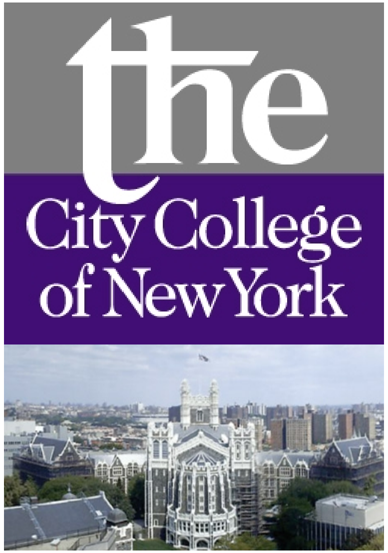
How does Direct Current Stimulation (DCS) work?

DCS boosts Hebbian plasticity







Greg Kronberg
Yu Huang
Asif Rahman
Anli Liu
Lucas Parra

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Brain Stimulation, Vancouver, February 2019

Disclosure

Co-inventor in patents held by the City University of New York.

Co-founder of Soterix Medial, Neuromatters and Kcore Analytics – startup efforts to make neurotechnology broadly available.

Clinical perspective on mechanism of tDCS

Cathode (-)
decreased
excitability

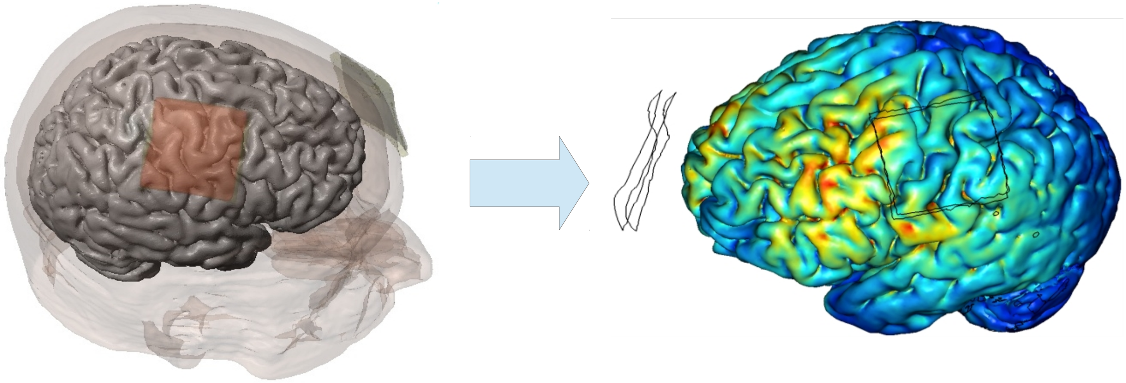
Anode (+)
increased
excitability

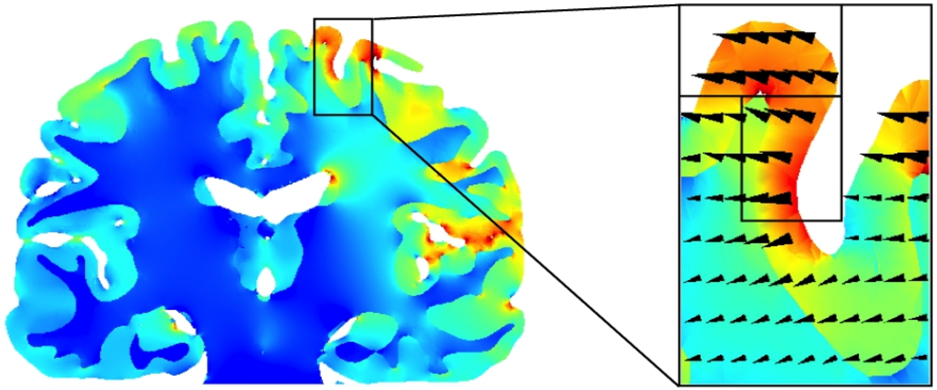
Perhaps too
simplistic

Direct currents cause complex E-fields


Abhi Datta

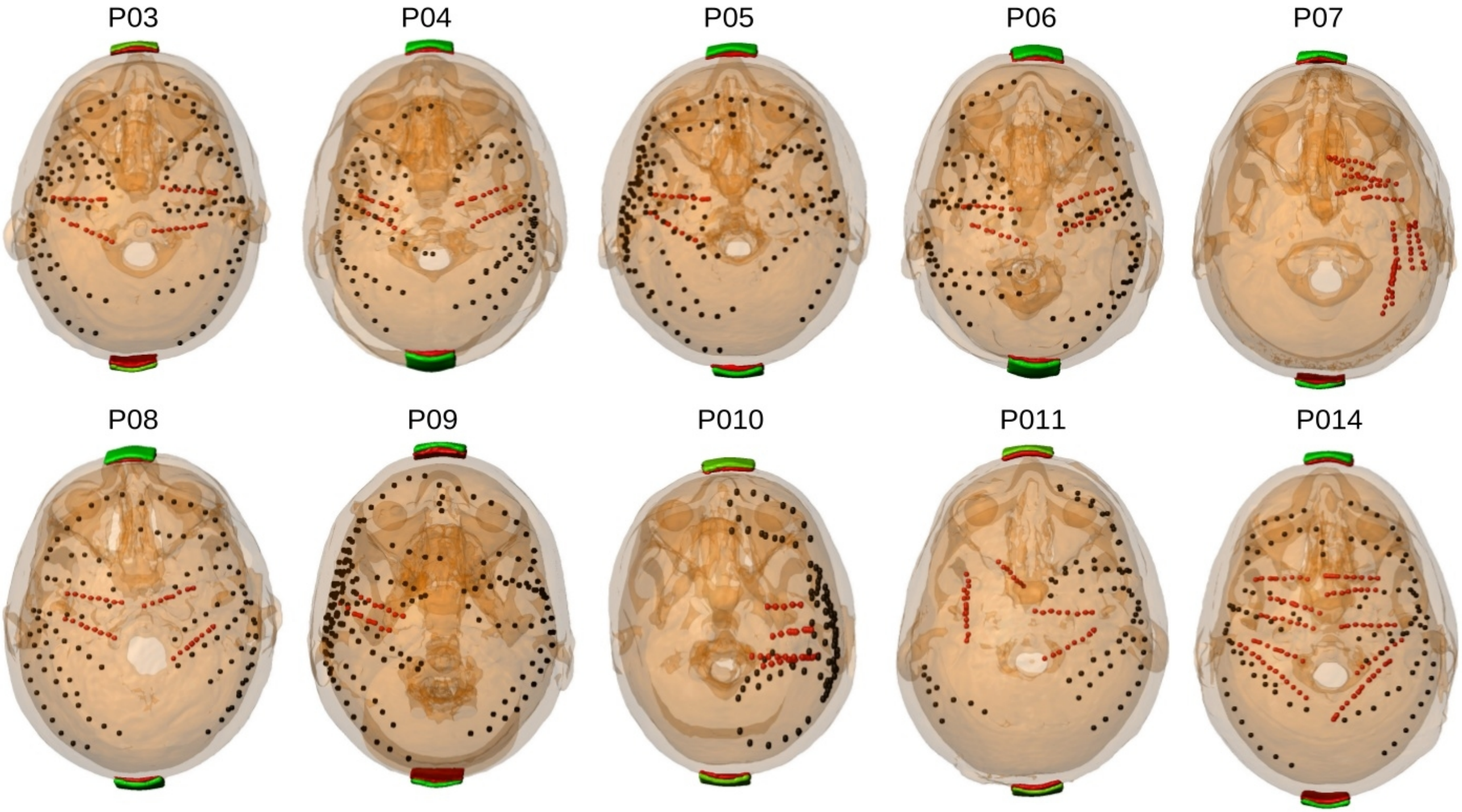

Asif Rahman

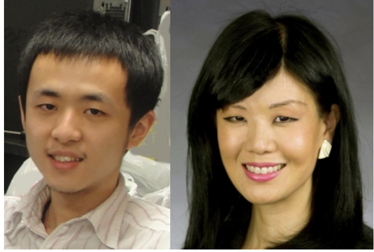

Datta, *Brain Stimulation*, 2009


Rahman, *J Physiology*, 2013

- Strongest E-field not always under the stimulation electrodes
- Cortical gyration cause mixed polarity E-fields

