Hippocampal place cells: neural substrates of navigation behavior

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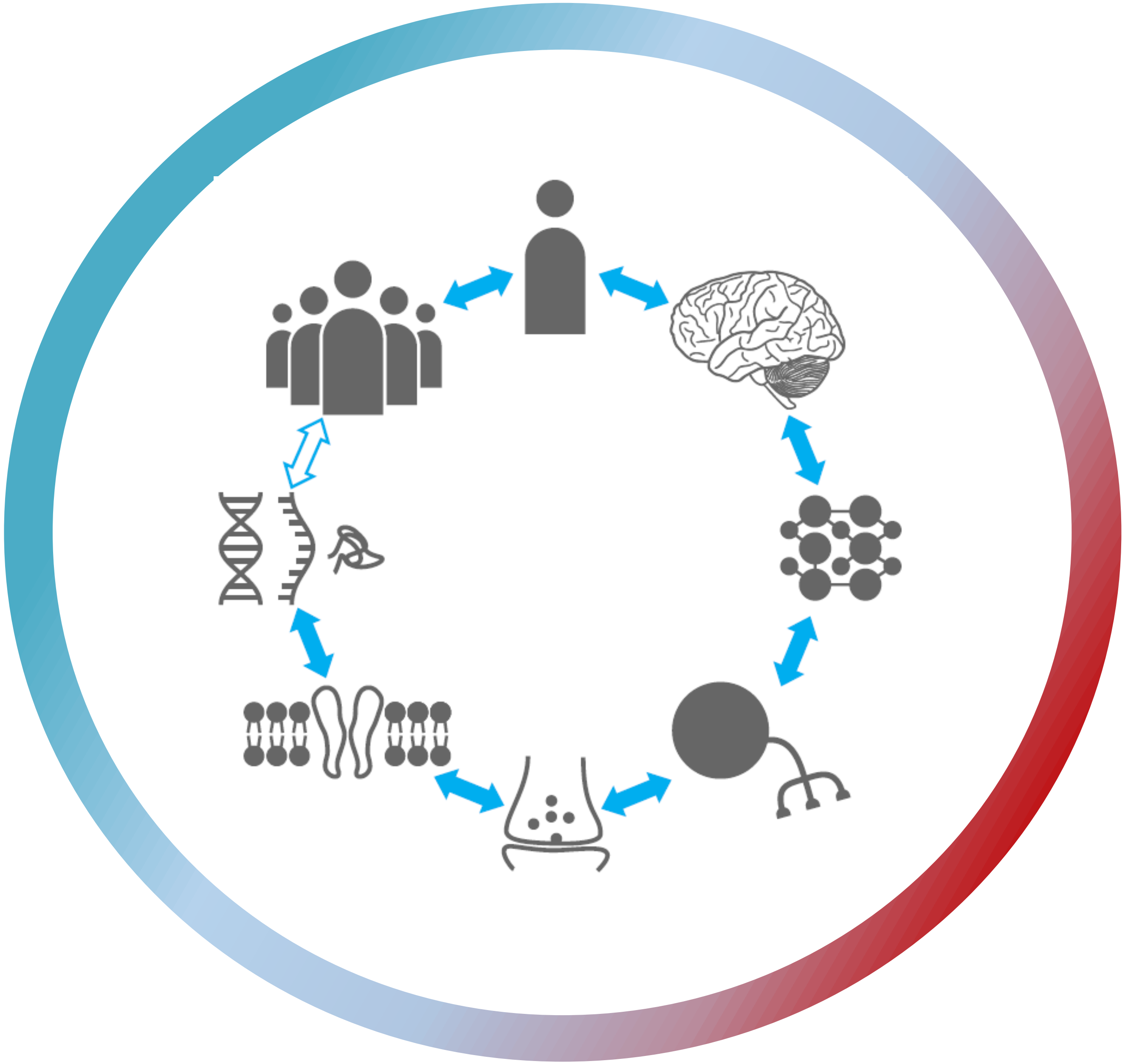
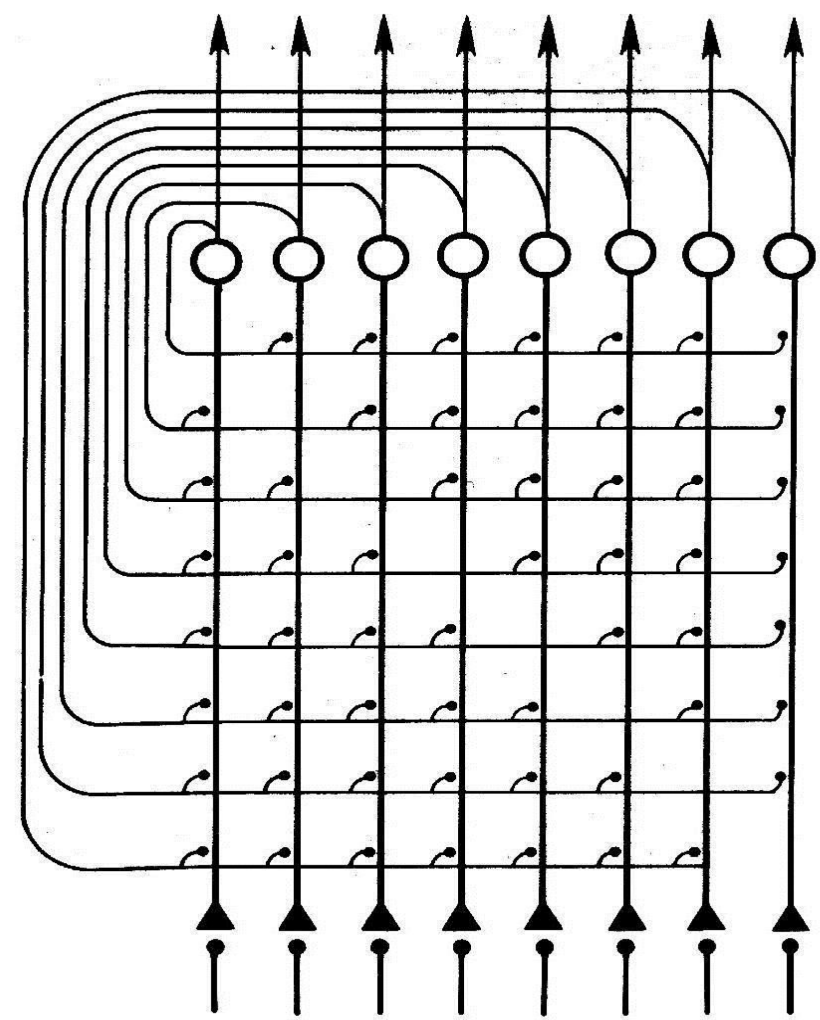
Multi-level approach of memory

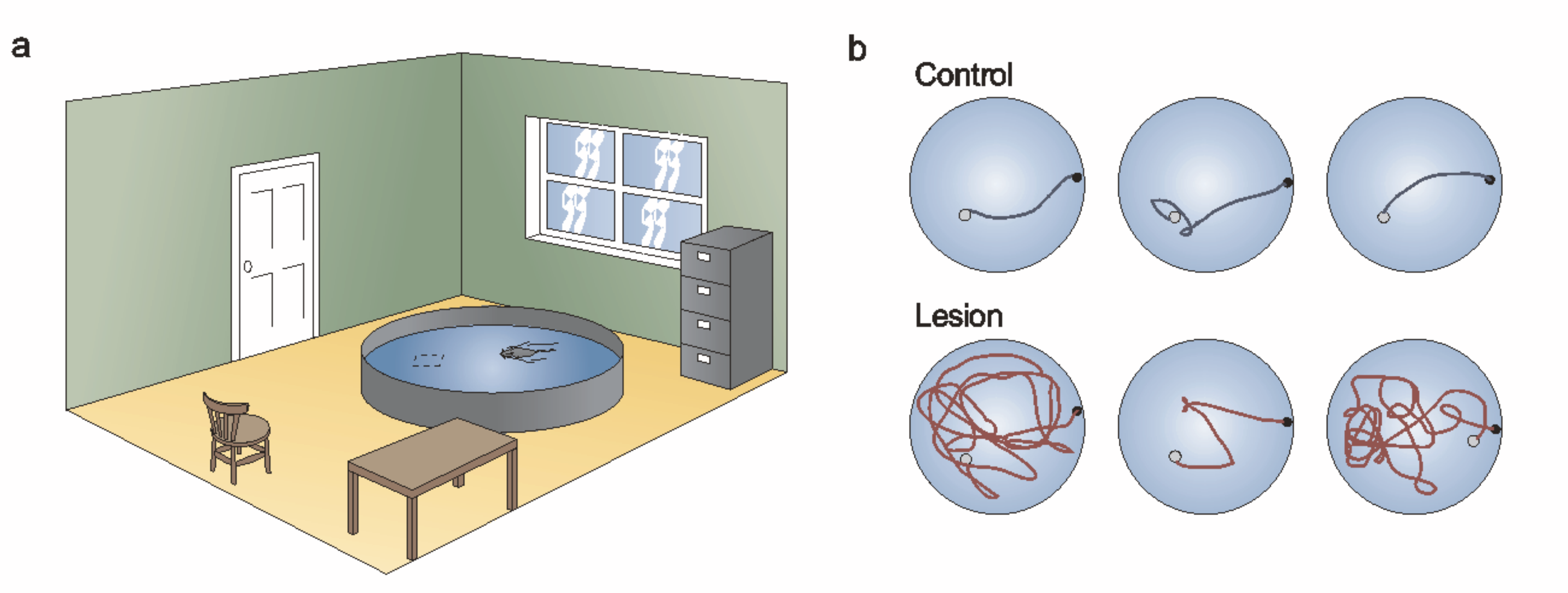


Your memories are in your connections

- An experience produces a pattern of activation over many neurons.
- The *memory trace* is adjustments to connections among the neurons.
- The *memory-as-recalled* is a pattern of activation reconstructed with the help of the affected connections.
- Connections are affected by many experiences, so 'recall' is always subject to influence from traces of other experiences.
- Remembering is thus always a process of reconstruction.



McClelland & Rumelhart (1985)



The rat hippocampus is involved in spatial navigation as shown by consistent impairments induced by lesions in most spatial tasks.

Plan général du cours

- Behavioral strategies in orientation
- Anatomy of the hippocampus
- Spatial memory and its neural substrate
- Memory properties of place cells
- Electrophysiological recordings in humans

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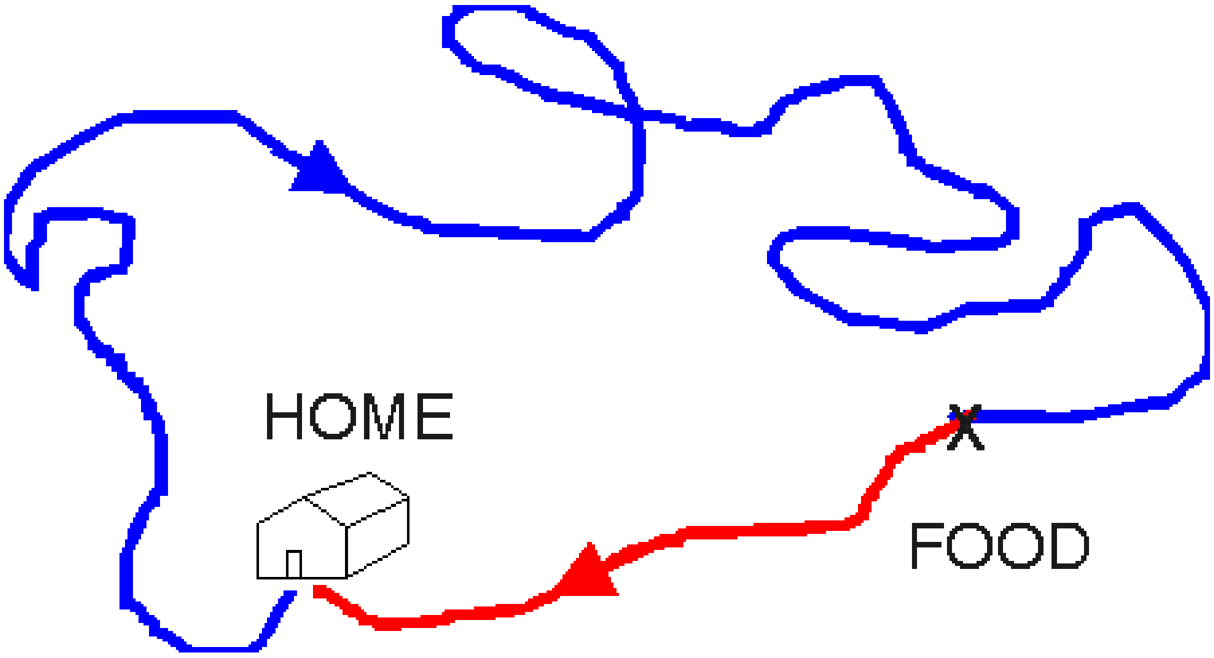
Navigation in animals

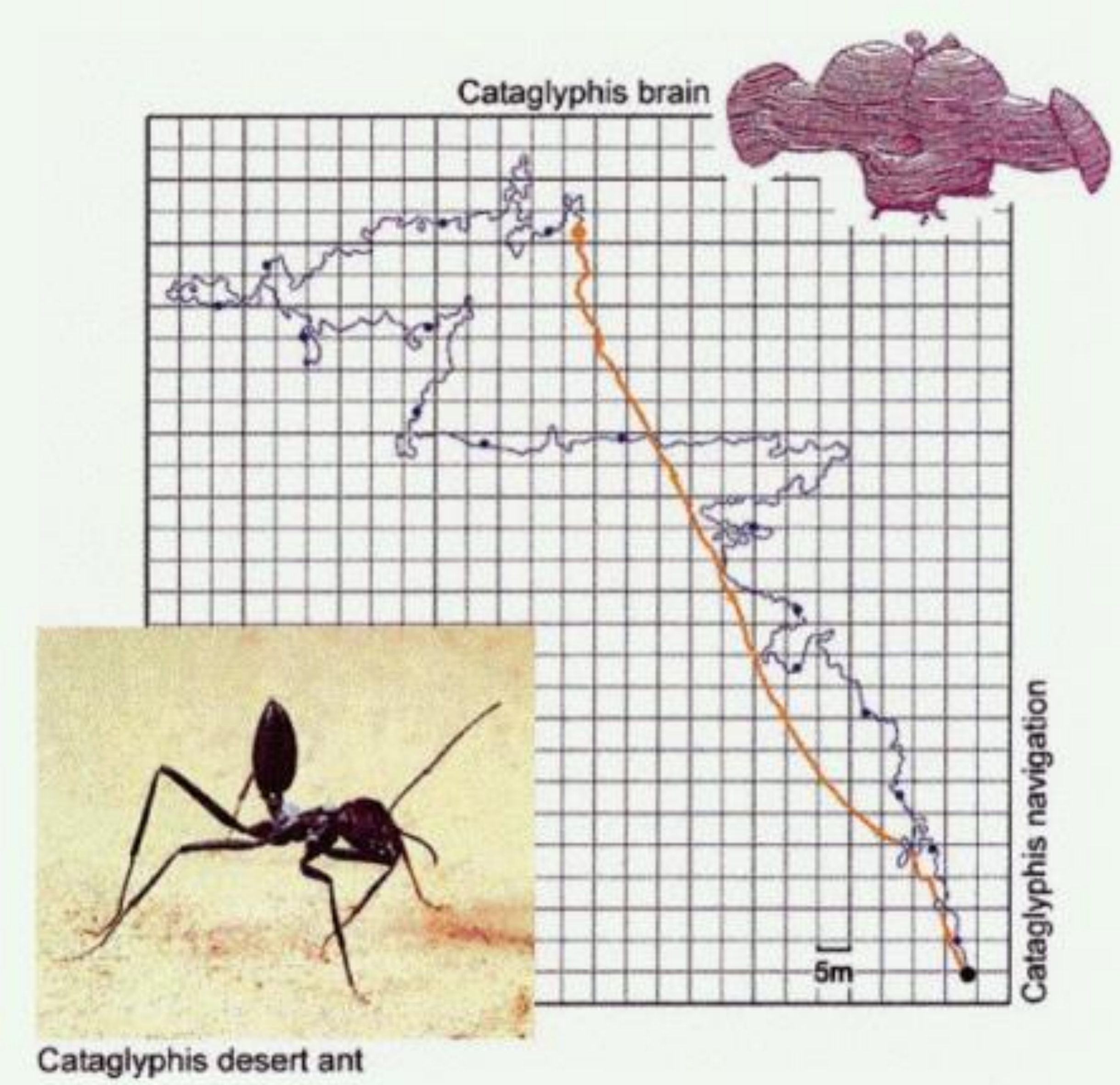


Egocentric localization

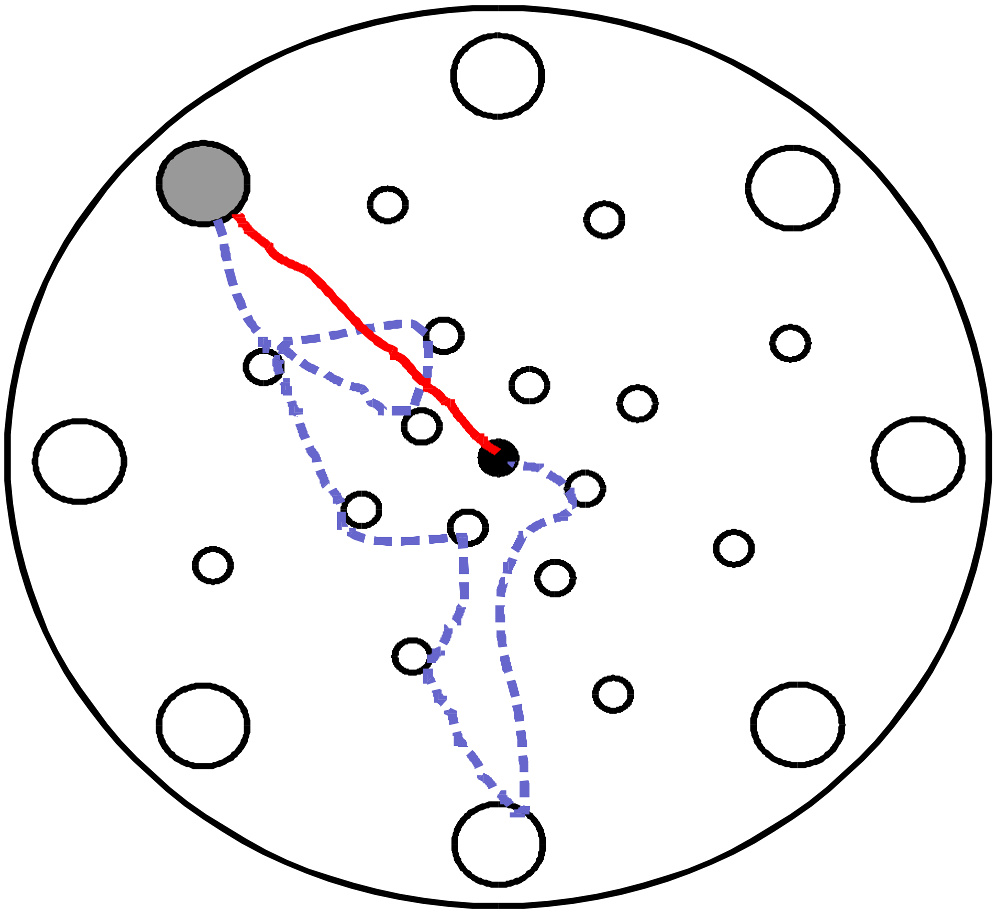
- Reference is the subject ’s position
- Behavior: Route navigation
- Requires a path integration mechanism for updating goal coordinates as one moves
- Works better with an external compass (insects, birds)

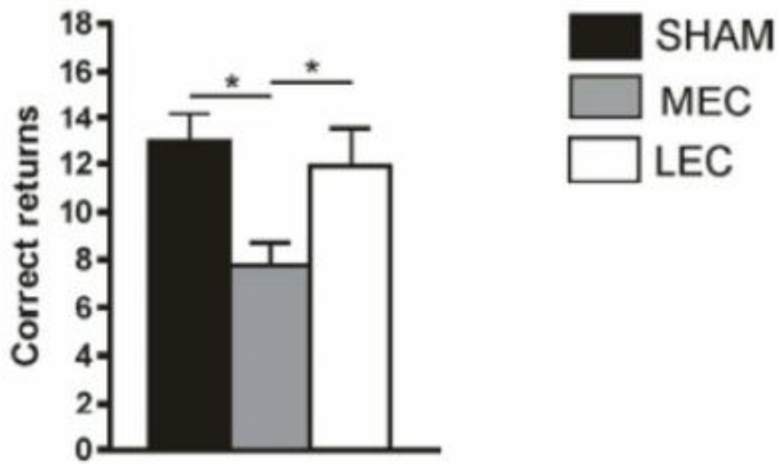
Exocentric localization

- Reference is the spatial layout of landmarks
- Behavior: Place navigation
- Requires a representation of the environment
- Birds, mammals

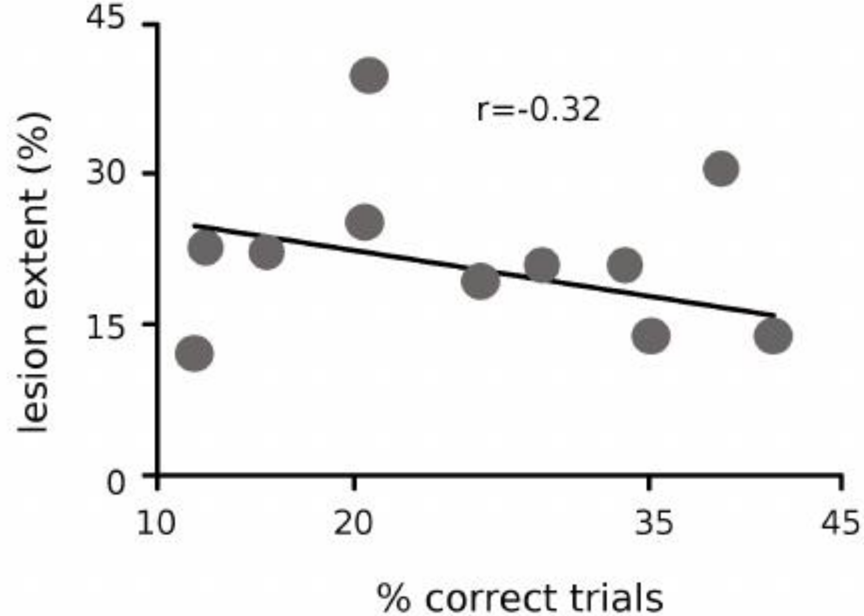

Cataglyphis brain
Cataglyphis navigation
5m
Cataglyphis desert ant

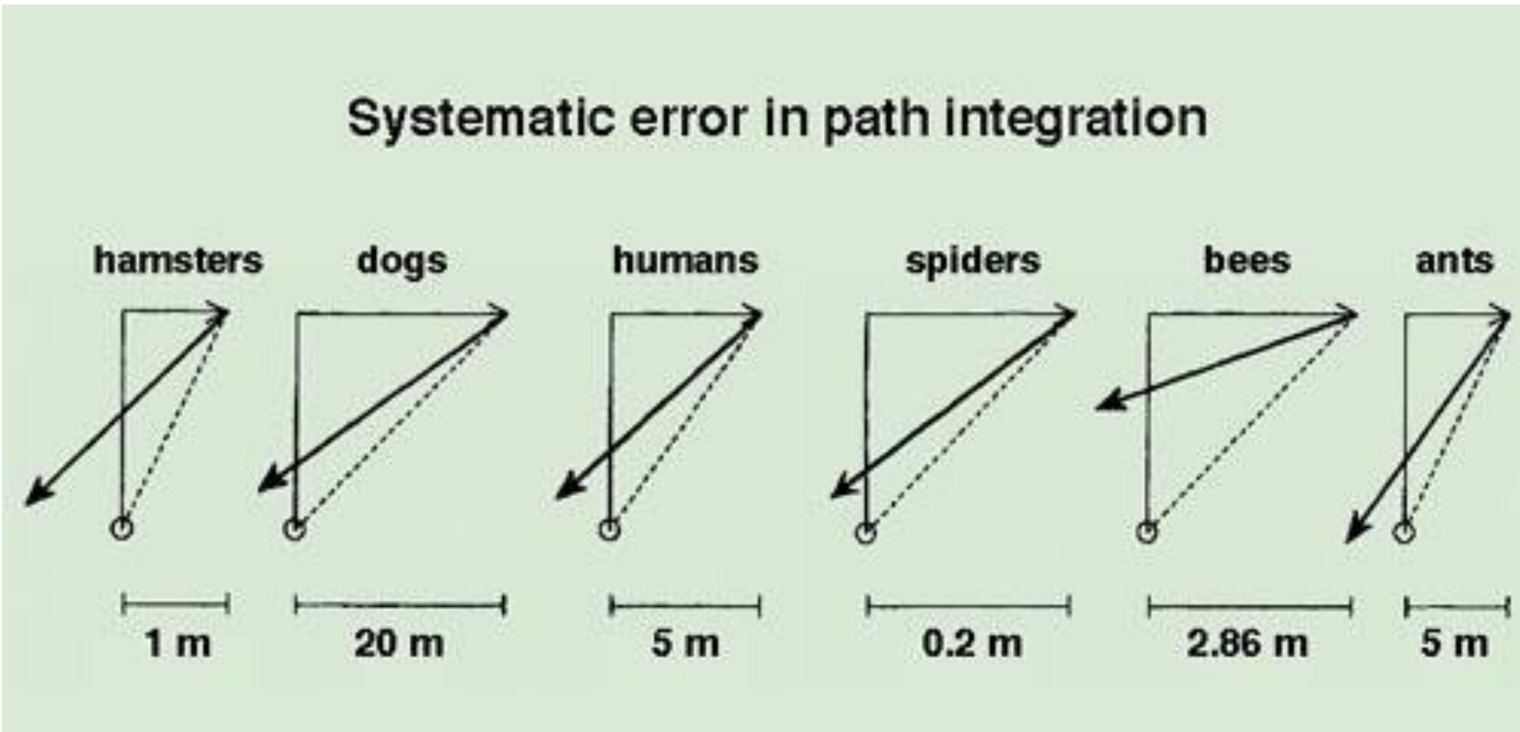
Path integration task





Van Cauter *et al.*, 2013 (*Cereb Cortex*)




Systematic error in path integration
hamsters
dogs
humans
spiders
bees
ants
1 m
20 m
5 m
0.2 m
2.86 m
5 m

Egocentric localization

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Behavior = association S-R (behaviorism)

I. P. Pavlov (1849-1936) : « The bell and the dog » - 1904
US + CS => UR then CS => UR
(meat) + (sound) => (salivation) then (sound) => (salivation)

E. L. Thorndike (1874-1949): Law of effect(1913-1928)- if an association is followed by a "satisfying state of affairs" it will be strengthened and if it is followed by an "annoying state of affairs " it will be weakened.

