Maintaining decodability of memories formed via Behavioural Timescale Synaptic Plasticity (BTSP)

Summary: Behavioural timescale synaptic plasticity (BTSP) enables synaptic changes based on neuronal activity at behaviourally relevant timescales [1]. In CA1 neurons, BTSP requires both plateau potentials in the apical dendrites and presynaptic input from CA3. These plateau potentials, driven by the Entorhinal Cortex (EC), act as instructive signals (IS) guiding synaptic changes [2, 3]. BTSP's capacity for one-shot learning suggests it plays a key role in episodic memory formation [4–7].

A key challenge is understanding how downstream regions like EC(out) maintain stable memory decoding as CA1 representations evolve. While additional plasticity mechanisms could link CA1 activity to downstream targets like EC(out), this would demand flexible, context-dependent adaptation. Another hypothesis we explore here is that the IS carries memory-related information, ensuring future reactivations of CA1 neurons align with original memory content. Our model suggests that the IS approximates an autoencoder EC(in)→CA1→EC(out) loop, allowing BTSP-modified CA1 neurons to reactivate during similar CA3 input, enabling EC(out) to decode the original memory.

Simulations in a circular track paradigm demonstrate that EC(out) reliably reconstructs original EC(in) patterns across multiple BTSP learning episodes. When the IS is randomized, this process breaks down, underscoring the IS's role in decoding. The model also generates context-dependent place fields, consistent with experimental findings in episodic memory tasks. We predict that the IS encodes sensory information alongside spatial cues, resulting in place-independent sensory selectivity in CA1 neurons—a hypothesis testable through axonal activity measurements [3].

