

Special Issue: Space, Time and Number

A manifold of spatial maps in the brain

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Two neural systems are known to encode self-location in the brain: Place cells in the hippocampus encode unique locations in unique environments, whereas grid cells, border cells and head-direction cells in the parahippocampal cortex provide a universal metric for mapping positions and directions in all environments. These systems have traditionally been studied in very simple environments; however, natural environments are compartmentalized, nested and variable in time. Recent studies indicate that hippocampal and entorhinal spatial maps reflect this complexity. The maps fragment into interconnected, rapidly changing and tightly coordinated submaps. Plurality, fast dynamics and dynamic grouping are optimal for a brain system thought to exploit large pools of stored information to guide behavior on a second-by-second time frame in the animal's natural habitat.

Spatial maps in the brain

More than 60 years ago, Tolman proposed that animals form internal cognitive maps of their spatial environment [1]. Cognitive maps were thought to represent a mental knowledge base in which information is stored according to its relationship to locations in the environment. Following the discovery of place cells two decades later [2–4], O'Keefe and Nadel hypothesized that the location of the Tolmanian cognitive map of space was in the hippocampus [3]. They proposed that hippocampal cells represent the animal's location in an internal map of the local environment, with entity and event information linked to locations in the map, similar to Tolman's model. The view that animals form internal maps of the spatial environment continues to be supported; however, new research indicates that space is represented in several brain systems, each hosting a variety of representations involving functionally specialized cell types. These systems span wide regions of cortex, including not only the hippocampus but also the adjacent entorhinal cortex [5], pre- and parasubiculum [6], retrosplenial cortex [7,8], parietal cortex [9,10], frontal cortex [10,11] and other areas. The aim of the present review is to highlight how recent experimental work in the hippocampus and entorhinal cortex of the rat brain is revising and refining the concept of spatial maps. We will show that space is represented in these structures by a manifold of rapidly interacting maps generated in conjunction by functionally specific cell types such as place cells and grid cells.

Hippocampal maps

Place cells are hippocampal pyramidal cells that fire when the animal is at specific positions in the environment (Figure 1a; Box 1). Place cells are active both in light and dark, suggesting that a single modality such as vision is not responsible for their positional firing [12]. Different place cells fire at different positions; there is no apparent topography among their firing fields [13,14]. The brain can read out the activity of a local population of place cells to determine the position of the rat in the box. In experiments where activity is recorded from a large number of cells, the position of the rat can be reconstructed with considerable accuracy [13], indicating that the population of place cells forms a spatial map of the environment. This map could be innate, as is suggested by the fact that place cells are present as early as postnatal day 15 (P15) soon after young rats (pups) open their eyes [15,16] (Box 2). The same population of place cells can encode or retrieve different maps in different environments or different configurations of the same environment [17–19]. The process of switching to a different map is called remapping (Box 3) [17].

Place cells do not convey only spatial information. For example, place cells can be shown to encode conjunctions

Glossary

Allocentric coordinates: World-based coordinates. Opposite of egocentric coordinates.

Attractor dynamics: Attractor networks are neural networks with one or more stable states. These stable states are determined by the strengths of the recurrent connections between the individual neurons of the network. When the system is started from a location in state space other than the stable state, it will evolve until it arrives at one of the stable states and will then tend to stay there.

Azimuth: Orientation relative to world coordinates.

Fourier-like transform: A classical mathematical Fourier-transform transforms between the description of a signal in position terms to a description of the signal in spatial-frequency terms. The Fourier transform of a sine wave is a narrow pulse. In two dimensions, this resembles the transformation from grid cells (which are oscillatory sine waves) to place cells (which resemble a narrow pulse in space).

Grid orientation: The orientation of the grid pattern relative to an external reference orientation.

Grid phase: The position of the vertices of a grid cell in the x - y plane.

Grid spacing: The distance between adjacent grid vertices, expressed as the average distance from the central peak to any of the vertices of the inner hexagon in the spatial autocorrelogram.

Path integration: Position is the integral of velocity in time. Therefore one way to determine the current position is to sum up all momentary velocities and directions until the current moment. Path integration is a method to determine one's position from one's own self movement in this manner, without relying on external landmarks.

Reference frame: An external configuration of landmarks and geometry to which neuronal firing coordinates are associated

Theta rhythm: A dominant regular ~ 8 Hz rhythm recorded in local-field potential signals in many brain areas, such as the hippocampus, the entorhinal cortex and the septum. Neuronal firing of individual cells is phase-modulated by this population rhythm. It occurs mostly when the rat is in movement.

