Offsembles:
precise stimulus encoding by selective silencing of neurons

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PSTR223.02

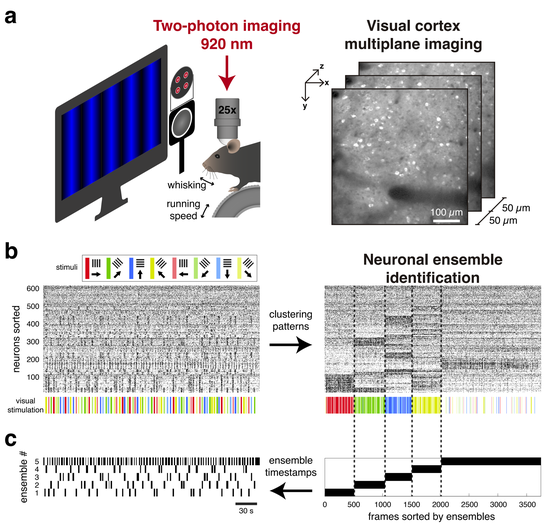
Introduction

Coactive groups of neurons, known as neuronal ensembles, are associated with motor, sensory, and cognitive functions. We have discovered that, when an ensemble is active, a group of neurons, which we term an "OFFsemble", becomes selectively supressed (Pérez-Ortega et al., Nat. Comm. 2024). Thus, each ensemble is composed of an ON and an OFFsemble. Here, we explore the properties and functional relevance of OFFsembles. We find that OFFsemble neurons are specifically inhibited during stimulus presentation and enhance the coding potential of ensembles.

We studied the neuronal population responses to drifting gratings in the mouse visual cortex. Our objectives are:

1. Detect neuronal ensembles usign an unsupervised method.
2. Identify ONsemble and OFFsemble neurons.
3. Compute orientation selectivity.
4. Evaluate the orientation predicting accuracy.
5. Characterize the neuronal composition of ensembles.

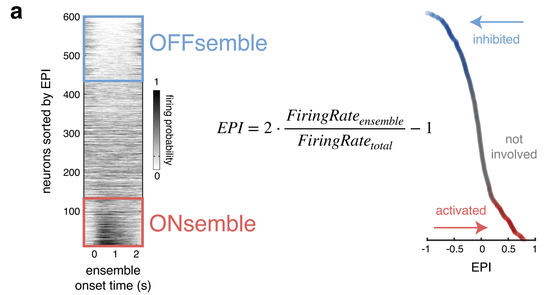
1. Ensemble detection using Xsembles2P



We performed volumetric two-photon calcium imaging in layer 2/3 of mouse primary visual cortex in vivo. Mice were head-fixed and free to run on a wheel in front of a screen displaying drifting gratings. We analyzed data from n = 12 mice.

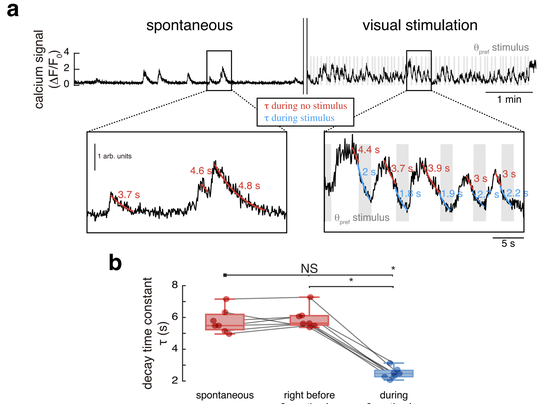
We use our software tool Xsembles2P to identify ensembles from calcium imaging videos. The steps are as follows: first, the software reads the calcium videos and performs registration. Next, it finds active neurons and extracts calcium signals, followed by spike inference to obtain population activity in the form of a binary raster. Finally, it applies an unsupervised method to find ensembles (ONsembles and OFFsembles) by clustering activity patterns and identifying neurons that are significantly activated or supressed.

2. Ensemble Participation Index (EPI)



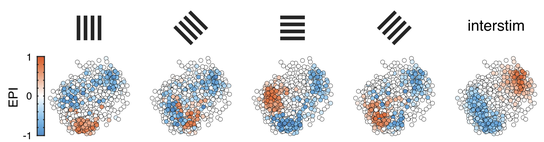
To quantify individual neuron participation within each ensemble we define an Ensemble Participation Index (EPI). We introduce the terms ONsemble to refer to a group of neurons simultaneously activated, and OFFsemble for a group of neurons simultaneously inhibited.

