Stimulus field formation and erasure in somatosensory cortex

NEUROSIM LAB

Cliff C. Kerr[1,2], Lee von Kraus[1], Jordan Iordanou[1], Samuel A. Neymotin[1,3], Joseph T. Francis[1], William W. Lytton[1,4]

[1] SUNY Downstate, Brooklyn, NY; [2] University of Sydney, Australia; [3] Yale University, New Haven, CT ; [4] Kings County Hospital, Brooklyn, NY

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.

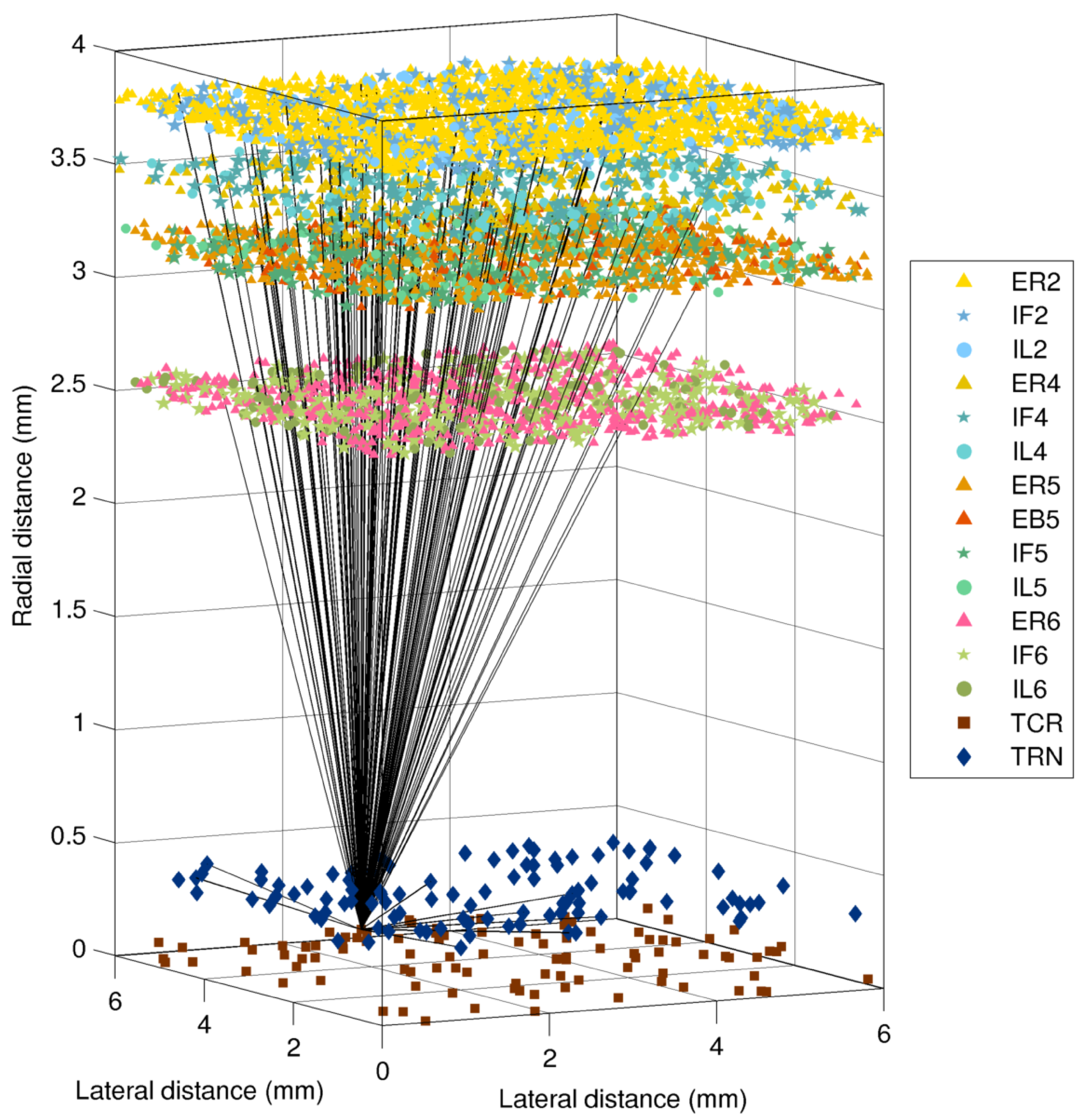


Fig. 1: Geometry of the spiking neuronal network model. The model has 15 cell types distributed across 6 cortical layers and the thalamus, for 5000 cells and 150,000 connections in total. All efferent connections from a single thalamocortical relay cell are shown (lines). **ER** = excitatory regular-firing pyramidal neuron; **EB** = excitatory bursting pyramidal neuron; **IF** = inhibitory fast-spiking interneuron; **IL** = inhibitory low-threshold-spiking interneuron; **TCR** = thalamocortical relay; **TRN** = thalamic reticular nucleus.

