

## Dispatches

# Spatial cognition: Uncovering navigational representations in prefrontal cortices

Kiah Hardcastle

Harvard University, Department of Organismic and Evolutionary Biology, 52 Oxford St, Cambridge, MA 02138, USA

Correspondence: [kiahhardcastle@gmail.com](mailto:kiahhardcastle@gmail.com)<https://doi.org/10.1016/j.cub.2023.07.012>

**A new study identifies representations of navigational variables in six prefrontal regions in freely moving macaques, expanding our view of how the brain represents space outside of the broader hippocampal formation.**

As anyone who has tried to navigate a new city without a smartphone knows, navigation is an immensely complex yet essential behavior. How the brain supports navigation, which often requires the construction of a ‘mental map’ and continuous updating of our location within it, has long been a mystery. To tackle this challenge, considerable effort has gone towards identifying the brain regions representing key navigational variables, like position, and elucidating the nature of these representations. In recent decades, the Nobel-Prize-winning discoveries of hippocampal place cells and entorhinal grid cells have focused much of our attention on the broader hippocampal formation<sup>1</sup>. While in many ways this has paid off with the rapid development of mechanistic theories of path-integration, the highly multifaceted nature of navigation suggests that other higher-order cortical regions likely also support this behavior. While recent work has supported this idea<sup>2</sup>, our understanding of putative spatial codes in various cognitive regions remains nascent. A study reported in this issue of *Current Biology* by Maisson, Cervera *et al.*<sup>3</sup> explicitly considers this possibility by exploring whether six distinct prefrontal regions in freely moving macaques encode navigational information. Strikingly, the authors uncover a diverse array of navigational signals in all regions, contributing to a more comprehensive understanding of brain-wide navigation processes.

To explore navigational codes across prefrontal cortex, Maisson, Cervera *et al.*<sup>3</sup> leveraged an impressive experimental set-up in which 62 cameras are used to track rhesus macaques as they perform a

foraging task in a large environment<sup>4</sup> (Figure 1, left). The task involved multiple reward stations, between which the animals had to navigate to continually receive reward. This not only encouraged exploration but also allowed the authors to examine how spatial codes might intermix with other cognitive signals more traditionally associated with prefrontal cortex, such as choice and reward. Using a wireless recording device that promoted unrestricted movement, the authors recorded electrical activity from an impressive 8,276 neurons over 196 sessions from two animals and six structures throughout the prefrontal cortex: orbitofrontal cortex (OFC), dorsal anterior cingulate cortex (dACC), supplementary motor area (SMA), ventrolateral prefrontal cortex (vIPFC), dorsolateral prefrontal cortex (dlPFC), and dorsal premotor cortex (PMd).

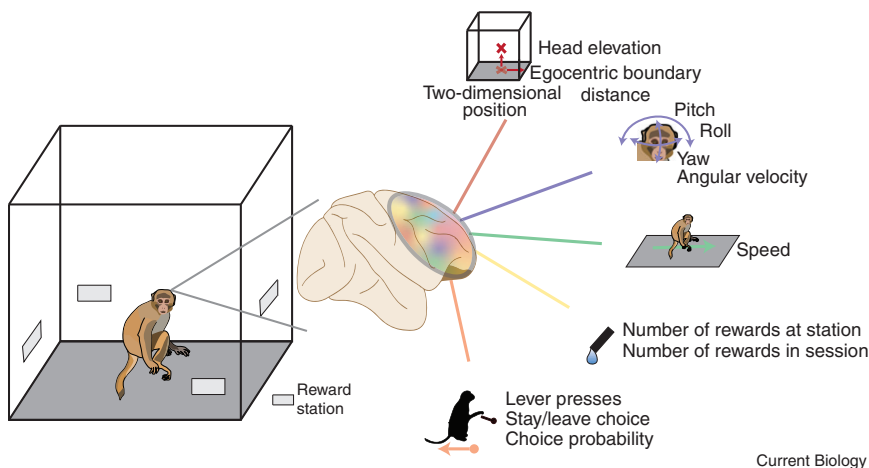
Using this system, Maisson, Cervera *et al.*<sup>3</sup> tracked various navigational variables, such as two-dimensional position, head elevation, allocentric head direction (yaw), head tilt (pitch and roll), egocentric boundary distance, angular velocity, and running speed. To determine which neurons encoded these features, the authors employed a generalized linear modeling framework that has been used in other regions to characterize navigational signals<sup>5</sup>. Broadly speaking, this approach determines whether neural activity is significantly modulated by each variable, such that neural activity can be predicted from that variable’s value (e.g., an animal’s position). To identify the minimum set of variables encoded by each cell, the authors used a greedy feature selection procedure, iteratively adding variables to the model

until the ability to predict neural spiking plateaued.

