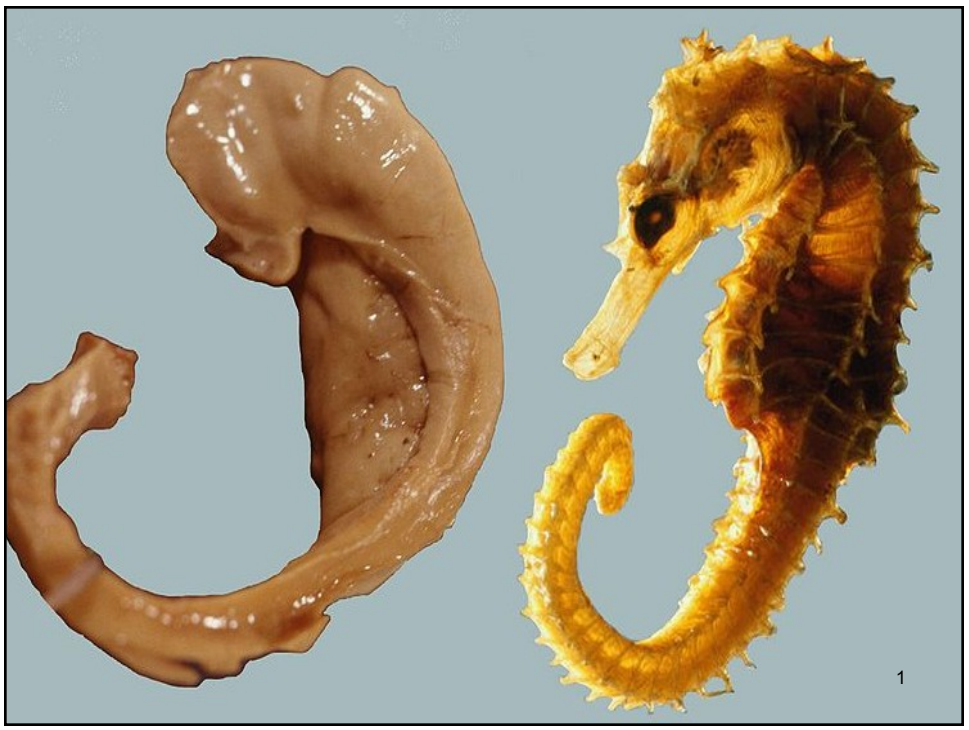
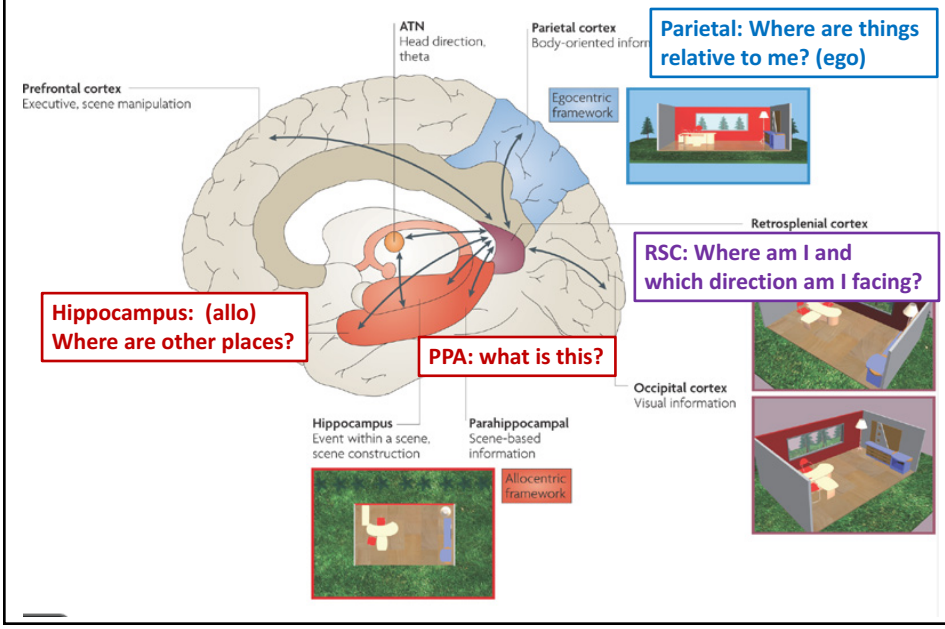
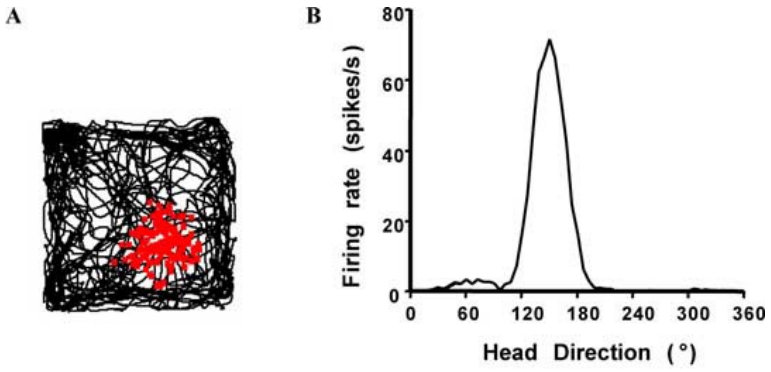


