



Spatial Navigation in Humans and Rodents

Bridging Levels of Analyses

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Abstract This chapter reviews and synthesizes current understanding of the neural and cognitive mechanisms that support spatial navigation, with the goal of linking neuronal activity to complex spatial behavior across species. Single-neuron recordings in rodent studies have identified key neuronal representations such as place cells, grid cells, and head-direction cells that form the basis of cognitive maps. Human neuroimaging and intracranial studies have identified indirect homologues of the neural spatial signals and have provided insights into the neural basis of higher-order spatial processes, including path planning and vector computation. Despite this progress, the generation of a unified account that integrates across different processing levels has remained challenging due to methodological differences across species and techniques. To bridge these gaps, three strategies are proposed: (a) methodological bridges, in which cellular-level and macroscopic measures, obtained from rodent and human studies respectively, are aligned through computational modeling and signal alignment; (b) behavioral bridges, in which comparable navigation tasks are employed across species in naturalistic or large-scale environments; and (c) developmental bridges, in which rodent neurodevelopment is used to identify milestones in the emergence of navigational abilities across species. By integrating findings from neurophysiology, neuroimaging, computational modeling, and developmental studies, a comprehensive framework linking neuronal mechanisms with spatial behavior can be achieved.

Keywords Navigation, rodents, humans, cognitive map, spatial cells

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1 Introduction

Understanding how humans and other animals navigate in search of food, shelter, and mates is a central goal in biology, psychology, and neuroscience. Over the past decades, research efforts have focused on elucidating the neuronal networks and cellular representations that underpin spatial navigation. Human neuroimaging studies have provided a comprehensive overview of the network of brain regions that underlie spatial navigation and the specific functional contributions of individual regions (for reviews see Dilks et al. 2022; Epstein 2008; Epstein et al. 2017; Julian et al. 2018b). In addition, human intracranial recording studies have yielded important insights about how spatial information is encoded at the neuronal level (e.g., Ekstrom et al. 2003; Jacobs et al. 2013; Tsitsiklis et al. 2020). However, as intracranial studies are only possible in small clinical populations (e.g., individuals with drug-resistant epilepsy), and the recording locations and techniques are determined by clinicians rather than researchers, it is essential for insights gained from human research to be complemented by data acquired from animal models, where neuronal circuit mechanisms and representations can be studied systematically.

The most studied animal model in the field is the rodent (mice, rats). Although rodents and humans differ in important ways (see [Section 2.2](#)), they share a similar ecological niche as central-place foragers (Metcalf and Barlow 1992), rely on similar strategies during navigation and some of the anatomical structures that support navigation are conserved across the two taxa. Indeed, nonhuman, tree-dwelling primates that are evolutionarily closer to humans have radically different foraging patterns. Rodent studies have provided detailed insight into the neuronal representations and mechanisms that support mammalian spatial behavior. These studies have, in turn, inspired detailed computational models of diverse spatial cognitive processes. Thus, the field of spatial navigation is in a promising position to integrate the different processing levels—from single-cell and cell population activity to complex spatial behaviors—to create a comprehensive framework that links brain and behavior.

Connecting different processing levels, however, has been impeded by fragmentation in the research field. Systems neuroscientists studying the spatial responses of single neurons in the rodent brain, for example, interact only occasionally with cognitive neuroscientists studying navigation-related responses in humans via noninvasive brain imaging techniques. To create a comprehensive, cross-level description of navigation, these separate areas of research must be connected. Here, our aim is to link these areas by creating three bridges. We begin by reviewing and comparing side-by-side research derived from human and rodent studies that employ different neuronal recording methods to enable a unified account of the neuronal representations and population mechanisms that underlie our ability to orient ourselves in space and navigate to spatial goals. We then discuss areas where methodological differences between studies hinder the creation of a cross-level description of navigation and propose solutions to bridge these gaps (methodological bridge). Thereafter we discuss aspects of spatial behavior that lack a cross-level explanation and offer concrete suggestions for tasks and approaches to fill these knowledge gaps (behavioral bridge). Finally, we explore how recent studies on rodent neurodevelopment provide an alternative approach for creating a cross-level description of navigation, offering

insights into the neurodevelopmental milestones that underlie navigation development (developmental bridge) as well as suggestions for future research.

2 The Neural Basis of Spatial Navigation

2.1 Cognitive Maps in Rodents and Humans

To navigate efficiently from place to place, humans and other animals rely on internal representation of spaces, which are sometimes referred to as a “cognitive map” (Tolman 1948). The reference frame of a cognitive map is world-(allo)centric: it emphasizes the independence of the cognitive map representation from the current position or orientation of the organism and enables flexible navigation, such as taking shortcuts or detours. In the classical view, the reference frame of the cognitive map is Euclidean (O’Keefe and Nadel 1978), but alternative views suggest that maps may take a more graph-like format and violate Euclidean properties of distances between places (Chrastil and Warren 2014; Peer et al. 2024; Warren 2019).

A wealth of human and rodent studies have identified the central involvement of the medial temporal lobe (MTL) and, in particular, the hippocampus in mediating cognitive maps (Hartley et al. 2003; O’Keefe and Conway 1978; O’Keefe and Dostrovsky 1971; Vargha-Khadem et al. 1997). Single-neuron electrophysiological recording studies in freely moving rodents (Figure 9.1a, i) have shown that hippocampal principal cells (recorded from the CA1–CA3 subregions) encode a unique position in space (Figure 9.1a, ii) and, as a population, keep track of an animal’s spatial location (O’Keefe and Dostrovsky 1971; O’Keefe and Nadel 1978). Importantly, the population of place cells that are active in different environments as well as the position in which they fire in these environments are not correlated; that is, place cells form a new map for each environment, a process termed *remapping* (Muller and Kubie 1987). Place cells, however, seem to be metric free, lacking an important property of maps. Aside from place cells with neighboring place fields that overlap partially, place cells alone cannot be used to infer relative distances. Grid cells likely provide a metric for distance metric and path-integration abilities (Hafting et al. 2005; Mittelstaedt and Mittelstaedt 1982 and discussed further below).

Cognitive maps are anchored to the environment via allothetic cues such as landmarks (e.g., tall buildings, statues, or other prominent visual cues) and environmental geometry (Cheng 1986; Epstein and Vass 2014). For example, when walking out of a London underground station in search of a restaurant located on the river Thames, one may look for the Big Ben tower to determine in which direction and how far to walk. One could also rely on geometric cues about the shape of the environment, particularly in small, confined spaces such as rooms. In the classic reorientation task, if organisms learn that a target object can be found in one corner of a rectangular environment and undergo disorientation before testing, they are equally likely to search in a location that is diagonally opposite to the correct location, an area that is geometrically equivalent to the location where they had found the object previously (Cheng 1986).

