

# Making our way through the world: Towards a functional understanding of the brain's spatial circuits

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## Abstract

Many animals make return trips from a home base to gather food and supplies, mate, or survive the seasons. In a world of unreliable and ambiguous cues, localizing within familiar environments and mapping new environments – functions critical for making successful return trips – is a complex problem requiring memory, integration, and inference. We review some key features of the mammalian brain's navigation system and its computational challenges, as well as the task neuroscientists face in understanding how its components interact and function. We argue that synthesizing the wide body of neural phenomenology requires formalization of the navigation problem as one of sequential probabilistic inference, as done in the robotics field of simultaneous localization and mapping (SLAM).

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## Keywords

Navigation, Hippocampus, Entorhinal cortex, Computational modelling, Simultaneous localization and mapping, Probabilistic inference.

Keeping track of one's location in space while navigating through it is a high-level cognitive problem handled by areas including the entorhinal cortex and hippocampus, which sit atop the mammalian brain hierarchy. Location coordinates are not simple sensory variables – they are estimated by combining a number of somewhat reliable cues, including self-motion and various external sensory landmarks in visual, tactile, auditory and olfactory space. For accurate localization, these partially informative cues must be integrated over time and fused together according to their reliability, in the context of learned maps of the environment. Navigation further requires goal selection and path planning, which in turn involve balancing exploration of new parts of the world with

exploitation of known venues. Thus, navigation is a wonderfully rich problem domain for understanding how the brain solves hard problems involving time-varying inputs, multisensory fusion, integration, memory, ongoing inference, decision making and optimization. In this review, we will focus on the problems of localization and mapping.

Various neuron populations in the mammalian brain have been discovered to encode spatial variables. However, our understanding of these representations is piecemeal. We propose that models that recognize the localization problem as one of real-time probabilistic inference, and generate neural solutions to challenging versions of this problem, will recapitulate and help to build a functional synthesis of the phenomenology of the brain's navigational circuits.

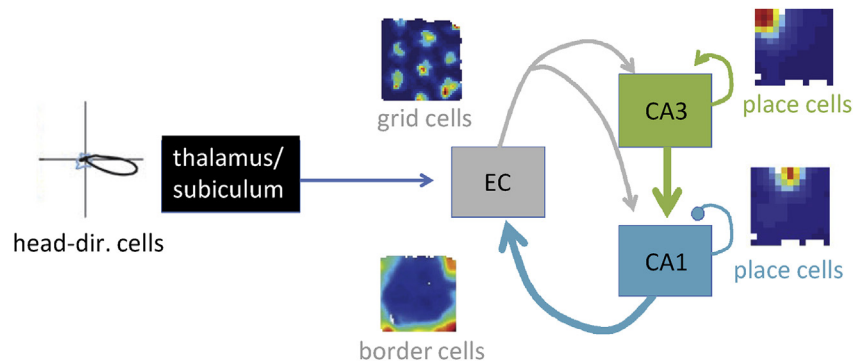
## Neural representations of spatial variables

One way to begin to understand how the brain computes is to characterize how it represents key variables. The classic approach to characterizing neural representations has been to construct tuning curves: the average response of a neuron to different values of an independent variable. Tuning curve-based characterizations of spatially responsive cells are not sufficient for understanding how the brain performs spatial computations, as discussed later. However, they have laid the essential groundwork for understanding how spatial computations are performed in the brain by showing where and how spatial variables are represented.

## Discovery of spatial tuning

The tuning curve approach has led to the discovery of cells involved in computing a broad assortment of spatial and navigation-related quantities ([Figure 1](#)): A place cell in the hippocampus fires whenever the animal is in a specific spatial location [\[2\]](#); a grid cell in medial entorhinal cortex (MEC) fires at multiple locations arranged on a regular triangular grid [\[3\]](#); a head direction cell in the postsubiculum, retrosplenial cortex, entorhinal cortex or thalamus [\[4–6\]](#) fires whenever the animal's head is pointing in a given direction (relative to some external reference); border [\[1,7\]](#) and boundary vector cells [\[8\]](#) in the entorhinal cortex and subiculum respond at or parallel to environment boundaries; speed cells in the medial entorhinal cortex [\[9\]](#) are sensitive to the animal's running speed; and landmark cells in lateral entorhinal cortex respond to local objects in a space based on their identity and the local reference frame [\[10,11\]](#).

