Computational Neuroscience: Systems Neuroscience in the Context of the Hippocampus

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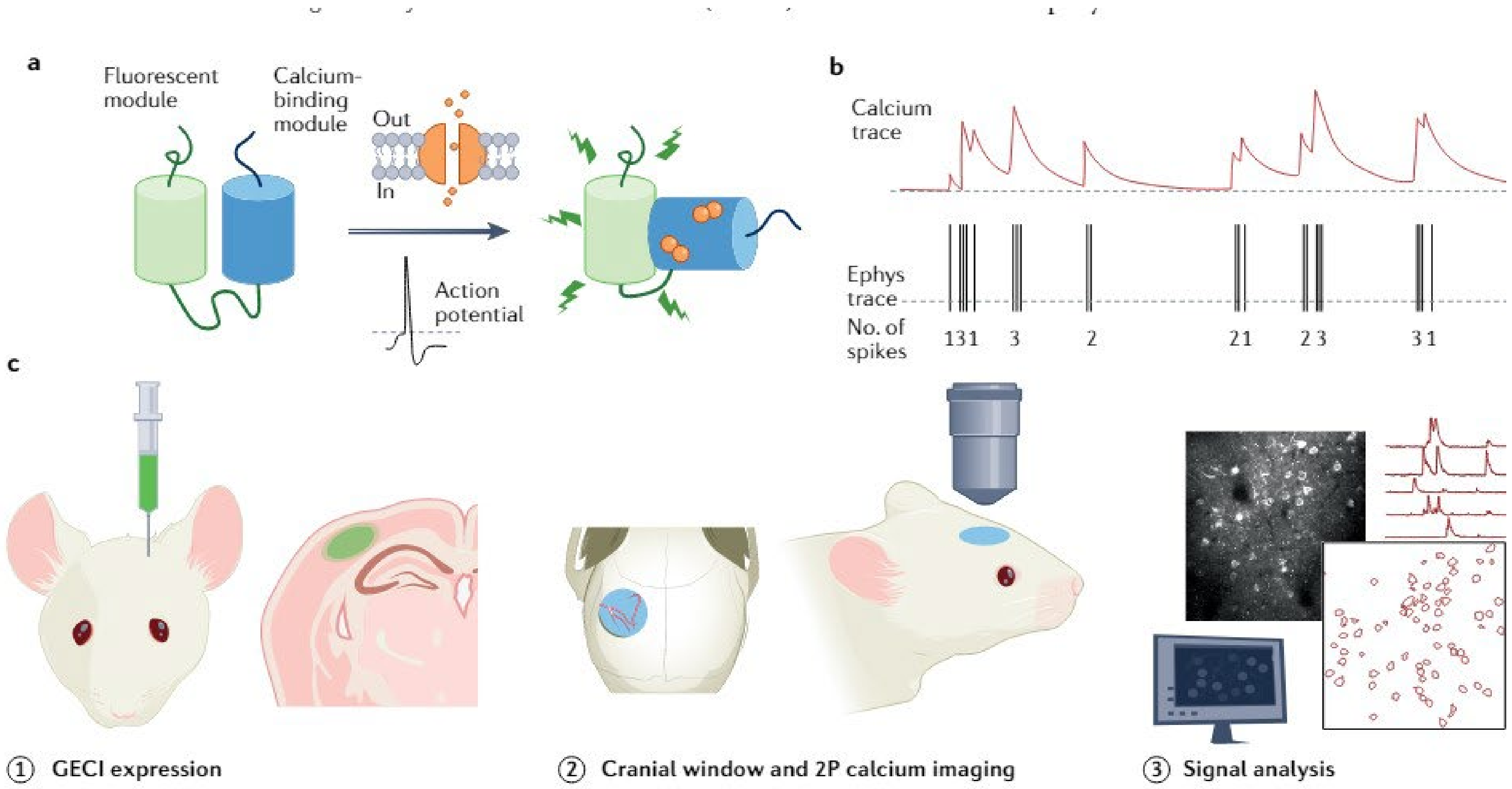
CWRU Undergraduate Neuroscience

Objectives

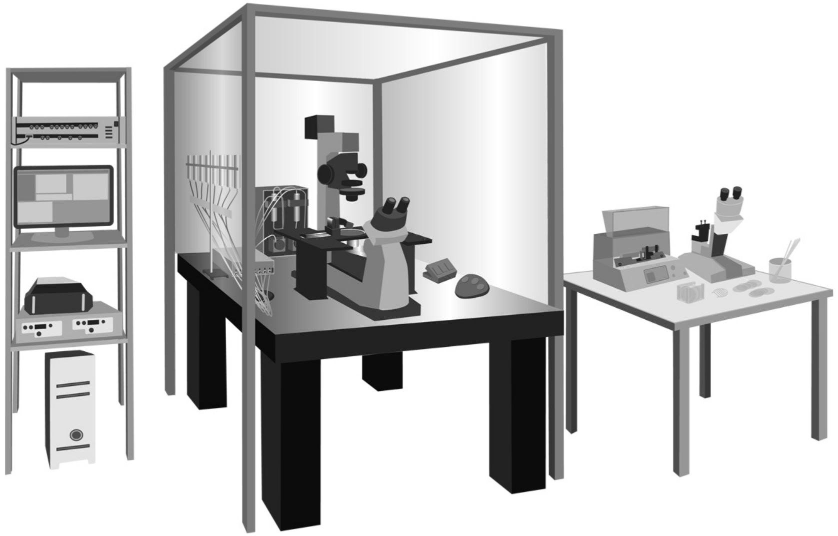
1. Understand the different methodologies used to record the brain *in vivo*
2. Understand the differences between EEG, ECoG, and LFP
3. Understand the physiology of place cells fire and reactivation during SWRs
4. Understand the importance of cell assemblies

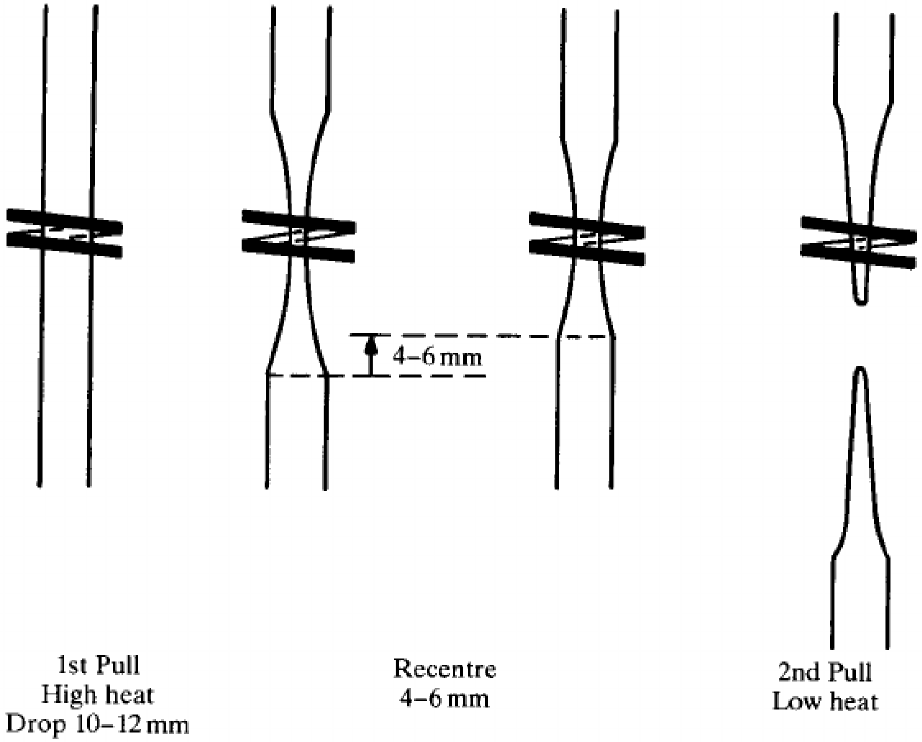
Techniques in Systems Neuroscience – Single cell recording – Calcium transients from Calcium Imaging



Grienberger…Portera-Callilau *Nature Reviews Method Primer* 2022

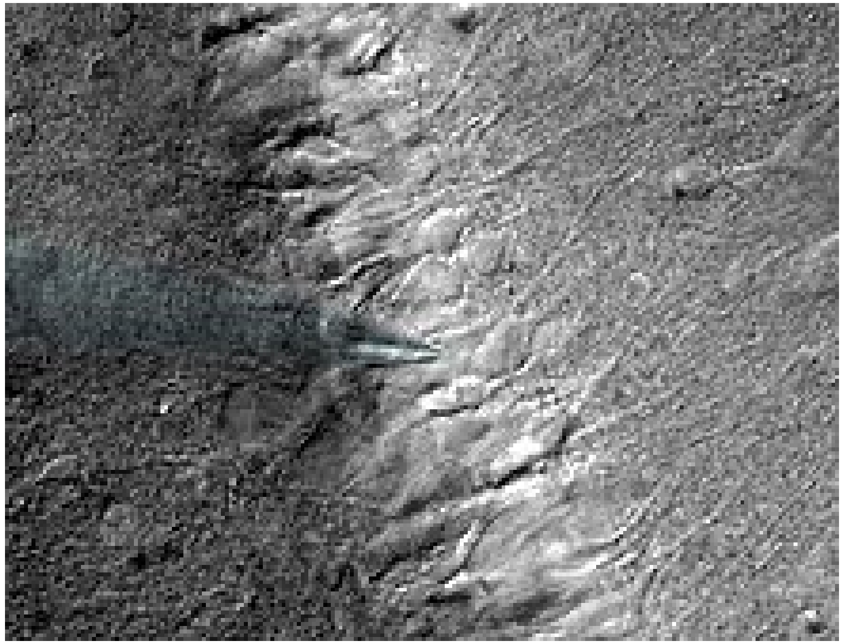
Techniques in Systems Neuroscience – Single cell recording – Patch Clamp

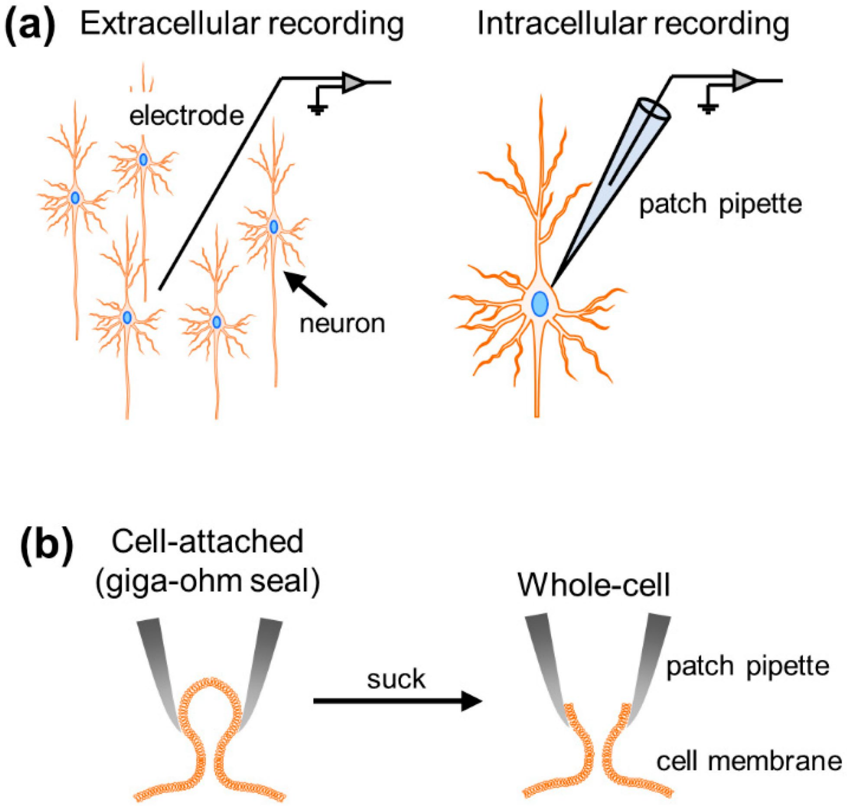


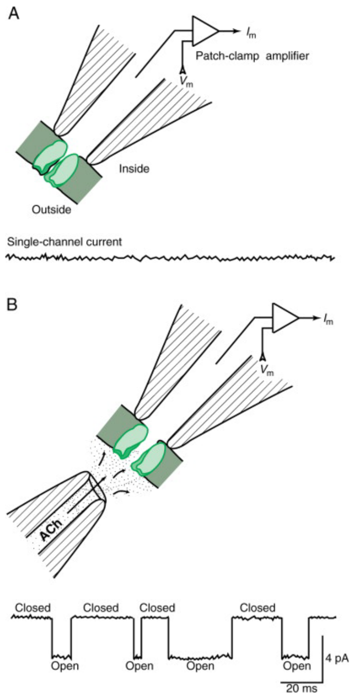


Ogden and Stanfield.(1994) *Patch clamp techniques for single channel and whole-cell recording.*

Slice In Vitro Electrophysiology

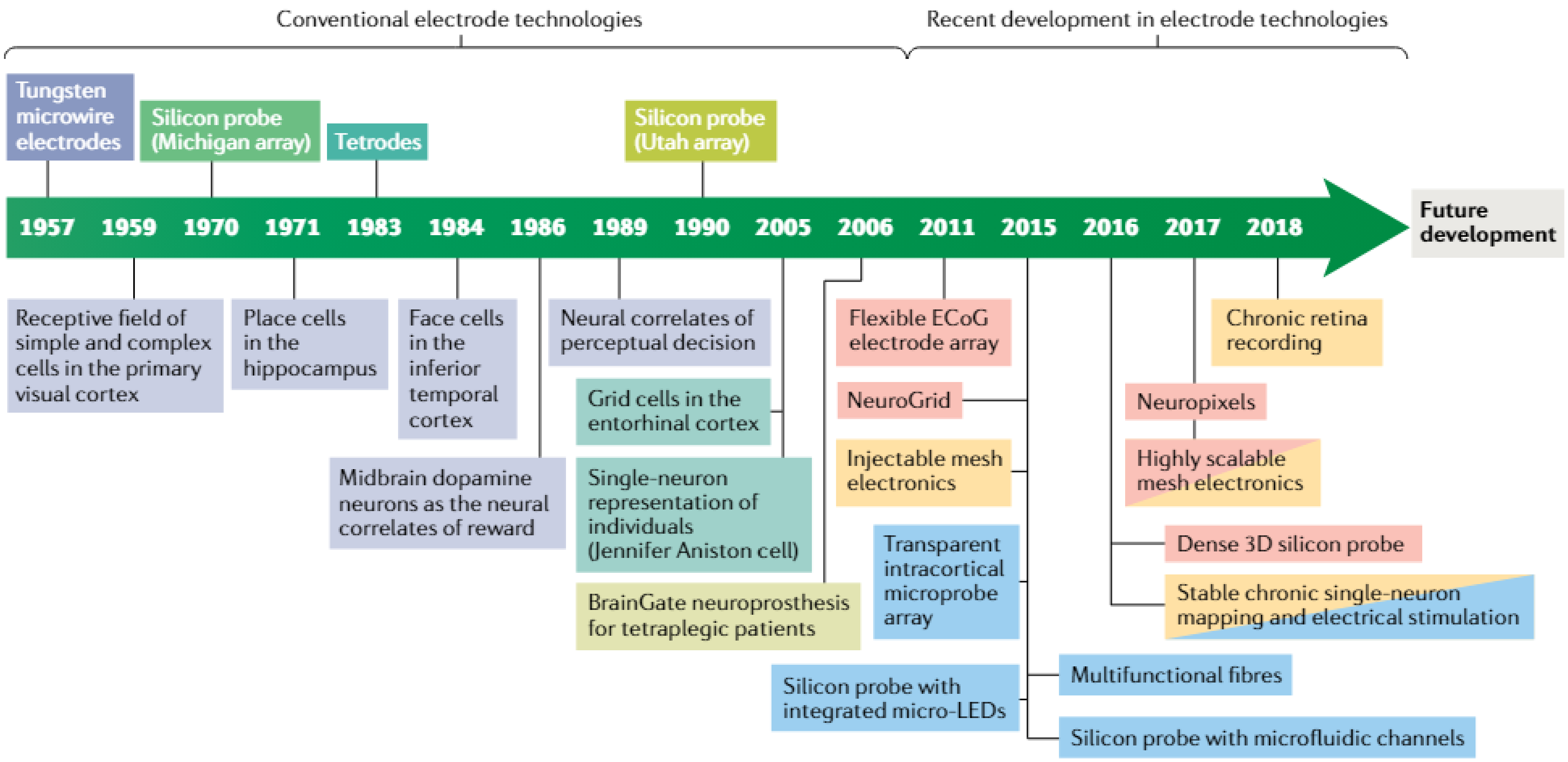






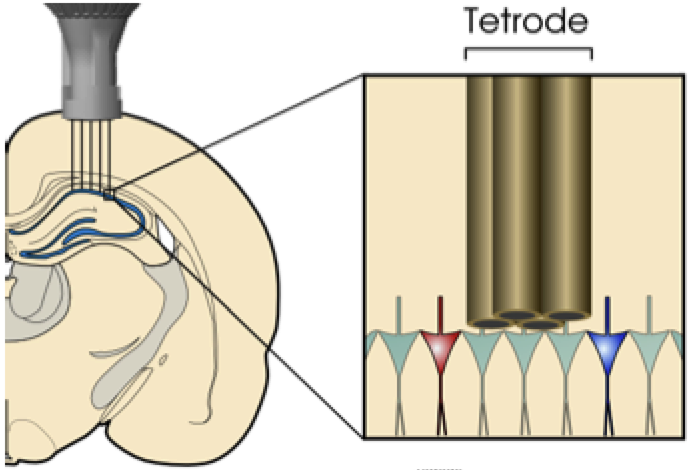
Wikipedia

Techniques in Systems Neuroscience – Single cell recording – Tetrodes and Silicon Probes