With this model and data in hand, Maisson, Cervera *et al.*<sup>3</sup> next examined whether neurons encoded navigational signals. Remarkably, despite the disparate proposed functions of these regions, with most thought to support navigation only indirectly, they observed nearly 20–40% of neurons encoded each variable in every single region (Figure 1, right). Specifically, 20–30% of neurons encoded three-dimensional location (two-dimensional position plus elevation); 20–30% of neurons encoded three-dimensional head orientation (yaw, pitch, and roll); and 25–35% of neurons encoded egocentric boundary distance, running speed, or angular velocity. Nearly all regions exhibited similar proportions of tuned neurons. Notably, the spatial tuning curves did not exhibit place cell-like characteristics, nor did the directional tuning curves resemble those of head-direction cells with narrow tuning. As with other prefrontal areas<sup>6</sup> and navigational areas<sup>5</sup>, however, the authors observed a high degree of mixed selectivity, with neurons representing nearly every possible combination of variables.

Maisson, Cervera *et al.*<sup>3</sup> next determined how these signals coexisted with five other task-relevant ‘economic’ variables, including rewarded lever presses, the number of rewards remaining in the environment or at each station, stay/leave choice, and predicted choice probability (Figure 1, right). Again, the authors found that 20–40% of neurons in each region encoded each variable, except for the rewards remaining at the reward station. Nearly all neurons encoding economic variables also





**Figure 1. Schematic of the task and main findings.**

Left: schematic of rhesus macaque exploring in an open environment with four reward stations (gray box). Right: regions across the prefrontal cortex encode a mixture of navigational variables (three-dimensional position, head orientation, angular velocity, speed) as well as task-relevant variables (number of rewards in the environment, number of rewards at the station, lever pressing, stay/leave choice, choice probability). Monkey image by Tom Baden/Scidraw (CC BY 4.0); brain image by Macauley Smith Breault/Scidraw (CC BY 4.0); lever pressing image by Klara Gerlei/Scidraw (CC BY 4.0).

encoded at least one navigational variable, revealing a blending of these coding schemes. Further, application of a previously developed analysis<sup>7,8</sup> aimed at categorizing cells based on the variables they encoded and how they encoded them did not reveal any distinct clustering. This suggests that coding for economic and navigational variables are thoroughly intermixed in prefrontal cortex, with few distinguishing factors across cortical areas. However, the authors also observed that encoding for both economic and navigational variables was generally stronger in dorsal regions, revealing at least one distinguishing factor across cortex.

Taken together, the new results of Maïsson, Cervera *et al.*<sup>3</sup> provide further evidence that navigational signals exist outside of the broader hippocampal formation<sup>2</sup>. While head direction signals have been identified widely throughout the brain, only recently have spatial signals been identified across cortical areas<sup>9–11</sup>. One intriguing future direction then is to determine precisely how signals in these cortices differ from those in hippocampal and parahippocampal regions. With any luck, contrasting these encoding schemes will shed light on the underlying function of, or computation in, the various regions that support navigation. In particular, hippocampal place cells possess key properties, like

well-defined place fields that persist in darkness yet remain influenced by prominent visual cues, which have been instrumental in the inference of their function of forming a cognitive map<sup>1</sup>. Given the observed difference in spatial signals in prefrontal cortex compared to hippocampus, it seems likely that prefrontal regions utilize spatial information for a different purpose.

