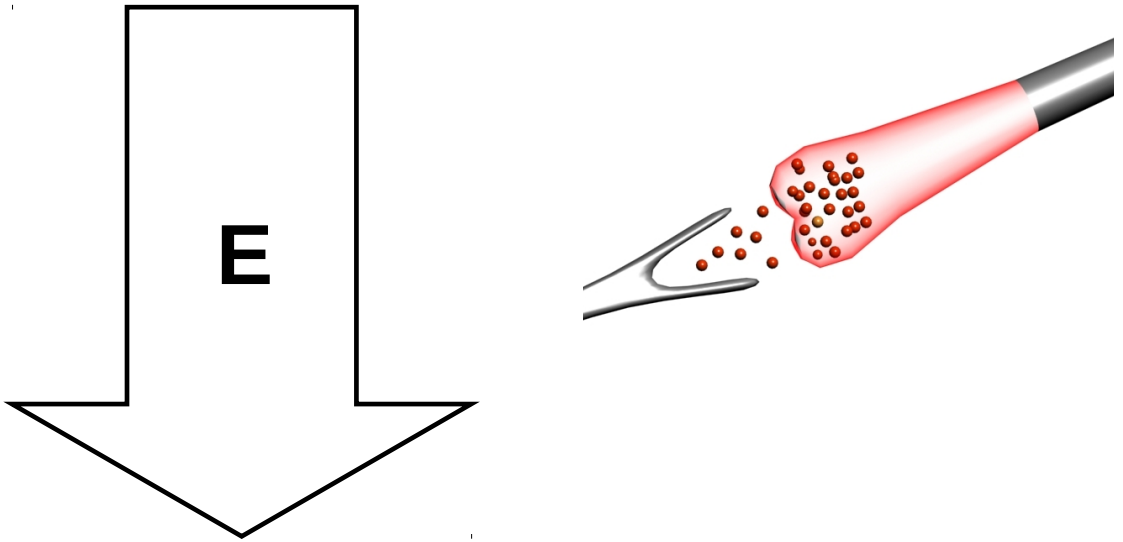


→ 1% firing rate
→ 1% synaptic efficacy
→ 1ms timing → entrainment

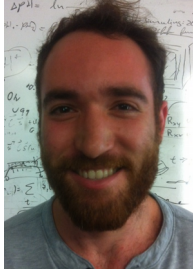
Reato, *Frontiers in Human Neuroscience*, 2013

Long Term effects?