Figure 1



Neural representations for spatial navigation. Summary of notable types of neural tuning for navigation-related variables; the brain areas where they appear; and major anatomical connections between areas. Head direction and border cell data from Ref. [1] (Reprinted with permission from AAAS). Grid cell data from Boccara, C.N., Sargolini, F., Thoresen, V.H., Solstad, T., Witter, M.P., Moser, E.I., Moser, M.-B. Grid cells in pre- and parasubiculum, *Nat Neurosci* 13 (8), 987–94 (2010) (Reprinted by permission from Macmillan Publishers Ltd). Place cell data from Colgin, L.L., Leutgeb, S., Jezeq, K., Leutgeb, J.K., Moser, E.I., McNaughton, B.L., Moser, M.-B. Attractor-map versus autoassociation based attractor dynamics in the hippocampal network, *J Neurophysiology* 104 (1), 35–50 (2010) (Reprinted with permission from APS).

### Mechanisms of spatial tuning in individual neural populations

The discoveries of neural tuning motivated the development of circuit models capable of generating such representations. Continuous attractor models of head direction cells [12], place cells [13,14] and grid cells [15,16] show how forgetful neurons could collectively represent and store spatial variables while integrating motion inputs to update these representations. These models, which were constructed to recapitulate individual tuning curves, have met with substantial recent successes in tests of their circuit-level predictions about cell–cell relationships constrained by internal dynamics rather than external inputs [5,6,17–19].

### Gaps between mechanistic models and observed tuning in homogeneous populations

We may arguably have a first-order understanding of the mechanisms of spatial tuning in groups of cells with homogeneous (but spatially offset) tuning curves, through hand-designed network models. However, even within this framework, there are notable gaps between our understanding and observed phenomena.

Examples of such gaps include understanding how multiple subnetworks of grid cells with different spatial periods [20,21] could emerge and modularize through plasticity and development; what drives the consistent skew in the grid cell response across familiar square enclosures [22] and the distortion of grid tuning in non-square environments [23,24]; whether periodic [16,25] or aperiodic attractor networks [15,16] or some combination of feedforward/oscillatory and attractor dynamics [26] underlies the grid cell response. Filling these gaps requires an elaboration of existing types of models, coupled with experimental study and data analysis for testing the elaborated models.

### More complex realities and questions

The realities of representation and requirements for computation in the navigation circuit are more complex than models that generate homogeneous tuning curves capture. Further, the description of neurons based on spatial tuning is a static view that neglects temporally changing responses, versions of which are required for navigational computations and are richly observed in spatial circuits.

### Sparse location tuning

Only a fraction of cells across navigation-related circuits display clearly discernible tuning to a navigation-relevant variable [27]. Even among spatially tuned cells, strong location specificity seems sparse [28]: high spatial information appears to reside in a small subset of neurons across environments [29]. From a coding-theoretic perspective, which would support maximally whitened representations with equalized information-sharing of the encoded variable across neurons, this is a puzzling result – why not dispense with the cells that, across environments, fail to exhibit strong location specificity? Are the less discriminating cells sidelined in spatial computations or essential to some other aspect of the computation? Mechanistically, are the low- and high-spatial information cells part of the same recurrent network or uncoupled populations?

### Mixed (conjunctive) representations and remapping

The navigation circuits contain various examples of mixed selectivity or conjunctive tuning: when a cell is tuned to one navigation-related variable, it is frequently jointly tuned to another. On the most basic level, the joint representation of grid cells (or place cells) to both spatial coordinates is a form of conjunctive coding. Cell in layers III–V of medial entorhinal cortex exhibit

conjunctive tuning to location and head direction [30], while other cells in these and more superficial layers are now also found to be conjunctively tuned to speed and other variables [23,89].

In attractor models of grid cells, conjunctive tuning to location, head direction and speed arises naturally from the requirement that the activity bump be updated by velocity input, but such models are not sufficient to explain its strength: Model cells can be tuned to exhibit conjunctive space-velocity tuning or nearly pure spatial tuning, without compromising their velocity-integration functionality [16,37]. Given such mechanism-level neutrality, it is interesting to understand why the neural circuit contains both grid cells and conjunctive grid-velocity cells (and why place cells in open fields in rats are not as conjunctive for these variables [31] but do exhibit clear direction tuning in Egyptian fruit bats, which use directed sensory systems for echolocation [34]).

Rate remapping of place cells in altered environmental contexts (e.g. by changing the color of the walls) [90] can be viewed as a conjunctive code for environmental context and location. Global or total remapping [58] is a form of conjunctive coding for environment identity and location. Joint codes are costly if the tuning for each variable is narrow (this is not the case for location coding conjunctive with speed since the latter is broadly tuned; but for joint coding of  $K$  coded variables with narrow tuning along each variable, the number of neurons required grows as  $\sim M^K$ , compared with  $\sim MK$  if the  $K$  variables were encoded independently by separate populations or jointly coded by a product of broadly-tuned responses along each variable) [35]. Joint codes for multiple variables can allow for easy adjustment of which variable is being read-out from the population [36], with little cost if tuning is broad. But it remains to be seen why the spatial circuit exhibits joint narrow tuning (e.g. head direction and location in conjunctive grid cells or location and environment identity in place cells).

