The neuroethology of spatial cognition

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A key challenge for animals is recognising locations and navigating between them. These capacities are varied: we can remember where our car is parked at the mall, rats are able to remember where their nest location is while foraging for food morsels, and bats are able to fly directly to a favourite fruit tree 20 kilometers from their home cave.

These spatial abilities, both commonplace or remarkable, raises fundamental questions. First, how *do* animals find their way? Second, how does the brain represent the outside world? In this primer, we will attempt to answer both questions from the perspective of rodent cognition and neuroscience.

Rodent behavior basics

A model organism for understanding basic mammalian brain processes, and increasingly disease states, is the rodent. At the beginning of the 20th century, rats were used to answer basic learning and memory questions, often in mazes. Much is now known about their behavior and neural systems, but it is useful to consider their natural behaviour – or at least the unstructured behaviour of a laboratory rat foraging for food - on an open platform.

Exploration Rats are cautiously curious. If you were to place a rat on a table, in the absence of strong light (which they find aversive), it would engage in bouts of movement

that gradually cover more of the environment. Each bout would typically conclude with a return to the point that the rat was placed into the environment. If a feature of the environment afforded protection, the rat would adapt this as a homebase (Whishaw et al., 2006); otherwise, it would use the introduction point as a home base (Nemati & Whishaw, 2007). Mice (*Mus musculus domesticus*) are also inclined to establishing a home base in an open platform environment, with visual, tactile, and olfactory cues influencing the position of the home base (Gorny et al., 2002; Clark et al., 2006). For rodents, the location of the home base is typically marked by grooming, rearing, and circling behaviors (Eilam & Golani, 1989). Once the home base is established, all subsequent behaviors are organized around this location.

Behaviors observed after home base establishment are kinematically and topographically organized. For example, movements away from the home base are slower and more circuitous relative to movements towards the home base (Tcherenichovski & Golani, 1995; for a review see Eilam, 2014). This organization allows division of exploratory behavior into a sequence of trips focused on the home base (Whishaw et al., 2001; Wallace et al., 2006). The initial or outward segment of these trips reflects relatively slow, non-circuitous progressions, punctuated by stops of varying duration and by changes in heading (Figure 1, panel A). The terminal or homeward segment follows the last stop and is a fast, non-circuitous path that ends at the home base (Figure 2, panel B). Although features of the environment can influence this behavior (e.g., walls can elicit thigmotaxic behavior), this organization is a ubiquitous characteristic of rodent open field behavior that may extend to humans (Blumenfeld-Lieberthal & Eilam, 2016).

Rats use path integration - an internal tracking of movements - to organize exploratory behavior. Specifically, self-movement cues generated as the rats moves away from the home base are used to update a representation of current position. Spontaneity in homeward segment initiation suggests that rats use this online representation to estimate direction to the home base, rather than encoding a fixed sequence of progressions and turns or a route engram. This online representation may also be used to estimate distance. For the homeward journey, peak speeds cluster at the midpoint and scale to Euclidean distance of the path, indicating that rats using distance estimates to guide return behavior. Both direction- and distance-based estimates do not depend on environmental cues. For example, exploratory trip organization is independent of access to visual (Wallace et al., 2006) or olfactory cues (Hines & Whishaw, 2005). As novelty of the environment abates, a reduction in frequency exploratory behavior follows with an increase in the willingness to eat or to carry food to a home base.

Homing Rodent foraging behavior has been used to dissociate navigational strategy preference (Maaswinkel & Whishaw, 1999). Rats readily search familiar environments for randomly located food items. Upon finding a food item, rats will carry it directly to an established home base (see Figure 2) if the estimated consumption time exceeds estimated carry time (Whishaw, 1990). Similar demonstrations of homing have been described in the female desert mouse (Mittelstaedt & Mittelstaedt, 1980) and the golden hamster (Etienne, 1980). In the field, deer mice have been reported to return to a home base even following displacements of 1.2 kilometers (Calisher et al., 1999).

