*Sloan-Swartz Centers 2010 Meeting*

**Yale Univ., June 30th**

# Mechanisms for representing and remembering space

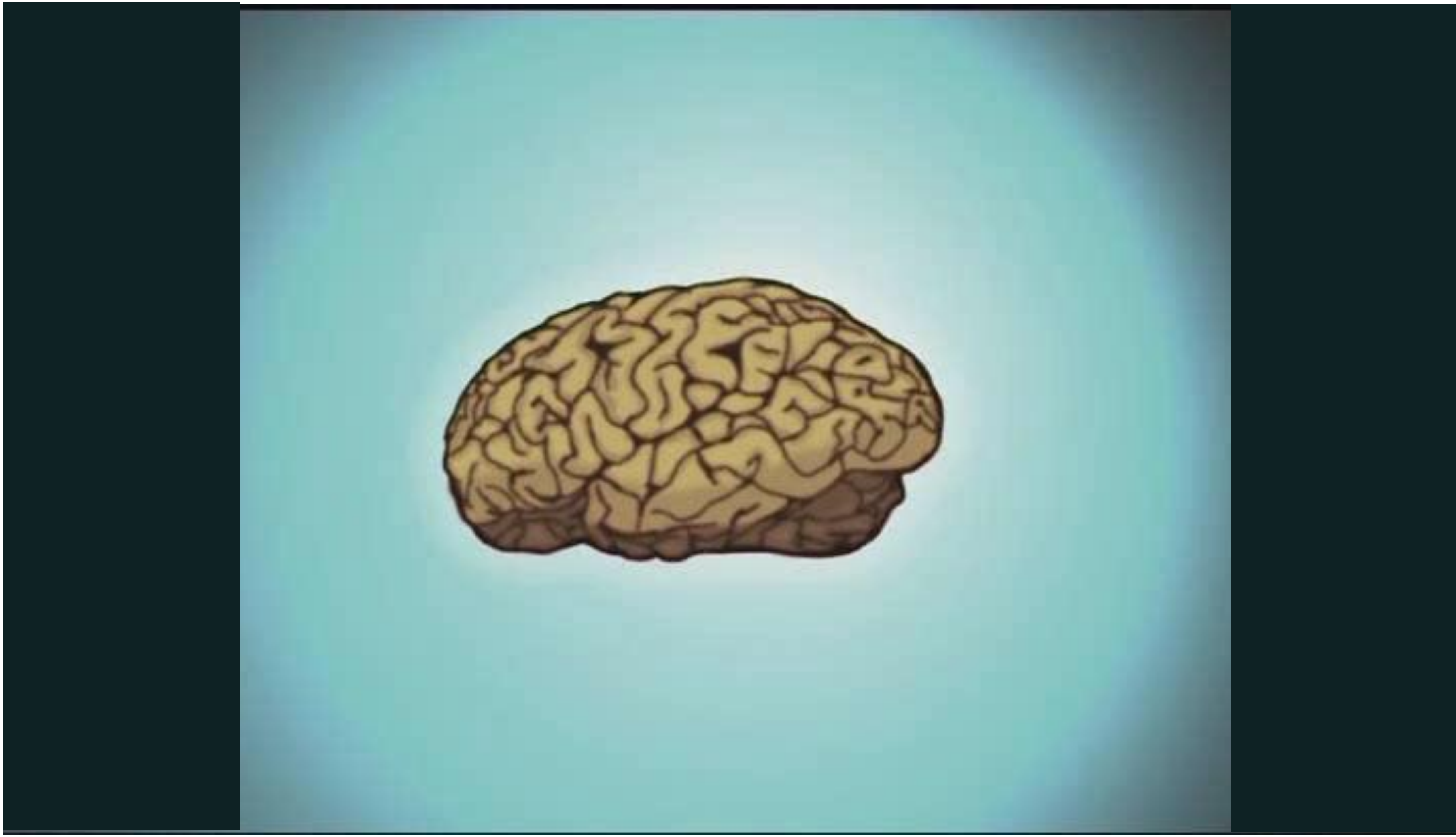
**May-Britt Moser**

**Kavli Institute for Systems Neuroscience,**

**Centre for the Biology of Memory,**

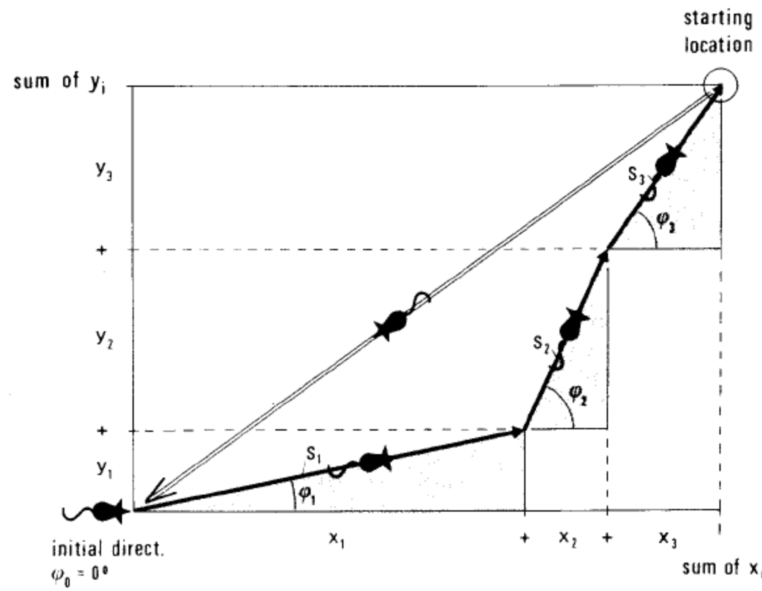
**NTNU, Trondheim, Norway**

# Can we understand computation in the brain?



100 billion ($10^{11}$) neurons, 10 000 synapses per neuron

# Starting with a simple question: Where am I?




McNaughton et al. (2006), Nature Rev Neurosci 7, 663-678.

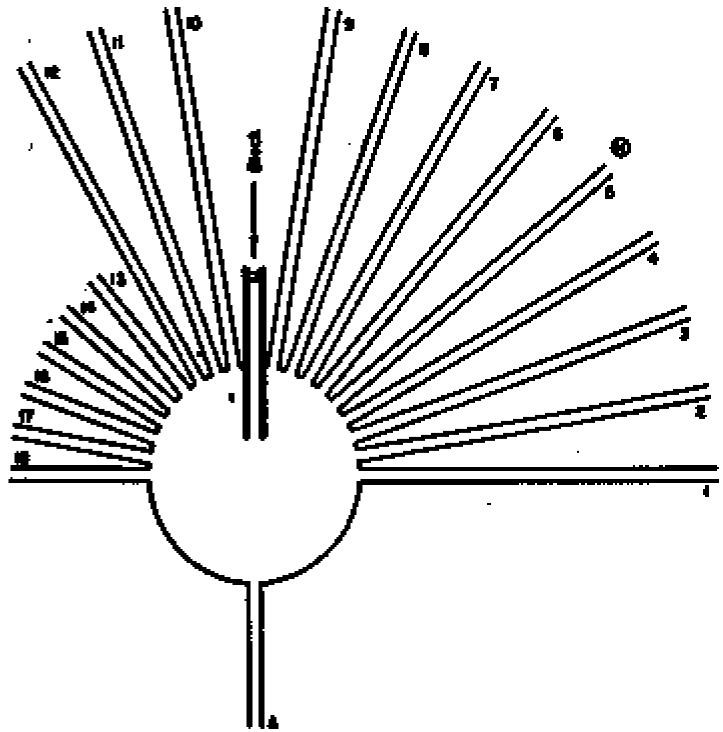
How does the brain compute position?

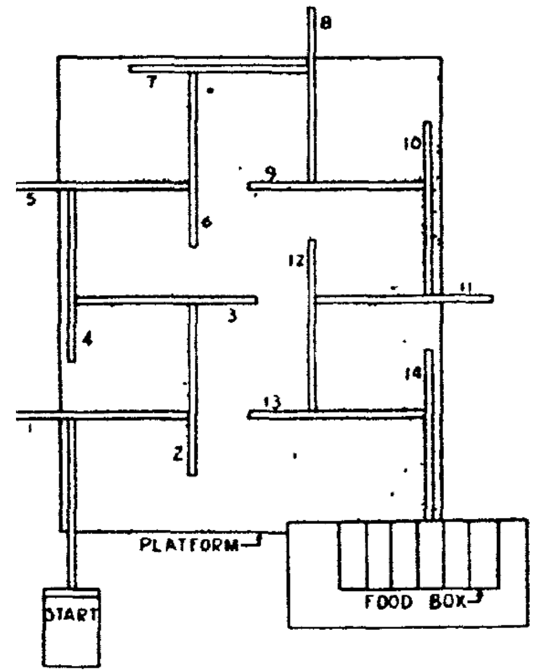
How does the brain maintain and update a representation of self-location?

How is information about location stored in memory?

# Experimental study of spatial mapping has a long history

Edward C.Tolman (1948):
”Cognitive maps in rats and men”






Apparatus used in the test trial

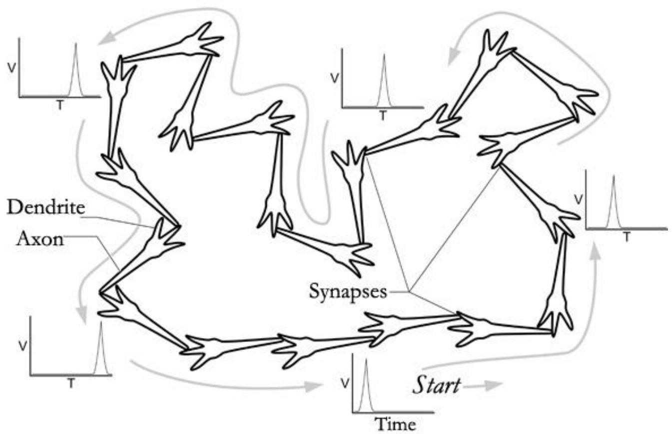
FIG. 16

(From E. C. Tolman, B. F. Ritchie and D. Kalish, Studies in spatial learning. I. Orientation and short-cut. *J. exp. Psychol.*, 1946, 36, p. 17.)

# Taking cognition into the brain

Donald O. Hebb

***The Organization of Behavior*** **(1949)**



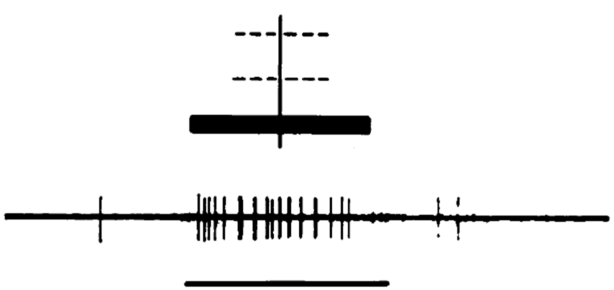

Concepts: * activity dependent plasticity
* cell assemblies

David Hubel and Torsten Wiesel

Tools: *single unit recordings

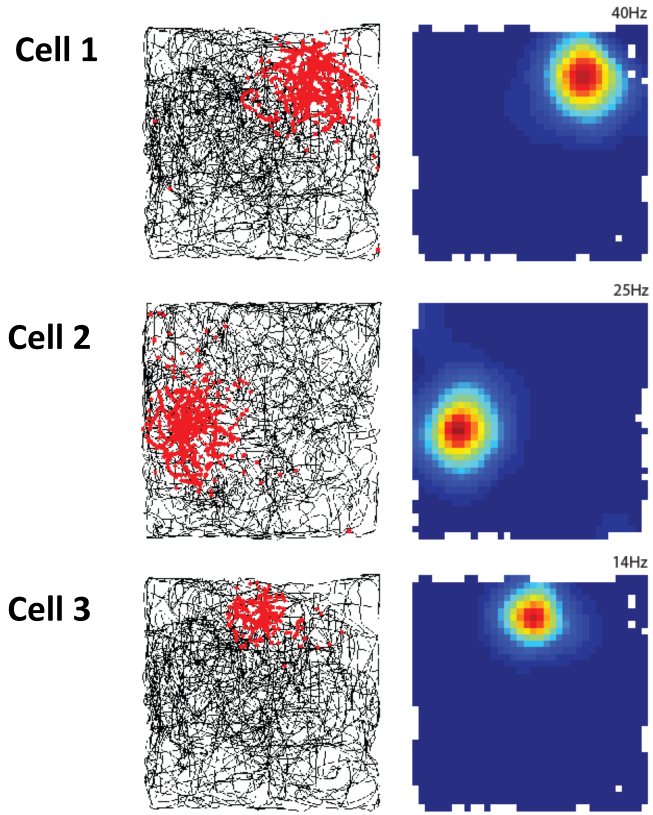
**Stimulus:**

**Response:**



# Place cells in the hippocampus (O'Keefe & Dostrovsky, 1971) – a window to cortical computation

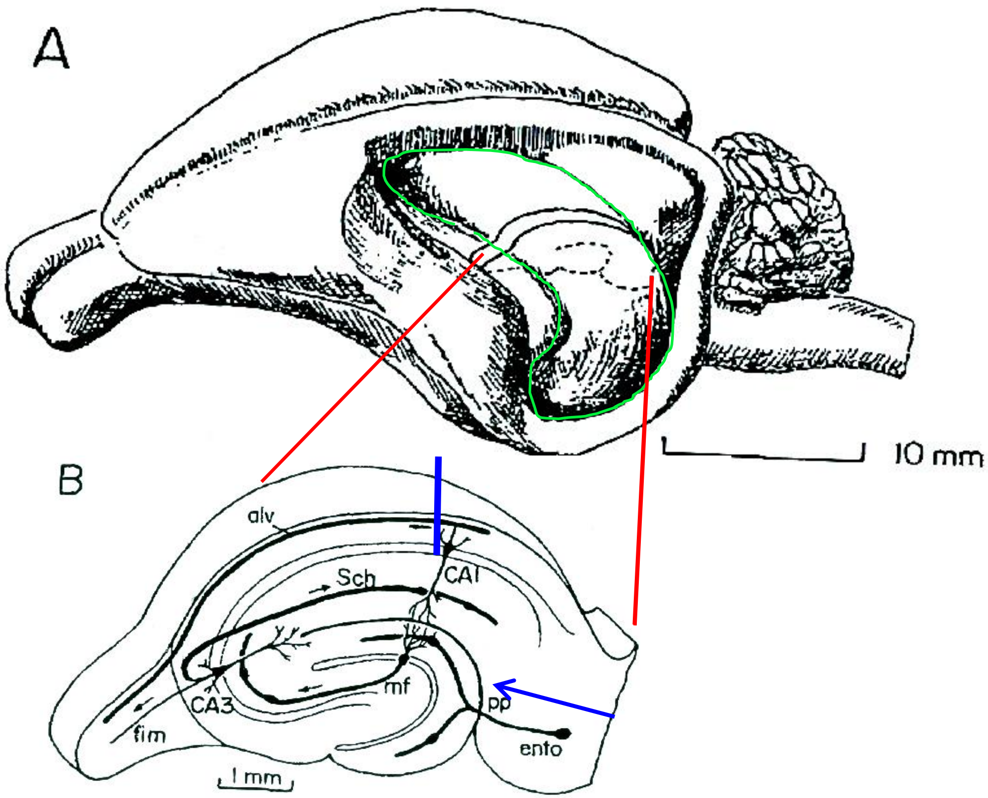
John O'Keefe: 1971-




Laura Colgin, Kavli Institute for Systems Neuroscience

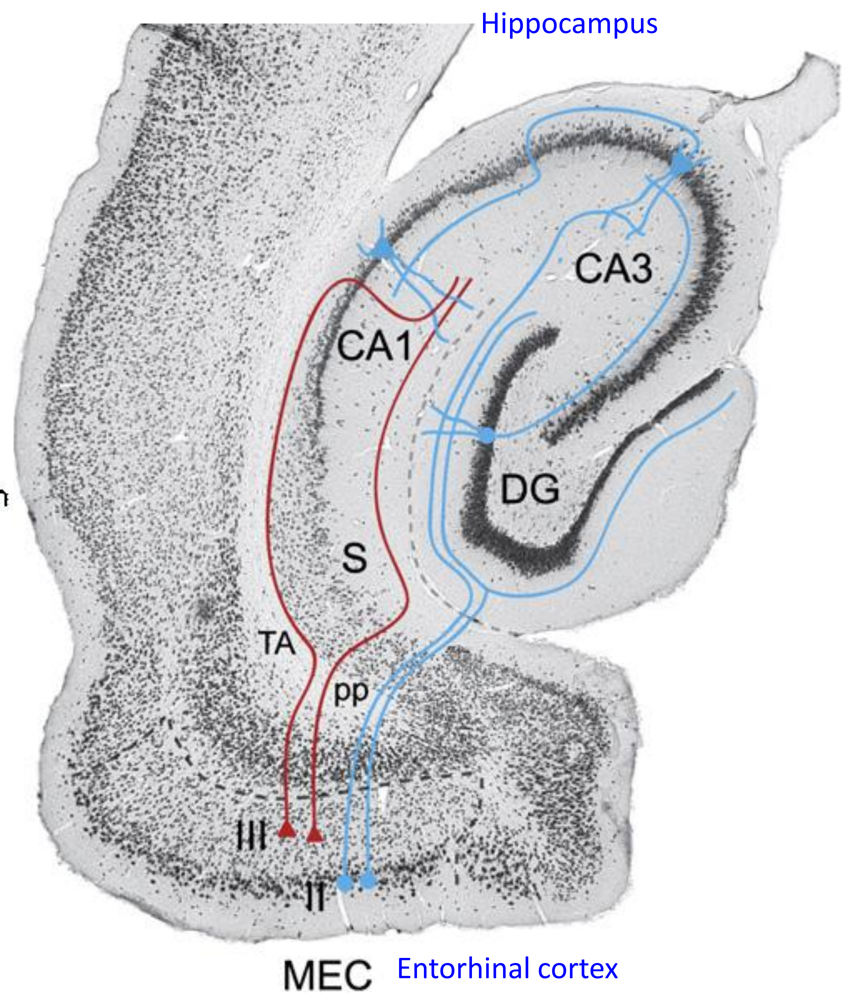
# Where and how are the place signals computed?

