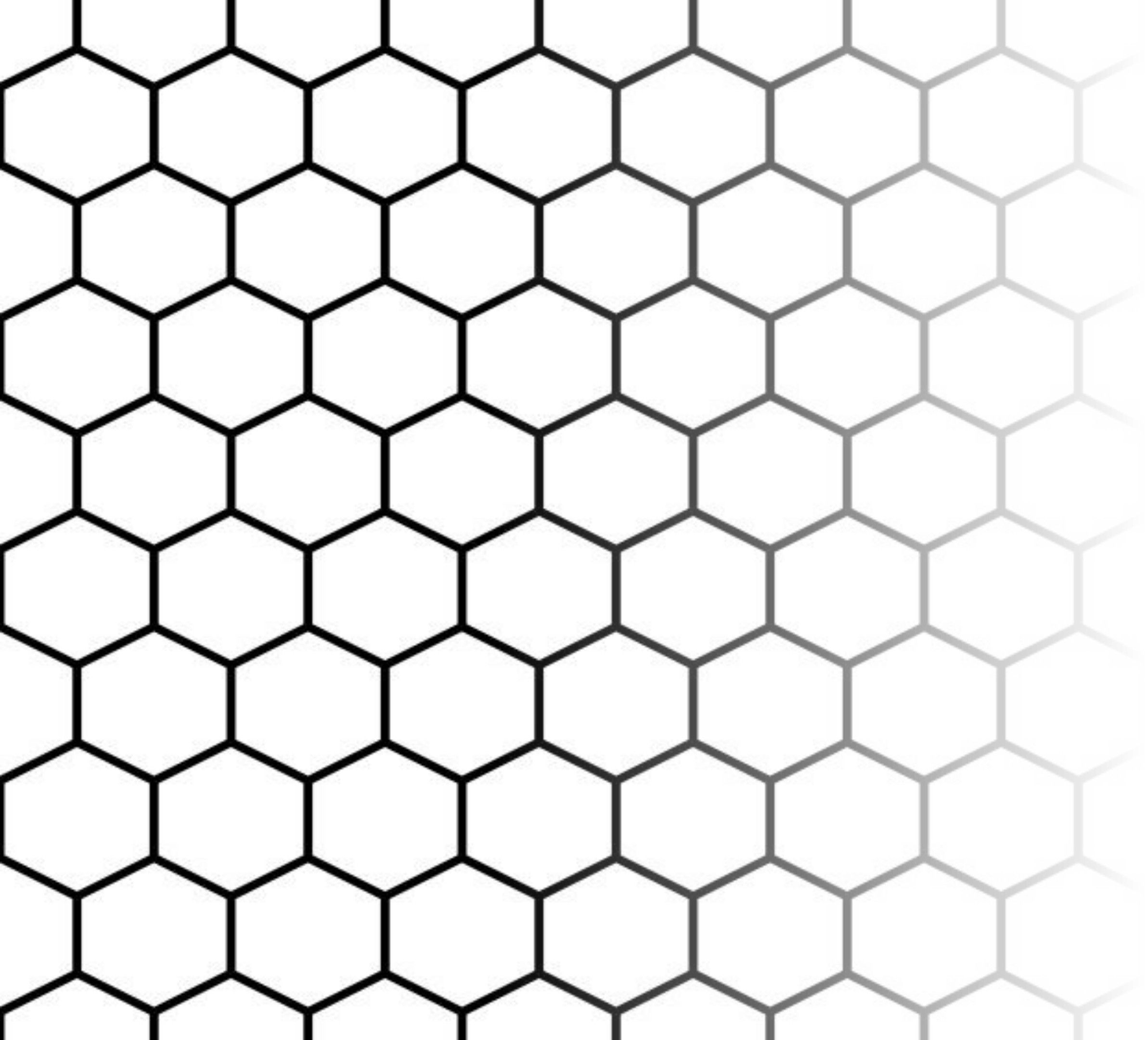


Section:
Hafting et al. 2005

Background Recap:

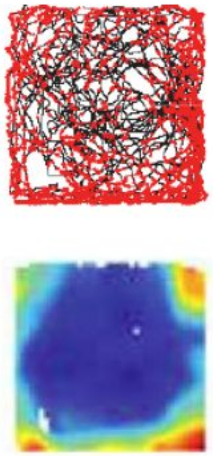
Section W8

The cognitive map

Medial entorhinal cortex

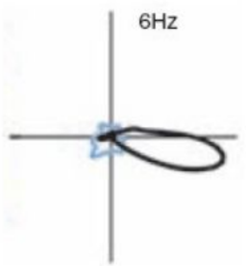
Hippocampus

Border cells



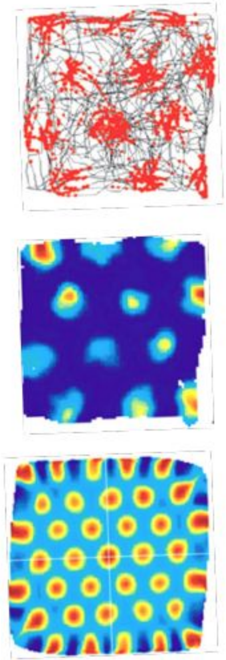
Mosers, O’Keefe, Knierim 2008

Head-direction cells



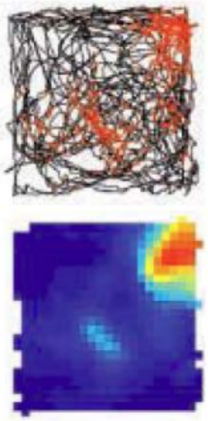
Ranck, Taube 1980s

Grid cells



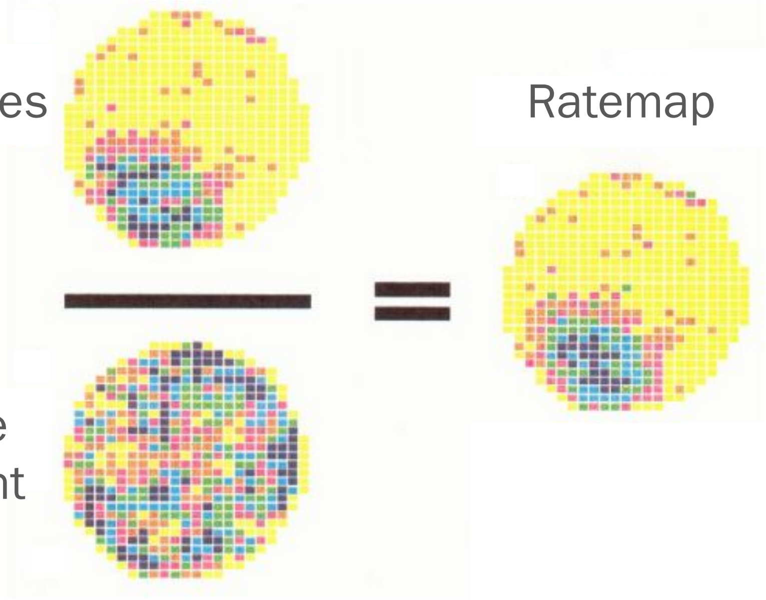
Mosers 2005

Place cells



O’Keefe 1971

Reminder: Ratemaps

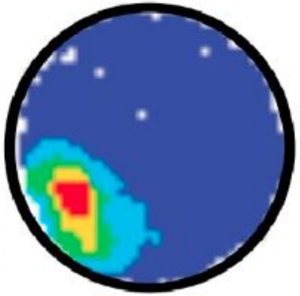


Spikes

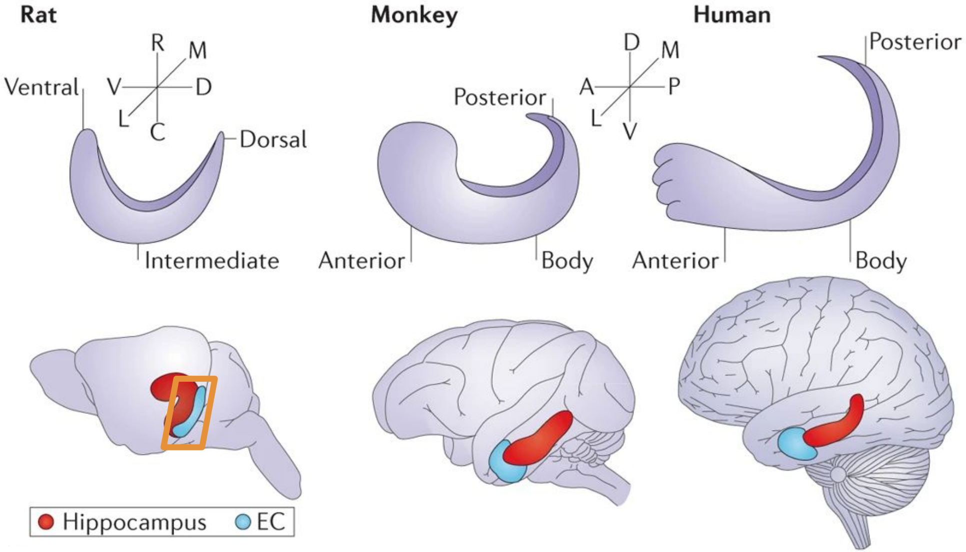
Time
spent

Ratemap

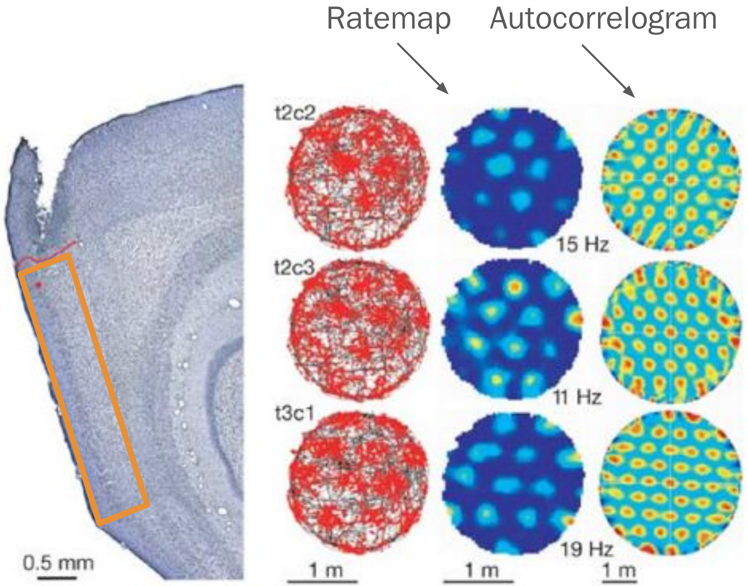
More bins
Different colormap



Grid cells in medial entorhinal cortex



Strange et al. 2014

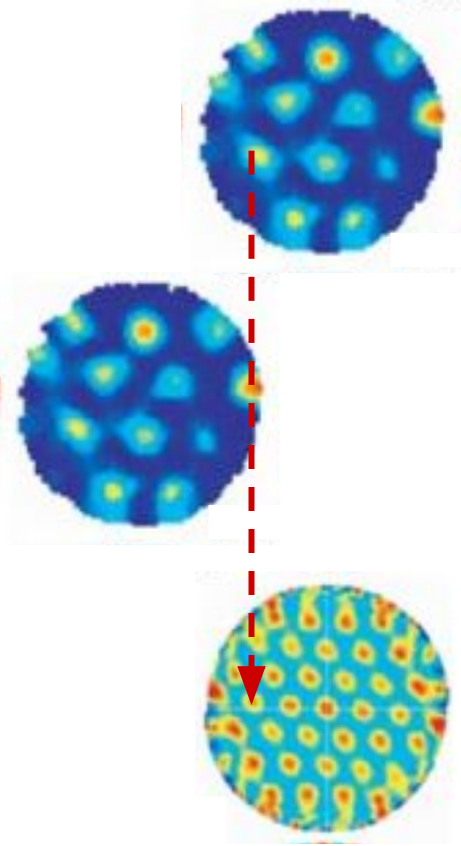


Entorhinal cortex (EC) is a major form of input to the hippocampal formation and is further split into medial (MEC) and lateral (LEC) entorhinal cortex

Animal trajectory is visualized in grey and the spikes are overlayed in red

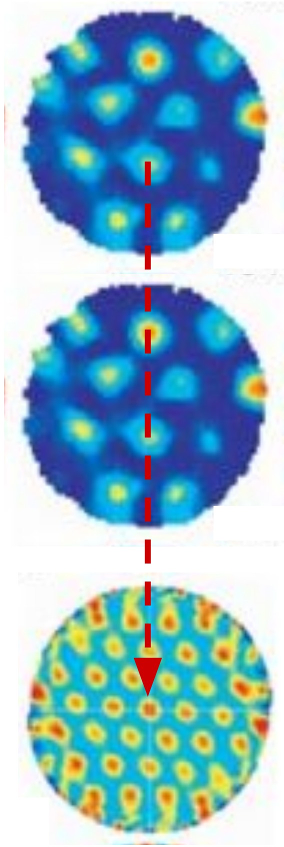
Autocorrelogram

Correlate ratemap to a shifted version of itself and then visualize the correlation coefficient



