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Perspective

Are grid cells used for navigation? On local metrics, subjective spaces, and black holes

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SUMMARY

The symmetric, lattice-like spatial pattern of grid-cell activity is thought to provide a neuronal global metric for space. This view is compatible with grid cells recorded in empty boxes but inconsistent with data from more naturalistic settings. We review evidence arguing against the global-metric notion, including the distortion and disintegration of the grid pattern in complex and three-dimensional environments. We argue that deviations from lattice symmetry are key for understanding grid-cell function. We propose three possible functions for grid cells, which treat real-world grid distortions as a feature rather than a bug. First, grid cells may constitute a local metric for proximal space rather than a global metric for all space. Second, grid cells could form a metric for subjective action-relevant space rather than physical space. Third, distortions may represent salient locations. Finally, we discuss mechanisms that can underlie these functions. These ideas may transform our thinking about grid cells.

GRID CELLS AS A METRIC FOR SPACE

Grid cells produce one of the most intriguing signals in the brain and are widely thought to be involved in navigation. When a rodent runs in a box of typically 1 × 1 m in size, grid cells fire in multiple firing fields across the floor of the box. The firing fields of a grid cell are arranged in a symmetric pattern, forming the vertices of a repetitive hexagonal lattice that spans the entire space.[1–3] Although the role of this exquisite hexagonal grid pattern in navigation is not entirely clear, a major line of thought suggests that the grid's role is to provide a global metric for space.[1,4–6]

Animals and humans employ multiple strategies as they navigate.[7,8] Two of these strategies—*path integration* and a *cognitive map*—indeed require that the explored space possess a global metric: a way in which distances can be measured uniformly and veridically across the entire space (see Box 1 for theories of how the grid pattern is utilized for self-positioning). When an animal navigates using *path integration*, the animal's traveled path, composed of the traversed distances and angles, is integrated over time. This process utilizes an internal velocity signal representing the animal's movement speed and direction, which is used to compute and update an ongoing estimate of the present position based on the past trajectory.[6,9,10] Such a scheme requires a metric for space to ensure that distances are computed in the same manner across different parts of the traveled space. A prevailing idea is that the grid pattern provides such a metric for space—reminiscent of the Roman milestones, which were positioned at known distances along a road. The grid pattern is also thought to provide a metric for space in the framework of a *cognitive map*, where one's position is estimated by comparing sensory input to internal representations, using both absolute cues from the environment and one's relative orientation toward those cues.[8] When an animal navigates using a cognitive map, a reliable metric would ensure that the distances measured—either between one's position and environmental landmarks or between the different landmarks—are represented reliably in an undistorted manner across the entire space. In the cognitive map framework, the grid pattern may resemble the longitude and latitude lines in a geographic map, binding distant cues and landmarks onto a coherent coordinate system.

But what should we expect to find when we speak of a metric for space? A metric for a space provides the notion of distance between points in that space. For Euclidean space, the distances given by a metric system should satisfy the following: *identity*—the distance between a point and itself should be zero; *symmetry*—the distance from A to B should equal the distance from B to A; and the *triangle inequality*—requiring that the direct distance from A to B is shorter or equal to the distance from A to B via any third point C. Importantly, for Euclidean spaces—such as physical space—we expect lines and angles to remain undistorted throughout the entire space, being invariant to translation and rotation.

With these requirements in mind, the classic hexagonal firing pattern of grid cells, as recorded in square boxes of typically 1 × 1 or 2 × 2 m in size, is indeed a strong candidate for serving as a metric for physical space. The grid pattern is composed of firing fields, which are the nodes of a spatial lattice pattern in

Box 1. Grid cells and spatial geometric computations

Several lines of theoretical work suggested that the function of the hexagonal grid pattern is to provide spatial information through *geometric computations*. One example for such a computation is *path integration*, which uses speed and direction signals to update the estimate of the current position of the animal with respect to its last known position.[6,10] Other examples of geometric computations focus on decoding the animal's current position utilizing several discrete grid scales, which were found experimentally.[11,12] Specifically, when an animal moves through space, grid cells from the same module (same spatial scale) fire in the same pattern and same orientation, but at different phases. The suggested *modulo code* treats the different grid scales as a mathematical basis.[13] The neuron's grid phase with respect to its grid scale is treated as the "remainder" that remains after projecting the animal's location on that basis (inspired by the mathematical modulo operation where the remainder equals the position modulo the grid scale). The remainders from multiple neurons can then be combined to decode the animal's position. A mathematical theorem (the Chinese remainder theorem) postulates that the position can be represented by the assembly of remainders from each scale, i.e., by using different grid cells with different scales.[13] Interestingly, this computation requires only a small number of different grid scales, in accordance with experimental findings, and the coded distances can be far greater than the largest grid spacing. Using the closely related *nested code*,[14,15] the animal's current position can be decoded from the intersection of the firing of all the different scales. Finally, the hexagonal geometry of grid cells was also suggested to allow *vector navigation*[15–17] by providing a vector to a specific place of interest, such as a roost or a reward location. This vector computation requires, however, having a perfect global grid with fixed spacing and fixed angles throughout the environment.[15,17] The various grid distortions that we review here pose a major challenge for all of these ideas.

We note that some of these geometric computations were shown to be possible under several types of distorted grids: Edvardsen[18] demonstrated the possibility to navigate with sheared grids and distorted grids. However, their simulated distortions occurred away from the goal location (unlike experimental data) and affected different modules differently, such that at least some spatial information remained undistorted at all locations. Stemmler et al.[15] demonstrated that geometric computations were possible under noise that is akin to grid-field jitter. However, this scheme preserves the underlying global structure of the grid pattern and does not account for the distortions reviewed here. Thus, these suggestions do not solve the problem of how navigation could occur, given the experimentally observed local distortions that are caused by the geometry and dimensionality of the arena and by the high-valence locations within it.

In summary, geometric computations by grid cells generally rely in a fundamental manner on the perfect lattice-like periodic repetition of the grid pattern. For these models to work (i.e., for animals to navigate using these proposed schemes), the pattern of a single neuron must be precisely periodic across the entire space. Therefore, the experimentally observed deviations from perfect lattice-structure, as reviewed in the current perspective, pose difficult challenges for these kinds of models.

which both distances and angles are repetitive and uniform across space. Furthermore, the grid pattern satisfies the requirements of a metric. First, it satisfies the *identity* requirement: once learned, the grid pattern in the classical experiments was stable, and fields were shown to remain in the same locations over several hours.[1] This implies that a firing field representing position A will continue to represent that position over time, and would not gradually drift to a different position in space. Second, the stability of the hexagonal grid pattern satisfies *symmetry*: the firing pattern in a two-dimensional (2D) open field is unaffected by the direction of travel and by the specific path trajectory.[19] This indicates that the distance from node A to node B in the grid pattern equals the distance from B to A—corresponding to the Euclidean distance through space and not to the animal's specific navigational trajectory. Third, because grids are embedded in physical Euclidean space, they naturally satisfy the *triangle inequality*. As expected from a metric, the grid pattern was classically shown to maintain its fixed distances and angles in different familiar environments,[20] indicating that the grid represents the geometric backbone of physical space and that the geometry is maintained irrespective of the details of the enclosure. Taken together, experiments in small empty symmetric environments are nicely compatible with the notion that grid cells are a metric for physical space and thus can be used for navigation.[4]

DIFFICULTIES WITH THE IDEA THAT GRID CELLS ARE A METRIC FOR SPACE

Although the characteristics of the grid pattern fit the notion of a metric for space when animals navigate in empty symmetric boxes—as typically studied in laboratory conditions—evidence that accumulated in recent years has suggested that this may not be the case in more complex situations. Multiple recent studies shifted away from symmetrical and uniform laboratory settings toward more naturalistic conditions, including using irregularly shaped environments or introducing salient locations or prominent objects.[21–23] These experiments revealed that under more ethological settings, the grid pattern may become distorted and is no longer globally ordered throughout the entire space.[19,21–26] Further, in three-dimensional (3D) space, the departure from hexagonal lattices is even more pronounced.[27,28]

In this perspective, we will discuss in detail these various grid distortions, and the different natural-world elements that induce distortions and deviations from the classical hexagonal grid pattern. We will argue that these distortions indicate that the grid pattern cannot be used as a reliable metric for physical space in real-world scenarios, and therefore it is unlikely to be used for long-distance navigation. Furthermore, we will suggest that these results are at odds with some leading theories of grid formation, such as continuous attractor networks (see also

Box 2. Continuous attractor models of grid cells

Hexagonal grid firing was widely suggested to emerge from a continuous attractor network[5,29] in which the hexagonal pattern arises out of recurrent network activity rather than being solely due to feed-forward inputs or to processes at the single-cell level. In this framework, grid cells in the same module (exhibiting the same spacing and orientation, but different phases) are wired by connections following a Mexican hat anatomical profile: neurons with close-by phases have excitatory connections, while neurons with very different phases have inhibitory connections. This connectivity creates an effective "neural sheet" in which the distances between the interconnected neurons can be geometrically described on a 2D surface (which does not necessarily map onto the physical surface of the brain). The Mexican hat connectivity implies that when a cell fires, other cells with non-overlapping selectivity (i.e., with a different grid phase and hence located away on the neural sheet) are inhibited, while cells with similar selectivity (close-by on the neural sheet) are activated. This architecture creates a bump of activity on the neural sheet, composed of the active cell and its close-by cells (with which it forms excitatory connections). This "activity bump" then continuously moves along the neural sheet with the animal's movement. In some variations of the attractor network models there is a single activity bump,[30,31] while in other variations the Mexican hat connectivity creates multiple activity bumps arranged in a hexagonal pattern.[5,29] There is substantial evidence for grid cells arising from such attractor networks, as this framework has been successful in predicting many experimentally observed phenomena in grid cells.[32] This evidence includes the preservation during sleep or during hippocampal inactivation of the pairwise correlation structure observed during behavior,[33,34] the preservation of the relative phases of grid fields during remapping,[20,35] the discrete jumps in grid spacing between different modules,[12] and a toroidal topological structure that was recently discovered in the activity of large ensembles of recorded grid cells.[29,36]

Box 2). We shall focus here on grid distortions created by movements of fields from their lattice position, and will not treat the interesting question of *firing-rate* deviations from a perfect grid, whereby field positions remain hexagonal but the firing rates of different fields are altered.[37,38] We will start with discussing three aspects that lead to grid distortions: geometry, non-uniformity of space, and dimensionality of space. We will then present three alternative interpretations for the *function* of grid cells, and will subsequently discuss the *mechanisms* that may underlie them.

Geometry

A major difference between navigating in real-world scenarios versus in symmetric small laboratory boxes is the geometry of the environment. Unlike a square box, the natural world is geometrically complex and non-symmetric. Rodents in the real world, outside of the laboratory, need to navigate through non-symmetric natural countryside,[39,40] in compartmentalized burrow systems,[41] and sometimes through the complexity of our kitchens or sewage systems—all being environments with complex geometries. Experiments from the last few years suggested that the grid pattern is sensitive to geometric variations, with non-symmetric geometries leading to distortion of the hexagonal grid pattern via translocation of grid fields in the vicinity of the symmetry-breaking regions in the environment. For example, when recorded in a trapezoid arena, field arrangement was no longer hexagonal, with the grid pattern being particularly disrupted in the narrow part of the trapezoid (Figure 1A, middle panel; compare the actual field positions to the positions predicted by a perfect lattice [white circles]).[21] When the symmetry of a rectangular arena was broken by adding a diagonal movable wall, individual firing fields located in the vicinity of the movable wall shifted away from their global lattice position[25] (Figure 1B, note that the only field that moved substantially [marked with an arrow] was the field closest to the diagonal wall). An interesting interpretation suggested that these effects are a consequence of the grid pattern being anchored to the borders of the arena, possibly through an interplay between grid cells and border cells.[43–45] According to this interpretation, in asymmetric boxes such as the trapezoid arena, the anchoring of the grid pattern to arena borders may indeed produce such distortions because the neuron's hexagonal pattern is anchored to multiple borders at various wall-angles, which together distort the grid and form a non-coherent pattern.

The grid pattern also breaks in spaces made of multiple compartments that allow seeing only the immediate vicinity ("vista space"[46]), similar to burrows and narrow passageways. In such compartmentalized arenas, the hexagonal grid pattern has been shown to disintegrate into multiple local patterns, with a similar firing pattern for each visually similar compartment of the arena (Figure 1C).[19,47] These results suggest that in natural-world geometries, which are often compartmentalized and occlude vision of the surroundings, the grid pattern's global order may not hold.

