Electric Fields in the Brain: Bug or Feature?

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Acknowledgments

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Two distinct problems

- Forward Problem: How do the transmembrane currents across synapses, dendrites, axons & glia add up to give rise to the extracellular potential? That is, how do the micro-variables constitute the macro-variables?
- Inverse Problem: Does the extracellular field influence the electrical properties of individual neurons or is the field useful to the experimentalist but otherwise an epiphenomenon (like the sound made by a beating heart)? That is, do the macro-variables influence the micro-variables?

The forward problem

From neurons to the field

The brain as a physical system

Calculation of extracellular potential due to point source via solution of Poisson's PDE

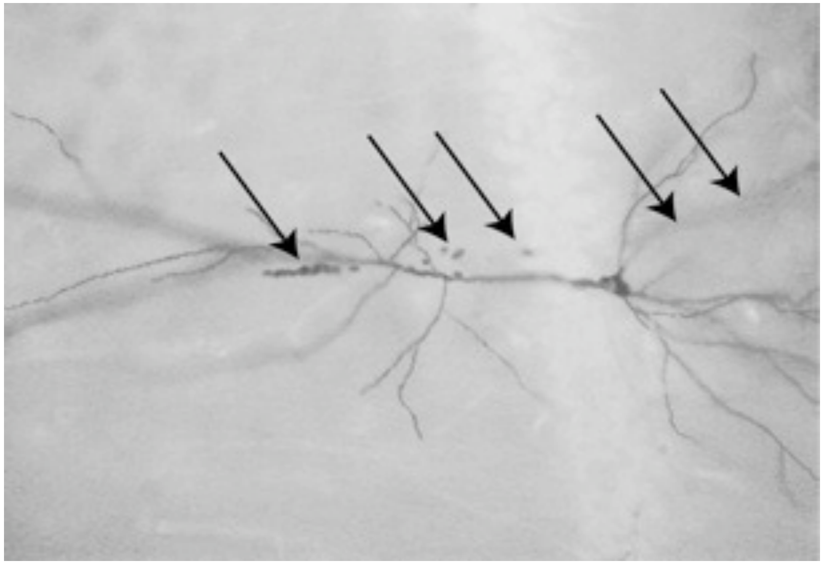
$$\phi = \frac{\rho I}{4\pi r}$$

Recall also the definition of the electric field

$$E = -\nabla \phi$$

Simultaneous intra & extracellular recordings

And histology

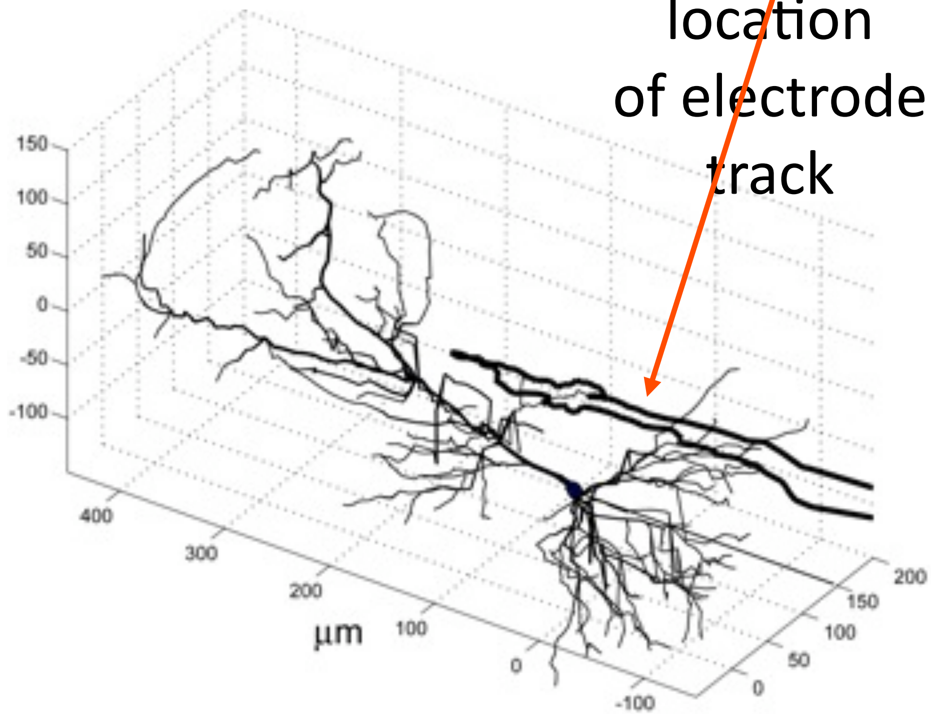


Arrows show electrode track visible at 20x
(most of track is in next section)

Henze et al. *J. Neurophysiol.* (2000)

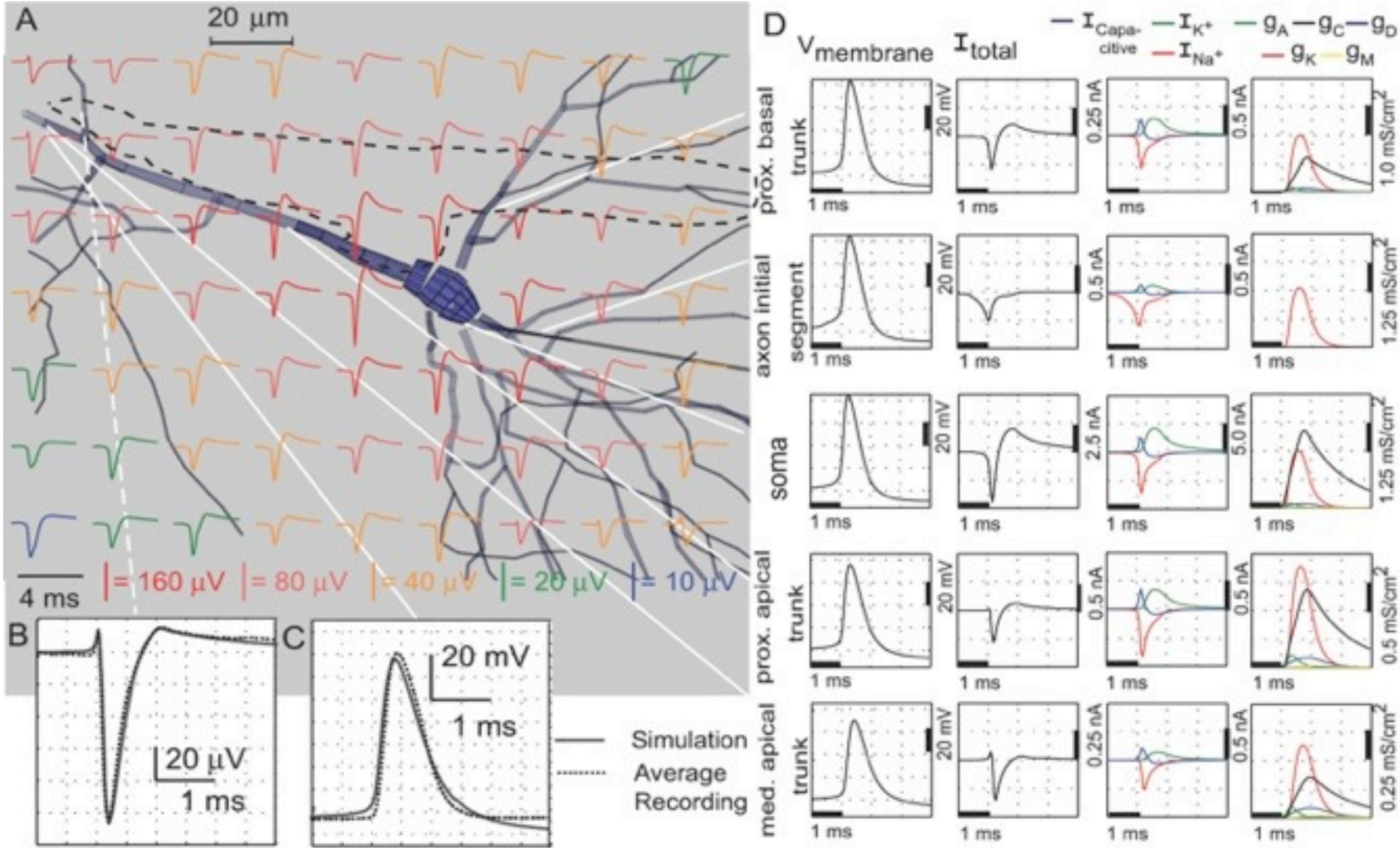
We create 3-D reconstruction

Measured location of electrode track



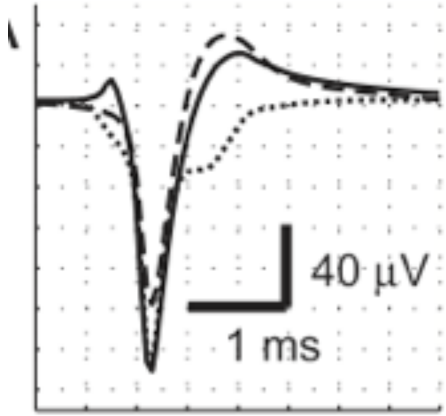
then simulate in NEURON…

Simulating CA1 pyramid D151



Gold et al. *J. Neurophysiol*. (2006; see also Holt & Koch 1999)

