Navigation & Encoding of Space

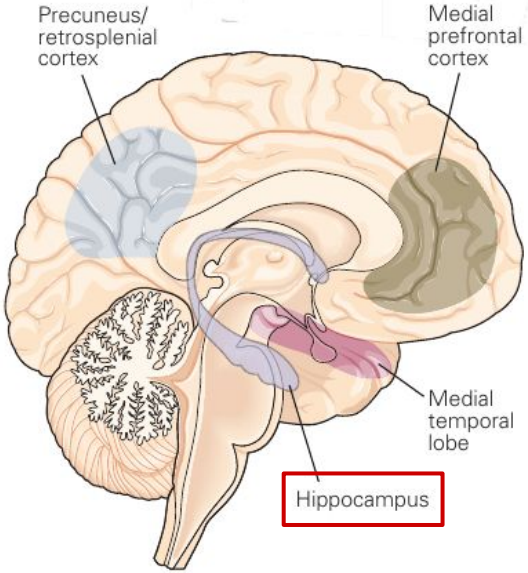
Markus Frey, PhD
& Mackenzie Mathis, PhD

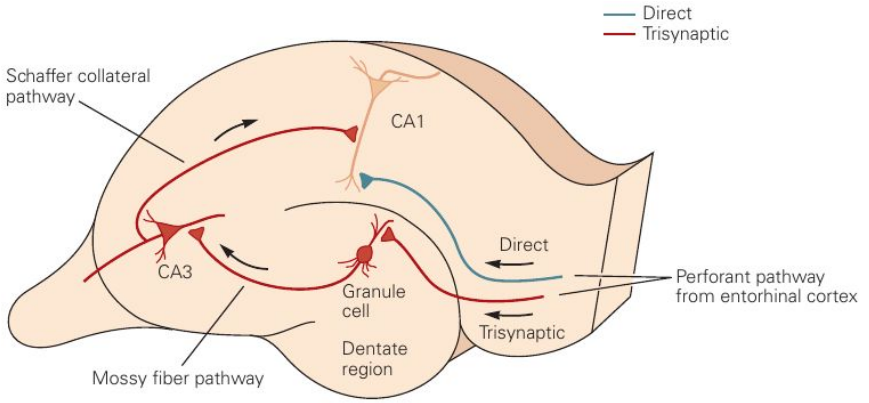
Recap - The Hippocampus

The two structures in the mammalian brain that are critical for encoding and storing explicit memories are the **prefrontal cortex** and the **hippocampus.**

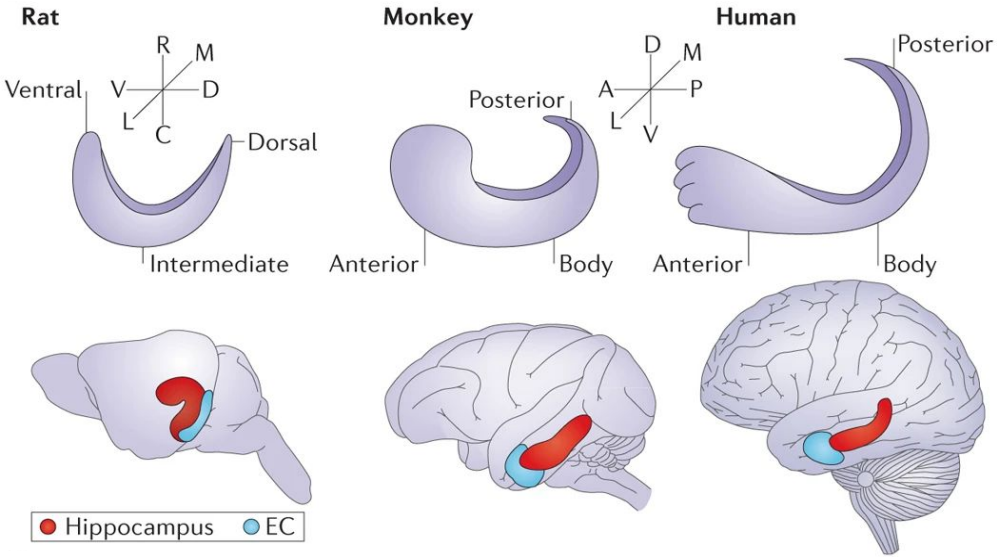
The prefrontal cortex mediates short-term memory. Information stored in short-term memory can be actively maintained for very short periods and then rapidly forgotten, such as a telephone number that is remembered only until it is dialed, or it can be stored elsewhere in the brain as long-term memory. **The hippocampus stores declarative information (facts and events) in a more stable form for periods ranging from days to weeks to years, up to a lifetime.**

The hippocampus is also the place where a cognitive map of the environment is stored - **an internal map of space which can be used as a form of database which stores information in relation to the animals position**





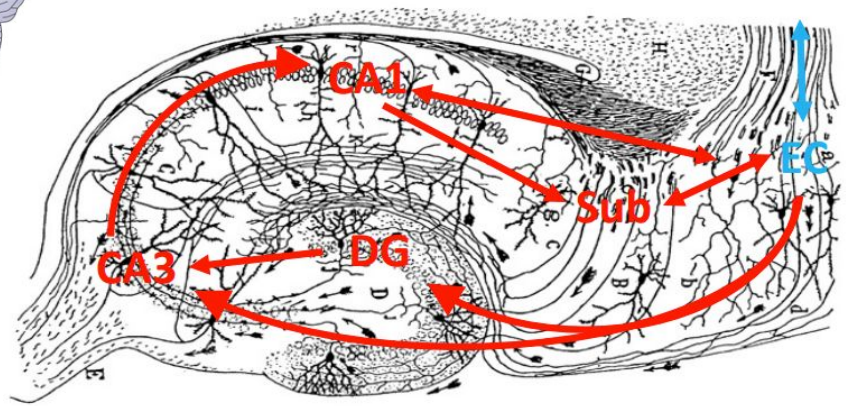
Recap - The Hippocampus



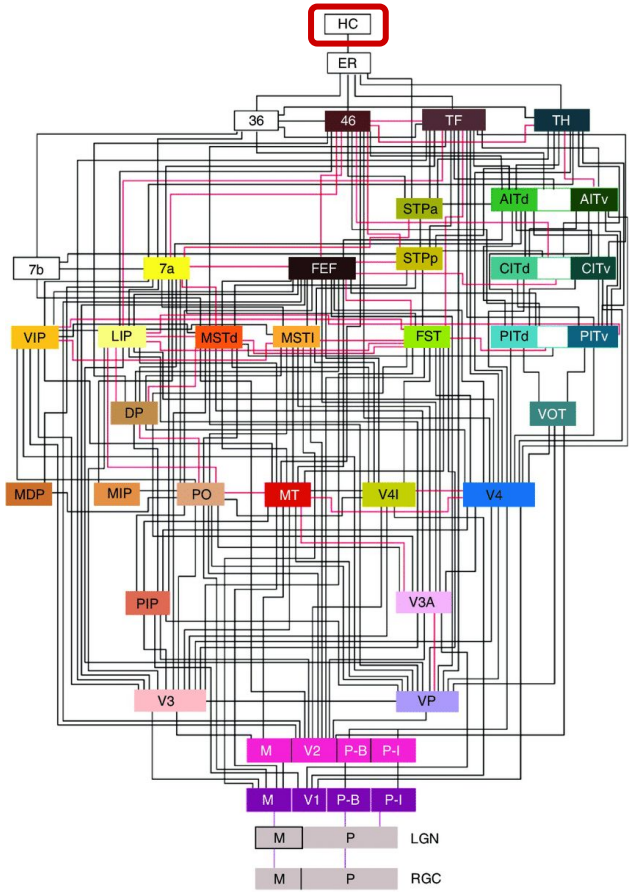
The hippocampus is a **highly conserved brain structure** across all mammals, including humans

Primarily **uni-directional processing loop**: entorhinal cortex -> hippocampus -> entorhinal cortex

EC -> Entorhinal cortex
Ca1: Cornu Ammonis 1
Ca3: Cornu Ammonis 3
DG: Dentate Gyrus
Sub: Subiculum



Recap - The Hippocampus



Huge amount of visual processing until any external sensory information reaches the hippocampus

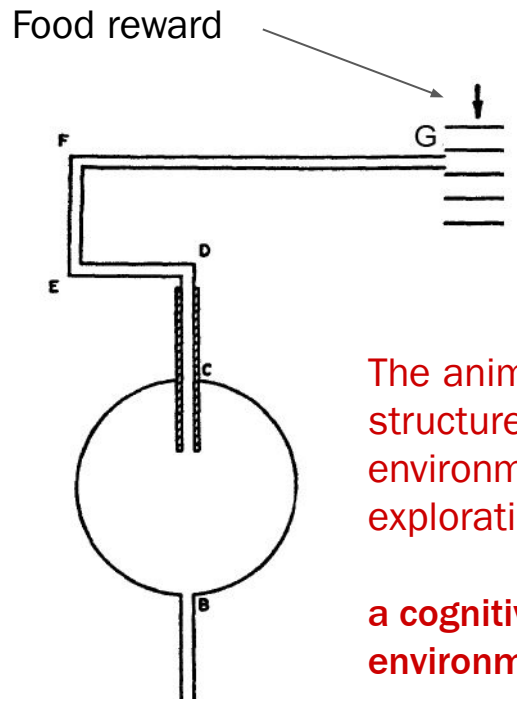
In other senses (auditory, somatosensory) there is similarly complex processing upstream of the hippocampus – except olfactory inputs that reach the hippocampus much more directly (olfactory bulb -> entorhinal cortex)

The hippocampus stores a world-centered (allocentric) map, derived from self-centered (egocentric) sensory information, a cognitive map of the environment

Fellemann & Van Essen 1991

The cognitive map

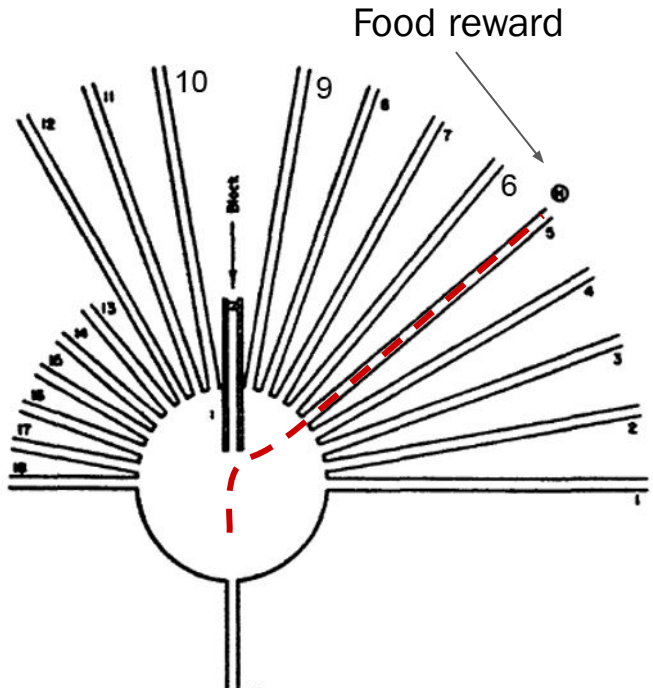
Initial training setup



The animal acquires a structure of the environment during initial exploration

a cognitive map of the environment

Test setup



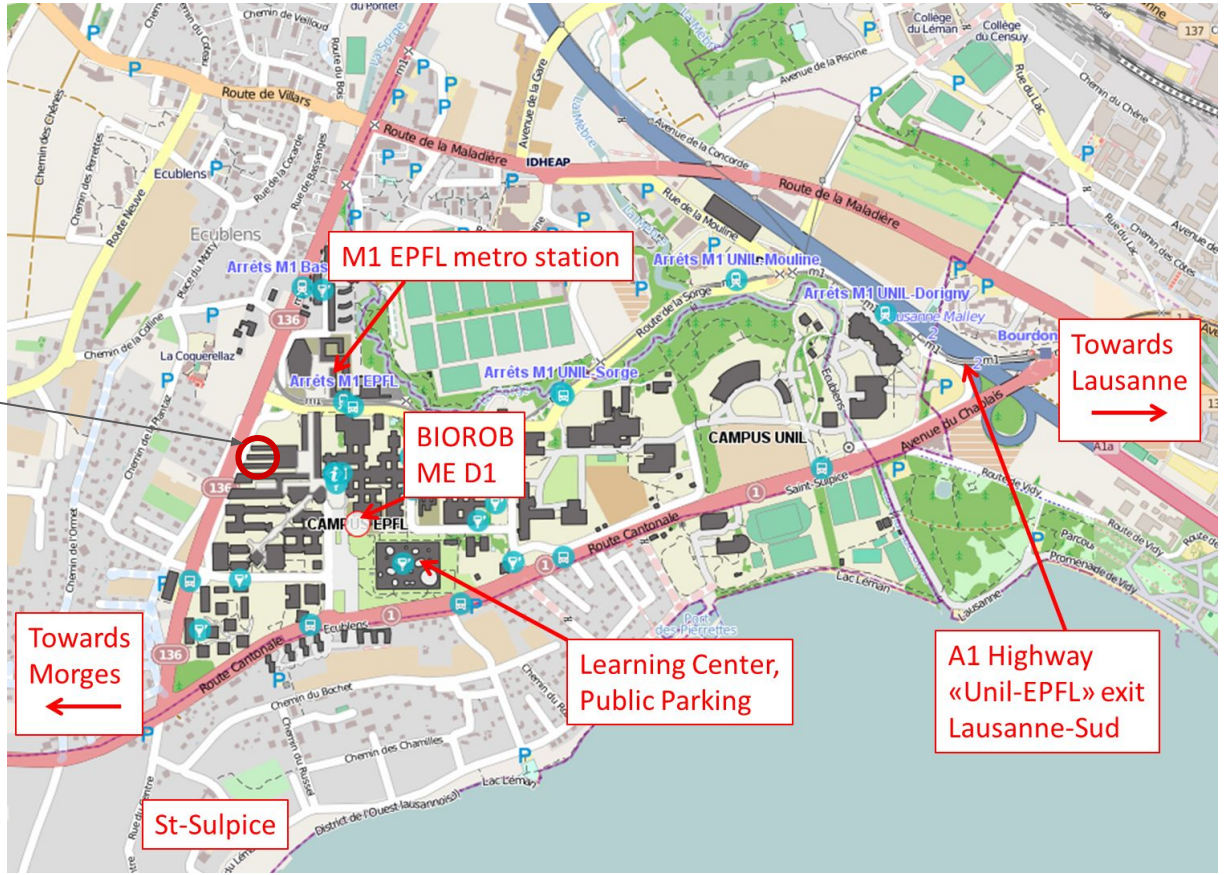
Tolman, Ritchie, Kalish 1946
Edward C. Tolman, 1948