Interestingly, substantial distortions of the grid pattern are apparent even in the well-studied symmetric and small environments. First, two studies showed that as an animal travels away from a boundary, the hexagonal grid pattern drifts in space with the passage of time since the last boundary encounter.[44,45] The grid pattern is then reset to its original position upon a renewed visit to a boundary. Consequently, the pattern depends on the animal's travel history: the represented distance between points A and B may be coded differently depending on when the animal last visited the boundary, which violates the demand for *identity* ($\text{distance}_{A\rightarrow B} \neq \text{distance}_{A\rightarrow B}$). Likewise, the represented distance from point A to the boundary may differ from the represented distance in the opposite direction, which begins with a resetting-encounter with the boundary—violating the demand for *symmetry* ($\text{distance}_{A\rightarrow B} \neq \text{distance}_{B\rightarrow A}$). These results indicate that the grid pattern drifts in space and that the arena boundaries serve as an error-correction mechanism for this drift. Second, symmetric arena boundaries may also induce distortions of the entire grid pattern (rather than of an individual field). Such a boundary-induced global distortion has been shown in the "shearing effect" (Figures 1D and 1E).[42] Shearing of the

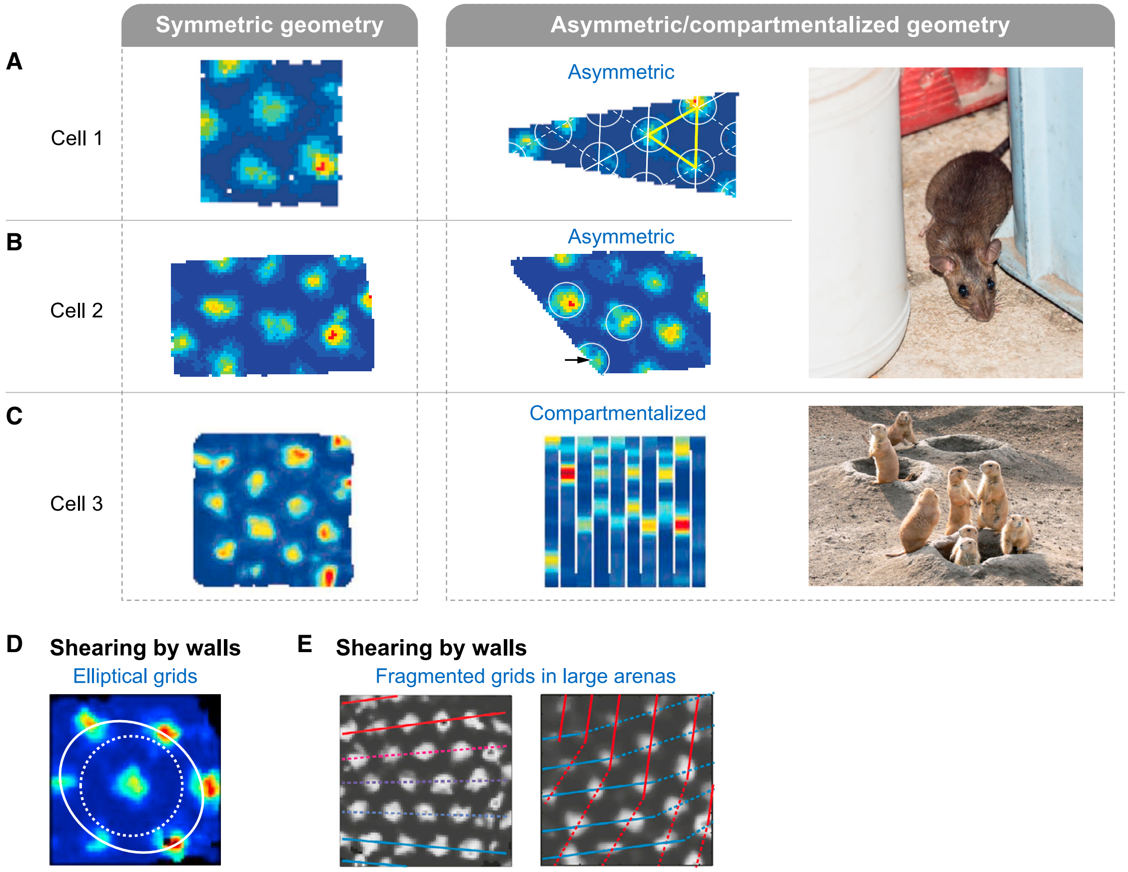


Figure 1. The geometry of the experimental arena can distort the grid pattern

(A–C) Three examples of grid cells that showed a hexagonal lattice when recorded in rectangular boxes (left column), but exhibited a distorted grid pattern or completely broken grid when the same cells were recorded in non-rectangular asymmetric arenas with complex geometry (middle column). Left and middle columns show 2D firing-rate maps, color-coded from zero (blue) to maximal firing rate (red). Right column shows examples of naturalistic scenarios corresponding to these asymmetric experimental arenas (photos: Shutterstock).

(A) The grid is distorted in a trapezoid arena. White circles in the middle panel depict the expected field positions of a perfect hexagonal grid; note the deviations of the real grid fields in the narrow part of the trapezoid, indicating grid distortion. Taken with permission from Krupic et al.[21]

(B) The grid is distorted in asymmetric environments. The arrow in the middle panel shows the movement of the field that was closest to the diagonal wall, from its original position (the base of the arrow) to its new position (the tip of the arrow). White circles depict approximate field positions; note that the field movement created a non-equilateral triangle. Taken with permission from Krupic et al.[25] Right: in natural conditions, animals often navigate through asymmetric environments.

(C) The grid pattern breaks down in a multi-compartment environment where vision is restricted to one compartment at a time. Taken with permission from Derdikman et al.[19] Right: prairie dogs are rodents that build complex underground tunnel systems consisting of multiple compartments. Many other rodents, such as rats, also build multi-compartment tunnel systems.[41]

(D and E) Shearing effect, taken with permission from Stensola et al.[42]

(D) The grid pattern is affected by arena boundaries, which can distort the grid even in a square symmetric arena. Compare the solid-line ellipse, which marks the ellipticity of this neuron's field arrangement, with the dotted circle that corresponds to a hypothetical perfect undistorted hexagon.

(E) Wall-induced shearing and fragmentation of the grid is more pronounced in large environments. Depicted are grid patterns recorded in rats in a 2.2 × 2.2 m box.

pattern describes a phenomenon in which the firing fields move along the axis of the boundary, as if the boundary were exerting a "force" on the grid fields, resulting in an elliptical grid pattern. Fields close to the boundary move together, as if the exerted force is strongest near the boundary and weaker away from it. This is in contrast to the above-mentioned drift, in which the pattern close to the boundary is more reliable; here, the opposite is true: the force is larger on fields located in the vicinity of the boundary and they are less reliable than those in the middle of the arena. The border-induced shearing effect has been shown to be coupled to a border-induced compression effect, which locally moves fields from their perfect-lattice positions.[48] Notably, the shearing effect was more pronounced in larger arenas in which the grid pattern may also be locally fragmented (Figure 1E).[42] These results suggest that distortions would be more severe in the real world, where open environments are much larger than typical laboratory boxes, and therefore shearing distortions would be even more dramatic and pattern drifts may not be easily corrected.

Some of the geometry-induced grid distortions were shown to be transient in time. For example, when an animal encounters a novel environment, the grid pattern was shown to expand at first

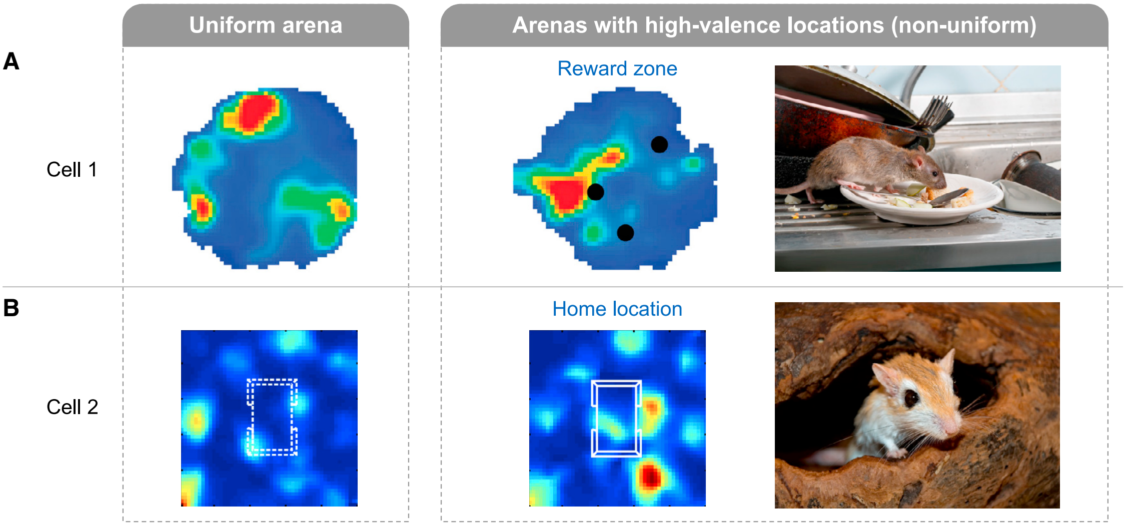


Figure 2. Areas of interest and valence distort the grid pattern
Examples of experimental arenas with "hotspots" of high valence locations: such non-uniform arenas distort the grid pattern locally around the locations of importance. Left column: the grid pattern when recorded in uniform boxes with no distinct areas of high behavioral valence. Middle column: when the same two cells were recorded in non-uniform arenas, the hexagonal pattern was distorted. Right column: examples of naturalistic scenarios corresponding to these experimental arenas (photos: Shutterstock).
(A) Grid fields shift toward distinct areas of reward (such as a sink full of food scraps in a real-world scenario; this was mimicked here with a stable location in which food was present). These shifts locally break the global hexagonal pattern. Black circles represent reward locations. Taken with permission from Boccara et al.[23]
(B) Grid fields shift toward areas of valence; in this case, toward a sheltered area (such as a sheltered nest in a real-world scenario; this was mimicked here with a box with high walls providing shelter in an open-field arena—this box could be either the home box or a cardboard box). This local field-shift breaks the global hexagonal grid pattern. Left panel: first session, without box; dashed white line marks future box position. Middle panel: second session; solid white line marks the position of the box, which provides shelter. Taken with permission from Sanguinetti-Scheck and Brecht.[22]

but then shrink back during familiarization.[11,49] Patterns changing over time are unlikely to form a reliable metric because the distances and angles between nodes are different at different times. When an animal visits two compartmentalized areas, such as two boxes connected by a corridor[47] or separated by a wall,[50] the grid patterns in the two boxes were shown to be initially incongruent, being shifted in spatial-phase relative to each other. However, once the corridor was opened or the separating wall was removed, and the animal started traveling in the combined environment, the two separate firing patterns gradually morphed into a continuous pattern that covered both compartments.[47,50] Interestingly, Wernle et al.[50] demonstrated that after removal of the wall, the grid pattern changed in the vicinity of the removed wall but never reached a global lattice structure, and remained locally distorted in the region where the separating wall used to be. These field-rearrangement processes lasted between a few hours and several weeks.[11,47,49,50] Such temporal dynamics are inconsistent with the stability required for a spatial metric.

Overall, recent studies have shown that the geometry of the arena's boundaries often modifies and distorts the grid pattern. These distortions appear in multiple forms, such as translocation of individual fields, shearing of the entire grid pattern, and fragmentation of the grid; and some of these distortions are influenced not just by the spatial geometry per se but also by the animal's travel history. These changes may be permanent or transient in time—but in either case, such distortions present difficulties for the notion that the grid serves as a veridical and reliable global metric for space.

Non-uniformity of space

An additional factor that affects the grid pattern is the non-uniformity of the environment in the real world. Whereas the inside of a laboratory box is usually uniform, with food being delivered randomly and uniformly throughout the box, this is rarely the case in natural environments. In naturalistic settings, valence is not uniform across space; instead, there is a non-uniform distribution of rewards, goals, shelters, and other important places of high valence that shape animals' behavior. Interestingly, the grid pattern has been shown recently to engage with high-valence locations. For example, in the presence of a food reward, individual fields in the vicinity of the reward were shown to move toward it, distorting the hexagonal pattern locally around the reward location (Figure 2A).[23] Individual fields could also move toward areas of motivational importance, such as a sheltered area or the home cage (Figure 2B).[22] Such distortions, manifested by local displacements of individual firing fields, pose a problem for the notion that the grid pattern constitutes a rigid and uniform global metric for space.

Interestingly, these studies[22,23] utilized *novel* locations of reward (such as food or shelter)—so novelty and learning could play a role in the reported grid distortions. By contrast, another study[26] used a highly familiar reward location and found that the individual grid fields did not strongly shift toward the reward; rather, the entire grid pattern shifted (remapped) rigidly to position a grid field next to the reward location. This may indicate that at the population level, across many grid cells, there is an over-representation of grid fields near the reward, which means that the population of grid cells does not cover space uniformly anymore.