F. Skinner (1950-1970):S-R learning through progressive conditioning. Rewards strenghten associations.

E.C. Tolman (1886-1959) : « Cognitive maps »

Rats build a mental representation, or « cognitive maps » of the environment. In such cognitive maps, places are represented relative to each other rather than relative to the animal.

Vol. 55, No. 4 July, 1948

THE PSYCHOLOGICAL REVIEW

COGNITIVE MAPS IN RATS AND MEN [1]

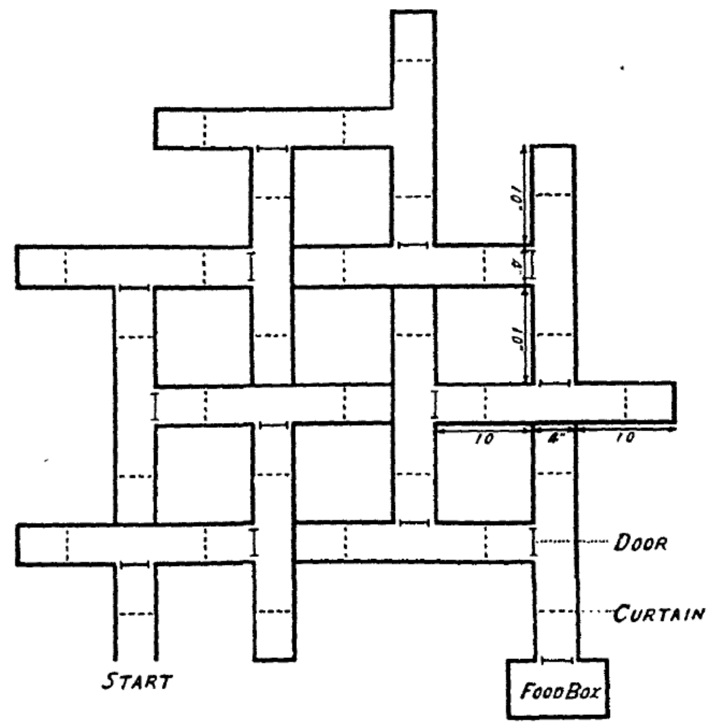
BY EDWARD C. TOLMAN

University of California

COGNITIVE MAPS IN RATS AND MEN [1]

BY EDWARD C. TOLMAN

- « In the typical experiment a hungry rat is put at the entrance of the maze [...], and wanders about through the various true path segments and blind alleys until he finally comes to the food box and eats. »

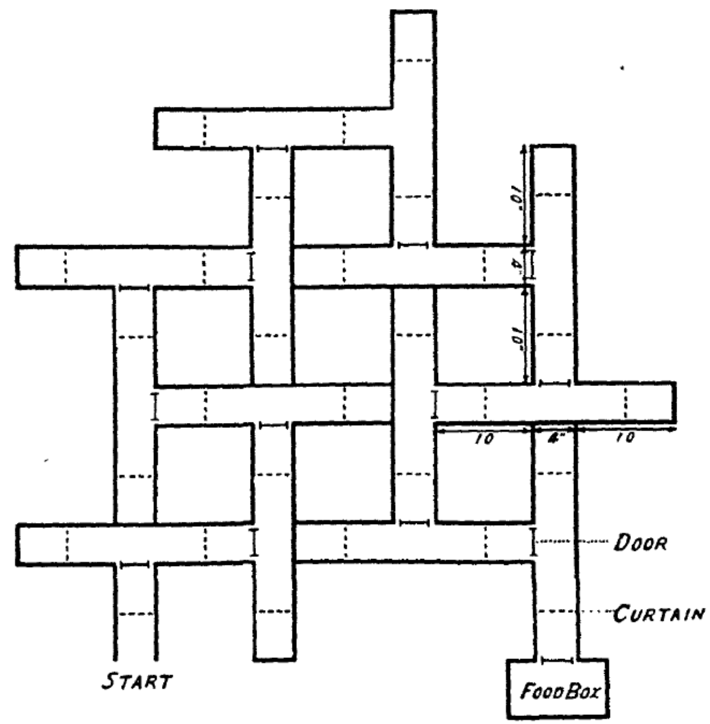


Plan of maze
14-Unit T-Alley Maze

COGNITIVE MAPS IN RATS AND MEN [1]

BY EDWARD C. TOLMAN

- « [...] the animal tends to make fewer and fewer errors [...] and to take less and less time between start and goal-box. »
- « All students agree as to the facts. They disagree, however, on theory and explanation. »



Plan of maze
14-Unit T-Alley Maze

COGNITIVE MAPS IN RATS AND MEN [1]

BY EDWARD C. TOLMAN

- « (1) First, there is a school of animal psychologists which believes that the maze behavior of rats is a matter of mere simple stimulus-response connections. »
- « (2) […] the second main school […] may be called the field theorists. We believe that in the course of learning something like a field map of the environment gets established in the rat's brain. »

- Field psychology was formulated by Gestalt psychologist Kurt Lewin (1936).
- This theory is an attempt to unify several branches of psychology (developmental psychology, animal psychology, psychopathology).

$$B = f(P, E)$$

Where: B = behavior, P = person et E = environment.

The two major lines of evidence for cognitive maps

- Latent learning
- Behavioral flexibility (shortcuts, detours)

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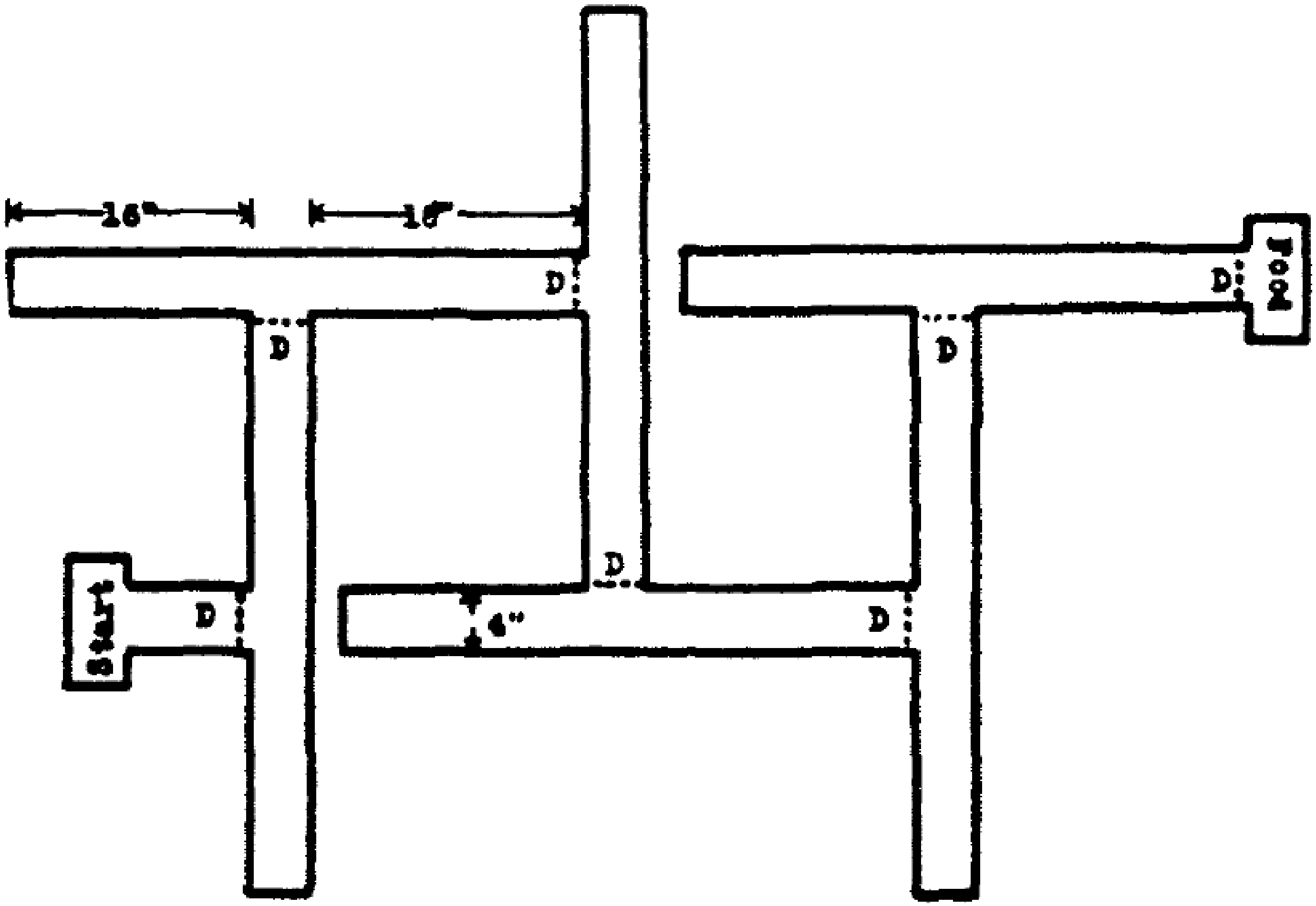
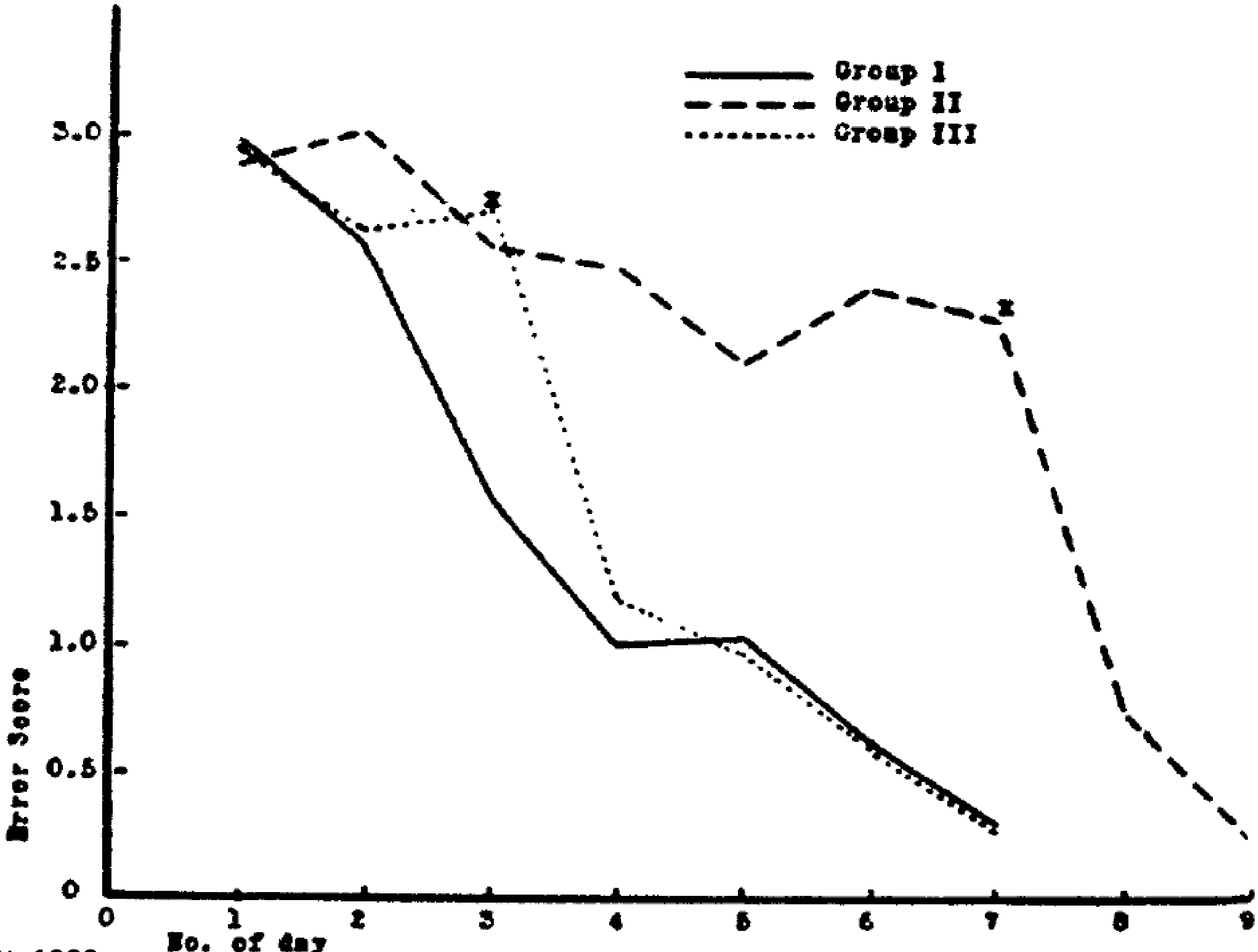
latent learning



6-Unit Alley T-Maze

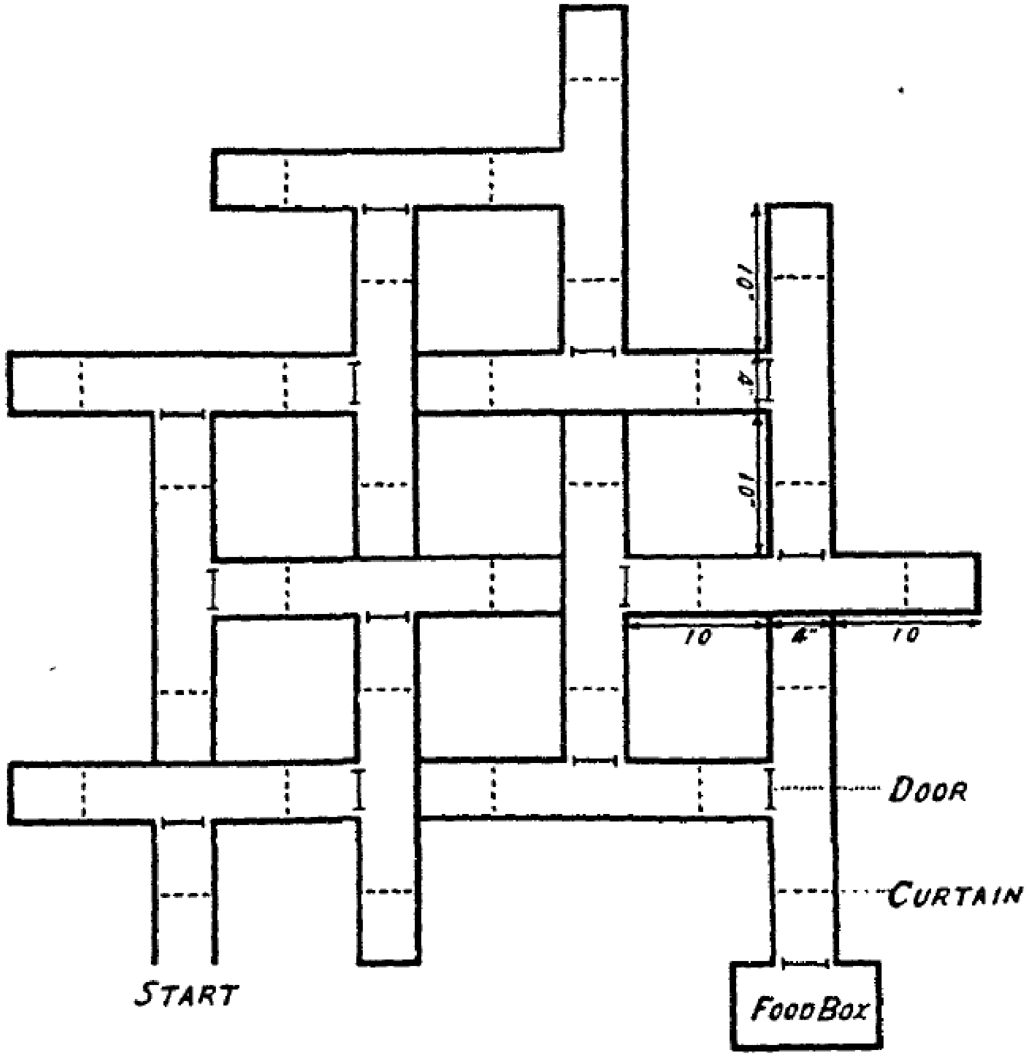
Blodgett, 1929.

latent learning



Blodgett, 1929.

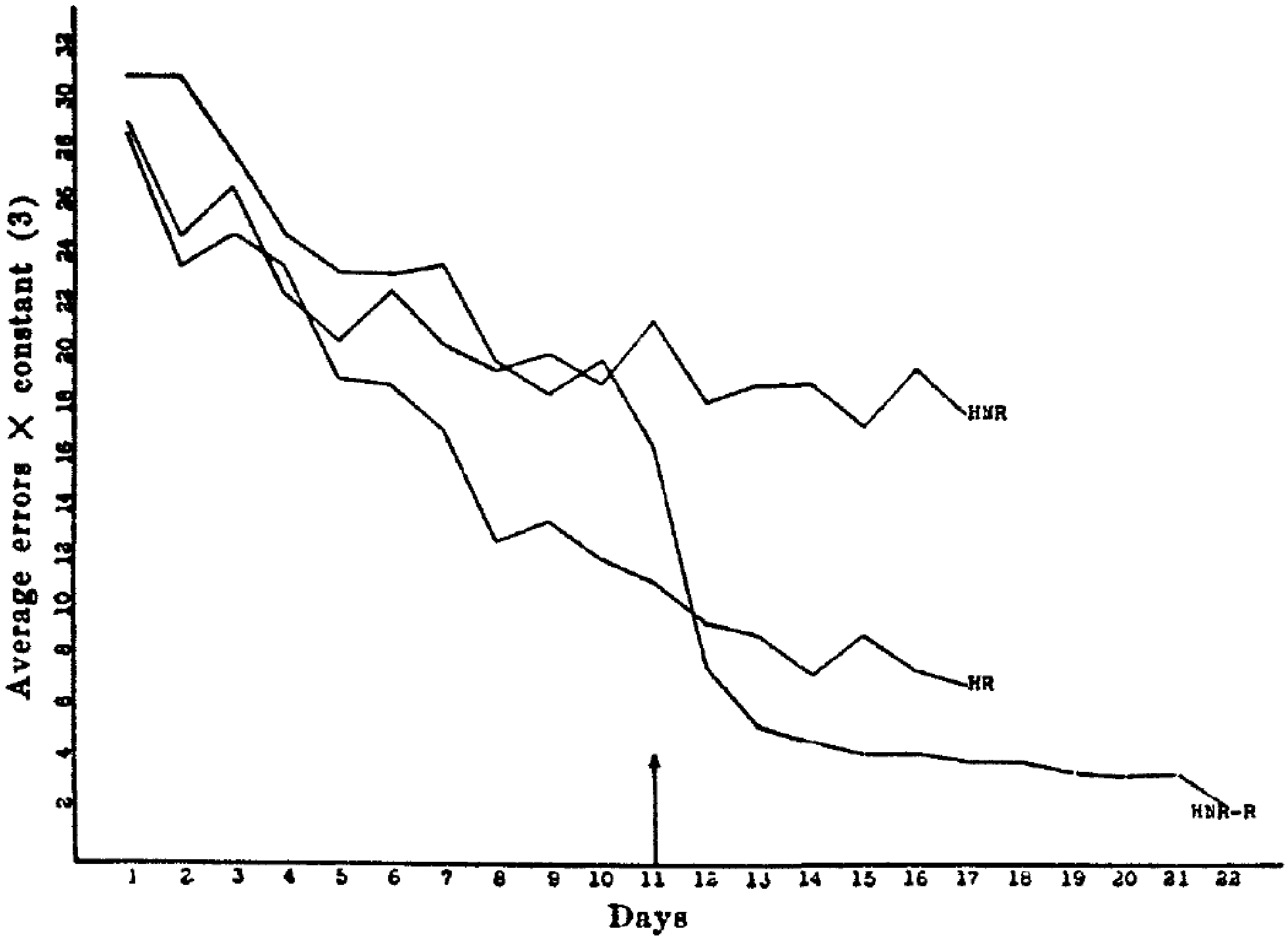
latent learning



Plan of maze
14-Unit T-Alley Maze

Tolman and Honzik, 1930.

latent learning



Error curves for HR, HNR, and HNR–R

Tolman and Honzik, 1930.

latent learning

- « Interpreting these results anthropomorphically, we would say that as long as the animals were not getting any food at the end of the maze they continued to take their time in going through it—they continued to enter many blinds. »
- « Once, however, they knew they were to get food, they demonstrated that during these preceding non-rewarded trials they had learned where many of the blinds were. They had been building up a 'map,' and could utilize the latter as soon as they were motivated to do so. »

The two major lines of evidence for cognitive maps

- Latent learning
- Behavioral flexibility (shortcuts, detours)

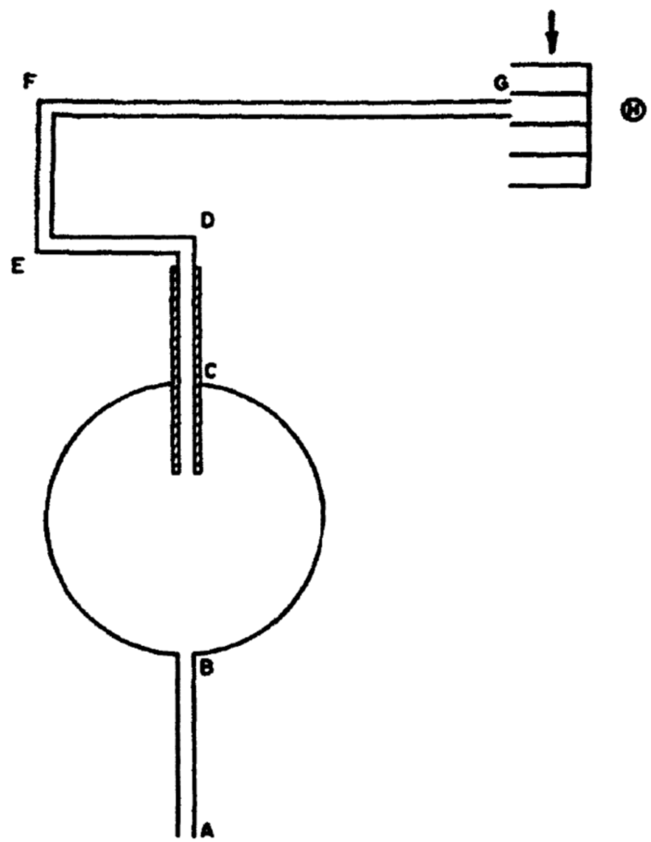
behavioral flexibiliy

- « As early as 1929, Lashley reported incidentally the case of a couple of his rats who, after having learned an alley maze, pushed back the cover near the starting box, climbed out and ran directly across the top to the goal-box where they climbed down in again and ate. »

behavioral flexibiliy

- « All such observations suggest that rats really develop wider spatial maps which include more than the mere trained-on specific paths. »

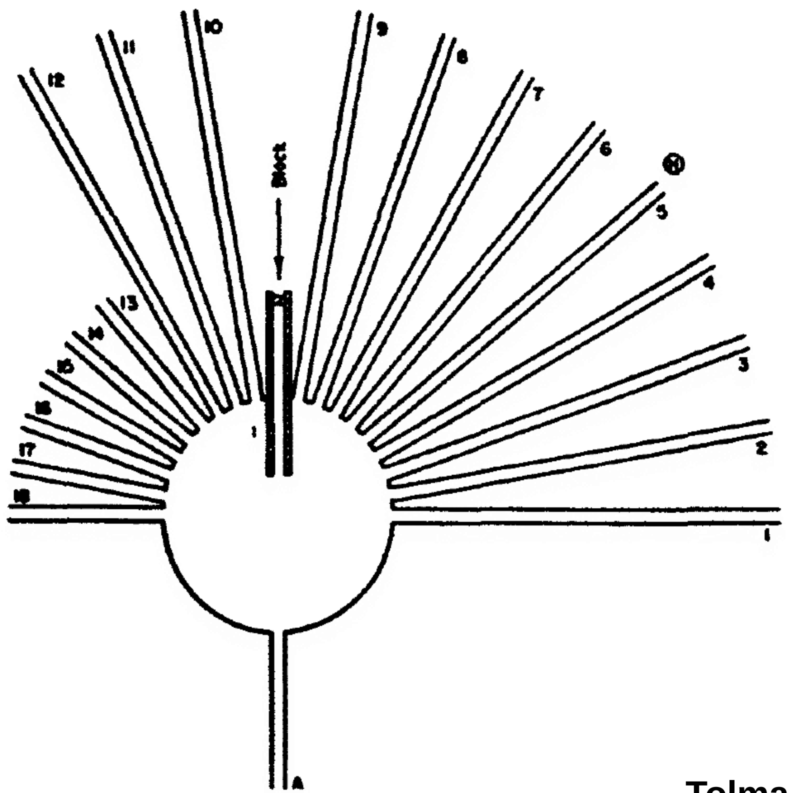
behavioral flexibility | shortcuts



Apparatus used in preliminary training

Tolman et al., 1946.

