Hippocampus in spatial memory and temporal sequence processing

- The hippocampus is involved in the formation of episodic memory as well as spatial memory used in navigation.
- Navigation - linkage of spatial locations
- Episodic memory - linkage of events
- Both may involve encoding and evaluation of temporally sequenced information.

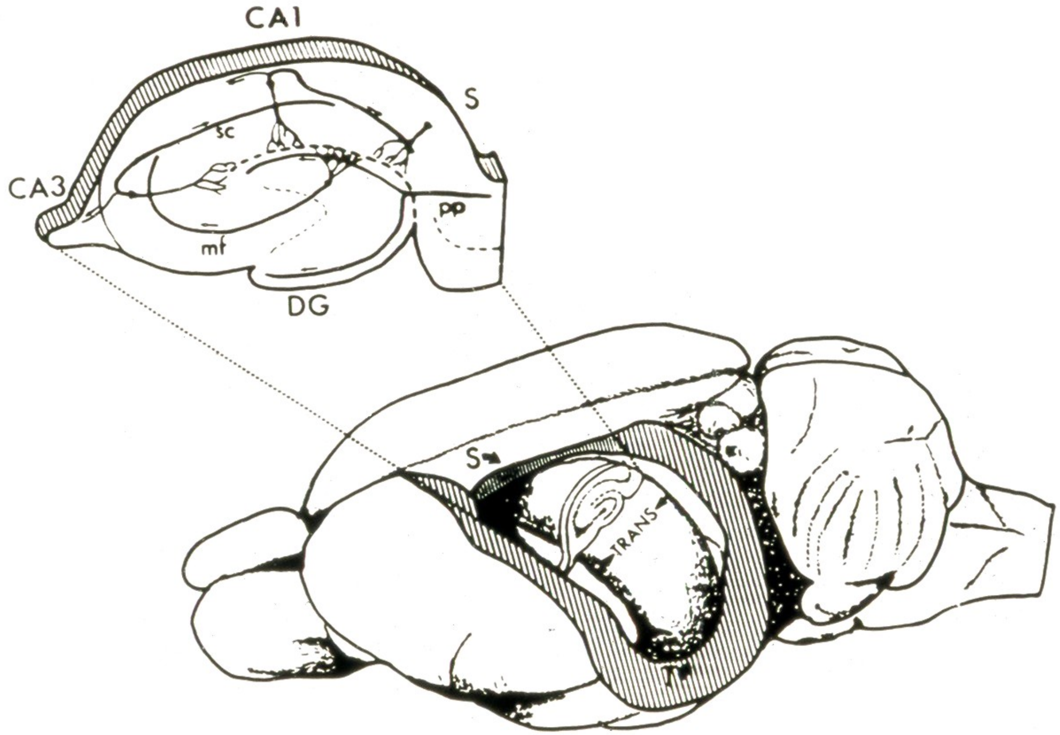
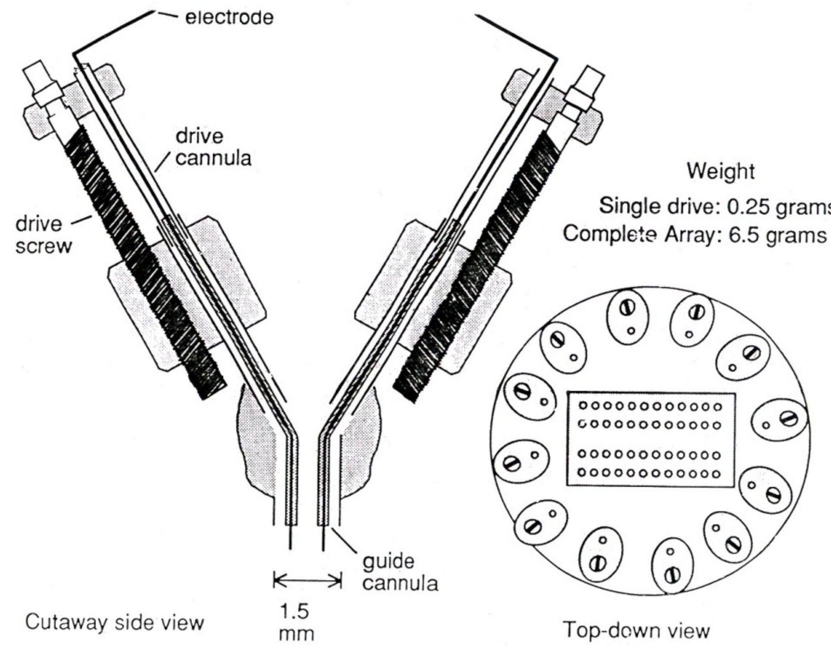


Fig. 2. The position of the hippocampal formation in the rat brain is shown in this drawing of a preparation in which the cortical surface overlying the hippocampus has been removed. The hippocampus is an elongated, C-shaped structure with the long or septotemporal axis running from the septal nuclei rostrally (S) to the temporal cortex (T) ventrocaudally. The short or transverse axis (TRANS) is oriented perpendicular to the septotemporal axis. The major fields of the hippocampal formation (except for the entorhinal cortex) are found in slices taken approximately midway along the septotemporal axis. The slice pictured at top left is a representation of the summary of the major neuronal elements and intrinsic connections of the hippocampal formation as originally illustrated by Andersen *et al.* (see text for details).

Abbreviations: DG, dentate gyrus; mf, mossy fibers; pp, perforant path; sc, Schaffer collaterals.

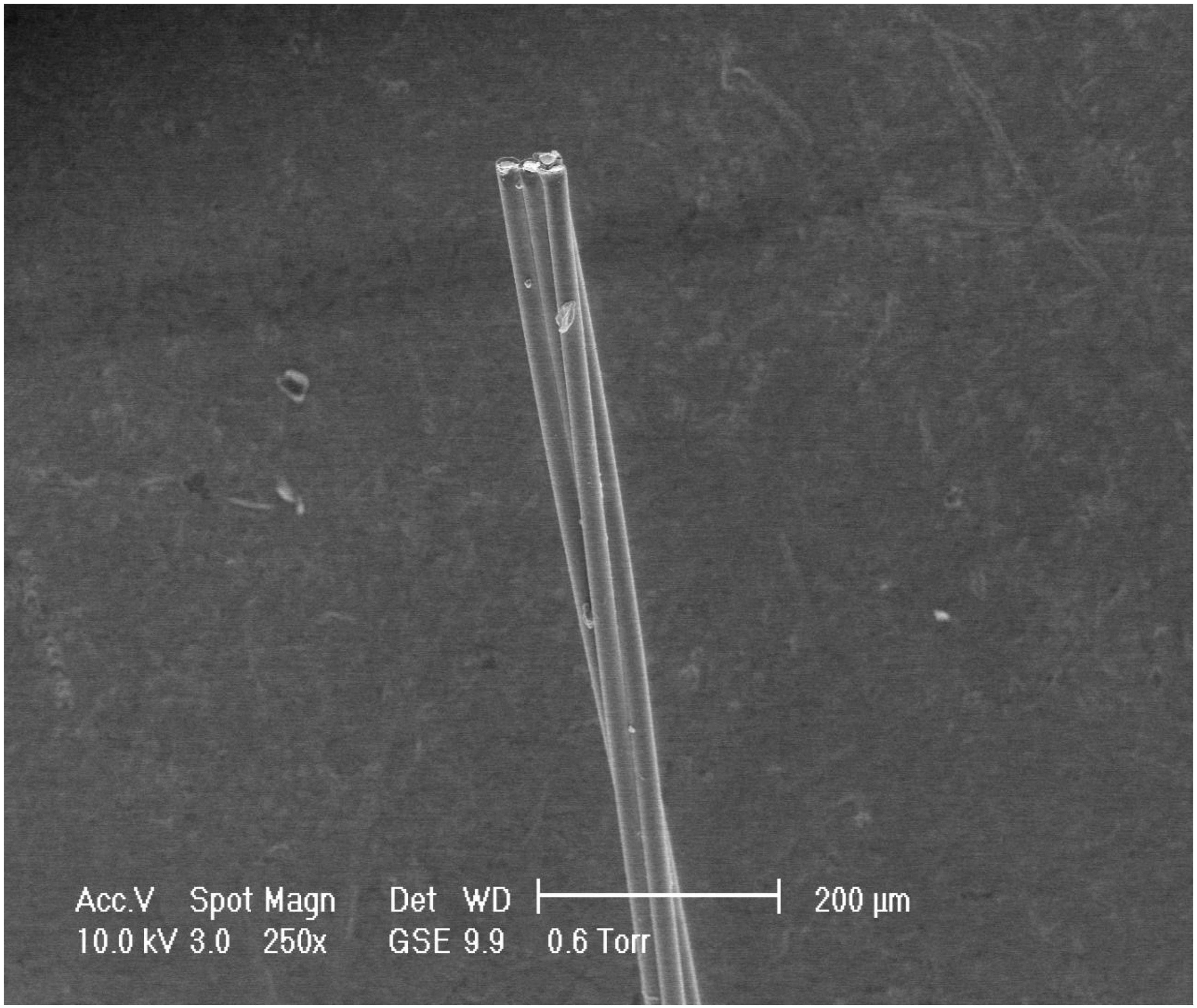
From Amaral and Witter, 1989

Microelectrode Microdrive Array for Chronic Recording



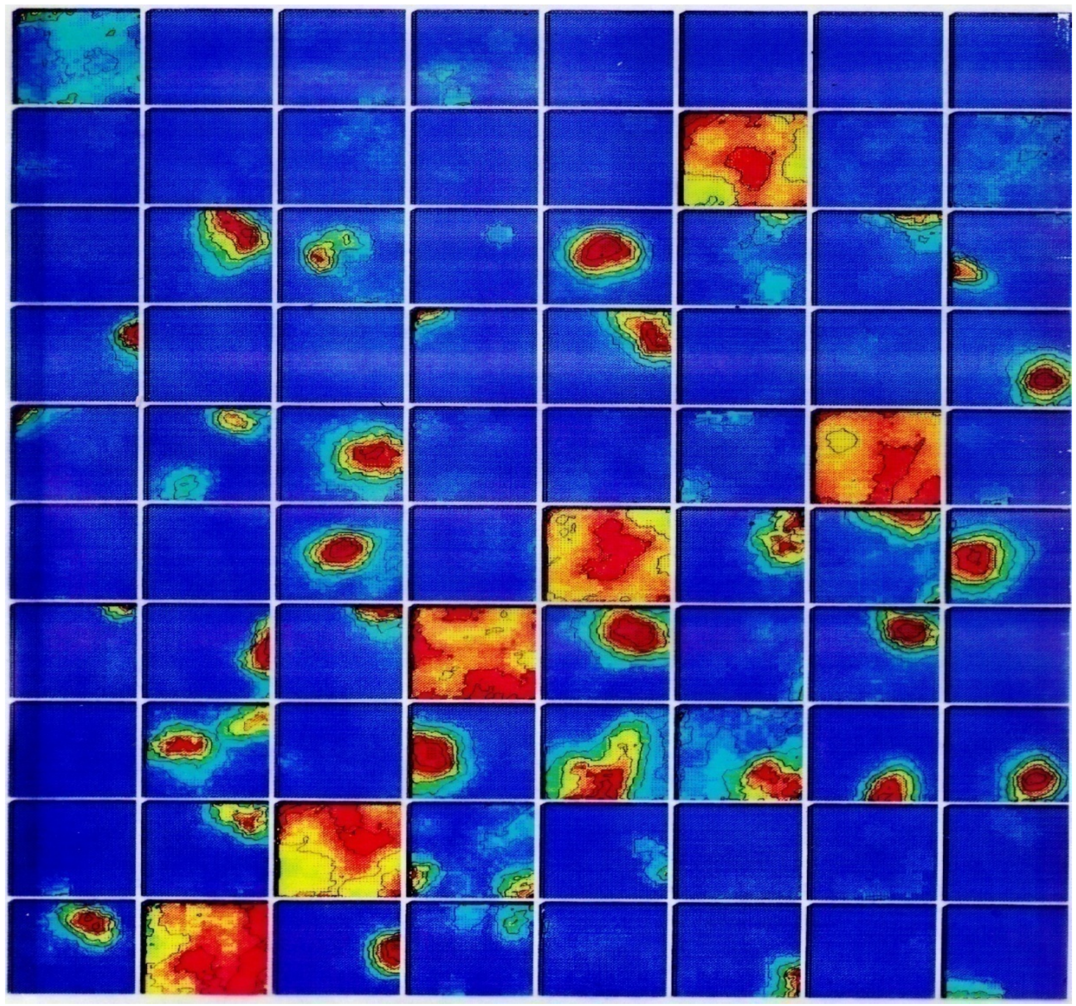
Allows simultaneous recording of 100 or more neurons at distributed sites around the brain in the behaving animal

