Development of the hippocampal spatial and memory networks in the rat

OR

How to build a brain circuit for a higher-cognitive function.

Tom Wills

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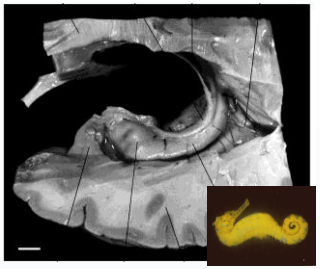
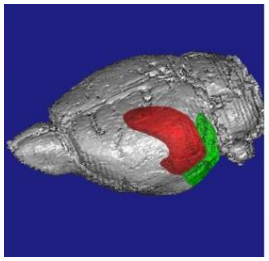
The hippocampus, spatial navigation and episodic memory

- The hippocampus (‘seahorse’) is involved in spatial memory and navigation across the Vertebrate group.

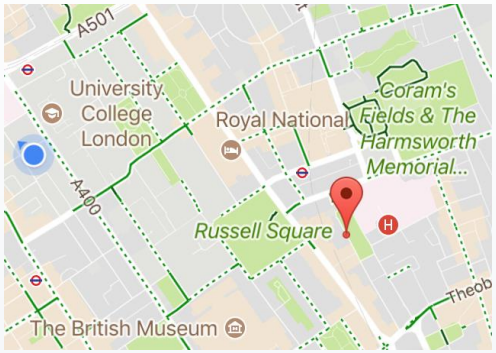
Human



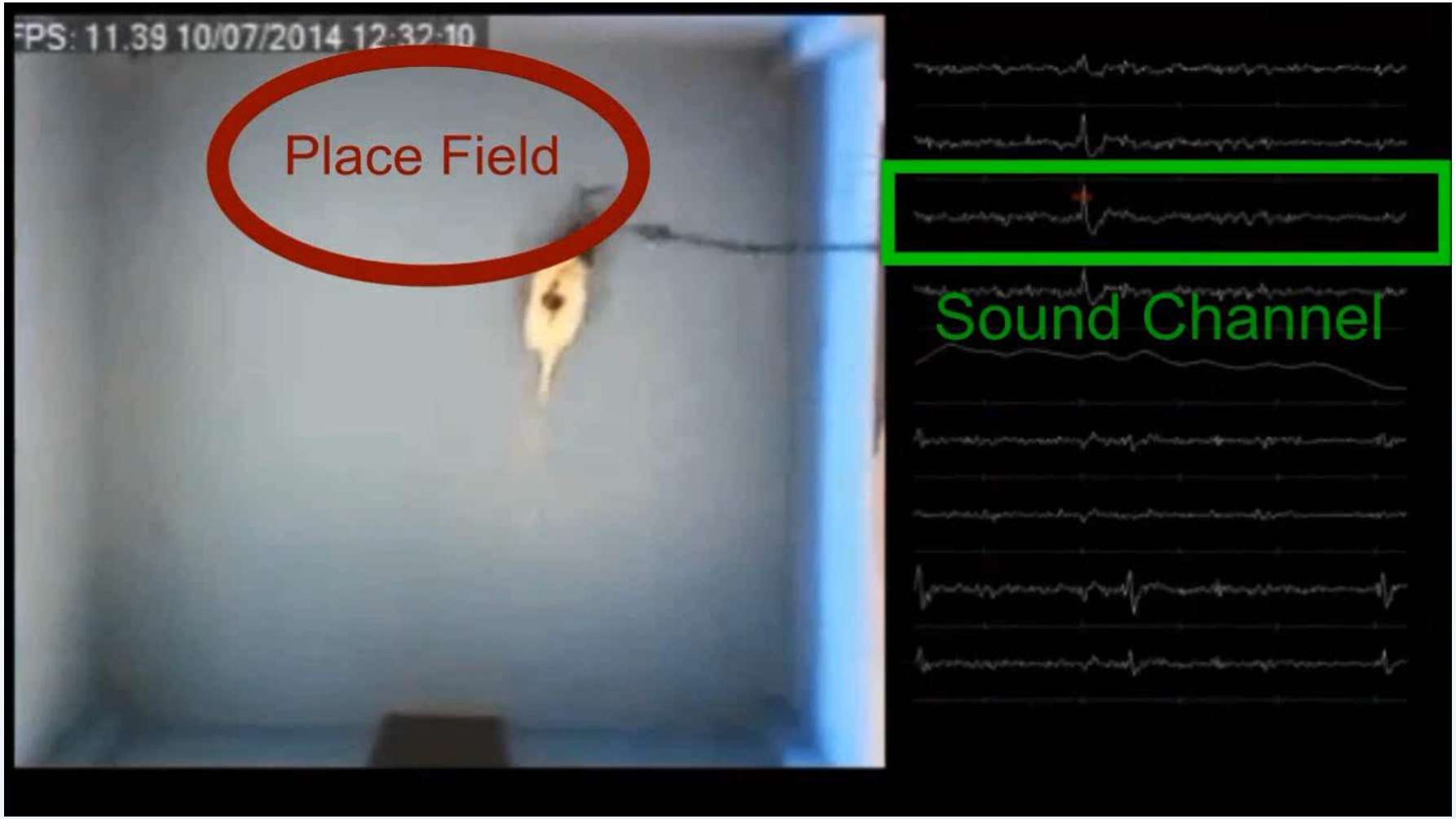
Rat



The hippocampus contains a neural representation of space: it is the seat of Tolman’s ‘Cognitive map’.



