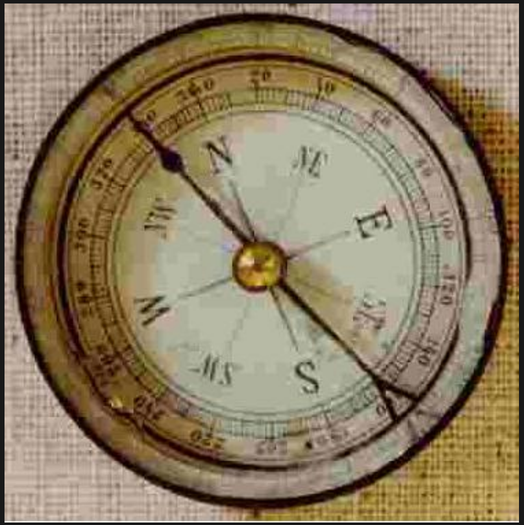
Learning & Memory in the Head Direction Cell Circuit



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What our Lab studies:

- Circuitry issues – How the Head Direction signal is generated?
- Involvement of vestibular & motor cues
- How visual landmark information is processed
- How HD signals guide behavior
- How head direction cells respond in 3-D, as well as under micro-gravity conditions?

What our Lab studies:

- Circuitry issues – How the HD signal is generated?
- Involvement of vestibular & motor cues
- How visual landmark information is processed
- How HD signals guide behavior
- How head direction cells respond in 3-D, as well as under micro-gravity conditions?

- Grid cell generation

Review a number of HD cell studies that we have conducted that involve learning and memory and inform us about some of the underlying neural processes involved in navigation.

Contributors

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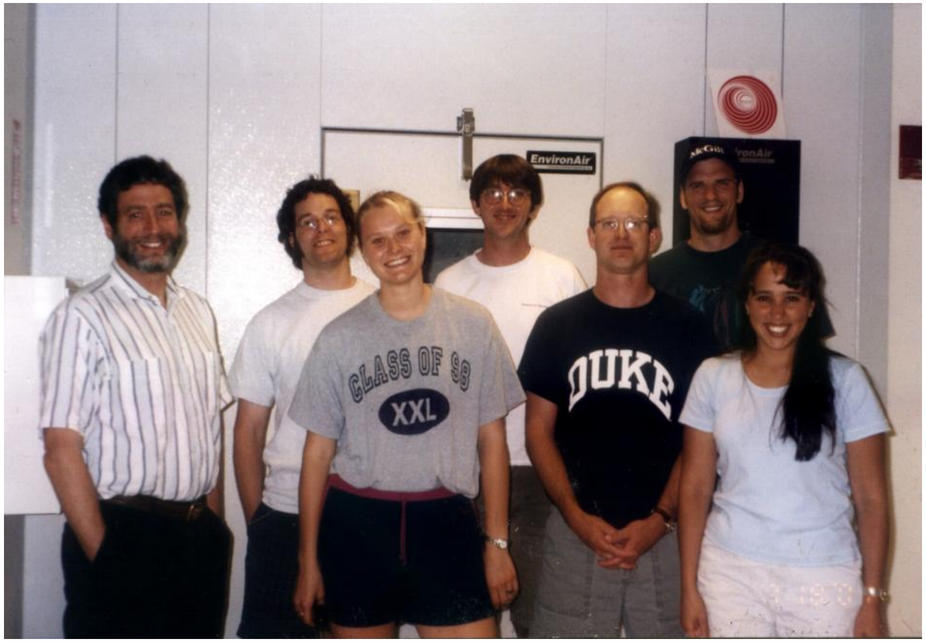
Gary Muir Jeffrey Calton



Brett Gibson

Jeremy Goodridge

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<u>Others</u>:

Josh Bassett	Joel Brown
Paul Dudchenko	Russ Frohardt
Jennifer Rilling	Mike Shinder
Bob Stackman	Sarah Wang
Shawn Winter	Ryan Yoder

Two Components of Spatial Orientation

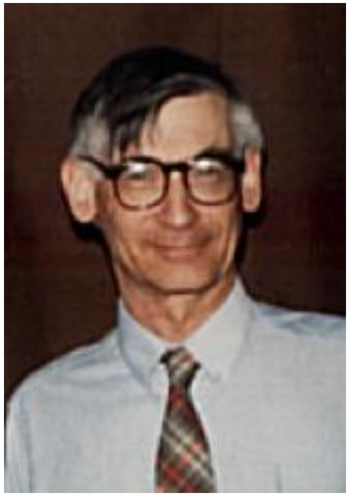
- Location - Place cells - 1971 - John O’Keefe
- Directional heading

But place cells do not provide information about directional heading.

A second category of spatial cells encodes for directional heading :

Head Direction cells

- Postsubiculum (dorsal presubiculum)
- found in many limbic system structures

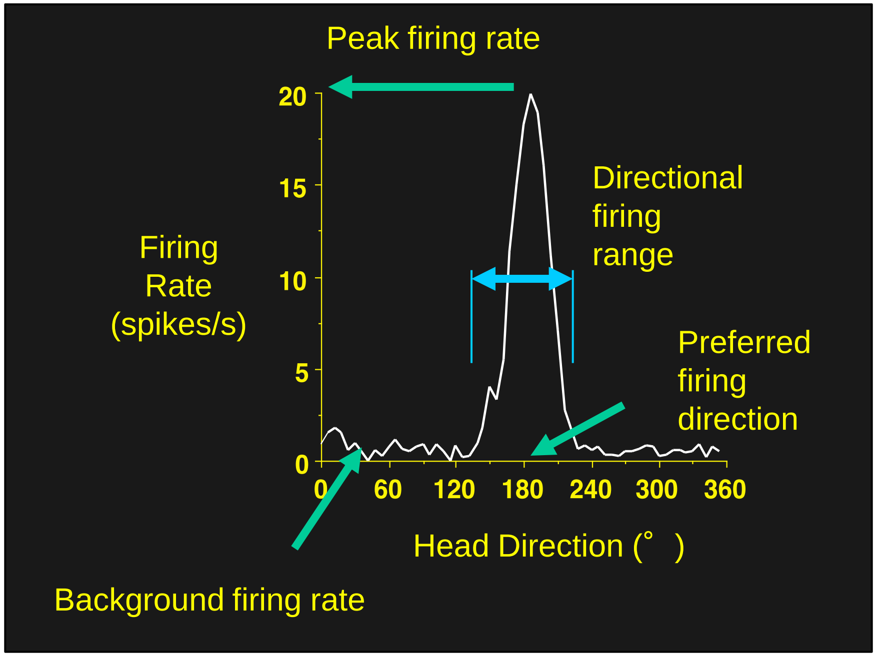


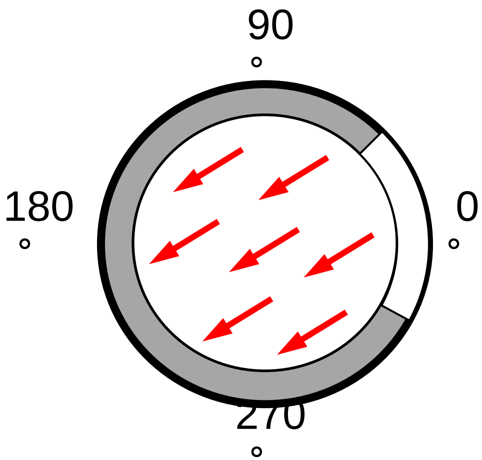
1984 - James Ranck

Head Direction Cell Video

Head Direction Cell Properties

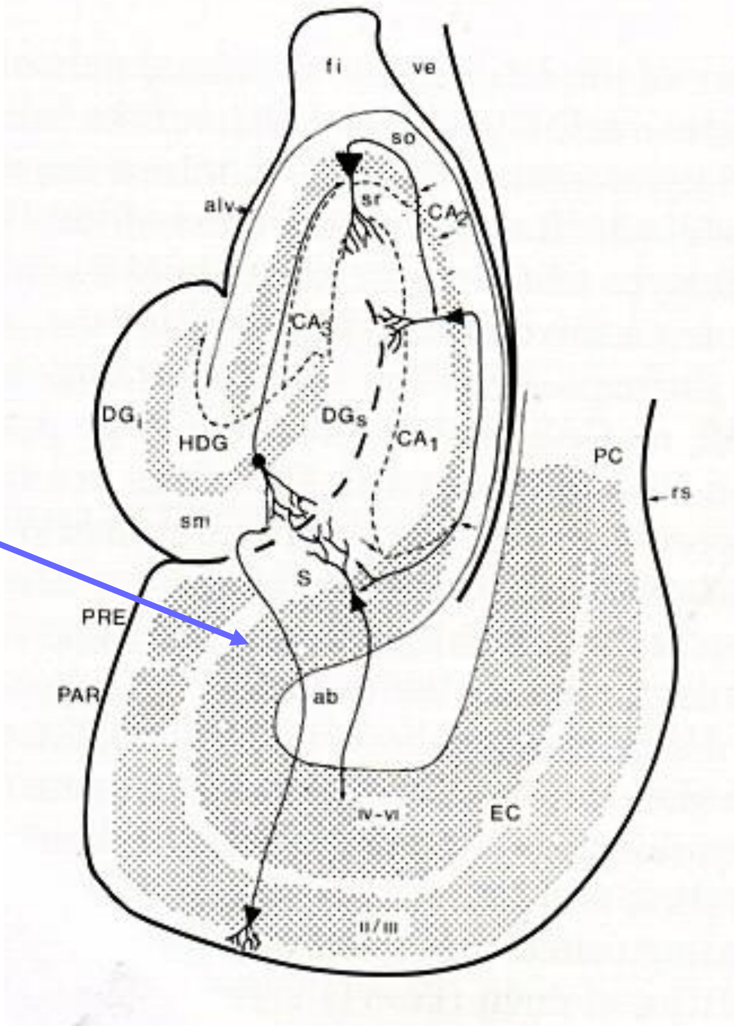
- Direction of head, not body position.
- Head direction in the horizontal plane.
- Fires whether animal is moving or still.
- Firing is independent of location and behavior.
- Each cell exhibits one preferred firing direction.
- Preferred firing directions distributed equally around 360º.





Where is the Postsubiculum?

Postsubiculum
- Deep layers

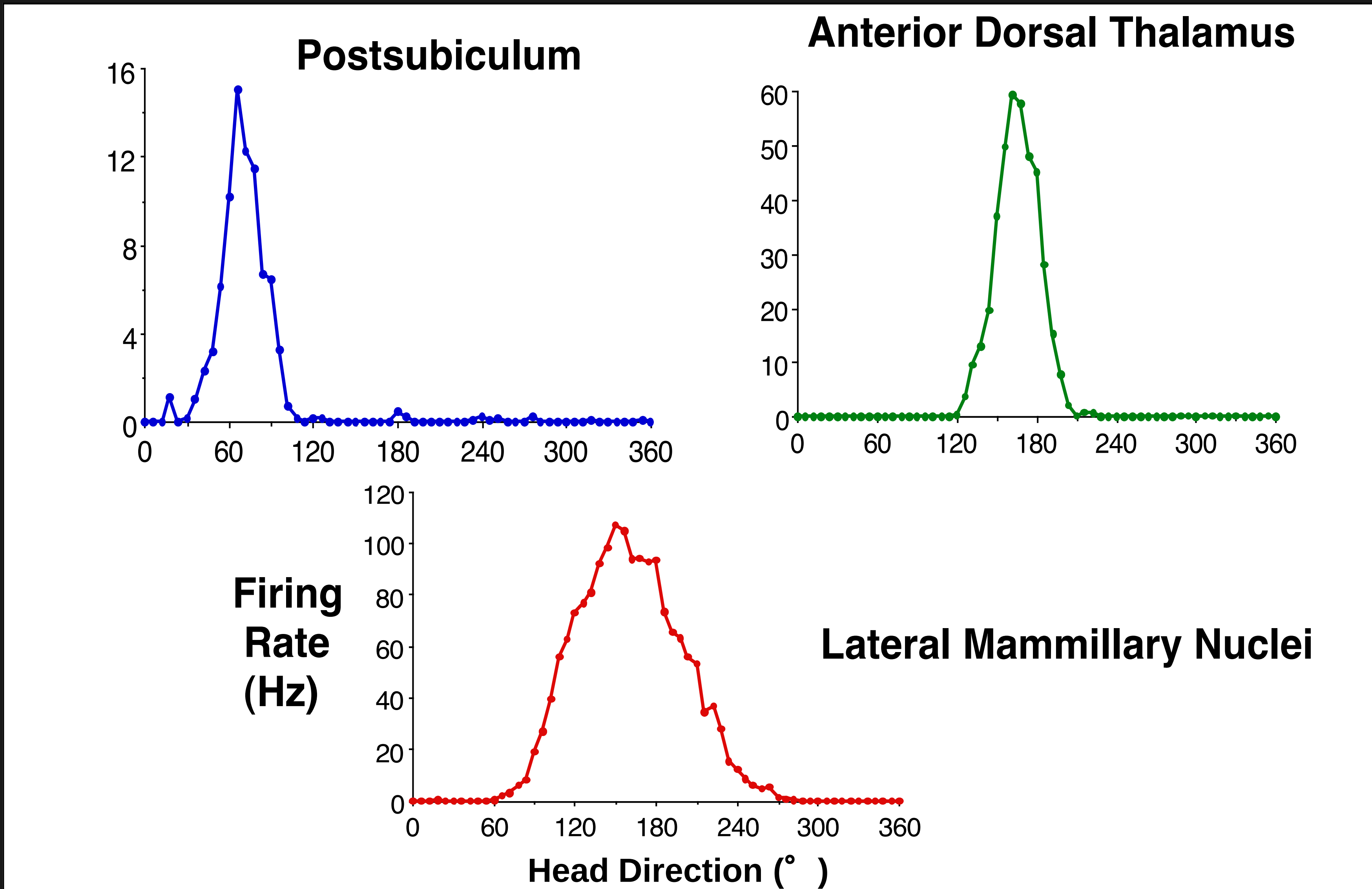


<u>Subicular Complex</u>
- Subiculum (S)
- Presubiculum (PRE)
- Parasubiculum (PAR)

Dorsal portion of Presubiculum = Postsubiculum

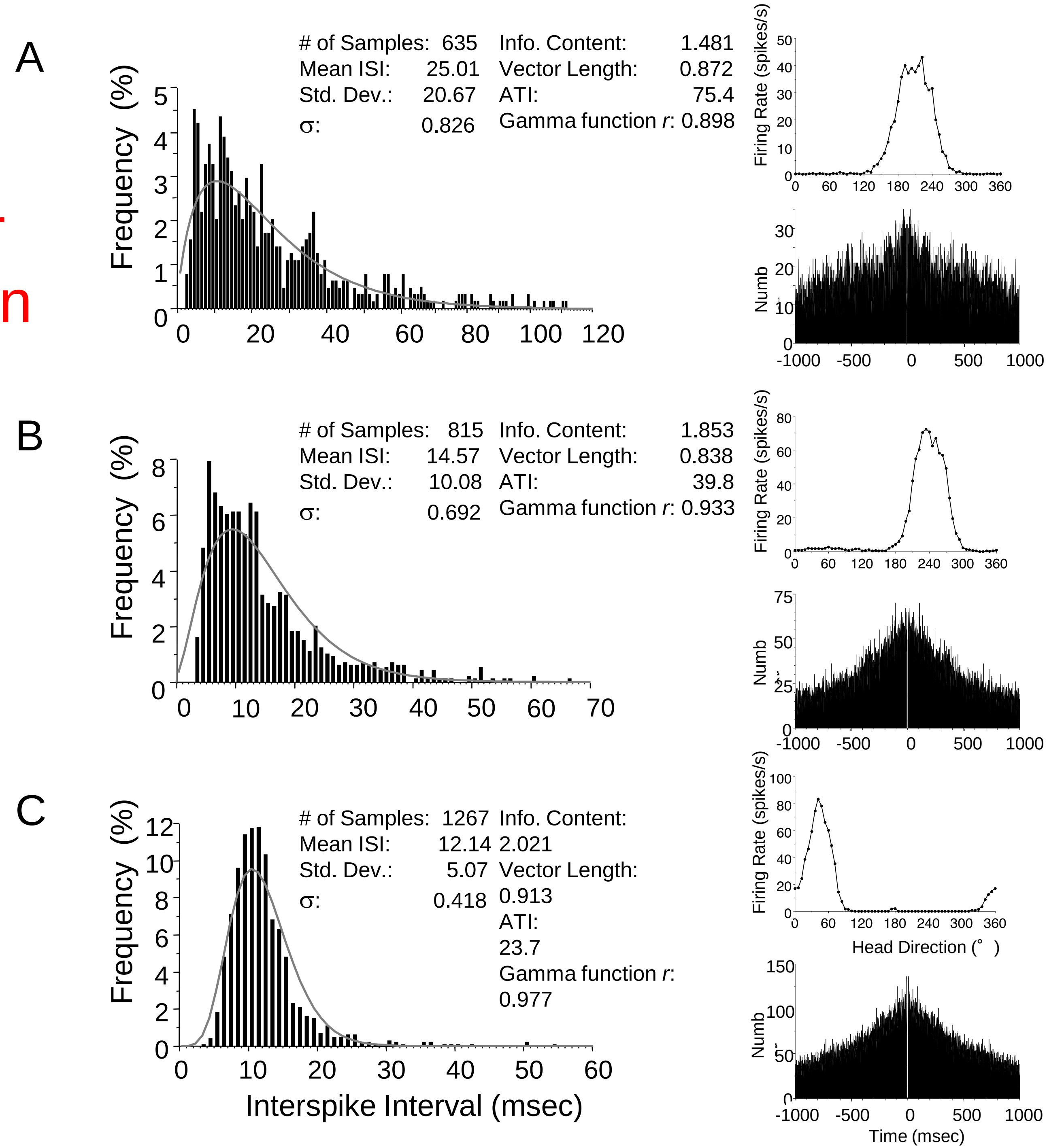
M Witter (1989) In *Hippocampus: New Vistas*

3 Typical HD cells from different brain areas

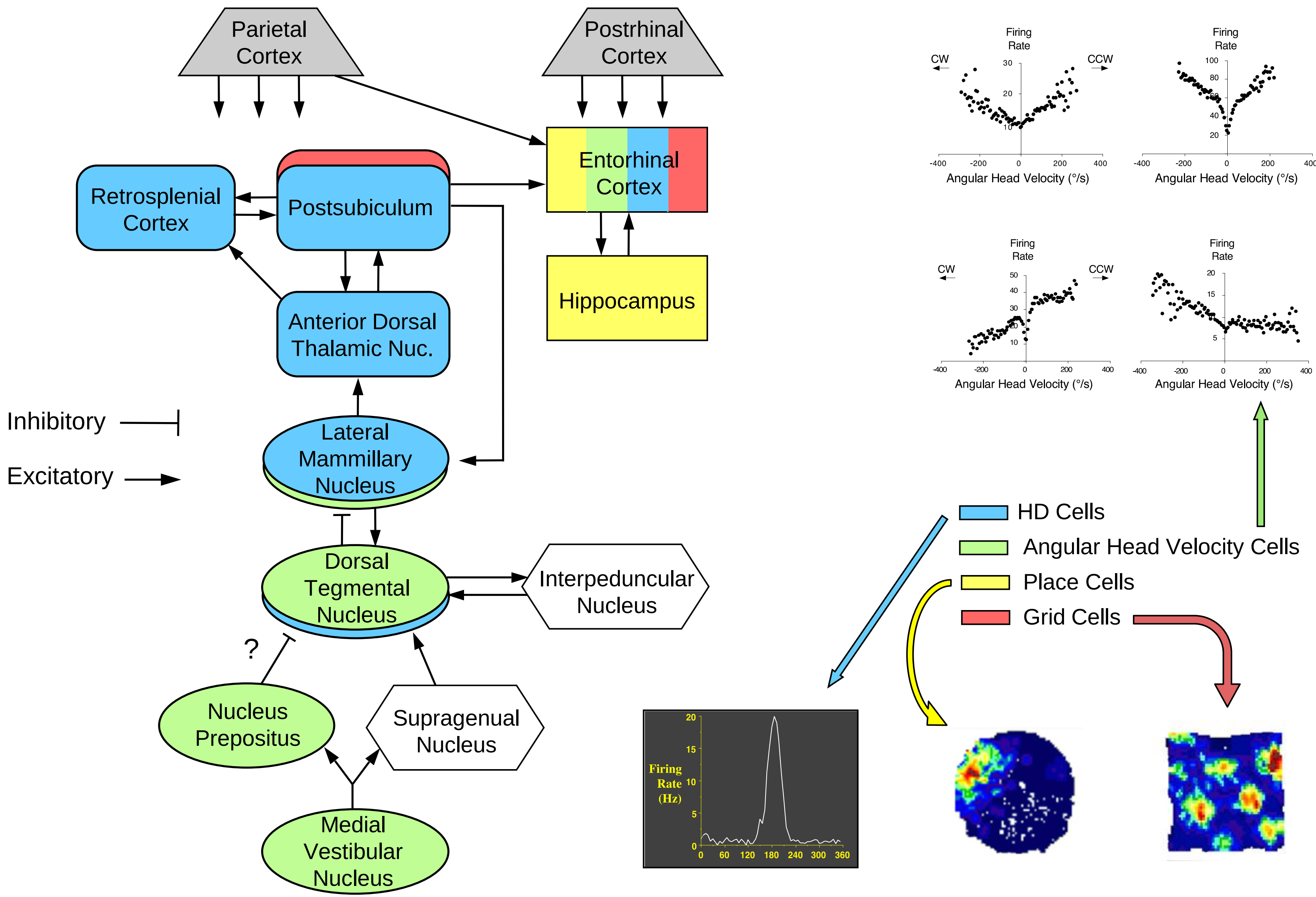


Taube, Muller, Ranck (1990) J Neurosci; Taube (1995) J Neurosci; Stackman & Taube (1998) J Neurosci

No evidence for theta-modulation

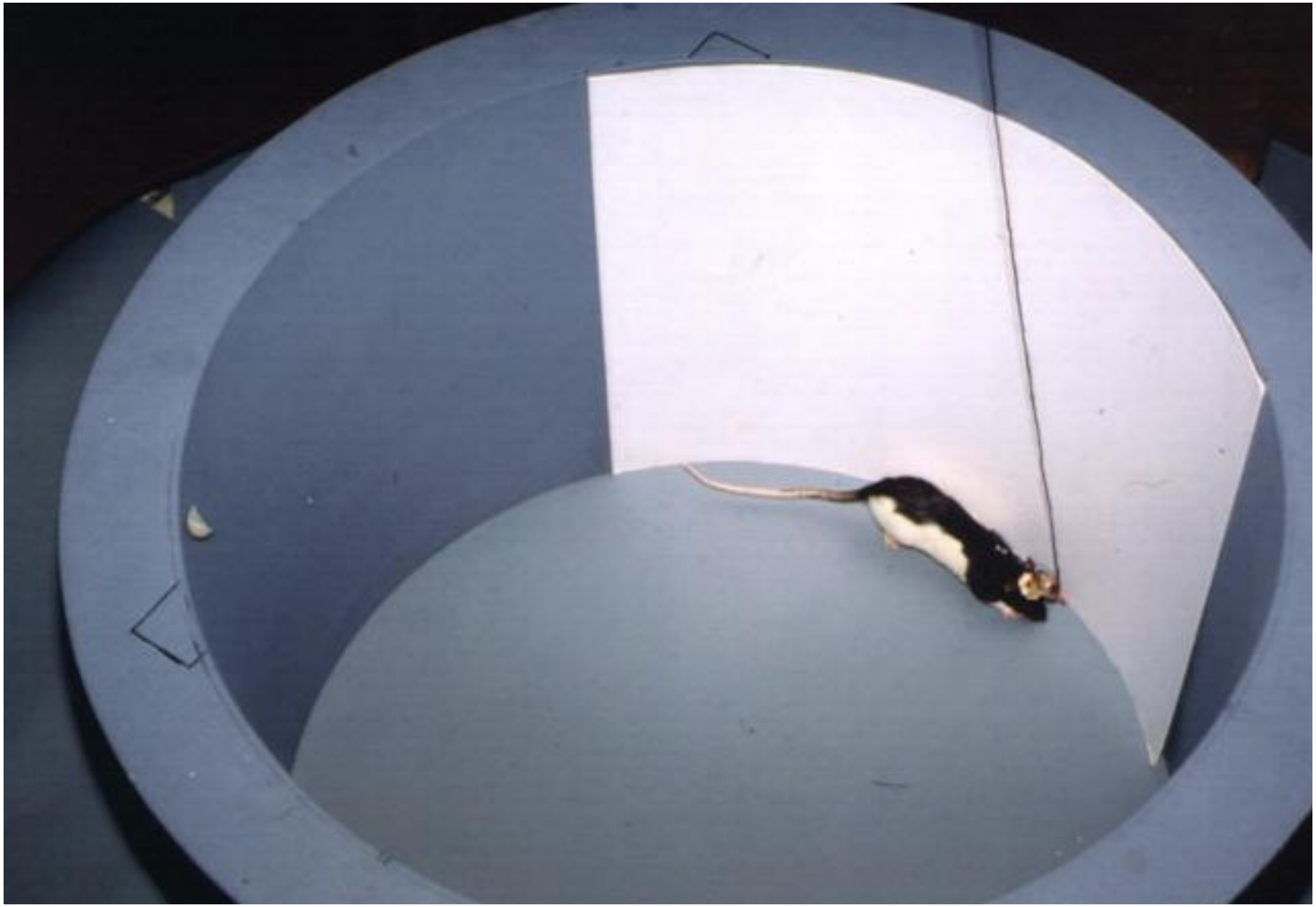


Head Direction Cell Circuitry

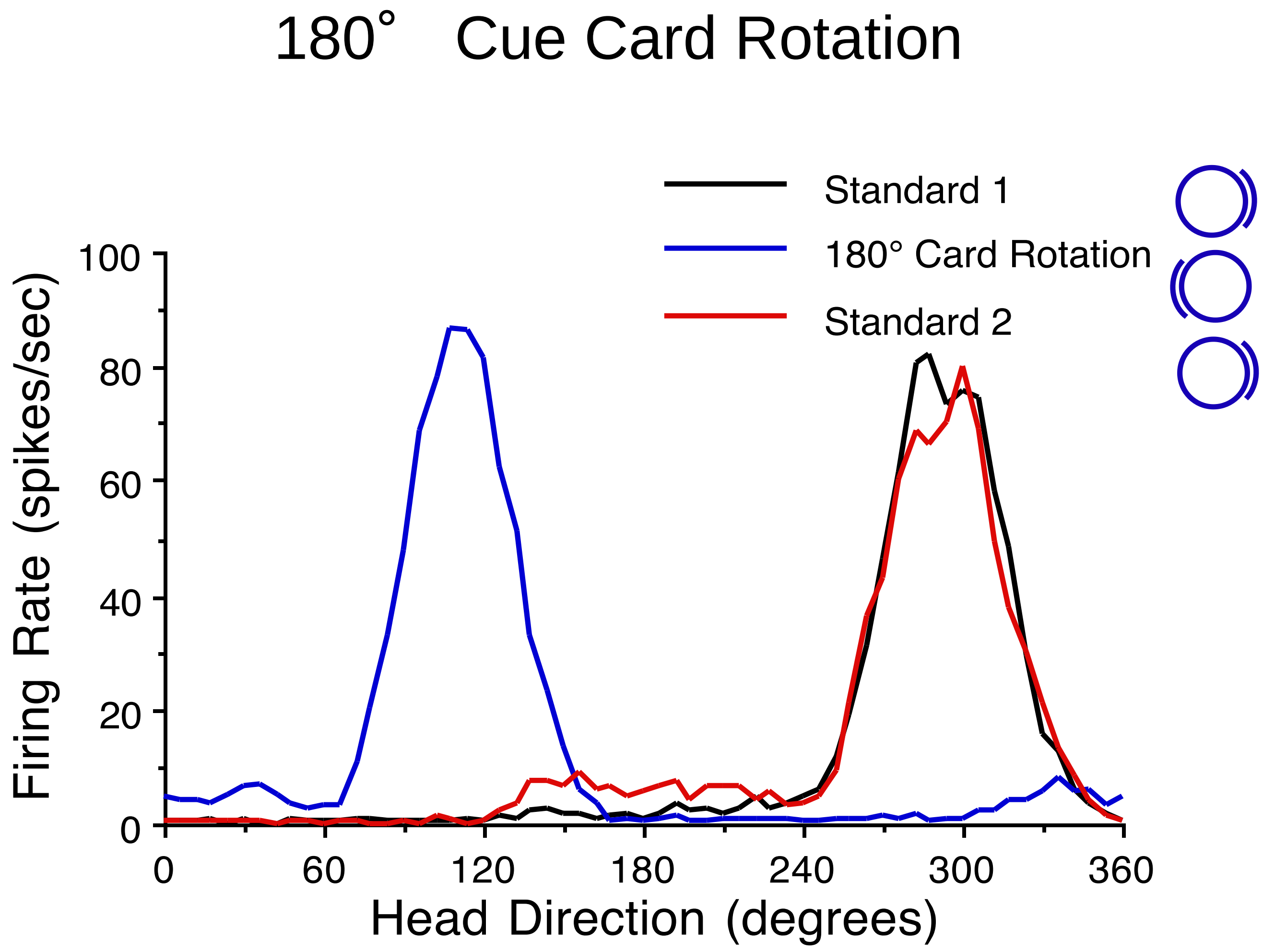


Taube (2007) Ann Rev Neurosci

White cue card acts as the sole intentional orienting cue.



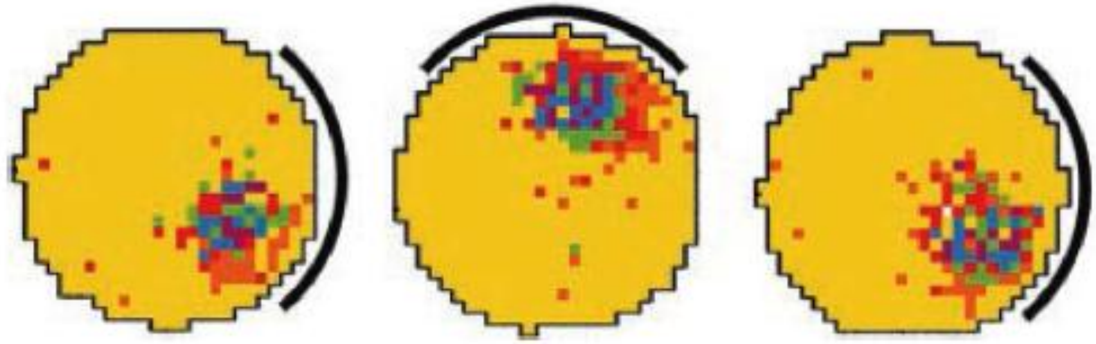
The cue card exerts stimulus control over head-direction cell firing



Taube et al. (1990) J Neurosci

Place cell place fields also shift following rotation of the salient visual cue

Place cell



What brain areas are important for visual landmark control of Head Direction & Place Cell activity?

