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3-D Maps and Compasses in the Brain

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spatial cognition, 3-D topology, place cells, grid cells, head-direction cells, rodents, primates, bats

Abstract

The world has a complex, three-dimensional (3-D) spatial structure, but until recently the neural representation of space was studied primarily in planar horizontal environments. Here we review the emerging literature on allocentric spatial representations in 3-D and discuss the relations between 3-D spatial perception and the underlying neural codes. We suggest that the statistics of movements through space determine the topology and the dimensionality of the neural representation, across species and different behavioral modes. We argue that hippocampal place-cell maps are metric in all three dimensions, and might be composed of 2-D and 3-D fragments that are stitched together into a global 3-D metric representation via the 3-D head-direction cells. Finally, we propose that the hippocampal formation might implement a neural analogue of a Kalman filter, a standard engineering algorithm used for 3-D navigation.

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Place cells:

hippocampal neurons that discharge when the animal passes through a specific location in the environment, called the place field

Head-direction cells:

neurons found in multiple brain regions that discharge when the animal's head points toward a specific absolute (allocentric) direction, providing a compass signal

Grid cells: neurons that discharge when the animal passes through the vertices of a periodic hexagonal lattice that tiles the environment

INTRODUCTION

Most animals, including insects, fish, birds, and mammals, navigate actively through space to find food, mating partners, and shelter. Decades of research on the neurobiology of navigation focused on two-dimensional (2-D) navigation on flat surfaces, which laid the foundations for understanding the neural basis of 2-D spatial representations (Hafting et al. 2005, O'Keefe & Dostrovsky 1971, O'Keefe & Nadel 1978, Taube et al. 1990a, Tolman 1948). However, we live in a 3-D world, and many animals need to orient and move through 3-D space—but until recently, very little was known about how 3-D space is encoded in the brain. The extra dimension may complicate the required brain computations and poses technical challenges to the experimenters who wish to study 3-D navigation. Here we review the emerging data on the neural basis of 3-D navigation in mammals, primarily from rodents and bats, and propose a synthesis of findings across species. Notably, although this review focuses on neural representations of allocentric (absolute) navigable 3-D space, similar questions were also studied for egocentric (body-referenced) 3-D space (see the sidebar, 3-D Maps of Egocentric Space).

The review consists of four parts. First, we describe the neural basis of maps and compasses for allocentric space during different navigation modes in 3-D, focusing on 3-D place cells and head-direction cells. Second, we discuss whether 3-D maps and compasses are local or global and offer predictions for 3-D grid cells. Third, we discuss the possible principles guiding the development of neural maps and compasses for 3-D space. Specifically, we propose that the neural representations of 3-D maps and 3-D compasses are flexible and are set largely by the ongoing behavior of the animal and by the behavioral repertoire experienced during ontogeny—and not only by phylogeny. Fourth, we describe how 3-D maps and compasses might interact, and we draw functional parallels to engineering approaches to 3-D navigation.

3-D MAPS OF EGOCENTRIC SPACE

In addition to the emerging study of the neural representation of 3-D allocentric space, which is the focus of this review, a large body of research points to the existence of a metric 3-D representation of egocentric, body-centered space—primarily in the parietal cortex (Buneo et al. 2002, Whitlock et al. 2012). This body-centered 3-D reference frame supports eye movements and arm reaching in primates and may underlie our ability to catch a flying ball in 3-D (Blohm et al. 2009, Breveglieri et al. 2012, Rosenberg et al. 2013). In fact, humans are ecologically quite 3-D animals when it comes to stereoscopic vision and our ability to perform complex 3-D movements in egocentric space (Cohen & Rosenbaum 2004, Klatzky & Giudice 2013), although we note the imperfections of visual depth perception (Foley 1980). The existence of a 3-D metric representation of egocentric space in monkey parietal cortex likely results from the high ethological importance of precise calculations of 3-D spatial movements for primates (Bueti & Walsh 2009). How egocentric and allocentric 3-D representations are related remains an important open question (Chen et al. 2013, Nitz 2012, Wang 2012). The 3-D head-direction system in the dorsal presubiculum (Finkelstein et al. 2015) may be important for linking these two major 3-D reference frames. An important future challenge will be to understand how the allocentric 3-D map and 3-D compass signals in the hippocampal formation are integrated with the 3-D egocentric system in the parietal cortex to enable 3-D hand and eye movements and whole-body locomotion.

3-D NAVIGATION MODES AND THEIR NEURAL CORRELATES

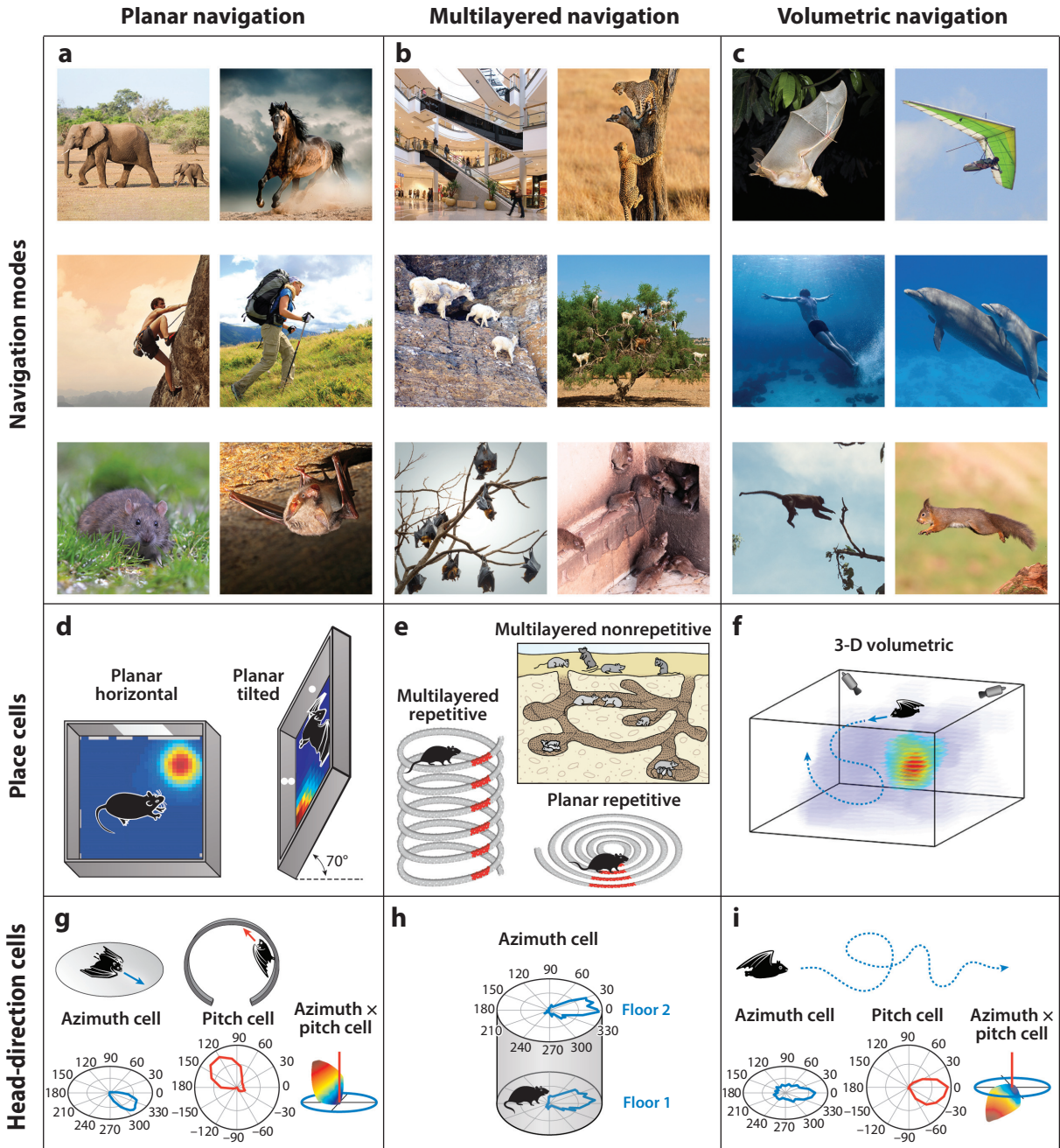
Navigation Modes in 3-D Space

All animals live in a 3-D world. However, 3-D navigation is not a unitary behavior but consists of several categories that may give rise to different neural representations. We propose to distinguish between three different behavioral modes of 3-D navigation: planar, multilayered, and volumetric navigation (**Figure 1a–c**).

1. Planar navigation implies movement along a 2-D surface embedded in 3-D space (**Figure 1a**) (O’Keefe & Nadel 1978, Tolman 1948). Planar navigation is 2-D in nature—whether it is performed on a horizontal, tilted, or vertical surface—and therefore may not require any explicit information about the dimension that is orthogonal to the locomotion plane.
2. Multilayered navigation requires movement across several interconnected planes (**Figure 1b**) (Thibault et al. 2012). Although navigation along each branch or layer of a multilayered space can be described as being 1-D or 2-D, navigating a multilayered environment requires an explicit 3-D representation—including the ability to discriminate between planes (e.g., floors), understand their 3-D spatial relations, and make novel 3-D shortcuts (Montello & Pick 1993).
3. Volumetric navigation is not limited by locomotion surfaces and involves an unconstrained movement through 3-D space (**Figure 1c**) (Grobéty & Schenk 1992, Jovalekic et al. 2011). Nevertheless, it can still be restricted by the 3-D boundaries of the environment, as well as by the animal’s ability to jump, glide, fly, or swim in 3-D. Similar to multilayered navigation, successful volumetric navigation requires an explicit 3-D representation of space.