Hypothesis: long term effects are mediated by synaptic plasticity

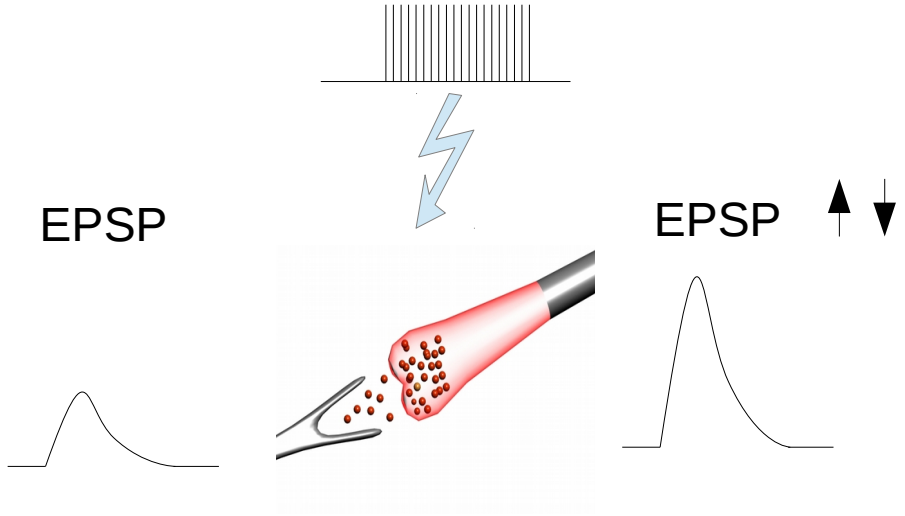


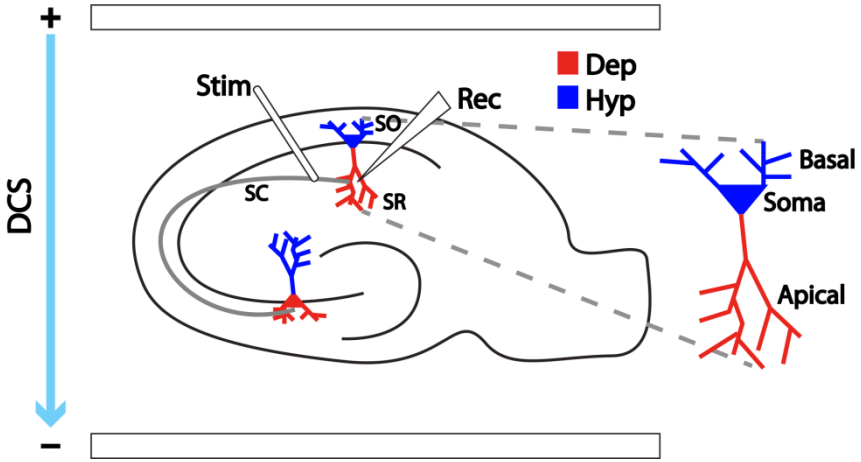
LTP/LTD + DC stimulation



Greg Kronberg

Long term synaptic plasticity induced with pulsed-stimulation.





