COMS30127/COMSM2127 Computational Neuroscience

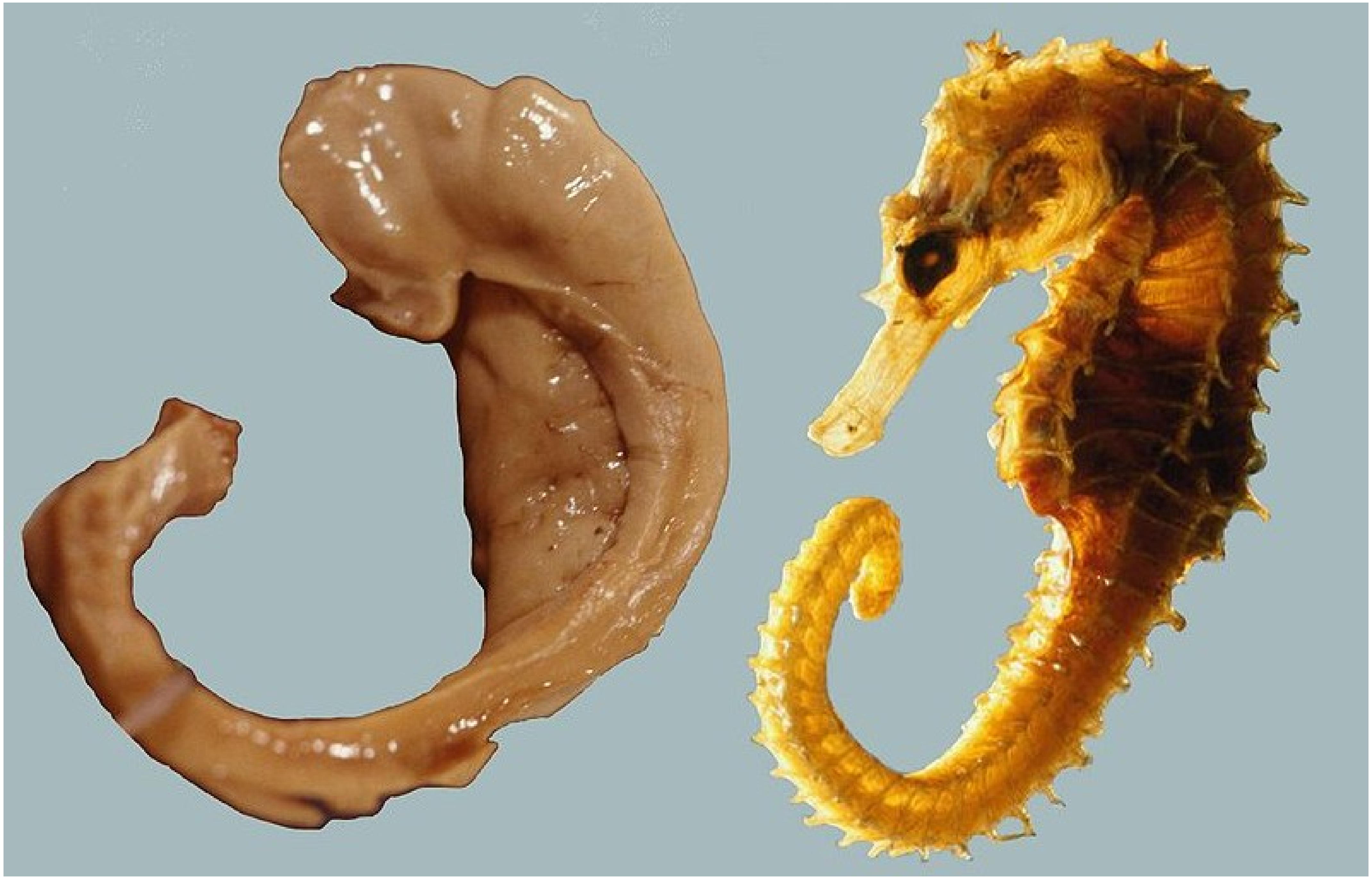
Lecture 8: The Hippocampus

Thanks go to Dr. Cian O’Donnell who let me edit some of his slides

What we will cover today and Tuesday

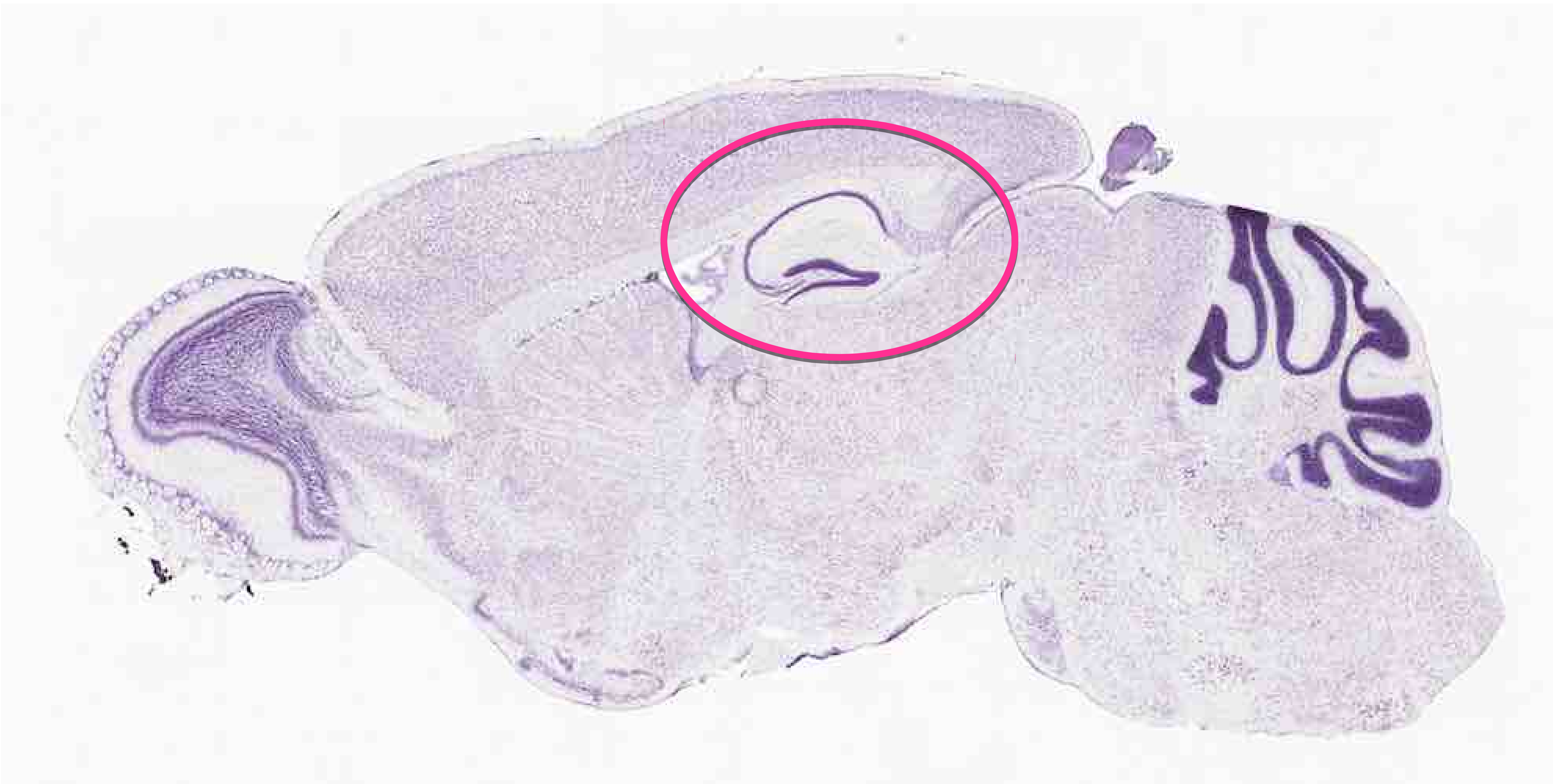
- Anatomy of the hippocampus.
- What does the hippocampus do?
  - Long-term memory
  - Spatial navigation
- What computations does the hippocampus do?
  - Pattern separation vs pattern completion
  - Path integration.
- Computational models of memory encoding and recall in the hippocampal circuit.
- Computational models of spatial navigation in the hippocampal circuit.

Hippocampus, from the greek words for “horse" and “sea-monster”



