Introduction to Neuroscience: Behavioral Neuroscience

Navigation and Spatial Memory: Brain Mechanisms

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2009-2010, 1st semester

Outline of today's lecture

- **Hippocampus and spatial memory: early discoveries**
- **Hippocampus and large-scale navigation**
- **Back to small-scale navigation in the laboratory:**
  - **Place cells**
  - **Head direction cells**
  - **Grid cells**
  - **Other brain areas involved in navigation**
- **Summary**

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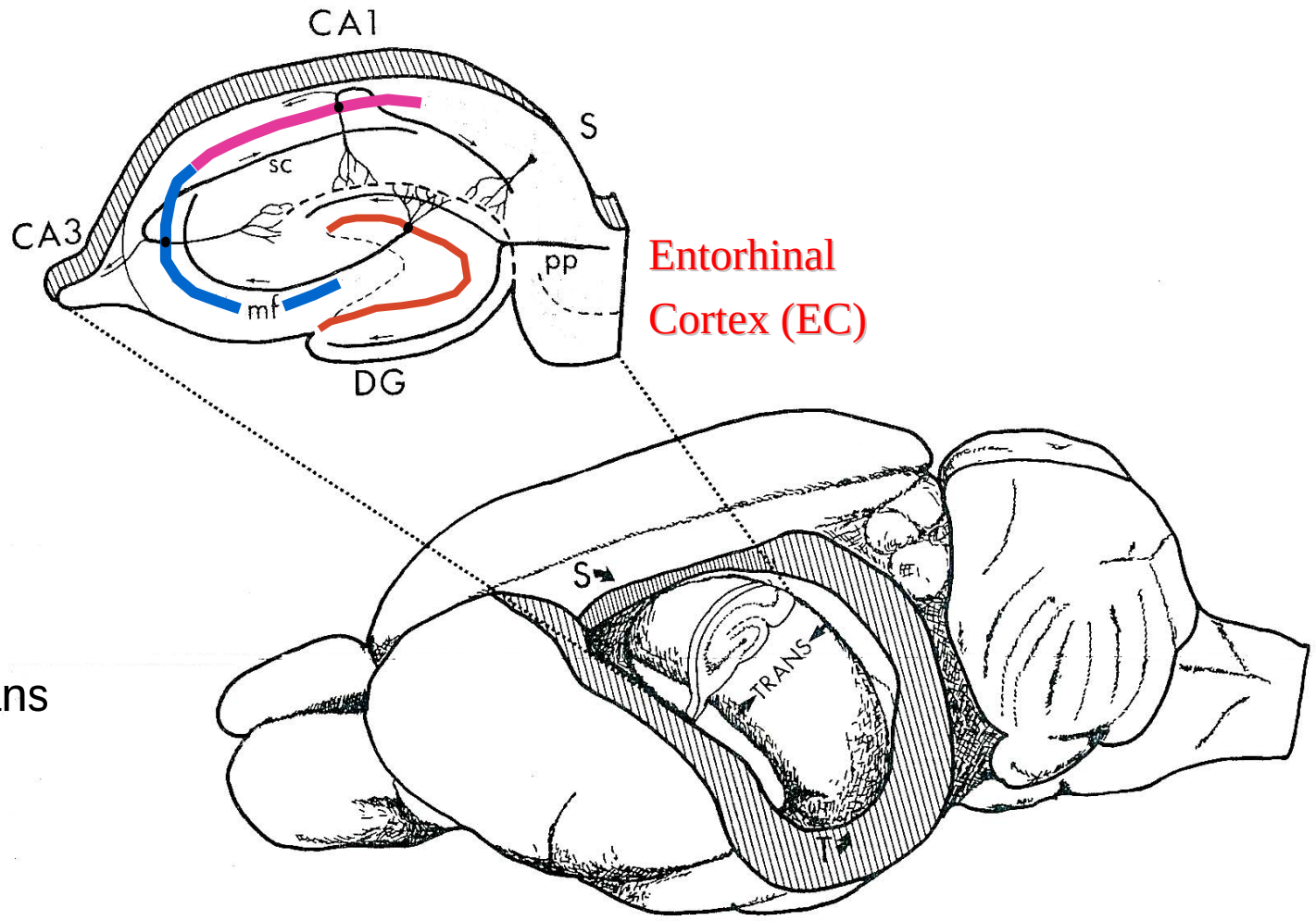
The hippocampus

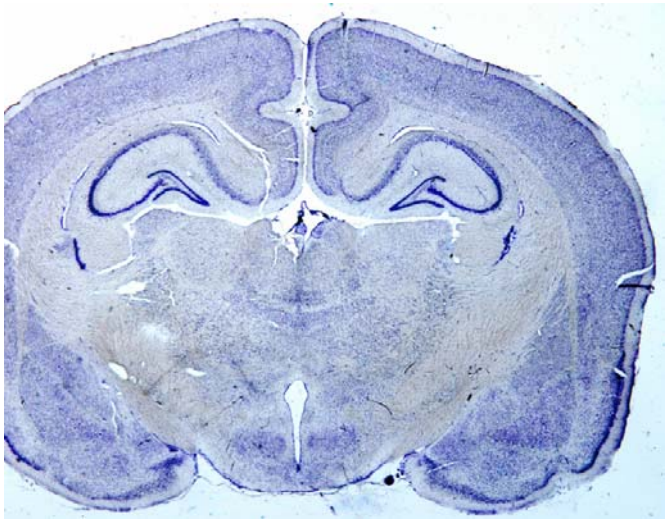


- Highly conserved brain structure across all mammals, including humans (exists also in birds, but looks quite different)
- The most important brain region, clinically

(Amaral and Witter 1989)

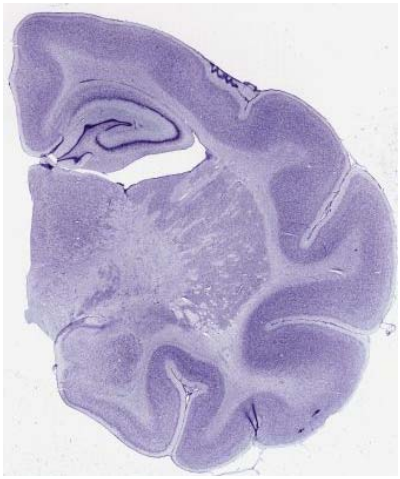
The hippocampus

Egyptian fruit bat



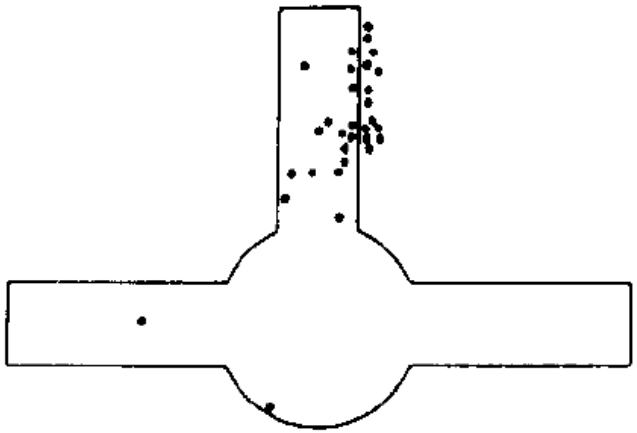
Rat

Echidna
(ancient egg-laying mammal)



In primates: The hippocampus is at the bottom of the brain and rotated 90°, but otherwise very similar.

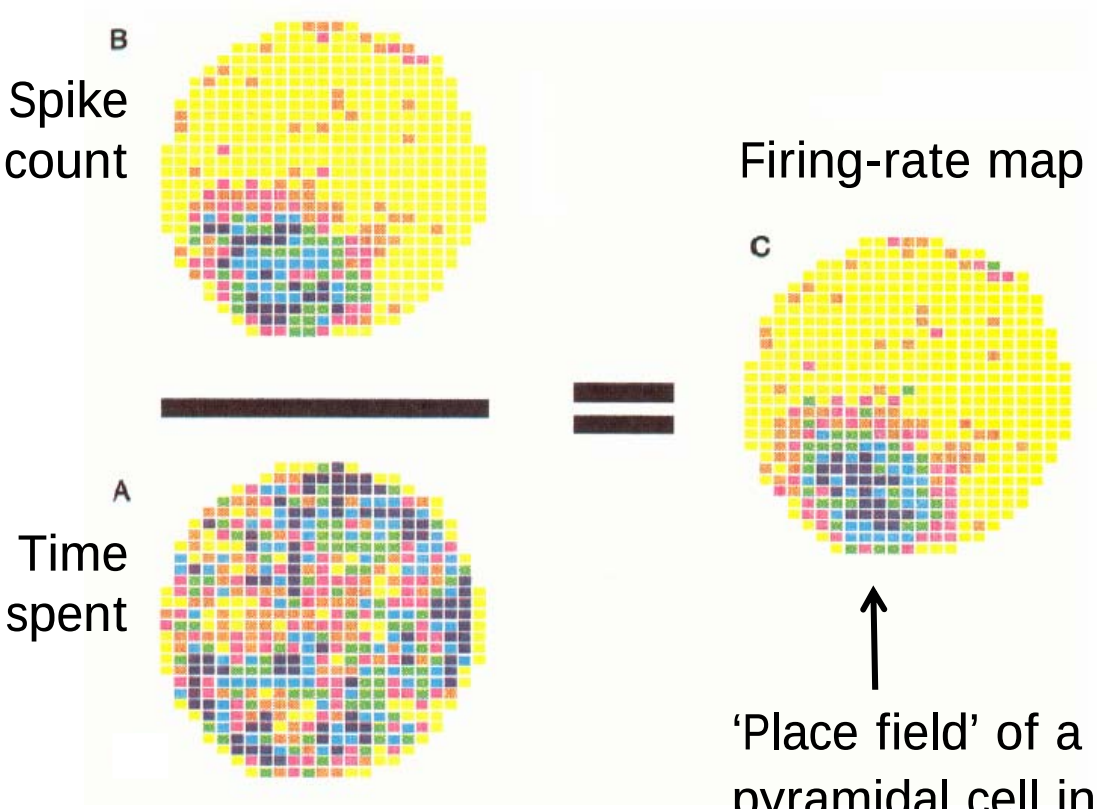
Hippocampal place cells in rats



(O'Keefe & Nadel 1978)

(O'Keefe & Dostrovsky 1971)

John O'Keefe



'Place field' of a pyramidal cell in rat hippocampus

(Muller et al. 1987)

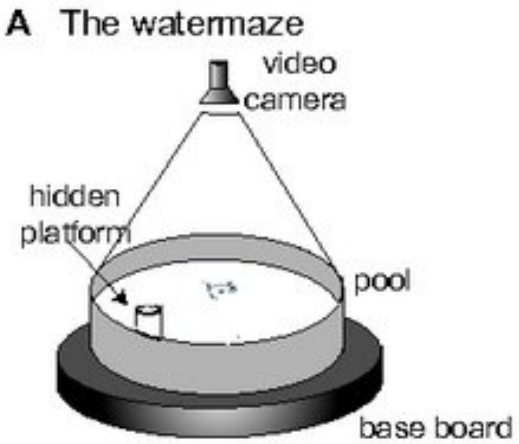
Movie of a rat hippocampal place cell in action

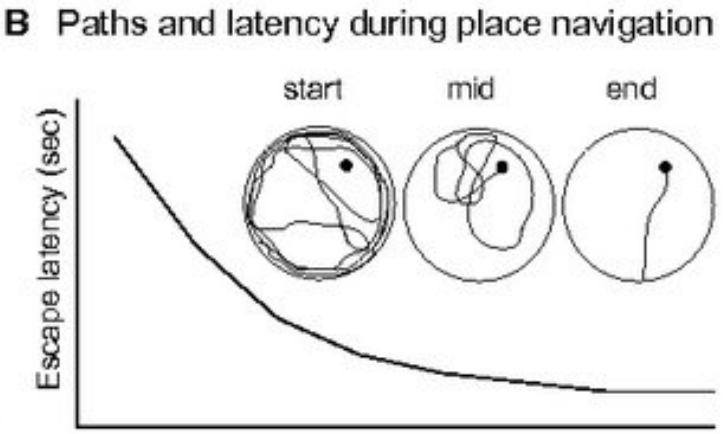
Movie of place cell

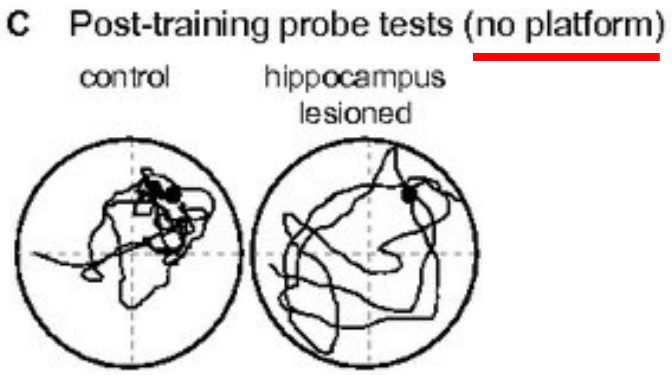
(Courtesy of Colgin, Moser & Moser)