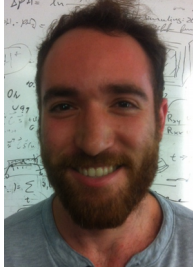
Rat hippocampus

High Frequency → LTP

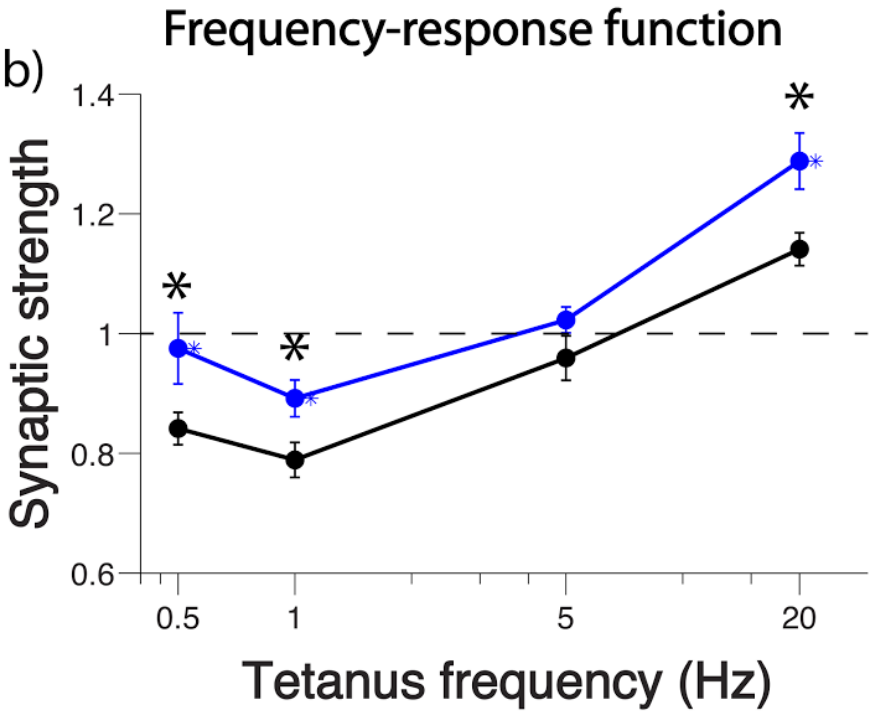
Low Frequency → LTD

Kronberg, *Brain Stimulation*, in press, 2016

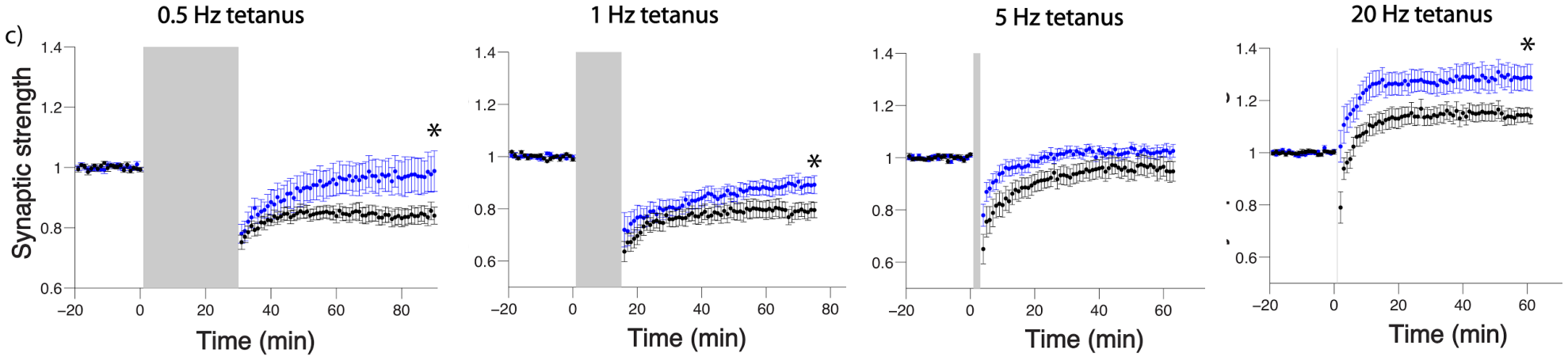
LTP & LTD are both modulated



Greg Kronberg



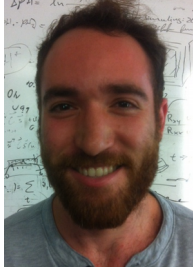
- dendrite depolarizing (20V/m)
- control



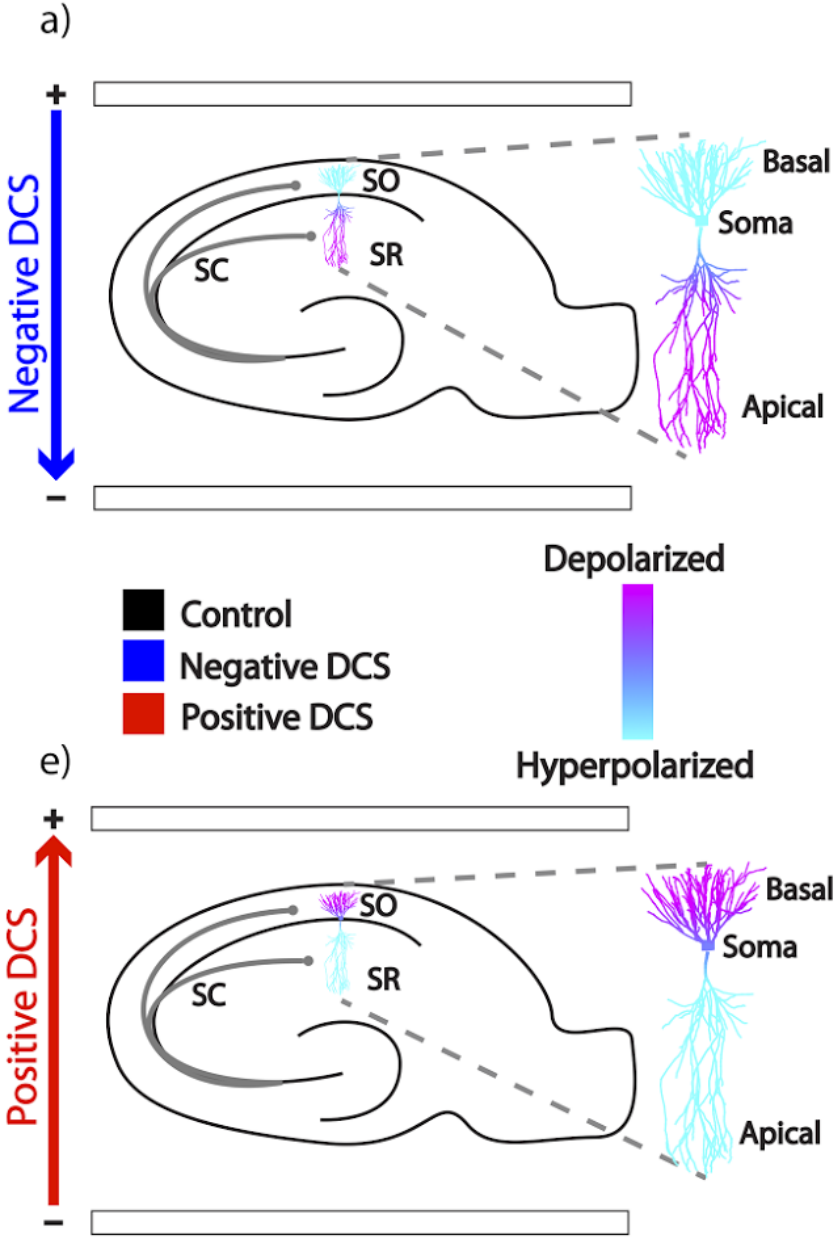
Tetanus (900 pulses)