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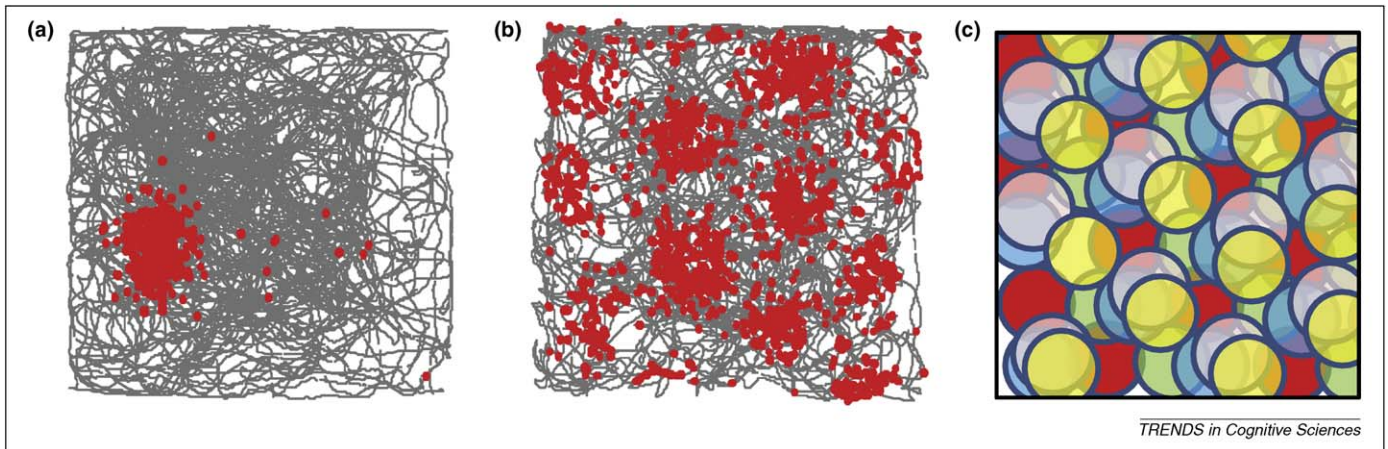


Figure 1. Place cells and grid cells form maps of the environment. (a) Example of a place cell in an open-field box. The trajectory of a rat is marked by a gray line and the positions where the cell fires are marked with a red dot. Most of the spikes of the cell occur when the rat is at a specific position inside the box. (b) Example of a grid cell in an open-field box. Positions of firing of grid cell are marked in red. The positions of firing form a hexagonal grid. (c) The population of grid cells forms a map of the environment. Firing vertices of different grid cells are marked with different colored circles. A specific position can be read out by determining what combination of grid cells fired at that position.

between spatial and olfactory information when this is relevant for the task [20–24]. When rats are rewarded in an odor discrimination task, in which they need to recognize odors that do not match a previously presented one, hippocampal neurons can encode not only position but also odor and training rule [20–22,24]. In some situations, the cells encode time intervals rather than positions, such as when the animal is using time to guide its behavior [22,25]. These examples suggest that place cells can link place to a

variety of features in the environment. The capacity to associate locations with particular experiences could be useful for episodic memory encoding in the hippocampus [19,26–29].

Entorhinal maps

The brain contains another class of position-selective neurons: grid cells. These cells were recently discovered in the medial entorhinal cortex (MEC) [30,31] (Box 1) but are

Box 1. Anatomy of the hippocampal formation

We present here a simplified sketch of the connections between the neocortex, the parahippocampal regions (PHR) and the hippocampal formation (HF) (Figure 1). For a more comprehensive and detailed description see Witter and Amaral [88]. The neocortex is connected to the hippocampus mainly via two pathways through the parahippocampal cortex. One projects through the perirhinal cortex (PER) and the lateral entorhinal cortex (LEC); the other projects through the postrhinal cortex (POR) and the MEC. Cells that carry information about the position of the animal, such as grid cells, head-direction cells, and border cells, are found in MEC but not in LEC [30]. MEC and LEC project to the same regions in the hippocampus, both via direct

projections to each hippocampal subfield and via the indirect trisynaptic circuit through dentate gyrus and CA3. While axons from MEC and LEC to dentate gyrus and CA3 tend to target the same cells, connections to CA1 are split, such that MEC is linked preferentially to the proximal part of CA1, and LEC preferentially to the distal part. This differential connectivity leads to stronger spatial modulation in proximal than distal CA1 [89]. The arrow from CA3 to itself stresses the abundance of recurrent connections within area CA3. Signals are routed back from CA1 to the entorhinal cortex either via direct projections, or via the subiculum (Sub), the presubiculum or the parasubiculum (not shown in Figure 1).