Canonical Extracellular Spike

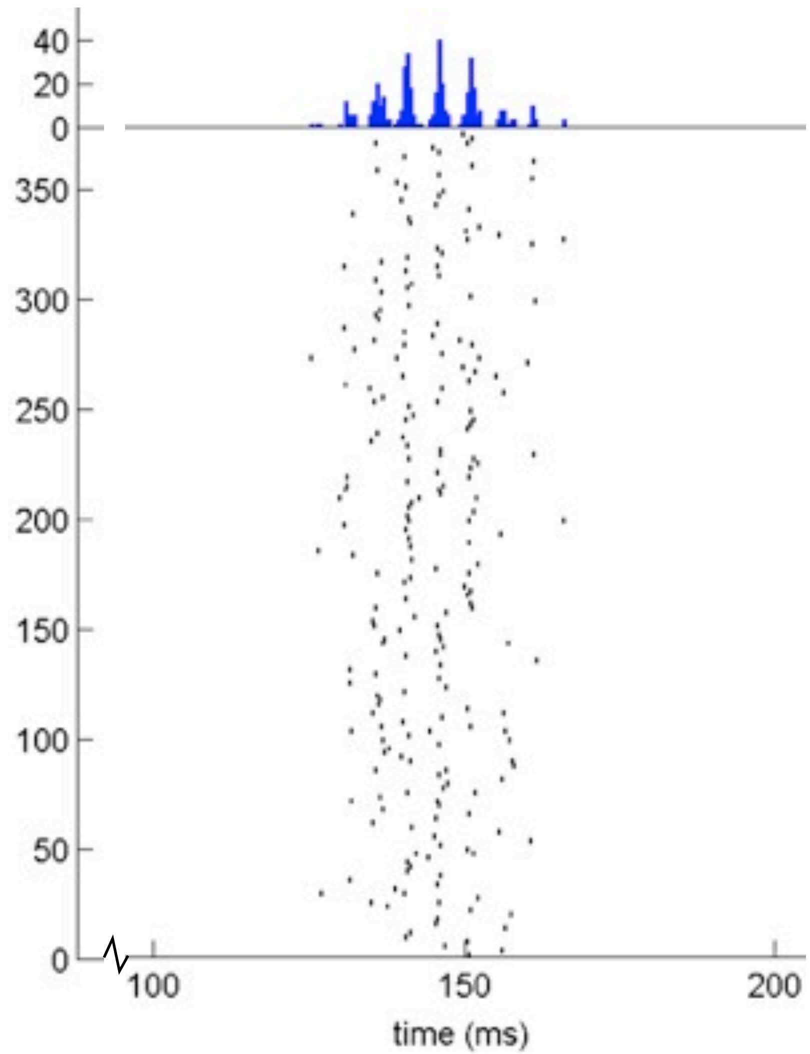


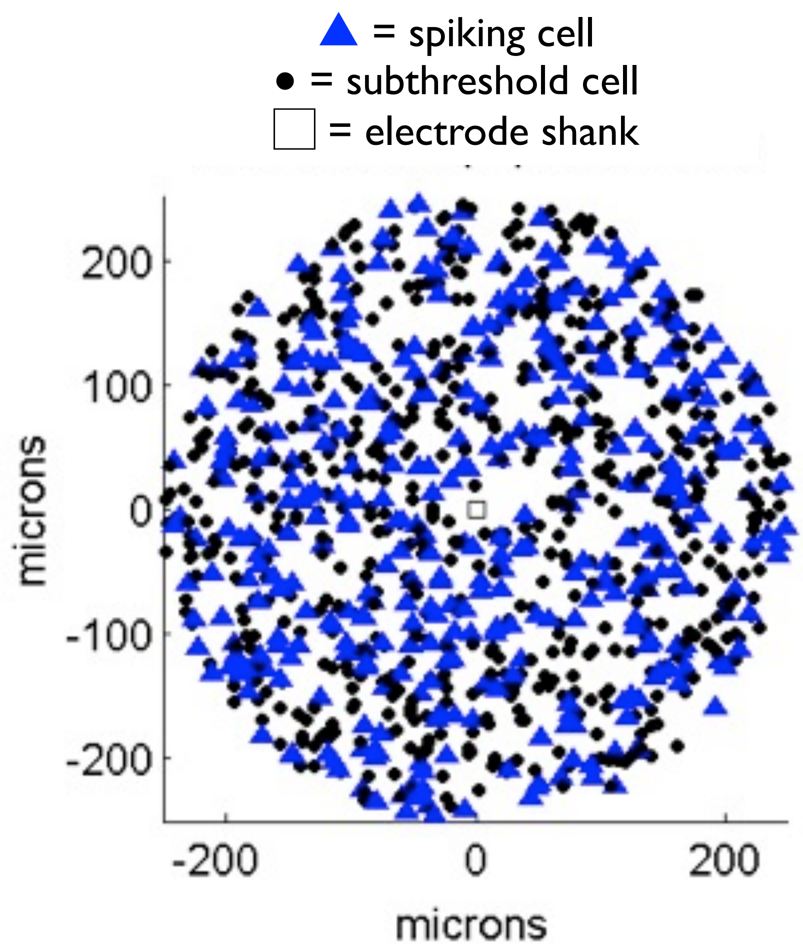
Three "phases":

- 1. phase is dominated by capacitive current: positive, due to initial membrane depolarization (is often not present)
- 2. phase is dominated by Na^+ current: negative, due to influx of Na^+ during action potential
- 3. phase is dominated by K^+ current: positive, due to efflux of K^+ during repolarization

All three currents are simultaneously active. The "phase" is which current is dominant at the time.

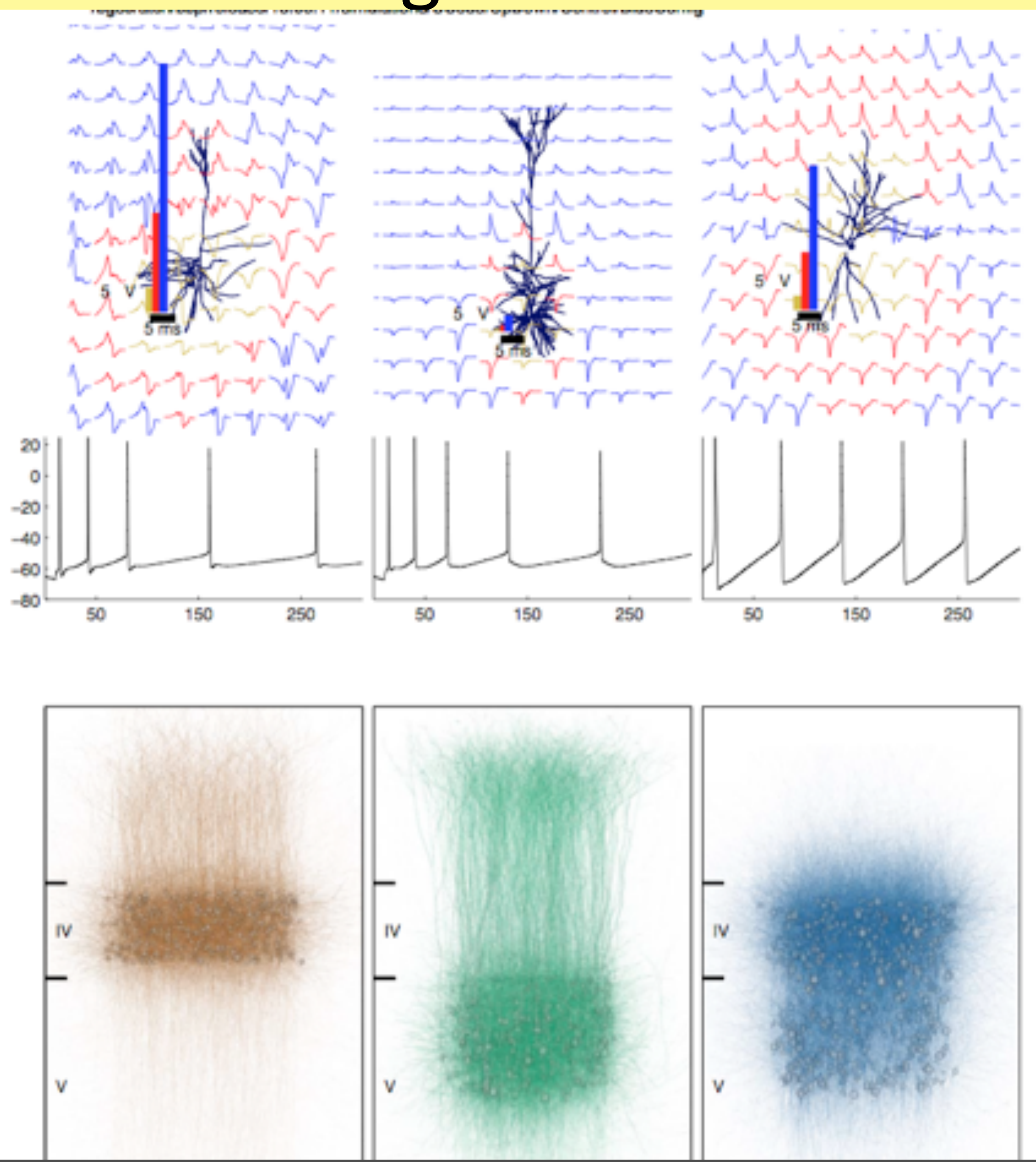
Modeling the LFP in Hippocampus





Schomburg, Anastassiou, Buzsaki & Koch (2011)

Modeling the LFP in Neocortex



Reiman, Anastassiou, Hill, Koch & Markram (2011)

The inverse problem

How does the field influence neurons?