Hong and Lieber *Nature Reviews Neuroscience* 2019

Techniques in Systems Neuroscience – Single cell recording – Tetrodes and Spike Sorting



Wikipedia

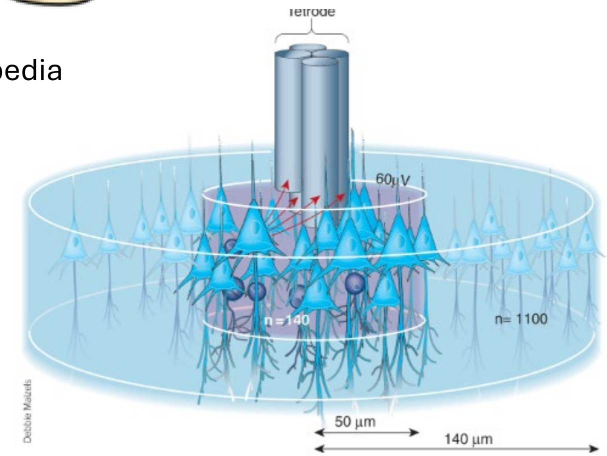
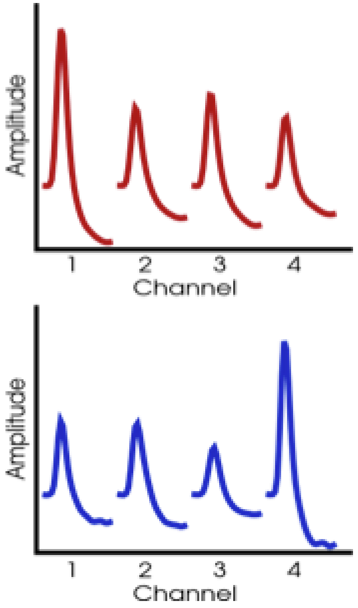
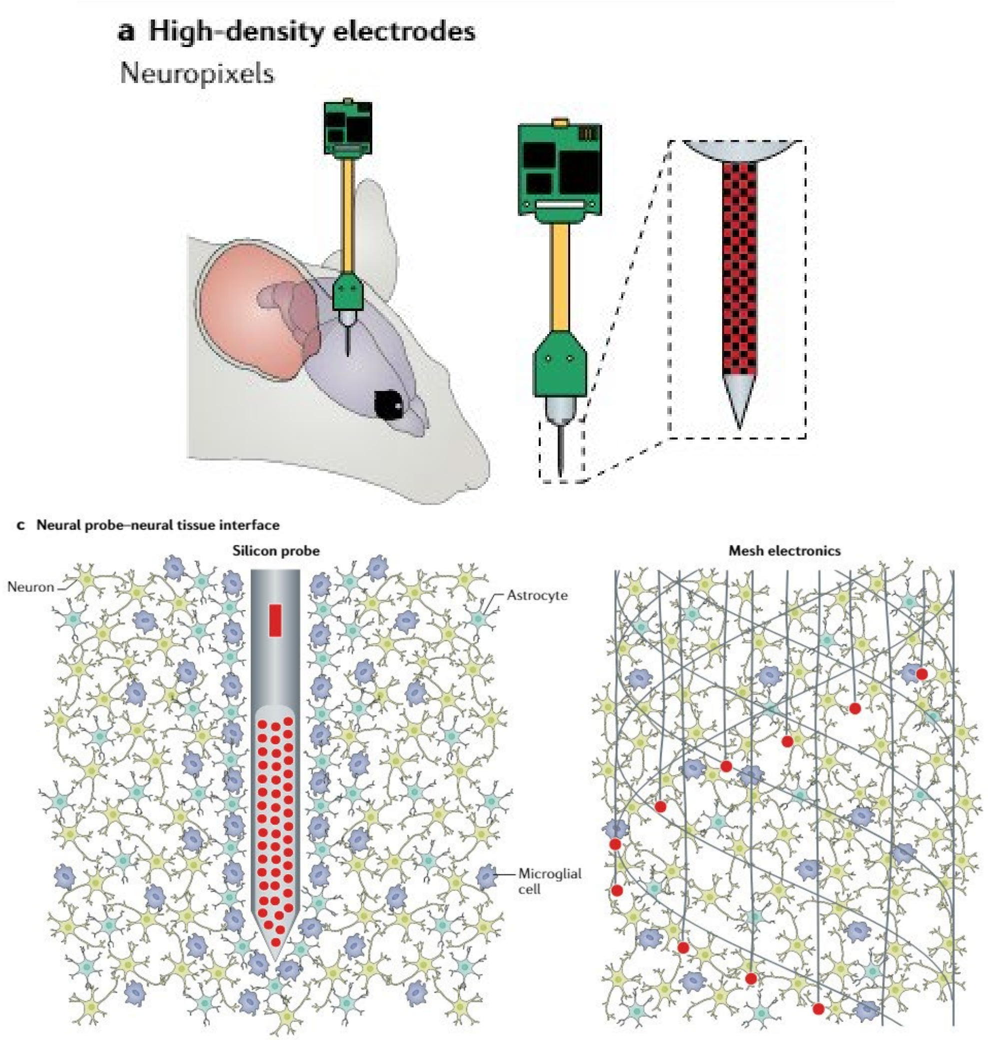


Figure 1 Unit isolation quality varies as a function of distance from the electrode. Multisite electrodes (a wire tetrode, for example) can estimate the position of the recorded neurons by triangulation. Distance of the visible electrode tips from a single pyramidal cell (triangles) is indicated by arrows. The spike amplitude of neurons (>60 μV) within the gray cylinder (50 μm radius), containing ~100 neurons, is large enough for separation by currently available clustering methods. Although the extracellularly recorded spike amplitude decreases rapidly with distance, neurons within a radius of 140 μm, containing ~1,000 neurons in the rat cortex[19,21], can be detected. Improved recording and clustering methods are therefore expected to record from larger number of neurons in the future. (Data are derived from simultaneous extracellular and intracellular recordings from the same pyramidal cells from ref. 19.)

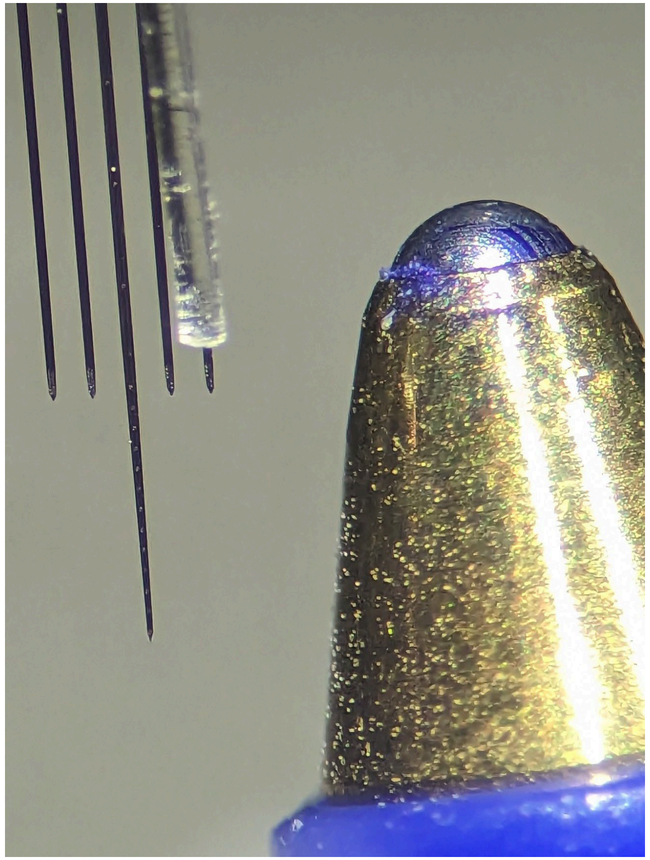
Buzsaki *Nature Neuroscience* 2004

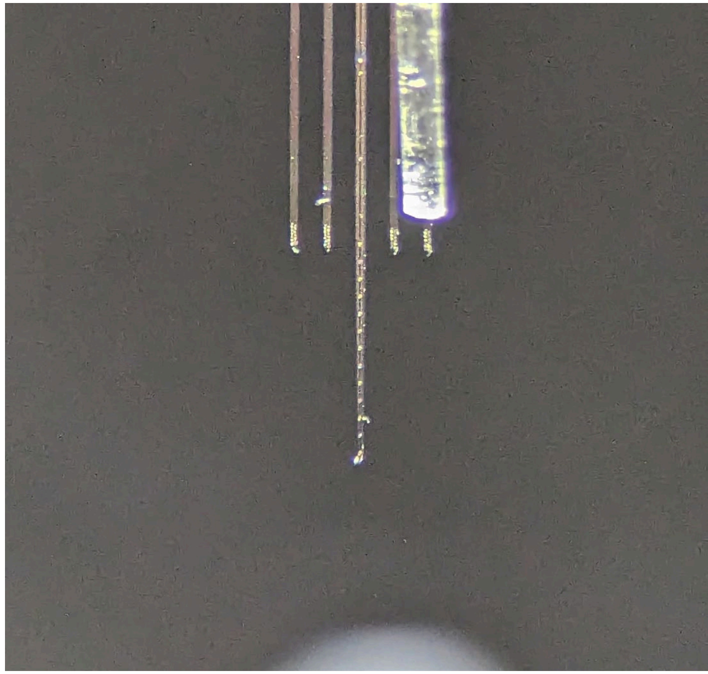


Techniques in Systems Neuroscience – Single cell recording – Tetrodes and Silicon Probes

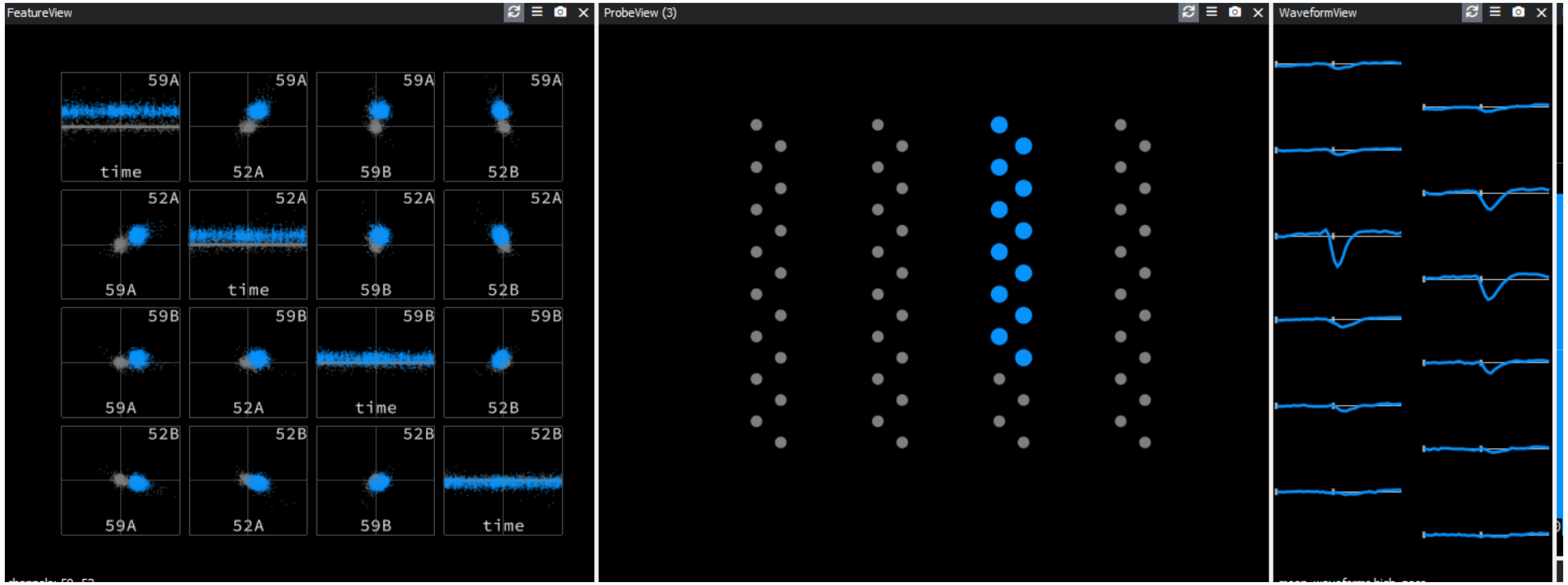


Hong and Lieber *Nature Reviews Neuroscience* 2019





Techniques in Systems Neuroscience – Single cell recording – Tetrodes and Silicon Probes



Techniques in Systems Neuroscience – Single cell recording – EEG, ECoG, LFP and Laminar Recordings

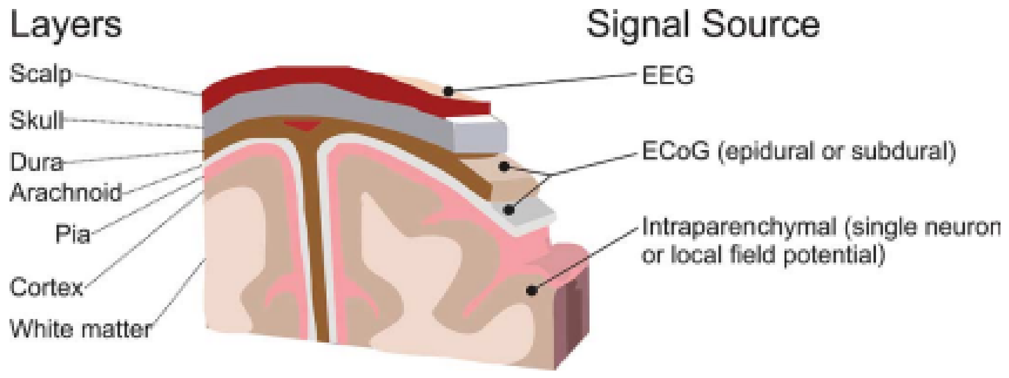
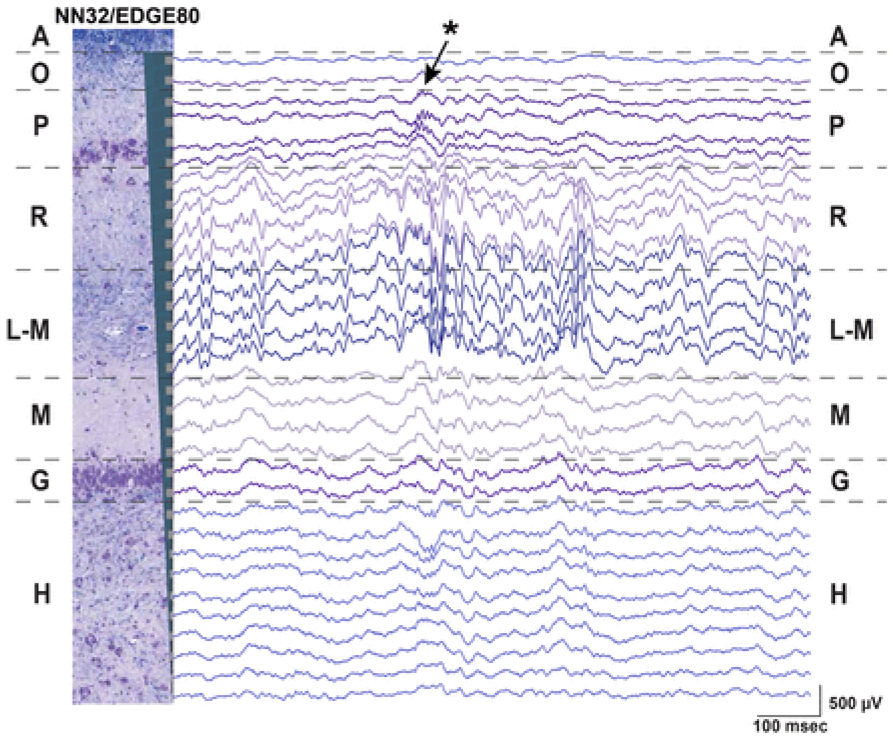


