

Embedding Analysis of Neuron Responses under Various Stimuli in Vision Systems

Huimiao Chen
Apr 11, 2025

Background

Retinal and cortical population encoding differ

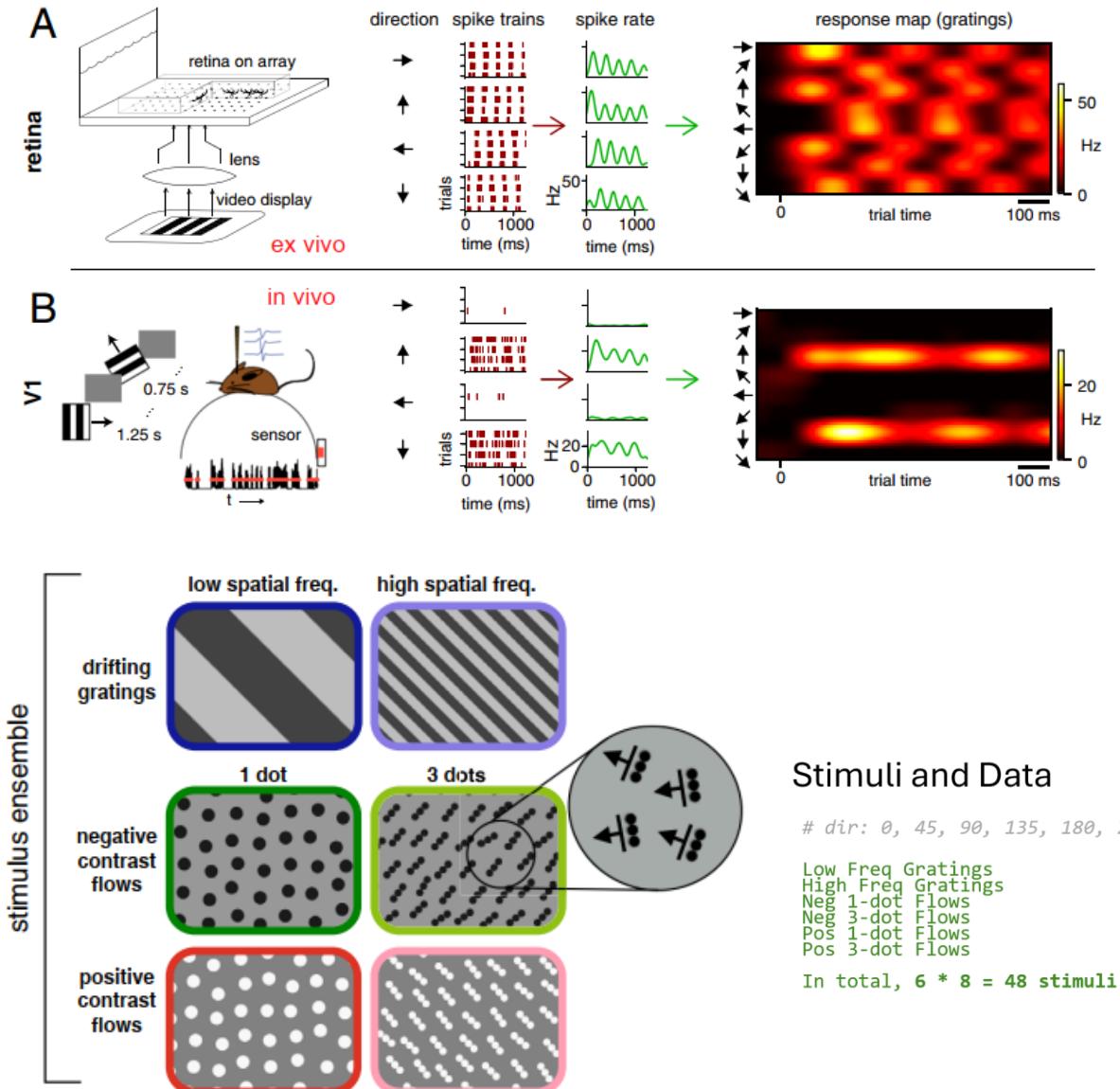
The retina consists of approximately 40 distinct types of retinal ganglion cells (RGCs), which encode visual features in a discrete manner.

In contrast, neurons in the primary visual cortex (V1) are thought to encode visual features more continuously.

This study proposes and applies an encoding manifold method to demonstrate that.

Neural responses to a common set of stimuli (drifting gratings and optical flows) were recorded from both the retina and V1.

The encoding manifold was constructed using non-negative tensor factorization (NMF) and diffusion maps, showing how neurons are organized in stimulus-response space.



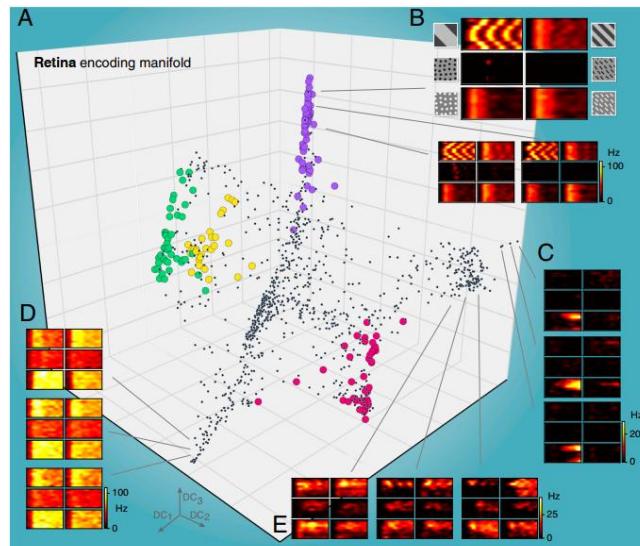
Retina: Discrete clusters; V1: Continuous encoding

Key Findings

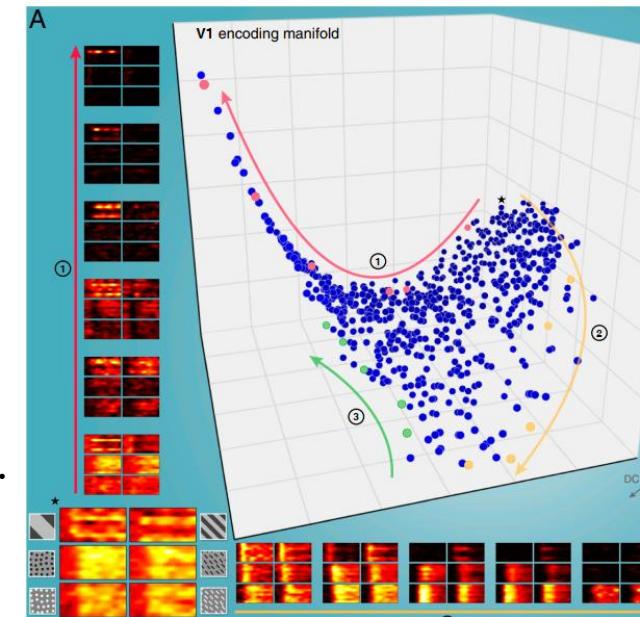
The retinal RGC encoding manifold shows clear clustering, with each cluster corresponding to a specific functional type.

The V1 neuron encoding manifold is continuously distributed, with feature selectivity and response dynamics varying smoothly across the manifold.

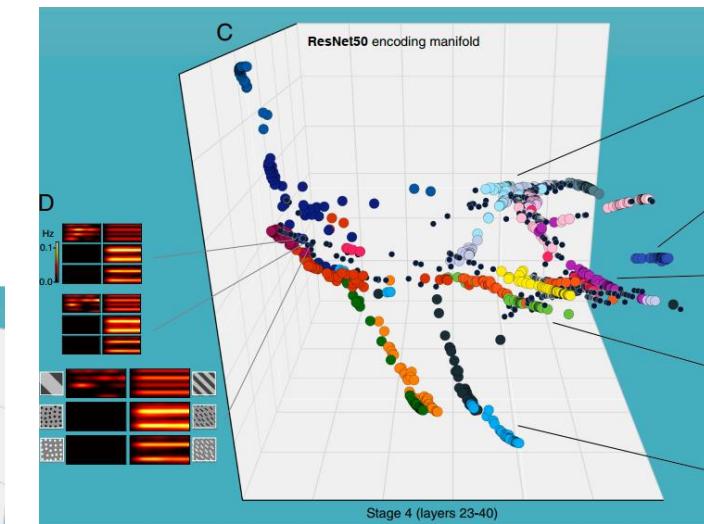
Convolutional neural networks (CNNs), such as ResNet50, were also tested. The encoding manifolds of CNNs were found to be highly clustered, even more discrete than the retina, and unlike V1.



Retinal neurons' encoding manifold showing **discrete clusters**.

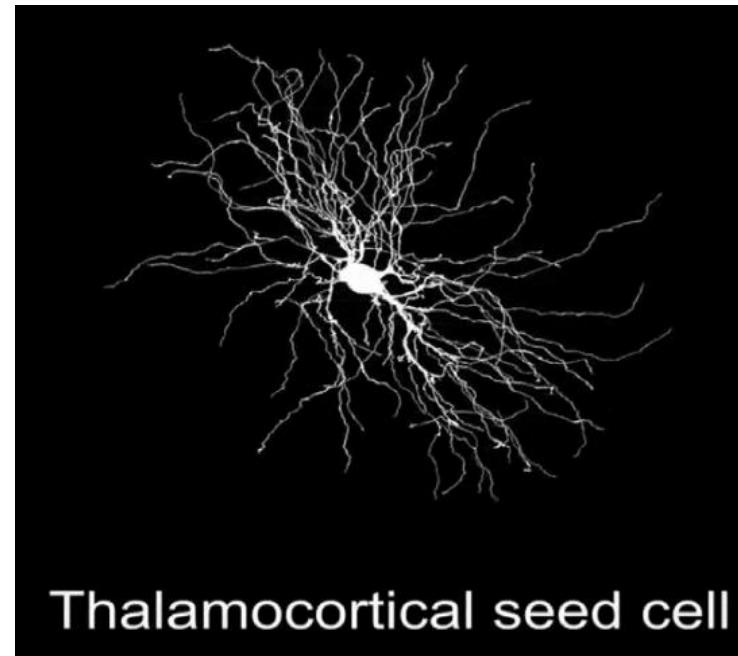
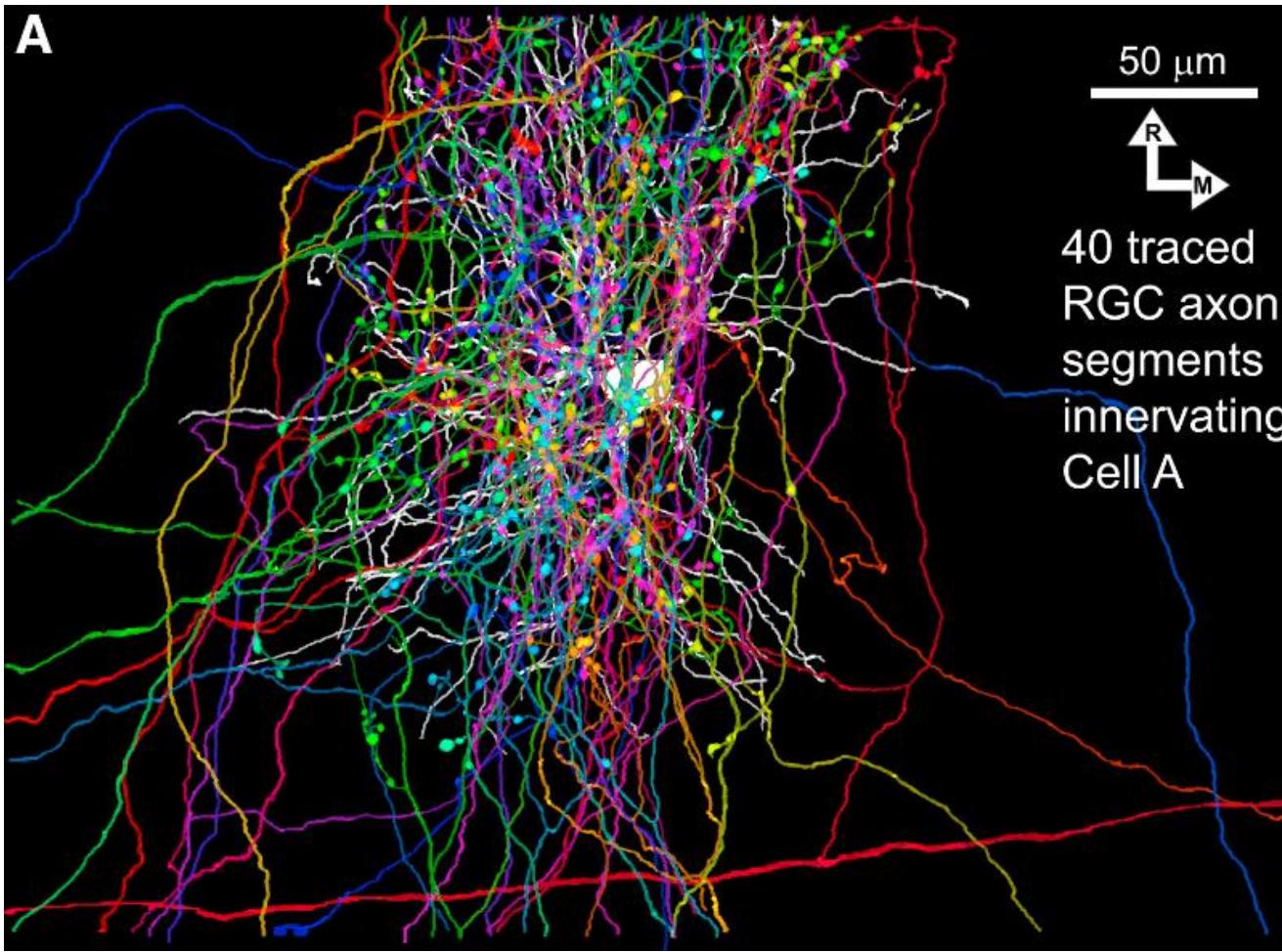


V1 neurons' encoding manifold showing a **continuous distribution**.



ResNet50 network's encoding manifold showing **strong clustering**.

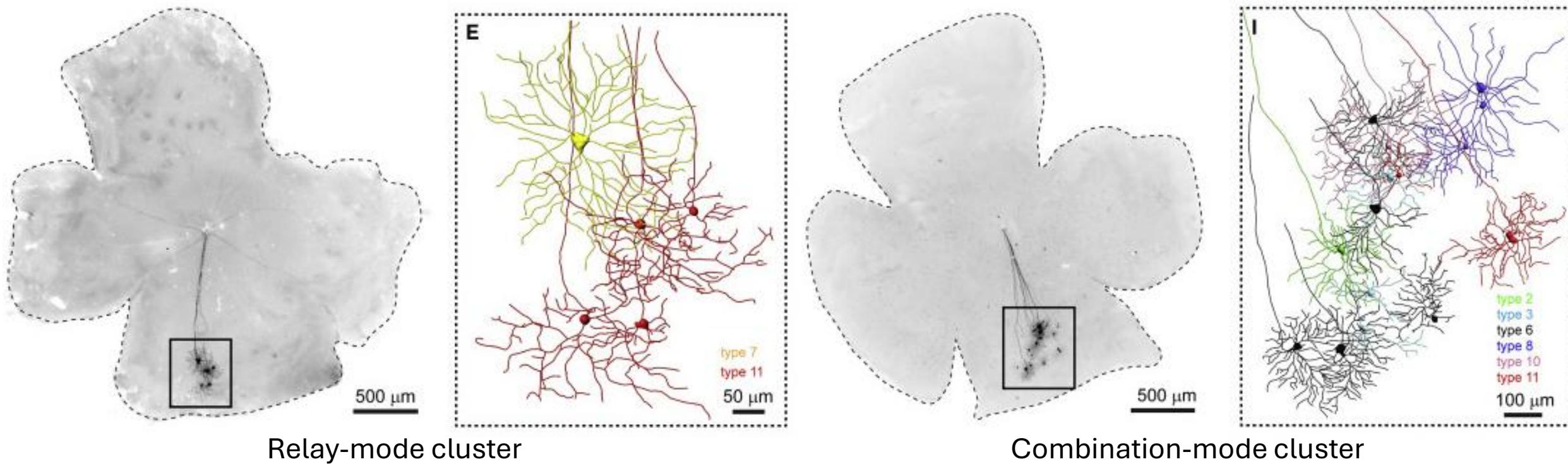
Tens of RGCs can converge to a single dLGN neuron



A single dLGN neuron (white) receives input from ~40 RGC axon segments (different colors).

Retrograde tracing shows inputs from multiple morphologically distinct RGC types.