Bilateral hippocampal lesions impair allocentric navigation

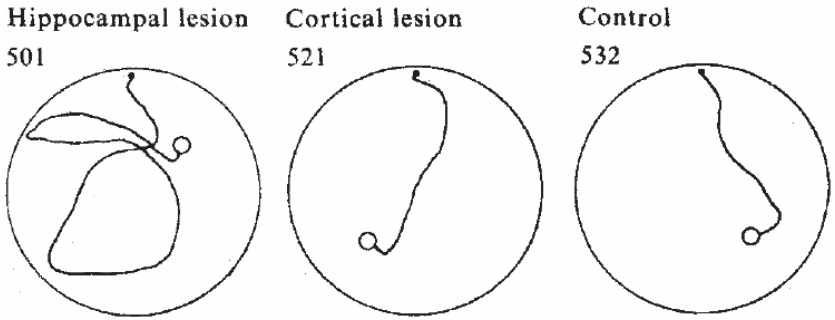
Richard Morris







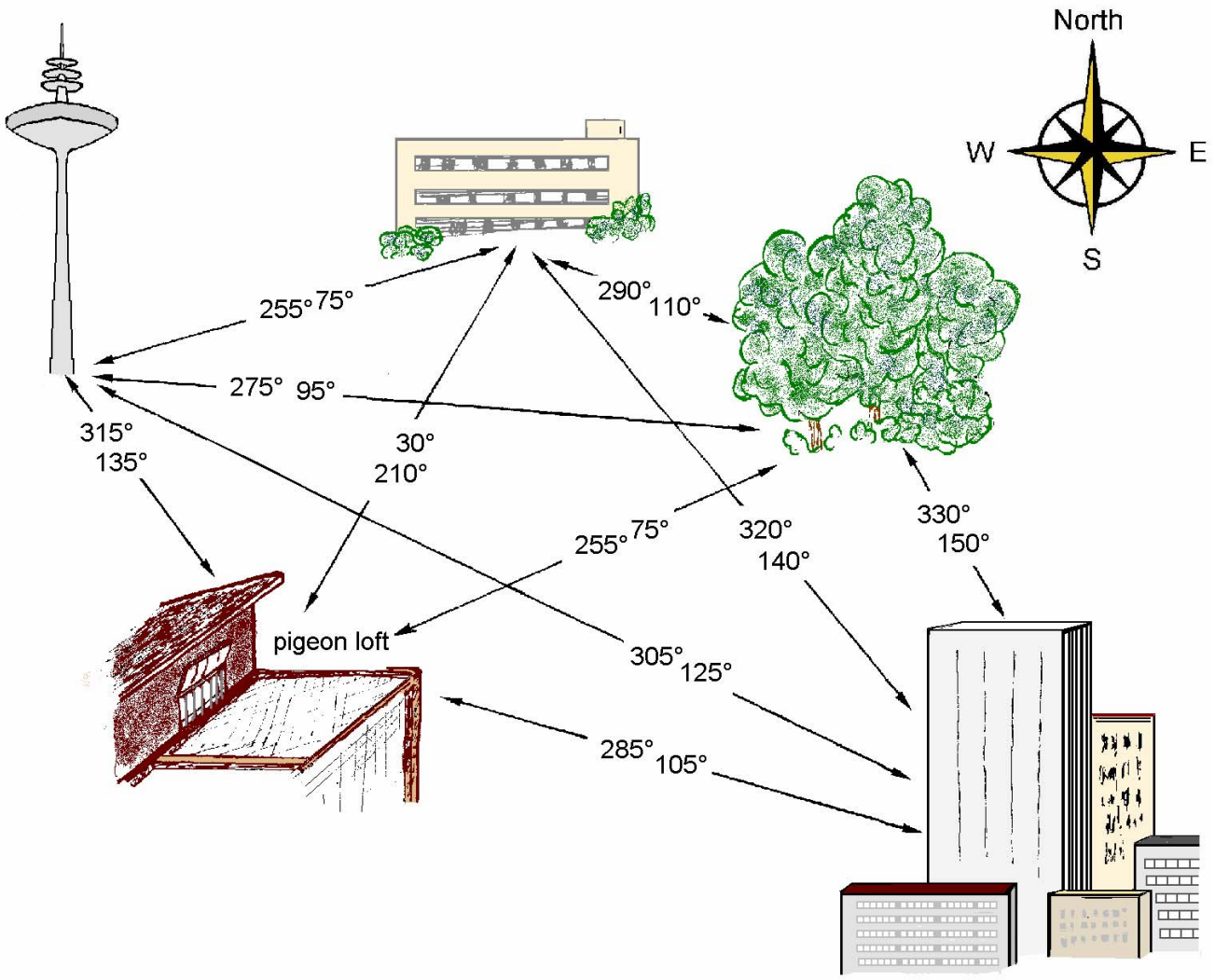
Original data from: Morris, Garrud, Rawlins, O'Keefe, *Nature* (1982) [with platform]



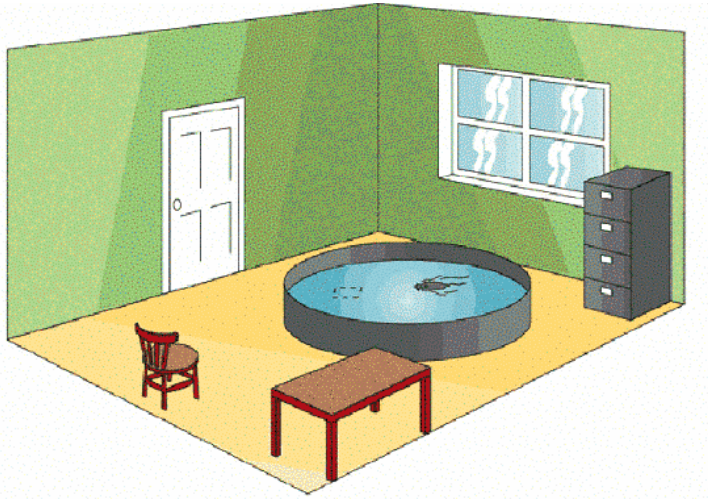
These deficits of spatial memory occur after lesions in dorsal hippocampus – not ventral hippocampus.

Rat navigation in a watermaze is thought to be similar to the concept of ‘Mosaic Map’ in birds: self-triangulation based on distal landmarks

Large-scale navigation by birds

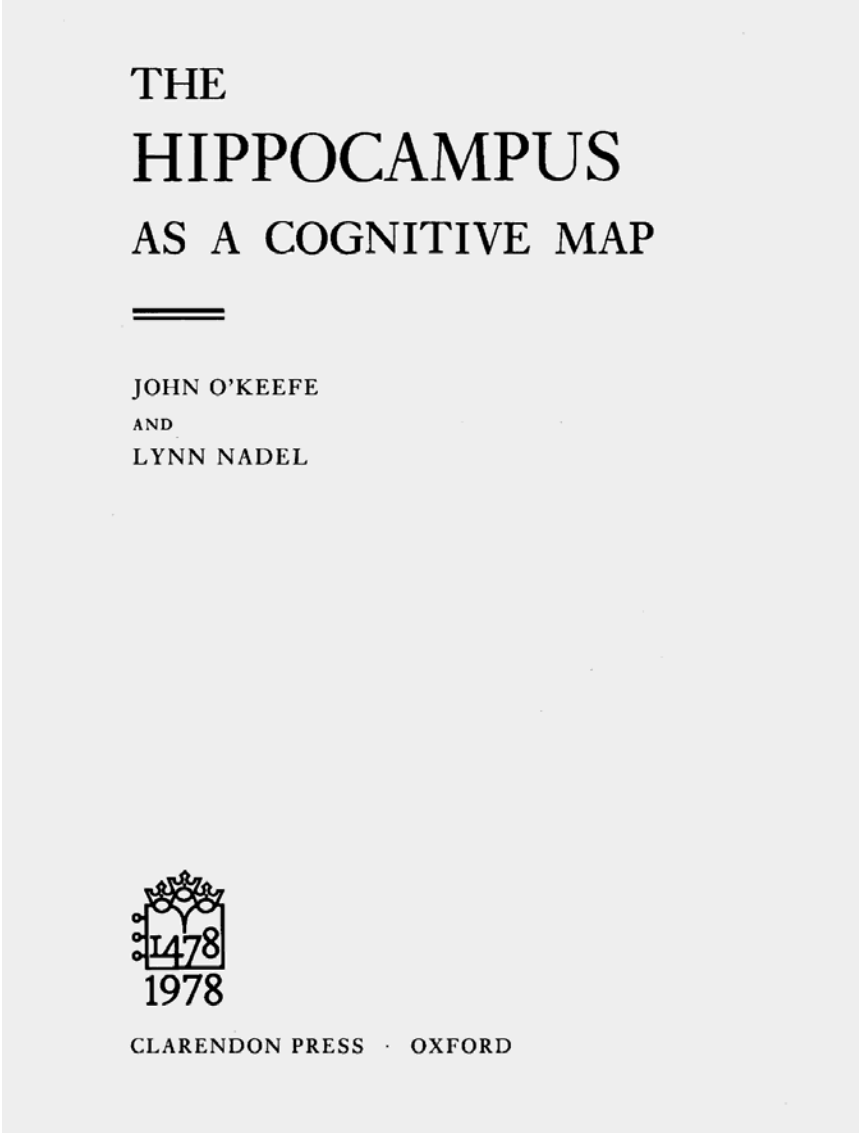


Small-scale navigation by rats in a watermaze



Neuroethology and the discovery of place cells

O’Keefe & Nadel, “The hippocampus as a cognitive map” (1978)



THE
HIPPOCAMPUS
AS A COGNITIVE MAP

JOHN O'KEEFE
AND
LYNN NADEL

1478
1978

CLARENDON PRESS · OXFORD

Neuroethology and the discovery of place cells

O'Keefe & Nadel, "The hippocampus as a cognitive map" (1978)

question, even with a good bit of luck and insight.* We suggest that during the exploratory phases of research into the function of a structure it is necessary to use a more information-rich methodology, the neuroethological one.

The neuroethological approach differs from the neuropsychological one in several respects. First, it seeks to study the activity of single units in as naturalistic a setting as possible, in the belief that an animal's behaviour in its natural environment maximizes the possibility of producing changes in unit activity that are meaningfully related to that unit's function. It thus embodies the reasonable assumption that the brain of a particular animal is built to operate in a specific environment. At the very

• • •

4.7.1. A NEUROETHOLOGICAL STRATEGY

The strategy used in our own work on single-unit activity in the hippocampus of the freely moving rat leans towards the neuroethological, rather than the neuropsychological, approach. The following is a general outline of this procedure.

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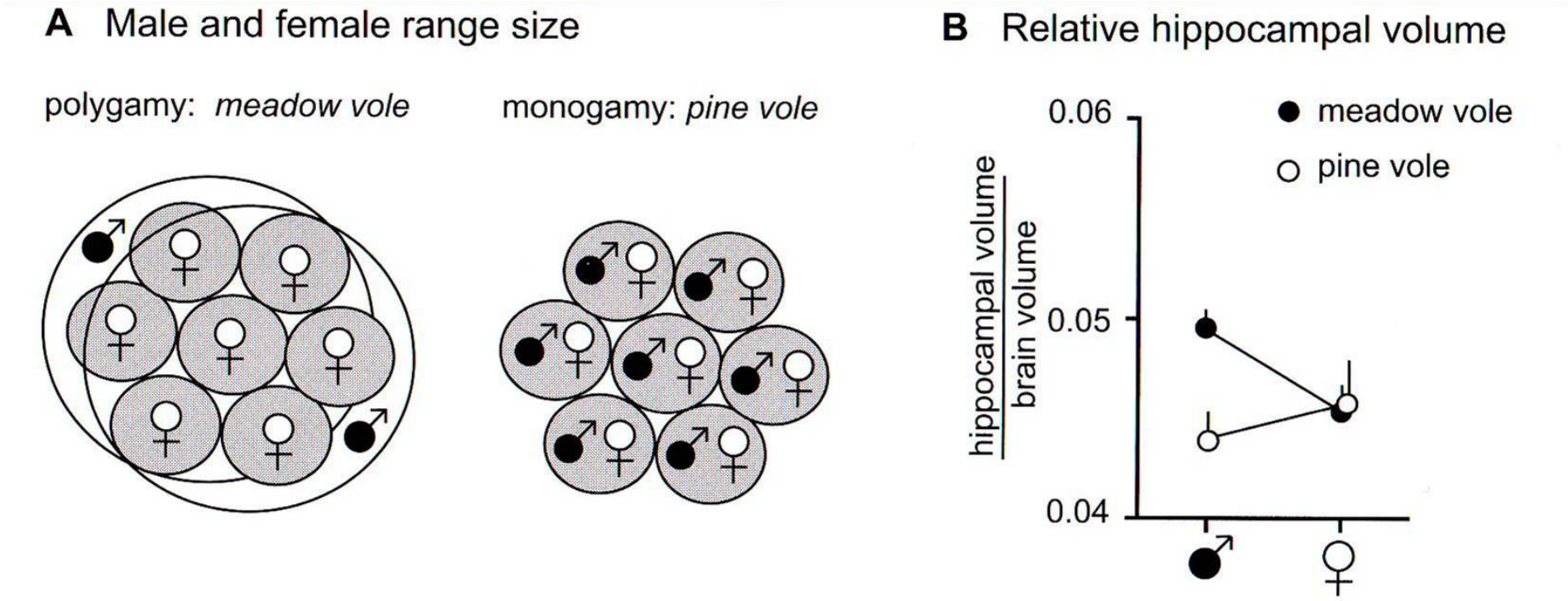
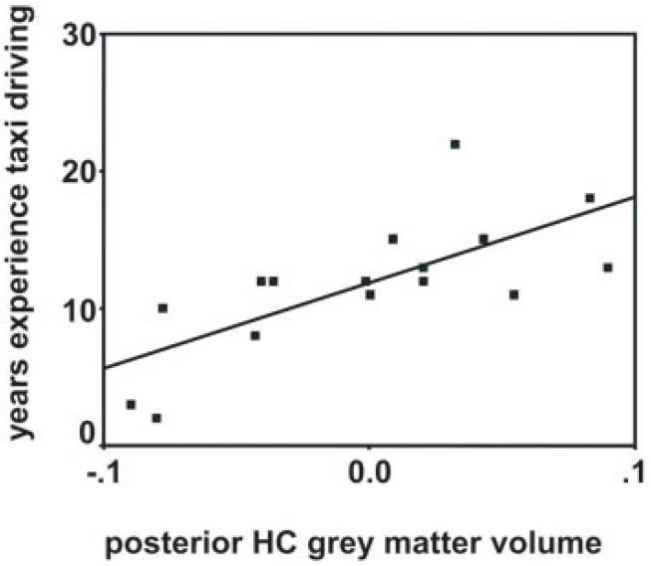
Hippocampal volume correlates with navigational load in rodents



Hippocampal volume correlates with navigational load in humans

Volume of posterior hippocampus in humans (equivalent to dorsal hippocampus in rats):

- Larger in London taxi drivers than in age-matched controls.
- Correlated with time spent as a taxi driver.
- Larger in Taxi drivers than in experience-matched Bus drivers.
- In Bus drivers, no correlation with experience was found.