Division of labor



Neural Navigation I:
constructing a cognitive map of space

1. Intelligent navigation: getting from here to there
2. A place hierarchy in the brain
3. Functions of the hippocampus
   - A. Representing space and spatial memory
   - B. Memory consolidation



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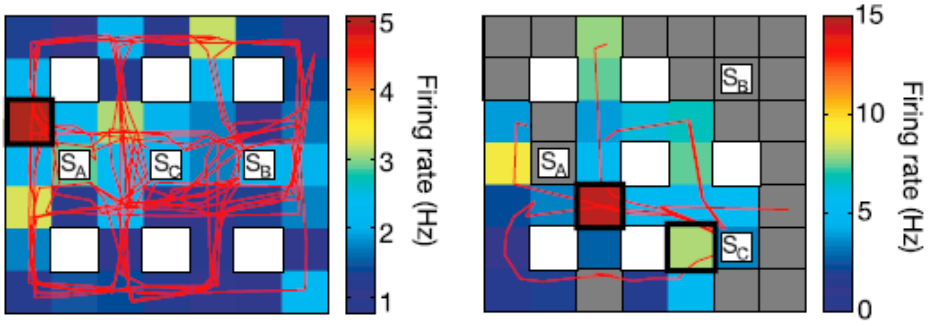
Place cells recorded in human hippocampus!



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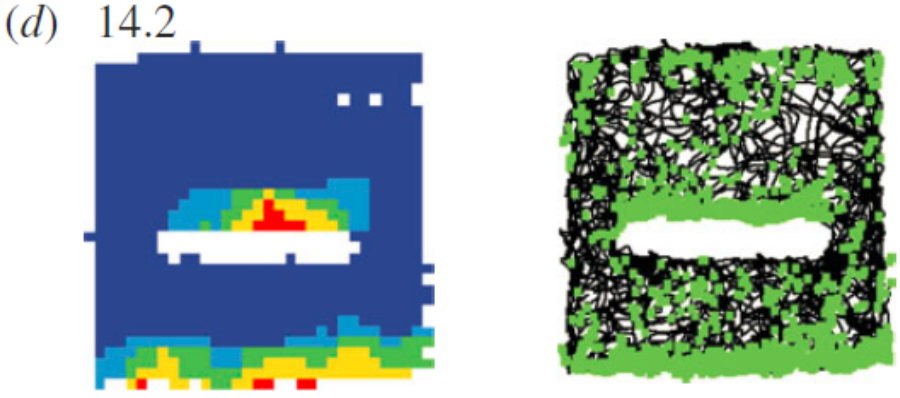
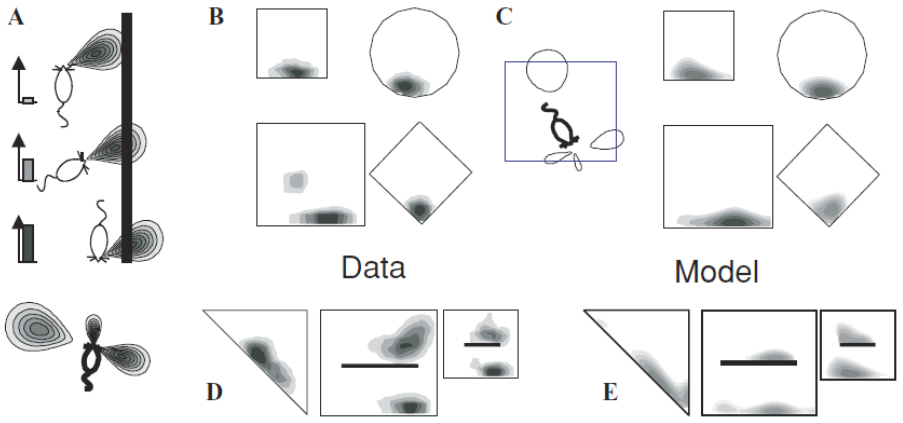
Boundary cell