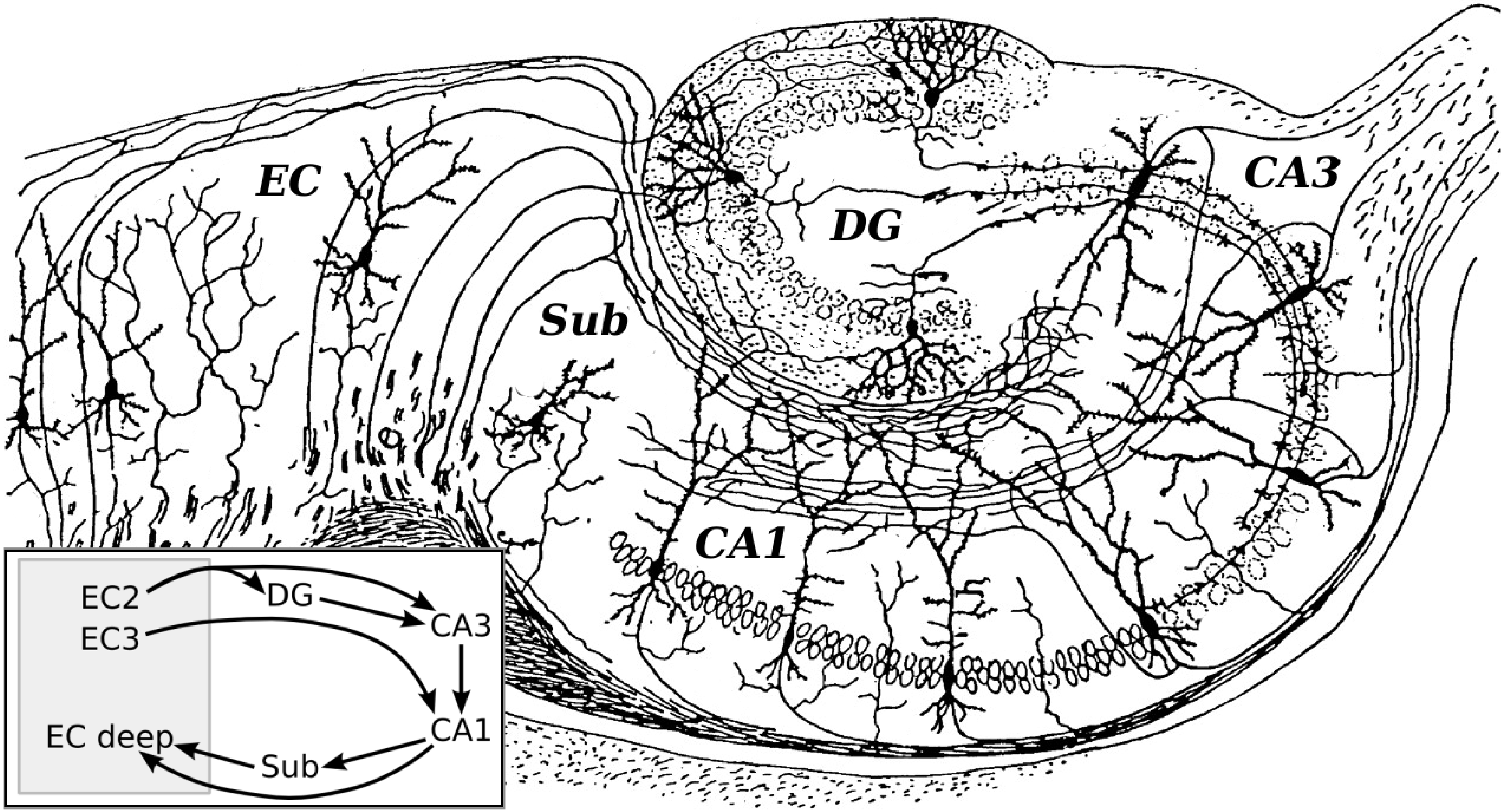
https://en.wikipedia.org/wiki/Hippocampus#/media/File:Hippocampus_and_seahorse_cropped.JPG

Anatomy of the hippocampus



https://mouse.brain-map.org

Anatomy of the hippocampus



Original drawing by Ramon y Cajal (circa 1900). The inset show approximate connectivity
https://en.wikipedia.org/wiki/Hippocampus#/media/File:CajalHippocampus_(modified).png

Hippocampal anatomy

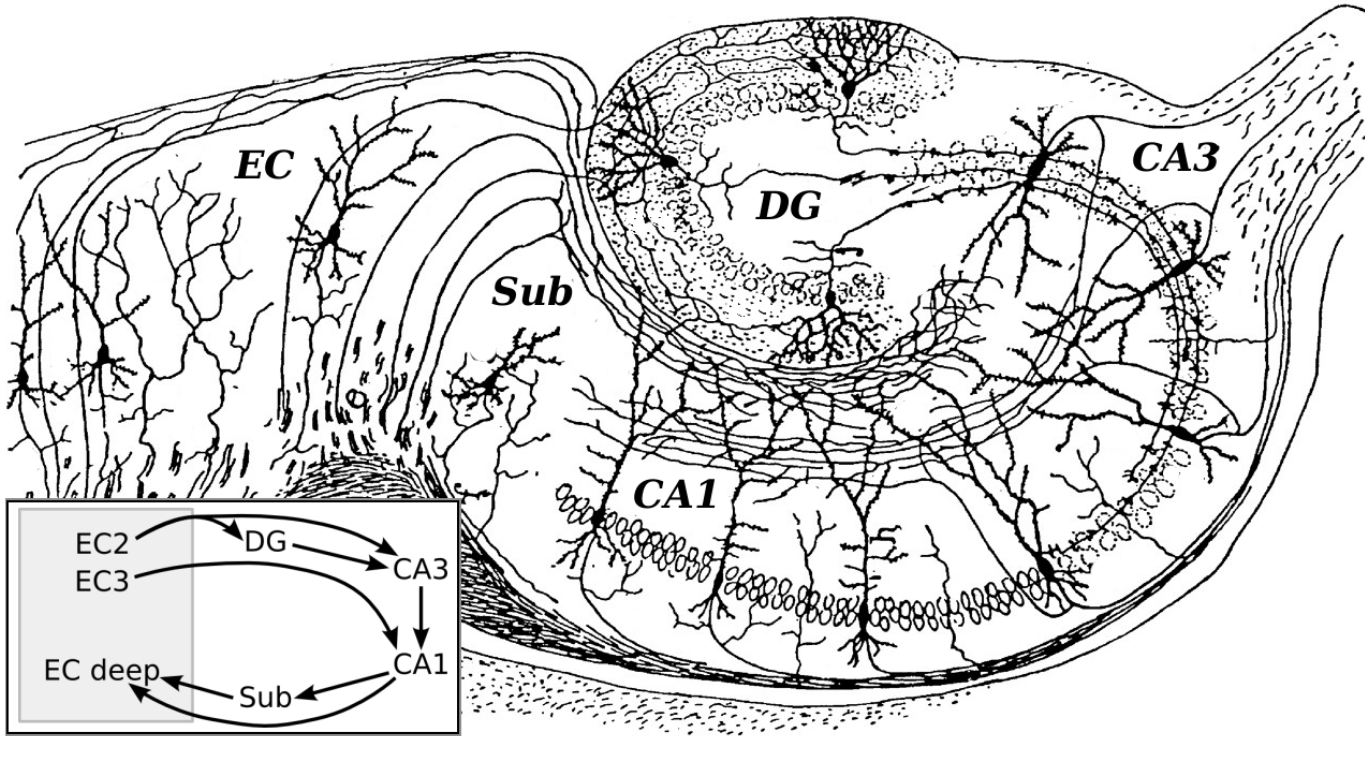
The hippocampus complex has a distinctive in shape and regions within the hippocampus are named based upon shape

- Cornu Ammonis (CA) - meaning the horn of Ammon, an Egypian god of ferility with curved horns. The CA is usually divided into four regions, labelled CA1 through to CA4.

- Dentate Gyrus (DG)- gyrus is the name given to the ridges in the cortex, dentate meanswith teeth. The dentate gyrus is one of the few areas of the adult brain that exhibits neurogenesis.

The main input to hippocampus comes from the Entorhinal Cortex (EC) - entorhinal means near the smell processing area.

In this discussion we include EC with the hippocampus since it participates in HPC processing

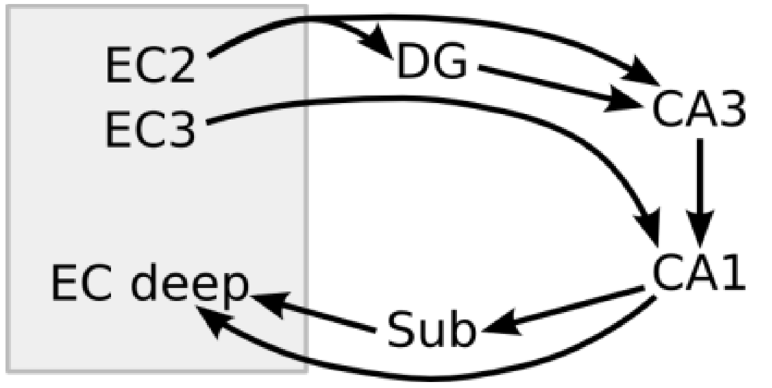


The tri-synaptic loop

- Information flows in a mostly feed-forward way through the hippocampus.

- Entorhinal cortex (EC) is sometimes described as “the gateway to the hippocampus” (most external signals to the hippocampus are routed via the EC).

- Inside the hippocampus, information propagates along the “trisynaptic loop”:
  - dentate gyrus (DG) → CA3
  - CA3 → CA1
  - CA1 → subiculum



- CA3 is the only subregion with substantial recurrent (feedback) excitatory connectivity (may be mediating attractor networks).

Connectivity pathways

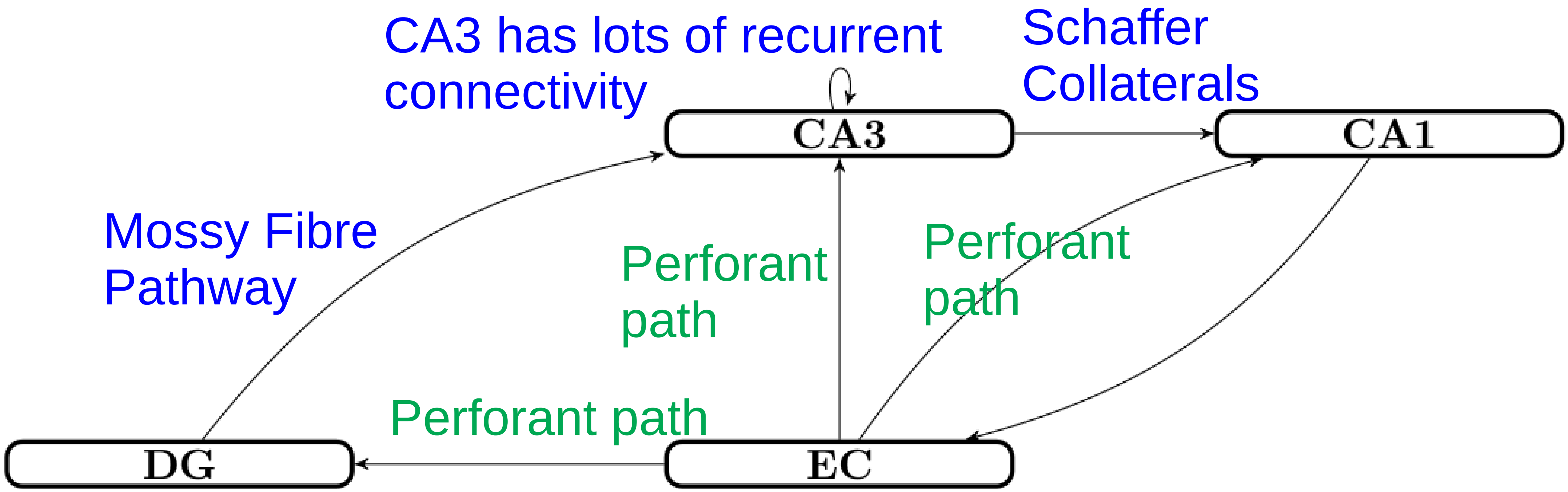


Figure 2: Connectivity of the hippocampus. A rough diagram showing the major connections between the areas of the connectivity. The set of axons running from EC to DG, CA3 and CA1 is called the perforant pathway, the mossy fibres run from DG to CA3 and the Schaffer collateral fibers go from CA3 to CA1. The loop on CA3 is supposed to represent the high level of recurrent connections in that regio.