Maguire et al., *PNAS* (2000)

Maguire et al., *Hippocampus* (2006)

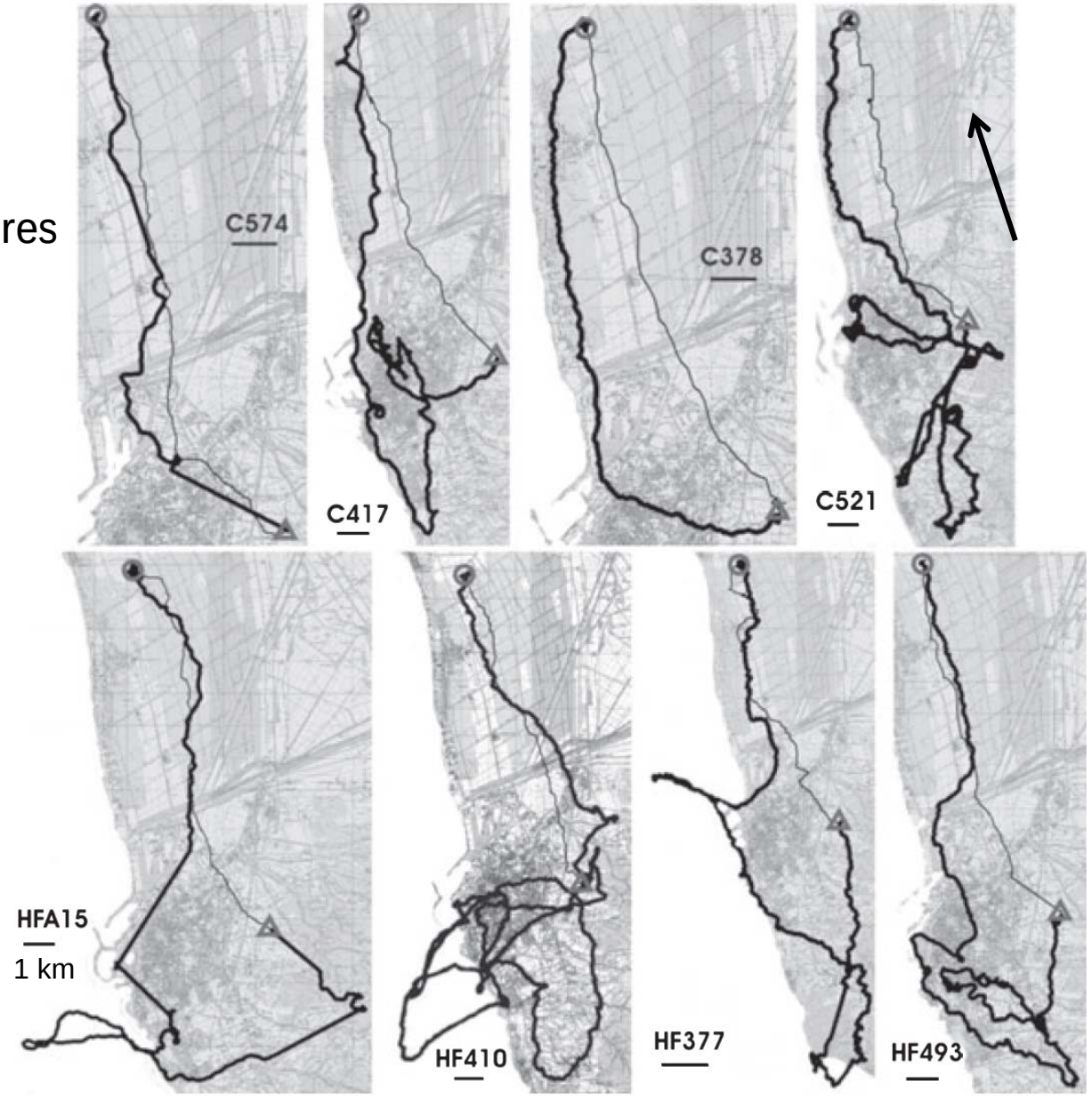
Interpretations:

- The hen and the egg problem: Does posterior hippocampus grow with experience (plasticity), or is a large hippocampus needed in order to do well and "survive" for many years in the demanding profession of a London taxi driver?
- Navigation based on a cognitive-map strategy (taxi drivers) requires/causes a larger hippocampus than route-based navigation (bus drivers) ?

Lesions in the hippocampus of homing pigeons affect navigation

— Regular release

— Clock-shifted (requires re-orientation)



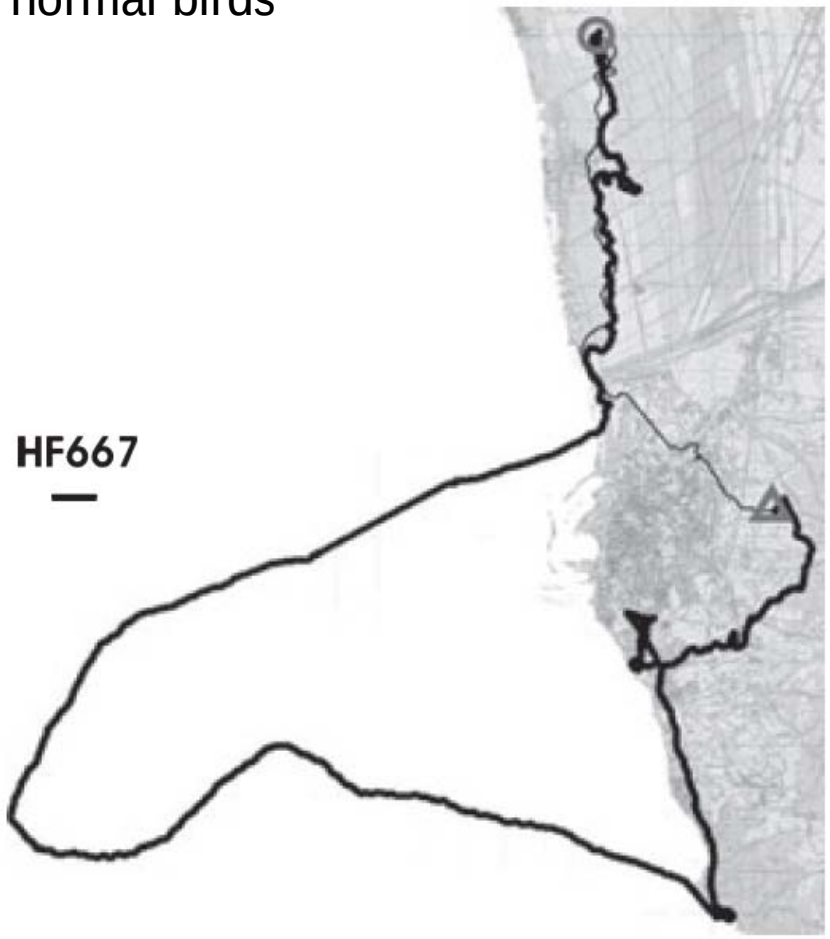
4 Controls

4 hippocampus lesioned birds

Note flight over the sea →

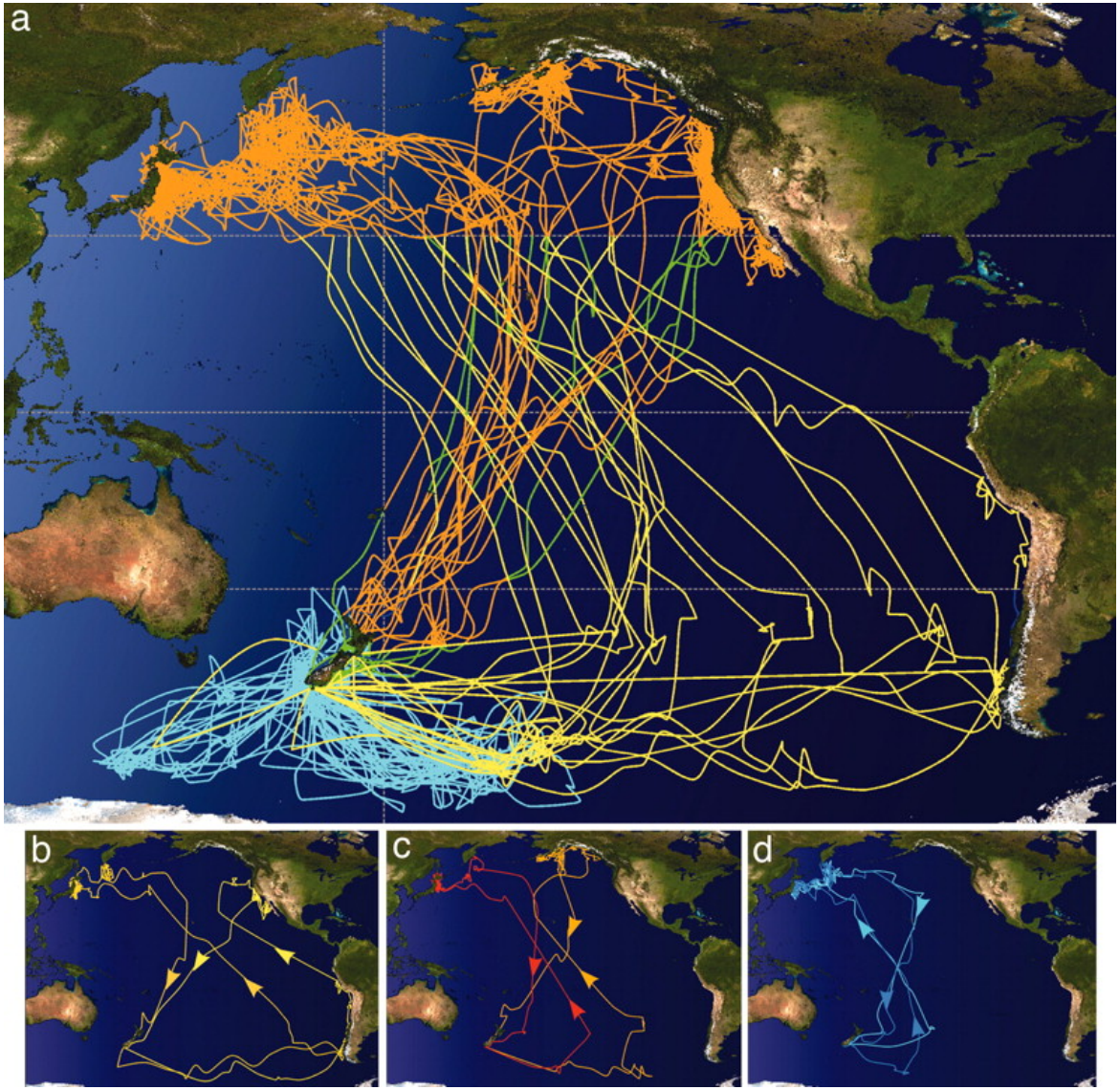
Lesions in the hippocampus of homing pigeons affect navigation

Extraordinary flight of a hippocampus-lesioned bird above the sea: Never occurs in normal birds



- *Interpretation*: The map is not stored in the hippocampus, since hippocampus-lesioned birds could home; only re-orientation seems to depend on the hippocampus
- *Caveat*: Bird hippocampus differs substantially in morphology from mammalian hippocampus

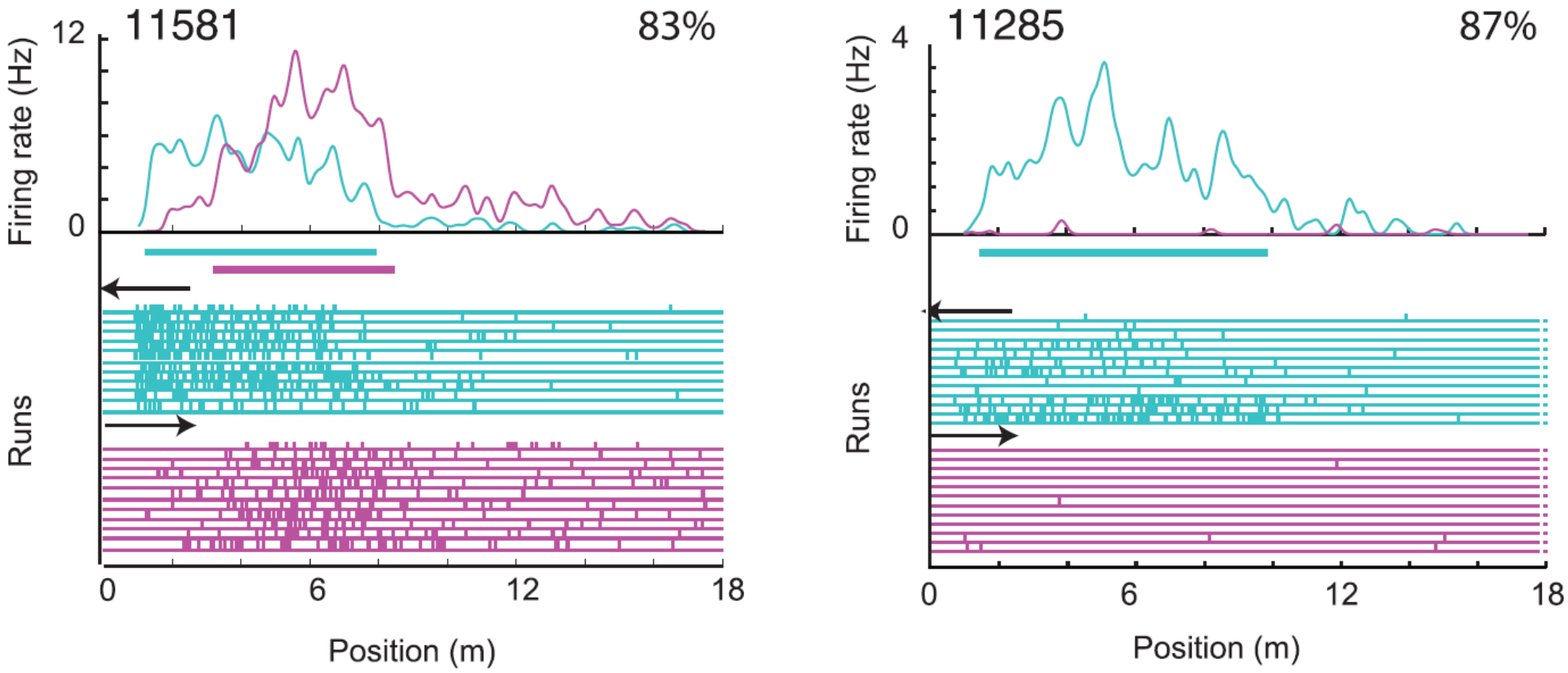
CAVEAT: No studies of place cells were done on this scale...



Shaffer et al. *PNAS* (2006)

... and not even on this scale

... Largest place fields demonstrated to date: ~10 meters



Still not large enough… Rats in the wild (real rats, not laboratory rats) move much larger distances than 10 meters.