One possibility is that the hippocampus sends spatial information to cortical regions, as has been recently suggested for spatial codes identified in dorsal posterior cortex in mice<sup>12</sup>. Following this suggestion, a trivial possibility is that these signals result from general broadcasting. As Maïsson, Cervera *et al.*<sup>3</sup> note in their discussion, “the fact that we observe widespread correlates of navigational information in these regions does not prove they play a causal role in navigation”. A more interesting possibility, though, is that prefrontal regions receive spatial signals from the broader hippocampal formation but utilize these signals to bind other task-relevant features, like choice, to location. Future experiments in which neurons from hippocampal and prefrontal regions are casually manipulated will be necessary to dissociate these possibilities. Further, this experimental approach would benefit from the development of mechanistic theories that lead to hypothesis-driven

experiments testing how the prefrontal cortex might use these spatial or self-motion signals to support navigation.

More broadly, the findings of Maïsson, Cervera *et al.*<sup>3</sup> contribute to an emerging body of work that examines modular versus distributed codes in the brain. The modular view, which assumes distinct functions and representations across brain regions, has been a long-guiding principle in our approach to understanding how the brain drives behavior. This reductionist view is clearly attractive. In its most extreme interpretation, it even provides a straightforward approach: determine the function of each region individually, and then combine them to understand how they interact to support a specific behavior. But as presented in this new paper, a wrinkle in this perspective is that many different regions exhibit similar coding properties, with few clear distinctions between regions. This finding is not limited to a specific system but has thus far been observed in action and choice coding<sup>13</sup>, movement<sup>14</sup>, and navigationally-relevant variables<sup>15</sup>. This has led to the popular question of whether there are meaningful functional distinctions between traditionally-defined brain regions<sup>16</sup> or if, instead, ‘everything is everywhere’.

A possible reconciliation between these perspectives, which has been mentioned elsewhere and is consistent with the findings here, is that while there is distributed coding, not all regions are the same. Rather, even though different regions may encode the same variables, they encode them to different extents, and use these signals for different purposes. These differences may not adhere to traditional regional boundaries, but instead may form a gradient along the cortical mantle. Thus, when the encoding properties of all variables are considered together, a complex landscape of coding emerges across the cortex, such that nearby areas, even within traditionally defined regions, exhibit distinct encoding profiles<sup>15</sup>. It is intriguing to consider whether a similar situation is occurring in the Maïsson, Cervera *et al.*<sup>3</sup> study, given that a ventral-to-dorsal gradient in coding is observed for both economic and navigational variables.

The ability to examine widespread coding for cognitive variables in freely

moving animals makes for an exciting time in systems neuroscience. While many challenges undoubtedly lie ahead, especially as we confront the dizzying complexity of spatial codes and grapple with turning neural correlates into mechanistic hypotheses, so do many opportunities for new insight.

#### DECLARATION OF INTERESTS

The author declares no competing interests.

