**NEURAL PATTERNS OF HIPPOCAMPUS AND AMYGDALA SUPPORTING MEMORY OVER LONG TIMESPANS**

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# ABSTRACT

Episodic memory is an imperfect record of events arranged in time and space. When dealing with the storage of memories, the brain is faced with a predicament: it must retain an acceptably faithful facsimile of transpired events while simultaneously permitting inevitable modifications to accommodate learning new information. In this thesis, I first review contemporary theories of how memories can be stored in a neural substrate within the hippocampus, particularly in regards to how they can be arranged in time. Next, using *in vivo* calcium imaging, I detail how hippocampal “time cell” sequences could support encoding of behavioral events along multiple temporal dimensions. In this study, I trained mice to run in place on a treadmill, thereby measuring single-cell activity in CA1 as a function of time. Neurons in CA1 formed sequences, each cell firing one after another as if forming a scaffold upon which memories can be laid. These sequences were relatively well-preserved over a period of four days, satisfying the first requirement that information must be stored for a memory to persist. Additionally, these sequences also changed over time, which may be revealing a mechanism for how memories can change over time to assimilate new information. In the next experiment, I describe a collaborative project where we used immunohistochemistry, optogenetics, and calcium imaging to investigate the long-term dynamics of a fear memory. After mice initially associated a context with an aversive stimulus, they were placed in the same context over two days where they gradually relearned that the context was harmless. This produced molecular and neurophysiological signatures consistent with memory modification. However, after re-triggering fear, mice reverted to fearful expression with commensurate neural correlates. Using optogenetics, these behaviors could also be reliably suppressed. Finally, I conclude by synthesizing these findings with hippocampal literature on sequence formation and consolidation by proposing a holistic view of how these features can support episodic memory.