What does the hippocampus do?

The role of any brain region is complex and the hippocampus is no exception. It may play a role in olfaction for example, however, it is widely believed that its principle role is in memory and in constructing spatial maps.

There are therefore two main theories:

1. Long-term memory

2. Spatial navigation

1. Hippocampus and memory

Hippocampus and memory

Studying patients with hippocampal damage shows that it is involved in declarative memory

- that is the sort of memory that can be described in words.

Patient HM (who had his hippocampus surgically removed) could not form new long-term memories, and also had time-limited retrograde amnesia.

The hippocampus is specifically needed for declarative/explicit memory: encoding new episodic memories (memory for events, facts)

It is not necessary for procedural memory, the memory process which allow us to learn how to do things (mostly motor skills), which usually occurs beneath conscious awareness.

Memory encoding requires synaptic plasticity in the hippocampus.

… But, it appears, again from patients with hippocampal damage, that some long term memories are stored outside the hippocampus.

Hippocampus is needed for forming episodic memories

Long-term memory types

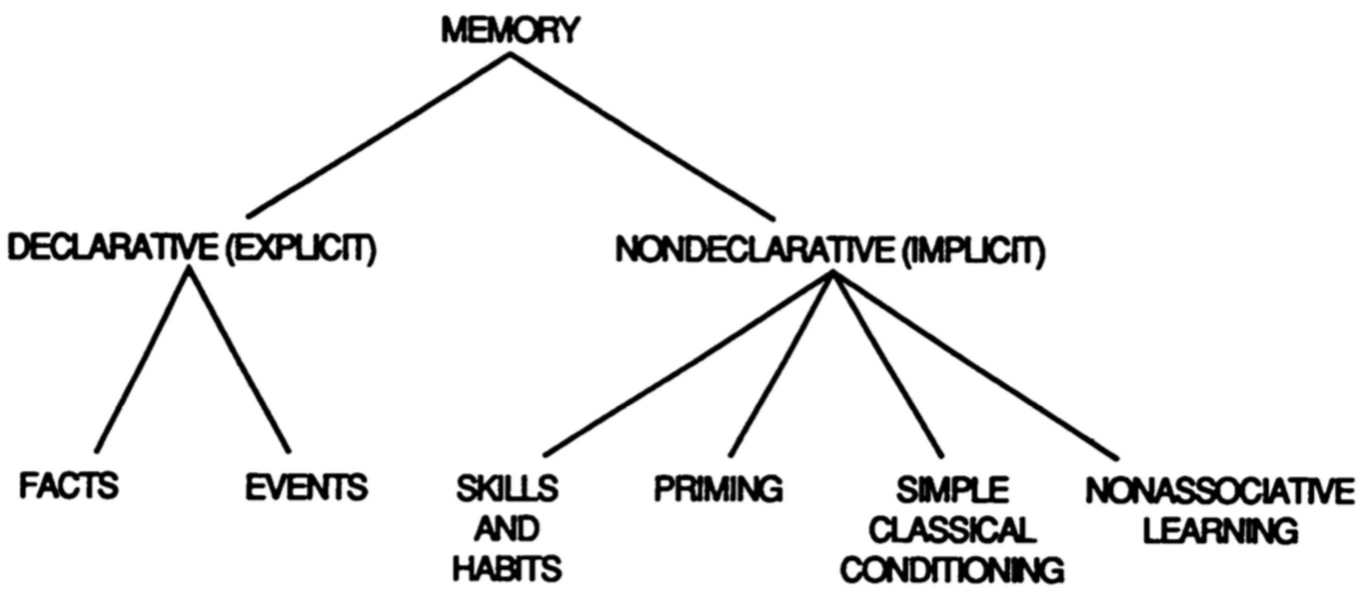
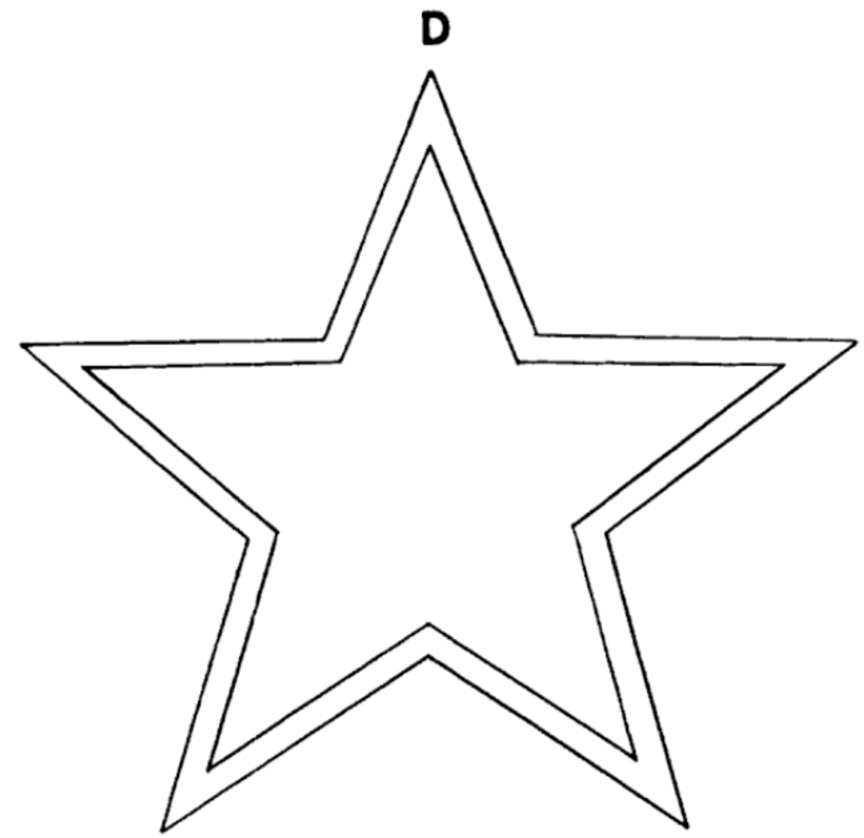


Fig. 3. Classification of memory. Declarative (explicit) memory refers to conscious recollections of facts and events and depends on the integrity of the medial temporal lobe (see text). Nondeclarative (implicit) memory refers to a collection of abilities and is independent of the medial temporal lobe (*60*). Nonassociative learning includes habituation and sensitization. In the case of nondeclarative memory, experience alters behavior nonconsciously without providing access to any memory content (*19, 20*).