This possible difference between novel and familiar reward locations raises several interesting questions. The first question concerns the role of experience. It would be interesting to examine the dynamics of the grid distortions over time, while the reward location ceases to be novel and becomes highly familiar. In particular, how do grid cells transition from local distortions to global shifting toward the reward? Second, does the *removal* of a reward elicit the return of the grid to its original structure? The third question concerns the encoding of multiple reward locations. Although it is easy to envision how a local-distortion mechanism[22,23] could represent an arena containing several rewards—the grids could simply distort independently, locally near each one of the rewards—it is unclear how multiple rewards could be encoded via a global-shifting mechanism.[26] Toward which reward should each pattern shift? Does the population of grid cells split such that some neurons shift their grid pattern toward one reward and other neurons shift toward another reward? One possibility is that this phenomenon[26] reflects shifts of hippocampal place fields toward rewards, and perhaps different subpopulations of place cells shift toward different rewards.

In summary, several studies have shown that high-valence locations cause distortions in the grid pattern. However, there are also many open questions regarding the precise nature of these distortions, and what exactly constitutes a "high-valence location."

Dimensionality of space

A final problem with the notion that grid cells serve as a metric for space is posed by the structure of the grid pattern in 3D. Surface-dwelling animals regularly traverse non-horizontal surfaces, while other animals move in a volumetric manner through 3D space. On one hand, when recorded on mildly slanted surfaces (40° slant), the firing patterns of rodent grid cells were almost unaltered.[51] On the other hand, on vertical walls, the picture was completely different.[52] When comparing grid cells on a vertical wall versus a horizontal floor, the grid pattern was dramatically disrupted on the wall: more than 60% of the neurons that exhibited a clearly hexagonal grid on the horizontal plane lost their grid pattern on the vertical wall. Most of the remaining neurons exhibited an increased grid scale or a disrupted grid on the vertical wall (Figure 3A).[52] Such dramatic elimination and distortion of grid coding on vertical walls seems inconsistent with the notion of a global metric for space.

In bats flying volumetrically through 3D space and in rats climbing inside a 3D volumetric structure, grid cells were recently shown to exhibit distinct, roughly spherical firing fields; however, the multiple spherical fields of 3D grid cells lacked any global lattice arrangement—in both bats and rats (Figures 3B and 3C).[27,28] Instead, grid cells in flying bats exhibited firing fields that were arranged in a *local order* in which there is a characteristic distance between neighboring fields. This local order could not be explained via shearing of the grid by the room's walls, as was verified by "un-shearing" analysis; thus, the grid geometry in 3D is genuinely different from 2D.[27]

The lack of a global lattice in 3D grid cells is of concern. As argued above, a metric for a Euclidean space requires global order (i.e., conservation of both distances and angles), and this order must be uniform across space. In 3D grid cells, these requirements are only partially satisfied. In bats, while the local distances between neighboring fields remained relatively uniform throughout the space, the angles between triplets of fields were not constant, and thus a global periodic lattice did not emerge.[27] The lack of a globally ordered 3D grid pattern in bats and rats suggests that grid cells are unlikely to serve as a global metric for 3D space.

IF GRIDS ARE NOT A GLOBAL METRIC FOR SPACE, WHAT IS THEIR FUNCTION?

Most theories on the possible functions of grid cells strongly rely on the notion of a globally ordered periodic hexagonal lattice (Box 1). However, as discussed above, multiple recent studies have shown that the grid pattern deviates dramatically from a globally ordered hexagonal lattice whenever the environment is large, non-empty, 3D, contains multiple compartments, displays non-symmetric geometry, or has a non-uniform valence of its contents. Most of the studies we surveyed above showed that from 60% up to nearly 100% of the grid cells exhibited deviations from hexagonality. All these conditions are expected to be even more severe in natural real-world complex environments, making the grid distortions and the associated problems reviewed above even more pronounced during naturalistic navigation.

These distortions may undermine the classical view of grid cells as providing a global Euclidean metric for space. However, cognition may still require a metric that can be used for navigation, even if this metric is non-Euclidean. This raises the obvious question: what navigational information does a distorted grid pattern provide? We propose that grid distortions can shed light on the function of grid cells. We will consider functional implications along three different axes. In the first axis, we will discuss whether grid cells provide a *global* versus a *local* metric for space. In the second axis, we will discuss whether grid cells provide a metric for *objective* physical space or rather for *subjective*, action-relevant space. In the third axis, we will discuss whether the grid pattern represents continuous *space itself*, or rather whether it represents discrete *entities within space*. Although these are three separate axes—addressing three separate questions—they are not necessarily mutually exclusive. We also note that grid distortions have interesting implications for the *mechanisms* of grid cells, which we will review subsequently. But we shall start with grid function.

Functional hypothesis 1: Grid cells form a local metric system

The first axis that we will discuss in light of grid distortions concerns the question of whether grid coding constitutes a *global* metric for space or a *local* metric for space. Distortions of the grid pattern mean that the pattern's characteristic global order is disrupted. The grid pattern is classically thought to provide a global metric for space due its repetitive pattern throughout the space. How can the grid serve as a metric for space if it exhibits distortions? One may reconcile the existence of distortions with the idea of a metric for space by relaxing the requirement for a *global* metric. A *local metric system* (Figure 4A) could provide a measure of distances or angles in space, but only

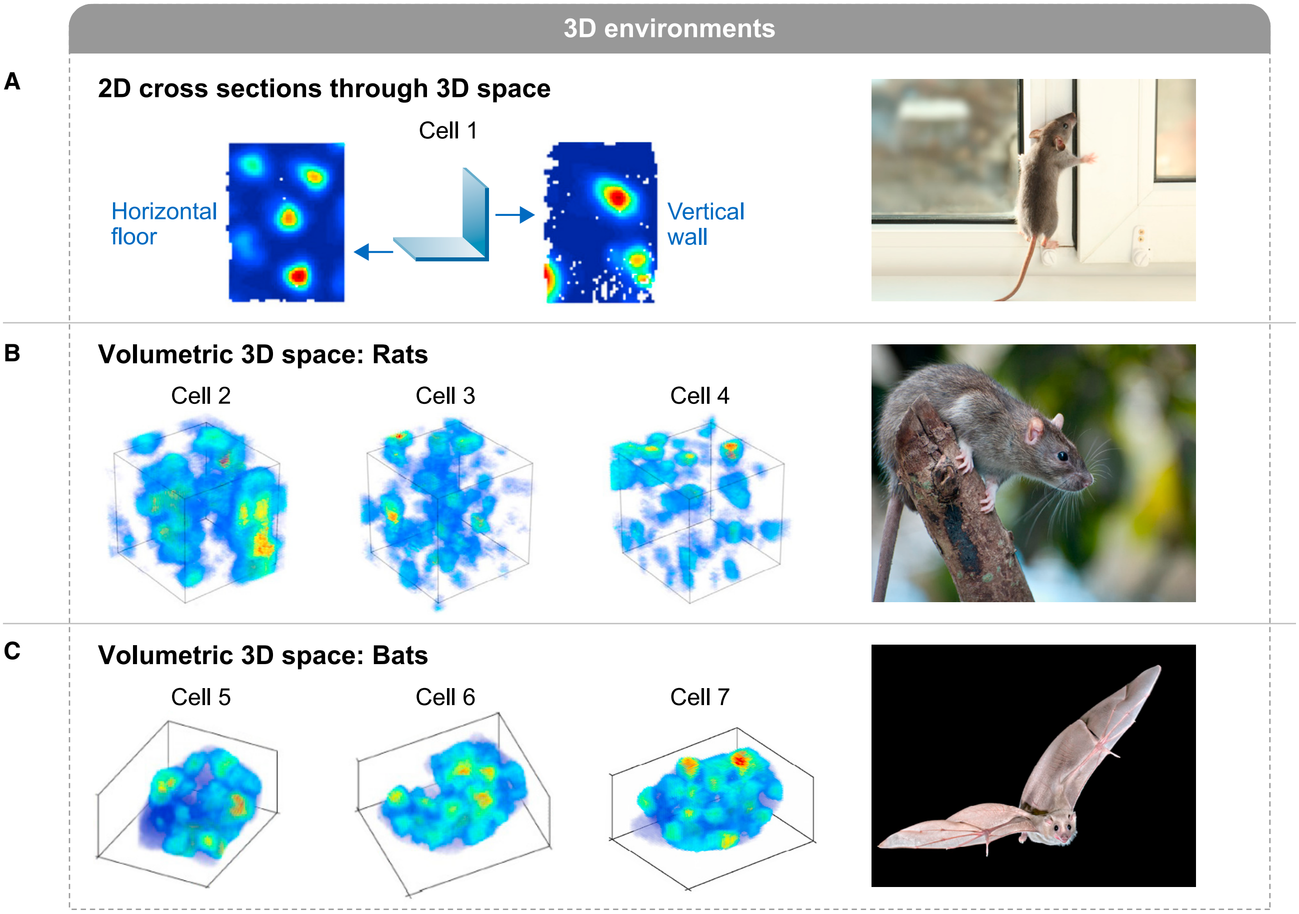
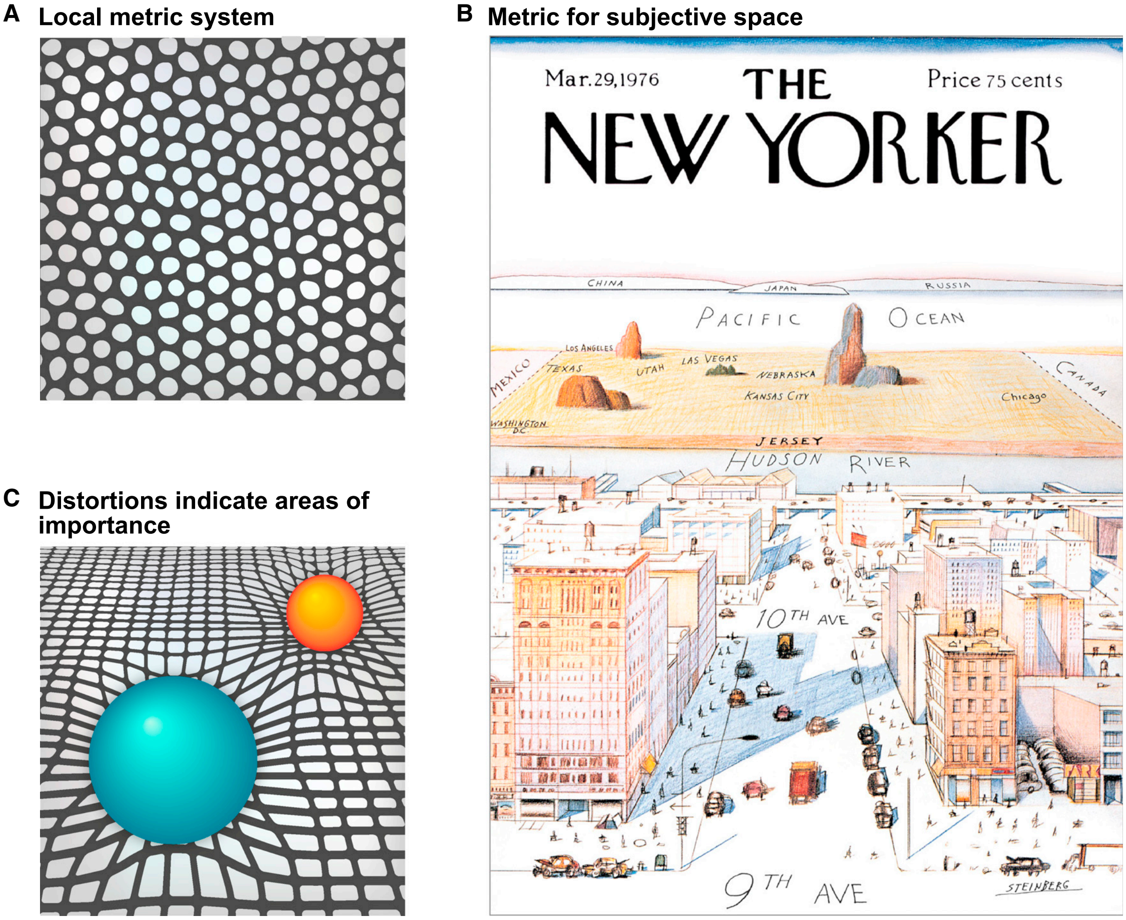


Figure 3. Dimensionality fundamentally affects the structure of the grid pattern: 3D grid cells do not exhibit a global hexagonal lattice
(A–C) Examples of grid cells recorded in non-classical arenas with a 3D component.
(A) Example of a grid cell in which the grid pattern was distorted when recorded on a vertical 2D surface (right) as compared with the same cell recorded in the classical manner on a horizontal 2D surface (left). Taken with permission from Casali et al.[52] Right column: surface-bound animals such as rodents are excellent climbers and often traverse vertical 2D surfaces. Photo: Shutterstock.
(B) Three examples of 3D grid cells in rats, which were recorded in medial entorhinal cortex (MEC) while the rats climbed a 3D volumetric structure. Field arrangements lack a global order (no lattice). Taken with permission from Grieves et al.[28] Photo: Shutterstock.
(C) Three examples of 3D grid cells in bats, which were recorded in the bat MEC while the bats flew volumetrically in 3D space. Field arrangements lack a global order but were found to exhibit a local order, with fixed local distances between neighboring fields, suggesting a *local* metric for space. Taken from our work in Ginosar et al.[27] Photo credit: Steve Gettle.

locally. We suggest that a pattern which is useful locally may either contain angles and distances that are fixed only on average (see illustration in Figure 4A), or it may be created from patches of perfectly ordered patterns sewn together with distortions. Such a system would be reliable at short distances from a known position (such as a landmark). However, upon traveling long distances, a local metric will accumulate errors and will not suffice for navigation.