Model validation in human



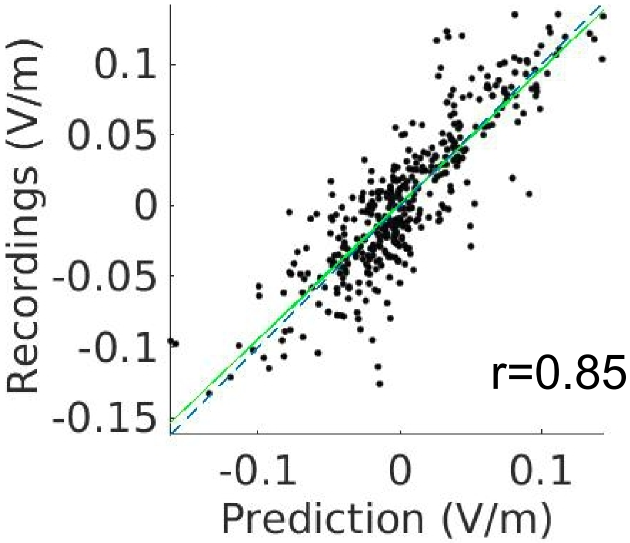


Huang, Liu, *eLife*, 2017

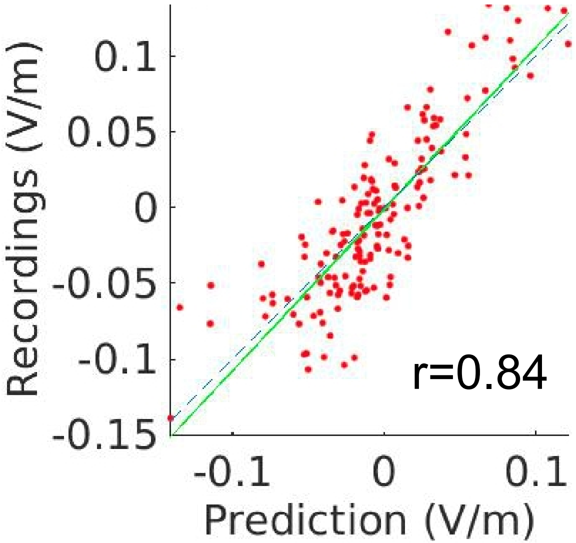
E-field models are generaly accurate


Yu Huang   Anli Liu

Cortical surface



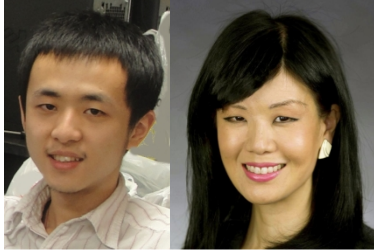
Deep brain



Huang, *eLife*, 2017

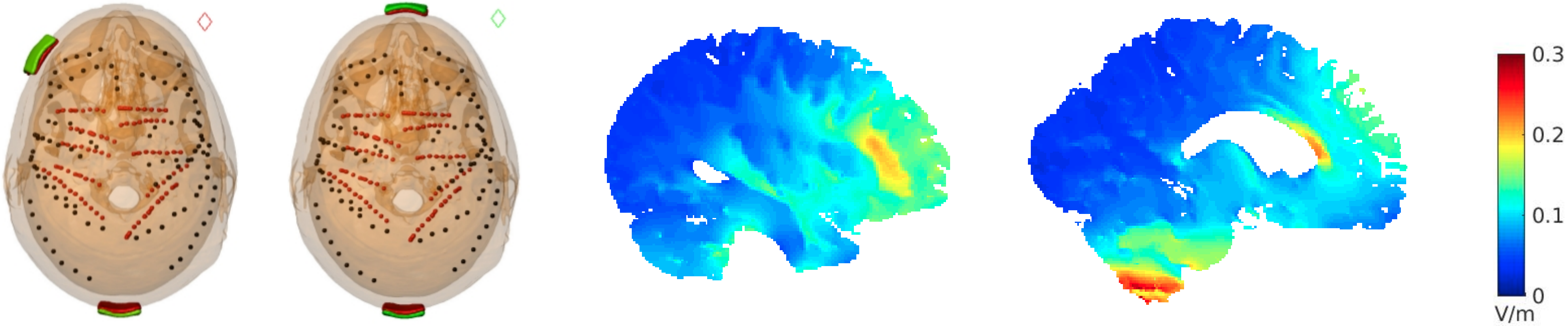
- Magnitude and spatial distribution of E-field generated by TES reasonably well predicted.

TES can reach deep targets

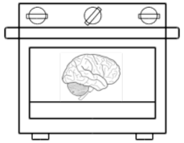


Yu Huang Anli Liu

- Maximum cortical stimulation for 2mA → 1 V/m
- Deep targets can be equally strong
- Individual subject anatomy matters

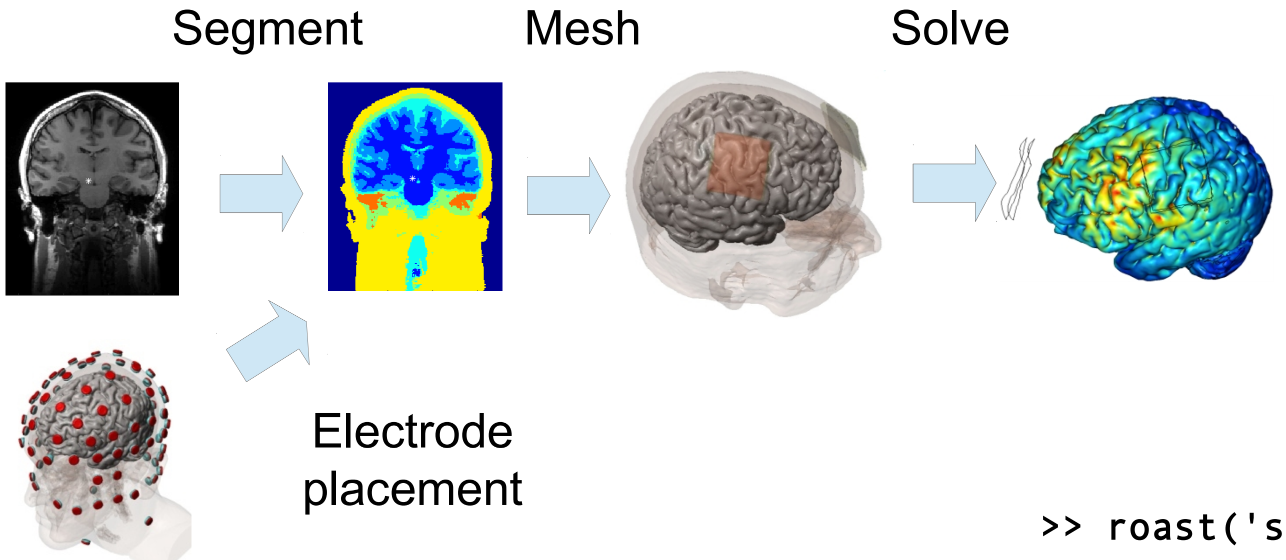


Huang, *eLife*, 2017



ROAST pipeline

Yu Huang



- Free
- Fast: 10~30 min
- Fully automated
- Easy to use

```
>> roast('subject.nii',{'F1',2,'P2',-2})
```