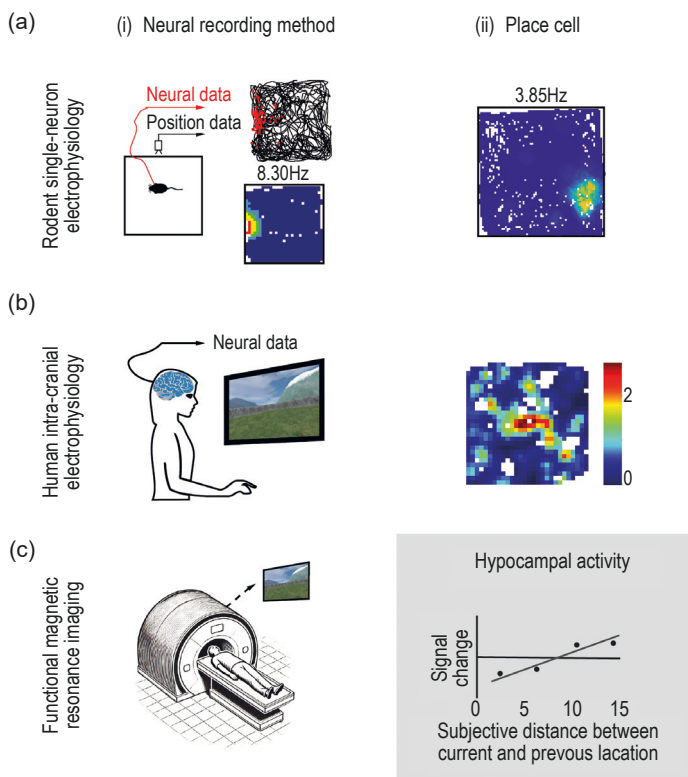


Figure 9.1 Studying the hippocampal cognitive map in humans and rodents. (a) Rodent neuronal hippocampal recording and spatial representation. (i) Schematic drawing of a setup to record spatial cell types in the rodent brain. While single-neuron activity is recorded (left), the position of the animal is recorded on a moment-to-moment basis with an overhead camera. Spikes recorded from a single hippocampal place cell (top right, red dots) are plotted on top of the animal's path (black lines). Spatial rate map of a cell's activity in the square environment (bottom right); hotter colors indicate higher activity. (ii) A rate map of an example place cell, showing peak firing rate of cell. (b) Single-neuron hippocampal representations recorded in the human brain using intracranial electrophysiological techniques. (i) Schematic of a standard setup to record spatial representations. As subjects engage in virtual reality (VR) spatial navigation tasks, electrophysiological signals are recorded from the brain. (ii) Example rate map of a human hippocampal place cell recorded during a VR navigation task (Jacobs et al. 2013, used with permission from Springer Nature). (c) Evidence for hippocampal spatial representations in the human brain obtained via fMRI experiments. (i) Schematic of subject undergoing fMRI while conducting VR navigation tasks. (ii) Change in hippocampal fMRI BOLD signal (y-axis) in relation to distance between landmarks shown on successive trials (after Morgan et al. 2011, used with permission).

Akin to the cues known to guide orientation behavior, visual landmarks and environmental geometry are known to influence place-cell activity. For example, if a prominent distal visual cue rotates around the environment, the spatial firing fields (place fields) of place cells rotate by a proportional amount (Muller and Kubie 1987; O'Keefe and Conway 1978). Similarly, morphing a square-shaped environment into a circular-shaped environment has been found to induce remapping (Wills et al. 2005); even a mere stretch of one axis of an environment can lead to a concomitant "stretching" of place fields (Burgess and O'Keefe 1996). However, place cells are not exclusively influenced by allothetic cues. Place cells can maintain their

place fields in the dark (Save et al. 1998; Save et al. 2000), and a wealth of studies have shown that self-motion (idiothetic) cues are critical for place-cell activity (Terrazas et al. 2005). This demonstrates sensitivity to internal (idiothetic) cues (e.g., vestibular and proprioceptive cues) as well as signals relayed from the motor system (motor efference copy) and optic flow, all of which are known to guide navigation through a process called *path integration* (Darwin 1873). Navigation seldom relies exclusively on path integration as it is inherently error prone: it relies on the addition of multiple incremental movement steps—errors which could be catastrophic in larger environments. Thus, accurate navigation is thought to rely on the integration of both allo- and idiothetic cues (e.g., Cheung et al. 2012; Parra-Barrero et al. 2023), with different cues being weighted according to the reliability of sensory information (Chen et al. 2013; Evans et al. 2016; Gothard et al. 1996). Hippocampal place cells are sensitive to both types of inputs.

Neurons with similar activity properties have also been identified in humans implanted with intracranial electrodes as they navigate through virtual reality (VR) environments (see [Figure 9.1b](#), i) (Ekstrom et al. 2003; Kunz et al. 2021; Kunz et al. 2024; Miller et al. 2013; Tsitsiklis et al. 2020). Similar to rodent place cells, these cells increase their activity when a participant occupies a specific location in (virtual) space ([Figure 9.1b](#), ii). Furthermore, functional magnetic resonance imaging (fMRI) studies ([Figure 9.1c](#), i), which examine hemodynamic correlates of brain activity at a more macroscopic level ($\sim 1\text{--}27\text{ mm}^3$), have reported findings consistent with the idea that the hippocampus encodes a map-like representation of space. For example, studies have shown that positions located near each other in VR space are represented as being similar ([Figure 9.1c](#), ii) (Deuker et al. 2016; Morgan et al. 2011; Nielson et al. 2015). Moreover, fMRI studies have shown that the hippocampus is preferentially engaged when participants participate in map-based navigation tasks (Chadwick et al. 2015; Hartley et al. 2003; Howard et al. 2014).

As noted above, although the human hippocampus may represent space in a manner similar to the rodent, neurons in the human hippocampus may display additional encoding capabilities. For example, in certain tasks, the activity of human hippocampal neurons can couple to the position of a spatial target (i.e., spatial target cells; Tsitsiklis et al. 2020). Nonhuman primate (NHP) research has reported cells that encode remote places, such as where a NHP is looking regardless of their own position (Mao et al. 2021; Rolls and O'Mara 1995; Wirth et al. 2017). In addition, the encoding of abstract representations of objects (concept cells) has been reported in human intracranial studies (Quiroga et al. 2005). These cells are thought to contribute to the hippocampus's role in episodic memory. Whether these findings point to divergent- or convergent-encoding mechanisms across species is still a matter of debate, a topic we explore next.

2.2 Alternative Model Organism for Bridging Analysis Levels in Navigation Research

Evolutionarily closer to humans than rodents, NHPs offer the possibility of bridging brain activity and navigation behavior and allow intracranial recordings to be

conducted. A prominent early study of NHP hippocampal responses emphasized their primary function as “spatial view” cells; that is, hippocampal neurons fired not according to where an animal was, but rather to where it was currently looking (Rolls and O’Mara 1995). This finding diverged notably from the established place-cell coding observed in rodents, and subsequent controversy focused on whether the information processed in primate and rodent hippocampal systems was fundamentally different (Mao et al. 2021; Rolls and Wirth 2018; Zhu et al. 2023). A key point of contention was whether the immobility of the experimental primate subjects (fixed in a chair) altered the activity of hippocampal neurons in a fundamental way such that freely moving subjects would have demonstrated place-tuned activity in their hippocampus, akin to that observed in rodents. Resolution of this controversy came through experiments that had NHPs actively navigate in VR (Furuya et al. 2014; Gulli et al. 2020; Wirth et al. 2017) or that freely moved in a manner analogous to rodent experiments (Mao et al. 2021; Xu et al. 2024) as well as a recent avian study that recorded the activity of place cells in relation to spatial and gaze behavior (Payne and Aronov 2025). Key consensus points emerged from these studies:

- The majority of NHP hippocampal neurons appear to encode complex multivariate information, including combinations of position, facing or gaze direction, linear and angular speed, and head tilt.
- Both the current position and the position being looked at or faced are among the variables consistently coded. Indeed, of all gaze-tuned hippocampal neurons in the black-capped chickadee, 95% exhibited place-specific responses when the bird occupied the location corresponding to their preferred gaze target (Payne and Aronov 2025).

Comparable findings have been reported in human intracranial studies, where cells that encode the position of a spatial target have been observed (Tsitsiklis et al. 2020). Thus, although differences may exist in terms of the inputs that underpin spatial representations in different species, and view-based coding may dominate, it appears that the “place-coding” function of the hippocampus is preserved across species and that an important “remote” place-coding function emerged in the primate order.

Human intracranial studies have also reported neurons in the MTL that encode abstract representations of a person (e.g., Jennifer Aniston) or building (e.g., Sydney Opera House) (Quiroga et al. 2005). These abstract representations, termed *concept cells*, have been argued to be evidence for encoding divergence between rodent and humans and are hypothesized to give rise to episodic memory capabilities, which may be unique to humans (but see Bicanski 2025; Buzsaki and Tingley 2018). At this point, however, we caution against such an interpretation because the encoding of concepts has not been investigated explicitly in rodents. Thus, with the right paradigm, comparable neuronal representations may be found in rodents. Furthermore, rodent place-cell activity has been linked to memory processes such as recall (e.g., during replay when nonlocal place-cell representations are activated, sometimes reflecting upcoming paths) (Pfeiffer and Foster 2013; Wilson and McNaughton 1994). Even more tantalizing evidence comes from a recent brain-machine interface study, which showed that rodents

can volitionally activate remote place representations (Lai et al. 2023). Mounting evidence suggests that hippocampal neuronal representations show a considerable degree of convergence across species. Based on common anatomical features of the hippocampal formation and some convergence in neural responses, we suggest that, to a first approximation, the hippocampal formation performs similar computations across species, albeit operating on different kinds of inputs: rodents predominantly explore with their body, whereas primates also use eye movements to explore space. We encourage researchers interested in species-specific differences to employ paradigms suited for cross-species testing so that such differences can be identified without bias.