The cable equation

Cable equation (Rall 1962) together with proper boundary conditions

$$-\frac{d^2 v_m}{dx^2} + \frac{r_i}{r_m}(v_m - v_{rest}) = \frac{d^2 v_e}{dx^2}$$

And an harmonic, stationary external field

$$v_e = v_0 \sin\left(2\pi f_s x + \phi_s\right)$$

Anastassiou, Montgomery, Barahona, Buzsaki & Koch *J Neurosci* (2010)

The amplitude of ephaptic potentials

In order for the ephaptic potential to become $O(v_0)$

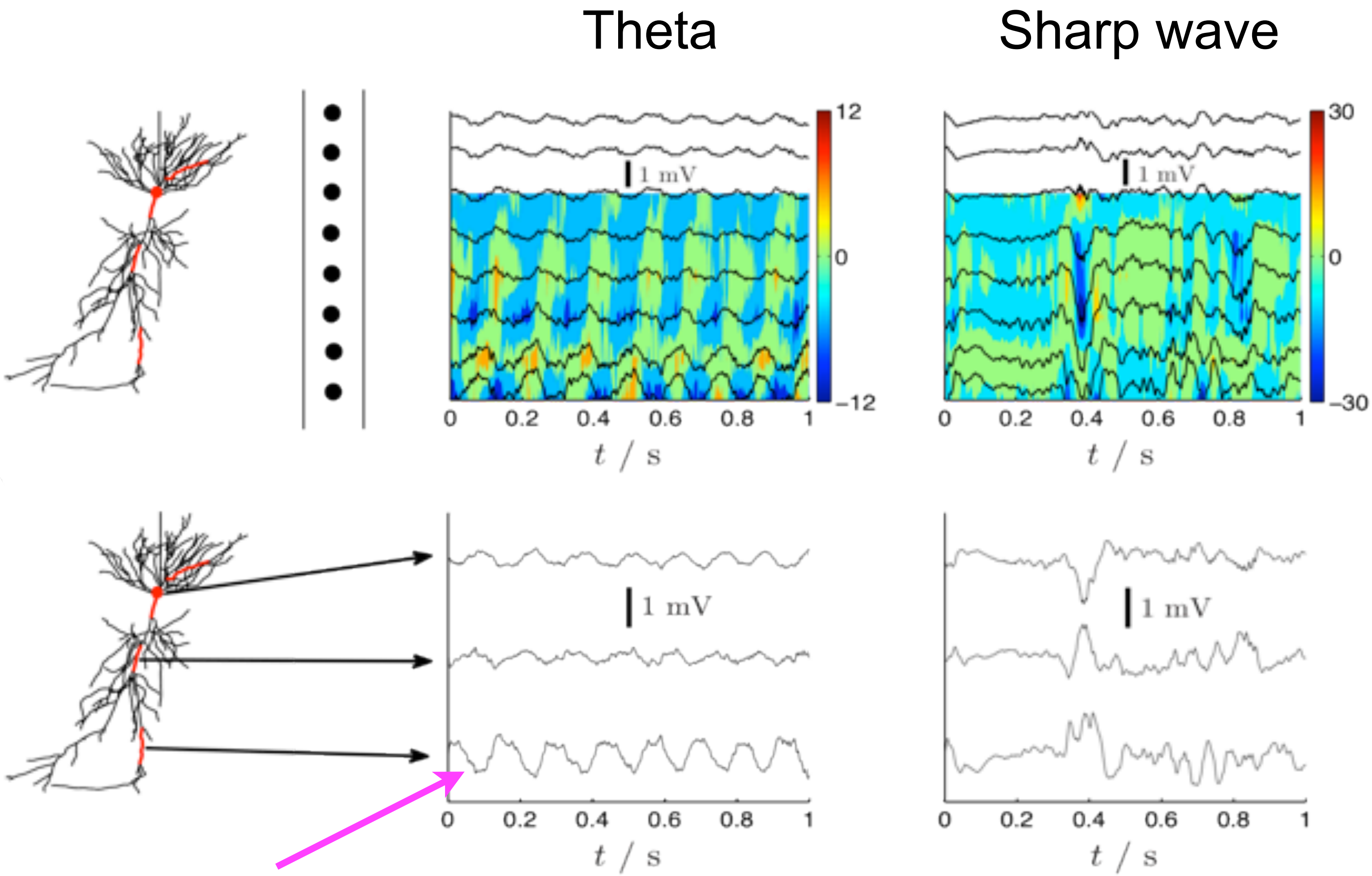
$$\Omega = 2\pi f_s \lambda > 1$$ and $$\Omega L > 1$$

with

$$v_m < 1.5 v_0$$

Anastassiou *et al, J Neurosci* (2010)

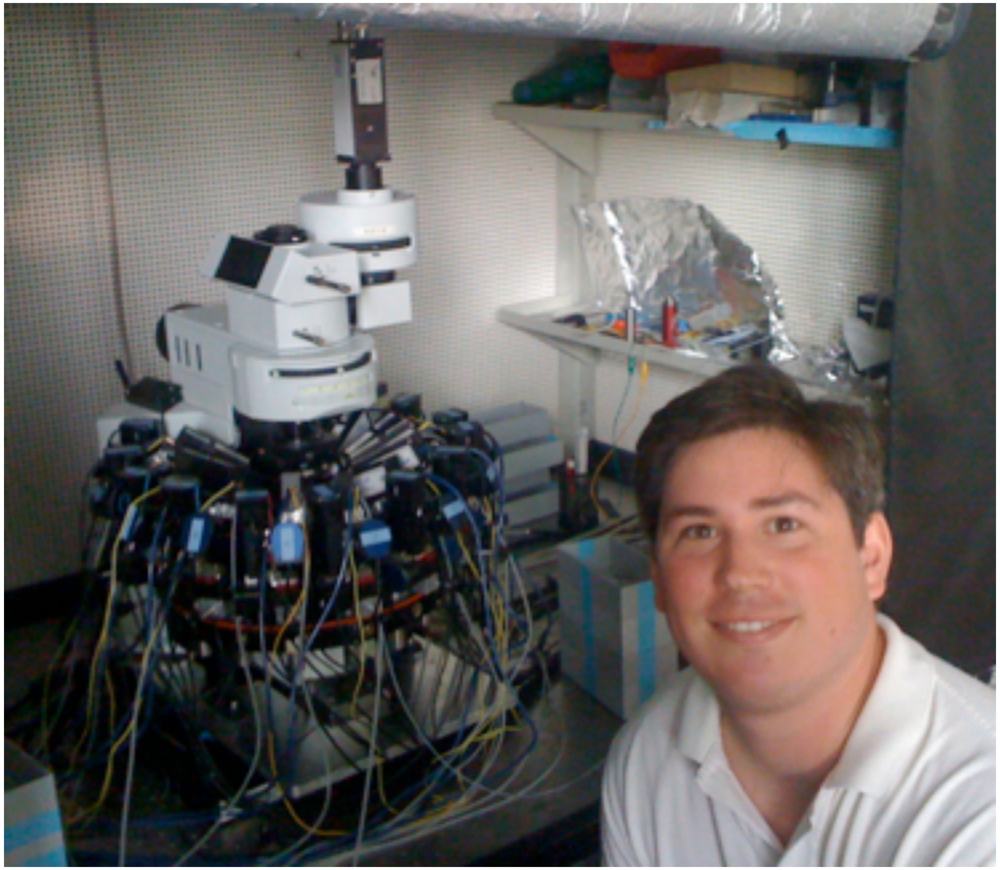
Computer simulations

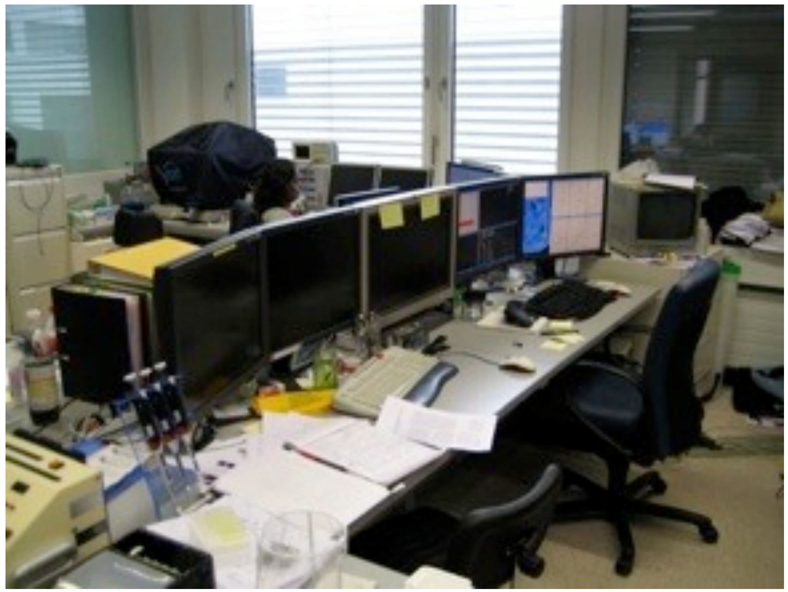


The expected ephaptic potentials

Anastassiou et al, *J Neurosci* (2010)

