Place cell as a significant organizer of cognitive map

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Abstract: Affected by the wave of research on hippocampus, place cell has been investigated on its functions in spatial information processing densely for over 3 decades, as a consequence, great findings on place cell emerged continuously. We see place cell could process information not only the space, but also its relative elements like odors; with its remapping capability, it could differentiate the similar information ensembles in real time and also in memory; and it was found to also be able to represent the conspecifics location. Based on the classic findings and recent research, this review will introduce the basic properties of place cell, describe its neural representation in different animals to see how the place cell represent the spatial information using place fields. Afterwards and most importantly, an overview of place cell functions would be presented to depict how it organize the cognitive maps of minds.

Key words: place cell; navigation; cognitive map; hippocampus; place field; remapping

Cognitive map is a type of mental representation of spatial information, which serves individuals to construct and accumulate the spatial knowledge of the environment. Its concept was first introduced by Edward Tolman[1] in 1948 when he investigated the navigation ability of mouse in the maze. For decades, researchers have found a series of specific neurons related to spatial cognition and navigation functions in mammalian brain, such as place cell[2], grid cell[3], head-direction cell[4-5], border cell[6], and speed cell[7]. Among these, hippocampal place cell and entorhinal grid cell discovery has won the 2014 Nobel Prize in Physiology or Medicine.

Place cell is a kind of pyramidal neuron in hippocampus CA1 and CA3 regions, it process spatial information of a selective location in its spatial environment, which also known as place field. When place cells act collectively, it could be considered to

construct a cognitive locations set; and when it cooperates with other spatial-related cells like grid cell as we mentioned above, animals are believed be able to organize their cognitive maps, therefore interpret the environmental information and make flexible decisions and actions.

So far, researchers have mainly used rodents, primates and bats as model animals to investigate on place cells, and sometimes people with serious hippocampal disease would be investigated on their place cell pattern for medical and incidentally scientific purpose. Gradually, while place cell's role of organizing the cognitive map has been addressed more deeply and clearly, its function in our cognition has been recognized more sophisticated. How place cell functions has been a valuable question for scientists to discover. As investigations on place cell keep providing worthy insights into hippocampus functions, boosting its significant role in the memory and navigation; in the future, the diseases related to hippocampus could be clarified much more according to its discovery progress.

1. Properties of Place Cell

1.1. Place field

Place field is referred to the specific location which place cell fires (Fig. 1). It is roughly analogous to the receptive field in sensory neurons, with the difference that place field is allocentric, not in the body like other sensory neurons. This property should be considered as the most basic one to ensure the function of place cell.

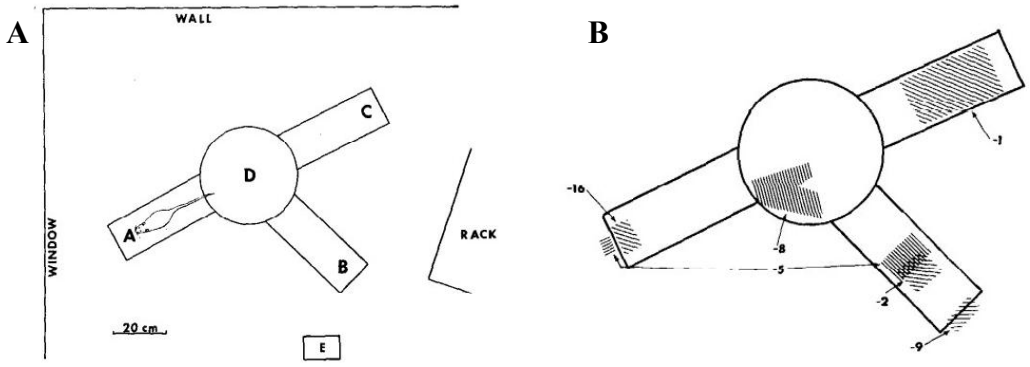

Figure 1 The explanation of place field. **(a)** Navigation testing maze (spatial environment). **(b)** Illustration of place fields(dark area) of an animal. (O'Keefe 1976)

1.2. Remapping

Remapping is the place field change of the place cell, associated with the change of spatial environment(Fig.2a). It is usually categorized by global remapping and partial remapping . As they literally means, when global remapping occurs, most place cells remap, which reflects a new map; while partial remapping occurs with only a small portion of place cells remap, which is usually considered as a reaction to spatial environment modification like the change of an object color. Place cell's remapping enable it to react to the different spatial environments, combined with its location at hippocampus, it's been theorized to be associative with the spatial memory[8].