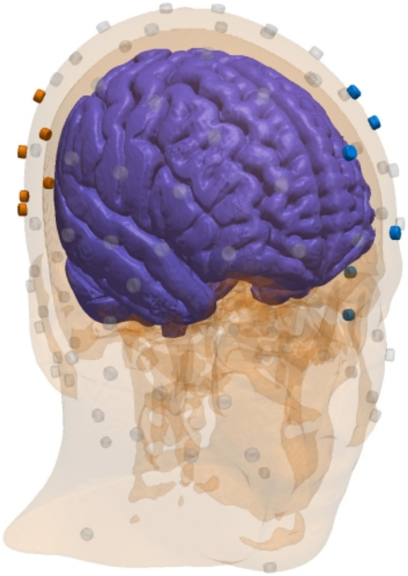
parralab.org/roast

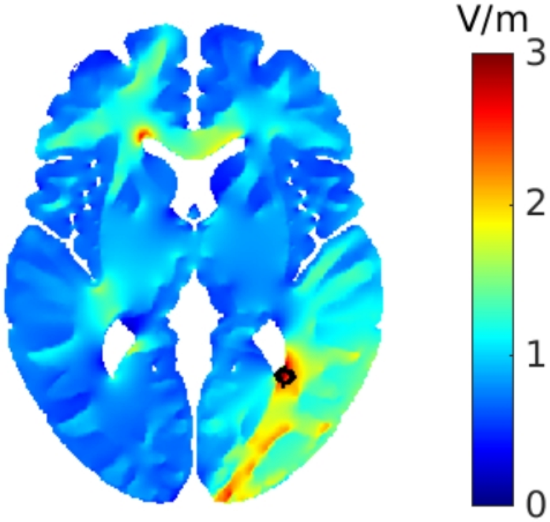
Huang et al. Realistic vOlumetric-Approach to Simulate Transcranial electrical stimulation, *bioRxiv*, 2019

Stimulation intensity

Yu Huang

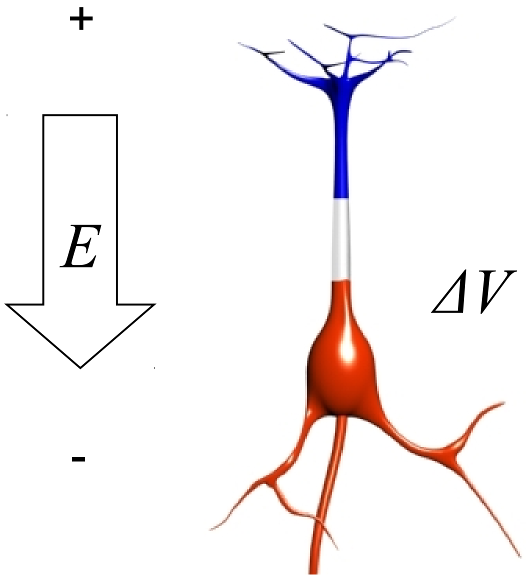
- “Intersectional Pulsed Stimulation” (IPS) uses multiple 1mA electrodes to achieve stronger stimulation in depth.
- Targeting of IPS is equivalent to High Definition TES which can be optimized.

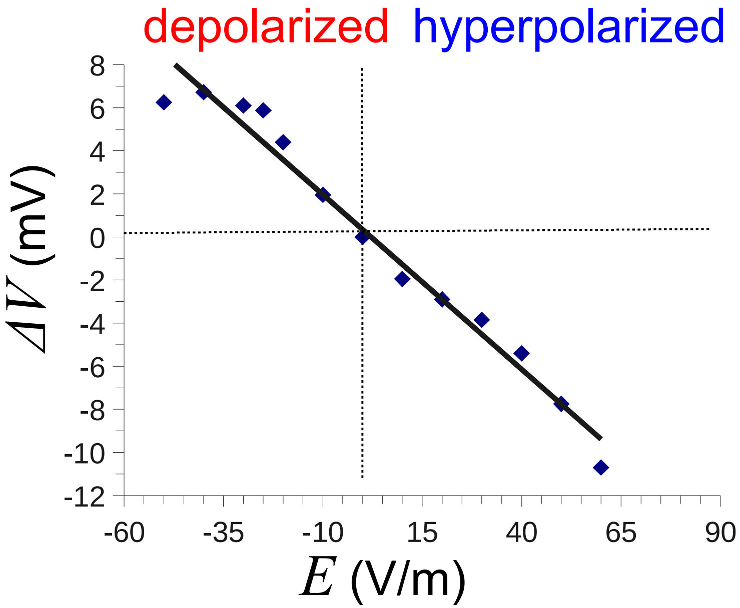




Huang, *Brain Stimulation*, 2018

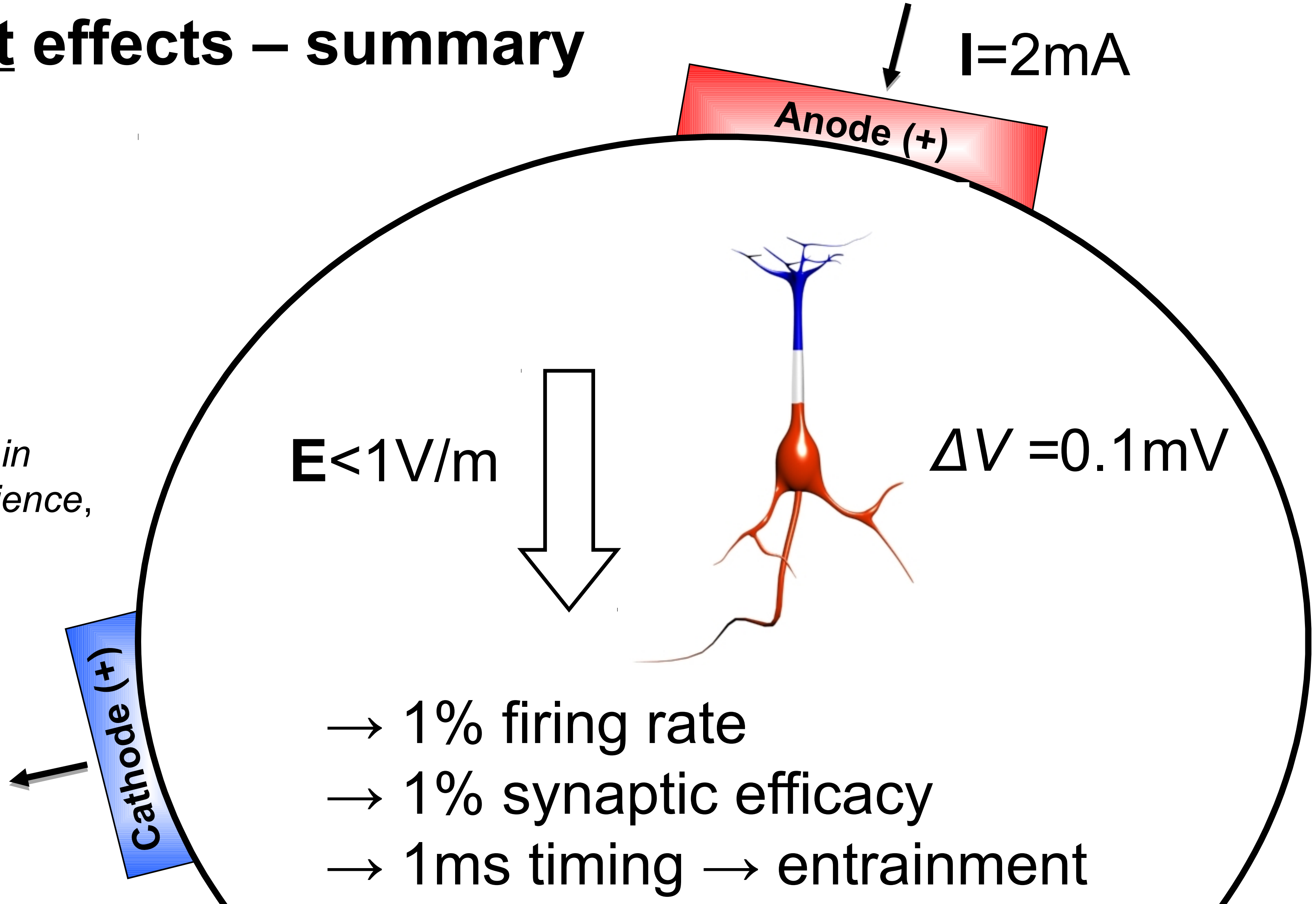
Fields polarize the membrane linearly





Bikson, *J Physiology*, 2004

Transient effects – summary



Reato, *Frontiers in Human Neuroscience*, 2013

Long term effects?

