Role of Behavioral State-dependent Cortical Neurons in Local Processing

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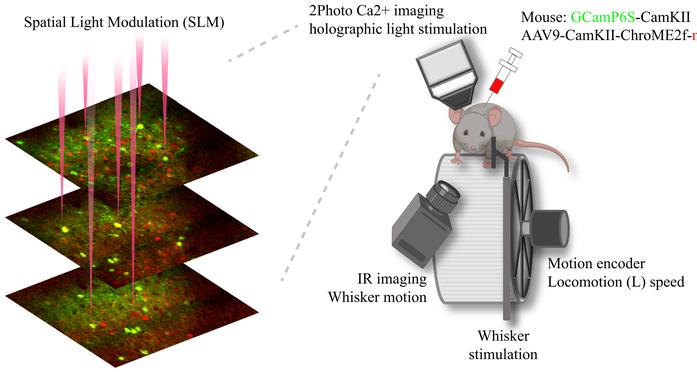
INTRODUCTION

Our recent work reveals distinct brain-wide presynaptic wiring patterns among functional defined neuron populations in somatosensory cortex: sensory cells and locomotion cells. Sensory cells exhibit strong passive response with whisker stimuli, while the locomotion cells encode animal's locomotor state and active whisker motion. These functional characteristics are both consistent and robust across days. Despite sharing similar local presynaptic connectivity pattern, locomotion cells received less input from motor cortex, and larger thalamic input, which is not simply driven by sensory feedback from whisker movements. These observations suggest that locomotion cells reliably convey behavioral state information to both the local network and other brain regions.

In this study, we investigate the specific contributions of locomotion cells to local processing and their influence on downstream targets within primary sensory cortex. To address this question, we monitor activities of excitatory neurons in layer 2/3 with two-photo calcium imaging, while selectively activate either locomotion cells or sensory cells with holographic light stimulation.

EXPERIMENTAL DESIGN AND METHODS

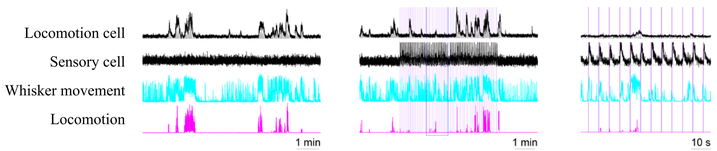
Identify different functional cell groups → Custermization of SLM Power for Single Cells → Activate functional groups of cells under different behaviors



This experimental framework allows us to examine how targeted manipulation of specific behavioral-state-dependent neuronal populations modulates intra- and inter-group neuronal dynamics across different behavioral states.

1 Neural acitivities during voluntary behavior

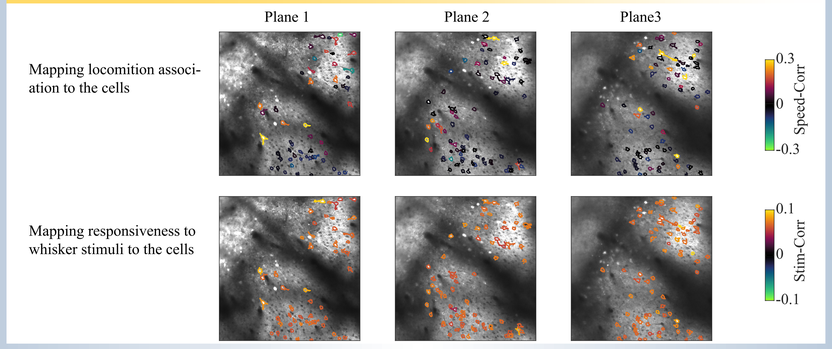
Diverse behaioral dependency of neural activities in primary somatosenory cortex (Layer 2/3)



Adapted from Inacio et al., Nature 2025

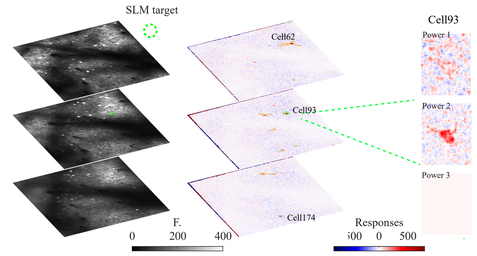
20 minutes recording during voluntary behavior, with 20 whisker stimulations. Quick processing of the imaging data using suite2p package

2. Identify behavioral dependency of all cells

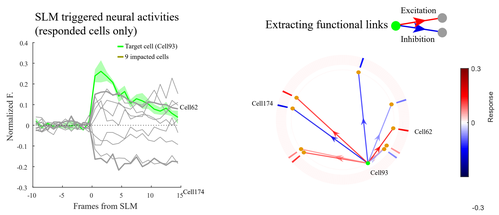


3 Custermization of SLM power for single cells

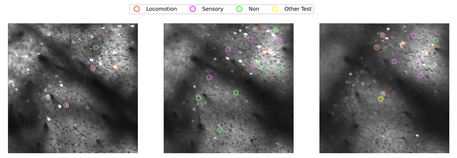
3.1 Choose minimal of the three stimulating power levels to significantly increase the target neural activities.