Indirect pathway (trisynaptic circuit)




The rodent hippocampus
(Andersen, Bliss and Skrede, 1971)

Direct pathway

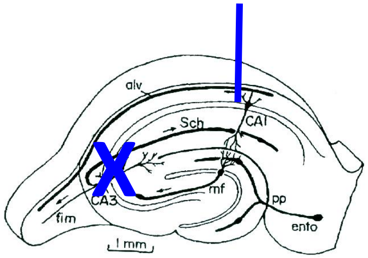


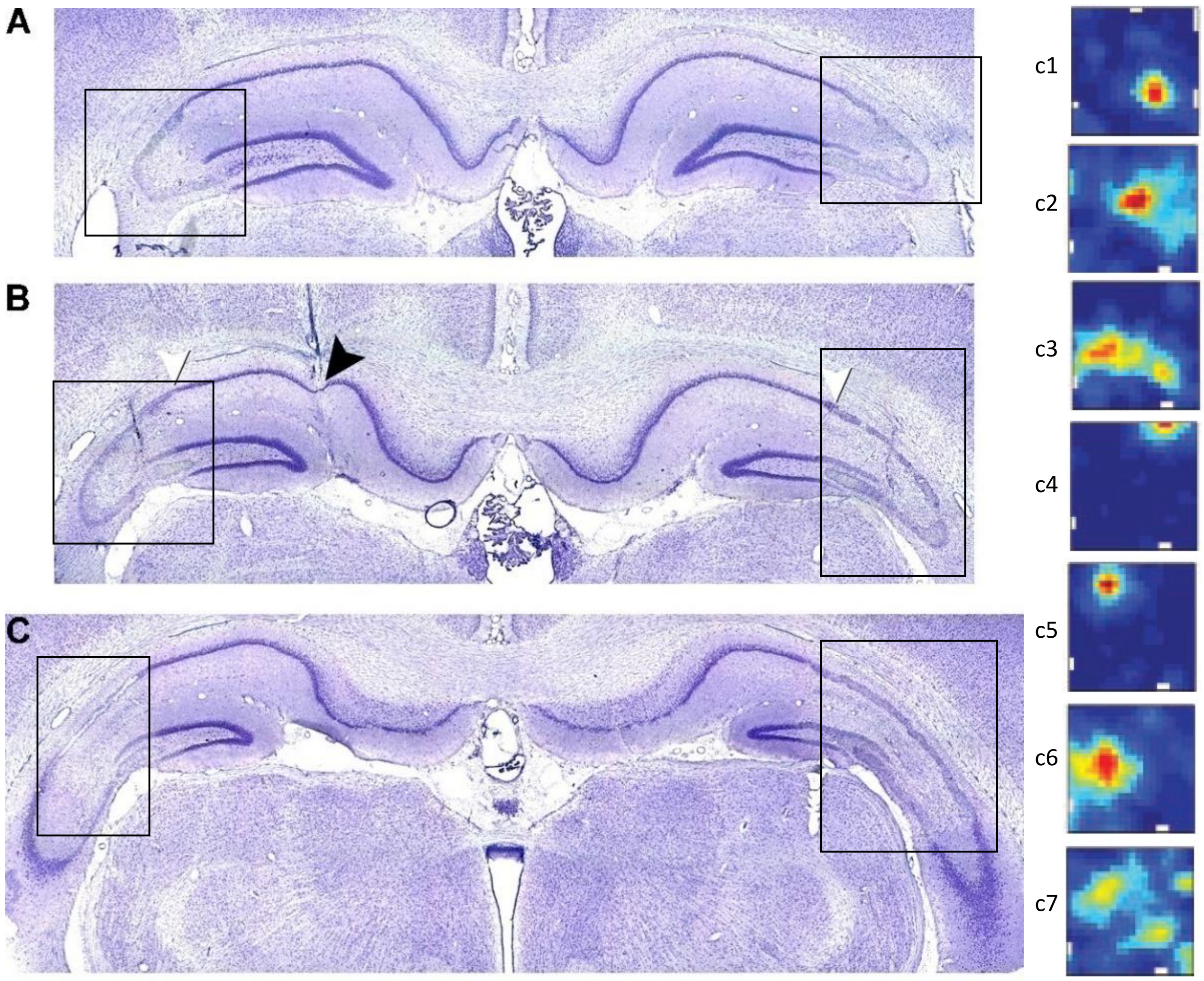

Brun et al., (2008). *Neuron*, 57, 290-302

# Place information may be imported from entorhinal cortex

CA1 cells continue to express place fields after lesion of the indirect intrahippocampal pathway,

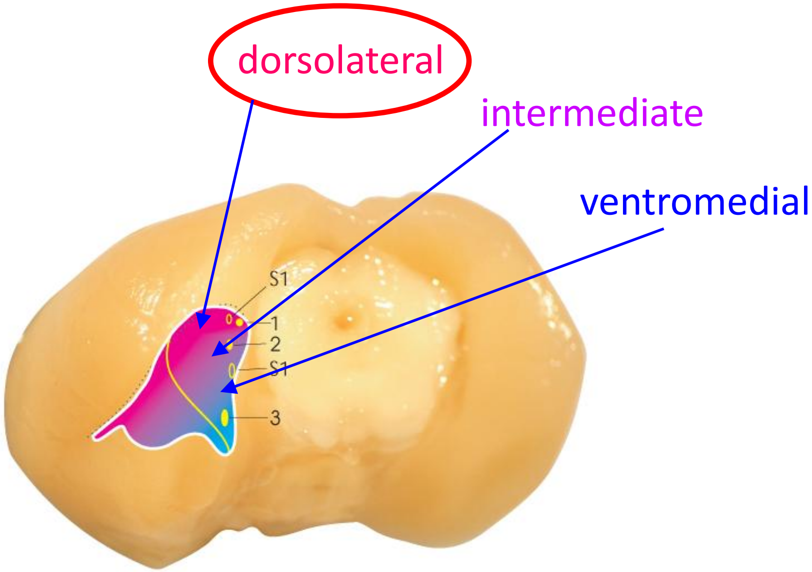
i.e. spatial signals may be conveyed by the direct entorhinal-hippocampal pathway



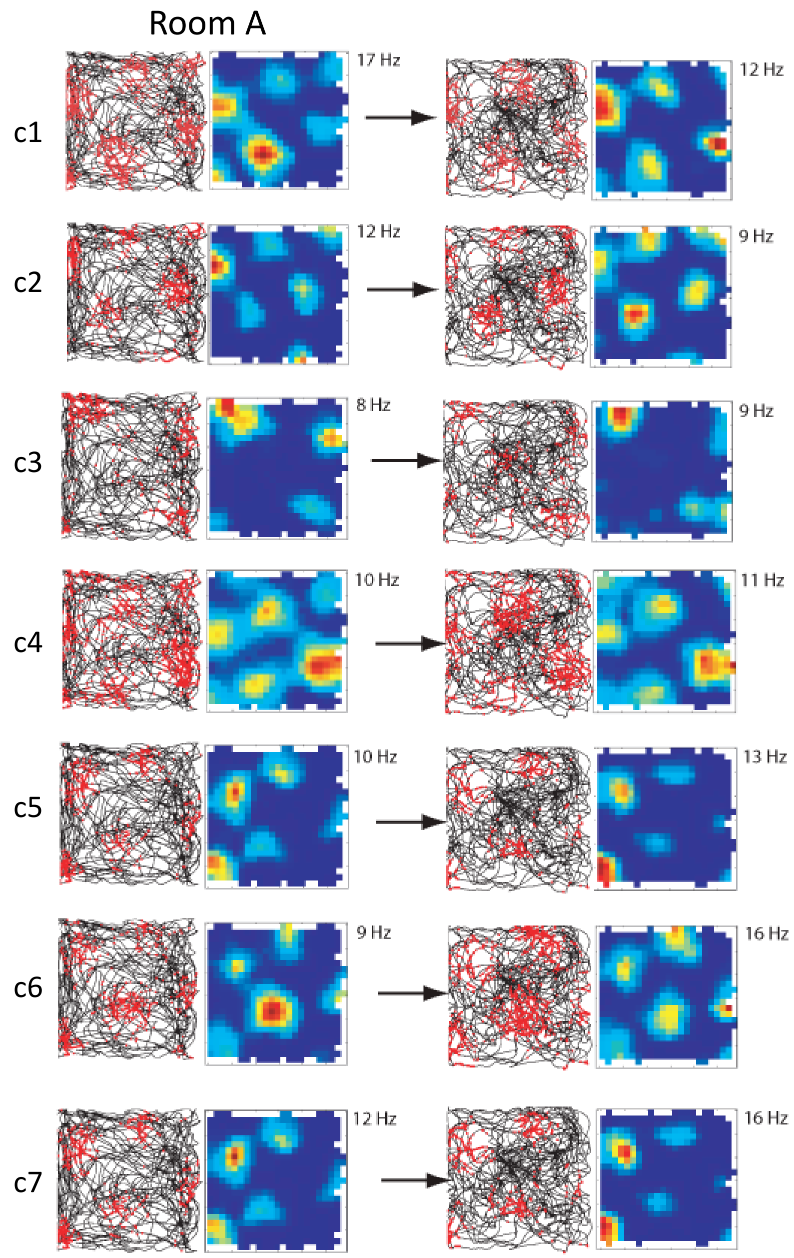




Brun et al. (2002). *Science* 296:2243-2246

We recorded from the part of medial entorhinal cortex that provides the strongest input to the dorsal hippocampus, where most place cells have been recorded

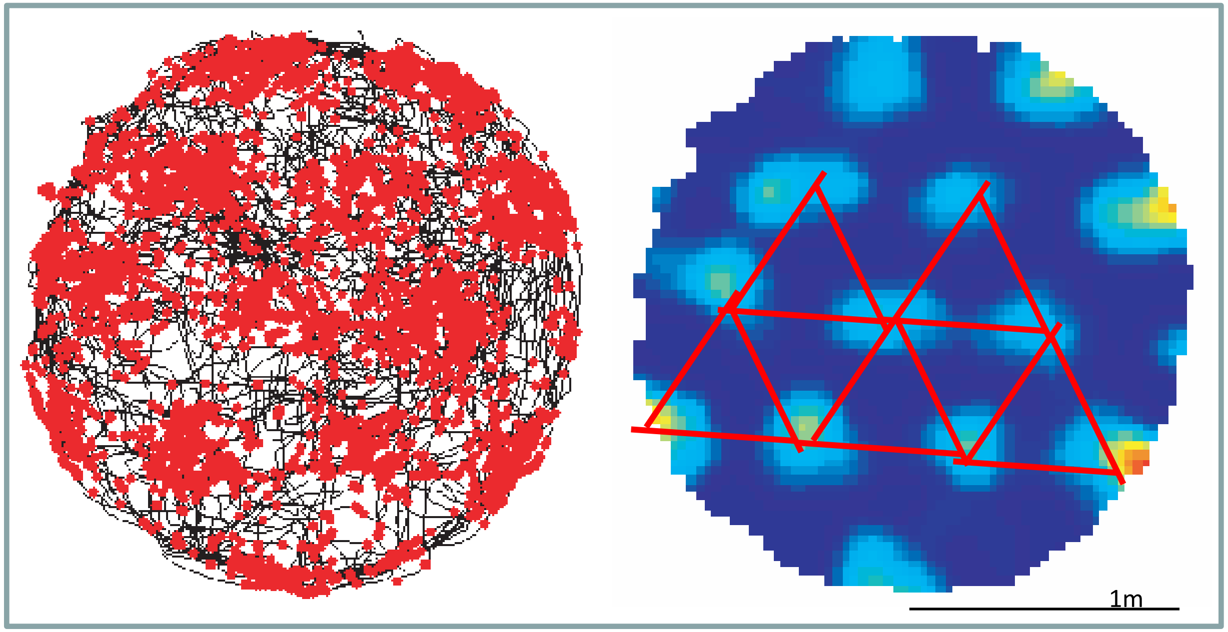



Fyhn et al. (2004). *Science* 305:1258-1264

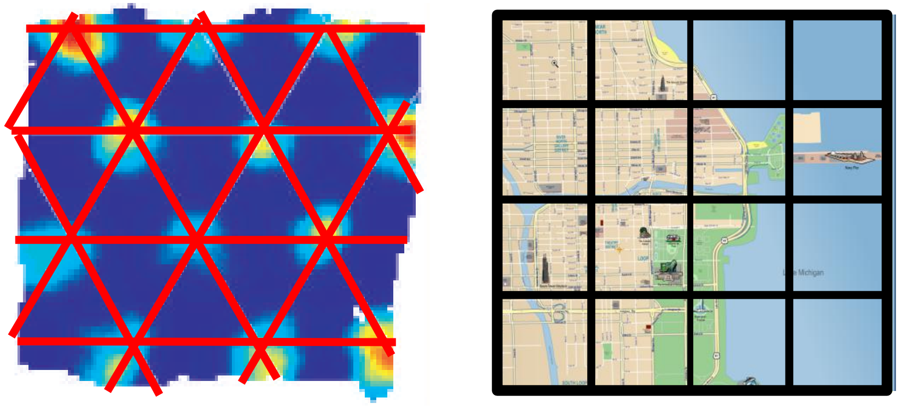



Entorhinal cells have sharp firing fields but each cell has multiple fields and the fields exhibit a regular pattern

# Grid-cells : the metric of the spatial map




**The firing pattern is similar to the grid of a map**

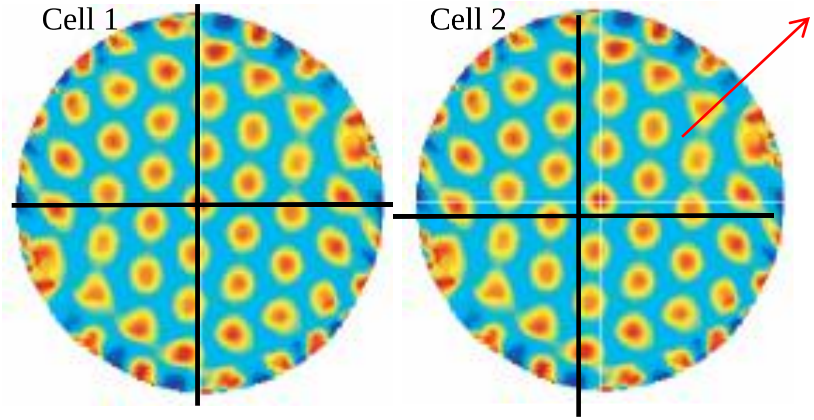


Hafting et al. (2005).
*Nature* 436:801-806

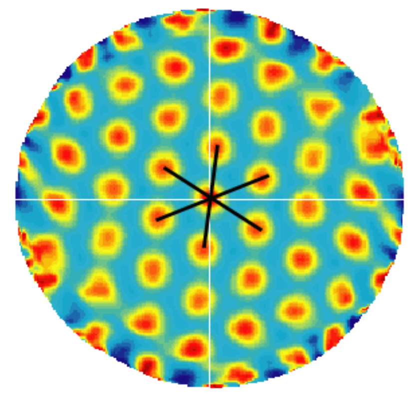
# 1. The anatomical structure of the grid map

# Grid cells have three dimensions of variation

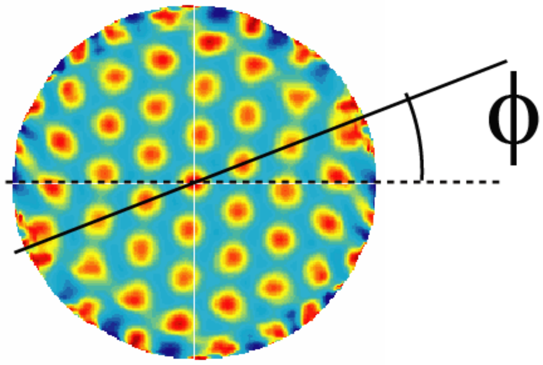
1. Spatial phase (displacement of nodes in x-y coordinates)




