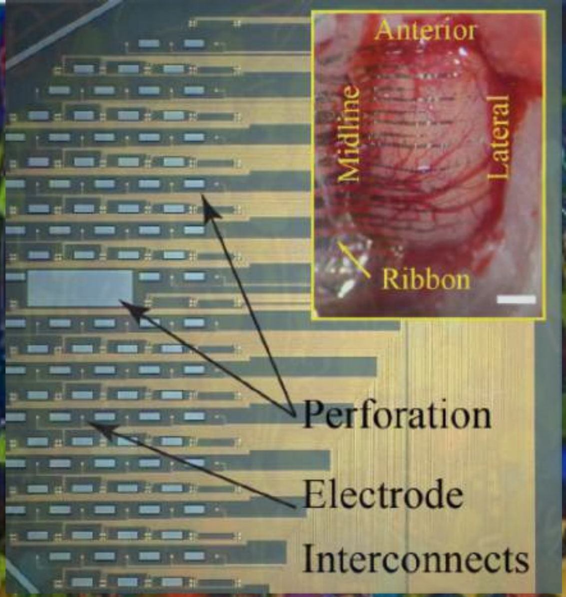
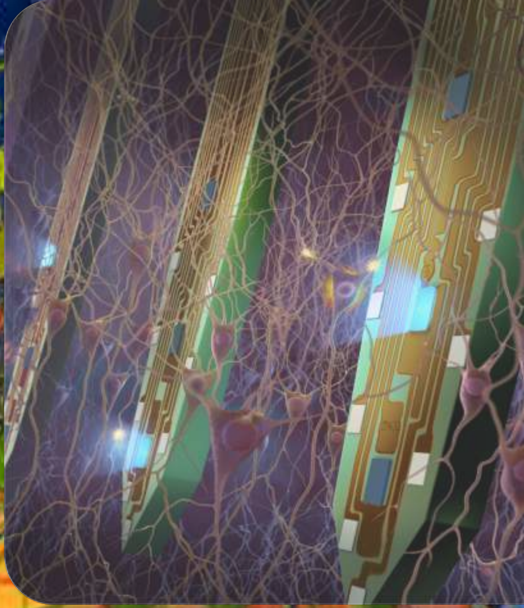
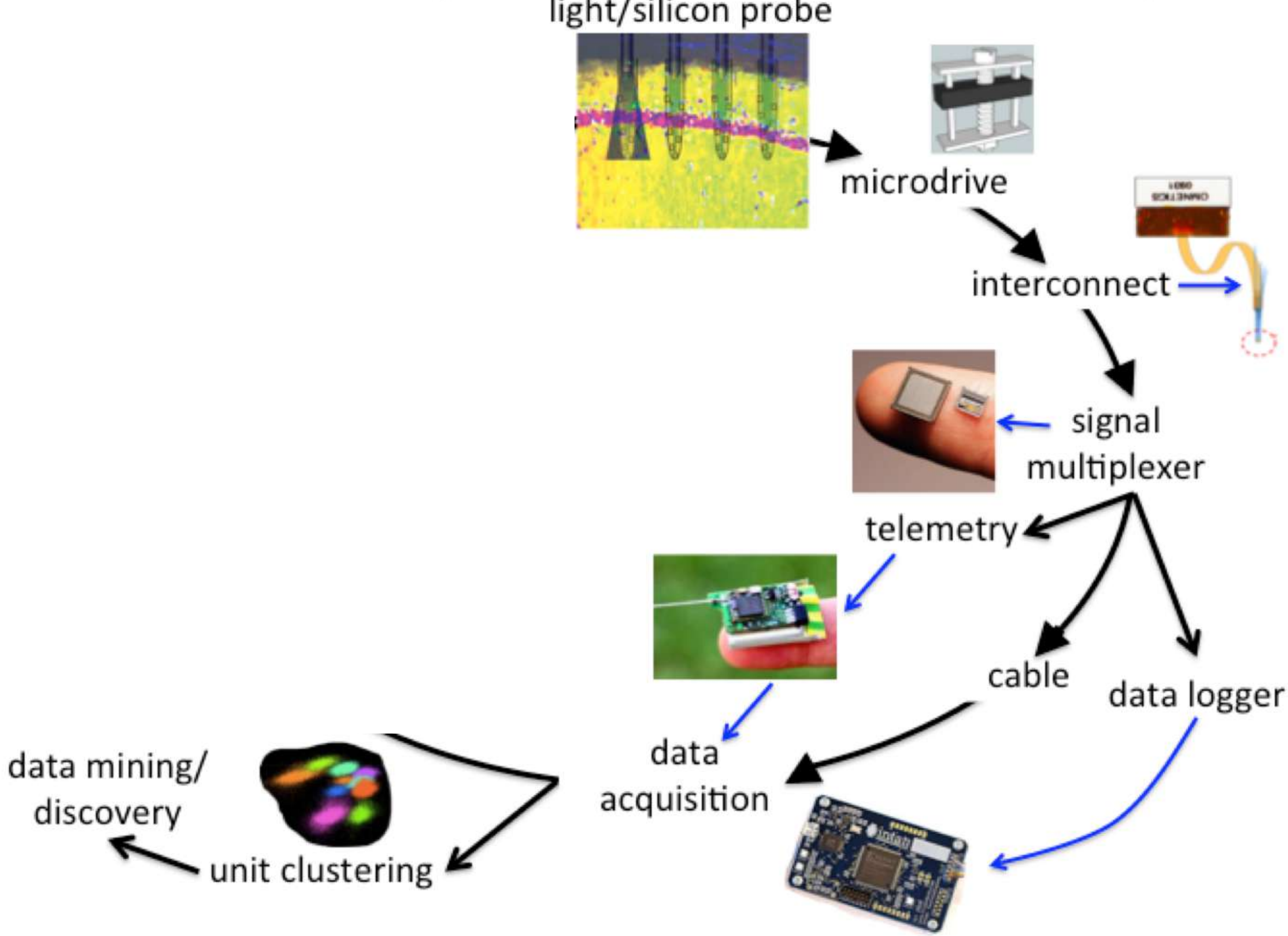




Perturbing circuits and networks

www.buzsakilab.com

Closed-loop control of neuronal activity

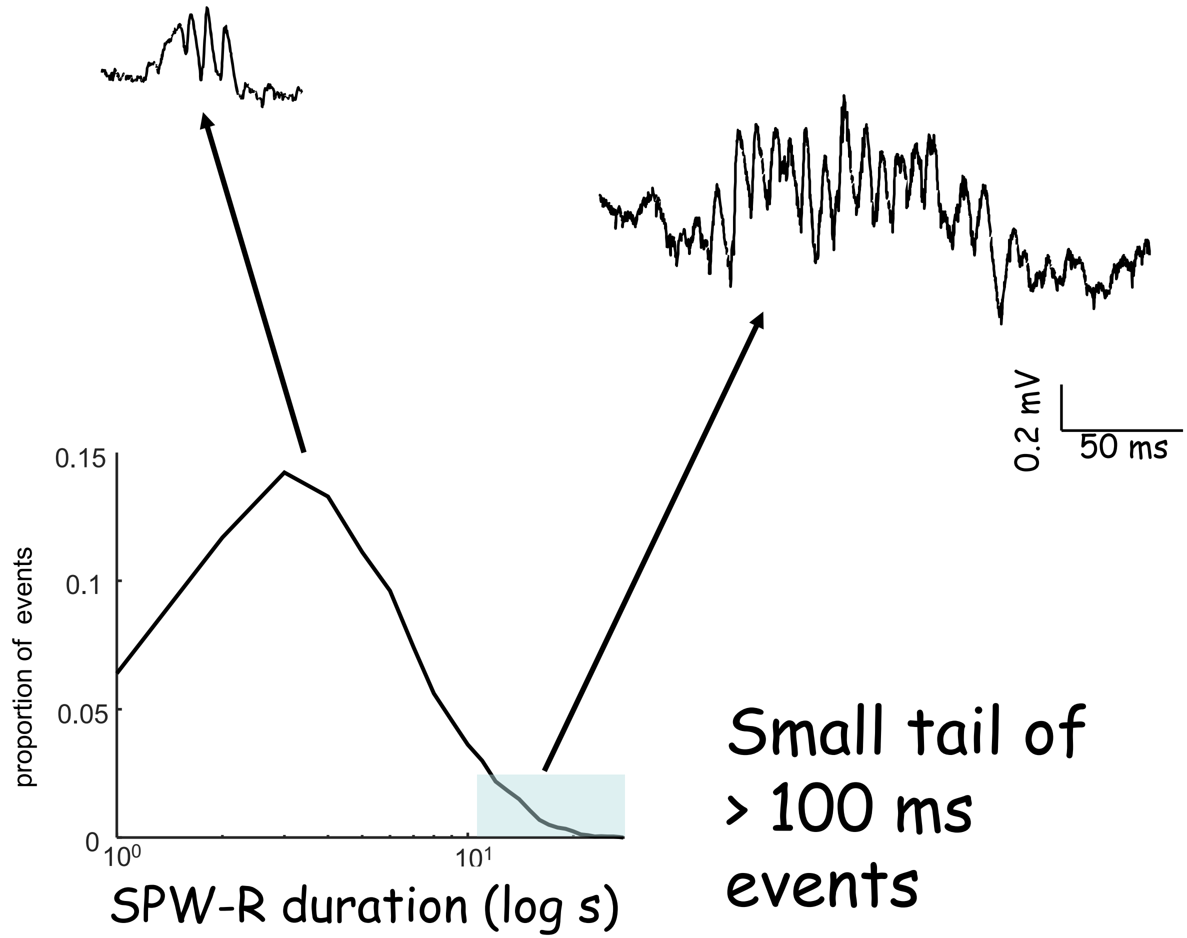


Buzsaki, Stark, Berenyi, Khodagholy, Kipke, Yoon, Wise **Neuron** (2015)