### Path integration-based accounts of localization and spatial tuning are inadequate

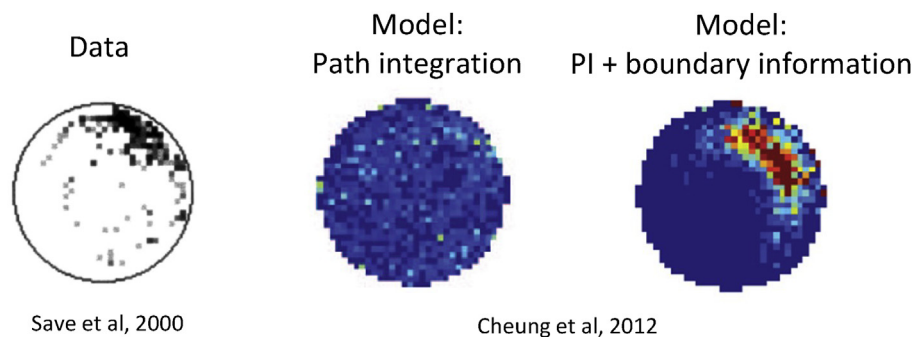
While animals are known to integrate motion cues to update their location estimates [41–43], integration alone is an invariable strategy for localization: Errors in motion estimate are unavoidable, thus the integrated location estimate will degrade with accumulating effect, resulting in washed-out tuning curves and a disoriented animal [44–46] (Figure 2).

### Inter-areal interactions

Spatial tuning in one cell type might arise from that in another, as shown in models of place tuning from boundary vector cells [47], grid tuning from place cells [52,53], and place tuning from grid cells [48,49] (however, the persistence of place tuning after grid cell lesions [50] suggests that grid cell input is not the sole determinant of place cell firing, consistent with the long-held view that hippocampal activity is informed by multiple inputs [41,51] and is a high-level associative memory area). These models operate on the level of tuning curves, and so do not provide a time-resolved view of how dynamical spatial inferences may be performed iteratively by temporally regular feedback interactions between these areas. Contrary to what is suggested in some of the above models, we believe it is unlikely that the brain simply recodes information from one area, and re-represents it in a different form in the next. Rather, we expect that the different spatially tuned cells are pooling information from different (perhaps overlapping sets of) sources and performing distinct spatial computations.

It has been proposed that interactions between place cells and grid cells might underlie intrinsic error-correcting mechanisms between grid and place cells to correct drifting estimates of location from path integration [39,40], while extrinsically-driven border and place cells activation could do the same based on external spatial cues, using the same architecture as for the intrinsic error-correcting mechanism [38,39,54,55] (using the same

Figure 2



*Stability of place fields in darkness.* Left: Place cell of example neuron in rat hippocampus after the animal spent 32–48 min in darkness in a circular enclosure. Olfactory cues were removed by regular wiping of the floor. Adapted from Figure 3, Unit #1 of [65] (Reprinted with permission by John Wiley & Sons, Inc). Middle and Right: Predicted place field after 32–40 min in darkness if animal is only using path integration or also performing corrective resets at the boundary. Adapted from Figure 4 of [44].

architecture as internal error-correcting mechanisms [39]), a possibility validated through the analysis of neural data [56,57].

### Beyond static tuning: dynamical phenomena

Spatial representations in the brain can unfold, evolve, or change on fast time-scales: The flickering between past and present environmental representations when a space is suddenly changed [61]; the acquisition of directional tuning by place cells in 1D spaces and during directional tasks compared to their relatively directionally insensitive responses during random foraging in 2D spaces [32,33]; the turnover, over days, in the ensemble of place cells that represent a familiar environment [59]; the selectivity of some landmark cells to the old location of an object after it is moved [60]; the phenomena of replay and preplay of place field sequences [62,63]; and the role of replay in spatial learning and planning [63,64]. Our understanding of how these dynamical phenomena are generated, and how they fit together to subserve navigational computations, is poor.

### From “how?” to “why?”

Piecewise mechanistic models can explain “how” a circuit can work, but usually have little to say about “why” certain representations and architectures are selected, as in several of the questions raised above. To answer some of the “why” questions, and arrive at a better understanding and synthesis of the diverse phenomenology in the brain's navigation circuits, we suggest that a more comprehensive, function-driven approach to the hard problems of navigation is necessary.