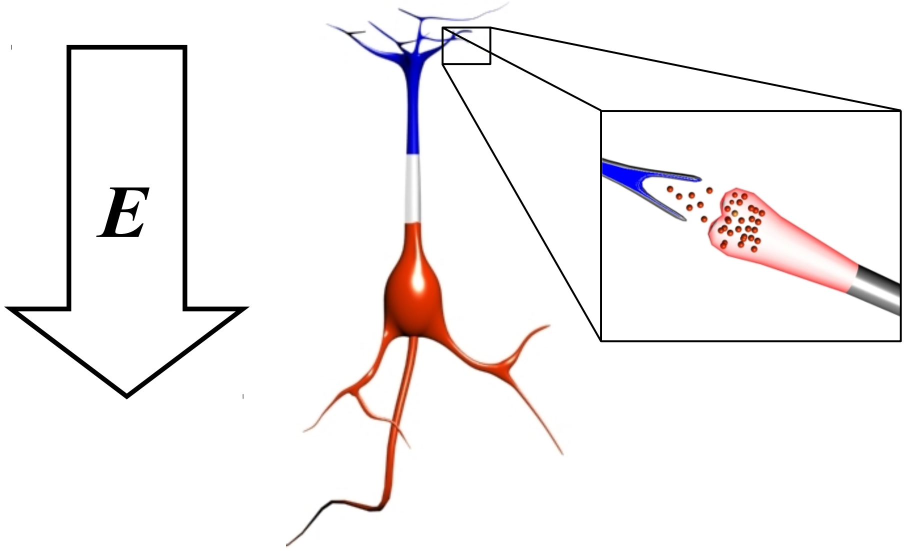
Hypothesis: Long term effects are mediated by synaptic plasticity

Hypothesized mechanism:

- E-fields polarize the membrane.
- In “Hebbian” plasticity the membrane depolarization captures post-synaptic activity.

Prediction:

- E-field interact with long-term synaptic plasticity via membrane depolarization.

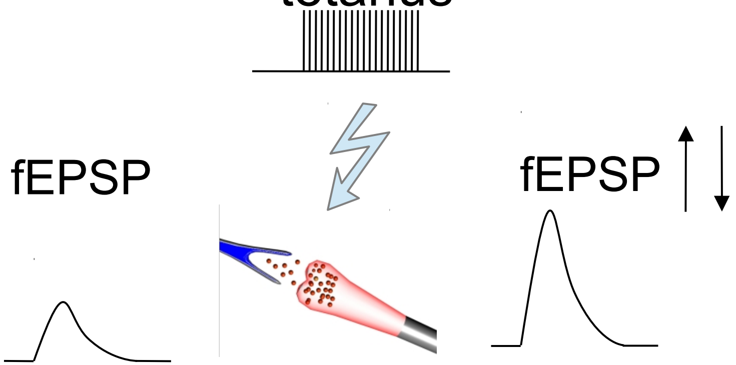


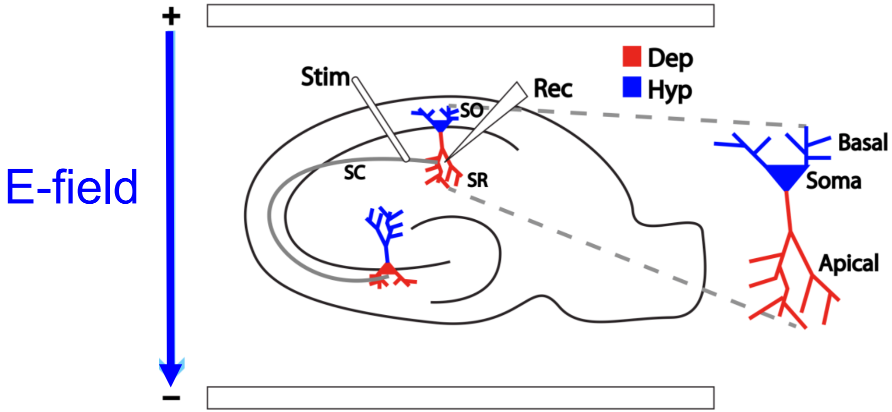
Kronberg, *Brain Stimulation*, 2017

Greg Kronberg

Plasticity induction + DC stimulation

- Induce long term potentiation/depression (LTP/LTD) in vitro in hippocampus.
- Record synaptic efficacy with field excitatory postsynaptic potentials (fEPSP).





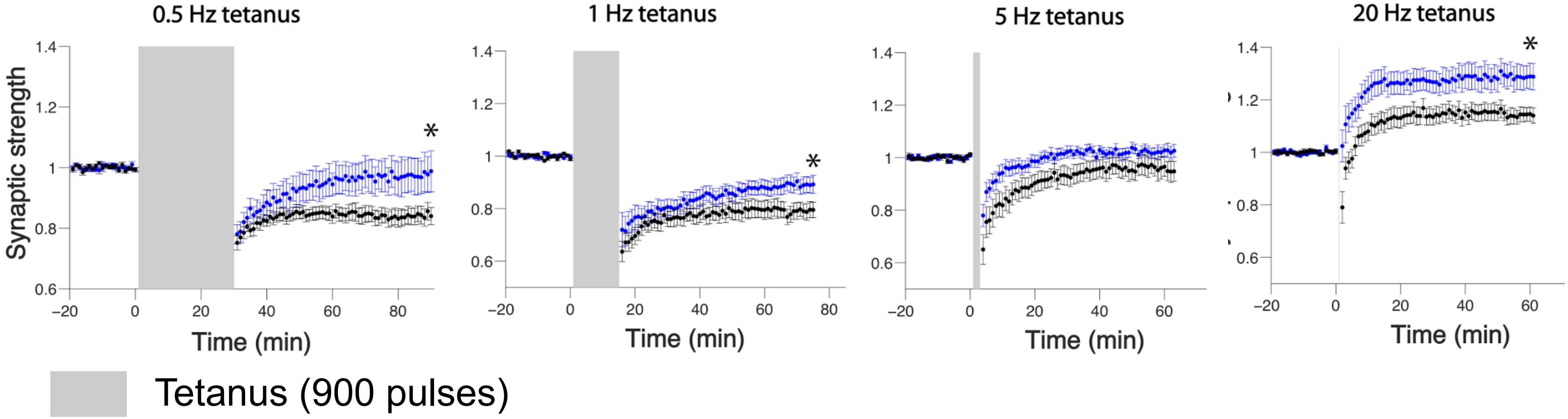
High frequency tetanus → LTP ↑
Low frequency tetanus → LTD ↓