Squire & Zola-Morgan, Science 1991

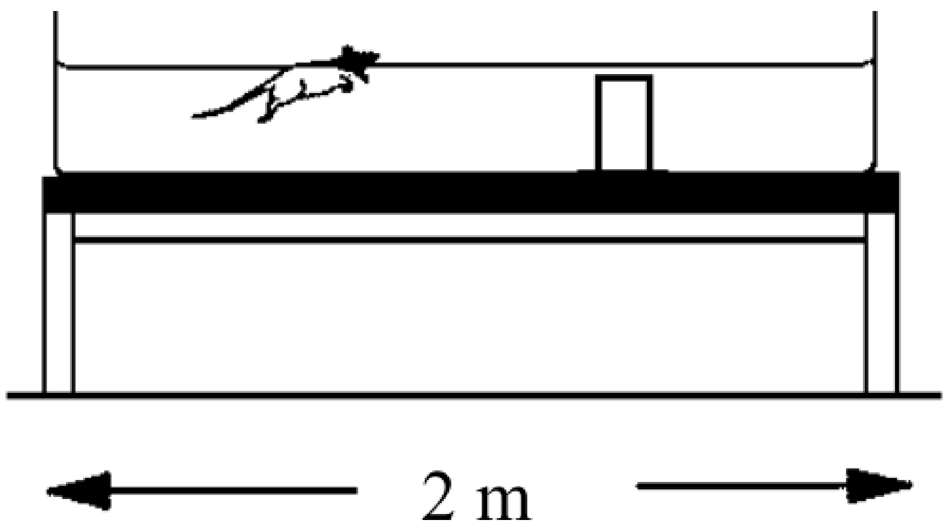
H.M. could form new motor memories

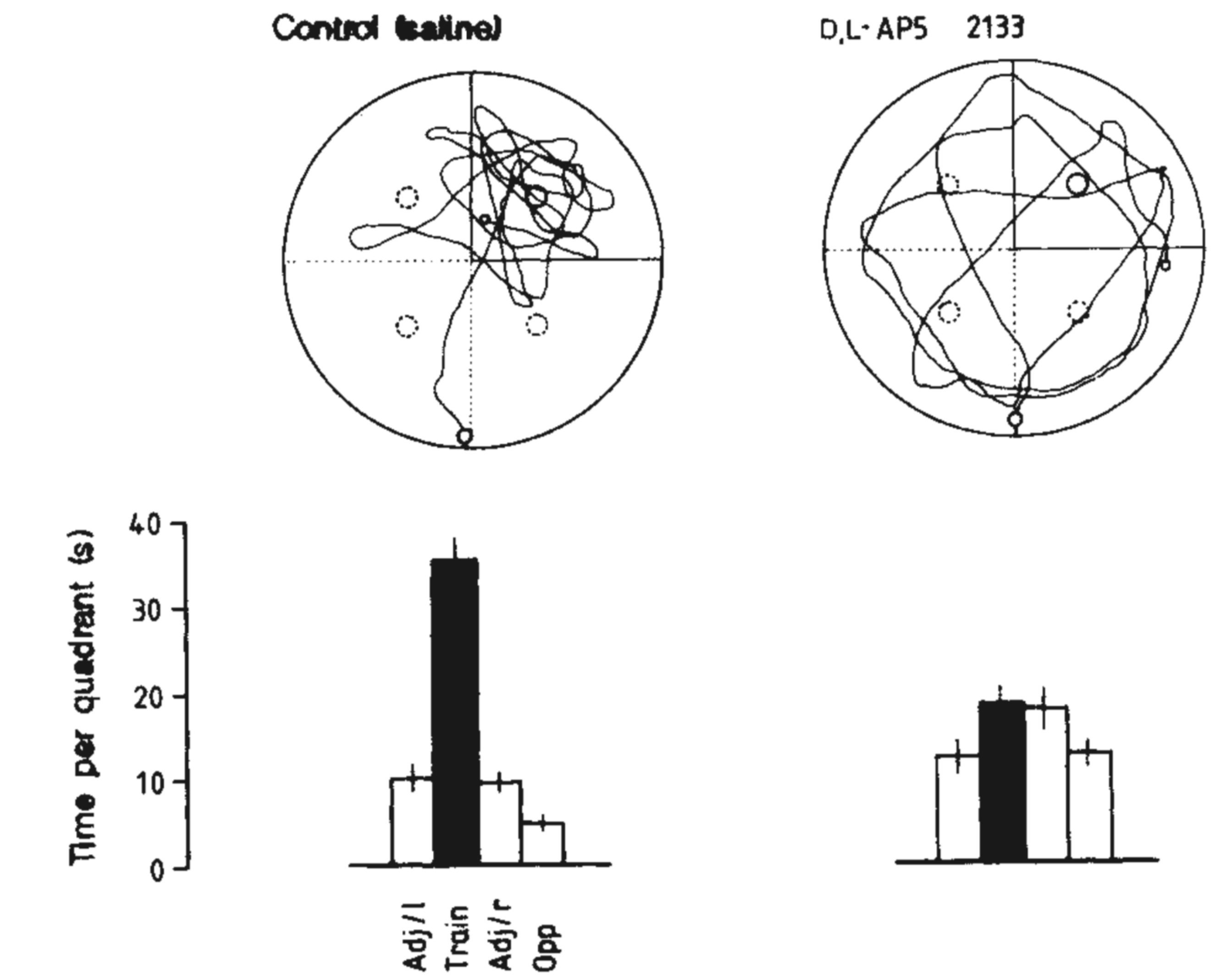


Milner (1962)

Synaptic plasticity in the hippocampus is needed for learning

The Morris water maze

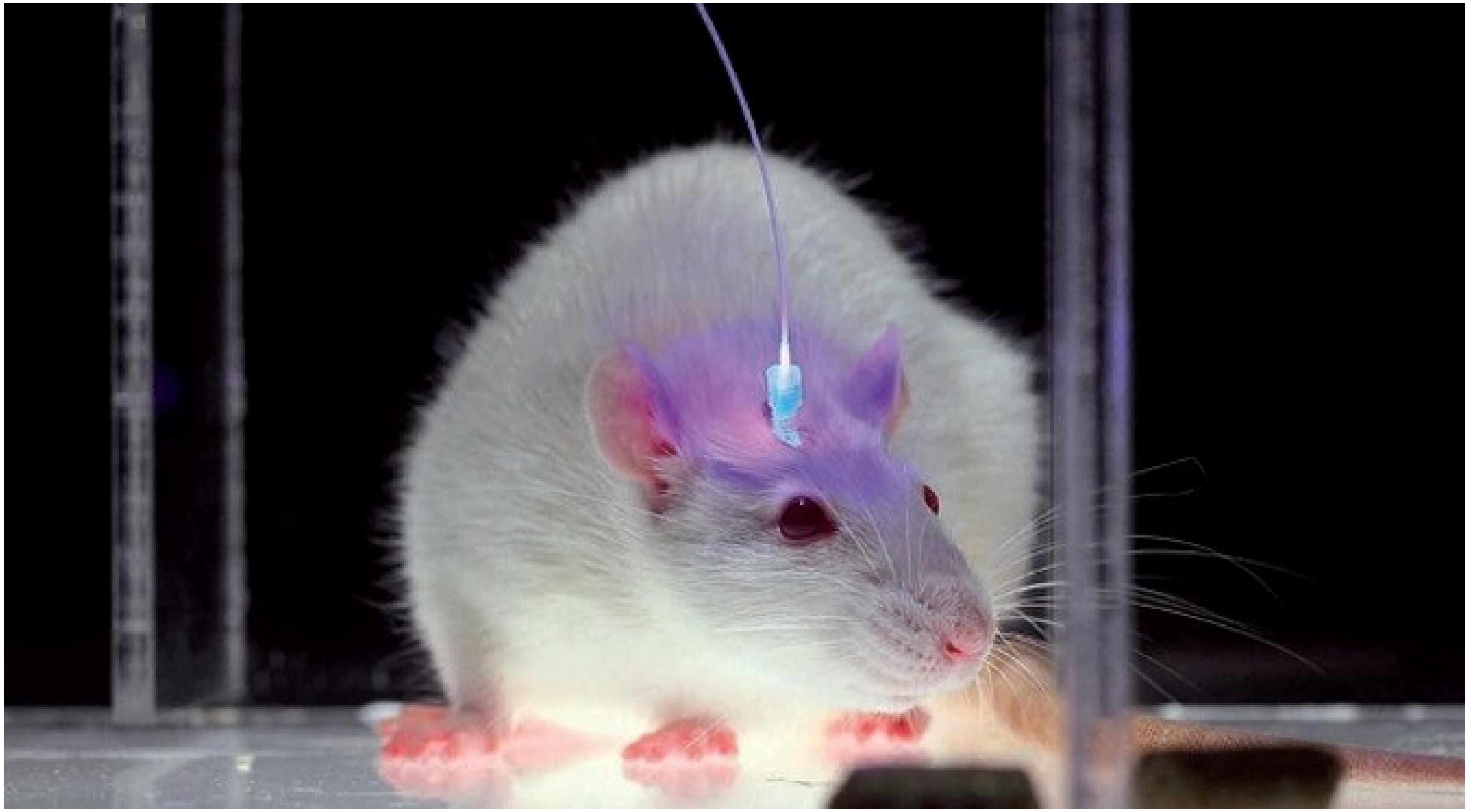




Morris et al, Nature 1986

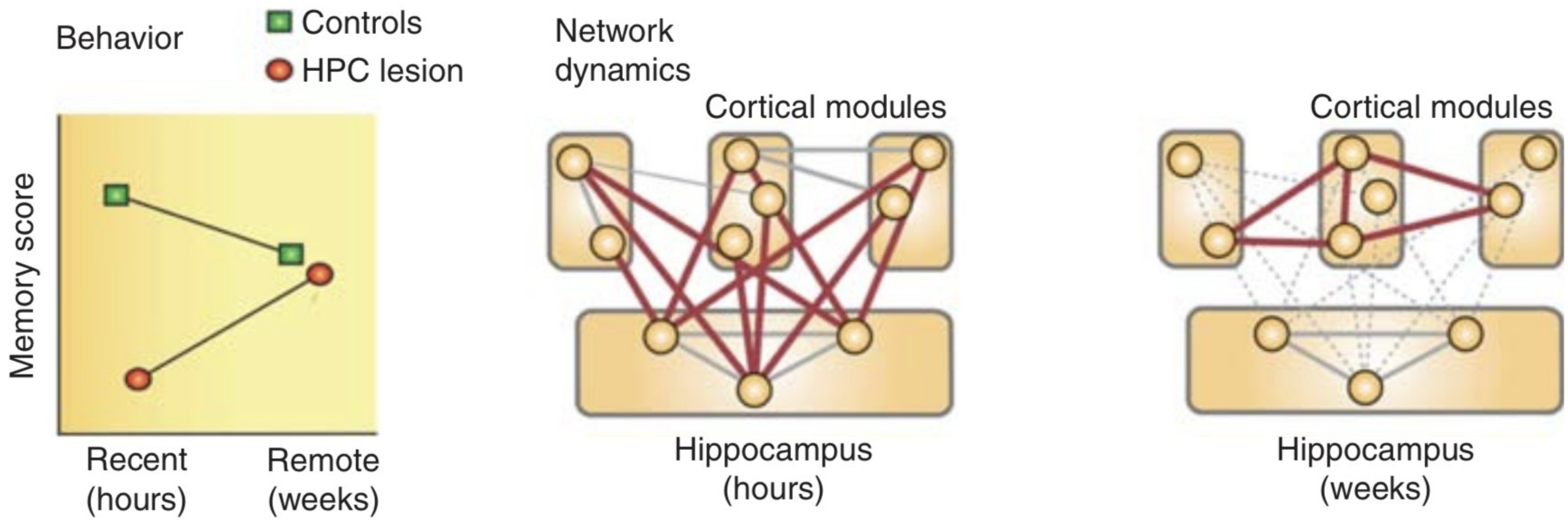
- A drug that blocks NMDA receptors blocks both synaptic plasticity and performance on a spatial learning task (left side is data from control animals, right side data from animals with drug).

False memories (the Inception experiment)



Tonegawa group (MIT) and Mayford group (UC San Diego)

Systems consolidation for memory



Squire et al. Cold Spring Harb Perspect Biol 7, a021766.

- New episodic memories are mainly encoded in the hippocampus during the day.
- During subsequent sleep, hippocampus replays the neural activity. This encodes the memory and triggers learning in the cortex.
- Over time, the memories get transferred to the cortex (the cortex learns the memories), and they become hippocampus-independent.

2. Hippocampus and spatial navigation

Spatial maps

The best studied function of the hippocampus is spatial memory.

There are cells in rat CA1 known as place cells which fire in response to specific location.

These were first discovered in 1971 and show both that the hippocampus has a role in spatial memory and that the memory encoding is very sparse.

Another, striking, example was discovered in 2005 in humans!

Some cells respond to very specific stimuli -these stimuli can be quite abstract. In the most quoted example, a cell in hippocampus in one patient was found which responded to pictures of Jennifer Aniston. It did this irrespective of how she appeared, but did not respond to other famous and non-famous faces, or curiously to pictures of Jennifer Aniston with Brad Pitt, her spouse at that time.