Twisted 4-wire electrode



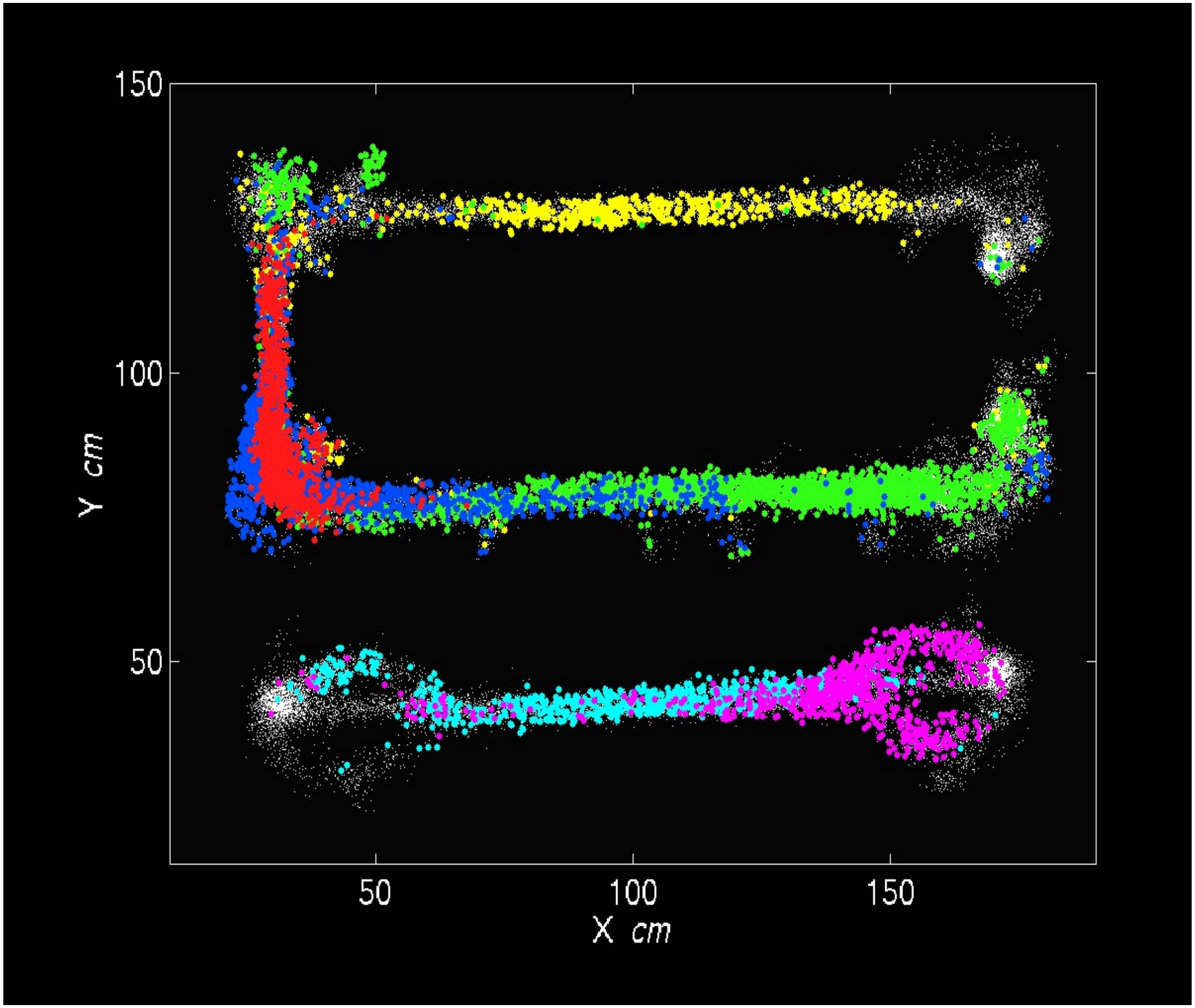
Example of a Simple Spatial Environment

Ensemble Activity in Area CA1 During Spatial Exploration



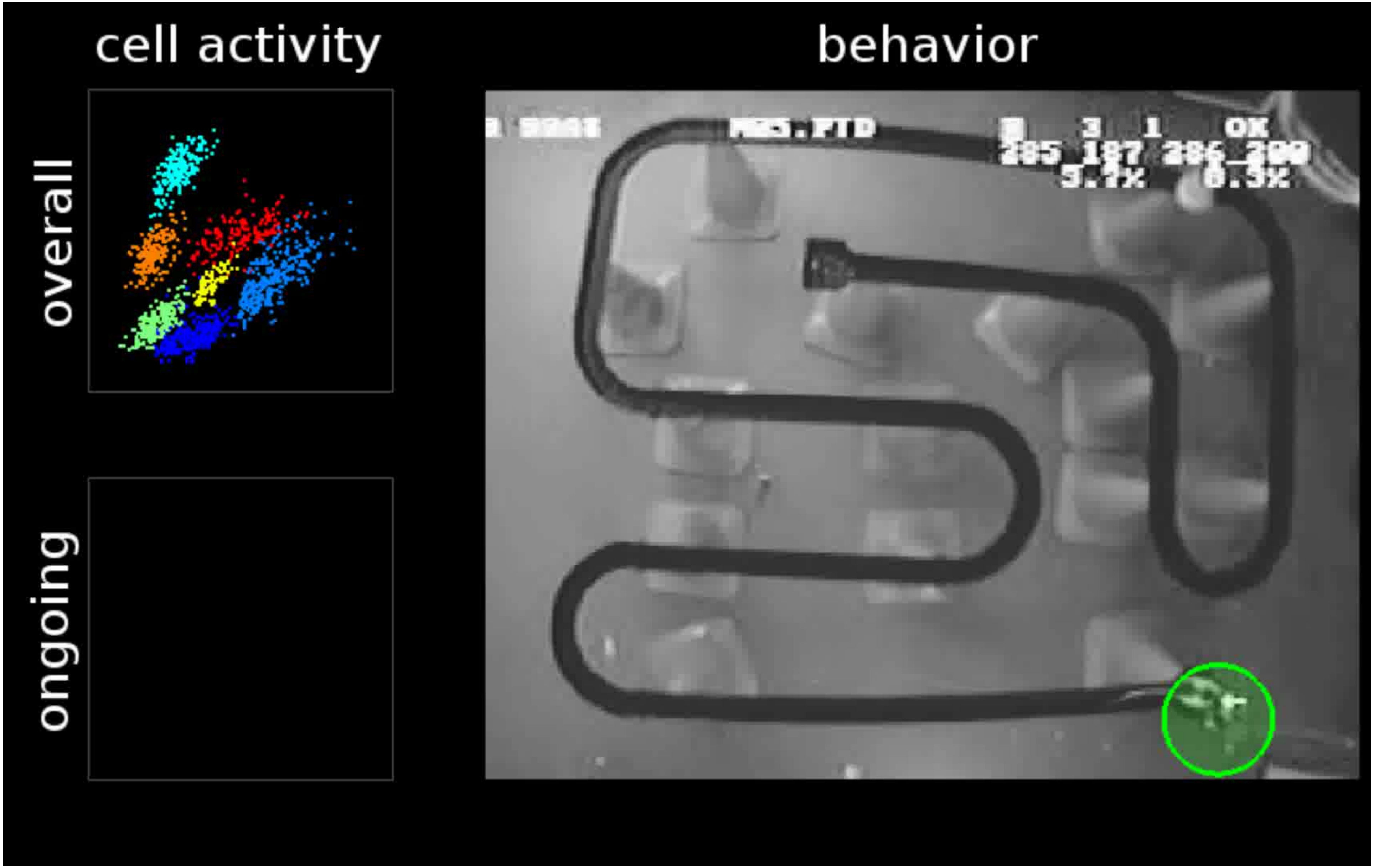
Wilson and McNaughton, *Science*, 1993

Place Fields on Linear Tracks

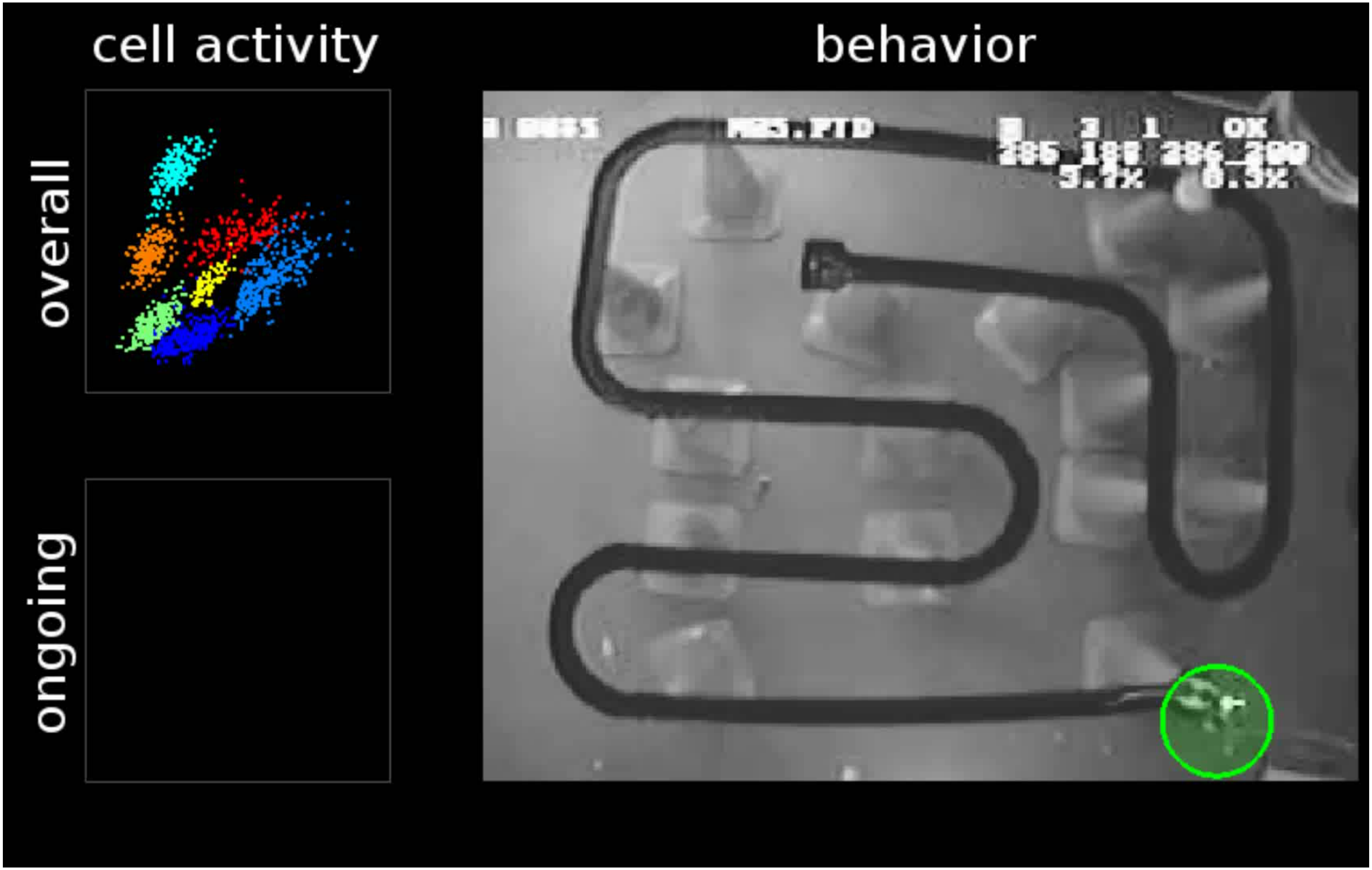


Mehta et al., *Neuron*, 2000

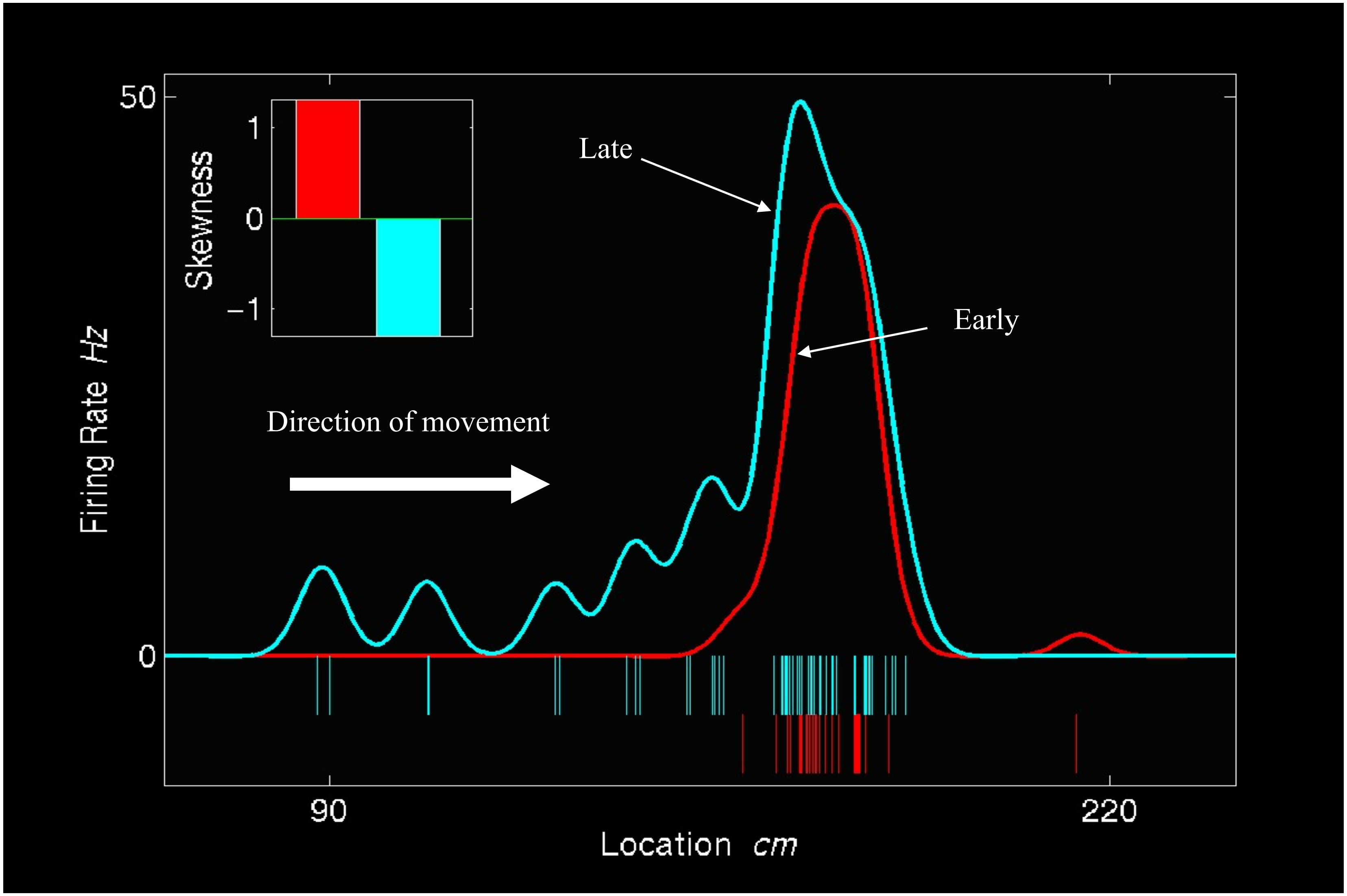
Hippocampal Place Cells



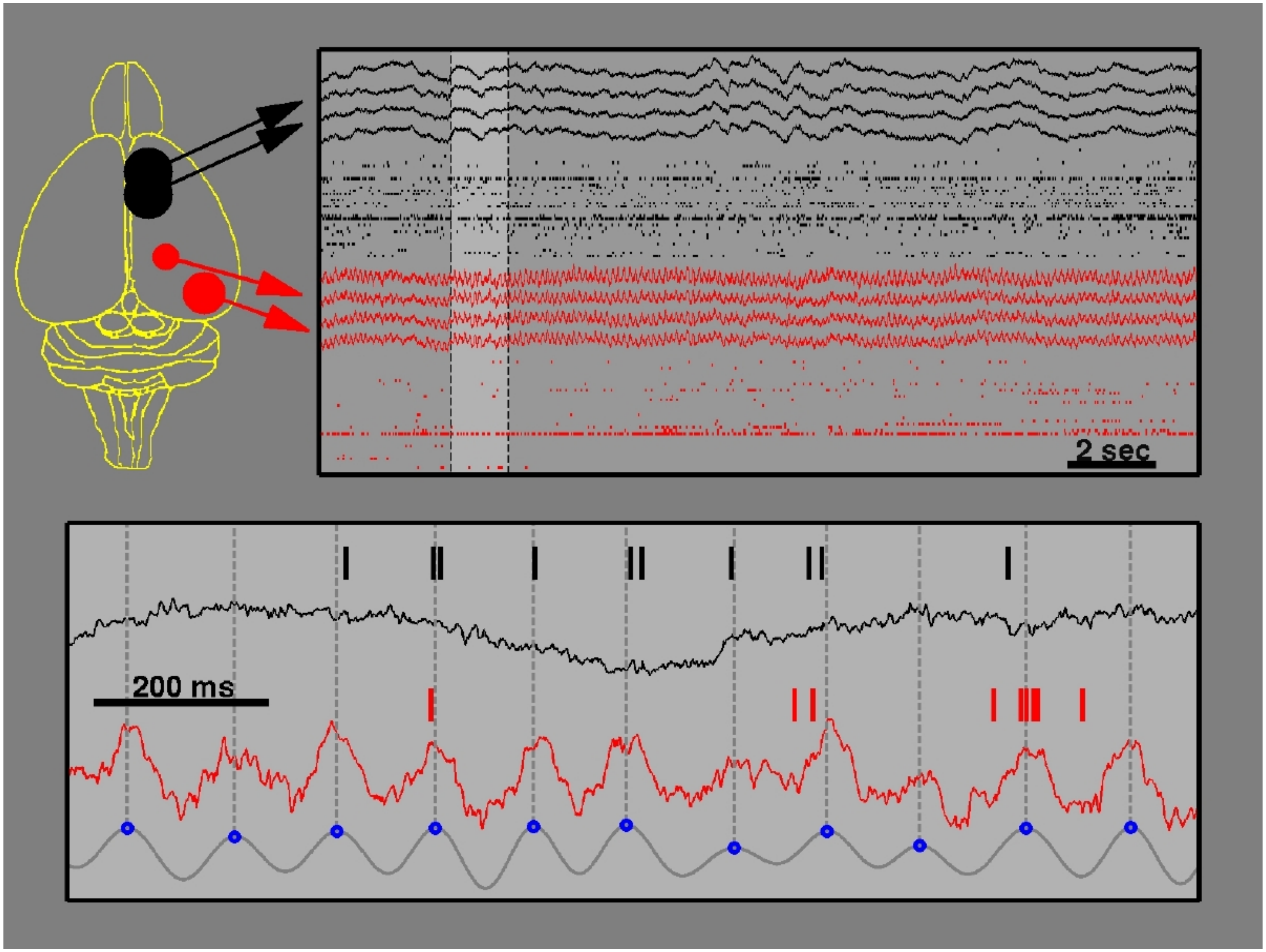
Hippocampal Ensemble Decoding



Place Fields Become Spatially Asymmetric with Experience

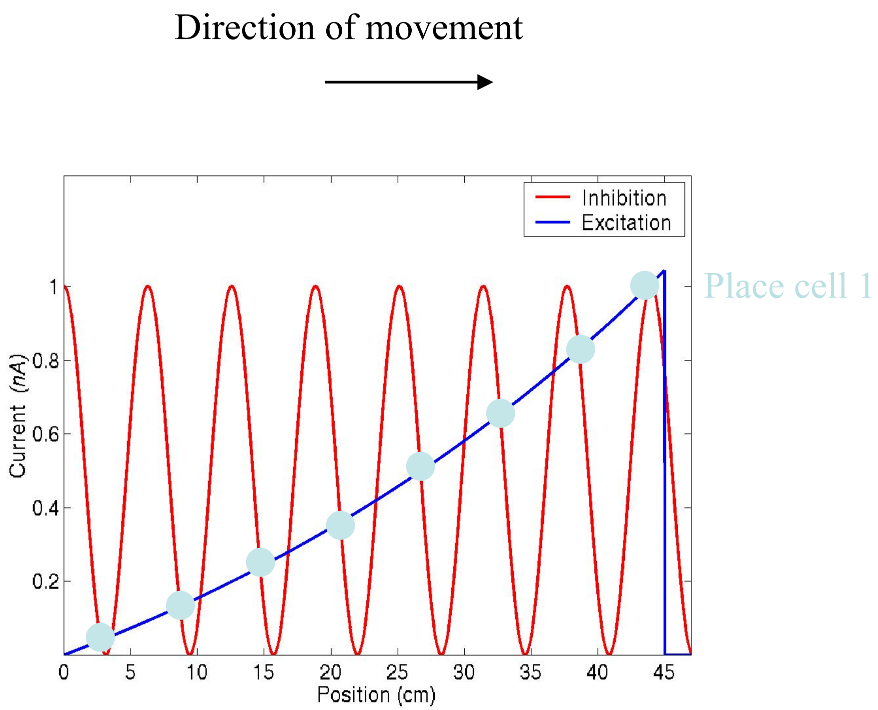


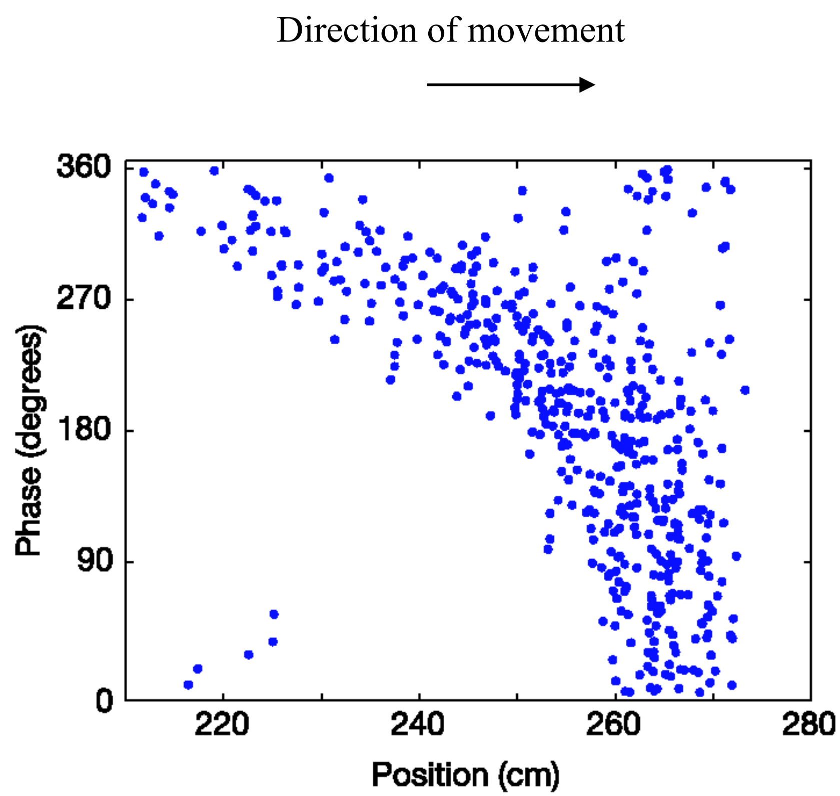
Mehta et al., *Neuron*, 2000


2 sec
200 ms

Interaction of asymmetric excitation with oscillatory variation in inhibition can translate one linear dimension (space) into another (time).

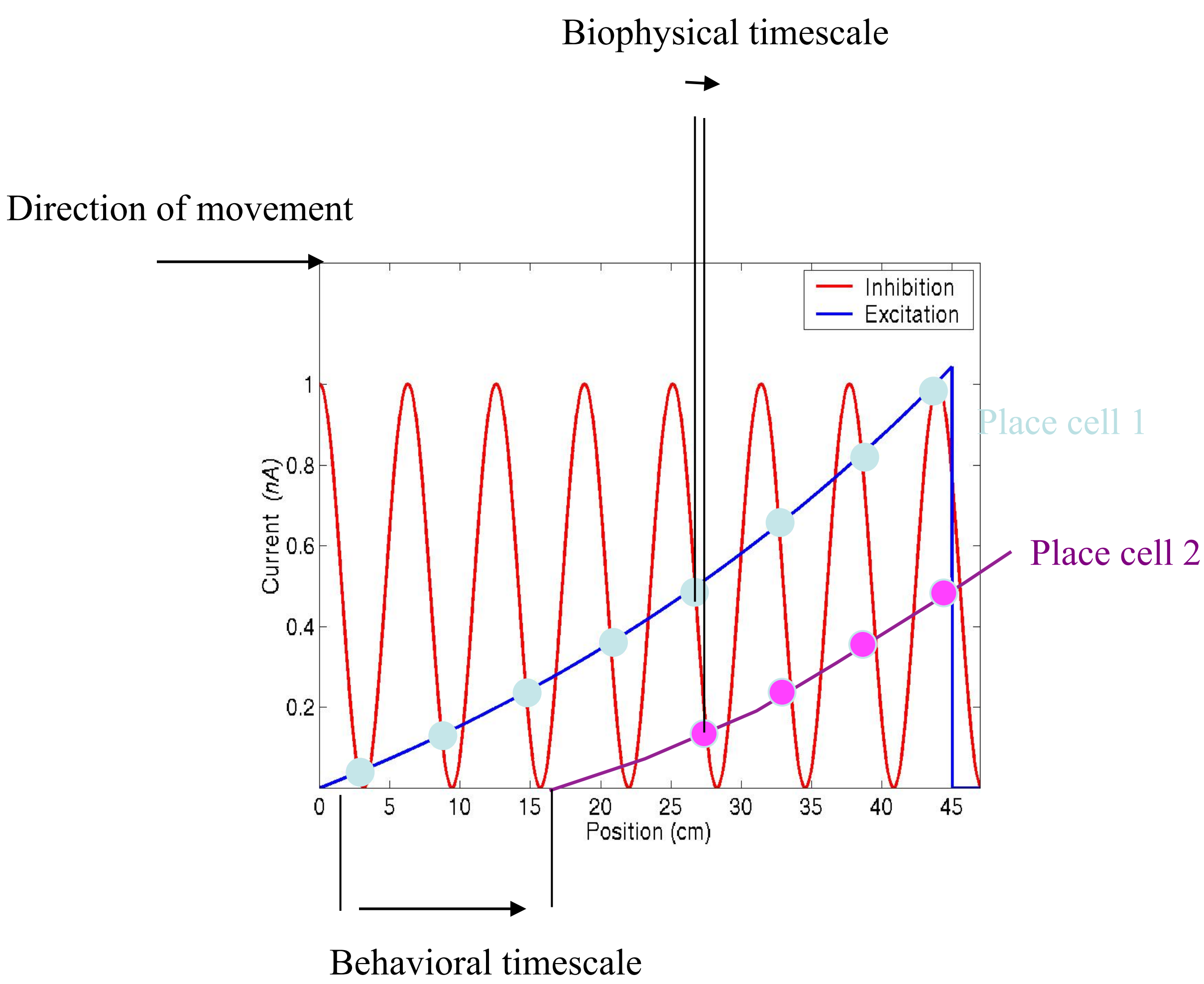
Hippocampal phase precession may be a demonstration of that process.



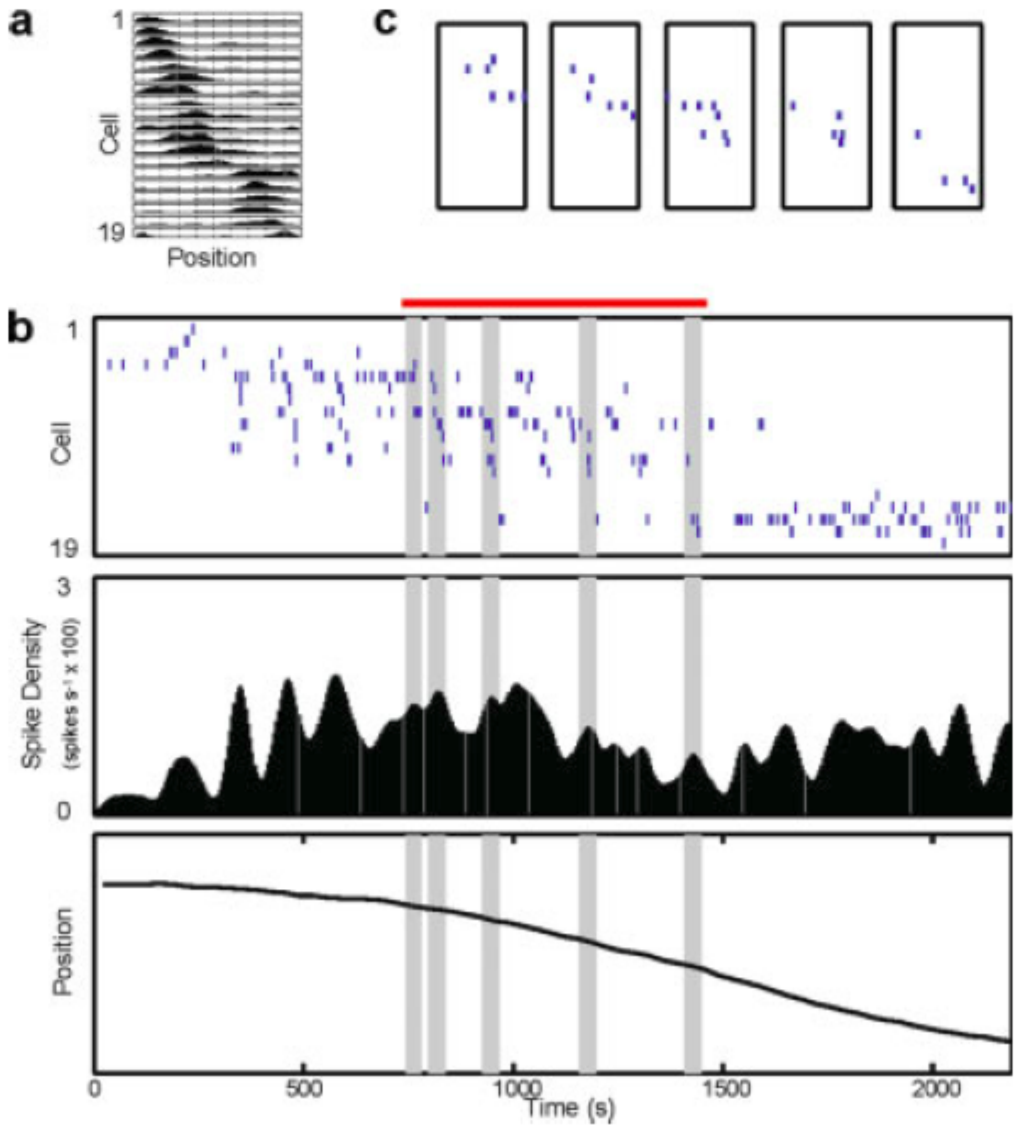


Mehta, Lee, and Wilson, *Nature*, 2002

Overlapping asymmetric place fields with oscillatory variation in excitability translate behavioral time relationships to biophysical timescales with preserved temporal order

