Lecture 2
Dynamical models for single neurons. Measuring experimental neural data.

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The Hodgkin – Huxley model

Using **pioneering experimental techniques** of that time, Hodgkin and Huxley (1952) determined not only the equations but **measured all the parameters values** :

$$
\begin{aligned}
C\,\dot V &= I - \overbrace{\bar g_{\rm K} n^4 (V - E_{\rm K})}^{I_{\rm K}} - \overbrace{\bar g_{\rm Na} m^3 h (V - E_{\rm Na})}^{I_{\rm Na}} - \overbrace{g_{\rm L}(V - E_{\rm L})}^{I_{\rm L}} \\
\dot n &= \alpha_n(V)(1-n) - \beta_n(V) n \\
\dot m &= \alpha_m(V)(1-m) - \beta_m(V) m \\
\dot h &= \alpha_h(V)(1-h) - \beta_h(V) h \,,
\end{aligned}
$$

$$
\begin{aligned}
\alpha_n(V) &= 0.01 \frac{10-V}{\exp(\frac{10-V}{10}) - 1}\,, \\
\beta_n(V) &= 0.125 \exp\left(\frac{-V}{80}\right)\,, \\
\alpha_m(V) &= 0.1 \frac{25-V}{\exp(\frac{25-V}{10}) - 1}\,, \\
\beta_m(V) &= 4 \exp\left(\frac{-V}{18}\right)\,, \\
\alpha_h(V) &= 0.07 \exp\left(\frac{-V}{20}\right)\,, \\
\beta_h(V) &= \frac{1}{\exp(\frac{30-V}{10}) + 1}\,.
\end{aligned}
$$

Values of shifted Nernst equilibrium potentials (so that $V_{rest} = 0$) :

$$E_{\rm K} = -12 \text{ mV}\,, \qquad E_{\rm Na} = 120 \text{ mV}\,, \qquad E_{\rm L} = 10.6 \text{ mV};$$

Values of maximal conductances:

$$\bar g_{\rm K} = 36 \text{ mS/cm}^2\,, \qquad \bar g_{\rm Na} = 120 \text{ mS/cm}^2\,, \qquad g_{\rm L} = 0.3 \text{ mS/cm}^2.$$

Value of membrane capacitance:

$$C = 1\,\mu\text{F/cm}^2$$

4-dimensional system: difficult to study the dynamics

A lot of parameters to be determined to model a neuron!
This is generally hard to measure!

The Hodgkin – Huxley model, simplified

Many interesting features of single neuron dynamics can be illustrated using two-dimensional systems

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{g_{\mathrm{L}}(V-E_{\mathrm{L}})}^{\text{leak } I_{\mathrm{L}}} - \overbrace{g_{\mathrm{Na}}\, m_\infty(V)\,(V-E_{\mathrm{Na}})}^{\text{instantaneous } I_{\mathrm{Na,p}}} - \boxed{\overbrace{g_{\mathrm{K}}\, n\,(V-E_{\mathrm{K}})}^{I_{\mathrm{K}}}}\,, \\
\dot{n} &= (n_\infty(V) - n)/\tau(V)\,,
\end{aligned}
$$

Definition: x-Nullcline:
curve such that $\frac{dx}{dt} = \dot{x} = 0$

The V-nullcline is given by the equation $I - g_{\mathrm{L}}(V-E_{\mathrm{L}}) - g_{\mathrm{Na}}\, m_\infty(V)\,(V-E_{\mathrm{Na}}) - g_{\mathrm{K}}\, n\,(V-E_{\mathrm{K}}) = 0$

which has the solution
$$\boxed{n = \frac{I - g_{\mathrm{L}}(V-E_{\mathrm{L}}) - g_{\mathrm{Na}}\, m_\infty(V)\,(V-E_{\mathrm{Na}})}{g_{\mathrm{K}}\,(V-E_{\mathrm{K}})}}$$

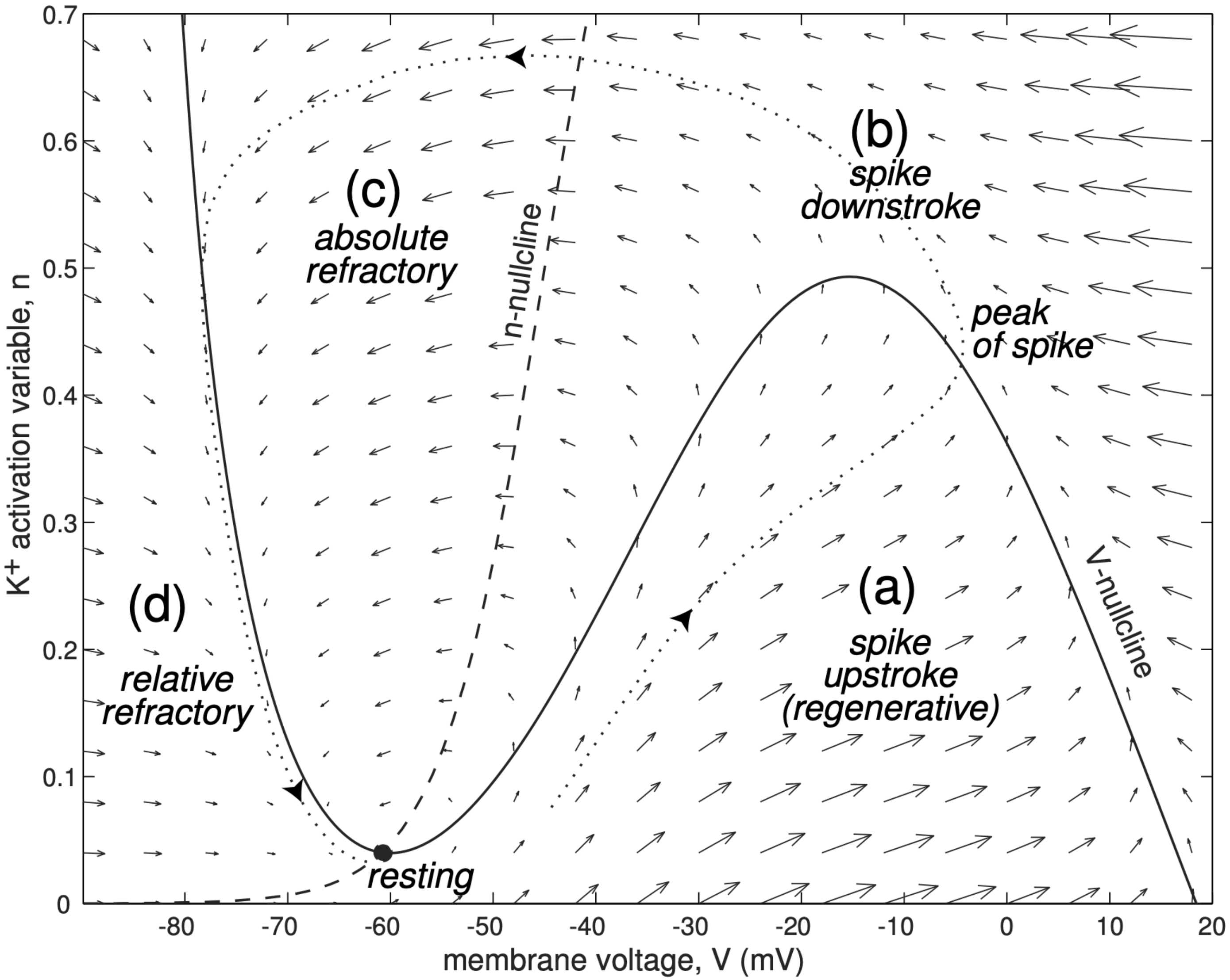
The equation $n_\infty(V) - n = 0$ defines the n-nullcline $\boxed{n = n_\infty(V)}$

The Hodgkin – Huxley model, simplified

Nullclines:

$$\boxed{n = \frac{I - g_{\mathrm{L}}(V - E_{\mathrm{L}}) - g_{\mathrm{Na}}\, m_\infty(V)\,(V - E_{\mathrm{Na}})}{g_{\mathrm{K}}\,(V - E_{\mathrm{K}})}}$$

$$\boxed{n = n_\infty(V)}$$



FitzHugh-Nagumo model

The system

$$\dot{V} = V(a-V)(V-1) - w + I \,,$$
$$\dot{w} = bV - cw \,,$$

imitates generation of action potentials by Hodgkin-Huxley-type models having cubic (N-shaped) nullclines (similar to the Figure in the previous slide)

- Parameter I mimics the injected current. For the sake of simplicity, we set $I = 0$
- Parameter a describes the shape of the cubic parabola $V(a-V)(V-1)$

The nullclines of the FitzHugh-Nagumo are:

$$w = V(a-V)(V-1) + I \qquad (V\text{-nullcline})$$
$$w = b/c\,V \qquad (w\text{-nullcline}),$$

FitzHugh-Nagumo model

The nullclines of the FitzHugh-Nagumo are:

$$w = V(a - V)(V - 1) + I \qquad (V\text{-nullcline})$$
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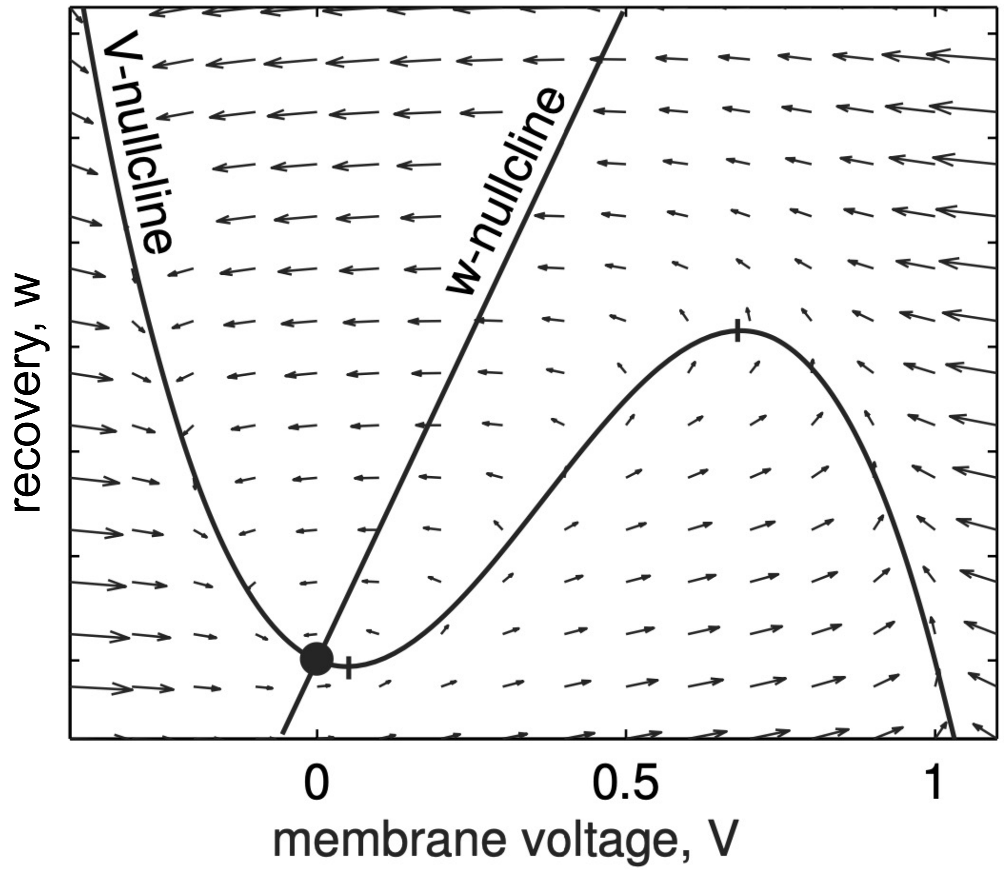
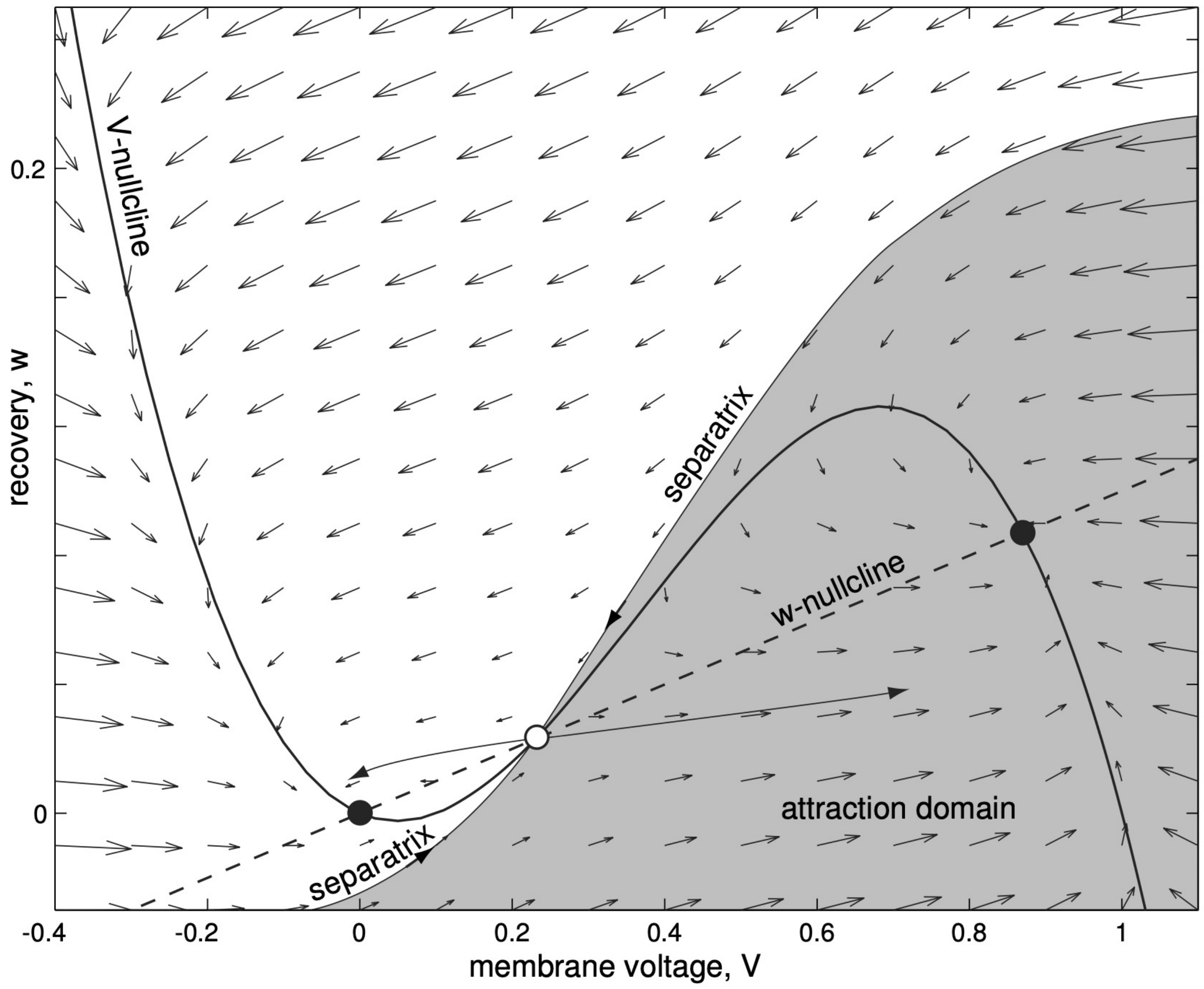
Spike



Spike and bi-stability



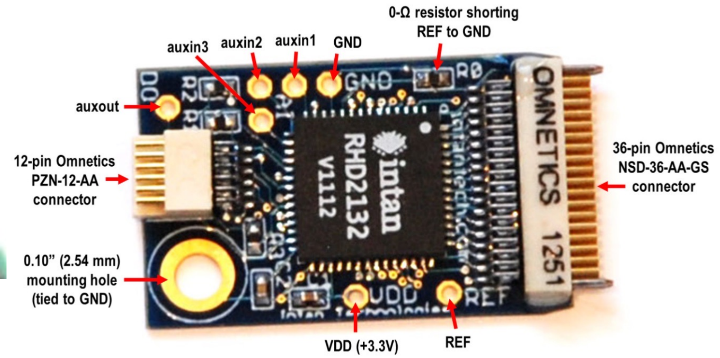
Recording neural activity

Now that we have a model for spikes,
we want to record real spikes!