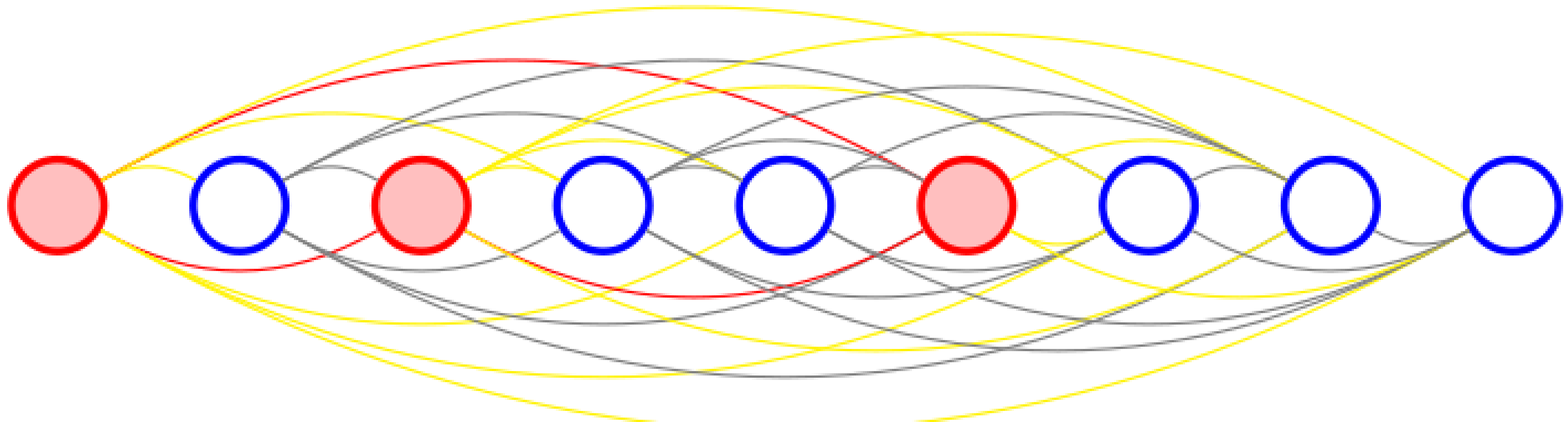
Again, this demonstrates a role in memory, but one that involves very sparse responses.

Sparseness

Sparseness is the idea that only a few neurons within a network of neurons encode each stimulus, or pattern to be remembered.

Therefore only a small percentage of neurons are active for any given pattern.

This is critical for enhancing capacity.



Red = large increase in the connection weights between two active neurons
Grey = small increase in the connection weights between two inactive neurons
Yellow = medium decrease in the strength of the connection weights between one active and one inactive neuron

Sparseness

If a pattern needed to turn on a large proportion of the neurons in a network it would need to modify a large proportion of the synaptic connections so that a lot of them are very strong. This is unlikely to be possible. The brain has limited resources and maintaining huge amounts of strong connections over time is energetically expensive.

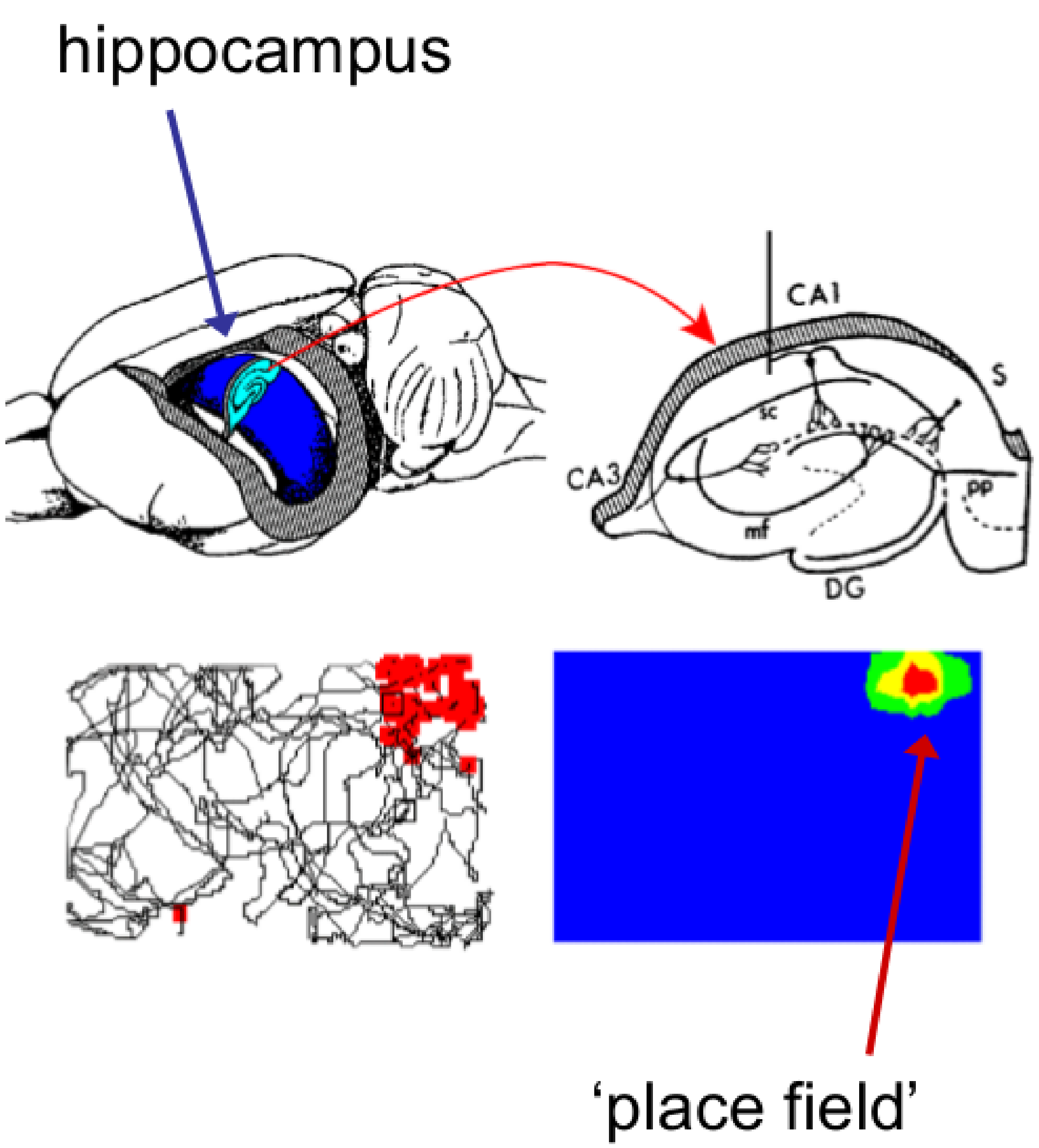
It would also lead to lots of interference between patterns.

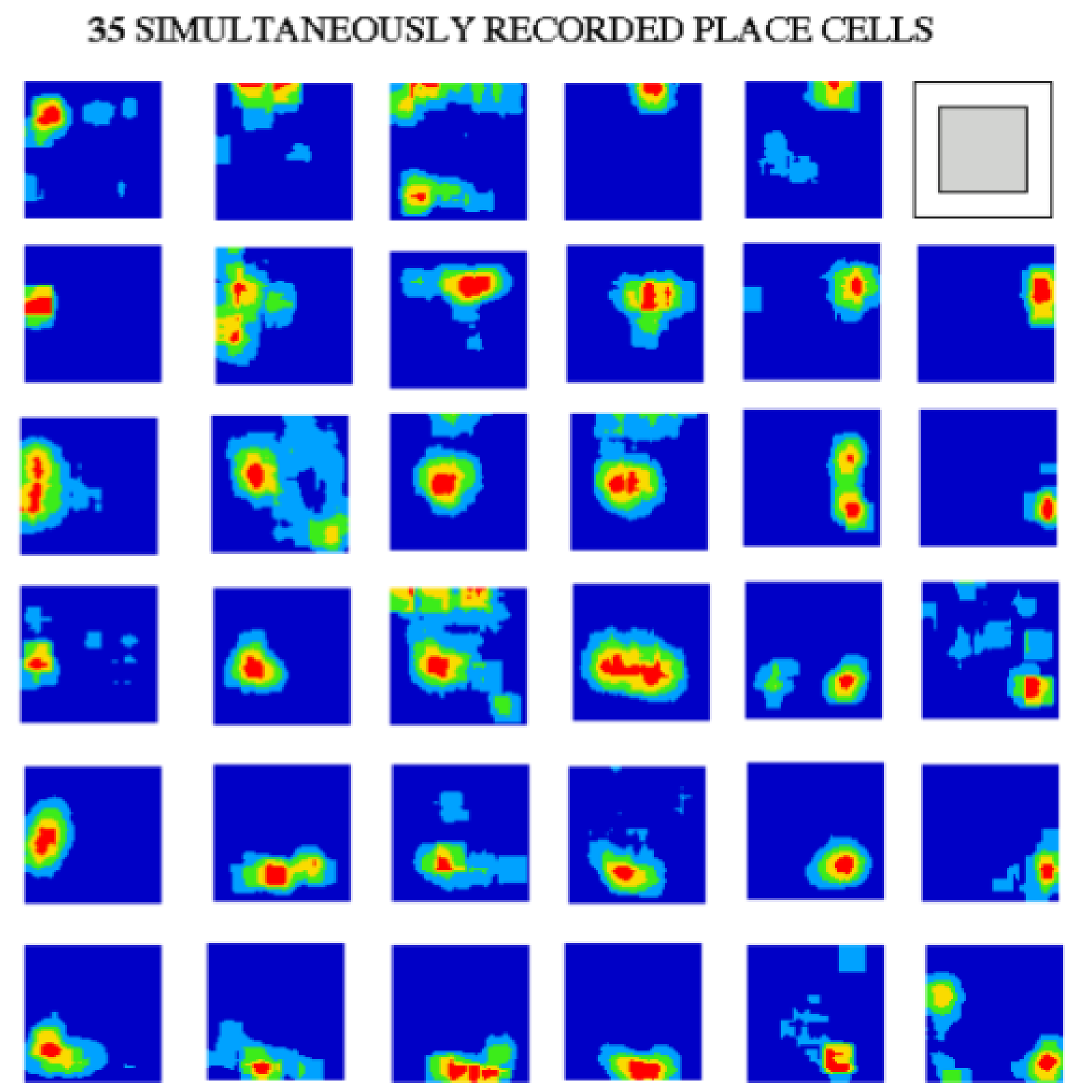
In a computational network model containing MP neurons, the connection weights, w, tend to be capped so that they all sum to 1. It would therefore not be possible to have many many strong connections as the connection strengths need to be shared across the population of neurons. In a network that wasn't sparse, the connection weights would get diluted and may not be strong enough to cause all of the neurons necessary for pattern recall to turn on.