Lognormal distribution of SPW-R durations

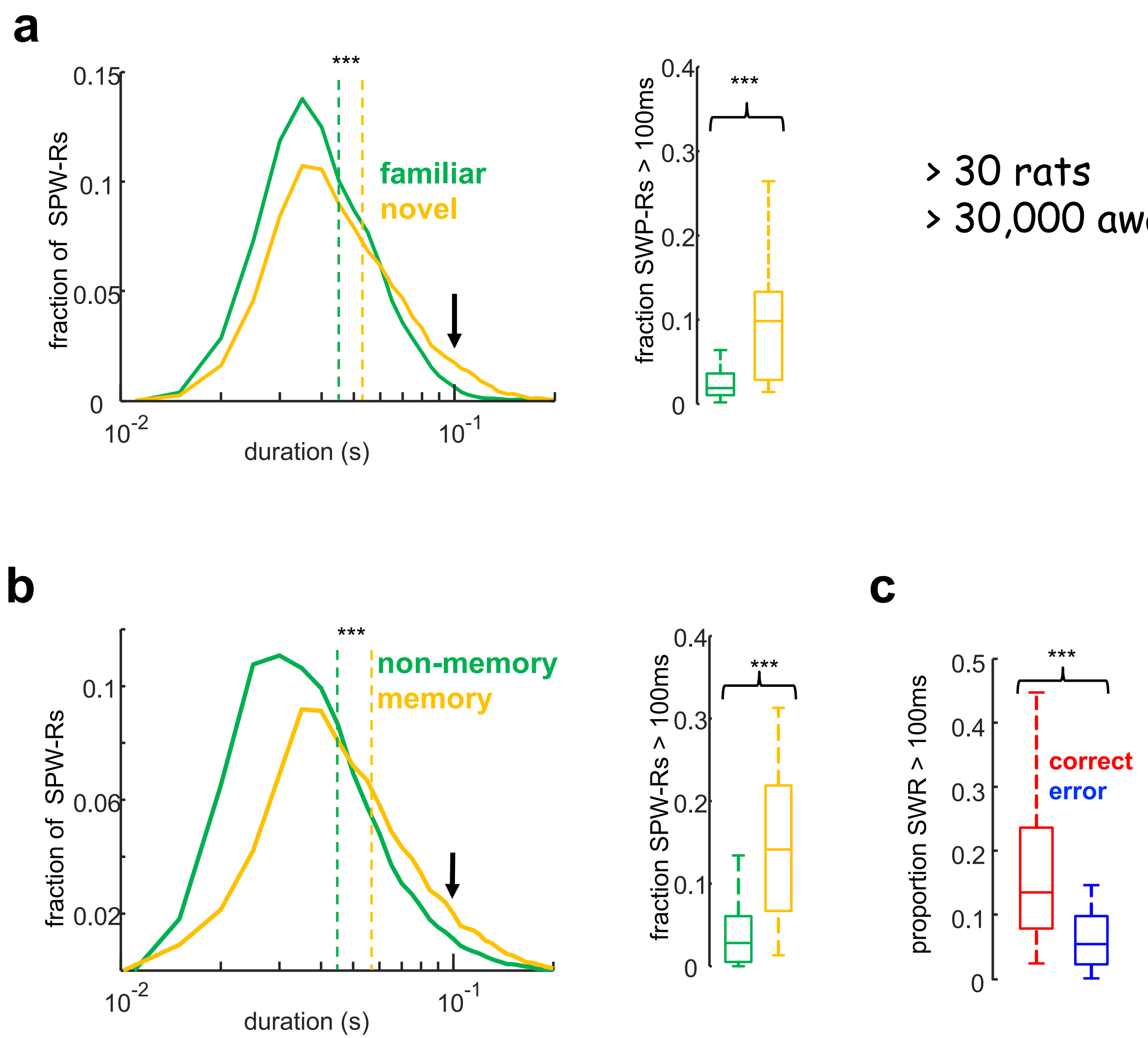
Antonio Fernandez-Ruiz

Azahara Oliva



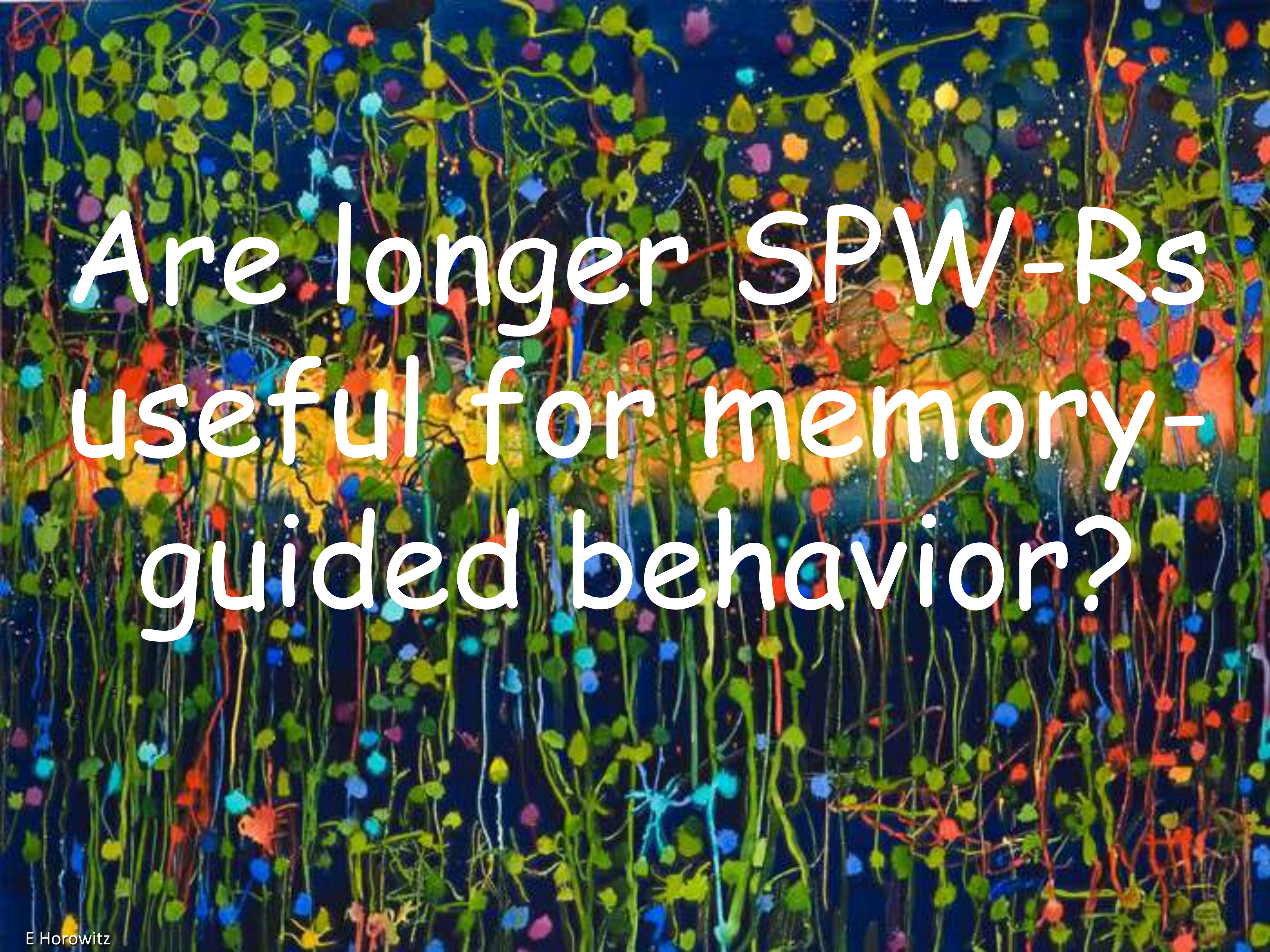
Small tail of
> 100 ms
events

SPW-Rs are longer in novel environments and memory tasks



> 30 rats
> 30,000 awake ripples

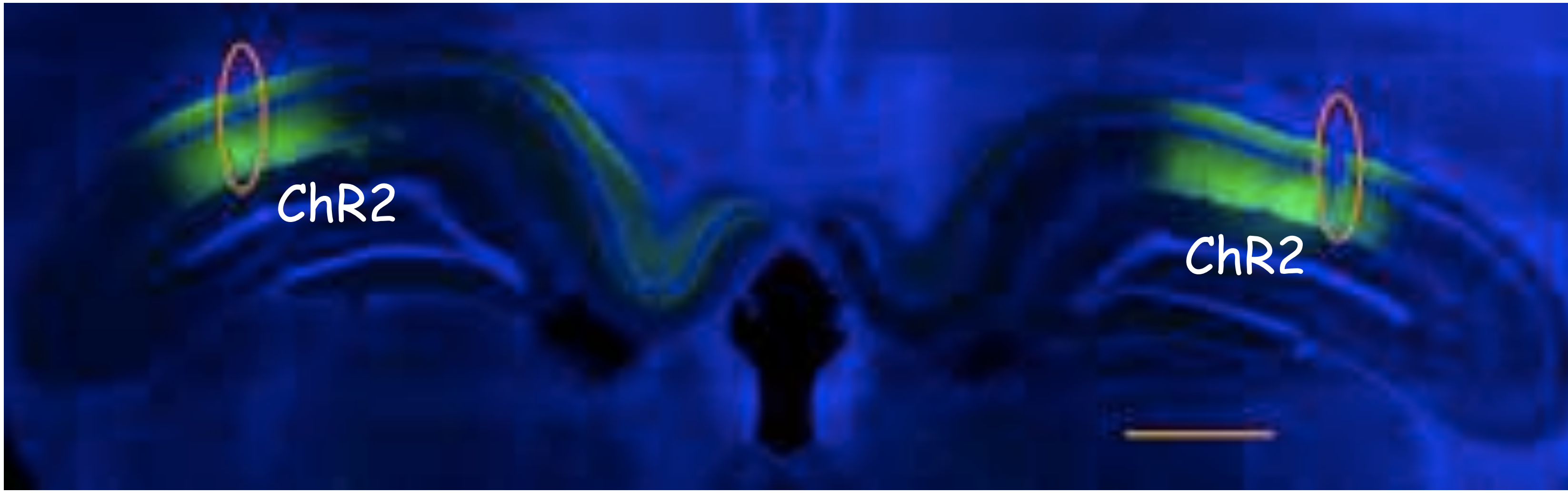
Fernandez-Ruiz, Oliva, Oliveira, Rocha-Almeida, Tingley, Buzsaki, Science, 2019



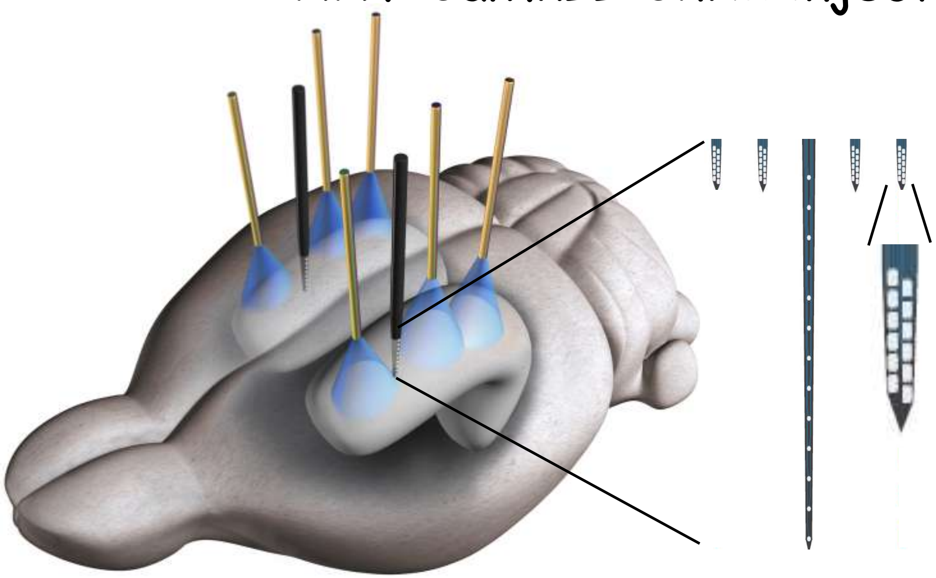
Are longer SPW-Rs useful for memory-guided behavior?

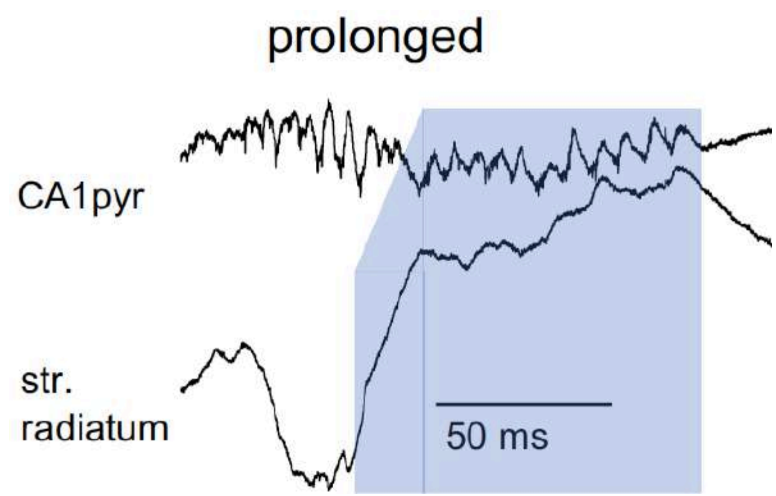
E Horowitz

Optogenetic prolongation of CA1 ripples



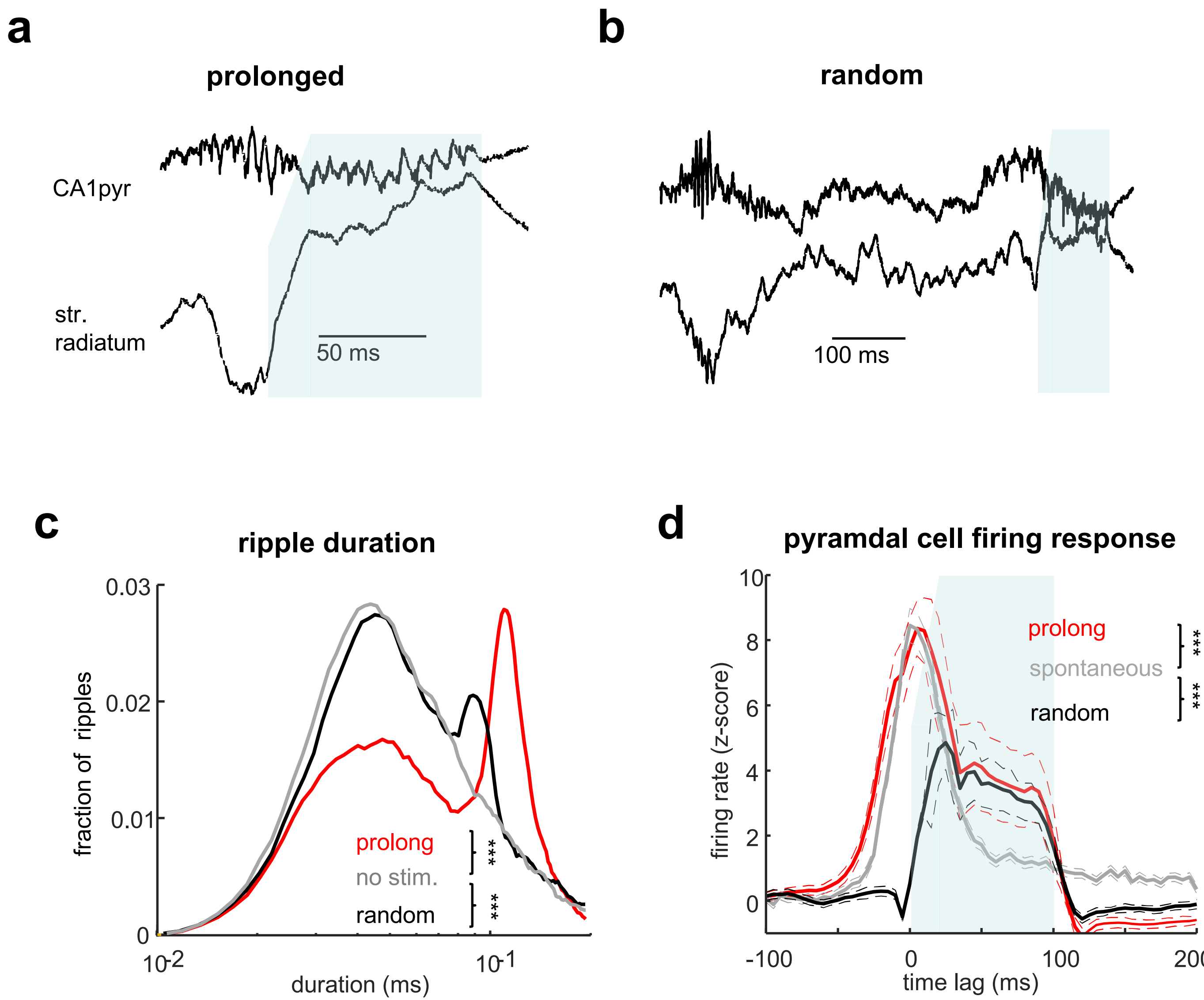
AAV-CaMkII-ChR2 injections in dorsal CA1 of rats





Fernandez-Ruiz, Oliva, Oliveira, Rocha-Almeida, Tingley, Buzsaki, **Science** 2019

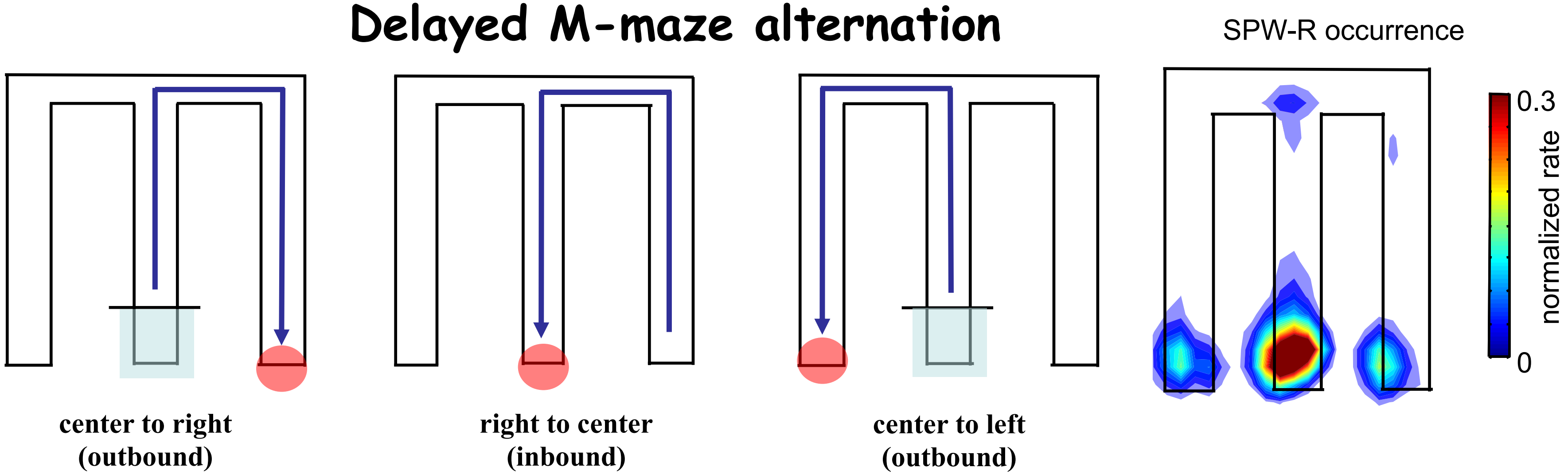
Closed-loop ripple prolongation



Fernandez-Ruiz, Oliva, Oliveira, Rocha-Almeida, Tingley, Buzsaki, **Science** 2019