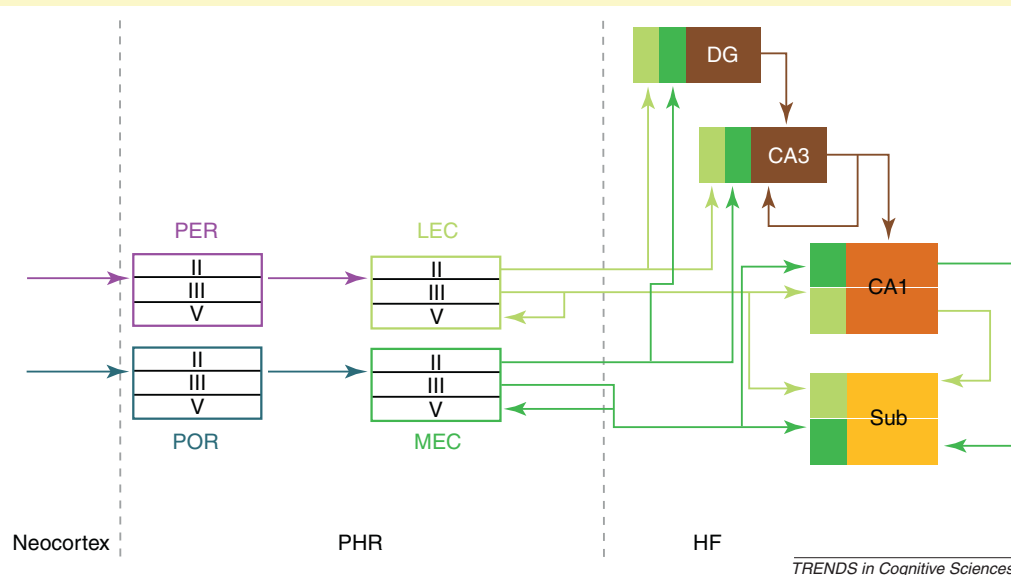


Figure 1. Major anatomical connections in the HF and PHR. Reproduced with permission from [90].

Box 2. Development of spatial maps

Questions about whether spatial representations are innate or rather experience-dependent have a long history, dating back to the Greek philosophers, the British empiricists and Immanuel Kant. Two recent studies have addressed these old questions at the cellular level by asking if rudiments of the brain's spatial representation system are present at the time when rat pups make their first navigational movements at approximately 2.5 weeks of age [15,16]. The pups were implanted with tetrodes on P13, before the eyelids unsealed, and recordings were made a few days later when the animals explored an environment outside the nest for the first few times. Both studies show that a rudimentary brain map of space is present from the first day of outbound movement.

The most rapidly developing component of the brain map is the directional representation in the pre- and parasubiculum. Strong directional tuning was apparent already at P15 and P16 when activity was recorded from these regions for the first time (Figure 1a). The proportion of direction-tuned cells was similar to that of adult rats, and the degree of directional tuning was not different. Young animals exploring an open space for the first time also had place cells. The number of place cells in CA1 was only slightly lower at P16–P18 than at older ages, although the spatial tuning and stability of the cells continued to show some development (Figure 1b). Finally, young rats

also had rudiments of grid cells. The number of grid cells was lower at P16–P19 than in older rats and the periodic structure of the grid fields was weaker than in the adults [15,16]. The number of grid cells, and their spatial periodicity, reached adult levels during the first week or two after the onset of navigation (Figure 1c). Therefore it seems that a rudimentary map of cells with directional and spatial firing correlates is present when animals navigate the outside world for the first time.

Although head-direction cells, place cells and grid cells show slightly different developmental profiles, these cells, or their predecessors, might interact from the outset. The adult-like representation of direction in pre- and parasubiculum in the youngest animals could guide the development of spatial representations in entorhinal cortex and hippocampus, and rudimentary grid cells in entorhinal cortex might provide sufficiently patterned input to the hippocampus to generate place-specific responses in the hippocampal areas. It could also be that in young pups place cells are constructed by a larger proportion of head-direction cells and border cells, and that the contribution of grid cells to the construction of place cells grows with age. The evolution of functional intrinsic connections in MEC during the fourth week [15] could be an essential component for the generation of a combined entorhinal–hippocampal representation of space.