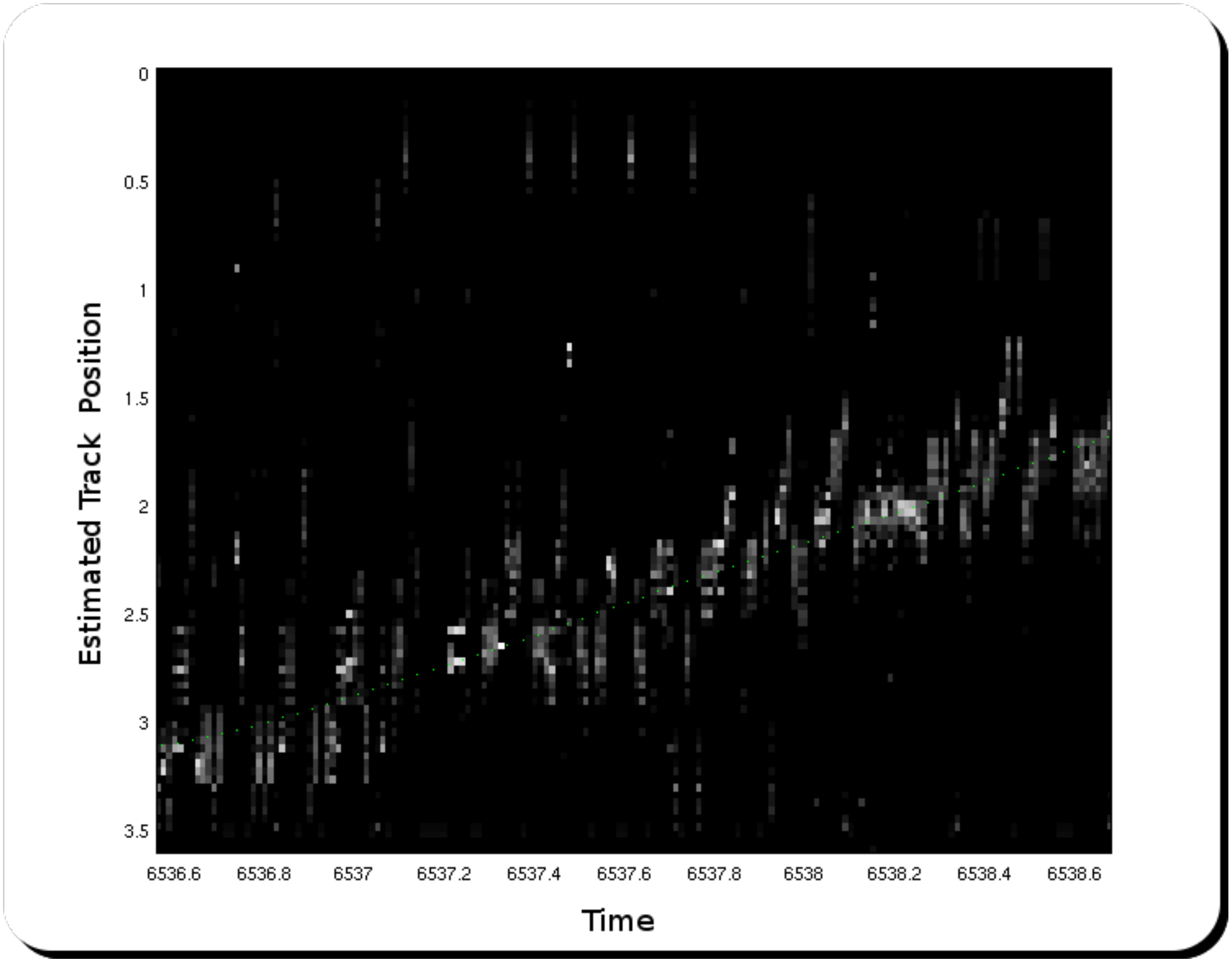


Hippocampal theta sequences: spikes



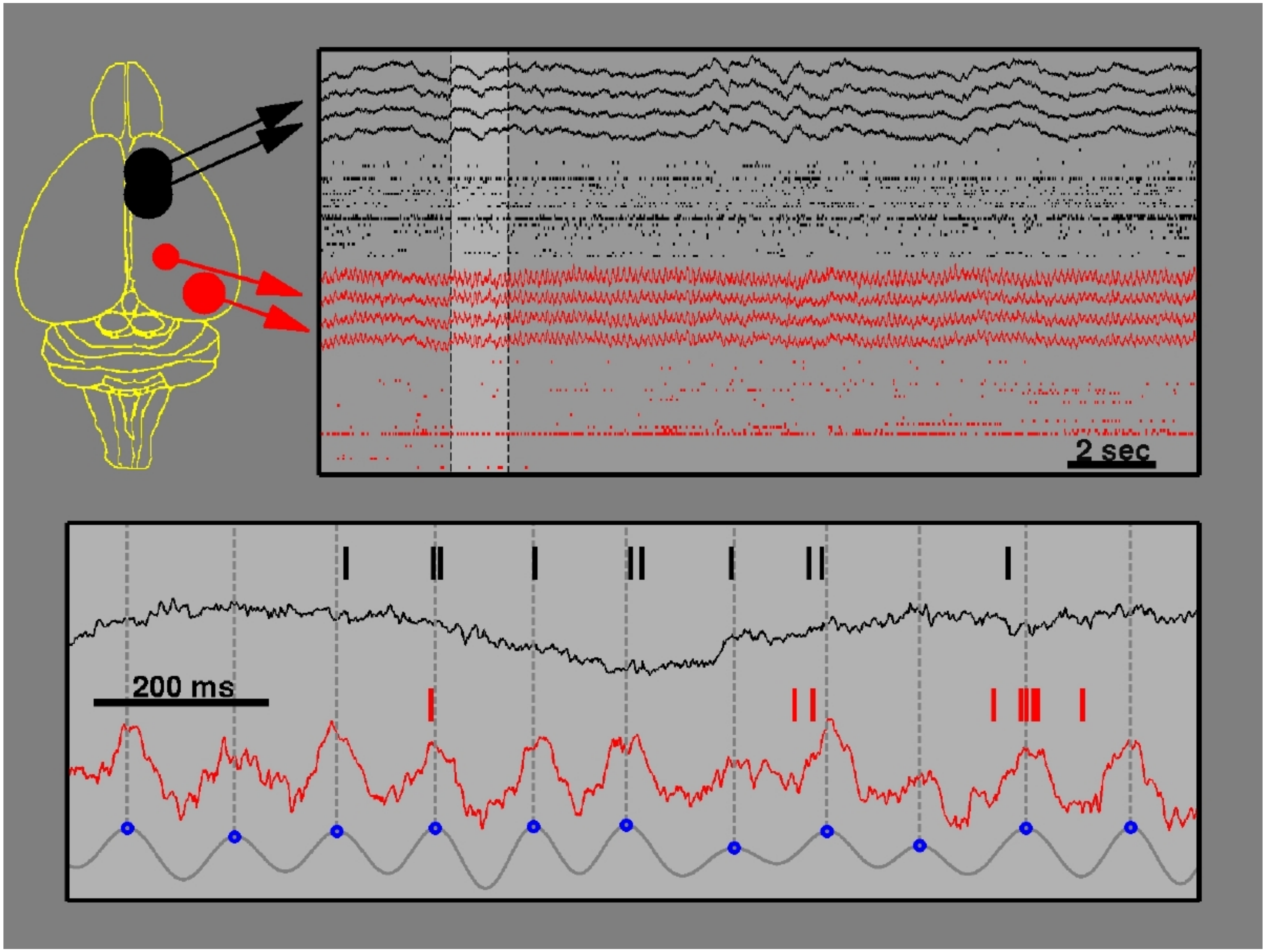
Foster and Wilson, 2007

Hippocampal theta sequences: spatial reconstruction

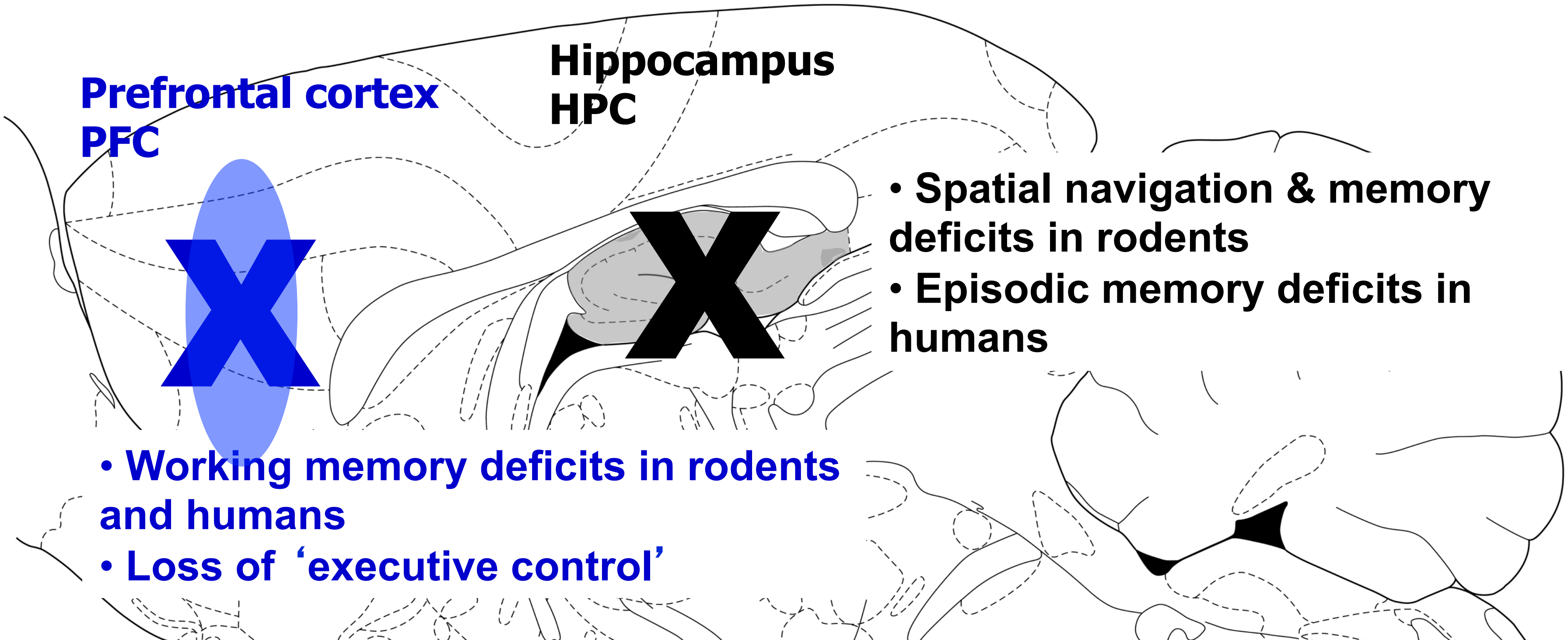


Properties of Place field Asymmetry and Phase Encoding

- Hippocampal place fields become temporally asymmetric in an experience dependent manner.
- This asymmetry may provide a mechanism for temporal sequence memory encoding.


2 sec
200 ms

HPC-PFC: functionally connected



The hippocampus: **encoding and recognising spatial context**

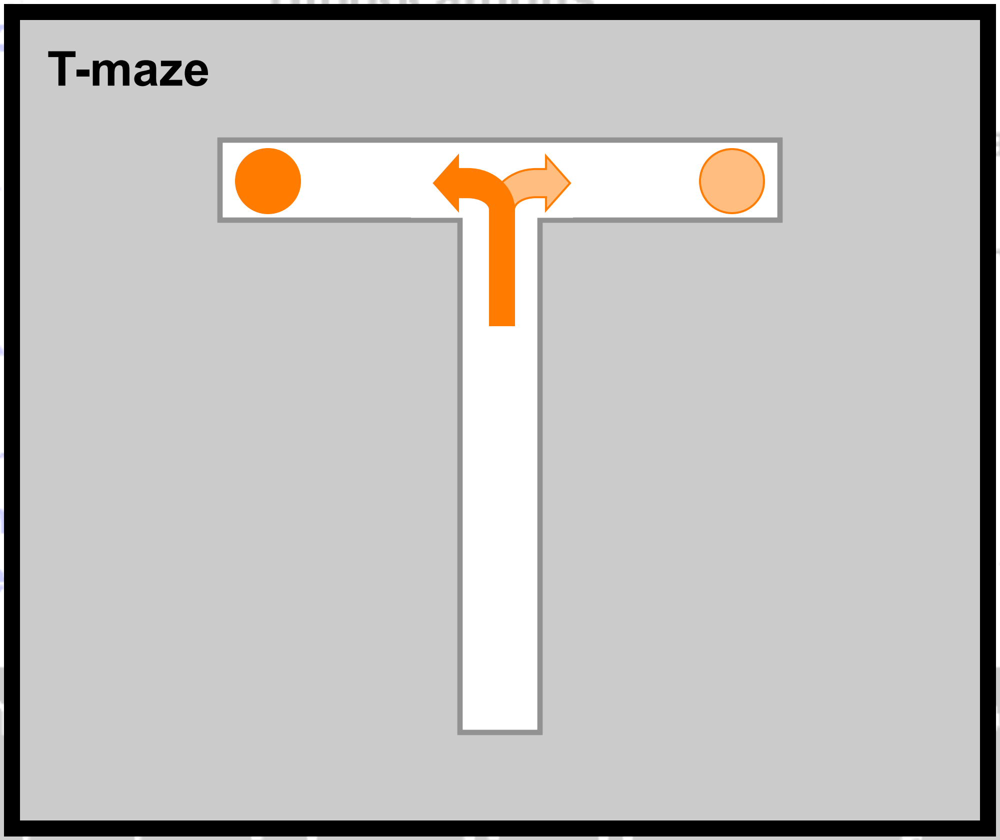
The prefrontal cortex: **integrating the cues of current context (held on-line in working memory) to control appropriate behaviour**

HPC-PFC: functionally connected during spatial working memory tasks

Prefrontal c

PFC

Hippocampus



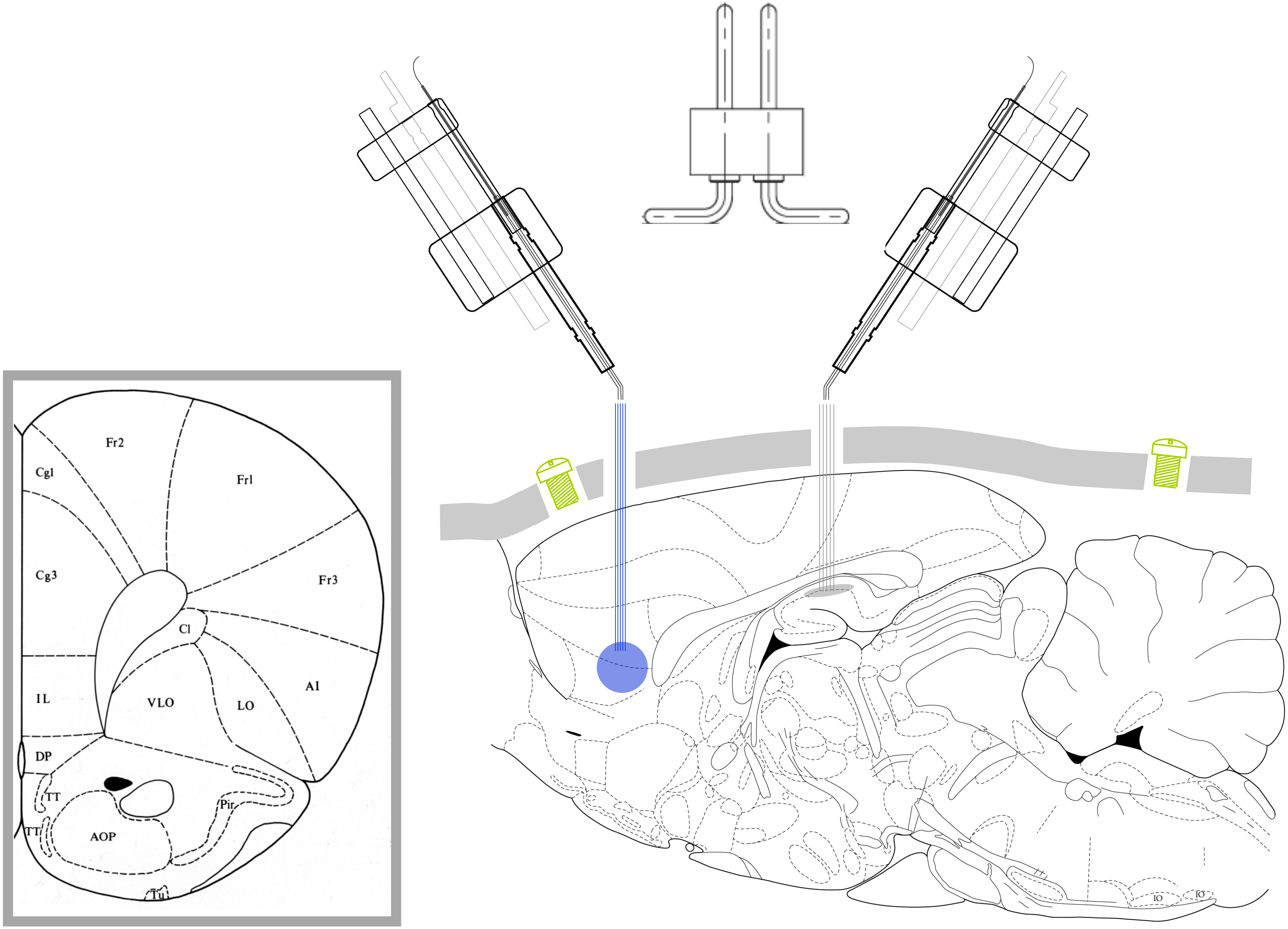
ation & memory
nts
nory deficits in

• Working r
and human
• Loss of 'e

The hippocam … atial context

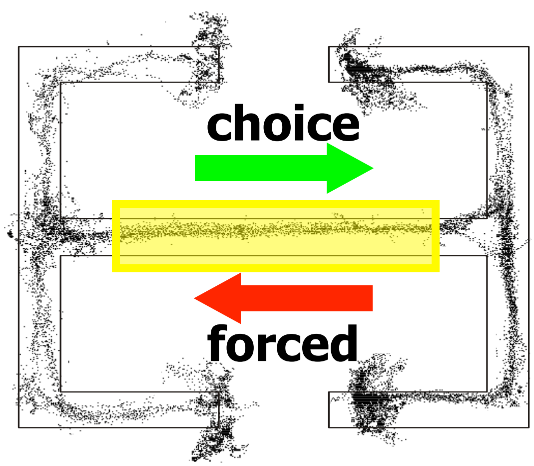
The prefrontal cortex: **integrating the cues of current context (held on-line in working memory) to control appropriate behaviour**

Multiple units from multiple electrodes in multiple sites

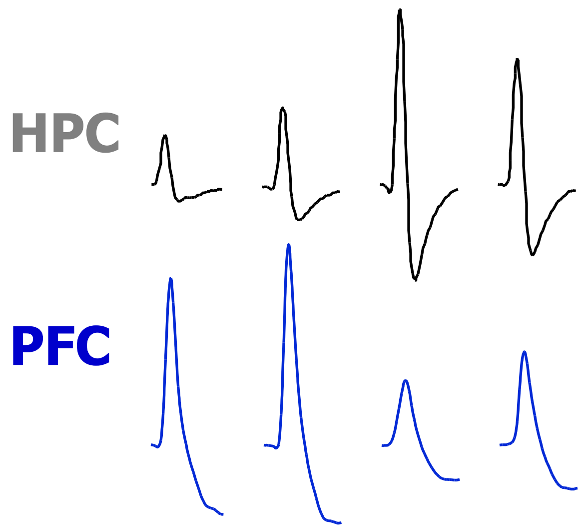


Data

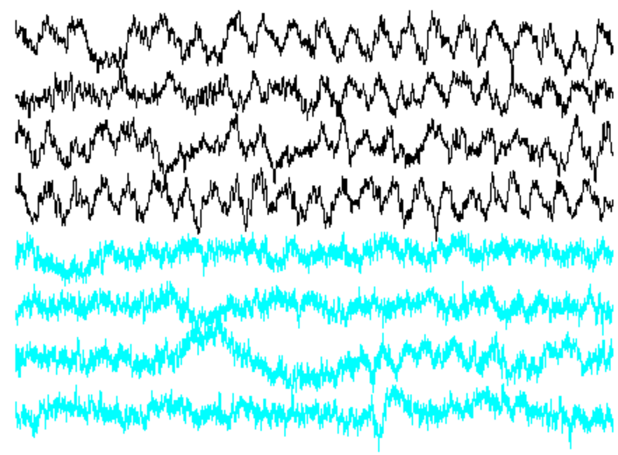
Behaviour & Position



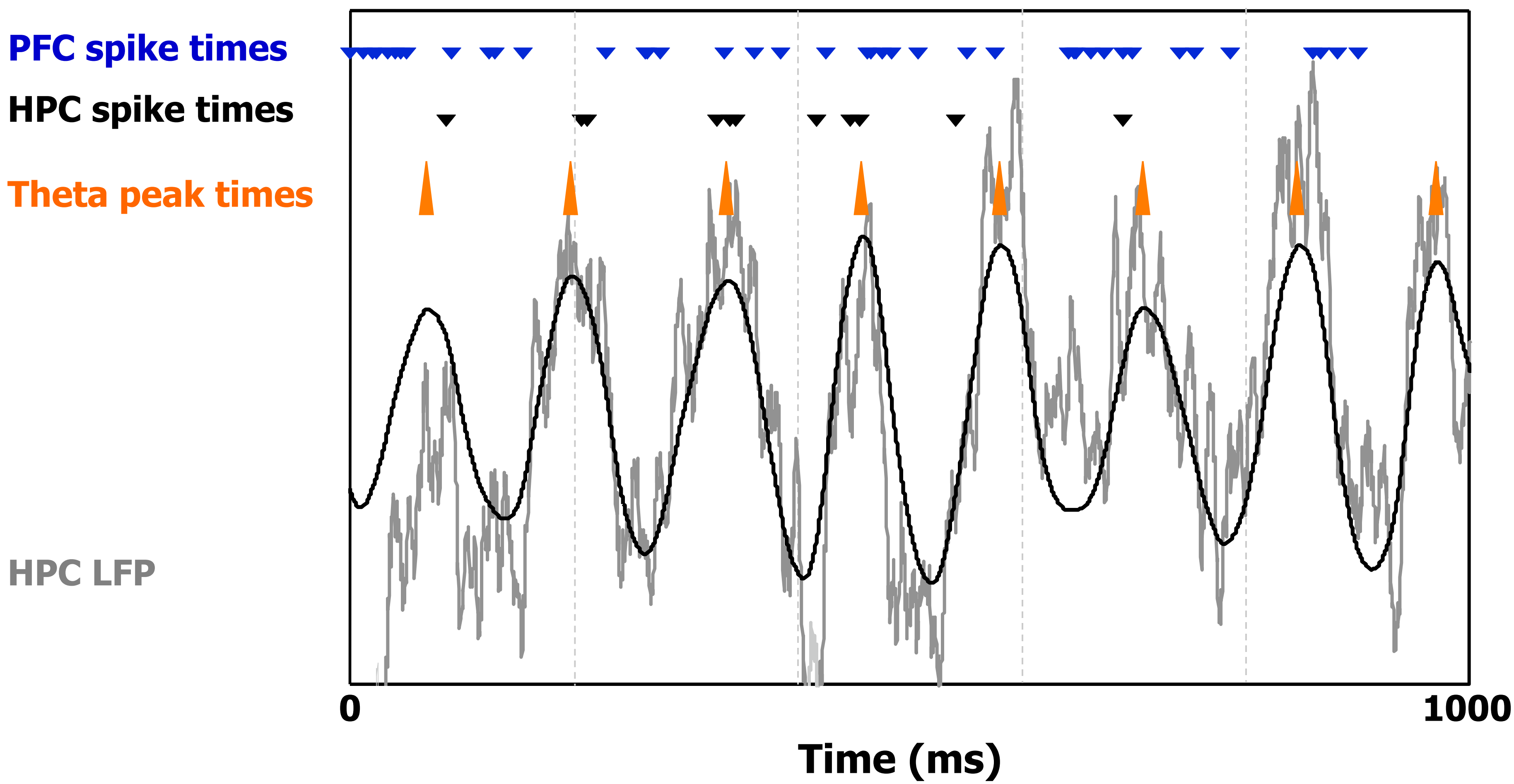
Extracellular Action Potentials (spikes)