Although some species exhibit only one of these navigation modes (e.g., horses navigate always in a planar fashion, and dolphins always navigate volumetrically), most mammals can flexibly switch between navigation modes according to the spatial layout of the environment and the behavioral

needs of the animal. For example, rats can switch from planar navigation during open-field foraging to multilayered navigation in burrows or dense vegetation; and other rodents, such as squirrels, also navigate volumetrically (**Figure 1c**). Monkeys are typically engaged in all three modes of 3-D navigation, moving in a planar fashion on the ground and in multilayered and volumetric modes in complex environments (e.g., the tree canopy). Humans exhibit terrestrial planar navigation,



as well as multilayered navigation in modern buildings, and can navigate volumetrically as they swim, dive, or pilot an aircraft (**Figure 1a–c**). Finally, bats—mammals capable of both crawling and flying—have mastered all three navigation modes, as their habitat spans from rock surfaces to complex caves, foliage, and large 3-D open spaces; this makes bats an ideal animal model to study the neural basis of 3-D navigation (Geva-Sagiv et al. 2015).

Neural Correlates of 3-D Navigation

Decades of neurophysiological studies in rodents revealed that the hippocampal formation is crucial for navigation and contains neurons whose functional properties can support map-and-compass navigation (Moser et al. 2008, O’Keefe & Nadel 1978). These neurons include place cells (O’Keefe & Dostrovsky 1971), head-direction cells (Taube et al. 1990a), grid cells (Hafting et al. 2005), and border/boundary cells (Lever et al. 2009, Solstad et al. 2008).

Place cells discharge selectively when the animal passes through a certain spatial location on a 2-D horizontal surface and were suggested to be the neural substrate of a “cognitive map” of the environment (O’Keefe & Nadel 1978, Tolman 1948). Similarly, during planar navigation on tilted or vertical surfaces, place cells in rodents, monkeys, and bats exhibit circular place fields at a specific vertical \times horizontal position—suggesting sensitivity of place cells to the vertical dimension (see **Figure 1d**) (Jeffery et al. 2005, Knierim & McNaughton 2001, Knierim et al. 2000, Ludvig et al. 2004, Ulanovsky & Moss 2007). In contrast, during multilayered navigation in rats moving along a vertical helix, Hayman et al. (2011) suggested that place cells were tuned in the horizontal dimension but were relatively insensitive to the vertical dimension, with place fields of a given neuron appearing stacked above each other (illustrated schematically in **Figure 1e, left**). Notably, in this experiment, the different layers (loops) of the helical apparatus were exact repetitions of each other (**Figure 1e, left**: multilayered repetitive). Such a geometric repetition is known in 2-D horizontal environments to result in repeating place fields in equivalent segments (**Figure 1e, bottom**: planar repetitive) (Cowen & Nitz 2014, Derdikman et al. 2009, Singer et al. 2010, Spiers et al. 2015)—and therefore the repetitiveness of place fields on the

Border/boundary cells: neurons that signal environmental geometry by discharging whenever the animal is close to a salient border of the environment

Figure 1

3-D navigation modes and their neural correlates. (a–c) Navigation modes in 3-D space across mammalian species: (a) planar, (b) multilayered, and (c) volumetric navigation. (d–f) 3-D tuning of place cells during the different 3-D navigation modes. (d) In planar navigation, place cells in a horizontal arena (*left*; Whitlock et al. 2008) and on a tilted 2-D surface (*right*; Ulanovsky & Moss 2011) exhibit circular place fields within the 2-D plane. (e) During multilayered navigation, place cells were tested in repetitive multilayered environments (*left schematic*) (Hayman et al. 2011), yielding repetitive place fields (*red, spikes*); this could stem from the repetitive nature of the environment because repetitive place fields are also observed in planar repetitive environments (*bottom right*) (Cowen & Nitz 2014). Place cells have yet to be recorded in multilayered nonrepetitive environments, such as a rat’s burrow system (*top right*). (f) During volumetric navigation, place cells were recorded in a bat flying through 3-D volumetric space (5.8 \times 4.6 \times 2.7-m room); these neurons exhibited spherical (isotropic) tuning to all three dimensions, as shown in this example (Yartsev & Ulanovsky 2013). (g–i) 3-D tuning of head-direction cells during the different 3-D navigation modes. (g) Head-direction cells tuned to azimuth, pitch, or azimuth \times pitch were recorded in bats during planar navigation on a horizontal-arena floor or on a vertical ring (Finkelstein et al. 2015). (h) Azimuthal head-direction cells exhibit the same directional preference during multilayered navigation in rats tested on two different floors (Stackman et al. 2000). (i) In bats flying through 3-D volumetric space, head-direction cells exhibited similar types of tuning to those found in planar navigation (shown in panel g; numbers indicate degrees); namely, neurons were tuned to azimuth, pitch, or azimuth \times pitch (Finkelstein et al. 2015). 3-D head-direction cells thus provide a global 3-D compass signal that could underlie 3-D navigation in bats. Such 3-D head-direction tuning was found so far only in the dorsal presubiculum of bats (Finkelstein et al. 2015), but 3-D tuning has never been tested in this brain region in other species; it therefore remains to be seen whether 3-D head-direction cells will be found in the presubiculum of mice, which are well adapted to 3-D multilayered navigation, and monkeys, which can also navigate in 3-D volumetrically. Panel d (*left*) adapted with permission from Whitlock et al. (2008); copyright (2008) National Academy of Sciences U.S.A. Panel f adapted from Yartsev & Ulanovsky (2013), adapted with permission from AAAS. Panel b based on data from Stackman et al. (2000).

Dorsal presubiculum (postsubiculum):

a cortical area where head-direction cells were first discovered in rats; it provides the major head-direction input to the medial entorhinal cortex

vertical helix might have resulted from the repetitive nature of the setup, rather than reflecting an underlying lack of altitude encoding in rats. It remains to be seen how place cells encode a naturalistic, multilayered environment not composed of repeating elements (**Figure 1e**, *top*: multilayered nonrepetitive). Finally, our recent recordings in the hippocampal formation of freely flying bats demonstrated the existence of 3-D place cells under fully volumetric 3-D conditions (Yartsev & Ulanovsky 2013). These neurons discharged when the animal passed through a 3-D spherical place field (**Figure 1f**, *red portion of space*)—thus providing an explicit 3-D neural representation, including the encoding of altitude, that could support 3-D volumetric navigation.

Head-direction cells (Ranck 1984, Taube et al. 1990a) are neurons that discharge selectively when the animal's head points at a specific azimuthal direction on a 2-D planar surface, and researchers have suggested these cells are the neural analogue of a compass (Taube 2007). Studies in subcortical regions of the rat brain showed that azimuthal head-direction cells are insensitive to head pitch; moreover, no pitch cells that span the behaviorally relevant pitch range were found in rodents (Stackman & Taube 1998). However, our recent study of a cortical area—the dorsal presubiculum of bats—revealed azimuth cells (**Figure 1g**, *left*) that resembled the head-direction cells found in rodents (Taube et al. 1990a), but we also found neurons tuned to head pitch (**Figure 1g**, *middle*) (Finkelstein et al. 2015). Additionally, bat dorsal presubiculum contained 3-D head-direction cells that responded to a particular combination of azimuth \times pitch, thus representing the direction of the head vector in 3-D space (**Figure 1g**, *right*). Notably, all the 3-D studies in rats were conducted in subcortical nuclei, whereas our study in bats was the first to examine 3-D coding in the presubiculum of any species. Because rodents move their head extensively in 3-D (Wallace et al. 2013), it would be interesting to examine 3-D representations in the presubiculum of rodents, where 3-D tuning has never been studied, as well as in the presubiculum of primates.

During multilayered navigation in an apparatus comprised of two visually distinct floors, head-direction cells of rats fired in the same azimuth direction on both floors (**Figure 1b**) (Stackman et al. 2000). This result is consistent with the notion that the head-direction signal is global and is not compartmentalized (as shown also in 2-D; see Whitlock & Derdikman 2012, Yoder et al. 2011)—a point to which we return below.

Head-direction tuning during 3-D volumetric navigation has been studied to date only in flying bats (Finkelstein et al. 2015). This study found head-direction cells that were tuned to azimuth, pitch, or conjunctively to azimuth \times pitch (**Figure 1i**)—similar to the tuning found during planar navigation (**Figure 1g**). Thus, the head-direction signal in dorsal presubiculum of bats is invariably 3-D during both planar and volumetric navigation, suggesting the head-direction signal is global and does not anchor to a specific locomotion plane. In contrast, we argue below that the dimensionality of spatial representation by place cells would switch flexibly from 2-D to 3-D, according to the navigation mode. Furthermore, because many mammalian species navigate in 3-D, we predict that similar representations will be found in other mammals, including mice and primates—both of which orient very well in 3-D.

A MOSAIC OF 2-D AND 3-D MAPS STITCHED BY A GLOBAL 3-D COMPASS

An important question is, how are the map and compass signals related to each other? Do they integrate into a global 3-D representation of the environment, and if so, how? For instance, does the brain use a global 3-D map and compass or a mosaic of local representations for different locomotion planes? In the next two sections, we discuss the intriguing possibility that separate sets of maps exist for 2-D and 3-D space, and these can be combined into a coherent spatial representation using a global 3-D compass.