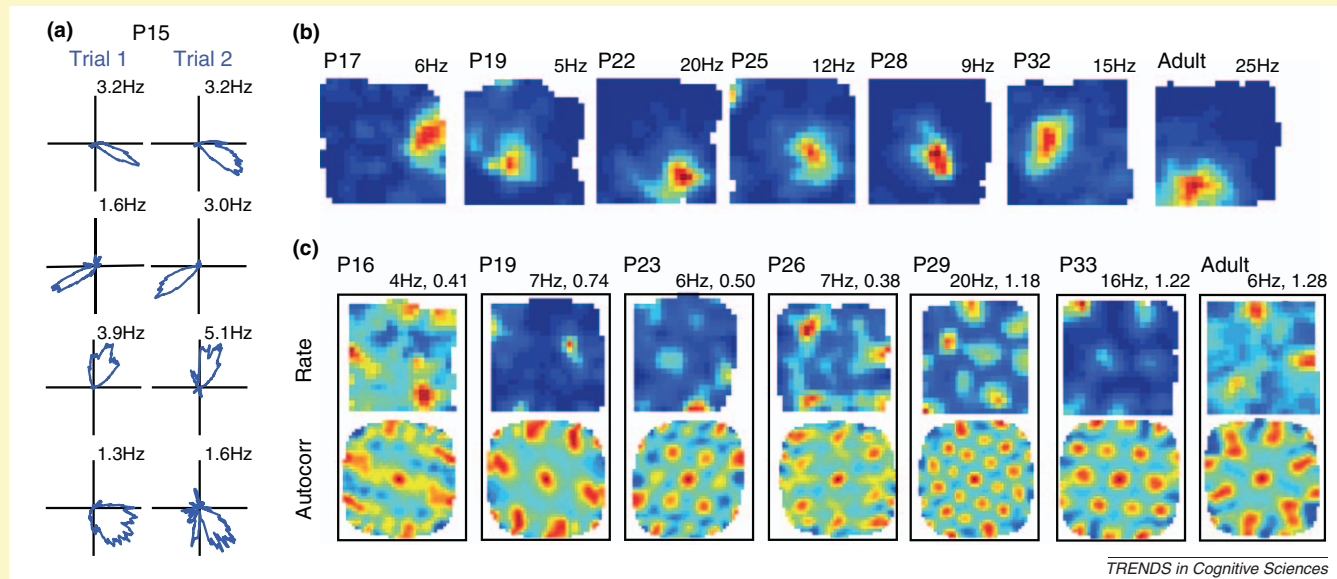


Figure 1. Rudiments of head-direction cells, place cells and grid cells in rat pups. (a) Strong directional tuning of presubiculum cells on P15. Traces show firing rate as a function of head direction on consecutive trials. Peak firing rate is indicated. (b) Firing fields of CA1 place cells between P17 and P35. Rate maps are color coded from blue to red; postnatal day and maximal rate are indicated. (c) Firing fields of entorhinal grid cells from P16 to P34 (top: rate maps, as in (b)); bottom: spatial autocorrelations, color scale from blue ($r = -1$) to red ($r = 1$). Postnatal day, maximal rate and grid scores [15] are indicated. Adapted from [15].

abundant also in the presubiculum and the parasubiculum [6]. Grid cells are characterized by multiple firing locations that, in an open-field arena, collectively form a hexagonal grid over the entire space available to the animal (Figure 1b). Grid cells can differ from each other in their grid spacing, grid phase and grid orientation [30,31]. It is known that the spacing of grid cells increases along the dorsal–ventral axis of the entorhinal cortex [30–32]. Similar to place cells, grid cells can be used to reconstruct the position of the rat in the environment [31] and so function as a map of the animal's position (Figure 1c).

The same parahippocampal brain regions that accommodate grid cells [6] also contain two additional types of cells of potential relevance for spatial mapping: head-direction cells and border cells. Head-direction cells are cells that respond only when the animal is facing a specific

azimuth [33,34]; different head-direction cells are tuned to different allocentric orientations. All directions are represented equally in the cell population. Head-direction cells were discovered in the presubiculum [33,34] but were later found also in MEC [35], as well as in several other brain regions [6,36,37]. Border cells respond when the animal is near a boundary of the local environment [38,39]. Boundary-related cells have been recorded also in the subiculum (Sub), which indirectly links the feedback from CA1 to the MEC, the presubiculum and the parasubiculum (Box 1) [40]. Grid, head-direction, and border cells might have strong innate components, given that rudiments of all three cell types are present when rat pups explore open spaces for the first time between P15 and P20 [15,16] (Box 2). Together, these cell types could be part of a metric navigation system able to map distances (grid cells),

Box 3. Remapping

Changes in the environment cause consistent changes in spatial maps in the hippocampus and the entorhinal cortex. These transformations are referred to as remapping [18].

Three main types of transformations can be considered:

- **Place cell deformations:** Squeezing or stretching the environment can cause a systematic move of the position of the place fields relative to the surrounding boundaries (Figure 1a). Such deformation was reported in 2-D boxes [50] but also along linear tracks [65]. In situations where place cells undergo spatial deformation, grid cells deform too [91].
- **Rate remapping:** In some cases, environmental transformations cause a dramatic change in the distribution of firing rates among place cells without an accompanying change in firing positions (Figure 1b). An example of a manipulation of the environment that induces rate remapping is to change the wall color of the box the rat is in from black to white [92]. When place cells undergo rate remapping, simultaneously recorded grid cells do not change their firing in a consistent way [68].

- **Global (place) remapping:** In some cases, environmental changes can change the position of the place fields in an unpredictable way. For example, when the rat is walking in a box in one room (room A) and then in a similar box in another room (room B), the positions and firing rates of the different place cells are apparently unrelated [93,94] (Figure 1c). Global remapping might also occur in the same location when the geometry or other salient properties of the environment change radically [18,68]. When place cells undergo global remapping, the firing vertices of grid cells undergo changes such as shifts in grid phase, grid orientation or grid scale [68]. Place cells do not preserve distance information during global remapping whereas grid cells do; that is, two place cells which had adjacent place fields in one environment might have very distant place fields in a second environment, whereas two grids with similar spacing will shift together such that the spatial phase relationships between the grid fields are conserved [30,68].