Place cell

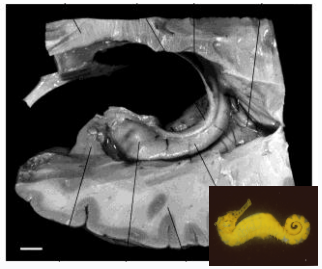


Video courtesy of Roddy Grieves (youtube)

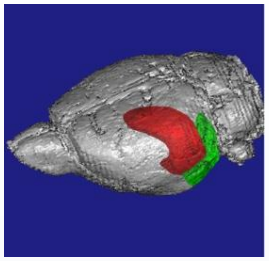
The hippocampus, spatial navigation and episodic memory

- The hippocampus ('seahorse') is involved in spatial memory and navigation across the Vertebrate group.

Human



Rat



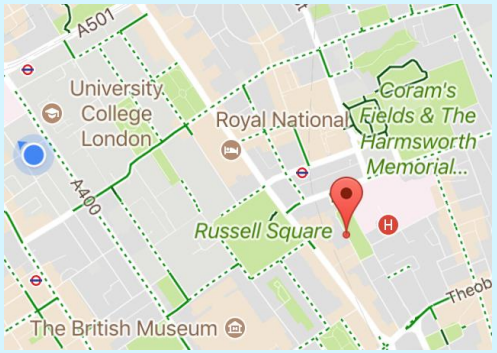
In humans, the hippocampus supports episodic memories.

Henry Molaison ('Patient H.M.')

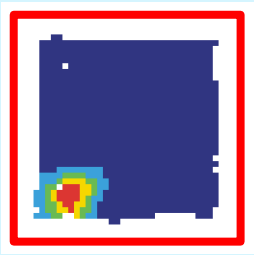
Damage to brain areas which contain place, grid and head direction cells result in amnesia in humans.

MEMORY

The hippocampus contains a neural representation of space: it is the seat of Tolman's 'Cognitive map'.

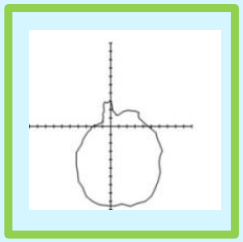


Place (Place Cells)



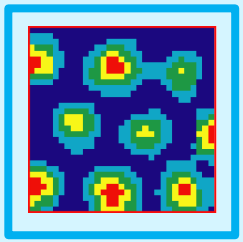
O'Keefe & Dostrovsky, 1971

Direction (Head Direction Cells)



Taube, Muller & Ranck, 1990

Distance (Grid Cells)



Hafting, Fyhn, Molden, Moser & Moser, 2005

SPACE

The development of the neural map of space

Key theme: How do neural representations of space and memory emerge during development?

- Kant proposed that space and time are 'innate';
- Which aspects of the hippocampal map (if any) are likely to develop independently from sensory experience?
- Conversely, are there any sensory inputs which are necessary for development?

Space […] exists in the mind *a priori,* […], it can contain, prior to all experience, principles which determine the relations of these objects' *(Immanuel Kant, Critique of Pure Reason*).

Talk outline:

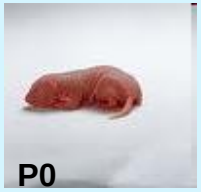
1) Maturation of **spatial responses**;

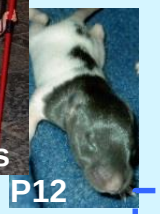
   1a) Place cells: the role of boundaries in development.

   1b) Head direction cells: interplay of sensory input and pre-configured circuits

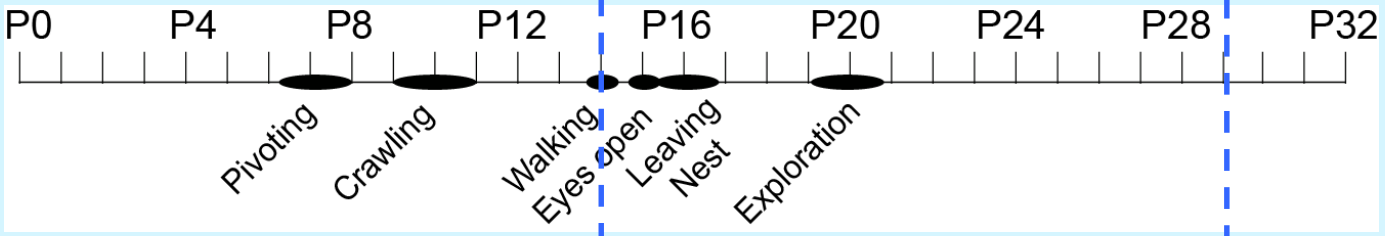
2) Development of **neural correlates of memory**.

