BuzsákiLab

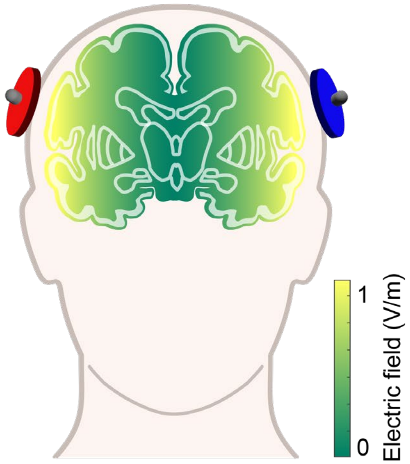
NYU

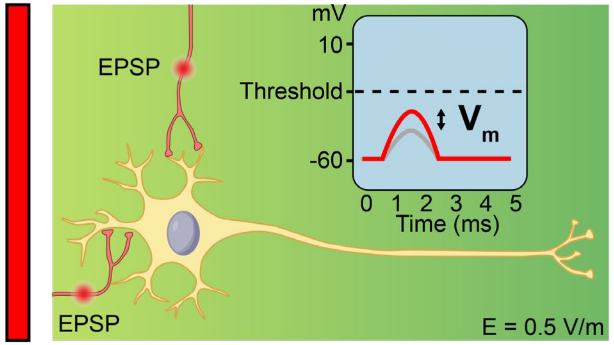
# How small electric fields still affect neurons

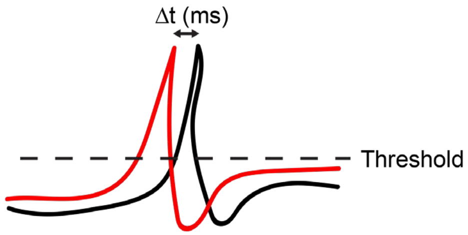
**Mihaly (Misi) Voroslakos**
Postdoctoral Researcher
Buzsaki Lab
NYU

Neuroergonomics Conference & NYC Neuromodulation Conference
2022. July 31.

# Electrical stimulation induced neuromodulation




Anode Cathode

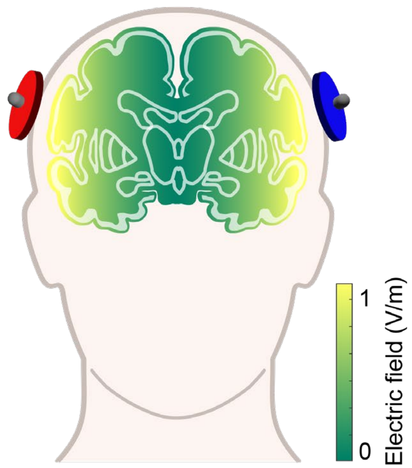
**tDCS**

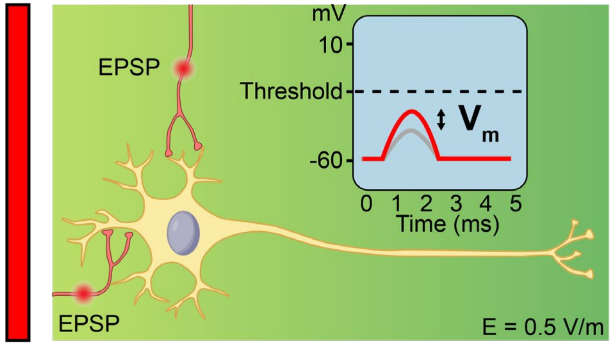
**Electric field**

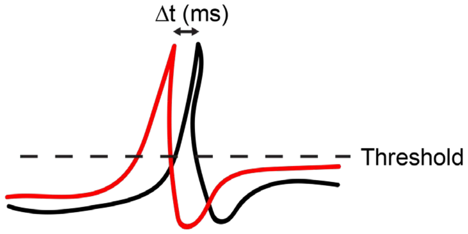
**Change in $V_m$**
(subthreshold)