Related to the issue of accumulation of errors, another important notion is that of path integration, which was strongly linked to grid cells.[6] As mentioned above, path integration is the process of estimating the animal's current position by integrating its past trajectory.[10] It is noteworthy that most animals (with the exception of desert ants) are in fact not capable of successful path integration over long distances, when sensory cues are eliminated entirely. Rodents are completely disoriented after they perform as few as 3 rotations in the dark and are then not able to path-integrate anymore.[54] Likewise, humans were shown to lose their way very quickly during a blindfolded walk.[55,56] Further, it is questionable whether there is an ecological need for mammals such as humans and rodents to navigate long distances without any cues such as boundaries or landmarks. We therefore suggest that it is much more likely that the activity of grid cells is used as a metric for space only over short distances from informative locations—possibly by path-integrating over short distances.[44]

Indeed, the grid pattern was proposed to anchor to specific boundaries of the arena and produce an ordered pattern in the local vicinity of the boundary.[44,45,57] This is consistent with the notion that the grid serves as a local metric system, which provides a means for local path integration near areas of information, where the animal knows where it is, e.g., near the boundary.



Local metric system

Metric for subjective space

Distortions indicate areas of importance

Figure 4. Possible interpretations of grid distortions

(A) Hypothesis 1: the grid pattern consists of characteristic fixed distances between neighboring fields (local hexagons), which can be utilized as a local metric for space.

(B) Hypothesis 2: the grid pattern is a metric for subjective action-relevant space. Shown is a cartoon illustrating a subjective action-relevant representation of Manhattan for New Yorkers. Reproduced with permission from Saul Steinberg, "View of the World from 9th Avenue," cover of The New Yorker, March 29, 1976.[53]

(C) Hypothesis 3: in a loose analogy to general relativity theory, where a distortion of spacetime indicates the presence of a large mass, we suggest here that the ordered grid pattern is used as a backbone map, whose distortions indicate the presence of a high-valence location (as in Figure 2). Thus, the deviations from a perfect hexagonal grid can encode information about areas of interest and valence.

If so, the grid should be anchored to the boundary, and movement of the boundary would cause a grid distortion near it—as was found experimentally.[25] Further, the notion that grids provide a local metric for space may also explain how grid cells could be useful, despite the shearing phenomenon,[42] because the effect of shearing on local distances may be negligible.

The idea of grids serving as a local metric system begs the question of how different local hexagonal grid patches with a local metric are "sewn" together to enable long-range navigation. The concern is that self-localization errors would accumulate rapidly as the animal passes from one local patch to another, where each patch may have a different orientation (this would be problematic, assuming that the grid is also used to encode direction). For example, if we take Figure 4A and assume a 1-m spacing (wavelength) for this pattern, then if an animal needs to navigate over a 100-m distance using such a pattern—passing through ~100 local patches of ~1-m size each—then the error accumulating over these 100 "sewing" operations will inevitably lead to complete disorientation.[58] One potential solution for this concern lies in the fact that the local grid patches are registered through external localizing input, such as vision, audition, or somatosensation, by resetting the estimated orientation of the animal at specific landmarks or encountered boundaries.[45,58–60] Alternatively, grids may be used only for local navigation or for locally "filling holes" in positional information when no sensory cues are available, while long-range navigation is performed elsewhere in the brain. The latter possibility is consistent with the recent experimental results on 3D grid cells in bats, where we found fixed local distances between grid fields in 3D, and proposed that 3D grid cells could be used for 3D local navigation—despite not exhibiting a global 3D lattice.[27] Our finding of a local metric in 3D prompted us to suggest a phenomenological model of interactions between the grid fields of each neuron. These interactions lead to local order and can explain both the classical global hexagonal grids in 2D as well as our findings of local order in 3D in bats. Specifically, in that work,[27] we showed that when we impose in the model a roughly characteristic local distance between fields along a 2D surface, the fields become arranged in a hexagonal grid pattern along the surface. When imposing this same local-distance constraint in 3D, spherical fields were arranged in a local, but not global, order. We will discuss in more detail below (in the section on grid cell mechanisms) the relationship between this type of model and mechanisms supporting a local metric system.

Functional hypothesis 2: Grid cells provide a metric for subjective action-relevant space

In the second axis, we propose that the existence of grid distortions raises the need to rethink the role of grid cells as providing a metric for the *objective Euclidean space*. Given that the Euclidean space itself is not distorted, why should its underlying metric be distorted? We suggest that the distortions that we reviewed here, which often align with areas of subjective interest, might indicate that the grid pattern serves as a metric for *subjective action-relevant space* (see also Jeffery[61]). The subjective space itself may differ from the physical space, and we propose that these differences could be encoded by different grid spacing, being morphed continuously across space in accordance with subjective perception. A navigating animal may in fact benefit from having higher resolution and accuracy in representing areas of high interest (such as areas with higher density of rewards, higher behavioral relevance, etc.). Evidence of grid fields moving toward specific rewarded locations[23] may support this idea. However, we propose that the grid pattern should also be tested in large rewarding zones (beyond punctate locations of reward) and that it should be compared with the grid pattern in a zone of the same size with a neutral importance. For example, think of the floor of a bakery or a chocolate factory compared with a neutral warehouse of the same size. Likewise, an animal may benefit from having a different resolution in areas that are best avoided—for example, short distances in the physical space may be deemed long in the action-relevant space if it presents danger (or vice versa). Indeed, coding of space by hippocampal place cells is altered by fearful experiences.[62,63] However, this was not examined in grid cells. Another variable that may affect the subjective space is the ease of travel through different areas of space, which may alter the velocity signal in the animal's brain. This was suggested to explain the increased grid scale in rats on vertical walls,[52] which require large effort to traverse. In this respect, it would be interesting to examine how the activity of speed cells in the medial entorhinal cortext (MEC)[64] is altered depending on the perceived ease of travel. Similarly, a short distance between the two sides of an unpassable barrier would be encoded as a much larger distance in the action-relevant space, discouraging the animal from hopelessly trying to pass through it.[65] Thus, according to this hypothesis, the grid pattern does not provide a veridical representation of Euclidean space, but instead it provides something that may be more useful for guiding actions during navigation: a veridical metric representation for subjective, action-relevant space. Such a representation is reminiscent of how we often perceive space in a non-Euclidean manner that is incongruent with physical space itself. Consider the famous cover of The New Yorker created by Saul Steinberg in 1976, which illustrates a well-known subjective feeling (Figure 4B). In this illustration, space is morphed by subjective importance, relevance, and actions, in a manner that may be consistent with data on grid distortions. Indeed, a recent study tested human memory in a trapezoid environment that was similar to the one shown in Figure 1A and found distortions in human spatial memory at the same locations where rodent grid cells were distorted in the trapezoid.[66] However, a direct link between neural representation and subjective perception is yet to be shown. Overall, we speculate that animals may benefit from maintaining a metric that varies in different areas, where space is subjectively perceived differently; for example, they may hold one metric for a difficult-to-pass high grass and another metric for an easily traveled pavement. At the same time, the exposed and dangerous parts of the pavement may be represented at a different resolution than the sheltered, well-acquainted parts.

Many of the models that treat grid cells as a positioning system rely on the repetitive and ordered geometry of the grid pattern (Box 1), but this was shown to be distorted in the experimental studies reviewed above. Thinking of grid cells as a positioning system in a subjective action-relevant space (which may be prone to distortions itself) may resolve this discrepancy. Specifically, the distorted grid may represent position within the distorted subjective space. A related idea was proposed in the framework of the "successor representation," in which hippocampal place cells do not encode space per se; instead, place cells code typical behavioral trajectories through space[65,67] (this applies to both physical space and abstract spaces; see Box 3 for discussion of grid cells in abstract spaces). Place cells simulated via the successor representation framework capture place-field deformations near boundaries or near points of interest. Further, it has been shown in these studies that computing the leading principal components of place cells' activity yields periodic neural activity patterns akin to grid cells.[65,67,74] It therefore follows that the behaviorally induced deformation of place cells, as predicted by the successor representation, propagates to yield deformation of grid cells. Indeed, Stachenfeld et al.[65] found the predicted deformations of simulated grid cells in the hairpin maze and in trapezoid environments. It would be interesting to conduct similar analysis for reward locations.

Finally, we note that the proposal that the grid pattern veridically and accurately represents an action-relevant subjective space (which is distorted relative to objective space) raises key questions regarding the interplay between distortions of the grid pattern and distortions of subjective perception. We will return to this issue below.

Functional hypothesis 3: Grid distortions carry useful information

Finally, distortions of the grid pattern seem too common to be treated as a "bug"; in fact, these distortions are so prevalent and easy to elicit experimentally that they may be a *feature* of the grid system. With this in mind, in the third axis we propose to rethink the basic assumption that the grid pattern's order is what carries information about continuous space. Instead, the grid pattern distortions could represent *discrete locations within the space* through deviations from order, where these deviations serve as "flags" marking locations of interest. This would mean

Box 3. Utilizing grid distortions for understanding grid cells in abstract spaces

The hexagonal grid pattern was discovered in the context of 2D spatial surfaces on which rodents navigate, and thus the grid pattern is thought to represent physical 2D space. Consistent with this, studies of humans using functional magnetic resonance imaging (fMRI) revealed a hexadirectional signal as the subjects navigated in a virtual 2D space, thus providing indirect evidence for grid cells in the human entorhinal cortex.[68] Surprisingly, a similar hexadirectional signal was found also when subjects mentally ‘‘navigated’’ through a 2D abstract space in which one dimension was a bird’s beak size and the other dimension was a bird’s leg size[69]—suggesting that the grid pattern represents 2D abstract spaces as well.

The discovery of a hexadirectional signal in abstract spaces, indicating grid-like activity, supported the idea that the grid pattern may create a representation of any continuous 2D topology, which could be an abstract space or physical space. It was thus suggested that the features of stimuli (e.g., the beaks and legs of birds) might form the dimensions of an abstract space[70] and that the grid pattern creates a metric for these stimuli and provides a framework for learning their relationships.[71] Another possible explanation for the emergence of the hexadirectional signal in both physical and abstract spaces, treats grid cells as encoding an item’s serial position within a sequential series of events.[72] Such a series could be a spatial series of locations in the case of spatial navigation or a non-spatial series in some abstract space if the behavior is non-spatial. Although most contemporary ideas suggest that the grid system represents spaces—of which the physical space is one example—Spiers[73] suggested that while the grid system can code both physical and abstract spaces, the maps for physical and abstract spaces are separated in the brain. According to this suggestion, spatial maps are located in the posterior/dorsal parts of the hippocampal formation (which have spatial inputs), whereas non-spatial maps are located in the anterior/ventral parts (with non-spatial inputs).

In order to examine whether the grid pattern is indeed a general metric for any space, be it physical or abstract, one could ask whether the grid pattern behaves in the abstract space as it does in the physical space. This can be done by studying the grid system when it deviates from its classical hexagonal symmetric pattern. We propose harnessing the deviations from perfect hexagonality, as were reviewed in this perspective, to glean insights on the relations of maps for physical and abstract spaces in the brain. Specifically, we suggest that the hexadirectional signal in abstract spaces should be examined in: (1) an abstract space with an area of valence, analogous to reward zones in the experiments done for 2D physical space[22,23] (Figure 2); and (2) a 3D abstract space, for example, a space consisting of birds’ beak-length × leg-length × head-height. Would one find local-but-not-global order in such 3D abstract space, akin to the bat grid cells that we recorded in 3D physical space[27] (Figure 3C)? Such experiments should probably be done using single-neuron electrophysiological recordings in human patients, rather than fMRI. This is because fMRI methodology may not be suitable for revealing localized distortions or a local order, as these would not induce a hexadirectional global signal that could be detected using fMRI. These experiments would therefore be quite challenging; however, it is important to conduct them because they could shed light on whether grid cells behave similarly in physical and abstract spaces, and whether the grid system is adequate to serve as a metric for abstract spaces.

that *the important information of the grid pattern lies in the deviations from order rather than in the order itself*.