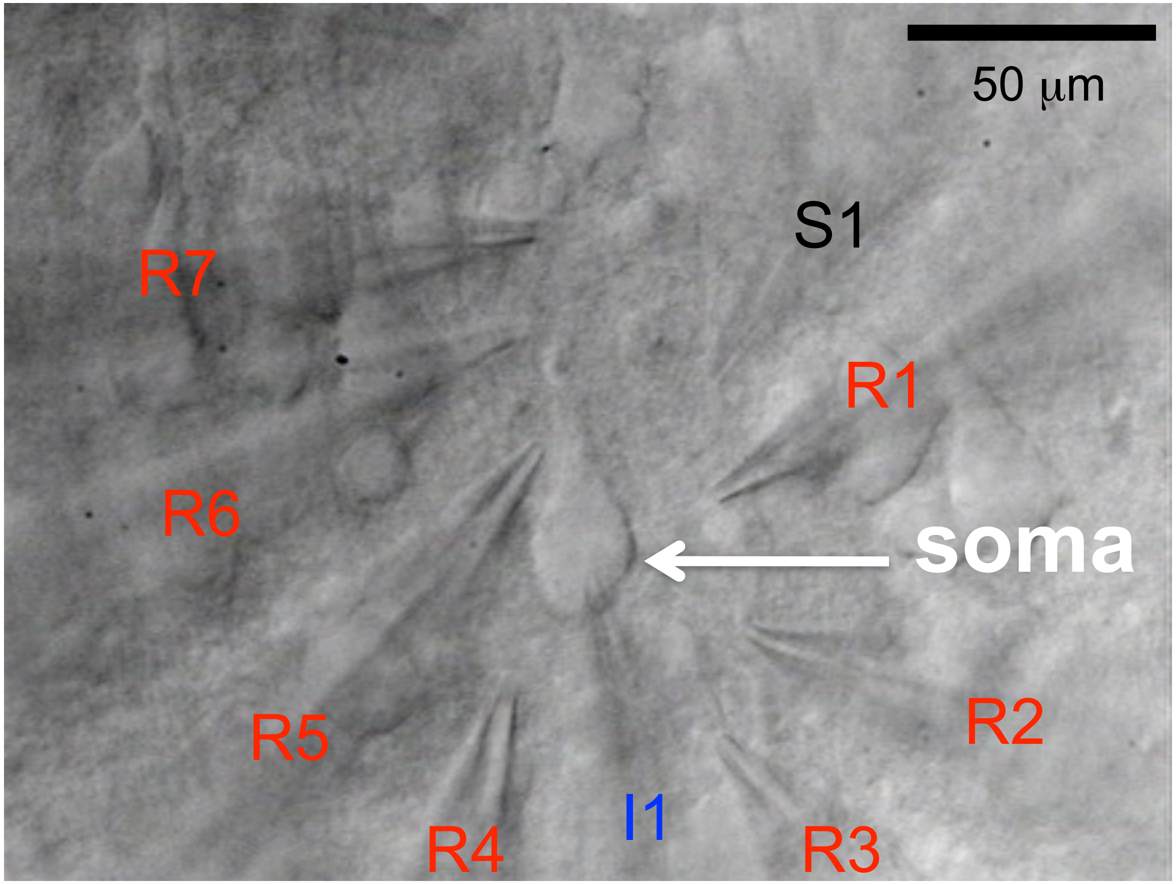
EPFL-Lausanne - 12 patch rig





Work with Costas Anastassiou, Rodrigo Perin & Henry Markram

Single cell measurements

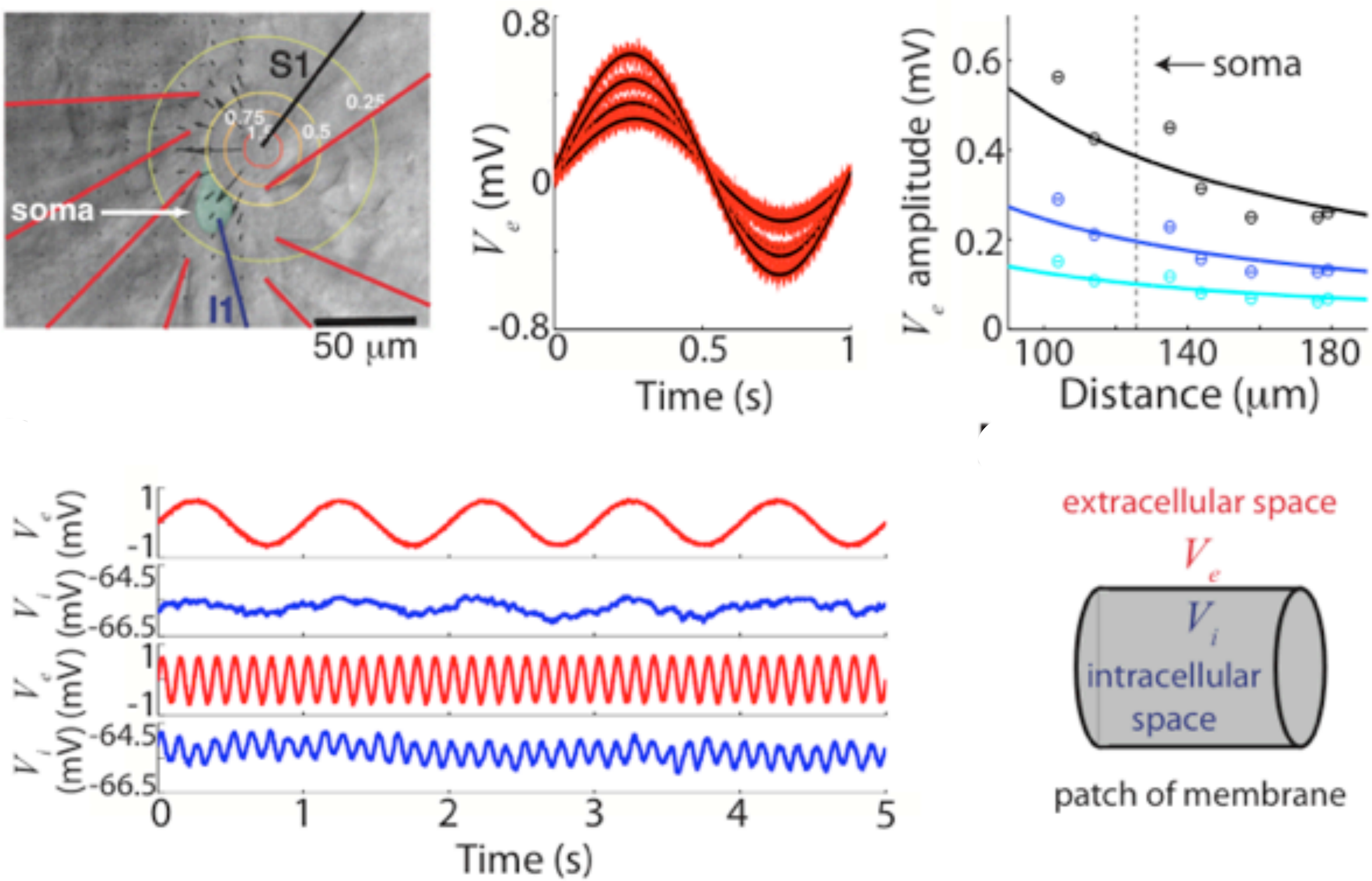


- 14-16 d old rats
- Somatosensory cortex
- Seal > 2 GOhm; average 4.4 GOhm

Pharmacologically silenced synaptic activity:

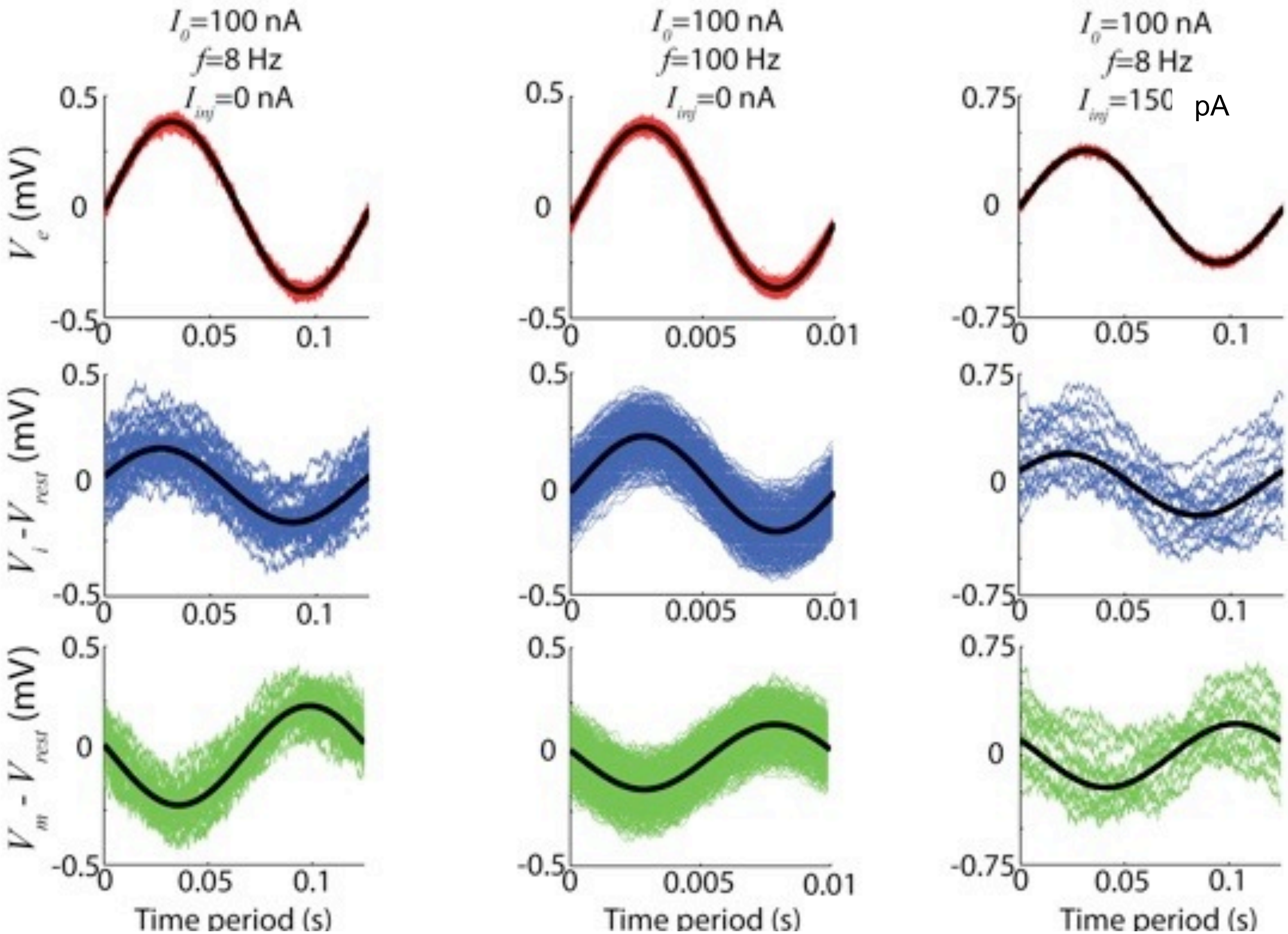
- AMPA – CNQX
- GABA – Gabazine / Bicuculine
- NMDA – APV

Subthreshold measurements



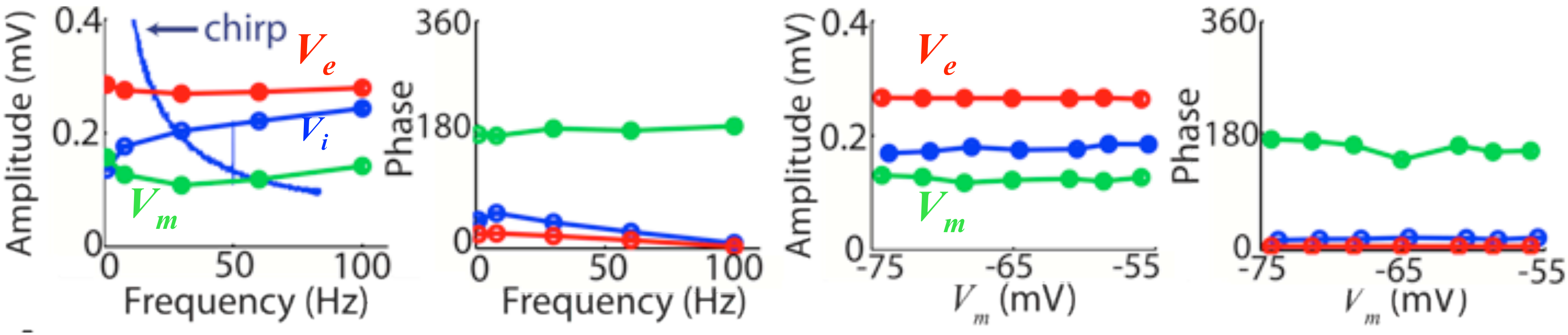
Anastassiou, Perin, Markram & Koch, *Nat Neurosci* (2011)

Subthreshold analysis



Subthreshold analysis

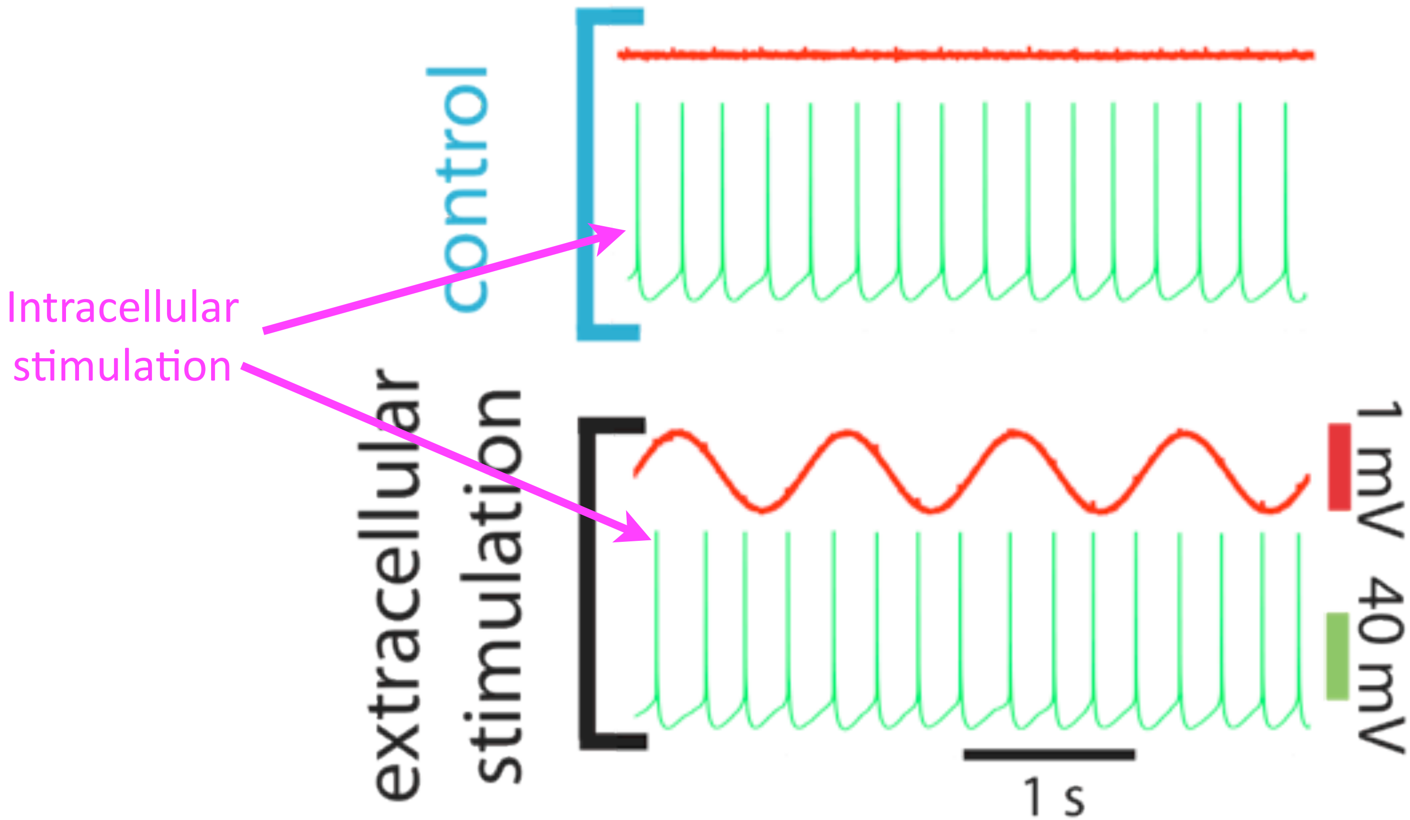
I_{inj}=100 nA, f=1-100 Hz (23 cells) I_{inj} = -150 to +150 nA, f =8 Hz (17 cells)