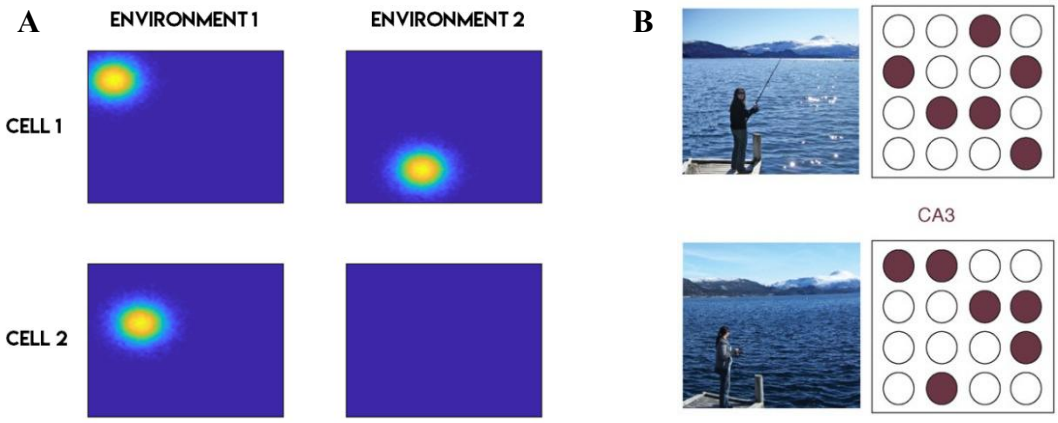

Figure 2 Schematic description of remapping. **(a)** Heat map of modeled place fields to illustrate remapping. Cell 1 changes the location of its place field and cell 2 losing its place field altogether in the change of the environment. (*Achaea, CC BY-SA 4.0 <https://creativecommons.org/licenses/by-sa/4.0>, via Wikimedia Commons*) **(b)** Schematic illustration of place cell remapping. Remapping helps distinguish the environmental difference, prevent interference between similar memory episodes. The colored circles mean active neurons, while the uncolored mean inactive neuron. (Modified from Colgin, Moser and Moser 2008 fig.1)

1.3. Relationship with sensory inputs

Place cell shows its properties of firing at a localized place and remapping to environmental changes, while its firing activities in this two properties could be

modulated by both geometric information (e.g., distances and directions) and nongeometric information (e.g., colors, odors and possibly behaviors) with different weights and strategies[9] (fig.3), which suggests that place cell processes both metric and contextual information to encode where should it fire and at which context should it fire[10]. When both requirements are satisfied, place cell fire to decode the spatial information to a map.

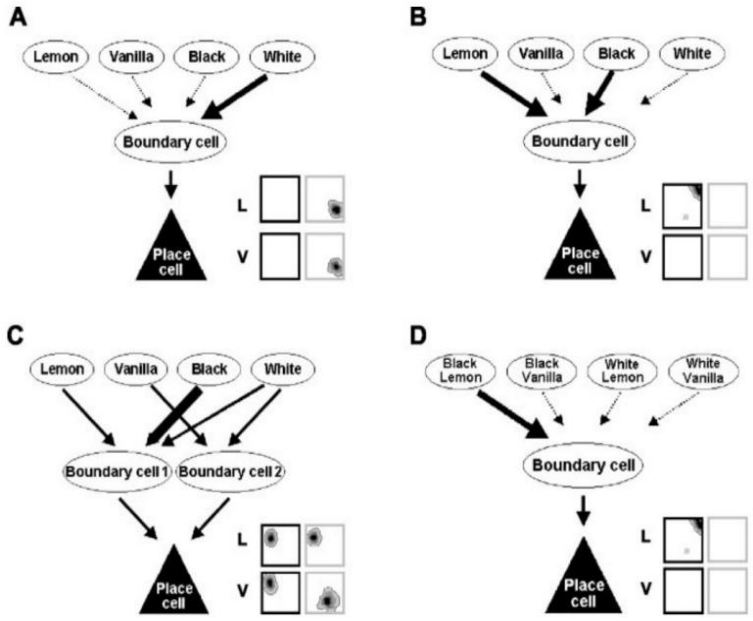

Figure 3 A model of the contextual remapping of place cells. Heavy lines indicate strong connections. L and V indicate odors, lemon and vanilla, while the colors of square lines indicate black or white. **(a-d)** Place cells show different remapping strategies to the change of contextual elements. (Anderson and Jeffery 2003)

1.4. Theta rhythm

Theta rhythm is referred to the neural oscillation of local field potential(LFP) which underlies various cognition and behavior, especially related to the hippocampus[11]. Place cell get this intriguing property with its firing at place fields, when the animal enters the place field, the place cell fires at particular phase of the theta wave. And its phase continues descending when the animal get across the place field, with its maximal firing rate at the trough of the wave(Fig.4), which means

different intensity of place cell firing has its specified phase in the LFP oscillation. This phenomenon is specified as theta-phase precession, which is considered to provide a possible mechanism for sequence information processing.