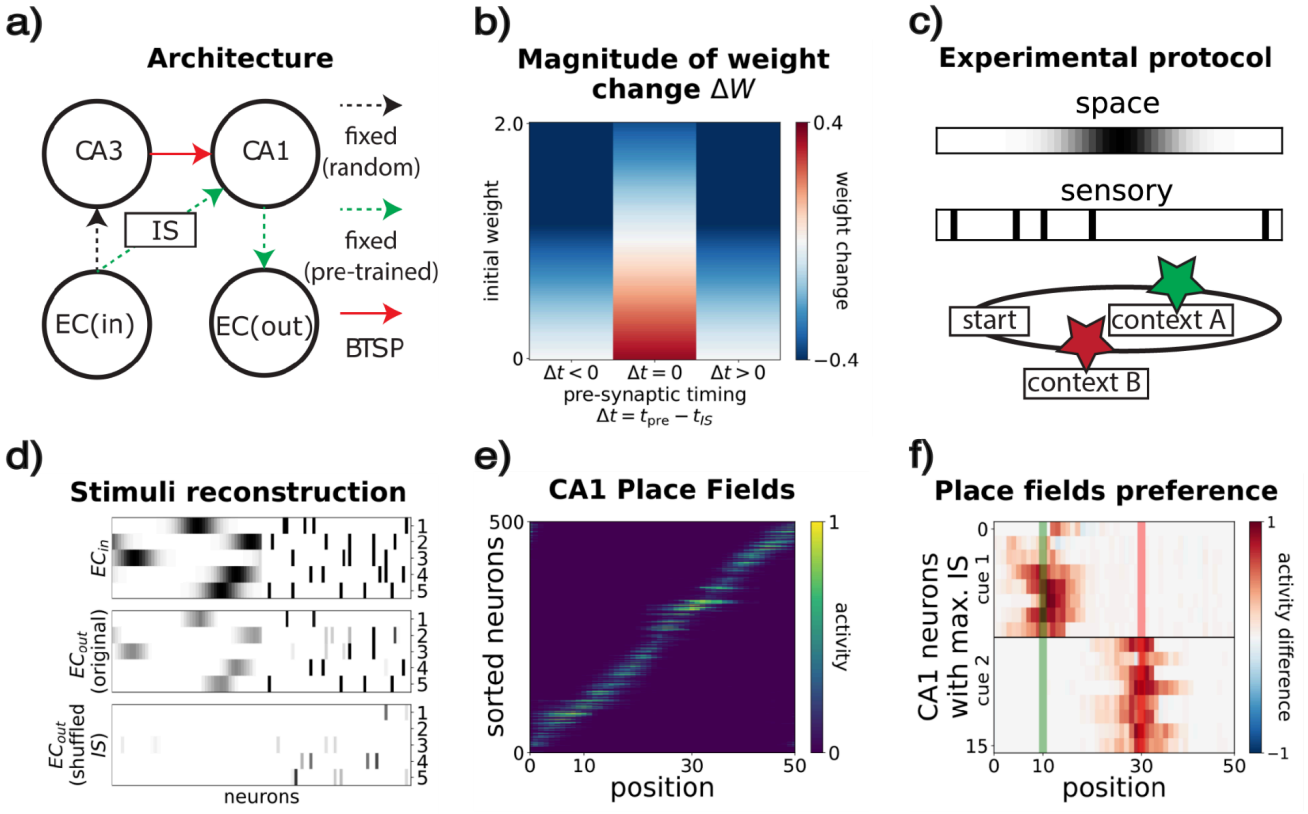

Figure 1: **a)** Model architecture. A pre-trained loop provides an IS to CA3→CA1 synapses undergoing BTSP. **b)** Weight change in neurons selected by the IS. **c)** Experimental protocol used in simulations. EC(in) contains spatial and sensory information. A circular track contains cue A (B) when context is A (B). **d)** Reconstruction of input after BTSP. **e)** Place fields formed in CA1 after BTSP. **f)** Context-dependent place fields in CA1.

Model Overview: We propose an autoencoding loop between EC(in), CA1, and EC(out). This loop ensures that BTSP-modified CA1 neurons are reactivated when similar activity arises in CA3, allowing EC(out) to decode the same memory content as during memory formation. Our computational model, consistent with hippocampal anatomy, includes two key circuits: one from EC(in) to CA1 apical dendrites and back to EC(out) (Fig. 1A, red), and another involving the CA3 to CA1 basal dendrites pathway (Fig. 1A, green). During an initial learning phase, the EC(in)→CA1→EC(out) circuit is trained to minimize EC(out)–EC(in) errors, forming stable representations in CA1 that are linked to memory content. CA3 to CA1 synapses undergo a simplified version of BTSP (Eq. 1, Fig. 1B), guided by the instructive signal from the EC(in)→CA1 apical circuit. In this way, reactivation of CA3 patterns triggers reactivation in EC(out) that aligns with the original memory, preserving the decodability of memories across multiple BTSP learning episodes. Intuitively, in Eq. 1, postsynaptic neurons receiving a high instructive signal potentiate/depress synapses depending on presynaptic activity in CA3. Those not receiving an instructive signal remain unchanged.

$$W_{\mathrm{CA3}\to\mathrm{CA1}}^{(t+1)} = (1 - \vec{\mathrm{IS}})W_{\mathrm{CA3}\to\mathrm{CA1}}^{(t)} + \vec{\mathrm{IS}}\vec{X}_{\mathrm{CA3}}^{\top} \tag{1}$$

Experiments and Results: We tested the model using a circular track paradigm, simulating place-like and sensory-tuned cells in the EC. The model was trained to represent spatial positions and random sensory cues (Fig. 1C, top). We observed that, when the original EC(in) activity was presented again, the EC(out) activity closely matched the memory-related EC(in) pattern (Fig. 1D), demonstrating the model's ability to preserve decodability. In contrast, shuffling the instructive signal disrupted memory decoding, highlighting the importance of an environment-specific IS for maintaining decodability.

In a second set of simulations, we introduced two contexts (A and B), each associated with distinct sensory cues at specific track positions (Fig. 1C, bottom). The BTSP learning rate was modulated based on the presence of salient cues. The model produced over-representation of CA1 place fields in contextually relevant positions (Fig. 1E), consistent with experimental findings [3], and exhibited cue selectivity at these positions (Fig. 1F).

Predictions

Our model predicts that plateau potentials in CA1 apical dendrites encode a population code containing both spatial and sensory information. This suggests that axonal activity should show place-independent selectivity to sensory cues, as measured in recent experimental studies [3].

References

[1] Bittner et al., 2017, Science; [2] Milstein et al., 2021, Elife; [3] Grienberger & Magee, 2022, Nature; [4] Yujie & Maass, 2023, bioRxiv; [5] Li & Roxin, 2023, PLoS Comp. Bio; [6] Vaidya et al., 2023, bioRxiv; [7] Pang & Recanatesi, 2024, bioRxiv.