A screenshot of a computer screen

Description automatically generated

Associative memories are hypothesized to be stored as strengthened connectivity between ensembles of hippocampal neurons, termed *engram cells*. Via these strengthened connections, stimulating a portion of the engram cells activates the remainder of the engram cells, allowing for memory recall. Mathematical models predict that strengthening the connectivity between engram cells while holding everything else constant leads to an increase in both the firing rates of engram cells and the correlations between engram cells during spontaneous activity. For instance, in a linear spiking network model (Figure B) with connectivity based on the hippocampus (Figure C), we see that increasing the parameter *h* describing the relative strength of engram-to-engram synapses leads to an increase in the firing rates of and correlations between engram cells, and—to a lesser extent—the non-engram excitatory cells (Figure D).

However, we did not observe an increase in either firing rates of or correlations between c-Fos tagged putative engram cells in CA1 following a contextual fear conditioning task (Figure A). Further, such an increase in rates and correlations of engram cells during spontaneous activity following learning could have deleterious behavioral consequences, such as freezing the absence of the conditioned stimulus. Thus, we consider modifications to our model of neural activity that suppress this increase in rates and correlations of engram cells during spontaneous activity, while preserving the ability of the engram cells to be reactivated in response to stimulation of a portion of the engram cells.

We show that increasing the relative strength of inhibition, both before and after learning, reduces the change in both correlations and rates after learning (Figure D). We also introduce inhibitory plasticity into our model: engram cells recruit increased inhibition, either from the entire population of inhibitory neurons or from a subpopulation of “inhibitory engram cells”. We show that this also moderates the increased rates and correlations which happen as we strengthen engram-to-engram synapses. Finally, in order to preserve the ability of the system for stimulating a portion of the engram cells increases the activity of all engram cells, we modify the nonlinearity in the network, replacing the flat threshold-linear activation function with a convex increasing function.