

Persistent Neural Activity in Head Direction Cells

Jeffrey S. Taube and Joshua P. Bassett

Department of Psychological & Brain Sciences, Center for Cognitive Neuroscience, Dartmouth College, 6207 Moore Hall, Hanover, NH 03755, USA

Many neurons throughout the rat limbic system discharge in relation to the animal's directional heading with respect to its environment. These so-called head direction (HD) cells exhibit characteristics of persistent neural activity. This article summarizes where HD cells are found, their major properties, and some of the important experiments that have been conducted to elucidate how this signal is generated. The number of HD and angular head velocity cells was estimated for several brain areas involved in the generation of the HD signal, including the postsubiculum, anterior dorsal thalamus, lateral mammillary nuclei and dorsal tegmental nucleus. The HD cell signal has many features in common with what is known about how neural integration is accomplished in the oculomotor system. The nature of the HD cell signal makes it an attractive candidate for using neural network models to elucidate the signal's underlying mechanisms. The conditions that any network model must satisfy in order to accurately represent how the nervous system generates this signal are highlighted and areas where key information is missing are discussed.

Introduction

Many neurons throughout the classical 'Papez circuit' discharge as a function of an animal's directional heading in the horizontal (or yaw) plane. These neurons are referred to as head direction (HD) cells (Taube *et al.*, 1990a). Each neuron is tuned to a different firing direction and all directional headings are equally represented within a population of these cells. HD cells are quiescent when the animal's head is not pointing in the cells' preferred direction of firing, and then increase their rates of firing linearly as the animal moves its head into the proper orientation. Cell firing is largely unaffected by pitch or roll of the animal's head within $\sim 90^\circ$ of the horizontal plane. As long as the animal's head is in a given cell's directional range, cell firing will continue whether the animal is moving or still and is independent of the animal's on-going behavior. There is little adaptation of cell firing when the animal is holding its head in the cell's preferred firing direction (Taube and Muller, 1998).

Fundamental Properties

Each HD cell can be characterized by a number of parameters based on its tuning curve, which is plotted on a firing rate versus head direction graph (Fig. 1A–C). The range of directional headings over which activity is elevated above baseline (background) levels is referred to as the *directional firing range*. Tuning curves generally have directional firing ranges of 90° , but they can vary from 60° up to 150° . Tuning curves are generally triangular or Gaussian in shape. The peak of the tuning curve is referred to as the *peak firing rate* of the cell and the animal's HD at the peak is the *preferred firing direction* of the cell. Peak firing rates vary across different HD cells and range from

~ 5 spikes/s to >120 spikes/s. The determinants of a cell's peak firing rate, and the role served by having cells with different characteristic peak firing rates are not known.

The preferred firing direction of a HD cell is controlled by a number of different cues. These cues can come from external or *allothetic* sources (e.g. visual, auditory, somatic) or internal or *idiothetic* sources (e.g. vestibular, proprioceptive, motor efference copy). For example, rotation of a salient visual landmark will lead to a corresponding shift in the preferred firing direction of HD cells, indicating that they can be controlled by landmarks (Taube *et al.*, 1990b; Taube, 1995). However, removing the visual cues or turning off the lights does not lead to a change in cell activity although the preferred firing direction may drift after some time (Taube *et al.*, 1990b; Goodridge *et al.*, 1998). Thus, the preferred firing direction of HD cells can be maintained purely via idiothetic information as the animal moves in its environment. Furthermore, firing at the peak rate may continue indefinitely even when the rat remains motionless, with very little adaptation. This combination of characteristics – that HD cells are clearly responsive to external cues and dynamic self-motion information, yet at the same time may continue to fire in the absence of visual or auditory stimulation, motor signals, or vestibular modulation – identifies HD cells as exemplars of persistent neural activity. This article will explore how the persistent activity observed in HD cell firing is generated from known sensory inputs and will raise key issues that remain to be elucidated. For other reviews of HD cell activity see Taube (1998), Sharp *et al.* (2001a) and Brown *et al.* (2003). The extent to which HD cell activity is important in spatial and navigational tasks was recently reviewed by Muir and Taube (2002a).

Brain Areas that Contain HD Cells

HD cells were originally discovered in the rat dorsal presubiculum (often referred to as postsubiculum) (Fig. 1A) (Ranck, 1984; Taube *et al.*, 1990a), but have been identified in other brain areas of the classical 'Papez circuit'. These areas include the anterior dorsal thalamic nucleus (ADN) (Fig. 1B), lateral mammillary nuclei (LMN) (Fig. 1C) and retrosplenial cortex (both granular and agranular regions) (Chen *et al.*, 1994; Taube, 1995; Stackman and Taube, 1998; Cho and Sharp, 2001). HD cells have also been identified in significant numbers in the lateral dorsal thalamus and dorsal striatum (Mizumori and Williams, 1993; Wiener, 1993). Other areas where they have been reported in smaller numbers include the medial prestriate cortex, medial precentral frontal cortex, CA1 hippocampus, and the dorsal tegmental nucleus (DTN) (Chen *et al.*, 1994; Guazzelli *et al.*, 2000; Leutgeb *et al.*, 2000; Sharp *et al.*, 2001b). HD cells have been primarily studied in rats, but have also been identified in the ADN of mice and chinchillas (Khabbaz *et al.*, 2000; Muir

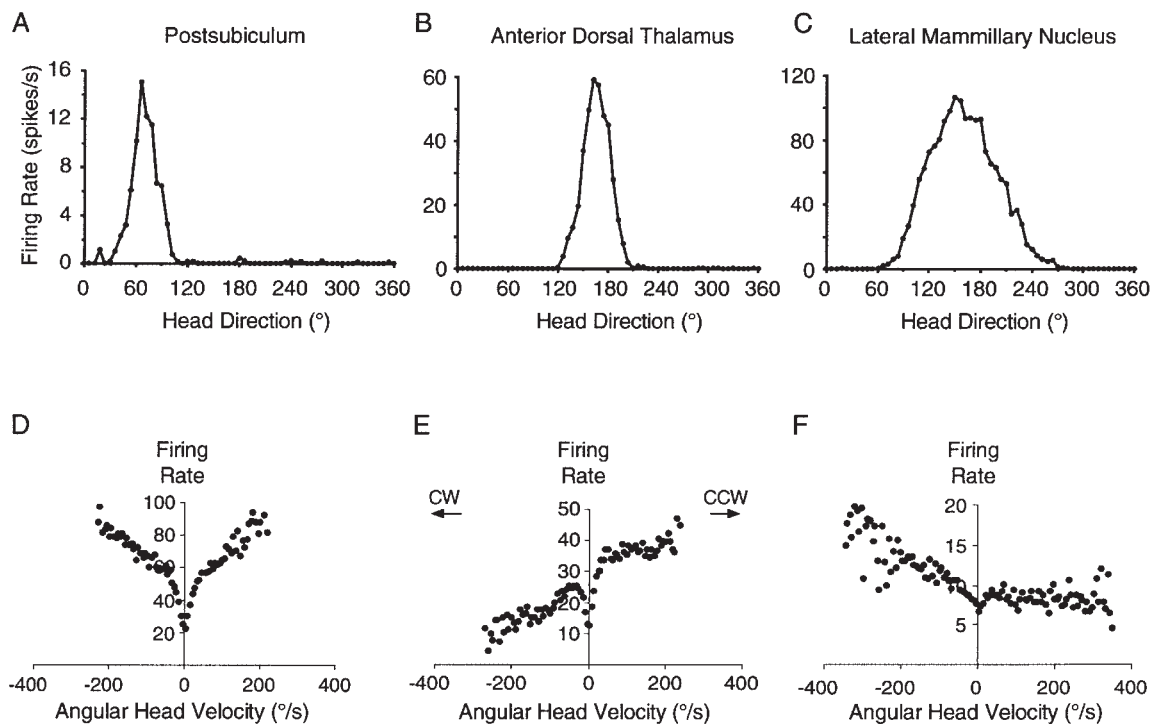


Figure 1. Representative HD cell and angular head velocity cell tuning curves. Data for these cells was recorded over 8 (HD cells) or 16 min (angular head velocity cells) sessions while the rat foraged for randomly placed food pellets about the floor of a cylindrical enclosure. (A–C) HD cell tuning curves for three different cells. Note that each cell has a different peak firing rate and preferred firing direction. The cell in C has a larger directional firing range compared to the other two cells. Cells were recorded in (A) postsubiculum, (B) anterior dorsal thalamus and (C) lateral mammillary nucleus. Ordinate for (B) and (C) are as noted in (A). (D–F) Different types of angular head velocity cells recorded in the dorsal tegmental nucleus. (D) Symmetric angular head velocity cell. Note that firing rate increases linearly as a function of angular speed for both clockwise (CW) and counter-clockwise (CCW) head turns. (E) Asymmetric angular head velocity cell. Note that except for very slow angular head velocities ($<12^\circ/\text{s}$) firing rate is proportional to head turning speed for both CW and CCW directions, but that firing rate increases for faster head turns in only one direction (CCW) and decreases for faster head turns in the opposite direction (CW). Nonetheless, the gain in firing rate is similar for both turn directions. (F) Asymmetric angular head velocity cell. Note that the firing rate is proportional to head turning speed in only one direction (CW) and is not influenced by head turning speed in the opposite direction (CCW). This cell thus has unequal gains in firing rate. CW and CCW directions for (D) and (F) are as noted in (E).