Rodents have been observed to use several sources of information (e.g., visual, olfactory, self-movement cues) to guide behavior on the homeward segment. First, under

light conditions, a rat can use environmental or self-movement cues guide movement toward the home base (see panel A of Figure 3). Next, in the dark, rats encountering a food item will carry it back to the home base accurately (see panel B of Figure 2). This performance may reflect rats using self-movement cues or odor cues associated with the table or home base to organize behavior (Wallace et al., 2002). Evidence suggests that that rats prefer to use self-movement cues under dark condition. When the location of the home base is shifted prior to the start of dark testing, rats accurately return to new home base location (see panel C of Figure 2). This indicates that rats do not use odor cues on the surface of table or within the room to guide movement. Further, when the home base is removed as the rat searches for food under dark conditions, returns are focused on location the refuge occupied before its removal. This observation is inconsistent with odor cues associated with the home base guiding food hoarding behavior.

Interestingly, a different pattern of behavior is observed if the position of the home base is shifted in a familiar environment in the light (see panel D of Figure 2). When the home base is positioned to a new location, rat quickly exit the refuge and search for the food item. Upon finding the food item, rats carry it to the previous location of the home base, consistent with the use of familiar visual cues. Failing to find the home base at the former location, rats follow a non-circuitous path to the new home location of the base. Together, these findings suggest that rats use learned associations between visual cues and the home base over self-movement cues; however, path integration is retained as a reliable backup strategy that is applied to self-movement cues during rapid environmental changes.

Alternation and perseverative behavior Rodent behavior also depends on the environment. On dry land, rats will alternate between visited locations, and this is the

4

foundation for many spatial tasks used to investigate mnemonic processes. For example, different types of memory have been dissociated on the radial arm maze - an apparatus in which several maze arms radiate from a central platform (Olton & Paras, 1979). In one form of the maze, food reward is consistently located at the end of a subset of arms. Rats learn to visit only the baited arms (reference memory) and do not return to a previously visited arm (working memory). However, rats will adopt a win-stay strategy (returning to a rewarded location) if the reward encountered at the end of a maze arm is not exhausted in a given visit. In aversive, water-based tasks, such as the Morris water maze, perseverative responding facilitates learning the location of a hidden escape platform (Whishaw & Pasztor, 2000).

Landmarks, environmental shape, and path integration

Rodents use multiple sources of information to navigate. For the most part, these have been identified in careful laboratory studies, where the number of cues available to the animal is limited, and manipulation of specific types of cues (for example, visual landmarks) is possible. Broadly, rodents (and humans), preferentially use visual cues at the edge of the perceived environment for orientation. Under certain conditions, the shape of the environment can be sufficient for identifying locations (Cheng & Newcombe, 2005; Mesa et al., 2017). Rat eyes, however, lack foveas, and the rat's visual acuity is much less than that of a human. In addition, the rat's eyes are laterally placed, and not precisely coordinated with one another. Thus, rat vision consists of two overlapping monocular fields, and appears to be particularly tuned to detecting moving overhead stimuli (and, presumably, predators) (Wallace et al., 2013). As described in the behavioural studies

above, in the dark or in the absence of a salient visual cue, rodents can use self-movement cues (e.g., vestibular, proprioception, optic flow) to keep track of their location as they move about. Rodents have a keen sense of smell, and can also follow odor trails left by other rodent, or by the experimenter (Wallace et al., 2002).

Place cells, head direction cells, and grid cells

As is clear from the preceding discussion, rodent spatial behavior is structured, and rodents can use many cues to identify their location. But there is another reason why rodent spatial cognition is of interest: one of the success stories of contemporary systems neuroscience is the discovery of neural circuits in the rodent dedicated to the recognition of locations and headings (Moser et al., 2017). In the early 1970s, John O'Keefe and Jonathan Dostrovsky described neurons in the hippocampus which fired when an animal occupied a specific location within its environment (Figure 4B). Different place cells, as they were to be termed, possessed different place fields - locations in which they fired - and together these provided a representation of the animal's entire environment. This phenomenon, together with evidence from studies of the effects of hippocampus damage, led O'Keefe and Lynn Nadel to argue that the hippocampus provided the neural substrate for a cognitive map.