Kronberg, *Brain Stimulation*, 2017

LTP & LTD are both modulated

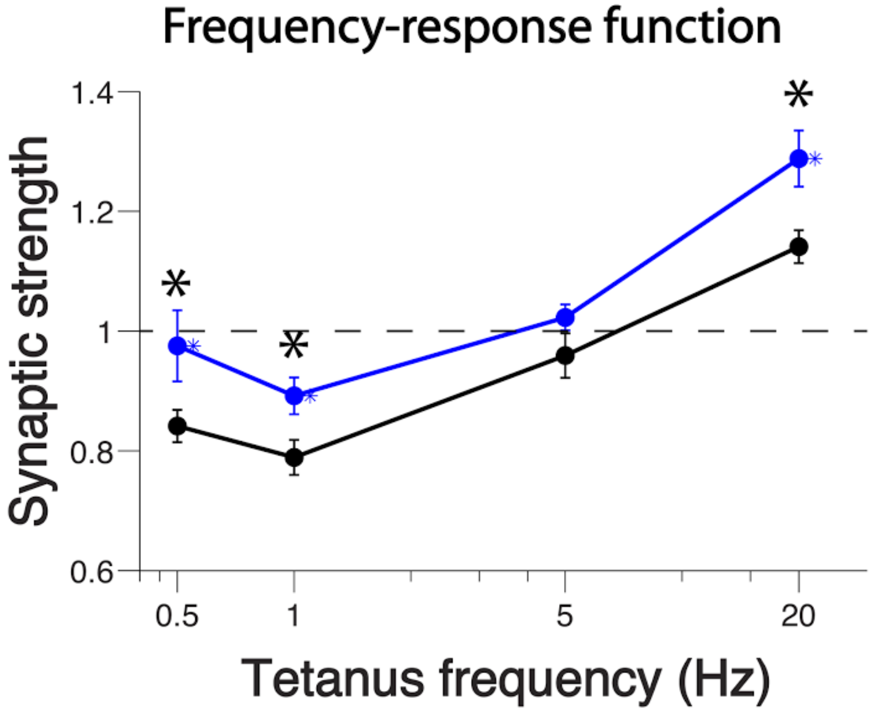
Greg Kronberg

- Cathodal DCS
- control



Kronberg, *Brain Stimulation*, 2017

Depolarizing field → stronger synapses

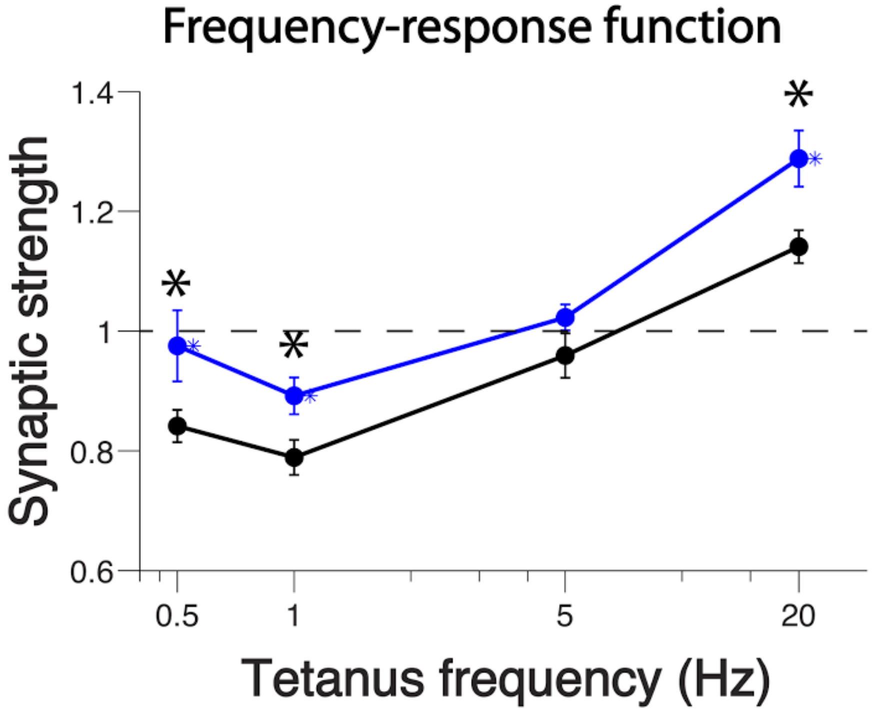


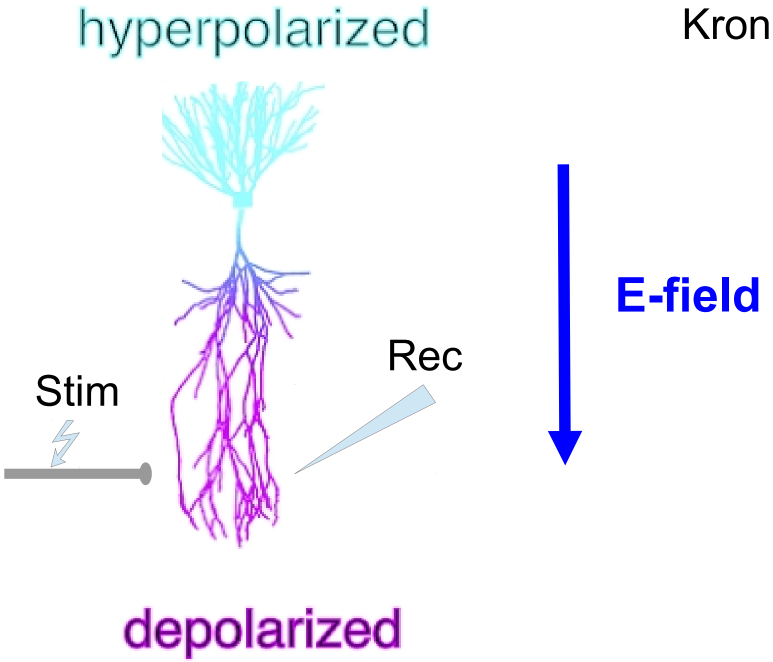
Greg Kronberg

Kronberg, *Brain Stimulation*, 2017

Depolarizing field → stronger synapses

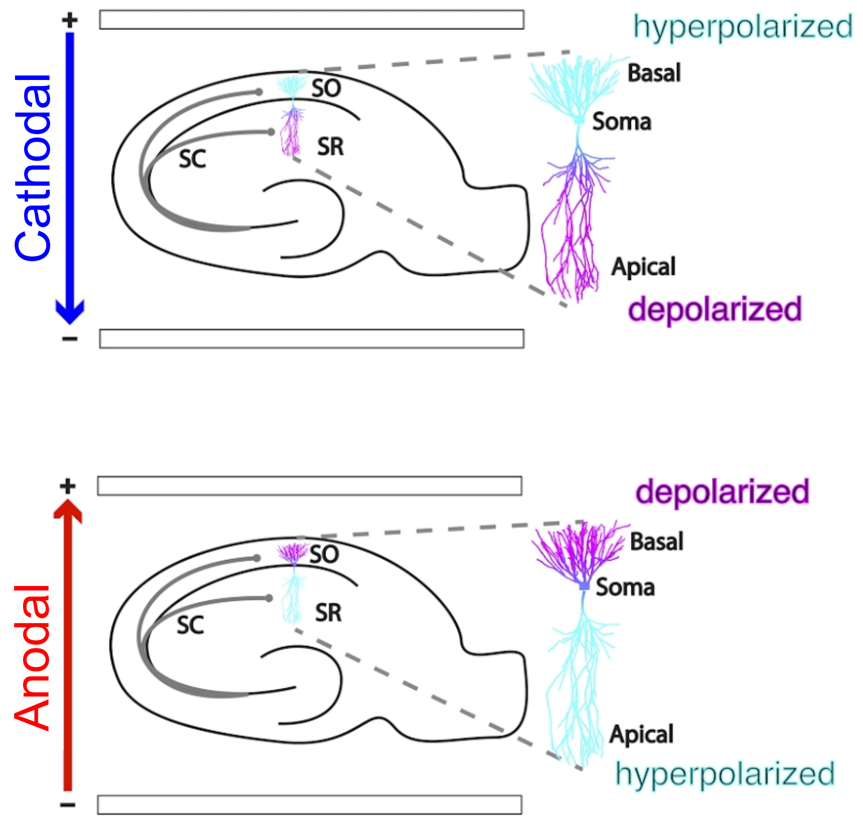
Greg Kronberg

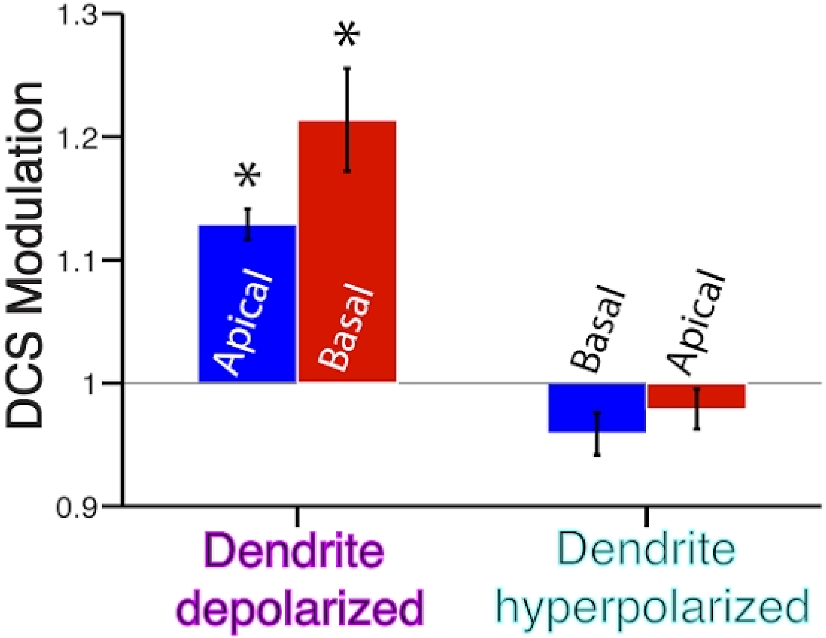




Kronberg, *Brain Stimulation*, 2017

Affected pathway depends on polarity



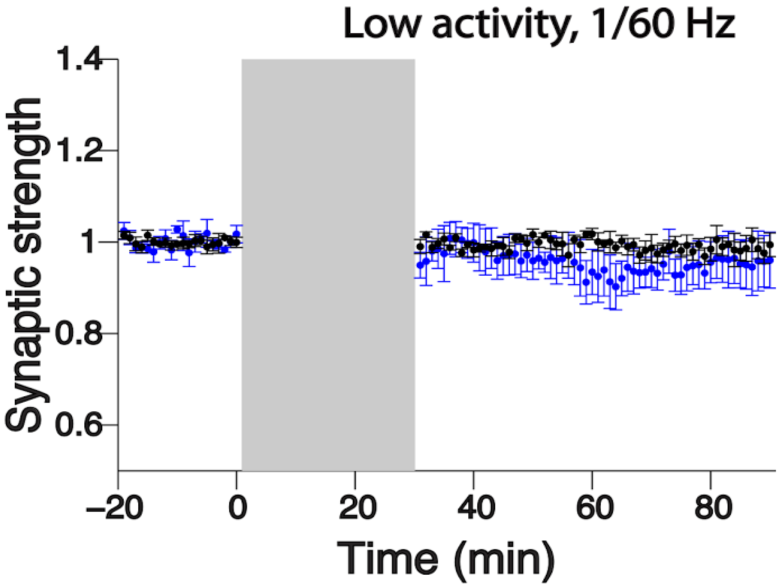


Kronberg, *Brain Stimulation*, 2017

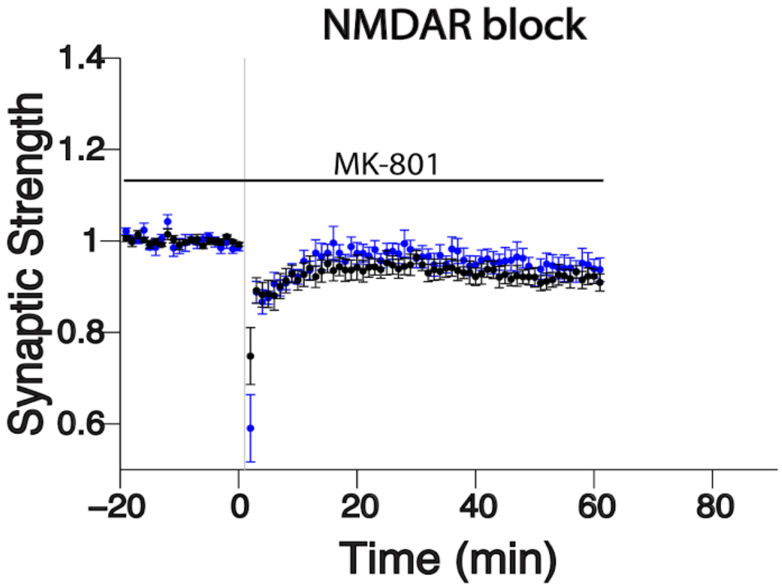