and Taube, 2002b), and in the presubiculum of monkeys (Robertson *et al.*, 1999). The latter study with monkeys showed that HD cell activity was not dependent on eye movements or where the monkey was directing its gaze. Of the quantitative analyses that have been conducted on HD cells across different brain areas, the tuning curves are remarkably similar, although there are some differences. For example, LMN HD cells tend to have broader directional firing ranges and ADN HD cells tend to have higher peak firing rates. In addition, many LMN cells are modulated by turn direction, that is, they exhibit higher peak firing rates for head turns that pass through the preferred direction in one direction of turn as opposed to the opposite turn direction (Stackman and Taube, 1998).

The percentage of cells that are classified as HD cells varies among different areas. No brain area contains solely HD cells. They are most abundant in the ADN where about 60% of the cells exhibit directional firing (Taube, 1995). The percentage of HD cells in other brain areas are estimated to be as follows: postsubiculum, 25% (Taube *et al.*, 1990a); LMN, 25% (Stackman and Taube, 1998); retrosplenial cortex, 10% (Cho and Sharp, 2001); lateral dorsal thalamus, 30% (Mizumori and Williams, 1993); striatum, 6% (Mizumori *et al.*, 2000). Because the ADN contains such a high percentage of HD cells, it might be interesting to consider how many total HD cells are present within this nucleus. Since each population of ADN HD cells potentially constitutes a complete representation of 360° of space, knowing

the absolute number of cells in this population may set useful constraints for modeling how directionally selective networks arise and behave. We therefore estimated the number of cells in the rat ADN by estimating the neuronal density in one coronal brain section stained with thionin at -1.35 mm posterior to bregma. Neurons occupied $\sim 51.6\%$ of tissue space. We then estimated the total volume of ADN based on the cross-sectional area through seven equally spaced $30 \mu\text{m}$ sections and calculated the total number of cells based on the average neuronal density. With a total volume of $145.81 (10^6) \mu\text{m}^3$ and an average cell volume of $3900 \mu\text{m}^3$ we estimate that the total number of neurons in the ADN is $\sim 19\,307$. If 60% of the cells in this nucleus are classified as HD cells, then there are $\sim 11\,584$ total HD cells in the ADN on one side of the brain. While this number should be viewed as a rough estimate, it nonetheless provides a starting point for constructing realistic network models concerned with HD cell discharge.

Mulders *et al.* (1997) estimated the number of cells in layers II/III of the rat presubiculum to be 334 000 and estimated the number of cells in layers V/VI of combined presubiculum + parasubiculum to be 218 000. Using these values, we estimate the total number of cells in the postsubiculum (the dorsal portion of presubiculum) to be $\sim 227\,000$ and if 25% of these cells are classified as HD cells, then there are $\sim 56\,750$ HD cells in the postsubiculum. Table 1 summarizes these estimates.

Table 1

Estimated percentage and number of HD and angular head velocity (AHV) cells across different brain areas

| Brain area | Total cell number | Percentage of HD cells | Percentage of AHV cells | Number of HD cells | Number of AHV cells | References |
|---------------------------------|----------------------|------------------------|-------------------------|--------------------|---------------------|---|
| Dorsal tegmental nucleus (DTN) | 1830 | 0 ^a | 75 | 0 | 1370 | Bassett and Taube (2001a) |
| | | 12.5 ^a | 83 | 230 | 1520 | Sharp <i>et al.</i> (2001b) |
| Lateral mammillary nuclei (LMN) | 4260 | 25 | 44 | 1060 | 1660 | Stackman and Taube (1998) |
| Anterior dorsal thalamus (ADN) | 19 300 | 60 | – | 11 600 | – | Taube (1995) |
| Postsubiculum (PoS) | 227 000 ¹ | 25 ² | 10 ³ | 56 750 | 22 700 | ¹ Mulders <i>et al.</i> (1997) |
| | | | | | | ² Taube <i>et al.</i> (1990b) |
| | | | | | | ³ Sharp (1996) |

^aBassett and Taube (2001) did not report any 'classic' HD cells in the DTN, whereas Sharp *et al.* (2001b) reported a small number.

Temporal HD Cell Properties

Interestingly, temporal analyses of HD cells in the ADN, LMN, and retrosplenial cortex reveal that firing parameters for cells in these areas are optimized just before the head reaches the cell's preferred firing direction: peak firing rates are higher and directional firing ranges are narrower. Thus, the cell's activity appears to be anticipating where the head will be in the future. For example, for a cell with a preferred firing direction at 45°, cell firing is highest at directions <45° for CCW head turns and >45° for CW head turns. The amount of anticipation is greatest for LMN HD cells (75 ms, Stackman and Taube, 1998; 40 ms, Blair and Sharp, 1998) and ~25 ms for HD cells in the ADN and retrosplenial cortex (Blair and Sharp, 1995; Taube and Muller, 1998; Cho and Sharp, 2001). In general, HD cells in the postsubiculum neither lag nor anticipate the cell's preferred firing direction. This type of analysis has not been conducted for HD cells in the remaining brain areas where HD cells have been reported. Another analysis that has been conducted for HD cell firing concerns their relationship to angular and linear head velocity. HD cells in the postsubiculum, ADN and LMN discharge at slightly higher rates when the animal moves faster linearly. Similarly, HD cell firing rates in the ADN and LMN, but not in the postsubiculum, are a little higher for faster rotational head turns through the cell's preferred firing direction, although angular head velocity only accounts for ~1% of the firing rate variance (Taube *et al.*, 1990a; Taube, 1995; Stackman and Taube, 1998; Taube and Muller, 1998).

Generation of the HD Cell Signal

Most work that has investigated how HD cell activity is generated has focused on brain areas within the Papez circuit. Figure 2 shows a mid-sagittal view of a rat brain indicating major areas where HD cells have been identified and the major connections between these areas. Many of these areas are interconnected, which complicates understanding how the signal is generated. However, lesion studies have begun to unravel how the directional signal is processed. Importantly, permanent lesions of the vestibular labyrinth abolish HD cell activity in the ADN (Stackman and Taube, 1997). Similarly, intratympanic injections of tetrodotoxin into the middle ear inactivate the vestibular hair cells for ~48 h and abolish directional activity in postsubiculum HD cells (Stackman *et al.*, 2002). With both types of lesions, the background activity of HD cells increases compared to pre-lesion controls. In addition, non-HD cells in the ADN are

observed to burst periodically. This bursty activity is not observed in intact animals and HD cells in lesioned animals do *not* become bursty following the lesions. We will return to this point below as it has important implications for models that use attractor networks to simulate HD cell activity. The absence of directional firing is all the more surprising when considering two points: (i) the presence of familiar landmark cues, normal motor/proprioceptive cues, and optic flow are insufficient to generate directional activity, even though HD cells are known to be responsive to these cues (Taube *et al.*, 1990b; Blair and Sharp, 1996; Stackman *et al.*, 2003) and (ii) tonic firing returns to secondary vestibular neurons in the vestibular nuclei, reaching 50% of normal rates within 24 h, and recovering to pre-lesion rates by one week following the labyrinthectomies (Ris and Godaux, 1998). Although it is not clear what mechanisms contribute to the return of the resting discharge rate in vestibular neurons, these observations clearly indicate that the generation of the directional activity is *not* due to the tonic firing of vestibular neurons.