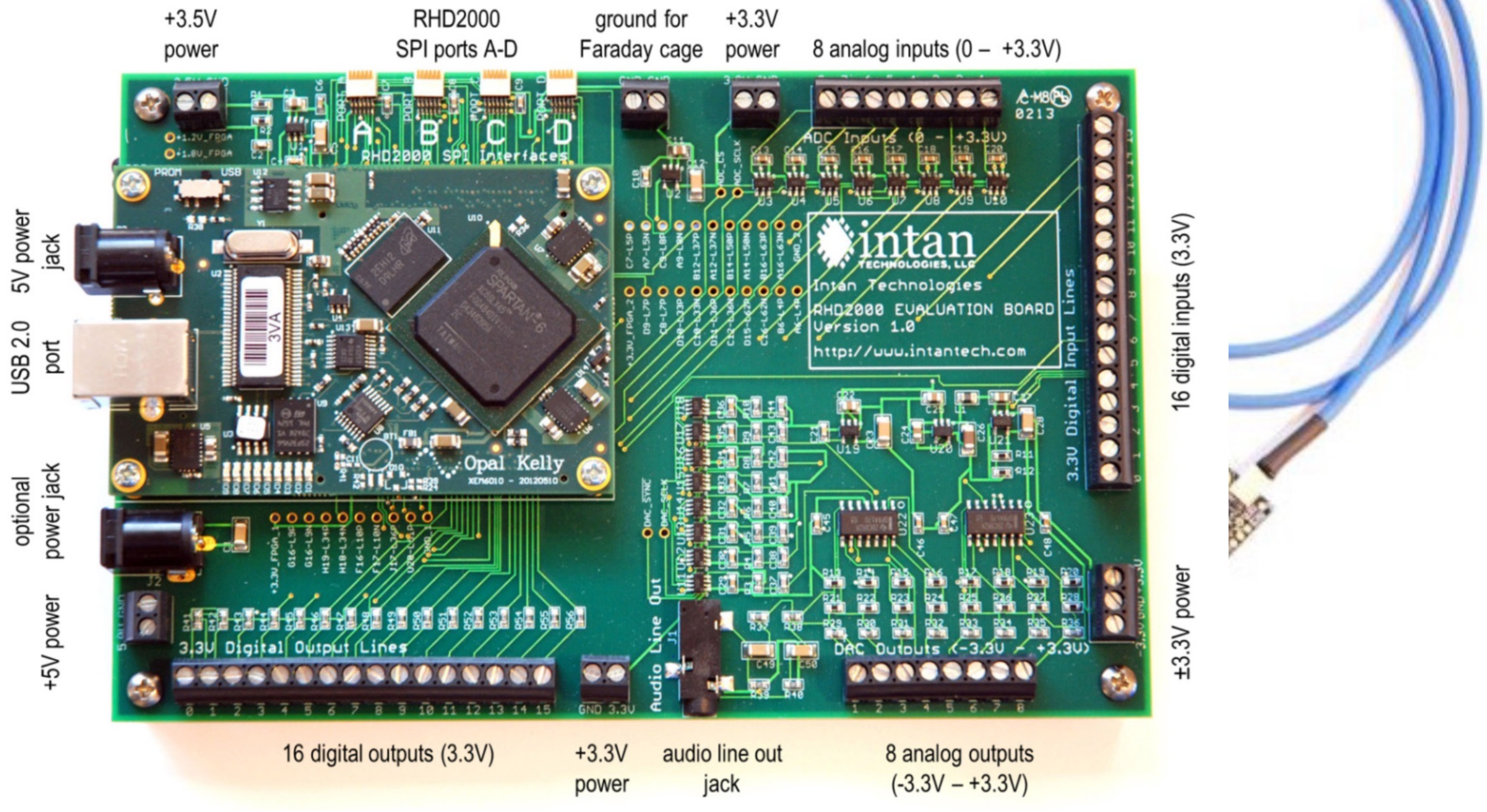
Or is it the other way around?

We first make **recording of spikes** and propose to use
dynamical models of spikes
to make sense of our recordings
(we are just measuring few spikes out of many, many more!)

Measuring electrical activity in the brain

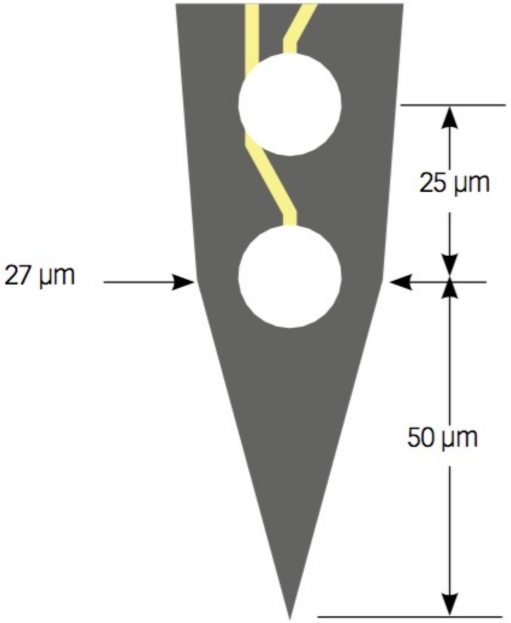


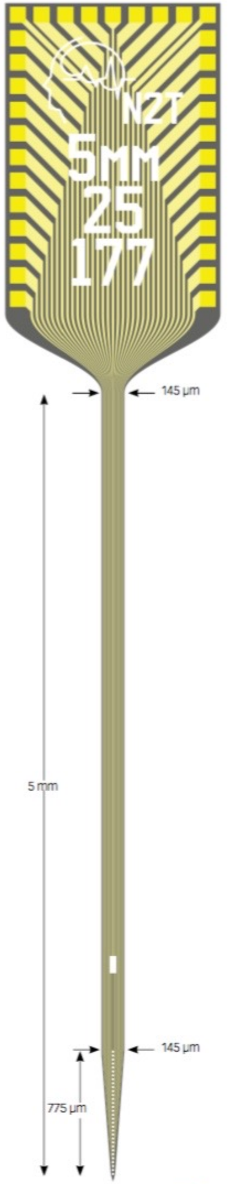
RHD2000 USB Interface Board



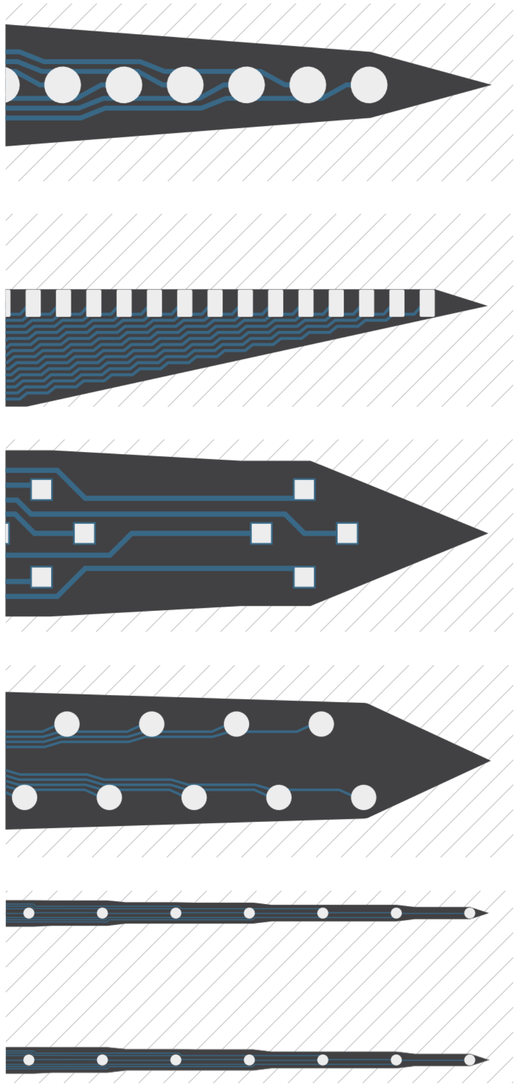
INTAN + Neuronexus

32-channel silicon probe





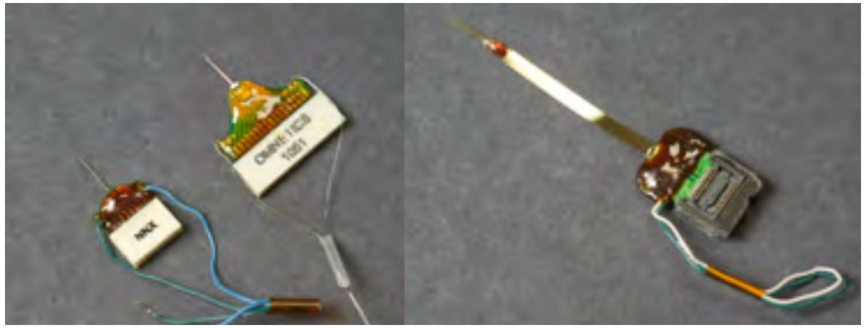
Measuring electrical activity in the brain

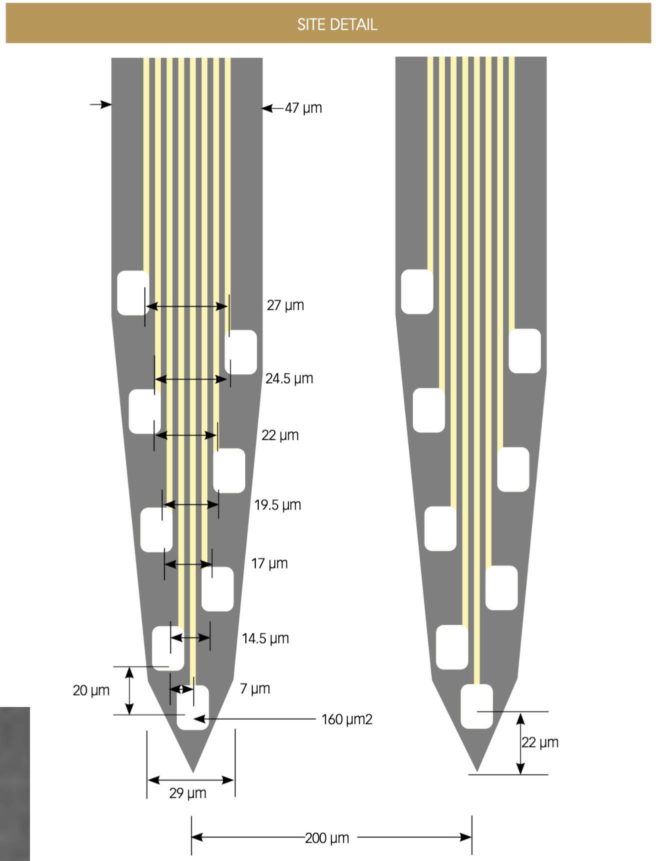


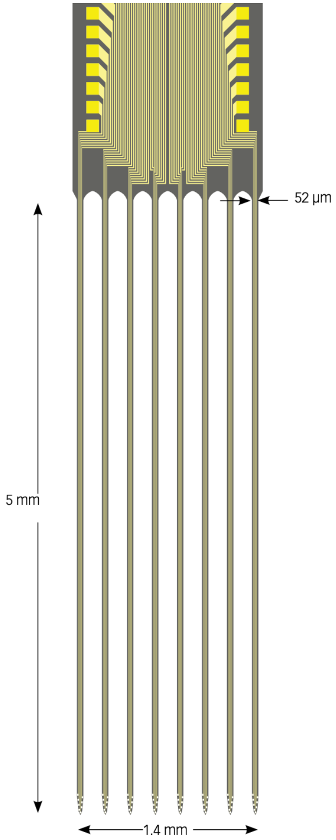
NeuroNexus

Micromachined silicon
probes

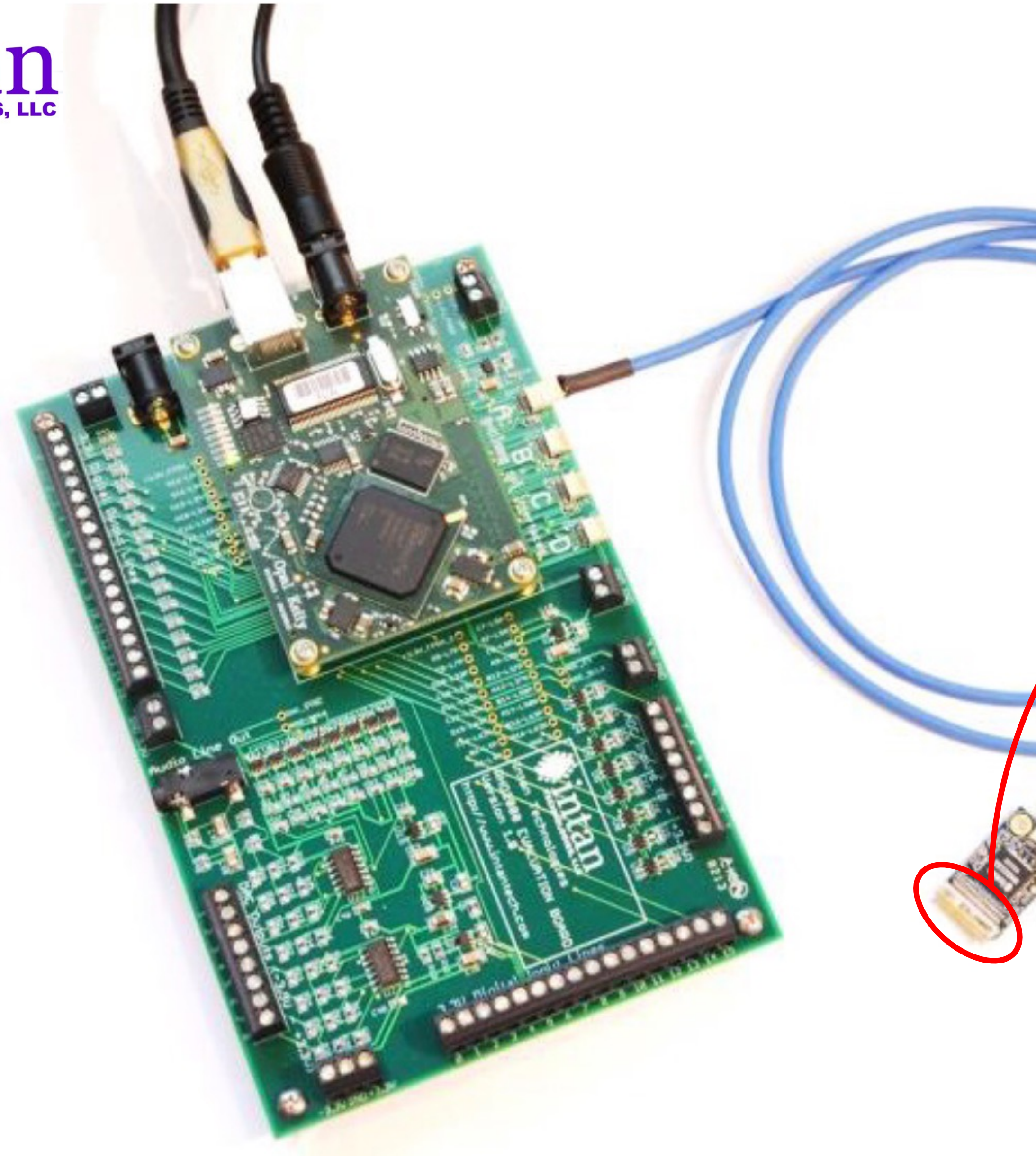
Value: around USD 1000







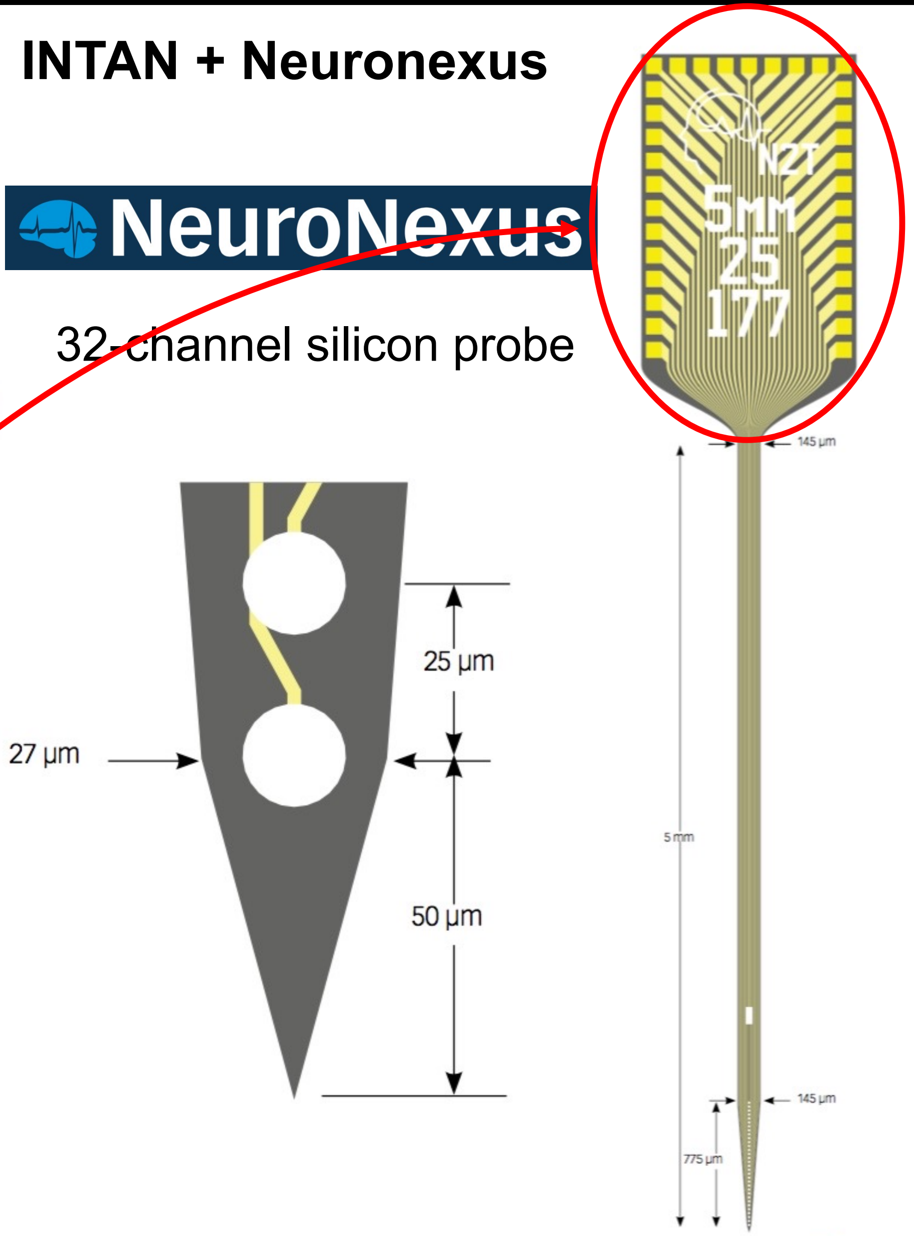
Measuring electrical activity in the brain



