The Neurobiology for a Sense of Direction

Outline
Nature of Head Direction Cell activity
Sensory Properties
Circuitry - How and where is the signal generated
Navigation
Responses in 3-D

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Neural Substrates of Spatial Cognition
Navigation and the Hippocampus

1. Behavioral studies with animals
   Morris water task
   Rats with hippocampal lesions are impaired in finding the platform.

2. fMRI and PET studies with humans
   London taxi cab drivers
   Activation of right hippocampus when recalling routes

3. Physiological recordings from single neurons in the hippocampus of freely-moving animals - Place cells

Human Data

• Maguire et al. (1997), J Neurosci. 17: 7103-7110
Two Components of Spatial Orientation

• Location - Place cells
• 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

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 360°.
- Little adaptation in cell firing when the rat holds its head in the cell’s preferred firing direction.

Head Direction Cell Tuning Curve

- Peak firing rate
- Directional firing range
- Preferred firing direction
- Background firing rate

- Firing Rate (Hz)
- Head Direction (°)
- 0°, 90°, 180°, 270°
3 typical HD cells, each with a different peak firing rate

Low

Medium

High

What controls the preferred firing direction of HD cells?

Does the cue card exert stimulus control over head-direction cell firing?

Experiment: Rotate the cue card.
Does removing the salient visual cue alter cell firing?

Experiment: Remove the cue card.
Preferred Firing Direction is Maintained in the Absence of the Cue Card

Does a change in the shape of the environment have an effect on cell firing?

Experiment: Place the animal in a rectangular or square enclosure with the cue card in the same relative position.
How is the HD Cell Signal Generated?

M Witter (1989) In Hippocampus: New Vistas
Neuro Biology for a Sense of Direction

Circuit Diagram - 1

Hippocampus → Entorhinal Cortex → Postsubiculum → Posterior Parietal Cortex → Posterior Cingulate Cortex → Anterior Dorsal Thalamus → Lateral Dorsal Thalamus → Lateral Mammillary Nuclei

Subiculum → Postsubiculum

Place Cells: Hippocampus, Entorhinal Cortex, Postsubiculum, Lateral Dorsal Thalamus, Lateral Mammillary Nuclei
HD Cells: Hippocampus, Entorhinal Cortex, Postsubiculum, Lateral Dorsal Thalamus, Lateral Mammillary Nuclei

3 Typical HD Cells

Postsubiculum → Anterior Dorsal Thalamus → Lateral Mammillary Nuclei

Firing Rate (Hz)
Where are HD cells located?

How is the HD Cell Signal Generated?

Given that the HD cells have been identified in several brain areas, which areas are critical for generating the signal?
Lesions in any of several different nuclei do not abolish HD cell firing in the AD Thalamus, but lesions in the AD Thalamus do abolish HD cell activity in the Postsubiculum.

Lesions in the Lateral Mammillary Nuclei disrupt HD activity in the Anterior Dorsal Thalamus.
Lesion Studies Conclusions

Lesions of the Lateral Mammillary Nuclei (LMN) led to the absence of finding HD cells in the Anterior Dorsal Thalamus.

The LMN and neural information projected to it are critical for the generation of HD cell activity.

So, what brain areas and what type of information is projected to the LMN?

Vestibular Apparatus

Interaction of the Vestibular System

• HD cell firing in the Anterior Dorsal Thalamus and in the Lateral Mammillary Nuclei (but not in the Postsubiculum) is modulated by angular head velocity.

• Vestibular deficient humans - Mild navigational impairments due to enhanced reliance on visual cues. But more severe deficits are seen during navigation in the dark or when blindfolded.

• Following a head turn, perhaps a vestibular system signal is fed forward onto HD cells to update the new head direction?

Influence of Vestibular Lesions on Head Direction Cells

Protocol:
A. Isolate Head Direction cell.
B. Under anesthesia, inject intra-tympanic sodium arsenilate.
C. Following recovery after ~ 1 hr, monitor HD cell over the course of the vestibular lesion.
Inhibition of contact-righting by foot contact in the labyrinthectomized rat.