In the late 1980s, James Ranck Jr. described a second class of spatially-tuned neurons which fired when the rat faced a specific direction. These head directions cells, as they were termed, were shown in careful experiments by Ranck, Robert Muller, John Kubie, and Jeffrey Taube to be anchored to the animal's external environment, and fire over about a 90° range (Figure 4C). Subsequent work by a number of investigators showed that these

cells were found in an interconnected set of brain structures, ranging from brainstem nuclei to regions of the cortex.

More recently, the lab of May-Britt and Edvard Moser described neurons in the entorhinal cortex - an input structure to the hippocampus - which exhibited multiple, hexagonally arranged firing fields (Figure 4D). Strikingly, the size of the fields and their spacing vary along the medial entorhinal cortex, in a manner that matches the change in size of place fields along the hippocampus dorsal-ventral axis, suggesting a close tie between the two.

Other spatially-tuned neurons include boundary-vector or border cells, described by Colin Lever and colleagues as well as the Mosers. These appear to fire at a specific distance and direction from a boundary, for example a maze wall (Figure 4E). The existence of such cells was predicted by Neil Burgess and colleagues, who argued that such representations could give rise to place cells. There are also cells in the medial entorhinal cortex that encode the speed of the rodent's locomotion (Kropff et al., 2015). Such cells could contribute to the animal's ability to path integrate. Lastly, again within the medial entorhinal cortex, there are object-vector cells, whose firing is tuned to a distance and direction from an object within an environment (Høydal et al., 2017). Earlier work by Deshmukh and Knierim (2013) observed a potentially similar phenomenon, landmark-vector (place) cells, within the hippocampus. How object- and landmark-vector contribute to navigation is not fully understood, but it is not hard to imagine that they provide one means of identifying local locations.

Together, the representations described above appear to provide many of the essential elements for the recognition of locations, the tracking of movement, and

potentially the linkage of environments beyond the animal's immediate vista. The brain

regions involved may well serve similar functions across species, as there is evidence that

the hippocampus, for example, varies in size for food-caching birds, suggesting that this

structure's volume varies as a function of spatial memory demands (Clayton, 1998; Sherry et

al., 1999).

The challenge of long-range navigation

As described above, a good deal is known about rodent exploration and spatial

cognition in laboratory-scale environments. In parallel, the elements of a neural

representation of space have also been identified, again almost exclusively from controlled

laboratory environments.   Correlations between the responses of neural representations

and spatial behaviour have been observed (e.g., van der Meer et al., 2010; Kenath et al.,

2017; Butler et al., 2017), though not in every instance (Weiss et al., 2017). A challenge is to

link these behavioural and neural observations with navigation over distances encountered

in the wild (Poucet, 1993; Jeffery et al., 2013).

One answer may be that as the rodent moves from one location to another, it links

the representations of each (e.g., Taube & Burton, 1995; Dudchenko & Zinyuk, 2005;

Carpenter et al., 2015). In this way, local representations give rise to larger, global maps.

With a stable direction frame provided by head direction cells, it's possible that place and

grid representation come to represent the entirety of an animal's locomotion.

However, as argued by Geva-Sagiv et al. (2015), the resolution of place cells in small

environments isn't feasible biologically for long range navigation. Their proposal, based on

elegant studies in the bat from Nachum Ulanovsky and colleagues, is that space is represented at different scales. Thus, over longer distances, place cell fields are considerably larger.

Together, head direction-, place- and grid cells may link independently perceived environments with a consistent directional heading and represent locations at different scales, allowing efficient navigation over a range of distances and environments. Such a neural architecture may allow a representation of space this is anchored to the external world, updated by the animal's motion, and fit for recognising locations and navigating between them.