Multiple Maps for 3-D Space

As discussed above, navigation is not a unitary behavior: Animals can switch abruptly between 2-D and 3-D navigation modes (**Figure 2a**). This suggests three possible neuronal representations. The first possibility is that a 3-D volumetric neural map is present at all times, during both 3-D and 2-D behavioral modes. According to this option, all place cells have 3-D tuning, including silent cells—those neurons that are inactive in a given 2-D environment (Alme et al. 2014)—which in fact might be 3-D place cells anchored to a global map whose 3-D place field happens to lie outside the 2-D locomotion surface. A second possibility is that rapid switches between behavioral modes imply rapid switches between the dimensionality of the neural representations. According to this possibility, place cells will have a 2-D tuning during planar navigation and a 3-D tuning during 3-D volumetric or multilayered navigation (Ulanovsky & Finkelstein 2013). A third possibility is that of attentional switches: For example, even during navigation on a 2-D surface, we may expect switches between a 2-D tuning when the animal attends to local surface cues (e.g., local odors and textures on the floor) and a 3-D tuning when the animal attends to global cues (e.g., distal visual landmarks that are embedded in 3-D space). This latter notion is consistent with the known flexibility of the hippocampal spatial code, manifested in switches of the place-cell map between local and global reference frames (Knierim & Hamilton 2011) (see the sidebar, Reference Frames).

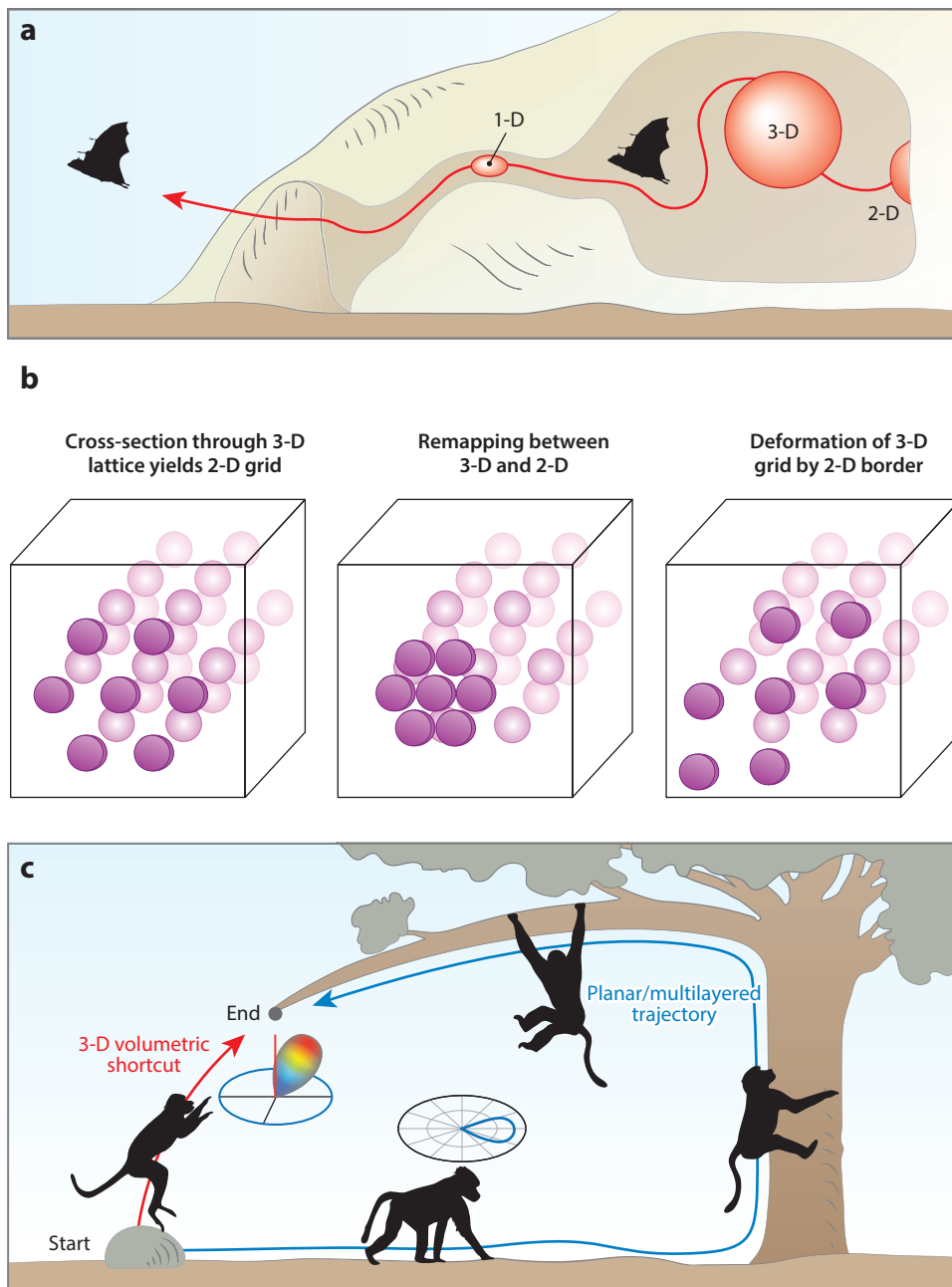
Notably, switches between reference frames might complicate the interpretation of studies on 3-D place cells during 2-D navigation. Specifically, two different studies in rats attempted to measure 3-D tuning of place cells by moving the plane of locomotion in 3-D space. In the first study, a horizontal arena was rotated in pitch (tilted upward by 45°), and many place cells in hippocampal area CA1 changed their firing pattern at a certain altitude (Knierim & McNaughton 2001)—indicating either 3-D tuning or a change in the anchoring reference frame, leading to remapping. In the second study, the arena was shifted upward by translation, which did not alter the firing pattern of place cells (Knierim & Rao 2003). These different results may stem from variations in how the locomotion plane was moved in 3-D space and by the identity of the sensory cues that determined the place-field tuning. For instance, if place cells are anchored to visual cues on the room's ceiling, a large part of these cues may become occluded once the arena is tilted, which will likely lead to remapping, as was observed in the first study. In contrast, shifting the arena upward (without rotating it) should not alter substantially the visual cues available above the animal, and hence the place-cell tuning would remain stable, as was shown in the second study. These differences illustrate the inherent difficulties posed by studying animals moving on 2-D planar surfaces (horizontal, tilted, or vertical) to elucidate the underlying 3-D representation.

The problem of a global map versus many different local maps is also relevant for tuning of grid cells in 3-D. Although grid-cell activity during 3-D volumetric navigation has not been tested

REFERENCE FRAMES

A reference frame defines the coordinate system in which measurements are conducted. An allocentric reference frame describes the orientation of the animal in external (world) coordinates (e.g., “north”), whereas an egocentric reference frame defines the orientation of one body part relative to another (e.g., right turn of the head with respect to the body). Furthermore, for an allocentric reference frame, the external coordinate system can be anchored to local cues (e.g., tactile cues on the floor of the behavioral apparatus) or global cues (e.g., cave walls for a bat navigating indoors, or distal landmarks such as mountains during navigation outdoors).

experimentally yet, several models predicted that 3-D grid cells would exhibit regular 3-D lattice patterns (Horiuchi & Moss 2015, Mathis et al. 2015); for further details on possible optimal 3-D lattices, see Jeffery et al. (2015). If 3-D grid cells in the brain indeed exhibit a regular 3-D lattice, an interesting question would be, how will the 2-D borders of the environment affect this putative 3-D lattice? One possibility is that 2-D grid patterns observed while animals locomote on the floor or walls of the environment are simply a cross-section through the full 3-D lattice (**Figure 2b, left**).



This notion is consistent with studies suggesting that grid-cell firing patterns on 1-D linear tracks are cuts through a perfect 2-D grid lattice (Domnisoru et al. 2013, Yoon et al. 2016)—suggesting that perhaps grid-cell representations might be of a higher dimensionality than the dimensionality of the experimental apparatus. However, a recent study in rats running on horizontal versus sloped surfaces did not find the changes in grid pattern that would be expected from planar 2-D cuts through a global 3-D volumetric map, arguing against this possibility (Hayman et al. 2015). A second possibility is that there will be remapping (phase-shift/rescaling/rotation) between 3-D and 2-D because of the changes in behavior under different locomotion modes, so that the grid patterns in 3-D and 2-D will be uncorrelated (**Figure 2b, middle**). A third possibility is that the 2-D walls will deform the 3-D grid (**Figure 2b, right**), akin to the border-induced shearing deformation of 2-D grids reported recently in rats (Stensola et al. 2015). It remains to be seen which of these possibilities (or perhaps a combination) holds at the interface between 3-D volumes and their 2-D borders. Importantly, here we assumed a highly regular lattice structure for 3-D grid cells—but another theoretical study (Stella & Treves 2015) predicted that in fact, 3-D grid cells would exhibit spherical firing fields, but these fields would be arranged much less regularly than expected from optimal-packing lattices. An important future challenge will therefore be to record from grid cells in 3-D.

Assuming a separate set of maps for 2-D and 3-D, how are these multiple maps stitched together? This also relates to the question of how multiple 2-D maps for different compartments are stitched in 2-D. A recent study in rats running between two interconnected 2-D compartments showed that each compartment was encoded initially by a distinct local grid map, but as the animals acquired experience in the environment, these two grid maps merged gradually into one global grid representation that was coherent across both compartments (Carpenter et al. 2015). Likewise, with experience, the 2-D map fragments (e.g., fragments representing open spaces, passageways, or different locomotion planes such as floors, walls, and ceilings) may merge into a global 3-D representation of the navigable environment. Such fusion is expected to occur as a result of the continuity of movements through 2-D and 3-D space and may be aided by a 3-D neural compass, as discussed in the next section.