2. Spatial frequency (scale, spacing)



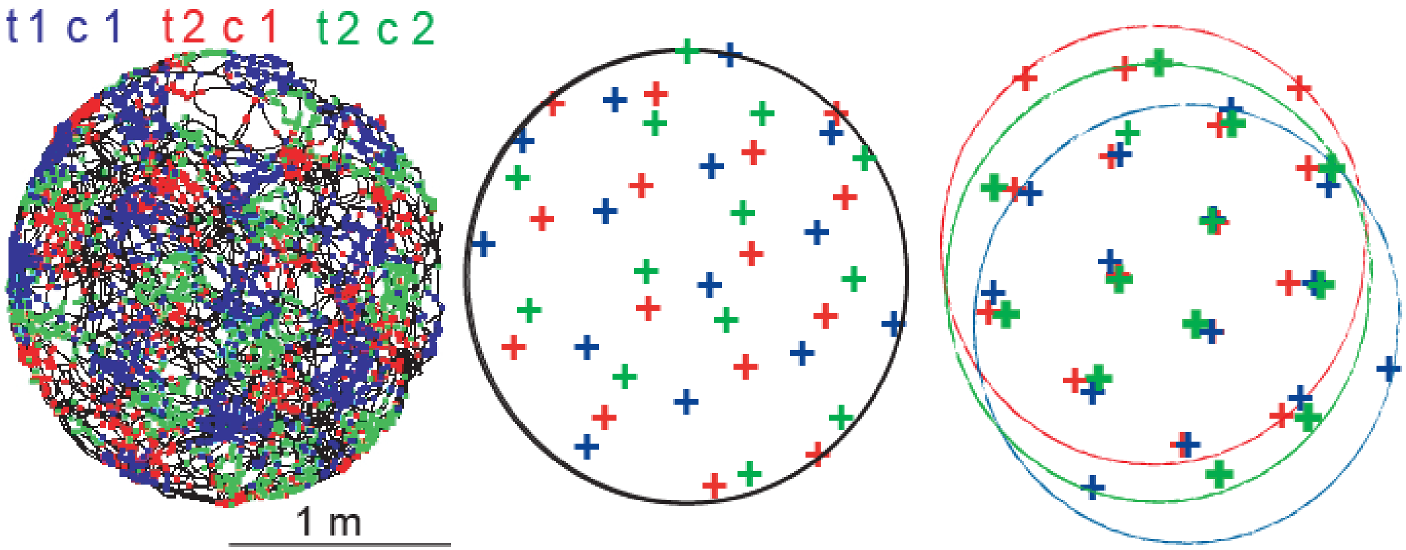
3. Spatial orientation (tilt)




Grid cells may be organized according to these dimensions

# 1. Grid phase is distributed

**3 colocalized grid cells:**

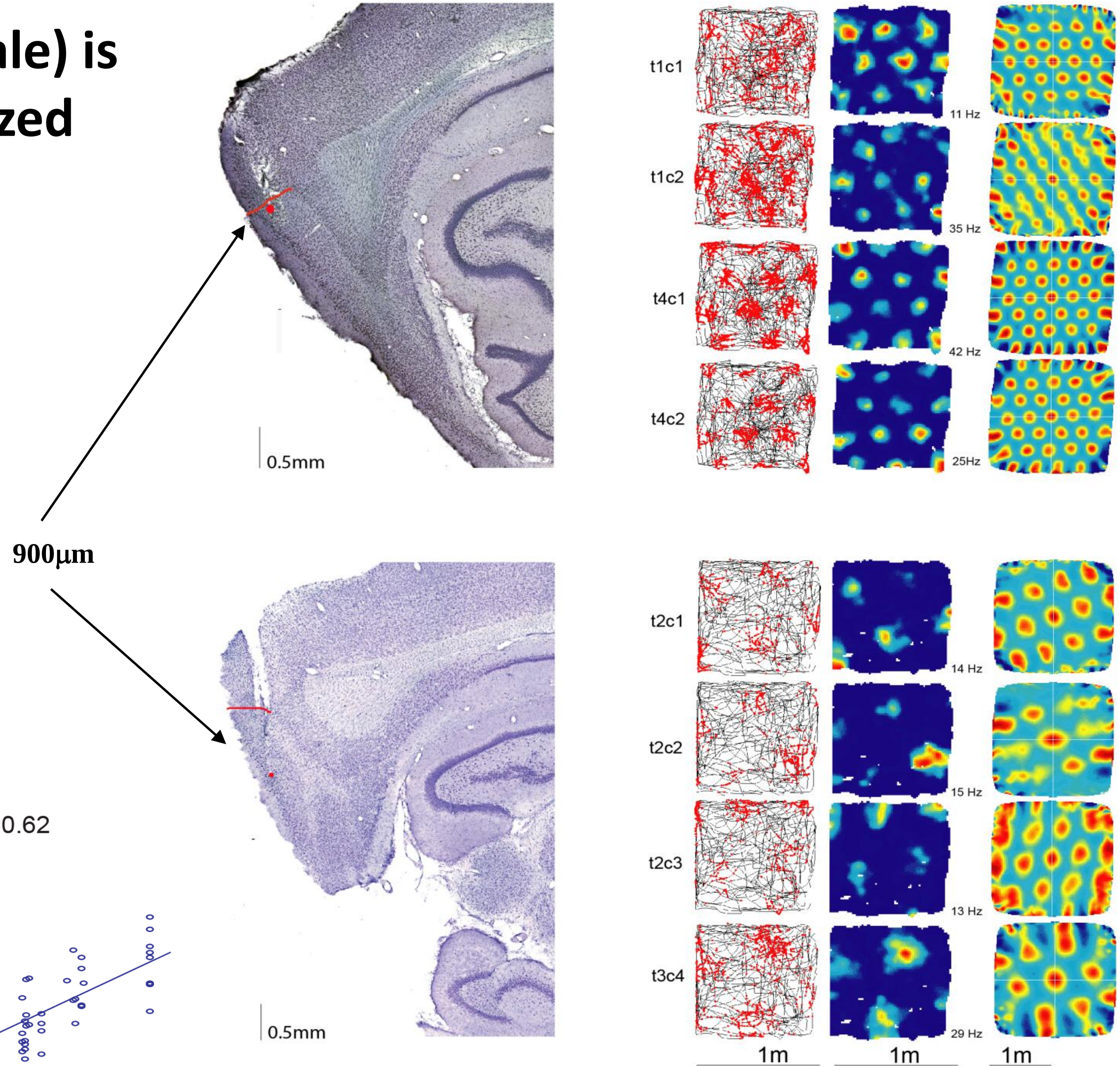


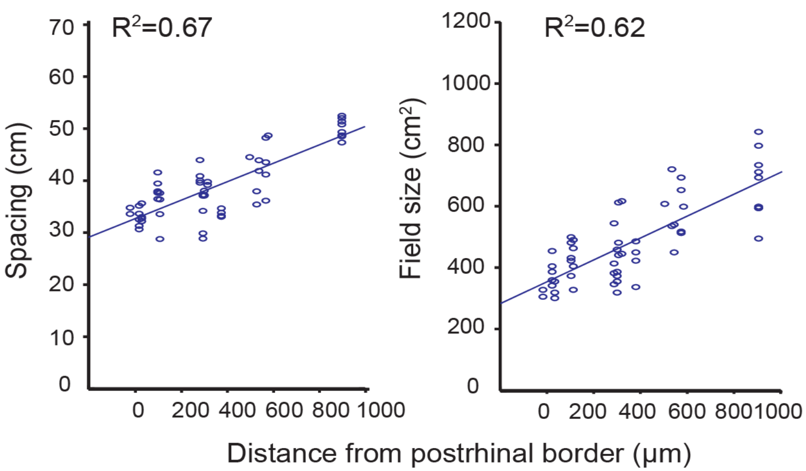

Hafting et al. (2005). *Nature* 436:801-806

**Thus, the complete environment is represented throughout the medial entorhinal cortex**

# 2. Grid frequency (scale) is topograhically organized

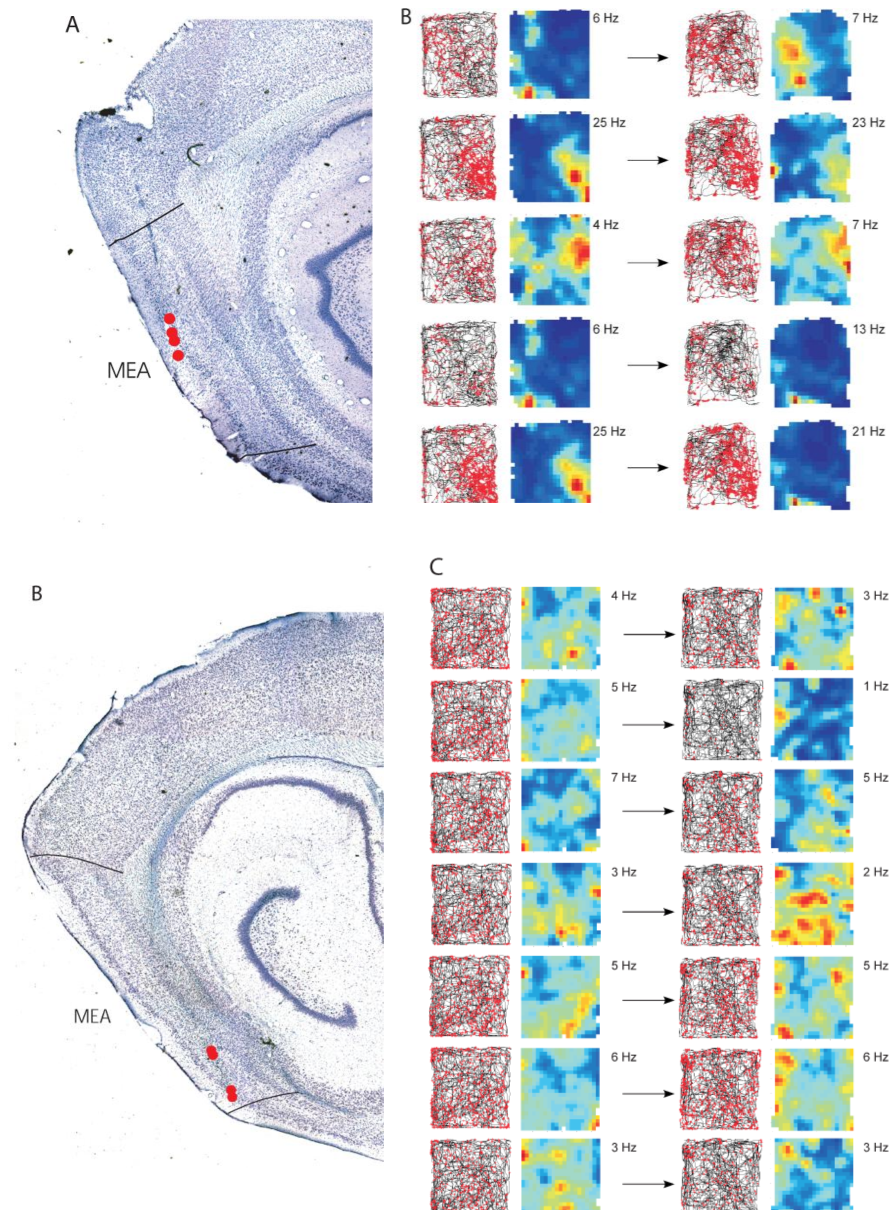
**Grid size increases from dorsal to ventral MEC**




Hafting et al. (2005). *Nature* 436:801-806

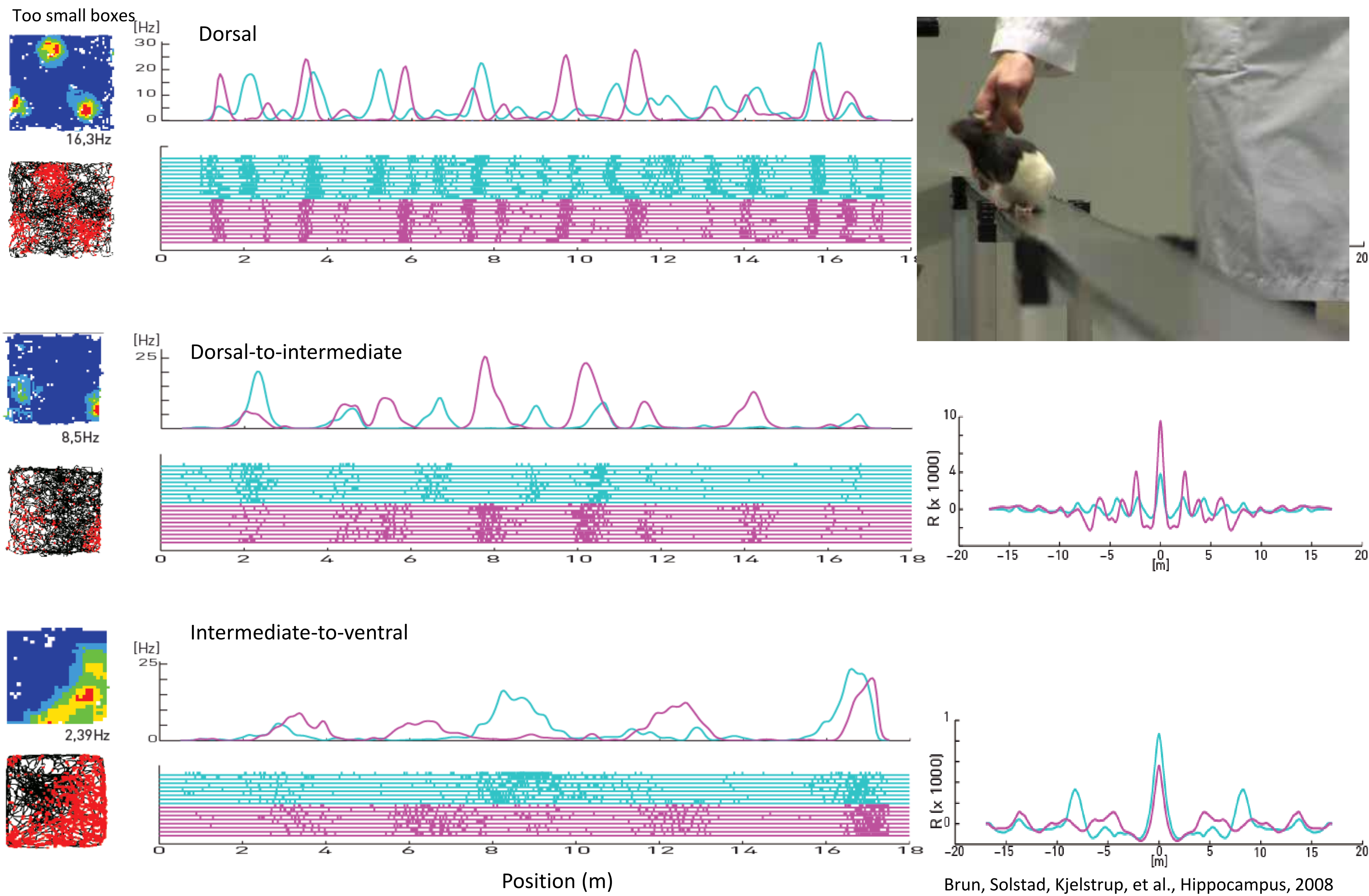
# Is the entire dorsoventral axis involved in the spatial map?




Fyhn et al. (2004). *Science* 305:1295-1298

Larger environments may be needed

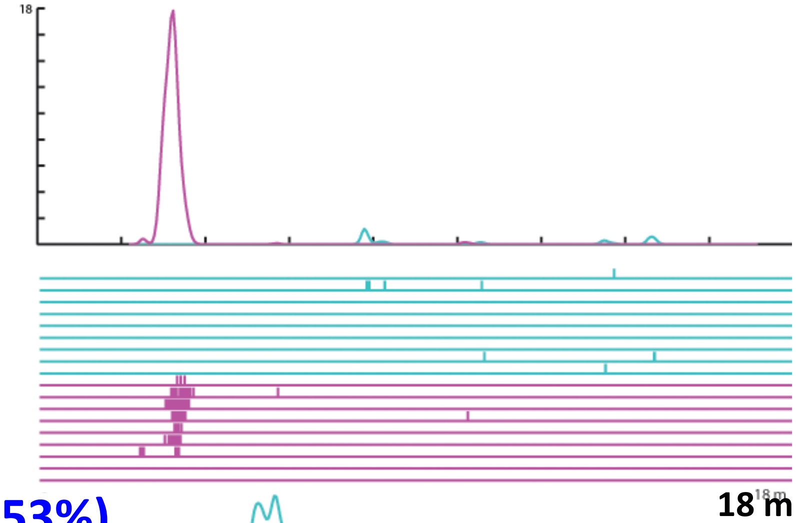
# Grids scale up from dorsal to ventral MEC



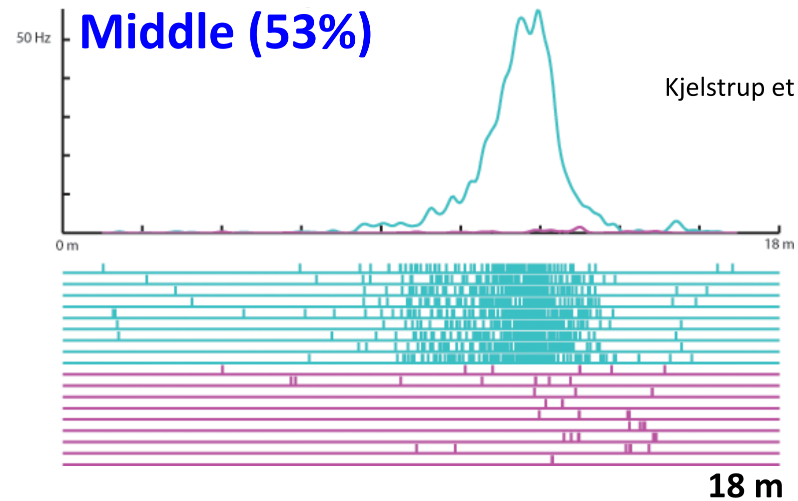

Brun, Solstad, Kjelstrup, et al., Hippocampus, 2008

The gradient in grid scale is mirrored in place cells in the hippocampus

Dorsal (30%)