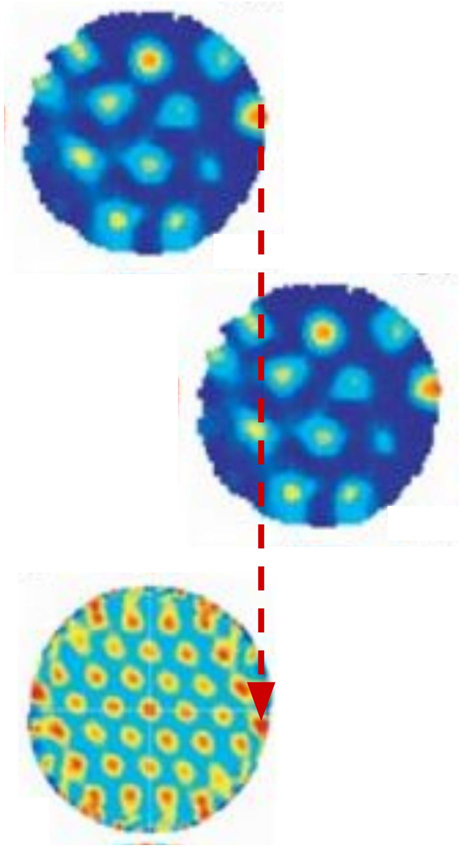
Autocorrelogram

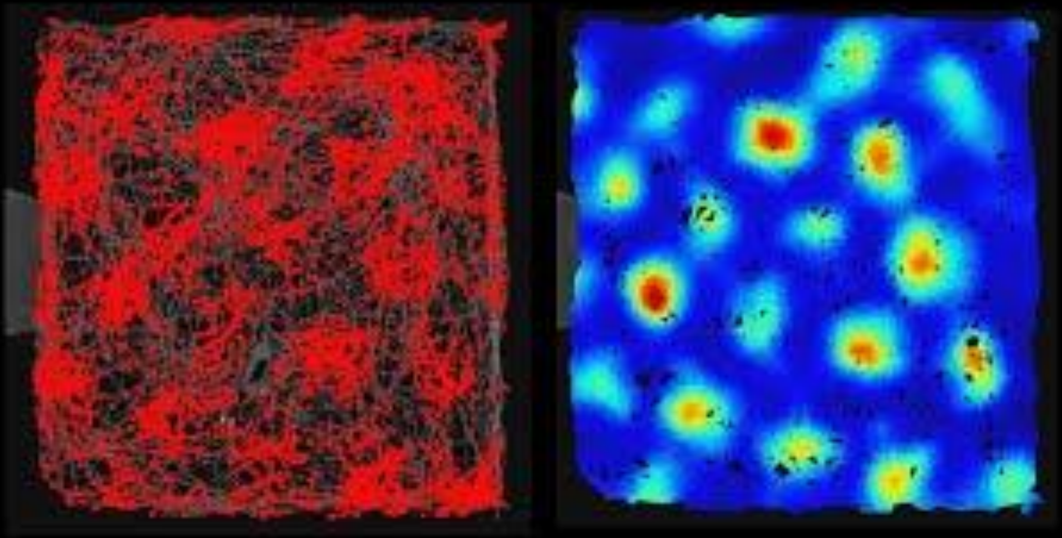
Correlate ratemap to a shifted version of itself and then visualize the correlation coefficient



Autocorrelogram

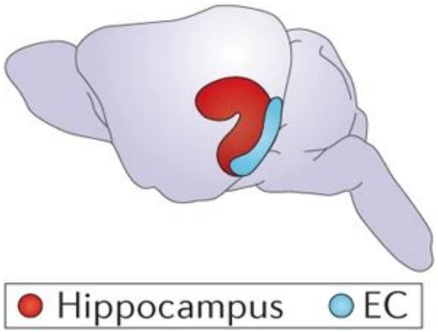
Correlate ratemap to a shifted version of itself and then visualize the correlation coefficient

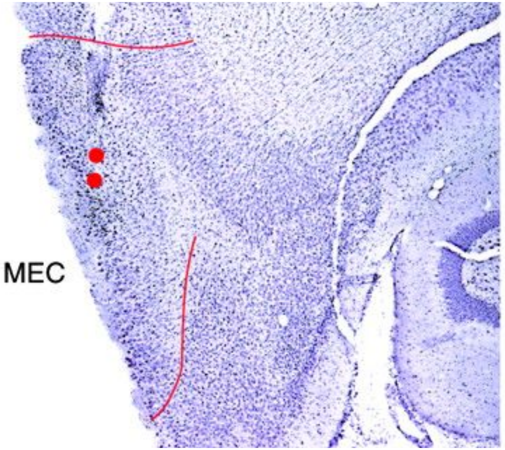


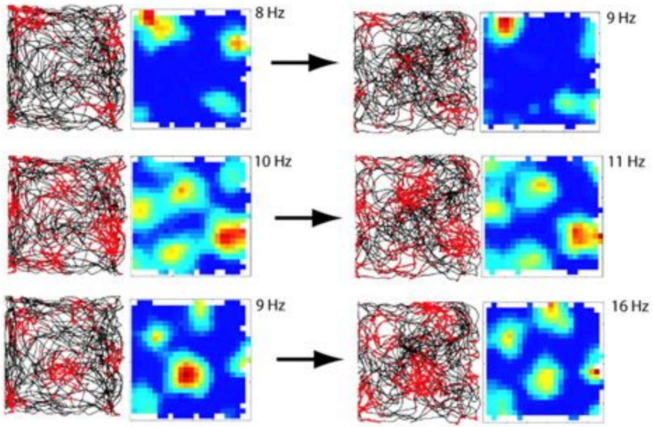


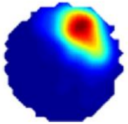
Grieves, Jefferey 2020

Previous findings from entorhinal cortex









?

Location is accurately represented in entorhinal cortex

However, “place cells” have multiple discrete fields of similar amplitude

Environment was too small to quantify periodicity

Fyhn et al. 2004

Is there a map-like structural organization in the medial entorhinal cortex (dMEC)?

Section Paper:

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Microstructure of a spatial map in the entorhinal cortex

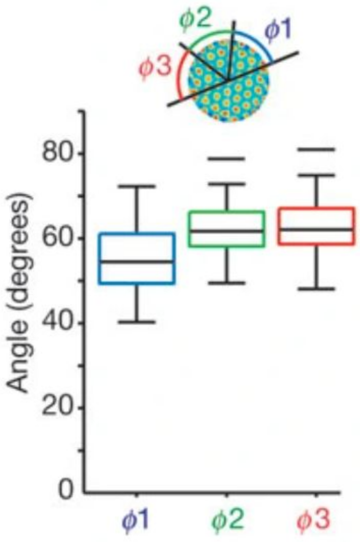
Torkel Hafting[1]*, Marianne Fyhn[1]*, Sturla Molden[1]†, May-Britt Moser[1] & Edvard I. Moser[1]

The ability to find one's way depends on neural algorithms that integrate information about place, distance and direction, but the implementation of these operations in cortical microcircuits is poorly understood. Here we show that **the dorsocaudal medial entorhinal cortex (dMEC) contains a directionally oriented, topographically organized neural map of the spatial environment.** Its key unit is the ‘grid cell’, which is activated whenever the animal's position coincides with any vertex of a regular grid of equilateral triangles spanning the surface of the environment. Grids of neighbouring cells share a common orientation and spacing, but their vertex locations (their phases) differ. The spacing and size of individual fields increase from dorsal to ventral dMEC. The map is anchored to external landmarks, but persists in their absence, suggesting that grid cells may be part of a generalized, path-integration-based map of the spatial environment.

Figure 1: Firing fields of grid cells have a repetitive triangular structure

In what sense is the experimental setting novel?

By using a bigger recording environment, they are able to see spatial organization of the subfields that was not apparent in conventionally sized environments.

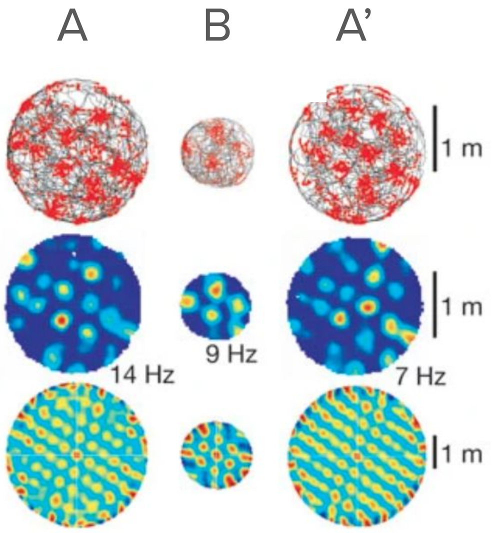


Why are the spatial autocorrelation maps computed on top of the rate maps?

Get clearer peaks as ratemaps can be noisy so that can measure the distance and angle from central peak to surrounding peaks.