The cognitive map

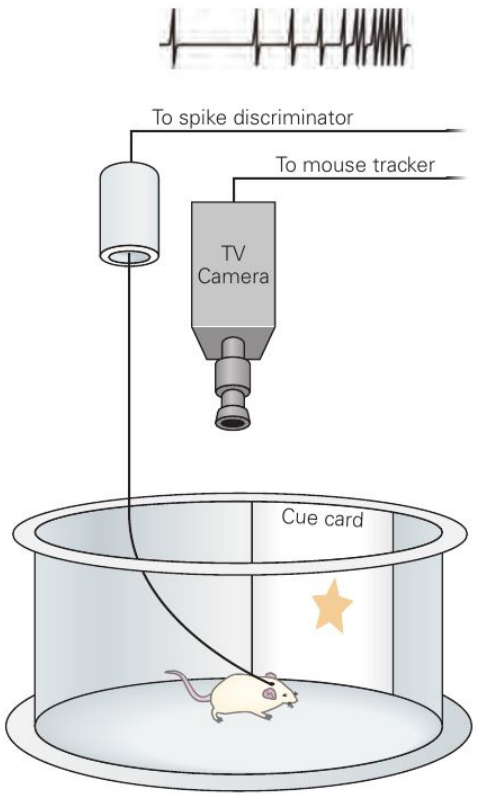
You are here

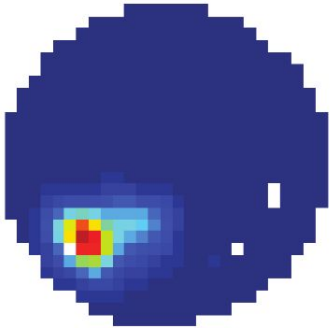
How do you know?

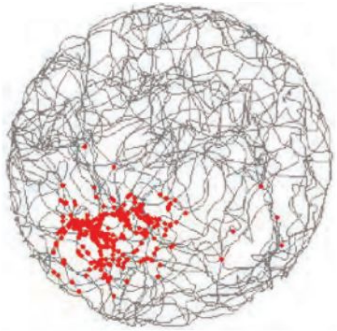
You have a cognitive map of the EPFL campus with **place cells** encoding specific places within it



Place cells in hippocampal subfield CA1

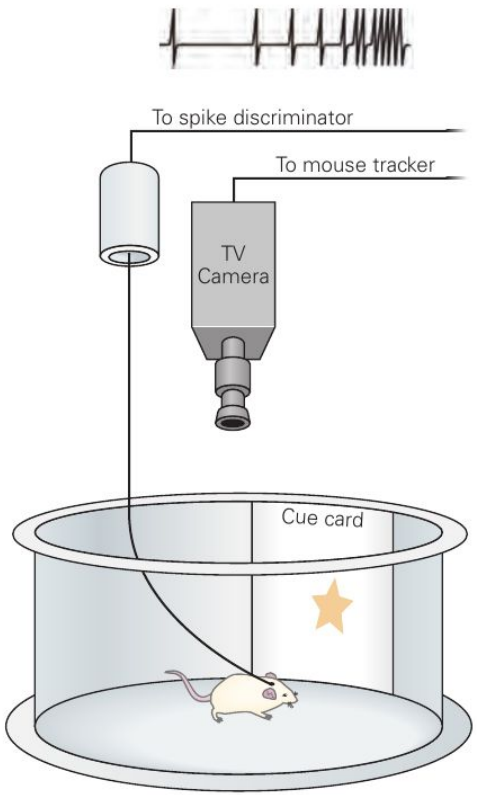


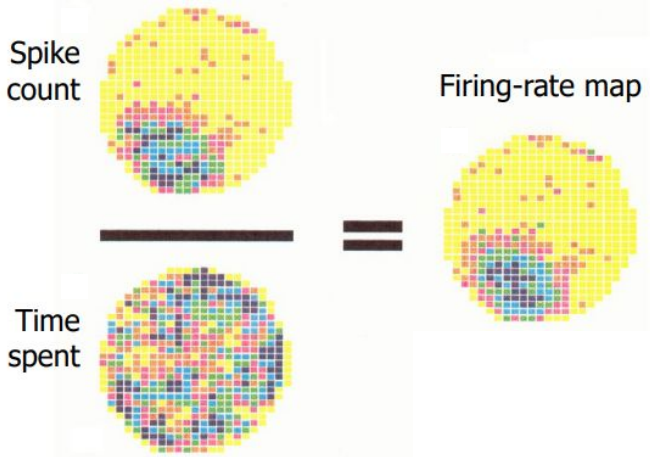




O'Keefe et al. 1971
O'Keefe & Nadel, 1978

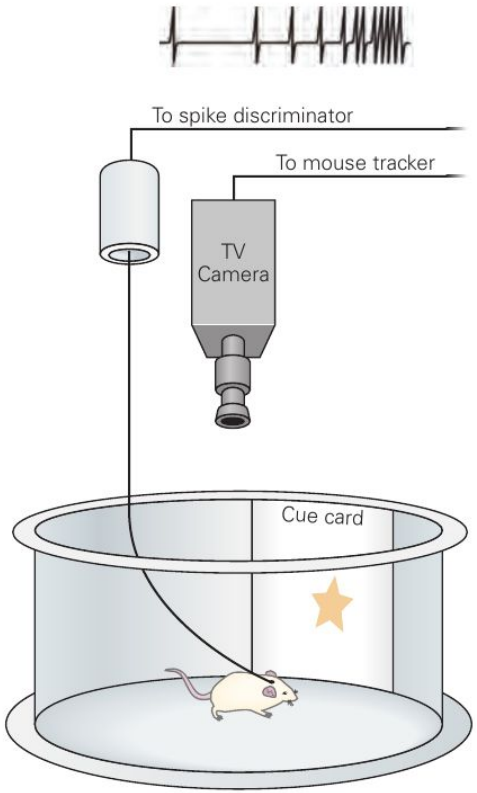
Place cells in hippocampal subfield CA1

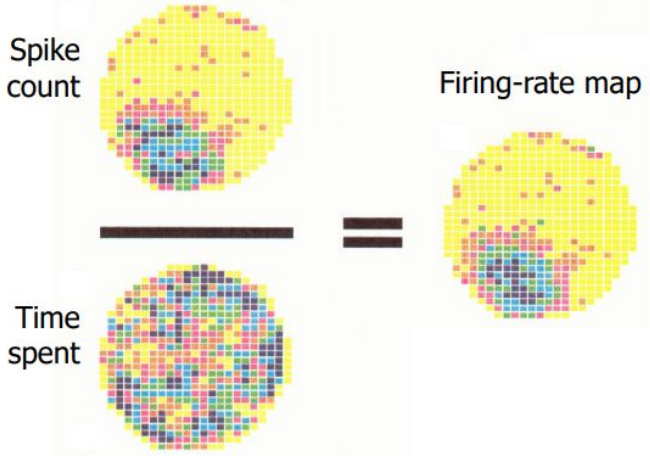


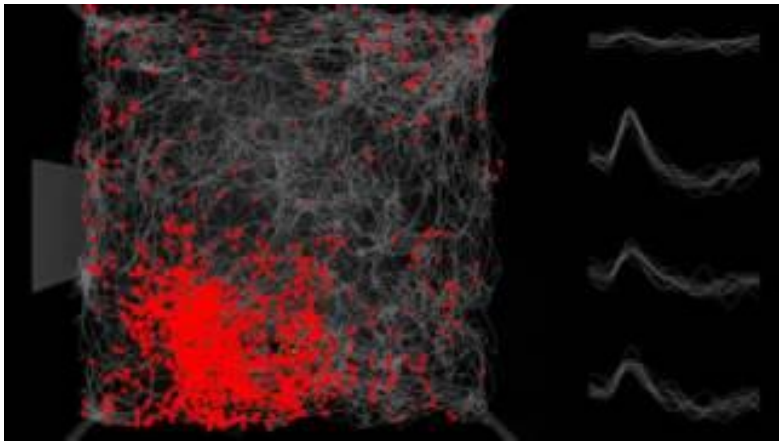


O'Keefe et al. 1971
O'Keefe & Nadel, 1978

Place cells in hippocampal subfield CA1

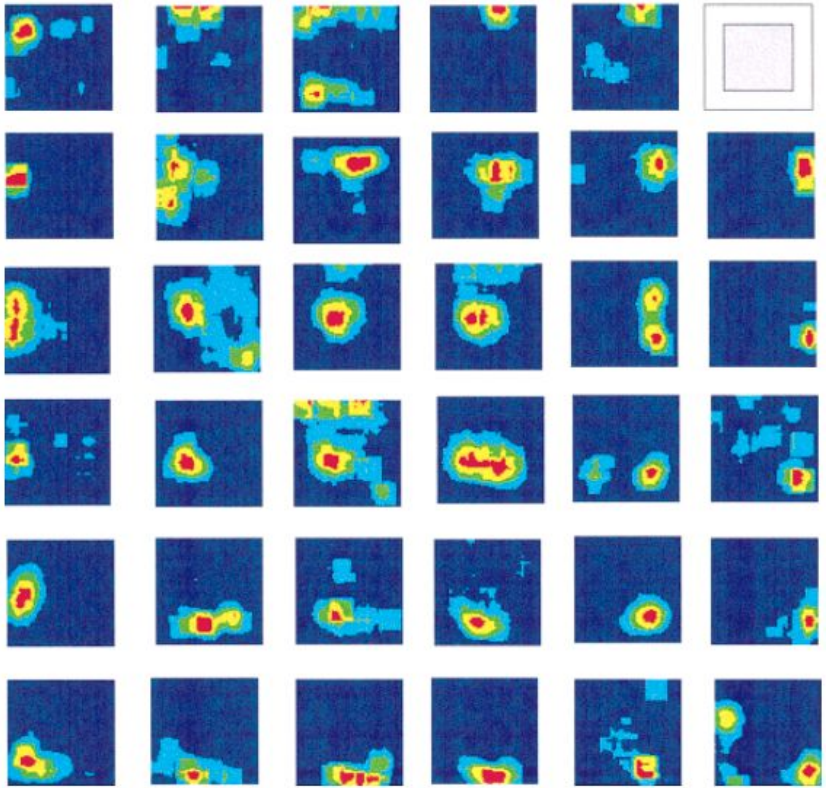






O'Keefe et al. 1971
O'Keefe & Nadel, 1978

Place cells in hippocampal subfield CA1



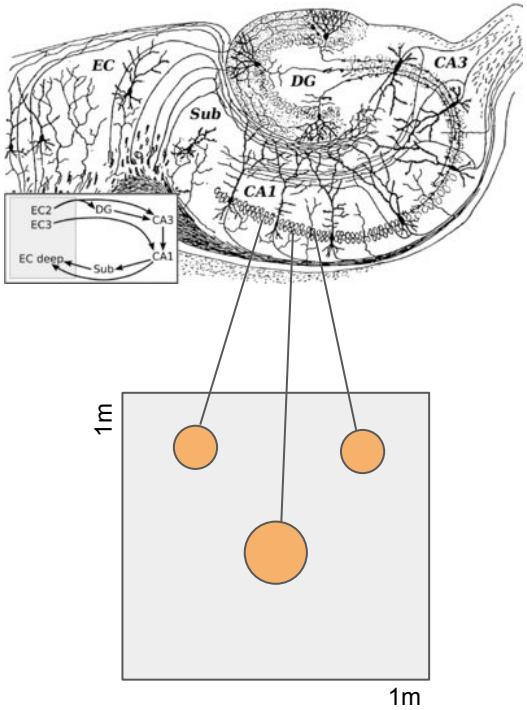
Many place cells together **tile the whole environment**

They provide a map of the environment, in the sense that the combination of currently active cells is sufficient to read out **precisely where the animal is** in the environment

Physical space is encoded in reference to the world (allocentric) - it is **fixed with respect to a point in the outside world**

O'Keefe et al. 1999

Place cells remap in novel contexts



200000 - 800000 neurons in CA1 (mice - rat)

Not enough neurons to encode larger (real-world) environments

Tiling a much larger space with typical place fields as measured in the laboratory (~10 to 20 cm diameter, single field per neuron) **would require 10^13 neurons**.