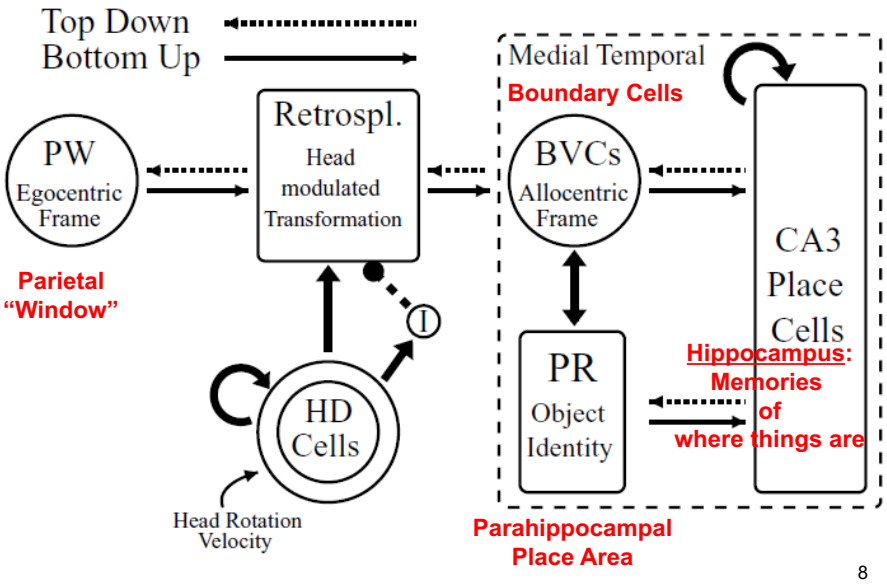
6

Boundary Vector Cell model of the sensory input to place cells



7

Egocentric sensory → Allocentric abstract representation of space



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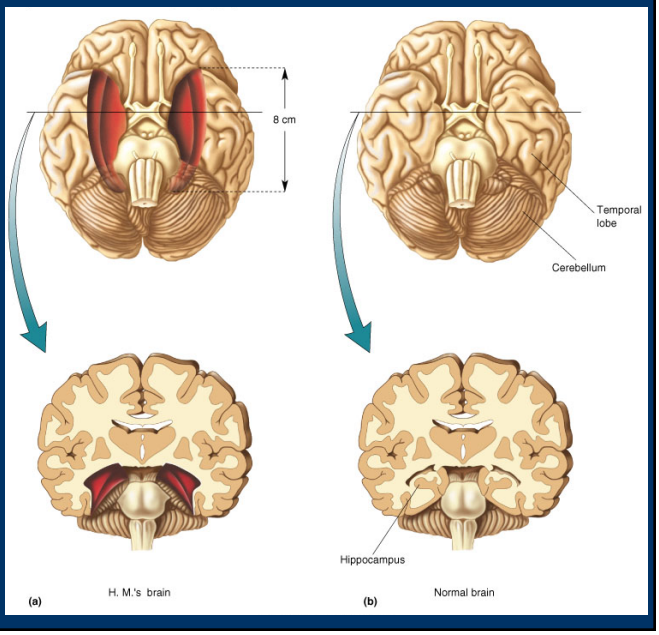
Neural Navigation I:
constructing a cognitive map of space

1. **Intelligent navigation: getting from here to there**
2. **A place hierarchy in the brain**
3. **Functions of the hippocampus**
   - **A. Representing space and spatial memory**
   - **B. Memory consolidation**

The medial temporal lobe and anterograde amnesia

H.M.: surgical removal of 8 cm of medial temporal lobe, including cortex, amygdala, and anterior 2/3s of the hippocampus