Developmental timeline



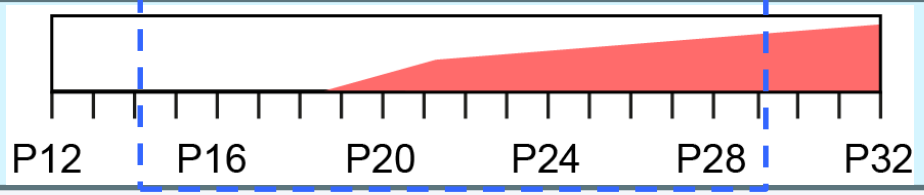


Sensory/ Motor Milestones



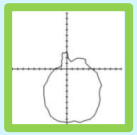
Record Neural Responses

Hippocampal memory

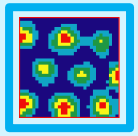


Spatial responses

Head Direction Cells



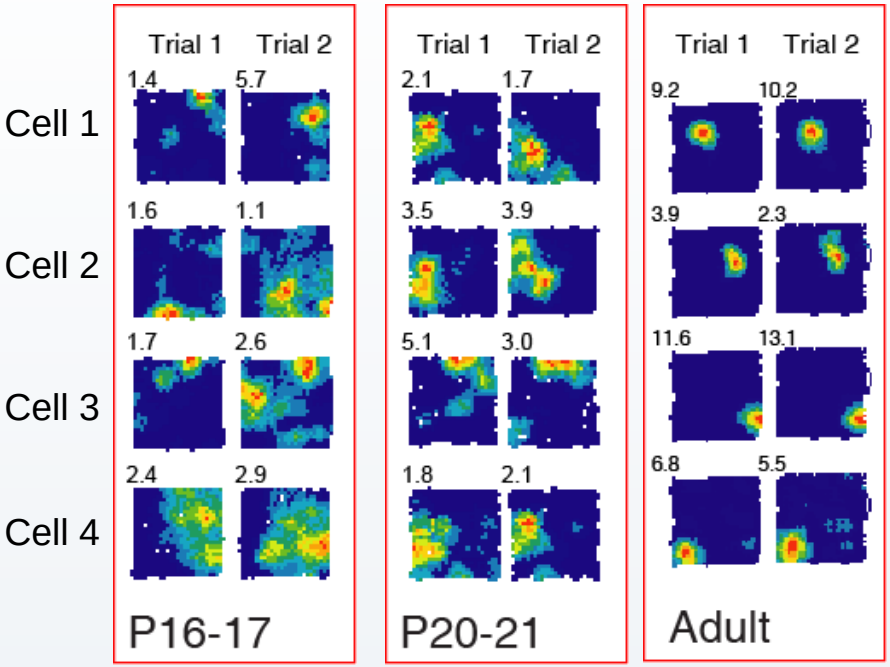
Grid Cells



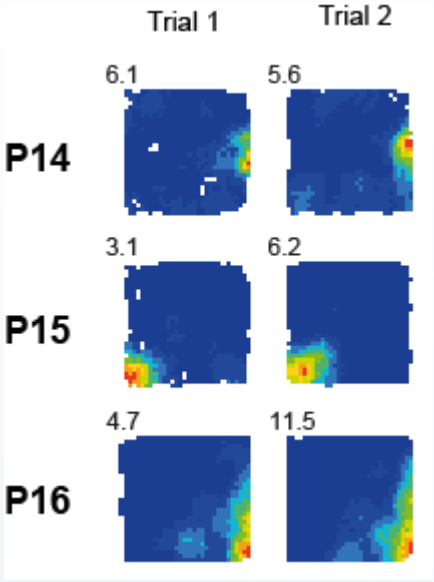
Place Cells

Wills, Cacucci et al, 2010, Science; Tan, Bassett et al, 2015, Current Biology; Bassett et al 2018, Current Biology.

Place cells: appear early, improve gradually



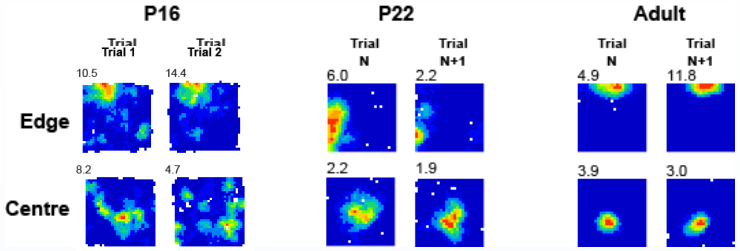
Some adult-like place cells are found even in very young pups:



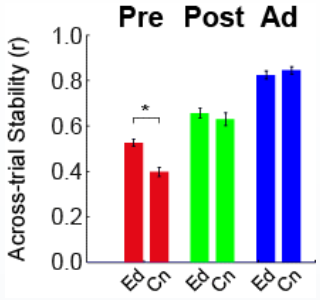
- What is supporting adult-like place cells in these animals?

Wills, Cacucci, Burgess and O'Keefe, Science, 2010.