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General view for processing visual information:

Dorsal stream important for processing spatial information - Parietal cortex

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Dorsal stream important for processing spatial information - Parietal cortex

Ventral stream important for processing object recognition - Inferior temporal cortex

What brain areas are important for visual landmark control of Head Direction & Place Cell activity?

General view for processing visual information:

Dorsal stream important for processing spatial information – Parietal Cortex

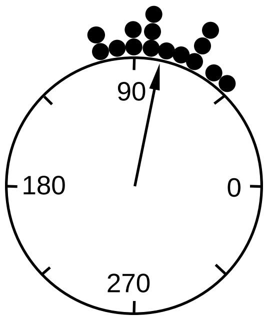
Ventral stream important for processing object recognition – Inferior Temporal Cortex

Visual Tectal Pathway - Attention

To test this, we conducted 90° landmark rotation experiments on HD cells in animals with lesions of various brain areas.

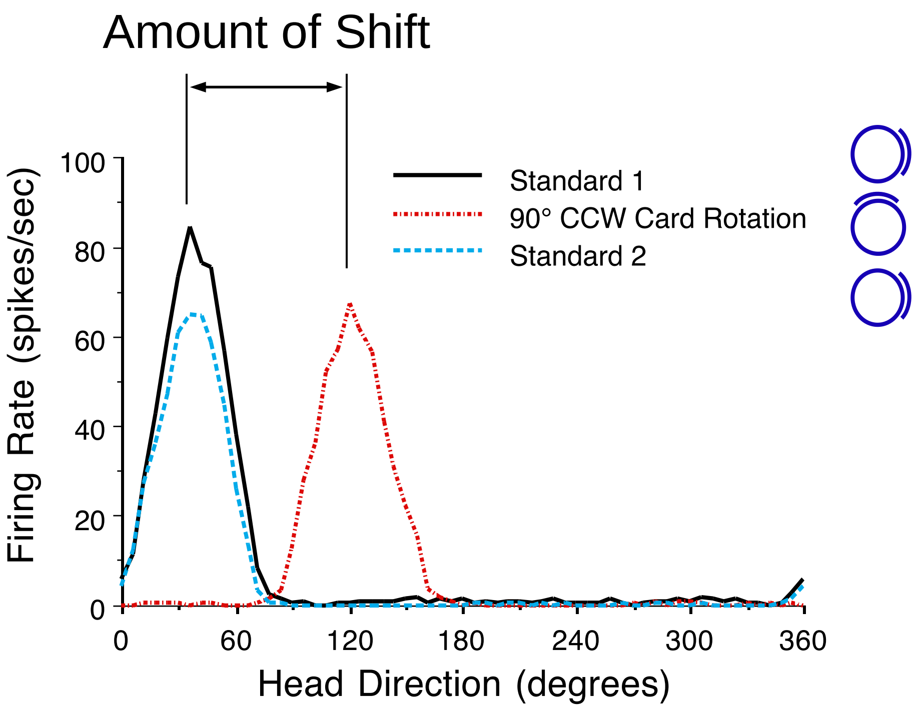
Head Direction cell responses to 90˚ cue card rotations

Frequency Distribution
for Shift Amounts

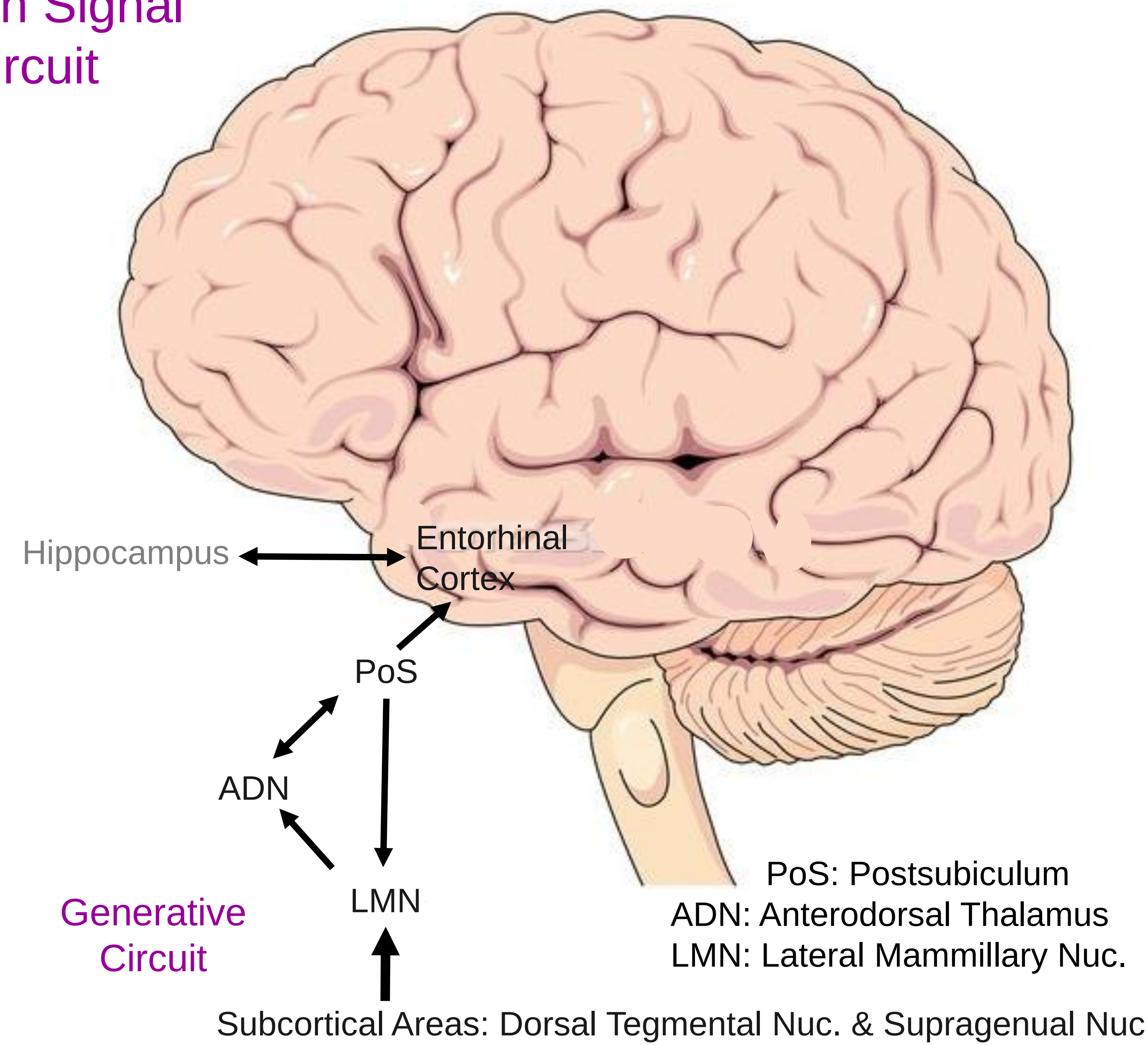


Control

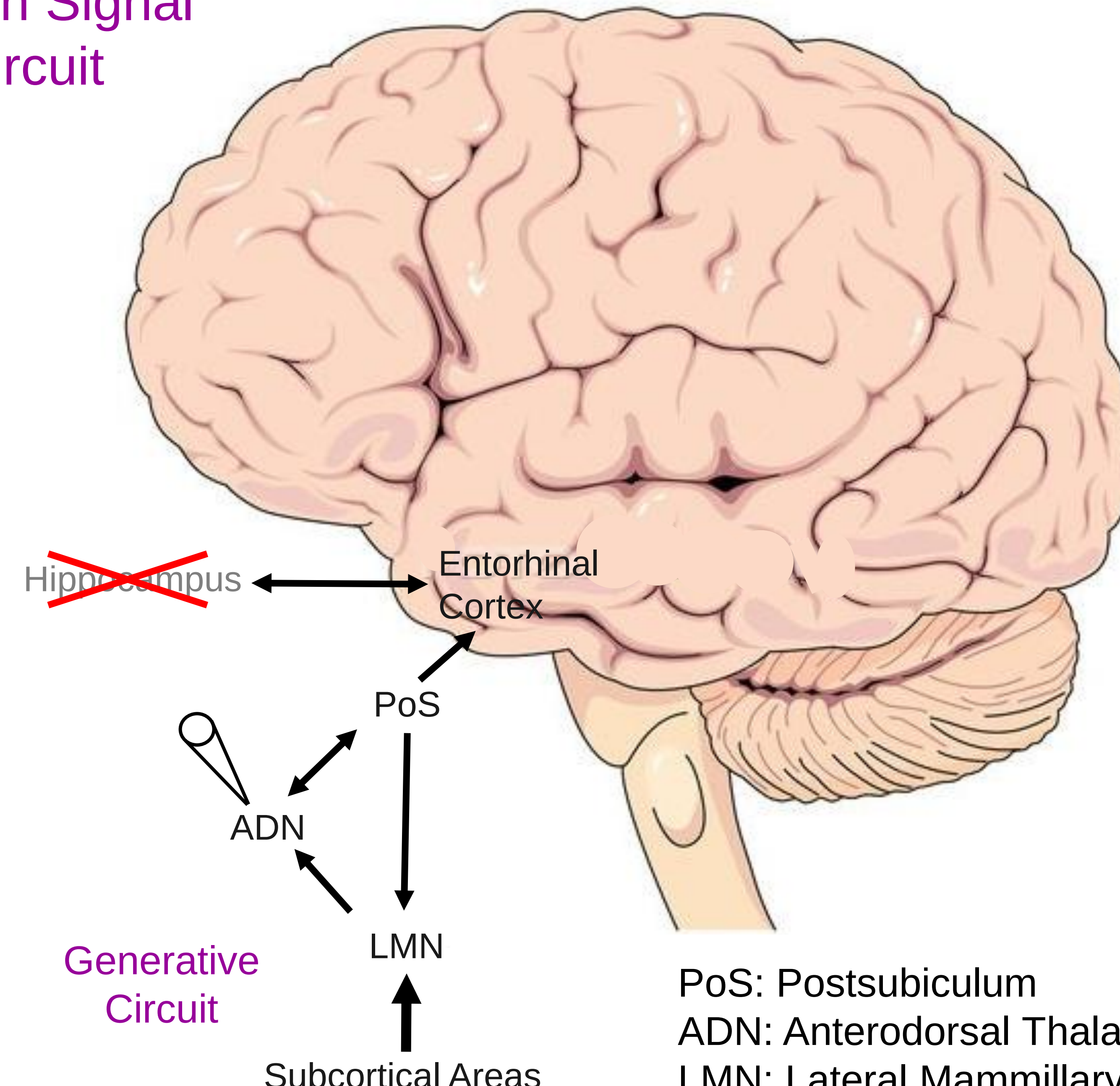
Arrow represents
the mean vector



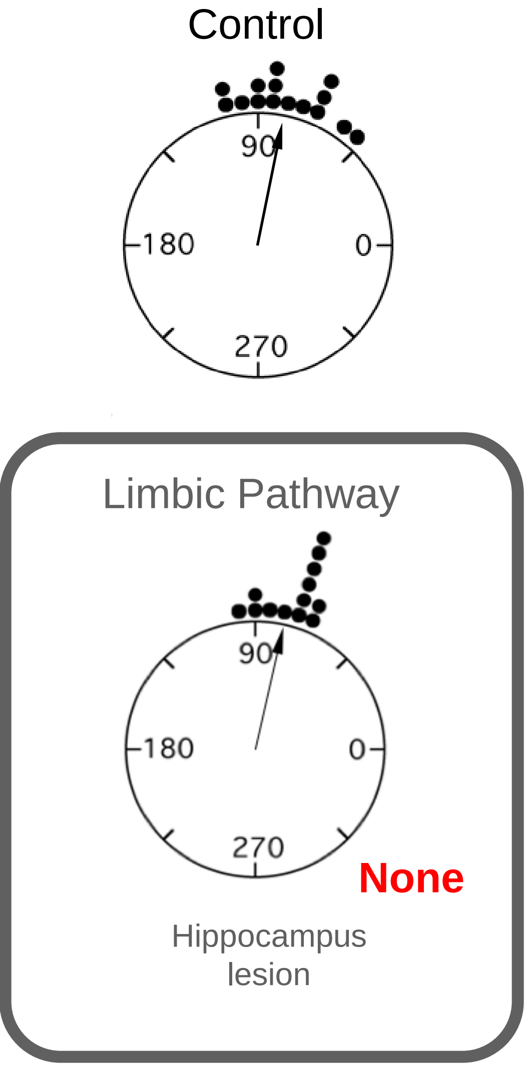
Head Direction Signal Generative Circuit



Head Direction Signal Generative Circuit



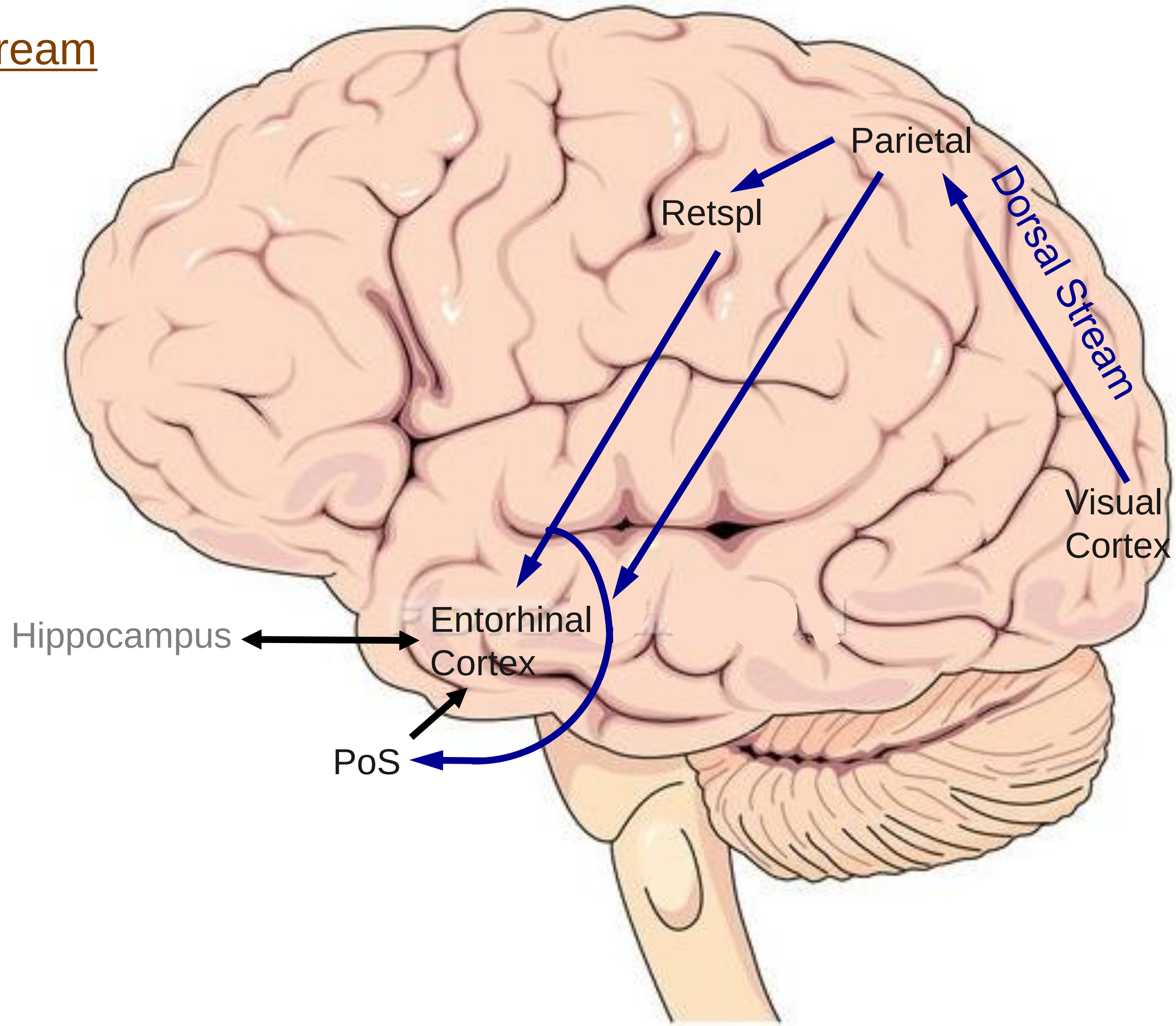
PoS: Postsubiculum
ADN: Anterodorsal Thalamus
LMN: Lateral Mammillary Nuc.



Control
90
180
0
270
Limbic Pathway
90
180
0
270
None
Hippocampus
lesion

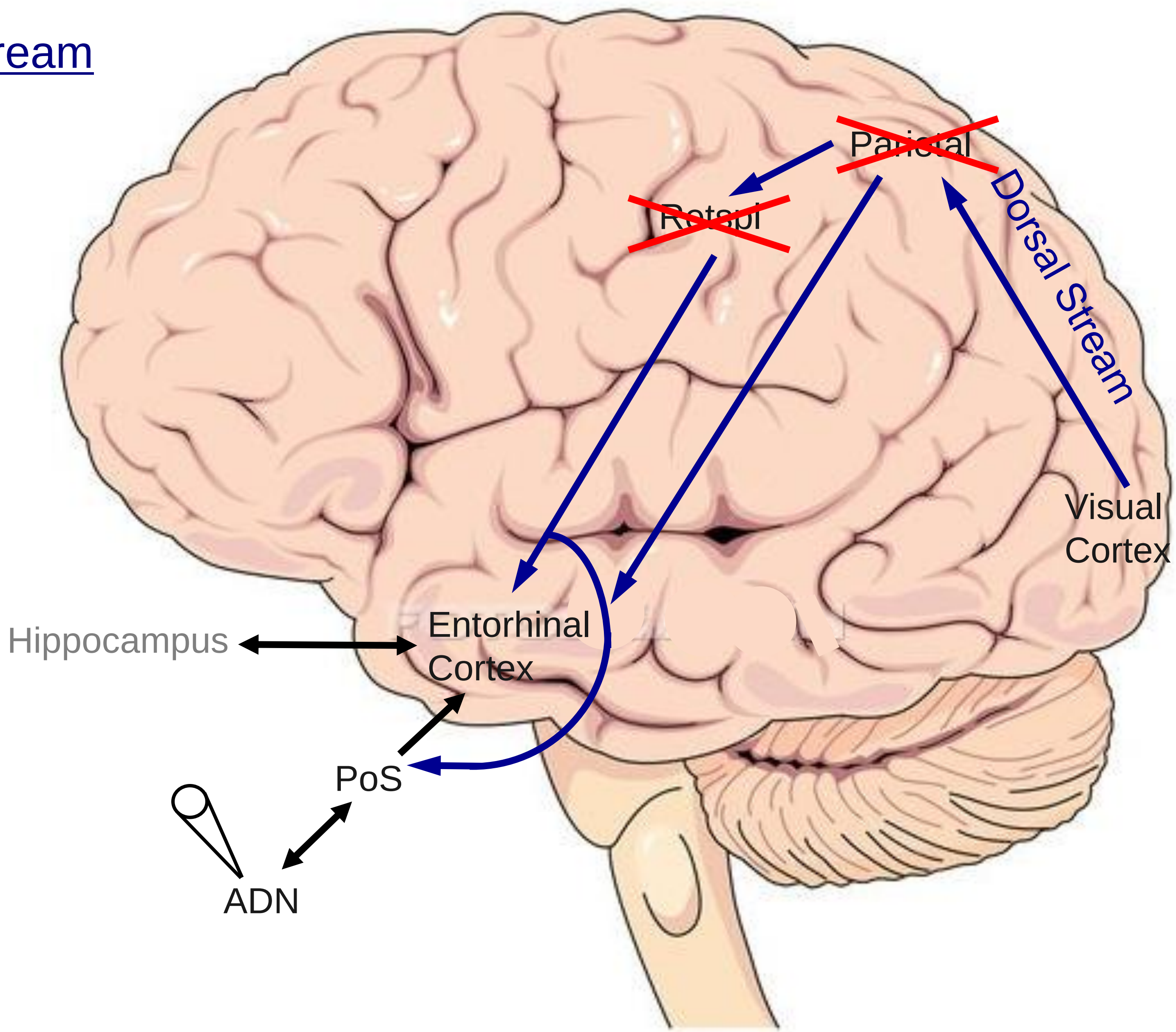
Visual Streams for Processing Landmark Information:

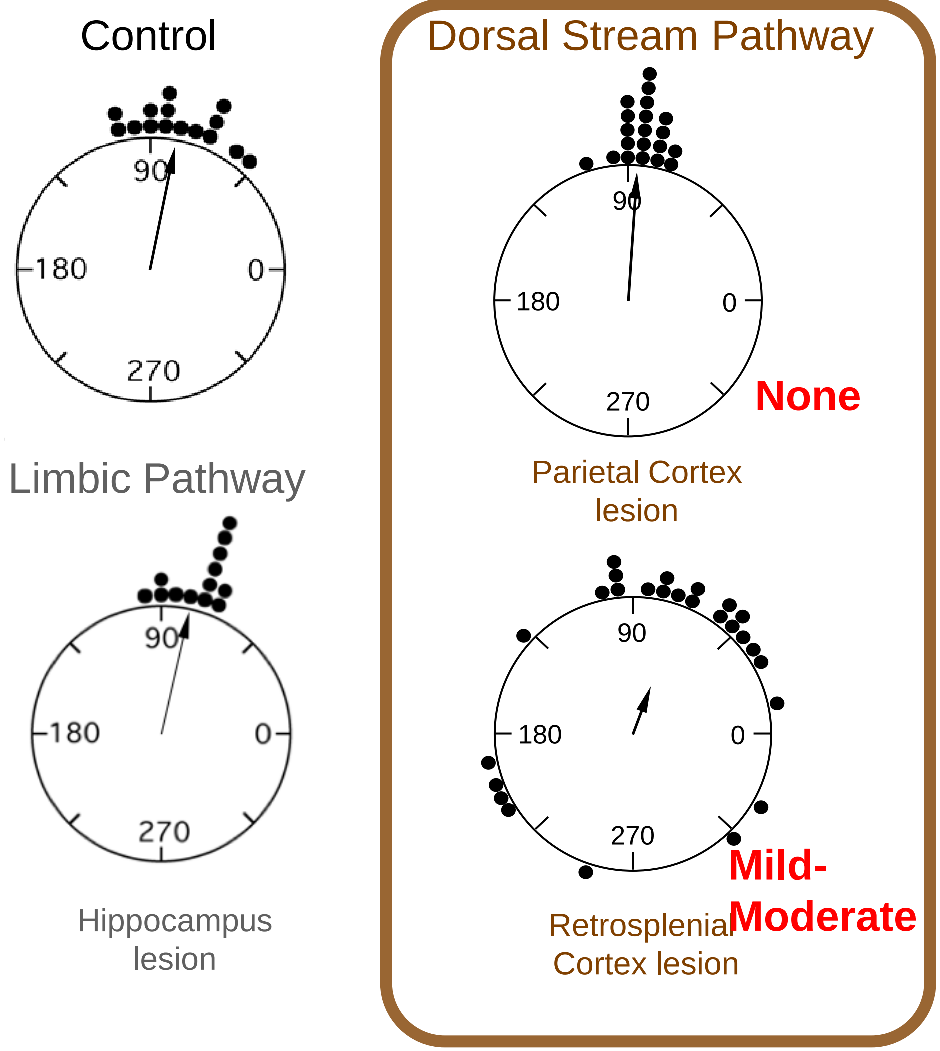
Dorsal Stream



Visual Streams for Processing Landmark Information:

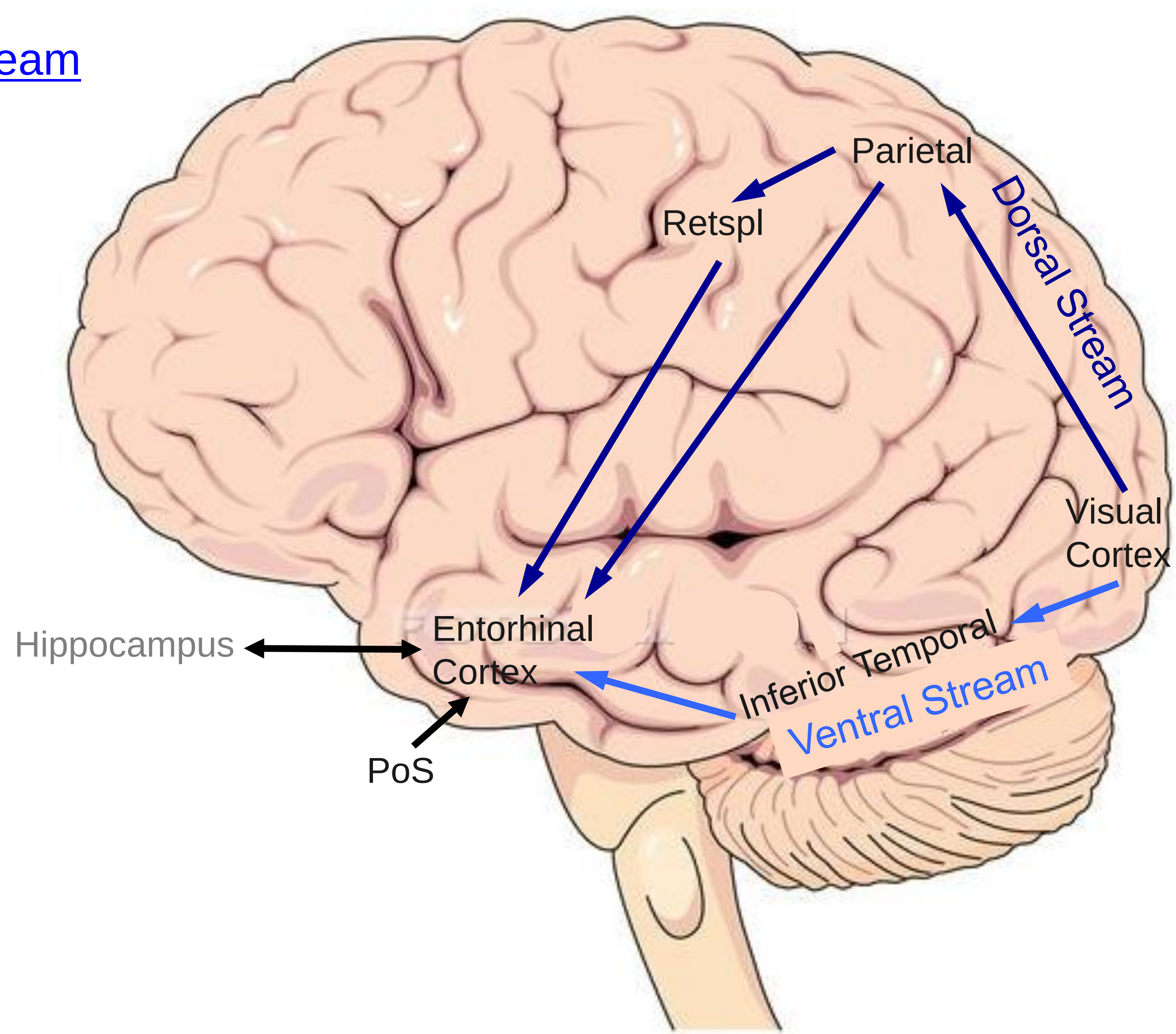
Dorsal Stream




Control
90
180
0
270
Limbic Pathway
90
180
0
270
Hippocampus lesion
Dorsal Stream Pathway
90
180
0
270
None
Parietal Cortex lesion
90
180
0
270
Mild-Moderate
Retrosplenial Cortex lesion

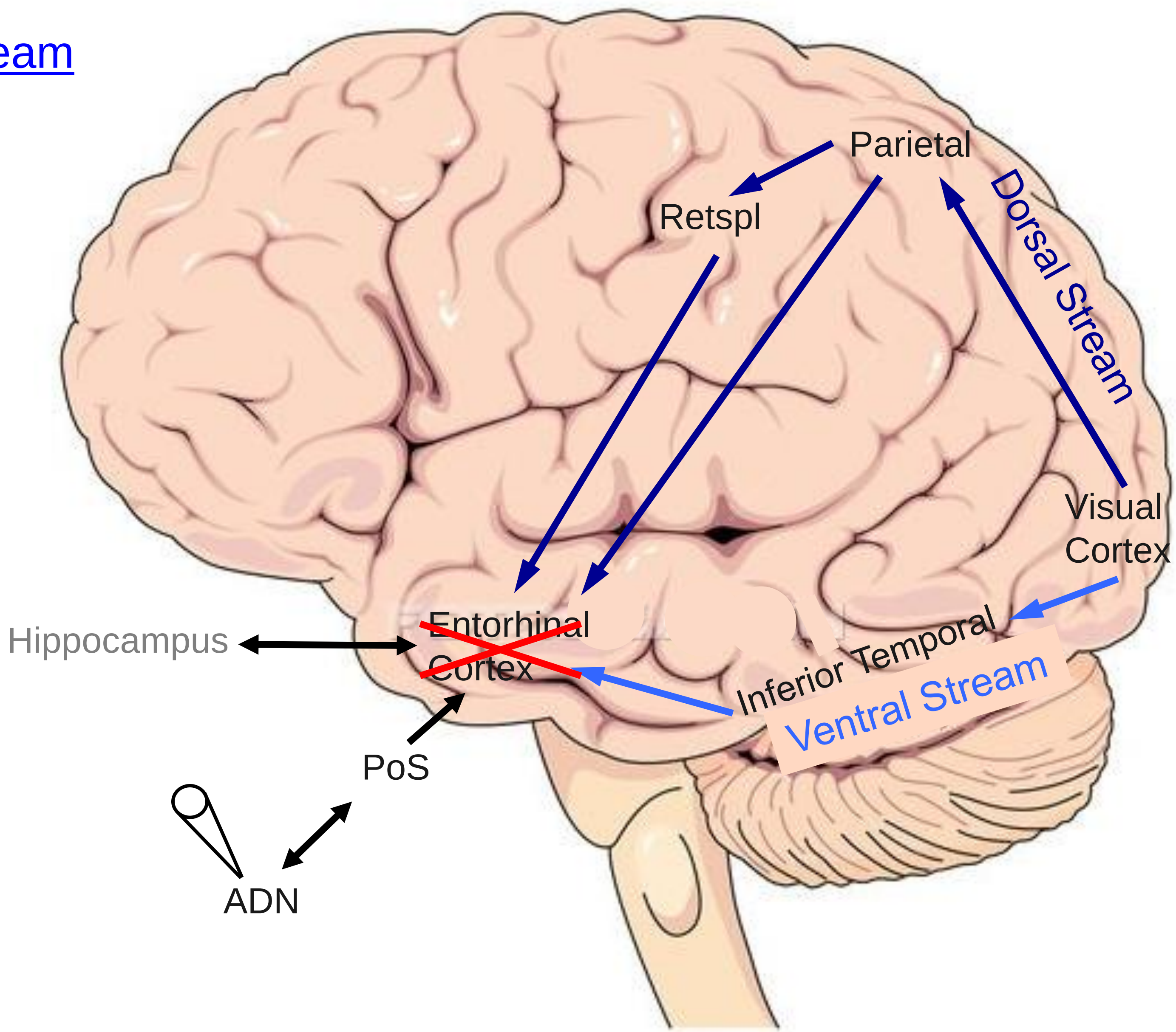
Visual Streams for Processing Landmark Information:

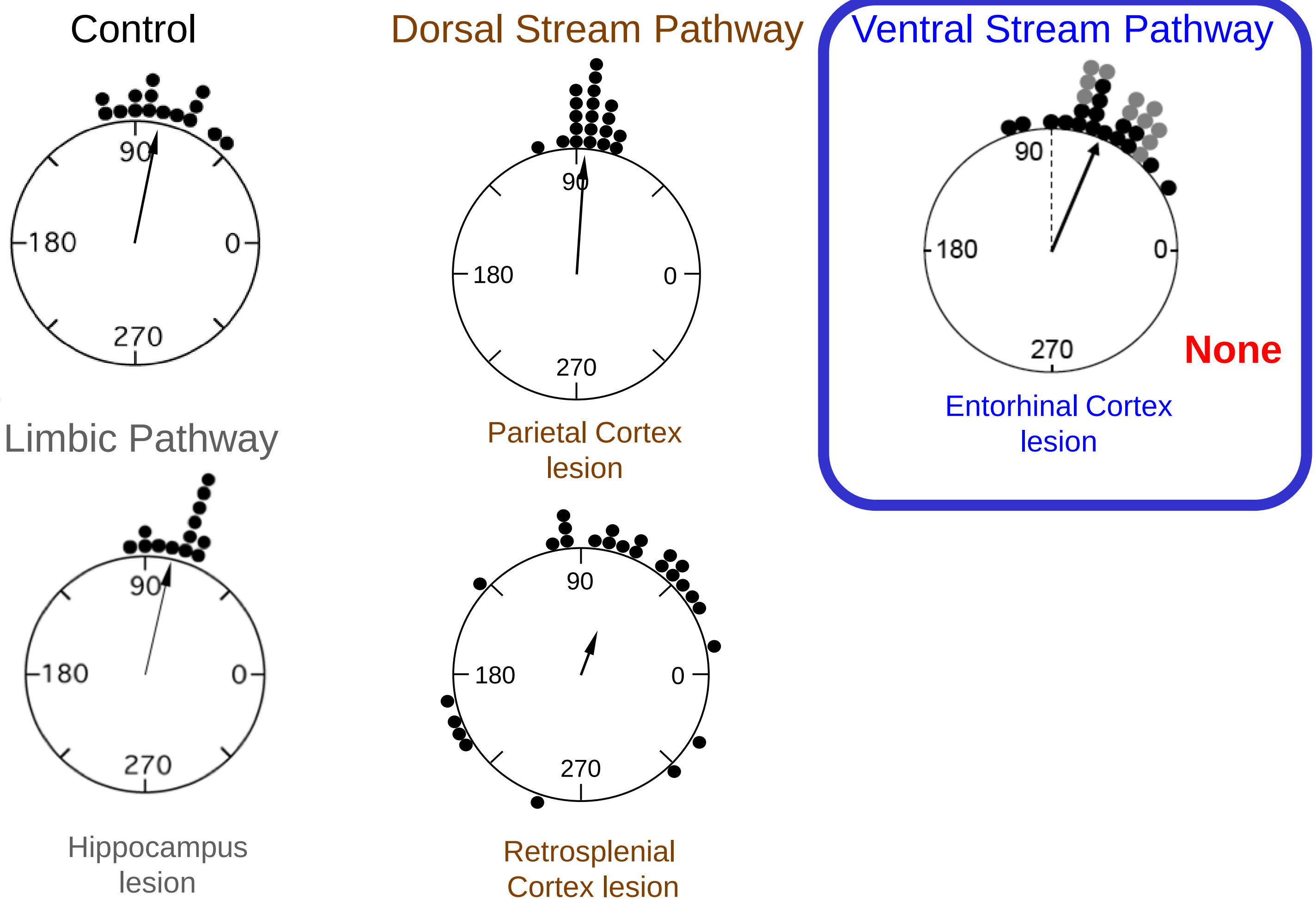
Ventral Stream



Visual Streams for Processing Landmark Information:

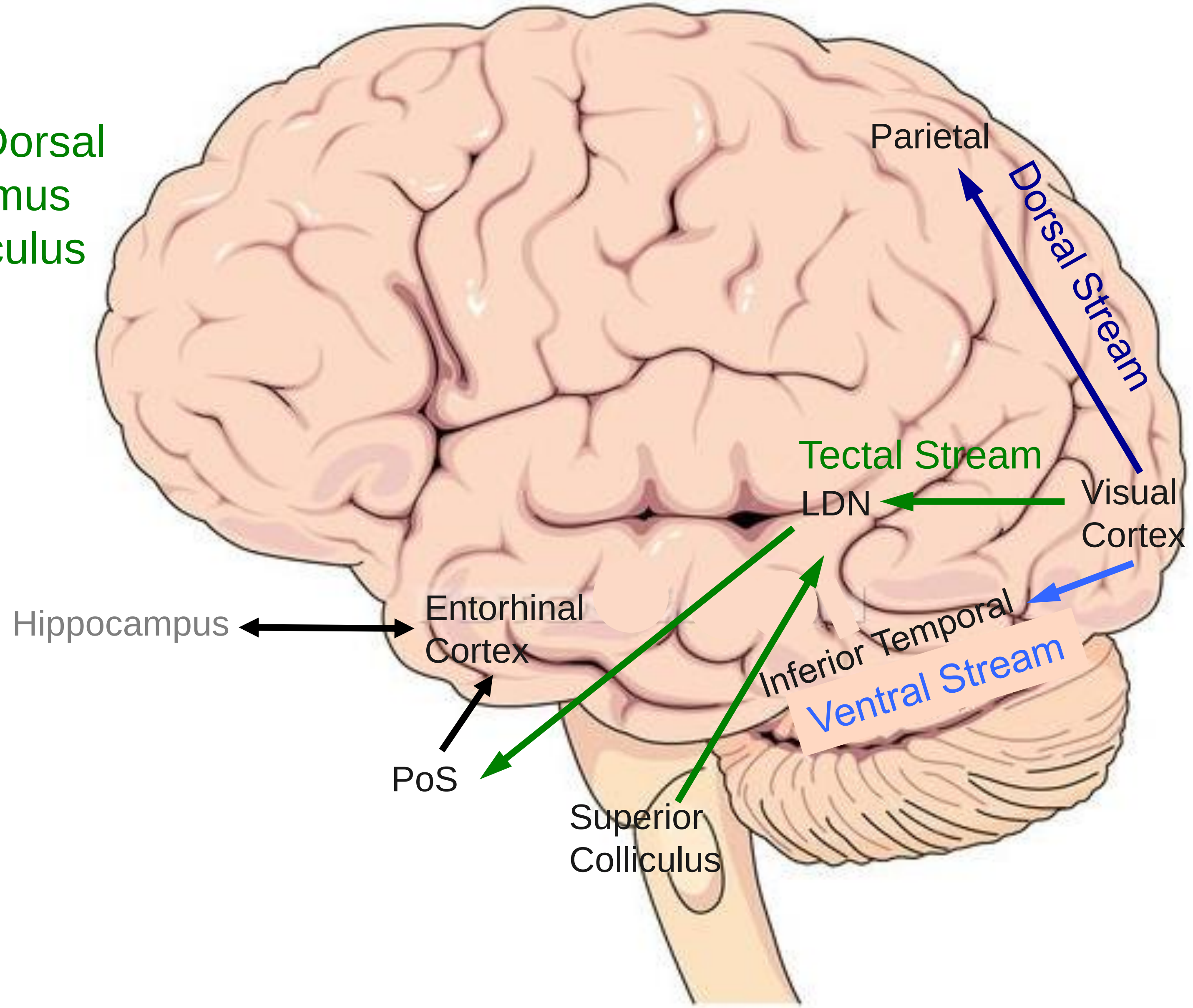
Ventral Stream




Control
90
180
0
270
Dorsal Stream Pathway
90
180
0
270
Parietal Cortex lesion
Ventral Stream Pathway
90
180
0
270
None
Entorhinal Cortex lesion
Limbic Pathway
90
180
0
270
Hippocampus lesion
90
180
0
270
Retrosplenial Cortex lesion

Visual Streams for Processing Landmark Information:

<u>Tectal Stream</u>
via
LDN: Lateral Dorsal Thalamus
Superior Colliculus
Pulvinar



Visual Streams for Processing Landmark Information:

Tectal Stream
via
LDN: Lateral Dorsal Thalamus
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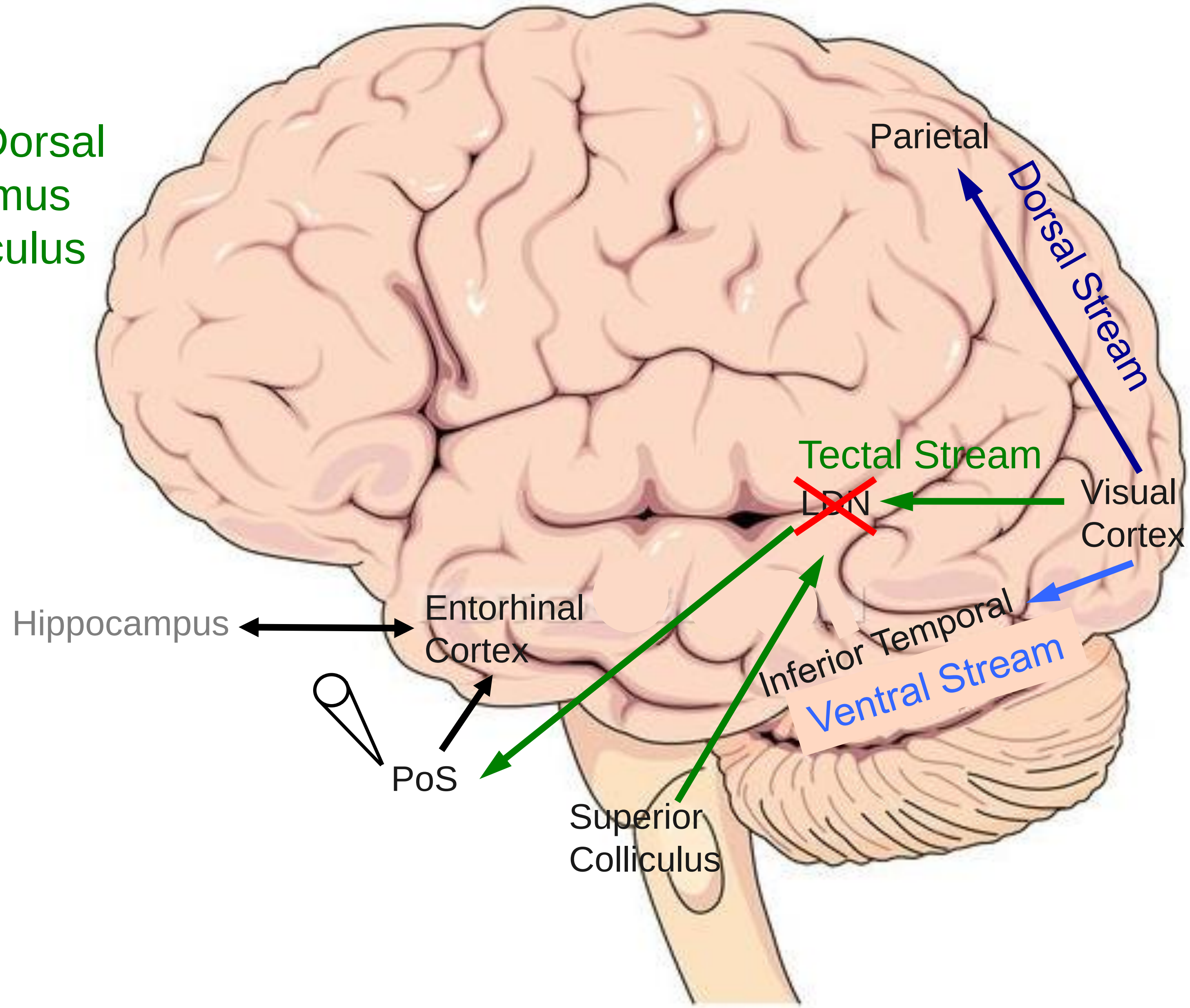
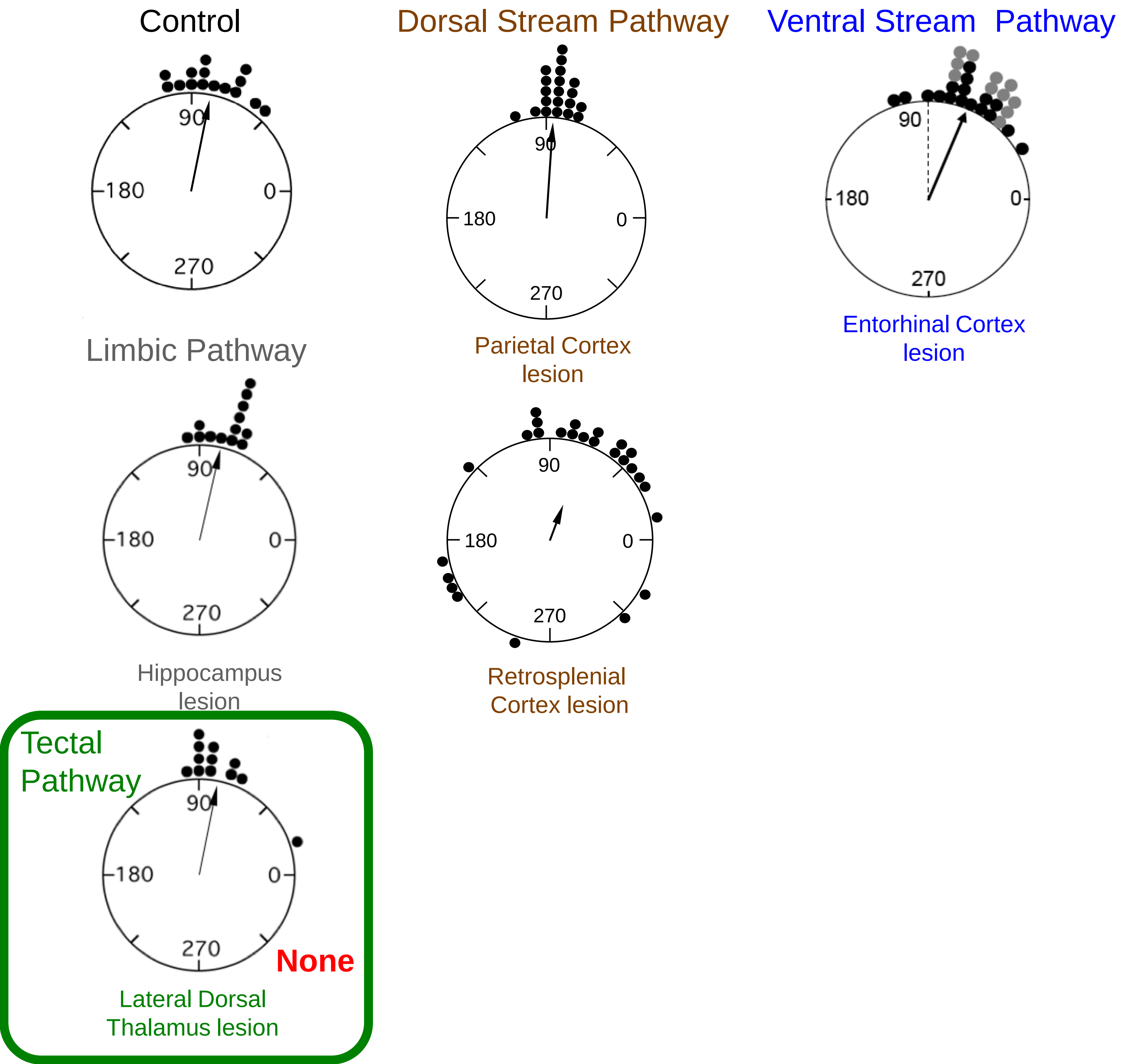
Pulvinar

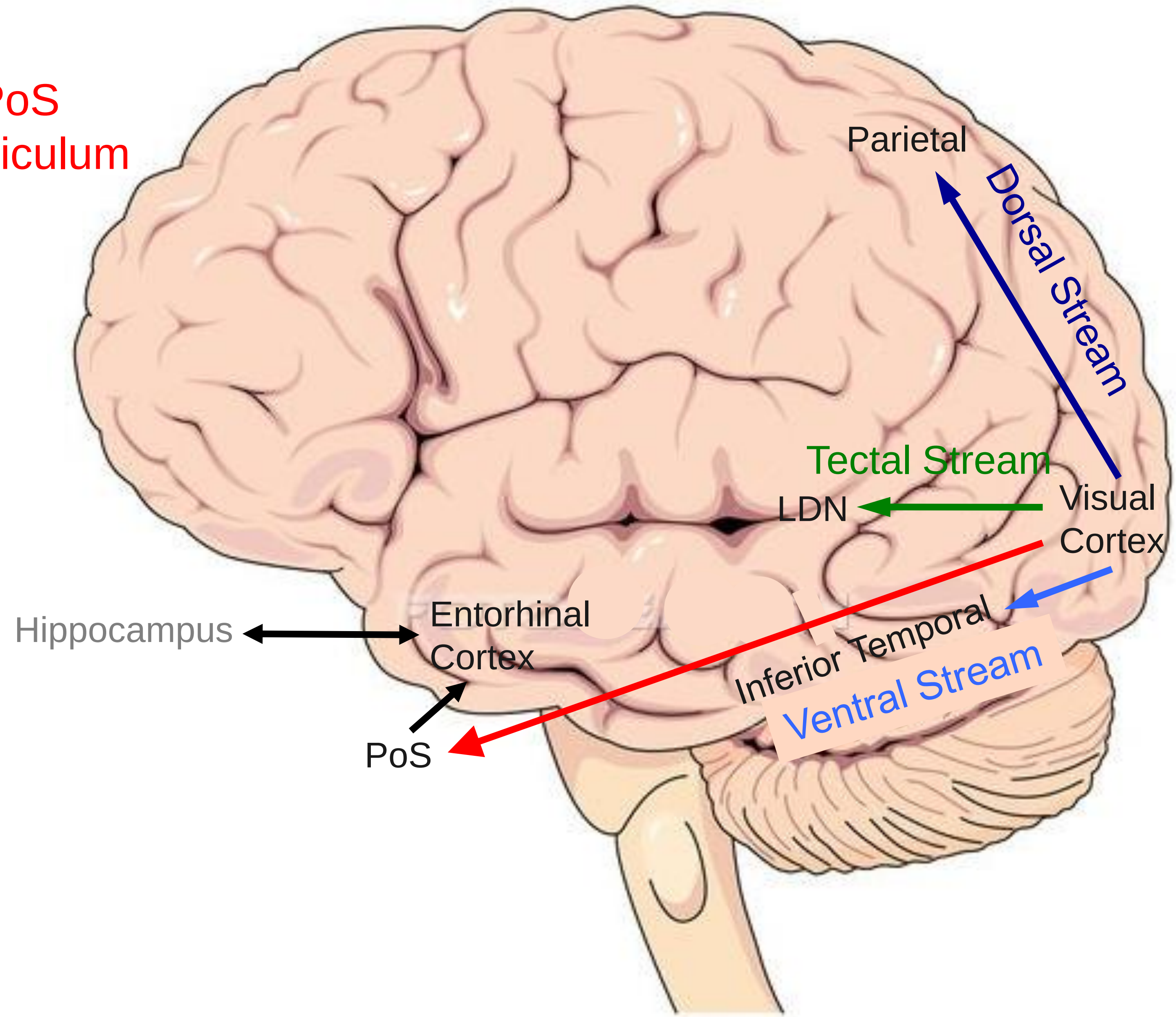



Control
90
180
0
270
Dorsal Stream Pathway
90
180
0
270
Parietal Cortex lesion
Ventral Stream Pathway
90
180
0
270
Entorhinal Cortex lesion
Limbic Pathway
90
180
0
270
Hippocampus lesion
90
180
0
270
Retrosplenial Cortex lesion
Tectal Pathway
90
180
0
270
None
Lateral Dorsal Thalamus lesion

Visual Streams for Processing Landmark Information:

Direct Projection:

Visual Cortex → PoS
Postsubiculum



Visual Streams for Processing Landmark Information:

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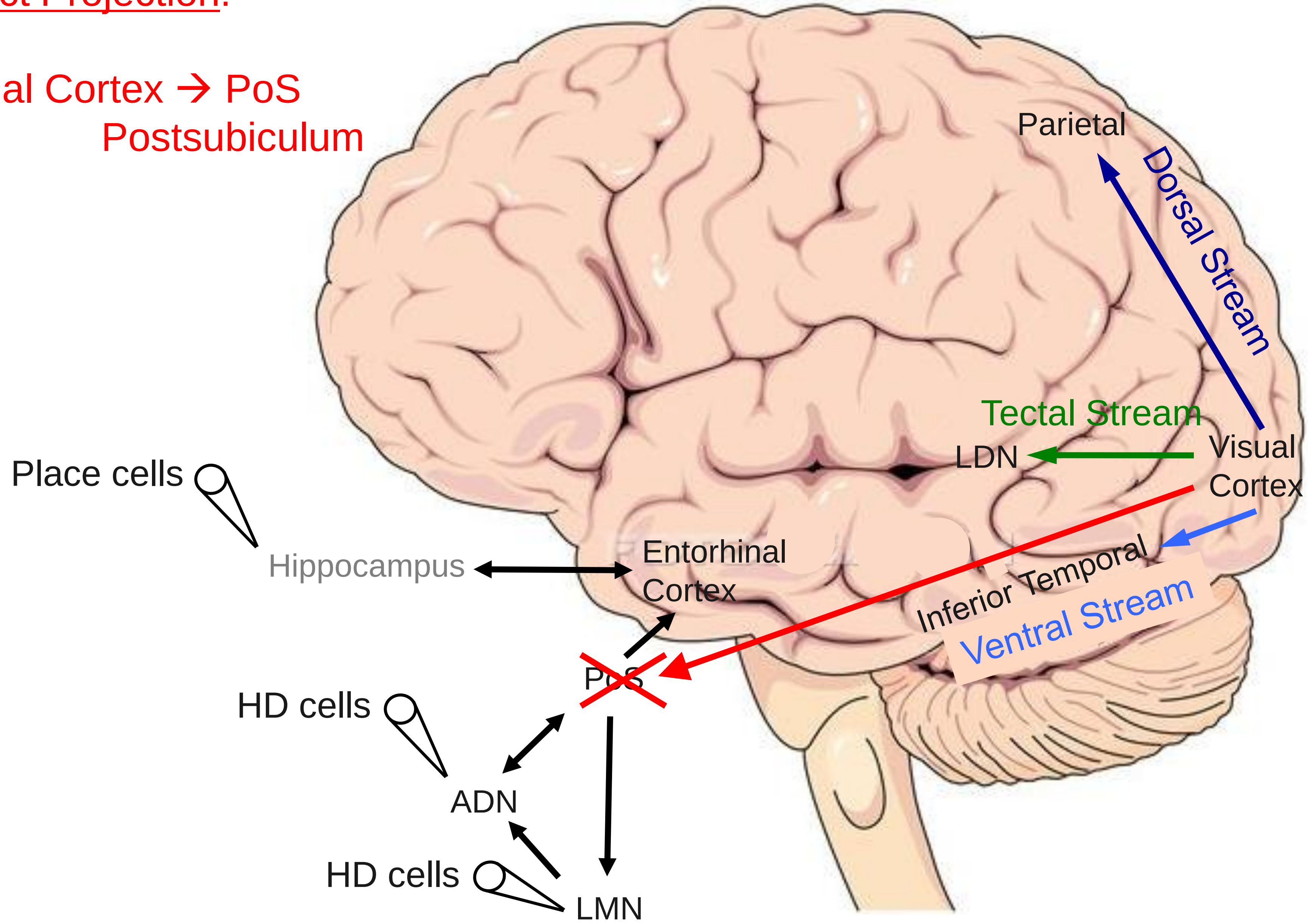
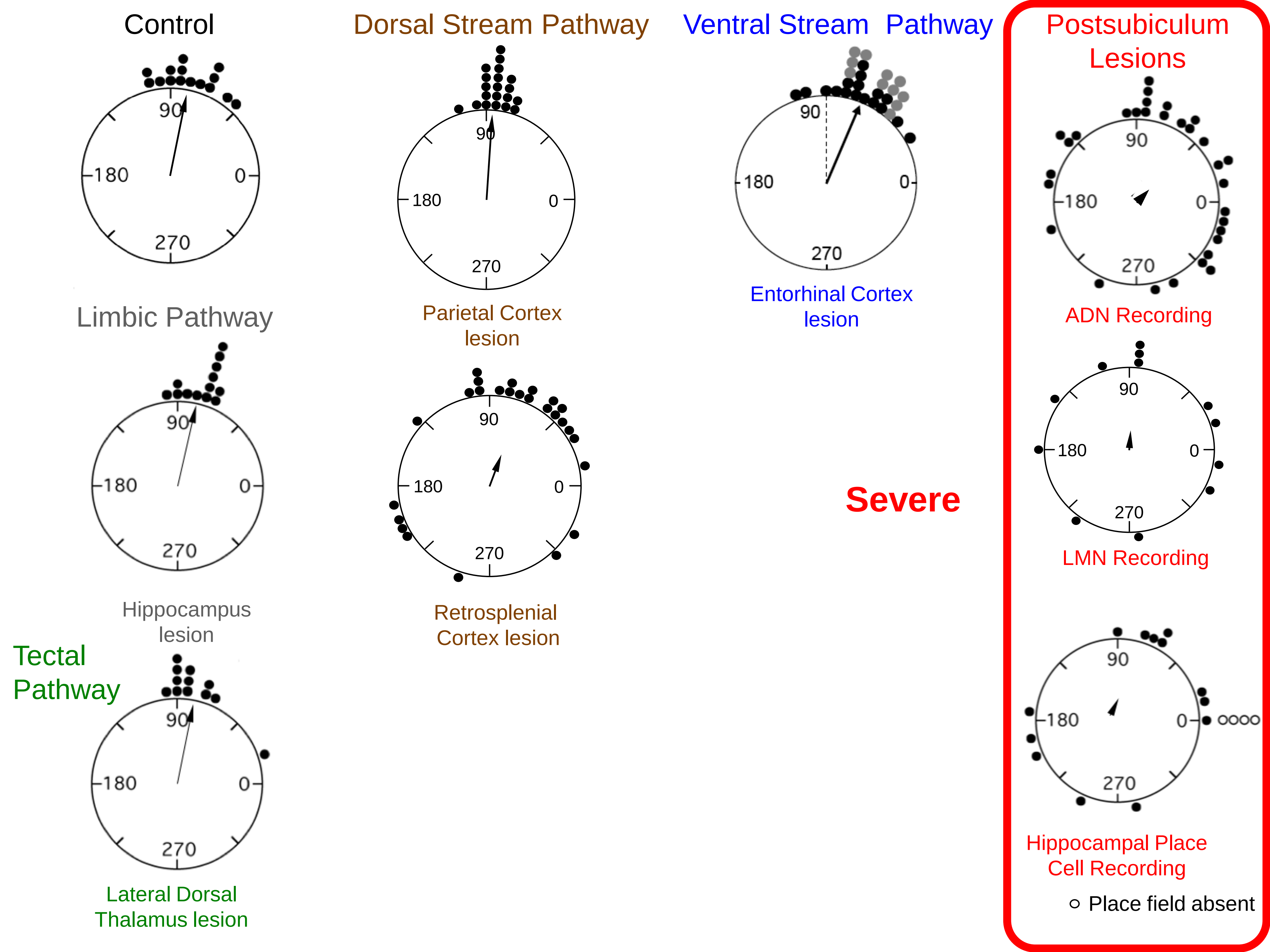
Visual Cortex → PoS
Postsubiculum