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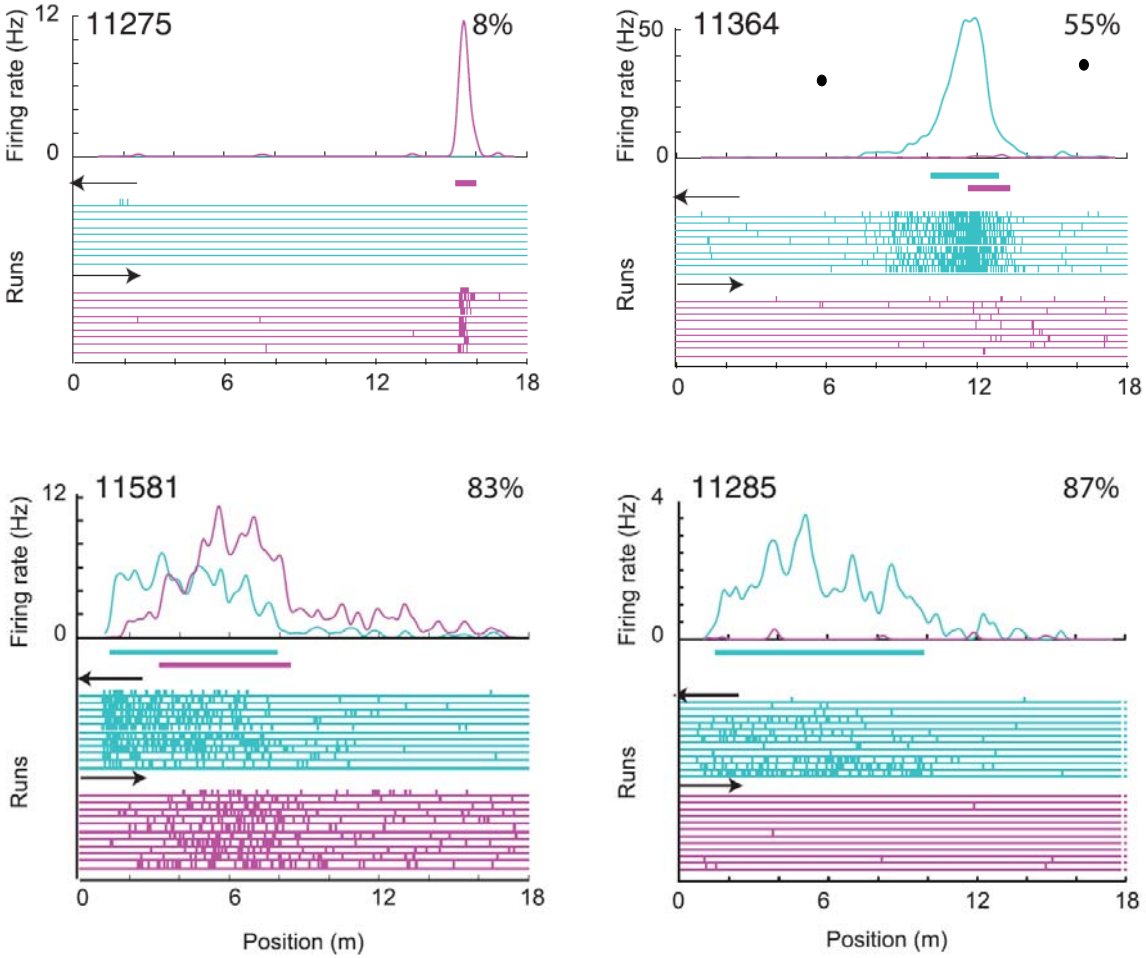
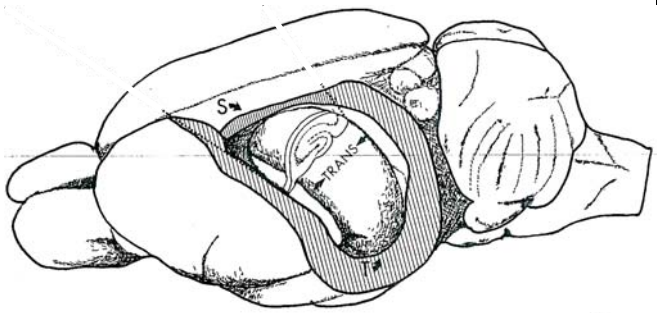
Place fields increase in size along the dorso-ventral (septo-temporal) axis in the hippocampus



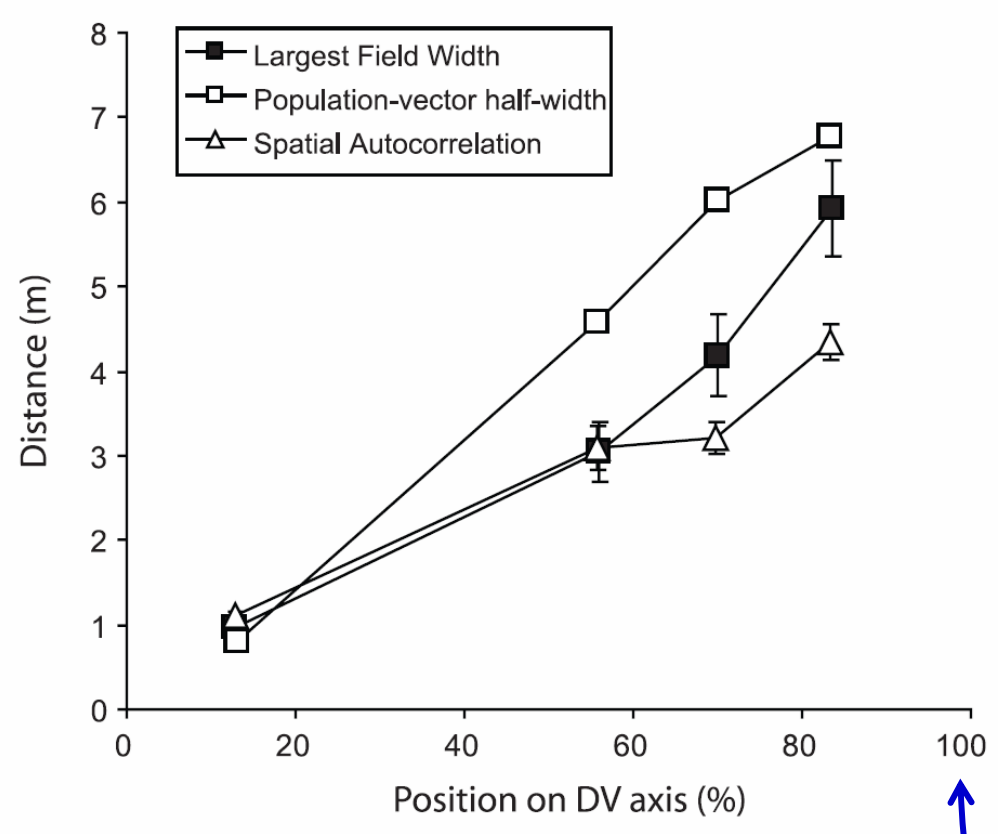
2 cells in dorsal hippocampus

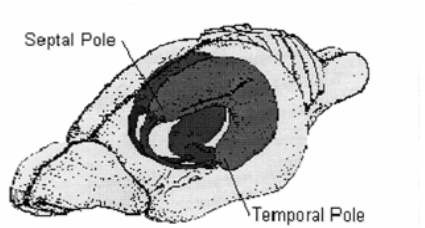


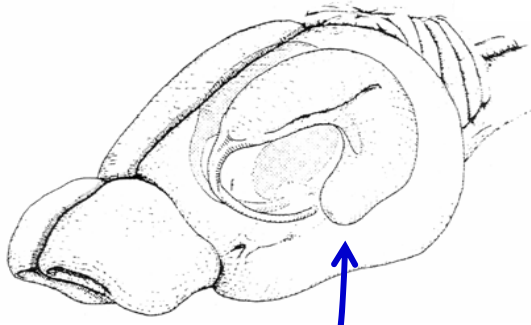
2 cells in ventral hippocampus

Kjelstrup et al., *Science* (2008)

Place fields increase in size along the dorso-ventral (septo-temporal) axis in the hippocampus

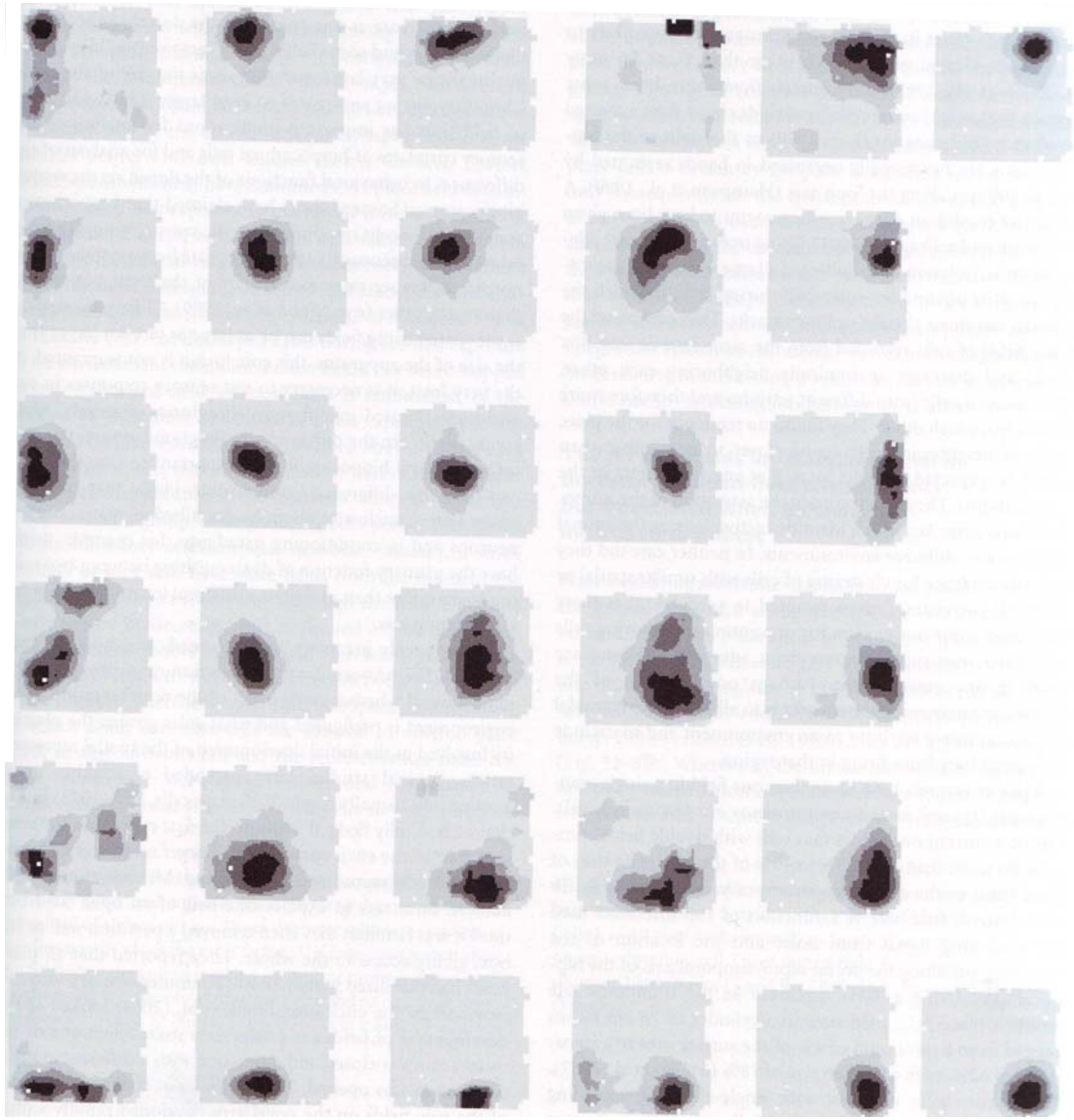






Hypothesis: very large-scale place fields here, at the temporal pole??

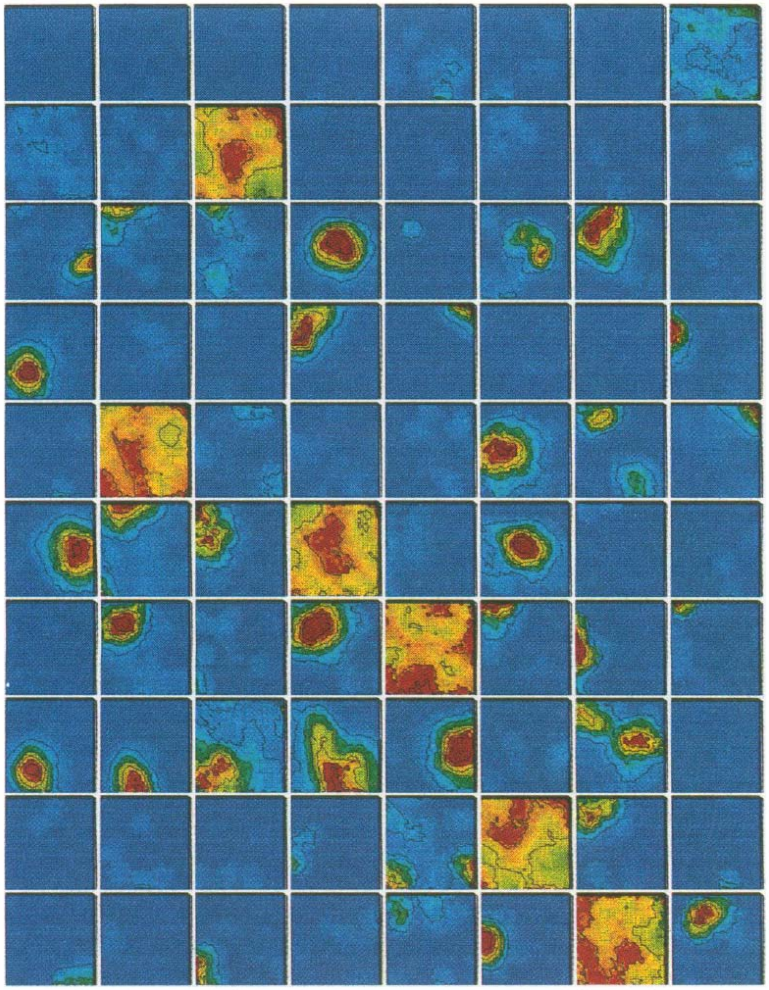
The place fields of hippocampal place cells tile the environment

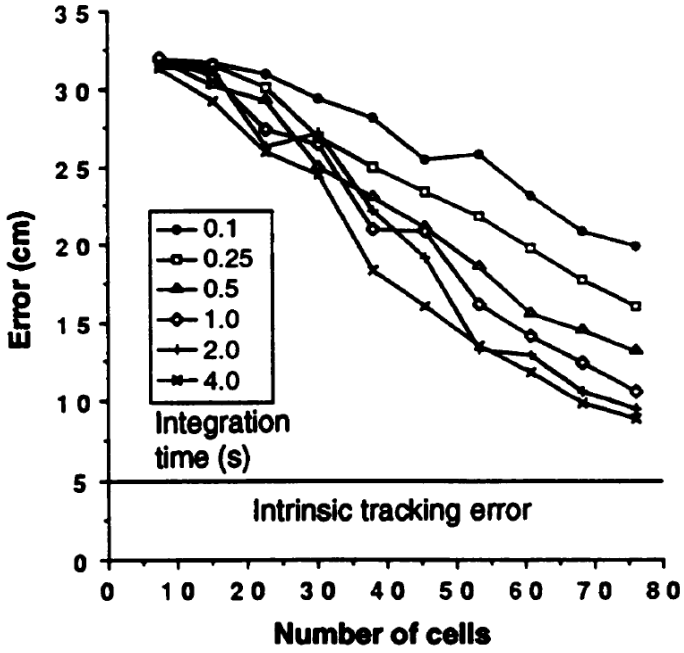


- An important property of place cells in a 2-D environment is that they are (generally) not directional, i.e. they do not have tuning to head direction.
- In 1-D environments, place cells may be directional (i.e. fire differently when running in one direction over another).