Further reading

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Figure captions

Figure 1: Topographic (top panels) and kinematic (bottom panels) characteristics plots for two representative exploratory trips by a rat. The outward segments (blue lines) are a set of slow, non-circuitous progressions punctuated by stops of varying duration. The homeward segment (red lines) is a single progression with peak speed at the midpoint of the journey and magnitude scaled to the Euclidean distance to the home base. Longer homeward segment Euclidean distances elicit faster peak speeds (left panels), whereas shorter homeward segment Euclidean distance elicit slower peak speeds (right panels).

Figure 2: Food hoarding in the rat. The rat exits the home base (panel A) to locate a food item (panel B). Upon locate the food item the rats will use a combination of environmental and self-movement cues to guide movement toward the refuge (panels C, D, and E). The rat will enter the home base prior to consuming the food item (pane F).

Figure 3: Homing in the light and the dark. Representative outward (blue lines) and homeward (red lines) paths are plotted for food hoarding behavior under various conditions. The hidden probe (panel A) involves testing under light conditions with the home base located below the surface of the table. The dark probe (panel B) involves testing under dark conditions with the home base located below the surface of the table. When the location of the home base is shifted to the opposite side of the table in the dark (panel C), rats are still able to make a direct return to it, indicating that they are able to track their movements in the dark. However, if the home base is moved in the light (panel D), rats

return to the former location of the home base first, before then moving to the new location. This suggests that the rats use an association between the home base and visual landmarks beyond the table to guide their homeward journey initially, and then use path integration once they discover that the base has been shifted.

