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Replay of cortical spiking sequences during human memory retrieval

Alex P. Vaz, John H. Wittig Jr., Sara K. Inati, Kareem A. Zaghloul

Presented by YM Zhu
04/04/2020

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- MIT, BS,1995
- UPenn, MD/PhD, 2003; Residency in Neurological Surgery & Postdoc, 2010
- NINDS, Staff Clinician, 2010; Investigator, 2013
- PhD: developing silicon models of visual processing in the mammalian retina, Dr. Kwabena Boahen @ Stanford
- Postdoc: neural correlates of human memory encoding, decision, and reward, w/ Dr. Michael Kahanas @ UPenn
- Clinical fellowship: Epilepsy Surgery and in DBS Surgery
- Research interest: neural mechanisms underlying human cognitive function
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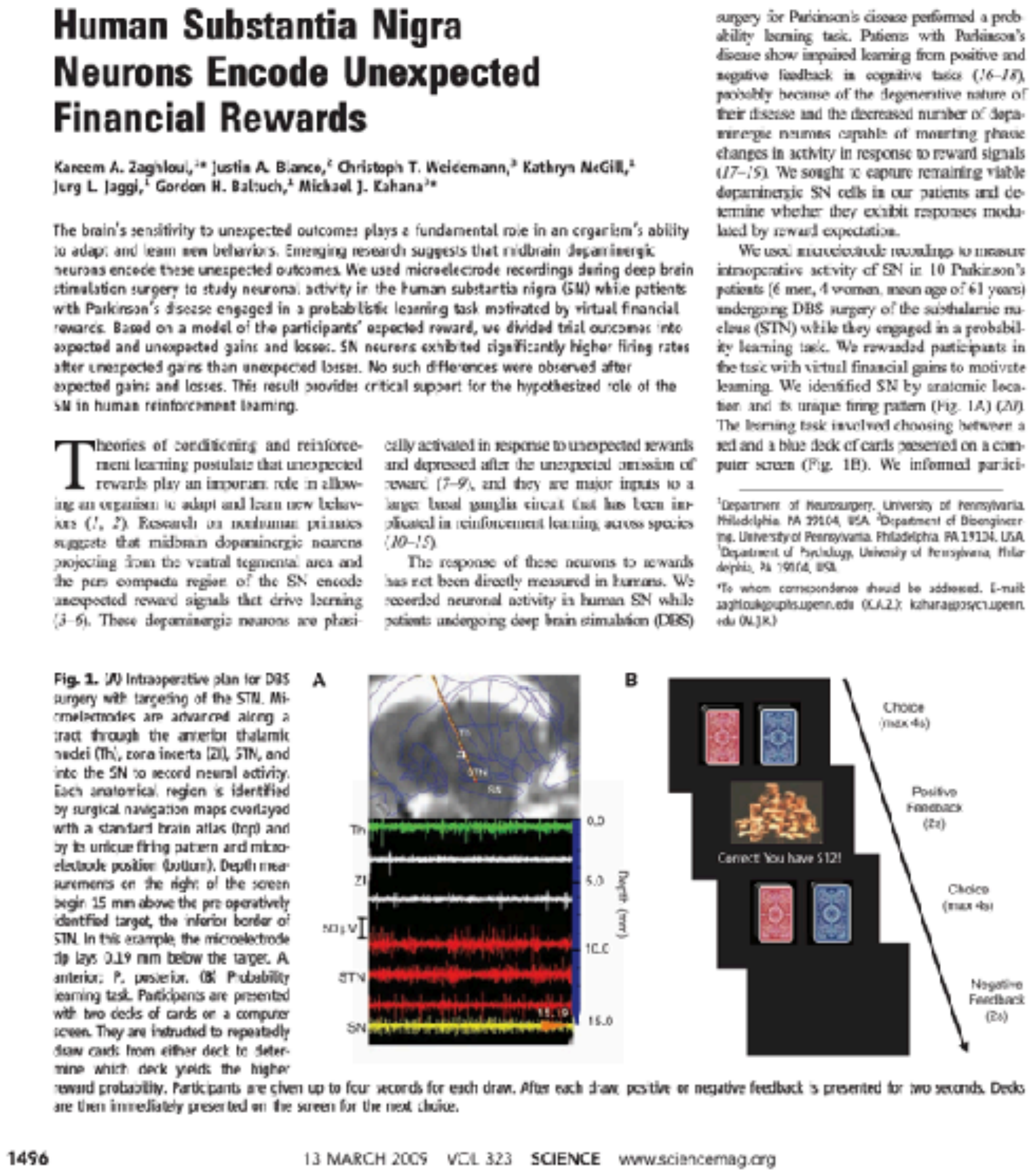

Human Substantia Nigra Neurons Encode Unexpected Financial Rewards

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The brain's sensitivity to unexpected outcomes plays a fundamental role in an organism's ability to adapt and learn new behaviors. Emerging research suggests that midbrain dopaminergic neurons encode these unexpected outcomes. We used microelectrode recordings during deep brain stimulation surgery to study neuronal activity in the human substantia nigra (SN) while patients with Parkinson's disease engaged in a probabilistic learning task motivated by virtual financial rewards. Based on a model of the participants' expected reward, we divided trial outcomes into expected and unexpected gains and losses. SN neurons exhibited significantly higher firing rates after unexpected gains than unexpected losses. No such differences were observed after expected gains and losses. This result provides critical support for the hypothesized role of the SN in human reinforcement learning.

Theories of conditioning and reinforcement learning postulate that unexpected rewards play an important role in allowing an organism to adapt and learn new behaviors (1, 2). Research on nonhuman primates suggests that midbrain dopaminergic neurons projecting from the ventral tegmental area and the pars compacta region of the SN encode unexpected reward signals that drive learning (3–6). These dopaminergic neurons are phasically activated in response to unexpected rewards and depressed after the unexpected omission of reward (7–9), and they are major inputs to a larger basal ganglia circuit that has been implicated in reinforcement learning across species (10–15).

The response of these neurons to rewards has not been directly measured in humans. We recorded neuronal activity in human SN while patients undergoing deep brain stimulation (DBS) surgery for Parkinson's disease performed a probability learning task. Patients with Parkinson's disease show impaired learning from positive and negative feedback in cognitive tasks (16–18), probably because of the degenerative nature of their disease and the decreased number of dopaminergic neurons capable of mounting phasic changes in activity in response to reward signals (17–19). We sought to capture remaining viable dopaminergic SN cells in our patients and determine whether they exhibit responses modulated by reward expectation.

We used microelectrode recordings to measure intraoperative activity of SN in 10 Parkinson's patients (6 men, 4 women, mean age of 61 years) undergoing DBS surgery of the subthalamic nucleus (STN) while they engaged in a probability learning task. We rewarded participants in the task with virtual financial gains to motivate learning. We identified SN by anatomic location and its unique firing pattern (Fig. 1A) (20). The learning task involved choosing between a red and a blue deck of cards presented on a computer screen (Fig. 1B). We informed partici-

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A B
Th
ZI
STN
SN
0.0
5.0
10.0
15.0
Depth (mm)
Choice (max 4s)
Positive Feedback (2s)
Correct! You have $12!
Choice (max 4s)
Negative Feedback (2s)

Fig. 1. (A) Intraoperative plan for DBS surgery with targeting of the STN. Microelectrodes are advanced along a tract through the anterior thalamic nuclei (Th), zona incerta (ZI), STN, and into the SN to record neural activity. Each anatomical region is identified by surgical navigation maps overlayed with a standard brain atlas (top) and by its unique firing pattern and microelectrode position (bottom). Depth measurements on the right of the screen begin 15 mm above the pre operatively identified target, the inferior border of STN. In this example, the microelectrode tip lays 0.19 mm below the target. A, anterior; P, posterior. (B) Probability learning task. Participants are presented with two decks of cards on a computer screen. They are instructed to repeatedly draw cards from either deck to determine which deck yields the higher reward probability. Participants are given up to four seconds for each draw. After each draw, positive or negative feedback is presented for two seconds. Decks are then immediately presented on the screen for the next choice.

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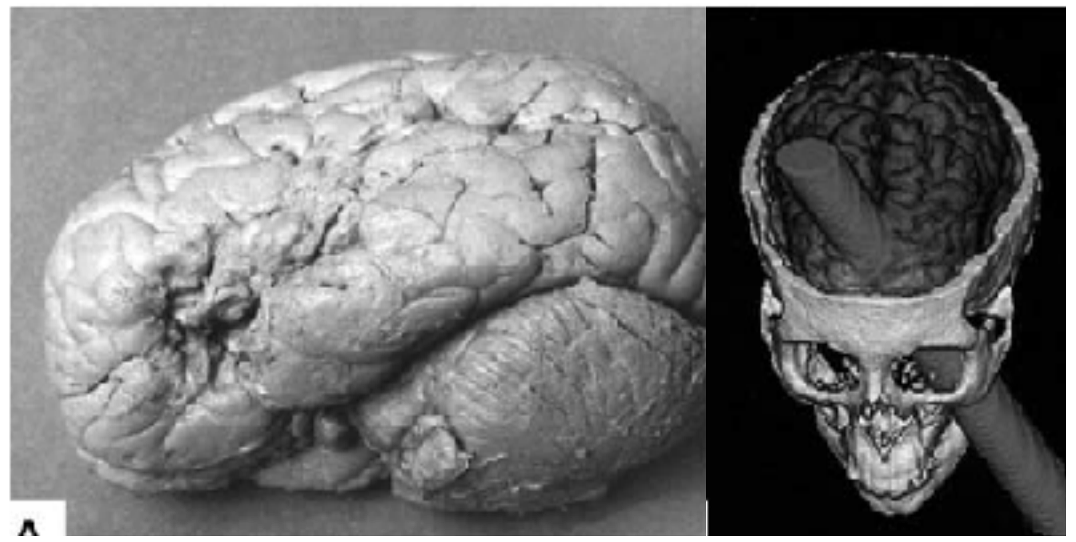
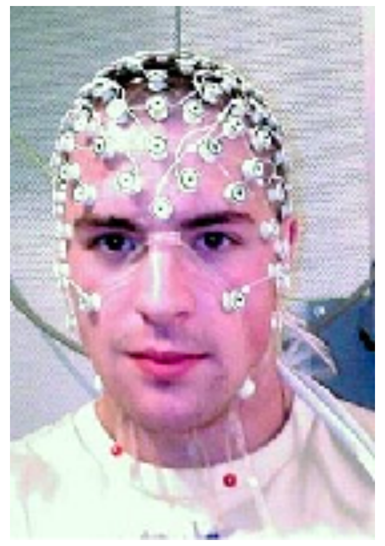
Methods studying human brain function

Lesion

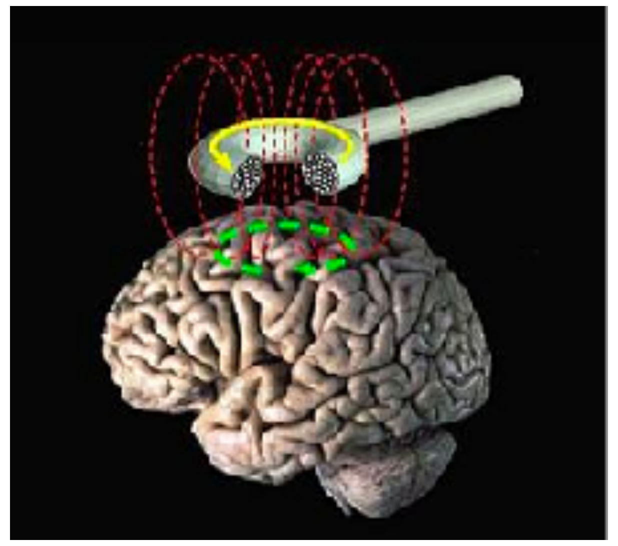


Electroencephalography (EEG)

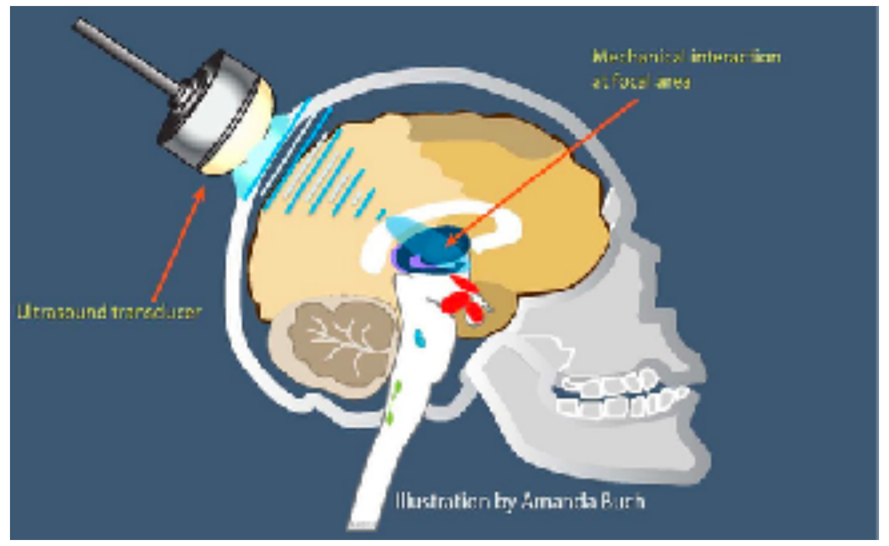


Magnetoencephalography (MEG)

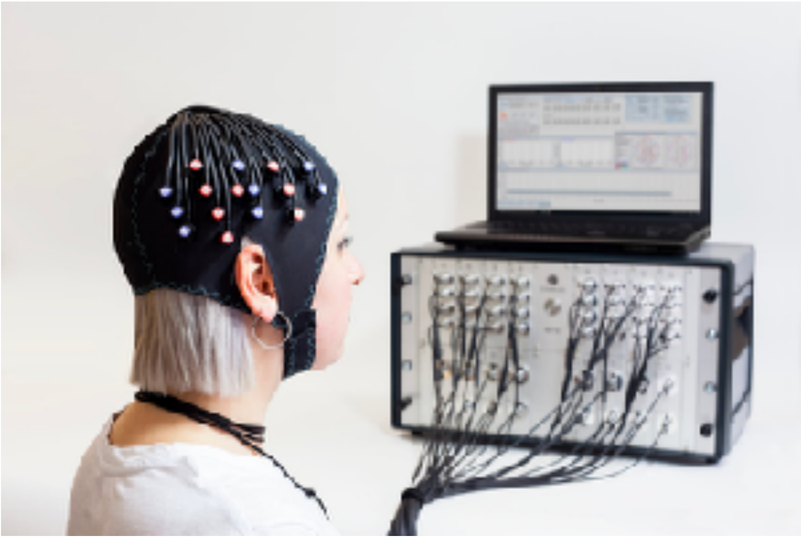
Transcranial magnetic stimulation (TMS)



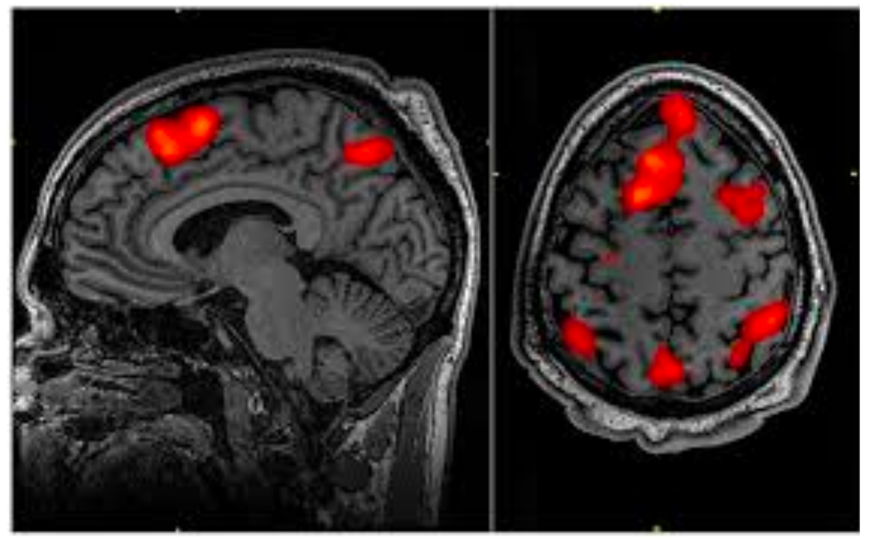
Transcranial focused ultrasound (tFUS)



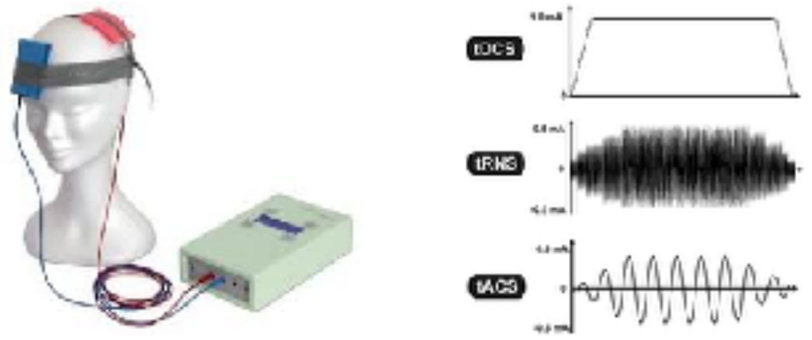
Functional near-infrared spectroscopy (fNIRS)



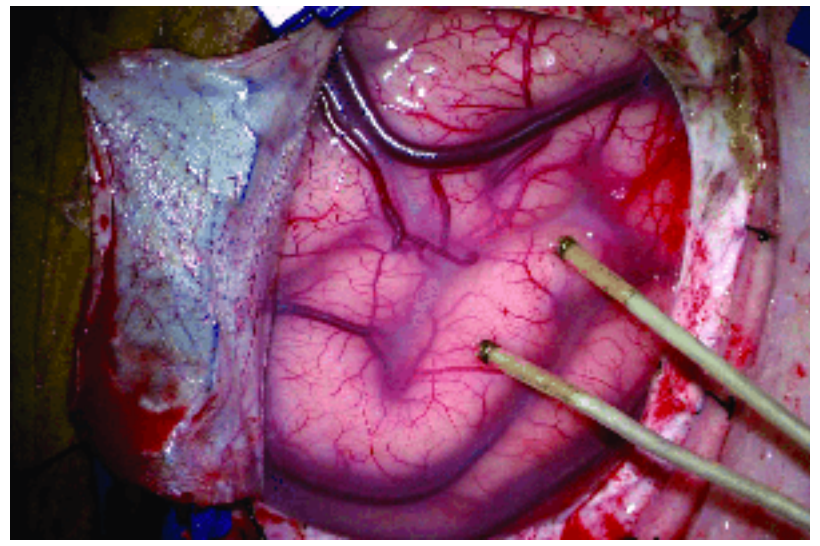
Functional magnetic resonance imaging (fMRI)