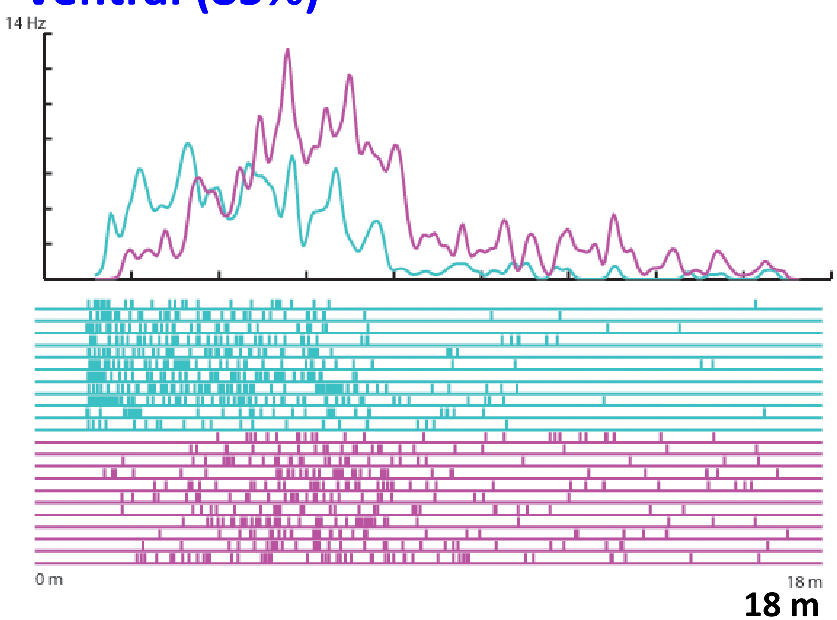


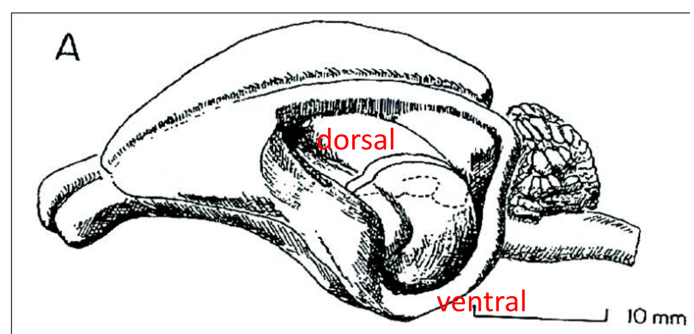

Middle (53%)



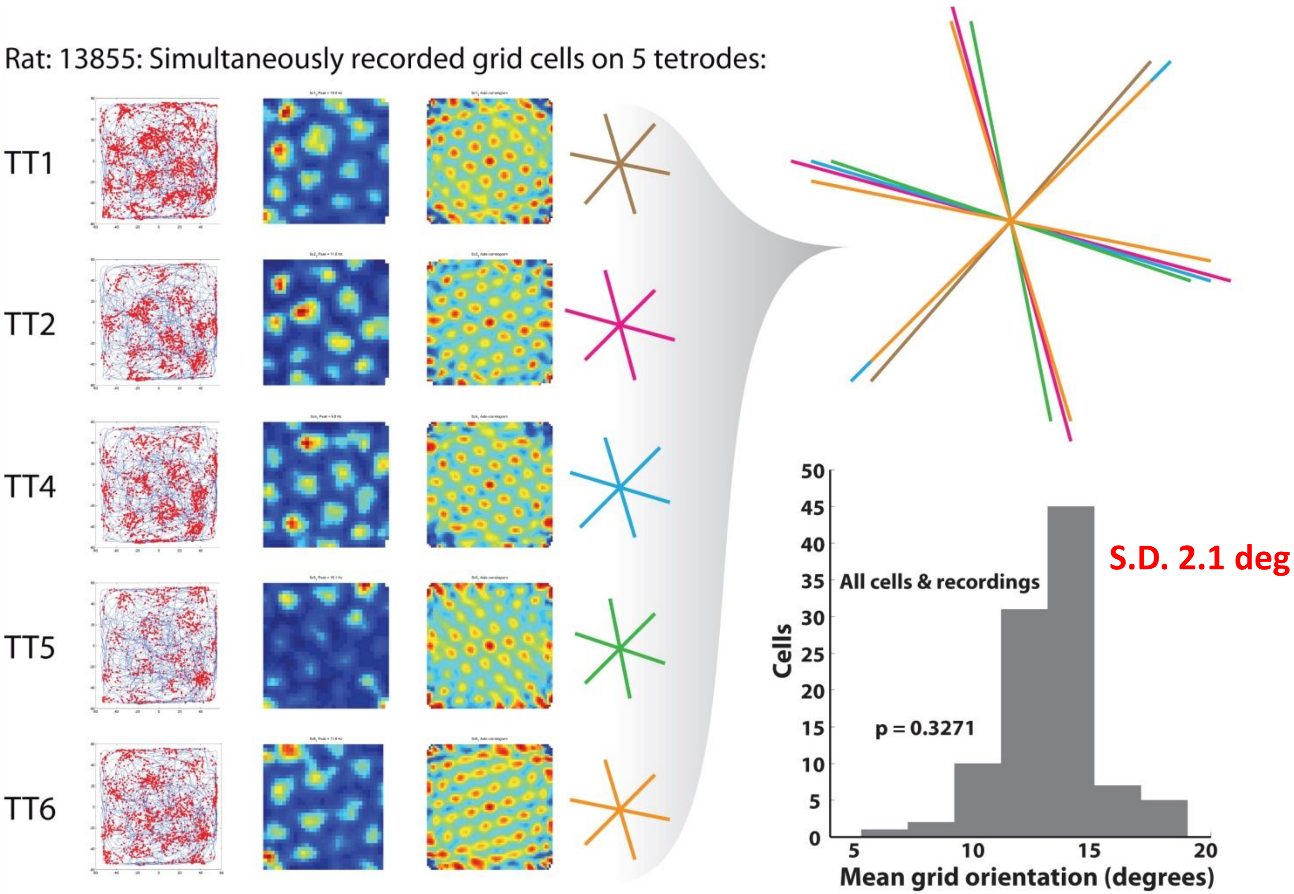

Kjelstrup et al., *Science*, 2008

Ventral (85%)

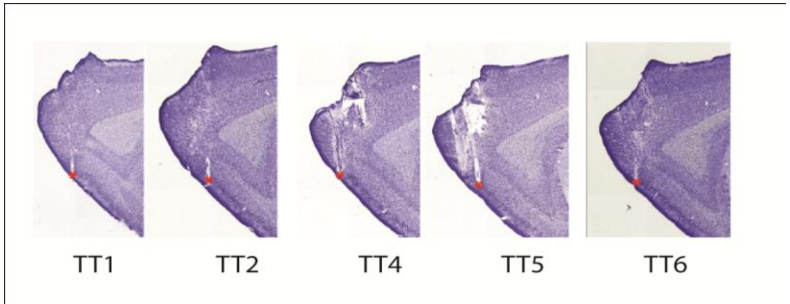


# 3. Grid orientation is usually similar for co-localized grid cells




**Distance between TT1 and TT6: 1.2 mm**

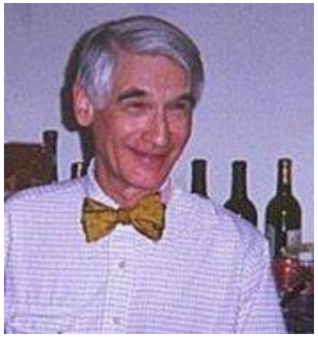


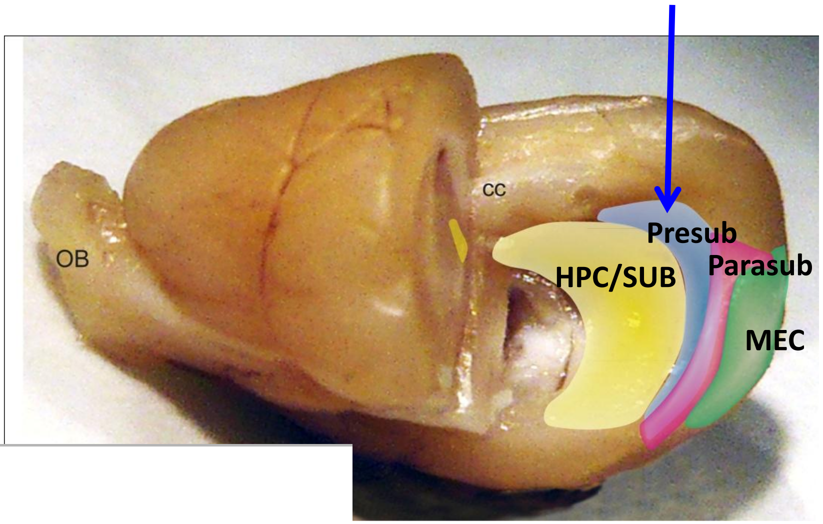

**Looks quite similar across large parts of dorsal MEC…**

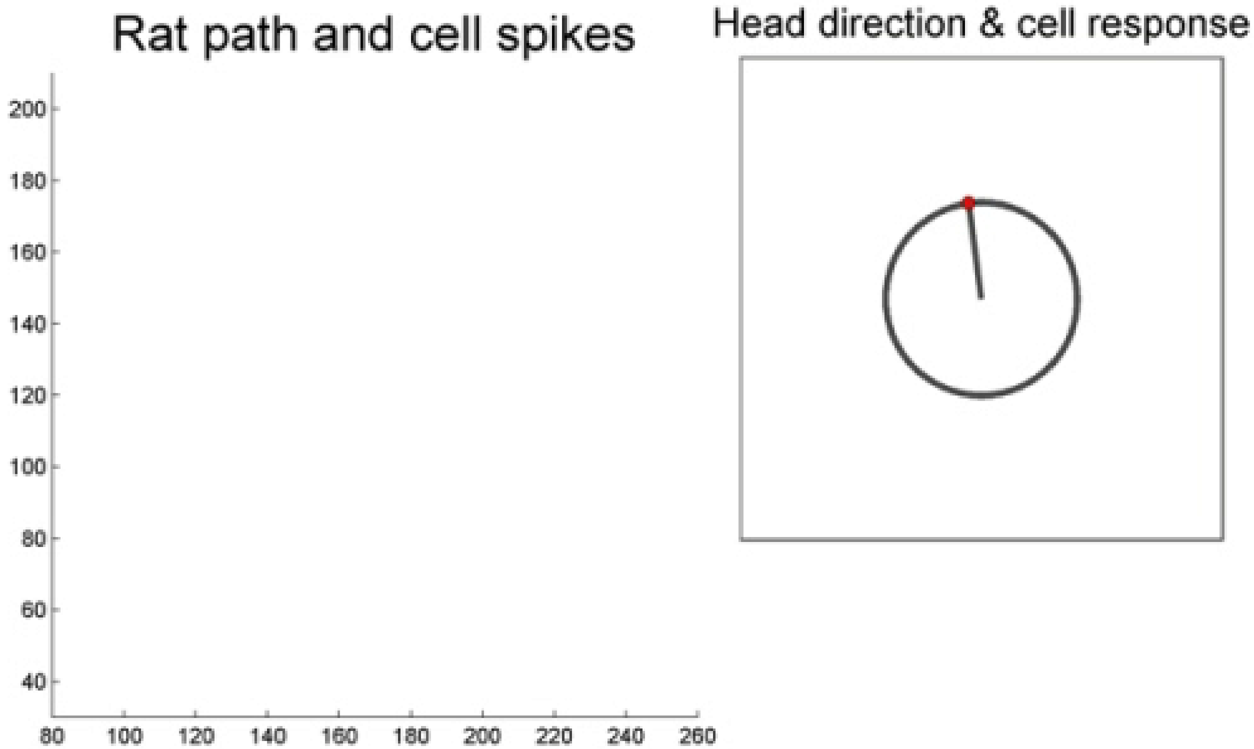
Stensland, Kirkesola, Moser, Moser, unpublished

**2. The entorhinal map contains multiple cell types that collectively contribute to representation of self-location**

Head direction cells in the presubiculum – an internal compass (Ranck, 1985)

