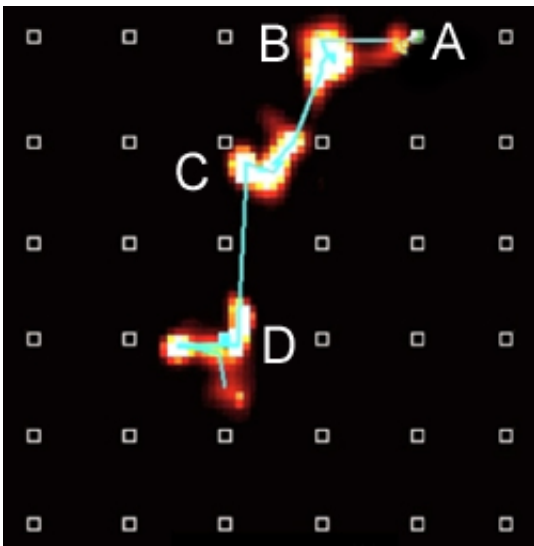


Going places: Rat brain 'GPS' maps routes to rewards

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Unique combinations of the brain's place cells fire (red lights) in sequence to represent each part of the path (A, B, C, D) that the rat will take. This image was compiled over a few milliseconds. Credit: David Foster, courtesy of *Nature*

While studying rats' ability to navigate familiar territory, Johns Hopkins scientists found that one particular brain structure uses remembered spatial information to imagine routes the rats then follow. Their discovery has implications for understanding why damage to that structure, called the hippocampus, disrupts specific types of memory and learning in people with Alzheimer's disease and age-related cognitive decline. And because these mental trajectories guide the rats' behavior, the research model the scientists developed may be useful in future

studies on higher-level tasks, such as decision-making.

The details of their work are scheduled for publication online in the journal *Nature* on April 17.

"For the first time, we believe we have evidence that before a rat returns to an important place, it actually plans out its path," says David Foster, Ph.D., assistant professor of neuroscience at the Johns Hopkins University School of Medicine. "The rat finds that location in its mind's eye and knows how to get there."

Foster and his team found that, at least for the purposes of navigation, the "mind's eye" is located in the hippocampus, which is composed of two banana-shaped segments under the [cerebral cortex](#) on both sides of the brain. It is best known for creating memories. In people with Alzheimer's, it is one of the first [parts of the brain](#) to sustain damage.

The Foster lab experiments focused on a group of neurons in the hippocampus called place cells because they are known to fire when animals are at a given location within a given environment. What was not known, Foster says, was how and when the brain uses that information.

By miniaturizing an existing technology, Foster and a postdoc in his lab, Brad Pfeiffer, Ph.D., were able to implant 20 microwires into each side of the hippocampus of four [rats](#). The tiny wires let them record [electrical activity](#) from as many as 250 individual place cells at the same time, more than ever achieved before.

Over a two-week training period, the rats became familiar with the testing area which was surrounded by a variety of objects, so that the rats could tell where they were in relation to the objects outside. The space was 2 meters square with 36 tiny "dishes" placed at regular intervals in a grid. A single dish at a time would be filled with the rats' reward: liquid

chocolate.

The rats' navigation tests involved as many as 40 sets of alternating "odd" and "even" trials per day. The odd trials required the rats to "forage" through the arena to find a chocolate-filled dish in a random location; the even trials required the rats to return each time to a "home" dish to receive their reward. While the rats fulfilled their tasks, the researchers recorded the firing of their place cells.

They found that as a rat travels randomly through the box without knowing where it needs to go, different combinations of place cells fire at each location along its path. The same set of cells fires every time the rat travels the same spot. These unique combinations of firings "mark" each spot in the rat's brain and can be reconstructed into what seems like a virtual map, when needed.

When a rat is about to go to a specific location, e.g., "home," place cells in its hippocampus fire in a sequence that creates a predictive path, which the rat then follows, somewhat like Hansel and Gretel following an imagined bread crumb trail.

Foster says that "unlike a Hansel and Gretel bread crumb trail, which only allows you to leave by the same route by which you entered, the rats' memories of their surroundings are flexible and can be reconstructed in a way that allows them to 'picture' how to quickly get from point A to point B." In order to do this, he says, the rats must already be familiar with the "terrain" between point A and point B, but, like a GPS, they don't have to have previously started at point A with the goal of reaching point B.

Foster says the elderly can get lost easily, and research on aged mice shows that their place cells can fail to distinguish between different environments. His team's research suggests that defective place cells

would also affect a person's ability to "look ahead" in their imaginations to predict a way home. Similarly, he says, higher-order brain functions, like problem solving, also require people to "look ahead" and imagine themselves in a different scenario.

"The [hippocampus](#) seems to be directing the movement of the rats, making decisions for them in real time," says Foster. "Our model allows us to see this happening in a way that's not been possible before. Our next question is, what will these [place cells](#) do when we put obstacles in the rats' paths?"

More information: Paper: [dx.doi.org/10.1038/nature12112](https://doi.org/10.1038/nature12112)

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