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Dynamic coding in the hippocampus during navigation

Spatial navigation, which enables animals to move in an oriented way, is a complex, dynamic behavior fundamental for everyday survival. Animals navigate their environments using cognitive maps, which are internal representations of external space acquired by the brain through integration of multisensory cues. Deficits in spatial navigation skills are often preclinical signs of Alzheimer's disease in seniors and neurodevelopmental disorders in children and adolescents (Coughlan et al., 2018; Faedda et al., 2022). Understanding the principles of spatial navigation is thus of great importance as it will facilitate research in neurological disorders, as well as applications of mobile robotics. The 2014 Nobel Prize in Physiology or Medicine was awarded to three navigation researchers for their discovery of the inner positioning system in the rat brain – a giant step toward navigation studies in laboratory animals.

In the past few decades, numerous studies in rodents have revealed that the hippocampus presents cognitive maps by the collective firing of location-specific excitatory neurons. These neurons (known as place cells) fire strongly whenever the animal visits a specific region in the environment (O'Keefe & Nadel, 1978). Studies have also demonstrated that hippocampal place cell activity is not only tuned to an animal's position in navigable space, but also to motivation and non-spatial environmental factors, such as geometry, color, and odor, during active navigation, as illustrated by notable changes in the firing rates of neuronal populations without changes in firing location (Colgin et al., 2008; Lu et al., 2015). However, most of these studies have been carried out on animals trained to explore open arenas with limited environmental cues to chase food rewards, which is insufficient for deciphering the neural basis of cognitive maps in real life. There are three main reasons: first, navigation in a two-dimensional open arena is unlikely to elucidate spatial coding in the three-dimensional world; second, mental maps of small and simple laboratory enclosures are distinct from those representing large-scale real-world environments with complex landforms and heterogeneous surfaces; third, stationary tasks do not evoke behavioral switches, and therefore do not mimic the rich dynamism of navigation in the real world, although objects or restrained conspecifics have been introduced to subjects in some studies (Alexander et al., 2016; Deshmukh & Knierim, 2011). Navigation researchers have recognized that highly simplified tasks and mazes are limiting factors in such experiments, and recent studies have shifted focus to uncovering new aspects of spatial coding in more natural environments (Figure 1).

The Ulanovsky lab at the Weizmann Institute of Science has been training fruit bats to explore how their navigation systems compute large distances (Eliav et al., 2021), as well as the third dimension along the z-axis (Finkelstein et al., 2016). Their research on how the hippocampal circuit dynamically encodes changes in navigational behaviors has also been fruitful. In a recent study published in *Nature*, Sarel et al. (2022) trained bats to fly back and forth in a 135 m long tunnel and wirelessly recorded spike activities of single units in the CA1 subregion of the hippocampus. They reported that when flying in the tunnel, the firing patterns of the CA1 neurons represented the bat's position along the trajectory; when a second bat was flying toward the test bat from the other end of the tunnel, the activity of many hippocampal CA1 neurons changed dramatically as the two bats were about to pass each other, irrespective of their position in the tunnel. This modulation of place cell activity was accompanied by collision avoidance behaviors, such as decreased flying speed and increased rate of echolocation clicks, a proxy of attention, indicating that changes in behavioral modes can be reflected in the neural network state. However, control analyses indicated that this firing rate change in single units could not be explained by elevated echolocation click rates per se or by reduced flying speed during cross-over, but rather by the instant distance between the two bats. In addition, the fast gain and loss of inter-bat distance coding in these neurons near cross-overs coexisted with a transient but significant decrease in spatial tuning, suggesting a fast switch of coding schemes between pure place coding and joint coding of inter-bat distance and self-position. Further analyses indicated that different place cells displayed different degrees of distance tuning, while individual place fields of the same CA1 neuron