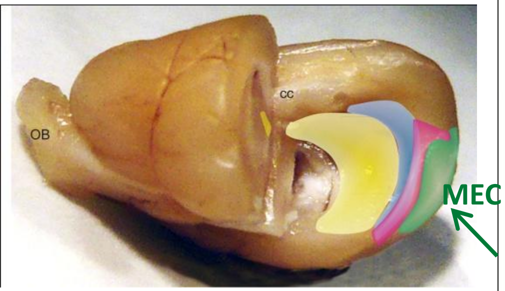

James B. Ranck Jr

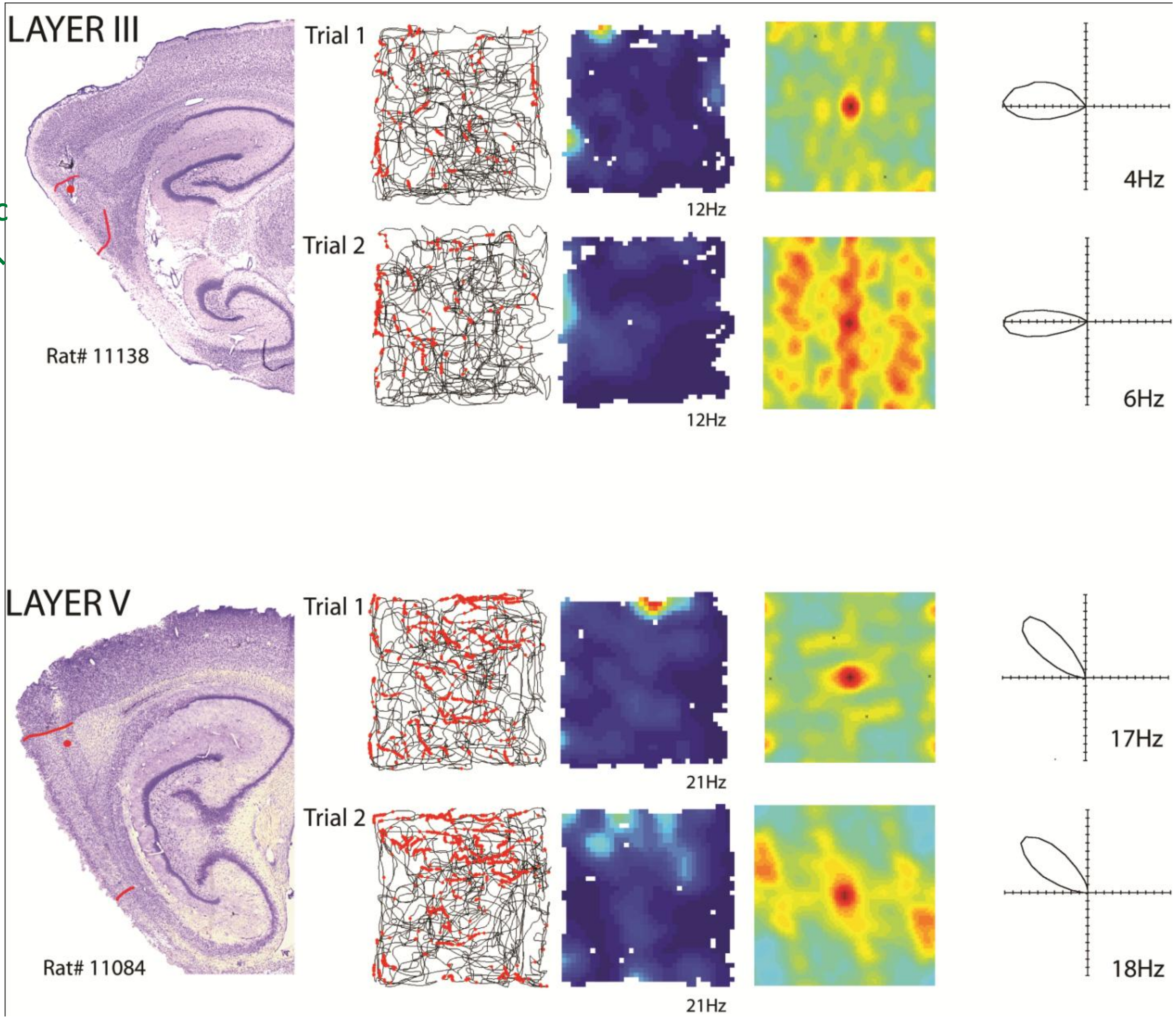



Tor Kirkesola, 2010

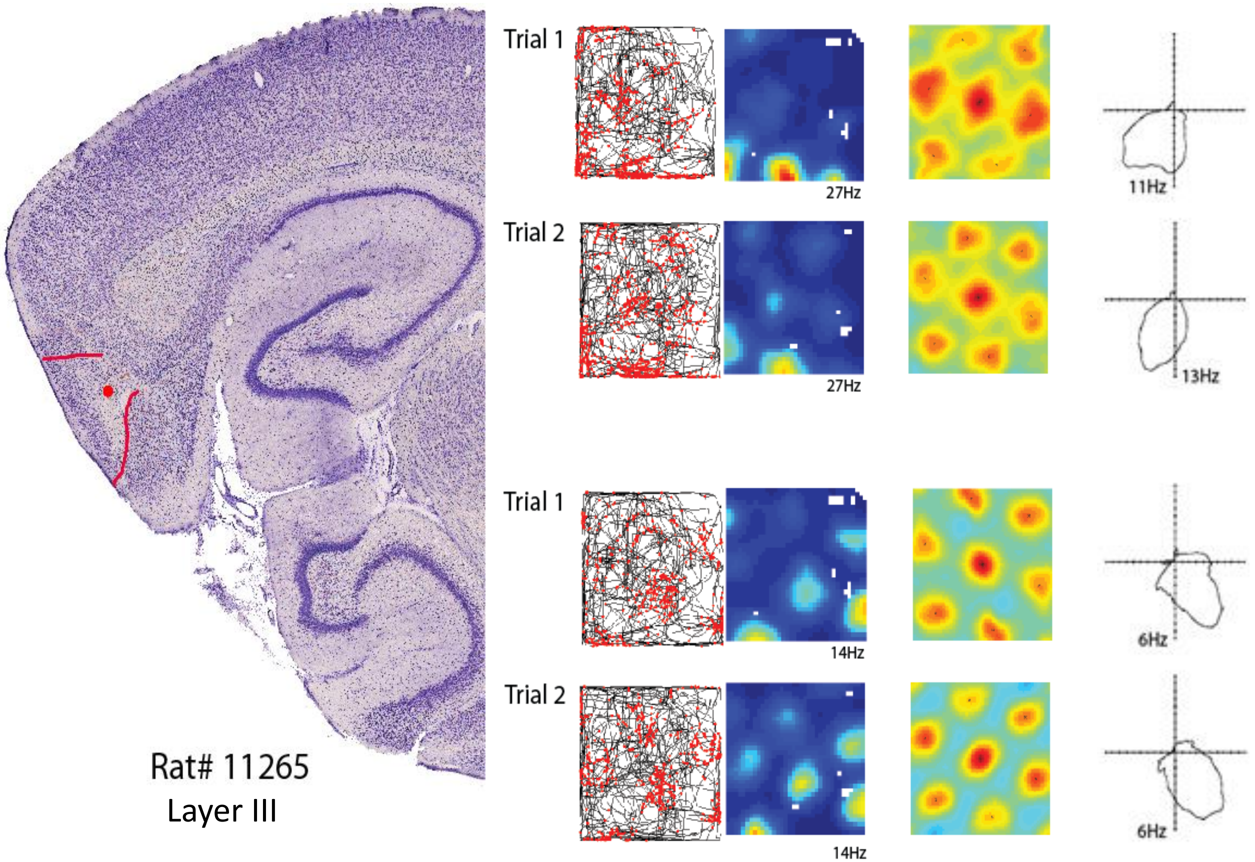
# Head-direction cells are abundant also in medial entorhinal cortex




Sargolini et al. (2006), *Science* 312, 758-762

# Many entorhinal head direction cells are also grid cells (conjunctive grid X head-direction cells)

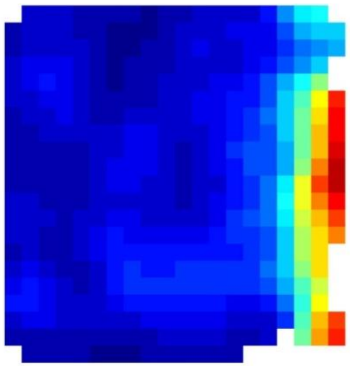



Sargolini et al. (2006), *Science* 312, 758-762

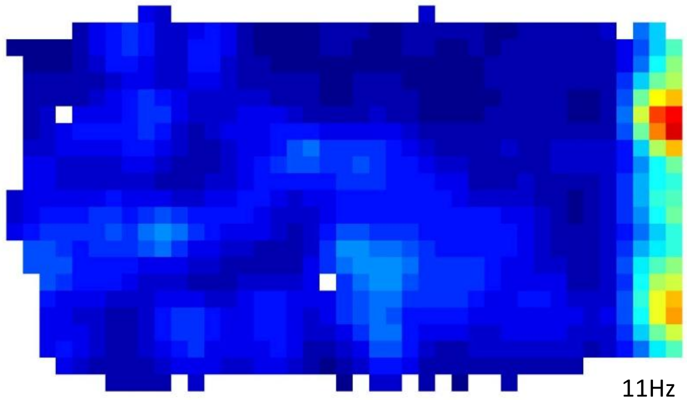
# A third entorhinal cell type responds to local geometric **borders**

The firing fields of the border cells follow the walls of the box when the box is stretched…

….in the *x* direction:

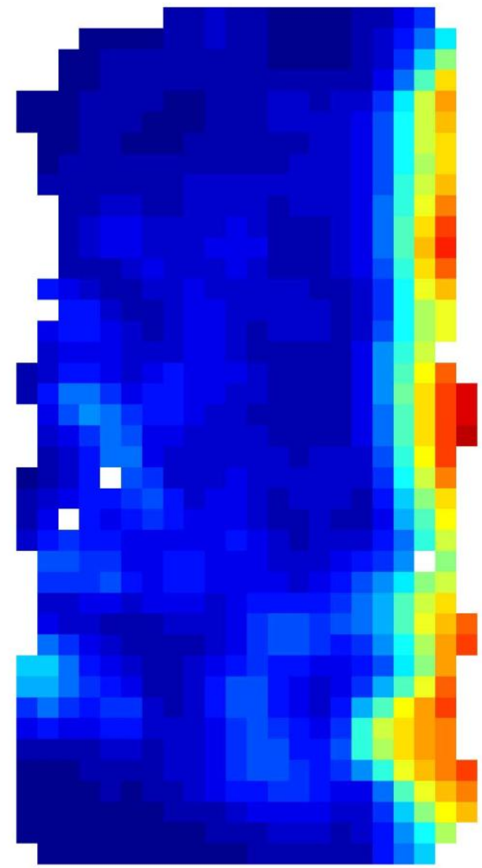


13Hz



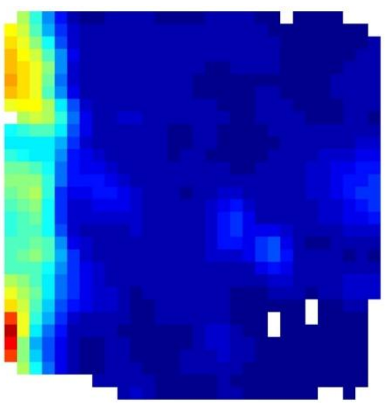
11Hz

….and in the *y* direction:

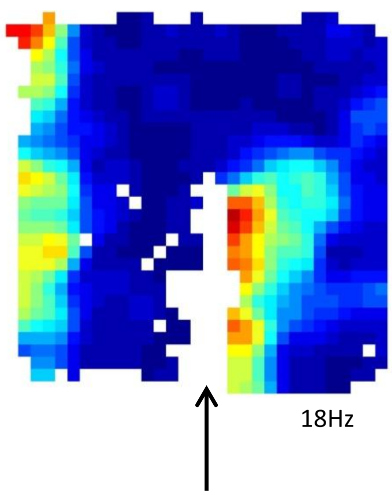


9Hz

Introducing a barrier duplicates the firing field:



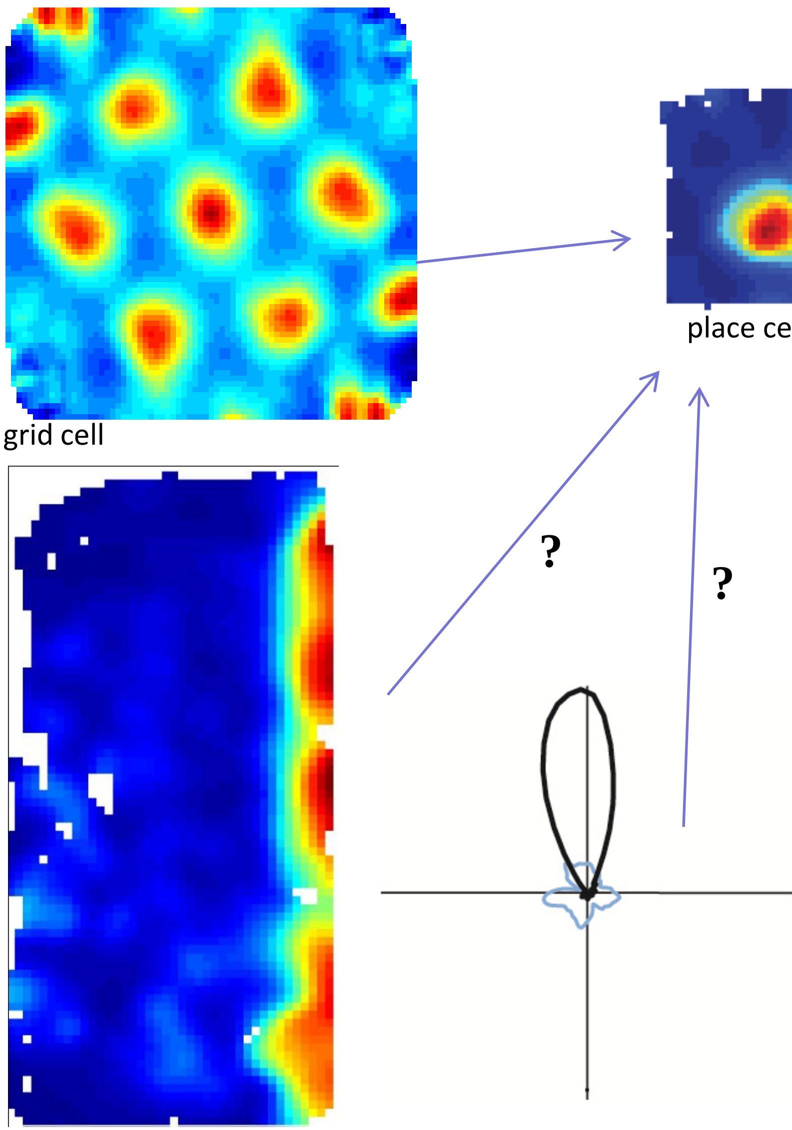
24Hz

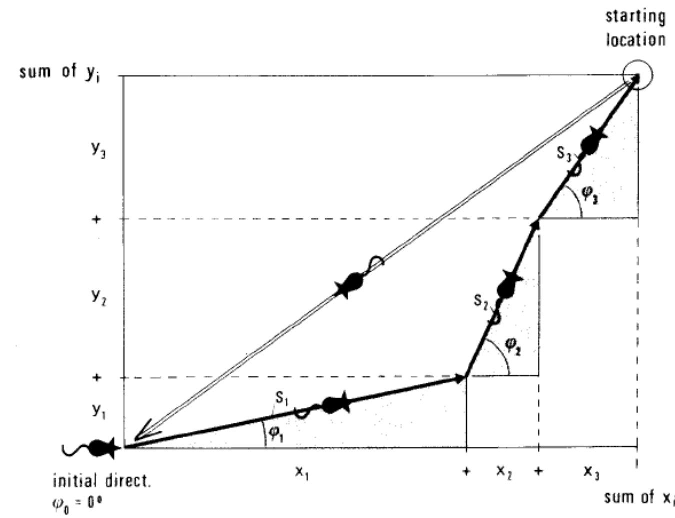


18Hz

Solstad et al. (2008), *Science* 322, 1865-1868)

# Are these cell types elements of a metric path integration-based navigation system?



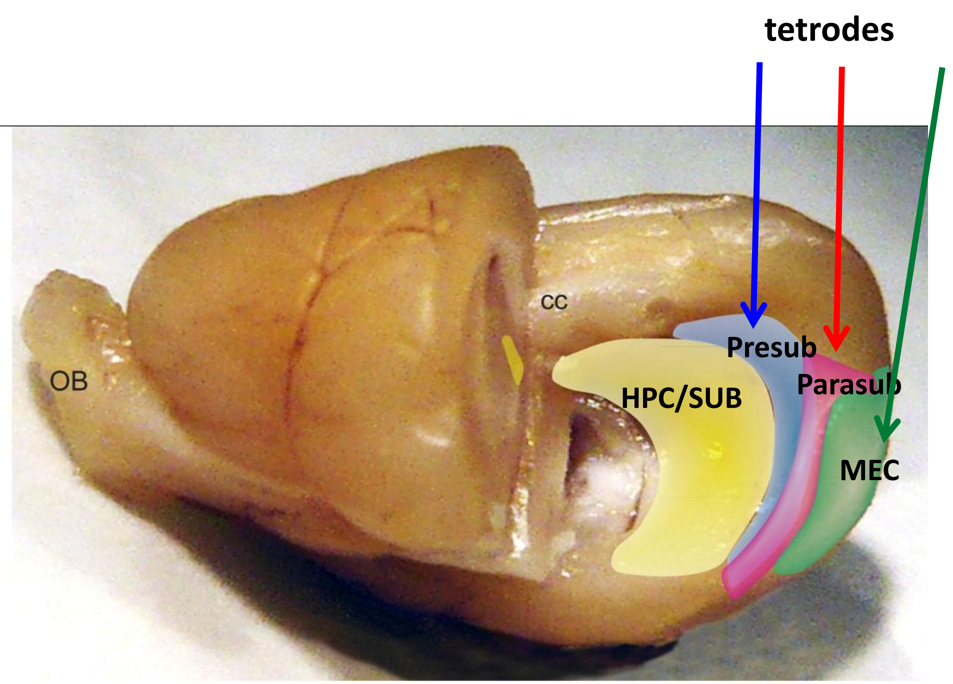

McNaughton et al. (2006), Nature Rev Neurosci 7, 663-678.

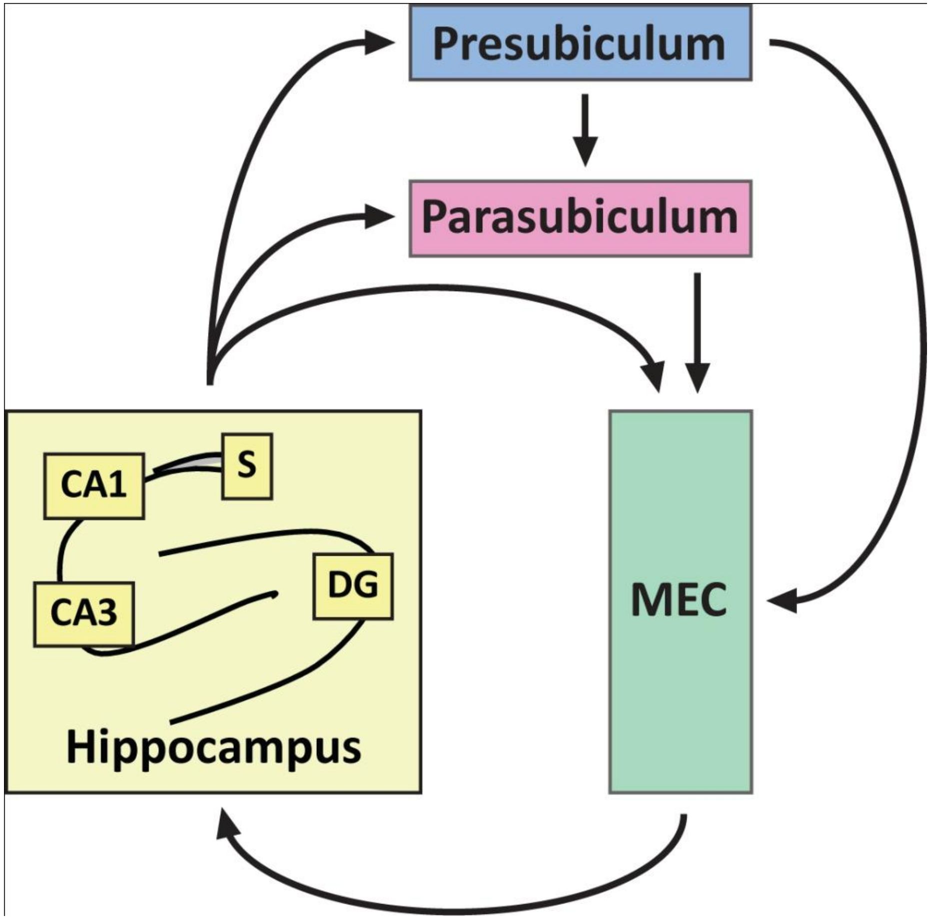
The entorhinal map contains a variety of cells types that together integrate distance and express direction and vicinity to local borders. This may be sufficient to generate a stable but **continuously updated metric representation** of the animal's location in the environment.

3. **Which network architectures** can support grid and direction firing; what are their common properties?