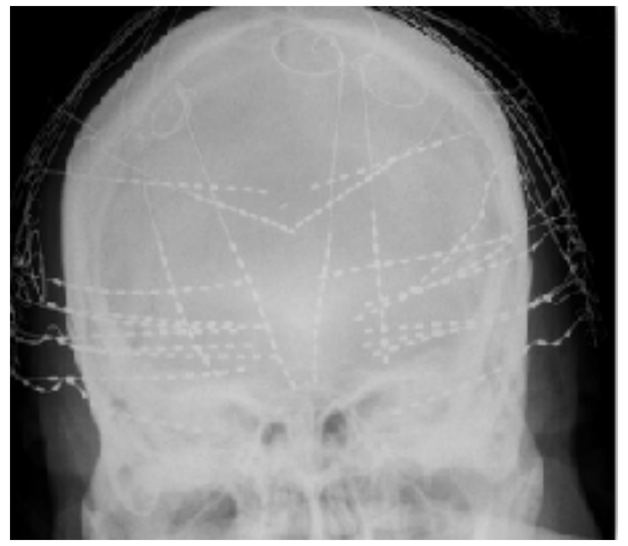
Transcranial alternating current stimulation (tACS)
Transcranial direct-current stimulation (tDCS)
Transcranial random noise stimulation (tRNS)
Transcranial pulsed current stimulation (tPCS)



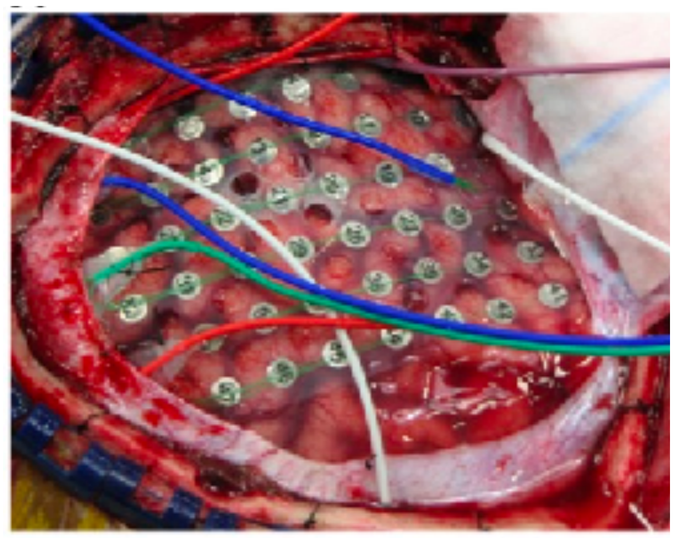
Direct cortical stimulation (DCS)



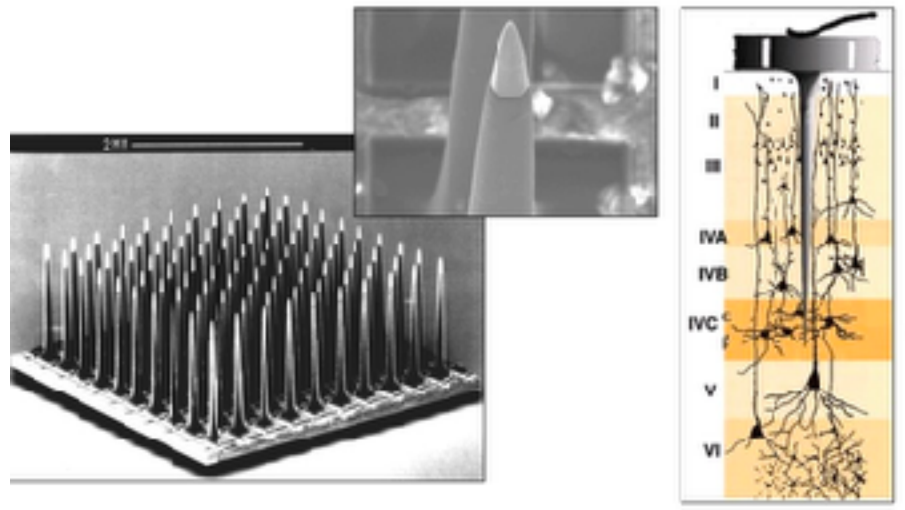
Stereo-EEG



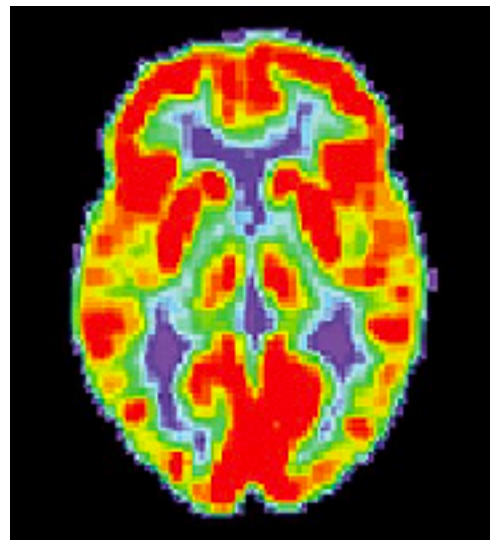
Electrocorticography (ECoG)



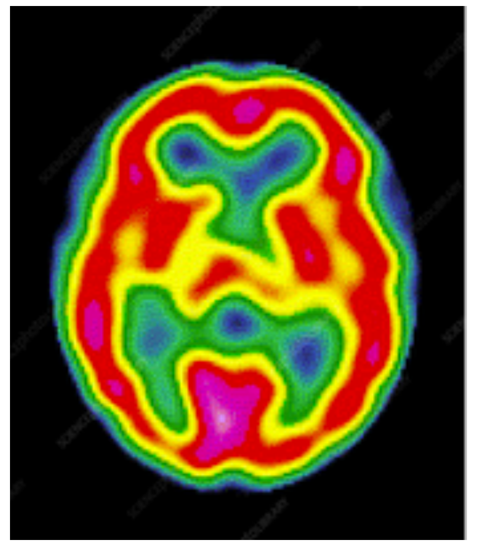
Utah array



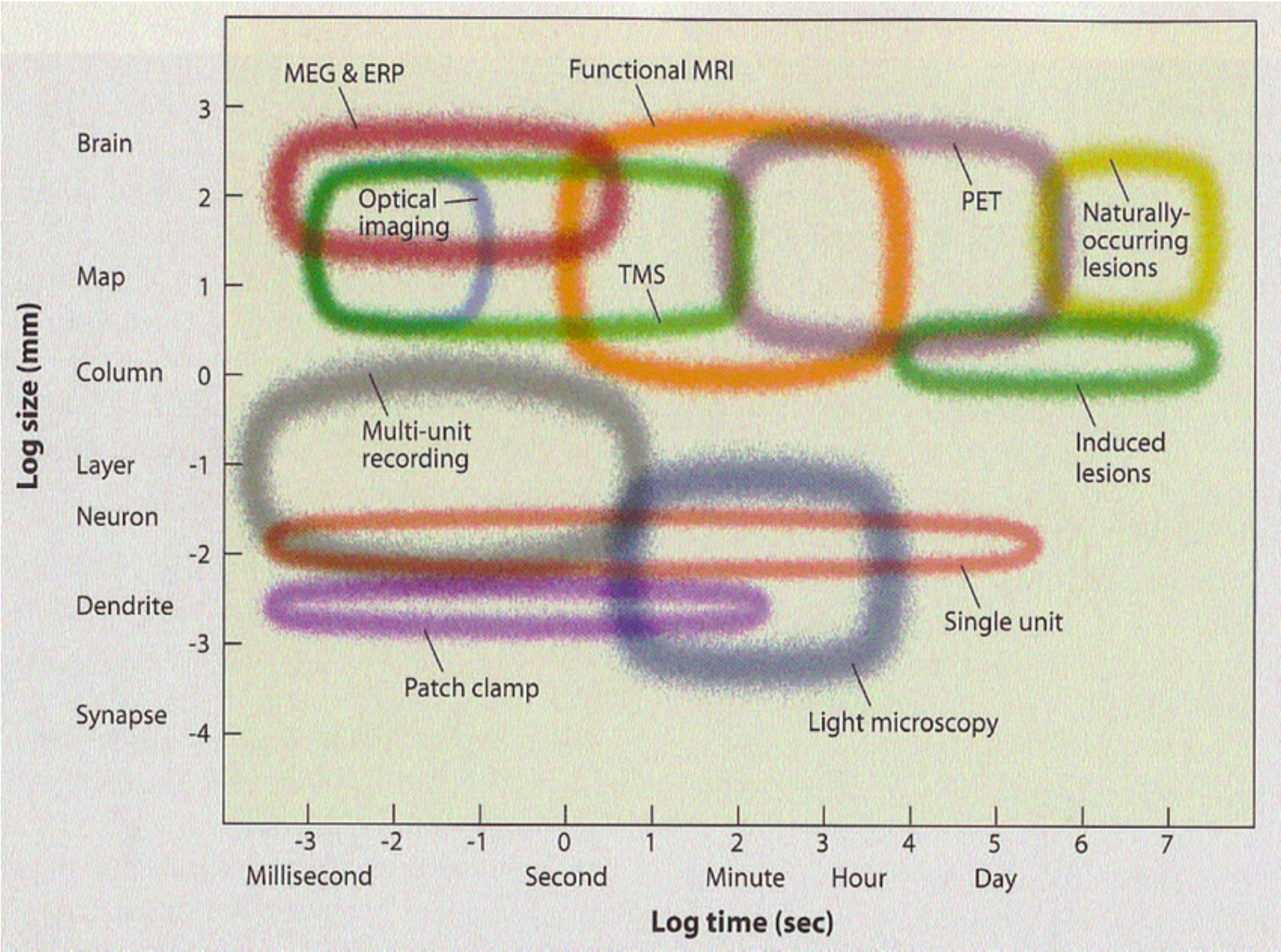
Positron emission tomography (PET)



Single-photon emission computed tomography (SPECT)

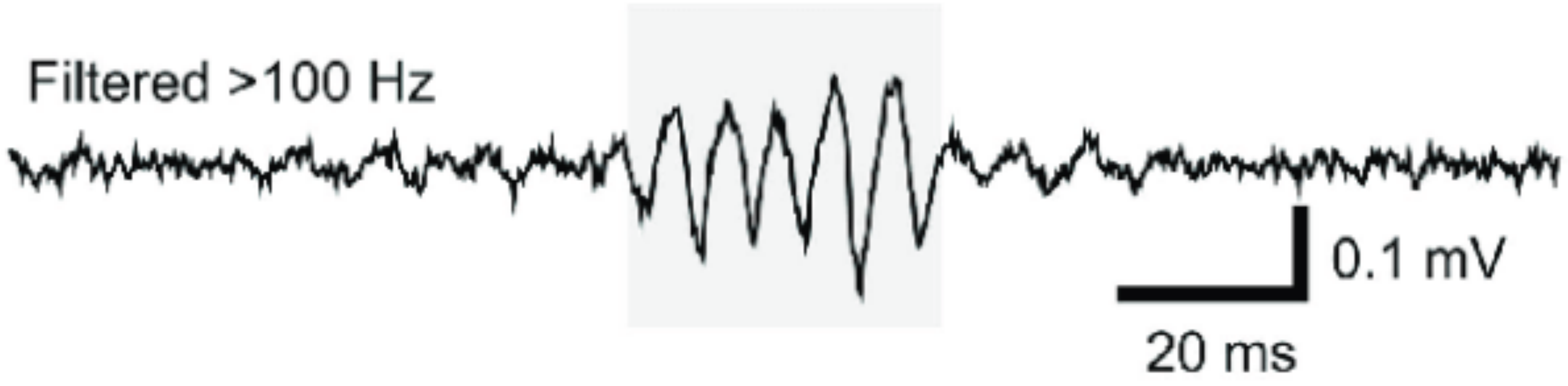


Comparison between methods

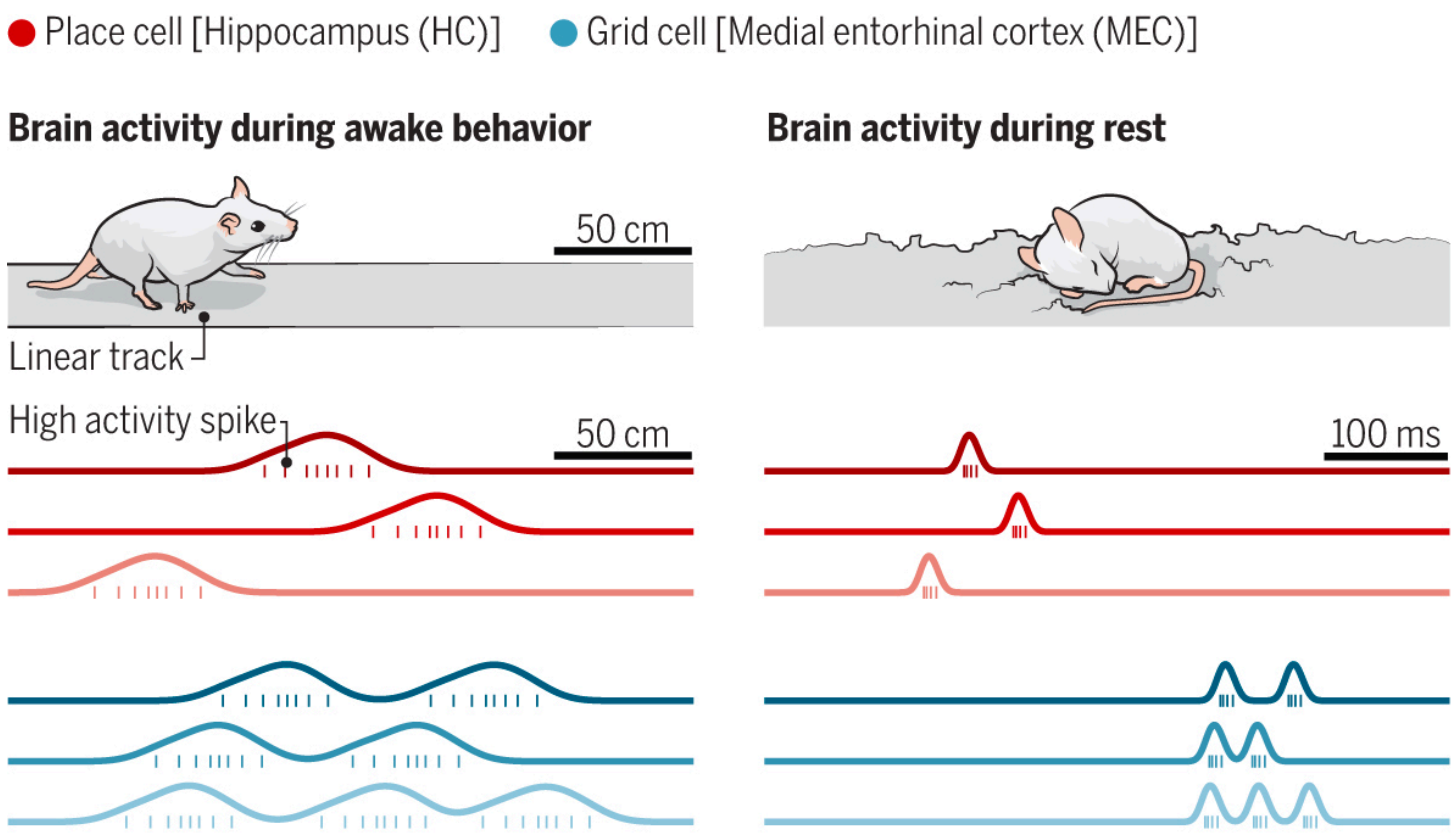


Background - ripple

- First found in hippocampus
- Large amplitude sharp waves in local field potential and associated fast field oscillations
- Involved in memory consolidation and the replay of wakefulness-acquired memory