3. Stimulus fields

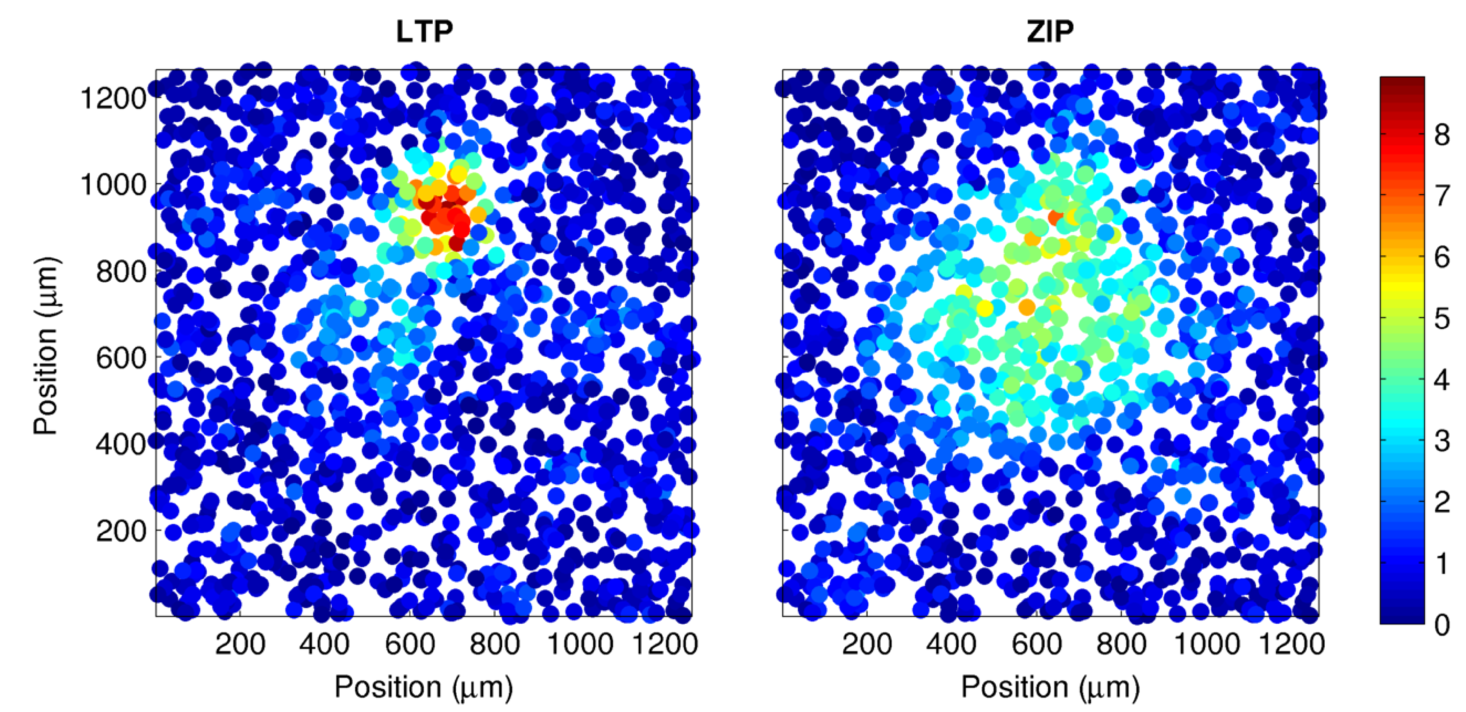