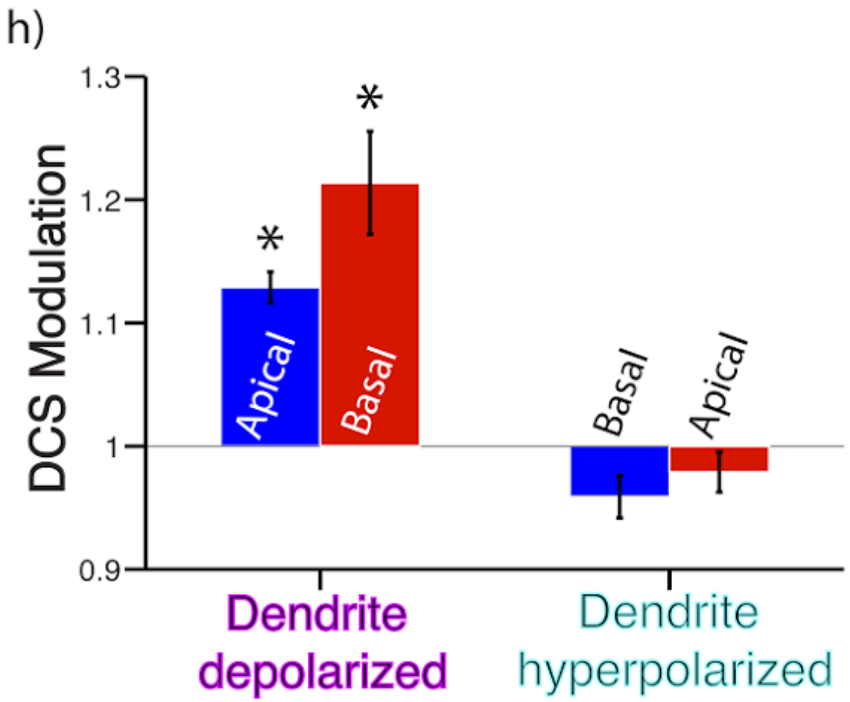
Kronberg, *Brain Stimulation*, in press, 2016

Consistent with dendritic polarization



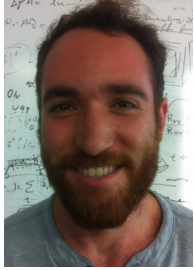
Greg Kronberg





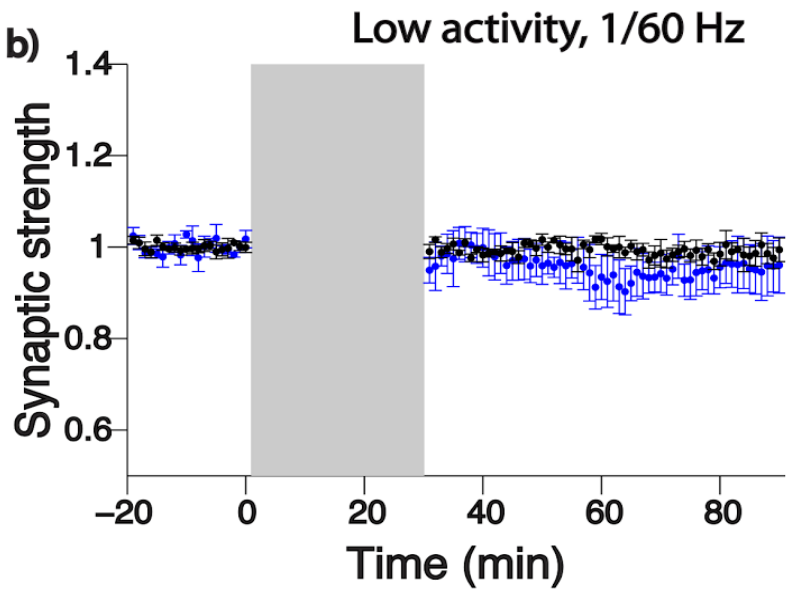
Kronberg, *Brain Stimulation*, in press, 2016