If an intact vestibular system is essential for establishment of HD firing then lesions of structures in between the vestibular nuclei and postsubiculum should interfere with directional activity in rostrally-projected areas. This notion follows from the observation that, in general, there appears to be a hierarchical processing of information as it flows from the vestibular nuclei to the postsubiculum, making synaptic connections in the nucleus prepositus (nPH) → DTN → LMN → ADN → postsubiculum (see Fig. 2) (Sripanidkulchai and Wyss, 1986; Liu *et al.*, 1984; Shibata, 1987, 1992, 1993a; Allen and Hopkins, 1989; Hayakawa and Zyo, 1990; van Groen and Wyss, 1990, 1995; Wyss and van Groen, 1992). There are also additional pathways that add to the complexity of the circuit. As shown in Figure 2, there is a pathway from ADN → retrosplenial cortex → postsubiculum (Sripanidkulchai and Wyss, 1987; Shibata, 1993b, 1994), and a return pathway from the postsubiculum to LMN (Shibata, 1989; van Groen and Wyss, 1990). Not shown in Figure 2 is a pathway from the DTN → interpeduncular nucleus (both directly and indirectly via the habenular nuclei) → DTN (Contestabile and Flumerfelt, 1981; Groenewegen and van Dijk, 1984; Liu *et al.*, 1984; Groenewegen *et al.*, 1986). Although these other pathways can still be considered a part of the overarching hierarchical scheme, the circuit becomes considerably more complex when considering the presence of reciprocal connections between many of these structures (e.g. DTN and LMN; ADN and postsubiculum; retrosplenial cortex and post-

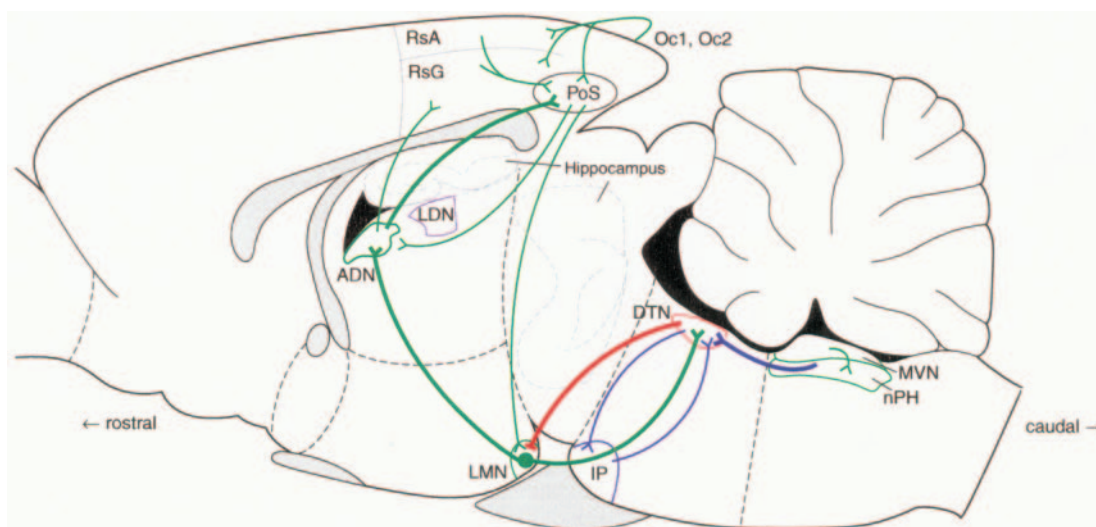


Figure 2. Schematic view of HD cell circuit, sagittal plane. Angular head velocity signals enter the system via vestibular afference to the MVN, conveyed in turn to nPH and then DTN. DTN makes a prominent inhibitory projection to LMN, which makes excitatory projections back to DTN. DTN has a similar connectivity relationship with IP. Single neurons within LMN project both to ADN bilaterally and to DTN ipsilaterally. ADN projects to PoS and RsG. Descending information about landmark cues, particularly visual, most likely enter the HD cell system via projections to retrosplenial cortex and/or PoS from visual cortex (Oc1 and Oc2). This input may then reach subcortical structures through PoS projections to LMN and ADN. Green lines indicate projections known or hypothesized to be excitatory; red lines are inhibitory. Blue lines are unknown. Thick lines denote the hypothesized hierarchical progression in the processing of the HD cell signal — from DTN to PoS. Subdivisions of the DTN and the habenular nuclei, and their respective connections, are not shown. (Abbreviations: ADN, anterodorsal thalamic nucleus; DTN, dorsal tegmental nucleus of Gudden; IP, interpeduncular nucleus; LDN, laterodorsal thalamic nucleus; LMN, lateral mammillary nucleus; MVN, medial vestibular nucleus; nPH, nucleus prepositus; Oc1, primary visual cortex; Oc2, secondary visual cortex; PoS, postsubiculum; RsA, agranular retrosplenial cortex; RsG, granular retrosplenial cortex.) The sagittal diagram is modified from Paxinos and Watson (1998).

subiculum), as well as descending connections from the postsubiculum to LMN. Importantly, the pathway from DTN → LMN is inhibitory and uses GABA as a neurotransmitter (Gonzalo-Ruiz *et al.*, 1993; Wirtshafter and Stratford, 1993). Commissural projections further complicate the connectivity as crossing fibers connect both the postsubiculum and the DTN to their respective contralateral counterparts, and the LMN sends a significant projection to the contralateral ADN, in addition to its ipsilateral projection. Finally, there is a distinct segregation of connectivity among the subdivisions of the DTN, with the ventral division, or pars centralis, bearing a prominent reciprocal connection with the LMN, and the dorsal division, or pars pericentralis, containing a parallel reciprocity with the interpeduncular nucleus (Hayakawa and Zyo, 1990). Visual information concerning landmarks is believed to originate in secondary visual areas (Oc2M, Oc2L) and projects to the HD cell network either directly to postsubiculum, or indirectly through the retrosplenial cortex (Vogt and Miller, 1983). The directional signal is thought to be conveyed to the hippocampus via postsubicular projections to the superficial layers of entorhinal cortex (Shiple, 1975; van Groen and Wyss, 1990). Taken together, what first appears as a simple circuit is actually a highly complex circuit with many reciprocal connections and side pathways. This situation makes it difficult to decipher how the HD cell signal is processed and what physiological role each brain area serves.

To date, all lesion studies are consistent with this hierarchical processing scheme. Lesions of the ADN abolish directional tuning in the postsubiculum, but not the reverse (Goodridge and Taube, 1997). Bilateral, but not unilateral, lesions of the LMN abolishes HD cell activity in the ADN (Tullman and Taube, 1998; Blair and Sharp, 1999). The primary projections to the LMN originate in the DTN and lesions of this structure abolish directional

firing in the ADN (Bassett and Taube, 2001b). Lesions in other brain areas that either contain HD cells, or have intimate connections with ADN, do not abolish the directional signal. Thus, lesions of the hippocampus, lateral dorsal thalamus, or retrosplenial cortex do not disrupt the directional-specific firing of cells in ADN (Golob and Taube, 1997; Golob *et al.*, 1998; Bassett and Taube, 1999). Preliminary studies also indicate that lesions of the posterior parietal cortex do not abolish HD cell activity in ADN (Calton and Taube, 2001). Together with the results from the labyrinthectomies, these lesion studies clearly indicate that subcortical sites are critical for the generation of HD cell activity in limbic system areas.

What types of signals are important for generating HD cell activity? For the most part, HD cells appear confined to rostral areas within the brain including diencephalic and telencephalic structures. But the generation of the directional signal stems from areas within the brainstem that contain cells that are sensitive to the animal's angular head velocity — most notably the DTN and nPH. Except for a few cells that were sensitive to directional heading, the most common neural correlate for DTN cells was angular head velocity, with ~75% of the cells sensitive to this parameter (Bassett and Taube, 2001a; Sharp *et al.*, 2001b). Bassett and Taube (2001a) observed two different types of angular head velocity cells. One type increased its firing rate proportionately to the speed to which the animal turned its head in either direction — clockwise or counter-clockwise (Fig. 1D). These cells were referred to as symmetric angular head velocity cells and accounted for almost 50% of the total cells in the DTN. The firing rate of the second type was positively correlated to the speed at which the animal turned its head, but only in one turn direction. Turning in the opposite direction led either to no change (Fig. 1F) or a decrease in the cell's activity (Fig. 1E). These cells were referred to as asymmetric angular head velocity

cells and composed ~25% of the DTN population. Most, but not all, asymmetric cells were localized to the hemisphere opposite the preferred turning direction. The firing of about half of the angular head velocity cells, both symmetric and asymmetric, was also modulated by the animal's linear velocity, although no cell's firing rate correlation to linear velocity exceeded its correlation to angular head velocity.

Vestibular nucleus neurons are often classified by their pattern of firing when the head is stationary (Goldberg and Fernández, 1971). Regular firing neurons discharge in a regular, periodic pattern with a fixed interspike interval. In contrast, irregular firing neurons discharge more variably with no definitive peak in the interspike interval histogram. Both symmetric and asymmetric angular head velocity neurons in the DTN were found to contain irregular discharge patterns.