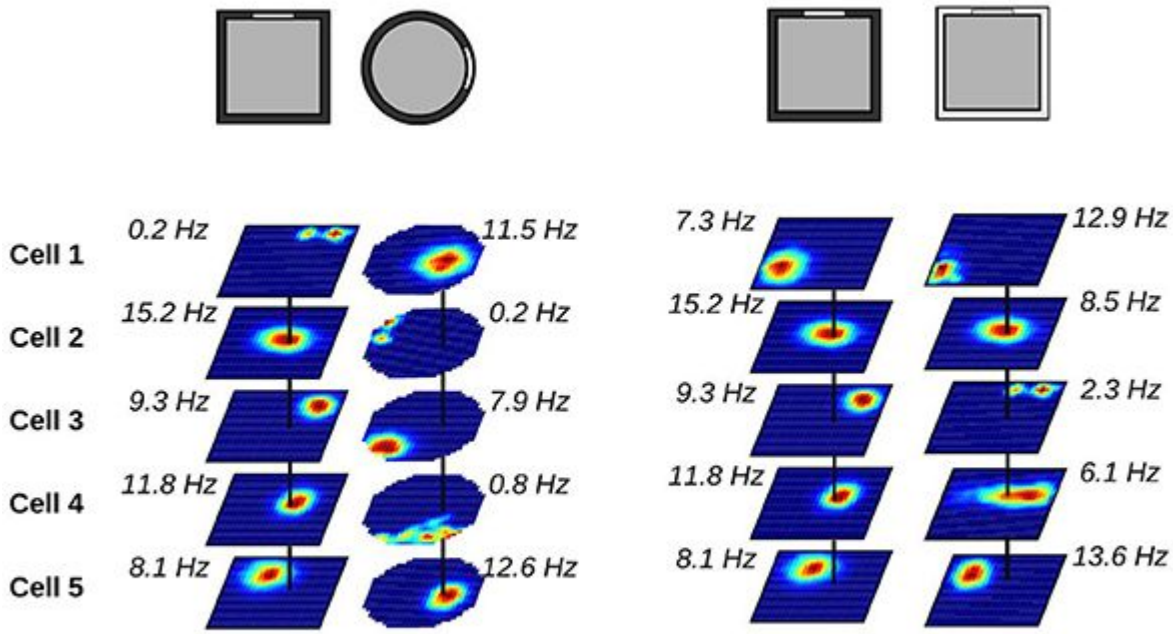
This is ~10^8 times more neurons than the number of cells in the entire dorsal hippocampal area CA1

Place cells remap in novel contexts

Place cell locations remap when context changes drastically (*global remapping*)

Smaller context changes are encoded as changes in firing rate (*rate remapping*)

Allows place cells to **encode multiple spaces and adapt to new environments**

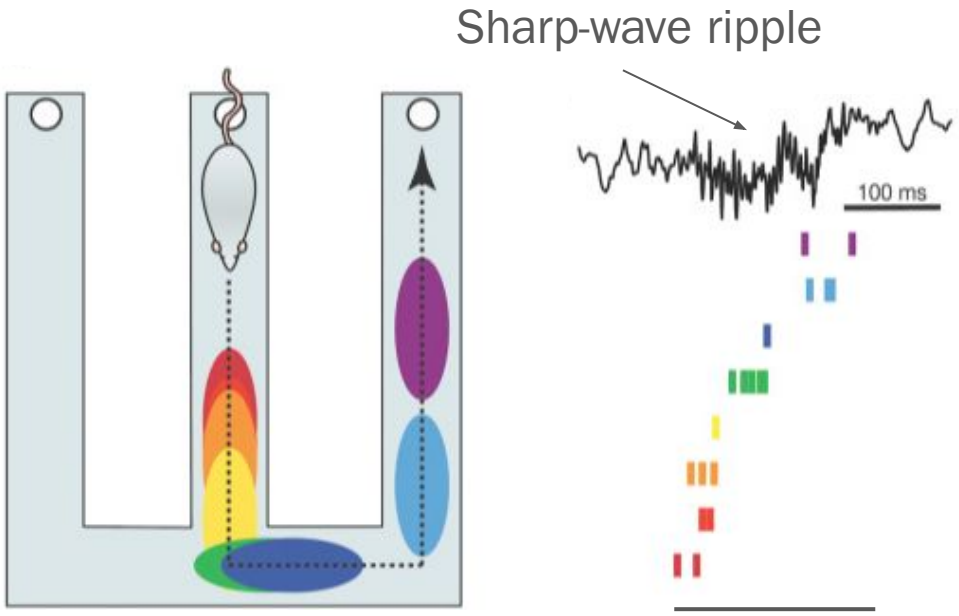


Global remapping

Rate remapping

Latuske et al. 2018

Place cells replay previously experienced trajectories



Environment setup

Replay event

Replay of previously experienced trajectories in **a temporally compressed** manner

Replay is a form of mental rehearsal by which certain **memories are gradually consolidated (to cortex)** and thus may be a crucial aspect of the role of the hippocampus in memory

Zielinski et al. 2017

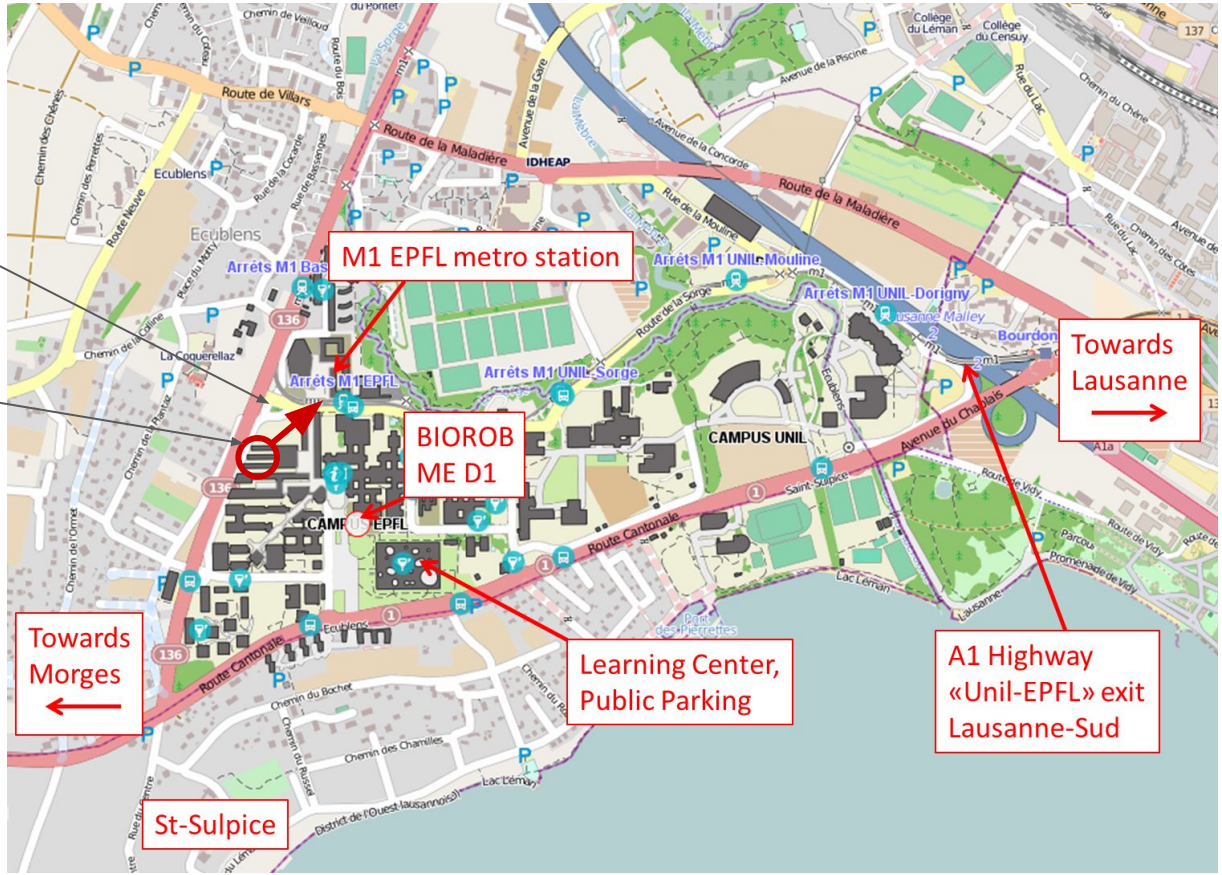
The cognitive map

The cognitive map

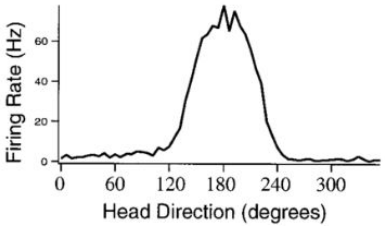
Where are you heading?

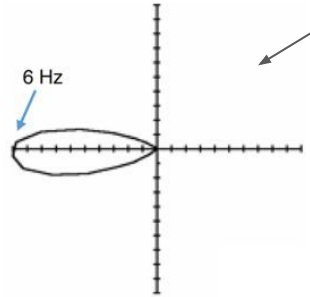
Place cells: Where you are?

Head direction cells encode the angular position of your head with respect to the world

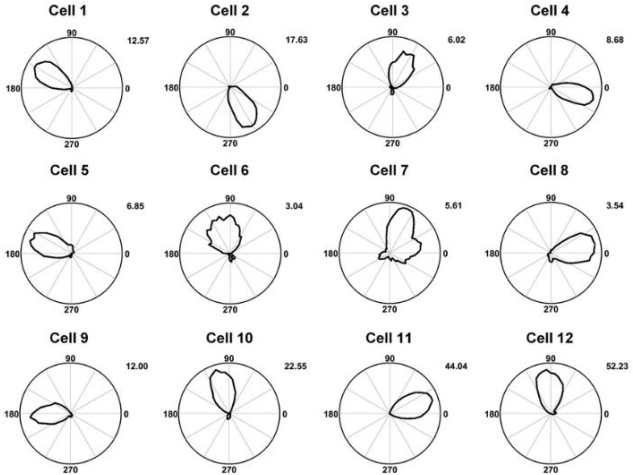


Head direction cells



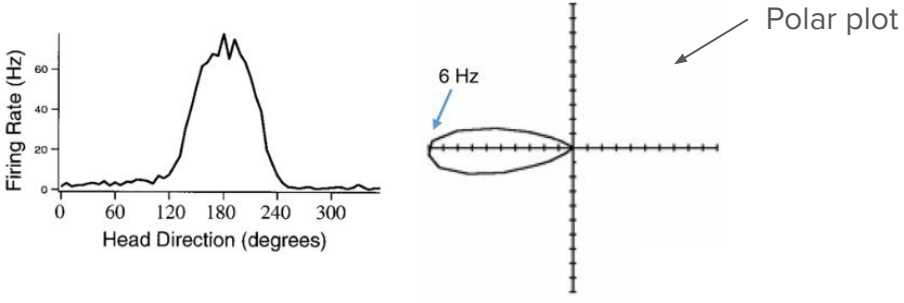


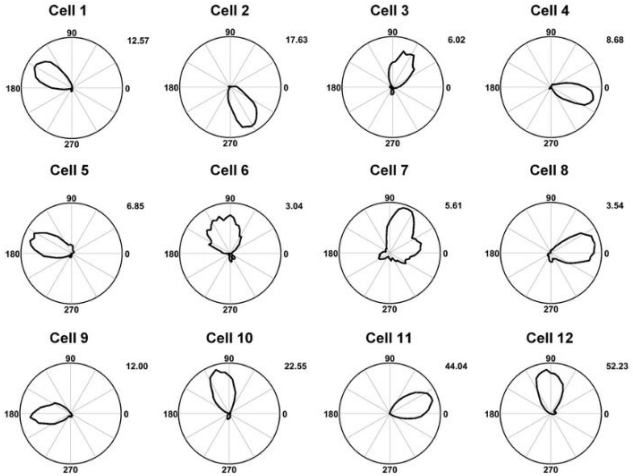
A given population of head direction cells encodes the full 360 degrees