**Change in AP timing**

# Stimulation intensity – response relationship

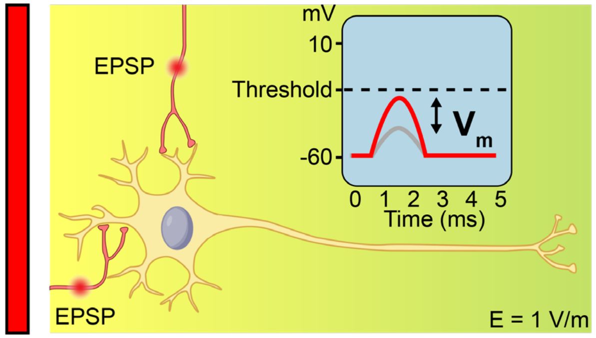


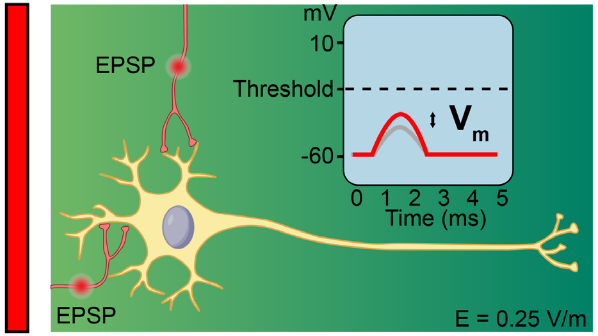




Anode Cathode

↑ Intensity ↑ E-field ↑ $V_m$

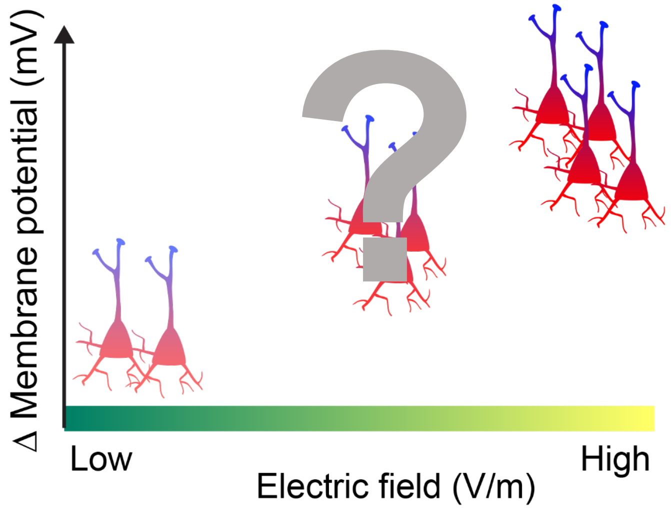



↓ Intensity ↓ E-field ↓ $V_m$




## In vitro

Linear relationship between **E - $V_m$**



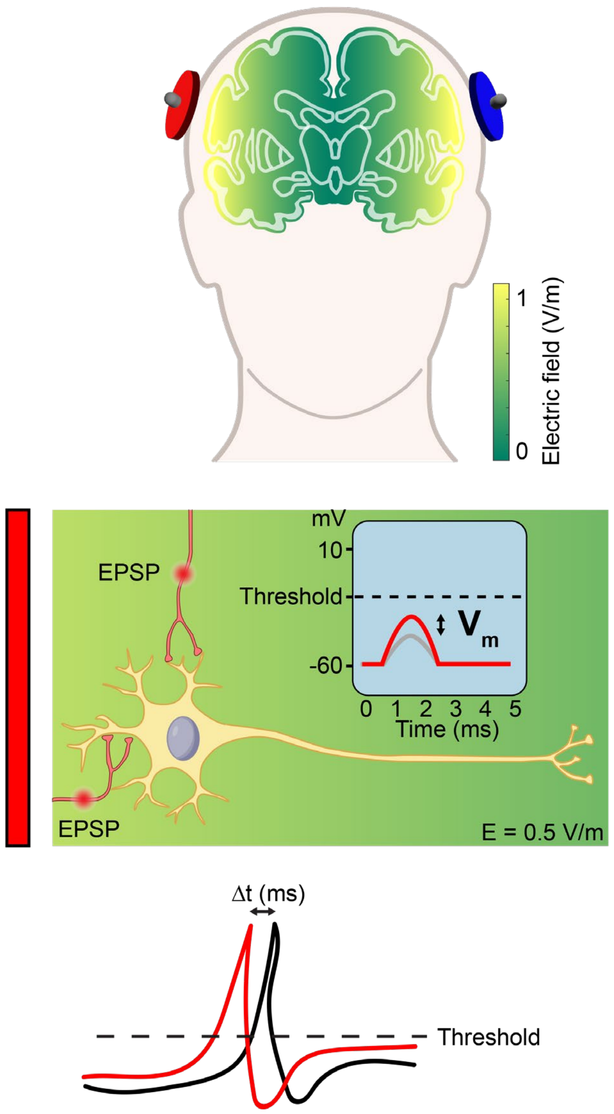

Memory
Pain
Alzheimer's
Epilepsy
Stroke

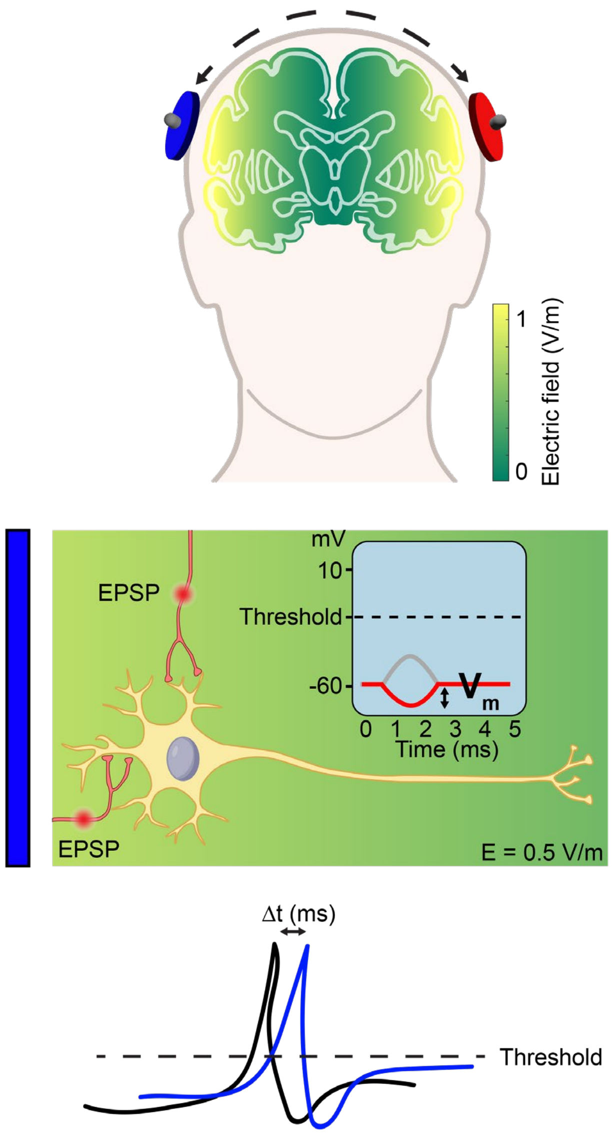
## In clinical practice

Is there an intensity - response relationship?

Esmaeilpour et. al., 2018

# Stimulation polarity – response relationship

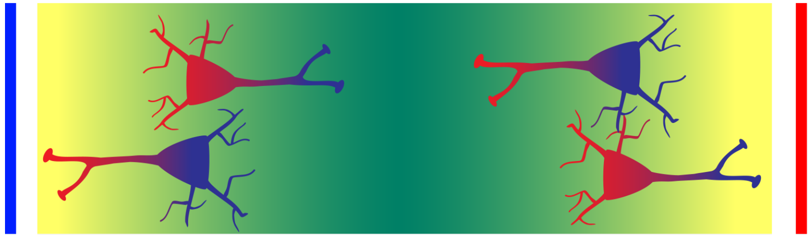


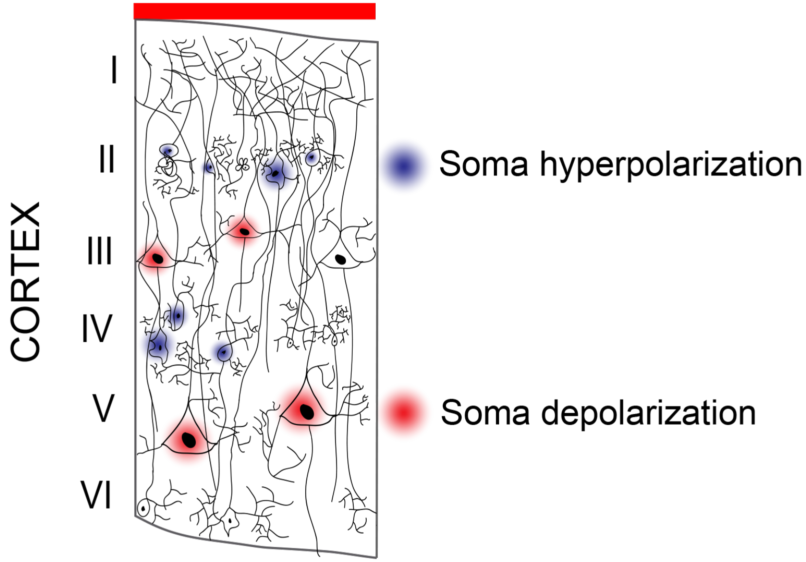




Anode Cathode

## In vitro

Soma depolarizing / hyperpolarizing effects

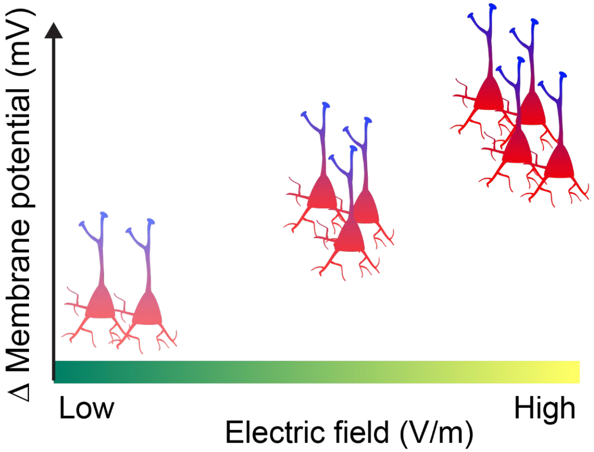


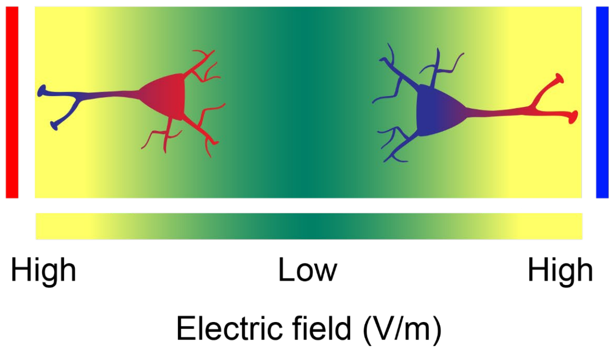



Memory
Pain
Alzheimer's
Epilepsy
Stroke

**In clinical practice?**

# Physiological effects depend on tDCS dose


**1. Electrode montage**

- Location, size and configuration
- E-field is highest below electrodes[1]