INTAN + Neuronexus

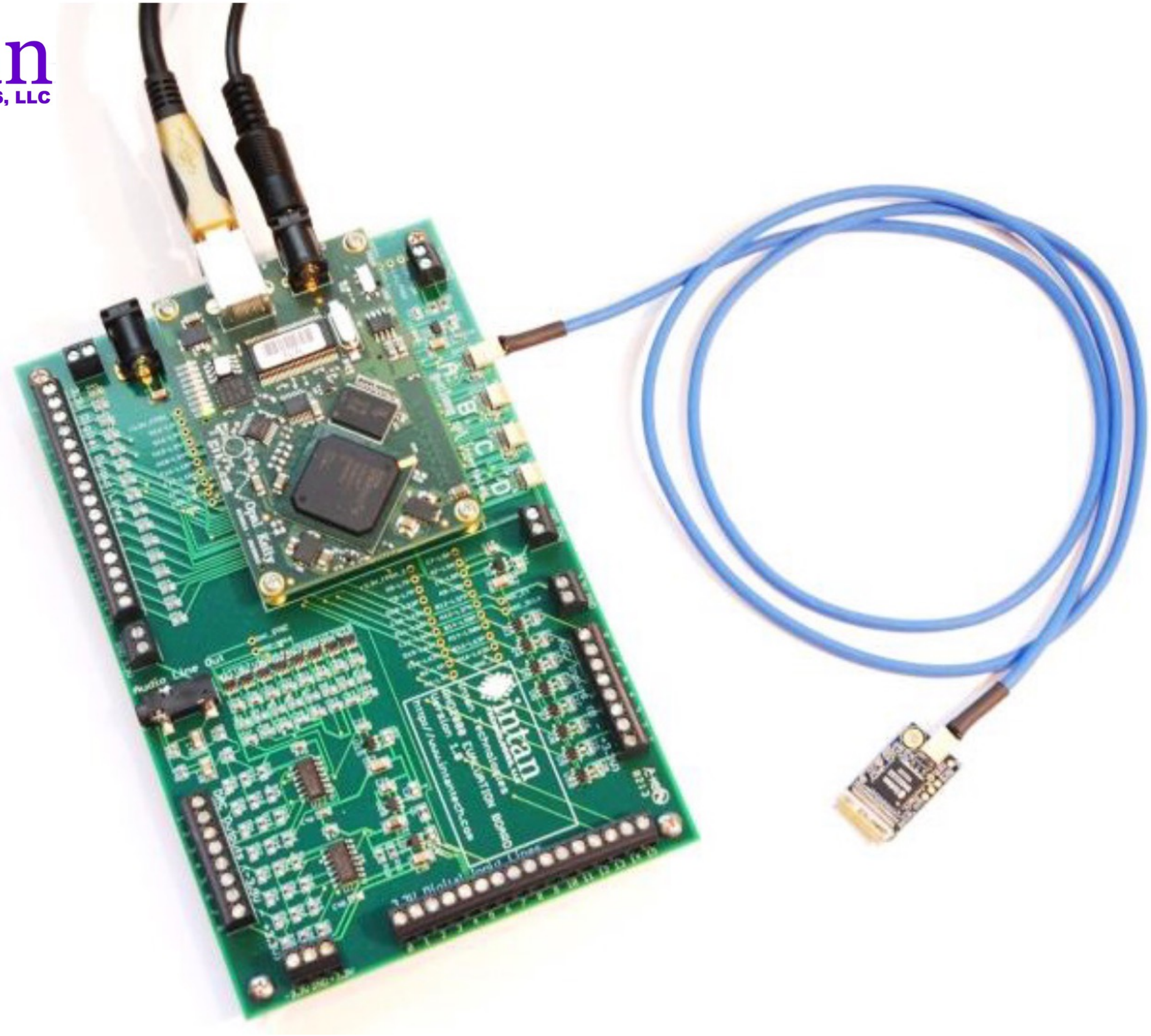
NeuroNexus

32-channel silicon probe

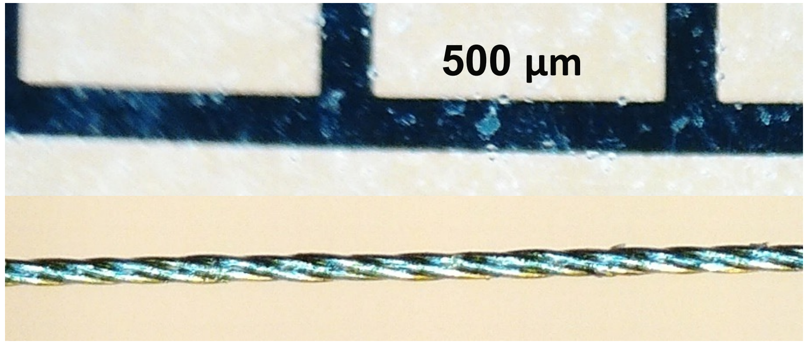


Measuring electrical activity in the brain

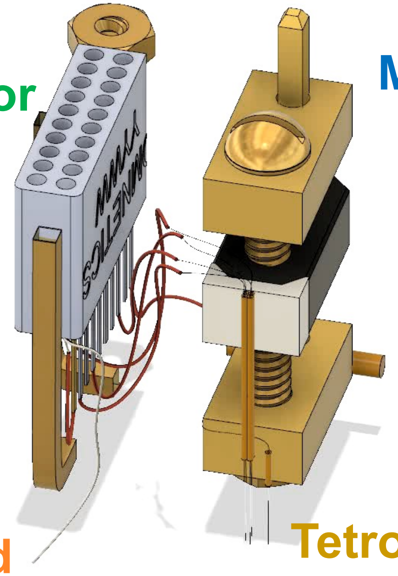
intan
TECHNOLOGIES, LLC



In-house manufactured tetrodes

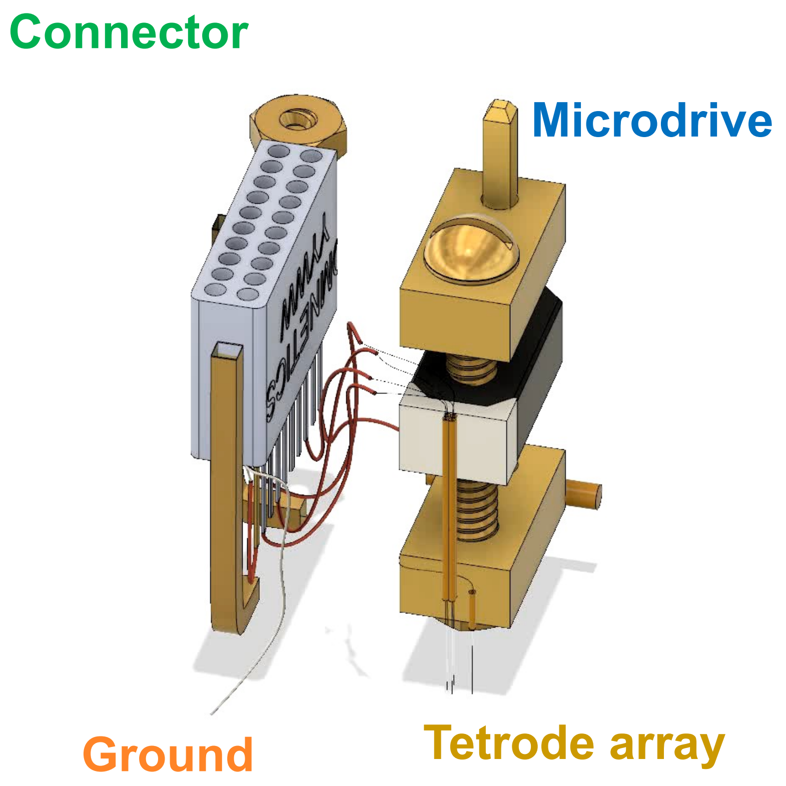


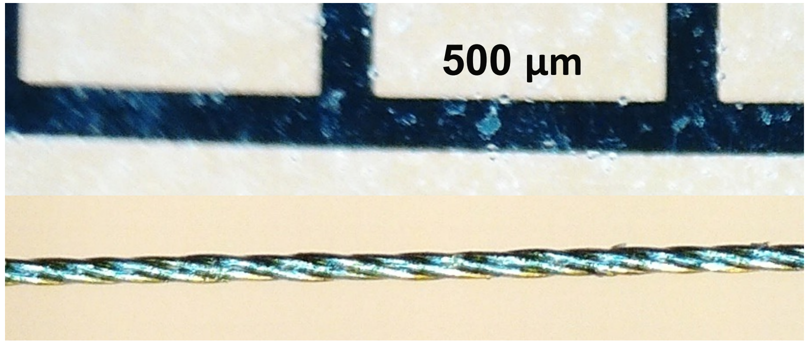
- Diameter 0.0005” (12.7 µm)
- Tungsten, HML coating
- Impedances: 500k to 3 MOhm



Measuring electrical activity in the brain

- **ultra-lightweight**
- **compact**
- **customizable**
- **low-cost**





- Tetrodes manufactured in-house
- Diameter 0.0005” (12.7 µm)
- Tungsten, HML coating
- Impedances:
  500k to 3 MOhm

In collaboration with M. Belluscio

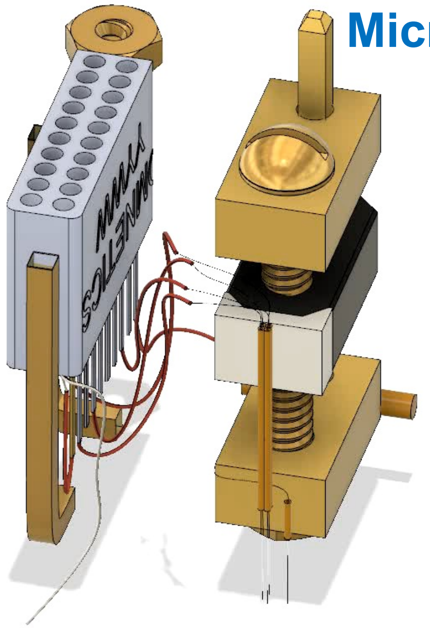
Credits: Cecilia T. Herbert

Lightweight recording device

- **ultra-lightweight**
- **compact**
- **customizable**
- **low-cost**

Connector

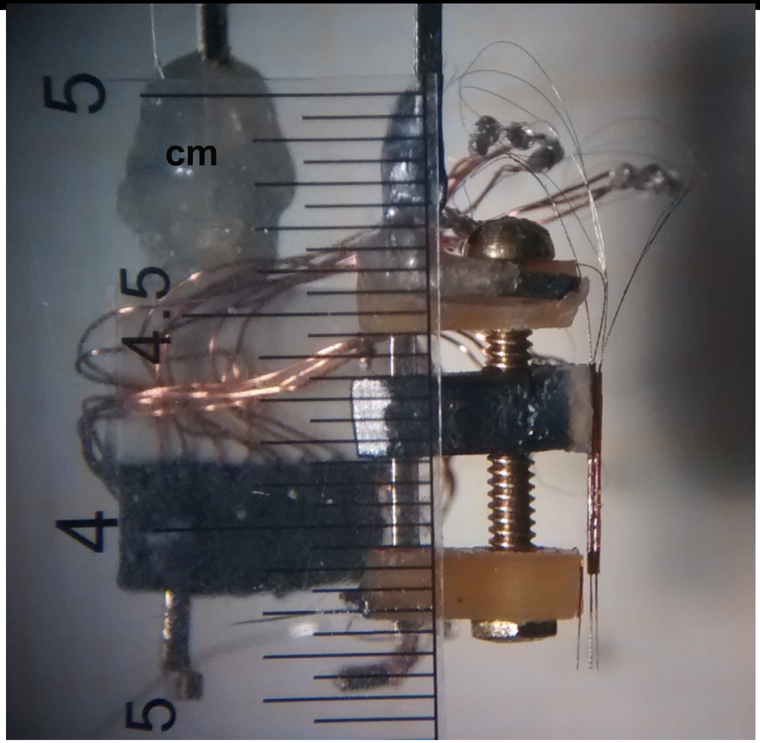
Microdrive



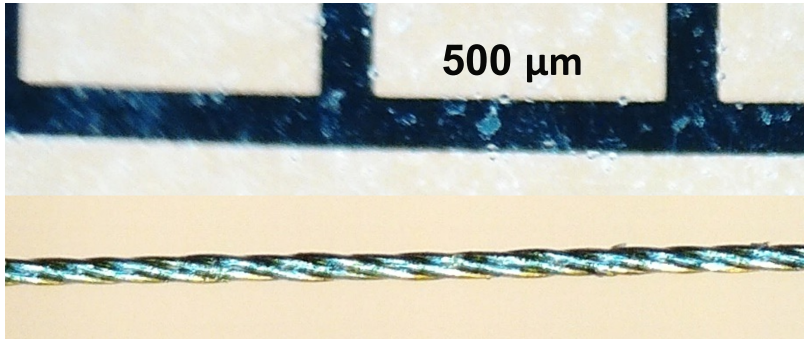
Ground

Tetrode array

In collaboration with M. Belluscio



- Pitch 90 TPI = 282 µm/turn (manual step ≈25 µm)
- Mass <1g
- 15mm tall, 13mm^2 footprint
- Tetrode geometry easy to modify.