What is the geometric structure they observed in the maps?

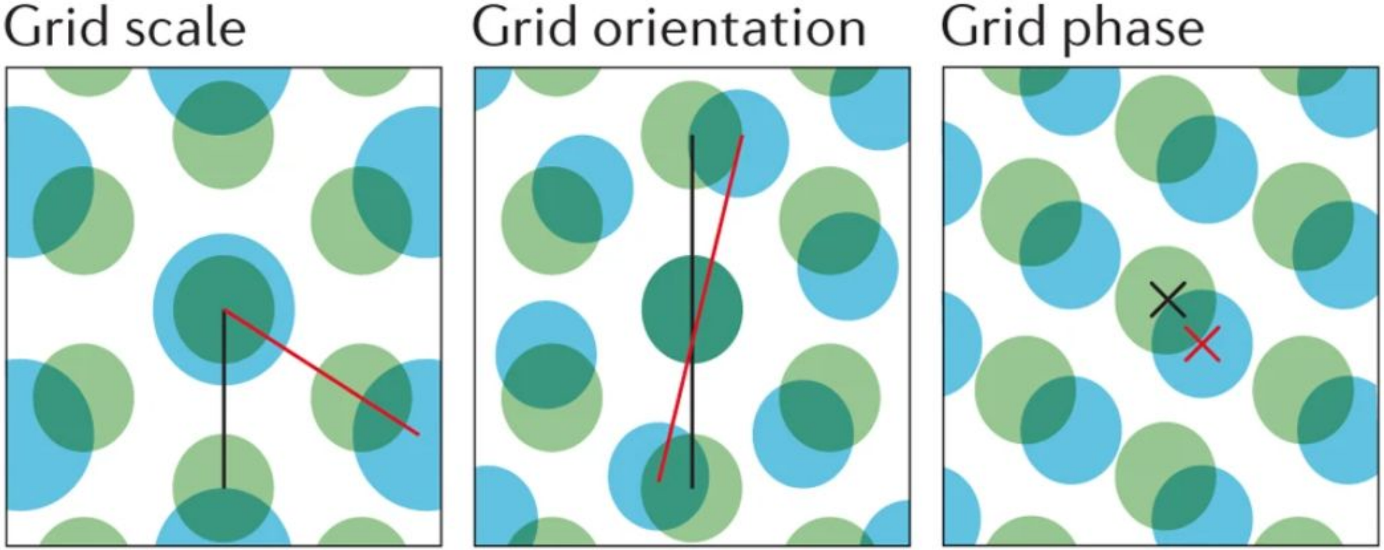
Equilateral triangle.
*- center peak to 6 nearest peaks distance → constant = **spacing**.*
- angular separation between central peak and closest firing fields → multiples of 60°.
- phase → stable across recordings.



What happens to the grid cell responses when the environment is smaller?

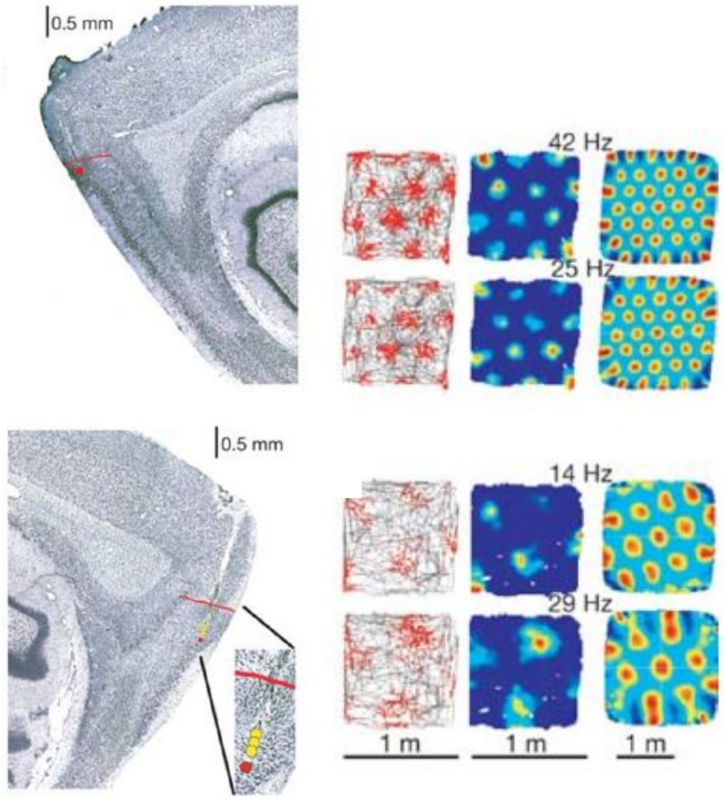
This geometric structure is also observed in smaller enclosures. Constant density!

Reminder: grid cells properties



Moser et al. 2014

Figure 2: Grid cells recorded simultaneously at two electrode locations in the same rat



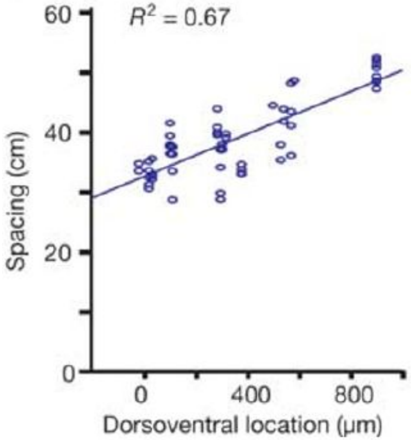
What are the observations made on spacing, orientation and field size?

- Almost invariant at individual recording locations.

- Spacing and field size between adjacent firing fields increases ***from dorsal to ventral.***

Discuss this finding considering the concept of "modules" (saw in the course).

The changes are not continuous, but clustered in modules across the dorsoventral levels.



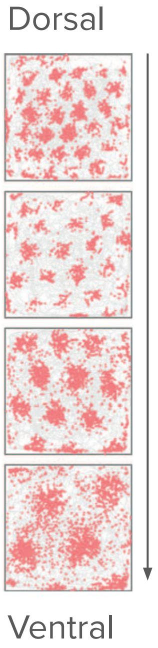


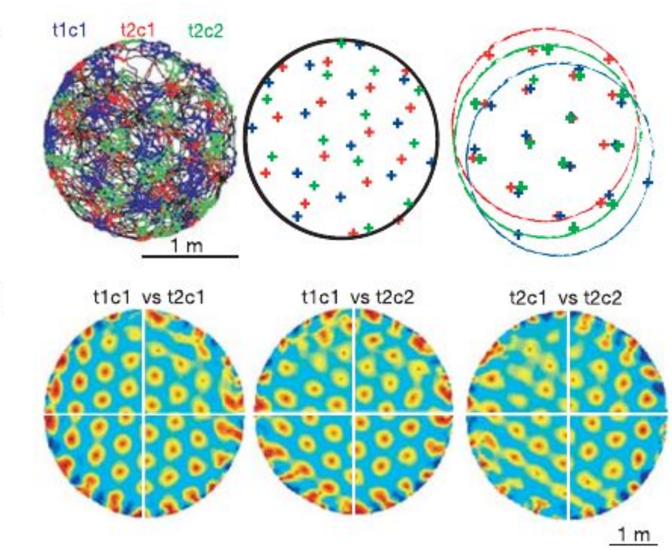
Figure 3: Distributed spatial phase of co-localized grid cells

What are the observations made on phase of co-localized cells?