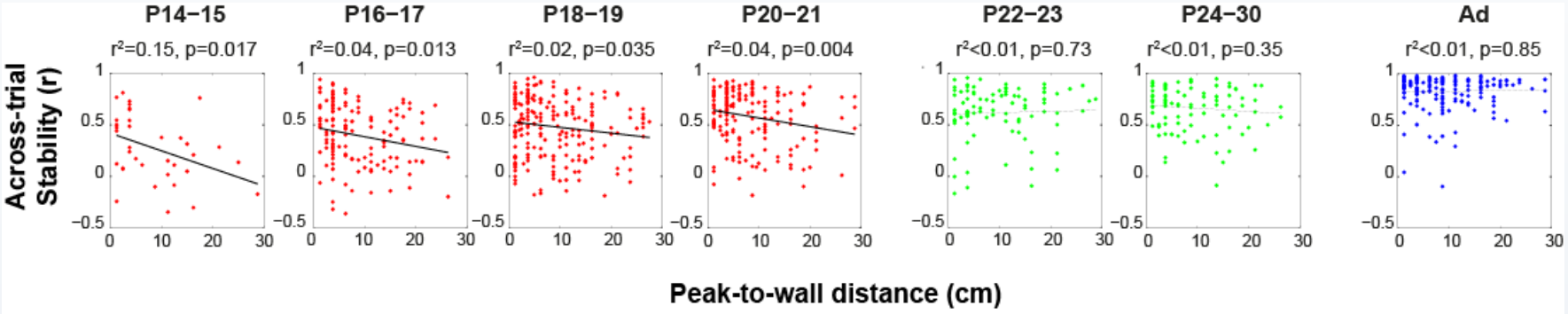
Boundaries stabilise place fields in pre-weanling pups



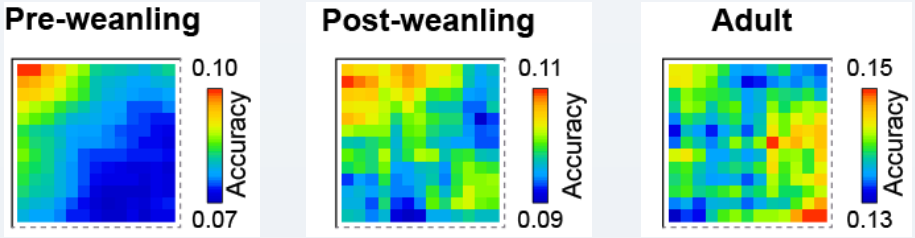
Place field stability at Edge and in Centre of the Environment



- Before weaning, significant correlation between place field proximity-to-wall and stability.
- After weaning and in adulthood, equal stability throughout environment.



Accuracy of Place Cell encoding of location:



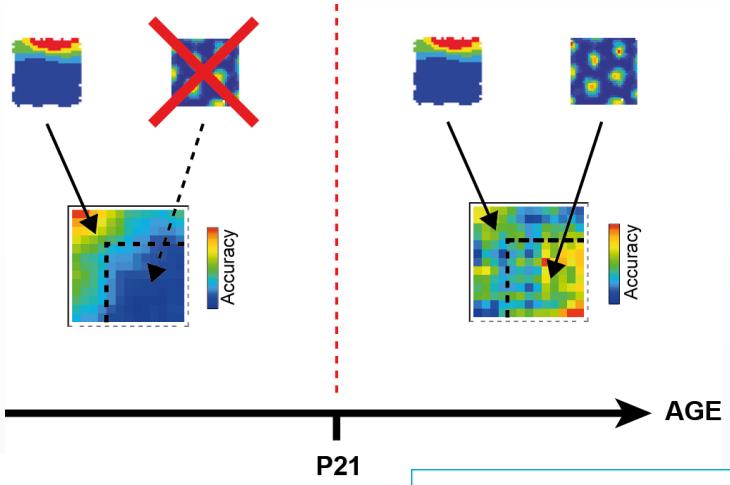
Muessig, et al, (2015), Neuron

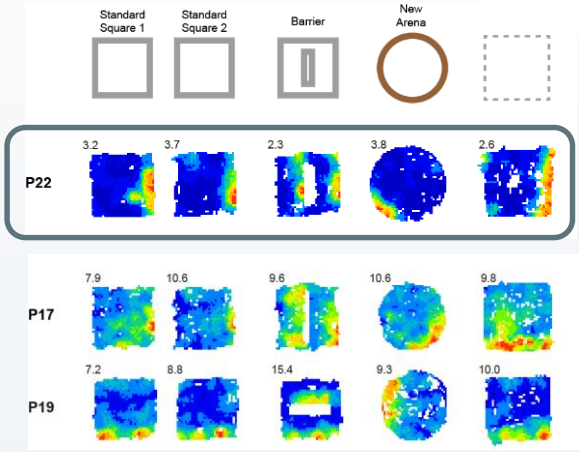
One possible mechanism …


Laurenz Muessig


Fabio Ribeiro Rodrigues

- **Boundary cells** may provide the input that drives and stabilises early place fields.