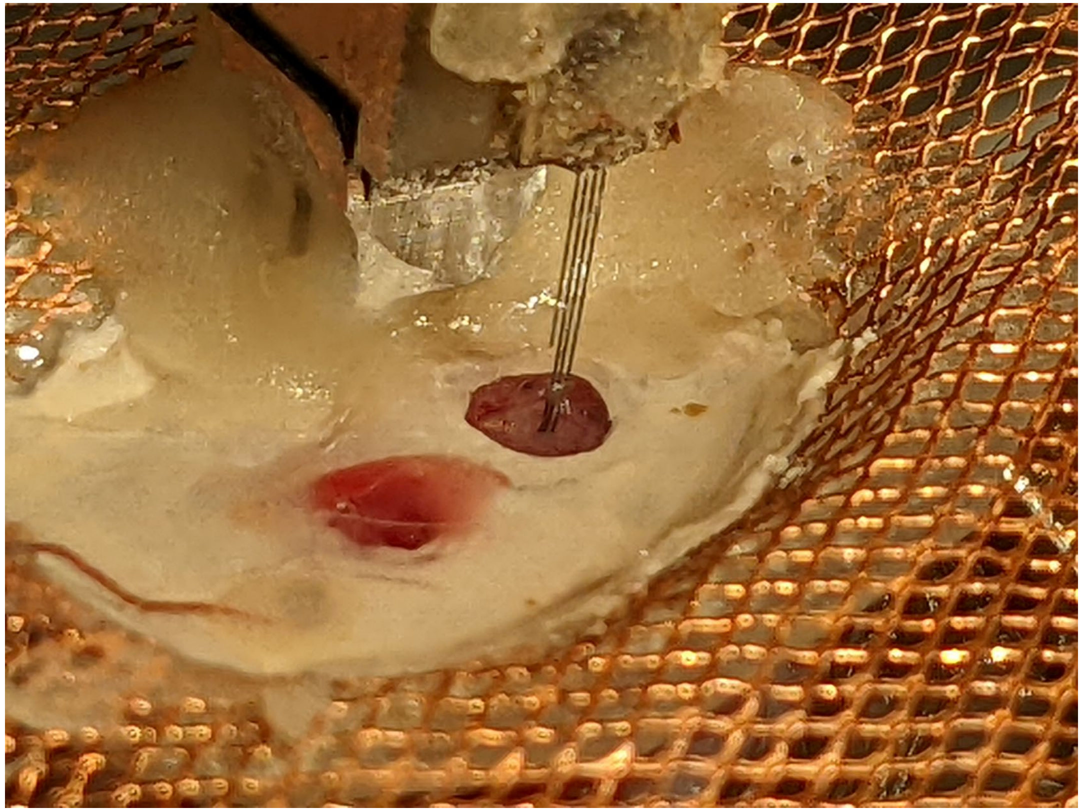
Fig. 1. Recording domains: from single-unit recordings within the brain to EEG recordings on the surface of the scalp. From [1].

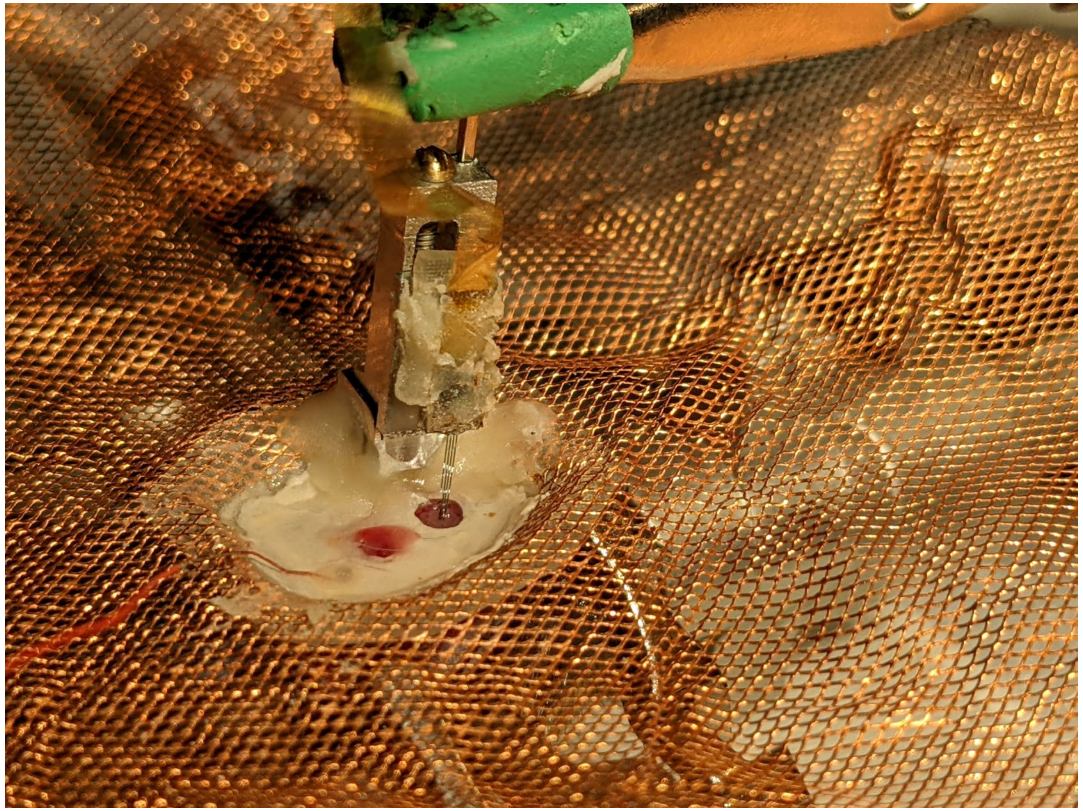
Schalk and Leuthardt *IEEE Reviews in Biomedical Engineering* 2011



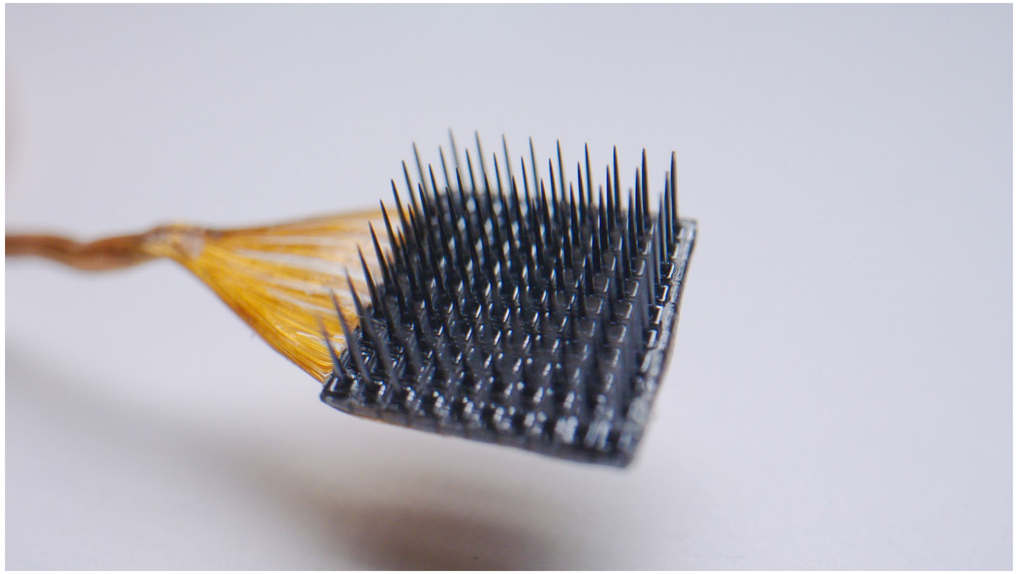
Ulyanova et al. *Frontiers in Neuroscience* 2019

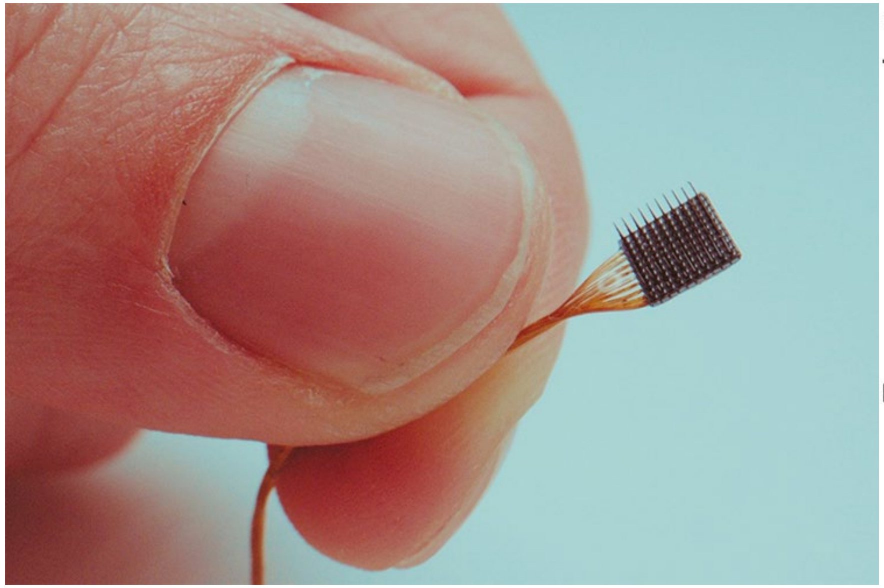
Techniques in Systems Neuroscience – Single cell recording – Silicon Probes

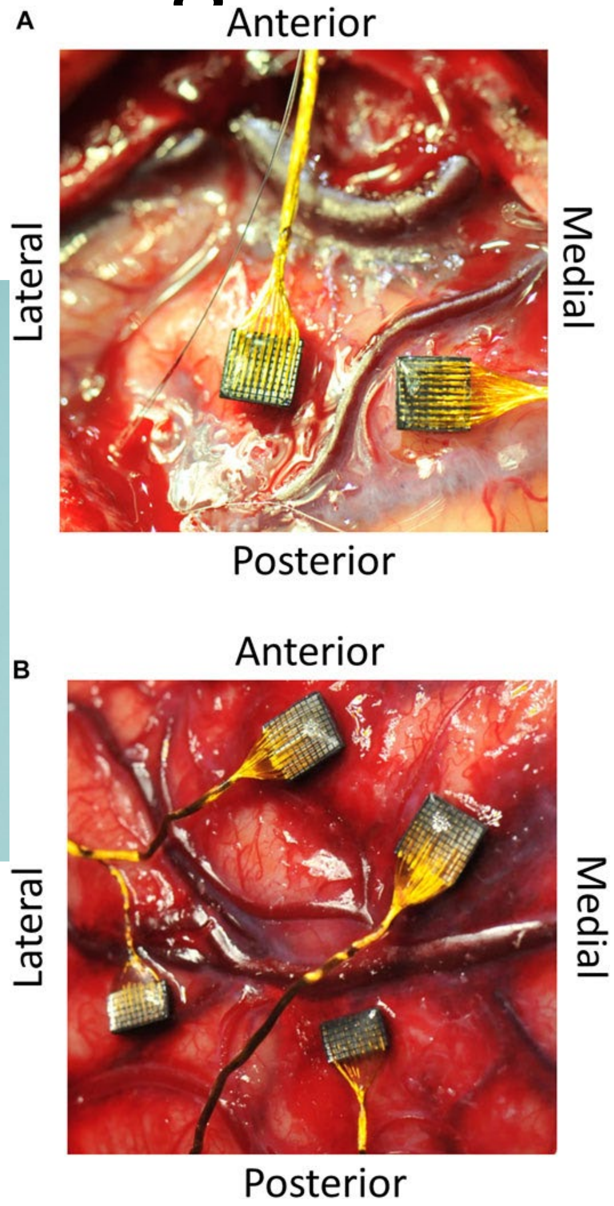




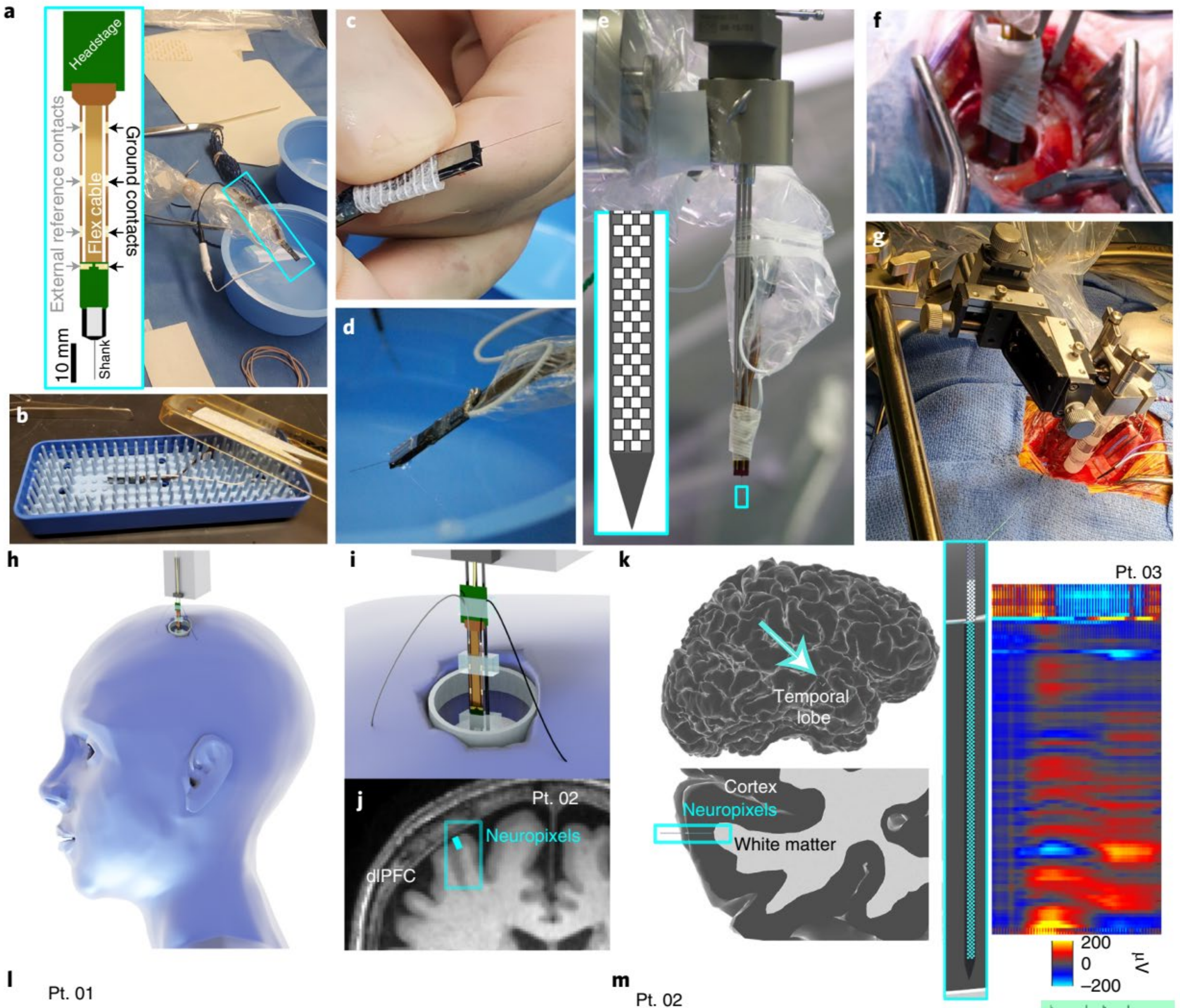
Techniques in Systems Neuroscience – Single cell recording – Utah Array