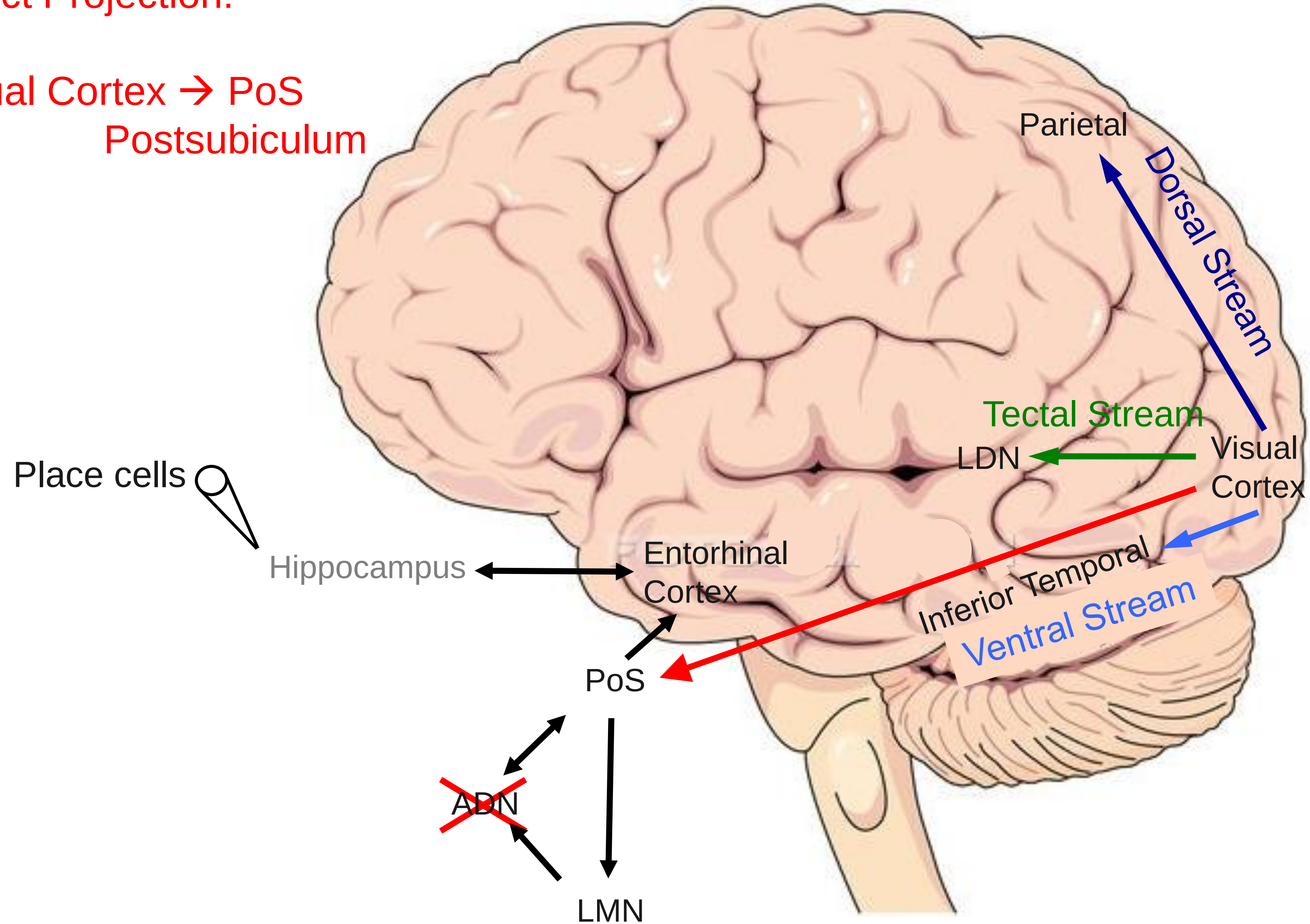


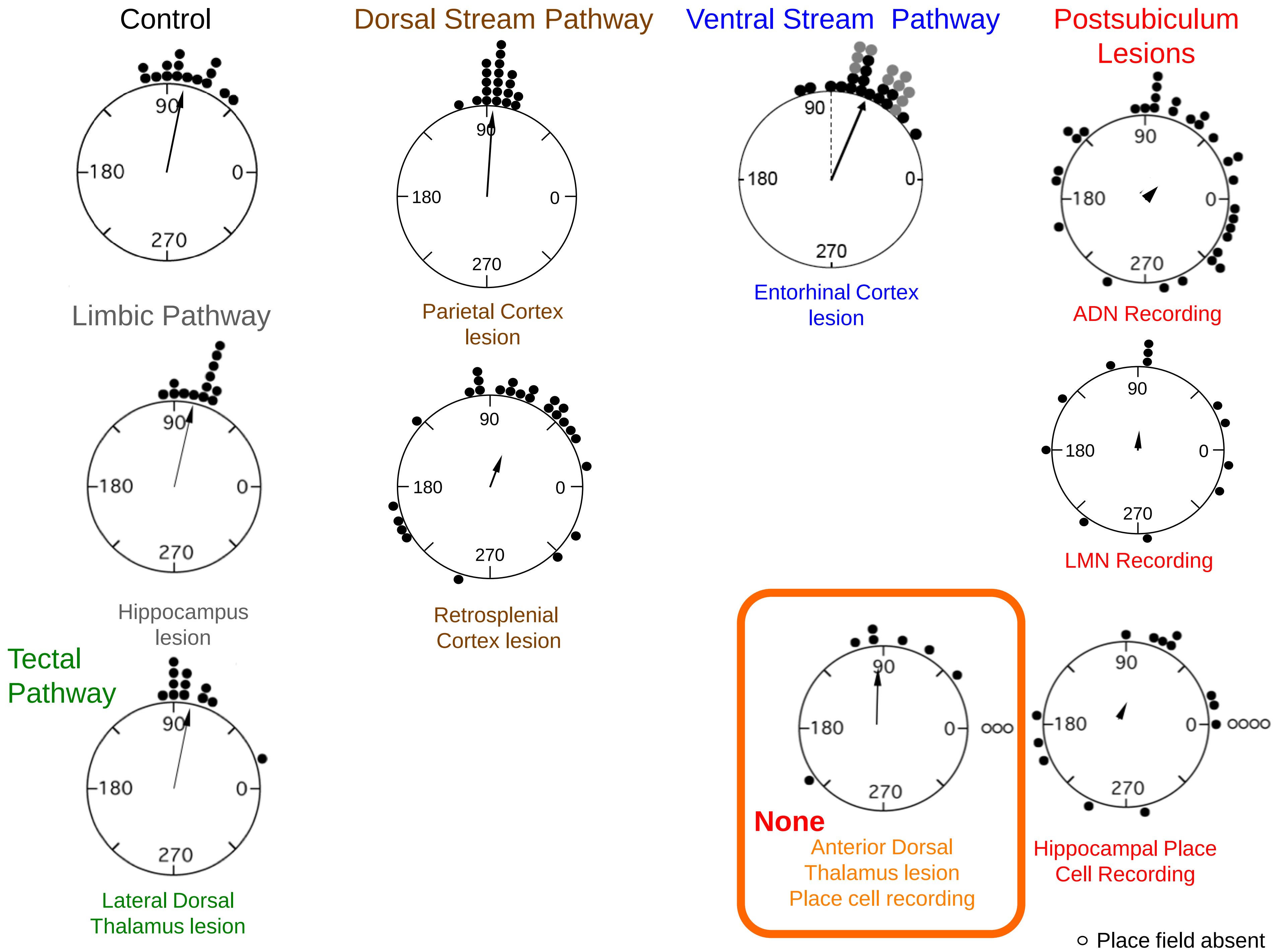
Control
90
180
0
270
Dorsal Stream Pathway
90
180
0
270
Parietal Cortex lesion
Ventral Stream Pathway
90
180
0
270
Entorhinal Cortex lesion
Postsubiculum Lesions
90
180
0
270
ADN Recording
Limbic Pathway
90
180
0
270
Hippocampus lesion
90
180
0
270
Retrosplenial Cortex lesion
Severe
90
180
0
270
LMN Recording
Tectal Pathway
90
180
0
270
Lateral Dorsal Thalamus lesion
90
180
0
270
Hippocampal Place Cell Recording
○ Place field absent

Visual Streams for Processing Landmark Information:

Direct Projection:

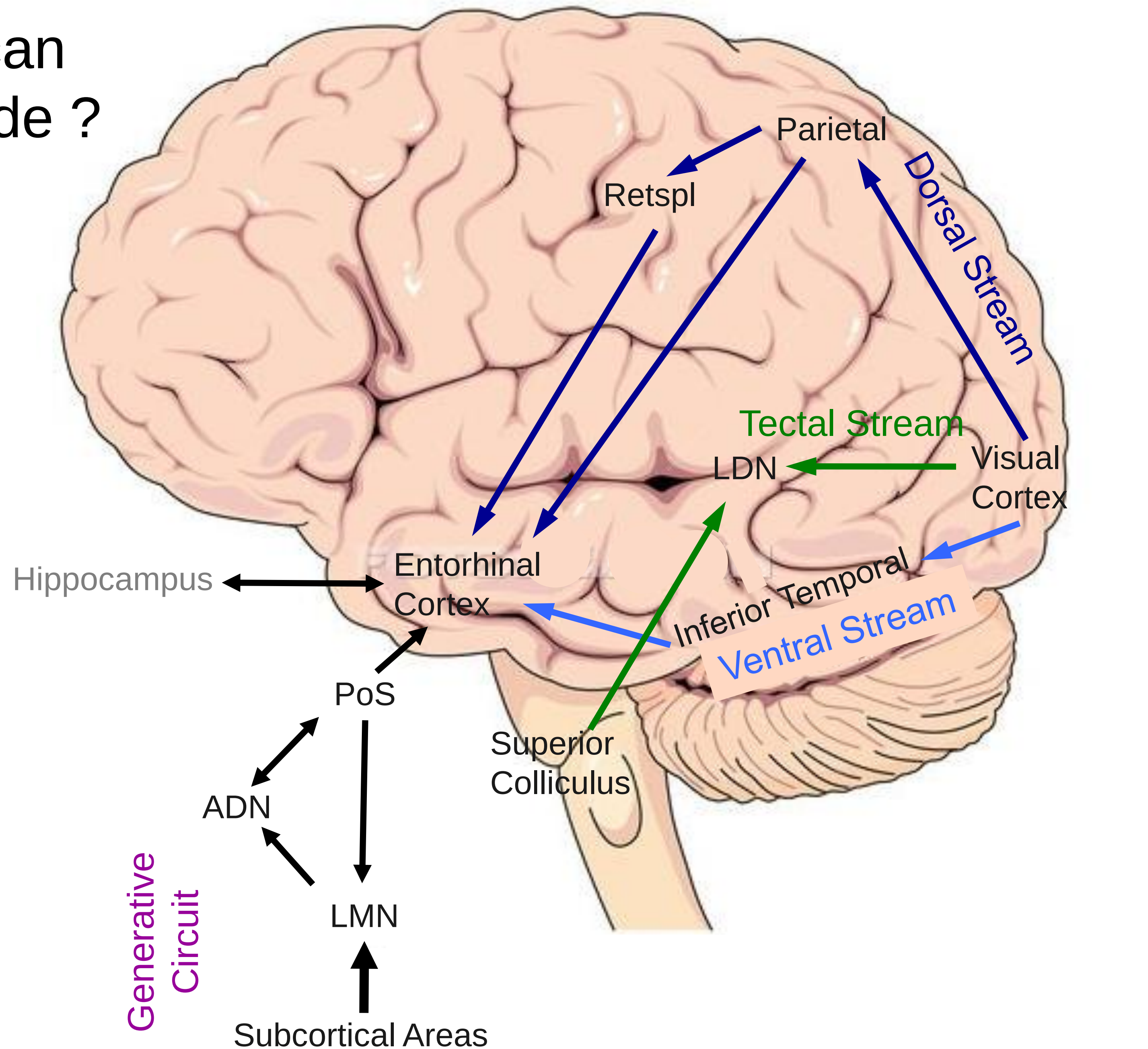
Visual Cortex → PoS
Postsubiculum





Control
Dorsal Stream Pathway
Ventral Stream Pathway
Postsubiculum Lesions
90
180
0
270
Parietal Cortex lesion
Entorhinal Cortex lesion
ADN Recording
Limbic Pathway
Hippocampus lesion
Retrosplenial Cortex lesion
LMN Recording
Tectal Pathway
Lateral Dorsal Thalamus lesion
None
Anterior Dorsal Thalamus lesion
Place cell recording
Hippocampal Place Cell Recording
○ Place field absent

So, what can we conclude ?



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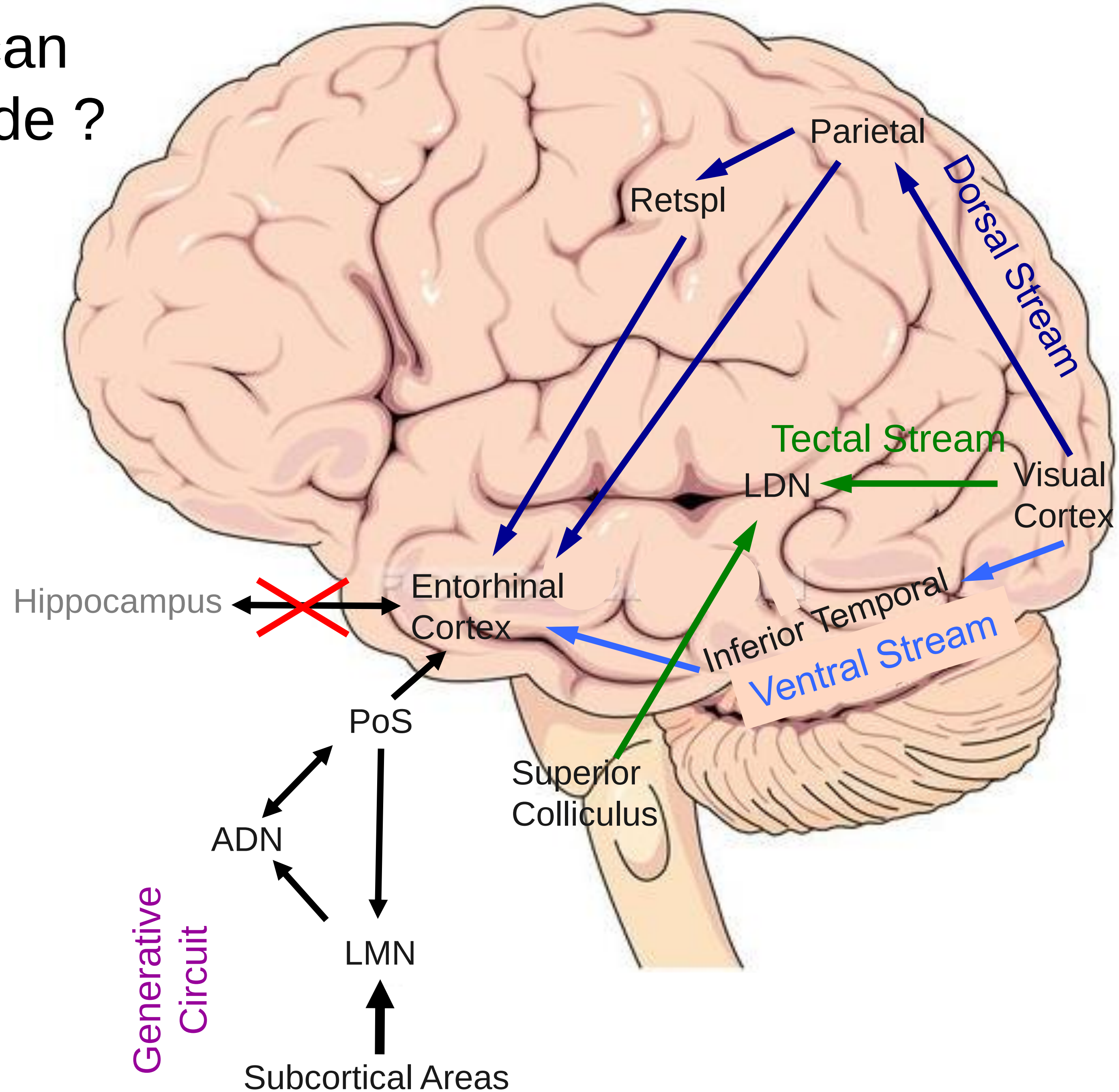

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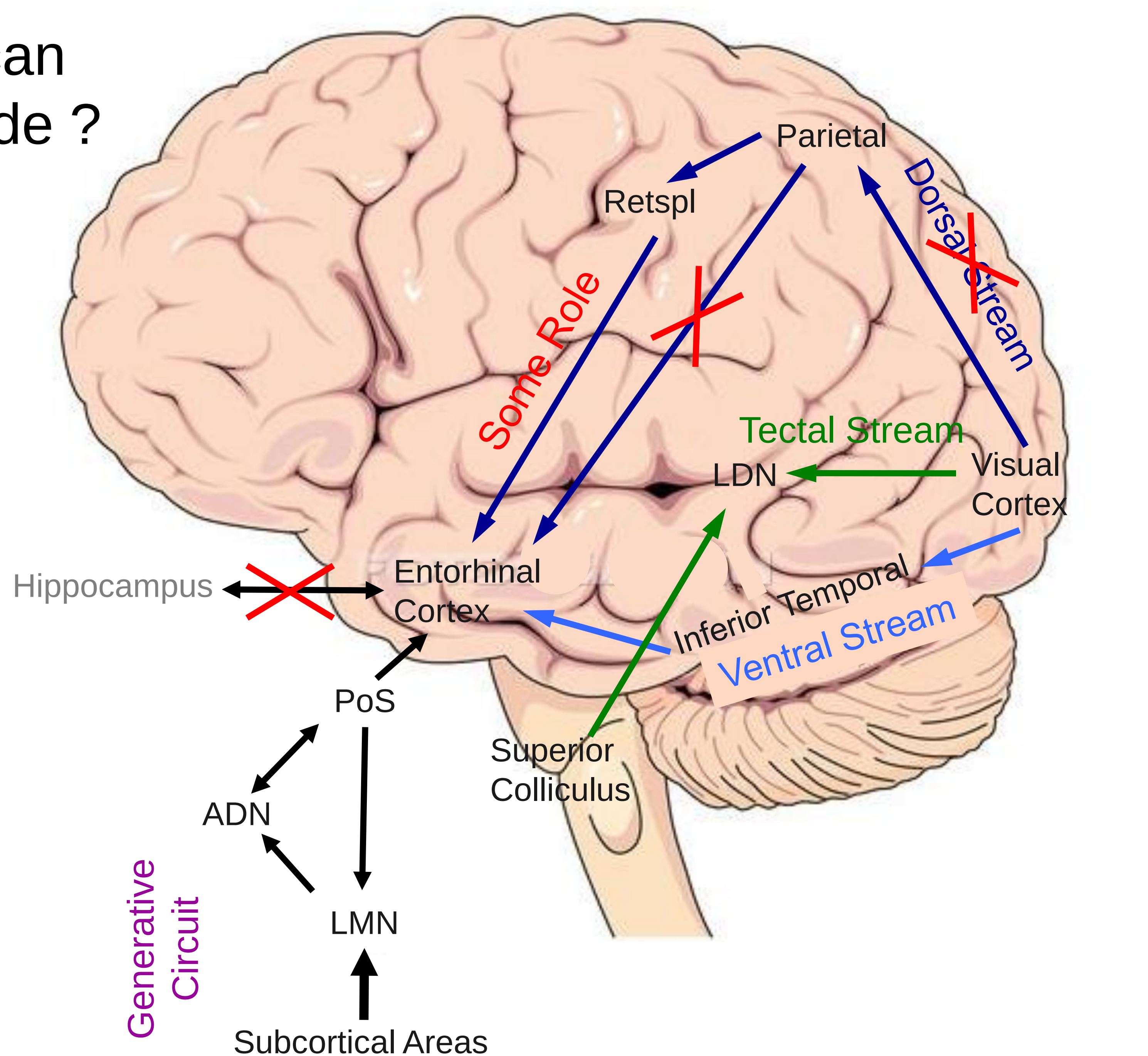

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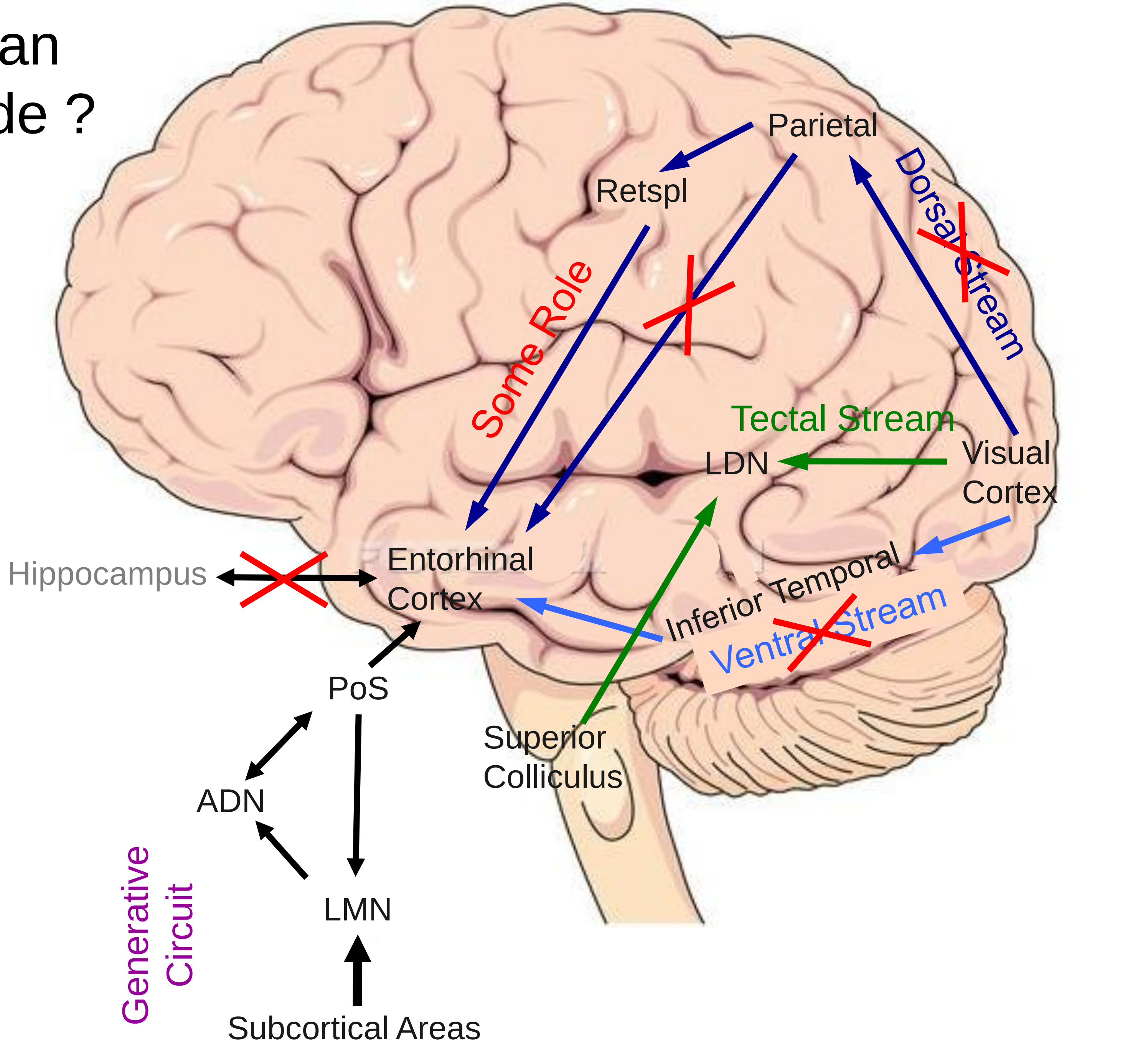
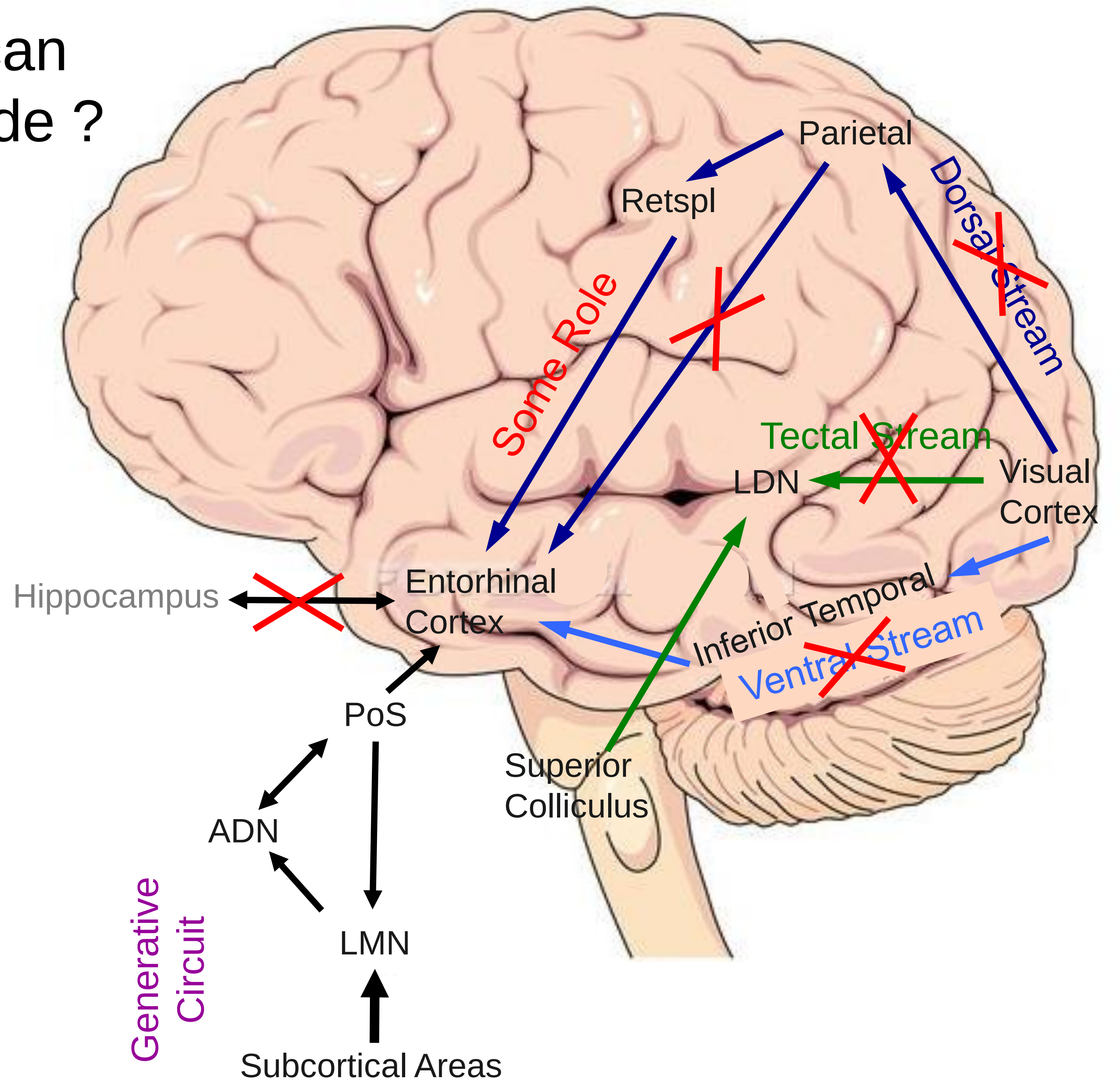
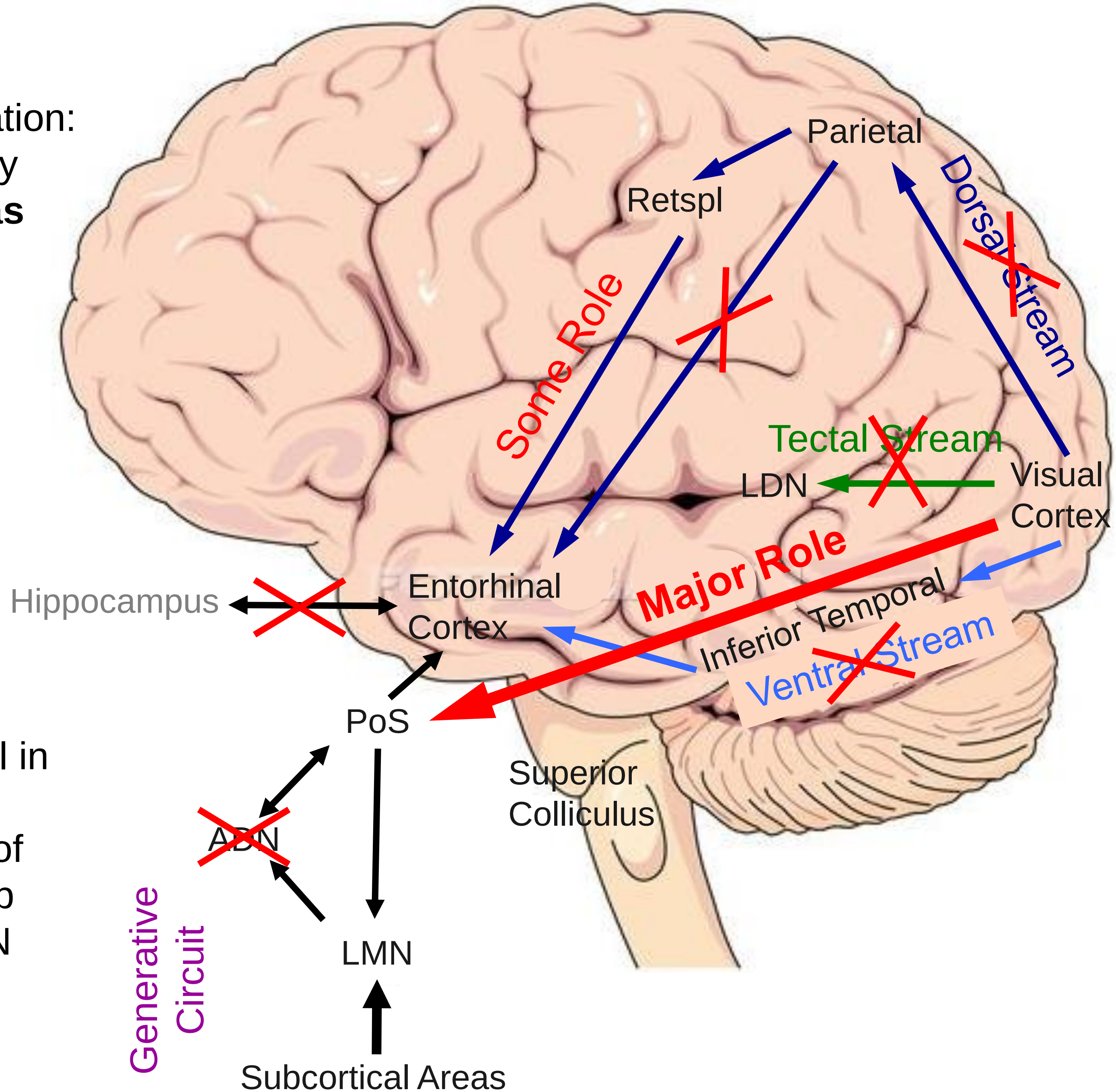


So, what can we conclude ?



<u>Conclusion</u>: For processing visual landmark information: the direct pathway from **Visual Areas 17, 18 --> PoS** is critical.