As predicted by our model, the ephaptic potentials in the subthreshold domain are < 1 mV, far away from being able to initiate spikes

Anastassiou *et al, Nature Neurosci.* (2011)

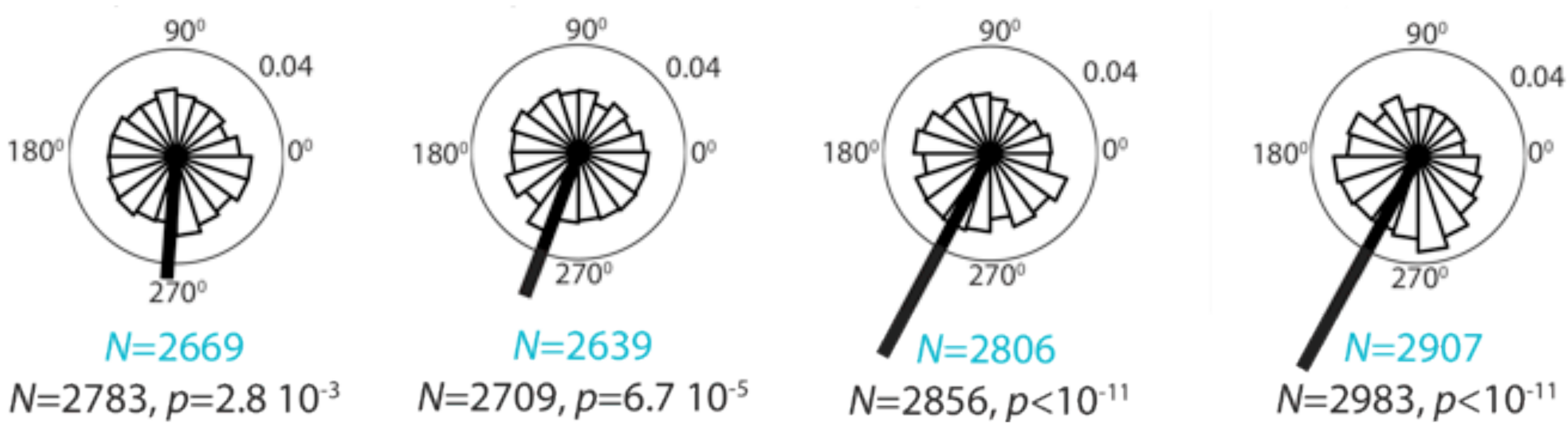
Ephaptic coupling of spiking



A 9 sec sustained current is injected into the cell

Population vector
1 Hz extracellular stimulation

I_0= 25 nA I_0= 50 nA I_0= 100 nA I_0= 200 nA



p-values as calculated by the Rayleigh test

25 cells

Control experiments performed before each extracellular stim. experiment

Field entrainment of spikes
leads to a non-uniform
spike-phase distribution

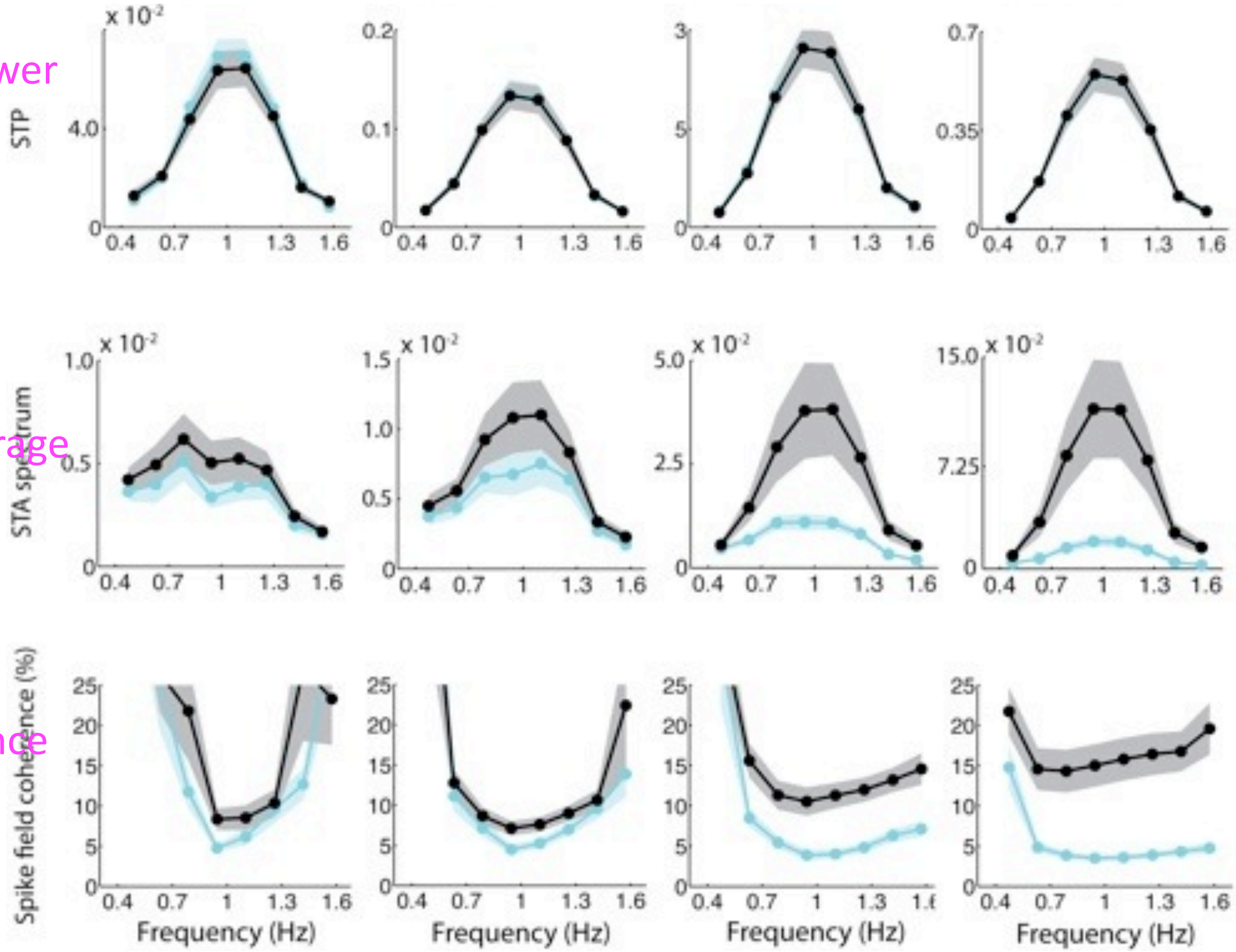
Spike-field coherence (SFC) analysis
1 Hz extracellular stimulation

I_0 = 25 nA I_0=50 nA I_0=100 nA I_0=200 nA

Spike-triggered power

Spike-triggered average

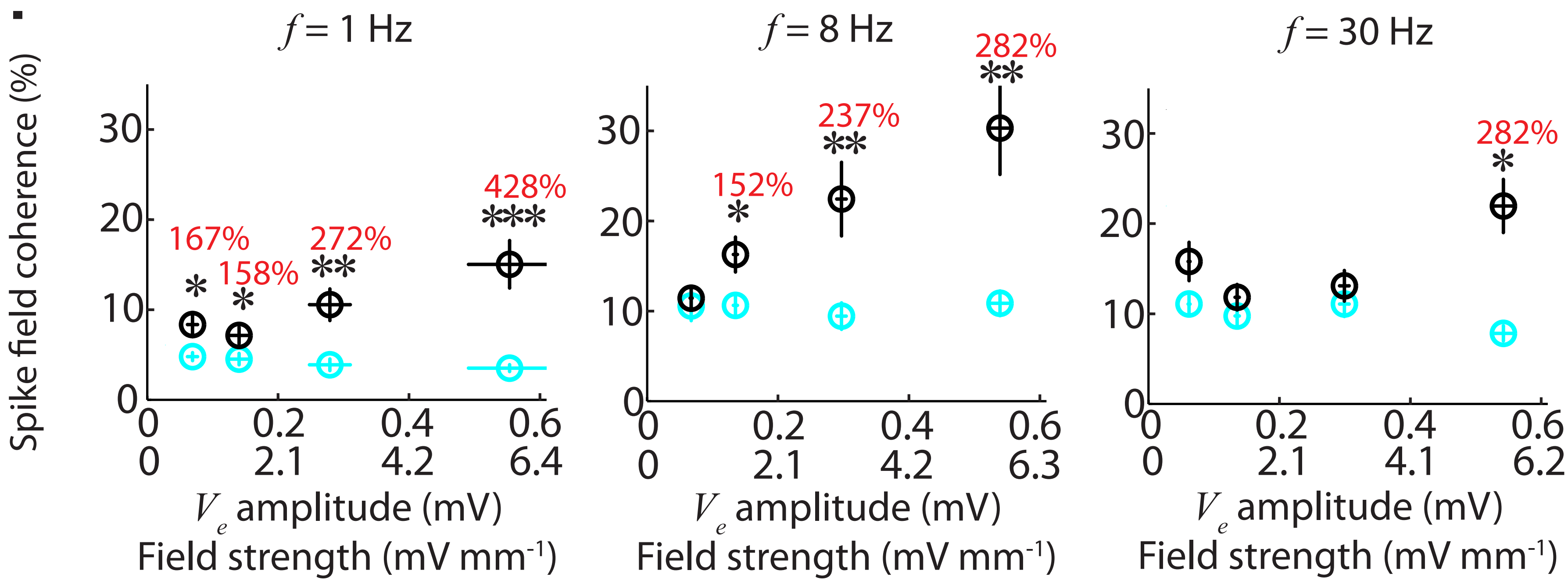
Spike field coherence (STA/STP)