In summary, we suggest that space is represented by a mosaic of multiple neural maps. This mosaic is composed of distinct 2-D planar maps and 3-D volumetric maps. Switching between such 2-D planar maps and 3-D volumetric maps may stem from toggling in reference frames and, in

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Figure 2

A mosaic of multiple 2-D and 3-D maps anchored by a global 3-D compass. (a) Animals can switch between different navigation modes and different dimensions (1-D, 2-D, and 3-D navigation), and the neural representations may switch accordingly. Illustrated here are hypothetical examples of a place cell with a 1-D place field during 1-D movement through a narrow tunnel, a 2-D place field on the surfaces of the environment (e.g., the wall of a cave), and a 3-D volumetric place field during volumetric 3-D flight. (b) Different hypotheses on the possible relations between the 2-D grids of grid cells (e.g., on the cave wall) and 3-D grids (e.g., during flight). (*Left*) Grid fields in 3-D are assumed to be arranged according to a 3-D lattice, and the 2-D grid on a plane is suggested to be a direct cross-section of that plane through the full 3-D volumetric grid. (*Middle*) 3-D grid cells might undergo remapping when the animal switches from 3-D to 2-D locomotion, such that the 2-D grid pattern is unrelated to the 3-D grid. (*Right*) The 3-D grid might be deformed by 2-D environmental borders, and thus its fields would appear in 2-D as a deformed 2-D grid. (c) Azimuthal head-direction cells referenced to the locomotion plane may be sufficient for orienting the animal during planar or even during multilayered navigation (*blue arrow*), but they would not allow volumetric 3-D shortcuts (*red arrow*). Instead, we propose that 3-D shortcuts are computed based on 3-D head-direction cells tuned to both azimuth and pitch, which provide a global 3-D compass that encodes the direction of the heading vector in 3-D (see also Finkelstein et al. 2015).

turn, could support rapid switching between different navigation modes. Finally, with experience, the different 2-D and 3-D maps may merge into one global representation.

A Global 3-D Compass

We propose that the correct alignment and stitching of different map fragments into a coherent representation might depend on the existence of a global 3-D compass system, required for preserving the overall sense of direction across environments. Such a global 3-D compass signal might be implemented neurally by the 3-D head-direction system in the dorsal presubiculum (Finkelstein et al. 2015). The 3-D head-direction cells that we found in bats (tuned to azimuth \times pitch) were tuned to 3-D regardless of the navigation mode—during both planar and volumetric navigation. Moreover, pitch cells were found to maintain their preferred pitch angle during navigation in a complex environment that consisted of a horizontal arena and a vertical ring positioned inside the arena, which enabled full pitch maneuvers (**Figure 1g, middle**) (Finkelstein et al. 2015), suggesting a global allocentric 3-D head-direction signal. Similarly, in rats, the azimuthal head-direction signal was maintained across multiple compartments, rooms, and floors—as long as the animal could move actively between the different parts of the environment (**Figure 1b**) (Stackman et al. 2000, Yoder et al. 2011). Furthermore, in rats running in a hairpin maze, the head-direction signal was maintained in all the subsections of the maze, despite fragmentation of the place-cell map and grid map (Whitlock & Derdikman 2012). Finally, rat head-direction cells were shown to be controlled by global distal cues and ignored the local cues unless distal cues became unavailable (Zugaro et al. 2001). Taken together, the studies from bats and rats suggest that the head-direction signal is global and is maintained across different compartments of the environment.

Is the head-direction signal global under all circumstances? Although during active navigation the head-direction signal seems to be global, under passive-translocation conditions the head-direction cells might stop using the global (room) reference frame and become anchored to the local locomotion plane, thus undergoing remapping (Taube et al. 2013). This remapping was shown for azimuthal head-direction cells; it would be interesting to examine whether the azimuth and pitch components of the 3-D compass might remap differently. Specifically, the preferred direction of azimuth cells is set primarily by visual landmarks (Zugaro et al. 2001), but pitch cells might in principle compute the vertical tilt of the head from gravity alone (Laurens et al. 2013). Therefore, whereas azimuth cells may undergo remapping (Taube et al. 1990b), pitch cells might always exhibit the same preferred direction, set by gravity—and therefore, the pitch signal might always be global, even when the azimuth signal is not. Notably, during natural navigation outdoors, the azimuthal component of the compass can be set reliably by global sensory cues, such as the direction of the sun, stars, wind, or distal mountains (Childs & Buchler 1981, Wallraff 2005). Together with gravity, these cues could create a global 3-D reference frame that may always be available for anchoring a global 3-D compass for outdoor navigation.

But how does the 3-D neural compass integrate horizontal and vertical information? For rats performing planar navigation on vertical surfaces, the preferred azimuthal head direction on the vertical wall follows the preferred direction on the horizontal surface after a 90° pitch rotation (Calton & Taube 2005, Stackman et al. 2000); this has led to the suggestion that in rats, the vertical wall might be encoded as an unfolded extension of the horizontal floor, as if the vertical walls were felled down (Taube et al. 2013). In light of these findings, Jeffery and colleagues (2013) proposed that the brain contains not a 3-D volumetric map but a mosaic of connected planar maps whose relative direction is updated via the azimuthal head-direction signal. Consequently, to move from point A to a higher or lower point B, a surface-dwelling animal would always have to follow a route along interconnected locomotion planes. However, this does not account for the

ability of many animals to perform 3-D volumetric shortcuts, such as monkeys leaping in arboreal environments (**Figure 2c**, 3-D volumetric shortcut) (Channon et al. 2010) or humans' ability to point toward the 3-D direction of a hidden target (Montello & Pick 1993, Wilson et al. 2004). Such 3-D shortcut behaviors require 3-D metric knowledge and a 3-D compass. This is consistent with our recent findings in bats, which demonstrated that head-direction cells in the presubiculum encode both azimuth and pitch directions, providing a direction in 3-D space (Finkelstein et al. 2015). Thus, the 3-D head-direction signal in the presubiculum can serve as an omnipresent 3-D compass that stays invariant between the different navigation modes. Taken together, such a global 3-D compass, anchored to a global 3-D reference frame, could be used to interconnect between the different locomotion planes during planar navigation or to calculate 3-D shortcuts during volumetric navigation (**Figure 2c**, 3-D volumetric shortcut)—facilitating the binding of different 2-D and 3-D map fragments into a coherent spatial representation.

PROPERTIES OF 3-D MAPS AND COMPASSES MAY DEPEND ON THE STATISTICS OF BEHAVIOR

Topology of 3-D Spatial Representations

During ontogeny, the movements of animals typically become increasingly more complex and 3-D. Therefore, an important question is, Do the properties of 3-D maps and compasses depend on ontogeny and on adult behavior, or are they hard-wired phylogenetic determinants? The head-direction signal appears in rat pups even before eye opening, suggesting that its formation is independent of visual cues (Bjerknes et al. 2015, Tan et al. 2015). In contrast, place cells develop later in ontogeny, followed by the appearance of adult-like grid cells (Langston et al. 2010, Wills et al. 2010). These findings may imply that the head-direction signal is hard-wired, whereas place and grid representations are experience-dependent. Alternatively, these data are also consistent with the idea that experience during ontogeny influences all these spatial codes. According to this notion, the head-direction signal develops early because pups move their head early in ontogeny (even in utero), whereas the formation of place and grid representations is delayed because pups start to move their center of mass voluntarily only later in life.

Do the statistics of spatial behaviors during ontogeny also shape the detailed properties of the neural representation? First, some theoretical models suggest that the metric of grid cells should reflect the metric of the environment—for example, grid cell development in non-Euclidian hyperbolic spaces was predicted to result in hyperbolic grids (Urdapilleta et al. 2015), and experiments are under way to test grid cells in rats raised in spherical environments (Kruge et al. 2013). Second, both theoretical and experimental studies have suggested that the temporal structure of place-cell population dynamics may be shaped by the statistics of the animal's movement through space and would therefore reflect the topology of the environment (Chen et al. 2012, Curto & Itskov 2008, Dabaghian et al. 2014, Poucet 1993, Stella et al. 2013)—again supporting the importance of movement statistics and movement topology for understanding the properties of spatial mapping.