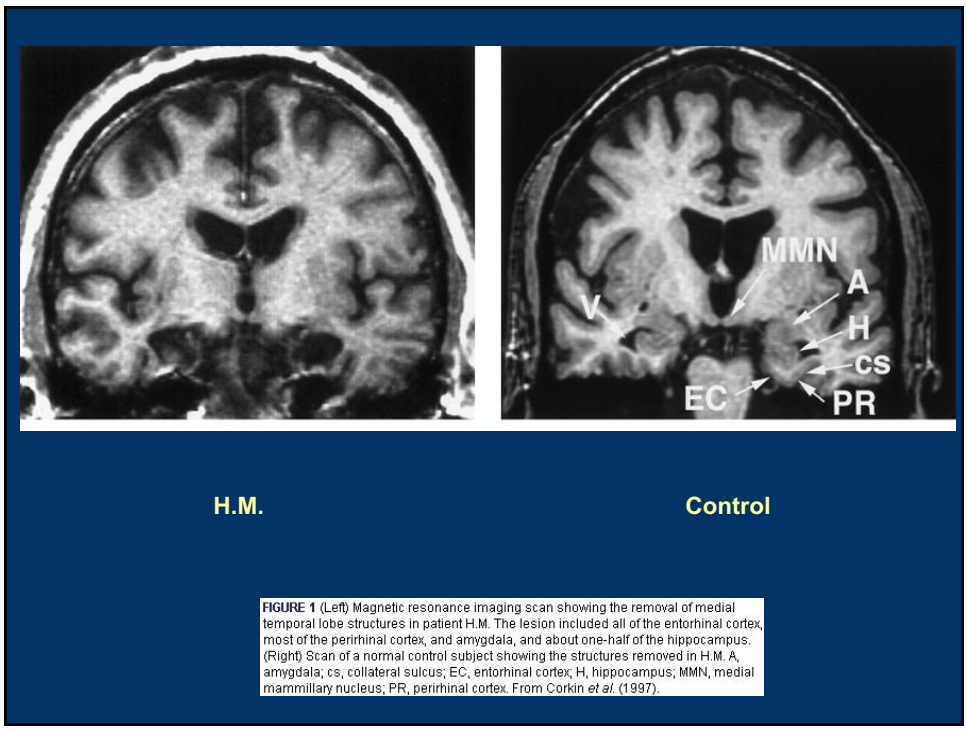
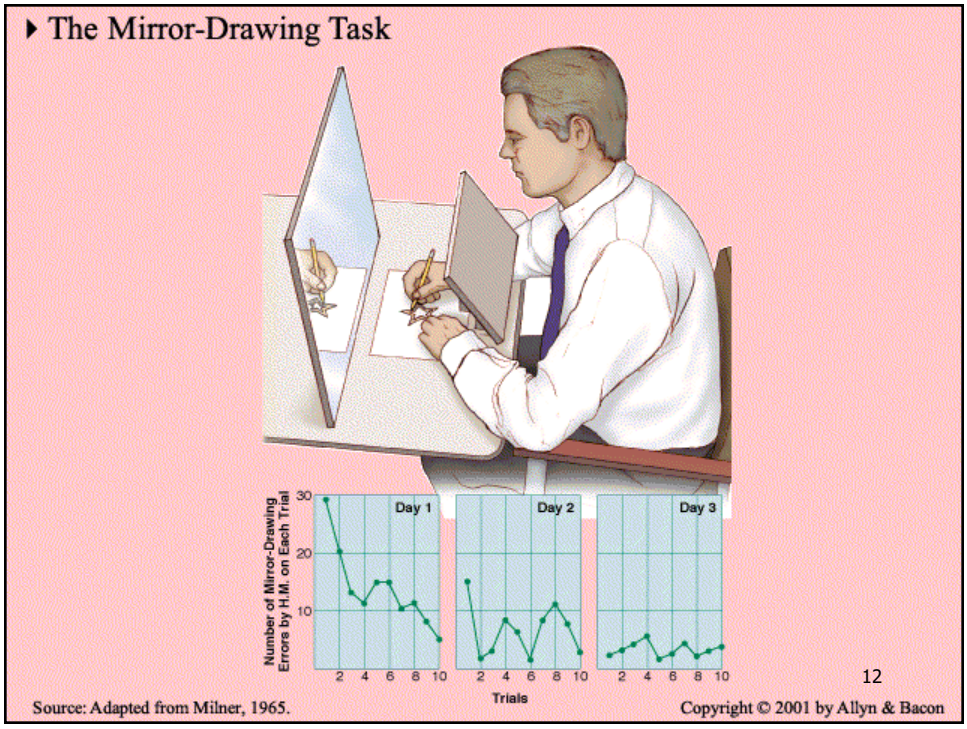


FIGURE 1 (Left) Magnetic resonance imaging scan showing the removal of medial temporal lobe structures in patient H.M. The lesion included all of the entorhinal cortex, most of the perirhinal cortex, and amygdala, and about one-half of the hippocampus. (Right) Scan of a normal control subject showing the structures removed in H.M. A, amygdala; cs, collateral sulcus; EC, entorhinal cortex; H, hippocampus; MMN, medial mammillary nucleus; PR, perirhinal cortex. From Corkin *et al.* (1997).



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What did we learn from H.M.?

- Medial temporal cortex and hippocampus may be involved in **consolidation**
- Declarative memory depends on medial temporal cortex but procedural memory does not

Henry Molaison RIP

Memory consolidation

"A poorly defined set of processes which take an initial, unstable memory representation and convert it into a form that is both more stable and more effective."

Stickgold 2007

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Neural Navigation II:
constructing a cognitive map of space

1. Sleep, hippocampal replay, and preplay
2. Beyond space: cognitive map of everything

Consolidate by replay?