**2. Stimulation intensity**

- Subthreshold change in membrane potential
- Higher intensity ➡ Higher E-field

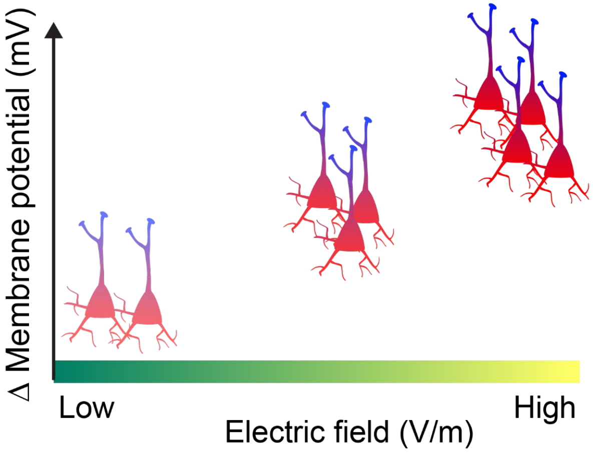
**3. Stimulation polarity**

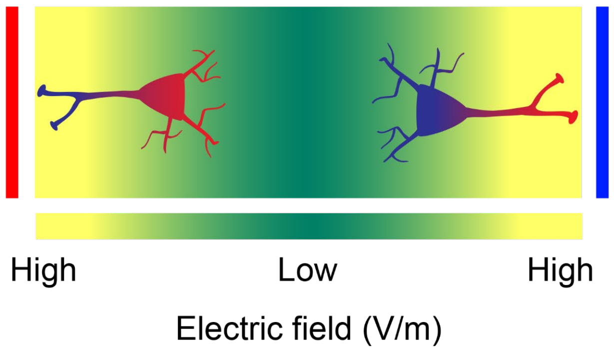
- Soma depolarizing / hyperpolarizing effects
- Neuronal morphology, orientation

[1]But see model predictions around ventricles – Huang et. al., 2019, Brain Stim.

# Physiological effects depend on tDCS dose




1. Electrode montage
   - Location, size and configuration
   - E-field is highest below electrodes

**1. Clinically relevant electric fields ( 1V/m)**

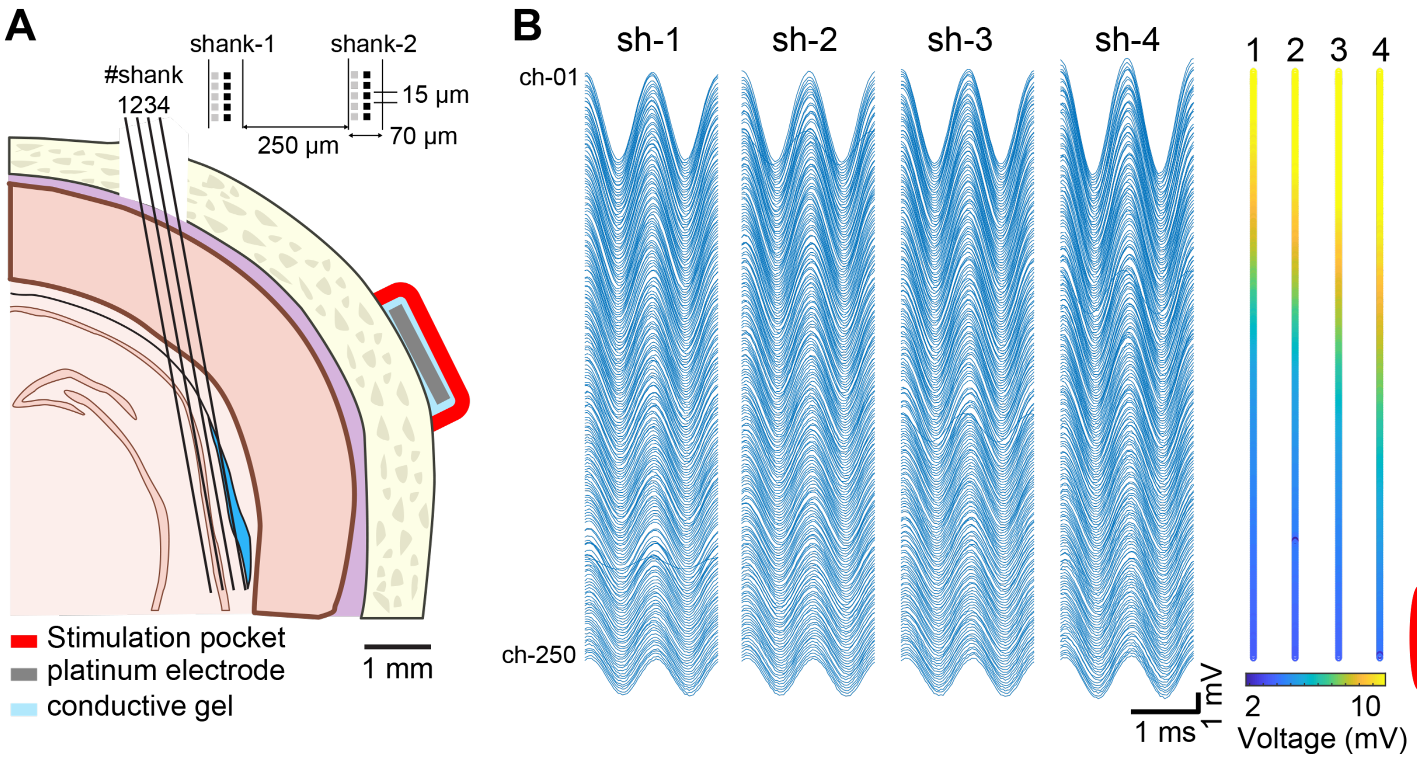
2. Stimulation intensity
   - Subthreshold change in membrane potential
   - Higher intensity Higher E-field

**2. Intensity-response relationship in vivo**

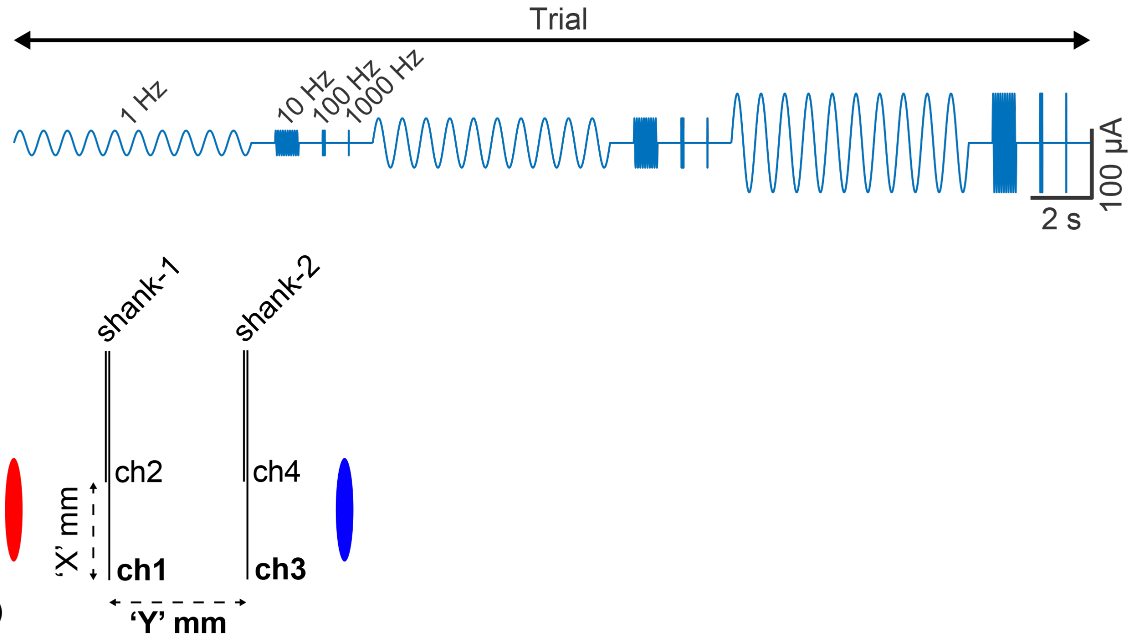
3. Stimulation polarity
   - Soma depolarizing / hyperpolarizing effects

