

Hippocampus: Mapping or memory?

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The identification of ‘place cells’ in the hippocampus has suggested a special role for this brain structure in spatial mapping, but other studies have indicated a more general role in memory. New findings on place cells point the way towards a reconciliation of the mapping and memory views.

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One of the most striking physiological properties of the hippocampus is the presence of what are referred to as ‘place cells’. These are pyramidal cells that fire when an animal is in a particular location in its environment. They are fascinating. As a rat forages for food or performs a well-learned routine that takes it through the environment, these neurons burst with spike activity, sounding — when amplified recordings are heard through speakers — like a geiger counter detecting a mysterious radiation from a particular place on the floor. But what is it that place cells ‘detect’? The immediate intuition was that these cells signal occupancy of a coordinate locus in a cognitive map, a Cartesian representation of the environment contained within the hippocampus [1,2]. But several recent studies, in particular new evidence [3] that place cells are influenced by the recent history and ongoing behavior of the animal, suggest that the cognitive mapping view is too simple.

While the phenomenon of place cells is not disputed, the notion that the hippocampus is dedicated to creating spatial maps is controversial. One major problem for the generality of the spatial mapping view is that damage to the hippocampus in humans results in global amnesia, an impairment in memory for facts and personal experiences including both spatial and non-spatial information [4,5]. In animals, hippocampal damage produces severe deficits in spatial learning and memory. There are, however, also reports of deficits in non-spatial learning and memory following hippocampal damage, most recently providing compelling evidence that the hippocampus is involved in learning relations between distinct experiences involving non-spatial stimuli [6]. Furthermore, across a variety of learning paradigms hippocampal cells have been found to fire in association with with non-spatial stimuli and acquired behaviors [7–9].

Moving from map to memory

It is a big leap to go from the representation of a ‘place’ to an organized mapping of space. Place-specific activity could simply reflect the recognition of a combination of sensory and behavioral features that have previously been experienced together at a particular location. To demonstrate the existence of a full map, one must show the hippocampus contains a complete representation of geometric parameters (angle and distance information) or a systematic topography of connected place representations. But there is no evidence that the hippocampus represents angles or distances, and place representations are not bound to one another in any systematic organization. So, is there another plausible interpretation of place representations in the hippocampus, something more consistent with a general role in memory?

Recent studies on place cells have begun to offer a reconciliation between the mapping and memory views. Early on, the cognitive map theory was strongly supported by reports that place cells provide faithful indicators of an animal’s position, regardless of its orientation in space or ongoing behavior. But later discovered characteristics of place cells that seem contrary to this characterization have forced researchers to alter the notion of a map in the direction of global memory representation. Here I shall consider three of the more prominently discussed findings (for a full review see [10]).

First, it was found that place cells can be ‘directional’, that is, fire only when the animal is moving in one direction through space [11]. This occurs in situations where the animal’s direction of movement is behaviorally significant with regard to the ongoing testing experience, such as when a rat runs to or from rewarded places in a maze. The finding of directionality was initially interpreted as a ‘vector’ quality of spatial representation, and little consideration was given to the problem that directional place cells do not reliably signal the occurrence of the animal in a particular place.

Second, more recently it was observed that place cells do not necessarily fire in relation to the consistent constellation of spatial cues that define an environment. Instead, their spatially selective activity is bound to individual important targets in space, such as a starting box or goal, that are moved to different places around the environment [12]. This observation obviously refutes the notion that the hippocampus contains a representation of the fixed environmental structure. But rather than abandoning the spatial mapping view, its discoverers concluded that the

hippocampus creates multiple spatial maps based on different 'reference frames', in the case of this study, separate maps referred to a starting point or goal. By extension, in an environment with many moveable objects of interest, there presumably could be a very large number of maps for the same space.

Third, Frank *et al.* [3] have now described yet another revision of the mapping hypothesis. In their protocol, rats ran through 'W' and 'U' shaped tracks located within the same recording room. The animals traversed the mazes from end to end in both directions, allowing comparison of firing properties of cells as the animals made similar runs and turns in different directions and at different locations in the environment. Also, in the W-maze the firing pattern of the cells that fired when the rat was in the middle arm could be compared under conditions where the rat came from, or was heading towards, different side arms.

Frank *et al.* [3] reported two new properties of place cells. First, in the middle arm of the W-maze, some cells of the hippocampus and adjacent entorhinal cortex fired differentially, depending on the preceding or forthcoming arm, even when the location and direction of movement was identical. Second, in both mazes some cells fired similarly when the rat was at the same segment (for example halfway) or executing the same behavior (such as turning left) during journeys that occurred in completely different areas of the environment. The combination of these firing patterns were interpreted as evidence for hippocampal coding of 'trajectories', a term that suggests the hippocampus performs mathematical computations in a domain usually associated with rocket science.

Note how the researchers who performed each of the studies described above cling to a geometrical terminology and conceptualization of these cells. Yet there still is no direct evidence that hippocampal cells systematically encode the metrics necessary for straightforward geometrical computations of vectors, maps to reference frames, or trajectories. Instead, the emerging evidence favors an alternative view that hippocampal networks encode journeys through space as memory episodes defined by sequences of events and the locations where they occur [10]. This notion can explain each of the phenomena just outlined. Place cells appear to be 'directional' when movements in different directions concur with episodes that have distinct behavioral significance, such as the distinction between running to a goal versus returning to start another trial. Similarly, from this perspective place cells appear to be governed by different 'reference frames' when behavioral episodes are defined by a sequence of actions and locations centered on objects independently of their positions within the overall spatial environment. And finally, from this view a 'trajectory' can be straightforwardly characterized as the representation of a journey

defined by a sequence of locations and behaviors recorded in memory.

Our own recent findings [13] support and extend this view. We trained rats to perform a spatial alternation task, in which on each trial a rat runs through the stem of a T-shaped maze and then alternately selects the left and right choice arms to obtain rewards. The task requires the rat to distinguish between left-turn and right-turn trials, and to remember the last trial in order to make the alternative choice on the next trial. Replicating the basic phenomenon of place cells, we found neurons that fired associated with locations throughout the maze. Our new finding was that most cells that fired when the rat was on the stem of the T, the area of the maze traversed on all trials, were predominantly active only on left-turn or on right-turn trials. Small differences in the animal's location on the stem, head direction or speed of movement did not account for the trial-type specific firing. Thus, it appears that separate networks of hippocampal neurons distinctly encode elements of the sequences of behaviors and places that compose separate left-turn episodes and right turn episodes.

Memory space, not spatial memory

Notably, in both the Frank *et al.* study [3] and in our own [13], whereas some cells fired in association with the combination of event and place specific to a particular type of trial, other cells appeared to encode behaviors or places that reflect common aspects of the distinct episodes. We have recently suggested [9] that this combination of episode-specific codings and the representation of common elements might reflect the existence of a 'memory space', an organized representation of memory episodes linked by their common features. Unlike cognitive mapping, the notion of a memory space is readily extended to the coding and linking of non-spatial episodic memories, and therefore is consistent with the emerging findings of deficits in non-spatial memory following hippocampal damage and reports of non-spatial coding by hippocampal neurons. Furthermore, this conception of hippocampal function fits nicely with the neuropsychological literature on human and animal amnesia that indicates a strong reliance on hippocampal function in memory for episodes and for common factual information accrued across memory episodes [14].

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