- Tetrodes manufactured in-house
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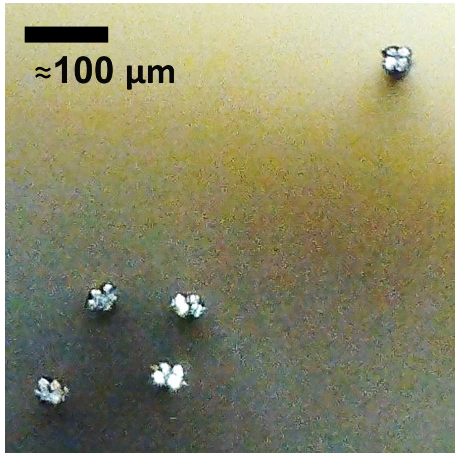
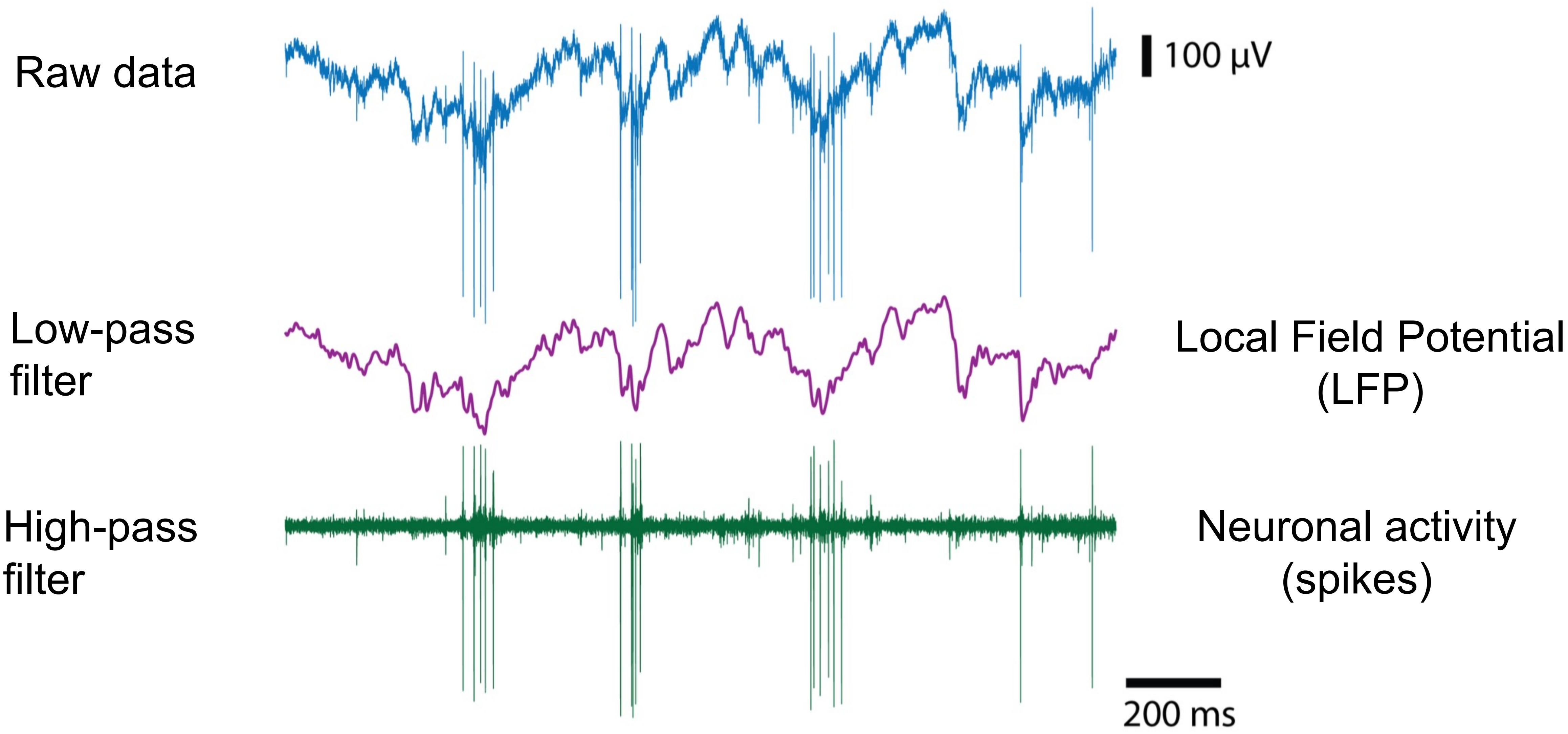