SFC analysis-summary

Control experiments

Extracellular stimulation experiments

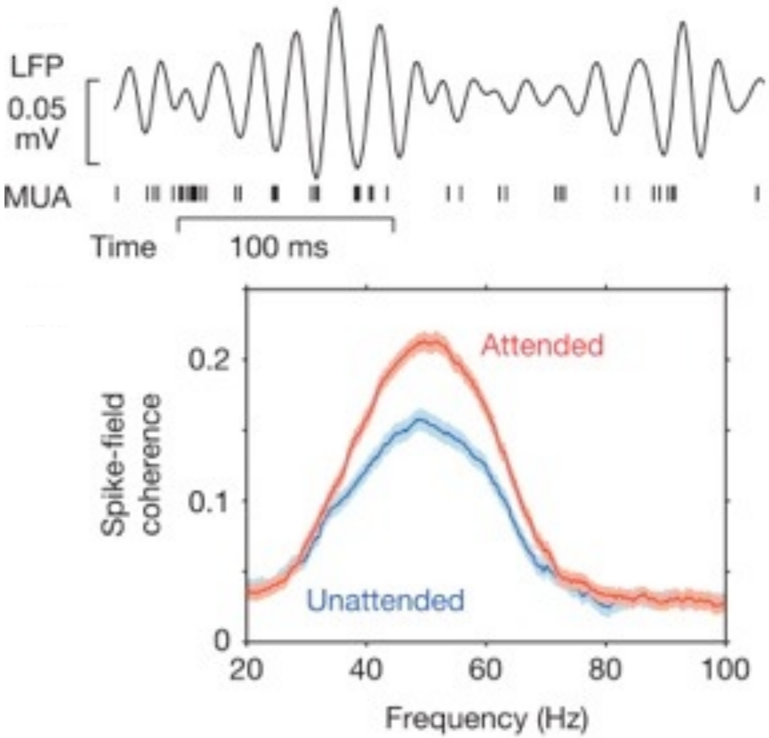


25 cells

Significance levels as calculated by paired t-test fdr-corrected for multiple comparisons

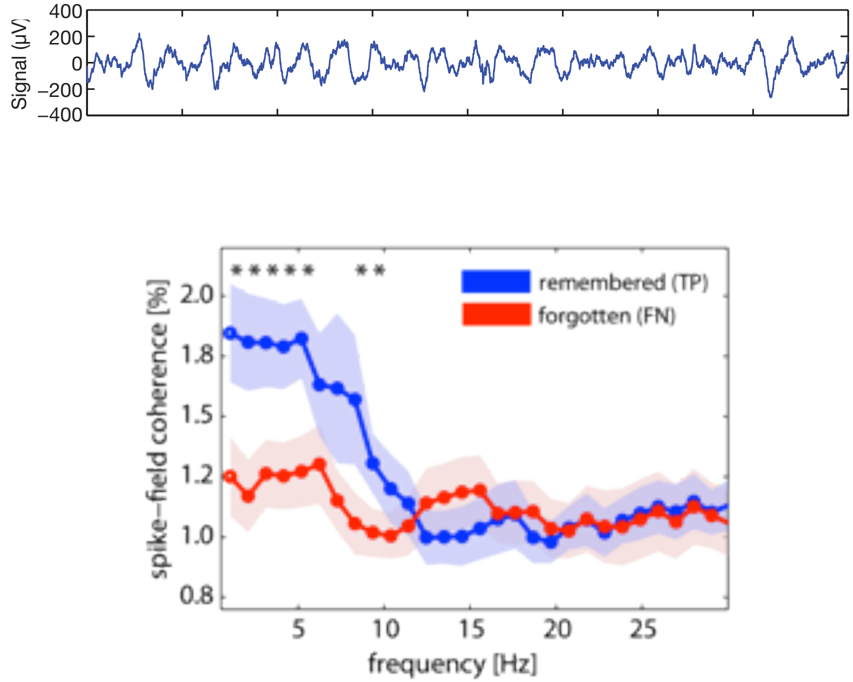
Anastassiou *et al, Nature Neurosci.* (2011)

Functional implications - SFC



Phase-locking of monkey V4 neurons
to gamma field potential

Womelsdorf, Fried, Mitra & Desimone *Nature* (2006)



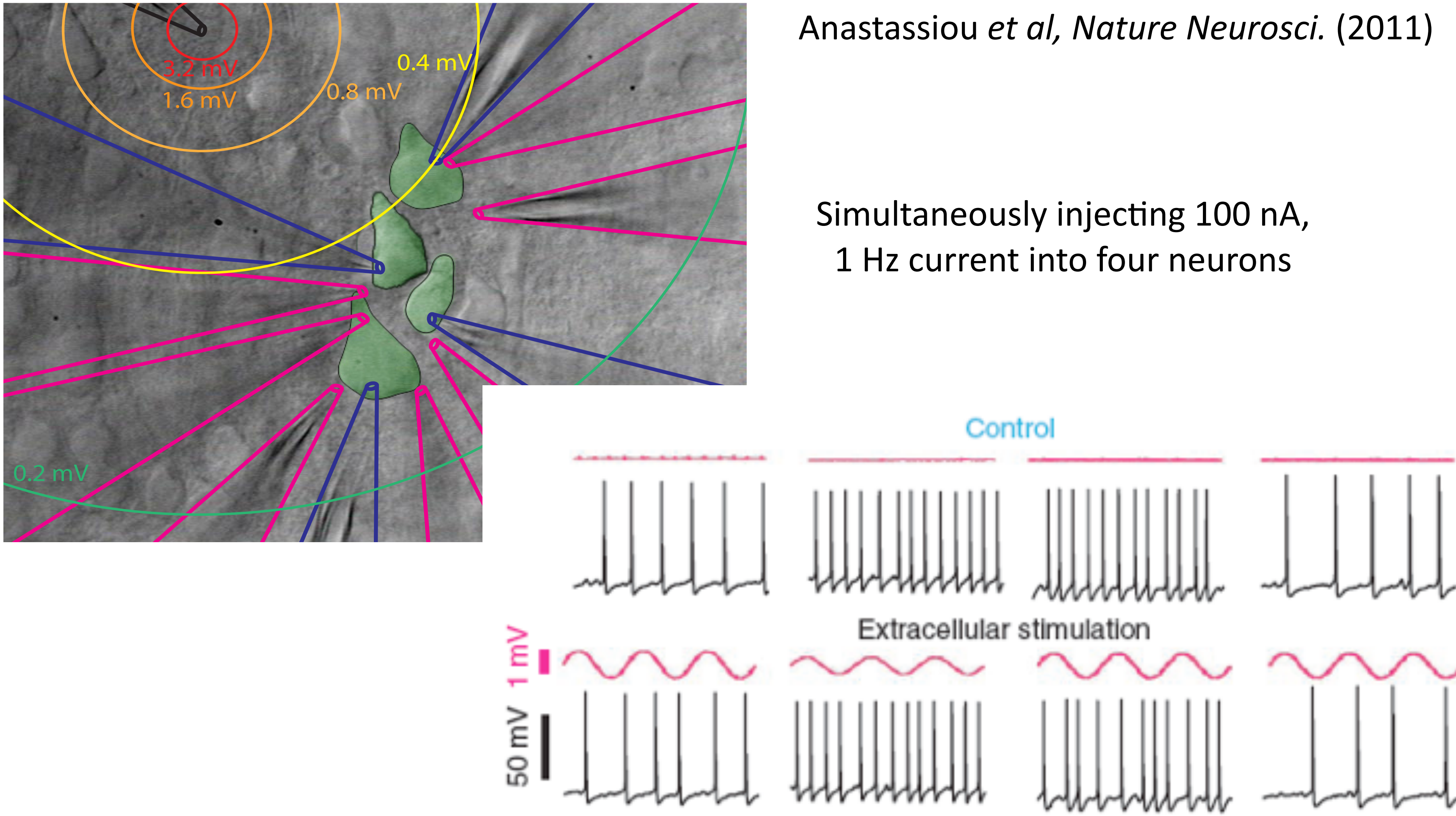
Phase-locking of human MTL neurons
to theta field potential