**3. Polarity-response relationship in vivo**

# Measuring electric fields in rats




**How can we measure electric fields?**



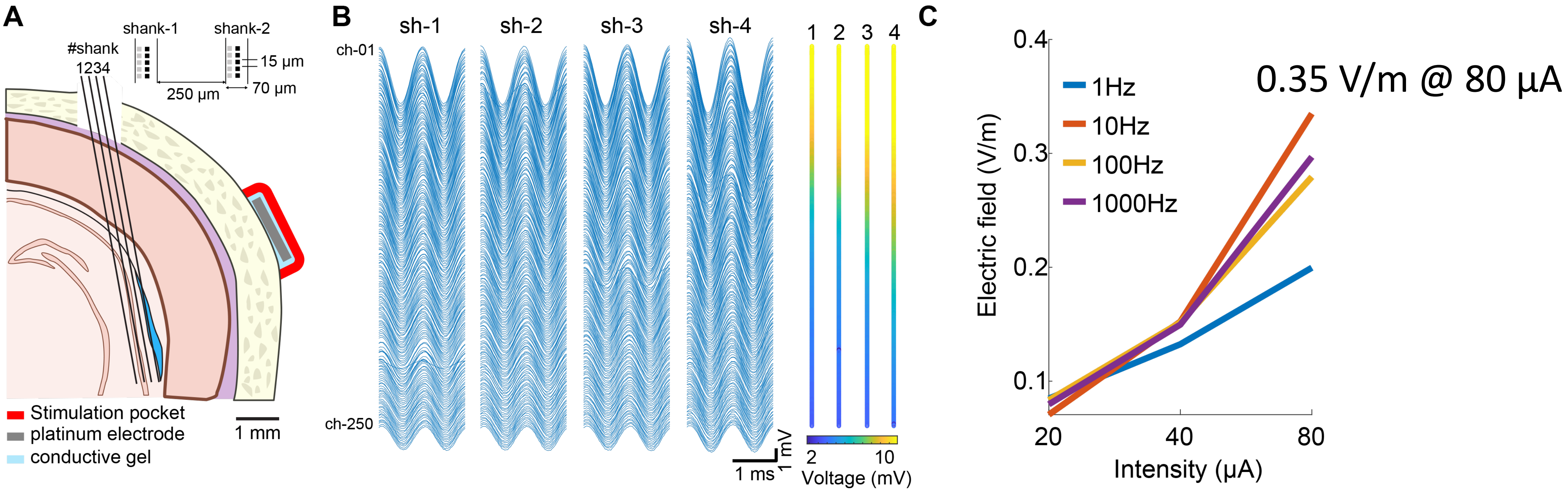

Neuropixels 2.0

- 1280 recording sites / shank

Shank-by-shank recording

- 4 x 250 channels = 1000 channels

# Stimulation induced electric fields in rats




Neuropixels 2.0
- 1280 recording sites / shank

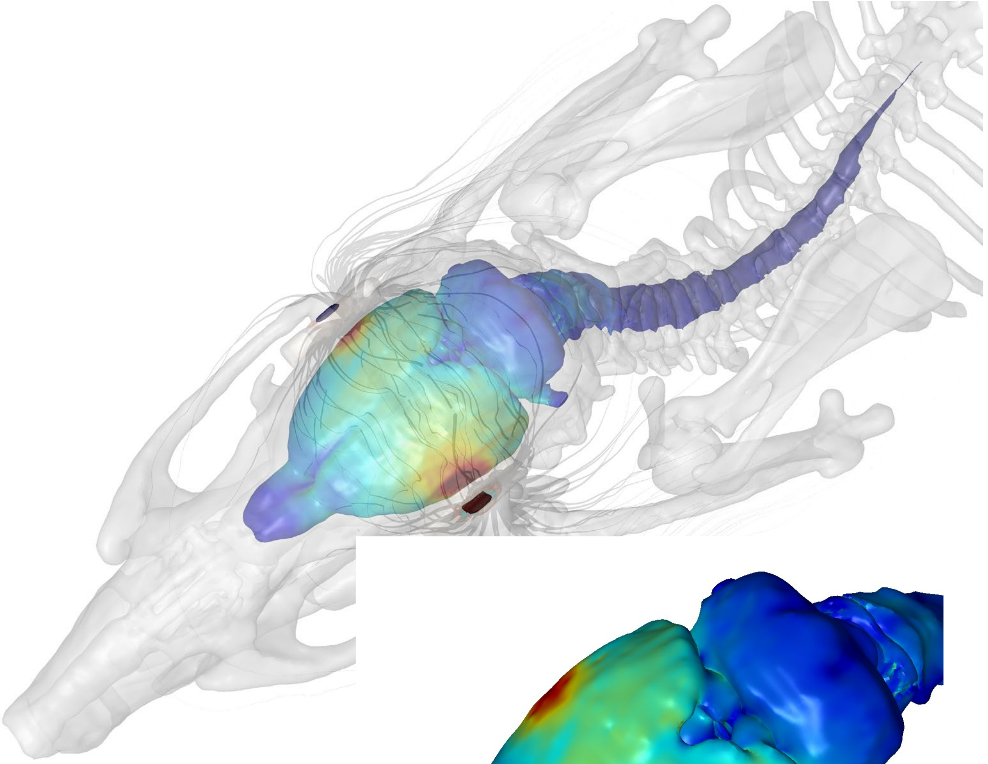
Shank-by-shank recording
- 4 x 250 channels = 1000 channels