In the theory of general relativity, distortions of spacetime indicate the presence of a large mass, such as a star or a black hole.[75] We suggest, in a very loose analogy, that the distortions of the grid pattern carry information about areas of importance—much like the distortions of spacetime in general relativity that carry information about regions with a large mass. Thus, perhaps the function of the perfectly ordered hexagonal grid, which is observed in symmetric environments, is not to represent metric spatial information. Rather, the perfect order makes the deviations from it stand out, and it is these deviations from the grid—rather than the grid itself—that are the key feature, as these deviations encode places of importance in space (see illustration in Figure 4C). This idea may explain the local distortions in 2D grids that are created by reward zones, home boxes, and other areas of high valence (Figure 2).[22,23,26] Borders of asymmetric parts of the environment may also be regarded as high-valence locations, as they provide useful information about the animal’s whereabouts, meaning that this third hypothesis may possibly also explain geometry-based grid distortions.

In contrast to axis 1, axes 2 and 3 both entail an element of the subjective world of the animal. In axis 2, the grid is morphed and scaled by the animal’s areas of interest as it creates a metric for the continuous space that is being used subjectively; for example, the same neuron may exhibit one grid-spacing in an agricultural field but a different grid spacing in nearby moors, reflecting their different subjective value. In axis 3, on the other hand, space itself is not represented continuously. Rather, the grid pattern is used to mark and represent the discrete locations of interest that lie within the space; e.g., a fruit tree in the middle of an agricultural field or a resting boulder in the middle of the moors. Therefore, axes 2 and 3 lead to distinct predictions regarding grid distortions. If the grid pattern creates a metric for subjective space (hypothesis 2), the pattern would exhibit different resolutions in different zones that have different subjective meaning, e.g., agricultural field versus moor, as in the example above. Importantly, we expect that the changes in grid spacing will unfold slowly over space, such that each grid resolution will cover entire large zones. However, if the grid pattern mostly marks locations of importance through discrete punctate distortions (hypothesis 3), we expect to find a regular grid across the entire space, dotted with punctate very-local distortions marking distinct locations of interest. In the example above, we will expect a perfect uniform grid that covers both the agricultural field and the moor, and the grid should be distorted only near the punctate fruit-tree and boulder, which are

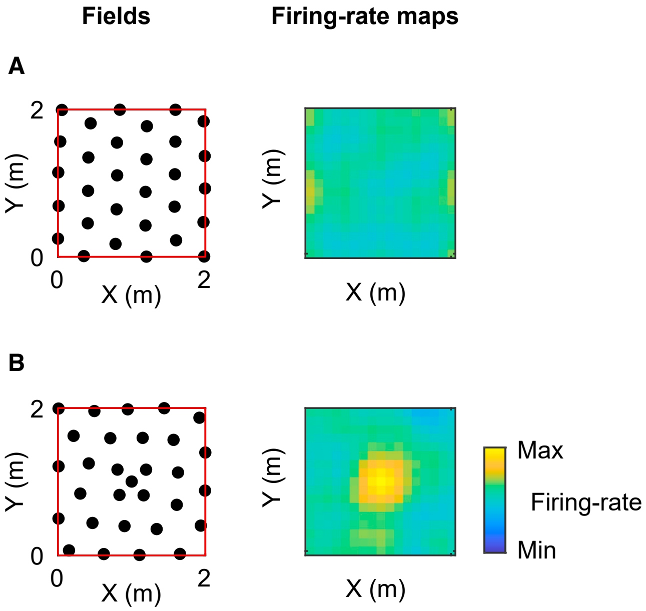


Figure 5. Possible read-out of grid distortions

Detecting grid distortions based on local distances between grid-fields. Shown are examples of two simulated grid cells. Left: field locations. Right: field locations after Gaussian smoothing, constituting an effective firing-rate map.

(A) Example of a simulated grid cell in an empty 2D square arena. This cell does not show any grid-distortions.

(B) Grid cell in an arena with reward in the middle—showing grid-distortions. Note on the right the region of high firing rate at the reward position (yellow hotspot). Spatial smoothing in both (A) and (B) was done with $\sigma = 0.2$ m and bin size = 0.1 m. Notably, a similar output would result from a temporal smoothing operation by a downstream reader (decoder), as biological neurons typically perform temporal smoothing. The high firing rate of the neuron in (B) signals the presence of a high-valence location, such as a reward location, without the need to compare to any "reference" grid with a perfect hexagonal lattice.

the only two specific locations of interest. In other words, here we expect to see very discrete and localized distortions, and these distortions should occur at discrete, punctate locations of interest. Of course, there could also be a combination of hypotheses 2 and 3: grid cells may show different spacings in zones of different subjective value, such as the agricultural field versus the moor (hypothesis 2), and also show distortions near punctate locations, such as the fruit-tree and the boulder (hypothesis 3).

In the case of hypothesis 3, we may ask: how could discrete punctate distortions be read out? A downstream decoder needs to detect these deviations from a fixed local distance, signaling important areas. One possibility is that the distorted grids are compared with a non-distorted veridical map. This requires the existence of perfect "ground-truth" grids that are never distorted, which could serve as a veridical reference map. A second possibility is that the distortions are not compared with any perfect grid, i.e., there is no veridical map. Instead, the read-out can be based on changes in *local distances* between grid fields (compare Figure 5A, left and Figure 5B, left) or on changes in *local density* of grid fields, inducing heightened activity at locations of interest (compare Figure 5A, right and Figure 5B, right; note the hotspot indicating the existence of a location of interest). As shown in Figure 5, it is indeed possible to read out the local distortions in the grid—which encode high-valence locations—without comparing to any perfect veridical grid as a reference; thus, there is no requirement for having a perfect grid anywhere in the brain. Importantly, it is the distortion of the grid pattern, rather than its order, which is informative—providing information about important objects and rewards and high-valence locations. It thus suggests that the essence of the locally ordered equidistant fields is in fact to provide a useful "canvas" that can accommodate the deviations from the characteristic distance between fields, while binding different areas of importance together in the same backbone. Additional experimental work would need to also validate this interpretation for 3D space by examining whether the local arrangement of 3D grids is distorted near locations of high behavioral valence.

Following our discussion of possible *functions* of grid cells and their distortions, we next discuss the *mechanisms* through which such functions could be implemented and read out.

GRID CELL MECHANISMS CONSISTENT WITH THE THREE PROPOSED FUNCTIONS

Possible mechanism I: Local pairwise interactions

A possible mechanism that may accommodate grid distortions and the three proposed grid functions is pairwise interactions between grid fields. In Ginosar et al.,[27] we modeled the grid pattern as emerging from effective pairwise interactions between fields—akin to interactions between particles in physical systems (see also Krupic et al.[24]). According to the pairwise interactions model, close-by fields repel each other while far-away fields attract each other, resulting in a fixed characteristic distance in-between adjacent grid fields (determined by the distance of the "well" in the potential energy function shown in Figure 6A, left). These types of interactions between firing fields could be created by plasticity mechanisms in feed-forward synaptic inputs to grid cells.[76] Such plasticity mechanisms acting in synapses from hippocampal area CA1 to MEC neurons were shown, theoretically, to create effective pairwise interactions between firing fields of grid cells.[77–79] We demonstrated that when applying such a model to fields residing on horizontal 2D surfaces, a hexagonal globally ordered grid pattern emerges in many of the neurons (Figure 6B, left; 2D square arena). However, when applied to fields in 3D space, the pattern does not crystallize into a hexagonal grid but rather exhibits an arrangement with equidistant fields only locally—as seen in the bat experimental data in 3D (Figure 6B, right; 3D arena).[27]

Here, inspired by Krupic et al.,[24] we extended our model of pairwise interactions between fields to include repulsion of fields away from nearby geometric borders of the environment, and attraction of fields toward nearby high-valence zones such as reward locations. The energy function used in this extended model describes a field's potential energy and is composed of three terms, indicating the three entities that a field interacts with, as follows (see also Figure 6A):

$$E_i = A_f \sum_{i \neq j}^{N} \left(\left(\frac{r_0}{r_{ij}} \right)^{12} - \left(\frac{r_0}{r_{ij}} \right)^{6} \right) + A_w \sum_{walls} e^{-\frac{r_i^w}{r_0^w}} - A_r e^{-\frac{r_i^r}{r_0^r}}$$

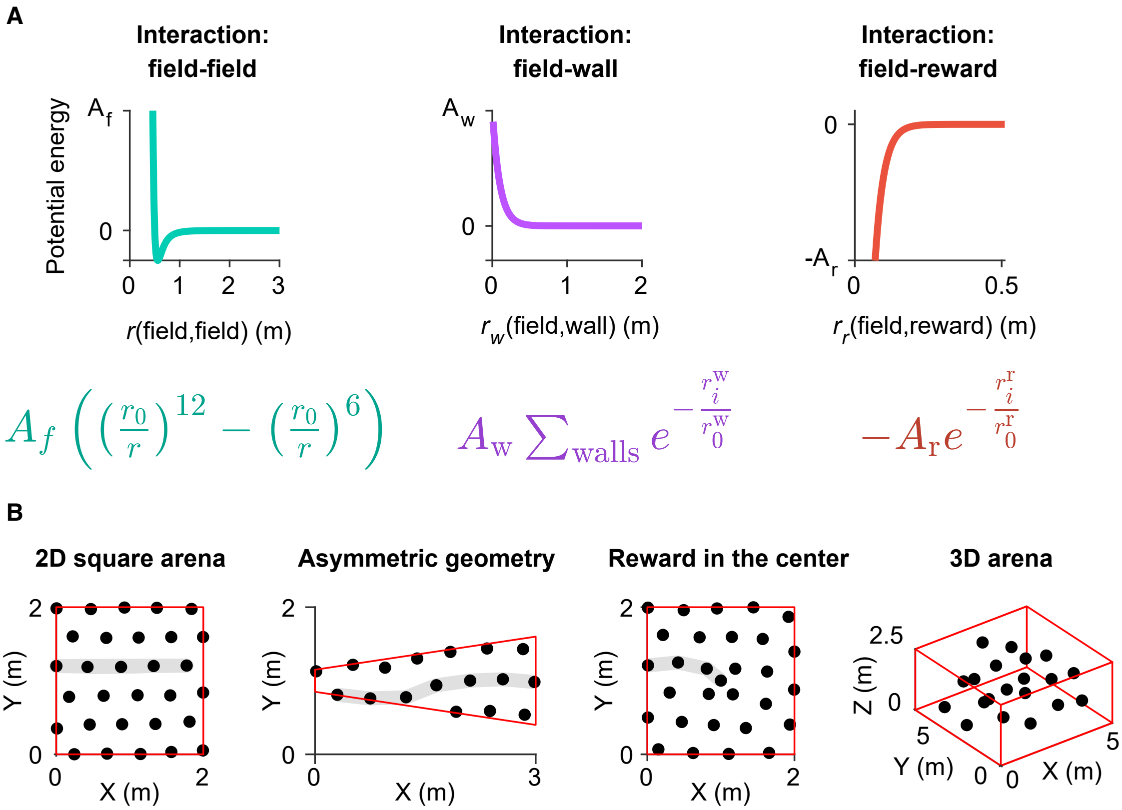


Figure 6. A model of pairwise interactions captures grid distortions elicited by geometry, reward zones, and dimensionality

(A) Energy potential used in our model. The three plots depict separately the three components of the model as a function of distance, in meters (the three potential energy functions are indicated). Left: interactions between fields, according to the Lennard-Jones potential, as used in Ginosar et al.[27] The Lennard-Jones potential exhibits repulsion at close-by distances and attraction at farther distances, creating a characteristic stable distance between fields at the minimum of the potential energy. A noise term (temperature, T) allows deviations from precisely fixed distances. Middle: interaction between a field and the wall of the experimental arena in which fields are repelled from the wall. Right: interaction between a field and a reward zone or other high-valence location, whereby fields are attracted to high-valence areas. Each type of interaction (field-field, field-wall, and field-reward) was simulated using a scaling factor $A_\mathrm{interaction}$ and a length-scale parameter r_0, indicating the interaction distance. See the full potential-energy equation of the model in the main text. For interactions between fields, we used $A_f = 4$ and $r_0 = 0.5$ m for 2D arenas, and $r_0 = 1$ m for 3D arenas (as in Ginosar et al.[27]). For the repulsion of fields from walls, we used $A_w = 50$ and $r_0^w = 0.1$ m. For the attraction of fields to reward sites, we used $A_r = 10^8$ and $r_0^r = 0.03$ m. In all scenarios, we used the same temperature as fitted to the 3D experimental data from the bat, namely $T = 10^{0.5}$.[27]

(B) Examples of simulations using the pairwise interactions model in a 2D square arena, an arena with trapezoid asymmetric geometry, an arena with a reward zone in the center, and a 3D arena. The model captured the hexagonal grid pattern in the 2D square arena (left) as well as the experimentally reported distortions of the global grid pattern exerted by asymmetric geometry and by a reward zone (middle two panels), and also the local-but-not-global grid arrangement in 3D arenas, which was found in flying bats (right). The gray lines in the 2D arenas highlight the grid distortion in the arena with asymmetric geometry and the arena with reward. We used the same density of fields in all 2D simulations (2D square arena, asymmetric geometry, and arena with reward in the center). Note that the 2D square arena and arena with reward in the center also contain the same number of fields (N = 30).