Phase offset between co-localized cells → regular multi-peaked surface to tile the full environment.

What are the observations made on phase of cells at different locations?

The phase shift between cells is homogeneously distributed → complete representation at each dorsoventral level.



Blue: Circular environment
Red: Square environment

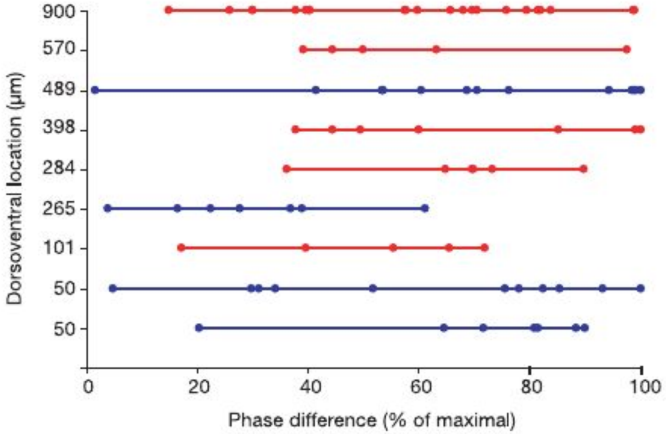
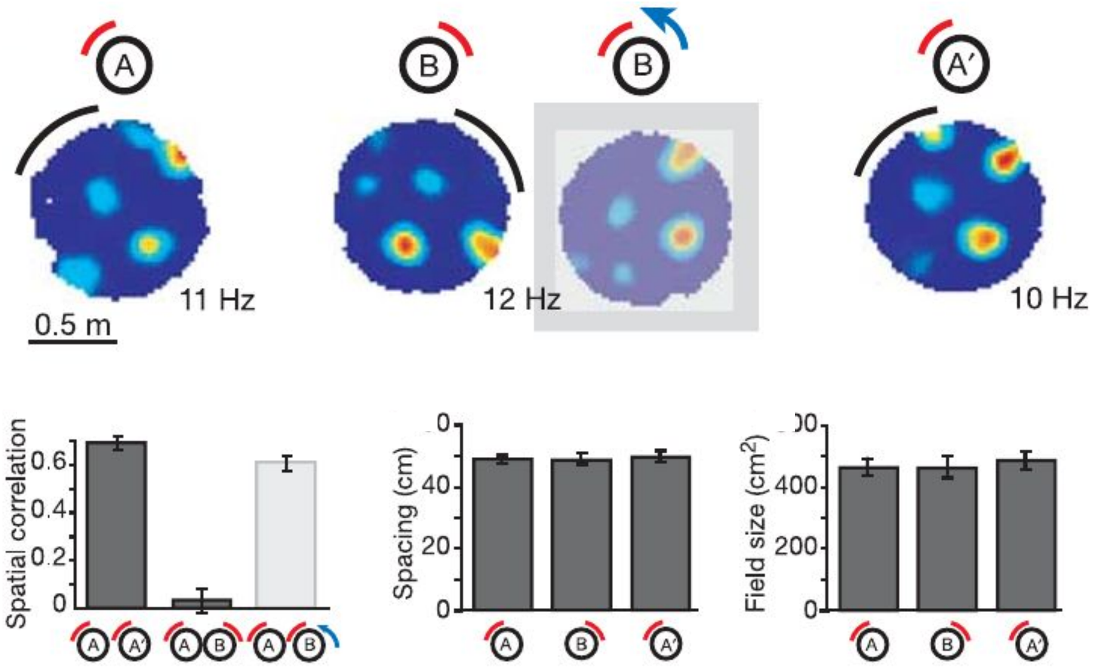


Figure 4: Grids are aligned to environment-specific landmarks.



From previous figures, what is the hypothesis?

Stability of the grid vertices across successive trials in the same enclosure → influence of external landmarks?

What is the difference between allothetic cues and idiothetic cues?

External landmarks vs information generated by the rat's movements.

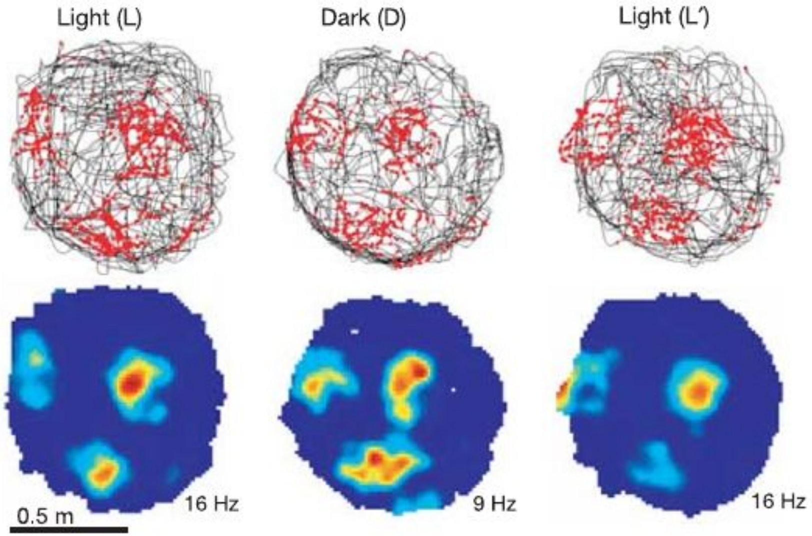
What happens to the grid cell responses when cue card is rotated?

The grid also rotates: change in orientation/phase, not in spacing or field size.

Figure 5: Grids persist in darkness.

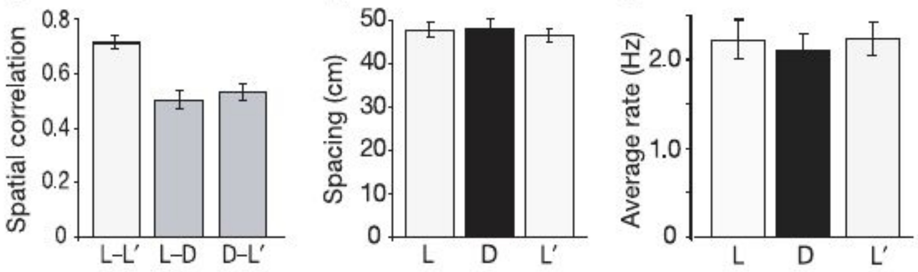
Allothetic cues anchor the grid map. Is it necessary to maintain the map?

Grid maintained in darkness → existence of the map is independent from the allothetic cues.



What can you say about the weak decrease in spatial correlation?