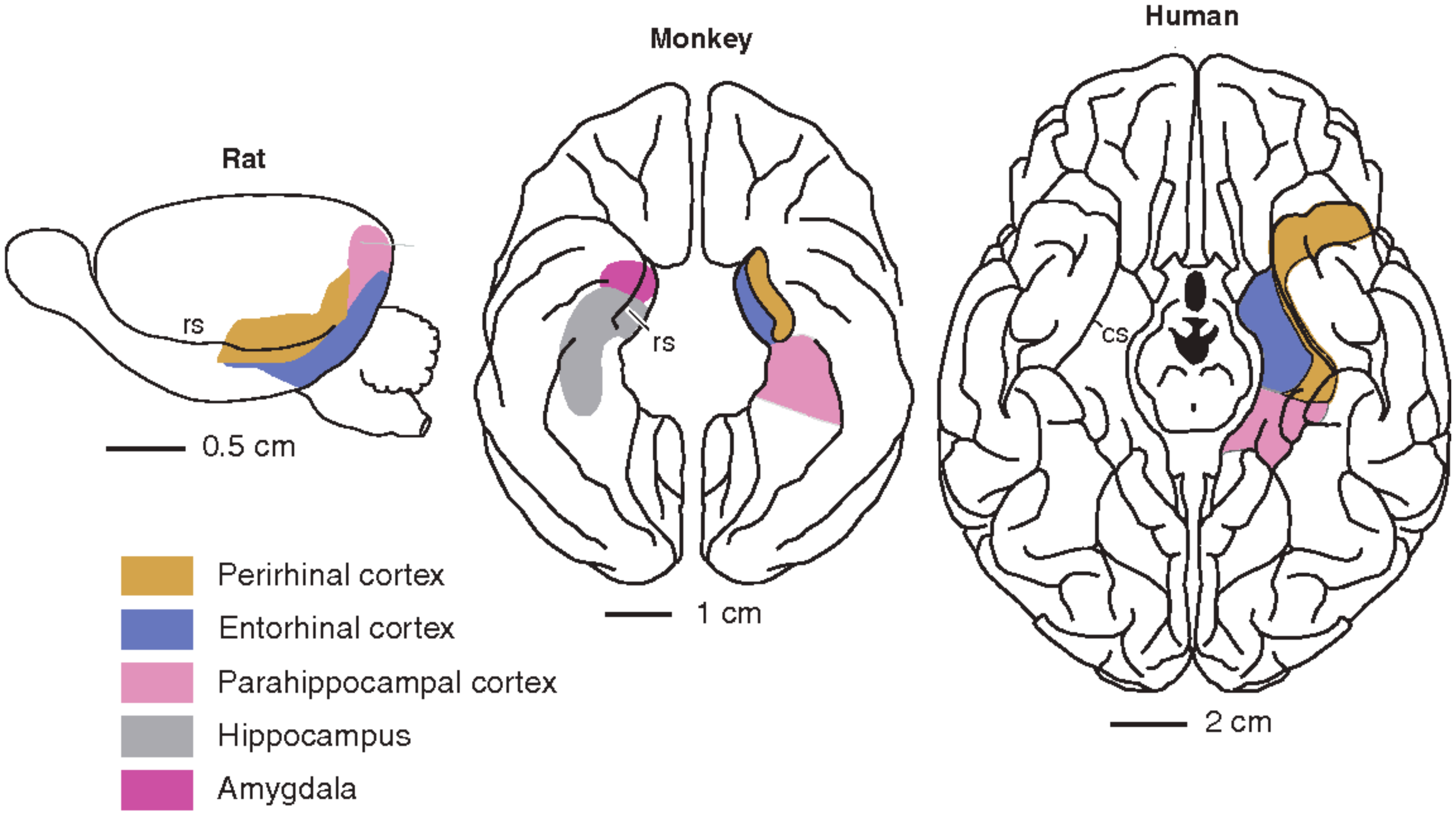
Background - rodents spatial memory



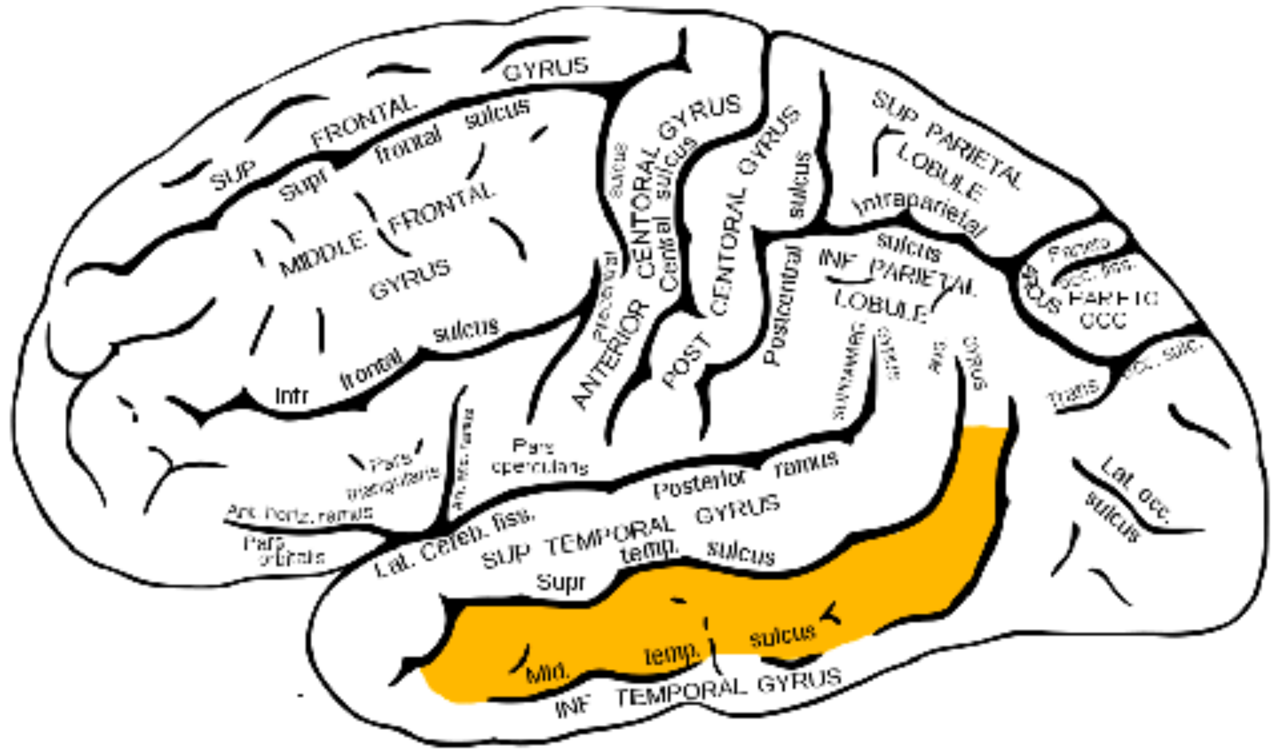
Background - anatomy

Medial temporal lobe (MTL)

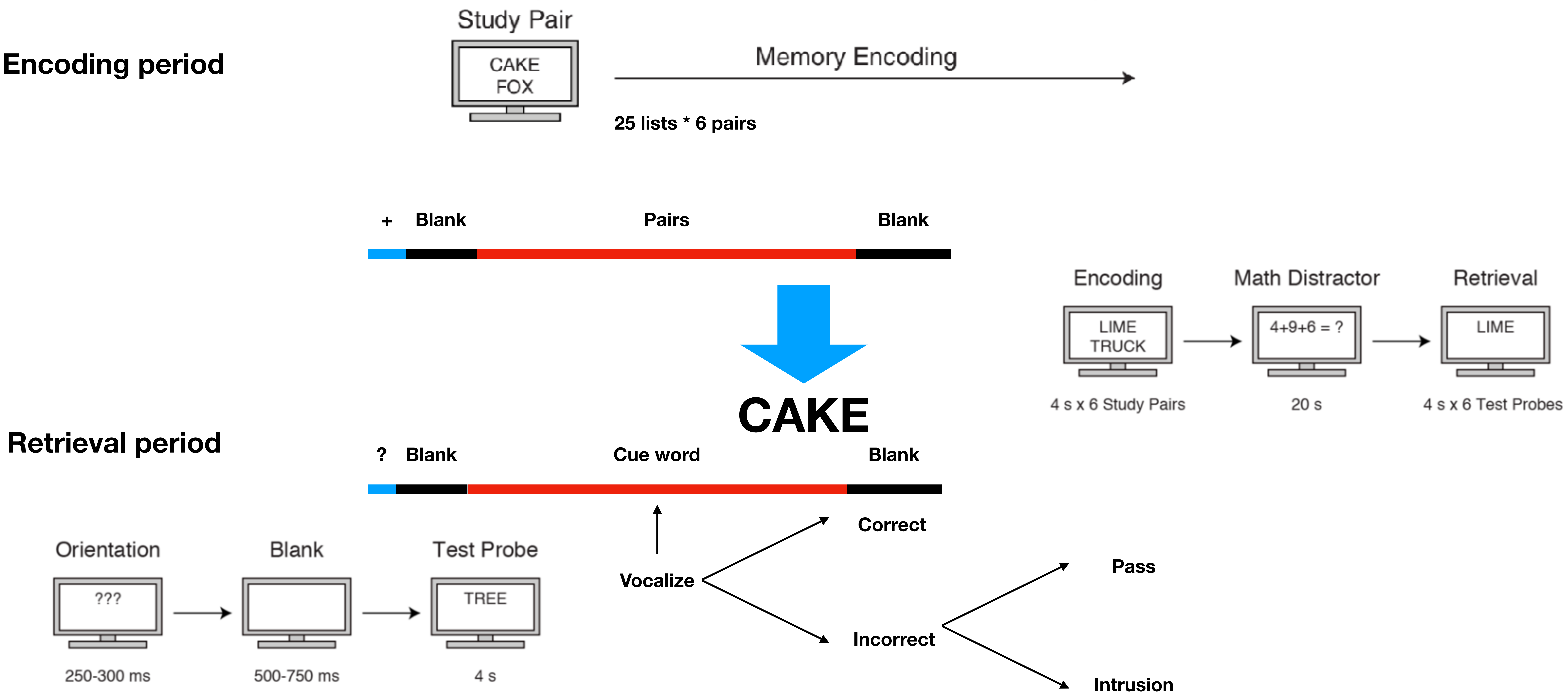
the hippocampus, along with the surrounding hippocampal region consisting of the perirhinal, parahippocampal, and entorhinal neocortical regions



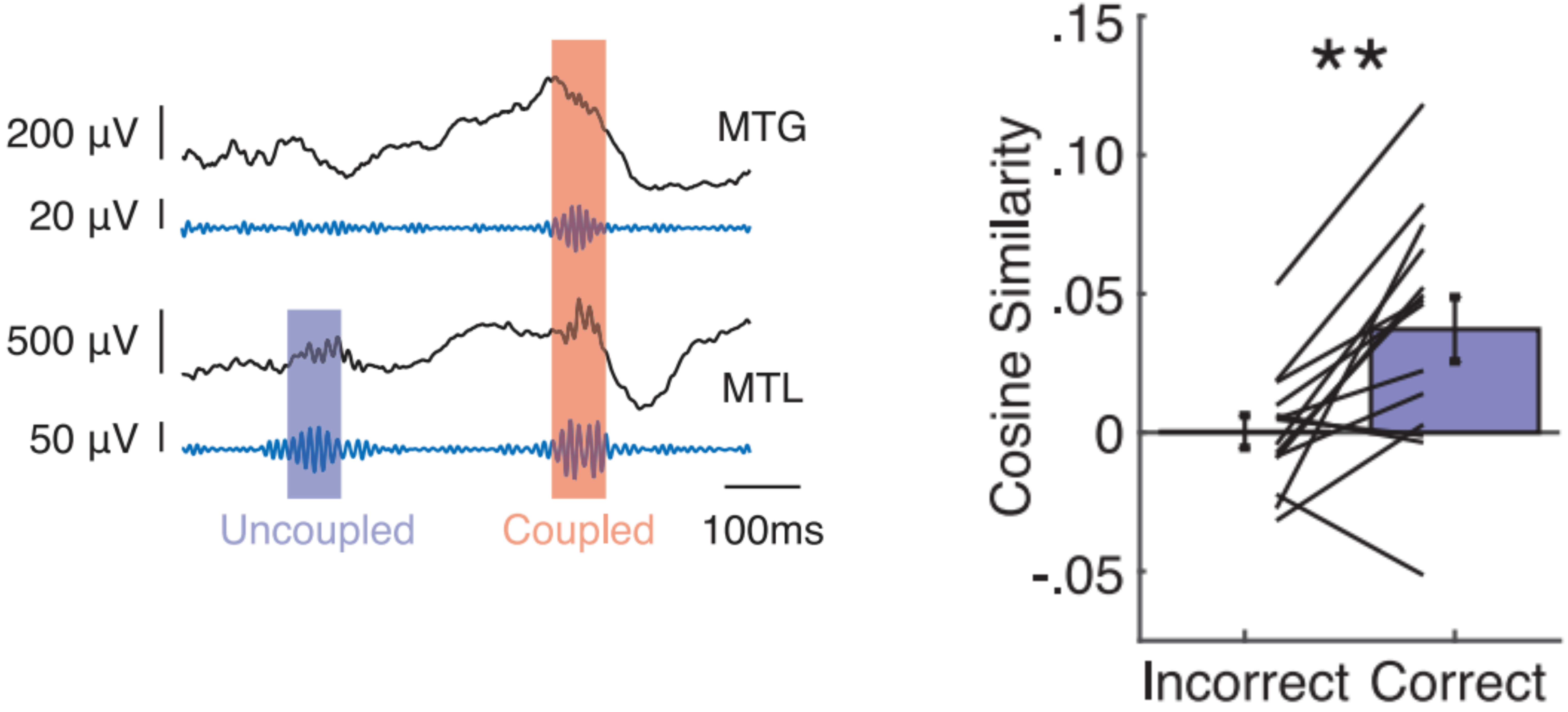
Middle temporal gyrus (MTG)