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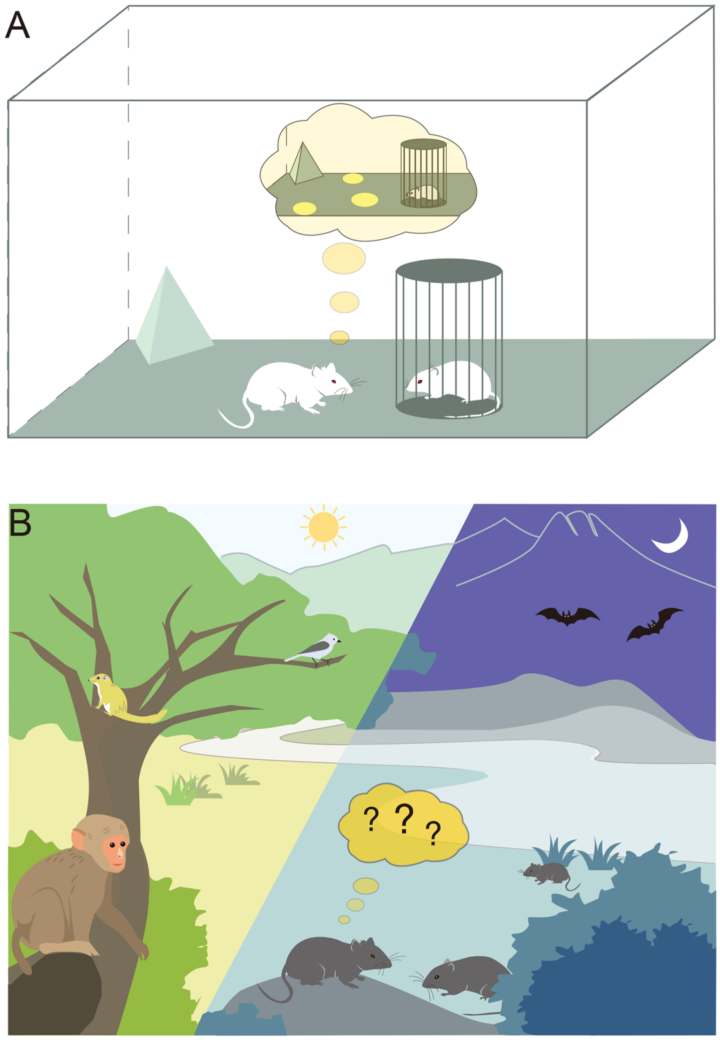

Figure 1 Laboratory environment vs. natural environment

Laboratory environments (A) are typically two-dimensional, small, with or without objects and restrained conspecifics; while natural environments (B) are large, dynamic, and rich in complex landforms and heterogeneous surfaces.

often exhibited independent modulation by inter-bat distance, suggesting that position and distance coding during cross-overs may be inseparable, which may facilitate efficient coding of both parameters according to theoretical models. In summary, the authors discovered that the hippocampus switched to a more efficient, non-separable position by the distance coding scheme when the bat's navigational behavior changed from regular flying mode to collision-avoidance mode triggered by an oncoming bat. These findings are of significance as they suggest a plausible mechanism for how the hippocampus dynamically encodes interchanging navigational behaviors: first, the hippocampal code is multiplexed and dynamic, yet not every individual hippocampal neuron must be continuously ready to process multiple incoming information streams; second, the hippocampus actively switches its core computation to support behavioral changes in response to sudden events during navigation, during which the firing patterns of individual place cells interchanges between distinct information processing states.

Animals need to rapidly switch behavioral modes during navigation to deal with the complex and dynamic situations of daily life. For example, a wild rat must rapidly switch to escape behavior when it encounters a predator during food foraging, and if it manages to escape, then it needs to reroute the way back to its burrow. How navigational strategies are updated in a timely manner to meet immediate behavioral demands remains an open question. In the above study, inter-bat distance coding was observed in the hippocampus near cross-over when two bats were flying toward each other but was rarely detected when the two bats were flying in the same direction at short inter-bat distances, suggesting that hippocampal coding may provide valuable information for ongoing behaviors, e.g., computation of inter-bat distance was critical for collision-avoidance behavior in cross-over flights, but was less useful during tracking flights. It will be interesting to test whether distance coding in the hippocampus becomes more intensive when the test bat is chased by a predator or a high-speed drone. The observations of Sarel et al. (2022)

have shed some light on our understanding of how internal navigation system works to guide an animal's navigational behaviors, and will inspire future studies designed to elucidate the neural basis of how joint computation of distance by position is achieved in the hippocampal circuit, how various coding schemes are adapted by an animal's inner positioning system under diverse navigational conditions, and how an animal's behavior is influenced by information selectively processed and presented in the navigation system.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

L.L. conceived and prepared the draft. J.L.L. created the figure. All authors read and approved the final version of the manuscript.

Jia-Li Long[1], Li Lu[1,2,3,*]

[1] *Key Laboratory of Animal Models and Human Disease Mechanisms of Yunnan Province*, *Kunming Institute of Zoology*, *Chinese Academy of Sciences*, *Kunming*, *Yunnan* 650201, *China*

[2] *National Research Facility for Phenotypic* & *Genetic Analysis of Model Animals (Primate Facility)*, *Kunming Institute of Zoology*, *Chinese Academy of Sciences*, *Kunming*, *Yunnan* 650107, *China*

[3] *Center for Excellence in Brain Science and Intelligence Technology*, *Chinese Academy of Sciences*, *Shanghai* 200031, *China*

*Corresponding author, E-mail: luli@mail.kiz.ac.cn

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