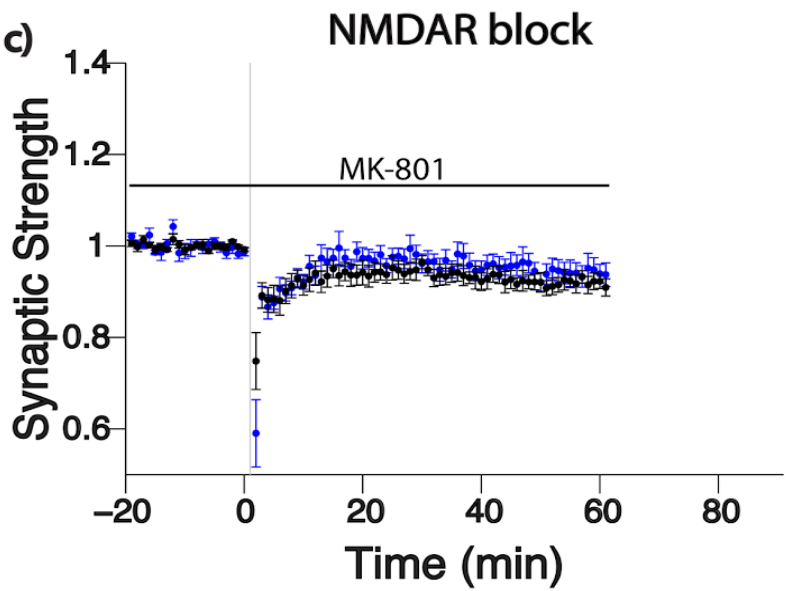
Activity and NMDA dependent



Greg Kronberg

- dendrite depolarizing (20V/m)
- control



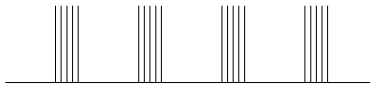


Kronberg, Bridi, Abel, Bikson, Parra, Direct current stimulation modulates LTP and LTD: activity dependence and dendritic effects, *Brain Stimulation*, in press, October 2016.

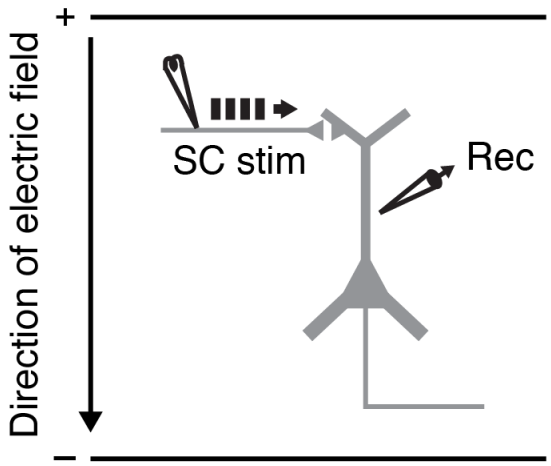
Theta Burst Stimulation, effect consistent with somatic polarization