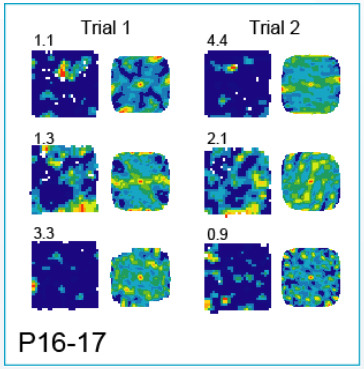


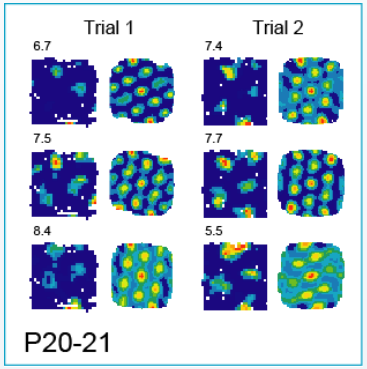


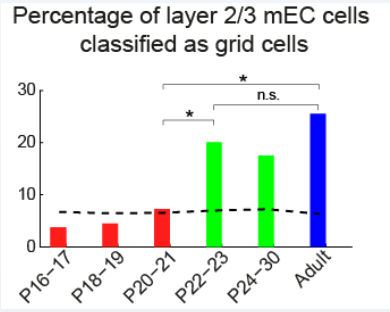
Muessig et al, in preparation

- Boundary cells can be recorded as early as P17 in both the subiculum (Muessig et al, in prep) and in the entorhinal cortex (Bjerknes et al., 2014).

- **Grid cells** may stabilise place maps in locations away from boundaries.







- The abrupt emergence of grid cells around weaning (P21) coincides with the shift from boundary to centre coding in CA1.

What have we learnt?

- Boundaries are a fundamental input to the hippocampal mapping system.
- Grid cells may allow accurate navigation when far from boundaries (or other landmarks).

Open questions?

- What happens if you develop without experience of boundaries?

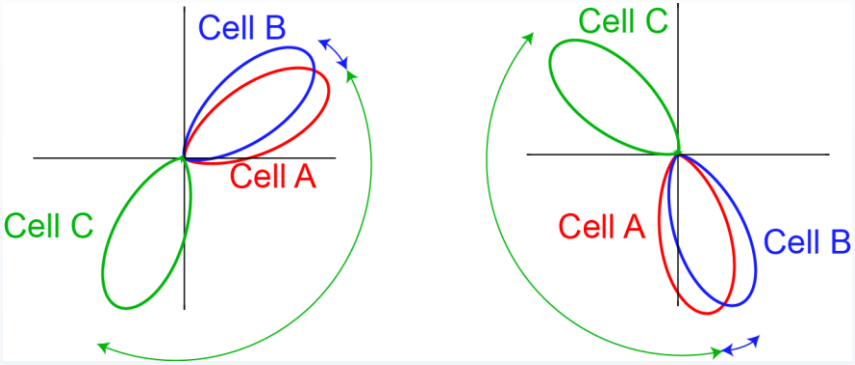
What underlies sudden appearance of stable HD cells?

- Adult HD cells maintain fixed offsets between tunings following rotation or disorientation.

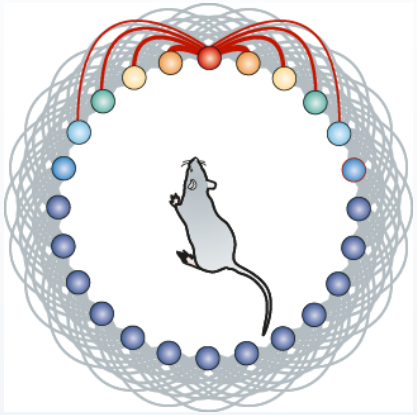
• This is thought to reflect network architecture (Skaggs et al 1995, Zhang, 1996).

Co-recorded cells rotate together

Trial 1 **Trial 2**



Network connectivity



McNaughton et al, 2006

Hypotheses

1. Self-organised mechanism

2. Spatially stable Instructive Input

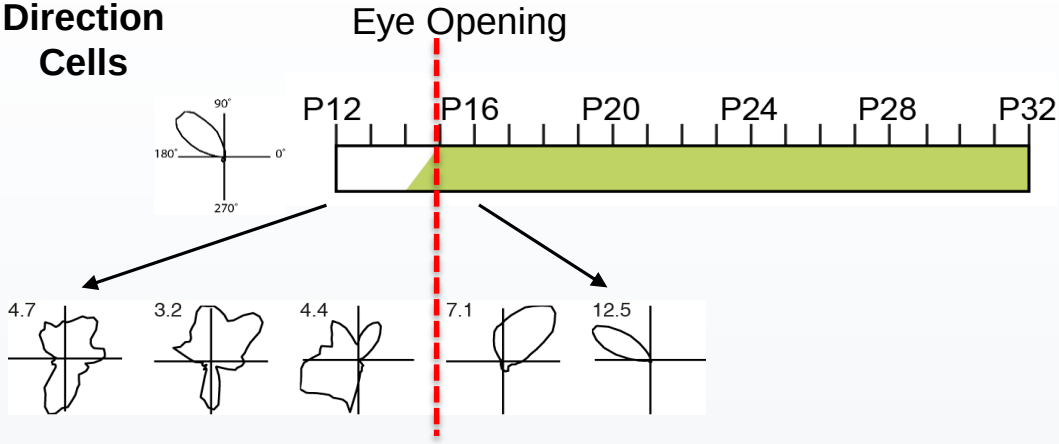
Learning

Connectivity

- How does connectivity arise during development? Does this process depend on the presence of stable landmarks or is it self-organised?

