Research Award Brief

LEARNING TO EXPLORE PATHS THROUGH SPACE (2016 – 2018)

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Research Question: How do neuronal networks of the hippocampus learn to generate sequences of spatial activity that help animals find their way in a changing world?

Interdisciplinary Approach: High-density neurophysiology data will drive mathematical analysis and computational modeling to develop a new learning theory for spatial route planning.

Potential Implications of Research: This research project will reveal neural mechanisms of synaptic plasticity that allow hippocampal networks to flexibly generate goal-directed sequences for navigation and memory. Theoretical predictions may reveal new approaches to treating neurological disorders affecting learning and memory.

As we explore the world, humans and other animals learn routes, maps, and landmarks that enable us to mentally imagine the various ways to get where we want to go. Spontaneous bursts of activity in the hippocampus are thought to be a primary mechanism for the navigational sequences underlying this process, but current theories of neural function cannot explain how flexible paths through space are learned and expressed.

Imagine that it has been a slightly unusual day. Not that any particular thing was out of the ordinary. There's that wedding coming up, so you drove downtown to pick up a suit and dress from the dry cleaners. Leaving the cleaners, you noticed how nice the day was turning out, reminding you of the city park which was only a handful of blocks to the north. You left the car behind and strolled to the park, wending along the paths to a good spot to enjoy the prominent willow tree you noticed the last time you were here, a few years back. You walked to the far side to visit the pond, where you watched a school of minnows dancing around the slower moving Koi. That's when you realized you were starving. Thoughts of food and being back in this part of town brought one place to mind: that great ramen spot you used to frequent a few blocks northwest of your old apartment. You've never walked from the park to the ramen place before, but you knew it was mostly east and a little south. You imagined the route and, mysteriously, just seemed to know that the quickest path would take the side exit from the park, a few blocks to the main avenue, a jog past your old bank, and spicy noodles would be waiting for you up ahead on the right.

For many decades, the hippocampus has been studied as a critical brain structure for learning and memory. Its role has been understood to have two major parts. First, that it stores memories of life's experiences. Second, that it constructs spatial maps for navigating from point A to point B in the world. More recent studies, including those from the co-investigator Dr. Foster, have revealed a third major component of the role of the hippocampus: to generate sequences of neural activity patterns driven by an animal's experience of the world. Studied in rats, these sequences consist of a series of spatial locations representing paths through the environment. Often these sequences are simply replays of paths already taken. However, Dr. Foster's work has discovered sequences that follow unexplored paths to future goals. These 'trajectory sequences' can predict which paths the rats will actually take to the goal, demonstrating that they have a critical role in the cognitive processing for finding spatial paths.

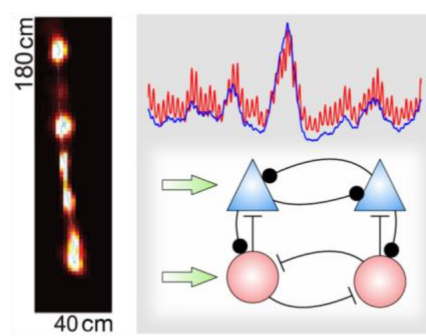

Figure 1. A trajectory sequence with discrete steps (left). Simulation of a hippocampal burst (top, blue; oscillations in red) in a recurrent network (bottom).

In this project, hippocampal data from rats will be analyzed for particular spatial and temporal characteristics. A major hypothesis is that these sequences do not travel smoothly through space, but jump from point to point (see figure, left) in time with certain brain oscillations. These data will inform mathematical (Dr. Zhang) and computational modeling (Dr. Monaco) studies that will develop a new learning theory of hippocampal sequences. The models will focus on how hippocampal networks learn to produce the spontaneous bursts (see figure, right) that drive trajectory sequences. This new theoretical foundation will clarify neural mechanisms of learning and memory, and enable predictions for impairments with age and disease.

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