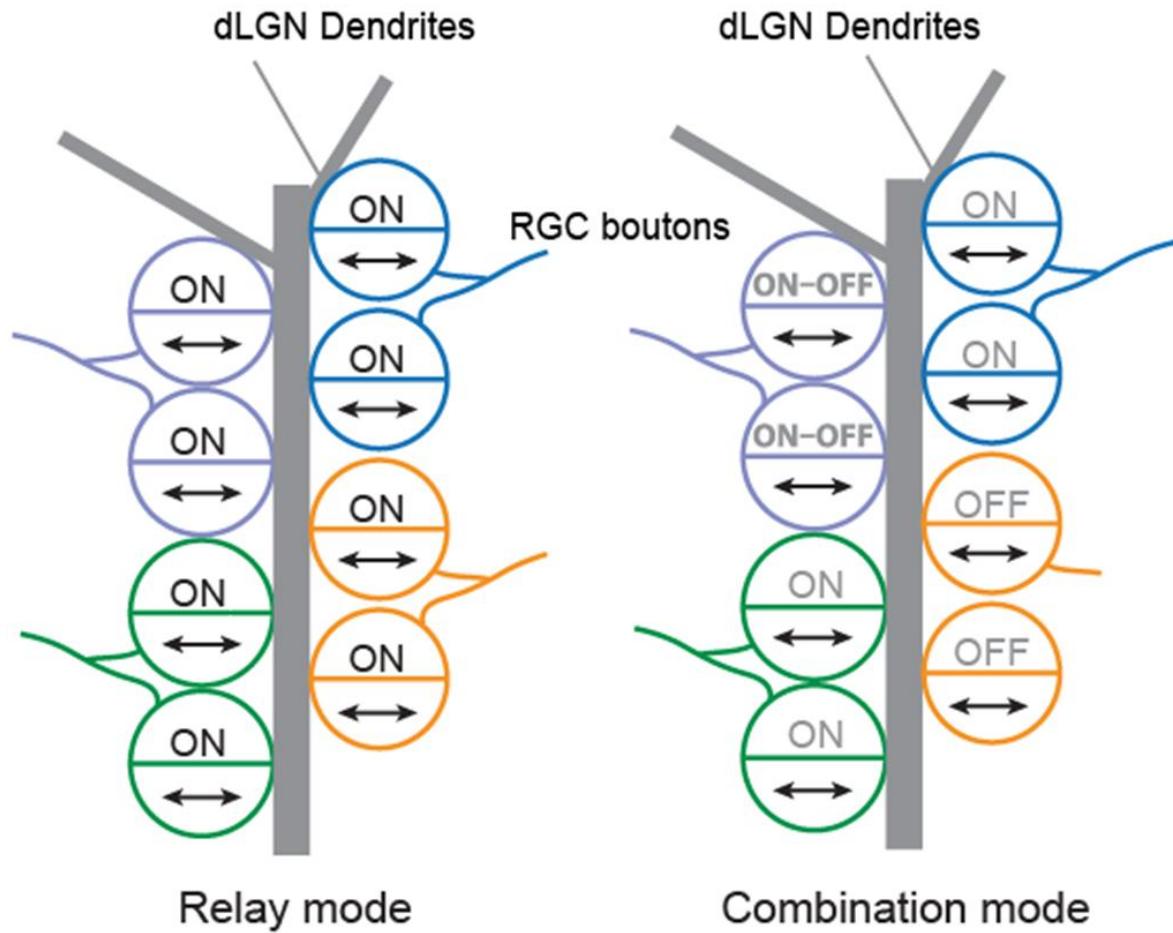
dLGN cells integrate retinal inputs in relay and combination mode



In addition to labeled-line connections (single RGC type), combination-mode connections (multiple RGC types) were observed.

More monocular LGN cells (8/15) received inputs from 2–6 different RGC types.

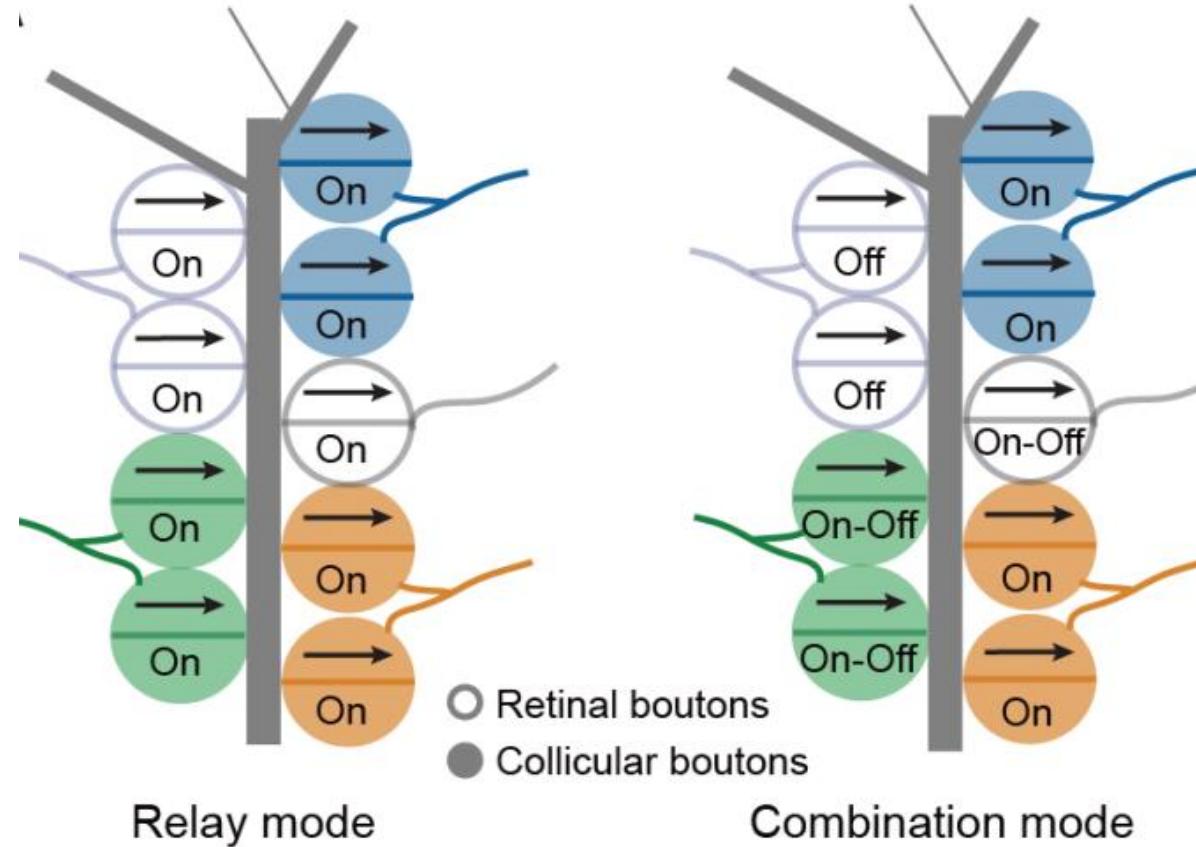
Nearby RGC boutons share one or several similar visual feature preference



Visual responses of RGC boutons in dLGN show local clustering by feature preference.

Nearby boutons tend to prefer similar visual features, beyond coarse retinotopy.

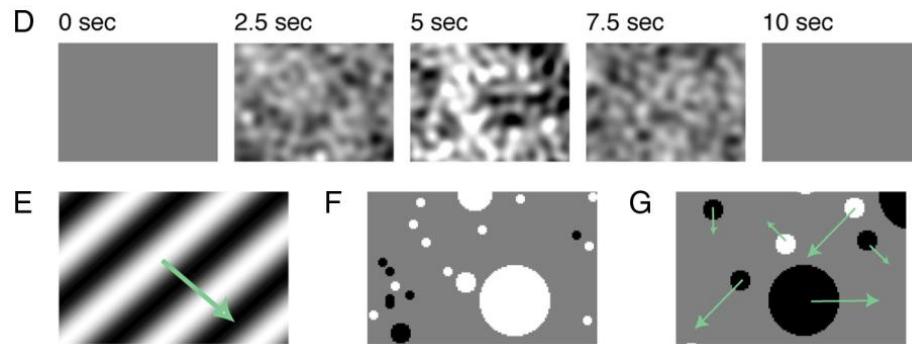
Nearby RGC boutons share one or several similar visual feature preference



Relay mode: nearby boutons share preferences for a single feature

Combination mode: nearby boutons exhibit similar preferences for multiple features between retinal and collicular boutons.

Functional Diversity of dLGN Neurons



Four stimulus sets used for visual response characterization. **D**, Contrast modulated band-limited noise. **E**, Drifting sinusoidal gratings. **F**, Flashing spots. **G**, Moving spots.

Denise M. Piscopo

Unsupervised clustering (k-means) based on responses to flashes, drifting gratings, and noise movies.

7 Discrete Cell Types Identified:

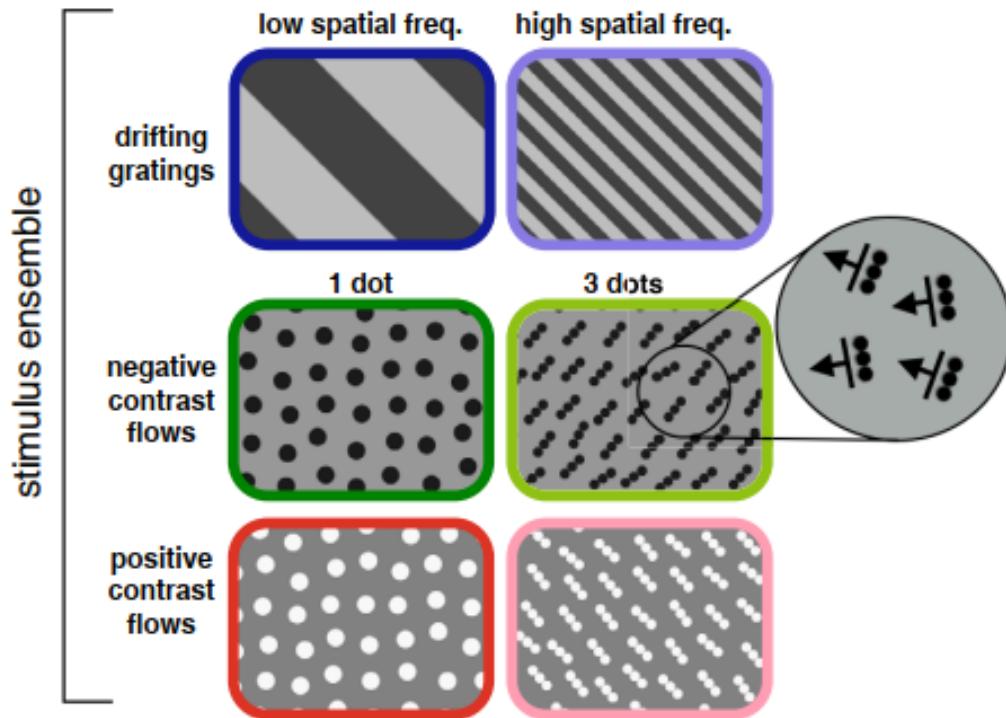
- **ON sustained:** Persistent response to bright stimuli
- **OFF sustained:** Persistent response to dark stimuli
- **ON transient:** Brief response to bright stimuli
- **OFF transient:** Brief response to dark stimuli
- **ON-OFF:** Responsive to both bright and dark stimuli
- **Suppressed-by-contrast:** Reduced activity during stimulus
- **Orientation/Direction selective (OS/DS):** Selective for stimulus orientation or direction

Hypothesis on dLGN Cell Type Organization

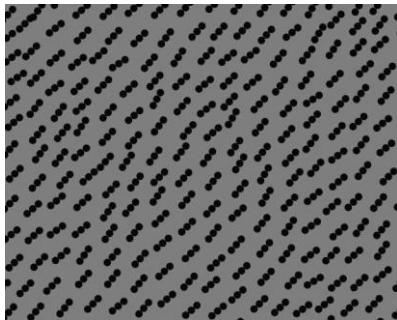
We hypothesize that dLGN neurons are not as discretely organized into cell types as RGCs.

Instead, dLGN may exhibit a more continuous distribution of response properties, resembling an intermediate stage between the discrete organization in the retina and the continuous representations in V1.

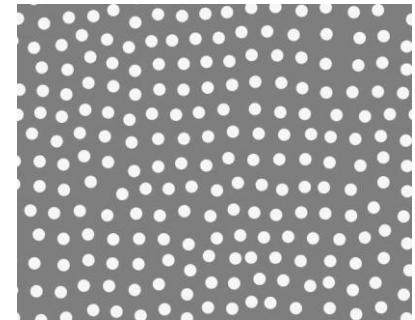
Data, Methods, Results



Luciano et al., 2024



neg_3flows_315



pos_1flows_225



gratings_lf_45

Stimuli and Data

dir: 0, 45, 90, 135, 180, 225, 270

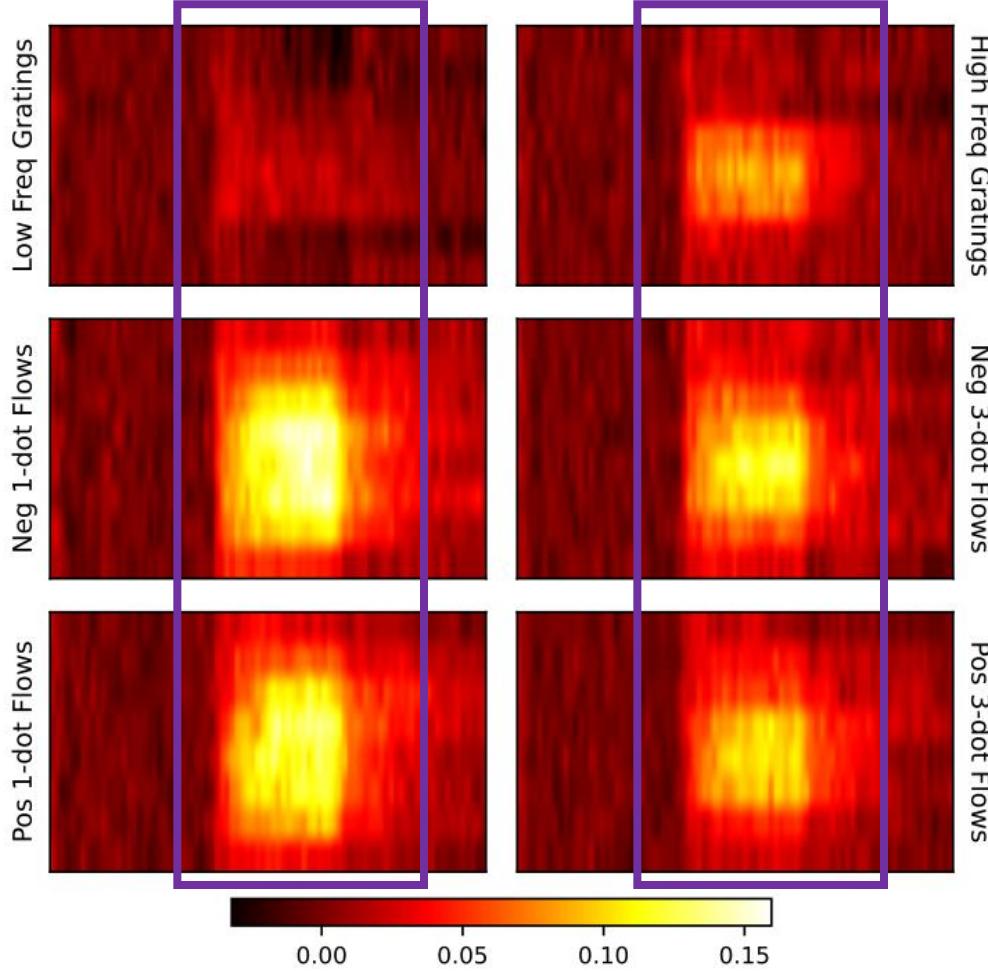
Low Freq Gratings
High Freq Gratings
Neg 1-dot Flows
Neg 3-dot Flows
Pos 1-dot Flows
Pos 3-dot Flows

In total, $6 * 8 = 48$ stimuli

Flow stimuli were chosen because they mimic certain features of naturalistic stimuli, and previous work has shown that they engage nonlinearities in V1 that are not predicted based on the responses to gratings.

Luciano et al., 2018

Example Response Map of a Neuron



85 frames is 2s off + 1.5s on + 2s off

1-31 frames are stimulus off,
32-54 frames are stimulus on, and
55-85 frames are stimulus off

For our data, we remove some frames to do analysis.

remove first 1.5s pre-inter-trial and last 1s post-inter-trial;

use **0.5s pre-inter-trial + 1.5s trial + 1s post-inter-trial**.

Methods

1. Data processing
2. Tensor decomposition
3. Diffusion maps
4. Post-analysis like HDBSCAN.

Indices for Neuron

Selectivity indices for various visual features (Fig. 4b–e) were computed as follows. Let the maximum response (instantaneous mean firing rate) to any of the grating stimuli (flow stimuli, respectively) be denoted as G_{\max} (F_{\max} , resp.). A **grating selectivity index** for a given neuron was computed as the ratio $G_{\max}/(G_{\max} + F_{\max})$.

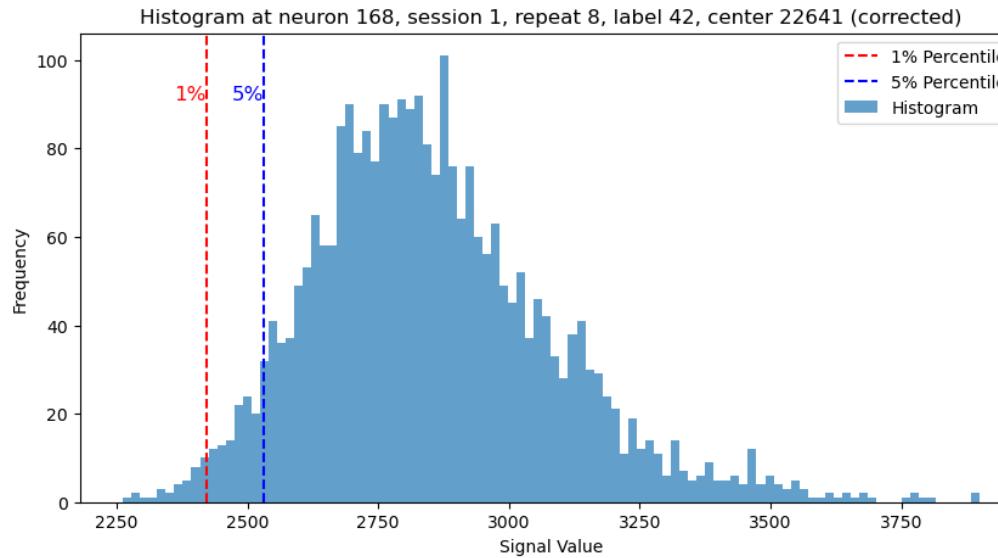
Let the relative response magnitude of a neuron to a given stimulus be defined as the ratio between its maximum response to that stimulus and its maximum response to any stimulus (therefore yielding a number between 0 and 1). Defining P_{rel} (N_{rel} , resp.) as the relative magnitude of a neuron's response to any positive contrast flow (negative contrast flow, resp.), a **flow polarity index** was computed as the difference $P_{\text{rel}} - N_{\text{rel}}$.

A **stimulus entropy index** was defined as 2^H , where H is the base-2 entropy of the vector containing the relative response magnitudes of a neuron to the 6 stimulus classes used in the experiments (divided by their sum). It therefore ranges between 0 (case in which the neuron responds to a single stimulus) and 6 (when it responds with uniform magnitude to all stimuli).