The rat's location can be reconstructed from the activity of an ensemble of simultaneously-recorded place cells

Tetrode recording of 80 neurons simultaneously



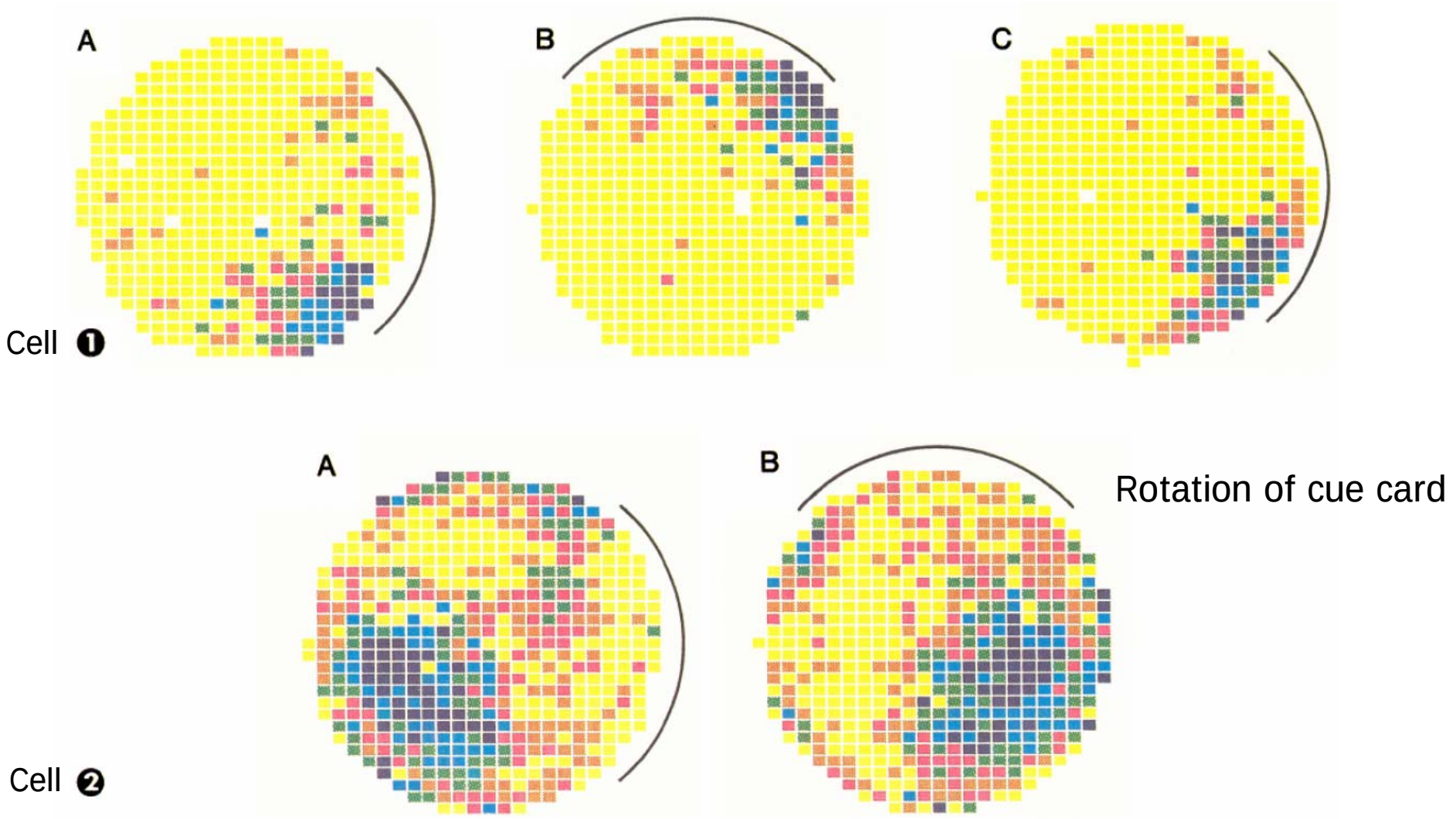


Putative pyramidal neuron (place cell)

Interneuron (very little spatial modulation)

Wilson and McNaughton, *Science* (1993)

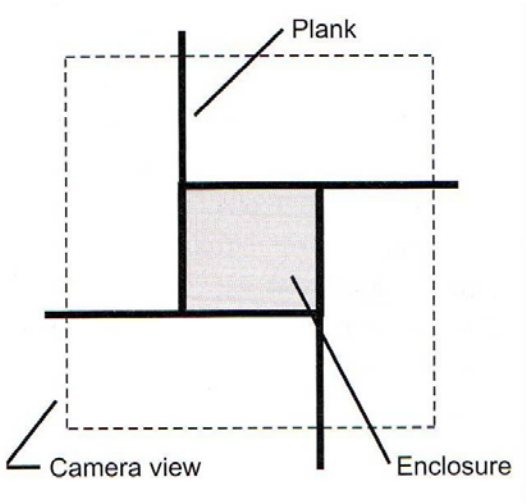
Place fields rotate with the rotation of external landmarks



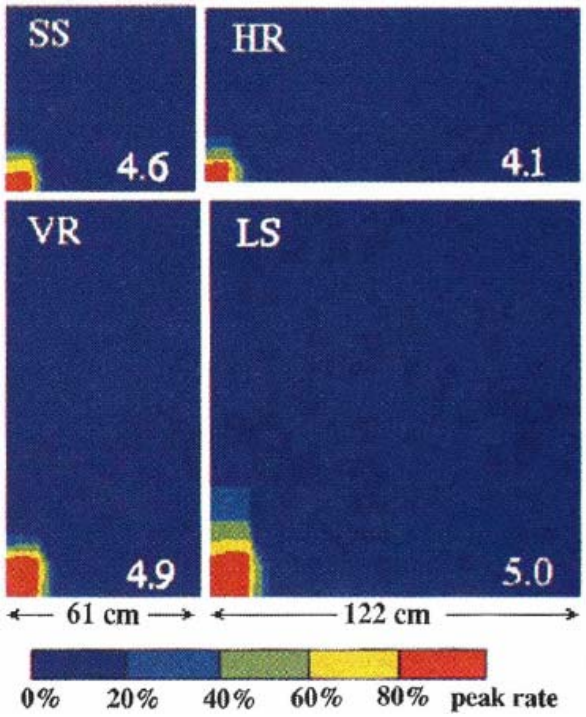
Also: Note that place field is quite <u>stable</u> (A vs. C)

(Muller and Kubie 1987)

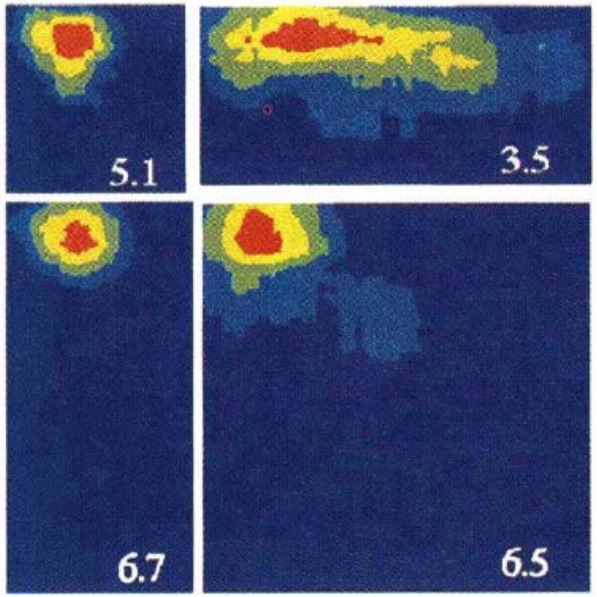
Place fields are affected by manipulations of the environment's geometry



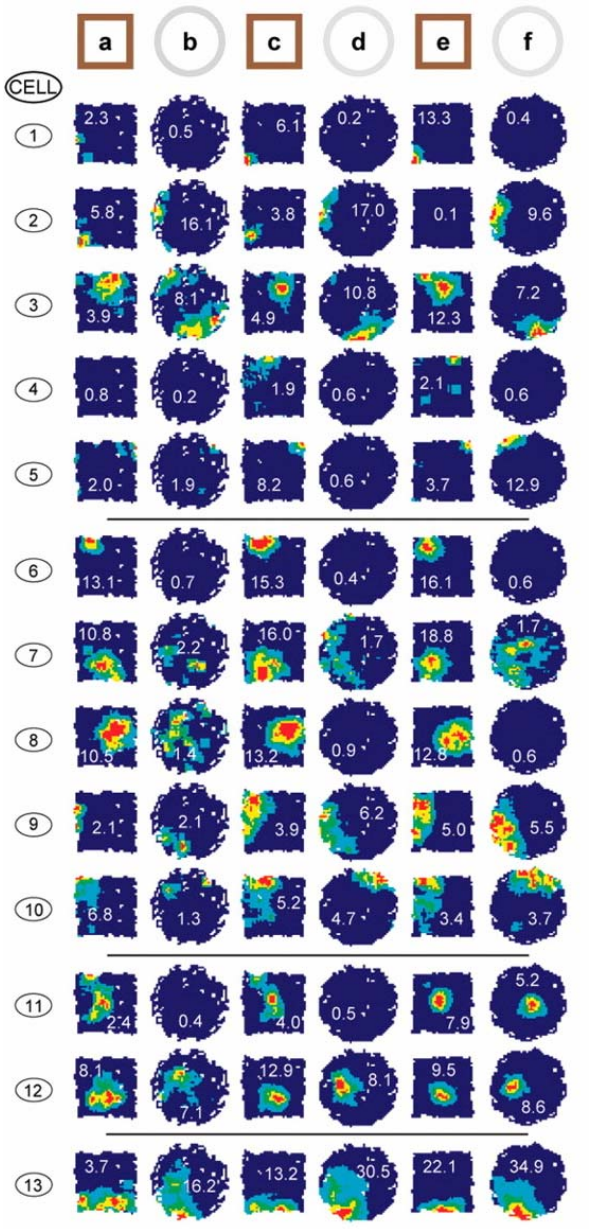
Cell 1



Cell 2



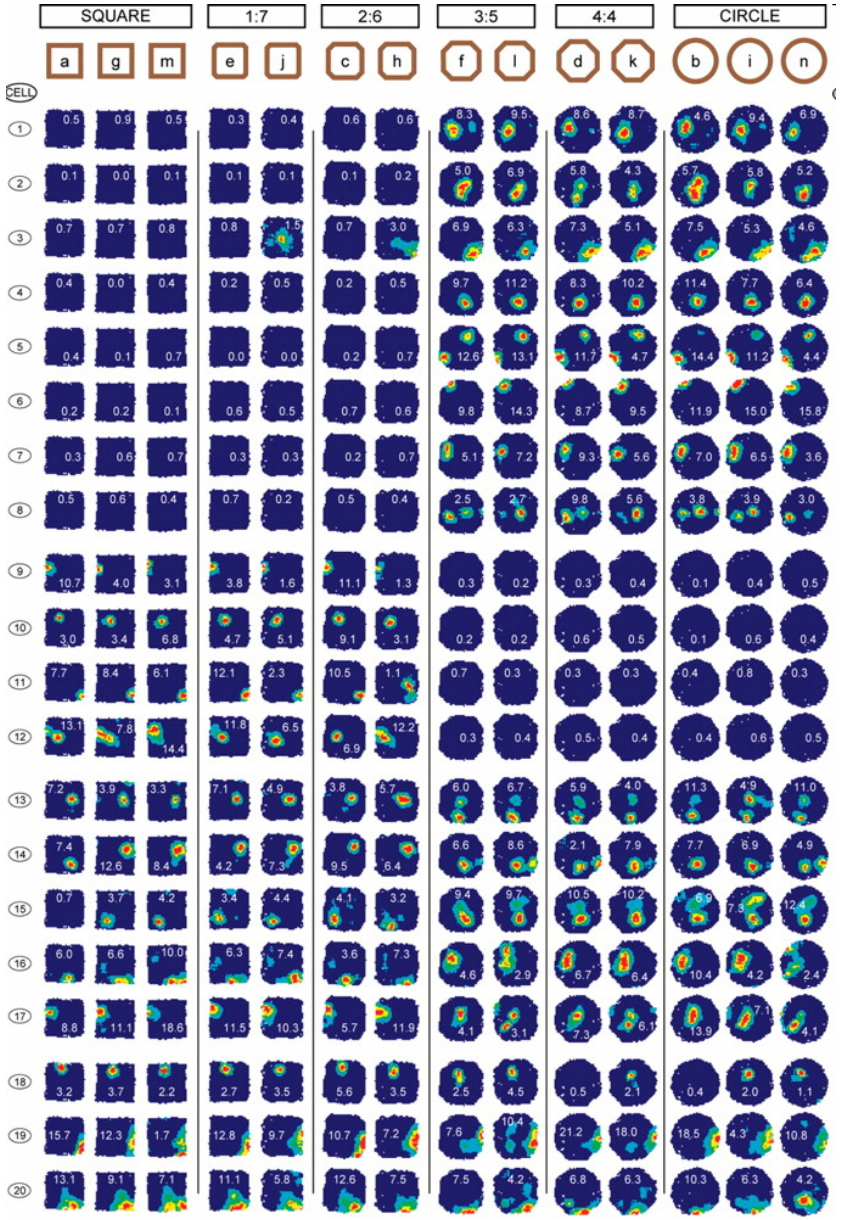
Multiple maps are stored simultaneously in the hippocampus



"Remapping" between representations of square and circular environments.

Wills et al., *Nature* (2005)

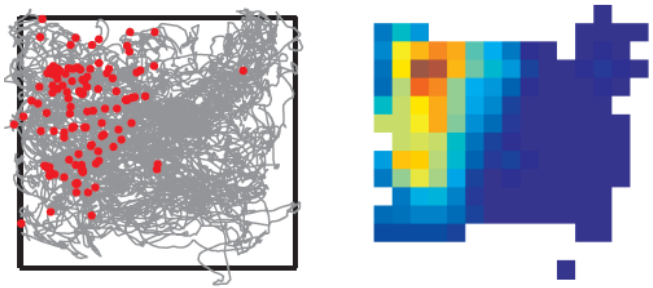
Multiple maps are stored simultaneously in the hippocampus



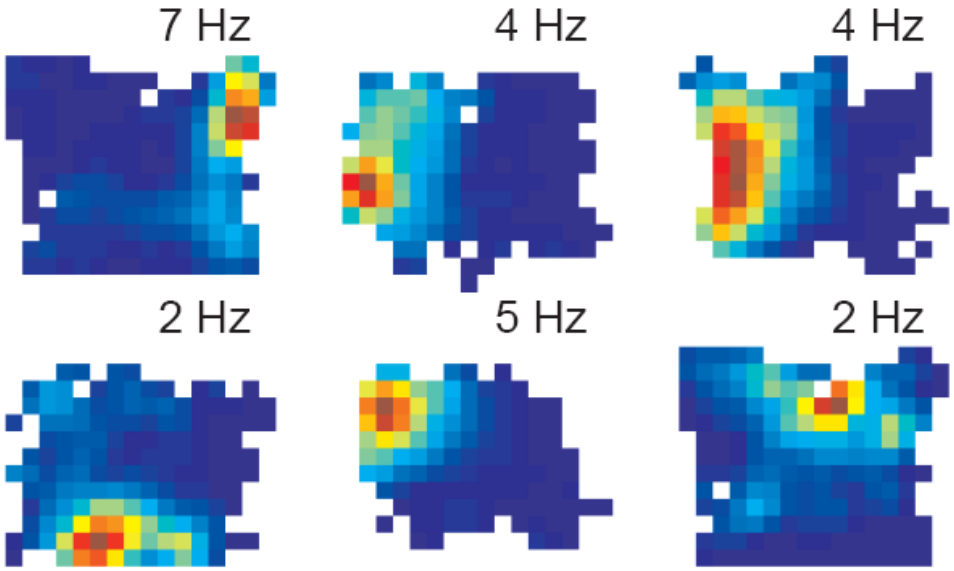
Abrupt phase transition between square-like and circle-like representations in intermediate octagonal environments.