### The computational problem of navigation: a function-centric approach

Here we advocate a function-first approach: Define the key hard computational problems associated with navigation, build a neurally plausible circuit model that can solve these problems, then study the correspondences between the model's tuning and dynamics and the neural phenomenology.

Let us focus first on the problem of localization, which involves two sub-problems. Even in a known environment, external spatial cues are often ambiguous and can be associated with several locations (e.g. multiple doors in a hallway, two similar-looking copses in a forest, or an extended boundary), and thus do not offer a unique correction for drifting motion-based estimators. Second, external cues (even ambiguous ones) are only of use if one has a map for the environment — that is, features of the environment have been endowed with spatial meaning and relationships which can be used in localization. Assigning a map to a space involves obtaining coordinates for its features, which assumes a solution to the localization problem — this is a chicken-or-egg problem.

Such problems are well-characterized in robotics, under the rubric of Simultaneous Localization and Mapping, or SLAM. In a typical example, a robot on wheels drives through an unknown environment, while the task is to infer both its own trajectory and a map of the environment from noisy wheel rotation estimates and laser-range measurements of distance from landmarks (Figure 3). Path integration is insufficient for the task, but sequential probabilistic inference algorithms can recover an accurate map, bootstrapping between noisy location estimates and noisy landmark estimates by inferring and jointly refining the probabilities of both [66].

Probabilistic SLAM algorithms update joint probability distributions over both self-location and external landmarks. With three spatial variables — location and orientation — and  $K$  landmarks, this requires the representation and updating of a  $(3 + K)$ -dimensional joint distribution (with  $M$  states per variable, the joint representation would consist of  $M^{(3 + K)}$  states), seemingly a complex demand for neural circuits.

In addition, extensions of robotic SLAM algorithms to goal selection and planning involve incorporating the well-characterized computational domains of reinforcement-based decision making and optimization to find the shortest path between locations.

### Do brains implement sophisticated spatial inference algorithms?

Wild rats live in complicated underground burrows with few global allothetic cues [67]. They are able to navigate over long distances within these burrows and in new places [68], which suggests that their spatial circuits can support navigation in familiar and novel environments.

In addition, a recent computational study shows that many grid cell phenomena including partial rescaling in resized environments [69] and grid cell fragmentation in hairpin mazes [70] can be explained by interpreting grid cell responses as reflecting the outcome of probabilistic SLAM computations [71], although the work does not provide a neural model of such computations.

Finally, several neural correlates of goal planning have been discovered in the spatial circuits: In flying bats, a subpopulation of hippocampal CA1 neurons exhibits angular tuning to the goal direction [72], while neurons in hippocampal area CA3 replay and preplay place field sequences when rats are either sleeping or stopping during a run [62], a phenomenon that has been linked to trajectory planning [63]. Recent models [73] suggest a functional explanation of preplay similar to reinforcement-based views of planning in the robotic literature.