The first term on the right hand side (A_f...) describes interactions between fields, using the Lennard-Jones potential, the same as we used previously[27] (Figure 6A, left). It consists of repulsion at short distances and attraction at long distances, and this energy is summed over all the field pairs. The second term (A_w...) represents the interaction between each field and the walls (Figure 6A, middle). We computed here the repulsion exerted on each field by all the walls. The third term (A_r...) captures each field's interaction with a nearby reward location (Figure 6A, right); here, the field is attracted to the reward (or to other locations of high valence), and the attraction is indicated by the minus sign. The parameters r_0, r_0^w, r_0^r represent interaction length scales with other fields, walls, and reward locations, respectively. The parameters A_f, A_w, A_r are the scaling factors of each energy term. This model, which successfully described grid-field arrangement in 2D square arenas and in 3D rooms,[27] was here able to also capture the grid distortions observed experimentally in asymmetric 2D trapezoid arenas and near reward locations (Figure 6B, asymmetric geometry—note the grid angle is changing across space; and Figure 6B, reward in the center—note the high density of fields in the center). These three interactions—field-field, field-wall, and field-reward—allowed the model to qualitatively capture the different grid patterns as recorded experimentally in different settings. The fact that a model that is based purely on short-distance local interactions can describe a host of different experimentally observed grid distortions reinforces the idea that grid distortions are largely local in nature.

This proposed mechanism is not only consistent with all the types of reported grid distortions but is also consistent with all our three functional hypotheses. Due to its local nature, the interfield interaction mechanism can support a grid used as a local metric for space—as in our functional hypothesis 1. By continuously adjusting the model's spacing parameter r_0 according to the subjective properties of the space (e.g., permissibility, danger, ease of locomotion), this model could also create a grid pattern whose spacing may be used as a metric for subjective space—as in functional hypothesis 2. By adding interactions with discrete, punctate locations of interest, this model creates distortions specifically next to these locations and can thus be used for marking such discrete locations of interest—as in functional hypothesis 3.

Possible mechanism II: Continuous attractor networks

Attractor network models of grid cells have been extremely successful in capturing the phenomenology of grid cells recorded in small and symmetric environments, namely hexagonal firing patterns (Box 2). However, the deviations from a perfect grid require modifying the current models and entail important implications for continuous attractor models.[72] How might we reconcile grid distortions and an attractor network? A first possibility is that the experimentally observed distorted grid pattern reflects a distorted pattern of the bumps of activity on the neural sheet itself (relevant for models of grid cells with multiple bumps).[5,29] Such a distortion could arise from a distortion in the "Mexican hat" anatomical connectivity pattern, which can occur, for example, due to competitive plasticity processes.[76,78,79] A local connectivity pattern could lead to a local—but not global—spatial firing structure, creating a local metric for space, as proposed in functional hypothesis 1. This possibility implies a slow emergence of the distortions due to the slow nature of plasticity mechanisms; it would therefore be important to study the dynamics of distortions from the first moment the animal is placed into an asymmetric arena. This experiment has not yet been undertaken. A second possibility is that while the pattern on the neural sheet is perfectly periodic and non-distorted, the velocity signal that moves the activity hotspot (bump of activity) is distorted. This velocity signal could be altered due to subjective variables, such as ease of movement, attention, or arousal, possibly creating a grid pattern that relates to subjective space—as proposed in functional hypothesis 2. The velocity signal may also be distorted only at the close vicinity of strong reward signals, creating discrete distortions near important locations while keeping the rest of the pattern unaltered—as proposed in functional hypothesis 3. A third possibility is that the grid pattern is being distorted by inputs from other cell types, such as border cells, or by sensory inputs incoming into the entorhinal cortex.

Recent advances in electrophysiological techniques allowed the recording of hundreds of neurons simultaneously, demonstrating that the joint activity of grid cells lies on a toroidal manifold[36]—as predicted by continuous attractor models. It would be important to conduct such multi-neuronal recordings in naturalistic distortion-inducing arenas, as this would shed light on the question of how grid distortions may be reconciled with continuous attractor models. This was done in part in Gardner et al.[36] by using a "wagon-wheel" maze. However, the wagon-wheel experiment had two key limitations: (1) this environment was highly symmetric; (2) there was no visual obstruction, and the entire environment was visible throughout—unlike the hairpin-maze experiments, which used high walls to yield strong grid breakdown.[19] The result of these two limitations was that the grid distortions reported by Gardner et al.[36] for the wagon-wheel were relatively mild (the gridness scores remained positive, on average). Therefore, such population-level experiments must be done systematically for much more strongly distortion-inducing environments, such as the hairpin maze, the trapezoids, or the asymmetric arenas shown in Figures 1A–1C. Specifically, such recordings could provide direct experimental support (or refutation) for the possibilities described above, namely that the bump of activity is changing its spacing or its movement speed on the torus in a manner that exactly corresponds to the distortions seen in the asymmetric arenas, such as the trapezoid. Such future experiments will elucidate the relationship between spatial distortions of the grid pattern—which affect the use of grid cells in navigation and are therefore important—and distortions (or lack of distortions) on the toroidal neural manifold.

SUMMARY AND OUTLOOK

In this perspective, we discussed several issues that lead us to depart from the notion that grid cells form a global metric for space that is used for long-distance navigation. We suggested three functional hypotheses, which retain a spatial function for grid cells, while being consistent with the recent experimental data. First, grid cells may constitute a local metric for space. Second, grid cells may code a subjective action-relevant space. Third, grid cells may encode locations of interest, such that the ordered hexagonal pattern forms a backbone for encoding distortions and the deviations from perfect order mark the positions of points of interest.

Although not necessarily mutually exclusive, these three functional proposals can be experimentally disentangled, as discussed above. Further, if the grid indeed creates a local metric that cannot be used in long-distance navigation, then we predict that the grid pattern, especially for grids with small spacings, will not maintain its regularity in large arenas. When simulating pairwise interactions between fields, we recently showed that the gridness scores of simulated 2D grids decreased in larger rooms—suggesting that the crystallization of hexagonal grids in 2D is affected by the ratio between arena size and grid scale.[27] With this in mind, we suggest that one way to provide experimental evidence supporting the local-metric framework would be to conduct experiments in very large 2D boxes, several meters across, and to record from grid cells belonging to different "modules"—i.e., grid cells with different spacings. If grid cells that possess a small-scale 2D grid compared with the room size exhibit a disrupted hexagonality—but at the same time large-scale 2D grids are perfectly hexagonal—this would be consistent with our simulations of local pairwise interactions and would support the notion of grid cells creating a local metric for space. Another possibility is that grid cells with different spacings have fundamentally different functions: for example, grids with large spacing might not be distorted at all and create a global metric for space, while grids with small spacing may be distorted and encode a local metric and/or subjective space and/or high-valence locations. This calls for experimental studies of grid cells with large spacing in very large asymmetric environments to examine whether these grid cells exhibit distortions; this has not been done to date.

Our second and third proposals both entail a subjective component and may thus be harder to tease apart, as both the valence of a location and its subjective behavioral relevance are related to the animal's own perception. The recent data we reviewed here revealed local pattern distortions near locations of subjective high valence, such as reward locations and shelters. Geometric asymmetries in the environment, which contain high levels of information for navigation, could also perhaps be thought of as high-valence or high-salience areas, which may explain the grid distortions in these areas. One possibility to test the second hypothesis without conflating it with the third hypothesis is to record grid cells in uniform arenas that do not contain punctate reward locations but rather differ in their *average* valence. For example, it would be interesting to compare the spacing of the same grid cells in a box where random reward is given versus a box where no reward is given—thus clearly differing in valence. Likewise, experiments can compare grid spacing in boxes with different surfaces (difficult versus easy to traverse), as well as boxes with different illuminations or different temperatures, which elicit different levels of stress and therefore entail different valences. One clue suggesting that grid spacing may differ in these conditions comes from an experiment on hippocampal place cells, which found that place fields are much smaller in an engaging area with very rich sensory stimuli as opposed to an empty area.[80]

A further issue that will have to be addressed in future experiments is the interplay with other cell types. Interestingly, while grid cells in bats flying in 3D did not exhibit a global hexagonal lattice—thus deviating dramatically from the 2D pattern—some other cell types in the hippocampal formation did show 3D tuning consistent with the 2D tuning. Thus, place cells showed spherical 3D place fields[81] and head-direction cells showed unimodal 3D tuning.[27,82] Similar results were also found in rodents in 3D.[83–85] Thus, in some sense, the "disintegration" of the 3D grid seems special. However, it will be important to compare tuning distortions in various cells types also in 2D. Specifically, future experiments will need to systematically record the various spatial cells types—grid cells, place cells, head-direction cells, as well as border cells and speed cells—in rodents navigating in 2D, and to examine the possible distortions of all these cells near reward zones and in asymmetric environments.

All theories describing the function of grid cells in spatial perception—including the three proposals that we described above—suffer from an important "missing link": a missing connection between the internal representation (i.e., the grid pattern) on the one hand and the spatial perception and spatial behavior on the other hand. For example, does a local distortion of the grid pattern in the narrow part of a trapezoid arena mean that the perception of space is distorted at that location? This is a fundamental question that is also important for the most basic question of all: is the grid pattern used at all for spatial perception and navigation? In fact, it has never been demonstrated directly that grid cells specifically (as opposed to other classes of spatially tuned neurons) are crucial for navigation—even though lesions and inactivations of the entorhinal cortex have been shown to affect some navigational tasks, albeit in varying degrees (see Box 4). Notably, some studies reported almost no effects of lesions and inactivations on navigation behavior (Box 4), which further argues against the notion that grid cells form a global metric for space because, if grid cells did form such a global metric, we would expect to see much larger effects of entorhinal lesions on navigation performance. Future work will thus need to show a direct link between grid cells and navigation behavior. Specifically, if the grid pattern indeed reflects an underlying spatial metric—be it a global or a local one—then whenever the grid pattern is distorted we may expect the spatial perception to be distorted accordingly. It may be particularly powerful to induce grid distortions causally (e.g., using optogenetics) and observe whether the subjective perception of space is being distorted accordingly. Measuring the link between distortions in the grid pattern and distortions in spatial perception poses a major challenge: while recording neural activity in animals is relatively straightforward, it is much more difficult to tap into an animal's subjective perception of space. In order to probe distortions in perception, one must design novel types of experiments. A promising first step has been made recently in rats by creating mazes that allow researchers to behaviorally measure subjective spatial-perceptual distortions.[97] In this dynamic maze, a rat needs to reach a goal location by making a series of choices on how to proceed toward the goal. The rat's choices at each decision point shed light on its perception of where the goal is and how to best navigate toward it, which allows inference of the rat's local subjective spatial distortions. In parallel with the difficulties in addressing this question via animal research, human research is challenging as well, but for opposite reasons: a human can easily report on their own spatial perception, and the perceptual distortions can be tested in a rather straightforward manner, but neural recordings of grid cells in humans are limited. Specifically, intracranial recordings are performed in virtual rather than in real environments,[98] while the hexadirectional functional magnetic resonance imaging (fMRI) signal found in the human entorhinal cortex is a global signal that is likely insufficient to study grid distortions.[68] However, interesting recent human studies have started closing this gap and have measured perceptual distortions by using size-varying arenas and asymmetric arenas, similar to those used in animal studies of grid cells.[66,99] An interesting recent study demonstrated that a non-symmetric trapezoid arena can distort human memory of space: after people navigated through a trapezoid arena, they remembered equal distances as shorter when they were in the narrow part of the trapezoid, presumably consistent with the distorted grid pattern.[66] Such efforts are important: we believe that a major future challenge for the field would be to further develop ways to measure distortions of spatial perception and correlate them with distortions of spatial-representation by grid cells—in both physical spaces and abstract spaces.