# Are grid cells limited to medial entorhinal cortex?

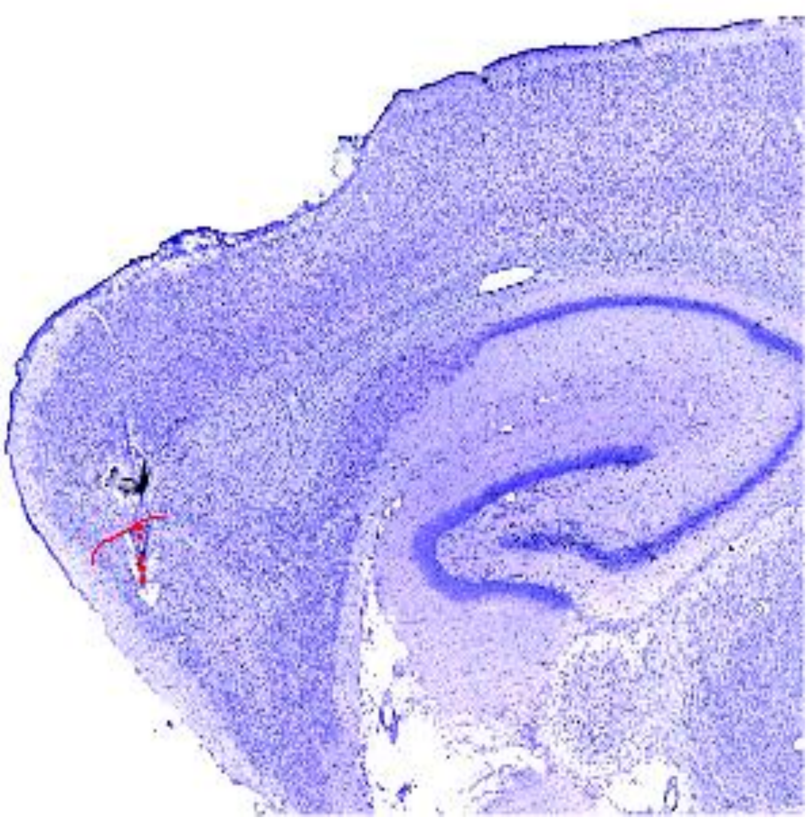
What is the distribution of the three cell types across the parahippocampal cortex?

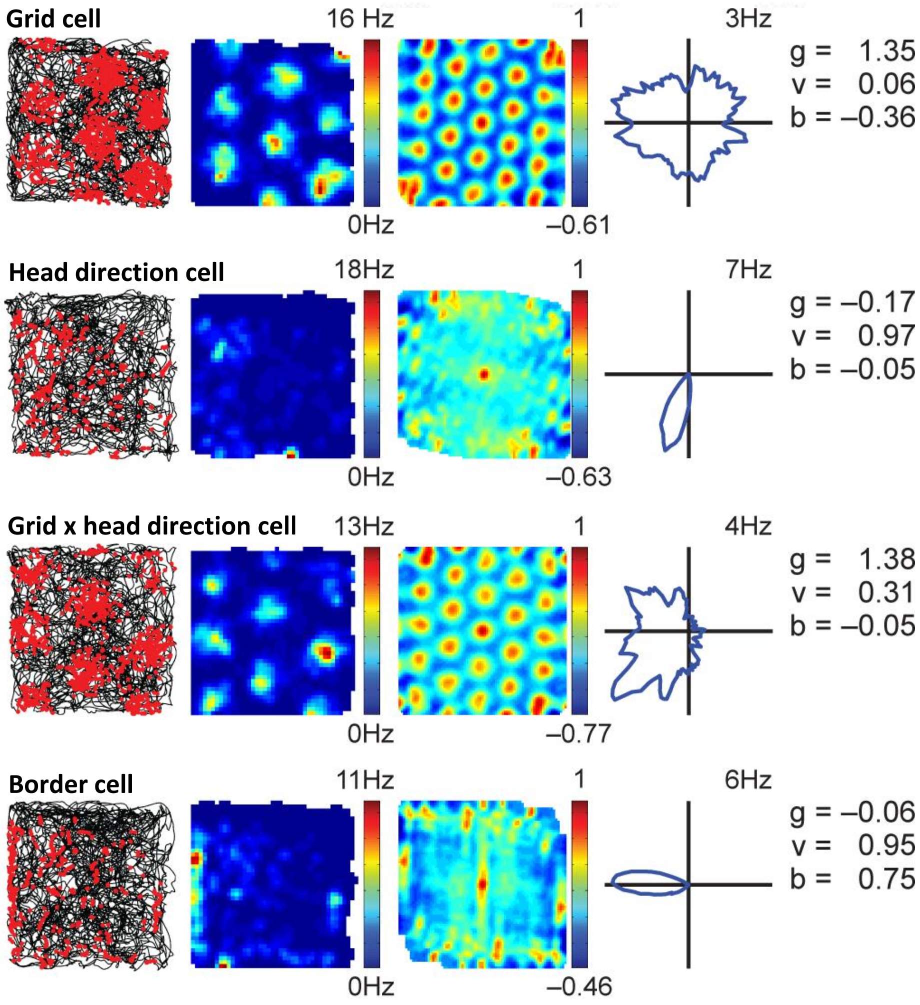



Boccara et al. (2010), Nature Neurosci., in press

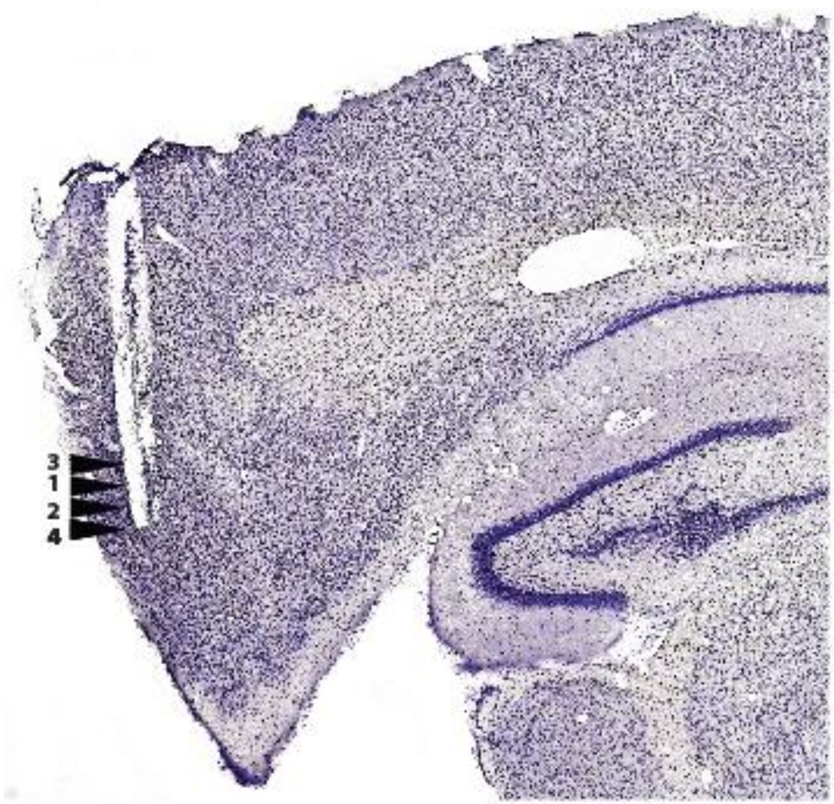
# Medial entorhinal cortex

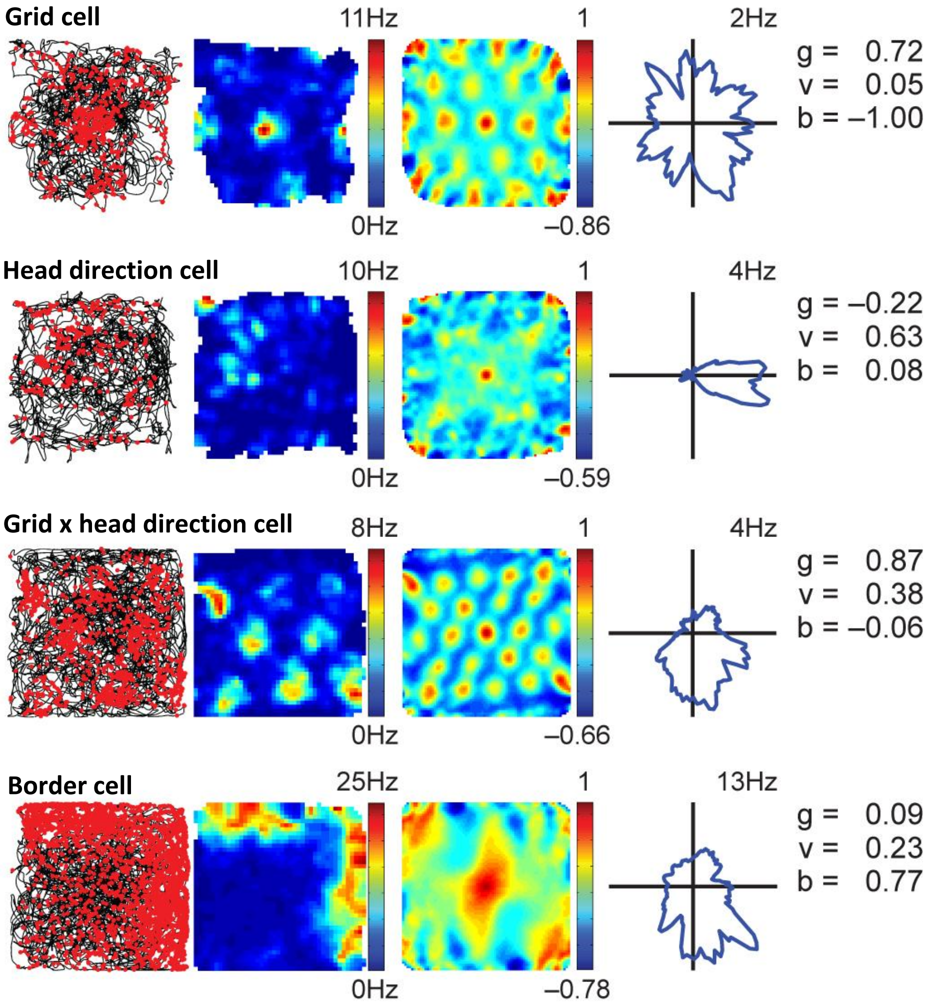





Boccara et al. (2010), Nature Neurosci., in press

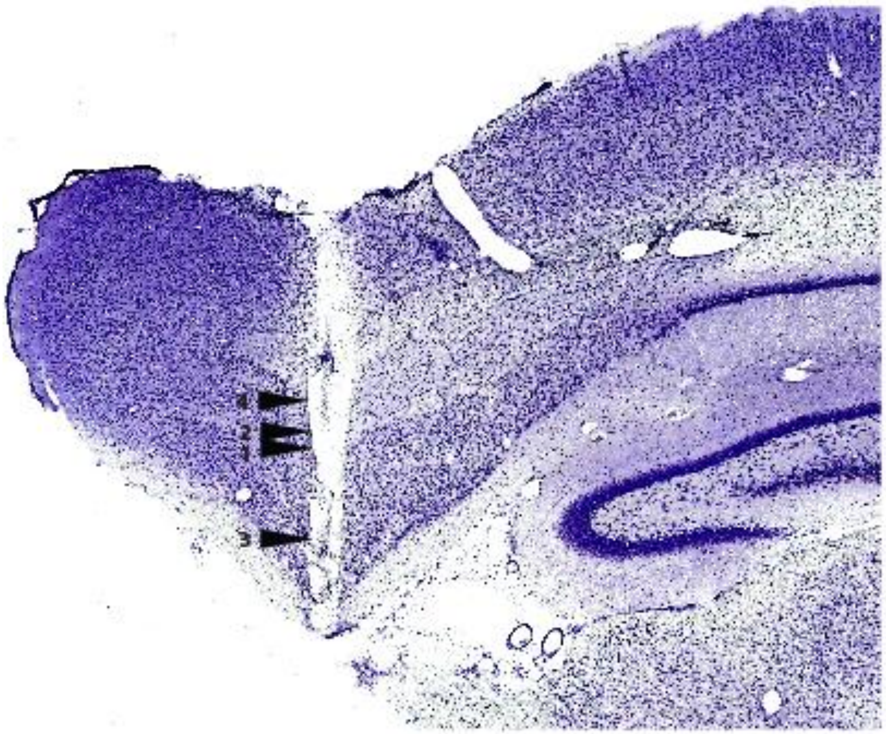
# Parasubiculum

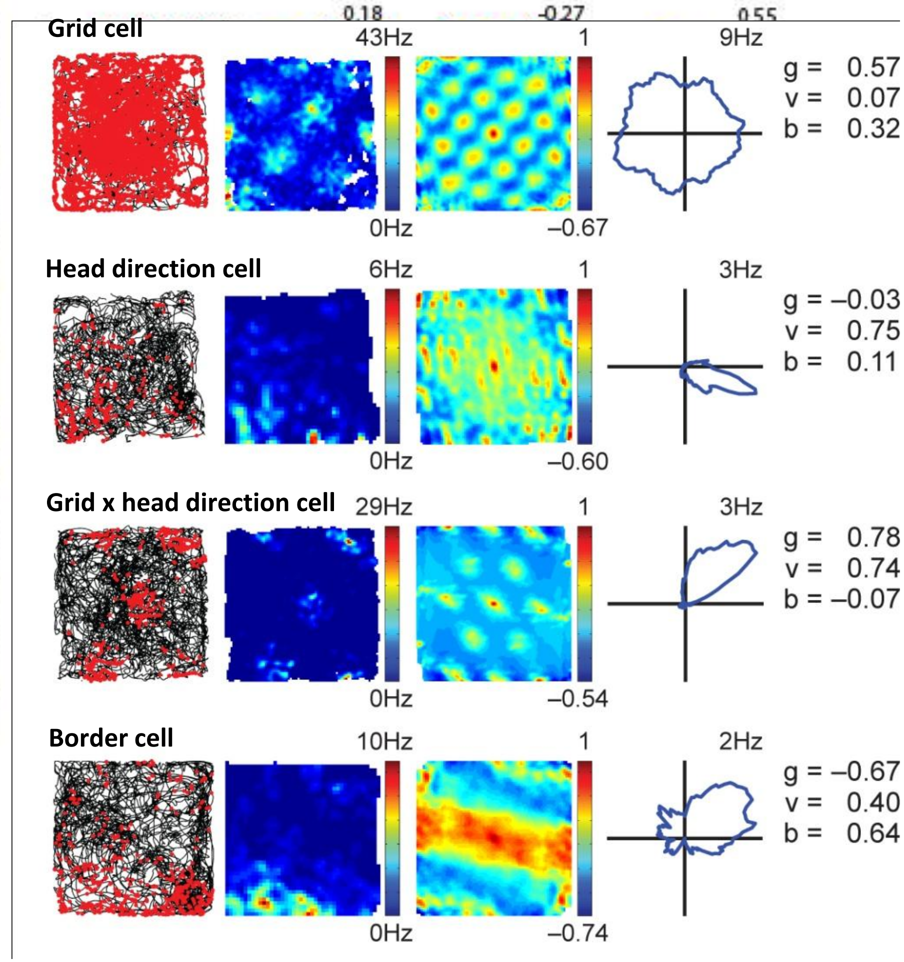



Boccara et al. (2010), Nature Neurosci., in press

# Presubiculum

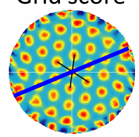




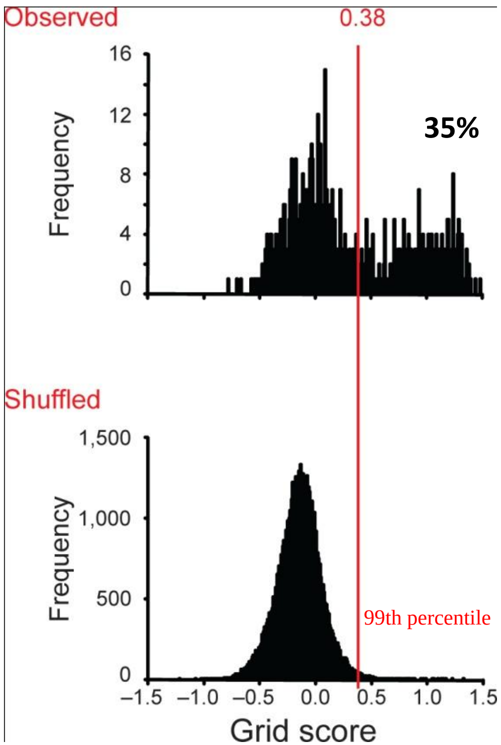

Boccara et al. (2010), Nature Neurosci., in press

# Grid cells are abundant in all parahippocampal regions

Grid score

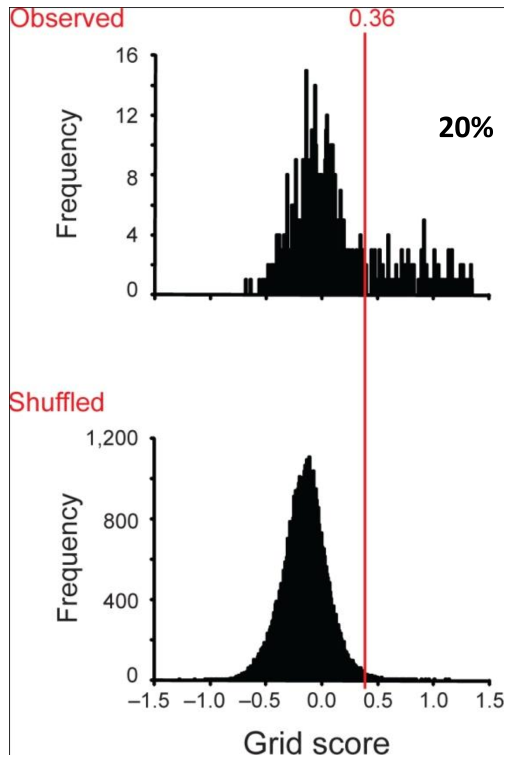


**Medial entorhinal cortex (n=630)**

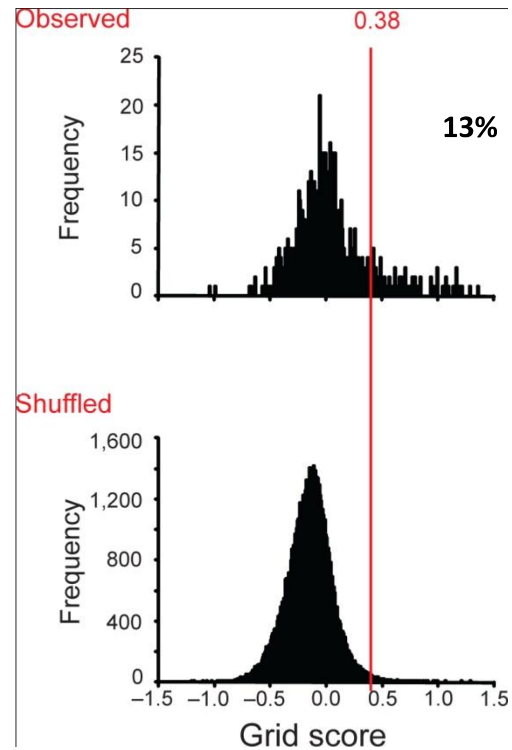



(60 deg rotational symmetry)