Best coding scheme is to have a few very strong connections to a few neurons and lots of weak or negative connections elsewhere.

Place cells and spatial maps

Place cells encode an animals current location. They are found mostly in CA1 (and CA3). Place cells are sparse.





Place cells and spatial maps

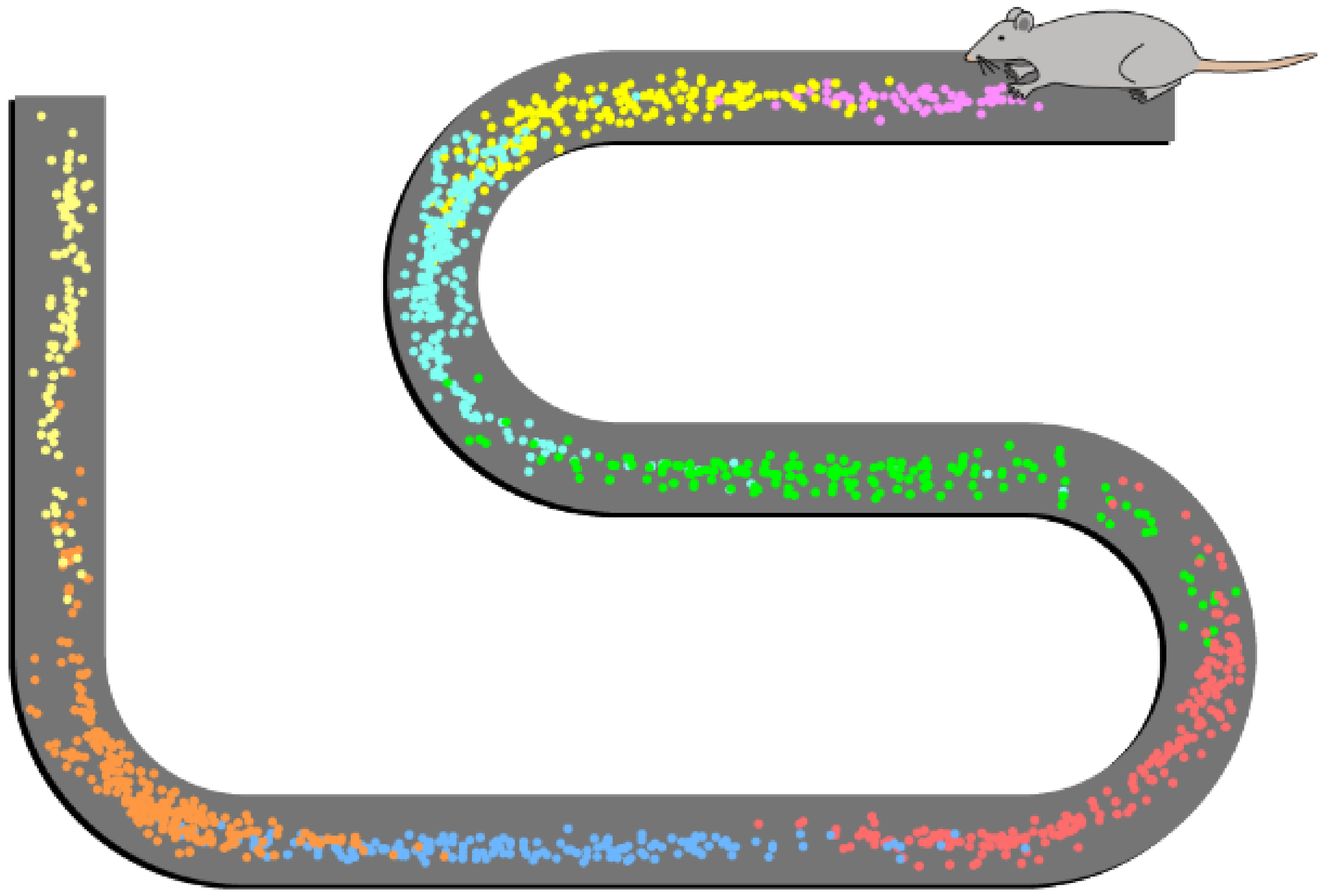
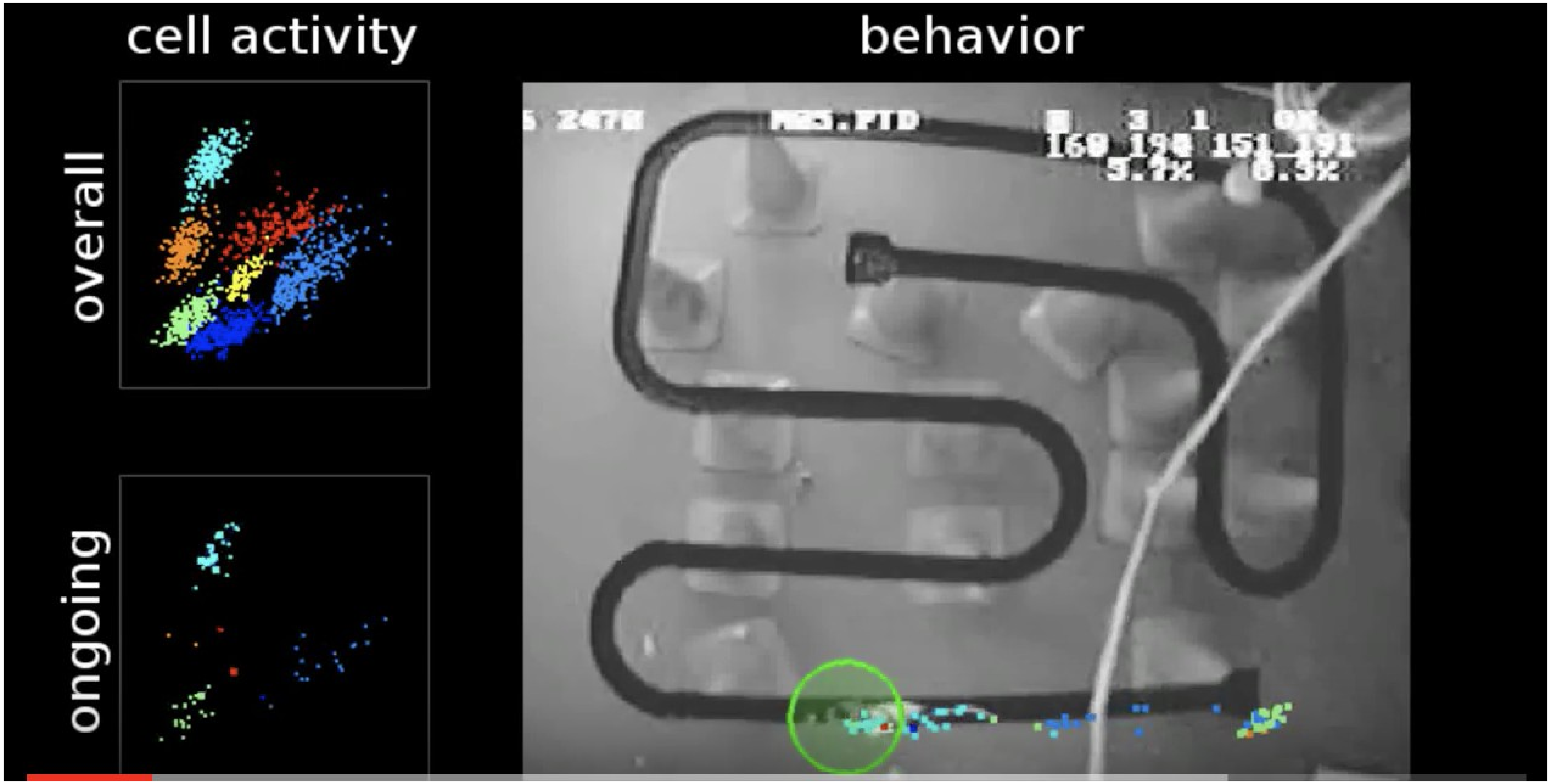


Figure 3: Place cells. This shows the firing activity of eight different cells in CA1 of a rat moving along a path, the dots correspond to spikes. [From http://en.wikipedia.org/wiki/Place_cell]