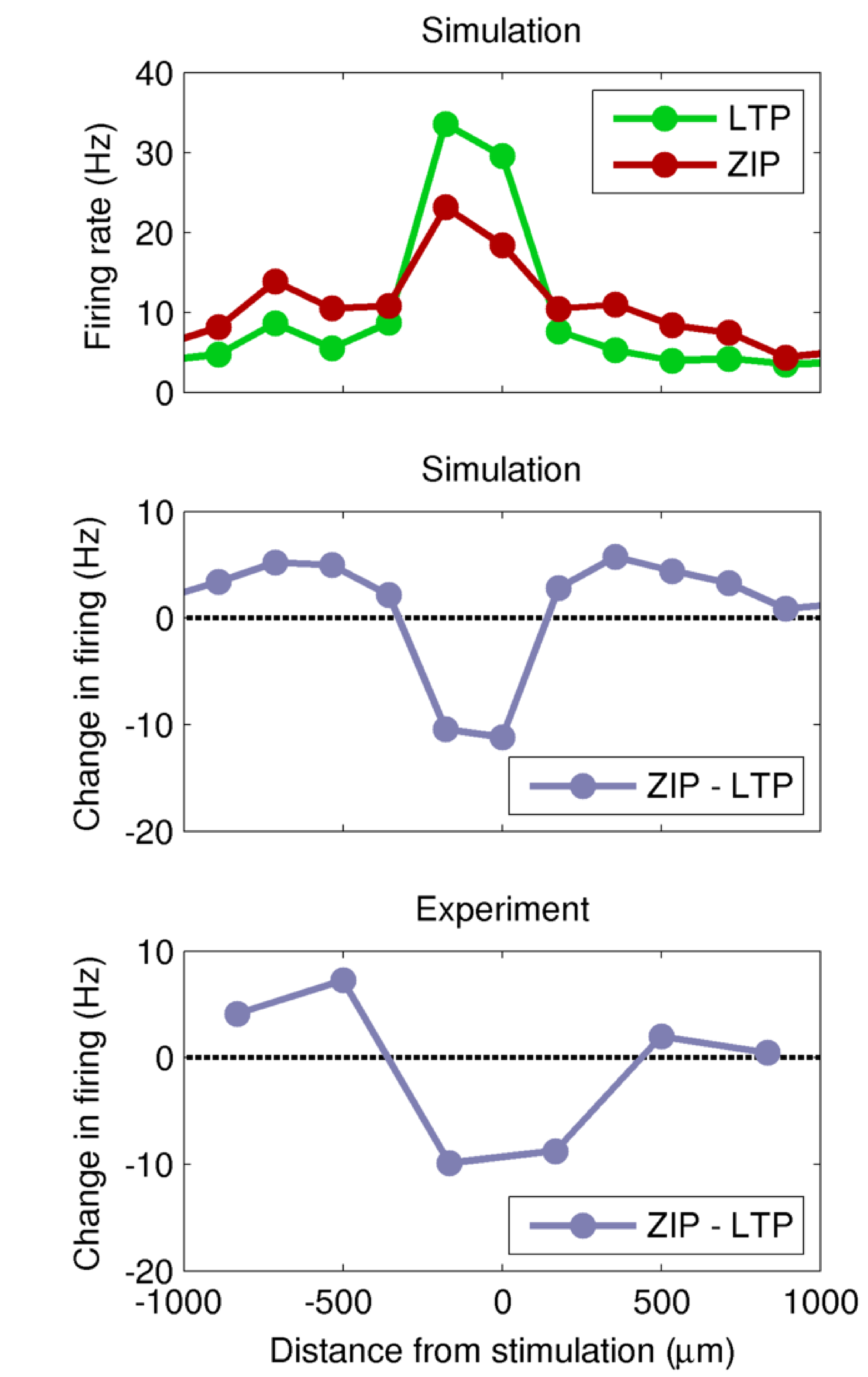