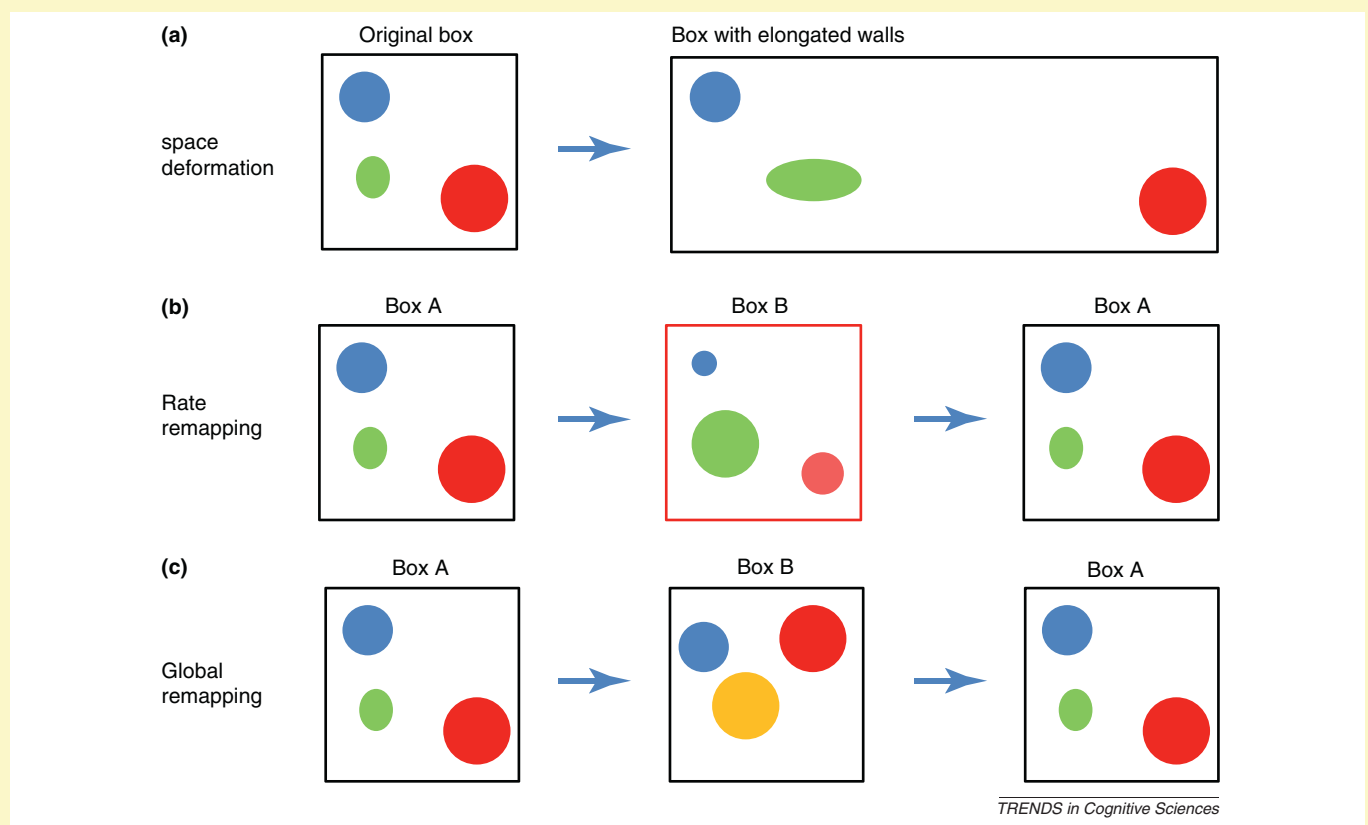


Figure 1. Transformation of place cell maps. (a) Illustration of a place cell deformation. When the box is elongated, different cells change their firing position to correspond to the deformation of the box. For example, the blue cell anchors its firing field to the left wall, the red cell anchors to the right wall, and the green cell elongates itself. (b) Illustration of rate remapping. The different cells in box A continue to fire at a different firing rate in box B but at similar positions. When returning to box A the rates return to the original values. (c) Illustration of global remapping. Some cells fire in one room and not in another; other cells change the position of firing from one room to another in an unpredictable way.

directions (head-direction cells), and vicinity to boundaries (border cells).

Relation between entorhinal and hippocampal maps

What are the relationships between place cells and the various cell types of the entorhinal cortex? Place cells in CA3 are contacted directly by axons from layer II cells in MEC (Box 1). Place cells in CA1 receive direct projections from layer III neurons in MEC. Both layers contain grid cells. Conversely, grid cells in layer V receive output from place cells in CA1. Thus it seems that grid cells and place

cells are only one synapse apart, suggesting that there exists a simple transformation between grid and place representations. Several models have proposed that place cells, by use of a Fourier-like transformation, can emerge as a sum of inputs from many grid cells with different spatial phases and orientations [5,41–48]. Place cells could also depend on input from other entorhinal cell types, such as border cells [38,40,49,50]. Lesions of ventral MEC, where grid fields are larger, lead to a decrease in the size of place fields in the hippocampus [51]. This is consistent with the proposed grid-to-place cell transformation [5,41–48]

because smaller place fields would be expected if inputs were restricted to grid cells with smaller grid fields. The view that place cells emerge from grid cell outputs is challenged by the finding that place cells mature earlier than grid cells during postnatal development of the nervous system [15,16]. The lag does not by itself exclude a role for grid cells in the formation of place cells because rudimentary grid fields can be sufficient to generate place fields (Box 2). However, if place cells can be constructed from a Fourier-like sum of grid cells, then it must also be possible to obtain the inverse transformation: the construction of grid cells as a Fourier-like sum of place cells [52]. Place-to-grid transformation models might not be able to explain the fact that grid structure persists for minutes after inactivation of the dorsal hippocampus (Bonnievie, Fyhn, Hafting, Derdikman, Moser and Moser, 2010, 40th Annual Meeting of the Society for Neuroscience, SfN, abstract 101.4); however, the gradual loss of stability and eventually all structure in grid fields of hippocampus-inactivated rats (*ibid.*) points to a role for hippocampal output in anchoring the grid fields to the local geometry and landmarks of the specific environment [48]. The reciprocal influences between grid cells and place cells will certainly remain a major target of study during the coming years.