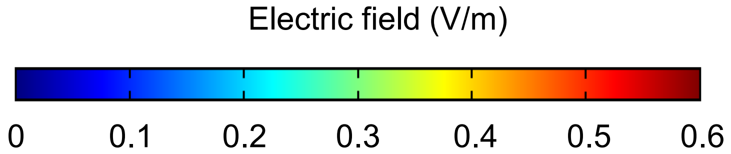
**Human limit < 200 µA**

# Validation of rat models

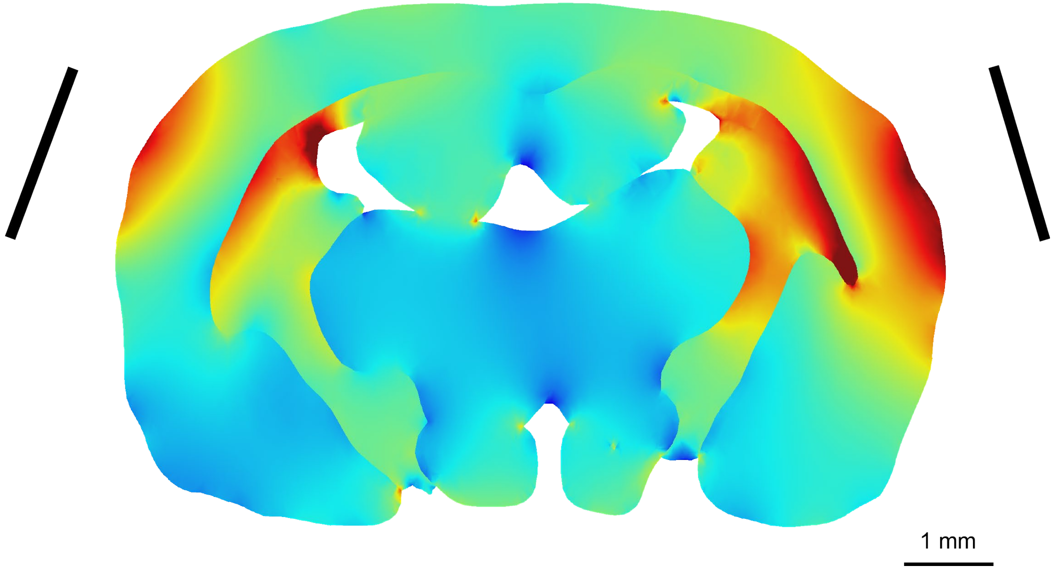
Niranjan Khadka

**Human limit < 200 μA**



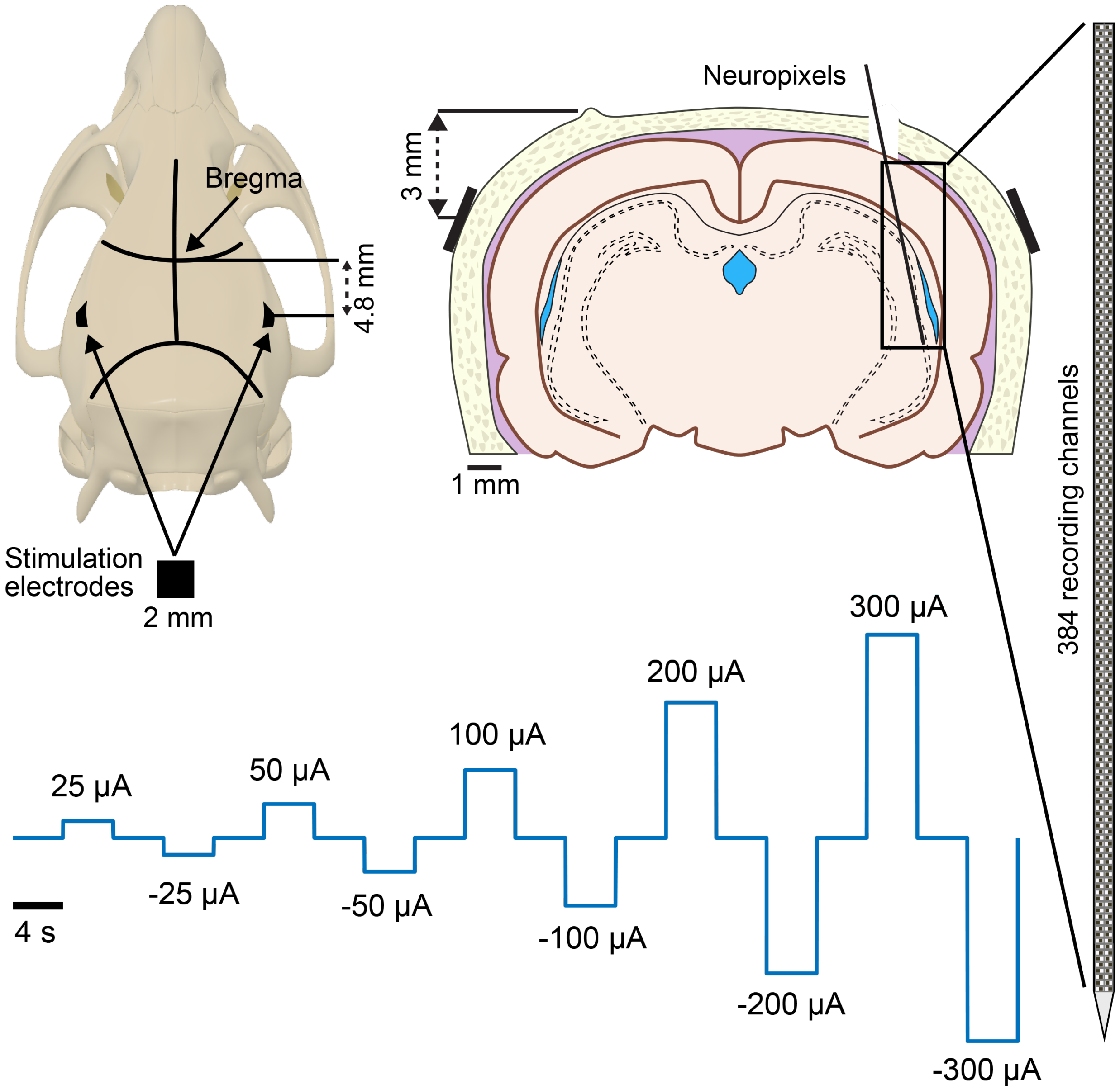



100 μA 0.6 V/m



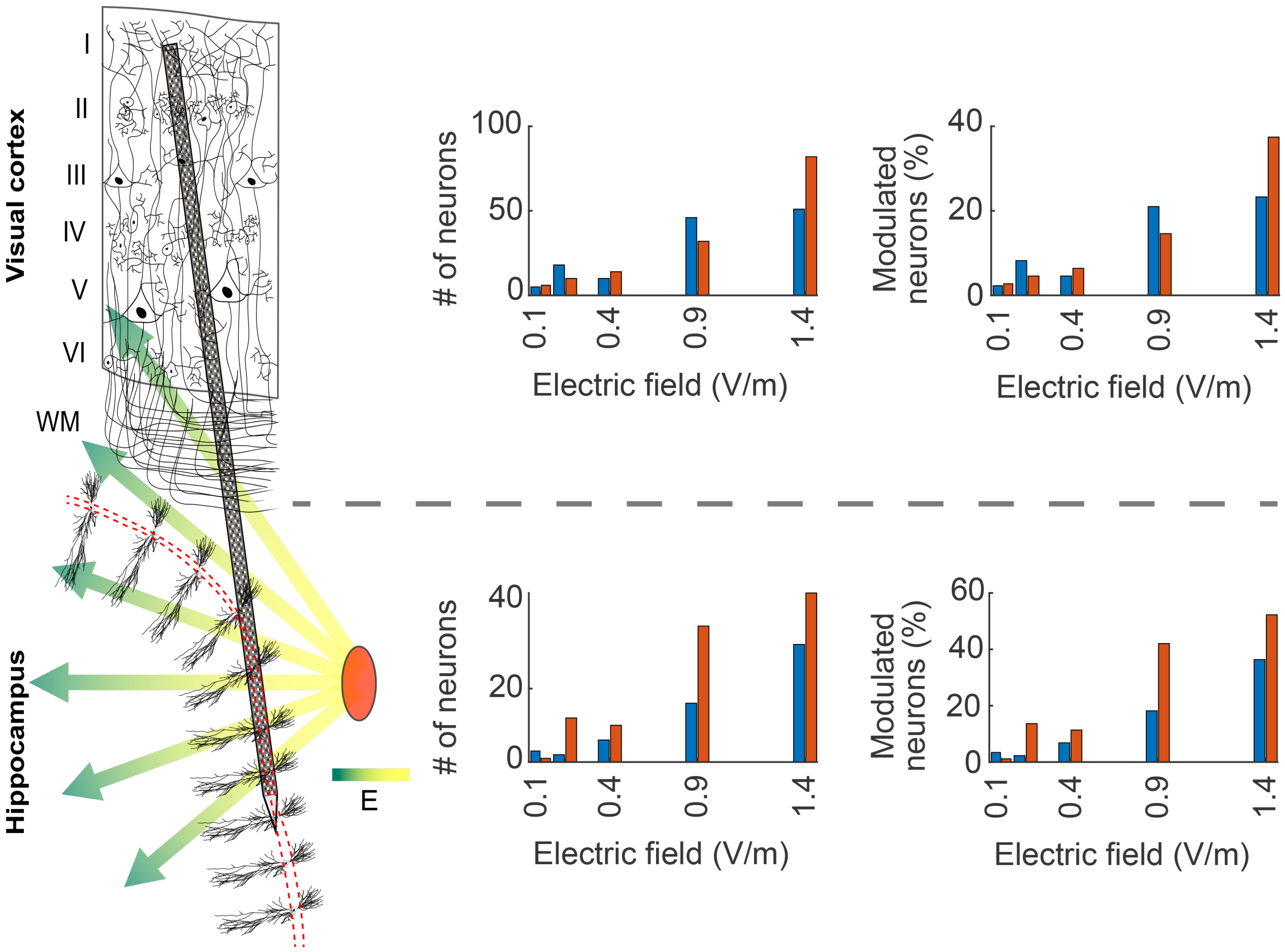
# Methods





Bregma
4.8 mm
Stimulation
electrodes
2 mm
Neuropixels
3 mm
1 mm
384 recording channels
25 µA
-25 µA
50 µA
-50 µA
100 µA
-100 µA
200 µA
-200 µA
300 µA
-300 µA
4 s