- 4-tetrode array (16ch) + Ref
- 2x2 geometry

Credits: Cecilia T. Herbert

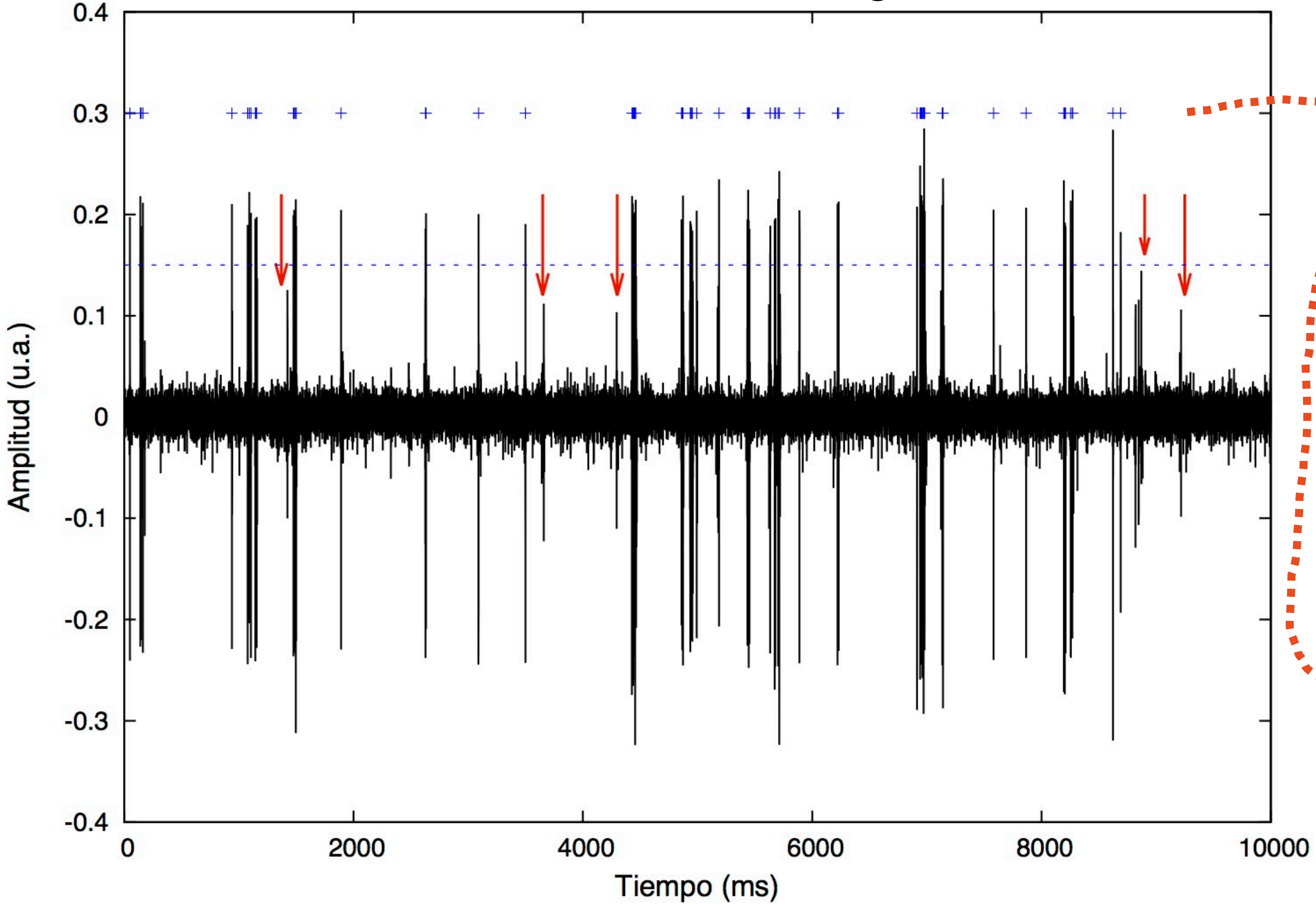
Neural recordings



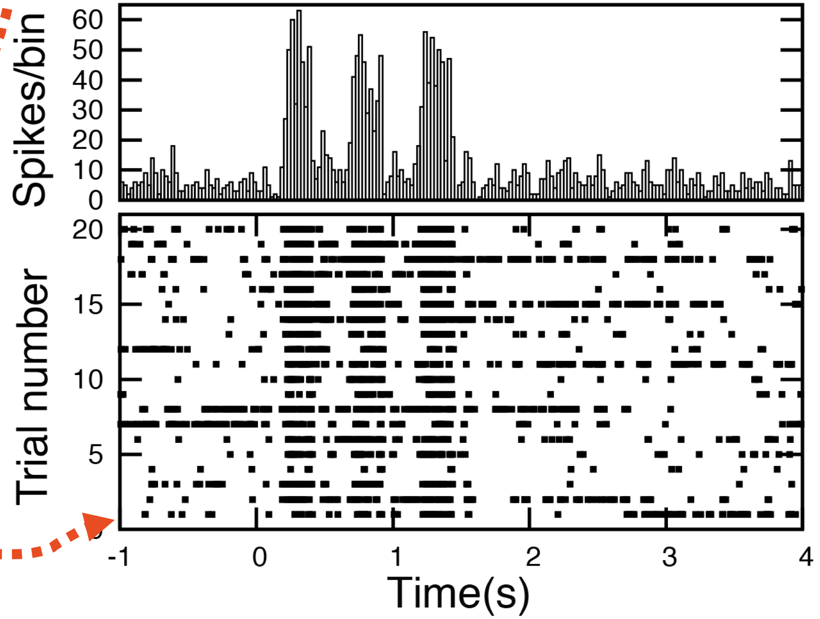
Work with Santiago Boari

Neural recordings

Multi-unit recordings

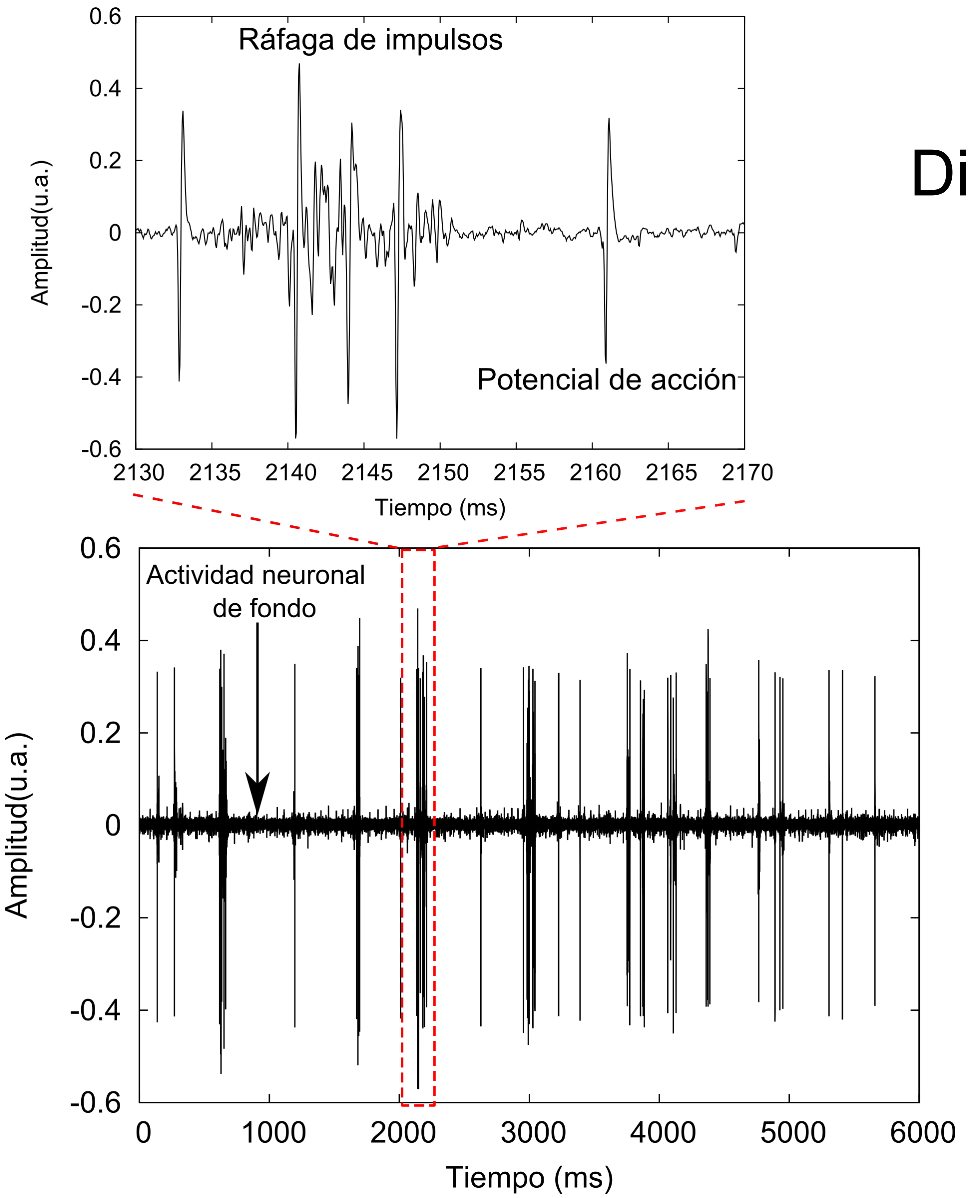


Spike sorting -
The simplest method:
threshold crossing



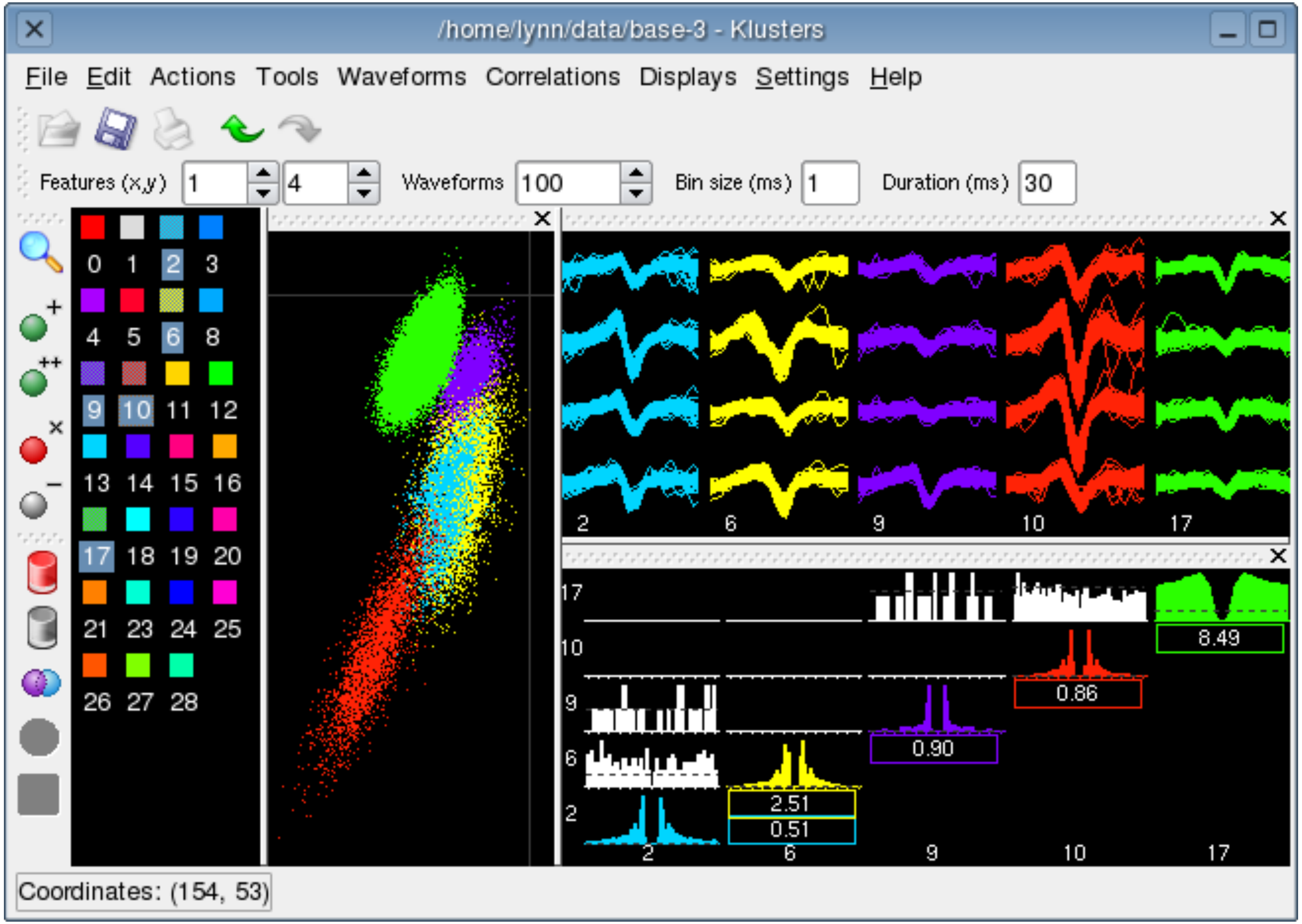
Grouped neuronal data

Neural recordings



Different neurons may present different spike shapes

Neural recordings

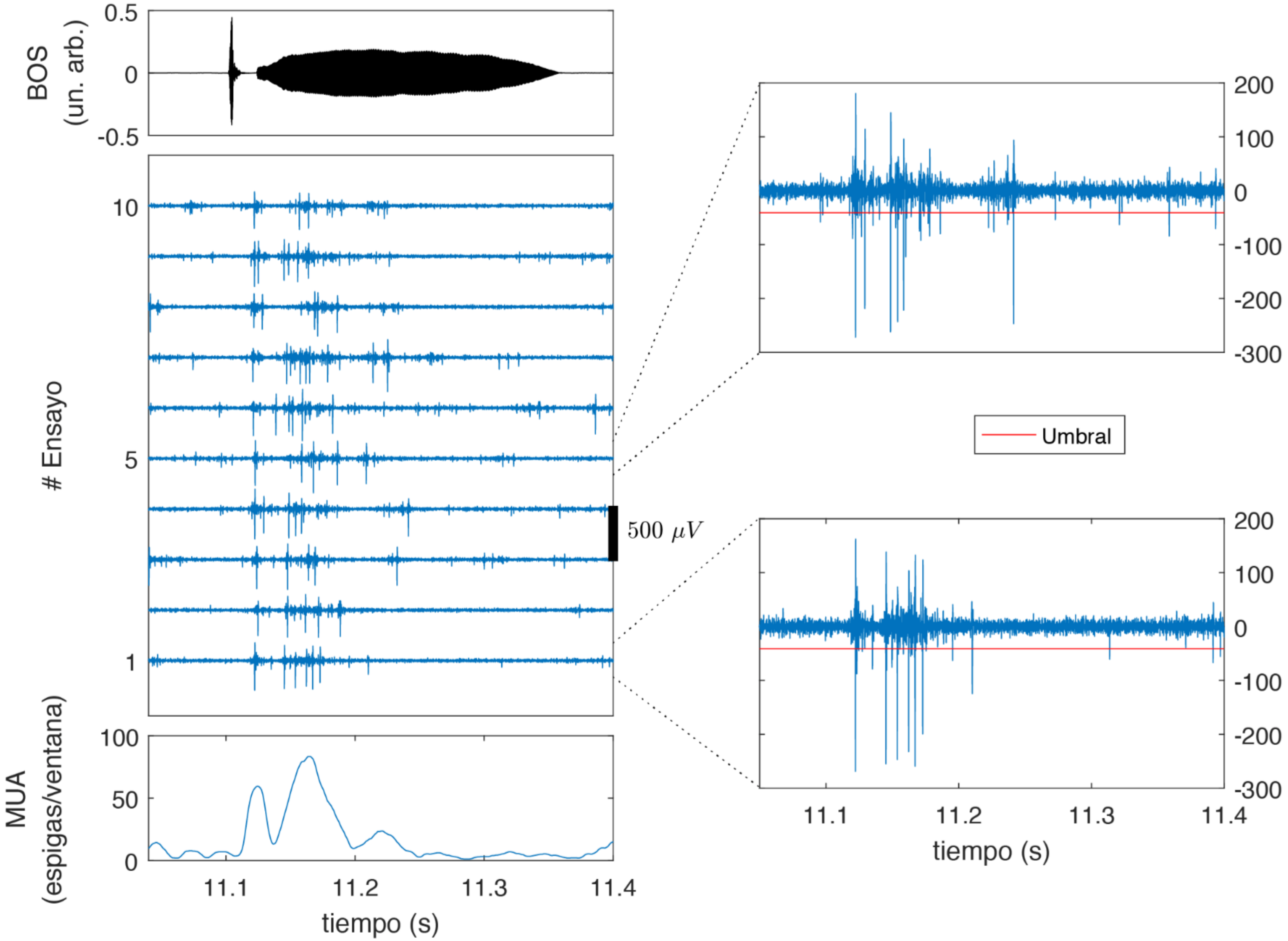


Spike sorting:
PCA analysis

Neural recordings

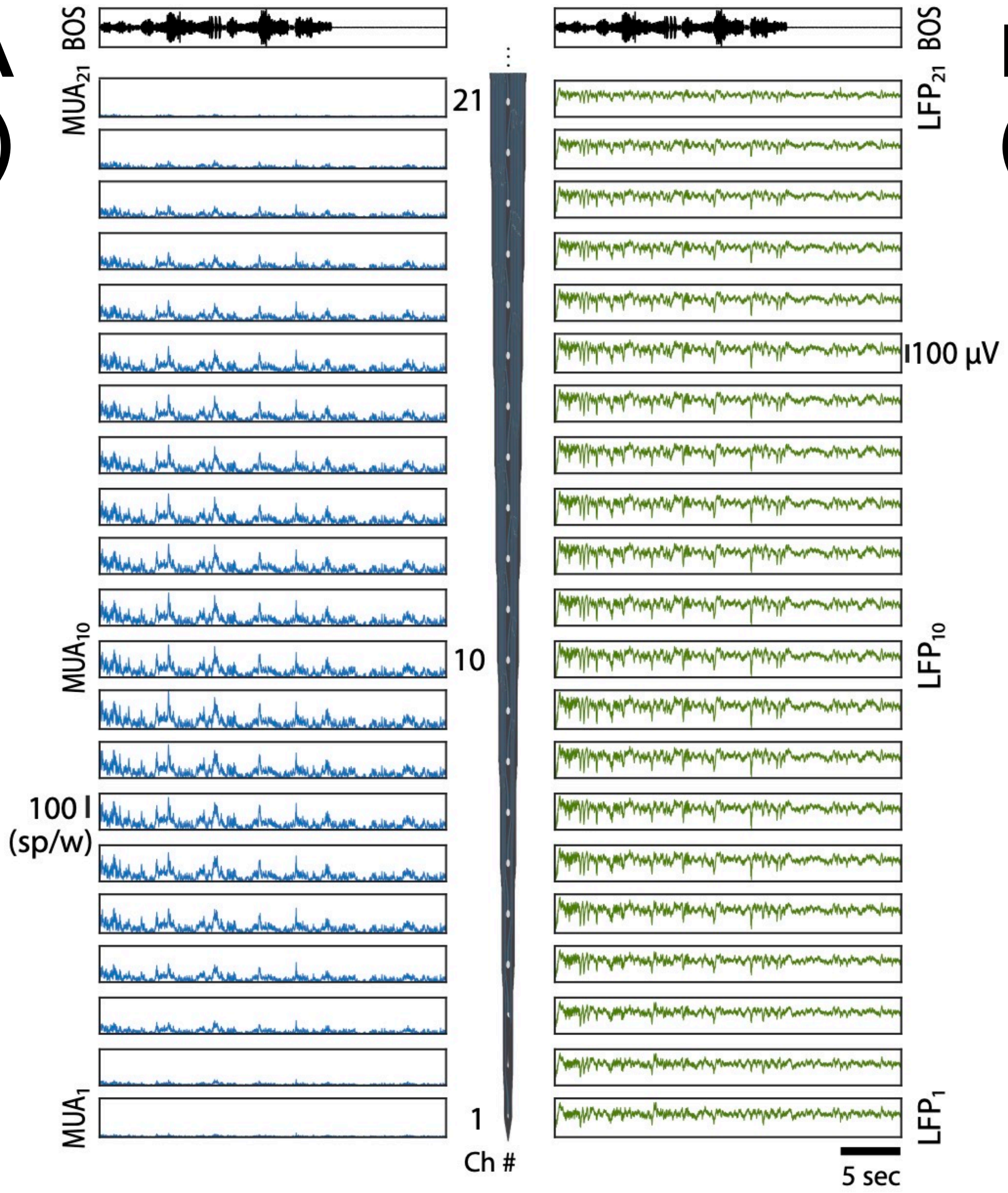
Neural activity in response to the Bird´s Own Song (BOS)

Multi-unit activity



Neural recordings: LFP and MUA

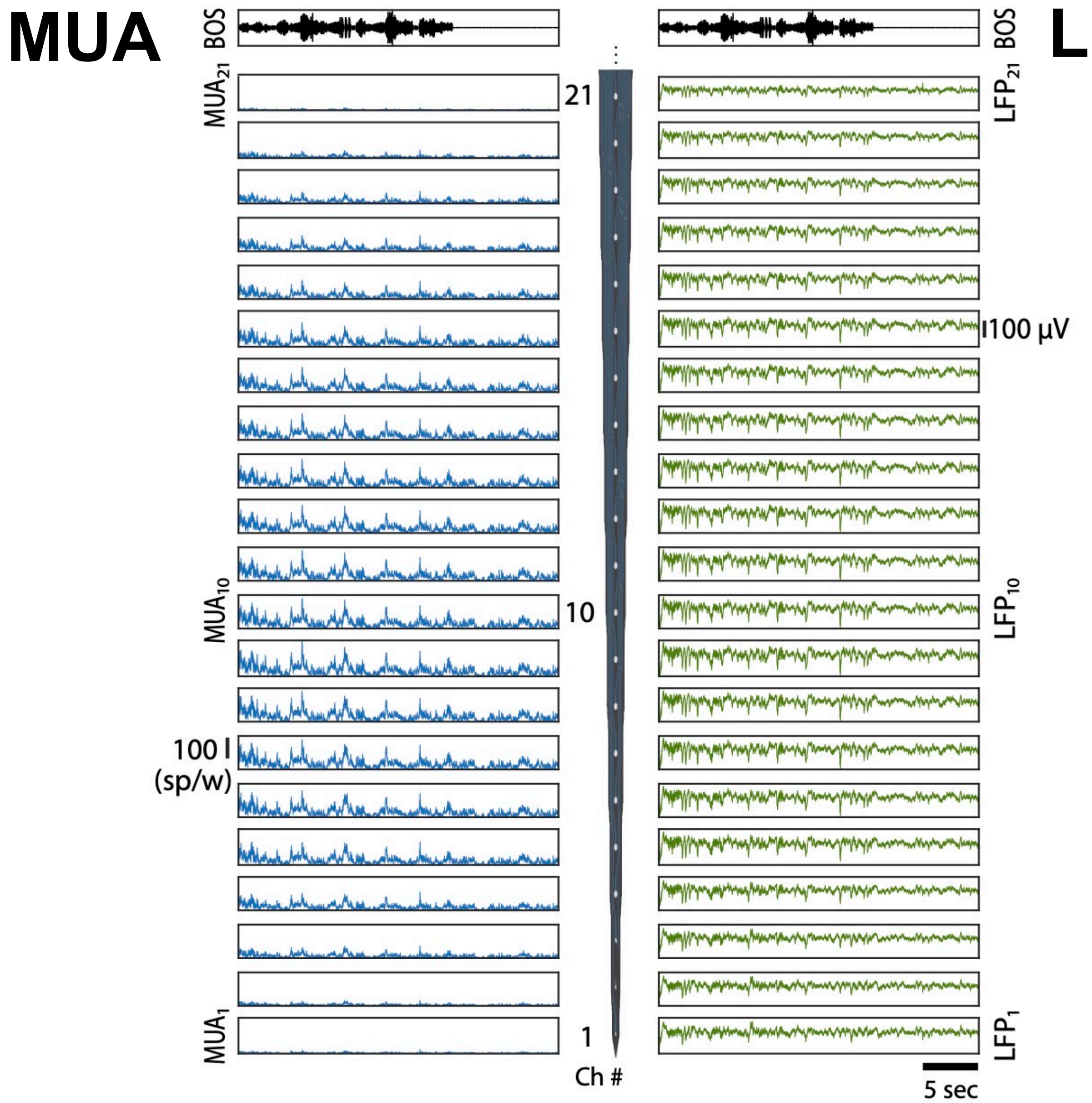
MUA
(Multi-Unit Activity)



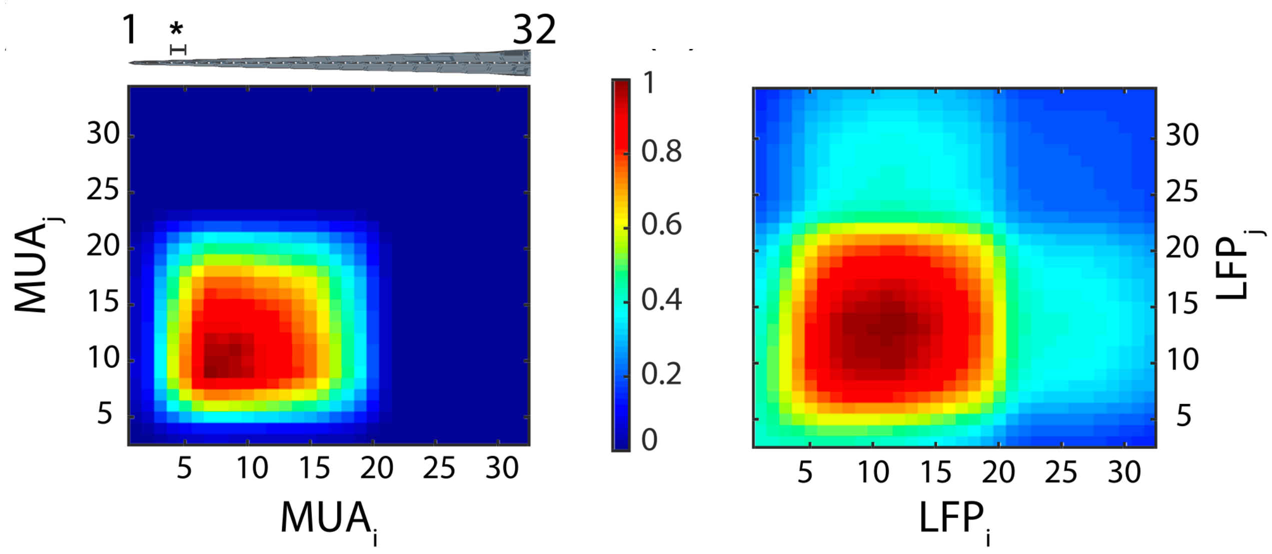
LFP
(Local Field Potential)

Boari, Mindlin and Amador, EJN 2021

Neural recordings: LFP and MUA

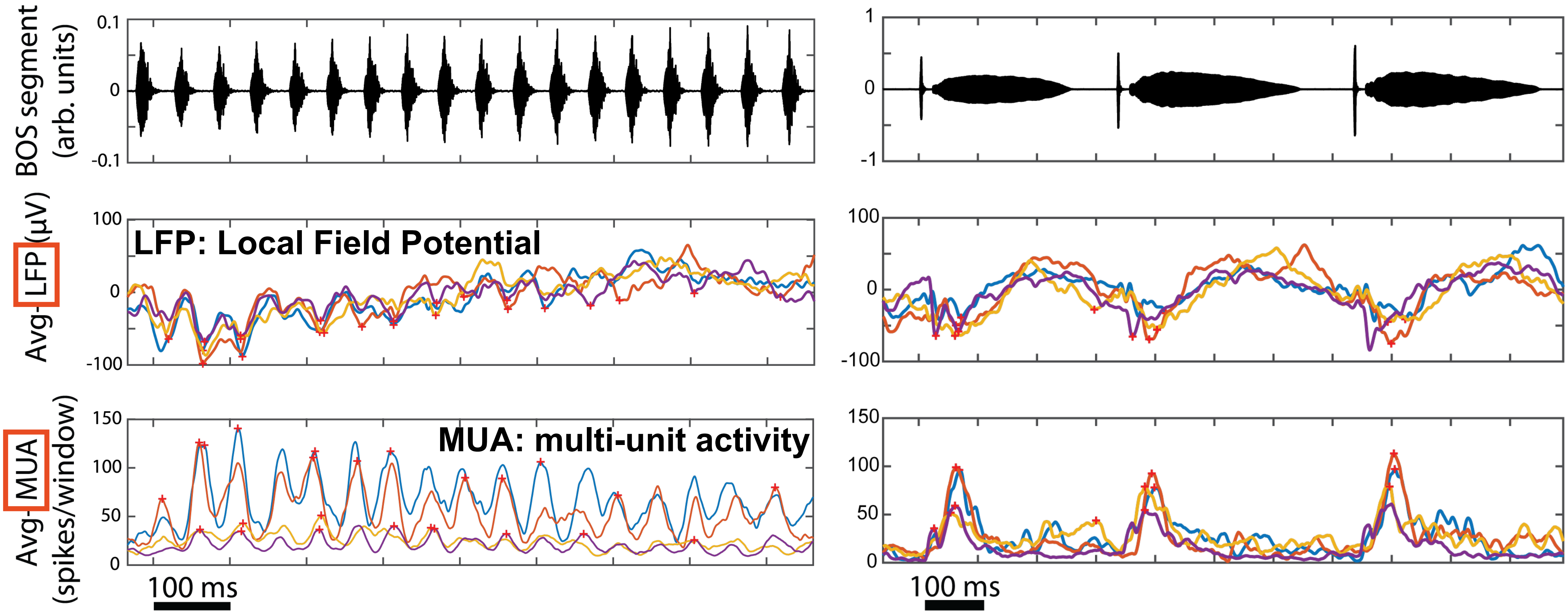


Spatial correlation
(amplitude weigthed)



Boari, Mindlin and Amador, EJN 2021

Neural recordings: LFP and MUA



Rhythms in the Brain?