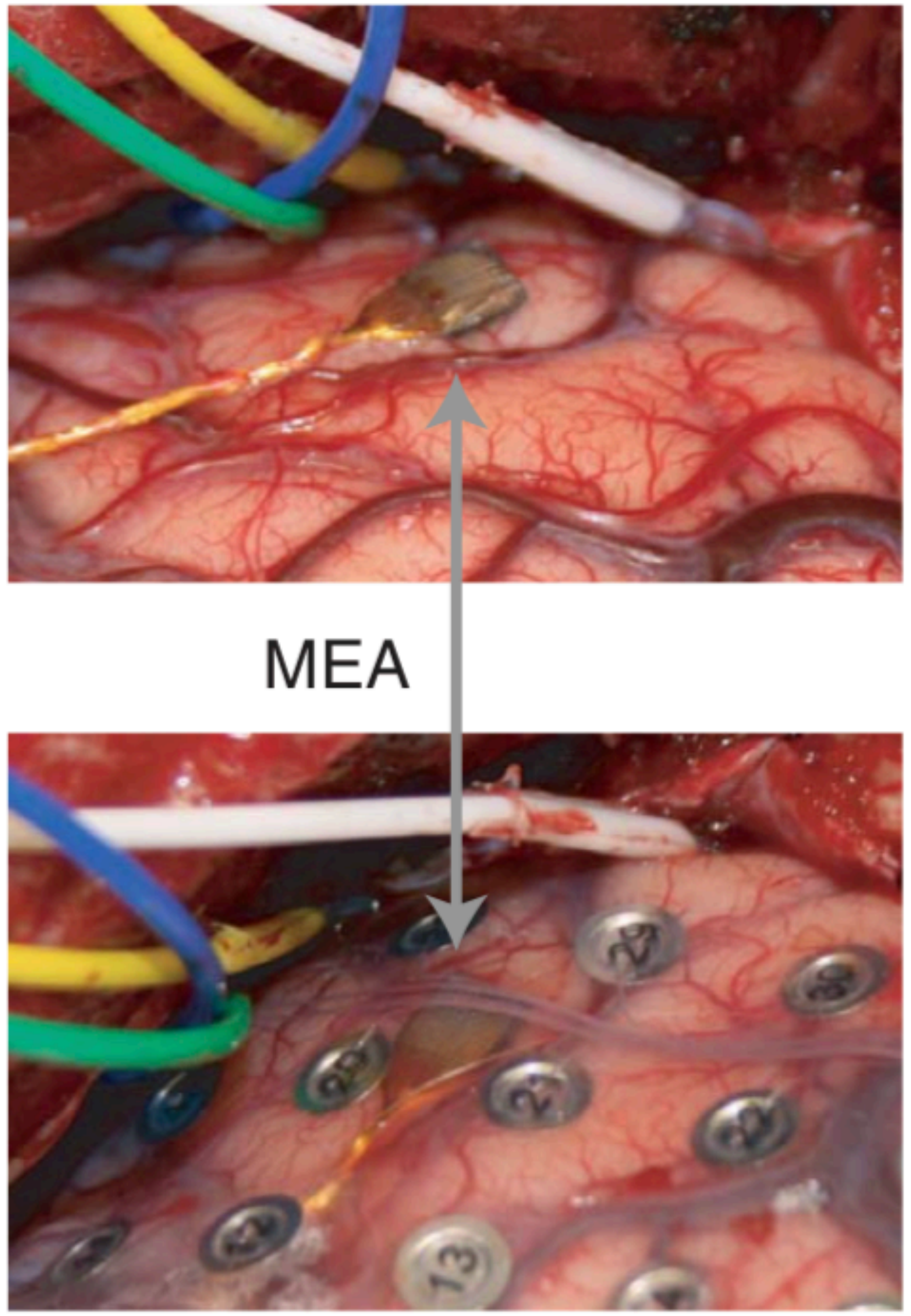
Paired associated memory task

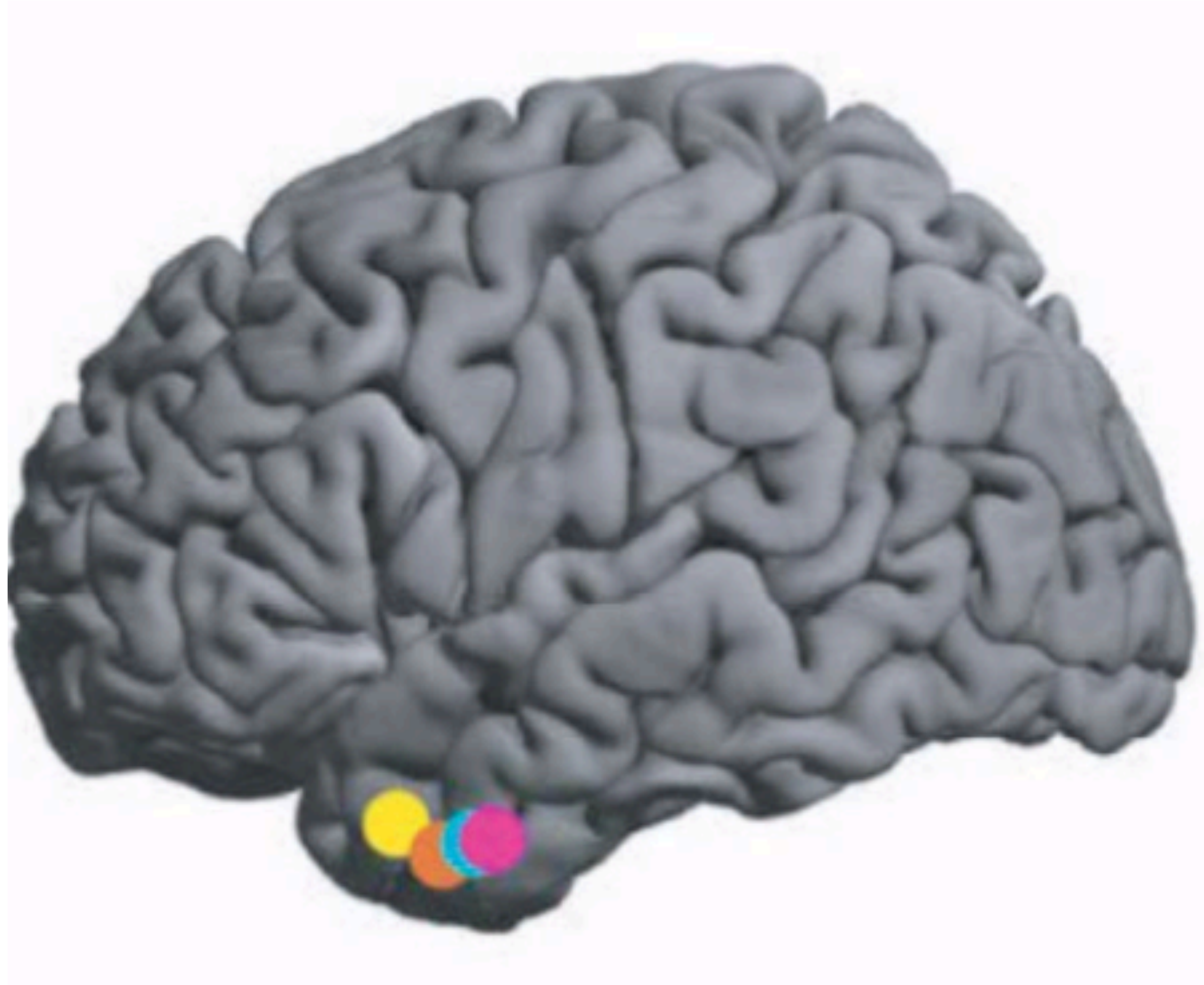


Previously - coupled ripple oscillations

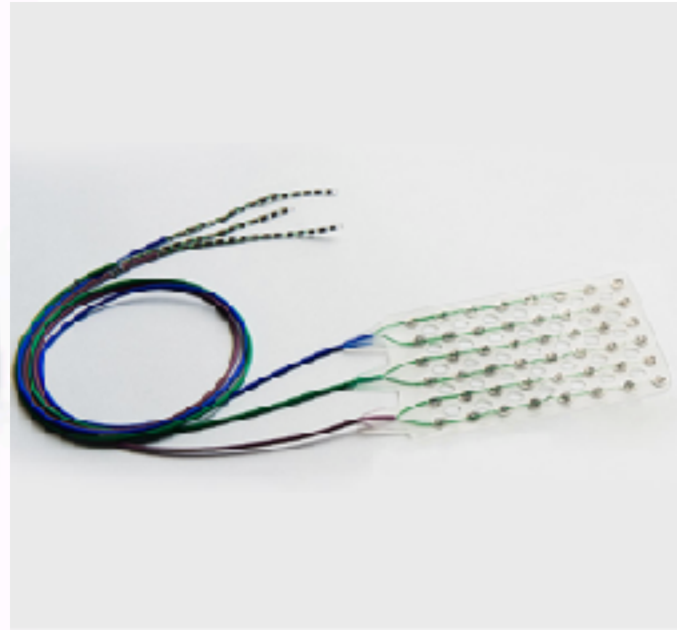


Intracranial recordings



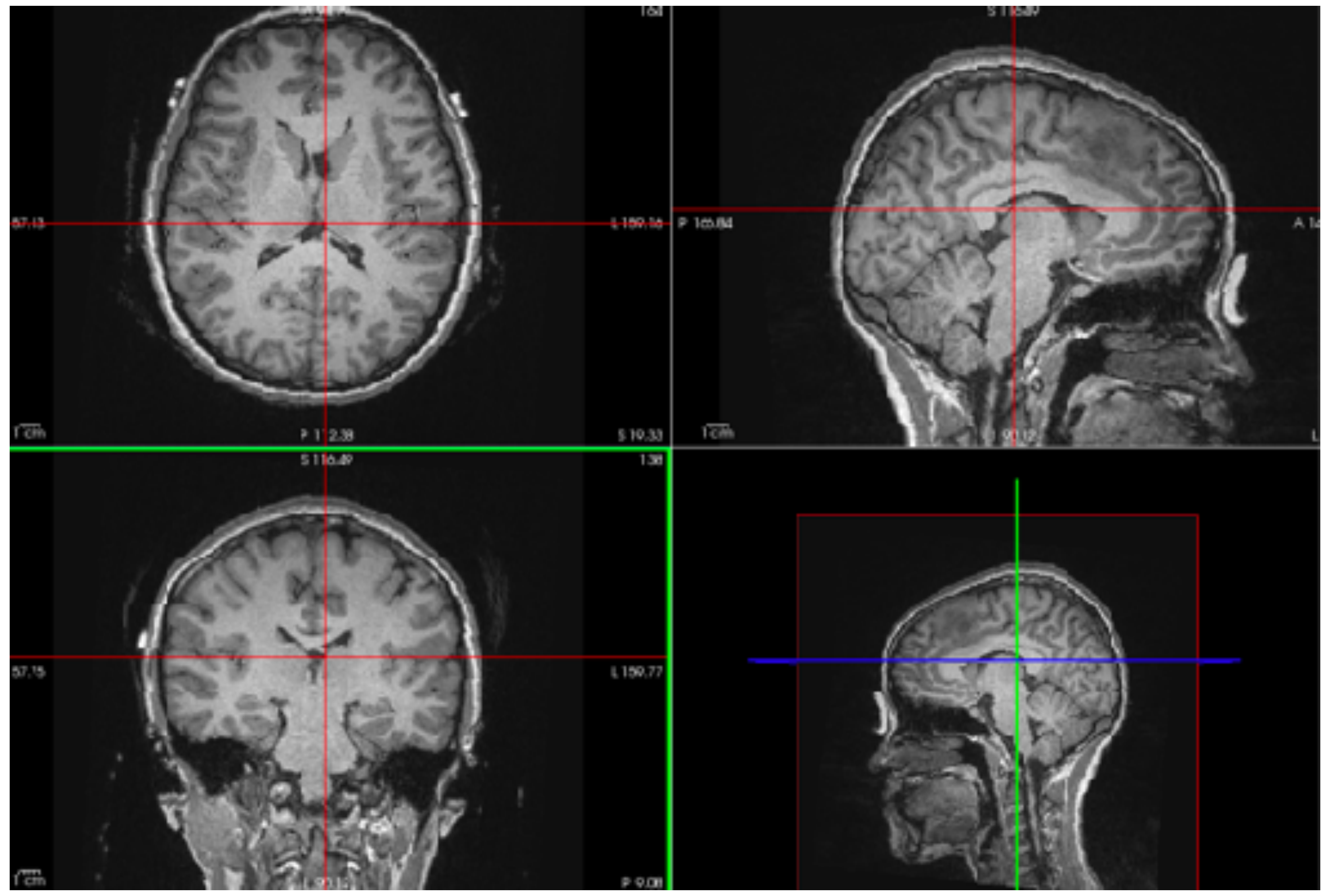


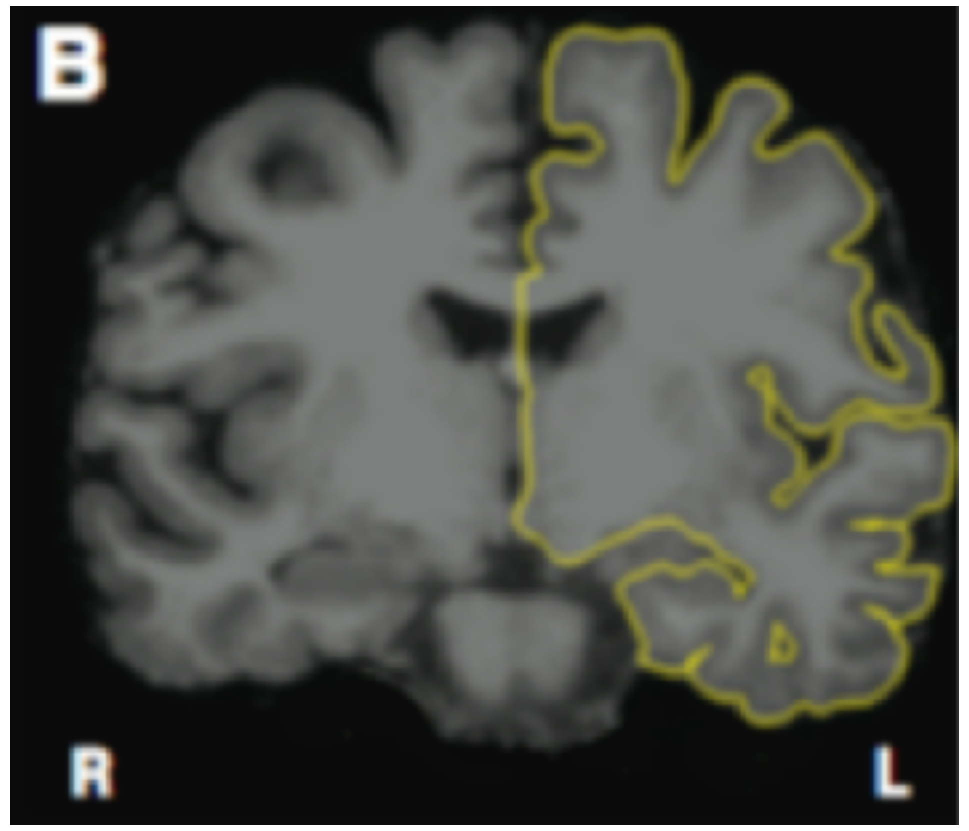
716 subdural and depth recording contacts
119 ± 16.0 per participant

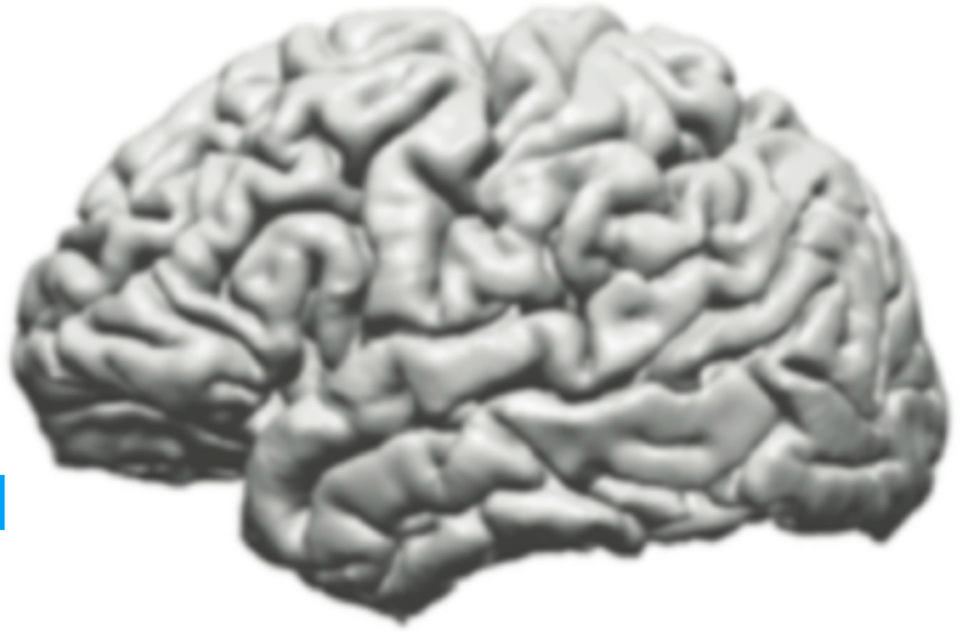


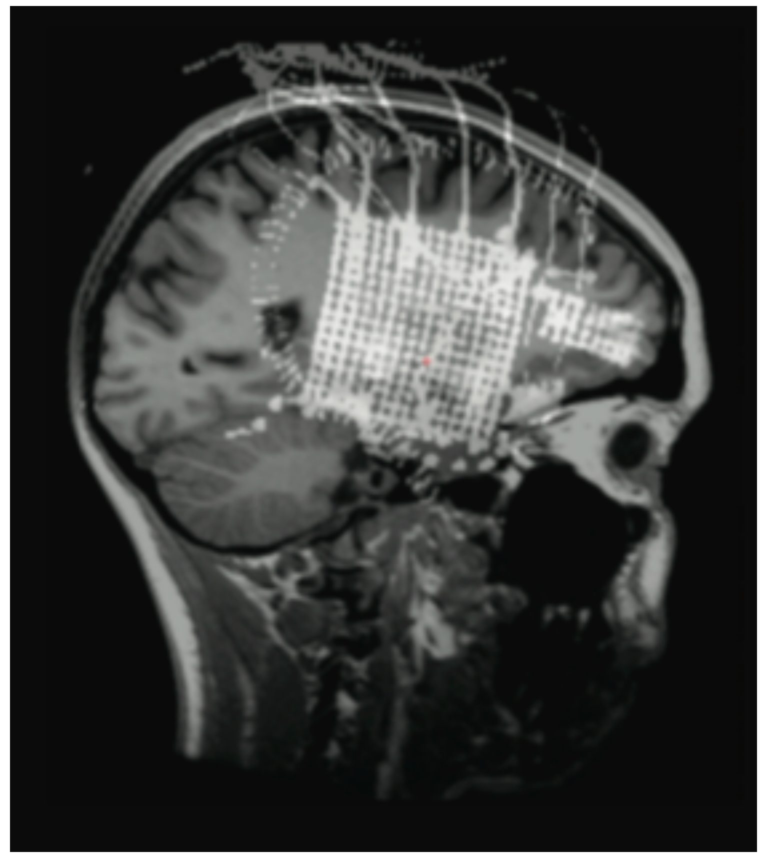
48 subdural contacts
8.0 ± 0.5 per participant