2.3 Coding of Orientation, Distance, and Boundaries

To generate a map-like representation, hippocampal place cells need to integrate orientation and distance information. This information is thought to derive from brain regions afferent to the hippocampus and is summarized here, along with the spatial representations they encode.

Orientation information is thought to be relayed to place cells by head-direction (HD) cells (Taube et al. 1990). These cells encode an animal's allocentric orientation in space irrespective of the animal's spatial position ([Figure 9.2a, ii](#)). HD cells have been extensively recorded in rats. First discovered in the postsubiculum (PoS) by Ranck (1984), they have since been found in multiple brain regions, with the main loci being the medial entorhinal cortex (MEC) (Sargolini et al. 2006), retrosplenial cortex (RSC) (Cho and Sharp 2001), the anterior dorsal thalamic nucleus (ADN), and the lateral mammillary nucleus (LMN) (Stackman and Taube 1998). HD cell activity is driven by vestibular input from the brain stem that projects to the HD circuit via the LMN and the dorsal tegmental nucleus (DTN) (Blair et al. 1998; Sharp et al. 2001). External cues such as landmarks, however, also exert strong influence over HD cells in all loci of the circuit (Taube 1995; Taube et al. 1990). The RSC and PoS are thought to be critical for registering HD tuning to landmark cues (Goodridge and Taube 1997; Vann and Aggleton 2005) and serve as a key gateway for visual information (Taube 2007). Modeling studies have shown the RSC is needed to correct for drift of the heading estimate coded by HD cells (Bicanski and Burgess 2016; Page et al. 2018; Yan et al. 2021). In addition, RSC has been suggested to play a role in egocentric-to-allocentric transformation of visually derived object and boundary representations (Bicanski and Burgess 2018; Byrne et al. 2007).

HD cells have not been studied directly in humans, due to the nonexistence of human single-neuron data during real-world navigation studies. Moreover, in human neuroimaging studies, subjects navigate VR environments while lying still in a scanner, thus observed neural correlates of head direction relate necessarily to *virtual*, or even imagined, orientation rather than actual head direction. Nonetheless, a few single-neuron studies have identified neurons in the human MTL (hippocampus, parahippocampal cortex, EC), where activity correlates with a person's direction in virtual space ([Figure 9.2b, ii](#)) (Jacobs et al. 2010; Kunz et al. 2021). In addition,

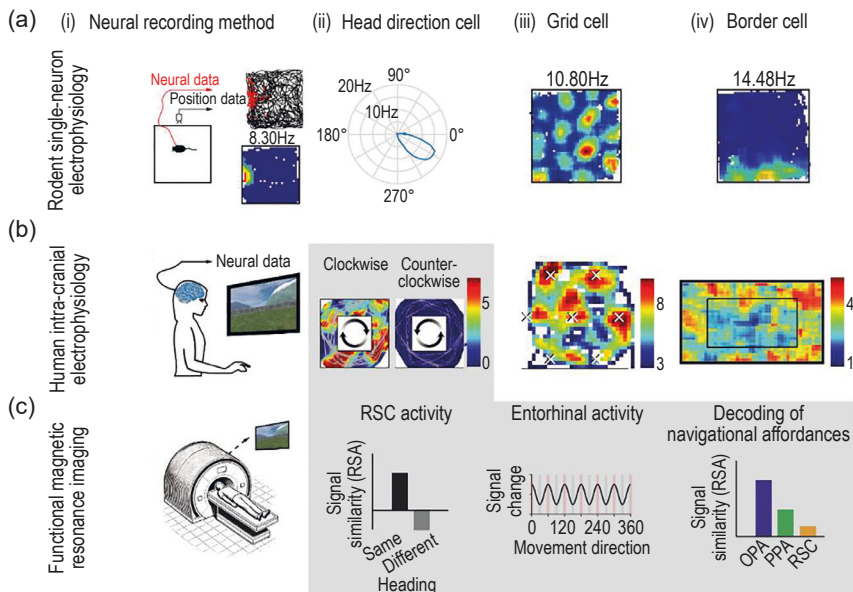


Figure 9.2 Neuronal representations for head direction, distance and boundaries in rodents and humans. (a) Rodent neuronal spatial representations. (i) Same as Figure 9.1. (ii) Polar plot showing directionally modulated activity of a HD cell in the anterior dorsal thalamic nucleus. Rate map of sample grid (iii) and border (iv) cells. (b) Spatial representations recorded in the human brain using intracranial electrophysiological techniques. (i) Same as Figure 9.1. (ii) Rate maps of a cell recorded in the entorhinal cortex while subjects navigated a virtual square-shaped corridor in a clockwise (left) or counterclockwise (right) manner (Jacobs et al. 2010, used with permission). (iii) Rate map of an entorhinal grid cell recorded during VR navigation (from Jacobs et al. 2013, used with permission). (iv) Rate map of local field potential theta power recorded from the subiculum while subjects learned the locations of objects in a rectangular-shaped environment (Lee et al. 2018, used with permission). (c) Evidence for spatial representations in the human brain obtained via fMRI experiments where subjects engage in VR navigation tasks. (i) Same as Figure 9.1. (ii) Similarity between BOLD signal recorded from the retrosplenial complex for the same and different head directions (Vass and Epstein 2016, used with permission from Oxford University Press). (iii) BOLD signal change, displaying sixfold symmetry, from the entorhinal cortex in relation to angular difference between sampled paths (after Bin Khalid et al. 2024). (iv) BOLD signal similarity from the parahippocampal place area (PPA), occipital place area (OPA), and RSComp in relation to the similarity of the navigational affordances of different scenes (after Bonner and Epstein 2017). Shaded panels indicate indirect evidence for a particular spatial representation.

fMRI studies have shown orientation-related signals in the EC and retrosplenial complex (RSComp, including the RSC) during VR spatial navigation (Figure 9.2c, ii), suggesting an orientation code may also exist in humans (Bellmund et al. 2016; Chadwick et al. 2015; Lu et al. 2025; Marchette et al. 2014; Persichetti and Dilks 2019; Vass and Epstein 2017). Still, it remains unclear whether this code is driven by inputs that are similar to rodent HD cell activity, which are generated by the same neural circuit (see Bicanski, Chapter 5).

Information about distance traversed is thought to be mediated by a class of MEC neurons known as grid cells (Hafting et al. 2005). Grid cells display periodic spatial firing fields that tessellate entire environments in a triangular grid-like array

(Figure 9.2a, iii) at different scales. Through their periodic activity, grid cells are thought to provide a continuous update regarding an animal's translational movements (i.e., odometry). In addition, a subset of MEC grid cells display a conjunctive code, responding only when an animal's head is oriented in a particular allocentric direction (Sargolini et al. 2006). In contrast to place cells, grid cells are active in all environments. Given the ubiquity of the grid code and its encoding of distance and orientation, these cells have been hypothesized to be the source of the path-integration signal in the hippocampal cognitive map, a hypothesis that has received some experimental support (Gil et al. 2018; Peng et al. 2025; Tennant et al. 2018).

Single neurons with grid-like properties have also been described in the human EC (Figure 9.2b, iii) (Jacobs et al. 2013; Miller et al. 2015). Yet because single-neuron recordings in the EC are rarely possible in humans, the vast majority of human grid-cell research comes from studies using fMRI. Given the macroscopic nature of the brain-activity signal recorded in fMRI, researchers have developed a method to identify a putative proxy for grid-cell activity, sometimes referred to as a grid-like signal (Doeller et al. 2010). Essentially, this method identifies six-peaked (with peaks 60° apart) modulation by movement direction of the fMRI BOLD signal in response to participants' motion through a VR environment (Figure 9.2c, iii). Although a mechanistic link between grid cells and the grid-like signal still remains unclear (Bin Khalid et al. 2024; Kunz et al. 2019; see also Chapter 6), multiple groups have independently found grid-like activity in the human EC during motion in VR environments (Doeller et al. 2010; Kunz et al. 2015) and mental navigation (Bellmund et al. 2016; Horner et al. 2016), as well as in abstract two-dimensional spaces (Bellmund et al. 2018; Constantinescu et al. 2016), suggesting a grid-cell code akin to that seen in rodents may also exist in humans.