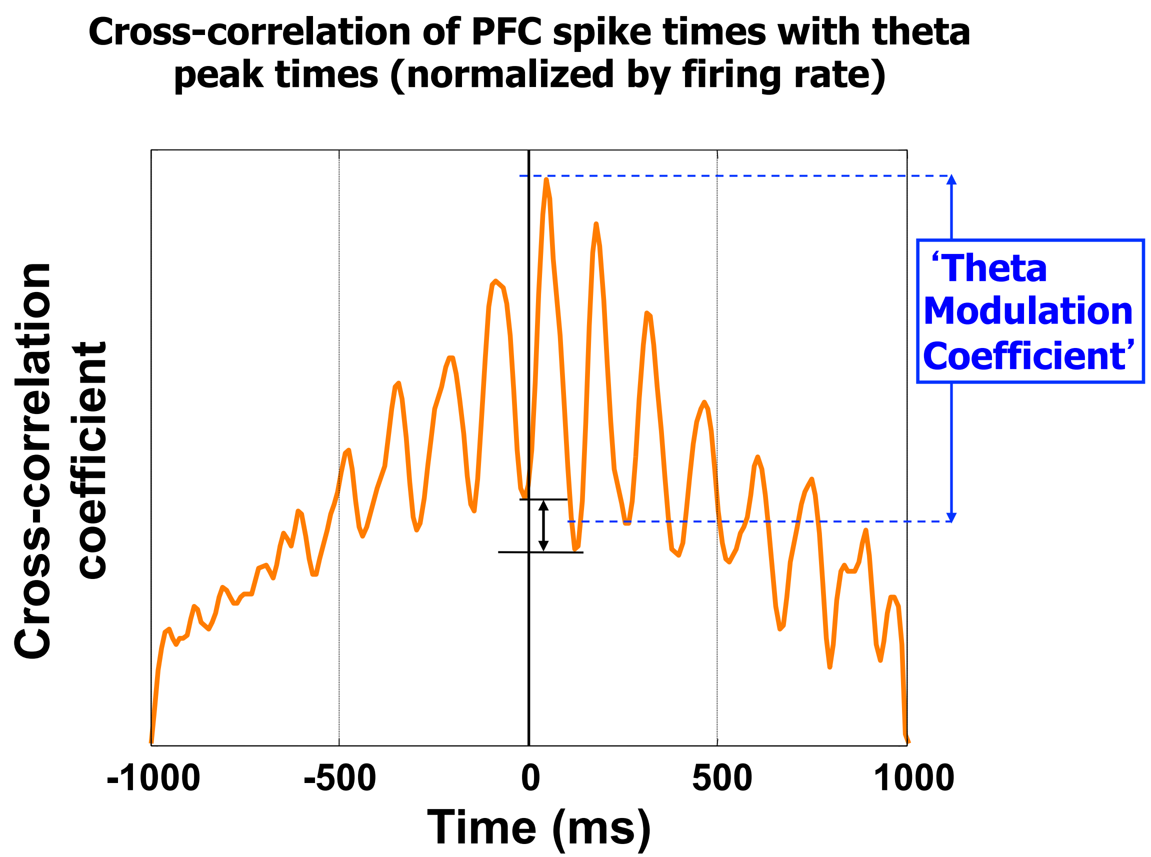
Local Field Potentials (LFP)



Interactions: spikes vs. LFP

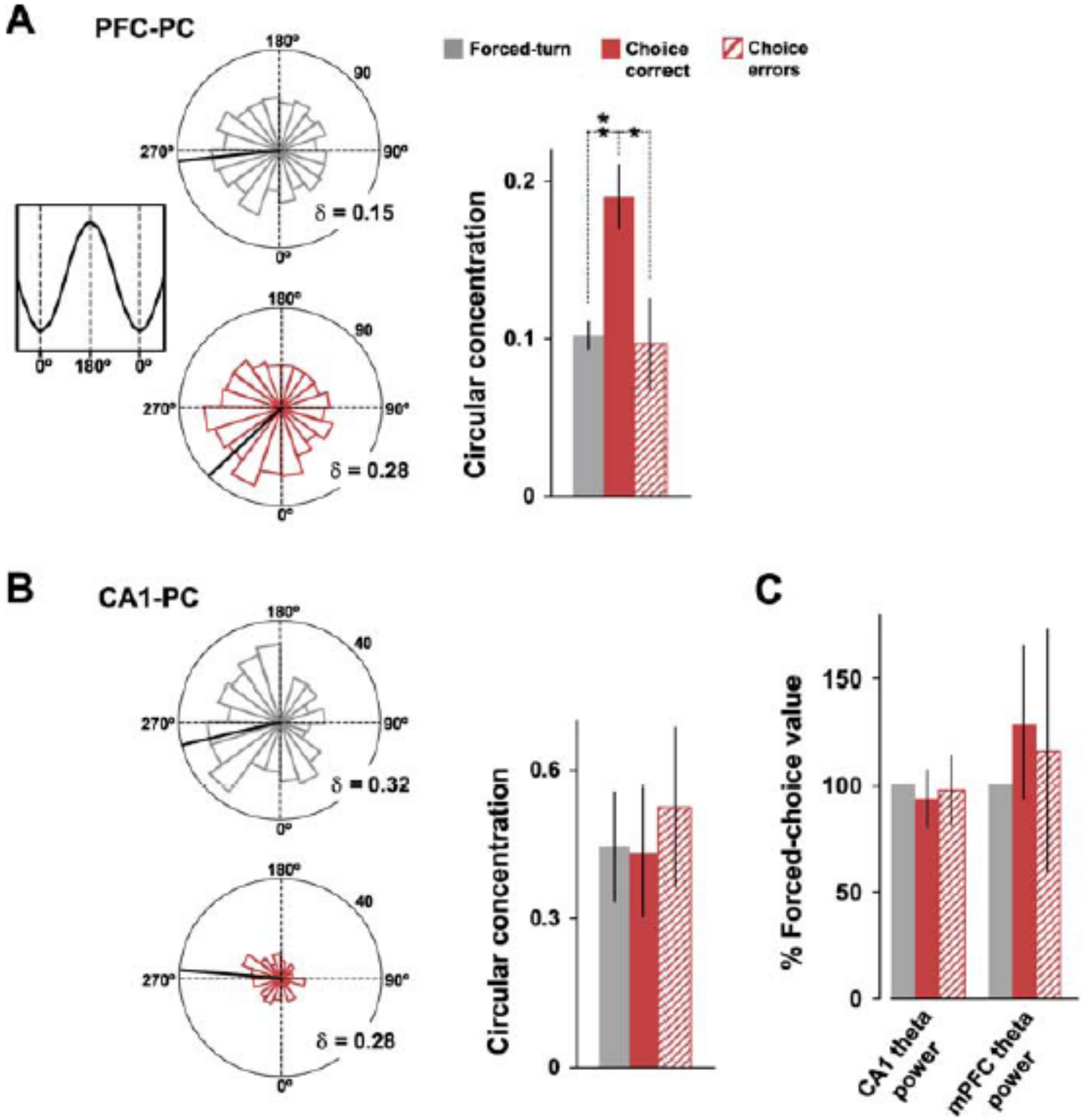


PFC Spikes *vs*. HPC LFP: theta modulation



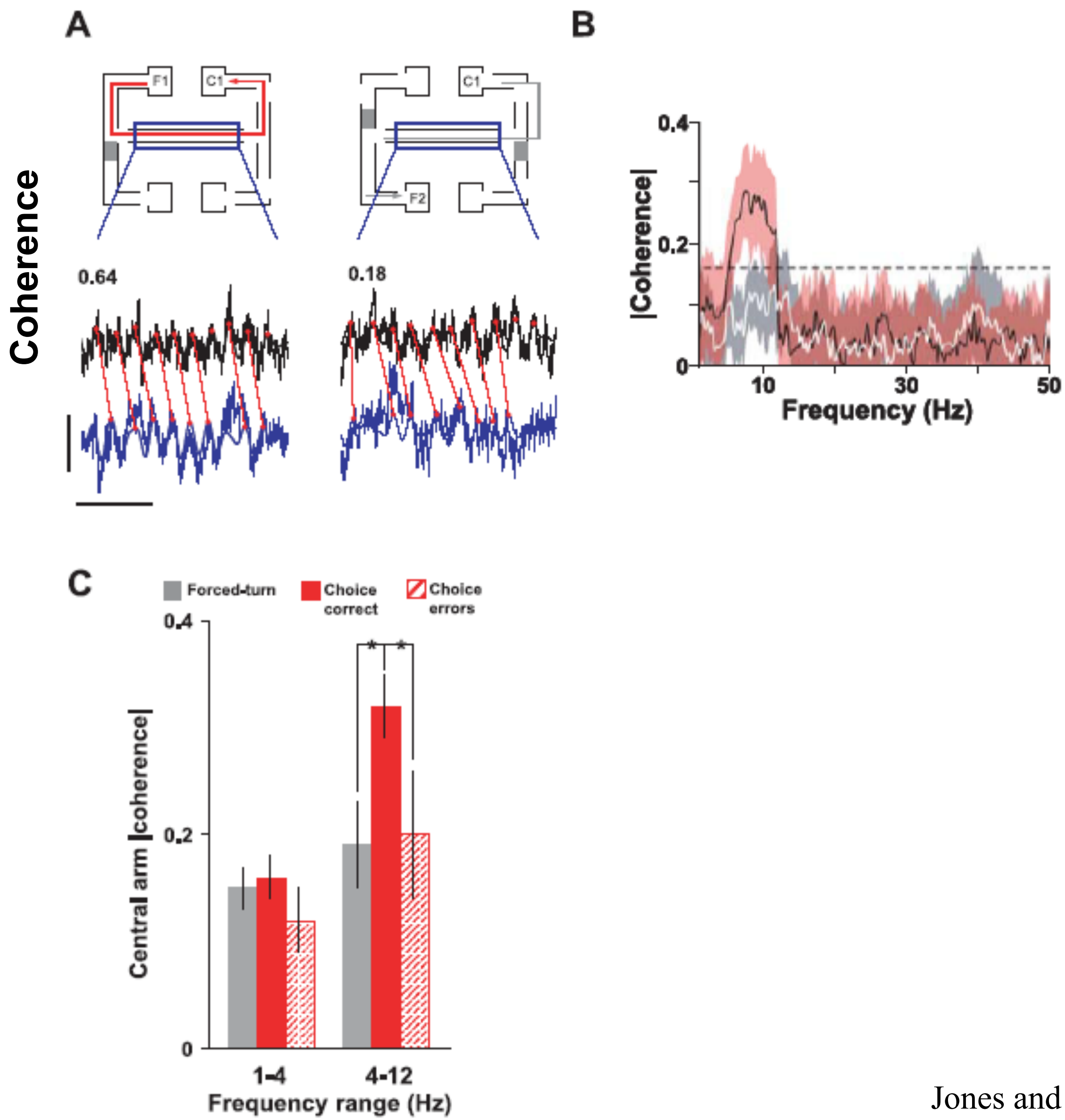
Jones and Wilson, *PLoS Biol.*, 2005

Enhanced theta-phase locking during ‘ correct choice’



Jones and Wilson, *PLoS Biol.*, 2005

LFP *vs.* LFP: Coherence

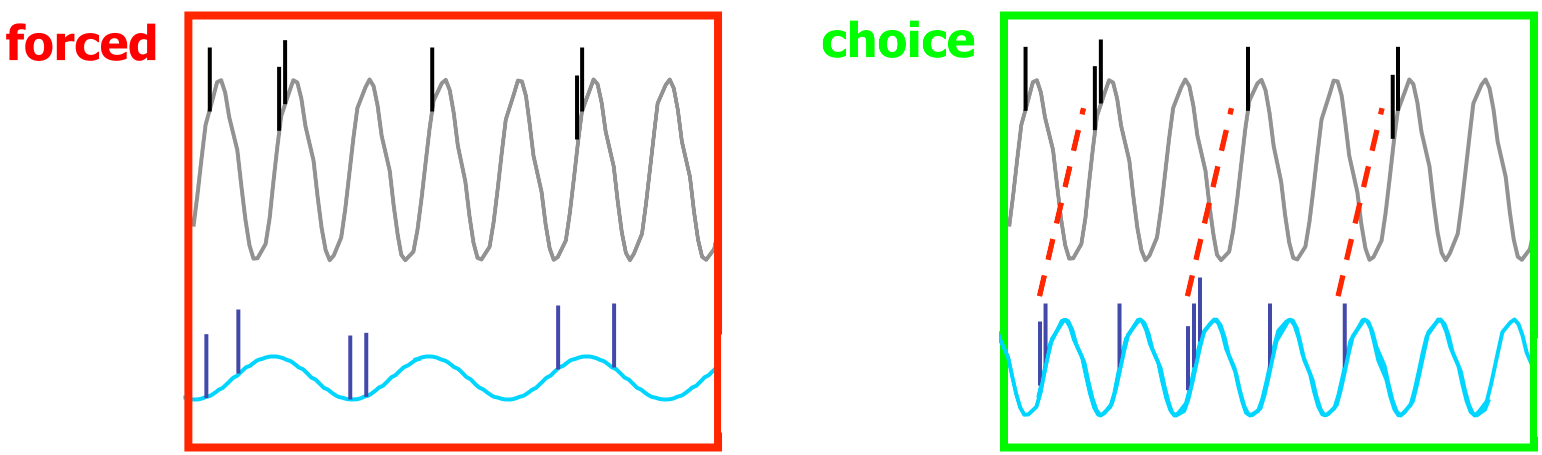


Jones and Wilson, *PLoS Biol.*, 2005

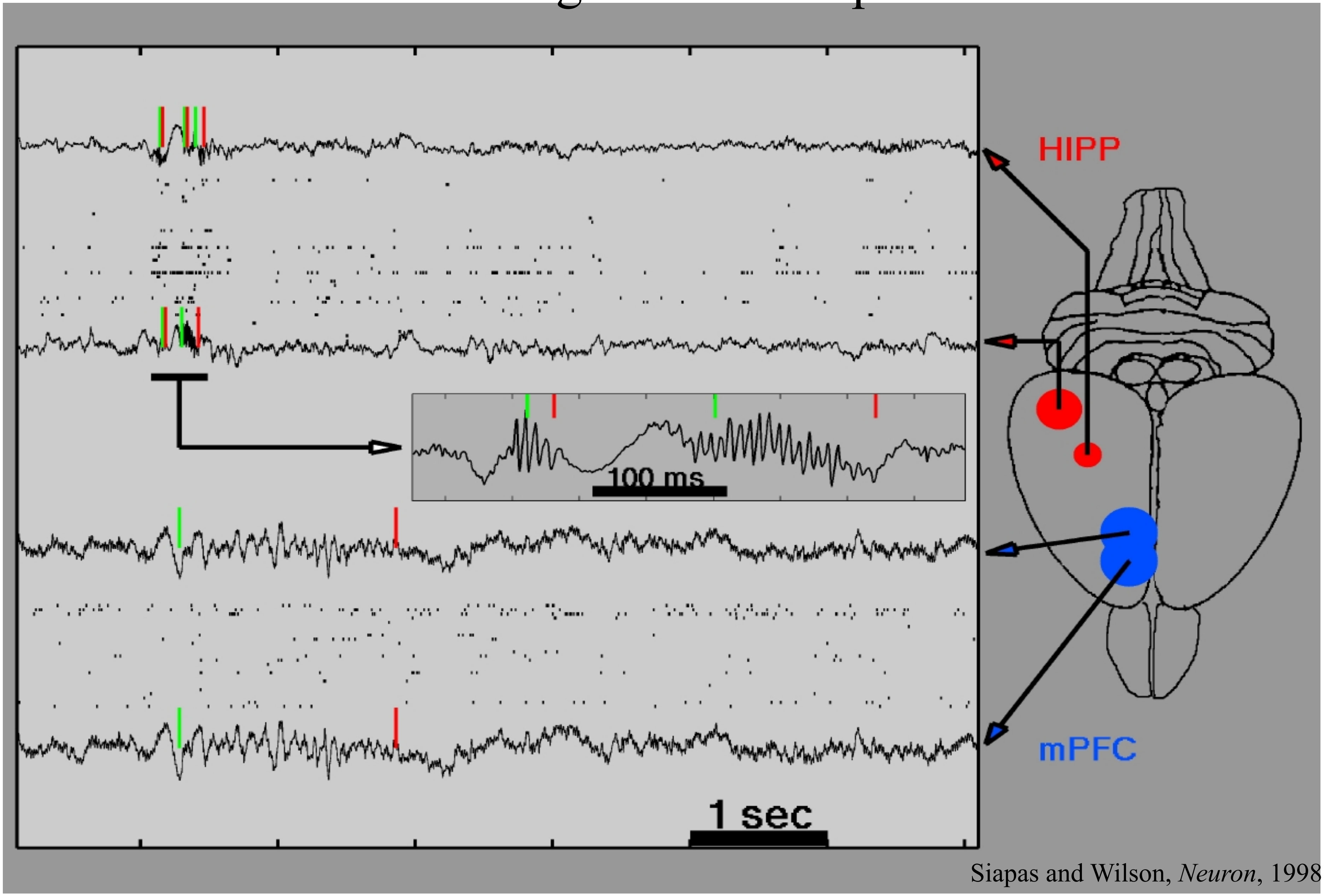
During the **choice** (as opposed to **forced**) condition:

- PFC *firing rates* on the central arm can discriminate between cue locations (reminiscent of primate working memory cells);
- More pronounced *theta modulation* of PFC firing (which in turn correlates with amount of spatial information carried by PFC)
- Increased phase-locking of PFC units to hippocampal theta rhythm.
- Increased phase-locking of hippocampal units to PFC theta rhythm.
- Increased PFC-hippocampal unit correlation.
- Increased LFP *coherence* in the theta frequency range.

- These parameters may reflect or underlie information transfer between HPC and PFC during spatial working memory.