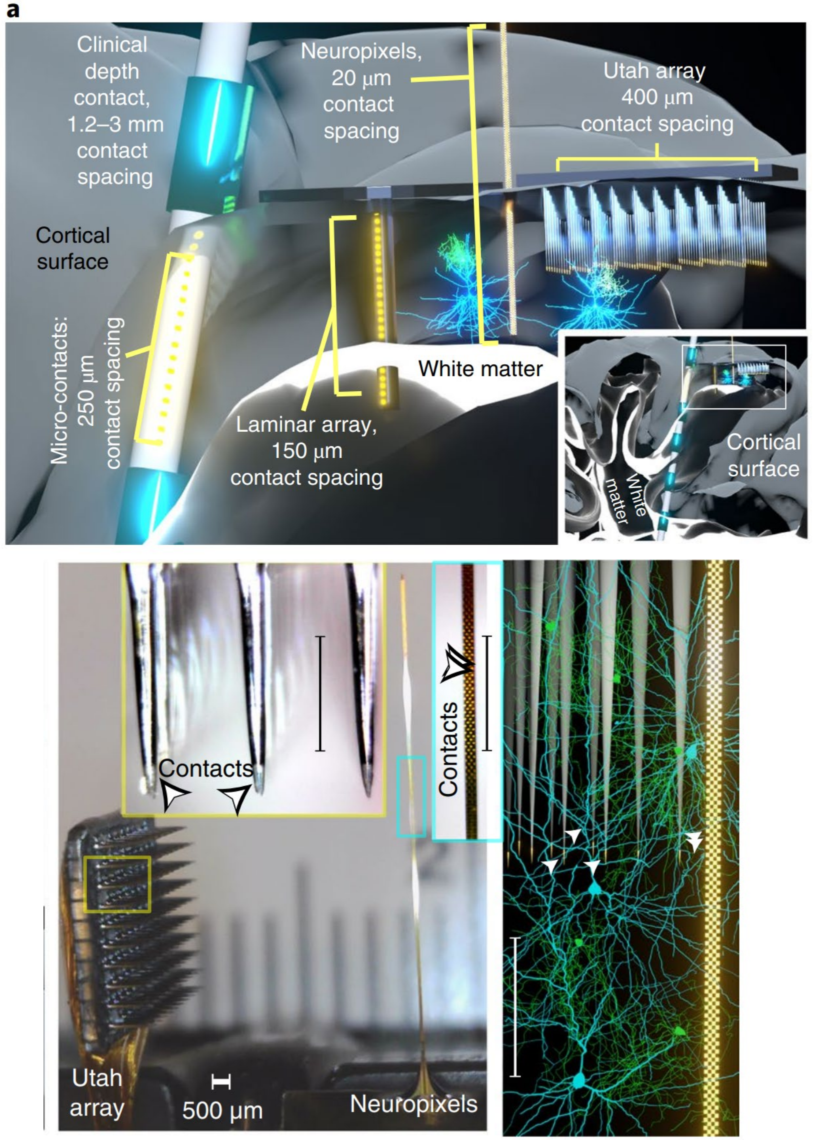


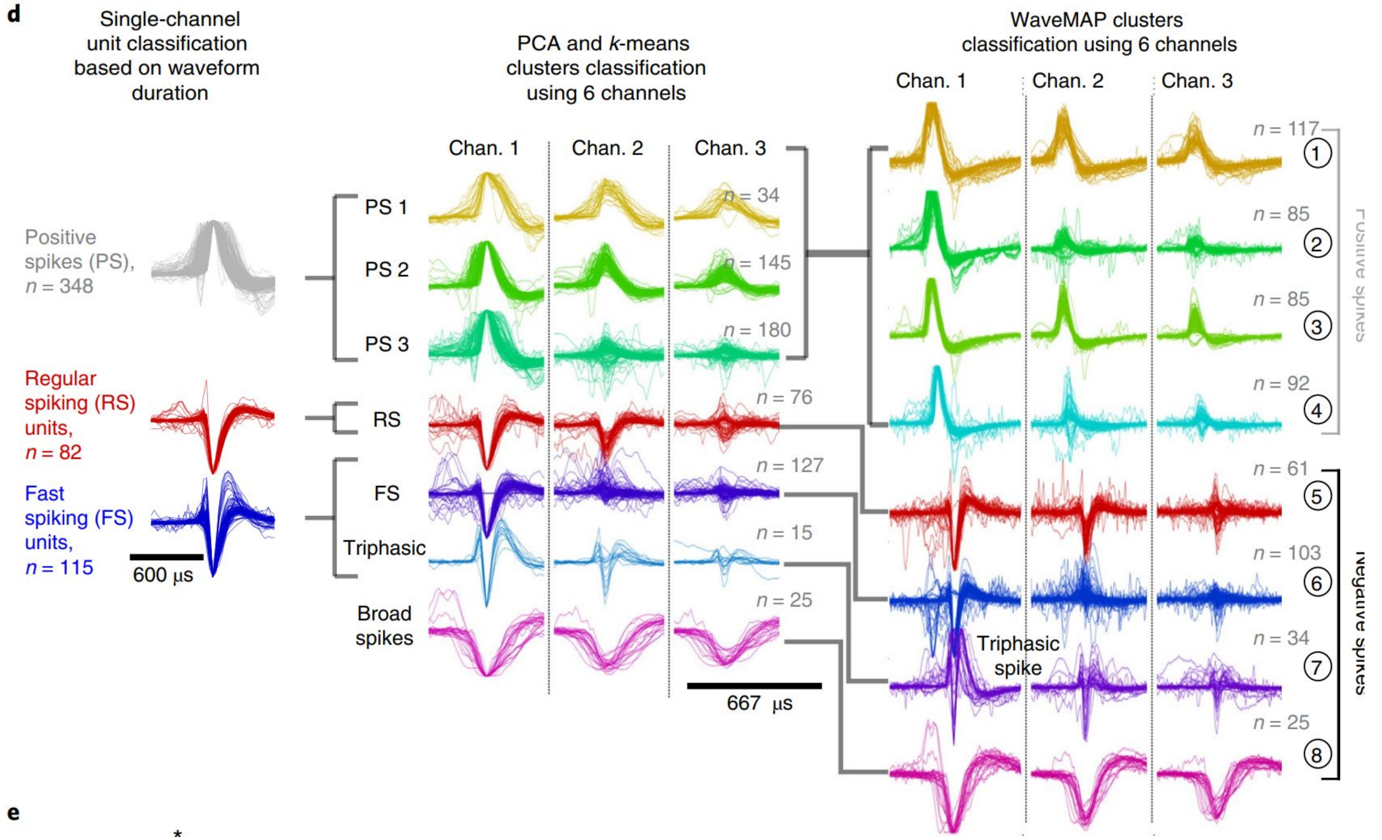
Techniques in Systems Neuroscience – Utah Array versus Silicon Probes



Paul et al. *Nature Neurosciencei* 2022c

Techniques in Systems Neuroscience – Utah Array versus Silicon Probes

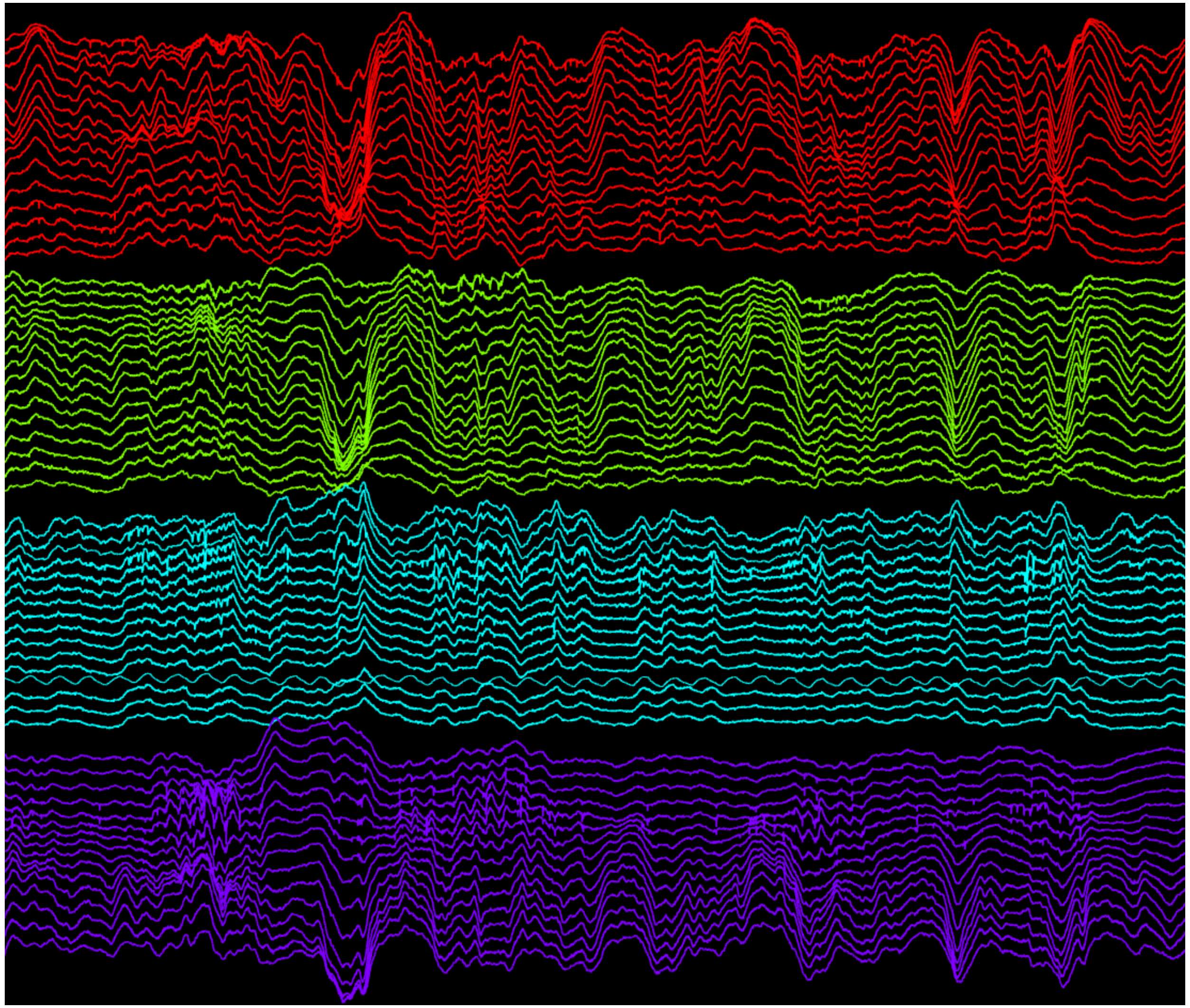




Schalk and Leuthardt *IEEE Reviews in Biomedical Engineering* 2011

So, what are we recording? And how do we make sense of it?

Techniques in Systems Neuroscience – Single cell recording – Hippocampus sleep recording



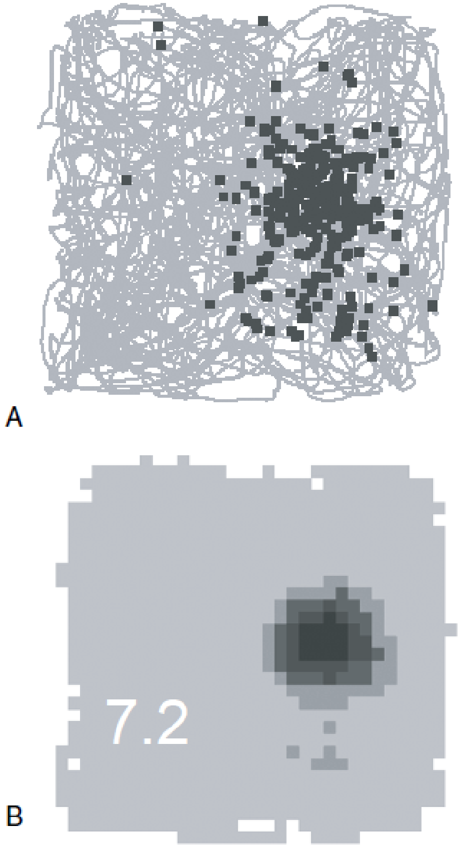
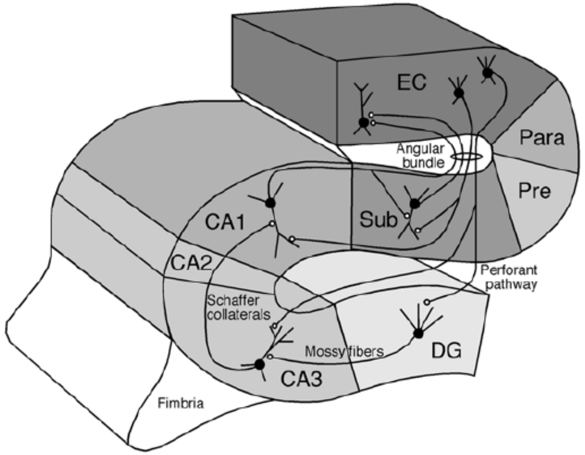
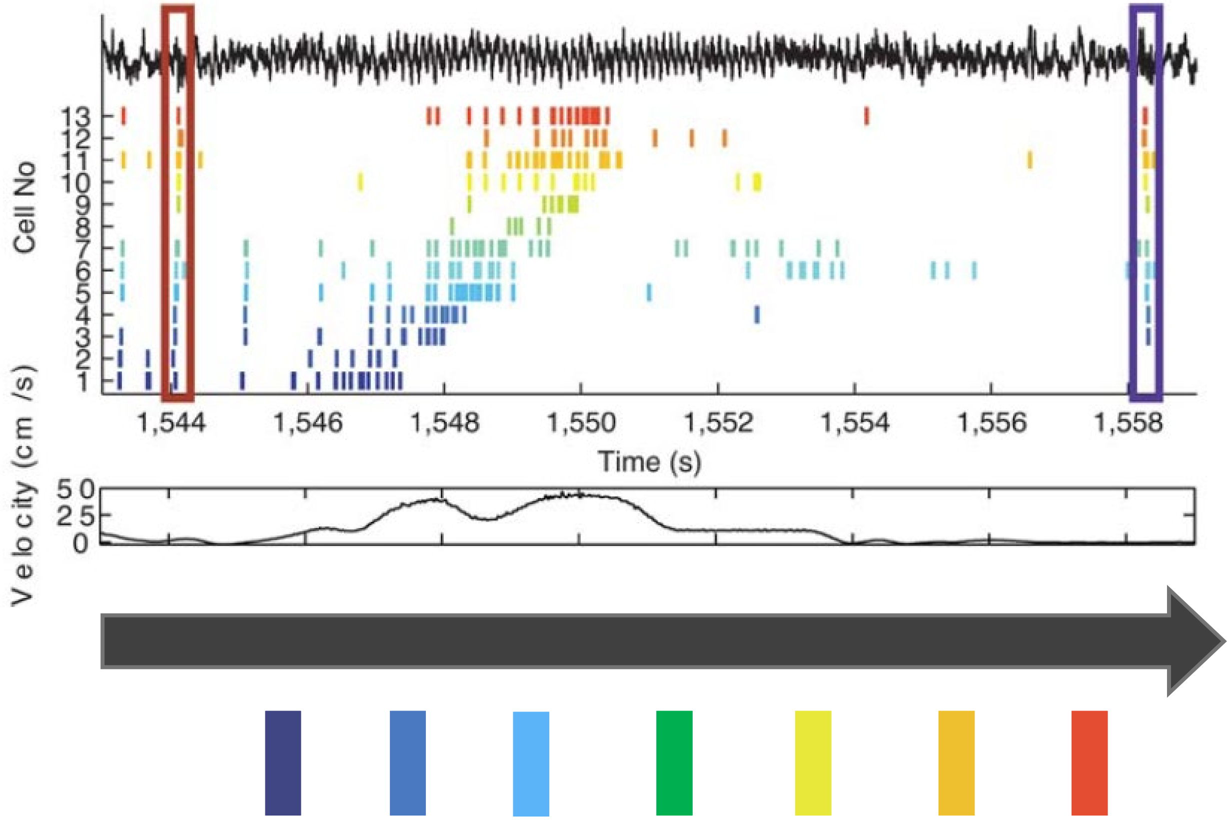


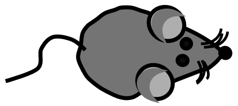
Figure 11–6. Firing field of a CA1 place cell. *A.* Raw data from a rat foraging for food in a square box for 10 minutes. Gray line traces the animal's path through the environment; black boxes show firing of place cell. *B.* Place firing field as a grayscale map where darker colors represent higher firing rates. Inset number in white gives the peak firing rate. (*Source:* After Wills et al., 2005, with permission.)