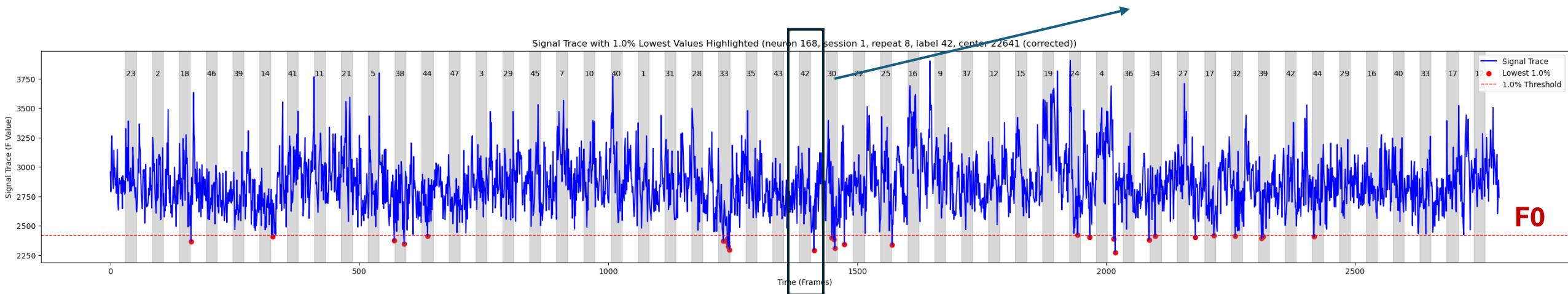
For firing rate data (positive data) and not considering suppressed cells

New normalization makes all dFF positive

neuron 168 (some negative response)



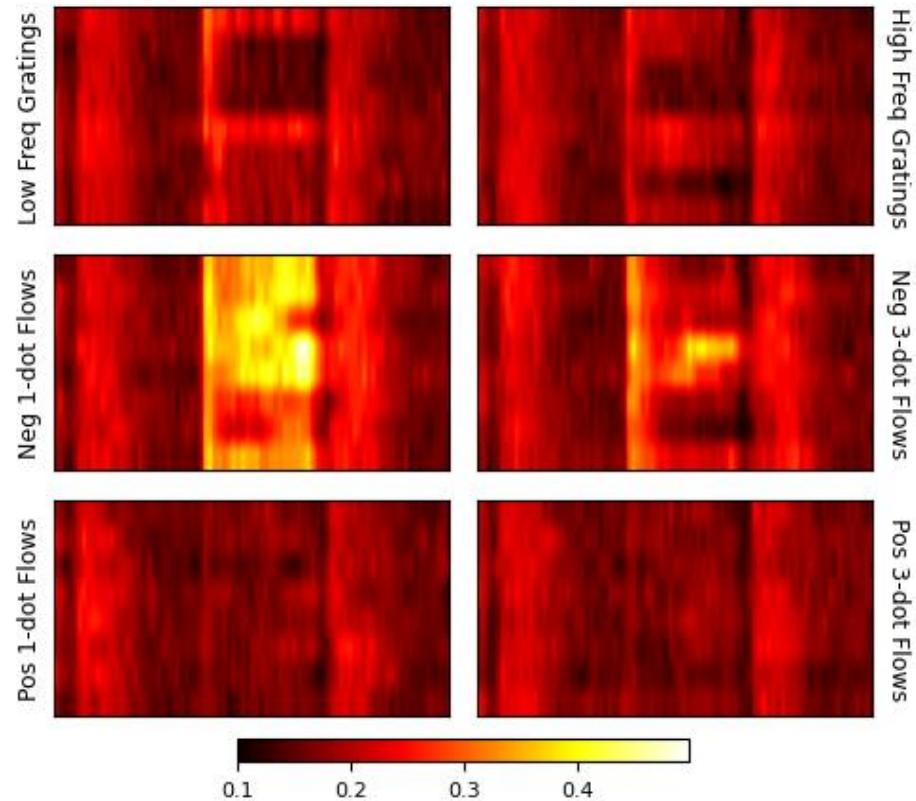
New $dF/F = (F - F_0) / F_0$
If negative (red points), let it be 0.



We use 5% lowest line as the baseline of F0 in data process.

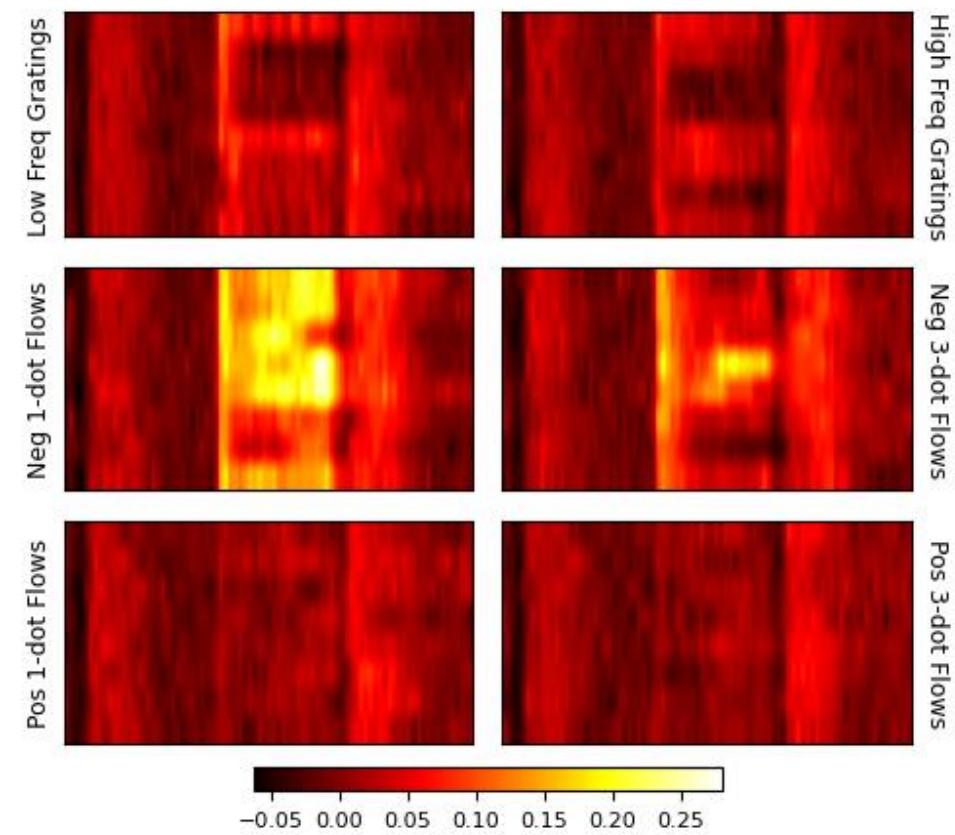
neuron 168 (negative response)

Neuron Response Heatmap (neuron idx: 168, newNorm)



New response map after
new norm (percentile 1%)

Neuron Response Heatmap (neuron index: 168)



Old response map

Definitions of indices (for our data)

$$\text{Grating Selectivity Index} = \frac{\Delta R_g - \Delta R_f}{|\Delta R_g| + |\Delta R_f|}$$

$$\text{Flow Polarity Index} = \frac{\Delta R_{\text{pf}} - \Delta R_{\text{nf}}}{|\Delta R_{\text{pf}}| + |\Delta R_{\text{nf}}|}$$

The Grating Selectivity Index measures the neuron's relative preference between grating and flow stimuli.

Its absolute value reflects the strength of selectivity.

The Flow Polarity Index measures the neuron's relative preference between positive and negative flow stimuli.

Its absolute value reflects the strength of polarity selectivity.

Stimulus Entropy Index

Step 1: Relative Response Magnitude

$$r_i = \frac{|\Delta R_i|}{|\Delta R_{\text{all}}|}$$

Step 2: Normalization to Probabilities

$$p_i = \frac{r_i}{\sum_{j=1}^6 r_j}$$

Step 3: Entropy Calculation

$$H = - \sum_{i=1}^6 p_i \log_2 p_i$$

Step 4: Stimulus Entropy Index

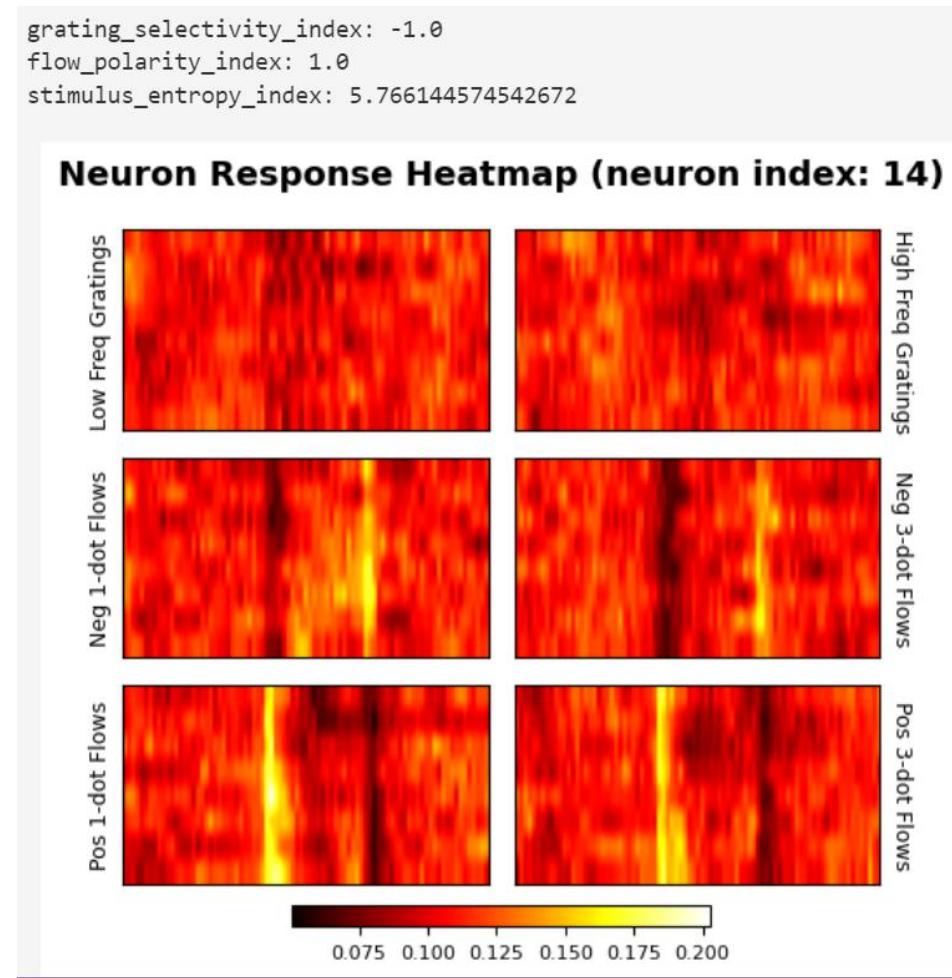
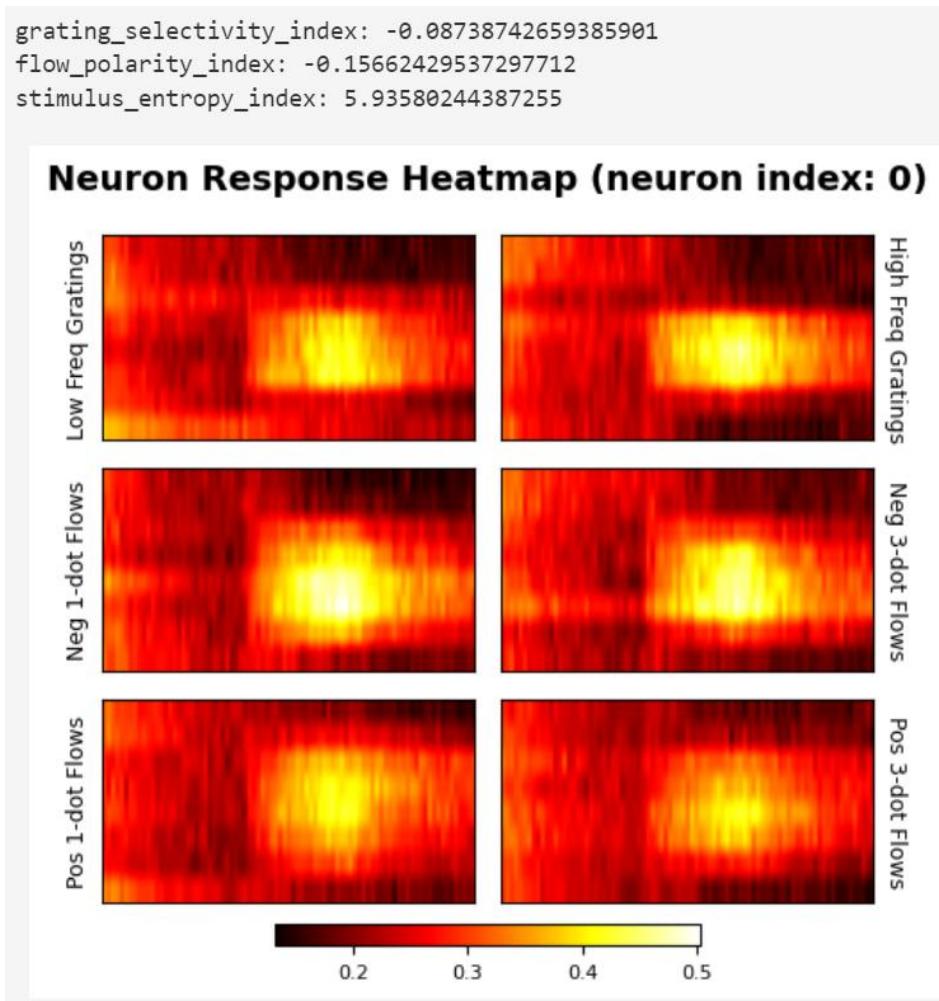
$$\text{Stimulus Entropy Index} = 2^H \quad \text{Ranges from 1 to 6}$$

Higher stimulus specificity: An index close to 1 indicates strong selectivity — the neuron responds strongly to a specific stimulus and weakly (or not at all) to others.

Uniform responses: An index close to 6 indicates no selectivity — the neuron has similar amplitudes across all six stimuli.

Note: the index only reflects the response magnitudes only. It does not distinguish the signs of responses.

Examples of neurons and their indices (our data, dLGN)



Suppressed neurons definition:

Find at least **one** stim with at least **one** direction:

- 1) QI > 0.3
- 2) 1/3 points during Trail with values < baseline mean - 2.5 baseline std

And

No positive response for this neuron.

Positive response means:

for the neuron we can find at least **one** stim with at least **one** direction:

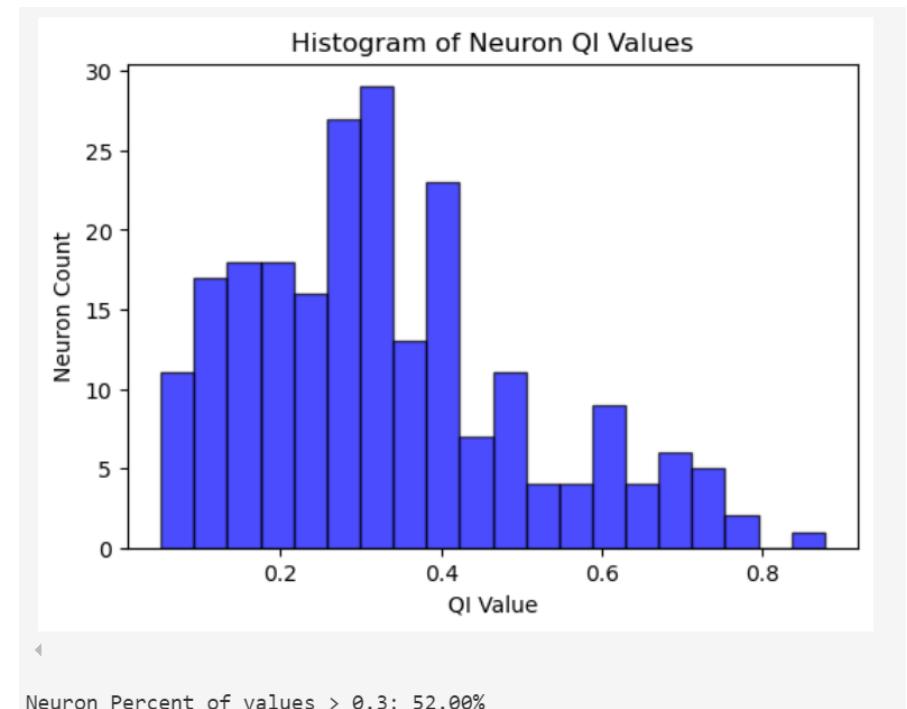
- 1) QI > 0.3
- 2) 1/3 points during Trail with values > baseline mean + 2.5 baseline std