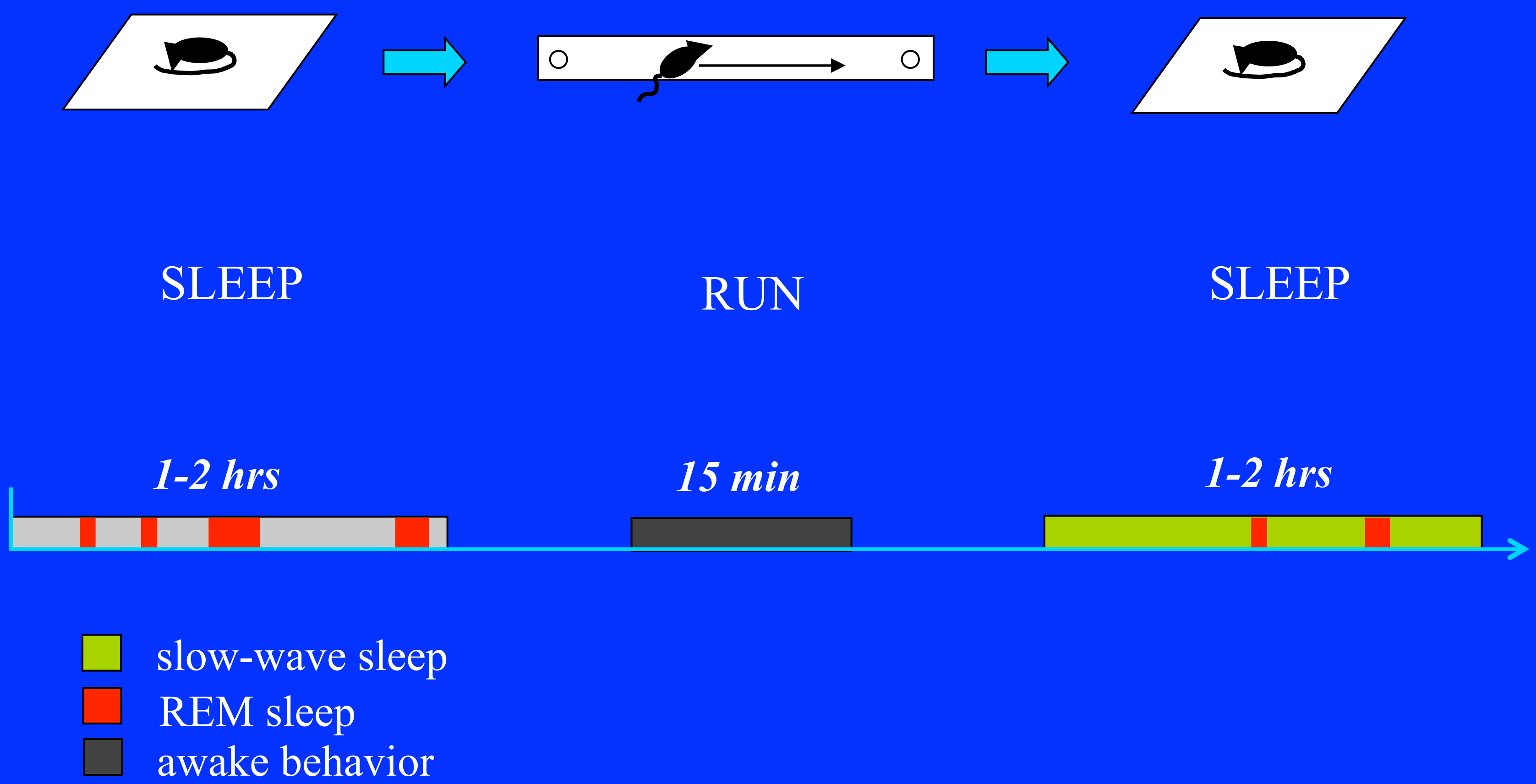


Interaction between the Hippocampus and the Neocortex during NREM Sleep

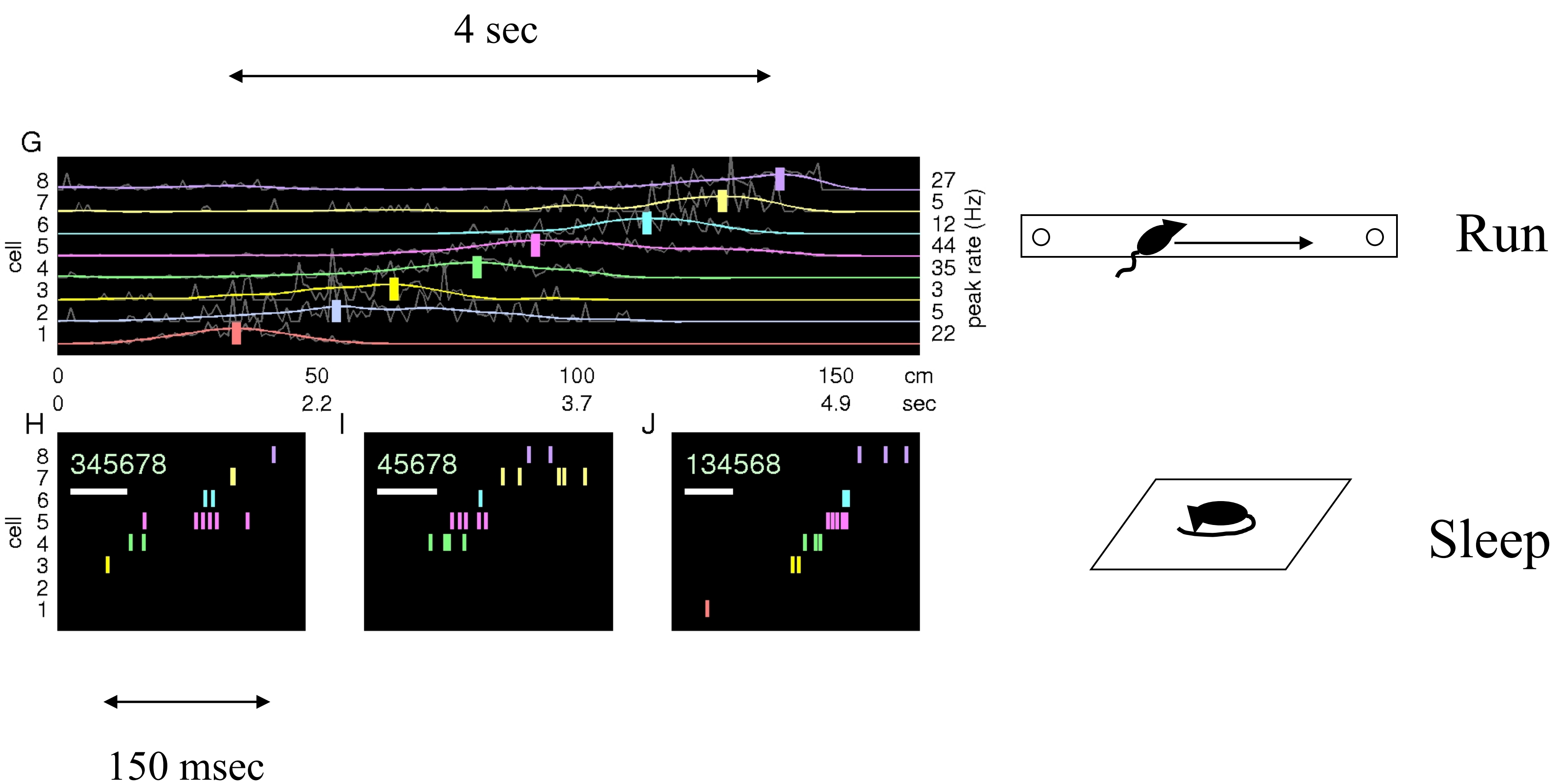


Siapas and Wilson, *Neuron*, 1998

Experimental design

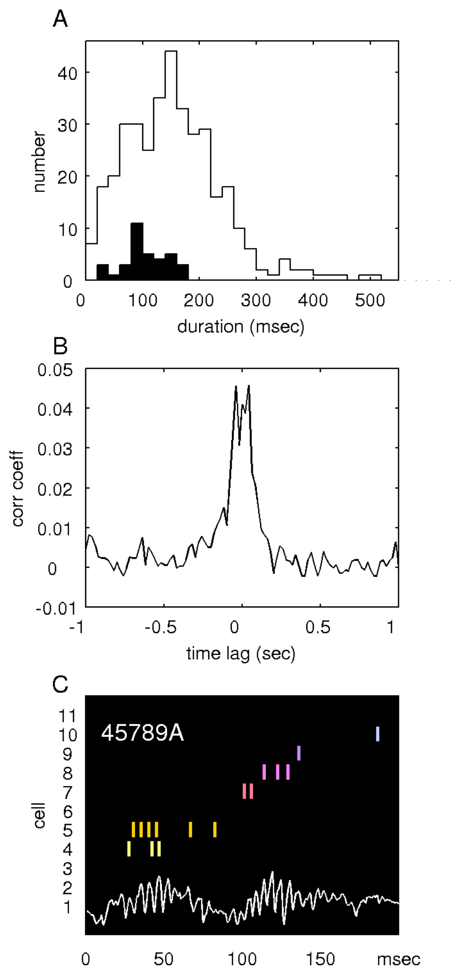


Compressed temporal sequences are expressed in hippocampus during NREM sleep



Lee and Wilson, *Neuron*, 2002

Sequences are re-expressed during CA1 ripple events



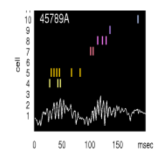
Duration of low probability sequences

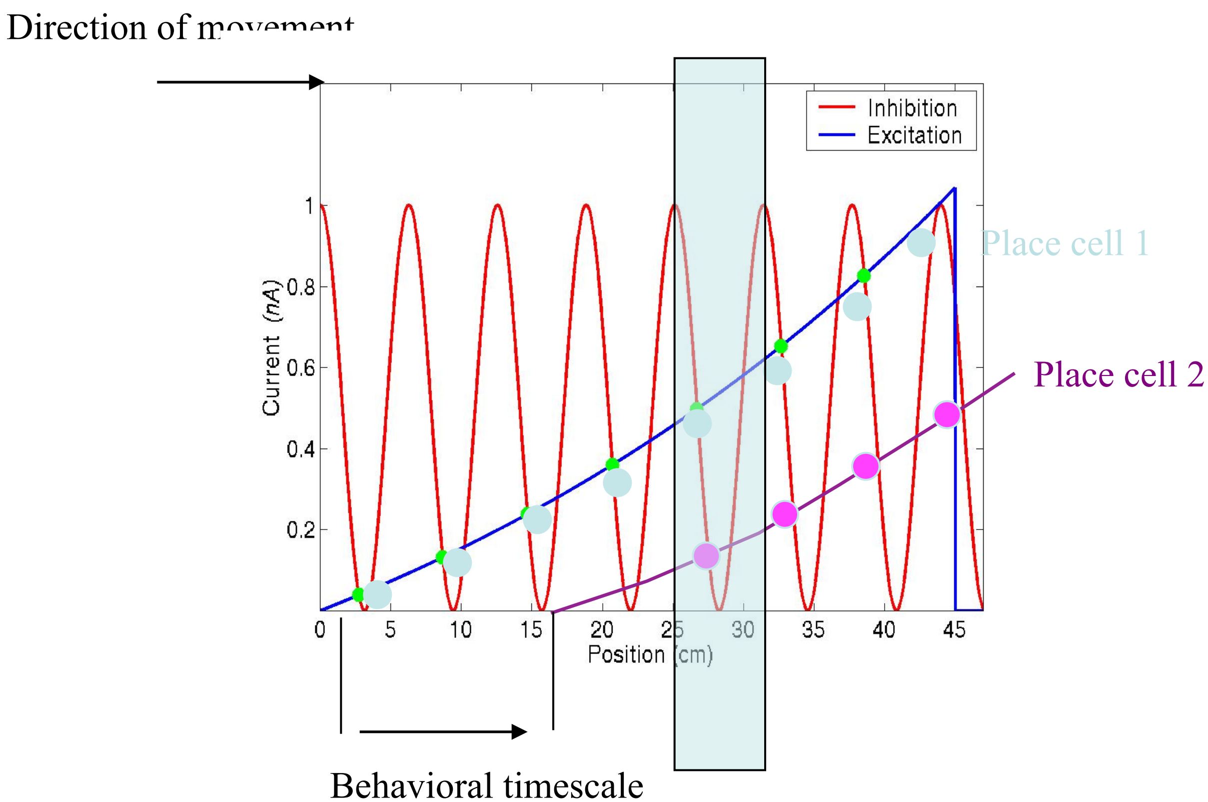
Correlation of low probability sequences and ripples

Example of a low probability sequence and a ripple event

Lee and Wilson, *Neuron*, 2002

Overlapping asymmetric place fields with oscillatory variation in excitability translate behavioral time relationships to biophysical timescales with preserved temporal order





Properties of memory reactivation in NREM sleep

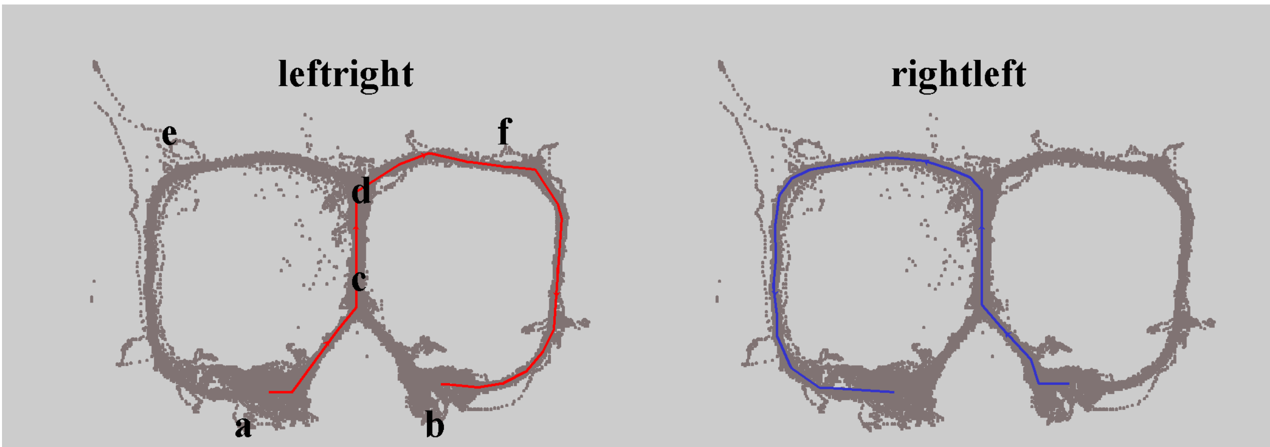
- Temporal sequence memory is replayed during NREM sleep.
- These sequences are compressed by a factor of approximately 10 .
- Replay is most robust in during sleep immediately following behavior (just after falling asleep).
- Memory for sequential experience appears to be broken up into short segments.

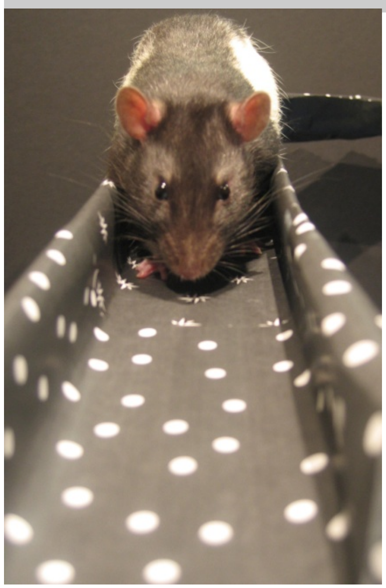
A

Experimental Design:

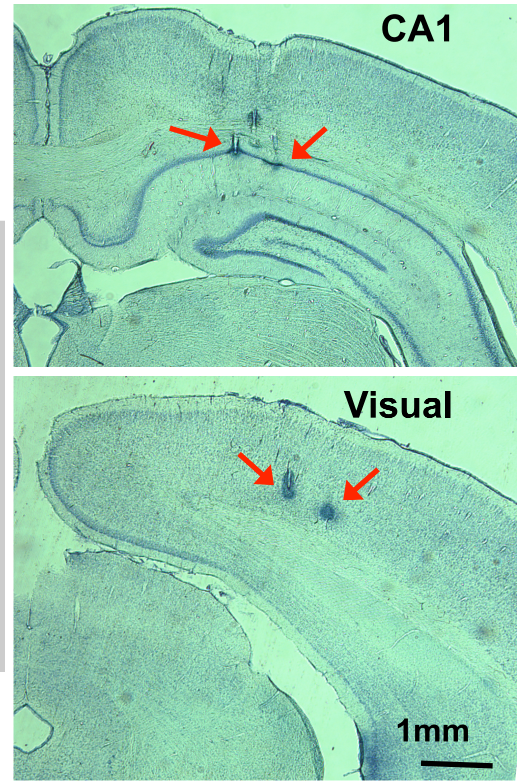
PRE (1-2hrs) — RUN (20-40mins) — POST (1-2hrs)

B



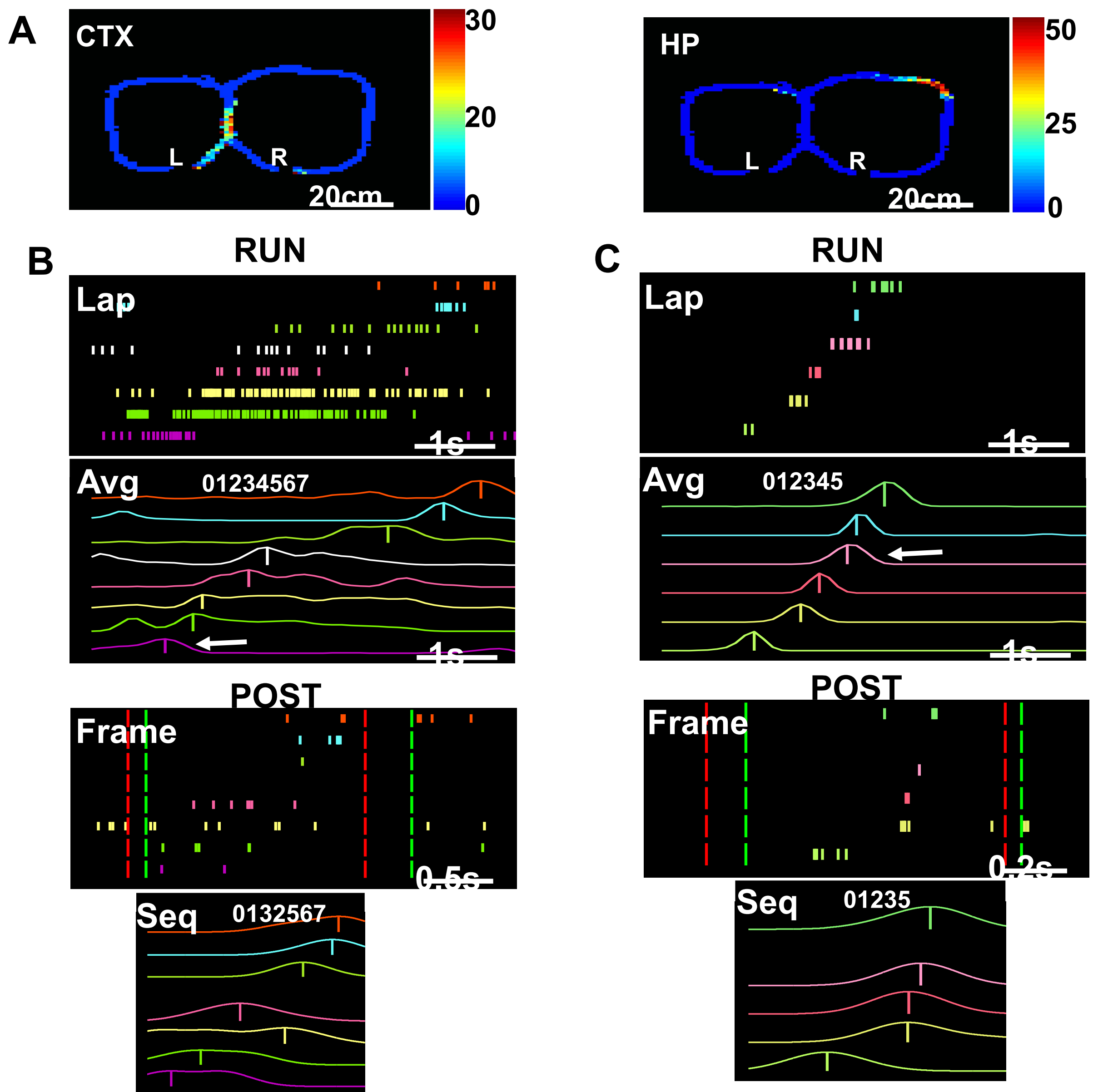


C



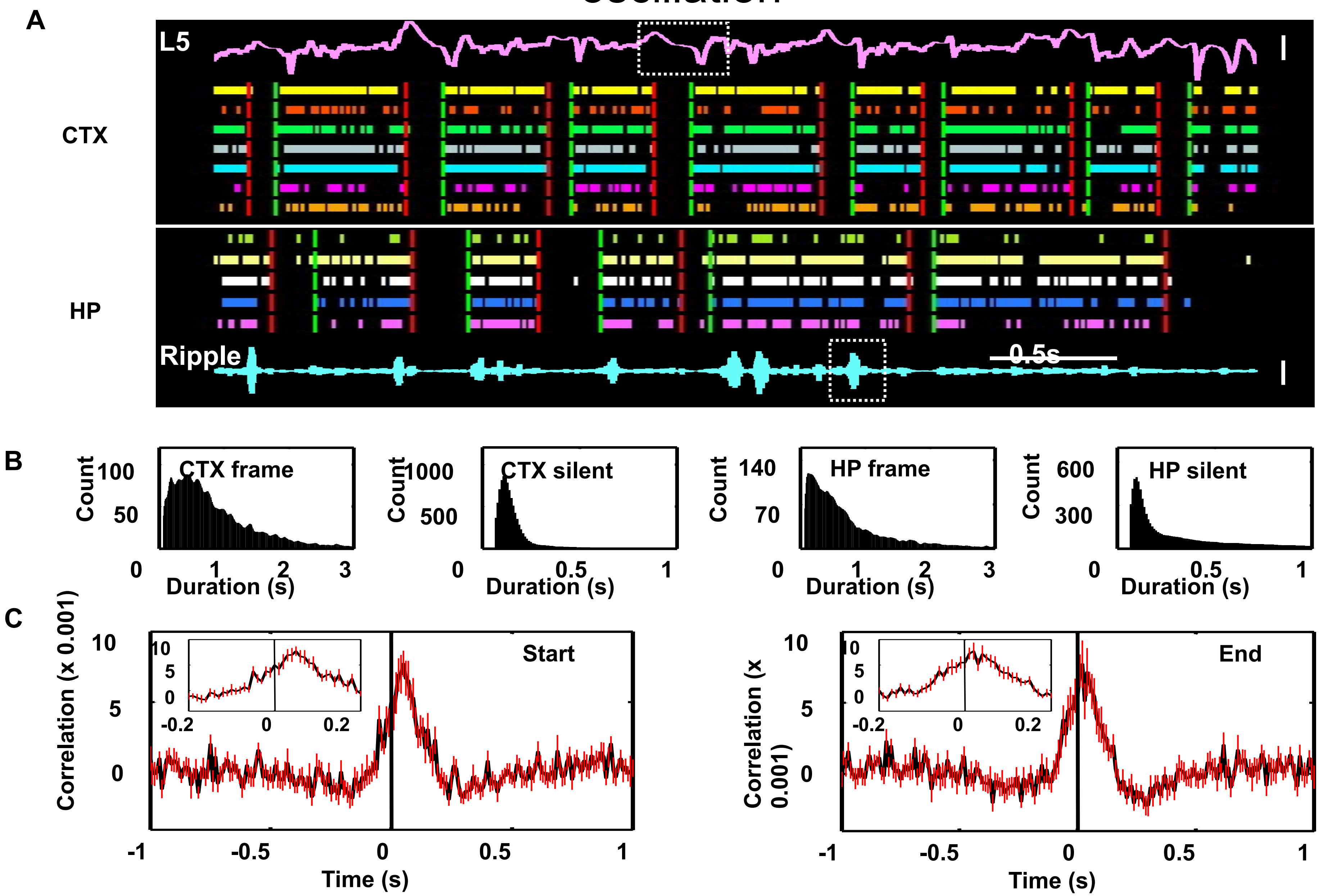
1. Intra-maze local cues, no prominent distal cues
2. Well trained animals: alternation task
3. Recording sites: visual cortex (Occ1, Occ2) and CA1
4. Sleep states (SWS, REM, Wake, Int) classified using EMG and hippocampal EEG

Sequence memory reactivation in hippocampus and visual cortex



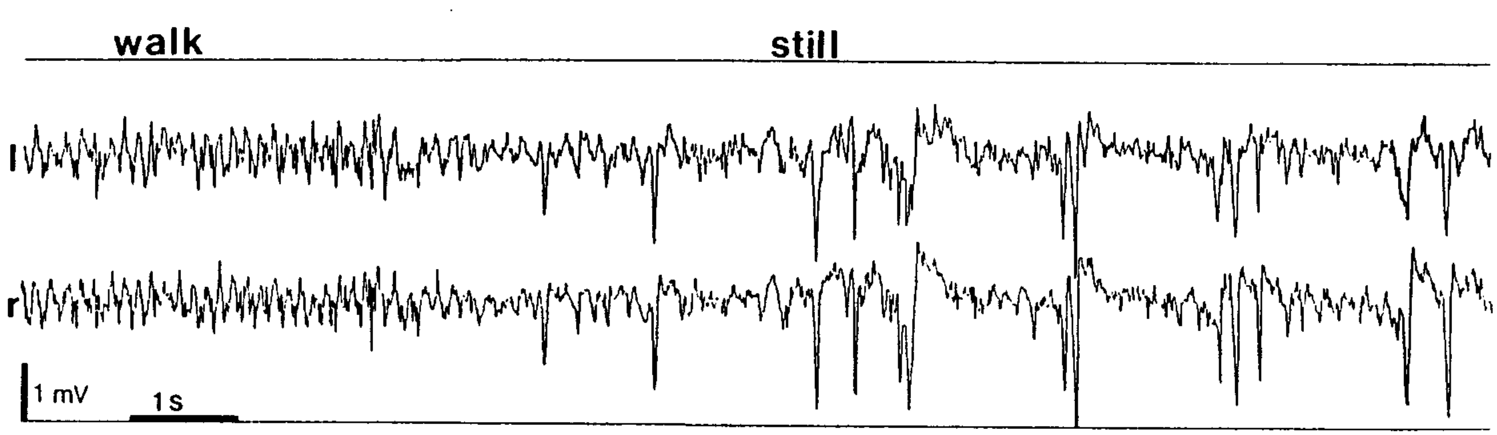
Ji and Wilson, *Nature Neuroscience*, 2007