Information about the geometry of an environment's boundaries (e.g., walls and drop edges) is thought to be integrated in rodents by boundary vector cells (BVCs) found in the subiculum (Lever et al. 2009) and border cells in the MEC (Solstad et al. 2008). BVCs fire at fixed distances from environmental boundaries that are located at a particular allocentric direction from the animal (e.g., west wall, see Figure 9.2a, iv). Border cells in MEC similarly code for boundary-related information, but they fire exclusively when the animal is located at or near an environmental border. No intracranial recording studies have investigated boundary-related single-neuron representations in humans, and only a few studies have investigated changes in intracranial EEG signals in the MTL in response to humans moving freely in space. These latter studies observed an increase in theta power when subjects navigated or learned items close to environmental boundaries (Figure 9.2b, iv) (Lee et al. 2018; Stangl et al. 2020). Similarly, a small number of studies have investigated boundary-related modulation of the BOLD signal. These studies identified a number of brain regions, such as the parahippocampal place area (PPA) and occipital place area (OPA), which respond when subjects are presented with an environmental boundary or an object that impedes their navigation through space (Figure 9.2c, iv) (for recent reviews, see Dilks et al. 2022; Epstein 2008; Julian et al. 2018b). Thus, there is some evidence for the representation of geometric information in the navigation network of the human brain, although the cortical regions implicated in geometric processing in the human brain may use boundary or object information for different purposes (Dilks et al. 2022).

Studies in humans have identified several neocortical regions that are proposed to provide the described spatial cell types with allothetic input. These include the PPA, the OPA, the RSComp, and the superior parietal lobe (Epstein and Baker 2019; Kennedy et al. 2024; Yoon et al. 2024). These regions are often activated in fMRI studies of navigation. They also respond strongly during mere passive viewing of spatial scenes (e.g., landscapes, cityscapes, or individual rooms) and are hence often referred to as the “scene network.” The OPA is specifically implicated in the processing of the local spatial layout of scenes (e.g., the location of boundaries and navigational affordances), information necessary to move about one’s immediately visible environment (often referred to as “visually guided navigation”) (Bonner and Epstein 2017; Dilks et al. 2011, 2013; Kamps et al. 2016a, 2016b; Persichetti and Dilks 2016, Dilks 2018). The PPA is thought to encode visual and spatial features that allow for the identification and categorization of scenes (Epstein and Kanwisher 1998; Persichetti and Dilks 2018). The RSComp, on the other hand, is purported to mediate between the local scene information encoded by the PPA and OPA and the map-based representation of the hippocampal cognitive map (Epstein 2008). Indeed, lesions to the RSComp are known to result in heading disorientation in humans (Ino et al. 2007); that is, the inability to understand the relationship between the local scene and distal locations. Recent rodent studies have shown that the RSC encodes head direction in terms of a local and a global reference frame (Jacob et al. 2017). RSComp may also be a cortical locus for spatial knowledge of familiar environments that has become consolidated over time (Wolbers and Büchel 2005). The superior parietal lobe has been less studied but exhibits similarities to RSComp (Dutriaux et al. 2024; Marchette et al. 2014) and OPA (Yoon et al. 2025).

It is important to note that the neuroanatomical organization of the scene network, as well as its rodent homologues, continues to be investigated. Scene regions can be reliably localized based on their response to scenes (Weiner et al. 2017, 2018), but these functionally defined regions do not correspond neatly to anatomically defined counterparts. For example, PPA is not the same as parahippocampal cortex, and RSComp is not the same as RSC. The mapping to the corresponding regions in rodents (e.g., postrhinal and retrosplenial cortices) is even more tentative, and for some regions (e.g., OPA), it is unclear whether there is a rodent equivalent. Recent work suggests a superseding organization that cuts across the scene regions, consisting of an anterior subnetwork (including anterior PPA and most of RSComp) that is more involved in mnemonic aspects of scene processing and a posterior network (including OPA and posterior PPA) that is more involved in perceptual aspects (Baldassano et al. 2013, 2016; Steel et al. 2021).

An alternative approach to mapping anatomical homologues between species is to draw on recent advances in molecular techniques, which have enabled the generation of spatially resolved atlases of gene expression and anatomical connectivity at single-cell resolution (e.g., Yao et al. 2023). These atlases hold transformative potential for comparative neuroanatomy. Just as classical neuronal staining allowed anatomists to identify parallels in cellular architectures across species, contemporary molecular approaches may now enable the discovery of fundamental genetic correspondences between rodent and human brains (Joglekar et al. 2024; Zemke et al. 2023). Critically, these genetic signatures could go

beyond identifying anatomical homologues and reveal meaningful evolutionary relationships that might otherwise remain undetected by anatomical or functional analyses alone.

2.4 Neuronal Mechanisms of Goal-Directed Navigation

Above, we described the neuronal representations that underlie our ability to orient ourselves in space. Navigation, however, requires more than just self-localization. Once we establish our spatial position and heading, we then need to estimate the distance and direction (i.e., a vector) between our current location and that of our goal. Furthermore, since most environments through which we navigate are complex (i.e., they contain multiple barriers or objects that obstruct a path), computing a vector that depicts the straight line distance to a goal is rarely sufficient. A route that respects the physical constraints of an environment must also be constructed. Here, we synthesize available knowledge on the proposed neuronal mechanisms that underlie these critical navigational processes.

Theoretical and experimental work has made progress in elucidating the neuronal computations that underlie vector-based navigation. Convergent findings suggest the EC and, more specifically, the grid cells of the MEC are the candidate neural substrates for computing a navigational vector (Bierbrauer et al. 2020; Bush et al. 2015; Erdem and Hasselmo 2012; Howard et al. 2014; Kubie and Fenton 2012). For example, in modeling the activity of grid cells across distinct anatomical modules (defined in terms of scale and orientation of the grid), Bush et al. (2015) showed that the activity of grid cells belonging to distinct modules was sufficient to resolve unambiguously the position (distance and direction) of a goal location, even in large environments where distance to the goal exceeds the largest grid scale (see also Edvardsen 2019; Mathis et al. 2012; Sreenivasan and Fiete 2011). Moreover, in studying the vectorial codes in the human brain while participants engaged in a VR navigation task inside an fMRI scanner, Howard et al. (2014) designed a task to decorrelate Euclidean and path distances to learned goals and found that entorhinal activity correlated positively with the Euclidean distance to a goal, and not the path distance. Subsequent work showed that entorhinal activity also tracks the (imagined) heading of a navigational goal (Chadwick et al. 2015) and exhibits grid-like responses that correspond to the goal vector (Bellmund et al. 2016). Relatedly, Bierbrauer et al. (2020) showed that fMRI grid-like activity in the EC predicted performance on a path-integration task, and that performance was impaired in carriers of the $\epsilon 4$ allele of the *APOE* gene, which carries an increased risk of developing Alzheimer disease (Corder et al. 1993) and is associated with neural degeneration in the EC in young adults.

The hippocampus, on the other hand, has been hypothesized to support the ability to plan navigational paths. For example, fMRI studies have shown that the hippocampus preferentially tracks path distance over Euclidean distance to a goal (Howard et al. 2014) and represents intermediate steps along the route when participants plan a route to a goal (Brown et al. 2016). Furthermore, MTL regions are thought to work in concert with neocortical regions, such as RSComp (Patai et al. 2019) and

prefrontal cortex (Patai and Spiers 2021), during path and vector planning. The neuronal mechanism for path planning may be time-compressed reactivation of rodent place-cell sequences, which encode paths an animal has already traversed (Jackson et al. 2006; Lee and Wilson 2002; Wilson and McNaughton 1994). These sequences occur either during oscillatory states associated with locomotion (theta sequences) or sleep/immobility periods (replay). Goal-directed paths are often preceded by replay that is centered at locations and paths near the animal; in some instances, replay even predicts future behavior (Olafsdottir et al. 2017; Pfeiffer and Foster 2013; Singer et al. 2013). At decision points, theta sequences have been found to depict upcoming paths (Johnson and Redish 2007; Wikenheiser and Redish 2015). When animals are unsure of their path in a complex maze, theta sequences continuously cycle between alternative paths (Kay et al. 2020), reminiscent of deliberative processes. In a task where animals alternated between random foraging and goal-directed navigation, replay only predicted upcoming goal-directed paths (Pfeiffer and Foster 2013). Similarly, the spatial extent of theta sequences has been found to be modulated by navigational goals, extending further ahead of the animal when they take place during vicarious trial-and-error behavior (Wikenheiser and Redish 2015). Finally, and important for its hypothesized role in path planning, replay is sensitive to an environment's navigational affordances (Widloski and Foster 2022). Such flexible navigation could result from the interplay of map-based planning and vector navigation (Edvardson et al. 2020). In an environment containing multiple barriers, replay sequences respected the topological structure of the environment, even when the structure changed on every visit (Widloski and Foster 2022).