Wills et al., *Nature* (2005)

Place cells in bat hippocampus



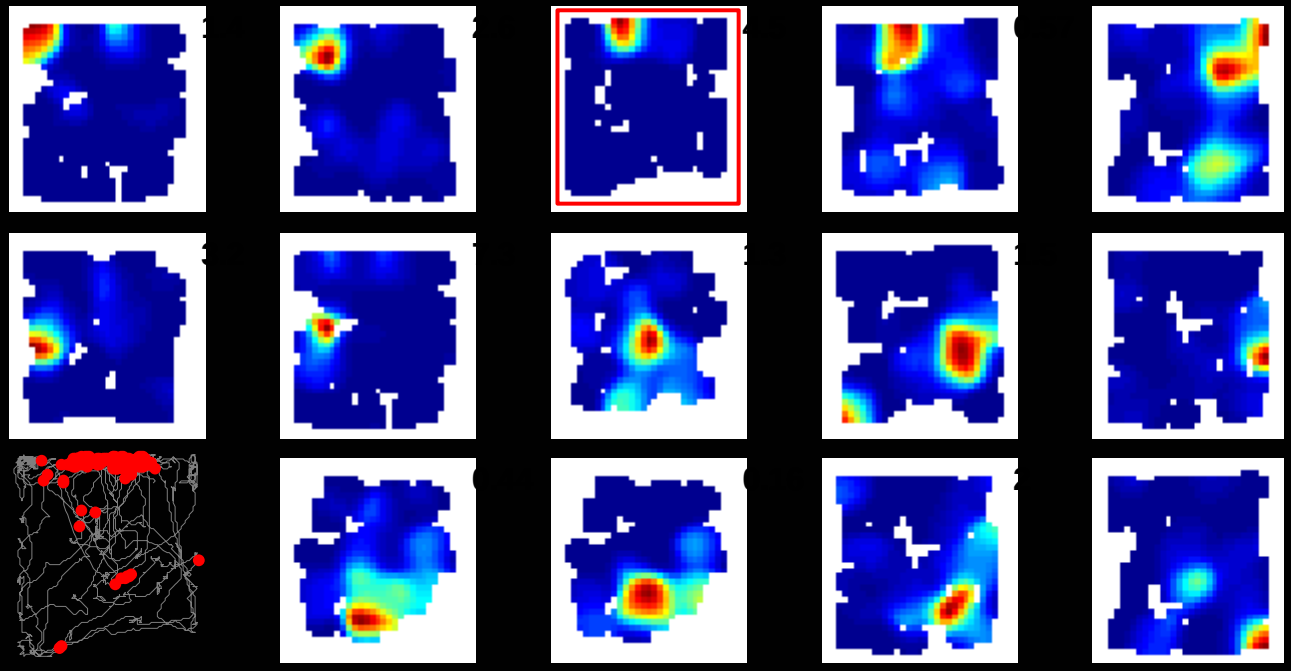
A single cell



More examples
of place fields
from 6 neurons

Ulanovsky & Moss,
Nature Neurosci. (2007)

And in another bat species: The Egyptian fruit bat



(Yes, bats can crawl)

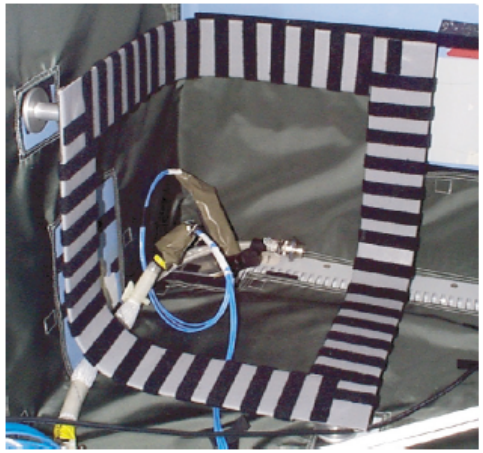
Movie of bat crawling

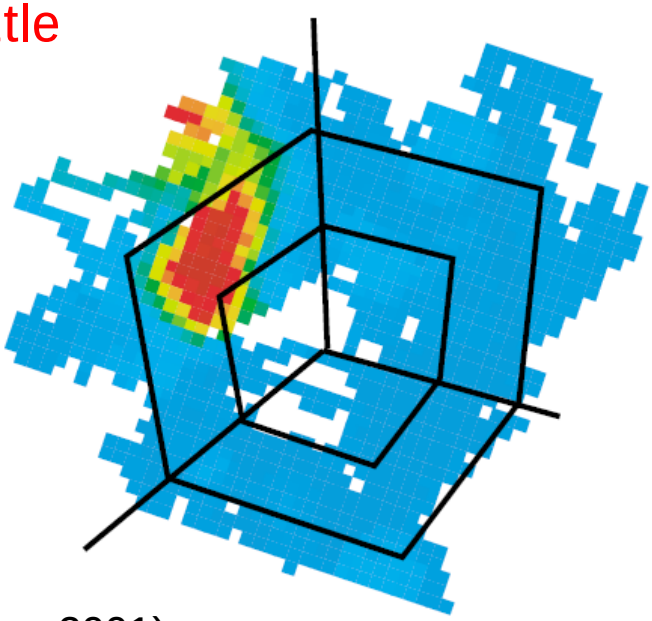
(Michael Yartsev)

Space rats

NeuroLab (1998)

On a NASA space shuttle

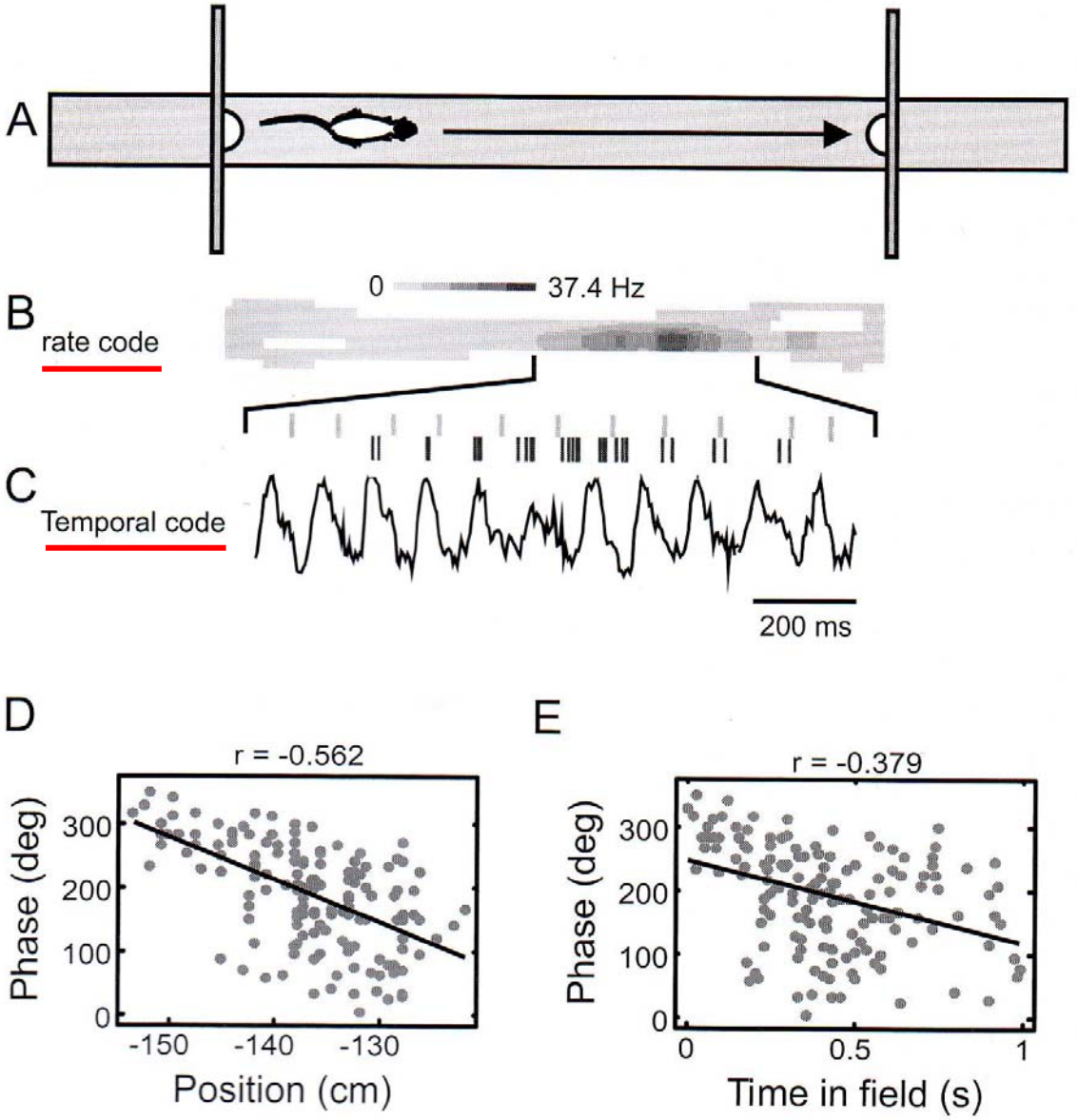




(Knierim, McNaughton & Poe 2001)

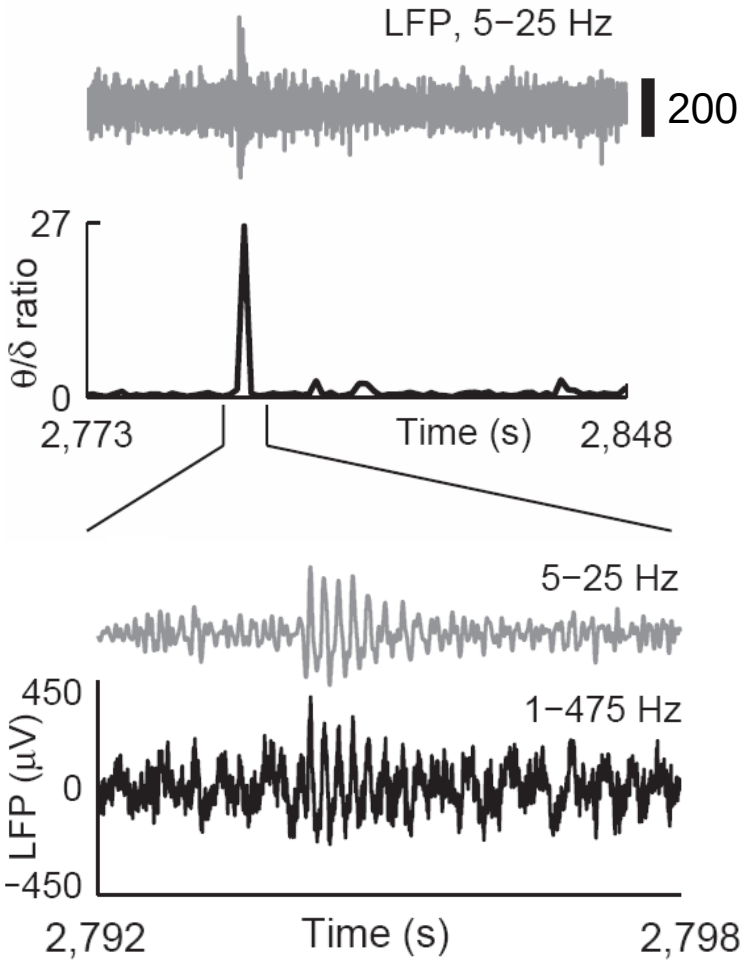
We are now working towards hippocampal neural recordings of 3-D place cells in freely flying bats, using a miniaturized telemetry system.

Temporal coding of location: Theta phase precession



Theta oscillation in bats is very different, casting doubt on the usefulness of theta-based temporal coding of location

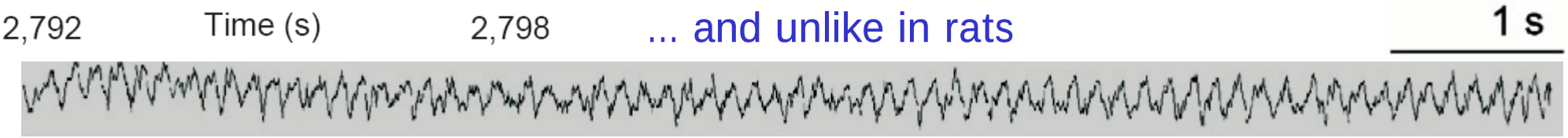
Short theta-bouts in bats



Like in humans...

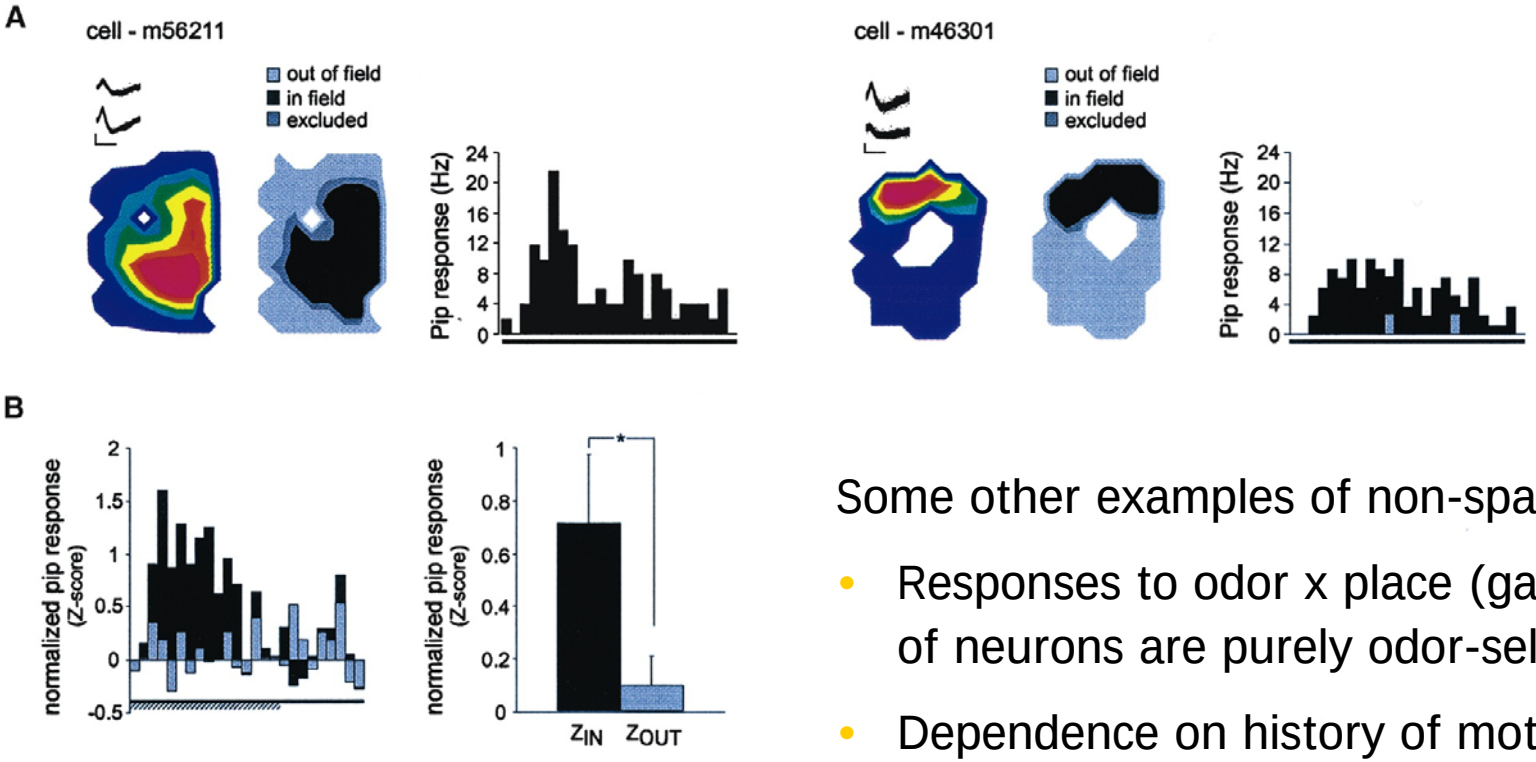
(Cantero et al. 2003)

... and unlike in rats



(Hollup et al. 2001)

Coding of place is not everything: Gating of auditory responses by hippocampal place cells



- Moita et al., *Neuron* (2003).