Angular head velocity neurons are also found in the LMN where they constitute ~43.7% of the cells (Stackman and Taube, 1998; Bassett and Taube, 2001a). Both symmetric and asymmetric cells are found within the LMN (termed 'fast' angular head velocity cells and compose 52.5% of the angular head velocity cells), in addition to a third type of angular head velocity cell, where firing rate is negatively correlated with the speed of head turn for both turn directions. These latter cells are referred to as 'slow' angular head velocity cells and were not observed in the DTN. These slow angular head velocity cells accounted for 47.5% of the angular head velocity cells within LMN. In general, the properties of fast LMN angular head velocity cells are similar to those in the DTN, although the correlation to angular head velocity is not as tight in the LMN compared to the DTN. Furthermore, the slope of the relationship between firing rate and angular head velocity is steeper for DTN than LMN cells. Finally, the firing of ~10% of the cells in the postsubiculum was correlated to angular head velocity – all the cells were classified as the asymmetric type (Sharp, 1996).

Cell count analyses for LMN and DTN similar to those used above for ADN resulted in a total of 4256 and 1832 cells for each area, respectively. These values indicate that LMN contains ~1064 HD cells, 979 fast angular head velocity cells, and 881 slow angular head velocity cells. The DTN contains ~916 symmetric and 458 asymmetric angular head velocity cells. The number of HD cells estimated for LMN compared to ADN – on the order of 1000 versus 10 000 – raises an interesting question: if the directional signal is already generated at the level of the LMN, then what function is served by having a tenfold increase in the number of cells encoding directional heading at the next rostral brain site?

Active versus Passive Motion

Recent studies in the vestibular field show the importance of observing cell firing when an animal is actively moving as opposed to passively turned. Vestibular nucleus neurons discharge in relation to angular head velocity for brief rotations when the animal is passively turned back-and-forth in a sinusoidal manner. Yet, when the animal initiates similar movements voluntarily, neuronal responses are severely attenuated (McCrea *et al.*, 1999; Roy and Cullen, 2001). The response of HD cells to similar passive rotations is more complex. If the animal is restrained tightly by wrapping it in a towel, direction-specific cell firing usually ceases (Taube, 1995). However, if the animal is restrained loosely by holding it in the experimenter's cupped hands, then directional cell firing persists but at a reduced rate

(Taube *et al.*, 1990b). Zugaro *et al.* (2001) reported similar results for animals that were passively rotated on a turntable. If firing of second order vestibular neurons is attenuated during active motion then these vestibular signals would be 'turned off' when the animal is in the freely-moving condition, and one might expect less influence from these neurons than other types of inputs, such as motor or visual cues, during active motion. On the other hand, a paradox arises from the finding that vestibular input is essential for establishing the directional signal.

How these seemingly disparate findings are to be resolved is presently unclear. It is possible that the angular head velocity signals in DTN represent motor and/or proprioceptive information rather than processed vestibular signals. The importance of motor/proprioceptive cues to HD cell discharge has to date been underestimated. Its importance is supported by recent findings showing that vestibular inputs were insufficient to maintain a HD cell's preferred firing direction when the animal was passively transported to a novel environment in the dark – active locomotion between the familiar and novel environments did not lead to this shift in the cell's preferred direction (Stackman *et al.*, 2003). Passive transportation to the novel environment would have activated the vestibular system without normal motor inputs. Other findings supporting a role for motor cues are the anticipatory properties of HD cells discussed above. These properties are more easily accounted for by motor/proprioceptive cues rather than vestibular or other sensory cues. In addition, it is clearly evident that the angular head velocity signals in the DTN have been highly processed because all angular velocity signals in the vestibular nucleus are of the asymmetric type (respond to head turns with increased firing in one direction and decreased firing in the opposite direction) whereas a significant portion of the neurons in the DTN show symmetric characteristics (respond with increased firing in both turn directions). In sum, motor and/or proprioceptive inputs are important contributors to the HD cell signal.

For these reasons it would be interesting to know how angular head velocity signals in the DTN or LMN respond to passive rotations. Would their firing remain robust as in the second order vestibular neurons or would their firing be attenuated similar to HD cells? The one study that addressed this issue examined passive rotations for 12 angular head velocity cells in the DTN and obtained mixed results (Sharp *et al.*, 2001b). Most cells became quiescent or lost their angular head velocity correlate during the passive rotations while only a few cells maintained their angular velocity correlates. These results emphasize the importance of motor cues for many of the DTN cells and provide further support for the notion that motor cues play an integral role in HD cell firing.

Modeling the HD Signal Using Attractor Networks

How angular head velocity signals in the DTN and LMN are processed and transformed into a signal yielding directional heading is one of the central issues in this field. Whether the persistent activity of HD cells arises from intrinsic cellular mechanisms or from network properties that emerge out of a population of these cells is not known. However, because the HD cell signal is so robust, with signal-to-noise ratios frequently over 100:1, it is an ideal signal to model using computational neural networks. Several models have been proposed and although it is beyond the scope of the present review to discuss all of them, each one shares one central feature in common: they all use attractor

network dynamics to generate the directional signal (Skaggs *et al.*, 1995; Redish *et al.*, 1996; Sharp *et al.*, 1996; Zhang, 1996; Goodridge and Touretzky, 2000; Xie *et al.*, 2002). This network contains a one-dimensional, continuous ring of HD cells that are interconnected with both excitatory and inhibitory connections. Each HD cell in the ring is tuned to a different directional heading. Cells with overlapping directional firing ranges are linked with excitatory connections, whereas cells with preferred firing directions far apart inhibit one another. This type of network architecture will force neural activity within the network to converge into a 'hill' of excitation that corresponds to one head direction. This hill can then be moved around to different directional headings depending on external influences, such as inputs from vestibular, motor or visual landmark cues.

This type of network architecture is particularly suitable for modeling the HD signal because attractor networks are generally stable and do not require external inputs to maintain their stable state. Instead, the external inputs function to move the hill to a new stable state when the animal turns its head. Attractor networks are also capable of performing a mathematical integration in time. Again, this is an attractive characteristic because 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. According to this view, the synaptic connections between different HD cells would maintain a stable state when the head is fixed. When the head moves, an angular head velocity signal from either vestibular or motor inputs would be integrated in time by the attractor network and move the activity hill to a new stable state. The amount the hill moves corresponds to the amount the head is displaced which is the integral of the angular head velocity signal. The activity of the hill is sustained (i.e. no adaptation of firing) either through the tonic firing of excitatory afferents in the recurrent network or by the internal membrane properties of the cells. In either case, once the new hill of activity is initiated it is maintained indefinitely until the next perturbation. Attractor network dynamics can also account for the slightly higher firing rates seen for faster head turns in LMN and ADN HD cells (Goodridge and Touretzky, 2000).

While attractor networks are appealing models for generating the HD cell signal they must be able to fulfill several experimental conditions in addition to satisfying the basic firing properties described above:

1. Removing external inputs will cease direction-specific firing in HD cells in 'downstream' brain areas. This condition follows from the finding that peripheral vestibular lesions abolish HD cell activity in the ADN and postsubiculum (Stackman and Taube, 1997; Stackman *et al.*, 2002). Thus, despite the fact that these vestibular effects are several synapses removed from the ADN, these vestibular lesions have a major impact on HD cell firing such that the activity hill is abolished. Presumably, the HD cell signal is also absent in LMN, although this has never been tested experimentally. Whether an angular head velocity signal is still present in DTN is also unknown. Most attractor networks that have been proposed for generating HD cell activity are designed in a way that removal of external inputs will not disrupt the activity hill. This condition follows from the fact that the hill

is derived through local interconnections within a single brain area [or connections across two areas as is the case for the Redish *et al.* (1996) model] and external inputs are only used to modulate or update the signal by moving the activity hill around. Thus, removal of external inputs will leave the activity hill either (i) stationary, where a subset of the neuronal population will be tonically active; or (ii) unstable such that it will continuously drift. In the latter condition, we would expect HD cells to show periodic bursts of activity. These bursts would occur whenever the activity hill passed through the cell's preferred firing direction and the frequency of the bursts would depend on the rate of drift in the activity hill. Note that in both the stationary and drifting cases, though, the activity hill is sustained. Our findings following peripheral vestibular lesions showed that neither of these predictions was borne out. Of eleven recorded HD cells, none of the cells remained tonically 'on' (i.e. activity hill locked in place). With directional firing ranges of 90°, statistics suggest that we should have observed at least two cells with tonic activity. Moreover, none of the 11 cells showed bursting activity. Bursting activity was observed in the ADN, but it was only seen in cells that were subsequently recorded after the lesion, and the authors attributed the bursting activity to the population of non-HD cells in this area. Importantly, while it is possible to design attractor networks that are dependent on external inputs for generating the activity hill, to date, none of the models that have been proposed for HD cell activity satisfy this requirement.