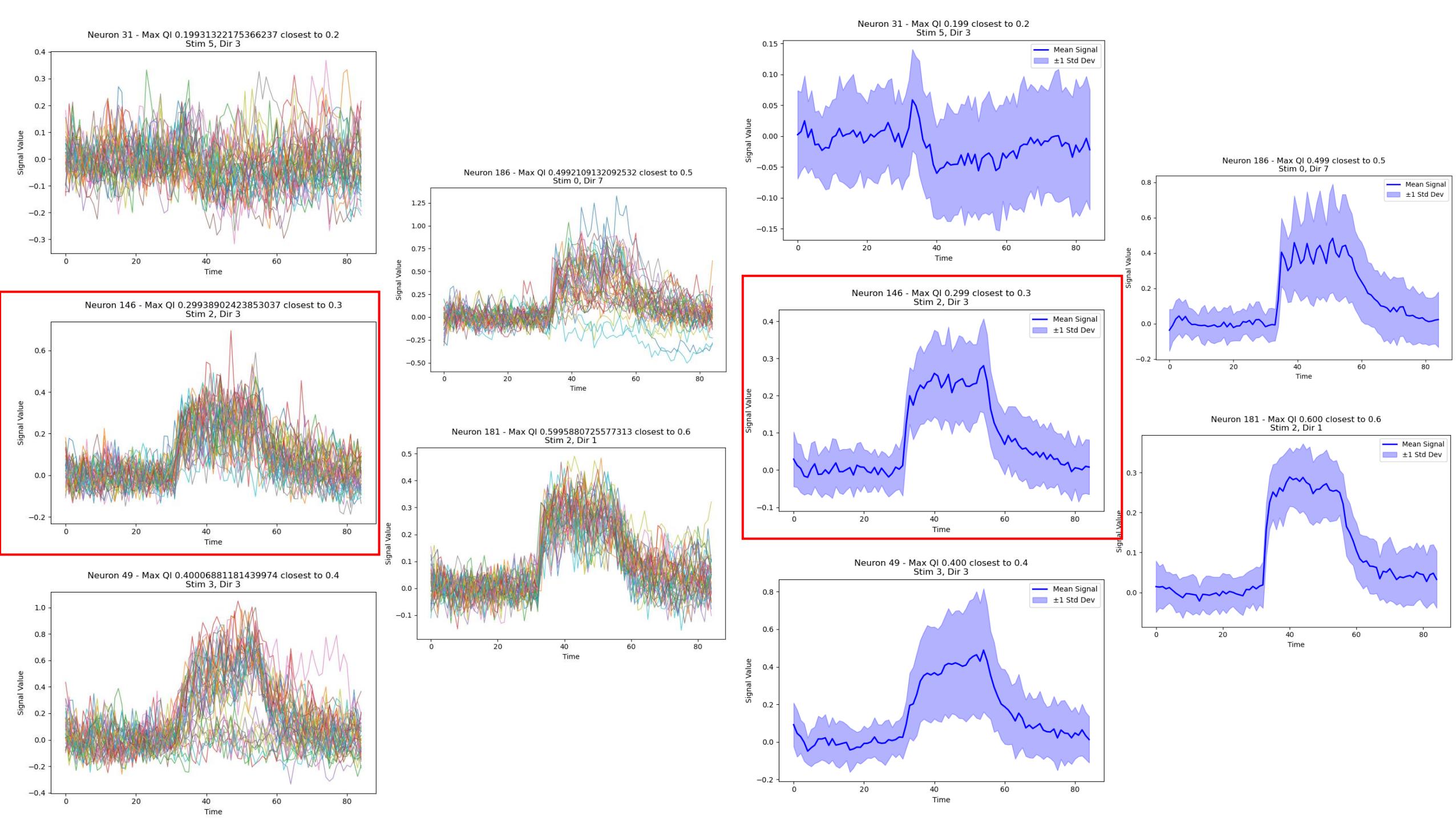
QI (quality index) calculation:

```
QI = var(mean(mat, axis=0)) / mean(var(mat, axis=1))
```

```
# QI = var of mean of repeats / mean of var of time
```

(Baden et al. *The functional diversity of retinal ganglion cells, 2016.*)

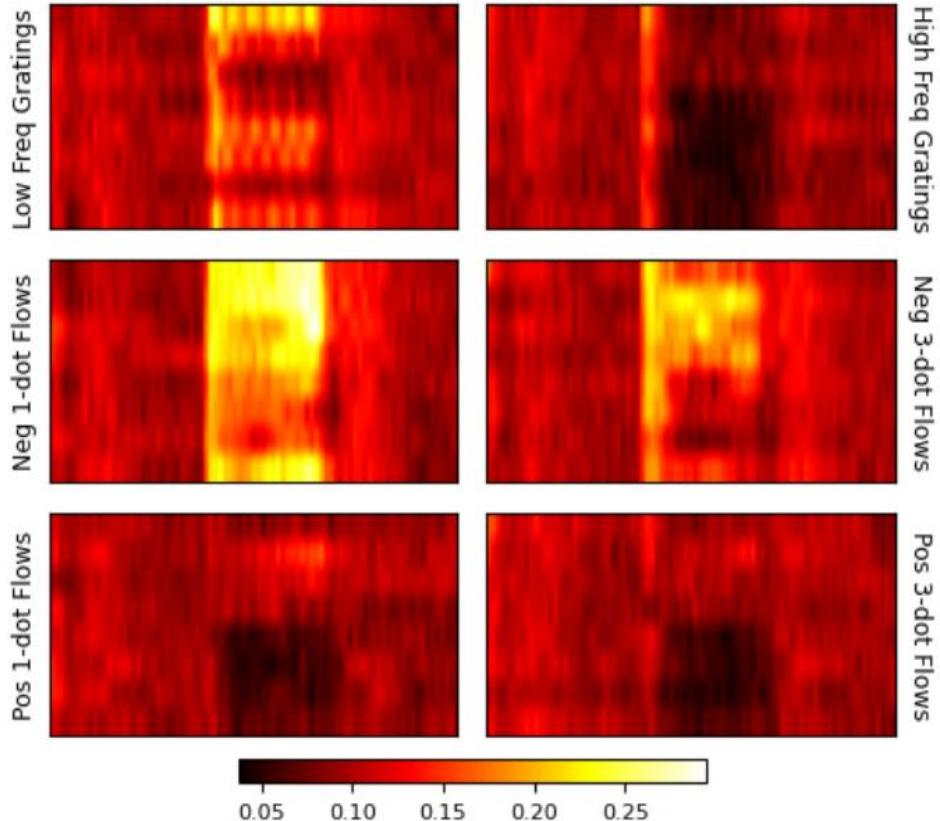




Found Neurons 122, 187, 212, 216, 221, 224 are suppressed. 6 out of 225 neurons

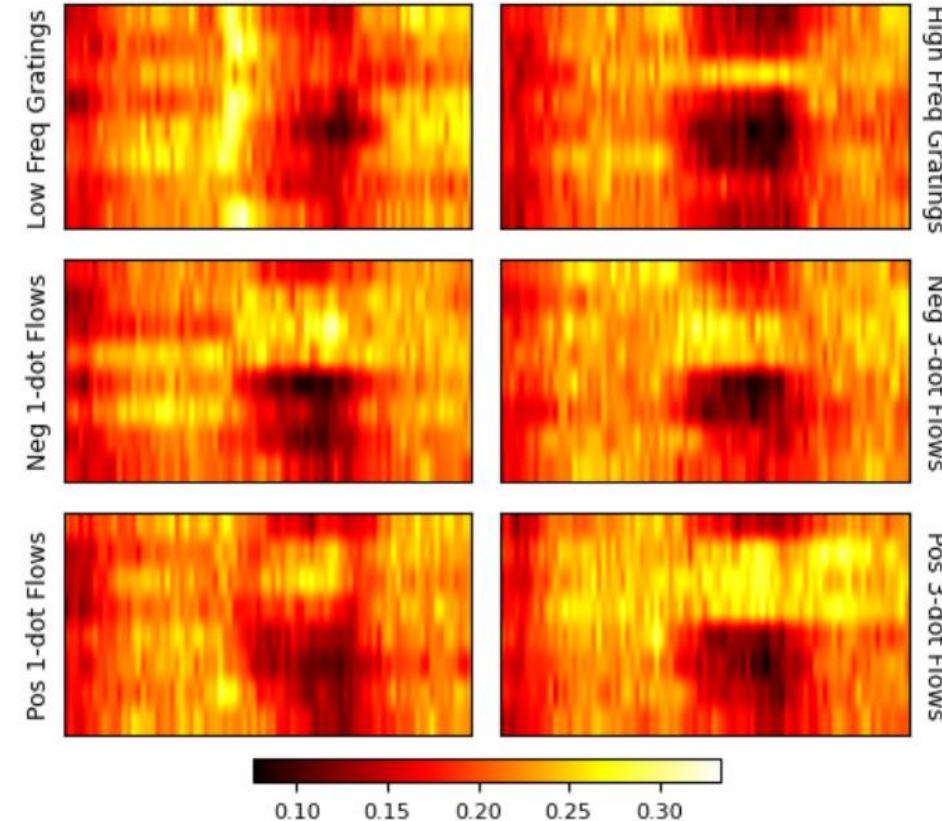
grating_selectivity_index: -0.09911803627733602
flow_polarity_index: -0.5336659007463342
stimulus_entropy_index: 5.386756488057938

Neuron Response Heatmap (neuron index: 122)



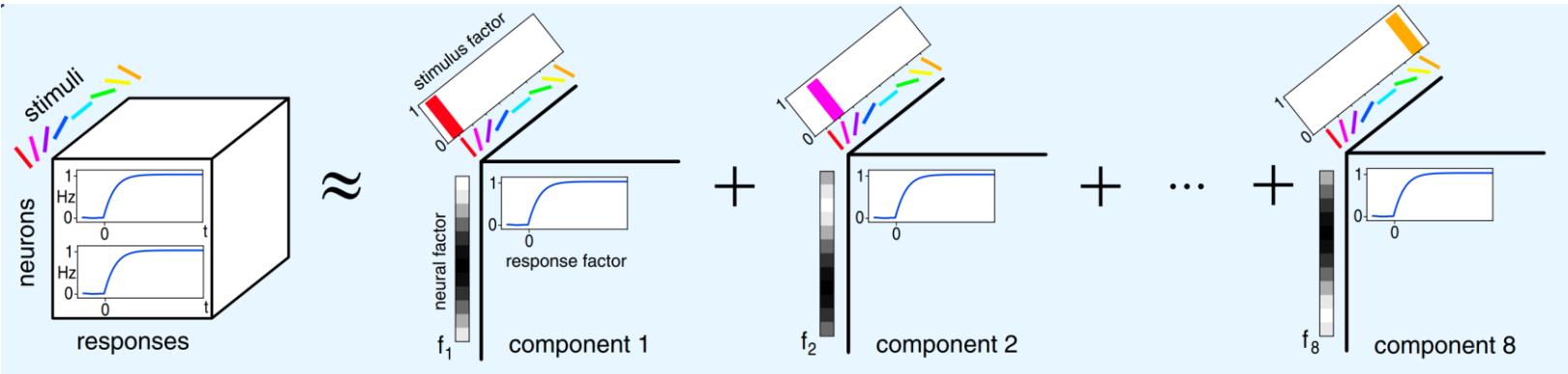
grating_selectivity_index: 0.008571895387512438
flow_polarity_index: 0.037486757551371576
stimulus_entropy_index: 5.98418084198213

Neuron Response Heatmap (neuron index: 187)



Manifold Embedding

Tensor Decomposition



Data here is a 3-D tensor (traces):
Neurons, Stimuli, Responses.

Neural factors: How each neuron responds to different stimuli.

Stimulus factors: The components of the stimuli that drive the neural responses.

Response factors: The temporal dynamics of the neural responses.

L. Dyballa et al 2024

- **Neuron factor matrix** $N \in \mathbb{R}^{I \times R}$,
- **Stimulus factor matrix** $S \in \mathbb{R}^{J \times R}$,
- **Response factor matrix** $R \in \mathbb{R}^{K \times R}$,

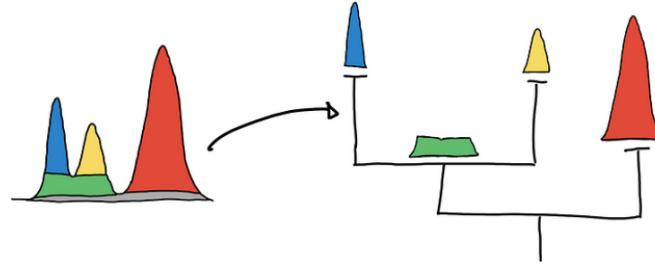
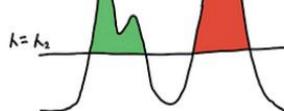
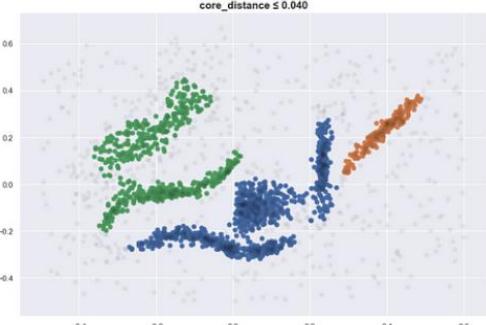
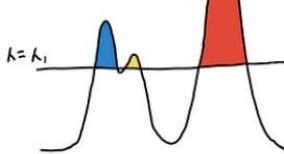
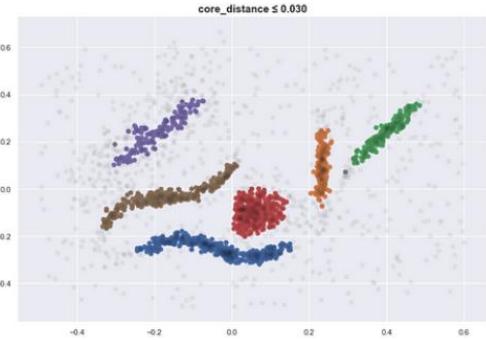
where R is the rank of the decomposition (i.e., the number of hidden components), and the number of columns R represents the number of latent factors.

$$\min_{N,S,R} \frac{1}{2} \|T - \sum_{r=1}^R N(:,r) \circ S(:,r) \circ R(:,r)\|_F^2$$

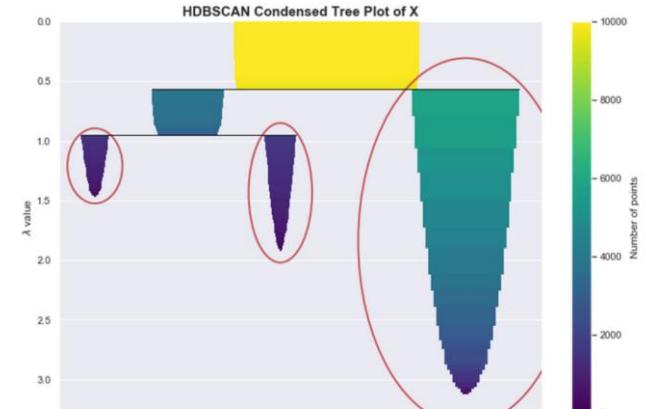
Then go through diffusion Map step, the basic idea of diffusion maps is making neurons with short distance closer and neurons with larger distance farther, based on some connection changes and iterations in the graph of neurons.

HDBSCAN (Hierarchical Density-Based Spatial Clustering of Applications with Noise)

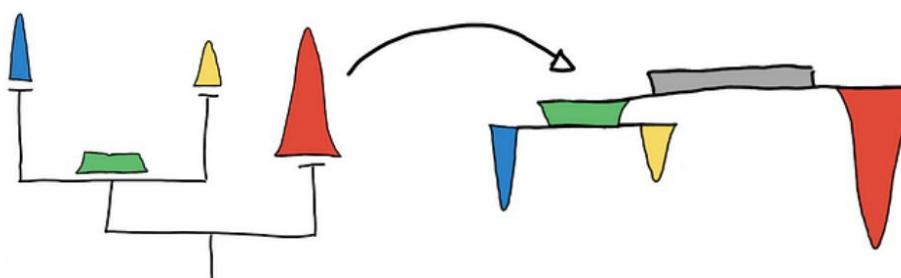
Used to see how discrete the neurons on final diffusion maps



Visualizing the cluster hierarchies as a tree



Condensed tree plot from HDBSCAN



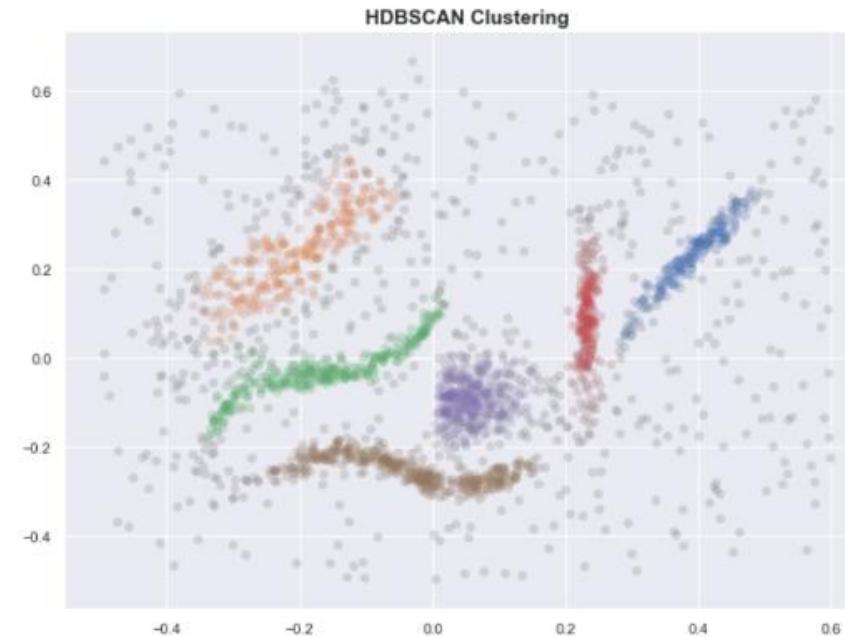
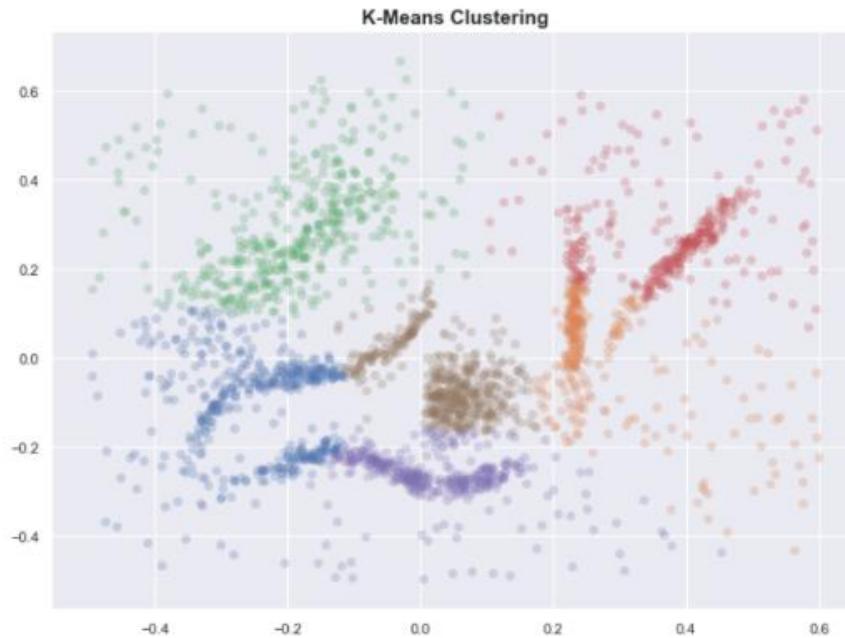
Visualizing the tree top-down

$$\lambda = \frac{1}{\text{core distance}}$$

<https://pberba.github.io/stats/2020/01/17/hdbscan/>

- **A larger λ value (Low Core Distance):**
higher density, meaning the point belongs to a more tightly clustered region.
- **A smaller λ value (High Core Distance):**
lower density, meaning the point is in a sparser region and may be separated earlier.