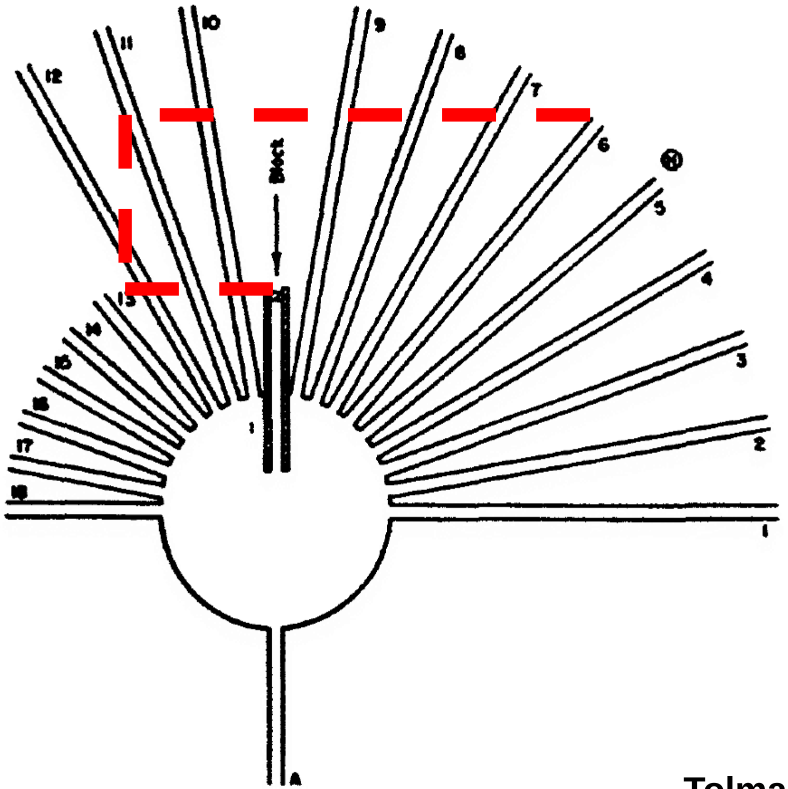
behavioral flexibility | shortcuts



Apparatus used in the test trial

Tolman et al., 1946.

behavioral flexibility | shortcuts



Apparatus used in the test trial

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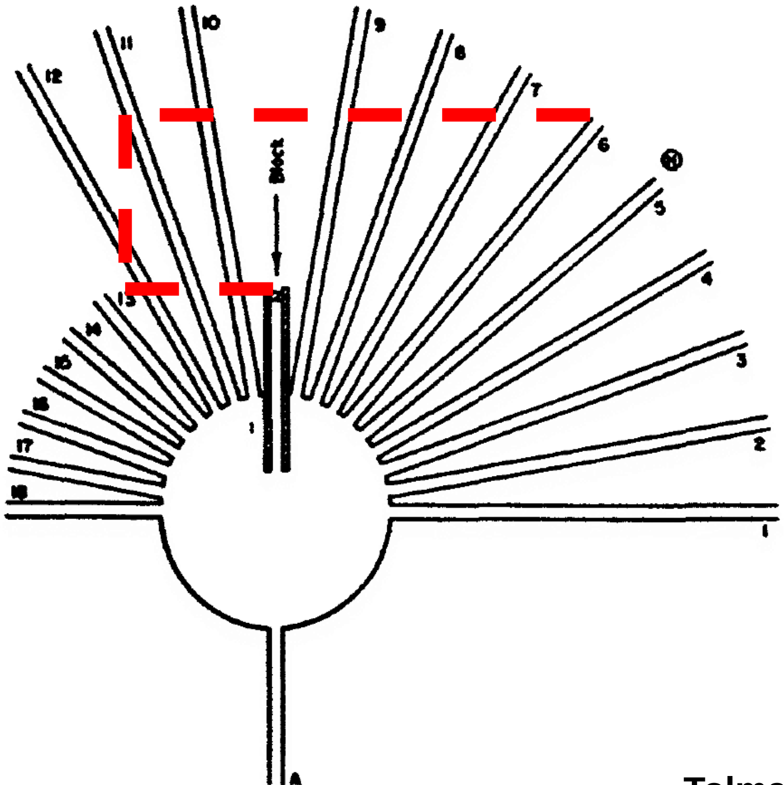
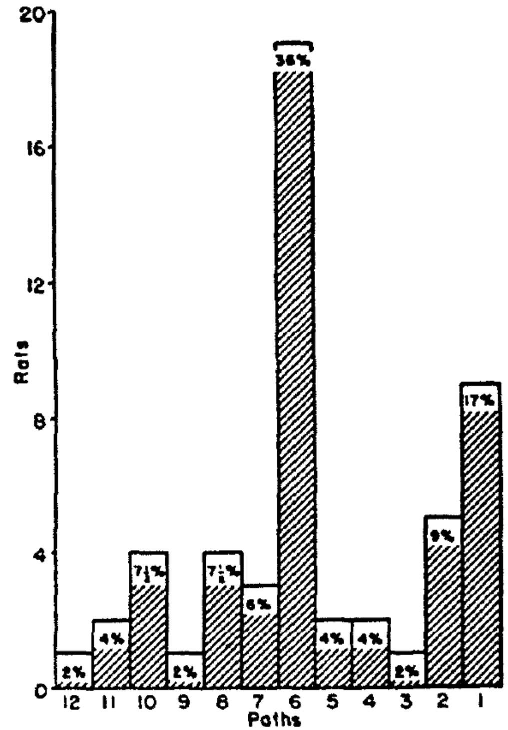
behavioral flexibility | shortcuts



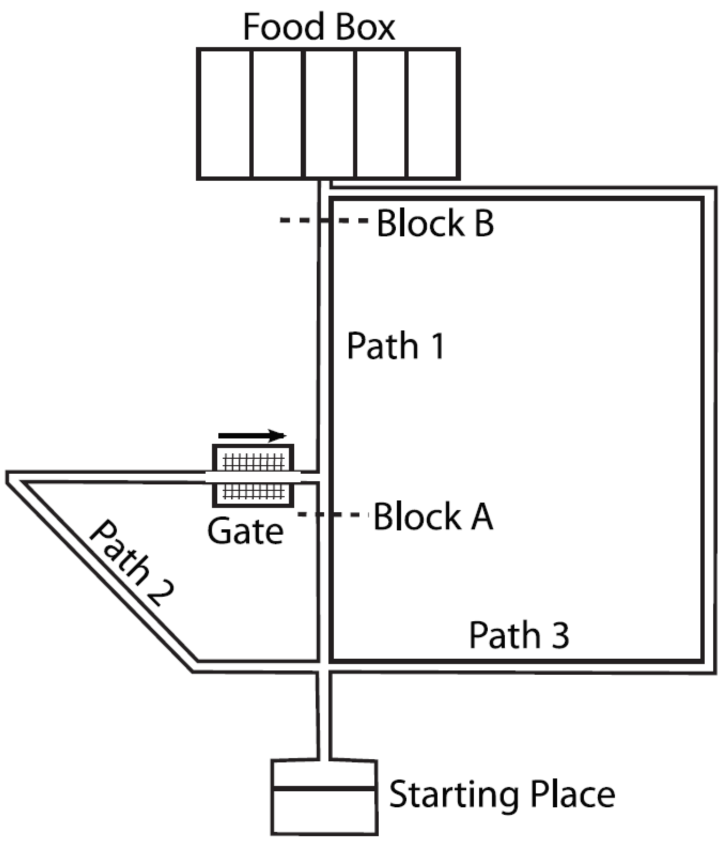
Apparatus used in the test trial



Numbers of rats which chose each of the paths

Tolman et al., 1946.

behavioral flexibility | detours



Tolman and Honzik, 1930.

THE
HIPPOCAMPUS
AS A COGNITIVE MAP

JOHN O'KEEFE
AND
LYNN NADEL

1478
1978
CLARENDON PRESS · OXFORD

Modern definition of Tolman cognitive map from a neurobiological perspective.

A map is "*the representation of a set of connected places which are systematically related to each other by a group of spatial transformation rules.*"

The cognitive map according to O'Keefe and Nadel

representation of distances and angles between locations, independent of the subject

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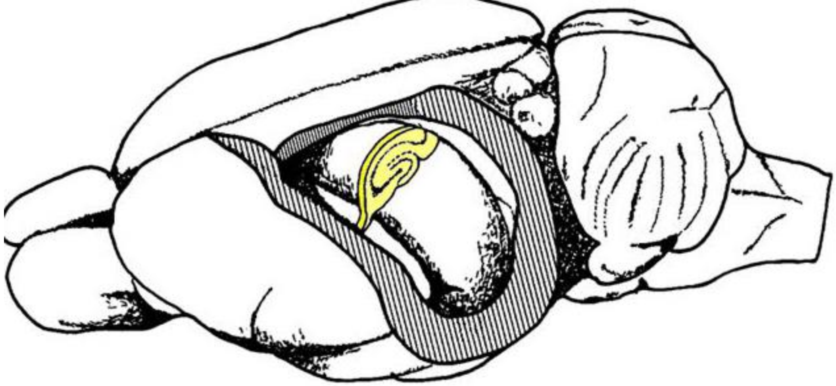
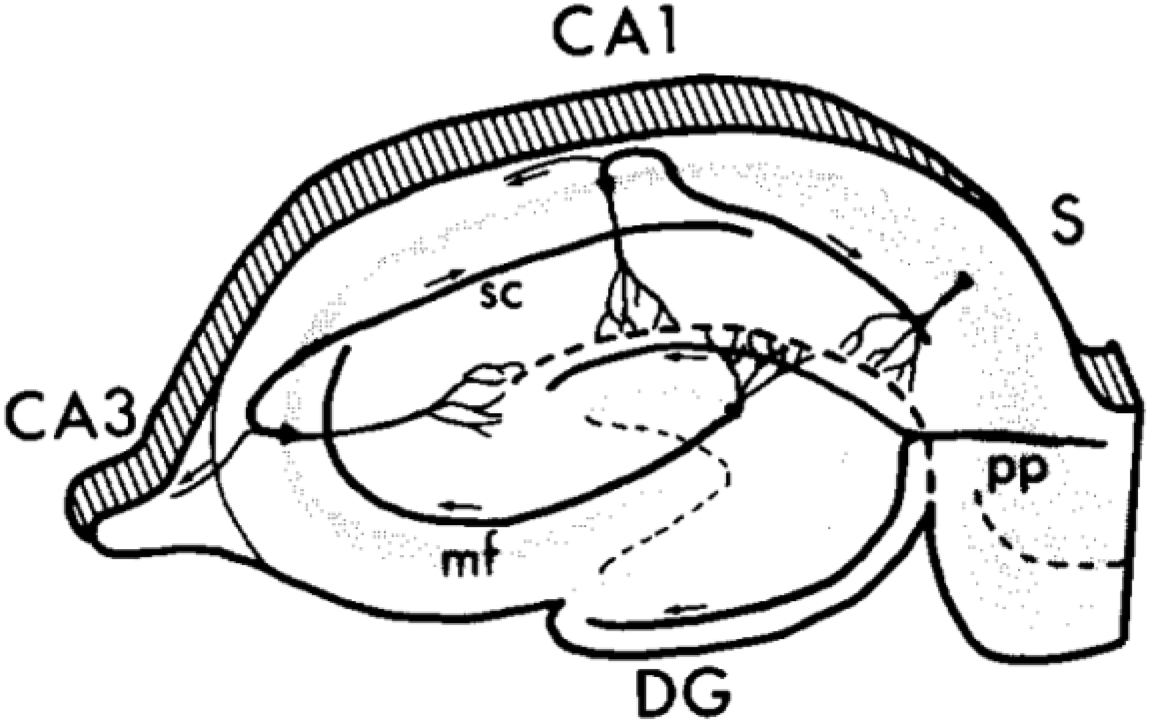
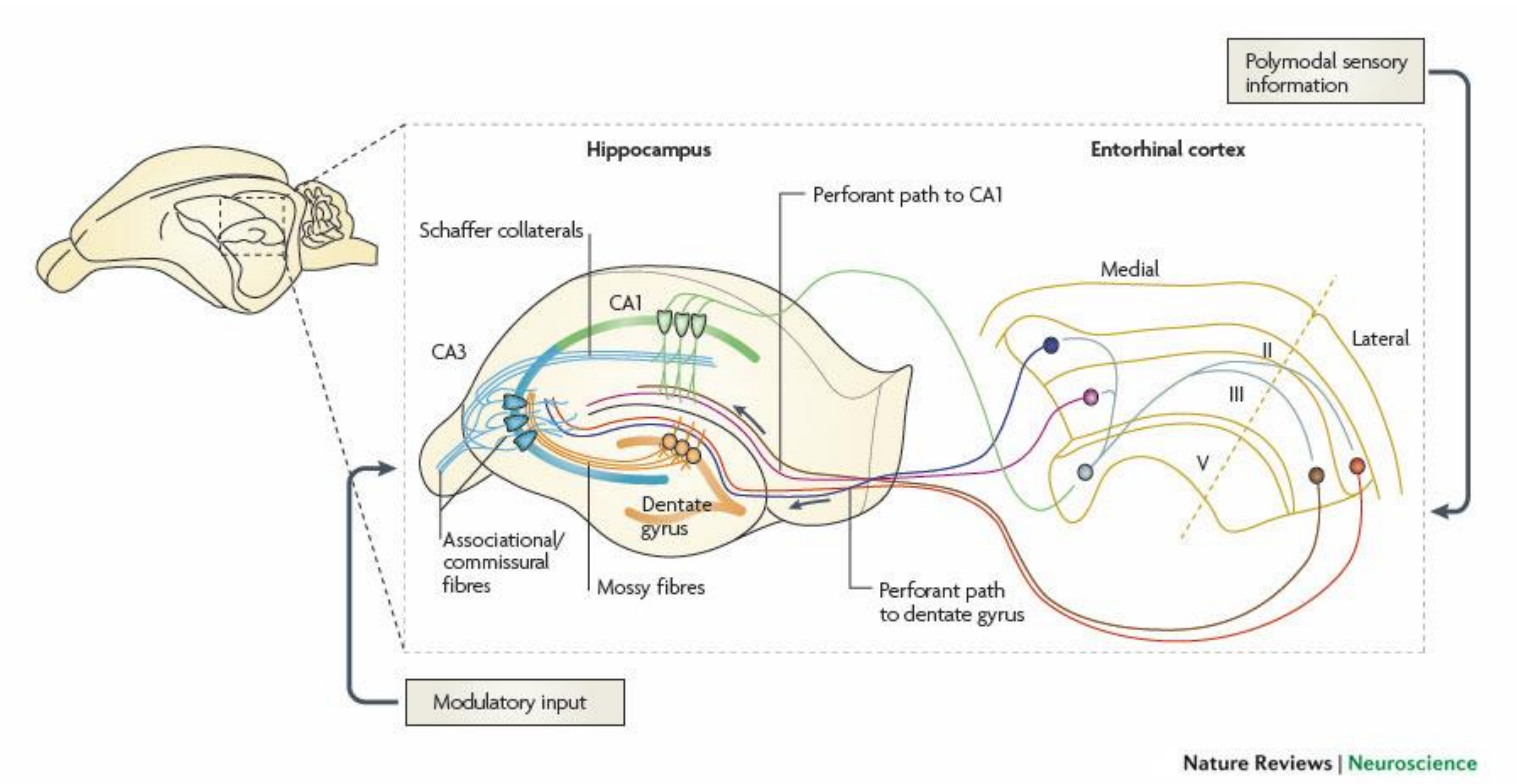
The trisynaptic pathway.





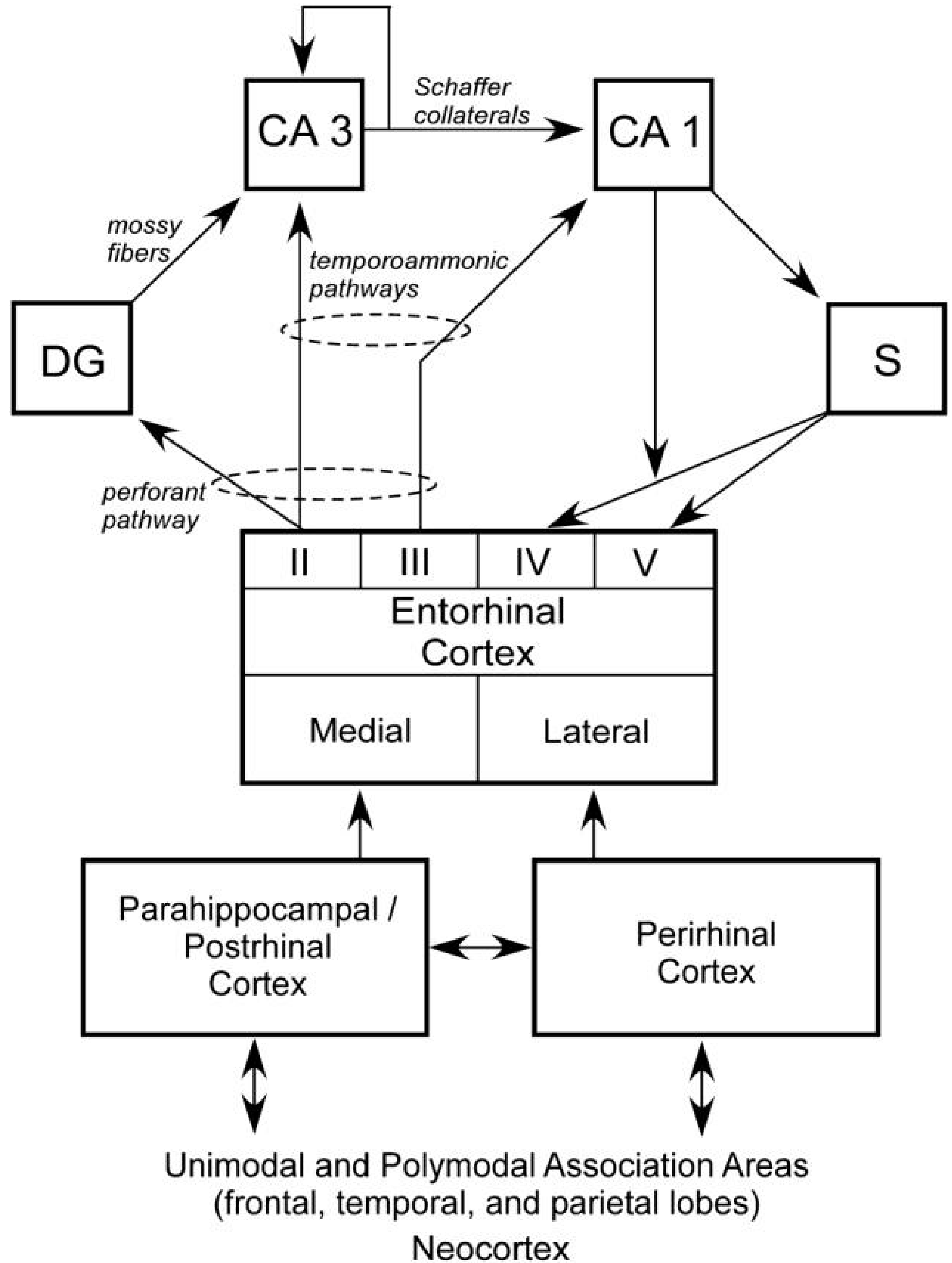
Enlarged portion of the hippocampus showing the trisynaptic pathway. S: Subiculum; DG: Dentate Gyrus; pp: perforant path; mf: mossy fibres; sc: Schaffer collaterals. Adapted from Amaral and Witter, 1989.

The trisynaptic pathway.

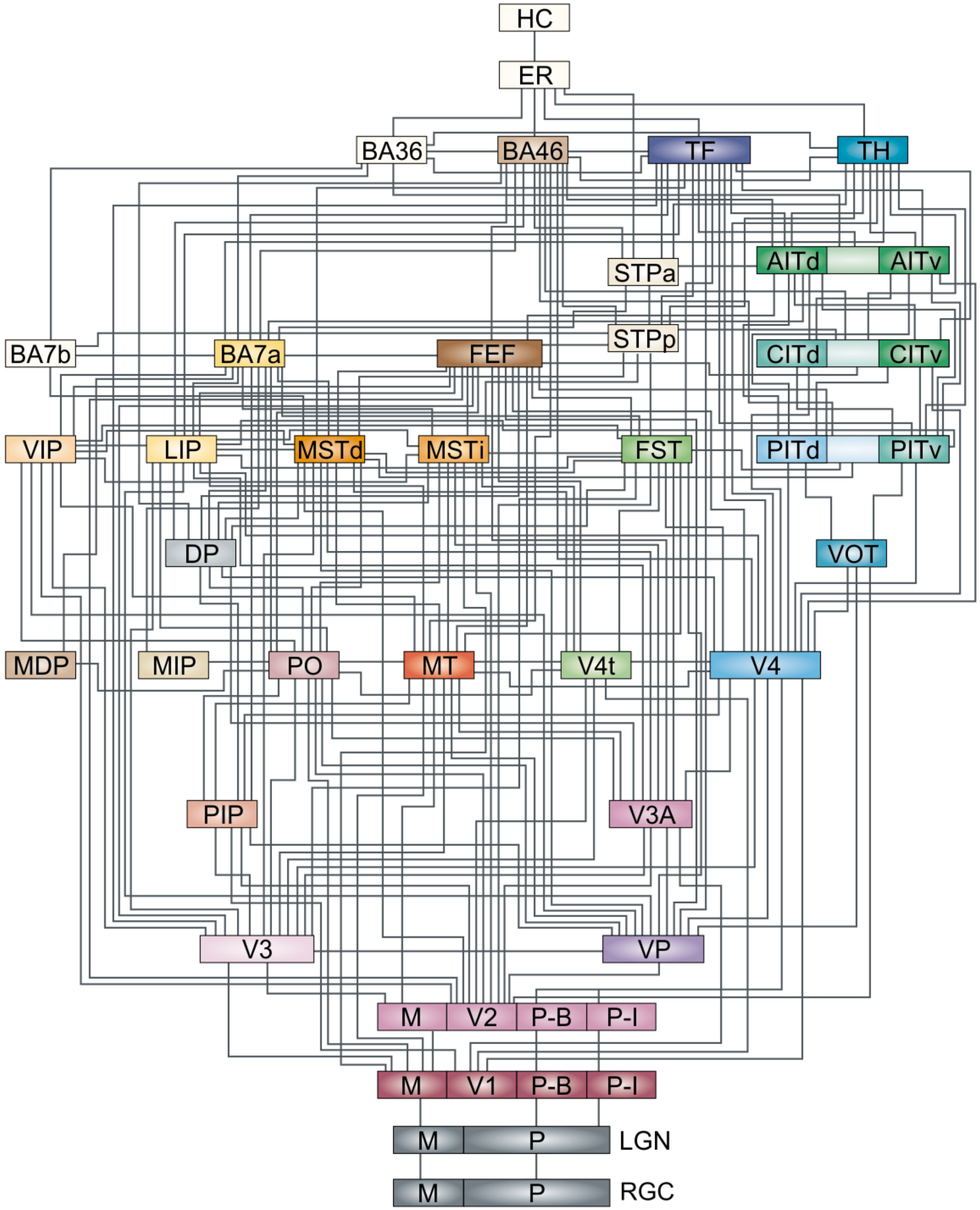


Guilherme Neves, Sam F. Cooke & Tim V. P. Bliss, Nature Reviews Neuroscience 9, 65-75 (January 2008), doi:10.1038/nrn2303

The trisynaptic loop and connections with neocortex.



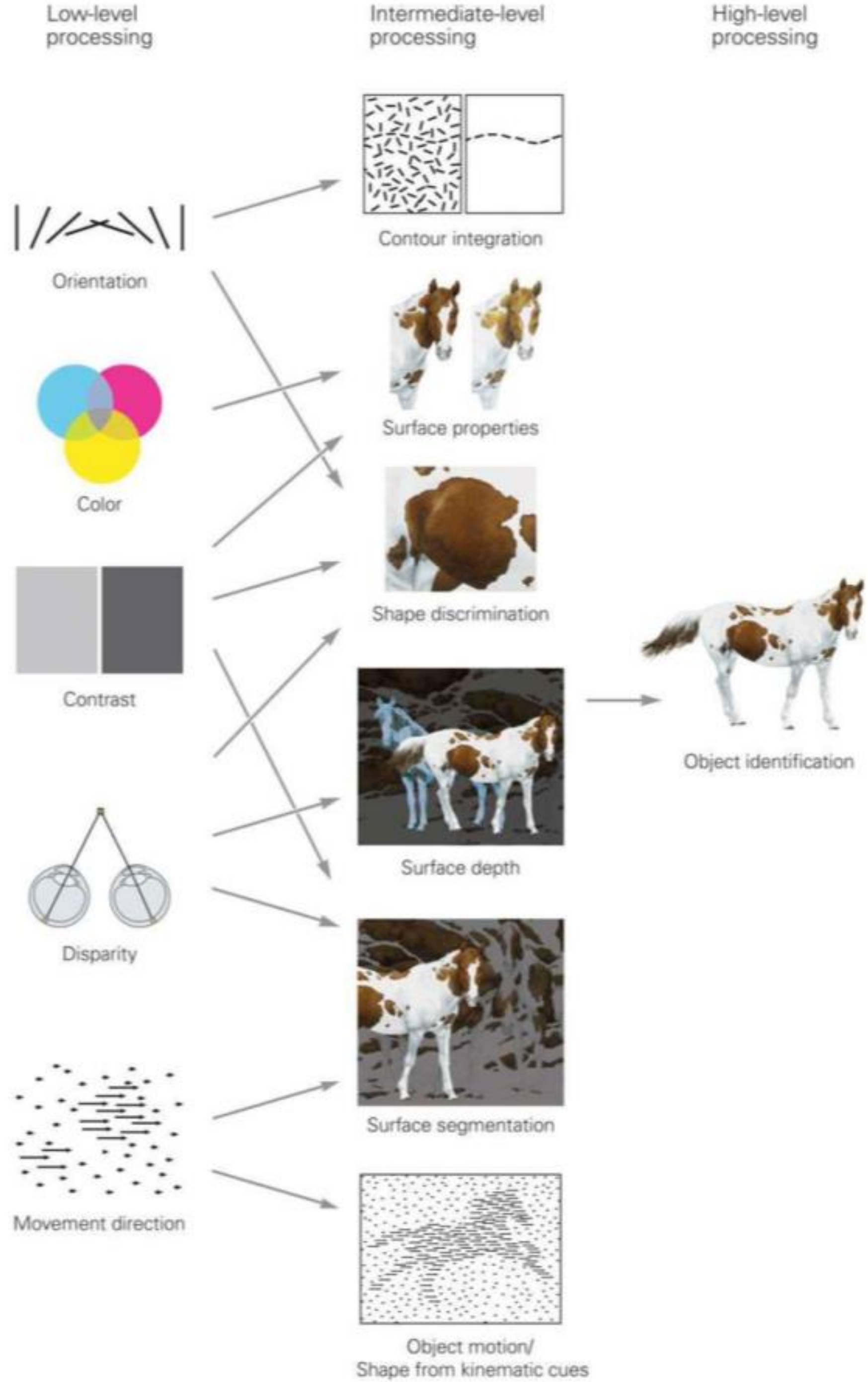
The trisynaptic loop and connections with neocortical regions. CA2 is not shown, however, it receives input from layer II and III of the MEC, and reciprocal input from CA3. It sends projections to CA1 and back to layer II of the MEC. From Clark & Squire, 2013.