Reactivation occurs during activity frames correlated with the slow oscillation



Ji and Wilson, *Nature Neuroscience*, 2007

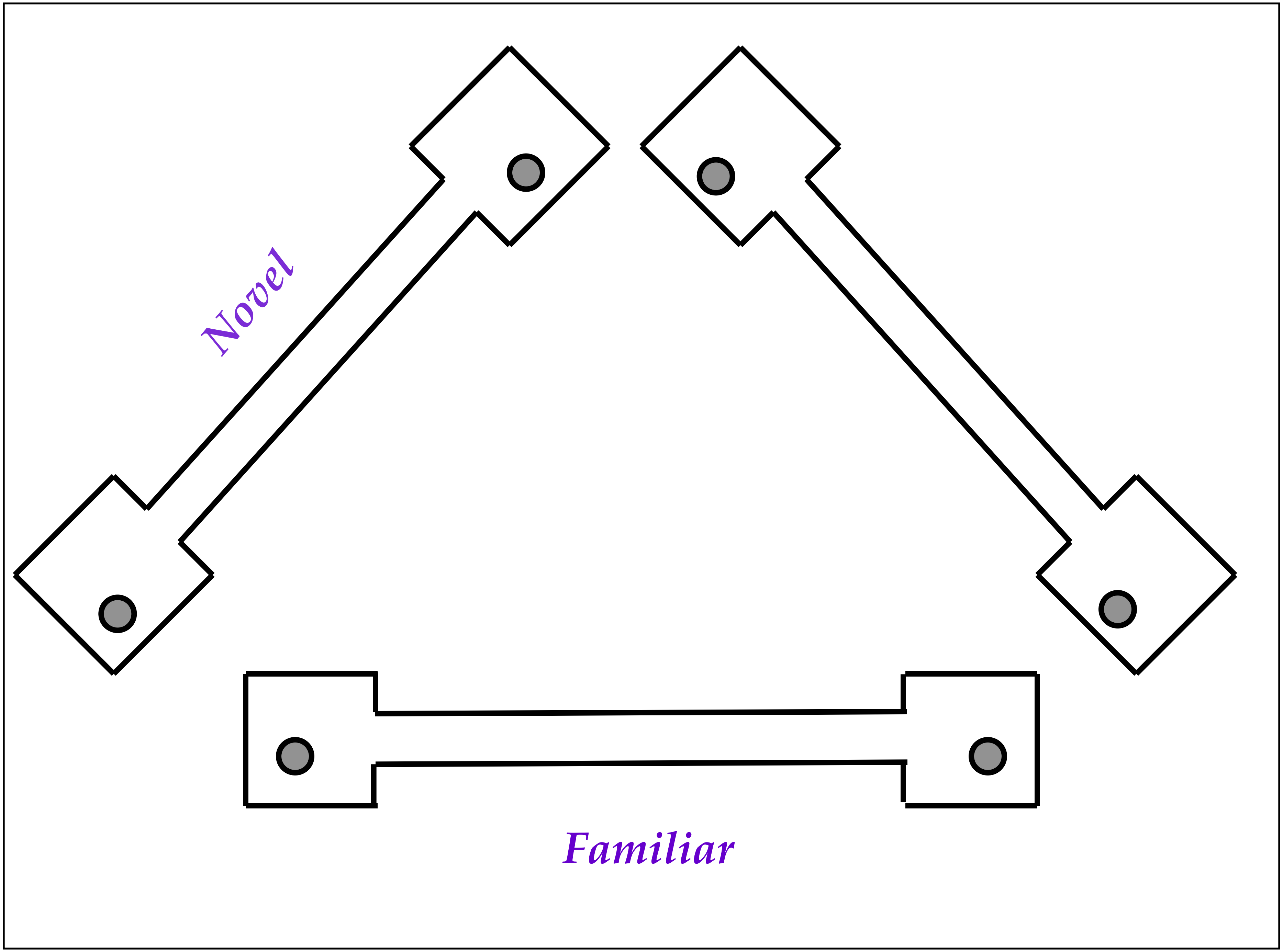
Sharp wave/Ripple activity during quiet wakefulness



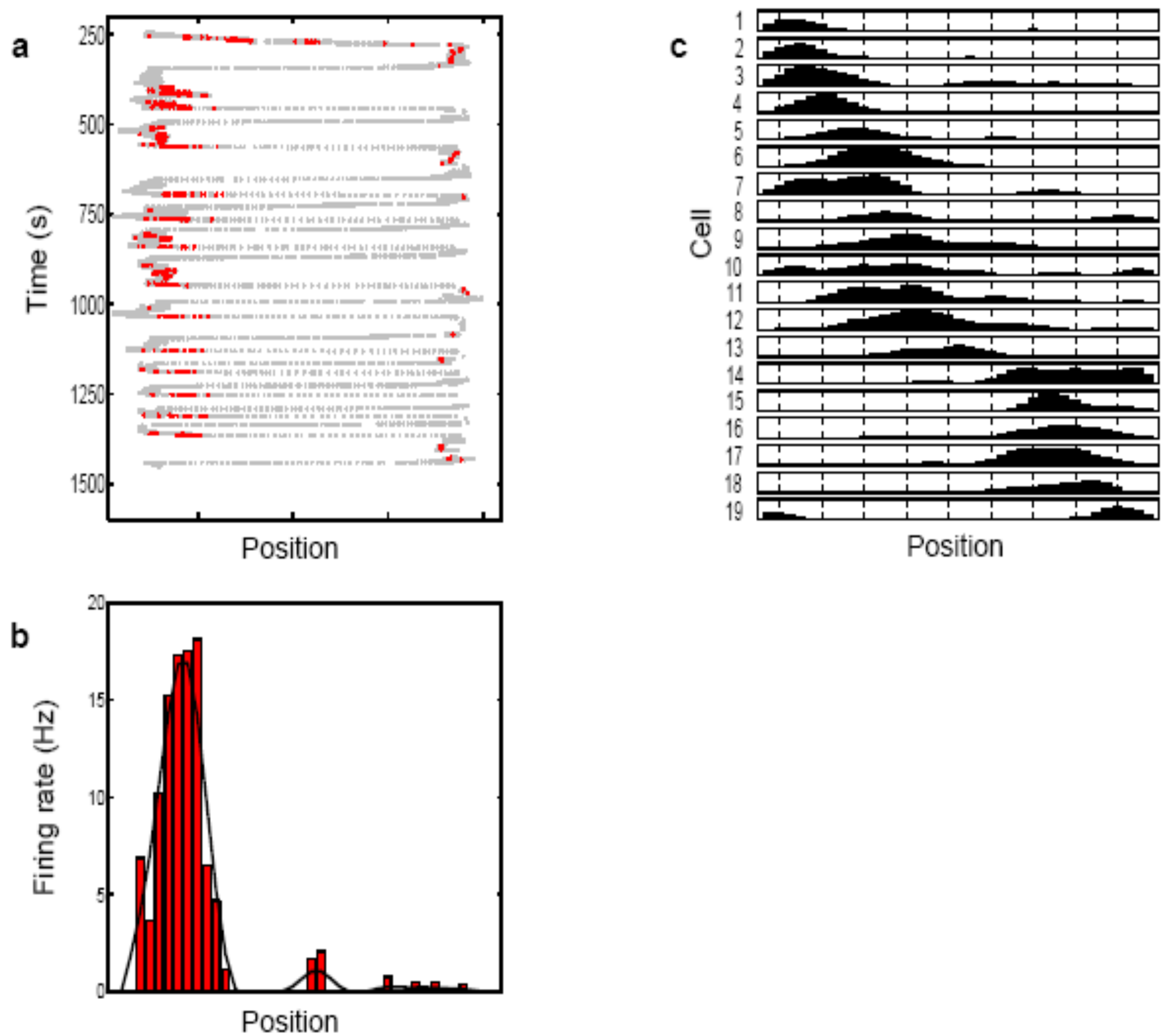
Buzsáki 1989

Hippocampal activity during quiet wakefulness

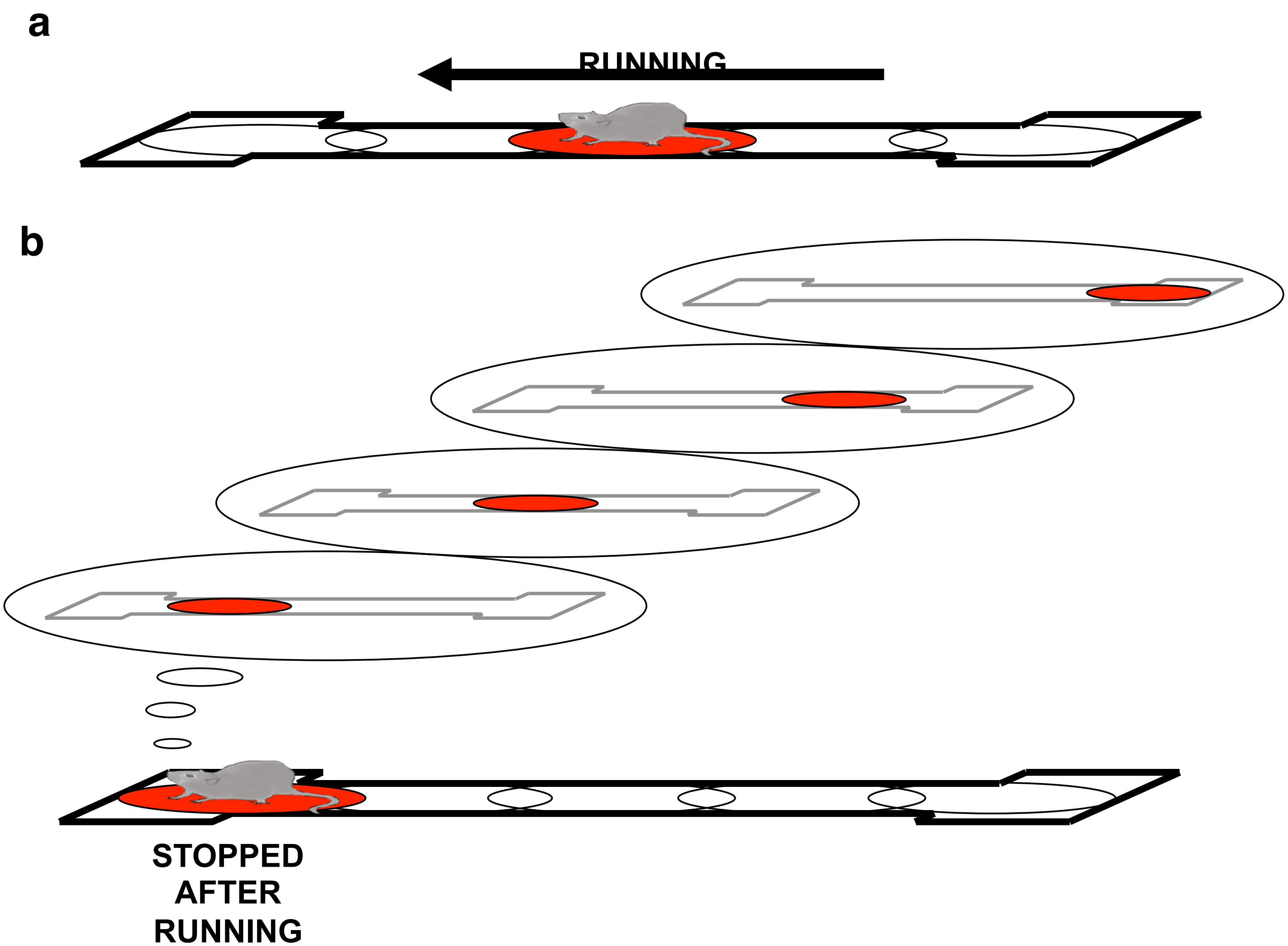
- During awake behavior, there are periods of quiet wakefulness that have EEG that is similar to NREM consisting of brief bursts of activity modulated by high frequency “ripple” oscillations.
- Is there structure to the patterns of multiple single neuron activity during this state?


Novel
Familiar

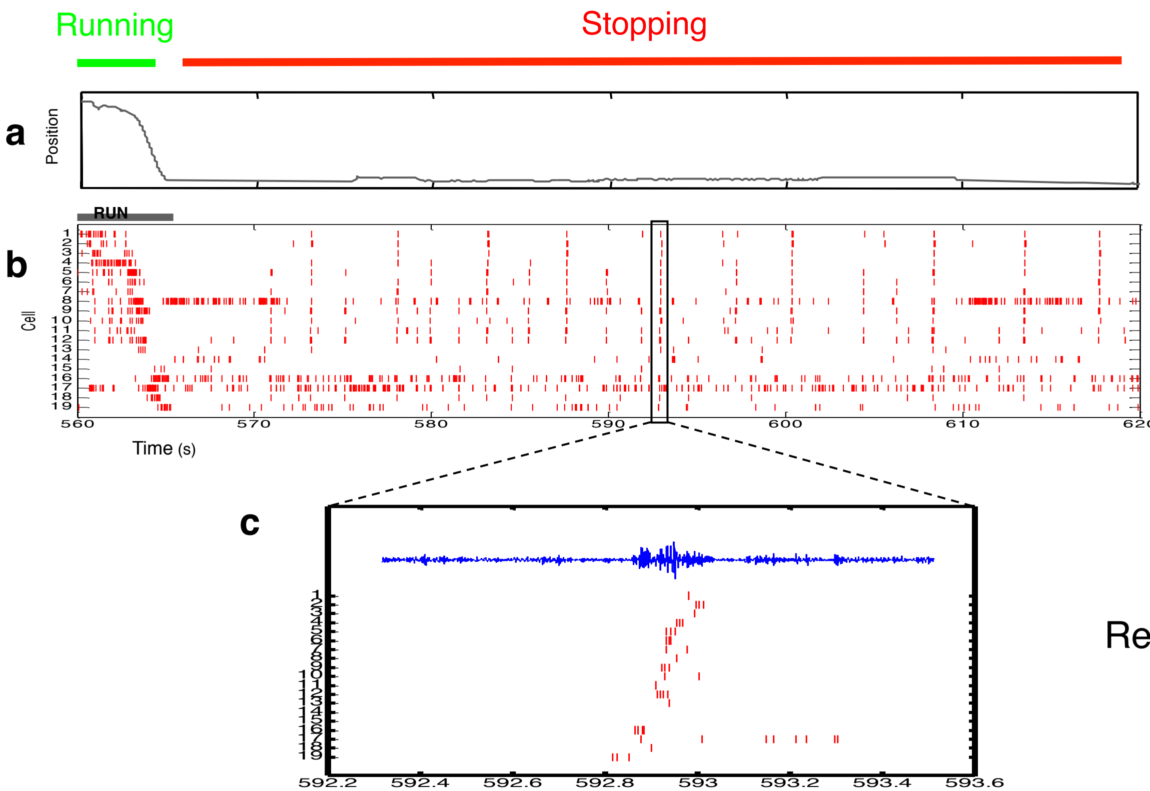
Place field sequences during running



Foster and Wilson, *Nature*, 2006


a
RUNNING
b
STOPPED
AFTER
RUNNING

Memory of recent spatial experience replayed in reverse-time order

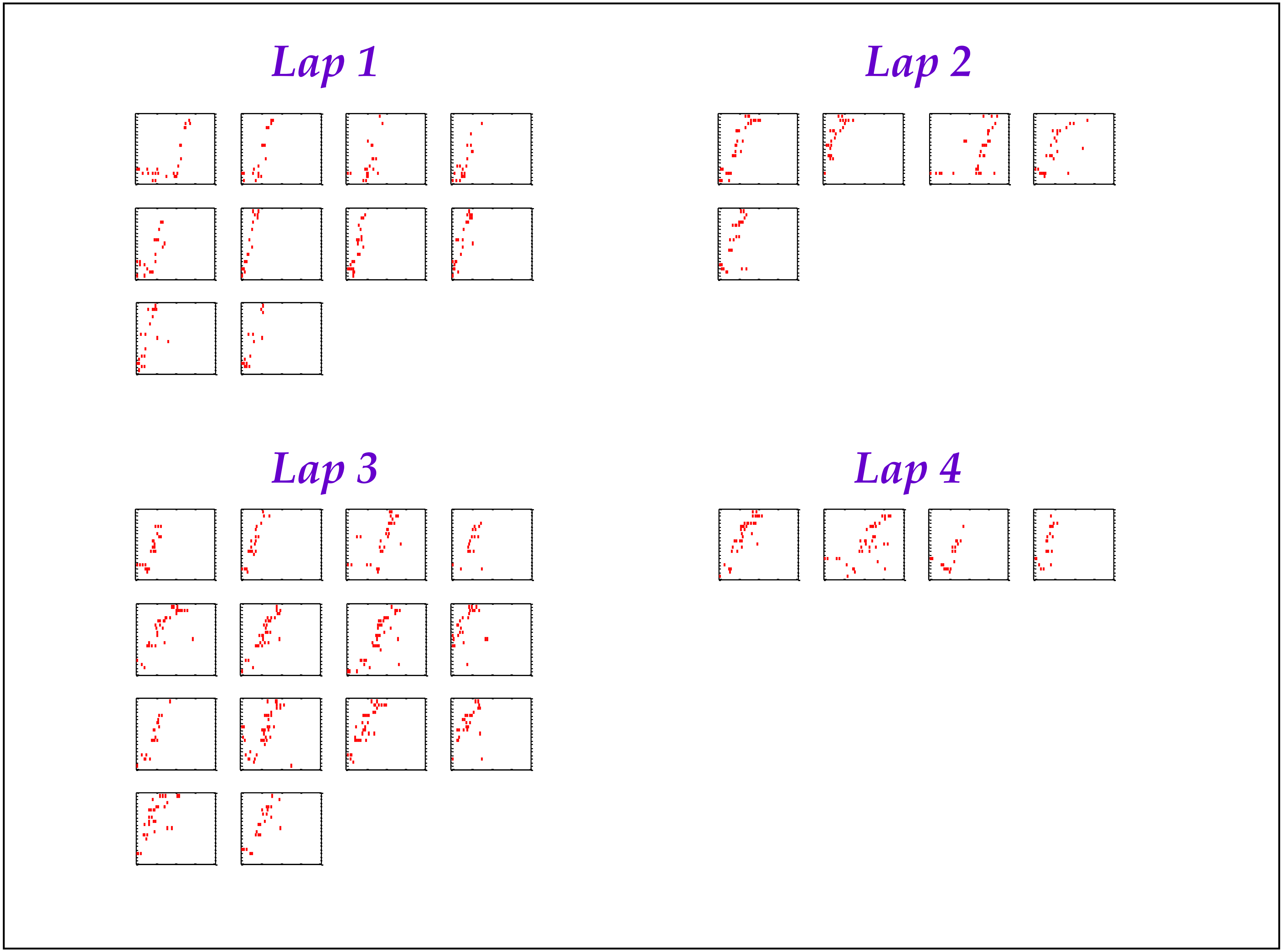


Position vs. time

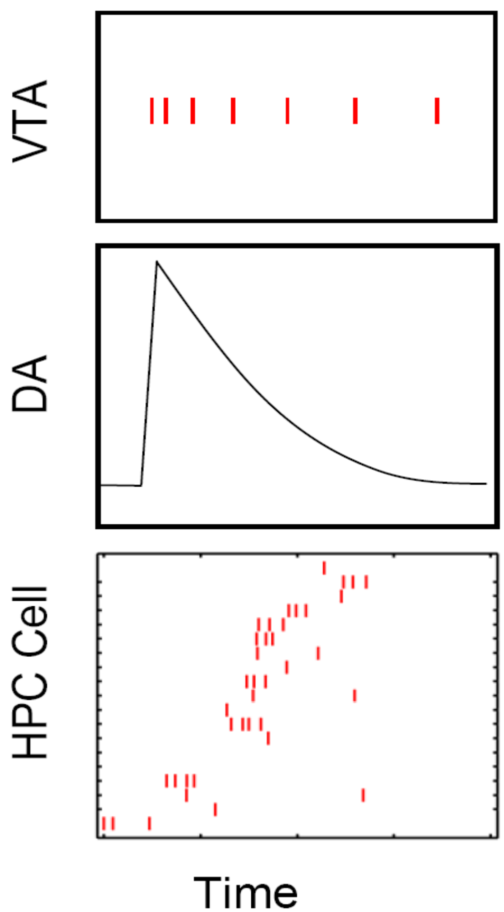
Hippocampal place-cell activity vs. time

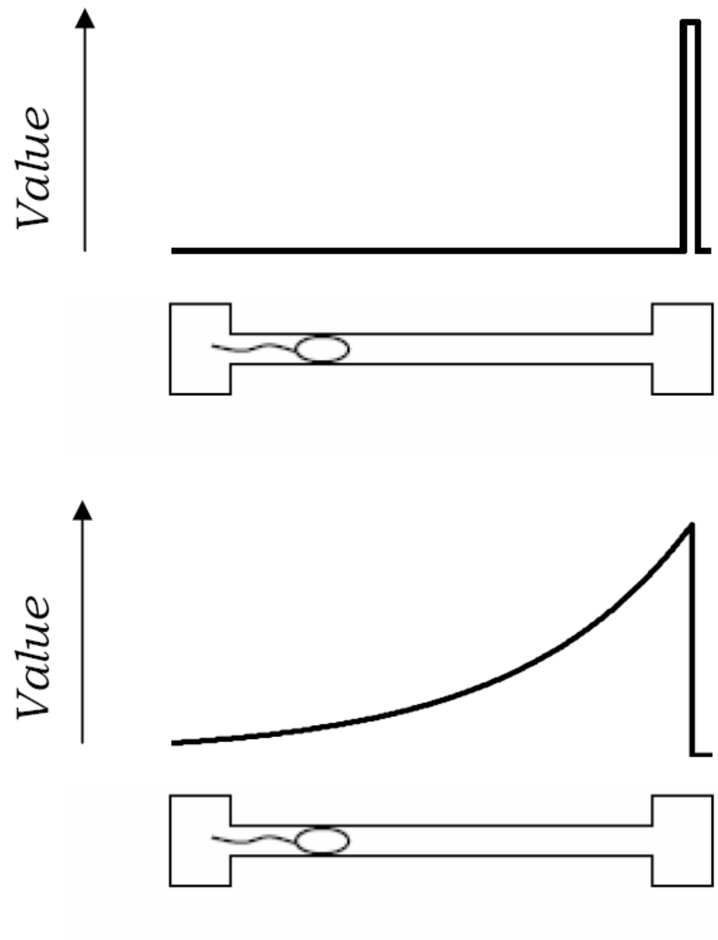
Reverse-time sequence replay during hippocampal ripples