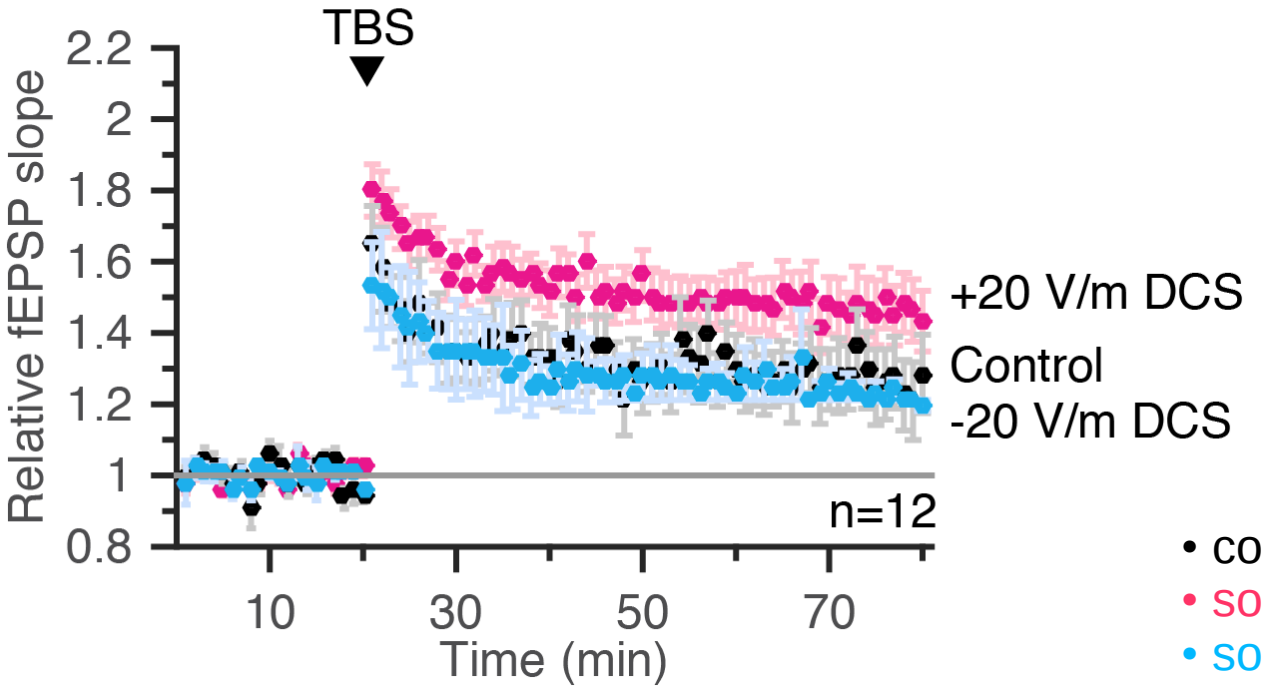
Asif Rahman

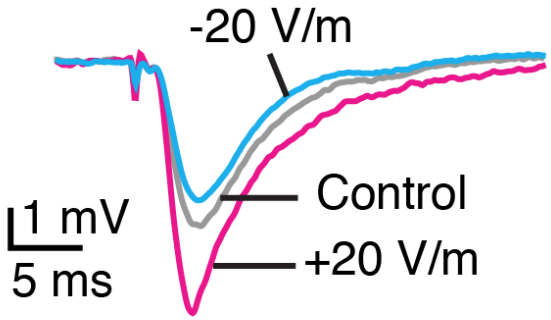
Theta burst stimulation (TBS)