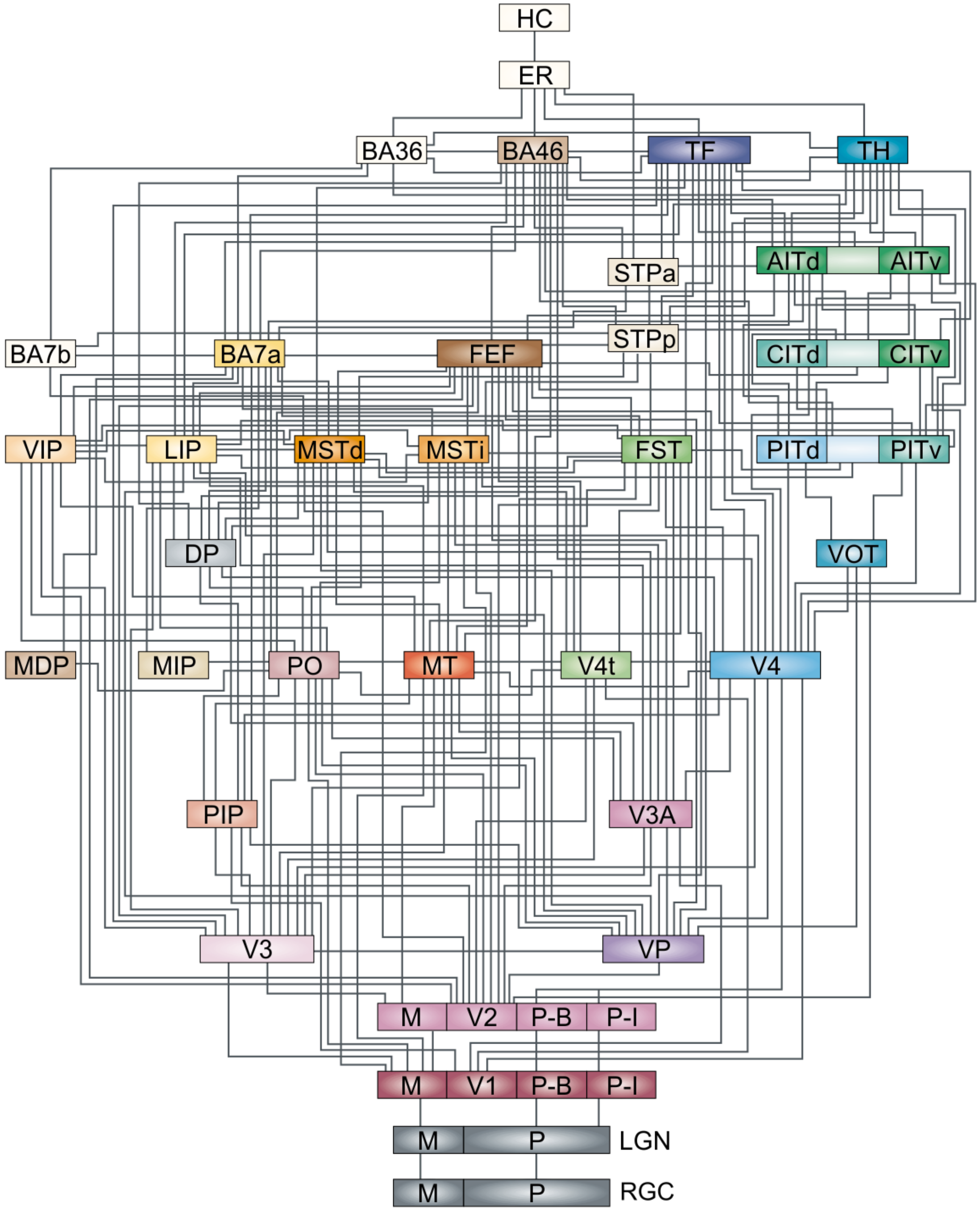


Anatomical hierarchy of visual areas in human and non-human primate

Rees, G., Kreiman, G., and Koch, C. (2002). Neural correlates of consciousness in humans. Nat. Rev. Neurosci. *3*, 261–270.

La nature constructive des traitements visuels.





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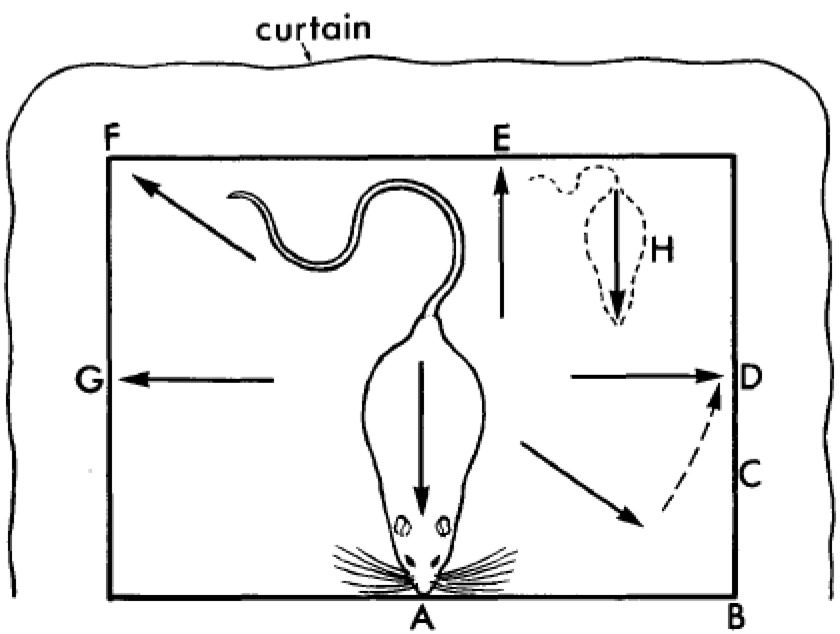
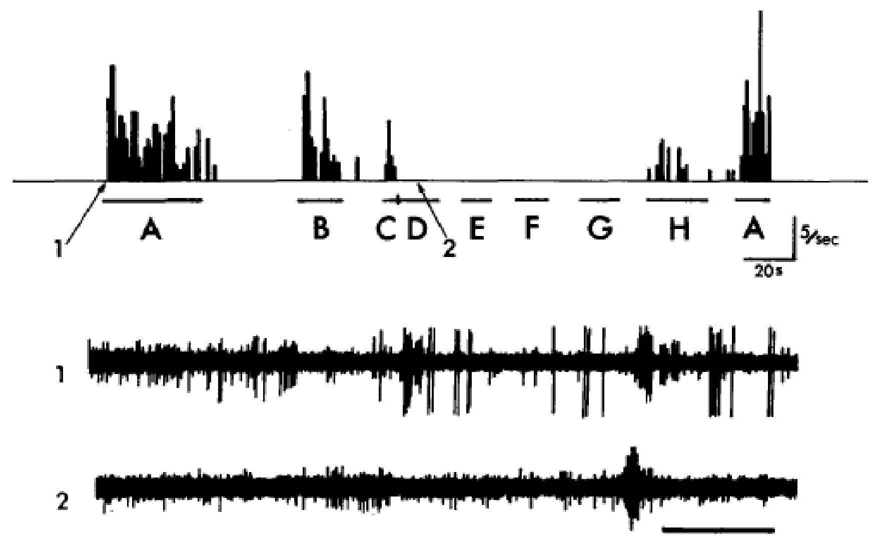
BRAIN RESEARCH

J. O'KEEFE
J. DOSTROVSKY*

Short Communications

The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat



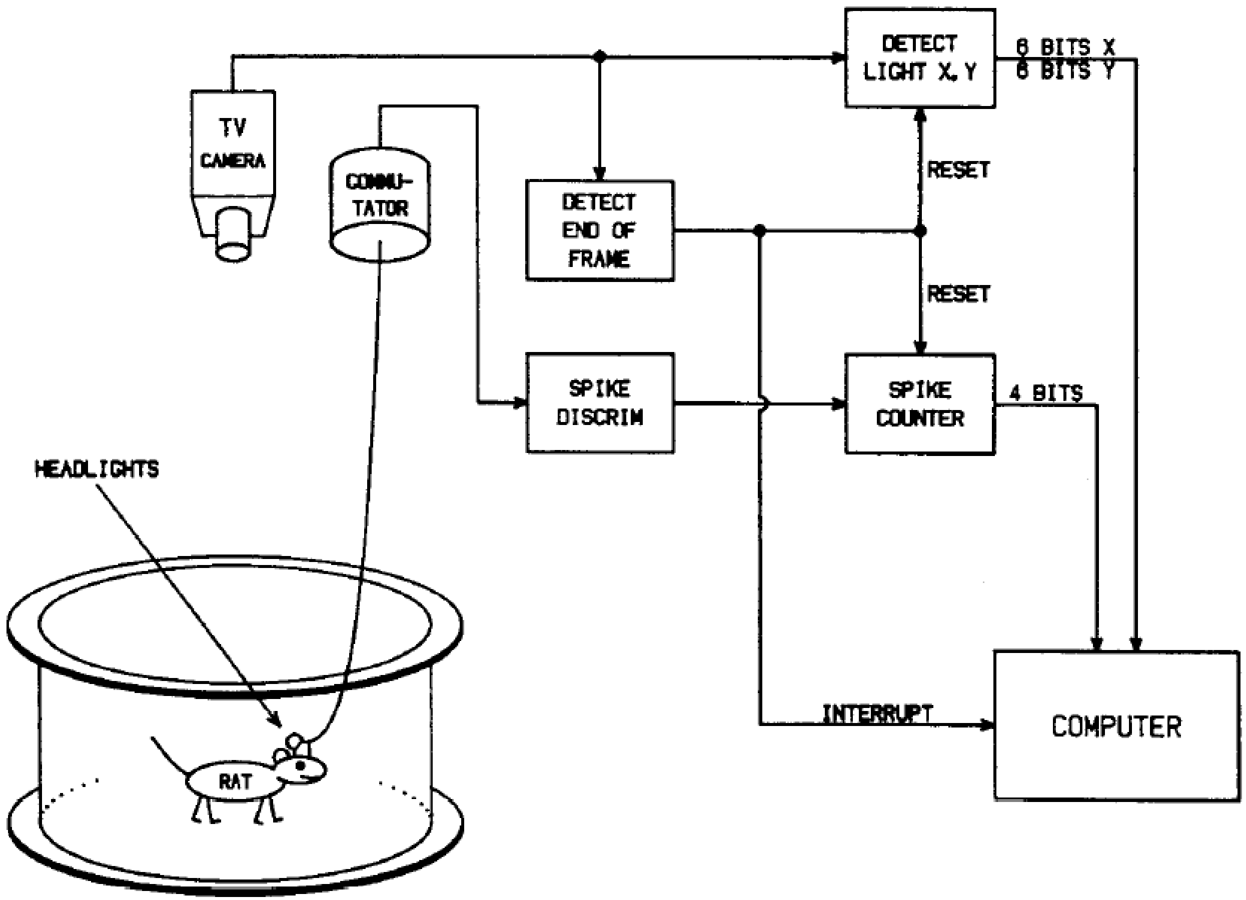


Brain Research, 34 (1971) 171–175

Spatial Firing Patterns of Hippocampal Complex-Spike Cells in a Fixed Environment

Robert U. Muller, John L. Kubie, and James B. Ranck, Jr.

Departments of Physiology and Anatomy and Cell Biology, Downstate Medical Center (SUNY), Brooklyn, New York 11203



The Journal of Neuroscience, July 1987, 7(7): 1935–1950

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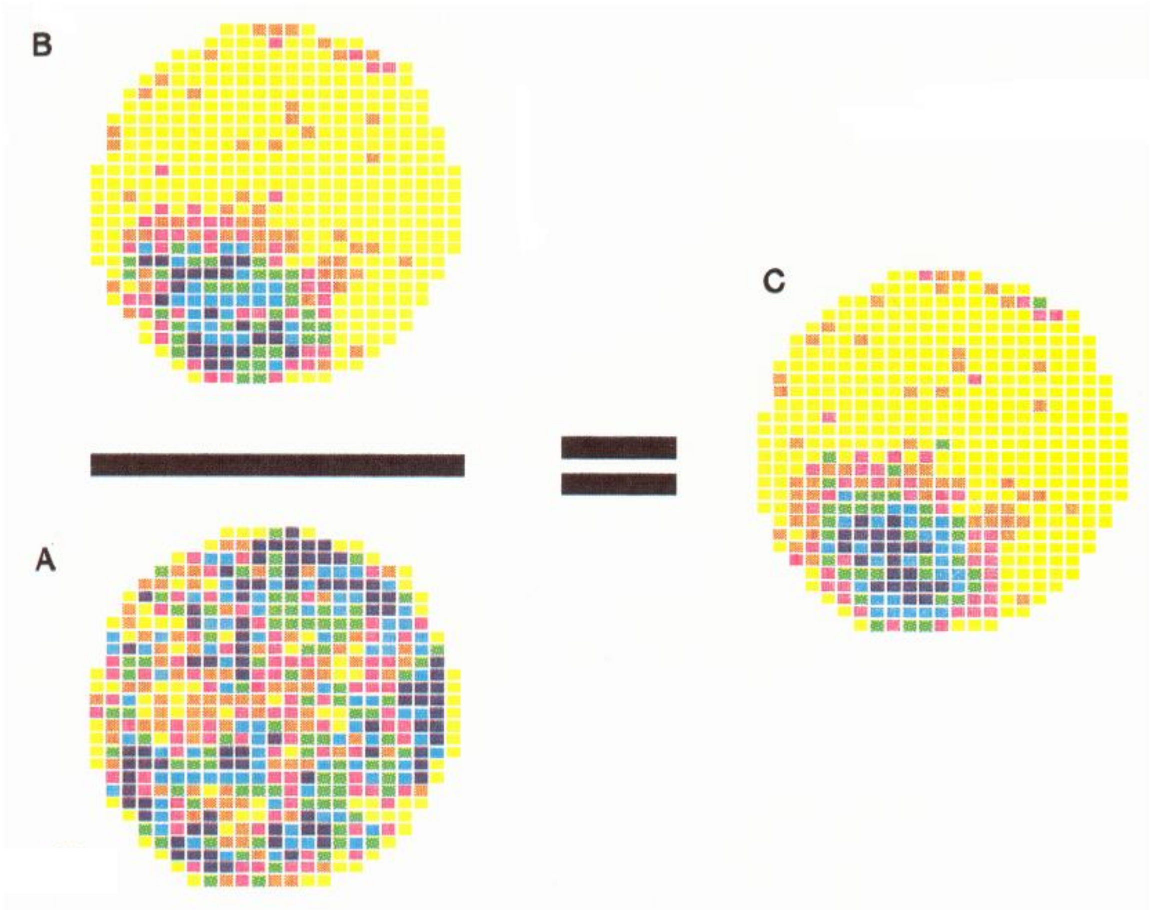

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Head-Direction Cells Recorded from the Postsubiculum in Freely Moving Rats. I. Description and Quantitative Analysis

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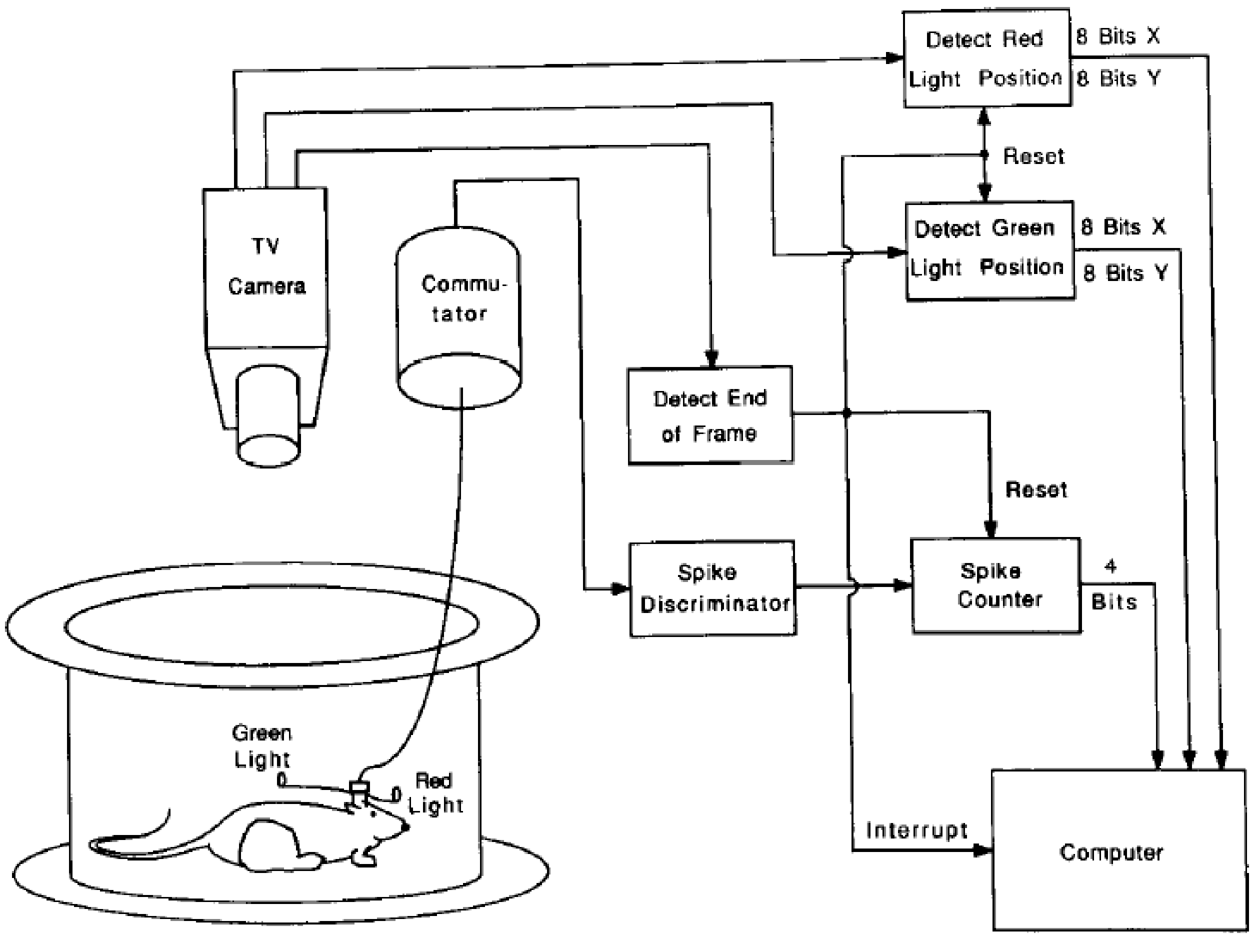
Department of Physiology, SUNY Health Sciences Center at Brooklyn, Brooklyn, New York 11203



The Journal of Neuroscience, February 1990, *10*(2): 420–435

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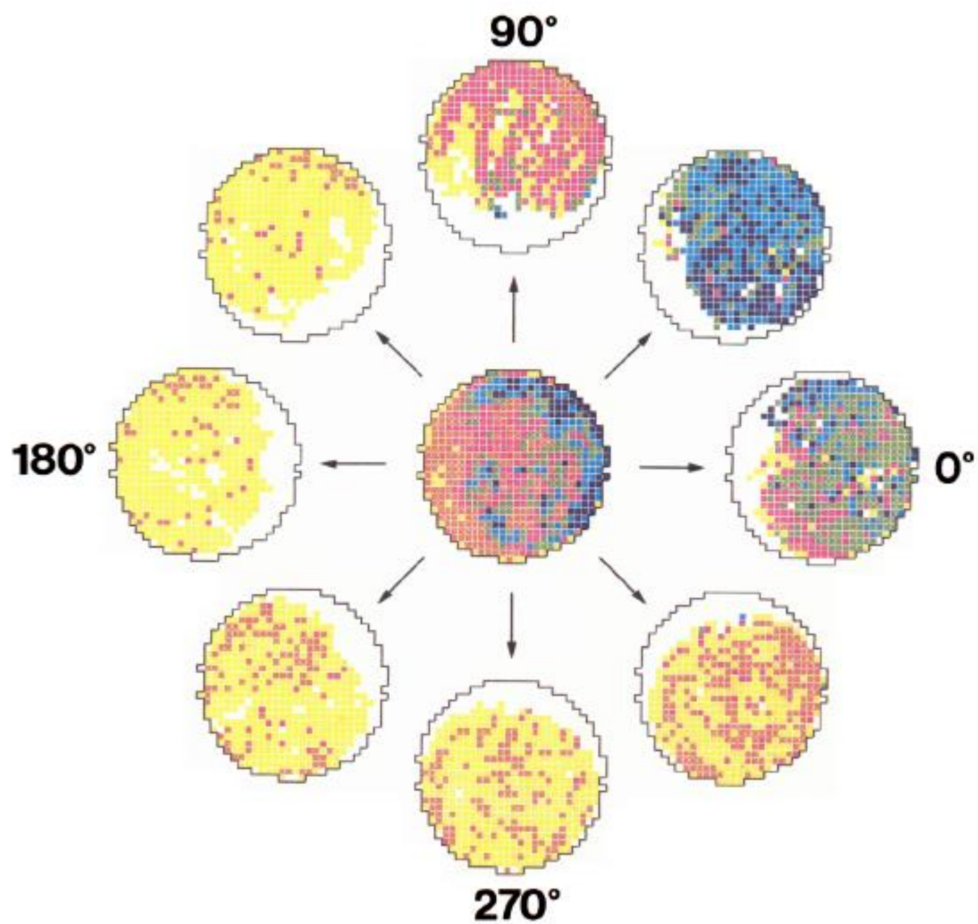

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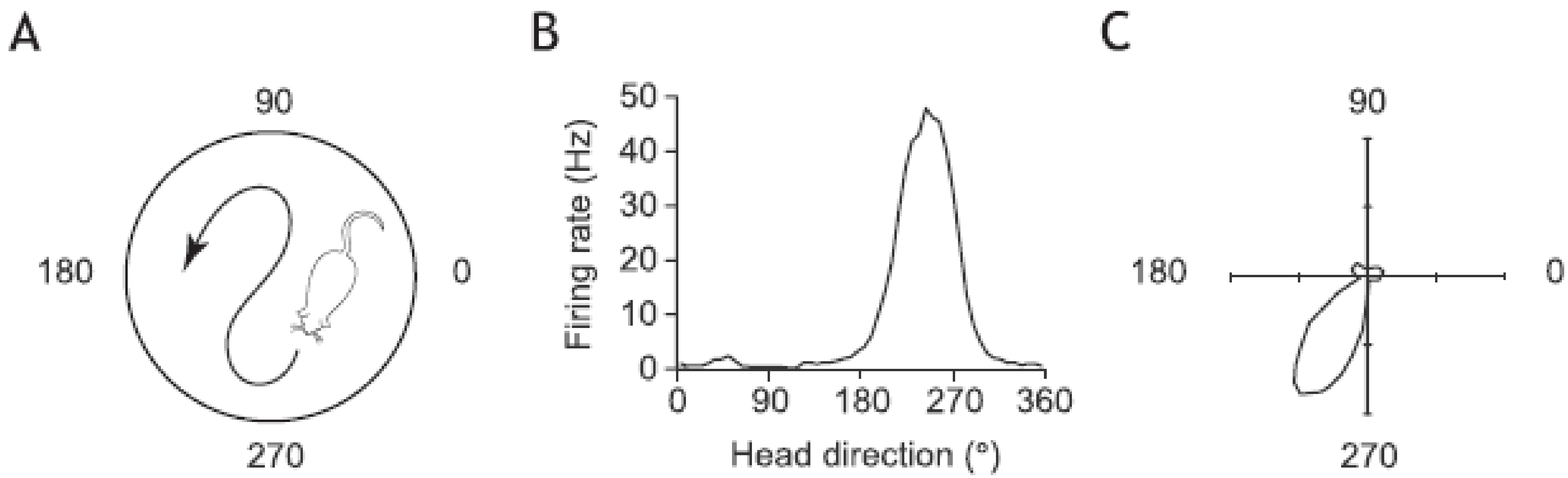
Head direction cells.