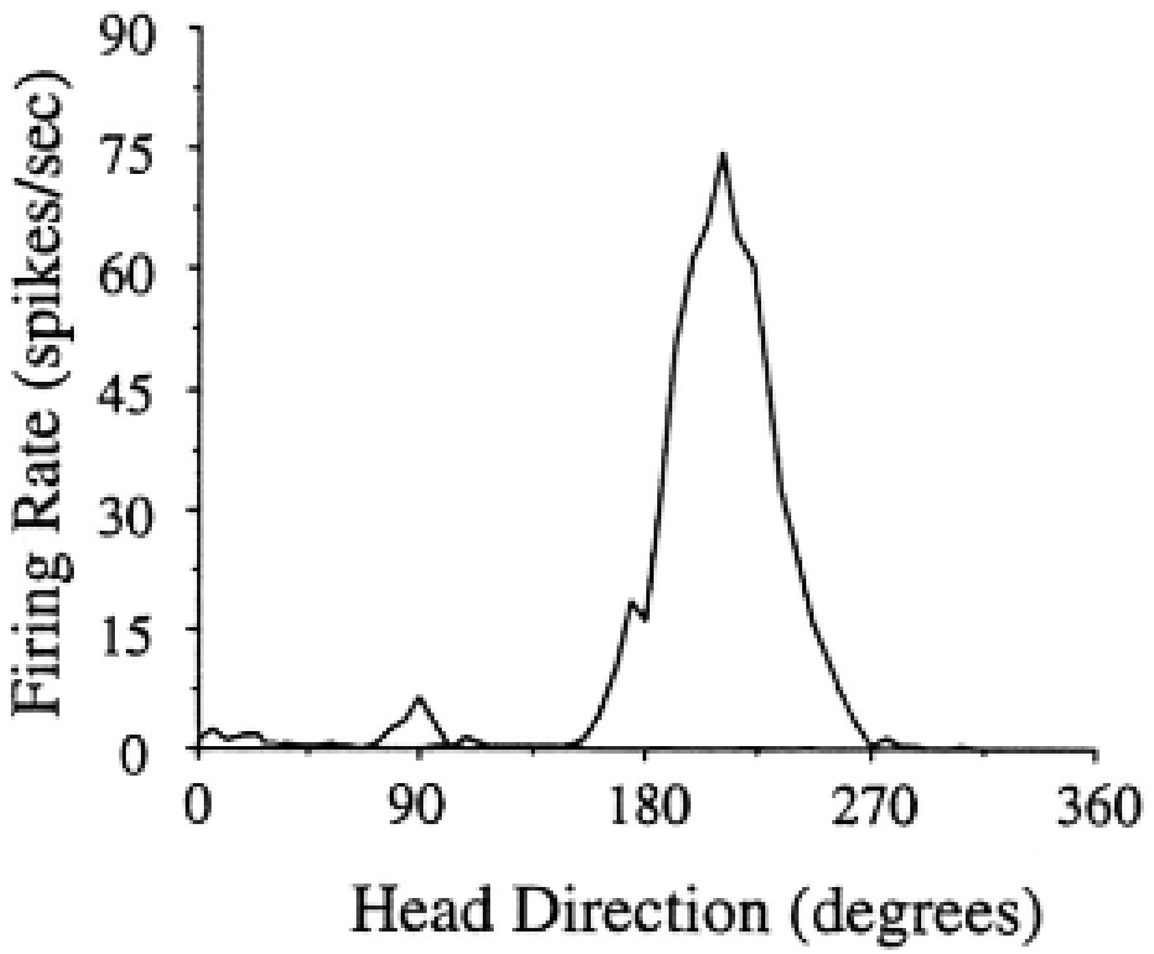
Place cell example video



https://www.youtube.com/watch?v=lfNVv0A8QvI

Head Direction Cells

If place cells tell the animal where it is, how does it know where to go?



Head direction cells are cells whose firing is tuned to specific angles of the head / heading direction

Ranck, 1984, Taube et al., 1997

Grid Cells

BUT, there is a problem with place cells:

- you are not able to calculate the heading vector between two points if they are separated by distances larger than the size of the largest place field

- this is because the place cell vector at the current location does not overlap with the place cell vector of the goal location

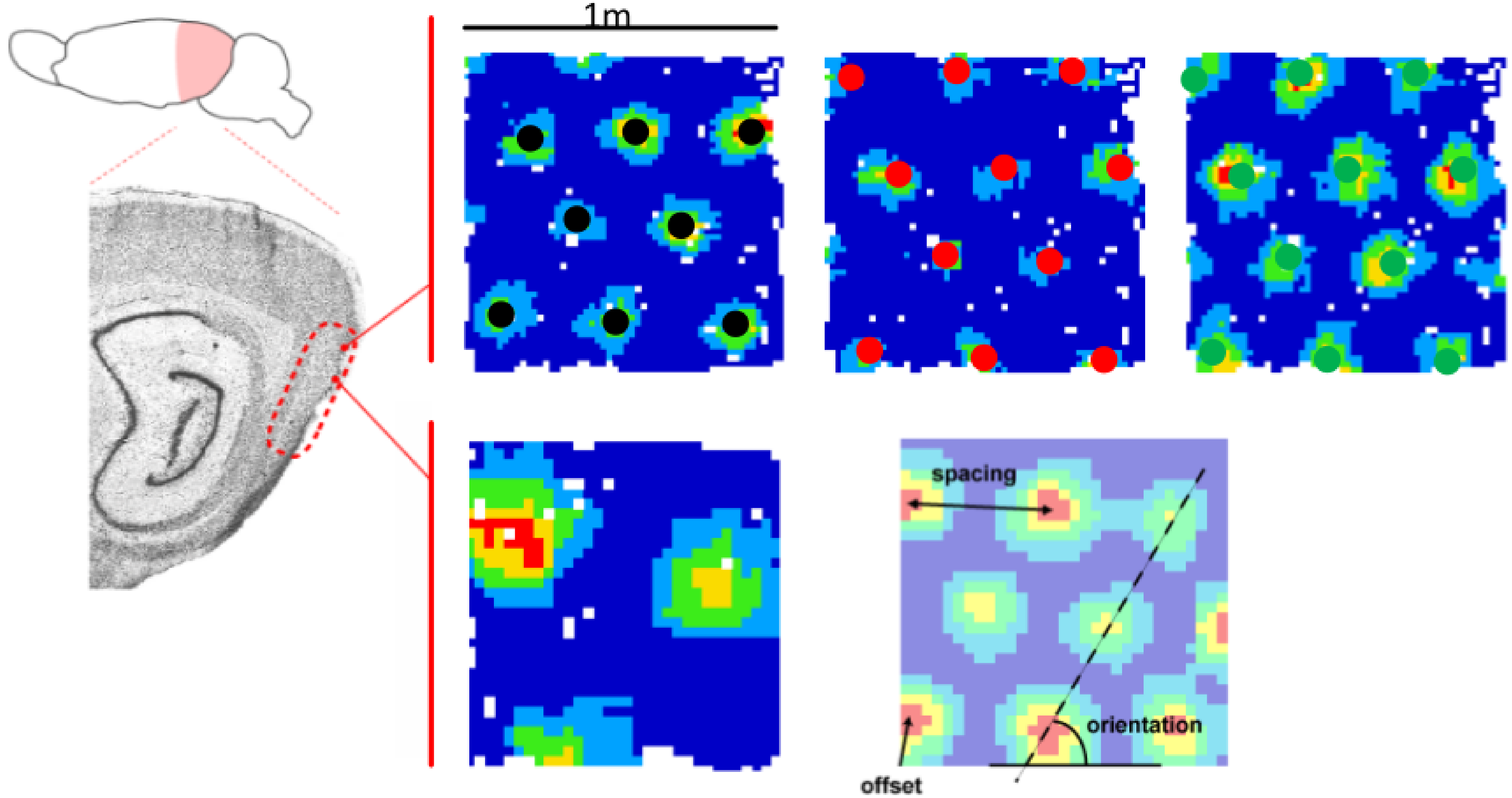
The solution is grid cells

Grid Cells

Grid cells make multiple, regularly spaced fields that tessellate the environment

Cells recorded simultaneously often have the same scale and orientation

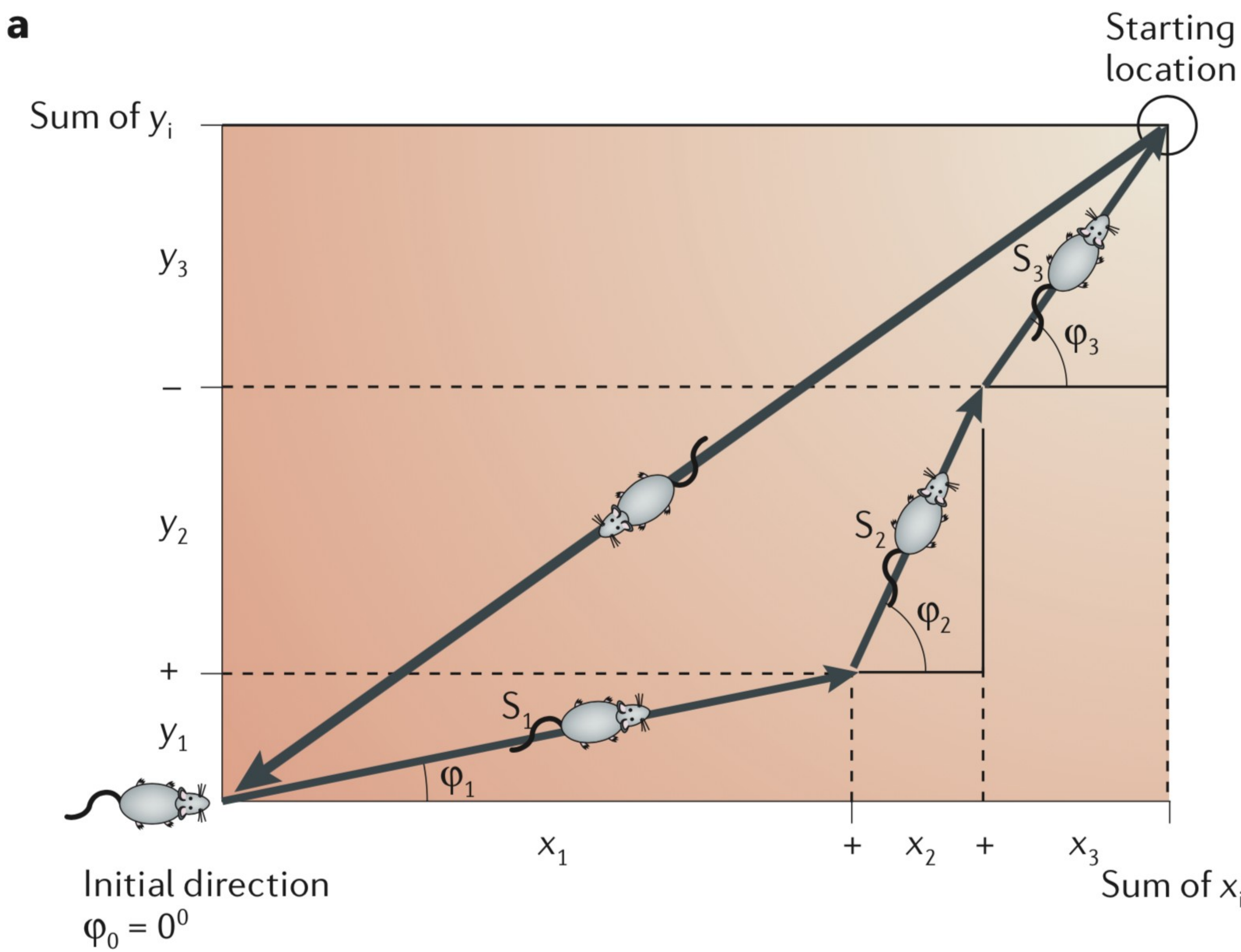
There are independent modules distributed along the entorhinal cortex



Path integration

Grid cells can be used, along with place cells and head direction cells, to recover the vector between two points and perform path integration.

