Spatial Neurons in the Hippocampus and Entorhinal Cortices

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Animal survival depends on accurate spatial coding

Clayton & Dickson, 1998
Wittlinger et al., 2006
Ancel et al., 1992
Morris, 1981
Aguirre & D’Esposito, 1999
What components are needed to navigate? Finding your car
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How does the brain represent our position in external space?
Mammalian representation of space is more complex

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

Tolman introduced the concept of an internal spatial map

Spatial navigation reflected the formation of spatial maps of the local environment

'Cognitive maps'
How do we find our way?

**Cognitive Maps**

Animals discover the relationships between places and events as they explore the environment and that exploration leads gradually to the formation of a “cognitive map.”
Where is the 'cognitive map' in the brain?

Henry Gustav Molaison (HM)

Could no longer form new episodic memories
The hippocampus is associated with memory formation.

Detection of nerve impulses from behaving rats provides a window into the sense of place.

What do hippocampal cells do during spatial navigation?
What are neurons in the hippocampus coding?
Place cells respond on the basis of spatial location cued by multiple different types of input.

Quirk et al., 1990

Knierim et al., J Neurosci, 1995
Where does this place code come from?
Where does this place code come from?
Recordings from the medial entorhinal cortex, which sends signals to the dorsal hippocampus, which is the structure where the majority of place cells have been recorded from.
The building blocks of an internal, neural navigation system

Grid cell periodicity requires continuous correction for changes in SPEED and DIRECTION.

The strict periodicity of the firing locations is thought to enable a metric representation of the animal’s own location in the spatial environment.
Grid neurons may represent a fundamental coding scheme generated by entorhinal neural circuits

Fyhn et al., Science, 2004
Hafting et al., Nature, 2005
Fyhn et al., Hippocampus, 2008
Yartsev et al., Science, 2011
Killian et al., Nature, 2012
Jacobs et al., Nature Neuroscience, 2013
How do neurons encode position: Head direction cells in the presubiculum

An inner compass
Ranck, 1985

Tor Kirkesola, 2010
How do neurons encode position: Head direction cells

Head direction cells encode local orientation; not based on magnetic poles

Different head direction cells fire in different directions

As a population, the entire 360 degree surround of the animal is represented
How do neurons encode position: Head direction cells

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How do neurons encode position: Head direction cells

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Different head direction cells fire in different directions

As a population, the entire 360 degree surround of the animal is represented
How do neurons encode position: Border cells in entorhinal cortex

Always fires along the border of the environment, even if the box is stretched or a new boundary inserted

Solstad et al., Science, 2008
The neural substrate for spatial representation

A way for encoding spatial maps in the brain

- Place cells
- Border cells
- Grid cells
- Head direction cells
Spatial navigation circuit
What is the role of self-motion and landmark cues in generating spatial codes?
Navigation leverages multiple types of cues to calculate our position in space.

Landmark cues support the creation of an internal map of our external world.

Self-motion cues provide directional information for navigation.

Supports the creation of an internal map of our external world.
The influence of landmark or self-motion cues on position estimates can differ based on how informative they are.

How are visual and locomotor cues combined to support navigation?
How are visual and locomotor cues combined during navigation: a behavioral perspective

Path-integration based navigation

Virtual reality setup: allows tight control over the mouse’s visual experience

Campbell, Ocko, Mallory, Low, Ganguli & Giocomo, Nature Neuroscience, In Press
How are visual and locomotor cues combined during path integration?

A path integration task that provides a read out of the animal’s estimate of position

**Experiment:**

On random trials, change rate of optical flow and measure where mice slow down

- **Gain increase**
  - Visual cues move faster

- **Gain decrease**
  - Visual cues move slower

*Campbell, Ocko, Mallory, Low, Ganguli & Giocomo, Nature Neuroscience, In Press*
Gain manipulation allows an examination of how mice weigh locomotor versus visual cues during path integration.

An asymmetry: Mice upweight the importance of visual speed when it is fast.

Campbell, Ocko, Mallory, Low, Ganguli & Giocomo, Nature Neuroscience, In Press
How is landmark input combined with path integration to form a unified map?

Examine neural activity in medial entorhinal cortex, a region thought to serve as a neural basis for navigation.

Grid cells show a periodic pattern despite changes in running speed and direction.

Grid cells may represent path integration calculations.

*Hafting et al., 2005*
Grid cell coding in virtual reality

Campbell, Ocko, Mallory, Low, Ganguli & Giocomo, Nature Neuroscience, In Press
A network-level attractor model for generating grid cell firing patterns

Grid cells

Recurrent Inhibition

Translation driven by velocity signals

Landmark input provides error correction

Burak & Fiete, 2009

Hardcastle, Ganguli, Giocomo, Neuron, 2015
A framework for understanding how self-motion and landmark cues control grid cell representations

Campbell, Ocko, Mallory, Low, Ganguli & Giocomo, Nature Neuroscience, 2018
Ocko, Hardcastle, Giocomo & Ganguli, PNAS, In Press
How do differences in the phase of the attractor and landmark inputs change during perturbations?

Gain manipulations de-couple landmark and self-motion cues

**Experiment**: Change rate of optical flow and measure grid cell response

*Gain increase* = Visual cues move faster

*Gain decrease* = Visual cues move slower

*Campbell, Ocko, Mallory, Low, Ganguli & Giocomo, Nature Neuroscience, 2018*

*Ocko, Hardcastle, Giocomo & Ganguli, PNAS, In Press*
Model-predictions for gain manipulations

Baseline:
path integration
matches landmarks

Small gain change:
Subcritical manipulation

Large gain change:
Critical manipulation

Small gain change = phase shift; Large gain change = re-scaling/remapping
Model-predictions for grid cell responses to gain manipulations

Because visual speed is up-weighted when it is fast and vice versa, 0.5x is a large gain change and 1.5x is a small gain change.

Therefore, gain decrease responses should be super-critical (rescaling/remapping) and gain increase responses should be sub-critical (phase shifts).
Grid cell responses to gain manipulations

Gain decrease (n = 40 grid cells): Remapping and rescaling (super-critical)

Gain increase (n = 41 grid cells): Phase shift (sub-critical)
Gain manipulations de-couple landmark and self-motion cues

**Small mismatch:**
- Subcritical manipulation
- Gain increase
- Visual cues faster

**Large mismatch:**
- Critical manipulation
- Gain decrease
- Visual cues slower
Principles of the integration of landmark and self-motion cues in MEC

Navigation – from the perspective of behavior and the neural codes supporting navigation - reflects self-motion and landmark cues in a dynamic but principled way.

Registration between position estimates based on MEC neural codes and behavior is consistent with a role for MEC in path-integration navigation.

Reveals quantitative principles for computing position across different environmental contexts or behavioral states.
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A sub-critical gain decrease manipulation

De-coherence

Gain

critical: rescaling

sub-critical: phase shift

0.5 0.75 1.5

sub-critical: phase shift

critical: rescaling

baseline
A-B (g=0.75)
A-B (g=0.5)

baseline
B-B (g=0.75)
B-B (g=0.5)