3.2 Confirm responsiveness of SLM target cell. Map functional connectivity

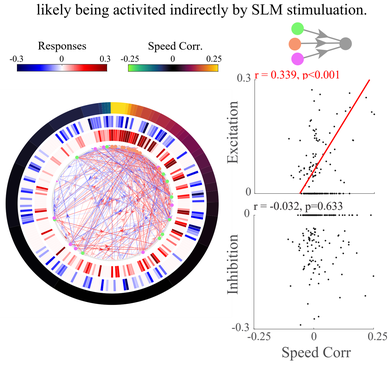


3.2 Identify three group of cells (10 cells/group), each cell has high responsive rate with SLM

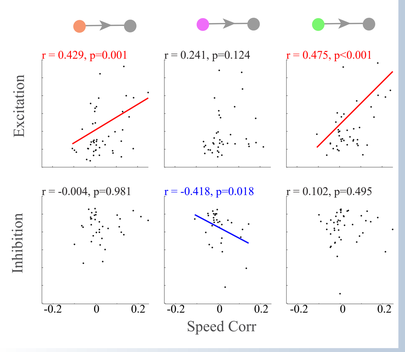


4 Integrative inputs from all cells to locomotion cells

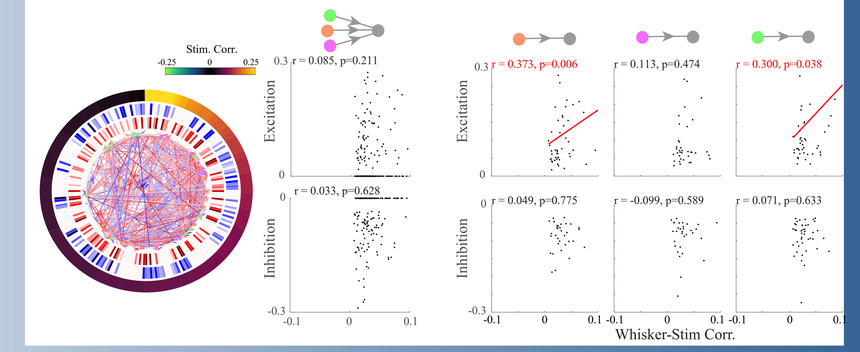
Cells with higher correlation with locomotion is more likely being activited indirectly by SLM stimuluation.



Break down by SLM target groups (responsive cells only)

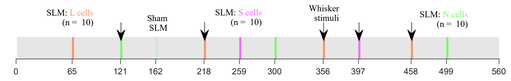


Much weaker activation dependency on whisker triggered cell responces.



5 Enhanced activities of locomotion-assocciate neurons by stimulating L group

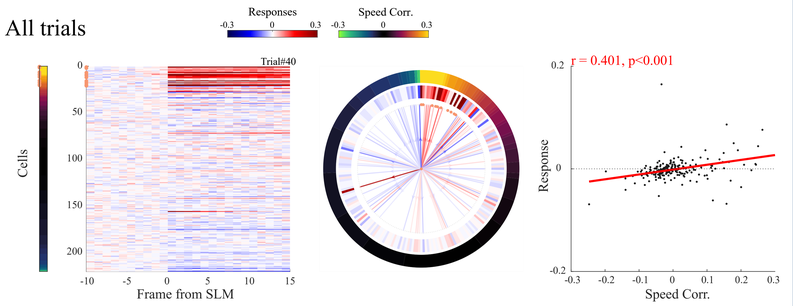
5.1 Randomized stimulating sequence during 2P recording



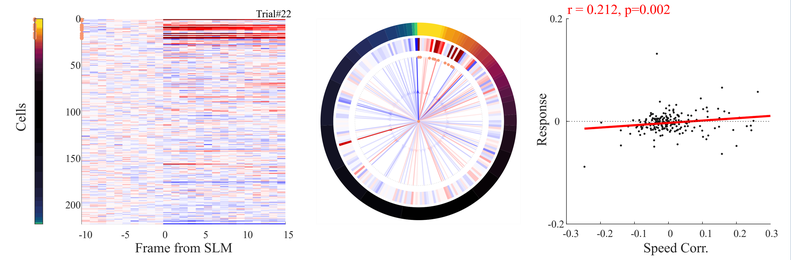
5.2 Cells response by stimulating L cells

SLM: L cells

All trials



Speed decreasing trials only



SUMMARY

1. We developed an experimental framework to examine how targeted manipulation of specific behavioral-state-dependent neuronal populations modulates intra- and inter-group neuronal dynamics across different behavioral states.
2. Primary results (1 animal) show locomotion-associated cells received local inputs broadly from other cell populations, with notably stronger inputs coming from L-cell group. Such connectivity pattern was not observed in sensory cells.
3. Optogenetic stimulation of a specific group of locomotion-associated cells significantly excited cells positively correlated with locomotion and simultaneously inhibited cells negatively correlated with locomotion.

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