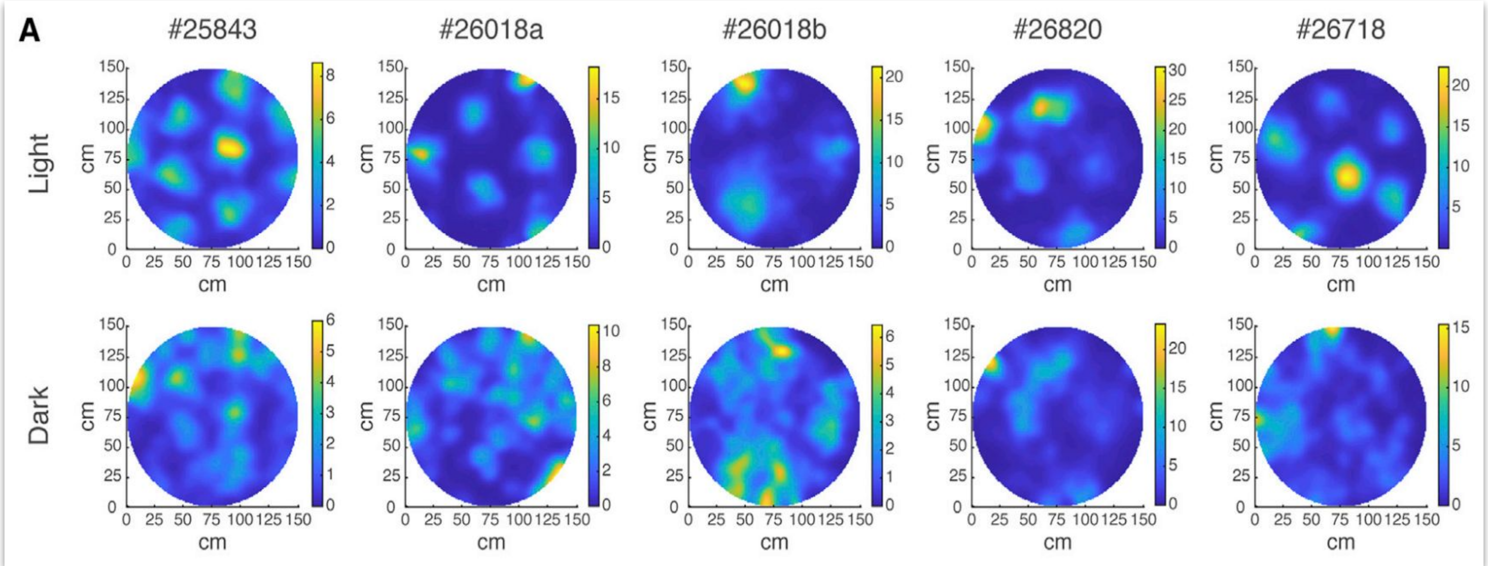
External cues used to determine the phase, but not the existence of the map → used for alignment to a reference frame.



Which other features could be used by the animal to anchor the grid map to its environment in the dark?

Combination of velocity, angular velocity, integrated based on last known position (idiothetic). Borders, scent (allothetic).

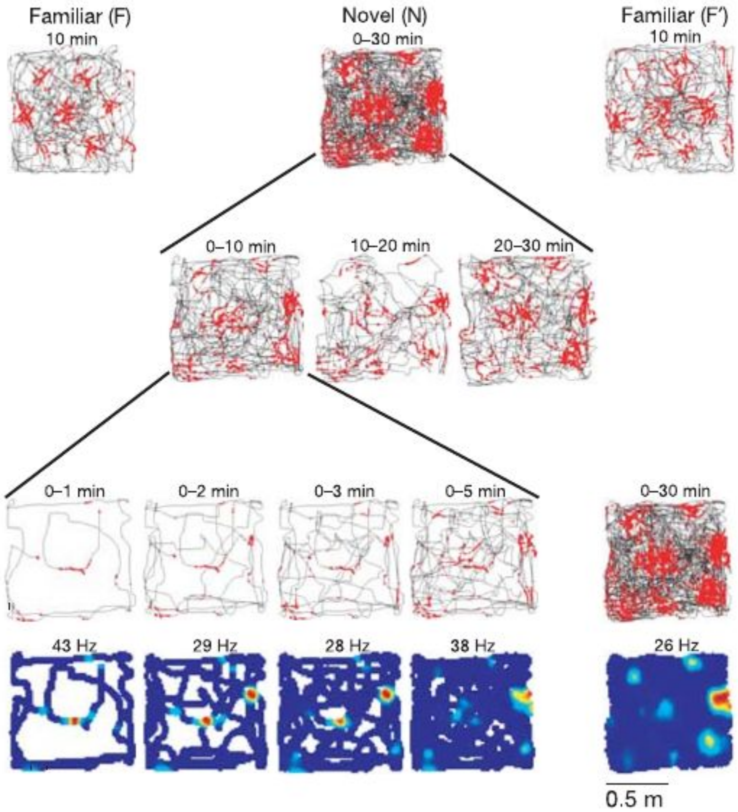
Updated findings: the grid actually doesn't persist



Waaga et al. 2023

"It was necessary in our study to take extreme measures (large circular arena, removing odors) to obtain strong degradation of the grid response patterns."

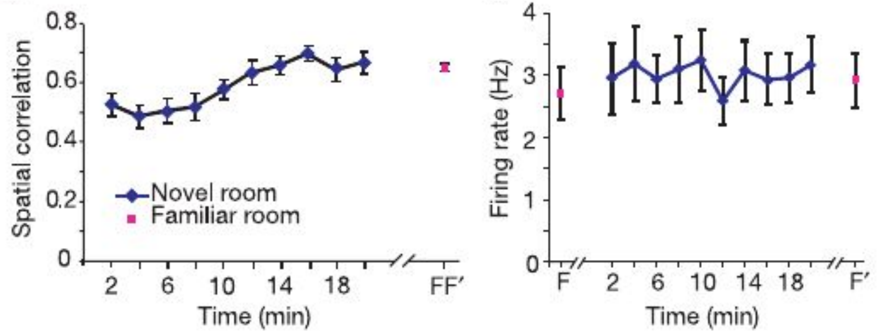
Figure 6: Grid structure of dMEC cells is expressed instantly in a novel environment.



Do you think the rat actually uses that map to navigate?

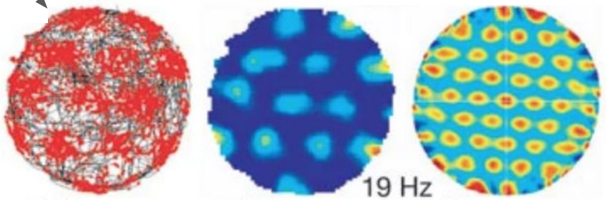
Map appears and is mostly stable from the first minutes in the environment.

Structure already there, and need to anchor it to the novel environment.