Fig. 2: Spatial characteristics of stimulus fields in the model. Each dot represents a single cortical pyramidal cell in layer 2/3; color shows evoked firing rates in spikes per cell per second. ZIP reduces the amplitude and increases the lateral extent of the cortical response.

Fig. 3: Cross-sections of stimulus fields in the model (top two panels) and experiment (bottom panel). With LTP, the response to stimuli is focally 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.

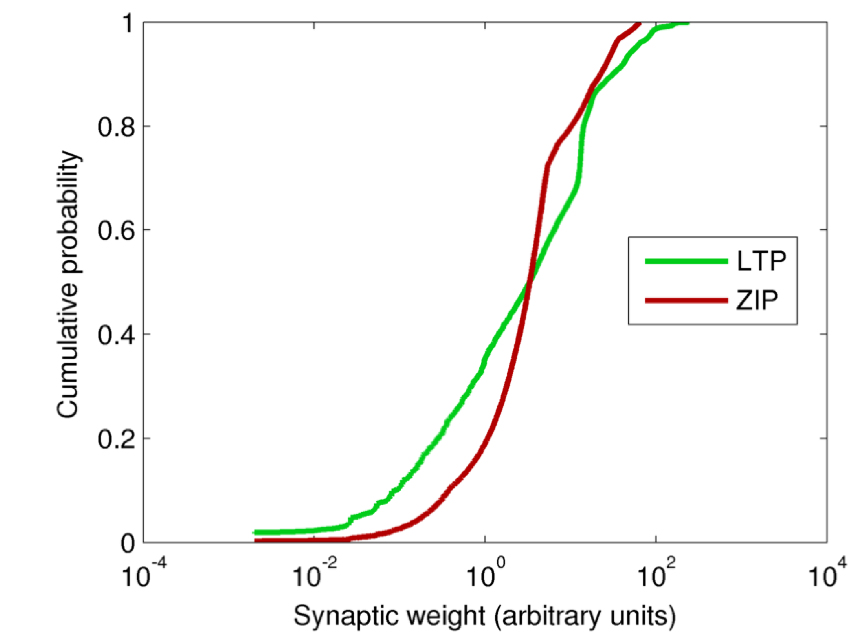


5. Summary

- 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 responses.
- 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.

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.



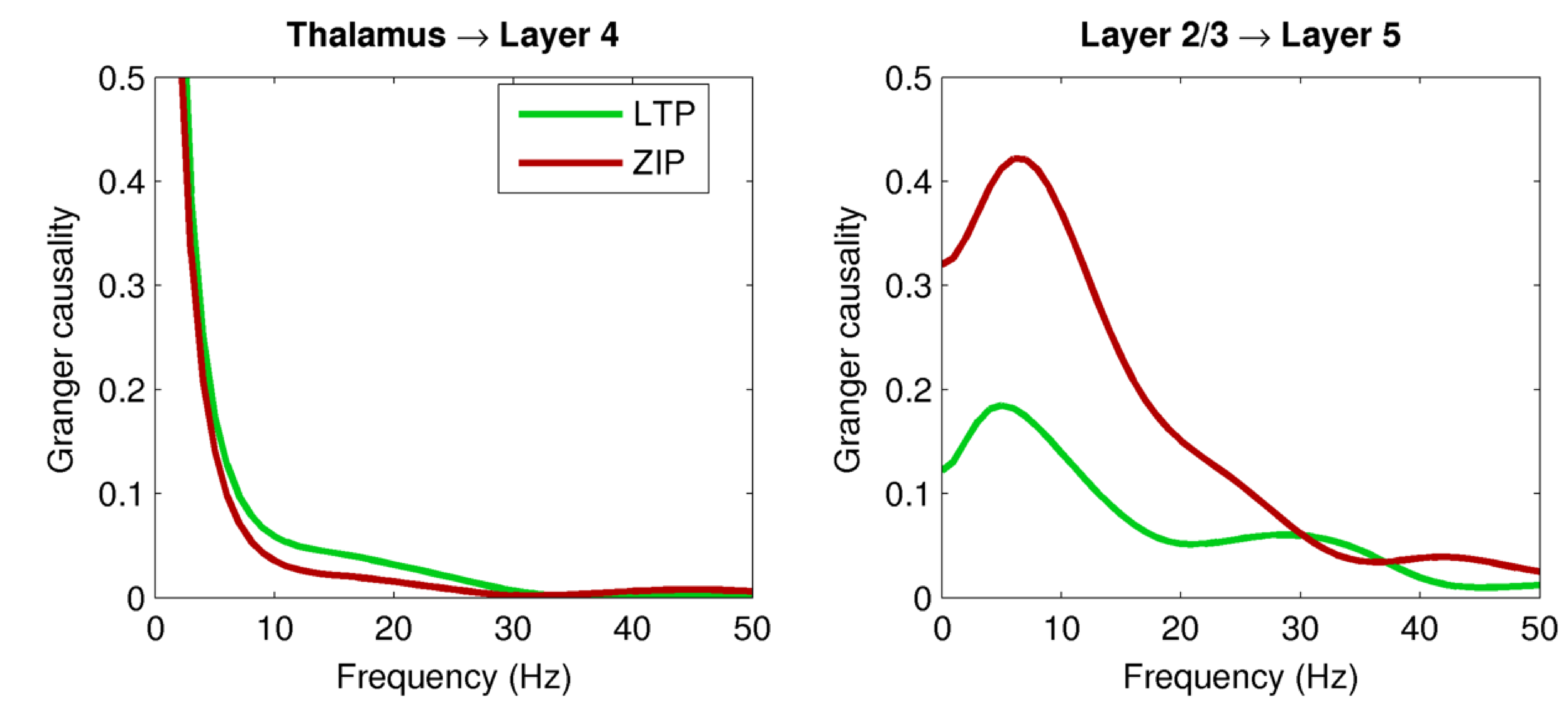


Fig. 5: Spectral Granger causality, a measure of information flow. In the simulation, LTP slightly enhanced feedforward information flow (left panel; information flowing from the thalamus to layer 4 of the cortex). It also significantly reduced intracortical information flow (right panel), consistent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