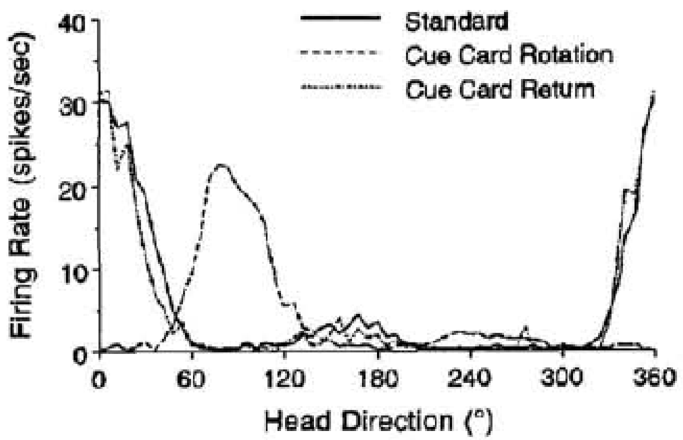
Landmark control in ADN and LMN occurs because of the feedback loop from PoS → LMN and ADN.

How fast can Head Direction cells learn about the visual landmarks ?

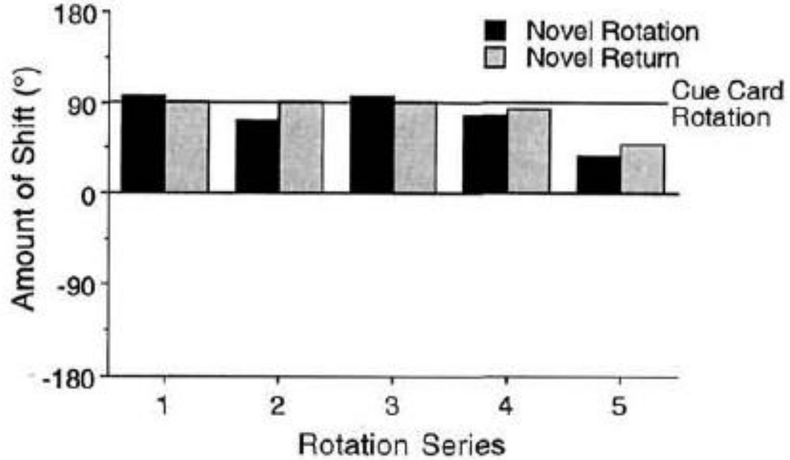
Rats can learn landmark information very fast

Here they learned about the visual cue card in a matter of minutes.

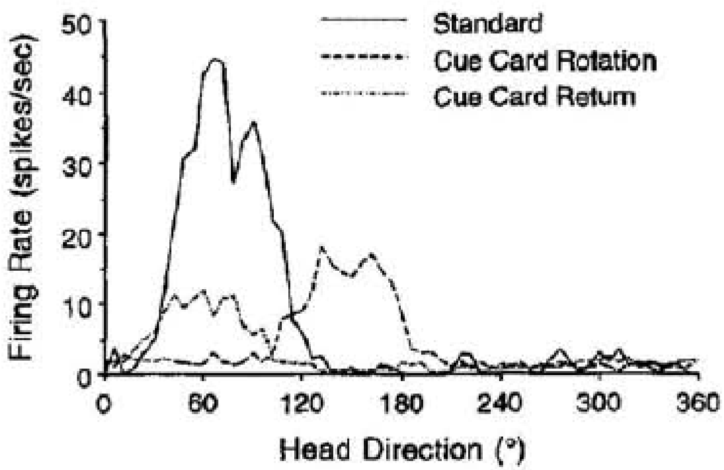
8 min Exposure



8 min Exposure

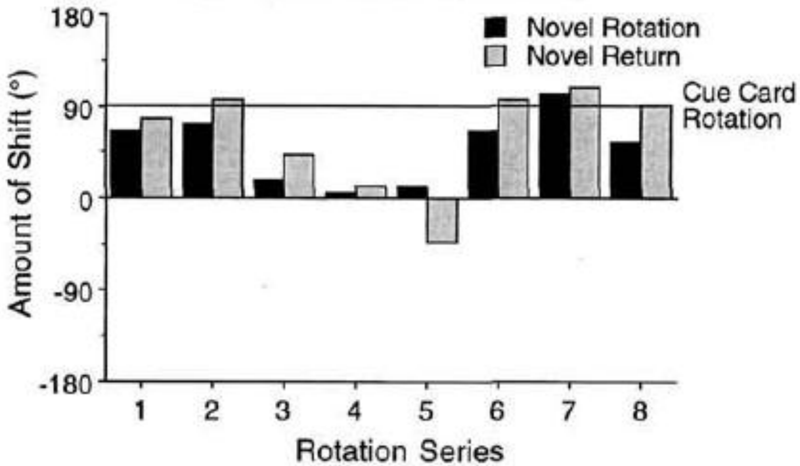


1 min Exposure



1 min Exposure

5 out of 8 rotated well



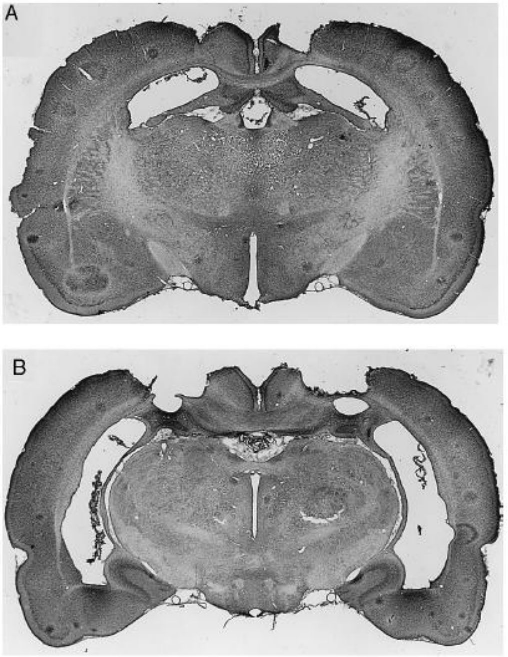
Goodridge et al. (1998) Beh Neurosci

Is the hippocampus important for HD cells to learn about novel visual landmarks?

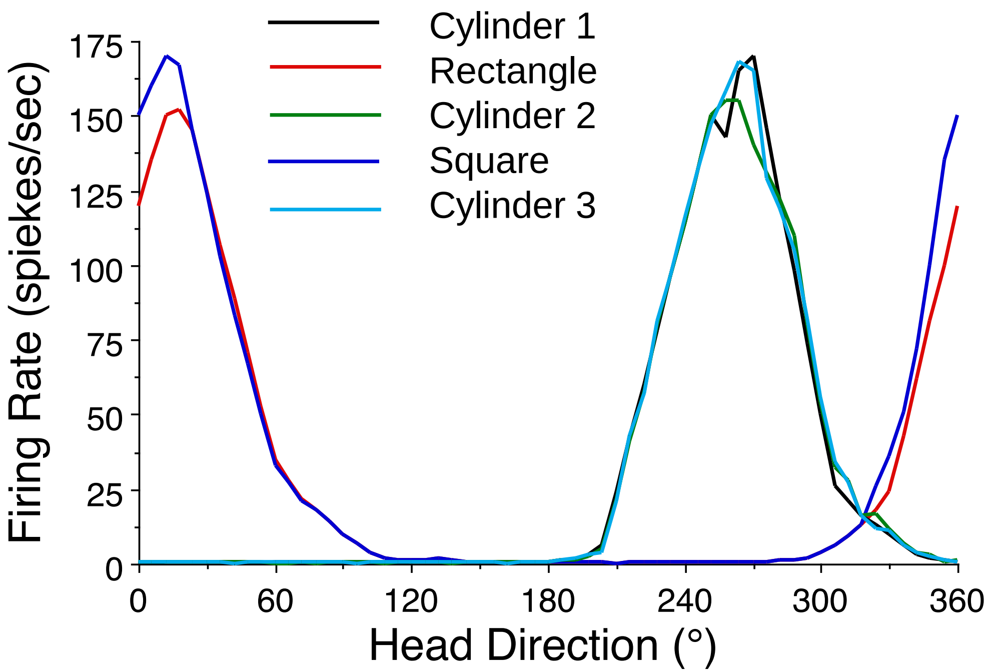
- We can take advantage of the fact that HD cells have different preferred directions in geometrically different environments.

- Thus, a change in the shape of the environment will usually lead to a shift in the cell's preferred firing direction

Hippocampal lesion

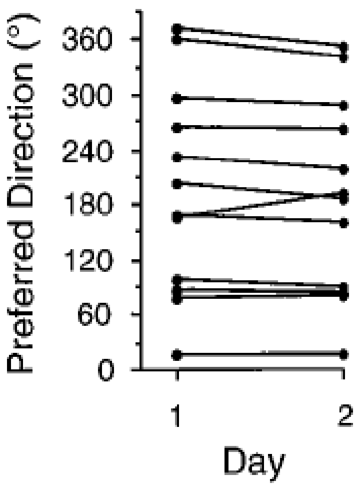


Cylinder vs. Rectangle & Square

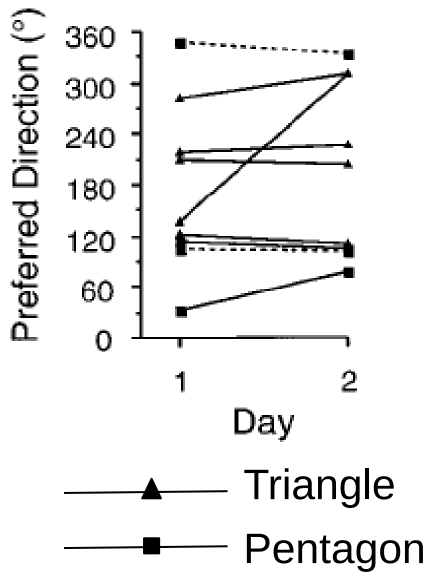


HD Cell preferred directions remain stable in a novel environment across days, despite the absence of hippocampus

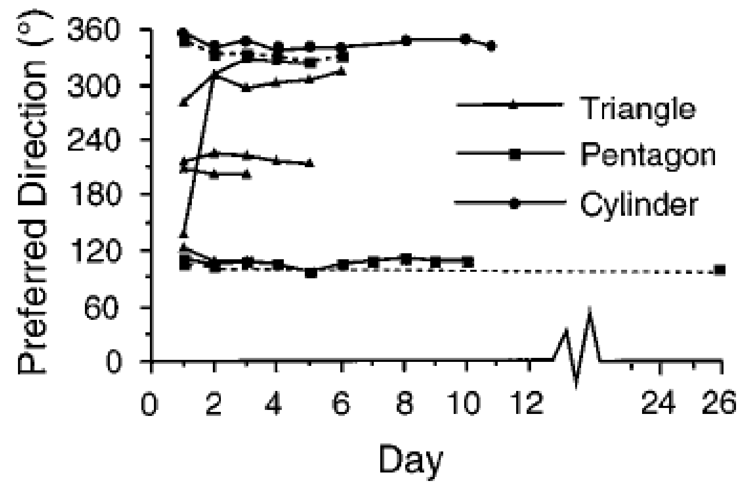
Cylinder – Familiar



Novel Enclosures



Novel Enclosures across days



Suggests that learning the spatial information about landmarks is more like **perceptual learning**, where visual information can drive the system directly – it is not like episodic learning, which involves the hippocampus.

Golob & Taube (1997) PNAS

What is the evidence that HD cells can guide behavior ?

Linkage between HD cell firing and behavior

•What you would like to see is that when a cell’s preferred firing direction shifts a certain amount, that the animal’s spatial behavior (choice) also shifts the same amount.

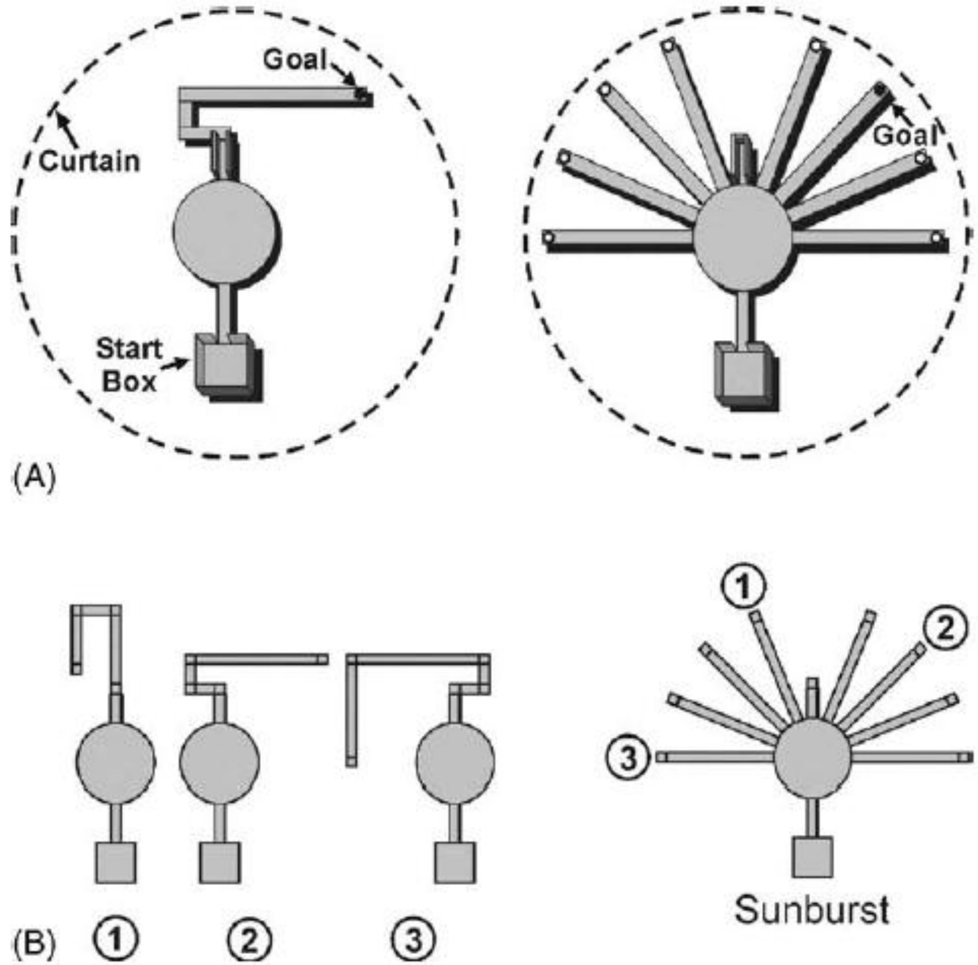
•Review a few studies with HD cells where we looked for this linkage.

•What happens with HD cells following a behavioral error?
Does the HD also show a shift in its PFD?

Example 1: HD Cell information is <u>not</u> always used for solving Spatial Tasks : Tolman Sunburst Maze

Training Trials

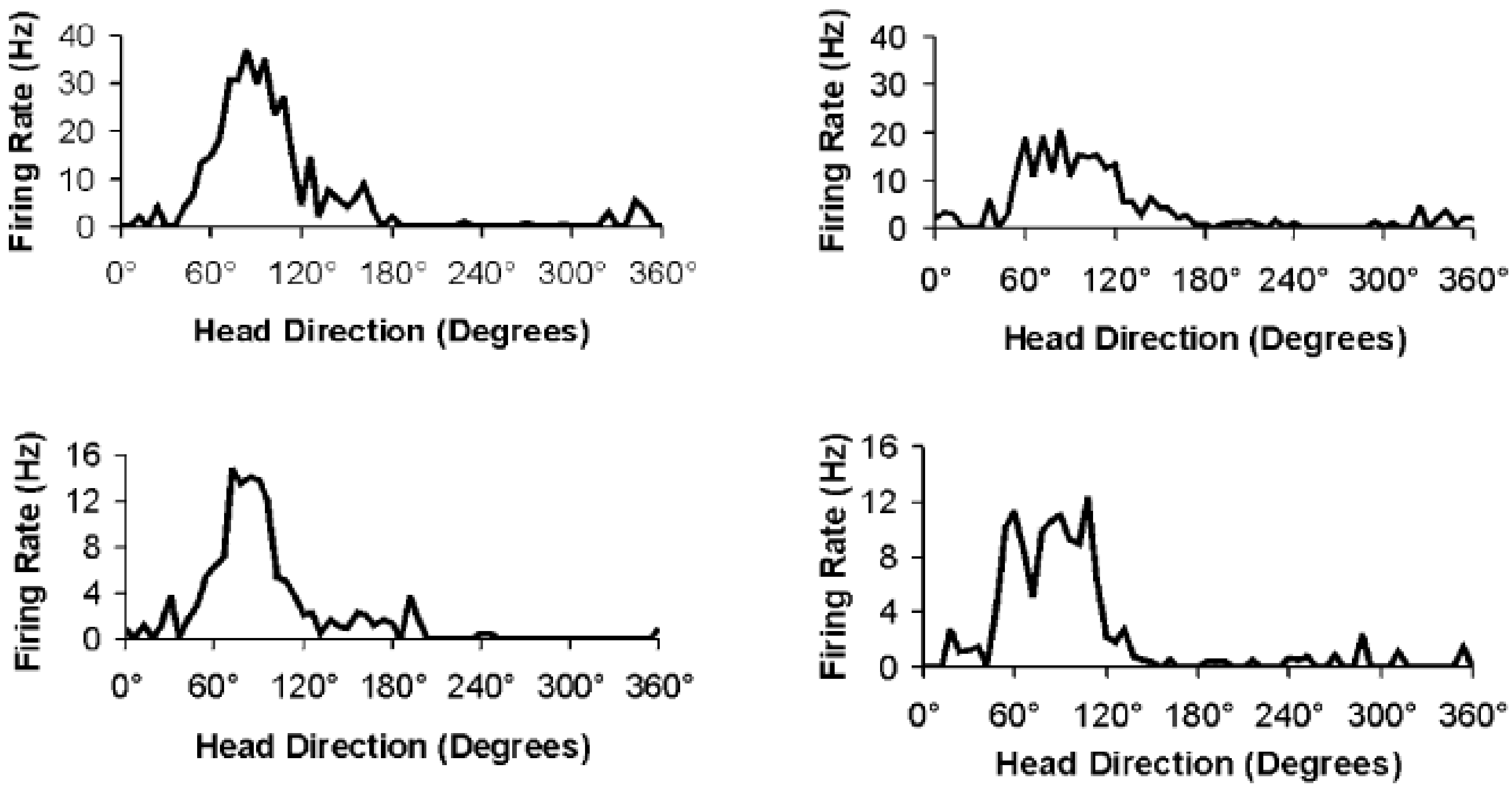
Test Trial



Muir & Taube (2004) Beh Brain Res

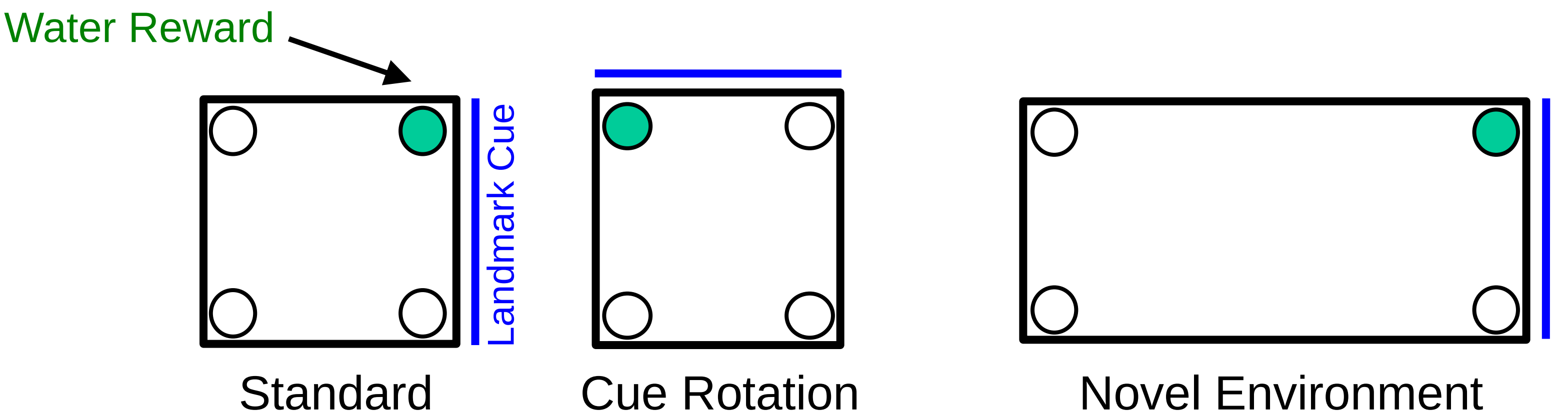
HD Cell Plots on Error Trials for 2 Different Cells

Training Trials | Test Trials in which rat made an error



……. thus, directional heading information was present,
but the animal did **not** use it to guide behavior.
This could explain why they had poor performance – no learning took place.

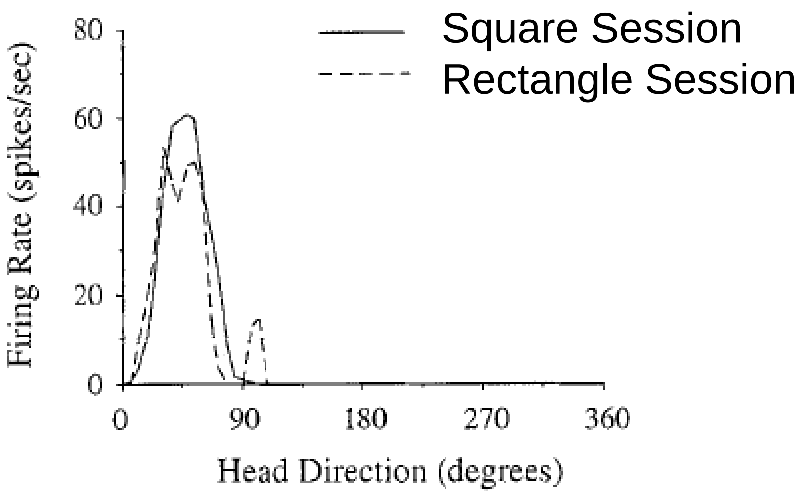
Example 2: Animal solves a spatial task, but is <u>not</u> using HD cell information to guide its behavior



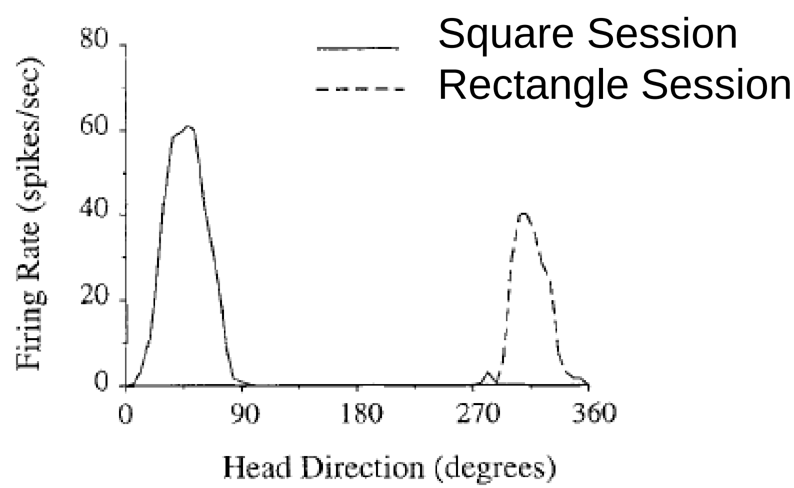
- Rat trained in square to go to a corner with water reward relative to landmark.
- Receives 40-60 trials in standard session and performing ~ 77% correct.
- Rotation of landmark leads to an equal shift in the animal's behavior and the HD cell's preferred firing direction.
- Rat generalizes well in the rectangle – and goes to the correct corner – 78% correct.
- But HD cells shifted their preferred directions > 72° in 12 / 13 sessions (<u>but their behavior did not shift the same amount</u>) → little evidence that HD cell firing was guiding the animal's behavior.

→ Behavior was <u>**not**</u> in register with the shift in the cell's preferred direction.

- Recordings from same cell on two consecutive trials in the rectangle.
- In both cases, rat generalized well from training in the square and selected the correct corner in the rectangle.
- Cell's preferred direction was <u>different</u> on both trials – but behavior was <u>similar</u>.
- Suggests that this cell's firing was not strongly linked to the animal's behavior.



HD cell preferred direction remains the same



HD cell preferred direction shifts

Golob et al (2001) Beh Neurosci

Head Direction cells and responses in 3D

Array of Disorientation Problems & Illusions in Space

Astronauts are frequently disoriented when working in space (0-g) and often experience several types of illusions, including:

- Visual Reorientation Illusion (VRIs)
- Inversion Illusion
- Extra Vehicular Activity (EVA) acrophobia

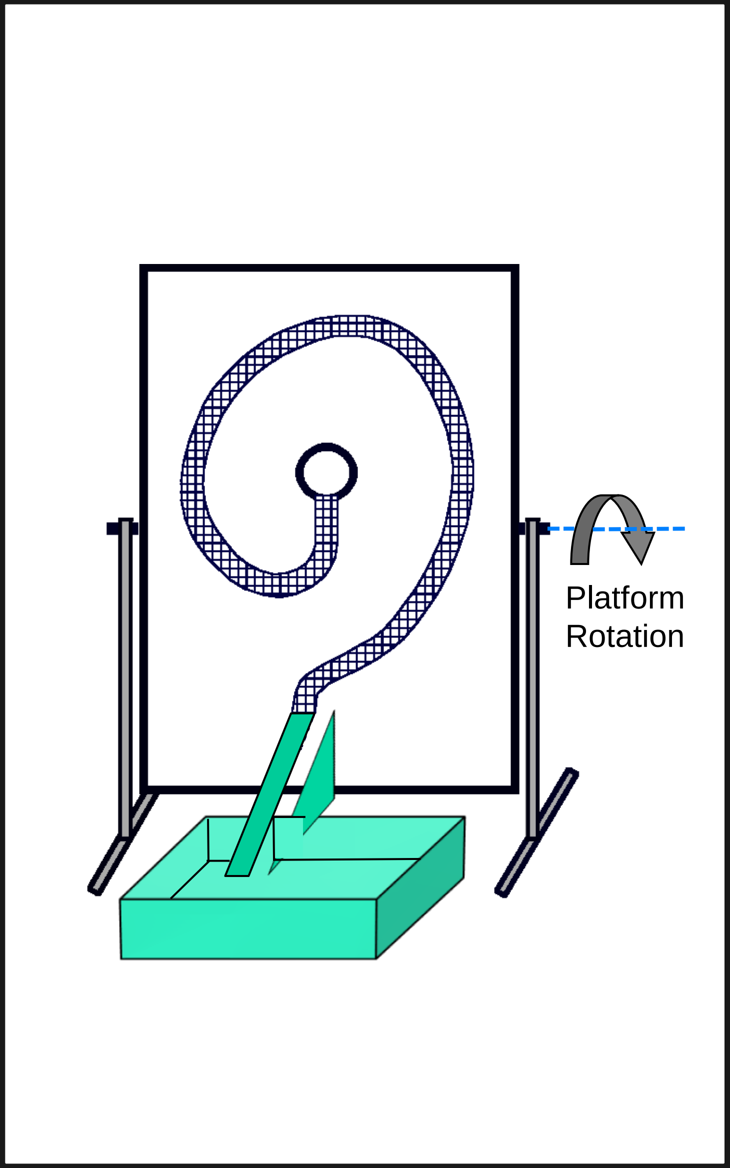
Which leads to a number of problems:

- Space motion sickness
- Poor spatial awareness – worry about emergency egress
- Inability to do work
- Flipping switches in wrong direction
- Otolith reinterpretation upon return to a gravitational environment