Which sensory inputs can anchor HD signals to the external world?

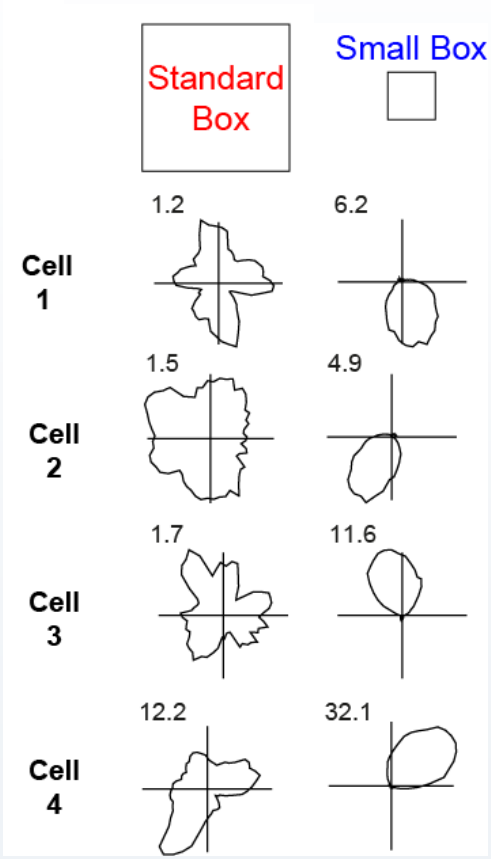
Head Direction Cells



Hui Min Tan

Tan, Bassett,O'Keefe,Cacucci and Wills, 2015, Current Biology; Bjerknes et al, 2014, Current Biology.