Andersen et al. *The Hippocampus Book* 2007. Oxford University Press

Hippocampus Place Cell Progression through a Linear Maze – rate coding





Diba and Buzsáki *Nature Neuroscience* 2007

Hippocampus Place Cell Progression through a Linear Maze – temporal coding (ie Phase Procession)

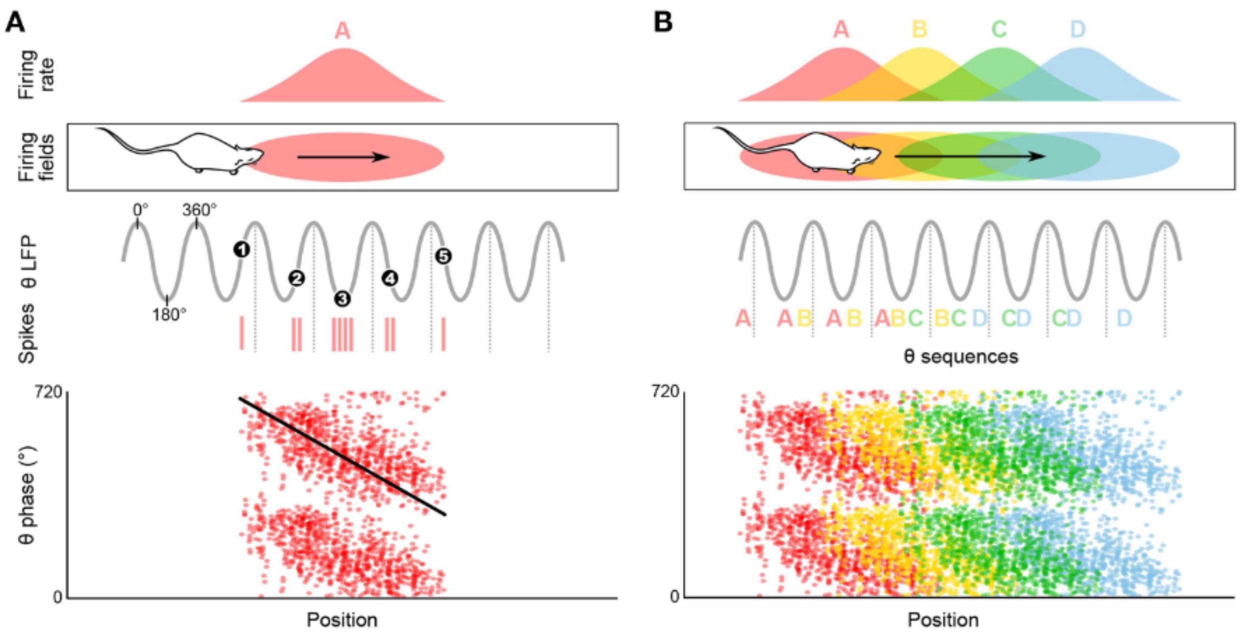


FIGURE 2 | Temporal coding in the hippocampus and emergence of theta sequences. **(A)** Theta spike phase precession. Top, schematic representation of the temporal organization of successive place cell bursts relative to theta as a rat runs along a linear track. When the rat enters the firing field (pink ellipse), the cell fires near the end of the theta cycle, i.e., with a phase of ~360°. As the rat progresses through the field, bursts occur on earlier and earlier phases (red vertical ticks, action potentials; black numbered dots, mean burst times within individual theta cycles). Bottom, phase precession plot. For each spike, phase is represented as a function of position (tilted black line, best linear-circular regression line). **(B)** Top, four schematic overlapping firing fields. Middle, in their overlap region the cells discharge in sequence (A, AB, ABC, etc.) within each theta cycle, reflecting the order of field traversal at a compressed time-scale. Bottom, these past-present-future "sweeps" may require coordination between individual phase precessing cells.

Drieu and Zugaro *Frontiers in Cellular Neuroscience* 2019

Hippocampus Place Cell Progression through a Linear Maze – temporal coding (ie Phase Procession)

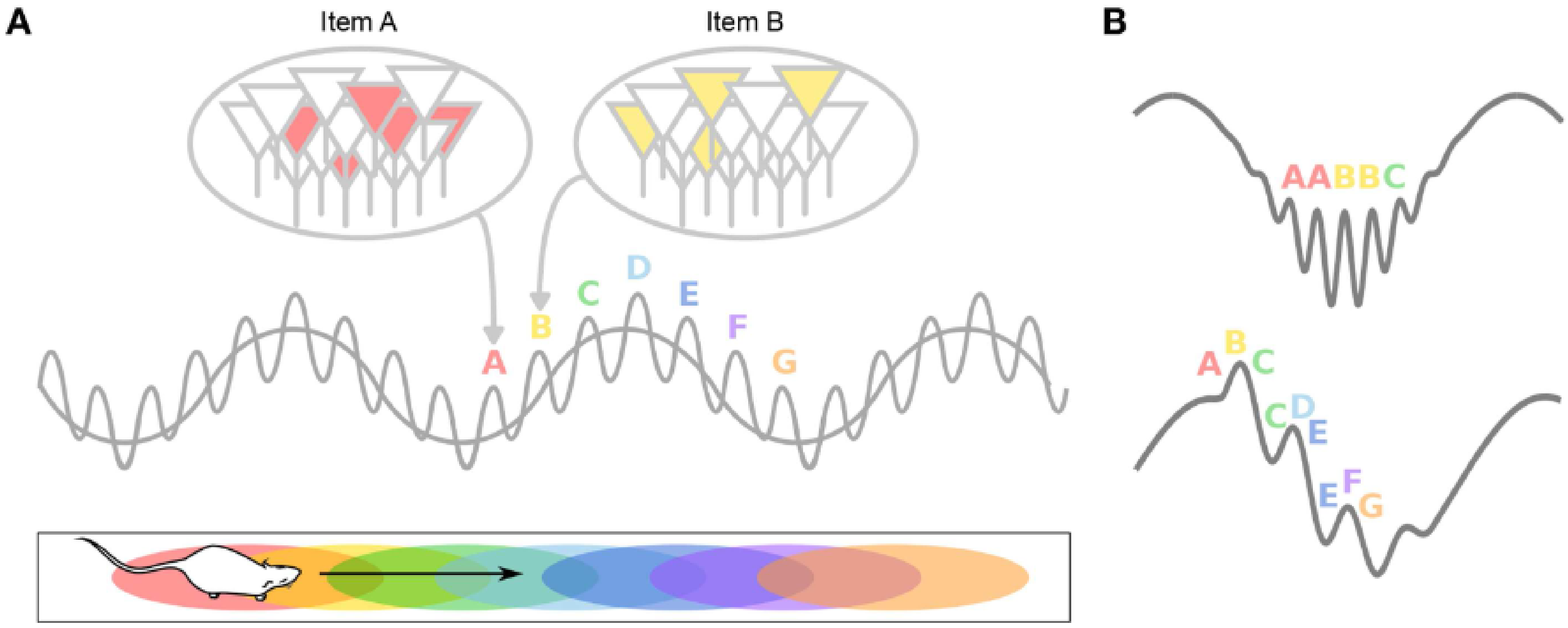
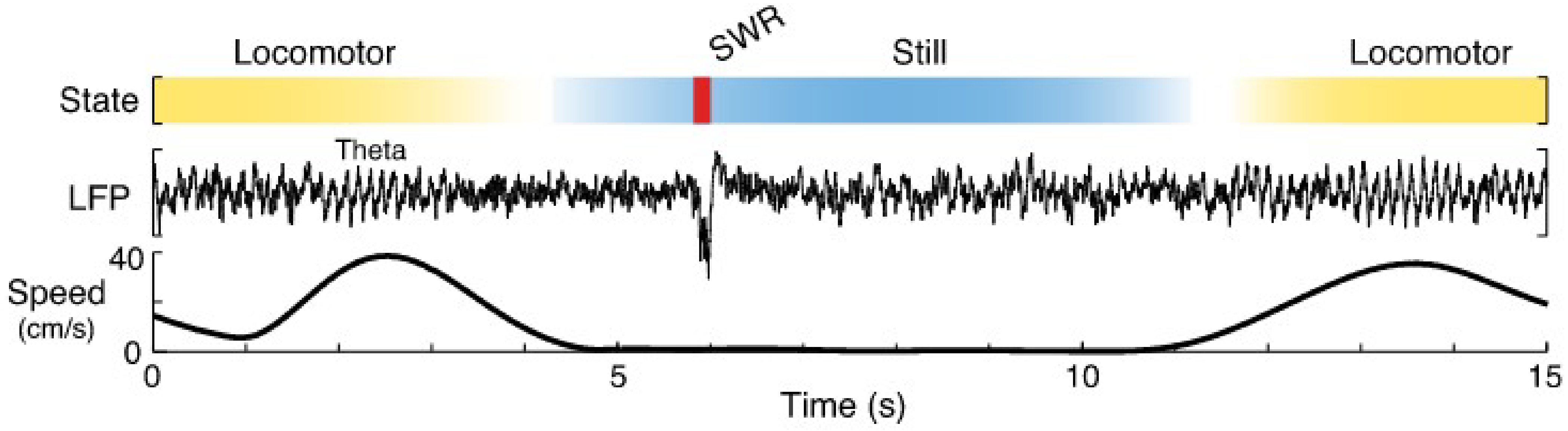


FIGURE 4 | Theta-gamma neural code. **(A)** Individual memory representations (cell assemblies, identified by letters) are repeatedly activated within each new theta cycle. The gamma rhythm separates the respective representations in time. The number of gamma cycles per theta cycle determines the span of working memory. **(B)** If discrete locations (i.e., A–G) are encoded within individual gamma cycles, longer paths would be encoded during fast gamma than during slow gamma. Alternatively, slow (but not fast) gamma cycles encode sequences of locations, rather than single locations. This results in longer paths encoded during slow gamma than during fast gamma.

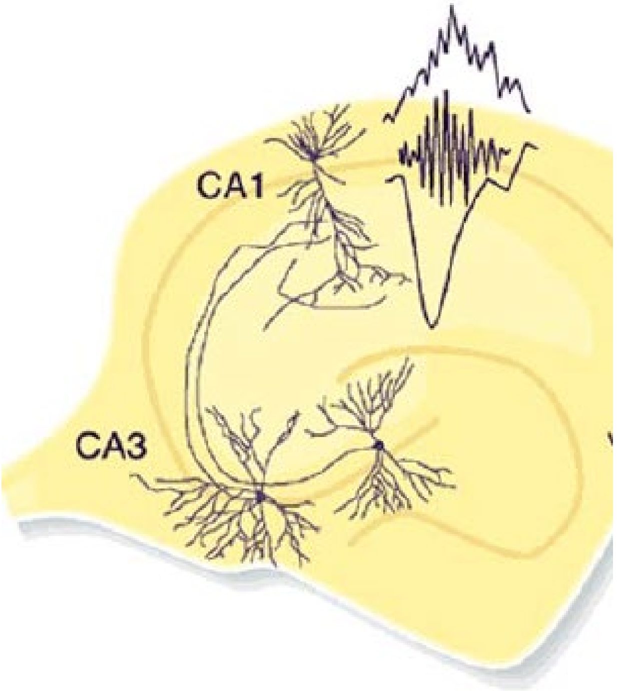
Drieu and Zugaro *Frontiers in Cellular Neuroscience* 2019

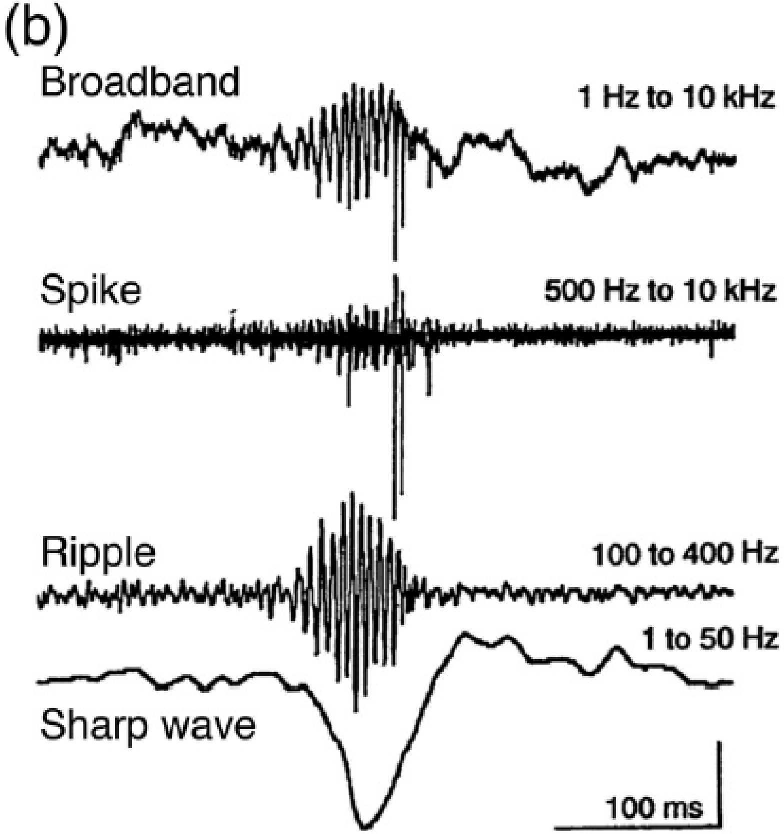
Hippocampus States – Theta and SWRs

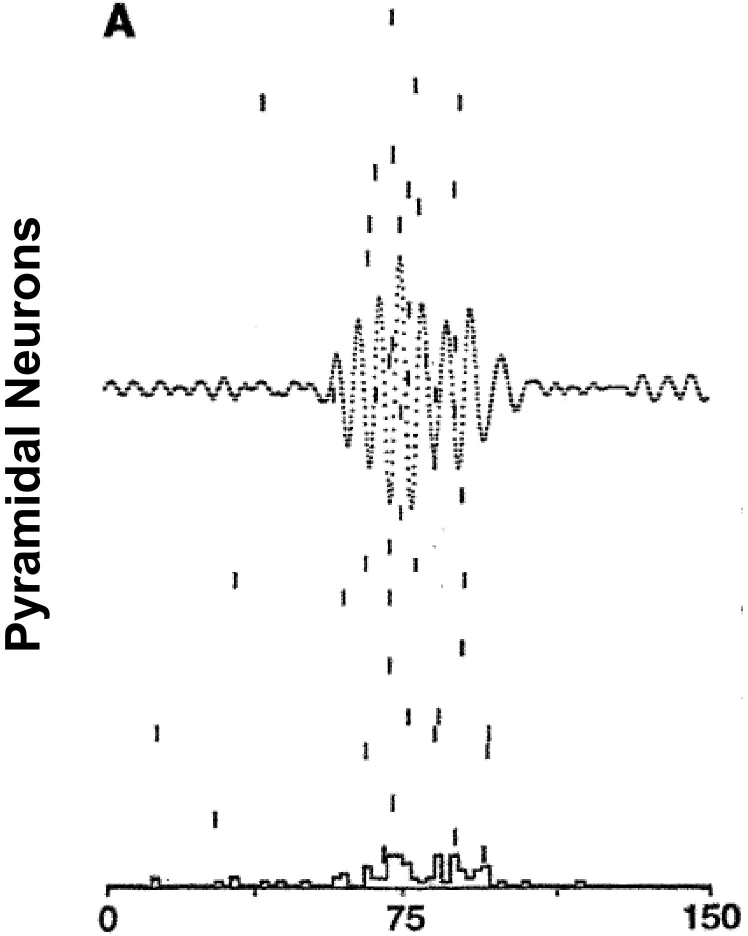


Diba and Buzsáki *Nature Neuroscience* 2007

Hippocampus Place Cell Progression through a Linear Maze – Sharp Wave Ripples reactivation state