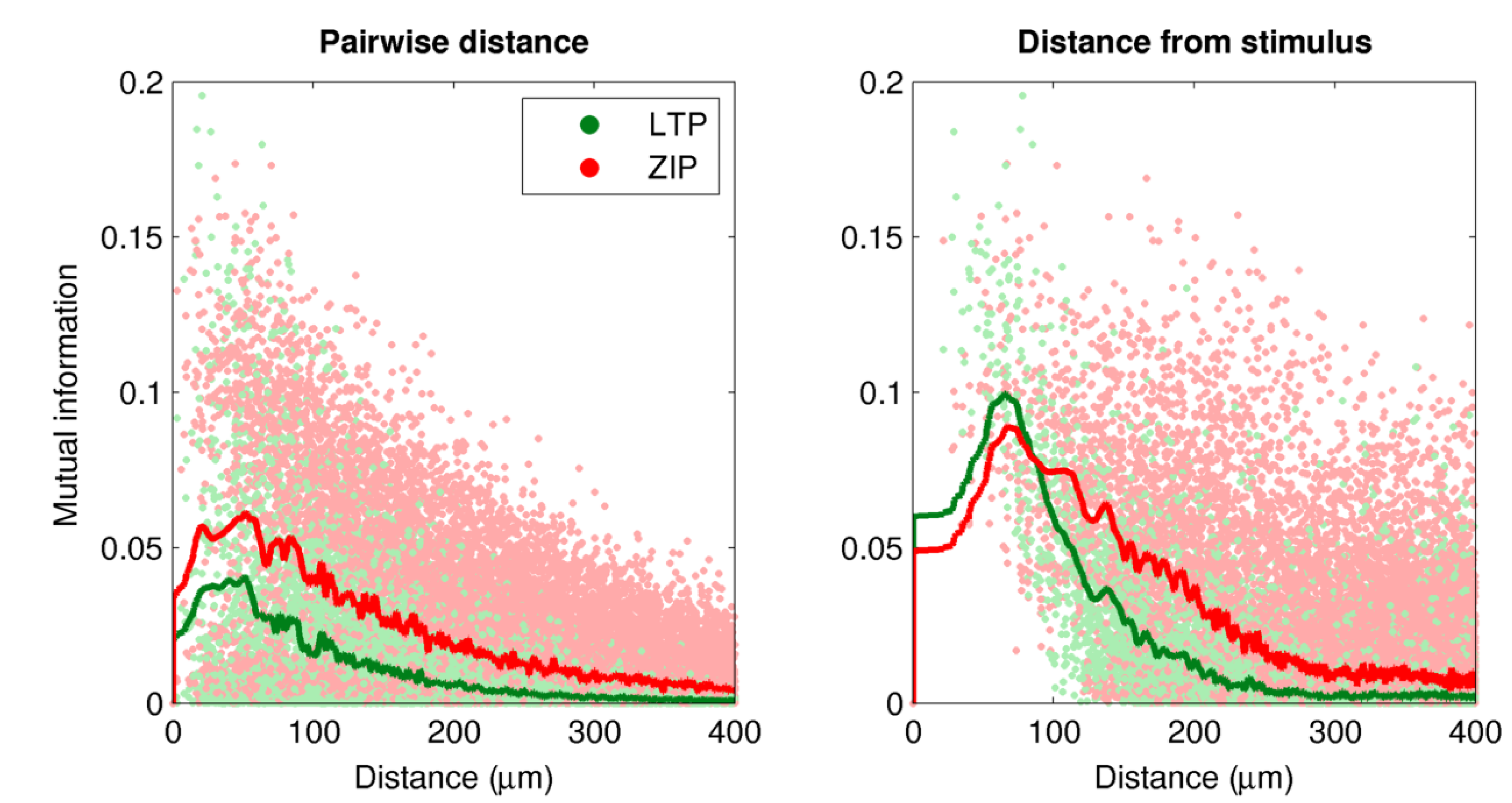


Fig. 6: Mutual information between pyramidal cell pairs in layer 2/3 in the simulation. Each dot represents a single pair of cells; lines show moving averages across multiple cell pairs. When cell pairs are sorted by their pairwise distance (left panel), mutual information is always higher in the ZIP condition, as a result of reduced lateral inhibition in the cortex. In contrast, when cell pairs are sorted by their distance from the center of the stimulus (right panel), mutual information near the stimulation site is higher in the LTP condition, indicating that LTP enhances focal information flow.

Acknowledgement

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

Further information

E-mail: cliffk@neurosim.downstate.edu
Web: neurosimlab.org