The 3-D head-direction system in bats (**Figure 1g,i**) (Finkelstein et al. 2015) provides an interesting case study for how movement statistics influence neural representations. During both flight and crawling, bats maneuver across 360° of azimuth (**Figure 3a, top**) and 360° of pitch, with pitch angles spanning both upright and inverted positions (**Figure 3a, bottom**). Importantly, the simplest way to describe such continuous angular rotations of 360° azimuth × 360° pitch is by using a toroidal coordinate system (**Figure 3b,c**) (see the sidebar, Toroidal Coordinates for 3-D Head Direction). In such coordinates, every combination of azimuth and pitch (each spanning a cyclical range of 360°) is described as a point on the toroidal manifold. Thus, angular movement in

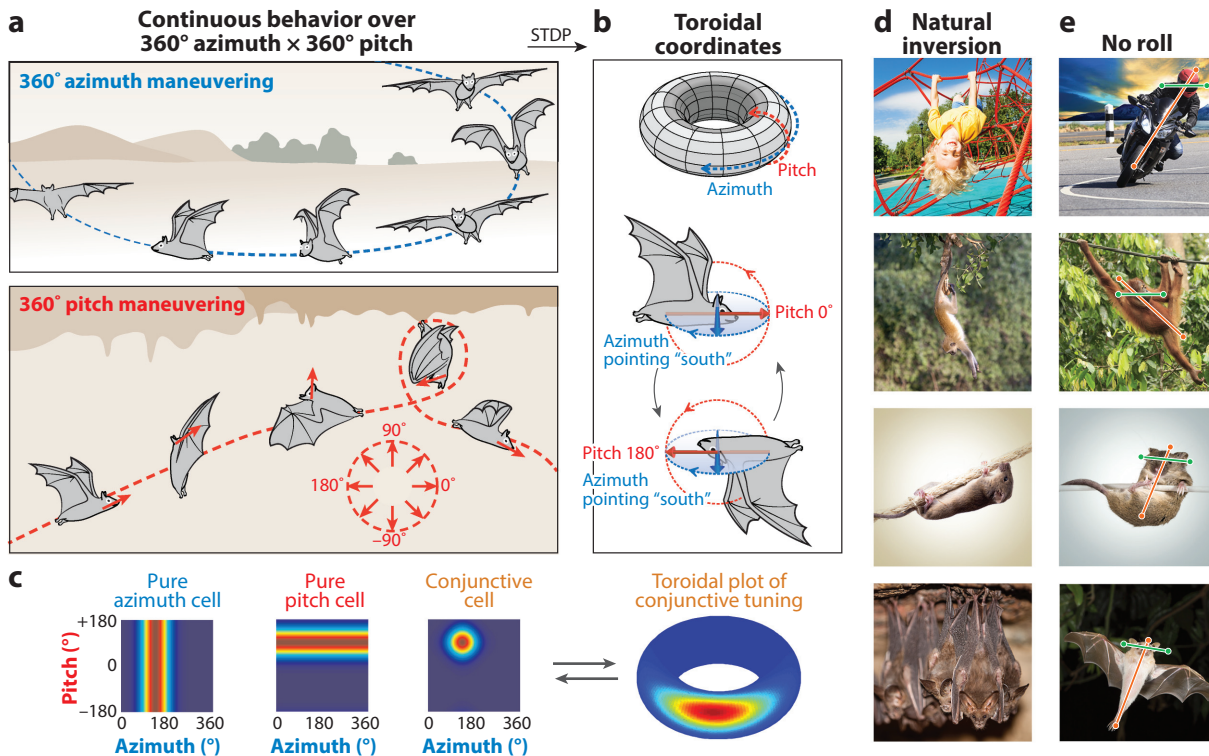


Figure 3

Topology of 3-D natural movements translates to topology of 3-D neural representations. (*a*) During 3-D volumetric navigation, bats maneuver across all possible combinations of 360° azimuth (*top*) and 360° pitch (*bottom*), creating a continuous behavioral coverage of 360° azimuth × 360° pitch. (*b*) The neural representation of head direction (*top*) in toroidal coordinates covers 360° azimuth × 360° pitch cyclically and can result from spike-timing-dependent plasticity (STDP) mechanisms combined with the continuous behavioral coverage of 360° azimuth × 360° pitch. Toroidal azimuth (*middle*) is defined as the azimuthal direction of the interaural axis (blue arrow, pointing “south”), whereas pitch is defined as the angle of the naso-occipital axis above or below the horizontal plane (red arrow). In toroidal coordinates, rotations in pitch (*bottom*) do not change the azimuth (note the naso-occipital axis, in blue, is still pointing “south”). The decoupling of the two axes of azimuth and pitch allows a continuous representation of azimuth × pitch, without any discontinuities (singularities) at the poles. (*c*) A neuronal representation of head direction in toroidal coordinates spans 360° azimuth × 360° pitch and can be represented on unfolded plots of the torus (see three leftmost plots). Shown schematically are three head-direction cells: a pure azimuth cell, a pure pitch cell, and a conjunctive cell tuned to a particular 3-D combination of azimuth × pitch. The conjunctive azimuth × pitch cell is also plotted on the toroidal manifold (*right*). (*d*) Many animals maneuver upside-down, exhibiting natural inversion. (*e*) Many animals, including humans, actively stabilize their head to avoid head-roll and maintain horizontal head (green lines) even during extreme body postures (red lines).

azimuth and pitch follows a continuous trajectory along the toroidal manifold—in sharp contrast to spherical coordinates, in which any rotation in pitch beyond $\pm 90^\circ$ (beyond the poles of the sphere) will cause an abrupt 180° switch in the azimuth direction. If continuity of movement determines the continuity of the neural representation, one would predict that head-direction cells in bats would represent the 3-D head direction in toroidal, continuous coordinates—as indeed we found in the bat dorsal presubiculum (Finkelstein et al. 2015).

The continuity of movement through space can be translated into a continuous neural representation by means of spike-timing-dependent plasticity (STDP) (Dan & Poo 2004). Specifically, a continuous spatial movement will lead to short temporal delays between the activity of

TOROIDAL COORDINATES FOR 3-D HEAD DIRECTION

A toroidal coordinate system utilizes two independent axes for azimuth and pitch, each spanning a range of 360° —in contrast to the spherical coordinate system, in which azimuth spans 360° but pitch spans only 180° (see Finkelstein et al. 2015). Toroidal azimuth is defined by the horizontal direction of the interaural axis (i.e., the axis going through the ears), and the toroidal pitch is defined as the vertical angle of the naso-occipital axis (i.e., going from tail to nose). Importantly, pitching of the naso-occipital axis does not change the azimuthal angle of the interaural axis, and vice versa—making these axes independent. Note that the toroidal coordinates use only two of the Euler angles—yaw (azimuth) and pitch—while ignoring the third angle, roll; this is justified in the context of navigation, because for a navigating animal, azimuth and pitch define the vector of heading-direction in 3-D space, with respect to external room coordinates, whereas roll is merely a rotation around this vector and hence is less important for navigation.

similarly tuned head-direction cells, which would selectively potentiate the synapses between similarly tuned neurons—and this in turn would lead to continuity of the neural representation. Such an STDP-based model can explain mechanistically how a continuous toroidal representation (**Figure 3b**) emerges in an animal that maneuvers in a continuous angular manner (**Figure 3a**). Therefore, we predict that head-direction cells with similar preferred directions (in azimuth \times pitch) would become more strongly interconnected during ontogeny—akin to the experience-dependent increase in connectivity between co-tuned neurons in visual cortex (Ko et al. 2013). Conversely, if the animal has not experienced a specific orientation during the development of the network, the appropriate neural representation might not form. Indeed, in rats (which do not typically locomote upside-down), the majority of azimuthal head-direction cells shut down when the rat assumed an inverted orientation (Calton & Taube 2005), suggesting a hemitorus model that does not represent the inverted pose (Stackman et al. 2000). Interestingly, some cells did not abolish their firing in inverted rats but became moderately tuned to the opposite direction as compared to the upright orientation (a 180° azimuth shift; Taube et al. 2004), consistent with a full toroidal topology. This suggests that perhaps with enough experience, a toroidal representation would be formed in rats.

Although behavioral experience can shape neural representations, the converse may also be true: The neural representation can shape and constrain behavior. For example, if the animal developed a toroidal representation during ontogeny, it will likely be able to maneuver behaviorally over 360° of pitch and navigate while inverted. However, if an animal did not experience a certain behavioral state, this may prevent the formation of the appropriate neural representation, which might later restrict the animal from navigating under similar conditions. This was observed, for example, in rats raised in laboratory cages; these animals were severely impaired during inverted navigation (Valerio et al. 2010). In contrast, many species—including monkeys and mice (which climb upside-down naturally)—can locomote in the inverted pose while maneuvering extensively in pitch (**Figure 3d**). Because such azimuth \times pitch movements are continuous in space, we predict that mice and primates might also develop a toroidal representation of head azimuth \times pitch, which would support 3-D navigation. Taken together, toroidal encoding of the 3-D compass might exist in the brain of multiple species; its existence in bats demonstrates empirically how topology of movement could translate into topology of the neural representation.

Commutativity of the 3-D Neural Compass

Coding of 3-D angles poses a potentially difficult problem. A 3-D orientation of a rigid body in space can be described by the three Euler angles, corresponding to azimuth (yaw), pitch, and

roll rotation angles. This 3-D rotations group is mathematically noncommutative, meaning that changing the order of rotations (e.g., whether you first rotate in azimuth, then pitch, then roll, or vice versa) will lead to a different final orientation. Such strong dependence on movement history would make any directional-trajectory computations very difficult. One possible solution to this noncommutativity problem is to avoid rotations in roll and to use the toroidal representation, which does not incorporate roll, because toroidal azimuth \times pitch coordinates are commutative (Finkelstein et al. 2015). Consistent with this idea, we found that only a small fraction of neurons in the bat presubiculum were modulated by roll. Furthermore, behaviorally, many terrestrial and flying animals (across all phyla, including insects, birds, and many mammals) stabilize their head actively to avoid roll (**Figure 3e**) (Dunbar et al. 2008, Iriarte-Díaz & Swartz 2008, Kress & Egelhaaf 2012, Pozzo et al. 1990, Viollet & Zeil 2013). Thus, we propose that the need for a commutative neural representation of head direction explains why most animals typically exhibit very small roll angles (**Figure 3e**). This proposal complements more classical explanations of roll avoidance, such as sensory stabilization (Laurens et al. 2013). Taken together, the need for commutativity might explain why most animals avoid roll and why azimuth \times pitch directions are represented in the brain in toroidal coordinates.