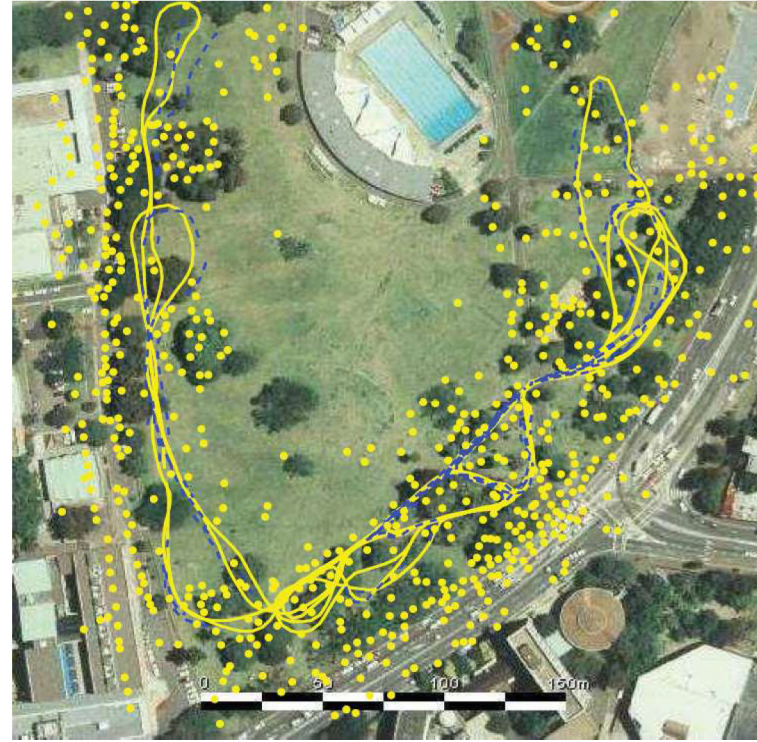


Figure 3

## Pure path integration



## Probabilistic SLAM



*Robotic solutions for robust navigation. Left:* Estimation of a robot trajectory using path integration: accumulation of errors causes large deviations. *Right:* Joint inference of trajectory and landmark locations in the same environment by a probabilistic Simultaneous Localization and Mapping (SLAM) algorithm. Adapted from Figure 1 of Montemerlo M., Thrun S., Koller D., Wegbreit, B. FastSLAM 2.0: An improved particle filtering algorithm for simultaneous localization and mapping that provably converges. In *Proceedings of the Sixteenth International Joint Conference on Artificial Intelligence (IJCAI)*, Acapulco, Mexico, 2003. IJCAI.

How does the diverse phenomenology observed in the brain's spatial circuits support its ability to solve problems similar to those addressed by probabilistic SLAM algorithms?

### Tools for a functional approach

As we have discussed, mechanistic circuit models built by hand-wiring a network to reproduce specific observed spatial tuning curves does not answer various “why” questions. It also does not necessarily provide a generic or especially robust solution. Finally, for sufficiently difficult problems it may not be feasible to find a mechanism by hand. How can we transcend these limitations?

Hand-wiring a solution shows that there is a solution to a computational problem, but a network organized through unsupervised or supervised learning likely represents a more generic and possibly more robust solution. Such models in the domain of navigation show how the head direction and grid cell circuits could form through structured input and spike time-dependent plasticity (STDP) [12,15,55], how place cells could wire up to grid cells with the right phase through associative learning [39], and (potentially relevant to hippocampal sequences though modeled in other systems) how sequences could form through STDP or other rules [74–76].

For more complex problems like the high-level functions of visual object recognition and speech recognition, an approach using supervised learning in multilayered feedforward networks (fueled by refinements in machine learning strategies [77], gains in computing power for supervised learning in neural networks, and plenty of labeled image data) has been successful in recapitulating high-level sensory representations in the visual [78–80] and auditory [81] pathways.

The SLAM problem represents the opportunity to understand, using supervised and reinforcement learning in recurrent networks as tools, how a high-level cognitive neural network that involves memory, integration and the fusion of noisy and ambiguous multisensory cues can take lower-level time-varying inputs and perform ongoing inference about a set of (latent) low-dimensional variables, and make plans and decisions about future trajectories. One can connect the representations that emerge from neural models of these complex computations to the rich phenomenology of the brain's spatial navigation circuit. Recent unpublished work by the authors has begun to exploit this opportunity [82].

On the experimental side, it will be important to study animal behavior and neural activity during demanding spatial tasks, in environments that contain ambiguous

external cues, involve (possibly tuneable levels of) sensory noise, at the same time challenging the animal to distinguish between multiple familiar environments or to map novel environments.

Finally, there is mounting evidence that the hippocampus is involved in navigation not just through space, but through events in time and other abstract conceptual spaces [83–87]. Informed by these experimental findings and longstanding hypotheses on the broader role of the hippocampus beyond spatial computations [83], we hypothesize that the hippocampus and associated areas comprise a general sequential inferential circuit for dealing with abstract tasks and spaces, and it stores and uses episodic memory including spatial memory to assist in inference given incomplete information.

For some of the reasons discussed so far, the “cognitive map” [41,51] — a beautiful and detailed function-centered hypothesis on how animals navigate that has long served as a conceptual framework and inspired debates about whether the hippocampus contains a cognitive map — must be recast to be more general, and simultaneously, more specific, for continued modern resonance. It must be expanded to include the role of the hippocampus in computing with non-spatial variables, while being made more computationally specific and precise so that it can generate concrete predictions about neural tuning and dynamics. Recasting navigation as a problem of sequential spatial inference with ambiguous cues is a way to make links to the more general framework of hippocampus as performing inference.

Navigation is a behavior central to almost all animal species, and certainly those with a fixed home base [41,88]. Yet it involves highly sophisticated cognitive computations involving memory, multi-sensory fusion with noisy inputs, and continuous time-varying inference. As we have argued in this review, a functional approach centered on identifying, modeling, and doing experiments to explore how the brain can solve the hard problems associated with spatial inference can make sense of the rich phenomenology that has been collected over the last decades. It has the potential for not only describing how, but also explaining why, the brain chooses the observed spatial representations.

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- \* of special interest
- \*\* of outstanding interest



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