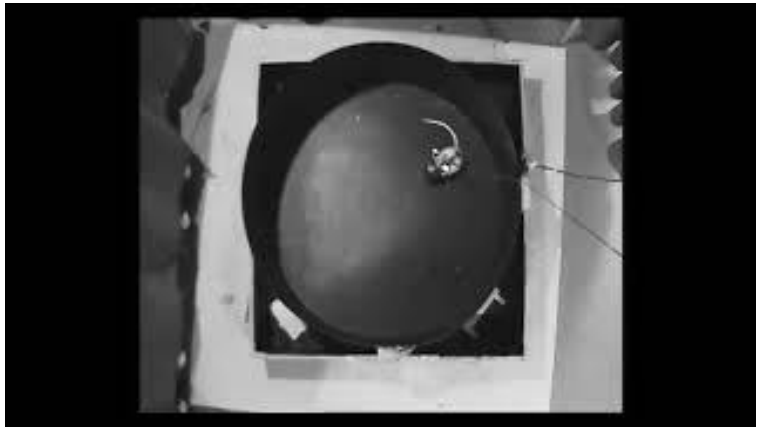
Taube et al. 1990
Preston-Ferrer et al. 2016

Head direction cells



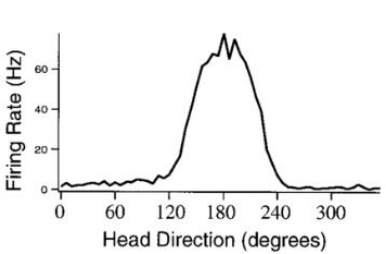


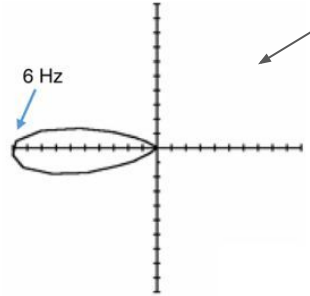
A given population of head direction cells encodes the full 360 degrees

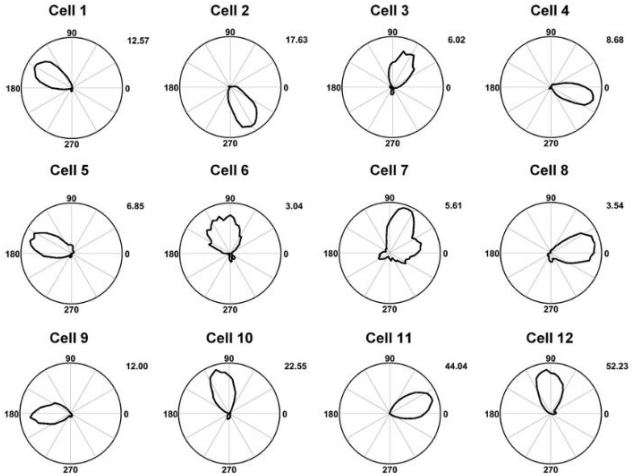


Taube et al. 1990
Preston-Ferrer et al. 2016

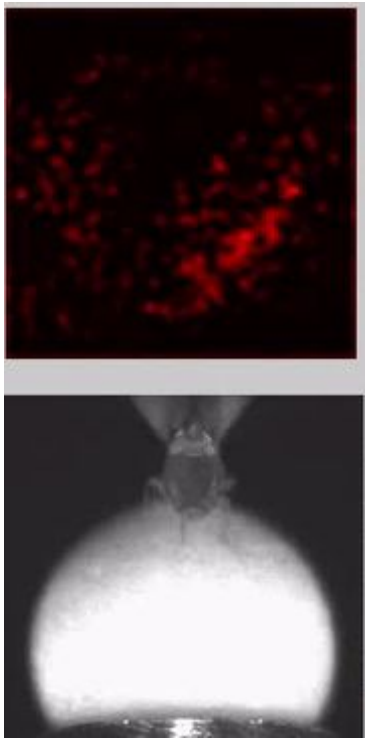
Head direction cells







A given population of head direction cells encodes the full 360 degrees



In drosophila the head direction circuit is arranged in **a topographical ring** with nearby cells encoding nearby angles

Taube et al. 1990
Preston-Ferrer et al. 2016

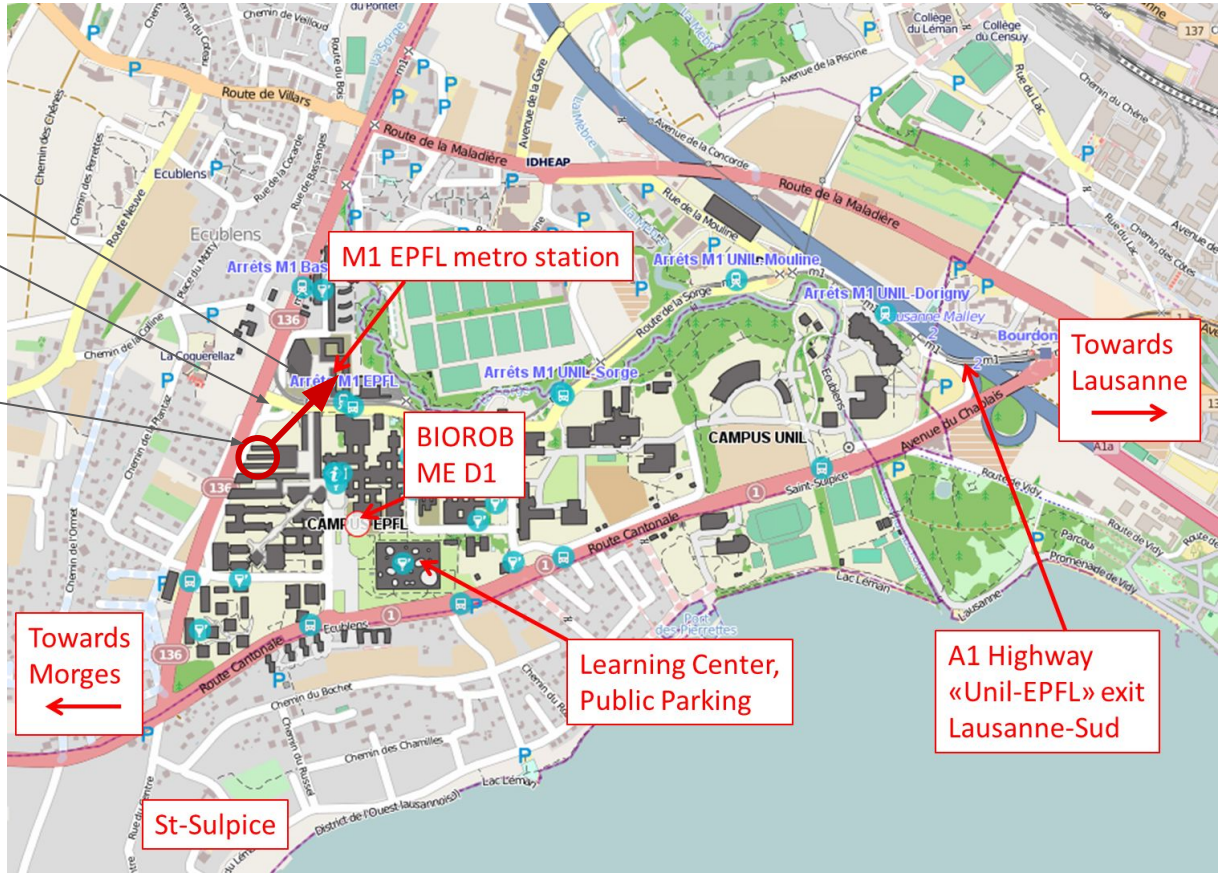
The cognitive map

Grid cells: Vector computation

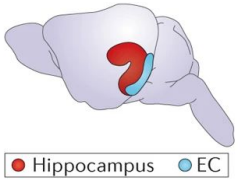
Head direction cells: Where you are heading?

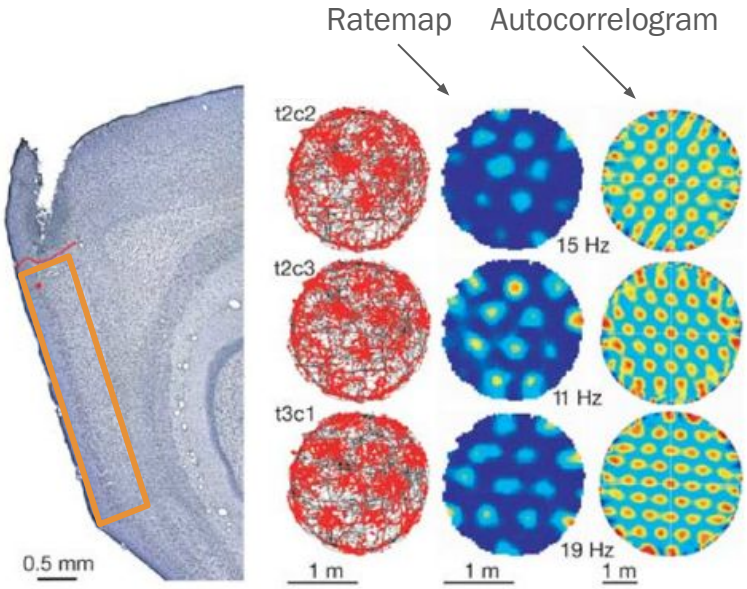
Place cells: Where you are?

Grid cells exhibit period firing as response to a non-period behavior, the position of the animal



Grid cells in entorhinal cortex (EC)

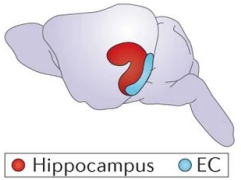


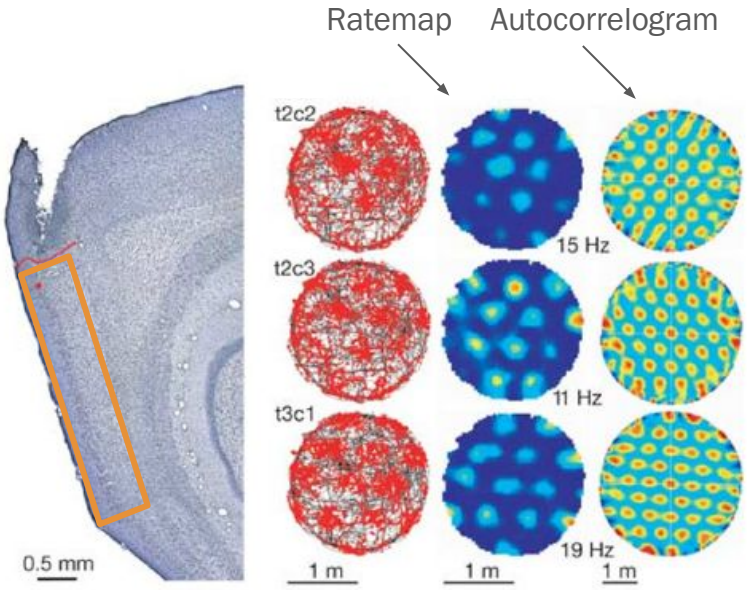


Hafting et al. 2005

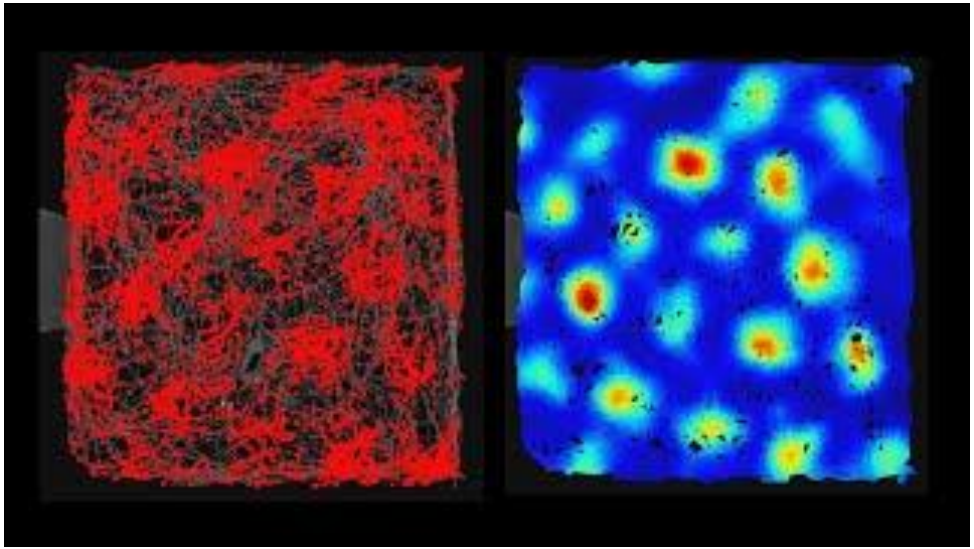
Grid cells in entorhinal cortex respond to multiple spatial locations in a unique triangular grid pattern.