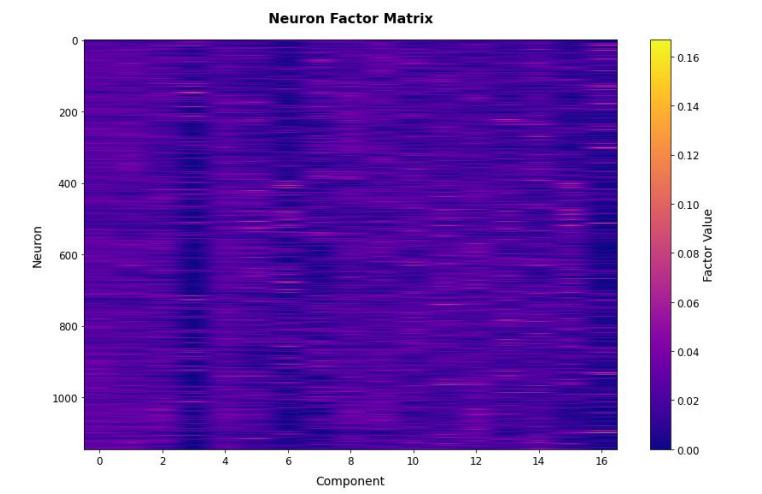
K-means vs HDBSCAN



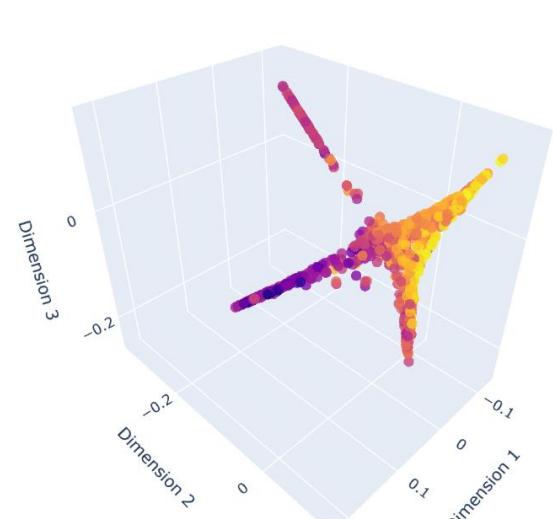
- “round” or spherical
- equally sized
- equally dense
- most dense in the center of the sphere
- not contaminated by noise/outliers

**More flexible shape
Can have outliers (noise)**

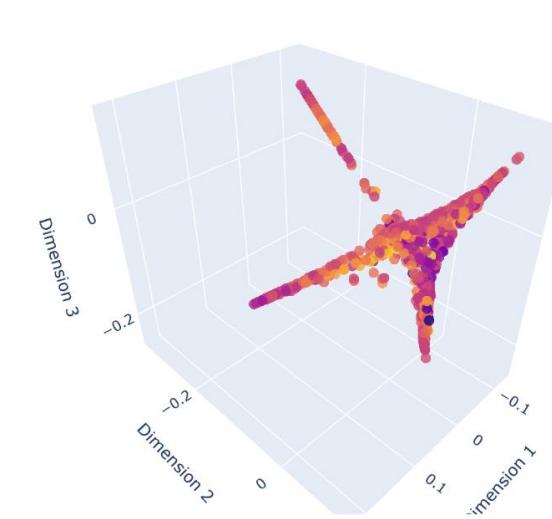
Retina (public data)



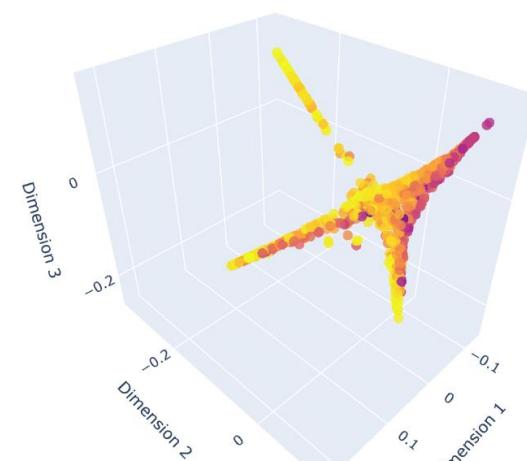
Neuron Diffusion Map (Flow Polarity Index)



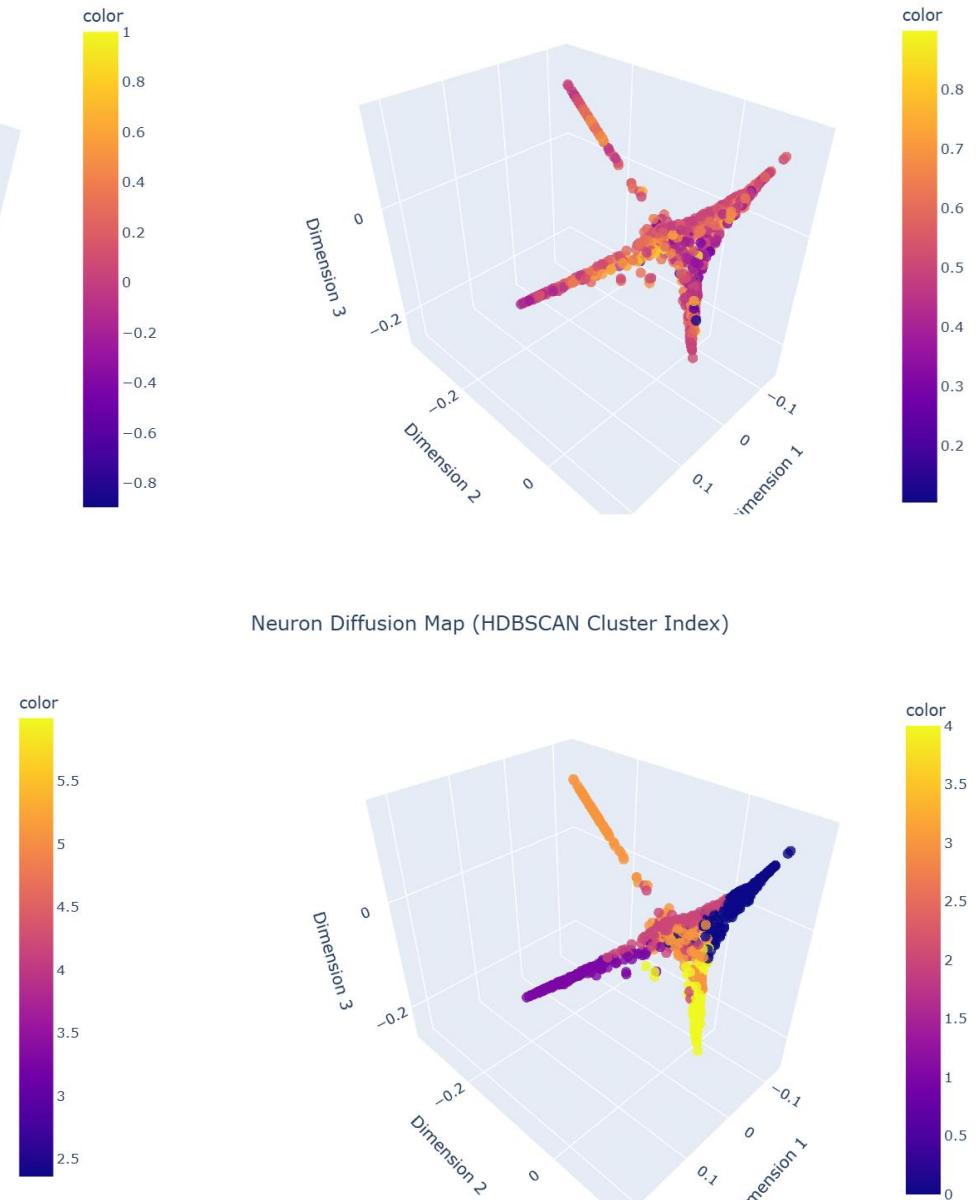
Neuron Diffusion Map (Grating Selectivity Index)

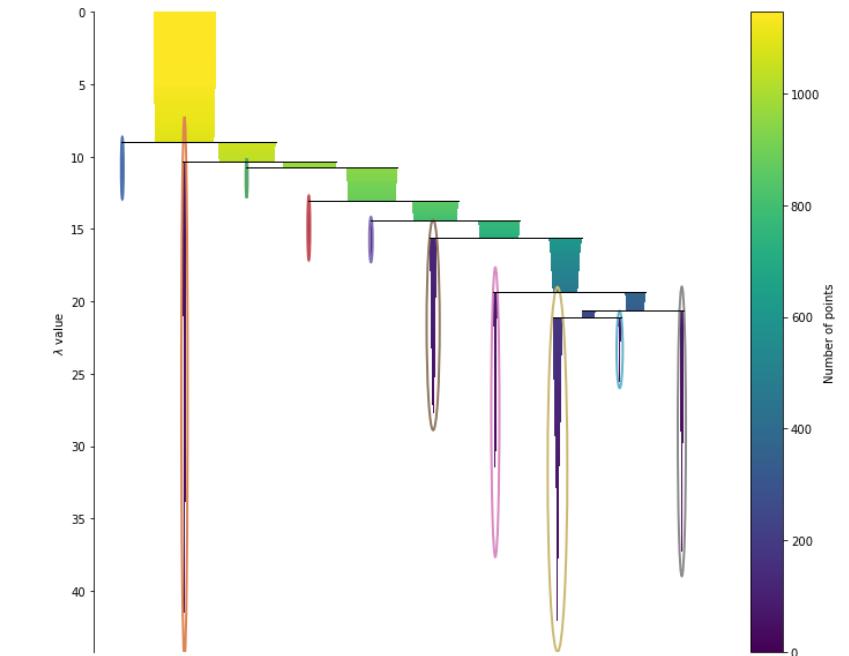
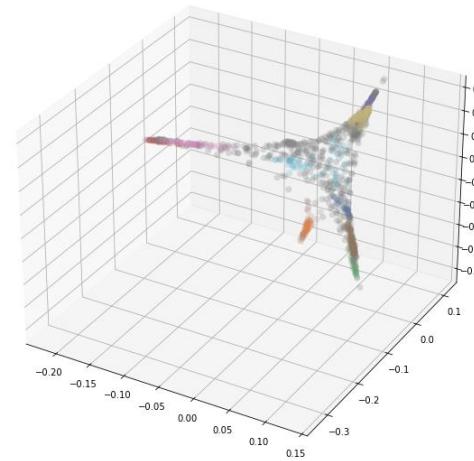
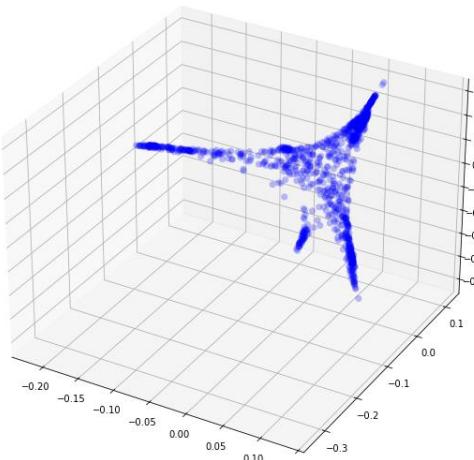
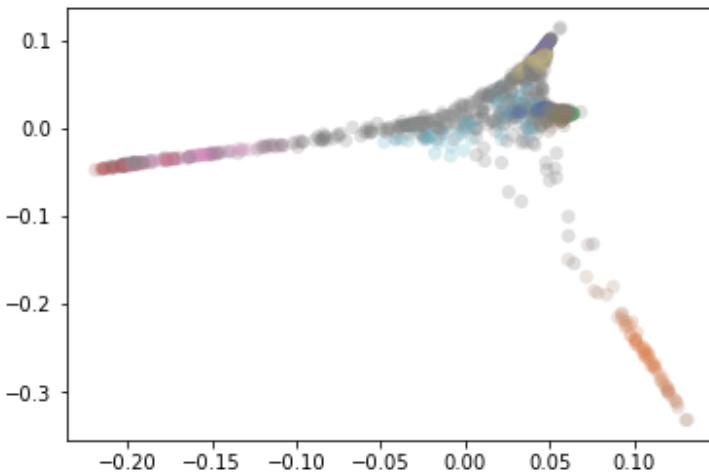
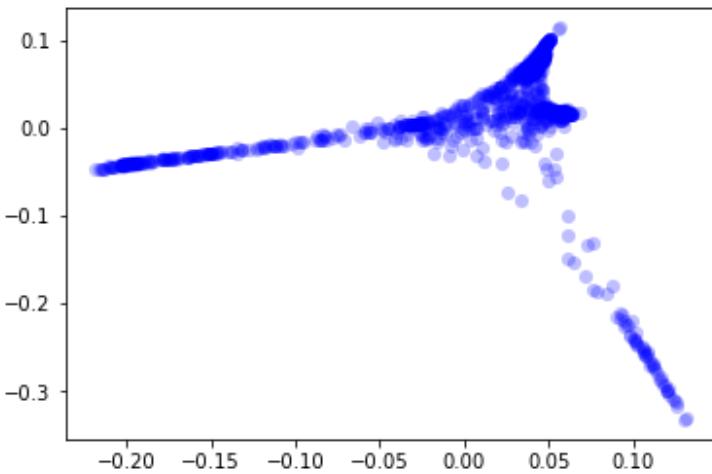


Neuron Diffusion Map (Stimulus Entropy Index)

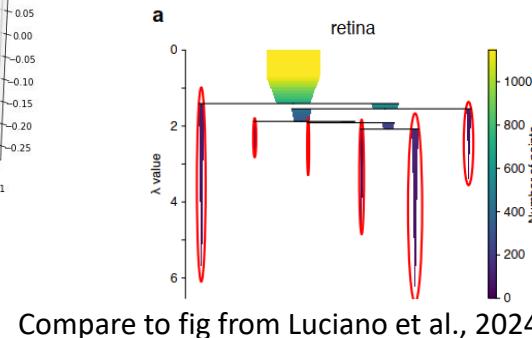


Neuron Diffusion Map (HDBSCAN Cluster Index)





a

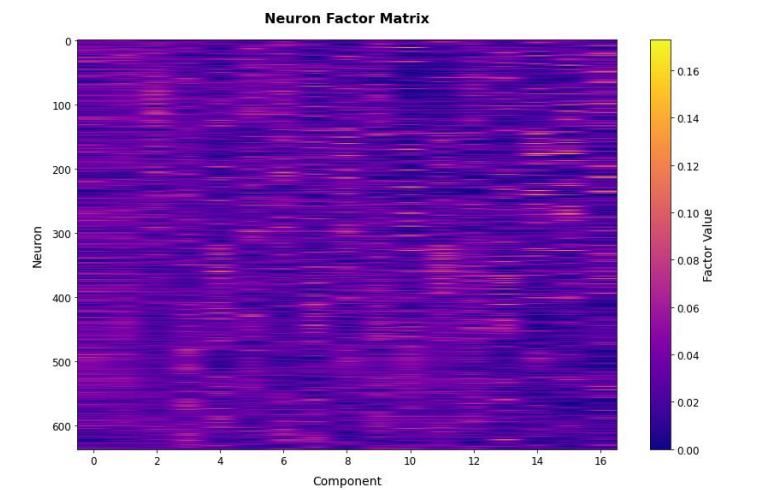


Compare to fig from Luciano et al., 2024

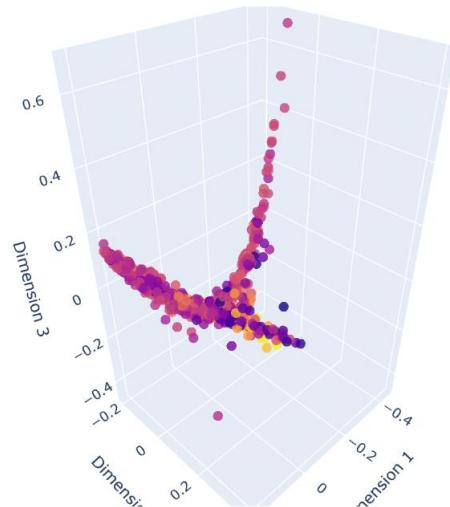
$$\lambda = \frac{1}{\text{core distance}}$$

- **A larger λ value (Low Core Distance):**
higher density, meaning the point belongs to a more tightly clustered region.
- **A smaller λ value (High Core Distance):**
lower density, meaning the point is in a sparser region and may be separated earlier.