# Single unit response induced by TES



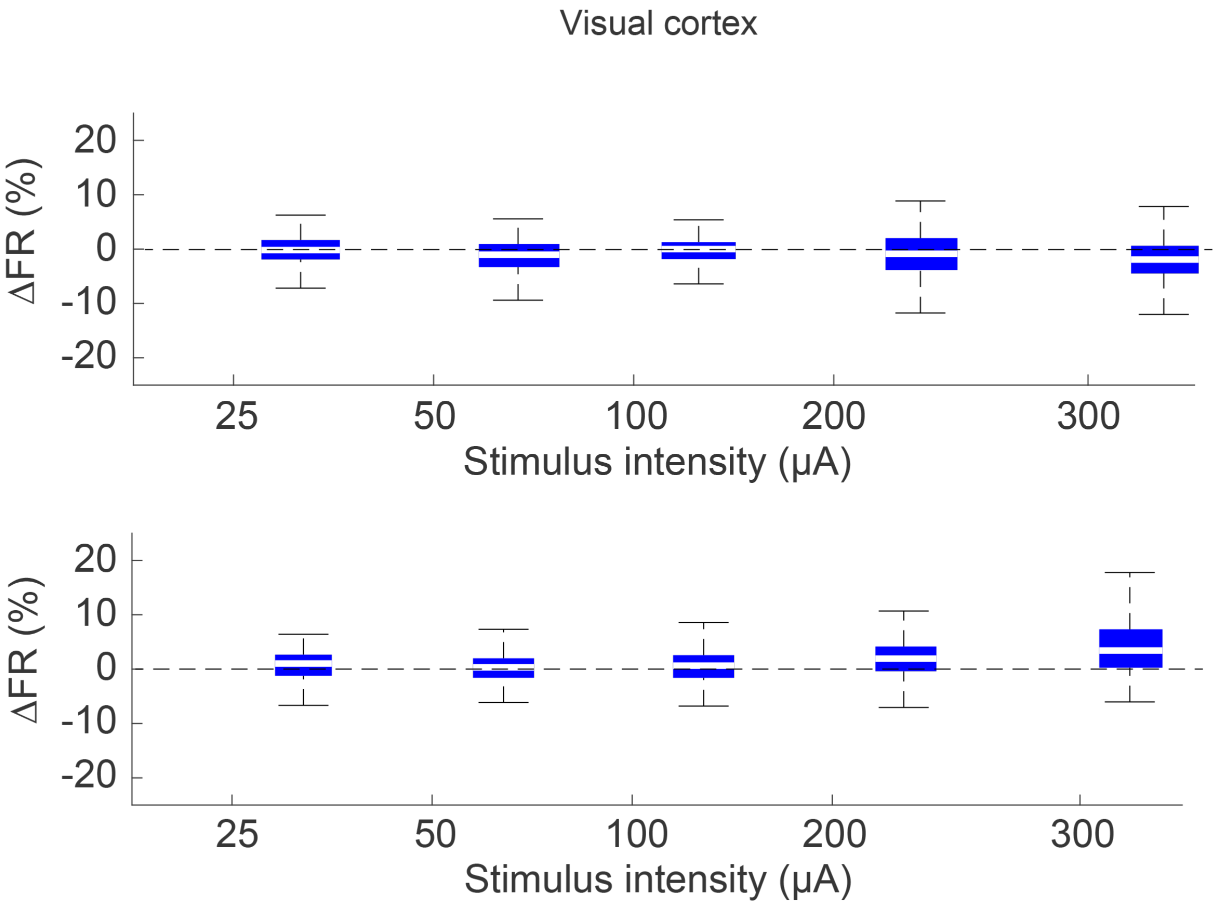

- n = 203 single units in visual cortex
- 40 % of cortical cells @ 1.4 V/m

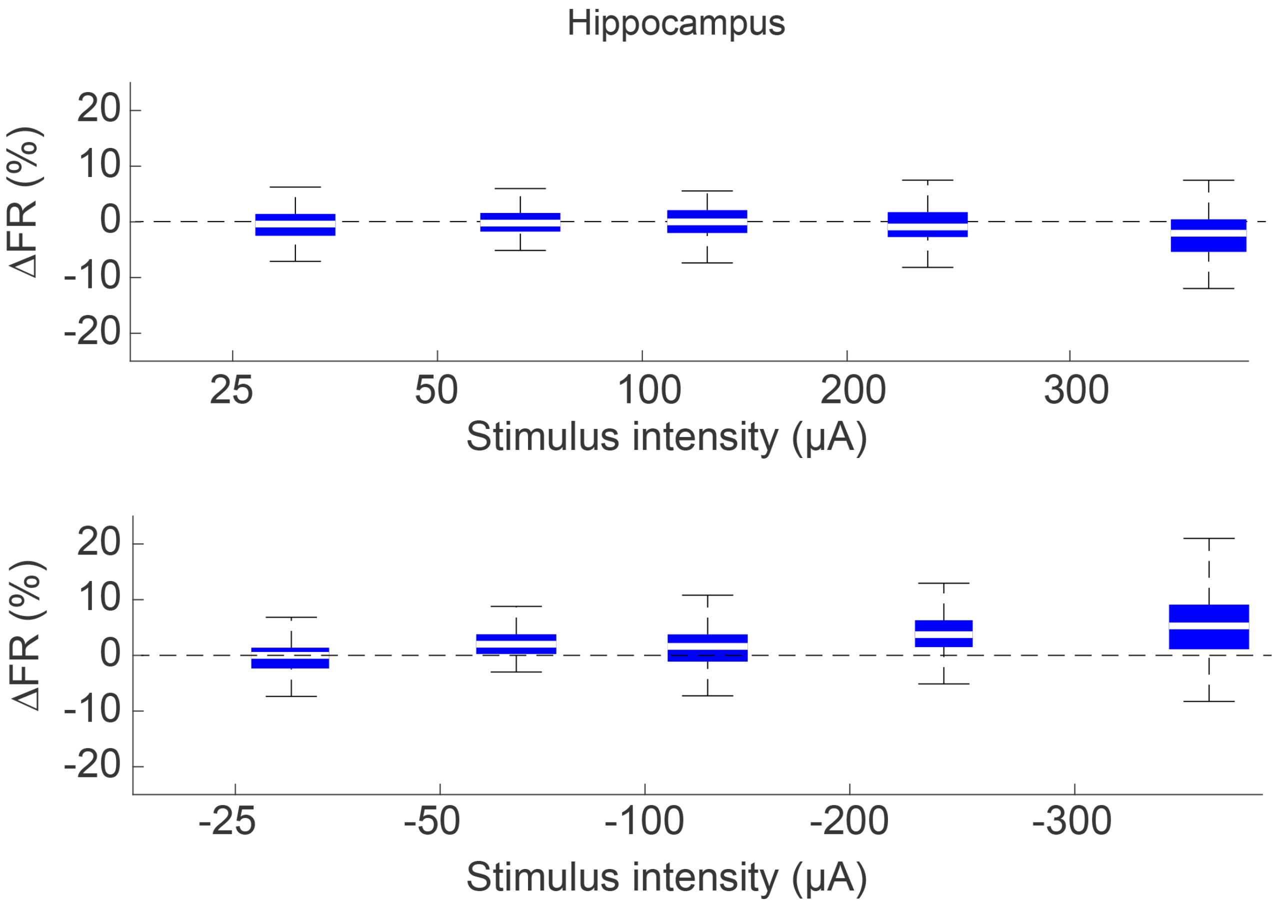
- n = 88 single units in hippocampus
- 54 % of hippocampal cells @ 1.4 V/m

# Single unit response induced by TES

ΔFR = -1.9% @ 300 μA (1.4 V/m)
ΔFR = 3.4% @ -300 μA (1.4 V/m)

ΔFR = -2% @ 300 μA (1.4 V/m)
ΔFR = 5.3% @ -300 μA (1.4 V/m)