Memory task design

Delayed M-maze alternation



Inbound component:

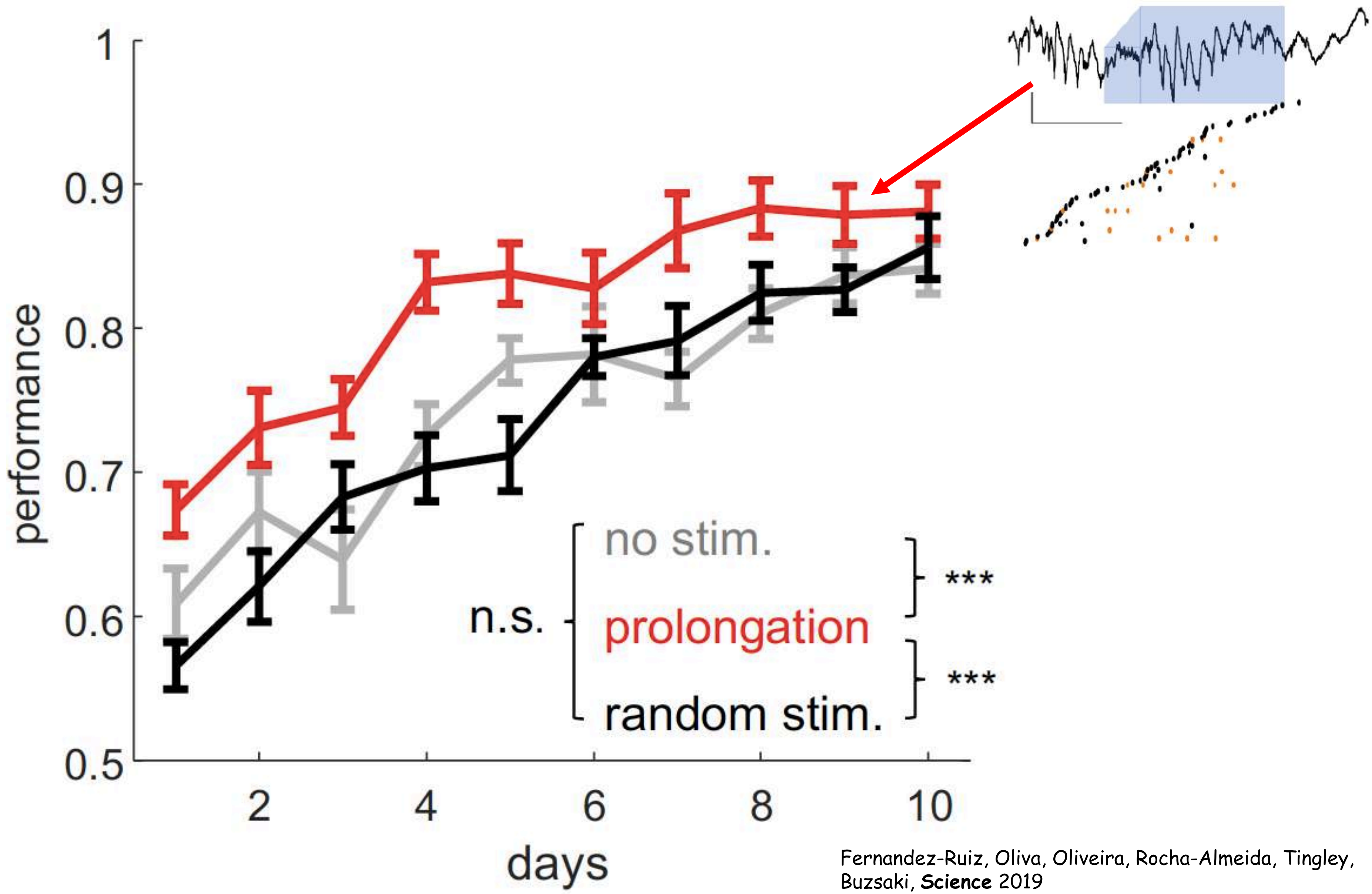
- "Reference" memory
- History independent

Outbound component:

- "Working" memory
- History dependent

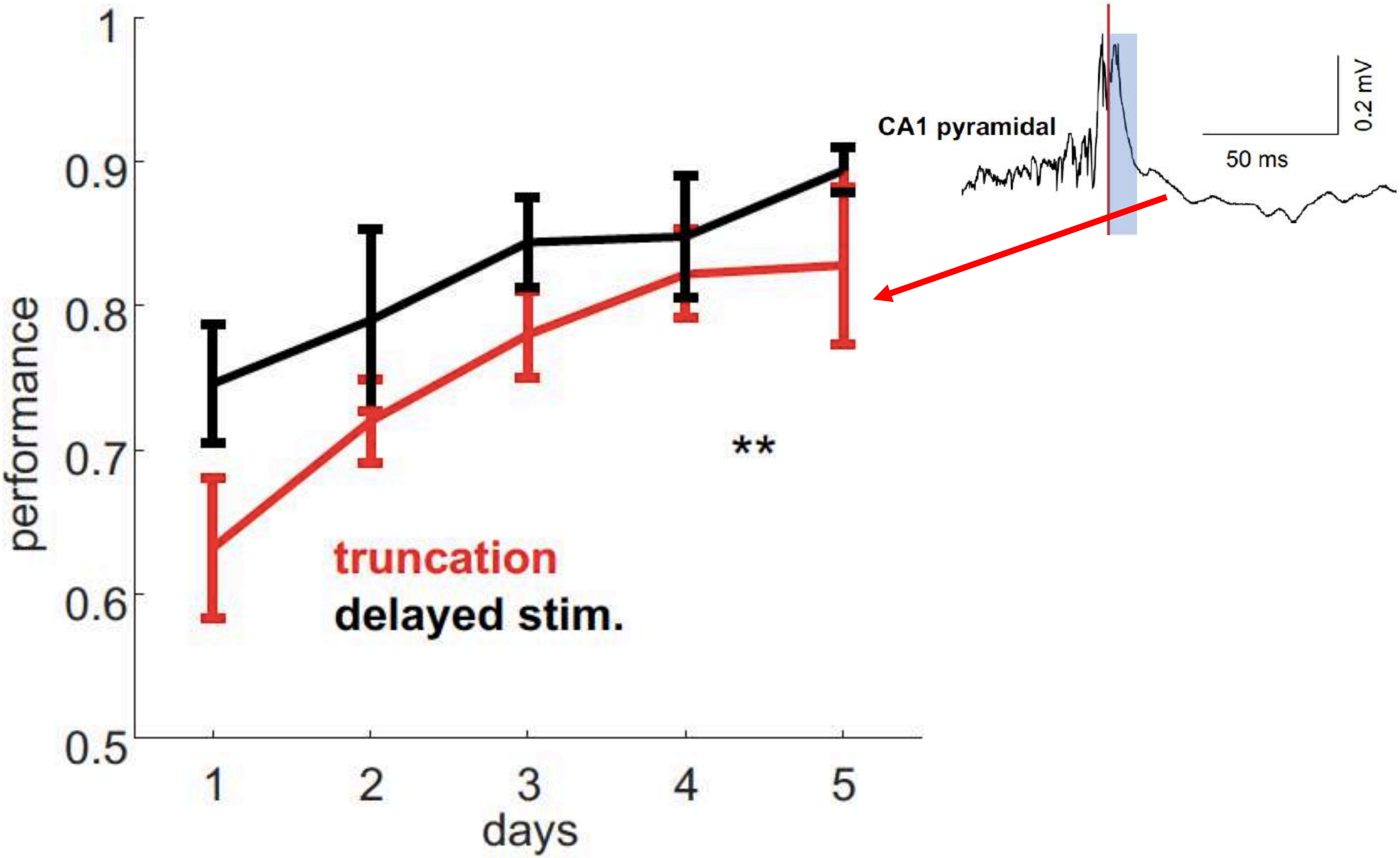
(Modified from Jadhav et al., 2012)

Prolongation of ripples improves memory



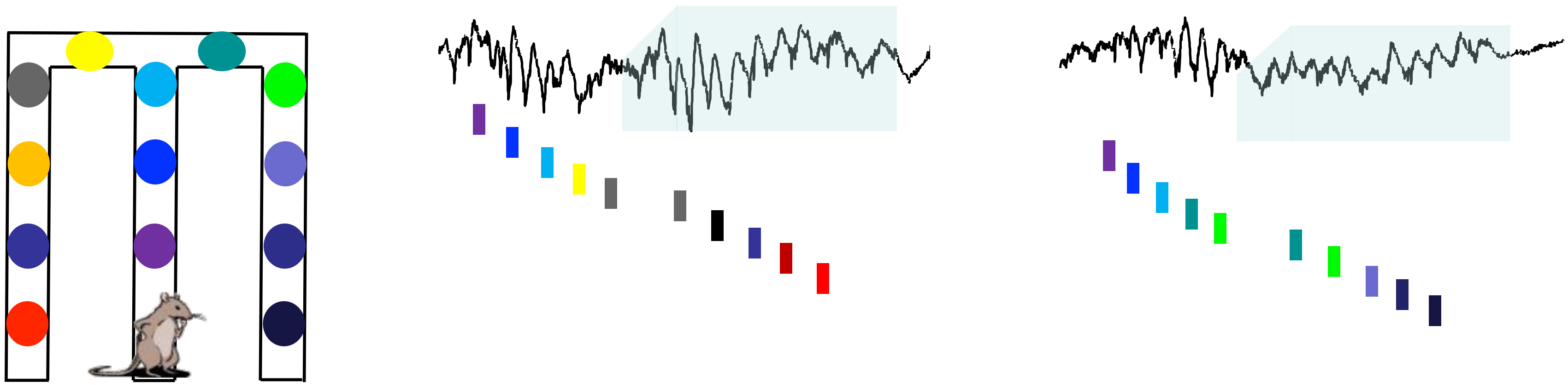
Fernandez-Ruiz, Oliva, Oliveira, Rocha-Almeida, Tingley, Buzsaki, **Science** 2019

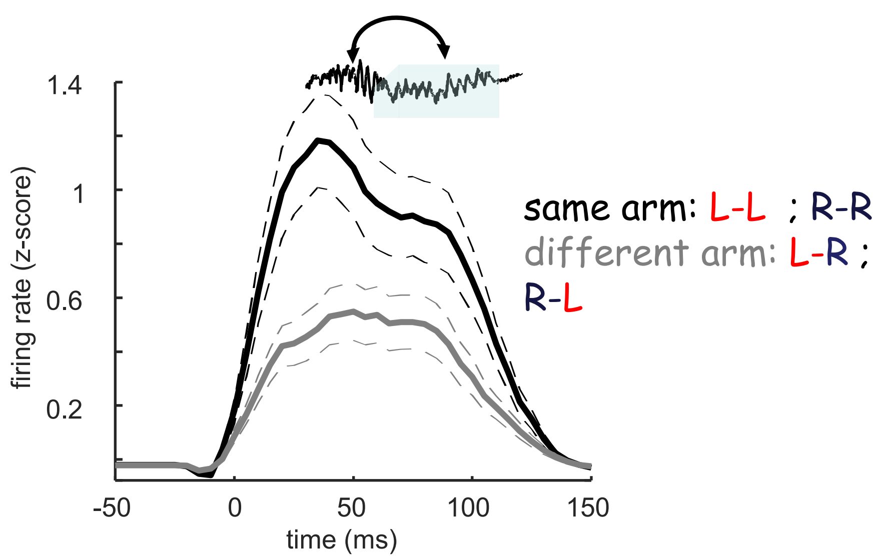
Truncating ripples deteriorates memory

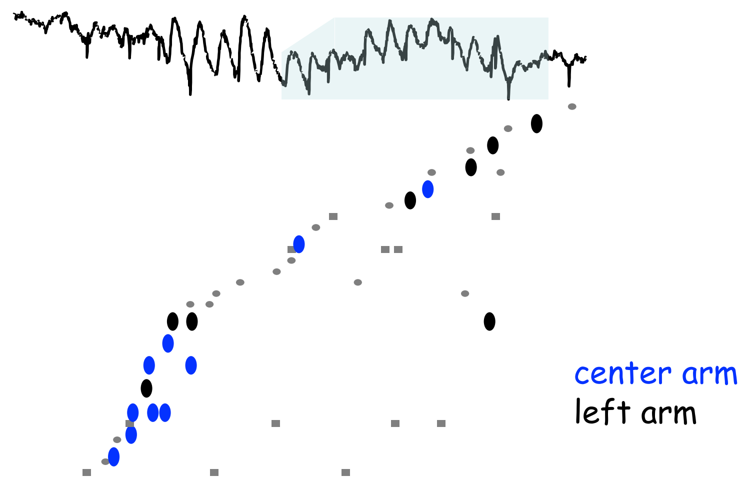


Replicates previous report with closed-loop electrical disruption of SWRs (Jadhav et al., Science, 2012)

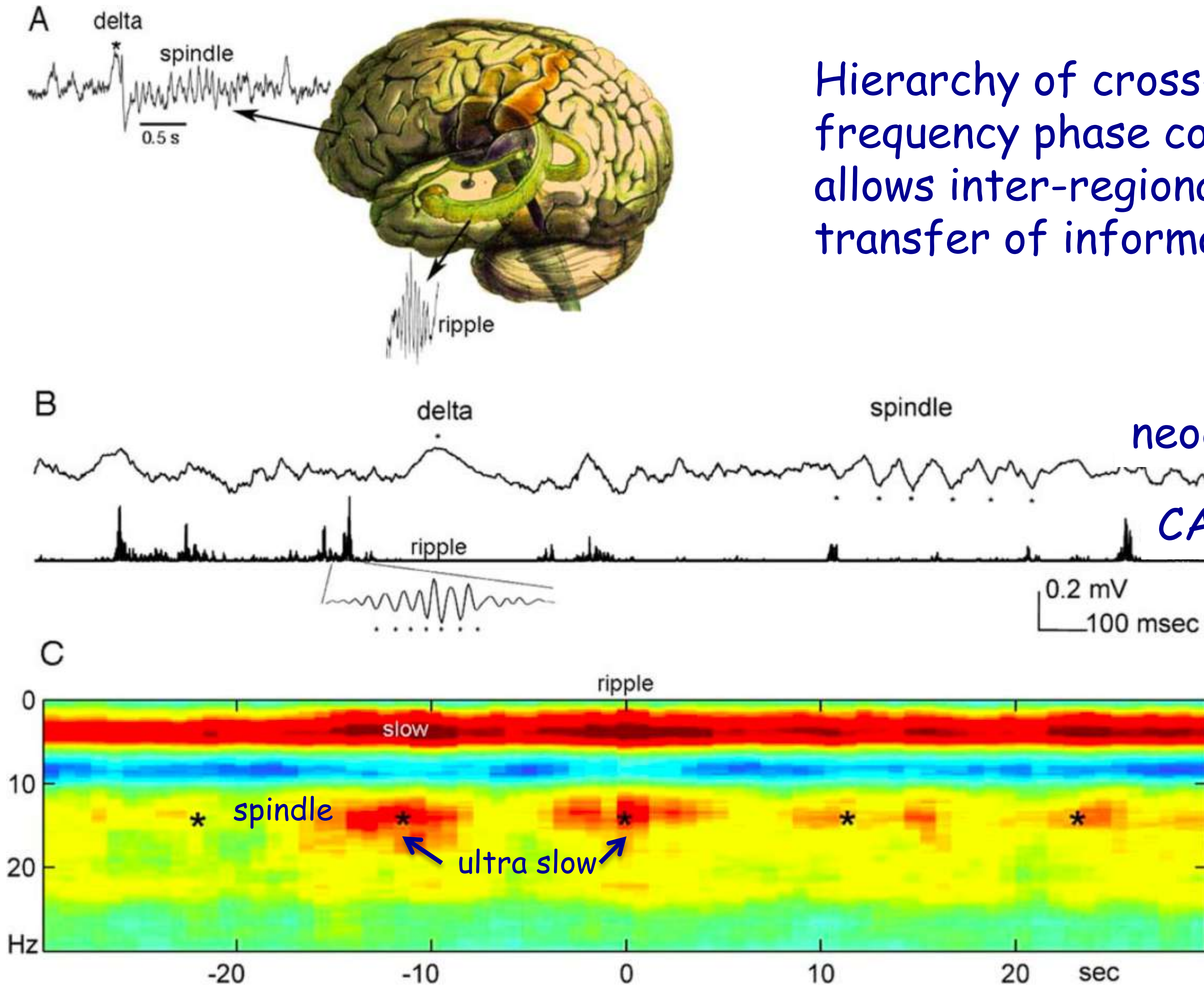
Optogenetic stimulation prolong ongoing place cell sequences