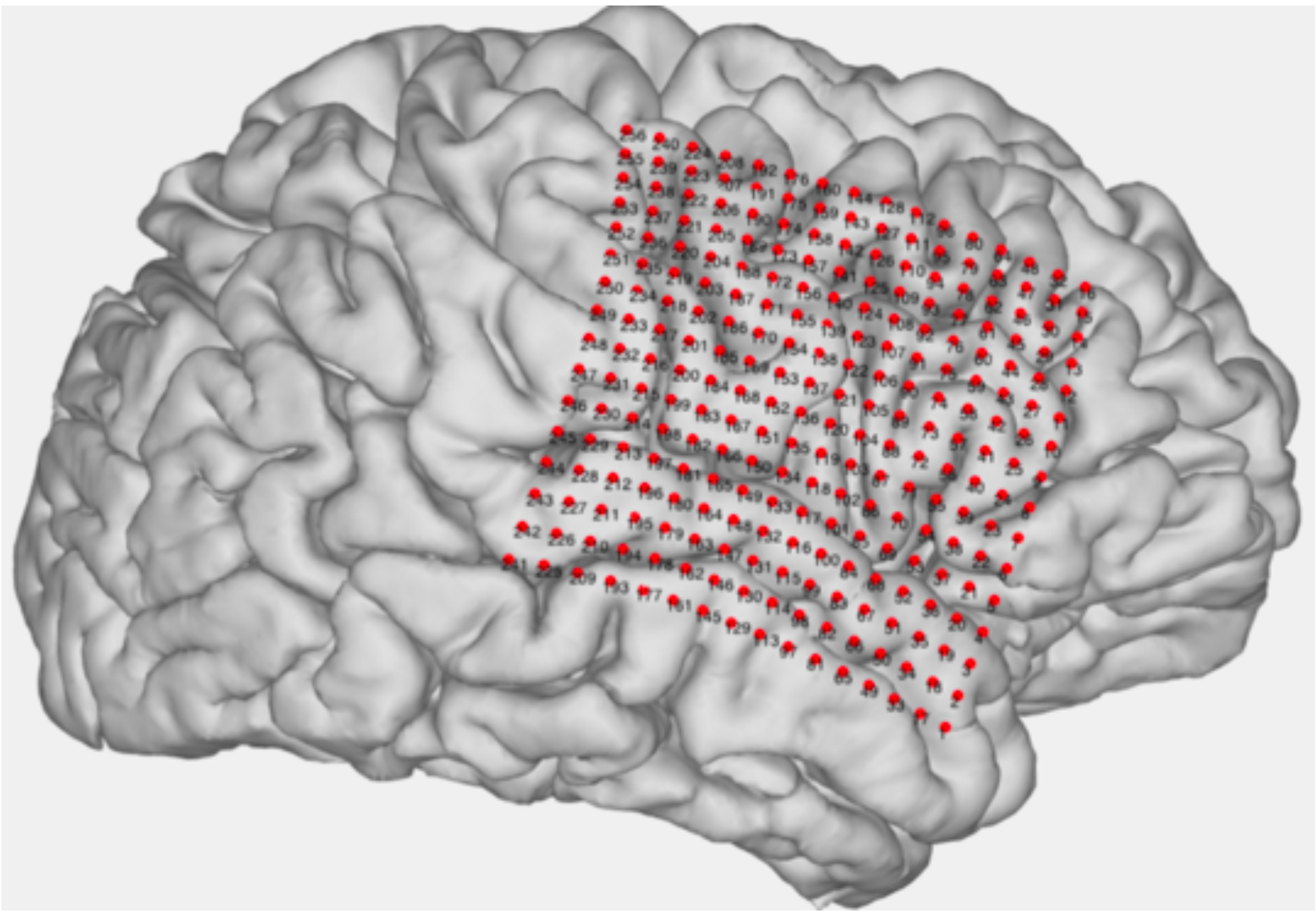
Grid localization

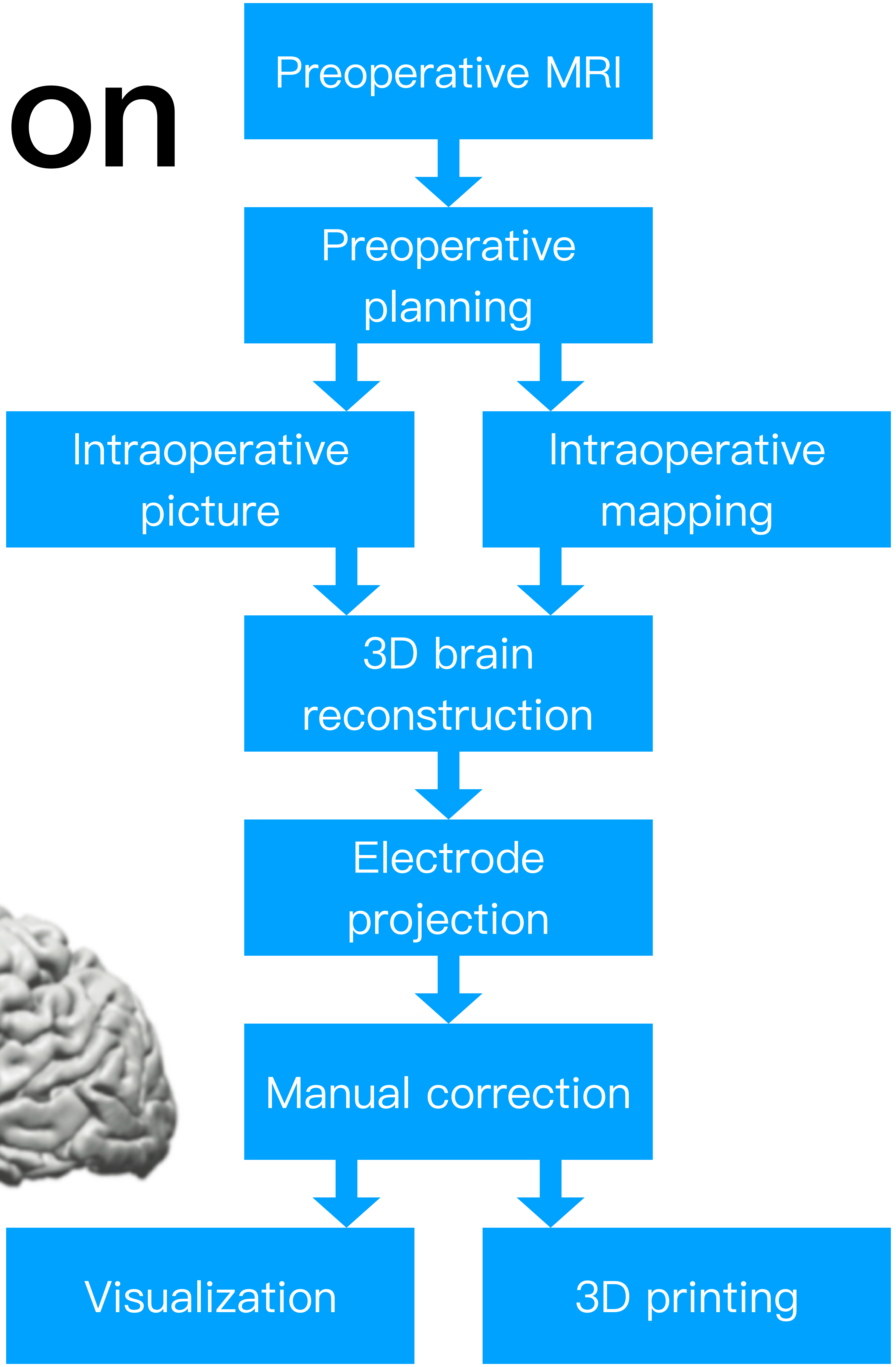












Data extraction - Macro iEEG

Data acquisition — Recording @ 1000Hz or 2000Hz

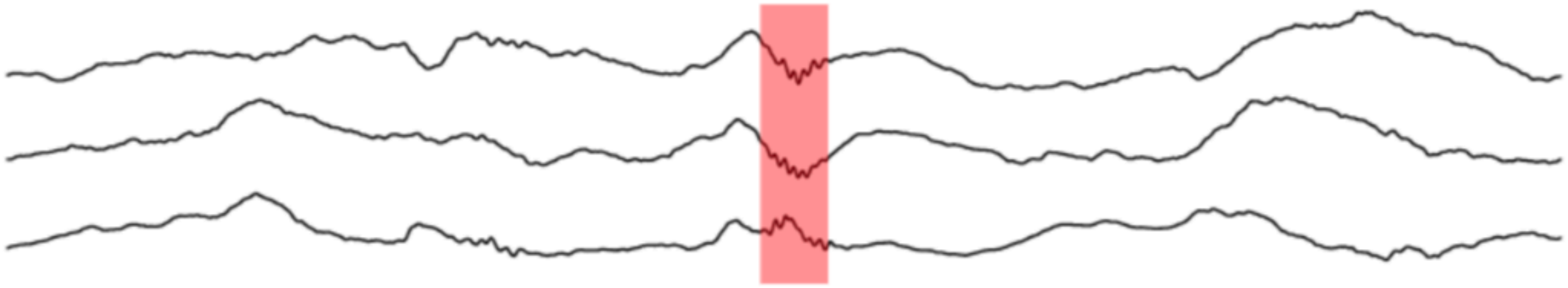
Down sampling — Downsample to 1000Hz

Notch filter — 60Hz

Quantify spectral power — Morlet wavelets

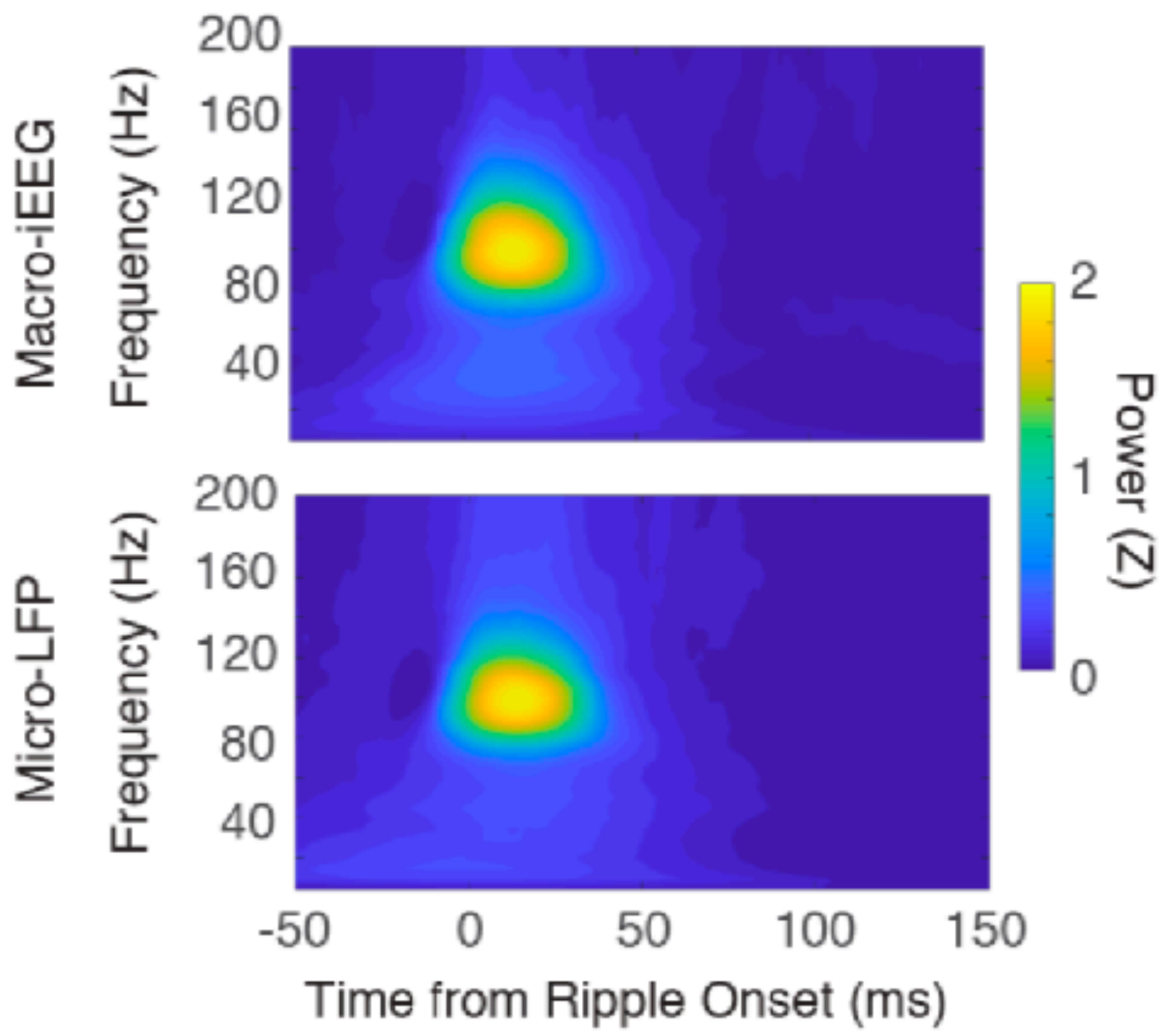
Hilbert transformation — 5 and 200 Hz

Analysis — 80Hz - 120Hz z-score

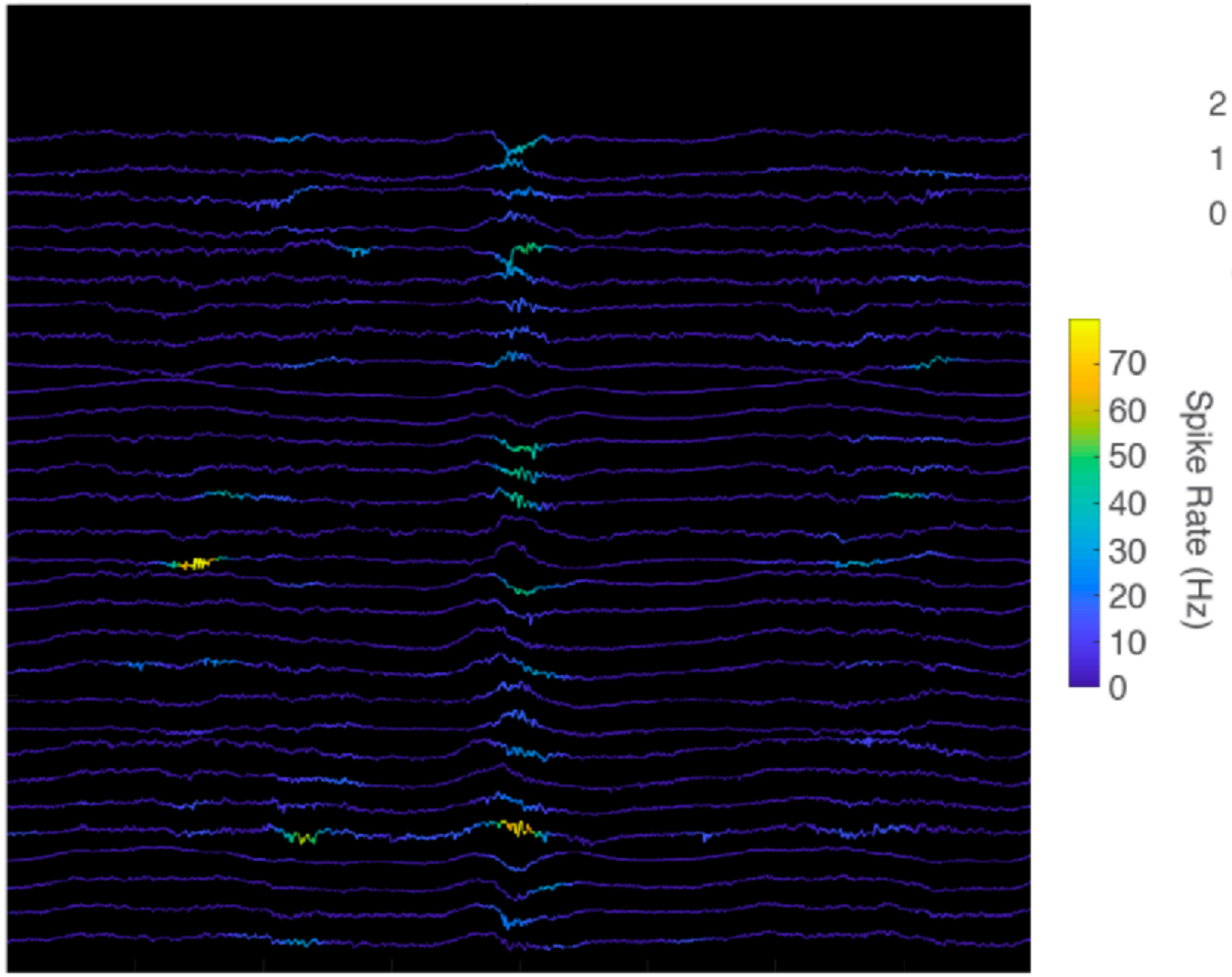


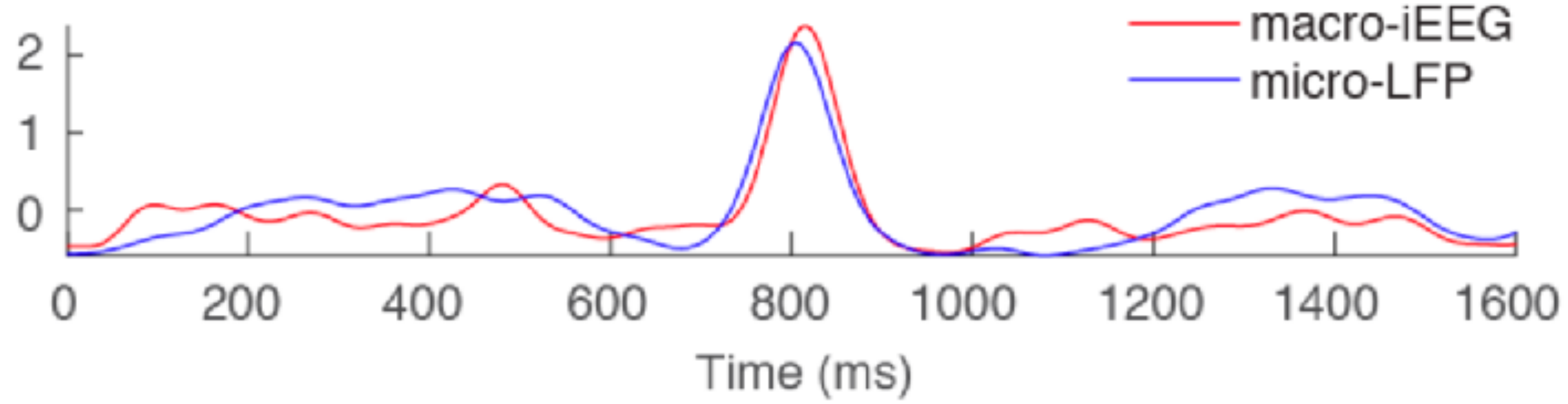
at least 25 ms in duration and had a maximum amplitude greater than 3 standard deviations