Figure 4. Spatially tuned neurons in the rodent brain. A) In the laboratory, recording of spatial neurons have often been conducted in a cylindrical environment with a cue card affixed to the wall to provide orientation. B) Overhead view of a hippocampal place cell firing field in such an environment. Recording are conducted over several minutes, and a color-code rate map show areas of the cylinder floor where there neuron fired at a high rate (warmer colors) and where no firing occurred (dark blue). C) Polar plot of a head direction cell. This cell fired when the rat faced about 45°, and little firing was observed when the animal faced other directions. D) Example of a grid cell. First described in the medial entorhinal cortex, these cells exhibit multiple, hexagonally arranged firing fields (example courtesy of Dr James Ainge). E) Example of a boundary-vector/border cell (example courtesy of Dr Anna Smith).
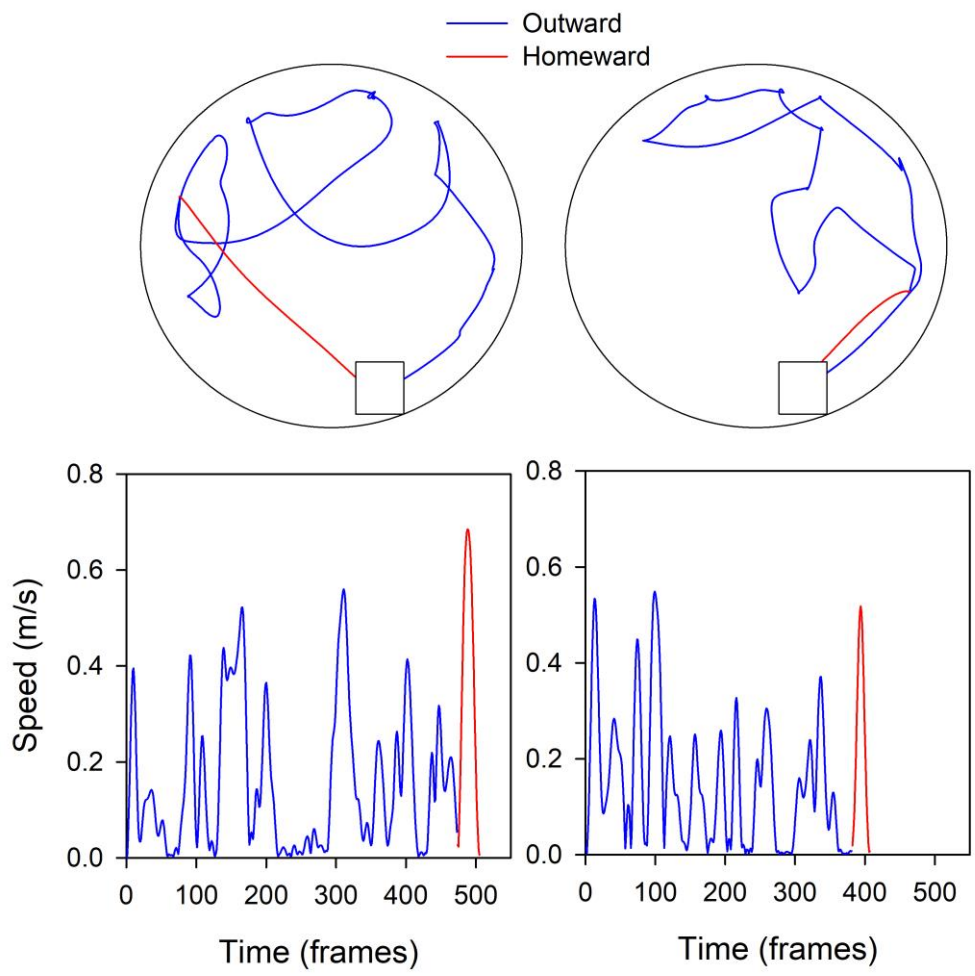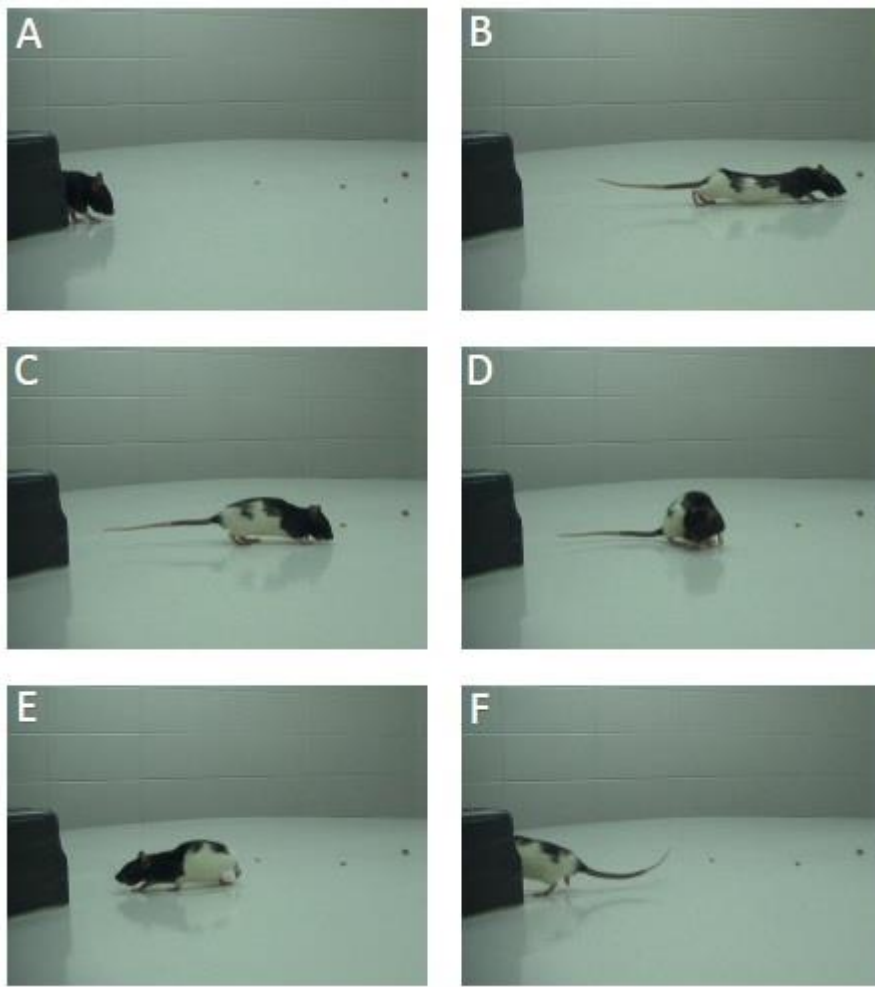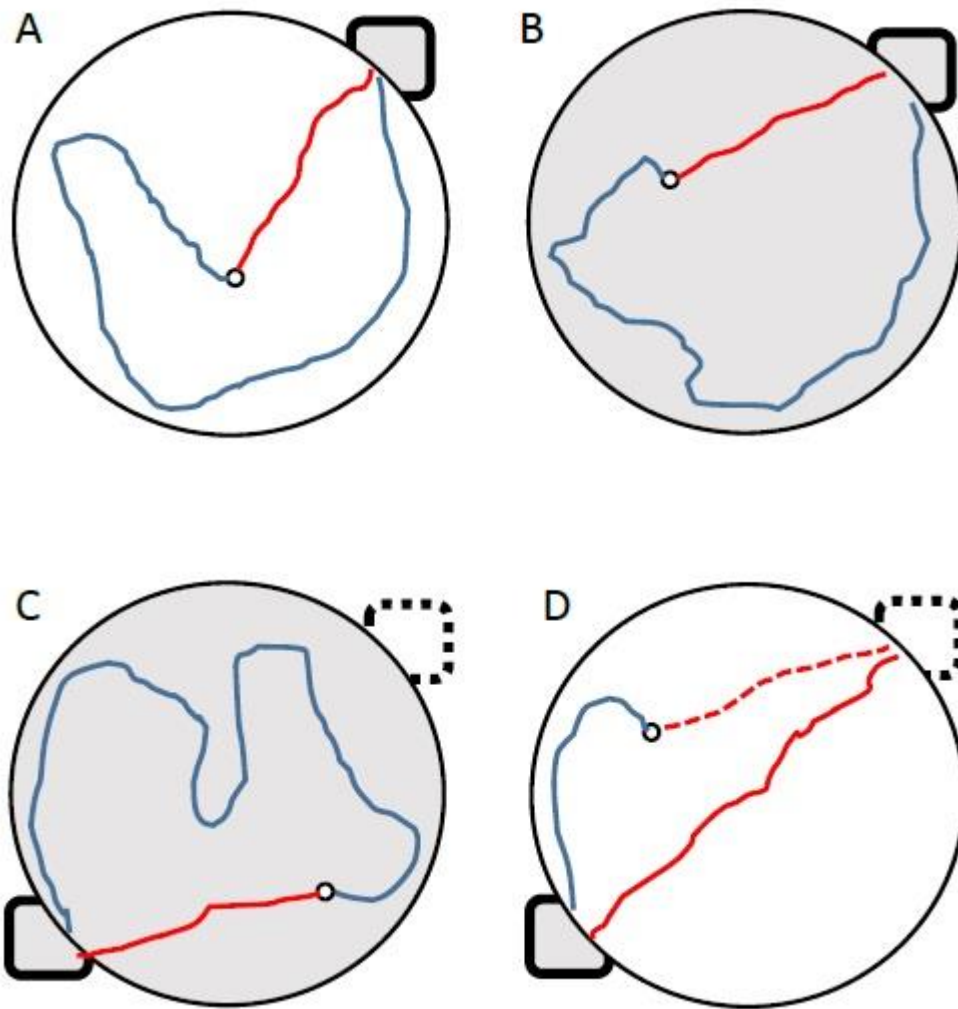
Figure 1

Figure 2

Figure 3

Figure 4

A)

B)

C)

90º

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270º

D)

E)