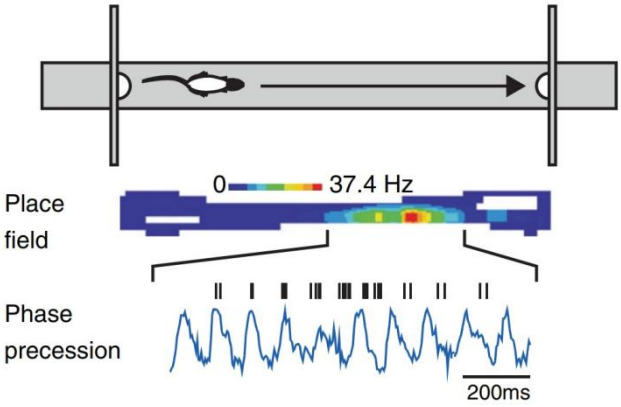

Figure 4 Theta phase precession of place cell firing. From top to bottom, the three diagrams indicates the running track of the rat, the place field and the phase precession of the place cell. When the rat moves from the left to the right, the LFP phase of action potentials moves from the right to the left in the opposite direction. (Burgess and O'keefe 2011)

1.5. Cooperation with grid cells

It's not enough to construct the cognitive map just through the collection of locations by place cells, thus place cell has to cooperate with other spatial cell, of which cooperation with entorhinal grid cell is much more investigated. In the circuits of dynamic representation of location, place cell and grid cell has been suggested to cooperate to form the basis of the brain's spatial representation system, which could process the spatial information in replay and also preplay[12].

2. Neural Representation of place cell

Knowing how place cell represents space is crucial for understanding how it works on spatial cognition, it describes the role of place cell during a animal behavior. And it's also interesting to know whether place cells functions in 3D movement as 2D.

2.1. Mouse in 2D space

The discovery of place cell began in rats, whose movements are mostly based in 2D space, so the investigation on the place cell neural representation also starts in 2D. Usually, we use heat map to describe the place cell activity in an environment (Fig.5a), locate the place field of a specified place cell with the warmest part in the place field

contours.

2.2. Mouse in virtual space

Navigation tasks in virtual space have emerged to be a promising tool for spatial behavior assessment in recent years, with advantages of limited animal position, which provides access to complex design of recording and modulating animals neural activity, also the variable design of spatial environment. In Figure 5B, we show a ordered neuron activity of mouse in a 2D narrow tube virtual space[13].

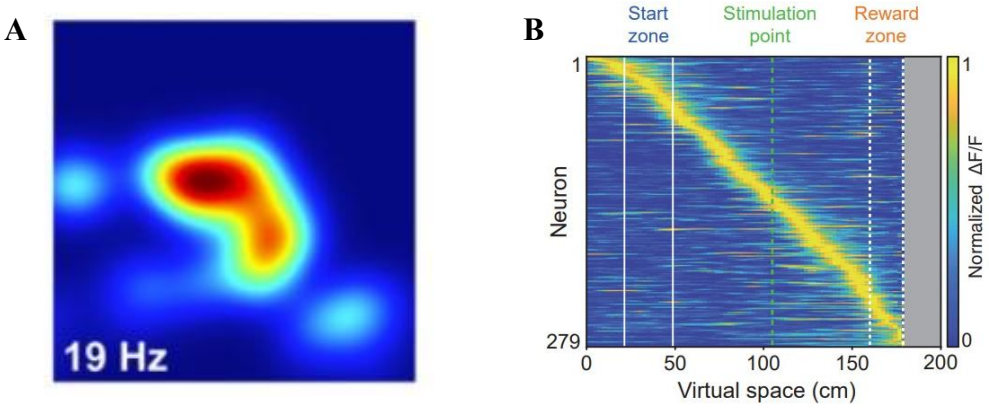

Figure 5 Neural representation of mouse place cells in 2D and virtual space. **(a)** Representative firing rate map of mouse in 2D space, the number on the left corner of the bottom indicates the maximal firing rates. (Modified from Chang, Volpe and Mackay et al. 2015) **(b)** Representative neural representation of mouse in a virtual space. All place cells recorded from an example baseline epoch on a stimulation day and average ΔF/F across space for each neuron and ordered by peak location on the track. (Robinson et al. 2020)

2.3. Bat and rat in 3D space

The key to differentiating between species specializations and general principles lies in comparative research, it's also apply to the place cell in rat and bat. While rat and bat have extremely different spatial behaviors in reality, it's intriguing to see whether the place cell in bat could represent the spatial cues as rats. And for rat, a commonly 2D-based animal, it's also intriguing to see whether the place cell have similarly strong selectivity on location in 3D. And the results indicated that, bat

showed many firing features parallel to the rat literature with slight species differences[14], while rat showed differences in volumetric place fields as a possible consequence of the gravity[15].