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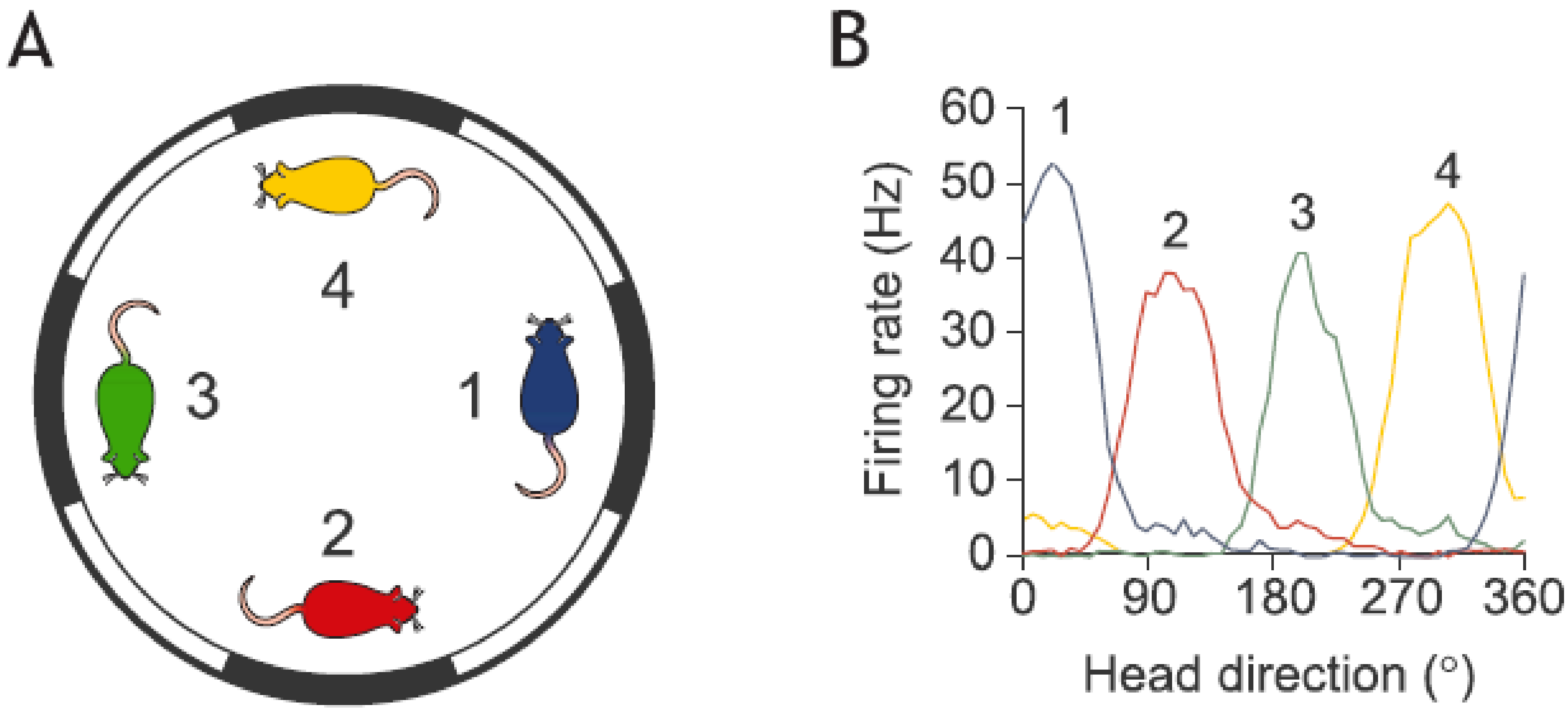
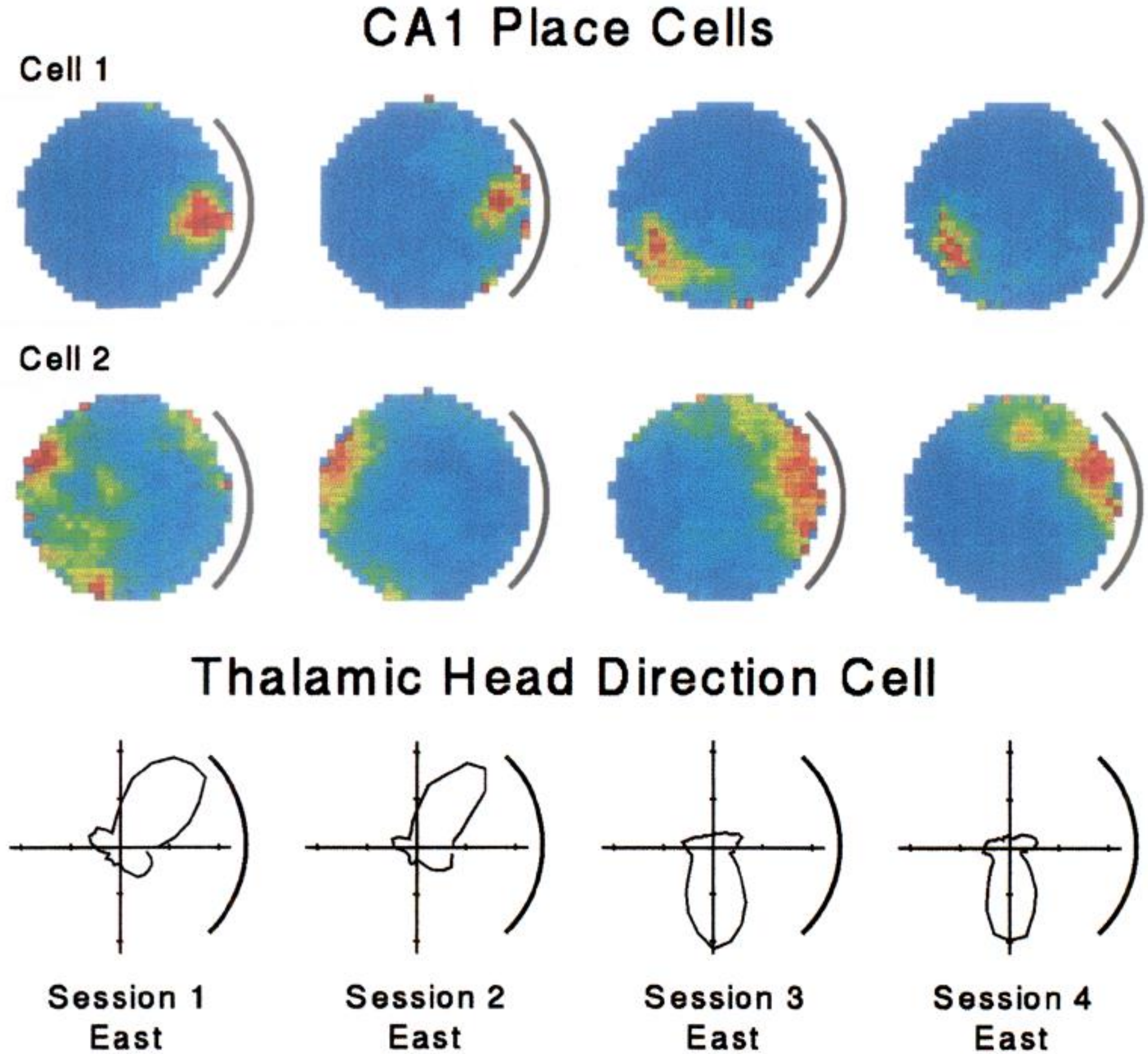
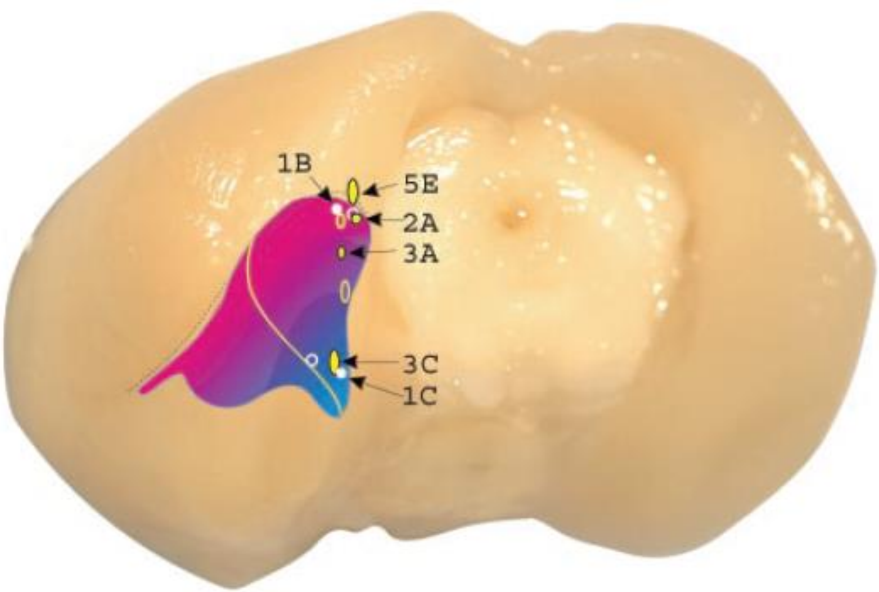


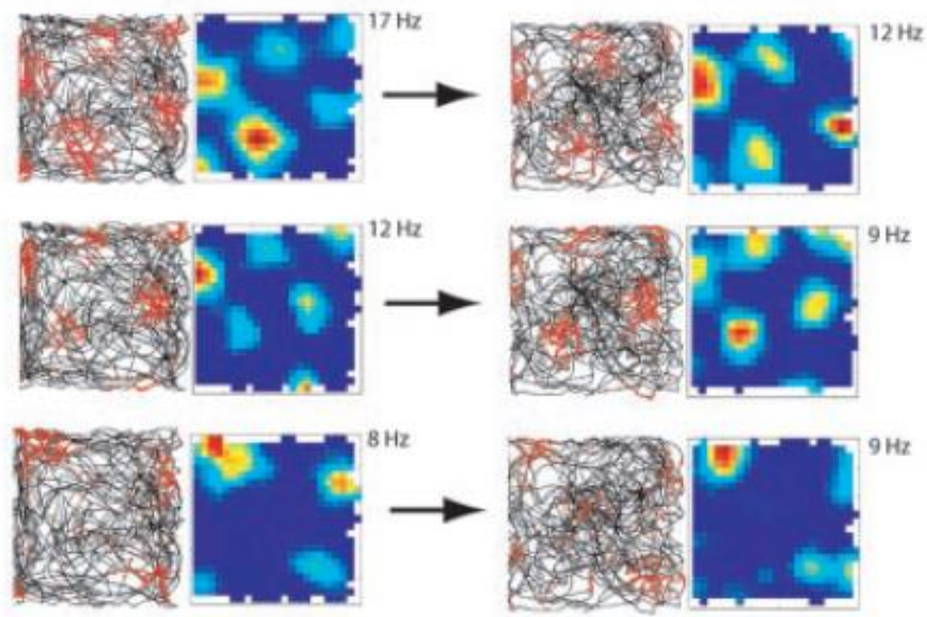


Knierim, J.J., Kudrimoti, H.S., and McNaughton, B.L. (1995). Place cells, head direction cells, and the learning of landmark stability. J. Neurosci. *15*, 1648–1659.

Spatial Representation in the Entorhinal Cortex

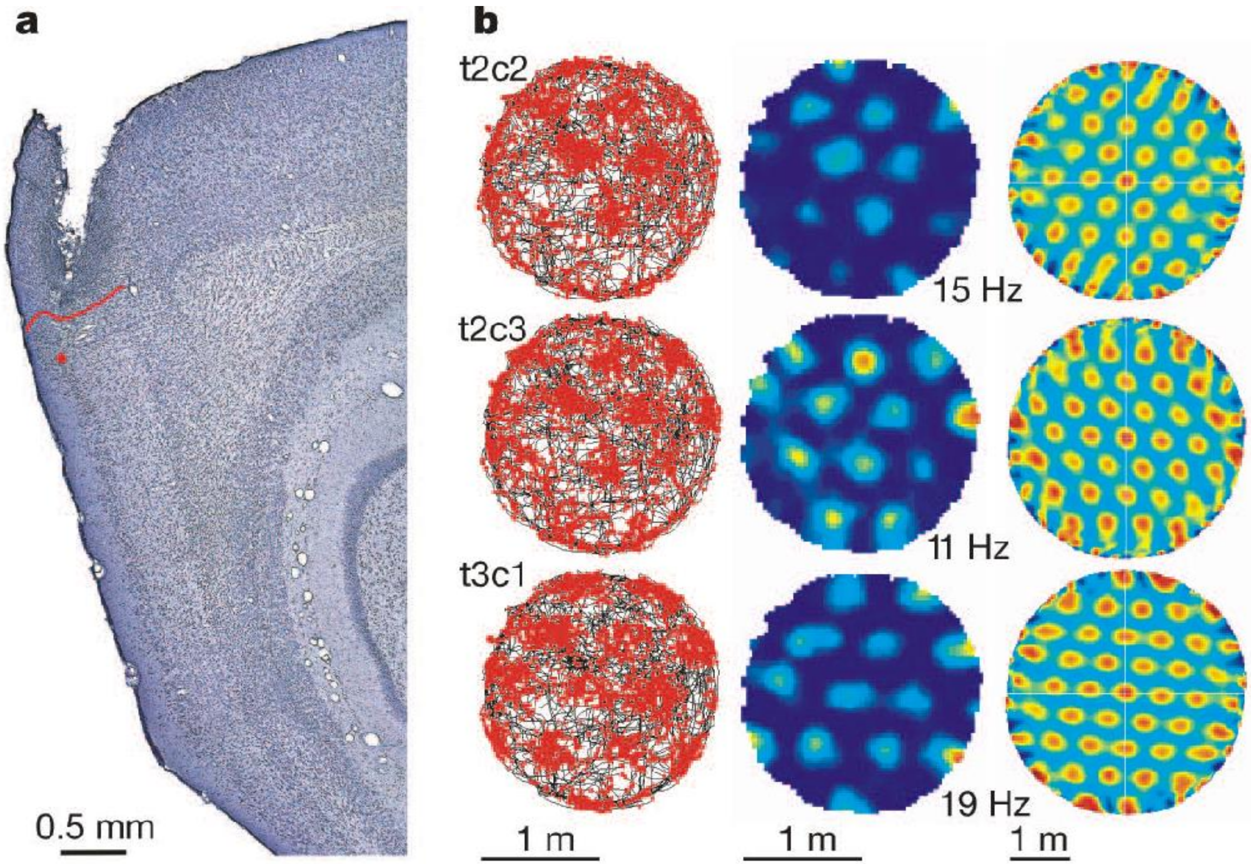
Marianne Fyhn,[1] Sturla Molden,[1] Menno P. Witter,[1,2]
Edvard I. Moser,[1*] May-Britt Moser[1]





Microstructure of a spatial map in the entorhinal cortex

Torkel Hafting[1]*, Marianne Fyhn[1]*, Sturla Molden[1]†, May-Britt Moser[1] & Edvard I. Moser[1]



2005 Nature *436*, 801–806.

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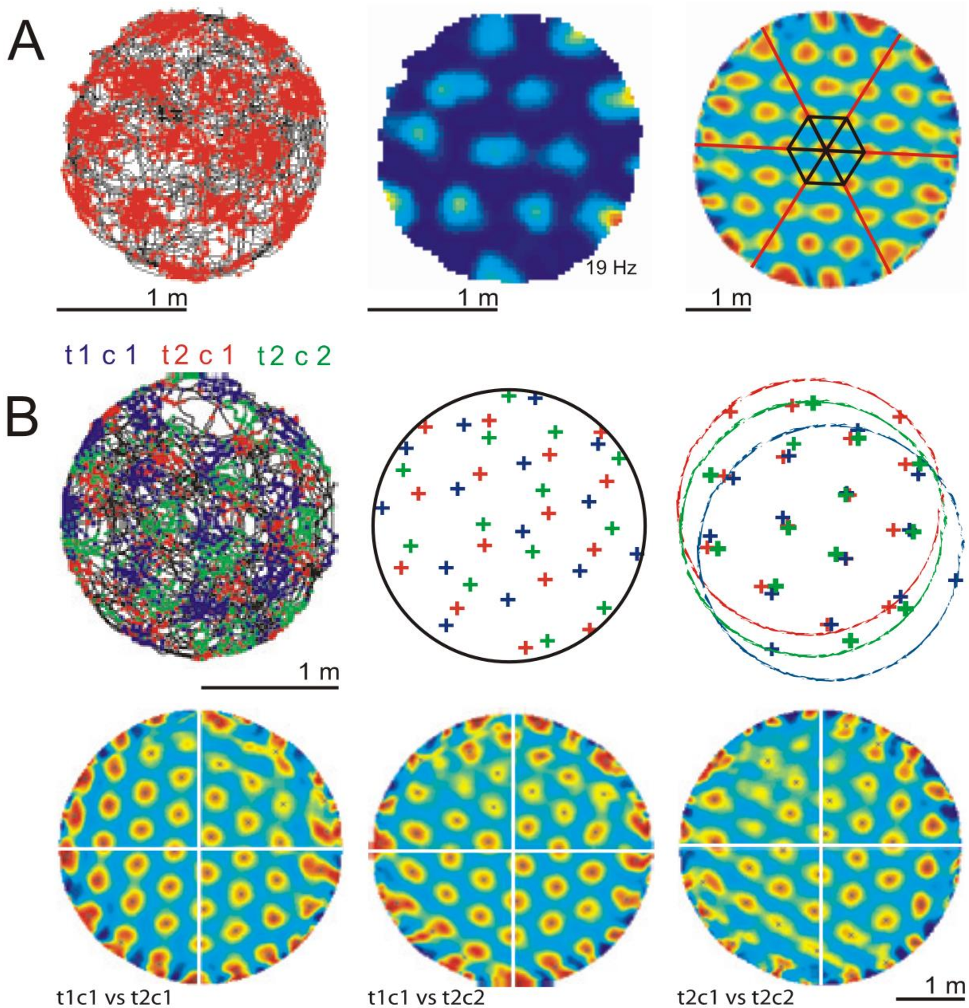
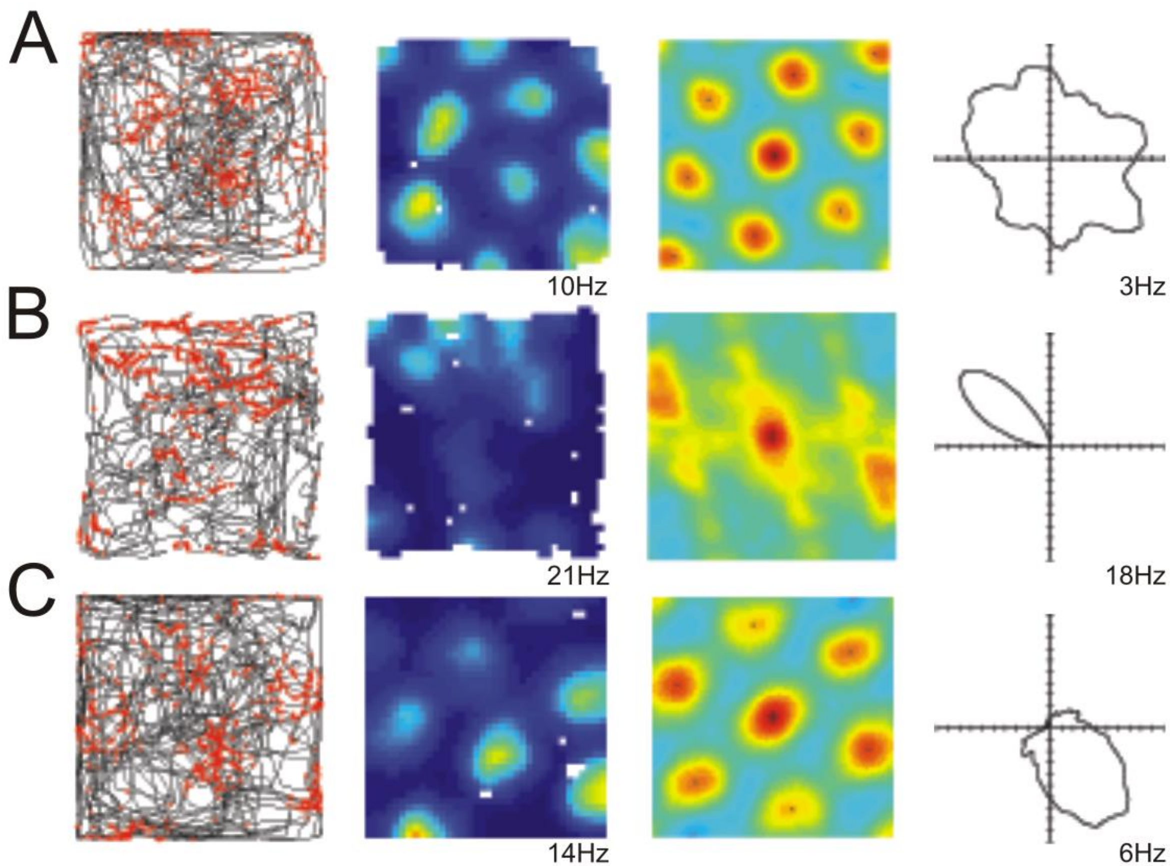
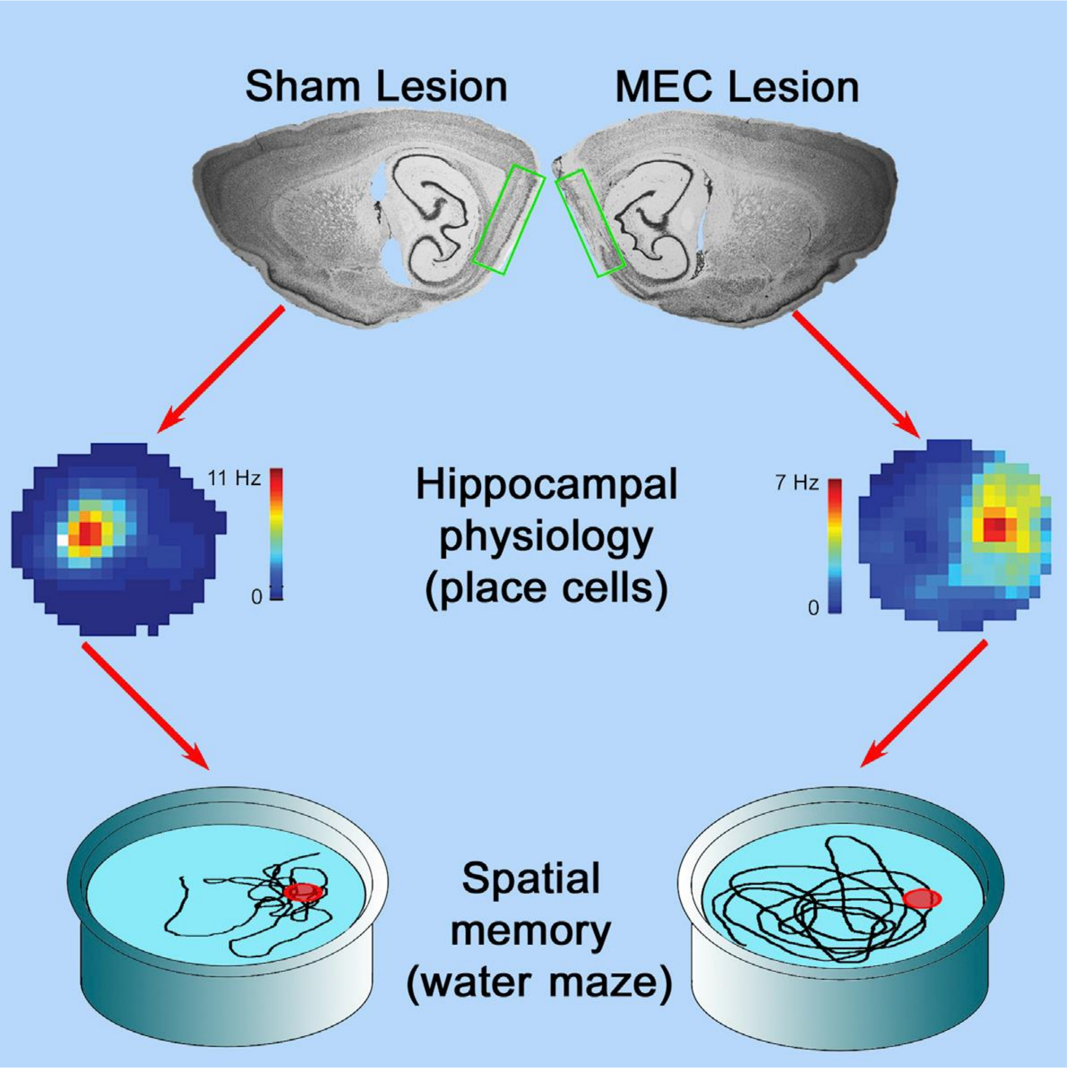


2005 Nature *436*, 801–806.

Conjunctive Representation of Position, Direction, and Velocity in Entorhinal Cortex

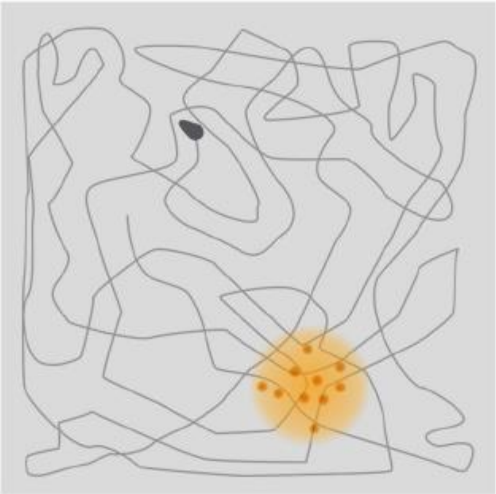
Francesca Sargolini,[1] Marianne Fyhn,[1] Torkel Hafting,[1] Bruce L. McNaughton,[1,2] Menno P. Witter,[1,3] May-Britt Moser,[1] Edvard I. Moser[1]*

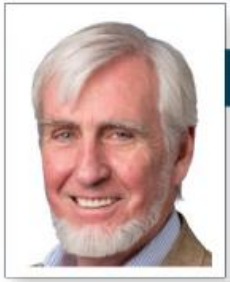




Hales, J.B., Schlesiger, M.I., Leutgeb, J.K., Squire, L.R., Leutgeb, S., and Clark, R.E. (2014). Medial Entorhinal Cortex Lesions Only Partially Disrupt Hippocampal Place Cells and Hippocampus-Dependent Place Memory. Cell Reports *9*, 893–901.