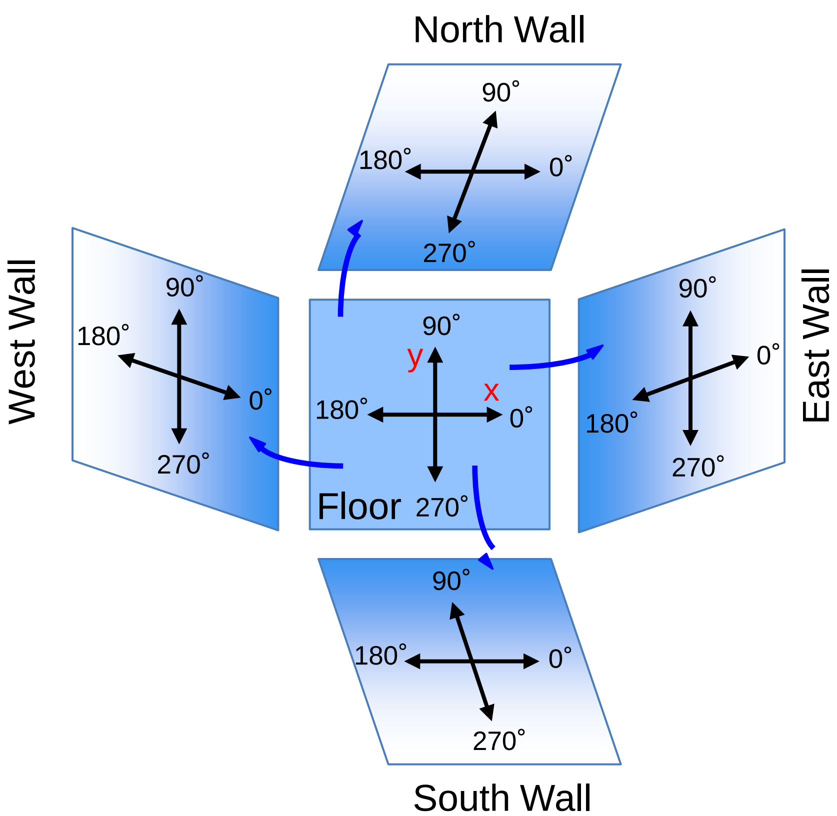
HD cell responses in Vertical Plane

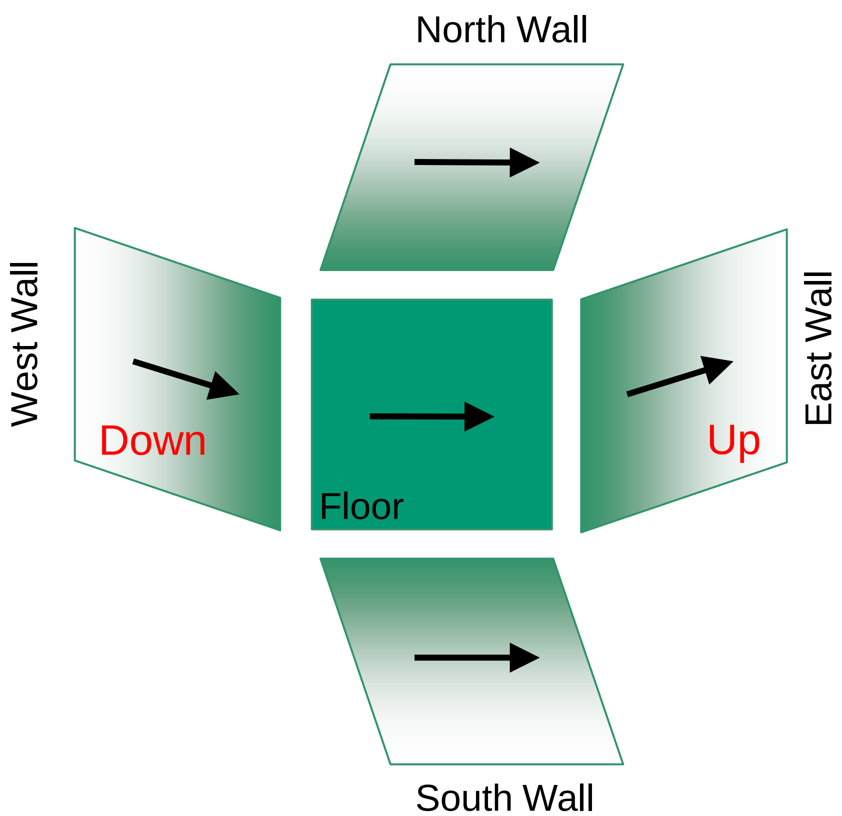
Experiment 1

Experiment 2



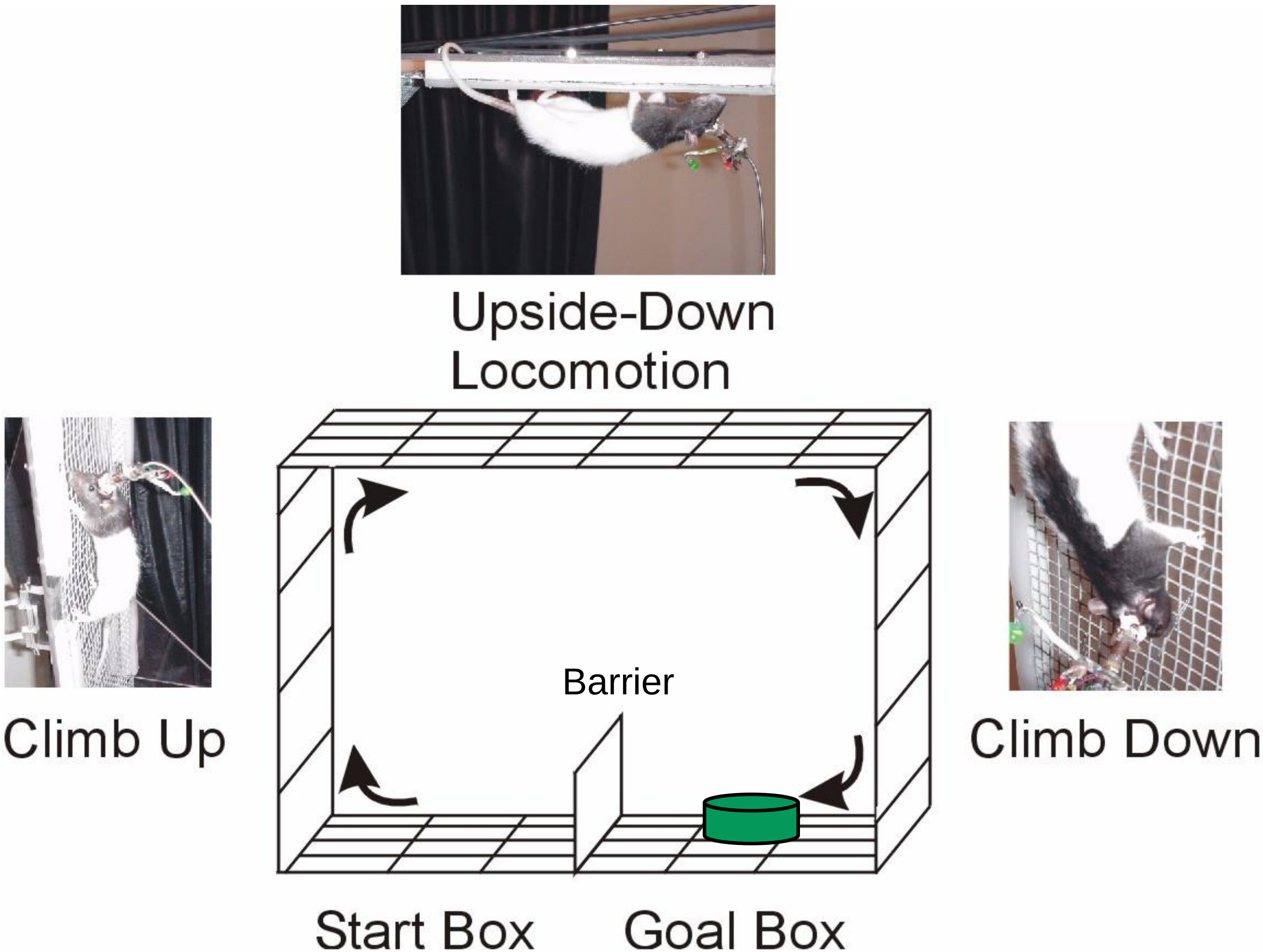
Animal defines its horizontal reference frame as the plane it happens to be locomoting in. Thus, it rotates its plane of locomotion by 90° as it moves into the vertical plane and defines this new surface as its horizontal reference frame.





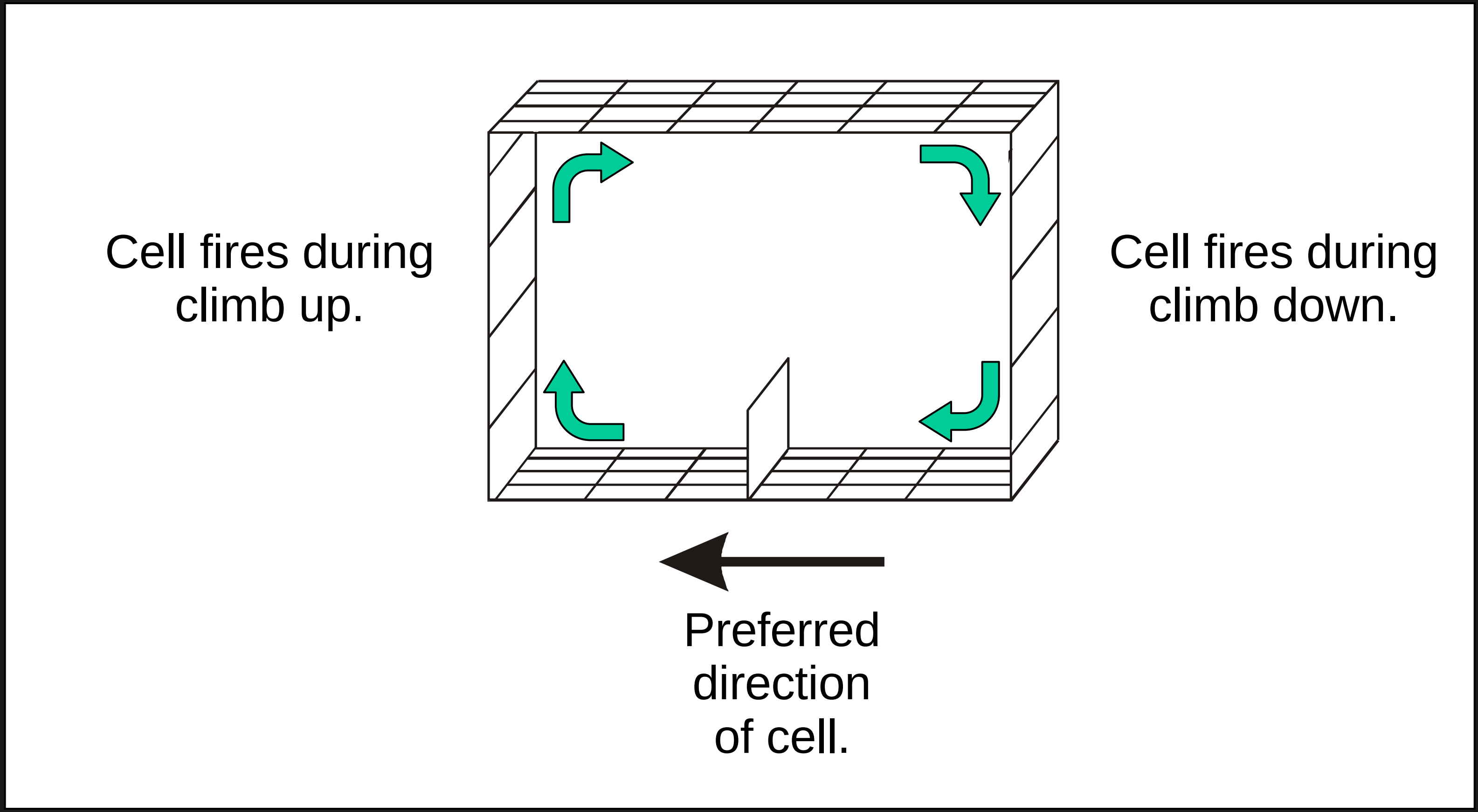
Direction of Cell Firing Along Walls

HD cell responses in 3D: Vertical plane and when Upside-down on ceiling

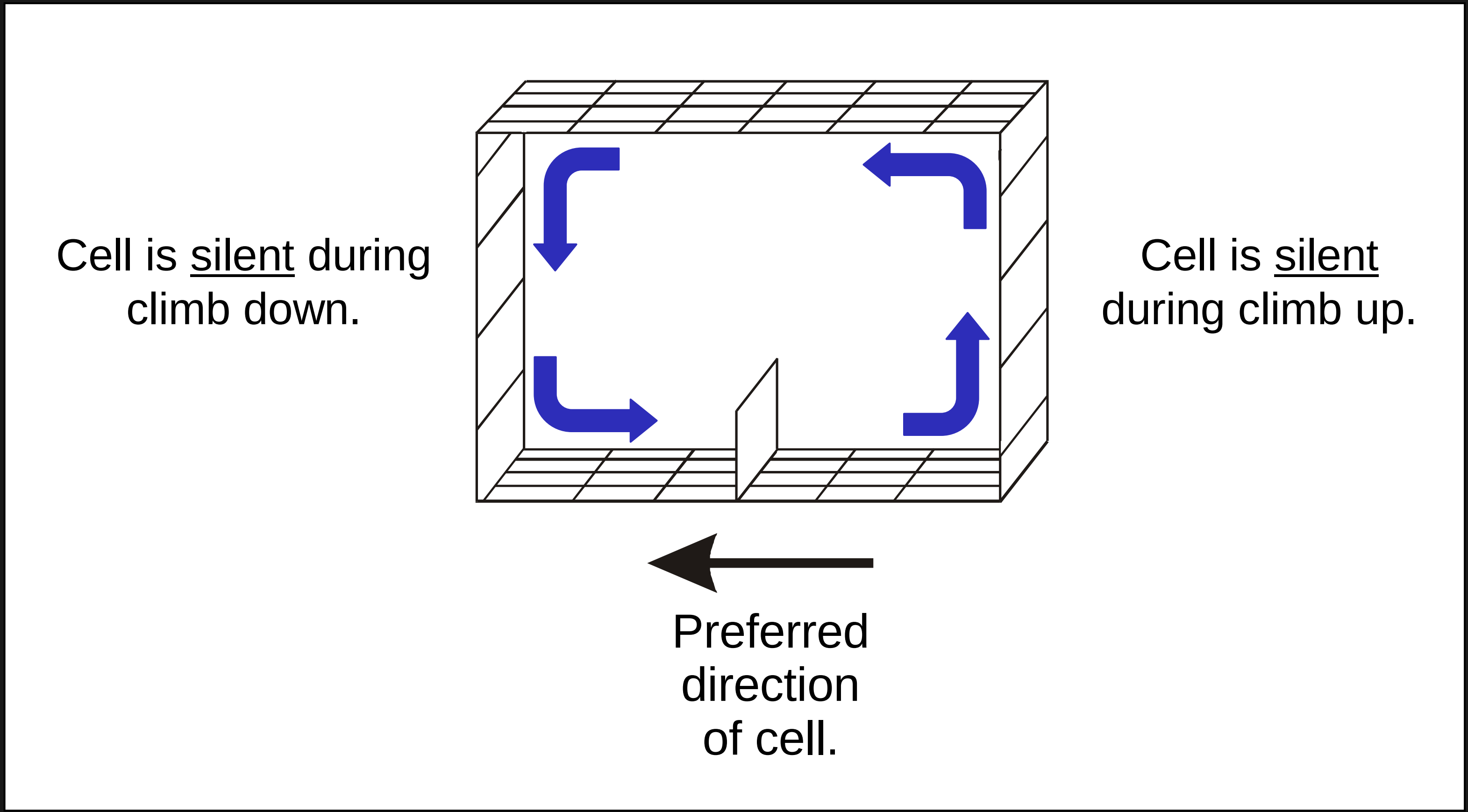


Calton & Taube (2005) J Neurosci

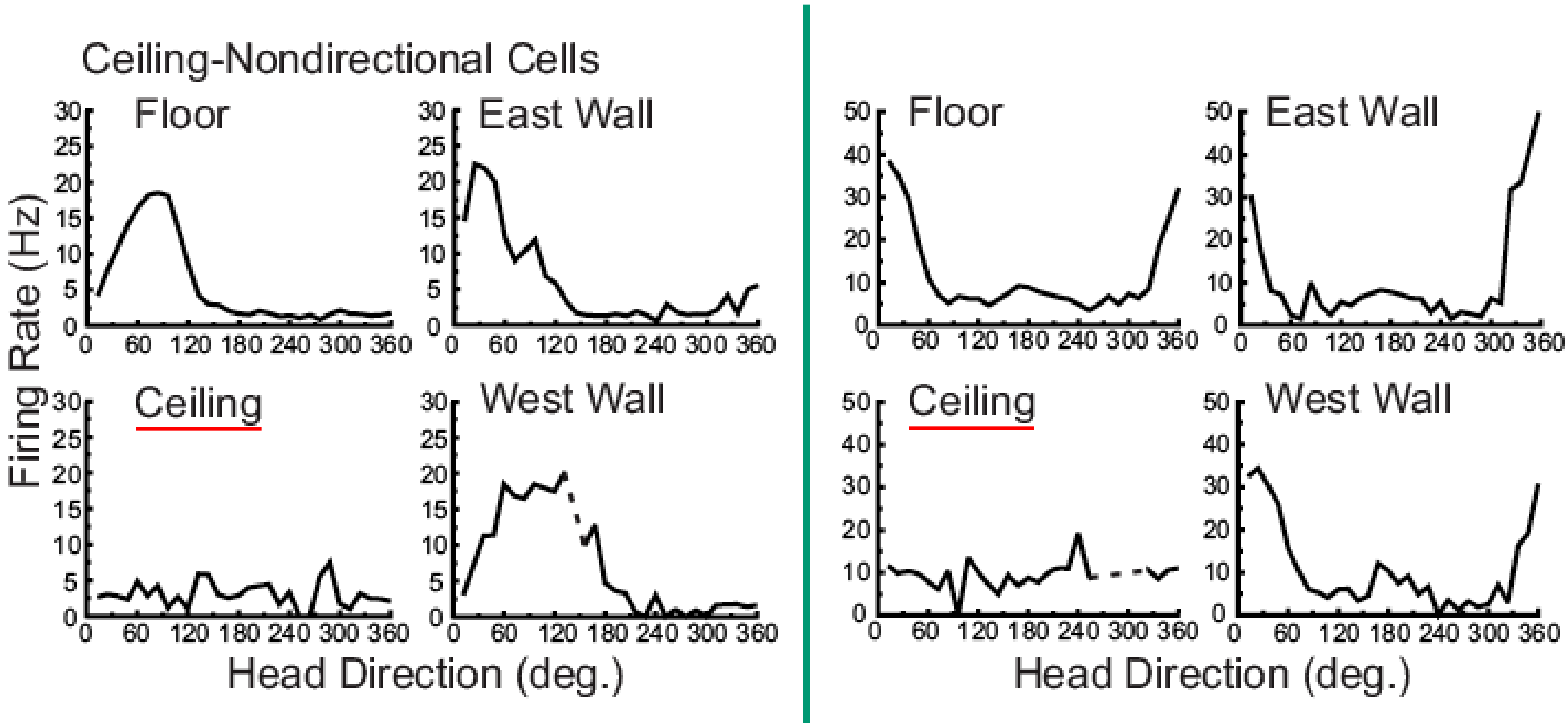
Similar to our wall-climbing findings, HD cells treated the walls as though they were an extension of the floor.



Running in the reverse direction, the cell is silent on both walls.



For most cells: Loss of directional tuning on ceiling, with increased background firing rate

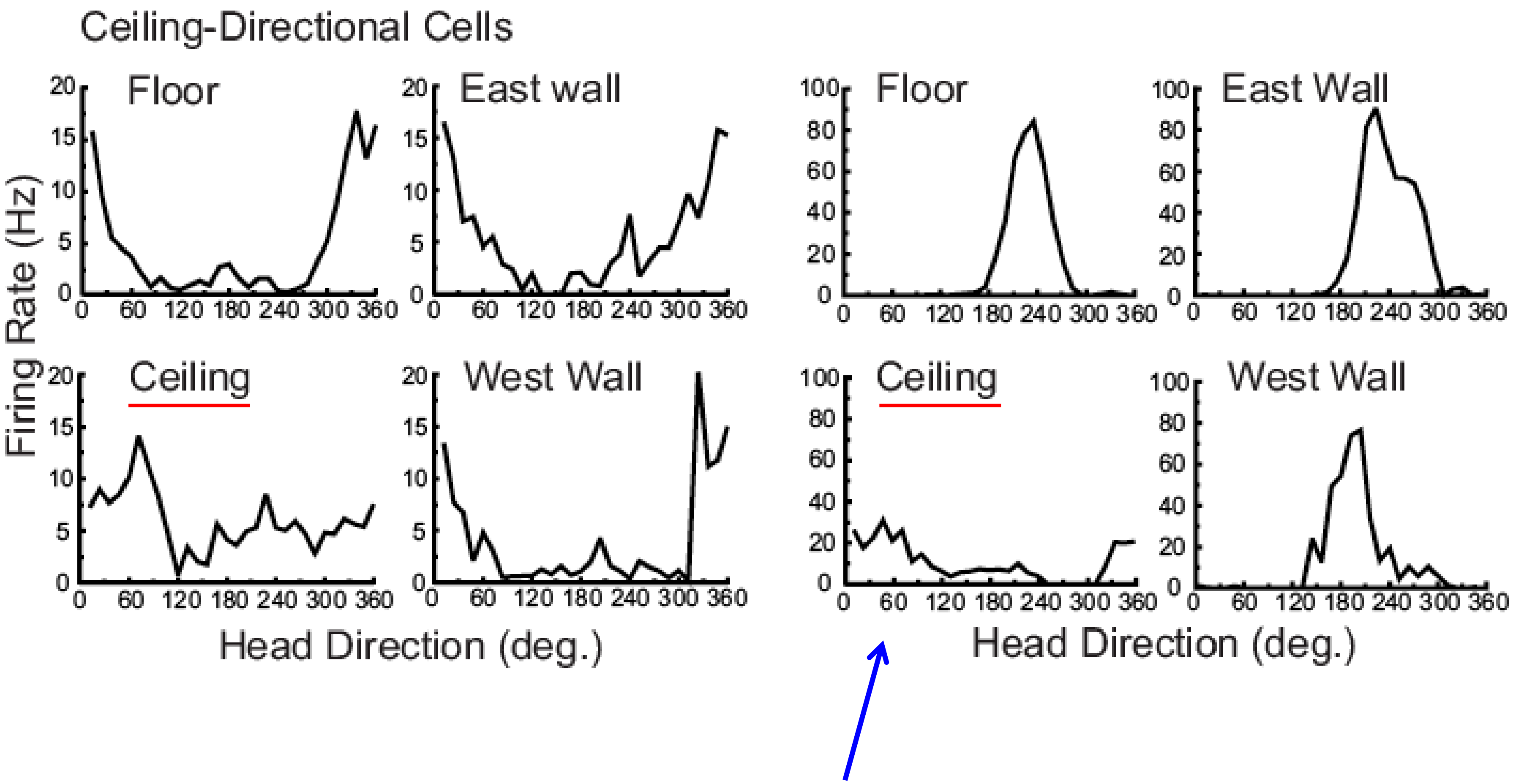


Cell 1

Cell 2

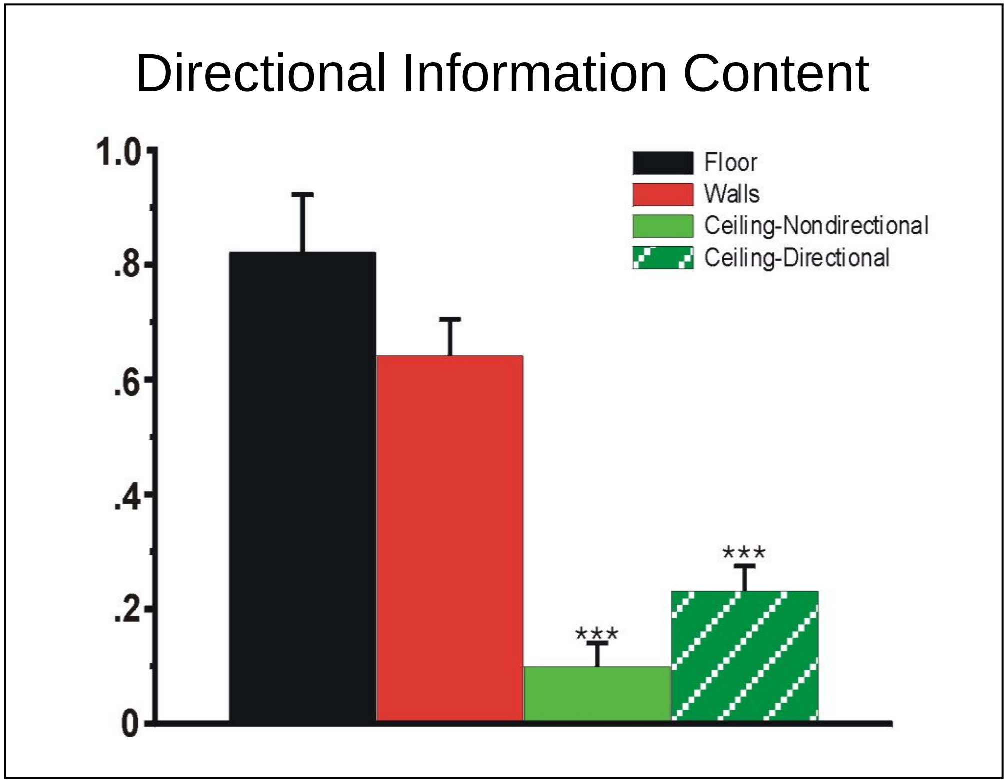
A few Cells Remained Directionally-tuned

Two examples:



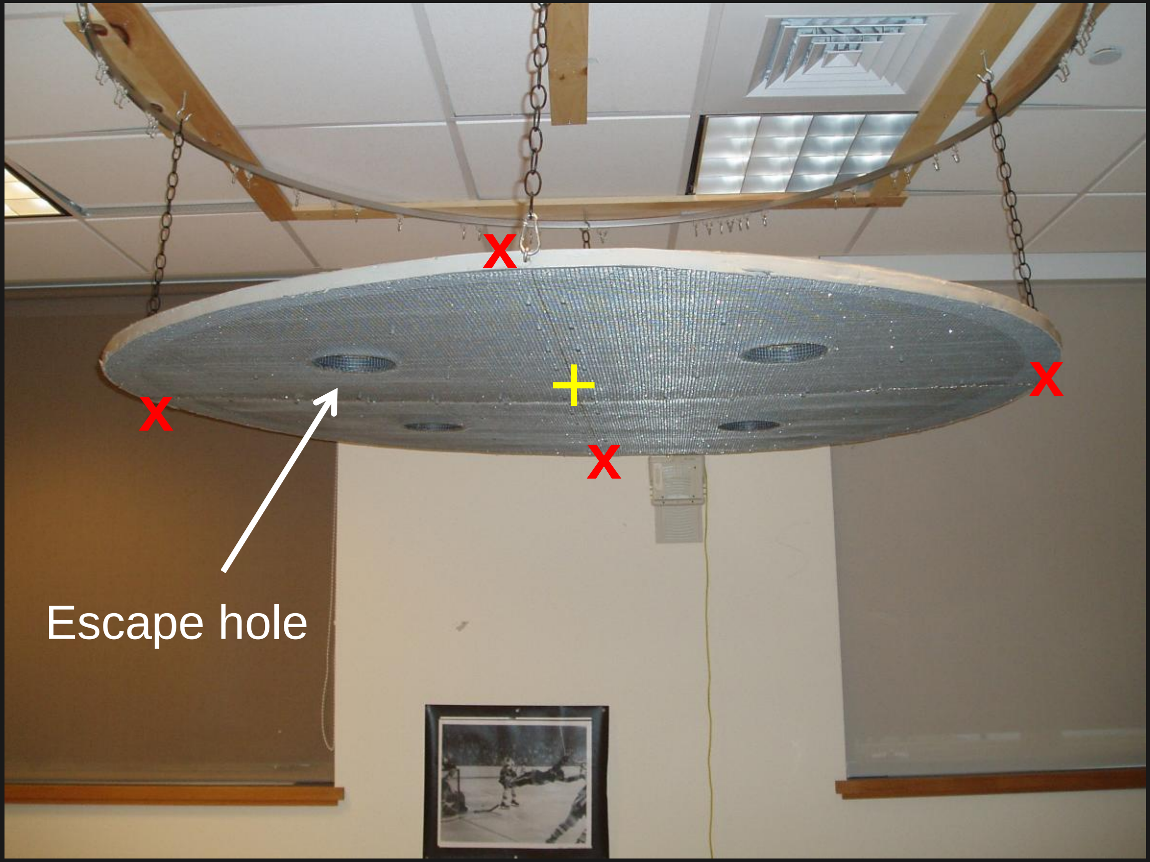
…. but even most of these cells had markedly reduced peak firing rates.

During inverted locomotion on the ceiling, cells had a lower directional information content score.



Could animals learn a spatial task upside-down ?

Inverted Hole Board Escape Task

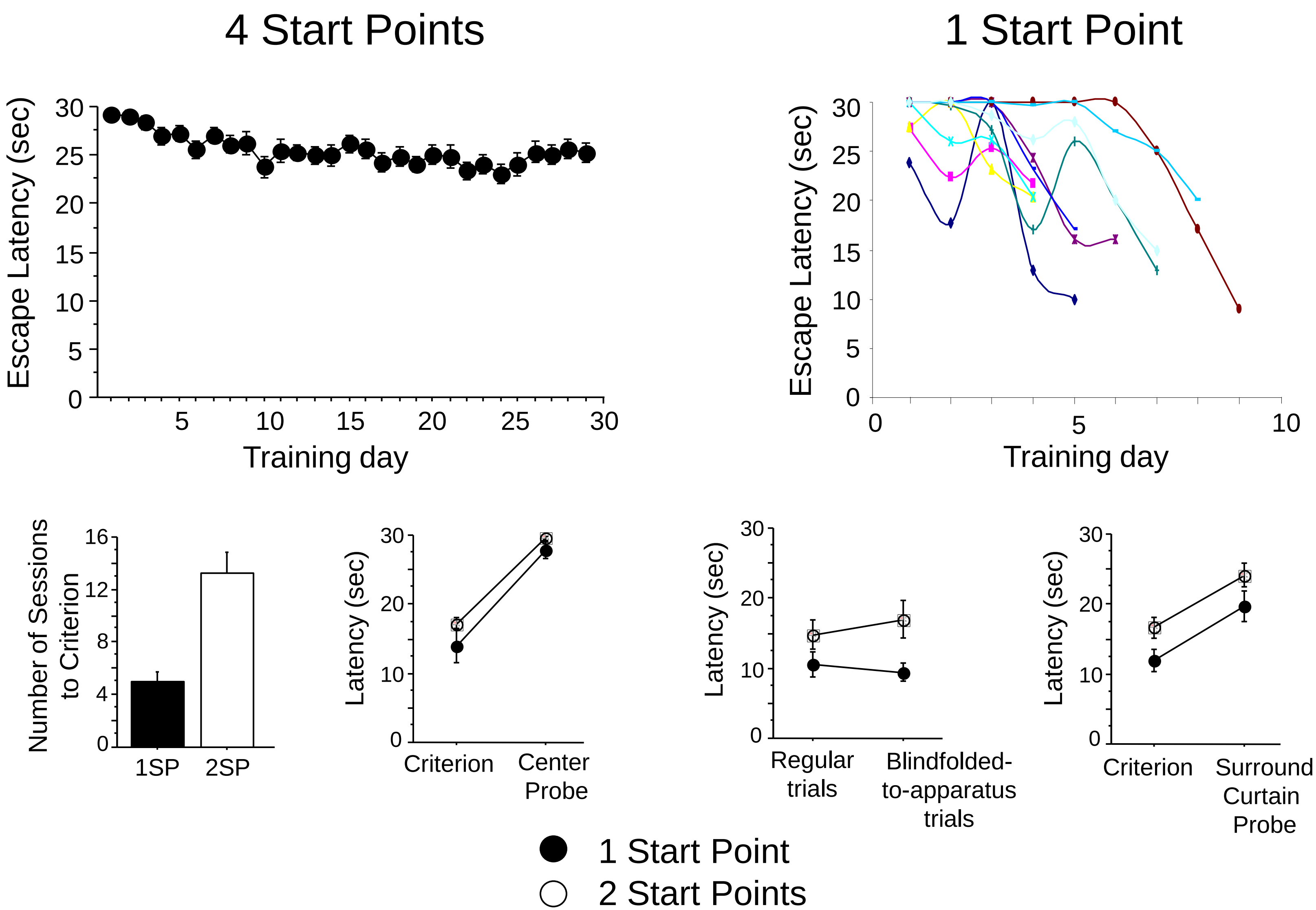


X = Four Release Points

+ = Center Release Point

Valerio, Clark et al. (2010) Neurobiol Learning & Memory

Performance in the Inverted Hole Board Escape Task



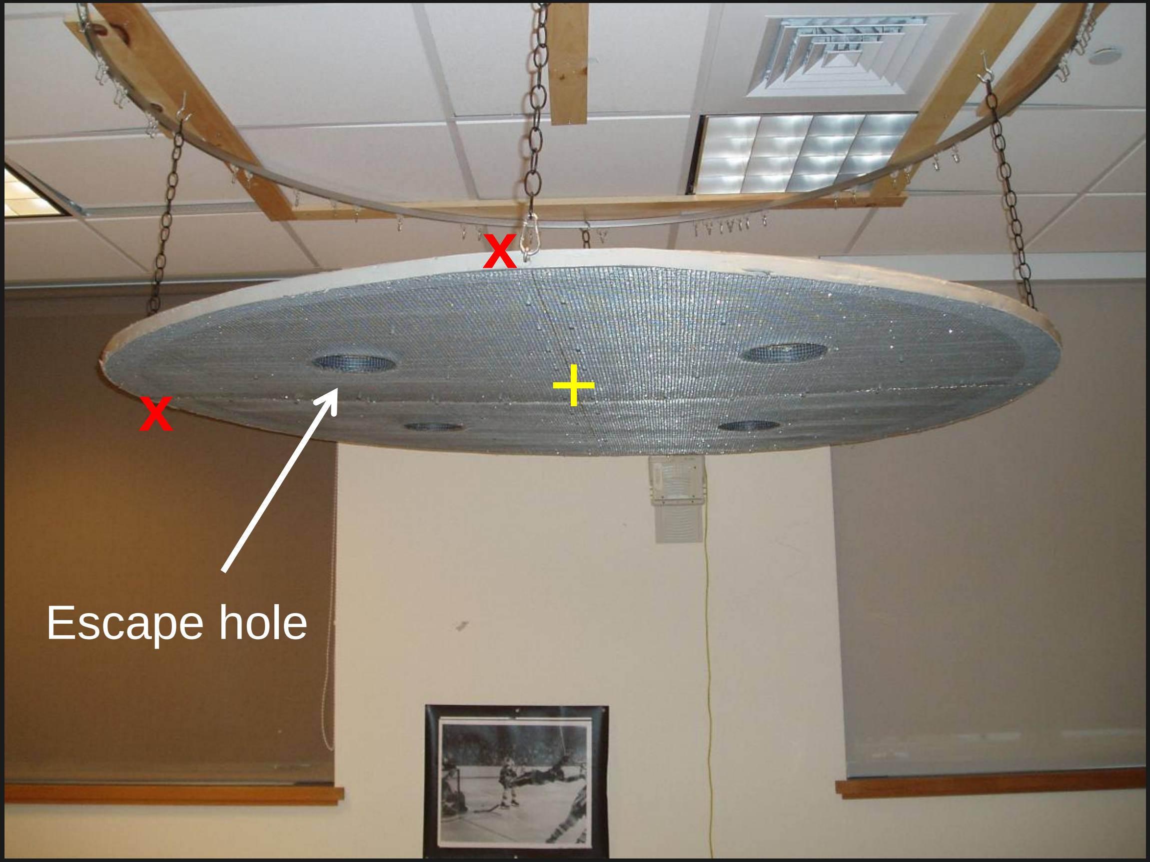
Conclusions from Behavioral Task:

When task was simple (1 or 2 start points) – animals could use a directional (or beacon) strategy – move toward a particular landmark.