Isotropy and Scale of 3-D Spatial Representations

In the section above, we suggested that movement statistics shape the topology of the neural representation. Another aspect of movement statistics is that animal navigational behavior may be nonisotropic (not identical in all directions), which could potentially create a 3-D spatial representation with different resolution in different directions. In addition to nonisotropic behaviors, sensory inputs are also nonisotropic—as exemplified by vertical gravity information in vestibular processing and by the limited depth accuracy provided by stereoscopic vision along the line of sight. This problem might be alleviated during navigation, when additional depth cues are present (e.g., motion parallax). This highlights the importance of studying the possible factors governing the resolution and isotropy of allocentric spatial codes.

Many animals process the horizontal and vertical dimensions differently during 3-D navigation (Davis et al. 2014, Grobéty & Schenk 1992, Jovalekic et al. 2011, Wilson et al. 2015). For instance, rats were shown to explore a 3-D lattice maze using a layer-like strategy, performing horizontal movements first and then vertical movements—creating a preference for horizontal routes (Jovalekic et al. 2011); however, another study in a similar task showed that rats exhibited a higher spatial accuracy in the vertical dimension (Grobéty & Schenk 1992). Behavioral studies in humans showed that in pointing experiments on imagined 3-D directions in familiar multilayered environments, the mental representation is distorted in both the horizontal and the vertical plane, resulting in imagined buildings being taller and narrower (Brandt et al. 2015). Importantly, the way we explore and learn 3-D routes affects our performance: Horizontal exploration results in better horizontal accuracy, whereas vertical exploration yields better vertical accuracy (Thibault et al. 2012), highlighting the fact that movement statistics affect the nature of spatial representations.

So is the neural map isotropic? When rats were trained to move on a vertical wall with protruding pegs, hippocampal place fields were found to be elongated in the vertical dimension, suggesting that under these conditions, place fields are tuned nonisotropically and provide less information about the animal's altitude (Hayman et al. 2011). However, in this experimental setup, the rats explored the vertical wall using mostly horizontal movements and jumped vertically between rows of pegs only occasionally (Hayman et al. 2011)—a nonisotropic sampling of the horizontal and vertical dimensions. In contrast, during navigation on tilted surfaces, when the movement was likely more isotropic for both the vertical and horizontal components, place-field tuning appeared

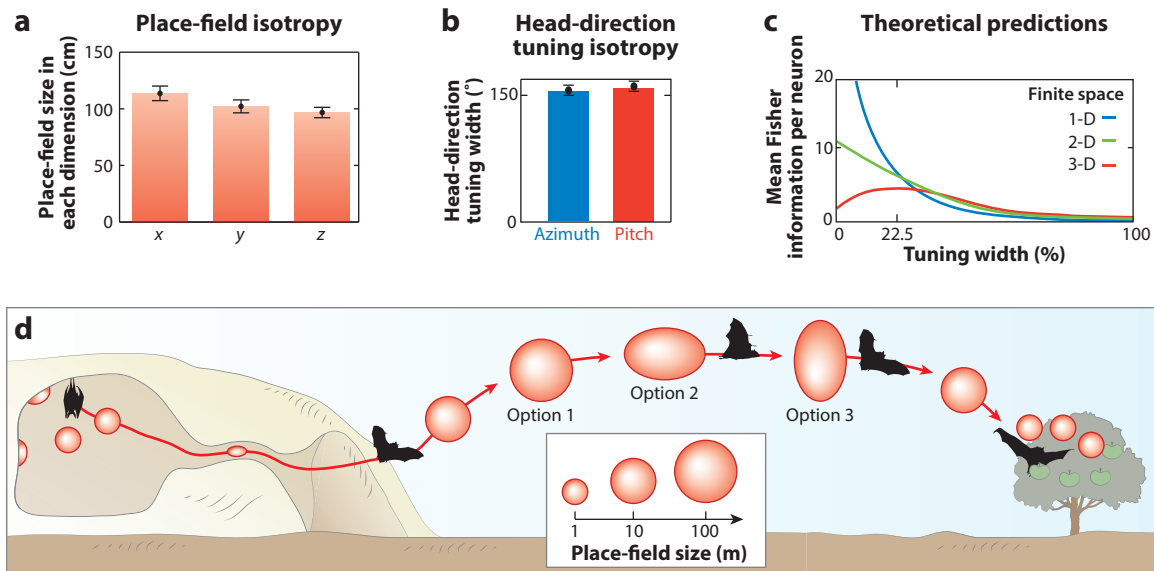


Figure 4

Isotropy and scale of 3-D neural representations. (a) 3-D place cells in bats during 3-D volumetric flight (measured as in **Figure 1f**) exhibit spherical place fields with a very similar size in all three dimensions, suggesting that 3-D place fields are isotropic. (b) Head-direction cells in bats have similar tuning widths in azimuth and pitch, suggesting that 3-D head-direction tuning is isotropic. (c) Theoretical predictions for the positional information encoded by a population of neurons tuned to 1-D, 2-D, or 3-D for finite-sized space (Brown & Bäcker 2006). Note that for 3-D navigation, there is an optimal tuning width at approximately 22.5% of the total range, i.e., place-field size is predicted to be 22.5% of the room size. (d) There are three different possibilities for place-field representation during large-scale (kilometer-sized) navigation of an Egyptian fruit bat. In option 1, place fields would be isotropic. In option 2, place fields might be compressed vertically because the volume through which the bat typically navigates outdoors (the behavioral space) is compressed vertically, spanning 15–30 km horizontally but only about 700 m vertically (Tsoar et al. 2011). In option 3, place fields will be elongated vertically, reflecting the behavioral demands for long-range navigation. For all the options, we predict that place fields will be much larger during large-scale navigation. Panel *a* based on data from Yartsev & Ulanovsky (2013). Panel *b* based on data from Finkelstein et al. (2015). Panel *c* adapted with permission from Brown & Bäcker (2006).

to be isotropic (circular) in both rats and bats (Jeffery et al. 2005, Knierim & McNaughton 2001, Ulanovsky & Moss 2007). Furthermore, 3-D place fields in bats were isotropic (spherical) during 3-D volumetric navigation (**Figure 1f**), exhibiting similar tuning width in all dimensions (**Figure 4a**) (Yartsev & Ulanovsky 2013). Likewise, 3-D head-direction representation in bats is also isotropic, with similar tuning width for azimuth cells and pitch cells (**Figure 4b**) (Finkelstein et al. 2015). Notably, the observation that under certain conditions the spatial resolution of place cells can be nonisotropic (Hayman et al. 2011, Jeffery et al. 2013) does not necessarily mean it is nonmetric. This is analogous to the global positioning system (GPS) that provides a metric 3-D position in all dimensions (x, y, z coordinates in GPS are all given literally in meters), although this metric information is more accurate in longitude and latitude (x and y) than in altitude (z) (Kaplan & Hegarty 2005). Therefore, we propose that the accumulated evidence on 3-D representations across species suggests the following: First, nonisotropic movements lead to nonisotropic neural representations, whereas isotropic movements result in isotropic representations (Ulanovsky 2011). Second, the 3-D spatial map is likely represented metrically in all three dimensions.

Another key factor that can influence the tuning width of 3-D place cells is the physical scale (size) of the environment. This point was reviewed in detail by Geva-Sagiv et al. (2015), and

hence we discuss it here only briefly. Experimental findings in 2-D showed that, first, expanding the environment along one of the dimensions results in elongation of the place field along that dimension (O'Keefe & Burgess 1996). Second, larger place fields are observed in larger environments (Kjelstrup et al. 2008, O'Keefe & Burgess 1996). Such place-field expansion is also predicted from theoretical considerations of optimal tuning width, which suggest that the tuning width of neurons may depend both on the dimensionality of space (one, two, or three dimensions) and on its spatial scale (size) (Brown & Bäcker 2006, Zhang & Sejnowski 1999). For finite 3-D space, Fisher information calculations predicted an optimal tuning width of approximately 22.5% of the environment size in each dimension (**Figure 4c**, *red curve*)—which, interestingly, was close to the relative size of place fields that we found for bat 3-D place cells during volumetric navigation (Yartsev & Ulanovsky 2013). This theoretical consideration predicts huge place fields for kilometer-sized environments; however, we note that other theoretical studies suggested instead that larger environments should lead to multiple small fields, not to larger fields (Hedrick & Zhang 2013). Future experiments should test how 3-D place fields look under kilometer-scale natural navigation (Geva-Sagiv et al. 2015).

Finally, the size and shape of 3-D place fields could be determined by complex combinations of the size and shape of the environment, as well as the degree of sensory isotropy and movement isotropy. For example, one possibility is that in open-field volumetric navigation, 3-D place cells would be isotropically tuned to all three dimensions but would have larger place fields compared to smaller environments (**Figure 4d**, option 1). However, even for infinite 3-D space, the behavioral space is anisotropic: For example, Egyptian fruit bats commute distances of 15–30 km horizontally, but their flight altitudes reach only up to about 700 m (Tsoar et al. 2011)—an approximately 30:1 ratio between the scales of horizontal and vertical movements, which can be viewed as a 2.5-D behavioral space. According to the aforementioned theoretical studies of optimal tuning (**Figure 4c**), in such a 2.5-D scenario, the place fields should shrink along the vertical dimension, maintaining a proportionally scaled optimal tuning width, yielding vertically compressed place fields (**Figure 4d**, option 2). Note that we assumed here that in outdoor open spaces, the relevant scale is the scale of the behavioral space of the animal and not the absolute environmental scale, which is practically infinite. A third possibility is that during volumetric navigation toward a distant target, the bat might not need to have a precise estimation of its altitude aboveground (as long as it is not hitting it), whereas estimating horizontal distance is more important. This might result hypothetically in elongation of place fields along the vertical dimension (**Figure 4d**, option 3), reflecting spatial uncertainty along the nonsalient dimension. Experiments in kilometer-sized environments are needed to test these contrasting possibilities.