Foster and Wilson, *Nature*, 2006


Lap 1
Lap 2
Lap 3
Lap 4

Reverse sequence evaluation can be used to rapidly solve the temporal credit assignment problem

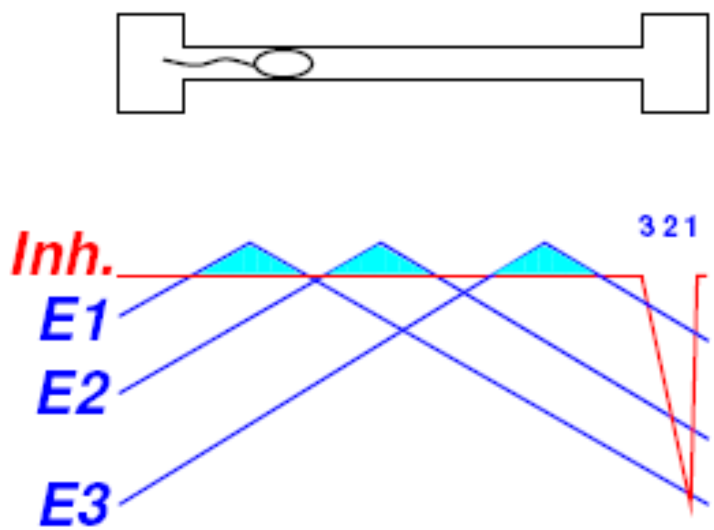




Reverse Evaluation

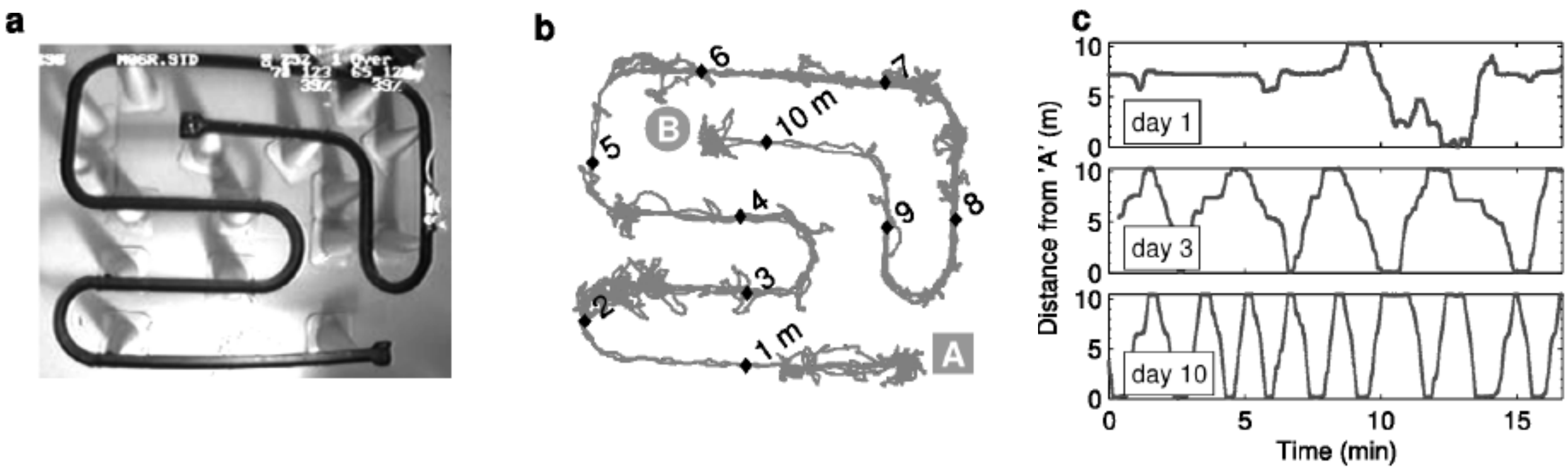
- Dynamic Programming
- Reinforcement Learning
- Temporal Difference (TD) Learning
- Q Learning
- Offline Learning in Reinforcement Learning
- Classical & Operant Conditioning

Model of Reverse Replay



Sharp Waves Reveal Sub-Threshold Fields

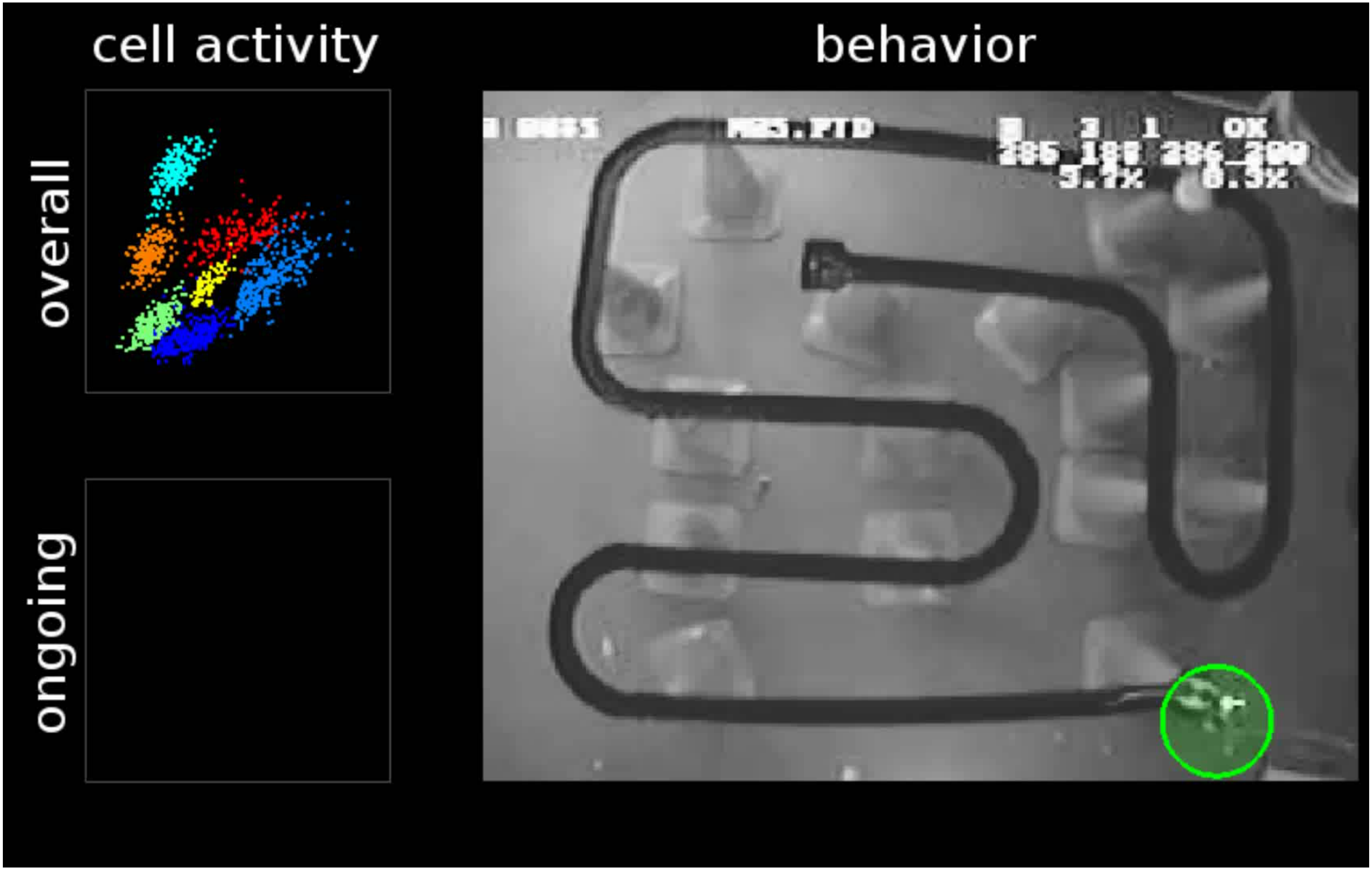
Long behavioral sequences on a 10m track



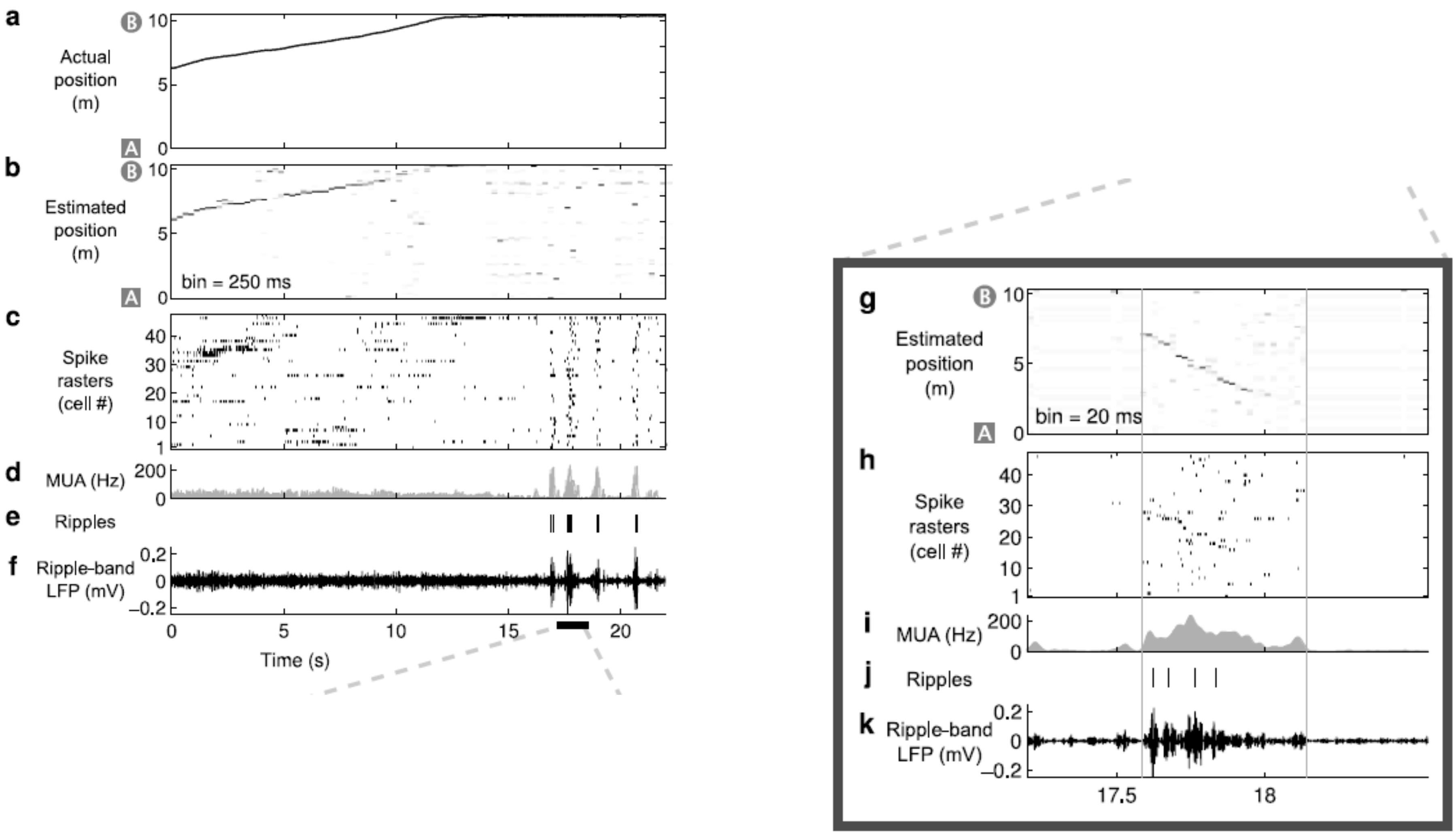
[Place fields]()

Davidson, Kloosterman, and Wilson, *Neuron*, 2009

Hippocampal Ensemble Decoding

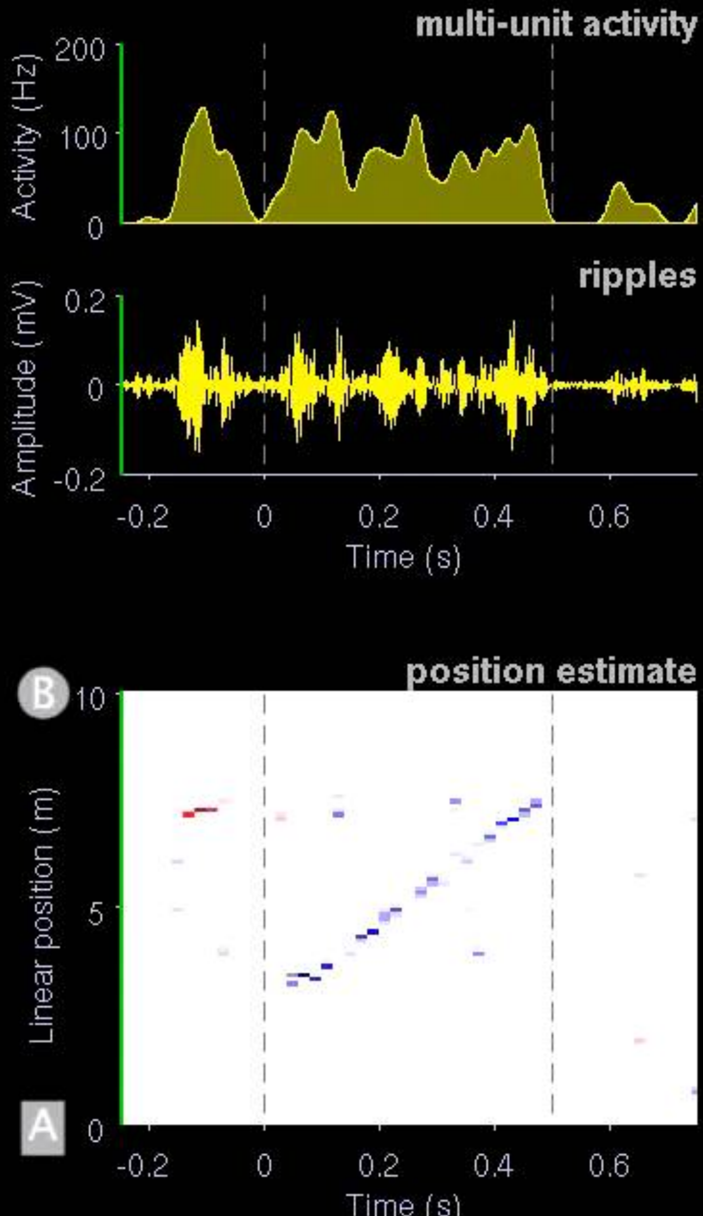


Reconstruction of extended sequence replay during quiet wakefulness



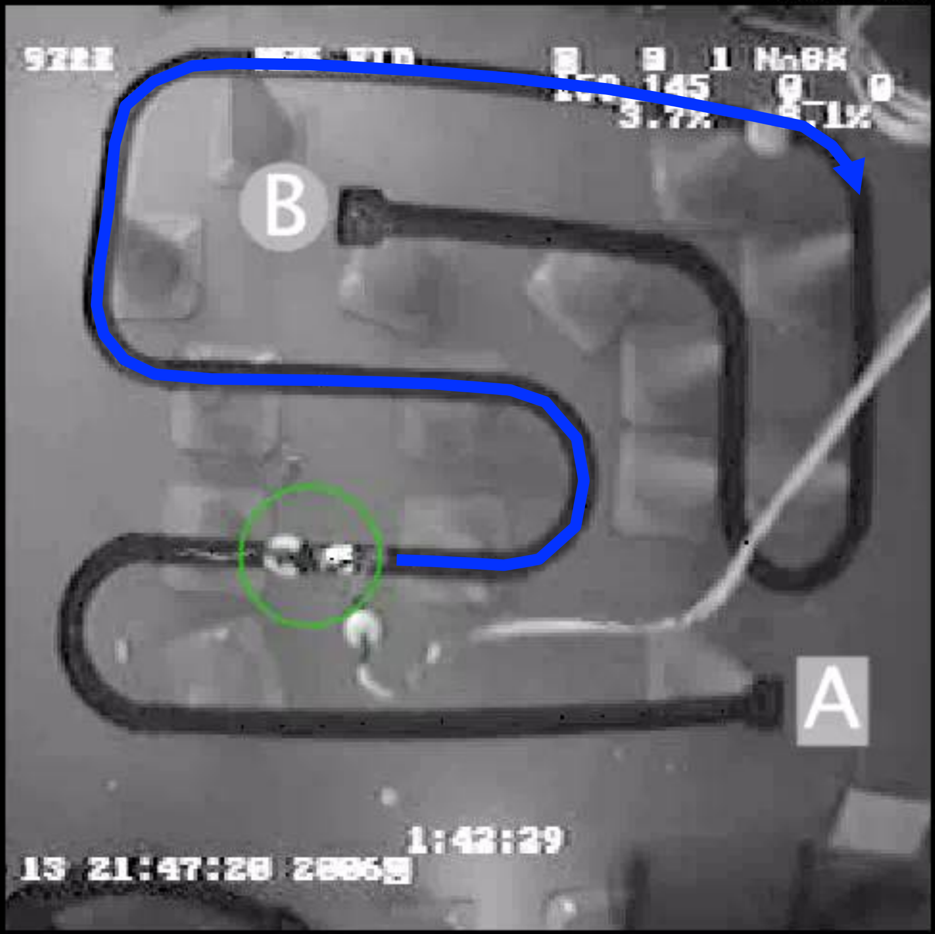
Davidson, Kloosterman, and Wilson, *Neuron*, 2009