Chen et al., 1986, Physiol Behav 37: 805-814.
Vestibular Lesion: Intact Neuronal Discharge
Transient Vestibular Lesion using TTX

Vestibular inputs may also be important for establishing spatial representations for location.
Transient Vestibular Inactivation Disrupts CA1 Place Cell Firing

If the HD cell signal generation is dependent upon vestibular input, then …

How is a vestibular signal conveyed to the HD cell circuitry?
Traditional View

Vestibular Pathway to the Limbic System & Hippocampus

Vestibular Nuclei → Ventral Posterior Thalamus → Somatosensory Cortex → Parietal Insular Vestibular Cortex → Entorhinal Cortex → Papez Circuit → Limbic System & Hippocampus

Alternative View for Vestibular Pathway to Limbic System

Nucleus Prepositus → Medial Vestibular Nucleus → Dorsal Tegmental Nucleus → Lateral Mammillary Nuclei → Anterior Dorsal Thalamus → Postsubiculum
What type of neuronal signal is projected onto Lateral Mammillary Nuclei cells from the Dorsal Tegmental Nucleus?

• ~75% of cells had firing rates correlated to the animal’s angular head velocity.

• Two different types of angular head velocity correlates were found.

DTN Symmetric AHV Cells

63.6% of AHV cells
DTN Asymmetric AHV Cells

36.4% of AHV cells

Alternative View for Vestibular Pathway to Limbic System
Neural Integrator

\[ \int v \, dt = \theta \]

- Starting from a known directional heading, a mathematical integration in time of angular head velocity yields angular head displacement.

- Perhaps a neural integrator, similar to the one involved in the vestibulo-ocular reflex (VOR), is present in the DTN --> LMN pathway and is responsible for generating the HD cell signal.

Working Model for integrating angular head velocity

[Diagram of neural pathways involving various nuclei and their interactions, including excitatory and inhibitory signals, and labels such as Postsubiculum, Lateral Mammillary Nuc., Anterior Dorsal Thalamic Nuc., Dorsal Tegmental Nuc., Medial Vestibular Nuc., Interpeduncular Nuc., Medial Habenular Nuc., Head Direction signal, Angular Head Velocity signal.]
Continuous Attractor Network

Vestibular/Motor
CW or CCW turns

On
90°

Excitatory

Visual Inputs

Inhibitory

Off

Off

Off

270°

Proposed by:
Skaggs, McNaughton et al., 1995
Blair, Sharp, 1995
Redish, Goodridge, Touretzky, 1996, 1999
Zhang, 1996

Some thoughts to ponder ....

• Assume that HD cell firing arises from a continuous attractor network.

• Then removing inputs into the attractor network may either:

  • a) leave the hill of activity stationary - and a subset of HD cells from the population might be continuously active, or

  • b) the hill of activity might be unstable and will drift around continuously. In this condition, we might expect to see some cells have bursts of activity as the hill passes through the cell’s preferred direction.
Our findings following vestibular disruption showed neither prediction.

- Of 11 recorded HD cells, none of the 11 cells was tonically “on”.
- Moreover, none of the 11 cells showed bursty activity.
- Bursty activity was only seen in non-HD cells.

A. Bursty cell in vestibular-lesioned rat
B. HD cell in normal rat
Navigational Systems

**Landmark based Navigation:**
- taking a positional fix
  - Use of familiar salient external landmarks
  - Episodic monitoring

Examples:
Visual, Auditory, Olfactory, Somatosensory cues
Navigational Systems

**Internal Navigation or Path Integration:**
- Use of internal (idiothetic) cues resulting from movements
- Continuous monitoring

**Examples:**
- Vestibular, Proprioceptive, Kinesthetic cues
- Motor efference copy, Optic and Auditory flow

Head Direction Cells - Idiothetic Cues

Rat is placed into arenas - preferred firing direction usually shifts by > 50°

What happens when the rat walks from the cylinder into the rectangle?
HD Cells use internal cues

Rat walks from cylinder into rectangle
preferred firing direction shifts by a mean of ± 18°

Recording Session Sequence: Novel Conditions

1. Standard Cylinder
   Door closed

2. Novel Session
   Door open
   Novel-Rectangle
   Return-Cylinder
Standard Session

Novel Session
Idiothetic Cues and HD Cells

What is the influence of motor efference copy cues or optic flow in updating the cell’s preferred direction in the Novel condition?

During Initial Exposure to Novel Environment:

<table>
<thead>
<tr>
<th>Cue Source</th>
<th>Manipulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Efference</td>
<td>Passive Transport via wheeled cart</td>
</tr>
<tr>
<td>Optic Flow</td>
<td>Room Lights On/Off</td>
</tr>
</tbody>
</table>
Idiothetic Cues and HD Cells

<table>
<thead>
<tr>
<th>Optic Flow</th>
<th>ROOM LIGHTS ON</th>
<th>ROOM LIGHTS OFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Efference</td>
<td>• all cues available • PFD maintained</td>
<td>• intact motor efference • disrupts optic flow • intact vestibular</td>
</tr>
<tr>
<td>RAT WALKS IN</td>
<td>• disrupts motor efference • intact optic flow • intact vestibular</td>
<td>• disrupts motor efference • disrupts optic flow • intact vestibular</td>
</tr>
<tr>
<td>PASSIVE TRANSPORT ON CART</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Passive Transport - Room Lights Off