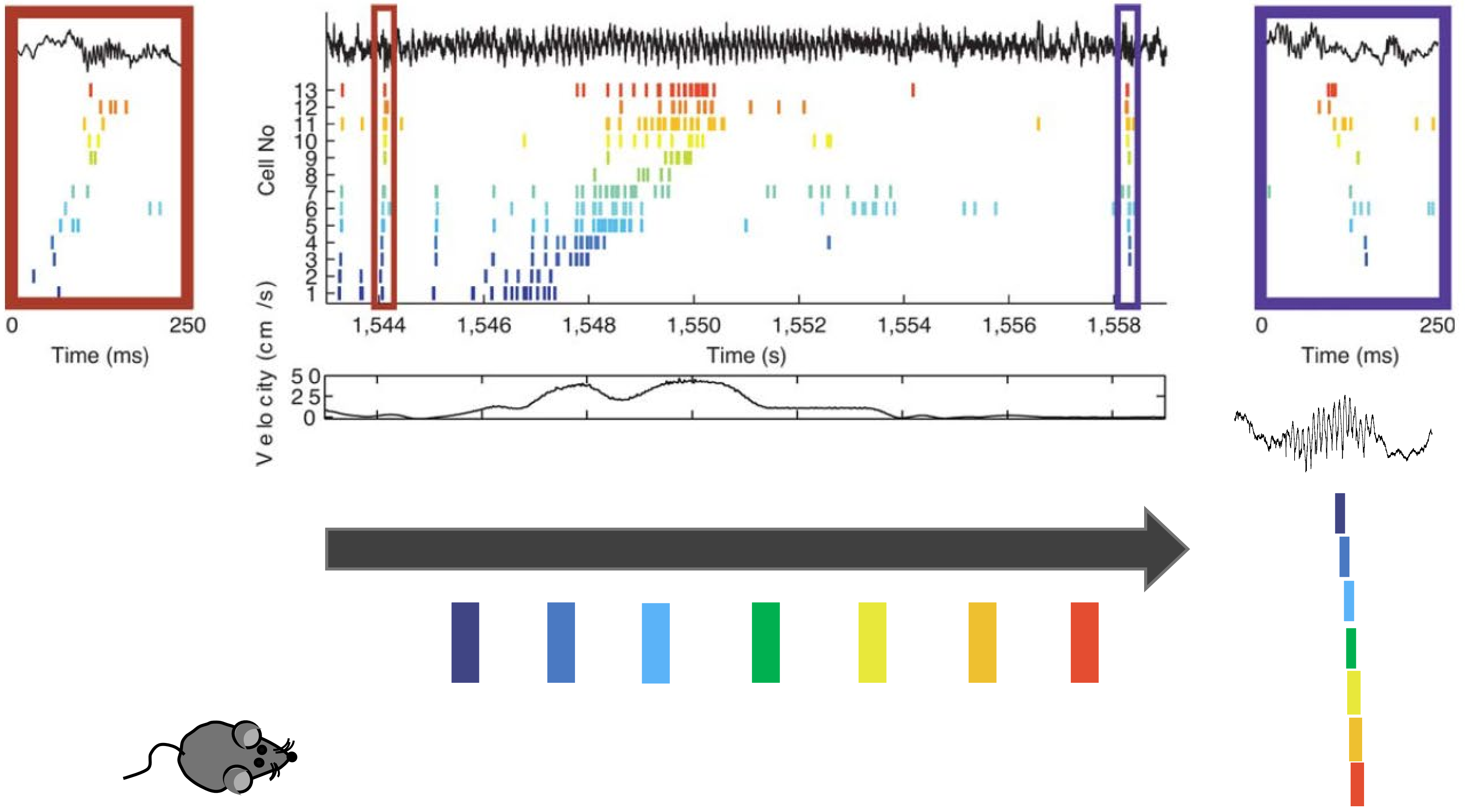






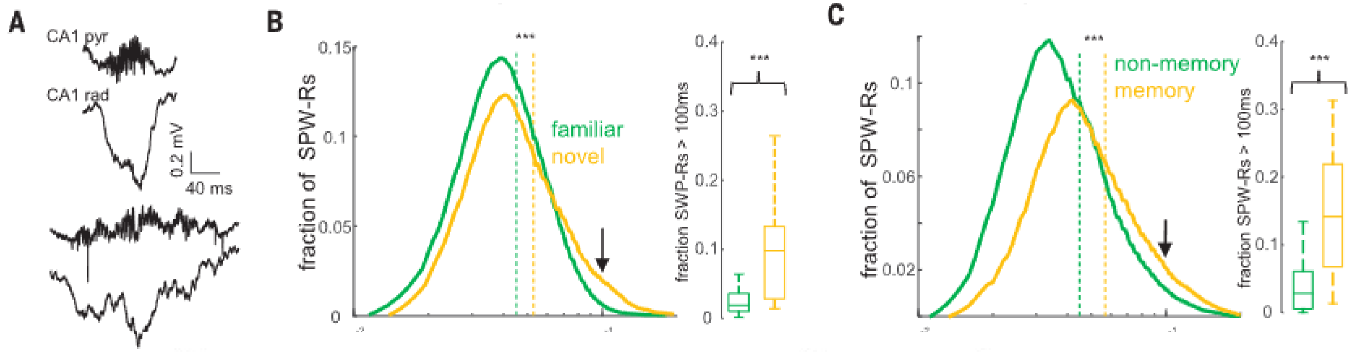
Buzsáki and Chobrak *Nat. Neuroscience* 2005
Buzsáki *Progress in Neurobiology* 1984
Buzsáki *Brain Research* 1986
Buzsáki…Wise *Science* 1992

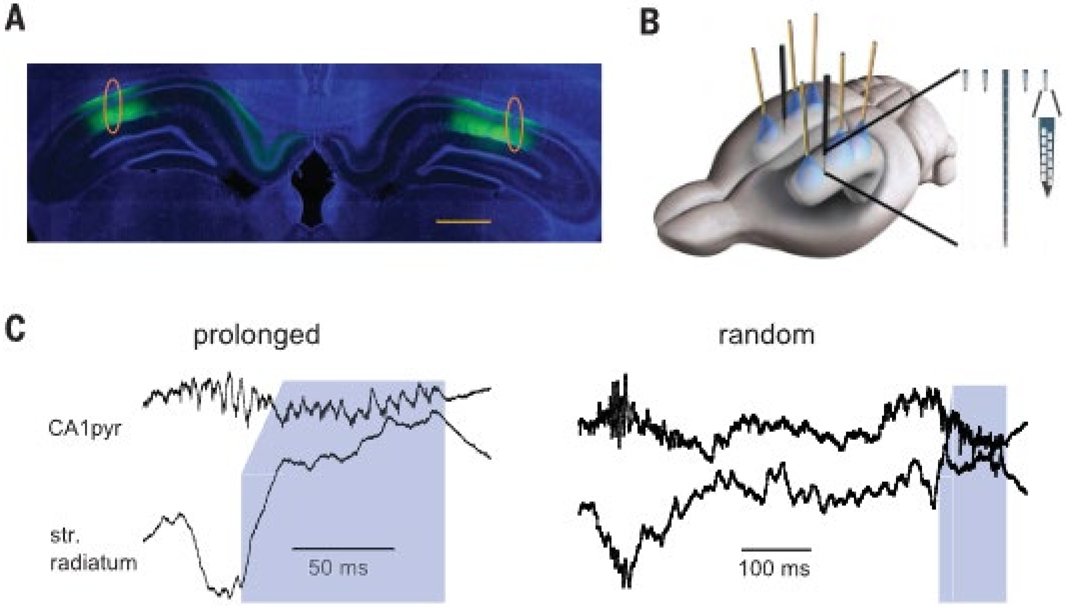
Hippocampus Place Cell Progression through a Linear Maze – Sharp Wave Ripples reactivate place cells