Grid cells in entorhinal cortex (EC)





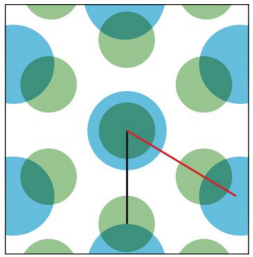
Hafting et al. 2005



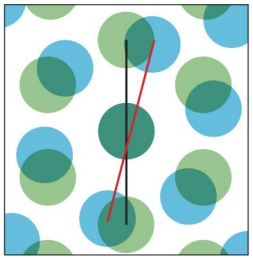
Grieves, Jefferey 2020

Grid cells in entorhinal cortex respond to multiple spatial locations in a unique triangular grid pattern.

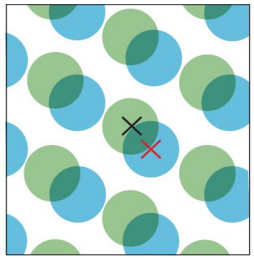
Grid cells form modules along the dorsoventral axis of EC



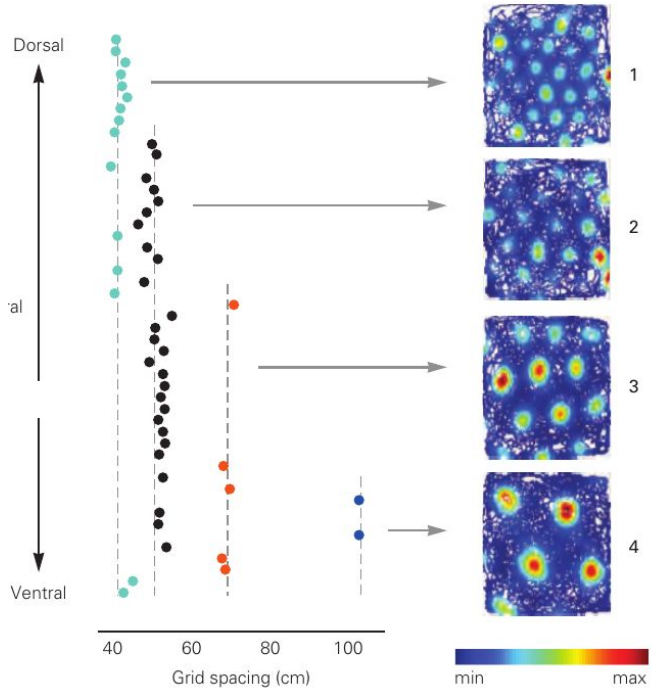
Scale / Spacing

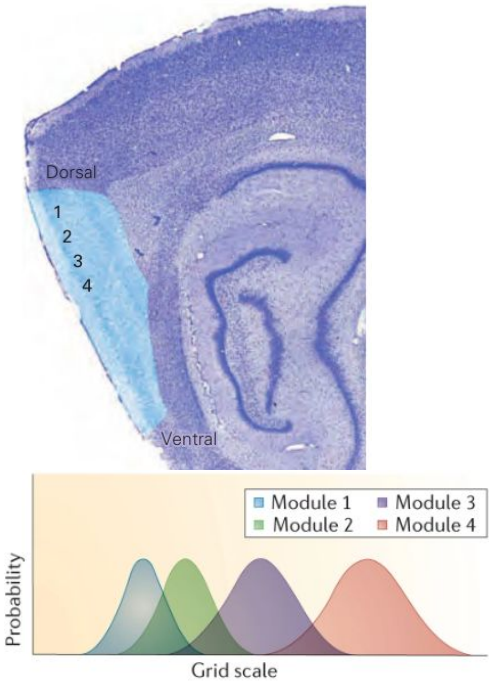


Orientation



Phase



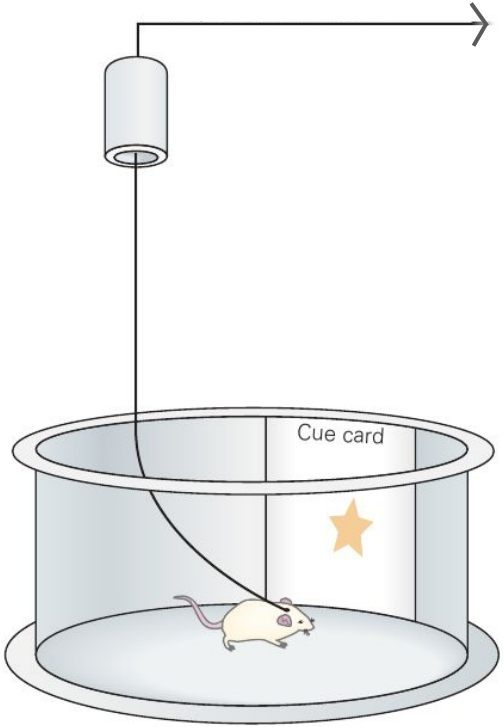


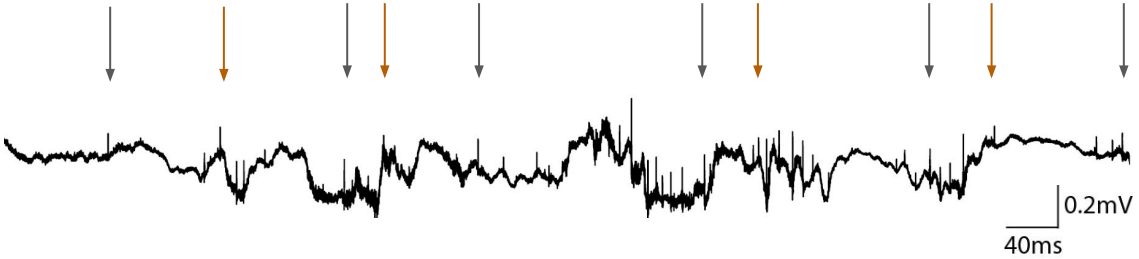
Scale of grid cells **increases topographically from dorsal to the ventral** part (~30cm dorsal to several metres ventral)

The expansion is **not linear but step-like**, suggesting that the grid-cell network is modular.

PoNS 6th Ed. 54–13
Moser et al. 2015

Decoding multiple behaviors from raw neural activity





Spike time vector, Cluster 1

[2.5, 3.3, 4.4, 5.1, ...]

Spike time vector, Cluster 2

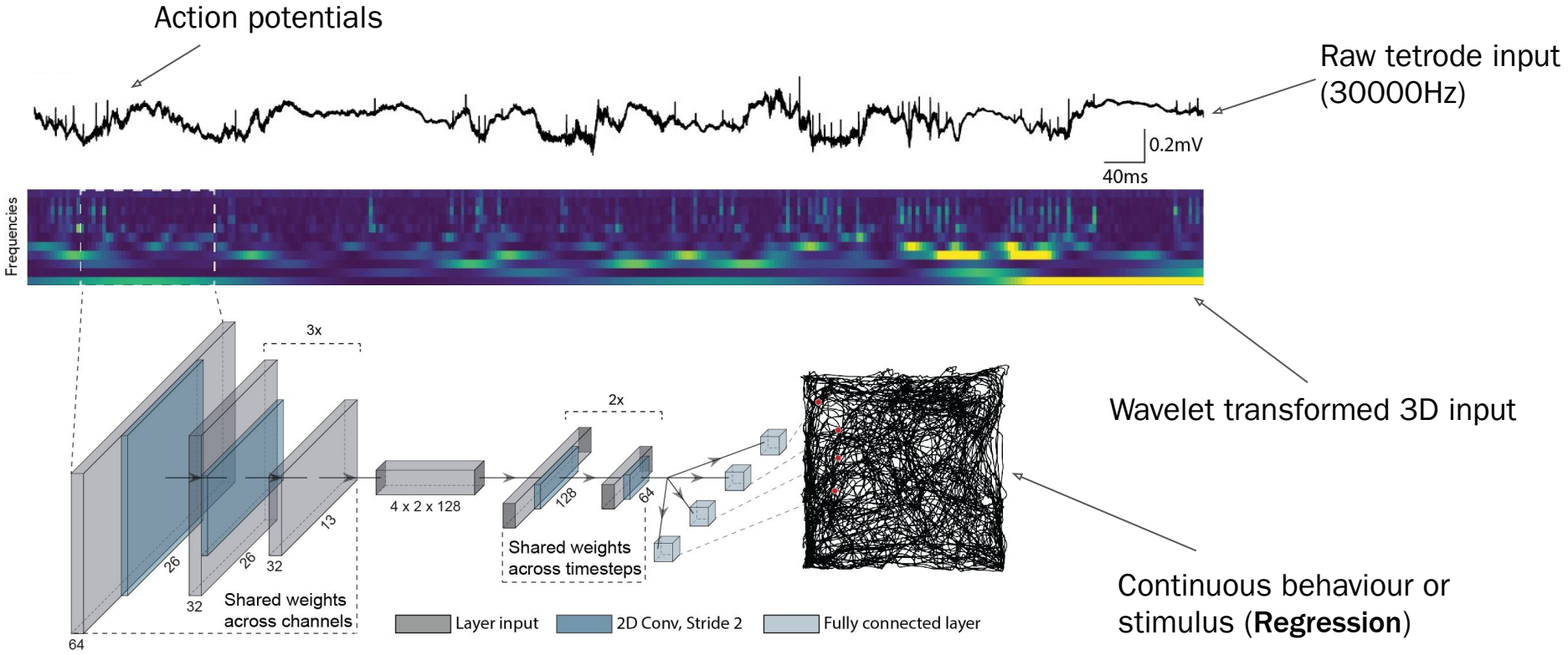
[2.7, 5.8, 7.2, ...]

Spike sorting helps in removing noise and clustering neurons, however

Results of spike sorting may vary from person to person (subjective)

Spike sorting discards information outside the spike range

Decoding multiple behaviors from raw neural activity

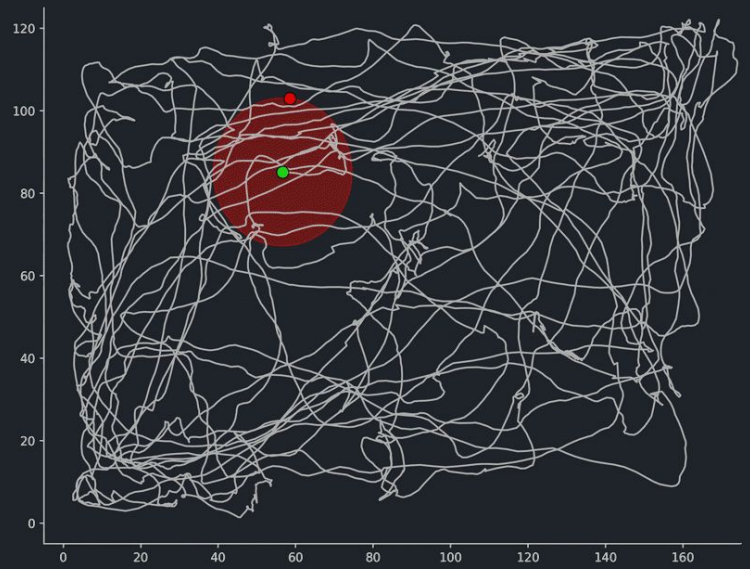


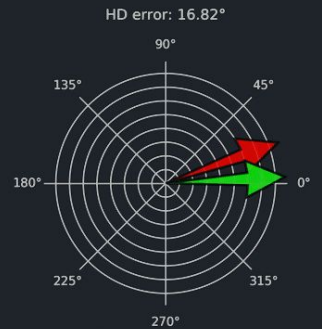
Frey et al. 2021

Decoding multiple behaviors from raw neural activity

Position

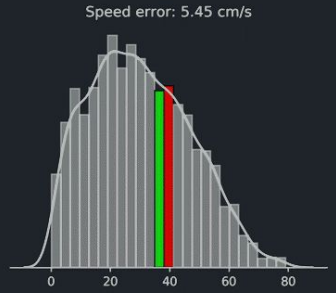
$$\mathcal{L}p(y_p, o_p) = \sqrt{\sum_{i=1}^{N}(o_p - y_p)^2}$$





Head Direction

$$\mathcal{L}_h(y_h, o_h) = \min[(o_h - y_h)^2, (o_h - y_h)^2 + \pi, (o_h - y_h)^2 - \pi]$$