Neuron, Vol. 36, 1183–1194, December 19, 2002, Copyright ©2002 by Cell Press

Memory of Sequential Experience in the Hippocampus during Slow Wave Sleep

Albert K. Lee[1] and Matthew A. Wilson[1]
Picower Center for Learning and Memory
RIKEN-MIT Neuroscience Research Center
Department of Brain and Cognitive Sciences
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

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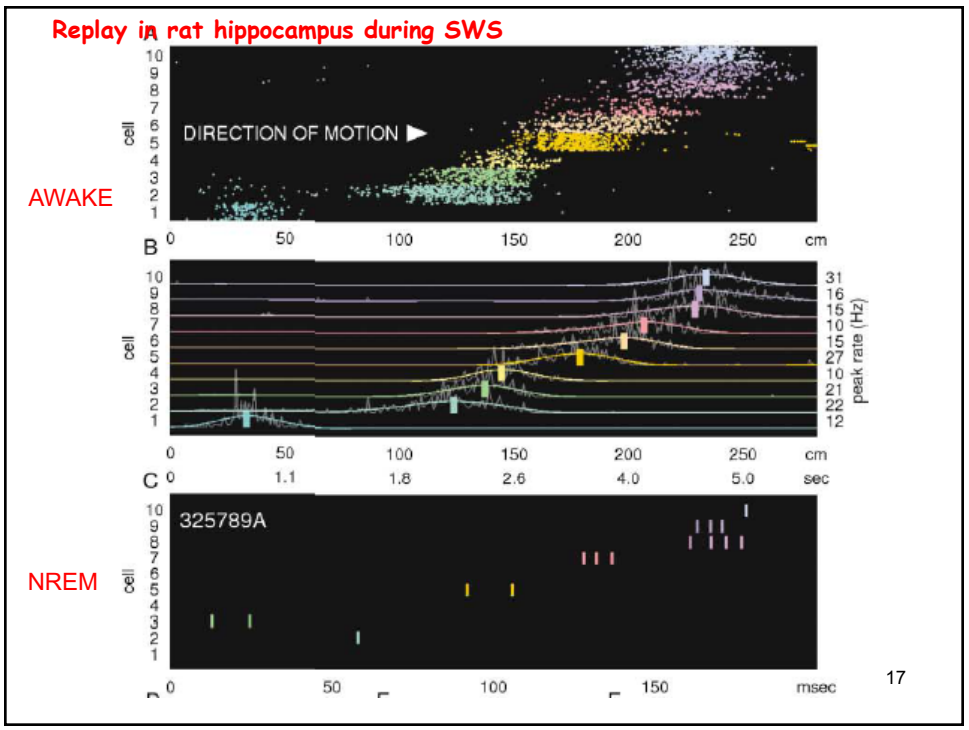
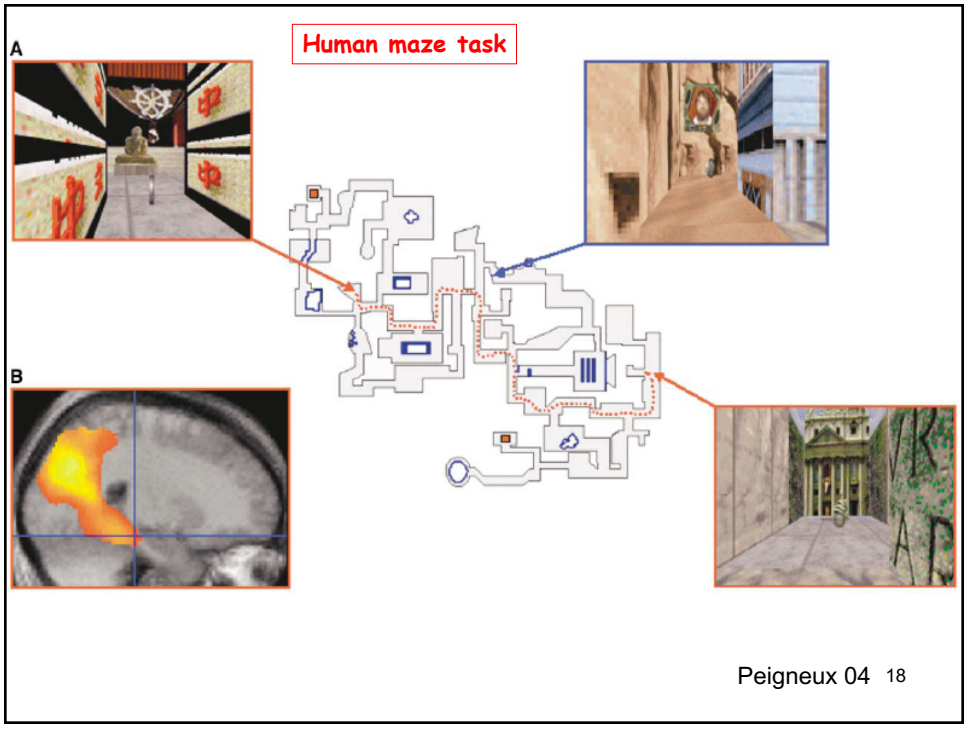
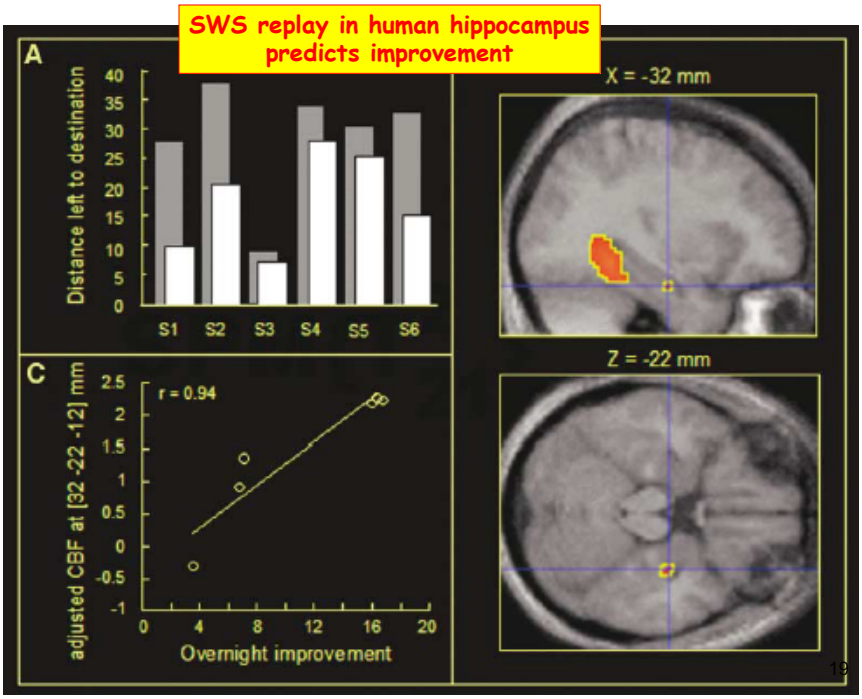