7Hz bursts





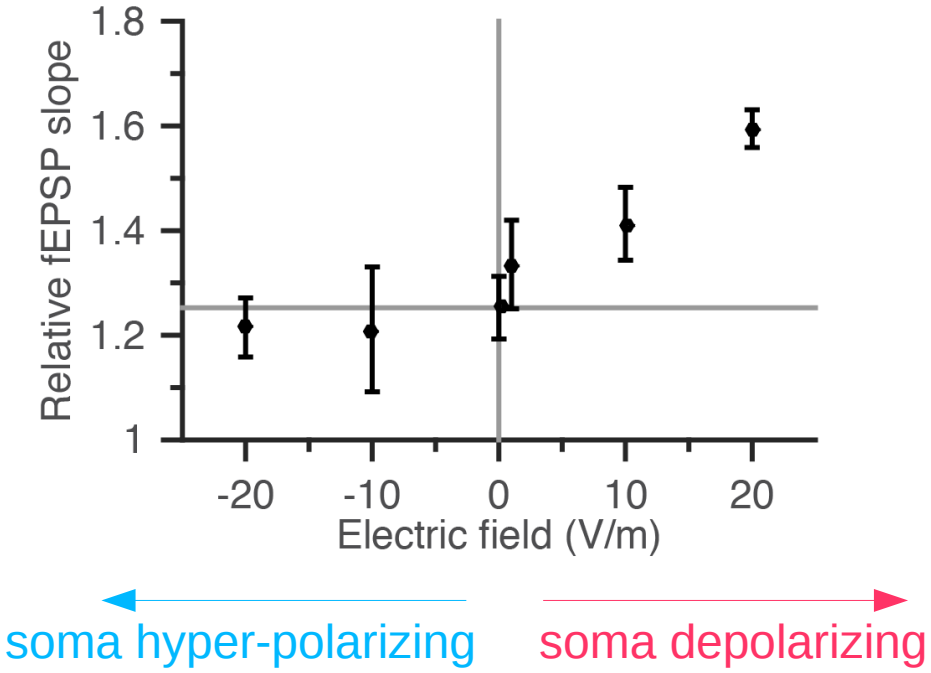


- control
- soma depolarizing
- soma hyper-polarizing

Rahman et al., in preparation

Monotonic, bias to potentiation

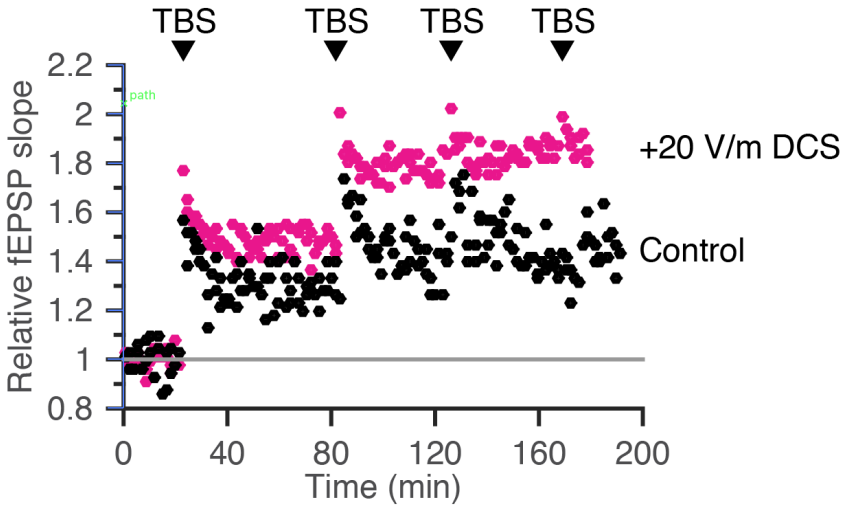
Asif Rahman

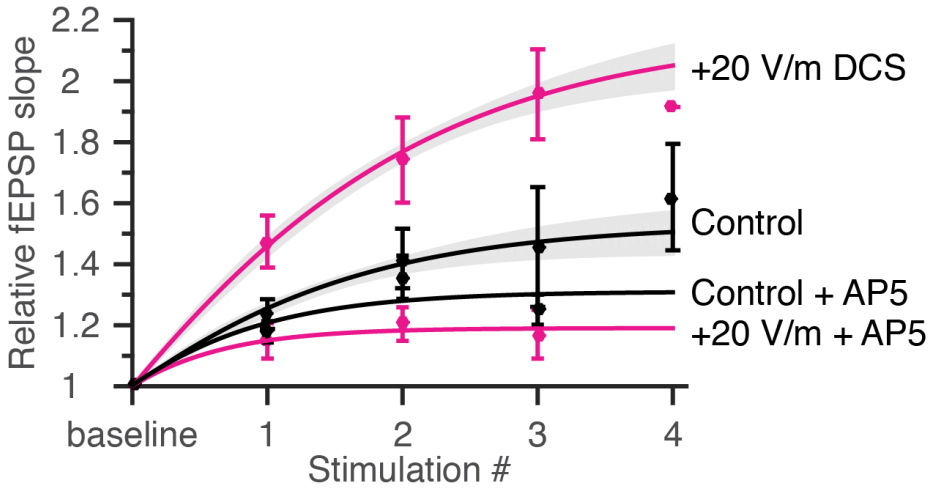


Rahman et al., in preparation

Repeated TBS boost ceiling of LTP

Asif Rahman

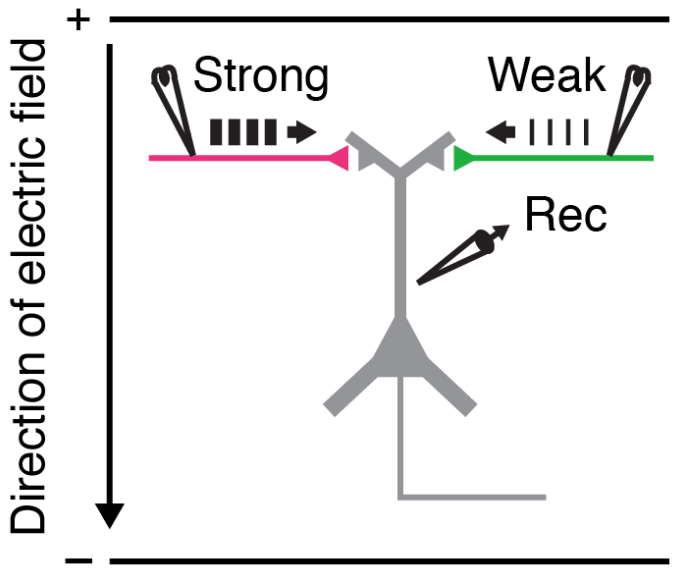




Rahman et al., in preparation

Associative LTP

Asif Rahman

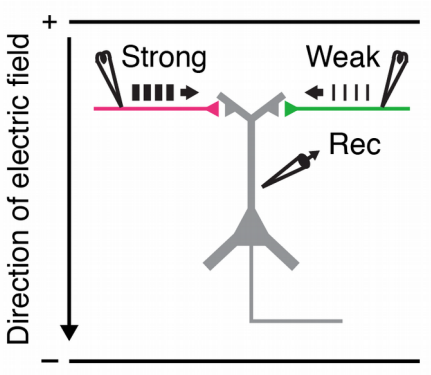


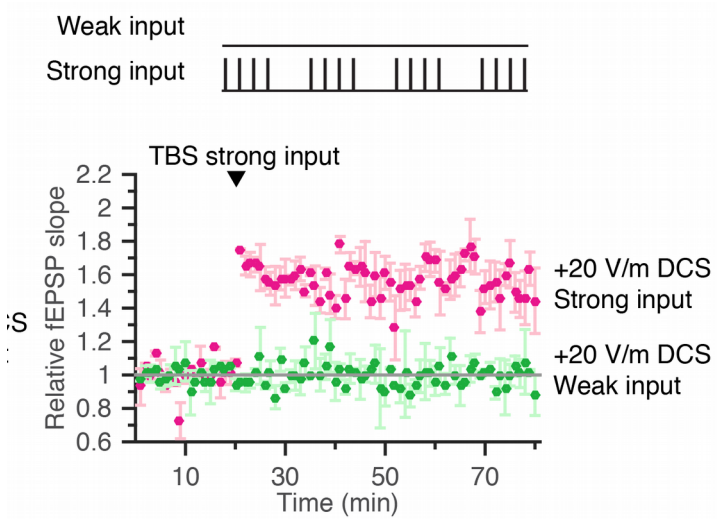
Strong stimulation known to induced LTP in weakly co-activated pathway.