The Nobel Prize in Physiology or Medicine 2014

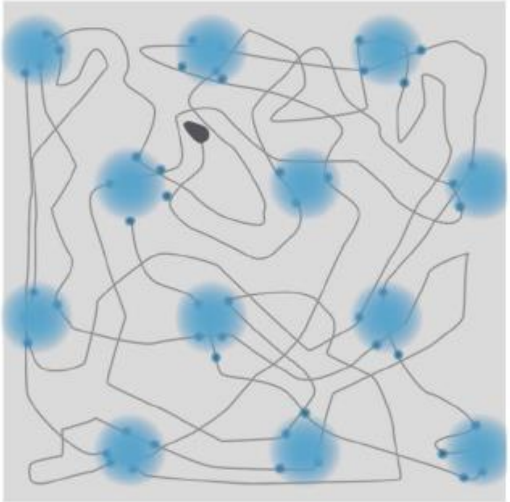




John O'Keefe

John O'Keefe discovered, in 1971, that certain nerve cells in the brain were activated when a rat assumed a particular place in the environment. Other nerve cells were activated at other places. He proposed that these "place cells" build up an inner map of the environment. Place cells are located in a part of the brain called the hippocampus.

May-Britt Moser and Edvard I. Moser



May-Britt och Edvard I. Moser discovered in 2005 that other nerve cells in a nearby part of the brain, the entorhinal cortex, were activated when the rat passed certain locations. Together, these locations formed a hexagonal grid, each "grid cell" reacting in a unique spatial pattern. Collectively, these grid cells form a coordinate system that allows for spatial navigation.

The Nobel Prize in Physiology or Medicine 2014

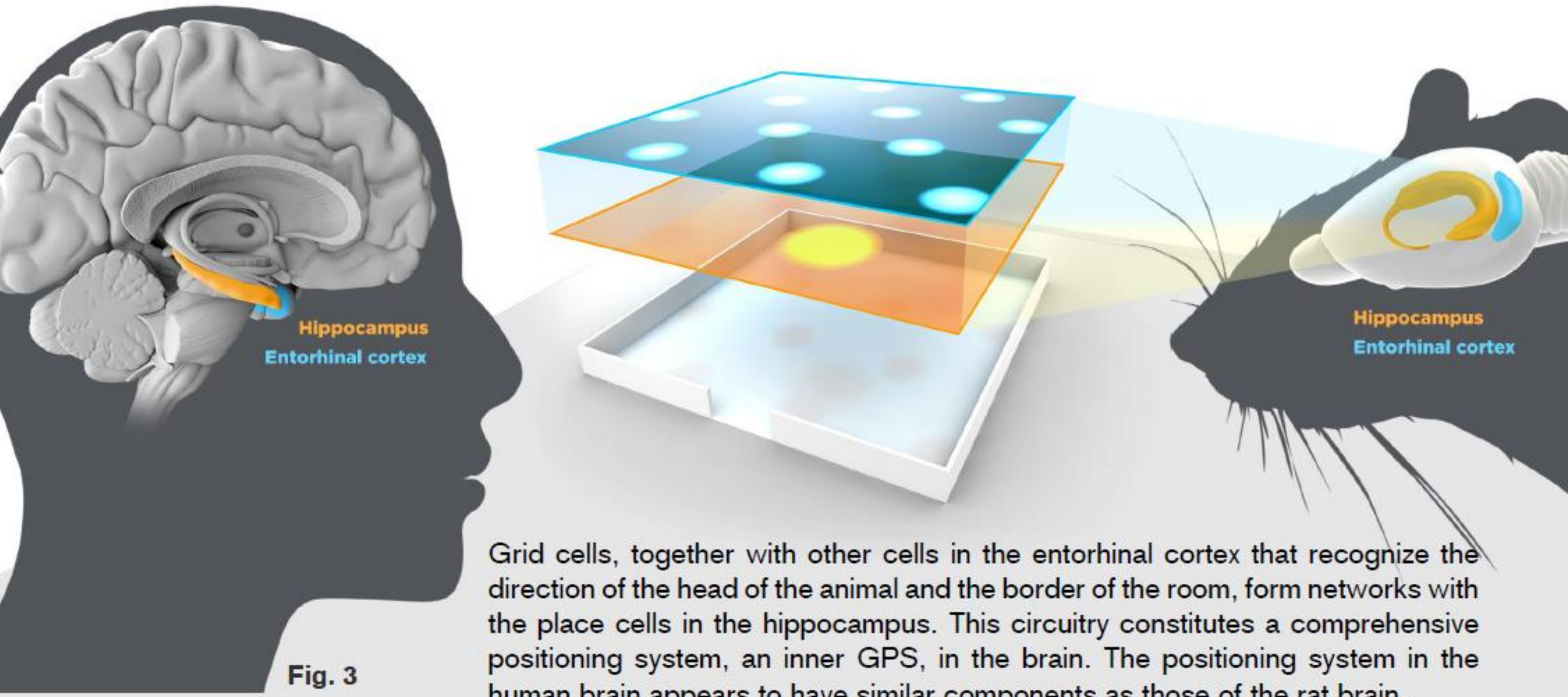
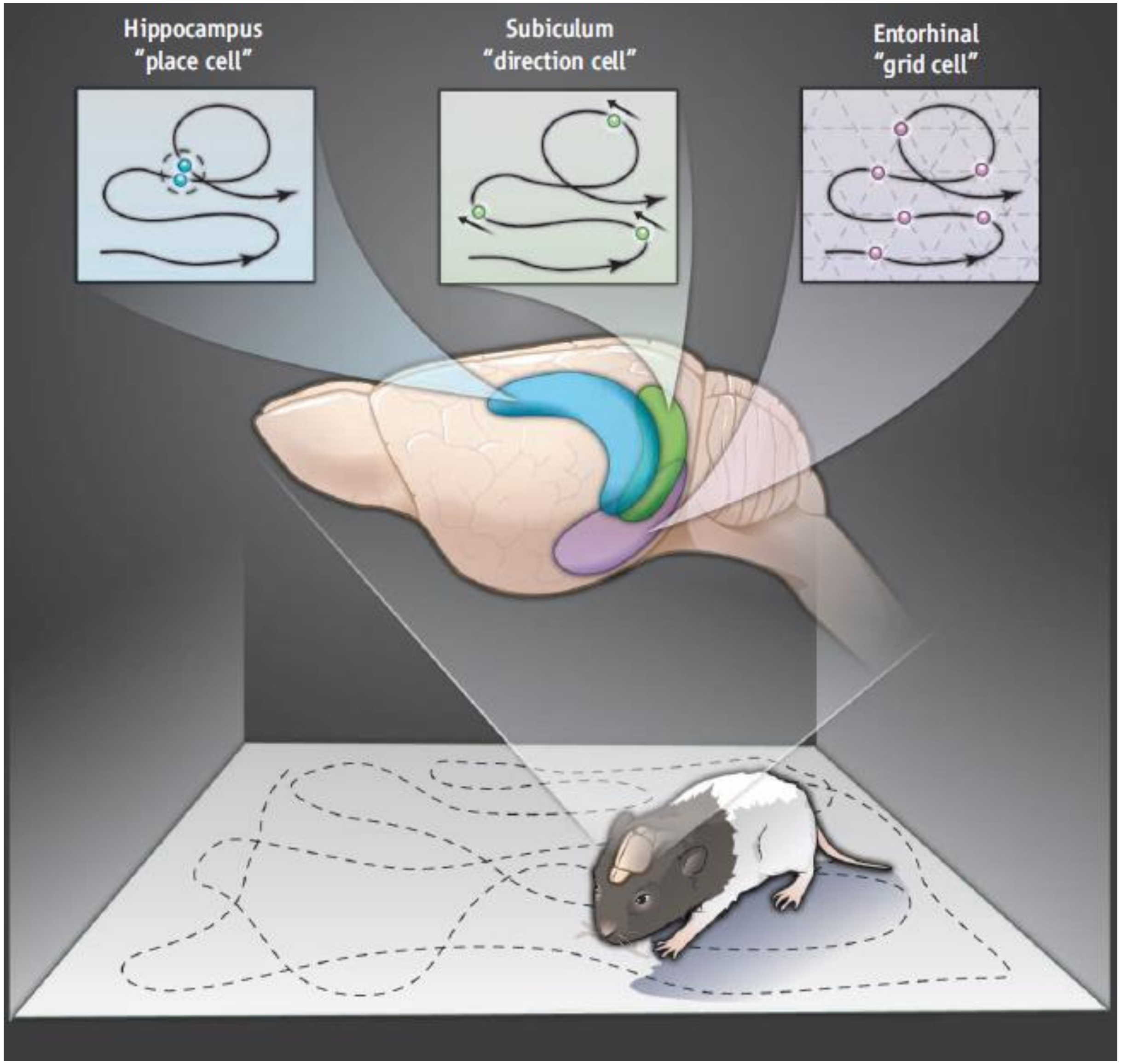


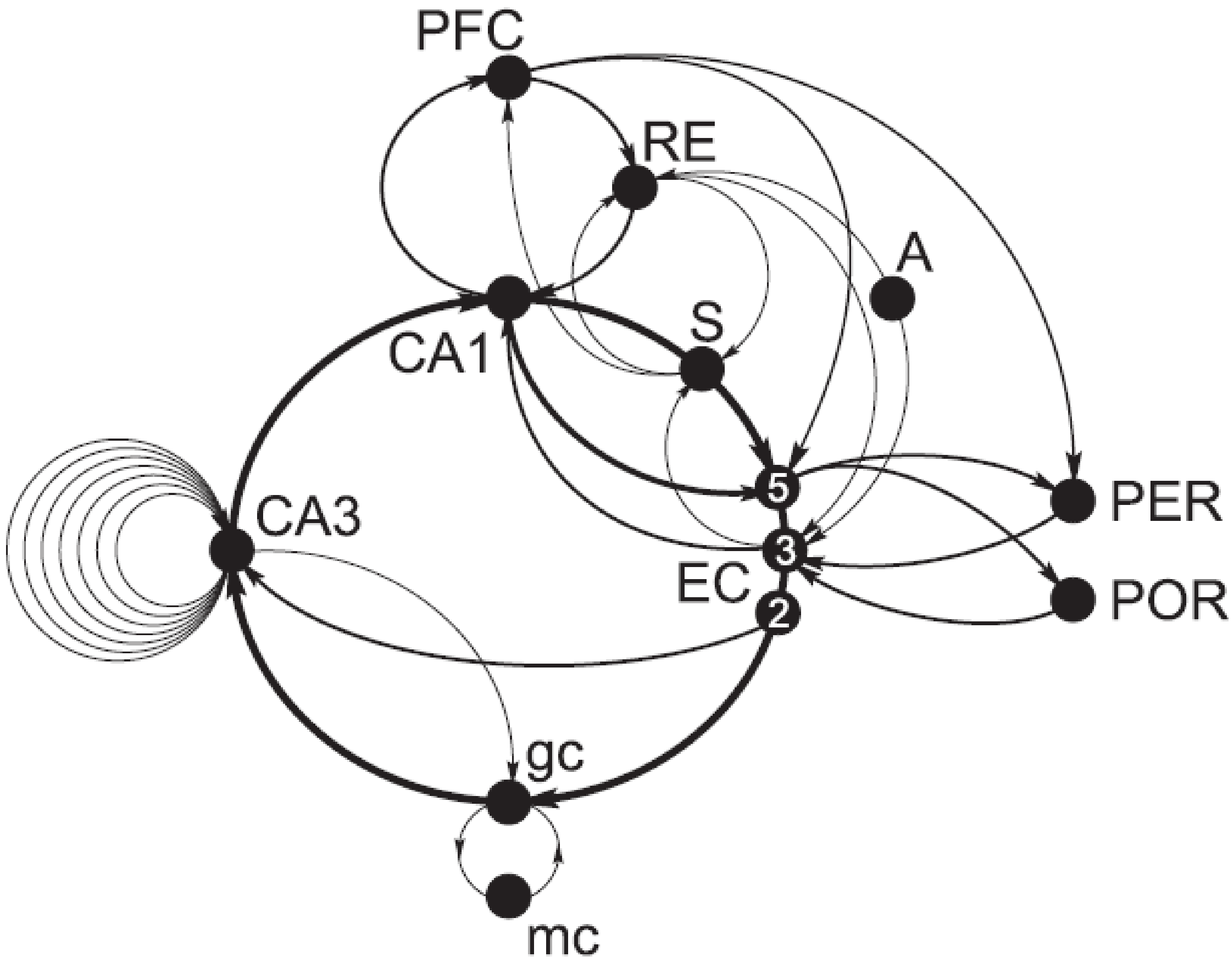
Fig. 3

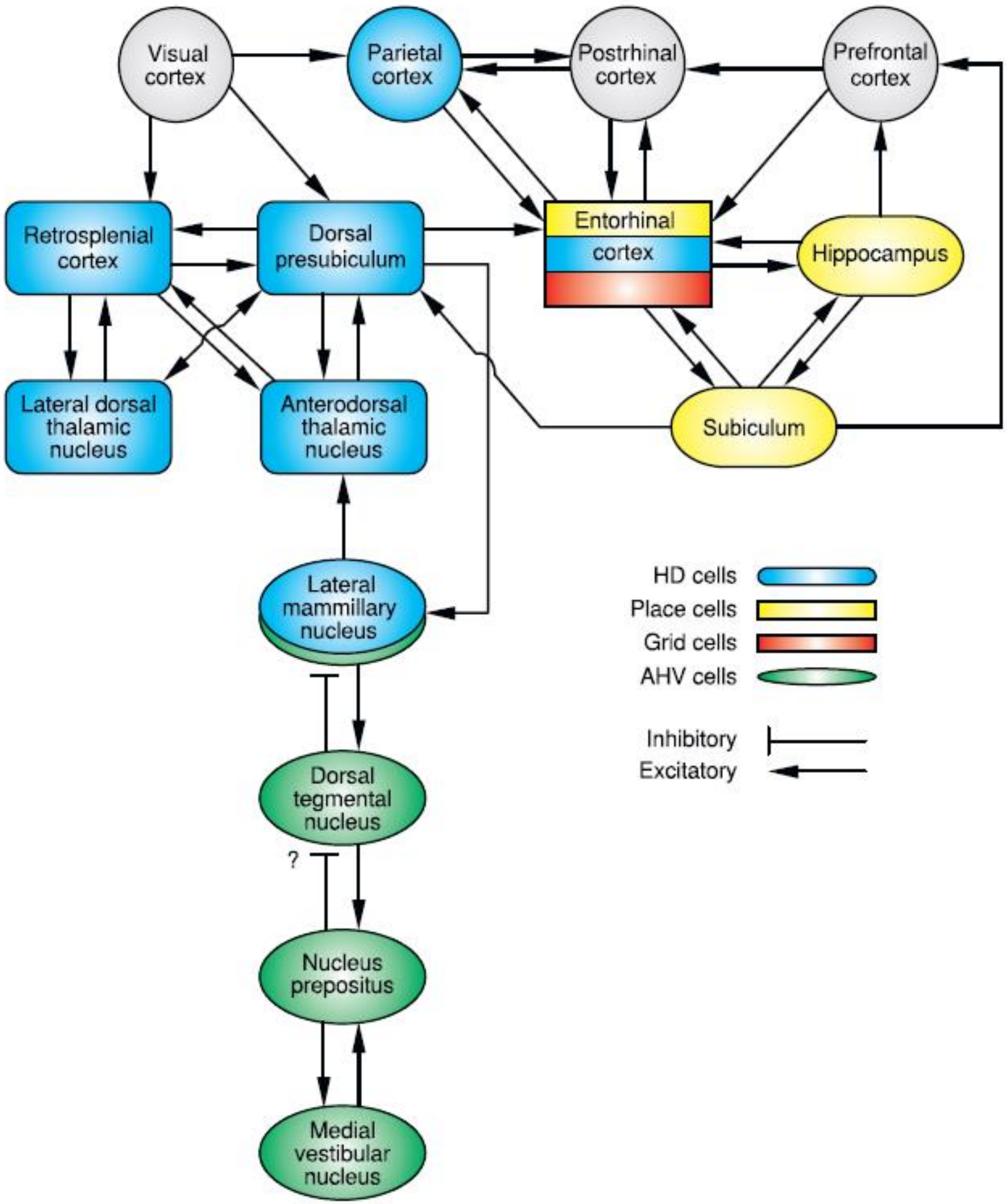
Grid cells, together with other cells in the entorhinal cortex that recognize the direction of the head of the animal and the border of the room, form networks with the place cells in the hippocampus. This circuitry constitutes a comprehensive positioning system, an inner GPS, in the brain. The positioning system in the human brain appears to have similar components as those of the rat brain.

The Nobel Prize in Physiology or Medicine 2014



Summary of the excitatory connections.





Networks of spatio-selective cells.

Plan général du cours

- Behavioral strategies in orientation
- Anatomy of the hippocampus
- Spatial memory and its neural substrate
- Memory properties of place cells
- Electrophysiological recordings in humans

Historical context

1960 – 1970 : Importance of the hippocampus in memory functions

1. First studies of field potentials, which will ultimately lead to the discovery of LTP (Bliss & Lømo, 1973)
2. Patients with medial temporal lobe lesions have impaired episodic memory (Scoville & Milner, 1957).
3. The hippocampus supports key functions of memory such as pattern completion and memory consolidation Marr (1971)

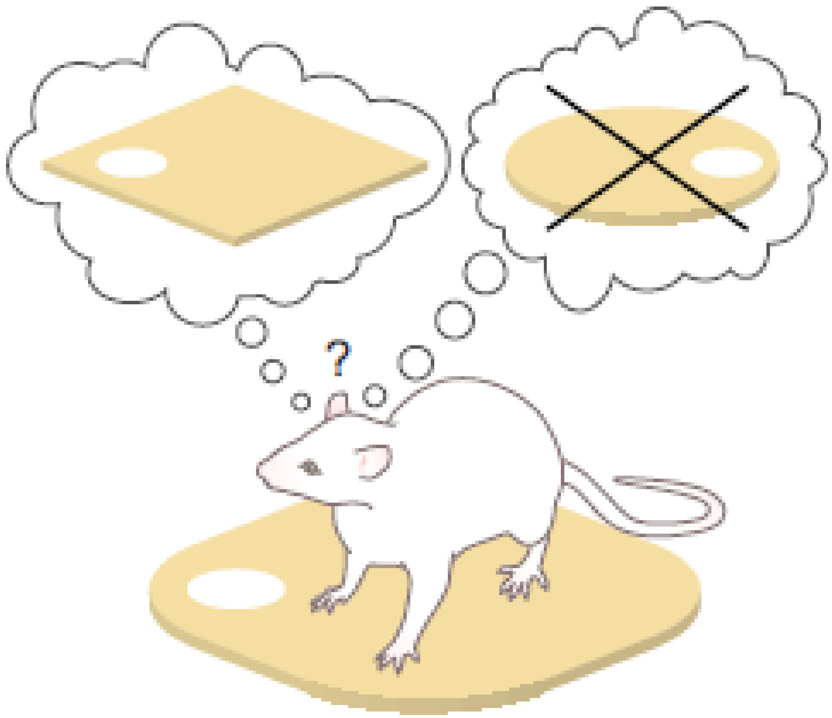
1970 – 1990 : The hippocampus and spatial memory

1. Discovery of place cells (O'Keefe & Dostrovsky, 1971) : The hippocampus supports a spatial map of the animal's local environment
2. Discovery of head direction cells by Ranck (1985), and much later of entorhinal grid cells (Hafting et al, 2005), strongly supports the spatial nature of this memory

1990 – today : Spatial memory, neural coding, and semantic/episodic memories

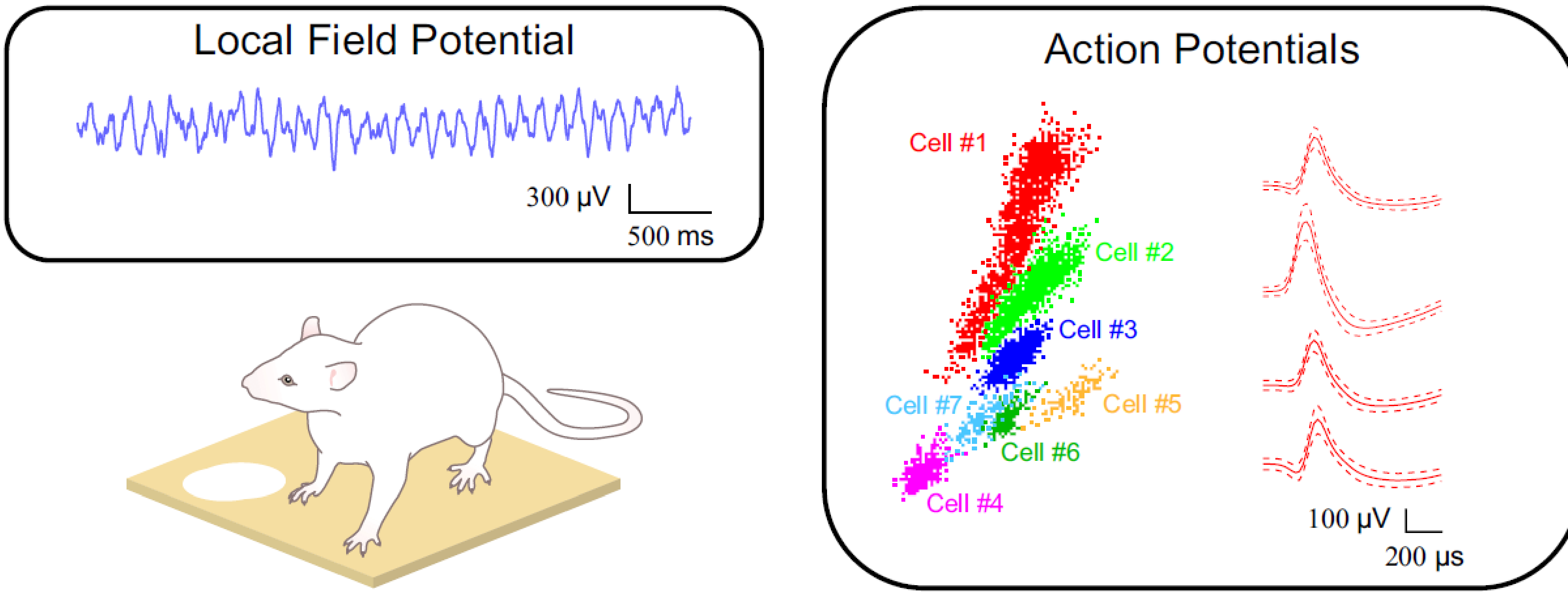
1. Place cells reflect the operation of a long-term memory system allowing recognition of slightly altered environments (pattern completion) and disambiguation of local environments (pattern separation).
2. Place cells have functions beyond spatial mapping. Their firing reflects both the place and the experience associated with that place – past or present. They may be an essential ingredient of « episodic » memories.

Neural Bases of Spatial Cognition

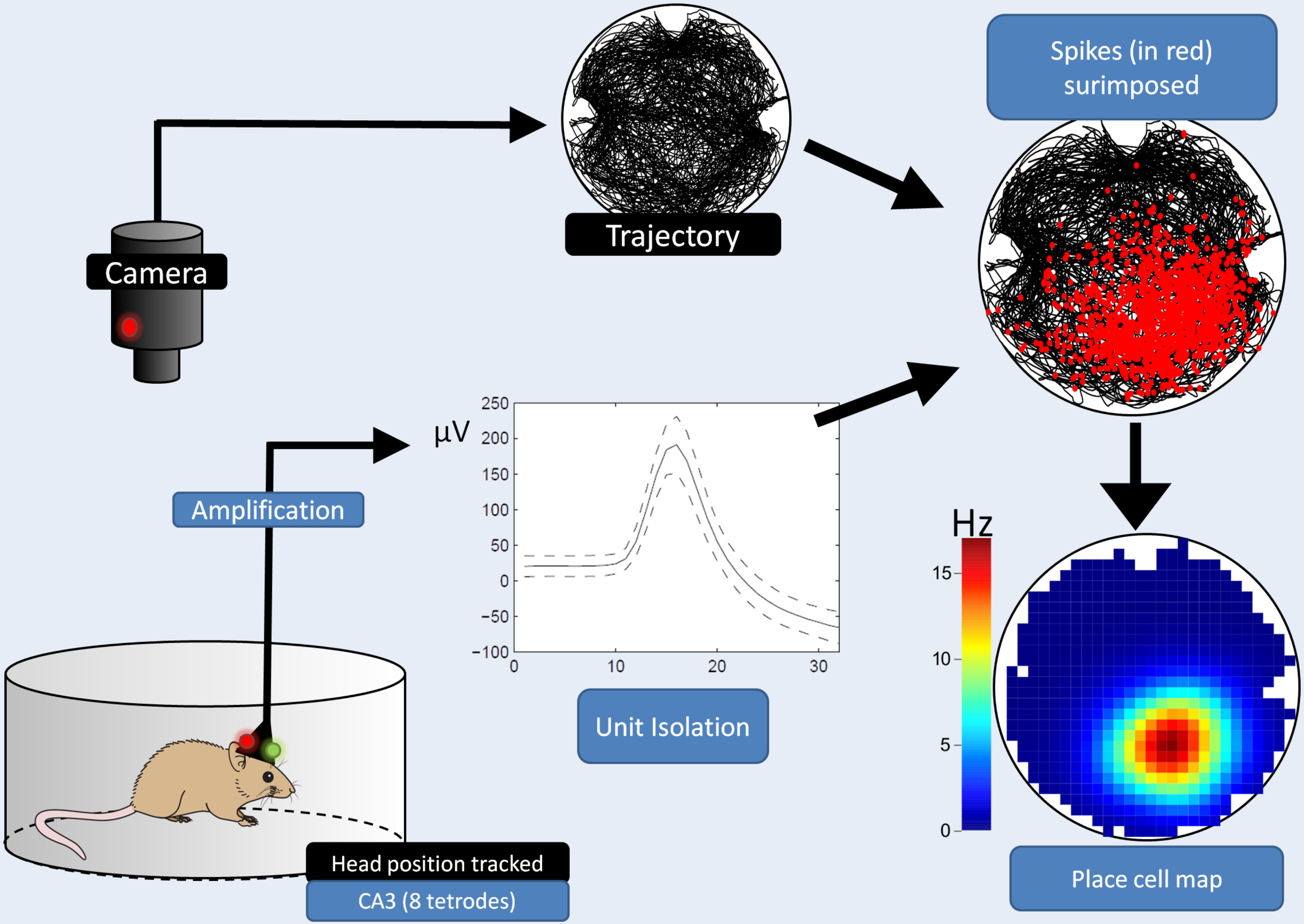


1. Identifying the neural circuits involved in spatial behavior.
2. Understanding how the activity of hippocampal place cells contribute to create new memories.