Bassett, Wills & Cacucci, Current Biology, 2018



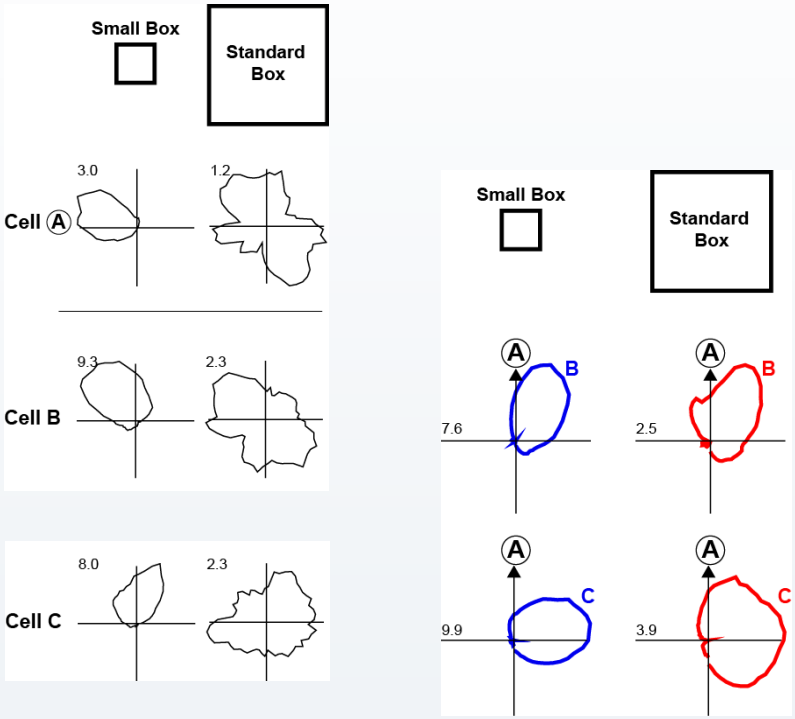
Josh Bassett

1) Vision

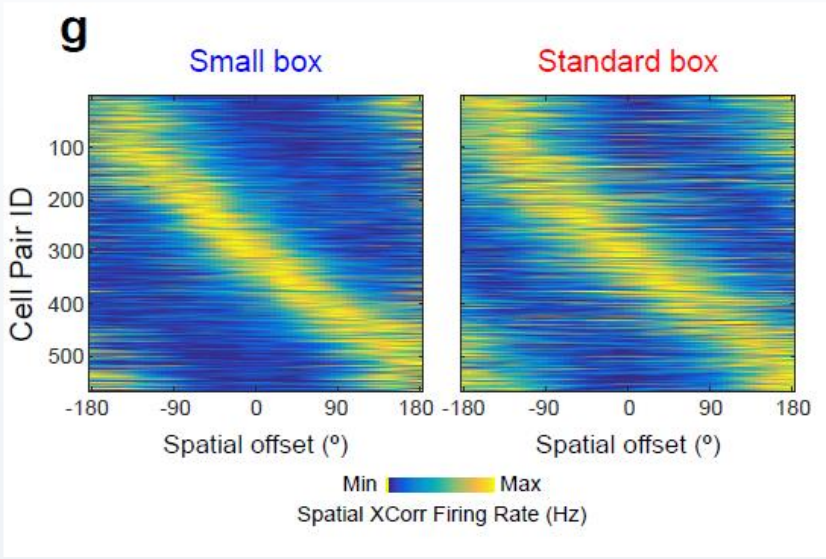
2) Closer boundaries

Attractor dynamics in drifting HD cells

- Are attractor dynamics present in HD cells before they are stable?
- Test the spatial distribution of Cell B firing, *relative to Cell A firing*, in a 10 sec time window.



All recorded HD cell pairs, sorted by preferred direction offset in small box.



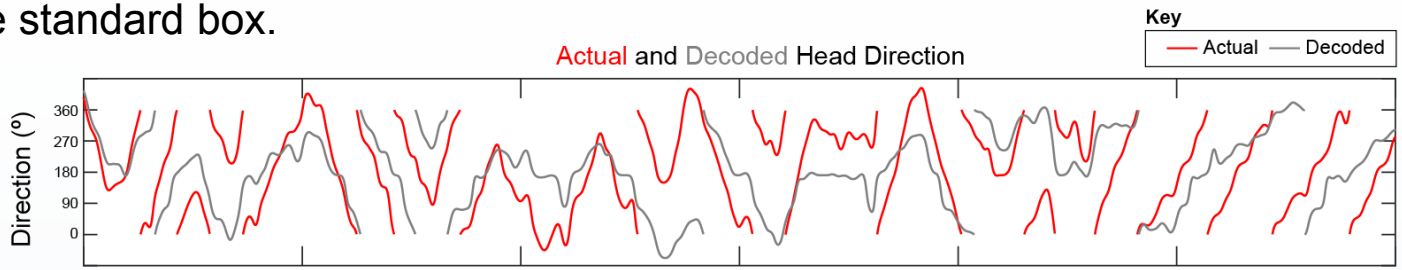
- Spatial coherence of co-recorded HD cells is preserved when HD tuning drifts (is un-anchored to allocentric reference frame).

Bassett, Wills & Cacucci, Current Biology, 2018

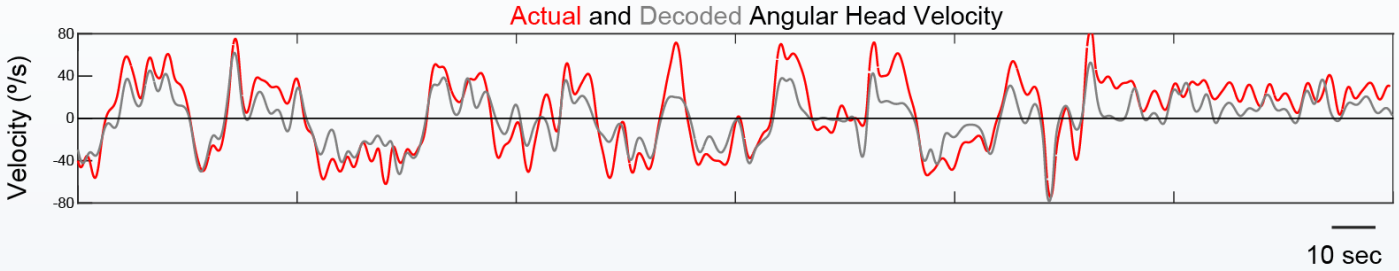
How and why do early HD cells drift?

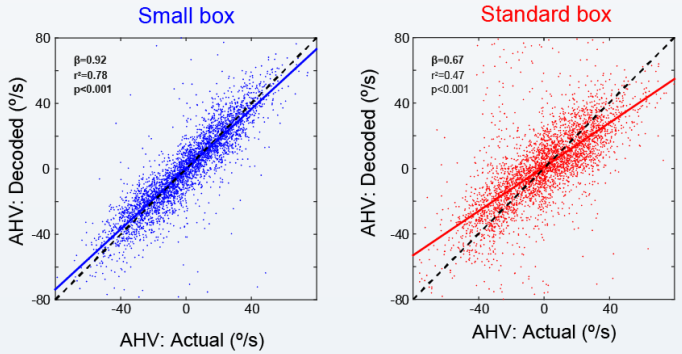
- We used the known spatial offsets of HD cells in the small box to decode the ‘signalled direction’ in the standard box.