2. Attractor networks are frequently characterized as having activity hills that move to new stable states by transitioning through intermediate states that are in between the initial and final states. In other words, if the hill of activity is at 60° and a head turn results in a new directional heading of 150°, then the hill of activity will briefly pass through all the directional headings in between 60 and 150°. The time spent in these intermediate states may be very short, but nonetheless, some activity may be observed in them. However, attractor networks can be designed such that these intermediate states are not mandatory and the activity hill appears to jump from one state to the next. In this scenario, the activity hill at the initial stable state begins to fade as a new hill forms at a different location on the ring attractor (Samsonovich and McNaughton, 1997; Redish, 1999). This latter type of design is more pertinent for HD cells because sensory cue conflict experiments show that HD cells can change their preferred firing directions rapidly without any evidence that intermediate states were activated during the transition (Goodridge and Taube, 1995; Taube and Burton, 1995). Indeed, Zugaro *et al.* (2003) recently showed that reorientation amongst HD cells can occur as rapidly as 80 ms after a familiar visual landmark appears in the scene.
3. As discussed above attractor networks usually rely on a set of recurrent excitatory connections within the network to sustain the activity hill in a stable state. They also rely on inhibitory connections to attenuate any activity for cells outside the current directional firing range. This architecture is paramount for the attractor network to function properly. However, the existence of these excitatory and inhibitory connections within the ADN or LMN is not readily apparent in the few anatomical studies that have been conducted on these areas. It is possible, however, that this pattern of connectivity exists, but it is spread over multiple brain

areas – in particular, the LMN and DTN. These two areas are attractive candidates because the projection from DTN → LMN is inhibitory while the reciprocal connection is excitatory. Furthermore, larger sized neurons in LMN send projections to both ADN and DTN (Hayakawa and Zyo, 1989), making it easy to imagine LMN HD cells passing directional signals on to their ADN targets while simultaneously inhibiting their out-of-direction neighbors by activating their inhibitory targets in the DTN. Some attractor network models for HD cell activity use two rings of cells (Redish *et al.*, 1996; Xie *et al.*, 2002) or do not rely on recurrent excitatory connections (Rubin *et al.*, 2001).

4. Visual cues must be able to override control of the preferred direction because most experiments have shown that prominent visual landmarks can control the preferred direction, even when its spatial information conflicts with the on-going spatial information derived from motor and vestibular cues (Goodridge and Taube, 1995; Taube and Burton, 1995; Blair and Sharp, 1996; Zugaro *et al.*, 2000). The model proposed by Skaggs *et al.* (1995) theoretically showed how visual inputs could override the internal attractor dynamics, although this model was not formally tested. Subsequent models have usually not addressed this issue as they have been more concerned with addressing the internal dynamics of how the activity hill is generated and moved around following head turns (e.g. Redish *et al.*, 1996; Sharp *et al.*, 1996; Zhang, 1996).
5. In designing a network model that simulates the neural processing between LMN and DTN, the network should contain both symmetric and asymmetric angular head velocity cells in DTN and fast and slow type angular head velocity cells in the LMN. This requirement follows from the relative abundance of these cell types in the two nuclei.

Key Information Needed

There are several areas where key information is needed that would aid understanding of how the HD cell signal is processed. Foremost among these areas is a better understanding of the internal circuitry for each of the brain areas where HD cells are present. Whereas researchers have a good understanding of how the areas containing HD cells are interconnected, little is known about the microcircuitry for these brain areas. Anatomical and electrophysiological techniques are available that could provide important new information. For example, the extent of recurrent excitation or inhibition among individual neurons within a brain region could be determined by using electrophysiological recordings in brain slices. Anatomical techniques could uncover whether the projections from nucleus prepositus → DTN are excitatory or inhibitory. In the future it would be nice to determine how HD cells within one brain area are interconnected with each other as well as to other nearby non-HD cells.

Each of the brain areas where HD cells are present contains many neurons that are not characterized by direction-specific firing. What is the role of these neurons? Are they interconnected with the local HD cells? Are angular head velocity cells within the LMN interconnected with HD cells in this same area? Is the connection only one way or is it reciprocal? Moreover, are all three types of angular head velocity cells within LMN (fast symmetric, fast asymmetric, slow) connected with the HD cells? Which types of DTN angular head velocity cells (symmetric or asymmetric) project to LMN? Finally, what cell types project

back to DTN – is it the HD cells or is it angular head velocity cells, and if the latter, which type of angular head velocity cells? It is known that the LMN cells that project to the ADN are the same cells that project back to the DTN (Hayakawa and Zyo, 1989). As one can see, these are all important anatomical questions that must be addressed if researchers want to model the generation of the HD cell signal accurately.

An even more fundamental issue is whether the HD cells in postsubiculum, ADN, and LMN project directly to their principal target regions – namely the entorhinal cortex, postsubiculum and ADN, respectively. While it is assumed that HD cells are the projection cells in these brain areas, there is no direct evidence supporting this notion, and it is quite possible that non-HD cells in these areas are the projection neurons. Simultaneous recording of a HD cell while trying to stimulate it antidromically from a downstream projection area could provide information on this important issue. In addition, as mentioned above, peripheral vestibular lesions abolish the direction-specific activity of HD cells. How these lesions influence the angular head velocity cells in the DTN and LMN is not known. Addressing this issue would provide important information on how HD cell information is processed.

Comparison to the Oculomotor System

Finally, in formulating critical questions for future research on head direction cells, it may help to consider the analogy between the activity of HD cells and that of neurons in another system that has the benefit of many more years of empirical study and modeling. The oculomotor integrator, like the HD cell system, has been identified as an example of persistent neural activity, and has been modeled as a continuous attractor (e.g. Anastasio, 1998; Seung *et al.*, 2000). The two systems share a number of other relevant features, such as some overlapping neural circuitry (i.e. the nucleus prepositus), an interaction between visual and vestibular afference in the case of reflexive (non-saccadic) eye movements, and most importantly, some common computational ends.

Oculomotor integrator neurons have been observed in both mammals (Lopez-Barneo *et al.*, 1982; McFarland and Fuchs, 1992) and fish (Pastor *et al.*, 1994); they discharge linearly as a function of eye position, with higher firing rates reached at more eccentric positions in the orbit. Bursting inputs to the integrator neurons correspond to motor signals that drive movement of the eye, while sustained firing persisting at a constant rate corresponds to the integrated position signal (Robinson, 1989). At this level, there is a clear parallel between the excitatory or inhibitory bursts that drive oculomotor integrator neurons to higher or lower persistent firing rates, and putative bursts of clockwise or counterclockwise vestibular modulation signaling angular head velocity that forces the activity hill around a HD cell ring attractor. This parallel makes clear several critical comparisons between the two systems.

In the oculomotor integrator, a single neuron may vary its firing rate linearly with eye position and will not fire at all below a threshold position. HD cells fire linearly as a function of angular displacement from the preferred firing direction and will cease firing beyond a threshold angle that corresponds with the directional firing range. As with the peak firing rate and the directional firing range of HD cells, the slope of firing rate to position and the positional threshold of oculomotor integrator neurons vary from one neuron to another. A property of oculo-

motor integrator neurons that is useful for experimental purposes is that they are not perfect; there is a tendency to 'leak' in these imperfect integrators. An animal attempting to hold an eccentric eye position in the dark (thereby having no visual stimuli to direct gaze) will inevitably exhibit a slow drift of the eye back toward a neutral position in the orbit, often referred to as the zero point. This neutral position is determined by the alignment and elasticity of the eye muscles. The drift in eye position toward 'orbit-zero' correlates to a decline in the firing rate of the oculomotor integrator neurons according to a characteristic time constant. As the eye continues to drift, the oculomotor neurons reach quiescence below their positional thresholds.

HD cells, in contrast, do not have a clearly identifiable directional zero. If we are to continue the analogy between the two systems further, then an important question is whether the neural integrator in the HD system is perfect or imperfect. Clearly, the HD cell system does not have the same physical constraints as the oculomotor system, which requires mechanisms to overcome the elastic properties of the eye muscles and the viscous drag of the orbit. Since the HD cell network is not considered a motor system controlling head movement, there is no *a priori* reason for why the HD cell system could not contain a perfect integrator. On the other hand, if the integrator is imperfect, then how are we to conceptualize leak in the HD cell system? In the oculomotor system, leak corresponds both to a decline in firing rate, and movement of the eye toward zero, and the two are closely correlated because they are causally related. The firing rate of a HD cell and its preferred firing direction do not have such a clear relationship. In fact, if one were to record a declining firing rate from a single HD cell, it would be impossible to distinguish between movement of the activity hill away from the cell's preferred firing direction and decay of activity in the system overall, yet leak in the HD integrator could be conceptualized as taking either of these two forms.