The manifold of entorhinal and hippocampal maps

Most environments are more complex than the regular box and linear track environments in which most experiments on place cells and grid cells have been conducted. Environments such as a house with many rooms or a landscape

with barriers such as rivers and fences are hard to describe purely in two-dimensional coordinates. An alternative way to represent such environments is to use a stack of maps where each subdivision of the environment has its own representation.

Several models have proposed that spatial environments are stored as large numbers of independent fragments or reference frames. Worden proposed that mammals store memories of their geographical environment as a collection of fragments each consisting of a small number of landmarks, their geometric relationship, and additional non-geometric properties [53]. In this model, fragments were rotated and pieced together to form a local map during navigation, in the same way that pieces are assembled in a jigsaw puzzle. Worden proposed that this geometric operation took place in the hippocampus and associated structures. The concept of multiple maps was further developed when McNaughton and colleagues introduced continuous attractor networks to understand translocation in hippocampal maps [54,55]. In their model, unique sets of place cells were active at different position coordinates in a virtual two-dimensional space called a chart. When the rat moved to a different position in the environment, its self-movement caused a movement of the place-cell activity bump to a different position in the chart, manifesting a neuronal implementation of path integration. Different spatial environments were associated with different, mutually exclusive charts. Redish and Touretzky provided additional theoretical support for a key role for path integration in the formation of hippocampal maps and

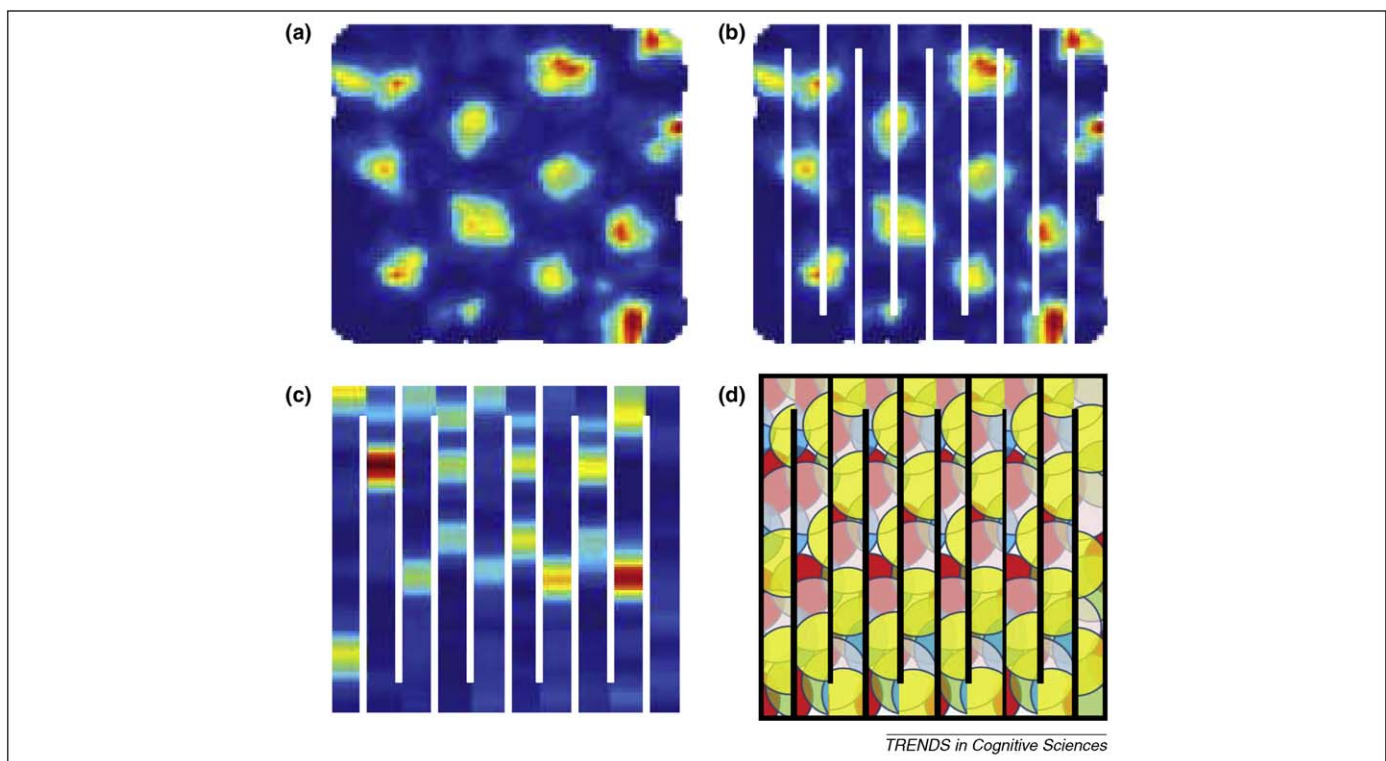


Figure 2. Grid pattern breaks up in a multi-compartment environment. (a) In the open-field box, a grid cell fires at multiple positions creating a hexagonal grid (red – high firing regions, blue – low firing regions). (b) When inserting walls into the same box, it could be hypothesized that the grid fields remain in the same positions. (c) However, what happens is that the grid breaks up, such that a similar map is expressed in every corridor with a similar running direction: every second corridor. (d) The multi-compartment environment is composed of multiple fragmented maps, one for each corridor. Multiple grid cells fire in different locations (color coded in different colors) such that the ensemble of grid cells maps each corridor separately. Remapping occurs when the rat turns from one corridor to the next. This is different from the continuity of the grid map in the open field, as demonstrated in Fig. 1c (adapted from [59]).

