**1.** I’m Adam Miller, a postdoc in Paul Frankland’s Lab in Toronto. My project looks at how mice form memories by combining information across multiple learning experiences.

**2.** It is well known that mice can form memories about single experiences, such as in contextual fear conditioning. However, they are also able to form memories by accumulating information over multiple experiences, such as in this work by Richards et al., showing that mice trained to find a new platform location each day in a water maze learned to search areas where platforms were most common, leading to faster escape times.

**3.** This ability to accumulate information may be related to the role of the hippocampus in memory integration. For example, a study by Cai et al found that memories learned in one context became associated with a second context if the same hippocampal neurons were active in both. Similarly, work by Schlichting & Preston found that when people have an experience that reminds them of another experience, they will reactivate the hippocampal state associated with that other experience, allowing them to link the two experiences in memory. These studies show that hippocampal reactivation can support memory integration. However, accumulating information across many experiences has the additional challenge of determining whether any particular memory should be integrated or not.

**4.** To investigate this, I trained mice on a series of problems that they initially treat as independent, before later integrating what they’ve learned into unified strategy. The task is made up of six two-tone discrimination problems, with mice expressing their preference for a tone by increasing how long they will wait for a reward when that tone is on. Crucially, however, by integrating across problems, the mice can learn that the rewarded tones all fall within a specific frequency range, and that they can predict whether a novel tone will be rewarded depending on if it is in this range. Now, to directly observe how their memories change as they learn, I give probe tests before and after each problem, shown here as gray bars. And the performance of mice trained to integrate is compared to a non-integration control group.

**5.** As expected, mice undergoing integration training showed improved discrimination, even for problems that they hadn’t been trained on yet. Looking at the probe tests we see that early on, both groups responded by preferring tones beyond the rich training tone. Later however, the integration group selectively preferred the range of tones that were rewarded across all of the problems. By comparing the similarity of all the probe responses, we can also see that the memories of mice in the integration group converged with training and then remained stable throughout the later problems, while the non-integration group changed their probe responses after each problem.

**6.** I hypothesized that mice might maintain, update, or even abandon their existing memories based on whether the memories helped them learn new problems. To test this, I computed a prediction score from their responses on the probe test before they started learning a new problem. I found that mice with good predictions were much better at learning new discrimination problems. I also found that mice with good predictions made fewer changes to their memory, by which I mean that their pre and post probe tests were highly correlated. This suggests that memories that support new learning are maintained, while less accurate memories are either updated or abandoned.

**7.** Next, I used calcium imaging to observe hippocampal CA1 activity as mice learned. I found that mice undergoing integration training incorporated a greater proportion of *reactivated* neurons into their active populations, which resulted in greater overlap among active populations throughout the later sessions, when the mice began to integrate.

**8.** I also found that hippocampal neurons form clear firing rate fields anchored in the sequence of events on each trial. Interestingly, the stability of the fields across sessions followed a pattern similar to what we just saw. Early in training, the neurons of both groups had sloppy firing fields and changed the timing of their fields between sessions. However, the firing fields of mice in the integration group became more stable with training, resulting in a reliable population code across the later sessions.

**9.** Together this suggests that the hippocampus supports the accumulation of information by gating memory retrieval and integration. This may happen when each new learning event is also a retrieval cue, leading to the reactivation of hippocampal states associated with related memories. Learning new information under these conditions leads to memory integration. However, interfering memories can cause the hippocampus to switch to a new population state, discouraging retrieval and enabling interference-free learning.

**10.** Again, I am Adam Miller. The people shown here, some from Paul’s lab and some from Sheena Josselyn’s lab, have also contributed to the project. I also note the funding agencies that supported this work. Please reach out to me if you have any questions or comments about the project.