Fernandez-Ruiz, Oliva, Oliveira, Rocha-Almeida, Tingley, Buzsaki, **Science** 2019



Hierarchy of cross-frequency phase coupling allows inter-regional transfer of information

neocortex

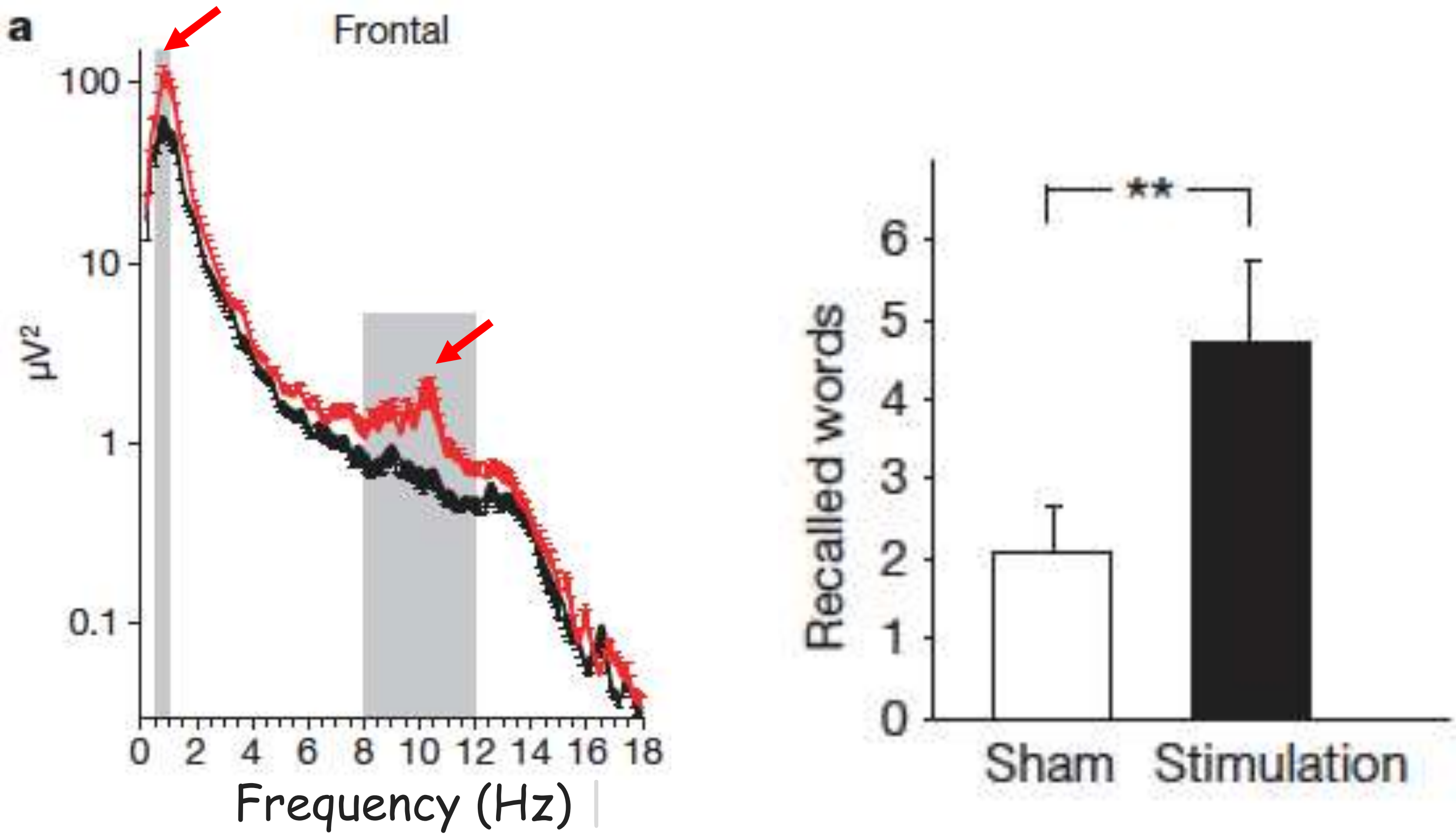
CA1 hippo

ripple ← sleep spindle ← slow oscillation ← ultraslow

140-200 Hz ← 12-20 Hz ← 0.5-1.5 Hz ← 0.1 Hz

Sirota, Csicsvari, Buhl, Buzsaki **PNAS** 2003

Boosting slow oscillations by transcranial electric stimulatioon during sleep potentiates memory

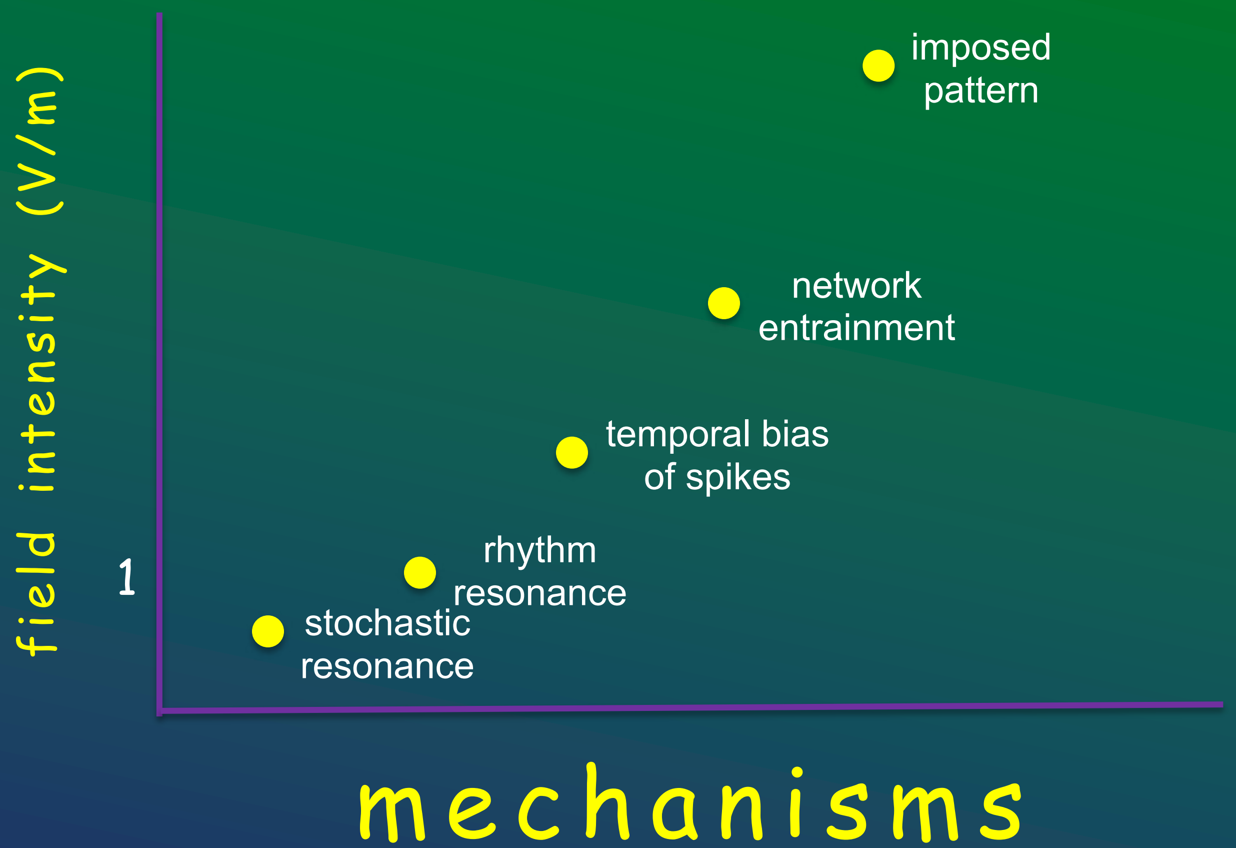


Marshall, Helgadóttir, Mölle Born **Nature** 2006

- # Diffuse spatial methods

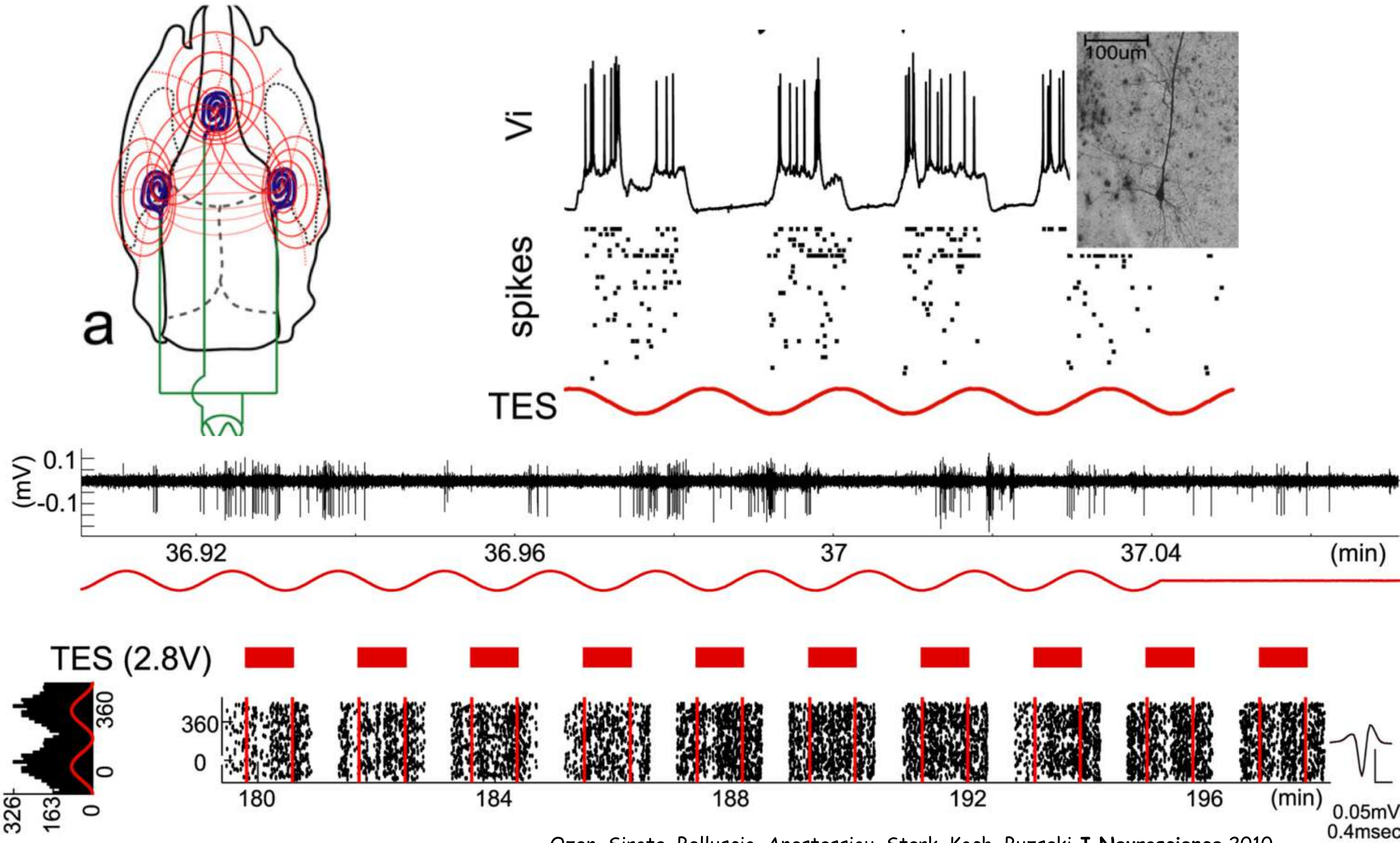
Transcranial electrical stimulation, TES;
Transcranial magnetic stimulation, TMS;
Transcranial ultrasound stimulation, TUS;
Transcranial radio frequency stimulation