#### REFERENCES

- Moser, E.I., Kropff, E., and Moser, M.-B. (2008). Place cells, grid cells, and the brain's spatial representation system. *Annu. Rev. Neurosci.* *31*, 69–89.
- Maisson, D.J.-N., Wikenheiser, A., Noel, J.-P.G., and Keinath, A.T. (2022). Making sense of the multiplicity and dynamics of navigational codes in the brain. *J. Neurosci.* *42*, 8450–8459.
- Maisson, D.J.-N., Cervera, R.L., Voloh, B., Conover, I., Zambre, M., Zimmermann, J., and Hayden, B.Y. (2023). Widespread coding of navigational variables in prefrontal cortex. *Curr. Biol.* *33*, 3478–3488.
- Bala, P.C., Eisenreich, B.R., Yoo, S.B.M., Hayden, B.Y., Park, H.S., and Zimmermann, J. (2020). Automated markerless pose estimation in freely moving macaques with OpenMonkeyStudio. *Nat. Commun.* *11*, 4560. <https://doi.org/10.1038/s41467-020-18441-5>.
- Hardcastle, K., Maheswaranathan, N., Ganguli, S., and Giocomo, L.M. (2017). A multiplexed, heterogeneous, and adaptive code for navigation in medial entorhinal cortex. *Neuron* *94*, 375–387.e7. <https://doi.org/10.1016/j.neuron.2017.03.025>.
- Rigotti, M., Barak, O., Warden, M.R., Wang, X.-J., Daw, N.D., Miller, E.K., and Fusi, S. (2013). The importance of mixed selectivity in complex cognitive tasks. *Nature* *497*, 585–590. <https://doi.org/10.1038/nature12160>.
- Raposo, D., Kaufman, M.T., and Churchland, A.K. (2014). A category-free neural population supports evolving demands during decision-making. *Nat. Neurosci.* *17*, 1784–1792.
- Hirokawa, J., Vaughan, A., Masset, P., Ott, T., and Kepecs, A. (2019). Frontal cortex neuron types categorically encode single decision variables. *Nature* *576*, 446–451.
- Poo, C., Agarwal, G., Bonacchi, N., and Mainen, Z.F. (2022). Spatial maps in piriform cortex during olfactory navigation. *Nature* *607*, 595–599.
- Saleem, A.B., Diamanti, E.M., Fournier, J., Harris, K.D., and Carandini, M. (2018). Coherent encoding of subjective spatial position in visual cortex and hippocampus. *Nature* *562*, 124–127.
- Long, X., and Zhang, S.-J. (2021). A novel somatosensory spatial navigation system outside the hippocampal formation. *Cell Res.* *31*, 649–663.
- Esteves, I.M., Chang, H., Neumann, A.R., Sun, J., Mohajerani, M.H., and McNaughton, B.L. (2021). Spatial information encoding across multiple neocortical regions depends on an intact hippocampus. *J. Neurosci.* *41*, 307–319.
- Steinmetz, N.A., Zatzka-Haas, P., Carandini, M., and Harris, K.D. (2019). Distributed coding of choice, action and engagement across the mouse brain. *Nature* *576*, 266–273.
- Musall, S., Kaufman, M.T., Juavinett, A.L., Gluf, S., and Churchland, A.K. (2019). Single-trial neural dynamics are dominated by richly varied movements. *Nat. Neurosci.* *22*, 1677–1686.
- Minderer, M., Brown, K.D., and Harvey, C.D. (2019). The spatial structure of neural encoding in mouse posterior cortex during navigation. *Neuron* *102*, 232–248.
- Hayden, B.Y. (2023). The dangers of cortical brain maps. *J. Cogn. Neurosci.* *35*, 372–375.

## Biogeography: The origin and spread of bee lineages

Santiago R. Ramírez

Department of Evolution and Ecology, University of California Davis, Davis, CA, USA

Correspondence: [sanram@ucdavis.edu](mailto:sanram@ucdavis.edu)

<https://doi.org/10.1016/j.cub.2023.07.025>

Where and when bees originated and how they dispersed and diversified across ancient continents has remained ambiguous. A new study that combines phylogenetics with fossil data reconstructs the origin and diversification of bees across geological time and space.

With more than 20,000 species worldwide, bees are the most prominent and specialized insect pollinators on Earth. The intricate association between bees and flowering plants, which began sometime during the mid-Cretaceous, has produced magnificent adaptations on both sides of this ancient liaison. Bees exhibit astonishingly diverse behaviors, including solitary nesting, brood parasitism, social parasitism and eusociality. Moreover, bees have evolved numerous adaptations for foraging, navigation, cognition, communication, brood provisioning and host-plant

specialization. However, despite the importance of bees in the evolution and maintenance of modern plant biodiversity, their origin and early evolution have remained obscure due to their sparse fossil record. A new study by Almeida, Bossert *et al.*<sup>1</sup> in this issue of *Current Biology* presents a comprehensive phylogenomic reconstruction coupled with a biogeographic analysis of all major bee groups. Their detailed analysis reconstructs when and where bees originated and how different lineages dispersed and diversified across ancient continents in geological time.

Bees belong to one of the largest groups of insects — the order Hymenoptera — along with ants, hunting wasps, parasitic wasps and sawflies<sup>2,3</sup>. Although bees depend entirely on pollen and nectar gathered from flowers to feed their larvae, the closest relatives of bees consist of a small group of hunting wasps that specializes in catching insect prey<sup>4</sup>. Bees, therefore, originated when an ancestral carnivorous wasp lineage transitioned into a vegan lifestyle.

But when and where did this evolutionary transition take place? What ecological conditions and habitats