3. OFFsemble neurons specifically inhibited



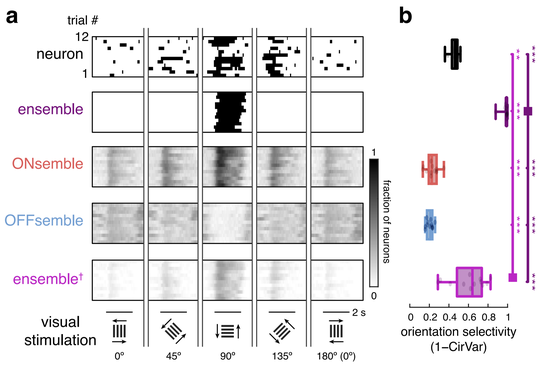
OFFsemble neurons had faster calcium decays during stimulus presentation, compared to other decays, indicating an active inhibitory mechanism. *p < 0.05

4. Graph representation of ensembles



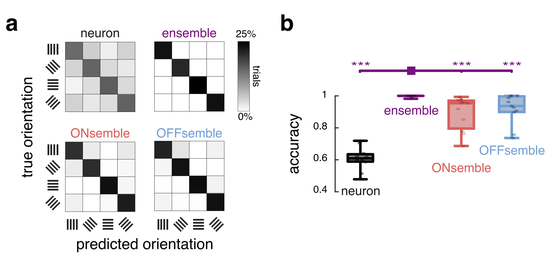
Neuronal ensembles are selectively tuned to specific orientations and interstimulus periods. In every ensemble, each neuron has an EPI value. Neurons can be part of multiple ONsembles and OFFsembles, and nonparticipants in one ensemble may actively participate in another.

5. Ensemble = ONsemble + OFFsemble



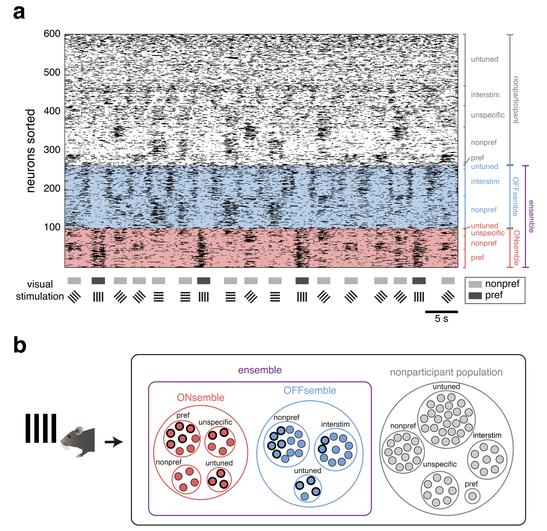
Neuronal ensembles exhibit higher orientation selectivity compared to individual tuned neurons, or even the summed activity of ONsemble neurons. In this study, we redefined neuronal ensembles to include specifically supressed groups of neurons, which we refer to as OFFsembles. **p < 0.01; ***p < 0.001

6. Offsembles enhance orientation encoding



Using confusion matrices, ONsembles and, surprisingly, also OFFsembles, had higher accuracy than individual sets of neurons. However, neuronal ensembles (ONsembles + OFFsembles) had overall superior accuracy. ***p < 0.001

7. Diverse neuronal tuning in an ensemble



Neuronal ensembles had neurons with different tuning properties, belonging to five distinct categories, as neurons preferring: the same orientation ("pref"), different orientations ("nonpref"), multiple orientations ("unspecific"), interstimulus periods ("interstim"), or no significant tuning ("untuned"). The tuning properties of individual neurons within an ensemble, combined with the sharing of neurons across ensembles, demonstrate that diverse types of neurons process visual stimuli.

Conclusion

Cortical circuits use both ONsembles (activation) and OFFsembles (inhibition) to encode information. This suggests that neural circuits involved in perception use an emergent distributed code.

Funding: The Revson Foundation (No. 22-21), NINDS (RM1NS132981), NIMH (R01MH115900), NSF (2203119), The Vannevar Bush Faculty Award (ONR N000142012828), and NEI (F32EY029161, K99EY033974).

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