Some other examples of non-spatial coding:

- Responses to odor x place (gating). A small handful of neurons are purely odor-selective (Wood et al 2000).
- Dependence on history of motion (trajectory) or on future planned motion.
- Responses to behavioral events.

→ **Nevertheless, place tuning in hippocampal place cells in the most robust neural correlate of behavior.**

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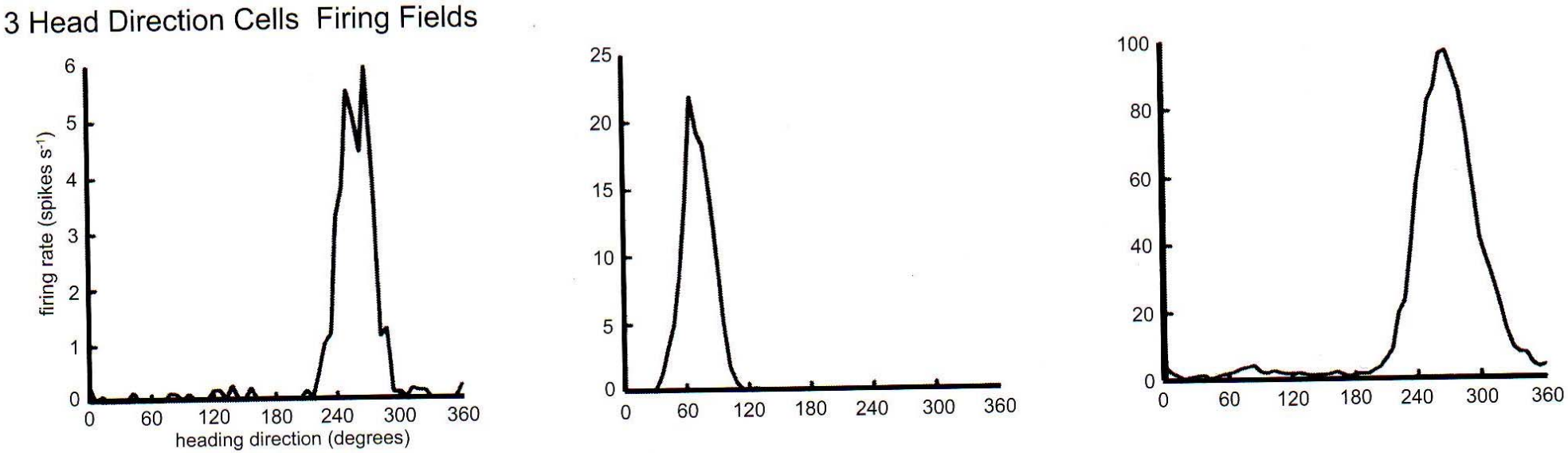
Head direction cells in dorsal presubiculum

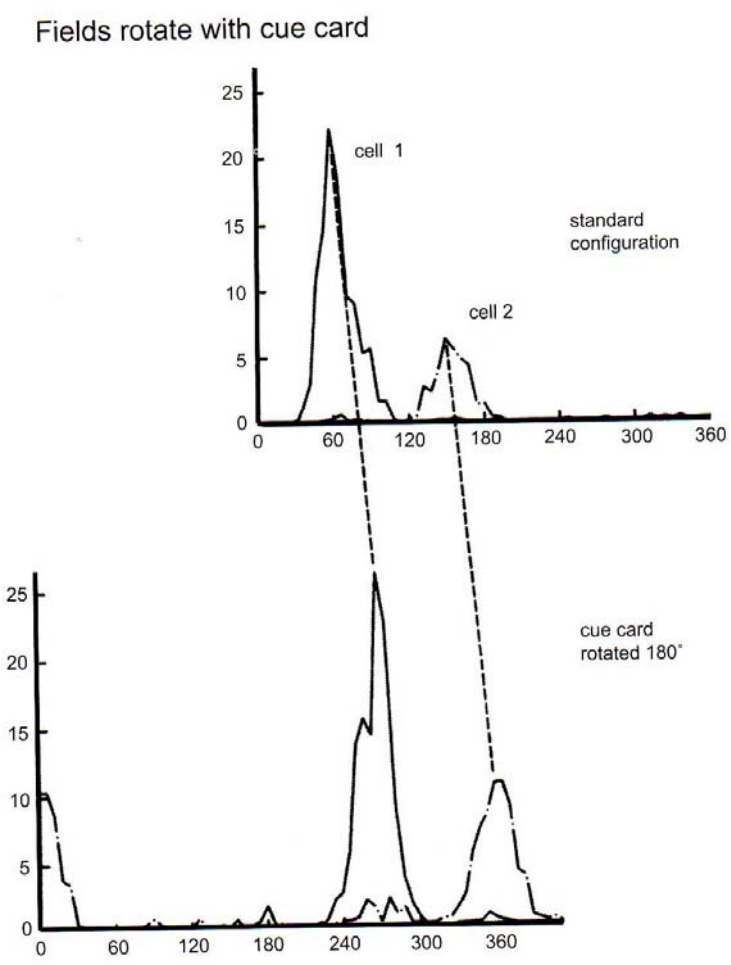


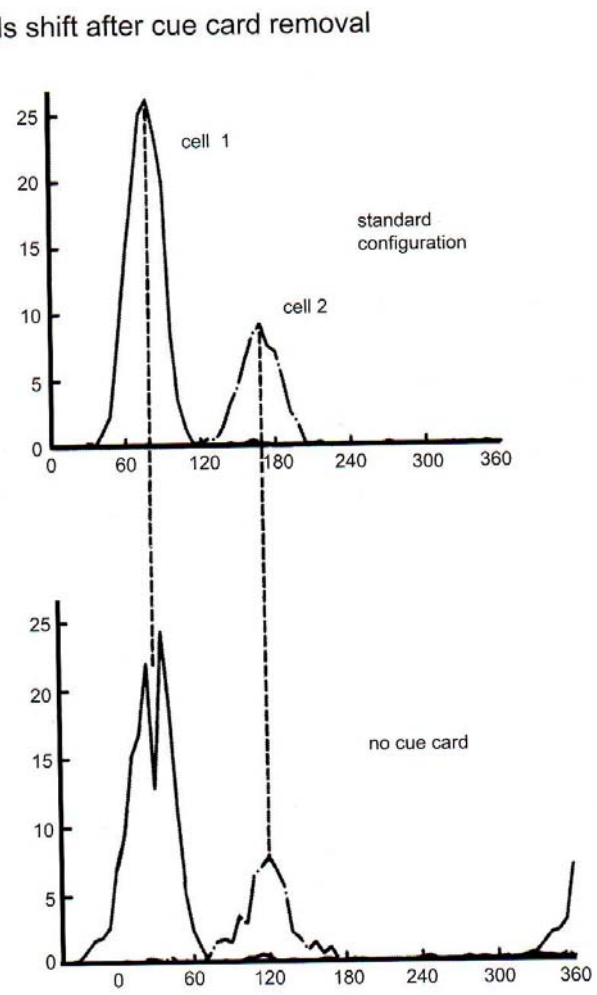
- Head direction cells are found in the dorsal presubiculum, anterior thalamus, medial entorhinal cortex, and in several other brain areas adjacent to the hippocampus.
- These cells are tuned to head direction, but *not* to place – i.e. they fire more or less uniformly with respect to the animal's location.

Head direction cells in dorsal presubiculum

Head direction cells rotate together

Head direction cells “remap” to a new random direction upon removal of cue card – but they remap *together*





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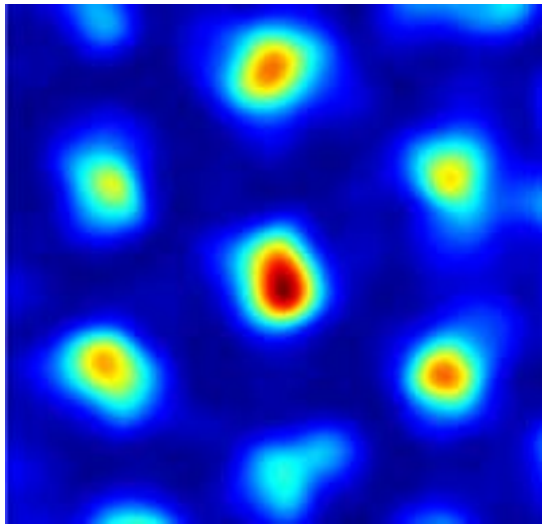
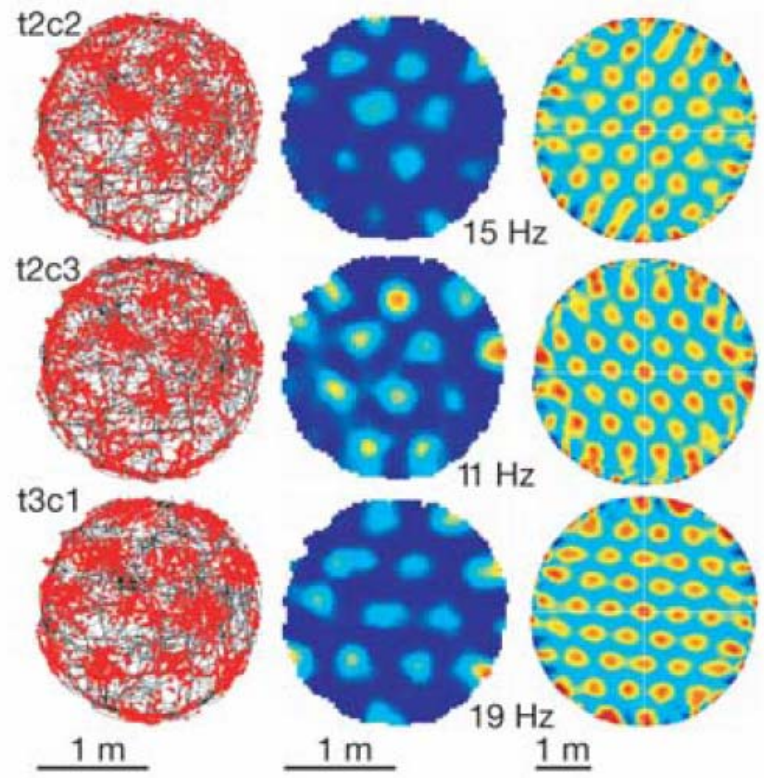
  - Head direction cells
  - **Grid cells**
  - Other brain areas involved in navigation
- Summary

Grid cells in dorsocaudal medial entorhinal cortex (dMEC)

Cell 1



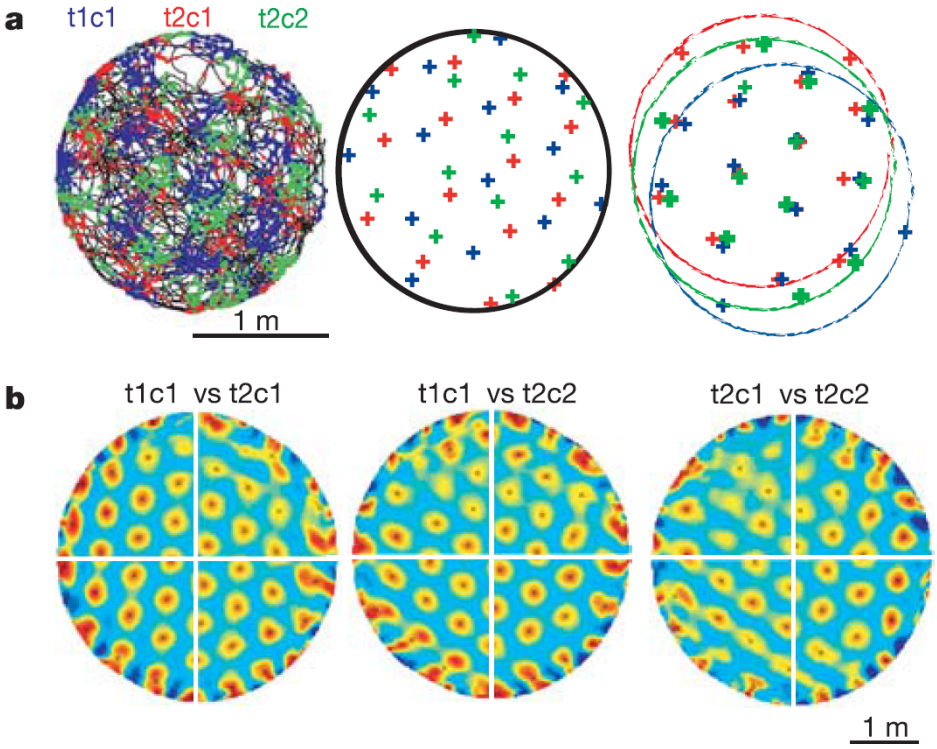


Cell 2

Cell 3

Cell 4

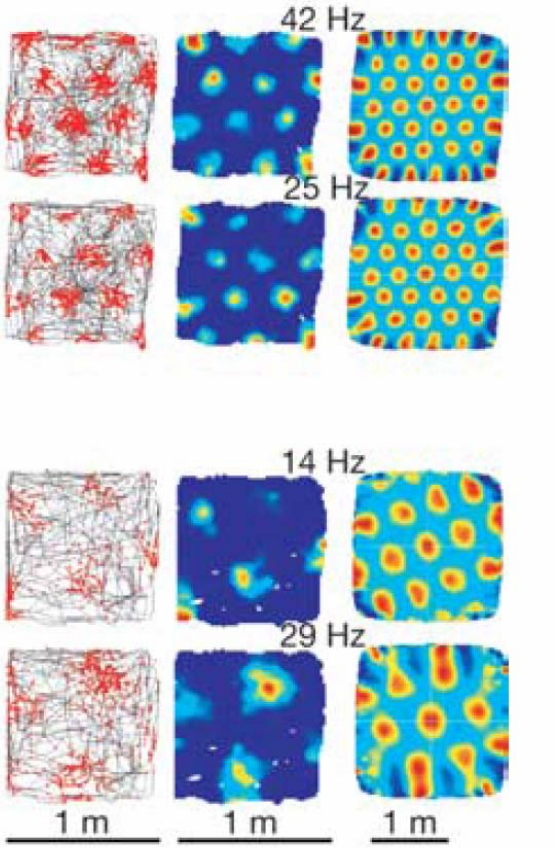
Nearby grid cells have the same grid spacing and orientation, but random grid phase