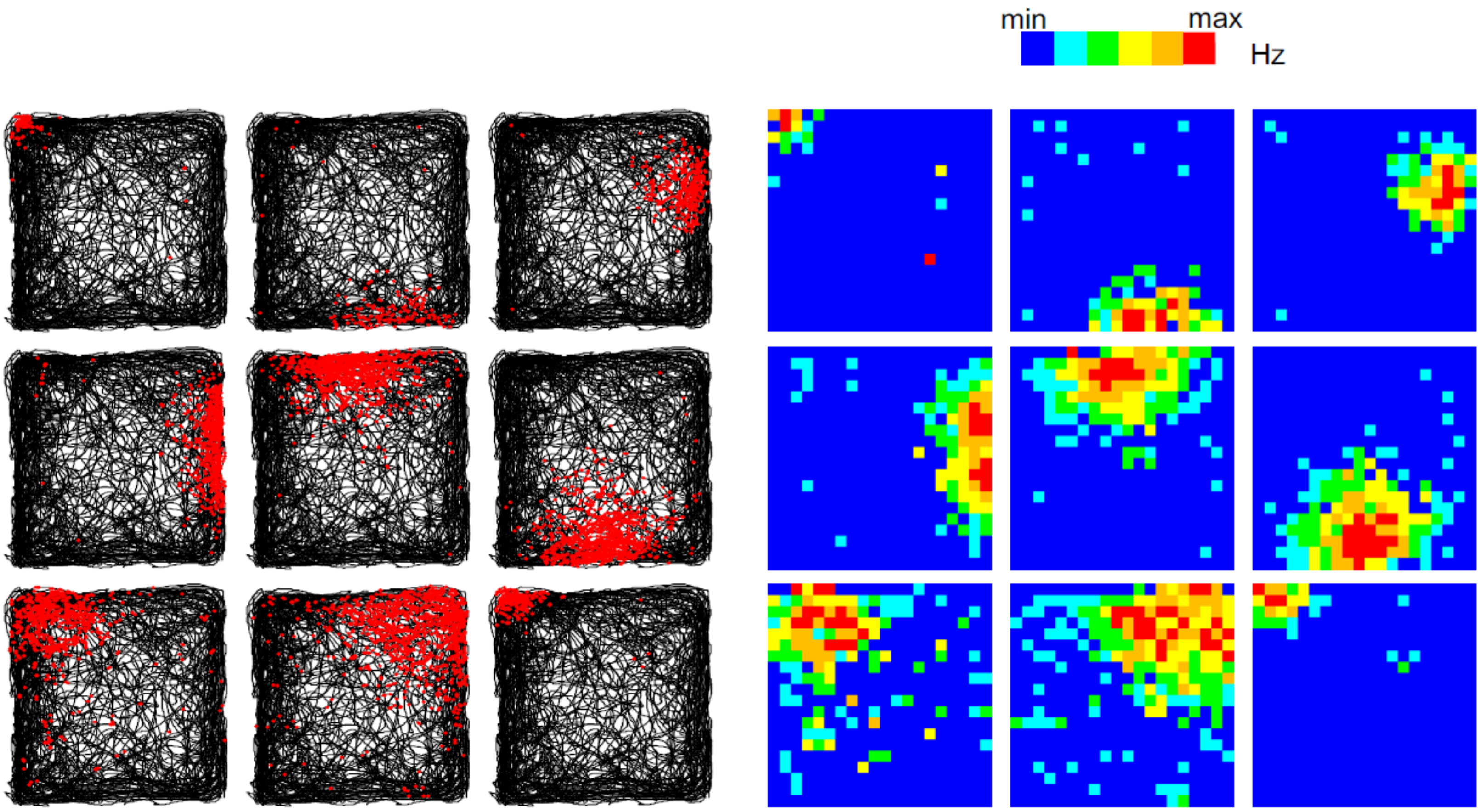
Extracellular electrophysiological recordings.



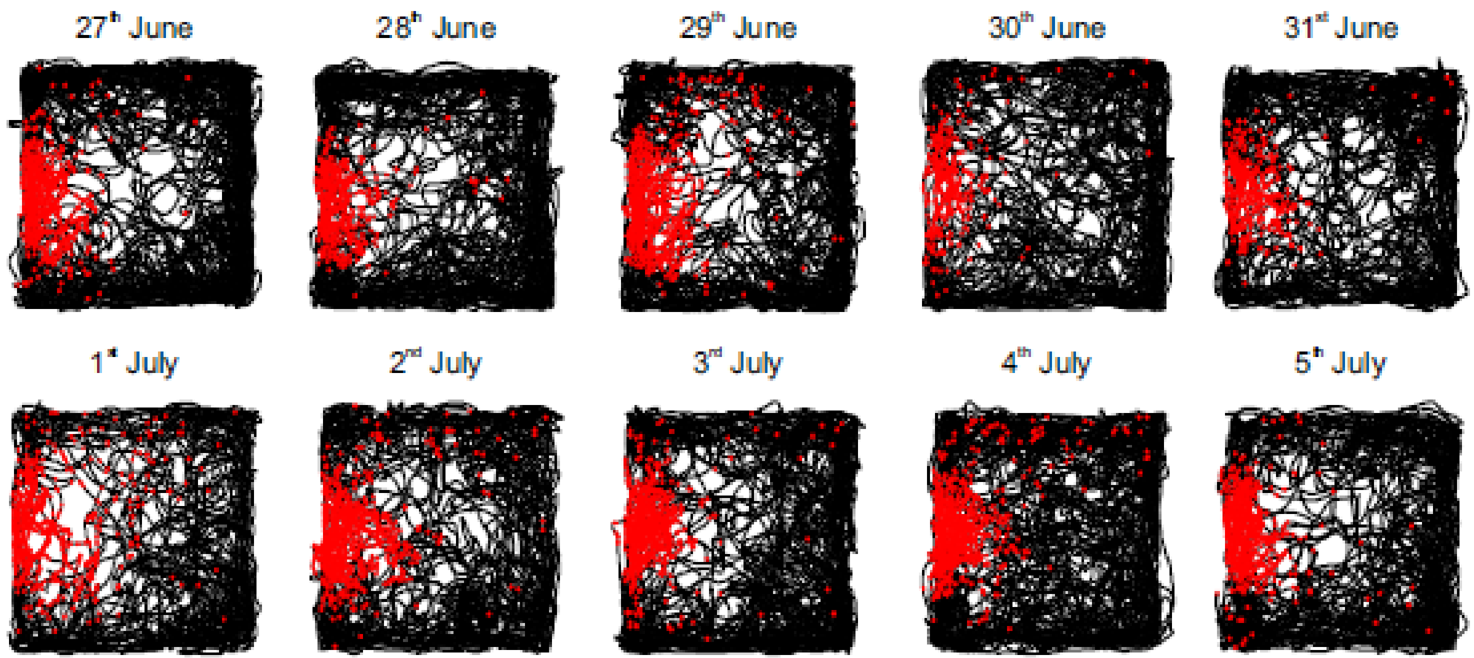
Place cells recording: principles



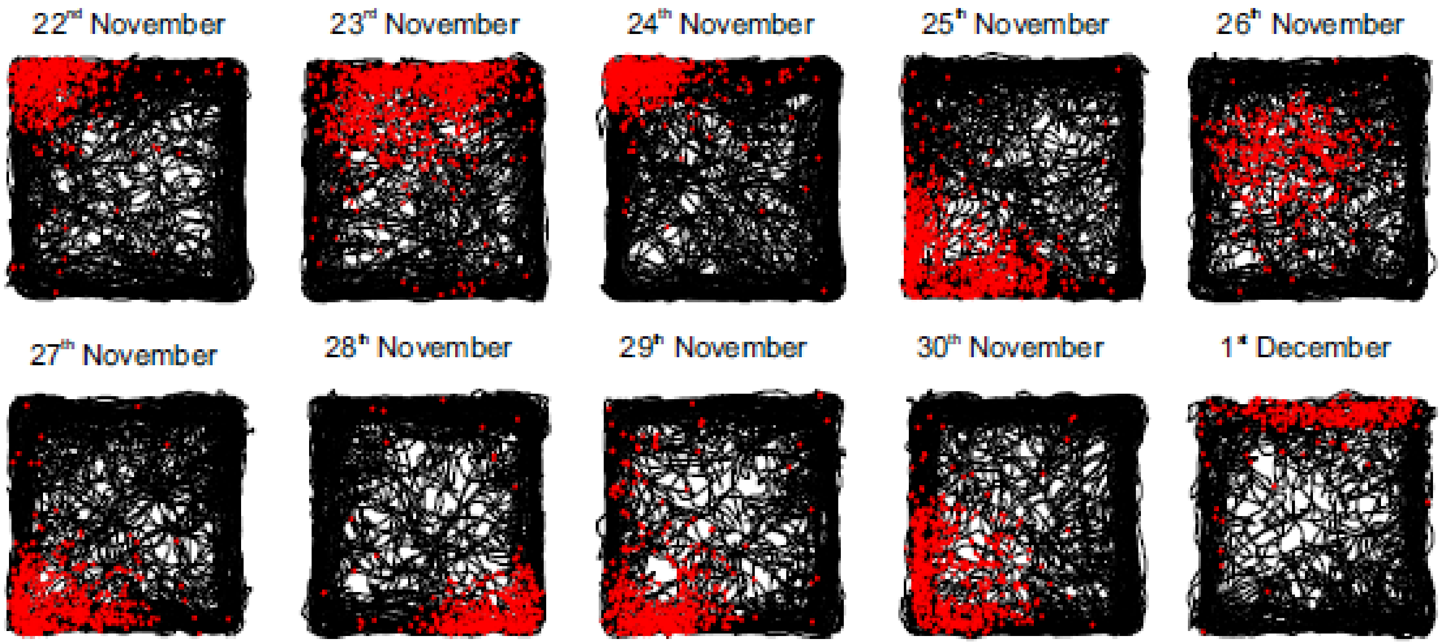
Simultaneous recordings.



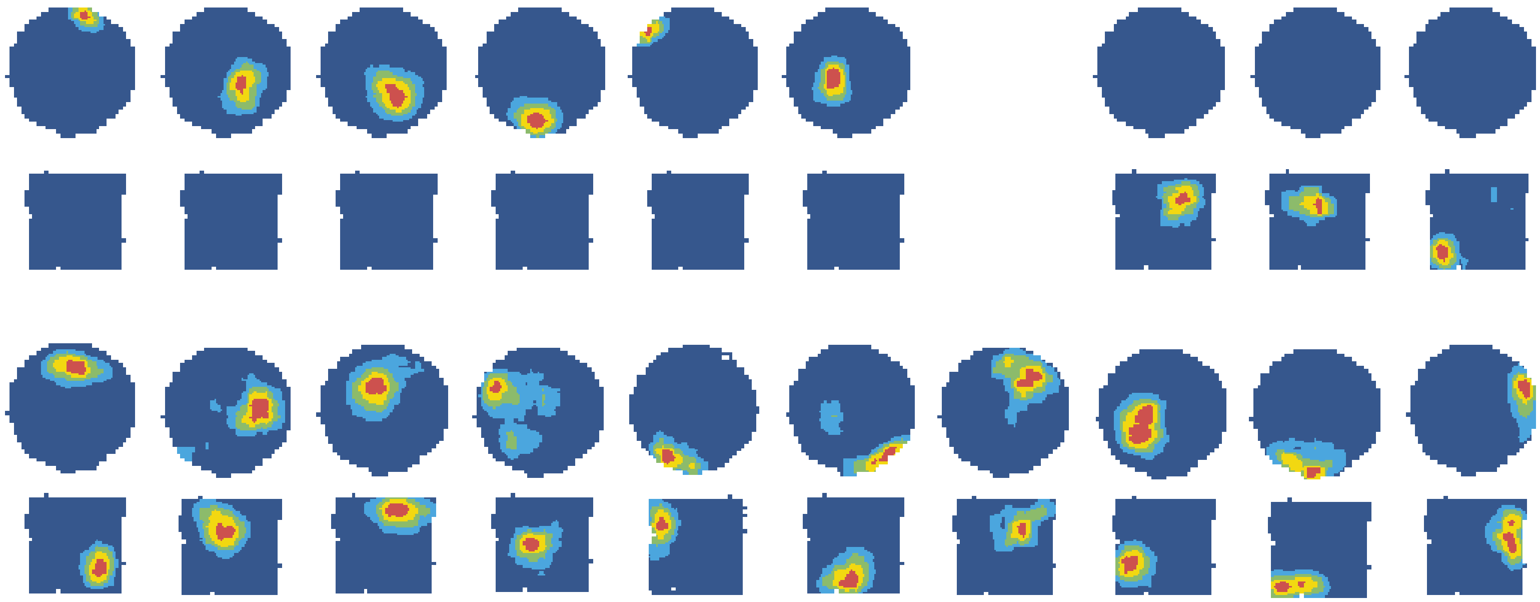
Place fields are spatially stable through time (days, weeks even months) in normal conditions.

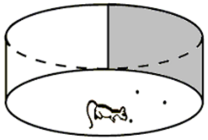


Place fields in aged rats (and cognitively impaired) are spatially unstable.



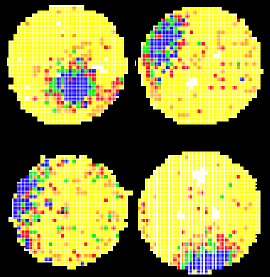
Global remapping: three possibilities.





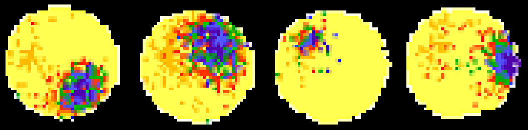
Memory properties of place cells

- Collective representation of space by place fields



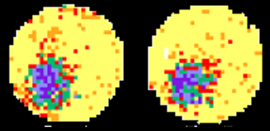
Different place fields

- No spatiotopic organization

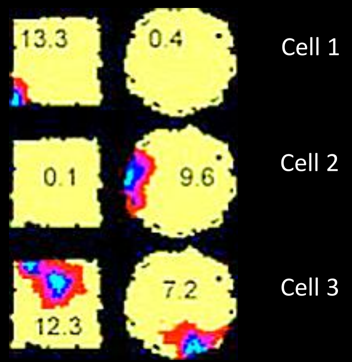


4 cells recorded from the same tetrode

- Long-term stability of place fields



- Place fields are specific to each environment (orthogonal representations)



Pattern separation and pattern completion

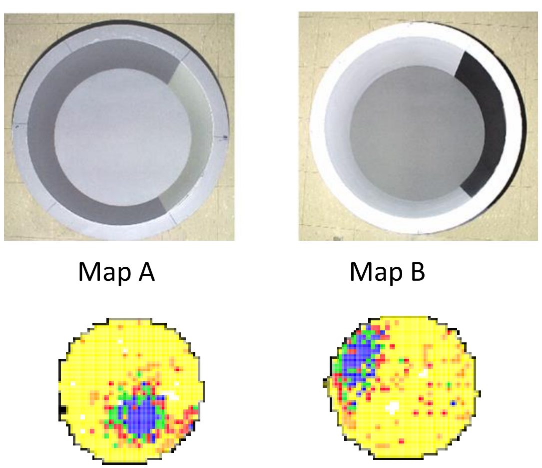
- An efficient memory system requires two mechanisms :

  1) A *pattern separation* process which allows to generate <u>distinct</u> representations of specific events, situations, etc.;

  2) A *pattern completion* process, which allows to generate <u>stable</u> representations of the environment in spite of its changes.

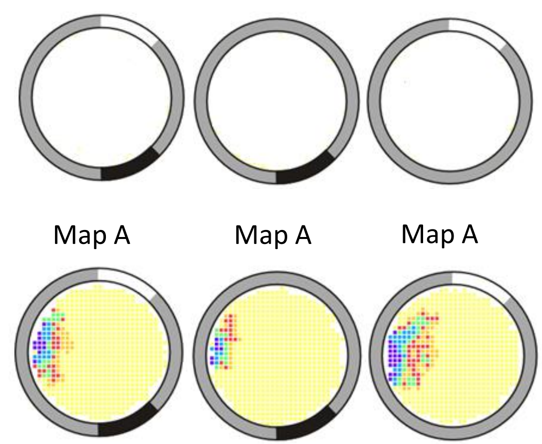
- These two complementary mechanisms are implemented in hippocampal place cells.

Pattern separation



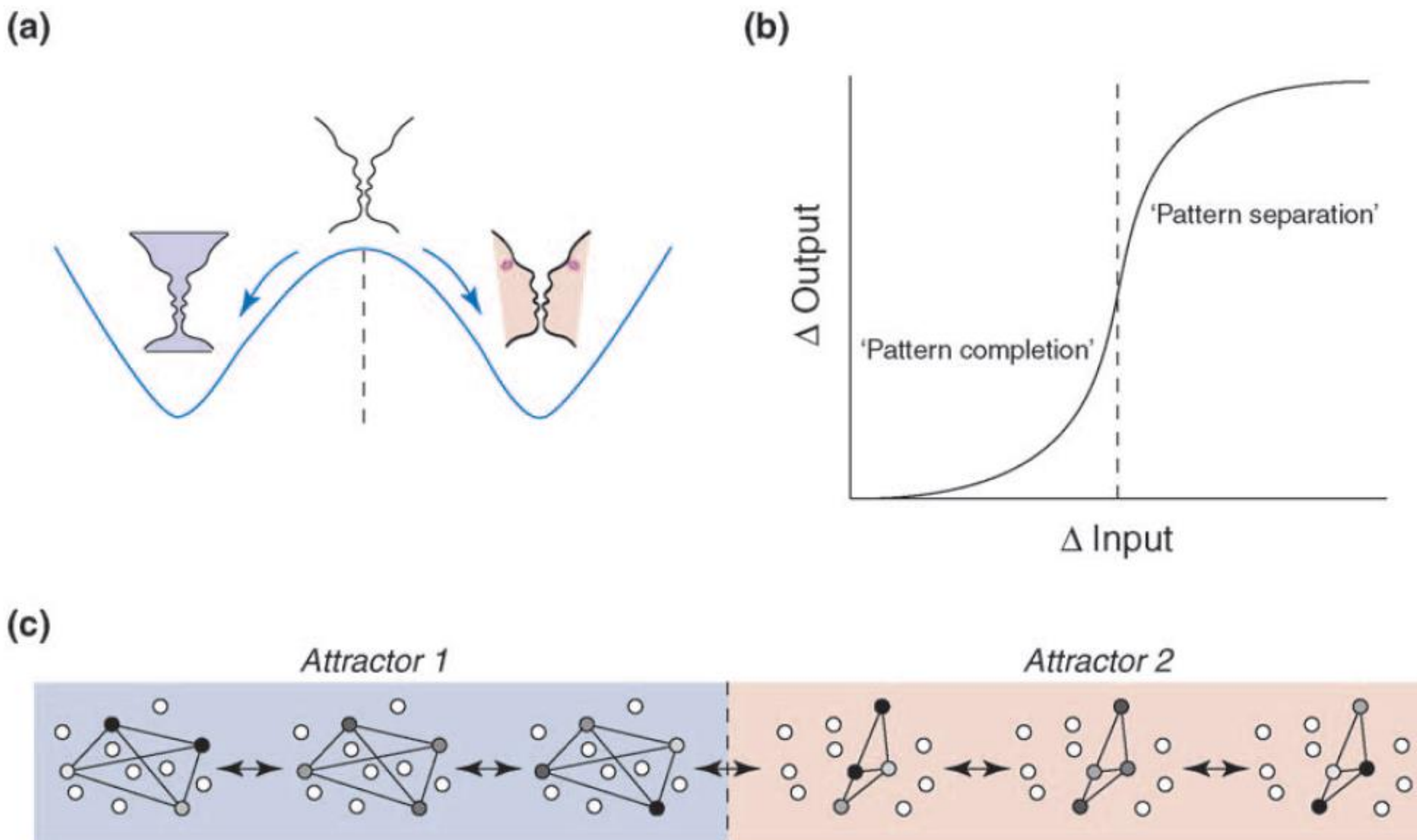
From Hok et al. (unpublished)

Pattern completion



From Fenton et al. (2000)

Place cells, spatial maps and the population code for memory
Stefan Leutgeb, Jill K Leutgeb, May-Britt Moser and Edvard I Moser



Place cells, spatial maps and the population code for memory

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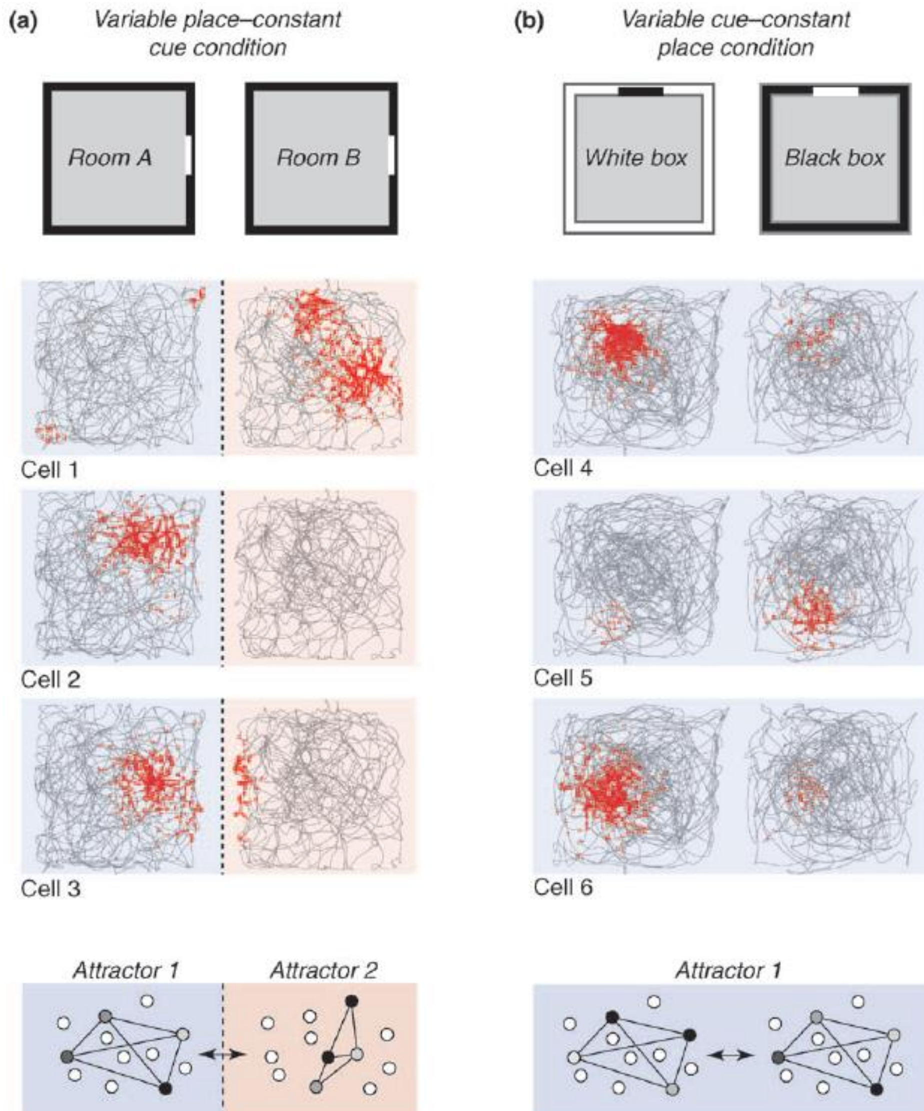
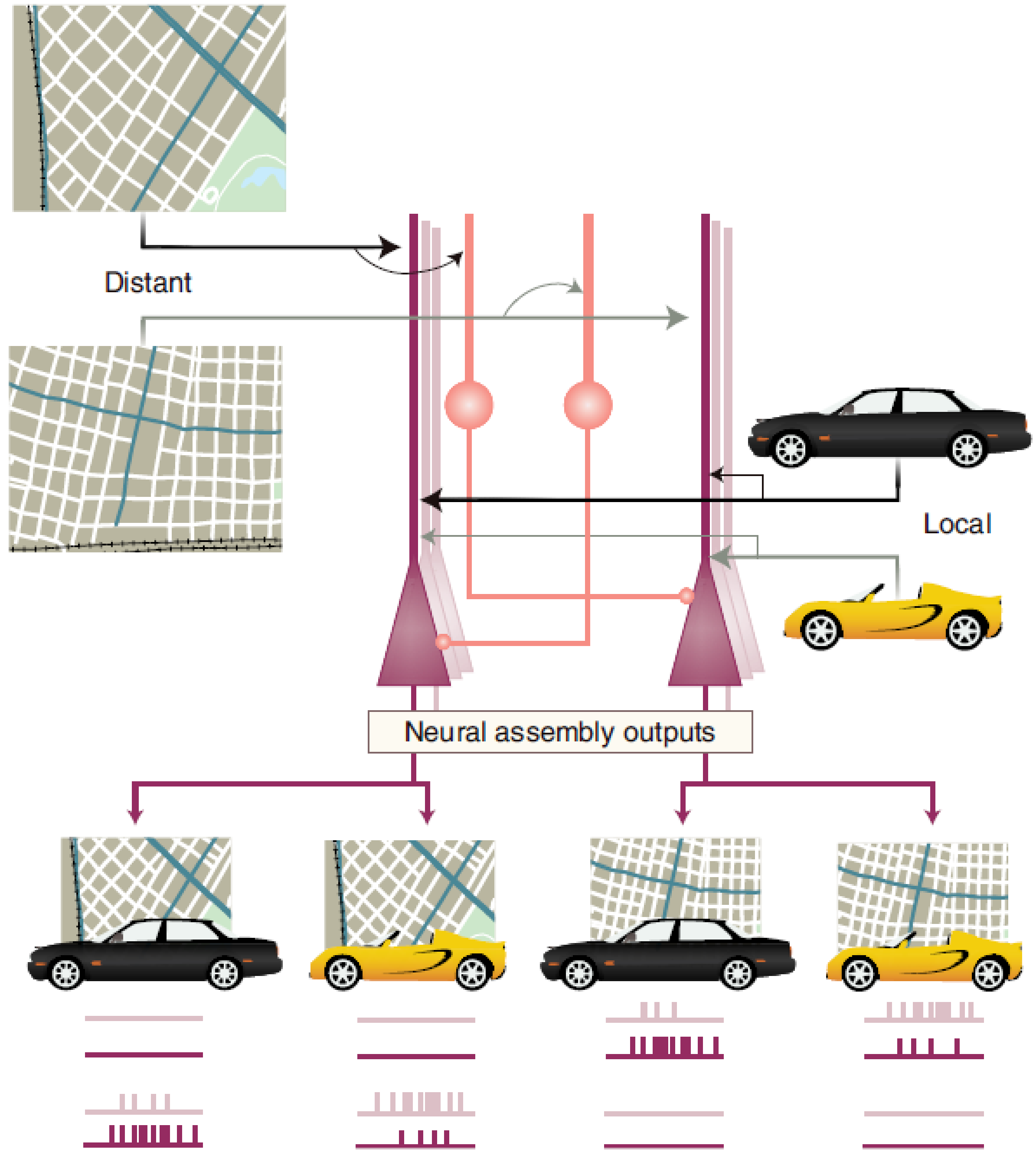
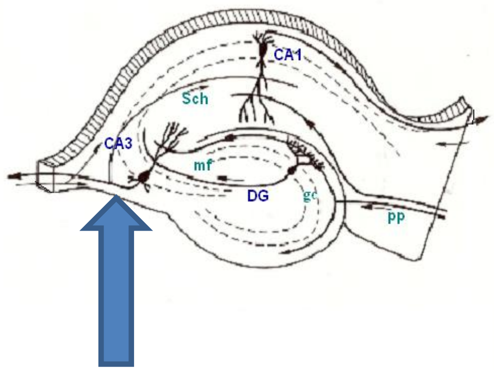