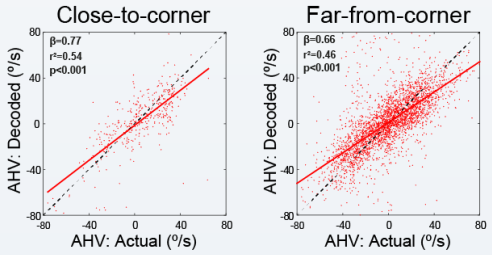
Decode **Position**



Reconstruct **Angular Head Velocity** from decoded position



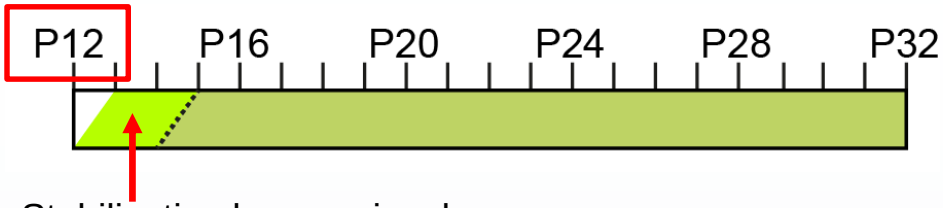




- Angular velocity is under-signalled when HD cells drift in the standard box

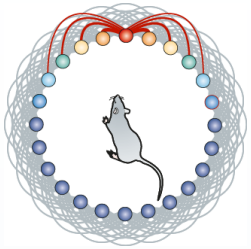
- Angular velocity under-signalling greater when far from corners.

When does attractor network connectivity emerge? (I)

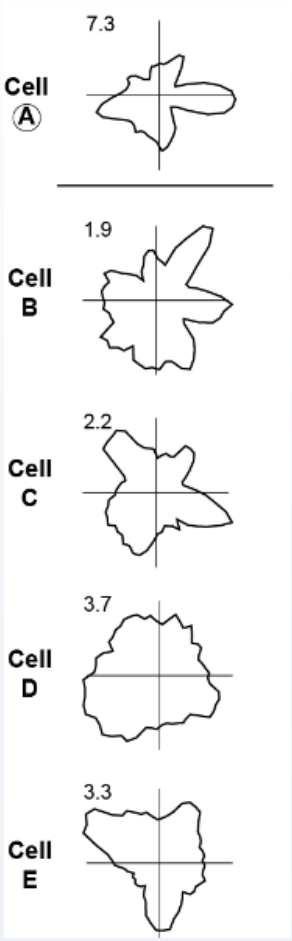


Stabilisation by non visual cues

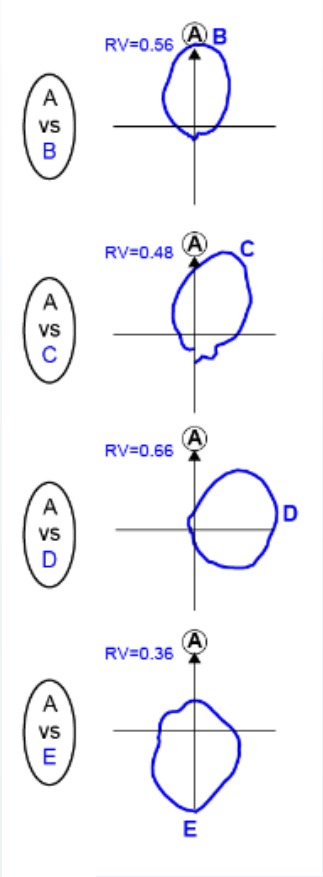
- At P12 putative HD cells cannot be anchored to external environment.
- Is attractor connectivity already present at P12, in spite of spatial instability?



Rate Maps

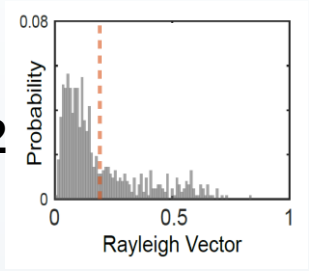


10 sec Time-window maps

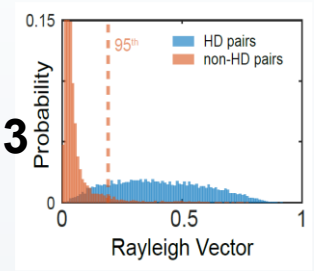


Time-window Rayleigh Vectors from all cell pairs

P12



≥P13



Hypotheses

1. Self-organised mechanism
2. ~~Spatially stable Instructive Input~~

Learning

Connectivity

- Spatial offsets between putative HD cells are fixed even at P12, before environmental anchoring. Network connectivity likely self-organised.

What have we learnt?

- Velocity inputs are under-signalled in the immature HD system, leading to integration error.
- Error is corrected by vision when eyes open, by boundaries (corners?) before then.
- Head direction network topology may be self-organised.

Open questions?

- How does the connectivity of head direction and grid cell networks arise? (Genetic programming? Electrical waves of spontaneous activity?)

Thanks to:

Tom Wills lab: **Laurenz Muessig**
Isabella Varsavsky
Tara O'Driscoll
Alice O'Leary

Collaborators: **Francesca Cacucci**
(Josh Bassett)

Alumni: **Hui Min Tan**
Jonas Hauser
Fabio Rodrigues

We are hiring!
Francesca will have two post-doctoral positions available early 2019 – applications from computational or engineering backgrounds are very welcome!

Thanks for listening!