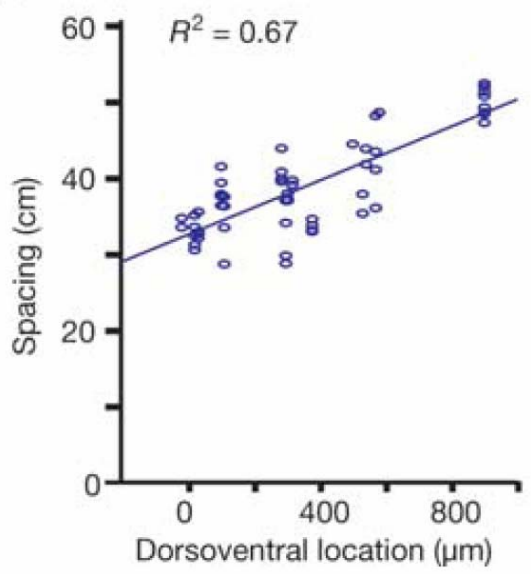


Grid spacing increases in size in the dorso-ventral direction

Dorsal

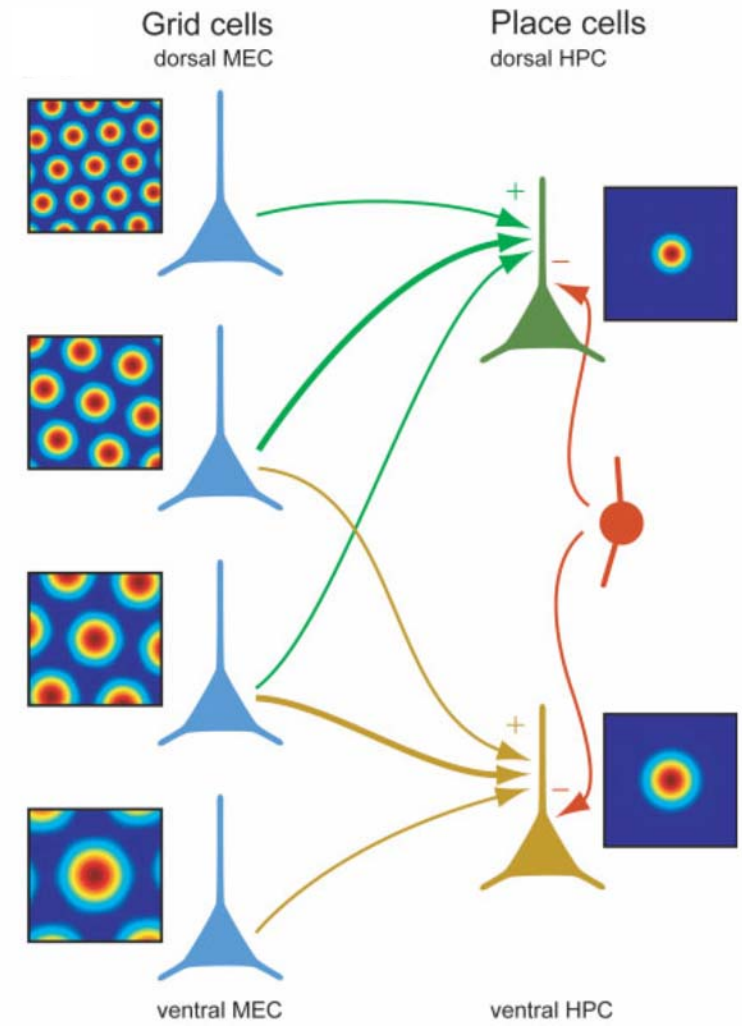
Ventral





- Historically the dorsal-to-dorsal and ventral-to-ventral connectivity between the dMEC and hippocampus was the “clue” that led the Mosers to try and record from more dorsal areas of MEC – which led to the discovery of grid cells.

Entorhinal grids might be combined to produce hippocampal place fields: Hexagonal Fourier-like decomposition



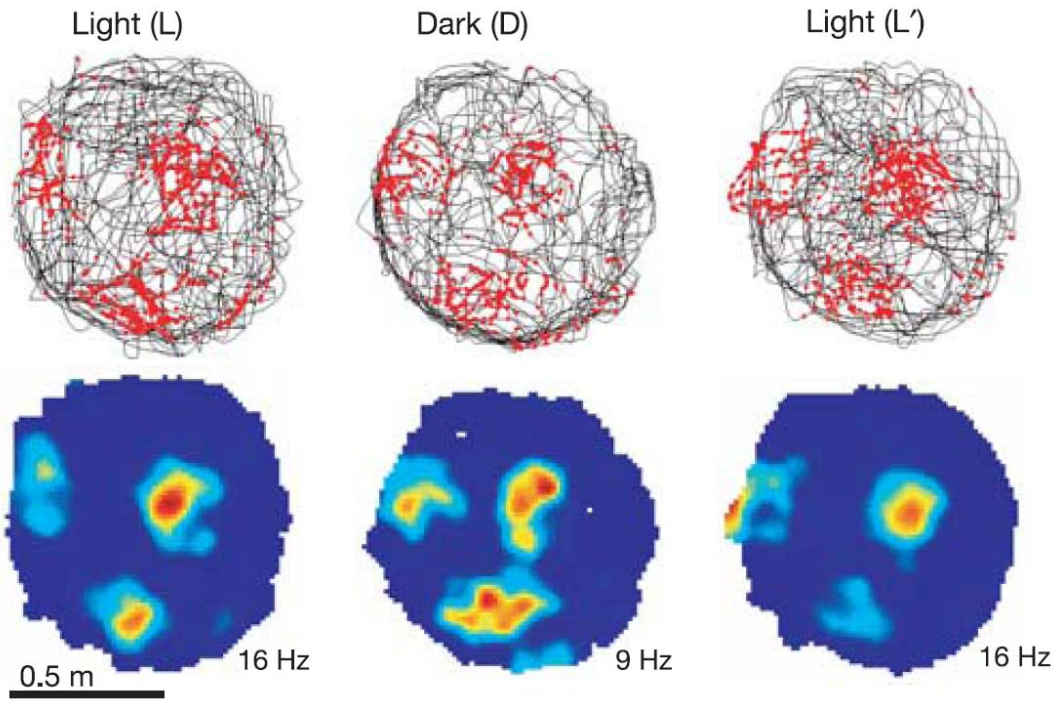
Model

by Solstad et al. (2006)

Additional interesting properties of grid cells:

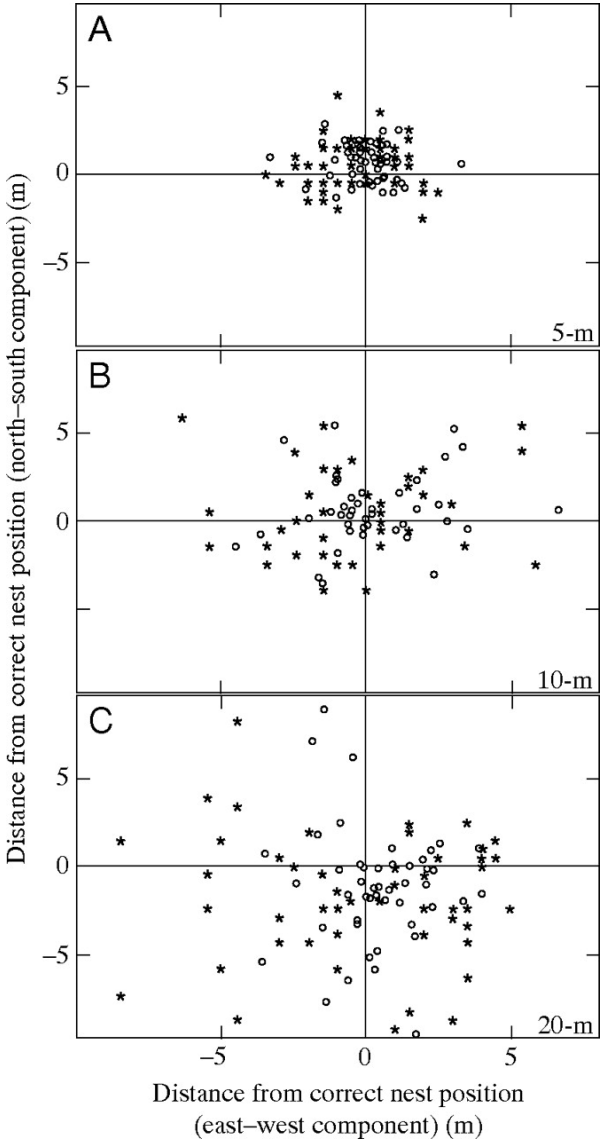
- During global remapping of hippocampal place cells, the grid cells exhibit a coherent shift & rotation (all of them shift & rotate together).
- Some grid cells have also clear directional tuning (and some don't); these differences are, to a certain degree, specific to the *layer* of the cortex.

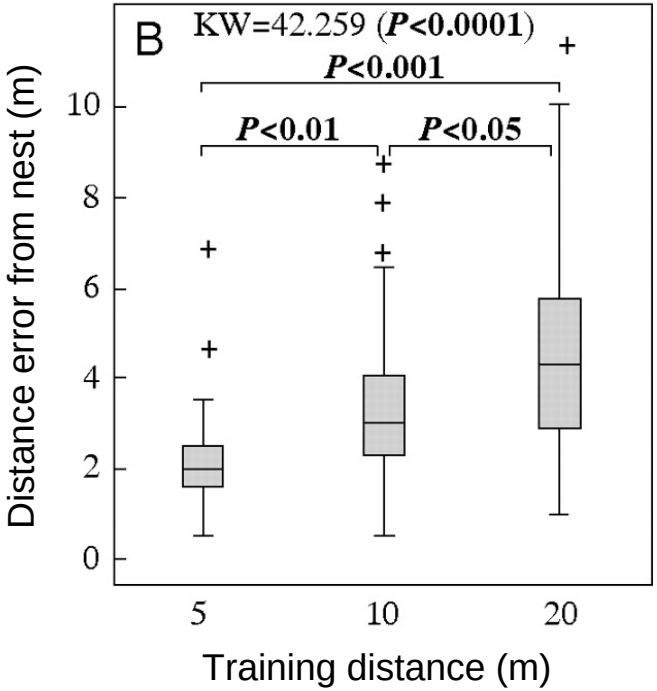
Proposed role of grid cells in path integration



- *Finding*: Grid cells persist after turning off the light (Hafting et al. 2005, see example above).
- *Caveat*: In these experiments, there was no attempt to remove odors (local cues): i.e., the rats could have been using a route-following navigational strategy (via local olfactory landmarks) to know their location – and not necessarily path integration.

Another caveat: Path integration is error prone



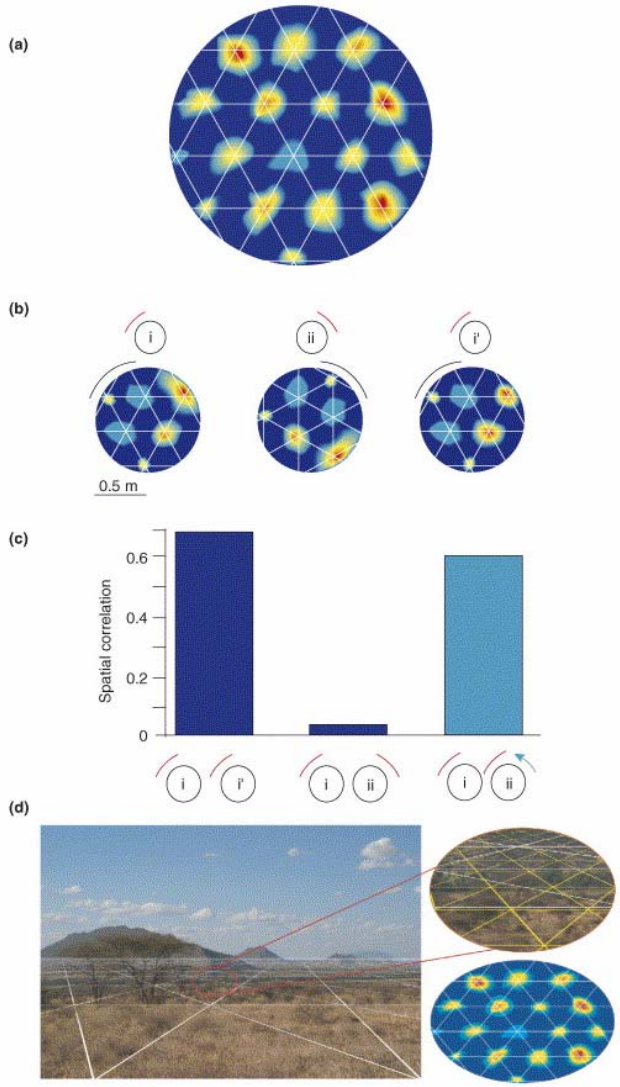


Graphs from last week:

In <u>desert ants</u>:
Random errors of **~25%** in **distance**

Mammals are less good path integrators that the desert ant. Rodents are not able to path-integrate reliably for more than 1–3 m (Etienne et al, *Nature* 1998).

Hypothesized role of grid cells in large-scale navigation



How a researcher of bird magnetic navigation imagines grid cells might be useful for long-distance navigation (Frost & Mouritsen, *Curr. Opin. Neurobiol.* 2006)

BUT: No such huge grids were found yet (and it is difficult to look for them).

Outline of today's lecture

- Hippocampus and spatial memory: early discoveries
- Hippocampus and large-scale navigation
- Back to small-scale navigation in the laboratory:
  - Place cells
  - Head direction cells
  - Grid cells
  - **Other brain areas involved in navigation**
- Summary

Other brain areas involved in navigation

* Beaconing / “response strategy” – **striatum**. That is, if you train a rat to always turn left (response strategy): this depends on the striatum. But if you train the rat to reach some *absolute* location in space: this depends on intact hippocampus & entorhinal cortex.

* Route-based navigation, transformations from organism-based (“egocentric”) coordinate frame to absolute-space-based (“allocentric”) coordinate frame – **parietal cortex** ?

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- **Summary**

Summary of some caveats

- Gap in spatial scale: Even rats (let alone bats) would require in the wild much larger place fields & grid fields than shown to date in the laboratory.
- Not only navigation and spatial memory: Other roles for hippocampus in learning & memory.
- Too little is known about the neural basis of the “higher” components of navigation (apart of the “you are here” component): How do animals compute the Home Vector ? Trajectory planning ? Decision making ?