It is important to note that not all replay studies report results that are consistent with its proposed planning function. For example, Gillespie et al. (2021) recorded replay while animals engaged in a flexible goal-directed navigation task on a multi-arm maze and found no bias for replay of paths leading to an animal's current navigational goal. Instead, they observed a strong bias for past rewarded paths. Replay during sleep has long been hypothesized to support memory consolidation (i.e., the stabilization of new memories) (Wilson and McNaughton 1994), a hypothesis that has considerable experimental support (Ego-Stengel and Wilson 2010; Girardeau et al. 2009; Gridchyn et al. 2020; Maingret et al. 2016). Whether replay recorded during waking periods serves exclusively to support memory consolidation or is additionally involved in planning remains an area of ongoing research (e.g., Mallory et al. 2025).

In summary, research conducted in humans and rodents over the past decades has elucidated a network of brain regions and their neuronal representations that encode spatial variables critical for self-orientation, and an emerging body of research has highlighted candidate neuronal mechanisms that may support goal-directed navigation. There are, however, areas of contention. For example, due to methodological differences in the way neuronal representations are studied in rodents and humans, questions remain regarding the nature of neuronal spatial encoding in different species and even whether brain regions strongly implicated in spatial behavior in rodents encode space in humans. Moreover, the interplay of different navigation strategies (e.g., landmark-based, map-based, vector-based) is also understudied. We turn to these issues next and discuss possible solutions.

3 Bridging Methodologies in Navigation Research

A key challenge to creating a cross-level description of navigation is to bridge the varied methodologies employed to study the neural basis of navigation, particularly when methods vary between species-specific researchers. Findings reported in rodent research are often derived from direct measurements of neuronal activity that operate at the timescale of brain activity (< 1 ms) and allow the activity of single cells to be resolved. Human research, on the other hand, often relies on indirect, hemodynamic correlates of brain activity (e.g., via the fMRI BOLD signal) over long timescales (i.e., seconds) with limited spatial resolution ($1\text{--}27\text{ mm}^3$ in typical fMRI studies). Thus, obtaining unequivocal evidence for the existence of the distinct spatial cell types in the human brain has been challenging. To address this issue, we propose the use of (a) computational modeling of rodent data to predict how a single-neuron functional representation would be expressed in population activity that fMRI measures and (b) signal alignment of rodent and human data so that comparable representations can be studied in the two species.

3.1 Computational Modeling: Linking Macroscopic and Neural Signals

As described above, grid-like signals have been reported in fMRI research (Doeller et al. 2010), yet how do these signals relate to cellular responses? Computational simulations of single-neuron signals have explored several plausible accounts. One view, the *conjunctive hypothesis*, is that the fMRI grid signal may emerge from population activity of conjunctive grid $\times$ HD cells (Figure 9.3a) (Bin Khalid et al. 2024; Kunz et al. 2019). As these conjunctive cells may increase their activity when individuals navigate along the grid axes, this could result in a heightened BOLD response when participants move along the axes of the grid-cell network. An alternative view, the *repetition suppression hypothesis*, is that grid cells and/or related fMRI activations show repetition suppression (Figure 9.3b), leading to reduced fMRI activity when individuals move along the grid axes (because the traversed grid fields repeatedly come from a smaller set of unique neurons). A potential third option, the *clustering hypothesis*, is that grid cells with similar phase offsets relative to environmental boundaries cluster anatomically, resulting in stronger signals in these anatomical subregions when subjects move along the axes of the grid cells belonging to a given cluster. This signal could then potentially modulate the BOLD signal, as long as the size of the grid-cell cluster does not exceed the spatial resolution of fMRI (Figure 9.3c).

Computer simulations of populations of grid cells showed that the conjunctive and repetition suppression hypotheses are good candidates for explaining grid-like signals, whereas the clustering hypothesis is less plausible (Bin Khalid et al. 2024). Furthermore, the repetition suppression hypothesis is dependent on the exact type of navigation paths, triggering new ideas for designing fMRI experiments on grid-like signals. Future studies could examine whether grid-like signals show alterations due to environmental changes, such as the reported elliptic distortions in individual grid cells (Stensola et al. 2015), which would provide useful additional information

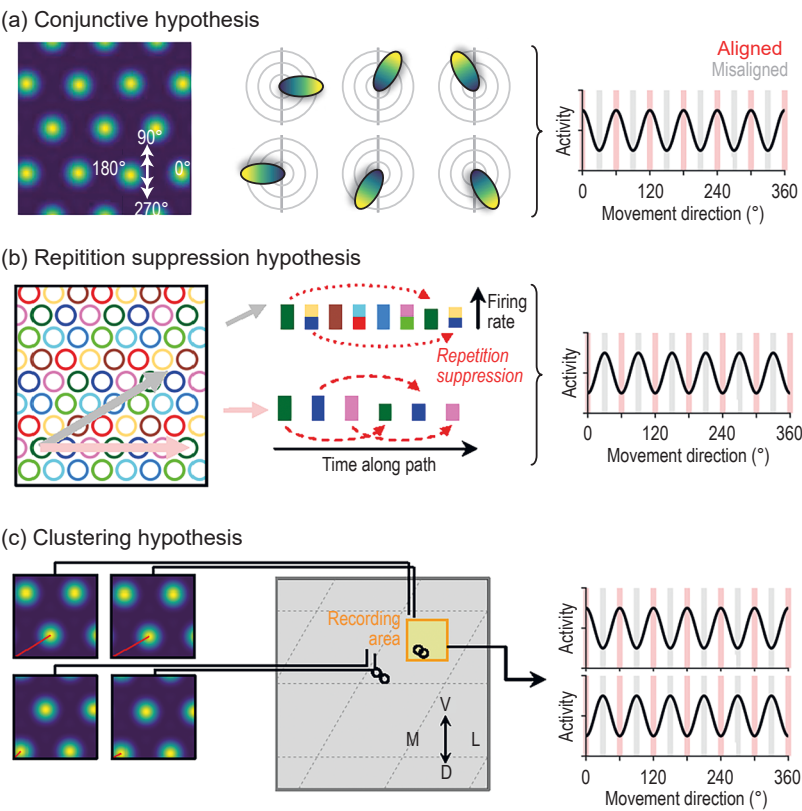


Figure 9.3 Computational modeling of macroscopic grid-like signals. Reused with permission from Bin Khalid et al. (2024) <http://creativecommons.org/licenses/by/4.0/>. (a) Conjunctive hypothesis: Macroscopic grid-like representations (right) may emerge from the firing of conjunctive grid by HD cells (left and middle panels) that exhibit increased firing when the subject moves aligned as compared to misaligned with the grid axes (right) (Doeller et al. 2010). This relies on directional preference across the grid-cell population being biased toward on-axis directions (middle, which shows preferred HD tuning for grid cells akin to the left panel). (b) Repetition suppression hypothesis: In a grid-cell population with similar grid orientations and grid spacings but with distributed phases (left: colored circles represent firing fields of different grid cells), aligned movements (horizontal pink arrow) lead to more frequent activation of a smaller number of different grid cells, whereas misaligned movements (diagonal gray arrow) lead to less frequent activation of a higher number of different grid cells (Doeller et al. 2010). Thus, aligned movements may lead to more pronounced repetition suppression as compared to misaligned movements (middle), resulting in a hexadirectional modulation of population spiking activity (right). (c) Clustering hypothesis: Because anatomically adjacent grid cells exhibit similar grid phase offsets, in addition to similar grid orientations and grid spacings (Gu et al. 2018), recordings from a limited number of grid cells with a nonrandom distribution of phase offsets may lead to macroscopic grid-like representations. Left: grid phase offset of four different grid cells, whose anatomical locations are illustrated in the middle panel. Depending on the subject's starting location relative to the phase offset of the grid fields, movements aligned or misaligned with the grid axes lead to higher total grid-cell activity compared to misaligned or aligned movements; upper and lower portions of the right panel illustrate hexadirectional modulation for two different anatomical clusters. Moreover, the orientation of hexadirectional modulation may shift when recording from neighboring voxels in anatomical space due to a shift in the clustered phase offsets.

for computational studies and enhance confidence in the fMRI grid-like signal. For a discussion of how fMRI grid-like signals are modulated by the shape and orientation of the environment, see Julian et al. (2018a).