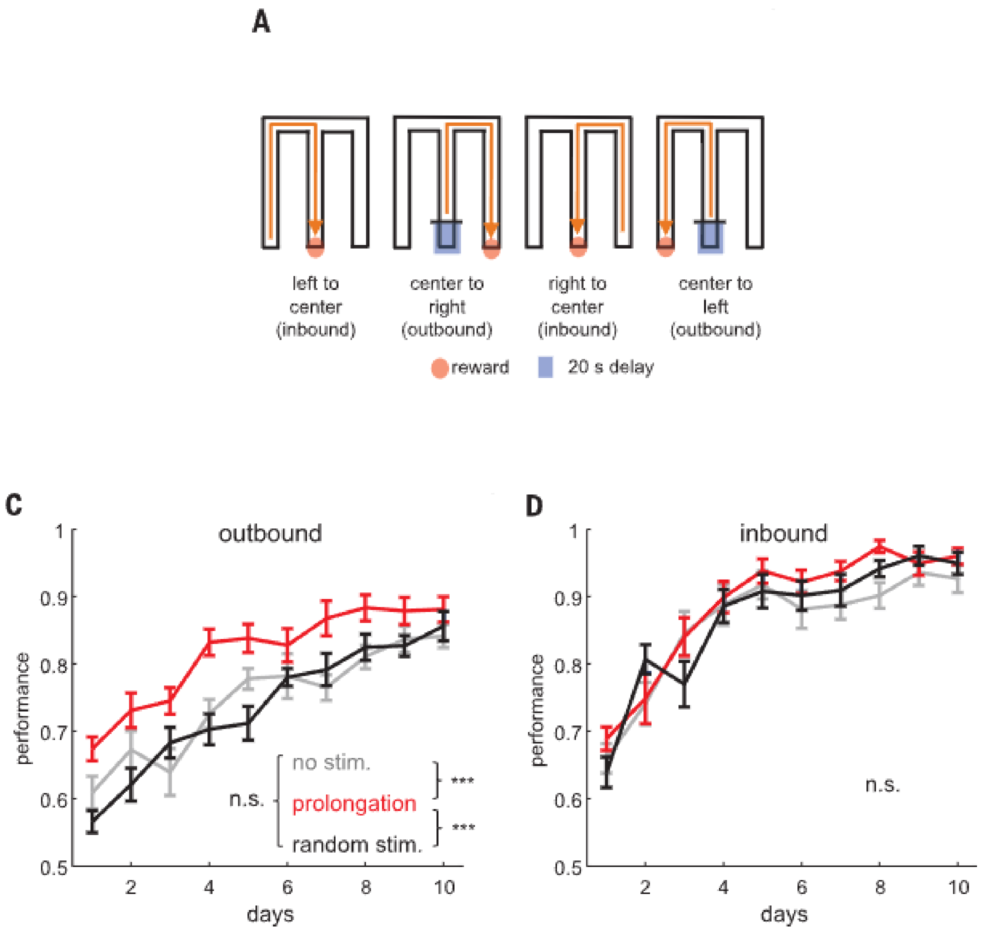


Diba and Buzsáki *Nature Neuroscience* 2007

Increasing the Length of Awake SWRs Artificially Increases Spatial Memory

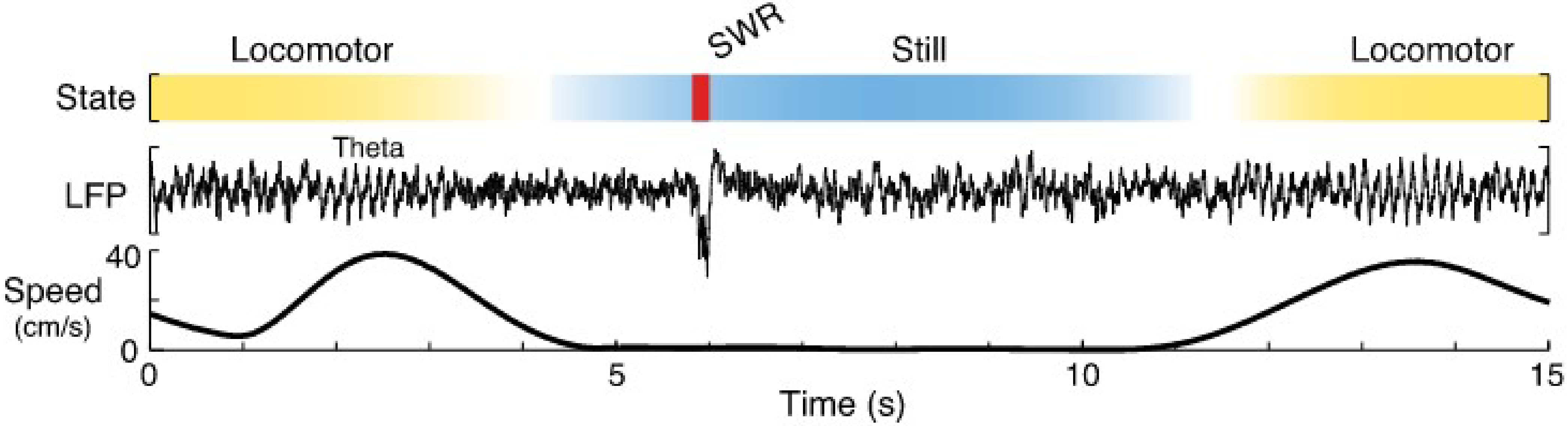






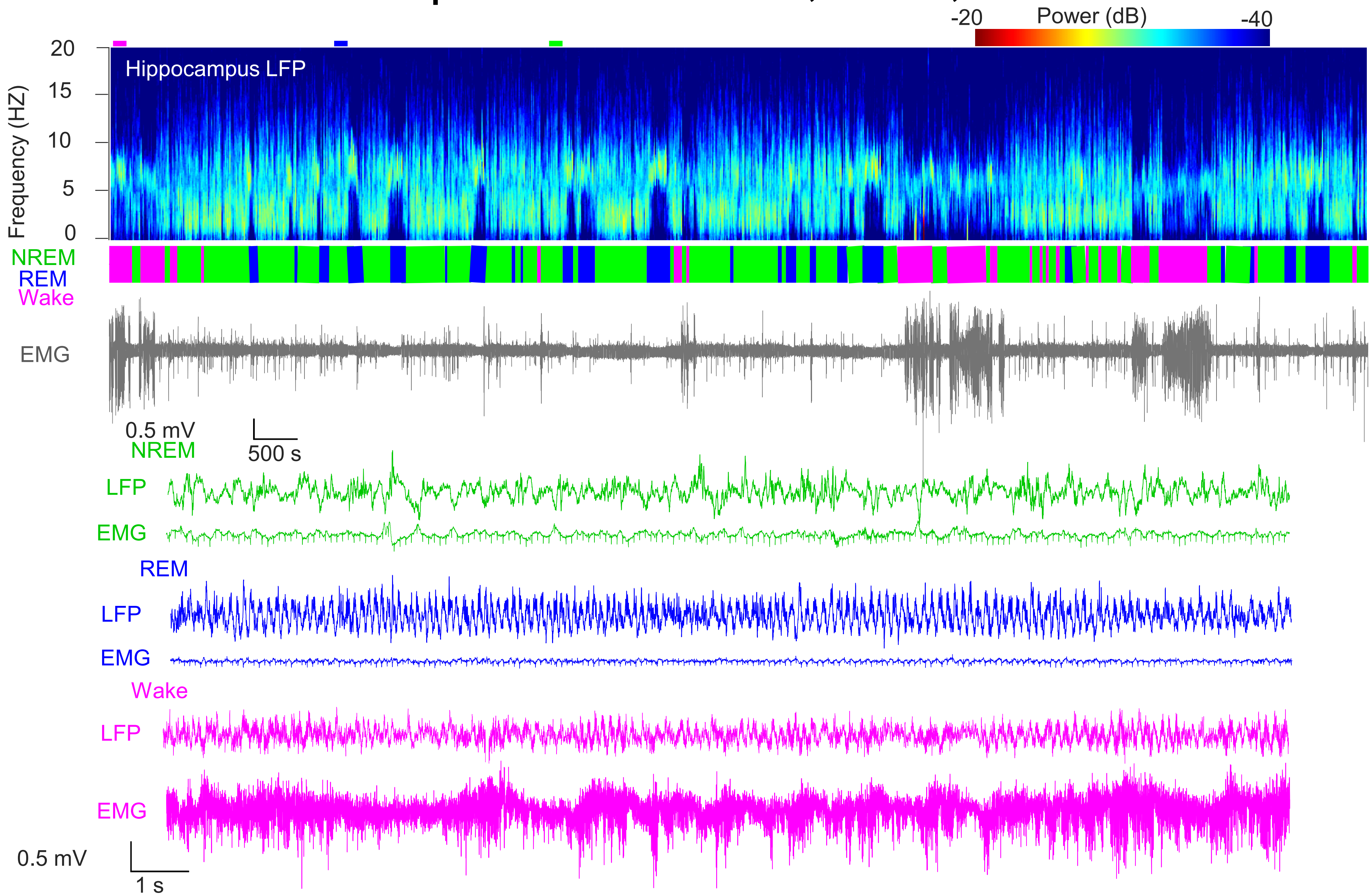
Fernandez-Ruiz, Oliva *Science* 2017

Hippocampus States – Theta and SWRs



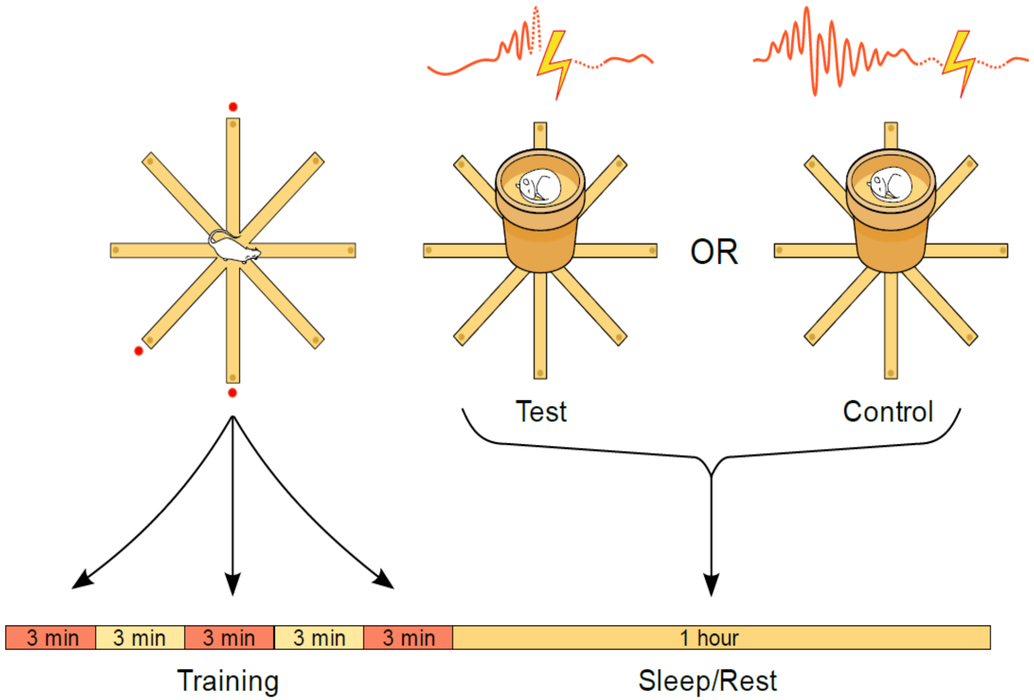
Diba and Buzsáki *Nature Neuroscience* 2007

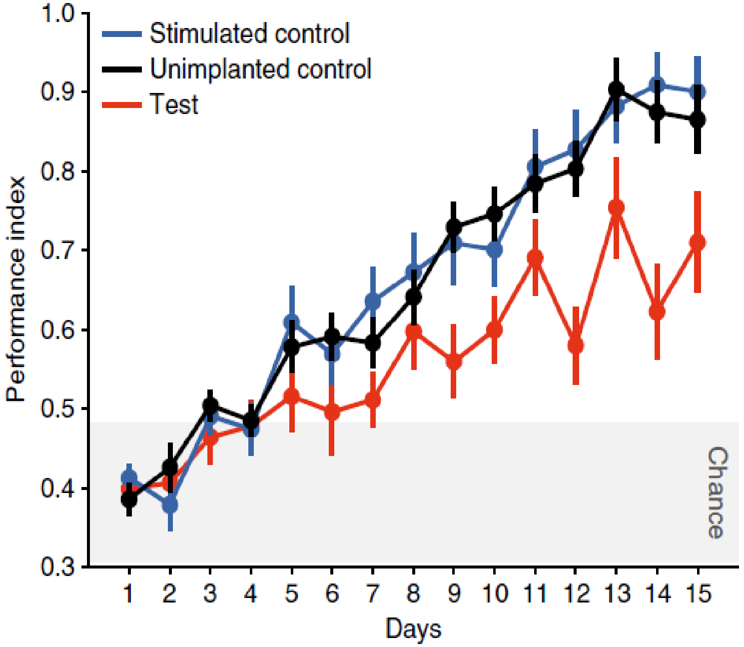
Sleep States – Wake, REM, NREM



Robinson et al. *The Journal of Neuroscience* 2021

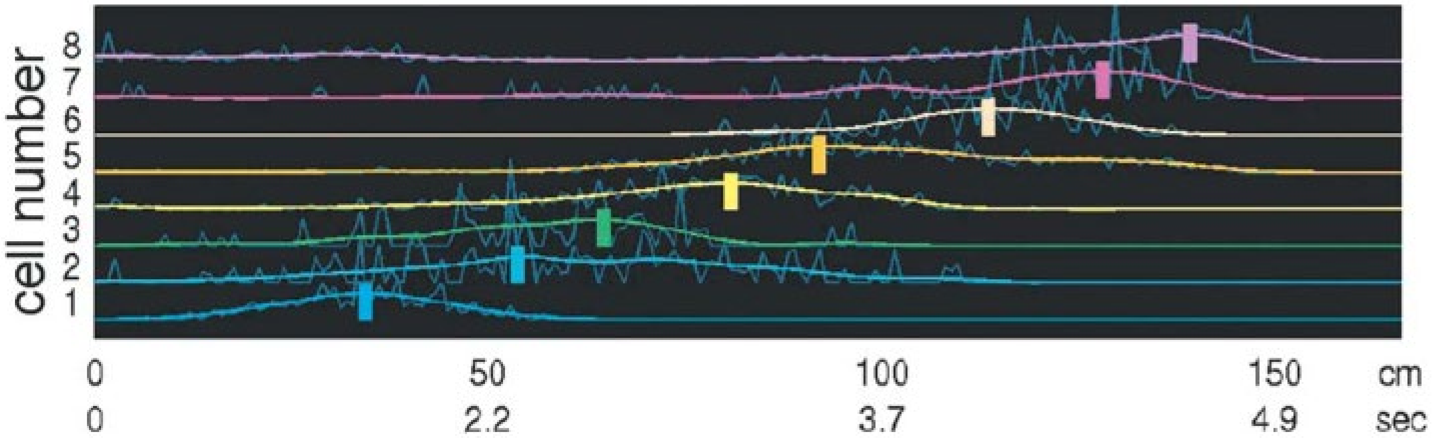
Impairing Sleep SWRs Impairs Spatial Memory

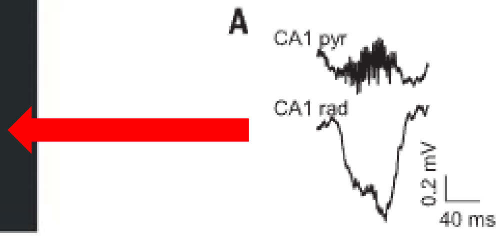




Girardeau…Zugaro *Nat. Neuroscience* 2009

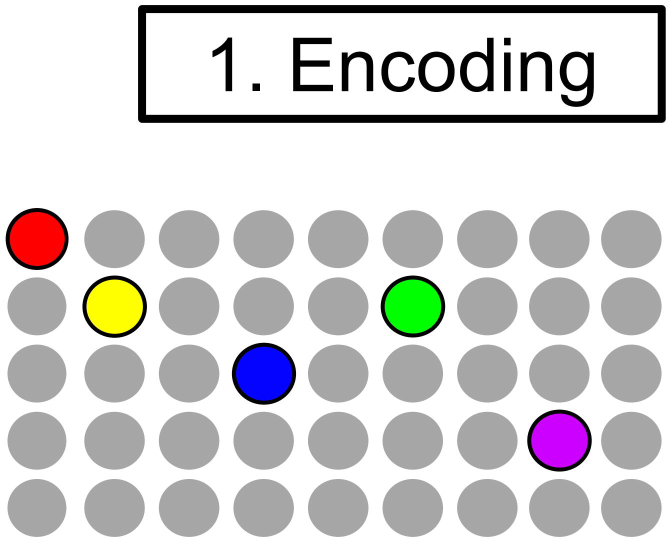
Sleep SWRs Reactivate Trajectories from Previous Experience

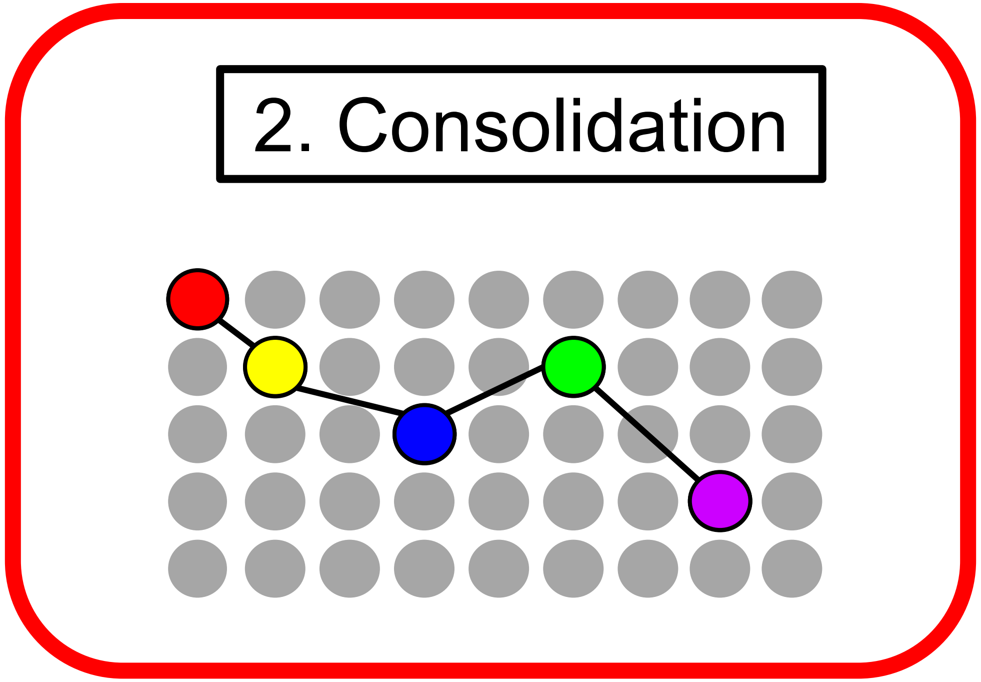




Lee and Wilson *Neuron* 2002

Two stage Model of Memory in Hippocampus – Encode, then Consolidate





How does the brain-firing activity present itself?

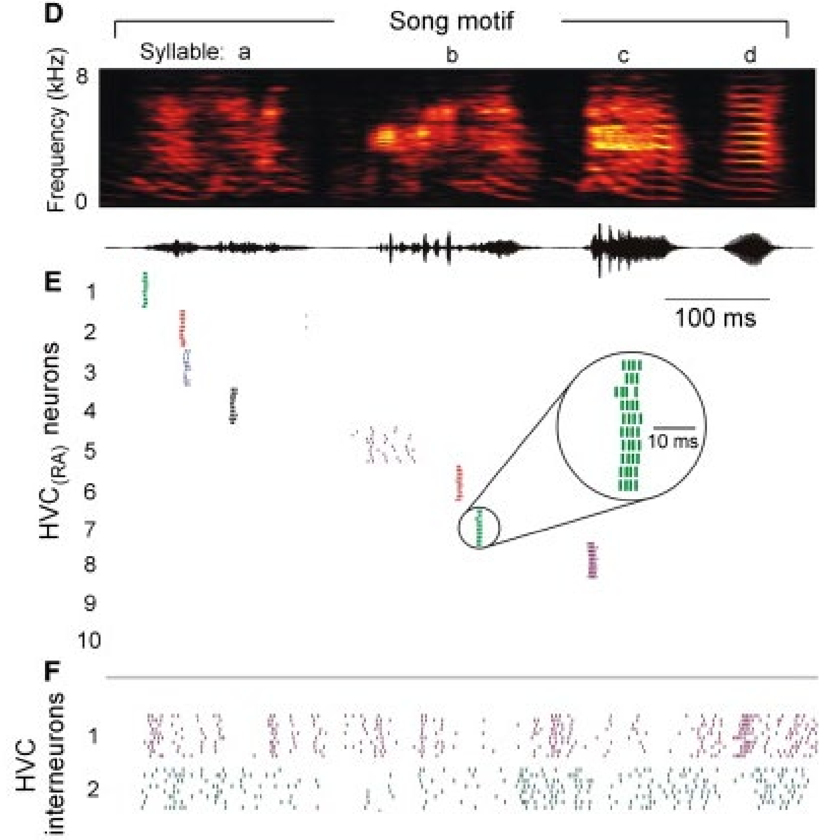
How Does the Brain Present Neural Patterns – Groups of Assemblies and Hebbian Plasticity

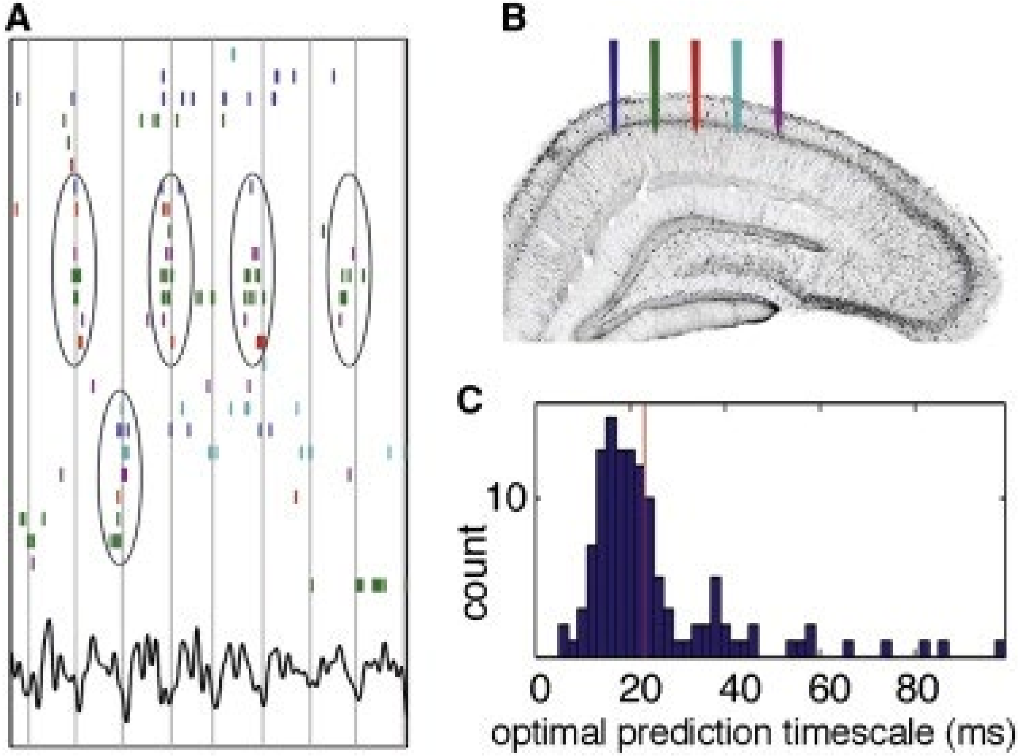
"*Let us assume that the persistence or repetition of a reverberatory activity (or "trace") tends to induce lasting cellular changes that add to its stability.... When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.*"

-**Donald Hebb** *The Organization of Behiavor: A Neuropsychological Theory.* 1949

"Neurons that fire together wire together"

How Does the Brain Present Neural Patterns – Groups of Assemblies and Hebbian Plasticity





Buzsáki *Neuron* 2010
Hahnloser, Kozhevnikov, Fee *Nature 2002*
Harris… Buzsáki *Nature* 2003

