Simulating inhibitory control over associative learning in the basolateral amydala

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[Introduction/Motivation:]

Associative learning in animals is necessary to extract predictive cues from the environment. But what neural mechanisms are responsible for this form of learning and how is it implemented at the circuit level? The focus of this work is to study the control of associative learning by complex inhibitory circuits using mechanistic simulations. We propose to study this problem in the amygdala where intricate disinhibitory circuits have been characterized experimentally[1,2]. The amygdala is involved with tagging stimuli with affective valence, e.g. learning whether a stimulus predicts a rewarding or noxious outcome. Learning in the amygdala is an orchestrated process under tight control of inhibitory cells. Two particular populations of inhibitory cells are critically involved, parvalbumin (PV) and somatostatin (SOM) cells. PV cells synapse unto the cell body of the principal cells and SOM cells unto the distal dendrites. Intriguingly, PV cells also synapse unto SOM cells, creating a disinhibitory effect when they are activated. Sensory stimuli recruit PV cells, thereby disinhibiting principal cell dendrites through their action of SOM cells, but inhibiting the soma of the principal cells[1]. A shock acting as an unconditioned stimulus inhibits both the PV and SOM cells, fully disinhibiting the principal cell and permitting a window of opportunity for plasticity[1]. We aim to simulate this system and study how information from real spike trains is encoded in the simulated network.

[Methods:]

Here we propose to study a circuit with multiple types of interconnected inhibitory neurons using multi-compartmental principal cells, receiving inhibitory inputs at the soma or the dendrite according to the cell type of the inhibitory neuron (SOM or PV inhibitory neurons), as in [3]. As input stimuli to the network, we use real spike trains recorded from the medial prefrontal cortex (mPFC) during a reward-acquisition working memory task[4,5]. The mPFC is reciprocally connected to the amygdala and carries highly processed task information. Pyramidal cells and amygdala cells both receive mPFC input spike trains. We inhibit the PV cells at cue times and both SOM and PV neurons at reward times. To study the distal reward problem stemming from the fact that the cue and the reward are separated in time, we introduce an eligibility trace at the principal cell synapses[6]. This eligibility trace is used to update synaptic weights when a reward is presented. We compare the responses of the principal cells to input stimuli from the mPFC before and after learning and with and without inhibitory gating by using spike-triggered averages and covariances with mPFC firing rates as stimuli. The aim of this computational analysis is to characterize how the disinhibitory circuit shapes what patterns of the input spikes the principal cells become responsive to.

[Discussion:]

Due to the complexity of the neural circuits, it is difficult to test theories without a recourse to mechanistic simulations that encode our understanding about the system. The disinhibitory circuit in the amygdala has been characterized experimentally, but the precise interactions have not been tested in simulations. It is the aim of this work to address this gap through realistic simulations that incorporate real spiking data and reward-modulated plasticity rules to formalize our understanding of the role of the disnhibitory circuit in associative learning.

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