Forward Replay from A to B

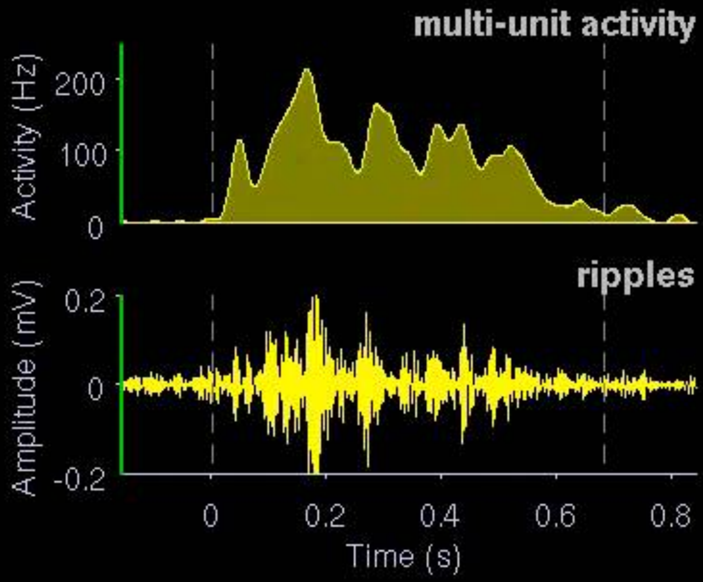


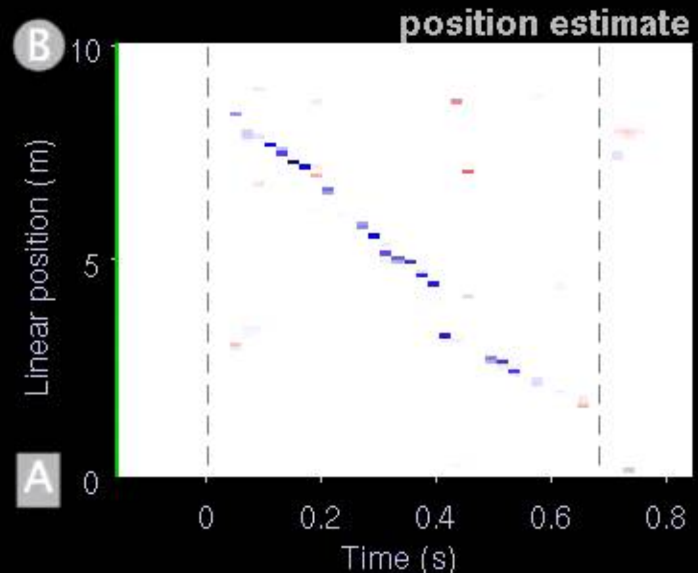
Forward replay

-250 ms



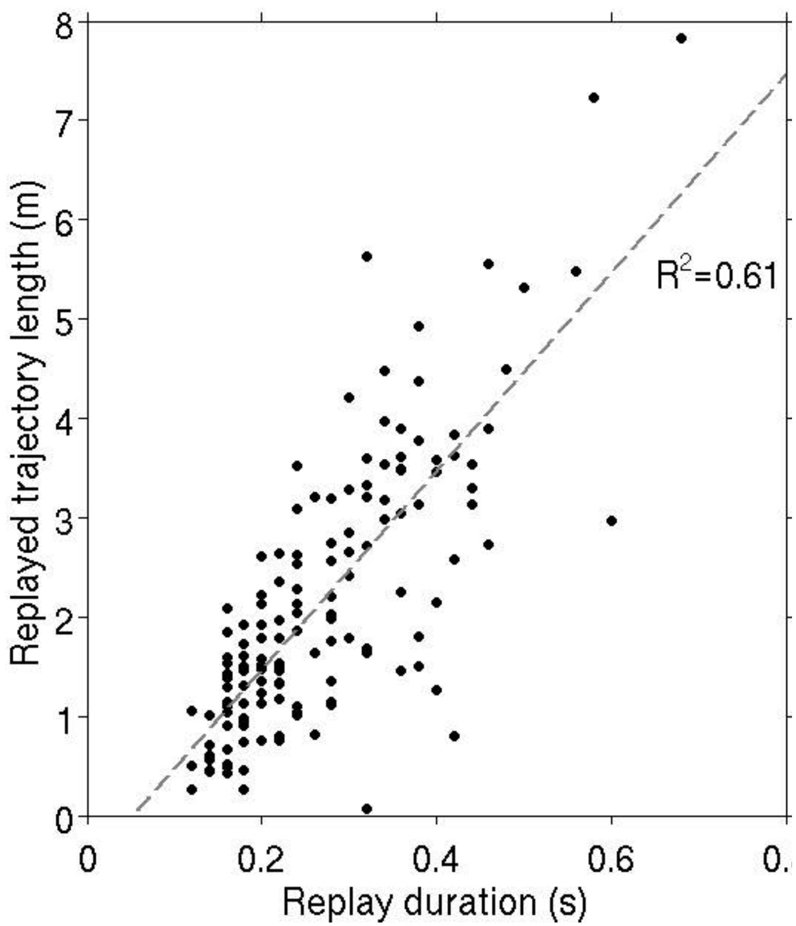
Reverse Replay from B to A

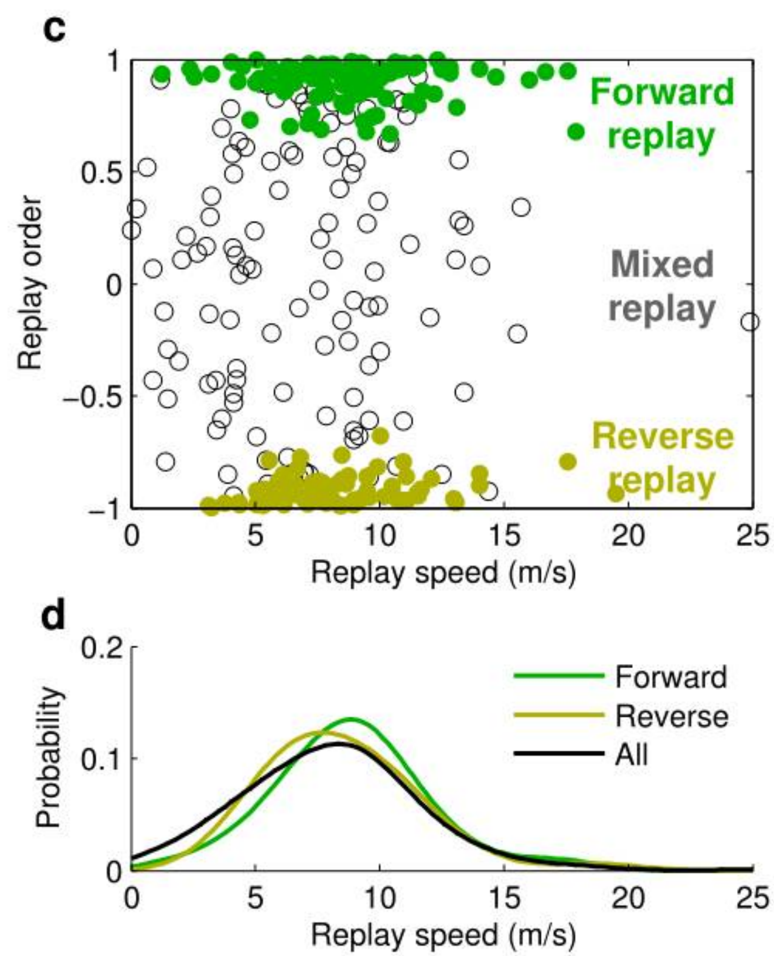




Reverse replay

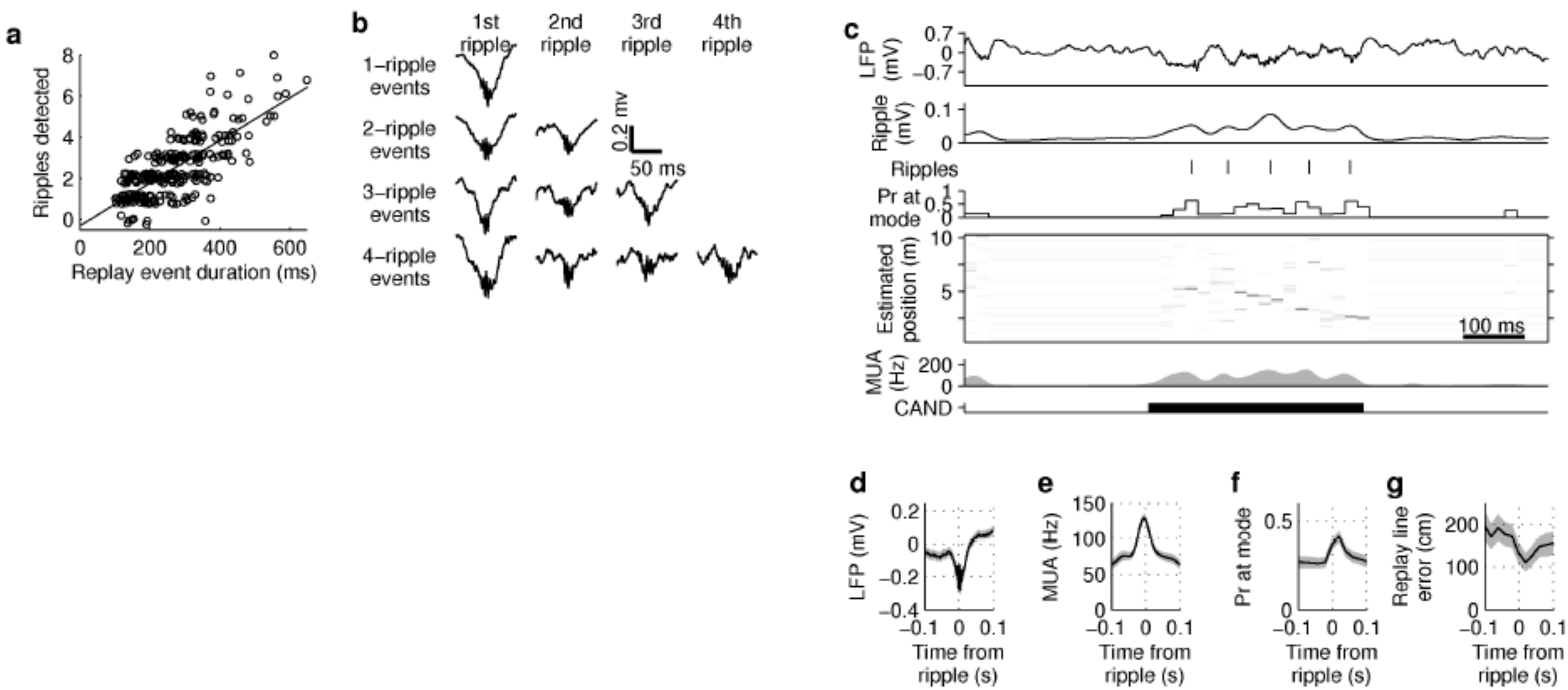
Extended replay has a characteristic speed





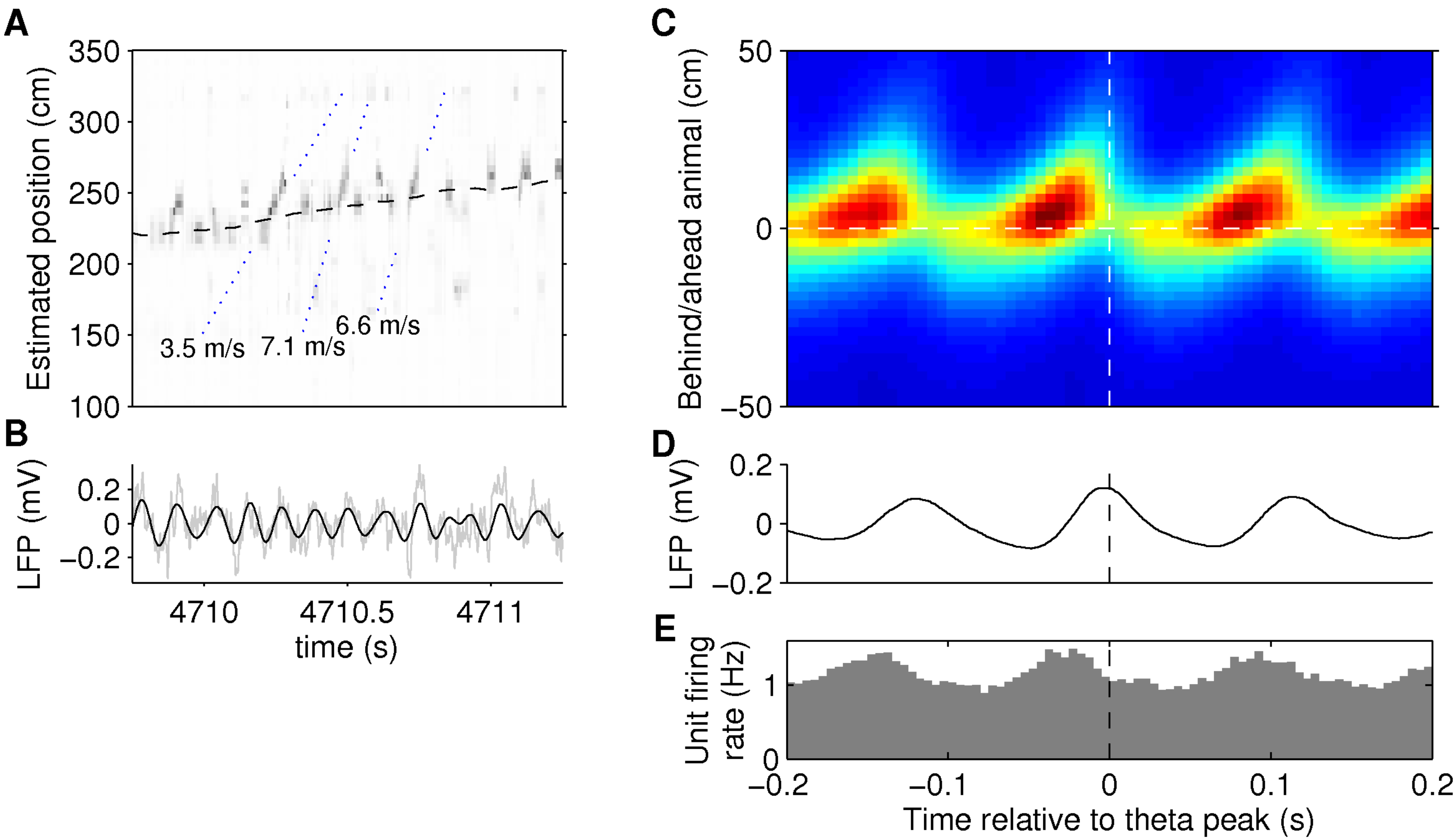
Davidson, Kloosterman, and Wilson, *Neuron*, 2009

Extended replay spans multiple ripple events



Davidson, Kloosterman, and Wilson, *Neuron*, 2009

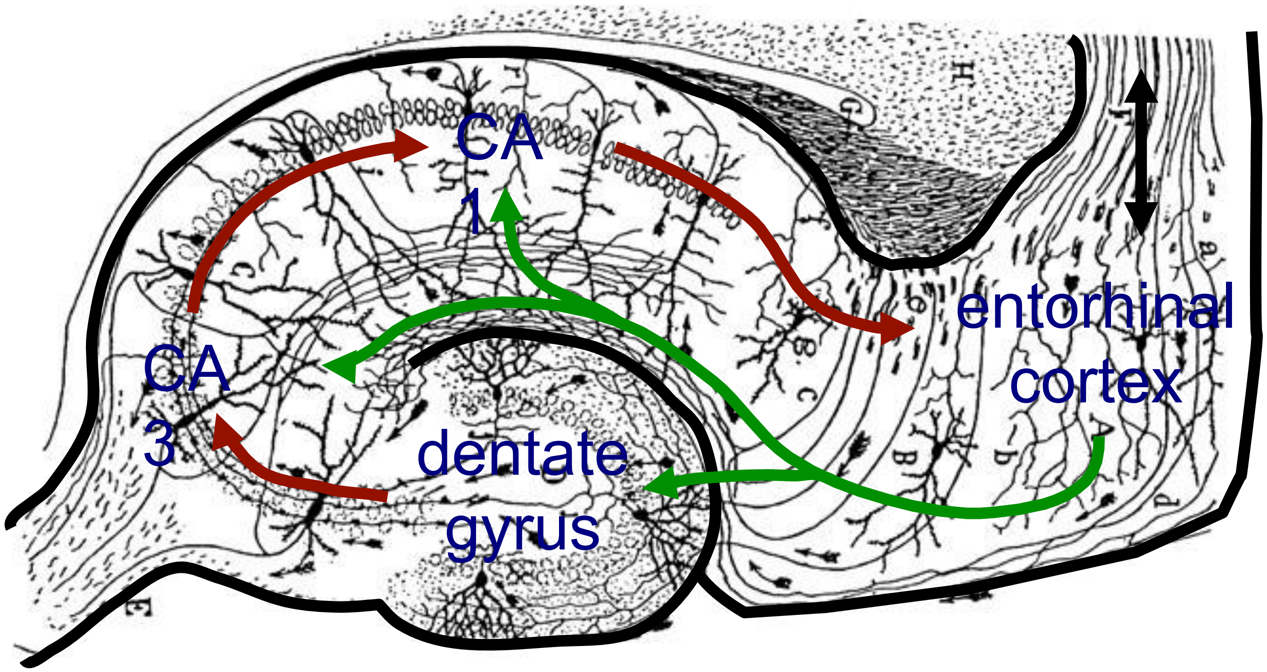
Single ripple sequences are at same scale as theta sequences



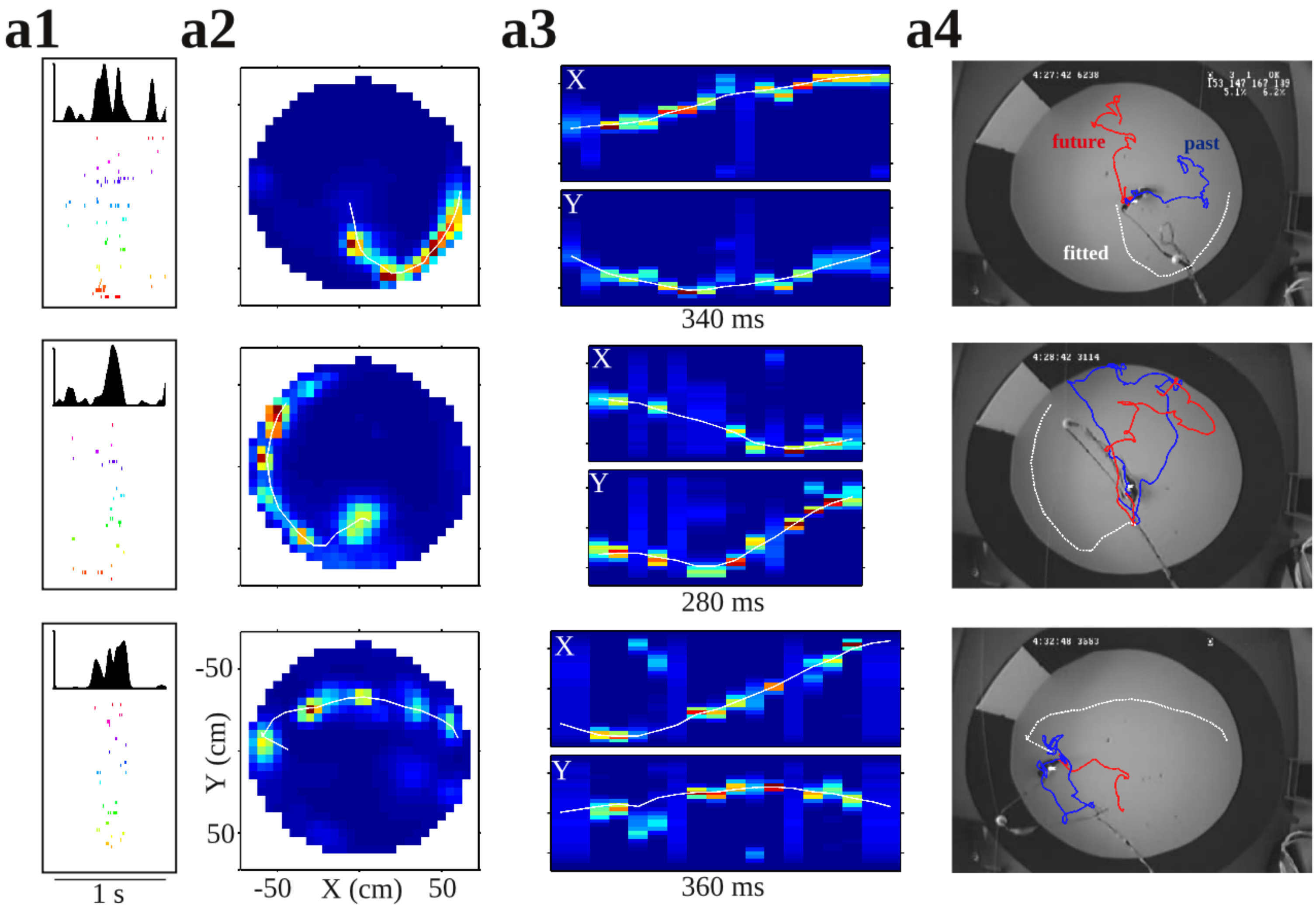
Davidson, Kloosterman, and Wilson, *Neuron*, 2009

Chaining of sequences

$A \rightarrow A' \rightarrow A''$



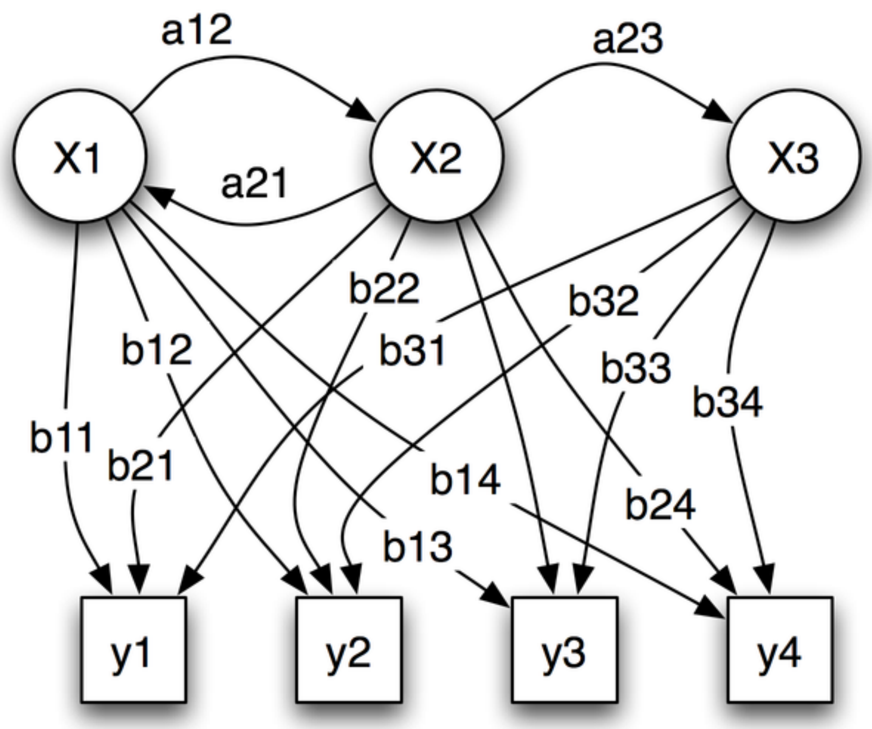
Open field sequence reactivation



Summary

- ✓ Replay occurs at a typical speed of ~8 m/s, spans many meters and last hundreds of ms, and is associated with trains of ripples.
- ✓ Replay is not exclusive to reward sites
- ✓ Start of replayed trajectories is not exclusively tied to the actual position of the animal
- ✓ Sequences can be in forward or reverse time order
- ✓ Replayed trajectories can be ahead or behind the animal

Hidden Markov Model



Probabilistic parameters of a hidden Markov model (example)
x — states
y — possible observations
a — state transition probabilities
b — output probabilities

Hinton's Recurrent Temporal Restricted Boltzmann Machine (RTBM) architecture

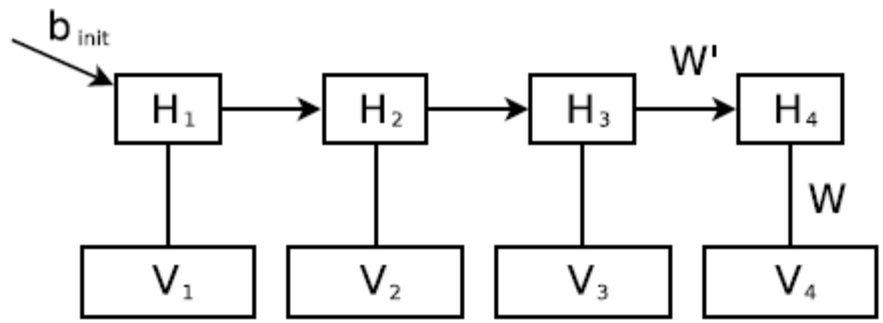


Figure 1: The graphical structure of a TRBM: a directed sequence of RBMs.

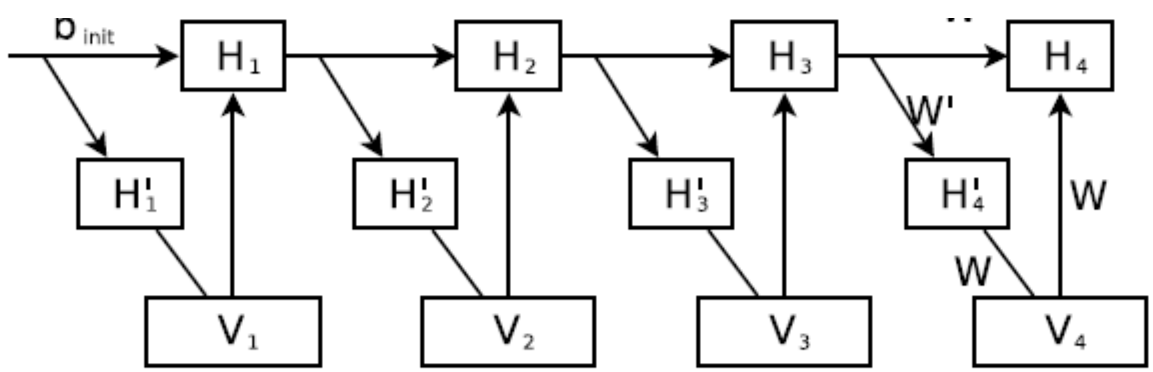


Figure 2: The graphical structure of the RTRBM, Q. The variables H_t are real valued while the variables H'_t are binary. The conditional distribution $Q(V_t, H'_t|h_{t-1})$ is given by the equation $Q(v_t, h'_t|h_{t-1}) = \exp\left(v_t^\top W h'_t + v_t^\top b_V + h'_t(b_H + W'h_{t-1})\right)/Z(h_{t-1})$, which is essentially the same as the TRBM's conditional distribution P from equation 5. We will always integrate out H'_t and will work directly with the distribution $Q(V_t|h_{t-1})$. Notice that when V_1 is observed, H'_1 cannot affect H_1.