proposed that the location of the path integrator involved regions both inside and outside the hippocampus, including the entorhinal cortex [56,57]. Different environments were suggested to be encoded by different spaces of path integrator coordinates reminiscent of the charts of McNaughton and colleagues [54,55].

The proposed multiplicity of the hippocampal-entorhinal map has received experimental verification. First, the presence of independent maps was supported by the fact that hippocampal place cells can undergo complete remapping even after small changes in the location or nature of the spatial environment [17–19]. Second, accumulating evidence indicates that hippocampal and entorhinal maps consist of fragmented submaps instead of a single universal representation. Frank and colleagues observed that entorhinal and hippocampal cells had similar firing patterns when rats were running along parallel corridors of the same complex maze [58]. Based on that, and to test whether entorhinal and hippocampal representations are decomposed into mosaics of connected maps, Derdikman *et al.* [59] recorded grid cells and place cells when rats were running in a square box of ten parallel corridors through which the animal had to run in a zigzag fashion to obtain reward at the ends (Figure 2a). Grid cells did not exhibit periodic two-dimensional firing fields in this hairpin maze. Instead, the grid pattern broke up and similar maps were generated in every corridor where the rat was running in the same direction, creating repeating patterns across the alleys of the maze (Figure 2c). Sharp transitions from one map to the next were observed whenever the rat turned from one corridor into the next. Because barriers could evoke local rate changes also in place cells [18,59] the fragmentation might apply across the grid and place map as a whole.

Are large natural spaces mapped in the same way as in the small confined space of a typical experimental study? Recordings from very large laboratory environments indicate that place cells extend in size from dorsal to ventral hippocampus [60,61]. The increase is finite, with an approximate field diameter of 10 meters at the ventral pole [60]. A similar finite scale expansion has been observed in entorhinal grid cells [32]. Therefore, the largest place fields and grid fields are probably substantially smaller than the largest environments visited by animals in their natural habitat. How are the latter environments then represented? One possibility would be to construct a more widely spaced representation based on interference between inputs from grid cells with different grid frequencies. The frequency of repetition of two grids with different spacing (the beat frequency) is equal to the least common multiplier of their spacing, which is generally larger than the spacing of each individual grid on its own [42,43]. The exploitation of beat frequencies would allow larger spaces to be represented but would not suffice to represent distances such as those covered during migration in animals or intercity travel in humans. A different solution would be to represent large environments as mosaics of smaller maps, breaking up along geometrical borders and landmarks, similar to the fragmentation described for the grid map in the hairpin maze [59]. Representations of relationships between such map fragments might not use the

metrics of grid and place cells but could rather depend on different mechanisms and brain systems.

Dynamic maps

The hippocampus hosts several maps, each anchored to a different reference frame or constellation of landmarks. Gothard and colleagues recorded place cells in an open-field task [62] in which the rat ran from a small start-box to a small end-box in such a way that the relative positions of the start-box, end-box and goal in the arena were changed on every trial. Whereas some place cells seemed to fire anchored to the coordinates of the arena, other place cells changed their position when the goal or the start-/end-boxes were moved, apparently indicating that different cells were anchored to different reference frames (arena, start-box, end-box and goal). Place cells with different reference frames were never observed simultaneously; rather, different frames could be active in the population at different times, that is at any given time, the active map might be aligned with one frame and misaligned with another. Similar results were reproduced in a more recent study, in which a subset of the hippocampal cells were anchored to the reference frame of a local barrier, whereas other cells were locked to the external room frame [63].

Subsequent research has shown that the hippocampus can undergo remapping very rapidly, often within a few seconds or less [64]. In a second study, Gothard and colleagues [65] demonstrated that when the rat was running along a linear track from a start-box to an end-box, which was moved to various distances from the start box, place fields anchored to the start-box at the beginning of the track and to the end-box at the end of the track. When the end-box was moved to a new distance from the start-box, the position of the place fields nearer the end box moved accordingly, whereas the position of the fields near the start box remained constant. This meant that there was a relatively sharp realignment on the middle of the track from the start-box frame to the end-box frame. Derdikman and colleagues [59] demonstrated a similarly rapid transition between entorhinal maps as rats turned from one alley to the next in the hairpin maze (Figure 2d). Such realignments seem to be coherent across the entire population of place cells, grid cells, head-direction cells and border cells, both within each population and between the populations [38,66–69]. Rotations of key landmarks cause coherent rotation of firing fields [38,66,67]. Remapping in place cells is accompanied by coherent changes in the phase and orientation of co-localized grid fields [68] and the orientation of direction fields and border fields [38]. The exact time scale or mechanisms of these global ensemble transitions has not been determined. It is not clear, for example, whether the transitions are all-or-none or pass smoothly through continua of intermediate network states. However, recordings from head-direction cells have shown that local ensembles can reset their firing preferences almost instantaneously, at a time scale of approximately 80 ms [70], and ongoing work in place cells, focusing specifically on the transition moment, indicates that hippocampal ensembles might switch from one map to another within less than a single theta cycle (Jezek, Treves, Moser and Moser, 2010, 40th Annual Meeting of the Society for

Neuroscience, SfN, abstract 101.11). Such fast transitions are often followed by one or several discrete flashbacks to the original representation, before the network settles, but only one state is expressed at a time (*ibid.*).