**Parasubiculum (n=528)**



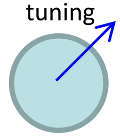

**Presubiculum (n=654)**



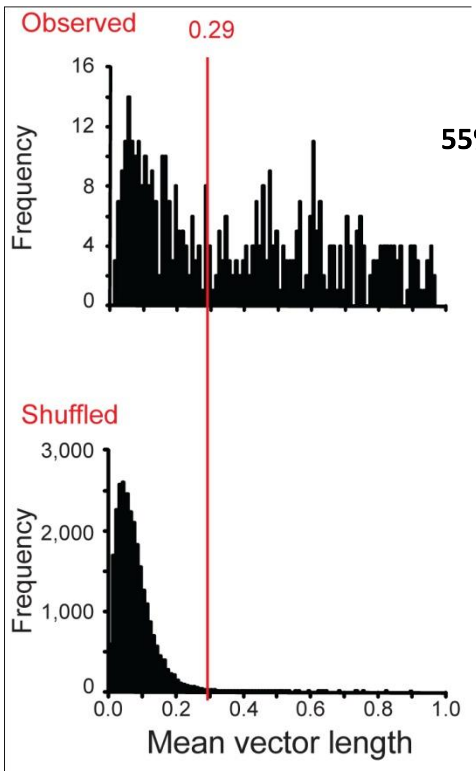

Boccara et al. (2010), Nature Neurosci., in press

# Head direction cells are abundant in all parahippocampal regions

Directional tuning

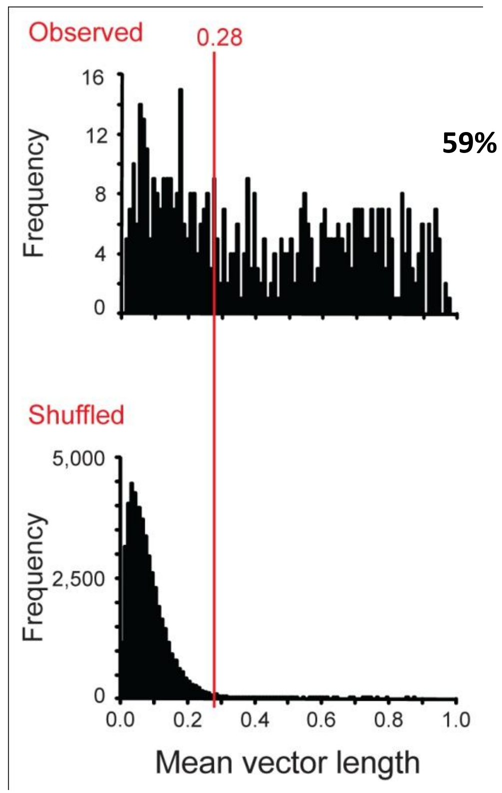


**Medial entorhinal cortex (n=435)**

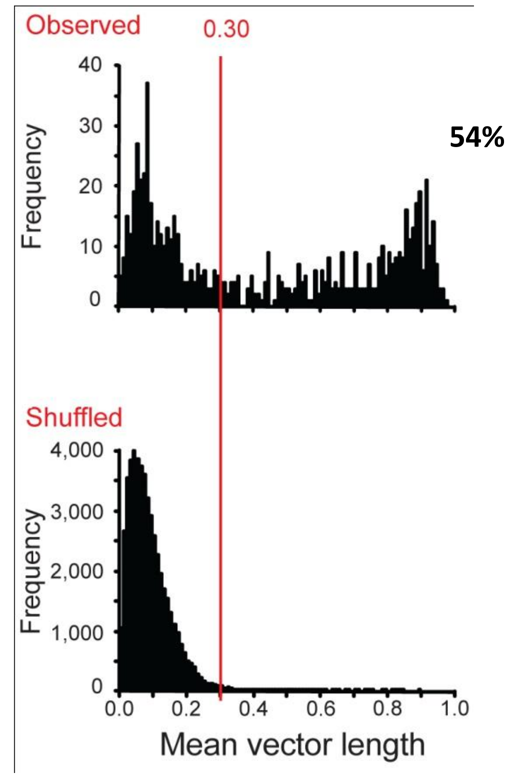



(directional bias)

**Parasubiculum (n=528)**




**Presubiculum (n=654)**

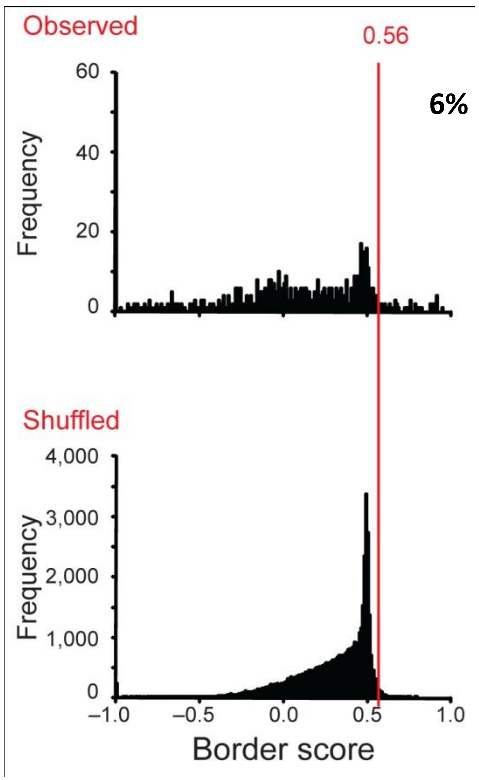



Boccara et al. (2010), Nature Neurosci., in press

# Border cells exist in all parahippocampal regions

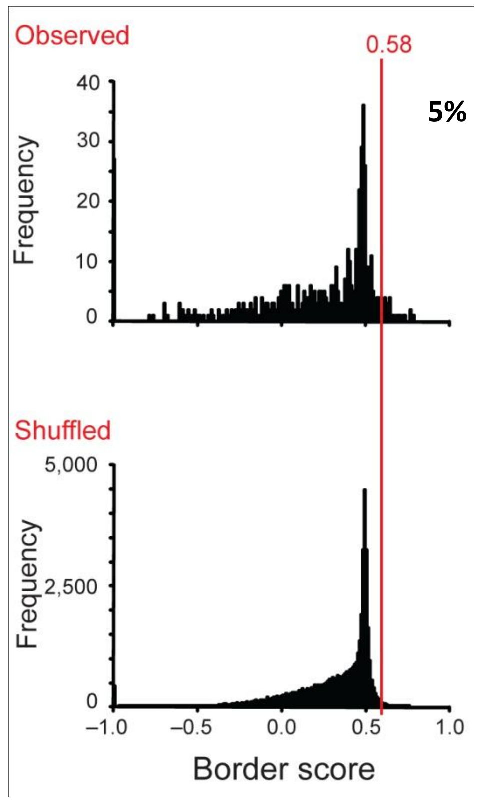
**Medial entorhinal cortex (n=630)**

Border score

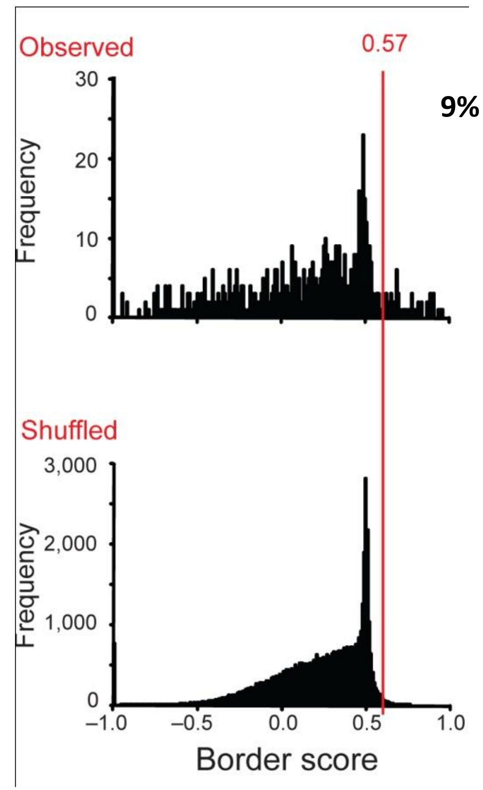



(firing along walls)

**Parasubiculum (n=528)**

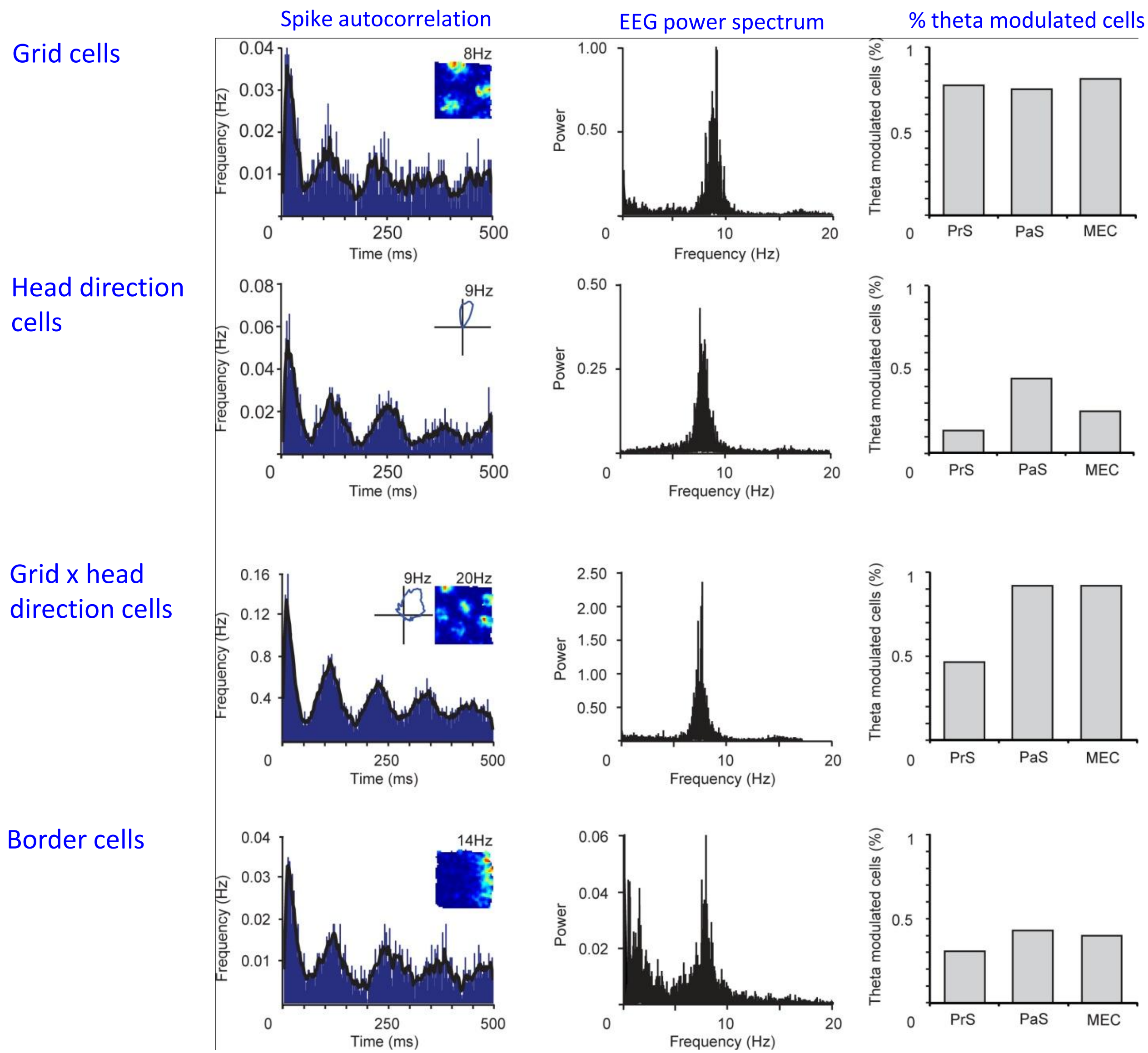



**Presubiculum (n=654)**




Boccara et al. (2010), Nature Neurosci., in press

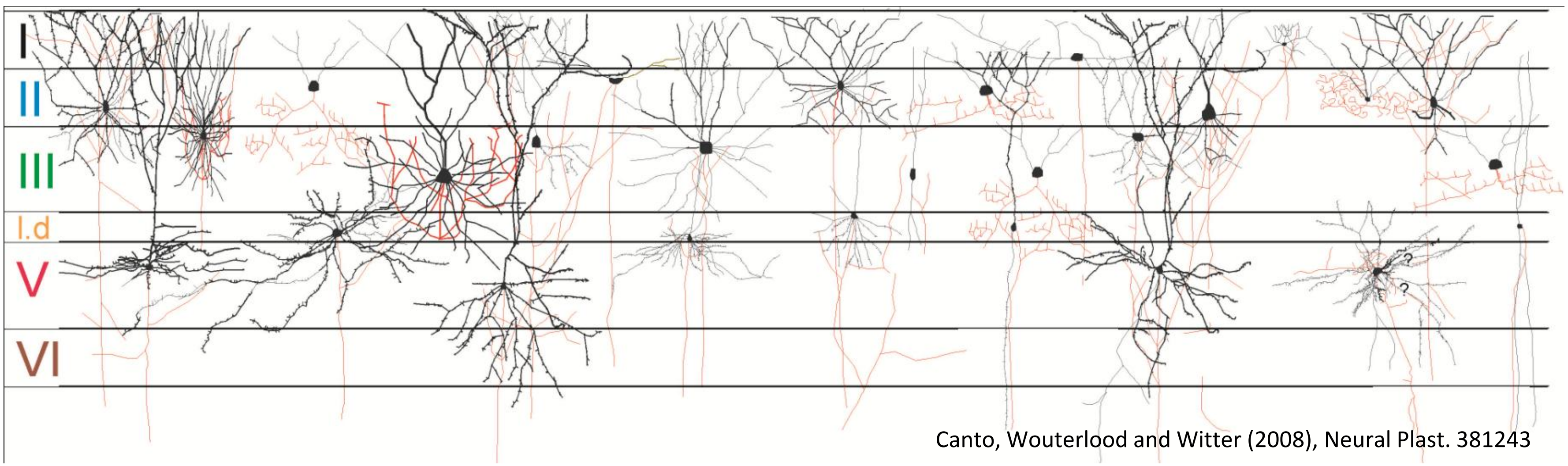
# All parahippocampal areas have theta-modulated cells




**Most grid cells were theta modulated independently of brain area**

Boccara et al. (2010), Nature Neurosci., in press

## What is the common factor of pre/parasubiculum and medial entorhinal cortex?




Canto, Wouterlood and Witter (2008), Neural Plast. 381243

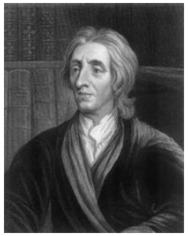
* All three areas  seem to have strong recurrent connections

* Theta-modulated cells exist in all areas

* Intracellular subthreshold theta oscillations have been reported in MEC as well as parasubiculum

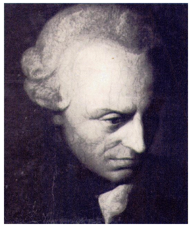
# 4. Development of the spatial map

# Nature/nurture and the spatial representation system



## John Locke (1632-1704):

**The human mind is at birth *a tabula rasa* ("a blank slate") without rules for processing data**; such rules are formed solely by one's sensory experiences.



## Immanuel Kant (1724-1804):

**Time and space are *a priori* forms of** intuition imposed by our own minds. They precede and structure all experience.