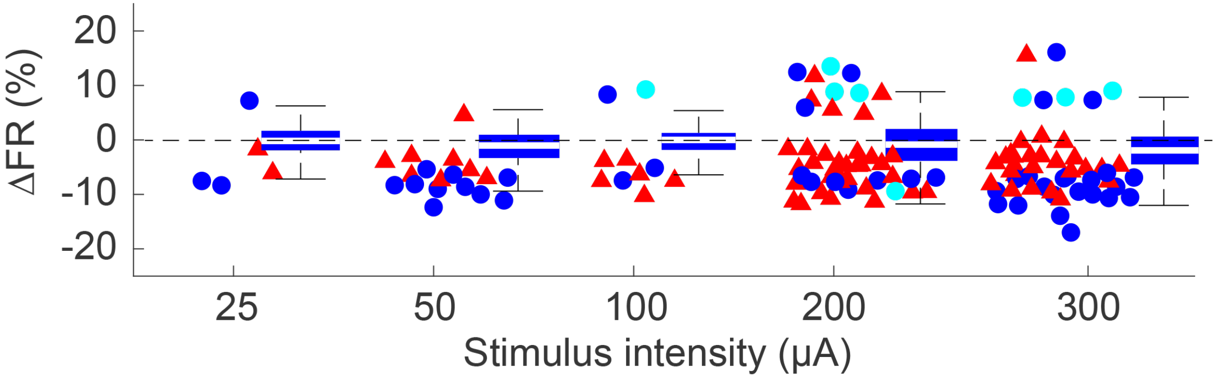


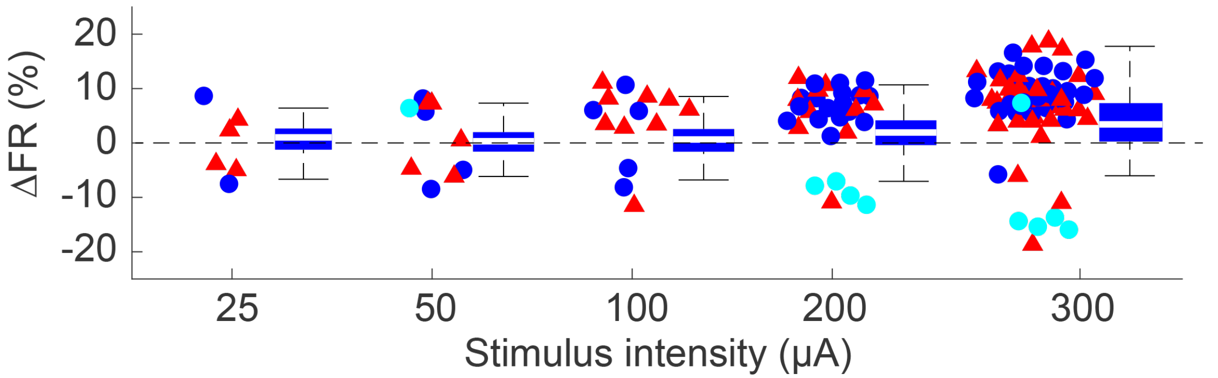



# Single unit response induced by TES

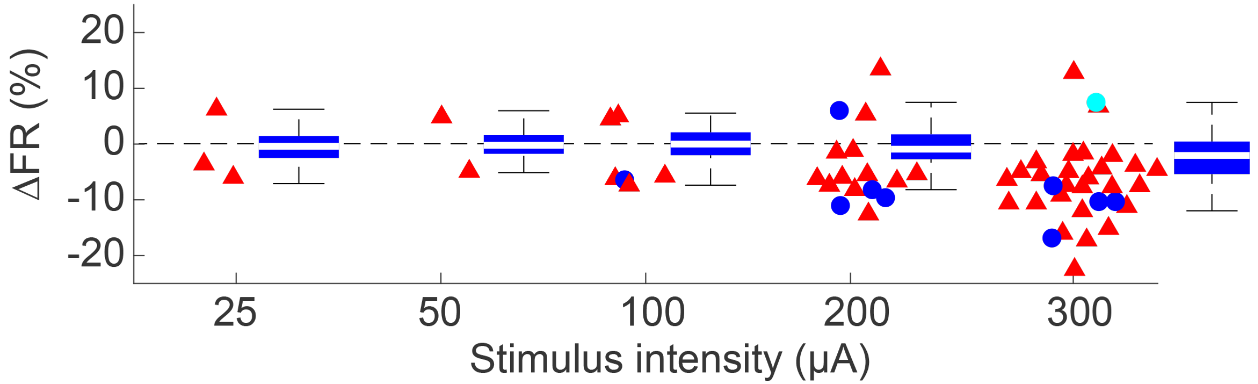
**Both putative pyramidal cells and interneurons are affected by TES.**

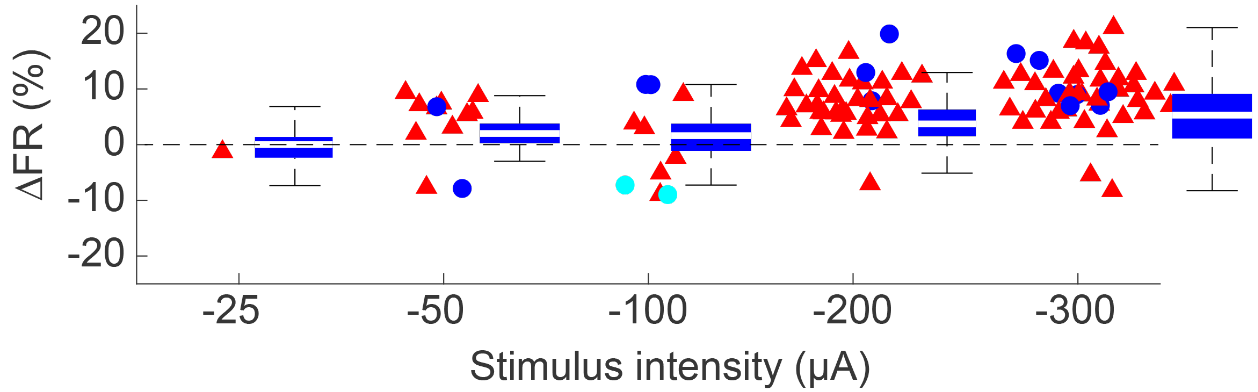
Visual cortex




Hippocampus



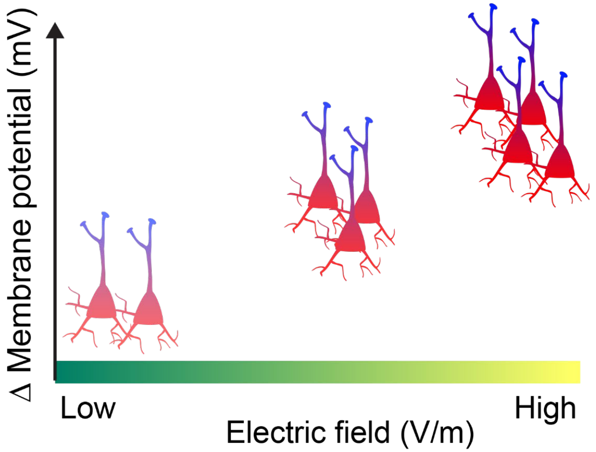




Putative pyramidal cell    Putative wide interneuron    Putative narrow interneuron