Rhythms in the Brain

Speech perception exhibits rhythmicity

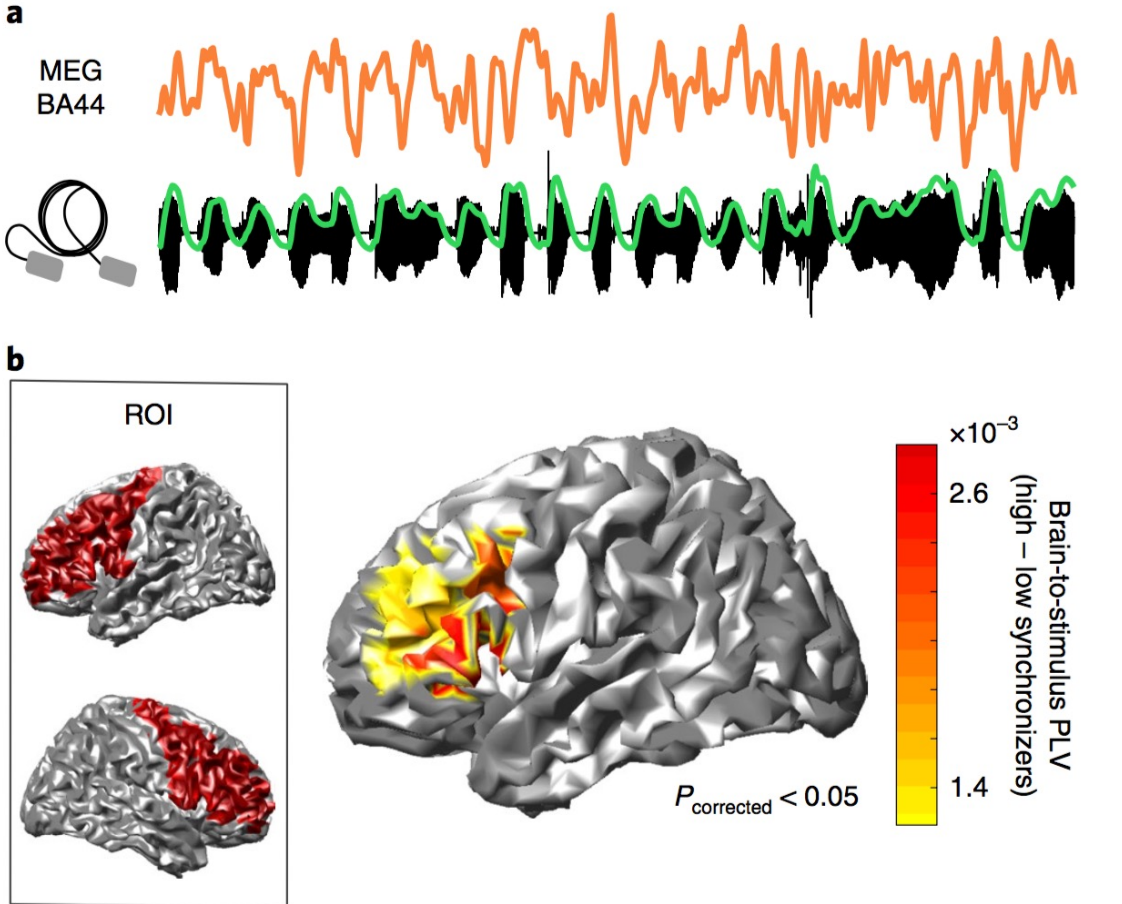
When presented with an
acoustic stimulus
(speech or modulated white noise) the auditory cortex tracks the amplitude modulation
of the input.

The speech rhythm enhances perception

nature neuroscience
ARTICLES
https://doi.org/10.1038/s41593-019-0353-z

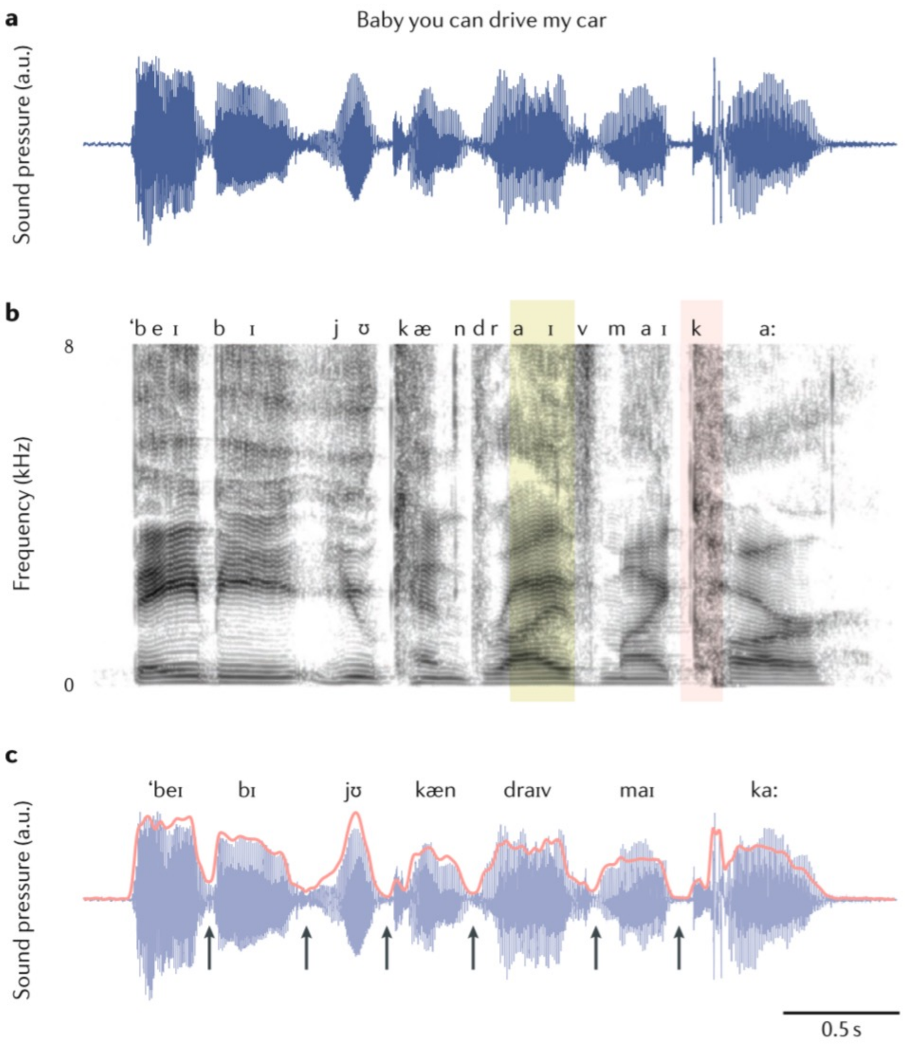
Spontaneous synchronization to speech reveals neural mechanisms facilitating language learning

M. Florencia Assaneo[1,7]*, Pablo Ripollés[1,7], Joan Orpella[2,3,4,7], Wy Ming Lin[1], Ruth de Diego-Balaguer[2,3,4,5,8] and David Poeppel[1,6,8]

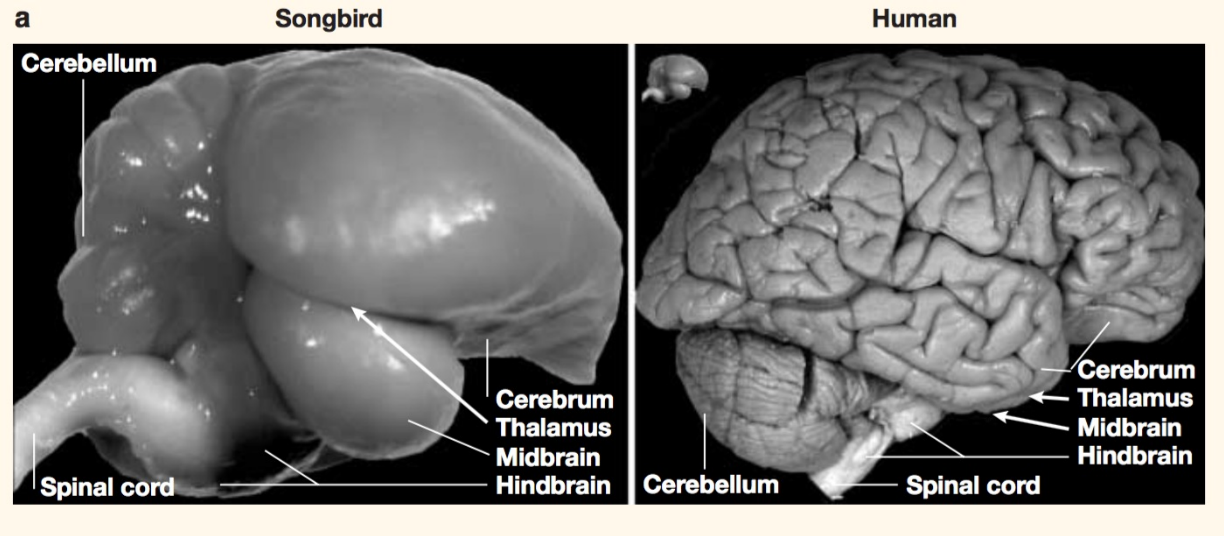


Rhythms in the Speech

Speech production exhibits rhythmicity



Rhythms in the Brain of a Songbird?



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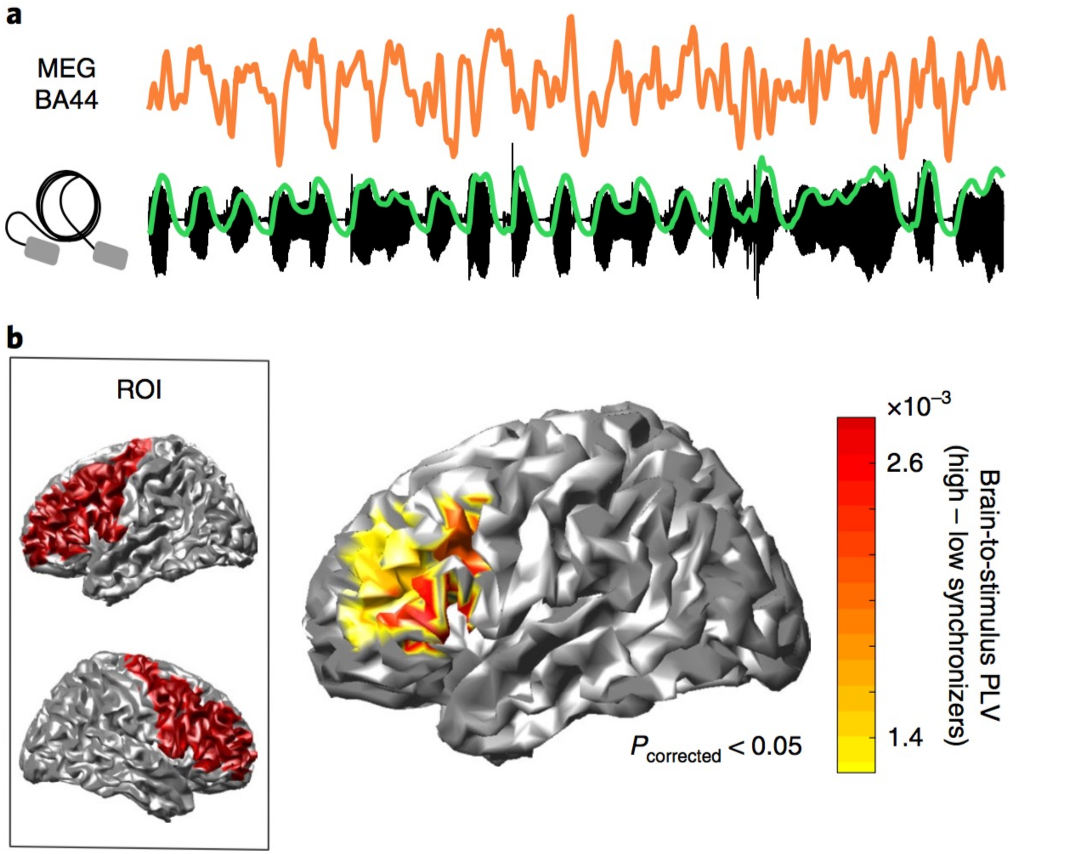

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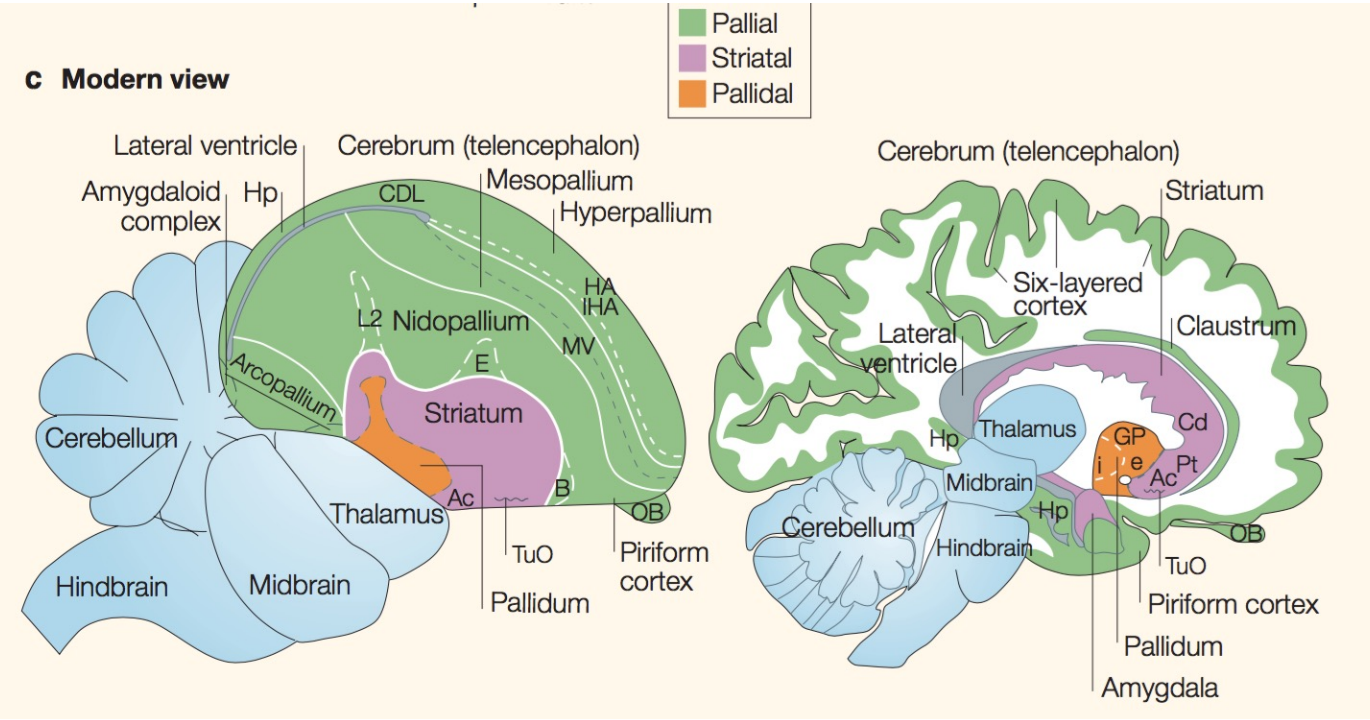

Similar structures mean similar properties?