FUNCTIONAL AND ANATOMICAL INTERACTIONS BETWEEN 3-D MAPS AND COMPASSES

Functional Anatomy of 3-D Spatial Circuits in the Hippocampal Formation

How are the map and compass systems in the brain wired anatomically to each other, and how does their wiring shape their function? We found a functional-anatomical gradient of head-direction cells along the transverse axis of the bat dorsal presubiculum, with 2-D azimuth cells located proximally in the presubiculum (close to the hippocampus) and 3-D azimuth \times pitch cells located distally (close to the entorhinal cortex). This 2-D-to-3-D functional gradient might arise from a combination of azimuthal directional inputs from subcortical nuclei such as the anterodorsal thalamic nucleus (Taube 2007)—which presumably projects to all parts of the dorsal presubiculum (**Figure 5a**, *blue arrows*)—and a putative pitch input that might project predominantly to the distal

part of the dorsal presubiculum (**Figure 5a**, red arrows). A convergence of azimuth and pitch inputs in the distal presubiculum may thus give rise to 3-D head-direction cells, whereas the proximal parts may receive only azimuthal input and therefore process mostly 2-D information.

This 2-D-to-3-D gradient of head-direction cells may affect other spatial cell types—in particular, grid cells in the medial entorhinal cortex (MEC), which were suggested to rely on head-direction inputs for computing the grid metric along each dimension (Burak & Fiete 2009). Interestingly, the transverse axis of the presubiculum, where we found the 2-D-to-3-D gradient of head-direction cells, projects in an inverted manner to the transverse axis of the MEC (**Figure 5a**) (Honda & Ishizuka 2004). Thus, distal MEC receives inputs from the proximal part of the dorsal presubiculum—which contains predominantly azimuthal head-directions cells—but does not receive pitch (vertical) head-direction inputs. If 3-D head-direction information is indeed crucial for grid formation in 3-D, then distal MEC grid cells would be insensitive to the vertical dimension and would discharge in 3-D space along vertically elongated hexagonal columns. In contrast, proximal MEC, which receives inputs predominantly from the distal presubiculum (that contains 3-D head-direction cells), is expected to contain 3-D grid cells tuned to all three axes, including altitude—namely, these 3-D grid cells should exhibit spherical firing fields, which could be arranged on a perfect 3-D lattice or might have a nonperfect 3-D arrangement.

Finally, we note that the entorhinal-hippocampal anatomical connectivity is very similar between bats and rats (Kleven et al. 2014), suggesting that the 2-D-to-3-D gradient of head-direction cells that we found in the presubiculum (and the corresponding predictions for grid cells in MEC) might be general across mammals. Because a 3-D head-direction tuning has never been studied in rodent presubiculum, this further highlights the need to record in the dorsal presubiculum of rats and mice during 3-D behaviors.

The Hippocampal Formation: A Neural Realization of a Kalman Filter?

A common problem encountered in human-made 3-D navigation systems, such as airplanes, spaceships, and submarines, is that directional and positional measurements by compasses and GPS can be noisy. In addition, similar information can also be computed from self-motion by an inertial navigation system (INS), which uses motion sensors and a set of navigational equations to compute the expected position, orientation, and velocity of a moving object via dead reckoning (path integration). Yet such estimation by an INS is very noisy and accumulates substantial errors over time. There is, however, a well-established engineering solution to this noisy-navigation problem: A recursive algorithm, known as the Kalman filter, can improve the navigational accuracy by comparing the GPS and compass measurements with those predicted by the INS and using both systems to generate a refined estimate of position and direction (Mohamed & Schwarz 1999).

In neuroscience, the Kalman filter was used to date mostly to model sensorimotor integration, such as tracking the hand position in space (Wolpert et al. 1995). In that case, researchers suggested that the brain generates an estimate of where the hand should be, based on an internal model of the arm kinematics (similar to INS), and compares it with the sensory-based estimation of the hand position (similar to GPS and compass). The error between the estimate of the internal model and the estimate based on sensory input is used by the Kalman filter to generate a more precise approximation of the hand position.

Here we hypothesize that, similar to the internal model that is needed to control 3-D arm movement (Wolpert et al. 1995), one would also need an internal model for controlling 3-D whole-body movement for navigation. Therefore, an intriguing possibility is that similar recursive interactions might exist in the hippocampal formation between the 3-D map and compass systems and the path-integration system (**Figure 5b**). These systems could mutually correct each other,

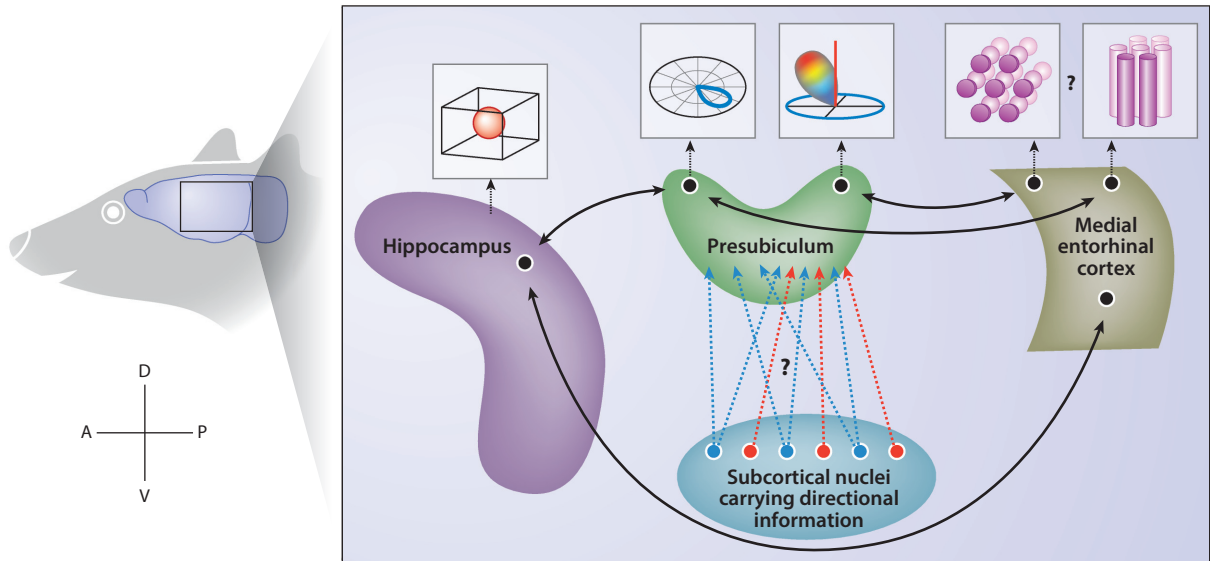
Kalman filter:

an optimal recursive estimation algorithm; in human-made navigation systems, it combines noisy sensor measurements with inertial measurements and an internal model to improve the estimation accuracy of location and orientation

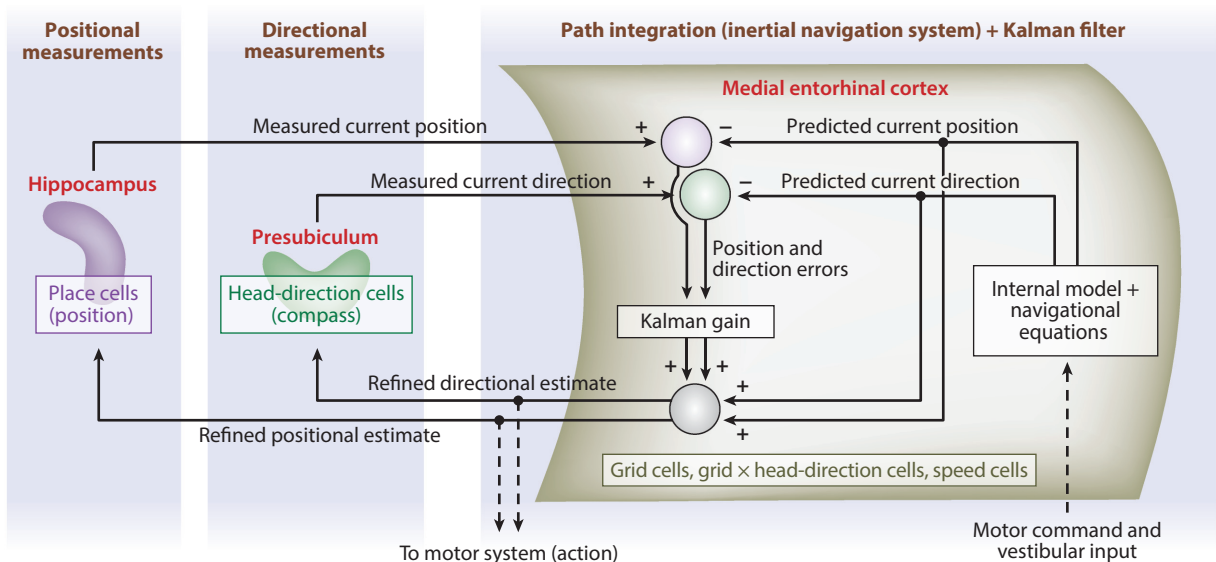
thus providing refined directional and positional estimates by implementing a neural analogue of a Kalman filter. According to our hypothesis, a sensory-based estimate of position and direction is computed in the hippocampus and the presubiculum by place cells and head-direction cells, respectively, which act as the neural analogue of a GPS and a compass. Additionally, we posit that the MEC forms an internal model of the animal's position and orientation, based on path integration (analogously to an INS).