When HD cells are recorded in the dark, the preferred firing directions often drift continuously over several min (Goodridge *et al.*, 1998). This drift in preferred firing direction is reminiscent of the drift of the eye in the dark from an eccentric to a central position, and suggests a failure of an integrator in the HD cell network. Thus, the eventual outcome of leak in the HD cell system might be an activity hill drifting freely with respect to the animal's actual directional heading. To test this hypothesis, we would want to record HD cells in the dark while the animal is immobile, pointing in the direction of a recorded cell's preferred firing direction. If the cell continues to fire indefinitely at its peak rate, then the integrator is perfect. If, over time, the peak firing rate of the cell declined, and the firing rate of a cell with a different preferred firing direction increased, then we could conclude that leak in the HD cell system results in drift of the directional signal (Fig. 3A). But should such a drift be thought of as 'leak'? It could be, from the standpoint of the single HD cell being monitored. In this scenario, after a head turn, the cell loses its activation in the absence of visual or vestibular information. On the other hand, what makes it unlike an oculomotor integrator neuron is that the activation is preserved elsewhere in the network, so as the firing rate declines in one cell, it must increase in another by virtue of the network connectivity. The 'zero point', then, would correspond to a state of constant instability of the activity hill, driven simply by the aggregation of small asymmetries in the velocity input

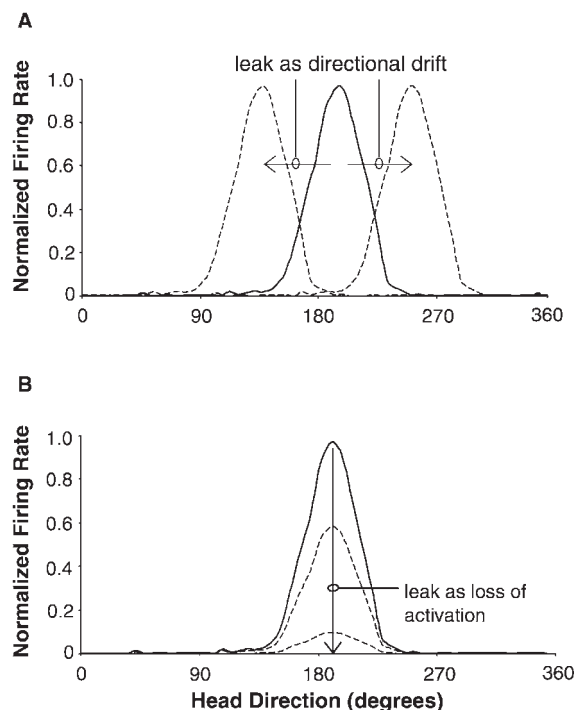


Figure 3. Alternate conceptions of leak in the HD cell system. Idealized HD cells are shown as if recorded during the hypothetical experiment described in the text. (A) Leak as directional drift. Firing rate is unchanged; preferred firing direction is initially stable (solid line) but drifts over time randomly with respect to head direction (dashed lines). Leak occurs on a cellular level but activity is preserved within the network. (B) Leak as loss of activation. Preferred firing direction remains stable (solid line) but firing rate declines gradually toward baseline (dashed lines). Loss of activation in the cell reflects loss of activation network-wide. Note that simultaneous recording from multiple cells is required to distinguish between (A) and (B). See text for detailed discussion.

while the head is motionless, rather like an eye suddenly cut free from the ocular muscles and left to drift in the socket. Furthermore, drift of the activity hill would imply that the persistent activity observed in HD cells is attributable primarily to the internal connectivity of the HD network, rather than depending upon extrinsic excitation, since some signal would persist even with no afferent input.

Alternatively, if in the same scenario directional firing failed over time in one HD cell without a corresponding increase in firing elsewhere in the HD network, then leak would be evident as a decrease in the firing rate of the cell towards its baseline firing rate, without a shift of the activity peak, implying an overall loss of activity in the network (Fig. 3B). This finding would show that persistent activity depends upon either intrinsic membrane properties of the HD cells, or excitatory input originating outside the system. Some models of oculomotor integration employ three mechanisms to account for the persistent neural activity: (i) saccadic bursts, originating outside the attractor network that drive the integrator signal from zero; (ii) a cellular time constant intrinsic to the integrator neurons; and (iii) the network connections that prolong the cellular time constant (Anastasio, 1998; Seung *et al.*, 2000). Unless we define a zero for HD cells that corresponds to the central position in the oculomotor integrator, from which a time constant of decay can be derived, the relative contribution of each mechanism is untestable using the methods employed for investigating the oculomotor integrator. Although firing rate adaptation has been

examined over relatively short time periods (Taube and Muller, 1998), the experiment described above for holding the head still over long periods remains to be done, and the previously described effects of restraint may make it difficult to execute. Unpublished observations, however, suggest a time constant for HD cells orders of magnitude longer than those for oculomotor integrator or vestibular neurons.

The results from vestibular lesion studies imply that the role of the vestibular system goes beyond moving the hill of activity around the network. It indicates that the vestibular system is particularly involved in driving the generation and persistence of the HD cell signal. If this situation is true, then a HD cell firing constantly in its preferred firing direction following a head turn may be seen as the integration of the velocity signal that corresponds to the head turn, just as the position-related firing of the oculomotor integrator neuron represents the integration of the velocity-related saccadic burst that moved the eye to its new position. It should be noted that when a rat is motionless and the head is at zero angular velocity, there is still a strong signal that could feed forward onto the HD cell network because of the tonic high firing rates in neurons within the vestibular nuclei. This condition is in contrast to the situation following labyrinthectomies when the activity hill in the attractor network has permanently broken down despite the eventual recovery of tonic firing rates within the vestibular nuclei (Stackman and Taube, 1997; Ris and Godaux, 1998).

Oculomotor integrator neurons continue to fire while holding the eye in an eccentric position, but some authors have postulated another type of integrator that resets to zero at the completion of each saccade (Jurgens *et al.*, 1981; Kustov and Robinson, 1995). In these models, a velocity-to-displacement integration occurs, but the eye displacement signal resets to zero immediately after each saccade by a rapid leak, so that the next saccade can be coded in terms of displacement from the current position. If an updated directional signal following a head turn is the result of an integration of angular velocity over time, then the HD cell system may also be comparable to the resettable displacement integrator in models of saccadic eye movements. Thus, each stable head position becomes a relative zero point to which the next integrated displacement is added when the head turns. In the light, resetting may be caused or facilitated by visual feedback from the environment. In the dark, the successive addition of displacement values without visual feedback may be responsible for the accumulation of error and observed as the preferred firing direction drifting in the dark. This suggestion is intriguing because it implies that a memory of the previous head direction is briefly preserved in the network, and is compared to a representation of desired head direction, an idea that is notable in light of the anticipatory firing properties of HD cells in the LMN and ADN (Blair and Sharp, 1995; Taube and Muller, 1998). As a measurable phenomenon, leak in this case would be altogether different than in our previous comparison and would not be evident in the firing activity of an isolated HD cell. In our postulated experiment described above, if the head were fixed in the dark after a single head turn, we would expect the HD integrator to reset to zero at the new direction and an external perturbation of the system would be required to elicit a drift of the activity hill back toward the original head direction. Such a finding would serve as indirect evidence of an incompletely reset displacement signal.

In addition to the oculomotor integrator and the resettable integrator of the saccade system, there is another example of a

neural integrator that prolongs a velocity signal, in this case one for the angular velocity of head turns. Within the brainstem circuits that mediate vestibular, vestibulo-ocular, and optokinetic reflexes, vestibular signals outlast the afferent signals in the VIIIth nerve. The longer time constant for the decay rate of vestibular signals in secondary vestibular neurons and other brainstem areas, including the nucleus prepositus, is referred to as velocity storage. This process is thought to play an important role in improving the VOR at low frequency (long duration) head turns and also functions to realign the eye movement axes with the direction of the current gravito-inertial acceleration of the organism (Leigh and Zee, 1999). There is also evidence that the vestibular signal subserving the subjective experience of angular velocity is affected by velocity storage (Okada *et al.*, 1999). Thus, one might wonder whether this mechanism makes a similar contribution to the HD cell signal, improving the accuracy of updated heading during low frequency head turns. Experimental manipulations of the velocity storage integrator may produce measurable effects on HD cell activity.