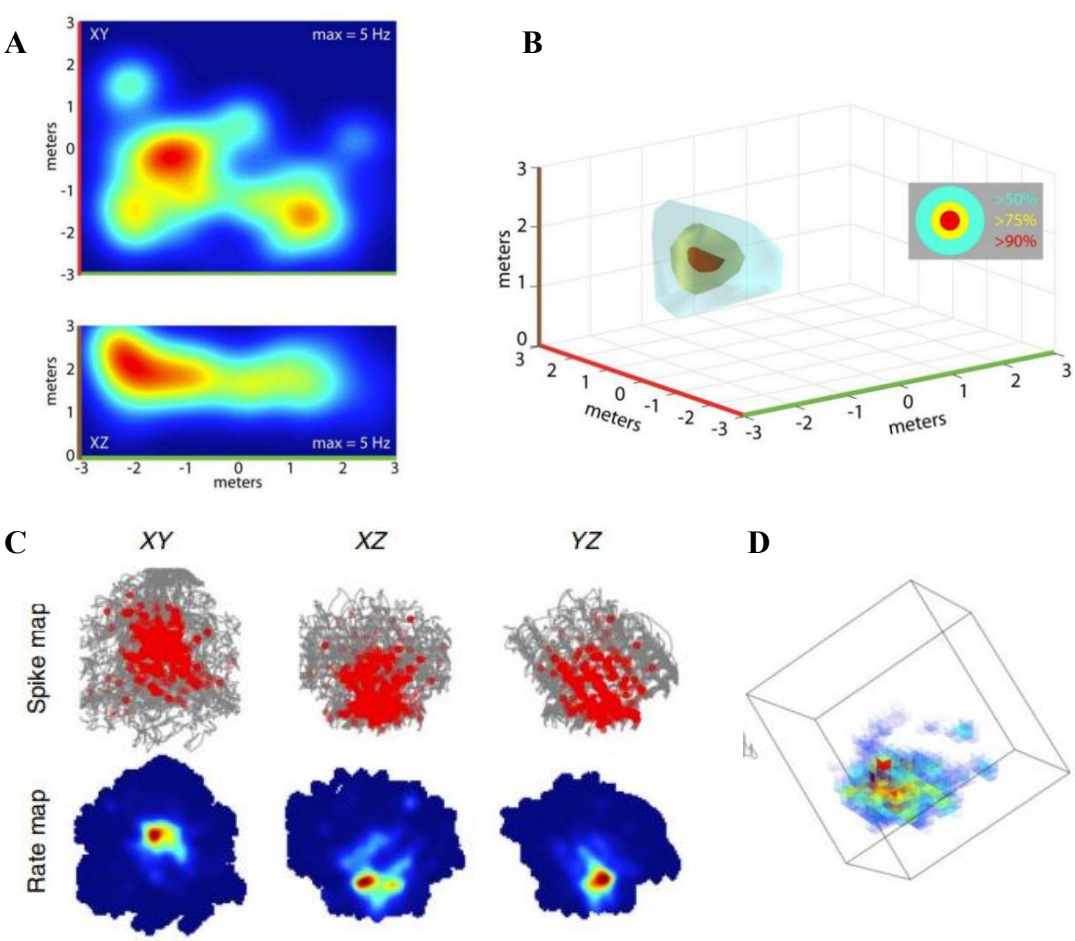

Figure 6 Neural representation of bat and rat place cells in 3D space. **(a-b)** Bat place cell neural representation example in 3D. (Wohlgemuth et al. 2018) **(a)** Heat map of spike rate in the projection to XY and XZ plane. **(b)** Construction of 3D place field for the neuron in **(a)**. The colors indicates the ratio to the maximal firing rate. **(c-d)** Rat place cell neural representation in 3D, a tilted aligned lattice. (Modified from Grieves et al. 2020 fig.3) **(c)** Spike map and heat map of spike rate in the projection to XY, XZ and YZ plane. **(d)** Construction of 3D place field for the neuron in **(c)**.