Finally, we return to our original question, which was posed in the title of this perspective: are grid cells used for navigation? As discussed above and in Box 4, to date there is still no direct causal evidence linking grid cells to navigation. Further, the grid

Box 4. Lesions and inactivations of entorhinal cortex put into question the role of grid cells as a global metric for space for navigation

Many lesion studies have been performed in the hippocampus and entorhinal cortex since the 1960s. Although hippocampal lesions tend to elicit a clear navigational deficit, studies of entorhinal lesions led to more variable behavioral effects on navigation, which were often rather weak. These differences may be influenced by the differences in the completeness of the lesions: the deep location and extended shape of the entorhinal cortex might make it harder to completely lesion it, as compared with the hippocampus. However, another possibility is that the variable and weak behavioral effects of lesions and inactivations of the entorhinal cortex, as compared with the strong effects of lesions and inactivations of the hippocampus, may also indicate that grid cells do not play a major causal role in navigation.

Studies with varied behavioral effects included rats with entorhinal lesions that navigated in a water-maze. Two studies[86,87] found no behavioral effect of entorhinal lesions on navigation, suggesting that the entorhinal cortex does not play a key role in navigation. By contrast, a different study[88] reported a deficit in the rats' ability to find a hidden platform; however, the deficit was milder than that observed in hippocampal-lesioned rats. Kanter et al.[37] showed that depolarization of MEC layer 2 cells, which caused rate remapping in grid cells, caused a navigational deficit in the Morris water maze. A different study demonstrated that entorhinal-lesioned rats had difficulties in water-maze navigation when relying on distal cues but not proximal cues.[89] This result is consistent with other data suggesting that entorhinal lesions impaired the use of distal (but not proximal) cues in a navigational task involving path integration on a platform with holes.[90] Another study also showed that path integration was impaired by MEC lesions in rats, whereby the lesions led to an impaired ability in estimating linear distances based on self-movement information.[91] When trying to dissect the role of grid cells in path integration, Gil et al.[92] selectively knocked out NMDA receptors in the MEC and nearby regions in mice. They demonstrated that grid cells disappeared in these mice while place cells remained intact. Although these mice had difficulties performing path integration, it is difficult to conclude the specific role of grid cells in the behavioral disruption because this manipulation may also have affected other entorhinal cells apart from grid cells and, in addition, the manipulation also affected brain areas outside of the MEC. When rats performed a delayed-match-to-position task on an elevated T-maze, entorhinal-lesioned rats consistently performed at a level comparable with that of unoperated controls—arguing against strong entorhinal involvement in spatial navigation, although they showed a degraded retention of the learning.[93] Overall, while a large body of hippocampal literature showed that hippocampal lesions lead to major deficits in navigation in the water-maze,[94] entorhinal lesions seem to yield milder behavioral effects than hippocampal lesions. However, it is unclear whether these results indicate that the MEC has a lesser role in navigation: these differences between entorhinal and hippocampal lesions may be due to the technical difficulties of achieving complete lesions in the entorhinal cortex.

Mixed behavioral effects were also reported in spatial tasks that were not strictly navigational. For example, when rats performed a spatial alternation task, which involves aspects of navigation but is not strictly a navigational task, rats with bilateral entorhinal lesions performed more poorly than rats without a lesion and rats with a unilateral lesion.[86,95] MEC lesions also affected performance in a spatial object translocation task.[96] In another experiment, targeted lesions of layer 3 of the MEC disrupted spatial working memory but did not show an effect on the consolidation of spatial memory.[87]

Overall, a corpus of data from MEC lesion studies exhibited heterogeneous navigational impairments of variable magnitudes. This heterogeneity may indicate a difficulty in creating complete lesions of the entorhinal cortex, or it may indicate that grid cells are not as central for navigation as originally envisioned. Under the latter possibility, these results suggest that while the MEC may be *involved* in navigation, it is not always *essential* for navigation. This argues against the notion that entorhinal grid cells provide a global metric for space. This is because a global spatial metric is expected to be essential for map-based navigation and its lesion should strongly disrupt navigation behavior, which is in contrast to the experimental findings. Importantly, the mild effects of entorhinal lesions and inactivations on navigation do not argue against our proposed functional hypothesis 1, whereby grid cells provide a local metric for space, because this hypothesis lends a weaker role for grid cells in navigation. Likewise, the lesion results do not argue against our proposed functional hypothesis 3, whereby grid distortions encode salient locations, because in this hypothesis navigation is not centrally dependent on grid cells. However, the lesion and inactivation studies may actually argue against our proposed functional hypothesis 2—that grid cells form a metric for subjective space—because then entorhinal lesions should have shown a more profound impairment in navigation.

distortions reviewed here, which argue against the notion that the grids provide a global metric for space, seem to also argue against the use of grid cells in long-distance navigation. However, our three functional hypotheses are in fact consistent with a role for grid cells in navigation. Hypothesis 1 suggests that grid cells may be used only for local, short-distance navigation. Hypothesis 2 suggests that grid cells may be used for navigation in spaces where different regions have different subjective values. Hypothesis 3 suggests that grid cells may be used as a backbone for navigation by signaling important high-valence locations. On the other hand, hypothesis 3 can also entail the notion that grid cells are not a key component in navigation because they do not represent continuous space itself but rather encode punctate entities within space. The jury is still out on this question.

In summary, here we reviewed recent data showing that grid cells are not a perfect lattice-like global metric for space as they were originally conceived.[1] Our three proposed alternative ideas on the function of grid cells provide testable predictions, and we hope that these ideas and predictions will shape future thinking and research in this field.

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DECLARATION OF INTERESTS

The authors declare no competing interests.

REFERENCES

1. Hafting, T., Fyhn, M., Molden, S., Moser, M.-B., and Moser, E.I. (2005). Microstructure of a spatial map in the entorhinal cortex. Nature *436*, 801–806.
2. Rowland, D.C., Roudi, Y., Moser, M.-B., and Moser, E.I. (2016). Ten years of grid cells. Annu. Rev. Neurosci. *39*, 19–40.
3. Moser, E.I., Moser, M.-B., and McNaughton, B.L. (2017). Spatial representation in the hippocampal formation: a history. Nat. Neurosci. *20*, 1448–1464.
4. Moser, E.I., and Moser, M.-B. (2008). A metric for space. Hippocampus *18*, 1142–1156.
5. Fuhs, M.C., and Touretzky, D.S. (2006). A spin glass model of path integration in rat medial entorhinal cortex. J. Neurosci. *26*, 4266–4276.
6. McNaughton, B.L., Battaglia, F.P., Jensen, O., Moser, E.I., and Moser, M.-B. (2006). Path integration and the neural basis of the 'cognitive map'. Nat. Rev. Neurosci. *7*, 663–678.
7. Geva-Sagiv, M., Las, L., Yovel, Y., and Ulanovsky, N. (2015). Spatial cognition in bats and rats: from sensory acquisition to multiscale maps and navigation. Nat. Rev. Neurosci. *16*, 94–108.
8. O'Keefe, J., and Nadel, L. (1978). The Hippocampus as a Cognitive Map (Oxford University Press).
9. McNaughton, B.L., Barnes, C.A., Gerrard, J.L., Gothard, K., Jung, M.W., Knierim, J.J., Kudrimoti, H., Qin, Y., Skaggs, W.E., Suster, M., and Weaver, K.L. (1996). Deciphering the hippocampal polyglot: the hippocampus as a path integration system. J. Exp. Biol. *199*, 173–185.
10. Mittelstaedt, M.L., and Mittelstaedt, H. (1980). Homing by path integration in a mammal. Naturwissenschaften *67*, 566–567.
11. Barry, C., Hayman, R., Burgess, N., and Jeffery, K.J. (2007). Experience-dependent rescaling of entorhinal grids. Nat. Neurosci. *10*, 682–684.
12. Stensola, H., Stensola, T., Solstad, T., Frøland, K., Moser, M.-B., and Moser, E.I. (2012). The entorhinal grid map is discretized. Nature *492*, 72–78.
13. Fiete, I.R., Burak, Y., and Brookings, T. (2008). What grid cells convey about rat location. J. Neurosci. *28*, 6858–6871.
14. Mathis, A., Herz, A.V., and Stemmler, M.B. (2012). Resolution of nested neuronal representations can be exponential in the number of neurons. Phys. Rev. Lett. *109*, 018103.
15. Stemmler, M., Mathis, A., and Herz, A.V. (2015). Connecting multiple spatial scales to decode the population activity of grid cells. Sci. Adv. *1*, e1500816.
16. Banino, A., Barry, C., Uria, B., Blundell, C., Lillicrap, T., Mirowski, P., Pritzel, A., Chadwick, M.J., Degris, T., Modayil, J., et al. (2018). Vector-based navigation using grid-like representations in artificial agents. Nature *557*, 429–433.
17. Bush, D., Barry, C., Manson, D., and Burgess, N. (2015). Using grid cells for navigation. Neuron *87*, 507–520.
18. Edvardsen, V. (2018). Navigating with distorted grid cells. ALIFE *2018*, 260–267.
19. Derdikman, D., Whitlock, J.R., Tsao, A., Fyhn, M., Hafting, T., Moser, M.-B., and Moser, E.I. (2009). Fragmentation of grid cell maps in a multicompartment environment. Nat. Neurosci. *12*, 1325–1332.
20. Fyhn, M., Hafting, T., Treves, A., Moser, M.-B., and Moser, E.I. (2007). Hippocampal remapping and grid realignment in entorhinal cortex. Nature *446*, 190–194.
21. Krupic, J., Bauza, M., Burton, S., Barry, C., and O'Keefe, J. (2015). Grid cell symmetry is shaped by environmental geometry. Nature *518*, 232–235.
22. Sanguinetti-Scheck, J.I., and Brecht, M. (2020). Home, head direction stability, and grid cell distortion. J. Neurophysiol. *123*, 1392–1406.
23. Boccara, C.N., Nardin, M., Stella, F., O'Neill, J., and Csicsvari, J. (2019). The entorhinal cognitive map is attracted to goals. Science *363*, 1443–1447.
24. Krupic, J., Bauza, M., Burton, S., Lever, C., and O'Keefe, J. (2014). How environment geometry affects grid cell symmetry and what we can learn from it. Philos. Trans. R. Soc. Lond. B Biol. Sci. *369*, 20130188.
25. Krupic, J., Bauza, M., Burton, S., and O'Keefe, J. (2018). Local transformations of the hippocampal cognitive map. Science *359*, 1143–1146.
26. Butler, W.N., Hardcastle, K., and Giocomo, L.M. (2019). Remembered reward locations restructure entorhinal spatial maps. Science *363*, 1447–1452.
27. Ginosar, G., Aljadeff, J., Burak, Y., Sompolinsky, H., Las, L., and Ulanovsky, N. (2021). Locally ordered representation of 3D space in the entorhinal cortex. Nature *596*, 404–409.
28. Grieves, R.M., Jedidi-Ayoub, S., Mishchanchuk, K., Liu, A., Renaudineau, S., Duvelle, É., and Jeffery, K.J. (2021). Irregular distribution of grid cell firing fields in rats exploring a 3D volumetric space. Nat. Neurosci. *24*, 1567–1573.
29. Burak, Y., and Fiete, I. (2006). Do we understand the emergent dynamics of grid cell activity? J. Neurosci. *26*, 9352–9354.
30. Guanella, A., Kiper, D., and Verschure, P. (2007). A model of grid cells based on a twisted torus topology. Int. J. Neural Syst. *17*, 231–240.
31. Samsonovich, A., and McNaughton, B.L. (1997). Path integration and cognitive mapping in a continuous attractor neural network model. J. Neurosci. *17*, 5900–5920.
32. Morris, G., and Derdikman, D. (2023). The chicken and egg problem of grid cells and place cells. Trends Cog. Sci. *27*, 125–138.
33. Trettel, S.G., Trimper, J.B., Hwaun, E., Fiete, I.R., and Colgin, L.L. (2019). Grid cell co-activity patterns during sleep reflect spatial overlap of grid fields during active behaviors. Nat. Neurosci. *22*, 609–617.
34. Almog, N., Tocker, G., Bonnevie, T., Moser, E.I., Moser, M.-B., and Derdikman, D. (2019). During hippocampal inactivation, grid cells maintain synchrony, even when the grid pattern is lost. eLife *8*, e47147.
35. Yoon, K., Buice, M.A., Barry, C., Hayman, R., Burgess, N., and Fiete, I.R. (2013). Specific evidence of low-dimensional continuous attractor dynamics in grid cells. Nat. Neurosci. *16*, 1077–1084.
36. Gardner, R.J., Hermansen, E., Pachitariu, M., Burak, Y., Baas, N.A., Dunn, B.A., Moser, M.-B., and Moser, E.I. (2022). Toroidal topology of population activity in grid cells. Nature *602*, 123–128.
37. Kanter, B.R., Lykken, C.M., Avesar, D., Weible, A., Dickinson, J., Dunn, B., Borgesius, N.Z., Roudi, Y., and Kentros, C.G. (2017). A novel mechanism for the grid-to-place cell transformation revealed by transgenic depolarization of medial entorhinal cortex layer II. Neuron *93*, 1480–1492.
38. Ismakov, R., Barak, O., Jeffery, K., and Derdikman, D. (2017). Grid cells encode local positional information. Curr. Biol. *27*, 2337–2343.