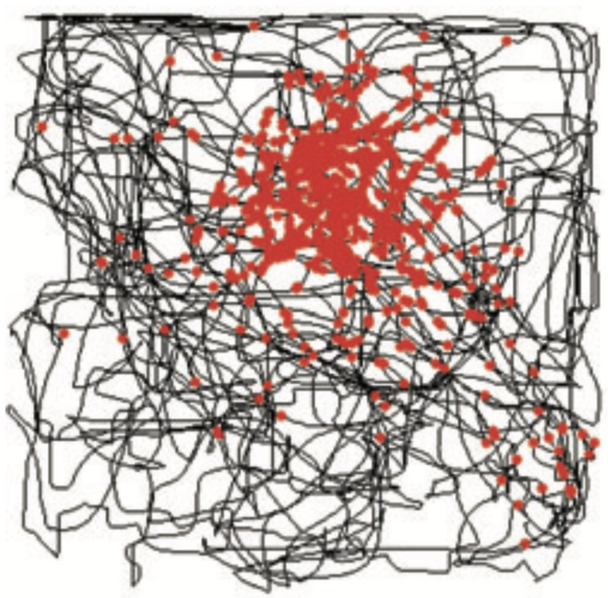
Path integration is the idea that an animal can use cues generated by its movements to monitor its trajectory and calculate an updated position of itself in relation to a start location.



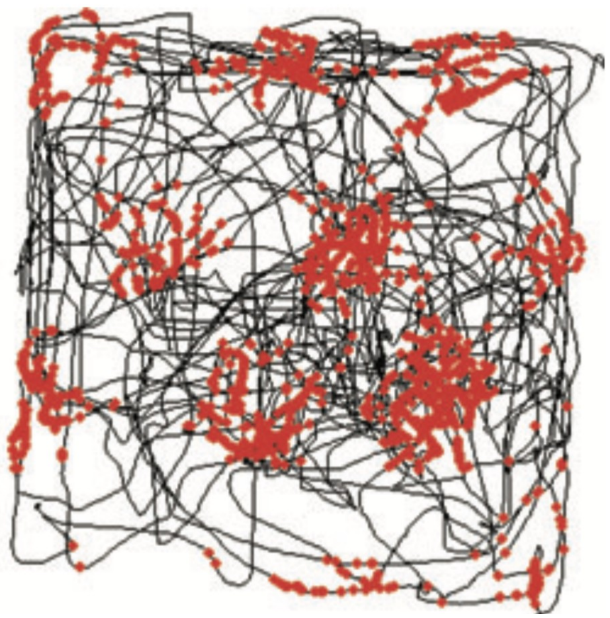
McNaughton et al, Nat Rev Neurosci (2006)

Place cells, grid cells, head direction cells

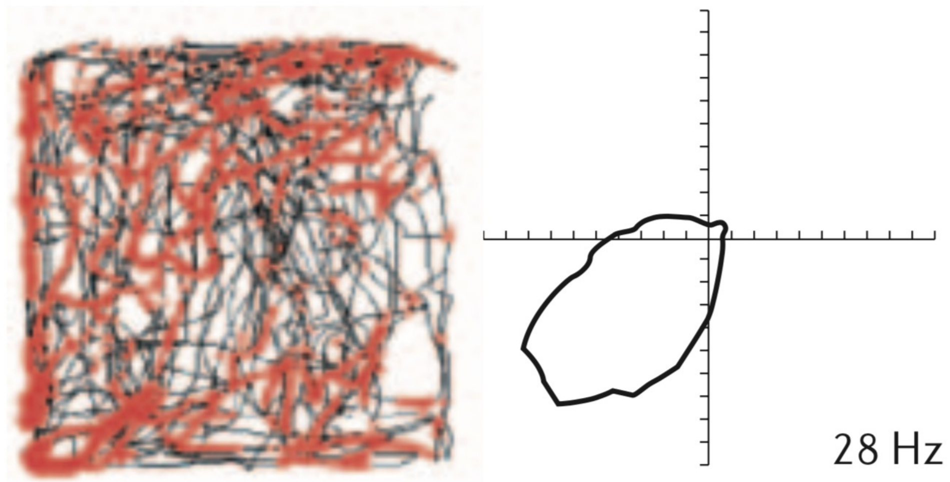
Place cell

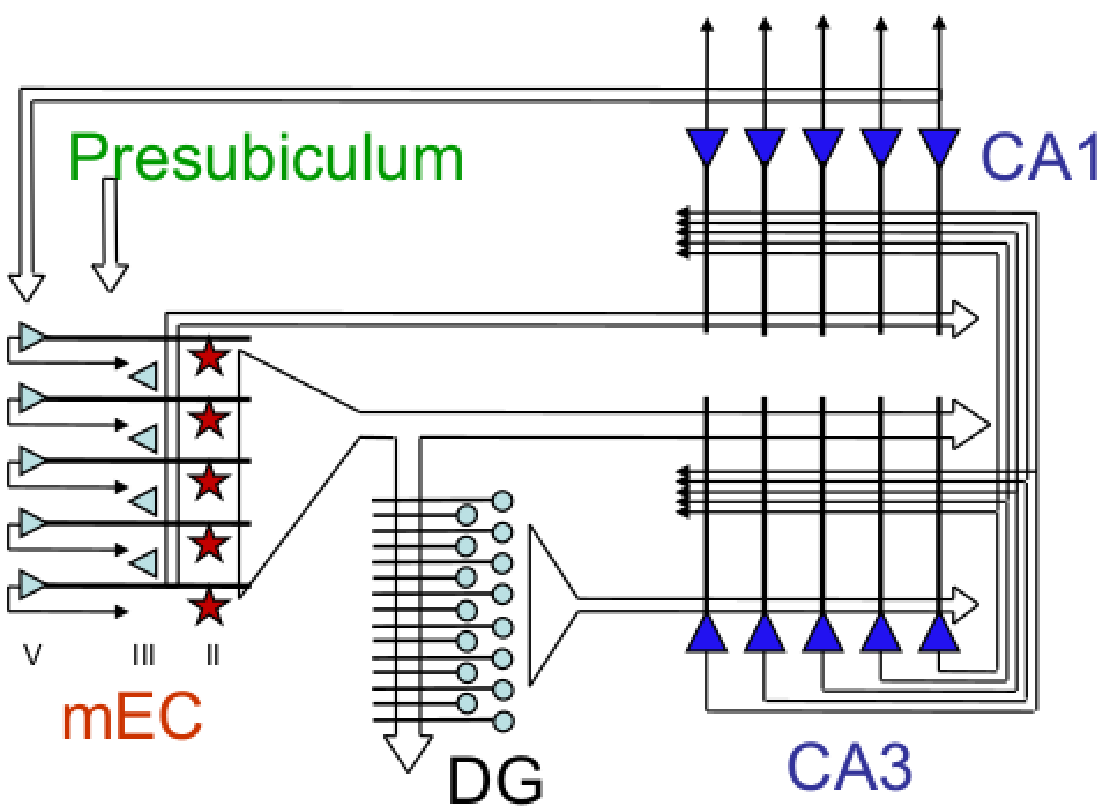


Grid cell



Head direction cell





Hippocampus and spatial navigation

Neurons in the hippocampus and surrounding regions respond to aspects of the spatial environment:

Place cells in CA3 and CA1 are active only when an animal is one particular **location**

Grid cells in entorhinal cortex are active when the animal is in any of a set of locations, arranged in a hexagonal grid. Essential for **path integration**

Head direction cells in subiculum (and also hippocampus, entorhinal cortex, and other neighbouring structures) tell the animal of it’s **orientation** don’t care where the animal is located, but are active only when the animal is facing a certain direction: the ‘heading direction’

Hippocampal computations

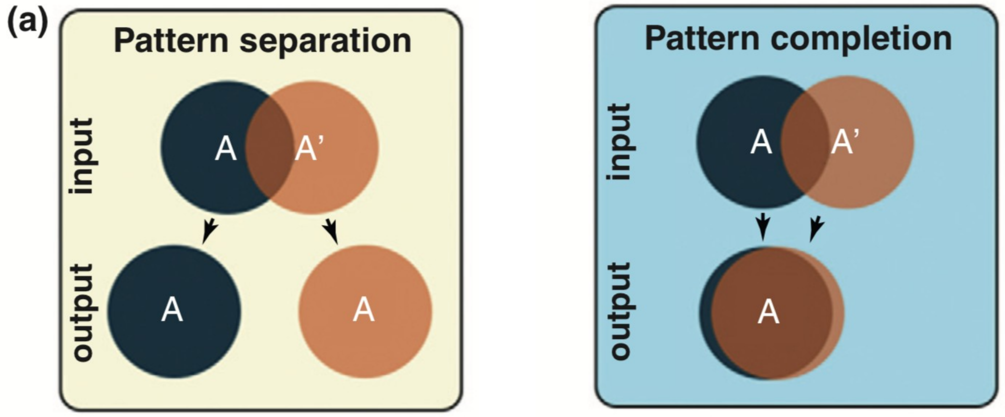
For both memory and spatial navigation, the hippocampus is thought to perform two key classes of computation:

- Pattern separation vs pattern completion.
- Path integration.

Pattern separation vs pattern completion

- Dentate gyrus is thought to do pattern separation.
- CA3 is thought to do pattern completion

  - an auto-associative network?



Yassa & Stark, Trends Neurosci (2011)

Conclusions

The hippocampus is associated with long term episodic memory and spatial navigation.

The DG is associated with pattern separation

CA3 is associated with pattern completion – similar to what we saw the Hopfield networks doing!

The hippocampus is essential for spatial navigation: animal location, orientation and path integration.

Spatial maps are supported by place cells, head direction cells and grid cells.

References

McNaughton, B., Battaglia, F., Jensen, O. et al. Path integration and the neural basis of the 'cognitive map'. Nat Rev Neurosci 7, 663–678 (2006). https://doi.org/10.1038/nrn1932

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