DCS effect requires LTP

Greg Kronberg

No activity → no effect



No NMDAR → no effect



Kronberg, *Brain Stimulation*, 2017

Conclusions of tetanus-induced LTP/LTD:

Greg Kronberg

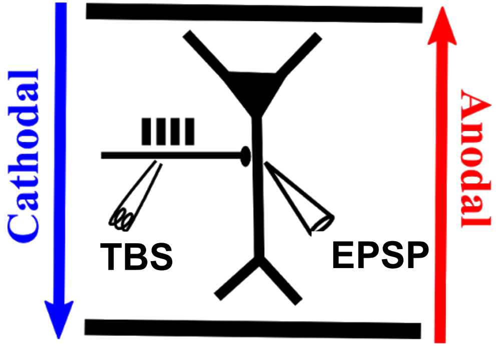
DCS effects on synaptic strength are specific:

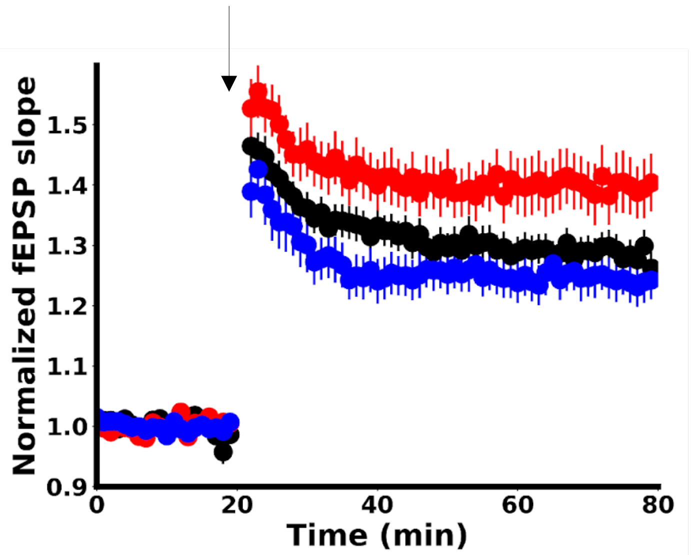
- Needs synaptic plasticity to affect plasticity
- Tends to potentiate, not depress synapses
- Cathodal vs anodal effect specific to dendritic location

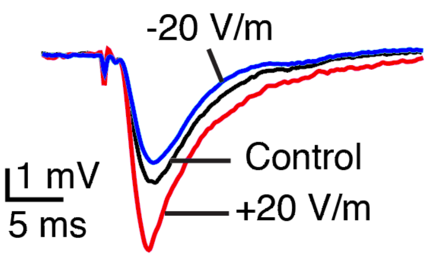
Kronberg, *Brain Stimulation*, 2017

Polarity interacts with type of activation

Theta burst stimulation (TBS): HF burst repeated at 7Hz.
TBS dominated by somatic activity and we target close to the soma.