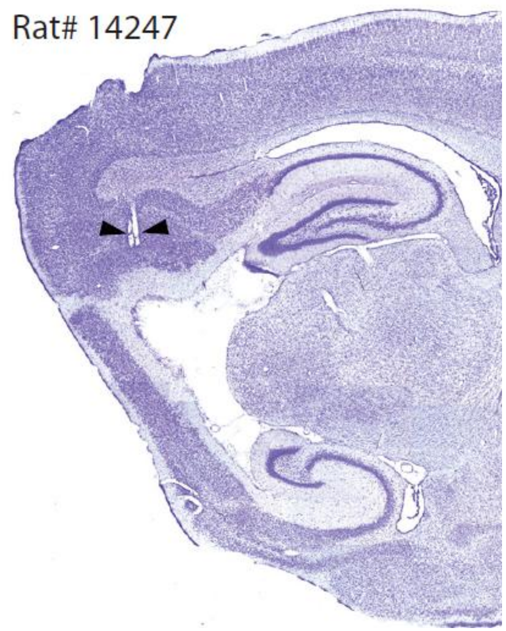

We implanted tetrodes in hippocampus and MEC at P13-P15, *before* eye opening (P15) and *before* exploration outside the nest (P15-17).

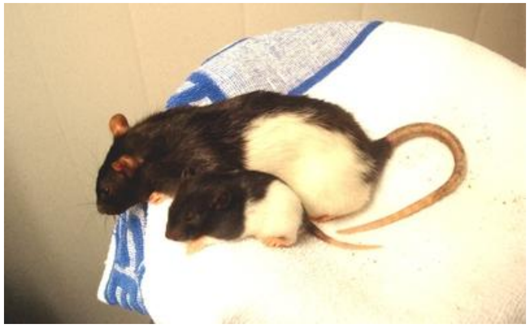
A similar study, with largely similar results, was conducted by Wills et al. (Science, 2010)

Langston et al. (2010), *Science* 328, 1576-1580

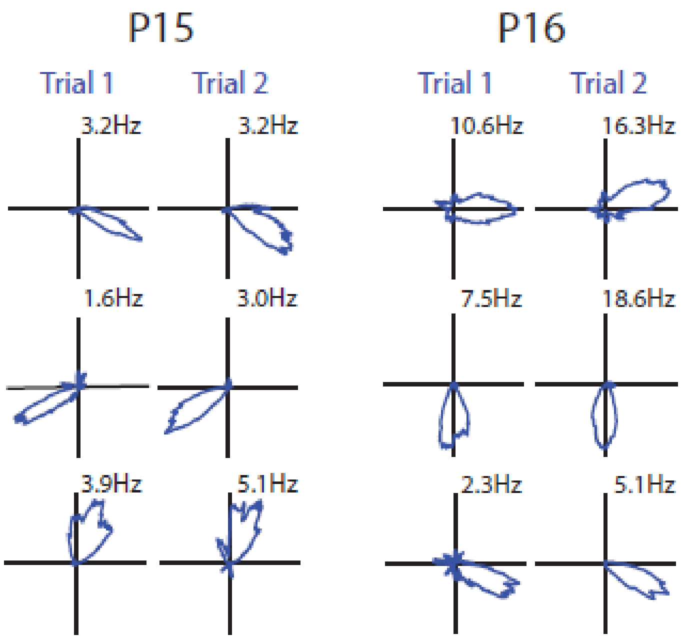
# Adult-like representation of head direction at eye opening (P15)

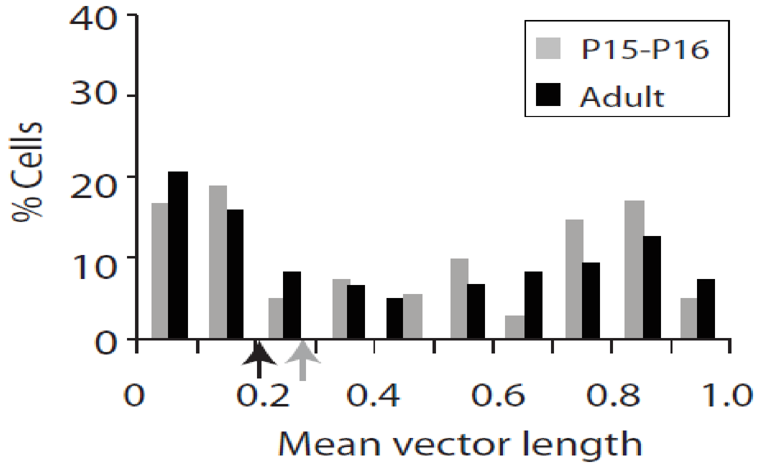
**Dorsal presubiculum**



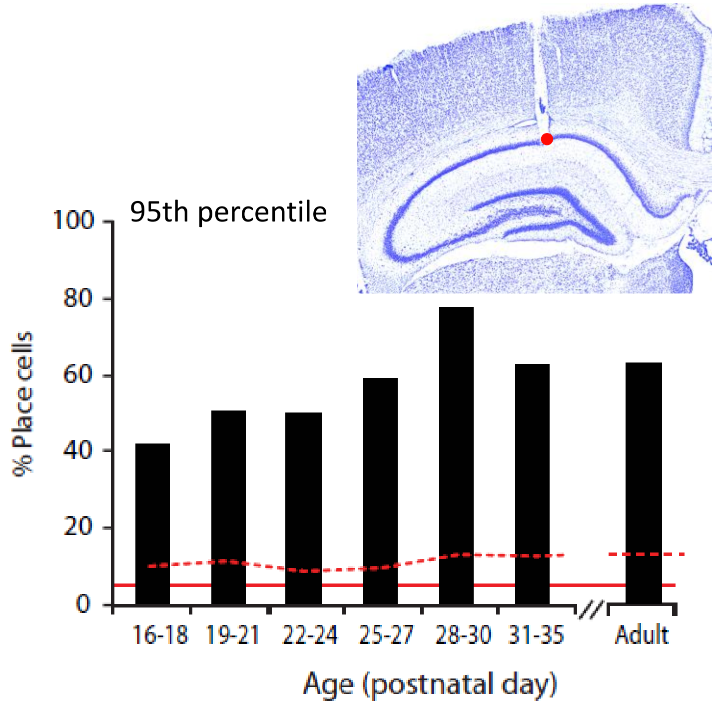



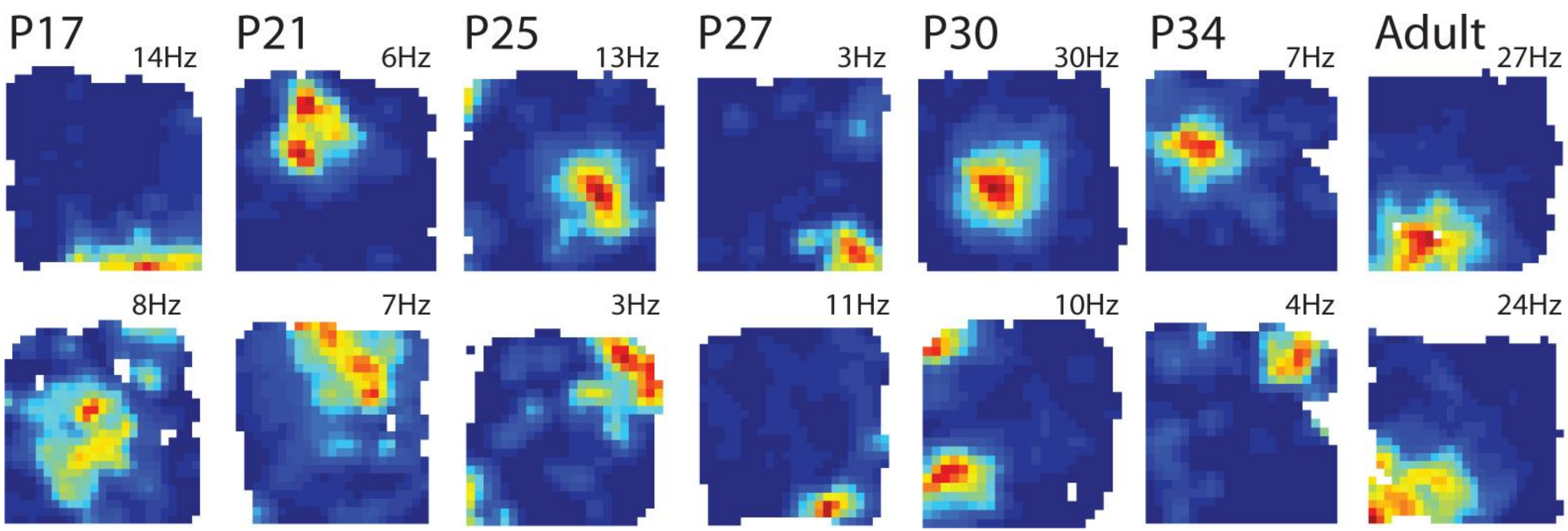
Langston et al. (2010), *Science* 328, 1576-1580



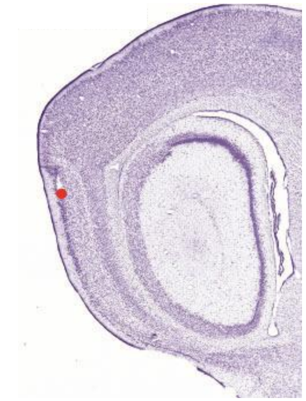
**Place cells are also present from the beginning but they continue to develop for 1-2 weeks**

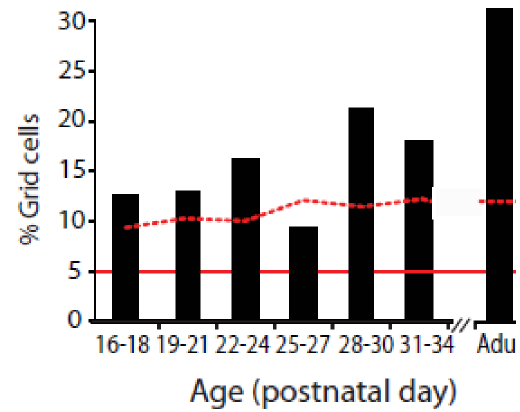


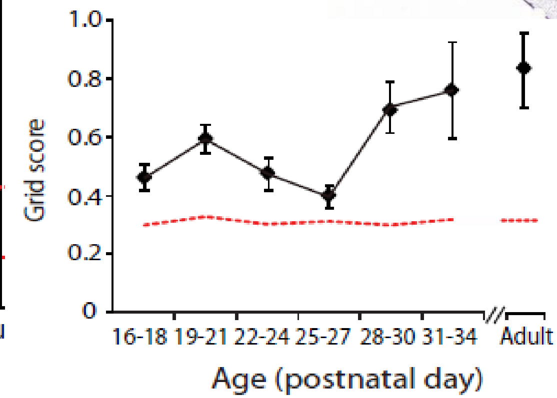



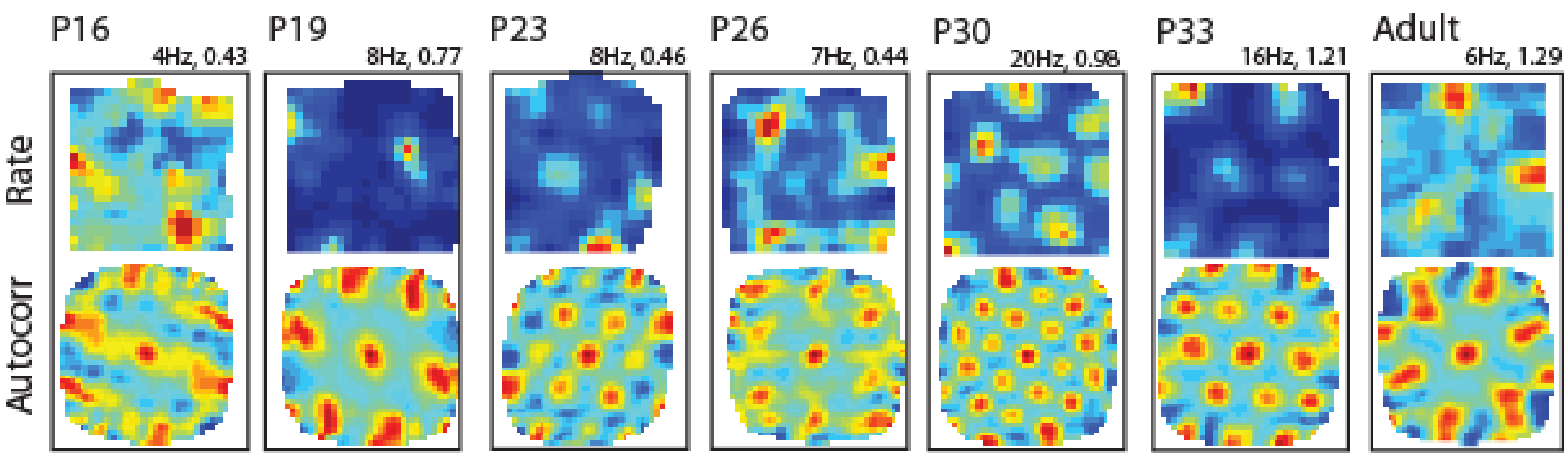

Langston et al. (2010), *Science* 328, 1576-1580

**Grid cells are present in rudimentary form but develop more slowly than place cells**

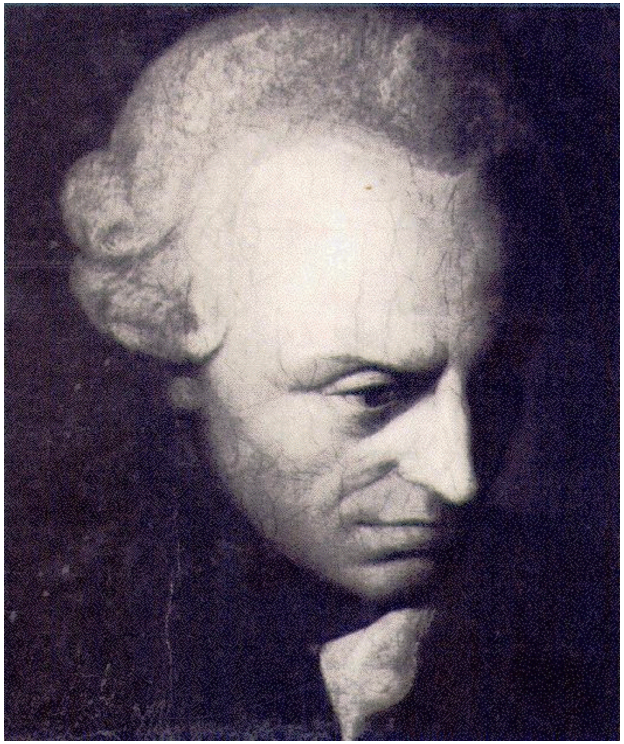





Langston et al. (2010), *Science* 328, 1576-1580



Preconfigured/innate/a priori?

Thus, a rudimentary map of space is present when 2 ½-week old pre-weanling rats explore open environments outside the nest for the first times; however, the directional map matures faster than the spatial map, suggesting that directional inputs from presubiculum may be instrumental in setting up networks for place and grid representations in hippocampus and entorhinal cortex.

# Conclusions

1. The navigational system contains multiple functional cell types: place cells, head direction cells, and grid cells, and ’border cells’. These cells are part of a brain system for metric representation of self-location.

2. Spatial frequency is mapped topographically along the dorsoventral axis of medial entorhinal cortex.

3. Spatial maps are present already when rats leave the nest but continue to be refined over the next two weeks. Head direction cells mature faster than place and grid cells, suggesting that directional inputs may be instrumental in setting up spatial maps.

4. Grid cells, head direction cells and border cells exist throughout much of the parahippocampus, not only in medial entorhinal cortex. The ability of different networks to sustain these firing patterns may provide clues about necessary conditions for expressing functional cell types.

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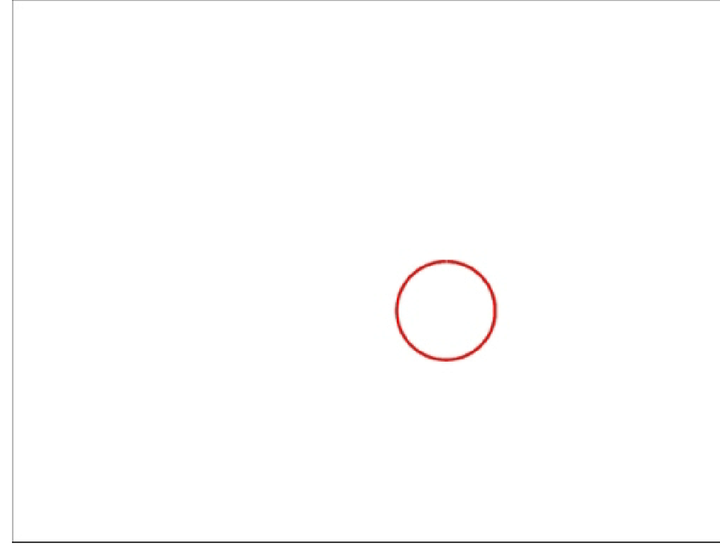
**Key contributors to this work:**

**Vegard Brun**
**Kirsten Kjelstrup**
**Marianne Fyhn**
**Torkel Hafting**
**Sturla Molden**
**Francesca Sargolini**
**Trygve Solstad**
**Charlotte Boccara***
**Emilio Kropff**
**Ros Langston***
**James Ainge**
**Hanne Stensland***
**Tor Kirksola***
**Sheng-Jia Zhang***
**Jing Ye***
**Chenglin Miao***
**Karel Jezek***

**Menno Witter***
**Carol Barnes**
**Alessandro Treves***
**Richard Morris**
**Bruce McNaughton**

**Edvard Moser***


The Norwegian University of Science and Technology (NTNU), Trondheim



**Raw data from our published studies on grid cells are available for download at:**
***http://ntnu.no/cbm/gridcell***