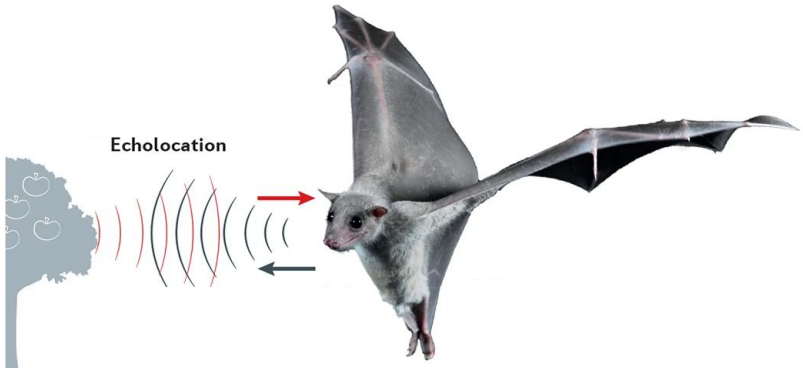
Speed

$$\mathcal{L}_s(y_s, o_s) = \frac{1}{N}\sum_{i=1}^{N}(o_s - y_s)^2$$

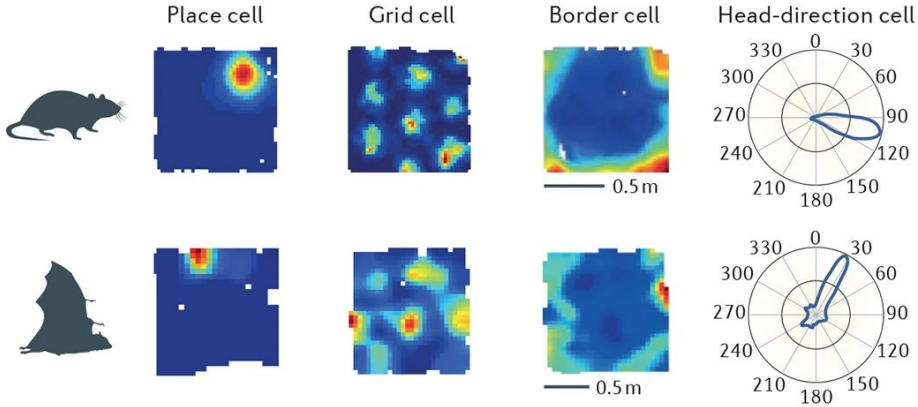
Frey et al. 2021

Navigating three-dimensional space

Navigating three-dimensional space



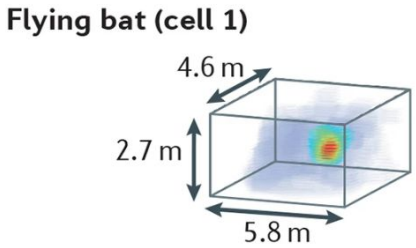
Ulanovsky Lab



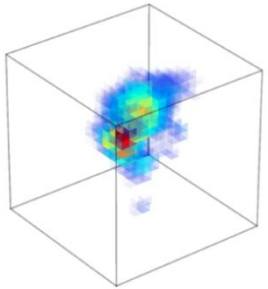
Same spatial cells in crawling bats (2D)

Geva-Sagiv et al. 2015
Ginosar et al. 2021

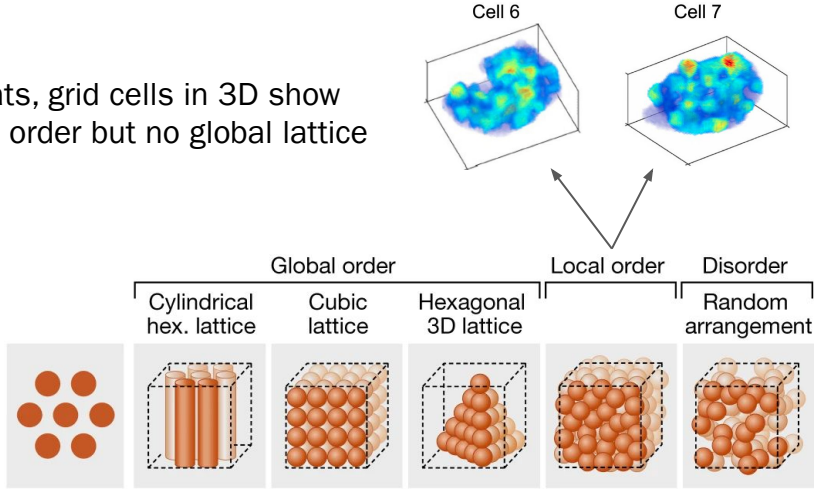
Navigating three-dimensional space



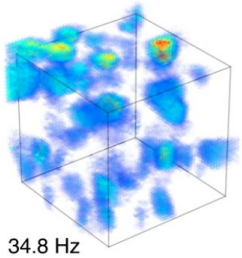
Place cells in rats & bats show similar firing properties in 3D



In bats, grid cells in 3D show local order but no global lattice

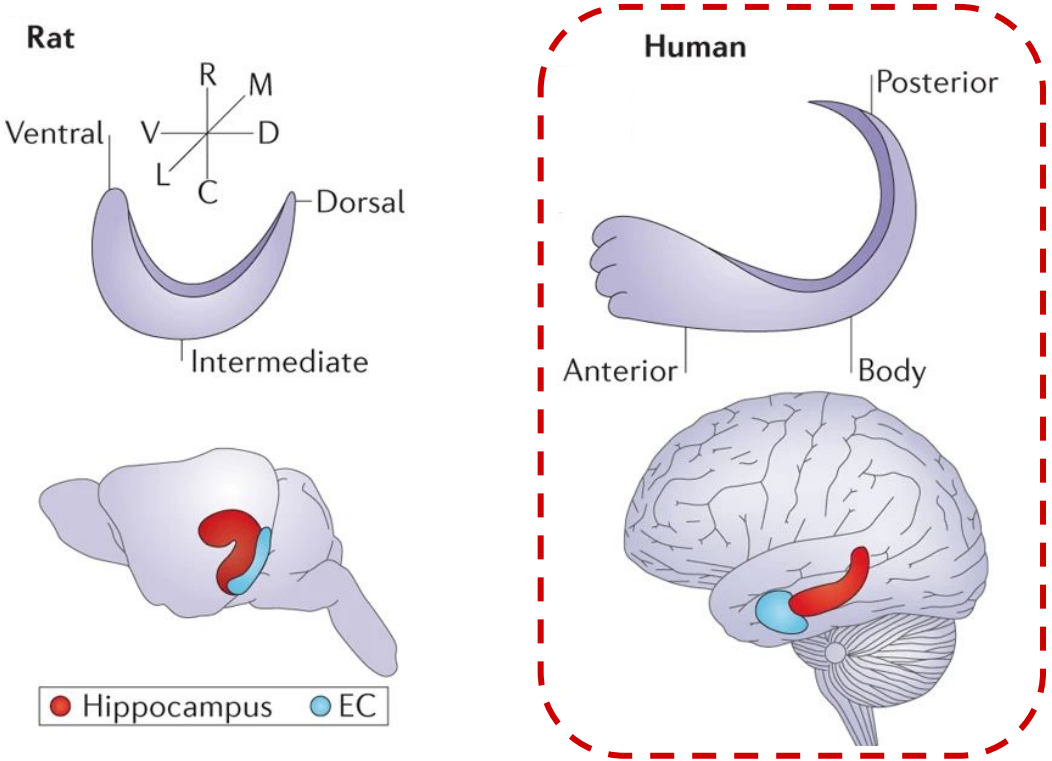


In rats, grid cells in 3D show purely random arrangement

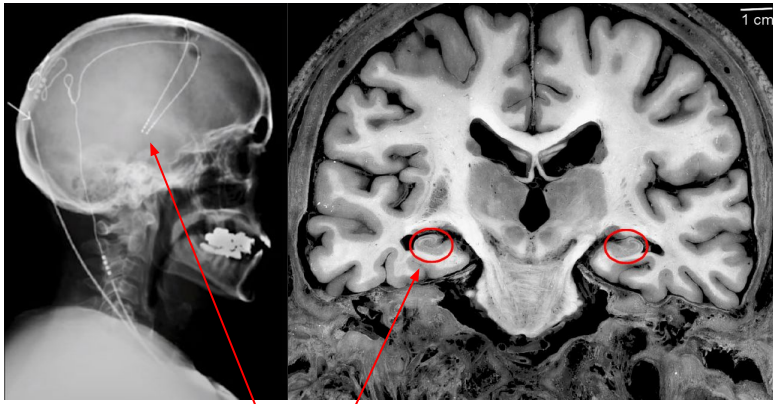


Ginosar et al. 2021
Grieves et al. 2020 & 2021

The cognitive map in humans

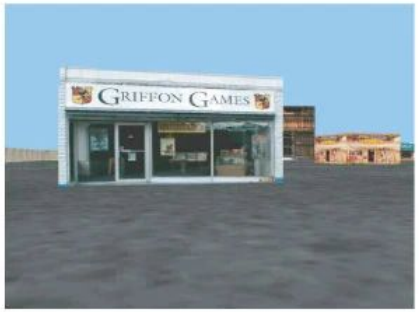


Place cells in human hippocampus



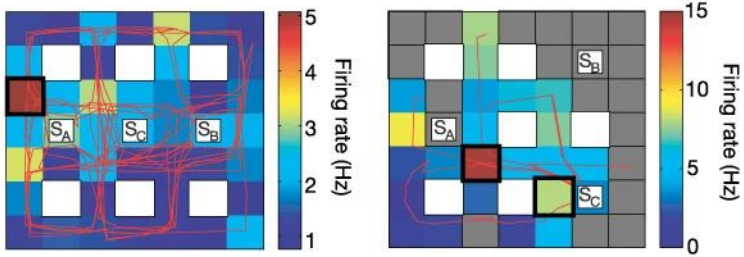
Patients with electrodes in the hippocampal formation

Participants navigating a virtual environment — Taxi task



Cells in human hippocampus show spatially selectivity, reminiscent of place cells in rodent experiments

Place field



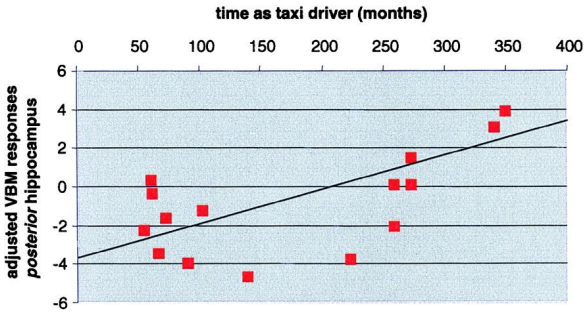
Ekstrom et al. 2003

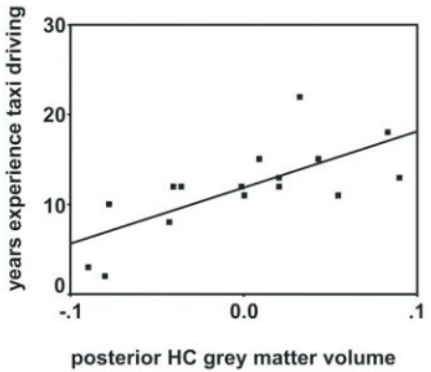
Hippocampal volume and navigation performance

Volume of posterior hippocampus in humans

Larger in London taxi drivers than in age-matched controls

Larger in Taxi drivers than in experience-matched Bus drivers & no correlation with experience in Bus drivers

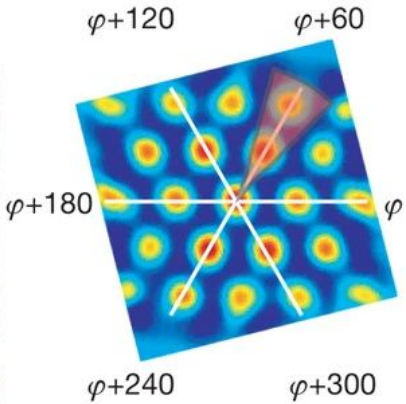


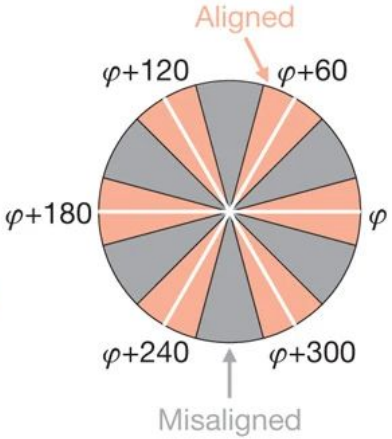


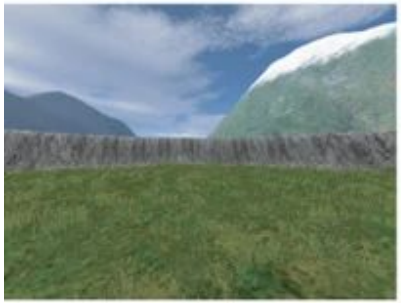
Navigation based on a cognitive-map, i.e. **an allocentric strategy (taxi drivers) requires a larger hippocampus than egocentric (route-based)** navigation (bus drivers) ?