A comparable approach could be adopted to investigate other spatial representations (e.g., boundary and HD cells) in the human brain. By considering the properties of these cell types in rodents and simulating populations of them, researchers could make predictions regarding the functional properties of these cells and the likelihood of observing population activity of boundary and HD cells with fMRI and intracranial EEG. For example, if a population of HD cells preferred a particular heading direction (e.g., toward a major distal cue), fMRI studies might record increased BOLD signals when participants face that direction. In contrast, if the cells' preferred heading directions were distributed randomly, a macroscopically visible population signal would become unlikely as the same magnitude of BOLD signal would be recorded along any heading direction. In relation to boundary representations, BVCs in the subiculum tend to fire near environmental boundaries (Muessig et al. 2024). Interestingly, recent intracranial studies have observed increased theta power in epilepsy patients when they were close to the boundary of a virtual rectangular room (Lee et al. 2018; Stangl et al. 2020), which may stem from the overrepresentation of short distances in BVCs. Accordingly, fMRI studies may also find increased fMRI signals related to BVCs when participants move along environmental boundaries as compared to when they move through the center of an environment. Furthermore, the preferred firing directions of BVCs align with environmental walls in a square-shaped environment, whereas they are evenly distributed in circular environments (Muessig et al. 2024). Hence, fMRI studies may find fourfold modulation while participants move along the edges of a rectangular environment but not in circular environments. Similar to models of the emergence of sixfold symmetry in the BOLD signal, computational modeling could help us to understand how and under which conditions a boundary signal could be measured in the fMRI BOLD signal by simulating populations of BVC cells with their known properties. Additionally, these models may elucidate why representations of boundaries and heading directions are most often observed in the theta band, by considering how strongly the spiking of individual neurons is modulated by theta rhythms (Lever et al. 2009).

3.2 Signal Alignment

An alternative approach is to try to match the neuronal signals recorded in rodent and human studies. For example, many human intracranial studies investigate representations in the local field potential (LFP), such as of environmental boundaries, rather than in single-neuron activity as is standard in rodent studies. Thus, a straightforward approach to determine whether results like these truly reflect a common functional representation is to assess whether rodent LFP shows similar spatial tuning. For example, by applying high-density, multisite electrophysiological probes, this approach might show whether regions with a higher density of place cells (e.g., dorsal vs. ventral CA1) are also more likely to contain LFP signals

modulated by specific locations (Agarwal et al. 2014). Conversely, human intracranial studies could use single-neuron recordings through Behnke-Fried electrodes (Fried et al. 1999) to detect the activity of individual neurons in addition to LFPs. Using this technique, studies in epilepsy patients have obtained evidence for grid and place cells in the human MTL (Jacobs et al. 2013; Kunz et al. 2021, 2024; Miller et al. 2013; Nadasdy et al. 2017; Qasim et al. 2019, 2021). More broadly, this line of research may show whether information encoded at the level of individual neurons and LFPs is redundant or complementary. For example, studies might show whether LFP signals are more likely to represent allocentric information if individual neurons in that brain region are also more specialized in processing allothetic instead of idiothetic cues. Consistent with this view, several studies in humans have demonstrated theta oscillations—an oscillatory signal implicated in core spatial and mnemonic processes—in the MTL related to allocentric distance coding (Bush et al. 2017; Buzsaki and Moser 2013; Solomon et al. 2019; Vass et al. 2016).

Matching signals acquired through indirect hemodynamic correlates of neural activity (e.g., the fMRI BOLD signal) with single-unit electrophysiological signals is more challenging. Using fMRI scanners, neuroimaging is possible in rodents. However, these experiments require the rodent to be at least lightly anesthetized, precluding the study of spatial representations. An alternative is to image hemodynamics in rodents via an optical approach (e.g., 1- and 2-photon microscopy, functional ultrasound imaging) that is compatible with *in vivo* experiments (both in head-fixed and freely moving animals). An added advantage of this approach is that neural activity could be simultaneously recorded via calcium imaging, allowing researchers to unequivocally ascertain whether, for example, the sixfold modulation of the hemodynamic signal truly reflects grid-cell activity. This approach has yet to be attempted in the context of navigation, yet it has been successfully implemented in experiments studying resting-state activity (Kozberg and Hillman 2016; Ma et al. 2016). Thus, it represents a potentially viable and exciting approach to bridging the diverse methodologies employed in navigation research.

4 Bridging Neuronal Activity to Navigation Behavior

Rodent neurophysiology research has provided crucial insights into the single-neuron code that supports spatial behaviors. However, the majority of rodent studies examine neuronal representations in the context of simple spatial behaviors in controlled experimental apparatuses (e.g., foraging in open field environments or traversals on linear tracks) in oriented subjects or when disoriented animals are not required to express any meaningful spatial behavior. As a result, it is difficult to link neural activity to navigation because it is unclear which processes and cues are guiding behavior. Furthermore, most rodent studies investigate spatial representations in vista environments (i.e., environments viewed from a single vantage point such as a single chamber) as opposed to large-scale and complex environments (environmental spaces) that better mimic real-world settings (but see Eliav et al. 2025; Ray et al. 2025). This point is particularly important as processes which guide spatial behavior are strongly affected by whether navigation occurs in a vista or

environmental space (Ekstrom and Isham 2017; Meilinger et al. 2016; for further discussion, see [Appendix 9.1](#)). Finally, future navigation research should strive to make their studies more naturalistic. Highly controlled and constrained experimental environments limit the range of spatial behaviors animals can exhibit and may cause researchers to overlook behaviors that occur only in the wild. Such naturalistic approaches have already been successfully applied in studies of flying bats and could readily be extended to research on other species (for further discussion, see Ulanovsky 2025).

We are only beginning to understand the neuronal processes that underlie higher-order navigational processes, such as planning and vector computation. Some initial insight has been gained from studies on replay (Pfeiffer and Foster 2013; Singer et al. 2013) and theta sequences (Johnson and Redish 2007; Kay et al. 2020; Wikenheiser and Redish 2015; Yu et al. 2025) as well as a small number of human fMRI studies that have mapped the neural networks engaged at different stages of navigation (e.g., Brown et al. 2016; Chadwick et al. 2015; Howard et al. 2014; Patai et al. 2019). Given the lack of consensus regarding the role of replay in planning and limited experimental evidence for the involvement of the MEC and grid cells in vector computation, more systematic studies are needed in these areas.

The reason for these knowledge gaps likely reflects (a) the difficulty with studying single-neuronal representations in experimental contexts which do not allow for extensive and repetitive sampling of the spatial firing fields of individual neurons, as is often the case in studies that employ spatial navigation tasks, and (b) technical challenges associated with carrying out electrophysiological experiments in complex environments. The advent of high-density single-neuron recording techniques like Neuropixels probes (Jun et al. 2017) may help address the first challenge. These probes enable researchers to record from hundreds of neurons simultaneously, allowing them to analyze a population code rather than relying solely on a single-neuron code, which requires less extensive spatial sampling. To address the second, technical challenge, emerging wireless electrophysiology technologies (e.g., neurologgers) offer a potential solution (for an extensive discussion, see Ulanovsky 2025). In recent years, neurologgers have rapidly improved: some models are capable of recording from 300–400 channels simultaneously, making them comparable to wired systems. Additionally, advances in lightweight battery technology now allow for long-duration wireless recordings for low channel-count systems (e.g., 32–64 channels), lasting several hours. Continued technological advances in wireless power transfer will hopefully soon enable wireless recordings to become on par with state-of-the-art wired solutions.