Replay in rat hippocampus during SWS
AWAKE
NREM
A
B
C
DIRECTION OF MOTION
cell
cm
sec
msec
peak rate (Hz)
325789A
17


Human maze task
A
B
Peigneux 04 18



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Sleep Conclusion

- Replay of place cell firing sequences during sleep (both REM and NREM, and while awake and "daydreaming") may help consolidate memories about paths the rat took while awake
- And may also simulate previously unexplored possible paths…

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Neural Navigation II:
constructing a cognitive map of space

1. Sleep, hippocampal replay, and preplay
2. Beyond space: cognitive map of everything

Functions of the hippocampus

- Represent space and spatial memory
- Episodic memory consolidation (by replay?)

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The phenomenon of hippocampal spatial representations and the hippocampal role in episodic memory retrieval remain two of the most puzzling mysteries in cognitive neuroscience that intuitively seem to be connected to each other. Since the finding that the hippocampus plays a pivotal role in long-term memory consolidation (Scoville and Milner 1957; Zola-Morgan and Squire 1986), many proposals have been made regarding its specific role (Teyler and Discenna 1985; Squire 1987; O'Reilly and McClelland 1994; McClelland et al. 1995). A prominent view of the mechanisms underlying consolidation of episodic memories involves fast formation (e.g., via Hebbian mechanisms) of strong associations between hippocampal sparse patterns of activity and distributed neocortical representations. As a result, the former subsequently serve as pointers to the latter. This memory-indexing theory that goes back to Teyler and Discenna (1985, 1986) and underlies several subsequent major theoretical contributions to the field (Nadel and Moscovitch 1997, 2001; Wheeler et al. 1997; Tulving 2002) assumes that a memory of an episode is retrieved by reactivating a hippocampal pointer to it. Consistent with this view, recent clinical and fMRI studies indicate that the hippocampus in humans is involved in and required for retrieval of all autobiographical, but not semantic memories (Vargha-Khadem et al. 1997; Ryan et al. 2001; Westmacot et al. 2001; Maguire and Frith 2003).