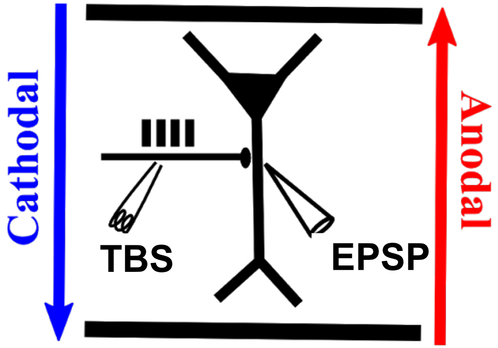


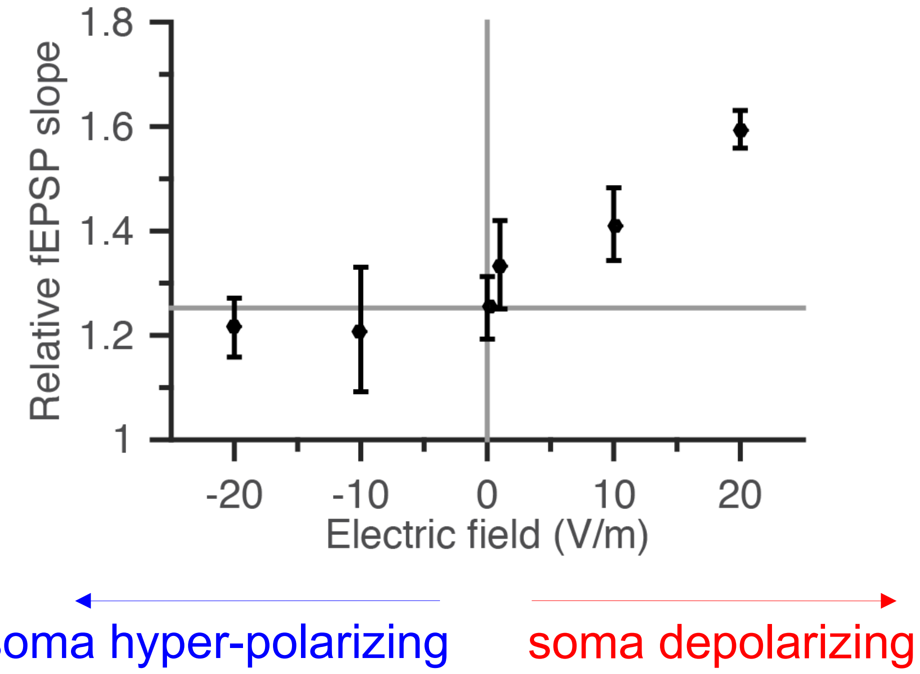


Kronberg, *bioRxiv*, 2019

Bias towards potentiation

Greg Kronberg   Asif Rahman

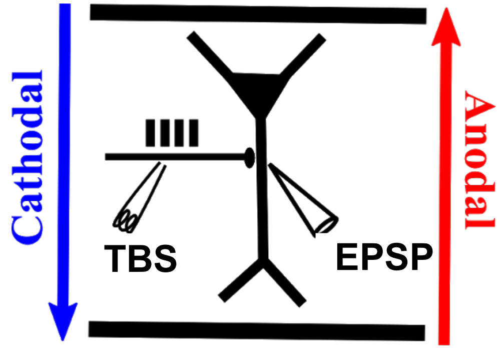


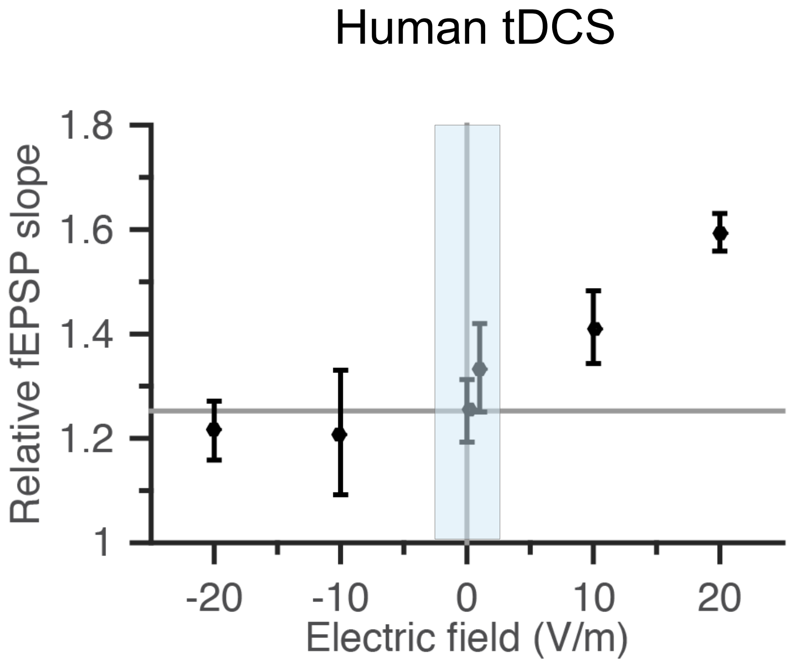


Kronberg, *bioRxiv*, 2019

Bias towards potentiation

Greg Kronberg Asif Rahman



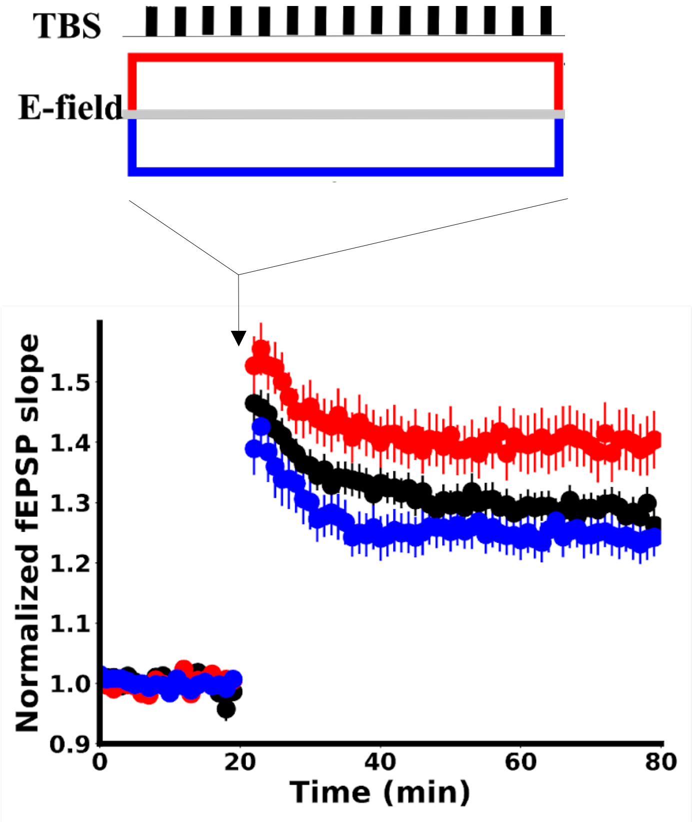


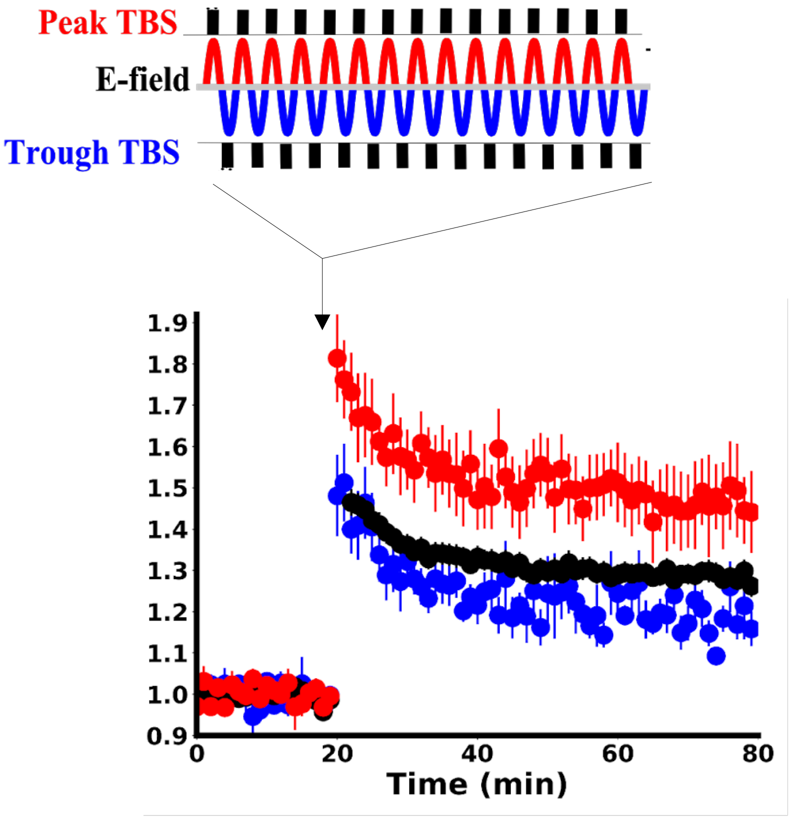
→ 1% in 1V/m

soma hyper-polarizing   soma depolarizing

Kronberg, *bioRxiv*, 2019

Instantaneous E-field is relevant





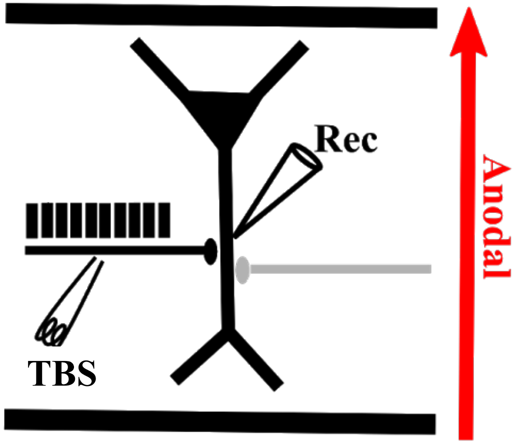
Greg Kronberg Asif Rahman

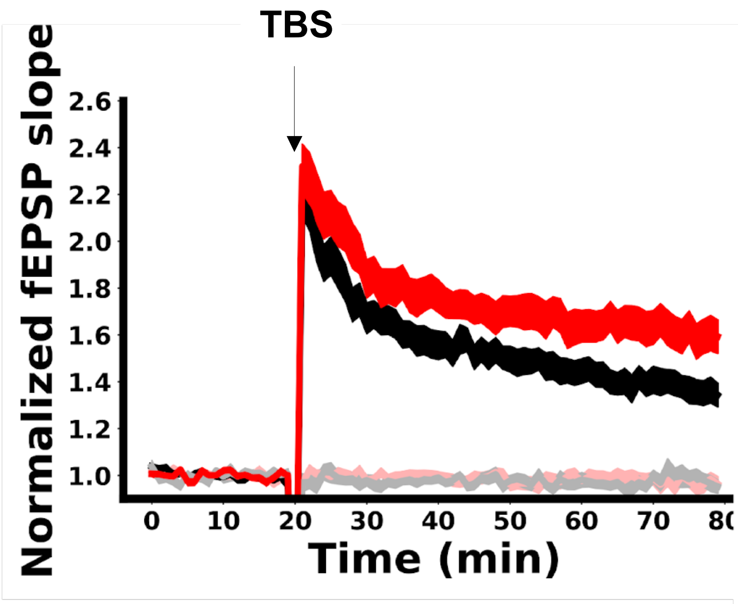
Kronberg, *bioRxiv*, 2019

Specific to the potentiated pathway

Greg Kronberg

Asif Rahman





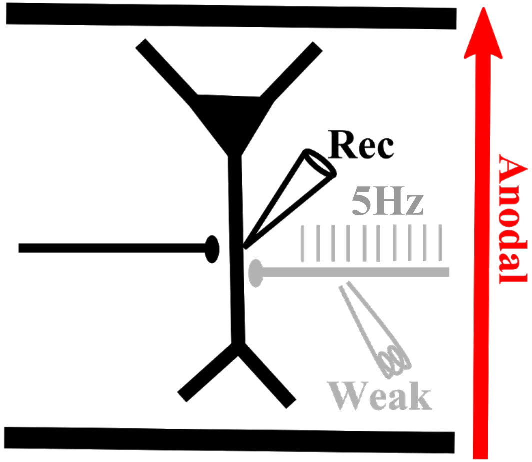
Kronberg, *bioRxiv*, 2019

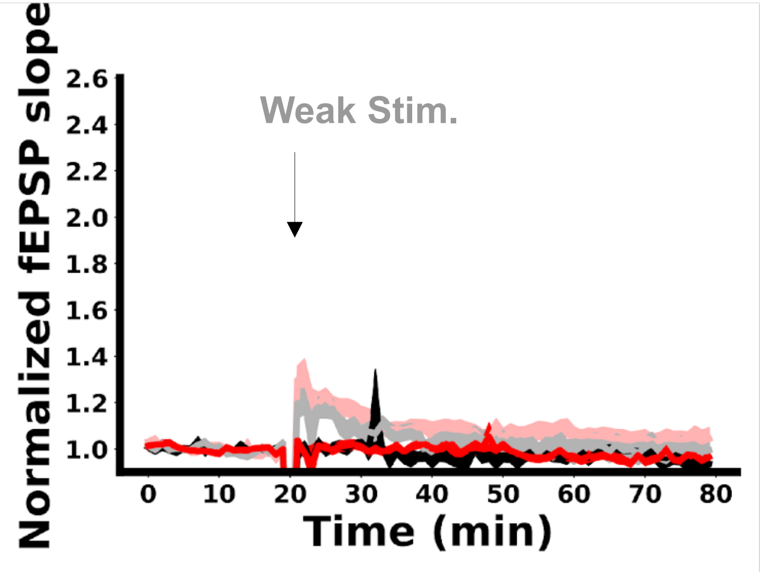
Specific to the potentiated pathway

Greg Kronberg

Asif Rahman

Weakly activated pathway is not enhanced.

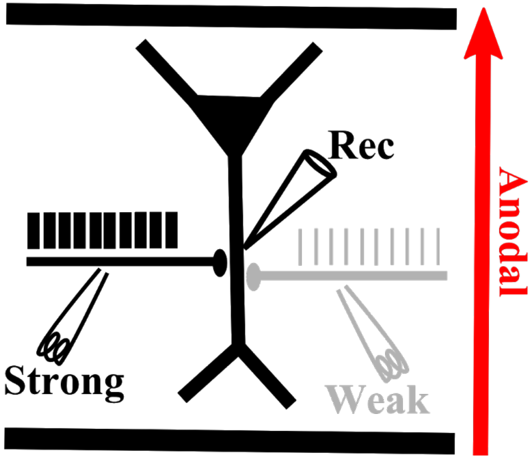