# Summary


**1. Clinically relevant electric fields ( 1V/m) in rats**

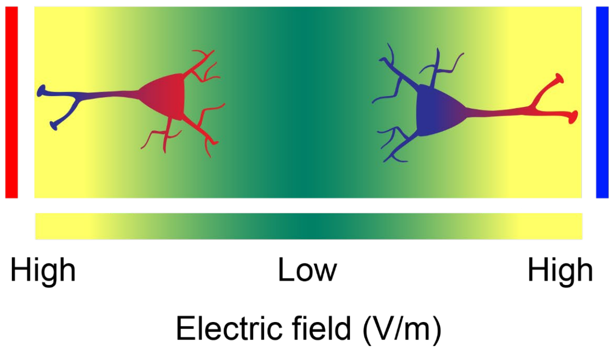
Validated FEM model for rats




**2. Intensity-response relationship**

Intensity – single unit response relationship

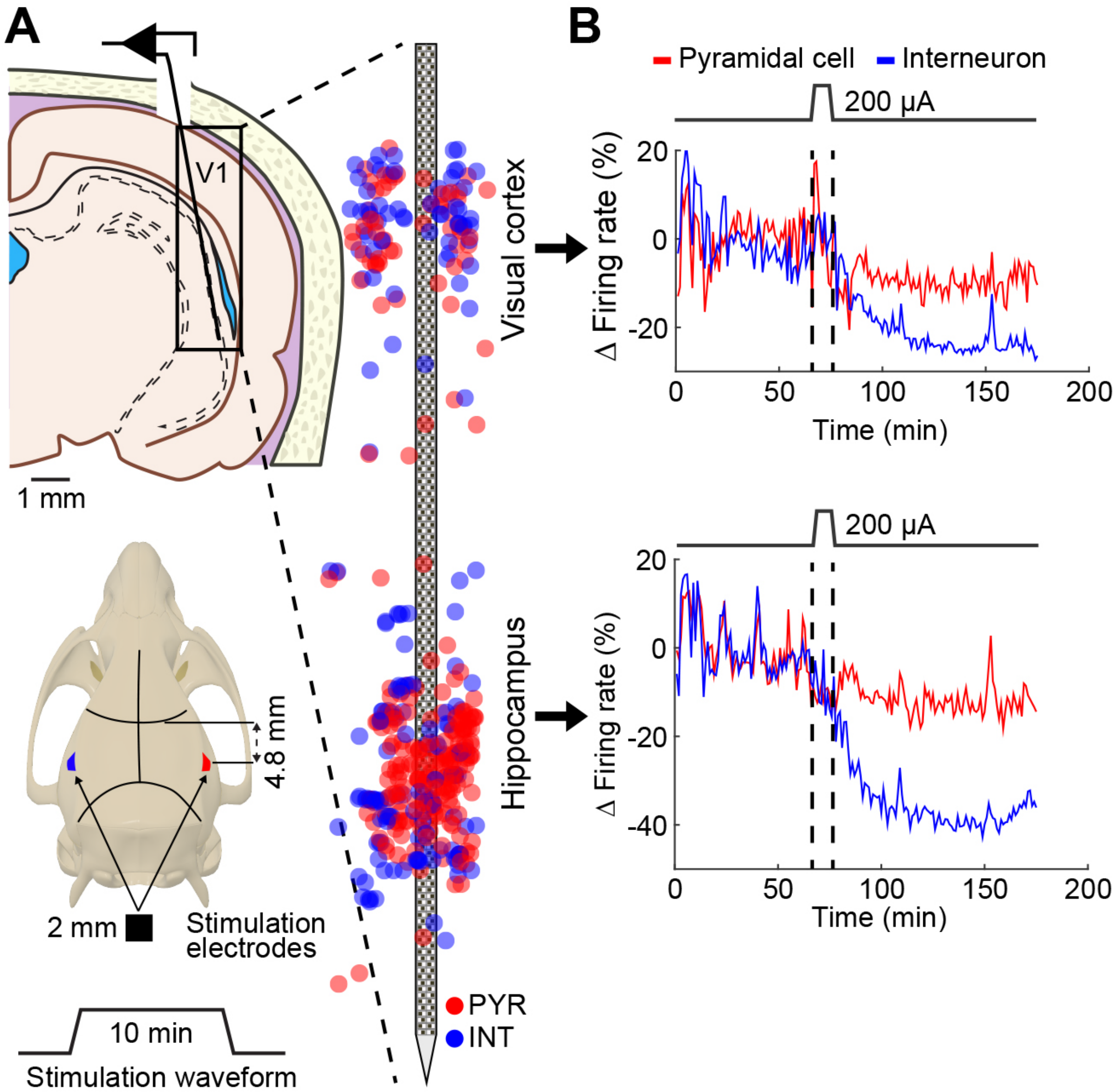
**Does this translate into behavioral response?**




**3. Polarity-response relationship**

Soma depolarization / hyperpolarization under both anode and cathode.

# tDCS-induced neuroplasticity in rats




ΔF - percent change in spiking between Pre and Stim, Post

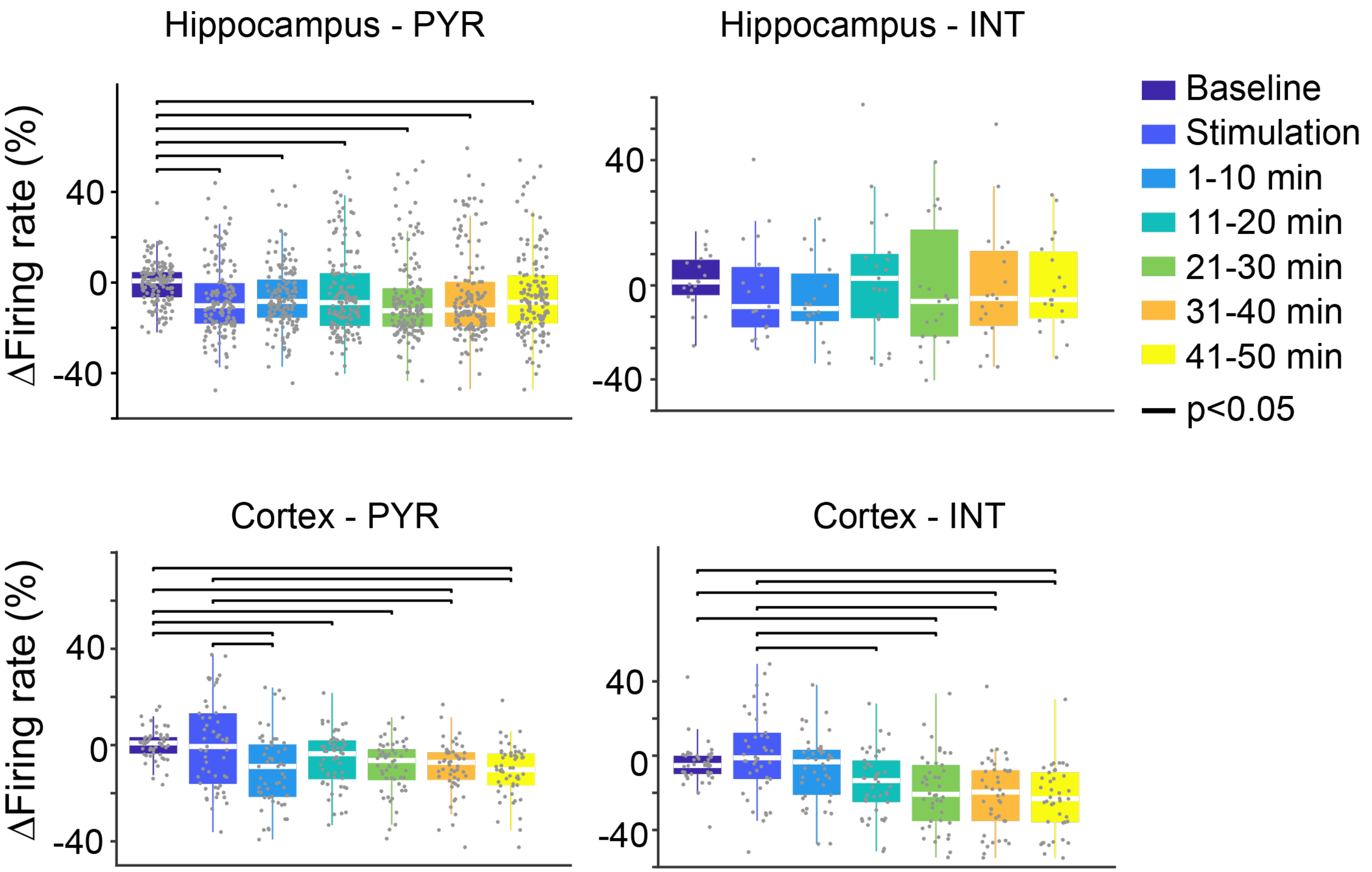
$$\Delta F = 100 \frac{F_{stim} - Fpre}{\max(Fpre, Fstim)}$$

# tDCS-induced neuroplasticity in rats

n = 2 rats

Hippocampus
- 145 PYR and 19 INT

Cortex
- 53 PYR and 42 INT




**tDCS-induced change in firing rate lasts 50 minutes**

# Acknowledgements


## Buzsaki Lab


## Modelling collaboration

Marom Bikson
Niranjan Khadka

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Forouzan Farahani