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A simple neural network model of the hippocampus suggesting its pathfinding role in episodic memory retrieval

Alexei V. Samsonovich[1,3] and Giorgio A. Ascoli[1,2]

[1]Krasnow Institute for Advanced Study and [2]Department of Psychology, George Mason University, Fairfax, Virginia 22030, USA

The goal of this work is to extend the theoretical understanding of the relationship between hippocampal spatial and memory functions to the level of neurophysiological mechanisms underlying spatial navigation and episodic memory retrieval. The proposed unifying theory describes both phenomena within a unique framework, as based on one and the same pathfinding function of the hippocampus. We propose a mechanism of reconstruction of the context of experience involving a search for a nearly shortest path in the space of remembered contexts. To analyze this concept in detail, we define a simple connectionist model consistent with available rodent and human neurophysiological data. Numerical study of the model begins with the spatial domain as a simple analogy for more complex phenomena. It is demonstrated how a nearly shortest path is quickly found in a familiar environment. We prove numerically that associative learning during sharp waves can account for the necessary properties of hippocampal place cells. Computational study of the model is extended to other cognitive paradigms, with the main focus on episodic memory retrieval. We show that the ability to find a correct path may be vital for successful retrieval. The model robustly exhibits the pathfinding capacity within a wide range of several factors, including its memory load (up to 30,000 abstract contexts), the number of episodes that become associated with potential target contexts, and the level of dynamical noise. We offer several testable critical predictions in both spatial and memory domains to validate the theory. Our results suggest that (1) the pathfinding function of the hippocampus, in addition to its associative and memory indexing functions, may be vital for retrieval of certain episodic memories, and (2) the hippocampal spatial navigation function could be a precursor of its memory function.

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Fear Conditioning

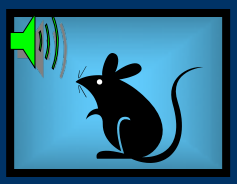
TRAINING

- Animal is placed in novel context
- Hears a tone
- Receives foot shock

CONTEXTUAL TEST

- Animal is returned to same context
- Test for freezing behavior
- **DEPENDS ON HIPPOCAMPUS**

CUED TEST



- Animal is placed in modified context
- Hears a tone
- Test for freezing behavior

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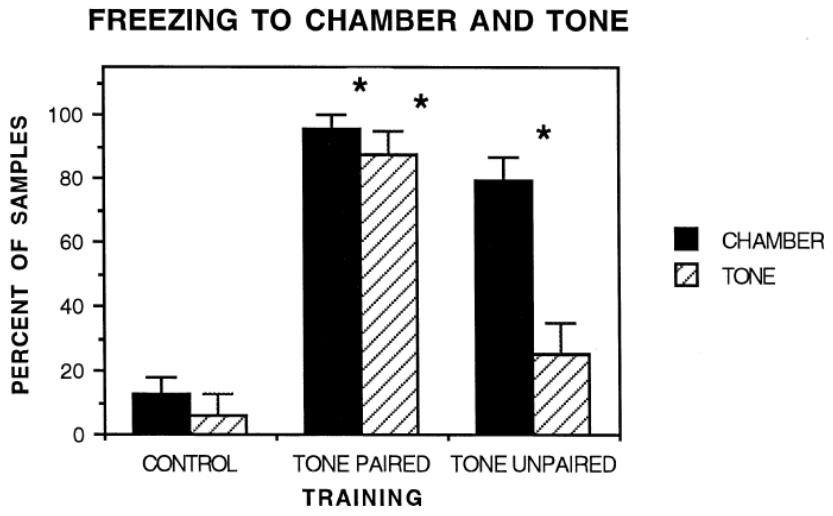
Hippocampal microtubule-associated protein-2 alterations with contextual memory [1]

Nancy J. Woolf [a,*], Marcus D. Zinnerman [b], Gail V.W. Johnson [b]



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Eye-Blink Conditioning in Rabbits

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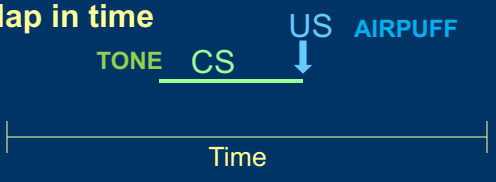
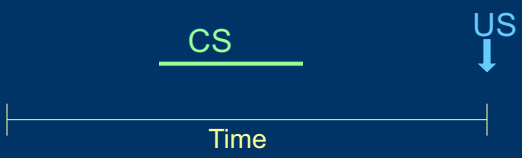
Two Types of Classical Conditioning