The process of path integration (McNaughton et al. 2006) uses self-motion information to generate predictions of the animal's position and orientation—similarly to the function of internal

a Functional connections in the 3-D navigation system



b The hippocampal formation as a Kalman filter?



models (forward models) in the motor system (Wolpert & Ghahramani 2000, Wolpert et al. 1995). The proposed internal model in the entorhinal cortex receives vestibular inputs (Jacob et al. 2014) that may update the model's prediction via navigational equations that are implemented by the entorhinal network, which includes grid cells (Hafting et al. 2005) and speed cells (Kropff et al. 2015), all of which were suggested to be important for path integration. The proposed involvement of grid cells and speed cells in path integration is one of the key reasons for our suggestion that the internal model for navigation resides in the MEC. We note that another component potentially important for path integration—angular velocity cells (Taube 2007)—was reported so far only in subcortical regions, and therefore it would be interesting to search for an angular-velocity signal in the MEC. Finally, we suggest that the sensory-based navigational measurements in the hippocampus and the presubiculum are compared with the prediction of the path-integration system in the MEC, and the resulting error is used by a neural analogue of a Kalman filter to weigh the relative contribution of each of the components and to refine the final positional and directional estimates, which are then sent back to the hippocampus and presubiculum (**Figure 5b**).

The proposed putative Kalman filtering (or a similar recursive error-correction algorithm that compares sensory measurements with an estimate of an internal model) could be implemented by a network with attractor dynamics (Denève et al. 2007) in the MEC (Yoon et al. 2013) and might depend specifically on directionally tuned grid cells (Sargolini et al. 2006). These neurons are tuned to both position and head direction, and they thus contain the information required to compute a refined directional and positional estimate. Notably, such a Kalman-based error-correction mechanism might be relevant not only for 3-D but also for 2-D navigation (Bousquet et al. 1998). Moreover, this proposed notion could reconcile the arguments on whether spatially tuned neurons in the hippocampal formation reflect sensory information or path integration:

Figure 5

Functional-anatomical interactions between 3-D maps and 3-D compasses. (*a*) The mammalian navigation circuit and its different functional cell types. Known excitatory projections are shown as black arrows. This illustration shows the functional gradient of head-direction cells along the transverse axis of the bat's dorsal presubiculum from 2-D to 3-D (see Finkelstein et al. 2015); this gradient can be explained by putative differences between subcortical azimuthal inputs that may project to the entire dorsal presubiculum (*blue arrows*) versus hypothesized pitch inputs from subcortical nuclei that may project only to the distal part of dorsal presubiculum (*red arrows*). The 2-D-to-3-D gradient in head-direction tuning might in turn give rise to a 2-D-to-3-D gradient of grid cells along the transverse axis of the medial entorhinal cortex. The diagram below the animal's head shows the directions of the dorsal-ventral (D-V) axis and anterior-posterior (A-P) axis. (*b*) The hippocampal-presubicular-entorhinal loop could implement a neural analogue of a Kalman filter—a standard 3-D navigation system used in airplanes, spaceships, and submarines—that is comprised of positional and directional sensors (e.g., GPS and compass); an inertial navigation system (INS) containing gyroscopes, accelerometers, and speedometers, which allow path integration; and a set of navigational equations that allow combining the positional and INS information to perform error-correction for computing a more accurate navigational estimate. We propose that, first, hippocampal place cells and presubicular head-direction cells, respectively, implement the positional system and compass system. Second, we posit that the entorhinal cortex contains an internal model that performs path integration via grid cells and speed cells—so the internal model functions similarly to an INS. Third, the error-correction is done by a neural analogue of a Kalman filter in the medial entorhinal cortex, where conjunctive grid \times head-direction cells might carry the refined navigational information. According to this view, the internal model is initialized by the previous location and orientation of the animal and is updated by self-motion cues (vestibular inputs as well as motor commands) to generate a prediction of the current position and orientation of the animal via path integration. This estimate is then compared in the medial entorhinal cortex to the measured current position and direction signals arising from the hippocampus and the presubiculum. The resulting error is used by the Kalman gain to weigh the sensory-based estimate versus the internal estimate (i.e., the signal from the hippocampus and presubiculum versus the prediction of the internal model in the medial entorhinal cortex) to generate a refined positional and directional estimate. This new estimate is then sent back to the hippocampus and presubiculum to refine the place-cell and head-direction-cell tuning; it also leaves the hippocampal formation toward the motor system to guide action.

We propose that this circuit combines both sensory information and path integration to guide navigation and that this is done via a recursive error-correction mechanism such as a Kalman filter.

What is the experimental evidence in favor of this hypothesis? First, both place cells and head-direction cells rely on a combination of external sensory processing and path integration (McNaughton et al. 2006). In the case of place cells, recordings in echolocating bats moving in darkness showed that place fields sharpen after each echolocation call (Ulanovsky & Moss 2011), as would be expected from a path-integration system that accumulates errors between the sensory inputs (between calls) and is then refined by each incoming sensory input. Similarly, head-direction representation accumulates errors in the absence of visual cues but can be corrected by positional cues such as the borders of the environment (Valerio & Taube 2012), indicating that head-direction computation also involves combined processing of external sensory inputs and path integration. Second, although the sensory-based positional and directional systems can function without each other, we predict that their estimate is refined via a Kalman filter (**Figure 5b**), and hence the accuracy of one type of system (i.e., place cells or head-direction cells) is expected to degrade if the other is impaired. Indeed, in rats with lesions of the dorsal presubiculum, place cells remained active, but their tuning became broader (Calton et al. 2003). Similarly, without the hippocampus, head-direction cells still provided direction information but became less stable (Golob & Taube 1999). Third, we expect that the components of a Kalman filter should be strongly affected in the absence of either the positional or directional systems; conversely, the positional and directional systems would still function (albeit more noisily) without the Kalman filter. Indeed, whereas grid cells lose their hexagonal firing pattern when either place-cell or head-direction-cell signals are disrupted (Bonnievie et al. 2013, Winter et al. 2015), the place and head-direction cells are affected only mildly by the loss of grid cells (Brun et al. 2008, Clark & Taube 2011, Hales et al. 2014, Koenig et al. 2011). Fourth, the Kalman model makes a specific prediction that if the positional input from the hippocampus is turned off, then the directional tuning in the entorhinal cortex should become sharper (because the Kalman filter gives higher weight to the more reliable input-channel)—which is exactly what was observed in experiments in which the hippocampus was inactivated, and medial entorhinal neurons were then shown to sharpen their head-direction tuning (Bonnievie et al. 2013). Fifth, if grid cells are implementing a Kalman filter, they should develop during ontogeny at a later stage than the positional and directional signals (i.e., place cells and head-direction cells). This is indeed the case (Langston et al. 2010, Wills et al. 2010). Sixth, the anatomy of the hippocampal-presubicular-entorhinal loop seems to suit particularly well a Kalman-filter implementation: compare **Figure 5a** and **b**. Taken together, it seems possible that the navigational function of the hippocampal formation is consistent with a biological realization of a Kalman filter—an algorithm that is used heavily for 3-D navigation in human-made vehicles. It remains to be seen in future experiments whether biology and technology indeed evolved similar solutions to the problem of 3-D navigation.

FUTURE OUTLOOK

Natural 3-D navigation behaviors are complex and consist of different navigation modes—planar, multilayered, and volumetric navigation—with most animals being able to switch flexibly between these different modes. In this review, we proposed that the properties of neural maps and compasses in the hippocampal formation depend strongly on behavior, being influenced both by pup behavior during ontogeny and by the adult behavioral repertoire. For example, the dimensionality of movement through space may determine the dimensionality of the map, and different map fragments will be formed consequently for 2-D and 3-D navigation. Similarly, the statistics and topology of movement through space define the topology of the neural representation, as

exemplified by the toroidal nature of the 3-D neural compass in bats. An important future challenge will therefore be to test systematically in multiple species how the properties of 3-D behavior affect the nature of 3-D maps and compasses.

We next suggested that hippocampal place cells form a mosaic of 2-D and 3-D spatial maps, and we proposed that a global 3-D compass may stitch these map fragments into a global 3-D spatial representation that allows novel 3-D shortcuts. We argued that current data suggest that 3-D place cells and 3-D head-direction cells embody a metric representation of 3-D volumetric space (as in GPS). An important future test for this idea would be to record from 3-D grid cells: Do they support the notion of a metric representation of 3-D space?

We also proposed that the hippocampal-presubicular-entorhinal loop may implement a Kalman filter recursive-prediction algorithm for 2-D and 3-D navigation. Wolpert et al. (1995) proposed similar ideas for the interaction between the body and the world in the motor system. We speculate here that, more broadly, a similar process of recursive prediction might form the basis for all two-way interactions between an organism and its environment.

Finally, a major challenge would be to elucidate the properties of 2-D and 3-D maps and compasses during natural 3-D navigation. What are the neural codes underlying real-life navigation in complex 3-D environments and over large naturalistic scales (kilometers)? Answering this question will be one of the key future challenges for the field of behavioral neuroscience.

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