This article has summarized the major properties of HD cell activity. The strength of this signal and the ability to measure it accurately provide an ideal system for understanding how the nervous system processes raw sensory information and transforms it into a high level cognitive signal that encodes the animal's perception of its directional heading in allocentric space. The nature of the HD cell makes it an attractive candidate for using neural network models to elucidate the underlying mechanisms.

Notes

This research was supported by grants from the National Institute of Mental Health (MH48924, MH01286) and the National Aeronautics and Space Administration through the NASA Cooperative Agreement NCC 9-58 with the National Space Biomedical Research Institute. We thank David Zee for helpful comments on portions of this manuscript.

Address correspondence to J.S. Taube, Dartmouth College, 6207 Moore Hall, Hanover, NH 03755, USA. Email: jeffrey.taube@dartmouth.edu.

References

- Allen GV, Hopkins DA (1989) Mamillary body in the rat: topography and synaptology of projections from the subicular complex, prefrontal cortex, and midbrain tegmentum. *Comp Neurol* 286:311-336.
- Anastasio TJ (1998) Nonuniformity in the linear network model of the oculomotor integrator produces approximately fractional-order dynamics and more realistic neuron behavior. *Biol Cybern* 79:377-391.
- Bassett JP, Taube JS (1999) Retrosplenial cortex lesions disrupt stability of head direction cell activity. *Soc Neurosci Abstr* 25:1383.
- Bassett JP, Taube JS (2001a) Neural correlates for angular head velocity in the rat dorsal tegmental nucleus. *J Neurosci* 21:5740-5751.
- Bassett JP, Taube JS (2001b) Lesions of the dorsal tegmental nucleus of the rat disrupt head direction cell activity in the anterior thalamus. *Soc Neurosci Abstr* 27:852.29.
- Blair HT, Sharp PE (1995) Anticipatory head direction signals in anterior thalamus: evidence for a thalamocortical circuit that integrates angular head motion to compute head direction. *J Neurosci* 15:6260-6270.
- Blair HT, Sharp PE (1996) Visual and vestibular influences on head-direction cells in the anterior thalamus of the rat. *Behav Neurosci* 110:643-660.
- Blair HT, Sharp PE (1998) Role of the lateral mammillary nucleus in the rat head direction circuit: a combined single-unit recording and lesion study. *Neuron* 21:1387-1397.

- Blair HT, Cho J, Sharp PE (1999) The anterior thalamic head-direction signal is abolished by bilateral but not unilateral lesions of the lateral mammillary nucleus. *J Neurosci* 19:6673–6683.
- Brown JE, Yates BJ, Taube JS (2003) Does the vestibular system contribute to head direction cell activity in the rat? *Physiol Behav* 77:743–748.
- Calton JL, Taube JS (2001) Head direction cell activity following bilateral lesions of posterior parietal cortex. *Soc Neurosci Abstr* 27:537.30.
- Chen LL, Lin LH, Green EJ, Barnes CA, McNaughton BL (1994) Head-direction cells in the rat posterior cortex. I., Anatomical distribution and behavioral modulation. *Exp Brain Res* 101:8–23.
- Cho J, Sharp PE (2001) Head direction, place, and movement correlates for cells in the rat retrosplenial cortex. *Behav Neurosci* 115:3–25.
- Contestabile A, Flumerfelt BA (1981) Afferent connections of the interpeduncular nucleus and the topographic organization of the habenulo-interpeduncular pathway: an HRP study in the rat. *J Comp Neurol* 196:253–270.
- Goldberg JM, Fernández C (1971) Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. III. Variations among units in their discharge properties. *J Neurophysiol* 34:676–684.
- Golob EJ, Taube JS (1997) Head direction cells and episodic spatial information in rats without a hippocampus. *Proc Natl Acad Sci USA* 94:7645–7650.
- Golob EJ, Wolk DA, Taube JS (1998) Recordings of postsubicular head direction cells following lesions of the lateral dorsal thalamic nucleus. *Brain Res* 780:9–19.
- Gonzalo-Ruiz A, Sanz-Anquela JM, Spencer RF (1993) Immunohistochemical localization of GABA in the mammillary complex of the rat. *Neuroscience* 54:143–156.
- Goodridge JP, Taube JS (1995) Preferential use of the landmark navigational system by head direction cells. *Behav Neurosci* 109:49–61.
- Goodridge JP, Taube JS (1997) Interaction between postsubiculum and anterior thalamus in the generation of head direction cell activity. *J Neurosci* 17:9315–9330.
- Goodridge JP, Touretzky DS (2000) Modeling attractor deformation in the rodent head-direction system. *J Neurophysiol* 83:3402–3410.
- Goodridge JP, Dudchenko PA, Worboys KA, Golob EJ, Taube JS (1998) Cue control and head direction cells. *Behav Neurosci* 112:749–761.
- Groenewegen HJ, van Dijk CA (1984) Efferent connection of the dorsal tegmental region in the rat, studied by means of anterograde transport of the lectin *Phaseolus vulgaris*-leucoagglutinin (PHA-L). *Brain Res* 304:367–371.
- Groenewegen HJ, Ahlenius S, Haber SN, Kowall NW, Nauta WJH (1986) Cytoarchitecture, fiber connections, and some histochemical aspects of the interpeduncular nucleus in the rat. *J Comp Neurol* 249:65–102.
- Guazzelli A, Ragozzino K, Leutgeb S, Cooper BG, Kunz B, Mizumori SJY (2000) Firing correlates of anterior cingulate and medial precentral cortex neurons of the rat. *Soc Neurosci Abstr* 26:473.
- Hayakawa T, Zyo K (1989) Retrograde double-labeling study of the mammillothalamic and the mammillotegmental projections in the rat. *J Comp Neurol* 284:1–11.
- Hayakawa T, Zyo K (1990) Fine structure of the lateral mammillary projection to the dorsal tegmental nucleus of Gudden in the rat. *J Comp Neurol* 298:224–236.
- Jurgens R, Becker W, Kornhuber HH (1981) Natural and drug-induced variations of velocity and duration of human saccadic eye movements: evidence for a control of the neural pulse generator by local feedback. *Biol Cybern* 39:87–96.
- Khabbazi A, Fee1 MS, Tsien JZ, Tank DW (2000) A compact converging-electrode microdrive for recording head direction cells in mice. *Soc Neurosci Abstr* 26:984.
- Kustov AA, Robinson DL (1995) Modified saccades evoked by stimulation of the macaque superior colliculus account for properties of the resettable integrator. *J Neurophysiol* 73:1724–1728.
- Leutgeb S, Ragozzino KE, Mizumori SJ (2000) Convergence of head direction and place information in the CA1 region of hippocampus. *Neuroscience* 100:11–19.
- Lopez-Barneo J, Darlot C, Berthoz A, Baker R (1982) Neuronal activity in prepositus nucleus correlated with eye movement in the alert cat. *J Neurophysiol* 47:329–352.
- Leigh R, Zee DS (1999) The neurology of eye movements. New York: Oxford University Press.
- Liu R, Chang L, Wickern G (1984) The dorsal tegmental nucleus: an axoplasmic transport study. *Brain Res* 310:123–132.
- McFarland JL, Fuchs AF (1992) Discharge patterns in nucleus prepositus hypoglossi and adjacent medial vestibular nucleus during horizontal eye movement in behaving macaques. *J Neurophysiol* 68:319–332.
- McCrea RA, Gdowski GT, Boyle R, Belton T (1999) Firing behavior of vestibular neurons during active and passive head movements; vestibulo-spinal and other non-eye-related neurons. *J Neurophysiol* 22:3077–3099.
- Mizumori SJ, Williams JD (1993) Directionally selective mnemonic properties of neurons in the lateral dorsal nucleus of the thalamus of rats. *J Neurosci* 13:4015–28.
- Mizumori SJY, Ragozzino KE, Cooper B (2000) Location and head direction representation in the dorsal striatum of rats. *Psychobiology* 28:441–462.
- Muir GM, Taube JS (2002a) The neural correlates of spatial navigation and performance: do head direction and place cells guide behavior? *Behav Cogn Neurosci Rev* 1:297–317.
- Muir GM, Taube JS (2002b) Firing properties of head direction cells, place cells, and theta cells in the freely-moving chinchilla. *Soc Neurosci Abstr* 28:584.4.
- Mulders WH, West MJ, Slomianka L (1997) neuron numbers in the presubiculum, parasubiculum, and entorhinal area of the rat. *J Comp Neurol* 385:83–94.
- Okada T, Grunfeld E, Shallo-Hoffman J, Bronstein AM (1999) Vestibular perception of angular velocity in normal subjects and in patients with congenital nystagmus. *Brain* 122:1293–1303.
- Pastor AM, de La Cruz RR, Baker R (1994) Eye position and eye velocity integrators reside in separate brainstem nuclei. *Proc Natl Acad Sci USA* 91:807–811.
- Paxinos G, Watson C (1998) The rat brain in stereotaxic coordinates, 3rd edn. San Diego, CA: Academic Press.
- Ranck JB Jr (1984) Head direction cells in the deep layer of dorsal presubiculum in freely moving rats. *Soc Neurosci Abstr* 10:599.
- Redish AD (1999) Beyond the cognitive map: from place cells to episodic memory. Cambridge, MA: MIT Press.
- Redish AD, Elga AN, Touretzky DS (1996) A coupled attractor model of the rodent head direction system. *Network* 7:671–685.
- Ris L, Godaux E (1998) Neuronal activity in the vestibular nuclei after contralateral or bilateral labyrinthectomy in the alert guinea pig. *J Neurophysiol* 80:2352–2367.
- Robertson RG, Rolls ET, Georges-François P, Panzeri S (1999) Head direction cells in the primate presubiculum. *Hippocampus* 9:206–219.
- Robinson DA (1989) Integrating with neurons. *Annu Rev Neurosci* 12:33–45.
- Roy JE, Cullen KE (2001) Selective processing of vestibular reafference during self-generated head motion. *J Neurosci* 21:2131–2142.
- Rubin J, Terman D, Chow C (2001) Localized bumps of activity sustained by inhibition in a two-layer thalamic network. *J Comp Neurosci* 10:313–331.
- Samsonovich A, McNaughton BL (1997) Path integration and cognitive mapping in a continuous attractor neural network model. *J Neurosci* 17:5900–5920.
- Seung HS, Lee DD, Reis BY, Tank DW (2000) Stability of the memory of eye position in a recurrent network of conductance-based model neurons. *Neuron* 26:259–271.
- Sharp PE (1996) Multiple spatial/behavioral correlates for cells in the rat postsubiculum: multiple regression analysis and comparison to other hippocampal areas. *Cereb Cortex* 6:238–259.
- Sharp PE, Blair HT, Brown M (1996) Neural network modeling of the hippocampal formation spatial signals and their possible role in navigation: a modular approach. *Hippocampus* 6:720–734.
- Sharp PE, Blair HT, Cho J (2001a) The anatomical and computational basis of the rat head-direction cell signal. *Trends Neurosci* 24:289–294.