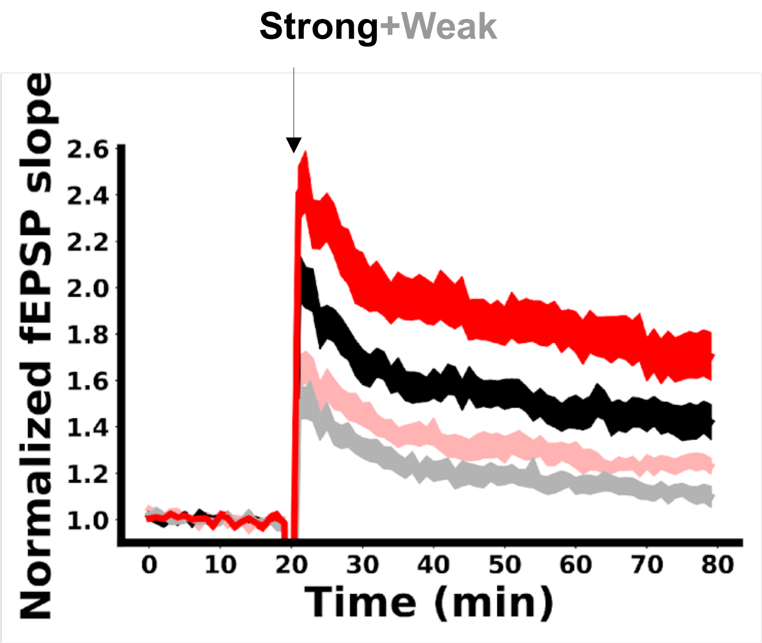


Kronberg, *bioRxiv*, 2019

Associative

Strong stimulation induces LTP in weakly co-activated pathway.
This associative effects is preserved and enhanced with DCS.





Kronberg, *bioRxiv*, 2019

Conclusion

DCS boosts Hebbian plasticity:

- Effect dependent on potentiating neural activity
- Specific to activated pathway
- Follows associative rule of learning

Clinical implications

Postulate

Human tDCS effects are highly task specific because they inherit exquisite specificity of Hebbian plasticity.

Predictions on tDCS:

- Efficacy improves when paired with a learning task instead of rest.
- Specificity comes from the task not focality of stimulation.
- Performance gains should be specific to the trained task.

Acknowledgments

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Asif
Rahman

Anli
Liu

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USAF
NYU

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