Remapping can occur at a rapid rate also when there are no external constraints to induce the transition. Hippocampal place cells are known to be extremely variable in their firing rates, more than expected from a Poisson-like distribution of the firing rates [71,72]. The apparent overdispersion in the hippocampus place code could actually result from rapid remapping; for example the spatial map might alternate between a range of representations associated with the same place (Box 3)[73–76]. The fact that overdispersion in a given cell can be predicted from changes in the activity state of other simultaneously recorded cells [77] adds support to this suggestion. It follows from these findings that maps are dynamic entities that are loaded to and from working memory during the course of behavior. Alternations between reference frames could result from intrinsic properties of the network, such as when reference frames change several times per second [76–78], but at longer time scales, switches might also occur in response to more global inputs similar to those thought to be responsible for selective attention [75,79].

Can several maps be active simultaneously?

The rapid time scale of hippocampal remapping raises the question whether hippocampal maps can co-occur completely simultaneously, or are always expressed in rapid succession. Early studies introduced the term partial remapping to characterize cases in which subsets of the place cell population remapped independently of each other [80]. In such cases, several maps, each associated with a different subpopulation of cells, were activated in the same trial. A paradigmatic example was the differential response of hippocampal place cells on trials on a circular track where proximal and distal cues were rotated in different directions [81–84]. A typical observation in such experiments was that one subset of the place cells rotated with the proximal cues in the environment, whereas another subset rotated with the distal cues. Similar to the cases described in the previous section, it could be hypothesized that there was a rapid alternation between a map anchored to the local cues and a map anchored to the distal cues, so the maps were not loaded simultaneously. Counter to this hypothesis, the authors of one of the studies [81] presented a single example in which the two maps were shown to be expressed completely simultaneously: Two different cells clearly belonging to different maps, one rotating with the proximal cues and another rotating with the distal cues, fired at the same time, as was evident from temporal cross-correlations between the two cells. In a conceptually similar set of studies in which rats were subjected to two shock-zones on a rotating arena, one rotating and one stationary, some place cells were anchored to the stationary shock-zone, whereas others were anchored to the rotating shock-zone [74,76]. Also in this case it is conceivable that the two maps, anchored to the two shock-zones, were never loaded simultaneously. However, the researchers reported a group of cells that was anchored to both shock-zones at once, firing only when the rat was at the same time at a certain position relative to both the

Box 4. Questions for future research

- What is the nature of the transformation between place cells and grid cells?
- If environments are mapped by fragmented representations, where are the fragments linked and how?
- Can multiple maps be expressed simultaneously? If not, can different maps alternate and if so, at what frequencies and under which conditions?
- How are very large environments represented?
- How do neuronal oscillations and synchrony contribute to retrieval of distributed maps in the hippocampus?
- Which components of spatial maps in the brain are genetically specified, and how are maps shaped by experience?
- What are the cellular and network mechanisms responsible for transitions between spatial maps?
- Do humans represent space in ways different from rodents?

stationary shock-zone and a the rotating shock-zone [76]. The presence of such cells would argue against temporal segmentation of stationary and rotating maps; however it should be noted that these cells appeared mostly near the centre of the disk where the difference between the reference frames was small. It therefore remains to be determined if discrete reference frames can be loaded simultaneously, or if conjunctions are always expressed by alternating expression of discrete representations.

Concluding remarks

Studies of place cells and grid cells have led to the insight that there is more than one spatial map in the brain. These studies are based almost exclusively on rats; however, the probable presence of place cells [85] and grid cells [86] in humans as well as phylogenetically distant species, such as echolocating bats [87] (Yartsev, Witter and Ulanovsky, 2010, 40th Annual Meeting of the Society for Neuroscience, SfN, abstract 203.15), suggests that the mechanisms could be more general.

The rat studies indicate that the brain hosts multiple maps representing different subsets of the environment at different times, in different brain regions, and at different scales. Spatial maps in the hippocampus and entorhinal cortex seem to be much more dynamic than previously appreciated. A map in these brain regions can be retrieved within a few hundred milliseconds and replaced soon after if a different map is relevant to the goal of the behavior. A major objective for the next few years will be to determine how the plurality and variety of maps interacts and how different cell types and components of the circuit contribute to the rapid dynamics of spatial mapping (Box 4). This will hopefully lead us to a comprehensive theory about how the brain is used for navigation and for representing the space around us.

Acknowledgements

We thank Laura Colgin for reading and commenting on the manuscript, and Menno Witter for advice about hippocampal anatomy.

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