nature neuroscience
ARTICLES
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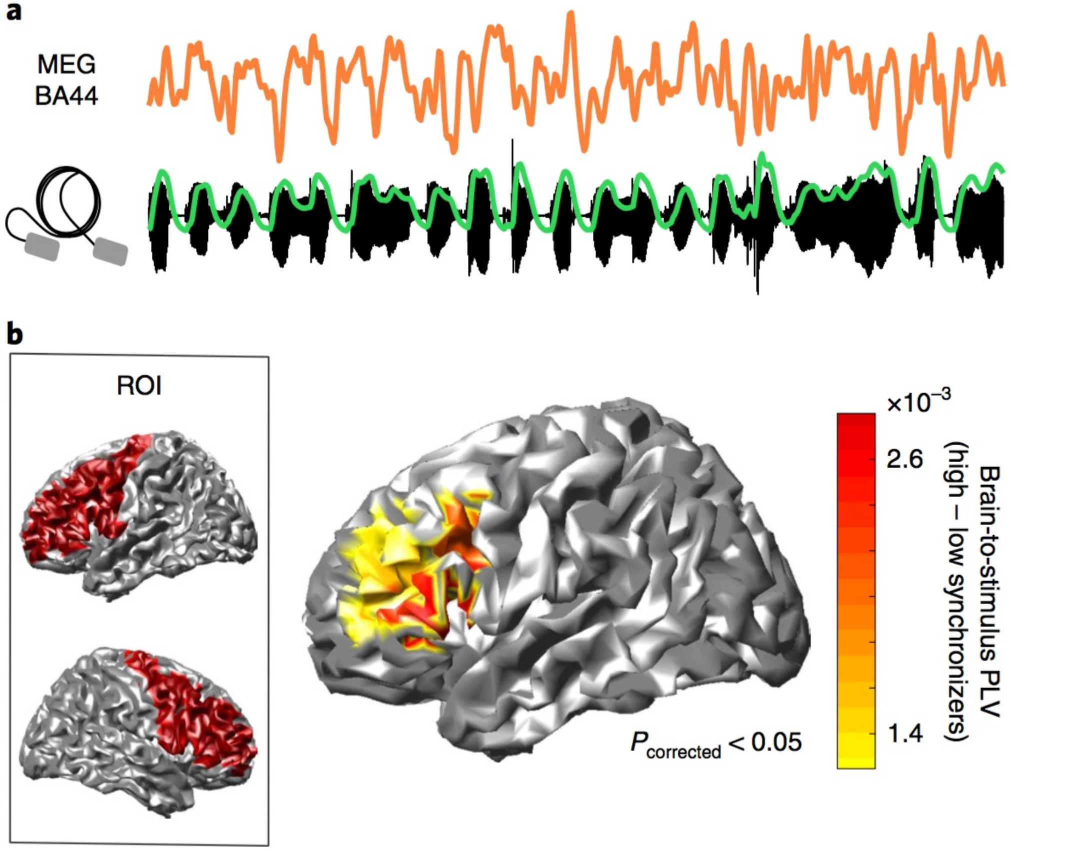
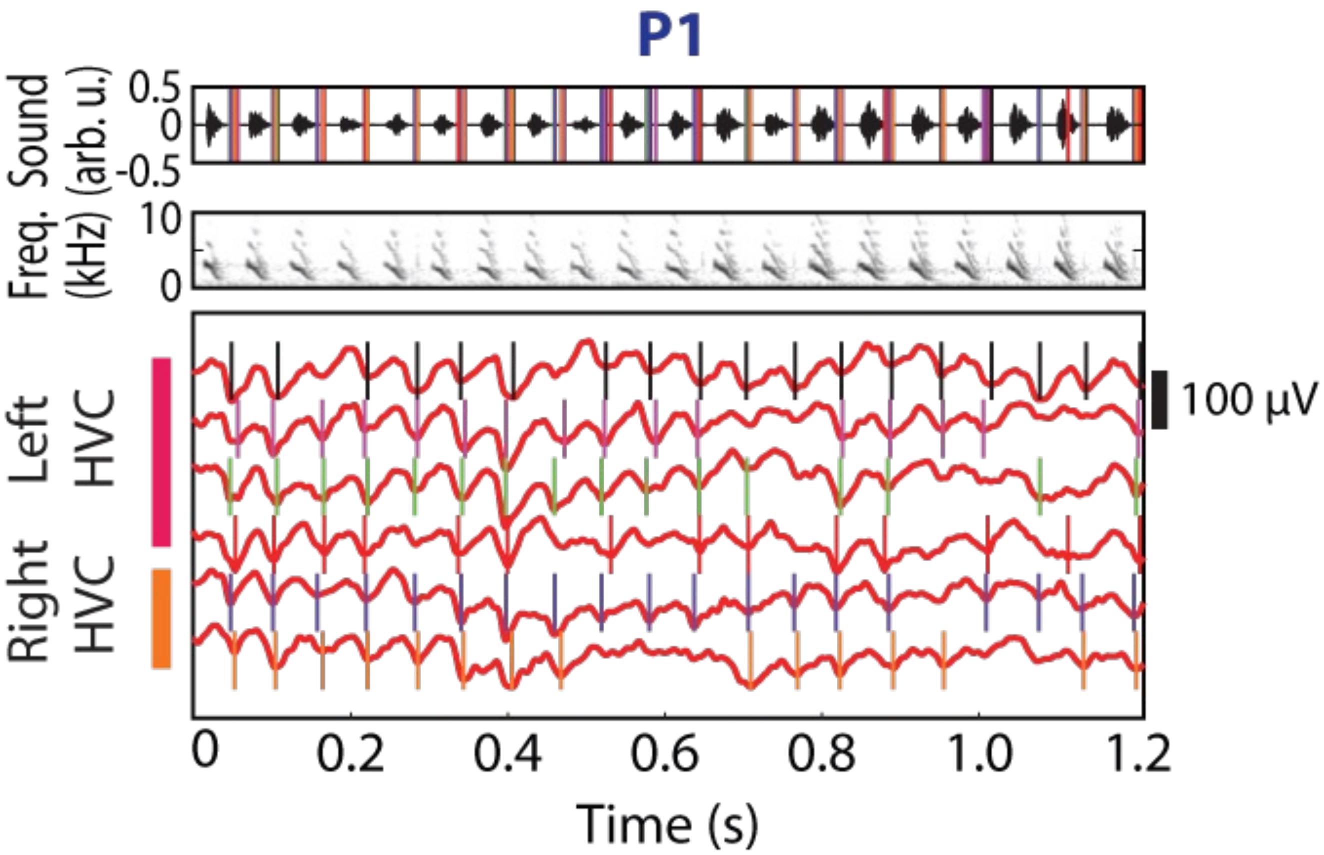


Rhythms in the Brain of a Songbird !



LFP oscillations are phase-locked (synchronization)

nature neuroscience

ARTICLES

https://doi.org/10.1038/s41593-019-0353-z

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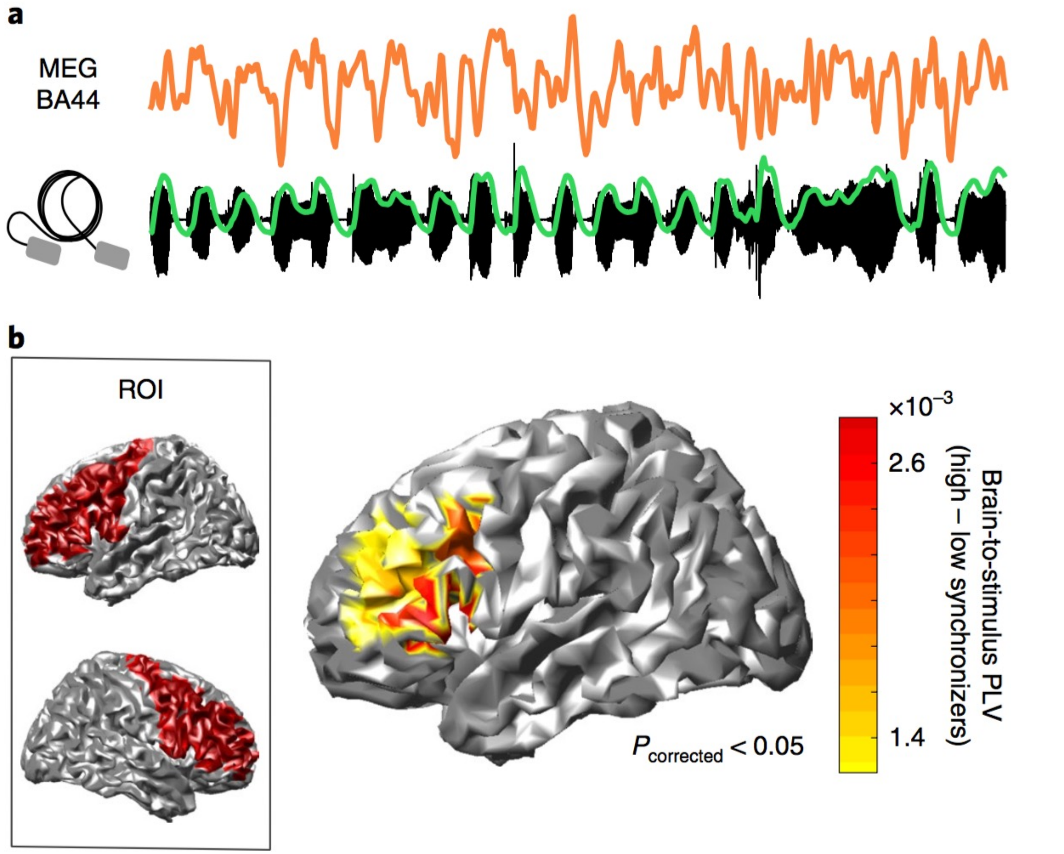
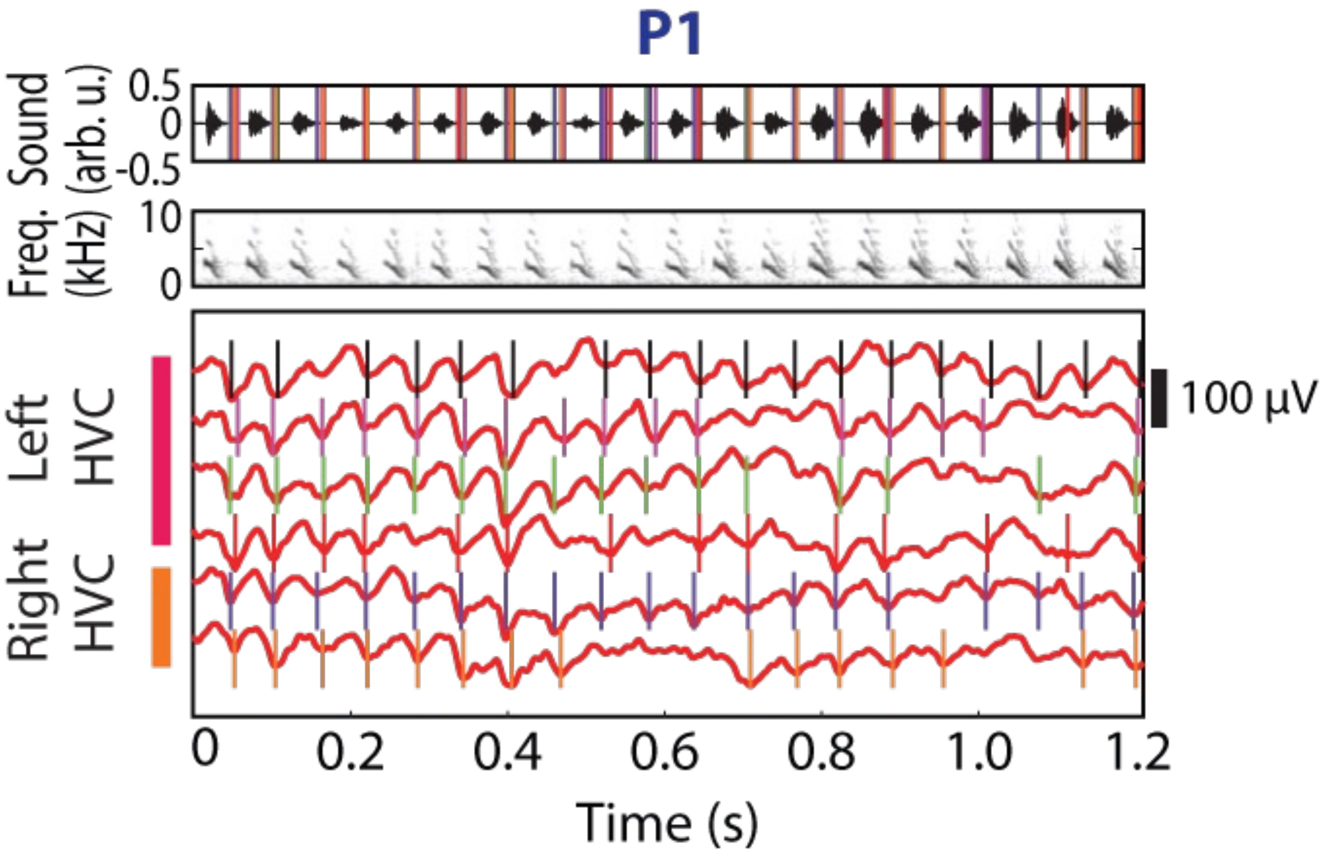
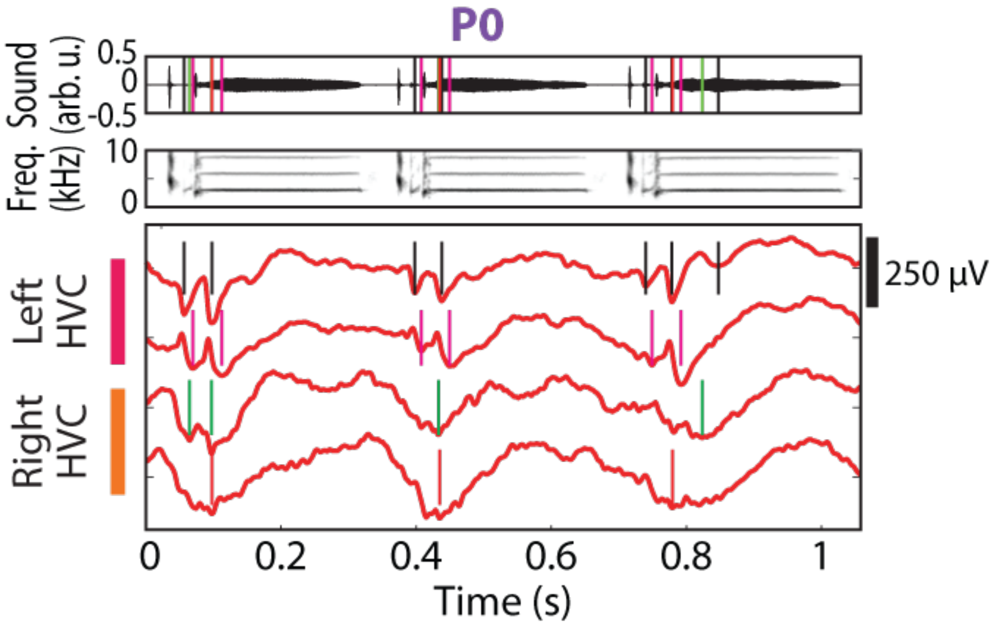
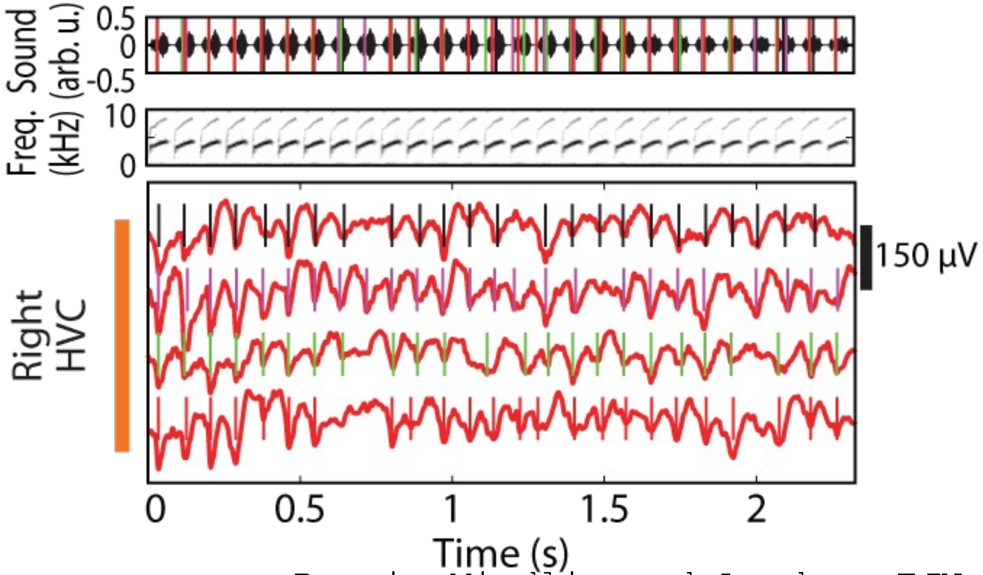


Rhythms in the Brain of a Songbird !