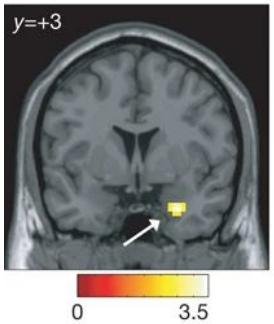
Maguire et al. 2000
Maguire et al. 2006
Ulanovsky 2021

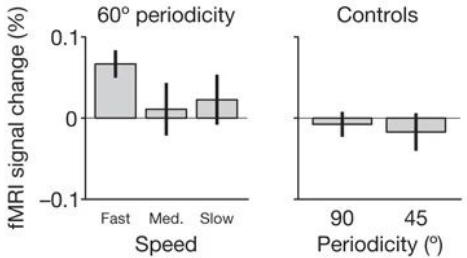
Grid cells in human entorhinal cortex











How to detect single-cell activity in fMRI tasks?

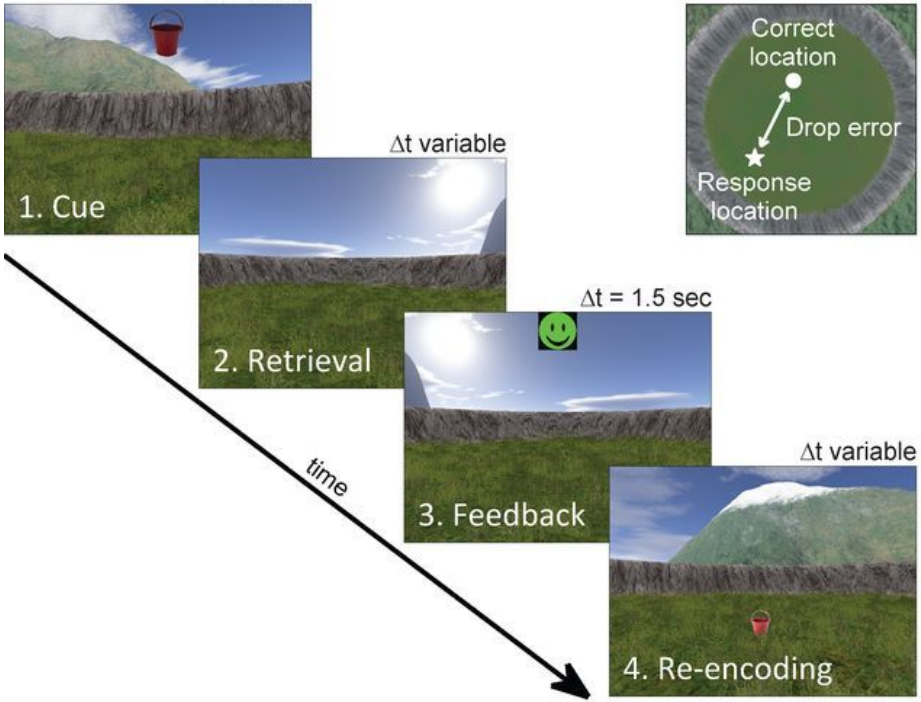
Calculate participants trajectory for aligned vs. misaligned paths, assuming hexagonal grid firing (60 degree)

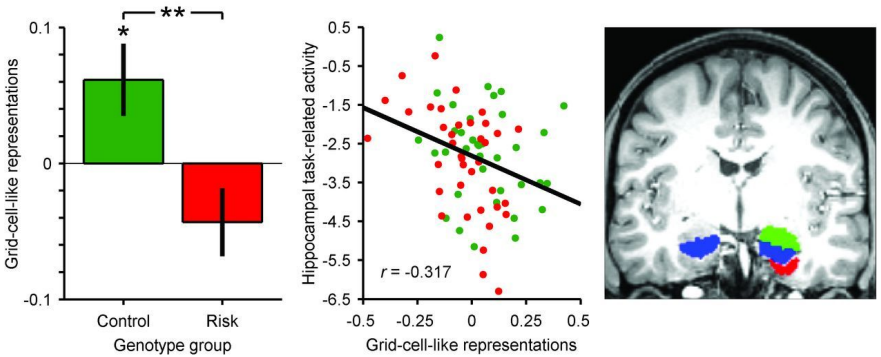
Compare activity in entorhinal cortex to other periodicities like 90 degree (square grids)

In entorhinal cortex **a 60 degree offset has the largest effect** between aligned and misaligned trajectories

Doeller et al. 2010

Reduced grid-cell like activity in Alzheimer's disease





Grid-cell-like activity in Alzheimer's patients is reduced during a virtual object retrieval task