Neuronal mechanisms of TES



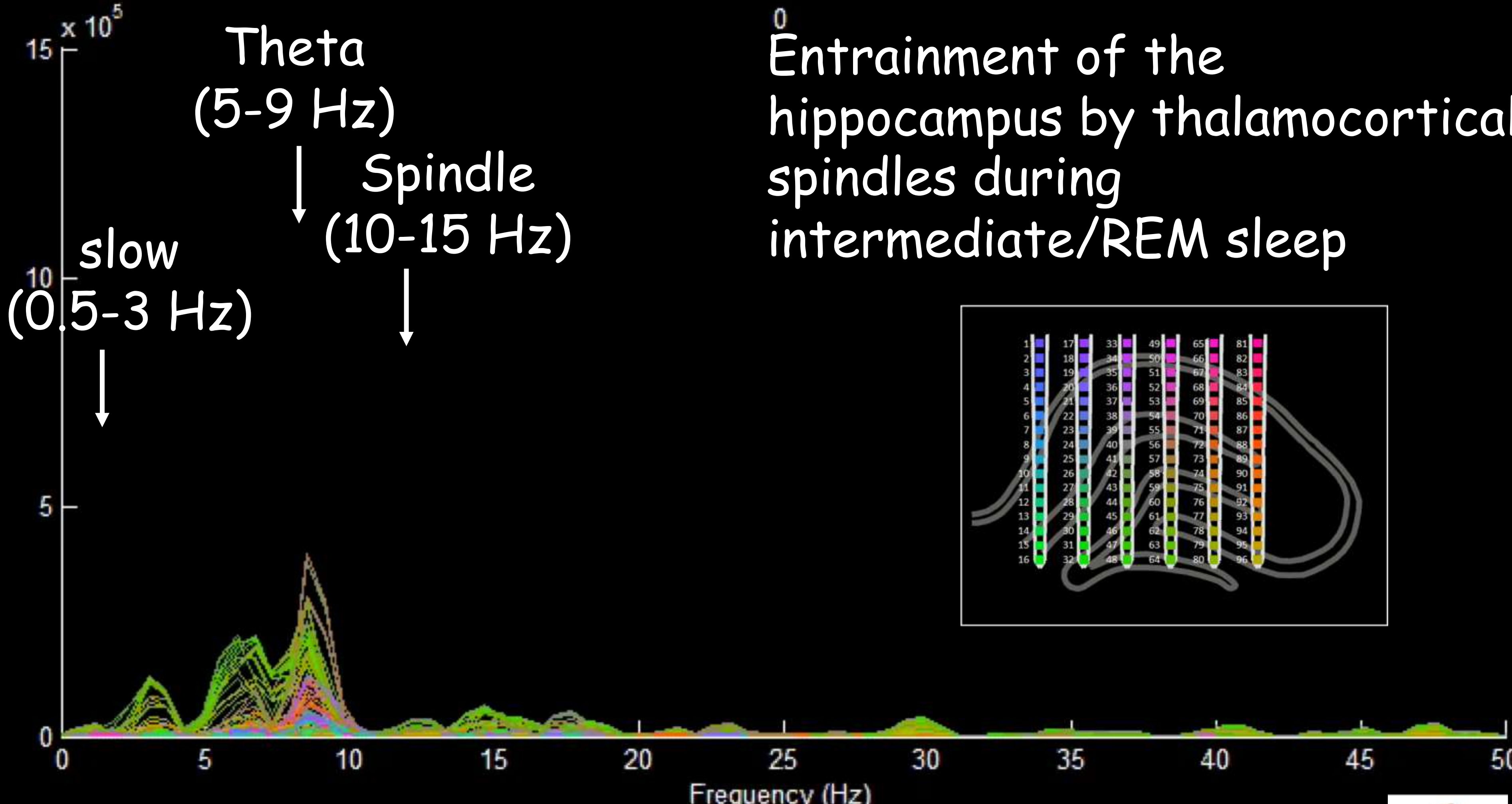
Liu, Vöröslakos,…. Buzsáki **Nature Communications** 2018

#3 Temporal bias of spikes by TES
(in vivo > 1 V/m)



Ozen, Sirota, Belluscio, Anastassiou, Stark, Koch, Buzsaki **J Neuroscience** 2010

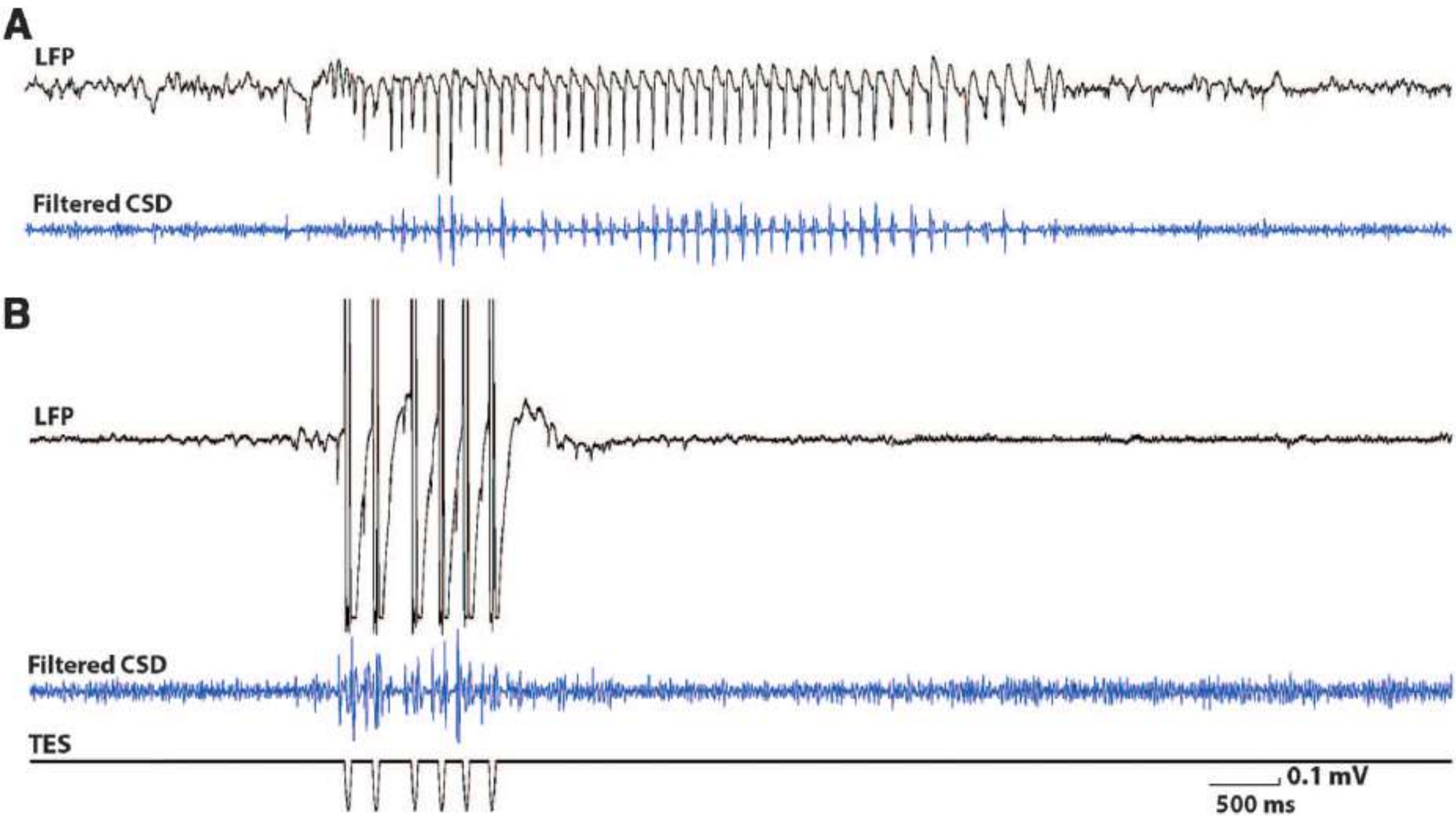
#4 Network entrainment



Entrainment of the hippocampus by thalamocortical spindles during intermediate/REM sleep

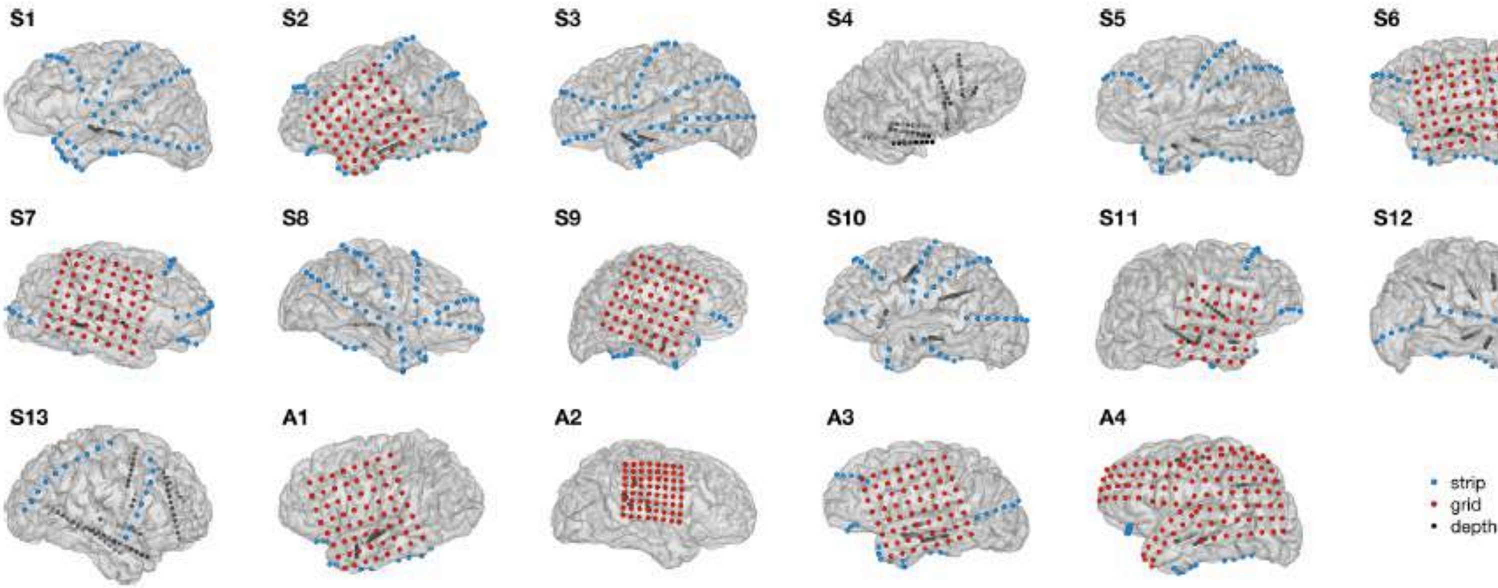
Emanuelle Tognoli, Buzsaki (unpublished)

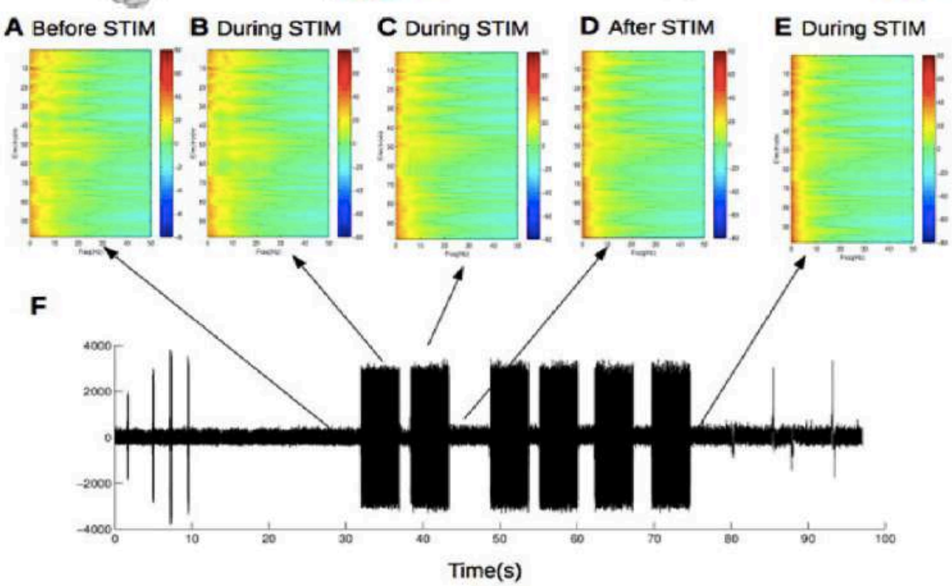
#5 Imposed pattern
(closed loop seizure control by TES; rat)



Berényi, Belluscio, Mao, Buzsáki **Science** 2012

TES (tACS) in patients with intracranial electrodes






Belen Lafon

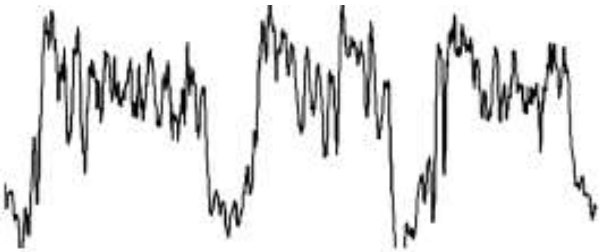

Orrin Devinsky


Anli Liu

Lafon, Henin, Huang, Friedman, Melloni, Thesen, Doyle, Buzsaki, Devinsky, Parra, Liu **Nat Comm** 2017

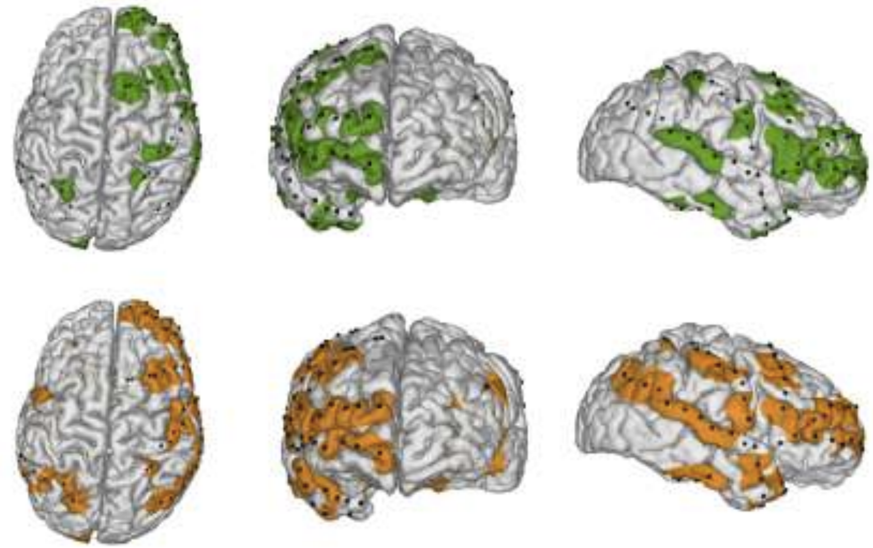
TES (tACS) fails to entrain cortical rhythms