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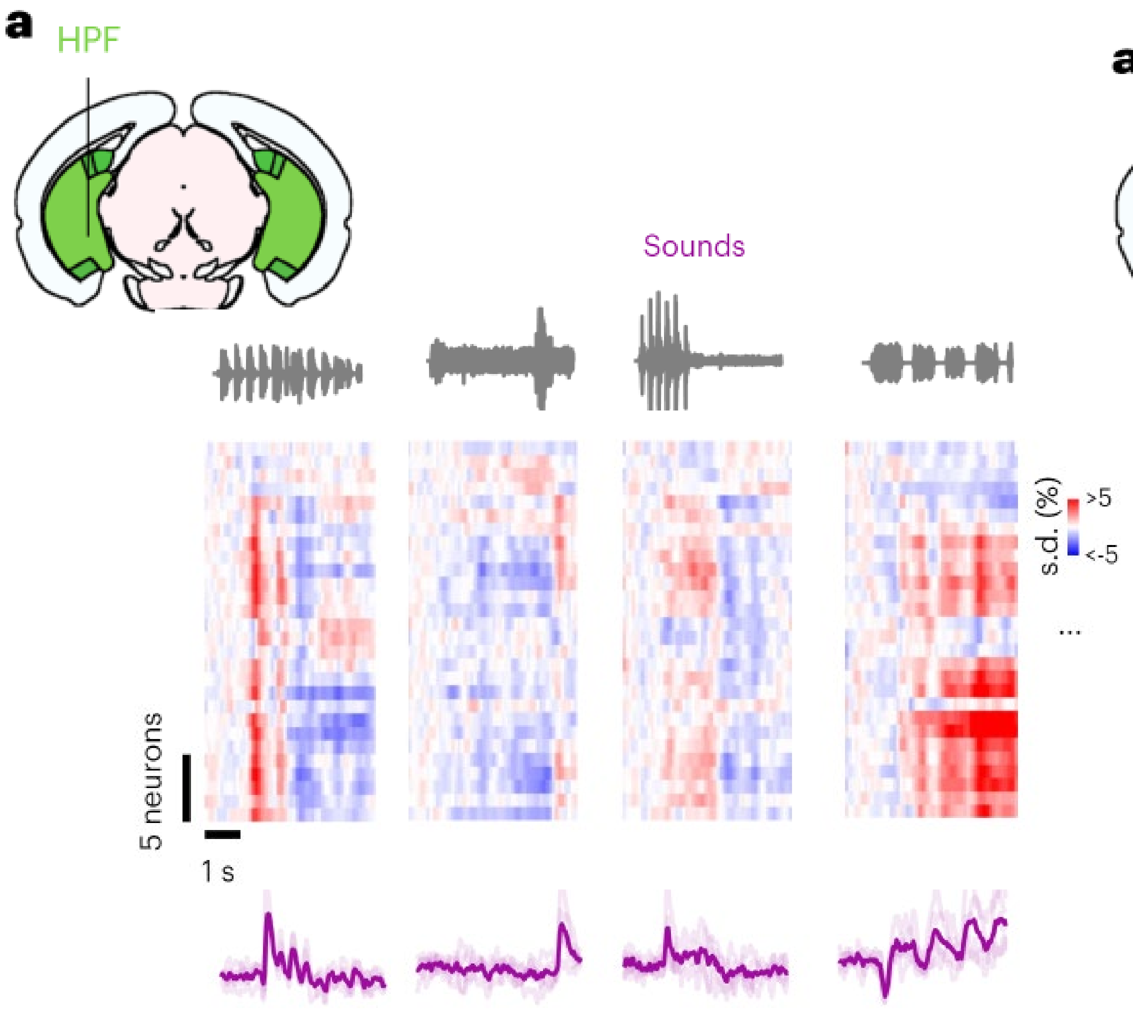
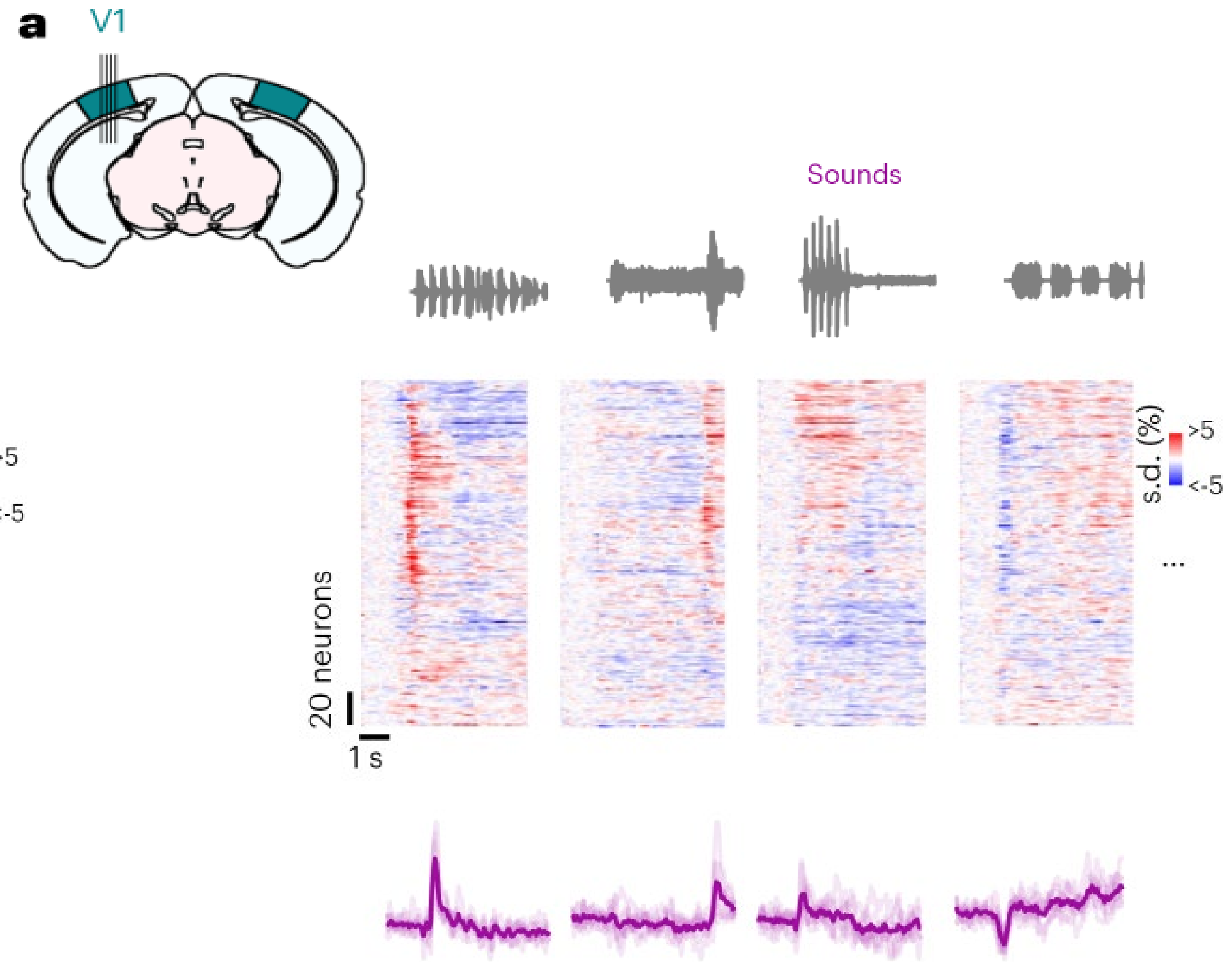
How Does the Brain Present Neural Patterns – Groups of Assemblies and Hebbian Plasticity





Bimbard et al. *Nature Neuroscience* 2023

The current state of Neuroscience – Understanding the Neurophysiology Underlying Behavior

From Netflix “Birds of Paradise”

"The problem of understanding behavior is the problem of understanding the total action of the nervous system, and vice versa.

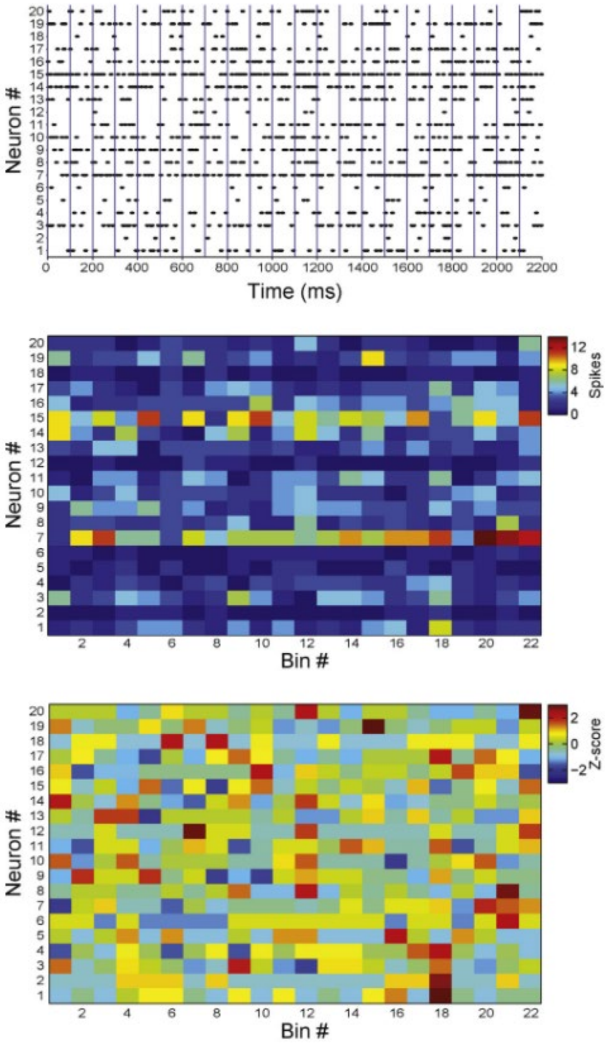
This has not always been a welcome proposition, either to psychologist or to physiologist"

-D.O. Hebb

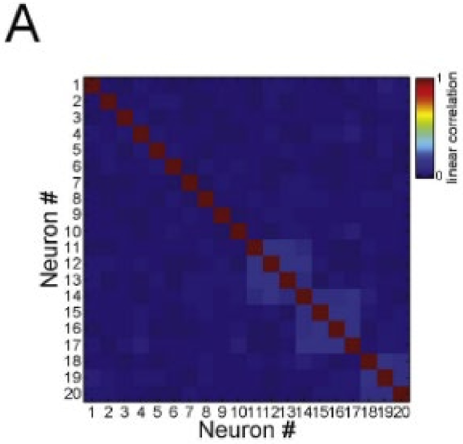
Thanks!

Bonus - Neuron Cell Assembly Detection

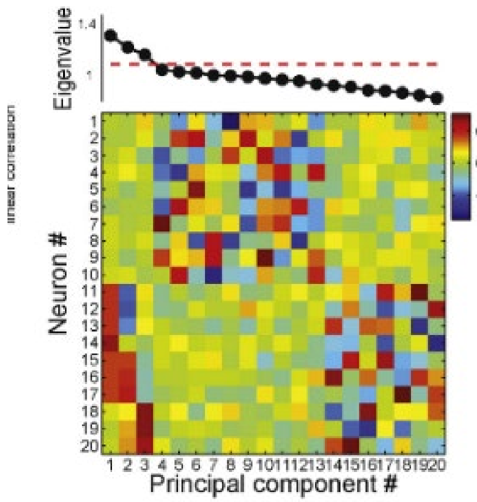
Bin and Z Score Spikes



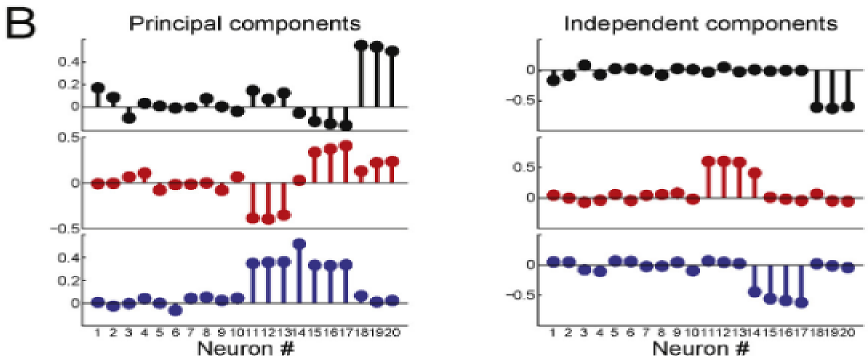
Correlation Matrix



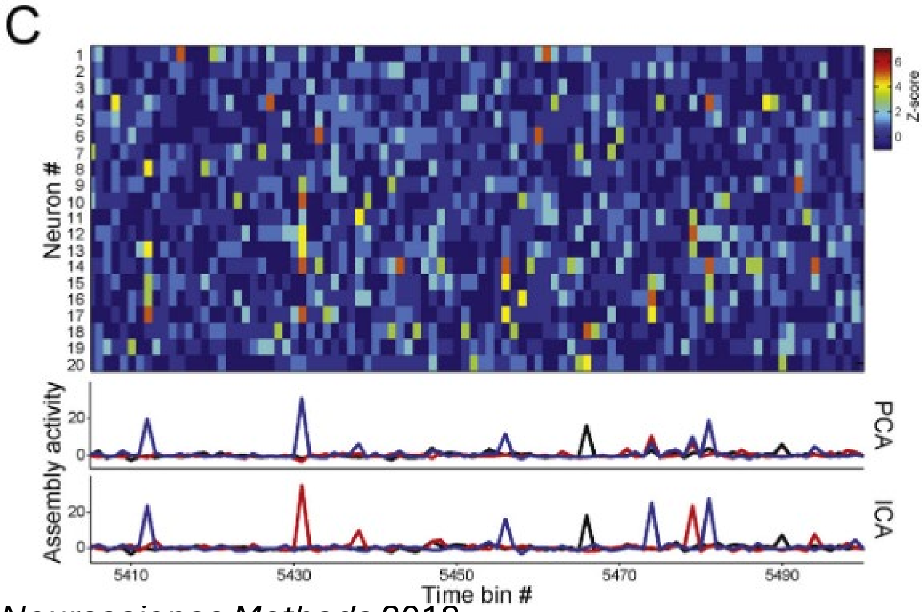
PCA and Determination of components (Marchenko -Pastur law)



ICA to determine the contribution (i.e. weight) of a neuron to each assembly (component)

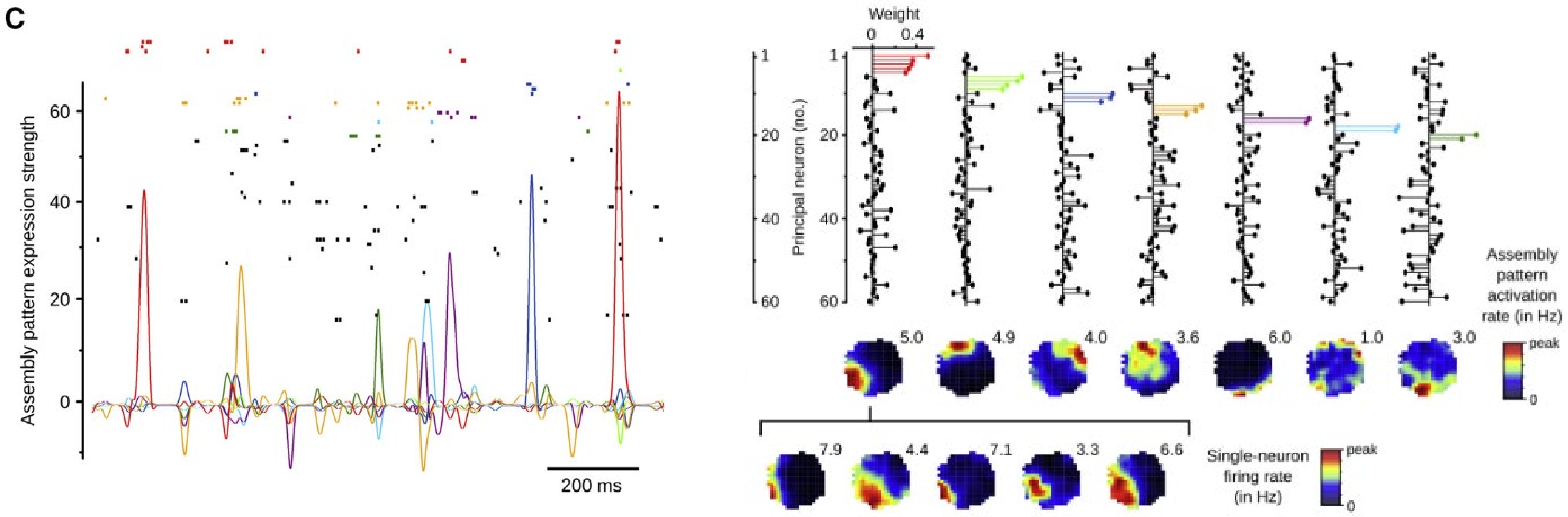


Project the Weight Matrix back onto the z-score binned data = Assembly Activity of each assembly over time



Lopes-dos-Santos, Ribeiro and Tort *The Journal of Neuroscience Methods* 2013

Bonus - Neuron Cell Assembly Detection



Van de Ven...Dupret *Neuron* 2016