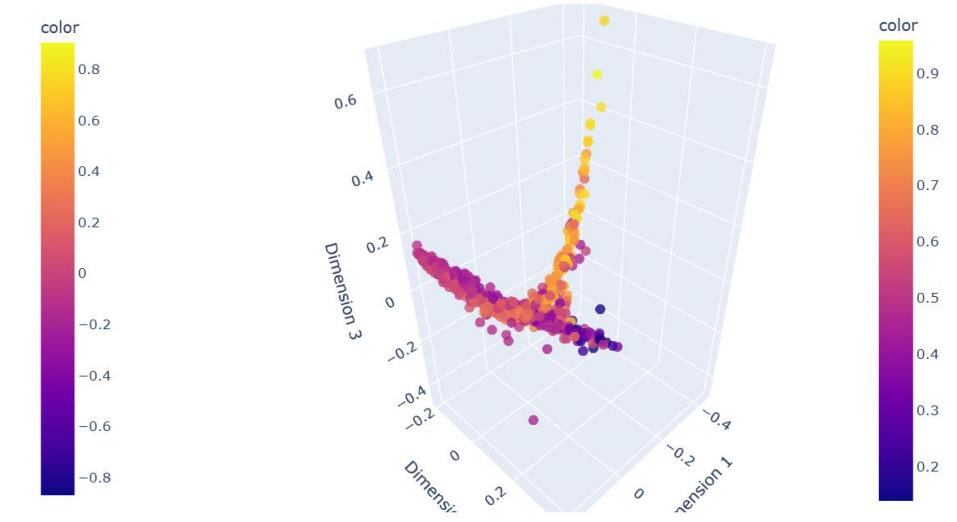
V1



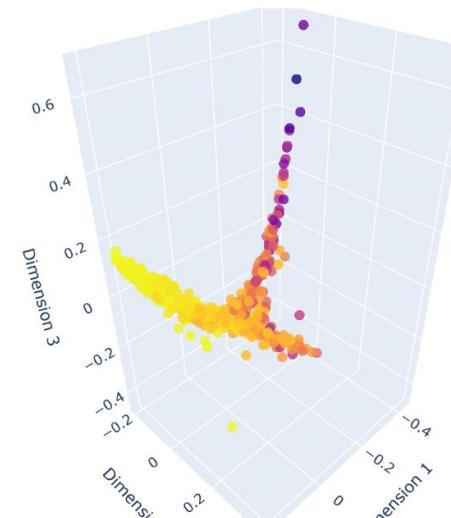
Neuron Diffusion Map (Flow Polarity Index)



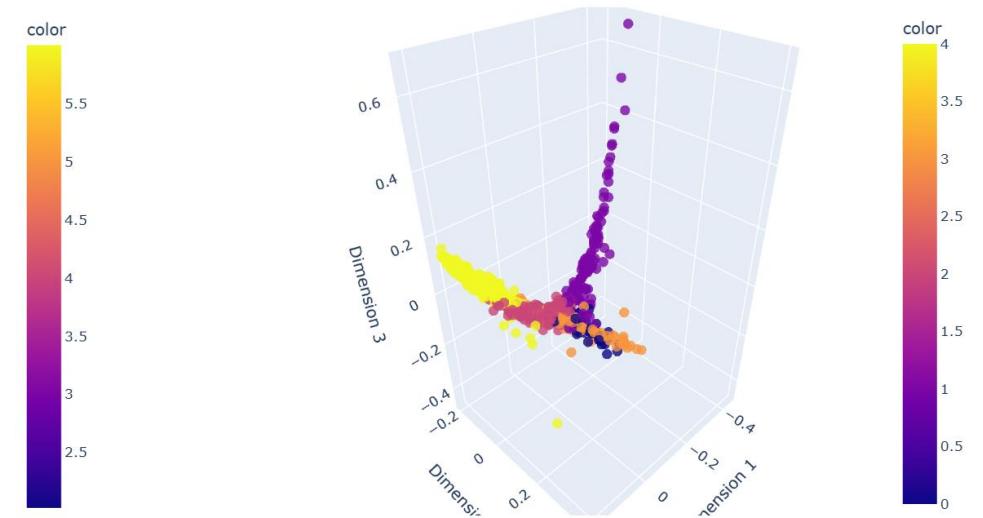
Neuron Diffusion Map (Grating Selectivity Index)

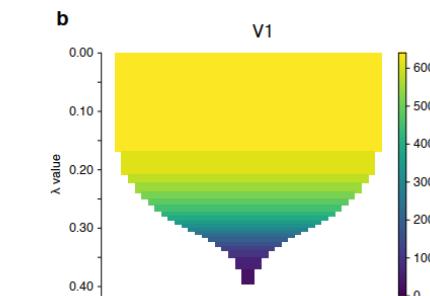
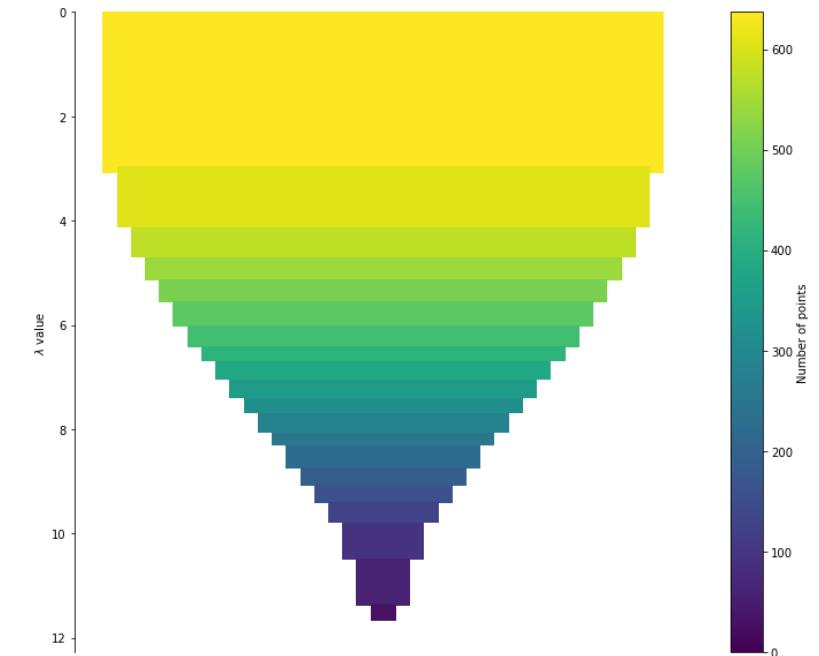
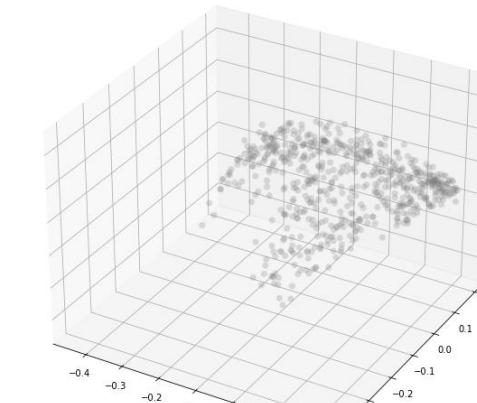
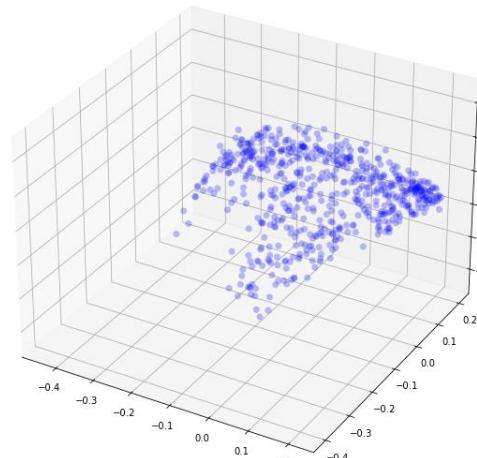
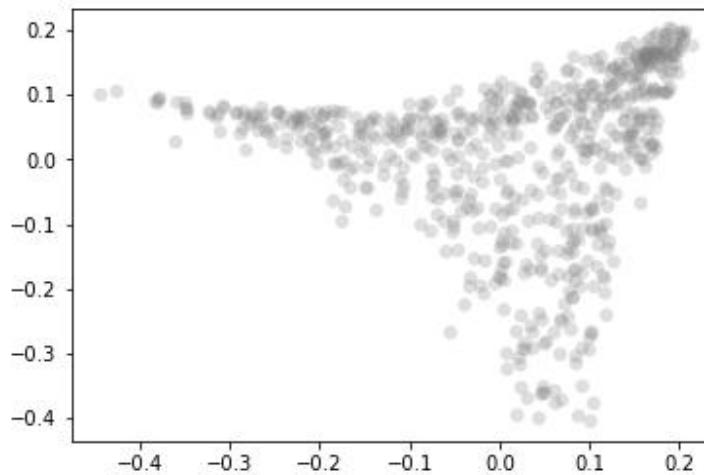
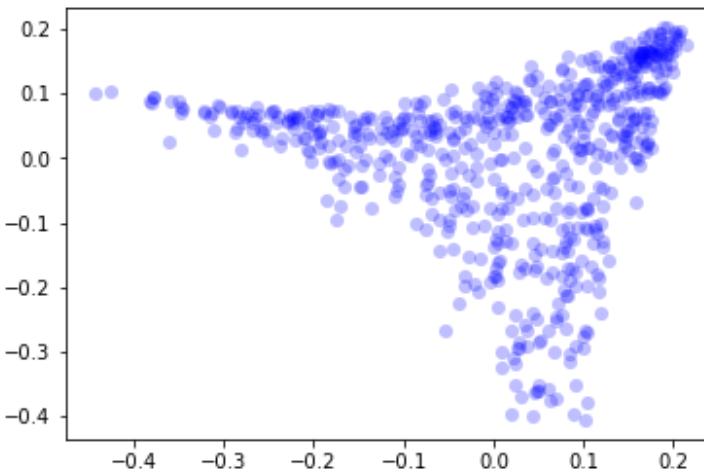


Neuron Diffusion Map (Stimulus Entropy Index)



Neuron Diffusion Map (HDBSCAN Cluster Index)



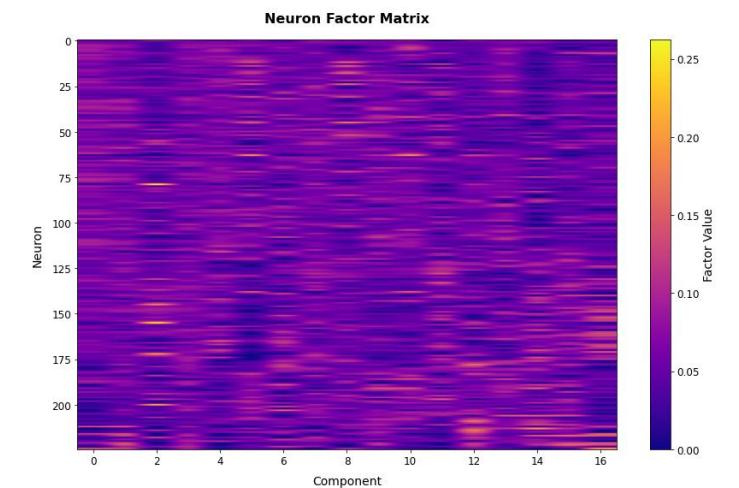


Compare to fig from Luciano et al., 2024

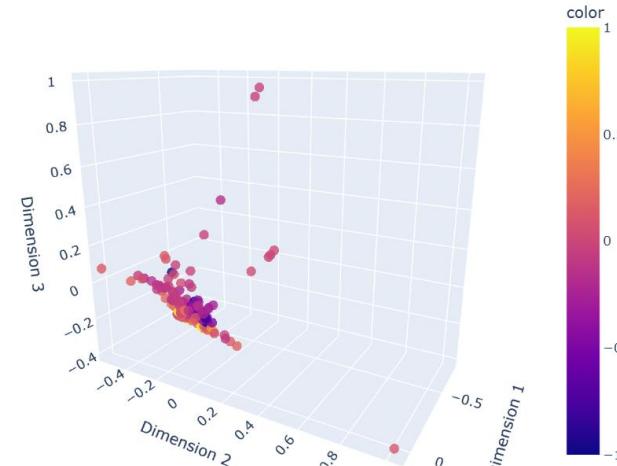
$$\lambda = \frac{1}{\text{core distance}}$$

- **A larger λ value (Low Core Distance):**
higher density, meaning the point belongs to a more tightly clustered region.
- **A smaller λ value (High Core Distance):**
lower density, meaning the point is in a sparser region and may be separated earlier.

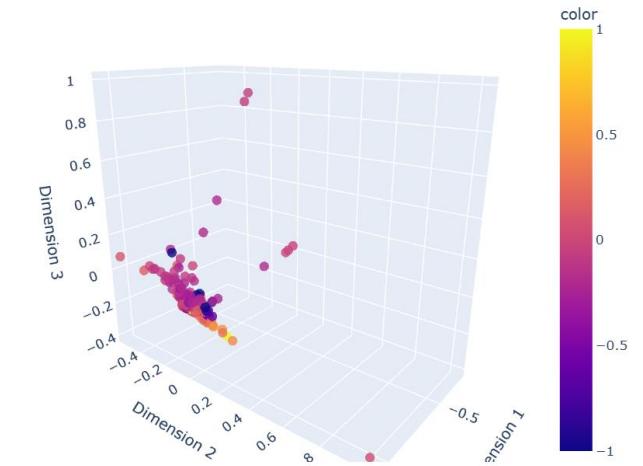
dLGN (our data)



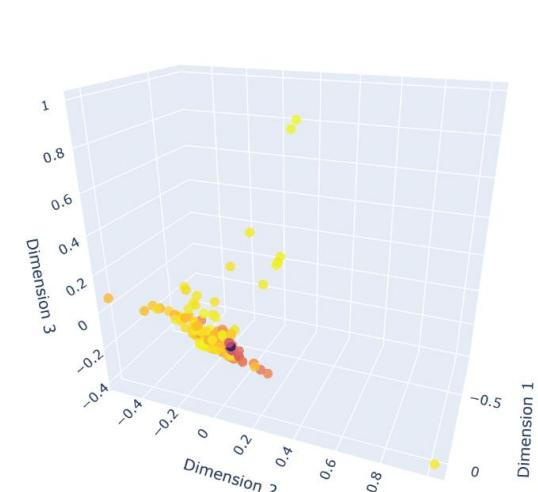
Neuron Diffusion Map (Flow Polarity Index)



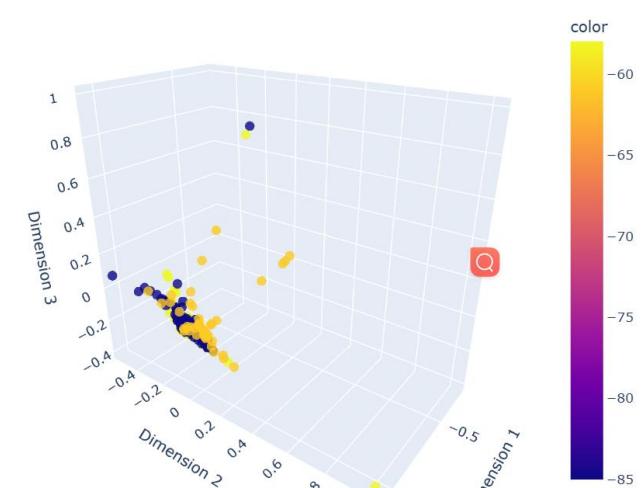
Neuron Diffusion Map (Grating Selectivity Index)



Neuron Diffusion Map (Stimulus Entropy Index)

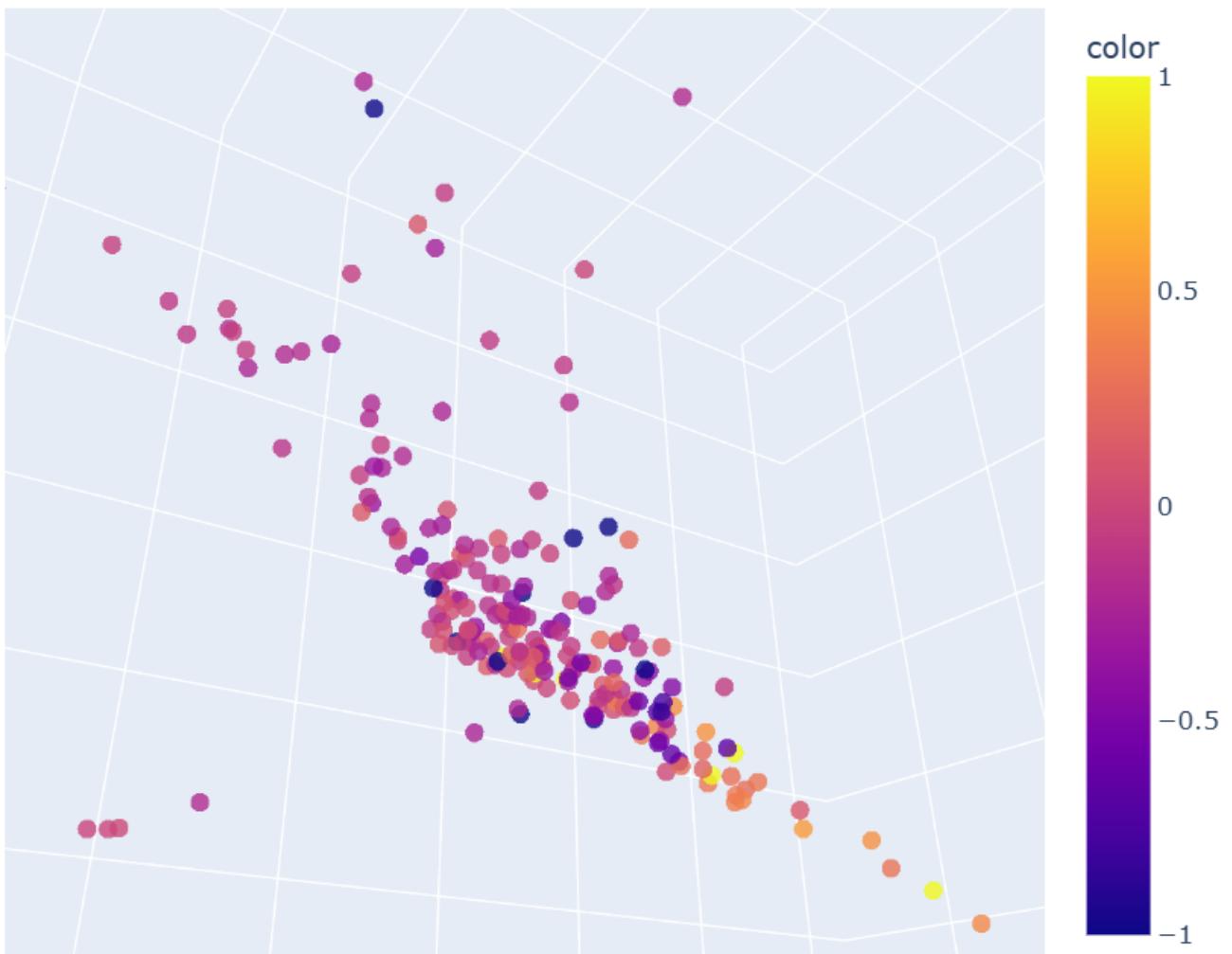


Neuron Diffusion Map (Depth in dLGN Index)