Slow oscillation-spindle cross-frequency coupling **(spontaneous)**

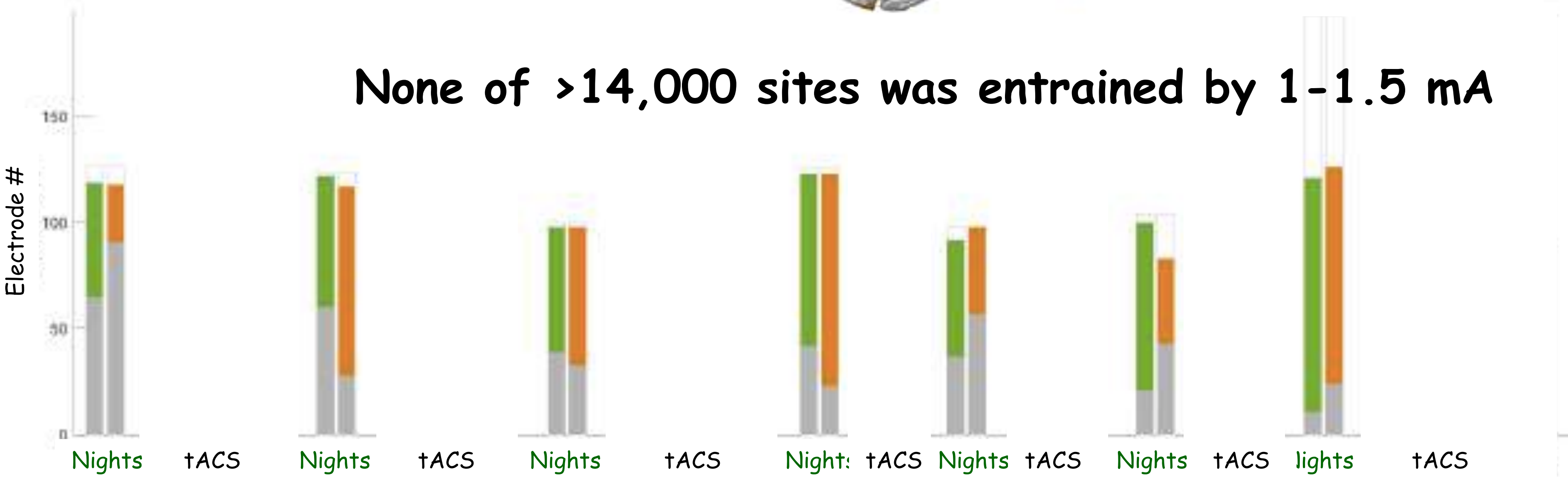


Night 1

Night 2

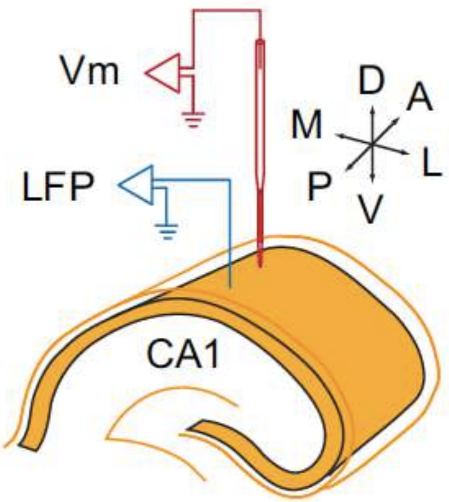


None of >14,000 sites was entrained by 1-1.5 mA

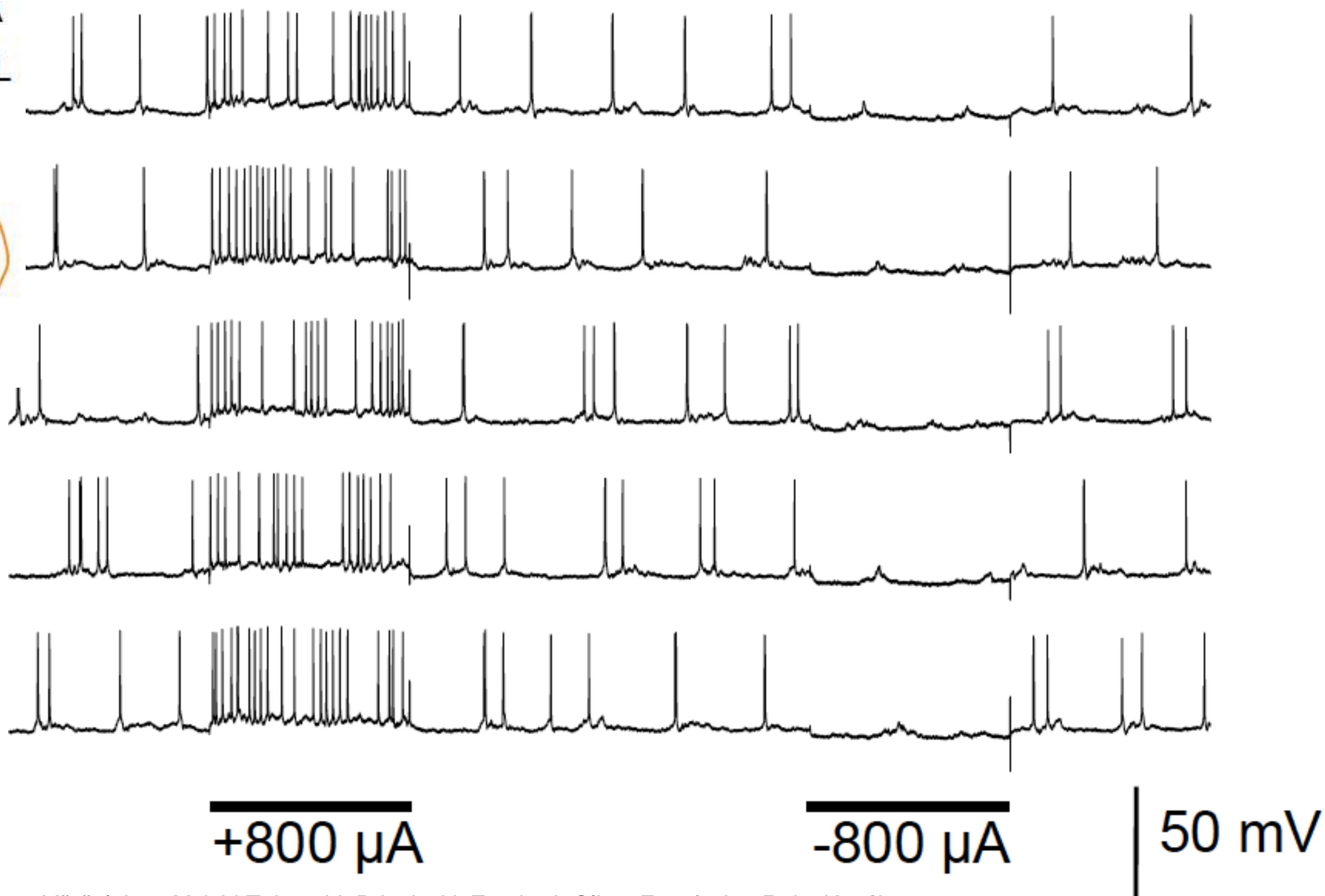


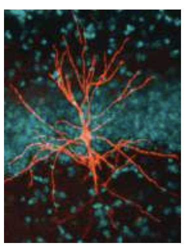
Lafon, Henin, Huang, Friedman, Melloni, Thesen, Doyle, Buzsaki, Devinsky, Parra, Liu **Nat Comm** 2017

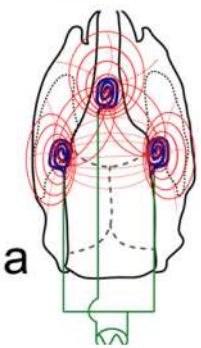
Intracellular responses to transcranial stimulation



Skull (in vivo > 1 V/m)