But when task was difficult (4 start points) – animals needed a more flexible representation of their environment.
They needed a flexible cognitive map-like spatial strategy.

It is possible that 'normal' HD activity is required for generation and use of a cognitive map.

Record HD cells in the Inverted Hole Board Escape Task

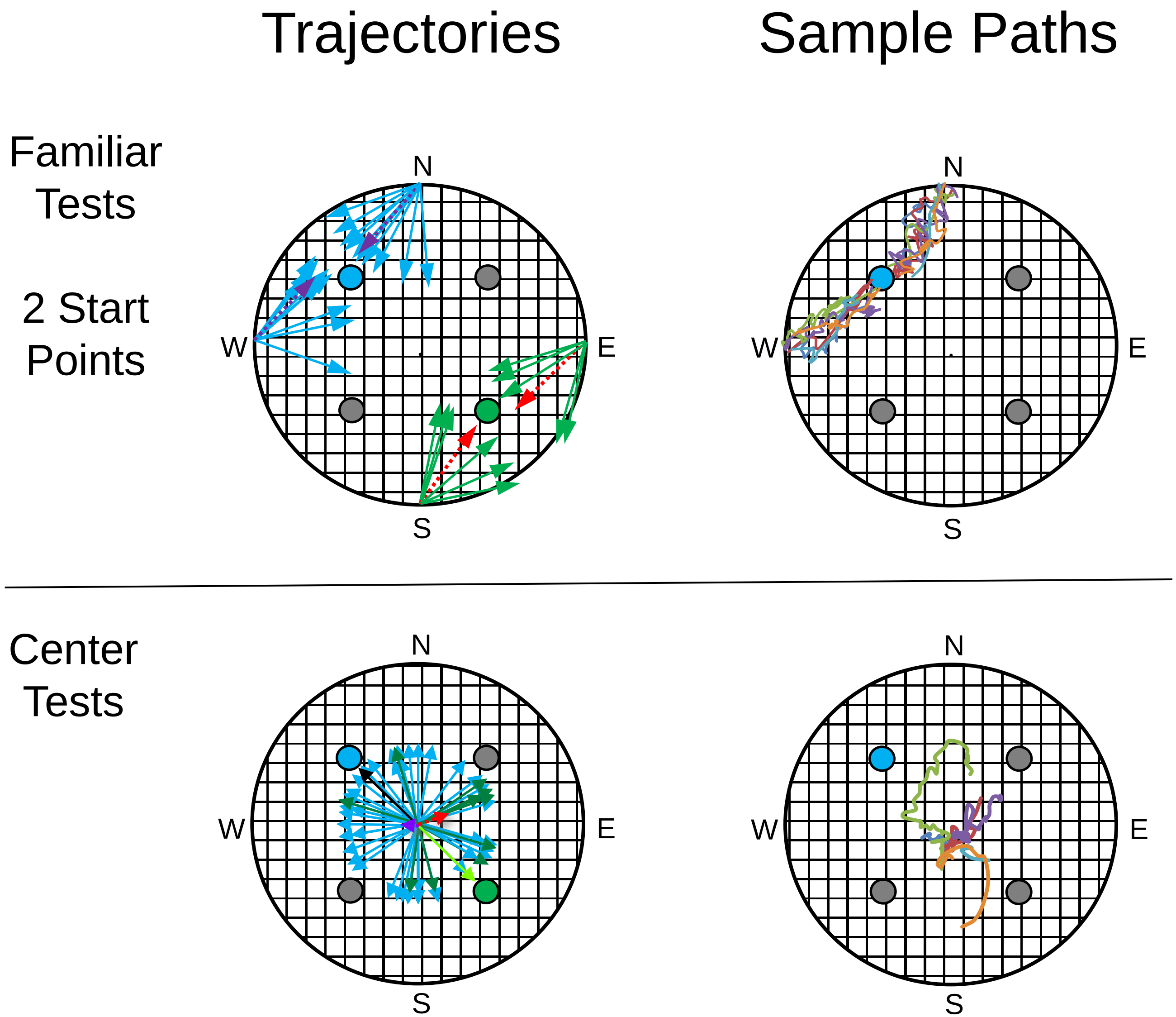


X = Familiar Release Point 1

X = Familiar Release Point 2

\+ = Center Release Point

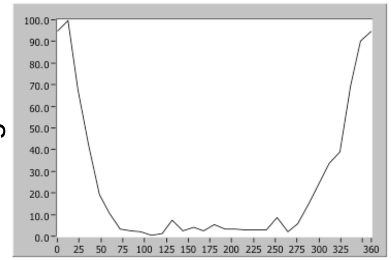
Valerio, Clark et al. (2010) Neurobiol Learning & Memory


Trajectories
Sample Paths
Familiar Tests
2 Start Points
Center Tests
N
S
E
W
N
S
E
W
N
S
E
W
N
S
E
W

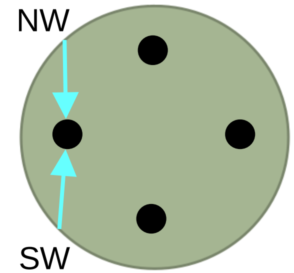
What are Head Direction Cells doing in this Task?

Session on Floor:
Upright

Firing Rate

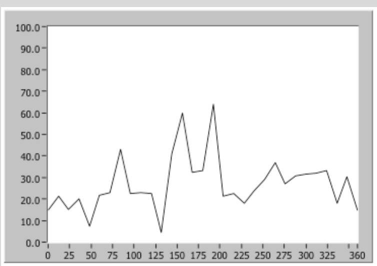


Head Direction

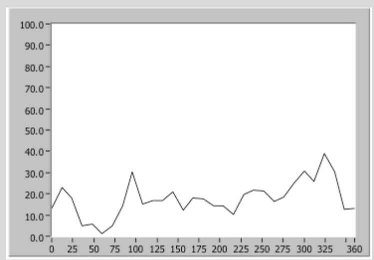


Rats trained from two locations

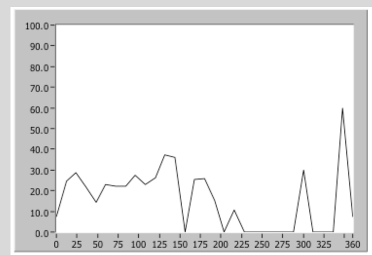
Inverted Trials



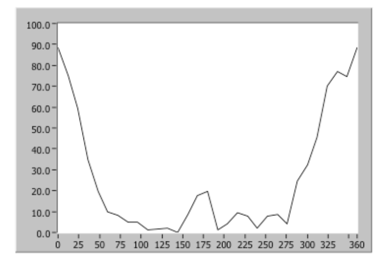
NW Inverted Trial
Correct



SW Inverted Trial
Correct



Inverted Trial: Center
Error



2nd Session on Floor:
Upright

Thus, rats were accurately performing the simple version of the inverted spatial task - despite the absence of a HD signal.

Conclusions

The results suggest that the head direction signal is needed for accurate navigation in situations that require a flexible representation of space (i.e., an allocentric cognitive-mapping strategy), but not for situations that utilize habit-like associative spatial learning.

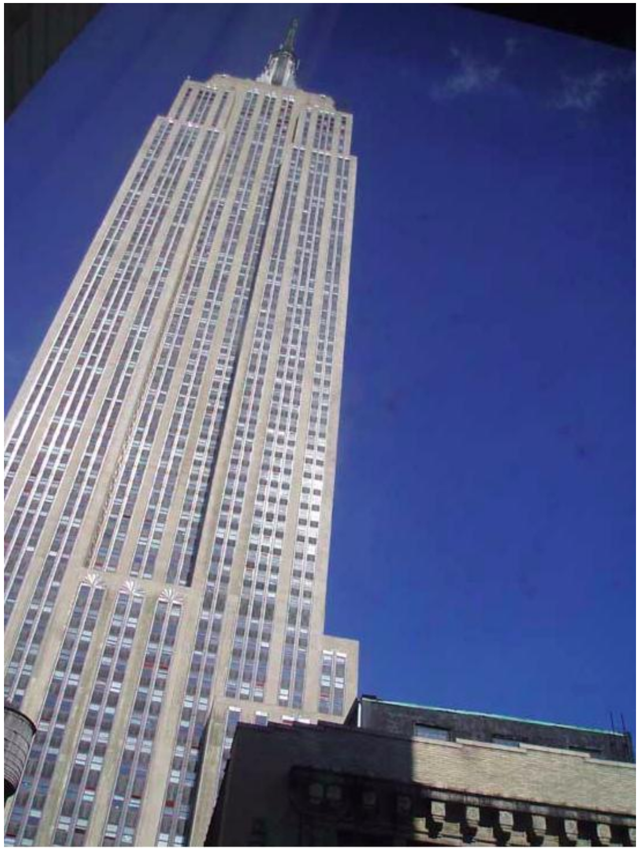
Looking for the linkage between HD cells and behavior using a task involving path integration.

What happens with HD cells following a behavioral error?

Reorientation

Cells get <u>Reset</u> to their previously established relationship with the familiar landmarks

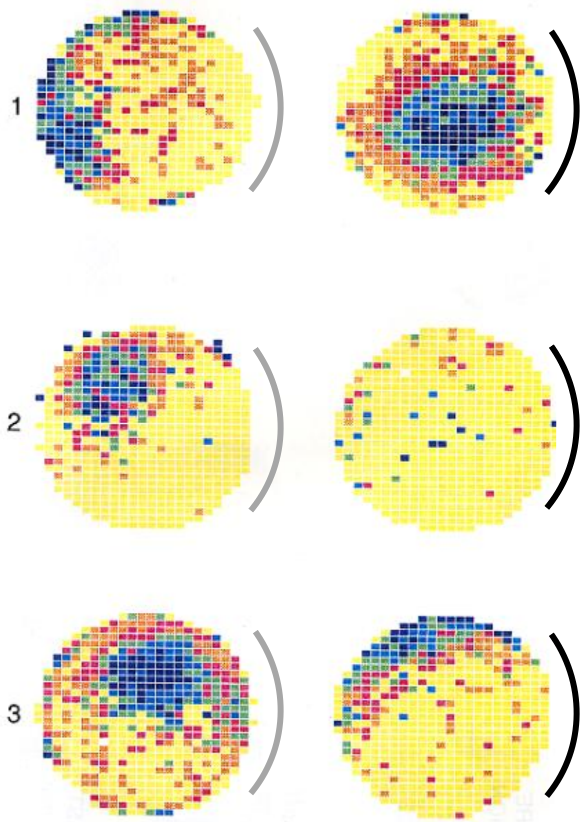
I thought that building would be on my left



In addition to Resetting, cells can also Remap

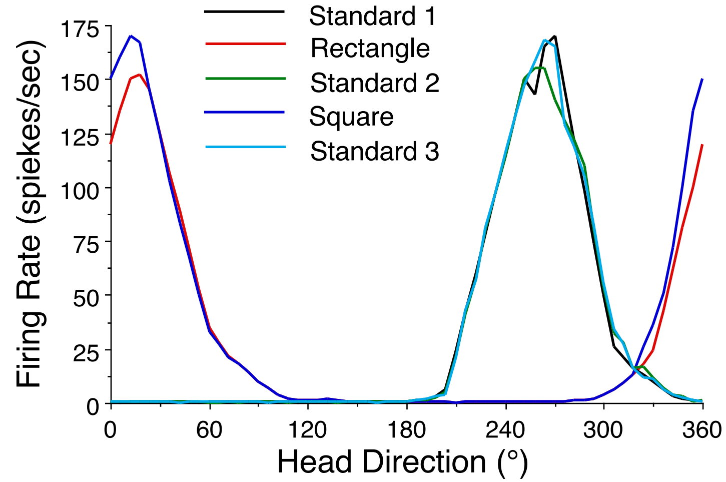
Place Cell Remapping

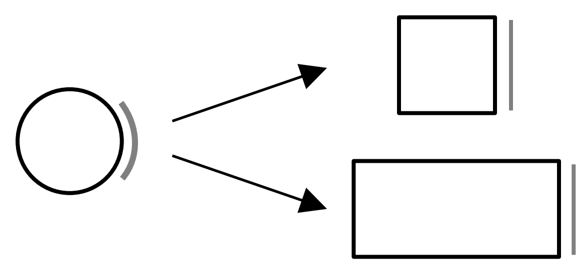
White Cue Card | Black Cue Card



Head Direction Cell Remapping

Cylinder vs. Rectangle & Square



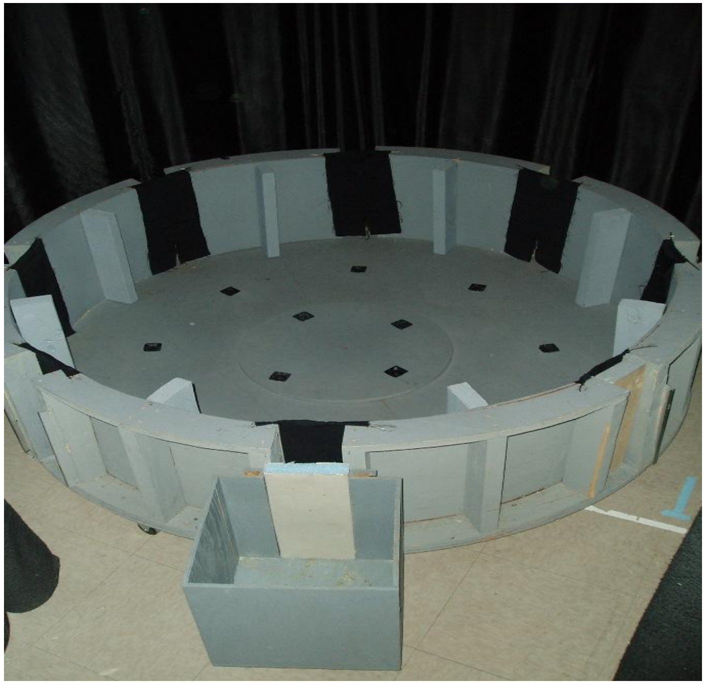


A change in the shape of the environment usually lead to a shift in the cell's preferred firing direction.

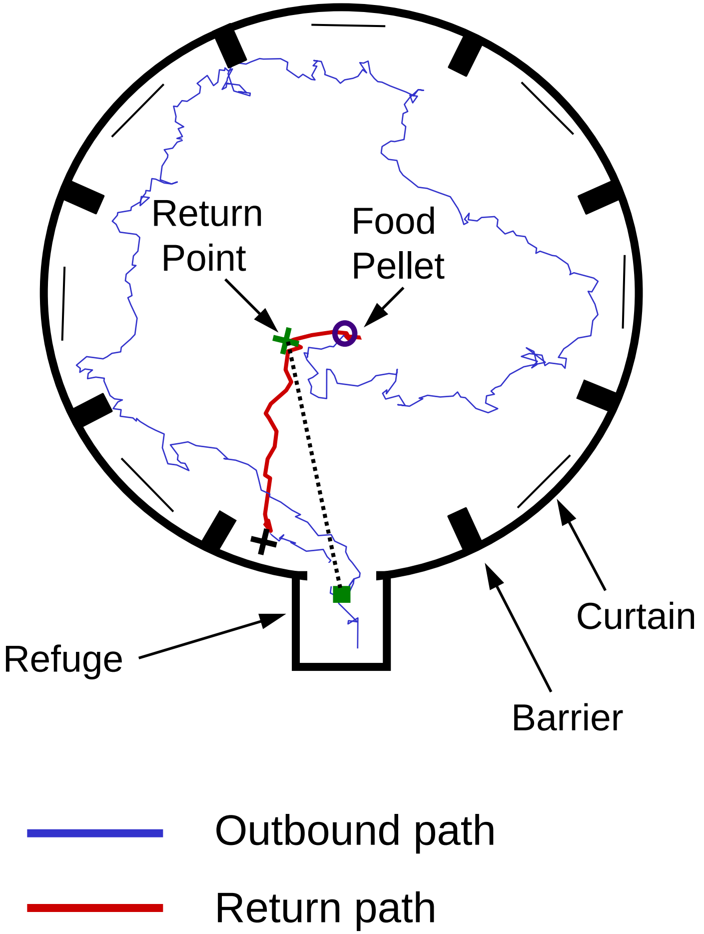
Bostock, Kubie, Muller, 1991, Hippocampus

Taube, Muller, Ranck, 1990, J Neurosci

Food-Carrying task requiring Path Integration: Behavior compared to Cell Activity



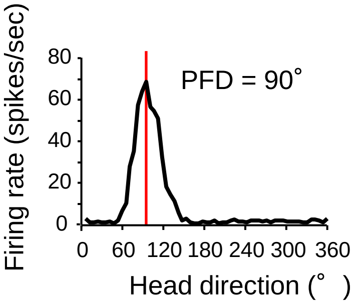
Rats are blindfolded



Valerio & Taube (2012) Nat Neurosci

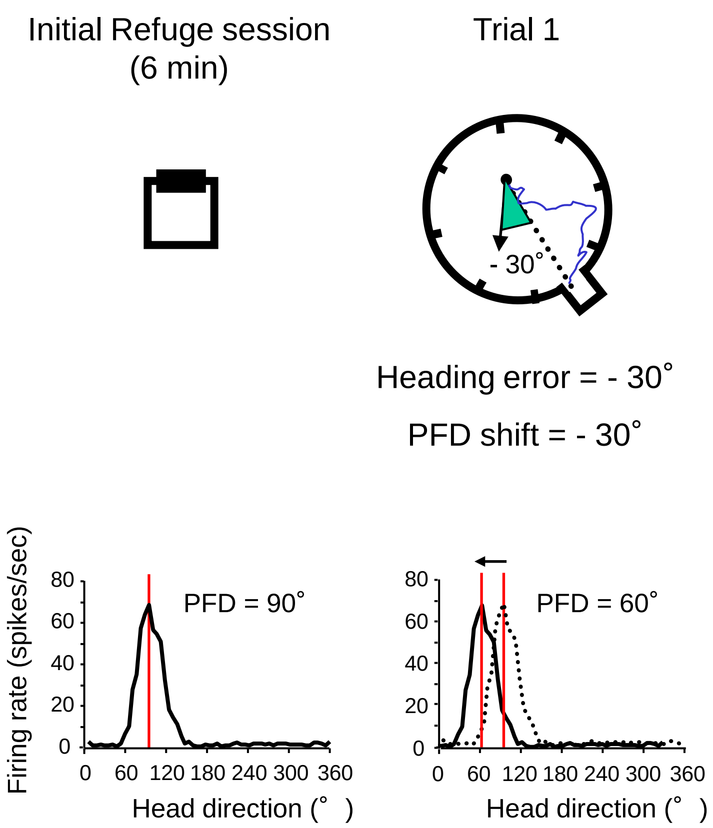
Hypothetical Results for Two Consecutive Trials

Initial Refuge session
(6 min)



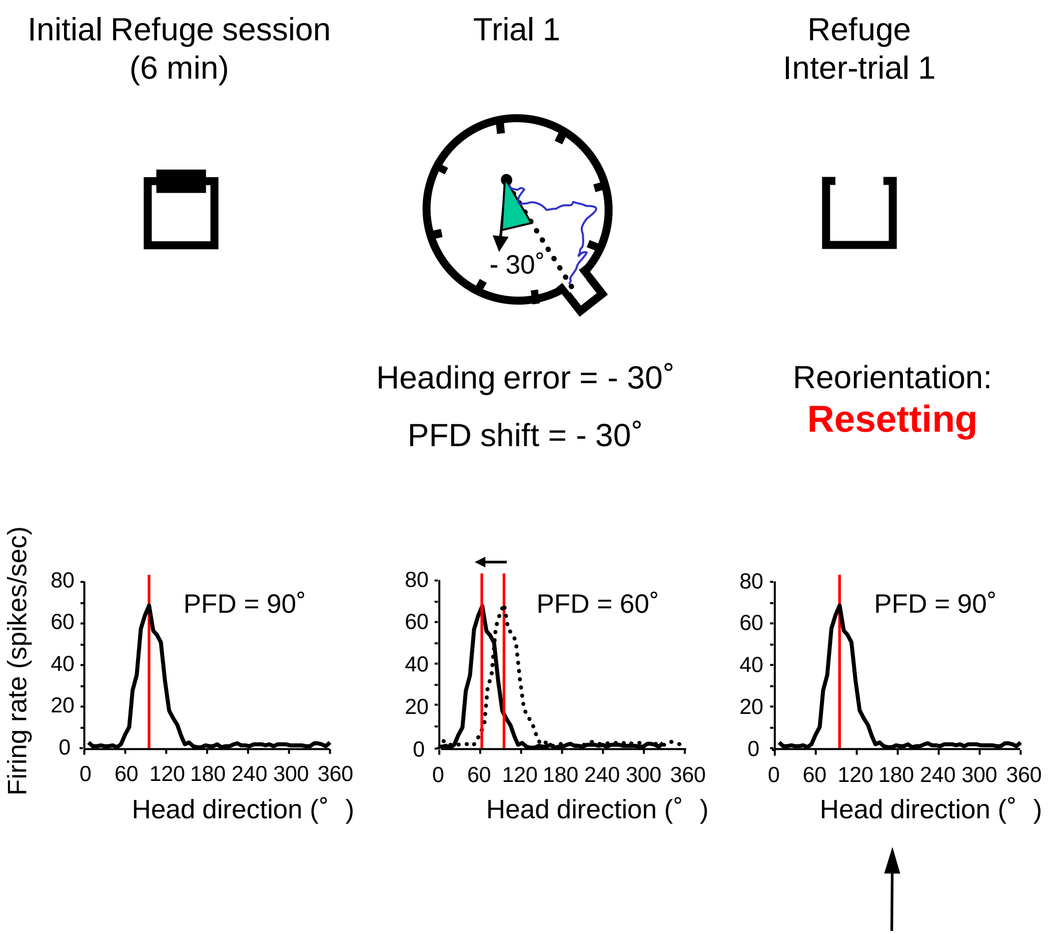
PFD = Preferred Firing Direction

Hypothetical Results for Two Consecutive Trials



PFD = Preferred Firing Direction

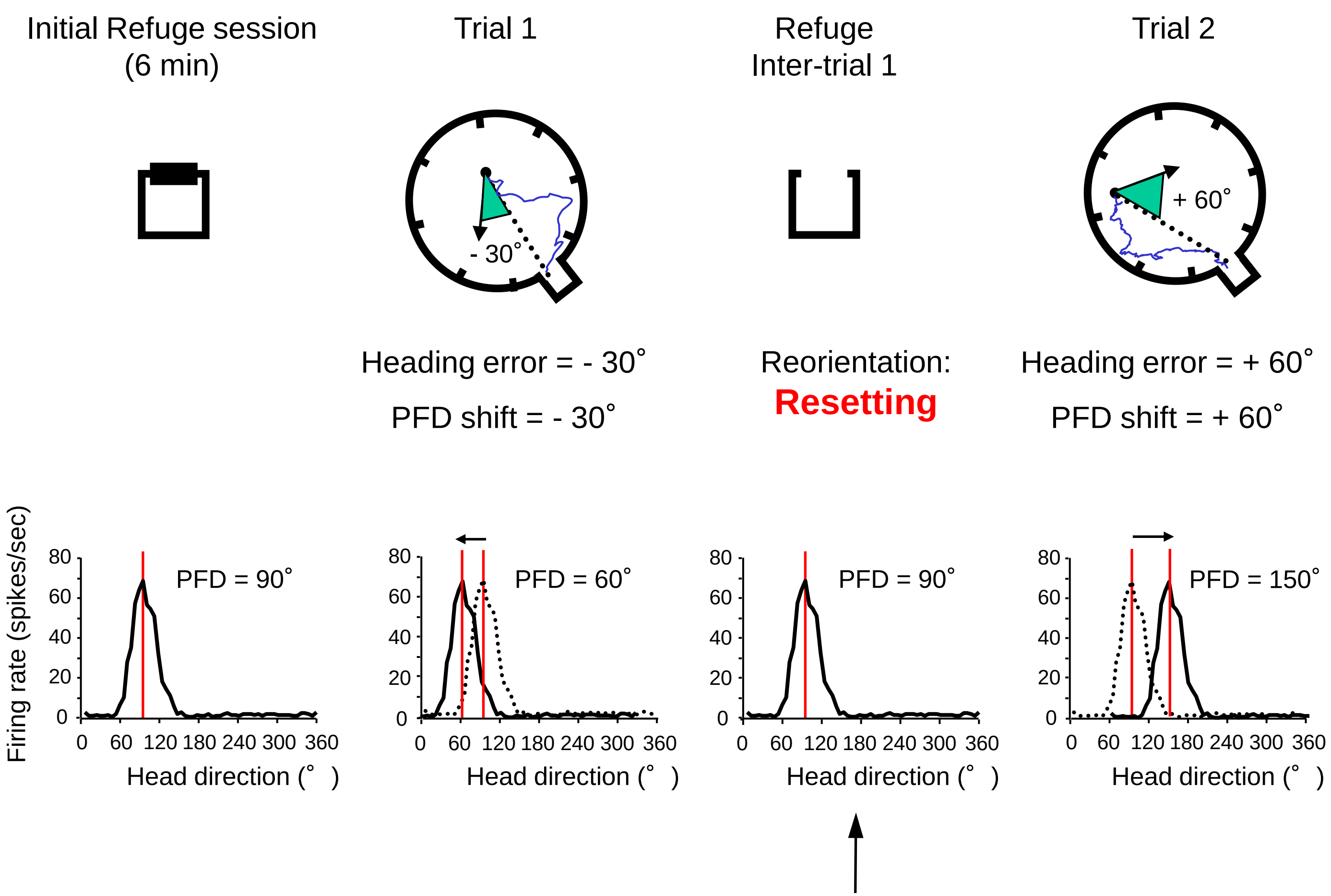
Hypothetical Results for Two Consecutive Trials



The PFD gets reset to the previous refuge value.