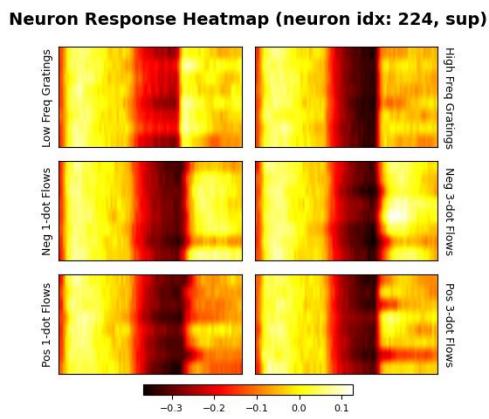
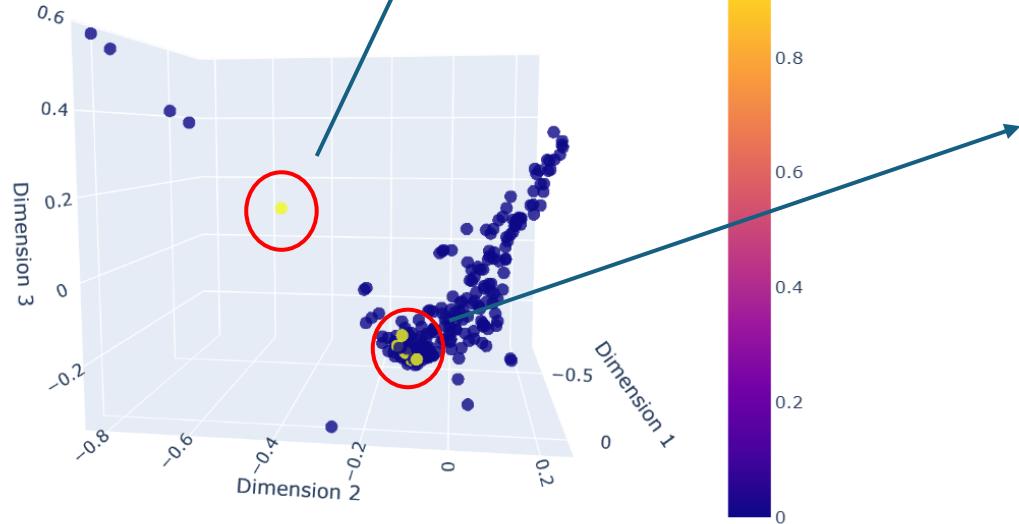
3 depths: -58, -85, -61 micrometer

Neuron Diffusion Map (Grating Selectivity Index)

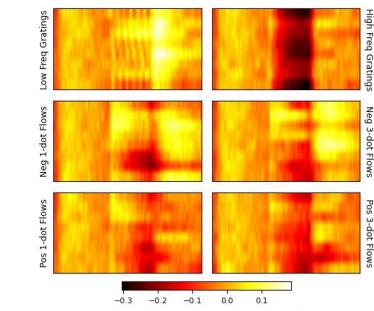


Suppressed neurons (our data, dLGN)

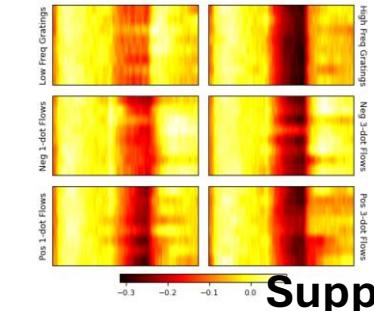
Neuron Diffusion Map (Negative Response Index)



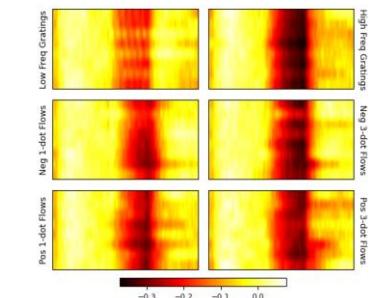
Neuron Response Heatmap (neuron idx: 221, sup)



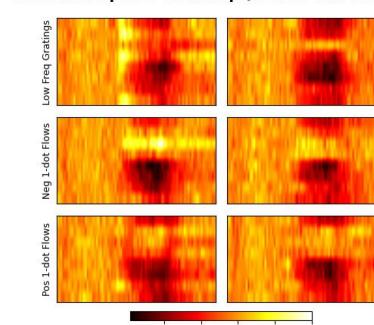
Neuron Response Heatmap (neuron idx: 216, sup)



Neuron Response Heatmap (neuron idx: 212, sup)



Neuron Response Heatmap (neuron idx: 187, sup)

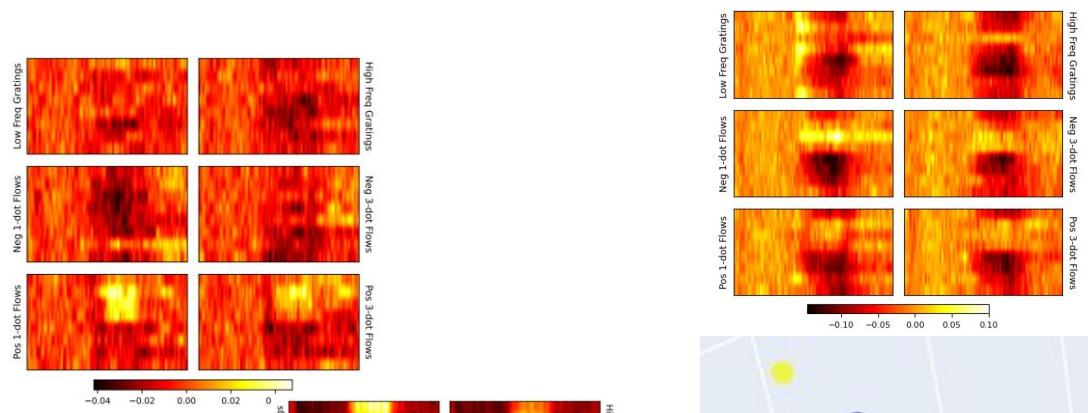


Suppressed neurons

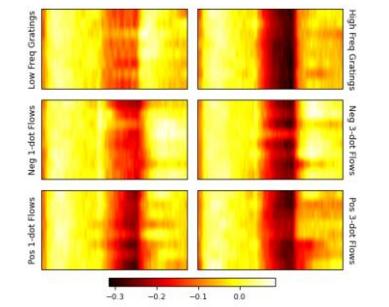
Nearby cells

Suppressed neurons

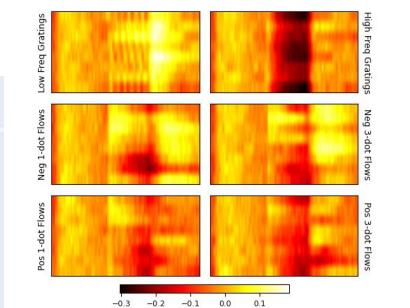
Neuron Response Heatmap (neuron idx: 187, sup)



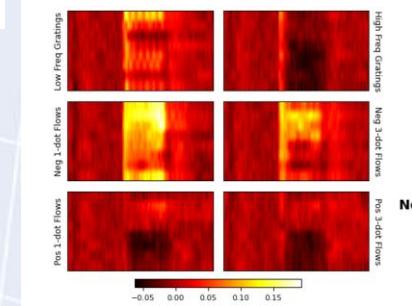
Neuron Response Heatmap (neuron idx: 216, sup)



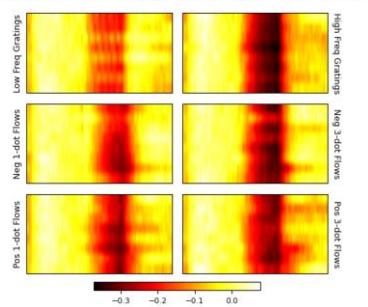
Neuron Response Heatmap (neuron idx: 221, sup)



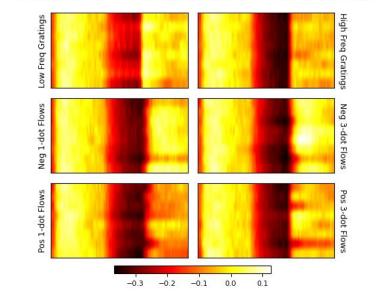
Neuron Response Heatmap (neuron idx: 122, sup)



Neuron Response Heatmap (neuron idx: 212, sup)

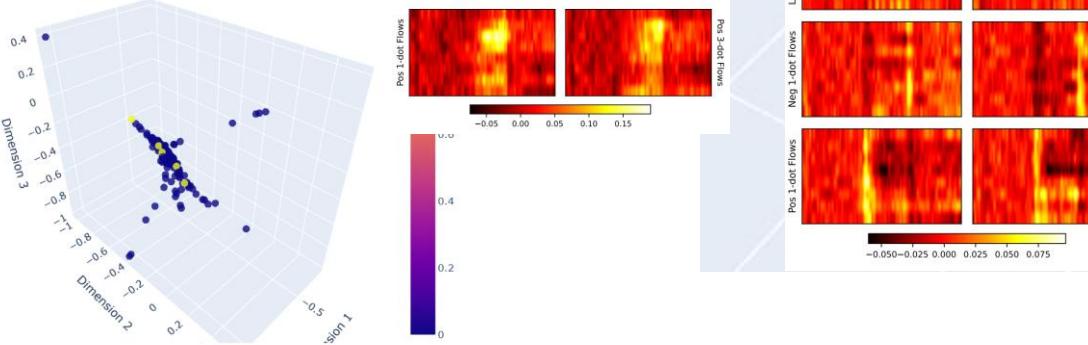
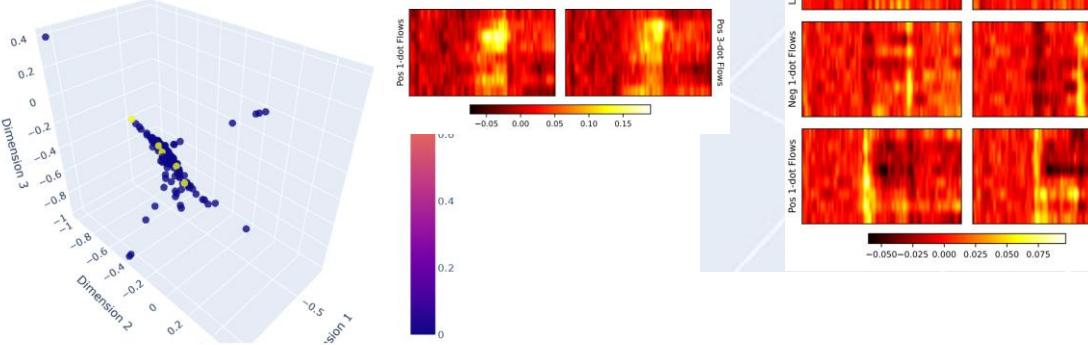
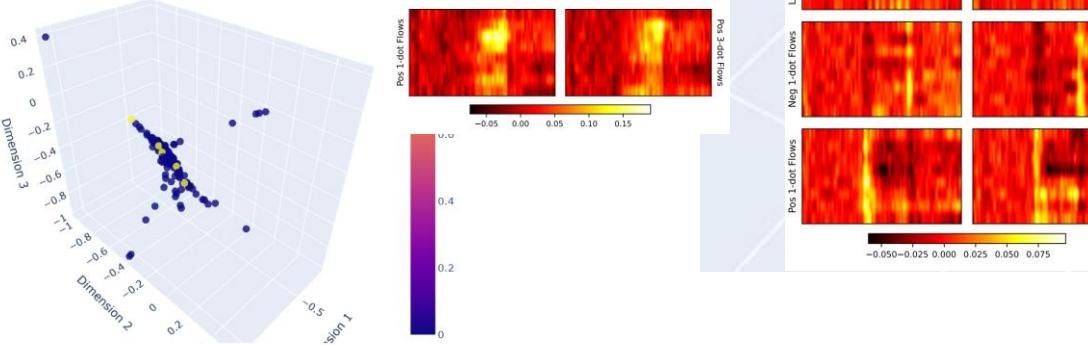
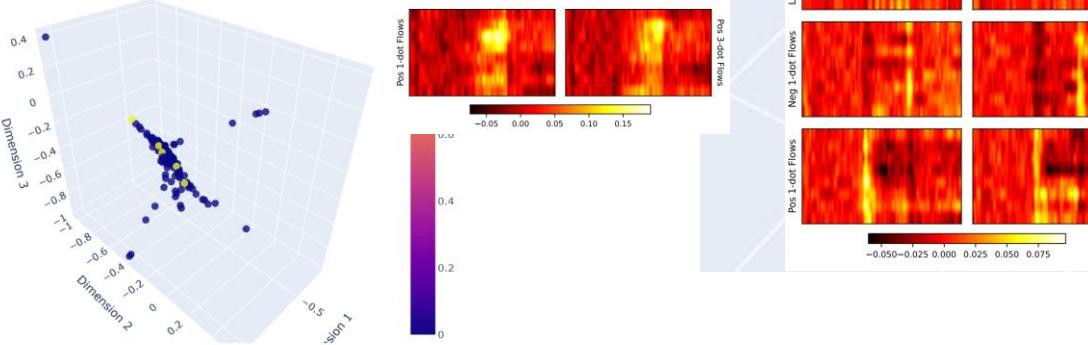
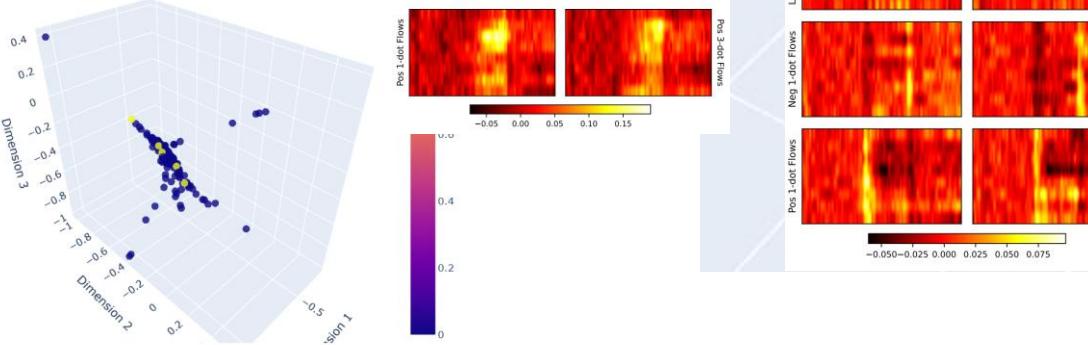
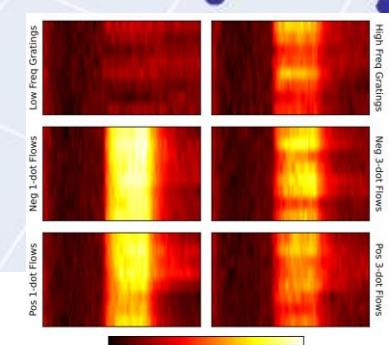
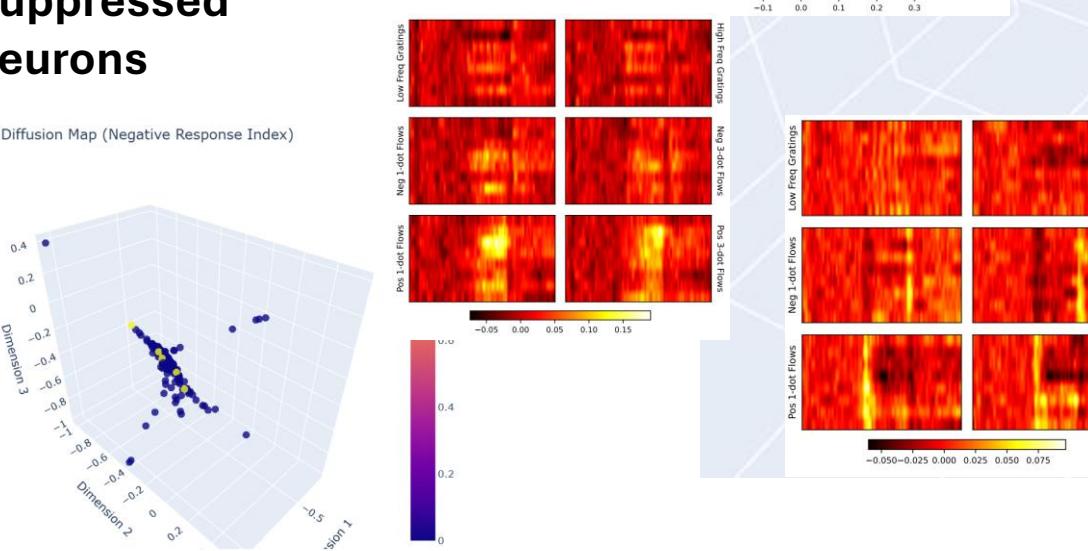


Neuron Response Heatmap (neuron idx: 224, sup)



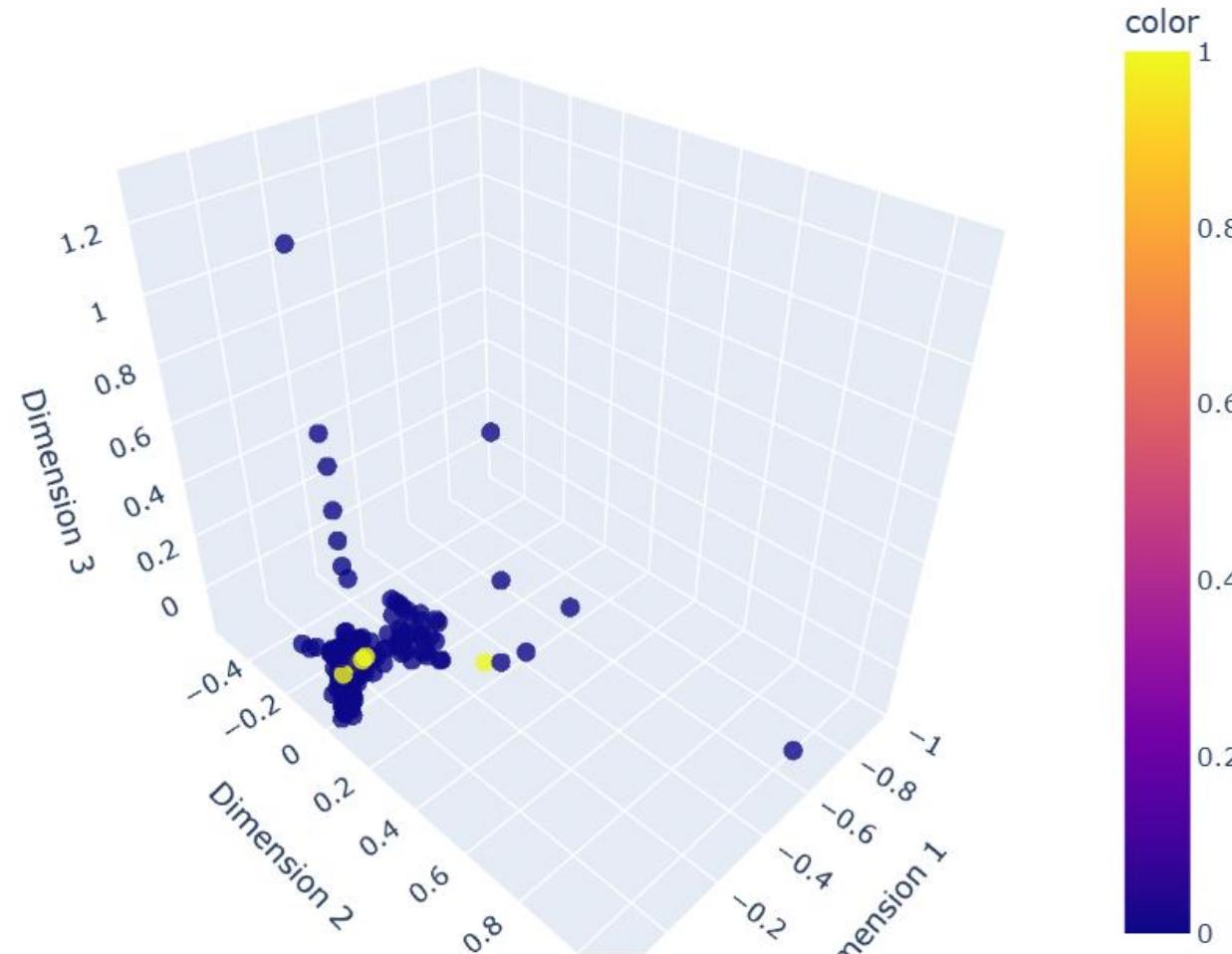
Nearby cells of Suppressed neurons

Neuron Diffusion Map (Negative Response Index)