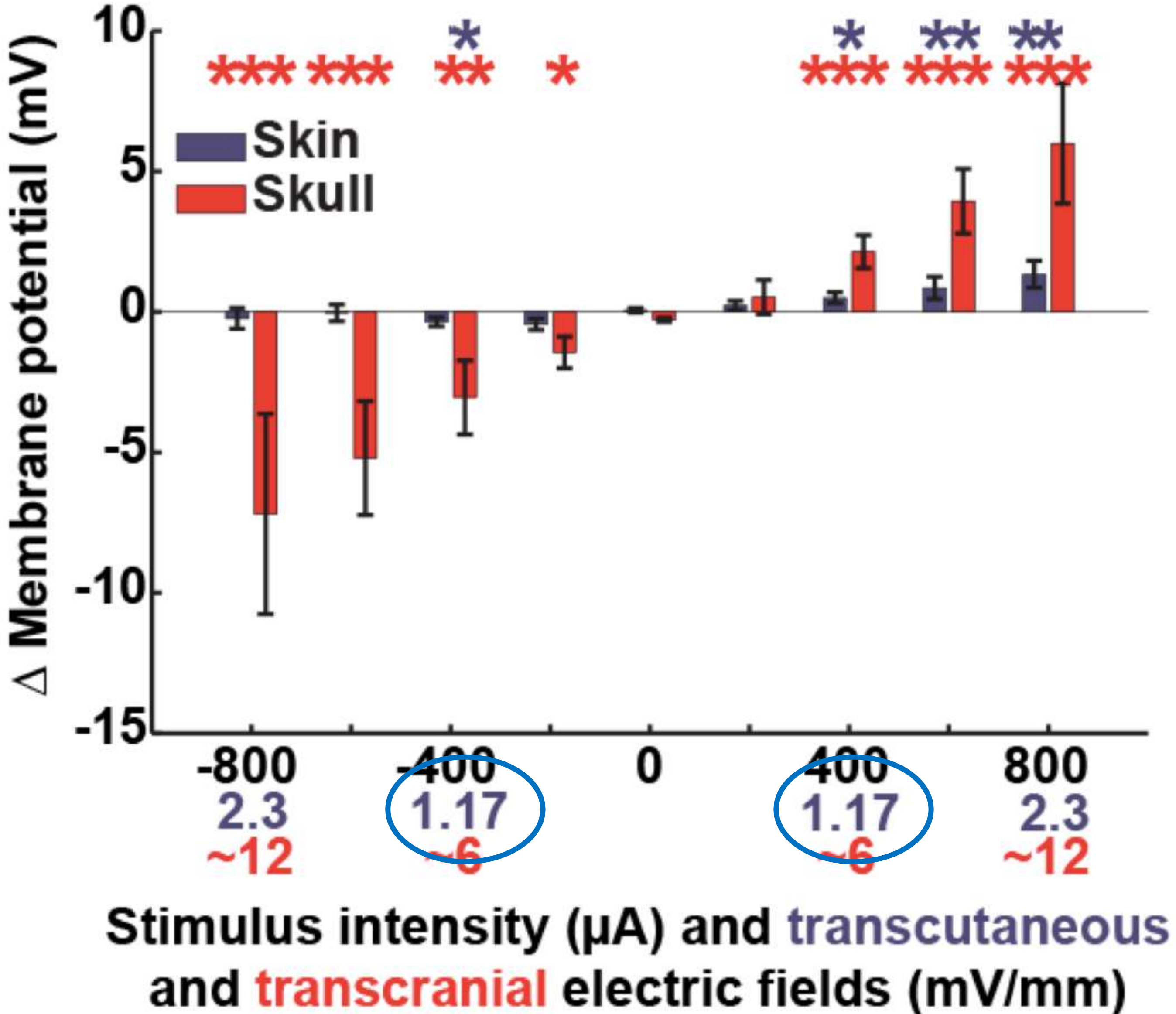


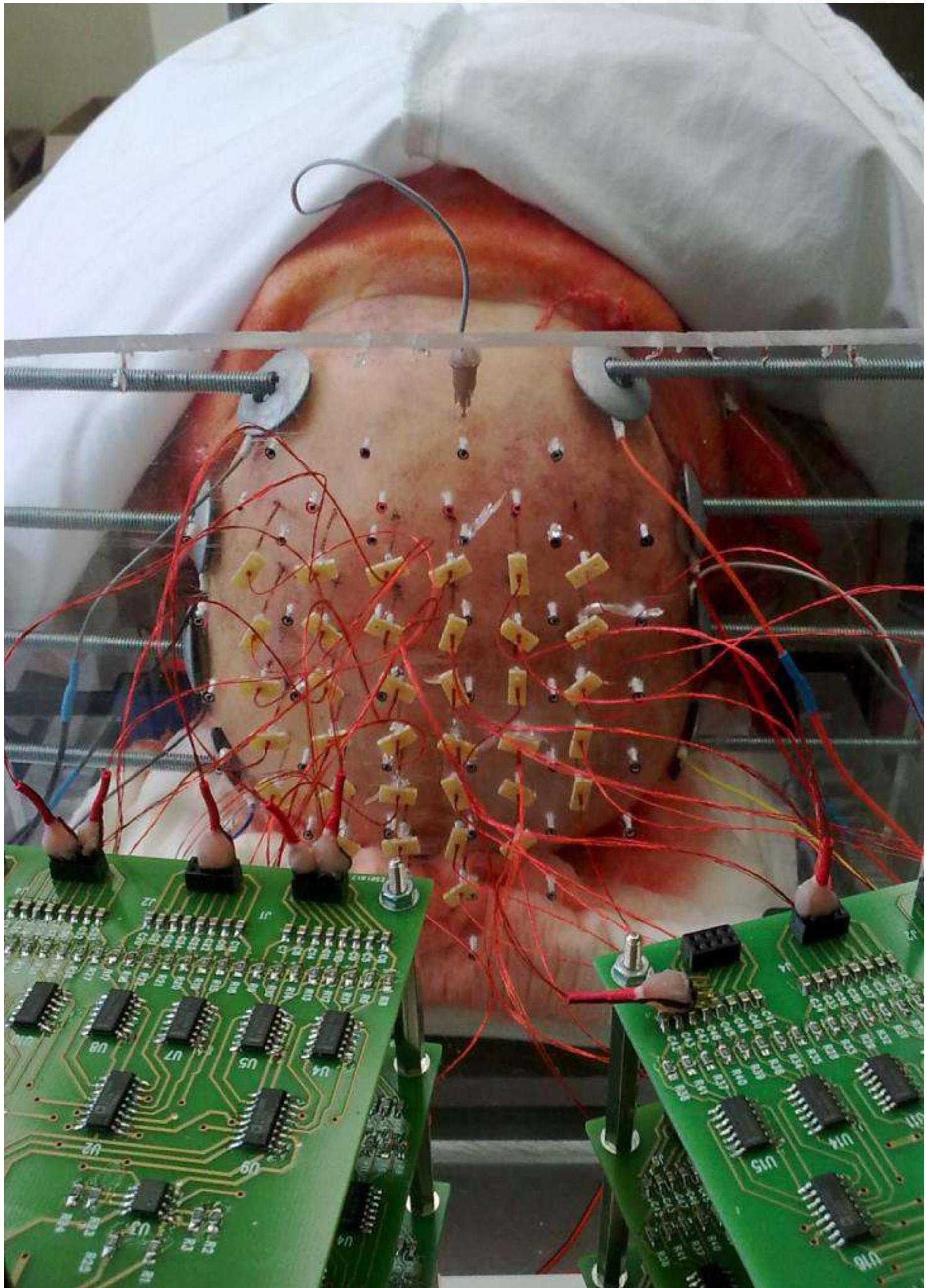


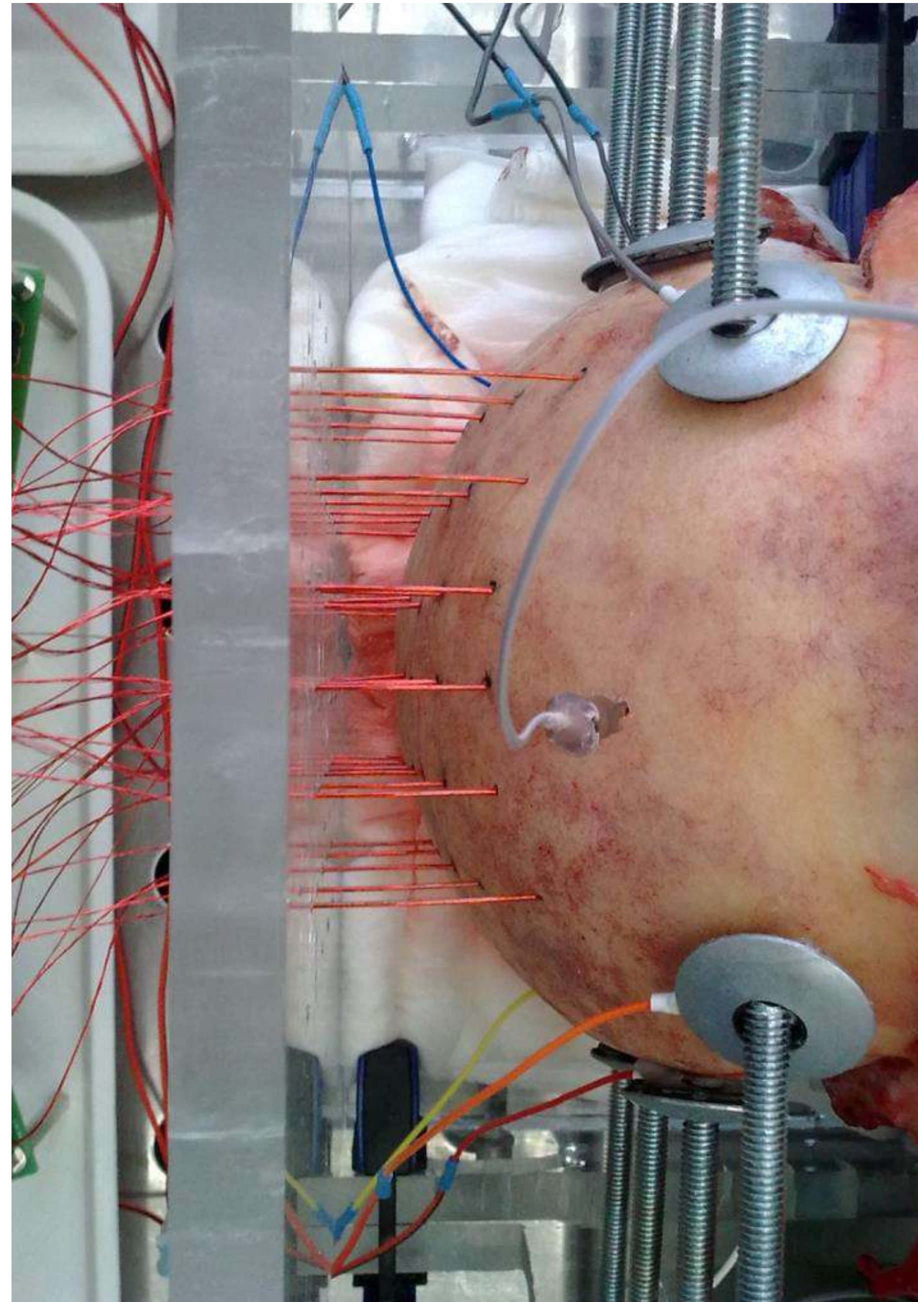
Mihaly
Vöröslakos

Vöröslakos, Yuichi Takeuchi, Brinyiczki, Zombori, Oliva, Fernández-Ruiz, Kozák, Kincses, Iványi, Buzsáki, Berényi **Nature Comm** 2018

Transcutaneous vs transcranial stimulation (~5-fold difference)

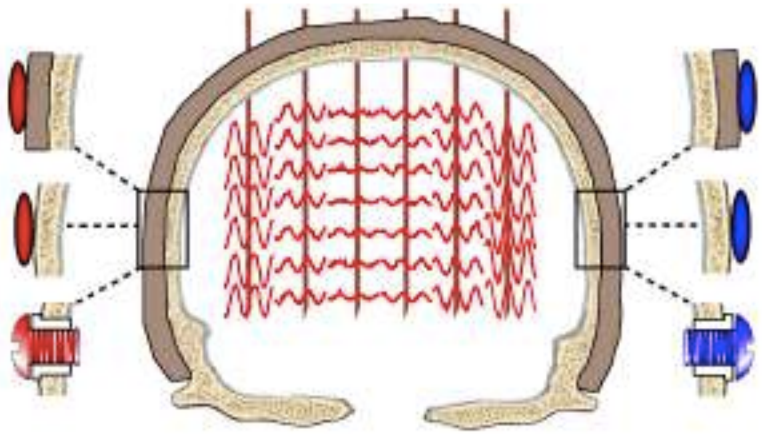


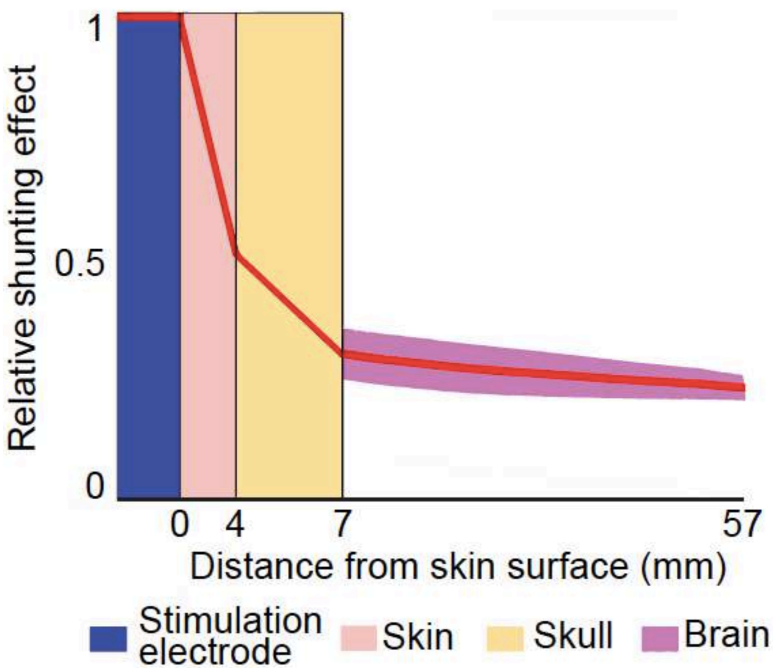


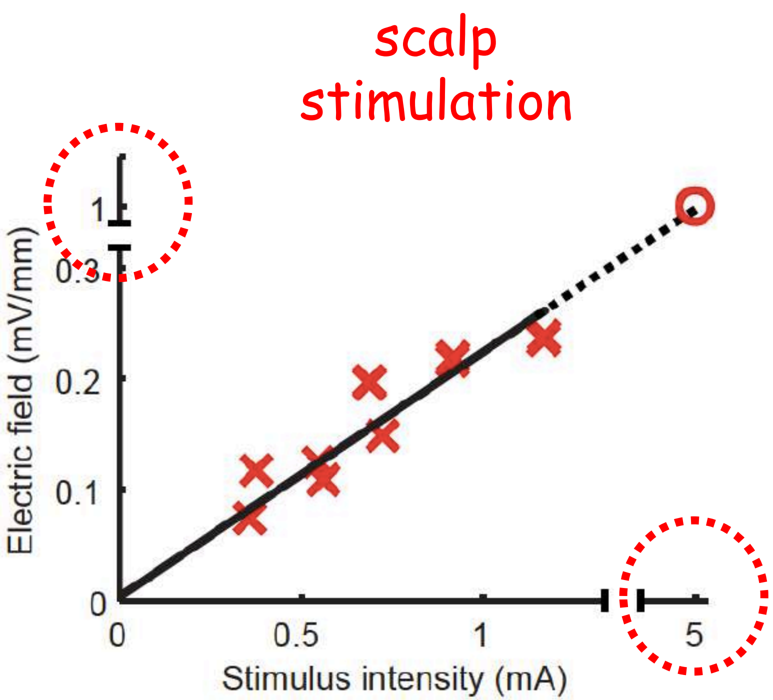


Vöröslakos, Yuichi Takeuchi, Brinyiczki, Zombori, Oliva, Fernández-Ruiz, Kozák, Kincses, Iványi, Buzsáki, Berényi **Nature Comm** 2018

Transcutaneous vs transcranial stimulation in human cadavers

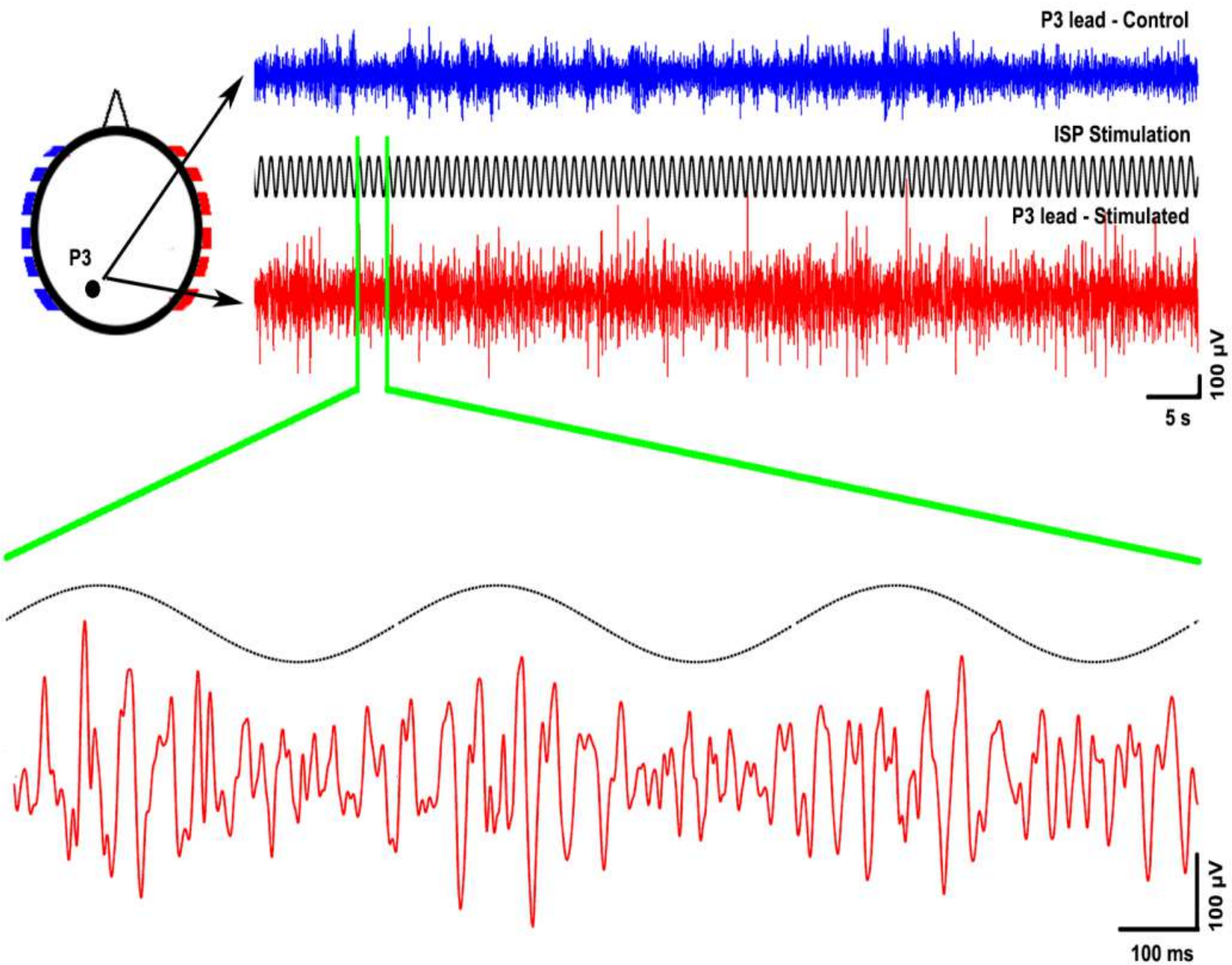






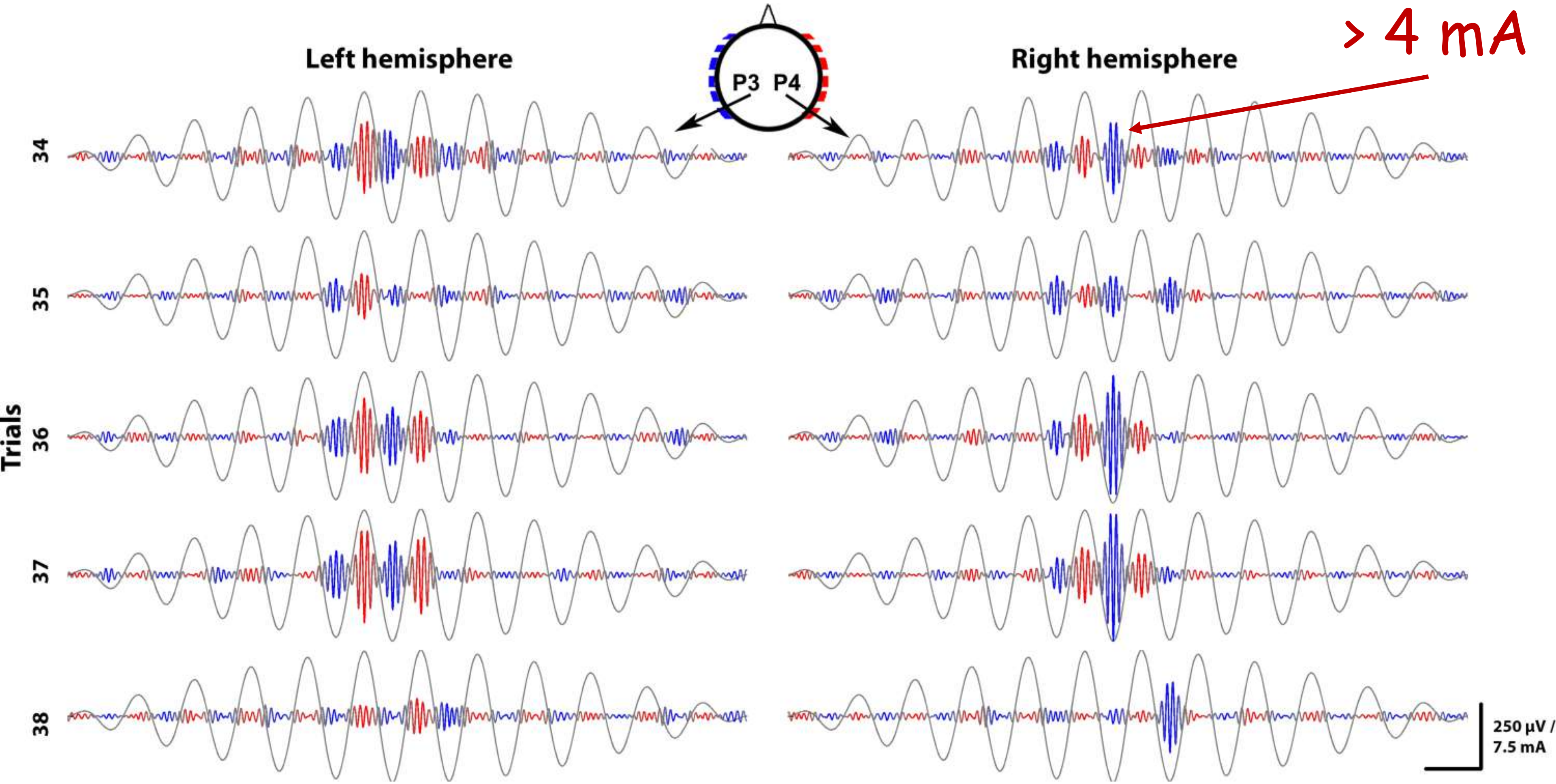
Vöröslakos, Yuichi Takeuchi, Brinyiczki, Zombori, Oliva, Fernández-Ruiz, Kozák, Kincses, Iványi, Buzsáki, Berényi **Nature Comm** 2018

