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Dear Editors,

We are submitting our manuscript titled "Memory in structurally unstable neural networks" for consideration for publication in *The Journal of Neuroscience*.

The impermanence of synaptic connections is an emerging theme in the study of hippocampal and cortical circuits of adult animals. The prevailing theory is that synapse loss through spine turnover would result in the erasure of stored memories. However, the structure with the highest observed percentage of unstable spines (hippocampus) appears to have remarkably stable cellular memory. Using computational modeling, we demonstrate that memory in neural networks undergoing synapse turnover can be stabilized by learning during reactivation events. Further, we show that learning during reactivations can stabilize the spatial receptive fields of hippocampal place cells in a model of the grid-cell-to-place-cell transformation.

Our results extend previous studies by suggesting that spine impermanence and memory persistence can coexist in the same neural circuit. Further, because our simulations involve only random rewiring, our results imply that while activity-dependent wiring plasticity may enhance memory capacity, learning of synaptic strengths alone is sufficient for memory persistence. Because our work addresses an apparent incongruity in the current literature and our findings highlight both biological and theoretical open questions, our work will be of interest to both experimental and computational neuroscientists.

The studies outlined in this manuscript were conceived and performed by Daniel Acker, PhD candidate in Neuroscience at Brandeis University, under the mentorship of Dr. Paradis (expertise in developmental neurobiology) and Dr. Miller (expertise in computational neuroscience). As such, Dan is the corresponding author on this manuscript. In addition, the late Dr. John Lisman (hippocampal expert extraordinaire) was a critical advisor on this project. Unfortunately, John passed away before seeing the completion of this work.

Thank you for considering our manuscript. We look forward to hearing from you soon.

Sincerely,

Suzanne Paradis

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