39. Taylor, K.D. (1978). Range of movement and activity of common rats (Rattus norvegicus) on agricultural land. J. Appl. Ecol. *15*, 663–677.

40. Russell, J.C., McMorland, A.J.C., and MacKay, J.W.B. (2010). Exploratory behaviour of colonizing rats in novel environments. Anim. Behav. *79*, 159–164.

41. Calhoun, J.B. (1963). The Ecology and Sociology of the Norway Rat (US Department of Health, Education and Welfare, Public Health Service).

42. Stensola, T., Stensola, H., Moser, M.-B., and Moser, E.I. (2015). Shearing-induced asymmetry in entorhinal grid cells. Nature *518*, 207–212.

43. Solstad, T., Boccara, C.N., Kropff, E., Moser, M.-B., and Moser, E.I. (2008). Representation of geometric borders in the entorhinal cortex. Science *322*, 1865–1868.

44. Hardcastle, K., Ganguli, S., and Giocomo, L.M. (2015). Environmental boundaries as an error correction mechanism for grid cells. Neuron *86*, 827–839.

45. Keinath, A.T., Epstein, R.A., and Balasubramanian, V. (2018). Environmental deformations dynamically shift the grid cell spatial metric. eLife *7*, e38169.

46. Wolbers, T., and Wiener, J.M. (2014). Challenges for identifying the neural mechanisms that support spatial navigation: the impact of spatial scale. Front. Hum. Neurosci. *8*, 571.

47. Carpenter, F., Manson, D., Jeffery, K., Burgess, N., and Barry, C. (2015). Grid cells form a global representation of connected environments. Curr. Biol. *25*, 1176–1182.

48. Hägglund, M., Mørreaunet, M., Moser, M.-B., and Moser, E.I. (2019). Grid-cell distortion along geometric borders. Curr. Biol. *29*, 1047–1054.

49. Barry, C., Ginzberg, L.L., O'Keefe, J., and Burgess, N. (2012). Grid cell firing patterns signal environmental novelty by expansion. Proc. Natl. Acad. Sci. USA *109*, 17687–17692.

50. Wernle, T., Waaga, T., Mørreaunet, M., Treves, A., Moser, M.-B., and Moser, E.I. (2018). Integration of grid maps in merged environments. Nat. Neurosci. *21*, 92–101.

51. Hayman, R.M., Casali, G., Wilson, J.J., and Jeffery, K.J. (2015). Grid cells on steeply sloping terrain: evidence for planar rather than volumetric encoding. Front. Psychol. *6*, 925.

52. Casali, G., Bush, D., and Jeffery, K. (2019). Altered neural odometry in the vertical dimension. Proc. Natl. Acad. Sci. USA *116*, 4631–4636.

53. Steinberg, S. (1976). View of the World from 9th Avenue. Cover of The New Yorker (The Saul Steinberg Foundation/Artists Rights Society).

54. Etienne, A.S., Maurer, R., Berlie, J., Reverdin, B., Rowe, T., Georgakopoulos, J., and Séguinot, V. (1998). Navigation through vector addition. Nature *396*, 161–164.

55. Harootonian, S.K., Wilson, R.C., Hejtmánek, L., Ziskin, E.M., and Ekstrom, A.D. (2020). Path integration in large-scale space and with novel geometries: comparing vector addition and encoding-error models. PLoS Comput. Biol. *16*, e1007489.

56. Loomis, J.M., Klatzky, R.L., Golledge, R.G., and Philbeck, J.W. (1999). Human navigation by path integration. In Wayfinding Behavior: Cognitive Mapping and Other Spatial Processes, R.G. Golledge, ed. (Johns Hopkins University Press), pp. 125–151.

57. Julian, J.B., Keinath, A.T., Frazzetta, G., and Epstein, R.A. (2018). Human entorhinal cortex represents visual space using a boundary-anchored grid. Nat. Neurosci. *21*, 191–194.

58. Cheung, A., Zhang, S., Stricker, C., and Srinivasan, M.V. (2007). Animal navigation: the difficulty of moving in a straight line. Biol. Cybern. *97*, 47–61.

59. Cheung, A., Ball, D., Milford, M., Wyeth, G., and Wiles, J. (2012). Maintaining a cognitive map in darkness: the need to fuse boundary knowledge with path integration. PLoS Comput. Biol. *8*, e1002651.

60. Keinath, A.T., Julian, J.B., Epstein, R.A., and Muzzio, I.A. (2017). Environmental geometry aligns the hippocampal map during spatial reorientation. Curr. Biol. *27*, 309–317.

61. Jeffery, K.J. (2021). How environmental movement constraints shape the neural code for space. Cogn. Process. *22*, 97–104.

62. Wang, M.E., Wann, E.G., Yuan, R.K., Ramos Álvarez, M.M., Stead, S.M., and Muzzio, I.A. (2012). Long-term stabilization of place cell remapping produced by a fearful experience. J. Neurosci. *32*, 15802–15814.

63. Moita, M.A., Rosis, S., Zhou, Y., LeDoux, J.E., and Blair, H.T. (2004). Putting fear in its place: remapping of hippocampal place cells during fear conditioning. J. Neurosci. *24*, 7015–7023.

64. Kropff, E., Carmichael, J.E., Moser, M.-B., and Moser, E.I. (2015). Speed cells in the medial entorhinal cortex. Nature *523*, 419–424.

65. Stachenfeld, K.L., Botvinick, M.M., and Gershman, S.J. (2017). The hippocampus as a predictive map. Nat. Neurosci. *20*, 1643–1653.

66. Bellmund, J.L.S., de Cothi, W., Ruiter, T.A., Nau, M., Barry, C., and Doeller, C.F. (2020). Deforming the metric of cognitive maps distorts memory. Nat. Hum. Behav. *4*, 177–188.

67. Momennejad, I. (2020). Learning structures: predictive representations, replay, and generalization. Curr. Opin. Behav. Sci. *32*, 155–166.

68. Doeller, C.F., Barry, C., and Burgess, N. (2010). Evidence for grid cells in a human memory network. Nature *463*, 657–661.

69. Constantinescu, A.O., O'Reilly, J.X., and Behrens, T.E.J. (2016). Organizing conceptual knowledge in humans with a gridlike code. Science *352*, 1464–1468.

70. Bellmund, J.L.S., Gärdenfors, P., Moser, E.I., and Doeller, C.F. (2018). Navigating cognition: spatial codes for human thinking. Science *362*, eaat6766.

71. Behrens, T.E.J., Muller, T.H., Whittington, J.C.R., Mark, S., Baram, A.B., Stachenfeld, K.L., and Kurth-Nelson, Z. (2018). What is a cognitive map? Organizing knowledge for flexible behavior. Neuron *100*, 490–509.

72. Rueckemann, J.W., Sosa, M., Giocomo, L.M., and Buffalo, E.A. (2021). The grid code for ordered experience. Nat. Rev. Neurosci. *22*, 637–649.

73. Spiers, H.J. (2020). The hippocampal cognitive map: one space or many? Trends Cogn. Sci. *24*, 168–170.

74. Dordek, Y., Soudry, D., Meir, R., and Derdikman, D. (2016). Extracting grid cell characteristics from place cell inputs using non-negative principal component analysis. eLife *5*, e10094.

75. Einstein, A. (1916). Die Grundlage der allgemeinen Relativitätstheorie. Ann. Phys. *354*, 769–822.

76. Kropff, E., and Treves, A. (2008). The emergence of grid cells: intelligent design or just adaptation? Hippocampus *18*, 1256–1269.

77. D'Albis, T., and Kempter, R. (2017). A single-cell spiking model for the origin of grid-cell patterns. PLoS Comput. Biol. *13*, e1005782.

78. Monsalve-Mercado, M.M., and Leibold, C. (2017). Hippocampal spike-timing correlations lead to hexagonal grid fields. Phys. Rev. Lett. *119*, 038101.

79. Weber, S.N., and Sprekeler, H. (2018). Learning place cells, grid cells and invariances with excitatory and inhibitory plasticity. eLife *7*, e34560.

80. Battaglia, F.P., Sutherland, G.R., and McNaughton, B.L. (2004). Local sensory cues and place cell directionality: additional evidence of prospective coding in the hippocampus. J. Neurosci. *24*, 4541–4550.

81. Yartsev, M.M., and Ulanovsky, N. (2013). Representation of three-dimensional space in the hippocampus of flying bats. Science *340*, 367–372.

82. Finkelstein, A., Derdikman, D., Rubin, A., Foerster, J.N., Las, L., and Ulanovsky, N. (2015). Three-dimensional head-direction coding in the bat brain. Nature *517*, 159–164.

83. Grieves, R.M., Jedidi-Ayoub, S., Mishchanchuk, K., Liu, A., Renaudineau, S., and Jeffery, K.J. (2020). The place-cell representation of volumetric space in rats. Nat. Commun. *11*, 789.

84. Angelaki, D.E., Ng, J., Abrego, A.M., Cham, H.X., Asprodini, E.K., Dickman, J.D., and Laurens, J. (2020). A gravity-based three-dimensional compass in the mouse brain. Nat. Commun. *11*, 1855.

85. Laurens, J., Kim, B., Dickman, J.D., and Angelaki, D.E. (2016). Gravity orientation tuning in macaque anterior thalamus. Nat. Neurosci. *19*, 1566–1568.

86. Bannerman, D.M., Yee, B.K., Lemaire, M., Wilbrecht, L., Jarrard, L., Iversen, S.D., Rawlins, J.N., and Good, M.A. (2001). The role of the entorhinal cortex in two forms of spatial learning and memory. Exp. Brain Res. *141*, 281–303.

87. Suh, J., Rivest, A.J., Nakashiba, T., Tominaga, T., and Tonegawa, S. (2011). Entorhinal cortex layer III input to the hippocampus is crucial for temporal association memory. Science *334*, 1415–1420.

88. Schenk, F., and Morris, R.G.M. (1985). Dissociation between components of spatial memory in rats after recovery from the effects of retrohippocampal lesions. Exp. Brain Res. *58*, 11–28.

89. Poitreau, J., Buttet, M., Manrique, C., Poucet, B., Sargolini, F., and Save, E. (2021). Navigation using global or local reference frames in rats with medial and lateral entorhinal cortex lesions. Behav. Brain Res. *413*, 113448.

90. Parron, C., Poucet, B., and Save, E. (2004). Entorhinal cortex lesions impair the use of distal but not proximal landmarks during place navigation in the rat. Behav. Brain Res. *154*, 345–352.

91. Jacob, P.Y., Gordillo-Salas, M., Facchini, J., Poucet, B., Save, E., and Sargolini, F. (2017). Medial entorhinal cortex and medial septum contribute to self-motion-based linear distance estimation. Brain Struct. Funct. *222*, 2727–2742.

92. Gil, M., Ancau, M., Schlesiger, M.I., Neitz, A., Allen, K., De Marco, R.J., and Monyer, H. (2018). Impaired path integration in mice with disrupted grid cell firing. Nat. Neurosci. *21*, 81–91.

93. Marighetto, A., Yee, B.K., and Rawlins, J.N. (1998). The effects of cytotoxic entorhinal lesions and electrolytic medial septal lesions on the acquisition and retention of a spatial working memory task. Exp. Brain Res. *119*, 517–528.

94. Andersen, P., Morris, R.G.M., Amaral, D.G., Bliss, T.V., and O'Keefe, J. (2007). The Hippocampus Book (Oxford University Press).

95. Scheff, S.W., and Cotman, C.W. (1977). Recovery of spontaneous alternation following lesions of the entorhinal cortex in adult rats: possible correlation to axon sprouting. Behav. Biol. *21*, 286–293.

96. Van Cauter, T., Camon, J., Alvernhe, A., Elduayen, C., Sargolini, F., and Save, E. (2013). Distinct roles of medial and lateral entorhinal cortex in spatial cognition. Cereb. Cortex *23*, 451–459.

97. Wood, R.A., Bauza, M., Krupic, J., Burton, S., Delekate, A., Chan, D., and O'Keefe, J. (2018). The honeycomb maze provides a novel test to study hippocampal-dependent spatial navigation. Nature *554*, 102–105.

98. Jacobs, J., Weidemann, C.T., Miller, J.F., Solway, A., Burke, J.F., Wei, X.X., Suthana, N., Sperling, M.R., Sharan, A.D., Fried, I., and Kahana, M.J. (2013). Direct recordings of grid-like neuronal activity in human spatial navigation. Nat. Neurosci. *16*, 1188–1190.

99. Keinath, A.T., Rechnitz, O., Balasubramanian, V., and Epstein, R.A. (2021). Environmental deformations dynamically shift human spatial memory. Hippocampus *31*, 89–101.