Intersectional short pulse (ISP) stimulation induces intracranial neuronal effects



Vöröslakos, Yuichi Takeuchi, Brinyiczki, Zombori, Oliva, Fernández-Ruiz, Kozák, Kincses, Iványi, Buzsáki, Berényi **Nature Comm** 2018

Intersectional short pulse **(ISP)** stimulation in human subjects
Reduced scalp effects, more intracerebral current delivery



Vöröslakos, Yuichi Takeuchi, Brinyiczki, Zombori, Oliva, Fernández-Ruiz, Kozák, Kincses, Iványi, Buzsáki, Berényi **Nature Comm** 2018

Transcranial electrical stimulation (TES)

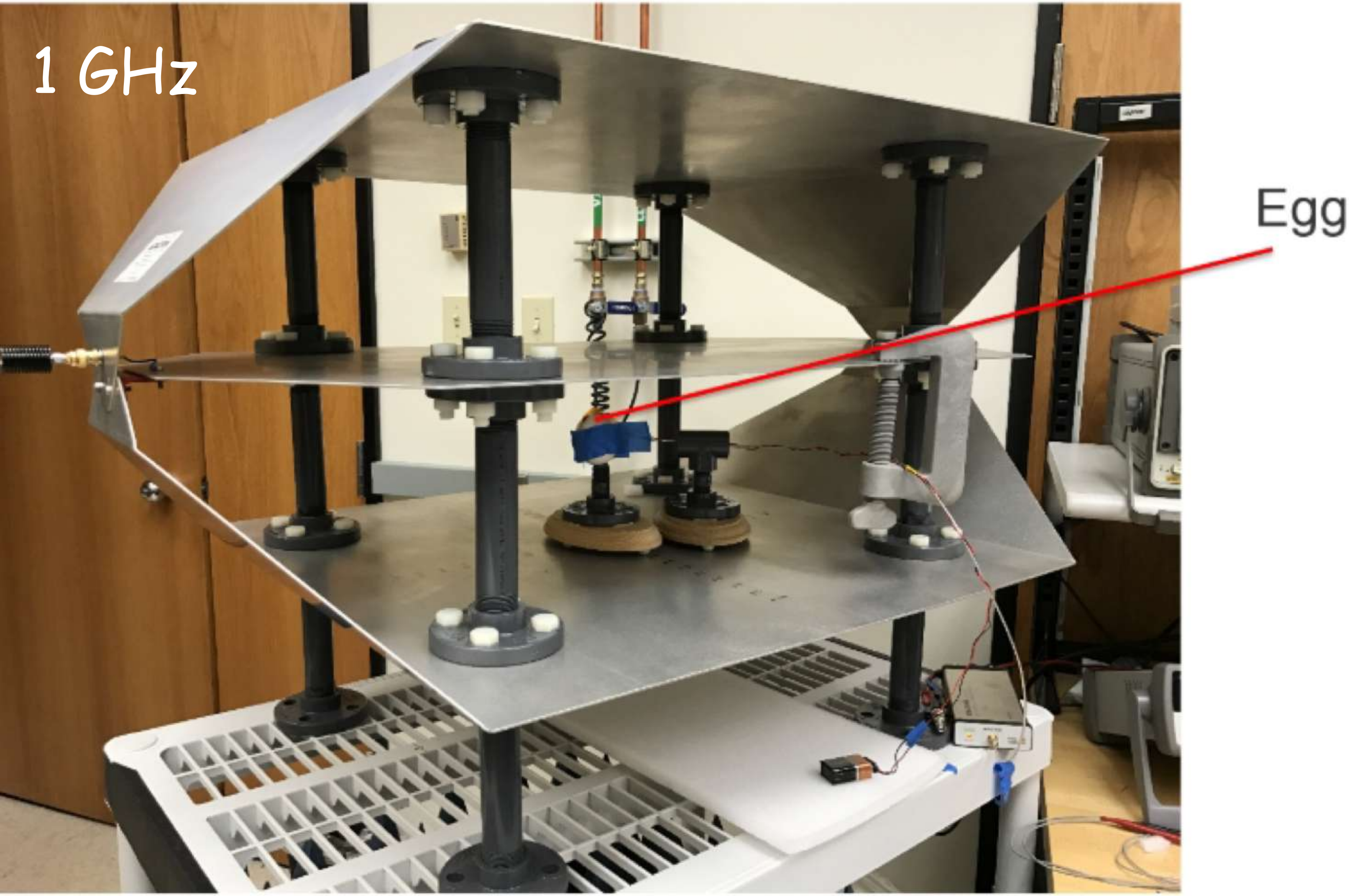
(i) Works! – under appropriate conditions

(ii) Intersectional pulse stimulation allows focused stimulation (increased brain/scalp current ratio)

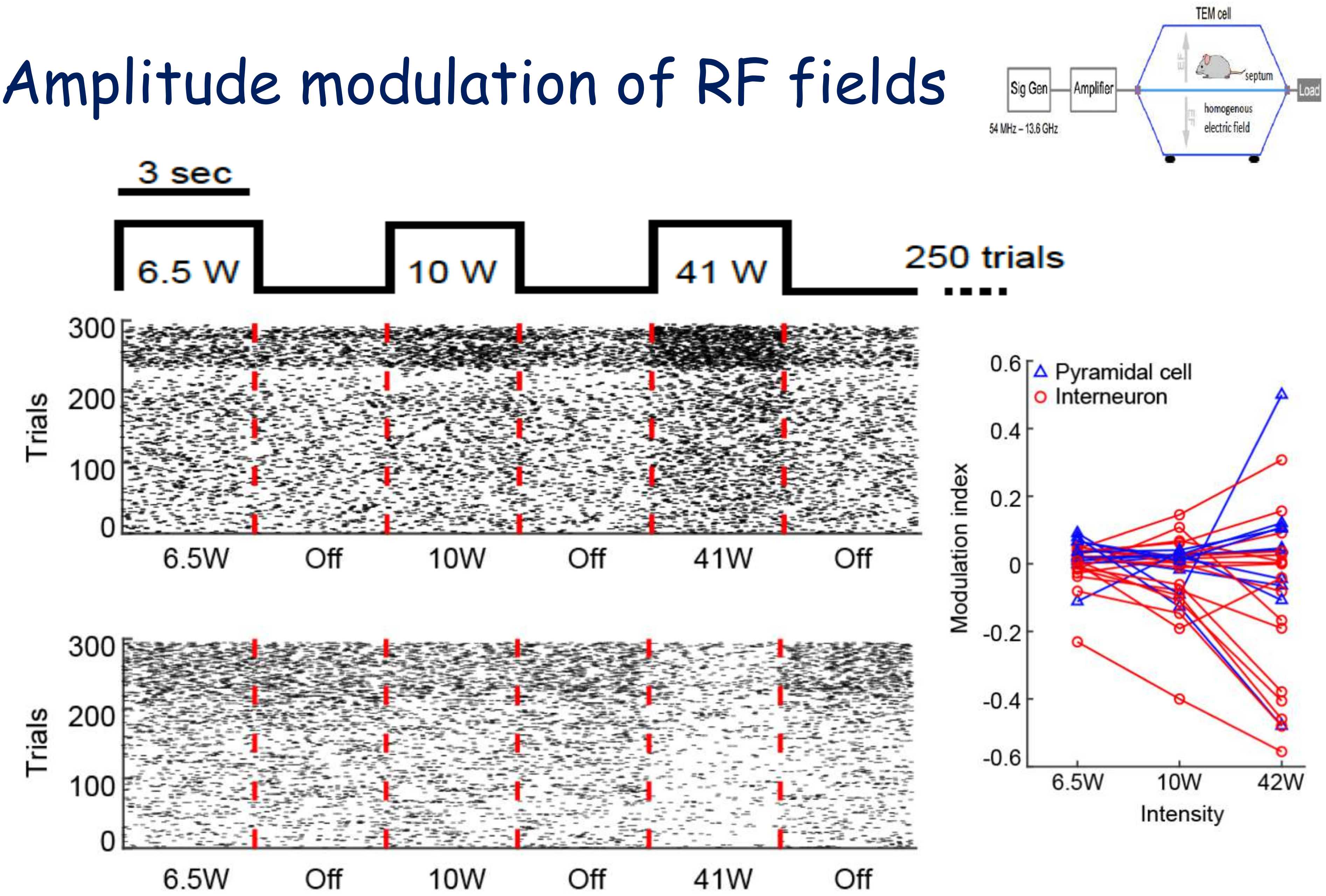
(iii) ~ 1 mV/mm voltage gradient is needed to entrain spikes and affect LFP (>4.5 mA scalp stimulation)

(iv) Our results do not contradict the efficacy of TES by non-network-mediated mechanisms at lower stimulus intensities

Non-invasive RF stimulation of neurons

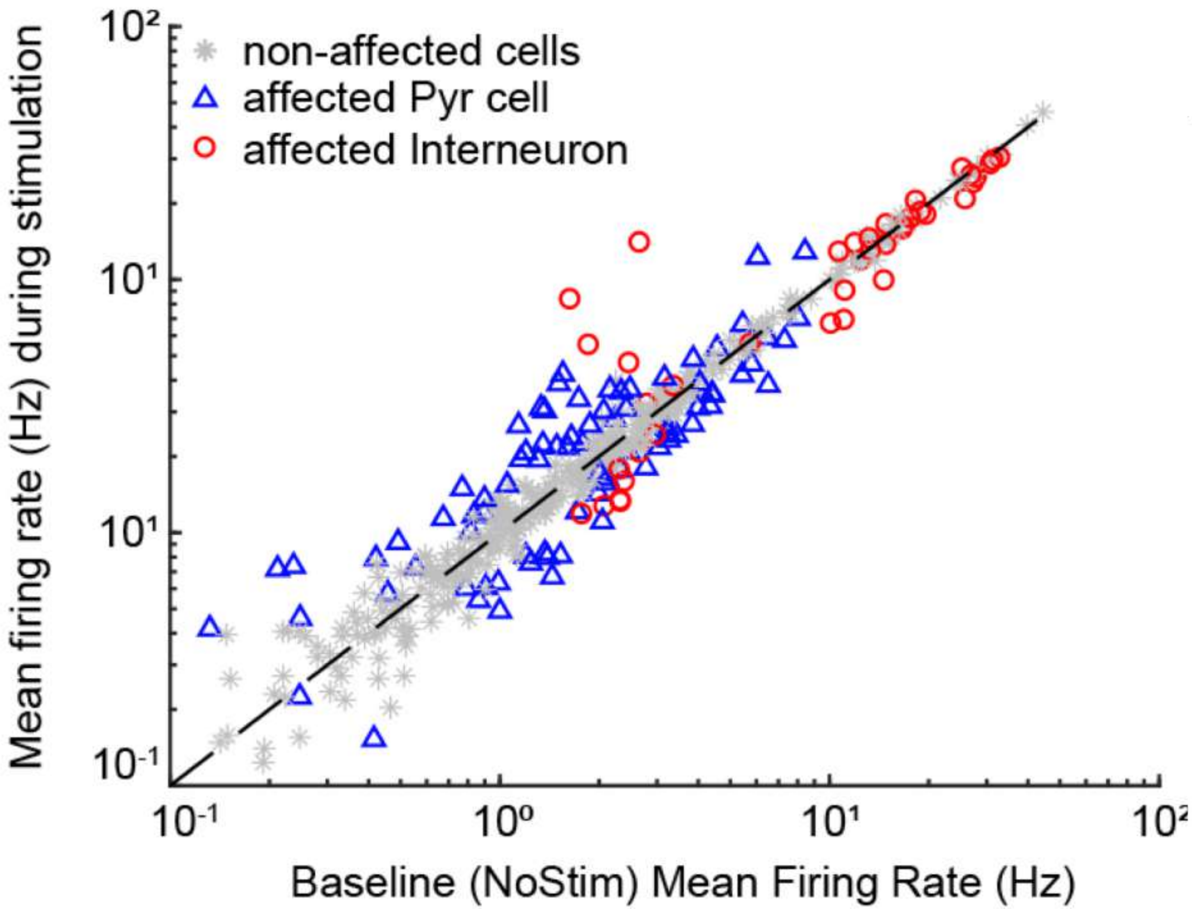


Amplitude modulation of RF fields

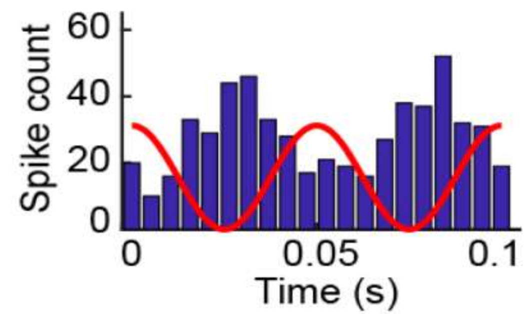


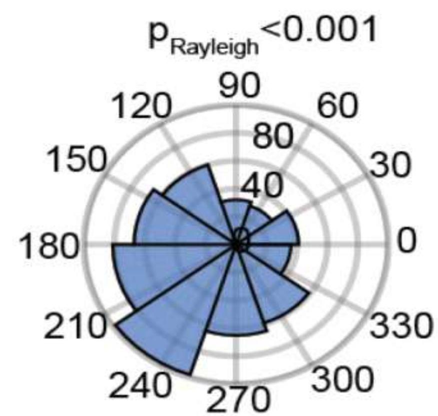
Yaghmazadeh, Vöröslakos, Buzsáki **SFN** 2018

Non-invasive RF stimulation of neurons



20 Hz entrainment





Yaghmazadeh, Vöröslakos, Buzsáki **SFN** 2018

Mihaly Voroslakos

Anli Liu

Antal Berenyi

Orrin Devinsky

Werner Doyle