Remove far-away-from-center neurons and redid the diffusion map

Neuron Diffusion Map (Negative Response Index)



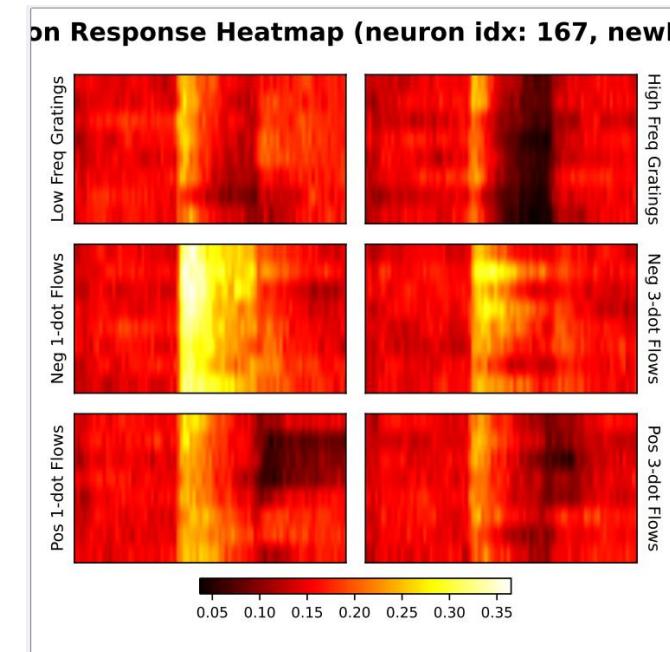
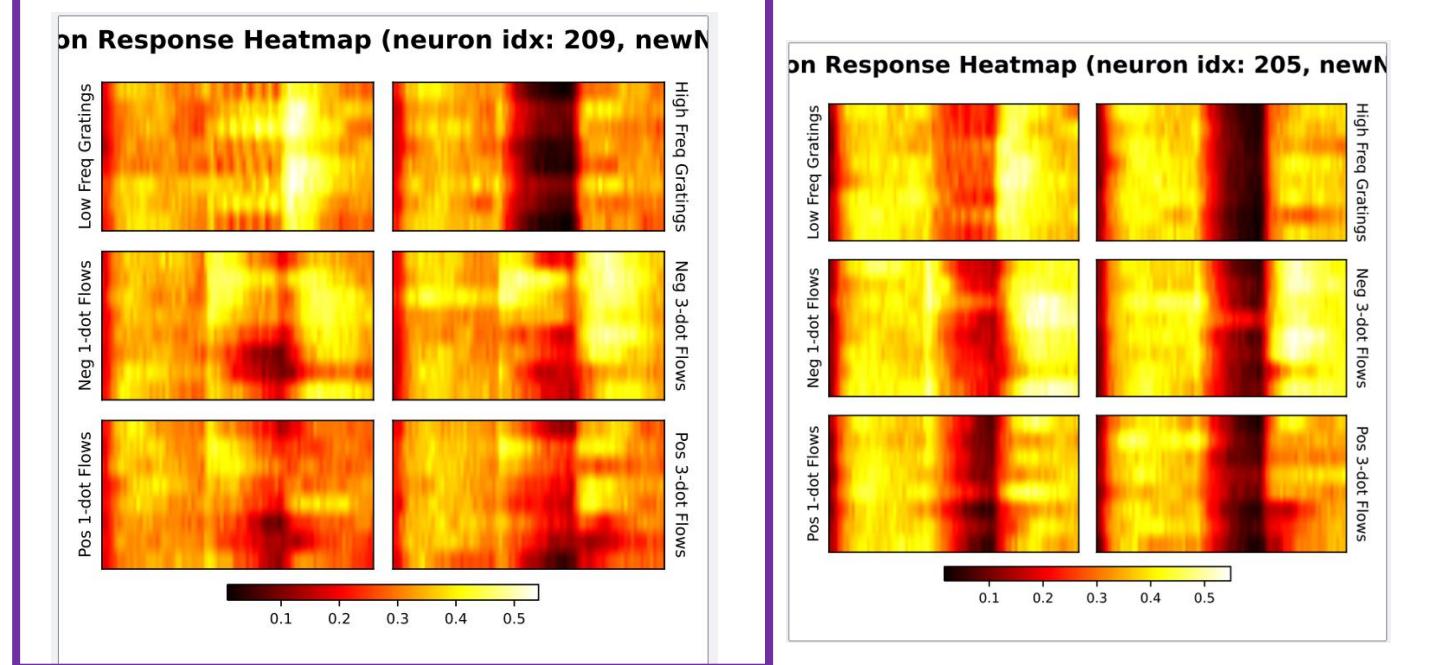
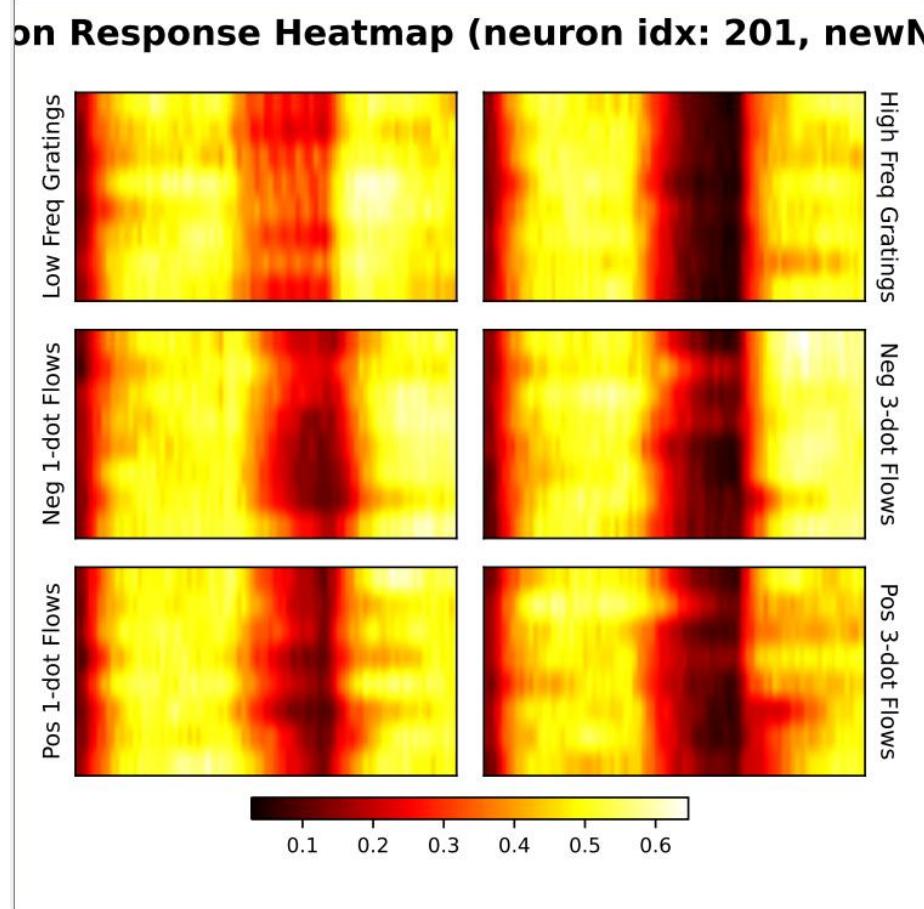
Suppressed-by-contrast neuron indices
= [116, 176, 201, 205, 209]

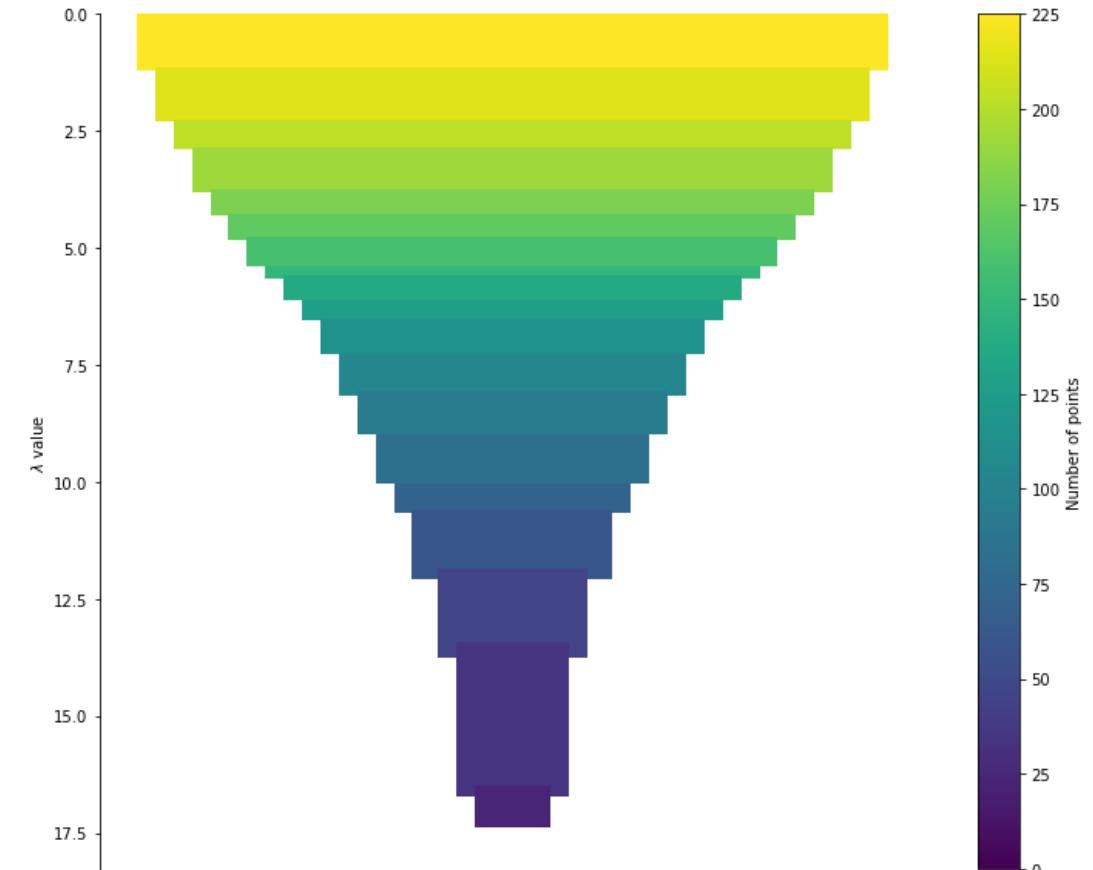
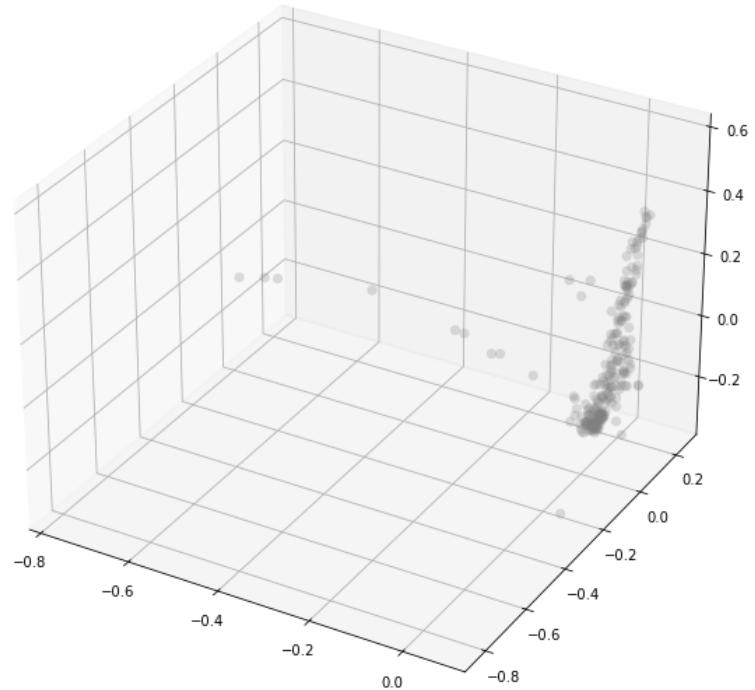
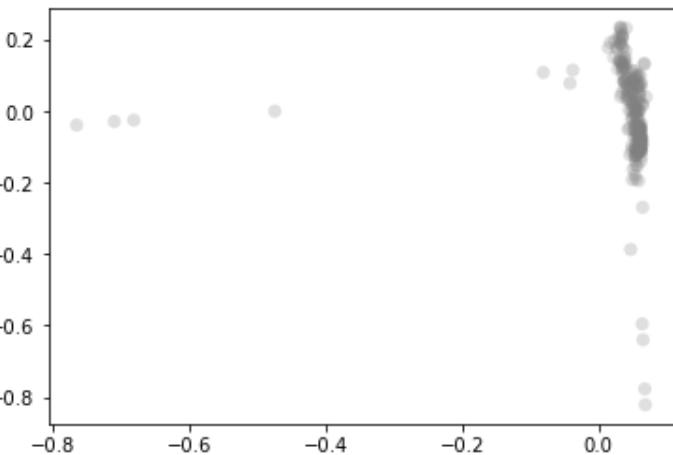
Actually, it's a 10-dim space. Find the 3 nearest neurons of above suppressed neurons in the 10-dim space.

Nearest neighbors

```
[[117 50 82]
[171 125 43]
[209 205 167]
[209 210 119]
[205 210 87]]
```

Suppressed-by-contrast neuron 3 and its 3 nearest neurons





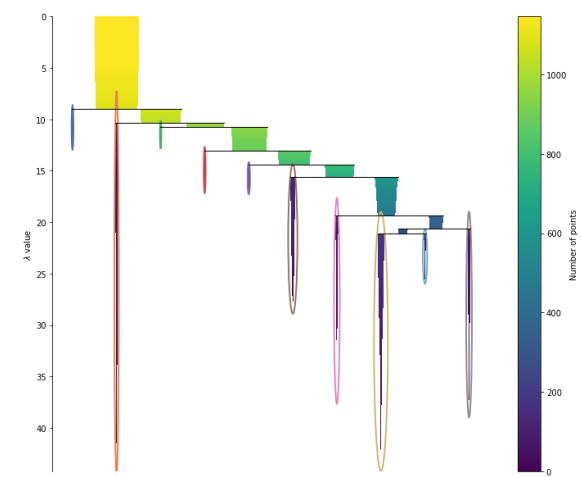
$$\lambda = \frac{1}{\text{core distance}}$$

- **A larger λ value (Low Core Distance):**
higher density, meaning the point belongs to a more tightly clustered region.
- **A smaller λ value (High Core Distance):**
lower density, meaning the point is in a sparser region and may be separated earlier.

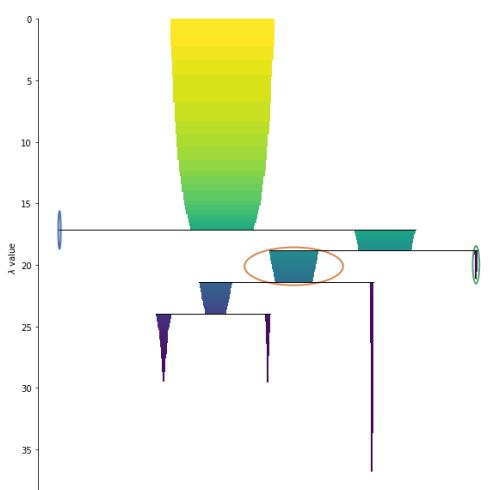
minimum cluster size = 15

Comparison

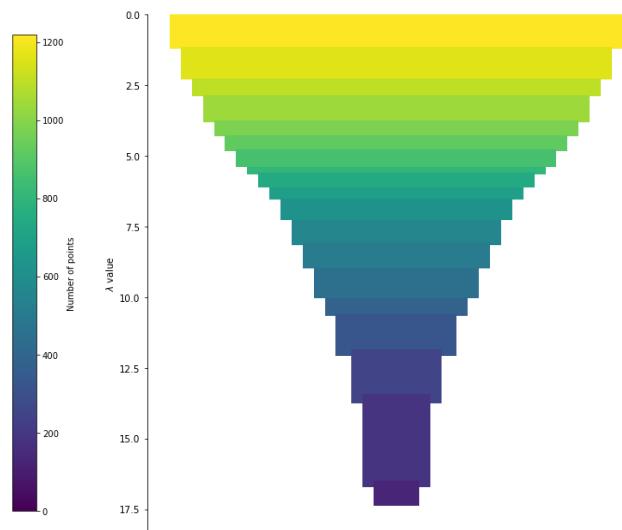
Retina



SC



dLGN



V1