3. Place cell's organizer role

We will illustrate place cell's organizer role of animal's cognitive map in navigation, memory, map construction and social activity using recent studies.

3.1. Navigation

Given the information of place cell, the intuitive thinking about its role may mostly be the navigation. Place cell respond to the selective location not only passively, but also actively as a cognitive process. When rats were in the T-maze, ran the decision-making task, studies[16] found that the rats place cell showed representations ahead of animal rather than behind the animal, indicated a active cognition by place cell might happen for the later decision making.

As for purer spatial task, reorientation is considered pure geometric in rat's spatial navigation[17], and by recent studies, hippocampal map made by place cell was shown to be aligned with the environmental geometry and realigned to control a navigational goal after distortion[18]. Together, These interpretations implied the high involvement of place cell in navigation work.

3.2. Memory

Place cell convey much more than just spatial information. Place cell is considered to play a great role in episodic memory, which is the collection of past personal experiences that occurred at particular times and places; for example, the party on one's birthday. Evidence from different laboratories is converging on the view that the hippocampus serves to process contextual information related with an episode, differentiate contexts to prime the relevant behavior and memory[19]. Thus place cell is suggested to process both the metric and contextual information of episodic memory as an integration in entorhinal cortex, colloquially where the episode occurs and what's the context of the episode.

While studies on targeted activation of place cell found it could trigger memory retrieval in its previous place field[13]. Mouse has been trained to get water reward at a specified location in the virtual reality space, through targeted activation of place cell which specified the reward location before mouse reached the original reward location, mouse showed advanced licking behaviors outside the original reward location. These results provide direct support for the cognitive map idea that, place cell link the interaction between our cognitive brain and the spatial information, as its exemplary connection of memory and its firing activity.

3.3. Map construction

To construct a map, at least place cell needs to be able to collect and differentiate the map elements(the representation of place cell to locations); and only in such a way, the map accuracy is believable. Satisfactorily, remapping property of place cell provides flexible reaction to the ever-changing environment, which would be the necessity to build versatility of place cell representation. As in most cases, animals could use partial or global remapping to react to the small or salient changes in the environment, separate the representations of different contexts[8]. It seems that cognitive map is organized already by the representations of different contexts.

While in recent work about bats, which have two sensory systems for space information, vision and echolocation; global remapping happens in a same spatial environment when bats change its major modality for space, as vision in light and echolocation in darkness[20]. Combined with the relationship with sensory inputs we mentioned in its properties, it could be hypothesized that place cell processes the integration of metric and contextual information to build a cognitive atlas, which forms a abstract map dependent on the using sensory modality, from this organize the cognitive map not just in multiple representations, but multiple representations in different sensory modalities.

3.4. Social activity

Social animals need to locate not only themselves, but also their conspecifics. Place cell's property on awareness of its own location has been revealed for a long time, while two recent papers showed us that place cell in rat[21] and bat[22] could process the spatial information of their conspecifics. In the experiment, the observer animal observe the demonstrater animal trajectory, and also move on its own. Researcher found that there are some place cells representing the location both for observer and demonstrater's trajectory, while some may only represent either one of they two, which means a group of place cell are there to be responsible for the representation of animals specifics, it's like when we playing team sports like basketball, we need to find our teammates and also recognize their locations. "These findings suggest that the 'place' part of the hippocampus is not just involved in

navigating the physical landscape. It plays an important role in navigating the social landscape, as well." Dr. Ulanovsky, one of the discoverers, said.

4. Discussion

So far, as we know more about the place cell, we are more surprised of what the hippocampus could do and how the computation principle is organized inside. From spatial information to contexts, vision to echolocation, and self to others, progress have been made and corroborated that place cell are constructing a magnificent cognitive map of our minds. Today, scientists try to use collaborative methods to understand the learning structures in cognitive map formation, which could help explain how animals learn and interpret the environment to act flexibly and imply new approaches to understand the hippocampal-cortical interactions[23]. Also, investigation on place cell could help explain the pathology of hippocampus related diseases like topographical disorientation, and may suggest some curing methods in the future. Though right now we haven't defined the theoretical framework under the cognitive map, research on place cell still appears to be a very interesting field for scientists to discover, as place cell has shown its significance of cognition.

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Acknowledegements:

I thank Professor Jing Yao for his dedicated work on the *Neorobiology* course, he imparted the knowledge and inspired me a lot on neuroscience. I thank *the Human Brain* course by Professor Nancy Kanwisher on MIT OpenCourseWare, which illuminate the place cell field to me.