Importantly, when studying navigation with the view of developing a cross-level analysis, efforts should be made to ensure that behavioral paradigms used are comparable between species-specific studies (e.g., test similar navigational processes), while respecting the ecological niches of different organisms. There are several tests in the field that meet this criterion. For example, the Morris water maze (Morris et al. 1982)—where subjects need to find an underwater escape platform located in a murky pool ([Figure 9.4a](#)) and for which VR alternatives exist (Astur et al. 1998; Cornwell et al. 2008; Doeller and Burgess 2008; Doeller et al. 2008)—allows researchers to assess the role of different orientation cues (landmarks, boundaries). Classic reorientation paradigms (Cheng 1986; Cheng et al. 2013) provide another

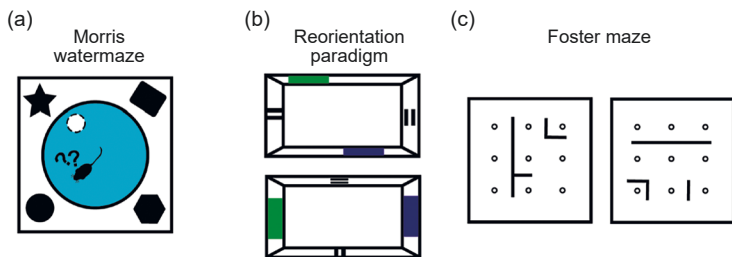


Figure 9.4 Navigational tasks suitable for cross-species investigation. (a) The Morris water maze: Organisms learn to locate a hidden escape platform in a circular pool. To solve the task, participants must learn the location of the escape platform in relation to a set of distal cues. (b) Reorientation paradigm: Participants learn the location of a target object in a rectangular environment with a set of visual cues (top). At testing (bottom), memory for the learned location is assessed after disorientation (e.g., visual cues rotated). (c) The Foster maze: Rodents learn the location of a reward in a square environment with configurable barriers. On each visit, the barrier may be reconfigured to change the topology of the environment.

example: subjects need to recover a learned location after disorientation (Figure 9.4b), and comparative data has been extensively collected. One recently developed alternative test is the Foster maze (Widloski and Foster 2022): its reconfigurable barriers (Figure 9.4c) allow researchers to examine how an environment's topology influences spatial behavior and resulting neural responses, and to disentangle the different types of goal-directed navigational processes (e.g., vector computation and path planning). These paradigms can be adapted to VR testing, making them suitable to test via a wide range of brain-recording methodologies. Efforts should also be made to further develop navigational paradigms that more closely match navigation in the real world, such as navigation in complex environments that contain multiple enclosures, passages and levels, and large-scale spaces (e.g., Eliav et al. 2021; Sarel et al. 2022). Similarly, it is important to determine whether the cognitive and neuronal processes that underpin navigation are similar in outdoor environments, where spatial cues often differ significantly from indoor spaces (e.g., no ceiling, no wall borders).

5 Studying Development to Bridge Neural Activity and Navigation Behavior

Another promising approach to bridging the gap between analysis levels is to look at the assembly of neural systems for navigation in development. The advantages of this approach lie in stereotyped developmental trajectories of navigation ability. Navigation does not emerge in an all-or-none fashion but through a series of incremental steps. Place learning (the ability to locate a target object relative to the location of distal cues) is known to develop relatively early, in both humans (~2 years) (Newcombe et al. 1998) and rodents (~3 weeks) (Brown and Whishaw 2000), but its full development is protracted (lasting years in humans and weeks in rodents). Moreover, human research has shown that children often rely on geometric cues over visual cues for orientation in small, enclosed spaces (Hermer and

Spelke 1994), although visual cues are used in larger environments (Learmonth et al. 2008), which are arguably closer to environmental space. Cross-species research has also shown that the ability to integrate and resolve conflicting cues develops over an extended period, continuing over the first decade in human development (Nardini et al. 2008) and over the first 2–3 months in a rodent's life (Rossier and Schenk 2003). Thus, studying the emergence of neuronal function in the early postnatal period allows a functional alternative to a lesion approach, whereby the system can be studied during a time period when certain components of it are naturally not active yet (see [Chapter 7](#) and Dilks et al. 2023).

Some notable successes of this approach have been seen in rodents (see [Chapter 8](#)). A series of descriptive studies have set out the core timeline for the maturation of neural networks for navigation in rodents, including some clear temporal dissociations between different functional spatial neuron types ([Figure 9.5c](#)) (Wills et al. 2014). HD cells emerge initially: by just over two weeks of age, HD cells display adultlike tuning (Bjerknes et al. 2015; Langston et al. 2010; Tan et al. 2015; Wills et al. 2010). Also, although less reliable and stable, HD signals can even be recorded before eye opening (Tan et al. 2015). Boundary-responsive cells show different developmental trajectories in different anatomical regions, with EC border cells developing early (adultlike from P17; Bjerknes et al. 2014). By contrast, subiculum BVCs show a protracted development, even into the fourth week of life (Muessig et al. 2024). Place cells have also been recorded from P16 (Langston et al. 2010; Wills et al. 2010). At this age, however, they are less stable and display more diffuse spatial firing fields relative to adults, particularly in locations far away from environmental boundaries (Muessig et al. 2015). They also are not yet able to encode for nonspatial variables (e.g., task phases; Bevanđić et al. 2024) as they do in adults. Place-cell development is thought to continue until at least five weeks of age, and in slow-developing individuals, full maturity may take several more weeks (Scott et al. 2010). Grid cells displaying clear, sixfold symmetry, on the other hand, have not been recorded before P20 (Wills et al. 2010). In contrast to place cells, however, grid-cell maturation is abrupt, with adultlike activity characteristics displayed at the earliest age at which they have been recorded. Interestingly, at the age when grid cells emerge, place-cell tuning improves, particularly for locations far away from environmental boundaries (Muessig et al. 2015), suggesting that place-cell tuning early in life may be preferentially influenced by the location of boundaries. Furthermore, hippocampal replay ([Figure 9.5a](#)) and theta sequences ([Figure 9.5b](#)) have been reliably identified in the fourth postnatal week (Farooq and Dragoi 2019; Muessig et al. 2019), and their emergence is tightly correlated, suggesting that a shared mechanism underlies both (Muessig et al. 2019).

In addition to bridging analysis levels, research on rodent development provides crucial insights into the neurodevelopmental milestones that underpin the maturation of human navigational capabilities. In school-aged children, fMRI studies have become increasingly common in recent years (e.g., Jung and Dilks 2025; Jung et al. 2024; Kamps et al. 2020; Mooney et al. 2021; Prabhakar et al. 2018). However, functional brain imaging remains rare in infants (but see, e.g., Deen et al. 2017; Yates et al. 2025) and is nearly impossible in young toddlers, thereby precluding direct examination of the neural development of navigation during the period in

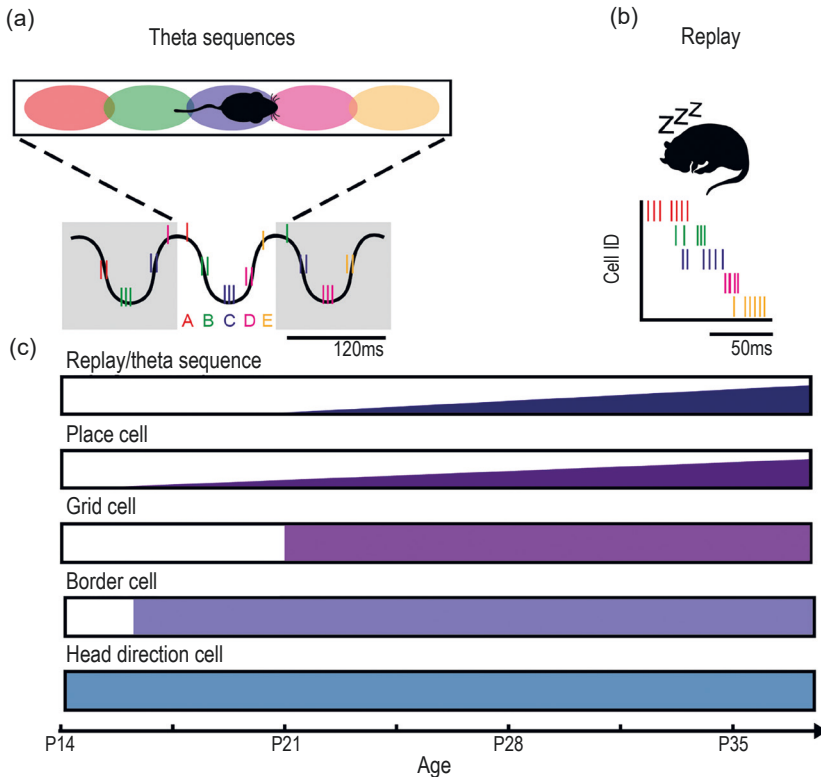


Figure 9.5 The ontogeny of neuronal spatial representations and mechanisms. (a) Traversals on a linear track are encoded by sequential activity of a group of place cells. During individual cycles of theta oscillations, place-cell sequences that reflect path segments are activated (theta sequences). (b) During sleep and rest periods, place-cell sequences that reflect paths taken are spontaneously replayed at a sped-up pace (~10–20 times faster than during behavior). (c) Developmental timeline for the emergence of different spatial cell types and replay and theta sequences in rats. P: postnatal day.