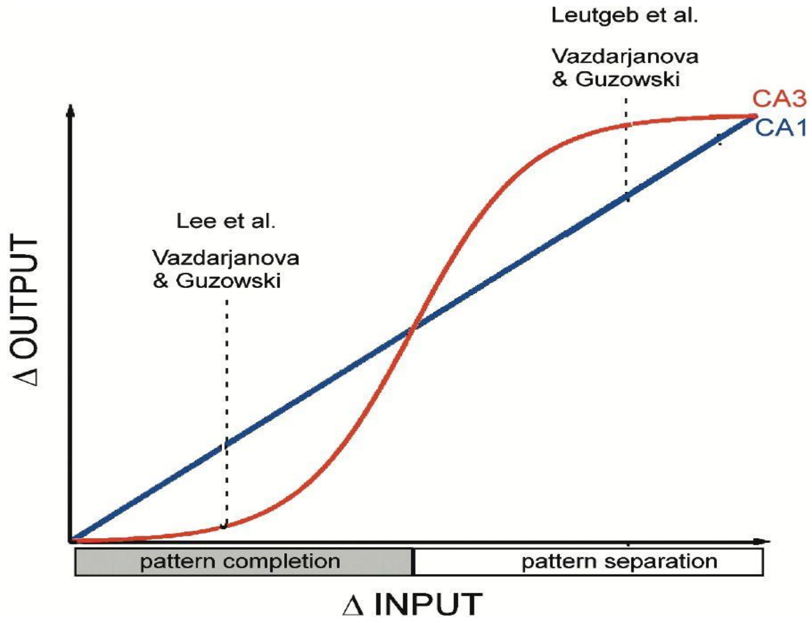
Similar is different in hippocampal networks.



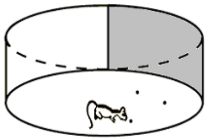
Buzsáki, G. (2005). NEUROSCIENCE: Similar Is Different in Hippocampal Networks. Science *309*, 568–569.

Neural bases of pattern separation and pattern completion



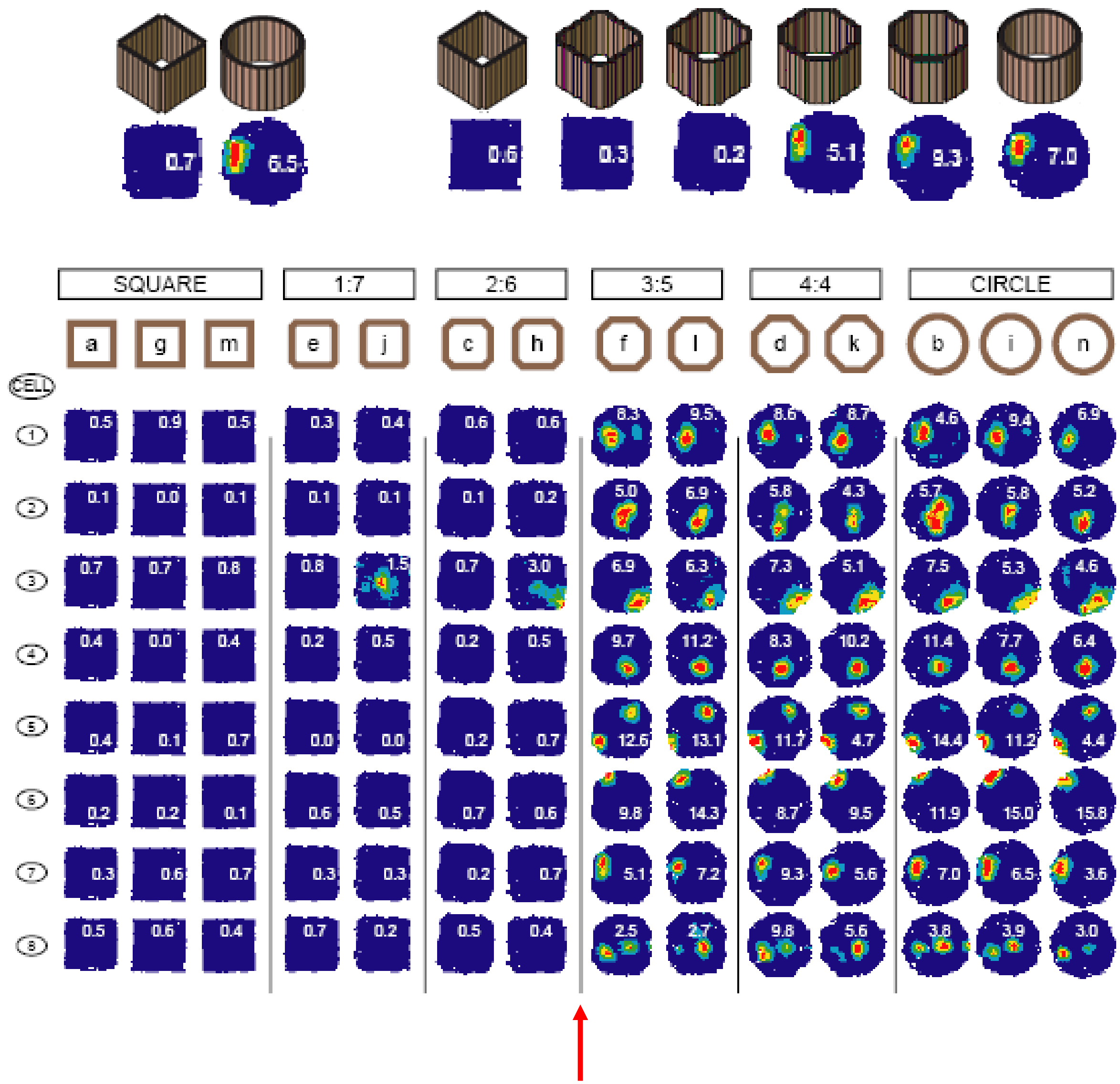


Complementarity and competition between pattern separation and pattern completion in CA3



Simple foraging (exploration)

Memory properties of place cells
Pattern separation



From Wills et al. (2005)

Plan général du cours

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What about the human hippocampus ?

Memory properties

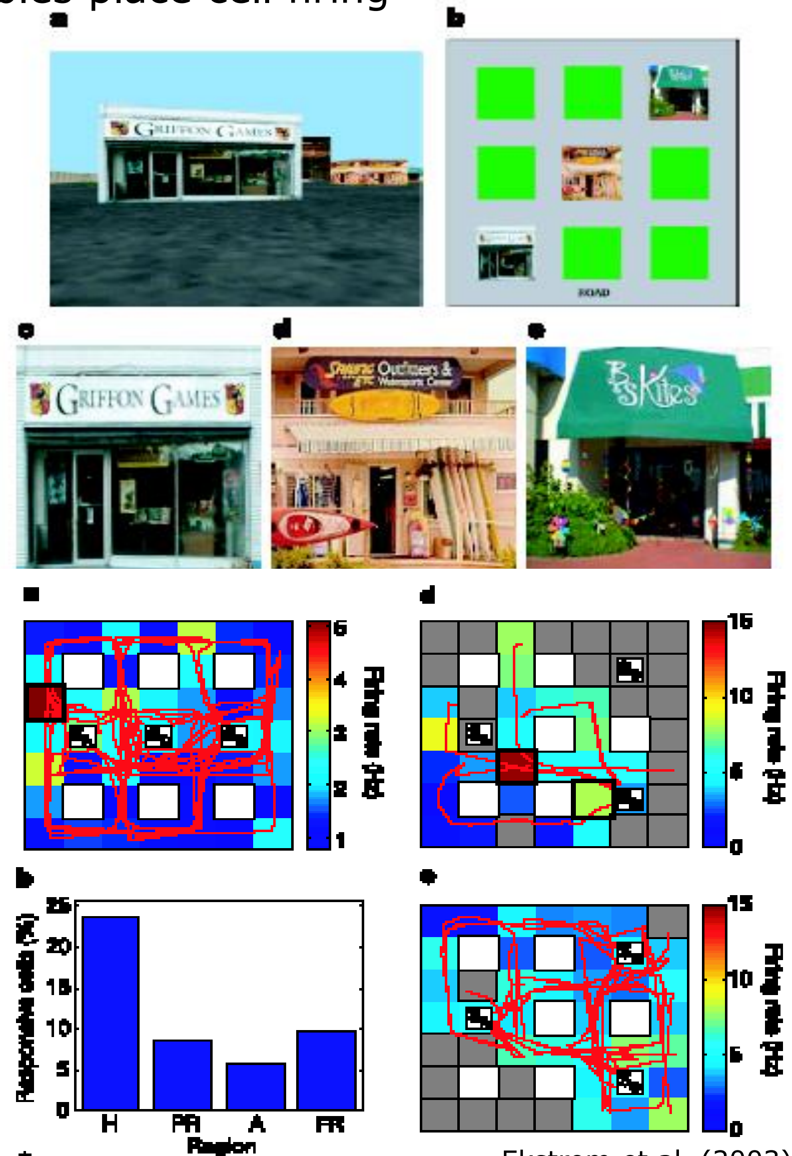
Hippocampal unit activity during a spatial memory task in a virtual environment resembles place cell firing

Cellular networks underlying human spatial navigation

Arne D. Ekstrom[1], Michael J. Kahana[1], Jeremy B. Caplan[1], Tony A. Fields[2], Eve A. Isham[2], Ehren L. Newman[1] & Itzhak Fried[2,3]

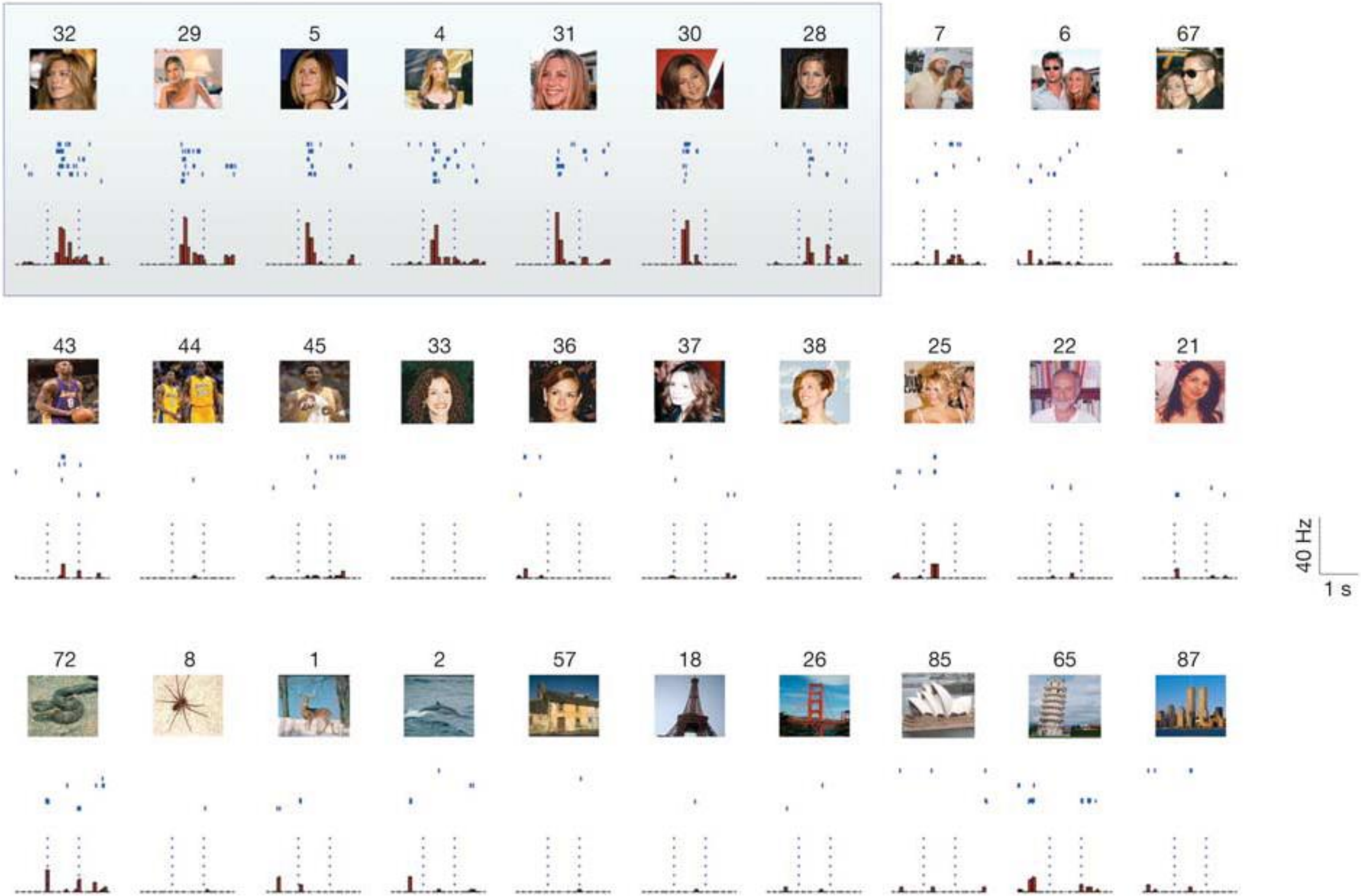
[1] *Volen Center for Complex Systems, Brandeis University, Waltham, Massachusetts 02454, USA*
[2] *Division of Neurosurgery and Department of Psychiatry and Biobehavioral Science, University of California, Los Angeles (UCLA), California 90095, USA*
[3] *Functional Neurosurgery Unit, Tel-Aviv Medical Center and Sackler School of Medicine, Tel-Aviv University, Tel-Aviv 69978, Israel*

Place cells of the rodent hippocampus constitute one of the most striking examples of a correlation between neuronal activity and complex behaviour in mammals[1,2]. These cells increase their firing rates when the animal traverses specific regions of its surroundings, providing a context-dependent map of the environment[3–5]. Neuroimaging studies implicate the hippocampus and the parahippocampal region in human navigation[6–8]. However, these regions also respond selectively to visual stimuli[9–13]. It thus remains unclear whether rodent place coding has a homologue in humans or whether human navigation is driven by a different, visually based neural mechanism. We directly recorded from 317 neurons in the human medial temporal and frontal lobes while subjects explored and navigated a virtual town. Here we present evidence for a neural code of human spatial navigation based on cells that respond at specific spatial locations and cells that respond to views of landmarks. The former are present primarily in the hippocampus, and the latter in the parahippocampal region. Cells throughout the frontal and temporal lobes responded to the subjects' navigational goals and to conjunctions of place, goal and view.



Ekstrom et al. (2003)

Invariant visual representation by single neurons in the human brain R. Quian Quiroga[1,2,5], L. Reddy[1], G. Kreiman[3], C. Koch[1] & I. Fried[2,4]
Nature **435**, 1102-1107 (23 June 2005)



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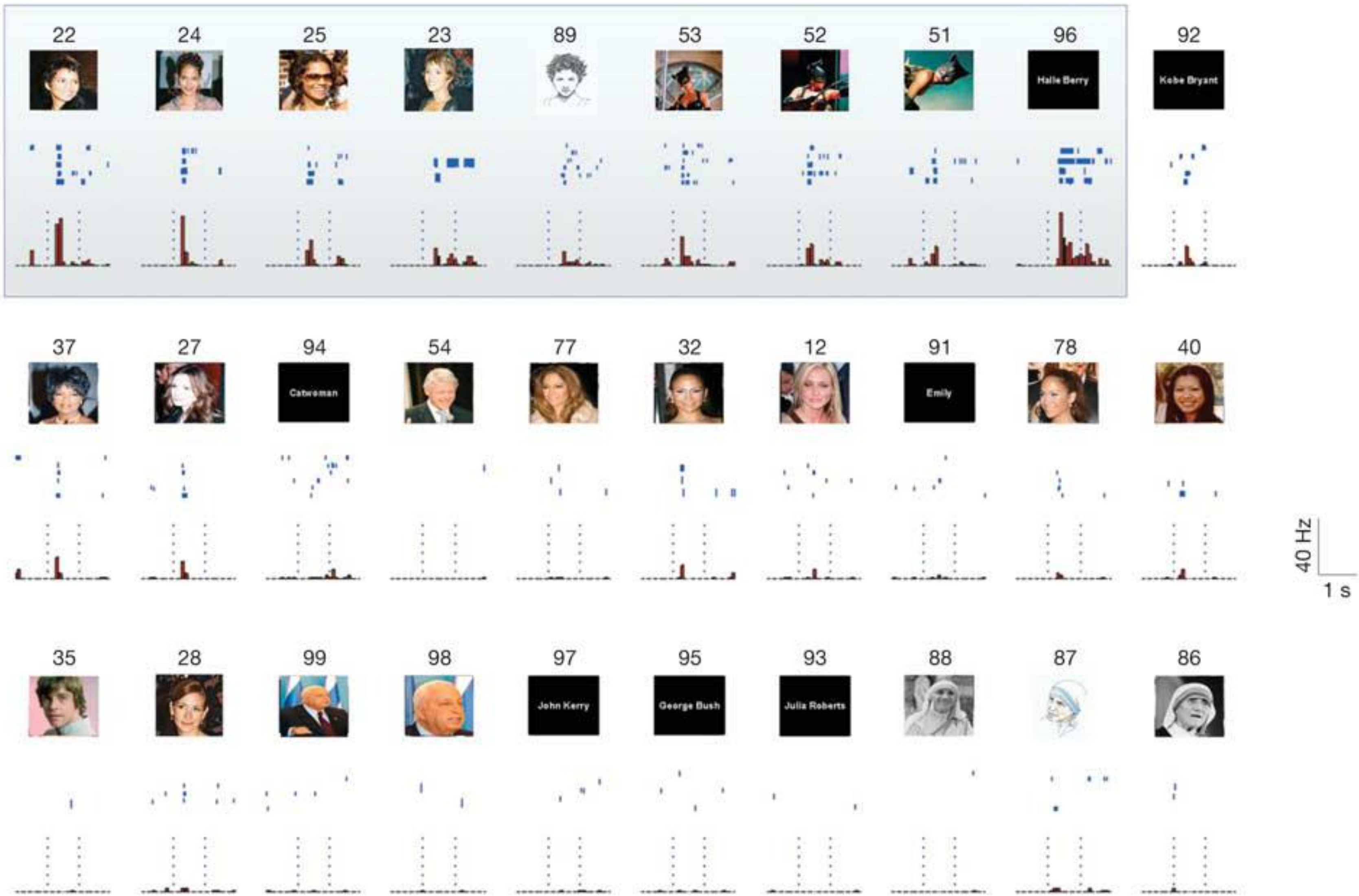

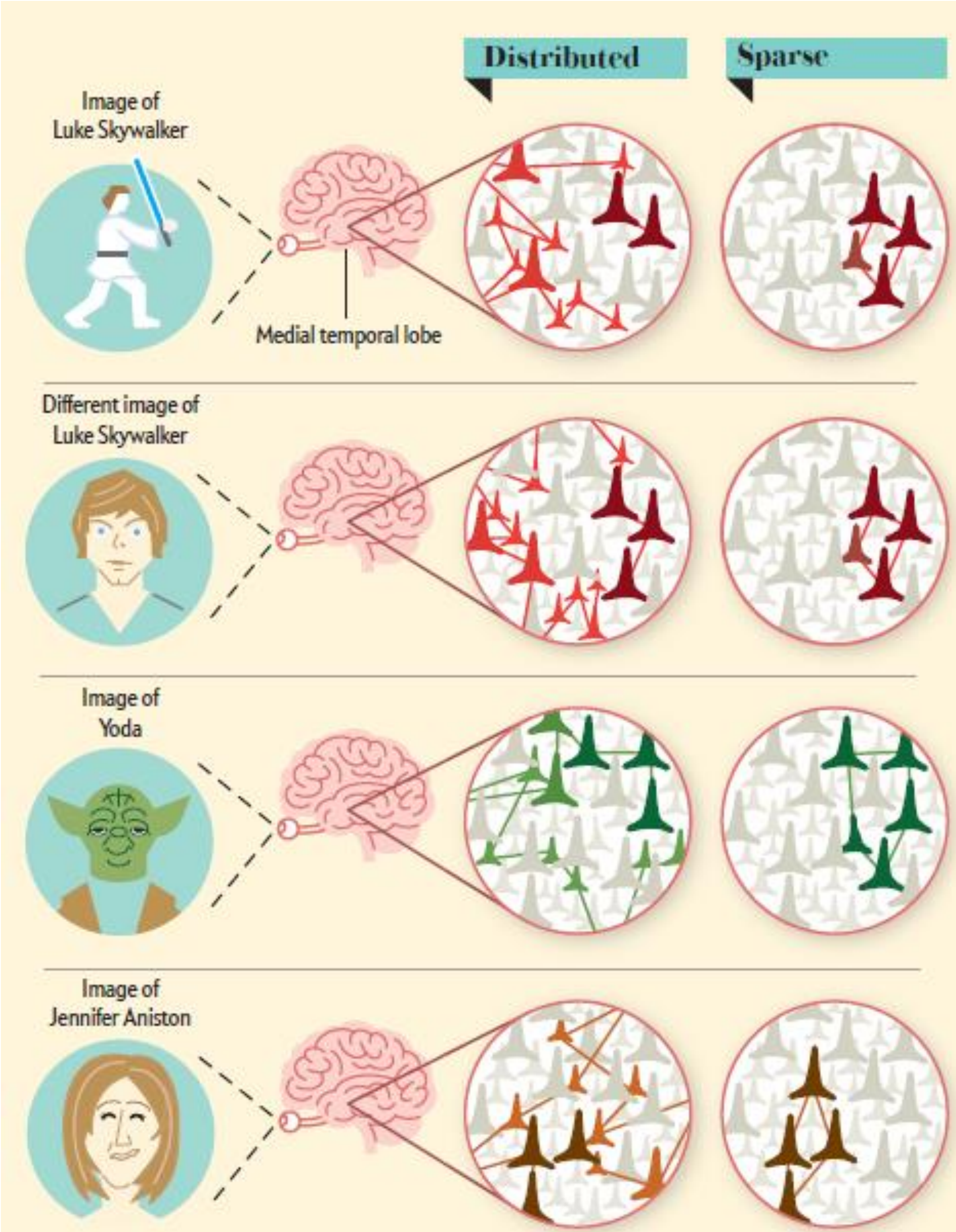

CONCEPT CELLS

Rodrigo Quian Quiroga, a native of Argentina, is professor and head of the Bioengineering Research Group at the University of Leicester in England. He is author of the recently published *Borges and Memory: Encounters with the Human Brain* (MIT Press, 2012).

Itzhak Fried is a professor of neurosurgery and director of the Epilepsy Surgery Program at the U.C.L.A. David Geffen School of Medicine. He is also a professor at the Tel Aviv Sourasky Medical Center and Tel Aviv University.

Christof Koch is professor of cognitive and behavioral biology at the California Institute of Technology and chief scientific officer at the Allen Institute for Brain Science in Seattle.