Rutishauser *et al. Nature* (2010)

Ephaptic coupling in neuronal assemblies

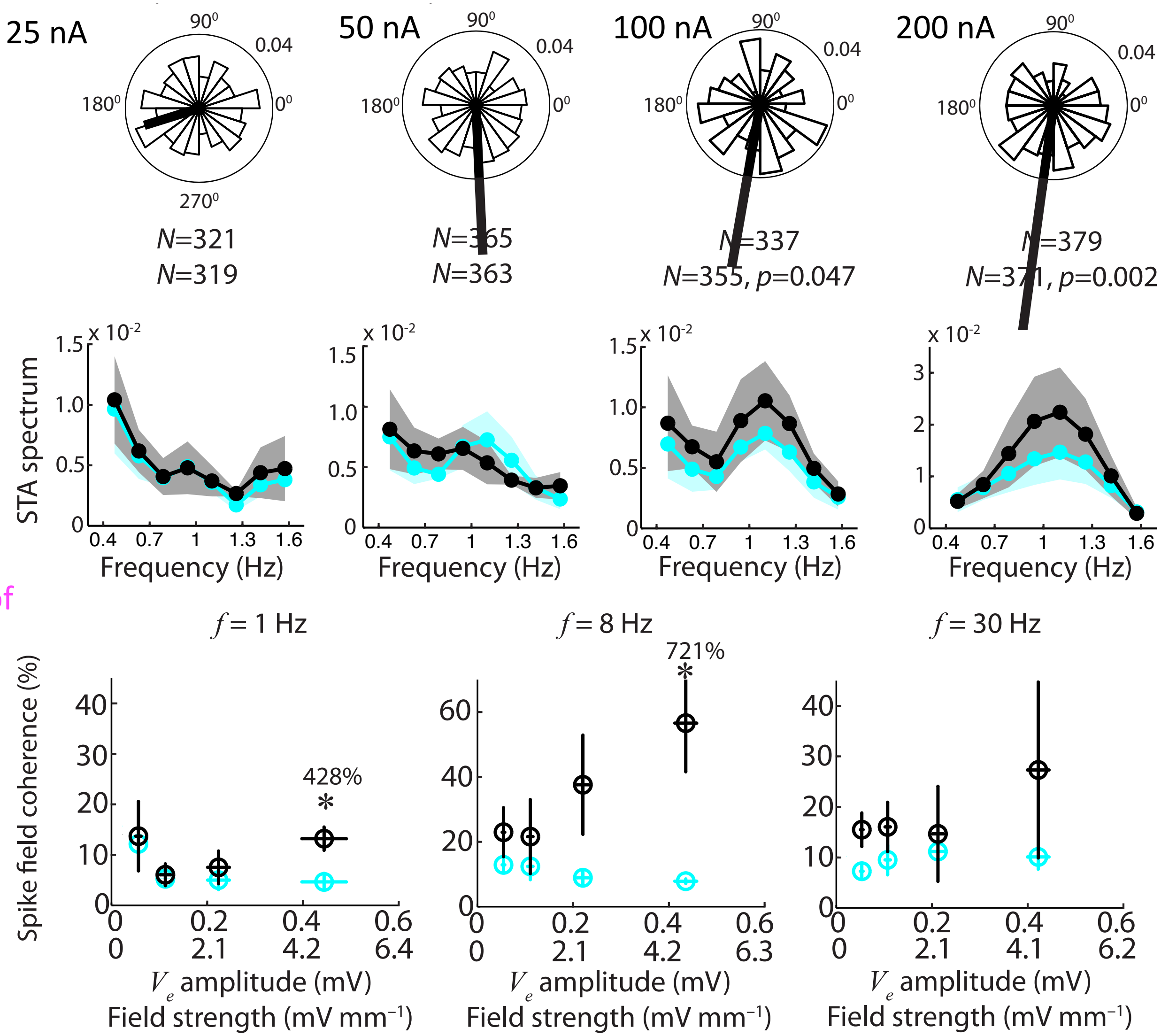
Anastassiou *et al, Nature Neurosci.* (2011)

Simultaneously injecting 100 nA, 1 Hz current into four neurons



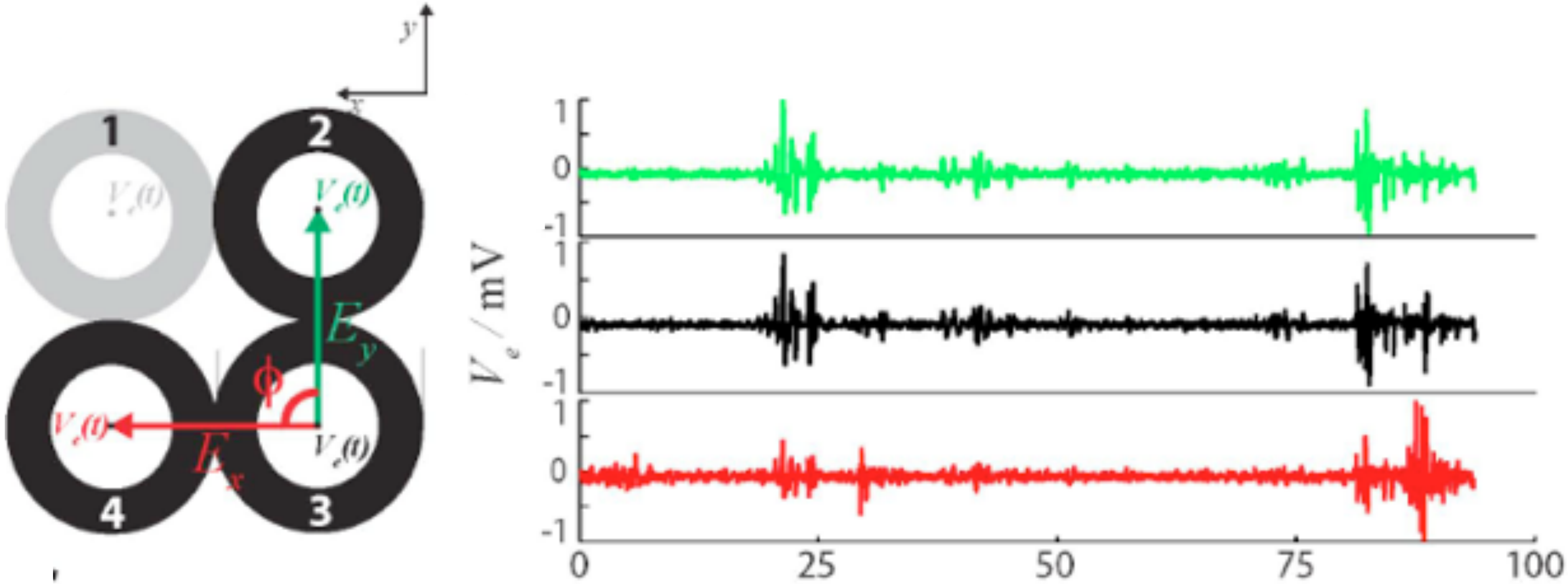
Ephaptic coupling in neural assemblies

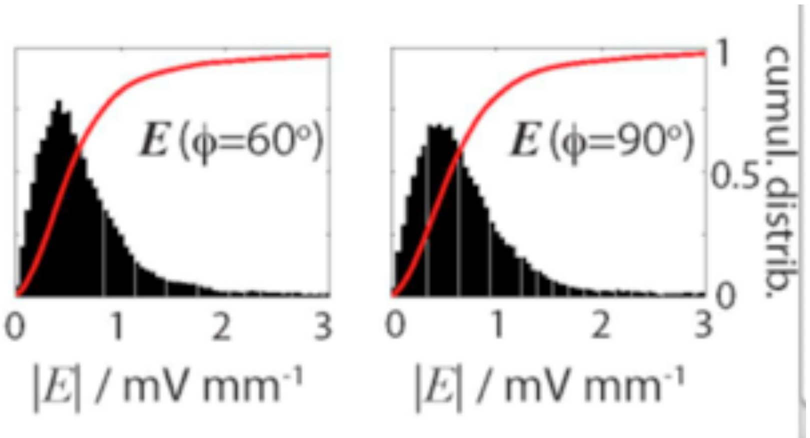
f = 1 Hz



Note the absence of
any synaptic input

Human tetrode recordings





Anastassiou, Hill, Koch & Fried (UCLA)

In summary

- Subthreshold field effects < 1 mV, and behave as expected from cable theory
- Supra-threshold field effects on layer 5 pyramidal neurons can be remarkable strong at low frequencies of the LFP
- Such ephaptic effects help to synchronize populations of neurons irrespective of their synaptic interconnectivity