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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 navigation.

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 insights into 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.

The importance of mentally exploring novel paths through space becomes clear by thinking about a day in the city. You drive downtown to pick up a suit and dress from the dry cleaners. Leaving the cleaners, you notice it was turning into a nice day, reminding you of a nearby city park which you hadn't been to in a few years. You look around and spot one of the taller buildings to get your bearings. You suddenly realize the park is only few blocks to the north, mentally imagining the café you have to pass and the intersection leading to the park entrance. At the park, you remember previous visits and a particularly prominent willow tree. There are many paths, but you just know which one will take you to that tree. That's when you realized you are starving, and one place comes to mind: that great ramen spot near your old apartment. You imagine the route and know you need to take the side exit from the park, head straight to the main avenue, jog past your old bank, and Spicy Noodles would be waiting for you ahead on the right. Each of these stops throughout the day depended on inferring a series of locations to your next goal.

The hippocampus is a critical brain structure for learning and memory, conventionally considered to have two primary roles. First, it helps create and keep track of long-term memories of life's experiences. Second, it helps to construct spatial maps supporting navigation from point A to point B. Recent studies, including from the laboratory of Dr. Foster, suggest a third major role of the hippocampus: to generate prospective sequences of neural activity patterns driven by an animal's experience of the world. Studied in rats, sequential activity during hippocampal bursts consists of a series of spatial locations that can represent paths through the environment. Often these 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' (shown in Figure 1) can predict which paths the rat will take to the goal, suggesting that they may have a critical role in the cognitive processes that evaluate spatial paths.

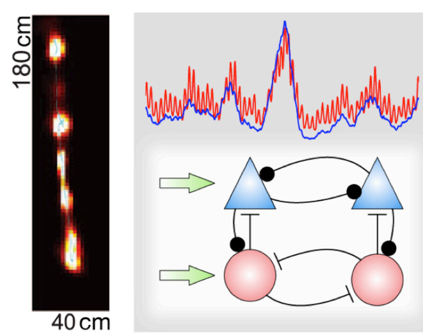

Figure 1. A rat's trajectory sequence with discrete steps (left). Simulation of a hippocampal burst (top, blue; oscillations in red) in a recurrent network (right).

In this project, hippocampal data from rats will be analyzed for particular spatial and temporal characteristics. We hypothesize that these sequences do not travel smoothly through space, but jump from point to point (see Figure 1, left) in time with certain brain oscillations. These data will inform mathematical analysis (Dr. Zhang) and computational modeling (Dr. Monaco) that will inform a new learning theory of hippocampal sequences. The models will focus on how hippocampal networks learn to produce the spontaneous bursts (see Figure 1, right) that drive trajectory sequences. This new theoretical foundation will clarify neural mechanisms of learning and memory with an explicit dynamical neuronal network model, which may help enable further study of hippocampal functions in health and disease.

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