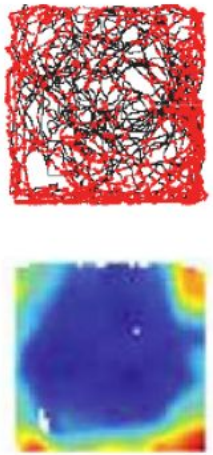
Kunz et al. 2015

The basic elements of the cognitive map

Medial entorhinal cortex

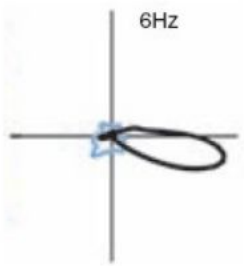
Hippocampus

Border cells



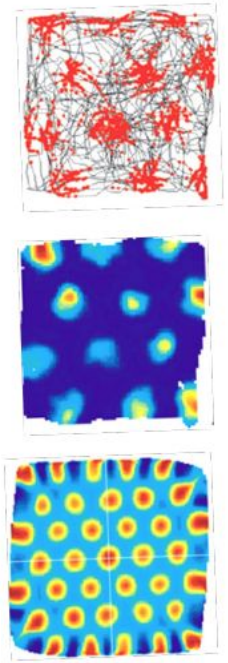
Mosers, O'Keefe, Knierim 2008

Head-direction cells



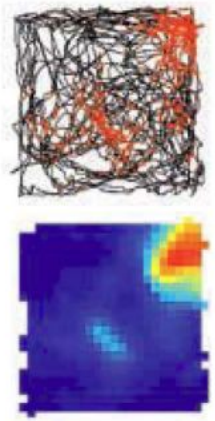
Ranck, Taube 1980s

Grid cells



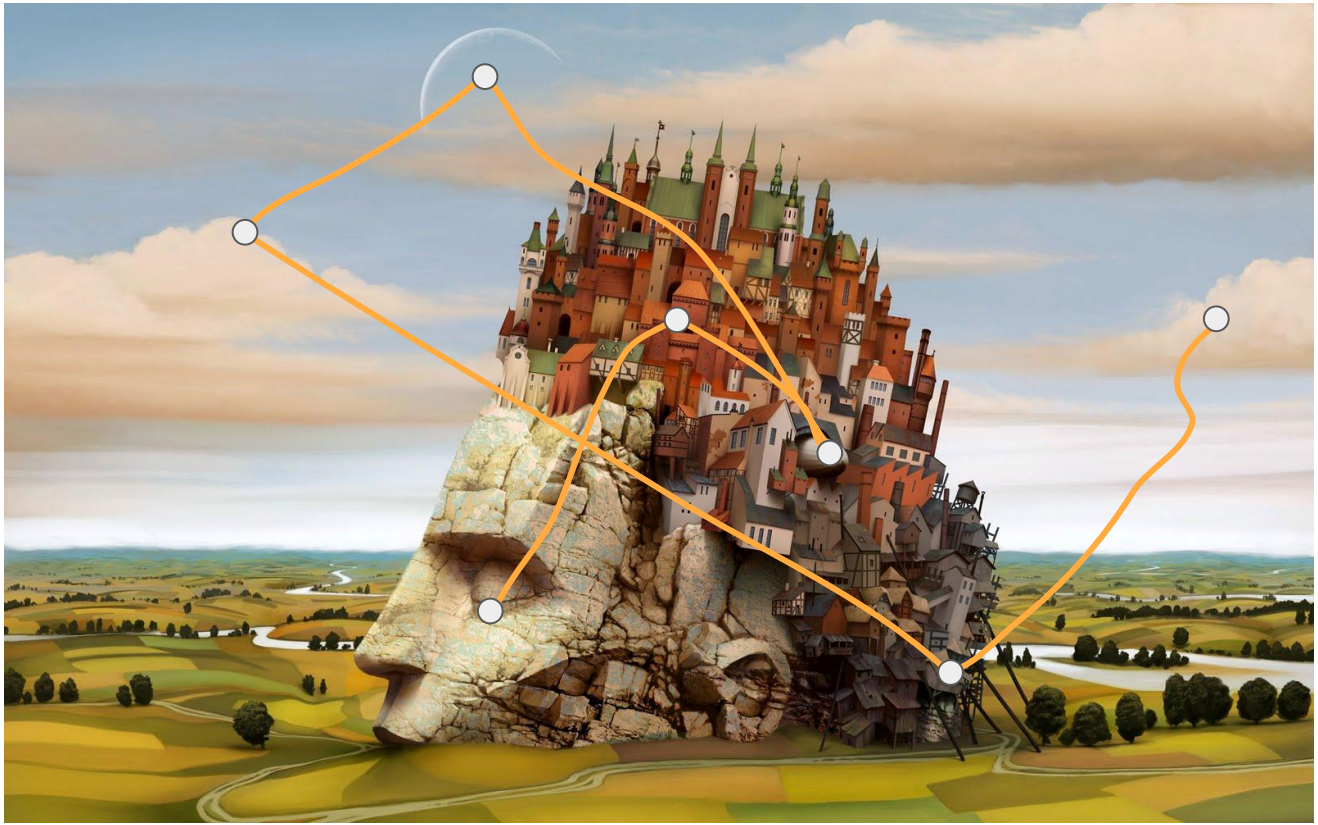
Mosers 2005

Place cells



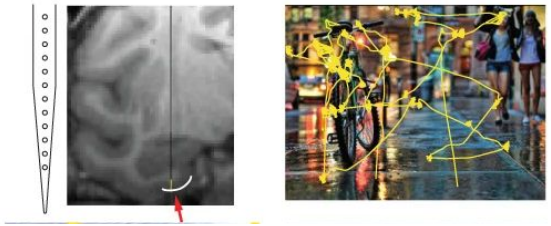
O'Keefe 1971

Encoding of visual space

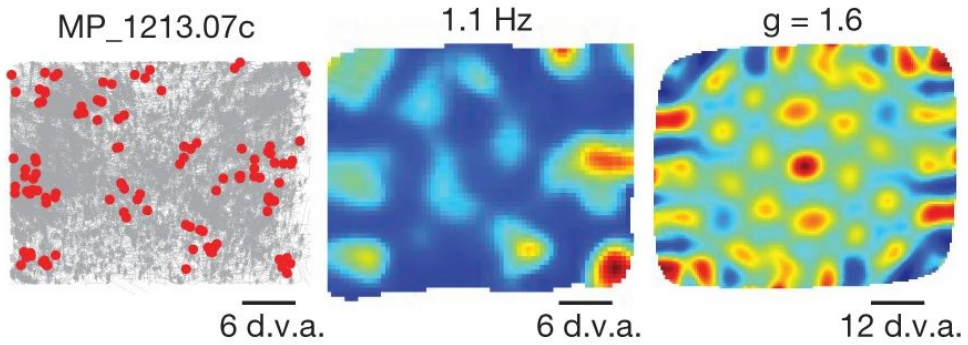


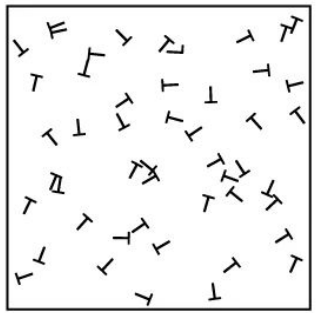
Jacek Yerka

Grid cells in entorhinal cortex encode visual space

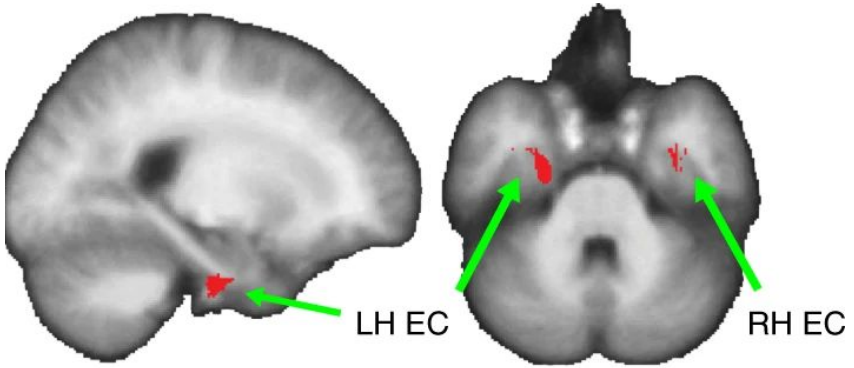


Eye-tracking during picture viewing



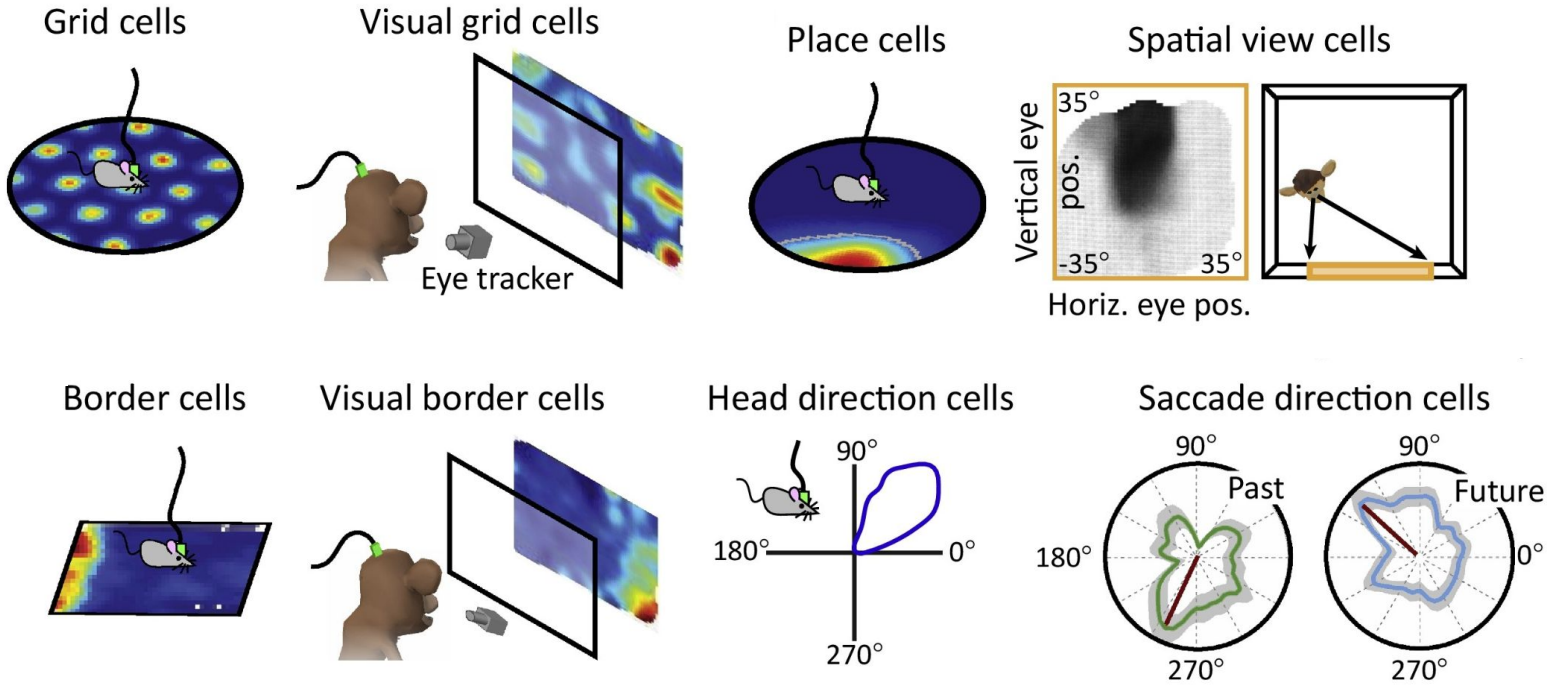


Find the letter L among the letter T



Kilian et al. 2012
Nau et al. & Julian et al., 2018

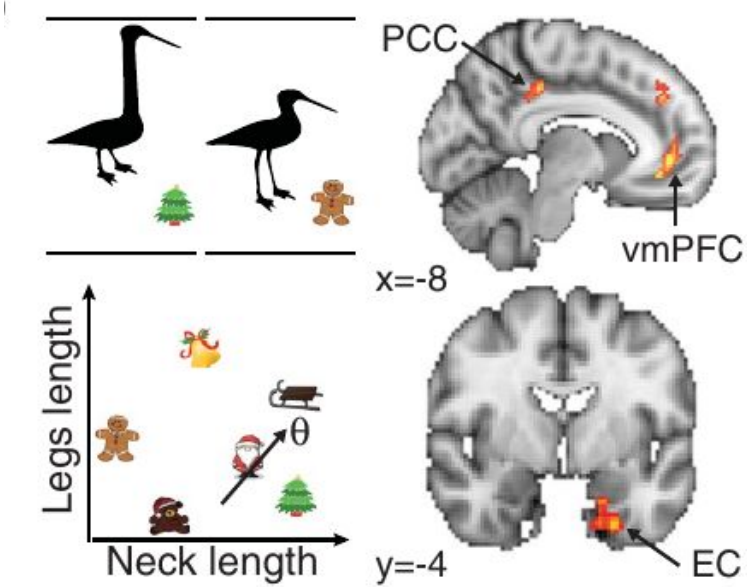
Cells encoding physical space also encode visual space



Hippocampus not only supports navigation but mediates a world-centered representation of visual space and guides viewing behavior

Nau, Julian et al. 2018

Encoding of abstract spaces



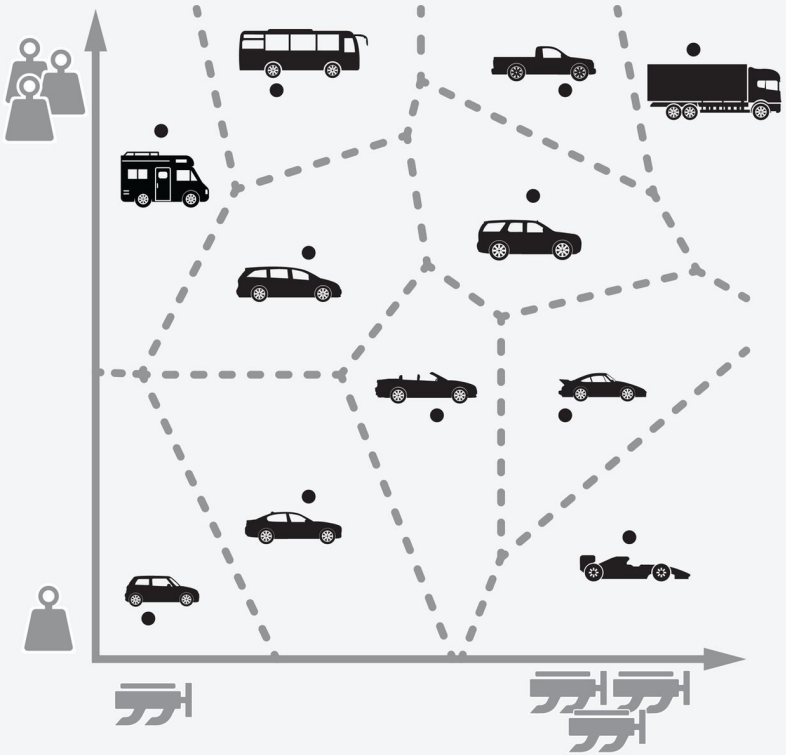
Participants in an fMRI scanner learned **association between objects and birds** (with variable neck and leg length) -> a novel abstract 2D space

During trajectories through that space **grid-like activity** in entorhinal cortex can be observed

This shows that the cells underlying **physical space also encode abstract space**

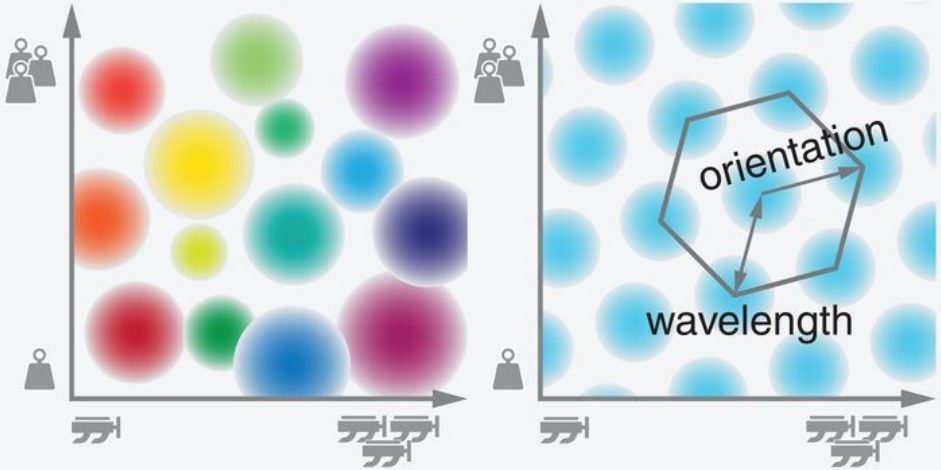
Constantinescu et al. 2016
Bellmund et al. 2018

Encoding of abstract spaces



A cognitive space spanned by the dimensions of car weight (*y* axis) and engine power (*x* axis)

This space can be tiled by place cells mapping each location and grid cells which provide the metrics for this space (distance and orientation)



Bellmund et al. 2018

Encoding of abstract spaces

Abstract knowledge is often represented at different hierarchical levels

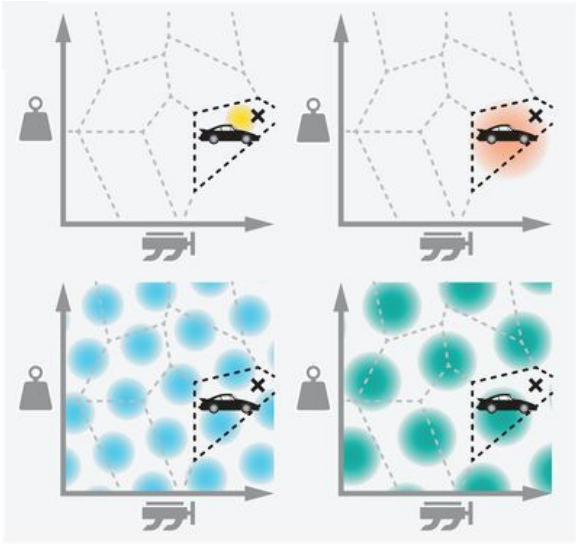
The different levels can be represented on the posterior-anterior (or dorsoventral in rodents) axis of the hippocampus or entorhinal cortex

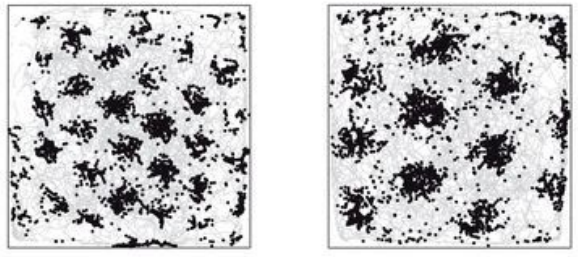
For example:

A vehicle characterized by low weight and high engine power might be a Porsche.

On a more general level, you can classify it as a sports car

On a more specific level you might wonder about the particular model and its associated characteristics.





Dorsal Ventral

Bellmund et al. 2018

Summary

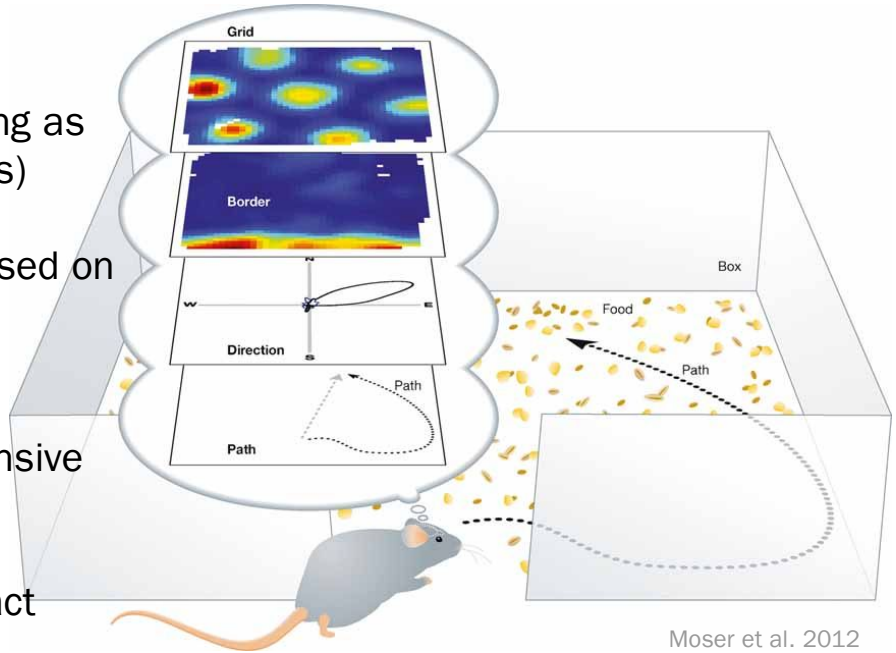
Place cells serve as landmarks in the brain's cognitive map, firing when an animal is in a specific location

Grid Cells create a hexagonal grid of spatial firing, acting as metric for the space (estimating of distances or vectors)

Head direction cells act as a neural compass, firing based on the animal's head direction, crucial for transforming egocentric to allocentric signals

The collective activity of these cells forms a comprehensive cognitive map for navigating complex environments.

These mechanisms also enable the encoding of abstract spaces, suggesting a fundamental role in imagination, planning, and memory.



Moser et al. 2012