which the foundational milestones for this ability emerge. If we apply the findings from rodent development, however, some insights may be gained. For example, the gradual development of place learning may reflect the gradual development of place-cell tuning. Furthermore, the presumed reliance on geometric cues over landmark cues early in life may reflect the early development of neurons with boundary-related tuning and place cells with stable spatial firing fields near environment walls. However, many knowledge gaps remain. For example, the development of allo- and idiothetic cue integration in the different spatial cell types has not been systematically investigated, and a number of nodes in the brain's navigation network have not been studied early in life (e.g., different head direction loci). Finally, most rodent developmental research does not focus on the maturation of neuronal function in the context of the development of spatial capabilities. Studying neuronal activity and behavior in tandem is critical, as significant individual variability exists in terms of age of inflection for spatial capabilities (Bevandić et al. 2024; Douglas et al. 1973; Nadel et al. 1992). In addition, we lack a consensus on the age equivalence between rodents and humans. Examining populations with unique

neurodevelopmental profiles (e.g., Williams syndrome) may offer a complementary approach to dissecting the navigational system (see [Appendix 9.2](#)) Hopefully, future research will address these knowledge gaps.

6 Conclusions

Over the past few decades, scientists from diverse methodological backgrounds and disciplines have provided detailed insights into the cognitive and neuronal processes that underlie spatial navigation. This work has put the research field in a promising position to create a cross-level description of navigation that links cellular activity to complex cognitive processes. Nonetheless, significant gaps in our understanding remain. The divergent brain-recording methodologies used in human and rodent studies currently make it hard for scientists to determine the consistency of neuronal spatial representations across different species. Moreover, as most rodent navigation studies do not study neural activity in tandem with complex spatial behavior or use environments that better represent natural spaces, linking neuronal mechanisms with specific navigational abilities applicable to real-world settings remains a challenge. Finally, we are only beginning to gain insights into the neurodevelopmental milestones that underpin the emergence of this critical capability early in life.

To address these challenges, methodological bridges through collaboration need to connect experimental researchers, who collect neuronal data, and computational scientists, who model how one type of neuronal signal translates into another, and their data should be aligned to match the signals recorded across techniques. Behavioral bridges could be advanced by recording from the brain's navigation network during naturalistic rodent navigation using state-of-the-art electrophysiology to overcome challenges of complex behavior (Ulanovsky 2025). To elucidate the neuronal basis of navigation development, we propose studying developing rodents, whose staggered developmental timeline for navigational capabilities closely resembles that of humans and for which tools for recording from the developing brain have been established in recent years. Connecting these areas of research will enable the field to generate a complete description of navigation, spanning multiple levels of analyses and linking single-neuron activity to complex cognition.

Appendix 9.1: Vista versus Environmental Spaces

Spatial environments can be differentiated into vista and environmental spaces by the visibility of the relevant surroundings (Montello 1993; Parra-Barrero et al. 2023; Peer et al. 2024). Vista spaces are environments that can be perceived from a single vantage point, such as in the Morris water maze, an open field, or a single room. Environmental spaces require traversal and multiple views to gather information and to integrate these views over different points of time, such as in a complex maze with multiple turns, a building, or a city. In studies with humans, vista and environmental spaces often correlate with the scale of the space (e.g., a vista-scale

room is typically smaller than an environmental-scale building or city). However, large-scale open environments whose features and layout can be perceived from a distance are also considered vista spaces.

Rodent navigation research typically employs small-scale vista spaces. In human neuroimaging and behavioral studies, large-scale environmental spaces—sometimes implemented as a VR setting—have become increasingly common (Wolbers and Wiener 2014). This difference poses a challenge for designing parallel tasks and environments suitable for cross-species comparisons of the neural mechanisms underlying navigation. There are important differences between vista and environmental spaces, both in terms of the timescale of navigation and the way information is acquired. Navigators are capable of locomoting through and forming spatial memories of both types of spaces, but human research shows that the types of spatial representations formed in these spaces are likely different (Ekstrom and Isham 2017; Meilinger et al. 2016). For example, borders of vista space influence the ease of spatial updating, with self-to-object locations more readily updated within the border than outside of the border (Avraamides and Kelly 2010). In a direct comparison of environmental and vista space (i.e., corridors present or removed from a VR building), memory for environmental space (but not vista) was influenced by distance traveled and number of objects encountered (Peer et al. 2024). Studies suggest that allocentric representations in environmental spaces are formed in an experience-dependent and compartmentalized way, building on representations of smaller interconnected units (Meilinger et al. 2016).

Appendix 9.2: What Can Special Populations Tell Us about the Neural Basis of Navigation?

Navigation can be studied in the context of neurodevelopmental conditions such as Williams syndrome, a genetic syndrome associated with moderate learning difficulties. Individuals with Williams syndrome exhibit an uneven cognitive profile, characterized by poorer spatial than verbal abilities (Farran and Karmiloff-Smith 2012), including significant impairments in navigation (e.g., Banta Lavenex and Lavenex 2021; Farran et al. 2010, 2015; Kamps et al. 2023). Notably, Williams syndrome is characterized by structural and functional abnormalities in brain regions implicated in navigation in typical development, including the hippocampus and parietal cortex (for a review, see Thom et al. 2023), raising the intriguing possibility of a causal link between these behavioral and neural navigation systems. However, individuals with Williams syndrome may rely on alternative strategies or brain regions (Karmiloff-Smith 1998), complicating attempts to draw definitive conclusions about the causal relationship between behavioral and neural systems underpinning navigation across development.

Indeed, several studies have demonstrated that individuals with Williams syndrome are impaired on several putative hippocampal abilities. For example, allocentric spatial coding (a known hippocampal function) has been investigated through tasks requiring participants to learn two routes (A to B and A to C) and then to find the shortest route between two places (B to C). In a task using a large-scale

VR environment, Farran et al. (2015) reported that only 35% of individuals with Williams syndrome walked the shortest route compared to 59% of neurotypical 5- to 11-year-old children (see also Broadbent et al. 2014a; Farran et al. 2010). In addition, individuals with Williams syndrome also exhibit impairments in other putative hippocampal abilities:

1. Geometric reorientation in a traditional version of the reorientation task (Ferrara and Landau 2015; Lakusta et al. 2010)
2. Boundary-based memory, but *not* landmark-based memory, in a “human version” of the water maze task (Julian et al. 2019)
3. Visuospatial memory in both a real-world radial arm maze task and the open field task with multiple rewards, as well deficits in understanding spatial layout (Foti et al. 2011; Mandolesi et al. 2009)

Landmark manipulation and view-matching tasks further suggest that individuals with Williams syndrome rely on a view-matching strategy for learning routes, thus providing an example of the alternative strategies discussed above (Broadbent et al. 2014b, 2015; Purser et al. 2015). In their studies of vista space, Banta Lavenex and Lavenex (2021) attribute the use of a view-matching strategy in Williams syndrome to activation of the parahippocampal and retrosplenial cortices and medial parietal regions.

Next, cortical systems, beyond the hippocampus, in the parietal cortex are hypothesized to be involved in navigation in typical development, albeit a different type of navigation. For example, the OPA has been hypothesized to support “visually guided navigation” (for a review, see Dilks et al. 2022). What, then, do we know about visually guided navigation in Williams syndrome—in which, curiously, cortical thinning in and around the OPA has been shown (Meyer-Lindenberg et al. 2004)? A recent behavioral study found that adults with Williams syndrome exhibit impaired visually guided navigation abilities, yet relatively proficient scene categorization abilities (i.e., the ability to recognize a place as a particular type of environment), relative to neurotypical mental age-matched controls. These findings suggest that OPA is casually involved in visually guided navigation.

While evidence indicates that individuals with Williams syndrome exhibit impaired navigation abilities, as well as structural and functional abnormalities in the hippocampus and parietal cortex, future research is needed to test whether these behavioral impairments result from these neural atypicalities. It is possible that individuals with Williams syndrome rely on alternative strategies or brain regions during navigation, complicating definitive conclusions about the behavioral and neural systems underlying navigation across typical development.

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