Removal of epileptiform activity & other noise



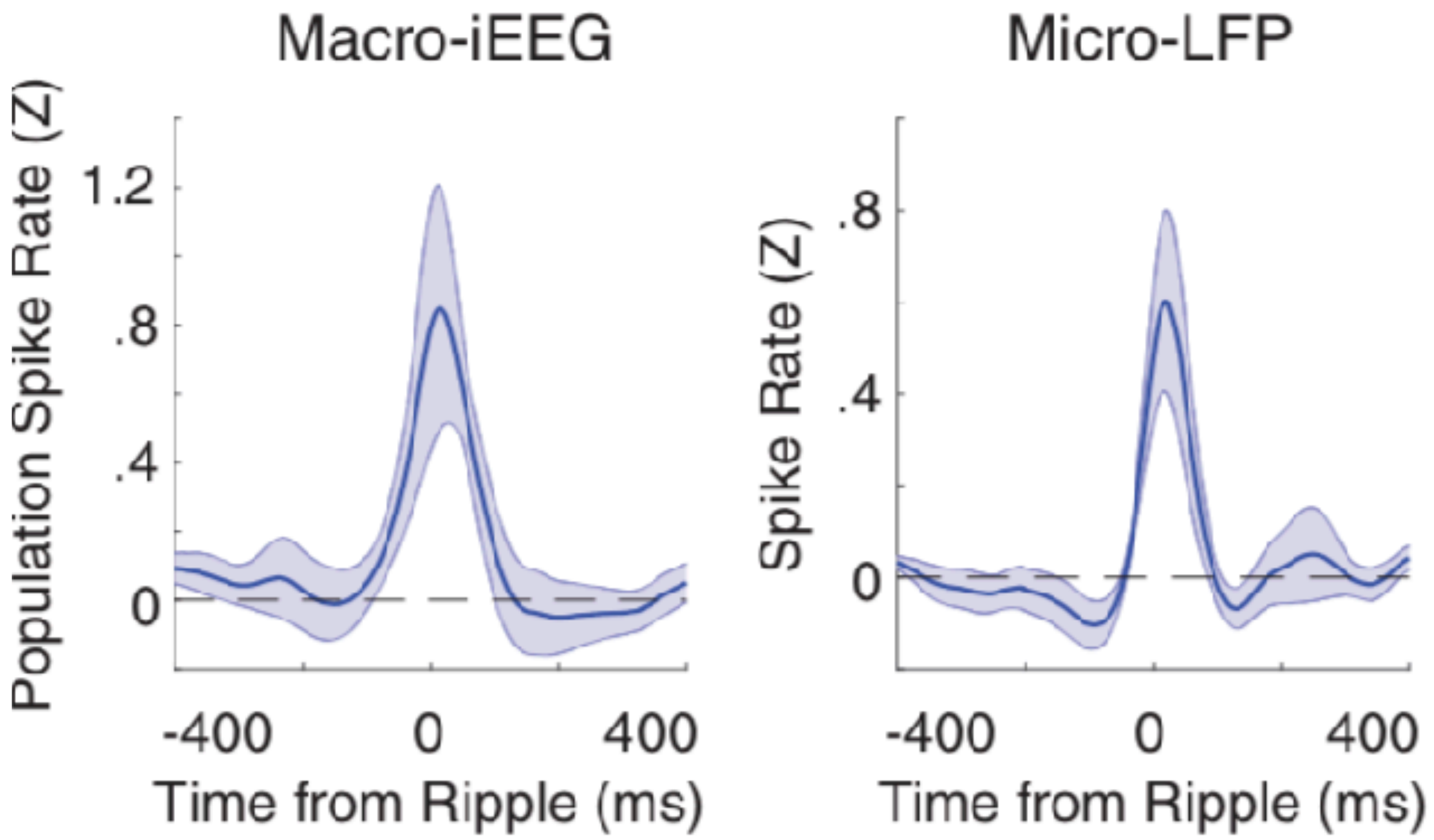
Data extraction - Micro LFP





Recording @ 30kHz

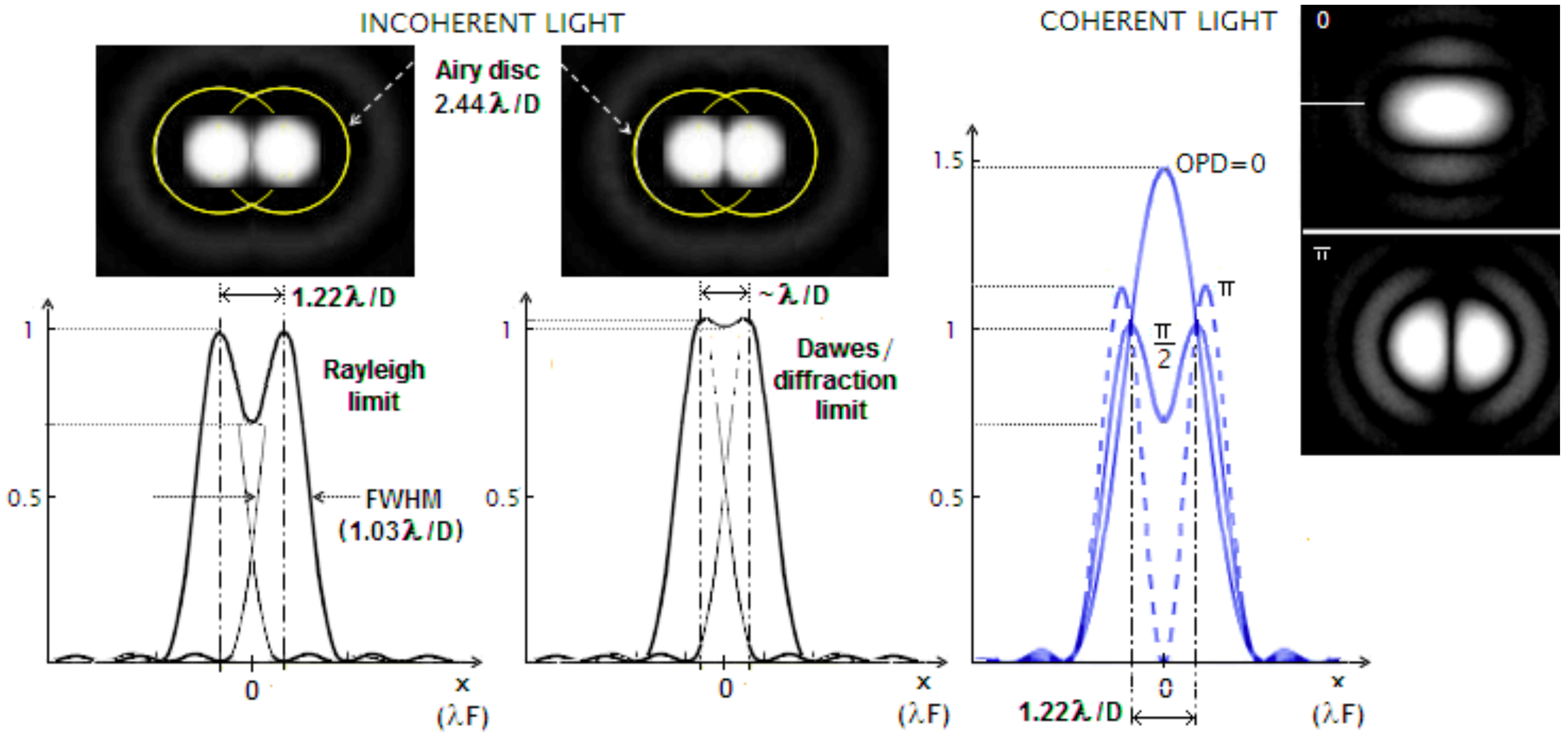
500 Hz low pass filter

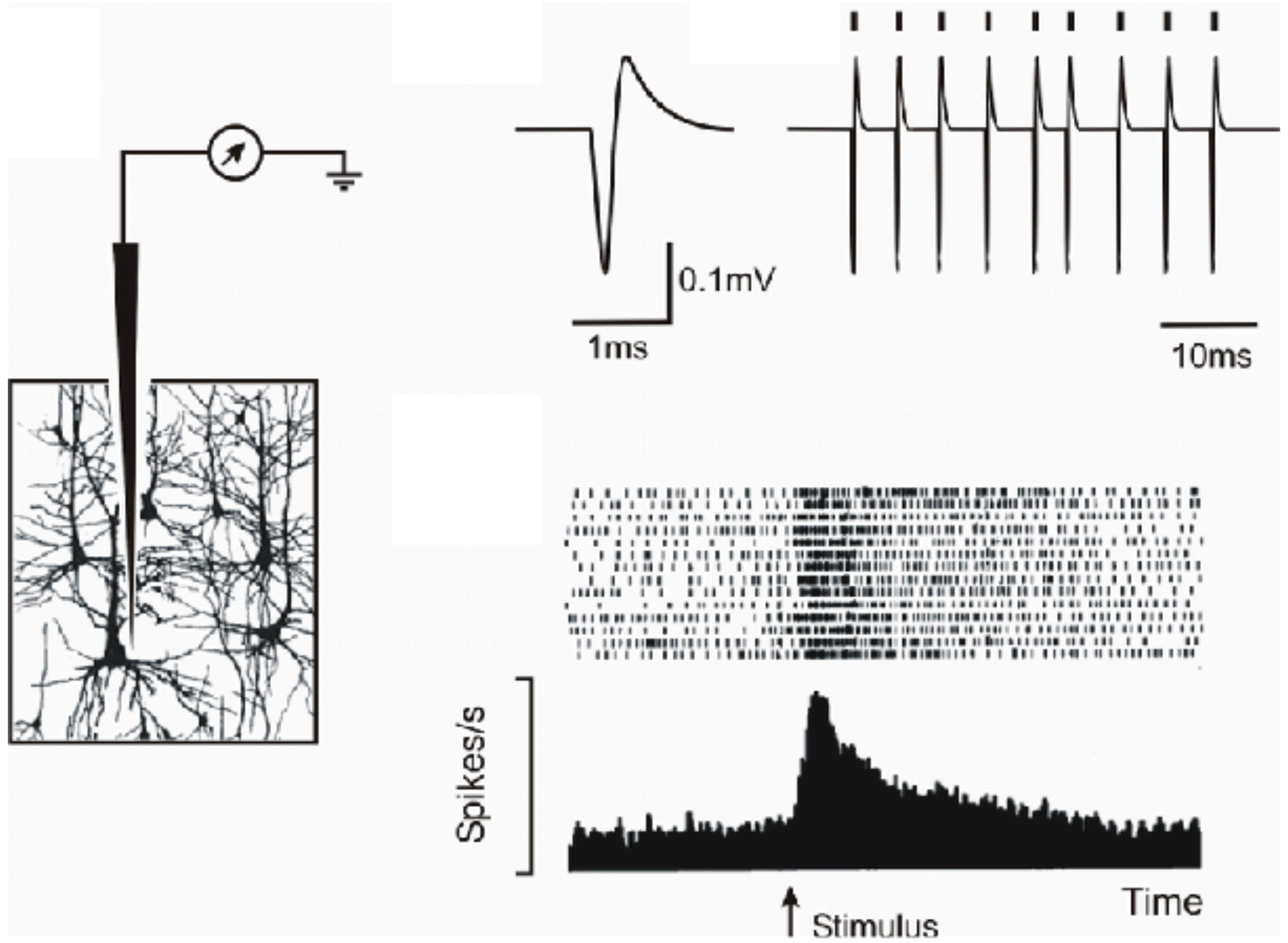


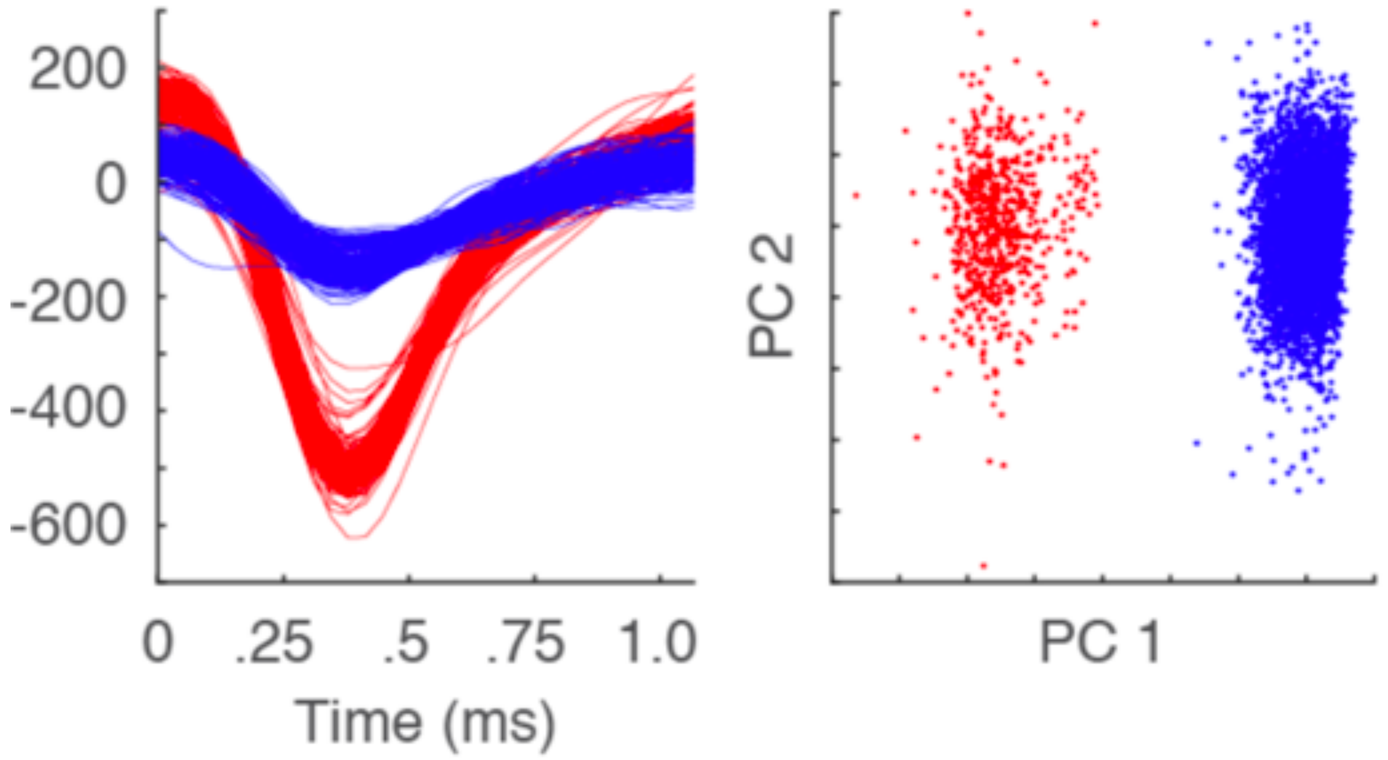
Data extraction - Single unit

Recording @ 30kHz

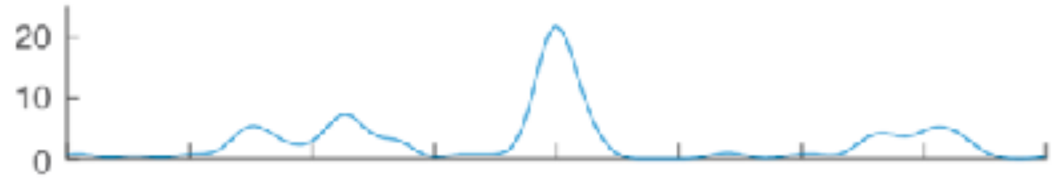
Downsample to 3000Hz



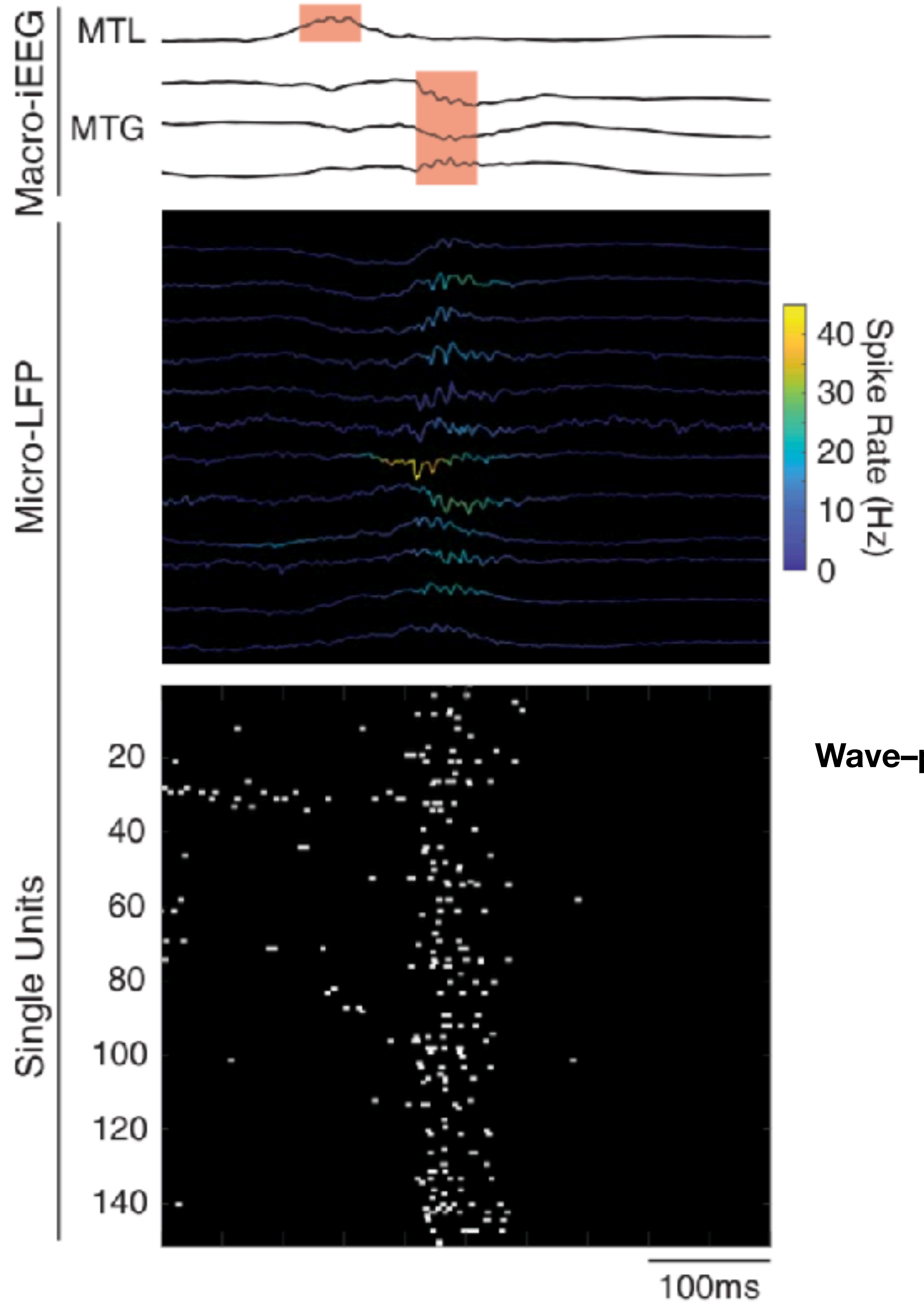




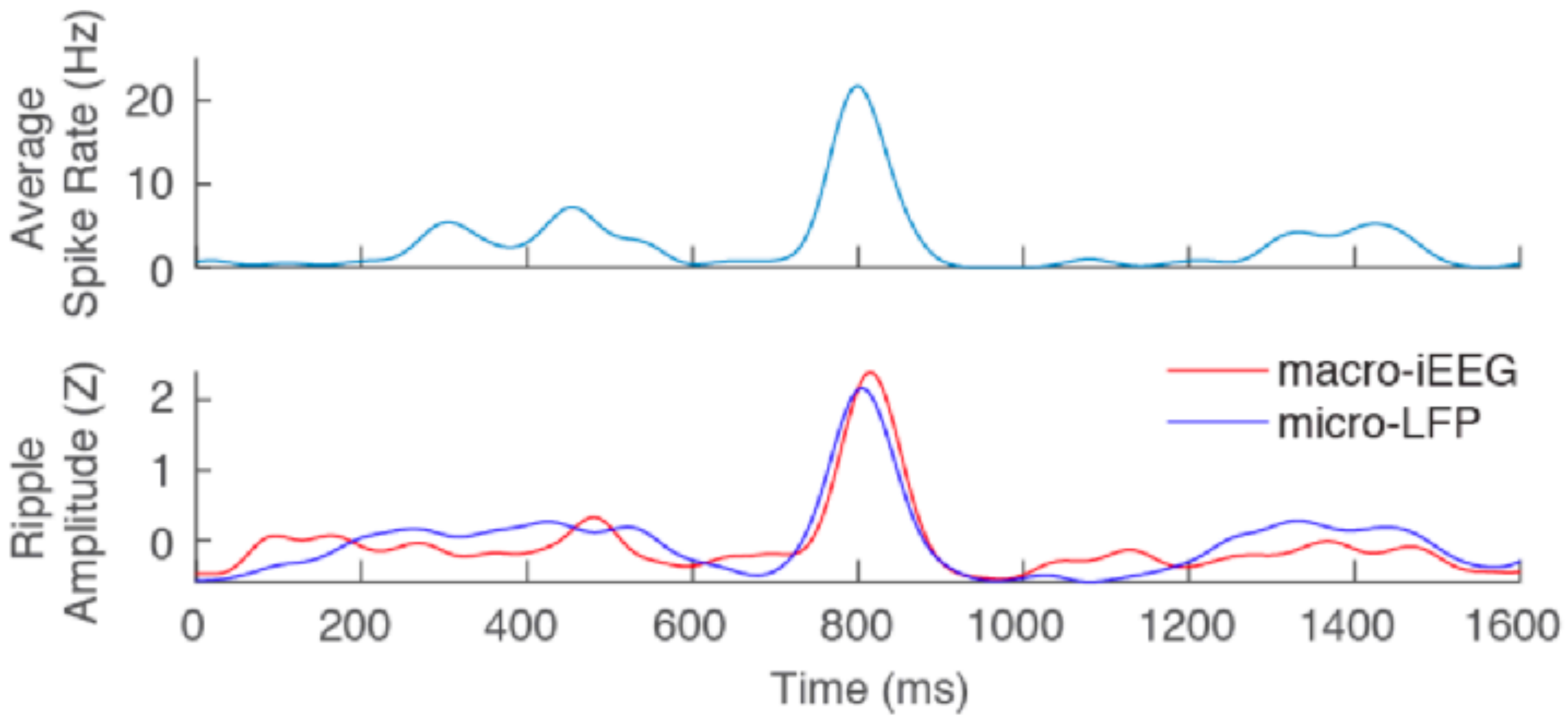
exceeding three standard deviations above the mean for at least 25 ms