PFD = Preferred Firing Direction

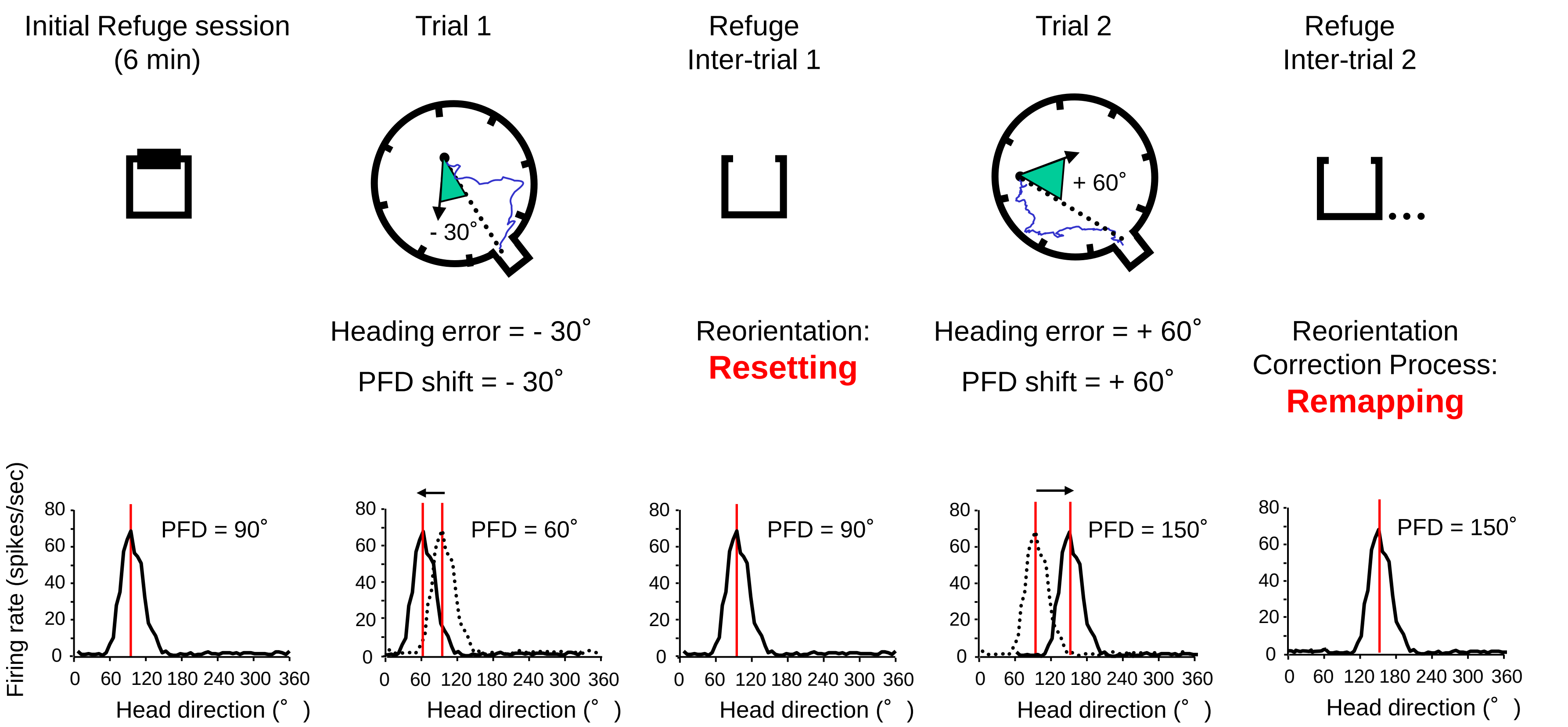
Hypothetical Results for Two Consecutive Trials



The PFD gets reset to the previous refuge value.

PFD = Preferred Firing Direction

Hypothetical Results for Two Consecutive Trials



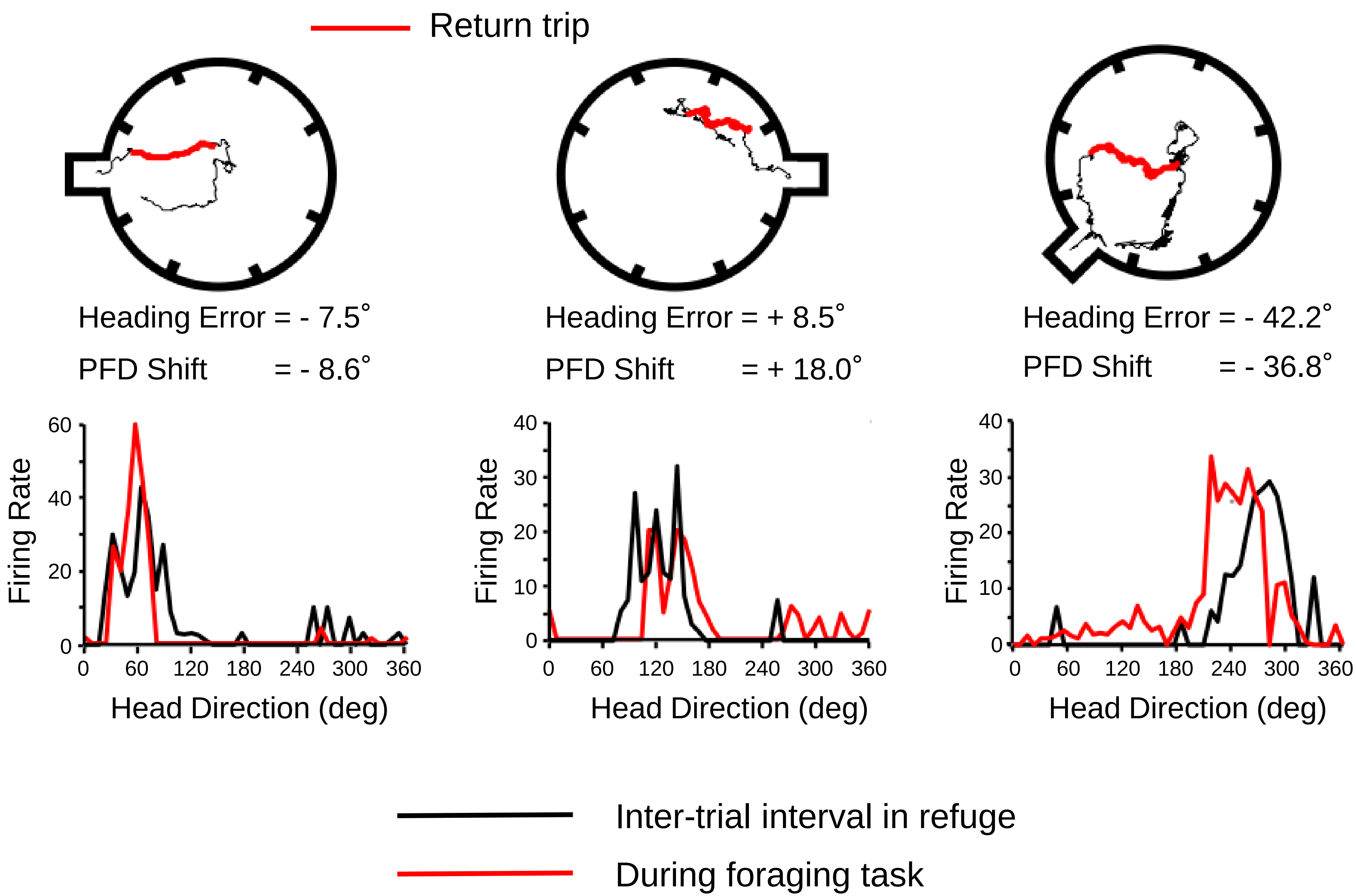
The PFD gets reset to the previous refuge value.

The PFD does **not** get reset to the previous refuge value.

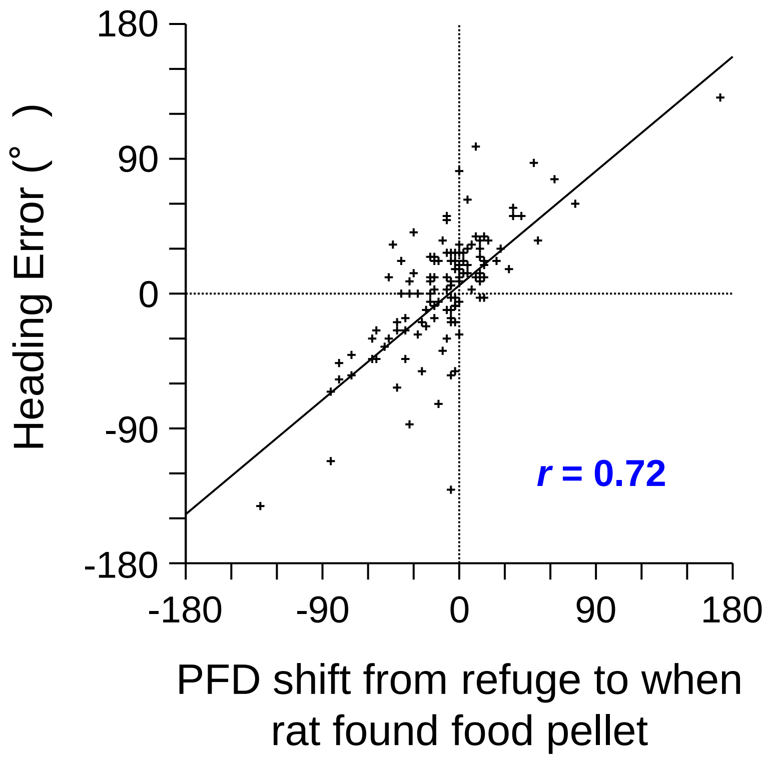
PFD = Preferred Firing Direction

Individual Trials for 3 Different Cells

Behavioral Heading Error correlates with Shift of HD cell's PFD



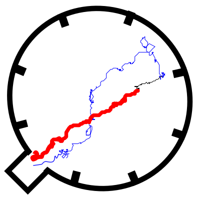
Correlation between Heading Error and the amount the Preferred Firing Direction (PFD) shifted during the outbound trip was good



Example When Resetting Process Occurred

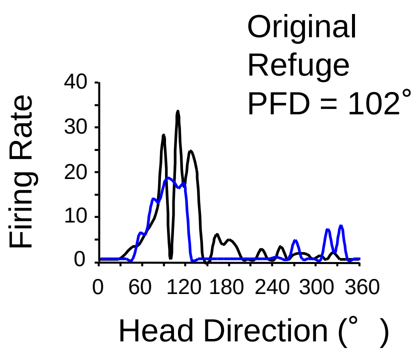
Outbound path
Return path

Trial 1



Heading Error = 5.7°

PFD Shift = -5.3°



Outbound Response

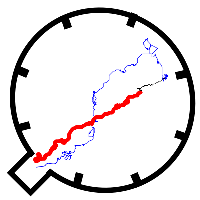
Original (initial) Refuge Response

Example When Resetting Process Occurred

Outbound path

Return path

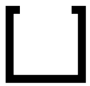
Trial 1

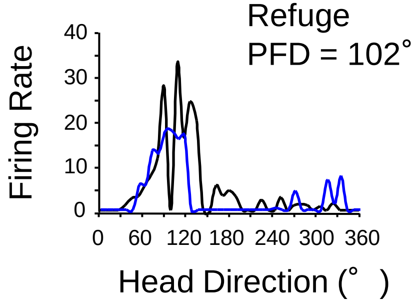


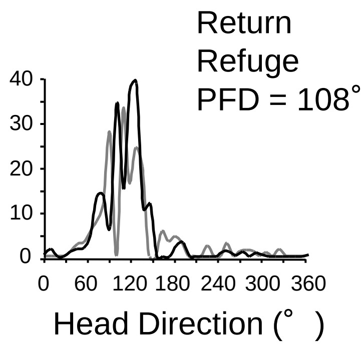
Heading Error = 5.7°

PFD Shift = -5.3°

Refuge
Inter-trial 1



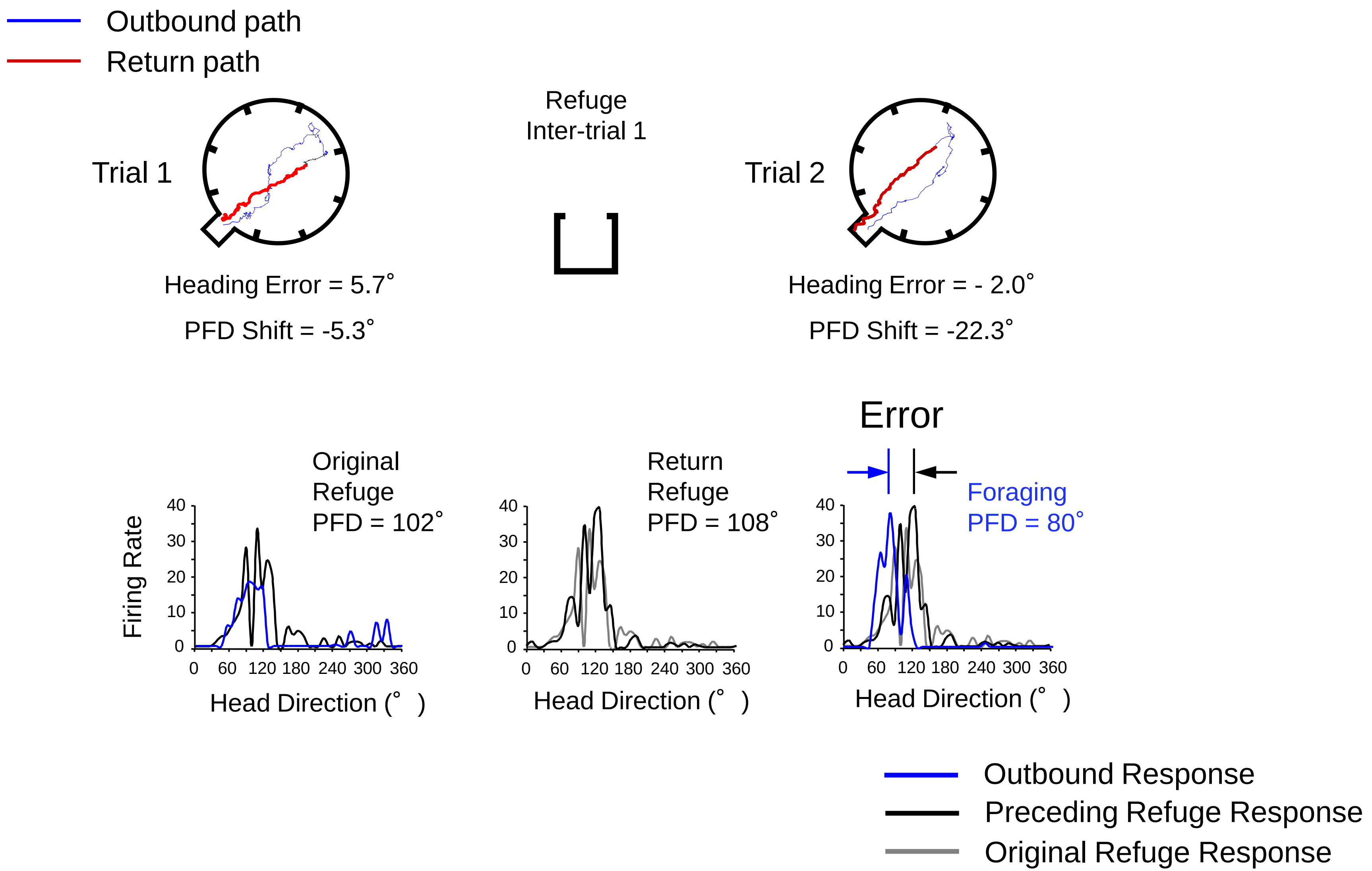




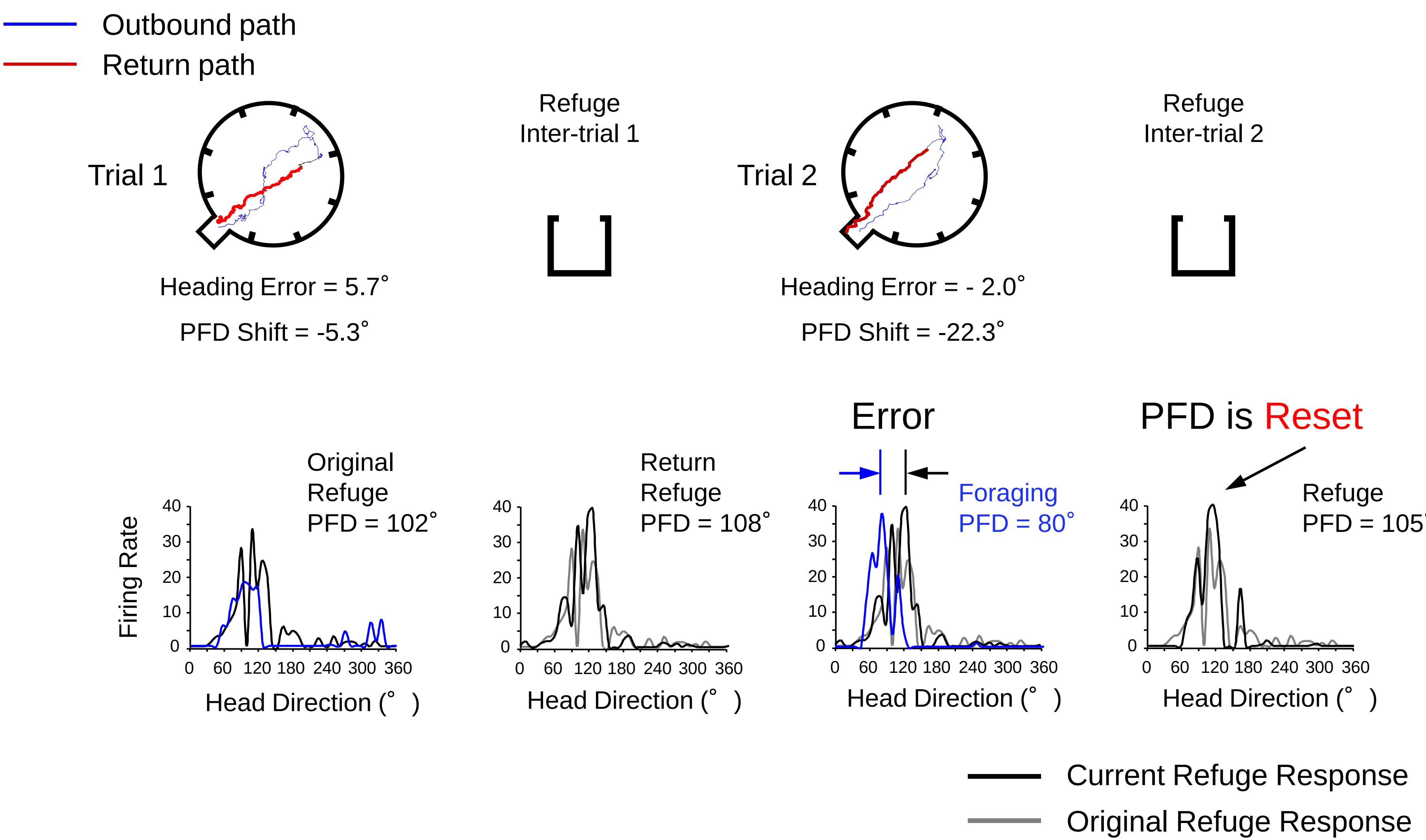
Original Refuge Response

Current Refuge Response

Example When Resetting Process Occurred



Example When Resetting Process Occurred



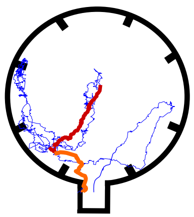
The PFD is <u>reset</u> to the refuge value upon return to the refuge.

Example When Remapping Process Occurred

Outbound path

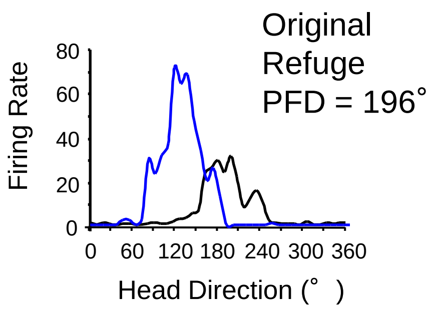
Return path

Trial 1



Heading Error = - 43.7°

PFD Shift = - 63.8°



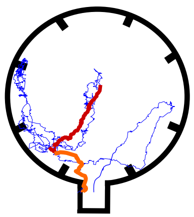
Refuge Response

Outbound Response

Example When Remapping Process Occurred

Outbound path
Return path

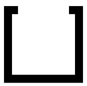
Trial 1



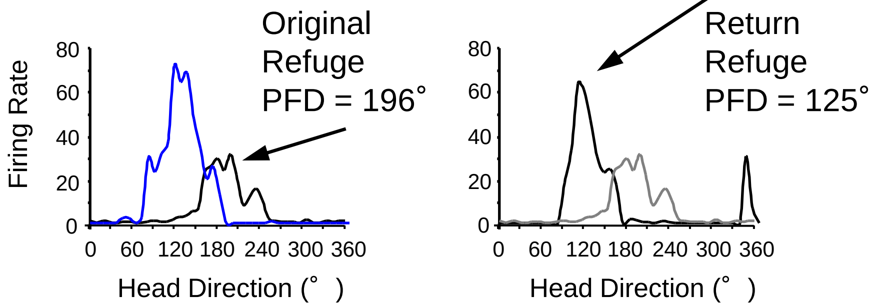
Heading Error = - 43.7˚

PFD Shift = - 63.8˚

Refuge
Inter-trial 1



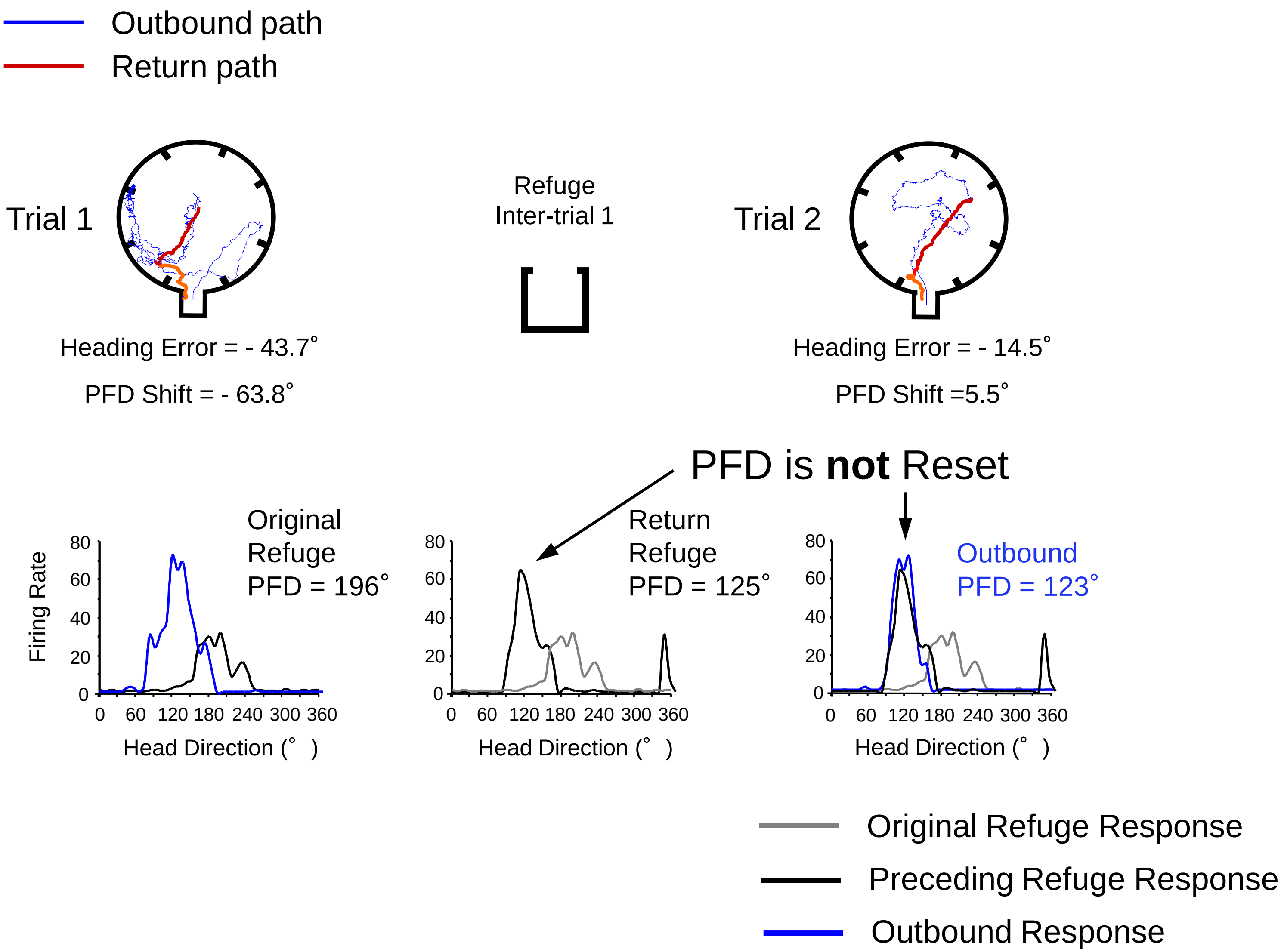
PFD is **not** Reset



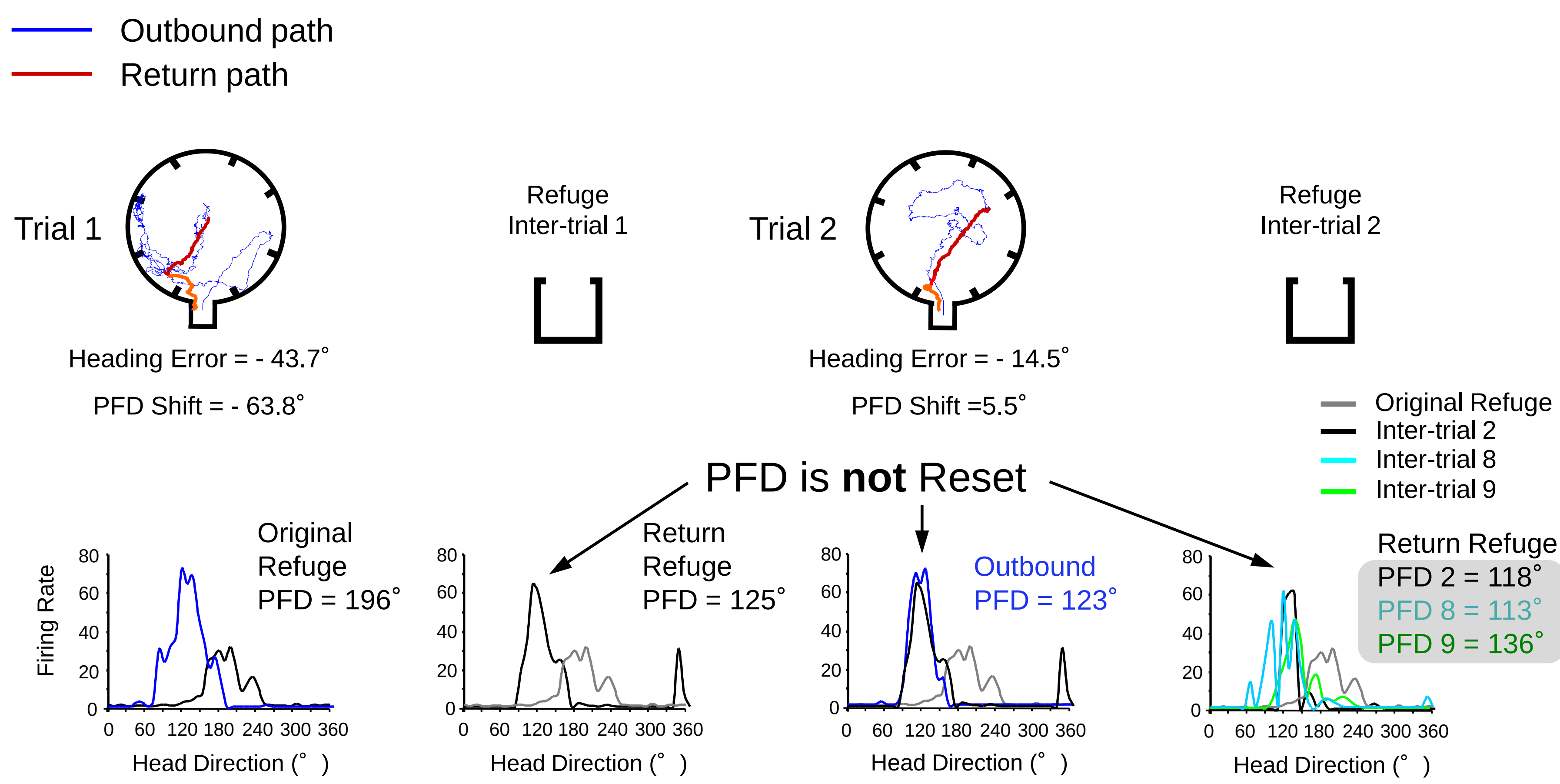
Original Refuge Response

Current Refuge Response

Example When Remapping Process Occurred

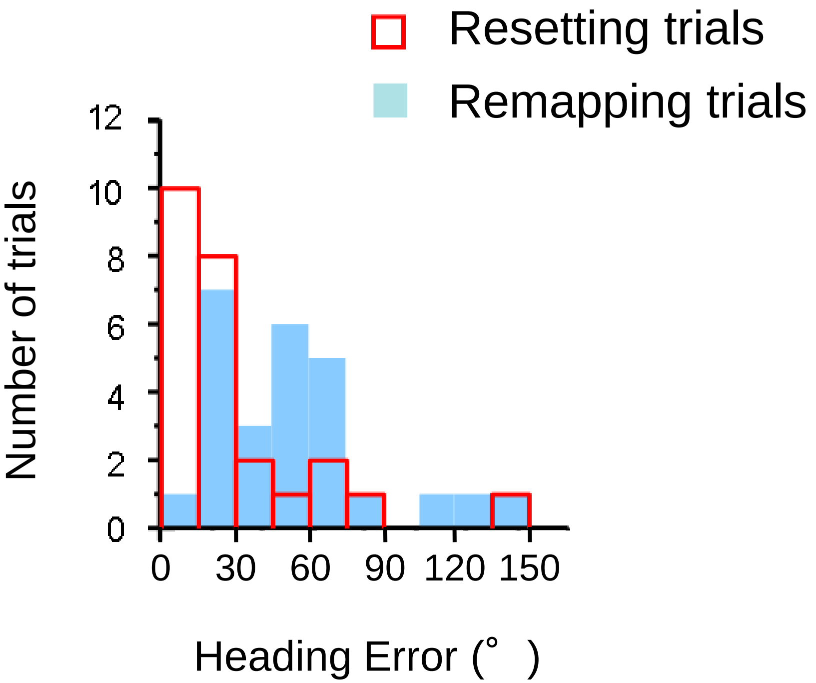


Example When Remapping Process Occurred



Remapping Occurs - the PFD is <u>not reset</u> to the refuge value upon return to the refuge, but instead retains the current PFD value (~120˚) for the next trial (#2) and subsequent trials (#s 8 and 9 are shown).

When did Resetting and Remapping trials occur?



Resetting occurred more often following **small** heading errors.

Remapping occurred more often following **large** heading errors.

Conclusions

•HD cells encode information about the animal's perceived directional heading in its environment.

•Can learn landmarks quickly and without the hippocampus.

•HD cells do not appear to be used when animal is using a directional 'beacon' strategy, but may be necessary for spatial strategies that require a flexible representation of the spatial environment - cognitive map.

•HD cell activity and behavioral performance correlated well when animal performed a task requiring path integration.

•When a behavioral error is made, there are two types of correction processes: resetting and remapping.

Grid Cell Signal Generation

Grid Cells & Motor/Proprioceptive Cues