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.
The lamellar hypothesis revisited

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, perirhinal 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

Place Fields on Linear Tracks
Hippocampal Place Cells
Hippocampal Ensemble Decoding
Place Fields Become Spatially Asymmetric with Experience

Mehta et al., Neuron, 2000

Direction of movement

Firing Rate Hz

Skewness

Late

Early

Location cm
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.

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.
HPC-PFC: functionally connected

- Spatial navigation & memory deficits in rodents
- Episodic memory deficits in humans
- Working memory deficits in rodents and humans
- Loss of ‘executive control’

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

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

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
Behaviour & Position

Extracellular Action Potentials (spikes)

Local Field Potentials (LFP)

Data

choice

forced

HPC

PFC
Interactions: spikes vs. LFP
Cross-correlation of PFC spike times with theta peak times (normalized by firing rate)

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
Experimental design

- **SLEEP**: 1-2 hrs
- **RUN**: 15 min
- **SLEEP**: 1-2 hrs

- slow-wave sleep
- REM sleep
- awake behavior
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 immediately following behavior (just after falling asleep).
• Memory for sequential experience appears to be broken up into short segments.
Experimental Design:

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

Reactivation occurs during activity frames correlated with the slow oscillation

Sharp wave/Ripple activity during quiet wakefulness
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
STOPPED AFTER RUNNING

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
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

multi-unit activity

ripples

Forward replay

-250 ms
Reverse Replay from B to A

multi-unit activity

ripples

Reverse replay

-160 ms

position estimate
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 → A' → 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 \( Q(v_t, h'_t|h_{t-1}) = \exp \left( v_t^T W h'_t + v_t^T b_V + h'_t(b_H + W'h_{t-1}) \right) / Z(h_{t-1}) \), 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 \( H_1 \).