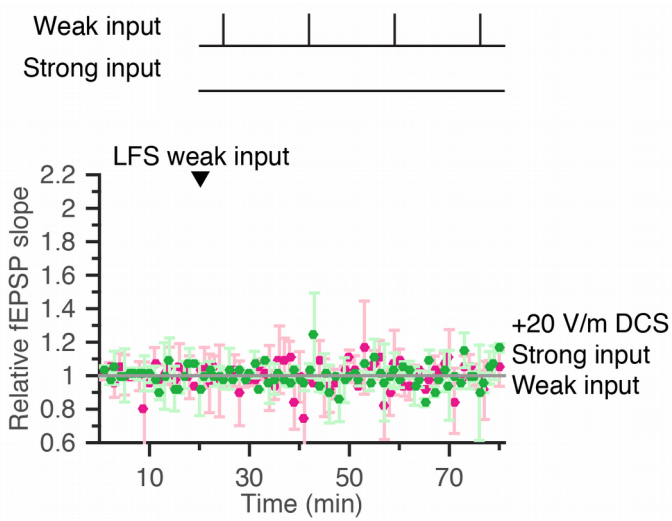
Rahman et al., in preparation

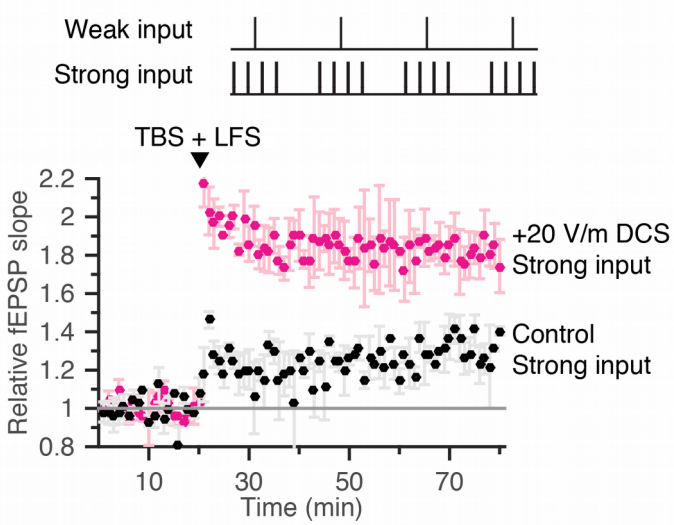
DCS boosts associative LTP

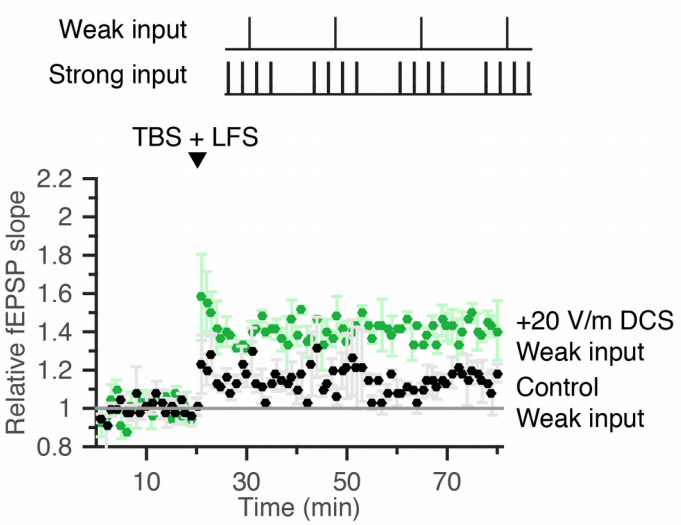
Asif Rahman











Rahman et al., in preparation

Summary: Lasting Synaptic Effects of DCS

- Require plasticity; do not happen in isolation.
- Polarity effects mixed, but tend to strengthen synapses.
- **“Hebbian”**: Dependent on activity and NMDA, are pathway specific, follows associative potentiation.

Postulate

Human tDCS effects are specific because DCS modulates Hebbian plasticity, which can be highly task specific.

Acknowledgments

Students
Belen Lafon
Greg Kronberg
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Anili Liu, NYU
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