- Sharp PE, Tinkelman A, Cho J (2001b) Angular velocity and head direction signals recorded from the dorsal tegmental nucleus of Gudden in the rat: implications for path integration in the head direction cell circuit. *Behav Neurosci* 115:571-588.
- Shibata H (1987) Ascending projections to the mammillary nuclei in the rat: a study using retrograde and anterograde transport of wheat germ agglutinin conjugated to horseradish peroxidase. *J Comp Neurol* 264:205-215.
- Shibata H (1989) Descending projections to the mammillary nuclei in the rat, as studied by retrograde and anterograde transport of wheat germ agglutinin-horseradish peroxidase. *J Comp Neurol* 285:436-452.
- Shibata H (1992) Topographic organization of subcortical projections to the anterior thalamic nuclei in the rat. *J Comp Neurol* 323:117-127.
- Shibata H (1993a) Direct projections from the anterior thalamic nuclei to the retrohippocampal region in the rat. *J Comp Neurol* 337:431-445.
- Shibata H (1993b) Efferent projections from the anterior thalamic nuclei to the cingulate cortex in the rat. *J Comp Neurol* 330:533-542.
- Shibata H (1994) Terminal distribution of projections from the retrosplenial area to the retrohippocampal region in the rat, as studied by anterograde transport of biotinylated dextran amine. *Neurosci Res* 20:331-336.
- Shiple MT (1975) The topographical and laminar organization of the presubiculum's projection to the ipsi- and contralateral entorhinal cortex in the guinea pig. *J Comp Neurol* 160:127-146.
- Skaggs WE, Knierim JJ, Kudrimoti HS, McNaughton BL (1995) A model of the neural basis of the rat's sense of direction. In: *Advances in neural information processing systems* (Tesauro G, Touretzky DS, Leen TK, eds), vol. 7, pp. 173-180. Cambridge, MA: MIT Press.
- Sripanidkulchai K, Wyss JM (1986) Thalamic projections to the retrosplenial cortex in the rat. *J Comp Neurol* 254:143-165.
- Sripanidkulchai K, Wyss JM (1987) The laminar organization of efferent neuronal cell bodies in the retrosplenial granular cortex. *Brain Res* 406:255-269.
- Stackman RW, Taube JS (1997) Firing properties of head direction cells in rat anterior thalamic neurons: Dependence upon vestibular input. *J Neurosci* 17:4349-4358.
- Stackman RW, Taube JS (1998) Firing properties of rat lateral mammillary single units: head direction, head pitch, and angular head velocity. *J Neurosci* 18:9020-9037.
- Stackman RW, Clark AS, Taube JS (2002) Hippocampal spatial representations require vestibular input. *Hippocampus* 12:291-303.
- Stackman RW, Golob EJ, Bassett JP, Taube JS (2003) Passive transport disrupts directional path integration by rat head direction cells. *J Neurophysiol* (in press).
- Taube JS (1995) Head direction cells recorded in the anterior thalamic nuclei of freely moving rats. *J Neurosci* 15:70-86.
- Taube JS (1998) Head direction cells and the neurophysiological basis for a sense of direction. *Prog Neurobiol* 55:225-256.
- Taube JS, Burton HL (1995) Head direction cell activity monitored in a novel environment and during a cue conflict situation. *J Neurophysiol* 74:1953-1971.
- Taube JS, Muller RU (1998) Comparison of head direction cell activity in the postsubiculum and anterior thalamus of freely moving rats. *Hippocampus* 8:87-108.
- Taube JS, Muller RU, Ranck JB Jr (1990a) Head-direction cells recorded from the postsubiculum in freely moving rats. I., Description and quantitative analysis. *J Neurosci* 10:420-435.
- Taube JS, Muller RU, Ranck JB Jr (1990b) Head-direction cells recorded from the postsubiculum in freely moving rats. II., Effects of environmental manipulations. *J Neurosci* 10:436-447.
- Tullman ML, Taube JS (1998) Lesions of the lateral mammillary nuclei abolish head direction cell activity in the anterior dorsal thalamus. *Soc Neurosci Abstr* 24:1912.
- van Groen T, Wyss JM (1990) The postsubicular cortex in the rat: characterization of the fourth region of the subicular cortex and its connections. *Brain Res* 529:165-177.
- van Groen T, Wyss JM (1995) Projections from the anterodorsal and anteroventral nucleus of the thalamus to the limbic cortex of the rat. *J Comp Neurol* 358:584-604.
- Vogt BA, Miller MW (1983) Cortical connections between rat cingulate cortex and visual, motor, and postsubicular cortices. *J Comp Neurol* 216:192-210.
- Wiener SI (1993) Spatial and behavioral correlates of striatal neurons in rats performing a self-initiated navigation task. *J Neurosci* 13:3802-3817.
- Wirtshafter D, Stratford TR (1993) Evidence for GABAergic projections from the tegmental nuclei of Gudden to the mammillary body in the rat. *Brain Res* 630:188-194.
- Wyss JM, van Groen T (1992) Connections between the retrosplenial cortex and the hippocampal formation in the rat: a review. *Hippocampus* 2:1-11.
- Xie X, Hahnloser RHR, Seung HS (2002) Double-ring network model of the head direction system. *Phys Rev E* 66, 041902.
- Zhang K (1996) Representation of spatial orientation by the intrinsic dynamics of the head-direction cell ensemble: a theory. *J Neurosci* 16:2112-2126.
- Zugaro MB, Tabuchi E, Berthoz A, Wiener SI (2000) Influence of conflicting visual, inertial and substratal cues on head direction cell activity. *Exp Brain Res* 133:198-208.
- Zugaro MB, Tabuchi E, Fouquier C, Berthoz A, Wiener SI (2001) Active locomotion increases peak firing rates of anterodorsal thalamic head direction cells. *J Neurophysiol* 86:692-702.
- Zugaro MB, Arleo A, Berthoz A, Wiener SI (2003) Rapid spatial reorientation and head direction cells. *J Neurosci* 23:3478-3482.