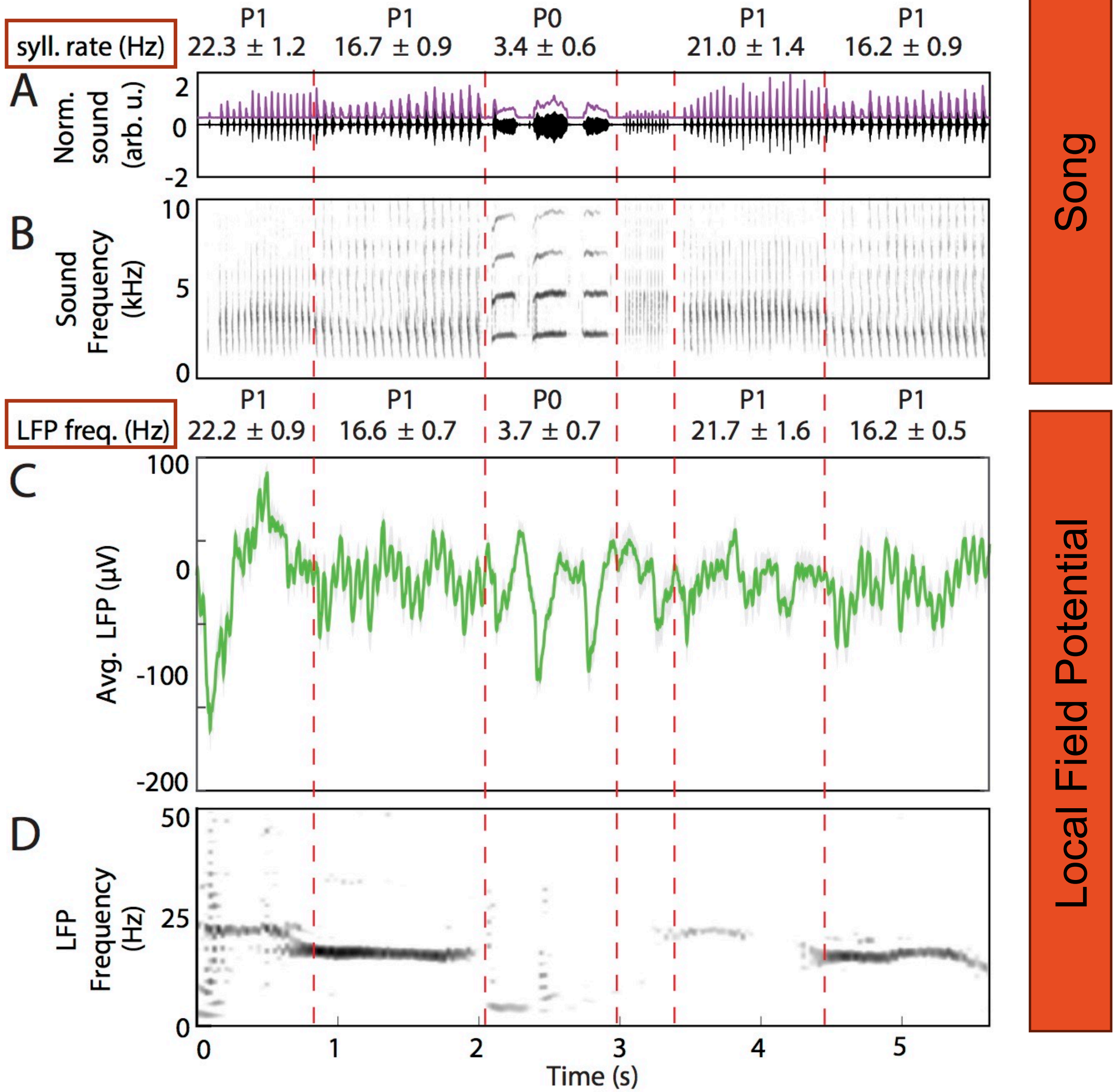




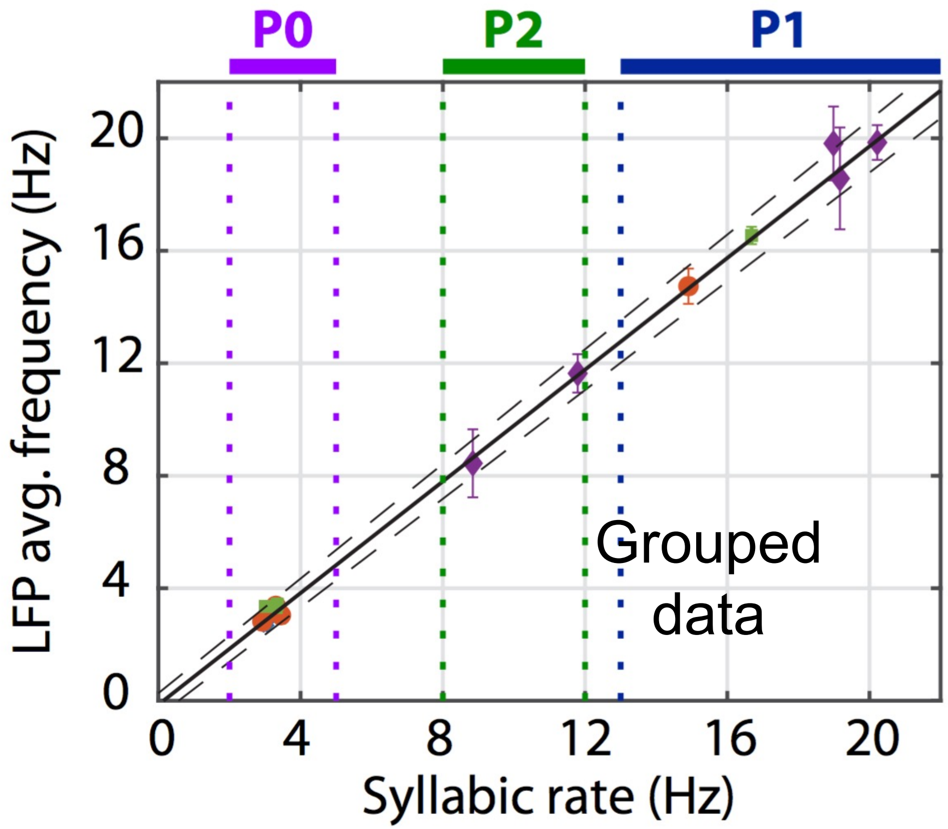
LFP oscillations are phase-locked (synchronization)

Boari, Mindlin and Amador, EJN 2021

LFP and coding of behavior (birdsong)



LFP oscillations occur at the song syllabic rate



$$LFP_{freq} = a + b\, s_r$$

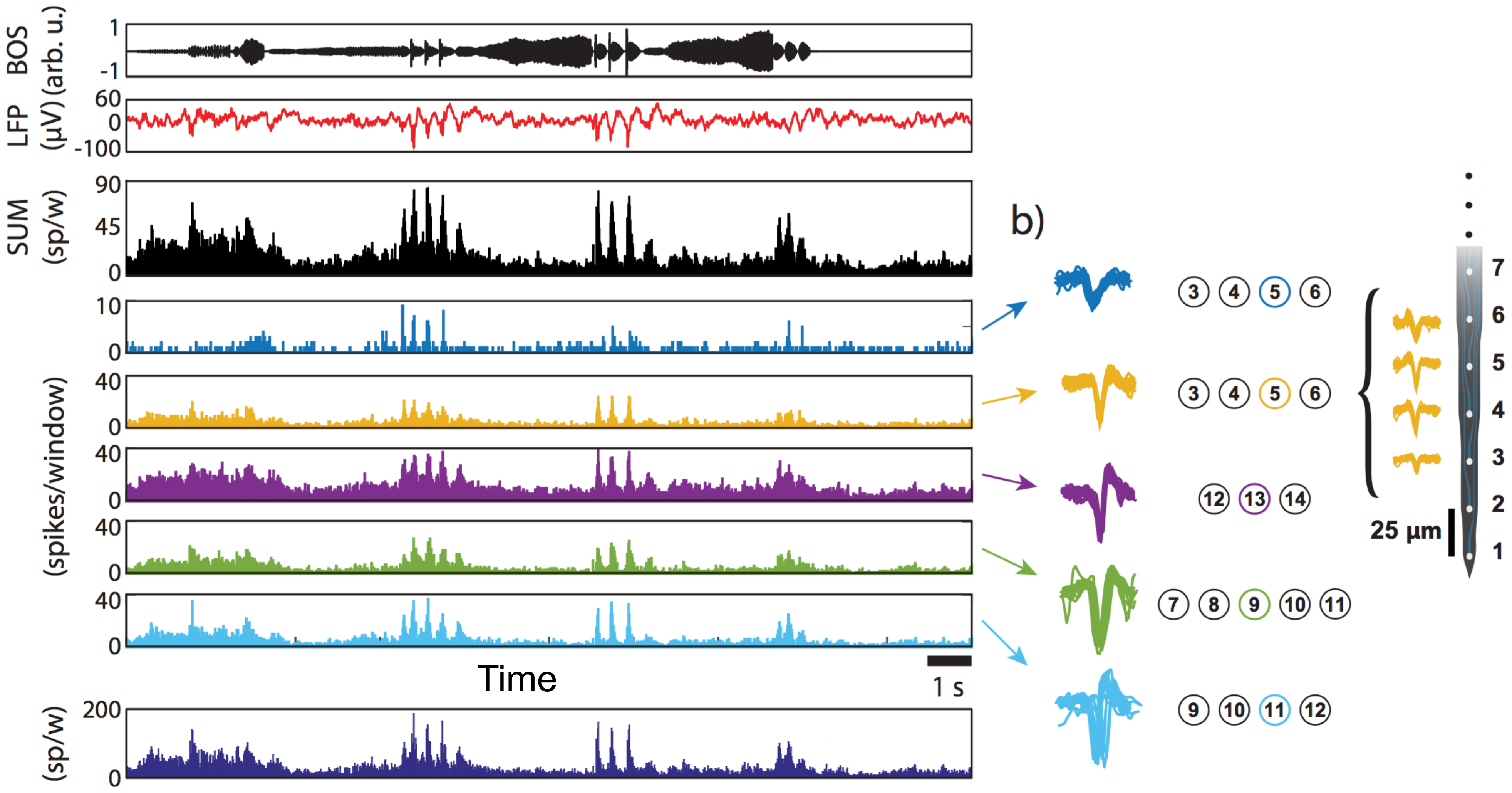
$a = -0.2 \pm 0.4\ Hz$

$b = 0.99 \pm 0.03$

Boari, Mindlin and Amador, EJN 2021

LFP vs. MUA vs. SUA

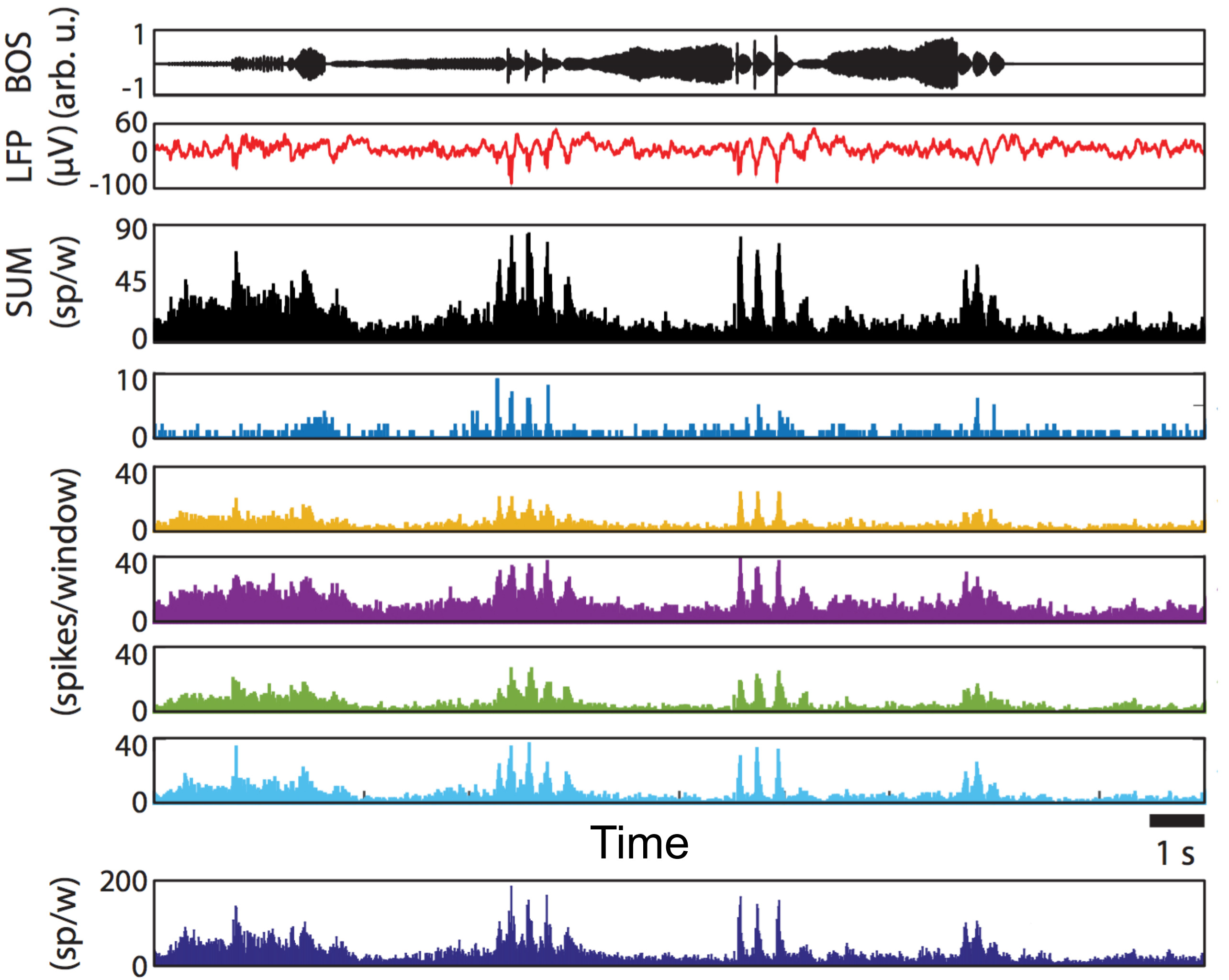
Extracellular recordings in canaries while hearing song (BOS)

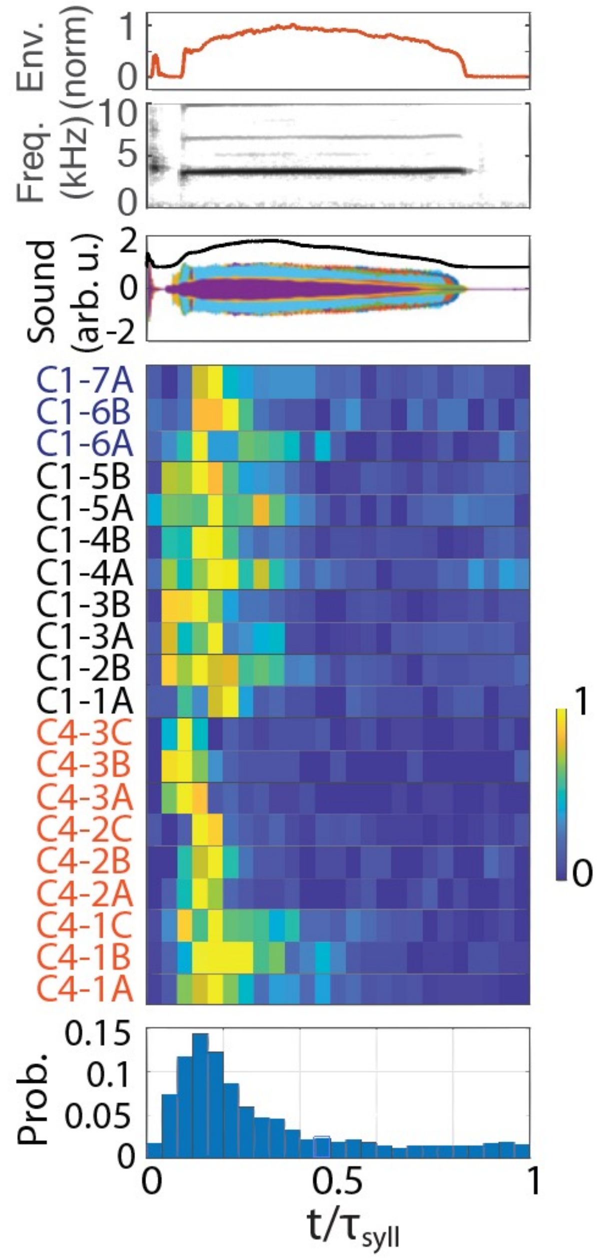


Color PSTHs below correspond to each colored cluster to the right.
Black PSTH represents the summed activity coming from
single units isolated in each protocol.

LFP vs. MUA vs. SUA

Extracellular recordings in canaries while hearing song (BOS)





Color PSTHs below correspond to each colored cluster to the right.
Black PSTH represents the summed activity coming from **single units** isolated in each protocol.

Gracias por su atención!

Collaborators

- Gabriel B. Mindlin (UBA, CONICET)
- Daniel Margoliash (Univ. of Chicago)

PhD Students

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