"Delay" Conditioning: tone and puff overlap in time



"Trace" Conditioning: no overlap



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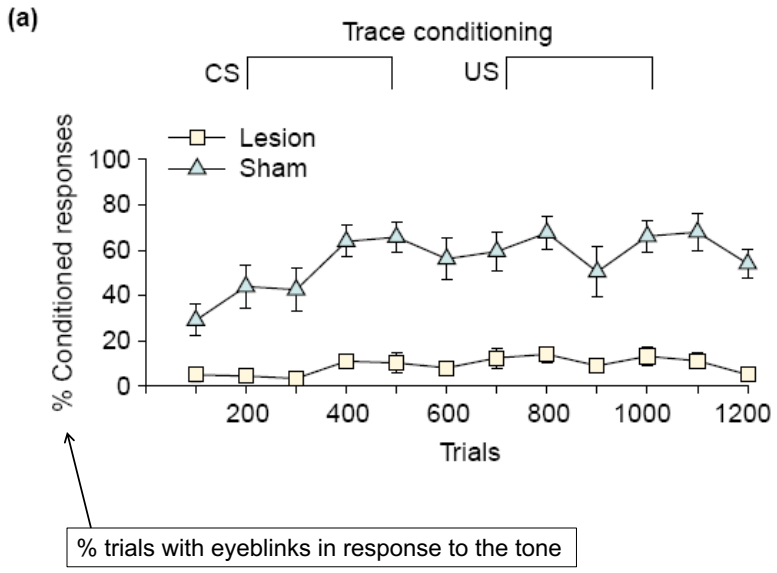
Trace eyeblink conditioning depends on the hippocampus



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Hippocampal "Time Cells" Bridge the Gap in Memory for Discontiguous Events

Christopher J. MacDonald,[1] Kyle Q. Lepage,[1] Uri T. Eden,[1] and Howard Eichenbaum[1,*]
[1]Center for Memory and Brain, Boston University, Boston, MA 02215, USA

The hippocampus is critical to remembering the flow of events in distinct experiences and, in doing so, bridges temporal gaps between discontiguous events. Here, we report a robust hippocampal representation of sequence memories, highlighted by "time cells" that encode successive moments during an empty temporal gap between the key events, while also encoding location and ongoing behavior. Furthermore, just as most place cells "remap" when a salient spatial cue is altered, most time cells form qualitatively different representations ("retime") when the main temporal parameter is altered. Hippocampal neurons also differentially encode the key events and disambiguate different event sequences to compose unique, temporally organized representations of specific experiences. These findings suggest that hippocampal neural ensembles segment temporally organized memories much the same as they represent locations of important events in spatially defined environments.

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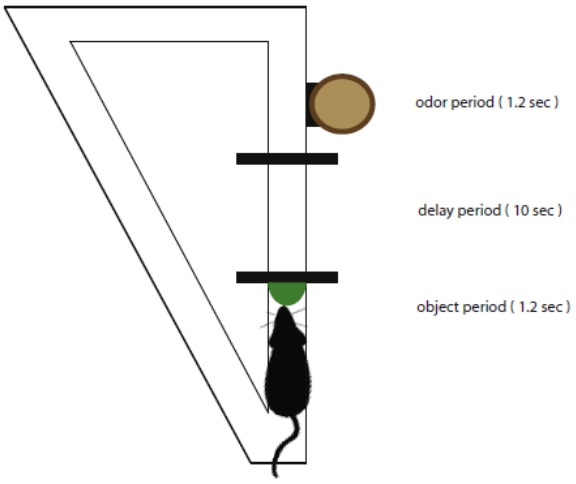

Figure 1. The Trial Structure for Object-Delay-Odor Sequences
The succession of events on each trial included an object period when the rat explored one of two objects, a delay period, and an odor period, when the rat sampled and responded to one of two odors. Green shape illustrates an object, brown circle illustrates an odor cup, and horizontal bars indicate removable walls that constrained the rat within each component of the apparatus during successive trial periods.

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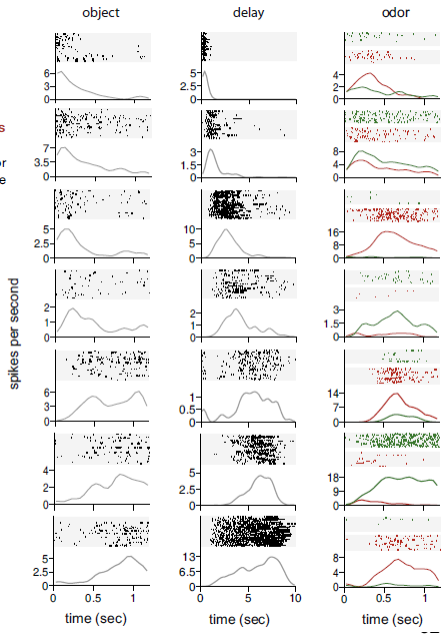
Figure 2. Hippocampal Neurons Activate at Successive Times during Each Trial Period
Raster plots for example trials and PSTHs for the entire session are shown for seven example neurons in each trial period. In the odor period, data are separated for go (green) and nogo (red) trials.



Hippocampus: Beyond space

- Episodic memory may use a similar hippocampal system as navigation, and may consolidate by replay
- Multisensory associations/contextual memories depend on hippocampus
- Hippocampal time cells encode time like place cells encode space

- Maybe it contains a cognitive map of when and where everything is, to be used for planning…