- Standard Cylinder
- Novel-Rectangle

Head Direction (°) vs. Firing Rate (spikes/sec)
Summary of Results

<table>
<thead>
<tr>
<th>Optic Flow</th>
<th>ROOM LIGHTS ON</th>
<th>ROOM LIGHTS OFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAT WALKS IN</td>
<td>Average shift of PFD: ± 18°</td>
<td>Average shift of PFD: ± 32°</td>
</tr>
<tr>
<td>PASSIVE TRANSPORT ON CART</td>
<td>Average shift of PFD: ± 65°</td>
<td>Average shift of PFD: ± 68°</td>
</tr>
</tbody>
</table>

Idiothetic Cues and HD Cells

- What do we know?

HD Cells are multi-modal:
- Vestibular: Generating HD cell signal
- Motor efference: Updating HD cell network
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**Place Cells**
- Hippocampus
- Entorhinal Cortex
- Subiculum
- Postsubiculum
- Lateral Dorsal Thalamus

**HD Cells**
- Posterior Parietal Cortex
- Posterior Cingulate Cortex
- Anterior Dorsal Thalamus
- Lateral Mammillary Nuclei
- Dorsal Tegmental Nucleus
- Medial Vestibular Nuclei

**Landmark Sensory Information**
- Visual Cortex
- Motor Cortex

**Idiothetic Information**
- Motor Information
- Landmark Sensory Information

**Other Sensory Cortex**
- Other Sensory Cortex
- Motor Cortex
- Landmark Sensory Information
- Idiothetic Information

**Landmark Sensory Information**
- Landmark Sensory Information
- Idiothetic Information

**Idiothetic Information**
- Idiothetic Information

**Motor Information**
- Motor Information
- Landmark Sensory Information

**Other Sensory Cortex**
- Other Sensory Cortex
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**Landmark Sensory Information**
- Landmark Sensory Information

**Idiothetic Information**
- Idiothetic Information

**Motor Information**
- Motor Information

**Other Sensory Cortex**
- Other Sensory Cortex

**Landmark Sensory Information**
- Landmark Sensory Information

**Idiothetic Information**
- Idiothetic Information

**Motor Information**
- Motor Information
Head direction Cells in 3D

- HD cells fire as a function of head direction in the horizontal plane.

- But how is the horizontal reference frame defined?

- How do HD cells respond during vertical plane locomotion?

Vertical Sampling Apparatus

- Food Cups
- Wire Mesh Ladder
- Annulus
- 74 cm
Example of Recording Protocol

MESH 0°  MESH 180°  MESH 270°  MESH 90°
(relative to HD cell's preferred firing direction)
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Mesh @ 180° Position

Mesh @ 90° Position
Vertical Plane Data Summary

Hemi-torus Model of HD Cell Firing in 3-D

Cell firing plotted in polar coordinates
Summary

- HD cell firing was maintained during vertical locomotion, if the rat approached the mesh in the cell's preferred firing direction.

- Horizontal reference frame was defined by the rat’s plane of locomotion, but …..

- How does an HD cell respond when a rat locomotes in a vertical plane >90°?
Loss of directional tuning on ceiling, with increased background firing rate.

Summary

- Head direction cells are multi-modal - receiving both sensory and motor information.

- They are observed in several areas of the brain (mostly within the limbic system).

- The vestibular system appears critical for generating the directional signal, but motor signals appear important for updating it.

- Brainstem circuitry involving the Dorsal Tegmental Nucleus and Nucleus Prepositus may act as an integrator for updating directional heading.

- The anterior thalamus may be a converging point for landmark and idiothetic information.
## Contributors

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Session Sequence: Sensory Conflict Conditions

3. Rotation Cylinder
   - Door closed
   - Cylinder cue card in rotated position

4. Conflict Condition
   - Door open
   - Cylinder cue card in rotated position

Conflict-Rectangle  Conflict-Cylinder

Novel  90° CCW Cue Rotation

Rectangle Conflict  Cylinder Conflict

Head Direction (°)  Firing Rate (spikes/sec)
Head Pitch Cell in LMN

Firing Rate (spikes/sec)

Head Pitch (°)

Transient Vestibular Inactivation Disrupts CA1 Place Cell Firing

Pre Post 1 hr 4 hr 12 hr

TTX

24 hr 36 hr 48 hr 60 hr

Recovery