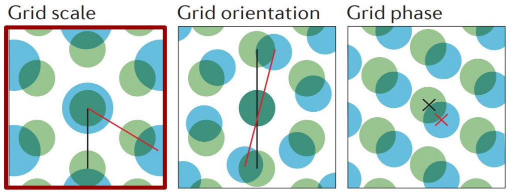


Summary

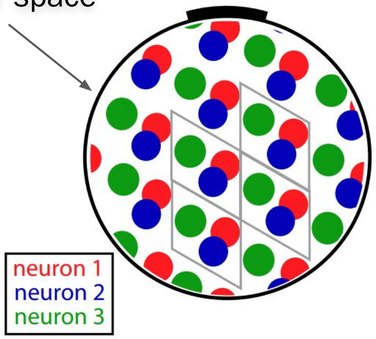
Periodic firing



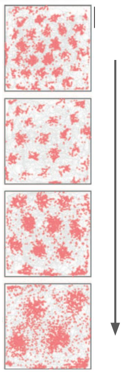
Grid cell parameters



Tiling of space

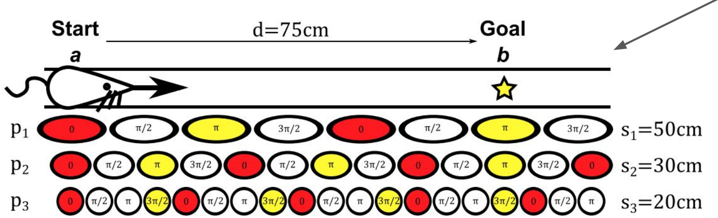


Dorsal

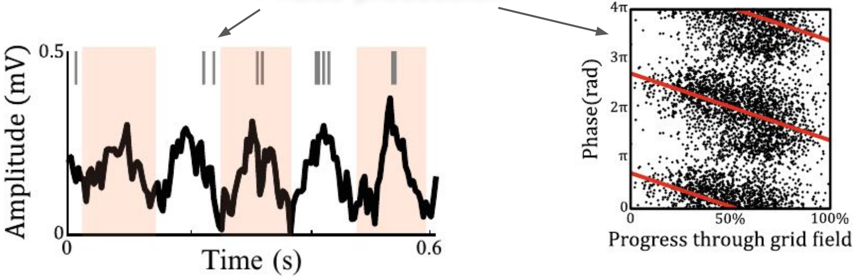


Ventral

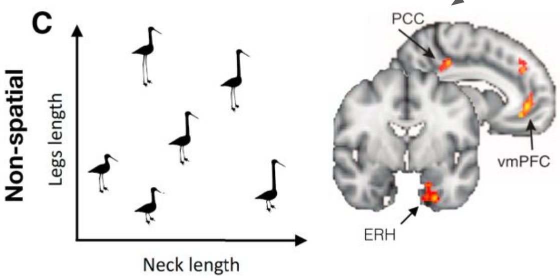
Vector computation



Phase precession



Encoding of abstract spaces!



Hafting et al. 2005
Fiete et al. 2008
Bush et al. 2015
Stemmler et al. 2015
Behrens et al. 2018

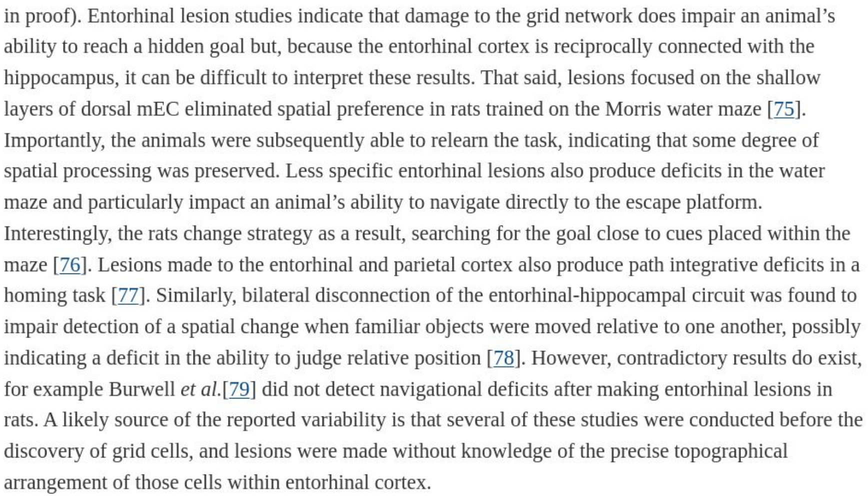
Paper round-up

- They propose that the dMEC is part of a neural map of the spatial environment.
- They find a novel cell type in the dMEC that would be the basic unit of the map: the grid cell, which shows periodic firing as a response to non-periodic behavior.
- They show that the grid spacing, orientation and field size are topographically arranged from dorsal to ventral entorhinal cortex.
- They show that the grid phase vary randomly among co-localized cells, so that the full surface of the environment is represented within a local cell ensemble, suggesting a modular local organization of the spacial map.
- They suggest that grid cells are aligned to external landmarks but also persist in darkness (further work challenged that last point!).
- They find that the grid structure in the dMEC is expressed instantly in a novel environment, suggesting that the periodic structure is encoded by default, and the phase and orientation are set in relation to context-specific landmarks.

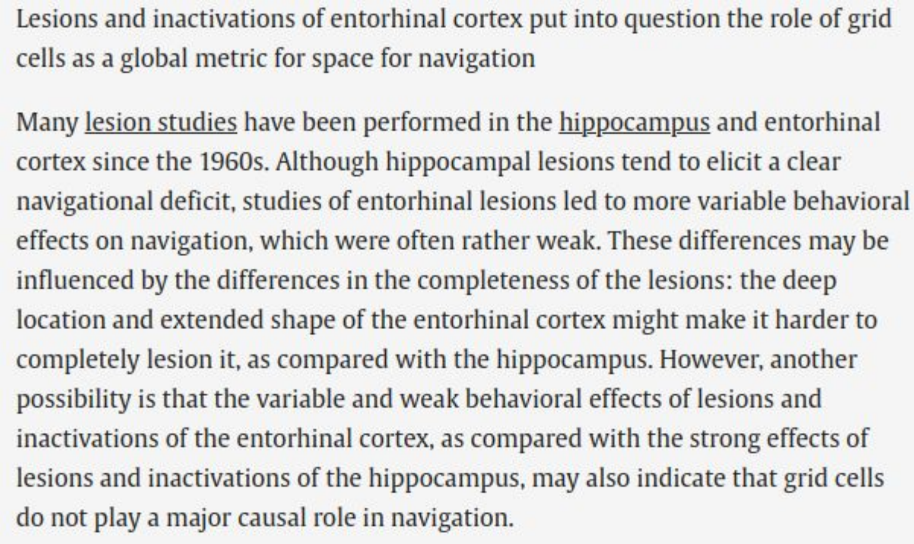
What did we learn? What questions do we have?

- What points do they make in the discussion?
- Is anything unclear?
- What would you do next if you had to design an experiment?
    - *How is the structure formed during development? from previous experience of the world? Ulsaker-Janke 2023, Tom Wills 2014*
    - *How does grid cells work in a 3D world? Work from Ulanovsky lab in Bats, clear place fields, noisy grid cells*
    - *Is the grid map actually used for navigation? Unclear lesion studies as EC is reciprocally connected to HC so hard to interpret but deficits in path integration are clear*
    - *How are larger scales represented? Multi-field place cells, Eliav et al. 2021*