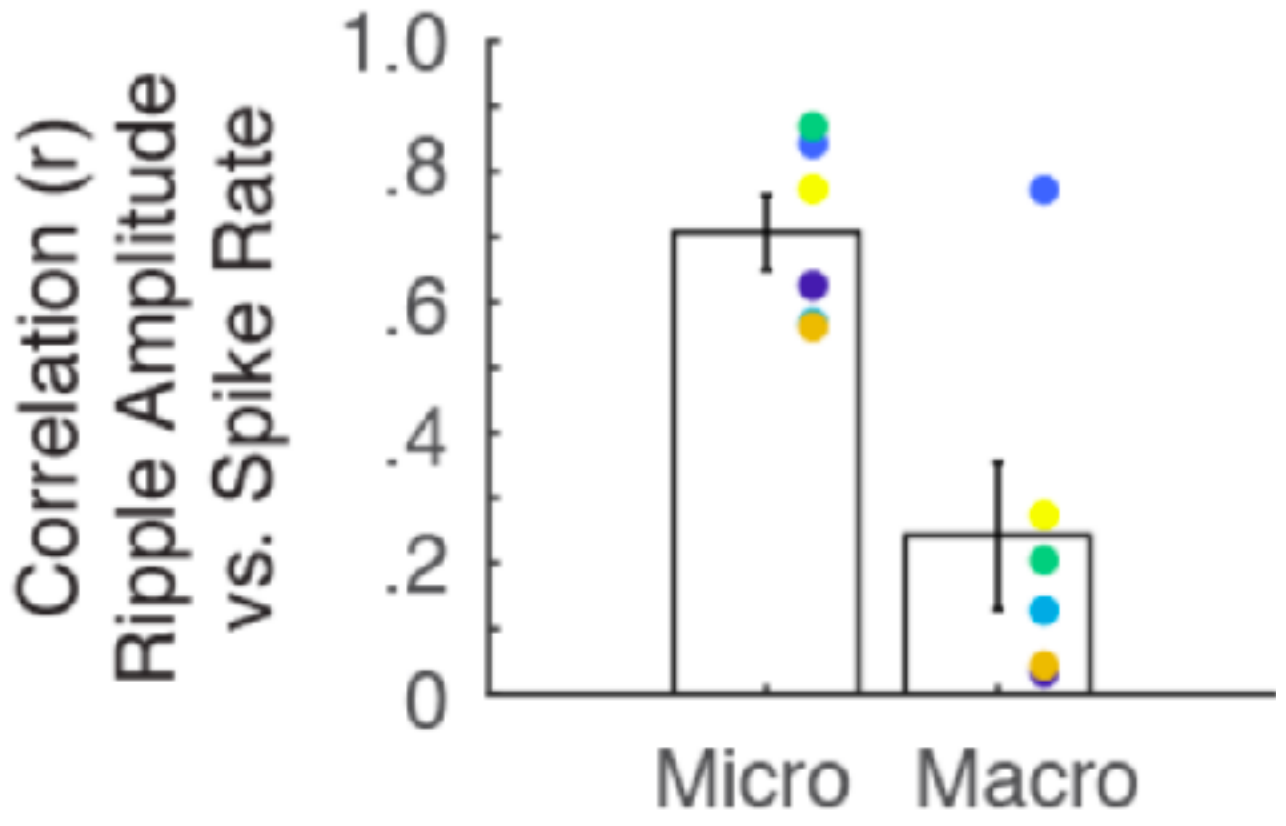


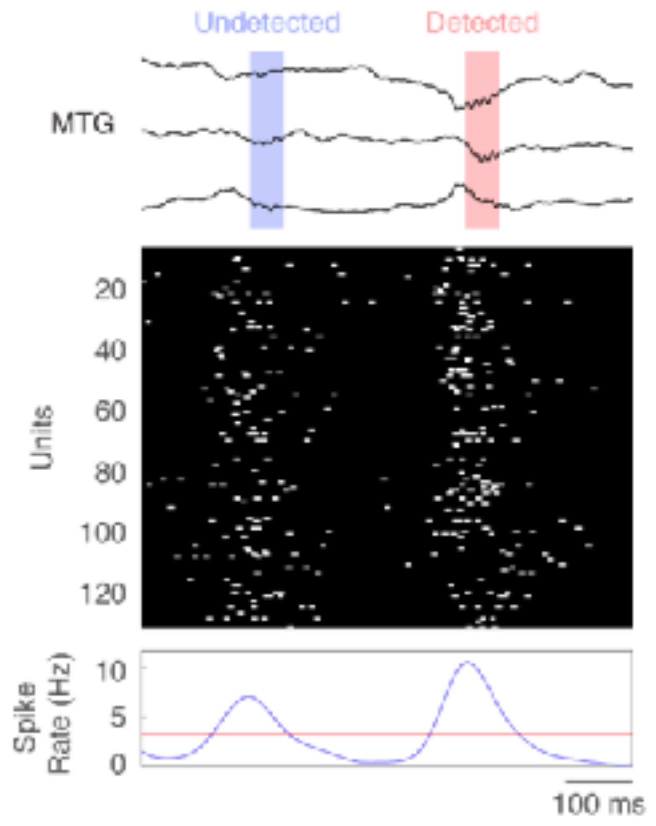
Correlation among macro iEEG, micro LFP and Single unit



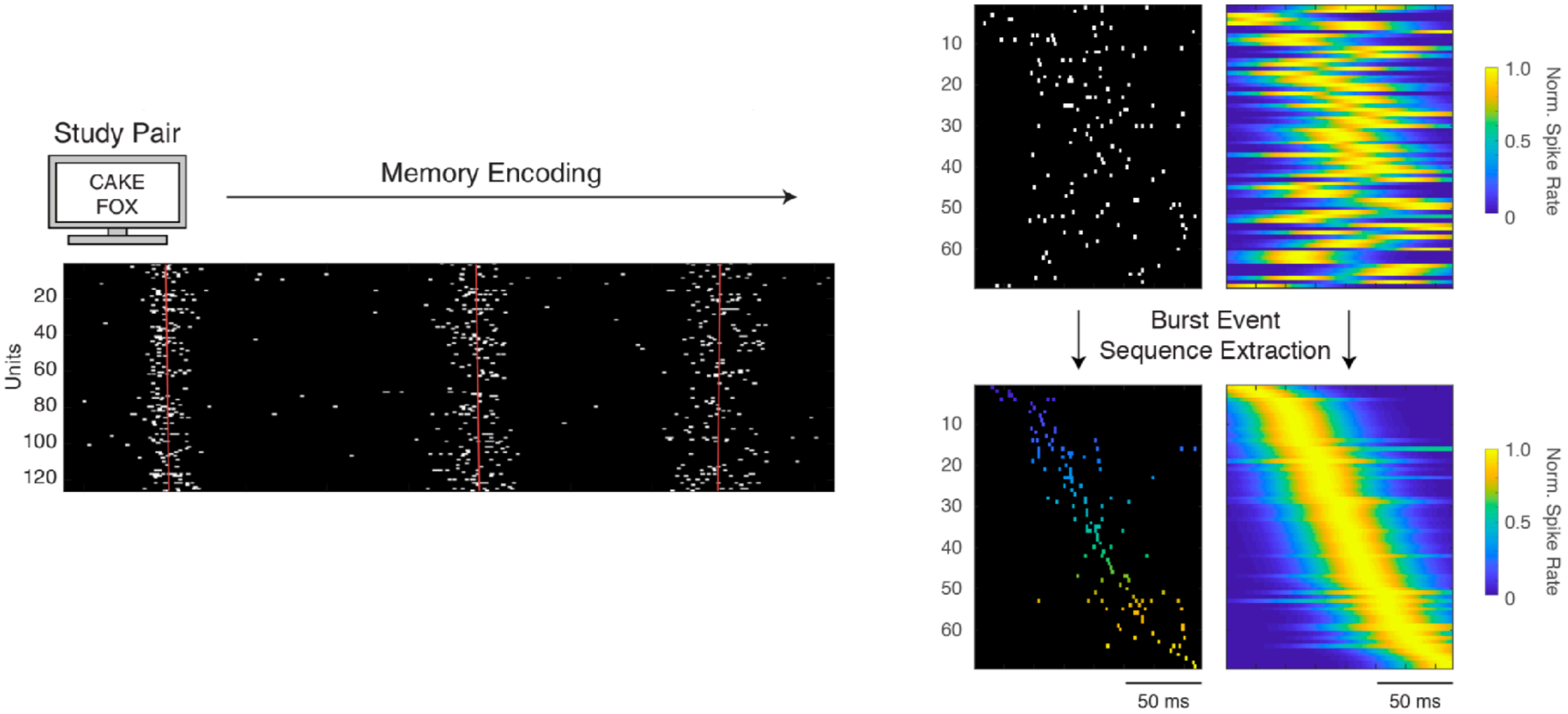
Wave–particle duality



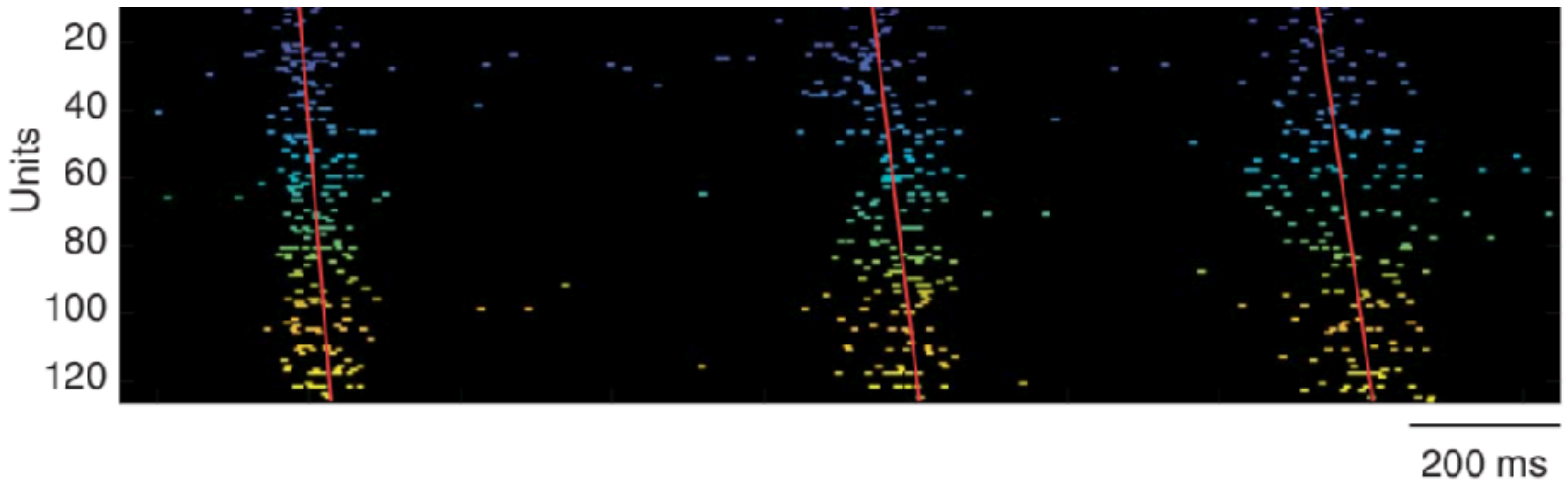


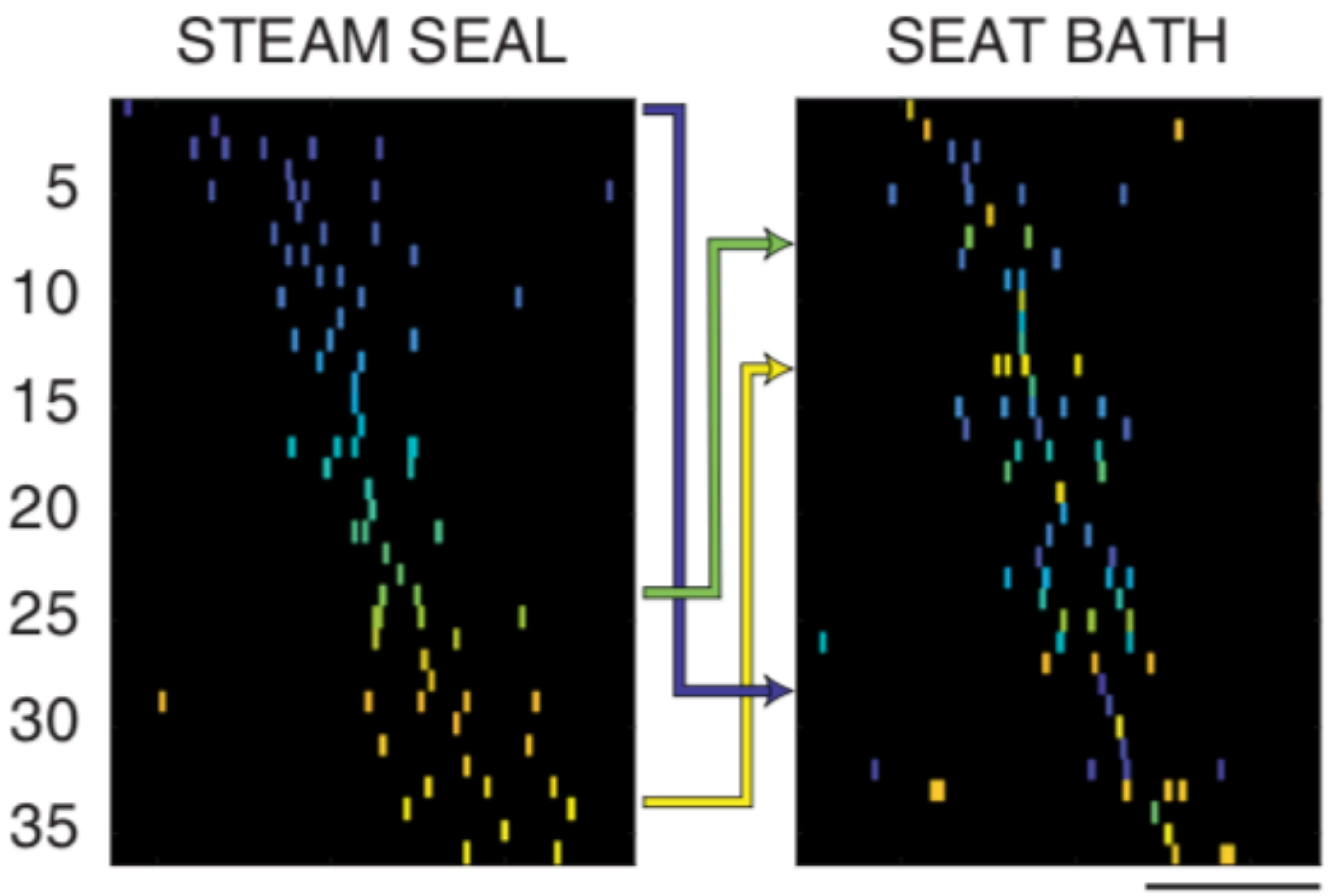


Burst events are organized into trial-specific sequences during successful memory formation

