1. Introduction
Long-term potentiation (LTP) provides the neural substrate underlying the formation of long-term memories. LTP has been suggested to be maintained by the persistently active kinase PKMζ. Inhibiting PKMζ, using zeta inhibitory peptide (ZIP) disrupts both recently and developmentally acquired sensorimotor memories. We developed a computer model of stimulus fields and their erasure via ZIP, and validated the findings of this model against in vivo microelectrode recordings.

2. Methods
- Experimental data were recorded from the S1 cortices of anesthetized rats and awake macaques. Touch stimuli of 50 ms duration were delivered to 15 locations on the subjects’ hands.
- The model consisted of event-driven integrate-and-fire neurons, divided into five cell types across the cortex and thalamus (Fig. 1).
- The effect of ZIP was modeled as a decrease in both excitatory-excitatory and excitatory-inhibitory connection strengths.

3. Stimulus fields

Fig. 2: Spatial characteristics of stimulus fields in the model. Each dot represents a single cortical pyramidal cell in layer 2/3; color shows evoked firing rates in spikes per cell per second. ZIP reduces the amplitude and increases the lateral extent of the cortical response.

Fig. 3: Cross-sections of stimulus fields in the model (top two panels) and experiment (bottom panel). With LTP, the response to stimuli is locally enhanced; when ZIP is applied, the response becomes both broader and lower in amplitude. The spatial profile of the change in firing rate (bottom two panels) is consistent between simulation and experiment. In the experiment, ZIP was injected to the left of the stimulation site; the asymmetry seen here is a result of the nonuniform ZIP concentration gradient.

4. Synaptic weights & information flow

Fig. 4: During normal learning of stimulus fields via spike-timing-dependent plasticity (STDP), most connections become slightly weaker while some become substantially stronger, producing a slight reduction in median weight but a large increase in mean weight. These changes are reversed after the application of ZIP.

Fig. 5: Spectral Granger causality, a measure of information flow. In the simulation, LTP slightly enhanced feedforward information flow (left panel, information flowing from the thalamus to layer 4 of the cortex). It also significantly reduced intracortical information flow (right panel), consistent with the narrowing of cortical response fields.

5. Summary
- We developed and validated a spiking network model of the effects of ZIP. Both experiment and simulation found that ZIP reduces the amplitude and increases the width of stimulus fields.
- The extra level of detail afforded by the simulation showed that these ZIP-induced changes lead to:
  - Increased layer 2/3 - layer 5 Granger causality;
  - Increased long-range mutual information and decreased short-range mutual information.

Acknowledgement
This work was supported by DARPA Grant N66001-10-C-2008.

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