Lesioning of grid cells - its complicated

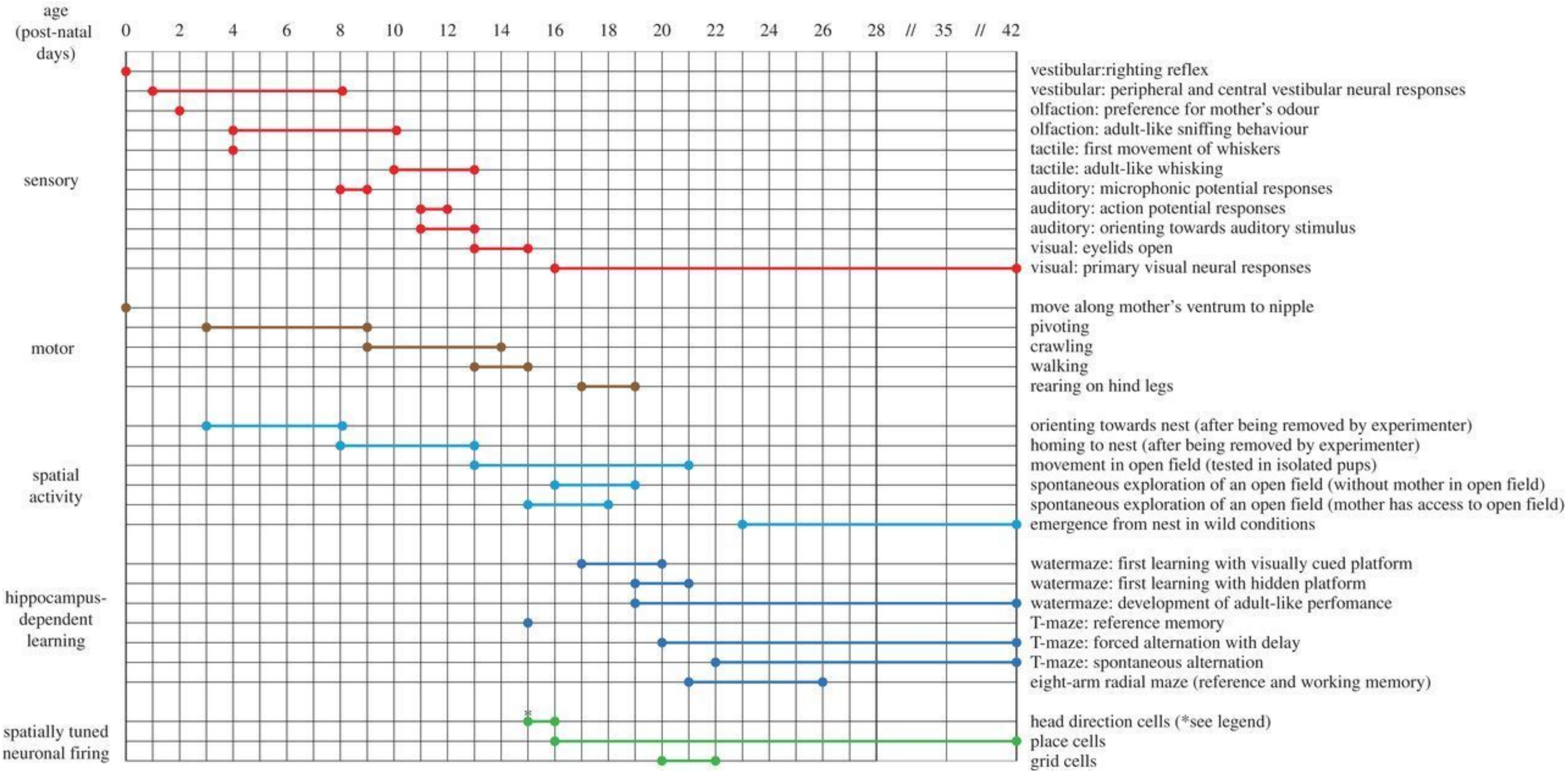


in proof). Entorhinal lesion studies indicate that damage to the grid network does impair an animal’s ability to reach a hidden goal but, because the entorhinal cortex is reciprocally connected with the hippocampus, it can be difficult to interpret these results. That said, lesions focused on the shallow layers of dorsal mEC eliminated spatial preference in rats trained on the Morris water maze [75]. Importantly, the animals were subsequently able to relearn the task, indicating that some degree of spatial processing was preserved. Less specific entorhinal lesions also produce deficits in the water maze and particularly impact an animal’s ability to navigate directly to the escape platform. Interestingly, the rats change strategy as a result, searching for the goal close to cues placed within the maze [76]. Lesions made to the entorhinal and parietal cortex also produce path integrative deficits in a homing task [77]. Similarly, bilateral disconnection of the entorhinal-hippocampal circuit was found to impair detection of a spatial change when familiar objects were moved relative to one another, possibly indicating a deficit in the ability to judge relative position [78]. However, contradictory results do exist, for example Burwell *et al.*[79] did not detect navigational deficits after making entorhinal lesions in rats. A likely source of the reported variability is that several of these studies were conducted before the discovery of grid cells, and lesions were made without knowledge of the precise topographical arrangement of those cells within entorhinal cortex.



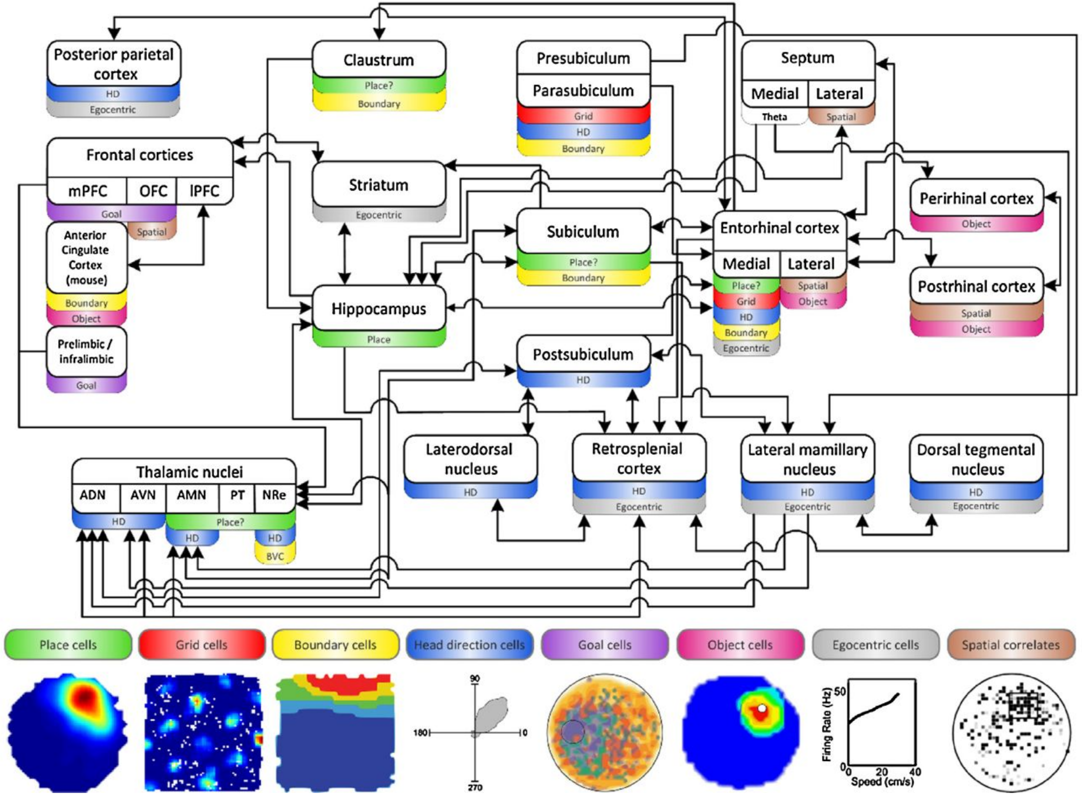
Lesions and inactivations of entorhinal cortex put into question the role of grid cells as a global metric for space for navigation

Many lesion studies have been performed in the hippocampus and entorhinal cortex since the 1960s. Although hippocampal lesions tend to elicit a clear navigational deficit, studies of entorhinal lesions led to more variable behavioral effects on navigation, which were often rather weak. These differences may be influenced by the differences in the completeness of the lesions: the deep location and extended shape of the entorhinal cortex might make it harder to completely lesion it, as compared with the hippocampus. However, another possibility is that the variable and weak behavioral effects of lesions and inactivations of the entorhinal cortex, as compared with the strong effects of lesions and inactivations of the hippocampus, may also indicate that grid cells do not play a major causal role in navigation.



Tom Wills 2014

The cognitive map theory



Grieves et al. 2017