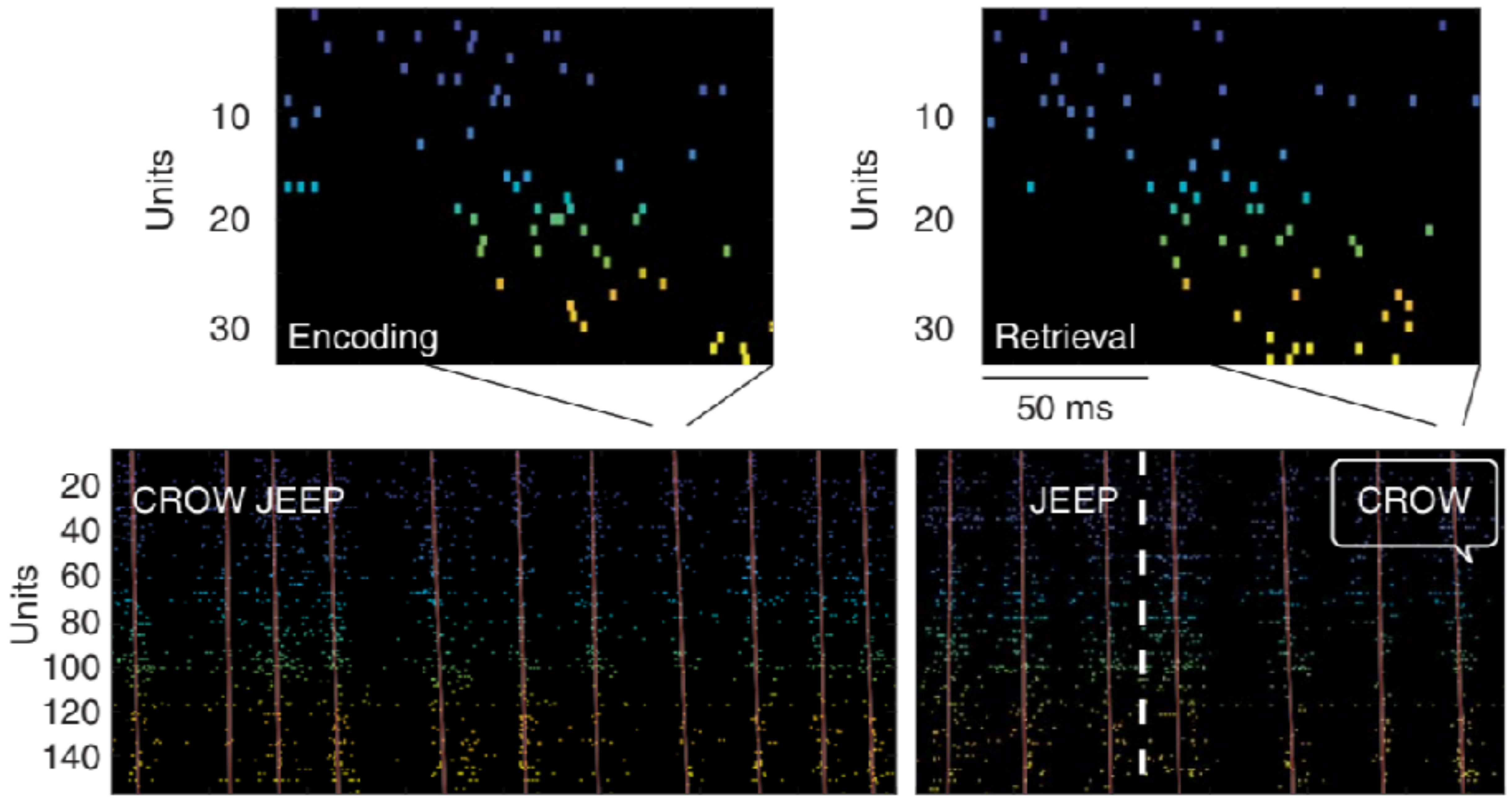


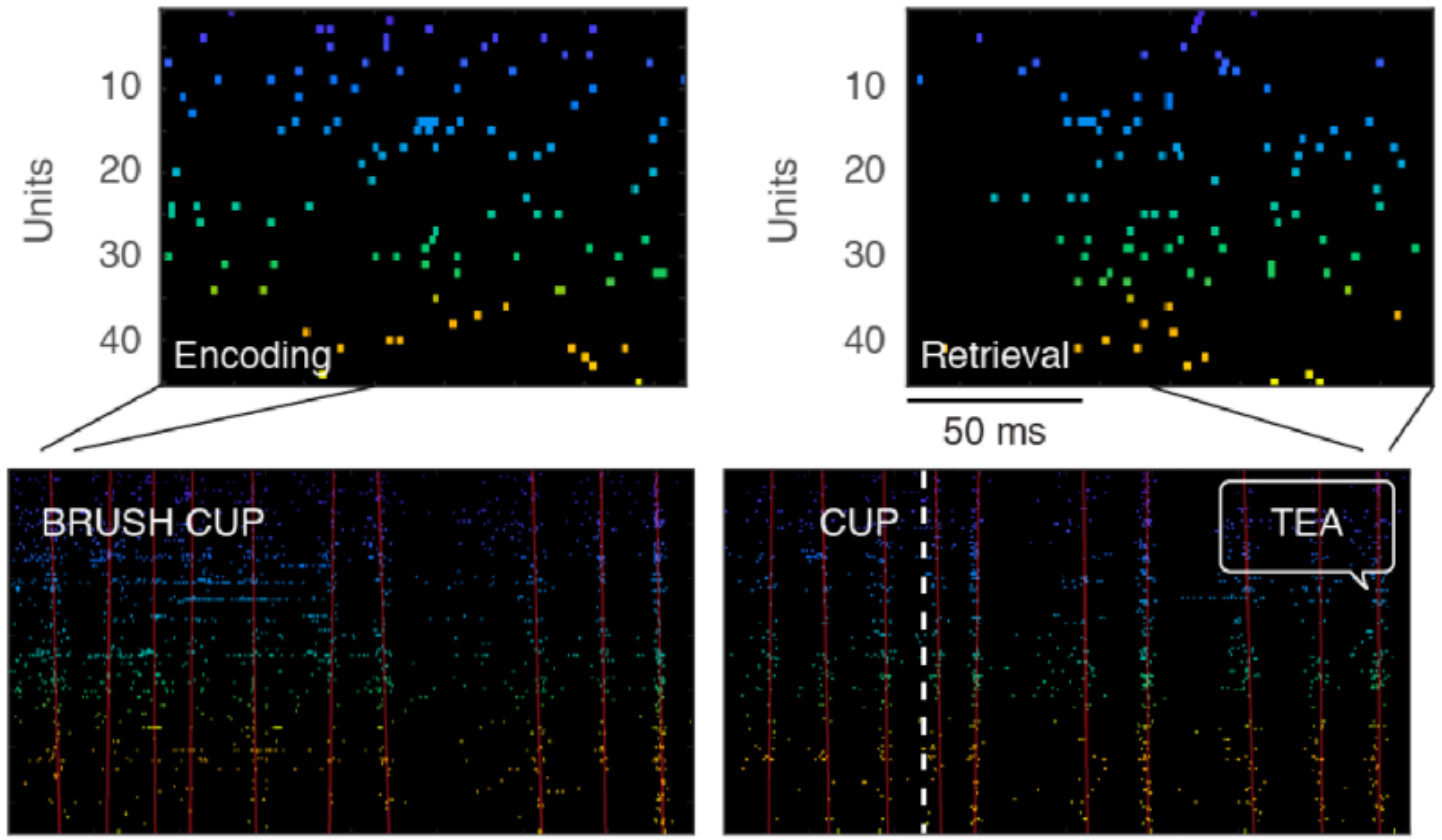
Burst events are organized into trial-specific sequences during successful memory formation





Memory-specific sequence replay occurs during successful memory retrieval

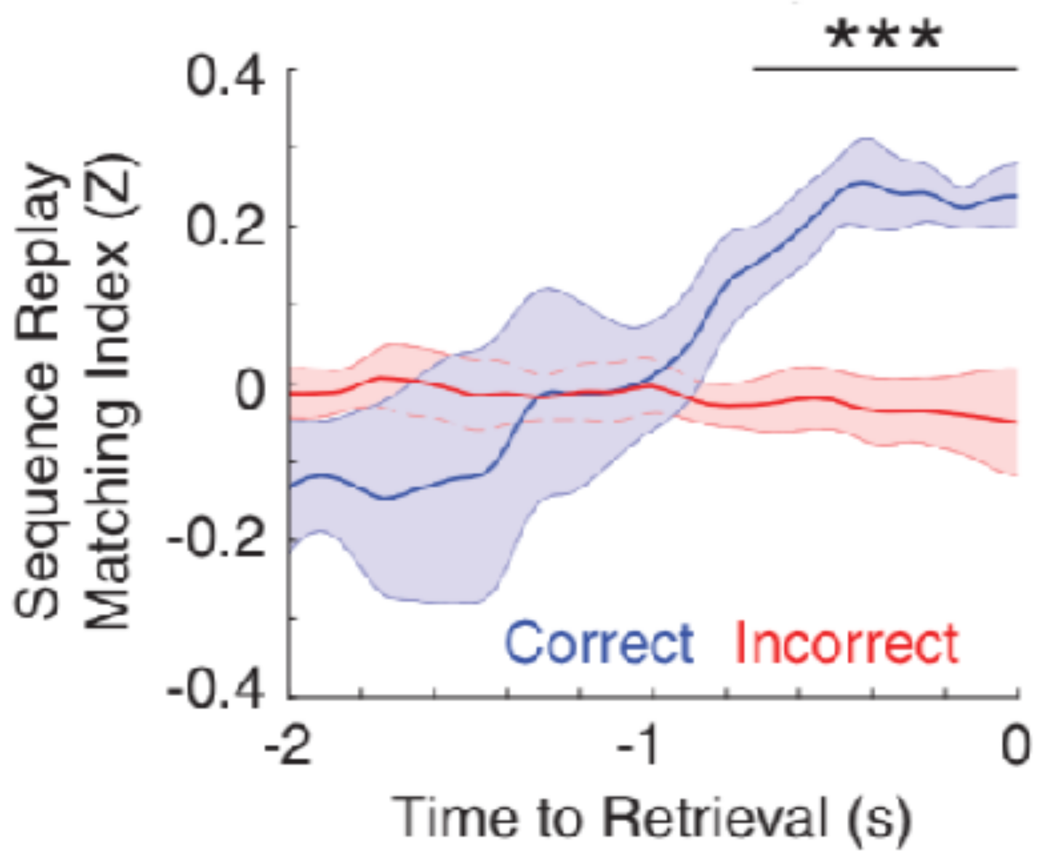




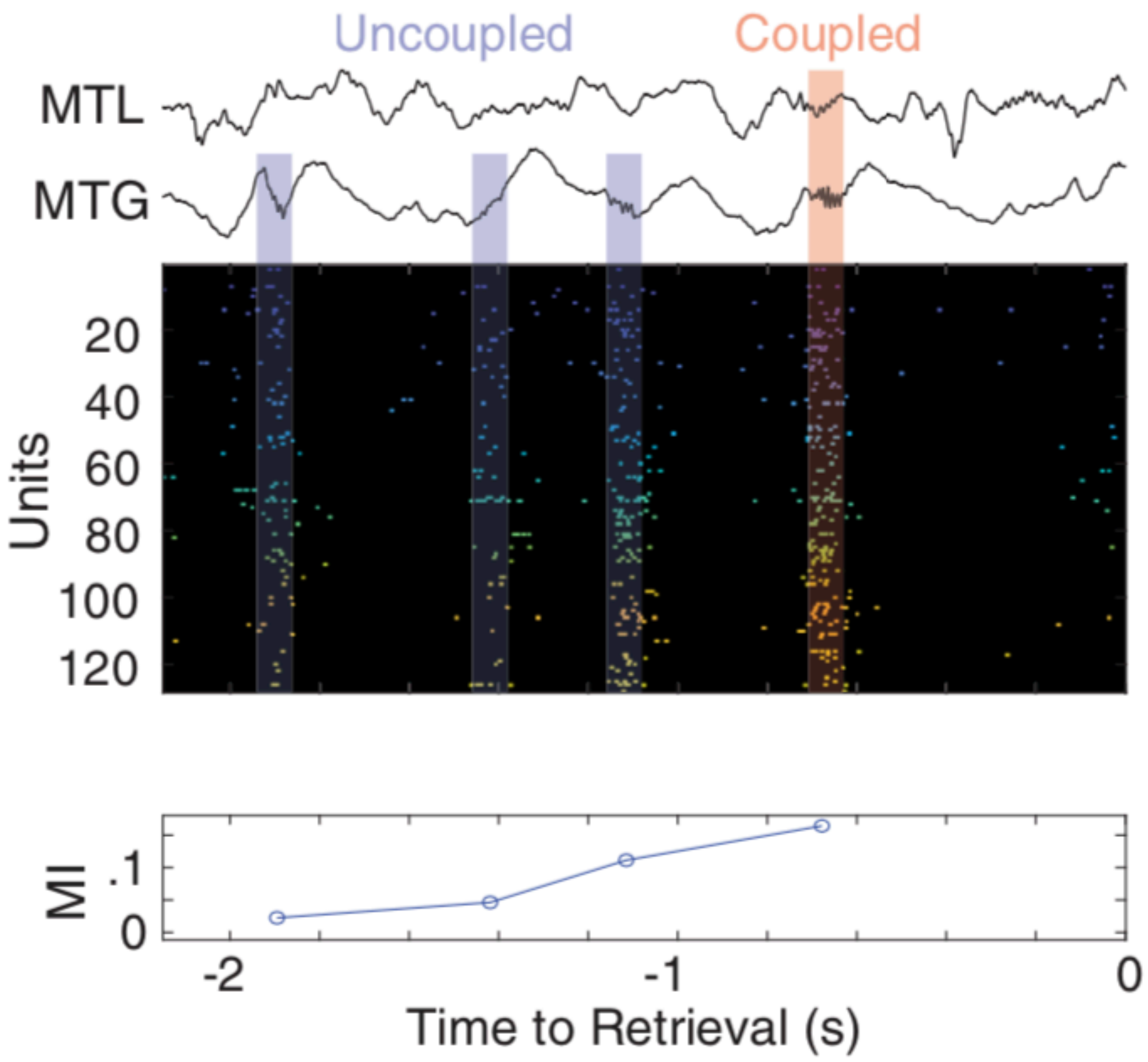
Correct

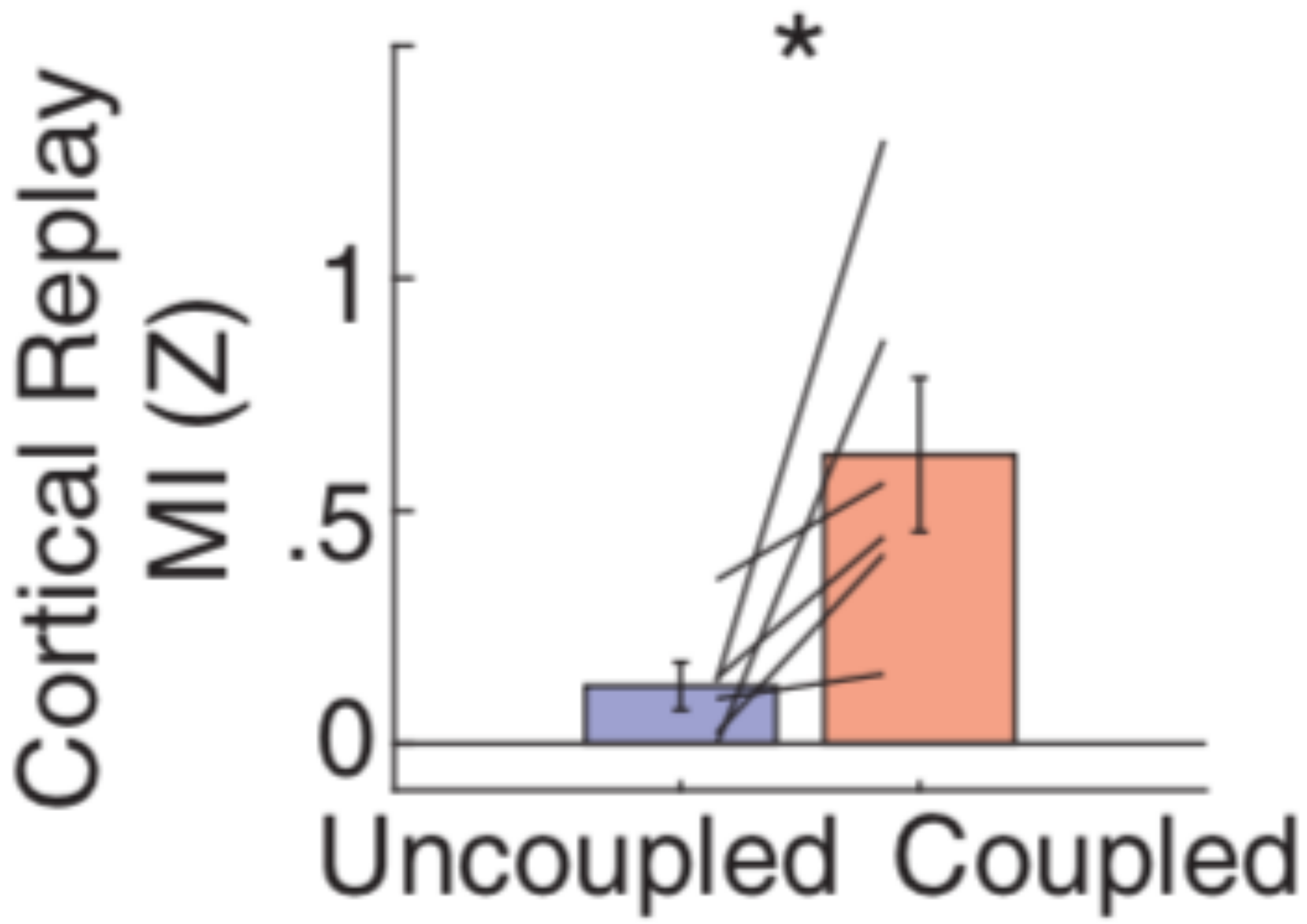
Incorrect

$$MI = (m - n) / (m + n)$$



MTL ripples precede cortical sequence replay

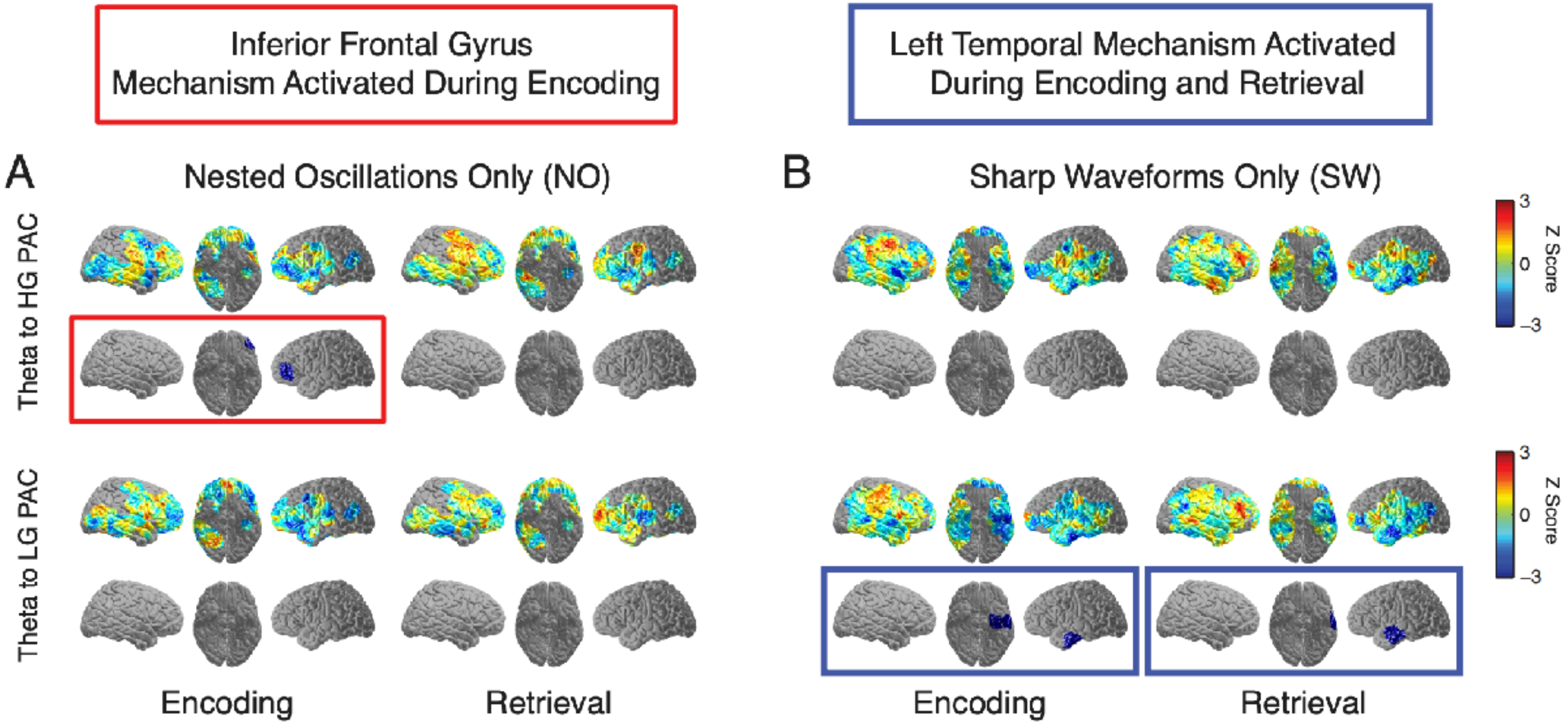




Summary

- Ripple strongly associated with burst activity
- Temporal pattern during encoding
- Replay of the temporal pattern during retrieval
- MTL ripples is more important for correct retrieval

What's next?



- Long term memory
- Interfering the burst/spiking
- Sleeping
- Association or concept

Slides will be uploaded on https://lingweizhang.github.io/JCN-FDU/